Synthesis of indoles, biindoles, indole alkaloids, pyrroloindoles and benzimidazoles from aromatic nitro compounds and a study of the chemoselectivity in the Kosugi-Migita-Stille coupling

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Synthesis of indoles, biindoles, indole alkaloids, pyrroloindoles and benzimidazoles from aromatic nitro compounds and a study of the chemoselectivity in the Kosugi-Migita-Stille coupling

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Dissertation submitted to
Eberly College of Arts and Sciences
West Virginia University
In partial fulfillment of the requirements
for the degree of

Doctor of Philosophy
in
Chemistry

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2017

Keywords: indoles, biindoles, indole alkaloids, pyrroloindoles, benzimidazoles, Kosugi-Migita-Stille coupling

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Abstract

Synthesis of indoles, biindoles, indole alkaloids, pyrroloindoles and benzimidazoles from aromatic nitro compounds and a study of the chemoselectivity in the Kosugi-Migita-Stille coupling

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Total syntheses of the three naturally occurring indole alkaloids alocasin A, scalaridine A and hyrtinadine A-B have been accomplished using three palladium catalyzed reactions, an alkyne hydrostannylation, a Kosugi-Migita-Stille coupling and a reductive N-heterocyclization as the key steps. A palladium catalyzed double reductive cyclization of 1,4-, 1,3-, and 2,3-bis(2-nitroaryl)-1,3-butadienes to afford 2,2’, 2,3’-, and 3,3’-biindoles, respectively, has been developed. In an attempt to synthesize indolo[2,3-b]- and indolo[3,2-b]-indoles from the reductive cyclizations of 1,1’, and 1,2’-bis(2-nitroaryl)ethenes respectively, nonselective product formation was observed giving rise to carbon monoxide insertion product as the sole or the major reaction product. The reductive cyclization strategy was extended to achieve the expedient synthesis of three naturally occurring polybrominated biindoles; 2,2’,5,5’-tetrabromo-3,3’-bi-1H-indole, 2,2’,6,6’-tetrabromo-3,3’-bi-1H-indole and 2,2’,5,5’,6,6’-hexabromo-3,3’-bi-1H-indole. In addition, palladium catalyzed, carbon monoxide mediated, double reductive N-heterocyclization of dialkenyldinitrobenzenes to the highly functionalized and highly elusive novel non-symmetrical pyrroloindoles has been developed for the first time. The methodology presents the first common synthetic routes to all isomeric pyrroloindoles which are of interest in a number of applications in addition to their presence as a core moiety in bioactive natural products. The highly functionalized isomeric cyclization precursors were prepared through the use of Kosugi-Migita-Stille coupling. The generally mild reaction conditions offer significant improvements over the previously reported synthetic routes. A facile base-mediated cyclization of enamines derived from the condensation of 2-nitroanilines with α-branched aldehydes, in the presence of a carbon-based electrophile, to give N-alkoxy-substituted benzimidazoles with or without an oxygenate side chain in the 2-position has also been developed. Finally, the chemoselectivity of Kosugi-Migita-Stille couplings of all isomeric permutations of bromphenyl- and bromonitrophenyl trifluoromethanesulfonates was examined in order to compare and contrast the reactivity of C-Br and C-OTf bonds under three different reaction conditions. To the best of our knowledge, the study presented here represents the first of its kind.
Dedicated to my parents and my wife

Shabana Tarannum
Acknowledgements

I would like to express my sincere gratitude to my research advisor professor Björn Söderberg for the continuous support, patience, motivation and immense knowledge. With his guidance, I learned organic chemistry and organic laboratory skills. I am very grateful to his guidance through all the difficulties that I encountered during my research work. His supervision and encouragement always helped me remain motivated in doing productive and meaningful research. This thesis which represents a milestone more than just a PhD requirement is a result of his insightful comments and discussions. In his lab, I gained the importance of honesty in the scientific world. I sincerely appreciate my committee members Dr. Kung Wang, Dr. Brian Popp, Dr. Jessica Hoover and Dr. Mark McLaughlin for their valuable involvement and suggestion in general throughout my graduate study at WVU. I truly appreciate Dr. Novruz Akhmedov’s kindness and helpfulness that enabled me to learn various NMR techniques.

I appreciate the friendship and assistance of my present and past group members in the Söderberg research lab. Chapter 2 had been initiated by Dr. Christopher Dacko. Part of the work in chapter 4 had been carried out by Arica Jordan. Part of the work in chapter 6 was continued from Dr. Matthew Cummings. Similarly, the foundation stone for chapter 7 was laid by Dr. Matthew Cummings and Dr. Serge Banini. I am very grateful to their contributions. Partial work in chapter 3 was performed by Matthew Taylor, an undergraduate student in our lab. Similarly, I like to thank Dr. Yilin Zhang for being helpful running $^{13}$C NMR spectra especially at night. I also like to thank my lab-mates Katharine Lambson, Ganesh Ghimire and SM Ashikur Rahman for their nice cooperation. I thank Katy for her impressive comments and suggestions during the organic divisional seminar talks. I appreciate Mr. Rahman’s help during my thesis writing. Overall, these people will remain a lifelong memory for me.

I want to express my appreciation to my family members in Nepal and my brother Khursded Ansari at University of Toledo, for their endless spiritual support and encouragement. My wife’s patience, bravery and encouragement served as an inspiration to make my graduate life productive. Through her patience was I able to complete seven research projects at WVU.

Last but not the least, I gratefully acknowledge the C. Eugene Bennett Department of Chemistry and funding from the National Institutes of Health (1 R15 GM122002-01) for support. The National Science Foundation-MRI program is also gratefully acknowledged for the funding of a 400 MHz NMR system (CHE-1228366). I would like to thank Dr. Stephen Valentine for HRMS analyses.
# Table of Contents

- Title page: i
- Abstract: ii
- Dedication: iii
- Acknowledgements: iv
- Table of Contents: v
- List of Tables: vii
- List of Schemes: viii
- List of Figures: x

**Chapter 1** Short syntheses of the indole alkaloids alocasin A, scalaridine A and hyrtinadine A-B
  - 1.A Introduction: 1
  - 1.B Results and Discussion: 3
  - 1.C Conclusion: 10

**Chapter 2** Double palladium catalyzed reductive cyclizations. Synthesis of 2,2’-, 2,3’-, and 2,2’-bi-1H-indoles, indolo[3,2-b]indoles, and indolo[2,3-b]indoles
  - 2.A Introduction: 11
  - 2.B Results and Discussion: 12
  - 2.C Conclusion: 21

**Chapter 3** Syntheses of three naturally occurring polybrominated 3,3’-bi-1H-indoles
  - 3.A Introduction: 22
  - 3.B Results and Discussion: 23
  - 3.C Conclusion: 29

**Chapter 4** A facile base-mediated synthesis of N-alkoxy-substituted benzimidazoles
  - 4.A Introduction: 30
  - 4.B Results and Discussion: 31
  - 4.C Mechanistic Discussion: 39
  - 4.D Conclusion: 40

**Chapter 5** A facile base-mediated synthesis of N-alkoxy-2H-benzimidazoles
  - 5.A Introduction: 41
  - 5.B Results and Discussion: 41
  - 5.C Conclusion: 44
<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Chemoselectivity in the Kosugi-Migita-Stille coupling of bromophenyl- and bromonitrophenyl-trifluoromethanesulfonates</td>
<td>45</td>
</tr>
<tr>
<td>6.A</td>
<td>Introduction</td>
<td>45</td>
</tr>
<tr>
<td>6.B</td>
<td>Results and Discussion</td>
<td>47</td>
</tr>
<tr>
<td>6.C</td>
<td>Conclusion</td>
<td>55</td>
</tr>
<tr>
<td>7</td>
<td>Synthesis of pyrroloindoles via a double reductive N-heterocyclization</td>
<td>56</td>
</tr>
<tr>
<td>7.A</td>
<td>Introduction</td>
<td>56</td>
</tr>
<tr>
<td>7.B</td>
<td>Results and Discussion</td>
<td>60</td>
</tr>
<tr>
<td>7.C</td>
<td>Synthesis of pyrroloindole (Type A-E) precursors</td>
<td>63</td>
</tr>
<tr>
<td>7.D</td>
<td>Synthesis of 1H,8H-pyrrolo[3,2-g]indoles (Type A)</td>
<td>72</td>
</tr>
<tr>
<td>7.E</td>
<td>Conclusion</td>
<td>84</td>
</tr>
<tr>
<td></td>
<td>Experimental Section</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>References and Footnotes</td>
<td>208</td>
</tr>
<tr>
<td></td>
<td>Appendix</td>
<td></td>
</tr>
</tbody>
</table>
List of Tables

Table 2.1 Synthesis of 2,2’-bi-1H-indoles 13
Table 2.2 Synthesis of 3,3’-bi-1H-indoles 15
Table 2.3 Synthesis of 2,3’-bi-1H-indoles 17
Table 4.1 Condition screening 32
Table 4.2 Base-mediated synthesis of benzimidazoles under condition A 34
Table 4.3 Base-mediated synthesis of benzimidazoles under condition B 36
Table 4.4 Base-mediated synthesis of N-oxygenated benzimidazoles from enamine 127 39
Table 5.1 Formation of N-methoxybenzimidazoles from enamines 43
Table 5.2 Base-mediated synthesis of N-oxygenated benzimidazoles from enamine 127 44
Table 6.1 Reactions of bromophenyl trifluoromethanesulfonates with ethenyltributyltin 48
Table 6.2 Cross-couplings of 213-222 with ethenyltributyltin 51
Table 7.1 Condition screening 61
Table 7.2 Synthesis of cyclization precursors by double Kosugi-Migita-Stille coupling 64
Table 7.3 Selective cross coupling of bromo- and iodo-phenyl triflates 66
Table 7.4 Synthesis of unsymmetrical cyclization precursors 69
Table 7.5 Synthesis of 1H,8H-pyrrolo[3,2-g]indoles (Type A) 73
Table 7.6 Attempted synthesis of pyrroloindoles (Type B-E) 76
Table 7.7 Synthesis of N-tosylated indoles 81
Table 7.8 Synthesis of N-tosylated pyrroloindoles (Type B-E) 82
List of Schemes

Scheme 1.1 Sperry’s synthesis of alocasin A 2
Scheme 1.2 Sperry’s synthesis of scalaridine A 2
Scheme 1.3 Tasch’s synthesis of hyrtinadine A 3
Scheme 1.4 Mosquera’s synthesis of scalaridien A 3
Scheme 1.5 Synthesis of alocasin A 5
Scheme 1.6 Attempted cross coupling of 4 with 3,5-dibromopyridine (9) 6
Scheme 1.7 Synthesis of scalaridine A 7
Scheme 1.8 Attempted cross coupling of 4 with 2,5-dibromopyrimidine (15) 8
Scheme 1.9 Synthesis of hyrtinadine A 9
Scheme 1.10 Synthesis of hyrtinadine B 10
Scheme 2.1 Synthesis of 5-bromo-2-nitrocinnamaldehyde (32) 13
Scheme 2.2 Synthesis of 4,4’-diaza-3,3’-bi-1H-indole 15
Scheme 2.3 Synthesis of unsymmetrical 3,3’-bi-1H-indole 16
Scheme 2.4 Reductive cyclization of 79 18
Scheme 2.5 Reductive Cyclization of 84 18
Scheme 2.6 Reductive cyclization of 88 19
Scheme 2.7 Reductive cyclization of 91 19
Scheme 2.8 Synthesis of indolo[2,3-b]indole (96) and indolo[2,3-c]quinolinone (97) 20
Scheme 2.9 Reductive cyclization of 99 21
Scheme 3.1 Palladium catalyzed double reductive cyclization to 3,3’-biindole 23
Scheme 3.2 Palladium catalyzed oxidative dimerization of 5-bromoindole 23
Scheme 3.3 Two common routes to 111 24
Scheme 3.4 Synthesis of precursor 111 25
Scheme 3.5 Bromination of 3-methylindole 25
Scheme 3.6 Synthesis of 2,2’,5,5’-tetrabromo- and 2,2’,5,5’,6,6’-hexabromobiindoles 26
Scheme 3.7 Synthesis of 2,2’,6,6’-tetrabromo-bi-1H-indole 27
Scheme 3.8 Polybromination of 113 27
Scheme 3.9 Bromination of 3,3-bi-1H-indole 56 28
Scheme 4.1 Formation of benzimidazoles 124-126 from enamine 122 30
Scheme 4.2 Formation of 2-ethenyl-N-propoxybenzimidazole 31
Scheme 4.3 Formation of N-methoxybenzimidazole 169 and benzophenone (170) 38
Scheme 4.4 Reaction of 127 with acetyl chloride 38
List of Figures

Figure 1.1 Structures of alocasin A, scalaridine A and hyrtinadine A-B 1
Figure 2.1 Possible cyclizations (A-E) of bis(2-nitrophenyl)butadienes and –ethenes 12
Figure 3.1 Naturally occurring polyhalogenated 3,3’-bi-1H-indoles 22
Figure 6.1 Isomeric bromonitrophenyl trifluoromethanesulfonates (213-222) 50
Figure 7.1 Isomeric pyrroloindoles 56
Figure 1.2 1H and 13C NMR of compound 2 220
Figure 1.3 1H and 13C NMR of compound 3 221
Figure 1.4 1H and 13C NMR of compound 4 222
Figure 1.5 1H and 13C NMR of compound 6 223
Figure 1.6 1H and 13C NMR of compound 7 224
Figure 1.7 1H and 13C NMR of compound 8 225
Figure 1.8 1H and 13C NMR of alocasin A 226
Figure 1.9 1H and 13C NMR of compound 11 227
Figure 1.10 1H and 13C NMR of compound 12 228
Figure 1.11 1H and 13C NMR of compound 13 229
Figure 1.12 1H and 13C NMR of compound 14 230
Figure 1.13 1H and 13C NMR of scalaridine A 231
Figure 1.14 1H and 13C NMR of compound 16 232
Figure 1.15 1H and 13C NMR of compound 17 233
Figure 1.16 1H and 13C NMR of compound 18 234
Figure 1.17 1H and 13C NMR of compound 19 235
Figure 1.18 1H and 13C NMR of compound 20 236
Figure 1.19 1H and 13C NMR of compound 21 237
Figure 1.20 1H and 13C NMR of compound 22 238
Figure 1.21 1H and 13C NMR of hyrtinadine A 239
Figure 1.22 1H and 13C NMR of compound 24 240
Figure 1.23 1H and 13C NMR of compound 25 241
Figure 1.24 1H and 13C NMR of compound 26 242
Figure 1.25 1H and 13C NMR of hyrtinadine B 243
Figure 2.2 $^1$H and $^{13}$C NMR of compound 28
Figure 2.3 $^1$H and $^{13}$C NMR of compound 29
Figure 2.4 $^1$H and $^{13}$C NMR of compound 30
Figure 2.5 $^1$H and $^{13}$C NMR of compound 32
Figure 2.6 $^1$H and $^{13}$C NMR of compound 34
Figure 2.7 $^1$H and $^{13}$C NMR of compound 35
Figure 2.8 $^1$H and $^{13}$C NMR of compound 36
Figure 2.9 $^1$H and $^{13}$C NMR of compound 37
Figure 2.10 $^1$H and $^{13}$C NMR of compound 38
Figure 2.11 $^1$H and $^{13}$C NMR of compound 39
Figure 2.12 $^1$H and $^{13}$C NMR of compound 40
Figure 2.13 $^1$H and $^{13}$C NMR of compound 41
Figure 2.14 $^1$H and $^{13}$C NMR of compound 42
Figure 2.15 $^1$H and $^{13}$C NMR of compound 43
Figure 2.16 $^1$H and $^{13}$C NMR of compound 48
Figure 2.17 $^1$H and $^{13}$C NMR of compound 49
Figure 2.18 $^1$H and $^{13}$C NMR of compound 50
Figure 2.19 $^1$H and $^{13}$C NMR of compound 51
Figure 2.20 $^1$H and $^{13}$C NMR of compound 52
Figure 2.21 $^1$H and $^{13}$C NMR of compound 53
Figure 2.22 $^1$H and $^{13}$C NMR of compound 54
Figure 2.23 $^1$H and $^{13}$C NMR of compound 55
Figure 2.24 $^1$H and $^{13}$C NMR of compound 56
Figure 2.25 $^1$H and $^{13}$C NMR of compound 57
Figure 2.26 $^1$H and $^{13}$C NMR of compound 58
Figure 2.27 $^1$H and $^{13}$C NMR of compound 59
Figure 2.28 $^1$H and $^{13}$C NMR of compound 60
Figure 2.29 $^1$H and $^{13}$C NMR of compound 62
Figure 2.30 $^1$H and $^{13}$C NMR of compound 63
Figure 2.31 $^1$H and $^{13}$C NMR of compound 64
Figure 2.32 $^1$H and $^{13}$C NMR of compound 66
Figure 2.33 $^1$H and $^{13}$C NMR of compound 67
Figure 2.34 $^1$H and $^{13}$C NMR of compound 68
Figure 2.35 $^1$H and $^{13}$C NMR of compound 69
Figure 2.36 $^1$H and $^{13}$C NMR of compound 71
Figure 2.37 $^1$H and $^{13}$C NMR of compound 72
Figure 2.38 $^1$H and $^{13}$C NMR of compound 73
Figure 2.39 $^1$H and $^{13}$C NMR of compound 74
Figure 2.40 $^1$H and $^{13}$C NMR of compound 75
Figure 2.41 $^1$H and $^{13}$C NMR of compound 76
Figure 2.42 $^1$H and $^{13}$C NMR of compound 77
Figure 2.43 $^1$H and $^{13}$C NMR of compound 78
Figure 2.44 $^1$H and $^{13}$C NMR of compound 81
Figure 2.45 $^1$H and $^{13}$C NMR of compound 82
Figure 2.46 $^1$H and $^{13}$C NMR of compound 88
Figure 2.47 $^1$H and $^{13}$C NMR of compound 89
Figure 2.48 $^1$H and $^{13}$C NMR of compound 90
Figure 2.49 $^1$H and $^{13}$C NMR of compound 91
Figure 2.50 $^1$H and $^{13}$C NMR of compound 92
Figure 2.51 $^1$H and $^{13}$C NMR of compound 93
Figure 2.52 $^1$H and $^{13}$C NMR of compound 94
Figure 2.53 $^1$H and $^{13}$C NMR of compound 95
Figure 2.54 $^1$H and $^{13}$C NMR of compound 96
Figure 2.55 $^1$H and $^{13}$C NMR of compound 97
Figure 2.56 $^1$H and $^{13}$C NMR of compound 99
Figure 2.57 $^1$H and $^{13}$C NMR of compound 100
Figure 2.58 $^1$H and $^{13}$C NMR of compound 101
Figure 2.59 $^1$H and $^{13}$C NMR of compound 102
Figure 3.2 $^1$H and $^{13}$C NMR of compound 113  
Figure 3.3 $^1$H and $^{13}$C NMR of compound 114  
Figure 3.4 $^1$H and $^{13}$C NMR of compound 115  
Figure 3.5 $^1$H and $^{13}$C NMR of compound 116  
Figure 3.6 $^1$H and $^{13}$C NMR of compound 111  
Figure 3.7 $^1$H and $^{13}$C NMR of compound 103  
Figure 3.8 $^1$H and $^{13}$C NMR of compound 105  
Figure 3.9 $^1$H and $^{13}$C NMR of compound 118  
Figure 3.10 $^1$H and $^{13}$C NMR of compound 119  
Figure 3.11 $^1$H and $^{13}$C NMR of compound 120  
Figure 3.12 $^1$H and $^{13}$C NMR of compound 104  
Figure 3.13 $^1$H and $^{13}$C NMR of compound 121
Figure 4.1 $^1$H and $^{13}$C NMR of compound 124
Figure 4.2 $^1$H and $^{13}$C NMR of compound 125
Figure 4.3 $^1$H and $^{13}$C NMR of compound 126
Figure 4.4 $^1$H and $^{13}$C NMR of compound 128
Figure 4.5 $^1$H and $^{13}$C NMR of compound 129
Figure 4.6 $^1$H and $^{13}$C NMR of compound 130
Figure 4.7 $^1$H and $^{13}$C NMR of compound 132
Figure 4.8 $^1$H and $^{13}$C NMR of compound 133
Figure 4.9 $^1$H and $^{13}$C NMR of compound 134
Figure 4.10 $^1$H and $^{13}$C NMR of compound 135
Figure 4.11 $^1$H and $^{13}$C NMR of compound 136
Figure 4.12 $^1$H and $^{13}$C NMR of compound 137
Figure 4.13 $^1$H and $^{13}$C NMR of compound 139
Figure 4.14 $^1$H and $^{13}$C NMR of compound 140
Figure 4.15 $^1$H and $^{13}$C NMR of compound 141
Figure 4.16 $^1$H and $^{13}$C NMR of compound 143
Figure 4.17 $^1$H and $^{13}$C NMR of compound 145
Figure 4.18 $^1$H and $^{13}$C NMR of compound 146
Figure 4.19 $^1$H and $^{13}$C NMR of compound 148
Figure 4.20 $^1$H and $^{13}$C NMR of compound 149
Figure 4.21 $^1$H and $^{13}$C NMR of compound 150
Figure 4.22 $^1$H and $^{13}$C NMR of compound 151
Figure 4.23 $^1$H and $^{13}$C NMR of compound 152
Figure 4.24 $^1$H and $^{13}$C NMR of compound 153
Figure 4.25 $^1$H and $^{13}$C NMR of compound 154
Figure 4.26 $^1$H and $^{13}$C NMR of compound 155
Figure 4.27 $^1$H and $^{13}$C NMR of compound 156
Figure 4.28 $^1$H and $^{13}$C NMR of compound 158
Figure 4.29 $^1$H and $^{13}$C NMR of compound 159
Figure 4.30 $^1$H and $^{13}$C NMR of compound 160
Figure 4.31 $^1$H and $^{13}$C NMR of compound 161
Figure 4.32 $^1$H and $^{13}$C NMR of compound 162
Figure 4.33 $^1$H and $^{13}$C NMR of compound 163
Figure 4.34 $^1$H and $^{13}$C NMR of compound 164

xiv
Figure 4.35 $^1$H and $^{13}$C NMR of compound 165
Figure 4.36 $^1$H and $^{13}$C NMR of compound 166
Figure 4.37 $^1$H and $^{13}$C NMR of compound 167
Figure 4.38 $^1$H and $^{13}$C NMR of compound 169
Figure 4.39 $^1$H and $^{13}$C NMR of compound 171
Figure 4.40 $^1$H and $^{13}$C NMR of compound 172
Figure 4.41 $^1$H and $^{13}$C NMR of compound 173
Figure 4.42 $^1$H and $^{13}$C NMR of compound 174
Figure 4.43 $^1$H and $^{13}$C NMR of compound 175
Figure 4.44 $^1$H and $^{13}$C NMR of compound 176
Figure 4.45 $^1$H and $^{13}$C NMR of compound 177
Figure 4.46 $^1$H and $^{13}$C NMR of compound 178
Figure 4.47 $^1$H and $^{13}$C NMR of compound 179
Figure 4.48 $^1$H and $^{13}$C NMR of compound 180
Figure 4.49 $^1$H and $^{13}$C NMR of compound 181
Figure 4.50 $^1$H and $^{13}$C NMR of compound 182
Figure 4.51 $^1$H and $^{13}$C NMR of 4-carbomethoxy-$^N$-methyl-$^N$-(2-methyl-1-propen-1-yl)-2-nitroaniline
Figure 4.52 $^1$H and $^{13}$C NMR of 2,4-dinitro-$^N$-methyl-$^N$-(2-methyl-1-propen-1-yl)aniline
Figure 4.53 $^1$H and $^{13}$C NMR of 5-chloro-$^N$-(2-methyl-1-propen-1-yl)-2-nitroaniline
Figure 5.1 $^1$H and $^{13}$C NMR of compound 190
Figure 5.2 $^1$H and $^{13}$C NMR of compound 191
Figure 5.3 $^1$H and $^{13}$C NMR of compound 192
Figure 5.4 $^1$H and $^{13}$C NMR of compound 193
Figure 5.5 $^1$H and $^{13}$C NMR of compound 195
Figure 5.6 $^1$H and $^{13}$C NMR of compound 196
Figure 5.7 $^1$H and $^{13}$C NMR of compound 197
Figure 5.8 $^1$H and $^{13}$C NMR of compound 198
Figure 5.9 $^1$H and $^{13}$C NMR of compound 199
Figure 5.10 $^1$H and $^{13}$C NMR of compound 200
Figure 5.11 $^1$H and $^{13}$C NMR of compound 201
Figure 6.2 $^1$H NMR of compound 204 378
Figure 6.3 $^{13}$C and $^{19}$F NMR of compound 204 379
Figure 6.4 $^1$H NMR of compound 205 380
Figure 6.5 $^{13}$C and $^{19}$F NMR of compound 205 381
Figure 6.6 $^1$H and $^{13}$C NMR of compound 211 382
Figure 6.7 $^1$H and $^{13}$C NMR of compound 215 383
Figure 6.8 $^1$H NMR of compound 216 384
Figure 6.9 $^{13}$C and $^{19}$F NMR of compound 216 385
Figure 6.10 $^1$H NMR of compound 217 386
Figure 6.11 $^{13}$C and $^{19}$F NMR of compound 217 387
Figure 6.12 $^1$H and $^{13}$C NMR of compound 219 388
Figure 6.13 $^1$H and $^{13}$C NMR of compound 222 389
Figure 6.14 $^1$H and $^{13}$C NMR of compound 224 390
Figure 6.15 $^1$H and $^{13}$C NMR of compound 225 391
Figure 6.16 $^1$H and $^{13}$C NMR of compound 226 392
Figure 6.17 $^1$H and $^{13}$C NMR of compound 227 393
Figure 6.18 $^1$H NMR of a mixture of compounds 226 and 228 394
Figure 6.19 $^1$H and $^{13}$C NMR of compound 229 395
Figure 6.20 $^1$H and $^{13}$C NMR of compound 232 396
Figure 6.21 $^1$H and $^{13}$C NMR of compound 233 397
Figure 6.22 $^1$H and $^{13}$C NMR of compound 234 398
Figure 6.23 $^1$H and $^{13}$C NMR of compound 235 399
<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.24</td>
<td>$^1$H and $^{13}$C NMR of compound 237</td>
<td>400</td>
</tr>
<tr>
<td>6.25</td>
<td>$^1$H and $^{13}$C NMR of compound 238</td>
<td>401</td>
</tr>
<tr>
<td>6.26</td>
<td>$^1$H and $^{13}$C NMR of compound 239</td>
<td>402</td>
</tr>
<tr>
<td>6.27</td>
<td>$^1$H and $^{13}$C NMR of compound 240</td>
<td>403</td>
</tr>
<tr>
<td>6.28</td>
<td>$^1$H and $^{13}$C NMR of compound 241</td>
<td>404</td>
</tr>
<tr>
<td>6.29</td>
<td>$^1$H and $^{13}$C NMR of compound 242</td>
<td>405</td>
</tr>
<tr>
<td>6.30</td>
<td>$^1$H and $^{13}$C NMR of compound 243</td>
<td>406</td>
</tr>
<tr>
<td>6.31</td>
<td>$^1$H and $^{13}$C NMR of compound 245</td>
<td>407</td>
</tr>
<tr>
<td>6.32</td>
<td>$^1$H and $^{13}$C NMR of compound 246</td>
<td>408</td>
</tr>
<tr>
<td>6.33</td>
<td>$^1$H and $^{13}$C NMR of compound 249</td>
<td>409</td>
</tr>
<tr>
<td>6.34</td>
<td>$^1$H and $^{13}$C NMR of compound 253</td>
<td>410</td>
</tr>
<tr>
<td>6.35</td>
<td>$^1$H and $^{13}$C NMR of compound 254</td>
<td>411</td>
</tr>
<tr>
<td>6.36</td>
<td>$^1$H and $^{13}$C NMR of compound 255</td>
<td>412</td>
</tr>
</tbody>
</table>
Figure 7.2 $^1$H and $^{13}$C NMR of compound 257
Figure 7.3 $^1$H of compound 258
Figure 7.4 $^{13}$C and $^{19}$F NMR of compound 258
Figure 7.5 $^1$H and $^{13}$C NMR of compound 261
Figure 7.6 $^1$H and $^{13}$C NMR of compound 262
Figure 7.7 $^1$H NMR of compound 264
Figure 7.8 $^{13}$C and $^{19}$F NMR of compound 264
Figure 7.9 $^1$H NMR of compound 265
Figure 7.10 $^{13}$C and $^{19}$F NMR of compound 265
Figure 7.11 $^1$H NMR of compound 266
Figure 7.12 $^{13}$C and $^{19}$F NMR of compound 266
Figure 7.13 $^1$H NMR of a mixture of 270 and 271
Figure 7.14 $^1$H NMR of compound 273
Figure 7.15 $^{13}$C and $^{19}$F NMR of compound 273
Figure 7.16 $^1$H and $^{13}$C NMR of a mixture of 274 and 275
Figure 7.17 $^1$H NMR of compound 276
Figure 7.18 $^{13}$C and $^{19}$F NMR of compound 276
Figure 7.19 $^1$H NMR of compound 277
Figure 7.20 $^{13}$C and $^{19}$F NMR of compound 277
Figure 7.21 $^1$H and $^{13}$C NMR of compound 279
Figure 7.22 $^1$H and $^{13}$C NMR of compound 280
Figure 7.23 $^1$H NMR of compound 281
Figure 7.24 $^{13}$C and $^{19}$F NMR of compound 281
Figure 7.25 $^1$H and $^{13}$C NMR of compound 285
Figure 7.26 $^1$H and $^{13}$C NMR of compound 286
Figure 7.27 $^1$H and $^{13}$C NMR of compound 287
Figure 7.28 $^1$H and $^{13}$C NMR of compound 289
Figure 7.29 $^1$H and $^{13}$C NMR of compound 290
Figure 7.30 $^1$H and $^{13}$C NMR of compound 291
Figure 7.31 $^1$H and $^{13}$C NMR of compound 292
Figure 7.32 $^1$H and $^{13}$C NMR of compound 293
Figure 7.33 $^1$H and $^{13}$C NMR of compound 294
Figure 7.34 $^1$H and $^{13}$C NMR of compound 295
Figure 7.35 $^1$H and $^{13}$C NMR of compound 296
Figure 7.104 $^1$H and $^{13}$C NMR of compound 364
Figure 7.105 $^1$H and $^{13}$C NMR of compound 365
Figure 7.106 $^1$H and $^{13}$C NMR of compound 366
Figure 7.107 $^1$H and $^{13}$C NMR of compound 368
Figure 7.108 $^1$H and $^{13}$C NMR of compound 369
Figure 7.109 $^1$H and $^{13}$C NMR of compound 370
Figure 7.110 $^1$H and $^{13}$C NMR of compound 371
Figure 7.111 $^1$H and $^{13}$C NMR of compound 372
Figure 7.112 $^1$H and $^{13}$C NMR of compound 373
Figure 7.113 $^1$H and $^{13}$C NMR of compound 374
Figure 7.114 $^1$H and $^{13}$C NMR of compound 375
Figure 7.115 $^1$H and $^{13}$C NMR of compound 376
Figure 7.116 $^1$H and $^{13}$C NMR of compound 377
Figure 7.117 $^1$H and $^{13}$C NMR of compound 378
Figure 7.118 $^1$H and $^{13}$C NMR of compound 379
Figure 7.119 $^1$H and $^{13}$C NMR of compound 380
Figure 7.120 $^1$H and $^{13}$C NMR of compound 381
Figure 7.121 $^1$H and $^{13}$C NMR of compound 382
Figure 7.122 $^1$H and $^{13}$C NMR of compound 383
Figure 7.123 $^1$H and $^{13}$C NMR of compound 384
Figure 7.124 $^1$H and $^{13}$C NMR of compound 385
Figure 7.125 $^1$H and $^{13}$C NMR of compound 386
Chapter 1 Short syntheses of the indole alkaloids alocasin A, scalaridine A and hyrtinadine A-B

1.A Introduction

A number of bisindole alkaloids have been isolated from marine sponges and tunicates. Specific examples include hemacanthins, dragmacidins, topsentins (spontogins), nortopsentins and rhopaladins. These metabolites possess diverse bioactivities such as cytotoxic, antiviral, antifungal, antibacterial and antiplasmodial activities. The common feature of these alkaloids is the presence of a pyrazinone/imidazole or a reduced derivative linker either attached directly to the 3 positions of the two indoles or attached via a carbonyl carbon and/or methine. Hydroxylation in the 6 or 7 position can also be found in some of the metabolites.

Alocasin A was recently isolated from the dried rhizomes of the herbaceous plant Alocasia macrorrhiza, collected in the People Republic of China (Fig. 1.1). This is the only heterocycle-linked bisindole isolated from a terrestrial source. The presence of hydroxyl groups in the two 5-positions is also unusual for this type of bisindoles, but can be found in hyrtinadine A isolated from the marine sponge Hyrtios sp. and scalaridine A and hyrtinadine B isolated from the marine sponge Scalarispongia sp. Hyrtinadine A and scalaridine A are the only examples of pyrimidine and pyridine linked bisindole alkaloids respectively. The structures of these natural products are depicted in Figure 1.1.

Figure 1.1 structures of alocasin A, scalaridine A, and hyrtinadine A-B

The structure elucidation of alocasin A, scalaridine A and hyrtinadine A-B was achieved using spectroscopic techniques.
Total syntheses of alocasin A, scalaridine A and hyrtinadine A using cross-coupling strategy have recently been reported. In the syntheses of the pyrazine, pyridine and pyrimidine linked bisindoles, a one pot double Suzuki-Miyaura cross coupling of 1-t-butoxycarbonyl-5-methoxy-3-boryl indole with 2,5-dibromopyrazine (alocasin A, Scheme 1.1),\textsuperscript{12} 3,5-dibromopyridine (scalaridine A, Scheme 1.2)\textsuperscript{13} and 2-iodo-5-bromopyrimidine (hyrtinadine A, Scheme 1.3)\textsuperscript{14} were used as the key step. In another synthesis of hyrtinadine A, a palladium catalyzed double cross coupling of a triindolylindium reagent and 2-chloro-4-bromopyrimidine was used (Scheme 1.4).\textsuperscript{15} Synthesis of hyrtinadine B has not been reported to date.

**Scheme 1.1** Sperry’s synthesis of alocasin A

![Scheme 1.1 Sperry’s synthesis of alocasin A](image)

**Scheme 1.2** Sperry’s synthesis of scalaridine A

![Scheme 1.2 Sperry’s synthesis of scalaridine A](image)
**Scheme 1.3** Tasch’s synthesis of hyrtinadine A

\[
\begin{align*}
\text{MeO} & \quad \text{I} \\
\text{N} & \quad \text{Boc} \\
\end{align*}
\]

\[
\begin{align*}
\text{Pd(PPh}_3)_4, \text{ HBPin} & \quad \text{MeO-} \\
\text{NEt}_3, \text{dioxane, 80 °C, 3 h} & \quad \text{H} \\
\text{then,} & \quad \text{ HO-} \\
\text{Br} & \quad \text{N} \\
\text{Cs}_2\text{CO}_3, \text{MeOH} & \quad \text{N} \\
\text{100 °C, overnight} & \quad \text{H} \\
\end{align*}
\]

64%

**Scheme 1.4** Mosquera’s synthesis of scalaridine A

\[
\begin{align*}
\text{MeO} & \quad \text{TBS} \\
\text{N} & \quad \text{In} \\
\text{TBS} & \quad \text{3} \\
\end{align*}
\]

\[
\begin{align*}
\text{Pd(PPh}_3)_4, \text{ THF} & \quad \text{MeO-} \\
\text{80 °C, 18 h} & \quad \text{H} \\
\end{align*}
\]

87%

1.B Results and Discussion

The objective of this work was to develop short and efficient synthetic routes to all the four natural products namely alocasin A, scalaridine A, hyrtinadine A and hyrtinadine B using a late stage palladium catalyzed reductive N-heterocyclization as the key indole forming step. This methodology has been emerging as a powerful tool for the synthesis of a wide variety of substituted indoles. A number of naturally occurring indole alkaloids have been synthesized including tjipanazoles, murrayquinone, bauerine A, carbazole alkaloids, mushroom metabolites, and the tetracyclic alkaloid ht-13-B using this reaction as the key indole forming step. The originally proposed plan was to use vinylstannane 4 as the common intermediate in the Kosugi-Migita-Stille cross coupling to assemble the reductive cyclization
precursors. Although the plan worked well for alocasin A, it proved problematic for the remaining three natural products calling for a change in the synthetic strategy.

Alocasin A was synthesized in 6 steps from 4-benzyloxy-2-bromo-1-nitrobenzene (1) using a palladium catalyzed reaction in five of the steps (Scheme 1.5). The synthesis commenced with a Sonogashira coupling of 1 with trimethylsilylethyne followed by a tetrabutylammonium fluoride (TBAF) mediated deprotection affording products 2 and 3 respectively, in high isolated yields. Use of highly \( \alpha \)-regioselective palladium catalyzed hydrostannylation of ortho-substituted arylakynes reported by Alami et al\(^{23} \) gave rise to the expected vinylstannane 4 in excellent yield.\(^{24} \) Palladium catalyzed reactions of halopyrazines\(^{25} \) including Sonogashira,\(^{26} \) Suzuki-Miyaura,\(^{27} \) Negishi,\(^{28} \) and Kosugi-Migita-Stille\(^{29} \) cross couplings have been reported. A double Suzuki-Miyaura cross coupling of 2,5-dibromopyrazine (5) with 3-borylated indoles was used to prepare 2,5-bisindolopyrazines.\(^{14,30} \) A sequential Suzuki-Miyaura and Kosugi-Migita-Stille cross coupling of 2,5-dibromo-3-methoxypyrazine was used in the total synthesis of bisindolopyrazine alkaloid dragmacidin D.\(^{31} \) In the present synthesis of alocasin A, the central pyrazine nucleus was installed by a one-pot double Kosugi-Migita-Stille cross coupling of vinylstannane 4 with 5 in a relatively low isolated yield along with the dimer 7 in 40% yield resulting from the dimerization of 4. The two products were readily separated by chromatography on a silica gel. Cross coupling of related styryltin derivatives with aryl bromides and iodides have been reported.\(^{32} \)

A double palladium catalyzed reductive \( N \)-heterocyclization of 6 using a bis(dibenzylideneactone)palladium-1,3-bis(diphenylphosphino)propane-1,10-phenanthroline catalyst system in the presence of carbon monoxide (pCO=6 atm, 120 °C) in \( N,N \)-dimethylformamide, furnished protected dibenzyloxyalocasin A 8 in excellent isolated yield. The benzyl groups were smoothly removed by hydrogenolysis using Pd/C-H\(_2\) (10% Pd, pH\(_2\)=4 atm) in ethanol at 60 °C affording the naturally occurring bisindolopyrazine alocasin A. Thus the synthesis of this natural product was completed in six steps in 21% overall yield starting from 1. The NMR, IR, HRMS, and melting point were compared with the literature reported data and all corroborated the originally proposed structure. It should be noted that all transformations from 6 to alocasin A involved reactions at two different centers making a total of nine connections/disconnections with an 84% average yield per step (Scheme 1.5).
Excited by the successful synthesis of alocasin A, a similar sequence of Kosugi-Migita-Stille cross coupling of 3,5-dibromopyridine (9) was envisioned for the synthesis of scalaridine A. While 9 has been utilized in cross coupling reactions with aryltin reagents, the use of vinyl tin reagents has not been reported. Disappointingly, all attempted cross coupling reactions of 4 with 9 using a number of palladium-based catalysts failed to give the desired coupling product. The only product obtained from these reactions was the homocoupling product 7 derived from the dimerization of 4. Low yields in addition to a preference for cine-substitution have been observed in palladium catalyzed cross couplings using 1-trimethylstannyl-1-phenylethene and 2- and 3-bromopyridines (Scheme 1.6).
Thus, a slightly different strategy was pursued for the synthesis of scalaridine A where the polarity of the coupling partners was reversed, that is, a Kosugi-Migita-Stille coupling of heteroaryl vinylstannane with an aryl halide. Hydrostannation of ethyne-substituted heterocycles are relatively rare in the literature. A single example of a copper catalyzed, $\alpha$-regioselective hydrostannation, of 2-ethynylpyridine using hexamethylditin was reported by Yoshida et al.\textsuperscript{32} A palladium catalyzed hydrostannation of an $N$-protected 3-ethynylindole also gave exclusively $\alpha$-stannylated product.\textsuperscript{36} In contrast, palladium catalyzed hydrostannation of 2-ethynylpyridine with an ionic liquid supported stannane was shown to be relatively unselective having an $\alpha/\beta$-ratio of 38:62.\textsuperscript{37}

In our case, palladium catalyzed hydrostannylation of 3,5-diethynylpyridine (10) gratifyingly furnished 11 with exclusive $\alpha$-selectivity. Subsequent Kosugi-Migita-Stille coupling of 11 with 4-benzyloxy-2-iodo-1-nitrobenzene (12) gave the expected product 13. Reductive cyclization followed by debenzylation afforded scalaridine A. Synthetic scalaridine A was spectroscopically and thermally identical to sample obtained from natural sources ($^1$H NMR, $^{13}$C NMR, IR, HRMS, mp). Starting from 10, the overall yield was 13\% in four synthetic transformations (Scheme 1.7).
2,5-Dichloropyrimidine has been shown to participate in Kosugi-Migita-Stille cross coupling reactions with vinylstannanes, reacting first in the 2-position then in the 5-position. However, the related compound 2,5-dibromopyrimidine (15) proved to be problematic substrate in cross coupling reactions. Attempted coupling of 4 with 15 gave three identifiable products, destannylated product 16, an inseparable mixture of homocoupling product 7 and an unknown impurity, and the monocoupled, debrominated pyrimidine 17. The site of cross coupling was determined to be the 2-position based on $^1$H NMR wherein a doublet resonance at $\delta$ 8.65 ppm integrating to two protons and a triplet at $\delta$ 7.10 ppm integrating to one proton with a coupling constant of $J$=5.2 Hz was observed. Similar chemical shifts and coupling constants have been reported for related 2-substituted pyrimidines (Scheme 1.8).
Here as well the reductive cyclization precursor was prepared by Kosugi-Migita-Stille coupling by reversing the polarity of the coupling partners. Double Sonogashira coupling\(^{40}\) of 2,5-dibromopyrimidine (15) with trimethylsilylethyne gave the expected product 18, which was used for desilylation using potassium carbonate in methanol/diethyl ether to give 2,5-diethynylpyrimidine (19). Palladium catalyzed hydrostannylation of 19 afforded the divinyltin-substituted pyrimidine 20, again with excellent α-regioselectivity. The subsequent steps, Kosugi-Migita-Stille coupling of 20 with 12, reductive N-heterocyclization, and debenzylation proceeded eventually to give hyrtinadine A. The spectroscopic data (\(^1\)H and \(^13\)C NMRs, HRMS) and melting point were fully consistent with those of the natural hyrtinadine A. The overall yield of hyrtinadine A starting from 15 was 12% in six steps (Scheme 1.9).
Finally, 5-ethynylpyrimidine (23) served as the starting material for the synthesis of the fourth alkaloid hyrtinadine B. Following same sequence of reactions used in the synthesis of hyrtinadine A, (1) palladium catalyzed hydrostannylation, (2) cross coupling, (3) reductive cyclization, and (4) debenzylation gave hyrtinadine B in 28% overall yield in four steps. The spectroscopic data of the synthetic sample matched with those of the isolated compound (Scheme 1.10).
1.10 Synthesis of hyrtinadine B

**Scheme 1.10** Synthesis of hyrtinadine B

1. C Conclusion

Expedient synthetic routes to four naturally occurring indole alkaloids, alocasin A, scalaridine A and hyrtinadine A-B have been developed. The overall yields were 21% (six steps), 13% (four steps), 12% (six steps), and 28% (four steps) respectively. Three palladium catalyzed reactions, namely, an alkyne hydrostannylation, a Kosugi-Migita-Stille cross coupling and a reductive \( N \)-heterocyclizations are the key steps in the syntheses. Results from the palladium catalyzed hydrostannylation of heteroarylethynes indicates that an *ortho*-substituent is not a requirement for high \( \alpha \)-regioselectivity when ethynyl substituted heterocycles are used.
Chapter 2 Double palladium catalyzed reductive cyclizations. Synthesis of 2,2’-, 2,3’-, and 3,3’-bi-1H-indoles, indolo[3,2-b]indoles, and indolo[2,3-b]indoles

2.A Introduction

Indoles and carbazoles can be synthesized by the reductive cyclization of 2-nitrostyrenes and 2-nitrobiphenyls using a number of reagents. Cadogan and Sundberg employed trialkyl phosphites or triphenylphosphine as reducing agents at elevated temperatures to carry out such transformations. More recently, however, reductive cyclizations using transition metal catalysts in the presence of carbon monoxide as the ultimate reducing agent have been developed. In fact, palladium complexes are the most commonly employed catalysts for effecting reductive cyclizations, and this facile method has been used in the total synthesis of a number of indole alkaloids. Therefore, we envisioned this methodology as an expedient pathway for the synthesis of a wide variety of compounds containing two indole units. Five different substrates in total, three bis(2-nitrophenyl)butadienes and two bis(2-nitrophenyl)ethenes were selected as biindole precursors (Figure 2.1). The formation of 2,2’-, 3,3’- and 2,3’-biindoles from 1,4-, 2,3-, and 1,3-bis(2-nitroaryl)-1,3-butadienes, respectively, was anticipated via a cyclization onto each of the two carbon-carbon double bonds of the butadienes (A-C, Figure 2.1). In related reactions, successful reductive cyclizations of 1,2-bis(2-nitroaryl)ethenes and 1,1-bis(2-nitroaryl)ethenes onto a shared olefin was hypothesized to furnish indolo[3,2-b]indoles and indolo[2,3-b]indoles respectively (D-E, Figure 2.1).

We disclose herein a short and efficient synthetic sequences to a variety of biindoles using a double reductive cyclization of 1,4-, 2,3-, and 1,3-bis(2-nitroaryl)-1,3-butadienes as the ultimate and key step leading to both the indole rings. Also disclosed are the nonselective reactions of 1,2-bis(2-nitroaryl)ethenes and 1,1-bis(2-nitroaryl)ethenes forming a mixture of products.
**Figure 2.1** Possible cyclizations (A-E) of bis(2-nitrophenyl)butadienes and –ethenes.

2.B Results and Discussion

The first biindole that was chosen for synthesis was 2,2’-bi-1H-indole (38). The cyclization precursor, 1,4-bis(2-nitrophenyl)-1,3-butadiene (33), was prepared following the procedure of Lowinger et al$^{46}$ via a Wittig reaction of 2-nitrocinnamaldehyde (31) with 2-nitrobenzyl triphenylphosphonium bromide in the presence of a base. To our delight, subjecting compound 33 to our standard condition of reductive N-heterocyclization using a bis(dibenzylideneacetone)palladium-1,3-bis(diphenyl)propane-1,10-phenanthroline catalyst sytem, in the presence of carbon monoxide (pCO=6 atm, 120 °C) in N,N’-dimethylformamide, afforded compound 38$^{47}$ in good isolated yield.

A number of synthetic pathways to access 2,2’-biindoles have been reported in the literature. For instance, the parent compound 38 has been accessed by iridium,$^{48}$ gold$^{49}$ and base$^{50}$ catalyzed cyclization of the
diamine corresponding to 33, Cadogan-Sunderberg type cyclizations using triphenylphosphine\textsuperscript{51} or triphenylphosphite,\textsuperscript{52} and double Madelung cyclization.\textsuperscript{53} Pertinent to the current methodology, Cenini et al. reported a Pd(TMB)\textsubscript{2}-TMphenanthroline\textsuperscript{54} catalyzed carbon monoxide (pCO=40 atm, 140 °C) mediated cyclization of 33 to give 38 (40%) in addition to the monocyclized product 2-(2-nitrophenyl)indole (26%).\textsuperscript{55} A related reaction has also been described by Davies et al. using a palladium catalyzed route without any experimental details or yields.\textsuperscript{56}

Excited by the above result, four additional substrates (34-37), in 55-75% yields, were prepared by the treatment of the Wittig salts (28-30) with 31 or 5-bromo-2-nitrocinamaldehyde (32) in the presence of a base. 5-Bromo-2-nitrocinamaldehyde, in turn, was obtained by the reaction of 5-bromo-2-nitrobenzaldehyde with (formylmethyl)triphenylphosphonium chloride in the presence of 4-(N,N-dimethylamino)pyridine (DMAP). Dienal 43 was also isolated resulting from two consecutive Wittig reactions in addition to 32 (Scheme 2.1). The dienes (34-37) were smoothly transformed to the corresponding 2,2'-bi-1H-indoles (39-42) under the same conditions. A good to excellent yield of product was observed for all substrates examined (Table 2.1).

**Table 2.1 Synthesis of 2,2'-bi-1H-indoles**

<table>
<thead>
<tr>
<th>Phosphane</th>
<th>Aldehyde</th>
<th>Diene</th>
<th>2,2'-Bi-1H-indole</th>
</tr>
</thead>
<tbody>
<tr>
<td>27 (R=H)</td>
<td>31 (R'='H)</td>
<td>33 (R=R'=H)</td>
<td>38 (R=R'=H, 73%)</td>
</tr>
<tr>
<td>28 (R=6-Cl)</td>
<td>31</td>
<td>34 (R=6-Cl, R'='H, 55%)</td>
<td>39 (R=4-Cl, R'='H, 94%)</td>
</tr>
<tr>
<td>29 (R=3-OMe)</td>
<td>31</td>
<td>35 (R=3-OMe, R'='H, 64%)</td>
<td>40 (R=7-OMe, R'='H, 93%)</td>
</tr>
<tr>
<td>30 (R=4-Br)</td>
<td>31</td>
<td>36 (R=4-Br, R'='H, 73%)</td>
<td>41 (R=6-Br, R'='H, 74%)</td>
</tr>
<tr>
<td>30</td>
<td>32 (R'=5-Br)</td>
<td>37 (R=4-Br, R'=5-Br, 75%)</td>
<td>42 (R=6-Br, R'=5-Br, 71%)</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Isolated yield of pure product after chromatography. \textsuperscript{b}Mixtures of EEZZ isomers obtained for 35-37.

**Scheme 2.1 Synthesis of 5-bromo-2-nitrocinamaldehyde (32)**

\[ \text{Br-CHO} \xrightarrow{\text{PPh}_3\text{Cl}, \text{DMAP, CHCl}_3, \text{rt-reflux}} \text{Br-CHO} + \text{Br-CHO} \]

\[ 32 (51\%) + 43 (21\%) \]
After the successful synthesis of 2,2′-bi-1H-indoles, double cyclization of 2,3-bis(2-nitrophenyl)-1,3-butadienes to give 3,3′-bi-1H-indoles was examined next, and the results are summarized in Table 2.2, Scheme 2.2, and Scheme 2.3. The parent cyclization precursor 2,3-bis(2-nitrophenyl)-1,3-butadiene (52) has previously been prepared using a palladium catalyzed double cross coupling of 2-nitrophenylboronic acid with 1,4-bis(carbonyloxy)-2-butyne.57 We have recently reported the formation of 7, a substituted analogue of 52, as a side product in Kosugi-Migita-Stille reaction of 4 with an aryl bromide.58 It seemed plausible that homocoupling of 4, and related alkenyltin reagents, would be the major reaction path in the absence of a cross-coupling partner. In order to examine this idea, tributyl(1-(2-nitrophenyl)tin (48) was prepared from 1-ethynyl-2-nitrobenzene (44) in excellent isolated yield using the regioselective palladium catalyzed hydrostannation developed by Alami and coworkers.23b As expected, the β-isomer was not detected by 1H NMR of the crude reaction mixture. To our delight, palladium catalyzed homocoupling of 48 proceeded smoothly in DMF to give dimer 52. Reductive cyclization of 52 resulted in the formation of 3,3′-bi-1H-indole (56)59 as the sole product (Table 2.2).

3,3-Biindoles are relatively rare in nature, but a handful examples of halogenated and/or sulfur containing alkaloids have been isolated from algae.60-63 In addition, the unsubstituted 3,3′-biindole 56 was isolated from a terrestrial fungus.64 Recent synthesis of 3,3′-biindoles include, for example, a Masuda indole borylation-Suzuki arylation sequence,65 a tellurium tetrachloride66 mediated and palladium catalyzed oxidative dimerizations of indoles.67

To briefly examine the ease of synthesis of 3,3′-biindoles by reductive N-heterocyclization, four additional 1-(2-nitrophenyl)ethenyl)tin derivatives (4, 49-51) were prepared in a similar fashion to 48 (Table 2.2). Although palladium catalyzed homocoupling of 4 gave the expected product 7 in good yield, the yield of chloro-substituted dimer 53 remained low and we were compelled to look for an alternative pathway. Homocoupling of organotin reagents have been reported using an excess of CuCl in DMF,68 an excess of Cu(NO₃)₂ in THF,69 or a catalytic amount of CuCl₂ in the presence of 0.5 equivalent of iodine in DMF.70 After several trials for the preparation of reductive cyclization precursors using the literature conditions, a combination of 2.5 equivalent of CuCl in DMF at ambient temperature was found to work well for our substrates (49-51) giving excellent yields of products (Table 2.2). These precursors (7, 53-55) were successfully converted to expected 3,3′-biindoles (57-60) in 64-100% isolated yields. The results are summarized in Table 2.2 below.
Table 2.2 Synthesis of 3,3’-bi-1H-indoles

<table>
<thead>
<tr>
<th>Alkyne</th>
<th>Vinyltin \textsuperscript{a}</th>
<th>Diene \textsuperscript{a}</th>
<th>3,3’-Bi-1H-indole \textsuperscript{a}</th>
</tr>
</thead>
<tbody>
<tr>
<td>44 (R=H)</td>
<td>48 (95%)</td>
<td>52 (67%\textsuperscript{b})</td>
<td>56 (R=H, 89%)</td>
</tr>
<tr>
<td>3 (R=5-OBn)</td>
<td>4 (96%)</td>
<td>7 (78%\textsuperscript{b})</td>
<td>57 (R=5,5’-OBn, 87%)</td>
</tr>
<tr>
<td>45 (R=4-Cl)</td>
<td>49 (96%)</td>
<td>53 (36%\textsuperscript{b}, 80%\textsuperscript{c})</td>
<td>58 (R=6,6’-diCl, 100%)</td>
</tr>
<tr>
<td>46 (R=4-CO\textsubscript{2}Me)</td>
<td>50 (78%)</td>
<td>54 (92%\textsuperscript{c})</td>
<td>59 (R=6,6’-diCO\textsubscript{2}Me, 100%)</td>
</tr>
<tr>
<td>47 (R=4-OMe)</td>
<td>51 (90%)</td>
<td>55 (98%\textsuperscript{c})</td>
<td>60 (R=6,6’-diOMe, 64%)</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Isolated yield of product after chromatography. \textsuperscript{b}PdCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2} used. \textsuperscript{c}CuCl used.

As an example of pyridine-linked biindole, 4,4’-diaza-3,3’-bi-1H-indole (64) was synthesized using hydrostannation, dimerization, cyclization sequence discussed above. Thus, 64 was prepared in three steps from the previously reported 2-ethynyl-3-nitropyridine (Scheme 2.2).

Scheme 2.2 Synthesis of 4,4’-diaza-3,3’-bi-1H-indole (64)

An unsymmetrical biindole 68 was also synthesized (Scheme 2.3). Treatment of 65 with HBr in 3-pentanone as a solvent furnished vinyl bromide 66\textsuperscript{71} in 57\% yield. The vinyl bromide was then subjected to Kosugi-Migita-Stille coupling with ethenyltin 48 to give 2,3-bis(2-nitrophenyl)-1,3-butadiene (67). Tin impurities from the cross coupling were removed by chromatography using a 9:1 SiO\textsubscript{2}/K\textsubscript{2}CO\textsubscript{3} stationary phase as described by Harrowven et al.\textsuperscript{72} Double reductive cyclization smoothly converted 67 to the desired 3,3’-biindole in quantitative yield (Scheme 2.3).\textsuperscript{73}
Scheme 2.3 Synthesis of unsymmetrical 3,3’-bi-1H-indole 68

The third permutation of the double cyclization of substituted 1,3-butadienes is the synthesis of 2,3’-bi-1H-indoles from 1,3-bis(2-nitrophenyl)-1,3-butadienes (Table 2.3). Synthesis of 2,3-bi-1H-indoles have previously been reported via the Fischer indole,\textsuperscript{74} acid mediated reaction of 3-bromoindole with indole,\textsuperscript{75} and Lewis acid mediated dimerization to give 2,3-dihydro-2,3’-bisindole, followed by oxidation.\textsuperscript{76} To date, only four natural products containing a 2,3’-bisindole have been isolated.\textsuperscript{77} All four natural compounds are connected by an ethylene bridge between the 2 and 3’ carbons of the respective indoles.

The parent cyclization precursor 71 was prepared in moderate yield by the treatment of the Wittig salt with 2-(2-nitrophenyl)-2-propenal (70)\textsuperscript{78} under basic conditions. Three additional substrates (72-74) were also synthesized in a similar fashion. Low to moderate yields of products were isolated. Treatment of (71-74) with carbon monoxide under palladium catalyzed conditions gave the anticipated 2,3’-bi-1H-indoles (75-78) in 61-72% yields. The results are summarized in Table 2.3.
The fourth variation of the double cyclization is the cyclization of the two adjacent nitro-groups onto a shared olefin bond with the anticipated formation of indolo[3,2-b]indole. In this case, subjecting the known parent compound 1,2-bis(2-nitrophenyl)ethene (79) to the palladium catalyzed reductive cyclization conditions for 56 h did not furnish the double cyclization product indolo[3,2-b]indole (80) but gave two isomeric tetracyclic compounds indolo[1,2-c]quinazolin-6(5H)-one (81) and 5,11-dihydro-6H-indolo[3,2-c]quinoline-6-one (82). The products were analyzed by 2D NMR experiments and by comparison of analytical data with literature reported values. It should be noted that Nishiyama et al. have reported a reductive cyclization, related to the transition metal catalyzed reactions. For example, treatment of 79 with a catalytic amount of selenium (40 mol%) under 30 atm of carbon monoxide at 100 °C gave 81 in 60% yield. In this catalytic process, carbon monoxide insertion to form an isocyanate was suggested as plausible intermediate that ultimately reacts with the indole N-H giving rise to the insertion product. Isocyanate 83 has previously been reported as an intermediate in a Curtius rearrangement of the corresponding acid, affording a 1:1 mixture of 81 and 82. Compound 82 was not observed in the selenium catalyzed reactions (Scheme 2.4). Products derived from insertion of carbon monoxide have been isolated in a few additional cases of transition metal catalyzed reductive cyclizations aromatic nitro compounds. An example is the rhodium catalyzed reductive cyclization of 84 that gave, in addition to indole 85 as the major product, quinolinone 86 and amine 87 (Scheme 2.5).
Scheme 2.4 Reductive cyclization of 79

\[
\text{79} \xrightarrow{\text{Pd(dba)}_2, \text{dppp}, 1,10\text{-phen, DMF, CO (6 atm), 120 °C}} \text{80 (not observed)} + \text{81 (76%) + 82 (12%)}
\]

Scheme 2.5 Reductive cyclization of 84

\[
\text{84} \xrightarrow{\text{Rh}6(\text{CO})_{16}, \text{PhMe, 220 °C, 80 atm}} \text{85 (35%)} + \text{86 (17%)} + \text{87 (5%)}
\]

The formation of indolo[1,2-c]quinazolin-6(5H)-one encouraged us to evaluate the palladium catalyzed pathway of 1,2-bis(2-nitrophenyl)ethenes as a general methodology toward these compounds. Two additional substrates 88 and 91 were prepared by Wittig reactions of 28 and 29 with 2-nitrobenzaldehyde. From the reductive cyclization of chloro-substituted alkene 88, both indolo[3,2-b]indole (90) and indolo[1,2-c]quinazolin-6(5H)-one (89) were isolated. The former compound 90 represents the first case of the formation of an indolo[3,2-b]indole from a transition metal catalyzed reductive cyclization, although as a minor product (Scheme 2.6). In contrast, the methoxy substituted substrate 91 did not participate in a double cyclization as readily as 79 and 88. In this case, two monocyclized products 92 and 93 were isolated in 10% and 74% respectively, together with a negligible amount of indolo[3,2-c]quinolin-6-one (94) (Scheme 2.7). Monocyclized indole 93 was hypothesized to be intermediate precursor to the tetracyclic compound 94; however, only a miniscule amount of 94 (2%) was isolated from an attempted cyclization of 93 under identical reaction conditions. Although all starting material was consumed in the reaction, no other side products were identified (Scheme 2.7).
Finally, the feasibility of palladium catalyzed double reductive N-heterocyclization of 1,1-bis(2-nitrophenyl)alkenes for the formation of indolo[2,3-b]indoles was also studied. The reductive cyclization precursor 95 was prepared by the Kosugi-Migita-Stille cross coupling of 1-ido-2-nitrobenzene in good yield.\textsuperscript{85} As observed in the previous palladium catalyzed reactions involving tin compound 48, dimer 52 was also isolated in low yield (11%). When subjected to palladium catalyzed reductive cyclization, compound 95 gave the anticipated product indolo[2,3-b]indole (96), although in a very low isolated yield together with the indolo[2,3-c]quinolinone (97) as the major product (Scheme 2.8). Cadogan-Sundberg type cyclizations of 3-(2-nitrophenyl)indoles using triphenylphosphine\textsuperscript{86} or triethyl phosphite\textsuperscript{87} to afford indolo[3,2-b]indoles have been reported.
**Scheme 2.8** Synthesis of indolo[2,3-b]indole (96) and indolo[2,3-c]quinolinone (97)

The reaction pathway seen in Scheme 2.8 represents a very short and efficient route to access indolo[2,3-c]quinolin-6-one starting from a symmetrical substrate like 95. A number of methodologies have been developed for the construction of the indoloquinoline-6-one skeleton. For example, cyclizations of N-arylindole-2-carboxamides utilizing a Heck reaction,\(^8^8\) photochemical cyclizations of indole-2-carboxylic acid arylamides,\(^8^9\) and 3-(2-azidophenyl)-N-phenylacrylamides,\(^9^0\) oxidative cyclizations of 3-arylindole-2-carboxamides,\(^9^1\) and a platinum catalyzed reduction of ethyl 3-(2-nitrophenyl)-1H-indole-2-carboxylates.\(^9^2\)

The unsymmetrical compound 99 containing a methoxy group *meta* to one of the nitro groups and a benzyloxy group *para* to the second nitro group was also synthesized by the Kosugi-Migita-Stille coupling of 4 with 98 (Scheme 2.9). Compound 99 was subjected to the cyclization conditions, and three different products were obtained after chromatography, an indolo[2,3-b]indole (100) and two isomeric indolo[2,3-c]quinolin-6-ones 101 and 102 in an approximately 1:1:1 ratio. The structures of the isomeric tetracycles (101-102) were elucidated using 2D NMR experiments (Scheme 2.9). It becomes clear that while the use of an unsymmetrical substrate will furnish two isomeric indolo[2,3-c]quinolin-6-ones, the methodology presented here may be of synthetic value employing symmetrical 1,1-bis(2-nitroaryl)alkenes as the starting materials.
Scheme 2.9 Reductive cyclization of 99

2.C Conclusion

A palladium catalyzed, carbon monoxide mediated, double reductive N-heterocyclization of 1,4-, 1,3-, and 2,3-bis(2-nitroaryl)-1,3-butadienes to afford 2,2’-, 2,3’-, and 3,3’-biindoles, respectively, have been developed. The methodology presented here clearly demonstrates potentially useful routes to access these ring systems. On the basis of the results in Schemes 2.4-2.8 and from the selenium catalyzed reactions reported in the literature, it appears that general syntheses of indolo[3,2-b]indoles and indolo[2,3-b]indoles via a palladium catalyzed carbon monoxide mediated reductive cyclizations of 1,2-bis(2-nitroaryl)ethenes or 1,1-bis(2-nitroaryl)ethenes, respectively are not feasible. Products derived from carbon monoxide insertion and/or monocyclized products are the predominant products observed in these reactions.
Chapter 3 Syntheses of three naturally occurring polybrominated 3,3'-bi-1H-indoles

3.A Introduction

Halogen and/or sulfur containing 3,3'-bi-1H-indoles are relatively rare in nature. A small number of such indole alkaloids have been isolated mainly from marine algae and also from a terrestrial fungus. In 1982, Norton et al. isolated 2,2',5,5'-tetrabromo-3,3'-bi-1H-indole (103) from *Rivularia firma* (Fig. 3.1).\(^{109}\) This was the first alkaloid of this family to be isolated and characterized. The related isomeric alkaloid 2,2',6,6'-tetrabromo-3,3'-bi-1H-indole (104) was later isolated from the same species.\(^{110}\) More recently was isolated 2,2',5,5',6,6'-hexabromo-3,3'-bi-1H-indole (105) from the red alga *Laurentia similis*.\(^{111}\) Compound 105 has been shown to be a protein tyrosine phospholipase 1B inhibitor.\(^{112}\)

In addition to the polyhalogenated indoles 103-105, sulfur containing alkaloids 106,\(^{60a}\) 107-108,\(^{60b}\) 109\(^{60c}\) also exist in the nature and they are all produced by the red alga *Laurencia bronngniartii*. The only example of a 3,3’-bi-1H-indole from a terrestrial source is the parent compound isolated from the fungus *Gliocladium catenulatum*.\(^{64}\) The polyfunctionalized biindole 110 was isolated from the green alga *Chaetomorpha basiretorsa Setchell*.\(^{63}\) To the best of our knowledge, the synthesis of none of these polyhalogenated alkaloids has been reported to date.

Figure 3.1 Naturally occurring polyhalogenated 3,3’-bi-1H-indoles

![Chemical structures of naturally occurring polyhalogenated 3,3’-bi-1H-indoles](image)

- **103** (R=Br, R’=H)
- **104** (R=H, R’=Br)
- **105** (R=R’=Br)
- **106** (R=R’=SMe)
- **107** (R=SMe, R’=SOMe)
- **108** (R=R’=SOMe)
- **109** (R=Br, R’=SMe)
We have recently disclosed palladium catalyzed double reductive cyclization of 2,3-bis(2-nitrophenyl)-1,3-butadienes for the synthesis of a variety of 3,3’-biindoles (Scheme 3.1). For instance, reductive cyclization of 2,3-bis(2-nitrophenyl)-1,3-butadiene (52) gave the parent 3,3’-bi-1H-indole (56) in excellent isolated yield. Herein are described synthetic routes to biindoles 103-105 based on this methodology.

**Scheme 3.1** Palladium catalyzed double reductive cyclization to 3,3’-biindoles

\[
\begin{align*}
\text{O}_2\text{N} & \quad \overset{\text{Pd(dba)}_2, \text{dppp, 1,10-phen}}{\text{CO (6 atm), 120 °C, DMF}} \\
\text{52} & \quad \text{56 (89%)}
\end{align*}
\]

3. B Results and Discussion

Biindole 120 has previously been prepared by a palladium catalyzed oxidative dimerization of 5-bromoindole (Scheme 3.2), reductive cyclization and a two-step procedure employing a nucleophilic addition of 5-bromoindole to 5-bromoisatin followed by borane reduction of the intermediate (Scheme 3.3).

**Scheme 3.2** Palladium catalyzed oxidative dimerization of 5-bromoindole

\[
\begin{align*}
\text{Br} & \quad \overset{\text{Pd(OTFA)}_2, \text{AgNO}_3, \text{MgSO}_4, \text{DMSO}}{\text{120 (69%)}}
\end{align*}
\]
We hypothesized that compounds 103 and 104 can be derived from compound 111 by the introduction of extra bromine atoms. Accordingly, our synthesis commenced with the known compound 5-bromo-2-nitro-1-iodobenzene (112) as the starting point for the synthesis of alkaloids 103 and 104. Sonogashira coupling of 112 with trimethylsilyl ethyne at ambient temperature gave 113. The silyl group was smoothly removed using potassium carbonate in a methanol-diethyl ether solvent system to afford 114. Treatment of 114 with tributyltin hydride in the presence of bis(triphenylphosphine)palladium dichloride in THF furnished the required vinyl tin derivative 115 with excellent $\alpha$-selectivity (Scheme 3.4). No trace of the $\beta$-isomer was observed by $^1$H NMR of the crude reaction mixture. Tin compound 115 was smoothly transformed into the reductive cyclization precursor 116 using an excess of copper chloride. Once in hand, diene 116 was dissolved in N,N-dimethylformamide (DMF) and subjected to carbon monoxide-mediated reductive cyclization (pCO = 6 atm, 120 °C) in the presence of a palladium catalyst system consisting of bis(dibenzylideneacetone)palladium - 1,3-bis(diphenyl)propane - 1,10-phenanthroline to give 5,5'-dibromo-3,3'-bi-1H-indole 111. The $^1$H NMR and $^{13}$C NMR data recorded for 111 were in complete accordance with the reported values.
Scheme 3.4 Synthesis of precursor 111

3-Substituted indoles have been selectively brominated in the 2-position using NBS. For example, bromination of 3-methylindole using NBS in carbon tetrachloride (CCl₄) gave 2-bromo-3-methylindole in 97% yield.¹¹⁵

Scheme 3.5 Bromination of 3-methylindole
Based on this result, biindole 111 was treated with 2.0 equivalents of NBS in CCl$_4$ affording the naturally occurring tetrabrominated alkaloid 103 in 59% yield after chromatographic purification. Reactions of 111 with 4-6 equivalents of NBS in CCl$_4$ were not clean and afforded a number of inseparable products with low mass balance. However, replacing CCl$_4$ with a 1: 1 mixture of tetrahydrofuran and dichloromethane as the solvent system gave 105 in 46% isolated yield upon treatment with six equivalents of NBS. All analytical data for 103$^{109}$ and 105$^{111}$ were in complete agreement with the data reported for the isolated natural products.

Scheme 3.6 Synthesis of 2,2’,5,5’-tetrabromo- and 2,2’,5,5’,6,6’-hexabromobiindoles

A synthetic sequence similar to the one depicted in Scheme 3.6 was used to prepare the remaining 2,2’,6,6’-tetrabrominated alkaloid 104. 1-(4-Bromo-2-nitrophenyl)ethyne (117) served as the starting point for the synthesis of 104 (Scheme 3.7). Both the regioselective palladium catalyzed hydrostannylation of 117 furnishing vinyl tin 118 and the subsequent copper mediated coupling affording dimer 119 proceeded uneventfully. Reductive cyclization of 119 afforded 6,6’-dibromo-3,3’-biindole (120) in 64% isolated yield. Compound 120 has previously been prepared via a palladium catalyzed oxidative dimerization of 6-bromoindole.$^{67}$

Similar to the synthesis of 103, biindole 120 was treated with 2.0 equivalents of NBS in CCl$_4$ affording the tetrabrominated biindole alkaloid 104 in 59% yield after chromatographic purification. All analytical data were in complete agreement with the data reported for isolated 104.$^{109}$
**Scheme 3.7** Synthesis of 2,2′,6,6′-tetrabromo-bi-1H-indole

Biindole 120 was perceived to be a suitable precursor to the hexabromo substituted natural product 105. In the event, treatment of 120 with 5 equivalents of NBS in a THF-dichloromethane solvent mixture gave a separable mixture of the expected product 105 along with a significant amount of 2,2′,5,6,6′-pentabromo-bi-1H-indole 121 (Scheme 3.8). Disappointingly, increasing the amount of NBS to eight equivalents gave roughly the same product ratio but in a much diminished yield (Scheme 3.8). In addition, an attempted bromination of the isolated pentabromobiindole 121 using three equivalents of NBS was unsuccessful. The starting material was recovered in high yield (94%) after chromatography.

**Scheme 3.8** Polybromination of 120
Reports for direct 2,6-dibromination and 2,5,6-tribromination of 3-substituted indoles can be found in the literature. For example, 2,6-dibromination of 3-cyanomethylindole using NBS-SiO$_2$ in dichloromethane gave 2,6-dibromo-3-cyanomethylindole (81%), 2,5-dibromo-3-cyanomethylindole (3%), and 2,4-dibromo-3-cyanomethylindole (5%). 3-Methylindole afforded selectively 2,6-dibromo-3-methylindole using NBS-SiO$_2$ in dichloromethane$^{117}$ and 3-phenylindole using NBS in acetic acid furnished a 6:1 ratio of 2,6-dibromo-3-phenylindole and 2,5-dibromo-3-phenylindole.$^{118}$ In contrast, a 3:4 ratio of 2,6: 2,5-dibromination was observed from brominations of methyltryptophan employing NBS in AcOH/HCOOH.$^{119}$ Tribromination of 3-methylindole with bromine in acetic anhydride gave 2,5,6-tribromo-3-methyl-N-acetylindole.$^{120}$ Based on these previously reported brominations, polybrominations of the parent 3,3'-biindole 56 to give either 104 or 105, depending on the stoichiometry of the reagents, were also pursued. Thus, 3,3'-biindole 56 was treated with 4.0, 5.1, and 8.0 equivalents of NBS in THF/dichloromethane (Scheme 3.9). The brominations proved to be substantially more difficult and only low yields of product(s) were obtained. Using 4.0 equivalents of NBS gave a mixture of 104 and 121 both in 8% isolated yield. Increasing the amount of NBS to 5.1 equivalents eliminated the formation of biindole 104 but gave instead pentabrominated and hexabrominated compounds 121 and 105, respectively. Finally, treatment of 56 with 8.0 equivalents of NBS gave 105 in 16% yield. No other products were isolated from the three reactions of 56.

Scheme 3.9 Bromination of 3,3-bi-1H-indole 56

![Scheme 3.9](attachment:image.png)
3.C Conclusion

The naturally occurring polybrominated indoles 2,2’,5,5’-tetrabromo-3,3’-bi-1H-indole, 2,2’,6,6’-tetrabromo-3,3’-bi-1H-indole, and 2,2’,5,5’,6,6’-hexabromo-3,3’-bi-1H-indole were synthesized for the first time using a palladium catalyzed, carbon monoxide mediated, double N-heterocyclization of 2,3-bis(2-nitro-4(or 5)-bromophenyl)-1,4-butadienes as the key indolization step. The synthetically derived compounds were in all aspects identical to the biindoles isolated from the natural sources.
Chapter 4 A facile base-mediated synthesis of N-alkoxy-substituted benzimidazoles

4.A Introduction

Benzimidazoles are a large class of heterocyclic aromatic compounds consisting of a benzene ring fused to imidazole. The benzo derivative of imidazole is referred to as benzimidazole. The parent compound of the series is commonly called benzimidazole although other name such as 1,3-benzodiazole is often used.

Our group has reported the synthesis of a series of N-substituted 2-nitrobenzenamines. We were proposing to use compound 123 as a precursor to quinolines via the palladium catalyzed, carbon monoxide, mediated reductive N-heterocyclization. With this in mind, compound 122 was dissolved in dimethylsulfoxide (DMSO) and the solution was added to a suspension of sodium hydride (NaH) in DMSO at an ambient temperature. After stirring the mixture for 1 h, the resulting solution was cooled to 0 °C and methyl iodide (MeI) was added. After slowly warming to ambient temperature over 1 h, the reaction mixture was worked up and purified. To our surprise, the expected N-methylated product 123 was not observed in the crude; instead 1-methoxybenzimidazole (124), 1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (125), and 1-methoxy-2-(2-hydroxy-2-propyl)benzimidazole (126) were obtained in 5%, 57%, and 15% yield, respectively (Scheme 4.1). Cyclization of N-phenacyl-2-nitroaniline121 and N-benzyl-2-nitroanilines to give N-oxygenated benzimidazoles122 has been reported.

Scheme 4.1 Formation of benzimidazoles 124-126 from enamine 122

The formation of the observed products in the preceding reaction can be accounted for based on the methodologies developed by Gardiner et al for the formation of 2-substituted N-alkoxybenzimidazoles from 2-nitrobenzenamines and organic halides in the presence of a base and by Popov and Kryshtalyuk for the formation of 2-substituted N-hydroxybenzimidazoles from 2-nitrobenzenamines (Scheme 4.2).123,124 N-alkoxybenzimidazoles can also be prepared from N-hydroxybenzimidazoles either via a Williamson type ether synthesis125 or by a Mitsunobu reaction126 with an alcohol. The reaction of 122 to give 124-126 differs in that either a loss of or oxygenation of the side chain is observed. The formation of compounds 125 and 126 was particularly interesting in the sense that no synthetic routes to N-alkoxy-2-(alkoxyalkyl)benzimidazoles or N-alkoxy-2-(hydroxyalkyl)benzimidazoles have been reported to date. This chapter presents detailed studies of the scope and limitation of the base mediated cyclization of
enamines to give \(N\)-oxygenated benzimidazoles. A plausible mechanism has also been included. \(N\)-Oxygenated benzimidazoles have been shown to exhibit anti-protozoa\(^{127}\) and anti-HIV activities.\(^{123d}\)

**Scheme 4.2** Formation of 2-ethenyl-\(N\)-propoxybenzimidazole\(^{123f}\)

\[
\text{H} \quad \text{N} \quad \text{O} \\
\text{N} \quad \text{O} \\
\text{N} \quad \text{O} \\
\text{Pr} \quad \text{NaH, Pr-Br} \quad \text{DMSO, 73\%} \\
\text{H} \quad \text{N} \quad \text{O} \\
\text{N} \quad \text{O} \\
\text{N} \quad \text{O} \\
\text{Pr}
\]

**4.B Results and Discussion**

In the reaction above, 3 equivalents of base and 3.2 equivalents of MeI were used to give rise to products 124-126. With the hope to control the selectivity of the reaction, we carried out a screening of the reaction conditions by varying the amounts of base and the electrophiles. We chose compound 127 for this purpose because it contains a methoxy group on the aromatic ring that may be useful to determine the product ratios in the crude reaction. As can be seen in table 4.1 (entries 1-3), increasing the amount of MeI while keeping the amount of base the same did not improve the reaction in favor of any of the products and the starting material was recovered in each case. Products 128 and 130 were inseparable by column chromatography; the approximate ratios of these products were determined by \(^1\text{H} \text{NMR.} \)

Gratifyingly, a significant improvement was observed when the amount of base was increased to 2.10 equivalents with 1.05 equivalents of MeI (table 4.1, entry 4). However, a mixture of products was observed upon increasing the amount of MeI while keeping the amount of base the same (table 4.1, entries 5-6). Finally, using 3.15 equivalents of both NaH and MeI resulted in a clean conversion of 127 to 129 with only trace amounts of the other two benzimidazoles observed in the \(^1\text{H} \text{NMR of the crude reaction mixture.} \)

Other possible solvents were also examined for the cyclization, however only a low yield of 129 was obtained. So, we concluded that DMF, NMP, and MeCN were not a good suit to this reaction.
Table 4.1 Condition screening

![Diagram of benzimidazole synthesis]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Eq. NaH</th>
<th>Eq. MeI</th>
<th>Solvent</th>
<th>Alkoxybenzimidazoles&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.05</td>
<td>1.05</td>
<td>DMSO</td>
<td>128&lt;sup&gt;c&lt;/sup&gt; -- --</td>
</tr>
<tr>
<td>2&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.05</td>
<td>2.10</td>
<td>DMSO</td>
<td>128 (1%) -- 130 (34%)</td>
</tr>
<tr>
<td>3&lt;sup&gt;e&lt;/sup&gt;</td>
<td>1.05</td>
<td>3.17</td>
<td>DMSO</td>
<td>128 (3%) -- 130 (30%)</td>
</tr>
<tr>
<td>4</td>
<td>2.10</td>
<td>1.05</td>
<td>DMSO</td>
<td>128 (2%) 129 tr. 130 (74%)</td>
</tr>
<tr>
<td>5</td>
<td>2.10</td>
<td>2.10</td>
<td>DMSO</td>
<td>128 (5%) 129 (17%) 130 (56%)</td>
</tr>
<tr>
<td>6</td>
<td>2.10</td>
<td>3.16</td>
<td>DMSO</td>
<td>128 (7%) 129 (18%) 130 (46%)</td>
</tr>
<tr>
<td>7</td>
<td>3.15</td>
<td>3.15</td>
<td>DMSO</td>
<td>128&lt;sup&gt;c&lt;/sup&gt; 129 (69%) 130&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>8</td>
<td>3.75</td>
<td>3.33</td>
<td>DMSO</td>
<td>128 (5%) 129 (64%) 130 (2%)</td>
</tr>
<tr>
<td>9</td>
<td>5.0</td>
<td>5.0</td>
<td>DMSO</td>
<td>128&lt;sup&gt;c&lt;/sup&gt; 129 (65%) --</td>
</tr>
<tr>
<td>10</td>
<td>3.74</td>
<td>3.20</td>
<td>DMF</td>
<td>128 (21%) 129 (8%) --</td>
</tr>
<tr>
<td>11</td>
<td>3.75</td>
<td>3.32</td>
<td>NMP</td>
<td>128&lt;sup&gt;c&lt;/sup&gt; 129 (2%) --</td>
</tr>
<tr>
<td>12</td>
<td>3.74</td>
<td>3.20</td>
<td>MeCN</td>
<td>128 (65%) 129 (13%) --</td>
</tr>
</tbody>
</table>

<sup>a</sup> Isolated yields of products after chromatography unless stated as ~%. The ~% are yields calculated from the <sup>1</sup>H NMR spectrum of an inseparable mixture. <sup>b</sup> The starting material was recovered in 48% yield. <sup>c</sup> Trace amount of the compound was observed in the <sup>1</sup>H NMR of the crude reaction mixture. <sup>d</sup> The starting material was recovered in 40% yield. <sup>e</sup> The starting material was recovered in 35% yield.

Based on the results from table 4.1, we devised two sets of reaction conditions. Experiments using 3.15 equivalents of both NaH and MeI to afford dimethylated benzimidazoles are referred to as Conditions A (See Table 4.1, entry 7); reactions using 2.1 equivalents of NaH and 1.05 equivalents of MeI to give monomethylated benzimidazoles as the major product are referred to as Conditions B (See Table 4.1, entry 4). The scope and limitation of the cyclization to give N-oxygenated benzimidazoles were probed using fifteen different enamines in total and the results are summarized in Table 4.2. Ten of the enamines were previously reported and five new were prepared by condensation of the appropriately substituted 2-nitroaniline with an aldehyde in dichloromethane or benzene in the presence of molecular sieves. Enamines derived from condensation of 2-nitroanilines bearing a substituent in the 4- or 5- position and 3-methylpropanal were selected in order to evaluate the effects of electronic properties and the relative position of the substituent on the benzene ring in a systematic fashion without a significant steric
contribution (Table 4.2, entries 1-25). The enamines were tested under both Conditions A and Conditions B and the results are summarized in Table 4.2. Although we initially considered acetonitrile and ratio of the reagents (Table 4.1, entry 12) to be plausible pathways for the synthesis of 2H-N-alkoxybenzimidazoles, complex mixtures of products in inferior yields were obtained when applied to other enamines.

As can be seen in Table 4.1, all substrates except 4-nitro-substituted enamine 144 furnished N-methoxybenzimidazoles under Condition A. Enamines 127, 131, 133, and 136 containing methoxy-, chloro-, bromo- and fluoro-substituent respectively at the 4-position gave good to excellent yields (69-94%) of dimethylated benzimidazoles as the sole product isolated after chromatography (Table 4.2, entries 1-8). In each of these reactions, an immediate color change to deep purple was observed upon mixing the enamine with the base in DMSO. In most cases, the purple color rapidly changed to brown or orange-brown within two minutes. The appearance of brown color was an indicative of a resting state of the reaction and no further reaction would occur until MeI had been added. For example, addition of MeI either after 2 minutes or 9 h of stirring at ambient temperature gave almost identical isolated yield of product 129 (entries 2-3). Similar color changes were observed for all substrate types although longer times were required in some cases before the purple color would disappear.

Apart from the selectivity observed for the first four substrates in Table 4.2, the rest of enamines gave either 2H-unsubstituted N-methoxybenzimidazoles, mixtures of N-methoxybenzimidazoles, or N-methylation of the starting material. The parent substrates 122, 138 and 153 gave rise to mixtures of three benzimidazoles when MeI was added at 0 °C (entries 9, 11, 24). In contrast monoalkylated benzimidazoles were not observed when MeI was added at ambient temperature (entries 10, 12, 15). The reason for this product distribution is not clear.

Two substrates containing an electron withdrawing group at the 4-position of the aromatic ring were also examined (Table 4.2, entries 13-16). Reaction of ester functionalized substrate 142 gave N-methylation product in 62% isolated yield when MeI was added at ambient temperature. In this reaction no sign of benzimidazoles was observed in the crude. However, when MeI was added after mixing the reaction mixture for 24 h at ambient temperature, N-methoxybenzimidazole was isolated as the only product in good yield. No trace of a 2-substituted product was observed in the crude reaction mixture. Reaction of 144 in a similar fashion gave N-methylated product in 85% isolated yield as the sole product. Extending the reaction time for the nitro analog 144 prior to addition of MeI did give neither benzimidazole, or any other product nor was the starting material observed in the crude reaction mixture. N-methylation was not limited to substrates containing electron withdrawing groups on the aromatic ring, but it was observed
with 5-methoxy- and 5-chloro-substituted enamines 145 and 147 when insufficient time was given before the mixing of MeI.

Two additional enamines 157 and 160 were also tested. The methoxy-substituted enamine 157 behaved similar to 127, affording the dialkylated product 158. In addition, a minor amount of the monoalkylated product 159 was isolated upon addition of MeI at ambient temperature (entry 27). Enamine 160 proved to be remarkably sensitive to temperature. All three N-oxygenated benzimidazoles were obtained in low yield at 0 °C. In contrast, only 134 was obtained when the reaction was carried out at ambient temperature.

Table 4.2 Base-mediated synthesis of benzimidazoles under Condition A

<table>
<thead>
<tr>
<th>Entry</th>
<th>Enamine</th>
<th>Time/Temp</th>
<th>% Yield</th>
<th>% Yield</th>
<th>% Yield</th>
<th>∑ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>127 (R=4-OMe)</td>
<td>1 h-0 °C</td>
<td>128d</td>
<td>129 (71)</td>
<td></td>
<td>71</td>
</tr>
<tr>
<td>2</td>
<td>127</td>
<td>2 min-rt</td>
<td></td>
<td>129 (71)</td>
<td></td>
<td>71</td>
</tr>
<tr>
<td>3</td>
<td>127</td>
<td>9 h-rt</td>
<td>128d</td>
<td>129 (69)</td>
<td></td>
<td>69</td>
</tr>
<tr>
<td>4</td>
<td>131 (R=4-Cl)</td>
<td>1 h-0 °C</td>
<td></td>
<td>132 (86)</td>
<td></td>
<td>86</td>
</tr>
<tr>
<td>5</td>
<td>131</td>
<td>1 h-rt</td>
<td></td>
<td>132 (94)</td>
<td></td>
<td>94</td>
</tr>
<tr>
<td>6</td>
<td>133 (R=4-Br)</td>
<td>1 h-0 °C</td>
<td>134d</td>
<td>135 (78)</td>
<td></td>
<td>78</td>
</tr>
<tr>
<td>7</td>
<td>133</td>
<td>4 min-rt</td>
<td>134d</td>
<td>135 (93)</td>
<td></td>
<td>93</td>
</tr>
<tr>
<td>8</td>
<td>136 (R=4-F)</td>
<td>1 h-rt</td>
<td></td>
<td>137 (75)</td>
<td></td>
<td>75</td>
</tr>
<tr>
<td>9</td>
<td>138 (R=4-Me)</td>
<td>1 h-0 °C</td>
<td>139 (28)</td>
<td>140 (52)</td>
<td>141 (5)</td>
<td>85</td>
</tr>
<tr>
<td>10</td>
<td>138</td>
<td>1 h-rt</td>
<td>139 (27)</td>
<td>140 (68)</td>
<td></td>
<td>95</td>
</tr>
<tr>
<td>11</td>
<td>122 (R=H)</td>
<td>1 h-0 °C</td>
<td>124 (5)</td>
<td>125 (57)</td>
<td>126 (15)</td>
<td>77</td>
</tr>
<tr>
<td>12</td>
<td>122</td>
<td>1 h-rt</td>
<td>124 (31)</td>
<td>125 (34)</td>
<td></td>
<td>65</td>
</tr>
<tr>
<td>13</td>
<td>142 (R=4-CO2Me)</td>
<td>10 min-rt</td>
<td></td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>14</td>
<td>142</td>
<td>24 h-rt</td>
<td>143 (74)</td>
<td></td>
<td></td>
<td>74</td>
</tr>
<tr>
<td>15</td>
<td>23 (R=4-NO2)</td>
<td>1 h-0 °C</td>
<td></td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>16</td>
<td>144</td>
<td>24 h-rt</td>
<td></td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>17</td>
<td>145 (R=5-OMe)</td>
<td>1 h-rt</td>
<td></td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>$^{145}$</td>
<td>24 h-rt</td>
<td>$^{146}$ (51)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>$^{147}$ (R=5-Cl)</td>
<td>6 min-rt$^k$</td>
<td>$^{149}$ (9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>$^{147}$</td>
<td>1 h-0 °C</td>
<td>$^{148}$ (56)</td>
<td>$^{149}$ (27)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>$^{147}$</td>
<td>1 h-rt</td>
<td>$^{148}$ (52)</td>
<td>$^{149}$ (31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>$^{150}$ (R=5-Br)</td>
<td>10 min-rt</td>
<td>$^{151}$ (67)</td>
<td>$^{152}$ (28)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>$^{150}$</td>
<td>1 h-rt</td>
<td>$^{151}$ (55)</td>
<td>$^{152}$ (29)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>$^{153}$ (R=5-Me)</td>
<td>1 h-0 °C</td>
<td>$^{154}$ (21)</td>
<td>$^{155}$ (22)</td>
<td>$^{156}$ (20)</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>$^{153}$</td>
<td>10 min-rt</td>
<td>$^{154}$ (31)</td>
<td>$^{155}$ (26)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>26</td>
<td>$^{157}$ (R=4-OMe)</td>
<td>1 h-0 °C</td>
<td>$^{128}$</td>
<td>$^{158}$ (78)</td>
</tr>
<tr>
<td>27</td>
<td>$^{157}$</td>
<td>2 min-rt</td>
<td>$^{128}$</td>
<td>$^{158}$ (84)</td>
</tr>
</tbody>
</table>

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>28</td>
<td>$^{160}$ (R=Br)</td>
<td>1 h-0 °C</td>
<td>$^{134}$</td>
<td>$^{161}$ (22)</td>
</tr>
<tr>
<td>29</td>
<td>$^{160}$</td>
<td>38 min-rt</td>
<td>$^{134}$ (92)</td>
<td></td>
</tr>
</tbody>
</table>

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>a. 3.15 equivalents of NaH and MeI were used. The Time/Temp is the time elapsed before addition of MeI and the temperature of the reaction mixture for the addition.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Isolated yields of pure products after chromatography unless stated as ~%. The ~% are yields calculated from $^1$H NMR spectrum of an inseparable mixture.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. Total yield of benzimidazoles isolated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. Trace amount of the compound was observed in the $^1$H NMR of the crude reaction mixture.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e. Trace amount of $^{138}$ was observed in the $^1$H NMR spectrum.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f. 4-Carbomethoxy-N-methyl-N-(2-methyl-1-propen-1-yl)-2-nitroaniline, the N-methylation product of $^{142}$ was isolated in 62% yield.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>g. 2,4-Dinitro-N-methyl-N-(2-methyl-1-propen-1-yl)aniline, the N-methylation product from $^{144}$, was isolated in 85% yield.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
h. No product or unreacted 144 was observed.

i. 5-Methoxy-2-nitro-N-methylaniline\(^{28}\) was isolated in 55% yield.

j. 5.0 Equivalents of NaH and 3.9 equivalents of MeI were used.

k. 5-Chloro-N-methyl-N-(2-methyl-1-propen-1-yl)-2-nitroaniline, the N-methylation product of 147, was isolated in 52% yield.

l. Trace amount of 128 was observed in the \(^1\)H NMR spectrum.

Finally, feasibility of formation of mono-alkylated benzimidazoles was evaluated next using Conditions B. Under this condition as well all enamines but except 4-nitro-substituted enamine 144, gave the expected products. In general, reactions under this condition were not as selective as the reaction of the 4-methoxy-substituted enamine 127 to give 130 (See Table 4.1, entry 4 and Table 4.3, entry 1). However, cyclization to produce benzimidazoles was observed in all cases. For all enamines except 4-carbethoxy- and the 5-methoxy-substituted compounds 142 and 145, the reaction went on smoothly to give monoalkylated benzimidazoles in 45-74% yields as the major product in addition to minor amounts of either 2H-N-methoxybenzimidazoles (2-21%) or dimethylated benzimidazoles (15-22%). Under conditions B, the position and the electronic properties of the substituents on the aromatic ring had little effect on the product distribution. Similar to Condition A, enamines 142 and 145 gave rise to 2H-N-methoxybenzimidazoles.

**Table 4.3** Base-mediated synthesis of benzimidazoles under Condition B

<table>
<thead>
<tr>
<th>Entry(^a)</th>
<th>Enamine</th>
<th>% Yield</th>
<th>% Yield</th>
<th>% Yield</th>
<th>(\sum (%)^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>122 (R=H)</td>
<td></td>
<td></td>
<td></td>
<td>126 (55)(^d)</td>
</tr>
<tr>
<td>2</td>
<td>123 (R=4-OMe)</td>
<td>128 (2)</td>
<td></td>
<td></td>
<td>130 (74)</td>
</tr>
<tr>
<td>3</td>
<td>131 (R=4-Cl)</td>
<td>132 (20)</td>
<td></td>
<td></td>
<td>163 (59)</td>
</tr>
<tr>
<td>4</td>
<td>133 (R=4-Br)</td>
<td>135 (22)</td>
<td></td>
<td></td>
<td>164 (68)</td>
</tr>
<tr>
<td>5</td>
<td>136 (R=4-F)</td>
<td>137 (15)</td>
<td></td>
<td></td>
<td>165 (56)</td>
</tr>
<tr>
<td>6</td>
<td>138 (R=4-Me)</td>
<td>139 (11)</td>
<td></td>
<td></td>
<td>141 (45)</td>
</tr>
<tr>
<td>7</td>
<td>142 (R=4-CO(_2)Me)(^e)</td>
<td></td>
<td></td>
<td></td>
<td>-</td>
</tr>
</tbody>
</table>

\(^a\) Enamine.
\(^b\) Alkoxybenzimidazoles.
\(^c\) \(\sum (\%)\) represents the sum of the yields of the major and minor products.
\(^d\) % Yield.
\(^e\) Reaction conditions: Base-mediated synthesis.
a. Condition B: 2.1 equivalents of NaH and 1.05 equivalents of MeI. The mixture was stirred for 1 h at ambient temperature then cooled to 0 °C prior to addition of MeI unless otherwise stated.

b. Isolated yields of pure products after chromatography unless otherwise stated. The % yields are calculated from the $^1$H NMR spectrum of an inseparable mixture.

c. Total yield of benzimidazoles.

d. Trace amount of 124 was observed in the $^1$H NMR spectrum.

e. A nearly 3:1 mixture of 4-carboxmethoxy-N-methyl-N-(2-methyl-1-propen-1-yl)-2-nitroaniline and 142 was observed in the $^1$H NMR spectrum of the crude reaction mixture.

f. The base substrate mixture was stirred for 24 h before addition of MeI.

g. Neither product nor starting material was observed.

The formation of 2H-N-alkoxybenzimidazoles in the above reactions involves a carbon-carbon bond fission during the reaction and a loss of three carbon unit probably in the form of acetone (see mechanism below). However, neither acetone nor acetophenone or cyclohexanone, the anticipated by-products from enamines 157 and 160 were recovered from the reactions. This is probably due to evaporative loss upon removal of solvents. With a hope to isolate, characterize and quantify any potential by-product derived from carbon-carbon bond cleavage, enamine 168 was prepared. The enamine was subjected to reaction

<table>
<thead>
<tr>
<th>8</th>
<th>142$^f$</th>
<th>143 (73)</th>
<th>73</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>145 (R=5-OMe)$^g$</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>145$^f$</td>
<td>146 (64)</td>
<td>64</td>
</tr>
<tr>
<td>11</td>
<td>147 (R=5-Cl)</td>
<td>149 (15)</td>
<td>66 (55)</td>
</tr>
<tr>
<td>12</td>
<td>140 (R=5-Br)</td>
<td>152 (16)</td>
<td>167 (63)</td>
</tr>
<tr>
<td>13</td>
<td>153 (R=5-Me)</td>
<td>-</td>
<td>156 (61)</td>
</tr>
</tbody>
</table>

14 | 157 (R=4-OMe) | 158 (19) | 159 (51) | 70 |

| 15 | 160 (R=4-Br) | 134 (22) | 162 (52) | 74 |
under Conditions A and a small amount of benzophenone (170) was obtained along with the expected product 169. Gratifyingly, when the base and the solvent system described by Gardiner et al\textsuperscript{123b} (t-BuOK/t-BuOH) was used, an almost quantitative yield of benzophenone was isolated in addition to the product 128 in 78% yield (Scheme 4.3).

Scheme 4.3 Formation of N-methoxybenzimidazole 169 and benzophenone 170

A small selection of other carbon-based electrophiles including benzyl bromide, allyl bromide, propargyl bromide, 3-bromo-1-butyne, diiodomethane, and acetyl chloride were also employed with enamine 127. Moderate yields of products were obtained. The result from acetyl chloride is presented in Scheme 4.4.

Scheme 4.4 Reaction of 127 with Acetyl Chloride
Table 4.4 Base-mediated synthesis of N-oxygenated benzimidazoles from enamine 127

<table>
<thead>
<tr>
<th>Entry</th>
<th>Time/Temp&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Electrophile (R-X)</th>
<th>Alkoxybenzimidazoles&lt;sup&gt;b&lt;/sup&gt;</th>
<th>∑ (%)&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 h-0 °C</td>
<td>Bn-Br</td>
<td><img src="image1" alt="Structure 171" /></td>
<td>171 (38%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><img src="image2" alt="Structure 172" /></td>
<td>172 (29%)</td>
</tr>
<tr>
<td>2</td>
<td>2 min-rt</td>
<td>Bn-Br</td>
<td><img src="image1" alt="Structure 171" /></td>
<td>171 (19%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><img src="image2" alt="Structure 172" /></td>
<td>172 (50%)</td>
</tr>
<tr>
<td>3</td>
<td>1 h-0 °C</td>
<td>Allyl bromide</td>
<td><img src="image3" alt="Structure 173" /></td>
<td>173 (5%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><img src="image4" alt="Structure 174" /></td>
<td>174 (14%)</td>
</tr>
<tr>
<td>4</td>
<td>1 min-rt</td>
<td>Allyl bromide</td>
<td><img src="image4" alt="Structure 174" /></td>
<td>174 (59%)</td>
</tr>
<tr>
<td>5</td>
<td>2 min-rt</td>
<td>CH₂I₂</td>
<td><img src="image5" alt="Structure 176" /></td>
<td>176 (40%)</td>
</tr>
<tr>
<td>6</td>
<td>1 min-rt</td>
<td>Propargyl bromide</td>
<td><img src="image6" alt="Structure 177" /></td>
<td>177 (6%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><img src="image7" alt="Structure 178" /></td>
<td>178 (47%)</td>
</tr>
<tr>
<td>7</td>
<td>1 h-0 °C</td>
<td>3-Bromo-1-butyne</td>
<td><img src="image8" alt="Structure 179" /></td>
<td>179 (9%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><img src="image9" alt="Structure 180" /></td>
<td>180 (41%)</td>
</tr>
<tr>
<td>8</td>
<td>2 min-rt</td>
<td>3-Bromo-1-butyne</td>
<td><img src="image9" alt="Structure 180" /></td>
<td>180 (66%)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Condition A: 3.15 equivalents of NaH and R-X. The Time/Temp is the time before addition of electrophile (R-X) and addition temperature.

<sup>b</sup> Isolated yields of pure products after chromatography unless otherwise stated. The yields are calculated from the <sup>1</sup>H NMR spectrum of an inseparable mixture.

<sup>c</sup> Total yield of benzimidazole(s) isolated.

A limitation of this methodology is the use of enamines derived from condensation of alpha-branched aldehydes and 4- or 5-substituted-2-nitroanilines. Attempts to prepare enamines from simple and unbranched aliphatic aldehydes, for example propanal and hexanal, were unsuccessful. In addition, 3- and 6-substituted 2-nitrobenzenamines did not form any enamines using the conditions described. Only unreacted starting materials were obtained from the reactions.

4.C Mechanistic Discussion

The formation of N-oxygenated benzimidazoles in the above transformations can be mechanistically understood as follows. Deprotonation of 122 forms anions of type 183 and 184. 1,7-Electrocyclization of 184 will give 185 which in turn may undergo ring opening to form nitroso-imine 186. 1,5-Electrocyclization of 186 to 187 is plausible. Aromatization of intermediate 187 would furnish alkoxybenzimidazole 188 by the loss of acetone or dialkoxybenzimidazole 189 via deprotonation. It is
unclear when the alkylation is taking place; it is possible that alkylation can occur both prior to and after aromatization. The proposed mechanism hints that two equivalents of a base will be required for the transformation of 122 to 125 and 126; one for the initial deprotonation to give 183/184 and another for deprotonation-aromatization of 187 to give 189. Although 2.10 equivalents of base proved optimal for the formation of monoalkylated products, it remained unclear why an addition equivalent of the base was required to maximize the yield of dialkylated products.

**Scheme 4.5 Proposed mechanism for the N-oxygenated benzimidazoles 124-126**

The mechanism outlined here is supported by previous studies in the literature. In the preparation of indazole-N-oxide from azomethine ylides, Nyerges et al proposed 1,7-electrocyclization. The authors suggested a ring-contraction with loss of formaldehyde followed by a nitroso-imine 1,5-electrocyclization. We have reported a related palladium catalyzed reductive cyclization of 2-nitrostyrenes in the presence of base to give oxygenated indoles.

**4.D Conclusion**

We have developed a mild base mediated cyclization of enamines derived from the condensation of 2-nitroanilines with α-branched aldehydes to give N-alkoxy-substituted benzimidazoles with or without an oxygenated side chain in the second position. A large number of carbon-based electrophiles can be employed.
Chapter 5 A facile base-mediated synthesis of N-alkoxy-2H-benzimidazoles

5.A Introduction

The methodology presented here can be viewed as a modification of the synthesis of N-alkoxy-2-substituted benzimidazoles discussed in chapter 4. Reaction of 2-nitrobenzenamines with an electrophile in the presence of sodium hydride in dimethylsulfoxide or acetonitrile is not specific giving rise to a mixture of 2-substituted N-alkoxybenzimidazoles. The product distribution was very much dependent on the amount of base used. For example, treatment of enamine 127 with MeI in dimethylsulfoxide (DMSO) in the presence of sodium hydride (NaH) with varying amount of base gave the following products (Scheme 5.1).136

Scheme 5.1 Reaction of enamine 127 with methyl iodide

<table>
<thead>
<tr>
<th>Reaction Conditions</th>
<th>Products</th>
<th>Yields</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.10 equiv. NaH/1.05 equiv. MeI</td>
<td>130 (74%)</td>
<td>129 (-)</td>
</tr>
<tr>
<td>3.50 equiv. NaH/3.50 equiv. MeI</td>
<td>130 (-)</td>
<td>129 (71%)</td>
</tr>
</tbody>
</table>

In the course of our investigation for suitable reaction conditions, we found that the reaction can be tailored to give N-alkoxy-2H-benzimidazole as the sole product when enamines are allowed to react with potassium t-butoxide (t-BuOK) for prolonged period of time followed by the trapping of the electrophile. Herein we report the scope and limitations of the cyclization to give N-oxygenated benzimidazoles from reactions of 2-nitrobenzenamines with an array of carbon-centered electrophiles.

5.B Results and Discussion

Very limited number of methods have been reported for the synthesis of N-alkoxybenzimidazoles. Direct alkylation of N-hydroxybenzimidazole or its tautomer 1H-benzimidazole-3-oxide has been used to prepare N-methoxy, N-ethoxy and N-allyloxybenzimidazoles.137 Gardiner et al has previously reported the synthesis of N-alkoxybenzimidazoles from 2-nitroanilines and an alkyl halide.123 However, mixtures of N-alkylated anilines and N-alkoxybenzimidazoles were observed in many cases. In addition, only one case of a 2H- N-alkoxybenzimidazole was reported (Scheme 5.2).
The objective of this work was to develop short and efficient synthetic routes to 2H-N-alkoxybenzimidazoles from easily accessible starting materials. A detailed study on the screening of reaction conditions and the suitable solvents can be found in chapter 4. Our group has disclosed the synthesis of a variety of N-(2-methyl-1-propen-1-yl)-2-nitrobenzenamines. Following the same procedure, we synthesized 2-nitrobenzenamines and subjected them to the reaction with t-BuOK for 24 h and then trapped the intermediates with the desired carbon-based electrophiles to afford 2H-N-alkoxybenzimidazoles in good to excellent yields (Table 5.1). Four equivalents of base and longer reaction time were required for the completion of the reaction. Reaction of 4-carbomethoxy-N-methyl-N-(2-methyl-1-propen-1-yl)-2-nitrobenzenamine and 2,4-dinitro-N-(2-methyl-1-propen-1-yl)benzenamine, however, did give neither the starting materials back nor any identifiable products for the similar reason discussed in the preceding chapter (chapter 4).
Table 5.1 Formation of $N$-methoxybenzimidazoles from enamines

<table>
<thead>
<tr>
<th>Entry</th>
<th>Enamine$^a$</th>
<th>Methoxybenzimidazole$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>127 (R=4-OMe)</td>
<td>128 (76%)</td>
</tr>
<tr>
<td>2</td>
<td>122 (R=H)</td>
<td>124 (100%)</td>
</tr>
<tr>
<td>3</td>
<td>138 (R=4-Me)</td>
<td>139 (76%)</td>
</tr>
<tr>
<td>4</td>
<td>131 (R=4-Cl)</td>
<td>191 (92%)</td>
</tr>
<tr>
<td>5</td>
<td>133 (R=4-Br)</td>
<td>134 (85%)</td>
</tr>
<tr>
<td>6</td>
<td>136 (R=4-F)</td>
<td>192 (67%)</td>
</tr>
<tr>
<td>7</td>
<td>142 (R=4-CO$_2$Me)</td>
<td>not observed</td>
</tr>
<tr>
<td>8</td>
<td>144 (R=4-NO$_2$)</td>
<td>not observed</td>
</tr>
<tr>
<td>9</td>
<td>145 (R=5-OMe)</td>
<td>146 (85%)</td>
</tr>
<tr>
<td>10</td>
<td>153 (R=5-Me)</td>
<td>154 (71%)</td>
</tr>
<tr>
<td>11</td>
<td>147 (R=5-Cl)</td>
<td>148 (71%)</td>
</tr>
<tr>
<td>12</td>
<td>150 (R=5-Br)</td>
<td>151 (73%)</td>
</tr>
<tr>
<td>13</td>
<td>190 (R=OMe)</td>
<td>128 (94%)</td>
</tr>
<tr>
<td>14</td>
<td>160 (R=Br)</td>
<td>134 (94%)</td>
</tr>
<tr>
<td>15</td>
<td>157</td>
<td>128 (76%)</td>
</tr>
<tr>
<td>16</td>
<td>168</td>
<td>128 (78%)</td>
</tr>
</tbody>
</table>

[a] A solution of the enamine in $t$-BuOH was treated with $t$-BuOK (4 equiv.) stirred for 24 h then treated with MeI (3 equiv.) b) Isolated yield of pure product after chromatography on silica gel.

Results from a number of other electrophiles are presented in Table 5.2 below. Of the various electrophiles tested, propargyl bromide and 3-bromo-1-butyne gave allenes instead of the normal products, albeit in low yield. Similarly, less reactive electrophiles, such as, 1-bromoheptane, 1-iodobutane and 2-iodopropane gave low isolated yield of the products. It should be born in mind that the pathway presented here represents the easiest and the cheapest route to access a wide variety of $2H-N$-
alkoxybenzimidazoles to date. Clean reaction, easy work up and isolation of compounds will make this methodology useful.

**Table 5.2** Base-mediated synthesis of $N$-oxygenated benzimidazoles from enamine 127

<table>
<thead>
<tr>
<th>Entry</th>
<th>Enamine$^a$</th>
<th>Electrophile</th>
<th>Benzimidazole$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Benzyl bromide</td>
<td>193 (82%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Allyl bromide</td>
<td>194 (100%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2-Methyl-3-bromopropene</td>
<td>195 (90%)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Propargyl bromide</td>
<td>196 (15%)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>3-Bromo-1-butyne</td>
<td>197 (12%)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Acetyl chloride</td>
<td>198 (54%)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1-Bromoheptane</td>
<td>199 (16%)</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>1-Iodobutane</td>
<td>200 (15%)</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>2-Iodopropane</td>
<td>201 (8%)</td>
<td></td>
</tr>
</tbody>
</table>

$^a$ A solution of the enamine in $t$-BuOH was treated with $t$-BuOK (4 equiv.) stirred for 24 h then treated with MeI (3 equiv.)

$b$ Isolated yield of pure product after chromatography on silica gel.

The formation of product can be rationalized via 1,7-electrocyclization$^{130,131}$ of the azomethine ylide followed by ring opening. The second ring closing step leads to a relatively unstable intermediate that loses the side chain possibly in the form of acetone opening the door for aromatization. The $N$-alkoxy anion then abstracts the electrophile giving rise to $N$-alkoxybenzimidazole. A detailed mechanistic viewpoint has been discussed in chapter 4. We have isolated benzophenone from the reaction of 168 with MeI in the presence of $t$-BuOK / $t$-BuOH.$^{136}$

**5.C Conclusion**

In summary, short and efficient synthetic route to a variety of 2H-$N$-alkoxybenzimidazoles from easily accessible $N$-(2-methyl-1-propen-1-yl)-2-nitrobenzenamines has been developed for the first time. This methodology presents a useful approach to the formation of NO-C bond. Mild reaction conditions, easy work up and isolation of compound are additional benefits.
Chapter 6 Chemoselectivity in the Kosugi-Migita-Stille coupling of bromonitrophenyl trifluoromethanesulfonates

6.A Introduction

Palladium catalyzed cross coupling reactions of aromatic halides and trifluoromethanesulfonates have long history of use in the modern organic synthesis. The reactions have undergone extensive modifications over the last four decades. In this chapter will be discussed the shortcomings and recent development related to Stille and Echavarren’s study on the relative chemoselectivity of carbon-bromine (C-Br) versus carbon-trifluoromethanesulfonate (C-OTf) in the palladium catalyzed cross couplings of bromophenyl- and bromonitrophenyl- trifluoromethanesulfonates with ethenyltributyltin. Stille and Echavarren disclosed that use of additives and varying reaction conditions can dramatically alter the product distribution. For example, treatment of 202 with vinyltin in the presence of Pd(PPh$_3$)$_4$ in dioxane at 98 °C gave product derived from highly selective oxidative addition to C-Br bond whereas product derived from highly selective oxidative addition to C-OTf bond was obtained when the reaction was carried out using PdCl$_2$(PPh$_3$)$_2$ and LiCl in DMF at 24 °C. In the same seminal work was reported the formation of products from both 4-iodophenyl trifluoromethanesulfonate and 1-bromo-4-iodobenzene via the completely selective oxidative addition to C-I bond. After a careful consideration, they proposed the following reactivity order:

1. I>Br>OTf>Cl in the presence of LiCl
2. I>OTf>Br>Cl in the absence of LiCl

However, the proposed reactivity order should not be taken as an absolute scale. The presence of other functional groups in the substrate, catalyst design and reaction conditions may greatly change the reactivity order where product derived from much less selective coupling site predominates. For example, reaction of 4-chlorophenyl trifluoromethanesulfonate with PhBu$_3$Sn in the presence of Pd$_2$(dba)$_3$-Pd(t-Bu)$_2$ and CsF in dioxane at ambient temperature gave exclusive C-Cl coupling products. The effect of added LiCl has been attributed to Ar-Pd-OTf to Ar-Pd-Cl metathesis followed by rapid transmetallation and reductive elimination. Thus, use of LiCl certainly affects chemoselectivity but literature reports suggest that the magnitude of effect is related to more than one factor. An increase in the rate of oxidative addition cannot be the sole reason behind the change in selectivity for C-Br to C-OTf bond with the added LiCl. To the best of our knowledge, there are no Kosugi-Migita-Stille couplings reported to date wherein even a fraction of C-Br or C-OTf coupling occurred on benzene ring also containing a C-I bond.
We have reported the synthesis of a wide variety of indoles, biindoles, and the total synthesis of a number of indole alkaloids via the palladium catalyzed carbon monoxide mediated en route reductive N-heteroannulation of orthonitrostyrene derivatives.\textsuperscript{45,113} We envisioned that chemoselective sequential introduction of two different alkenes to dinitrobenzenes may lead to dialkenyldinitrobenzenes that are the potential precursors to pyrroloindoles. We thought that the chemoselectivity reported by Stille and Echavarren would enable us to prepare a variety of dialkenyldinitrobenzenes that can be used for palladium catalyzed double reductive cyclization.

In order to test the hypothesis, 5-bromo-2,4-dinitrophenyl trifluoromethanesulfonate (204) was prepared in good yield by dinitration of 3-bromophenyl trifluoromethanesulfonate (203). Treatment of 204 with ethenyltributyltin in DMF under Stille-Echavarren conditions discussed above that should result in C-OTf coupling did not give any identifiable product. To simplify possible work up and the analysis of crude \textsuperscript{1}H NMR, the solvent was changed to toluene and the reaction was carried out at ambient temperature. However, no appreciable reaction was observed. The reaction temperature was then raised to 80 °C whereby all starting material was consumed within 17 h. The \textsuperscript{1}H NMR of the crude reaction mixture revealed the presence of one site coupling product. The crude reaction mixture was purified by chromatography on a silica gel to afford 205 in good isolated yield. The product was identified and characterized by \textsuperscript{1}H, \textsuperscript{19}F and \textsuperscript{13}C NMRs. A very indicative quartet (\textit{J}=320 Hz) in the \textsuperscript{13}C NMR and a resonance at -72.9 Hz in the \textsuperscript{19}F NMR confirmed the product to be 205; the expected C-OTf coupling product was not observed.

\textbf{Scheme 6.1 Preparation and Kosugi-Migita-Stille coupling of 204}

\begin{align*}
\text{Br} & \quad \text{OTf} \quad \xrightarrow{\text{Fum. HNO}_3} \quad \text{Br} \quad \text{OTf} \\
\text{203} & \quad \xrightarrow{\text{Conc. H}_2\text{SO}_4, 80 \, ^\circ\text{C}} \quad \text{Br} \quad \text{OTf} \\
\text{204} & \quad \xrightarrow{\text{PdCl}_2(\text{PPh}_3)_2} \quad \text{205} \\
80\% & \quad 78\% \\
\text{Not observed} &
\end{align*}

The absence of C-OTf coupling in the above reaction is in sharp contrast to what Stille and Echavarren reported. The structure of compound 204 suggests that both the coupling sites have to be activated by the adjacent nitro groups more or less to the same extent for the oxidative addition. In addition, the steric
environments for both the sites seem to be more or less equal as both are followed by an ortho nitro group and separated by a free carbon. The absence of the C-OTf coupling under the reaction conditions known to be selective for C-OTf coupling became a driving force for us to consider a detailed systematic study of chemoselectivity in the palladium catalyzed Kosugi-Migita-Stille cross couplings of halophenyl triflates and halonitrophenyl triflates with ethenyltributyltin. Thus, all possible permutations of bromophenyl trifluoromethanesulfonates and bromonitrophenyl trifluoromethanesulfonates were synthesized although few additional substrate types were also pursued in order to evaluate the selectivity more accurately. To the best of our knowledge, the study presented in this chapter represents the first of its kind.

6.B Results and Discussion

All the bromophenyl trifluoromethanesulfonates and bromonitrophenyl trifluoromethanesulfonates were tested under the following three different conditions:

1. Conditions A: Pd(dba)$_2$, PPh$_3$, 1,4-dioxane, ethenyltributyltin, reflux
2. Conditions B: PdCl$_2$(PPh$_3$)$_2$, LiCl, ethenyltributyltin, DMF, 24 °C
3. Conditions C: PdCl$_2$(PPh$_3$)$_2$, ethenyltributyltin, 1,4-dioxane, reflux

It is worth mentioning that Conditions A are the reported conditions for C-Br coupling, Conditions B are the reported conditions for C-OTf coupling. Under conditions A and B, efforts were focused on duplicating the results reported by Still and Echavarren. Under C-Br selective conditions, compound 202 is reported to give a 33:1 ratio of C-Br to C-OTf bond coupling based on $^1$H NMR of the crude reaction mixture (Table 6.1). When the reaction was repeated, in our hands only product 206 was detected in the $^1$H NMR of the crude reaction mixture (600 MHz, Table 6.1, entry 2). The palladium catalyst, (Pd(PPh$_3$)$_4$), used by Stille and Echavarren is not very air stable; handling and storage of this catalyst often results into diminished catalytic activity. In our hands, a combination of 2 mol% of Pd(dba)$_2$ and 8 mol% of PPh$_3$ gave the same exclusive selectivity as Pd(PPh$_3$)$_4$ (entry 3). So, this catalyst system (Pd(dba)$_2$ and PPh$_3$) was used as a substitute for Pd(PPh$_3$)$_4$ in order to minimize possible catalytic degradation under Conditions A. Under Conditions B, Stille and Echavarren reported exclusive C-OTf coupling (entry 4). In our hands, use of the same reaction conditions gave a much lower selectivity (1:6.7, entry 5). This product distribution is same as the one reported by Stille and Echavarren at higher temperature (70 °C, entry 6). It should be noted that products (206-207) are susceptible to decomposition/polymerization while performing chromatography on silica gel.

In order to examine the effect of relative position of bromide and trifluoromethanesulfonate on chemoselectivity, isomeric compounds 2-bromophenyl- and 3-bromophenyl- trifluoromethanesulfonates (208 and 203) were prepared according to literature procedures. Reactions of both the isomers displayed
the same high selectivity for C-Br coupling under Conditions A and a similar selectivity for C-OTf coupling under Conditions B as was observed with compound 202. Reaction of 203 under Conditions B using PdCl₂(dppp) has been reported. Only C-OTf coupling was reported in 25% yield although it remains unclear if the reported selectivity is based on crude reaction mixture or after chromatographic purification.

Table 6.1 Reactions of bromophenyl trifluoromethanesulfonates with ethenytributyltin

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>Product (s) &amp; ratio</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 b</td>
<td>Pd(PPh₃)₄, 1,4-dioxane, reflux</td>
<td>33 1 77%</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Pd(PPh₃)₄, 1,4-dioxane, reflux</td>
<td>&gt;30 1</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Pd(dba)₂, 4 PPh₃, 1,4-dioxane, reflux</td>
<td>&gt;30 1 30%</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>PdCl₂(PPh₃)₂, 1,4-dioxane, reflux</td>
<td>&gt;30 1 90%</td>
<td></td>
</tr>
<tr>
<td>5 b</td>
<td>PdCl₂(PPh₃)₂, LiCl, DMF, 24 °C</td>
<td>0 100 77%</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>PdCl₂(PPh₃)₂, LiCl, DMF, 24 °C</td>
<td>1 6.7</td>
<td></td>
</tr>
<tr>
<td>7 b</td>
<td>PdCl₂(PPh₃)₂, LiCl, DMF, 70 °C</td>
<td>1 5 45%</td>
<td></td>
</tr>
<tr>
<td>8 b</td>
<td>PdCl₂(PPh₃)₂, LiCl, 1,4-dioxane, reflux</td>
<td>1 6 75%</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Pd(dba)₂, 4 PPh₃, 1,4-dioxane, reflux</td>
<td>&gt;30 1 5%</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>PdCl₂(PPh₃)₂, LiCl, DMF, 24 °C</td>
<td>1 5.9</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Pd(dba)₂, 4 PPh₃, 1,4-dioxane, reflux</td>
<td>30 1 34%</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>PdCl₂(PPh₃)₂, 1,4-dioxane, reflux</td>
<td>30 1 47%</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>PdCl₂(PPh₃)₂, LiCl, DMF, 24 °C</td>
<td>1 6.3 75%</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>PdCl₂(dppp), LiCl, DMF 25 °C</td>
<td>0 100 25%</td>
<td></td>
</tr>
</tbody>
</table>
a) See experimental section for details. b) Ratio of products in crude reaction mixture. c) Isolated yield of pure product after chromatography. d) See reference\textsuperscript{138}. e) Less than nearly 10\% of decoupling product was also observed. f) A 19:30:1:6 ratio of 203/211/212:ethenyltributyltin was observed in the crude \textsuperscript{1}H NMR spectrum. g) Isolated as a mixture with 203. Yield calculated from \textsuperscript{1}H NMR spectrum. h) A significant amount of 203 remained unreacted even after 72 h. i) The reaction time was 39 h. j) A 5.6:1:6.3 ratio of 203/211/212 was observed in the crude \textsuperscript{1}H NMR spectrum. K) Product 212 was not isolated. l) See reference\textsuperscript{152}. m) The reaction time was 39 h.

Chemoselectivity of substrates containing both C-Br and C-OTf bonds can be significantly affected by electronic effects. For example, exclusive coupling at C-OTf bond was observed in the Suzuki-Miyaura coupling of 202 with triethylboron.\textsuperscript{151} On the other hand, reaction of 202 with 4-MeC\textsubscript{6}H\textsubscript{4}SnBu\textsubscript{3} in the presence of PdCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2}, PPh\textsubscript{3}, and CuBr in refluxing dioxane afforded C-Br coupling product exclusively.\textsuperscript{139} For Suzuki-Miyaura couplings with aryl/alkenyboronic acids, the C-Br bond generally undergoes selective coupling regardless of electron density of the substrate and regardless of the palladium based catalyst used.\textsuperscript{143a,152-156} For substrates containing two trifluoromethanesulfonate groups in Suzuki-Miyaura reactions, the cross coupling may take place either at the more electron deficient site\textsuperscript{157} or at the least hindered but more electron rich site.\textsuperscript{158} Oh-e, Miyaura and Suzuki established the order of reactivity as I>Br>OTf for Suzuki-Miyaura couplings with 9-BBN reagent.\textsuperscript{159} Fu and coworkers have shown that the chemoselectivity could be changed depending on the ligand system and the type of the reaction solvents.\textsuperscript{143} Similarly, Sonogashira coupling of 202 and 203 with phenylethyne gave exclusive coupling at C-Br bond in the presence of 10 mol\% of ZnCl\textsubscript{2} at ambient temperature\textsuperscript{160} whereas the same reaction gave only C-OTf coupling product when trimethylsilylethylene was used as a coupling partner in the presence of CuI.\textsuperscript{161} Kumada coupling of 202 and a variety of ortho bromo trifluoromethanesulfonates with phenylethynyl magnesium bromide or phenyl magnesium bromide afforded product derived from C-OTf coupling.\textsuperscript{152,162} Negishi coupling of 207 with organozinc reagents gave C-OTf coupling product in the presence of PdCl\textsubscript{2}(dppp)\textsuperscript{157}, [Pd\textsubscript{2}(dba)\textsubscript{3}]-dppb\textsuperscript{163}. In contrast, coupling of 202 with Me\textsubscript{2}Zn gave C-Br coupling product using Pd(OAc)\textsubscript{2}-AsPPh\textsubscript{3} and a 3:1 ratio of C-Br to C-OTf coupling products when PdCl\textsubscript{2}(dppe)\textsubscript{2} was used.\textsuperscript{164}

The effects of substituents on the coupling reactions were further examined with additional substrates. All the possible isomeric permutations of bromonitrophenyl trifluoromethanesulfonates (213-222) were prepared from the corresponding phenols using literature procedures. The phenols were treated with trifluoromethanesulfonic anhydride in the presence of either pyridine or triethylamine.
Figure 6.1 Isomeric bromonitrophenyl trifluoromethanesulfonates (213-222)

All the above isomeric compounds were tested under the previously mentioned three reaction conditions for the cross coupling results with ethenyltributytin. Under Conditions A, a combination of relatively air stable Pd(dba)$_2$ and PPh$_3$, a substitute for Pd(PPh$_3$)$_4$ was used. The reactions were carried out in refluxing 1,4-dioxane. This condition is known to afford product derived from highly selective oxidative addition to C-Br bond. Conditions B comprise of a combination of 2 mol% of PdCl$_2$(PPh$_3$)$_2$ and 3 equivalents of LiCl. The reactions were carried out in DMF at ambient temperature. This condition as reported by Stille and Echavarren is known to give product derived from highly selective oxidative addition to C-OTf bond. Under conditions C, the reactions were carried out in the presence of 2 mol% of PdCl$_2$(PPh$_3$)$_2$ in refluxing 1,4-dioxane. Under conditions A and B, all the reactions were carried out for 24 h regardless of whether the starting material was consumed or left over within 24 h. Starting materials were observed in the $^1$H NMR of the crude reaction mixture in many cases after the allocated reaction time. Under conditions C, a majority of reactions were run for approximately 24 h. For details, visit the experimental section. For all the reactions, the ratio of products was analyzed by $^1$H NMR of the crude reaction mixtures before chromatographic separation. Since the objective of this study was to examine the selectivity of the coupling reactions (C-Br vs C-OTf), no attempts were made to optimize the yield of a product for a particular substrate. High selectivity was observed under both conditions A and B for 216 and 219 wherein the bromo and the trifluoromethanesulfonate groups are both ortho or meta to the nitro group. Similarly, enhanced selectivity for C-OTf couplings was observed for 217-220 under Conditions B when the bromide was meta to the nitro group. Under Conditions C, a completely different selectivity pattern was observed for all the substrates tested regardless of positions of the groups on the aromatic rings. Under this condition, all substrates gave products derived from highly selective oxidative addition to C-Br or C-I bond. The results are summarized in the table below.
Table 6.2 Cross-couplings of 213-222 with ethenyltributyltin

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>C-Br coupling product</th>
<th>C-OTf coupling product</th>
<th>Additional product(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-A&lt;sup&gt;a&lt;/sup&gt;</td>
<td>213</td>
<td>223 (36%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-B&lt;sup&gt;c&lt;/sup&gt;</td>
<td>213 (~27%)</td>
<td>223 (20%)</td>
<td>224 (38%)</td>
<td>(~12%)</td>
</tr>
<tr>
<td>1-C</td>
<td>213</td>
<td>223 (77%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-D&lt;sup&gt;e&lt;/sup&gt;</td>
<td>213 (75%)</td>
<td>223 (19%)</td>
<td>224 (49%)</td>
<td>225 (10%) (11%)</td>
</tr>
<tr>
<td>1-E&lt;sup&gt;f&lt;/sup&gt;</td>
<td>213</td>
<td>223 (91%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-F&lt;sup&gt;g&lt;/sup&gt;</td>
<td>213</td>
<td>223 (91%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-A</td>
<td>214</td>
<td>226 (82%)</td>
<td></td>
<td>227 (9%)</td>
</tr>
<tr>
<td>2-B</td>
<td>214</td>
<td>226 (~9%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>228 (~37%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>227 (15%)</td>
</tr>
<tr>
<td>2-C</td>
<td>214</td>
<td>226 (68%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-D&lt;sup&gt;i&lt;/sup&gt;</td>
<td>213</td>
<td>226 (68%)</td>
<td></td>
<td>227 (4%)</td>
</tr>
<tr>
<td>3-A</td>
<td>215</td>
<td>229 (68%)</td>
<td>231 (36%)</td>
<td>230 (2%)</td>
</tr>
<tr>
<td>3-B</td>
<td>215 (17%)&lt;sup&gt;i&lt;/sup&gt;</td>
<td>229 (~23%)&lt;sup&gt;i&lt;/sup&gt;</td>
<td></td>
<td>230 (3%)</td>
</tr>
<tr>
<td>3-C</td>
<td>215</td>
<td>229 (81%)</td>
<td></td>
<td>230 (3%)</td>
</tr>
<tr>
<td>3-D&lt;sup&gt;i&lt;/sup&gt;</td>
<td>215</td>
<td>229 (74%)</td>
<td></td>
<td>230 (2%)</td>
</tr>
<tr>
<td>4-A</td>
<td>216</td>
<td>232 (60%)</td>
<td>233 (3%)</td>
<td>234 (30%)</td>
</tr>
<tr>
<td>4-B</td>
<td>216</td>
<td>232 (68%)</td>
<td>233 (61%)</td>
<td>234 (trace)</td>
</tr>
<tr>
<td>4-C</td>
<td>216</td>
<td>232 (68%)</td>
<td>233 (1%)</td>
<td>234 (23%)</td>
</tr>
<tr>
<td>5-A</td>
<td>217 (9%)</td>
<td>235 (24%)</td>
<td>236 (-5%)&lt;sup&gt;k&lt;/sup&gt;</td>
<td>225 (-5%)&lt;sup&gt;k&lt;/sup&gt;</td>
</tr>
<tr>
<td>-----</td>
<td>----------</td>
<td>-----------</td>
<td>-----------------</td>
<td>----------------</td>
</tr>
<tr>
<td>5-B</td>
<td>217 (5%)</td>
<td>235 (66%)</td>
<td>236 (-4%)&lt;sup&gt;k&lt;/sup&gt;</td>
<td>225 (-8%)&lt;sup&gt;k&lt;/sup&gt;</td>
</tr>
<tr>
<td>5-C</td>
<td>217</td>
<td>235 (66%)</td>
<td>236 (24%)</td>
<td>225 (7%)</td>
</tr>
</tbody>
</table>

6-A<sup>m</sup> | 218 (7%) | 237 (22%) | | | (7%) |
6-B<sup>n</sup> | 218 (8%) | 238 (57%) | | | (16%) |
6-C<sup>o</sup> | 218 | 237 (94%) | | | |

7-A | 219 (4%) | 239 (78%) | 240 (66%) | | |
7-B | 219 | 239 (89%) | | | |
7-C | 219 | 239 (89%) | | | |

8-A<sup>p</sup> | 220 | 241 (~41%)<sup>q</sup> | 242 (78%) | 230 (~8%) | |
8-B | 220 | | | | |
8-C | 220 (9%) | 241 (67%) | 242 (~3%) | 230 (~8%) | |

9-A | 221 | 243 (41%) | | | |
9-B | 221 (22%) | 243 (23%) | 244 (17%) | | |
9-C | 221 | 243 (74%) | 244 (~1%) | 227 (~5%) | |

10-A | 222 (20%) | 245 (48%) | | | |
10-B | 222 (31%) | 245 (31%) | 246 (7%) | | |
Details of the reaction Conditions A-C

A) Pd(dba)$_2$ (2 mol%), PPh$_3$ (8 mol%), 14,-dioxane, reflux

B) PdCl$_2$(PPh$_3$)$_2$ (2 mol%), LiCl (300 mol%), DMF, ambient temperature

C) PdCl$_2$(PPh$_3$)$_2$ (2 mol%), 1,4-dioxane, reflux

a) A ratio of 1:2 was observed for 213/223 in the $^1$H NMR of the crude reaction mixture. b) Isolated as a mixture with unknown impurities. c) A ratio of 1.14:1:1.93 was observed for 213/223/224 in the $^1$H NMR of the crude reaction mixture. d) A mixture of 213 and 2-bromo-3-nitrophenol was obtained from the $^1$H NMR of the mixture. e) PdCl$_2$(dppp)$_2$ (2 mol%), LiCl (300 mol%), DMF, ambient temperature used for the reaction. f) PdCl$_2$(dppp)$_2$ (2 mol%), DMF, ambient temperature was used for the reaction. g) Pd(PPh$_3$)$_4$ (2 mol%), toluene, reflux condition used for the reaction. h) An inseparable mixture of 226 and 228 was obtained; yield calculated from $^1$H NMR of the crude reaction mixture. i) An inseparable mixture of 215 and 229 was obtained; yield calculated from the $^1$H NMR of the crude reaction mixture. j) A ratio of 3.22:3.55:1.10:1 was observed for 217/235/236/225 in the crude reaction mixture. k) An inseparable mixture of 225 and 236 was obtained; yield calculated from $^1$H NMR of the crude reaction mixture. l) A ratio of 1:6.67 for compounds 217/236 was observed by $^1$H NMR of the crude reaction mixture. m) A ratio of 1:2.58 for compounds 218/237 was observed by $^1$H NMR of the crude reaction mixture. n) A ratio of 1:5 for compounds 218/239 was observed by $^1$H NMR of the crude reaction mixture. o) Reaction time 36 h. p) A ratio of 1:2.2 was observed for compounds 220/241 by the $^1$H NMR of the crude reaction mixture. q) Calculated from a mixture of 241 and dibenzylideneacetone.

Hayashi and Kamikawa have demonstrated that chemoselectivity of oxidative addition to C-Br vs C-OTf bond can be modulated by proper choice of ligands. Jutand and Mosleh have shown that a faster oxidative addition to C-OTf bond generally predominates when the OTf group sits para to an electron withdrawing group such as, a nitro group. 4-Cyanobromobenzene has been reported to be 326 times more reactive than the bromobenzene. Stille couplings of usually unreactive aryl fluorides have also been reported.

The chemoselectivity of C-I vs C-OTf bond was evaluated under all the three different conditions (A, B and C). The trifluoromethanesulfonate group was placed at an activated site. The results are outlined in the scheme below. In general, iodides are known to undergo coupling much faster than the OTf group even in the presence of LiCl. Reaction of 3-bromo-4-iodo-1-methoxybenzene with an alkenyltin reagent...
to give C-I coupling product had been reported although C-I is positioned at an electronically unfavorable site.\textsuperscript{170}

**Scheme 6.2** Kosugi-Migita-Stille coupling of 247 with ethenyltributyltin

Reaction of 5-bromo-2-trifloxybenzaldehyde has been shown to give C-OTf coupling product when the reaction is carried out with Pd\textsubscript{2}(dba)\textsubscript{3} and chiral ferrocenyldiphosphine in DMF at 80 °C without added LiCl. Only a very limited number of palladium catalyzed coupling reactions of bromophenyl trifluoromethanesulfonates containing an electron donating group has been reported.\textsuperscript{139,171}

Compound 250 was selected to minimize the possible steric interactions between the Br/OTf and the methoxy groups. Based on electronic considerations, the trifluoromethanesulfonate group may be expected to show less selectivity while the bromide in the less electron rich position should be more selective. This compound was also tested under all the three reaction conditions. The results are summarized in the scheme below. The reaction of 250 did not reach completion under Conditions C even with an excess of ethenyltributyltin.

**Scheme 6.3** Kosugi-Migita-Stille coupling of 250

As a final test substrate, compound 253 was chosen. The purpose here was to examine if the generalization of chemoselectivity may be extended to other electron withdrawing groups. Under all the
three reaction conditions, only one cross coupling product was observed in the $^1$H NMR spectrum of the crude reaction mixtures.

**Scheme 6.4** Kosugi-Migita-Stille coupling of 253

\[
\begin{align*}
\text{OTf} & \quad \text{SnBu}_3 \\
\text{Br} & \quad \text{Br}
\end{align*}
\]

<table>
<thead>
<tr>
<th>Compound</th>
<th>Reaction Conditions</th>
<th>Product</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>253</td>
<td>Conditions A</td>
<td>254</td>
<td>14%</td>
</tr>
<tr>
<td>253</td>
<td>Conditions B</td>
<td>255</td>
<td>58%</td>
</tr>
<tr>
<td>252</td>
<td>Conditions C</td>
<td>254</td>
<td>57%</td>
</tr>
</tbody>
</table>

**6.6 Conclusion**

The chemoselectivity of Kosugi-Migita-Stille couplings of all isomeric permutations of bromphenyl trifluoromethanesulfonates and bromonitrophenyl trifluoromethanesulfonates was examined in order to compare and contrast the reactivity of C-Br and C-OTf bonds under three different reaction conditions. Under all conditions, discrepancies were observed from the literature reported results. High selectivity was observed only for few of the compounds under both the reaction conditions (A and B). Enhanced selectivity for carbon-triflate bond was observed under conditions B only for some of the compounds. All substrates tested under conditions C showed very high selectivity for carbon-bromine bond coupling regardless of the type of functional groups and their positions on the aromatic rings. Although some generalizations can be made for some of the isomeric and potentially useful compounds, it is worth not to extend them to compounds having additional functional groups and/or more sterically demanding functionalities.
Chapter 7 Synthesis of pyrroloindoles via a double reductive N-heterocyclization

7.A Introduction
There are five isomeric pyrroloindoles. For simplicity, they have been grouped into five types (types A-E, Figure 7.1). The structures of these compounds remind of the notion that chemistry is indeed a creative science. Another interesting fact about these compounds is that they form a good basis for separate NMR studies. For example, the $^1$H and $^{13}$C NMRs of pyrroloindoles (of types A, C and D) look similar. Unless one knows the identity of the starting material, it is hard to tell what pyrroloindoles have been synthesized. In addition to their wide range of possible applications, the pyrroloindole skeleton can be found in natural products. Pyrroloindoles have been shown to possess bactericidal, antimicrobial, and antitumor activities. Among other representative examples of pyrroloindole containing natural products include terreusinone A, and indolo[3,2-$b$]carbazole. Terreusinone A possesses significant UV-A protecting properties.

Figure 7.1 Isomeric pyrroloindoles

1H,8H-Pyrrolo[3,2-$g$]indole
(Type A)

1H,7H-Pyrrolo[3,2-$f$]indole
(Type B)

1H,6H-Pyrrolo[3,2-$e$]indole
(Type D)

1H,5H-Pyrrolo[2,3-$f$]indole
(Type C)

1H,5H-Pyrrolo[2,3-$g$]indole
(Type E)
There are several methods reported to access these isomeric compounds. They can be broadly classified into two categories. One route consists of fusing a pyrrole ring onto a preformed indole or indoline ring, and the other route is the direct double ring closure of the precursors without a preformed indole or indoline. Examples of the first methodology includes a Fischer indole synthesis\textsuperscript{199} intramolecular cyclization of a bis-(β-aminoethyl)-hydroquinone derivative in presence of water.\textsuperscript{200} The second general methodology includes a double Reissert indole synthesis\textsuperscript{201,202} and a double Batcho-Leimgruber\textsuperscript{203} Shannon \textit{et al}. prepared pyrrolo[3,2-\textit{f}] and –[2,3-\textit{f}]-indoles through the Montmorillonite K-10 clay catalyzed Vilsmeier formylation of pyrrole.\textsuperscript{204}

\textbf{Scheme 7.1} Vilsmeier formylation route to pyrroloindoles

![Scheme 7.1 Vilsmeier formylation route to pyrroloindoles](image)

Samsoniya \textit{et al}. reported numerous methods to prepare pyrroloindoles.\textsuperscript{205,206} The first method utilized a Fischer-type bicyclization of bishydrazone to form the two pyrrole rings (Scheme 7.2). An inherent drawback of this methodology was the formation of four isomers.

\textbf{Scheme 7.2} Samsoniya \textit{et al} synthesis of pyrroloindoles

![Scheme 7.2 Samsoniya \textit{et al} synthesis of pyrroloindoles](image)

Although the second methodology by Samsoniya \textit{et al} attempted to circumvent the previously reported issue of isomer formation by using a pre-formed aminoindoline, two non-substituted pyrroloindoles were obtained only at the expense of additional steps.
**Scheme 7.3** Preparation of pyrroloindoles from Aminoindoline

![Diagram of Scheme 7.3](image)

While the palladium-catalyzed aerobic oxidative bicyclization route to the preparation of pyrroloindoles from N-aryl imines reported by Yoshikai et al.\(^{207}\) seemed to have broader substrate scope, the authors did not attempt to prepare non-symmetrical compounds. The yields of products were modest at best and the regioselectivities observed in the cyclizations were also not explained.

**Scheme 7.4** Preparation of pyrroloindoles from Diimines

![Diagram of Scheme 7.4](image)

Fujii and Ohno reported a copper-catalyzed bis-cyclization of di-alkynyl-dimesylamide (Scheme 7.5).\(^{208}\) This approach was limited to terminal alkynes, affording only non-substituted pyrroloindoles.

A related rhodium catalyzed hydroamination of di-alkynyl-diamines and di-alkynyl-acetylamide have been used to prepare type B and C benzoindoles.\(^{209}\) 2-Substituted pyrroloindoles cannot be made by this methodology.

**Scheme 7.5** Intramolecular Hydroamination route to pyrroloindoles

![Diagram of Scheme 7.5](image)
One serious limitation of the previously reported synthetic routes is that they allow only for the preparation of symmetrical pyrroloindoles. This is in part due to limitations associated with the methods used to prepare the required starting materials, most of which also involve symmetrical compounds. Therefore, methods to prepare non-symmetrical substrates that can be converted to non-symmetrical pyrroloindoles are highly desirable.

Over the last twenty years, our group has extensively studied applications of palladium catalyzed carbon monoxide mediated reductive cyclizations. This versatile methodology has been used to prepare a wide variety of indoles, bi-1H-indoles and indole alkaloids.45,113 We envisioned that this methodology could be applied in the synthesis of benzoindoles from dialkenyldinitrobenzenes. The relatively mild conditions used in such reactions could allow for broad functional group compatibility and offer significant improvements over the previously disclosed methods. With the goal of preparing non-symmetrical pyrroloindoles using the reductive cyclization methodology, efforts were made to establish routes to prepare the requisite dialkenyldinitrobenzenes. Specifically, efforts were focused on synthesizing non-symmetrical cyclization precursors in a controlled, sequential manner. For organizational clarity, each isomeric substrate is presented separately, although numerous commonalities were encountered in the preparation of each substrate. The synthetic strategy is presented below.

**Scheme 7.6 Possible routes to pyrroloindoles**

![Scheme 7.6 Possible routes to pyrroloindoles](image)
Accordingly, we hypothesized that pyrroloindole of type A could be obtained by reductive cyclization of 1,4-dialkenyl-2,3-dinitrobenzenes which, in turn, could be derived by Kosugi-Migita-Stille coupling with the appropriate tin reagents. A similar strategy was envisioned for the synthesis of the other pyrroloindole types.

7. B Results and Discussion

Compound 285 was chosen as a test substrate. Compound 285 was synthesized by a double Kosugi-Migita-Stille coupling of 1,4-dibromo-2,3-dinitrobenzene with vinyltin 282. Treatment of 285 under our standard conditions for reductive cyclization (Pd(dba)$_2$, dppp, 1,10-phen, CO (6 atm), DMF, 120 °C) afforded the expected product 336 in 23% isolated yield. The monocyclized product 337 was not observed. The problem, however, was the low yield of product. We hypothesized that the low yield (Table 7.1, entry 1) might be a result of the catalyst inactivity after prolonged period of reaction and is probably a call for the reevaluation of the catalytic systems. This catalyst was replaced with a robust catalyst system (Pd(OAc)$_2$, dppp, 1,10-phen) which improved the yield, but this was again not very satisfactory (Table 7.1, entry 2). Although a combination of Pd(dba)$_2$ and PPh$_3$ did improve the yield tremendously (64%, entry 3), the best result (70%, entry 6), was obtained with the combination of the very simple catalyst (Pd(OAc)$_2$, 1,10-phen). Notice that entries 4 and 5 are conditions leading to monocyclized product 337 although a minor amount of pyrroloindole was also isolated (9%, entry 5).
Table 7.1 Condition screening

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>Time (h)</th>
<th>% Yield</th>
<th>% Yield</th>
<th>Σ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Pd(dba)$_2$, dppp, 1,10-phen</td>
<td>89</td>
<td>23</td>
<td>-</td>
<td>23</td>
</tr>
<tr>
<td>2.</td>
<td>Pd(OAc)$_2$, dppp, 1,10-phen</td>
<td>100</td>
<td>35</td>
<td>-</td>
<td>35</td>
</tr>
<tr>
<td>3.</td>
<td>Pd(dba)$_2$, PPh$_3$</td>
<td>126</td>
<td>64</td>
<td>-</td>
<td>64</td>
</tr>
<tr>
<td>4.</td>
<td>Pd(OAc)$_2$, PPh$_3$</td>
<td>126</td>
<td>-</td>
<td>54</td>
<td>54</td>
</tr>
<tr>
<td>5.</td>
<td>Pd(OAc)$_2$, dppp</td>
<td>36</td>
<td>9</td>
<td>49</td>
<td>58</td>
</tr>
<tr>
<td>6.</td>
<td>Pd(OAc)$_2$, 1,10-phen</td>
<td>48</td>
<td>41</td>
<td>-</td>
<td>48</td>
</tr>
<tr>
<td>7.</td>
<td>Pd(OAc)$_2$, 1,10-phen</td>
<td>90</td>
<td>70</td>
<td>-</td>
<td>70</td>
</tr>
</tbody>
</table>

In order to validate the result presented in Table 7.1, we commenced to synthesize symmetrical as well as unsymmetrical cyclization precursors. Most of the cross-coupling precursors were novel and they were prepared as described below. All other starting materials were commercially available or prepared according to literature procedures. For the 1H,8H-pyrrolo[3,2-g]indole (Type A) precursors, 4-bromo-2,3-dinitrophenol (257) and 4-bromo-2,3-dinitrophenyltriflate (258) were prepared from 1,4-dibromo-2,3-dinitrobenzene (256) by a sequential nucleophilic aromatic substitution using an excess of sodium hydroxide in a water-THF mixture and triflation (Scheme 7.7).

Scheme 7.7 Preparation of 258

4-Bromo-2,3-dinitrophenol (257) can alternatively be obtained from nitration of 4-bromo-3-nitrophenol (259). In addition to 257, the isomeric nitration product 4-bromo-2,5-dinitrophenol (262) was also obtained. The latter is a plausible precursor to Type C pyrroloindoles. The isomers were readily separated.
and transformed into the corresponding triflates 258, and 265, respectively (Scheme 7.8). In a similar fashion, nitration of 4-iodo-3-nitrophenol (260)\textsuperscript{211} gave rise to two readily separable products, 4-iodo-2,5-dinitrophenol (263) and 4-iodo-2,3-dinitrophenol (261), and after triflation the corresponding triflates 266 and 264 respectively.

Scheme 7.8 Synthesis of bromo- and iodo-phenyl trifluoromethanesulfonates

\[
\begin{align*}
\text{H}_2\text{O} & \xrightarrow{X} \text{H}_2\text{O} \\
\text{NO}_2 & \xrightarrow{\text{HNO}_3} \text{NO}_2 \\
259 & (X=\text{Br}) & 257 & (51\%) & 262 & (37\%) & 258 & (82\%) & 265 & (80\%) \\
260 & (X=\text{I}) & 261 & (50\%) & 263 & (30\%) & 264 & (92\%) & 266 & (80\%)
\end{align*}
\]

A selective oxidative iodination of 2,5-dinitrophenol (267)\textsuperscript{212} using potassium iodide and benzyltriphenylphosphonium peroxymonosulfate to give 263 has been reported. However, we were unable to repeat the reported result using this procedure. Iodination of deactivated aromatic compounds using N-iodosuccinimide (NIS) in trifluoromethanesulfonic acid has been reported by Olah et al.\textsuperscript{213} In a slight modification of this procedure, treatment of 267 with NIS in sulfuric acid afforded the desired 4-iodo-2,5-dinitrophenol (263) in moderate yield (Scheme 7.9).

Scheme 7.9 Iodination of 2,5-dinitrophenol (267).

\[
\begin{align*}
\text{O}_2\text{N} & \xrightarrow{\text{NIS}, \text{H}_2\text{SO}_4} \text{O}_2\text{N} \\
\text{OH} & \xrightarrow{0-60 \, ^\circ\text{C}} \text{OH} \\
267 & \quad 263 & (57\%)
\end{align*}
\]

Nitration of 5-iodo-2-nitrophenol (269)\textsuperscript{214} with sodium nitrate in sulfuric acid afforded 5-iodo-2,4-dinitrophenol (274)\textsuperscript{215} as the major product along with the novel nitration product 3-iodo-2,4-dinitrophenol (275) as an inseparable mixture by chromatography (Scheme 7.10). Since the products were inseparable, they were treated with triflic anhydride to give the readily separated triflates 276 and 277. The same results were obtained using 5-bromo-2-nitrophenol (268) affording an inseparable mixture of dinitro bromophenols 270 and 271 and the readily separable corresponding triflates 204 and 273 (Scheme 7.10).
Scheme 7.10 Synthesis of bromo- and iodo-phenyl trifluoromethanesulfonates

\[
\begin{align*}
\text{HO} & \quad \xrightarrow{\text{NaNO}_3, \text{H}_2\text{SO}_4} & \text{HO} \\
\text{O}_2\text{N} & \quad \text{X} & \quad \text{O}_2\text{N}
\end{align*}
\]

\[\text{268 (X=Br)}\]

\[
\begin{align*}
\text{HO} & \quad \xrightarrow{\text{0 °C}} & \text{HO} \\
\text{O}_2\text{N} & \quad \text{X} & \quad \text{O}_2\text{N} \\
\text{NO}_2 & \quad & \text{NO}_2 \\
\text{270 + 271} & & (99\%) \\
\text{274 + 275} & & (99\%)
\end{align*}
\]

\[\text{269 (X=I)}\]

\[
\begin{align*}
\text{HO} & \quad \xrightarrow{\text{Tf}_2\text{O, Et}_3\text{N}} & \text{HO} \\
\text{O}_2\text{N} & \quad \text{X} & \quad \text{O}_2\text{N} \\
\text{NO}_2 & \quad & \text{NO}_2 \\
\text{204} & & (57\%) \\
\text{274} & & (62\%) \\
\text{277} & & (28\%)
\end{align*}
\]

Finally, the elusive Kosugi-Migita-Stille coupling precursor, 2-bromo-3,6-dinitrophenyl trifluoromethanesulfonate (281) was prepared in the same fashion as discussed above for compounds 204 and 273. A minor amount of the undesired product 280 was also obtained from the nitration reaction (Scheme 7.11).

Scheme 7.11 Synthesis of 281

\[
\begin{align*}
\text{HO} & \quad \xrightarrow{\text{NaNO}_3, \text{H}_2\text{SO}_4} & \text{HO} \\
\text{O}_2\text{N} & \quad \text{Br} & \quad \text{O}_2\text{N} \\
\text{NO}_2 & \quad & \text{NO}_2 \\
\text{278} & & (61\%) \\
\end{align*}
\]

\[
\begin{align*}
\text{HO} & \quad \xrightarrow{\text{0 °C-rt}} & \text{HO} \\
\text{O}_2\text{N} & \quad \text{Br} & \quad \text{O}_2\text{N} \\
\text{NO}_2 & \quad & \text{NO}_2 \\
\text{279, Tf}_2\text{O, Et}_3\text{N} & \xrightarrow{\text{CH}_2\text{Cl}_2, \text{0 °C-rt}} & \text{O}_2\text{N} \\
\text{281} & & (91\%)
\end{align*}
\]

7.C Synthesis of pyrroloindole (Type A-E) precursors

The Kosugi-Migita-Stille cross coupling was used to introduce the required alkenes onto the benzene ring. Some of the advantages of this type of coupling reaction include the vast array of alkenyltins already reported in the literature, their ease of preparation either from Grignard reagents or hydrostannation of alkynes and their stability relative to alternative reagents. Variation of the alkenyl tin used in either coupling step would allow for preparation of a number of structurally diverse pyrroloindoles. A double Kosugi-Migita-Stille cross-coupling was used for the synthesis of symmetrical cyclization precursors using 1,4-dibromo-2,3-dinitrobenzene (256), 1,5-dibromo-2,4-dinitrobenzene (288), 4-iodo-2,5-dinitrophenyl triflate (266) or 4-bromo-2,5-dinitrophenyl triflate (265), 5-bromo-2,4-dinitrophenyl triflate (204), 5-iodo-2,4-dinitrophenyl triflate (276), 3-bromo-2,6-dinitrophenyl triflate (273), and 2-bromo-3,6-dinitrophenyl triflate (281).

Thus, ethenyl (282), 1-propen-1-yl (283), and 1-propen-2-yl (284) tributyltin were treated with the appropriate substrate in the presence of PdCl₂(PPh₃)₂ and/or PPh₃ in 1,4-dioxane at 90-100 °C and the results are summarized in Table 7.2.
<table>
<thead>
<tr>
<th>Entry</th>
<th>Aryl-Br/OTf</th>
<th>Tin reagent</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><img src="image1" alt="" /></td>
<td>![image2]</td>
<td><img src="image3" alt="" /></td>
</tr>
<tr>
<td>1</td>
<td>256</td>
<td>282 (R=R'=H)</td>
<td>285 (R=R'=H, 67%)</td>
</tr>
<tr>
<td>2</td>
<td>256</td>
<td>283 (R=H, R'=Me)</td>
<td>286 (R=H, R'=Me, 85%)</td>
</tr>
<tr>
<td>3</td>
<td>256</td>
<td>284 (R=Me, R'=H)</td>
<td>287 (R=Me, R'=H, 70%)</td>
</tr>
<tr>
<td>4</td>
<td>288</td>
<td>282</td>
<td>289 (R=R'=H, 73%)</td>
</tr>
<tr>
<td>5</td>
<td>288</td>
<td>283</td>
<td>290 (R=H, R'=Me, 93%)</td>
</tr>
<tr>
<td>6</td>
<td>288</td>
<td>284</td>
<td>291 (R=Me, R'=H, 87%)</td>
</tr>
<tr>
<td>7</td>
<td>266</td>
<td>282</td>
<td>292 (R=R'=H, 60%)</td>
</tr>
<tr>
<td>8</td>
<td>266</td>
<td>283</td>
<td>293 (R=H, R'=Me, 52%)</td>
</tr>
<tr>
<td>9</td>
<td>266</td>
<td>284</td>
<td>294 (R=Me, R'=H, 54%)</td>
</tr>
<tr>
<td>10</td>
<td>288</td>
<td>282</td>
<td>295 (R=R'=H, 34%)</td>
</tr>
</tbody>
</table>
It was anticipated that the chemoselectivity between bromides and triflates (discussed in chapter 6) could be used to our advantage for the introduction of two different alkenes onto an aromatic ring. However, cross coupling of 258 proved to be relatively unselective under the two conditions established by Echavarren and Stille and under some additional conditions examined (Scheme 7.12). Inseparable mixtures of di- and C-OTf coupled products and C-Br coupled product and starting material in addition to unknown impurities were obtained in each case. Compound 258 was not further examined as a possible starting material to unsymmetrically substituted precursors for pyrroloindole type A.

Scheme 7.12 Attempted selective Kosugi-Migita-Stille coupling of 258

A selective introduction of one alkene was, however, feasible using iodo- and bromo-triflates and limited amounts of alkenyl tin reagent (Table 7.3). Attempted coupling at the triflate using an excess of lithium chloride resulted in an OTf–chloride exchange (Scheme 7.13, 7.14). Thus, all reactions were performed in the absence of LiCl.
Table 7.3 Selective cross coupling of bromo- and iodo-phenyl triflates.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aryl-Br/I/Cl/OTf</th>
<th>Tin reagent</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>264</td>
<td>282</td>
<td>300 (65%) 285 (2%)</td>
</tr>
<tr>
<td></td>
<td><img src="image1" alt="Structure" /></td>
<td><img src="image2" alt="Structure" /></td>
<td><img src="image3" alt="Structure" /></td>
</tr>
<tr>
<td>2</td>
<td>264</td>
<td>283</td>
<td>301 (64%)</td>
</tr>
<tr>
<td></td>
<td><img src="image4" alt="Structure" /></td>
<td><img src="image5" alt="Structure" /></td>
<td><img src="image6" alt="Structure" /></td>
</tr>
<tr>
<td>3</td>
<td>264</td>
<td>284</td>
<td>302 (64%) 287 (2%)</td>
</tr>
<tr>
<td></td>
<td><img src="image7" alt="Structure" /></td>
<td><img src="image8" alt="Structure" /></td>
<td><img src="image9" alt="Structure" /></td>
</tr>
<tr>
<td>4</td>
<td>264</td>
<td><img src="image10" alt="Structure" /></td>
<td>303 (50%)</td>
</tr>
<tr>
<td></td>
<td><img src="image11" alt="Structure" /></td>
<td><img src="image12" alt="Structure" /></td>
<td><img src="image13" alt="Structure" /></td>
</tr>
<tr>
<td>5</td>
<td>276</td>
<td>282</td>
<td>205 (35%)</td>
</tr>
<tr>
<td></td>
<td><img src="image14" alt="Structure" /></td>
<td><img src="image15" alt="Structure" /></td>
<td><img src="image16" alt="Structure" /></td>
</tr>
<tr>
<td>6</td>
<td>204</td>
<td>283</td>
<td>305 (75%) 290 (12%)</td>
</tr>
<tr>
<td></td>
<td><img src="image17" alt="Structure" /></td>
<td><img src="image18" alt="Structure" /></td>
<td><img src="image19" alt="Structure" /></td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>276</td>
<td>266</td>
<td>266</td>
<td>281</td>
</tr>
<tr>
<td>284</td>
<td>282</td>
<td>283</td>
<td>282</td>
</tr>
<tr>
<td>306 (51%)</td>
<td>307 (76%)</td>
<td>308 (70%)</td>
<td>309 (35%)</td>
</tr>
<tr>
<td>291 (6%)</td>
<td>292 (4%)</td>
<td>293 (7%)</td>
<td>295 (10%)</td>
</tr>
</tbody>
</table>
The second alkene was thought to be readily introduced by an aryl trflate–organotin cross coupling using the conditions described by Echavarren and Stille (PdCl₂(PPh₃)₂, LiCl, DMF, RT). However, attempted coupling of 300 and 307 resulted only in a replacement of the trflate with a chlorine to give 314 and 315, respectively (Schemes 7.13–7.14). Cross coupling of the chlorine was not feasible at ambient temperature but 317 underwent coupling at elevated temperature to give 316 in excellent isolated yield after chromatography. The trflate to chloride transformation could readily be avoided by either excluding lithium chloride at ambient temperatures or perform the reaction at elevated temperatures in the presence of lithium chloride. The results from the second Kosugi-Migita-Stille coupling of phenyl trflate are summarized in the following table (Table 7.13).

Scheme 7.13 Problem in Kosugi-Migita-Stille coupling

Scheme 7.14 Synthesis and attempted Kosugi-Migita-Stille coupling of 315
<table>
<thead>
<tr>
<th>Entry</th>
<th>Aryl-Br/I/Cl/OTf</th>
<th>Tin reagent</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Image" /></td>
<td>300, 283</td>
<td><img src="image2" alt="Image" /> 317 (66%)</td>
</tr>
<tr>
<td>2</td>
<td><img src="image3" alt="Image" /></td>
<td>300, 284</td>
<td><img src="image4" alt="Image" /> 318 (64%)</td>
</tr>
<tr>
<td>3</td>
<td><img src="image5" alt="Image" /></td>
<td>302, 283</td>
<td><img src="image6" alt="Image" /> 319 (45%)</td>
</tr>
<tr>
<td>4</td>
<td><img src="image7" alt="Image" /></td>
<td>300</td>
<td><img src="image8" alt="Image" /> 320 (51%)</td>
</tr>
<tr>
<td>5</td>
<td><img src="image9" alt="Image" /></td>
<td>301</td>
<td><img src="image10" alt="Image" /> 321 (51%)</td>
</tr>
<tr>
<td>6</td>
<td><img src="image11" alt="Image" /></td>
<td>303, 283</td>
<td><img src="image12" alt="Image" /> 321 (43%)</td>
</tr>
<tr>
<td></td>
<td>Reaction</td>
<td>Yield (%)</td>
<td></td>
</tr>
<tr>
<td>----</td>
<td>----------</td>
<td>-----------</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>[Image]</td>
<td>302 (\text{Bu}_3\text{Sn} \text{CO}_2\text{Et})</td>
<td>322 (55%)</td>
</tr>
<tr>
<td>8</td>
<td>[Image]</td>
<td>205 (\text{O}_2\text{N NO}_2)</td>
<td>284</td>
</tr>
<tr>
<td>9</td>
<td>[Image]</td>
<td>305 (\text{O}_2\text{N NO}_2)</td>
<td>284</td>
</tr>
<tr>
<td>10</td>
<td>[Image]</td>
<td>307 (\text{O}_2\text{N NO}_2)</td>
<td>283</td>
</tr>
<tr>
<td>11</td>
<td>[Image]</td>
<td>308 (\text{O}_2\text{N NO}_2)</td>
<td>284</td>
</tr>
<tr>
<td>12</td>
<td>[Image]</td>
<td>309 (\text{O}_2\text{N NO}_2)</td>
<td>283</td>
</tr>
</tbody>
</table>
The route to Type E pyrroloindoles involved the separation of isomeric nitration product affording the precursor in moderate to low yield. Thus, a second route to the precursors was pursued. Aniline 332 was converted to aryl iodide 333 via reaction of the corresponding diazonium salt with potassium iodide (Scheme 7.15). Employing Mundla’s methodology condensation of 333 with para-formaldehyde in the presence of a catalytic amount of potassium hydroxide afforded alcohol 334. Conversion of alcohol 334 to the corresponding mesylate, which was not isolated, followed by subsequent elimination afforded dinitrostyrene 330. Kosugi-Migita-Stille coupling between iodide 335 and 284 gave the expected substrate 330. Unfortunately, all attempts to broaden the scope of Mundla’s methodology substituting para-formaldehyde with other aldehydes, for example hexanal, were unsuccessful.
7.D Synthesis of 1H, 8H-pyrrolo[3,2-g]indoles (Type A)

After successful synthesis of symmetrically as well as unsymmetrically substituted cyclization precursors, they were subjected to the reductive cyclization conditions as discussed in table 7.1. To our delight, all diakenyl-dinitrobenzenes smoothly participated in the reactions to give rise to symmetrical as well as unsymmetrical pyrroloindoles of type A (Table 7.5). The symmetrical substrates 286 and 287 also behaved as 285 to give rise to monocyclized indoles 339 and 341 along with pyrroloindoles 338 and 340 respectively. In order to compare the reactivity of substituted and the unsubstituted double bonds, compound 317 was subjected to the monocyclization conditions (Pd(OAc)$_2$, PPh$_3$) as revealed in Table 7.1. Only double cyclization product 342 (53%) was obtained; the expected monocyclization product was not detected. The formation of unsymmetrically substituted pyrroloindoles here represents the first synthesis of these compounds. All the results are summarized the table below (Table 7.5).
Table 7.5 Synthesis of $1H,8H$-pyrrolo[3,2-g]indoles (Type A)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Reaction conditions</th>
<th>Pyrroloindole</th>
<th>Indole</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>286</td>
<td>Pd(OAc)$_2$-phen</td>
<td>338 (67%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>286</td>
<td>Pd(OAc)$_2$-dppp</td>
<td>338 (9%)</td>
<td>339 (69%)</td>
</tr>
<tr>
<td>3</td>
<td>286</td>
<td>Pd(OAc)$_2$-dppp-phen</td>
<td>338 (36%)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>287</td>
<td>Pd(OAc)$_2$-phen</td>
<td>340 (54%)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>287</td>
<td>Pd(dba)$_2$-dppp-phen</td>
<td>340 (67%)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>287</td>
<td>Pd(dba)$_2$-PPh$_3$</td>
<td>340 (62%)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>287</td>
<td>Pd(dba)$_2$-dppp</td>
<td>340 (16%)</td>
<td>341 (78%)</td>
</tr>
<tr>
<td>8</td>
<td>317</td>
<td>Pd(OAc)$_2$-phen</td>
<td>342 (63%)</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>317</td>
<td>Pd(OAc)$_2$-PPh$_3$</td>
<td>342 (25%)</td>
<td></td>
</tr>
</tbody>
</table>
The results summarized in Table 7.5 are exciting in the sense that they open the door for the synthesis of unsymmetrically substituted pyrroloindoles of type A. Encouraged with these results, we were very sure that a combination of Pd(OAc)$_2$-1,10-phen would be a good catalyst for the synthesis of rest of the pyrroloindole types. Problems then started arising. Although compound 291 gave pyrroloindole in moderate yield (53%), the case of formation of pyrroloindole 350 was realized only with Pd(dba)$_2$-dppp-1,10-phen; all other conditions gave monocyclized indole (Table 7.6, entries 4). Compound 290 gave monocyclized indole even after prolonged reaction time (Table 7.6, entries 2, 3). On the other hand, the non-substituted 1,5-diethenyl-2,4-dinitrobenzene (289) did not afford any identifiable monocyclized or double cyclized product although all the starting material was consumed under any of the several conditions tested. A possible route is the polymerization but this possibility was also ruled out when similar result was obtained with Pd(dba)$_2$-dppp-1,10-phen, BHT. The unsymmetrically substituted 1,5-
dialkenyl-2,4-dinitrobenzenes of this series (compounds 323 and 324) afforded monocyclized products in very diminished yields along with an inseparable mixture of unknown impurities under all reaction conditions tried. We were unable to find a good condition for the cyclization of compounds 323 and 324. Similar results were obtained when we attempted to synthesize pyrroloindoles of type C. The non-substituted 1,4-dialkenyl-2,5-dinitrobenzene 292 participated in double cyclization to afford pyrroloindole 351 (60%) uneventfully. The related cyclization precursor 294 gave pyrroloindole 387 only with Pd(dba)$_2$-PPh$_3$ albeit in low yield (26%). Under all other conditions tried, compounds 293 and 294 gave monocyclized normal indoles 352 and 353 respectively. Here also the unsymmetrically substituted cyclization partners gave monocyclized indoles in diminished yield along with an inseparable mixture of unknown impurities. These compounds were not further explored for the unsymmetrically substituted pyrroloindoles of type C.

The results from the attempted cyclizations of 298, 330 and 331 that are possible precursors to pyrroloindoles of type E are outlined in Table 7.6. As can been, compound 298 gave monocyclized and dicyclized products 364 (20%) and 363 (50%) respectively whereas the unsymmetrical partners 330 and 331 gave indoles. Compound 366 was obtained along with minor amount of pyrroloindole 367 as an inseparable mixture by chromatography.

The cyclization precursors to type D were also tested for any possibility of formation of pyrroloindoles. Unsurprisingly, however, all the symmetrical dialkenyl-dinitrobenzenes went on smoothly to give rise to indoles in high isolated yields after chromatography. Completely different observations were noticed when the unsymmetrically substituted dialkenyl-dinitrobenzenes were subjected to double cyclization; these compounds gave rise to two indoles resulting from each of the double bond cyclization as an inseparable mixture in nearly 1:1 ratio. The results are included in Table 7.6.
<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Conditions</th>
<th>Pyrroloindole</th>
<th>Indole</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>289</td>
<td>Pd(OAc)$_2$&lt;sub&gt;2&lt;/sub&gt;, phen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>290</td>
<td>Pd(OAc)$_2$, phen</td>
<td>348 (37%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>290</td>
<td>Pd(dba)$_2$, PPh$_3$</td>
<td>348 (64%)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>291</td>
<td>Pd(dba)$_2$, dppp, phen</td>
<td>349 (56%)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>291</td>
<td>Pd(dba)$_2$, dppp</td>
<td>349 (16%)</td>
<td>350 (78%)</td>
</tr>
<tr>
<td>6</td>
<td>291</td>
<td>Pd(dba)$_2$, phen</td>
<td>350 (20%)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>291</td>
<td>Pd(dba)$_2$, PPh$_3$</td>
<td>350 (85%)</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>292</td>
<td>Pd(OAc)$_2$, phen</td>
<td>351 (60%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 7.6 Attempted synthesis of pyrroloindoles (Type B-E)
9  293  Pd(OAc)$_2$, phen  352 (31%)
10  293  Pd(dba)$_2$, PPh$_3$  352 (100%)
11  294  Pd(dba)$_2$, PPh$_3$  353 (73%)
12  295  Pd(OAc)$_2$, phen  354 (44%)
13  295  Pd(dba)$_2$, PPh$_3$  354 (68%)
14  296  Pd(OAc)$_2$, phen  355 (74%)
15  296  Pd(dba)$_2$, PPh$_3$  355 (70%)
16  297  Pd(OAc)$_2$, phen  356 (86%)
<table>
<thead>
<tr>
<th>No.</th>
<th>Reaction</th>
<th>Intermediate</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>$\text{Pd(OAc)}_2$, dppp, phen</td>
<td>356 $(51%)$</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>$\text{Pd(OAc)}_2$, PPh$_3$</td>
<td>356 $(84%)$</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>$\text{Pd(OAc)}_2$, dppp, phen</td>
<td>$357 + 358$ $(46%, 1:1)$</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>$\text{Pd(OAc)}_2$, phen</td>
<td>$359 + 360$ $(70%, 1:1)$</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>$\text{Pd(OAc)}_2$, phen</td>
<td>$361 + 362$ $(77%, 1:1)$</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>$\text{Pd(OAc)}_2$, phen</td>
<td>$363$ $(50%)$, $364$ $(20%)$</td>
<td></td>
</tr>
</tbody>
</table>
A second cyclization of the indoles 348 and 352 was also attempted. Submitting the mono-cyclized product from 290 to the reaction conditions Pd(OAc)$_2$-PPh$_3$ -30h gave only 38% of recovered starting material whereas quantitative amount of starting material was recovered from the attempted second cyclization of 352 under the reaction conditions Pd(OAc)$_2$-PPh$_3$ -30h. A possible hindrance to the second cyclization may be the electronic factor associated with the indoles resulting from the first cyclization. Once the indole is formed, the ring becomes electron rich and this may be acting as an obstacle to the second cyclization. We then considered introducing electron withdrawing group to the NH group of the indole and subjecting the resulting indole to the second cyclization. The first electron withdrawing that came into our consideration was the acetyl group. Accordingly, we synthesized the acetylated indoles 368 and 369 and submitted them to our standard conditions of reductive cyclization.
Scheme 7.16 Attempted reductive cyclization of 368 and 369

Although the result from the attempted cyclization of 368 was frustrating, the presence of a minor amount of pyrroloindole in the isolated starting material from the reductive cyclization of 369 was an indication that an electron withdrawing group may play a crucial role in the second cyclization. With this in mind, we synthesized the tosylated indole 370 by reacting 356 with TsCl in the presence of a base in DMF and subjected to reductive cyclization. To our delight, the tosylated pyrroloindole 371 was obtained in excellent yield (88%) after chromatographic separation.

Scheme 7.17 Reductive cyclization of 370

Encouraged with this result, the tosylated indoles 372-379 were prepared in a similar fashion and subjected to reductive cyclization. The results are summarized in the table below.
<table>
<thead>
<tr>
<th>Entry</th>
<th>Indole</th>
<th>Reaction conditions</th>
<th>N-Tosyl indole</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Indole 1" /></td>
<td>NaH, TsCl, DMF, 0 °C-rt</td>
<td><img src="image2" alt="Indole 2" /></td>
</tr>
<tr>
<td>2</td>
<td><img src="image3" alt="Indole 3" /></td>
<td><img src="image4" alt="Indole 4" /></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td><img src="image5" alt="Indole 5" /></td>
<td><img src="image6" alt="Indole 6" /></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td><img src="image7" alt="Indole 7" /></td>
<td><img src="image8" alt="Indole 8" /></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td><img src="image9" alt="Indole 9" /></td>
<td><img src="image10" alt="Indole 10" /></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td><img src="image11" alt="Indole 11" /></td>
<td>NaH, TsCl, DMF, 0 °C-rt</td>
<td><img src="image12" alt="Indole 12" /></td>
</tr>
</tbody>
</table>

*Table 7.7 Synthesis of N-tosylated indoles*
As is clear, all the problematic substrates but 379 smoothly participated in cyclization giving rise to pyrroloindoles in high to excellent isolated yields. Compound 379 was tested for cyclization under two different catalytic conditions (Table 7.8, entries 8, 9). The use of tosyl group as an electron withdrawing group has several advantages, for example, it improves the yields and leads to enhanced stability of the pyrroloindoles and diminishes the overall reaction time. The non-tosylated indoles are relatively unstable in air. The results are summarized in Table 7.8.

Table 7.8 Synthesis of N-tosylated pyrroloindoles (Types B-E)

<table>
<thead>
<tr>
<th>Entry</th>
<th>N-Tosyl indole</th>
<th>Reaction conditions</th>
<th>Pyrroloindole</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="" /></td>
<td>Pd(dba)$_2$, dppe, 1,10-phen</td>
<td><img src="image2" alt="" /></td>
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<tr>
<td></td>
<td>372</td>
<td>CO (6 atm), DMF, 120 °C</td>
<td>380 (79%)</td>
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<tr>
<td>2</td>
<td><img src="image3" alt="" /></td>
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<td>373</td>
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<td>381 (70%)</td>
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3  \[ \text{374} \]

4  \[ \text{375} \]

5  \[ \text{376} \]

6  \[ \text{377} \]

7  \[ \text{378} \]

8  \[ \text{379} \]
Pd(OAc)$_2$, 1,10-phen, CO (6 atm), DMF, 120 °C  

7.E Conclusion Palladium catalyzed, carbon monoxide mediated, double reductive $N$-heterocyclization of dialkenylnitrobenzenes to the functionalized and novel non-symmetrical pyrroloindoles has been developed for the first time. This methodology represents the first common synthetic routes to all the isomeric pyrroloindoles which are of interest in a number of applications in addition to their presence as a core moiety in a wide range of bioactive natural products. The functionalized isomeric cyclization precursors were prepared through use of Kosugi-Migita-Stille coupling reaction. The generally mild catalyst conditions offer significant improvements over previously reported methods that utilize harsh conditions. This pathway opens the door for the synthesis of all the otherwise synthetically challenging unsymmetrically substituted pyrroloindoles in general.
Experimental Section

General Procedures. All NMR spectra were recorded in CDCl₃ at 600 MHz (¹H NMR), 150 MHz (¹³C NMR, 1H broadband decoupled) and 376 MHz ¹⁹F NMR at ambient temperature unless otherwise stated. The chemical shifts are expressed in δ values relative to SiMe₄ (0.0 ppm, ¹H and ¹³C) or CDCl₃ (77.0 ppm, ¹³C) internal standards. HRMS data were obtained via electrospray ionization (ESI) with an ion trap mass analyzer. THF, dichloromethane and toluene were purified and dried via a two consecutive columns composed of activated alumina and Q5 catalyst on a Glass Contours solvent purification system. Anhydrous N,N-dimethylformamide was used as received. Hexanes, ethyl acetate, and 1,4-dioxane were distilled from calcium hydride. Chemicals prepared according to literature procedures have been footnoted the first time used; all other reagents were obtained from commercial sources and used as received. All reactions were performed under a nitrogen atmosphere in oven-dried glassware. Solvents were removed from reaction mixtures and products on a rotary evaporator at water aspirator pressure unless otherwise stated. Melting points (uncorrected) were recorded from the pure products obtained by chromatography.

2-(5-Benzylxy-2-nitrophenyl)-1-trimethylsilylethyne (2). 5-Benzylxy-2-nitro-1-bromobenzene⁴¹ (1) (3.91 g, 12.7 mmol) was dissolved in toluene (10 mL) and triethylamine (NEt₃, 40 mL) whereby bis(triphenylphosphinepalladium dichloride (PdCl₂(PPh₃)₂, 0.62 g, 0.88 mmol) and copper iodide (CuI, 0.17 g, 0.89 mmol) were added successively. The reaction mixture was stirred under a nitrogen atmosphere for five minutes. Trimethylsilylethyne (2.17 mL, 15.2 mmol) was added drop wise and the resulting mixture was stirred at 48 °C for 24 h. After cooling to ambient temperature, the mixture was filtered through celite, and the celite was washed with EtOAc. The solvents were removed from the filtrate under reduced pressure. The resulting residue was purified by chromatography (EtOAc/hexane, 1:9) affording 2 (3.71 g, 11.4 mmol, 90%) as a faint yellow solid. mp=96 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.07 (d, ³J=9.2 Hz, 1H), 7.43-7.36 (m, 5H), 7.18 (d, ³J=2.8 Hz, 1H), 6.97 (dd, ³J=9.2, 2.8 Hz, 1H), 5.14 (s, 2H), 0.29 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 161.8, 143.2, 135.3, 128.8, 128.5, 127.5, 127.0, 120.7, 120.1, 115.4, 103.7, 99.9, 70.7, 0.4; IR (APT) 1572, 1515, 1333. 1248, 836 cm⁻¹; HRMS (ESI) calcd for C₁₈H₂₀NO₃Si (M+H⁺) 326.1212, found 326.1195.

1-(5-Benzylxy-2-nitrophenyl)ethyne (3). A solution of tetrabutylammonium fluoride (1M in THF) was added drop wise to a 0 °C cold solution of 2 (2.32 g, 7.13 mmol) in THF (30 mL). The resulting mixture was stirred at 0 °C for 30 min. The solvent was removed under reduced pressure and the resulting residue was purified by chromatography (EtOAc/hexane, 2:8) to give 3 (1.63 g, 6.44 mmol, 90%) as a white solid. mp=122 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.10 (d, ³J=9.2 Hz, 1H), 7.45-7.36 (m, 5H), 7.22 (d,
$J=2.8$ Hz, 1H), 7.02 (dd, $J=9.2$, 2.8 Hz, 1H), 5.15 (s, 2H), 3.52 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 161.9, 143.2, 135.1, 128.8, 128.7, 127.5, 127.1, 120.8, 119.7, 115.7, 85.0, 79.0, 70.8; IR (APT) 3284, 1579, 1507, 1327, 1249, 1073 cm$^{-1}$; HRMS (ESI) calcd for C$_{15}$H$_{12}$NO$_3$ (M+H$^+$) 254.0817, found 254.0805.

1-(5-Benzyloxy-2-nitrophenyl)-1-tributylstannylethene (4). To a solution of 3 (1.60 g, 6.32 mmol) in THF (30 mL) under N$_2$ was added PdCl$_2$(PPh$_3$)$_2$ (0.44 g, 0.63 mmol) and tributyltin hydride (2.76 g, 9.48 mmol). The resulting dark brown mixture was stirred at ambient temperature under N$_2$ for 24 h. The mixture was diluted with EtOAc (30 mL) and washed with H$_2$O (3x30 mL) and brine (30 mL). The organic layer was dried (MgSO$_4$), filtered, and the solvents were removed under reduced pressure. The residue was purified by chromatography (EtOAc/hexane, 1:19) affording 4 (2.99 g, 5.49 mmol, 87%) as a brown viscous liquid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.10 (d, $J=9.2$ Hz, 1H), 7.45-7.33 (m, 5H), 6.86 (dd, $J=9.2, 2.4$ Hz, 1H), 6.63 (d, $J=2.4$ Hz, 1H), 5.72 (d, $J=2.4$ Hz, 1H), 5.41 (d, $J=2.0$ Hz, 1H), 5.14 (s, 2H), 1.56-1.37 (m, 6H), 1.27 (sext, $J=7.2$ Hz, 6H), 0.95-0.84 (m, 15H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 162.3, 155.7, 147.6, 139.1, 135.6, 128.7, 128.4, 127.5, 127.1, 124.8, 114.6, 112.7, 70.5, 28.8, 27.3, 13.6, 11.0; IR (ATR) 2954, 2922, 1567, 1329, 1283, 1243, 1228, 694 cm$^{-1}$; HRMS (ESI) calcd for C$_{27}$H$_{40}$NO$_3$Sn (M+H$^+$) 546.2030, found 546.2025.

2,5-Di(1-(5-benzylxoy-2-nitrophenyl)-1-ethenyl)pyrazine (6) and 2,3-di(5-benzylxoy-2-nitrophenyl)-1,3-butadiene (7). To a solution of 2,5-dibromo pyrazine (5) (100 mg, 0.420 mmol) and 4 (458 mg, 0.841 mmol) in dry DMF (2 mL) was added bis(dibenzylideneacetone)palladium (Pd(dba)$_2$, 19.4 mg, 0.034 mmol), CuI (160 mg, 0.841 mmol), and PPh$_3$ (35.3 mg, 0.135 mmol) respectively. The resulting brown mixture was stirred under an atmosphere of N$_2$ at 90°C for 41 h. EtOAc (25 mL) was added and the mixture was washed with H$_2$O (3x25 mL) and brine (3x25 mL). The organic layer was dried (MgSO$_4$), filtered, and the solvents were removed under reduced pressure. The residue was purified by chromatography on SiO$_2$/K$_2$CO$_3$ (10% K$_2$CO$_3$, EtOAc/hexane, 1:9, then 2:8) to give, in order of elution, 7 (85.5 mg, 0.168 mmol, 40%) followed by 6 (96 mg, 0.16 mmol, 39%) both as white solids. Analytical data for 6: mp=186-187°C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.51 (s, 1H), 8.15 (d, $J=9.0$ Hz, 1H), 7.45-7.33 (m, 5H), 7.04 (dd, $J=8.8, 2.4$ Hz, 1H), 7.01 (d, $J=2.4$ Hz, 1H), 6.29 (s, 1H), 5.57 (s, 1H), 5.17 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 162.7, 149.9, 144.7, 141.2, 140.5, 137.8, 135.4, 128.8, 128.5, 127.6, 127.3, 118.8, 118.4, 114.6, 70.8; IR (APT) 1578, 1508, 1326, 1242, 1001, 919, 750 cm$^{-1}$; HRMS (ESI) calcd for C$_{34}$H$_{27}$N$_4$O$_6$ (M+H$^+$) 587.1931, found 587.1925. Analytical data for 7: mp=158-160°C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.08 (d, $J=9.2$ Hz, 1H), 7.48-7.36 (m, 5H), 7.17 (d, $J=2.8$ Hz, 1H), 7.03 (dd, $J=9.2, 2.8$ Hz, 1H), 5.20 (s, 2H), 5.08 (s, 1H), 4.88 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 162.2, 145.6, 141.7,
138.3, 135.5, 128.7, 128.4, 127.8, 126.8, 117.5, 117.1, 114.9, 70.7; IR (ATR) 1573, 1513, 1343, 1230, 1007 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{30}\)H\(_{25}\)N\(_{2}\)O\(_{6}\) (M+H\(^{+}\)) 509.1713, found 509.1715.

5,5'-Dibenzyloxy-3,3'-(2,5-pyrazindiyli)bis-(1(H)-indole (8). To a solution of 5 (114 mg, 0.194 mmol) in dry DMF (2 mL), in a threaded ACE-Glass pressure tube, was added 1,3-bis(diphenylphosphino)propane (dppp, 6 mg, 0.014 mmol), 1,10-phenanthroline (phen, 5 mg, 0.027 mmol) and Pd(dba)\(_{2}\) (8 mg, 0.014 mmol). The tube was filled with a pressure head, and the solution was saturated with 3 cycles of CO (6 atm) and stirred at 120 °C (6 atm CO, 72 h). The reaction mixture was cooled to ambient temperature, diluted with EtOAc (30 mL), and washed with H\(_2\)O (3x30 mL) and brine (3x30 mL). The organic layer was dried (MgSO\(_4\)), filtered, and the solvents were removed under reduced pressure. The residue was purified by chromatography (EtOAc/hexane, 3:7, then 6:4) to afford 8 (90 mg, 0.172 mmol, 89%) as a yellow powder. mp=264-265 °C; \(^1\)H NMR (400 MHz, acetone-\(d_6\)) \(\delta\) 10.63 (s, 1H), 9.09 (s, 1H), 8.22 (d, \(J=2.5\) Hz, 1H), 8.14 (d, \(J=2.8\) Hz, 1H), 7.58 (d, \(J=7.6\) Hz, 2H), 7.46–7.29 (m, 5H), 6.98 (dd, \(J=8.8, 2.5\) Hz, 1H), 5.22 (s, 2H); \(^{13}\)C NMR (100 MHz, acetone-\(d_6\)) \(\delta\) 155.0, 148.0, 141.0, 139.2, 133.6, 129.2, 128.6, 128.5, 127.2, 126.3, 114.5, 113.8, 113.2, 106.3, 71.3; IR (APT) 3228, 2927, 1546, 1478, 1154 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{34}\)H\(_{26}\)N\(_{4}\)O\(_{2}\) (M+H\(^{+}\)) 523.2134, found 523.2116.

Alocasin A. To a solution of 8 (41 mg, 0.078 mmol) in EtOH (2 mL), in a threaded pressure tube, was added Pd/C (10%-Pd, 18 mg, 0.017 mmol). The tube was filled with a pressure head and the mixture was pressurized with H\(_2\) (4 atm) and stirred at 60 °C (12 h). After cooling to ambient temperature, the mixture was filtered through a pad of celite and the celite was washed with warm ethanol (5 mL). The solvent was removed under reduced pressure and residue was purified by chromatography (EtOAc/hexane, 7:3) to afford alocasin A (23 mg, 0.067 mmol, 86%) as a faint yellow solid. mp=244-245 °C (lit. mp=243-244 °C); \(^1\)H NMR (400 MHz, CD\(_3\)OD) \(\delta\) 8.94 (s, 2H), 7.90 (s, 2H), 7.72 (d, \(J=2.4\) Hz, 2H), 7.30 (d, \(J=8.4\) Hz, 2H), 6.79 (dd, \(J=8.8, 2.4\) Hz, 2H); \(^{13}\)C NMR (100 MHz, CD\(_3\)OD) \(\delta\) 152.8, 148.4, 141.4, 133.6, 127.3, 126.6, 113.8, 113.3, 113.2, 106.1; IR (ATR) 3228, 2927, 1546, 1478, 1154 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{20}\)H\(_{15}\)N\(_{4}\)O\(_{2}\) (M+H\(^{+}\)) 343.1195, found 343.1188.

2,3-Di(5-benzyloxy-2-nitrophenyl)-1,3-butadiene (7). To a solution of 3,5-dibromopyridine (9) (217 mg, 0.919 mmol) and 4 (1.00 g, 1.84 mmol) in dry DMF (6 mL) was added Pd(dba)\(_{2}\) (52.8 mg, 0.092 mmol), CuI (350 mg, 1.84 mmol), and PPh\(_3\) (96.4 mg, 0.367 mmol) respectively. The resulting brown mixture was stirred under an atmosphere of N\(_2\) at 80 °C for 24 h. EtOAc (25 mL) was added and the mixture was washed with brine (6x50 mL). The organic layer was dried (MgSO\(_4\)), filtered, and the solvents were removed under reduced pressure. The residue was purified by chromatography on SiO\(_2\)/K\(_2\)CO\(_3\) (10% K\(_2\)CO\(_3\), EtOAc/hexane, 1:9, then 2:8) to give 7 (139 mg, 0.273 mmol, 30%).
3,5-(1-Tributylstannyl-1-ethenyl)pyridine (11). Treatment of 3,5-diethynylpyridine (10)\(^{42}\) (150 mg, 1.18 mmol) with \(Bu_3SnH\) (1.03 mg, 3.59 mmol) in the presence of PdCl\(_2\)(PPh\(_3\))\(_2\) (100 mg, 0.142 mmol) in THF (4 mL), as described for 4 (36 h), gave after work up and chromatography (EtOAc/hexanes, 2:98) 11 (510 mg, 0.719 mmol, 61\%) as yellow oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.24 (d, \(J=2.4\) Hz, 1H), 7.23 (t, \(J=2.0\) Hz, 1H), 6.05 (d, \(J=2.4\) Hz, 1H), 5.51 (d, \(J=2.4\) Hz, 1H), 1.57 - 1.24 (m, 6H), 1.29 (sext, \(J=7.2\) Hz, 6H), 1.07 - 0.79 (m, 15H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 151.3, 145.4, 141.5, 130.4, 128.7, 29.0, 27.2, 13.6, 10.3; IR (ATR) 2956, 2925, 1463, 920 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{33}\)H\(_{62}\)NSn\(_2\) (M+H\(^+\)) 712.2926, found 712.2929.

2-Iodo-4-benzyl-1-nitrobenzene (12). A mixture of 3-iodo-4-nitrophenol (5.83 g, 22.0 mmol), benzyl bromide (4.86 g, 35.2 mmol) and K\(_2\)CO\(_3\) (5.64 g, 40.8 mmol) in absolute EtOH (50 mL) was heated at reflux for 18 h. The resulting mixture was concentrated under reduced pressure and EtOAc (50 mL) was added to the resulting residue. The mixture was washed with water (3x40 mL), dried (MgSO\(_4\)), and filtered. The filtrate was concentrated under reduced pressure and the resulting residue was purified by chromatography (EtOAc/hexanes, 2:8) to afford 12 (7.32 g, 20.6 mmol, 94\%) as an orange-yellow solid. mp=73-75 \(^o\)C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.97 (d, \(J=9.2\) Hz, 1H), 7.63 (d, \(J=2.8\) Hz, 1H), 7.00 (dd, \(J=8.8, 2.8\) Hz, 1H), 5.12 (s, 2H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 161.6, 145.4, 135.0, 128.8, 128.6, 128.0, 127.5, 127.5, 114.7, 88.1, 70.8; IR (ATR) 1575, 1507, 1332, 1241, 982 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{13}\)H\(_{11}\)INO\(_3\) (M+H\(^+\)) 355.9784, found 355.9785.

3,5-Di(5-benzyl-2-nitrophenyl)pyridine (13). Reaction of 11 (750 mg, 1.06 mmol) with 12 (1.13 g, 3.17 mmol) in the presence of Pd(dba)\(_2\) (61 mg, 0.11 mmol, PPh\(_3\) (111 mg, 0.423 mmol) and CuI (403 mg, 2.11 mmol) in DMF (6 mL), as described for 5 (120 \(^o\)C, 48 h) gave after work up and chromatography (EtOAc/hexanes, 2:8 then 3:7) 13 (216 mg, 0.369 mmol, 35\%) as viscous yellow oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.33 (d, \(J=2.0\) Hz, 2H), 8.07 (d, \(J=8.8\) Hz, 2H), 7.51 (t, \(J=2.0\) Hz, 1H), 7.46-7.37 (m, 10H), 7.04 (dd, \(J=9.2, 2.8\) Hz, 2H), 6.98 (d, \(J=2.8\) Hz, 2H), 5.73 (s, 2H), 5.36 (s, 2H), 5.17 (s, 4H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 162.4, 146.8, 144.1, 141.2, 138.4, 135.3, 134.4, 130.8, 128.8, 128.5, 127.6, 127.4, 118.2, 116.8, 114.7, 70.8; IR (ATR) 1572, 1507, 1332, 1241, 982 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{35}\)H\(_{28}\)N\(_3\)O\(_6\) (M+H\(^+\)) 586.1978, found 586.1979.

3,5-Bis(5-benzyl-3-indolyl)pyridine (14). Treatment of a solution of 13 (176 mg, 0.300 mmol) in the presence of Pd\(_2\)(dba)\(_3\) (28 mg, 0.030 mmol), dppp (12 mg, 0.030 mmol), and phen (11 mg, 0.060 mmol) in DMF (1.5 mL) with CO (6 atm), as described for 8 (120 \(^o\)C, 68 h), gave after work up and chromatography (EtOAc/hexanes, in order 7:3, 3:7) 14 (105 mg, 0.201 mmol, 67\%) as a viscous yellow oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.91 (br, s, 2H), 8.84 (d, \(J=2.0\) Hz, 2H), 8.12 (t, \(J=2.0\) Hz, 1H), 7.50
(d, J=2.4 Hz, 2H), 7.44-7.42 (m, 4H), 7.35-7.24 (m, 10H), 7.02 (dd, J=8.8, 2.4 Hz, 2H), 5.07 (s, 4H); ^13^C NMR (100 MHz, CDCl$_3$) δ 154.0, 145.2, 137.4, 132.6, 132.1, 131.9, 128.4, 127.7, 127.5, 125.9, 123.4, 114.1, 113.5, 112.4, 102.9, 70.9; IR (ATR) 3427, 3287, 1594, 1477, 1196 cm$^{-1}$; HRMS (ESI) calcd for C$_{35}$H$_{28}$N$_3$O$_2$ (M+H$^+$) 522.2181, found 522.2182.

Scalaridine A. Treatment of a solution of 14 (87 mg, 0.168 mmol) with Pd/C (10%, 21 mg, 0.020 mmol) in EtOH (1.5 mL), as described for alocasin A (4 atm, 60 °C, 12 h) gave after work up and chromatography (EtOAc), scalaradine A (45 mg, 0.13 mmol, 79%) as yellow solid. mp=321 °C dec. (lit. mp = 319-329 °C dec.);

$^{1}$H NMR (400 MHz, DMSO-d$_6$) δ 11.26 (br, s, 2H), 8.80 (s, 2H), 8.69 (br, s, 2H), 8.18 (s, 1H), 7.78 (d, J=2.4 Hz, 2H), 7.29 (d, J=8.8 Hz, 2H), 7.23 (d, J=2.4 Hz, 2H), 6.70 (dd, J=8.4, 2.0 Hz, 2H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 151.6, 143.7, 132.0, 131.8, 130.0, 125.6, 124.5, 112.6, 112.0, 111.5, 102.6; IR (ATR) 3427, 3286, 1594, 1475, 1195 cm$^{-1}$; HRMS (ESI) calcd for C$_{21}$H$_{16}$N$_3$O$_2$ (M+H$^+$) 342.1243, found 342.1240.

(5-Benzylthio-2-nitrophenyl)ethene (16), 2,3-di(5-benzylthio-2-nitrophenyl)-1,3-butadiene (7), 1-(5-benzylthio-2-nitrophenyl)-1-(2-pyrimidyl)ethene (17). Reaction of 2,5-dibromopyrimidine (15) (300 mg, 1.26 mmol) and 4 (2.06 g, 3.78 mmol) in the presence of Pd(dba)$_2$ (73 mg, 0.13 mmol), CuI (720 mg, 3.78 mmol), and PPh$_3$ (132 mg, 0.504 mmol) in dry DMF (5 mL) under argon as described for 5 (100 °C, 48 h), gave after work up and chromatography on SiO$_2$/K$_2$CO$_3$ (10% K$_2$CO$_3$, EtOAc/hexane, 1:9, then 2:8), in order of elution, 16 (101 mg, 0.396 mmol, 10%) as a white solid, an inseparable mixture of 7 and an unknown impurity (90 mg, <8%) as a white solid, and 17 (114 mg, 0.342 mmol, 27%) as a viscous greenish-brown oil. Analytical data for 16 mp=58-59 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 8.05 (d, J=9.2 Hz, 1H), 7.44-7.32 (m, 5H), 7.30 (dd, J=17.2, 10.8 Hz, 1H), 7.11 (d, J=2.8 Hz, 1H), 6.94 (dd, J=9.2, 2.8 Hz, 1H), 5.65 (dd, J=17.2, 0.8 Hz, 1H), 5.46 (dd, J=11.2, 0.8 Hz, 1H), 5.17 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 162.3, 140.9, 136.7, 135.5, 133.7, 128.8, 128.5, 127.5, 127.3, 118.6, 114.4, 114.0, 70.6; IR (ATR) 1581, 1501, 1238, 1078, 987, 930 cm$^{-1}$; HRMS (ESI) calcd for C$_{19}$H$_{16}$N$_3$O$_3$ (M+H$^+$) 334.1192, found 334.1190.

2,5-Di(2-trimethylsilyl-1-ethynyl)pyrimidine (18). A solution of 15 (2.25 g, 9.49 mmol), PdCl$_2$(PPh$_3$)$_2$ (666 mg, 0.949 mmol), and CuI (362 mg, 1.90 mmol) in toluene (9 mL) was stirred at ambient
temperature under an atmosphere of N$_2$ for 5 min. Triethylamine (25 mL) and a solution of trimethylsilylethyne (2.52 g, 25.6 mmol) in NEt$_3$ (4 mL) was added. The resulting dark brown reaction mixture was stirred at 50 °C for 24 h. After cooling to ambient temperature, the mixture was filtered through Celite and the bed was washed with Et$_2$O (25 mL). The filtrate was concentrated under reduced pressure and the resulting residue was purified by chromatography (EtOAc/hexanes, 5:95) to afford 18 (2.59 g, 0.949 mmol, 100%) as pale green solid. mp=99-100 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 8.72 (s, 2H), 0.29 (s, 9H), 0.27 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 159.2, 149.9, 118.2, 104.6, 102.1, 97.6, 96.8, -0.4, -0.6; IR (ATR) 2963, 2163, 1413, 1245, 838 cm$^{-1}$; HRMS (ESI) calcd for C$_{14}$H$_{21}$N$_2$Si$_2$ (M+H$^+$) 273.1243, found 273.1240.

2,5-Diethynylpyrimidine (19). A heterogeneous mixture of 18 (744 mg, 2.94 mmol), K$_2$CO$_3$ (2.43 g, 17.6 mmol) in MeOH/Et$_2$O (1:2, 15 mL) was stirred at ambient temperature under an N$_2$ atmosphere for 1 h. Water (20 mL) was added and the mixture was extracted in EtOAc (3x10 mL). The combined organic layer was concentrated under reduced pressure and the resulting crude product was purified by chromatography (EtOAc/hexanes, 1:1) to afford 19 (326 mg, 2.54 mmol, 93%) as a white solid. mp=97-98 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 8.79 (s, 2H), 3.49 (s, 1H), 3.26 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 159.6, 150.2, 117.8, 86.1, 81.5, 78.0, 76.7; IR (ATR) 3291, 3180, 2129, 2100, 1415 cm$^{-1}$; HRMS (ESI) calcd for C$_8$H$_5$N$_2$ (M+H$^+$) 129.0452, found 129.0448.

2,5-Di(1-tributylstannyl-1-ethenyl)pyrimidine (20). THF (4 mL) was added to a flask containing 19 (257 mg, 2.01 mmol) and PdCl$_2$(PPh$_3$)$_2$ (169 mg, 0.241 mmol) under an atmosphere of N$_2$. The mixture was stirred at ambient temperature for 5 min followed by slow addition of Bu$_3$SnH (1.75 g, 6.03 mmol) dissolved in THF (1 mL). The resulting brown mixture was stirred at the ambient temperature for 34 h. The mixture was then concentrated under reduced pressure and the residue was purified by chromatography (EtOAc/hexanes, 2:98) to give 20 (566 mg, 0.797 mmol, 40%) as pale yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.47 (s, 2H), 7.10 (d, $J$=2.8 Hz, 1H), 6.12 (d, $J$=2.0 Hz, 1H), 5.86 (d, $J$=2.8 Hz, 1H), 5.56 (d, $J$=2.4 Hz, 1H), 1.58-1.43 (m, 12H), 1.30 (dhex, $J$=7.2, 3.2 Hz, 12H), 1.04-0.84 (m, 30H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 166.7, 154.4, 153.9, 147.8, 147.8, 136.3, 132.4, 129.7, 29.1, 28.9, 27.3, 27.2, 13.7, 13.6, 10.4, 10.3; IR (ATR) 2955, 2922, 2852, 1427 cm$^{-1}$; HRMS (ESI) calcd for C$_{32}$H$_{61}$N$_2$Sn$_2$ (M+H$^+$) 713.2879, found 713.2883.

2,5-Di[1-(5-benzyloxy-2-nitrophenyl)-1-ethenyl]pyrimidine (21). Treatment of 20 (436 mg, 0.615 mmol) with 12 (655 mg, 1.84 mmol) in the presence of Pd$_2$(dba)$_3$ (56 mg, 0.061 mmol), PPh$_3$ (65 mg, 0.25 mmol) and Cul (234 mg, 1.23 mmol) in DMF (5 mL), as described for 5 (120 °C, 48 h), gave after work up and chromatography (EtOAc/hexanes, 1:9 then 8:2) 21 (189 mg, 0.323 mmol, 53%) as viscous
yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.52 (s, 2H), 8.16 (dd, $J$=8.0, 0.8 Hz, 1H), 8.12 (d, $J$=8.8 Hz, 1H), 7.44-7.35 (m, 10H), 7.06-7.01 (m, 3H), 6.96 (d, $J$=2.4 Hz, 1H), 6.86 (d, $J$=1.2 Hz, 1H), 5.81 (s, 1H), 5.76 (d, $J$=1.2 Hz, 1H), 5.37 (s, 1H), 5.17 (s, 2H), 5.16 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 162.7, 162.5, 162.5, 154.0, 146.4, 141.5, 141.5, 140.7, 138.1, 137.5, 135.5, 135.1, 130.1, 128.8, 128.7, 128.5, 128.4, 127.6, 127.6, 127.5, 126.9, 122.4, 118.2, 118.2, 116.9, 114.8, 114.0, 70.8, 70.6; IR (ATR) 1574, 1509, 1334, 1228, 1003 cm$^{-1}$; HRMS (ESI) calcd for C$_{34}$H$_{27}$N$_4$O$_6$ (M+H$^+$) 587.1931, found 587.1934.

3-[2-(5-benzylxoy-1H-indol-3-yl)-5-pyrimidinyl]-5-benzylxoy-1H-indole (22). Treatment of a solution of 21 (141 mg, 0.240 mmol) in the presence of tris(dibenzylideneacetone)dipalladium (Pd$_2$(dba)$_3$, 22 mg, 0.024 mmol), dppp (10 mg, 0.024 mmol), and phen (9 mg, 0.048 mmol) in DMF (1.5 mL) with CO (6 atm), as described for 8 (120 °C, 60 h), gave after work up and chromatography (hexanes/EtOAc, 3:7) 22 (85 mg, 0.163 mmol, 68%) as a yellow solid. mp=199-200 °C; $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 11.54 (br, s, 1H), 11.46 (br, s, 1H), 9.09 (s, 2H), 8.26 (s, 1H), 8.19 (s, 1H), 7.55-7.32 (m, 13H), 6.94 (d, $J$=8.4 Hz, 2H), 5.20 (s, 2H), 5.17 (s, 2H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 160.6, 153.7, 154.4, 153.2, 137.8, 137.7, 132.3, 132.0, 129.0, 128.3, 128.3, 127.8, 127.7, 126.6, 126.1, 125.0, 124.9, 124.6, 114.6, 112.8, 112.7, 112.5, 112.2, 109.3, 105.7, 102.3, 69.9, 69.9; IR (ATR) 3409, 2884, 1543, 1447, 1199 cm$^{-1}$; HRMS (ESI) calcd for C$_{34}$H$_{27}$N$_4$O$_6$ (M+H$^+$) 523.2135, found 523.2135.

Hyrtinandine A. Treatment of a solution of 22 (56 mg, 0.107 mmol) with Pd/C (10%-Pd, 14 mg, 0.013 mmol) in MeOH (2 mL), as described for alocasine A (4 atm H$_2$, 60 °C, 14 h) gave after work up and chromatography (EtOAc/hexanes, 9:1) hyrtinadine A (32 mg, 0.093 mmol, 87%) as a white solid. mp=290-291 °C (lit. mp = 296 °C); $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 11.38 (br s, 1H), 11.29 (br s, 1H), 8.99 (s, 2H), 8.84 (s, 2H), 8.11 (d, $J$=3.2 Hz, 1H), 7.97 (d, $J$=2.4 Hz, 1H), 7.80 (d, $J$=2.8 Hz, 1H), 7.30-7.25 (m, 2H), 7.20 (d, $J$=1.6 Hz, 1H), 6.73-6.68 (m, 2H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 160.7, 153.5, 151.8, 151.6, 131.4, 131.3, 128.7, 126.4, 125.4, 125.0, 124.2, 114.1, 112.6, 112.2, 112.1, 112.0, 108.6, 106.2, 102.7. IR (ATR) 3295, 1542, 1448, 1364, 1229 cm$^{-1}$; HRMS (ESI) calcd for C$_{20}$H$_{15}$N$_4$O$_2$ (M+H$^+$) 343.1195, found 343.1194.

1-(5-Pyrimidyl)-1-tributylstannylethene (24). Treatment of 5-ethynylpyrimidine 23 (388 mg, 3.73 mmol) with tributyltin hydride (1.63 g, 5.59 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (262 mg, 0.373 mmol) in THF (9 mL), as described for 4 (ambient temperature, 36 h), gave after work up and chromatography (EtOAc/hexanes, 5:95) 24 (1.02 g, 2.57 mmol, 69%) as pale yellow oil. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 9.04 (s, 1H), 8.52 (s, 2H), 6.10 (d, $J$=1.8 Hz, 1H), 5.62 (d, $J$=2.4 Hz, 1H), 1.52-1.42 (m, 6H), 1.29 (sext, $J$=7.8 Hz, 6H), 1.06-0.84 (m, 15H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 156.4, 153.9, 147.5,
139.7, 130.9, 28.8, 27.1, 13.5, 10.2; IR (APT) 2956, 2925, 1544, 1407 cm⁻¹; HRMS (ESI) calcd for C₁₈H₃₃N₂Sn (M+H⁺) 397.1666, found 397.1666.

1-(5-Benzyloxy-2-nitrophenyl)-1-(4-pyrimidyl)ethene (25). To mixture of 12 (584 mg, 1.64 mmol), PPh₃ (66 mg, 0.25 mmol), Cul (241 mg, 1.26 mmol) and Pd₂dba₃ (58 mg, 0.063 mmol) in DMF (5 mL) at ambient under an atmosphere of N₂, was added a solution of 24 (500 mg, 1.26 mmol) in DMF (1 mL). The resulting brown reaction mixture was heated at 120 °C for 36 h. After cooling to ambient temperature, the mixture was diluted with EtOAc (30 mL) and the organic layer was washed with water (4x20 mL) and brine (20 mL). The organic phase was dried over MgSO₄, filtered, and the solvent was removed under reduced pressure. The crude product was purified by column (EtOAc/hexanes, 3:7, then 1:1) to afford 25 (223 mg, 0.669 mmol, 53%) as viscous pale brown oil that slowly solidified. mp=113 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.11 (s, 1H), 8.62 (s, 2H), 8.17 (d, J=8.8, 1H), 7.45-7.37 (m, 5H), 7.09 (dd, J=8.8, 2.4 Hz, 1H), 6.99 (d, J=2.8 Hz, 1H), 5.82 (s, 1H), 5.44 (s, 1H), 5.19 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 162.5, 157.7, 153.9, 141.5, 137.3, 135.0, 132.6, 128.7, 128.5, 127.7, 127.4, 118.4, 117.7, 114.6, 70.7; IR (APT) 1575, 1510, 1340, 1223 cm⁻¹; HRMS calcd for C₁₉H₁₆N₃O₃ (M+H⁺) 334.1192, found 334.1190.

5-Benzylx-3-(4-pyrimidyl)indole (26). Treatment of a solution of 25 (200 mg, 0.600 mmol) in the presence of Pd₂(dba)₃ (33 mg, 0.036 mmol), dppp (15 mg, 0.036 mmol), and phen (13 mg, 0.072 mmol) in DMF (2 mL) with CO (6 atm), as described for 8 (120 °C, 28 h), gave after work up and chromatography (EtOAc/hexanes, 7:3) 26 (163 mg, 0.540 mmol, 90%) as a white solid. mp=189 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.14 (s, 1H), 9.00 (s, 2H), 8.52 (br, s, 1H), 7.48 (d, J=7.2 Hz, 2H), 7.45 (d, J=2.8 Hz, 1H), 7.42-7.31 (m, 5H), 7.05 (dd, J=8.4, 2.0 Hz, 1H), 5.12 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 156.0, 154.5, 154.4, 137.2, 131.9, 129.9, 128.6, 127.9, 127.6, 125.5, 123.3, 114.2, 112.6, 110.7, 102.3, 70.9; IR (ATR) 3017, 1533, 1486, 1157 cm⁻¹; HRMS (ESI) calcd for C₁₉H₁₆N₃O (M+H⁺) 302.1293, found 302.1291.

Hyrninadine B. Treatment of a solution of 21 (90 mg, 0.30 mmol) with Pd/C (10%, 28 mg, 0.026 mmol) in MeOH (1.5 mL), as described for alocasin A (4 atm H₂, 60 °C, 6 h) gave after work up and chromatography (EtOAc) hyrinadine B (53 mg, 0.251 mmol, 84%) as a white solid. mp=289-290 °C; ¹H NMR (400 MHz, CD₃OD) δ 9.05 (s, 2H), 8.89 (s, 1H), 7.62 (s, 1H), 7.24 (d, J=8.4 Hz, 1H), 7.16 (d, J=2.4 Hz, 1H), 6.72 (dd, J=8.8, 2.0 Hz, 1H); ¹³C NMR (100 MHz, CD₃OD) δ 155.5, 155.0, 153.3, 133.7, 133.1, 127.0, 126.1, 113.8, 113.8, 109.5, 103.8; IR (ATR) 3327, 2727, 1557, 1420, 1386 cm⁻¹; HRMS (ESI) calcd for C₁₂H₁₀N₃O (M+H⁺) 212.0824, found 212.0821.
[(6-Chloro-2-nitrophenyl)methyl]triphenylphosphonium bromide (28). To a solution of 2-chloro-6-nitrobenzylbromide (3.03 g, 12.1 mmol) in toluene (36 mL) was added, in portions, triphenylphosphine (PPh₃, 3.49 g, 13.3 mmol). The resulting solution was stirred under a nitrogen atmosphere, at 100 °C, for 12 h. A precipitate started to form after 15 min. The mixture was cooled to ambient temperature, the precipitate was removed by filtration, the solid was washed with Et₂O and the solvents were removed to afford 28 (6.21 g, 12.1 mmol, 100%) as a white solid. mp=235-243 °C; ¹H NMR (600 MHz, DMSO-d₆) δ 7.96 (d, J=8.4 Hz, 1H), 7.89-7.85 (m, 4H), 7.73-7.66 (m, 12H), 7.63 (td, J=7.8, 1.8 Hz, 1H), 5.34 (d, J=14.4 Hz, 2H); ¹³C NMR (150 MHz, DMSO-d₆) δ 149.7 (d, J=3.0 Hz), 133.8 (d, J=10.5 Hz), 131.8 (d, J=13.5 Hz), 124.9 (d, J=3.0 Hz), 123.5 (d, J=13.5 Hz), 117.9 (d, J=8.4 Hz), 25.9 (d, J=8.4 Hz); IR (ATR) 1533, 1434, 1355, 1107, 748 cm⁻¹; HRMS (ESI, negative ion mode) calcd for C₂₅H₂₀BrClNO₂P (M⁻) 511.0104, found 511.0133.

[(3-Methoxy-2-nitrophenyl)methyl] triphenylphosphonium bromide (29). Treatment of 3-methoxy-2-nitrobenzylbromide (1.48 g, 6.05 mmol) with PPh₃ (1.74 g, 6.64 mmol) in toluene (15 mL) as described for 28 (100 °C, 12 h), gave after work up 29 (2.67 g, 5.26 mmol, 87%) as a white solid. mp=213-215 °C; ¹H NMR (600 MHz, DMSO-d₆) δ 7.92 (t, J=7.8 Hz, 3H), 7.74 (dt, J=7.8, 3.6 Hz, 6H), 7.63 (dd, J=8.4, 7.2 Hz, 6H), 7.42 (t, J=8.4 Hz, 1H), 7.35 (d, J=9.0 Hz, 1H), 6.66 (dd, J=8.4, 2.4 Hz, 1H), 5.10 (d, J=15.0 Hz, 2H), 3.84 (s, 3H); ¹³C NMR (150 MHz, DMSO-d₆) δ 149.7 (d, J=6.0 Hz), 133.8 (d, J=8.4 Hz), 131.8 (d, J=8.4 Hz), 117.9 (d, J=8.4 Hz), 25.9 (d, J=8.4 Hz); IR (ATR) 1536, 1433, 1355, 1108, 685 cm⁻¹; HRMS (ESI, negative ion mode) calcd for C₂₅H₂₀BrNO₂P (M⁻) 507.0599, found 507.0628.

[(4-Bromo-2-nitrophenyl)methyl] triphenylphosphonium bromide (30). Treatment of 4-bromo-2-nitrobenzylbromide (208 mg, 0.705 mmol) with PPh₃ (203 mg, 0.774 mmol) in toluene (8 mL) as described for 28 (100 °C, 8 h), gave after work up 30 (393 mg, 0.705 mmol, 100%) as a white solid. mp=242-244 °C; ¹H NMR (400 MHz, DMSO-d₆) δ 8.24 (d, J=2.0 Hz, 1H), 7.97-7.90 (m, 3H), 7.92(d, J=1.6 Hz, 1H), 7.77-7.72 (m, 6H), 7.66-7.61 (m, 6H), 7.31 (dd, J=8.0, 2.4 Hz, 1H), 5.42 (d, J=15.2 Hz, 2H); ¹³C NMR (150 MHz, DMSO-d₆) δ 151.4 (d, J=2.2 Hz), 140.9(d, J=6.9 Hz), 135.3 (d, J=3.4 Hz), 133.9 (d, J=10.2 Hz), 132.1 (d, J=3.4 Hz), 130.2 (d, J=12.6 Hz), 123.1 (d, J=9.0 Hz), 121.8 (d, J=7.9 Hz), 117.1 (d, J=8.4 Hz), 114.3 (d, J=2.2 Hz), 57.0, 25.3 (d, J=49.2 Hz); IR (ATR) 1536, 1433, 1281, 1108, 685 cm⁻¹; HRMS (ESI) calcd for C₂₆H₂₁BrNO₃P (M) 570.0599, found 570.0628.

93
3-((5-Bromo-2-nitrophenyl)-2-propenal (32) and 5-(5-Bromo-2-nitrophenyl)-2,4-pentadienal (43). A mixture of 5-bromo-2-nitrobenzaldehyde (600 mg, 2.61 mmol), (formylmethyl)triphenylphosphonium chloride (1.78 mg, 5.22 mmol) and DMAP (956 mg, 7.82 mmol) in CHCl₃ (36 mL) was stirred at ambient temperature for 4 h followed by heating at reflux for 3 h. After cooling to ambient temperature, the solvent was removed under reduced pressure and the resulting crude product was purified by chromatography (hexane/EtOAc, 95:5) to afford, in order of elution, 32 (337 mg, 1.32 mmol, 51%) and 43 (153 mg, 0.542 mmol, 21%) both as pale yellow solids. Analytical data for 32: mp=125-130 °C; ¹H NMR (600 MHz, CDCl₃) δ 9.78 (d, J=7.2 Hz, 1H), 8.01 (d, J=3.0 Hz, 1H), 7.99 (d, J=9.6 Hz, 1H), 7.80 (d, J=1.8 Hz, 1H), 7.73 (dd, J=9.0, 1.8 Hz, 1H), 6.61 (dd, J=15.5, 7.8 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 192.5, 146.5, 145.7, 133.9, 133.4, 132.0, 131.9, 128.8, 126.7; IR (ATR) 1675, 1521, 1345, 1098, 834 cm⁻¹; HRMS (ESI, negative ion mode) calcd for C₉H₆BrNO₃ (M⁻) 254.9531, found 254.9530.

Analytical data for 43: mp=110-119 °C; ¹H NMR (600 MHz, CDCl₃) δ 9.68 (d, J=7.8 Hz, 1H), 7.92 (d, J=2.4 Hz, 1H), 7.62 (dd, J=9.0, 1.8 Hz, 1H), 7.50 (d, J=15.6 Hz, 1H), 7.30 (dd, J=15.6, 10.8 Hz, 1H), 6.96 (dd, J=15.6, 11.4 Hz, 1H), 6.36 (dd, J=15.0, 7.8 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 193.2, 149.8, 146.6, 135.0, 134.1, 133.1, 132.5, 131.8, 131.4, 128.4, 126.6; IR (ATR) 3417, 1676, 1512, 1345, 1334, 1117, 983 cm⁻¹; HRMS (ESI, negative ion mode) calcd for C₁₁H₈BrNO₃ (M⁻) 280.9688, found 280.9709.

E,E-1-(2-Chloro-6-nitrophenyl)-4-(2-nitrophenyl)-1,3-butadiene (34). A solution of freshly prepared sodium ethoxide (NaOEt, 1.5 M in EtOH, 6 mL, 9.0 mmol) was added drop wise to a solution of 31 (389 mg, 2.20 mmol) and 28 (1.13 g, 2.20 mmol) in absolute EtOH (9 mL) at ambient temperature. The reaction mixture turned dark purple slowly changing to red. After 36 h at ambient temperature, water (30 mL) was added, and the mixture was extracted with EtOAc (3 x 15 mL). The combined organic phases were dried (MgSO₄), filtered, and the solvents were removed under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 9:1, then 8:2) to give 34 (399 mg, 1.21 mmol, 55%) as an orange solid. mp=153-155 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.92 (dd, J=8.0, 0.8 Hz, 1H), 7.90 (dd, J=8.4, 1.2 Hz, 1H), 7.82 (dd, J=8.4, 1.2 Hz, 1H), 7.73-7.63 (m, 3H), 7.60 (td, J=7.2, 0.4 Hz, 1H), 7.51 (td, J=8.0, 0.8 Hz, 1H), 7.46-7.32 (m, 6H), 7.19 (d, J=15.2 Hz, 1H), 7.17 (d, J=15.2 Hz, 1H), 6.93 (dd, J=13.4, 10.0 Hz, 1H), 6.83 (d, J=15.6 Hz, 1H), 6.73-6.59 (m, 3H), 6.40 (dd, J=15.2, 10.0 Hz, 1H); ¹³C NMR (100 MHz, DMSO-d₆) δ 150.7, 150.3, 147.9, 147.8, 136.6, 135.7, 135.1, 133.7, 133.6, 133.2, 133.0, 133.0, 132.9, 132.2, 132.0, 130.8, 130.2, 129.7, 128.9, 128.4, 128.3, 128.3, 127.9, 127.7, 125.8, 124.7, 124.6, 124.3, 122.5, 122.4; IR (ATR) 1515, 1343, 986, 751, 725 cm⁻¹; HRMS (ESI) calcd for C₁₅H₁₂ClN₂O₂ (M+H⁺) 331.0485, found 331.0480.
**EE/EZ-1-(3-Methoxy-2-nitrophenyl)-4-(2-nitrophenyl)-1,3-butadiene (35).** Treatment of a solution of 31 (300 mg, 1.69 mmol) and 29 (861 mg, 1.69 mmol) in EtOH (18 mL) in the presence of NaOEt (1.7 M, 11 mL, 18.7 mmol), as described for 34 (24 h), gave after work up and chromatography (hexane/EtOAc, 8:2, then 7:3) 35 (354 mg, 1.08 mmol, 64%, EE/EZ=1:1) as an orange solid. mp=130-135 °C; 1H NMR (600 MHz, DMSO-d6) δ 7.97-7.95 (m, 3H), 7.76 (dd, J=7.9, 1.4 Hz, 1H), 7.71 (dd, J=7.8, 1.3 Hz, 1H), 7.68 (dd, J=7.9, 1.3 Hz, 1H), 7.59 (t, J=8.3 Hz, 1H), 7.56-7.51 (m, 4H), 7.41-7.30 (m, 3H), 7.25 (dd, J=8.3, 0.8 Hz, 1H), 7.17 (d, J=15.2 Hz, 1H), 7.16 (d, J=7.9 Hz, 1H), 7.13 (d, J=15.2 Hz, 1H), 7.03 (dd, J=15.2, 11.5 Hz, 1H), 6.73 (t, J=11.4 Hz, 1H), 6.59 (d, J=15.5 Hz, 1H), 6.45 (d, J=11.3 Hz, 1H), 3.92 (s, 3H), 3.90 (s, 3H); 13C NMR (150 MHz, CDCl3, major and minor) δ 150.3, 150.2, 147.9, 147.8, 139.9, 139.7, 134.4, 133.9, 133.6, 133.5, 133.2, 131.6, 131.3, 130.9, 130.9, 130.8, 129.3, 129.1, 129.1, 128.9, 128.7, 128.3, 128.2, 127.7, 125.5, 124.4, 124.4, 124.1, 121.9, 117.4, 112.8, 112.5, 56.7, 56.7; IR (ATR) 1519, 1369, 1343, 1285, 1063 cm⁻¹; HRMS (ESI) calcd for C17H15N2O3 (M+H⁺) 327.0981, found 327.0976.

**EE/EZ-1-(4-Bromo-2-nitrophenyl)-4-(2-nitrophenyl)-1,3-butadiene (36).** Treatment of a solution of 31 (51 mg, 0.29 mmol) and 30 (155 mg, 0.278 mmol) in EtOH (7 mL) in the presence of NaOEt (1.7 M, 7 mL, 11.9 mmol), as described for 34 (36 h), gave after work up and chromatography (hexane/EtOAc, 9:1) 36 (78.4 mg, 0.209 mmol, 73%, EE/EZ=1:2) as an orange solid. NMR data from the EE/EZ=1:2 mixture of 36: mp=141-142 °C; 1H NMR (600 MHz, DMSO-d6) δ 8.32 (d, J=2.1 Hz, 1H), 8.19 (d, J=2.1 Hz, 0.5H), 7.99-7.94 (m, 3H), 7.91 (dd, J=8.6, 2.0 Hz, 0.5H), 7.78 (dd, J=8.0, 1.3 Hz, 1H), 7.72 (t, J=6.7 Hz, 0.5H), 7.65 (dd, J=7.4, 0.7 Hz, 1H), 7.54-7.50 (m, 3H), 7.38 (dd, J=15.1, 10.5 Hz, 0.5H), 7.31 (dd, J=14.9, 10.6 Hz, 0.5H), 7.17-7.14 (m, 1.5H), 7.05-6.98 (m, 1.5H), 6.79 (d, J=11.4 Hz, 1H), 7.73 (t, J=11.2 Hz, 1H); 13C NMR (150 MHz, DMSO-d6) δ 148.3, 148.2, 147.9, 147.8, 136.3, 135.8, 134.6, 134.0, 133.7, 133.3, 133.2, 131.8, 130.9, 130.7, 130.4, 130.2, 129.3, 129.0, 128.9, 128.9, 128.5, 128.2, 128.2, 127.7, 127.2, 127.1, 126.9, 122.4, 124.3, 120.7, 120.6; IR (ATR) 3027, 1520, 1347, 1217, 748 cm⁻¹; HRMS (ESI) calcd for C18H13BrN2O4 (M+H⁺) 374.9980, found 374.9975.

**EZ/EE-1-(4-Bromo-2-nitrophenyl)-4-(5-bromo-2-nitrophenyl)-1,3-butadiene (37).** Treatment of a solution of 32 (320 mg, 1.25 mmol) with 30 (696 mg, 1.25 mmol) in the presence of NaOEt (2.0 M in EtOH, 2.81 mL, 5.62 mmol) in EtOH (16 mL), as described for 34 (24 h) gave after work up and chromatography (hexane/EtOAc, 9:1) 37 (424 mg, 0.934 mmol, 75%, EZ/EE=7:1) as an orange solid. mp=159-162 °C; 1H NMR data from the EZ/EE=7:1 mixture of 37, major isomer: 1H NMR (600 MHz, CDCl3) δ 8.29 (d, J=1.8 Hz, 1H), 7.83 (d, J=8.6 Hz, 1H), 7.78 (dd, J=8.3, 1.8 Hz, 1H), 7.60 (d, J=2.0 Hz, 1H), 7.51 (dd, J=8.8, 1.9 Hz, 1H), 7.35 (d, J=8.1 Hz, 1H), 7.22 (d, J=15.3 Hz, 1H), 6.90 (d, J=11.2 Hz, 1H), 6.78 (dd, J=15.2, 11.2 Hz, 1H), 6.64 (t, J=11.4 Hz, 1H); partial 1H NMR data for minor isomer: 1H
NMR (600 MHz, CDCl$_3$) $\delta$ 8.11 (d, $J$=1.6 Hz, 1H), 7.87 (d, $J$=2.5 Hz, 1H), 7.73 (dd, $J$=9.1, 1.8 Hz, 1H), 7.62 (d, $J$=8.3 Hz, 1H), 7.54 (dd, $J$=8.6, 1.7 Hz, 1H), 7.02-6.96 (m, 2H); $^{13}$C NMR (150 MHz, DMSO-d$_6$) $\delta$ 148.1, 148.0, 146.4, 146.3, 136.3, 136.2, 134.4, 134.2, 134.0, 133.7, 133.6, 131.5, 131.4, 131.0, 130.9, 130.8, 130.0, 129.5, 129.3, 129.2, 128.8, 128.6, 128.1, 128.0, 127.8, 126.5, 126.4, 126.4, 126.3, 121.9, 121.7; IR (ATR) 3381, 1589, 1517, 1335 cm$^{-1}$; HRMS (ESI, negative ion mode) calcd for C$_{16}$H$_{10}$Br$_2$N$_2$O$_4$ (M$-$) 451.9007, found 451.9018.

2,2'-Bi-1H-indole (38). 1,4-Di(2-nitrophenyl)-1,3-butadiene (33)$_{94}$ (51 mg, 0.17 mmol), Pd(dba)$_2$ (6 mg, 0.01 mmol), dppp (4 mg, 0.01 mmol) and phen (5 mg, 0.02 mmol) were dissolved in anhydrous DMF (1 mL) in a threaded ACE glass pressure tube. The tube was fitted with a pressure head, and the solution was saturated with carbon monoxide (four cycles of 6 atm of CO). The reaction mixture was heated at 120 °C under CO (6 atm) until all starting material was consumed (60 h), as judged by TLC (hexanes/EtOAc, 9:1). Brine (10 mL) was added and the red-brown solution was extracted with EtOAc (3x20 mL). The combined organic phases were dried (MgSO$_4$), filtered, and the solvent was removed under reduced pressure. The resulting crude product was purified by chromatography (hexane/EtOAc, 9:1) to afford 38 (29 mg, 0.13 mmol, 73%) as a white solid. mp 310-313 °C (lit. 95 mp 310-312 °C).

4-Chloro-2,2'-bi-1H-indole (39). Treatment of a solution of 34 (297 mg, 0.898 mmol) in DMF (2 mL) with Pd(dba)$_2$ (36 mg, 0.063 mmol), dppp (26 mg, 0.063 mmol) and phen (23 mg, 0.126 mmol), as described for 38 (CO 6 atm, 120 °C, 40 h), gave after work up and chromatography (hexane/EtOAc, 9:1) 39 (226 mg, 0.846 mmol, 94%) as a white solid. mp=186-187 °C; $^1$H NMR (400 MHz, Acetone-d$_6$) $\delta$ 11.03 (br, s, 1H), 10.81 (br, s, 1H), 7.60 (dd, $J$=7.6, 0.8 Hz, 1H), 7.46 (dd, $J$=8.0, 0.8 Hz, 1H), 7.39 (ddd, $J$=7.2, 2.4, 0.8 Hz, 1H), 7.18 (td, $J$=7.6, 0.4 Hz, 1H), 7.16 (t, $J$=7.6 Hz, 1H), 7.14-7.05 (m, 4H), 7.01 (dd, $J$=2.4, 0.8 Hz, 1H); $^{13}$C NMR (100 MHz, Acetone-d$_6$) $\delta$ 138.9, 138.3, 133.3, 131.5, 129.8, 128.6, 125.7, 123.5, 123.2, 121.2, 120.7, 120.1, 111.9, 110.8, 100.2, 97.6; IR (ATR) 3409, 3063, 1334, 1185, 747 cm$^{-1}$; HRMS (ESI) calcd for C$_{16}$H$_{12}$ClN$_2$ (M$+$H$^+$) 267.0689, found 267.0686.

7-Methoxy-2,2'-bi-1H-indole (40). Treatment of a solution of 35 (86 mg, 0.26 mmol) in DMF (2 mL) with Pd(dba)$_2$ (11 mg, 0.018 mmol), dppp (8 mg, 0.018 mmol) and phen (23 mg, 0.126 mmol), as described for 38 (CO 6 atm, 120 °C, 72 h), gave after work up and chromatography (hexane/EtOAc, 9:1) 40 (64 mg, 0.24 mmol, 93%) as a white solid. mp=228-229 °C; $^1$H NMR (400 MHz, Acetone-d$_6$) $\delta$ 10.68, (br, s, 1H), 10.58 (br, s, 1H), 7.58 (d, $J$=8.0 Hz, 1H), 7.42 (dd, $J$=8.0 Hz, 1.2 Hz, 1H), 7.17 (d, $J$=8.0 Hz, 1H), 7.13 (td, $J$=6.8, 1.2 Hz, 1H), 7.11 (d, $J$=1.2 Hz, 1H), 7.04 (td, $J$=6.8, 1.2 Hz, 1H), 6.98 (d, $J$=8.0 Hz, 1H), 6.94 (d, $J$=2.4 Hz, 1H), 6.68 (d, $J$=7.6 Hz, 1H), 3.94 (s, 3H); $^{13}$C NMR (100 MHz, Acetone-d$_6$) $\delta$ 147.2, 138.1, 132.3, 132.1, 131.3, 130.0, 128.3, 122.7, 121.2, 121.0, 120.5, 113.8, 111.8, 103.7, 100.2,
100.0, 55.6; IR (ATR) 3346, 1580, 1344, 1252, 1094, 729 cm⁻¹; HRMS (ESI) calcd for C₁₇H₁₅N₂O (M+H⁺) 263.1184, found 263.1184.

**6-Bromo-2,2’-bi-1H-indole (41).** Treatment of a solution of 36 (72 mg, 0.19 mmol) in DMF (1.5 mL) with Pd(dba)₂ (8 mg, 0.013 mmol), dppp (6 mg, 0.013 mmol) and phen (5 mg, 0.027 mmol), as described for 38 (CO 6 atm, 120 °C, 49 h), gave after work up and chromatography (hexane/EtOAc, 1:9) 41 (44 mg, 0.142 mmol, 74%) as a white solid. mp=251–252 °C; ¹H NMR (400 MHz, Acetone-d₆) δ 10.93 (s, 1H), 10.79 (s, 1H), 7.58 (s, 1H), 7.57 (d, J=8.8 Hz, 1H), 7.51 (d, J=8.0 Hz, 1H), 7.41 (dd, J=7.6, 0.8 Hz, 1H), 7.17 (dd, J=8.8, 2.0 Hz, 1H), 7.14 (dd, J=8.4, 1.2 Hz, 1H), 7.04 (t with further fine splittings, J=7.2 Hz, 1H), 6.96 (br s, 2H); ¹³C NMR (100 MHz, Acetone-d₆) δ 138.9, 138.2, 133.4, 131.7, 129.8, 129.0, 123.6, 123.1, 122.5, 121.1, 120.6, 115.6, 114.5, 111.9, 100.0, 99.5; IR (ATR) 3425, 1386, 1338, 1218, 741 cm⁻¹; HRMS (ESI) calcd for C₁₆H₁₂BrN₂ (M+H⁺) 311.0183, found 311.0176.

**5,6’-Dibromo-2,2’-bi-1H-indole (42).** Treatment of a solution of 37 (100 mg, 0.220 mmol) in the presence of Pd(dba)₂ (8.9 mg, 0.015 mmol), dppp (6.4 mg, 0.015 mmol) and phen (5.6 mg, 0.031 mmol) in DMF (1.5 mL) with CO (6 atm), as described for 38 (120 °C, 58 h), gave after work up and chromatography (hexane/EtOAc, 9:1) 42 (61.3 mg, 0.157 mmol, 71%) as a white solid. mp=275–276 °C; ¹H NMR (600 MHz, CDCl₃/DMSO-d₆) δ 11.73 (br, s, 1H), 11.69 (br, s, 1H), 7.74 (s, 1H), 7.53 (s, 1H), 7.50 (d, J=8.4 Hz, 1H), 7.34 (d, J=9.0 Hz, 1H), 7.19 (dd, J=8.4, 1.8 Hz, 1H), 7.12 (dd, J=8.4, 1.8 Hz, 1H), 6.94 (s, 1H), 6.90 (s, 1H); ¹³C NMR (150 MHz, CDCl₃/DMSO-d₆) δ 137.8, 135.6, 132.2, 131.6, 130.2, 127.3, 124.1, 122.3, 122.1, 121.6, 114.4, 113.5, 112.8, 111.9, 99.0, 98.3; IR (ATR) 3416, 1599, 1437, 1332, 802 cm⁻¹; HRMS (ESI) calcd for C₁₆H₁₁Br₂N₂ (M+H⁺) 388.9289, found 388.9286.

**Tributyl(1-(2-nitrophenyl)ethenyl)tin (48).** Tributyltin hydride (742 mg, 2.55 mmol) was added drop wise, at ambient temperature, to a solution of PdCl₂(PPh₃)₂ (119 mg, 0.170 mmol) and 1-ethynyl-2-nitrobenzene (44) (250 mg, 1.70 mmol) in THF (5 mL). The dark brown reaction mixture was stirred for 34 h followed by removal of the solvent under reduced pressure. Purification by chromatography (hexane/EtOAc, 9:1) gave 48 (707 mg, 1.61 mmol, 95%) as a pale green oil. ¹H NMR (600 MHz, CDCl₃) δ 7.99 (dd, J=8.4, 1.2 Hz, 1H), 7.52 (dt, J=7.8, 1.2 Hz, 1H), 7.31 (dt, J=7.2, 1.2 Hz, 1H), 7.11 (dd, J=7.8, 1.2 Hz, 1H), 5.74 (d, J=3.0 Hz, 1H), 5.45 (d, J=2.4 Hz, 1H), 1.43–1.48 (m, 6H), 1.26 (sext, J=7.8 Hz, 6H), 0.91–0.94 (m, 6H), 0.86 (t, J=7.2 Hz, 9H); ¹³C NMR (150 MHz, CDCl₃) δ 154.6, 146.0, 144.3, 133.2, 129.7, 126.3, 126.0, 124.3, 28.8, 27.3, 13.6, 10.9; IR (ATR) 2922, 1518, 1339, 1038 cm⁻¹; HRMS (ESI) calcd for C₂₀H₃₄NO₂¹²⁵Sn (M+H⁺) 440.1606, found 440.1607.

**Tributyl(1-(5-benzyloxy-2-nitrophenyl)ethenyl)tin (4).** Treatment of 3₈ (1.30 g, 5.15 mmol) in dry THF (15 mL) with tributyltin hydride (2.30 g, 7.90 mmol) in the presence of PdCl₂(PPh₃)₂ (362 mg, 0.515
mmol), as described for 48 (24 h), gave after solvent removal and chromatography (hexane/EtOAc, 9:1) 4 (2.70 g, 4.96 mmol, 96%) as a brown viscous oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.10 (d, $J=9.2$ Hz, 1H), 7.45-7.33 (m, 5H), 6.86 (dd, $J=9.2$, $J=2.4$ Hz, 1H), 6.63 (d, $J=2.0$ Hz, 1H), 5.72 (d, $J=2.4$ Hz, 1H), 5.41 (d, $J=2.0$ Hz, 1H), 5.14 (s, 2H), 1.56-1.37 (m, 6H), 1.27 (sext, $J=7.2$ Hz, 6H), 0.95 – 0.84 (m, 15H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 162.3, 155.7, 147.6, 139.1, 135.6, 128.7, 128.4, 127.5, 127.1, 124.8, 114.6, 112.7, 70.5, 28.8, 27.3, 13.6, 11.0; IR (ATR) 2954, 2922, 1567, 1329, 1283, 1243, 1228, 694 cm$^{-1}$; HRMS calcd for C$_{27}$H$_{40}$NO$_3$Sn (M+H$^+$) 546.2030, found 546.2030.

Tributyl(1-(4-chloro-2-nitrophenyl)ethenyl)tin (49). Treatment of a solution of 45$^{97}$ (215 mg, 1.18 mmol) in THF (3 mL) with tributyltin hydride (577 mg, 1.78 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (83.1 mg, 0.118 mmol), as described for 48 (24 h), gave after solvent removal and chromatography (hexane/EtOAc, 19:1) 49 (537 mg, 1.13 mmol, 96%) as a brown viscous oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.99 (d, $J=2.0$ Hz, 1H), 7.48 (dd, $J=8.4$, $J=2.4$ Hz, 1H), 7.05 (d, $J=8.0$, Hz, 1H), 5.73 (d, $J=2.4$ Hz, 1H), 5.46 (d, $J=2.4$ Hz, 1H), 1.51-1.43 (m, 6H), 1.30 (sext, $J=8.0$ Hz, 6H), 0.99-0.82 (m, 15H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 153.6, 146.1, 142.8, 133.2, 131.8, 130.8, 126.8, 124.2, 28.8, 27.2, 13.6, 10.9; IR (ATR) 2954, 2922, 1567, 1329, 1283, 1243, 1228, 694 cm$^{-1}$; HRMS (ESI, negative ion mode) calcd for C$_{20}$H$_{32}$ClNO$_2$Sn (M$-$) 473.1144, found 473.1188.

Tributyl(1-(4-carbox methoxy-2-nitrophenyl)ethenyl)tin (50). Treatment of a solution of 46$^{90}$ (100 mg, 0.487 mmol) in THF (2 mL) with tributyltin hydride (213 mg, 0.731 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (34 mg, 0.049 mmol), as described for 48 (35 h) gave after solvent removal and chromatography (hexane/EtOAc, 19:1) 50 (189 mg, 0.380 mmol, 78%) as a brown viscous oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.63 (d, $J=1.6$ Hz, 1H), 8.15 (dd, $J=7.6$, $J=1.6$ Hz, 1H), 7.17 (d, $J=8.0$ Hz, 1H), 5.75 (d, $J=2.8$ Hz, 1H), 5.48 (d, $J=2.8$ Hz, 1H), 3.96 (s, 3H), 1.51-1.43 (m, 6H), 1.25 (sext, $J=7.2$ Hz, 6H), 0.94-0.90 (m, 6H), 0.85 (t, $J=6.8$ Hz, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 165.0, 154.1, 148.7, 145.8, 133.5, 129.9, 128.6, 126.4, 125.6, 52.4, 28.7, 27.2, 13.6, 11.0; IR (ATR) 2954, 2922, 1567, 1329, 1283, 1243, 1228, 694 cm$^{-1}$; HRMS (ESI, negative ion mode) calcd for C$_{22}$H$_{35}$N$_2$O$_4$Sn (M$-$) 497.1588, found 497.1645.

Tributyl(1-(4-methoxy-2-nitrophenyl)ethenyl)tin (51). Treatment of a solution of 47$^{99}$ (1.10 g, 6.21 mmol) in THF (130 mL) with tributyltin hydride (2.71 g, 9.31 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (436 mg, 0.621 mmol), as described for 48 (32 h), gave after solvent removal and chromatography (hexane/EtOAc, 9:1) 51 (2.62 g, 5.58 mmol, 90%) as a brown viscous oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.52 (d, $J=2.8$ Hz, 1H), 7.10 (dd, $J=8.4$, 2.8 Hz, 1H), 7.01 (d, $J=8.0$, Hz, 1H), 5.72 (d, $J=2.4$ Hz, 1H), 5.42 (d, $J=2.8$ Hz, 1H), 3.86 (s, 3H), 1.51-1.32 (m, 6H), 1.26 (sext, $J=7.6$ Hz, 6H), 0.98-0.82 (m, 15H); $^{13}$C
NMR (100 MHz, CDCl₃) δ 157.9, 154.3, 146.1, 136.8, 130.7, 126.1, 120.6, 108.2, 55.8, 28.8, 27.3, 13.6, 10.8; IR (ATR) 2924, 1521, 1341, 1303, 1034 cm⁻¹; HRMS (ESI) calcd for C₂₁H₃₆NO₃¹²⁰Sn (M+H⁺-C₄H₈) 412.0935, found 412.0931.

2,3-Di(2-nitrophenyl)-1,3-butadiene (52).⁵³ To a solution of 48 (348 mg, 0.794 mmol) in DMF (10 mL) was added PdCl₂(PPh₃)₂ (28 mg, 0.040 mmol), PPh₃ (21 mg, 0.080 mmol) and CuI (113 mg, 0.595 mmol). The reaction was stirred at ambient temperature for 36 h. Et₂O (30 mL) was added and the organic phase was washed with NH₄OH (10%, aqueous, 3 X 30 mL), H₂O (30 mL), and brine (30 mL). The organic phase was dried (MgSO₄), filtered, and the solvents were removed under reduced pressure. The resulting solid was purified by chromatography (hexane/EtOAc, 95:5) to afford 52 (78 mg, 0.263 mmol, 67%) as a dark yellow solid. mp=122-124 °C; ¹H NMR (600 MHz, CDCl₃) δ 7.98 (dd, J=8.4, 1.2 Hz, 2H), 7.66 (dt, J=7.8, 1.2 Hz, 2H), 7.61 (dd, J=7.8, 1.2 Hz, 2H), 7.52 (dt, J=7.2, 1.2 Hz, 2H), 5.15 (s, 2H), 4.92 (s, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 149.0, 145.2, 135.3, 132.9, 132.4, 128.7, 124.0, 118.3; IR (ATR) 1514, 1332, 911, 790, 749, 697 cm⁻¹; HRMS (ESI) calcd for C₁₆H₁₂N₂ONaO₄ (M+Na⁺) 319.0695, found 319.0690.

2,3-Di(5-benzyloxy-2-nitrophenyl)-1,3-butadiene (7). Treatment of 4 (103 mg, 0.189 mmol) in DMF (1.5 mL) with Pd(dba)₂ (7.2 mg, 0.013 mmol), PPh₃ (14 mg, 0.053 mmol), and CuI (36 mg, 0.189 mmol), as described for 52 (28 h), gave after work up and chromatography¹⁰⁰ (hexane/EtOAc, 9:1) 7 (37.6 mg, 0.074 mmol, 78%) as a white solid. mp=158-160 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.08 (d, J=9.2, Hz, 1H), 7.48-7.36 (m, 5H), 7.17 (d, J=2.8 Hz, 1H), 7.02 (dd, J=9.6, 3.2 Hz, 1H), 5.19 (s, 2H), 5.08 (s, 1H), 4.88 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 162.2, 145.6, 141.7, 134.3, 135.5, 128.7, 128.4, 127.8, 126.8, 117.5, 117.1, 114.9, 70.7; IR (ATR) 1573, 1513, 1343, 1230, 1007 cm⁻¹; HRMS (ESI) calcd for C₃₀H₂₅N₂O₆ (M+Na⁺) 509.1713, found 509.1715.

2,3-Di(4-chloro-2-nitrophenyl)-1,3-butadiene (53). To a slurry of copper chloride (210 mg, 2.12 mmol) in DMF (2 mL) in a round bottomed flask covered with aluminum foil to exclude light was added a solution of 49 (400 mg, 0.846 mmol) in DMF (2 mL). The resulting mixture was stirred at ambient temperature for 1 h. A saturated solution of NH₄Cl (aqueous, 4 mL) was added and the mixture was allowed to stir for an additional hour. The mixture was diluted with EtOAc (30 mL), was washed with H₂O (3 x 30 mL) and brine (20 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed under reduced pressure. The residue was purified by chromatography¹⁰⁰ (hexane/EtOAc, 9:1) affording 53 (124 mg, 0.340 mmol, 80%) as a white solid. mp=182 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.98 (d, J = 2.0, Hz, 1H), 7.64 (dd, J=8.0, 1.6 Hz 1H), 7.54 (d, J = 8.4 Hz, 1H), 5.15 (s, 1H), 4.92 (s, 1H); ¹³C NMR (100 MHz, DMSO-d₆) δ 149.2, 143.4, 133.5, 133.3, 133.2, 132.6, 124.1, 119.4; IR (ATR)
3086, 1523, 1344, 914, 700 cm\(^{-1}\); HRMS (ESI, negative ion mode) calcd for C\(_{16}\)H\(_{10}\)Cl\(_2\)N\(_2\)O\(_4\) (M\(^{-}\)) 364.0018, found 364.0048.

2,3-Di(4-carboxyethoxy-2-nitrophenyl)-1,3-butadiene (54). Treatment of 50 (400 mg, 0.806 mmol) with CuCl (207 mg, 2.10 mmol) in DMF (2 mL), as described for 53 (3 h), gave after work up and chromatography\(^{100}\) (hexan/EtOAc, 9:1), 54 (306 mg, 0.742 mmol, 92%) as a white solid. mp=187-188 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.60 (d, \(J=1.2\) Hz, 1H), 8.29 (dd, \(J=7.6, 1.2\) Hz 1H), 7.68 (d, \(J=8.0\) Hz, 1H), 5.18 (s, 1H), 5.20 (s, 2H), 4.92 (s, 1H), 3.98 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 164.7, 148.9, 144.2, 139.0, 133.5, 132.6, 131.2, 125.3, 118.9, 52.8; IR (ATR) 1721, 1532, 1358, 1288, 1219 cm\(^{-1}\); HRMS (ESI, negative ion mode) calcd for C\(_{20}\)H\(_{16}\)N\(_2\)O\(_8\) (M\(^{-}\)) 412.0907, found 412.0937.

2,3-Di(4-methoxy-2-nitrophenyl)-1,3-butadiene (55). Treatment of 51 (100 mg, 0.214 mmol) in the presence of CuCl (55 mg, 0.56 mmol), in DMF (1.5 mL), as described for 53 (2 h), gave after work up and chromatography\(^{100}\) (hexan/EtOAc, 9:1) 55 (37.1 mg, 0.104 mmol, 98%) as a white solid. mp=163.5-164 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.48 (d, \(J=9.2\) Hz, 1H), 7.47 (d, \(J=2.4\) Hz 1H), 7.17 (dd, \(J=8.8, 2.8\) Hz, 1H), 5.09 (s, 1H), 4.90 (s, 1H), 3.90 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 159.3, 149.5, 145.3, 133.2, 127.6, 119.3, 118.0, 108.8, 55.9; IR (ATR) 1521, 1340, 1308, 1278, 1028 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{18}\)H\(_{17}\)N\(_2\)O\(_6\) (M+H\(^{+}\)) 357.1087, found 357.1081.

3,3'-Bi-1H-indole (56).\(^{101}\) Treatment of a solution of 52 (68 mg, 0.229 mmol) in the presence of Pd(OAc)\(_2\) (3 mg, 0.014 mmol), dppp (6 mg, 0.014 mmol), and phen (6 mg, 0.028 mmol), and in DMF (3 mL) with CO (6 atm), as described for 38 (120 °C, 39 h) gave, after chromatography (hexane/EtOAc, 8:2), 56 (36 mg, 0.155 mmol, 68%) as a white solid. All data in accordance with previously reported values.

5,5'-Dibenzyloxy-3,3'-Bi-1H-indole (57). Treatment of a solution of 7 (100 mg, 0.197 mmol) in the presence of Pd(dba)\(_2\) (9 mg, 0.016 mmol), dppp (6 mg, 0.016 mmol) phen (6 mg, 0.031 mmol) in DMF (2 mL) with CO (6 atm), as described for 38 (72 h), gave after work up and chromatography (hexane/EtOAc; 7:3) 57 (76.3 mg, 0.172 mmol, 87%) as a white solid. mp=125-126 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.10 (br, s, 1H), 7.46 (d, \(J=6.8\) Hz, 2H), 7.39-7.31 (m, 6H), 7.02 (dd, \(J=8.8, 2.4\) Hz, 1H), 5.07 (s, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 153.5, 137.6, 131.6, 128.4, 127.7, 127.6, 127.3, 122.4, 113.2, 111.9, 110.7, 103.6, 71.0; IR (ATR) 3406, 1452, 1186, 1151, 794 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{30}\)H\(_{24}\)N\(_2\)O\(_2\) (M\(^{+}\)) 444.1838, found 444.1834.

6,6'-Dichloro-3,3'-Bi-1H-indole (58). Treatment of a solution of 53 (23 mg, 0.064 mmol) in the presence of Pd(dba)\(_2\) (4 mg, 0.006 mmol), dppp (4 mg, 0.006 mmol), and phen (2 mg, 0.013 mmol) in DMF (1.5
mL) with CO (6 atm), as described for 38 (72 h), gave after work up and chromatography (hexane/EtOAc, 7:3) 58 (190 mg, 0.063 mmol, 100%) as a white solid. mp=225-226 °C; 1H NMR (400 MHz, Acetone-d$_6$) δ 10.52 (s, 1H), 7.77 (d, J=8.4 Hz, 1H), 7.69 (d, J=2.4 Hz, 1H), 7.53 (d, J=2.0 Hz, 1H), 7.09 (dd, J=8.4, 2.0 Hz, 1H); 13C NMR (100 MHz, Acetone-d$_6$) δ 138.1, 127.9, 126.3, 123.9, 121.7, 120.4, 112.2, 111.1; IR (ATR) 3411, 1448, 1376, 1227, 914, 802 cm$^{-1}$; HRMS (ESI) calcd for C$_{16}$H$_{11}$Cl$_2$N$_2$ (M+H$^+$) 301.0299, found 301.0292.

6,6’-Carbomethoxy-3,3’-Bi-1H-indole (59). Treatment of a solution of 54 (100 mg, 0.243 mmol) in the presence of Pd(dba)$_2$ (10 mg, 0.017 mmol), dppp (7 mg, 0.017 mmol) and phen (6 mg, 0.034 mmol) in DMF (2 mL) with CO (6 atm), as described for 38 (44 h), gave after work up and chromatography (hexane/EtOAc, 1:1) 59 (84.3 mg, 0.242 mmol, 100%) as a white solid. mp = 300-301 °C; 1H NMR (400 MHz, CDCl$_3$/DMSO-d$_6$) δ 11.67 (br, s, 1H), 8.13 (s with further fine splittings, 1H), 7.96 (d, J=2.4 Hz, 1H), 7.86 (d, J=8.4 Hz, 1H), 7.69 (dd, J=8.4, 1.6 Hz, 1H), 3.87 (s, 3H); 13C NMR (100 MHz, CDCl$_3$/DMSO-d$_6$) δ 167.1, 135.5, 129.2, 125.7, 122.3, 119.5, 113.6, 109.5, 51.4; IR (ATR) 3305, 1689, 1436, 1319, 1227 cm$^{-1}$; HRMS (ESI) calcd for C$_{20}$H$_{17}$N$_2$O$_4$ (M+H$^+$) 349.1188, found 349.1182.

6,6’-Dimethoxy-3,3’-Bi-1H-indole (60). Treatment of a solution of 55 (421 mg, 1.18 mmol) in the presence of Pd(dba)$_2$ (47 mg, 0.083 mmol), dppp (34 mg, 0.083 mmol), and phen (30 mg, 0.17 mmol) in DMF (2.5 mL) with CO (6 atm), as described for 38 (30 h), gave after work up and chromatography (hexane/EtOAc, 1:1) 60 (221 mg, 0.757 mmol, 64%) as a white solid. mp = 282-284 °C; 1H NMR (400 MHz, DMSO-d$_6$) δ 10.90 (s, 1H), 7.62 (d, J=8.8 Hz, 1H), 7.46 (d, J=2.0 Hz, 1H), 6.92 (d, J=2.4 Hz, 1H), 6.70 (dd, J=8.4, 1.6 Hz, 1H), 3.79 (s, 3H); 13C NMR (100 MHz, DMSO-d$_6$) δ 155.5, 137.1, 120.3, 120.2, 120.1, 109.8, 108.9, 94.5, 55.1; IR (ATR) 3379, 1626, 1298, 1155, 1026 cm$^{-1}$; HRMS (ESI) calcd for C$_{18}$H$_{17}$N$_2$O$_2$ (M+H$^+$) 293.1290, found 293.1284.

Tributyl(1-(3-nitro-2-pyridyl)ethenyl)tin (62). Treatment of a solution of 61 (100 mg, 0.675 mmol) in THF (2 mL) with tributyltin hydride (295 mg, 1.01 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (47 mg, 0.068 mmol), as described for 48 (36 h), gave after solvent removal and chromatography (hexane/EtOAc, 9:1), 62 (181 mg, 0.412 mmol, 61%) as a brown viscous oil. 1H NMR (400 MHz, CDCl$_3$) δ 8.70 (dd, J=4.8, 1.6 Hz, 1H), 8.10 (dd, J=8.4, 1.6 Hz, 1H), 7.24 (dd, J=8.0, 4.4 Hz, 1H), 5.95 (d, J=2.8 Hz, 1H), 5.64 (d, J=2.4 Hz, 1H), 1.49-1.43 (m, 6H), 1.30-125 (m, 6H), 1.00-0.83 (m, 15H); 13C NMR (100 MHz, CDCl$_3$) δ 159.6, 153.4, 152.0, 143.8, 131.8, 129.1, 120.7, 28.7, 27.2, 13.6, 10.9; (ATR) 2956, 2924, 1526, 1352, 808 cm$^{-1}$; HRMS (ESI) calcd for C$_{19}$H$_{33}$N$_2$O$_2^{120}$Sn (M+H$^+$) 441.1564, found 441.1558.

2,3-Di(3-nitro-2-pyridyl)-1,3-butadiene (63). Treatment of 62 (500 mg, 1.14 mmol) with CuCl (282 mg, 2.85 mmol) in DMF (3 mL), as described for 53 (5 h), gave after work up and chromatography100
(hexane/EtOAc, 1:1) 63 (91.4 mg, 0.306 mmol, 54%) as a white solid. mp=198-199 °C; 1H NMR (400 MHz, CDCl$_3$) δ 8.88 (dd, $J$=4.8, 1.6 Hz, 1H), 8.22 (dd, $J$=8.4, 1.6 Hz 1H), 7.48 (dd, $J$=8.4, 4.8 Hz, 1H), 5.40 (s, 1H), 5.24 (s, 1H); 13C NMR (100 MHz, CDCl$_3$) δ 152.6, 152.4, 146.4, 143.6, 132.0, 123.2, 120.0; IR (ATR) 3019, 1522, 1361, 1217, 932 cm$^{-1}$; HRMS (ESI) calcd for C$_{14}$H$_{11}$N$_4$O$_4$ (M+H$^+$) 299.0780, found 299.0774.

3,3’-Bi-1H-pyrrolo[3,2-b]pyridine (64). Treatment of a solution of 63 (90 mg, 0.302 mmol) in the presence of Pd(dba)$_2$ (12 mg, 0.021 mmol), dppp (9 mg, 0.021 mmol), and phen (8 mg, 0.042 mmol) in DMF (2 mL) with CO (6 atm), as described for 38 (36 h), gave after work up and chromatography (EtOAc) 64 (52.3 mg, 0.223 mmol, 74%) as a white solid. mp=309-310 °C; 1H NMR (400 MHz, DMSO-d$_6$) δ 11.26 (s, 1H), 8.63 (d, $J$=2.4 Hz, 1H), 8.44 (dd, $J$=4.8, 1.6 Hz, 1H), 7.81 (dd, $J$=8.0, 1.2 Hz, 1H), 7.16 (dd, $J$=8.4, 4.8 Hz, 1H); 13C NMR (100 MHz, DMSO-d$_6$) δ 143.7, 142.1, 128.6, 125.6, 118.5, 116.3, 108.9; IR (ATR) 3088, 3019, 1522, 1361, 1217 cm$^{-1}$; HRMS (ESI) calcd for C$_{14}$H$_{11}$N$_4$ (M+H$^+$) 235.0984, found 235.0978.

2-(1-Bromo-1-ethenyl)-5-methoxy-1-nitrobenzene (66). A mixture of 2-(2-trimethylsilyl-1-ethynyl)-5-methoxy-1-nitrobenzene (65) (756 mg, 3.03 mmol) and HBr (aq.-48%, 1.10 mL) in 3-pentanone (7 mL) was stirred at 100 °C for 2 h. After cooling to ambient temperature, the dark brown solution was diluted with EtOAc (15 mL) and the organic phase was washed with water (3x15 mL), dried (MgSO$_4$), filtered, and the filtrate was concentrated under reduced pressure. The resulting brown oil was purified by chromatography (hexane/EtOAc, 95:5) to give 66 (446 mg, 1.73 mmol, 57%) as a brown oil. 1H NMR (400 MHz, CDCl$_3$) δ 7.42 (d, $J$=2.0 Hz, 1H), 7.37 (d, $J$=8.4 Hz, 1H), 7.10 (dd, $J$=8.4, 2.8 Hz, 1H), 5.84 (d, $J$=2.4 Hz, 1H), 5.82 (d, $J$=2.4 Hz, 1H), 3.89 (s, 3H); 13C NMR (100 MHz, CDCl$_3$) δ 160.2, 148.2, 132.2, 127.5, 124.3, 121.2, 118.8, 109.4, 56.0; IR (ATR) 1611, 1526, 1352, 1245, 1029 cm$^{-1}$; HRMS (ESI) calcd for C$_9$H$_9$BrNO$_3$ (M+H$^+$) 257.9765, found 257.9763.

2-(4-Methoxy-2-nitrophenyl)-3-(2-nitrophenyl)-1,3-butadiene (67). To a mixture of 66 (320 mg, 1.24 mmol), CuI (307 mg, 1.61 mmol), CsF (382 mg, 2.52 mmol) and Pd(PPh$_3$)$_4$ (143 mg, 0.124 mmol) in DMF (3 mL) was added, under a N$_2$ atmosphere, a solution of 48 (706 mg, 1.61 mmol) in DMF (3 mL). The resulting mixture was stirred at 70 °C for 12 h. The mixture was cooled to ambient temperature and EtOAc (30 mL) was added. The mixture was washed with water (5x20 mL) and brine (20 mL), and the organic phase was dried (MgSO$_4$), filtered, and the filtrate was concentrated under reduced pressure. The resulting brown oil was purified by chromatography (hexane/EtOAc, 95:5) to give, in order of elution, 52 (66 mg, 0.22 mmol, 28%) as a white solid and 67 (247 mg, 0.756 mmol, 61%) as a yellow solid. mp=91-95 °C; 1H NMR (400 MHz, CDCl$_3$) δ 7.96 (dd, $J$=8.4, 1.2 Hz, 1H), 7.65 (dt, $J$=8.4, 1.2 Hz, 1H),
7.59 (dd, J=8.0, 1.6 Hz, 1H), 7.52-7.47 (m, 3H), 7.19 (dd, J=8.4, 2.8 Hz, 1H), 5.12 (d, J=2.8 Hz, 2H), 4.93 (s, 1H), 4.88 (s, 1H), 3.91 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 159.3, 149.4,148.9, 145.4, 145.0, 135.4, 133.1, 132.9, 132.3, 128.6, 127.3, 123.9, 119.2, 118.1, 117.9, 108.8, 55.8; IR (ATR) 1520, 1351, 1233, 1027, 910 cm⁻¹; HRMS (ESI) calcd for C17H13N2O5 (M+H⁺) 327.0981, found 327.0979.

6-Methoxy-3,3'-Bi-1H-indole (68). Treatment of a solution of 67 (200 mg, 0.613 mmol) in the presence of Pd2(dba)3 (56 mg, 0.061 mmol), dppp (26 mg, 0.063 mmol), and phen (22 mg, 0.123 mmol) in DMF (1.5 mL) with CO (6 atm), as described for 38 (30 h), gave after work up and chromatography (hexane/EtOAc, 7:3 then 1:1) 68 (161 mg, 0.613 mmol, 100%) as a white solid. mp=252 °C (dec.);

1H NMR (400 MHz, DMSO-d6) δ 11.11 (br s, 1H), 10.93 (br s, 1H), 7.77 (d, J=7.6 Hz, 1H), 7.64 (d, J=8.4 Hz, 1H), 7.61 (d, J=2.4 Hz, 1H), 7.49 (d, J=2.4 Hz, 1H), 7.43 (d, J=8.0 Hz, 1H), 7.13 (t, J=7.2 Hz, 1H), 7.05 (t, J=7.2 Hz, 1H), 6.94 (d, J=2.4 Hz, 1H), 6.72 (dd, J=8.4, 2.4 Hz, 1H), 3.80 (s, 3H); 13C NMR (100 MHz, DMSO-d6) δ 155.6, 137.1, 136.4, 126.0, 121.6, 121.2, 120.4, 120.3, 120.2, 119.6, 118.8, 111.5, 109.9, 109.7, 108.9, 94.5, 55.2; IR (ATR) 3395, 1629, 1454, 1239, 1105 cm⁻¹; HRMS (ESI) calcd for C17H15N2O (M+H⁺) 263.1184, found 263.1180.

[5-Bromo-2-nitrophenyl]methyl triphenylphosphonium bromide (69). Treatment of 5-bromo-2-nitrobenzyl bromide (486 mg, 1.65 mmol) with PPh3 (519 mg, 1.977 mmol) in toluene (6 mL) as described for 28 (100 °C, 10 h), gave after work up 69 (918 mg, 1.647 mmol, 100%) as a white solid. mp=249-250 °C, 1H NMR (600 MHz, DMSO-d6) δ 7.97 (d, J=9.0 Hz, 1H), 7.93 (td, J=8.4, 1.8 Hz, 3H), 7.87 (dt, J=7.2, 2.4 Hz, 1H), 7.75 (sext, J=3.6 Hz, 6H), 7.67-7.64 (m, 6H), 7.56 (d, J=2.4 Hz, 1H), 5.47 (d, J=15.0 Hz, 2H); 13C NMR (150 MHz, DMSO-d6) δ 147.3 (d, JCP=5.7 Hz), 136.3 (d, JCP=10.3 Hz), 136.3, 135.4, 134.0 (d, JCP=10.3 Hz), 133.3, 127.9 (d, JCP=4.5 Hz), 127.8, 125.9 (d, JCP=9.1 Hz), 116.9 (d, JCP=85.8 Hz), 26.6 (d, JCP=49.2 Hz); IR 1519, 1330, 1109, 884, 754 cm⁻¹; HRMS (ESI) calcd for C25H20Br2NO2P (M-Br) 476.0415, found 476.0416.

EZ/EE-1,3-Di(2-nitrophenyl)-1,3-butadiene (71). Treatment of a solution of 2-(2-nitrophenyl)propenal 70 (250 mg, 1.41 mmol) and 27 (810 mg, 1.69 mmol) in EtOH (10 mL) in the presence of NaOEt (1.8 M in EtOH, 5.5 mL, 9.90 mmol), as described for 34 (24 h), gave after work up and chromatography (hexane/EtOAc, 17:3) 71 (171 mg, 0.579 mmol, 41%, EZ/EE=10:1) as a faint yellow solid. mp =132-138 °C; Data from the mixture of isomers of 71, major isomer: 1H NMR (600 MHz, CDCl3) δ 7.77 (dd, J=7.9, 1.3 Hz, 1H), 7.53 (dd, J=8.0, 1.3 Hz, 1H), 7.22-7.06 (m, 6H), 6.83 (d, J=12.1 Hz, 1H), 6.58 (d, J=12.3 Hz, 1H), 5.51 (d, J=0.8 Hz, 1H), 5.20 (d, J=0.4 Hz 1H); partial data of minor isomer: 1H NMR (600 MHz, CDCl3) δ 8.01 (dd, J=8.2, 1.1 Hz, 1H), 7.90 (dd, J=8.2, 1.3 Hz, 1H), 7.68-7.65 (m, 2H), 7.57 (t with further fine splittings, J=7.2 Hz, 1H), 7.43 (dd, J=7.6, 1.3 Hz, 1H), 7.37 (dt, J=7.8, 1.4 Hz, 1H), 6.99 (d,
$J=16.0\text{ Hz, } 1\text{H})$, 5.59 (s, 1H), 5.30 (s, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 148.6, 147.8, 147.6, 146.9, 144.6, 142.0, 135.4, 134.4, 134.2, 133.2, 132.5, 132.4, 132.3, 132.1, 132.0, 131.0, 131.0, 128.9, 128.4, 128.2, 128.0, 127.9, 127.5, 126.8, 127.7, 124.3, 123.8, 123.7, 122.4, 122.0; IR (ATR) 1568, 1514, 1339, 912, 786 cm$^{-1}$; HRMS (ESI) calcd for C$_{16}$H$_{13}$N$_2$O$_4$ (M$+$H$^+$) 297.0875, found 297.0870.

**E-1-(3-methoxy-2-nitrophenyl)-3-(2-nitrophenyl)-1,3-butadiene (72).** Treatment of a solution of 70 (69.7 mg, 0.393 mmol) and 29 (200 mg, 0.393 mmol) in absolute EtOH (2 mL) in the presence of NaOEt (2 M, 1.1 mL, 2.2 mmol), as described for 34 (30 h), gave after work up and chromatography (hexane/EtOAc, 85:15) 72 (49.1 mg, 0.150 mmol, 38%) as a yellow-orange oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.65 (dd, $J=8.4, 1.6$ Hz, 1H), 7.27-7.23 (m, 1H), 7.21-7.15 (m, 2H), 6.92 (t, $J=8.0$ Hz, 1H), 6.74 (dt, $J=7.6, 1.2$ Hz, 1H), 6.67 (d, $J=8.4$ Hz, 1H), 6.55 (d, $J=12.4$ Hz, 1H), 6.44 (d, $J=12.0$ Hz 1H), 6.52 (d, $J=0.8$ Hz, 1H), 5.23 (s, 1H), 3.80 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 150.2, 148.2, 141.6, 139.8, 135.0, 133.8, 131.9, 131.4, 130.5, 129.9, 128.0, 123.7, 123.6, 123.0, 121.9, 56.4; IR (ATR) 1522, 1337, 1107, 8333, 756, 721, 690 cm$^{-1}$; HRMS (ESI) calcd for C$_{17}$H$_{15}$N$_2$O$_5$ (M$+$H$^+$) 327.0981, found 327.0977.

**E-1-(4-bromo-2-nitrophenyl)-3-(2-nitrophenyl)-1,3-butadiene (73).** Treatment of a solution of 70 (320 mg, 1.80 mmol) with 30 (1.20 g, 2.23 mmol) in the presence of NaOEt (2.0 M, 4.2 mL, 8.41 mmol) in EtOH (15 mL), as described for 34 (26 h), gave after work up and chromatography (hexane/EtOAc, 9:1) 73 (139 mg, 0.370 mmol, 21%) as a faint yellow solid. mp=119-121 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.92 (d, $J=2.0$ Hz, 1H), 7.58 (dd, $J=7.2, 1.2$ Hz, 1H), 7.27-7.19 (m, 3H), 7.10-7.05 (m, 2H), 6.92 (t, $J=8.0$ Hz, 1H), 6.74 (d, $J=12.0$ Hz, 1H), 6.55 (d, $J=12.4$ Hz, 1H), 6.44 (d, $J=12.0$ Hz 1H), 6.52 (d, $J=0.8$ Hz, 1H), 5.23 (s, 1H), 3.80 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 147.9, 147.2, 141.7, 135.2, 135.1, 133.3, 132.2, 131.8, 131.3, 131.1, 128.1, 126.8, 126.3, 123.9, 123.0, 121.0; IR (ATR) 1517, 1338, 1147, 859, 784 cm$^{-1}$; HRMS (ESI) calcd for C$_{16}$H$_{11}$BrN$_2$O$_4$ (M$-$) 373.9902, found 373.9898.

**E-1-(5-bromo-2-nitrophenyl)-3-(2-nitrophenyl)-1,3-butadiene (74).** Treatment of a solution of 70 (246 mg, 1.39 mmol) and 69 (850 mg, 1.53 mmol) in EtOH (8 mL) in the presence of NaOEt (2.0 M, 3.1 mL, 6.24 mmol), as described for 34 (26 h) gave after work up and chromatography (hexane/EtOAc, 9:1) 74 (113 mg, 0.301 mmol, 22%) as a yellow solid. mp=129-134 °C; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.66 (d, $J=8.4$ Hz, 1H), 7.60 (dd, $J=8.4, 1.2$ Hz, 1H), 7.29 (d, $J=2.4$ Hz, 1H), 7.24 (dd, $J=7.2, 1.2$ Hz, 1H), 7.20 (dd, $J=9.0, 2.4$ Hz, 1H), 7.13 (td, $J=8.4, 1.8$ Hz, 1H), 7.08 (dd, $J=7.8, 1.8$ Hz, 1H), 6.78 (d, $J=12.0$ Hz, 1H), 6.63 (d, $J=12.6$ Hz, 1H), 5.58 (s, 1H), 5.28 (s, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 147.7, 145.6, 141.8, 135.1, 135.4, 133.8, 132.3, 132.0, 130.9, 130.8, 128.2, 127.3, 125.8, 125.3, 124.0, 123.4; IR (ATR)
1598, 1518, 1340, 855, 754 cm\(^{-1}\); HRMS (ESI, negative ion mode) calcd for C\(_{16}\)H\(_{11}\)BrN\(_2\)O\(_4\) (M\(^-\)) 373.9902, found 373.9898.

**2,3’-Bi-1H-indole (75).** Treatment of a solution of 71 (200 mg, 0.675 mmol) in the presence of Pd(dba)\(_2\) (19 mg, 0.034 mmol), dppp (14 mg, 0.034 mmol), and phen (12 mg, 0.067 mmol) in DMF (2 mL) with CO (6 atm), as described for 38 (41 h), gave after work up and chromatography (hexane/EtOAc, 7:3) 75 (96 mg, 0.41 mmol, 61%) as a white solid. mp=206–207 °C; \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 11.32 (s, 1H), 11.14 (s, 1H), 8.00 (d, \(J=7.8\) Hz, 1H), 7.85 (d, \(J=1.8\) Hz, 1H), 7.50 (d, \(J=7.8\) Hz, 1H), 7.47 (d, \(J=7.8\) Hz, 1H), 7.36 (d, \(J=8.4\) Hz, 1H), 7.18 (t, \(J=6.0\) Hz, 1H), 7.16 (t, \(J=6.0\) Hz, 1H), 7.03 (t, \(J=7.2\) Hz, 1H), 6.96 (t, \(J=7.2\) Hz, 1H), 6.74 (d, \(J=1.2\) Hz, 1H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 136.6, 135.9, 134.1, 129.1, 124.6, 123.0, 121.5, 120.1, 119.6, 119.6, 118.9, 118.7, 111.8, 110.3, 108.4, 96.7; IR (ATR) 3405, 3054, 1596, 1456, 1308, 743 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{16}\)H\(_{13}\)N\(_2\) (M+H\(^+\)) 233.1078, found 233.1073.

7-Methoxy-2,3’-Bi-1H-indole (76). Reaction of a solution of 72 (46 mg, 0.14 mmol) in the presence of Pd(dba)\(_2\) (8.1 mg, 0.014 mmol), dppp (6.0 mg, 0.015 mmol) and phen (5.1 mg, 0.028 mmol) in DMF (0.8 mL) with CO (6 atm), as described for 38 (120 °C, 48 h), gave after work up and chromatography (hexane/EtOAc, 7:3) 76 (26.7 mg, 0.102 mmol, 72%) as a yellowish-brown oil. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 8.45 (br s, 1H), 8.29 (br s, 1H), 7.48 (d, \(J=2.6\) Hz, 1H), 7.45 (d, \(J=8.0\) Hz, 1H), 7.29 (dt, \(J=7.0, 1.2\) Hz, 1H), (7.25-7.23 (m, 3H), 7.05 (t, \(J=7.9\) Hz, 1H), 6.77 (d, \(J=2.2\) Hz, 1H), 6.66 (d, \(J=7.6\) Hz, 1H), 3.99 (s, 3H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 145.7, 136.4, 132.8, 130.7, 126.3, 125.4, 122.9, 121.3, 120.7, 120.3, 120.0, 112.9, 111.5, 110.4, 101.6, 99.7, 55.4; IR (ATR) 3395, 1703, 1598, 1576, 1254, 1094, 789, 742 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{17}\)H\(_{15}\)N\(_2\)O (M+H\(^+\)) 263.1184, found 263.1182.

6-Bromo-2,3’-Bi-1H-indole (77). Reaction of a solution of 73 (50 mg, 0.133 mmol) in the presence of Pd(dba)\(_2\) (4.6 mg, 0.008 mmol), dppp (3.3 mg, 0.008 mmol) and phen (3 mg, 0.016 mmol) in DMF (1.5 mL) with CO (6 atm), as described for 38 (120 °C, 43 h), gave after work up and chromatography (hexane/EtOAc, 7:3) 77 (27.4 mg, 0.102 mmol, 72%) as a white solid. mp=206–207 °C; \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 11.41 (br, s, 1H), 11.34 (br, s, 1H), 7.99 (d, \(J=7.8\) Hz, 1H), 7.90 (d, \(J=2.4\) Hz, 1H), 7.67 (d, \(J=1.8\) Hz, 1H), 7.49 (d, \(J=8.4\) Hz, 1H), 7.32 (d, \(J=8.4\) Hz, 1H), 7.22-7.13 (m, 3H), 6.77 (d, \(J=1.8\) Hz, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)/DMSO-d\(_6\)) \(\delta\) 136.9, 136.6, 135.2, 128.2, 124.5, 123.4, 121.7, 121.5, 120.5, 119.8, 119.4, 112.8, 112.6, 111.9, 107.9, 96.8; IR (ATR) 3410, 3381, 1588, 1317, 747 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{16}\)H\(_{12}\)BrN\(_2\) (M+H\(^+\)) 311.0184, found 311.0183.

5-Bromo-2,3’-Bi-1H-indole (78). Reaction of a solution of 74 (121 mg, 0.323 mmol) in the presence of Pd(dba)\(_2\) (13 mg, 0.023 mmol) and phen (8.2 mg, 0.045 mmol) in DMF (1.5 mL) with CO (6 atm), as described for 38 (120 °C, 44 h), gave after work up and chromatography
(hexane/EtOAc, 7:3) 78 (67.3 mg, 0.216 mmol, 67%) as a white solid. mp=205-206 °C ¹H NMR (600 MHz, DMSO-d₆) δ 11.46 (br, s, 1H), 11.42 (br, s, 1H), 7.99 (d, J=7.8 Hz, 1H), 7.90 (d, J=2.4 Hz, 1H), 7.67 (d, J=1.8 Hz, 1H), 7.49 (d, J=8.4 Hz, 1H), 7.32 (d, J=8.4 Hz, 1H), 7.22-7.15 (m, 3H), 7.14 (dd, J=7.8, 1.8 Hz, 1H), 7.27 (d, J=1.8 Hz, 1H); ¹³C NMR (150 MHz, DMSO-d₆) δ 136.6, 135.8, 134.7, 131.2, 124.5, 123.7, 122.6, 121.9, 121.1, 119.9, 119.5, 112.3, 112.0, 111.3, 107.9, 96.4; IR (ATR) 3412, 3356, 1589, 1234, 748 cm⁻¹; HRMS (ESI) calcd for C₁₇H₁₂BrN₂ (M+H⁺) 311.0184, found 311.0182.

**Indolo[1,2-c]quinazolin-6(5H)-one (81)** and **5,11-Dihydro-6H-Indolo[3,2-c] quinolin-6-one (82).**

Treatment of a solution of trans-2,2'-di(2-nitrophenyl)ethene (79) (200 mg, 0.740 mmol) in the presence of Pd(dba)₂ (25.6 mg, 0.044 mmol), dppp (18.3 mg, 0.044 mmol) and phen (16 mg, 0.089 mmol) in DMF (2 mL) with CO (6 atm), as described for 38 (120 °C, 56 h), gave after work up and chromatography (hexane/EtOAc, 9:1, 8:2, and 1:1), in order of elution, 81 (132 mg, 0.565 mmol, 76%) and 82 (21 mg, 0.090 mmol, 12%) both as white solids. Analytical data for 81: mp = 320-321 °C; ¹H NMR (600 MHz, CDCl₃/DMSO-d₆) δ 11.23 (br, s, 1H), 8.56-8.55 (m, 1H), 7.96 (d, J=9.6 Hz, 1H), 7.68-7.66 (m, 1H), 7.34 (t, J=8.4 Hz, 1H), 7.31-7.27 (m, 2H), 7.24 (d, J=8.4 Hz, 1H), 7.19-7.15 (m, 2H); ¹³C NMR (150 MHz, CDCl₃/DMSO-d₆) δ 147.0, 134.1, 133.9, 133.3, 129.4, 128.9, 123.1, 123.0, 122.5, 122.5, 119.8, 115.4, 115.2, 113.5, 97.7; IR (ATR) 2920, 1697, 1596, 1339, 739 cm⁻¹; HRMS (ESI) calcd for C₁₉H₁₂N₂O (M+H⁺) 335.0871, found 335.0868.

Analytical data for 82: mp=396-397 °C (dec.); ¹H NMR (600 MHz, DMSO-d₆) δ 12.55 (br, s, 1H), 11.42 (br, s, 1H), 8.20 (dd, J=7.8, 1.2 Hz, 2H), 7.62 (d, J=7.8 Hz, 1H), 7.51 (td, J=8.4, 1.2 Hz, 1H), 7.47(dd, J=8.4, 0.6 Hz, 1H), 7.38-7.35 (m, 1H), 7.30-7.25 (m, 2H); ¹³C NMR (150 MHz, DMSO-d₆) δ 159.8, 140.7, 137.9, 137.7, 129.1, 124.4, 124.0, 122.1, 121.5, 121.0, 120.7, 116.0, 111.9, 111.7, 106.4; IR (ATR) 3050, 2925, 1698, 1596, 1395 cm⁻¹; HRMS (ESI) calcd for C₁₅H₁₁N₂O (M+H⁺) 235.0871, found 235.0869.

**1-(5-Chloro-2-nitrophenyl)-2-(2-nitrophenyl)ethane (88).** Treatment of a solution of 2-nitrobenzaldehyde (531 mg, 3.51 mmol) with 28 (2.20 mg, 4.29 mmol) in EtOH (18 mL) in the presence of NaOEt (1.8 M, 10.5 mL, 18.9 mmol), as described for 34 (24 h) gave after work up and chromatography (hexane/EtOAc, 1:1) 88 (300 mg, 0.985 mmol, 28%) as a faint yellow solid. mp=139-140 °C; ¹H NMR (600 MHz, CDCl₃) δ 8.05 (d, J=8.4 Hz, 1H), 7.80 (d, J=8.4 Hz, 1H), 7.79 (d, J=9.6 Hz, 1H), 7.70 (d, J=8.4 Hz, 1H), 7.68 (t, J=7.8 Hz, 1H), 7.50 (t, J=7.2 Hz, 1H), 7.41 (t, J=8.4 Hz, 1H), 7.30 (d, J=16.8 Hz, 1H), 7.09 (d, J=16.8 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 150.4, 147.7, 135.5, 133.9, 133.6, 132.3, 132.1, 130.8, 129.2, 129.1, 128.8, 125.5, 124.8, 122.6; IR (ATR) 1525, 1347, 1217, 738 cm⁻¹; HRMS (ESI, negative ion mode) calcd for C₁₄H₁₂ClNO₂ (M⁻) 304.0251, found 304.0272.

106
2-(2-Nitro-6-chlorophenyl)indole (89) and 4-Chloro-5,10-dihydroindolo[3,2-b]indole (90). Reaction of 88 (250 mg, 0.822 mmol) in the presence of Pd(dbAc)$_2$ (23.6 mg, 0.041 mmol), dppp (16.9 mg, 0.041 mmol) and phen (14.8 mg, 0.082 mmol) in DMF (2 mL), as described for 38 (120 °C, 76 h), gave, after work up and chromatography (hexane/EtOAc, 9:1; 8:2; 1:1), in order of elution, 90 (26 mg, 0.107 mmol, 13%) and 89 (153 mg, 0.570 mmol, 69%) both as white solids. Analytic data for 89: mp=269-270 °C; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 11.52 (br, s, 1H), 8.52 (dd, $J=8.2$, 0.8 Hz, 1H), 8.24 (dd, $J=7.6$, 1.2 Hz, 1H), 7.48-7.44 (m, 3H), 7.35 (t, $J=8.2$ Hz, 1H), 7.28 (d, $J=8.2$ Hz, 1H), 7.26 (t, $J=7.8$ Hz, 1H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 146.8, 135.2, 134.4, 134.0, 130.0, 128.2, 124.1, 124.0, 123.8, 123.1, 123.0, 115.4, 114.4, 113.2, 96.0; IR (ATR) 3053, 1712, 1419, 1398, 748 cm$^{-1}$; HRMS (ESI) calcd for C$_{15}$H$_{10}$ClN$_2$O (M+H$^+$) 269.0482, found 269.0475.

Analytic data for 90: mp=182-183 °C; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 11.33 (br, s, 1H), 11.05 (br, s, 1H), 7.75 (d, $J=8.0$ Hz, 1H), 7.54 (d, $J=8.0$ Hz, 1H), 7.41 (d, $J=7.6$ Hz, 1H), 7.18 (t, $J=7.6$ Hz, 1H), 7.11-7.04 (m, 3H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 141.0, 140.7, 125.9, 123.3, 122.6, 122.0, 122.0, 118.2, 117.7, 117.4, 113.9, 113.5, 112.5, 110.9; IR (ATR) 3424, 1455, 1391, 1322, 730 cm$^{-1}$; HRMS (ESI) calcd for C$_{14}$H$_9$ClN$_2$O (M$^+$) 240.0454, found 240.0447.

Z/E-1-(3-Methoxy-2-nitrophenyl)-2-(2-nitrophenyl)ethene (91). Treatment of a solution of 2-nitrobenzaldehyde (500 mg, 3.31 mmol) with 29 (1.68 mg, 3.31 mmol) in EtOH (16 mL) in the presence of NaOEt (1.8 M, 12 mL, 21.6 mmol), as described for 34 (ambient temperature, 24 h) gave after work up and chromatography (hexane/EtOAc, 7:3 then 1:1) 91 (891 mg, 2.97 mmol, 90%, Z/E=1.8:1) as an orange solid. NMR data from the E/Z=1.8:1 mixture of 91, major isomer: $^1$H NMR (600 MHz, CDCl$_3$) δ 8.10-8.08 (m, 1H), 7.17 (d, $J=7.5$ Hz, 1H), 7.48 (t, $J=8.3$ Hz, 1H), 7.40-7.36 (m, 2H), 7.09 (t, $J=8.5$ Hz, 1H), 6.87 (d, $J=8.3$ Hz, 1H), 6.68 (d, $J=11.7$ Hz, 1H), 6.48 (d, $J=7.7$ Hz, 1H), 3.89 (s, 3H); minor isomer: $^1$H NMR (600 MHz, CDCl$_3$) δ 8.02 (d, $J=8.2$ Hz, 1H), 7.69 (d, $J=15.7$ Hz, 1H), 7.63 (t, $J=8.2$ Hz, 1H), 7.45 (d, $J=8.2$ Hz, 1H), 7.19-7.16 (m, 2H), 7.11 (d, $J=12.1$ Hz, 1H), 7.01 (d, $J=8.2$ Hz, 1H), 6.88 (d, $J=15.8$ Hz, 1H), 3.92 (s, 3H); Analytical data for both isomers from the mixture: mp=135-140 °C; $^{13}$C NMR (150 MHz, CDCl$_3$) δ 151.0, 150.8, 148.0, 147.9, 141.1, 140.7, 133.5, 133.3, 132.4, 132.4, 132.1, 132.0, 131.1, 130.6, 130.3, 130.0, 129.4, 129.0, 128.8, 128.7, 125.4, 124.9, 124.7, 124.6, 122.1, 118.1, 112.1, 111.5, 56.5, 56.4; IR (ATR) 1518, 1342, 1285, 1063, 852 cm$^{-1}$; HRMS (ESI) calcd for C$_{15}$H$_{13}$N$_2$O$_5$ (M$^+$) 301.0824, found 301.0817.

7-Methoxy-2-(2-nitrophenyl)indole (92), 2-(3-Methoxy-2-nitrophenyl)indole (93), and 5,11-Dihydro-4-methoxy-6H-indolo[3,2-c]quinolin-6-one (94). Reaction of 91 (439 mg, 1.46 mmol) in the presence of Pd(dbAc)$_2$ (50.4 mg, 0.088 mmol), dppp (36.2 mg, 0.088 mmol) and phen (31.6 mg, 0.175 mmol) in DMF
(3 mL) with CO (6 atm) as described for 38 (120 °C, 56 h), gave, after work up and chromatography (hexane/EtOAc, 9:1, 8:2, 1:1, 3:7), in order of elution 92 (38 mg, 0.14 mmol, 10%) as a viscous oil, 93 (290 mg, 1.08 mmol, 74%) as a yellow solid and 94 (23.2 mg, 0.088 mmol, 6%) as a white solid.

Analytic data for 92: ¹H NMR (400 MHz, CDCl₃) δ 8.69 (d, J=7.2 Hz, 1H), 8.11 (br s, 1H), 7.71 (dd, J=6.8, 2.4 Hz, 1H), 7.52 (d, J=8.0 Hz, 1H), 7.42-7.36 (m, 2H), 7.17 (t, J=8.0 Hz, 1H), 7.09 (s, 1H), 6.91 (d, J=8.0 Hz, 1H), 3.99 (s, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ 146.3, 134.0, 133.4, 129.6, 123.8, 123.5, 123.2, 123.0, 120.2, 115.6, 115.3, 114.1, 110.7, 98.4, 56.0; IR (ATR) 3424, 2230, 1611, 1535, 1052 cm⁻¹; HRMS (ESI) calcd for C₁₅H₁₃N₂O₃ (M+H⁺) 269.0926, found 269.0919.

Analytic data for 93: mp=158-160 °C; ¹H NMR (600 MHz, CDCl₃/DMSO-d₆) δ 11.57 (br s, 1H), 7.59 (t, J=8.4 Hz, 1H), 7.56 (d, J=7.6 Hz, 1H), 7.46 (d, J=8.4 Hz, 1H), 7.41 (d, J=7.6 Hz, 1H), 7.23 (d, J=8.0 Hz, 1H), 7.17 (t, J=7.6 Hz, 1H), 7.04 (t, J=8.0 Hz, 1H), 6.54 (d, J=1.6 Hz, 1H), 3.92 (s, 3H); ¹³C NMR (150 MHz, CDCl₃/DMSO-d₆) δ 150.4, 139.1, 137.0, 131.0, 130.6, 128.2, 125.2, 122.4, 120.4, 120.3, 119.6, 112.0, 111.5, 101.1, 56.5; IR (ATR) 3402, 1609, 1527, 1275, 1112 cm⁻¹; HRMS (ESI) calcd for C₁₅H₁₃N₂O₃ (M+H⁺) 269.0926, found 269.0919.

Analytic data for 94: mp=355-360 °C; ¹H NMR (600 MHz, DMSO-d₆) δ 12.57 (br, s, 1H), 10.16 (br, s, 1H), 8.20 (d, J=7.8 Hz, 1H), 7.79 (d, J=7.8 Hz, 1H), 7.62 (d, J=8.4 Hz, 1H), 7.37 (td, J=8.4, 1.2 Hz, 1H), 7.28-7.25 (m, 2H), 7.17 (d, J=7.8 Hz, 1H), 3.96 (s, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ 159.1, 146.3, 140.7, 137.7, 127.6, 124.4, 124.1, 121.7, 121.1, 120.8, 113.9, 112.4, 111.7, 110.0, 106.7, 56.1; IR (ATR) 3407, 1523, 1377, 1275, 1110 cm⁻¹; HRMS (ESI) calcd for C₁₆H₁₃N₂O₂ (M+H⁺) 265.0977, found 265.0971.

1,1-Bis(2-nitrophenyl)ethene (95) and 2,3-di(2-nitrophenyl)-1,3-butadiene (52). To a solution of 2-iodonitrobenzene (473 mg, 1.90 mmol) in DMF (10 mL) was added 48 (1.00 g, 2.28 mmol), PdCl₂(PPh₃)₂ (67 mg, 0.095 mmol), PPh₃ (50 mg, 0.190 mmol) and CuI (271 mg, 1.43 mmol). The reaction was stirred at ambient temperature for 24 h. Et₂O (30 mL) was added and the organic phase was washed with NH₄OH (10%-aqueous, 3x30 mL), H₂O (30 mL), and brine (30 mL). The organic phase was dried (MgSO₄), filtered, and the solvents were removed under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 9:1) to afford, in order of elution 52 (30 mg, 0.10 mmol, 11%) and 95 (320 mg, 1.18 mmol, 62%) both as a white solid. mp=132-134 °C; ¹H NMR (600 MHz, CDCl₃) δ 5.62 (s, 2H), 7.43-7.46 (m, 2H), 7.58-7.59 (m, 4H), 7.71 (dt, J=7.8, 0.6 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 121.3, 123.9, 129.1, 132.4, 133.1, 133.9, 142.4, 148.7; IR (ATR) 716, 774, 1351, 1516 cm⁻¹; HRMS (ESI) calcd for C₁₄H₁₀N₂NaO₄ (M+Na⁺) 293.0538, found 293.0534.
Indolo[2,3-b]indole (96) and 6H-Indolo[2,3-c]quinolin-6-one (97). Reaction of 95 (210 mg, 0.777 mmol) in the presence of Pd(OAc)$_2$ (17.5 mg, 0.078 mmol), dppp (32 mg, 0.078 mmol), phen (28 mg, 0.155 mmol), and CO (6 atm) in DMF (3 mL), as described for 38 (41 h), gave, after chromatography (hexane/EtOAc, 4:6), in order of elution, 96 (22.6 mg, 0.110 mmol, 14%) and 97 (106 mg, 0.451 mmol, 58%) both as white solids. Analytical data for 96: mp 340-343 ºC; $^1$H NMR (600 MHz, DMSO-$d_6$) δ 11.35 (br, s, 1H), 7.79 (d, J = 7.2 Hz, 1H), 7.40 (d, J = 7.8 Hz, 1H), 7.10 (dt, J = 7.2, 0.6 Hz, 1H); 7.05 (dt, J = 8.4, 1.8 Hz, 1H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) δ 144.5, 138.6, 121.9, 119.2, 119.0, 117.4, 111.5, 99.7; IR (ATR) 3413, 3363, 1450, 736, 696 cm$^{-1}$; HRMS (ESI) calcd for C$_{14}$H$_{11}$N$_2$ (M+H$^+$) 207.0922, found 207.0917.

Analytical data for 97: mp 312-314 ºC; $^1$H NMR (600 MHz, DMSO-$d_6$) δ 12.34 (br s, 1H), 11.85 (br s, 1H), 8.47 (d, J = 7.8 Hz, 1H), 8.44 (d, J = 7.2 Hz, 1H), 7.65 (d, J = 7.8 Hz, 1H), 7.51 (d, J = 8.4 Hz, 1H), 7.47 (t, J = 7.8 Hz, 1H), 7.41 (t, J = 7.2 Hz, 1H), 7.34 (t, J = 7.2 Hz, 1H), 7.32 (t, J = 7.2 Hz, 1H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) δ 155.7, 138.8, 134.9, 127.6, 125.9, 125.7, 123.0, 122.3, 122.2, 120.7, 118.2, 118.0, 116.1, 113.0, ; IR (ATR) 3316, 3158, 1648, 1620, 1328, 729 cm$^{-1}$; HRMS (ESI) calcd for C$_{15}$H$_{11}$N$_2$O (M+H$^+$) 235.0871, found 235.0867.

1-(5-Benzzyloxy-2-nitrophenyl)-2-(4-methoxy-2-nitrophenylethene (99). To a solution of 98 (500 mg, 1.79 mmol) in DMF (4 mL) was added CuI (34 mg, 0.18 mmol), CsF (546 mg, 3.62 mmol), Pd(PPh$_3$)$_4$ (124 mg, 0.108 mmol) and 4 (1.10 g, 2.01 mmol). The mixture was stirred at 50 ºC under N$_2$ for 8 h. After cooling to ambient temperature, the crude mixture was diluted with EtOAc (35 mL), washed with H$_2$O (3x35 mL) and brine (2x35 mL). The organic layer was dried (MgSO$_4$), filtered, and the solvents were removed under reduced pressure. The residue was purified by chromatography on SiO$_2$/K$_2$CO$_3$ (9:1) using (hexane/EtOAc, 9:1 then 85:15) to give, in order of elution, 7 (69.2 mg, 0.136 mmol, 15%) and 99 (503 mg, 1.24 mmol, 69%) both as white solids. Analytical data for 99: mp =127-128 ºC; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.81 (d, J=9.2 Hz, 1H), 7.50 (d, J=8.8 Hz, 1H), 7.45-7.34 (m, 5H), 7.17 (d, J=2.8 Hz, 1H), 7.11 (d, J=2.8 Hz, 1H), 7.09 (dd, J=8.8, 2.8 Hz, 1H), 6.95 (dd, J=8.8, 2.4 Hz, 1H), 5.55 (s, 1H), 5.52 (s, 1H), 5.16 (s, 2H), 3.85 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 161.6, 159.5, 149.1, 142.8, 141.6, 137.2, 135.5, 134.2, 128.7, 128.4, 127.7, 126.7, 126.0, 120.3, 119.1, 118.5, 114.7, 108.7, 70.7, 55.8; IR (ATR) 1515, 1348, 1228, 1004, 826 cm$^{-1}$; HRMS (ESI) calcd for C$_{22}$H$_{19}$N$_2$O$_6$ (M+H$^+$) 407.1243, found 407.1236.

6-Methoxy-indolo[2,3-b]-5-benzyloxyindole (100), 2-benzyloxy-5,7-dihydro-9-methoxy-6H-indolo[2,3-c]quinolin-6-one (101), and 10-benzyloxy-5,7-dihydro-3-methoxy-6H-indolo[2,3-c]quinolin-6-one (102). Reaction of 99 (300 mg, 0.738 mmol) in the presence of Pd(dba)$_2$, dppp (29.7
mg, 0.0527 mmol), phen (21.3 mg, 0.052 mmol) in DMF (2.5 mL), as described for 38 (pCO=6 atm, 41 h), gave, after chromatography (hexane/EtOAc, in order 7:3, 1:1, 3:7, 2:8), in order of elution, 100 (75.8 mg, 0.221 mmol, 30%), 101 (84.7 mg, 0.229 mmol, 31%) and 102 (104 mg, 0.281 mmol, 38%) all as white solids.

Analytical data for 100: mp=206-207 °C; ¹H NMR (400 MHz, DMSO-d₆) δ 10.59 (s, 1H), 10.50 (s, 1H), 8.16 (d, J=8.4 Hz, 1H), 8.01-7.97 (m, 2H), 7.95 (d, J=2.8 Hz, 1H), 7.87-7.81 (m, 2H), 7.79-7.75 (m, 1H), 7.74 (d, J=8.8 Hz, 1H), 7.47 (d, J=2.4 Hz, 1H), 7.25 (dd, J=8.8 Hz, 2.4 Hz, 1H), 7.22 (dd, J=9.2, 2.4 Hz, 1H), 5.65 (s, 2H), 4.26 (s, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ 153.9, 152.6, 144.9, 139.6, 138.0, 133.3, 128.3, 127.6, 127.6, 122.2, 117.8, 116.2, 111.7, 107.4, 107.0, 102.8, 99.6, 96.9, 69.9, 55.3; IR (ATR) 3373, 1577, 1452, 1148, 1022 cm⁻¹; HRMS (ESI) calcd for C₂₂H₁₈N₂O₂ (M⁺) 342.1368, found 342.1361.

Analytical data for 101: mp=285-286 °C; ¹H NMR (400 MHz, DMSO-d₆) δ 12.05 (s, 1H), 11.66 (s, 1H), 8.34 (d, J=8.4 Hz, 1H), 7.92 (d, J=2.4 Hz, 1H), 7.56 (d, J=6.8 Hz, 2H), 7.53 (d, J=9.2 Hz, 1H), 7.42 (t, J=7.2 Hz, 2H), 7.34 (tt, J=6.8, 1.2 Hz, 1H), 7.19 (dd, J=9.2, 2.4 Hz, 1H), 7.05 (d, J=2.8 Hz, 1H), 6.95 (dd, J=8.4, 2.4 Hz, 1H), 5.27 (s, 2H), 3.83 (s, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ 157.5, 155.9, 153.2, 137.5, 136.3, 134.2, 128.4, 127.8, 127.7, 126.6, 124.2, 122.0, 118.3, 117.0, 113.8, 111.9, 110.2, 104.8, 99.8, 70.1, 55.2; IR (ATR) 3437, 3026, 1621, 1288, 811 cm⁻¹; HRMS (ESI) calcd for C₂₃H₁₉N₂O₃ (M+H⁺) 371.1396, found 371.1389.

Analytical data for 102: mp=276-277 °C; ¹H NMR (400 MHz, DMSO-d₆) δ 12.16 (s, 1H), 11.65 (s, 1H), 8.27 (d, J=8.8 Hz, 1H), 7.80 (d, J=2.8 Hz, 1H), 7.56 (d, J=7.2 Hz, 2H), 7.44-7.40 (m, 3H), 7.34 (t, J=7.6 Hz, 1H), 7.12 (dd, J=8.8, 2.4 Hz, 1H), 7.05 (d, J=2.4 Hz, 1H), 6.94 (dd, J=8.8, 2.4 Hz, 1H), 5.29 (s, 2H), 3.86 (s, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ 158.3, 154.9, 153.7, 140.2, 137.4, 129.4, 128.4, 127.8, 127.7, 127.2, 123.1, 118.4, 118.4, 117.2, 116.2, 115.0, 111.5, 106.7, 94.8, 69.8, 55.2; IR (ATR) 3448, 1652, 1458, 1264, 1228 cm⁻¹; HRMS (ESI) calcd for C₂₃H₁₉N₂O₃ (M+H⁺) 371.1396, found 371.1389.
2-(5-Bromo-2-nitrophenyl)-1-trimethylsilylethylene (113). To a mixture of 5-bromo-2-nitro-1-iodobenzene (112) (3.50 g, 10.7 mmol), CuI (203 mg, 1.07 mmol) and bis(triphenylphosphine)palladium dichloride (PdCl$_2$(PPh$_3$)$_2$, 374 mg, 0.533 mmol) at ambient temperature under a N$_2$ atmosphere was added tetrahydrofuran (THF, 10 mL) followed by the addition of triethylamine (Et$_3$N, 16 mL). After stirring the mixture for 5 minutes, the solution of trimethylsilylethylene (1.40 g, 13.4 mmol) in Et$_3$N (4 mL) was added via syringe. The resulting dark brown mixture was stirred at this temperature for 36 h. The reaction mixture was then filtered through Celite, and the Celite was washed with EtOAc (30 mL). The solvents were removed from the filtrate under reduced pressure. The resulting residue was purified by chromatography (hexane/EtOAc, 95:5) to give 113 (2.93 mg, 9.82 mmol, 92%) as a yellow oil. $^1$H NMR (600 MHz, CDCl$_3$) δ 7.89 (d, $J=8.4$ Hz, 1H), 7.79 (d, $J=1.8$ Hz, 1H), 7.56 (dd, $J=8.4$, 1.8 Hz, 1H), 0.27 (s, 9H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 148.7, 137.6, 131.9, 127.4, 125.8, 120.1, 105.7, 98.0, 0.5; IR (ATR) 2958, 1596, 1523, 1341, 1248, 833 cm$^{-1}$; HRMS (ESI) calcd for C$_{11}$H$_{13}$BrNO$_2$Si (M+H$^+$) 297.9899, found 297.9883.

1-(5-Bromo-2-nitrophenylethynyl)ethyne (114). A heterogeneous mixture of 113 (2.56 g, 8.58 mmol) and K$_2$CO$_3$ (2.37 g, 17.2 mmol) in MeOH/Et$_2$O (1:1, 40 mL) was stirred at ambient temperature under a N$_2$ atmosphere for 2 h. The mixture was diluted with EtOAc (30 mL) and the organic layer was washed with water (3x20 mL). The resulting organic layer was dried (MgSO$_4$), filtered and the solvents were removed under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 9:1) to give 114 (1.76 g, 7.81 mmol, 91%) as a white solid. mp=89-90 °C; $^1$H NMR (600 MHz, CDCl$_3$) δ 7.93 (d, $J=8.4$ Hz, 1H), 7.83 (d, $J=2.4$ Hz, 1H), 7.63 (dd, $J=9.0$, 2.4 Hz, 1H), 3.58 (s, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 148.9, 138.0, 132.5, 127.6, 125.9, 119.2, 86.6, 77.3; IR (ATR) 3276, 2111, 1598, 1513, 1324, 836 cm$^{-1}$; HRMS (ESI) calcd for C$_8$H$_5$BrNO$_2$ (M+H$^+$) 225.9504, found 225.9502.

Tributyl(1-(5-bromo-2-nitrophenylethynyl)tin (115). Tributyltin hydride (1.98 g, 6.79 mmol) was added drop wise, at ambient temperature, to a solution of PdCl$_2$(PPh$_3$)$_2$ (318 mg, 0.453 mmol) and 114 (1.02 g, 4.53 mmol) in THF (10 mL). The dark brown reaction mixture was stirred for 36 h followed by removal of the solvent under reduced pressure. Purification by chromatography (hexane/EtOAc, 98:2) gave 115 (2.16 g, 4.185 mmol, 92%) as a brown viscous oil. $^1$H NMR (600 MHz, CDCl$_3$) δ 7.89 (d, $J=9.0$ Hz, 1H), 7.44 (dd, $J=8.4$, 1.8 Hz, 1H), 7.27 (d, $J=1.8$ Hz, 1H), 5.75 (d, $J=2.4$ Hz, 1H), 5.46 (d, $J=2.4$ Hz, 1H), 1.48-1.42 (m, 6H), 1.26 (sext, $J=7.8$ Hz, 6H), 0.94-0.91 (m, 6H), 0.86 (t, $J=7.2$ Hz, 9H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 153.8, 146.2, 144.6, 132.4, 129.4, 128.0, 126.7, 125.8, 28.8, 27.3, 13.6, 11.0; IR (ATR) 2955, 2923, 1525, 1339, 878 cm$^{-1}$; HRMS (ESI) calcd for C$_{20}$H$_{33}$BrNO$_2$Sn (M+H$^+$) 518.0717, found 518.0730.
2,3-Di(5-bromo-2-nitrophenyl)-1,3-butadiene (116). To a slurry of copper chloride (437 mg, 4.42 mmol) in DMF (5 mL) in a round bottomed flask covered with aluminum foil to exclude light was added a solution of 115 (914 mg, 1.77 mmol) in DMF (3 mL). The resulting mixture was stirred at ambient temperature for 3 h. A saturated solution of NH$_4$Cl (aqueous, 6 mL) was added and the mixture was allowed to stir for an additional hour. The mixture was diluted with EtOAc (50 mL), was washed with H$_2$O (3 x 40 mL) and brine (40 mL). The organic phase was dried (MgSO$_4$), filtered, and the solvent was removed under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 9:1) affording 116 (223 mg, 0.491 mmol, 56%) as a white solid. mp=235 °C (decomposed); $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.90 (d, $J=9.0$ Hz, 1H), 7.75 (d, $J=1.8$ Hz, 1H), 7.67 (dd, $J=8.4$, 1.8 Hz, 1H), 5.18 (s, 1H), 4.94 (s, 1H); $^1$H NMR (100 MHz, CDCl$_3$) $\delta$ 147.6, 143.8, 136.7, 135.0, 132.1, 128.0, 125.7, 119.0; IR (ATR) 1558, 1516, 1333, 1084, 868 cm$^{-1}$; HRMS (ESI) calcd for C$_{16}$H$_{11}$Br$_2$N$_2$O$_4$ (M+H$^+$) 452.9085, found 452.9068.

5,5'-Dibromo-3,3'-bi-1H-indole (111). 2,3-Di(5-bromo-2-nitrophenyl)-1,3-butadiene (116) (207 mg, 0.456 mmol), Pd(dba)$_2$ (26.2 mg, 0.046 mmol), dppp (22.6 mg, 0.055 mmol) and phen (20.0 mg, 0.111 mmol) were dissolved in anhydrous DMF (3 mL) in a threaded ACE glass pressure tube. The tube was fitted with a pressure head, and the solution was saturated with carbon monoxide (four cycles of 6 atm of CO). The reaction mixture was heated at 120 °C under CO (6 atm) for 60 h. After cooling to ambient temperature, the crude was diluted with EtOAc (30 mL) and was washed with water (20 mLx4) and brine (20 mLx1) respectively. The organic layer was dried (MgSO$_4$), filtered and the solvent was removed from the filtrate under reduced pressure. The resulting residue was purified by chromatography (hexane/EtOAc, 7:3) to give 111 (80 mg, 0.205 mmol, 45%) as a white solid. $^1$H NMR (600 MHz, DMSO-d$_6$) $\delta$ 11.42 (br s, 1H), 7.74 (d, $J=1.8$ Hz, 1H), 7.42 (d, $J=1.2$ Hz, 1H), 7.31 (dd, $J=8.8$, 2.0 Hz, 1H); $^1$H NMR (100 MHz, DMSO-d$_6$) $\delta$ 135.0, 127.7, 123.9, 123.8, 121.4, 113.6, 111.6, 108.6; IR (ATR) 3423, 1658, 1455, 1098, 794 cm$^{-1}$.

2,2',5,5'-Tetrabromo-3,3'-bi-1H-indole (103). A mixture of 111 (51.3 mg, 0.132 mmol) and N-bromosuccinimide (NBS, 46.8 mg, 0.263 mmol) in carbon tetrachloride (2 mL) was stirred at reflux (78 °C ) for 2 h. After cooling to ambient temperature, the dark brown mixture was filtered through silica gel and the silica gel was washed with EtOAc (3 mL). The combined filtrate was concentrated under reduced pressure and purified by chromatography (hexane/EtOAc, 9:1) to give 103 (42.8 mg, 0.078 mmol, 59%) as a colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.43 (br s, 1H), 7.45 (d, $J=1.2$ Hz, 1H), 7.31 (dd, $J=8.8$, 2.0 Hz, 1H), 7.24 (d, $J=2.8$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 134.7, 129.6, 125.6, 122.0, 114.0, 112.0, 111.1, 108.2; IR (ATR) 3404, 1452, 1432, 1397, 1327, 794 cm$^{-1}$; HRMS (ESI) calcd for C$_{16}$H$_8$Br$_4$N$_2$ (M$^+$) 547.7380, found 547.7359.
2,2’,5,5’,6,6’-Hexabromo-3,3’-bi-1H-indole (105). Reaction of 111 (70.1 mg, 0.180 mmol) and NBS (192 mg, 1.08 mmol) in THF/CH₂Cl₂ (1:1, 4 mL), as described for 103 (70 °C, 13 h), gave after work up and chromatography (hexane/EtOAc, 9:1) 105 (58.0 mg, 0.082 mmol, 46%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 8.43 (br s, 1H), 7.67 (s, 1H), 7.55 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 135.5, 128.4, 123.5, 118.1, 116.3, 115.3, 112.0, 107.8; IR (ATR) 3410, 1431, 1364, 1308, 936, 731 cm⁻¹; HRMS (ESI) calcd for C₁₆H₆Br₆N₂ (M⁺) 705.5570, found 705.5597.

Tributyl(1-(4-bromo-2-nitrophenyl)ethenyl)tin (118). Tributyltin hydride (2.56 g, 8.81 mmol) was added drop wise, at ambient temperature, to a solution of PdCl₂(PPh₃)₂ (412 mg, 0.587 mmol) and 1-(4-bromo-2-nitrophenyl)ethyne (117) (1.28 g, 5.88 mmol) in THF (13 mL). The dark brown reaction mixture was stirred for 24 h followed by removal of the solvent under reduced pressure. Purification by chromatography (hexane) gave 118 (2.95 g, 5.70 mmol, 97%) as a brown oil. ¹H NMR (600 MHz, CDCl₃) δ 8.13 (d, J=1.8 Hz, 1H), 7.63 (dd, J=8.4, 1.8 Hz, 1H), 6.98 (d, J=7.8 Hz, 1H), 5.73 (d, J=2.4 Hz, 1H), 5.46 (d, J=2.4 Hz, 1H), 1.47-1.42 (m, 6H), 1.26 (sext, J=7.2 Hz, 6H), 0.93-0.90 (m, 6H), 0.86 (t, J=7.2 Hz, 9H); ¹³C NMR (150 MHz, CDCl₃) δ 153.7, 146.3, 143.3, 136.1, 131.1, 127.1, 126.7, 119.0, 28.8, 27.3, 13.6, 10.9; IR (ATR) 2921, 1522, 1464, 1339, 878 cm⁻¹; HRMS (ESI, negative ion mode) calcd for C₂₀H₃₂BrNO₂Sn (M⁻) 517.0638, found 517.0638.

2,3-Di(4-bromo-2-nitrophenyl)-1,3-butadiene (119). To a slurry of copper chloride (CuCl, 579 mg, 5.85 mmol) in DMF (3 mL) in a round bottomed flask covered with aluminum foil to exclude light was added a solution of 118 (1.21 g, 2.34 mmol) in DMF (3 mL). The resulting mixture was stirred at ambient temperature for 2 h. A saturated solution of NH₄Cl (aqueous, 6 mL) was added and the mixture was allowed to stir for an additional hour. The mixture was diluted with EtOAc (50 mL), was washed with H₂O (3 x 40 mL) and brine (40 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 9:1) to give 119 (438 mg, 0.965 mmol, 82%) as a white solid. mp=185-187 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.13 (d, J=2.0 Hz, 1H), 7.79 (dd, J=8.0, 2.0 Hz, 1H), 7.47 (d, J=8.4 Hz, 1H), 5.15 (s, 1H), 4.92 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 149.2, 144.1, 136.1, 133.8, 133.6, 127.2, 122.1, 118.9; IR (ATR) 1555, 1522, 1336, 913, 840 cm⁻¹; HRMS (ESI, negative ion mode) calcd for C₁₆H₁₀Br₂N₂O₄ (M⁻) 453.8987, found 453.9017.

6,6’-Dibromo-3,3’-Bi-1H-indole (120). 2,3-Di(4-bromo-2-nitrophenyl)-1,3-butadiene (119) (320 mg, 0.705 mmol), Pd(dba)₂ (28.4 mg, 0.049 mmol), dppp (20.4 mg, 0.049 mmol) and phen (17.8 mg, 0.099 mmol) were dissolved in anhydrous DMF (3 mL) in a threaded ACE glass pressure tube. The tube was fitted with a pressure head, and the solution was saturated with carbon monoxide (four cycles of 6 atm of
The reaction mixture was heated at 120 °C under CO (6 atm) for 42 h. The combined organic phases were dried (MgSO₄), filtered, and the solvent was removed under reduced pressure. The resulting crude product was purified by chromatography (hexane/EtOAc, 19:1) to afford 120 (176 mg, 0.451 mmol, 64%) as a white solid. mp=239-240 °C; ¹H NMR (400 MHz, DMSO-d₆) δ 11.34 (br s, 1H), 7.70 (d, J=8.8 Hz, 1H), 7.68 (d, J=2.4 Hz, 1H), 7.61 (d, J=1.6 Hz, 1H), 7.18 (dd, J=8.4, 2.0 Hz, 1H); ¹³C NMR (150 MHz, DMSO-d₆) δ 137.2, 124.9, 123.0, 121.7, 121.2, 114.1, 114.0, 109.3; IR (ATR) 3382, 1589, 1519, 1335, 801 cm⁻¹; HRMS (ESI) calcd for C₁₆H₁₁Br₂N₂ (M+H⁺) 388.9289, found 388.9287.

2,2',6,6'-Tetrabromo-3,3'-bi-1H-indole (104). A mixture of 120 (41.2 mg, 0.106 mmol) and N-bromosuccinimide (NBS, 28.6 mg, 0.161 mmol) in carbon tetrachloride (1 mL) was stirred at reflux (78 °C) for 2 h. After cooling to ambient temperature, the dark brown mixture was filtered through silica gel and the silica gel was washed with EtOAc (3 mL). The combined filtrate was concentrated under reduced pressure and purified by chromatography (hexane/EtOAc, 9:1) to give 104 (32.9 mg, 0.060 mmol, 57%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 8.37 (br s, 1H), 7.55 (d, J=1.2 Hz, 1H), 7.22 (dd, J=8.4, 1.6 Hz, 1H), 7.20 (d, J=8.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 136.7, 126.9, 123.9, 120.9, 116.3, 113.5, 110.1, 108.9; IR (ATR) 3425, 1432, 1371, 1308, 910, 815 cm⁻¹; HRMS (ESI) calcd for C₁₆H₈Br₄N₂ (M⁺) 547.7380, found 547.7364.

2,2',5,5',6,6'-Hexabromo-3,3'-bi-1H-indole (105) and 2,2',5,6,6'-pentabromo-3,3'-bi-1H-indole (121). Compound 56 (40.1 mg, 0.173 mmol) was treated with NBS (123 mg, 0.690 mmol) in THF/CH₂Cl₂ (1:1, 4 mL), as described for 103 (70 °C, 6 h), gave after work up and chromatography (hexane/EtOAc, 9:1), in order of elution, 104 (7.8 mg, 0.014 mmol, 8%) and 121 (8.5 mg, 0.014 mmol, 8%) both as a colorless oil.

2,2',5,5',6,6'-Hexabromo-3,3'-bi-1H-indole (105) and 2,2',5,6,6'-pentabromo-3,3'-bi-1H-indole (121). Compound 56 (40.1 mg, 0.173 mmol) was treated with NBS (123 mg, 0.690 mmol) in THF/CH₂Cl₂ (1:1, 4 mL), as described for 103 (70 °C, 6 h). Work up and chromatography (hexane/EtOAc, 95:5) gave, in order of elution, 104 (7.8 mg, 0.014 mmol, 8%) and 121 (8.5 mg, 0.014 mmol, 8%) both as a colorless oil.

2,2',5,5',6,6'-Hexabromo-3,3'-bi-1H-indole (105) and 2,2',5,6,6'-pentabromo-3,3'-bi-1H-indole (121). Compound 56 (32.2 mg, 0.139 mmol) was treated with NBS (126 mg, 0.708 mmol) in
THF/CH$_2$Cl$_2$ (1:1, 3 mL), as described for 103 (70 °C, 16 h). Work up and chromatography (hexane/EtOAc, 95:5) gave, in order of elution, 121 (10.8 mg, 0.017 mmol, 12%) and 105 (10.1 mg, 0.014 mmol, 10%) both as a colorless oil.

2,2',5,5',6,6'-Hexabromo-3,3'-bi-1H-indole (105). Compound 56 (40.8 mg, 0.176 mmol) was treated with NBS (250 mg, 1.40 mmol) in THF/CH$_2$Cl$_2$ (1:1, 3 mL), as described for 103 (70 °C, 22 h). Work up and chromatography (hexane/EtOAc, 95:5) gave 105 (19.3 mg, 0.027 mmol, 16%) as a colorless oil.
5-Methoxy-2-nitro-N-(2-methyl-1-propen-1-yl)benzenamine (145). To a solution of 5-methoxy-2-nitrobenzenamine (1.00 g, 5.95 mmol) and 2-methylpropanal (515 mg, 7.14 mmol) in dichloromethane (DCM, 12 mL) at ambient temperature under a nitrogen atmosphere was added 4 Å molecular sieves (3 g, activated by heating at 120 °C under vacuum overnight, then stored under nitrogen). The reaction mixture was allowed to sit without agitation or stirring for 48 h. The mixture was then filtered and the sieves were washed with DCM (20 mL). The filtrate was concentrated under reduced pressure and the resulting residue was purified by chromatography (hexane/EtOAc, 9:1) to give 145 (484 mg, 2.18 mmol, 37%) as a red solid. mp=83-84 °C; 1H NMR (600 MHz, CDCl3) δ 9.86 (d, J=7.2 Hz, 1H), 8.14 (d, J=9.6 Hz, 1H), 6.32 (d, J=3.0 Hz, 1H), 6.29 (dd, J=9.6, 2.4 Hz, 1H), 6.20 (dpent, J=9.6, 1.2 Hz, 1H), 3.88 (s, 3H), 1.83 (s, 3H), 1.80 (s, 3H); 13C NMR (150 MHz, CDCl3) δ 165.7, 143.5, 129.0, 126.0, 119.0, 118.0, 106.1, 95.0, 55.7, 22.5, 16.8; IR (ATR) 2923, 1616, 1585, 1497, 1239 cm⁻¹; HRMS (ESI) calcd for C11H14N2O3Na (M+Na⁺) 245.0902, found 245.0896.

4-Bromo-2-nitro-N-(2-methyl-1-propen-1-yl)benzenamine (133). Treatment of a solution of 4-bromo-2-nitrobenzenamine (1.04 g, 4.78 mmol) and 2-methylpropanal (414 mg, 5.74 mmol) in dichloromethane (DCM, 12 mL) at ambient temperature under a nitrogen atmosphere in the presence of 4 Å molecular sieves (3 g), as described for 145 (24 h), gave after work up and chromatography (hexane/EtOAc, 95:5), 133 (726 mg, 2.68 mmol, 56%) as a violet solid. mp=119-120 °C; 1H NMR (400 MHz, CDCl3) δ 9.55 (d, J=8.0 Hz, 1H), 8.29 (d, J=2.4 Hz, 1H), 7.47 (dd, J=9.2, 2.4 Hz, 1H), 6.93 (d, J=9.6 Hz, 1H), 6.20 (d, J=9.6 Hz, 1H), 1.81 (s, 3H), 1.78 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 140.3, 138.8, 128.8, 119.9, 117.9, 116.0, 107.6, 22.5, 16.8; IR (ATR) 2912, 1564, 1340, 1165 cm⁻¹; HRMS (ESI) calcd for C10H12BrN2O2 (M+H⁺) 271.0082, found 271.0078.

5-Bromo-2-nitro-N-(2-methyl-1-propen-1-yl)benzenamine (150). Treatment of a solution of 5-bromo-2-nitrobenzenamine (455 mg, 2.10 mmol) with 2-methylpropanal (182 mg, 2.52 mmol) in benzene (6 mL), in the presence of 4 Å molecular sieves (4 g), at ambient temperature under a nitrogen atmosphere, as described for 145 (24 h), gave after work up and chromatography (hexane/EtOAc, 95:5), 150 (416 mg, 1.534 mmol, 73%) as a red solid. mp=94-95 °C; 1H NMR (600 MHz, CDCl3) δ 9.56 (d, J=7.2 Hz, 1H), 8.03 (d, J=9.0 Hz, 1H), 7.20 (d, J=1.2 Hz, 1H), 6.81 (dd, J=9.0, 1.8 Hz, 1H), 6.18 (d with further fine splitting, J=9.6 Hz, 1H), 1.83 (s, 3H), 1.79 (s, 3H); 13C NMR (150 MHz, CDCl3) δ 141.8, 131.6, 130.7, 128.1, 120.7, 119.8, 117.8, 117.0, 22.5, 16.9; IR (ATR) 3495, 3381, 1616, 1564, 1489, 1218 cm⁻¹; HRMS (ESI) calcd for C10H12BrN2O2 (M+H⁺) 271.0082, found 271.0078.
4-Fluoro-2-nitro-N-(2-methyl-1-propen-1-yl)benzenamine (136). Treatment of a solution of 4-fluoro-2-nitrobenzenamine (845 mg, 5.41 mmol) with 2-methylpropanal (390 mg, 5.41 mmol) in DCM (12 mL), in the presence of 5 Å molecular (12 g), at ambient temperature under a nitrogen atmosphere, as described for 145, (24 h), gave after work up and chromatography (hexane/EtOAc, 97:3), 136 (788 mg, 3.75 mmol, 69%) as a reddish-brown solid. mp=79-80 °C; 1H NMR (400 MHz, CDCl3) δ 9.48 (d, J=7.6 Hz, 1H), 7.87 (dd, J=9.6, 6.4, 2.4 Hz, 1H), 7.02 (dd, J=9.6, 4.8 Hz, 1H), 6.21 (d, J=9.6 Hz, 1H), 1.81 (s, 3H), 1.78 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 153.0 (d, J=239.0 Hz), 138.6 (d, J=1.0 Hz), 130.5 (d, J=8.0 Hz), 124.9 (d, J=24 Hz), 119.2, 118.2, 115.7 (d, J=8.0 Hz), 111.8 (d, J=26.0 Hz), 22.3, 16.7; IR (ATR) 1580, 1519, 1404, 1185, 1158, 1112 cm⁻¹; HRMS (ESI) C10H12FN2O2 (M+H⁺) 211.0883, found 211.0897.

5-Methyl-2-nitro-N-(2-methyl-1-propen-1-yl)benzenamine (153). Treatment of a solution of 5-methyl-2-nitrobenzenamine (200 mg, 1.31 mmol) and 2-methylpropanal (114 mg, 1.58 mmol) in benzene (3 mL), in the presence of 4 Å molecular sieves (1 g) at ambient temperature under a nitrogen atmosphere, as described for 145 (24 h), gave after work up and chromatography (hexane/EtOAc, 95:5), 153 (106 mg, 0.514 mmol, 39%) as a red solid. mp=75-76 °C; 1H NMR (600 MHz, CDCl3) δ 9.63 (d, J=7.8 Hz, 1H), 8.06 (d, J=9.0 Hz, 1H), 6.81 (s, 1H), 6.51 (dd, J=9.0, 1.2 Hz, 1H), 6.27 (d with further fine splitting, J=9.0 Hz, 1H), 2.35 (s, 3H), 1.82 (s, 3H), 1.79 (s, 3H); 13C NMR (150 MHz, CDCl3) δ 147.7, 141.4, 129.9, 126.8, 118.5, 118.4, 118.2, 113.8, 22.5, 22.1, 16.8; IR (ATR) 1618, 1578, 1332, 1210, 1183 cm⁻¹; HRMS (ESI) calcd for C11H15N2O2 (M+H⁺) 207.1133, found 207.1128.

4-Bromo-2-nitro-N-(2-phenyl-1-propen-1-yl)benzenamine (160). Treatment of a solution of 4-bromo-2-nitrobenzenamine (430 mg, 1.98 mmol) with 2-phenylpropanal (239 mg, 1.78 mmol) in DCM (7 mL), in the presence of 5 Å molecular sieves (3.5 g), at ambient temperature under a nitrogen atmosphere, as described for 145 (24 h), gave after work up and chromatography (hexane/EtOAc, 95:5), 160 (446 mg, 1.34 mmol, 67%) as a violet solid. mp=106-107 °C; 1H NMR (400 MHz, CDCl3) δ 9.93 (d, J=10.4 Hz, 1H), 8.37 (d, J=2.4 Hz, 1H), 7.56 (dd, J=9.2, 2.4 Hz, 1H), 7.42-7.34 (m, 4H), 7.29-7.25 (m, 1H), 7.09 (d, J=9.2 Hz, 1H), 6.87 (dq, J=10.4, 1.2 Hz, 1H), 2.21 (d, J=1.2 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ 140.9, 139.4, 138.9, 132.7, 129.0, 128.5, 126.8, 125.3, 120.6, 120.5, 116.0, 108.8, 14.7; IR (ATR) 1618, 1564, 1175, 1126, 749 cm⁻¹; HRMS (ESI) calcd for C15H13BrN2O2 (M+H⁺) 333.0238, found 333.0234.

A detailed experimental procedure for the experiment shown in Entry 1 in Table 1 is shown below. All other entries in Tables 1-3 are slight variations of this procedure. Detailed experimental procedures for all entries discussed can be found below the analytical data section.
1-Methoxybenzimidazole (124), 1-Methoxy-2-(2-methoxy-2-propyl)benzimidazole (125), and 2-(2-Hydroxy-2-propyl)-1-methoxybenzimidazole (126). A mixture of 2-nitro-N-(2-methyl-1-propen-1-yl)benzenamine (122) (160 mg, 0.833 mmol) and sodium hydride (NaH, 74.4 mg, 3.10 mmol) in dimethylsulfoxide (DMSO, 10 mL) was stirred at ambient temperature under a nitrogen atmosphere. After stirring for 1 h, the mixture was cooled to 0 °C and methyl iodide (379 mg, 2.67 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for 1 h. The resulting mixture was diluted with EtOAc (20 mL), washed with water (5x15 mL), dried (MgSO₄), and filtered. The solvents were removed from the filtrate under reduced pressure and the resulting residue was purified by chromatography (hexane/EtOAc, 7:3 then 3:7) to give, in order of elution 125 (105 mg, 0.477 mmol, 57%) as a colorless oil, 126 (25.3 mg, 0.123 mmol, 15%) as a white solid, and 124 (6.3 mg, 0.043 mmol, 5%) as a colorless oil.

Analytical data for all compounds:

1-Methoxybenzimidazole (124). Colorless oil; 1H NMR (400 MHz, CDCl₃) δ 8.08 (s, 1H), 7.78 (d, J=8.0 Hz, 1H), 7.49 (d, J=7.2, 1.2 Hz, 1H), 7.34 (td, J=7.2, 1.2 Hz, 1H), 4.17 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ 139.4, 137.4, 129.2, 123.6, 122.5, 120.9, 108.3, 67.2; IR (ATR) 1476, 1449, 1318, 1074, 962 cm⁻¹; HRMS (ESI) calcd for C₈H₉N₂O (M+H⁺) 149.0715, found 149.0710.

1-Methoxy-2-(2-methoxy-2-propyl)benzimidazole (125). Colorless oil; 1H NMR (400 MHz, CDCl₃) δ 7.75 (d, J=8.0 Hz, 1H), 7.45 (d, J=8.0 Hz, 1H), 7.32 (td, J=7.2, 1.2 Hz, 1H), 7.29 (td, J=8.0, 1.2 Hz, 1H), 4.17 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ 151.3, 136.9, 131.4, 123.4, 122.2, 120.4, 108.3, 74.5, 65.2, 51.3, 24.8; IR (ATR) 1244, 1176, 1151, 1066, 969 cm⁻¹; HRMS (ESI) calcd for C₁₂H₁₇N₂O₂ (M+H⁺) 221.1290, found 221.1285.

1-Methoxy-2-(2-hydroxy-2-propyl)benzimidazole (126). White solid; mp=121-122 °C; 1H NMR (400 MHz, CDCl₃) δ 7.71 (d, J=7.6 Hz, 1H), 7.43 (d, J=8.4 Hz, 1H), 7.31 (td, J=7.2, 1.2 Hz, 1H), 7.26 (td, J=8.0, 1.6 Hz, 1H), 4.22 (s, 3H), 3.51 (br s, 1H), 1.77 (s, 6H); 13C NMR (100 MHz, CDCl₃) δ 154.2, 136.9, 131.2, 123.3, 122.5, 120.4, 108.5, 69.8, 65.7, 28.8; IR (ATR) 3240, 1438, 1359, 1234, 1176, 1147 cm⁻¹; HRMS (ESI) calcd for C₁₁H₁₅N₂O₂ (M+H⁺) 207.1133, found 207.1118.

1,6-Dimethoxybenzimidazole (128). Colorless oil; 1H NMR (400 MHz, CDCl₃) δ 7.97 (s, 1H), 7.64 (d, J=9.6 Hz, 1H), 6.93-6.90 (m, 2H), 4.17 (s, 3H), 3.89 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ 157.3, 136.6,
133.9, 129.9, 121.6, 112.4, 91.3, 67.0, 55.8; IR (ATR) 1493, 1236, 1020, 815 cm$^{-1}$; HRMS (ESI) calcd for C$_9$H$_{11}$N$_2$O$_2$ (M+H$^+$) 179.0820, found 179.0814.

**1,6-Dimethoxy-2-(2-methoxy-2-propyl)benzimidazole (129).** Pale yellow oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.61 (d, $J$=9.6 Hz, 1H), 6.88 (dd, $J$=7.2, 2.4 Hz, 1H), 6.87 (s, 1H), 4.17 (s, 3H), 3.88 (s, 3H), 3.16 (s, 3H), 1.77 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.2, 150.5, 132.1, 131.3, 121.1, 111.8, 91.4, 74.5, 65.0, 55.8, 51.3, 24.9; IR (ATR) 2929, 1738, 1215, 1063, 817 cm$^{-1}$; HRMS (ESI) calcd for C$_{13}$H$_{19}$N$_2$O$_2$ (M+H$^+$) 251.1395, found 251.1389.

**2-(2-Hydroxy-2-propyl)-1,6-dimethoxybenzimidazole (130).** Data from a 37:1 mixture of 130 and 128: White solid; mp=119-120 °C, $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.59 (d, $J$=8.6 Hz, 1H), 6.90 (dd, $J$=8.8, 2.5 Hz, 1H), 6.87 (d, $J$=2.2 Hz, 1H), 4.21 (s, 3H), 3.89 (s, 3H), 3.26 (br s, 1H), 1.76 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.1, 153.4, 131.8, 131.4, 121.0, 111.8, 92.0, 69.8, 65.5, 55.9, 28.8; IR (neat) 3234, 1625, 1497, 1242, 1217, 1178, 1147, 1018, 956, 823 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{17}$N$_2$O$_3$ (M+H$^+$) 237.1239, found 237.1229.

**6-Chloro-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (132).** Orange solid; mp=66-67 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.05 (s, 1H), 7.66 (d, $J$=2.0 Hz, 1H), 7.63 (d, $J$=8.8 Hz, 1H), 7.38 (dd, $J$=8.4, 1.6 Hz, 1H), 4.17 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 152.4, 135.5, 132.1, 126.0, 122.3, 117.1, 111.5, 67.4; IR (ATR) 1462, 1347, 1220, 1086, 952 cm$^{-1}$; HRMS (ESI) calcd for C$_8$H$_8$BrN$_2$O (M+H$^+$) 226.9820, found 226.9814.

**6-Bromo-1-methoxybenzimidazole (134).** White solid; mp=46-47 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.05 (s, 1H), 7.66 (d, $J$=2.0 Hz, 1H), 7.38 (dd, $J$=8.4, 1.6 Hz, 1H), 4.17 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 153.0, 138.1, 130.3, 126.0, 122.3, 117.1, 111.5, 67.4; IR (ATR) 1462, 1347, 1220, 1086, 952 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{16}$BrN$_2$O (M+H$^+$) 265.0900, found 265.0893.

**6-Bromo-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (135).** Orange oil; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.57 (s, 1H), 7.56 (d, $J$=8.4 Hz, 1H), 7.32 (dd, $J$=8.4, 1.8 Hz, 1H), 4.15 (s, 3H), 3.15 (s, 3H), 1.74 (s, 6H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 152.3, 136.0, 132.6, 125.8, 121.8, 116.9, 111.5, 74.6, 65.6, 51.4, 24.8; IR (ATR) 2941, 1461, 1355, 1240, 1177 cm$^{-1}$; HRMS (ESI) calcd for C$_{13}$H$_{18}$BrN$_2$O$_2$ (M+H$^+$) 299.0395, found 299.0390.

**6-Fluoro-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (137).** Pale yellow oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.62 (dd, $J$=8.8, 4.8 Hz, 1H), 7.07 (dd, $J$=8.0, 2.4 Hz, 1H), 6.95 (td, $J$=9.6, 2.4 Hz, 1H), 4.17 (s, 3H), 3.88 (s, 3H), 3.16 (s, 3H), 1.77 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.2, 150.5, 132.1, 131.3, 121.1, 111.8, 91.4, 74.5, 65.0, 55.8, 51.3, 112; IR (ATR) 2929, 1738, 1215, 1063, 817 cm$^{-1}$; HRMS (ESI) calcd for C$_{13}$H$_{19}$N$_2$O$_2$ (M+H$^+$) 251.1395, found 251.1389.
4.13 (s, 3H), 3.14 (s, 3H), 1.73 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 159.9 (d, $^J_{CF}$=241.0 Hz), 152.2 (d, $^J_{CF}$=3.0 Hz), 133.2, 131.5 (d, $^J_{CF}$=13.0 Hz), 121.4 (d, $^J_{CF}$=10.0 Hz), 110.8 (d, $^J_{CF}$=25.0 Hz), 95.0 (d, $^J_{CF}$=28.0 Hz), 74.4, 65.2, 51.3, 24.7; IR (ATR) 1486, 1448, 1172, 1067, 965, 811 cm$^{-1}$; HRMS (ESI) calcd for C$_{13}$H$_{16}$FN$_2$O$_2$ (M+H$^+$) 239.1196, found 239.1191.

1-Methoxy-6-methylbenzimidazole (139). Colorless oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.02 (br s, 1H), 7.65 (d, $J$=8.4 Hz, 1H), 7.29 (s, 1H), 7.11 (dd, $J$=8.0, 1.2 Hz, 1H), 4.17 (s, 3H), 2.51 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 137.5, 137.0, 133.8, 129.4, 124.2, 120.4, 108.1, 67.1, 21.7; IR (ATR) 2922, 1457, 1060, 965, 806 cm$^{-1}$; HRMS (ESI) calcd for C$_9$H$_{11}$N$_2$O (M+H$^+$) 163.0871, found 163.0867.

1-Methoxy-2-(2-methoxy-2-propyl)-6-methylbenzimidazole (140). Colorless oil; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.60 (d, $J$=8.4 Hz, 1H), 7.21 (d, $J$=1.2 Hz, 1H), 7.06 (dd, $J$=8.4, 1.2 Hz, 1H), 4.15 (s, 3H), 3.15 (s, 3H), 1.76 (s, 6H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 150.8, 135.1, 133.6, 131.6, 123.9, 119.9, 108.1, 74.5, 65.1, 51.3, 24.9, 21.7; IR (ATR) 2947, 1242, 1176, 810 cm$^{-1}$; HRMS (ESI) calcd for C$_{13}$H$_{19}$N$_2$O$_2$ (M+H$^+$) 235.1446, found 235.1441.

2-(2-Hydroxy-2-propyl)-1-methoxy-6-methylbenzimidazole (141). White solid; mp=99-100 °C; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.58 (d, $J$=8.4 Hz, 1H), 7.22 (s, 1H), 7.08 (dd, $J$=8.4, 1.2 Hz, 1H), 4.21 (s, 3H), 3.44 (br s, 1H), 2.50 (s, 3H), 1.76 (s, 6H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 153.8, 135.0, 133.5, 131.4, 124.1, 119.9, 108.3, 69.8, 65.6, 28.8, 21.8; IR (ATR) 3241, 1145, 951, 815 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{17}$N$_2$O$_2$ (M+H$^+$) 221.1290, found 221.1285.

Methyl 1-methoxybenzimidazole-6-carboxylate (143). White solid; mp=126-127 °C; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 8.23 (br s, 1H), 8.19 (s, 1H), 7.99 (dd, $J$=8.4, 1.2 Hz, 1H), 7.78 (d, $J$=8.4 Hz, 1H), 4.22 (s, 3H), 3.95 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 167.0, 142.6, 140.0, 129.0, 125.6, 123.9, 120.7, 110.9, 67.7, 52.2; IR (ATR) 1698, 1441, 1320, 1260, 1226 cm$^{-1}$; HRMS (ESI) calcd for C$_{10}$H$_{11}$N$_2$O$_3$ (M+H$^+$) 207.0769, found 207.0763.

1,5-Dimethoxybenzimidazole (146). Colorless oil; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 8.01 (s, 1H), 7.35 (d, $J$=8.4 Hz, 1H), 7.23 (d, $J$=2.4 Hz, 1H), 6.98 (dd, $J$=8.4, 2.4 Hz, 1H), 4.15 (s, 3H), 3.85 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 156.4, 140.3, 137.4, 123.9, 114.1, 108.8, 102.7, 67.2, 55.7; IR (ATR) 1213, 1125, 969, 803 cm$^{-1}$; HRMS (ESI) calcd for C$_9$H$_{11}$N$_2$O$_2$ (M+H$^+$) 179.0820, found 179.0820.
5-Chloro-1-methoxybenzimidazole (148). Yellow oil; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 8.09 (s, 1H), 7.75 (d, $J$=1.8 Hz, 1H), 7.39 (d, $J$=8.4 Hz, 1H), 7.29 (dd, $J$=9.0, 1.8 Hz, 1H), 4.16 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 140.0, 138.5, 128.1, 127.8, 124.1, 120.5, 109.1, 67.3; IR (ATR) 1457, 1309, 1054, 965, 898 cm$^{-1}$; HRMS (ESI) calcd for C$_8$H$_7$ClN$_2$O (M+Na$^+$) 205.0144, found 205.0139.

5-Chloro-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (149). Yellow oil; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.71 (d, $J$=1.2 Hz, 1H), 7.35 (d, $J$=8.4 Hz, 1H), 7.28 (dd, $J$=8.4, 1.8 Hz, 1H), 4.18 (s, 3H), 3.18 (s, 3H), 1.77 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 152.7, 137.8, 130.2, 128.0, 124.0, 120.3, 109.2, 74.6, 65.5, 51.4, 24.8; IR (ATR) 2938, 1700, 1608, 1575, 1493, 1245 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{16}$ClN$_2$O$_2$ (M+H$^+$) 255.0900, found 255.0901.

5-Bromo-1-methoxybenzimidazole (151). Faint yellow oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.05 (s, 1H), 7.91 (d, $J$=1.6 Hz, 1H), 7.43 (dd, $J$=8.8, 2.0 Hz, 1H), 7.35 (d, $J$=8.8 Hz, 1H), 4.16 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 140.6, 138.4, 128.2, 126.8, 123.7, 115.6, 109.7, 67.4; IR (ATR) 1454, 1308, 1175, 1066, 729 cm$^{-1}$; HRMS (ESI) calcd for C$_8$H$_8$BrN$_2$O (M+H$^+$) 226.9820, found 226.9815.

5-Bromo-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (152). Red oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.87 (d, $J$=1.6 Hz, 1H), 7.41 (dd, $J$=8.4, 1.6 Hz, 1H), 7.31 (d, $J$=8.8 Hz, 1H), 4.17 (s, 3H), 3.17 (s, 3H), 1.77 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 152.6, 138.3, 130.5, 126.6, 123.4, 115.2, 109.6, 74.6, 65.5, 51.4, 24.8; IR (ATR) 1454, 1308, 1246, 1176, 1066 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{16}$BrN$_2$O$_2$ (M+H$^+$) 299.0395, found 299.0376.

1-Methoxy-5-methylbenzimidazole (154). Orange oil; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 8.04 (s, 1H), 7.56 (s, 1H), 7.37 (d, $J$=8.4 Hz, 1H), 7.17 (d, $J$=7.8 Hz, 1H), 4.17 (s, 3H), 2.48 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 139.9, 137.4, 132.3, 127.4, 125.2, 120.6, 107.9, 21.5; IR (ATR) 2931, 1686, 1607, 1523, 1341, 1077 cm$^{-1}$; HRMS (ESI) calcd for C$_9$H$_{11}$N$_2$O (M+H$^+$) 163.0871, found 163.0866.

1-Methoxy-5-methyl-(2-methoxy-2-propyl)benzimidazole (155). Orange oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.53 (br s, 1H), 7.32 (d, $J$=8.0 Hz, 1H), 7.14 (dd, $J$=8.0, 0.8 Hz, 1H), 4.17 (s, 3H), 3.17 (s, 3H), 2.47 (s, 3H), 1.78 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 151.2, 137.4, 132.0, 129.6, 124.9, 120.2, 107.9, 74.6, 65.2, 51.4, 25.0, 21.5; IR (ATR) 2939, 1455, 1314, 1248, 1067 cm$^{-1}$; HRMS (ESI) calcd for C$_{13}$H$_{19}$N$_2$O$_2$ (M+H$^+$) 235.1446, found 235.1439.
1-Methoxy-(2-hydroxy-2-propyl)-5-methylbenzimidazole (156). White solid; mp=99-100 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.50 (br s, 1H), 7.31 (d, $J$=8.0 Hz, 1H), 7.14 (dd, $J$=8.4, 1.2 Hz, 1H), 4.20 (s, 3H), 3.45 (br s, 1H), 2.47 (s, 3H), 1.76 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 154.2, 137.3, 132.3, 129.3, 124.7, 120.1, 108.0, 69.7, 65.6, 28.7, 21.5; IR (ATR) 3242, 1372, 1309, 1236, 1145 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{17}$N$_2$O$_2$ (M+H$^+$) 221.1290, found 221.1285.

6-Bromo-1-methoxy-(1-methoxy-1-phenylethyl)benzimidazole (161). Orange oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.67 (dd, $J$=8.8, 0.4 Hz, 1H), 7.51 (d, $J$=1.6 Hz, 1H), 7.38-7.27 (m, 3H), 3.90 (br s, 1H), 3.39 (s, 3H), 2.08 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 152.1, 144.0, 136.1, 128.2, 127.4, 125.9, 125.2, 122.0, 117.0, 111.5, 73.4, 64.8, 51.4, 25.0; IR (ATR) 1437, 1373, 1185, 981, 792 cm$^{-1}$; HRMS (ESI) calcd for C$_{17}$H$_{18}$N$_2$O$_2$ (M+H$^+$) 361.0551, found 361.0549.

6-Bromo-(1-hydroxy-1-phenylethyl)-1-methoxybenzimidazole (162). Colorless oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.62 (d, $J$=9.6 Hz, 1H), 6.88 (dd, $J$=9.6, 2.4 Hz, 1H), 6.87 (s, 1H), 4.16 (s, 3H), 3.89 (s, 3H), 3.10 (s, 3H), 2.34-2.31 (m, 2H), 2.16-2.10 (m, 2H), 1.76-1.64 (m, 2H), 1.62-1.56 (m, 3H), 1.42-1.35 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 154.2, 144.4, 136.0, 132.0, 128.6, 127.9, 126.1, 125.2, 122.0, 116.9, 111.5, 73.4, 65.0, 28.6; IR (ATR) 3233, 1449, 1364, 1251, 1089 cm$^{-1}$; HRMS (ESI) calcd for C$_{16}$H$_{16}$N$_2$O$_2$ (M+H$^+$) 347.0395, found 347.0395.

1,6-Dimethoxy-2-(1-methoxycyclohexyl)benzimidazole (158). Colorless oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.62 (d, $J$=9.6 Hz, 1H), 6.88 (dd, $J$=9.6, 2.4 Hz, 1H), 6.87 (s, 1H), 4.16 (s, 3H), 3.89 (s, 3H), 3.10 (s, 3H), 2.34-2.31 (m, 2H), 2.16-2.10 (m, 2H), 1.76-1.64 (m, 2H), 1.62-1.56 (m, 3H), 1.42-1.35 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.0, 149.9, 131.8, 131.4, 120.9, 111.7, 91.3, 75.8, 64.9, 55.7, 50.4, 32.5, 25.5, 21.7; IR (ATR) 2944, 1739, 1450, 1365, 1207 cm$^{-1}$; HRMS (ESI) calcd for C$_{16}$H$_{21}$N$_2$O$_3$ (M+H$^+$) 291.1708, found 291.1701.

1,6-Dimethoxy-2-(1-hydroxycyclohexyl)benzimidazole (159). White solid; mp=132-133 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.58 (dd, $J$=8.4, 1.2 Hz, 1H), 6.87 (dd, $J$=8.4, 2.4 Hz, 1H), 6.86 (s, 1H), 4.19 (s, 3H), 3.88 (s, 3H), 2.87 (br s, 1H), 2.17 (td, $J$=12.8, 4.0 Hz, 2H), 2.02-1.99 (m, 2H), 1.85-1.77 (m, 2H), 1.72-1.62 (m, 3H), 1.42-1.33 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.0, 153.2, 131.7, 131.5, 121.0, 111.7, 91.8, 71.3, 65.5, 55.9, 36.1, 25.3, 21.6; IR (ATR) 3281, 2940, 1504, 1451, 1435, 1237 cm$^{-1}$; HRMS (ESI) calcd for C$_{15}$H$_{21}$N$_2$O$_3$ (M+H$^+$) 277.1552; found: 277.1547.
6-Chloro-2-(2-hydroxy-2-propyl)-1-methoxybenzimidazole (163). White solid; mp=94-95 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.61 (d, J=8.8 Hz, 1H), 7.43 (d, J=2.0 Hz, 1H), 7.23 (dd, J=8.8, 2.0 Hz, 1H), 4.22 (s, 3H), 3.19 (br s, 1H), 1.77 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 155.1, 135.6, 131.8, 129.2, 123.3, 121.3, 108.6, 69.9, 66.0, 28.7; IR (ATR) 3286, 1457, 1309, 1054, 965 cm⁻¹; HRMS (ESI) calcd for C₁₁H₁₄ClN₂O₂ (M+H⁺) 241.0743, found 241.0739.

6-Bromo-2-(2-hydroxy-2-propyl)-1-methoxybenzimidazole (164). White solid; mp=118-119 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.58 (s, 1H), 7.56 (d, J=8.4 Hz, 1H), 7.36 (dd, J=8.4, 0.8 Hz, 1H), 4.21 (s, 3H), 3.36 (br s, 1H), 1.76 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 155.0, 135.9, 132.2, 126.0, 121.7, 116.6, 111.5, 69.8, 66.0, 28.7; IR (ATR) 3332, 1458, 1269, 1104, 729 cm⁻¹; HRMS (ESI) calcd for C₁₁H₁₄BrN₂O₂ (M+H⁺) 285.0238, found 285.0233.

6-Fluoro-2-(2-hydroxy-2-propyl)-1-methoxybenzimidazole (165). White solid; mp=123-124 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.61 (dd, J=9.2, 4.8 Hz, 1H), 7.10 (dd, J=8.0, 2.4 Hz, 1H), 6.99 (ddd, J=9.6, 8.8, 2.4 Hz, 1H), 4.19 (s, 3H), 3.46 (br s, 1H), 1.75 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 159.8 (d, J=C-F=241.0 Hz), 155.0 (d, J=C-F=3.0 Hz), 133.2, 131.2 (d, J=C-F=14.0 Hz), 121.3 (d, J=C-F=10.0 Hz), 111.0 (d, J=C-F=25.0 Hz), 95.3 (d, J=C-F=28.0 Hz), 69.8, 65.7, 28.7; IR (ATR) 3232, 1488, 1438, 1363, 1172, 960, 833 cm⁻¹; HRMS (ESI) calcd for C₁₁H₁₄FN₂O₂ (M+H⁺) 225.1039, found 225.1035.

5-Chloro-2-(2-hydroxy-2-propyl)-1-methoxybenzimidazole (166). Yellow oil; ¹H NMR (400 MHz, CDCl₃) δ 7.67 (d, J=2.0 Hz, 1H), 7.34 (d, J=8.8 Hz, 1H), 7.26 (dd, J=8.8, 2.0 Hz, 1H), 4.21 (s, 3H), 3.71 (br s, 1H), 1.76 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 155.4, 137.6, 129.8, 128.1, 123.7, 120.1, 109.2, 69.8, 65.9, 28.6; IR (ATR) cm⁻¹; HRMS (ESI) calcd for C₁₁H₁₄ClN₂O₂ (M+H⁺) 241.0727.

5-Bromo-2-(2-hydroxy-2-propyl)-1-methoxybenzimidazole (167). White solid; mp=109-110 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.83 (s, 1H), 7.40 (dd, J=8.8, 1.6 Hz, 1H), 7.29 (d, J=8.8 Hz, 1H), 4.20 (s, 3H), 3.49 (br s, 1H), 1.75 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 155.3, 138.1, 130.1, 126.4, 123.2, 115.4, 109.7, 69.8, 66.0, 28.7; IR (ATR) 3257, 1455, 1309, 1175, 918, 731 cm⁻¹; HRMS (ESI) calcd for C₁₁H₁₄BrN₂O₂ (M+H⁺) 285.0239, found 285.0233.

1,6-Dimethoxy-2-(1-hydroxy-1,1-diphenylmethyl)benzimidazole (169). Red viscous oil; ¹H NMR (600 MHz, CDCl₃) δ 7.24-7.21 (m, 2H), 7.19-7.16 (m, 1H), 7.15 (d, J=1.8 Hz, 1H), 7.14-7.13 (m, 1H), 7.09-
7.02 (m, 6H), 7.01 (d, J=9.0 Hz, 1H), 6.81 (dd, J=9.0, 3.0 Hz, 1H), 6.33 (br s, 1H), 3.72 (s, 3H), 3.12 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 154.8, 142.9, 142.6, 138.7, 135.9, 134.1, 130.4, 128.0, 127.6, 127.3, 127.0, 126.3, 126.0, 122.6, 120.5, 108.9, 55.9, 42.7; IR (ATR) 2835, 1529, 1493, 1228, 1040 cm⁻¹; HRMS (ESI) calcd for C22H21N2O3 (M+H⁺) 361.1552, found 361.1548.

1-Benzyl-2-(2-benzyl-2-propyl)-6-methoxybenzimidazole (171). Orange oil; 1H NMR (400 MHz, CDCl3) δ 7.64 (d, J=8.8 Hz, 1H), 7.38-7.20 (m, 10H), 6.87 (dd, J=2.8, 8.8 Hz, 1H), 5.18 (s, 2H), 4.48 (s, 2H), 3.78 (s, 3H), 1.93 (s, 6H); 13C NMR (100 MHz, CDCl3) δ 157.1, 150.9, 138.4, 134.2, 132.9, 131.2, 129.3, 129.1, 128.6, 128.2, 127.3, 126.9, 121.0, 111.9, 92.0, 79.8, 74.7, 65.6, 55.7, 25.5; IR (ATR) 2938, 1625, 1490, 1454, 1381, 1306 cm⁻¹; HRMS (ESI) calcd for C25H27N2O3 (M+H⁺) 403.2022, found 403.2014.

1-Benzyl-2-(2-hydroxy-2-propyl)-6-methoxybenzimidazole (172). White solid; mp=118-119 °C; 1H NMR (400 MHz, CDCl3) δ 7.57 (d, J=8.8 Hz, 1H), 7.53-7.50 (m, 2H), 7.45-7.42 (m, 3H), 6.85 (dd, J=8.8, 2.4 Hz, 1H), 6.69 (d, J=2.4 Hz, 1H), 5.36 (s, 2H), 3.79 (s, 3H), 3.46 (br s, 1H), 1.80 (s, 6H); 13C NMR (100 MHz, CDCl3) δ 156.9, 153.5, 133.9, 132.4, 131.2, 129.5, 129.4, 128.9, 120.8, 111.7, 92.2, 80.3, 69.9, 55.7, 28.9; IR (ATR) 3240, 1627, 1491, 1452, 1250, 1213, 1061, 932, 815 cm⁻¹; HRMS (ESI) calcd for C18H21N2O3 (M+H⁺) 313.1552, found 313.1547.

1-(2-Propen-1-yloxy)-6-methoxybenzimidazole (173). Pale yellow oil; 1H NMR (400 MHz, CDCl3) δ 7.88 (s, 1H), 7.61 (dd, J=9.6, 1.2 Hz, 1H), 6.90-6.87 (m, 2H), 6.07 (dt, J=17.2, 10.4, 6.8 Hz, 1H), 5.33 (dq, J=17.2, 1.2 Hz, 1H), 4.71 (dt, J=6.4, 1.2 Hz, 1H), 3.85 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 157.2, 137.6, 133.7, 130.5, 130.3, 123.1, 121.3, 112.1, 91.6, 79.7, 55.7; IR (ATR) 1624, 1495, 1212, 1158, 1026, 815 cm⁻¹; HRMS (ESI) calcd for C11H13N2O2 (M+H⁺) 205.0977, found 205.0961.

1-(2-Propen-1-yloxy)-2-(2-(2-propen-1-yloxy)-2-propyl)-6-methoxybenzimidazole (174). Yellow oil; 1H NMR (400 MHz, CDCl3) δ 7.60 (dd, J=8.8, 0.8 Hz, 1H), 6.87 (dd, J=8.4, 2.4 Hz, 1H), 6.85 (d, J=2.0 Hz, 1H), 6.15 (ddt, J=16.8, 10.4, 6.4 Hz, 1H), 5.87 (ddt, J=17.2, 10.4, 5.2 Hz, 1H), 5.50 (dq, J=17.2, 1.2 Hz, 1H), 5.41 (dd, J=17.2, 1.2 Hz, 1H), 5.23 (dq, J=17.2, 1.6 Hz, 1H), 5.10 (dq, J=10.4, 1.6 Hz, 1H), 4.84 (dt, J=6.4, 1.2 Hz, 2H), 3.87 (s, 3H), 3.85 (dt, J=5.2, 1.6 Hz, 2H), 1.82 (s, 6H); 13C NMR (100 MHz, CDCl3) δ 157.1, 150.7, 134.8, 132.7, 131.1, 130.9, 121.0, 120.9, 116.1, 111.7, 91.9, 78.7, 74.2, 64.5, 55.7, 25.3; IR (ATR) 2939, 1626, 1490, 1212, 1158, 1026 cm⁻¹; HRMS (ESI) calcd for C13H23N2O3 (M+H⁺) 303.1708, found 303.1702.
2-(2-Hydroxy-2-propyl)-6-methoxy-1-(2-propen-1-yloxy)benzimidazole (175). White solid; mp=110-111 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.56 (dd, $J$=8.4, 0.8 Hz, 1H), 6.87 (dd, $J$=8.8, 2.4 Hz, 1H), 6.84 (d, $J$=2.0 Hz, 1H), 6.13 (ddt, $J$=16.8, 10.4, 6.4 Hz, 1H), 5.52 (dq, $J$=17.2, 1.2 Hz, 1H), 5.44 (dq, $J$=10.8, 1.2 Hz, 1H), 4.86 (d, $J$=6.4 Hz, 2H), 3.86 (s, 3H), 3.48 (br s, 1H), 1.75 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 156.9, 153.6, 132.3, 131.2, 130.4, 121.5, 120.9, 111.7, 92.3, 79.0, 69.7, 55.8, 28.8; IR (ATR) 3208, 2991, 1490, 1252, 1176 cm$^{-1}$; HRMS (ESI) calcd for C$_{14}$H$_{19}$N$_2$O$_3$ (M+H$^+$) 263.1396, found 263.1390.

8-Methoxy-4,4-dimethyl-4$H$-benzo[4,5]imidazo[1,2-b]dioxazine (176). White solid; mp=121-122 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.55 (dd, $J$=8.8, 1.2 Hz, 1H), 6.88 (dd, $J$=8.4, 2.4 Hz, 1H), 6.86 (d, $J$=2.4 Hz, 1H), 5.44 (s, 2H), 3.83 (s, 3H), 1.76 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 156.6, 146.3, 131.6, 129.0, 120.4, 112.6, 91.3, 91.2, 75.8, 55.8, 27.4; IR (ATR) 1523, 1451, 1234, 1209, 1148 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{15}$N$_2$O$_3$ (M+H$^+$) 235.1082, found 235.1077.

6-Methoxy-1-(2-propyn-1-yloxy)benzimidazole (177). Pale yellow oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.03 (s, 1H), 7.62 (d, $J$=8.8 Hz, 1H), 6.92 (d, $J$=2.0 Hz, 1H), 6.90 (dd, $J$=8.4, 2.4 Hz, 1H), 4.86 (d, $J$=2.4 Hz, 2H), 3.85 (s, 3H), 2.68 (t, $J$=2.4 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.3, 137.8, 133.6, 130.1, 121.5, 112.4, 91.6, 79.1, 76.4, 66.0, 55.8; IR (ATR) 3286, 1626, 1496, 1298, 1021; HRMS (ESI) calcd for C$_{11}$H$_{11}$N$_2$O$_2$ (M+Na$^+$) 203.0820, found 203.0811.

2-(2-Hydroxy-2-propyl)-6-methoxy-1-(2-propyn-1-yloxy)benzimidazole (178). White solid; mp=150-151 °C (dec.); $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.57 (d, $J$=8.4 Hz, 1H), 6.89 (d, $J$=1.8 Hz, 1H), 6.87 (dd, $J$=8.4, 2.4 Hz, 1H), 5.26 (d, $J$=2.4 Hz, 2H), 3.87 (s, 3H), 2.89 (br s, 1H), 2.33 (t, $J$=3.0 Hz, 1H), 1.77 (s, 6H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 156.8, 156.2, 136.4, 135.7, 120.2, 111.4, 93.6, 77.8, 73.2, 71.2, 55.9, 34.5, 29.3; IR (ATR) 3282, 1627, 1490, 1214, 1146 cm$^{-1}$; HRMS (ESI) calcd for C$_{14}$H$_{16}$N$_2$O$_3$ (M+Na$^+$) 283.1058, found 283.1042.

1-(3-Butyn-2-yloxy)-6-methoxybenzimidazole (179). Colorless oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.04 (s, 1H), 7.62 (d, $J$=9.6 Hz, 1H), 6.89 (d, $J$=2.8 Hz, 1H), 6.88 (dd, $J$=9.6, 2.8 Hz, 1H), 5.02 (dq, $J$=6.4, 2.0 Hz, 1H), 3.85 (s, 3H), 2.63 (d, $J$=2.0 Hz, 1H), 1.70 (d, $J$=6.8 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.2, 138.3, 133.6, 130.7, 121.3, 112.1, 92.0, 80.6, 76.7, 74.1, 55.8, 20.3; IR (ATR) 1624, 1495, 1234, 1061, 816; HRMS (ESI) calcd for C$_{12}$H$_{13}$N$_2$O$_3$ (M+H$^+$) 217.0977, found 217.0968.
1-(3-Butyn-2-yl-oxy)-2-(2-hydroxy-2-propyl)-6-methoxybenzimidazole (180). White solid; mp=131-132 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.54 (d, $J$=8.8 Hz, 1H), 7.13 (d, $J$=2.4 Hz, 1H), 6.86 (dd, $J$=8.8, 2.4 Hz, 1H), 5.52 (dq, $J$=6.8, 2.0 Hz, 1H), 3.86 (s, 3H), 2.78 (br s, 1H), 2.56 (d, $J$=2.0 Hz, 1H), 1.83 (s, 3H), 2.74 (d, $J$=1.2 Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 156.8, 153.7, 133.9, 131.0, 120.5, 112.0, 93.9, 81.9, 74.3, 70.2, 55.8, 29.7, 28.4, 20.7; IR (ATR) 3168, 1489, 1251, 1217, 1179 cm$^{-1}$; HRMS (ESI) calcd for C$_{15}$H$_{19}$N$_2$O$_3$ (M+H$^+$) 275.1396, found 275.1391.

1-Acetoxy-2-(2-acetoxy-2-propyl)-6-methoxybenzimidazole (181). Yellow oil; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.60 (d, $J$=8.4 Hz, 1H), 6.87 (dd, $J$=8.4, 2.4 Hz, 1H), 6.57 (d, $J$=2.4 Hz, 1H), 3.84 (s, 3H), 2.46 (s, 3H), 1.82 (s, 6H), 1.76 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 167.1, 157.5, 150.4, 133.4, 130.8, 120.9, 112.0, 91.6, 55.8, 43.0, 31.5, 27.1, 18.9, 12.4; IR (ATR) 1809, 1630, 1491, 1213, 1158 cm$^{-1}$; HRMS (ESI) calcd for C$_{15}$H$_{19}$N$_2$O$_5$ (M+H$^+$) 307.1294, found 307.1275.

1-Acetoxy-2-(1-propen-2-yl)-6-methoxybenzimidazole (182). Pale yellow oil; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.63 (d, $J$=9.0 Hz, 1H), 6.89 (dd, $J$=9.0, 2.4 Hz, 1H), 6.63 (d, $J$=2.4 Hz, 1H), 5.69 (pent, $J$=1.2 Hz, 1H), 5.50 (pent, $J$=1.2 Hz, 1H), 3.84 (s, 3H), 2.27 (dd, $J$=1.8, 1.2 Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 167.2, 157.7, 148.3, 133.3, 133.0, 132.3, 121.2, 118.3, 112.4, 91.6, 55.8, 21.2, 18.3; IR (ATR) 1805, 1623, 1491, 1221, 1157, 813; HRMS (ESI) calcd for C$_{13}$H$_{15}$N$_2$O$_3$ (M+H$^+$) 247.1083, found 247.1066.

2,4-Dinitro-N-methyl-N-(2-methyl-1-propen-1-yl)benzenamine. Red oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.54 (d, $J$=2.8 Hz, 1H), 8.20 (dd, $J$=9.6, 2.8 Hz, 1H), 7.04 (d, $J$=9.6 Hz, 1H), 5.71 (sept, $J$=1.2 Hz, 1H), 3.09 (s, 3H), 1.71 (d, $J$=1.2 Hz, 3H), 1.42 (d, $J$=1.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 147.3, 141.3, 136.8, 132.3, 127.7, 127.0, 123.2, 117.3, 40.7, 21.4, 17.5; IR (ATR) 1601, 1580, 1501, 1311, 1137 cm$^{-1}$; HRMS (ESI) calcd for C$_{11}$H$_{14}$N$_3$O$_4$ (M+H$^+$) 252.0984, found 252.0980.

Methyl 4-N-methyl-N-(2-methyl-1-propen-1-yl)amino-3-nitrobenzoate. Red oil; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 8.27 (d, $J$=1.8 Hz, 1H), 7.96 (dd, $J$=9.0, 2.8 Hz, 1H), 6.99 (d, $J$=9.0 Hz, 1H), 5.64 (sept, $J$=1.2 Hz, 1H), 3.87 (s, 3H), 3.02 (s, 3H), 1.67 (s, 3H), 1.38 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 165.5, 146.3, 138.1, 133.5, 130.3, 128.2, 127.6, 118.7, 117.5, 52.0, 40.3, 21.4, 17.4; IR (ATR) 1704, 1607, 1525, 1290, 1259, 1126 cm$^{-1}$; HRMS (ESI) calcd for C$_{13}$H$_{17}$N$_2$O$_4$ (M+H$^+$) 265.1188, found 265.1171.
5-Chloro-2-nitro-N-methyl-N-(2-methyl-1-propen-1-yl)benzenamine. Yellow oil; \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 7.58 (d, \(J=8.4\) Hz, 1H), 7.01 (d, \(J=1.8\) Hz, 1H), 6.74 (dd, \(J=8.4, 1.8\) Hz, 1H), 5.60 (sept, \(J=1.8\) Hz, 1H), 2.97 (s, 3H), 1.68 (d, \(J=1.2\) Hz, 3H), 1.43 (d, \(J=1.2\) Hz, 3H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 144.4, 138.8, 137.7, 129.1, 127.7, 127.2, 118.5, 117.7, 40.5, 21.5, 17.5; IR (ATR) 1596, 1514, 1487, 1340, 1288 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{11}\)H\(_{14}\)ClN\(_2\)O\(_2\) (M+H\(^+\)) 241.0743, found 241.0733.

Table 4.1, Entry 1

4-Methoxy-N-(2-methyl-1-propen-1-yl)-2-nitrobenzenamine (127)
A mixture of 127 (120 mg, 0.540 mmol) and NaH (80%, 17.0 mg, 0.567 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere. After 1 h, the mixture was cooled to 0 °C and MeI (35 µL, 0.57 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for an additional 1 h. EtOAc (15 mL) was added and the mixture was washed with water (6x10 mL). The organic phase was dried (MgSO\(_4\)), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 95:5) to give 127 (57.9 mg, 0.261 mmol, 48%) as a deep red solid.

Table 4.1, Entry 2

4-Methoxy-N-(2-methyl-1-propen-1-yl)-2-nitrobenzenamine (127), 1,6-dimethoxybenzimidazole (128), and 2-(2-hydroxy-2-propyl)-1,6-dimethoxybenzimidazole (130)
A mixture of 127 (70 mg, 0.32 mmol) and NaH (80%, 9.9 mg, 0.33 mmol) in DMSO (9 mL) was stirred at ambient temperature under a nitrogen atmosphere. After 1 h, the mixture was cooled to 0 °C and MeI (41 µL, 0.66 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for an additional 1 h. EtOAc (12 mL) was added and the mixture was washed with water (8x7 mL). The organic phase was dried (MgSO\(_4\)), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 7:3) to give, in order of elution, 127 (28 mg, 0.126 mmol, 40%) as a deep red solid and an inseparable mixture of 128 and 130 (26.1 mg, 128 (1%) and 130 (34%) as calculated from \(^1\)H NMR spectrum) as a white solid.

Table 4.1, Entry 3

4-Methoxy-N-(2-methyl-1-propen-1-yl)-2-nitrobenzenamine (127), 1,6-dimethoxybenzimidazole (128), and 2-(2-hydroxy-2-propyl)-1,6-dimethoxybenzimidazole (130)
A mixture of 127 (80 mg, 0.36 mmol) and NaH (80%, 11.4 mg, 0.379 mmol) in DMSO (6 mL) was stirred at ambient temperature under a nitrogen atmosphere. After 1 h, the mixture was cooled to 0 °C and
MeI (71 µL, 1.1 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for an additional 1 h. EtOAc (13 mL) was added and the mixture was washed with water (7x8 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 7:3) to give, in order of elution, 127 (28.4 mg, 0.128 mmol, 35%) as a deep red solid and an inseparable mixture of 128 and 130 (27.8 mg, 128 (3%) and 130 (30%) as calculated from ¹H NMR spectrum) as a white solid.

Table 4.1, Entry 4

Table 4.1, Entry 6

1,6-dimethoxybenzimidazole (128), 1,6-dimethoxy-2-(2-methoxy-2-propyl)benzimidazole (129), and 2-(2-hydroxy-2-propyl)-1,6-dimethoxybenzimidazole (130)
A mixture of 127 (120 mg, 0.540 mmol) and NaH (80%, 34.0 mg, 1.13 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere. After 1 h, the mixture was cooled to 0 °C and MeI (71 µL, 1.1 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for an additional 1 h. EtOAc (15 mL) was added and the mixture was washed with water (6x10 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 7:3, then 1:1) to give, in order of elution, 129 (23.4 mg, 0.093 mmol, 17%) as a pale yellow oil and an inseparable mixture of 128 and 130 (75.5 mg, 128 (5%) and 130 (56%) as calculated from ¹H NMR spectrum) as a white solid.

Table 4.1, Entry 6

1,6-dimethoxybenzimidazole (128), 1,6-dimethoxy-2-(2-methoxy-2-propyl)benzimidazole (129), and 2-(2-hydroxy-2-propyl)-1,6-dimethoxybenzimidazole (130)
A mixture of 127 (70 mg, 0.32 mmol) and NaH (80%, 19.9 mg, 0.663 mmol) in DMSO (9 mL) was stirred at ambient temperature under a nitrogen atmosphere. After 1 h, the mixture was cooled to 0 °C and MeI (62 µL, 0.10 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for an additional 1 h. EtOAc (14 mL) was added and the mixture was washed with water (8x8 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 7:3) to give, in order of elution, 129 (14.2 mg, 0.056 mmol, 18%) as a pale yellow oil and an inseparable mixture of 128 and 130 (38.6 mg, 128 (7%) and 130 (46%) as calculated from ¹H NMR spectrum) as a white solid.
Table 4.1, Entry 7
1,6-Dimethoxy-2-(2-methoxy-2-propyl)benzimidazole (129). A mixture of 127 (115 mg, 0.518 mmol) and NaH (80%, 58.1 mg, 1.94 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for 9 h. MeI (171 µL, 2.75 mmol) was added and the mixture was stirred for 1 h. EtOAc (15 mL) was added and the mixture was washed with water (5x10 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3) to give 129 (89.1 mg, 0.356 mmol, 69%) as a pale yellow oil.

Table 4.1, Entry 8
1,6-dimethoxybenzimidazole (128), 1,6-dimethoxy-2-(2-methoxy-2-propyl)benzimidazole (129), and 2-(2-hydroxy-2-propyl)-1,6-dimethoxybenzimidazole (130)
A mixture of 127 (62.3 mg, 0.280 mmol) and NaH (80%, 31.5 mg, 1.05 mmol) in DMSO (2 mL) was stirred at ambient temperature under a nitrogen atmosphere. After stirring for 1 h, MeI (58 µL, 0.93 mmol) was added via a syringe. The resulting reaction mixture was stirred for an additional 1 h. EtOAc (10 mL) was added and the mixture was washed with water (7x6 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 7:3) to give, in order of elution, 129 (45.0 mg, 0.180 mmol, 64%) as a pale yellow oil and an inseparable mixture of 128 and 130 (4.0 mg, 128 (5%) and 130 (2%) as calculated from ¹H NMR spectrum) as a white solid.

Table 4.1, Entry 9
1,6-dimethoxy-2-(2-methoxy-2-propyl)benzimidazole (129)
To a mixture of 127 (165 mg, 0.741 mmol) and NaH (80%, 111 mg, 3.70 mmol) placed in ice bath at 0 °C under a nitrogen atmosphere was added DMSO (10 mL) followed by the immediate addition of MeI (231 µL, 3.71 mmol) via syringes. The reaction vessel was removed from the cold bath and the yellow solution was stirred at ambient temperature for 2 h. EtOAc (20 mL) was added and the mixture was washed with water (15x5 mL) and brine (15 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 7:3) to give 129 (120 mg, 0.479 mmol, 65%) as a pale yellow oil.
Table 4.1, Entry 10

1,6-Dimethoxybenzimidazole (128) and 1,6-Dimethoxy-2-(2-methoxy-2-propyl)benzimidazole (129).

A mixture of 127 (85.0 mg, 0.382 mmol) and NaH (80%, 42.9 mg, 1.43 mmol) in DMF (8 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1-2 min. MeI (72 µL, 1.16 mmol) was added and the mixture was stirred for 2 h. EtOAc (10 mL) was added and the mixture was washed with water (4x8 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3 then 1:1) to give, in order of elution, 129 (8.0 mg, 0.032 mmol, 8%) as a pale yellow oil followed by 128 (14.1 mg, 0.079 mmol, 21%) as a colorless oil.

Table 4.1, Entry 11

1,6-Dimethoxy-2-(2-methoxy-2-propyl)benzimidazole (129). A mixture of 127 (75.4 mg, 0.339 mmol) and NaH (80%, 38.1 mg, 1.27 mmol) in NMP (7 mL) was stirred at ambient temperature under a nitrogen atmosphere for 2 min. MeI (70 µL, 1.12 mmol) was added and the mixture was stirred for 2 h. EtOAc (10 mL) was added and the mixture was washed with water (5x8 mL) and brine (8 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3 then 1:1) to give 129 (25.0 mg, 0.100 mmol, 29%) as a pale yellow oil.

Table 4.1, Entry 12

1,6-Dimethoxybenzimidazole (128) and 1,6-Dimethoxy-2-(2-methoxy-2-propyl)benzimidazole (129).

A mixture of 127 (150 mg, 0.675 mmol) and NaH (80%, 75.7 mg, 2.52 mmol) in acetonitrile (MeCN, 10 mL) was stirred at ambient temperature under a nitrogen atmosphere for approximately 2 min. To the brown mixture was added MeI (134 µL, 2.15 mmol) and it was stirred for 2 h. An orange solution was obtained after 18-20 min. EtOAc (15 mL) was added and the mixture was washed with water (3x15 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3 then 1:1) to give, in order of elution 129 (21.5 mg, 0.086 mmol, 13%) as a pale yellow oil and 128 (78.1 mg, 0.438 mmol, 65%) as a colorless oil.

Table 4.2, Entry 1

1,6-Dimethoxy-2-(2-methoxy-2-propyl)benzimidazole (129). A mixture of 4-methoxy-2-nitro-N-(2-methyl-1-propen-1-yl)benzenamine 127 (191 mg, 0.859 mmol) and NaH (80%, 96.4 mg, 3.21 mmol) in
DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. The orange solution was cooled to 0 °C and MeI (171 µL, 2.75 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and the orange solution was stirred for 1 h. EtOAc (20 mL) was added and the mixture was washed with water (5×15 mL). The organic phase was dried (MgSO$_4$), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3) to give 129 (153 mg, 0.609 mmol, 71%) as a pale yellow oil.

**Table 4.2, Entry 2**

1,6-Dimethoxy-2-(2-methoxy-2-propyl)benzimidazole (129). A mixture of 127 (146 mg, 0.659 mmol) and NaH (80%, 98.7 mg, 3.29 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for 2 min. MeI (205 µL, 3.29 mmol) was added and the mixture was stirred for 2 h. EtOAc (15 mL) was added and the mixture was washed with water (4×10 mL) and brine 10 mL). The organic phase was dried (MgSO$_4$), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3) to give 129 (118 mg, 0.471 mmol, 71%) as a pale yellow oil.

**Table 4.2, Entry 3**

1,6-Dimethoxy-2-(2-methoxy-2-propyl)benzimidazole (129). A mixture of 127 (115 mg, 0.518 mmol) and NaH (80%, 58.1 mg, 1.94 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for 9 h. MeI (171 µL, 2.75 mmol) was added and the mixture was stirred for 1 h. EtOAc (15 mL) was added and the mixture was washed with water (5×10 mL). The organic phase was dried (MgSO$_4$), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3) to give 129 (89.1 mg, 0.356 mmol, 69%) as a pale yellow oil.

**Table 4.2, Entry 4**

6-Chloro-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (132). A mixture of 4-chloro-2-nitro-N-(2-methyl-1-propen-1-yl)benzenamine (131) (164 mg, 0.724 mmol) and NaH (80%, 110 mg, 3.66 mmol) in DMSO (13 mL) was stirred at ambient temperature under a nitrogen atmosphere 1 h. The mixture was cooled to 0 °C and MeI (144 µL, 2.31 mmol) was added. The reaction vessel was removed from the cold bath and the resulting orange solution was stirred for 1 h. EtOAc (20 mL) was added and the mixture was washed with water (5×15 mL). The organic phase was dried (MgSO$_4$), filtered, and the solvent was
removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 1:1) to give 132 (159 mg, 0.624 mmol, 86%) as an orange solid.

**Table 4.2, Entry 5**

6-Chloro-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (132). A mixture of 131 (133 mg, 0.587 mmol) and NaH (80%, 65.9 mg, 2.20 mmol) in DMSO (10 mL) was stirred at ambient temperature for 1 h. MeI (121 µL, 1.94 mmol) was added and the resulting orange solution was stirred for an additional 1 h. EtOAc (15 mL) was added and the mixture was washed with water (5x10 mL) and brine (10 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3) to give 132 (141 mg, 0.555 mmol, 94%) as an orange solid.

**Table 4.2, Entry 6**

6-Bromo-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (135). A mixture of 4-bromo-2-nitro-N-(2-methyl-1-propen-1-yl)benzenamine (133) (56 mg, 0.207 mmol) and NaH (80%, 23.0 mg, 0.767 mmol) in DMSO (4 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. The brown reaction mixture was cooled to 0 °C and MeI (41 µL, 0.66 mmol) was added. The reaction vessel was removed from the cold bath and the resulting orange solution was stirred for 1 h. EtOAc (10 mL) was added and the mixture was washed with water (5x10 mL) and brine (10 mL). The organic phase was concentrated under reduced pressure and the residue was purified by chromatography (hexane/EtOAc, 7:3) to give 135 (48.2 mg, 0.161 mmol, 78%) as an orange oil.

**Table 4.2, Entry 7**

6-Bromo-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (135). A mixture of 133 (96.2 mg, 0.355 mmol) and NaH (80%, 39.8 mg, 1.33 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for approximately 6 min. An immediate color change from purple to brown was observed. MeI (73 µL, 1.17 mmol) was added and the resulting orange solution was stirred for 4 h. EtOAc (15 mL) was added and the mixture was washed with water (5x10 mL) and brine (10 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3) to give 135 (104 mg, 0.329 mmol, 93%) as an orange oil.
Table 4.2, Entry 8
6-Fluoro-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (137). A mixture of 136 (134 mg, 0.636 mmol) and NaH (80%, 71.8 mg, 2.39 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere. After stirring for 1 h, MeI (132 µL, 2.12 mmol) was added via a syringe and the resulting yellow-orange solution was stirred for an additional 1 h. EtOAc (15 mL) was added and the mixture was washed with water (7x10 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 7:3) to give 137 (113 mg, 0.474 mmol, 75%) as a pale yellow oil.

Table 4.2, Entry 9
1-Methoxy-6-methylbenzimidazole (139), 1-Methoxy-2-(2-methoxy-2-propyl)-6-methylbenzimidazole (140), and 2-(2-Hydroxy-2-propyl)-1-methoxy-6-methylbenzimidazole (141). A mixture of 4-methyl-2-nitro-N-(2-methyl-1-propen-1-yl)benzenamine (138) (145 mg, 0.705 mmol) and NaH (80%, 78.9 mg, 2.63 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. The resulting orange mixture was cooled to 0 °C and MeI (140 µL, 2.25 mmol) was added. The reaction was removed from the cold bath and the resulting solution was stirred for an additional 1 h. EtOAc (20 mL) was added and the mixture was washed with water (5x15 mL) and brine (10 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, in order 7:3, 1:1, 3:7) to give, in order of elution, 140 (86.3 mg, 0.368 mmol, 52%) as a colorless oil, 141 (0.008 mg, 0.036 mmol, 5%) as a white solid and 139 (32.5 mg, 0.200 mmol, 28%) as a colorless oil.

Table 4.2, Entry 10
1-Methoxy-6-methylbenzimidazole (139) and 1-Methoxy-2-(2-methoxy-2-propyl)-6-methylbenzimidazole (140) A mixture of 138 (114 mg, 0.555 mmol) and NaH (80%, 62.3 mg, 2.08 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. MeI (111 µL, 1.78 mmol) was added and the resulting orange solution was stirred for 1 h. EtOAc (15 mL) was added and the mixture was washed with water (6X10 mL). The organic phase was dried (MgSO₄) filtered, and the solvent was removed from the filtrate under reduced pressure. The crude was purified by chromatography (hexane/EtOAc, 1:1) to give, in order of elution, 140 (88.6 mg, 0.378 mmol, 68%) and 139 (24.6 mg, 0.152 mmol, 27%) both as a colorless oil.
Table 4.2, Entry 11

1-Methoxybenzimidazole (124) and 1-Methoxy-2-(2-methoxy-2-propyl)benzimidazole (125) and 2-(2-Hydroxy-2-propyl)-1-methoxybenzimidazole (126). A mixture of 122 (160.2 mg, 0.833 mmol) and NaH (80%, 93 mg, 3.10 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere. After stirring for 1 h, the mixture was cooled to 0 °C and MeI (166 µL, 2.67 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for an additional 1 h. EtOAc (30 mL) was added and the mixture was washed with water (20x5 mL) and brine (20 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 7:3, then 3:7) to give, in order of elution, 124 (6.3 mg, 0.043 mmol, 5%) and 125 (105.1 mg, 0.477 mmol, 57%) both as a colorless oil and 126 (25.3 mg, 0.123 mmol, 15%) as a white solid.

Table 4.2, Entry 12

1-Methoxybenzimidazole (124) and 1-Methoxy-2-(2-methoxy-2-propyl)benzimidazole (125).

A mixture of 122 (160 mg, 0.832 mmol) and NaH (80%, 93.4 mg, 3.11 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. Methyl iodide (MeI, 166 µL, 2.67 mmol) was added via a syringe and the resulting orange solution was stirred for 1 h. EtOAc (20 mL) was added and the mixture was washed with water (6x15 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 7:3 then 1:1) to give, in order of elution, 124 (6.3 mg, 0.043 mmol, 5%) and 125 (105.1 mg, 0.477 mmol, 57%) both as a colorless oil.

Table 4.2, Entry 13

Methyl 4-N-methyl-N-(2-methyl-1-propen-1-yl)amino-3-nitrobenzoate. A mixture of methyl 4-(N-2-methyl-1-propen-1-yl)amino-3-nitrobenzoate (142) (195 mg, 0.779 mmol) and NaH (80%, 87.4 mg, 2.91 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for 10 min. MeI (104 µL, 1.67 mmol) was added and the mixture was stirred for an additional 1 h 50 min. EtOAc (20 mL) was added to the yellow-orange solution and the mixture was washed with water (5x15 mL) and brine (15 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 19:1) to give methyl 4-N-methyl-N-(2-methyl-1-propen-1-yl)amino-3-nitrobenzoate (128 mg, 0.484 mmol, 62%) as a red viscous oil.
Table 4.2, Entry 14
Methyl 1-methoxybenzimidazole-6-carboxylate (143). A mixture of 142 (83.5 mg, 0.334 mmol) and NaH (80%, 50.1 mg, 1.67 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for 24 h. To the resulting colorless solution was added MeI (104 µL, 1.67 mmol) and it was stirred for 1 h. EtOAc (15 mL) was added and the mixture was washed with water (5x10 mL) and brine (10 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 1:1) to give 143 (51.0 mg, 0.247 mmol, 74%) as a white solid.

Table 4.2, Entry 15
N-Methyl-N-(2-methyl-1-propen-1-yl)-2,4-dinitrobenzenamine. A mixture of N-(2-methyl-1-propen-1-yl)-2,4-dinitrobenzenamine (144) (45.1 mg, 0.190 mmol) and NaH (80%, 21.3 mg, 0.708 mmol) in DMSO (4 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. The red solution was cooled to 0 °C and MeI (38 µL, 0.61 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and the resulting solution was stirred for 1 h. EtOAc (15 mL) was added and the mixture was washed with water (5x10 mL) and brine (2x10 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 8:2) to give N-methyl-N-(2-methyl-1-propen-1-yl)-2,4-dinitrobenzenamine (40.6 mg, 0.162 mmol, 85%) as a red oil.

Table 4.2, Entry 16
A mixture of 144 (36 mg, 0.15 mmol) and NaH (80%, 22.7 mg, 0.758 mmol) in DMSO (5 mL) was stirred at ambient temperature under a nitrogen atmosphere for 24 h. MeI (47 µL, 0.76 mmol) was added via a syringe and the resulting solution was stirred for an additional 2 h. EtOAc (10 mL) was added and the mixture was washed with water (5x7 mL) and brine (2x7 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. No product or unreacted starting material was observed in the ¹H NMR of the crude reaction mixture.

Table 4.2, Entry 17
5-Methoxy-N-methyl-2-nitrobenzenamine. A mixture of 5-methoxy-2-nitro-N-(2-methyl-1-propen-1-yl)benzenamine (145) (156 mg, 0.703 mmol) and NaH (80%, 84.4 mg, 2.81 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. To the resulting orange mixture was added MeI (145 µL, 2.33 mmol) and the solution was stirred for 1 h. EtOAc (20 mL) was added and
the mixture was washed with water (5x15 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude was purified by chromatography (hexane/EtOAc, 9:1) to give the 5-methoxy-N-methyl-2-nitrobenzenamine (71.0 mg, 0.390 mmol, 55%) as an orange solid.

Table 4.2, Entry 18
1,5-Dimethoxybenzimidazole (146). A mixture of 145 (53 mg, 0.24 mmol) and NaH (80%, 35.7 mg, 1.19 mmol) in DMSO (5 mL) was stirred at ambient temperature under a nitrogen atmosphere for 24 h. To the resulting almost clear solution was added MeI (58 µL, 0.93 mmol) and the solution was stirred for 1 h. EtOAc (10 mL) was added and the mixture was washed with water (7x8 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude was purified by chromatography (hexane/EtOAc, 1:1) to give 146 (21.6 mg, 0.121 mmol, 51%) as a colorless oil.

Table 4.2, Entry 19
5-Chloro-2-nitro-N-methyl-N-(2-methyl-1-propen-1-yl)benzenamine and 5-chloro-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (149). A mixture of 147 (175 mg, 0.775 mmol) and NaH (80%, 87.0 mg, 2.90 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for 6 min. MeI (160 µL, 2.57 mmol) was added and the resulting solution was stirred for 2 h. EtOAc (20 mL) was added and the mixture was washed with water (5x15 mL) and brine (15 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 8:2 then 1:1) to give, in order of elution, 5-chloro-2-nitro-N-methyl-N-(2-methyl-1-propen-1-yl)benzenamine (109 mg, 0.452 mmol, 52%) and 149 (17.8 mg, 0.070 mmol, 9%) both as a yellow oil.

Table 4.2, Entry 20
5-Chloro-1-methoxybenzimidazole (148) and 5-chloro-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (149). A mixture of 5-chloro-2-nitro-N-(2-methyl-1-propen-1-yl)benzenamine (147) (225 mg, 0.991 mmol) and NaH (80%, 111 mg, 3.70 mmol) in DMSO (15 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. The orange solution was cooled to 0 ºC and MeI (205 µL, 3.29 mmol) was added. The reaction vessel was removed from the cold bath and stirred for 1 h. EtOAc (20 mL) was added and the mixture was washed with water (5x15 mL) and brine (15 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under

136
reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3 then 1:1) to give, in order of elution, 149 (68.2 mg, 0.268 mmol, 27%) and 148 (101 mg, 0.555 mmol, 56%) both as a yellow oil.

**Table 4.2, Entry 21**

5-Chloro-1-methoxybenzimidazole (148) and 5-chloro-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (149). A mixture of 147 (53.3 mg, 0.235 mmol) and NaH (80%, 26.4 mg, 0.879 mmol) in DMSO (2 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. MeI (49 µL, 0.783 mmol) was added. The reaction mixture was stirred for an additional 1 h. EtOAc (10 mL) was added and the mixture was washed with water (5x7 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3) to give, in order of elution, 149 (18.8 mg, 0.074 mmol, 31%) and 148 (22.5 mg, 0.123 mmol, 52%) both as a yellow oil.

**Table 4.2, Entry 22**

5-Bromo-1-methoxybenzimidazole (151) and 5-bromo-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (152). A mixture of 5-bromo-2-nitro-N-(2-methyl-1-propen-1-yl)benzenamine (150) (141 mg, 0.519 mmol) and NaH (80%, 58.4 mg, 1.95 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for approximately 10 min. An immediate color change from purple to brown was observed. MeI (107 µL, 1.72 mmol) was added and the resulting orange solution was stirred for 2 h. EtOAc (15 mL) was added and the mixture was washed with water (5x10 mL) and brine (10 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3 then 1:1) to give, in order of elution, 152 (43.4 mg, 0.145 mmol, 28%) as a red oil and 151 (79.3 mg, 0.349 mmol, 67%) as a pale yellow oil.

**Table 4.2, Entry 23**

5-Bromo-1-methoxybenzimidazole (151) and 5-bromo-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (152). A mixture of 150 (76.8 mg, 0.283 mmol) and NaH (80%, 32 mg, 1.07 mmol) in DMSO (9 mL) was stirred at ambient temperature under a nitrogen atmosphere for approximately 1 h. To the resulting orange solution was added MeI (59 µL, 0.943 mmol) was added and stirred for an additional 1 h. EtOAc (12 mL) was added and the mixture was washed with water (7x8 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under
reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3 then 1:1) to give, in order of elution, 152 (24.8 mg, 0.083 mmol, 29%) as a red oil and 151 (35.4 mg, 0.156 mmol, 55%) as a pale yellow oil.

Table 4.2, Entry 24
1-Methoxy-5-methylbenzimidazole (154), 1-Methoxy-2-(2-methoxy-2-propyl)-5-methylbenzimidazole (155), and 2-(2-Hydroxy-2-propyl)-1-methoxy-5-methylbenzimidazole (156). A mixture of 5-methyl-2-nitro-N-(2-methyl-1-propen-1-yl)benzenamine (153) (136 mg, 0.657 mmol) and NaH (80%, 73.4 mg, 2.45 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. The yellowish-brown solution was cooled to 0 °C and MeI (136 µL, 2.18 mmol) was added. The reaction vessel was removed from the cold bath and the resulting orange solution was stirred for 1 h. EtOAc (20 mL) was added and the mixture was washed with water (5x15 mL) and brine (15 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3 then 3:7) to give, in order of elution, 155 (33.6 mg, 0.143 mmol, 22%) as an orange oil, 156 (29.2 mg, 0.133 mmol, 20%) as a white solid and 154 (22.7 mg, 0.140 mmol, 21%) as an orange oil.

Table 4.2, Entry 25
1-Methoxy-5-methylbenzimidazole (154) and 1-Methoxy-2-(2-methoxy-2-propyl)-5-methylbenzimidazole (155). A mixture of 5-methyl-2-nitro-N-(2-methyl-1-propen-1-yl)benzenamine (153) (47.1 mg, 0.228 mmol) and NaH (80%, 25.6 mg, 0.854 mmol) in DMSO (5 mL) was stirred at ambient temperature under a nitrogen atmosphere for approximately 10 min. To the yellowish brown solution was added MeI (47 µL, 0.76 mmol) and the resulting orange solution was stirred for 2 h. EtOAc (8 mL) was added and the mixture was washed with water (5x5 mL) and brine (5 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3 then 1:1) to give, in order of elution, 155 (13.8 mg, 0.059 mmol, 26%) and 154 (11.5 mg, 0.071 mmol, 31%) both as an orange oil.

Table 4.2, Entry 26
1,6-Dimethoxy-2-(1-methoxycyclohexyl)benzimidazole (158). A mixture of 4-methoxy-2-nitro-N-(cyclohexylmethylene)benzenamine (157) (149 mg, 0.569 mmol) and NaH (80%, 63.5 mg, 2.12 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. The orange-yellow solution was cooled to 0 °C and MeI (113 µL, 1.82 mmol) was added. The reaction vessel was
removed from the cold bath and the resulting orange solution was stirred for 1 h. EtOAc (20 mL) was added and the mixture was washed with water (5x20 mL) and brine (20 mL). The organic phase was concentrated under reduced pressure and the residue was purified by chromatography (hexane/EtOAc, 7:3) to give 158 (129 mg, 0.446 mmol, 78%) as a colorless oil.

Table 4.2, Entry 27
1,6-Dimethoxy-2-(1-methoxycyclohexyl)benzimidazole (158), 1,6-Dimethoxy-2-(1-hydroxycyclohexyl)benzimidazole (159). A mixture of 157 (104 mg, 0.396 mmol) and NaH (80%, 44.5 mg, 1.48 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for 2 min. An immediate color change from purple to brown was observed. MeI (82 µL, 1.32 mmol) was added and the resulting orange solution was stirred for 2 h. EtOAc (20 mL) was added and the mixture was washed with water (5x20 mL) and brine (15 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3 then 4:6) to give, in order of elution, 158 (97 mg, 0.33 mmol, 84%) as a colorless oil and 159 (12.2 mg, 0.044 mmol, 11%) as a white solid.

Table 4.2, Entry 28
6-Bromo-1-methoxybenzimidazole (134), 6-Bromo-1-methoxy-(1-methoxy-1-phenylethyl)benzimidazole (161), and 6-bromo-(1-hydroxy-1-phenylethyl)-1-methoxybenzimidazole (162). A mixture of 4-bromo-2-nitro-N-(2-phenyl-1-propen-1-yl)benzenamine (160) (157 mg, 0.471 mmol) and NaH (80%, 52.6 mg, 1.75 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. The brown reaction mixture was cooled to 0 °C and MeI (94 µL, 1.51 mmol) was added. The reaction vessel was removed from the cold bath and the resulting orange solution was stirred for 1 h. EtOAc (20 mL) was added and the mixture was washed with water (5x15 mL) and brine (15 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3 then 3:7) to give, in order of elution, 161 (37.2 mg, 0.103 mmol, 22%) as an orange oil, 162 (20.5 mg, 0.059 mmol, 13%) as a colorless oil and 134 (25.7 mg, 0.113 mmol, 22%) as a white solid.

Table 4.2, Entry 29
6-Bromo-1-methoxybenzimidazole (134). A mixture of 160 (50.0 mg, 0.150 mmol) and NaH (80%, 16.9 mg, 0.563 mmol) in DMSO (5 mL) was stirred at ambient temperature under a nitrogen atmosphere for approximately 38 min. Color change was not observed in the specified period of time. MeI (31 µL,
0.50 mmol) was added and the resulting faint yellow solution was stirred for an 1h 22 m. EtOAc (10 mL) was added and the mixture was washed with water (5x5 mL) and brine (5 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3 then 3:7) to give 134 (34.1 mg, 0.150 mmol, 92%) as a white solid.

Scheme 4.3
2-(2-Hydroxy-2,2-diphenylmethyl)-1,6-dimethoxybenzimidazole (169) and benzophenone (170). A mixture of 4-methoxy-2-nitro-N-(2,2-diphenylethenyl)benzenamine (168) (124 mg, 0.358 mmol) and NaH (80%, 40.1 mg, 1.34 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for 35 min. MeI (74 µL, 1.19 mmol) was added and the resulting red solution was stirred for 1 h 25 min. EtOAc (20 mL) was added and the mixture was washed with water (5x15 mL) and brine (15 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3 then 3:7) to give, in order of elution, 170 (5.7 mg, 0.03 mmol, 9%) as a colorless oil and 169 (115 mg, 0.320 mmol, 89%) as a red viscous oil.

Scheme 4.3
1,6-Dimethoxybenzimidazole (128) and benzophenone (170). A mixture of 168 (124 mg, 0.385 mmol) and t-BuOK (201 mg, 1.79 mmol) in t-BuOH (5 mL) was stirred at ambient temperature under a nitrogen atmosphere for 24 h. MeI (89 µL, 1.43 mmol) was added and the mixture was stirred for 1 h. The resulting mixture was filtered through silica gel and silica gel was washed with EtOAc. The solvent was removed from the filtrate under reduced pressure and the resulting residue was purified by chromatography (hexane/EtOAc, 9:1 then 1:1) to give, in order of elution, 170 (63.6 mg, 0.349 mmol, 97%) and 128 (49.8 mg, 0.279 mmol, 78%) both as a colorless oil.

Table 4.3, Entry 1
2-(2-Hydroxy-2-propyl)-1-methoxybenzimidazole (126). A mixture of 122 (83.1 mg, 0.432 mmol) and NaH (80%, 27.3 mg, 0.908 mmol) in DMSO (8 mL) was stirred at ambient temperature under a nitrogen atmosphere. After stirring for 1 h, the mixture was cooled to 0 °C and MeI (28 µL, 0.454 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for an additional 1 h. EtOAc (13 mL) was added and the mixture was washed with water (7x8 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The residue
was purified by chromatography (hexane/EtOAc, 7:3 then 1:1) to give 126 (49.4 mg, 0.240 mmol, 55%) as a white solid.

Table 4.3, Entry 2
1,6-Dimethoxybenzimidazole (128) and 2-(2-Hydroxy-2-propyl)-1,6-dimethoxy-benzimidazole (130). A mixture of 127 (120 mg, 0.540 mmol) and NaH (80%, 34.0 mg, 1.13 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere. After 1 h, the mixture was cooled to 0 °C and MeI (35 µL, 0.57 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for an additional 1 h. EtOAc (15 mL) was added and the mixture was washed with water (6x10 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 1:1) to give an inseparable mixture of 128 and 130 (96.1 mg, 128 (2%) and 130 (74%) as calculated from ¹H NMR spectrum) as a white solid.

Table 4.3, Entry 3
6-Chloro-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (132) and 6-Chloro-2-(2-hydroxy-2-propyl)-1-methoxybenzimidazole (163). A mixture of 131 (121 mg, 0.534 mmol) and NaH (80%, 33.6 mg, 1.12 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere. After stirring for 1 h, the mixture was cooled to 0 °C and MeI (35 µL, 0.56 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for an additional 1 h. EtOAc (20 mL) was added and the mixture was washed with water (8x15 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 7:3, then 6:4)) to give, in order of elution, 132 (27.5 mg, 0.108 mmol, 20%) as a orange solid and 163 (76.0 mg, 0.316 mmol, 59%) as a white solid.

Table 4.3, Entry 4
6-Bromo-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (135) and 6-Bromo-2-(2-hydroxy-2-propyl)-1-methoxybenzimidazole (164). A mixture of 133 (71.3 mg, 0.263 mmol) and NaH (80%, 16.6 mg, 0.554 mmol) in DMSO (8 mL) was stirred at ambient temperature under a nitrogen atmosphere. After stirring for 1 h, the mixture was cooled to 0 °C and MeI (17 µL, 0.275 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for an additional 1 h. EtOAc (12 mL) was added and the mixture was washed with water (7x8 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by
chromatography (hexane/EtOAc, 6:4) to give, in order of elution, 135 (17.1 mg, 0.057 mmol, 22%) as an orange oil and 164 (51.0 mg, 0.178 mmol, 68%) as a white solid.

Table 4.3, Entry 5
6-Fluoro-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (137) and 6-Fluoro-2-(2-hydroxy-2-propyl)-1-methoxybenzimidazole (165). A mixture of 136 (80 mg, 0.381 mmol) and NaH (80%, 24 mg, 0.80 mmol) in DMSO (8 mL) was stirred at ambient temperature under a nitrogen atmosphere. After stirring for 1 h, the mixture was cooled to 0 °C and MeI (25 µL, 0.40 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for an additional 1 h. EtOAc (10 mL) was added and the mixture was washed with water (7x8 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 6:4)) to give, in order of elution, 137 (14 mg, 0.06 mmol, 15%) as a pale yellow oil and 165 (48.1 mg, 0.215 mmol, 56%) as a white solid.

Table 4.3, Entry 6
1-Methoxy-6-methylbenzimidazole (139) and 2-(2-Hydroxy-2-propyl)-1-methoxy-6-methylbenzimidazole (141). A mixture of 138 (83.0 mg, 0.402 mmol) and NaH (80%, 25.4 mg, 0.908 mmol) in DMSO (8 mL) was stirred at ambient temperature under a nitrogen atmosphere. After stirring for 1 h, the mixture was cooled to 0 °C and MeI (26 µL, 0.422 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for an additional 1 h. EtOAc (13 mL) was added and the mixture was washed with water (7x8 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 6:4) to give an inseparable mixture of 139 and 141 (57.5 mg, 139 (11%) and 141 (45%) as calculated from ¹H NMR spectrum) as a white solid.

Table 4.3, Entry 7
Methyl 4-N-methyl-N-(2-methyl-1-propen-1-yl)amino-3-nitrobenzoate. A mixture of 142 (83 mg, 0.33 mmol) and NaH (80%, 21 mg, 0.70 mmol) in DMSO (8 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. The dirty brown mixture was cooled to 0 °C and MeI (22 µL, 0.35 mmol) was added. The reaction vessel was removed from the cold bath and the resulting solution was stirred for an additional 1 h. EtOAc (12 mL) was added and the mixture was washed with water (8x8 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under
reduced pressure. An ~3:1 mixture of methyl 4-N-methyl-N-(2-methyl-1-propen-1-yl)amino-3-nitrobenzoate and 159 was observed in the $^1$H NMR of the crude reaction mixture.

**Table 4.3, Entry 8**

**Methyl 1-methoxybenzimidazole-6-carboxylate (143).** A mixture of 142 (110.2 mg, 0.440 mmol) and NaH (80%, 27.7 mg, 0.925 mmol) in DMSO (8 mL) was stirred at ambient temperature under a nitrogen atmosphere. After 24 h, the mixture was cooled to 0 °C and MeI (29 µL, 0.465 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for an additional 1 h. EtOAc (15 mL) was added and the mixture was washed with water (7x8 mL). The organic phase was dried (MgSO$_4$), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 1:1 then 3:7) to give 143 (66.2 mg, 0.321 mmol, 73%) as a white solid.

**Table 4.3, Entry 10**

**1,5-Dimethoxybenzimidazole (146).** A mixture of 145 (98.5 mg, 0.443 mmol) and NaH (80%, 27.9 mg, 0.930 mmol) in DMSO (8 mL) was stirred at ambient temperature under a nitrogen atmosphere. After 24 h, the mixture was cooled to 0 °C and MeI (29 µL, 0.465 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for an additional 1 h. EtOAc (15 mL) was added and the mixture was washed with water (7x8 mL). The organic phase was dried (MgSO$_4$), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 1:1 then 3:7) to give 146 (50.8 mg, 0.285 mmol, 64%) as a colorless oil.

**Table 4.3, Entry 11**

**5-Chloro-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (149) and 5-Chloro-2-(2-hydroxy-2-propyl)-1-methoxybenzimidazole (166).** A mixture of 147 (118 mg, 0.521 mmol) and NaH (80%, 32.7 mg, 1.09 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere. After stirring for 1 h, the mixture was cooled to 0 °C and MeI (34 µL, 0.55 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for an additional 1 h. EtOAc (15 mL) was added and the mixture was washed with water (7x10 mL). The organic phase was dried (MgSO$_4$), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 7:3, then 1:1)) to give, in order of elution, 149 (20.1 mg, 0.079 mmol, 15%) and 166 (69.1 mg, 0.287 mmol, 55%) both as yellow oils.
Table 4.3, Entry 12
5-Bromo-1-methoxy-2(2-methoxy-2-propyl)benzimidazole (152) and 5-Bromo-2(2-hydroxy-2-propyl)-1-methoxybenzimidazole (167). A mixture of 150 (73 mg, 0.27 mmol) and NaH (80%, 17 mg, 0.57 mmol) in DMSO (8 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. The reddish-brown solution was cooled to 0 °C and MeI (18 µL, 0.28 mmol) was added. The reaction vessel was removed from the cold bath and the mixture was stirred for 1 h. EtOAc (13 mL) was added and the mixture was washed with water (7x8 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 6:4) to give, in order of elution, 152 (12.9 mg, 0.043 mmol, 16%) as a red oil and 167 (48 mg, 0.17 mmol, 63%) as a white solid.

Table 4.3, Entry 13
2-(2-Hydroxy-2-propyl)-1-methoxy-5-methylbenzimidazole (156). A mixture of 153 (100 mg, 0.485 mmol) and NaH (80%, 30.5 mg, 1.017 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. After stirring for 1 h, the mixture was cooled to 0 °C and MeI (32 µL, 0.51 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for an additional 1 h. EtOAc (15 mL) was added and the mixture was washed with water (7x10 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 6:4) to give 156 (65.2 mg, 0.296 mmol, 61%) as a white solid.

Table 4.3, Entry 14
1,6-Dimethoxy-2-(1-methoxycyclohexyl)benzimidazole (158), 1,6-Dimethoxy-2-(1-hydroxycyclohexyl)benzimidazole (159). A mixture of 157 (73 mg, 0.28 mmol) and NaH (80%, 17.5 mg, 0.583 mmol) in DMSO (8 mL) was stirred at ambient temperature under a nitrogen atmosphere. After stirring for 1 h, the mixture was cooled to 0 °C and MeI (18 µL, 0.29 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for an additional 1 h. EtOAc (12 mL) was added and the mixture was washed with water (7x8 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 6:4) to give, in order of elution, 158 (15.4 mg, 0.053 mmol, 19%) as a colorless oil and 159 (39.4 mg, 0.143 mmol, 51%) as a white solid.
Table 4.3, Entry 15
6-Bromo-1-methoxybenzimidazole (134) and 6-Bromo-2-(2-hydroxy-2-phenylethyl)-1-methoxybenzimidazole (162). A mixture of 160 (73 mg, 0.22 mmol) and NaH (80%, 13.7 mg, 0.458 mmol) in DMSO (8 mL) was stirred at ambient temperature under a nitrogen atmosphere. After stirring for 1 h, the mixture was cooled to 0 °C and MeI (14 µL, 0.23 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and stirred for an additional 1 h. EtOAc (13 mL) was added and the mixture was washed with water (7x9 mL). The organic phase was dried (MgSO₄), filtered and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 6:4) to give, in order of elution, 162 (39.4 mg, 0.114 mmol, 52%) and 134 (10.6 mg, 0.047 mmol, 22%) both as a white solid.

Table 4.4, Entry 1
1-Benzyl oxy-2-(2-benzyloxy-2-propyl)-6-methoxybenzimidazole (171) and 1-benzyloxy-2-(2-hydroxy-2-propyl)-6-methoxybenzimidazole (172). A mixture of 127 (108 mg, 0.484 mmol) and NaH (80%, 54.0 mg, 1.80 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. The orange mixture was cooled to 0 °C and benzyl bromide (BnBr, 191 µL, 1.61 mmol) was added via a syringe. The resulting almost colorless solution was stirred for an additional 1 h. EtOAc (20 mL) was added and the resulting mixture was washed with water (5x10 mL) and brine (10 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3 then 1:1) to give, in order of elution, 171 (56.3 mg, 0.140 mmol, 29%) as an orange oil and 172 (56.8 mg, 0.182 mmol, 38%) as a white solid.

Table 4.4, Entry 2
1-Benzyl oxy-2-(2-benzyloxy-2-propyl)-6-methoxybenzimidazole (171) and 1-Benzyl oxy-2-(2-hydroxy-2-propyl)-6-methoxybenzimidazole (172). A mixture of 127 (104 mg, 0.469 mmol) and NaH (80%, 52.7 mg, 1.76 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for approximately 2 min. An immediate color change from purple to brown was observed. Benzyl bromide (185 µL, 1.56 mmol) was added via a syringe and the mixture was stirred for an additional 2 h. EtOAc (15 mL) was added and the resulting mixture was washed with water (5x10 mL) and brine (10 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3...
then 1:1) to give, in order of elution, 171 (94.5 mg, 0.235 mmol, 50%) as an orange oil and 172 (27.9 mg, 0.089 mmol, 19%) as a white solid.

**Table 4.4, Entry 3**

1-(2-Propen-1-yloxy)-2-(2-(2-propen-1-yloxy)-2-propyl)-6-methoxybenzimidazole (174) and 2-(2-Hydroxyl-2-propyl)-1-(2-propen-1-yloxy)-6-methoxybenzimidazole (175) and 1-(2-propen-1-yloxy)-7-methoxybenzimidazole (173). A mixture of 127 (80.3 mg, 0.389 mmol) and NaH (80%, 43.5 mg, 1.45 mmol) in DMSO (8 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. The orange mixture was cooled to 0 °C and allyl bromide (108 µL, 1.25 mmol) was added via syringe. The reaction vessel was removed from the cold bath and the resulting orange solution was stirred for an additional 1 h. EtOAc (15 mL) was added and the mixture was washed with water (5x10 mL) and brine (10 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3 then 1:1) to give, in order of elution, 174 (16.7 mg, 0.055 mmol, 14%) as a pale yellow oil and a mixture of 173 and 175 (36.3 mg, 173 (5%) and 175 (31%) as calculated from ¹H NMR spectrum) as a white solid.

**Table 4.4, Entry 4**

1-(2-Propen-1-yloxy)-2-(2-(2-propen-1-yloxy)-2-propyl)-6-methoxybenzimidazole (174). A mixture of 127 (178 mg, 0.803 mmol) and NaH (80%, 96.4 mg, 3.21 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for approximately 1 min. An immediate color change from purple to brown was observed. Allyl bromide (236 µL, 2.73 mmol) was added via syringe and the resulting orange mixture was stirred for an addition 2 h. EtOAc (20 mL) was added and the mixture was washed with water (5x15 mL) and brine (15 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc) to give 174 (142.6 mg, 0.472 mmol, 59%) as a yellow oil.

**Table 4.4, Entry 5**

8-Methoxy-4,4-dimethyl-4H-benzo[4,5]imidazo[1,2-b]dioxazine (176). A mixture of 127 (143 mg, 0.642 mmol) and NaH (80%, 72.0 mg, 2.40 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere for approximately 2 min. An immediate color change from purple to brown was observed. Diiodomethane (172 µL, 2.13 mmol) was added via a syringe and the resulting reddish-brown solution was stirred for an additional 2 h. EtOAc (20 mL) was added and the mixture was washed with water (5x15 mL) and brine (15 mL). The organic phase was dried (MgSO₄), filtered, and the solvent
was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 1:1) to give 176 (59.6 mg, 0.254 mmol, 40%) as a white solid.

Table 4.4, Entry 6
6-Methoxy-1-(2-propyn-1-yloxy)benzimidazole (177) and 2-(2-Hydroxy-2-propyl)-6-methoxy-1-(2-propyn-1-yloxy)benzimidazole (178). A mixture of 127 (311 mg, 1.400 mmol) and NaH (80%, 157 mg, 5.23 mmol) in DMSO (15 mL) was stirred at ambient temperature under a nitrogen atmosphere for approximately 1 min. An immediate color change from purple to brown was observed. Propargyl bromide (414 µL, 4.65 mmol) was added via a syringe and the resulting reddish-brown solution was stirred for an additional 2 h. EtOAc (20 mL) was added and the mixture was washed with water (7x10 mL). The organic phase was dried (MgSO$_4$), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 9:1, then 85:15) to give, in order of elution, 178 (171 mg, 0.656 mmol, 47%) as a white solid and 177 (17 mg, 0.084 mmol, 6%) as a pale yellow oil.

Table 4.4, Entry 7
1-(3-Butyn-2-yloxy)-6-methoxybenzimidazole (179) and 1-(3-Butyn-2-yloxy)-2-(2-hydroxy-2-propyl)-6-methoxybenzimidazole (180). A mixture of 127 (100 mg, 0.450 mmol) and NaH (80%, 50.7 mg, 1.69 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere. After 1 h, the reaction mixture was cooled to 0 °C and 3-bromo-1-butyn (135 µL, 1.49 mmol) was added via syringe and the reaction vessel was removed from the cold bath and light brown solution was stirred for an additional 1 h. EtOAc (20 mL) was added and the mixture was washed with water (5x15 mL) and brine (15 mL). The organic phase was dried (MgSO$_4$), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 1:1) to give, in order of elution, 180 (50.1 mg, 0.183 mmol, 41%) as a white solid and 179 (9 mg, 0.042 mmol, 9%) as a colorless liquid.

Table 4.4, Entry 8
1-(3-Butyn-2-yloxy)-2-(2-hydroxy-2-propyl)-6-methoxybenzimidazole (180). A mixture of 127 (180 mg, 0.871 mmol) and NaH (80%, 97.3 mg, 3.24 mmol) in DMSO (10 mL) was stirred at ambient temperature under a nitrogen atmosphere. After 1 h, the reaction mixture was cooled to 0 °C and 3-bromo-1-butyn (261 µL, 2.79 mmol) was added via syringe and the reaction vessel was removed from the cold bath and light brown solution was stirred for an additional 1 h. EtOAc (20 mL) was added and
the mixture was washed with water (5x15 mL) and brine (15 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3) to give 180 (157 mg, 0.572 mmol, 66%) as a white solid.

Scheme 4.4
1-Acetoxy-2-(2-acetoxy-2-propyl)-6-methoxybenzimidazole (181) and 1-Acetoxy-2-(2-propen-2-yl)-6-methoxybenzimidazole (182). A mixture of 127 (334 mg, 1.50 mmol) and NaH (80%, 169 mg, 5.62 mmol) in DMSO (15 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. The reaction mixture was cooled to 0 °C and acetyl chloride (355 µL, 4.97 mmol) was added via a syringe. The reaction vessel was removed from the cold bath and the resulting mixture was stirred for an additional 1 h. EtOAc (20 mL) was added and the mixture was washed with water (7x15 mL). The organic phase was dried (MgSO₄), filtered, and the solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 7:3, then 1:1) to give, in order of elution, 182 (20.6 mg, 0.084 mmol, 6%) as a pale yellow oil and 181 (80.9 mg, 0.264 mmol, 18%) as a yellow oil.
4-Methoxy-2-nitro-\(N\)-(2-phenyl-1-propen-1-yl)benzenamine (190). To a solution of 4-methoxy-2-nitrobenzenamine (500 mg, 2.974 mmol) and 2-phenylpropanal (399.1 mg, 2.974 mmol) in dichloromethane (DCM, 12 mL) at ambient temperature under a nitrogen atmosphere was added 4 Å molecular sieves (3 g, activated by heating at 120 °C under vacuum overnight, then stored under nitrogen). The reaction mixture was allowed to sit without agitation or stirring for 48 h. The mixture was then filtered and the sieves were washed with DCM (20 mL). The filtrate was concentrated under reduced pressure and the resulting residue was purified by chromatography (hexane/EtOAc, 95:5) to give 190 (501 mg, 1.762 mmol, 59%) as a red solid. mp=85-86 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.92 (d, \(J=10.8\) Hz, 1H), 9.83 (d, \(J=10.8\) Hz, 1H), 7.57 (d, \(J=2.8\) Hz, 1H), 7.49 (d, \(J=2.0\) Hz, 1H), 7.38-7.32 (m, 5H), 7.29-7.21 (m, 3H), 7.18-7.12 (m, 2H), 7.10-7.04 (m, 4H), 6.85 (dq, \(J=10.8, 0.8\) Hz, 1H), 6.50 (dq, \(J=10.8, 0.8\) Hz, 1H), 3.74 (s, 3H), 3.71 (s, 3H), 2.12 (d, \(J=1.2\) Hz, 3H), 2.06 (d, \(J=1.2\) Hz, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 151.1, 150.7, 141.4, 139.1, 136.0, 131.8, 131.3, 129.0, 128.5, 127.3, 127.3, 127.0, 126.9, 126.4, 125.2, 121.4, 119.9, 118.8, 118.4, 115.8, 115.6, 107.1, 107.0, 55.8, 55.8, 22.0, 14.6; IR (ATR) 3311, 1640, 1571, 1513, 1163, 1060 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{16}\)H\(_{17}\)N\(_2\)O\(_3\) (M+H\(^+\)) 285.1239, found 285.1225.

1-Methoxybenzimidazole (124).\(^{136}\) A mixture of \(N\)-(2-methyl-1-propen-1-yl)-2-nitrobenzenamine (122)\(^{134}\) (63.8 mg, 0.332 mmol) and \(t\)-BuOK (149 mg, 1.33 mmol) in \(t\)-BuOH (5 mL) was stirred at ambient temperature under a nitrogen atmosphere for 24 h. MeI (62 µL, 0.996 mmol) was added via a syringe and the mixture was stirred for an additional 1 h. The resulting orange mixture containing floating white solids was filtered through silica gel and the filtrate was washed with EtOAc (10 mL). The solvent was removed from the filtrate under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 1:1) to give 124 (0.049 mg, 0.332 mmol, 100%) as a colorless oil.

1,6-Dimethoxybenzimidazole (128).\(^{136}\) Reaction of a solution of 4-methoxy-2-nitro-\(N\)-(2-methyl-1-propen-1-yl)benzenamine (127)\(^{134}\) (216 mg, 0.973 mmol) with MeI (194 µL, 3.15 mmol) in \(t\)-BuOH (10 mL) in the presence of \(t\)-BuOK (437 mg, 3.89 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 1:1), 128 (131 mg, 0.735 mmol, 76%) as a colorless oil.

1-Methoxy-6-methylbenzimidazole (139).\(^{136}\) Reaction of a solution of 4-methyl-2-nitro-\(N\)-(2-methyl-1-propen-1-yl)benzenamine (138)\(^{136}\) (76 mg, 0.368 mmol) with MeI (69 µL, 1.105 mmol) in \(t\)-BuOH (5

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149
mL) in the presence of t-BuOK (165.4 mg, 1.474 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 1:1), 139 (45.5 mg, 0.281 mmol, 76%) as a colorless oil.

6-Chloro-1-methoxybenzimidazole (191). Reaction of a solution of 4-chloro-2-nitro-N-(2-methyl-1-propen-1-y1)benzenamine (131)134 (75 mg, 0.331 mmol) with MeI (62 µL, 0.993 mmol) in t-BuOH (5 mL) in the presence of t-BuOK (148.5 mg, 1.323 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 1:1), 191 (55.6 mg, 0.304 mmol, 92%) as a colorless oil. 1H NMR (400 MHz, CDCl3) δ 8.05 (s, 1H), 7.66 (d, J=8.8 Hz, 1H), 7.47 (d, J=2.0 Hz, 1H), 7.23 (dd, J=8.8, 2.0 Hz, 1H), 4.15 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 138.2, 137.9, 129.8, 129.6, 123.4, 121.8, 108.5, 67.4; IR (neat) 3293, 1623, 1473, 1346, 1214 cm⁻¹; HRMS (ESI) calcd for C8H7ClN2O (M+Na+) 205.0144, found 205.0139.

6-Bromo-1-methoxybenzimidazole (134).136 Reaction of a solution of 4-bromo-2-nitro-N-(2-methyl-1-propen-1-y1)benzenamine (133)136 (136.2 mg, 0.502 mmol) with MeI (94 µL, 1.506 mmol) in t-BuOH (8 mL) in the presence of t-BuOK (225.5 mg, 2.010 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 1:1), 134 (96.9 mg, 0.427 mmol, 85%) as a colorless oil.

6-Fluoro-1-methoxybenzimidazole (192). Reaction of a solution of 4-fluoro-2-nitro-N-(2-methyl-1-propen-1-y1)benzenamine (136)136 (118.1 mg, 0.562 mmol) with MeI (75 µL, 1.197 mmol) in t-BuOH (10 mL) in the presence of t-BuOK (252.2 mg, 2.248 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 1:1), 192 (62.6 mg, 0.377 mmol, 67%) as a colorless oil. 1H NMR (400 MHz, CDCl3) δ 8.06 (s, 1H), 7.70 (dd, J=5.6, 2.8 Hz, 1H), 7.16 (dd, J=5.6, 1.6 Hz, 1H), 7.03 (td, J=6.4, 1.6 Hz, 1H), 4.17 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 161.4, 158.9, 138.1, 135.8, 122.0 (d, Jc-F=10 Hz, 1C), 111.3 (d, Jc-F=25 Hz, 1C), 95.1 (d, Jc-F=28 Hz, 1C), 67.2; IR (neat) 3395, 1626, 1493, 1357, 1225 cm⁻¹; HRMS (ESI) calcd for C8H8N2O2 (M+H⁺) 167.0621, found 167.0614.

1,5-Dimethoxybenzimidazole (146).136 Reaction of a solution of 5-methoxy-2-nitro-N-(2-methyl-1-propen-1-y1)benzenamine (12)136 (77.2 mg, 0.347 mmol) with MeI (65 µL, 1.041 mmol) in t-BuOH (5
mL) in the presence of t-BuOK (155.9 mg, 1.389 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 1:1), 146 (45.4 mg, 0.255 mmol, 73%) as a colorless oil.

1-Methoxy-5-methylbenzimidazole (154). Reaction of a solution of 5-methyl-2-nitro-N-(2-methyl-1-propen-1-yl)benzenamine (153) (183 mg, 0.887 mmol) with MeI (166 µL, 2.662 mmol) in t-BuOH (10 mL) in the presence of t-BuOK (398.3 mg, 3.550 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 1:1), 154 (102.3 mg, 0.631 mmol, 71%) as an orange oil.

5-Chloro-1-methoxybenzimidazole (148). Reaction of a solution of 5-chloro-2-nitro-N-(2-methyl-1-propen-1-yl)benzenamine (147) (197.9 mg, 0.873 mmol) with MeI (163 µL, 2.619 mmol) in t-BuOH (10 mL) in the presence of t-BuOK (391.9 mg, 3.493 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 1:1), 148 (113.5 mg, 0.622 mmol, 71%) as a yellow oil.

5-Bromo-1-methoxybenzimidazole (151). Reaction of a solution of 5-bromo-2-nitro-N-(2-methyl-1-propen-1-yl)benzenamine (150) (86.9 mg, 0.321 mmol) with MeI (60 µL, 0.962 mmol) in t-BuOH (5 mL) in the presence of t-BuOK (143.9 mg, 1.282 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 1:1), 151 (53.5 mg, 0.236 mmol, 73%) as a faint yellow oil.

1,6-Dimethoxybenzimidazole (128). Reaction of a solution of 4-methoxy-2-nitro-N-(cyclohexylmethylene)benzenamine (157) (339.5 mg, 1.295 mmol) with MeI (258 µL, 4.144 mmol) in t-BuOH (10 mL) in the presence of t-BuOK (580.9 mg, 5.177 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 1:1), 128 (176.1 mg, 0.988 mmol, 76%) as a colorless oil.
1,6-Dimethoxybenzimidazole (128). Reaction of a solution of 4-methoxy-2-nitro-N-(2,2-diphenylethylene)benzenamine (168)\(^{134}\) (123.9 mg, 0.358 mmol) with MeI (89 µL, 1.432 mmol) in \(t\)-BuOH (5 mL) in the presence of \(t\)-BuOK (200.7 mg, 1.789 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 9:1, then, 1:1), in order of elution, benzophenone (170, 63.6 mg, 0.349 mmol, 98%) and 128 (49.8 mg, 0.279 mmol, 78%) both as a colorless oil.

6-Bromo-1-methoxybenzimidazole (134).\(^{136}\) Reaction of a solution of 4-bromo-2-nitro-N-(2-phenyl-1-propen-1-yl)benzenamine (160)\(^{136}\) (50.8 mg, 0.153 mmol) with MeI (29 µL, 0.459 mmol) in \(t\)-BuOH (3 mL) in the presence of \(t\)-BuOK (68.6 mg, 0.611 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 1:1), 134 (32.5 mg, 0.143 mmol, 94%) as a colorless oil that solidified upon standing.

1-Benzylxylo-6-methoxybenzimidazole (193). Reaction of a solution of 127 (109.7 mg, 0.494 mmol) with benzyl bromide (BnBr, 152 µL, 1.283 mmol) in \(t\)-BuOH (8 mL) in the presence of \(t\)-BuOK (208.3 mg, 1.856 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 95:5, 6:4) 193 (103.4 mg, 0.407 mmol, 82%) as a colorless oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.59 (d, \(J=8.8\) Hz, 1H), 7.57 (s, 1H), 7.41-7.34 (m, 3H), 7.31-7.28 (m, 2H), 6.87 (dd, \(J=8.8, 2.4\) Hz, 1H), 6.72 (d, \(J=2.4\) Hz, 1H), 5.19 (s, 2H), 3.80 (s, 3H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 157.1, 137.6, 133.8, 133.6, 130.3, 129.8, 129.6, 128.8, 121.3, 112.2, 91.5, 80.9, 55.6; IR (neat) 1624, 1494, 1234, 1061, 816 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{15}\)H\(_{14}\)N\(_2\)O\(_2\) (M+H\(^+\)) 255.1133, found 255.1123.

6-methoxy-1-(2-propen-1-yloxy)benzimidazole (194). Reaction of a solution of 127 (52.2 mg, 0.235 mmol) with allyl bromide (41 µL, 0.470 mmol) in \(t\)-BuOH (5 mL) in the presence of \(t\)-BuOK (105.4 mg, 0.939 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 1:1) 194 (47.9 mg, 0.235 mmol, 100%) as a colorless oil.

1-(2-Methyl-2-propen-1-yloxy)-6-methoxybenzimidazole (195). Reaction of a solution of 127 (106.4 mg, 0.479 mmol) with 3-bromo-2-methyl-1-propene (102 µL, 1.016 mmol) in \(t\)-BuOH (10 mL) in the presence of \(t\)-BuOK (214.9 mg, 1.915 mmol), at ambient temperature under a nitrogen atmosphere, as
described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 7:3) 195 (94.3 mg, 0.432 mmol, 90%) as a colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.85 (s, 1H), 7.59 (d, J=9.2 Hz, 1H), 6.88 (d, J=2.4 Hz, 1H), 6.86 (dd, J=9.6, 2.4 Hz, 1H), 5.05 (pentet, J=1.6 Hz, 1H), 4.93 (pentet, J=0.8 Hz, 1H), 4.59 (s, with further fine splitting, 2H), 3.83 (s, 3H), 1.94 (t, J=1.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.1, 138.2, 137.4, 133.6, 130.0, 121.3, 118.4, 112.0, 91.5, 82.9, 55.6, 19.6; IR (neat) 1629, 1499, 1449, 1230, 917, 822 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{15}$N$_2$O$_2$ (M+H$^+$) 219.1133, found 219.1123.

6-Methoxy-1-(1,2-propadien-1-yloxy)benzimidazole (196). Reaction of a solution of 127 (131.3 mg, 0.591 mmol) with propargyl bromide (112 $\mu$L, 1.259 mmol) in t-BuOH (8 mL) in the presence of t-BuOK (259.2 mg, 2.310 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 1:1) 196 (17.4 mg, 0.086 mmol, 15%) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.91 (s, 1H), 7.54 (d, J=8.8 Hz, 1H), 7.28 (d, J=2.4 Hz, 1H), 7.13 (t, J=6.4 Hz, 1H), 6.95 (dd, J=8.8, 2.4 Hz, 1H), 5.69 (d, J=6.4 Hz, 2H), 3.87 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 203.0, 156.5, 145.1, 141.8, 127.3, 113.5, 111.2, 102.6, 95.3, 88.2, 55.8; IR (neat) 3367, 1488, 1239, 1144, 850 cm$^{-1}$; HRMS (ESI) calcd for C$_{11}$H$_{11}$N$_2$O$_2$ (M+H$^+$) 208.0820, found 208.0811.

1-(1,2-Butadien-1-yloxy)-6-methoxybenzimidazole (197). Reaction of a solution of 127 (131.3 mg, 0.586 mmol) with 3-bromo-1-butyne (181 $\mu$L, 2.000 mmol) in t-BuOH (12 mL) in the presence of t-BuOK (449.6 mg, 4.007 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 1:1) 197 (26.1 mg, 0.121 mmol, 12%) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.01 (s, 1H), 7.63 (d, J=8.8 Hz, 1H), 6.93 (d, J=2.4 Hz, 1H), 6.90 (dd, J=8.8, 2.4 Hz, 1H), 4.82 (q, J=2.4 Hz, 2H), 3.86 (s, 3H), 1.85 (t, J=2.4 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.2, 138.4, 137.9, 133.7, 130.3, 121.4, 112.3, 91.7, 87.7, 72.3, 66.9, 55.8; IR (neat) 1624, 1495, 1418, 127.3, 113.5, 111.2, 102.6, 95.3, 88.2, 55.8; IR (neat) 3367, 1488, 1239, 1144, 850 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{13}$N$_2$O$_2$ (M+H$^+$) 217.0977, found 217.0968.

1-Acetoxy-6-methoxybenzimidazole (198). Reaction of a solution of 127 (130.3 mg, 0.586 mmol) with acetyl chloride (88 $\mu$L, 1.236 mmol) in t-BuOH (10 mL) in the presence of t-BuOK (449.6 mg, 4.007 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 6:4) 198 (65.4 mg, 0.317 mmol, 54%) as a white solid. mp=231-231.5 °C, $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 11.28 (br, s, 1H), 7.84 (d, J=8.8 Hz, 1H), 6.61 (dd, J=8.8, 2.4 Hz, 1H), 6.56 (d, J=2.4 Hz, 1H), 3.73 (s, 3H), 2.57 (s, 3H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 169.9, 156.6, 152.7, 129.5, 120.8, 115.6, 106.8, 95.4, 55.4, 25.0; IR (neat) 1709, 1634, 1377, 1332, 1158, 1014 cm$^{-1}$; HRMS (ESI) calcd for C$_{10}$H$_{10}$N$_2$O$_3$ (M+Na$^+$) 229.0589, found 229.0596.
1-(Heptyloxy)-6-methoxybenzimidazole (199). Reaction of a solution of 127 (113.6 mg, 0.511 mmol) with 1-bromoheptane (169 µL, 1.073 mmol) in t-BuOH (10 mL) in the presence of t-BuOK (229.4 mg, 2.044 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 7:3) 199 (21.8 mg, 0.083 mmol, 16%) as a colorless oil. 

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.93 (s, 1H), 7.63 (d, $J$=9.2 Hz, 1H), 6.91 (dd, $J$=8.4, 2.4 Hz, 1H), 6.88 (d, $J$=2.0 Hz, 1H), 4.28 (t, $J$=6.8 Hz, 2H), 3.88 (s, 3H), 1.84-1.76 (m, 3H), 1.52-1.48 (m, 1H), 1.39-1.29 (m, 6H), 0.90 (t, with further splitting, $J$=7.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.2, 137.3, 133.9, 130.4, 121.4, 112.2, 91.5, 79.7, 55.8, 31.6, 28.9, 28.2, 25.6, 22.5, 14.0; IR (neat) 2928, 1625, 1496, 1236, 1064 cm$^{-1}$; HRMS (ESI) calcd for C$_{15}$H$_{23}$N$_2$O$_2$ (M+H$^+$) 263.1759, found 263.1749.

1-(1-butyloxy)-6-methoxybenzimidazole (200). Reaction of a solution of 127 (111.5 mg, 0.502 mmol) with 1-iodobutane (120 µL, 1.054 mmol) in t-BuOH (8 mL) in the presence of t-BuOK (224.1 mg, 1.997 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 6:4) 200 (16.8 mg, 0.076 mmol, 15%) as a colorless oil. 

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.94 (s, 1H), 7.63 (d, $J$=8.8 Hz, 1H), 6.91 (dd, $J$=8.4, 2.4 Hz, 1H), 6.88 (d, $J$=2.0 Hz, 1H), 4.28 (t, $J$=6.4 Hz, 2H), 3.88 (s, 3H), 1.84-1.75 (m, 2H), 1.58-1.52 (m, 1H), 1.01 (t, $J$=7.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.2, 137.3, 133.9, 130.4, 121.4, 112.2, 91.5, 79.5, 55.8, 30.1, 18.9, 13.7; IR (neat) 2959, 1625, 1496, 1236, 1063, 1022, 816 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{17}$N$_2$O$_2$ (M+H$^+$) 221.1290, found 221.1280.

6-methoxy-1-(2-methylethylloxy)benzimidazole (201). Reaction of a solution of 127 (143.6 mg, 0.646 mmol) with 2-iodopropane (136 µL, 1.357 mmol) in t-BuOH (8 mL) in the presence of t-BuOK (290 mg, 2.584 mmol), at ambient temperature under a nitrogen atmosphere, as described for 124 (25 h), gave after work up and chromatography (hexane/EtOAc, 6:4) 201 (10.9 mg, 0.053 mmol, 8%) as a colorless oil. 

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.90 (s, 1H), 7.63 (d, $J$=8.8 Hz, 1H), 6.90 (dd, $J$=8.8, 2.8 Hz, 1H), 6.87 (d, $J$=2.4 Hz, 1H), 4.57 (heptet, $J$=6.0 Hz, 1H), 3.88 (s, 3H), 1.39 (d, $J$=6.4 Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.2, 138.2, 133.9, 131.2, 121.4, 112.2, 91.5, 79.5, 55.8, 30.1, 18.9, 13.7; IR (neat) 2959, 1625, 1497, 1105, 817 cm$^{-1}$; HRMS (ESI) calcd for C$_{11}$H$_{15}$N$_2$O$_2$ (M+H$^+$) 207.1133, found 207.1124.
2,4-Dinitro-5-bromophenyl trifluoromethanesulfonate (204) To a solution of fuming HNO₃ (2 mL) in H₂SO₄ (2 mL) was added 3-bromophenyl trifluoromethanesulfonate (203)¹⁷² (297 mg, 0.974 mmol) and the mixture was heated at 60 °C for 7 h. The resulting mixture was poured onto ice, the ice was allowed to melt, and the resulting mixture was extracted with EtOAc (3 x 20 mL). The combined organic phases were dried (MgSO₄), filtered, and the solvents were removed under reduced pressure. The crude product was purified by chromatography (hexanes/EtOAc, 9:1) affording 204 (307 mg, 0.777 mmol, 80%) as a pale yellow oil that solidified upon standing. mp = 33-35 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.73 (s, 1H), 7.90 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 148.2, 142.6, 140.1, 131.2, 124.0, 122.2, 118.4 (q, Jₐₙ-C-F = 319 Hz); IR (ATR) 1591, 1541, 1436, 1337, 1213, 1130 cm⁻¹.

5-Ethenyl-2,4-dinitro trifluoromethanesulfonate (205). A mixture of 204 (238 mg, 0.60 mmol), ethenyltributyltin (187 mg, 0.59 mmol), 2,6-di-t-butyl-4-methylphenol (22 mg, 0.10 mmol), LiCl (87 mg, 2.05 mmol), PPh₃ (25.2 mg, 0.098 mmol), and PdCl₂(PPh₃)₂ (33.7 mg, 0.048 mmol) in toluene (4 mL) was heated at 80 °C for 17 h. The solvent was removed at reduced pressure and the crude product was purified by chromatography (hexanes/EtOAc, 9:1) to give 205 (160 mg, 0.468 mmol, 78%) as a faint brown oil. ¹H NMR (600 MHz, CDCl₃) δ 8.82 (s, 1H), 7.69 (s, 1H), 7.26 (dd, J = 17.4, 10.8 Hz, 1H), 5.96 (d, J = 17.4 Hz, 1H), 5.84 (d, J = 11.4 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 145.3, 143.6, 140.5, 129.8, 127.4, 125.0, 124.4, 123.9, 118.5 (q, Jₐₙ-C-F = 319 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ -72.9; IR (ATR) 1614, 1590, 1539, 1437, 1345, 1223, 1134 cm⁻¹.

4-Bromo-3-nitrophenyl trifluoromethanesulfonate (215). To a solution of 4-bromo-3-nitrophenol¹⁷⁴ (269 mg, 1.23 mmol) in CH₂Cl₂ (5 mL) at 0 °C was added pyridine (200 µL, 2.48 mmol) and trifluoromethanesulfonic anhydride (Tf₂O, 250 µL, 1.48 mmol). The mixture was removed from the cold bath and allowed to stir at ambient temperature for 30 min. The resulting mixture was filtered through a small plug of silica gel and the solvent was removed under reduced pressure from the filtrate. Purification by chromatography (hexanes/EtOAc, 9:1) afforded 215 (391 mg, 1.12 mmol, 90%) as a yellow oil. ¹H NMR (600 MHz, CDCl₃) δ 7.88 (d, J = 9.0 Hz, 1H), 7.82 (d, J = 2.4 Hz, 1H), 7.41 (dd, J = 9.0, 3.0 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 150.1, 147.9, 136.8, 126.2, 119.3, 118.6 (q, Jₐₙ-C-F = 319 Hz), 114.6; IR (ATR) 3103, 1541, 1428, 1208, 1132 cm⁻¹; HRMS (ESI) calcd for C₇H₄BrNaN₃O₃F₃S (M+Na⁺) 371.8765; found 371.8760.

3-Bromo-2-nitrophenyl trifluoromethanesulfonate (216). Treatment of 3-bromo-2-nitrophenol¹⁷⁵ (298 mg, 1.37 mmol) in CH₂Cl₂ (5 mL) with pyridine (250 µL, 3.10 mmol) and Tf₂O (300 µL, 1.77 mmol), as described for 213, gave after chromatography (hexanes/EtOAc, 8:2) 216 (394 mg, 1.13 mmol, 80%) as a
red solid. mp 52-53 °C; 1H NMR (400 MHz, CDCl3) δ 7.74-7.72 (m, 1H), 7.50-7.49 (m, 2H); 13C NMR (150 MHz, CDCl3) δ 140.6, 133.4, 132.1, 121.6, 119.4, 117.3 (q, JCF = 319 Hz), 115.2; 19F NMR (376 MHz, CDCl3) δ -73.2; IR (ATR) 3099, 1538, 1434, 1360, 1219, 1132 cm^-1; HRMS (ESI) calcd for C7H3BrNNaO3F3S (M+Na^+) 371.8765; found 371.8767.

2-Bromo-6-nitrophenyl trifluoromethanesulfonate (217). Treatment of 2-bromo-6-nitrophenol176 (189 mg, 0.87 mmol) in CH2Cl2 (5 mL) with pyridine (150 µL, 1.85 mmol) and Tf2O (200 µL, 1.18 mmol), as described for 215, gave after chromatography (hexanes/EtOAc, 7:3) 217 (299 mg, 0.85 mmol 98%) as a colorless oil. 1H NMR (600 MHz, CDCl3) δ 8.03 (dd, J = 7.8, 1.2 Hz, 1H), 7.98 (dd, J = 8.4, 1.8 Hz, 1H), 7.45 (dt, J = 8.4, 1.2 Hz, 1H); 13C NMR (150 MHz, CDCl3) δ 143.6, 139.4, 139.1, 129.3, 125.6, 119.0, 118.4 (q, JCF = 319 Hz); 19F NMR (376 MHz, CDCl3) δ -73.2; IR (ATR) 3093, 1588, 1540, 1431, 1347, 1207 cm^-1; HRMS (ESI) calcd for C7H3BrNNaO3F3S (M+Na^+) 371.8765; found 371.8761.

3-Bromo-5-nitrophenyl trifluoromethanesulfonate (219). Treatment of 3-bromo-5-nitrophenol177 (329 mg, 1.51 mmol) in CH2Cl2 (10 mL) with pyridine (250 µL, 3.10 mmol) and Tf2O (300 µL, 1.78 mmol), as described for 215, gave after chromatography (hexanes/EtOAc, 7:3) 219 (316 mg, 0.90 mmol, 60%) as a red oil. 1H NMR (600 MHz, CDCl3) δ 8.44 (t, J = 1.8 Hz, 1H), 8.11 (t, J = 2.4 Hz, 1H), 7.80 (t, J = 1.8 Hz, 1H); 13C NMR (150 MHz, CDCl3) δ 149.2, 130.8, 126.8, 123.8, 118.6 (q, JCF = 319 Hz), 116.1; IR (ATR) 3097, 1732, 1542, 1427, 1344, 1210, 1134 cm^-1; HRMS (ESI) calcd for C7H3BrNNaO3F3S (M+Na^+) 371.8765; found 371.8764.

4-Bromo-2-nitrophenyl trifluoromethanesulfonate (220).164 Treatment of 4-bromo-3-nitrophenol178 (353 mg, 1.60 mmol) in CH2Cl2 (5 mL) with pyridine (260 µL, 3.22 mmol) and Tf2O (330 µL, 1.95 mmol), as described for 215, gave after chromatography (hexanes/EtOAc, 7:3) 220 (540 mg, 1.54 mmol, 97%) as a yellow oil. 1H NMR (600 MHz, CDCl3) δ 8.30 (d, J = 2.4 Hz, 1H), 7.88 (dd, J = 8.4, 2.4 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H); 13C NMR (150 MHz, CDCl3) δ 141.9, 140.5, 138.2, 129.7, 125.6, 122.3, 118.5 (q, JCF = 319 Hz); IR (ATR) 3105, 1540, 1431, 1207, 1131 cm^-1; HRMS (ESI) calcd for C7H3BrNNaO3F3S (M+Na^+) 371.8765; found 371.8764.

2-Bromo-5-nitrophenyl trifluoromethanesulfonate (222). Treatment of 2-bromo-5-nitrophenol179 (119 mg, 0.55 mmol) in CH2Cl2 (5 mL) with pyridine (90 µL, 1.12 mmol) and Tf2O (120 µL, 0.71 mmol), as described for 215, gave without further purification 222 (188 mg, 0.54 mmol, 98%) as a brown oil. 1H NMR (400 MHz, CDCl3) δ 8.22 (d, J = 2.4 Hz, 1H), 8.16 (dd, J = 8.8, 2.4 Hz, 1H), 7.93 (d, J = 8.8 Hz, 1H); 13C NMR (100 MHz, CDCl3) δ 147.6, 146.9, 135.2, 124.0, 123.9, 118.5 (q, JCF = 320 Hz), 118.3; IR
(ATR) 3104, 1534, 1431, 1348, 1211, 1134 cm⁻¹; HRMS (ESI) calcd for C₇H₇BrNNaO₅F₃S (M+Na⁺) 371.8765; found 371.8764.

**Conditions A**

**4-Ethenylphenyl trifluoromethanesulfonate (206).** To a solution of PPh₃ (7.5 mg, 0.029 mmol) and Pd(dba)₂ (4.3 mg, 0.007 mmol) in dioxane (1.5 mL), stirred for 5 min under an atmosphere of N₂, was added 4-bromophenyl trifluoromethanesulphonate (202) (102 mg, 0.34 mmol) followed by ethenyltributyltin (128 mg, 0.40 mmol). The solution was heated at reflux for 24 h. The solvent was removed under reduced pressure and the residue was dissolved in EtOAc (10 mL) and washed with NH₄OH (10% aqueous, 3 x 20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried (MgSO₄), filtered, and solvents were removed under reduced pressure. The crude product was purified by chromatography (hexanes/EtOAc, 97:3) to give 206 (25.2 mg, 0.10 mmol, 30%) as a colorless oil. Only 206 was observed by ¹H NMR (600 MHz, CDCl₃) of the crude reaction mixture.

**Conditions B**

**4-Ethenylphenyl trifluoromethanesulfonate (206) and 4-ethenyl-1-bromobenzene (207).** To a solution of LiCl (45.5 mg, 1.07 mmol) and Pd(PPh₃)₂Cl₂ (4.7 mg, 0.007 mmol) in DMF (1.5 mL), under an atmosphere of N₂, was added 202 (108 mg, 0.35 mmol) followed by ethenyltributyltin (141 mg, 0.44 mmol). After stirring at ambient temperature for 24 h, the solvent was removed by bulb-to-bulb distillation. The resulting residue was dissolved in EtOAc (15 mL) and washed with NH₄OH (10% aqueous, 3 x 20 mL) and brine (20 mL). The organic phase was dried (MgSO₄), filtered, and solvents were removed under reduced pressure. The terminal cis-alkene protons were clearly resolved in the ¹H NMR spectrum at 600 MHz and these signals were used to determine the ratio of 206 (δ 5.35, d, J = 10.8 Hz, 1H) to 207 (δ 5.27, d, J = 10.8 Hz, 1H). A 6.7:1 ratio of 207/206 was observed by NMR. The products decomposed upon attempted purification on silica gel.

**Conditions C**

**4-Ethenylphenyl trifluoromethanesulfonate (206).** To a solution of PdCl₂(PPh₃)₂ (4.3 mg, 0.007 mmol) in dioxane (4 mL), stirred for 5 min under an atmosphere of N₂, was added 202 (310 mg, 1.02 mmol) followed by ethenyltributyltin (340 mg, 1.07 mmol). The solution was heated at reflux for 24 h. The solvent was removed under reduced pressure. The product was purified by chromatography on SiO₂/K₂CO₃ (10% K₂CO₃, hexanes/EtOAc, 98:2) to give 206 (231 mg, 0.917 mmol, 90%) as a colorless oil. Only 206 was observed by ¹H NMR (600 MHz, CDCl₃) of the crude reaction mixture.
2-Ethenylphenyl trifluoromethanesulfonate (209). Cross coupling of 2-bromophenyl trifluoromethanesulphonate (208) (95.6 mg, 0.31 mmol) with ethenyltributyltin (121 mg, 0.38 mmol) in the presence of PPh₃ (6.9 mg, 0.026 mmol) and Pd(dba)₂ (3.8 mg, 0.007 mmol) in dioxane (1.5 mL) was performed as described for 206 under Conditions A. Work up and chromatography (hexanes/EtOAc, 9:1) gave 209 (4.1 mg, 0.016 mmol, 5%) as a colorless oil. Only 209 was observed by ¹H NMR (600 MHz, CDCl₃) of the crude reaction mixture after work up.

2-Ethenylphenyl trifluoromethanesulfonate (209) and 2-ethenyl-1-bromobenzene (210). Cross coupling of 208 (88.3 mg, 0.25 mmol) with ethenyltributyltin (98.0 mg, 0.31 mmol) in the presence of LiCl (32.2 mg, 0.76 mmol) and Pd(PPh₃)₂Cl₂ (3.8 mg, 0.005 mmol) in DMF (1.0 mL) was performed as described for 208 under Conditions B. A 5.9:1 ratio of 210/209 was observed by ¹H NMR (600 MHz, CDCl₃) of the crude reaction mixture after standard work up. The products decomposed upon attempted purification on silica gel. The terminal cis-alkene protons were clearly resolved in the ¹H NMR spectrum at 600 MHz and these signals were used to determine the ratios of 209 (δ 5.49, d, J = 11.1 Hz, 1H) to 210 (δ 5.37, dd, J = 10.9, 1.0 Hz, 1H).

3-Ethenylphenyl trifluoromethanesulfonate (211) and 3-Ethenylphenyl-1-bromobenzene (212). Cross coupling of 3-bromophenyl trifluoromethane sulphonate (203) (105 mg, 0.34 mmol) with ethenyltributyltin (127 mg, 0.40 mmol) in the presence of PPh₃ (7.6 mg, 0.03 mmol) and Pd(dba)₂ (4.0 mg, 0.007 mmol) in dioxane (1.5 mL) was performed as described for 206 under Conditions A. Work up and chromatography (hexanes/EtOAc, 9:1) to give an inseparable mixture of 203 and 211 (49.2 mg, calculated from ¹H NMR spectrum: 20.2 mg 203 and 28.8 mg 211, 34%) as a colorless oil. A ~30:1 ratio of 211/212 was observed by ¹H NMR (600 MHz, CDCl₃) of the crude reaction mixture after standard work up. The terminal cis-alkene protons were clearly resolved in the ¹H NMR spectrum at 600 MHz and these signals were used to determine the ratios of 211 (δ 5.38, d, J = 11.4 Hz, 1H) to 212 (δ 5.30, d, J = 10.8 Hz, 1H).

3-Ethenylphenyl trifluoromethanesulfonate (211) and 3-Ethenylphenyl-1-bromobenzene (212). Cross coupling of 203 (108 mg, 0.36 mmol) with ethenyltributyltin (140 mg, 0.44 mmol) in the presence of LiCl (45.6 mg, 1.08 mmol) and Pd(PPh₃)₂Cl₂ (5.4 mg, 0.008 mmol) in DMF (1.5 mL) was performed as described for 207 under Conditions B. A 5.3:6.3:1 ratio of 203/212/211 was observed by ¹H NMR (600 MHz, CDCl₃) of the crude reaction mixture after standard work up. The products decomposed upon attempted purification on silica gel or basic alumina.
3-Ethenylphenyl trifluoromethanesulfonate (211) Cross coupling of 203 (310 mg, 1.02 mmol) with ethenyltributyltin (490 mg, 1.54 mmol) in the presence of Pd(PPh₃)₂Cl₂ (13.3 mg, 0.019 mmol) in DMF (4 mL) was performed as described for 206 under Conditions C (100 °C, 50 h). Work up and chromatography on SiO₂/K₂CO₃ (10% K₂CO₃, hexanes/EtOAc, 98:2) gave 211 (121 mg, 0.480 mmol, 47%) as a colorless oil. Only 211 was observed by ¹H NMR (600 MHz, CDCl₃) of the crude reaction mixture Needs to be reintegrated some 212 can be seen. ¹H NMR (600 MHz, CDCl₃) δ 7.42-7.39 (m, 2H), 7.29 (d, J=1.2 Hz, 1H), 7.17-7.15 (m, 1H), 6.70 (dd, J = 17.4, 10.8 Hz, 1H), 5.81 (d, J = 17.4 Hz, 1H), 5.39 (d, J = 10.8 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 149.9, 140.3, 135.0, 130.2, 126.1, 120.2, 118.8, 118.7 (q, J_C-F = 319 Hz), 116.5; IR (ATR) 1574, 1420, 1205, 1136, 1117, 924, 825 cm⁻¹; HRMS (ESI) calcd for C₉H₈F₃O₃S (M+H⁺) 253.0146; found 253.0147.

2-Ethenyl-3-nitrophenyl trifluoromethanesulfonate (223). Cross coupling of 2-bromo-3-nitrophenyl trifluoromethanesulfonate (213) (105 mg, 0.30 mmol) with ethenyltributyltin (119 mg, 0.38 mmol) in the presence of in the presence of PPh₃ (6.5 mg, 0.03 mmol) and Pd(dba)₂ (3.7 mg, 0.006 mmol) in dioxane (1.5 mL) was performed as described for 206 under Conditions A. Work up and chromatography (hexanes/EtOAc, 97:3) gave , in order of elution, 223 (32.3 mg, 0.11 mmol, 36%) as a white solid and impure 2-bromo-3-nitrophenol (41 mg).

2-Ethenyl-3-nitrophenyl trifluoromethanesulfonate (223), 2-bromo-3-nitrophenol, and 2-bromo-3-ethenyl-nitrobenzene (224). Cross coupling of 213 (110 mg, 0.32 mmol) with ethenyltributyltin (123 mg, 0.39 mmol) in the presence of LiCl (40.9 mg, 0.96 mmol) and Pd(PPh₃)₂Cl₂ (4.8 mg, 0.007 mmol) in DMF (1.5 mL) was performed as described for 207 under Conditions B. Work up and chromatography (hexanes/EtOAc, 97:3) gave , in order of elution, 223 (18.5 mg, 0.06 mmol, 20%), 224 (27.6 mg, 0.12 mmol, 38%) as a colorless oil and an impure mixture of 213 and 2-bromo-3-nitrophenol (38.2 mg). Spectral data for 224: ¹H NMR (600 MHz, CDCl₃) δ 7.70 (d, J = 7.8 Hz, 1H), 7.57 (d, J = 7.8 Hz, 1H), 7.41 (t, J = 7.8 Hz, 1H), 7.10 (dd, J = 17.4, 10.8 Hz, 1H), 5.76 (d, J = 17.4 Hz, 1H), 5.52 (d, J = 10.8 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 147.2, 128.9, 128.3, 126.2, 125.7, 124.8, 123.8, 119.5; IR (ATR) 3110, 1533, 1423, 1358, 1210, 1135 cm⁻¹; HRMS (ESI) calcd for C₈H₆NNaO₂Br (M+Na⁺) 249.9474; found 249.9473.

2-Ethenyl-3-nitrophenyl trifluoromethanesulfonate (223). Cross coupling of 213 (127 mg, 0.362 mmol) with ethenyltributyltin (149 mg, 0.471 mmol) in the presence of Pd(PPh₃)₂Cl₂ (5.1 mg, 0.007 mmol) in dioxane (1 mL) was performed as described for 206 under Conditions C (23 h). Work up and chromatography on SiO₂/K₂CO₃ (10% K₂CO₃, hexanes/EtOAc, 98:2) gave 223 (83 mg, 0.28 mmol, 77%).
2-Ethenyl-3-nitrophenyl trifluoromethanesulfonate (223) and 1-bromo-2-ethenyl-nitrobenzene (224) 2,3-Diethenyl-nitrobenzene (225), and 2-ethenyl-3-nitrophenol. Cross coupling of 213 (143 mg, 0.41 mmol) with ethenyltributyltin (123 mg, 0.39 mmol) in the presence of LiCl (53.8 mg, 1.27 mmol) and 1,3-bis(diphenylphosphino)propanepalladium dichloride (5.3 mg, 0.009 mmol) in DMF (2 mL) was performed as described for 207 under Conditions B. Work up and chromatography (hexanes/EtOAc, 97:3) gave in order of elution, 225 (7.0 mg, 0.04 mmol, 10%), 223 (22.9 mg, 0.077 mmol, 19%), 224 (45.7 mg, 0.20 mmol, 49%) as a colorless oil, and 2-ethenyl-3-nitrophenol (7.7 mg, 0.046 mmol, 11%).

Spectral data for 225: 1H NMR (400 MHZ, CDCl3) δ 7.75 (dd, J = 8.0, 1.2 Hz, 1H), 7.71 (dd, J = 8.0, 1.2 Hz, 1H), 7.37 (t, J = 8.0 Hz, 1H), 6.96 (dd, J = 17.6, 10.8 Hz, 1H), 6.89 (dd, J = 17.6, 11.6 Hz, 1H), 5.71 (dd, J = 17.6, 0.8 Hz, 1H), 5.63 (dd, J = 11.6, 1.2 Hz, 1H), 5.37 (dd, J = 11.2, 1.2 Hz, 1H), 5.32 (d, J = 18.0, 1.2 Hz, 1H); 13C NMR (100 MHZ, CDCl3) δ 149.8, 138.7, 134.5, 131.4, 130.5, 130.0, 127.6, 122.8, 122.6, 117.3; IR (ATR) 1521, 1348, 985, 921, 810, 774, 753, 735 cm⁻¹; HRMS (ESI) calculated from C10H10NO2 (M+H⁺) 176.0711, found 176.0709.

2,3-Diethenyl-nitrobenzene (225). Cross coupling of 213 (70.2 mg, 0.201 mmol) with ethenyltributyltin (203 mg, 0.641 mmol) in the presence of Pd(PPh3)Cl2 (6.0 mg, 0.008 mmol) and LiCl (6.0 mg, 0.008 mmol) in dioxane (1 mL) was performed as described for 207 under Conditions B (100 °C, 24 h). Work up and chromatography on SiO2/K2CO3 (10% K2CO3, hexanes/EtOAc, 98:2) gave 225 (33.7 mg, 0.192 mmol, 96%).

3-Ethenyl-4-nitrophenyl trifluoromethanesulfonate (226) and 2,4-diethenyl-nitrobenzene (227). Cross coupling of 3-bromo-4-nitrophenyl trifluoromethanesulfonate (214) (67.6 mg, 0.19 mmol) with ethenyltributyltin (72.8 mg, 0.23 mmol) in the presence of PPh3 (4.5 mg, 0.02 mmol) and Pd(dba)2 (2.2 mg, 0.004 mmol) in dioxane (1 mL) was performed as described for 206 under Conditions A. Work up and chromatography (hexanes/EtOAc, 97:3), gave in order of elution, 227 (3.0 mg, 0.02 mmol, 9%) and 226 (47.3 mg, 0.16 mmol, 82%) as a colorless oil. Analytical data for 226: 1H NMR (600 MHZ, CDCl3) δ 8.06 (d, J = 9.0 Hz, 1H), 7.51 (d, J = 2.4 Hz, 1H), 7.33 (dd, J = 9.0, 3.0 Hz, 1H), 7.18 (dd, J = 17.4, 11.4 Hz, 1H), 5.81 (d, J = 17.4 Hz, 1H), 5.66 (d, J = 11.4 Hz, 1H); 13C NMR(150 MHZ, CDCl3) δ 151.7, 146.6, 136.4, 131.0, 127.0, 121.4, 121.3, 121.0, 118.6 (q, JCF = 319 Hz); IR (ATR) 3118, 1530, 1424, 1350, 1207, 1131 cm⁻¹; HRMS (ESI) calcd for C9H6NNaO5F3S (M+Na⁺) 319.9811; found 319.9809.

Analytical data for 227: 1H NMR (400 MHZ, CDCl3) δ 7.95 (d, J = 8.4 Hz, 1H), 7.57 (d, J = 1.6 Hz), 7.44 (dd, J = 8.4, 2.0 Hz, 1H), 7.23 (dd, J = 17.2, 10.8 Hz, 1H), 6.76 (dd, J = 17.6, 10.8 Hz, 1H), 5.92 (d, J = 17.6 Hz, 1H), 5.75 (dd, J = 17.2, 0.8 Hz, 1H), 5.51 (dd, J = 11.2, 0.8 Hz, 1H), 5.49 (dd, J = 11.2, 0.8 Hz,
1H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 146.6, 142.4, 134.9, 134.1, 132.9, 126.5, 125.5, 125.1, 118.9, 118.2; IR (ATR) 1600, 1575, 1509, 1337, 914, 835 cm$^{-1}$; HRMS (ESI) calculated for C$_{10}$H$_{10}$NO$_2$ (M+H$^+$) 176.0711, found 176.0709.

3-Ethynyl-4-nitrophenyl trifluoromethanesulfonate (226), 2,4-diethenyl-nitrobenzene (227), and 2-bromo-4-ethenyl-nitrobenzene (228). Cross coupling of 214 (75.2 mg, 0.22 mmol) with ethenyltributyltin (85.5 mg, 0.27 mmol) in the presence of LiCl (28.1 mg, 0.66 mmol) and Pd(PPh$_3$)$_2$Cl$_2$ (3.6 mg, 0.005 mmol) in DMF (1 mL) was performed as described for 207 under Conditions B. Work up and chromatography (hexanes/EtOAc, 97:3) gave, in order of elution, 227 (5.5 mg, 0.03 mmol, 15%) followed by a mixture of 228 and 226 (23.8 mg, calculated from $^1$H NMR spectrum: 18.0 mg of 228, 37%, 5.8 mg of 226, 9%) as a yellow oil. Spectral data for 228 from the mixture: $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.86 (d, $J$ = 8.4 Hz, 1H), 7.74 (d, $J$ = 1.8 Hz, 1H), 7.45 (dd, $J$ = 8.4, 1.2 Hz, 1H), 6.68 (dd, $J$ = 17.4, 10.8 Hz, 1H), 5.90, (d, $J$ = 17.4 Hz, 1H), 5.52 (d, $J$ = 10.8 Hz, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 142.9, 136.4, 133.7, 132.6, 126.1, 125.5, 119.3, 115.1; IR (ATR) 3095, 1573, 1526, 1346, 1217, 1139 cm$^{-1}$; HRMS (ESI) calcd for C$_8$H$_6$NNaO$_2$Br (M+Na$^+$) 249.9474; found 249.9474.

4-Ethynyl-3-nitrophenyl trifluoromethanesulfonate (229) and 2,5-diethenyl-nitrobenzene (230). Cross coupling of 215 (110 mg, 0.32 mmol) with ethenyltributyltin (134 mg, 0.42 mmol) in the presence of in the presence of PPh$_3$ (6.9 mg, 0.03 mmol) and Pd(dba)$_2$ (3.6 mg, 0.006 mmol) in dioxane (1.5 mL) was performed as described for 206 under Conditions A. Work up and chromatography (hexanes/EtOAc, 97:3) gave, in order of elution, 230 (1.2 mg, 0.0068 mmol, 2%) and 229 (63.3 mg, 0.21 mmol, 68%) as colorless oils. Spectral data for 230 were in accordance with literature values. Analytical data for 229: $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.90 (d, $J$ = 2.4 Hz, 1H), 7.74 (d, $J$ = 8.4 Hz, 1H), 7.53 (dd, $J$ = 8.4, 2.4 Hz, 1H), 7.18 (dd, $J$ = 17.4, 11.4 Hz, 1H), 5.79 (d, $J$ = 17.4 Hz, 1H), 5.60 (d, $J$ = 11.4 Hz, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 148.0, 147.7, 133.8, 131.1, 130.5, 126.2, 121.0, 118.6 (q, $J^{C-F}$ = 319 Hz), 118.0; IR (ATR) 3110, 1533, 1426, 1351, 1208, 1133 cm$^{-1}$; HRMS (ESI) calcd for C$_9$H$_6$NNaO$_2$F$_3$S (M+Na$^+$) 319.9811; found 319.9810.

4-Ethynyl-3-nitrophenyl trifluoromethanesulfonate (229), 2,5-diethenyl-nitrobenzene (230), and 2-bromo-5-ethenyl-nitrobenzene (231). Cross coupling of 215 (120 mg, 0.34 mmol) with ethenyltributyltin (135 mg, 0.43 mmol) in the presence of LiCl (48.2 mg, 1.13 mmol) and Pd(PPh$_3$)$_2$Cl$_2$ (4.8 mg, 0.007 mmol) in DMF (1.5 mL) was performed as described for 207 under Conditions B. Work up and chromatography (hexanes/EtOAc, 97:3) gave, in order of elution, 230 (1.7 mg, 0.0097 mmol, 3%), 231 (27.8 mg, 0.12 mmol, 36%) as a colorless oil and a mixture of 229 and 215 (42 mg, calculated from
1H NMR spectrum: 229 22 mg, 23% and 215 20 mg, 17%). Spectral data for 231 were in accordance with literature values.

3-Ethyl-2-nitrophenyl trifluoromethanesulfonate (232), 2-bromo-6-ethenyl-nitrobenzene (233), and 2,6-diethenyl-nitrobenzene (234). Cross coupling of 216 (104 mg, 0.30 mmol) with ethenyltributyltin (121 mg, 0.38 mmol) in the presence of in the presence of PPh₃ (6.7 mg, 0.03 mmol) and Pd(dba)₂ (3.7 mg, 0.006 mmol) in dioxane (1.5 mL) was performed as described for 206 under Conditions A. Work up and chromatography (hexanes/EtOAc, 97:3) gave, in order of elution, 234 (16.0 mg, 0.09 mmol, 30%) a colorless oil, 233 (2.3 mg, 0.01 mmol, 3%) and 232 (52.9 mg, 0.18 mmol, 60%) as faint yellow solids.

Analytical data for 232: mp = 38-39 °C; 1H NMR (400 MHz, CDCl₃) δ 7.67 (d, J = 8.0, 0.8 Hz, 1H), 7.57 (t, J = 8.4 Hz, 1H), 7.40 (dd, J = 17.6, 11.2 Hz, 1H), 6.68 (dd, J = 17.2 Hz, 1H), 5.91 (d, J = 17.2 Hz, 1H), 5.61 (d, J = 11.2 Hz, 1H); 13C NMR (150 MHz, CDCl₃) δ 137.2, 133.6, 132.1, 131.6, 128.5, 126.4, 121.9, 121.4, 118.4 (q, J_C-F = 319 Hz); IR (ATR) 3090, 1533, 1427, 1361, 1211, 1138 cm⁻¹; HRMS (ESI) calcd for C₁₀H₈NNaO₅F₃S (M+Na⁺) 319.9811; found 319.9809.

Analytical data for 233: mp = 42-44 °C; 1H NMR (600 MHz, CDCl₃) δ 7.57 (t, J = 7.2 Hz, 2H), 7.32 (t, J = 8.4 Hz, 1H), 6.57 (dd, J = 17.4, 11.4 Hz, 1H), 5.85 (d, J = 17.4 Hz, 1H), 5.51 (d, J = 10.8 Hz, 1H); 13C NMR (150 MHz, CDCl₃) δ 150.1, 132.6, 131.6, 130.9, 129.0, 125.5, 120.8, 112.9; IR (ATR) 3077, 1557, 1521, 1460, 1365, 1187 cm⁻¹; HRMS (ESI) calcd for C₈H₆NNaO₂Br (M+Na⁺) 251.9454; found 251.9454.

Analytical data for 234: 1H NMR (400 MHz, CDCl₃) δ 7.54 (d, J = 8.0 Hz, 2H), 7.43 (t, J = 7.2 Hz, 1H), 6.59 (dd, J = 17.2, 10.8 Hz, 2H), 5.82 (d, J = 17.6 Hz, 2H), 5.47 (d, J = 11.2 Hz, 2H); 13C NMR (150 MHz, CDCl₃) δ 148.6, 130.2, 129.8, 129.6, 125.8, 119.6; IR (ATR) 1513, 1365, 926, 850, 809, 731 cm⁻¹; HRMS (ESI) calcd for C₁₀H₁₀NO₂ (M+H⁺) 176.0711; found 176.0709.

2-Bromo-6-ethenyl-nitrobenzene (233). Cross coupling of 216 (119 mg, 0.34 mmol) with ethenyltributyltin (138 mg, 0.44 mmol) in the presence of LiCl (45.6 mg, 1.08 mmol) and Pd(PPh₃)₂Cl₂ (5.0 mg, 0.007 mmol) in DMF (1.5 mL) was performed as described for 207 under Conditions B. Work up and chromatography (hexanes/EtOAc, 97:3) gave 233 (47.1 mg, 0.21 mmol, 61%) as an off-white solid.

3-Ethyl-2-nitrophenyl trifluoromethanesulfonate (232), 2-bromo-6-ethenyl-nitrobenzene (233), and 2,6-diethenyl-nitrobenzene (234). Cross coupling of 216 (105 mg, 0.300 mmol) with ethenyltributyltin (140 mg, 0.442 mmol) in the presence of Pd(PPh₃)₂Cl₂ (4.2 mg, 0.006 mmol) in 1,4-dioxane (1 mL) was performed as described in Conditions C (100 °C, 27 h). Work up and purification...
gave after chromatography on SiO₂/K₂CO₃ (10% K₂CO₃, hexanes/EtOAc, 19:1), in order of elution, 234 (11.9 mg, 0.068 mmol, 23%) a colorless oil, 233 (0.9 mg, 0.004 mmol, 1%) and 232 (60.6 mg, 0.204 mmol, 68%).

6-Ethenyl-2-nitrophenyl trifluoromethanesulfonate (235). Cross coupling of 217 (135 mg, 0.39 mmol) with ethenyltributyltin (129 mg, 0.41 mmol) in the presence of in the presence of PPh₃ (8.2 mg, 0.03 mmol) and Pd(dba)₂ (4.5 mg, 0.008 mmol) in dioxane (2 mL) was performed as described for 206 under Conditions A. Work up and chromatography (hexanes/EtOAc, 97:3) to afford in order of elution, 236 and 225 (8.5 mg, 1:1 mixture), 2-bromo-6-nitrophenol¹⁸³ (22.7 mg mixed with dba), and a mixture of 217 and 235 (95.1 mg). The latter fraction was repurified by chromatography (hexanes/EtOAc, 97:3) to give in order of elution, 235 as a colorless oil (27.8 mg, 0.09 mmol, 24%) and 217 (12.3 mg, 0.04 mmol, 9%).

Analytical data for 235: ¹H NMR (600 MHz, CDCl₃) δ 7.98 (dd, J = 8.4, 1.8 Hz, 1H), 7.90 (dd, J = 7.8, 1.8 Hz, 1H), 7.52 (t, J = 7.8 Hz, 1H), 6.99 (dd, J = 18.0, 11.4 Hz, 1H), 5.95 (d, J = 18.0 Hz, 1H), 5.67 (d, J = 11.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 143.1, 137.9, 134.4, 132.0, 128.5, 128.0, 125.5, 121.4, 118.3 (q, J_C-F = 319 Hz); IR (ATR) 3103, 1539, 1429, 1351, 1210, 1131 cm⁻¹; HRMS (ESI) calcd for C₉H₆NNaO₅F₃S (M+Na⁺) 319.9811; found 319.9808.

3-Bromo-2-ethenyl-nitrobenzene (236).³⁸⁷ Cross coupling of 217 (99.8 mg, 0.29 mmol) with ethenyltributyltin (97.5 mg, 0.31 mmol) in the presence of LiCl (36.6 mg, 0.86 mmol) and Pd(PPh₃)₂Cl₂ (4.1 mg, 0.006 mmol) in DMF (1.5 mL) was performed as described for 207 under Conditions B. Work up and chromatography (hexanes/EtOAc, 9:1) gave, in order of elution, 236 as a yellow oil (28.3 mg, 0.12 mmol, 43%), 2-bromo-6-nitrophenol (7.4 mg, 0.03 mmol, 12%), and 217 (5.0 mg, 0.01 mmol, 5%). Spectral data for 236 were in accordance with literature values.

3-Ethenyl-6-nitrophenyl trifluoromethanesulfonate (235), 3-bromo-6-ethenyl-nitrobenzene (236), and 2,3-diethenyl-nitrobenzene (225). Cross coupling of 217 (117 mg, 0.334 mmol) with ethenyltributyltin (159 mg, 0.501 mmol) in the presence of Pd(PPh₃)₂Cl₂ (5.1 mg, 0.007 mmol) in 1,4-dioxane (1 mL) was performed as described in Conditions C (100 °C, 24 h). Work up and purification gave after chromatography on SiO₂/K₂CO₃ (10% K₂CO₃, hexanes/EtOAc, 97:3), in order of elution, a mixture of 236 and 225 (16.1 mg, 1:2 mixture, 8% and 4%, respectively) and 235 (65.3 mg, 0.220 mmol, 66%).

2-Ethenyl-4-nitrophenyl trifluoromethanesulfonate (237). Cross coupling of 2-bromo-4-nitrophenyl trifluoromethanesulfonate (218)⁶⁴ (102 mg, 0.29 mmol) with ethenyltributyltin (116 mg, 0.37 mmol) in
the presence of in the presence of PPh$_3$ (6.5 mg, 0.03 mmol) and Pd(dba)$_2$ (4.1 mg, 0.007 mmol) in dioxane (1.5 mL) was performed as described for 206 under Conditions A. Work up and chromatography (hexanes/EtOAc, 8:2) gave, in order of elution, a mixture of 218 and 237 (45.1 mg) followed by 2-bromo-4-nitrophenol (5.2 mg, 0.02 mmol, 7%). The mixture was repurified by chromatography (hexanes/EtOAc, 97:3) to afford, in order of elution, 237 (19.3 mg, 0.06 mmol, 22%) as a light pink oil and 218 (7.0 mg, 0.02 mmol, 7%). Analytical data for 237: $^1$H NMR (400 MHz, CDCl$_3$) δ 8.52 (d, $J$ = 2.8 Hz, 1H), 8.20 (dd, $J$ = 9.2, 2.8 Hz, 1H), 7.48 (d, $J$ = 9.2 Hz, 1H), 6.94 (dd, $J$ = 17.6, 11.2 Hz, 1H), 6.04 (d, $J$ = 17.6 Hz, 1H), 5.70 (d, $J$ = 11.2 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 149.9, 147.2, 132.7, 127.2, 124.0, 122.9, 122.6, 121.7, 118.5 (q, $J_{CF}$ = 319 Hz); IR (ATR) 3107, 1536, 1424, 1347, 1209, 1134 cm$^{-1}$; HRMS (ESI) calcd for C$_9$H$_6$NNaO$_5$F$_3$S (M+Na$^+$) 319.9811; found 319.9809.

3-Bromo-4-ethenyl-nitrobenzene (238). Cross coupling of 218 (110 mg, 0.32 mmol) with ethenyltributyltin (138 mg, 0.43 mmol) in the presence of LiCl (42.6 mg, 1.0 mmol) and Pd(PPh$_3$)$_2$Cl$_2$ (4.5 mg, 0.006 mmol) in DMF (1.5 mL) was performed as described for 207 under Conditions B. Work up and chromatography (hexanes/EtOAc, 85:15) to give a mixture of 218 and 238. The mixture was repurified by chromatography (hexanes/EtOAc, 97:3) to afford in order of elution, 238 (40.7 mg, 0.18 mmol, 57%) as a yellow oil, 218 (8.7 mg, 0.02 mmol, 8%), and 3-bromo-4-nitrophenol (11.1 mg, 0.05 mmol, 16%). Analytical data for 238: $^1$H NMR (600 MHz, CDCl$_3$) δ 8.43 (d, $J$ = 2.4 Hz, 1H), 8.14 (ddd, $J$ = 8.4, 2.4, 0.6 Hz, 1H), 7.69 (d, $J$ = 9.0 Hz, 1H), 7.08 (dd, $J$ = 17.4, 10.8 Hz, 1H), 5.88 (d, $J$ = 17.4 Hz, 1H), 5.60 (dd, $J$ = 10.8, 0.6 Hz, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 147.2, 143.7, 134.3, 128.2, 127.0, 123.3, 122.4, 120.8; IR (ATR) 3099, 1536, 1424, 1347, 1116, 1035 cm$^{-1}$; HRMS (ESI) calcd for C$_8$H$_6$NNaO$_2$Br (M+Na$^+$) 249.9479; found 249.9478.

2-Ethenyl-4-nitrophenyl trifluoromethanesulfonate (237). Cross coupling of 218 (89.1 mg, 0.255 mmol) with ethenyltributyltin (105 mg, 0.331 mmol) in the presence of Pd(PPh$_3$)$_2$Cl$_2$ (3.6 mg, 0.005 mmol) in 1,4-dioxane (0.8 mL) was performed as described for 206 as described under Conditions C (100 °C, 24 h). Work up and purification gave after chromatography on SiO$_2$/K$_2$CO$_3$ (10% K$_2$CO$_3$, hexanes/EtOAc, 98:2) gave 237 (71.4 mg, 0.240 mmol, 94%).

3-Ethenyl-4-nitrophenyl trifluoromethanesulfonate (239). Cross coupling of 219 (106 mg, 0.30 mmol) with ethenyltributyltin (130 mg, 0.41 mmol) in the presence of the presence of (6.4 mg, 0.02 mmol) and Pd(dba)$_2$ (3.4 mg, 0.006 mmol) in dioxane (1.5 mL) was performed as described for 206 under Conditions A. Work up and chromatography (hexanes/EtOAc, 97:3) gave, in order of elution, 219 (4.1 mg, 0.01 mmol, 4%) and 239 (70.0 mg, 0.24 mmol, 78%) as a colorless oil. Analytical data for 239: $^1$H
NMR (400 MHz, CDCl\textsubscript{3}) δ 8.30 (t, \(J = 1.6\) Hz, 1H), 8.02 (t, \(J = 2.4\) Hz, 1H), 7.60 (t, \(J = 2.0\) Hz, 1H), 6.77 (dd, \(J = 17.2, 10.8\) Hz, 1H), 5.98 (d, \(J = 17.6\) Hz, 1H), 5.60 (d, \(J = 10.8\) Hz, 1H); \(^{13}\)C NMR (150 MHz, CDCl\textsubscript{3}) δ 149.4, 149.2, 141.7, 133.2, 124.6, 120.6, 119.8, 118.6 (q, \(J_{C-F} = 319\) Hz), 115.6; IR (ATR) 3103, 1540, 1425, 1348, 1213, 1132 cm\(^{-1}\); HRMS (ESI) calcd for C\textsubscript{9}H\textsubscript{7}NO\textsubscript{5}F\textsubscript{3}S (M+H\(^{+}\)) 297.9997; found 297.9997.

3-Bromo-5-ethenyl-nitrobenzene (240). Cross coupling of 219 (109 mg, 0.31 mmol) with ethenyltributyltin (139 mg, 0.44 mmol) in the presence of LiCl (45.0 mg, 1.1 mmol) and Pd(PPh\textsubscript{3})\textsubscript{2}Cl\textsubscript{2} (4.7 mg, 0.007 mmol) in DMF (1.5 mL) was performed as described for 207 under Conditions B. Work up and chromatography (hexanes/EtOAc, 97:3) gave 240 (47.1 mg, 0.21 mmol, 66%) as an off-white solid. Analytical data for 240: mp = 37-39°C; \(^1\)H NMR (600 MHz, CDCl\textsubscript{3}) δ 8.23 (t, \(J = 1.8\) Hz, 1H), 8.16 (t, \(J = 1.8\) Hz, 1H), 7.82 (t, \(J = 1.8\) Hz, 1H), 6.70 (dd, \(J = 17.4, 10.8\) Hz, 1H), 5.90 (d, \(J = 18.0\) Hz, 1H), 5.50 (d, \(J = 10.8\) Hz, 1H); \(^{13}\)C NMR (150 MHz, CDCl\textsubscript{3}) δ 149.0, 140.8, 134.8, 133.6, 125.3, 122.9, 119.6, 118.5; IR (ATR) 3079, 1531, 1339, 1301, 1214 cm\(^{-1}\); HRMS (ESI) calcd for C\textsubscript{8}H\textsubscript{6}NNaO\textsubscript{2}Br (M+Na\(^{+}\)) 251.9454; found 251.9452.

3-Ethenyl-5-nitrophenyl trifluoromethanesulfonate (239). Cross coupling of 219 (104 mg, 0.296 mmol) with ethenyltributyltin (122 mg, 0.385 mmol) in the presence of Pd(PPh\textsubscript{3})\textsubscript{2}Cl\textsubscript{2} (4.3 mg, 0.006 mmol) in 1,4-dioxane (1 mL) was performed as described for 206 as described under Conditions C (100°C, 24 h). Work up and purification gave after chromatography on SiO\textsubscript{2}/K\textsubscript{2}CO\textsubscript{3} (10% K\textsubscript{2}CO\textsubscript{3}, hexanes/EtOAc, 98:2) gave 239 (78.5 mg, 0.264 mmol, 89%).

4-Ethenyl-2-nitrophenyl trifluoromethanesulfonate (241). Cross coupling of 220 (103 mg, 0.29 mmol) with ethenyltributyltin (112 mg, 0.35 mmol) in the presence of Pd(dba)\textsubscript{2} (3.4 mg, 0.006 mmol) in dioxane (1.5 mL) was performed as described for 206 under Conditions A. Work up and chromatography (hexanes/EtOAc, 9:1) gave, in order of elution, a mixture of 220 and 5-bromo-2-nitrophenol (11.3 mg) followed by 241 as a yellow oil mixed with dibenzylideneacetone (34.6 mg, 0.12 mmol, 41% of 241, calculated from \(^1\)H NMR spectrum).

5-Bromo-2-ethenyl-nitrobenzene (242). Cross coupling of 220 (111 mg, 0.32 mmol) with ethenyltributyltin (131 mg, 0.41 mmol) in the presence of LiCl (44.5 mg, 0.86 mmol) and Pd(PPh\textsubscript{3})\textsubscript{2}Cl\textsubscript{2} (4.2 mg, 0.006 mmol) in DMF (1.5 mL) was performed as described for 207 under Conditions B. Work up and chromatography (hexanes/EtOAc, 9:1) gave 242 as a yellow solid (56.3 mg, 0.25 mmol, 78%). Analytical data for 242: mp = 40-41°C; \(^1\)H NMR (600 MHz, CDCl\textsubscript{3}) δ 8.43 (d, \(J = 2.4\) Hz, 1H), 8.14 (ddd,
$J = 8.4, 2.4, 0.6 \text{ Hz, 1H})$, 7.69 (d, $J = 9.0 \text{ Hz, 1H}$), 7.08 (dd, $J = 17.4, 10.8 \text{ Hz, 1H}$), 5.88 (d, $J = 17.4 \text{ Hz, 1H}$), 5.60 (d, $J = 10.8 \text{ Hz, 1H}$); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 148.0, 136.1, 132.2, 131.5, 129.7, 127.3, 121.4, 119.7; IR (ATR) 3097, 1552, 1514, 1341, 1149 cm$^{-1}$; HRMS (ESI) calcd for C$_8$H$_6$NNaO$_2$Br (M+Na$^+$) 251.9454; found 251.9455.

4-Ethenyl-2-nitrophenyl trifluoromethanesulfonate (241). Cross coupling of 220 (122 mg, 0.348 mmol) with ethenyltributyltin (162 mg, 0.511 mmol) in the presence of Pd(PPh$_3$)$_2$Cl$_2$ (4.9 mg, 0.007 mmol) in 1,4-dioxane (2.5 mL) was performed as described for 206 as described under Conditions C (100 ºC, 26 h). Work up and purification gave after chromatography on SiO$_2$/K$_2$CO$_3$ (10% K$_2$CO$_3$, hexanes/EtOAc, 98:2) gave 241 (54.5 mg, 0.311 mmol, 89%). Analytical data for 241: $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.72 (dd, $J = 8.4, 1.8 \text{ Hz, 1H}$), 7.41 (d, $J = 9.0 \text{ Hz, 1H}$), 6.74 (dd, $J = 17.4, 10.8 \text{ Hz, 1H}$), 5.92 (d, $J = 17.4 \text{ Hz, 1H}$), 5.55 (d, $J = 10.8 \text{ Hz, 1H}$); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 141.6, 140.2, 139.2, 133.1, 132.2, 124.3, 123.8, 119.1, 118.5 (q, $J_{C-F} = 319 \text{ Hz}$); IR (ATR) 3117, 1581, 1519, 1431, 1343, 1207 cm$^{-1}$; HRMS (ESI) calculated for C$_9$H$_7$F$_3$NO$^+_5$S (M+H$^+$) 297.9997, found 297.9994.

3-Ethenyl-6-nitrophenyl trifluoromethanesulfonate (243). Cross coupling of 3-bromo-6-nitrophenyl trifluoromethanesulfonate (221) (100 mg, 0.29 mmol) with ethenyltributyltin (95.1 mg, 0.30 mmol) in the presence of LiCl (37.0 mg, 0.87 mmol) and Pd(PPh$_3$)$_2$Cl$_2$ (3.3 mg, 0.006 mmol) in dioxane (1.5 mL) was performed as described for 206 under Conditions A. Work up and chromatography (hexanes/EtOAc, 97:3) gave, in order of elution, a mixture of 221 and dba (17.2 mg) followed by 243 (34.6 mg, 0.12 mmol, 41%) as a yellow oil. Analytical data for 243: $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 8.15 (d, $J = 8.4 \text{ Hz, 1H}$), 7.55 (dd, $J = 9.0, 1.8 \text{ Hz, 1H}$), 7.41 (d, $J = 1.2 \text{ Hz, 1H}$), 6.75 (dd, $J = 17.4, 10.8 \text{ Hz, 1H}$), 5.97 (d, $J = 17.4 \text{ Hz, 1H}$), 5.63 (d, $J = 10.8 \text{ Hz, 1H}$); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 145.3, 141.9, 139.9, 133.3, 127.1, 126.3, 121.7, 120.9, 118.5 (q, $J_{C-F} = 319 \text{ Hz}$); IR (ATR) 3117, 1587, 1529, 1429, 1341, 1207 cm$^{-1}$; HRMS (ESI) calculated for C$_9$H$_7$NO$_3$F$_3$S (M+H$^+$) 297.9997; found 297.9995.

3-Ethenyl-6-nitrophenyl trifluoromethanesulfonate (243) and 4-Bromo-2-ethyl-nitrobenzene (244). Cross coupling of 221 (99.5 mg, 0.29 mmol) with ethenyltributyltin (98.1 mg, 0.31 mmol) in the presence of LiCl (37.0 mg, 0.87 mmol) and Pd(PPh$_3$)$_2$Cl$_2$ (4.0 mg, 0.006 mmol) in DMF (1.5 mL) was performed as described for 207 under Conditions B. Work up and chromatography (hexanes/EtOAc, 9:1) gave, in order of elution, 244 (11.0 mg, 0.05 mmol, 17%) as an off-white solid, 221 (22.9 mg, 0.07 mmol, 22%) and 243 (19.4 mg, 0.07 mmol, 23%). Spectral data for 244 were in accordance with literature values.
3-Ethenyl-6-nitrophenyl trifluoromethanesulfonate (243) Cross coupling of 221 (96.8 mg, 0.277 mmol) with ethenyltributyltin (114 mg, 0.360 mmol) in the presence of Pd(PPh3)2Cl2 (4.0 mg, 0.006 mmol) in 1,4-dioxane (0.7 mL) was performed as described for 206 as described under Conditions C (100 °C, 24 h). Work up and purification by chromatography on SiO2/K2CO3 (10% K2CO3, hexanes/EtOAc, 19:1) gave, in order of elution, a 6:1 mixture of 227 and 244 (5.1 mg, 0.024 mmol, 9% of 227 and 0.9 mg, 0.004 mmol, 14% of 244, calculated from 1H NMR spectrum) and 243 (60.9 mg, 0.205 mmol, 74%).

2-Ethenyl-5-nitrophenyl trifluoromethanesulfonate (245). Cross coupling of 222 (74.7 mg, 0.21 mmol) with ethenyltributyltin (83.2 mg, 0.26 mmol) in the presence of PPh3 (5.0 mg, 0.02 mmol) and Pd(dba)2 (2.7 mg, 0.005 mmol) in dioxane (1.5 mL) was performed as described for 206 under Conditions A. Work up and chromatography (hexanes/EtOAc, 97:3) gave, in order of elution, 222 (14.8 mg, 0.04 mmol, 20%) and 245 (30.2 mg, 0.10 mmol, 48%) as a yellow oil. Analytical data for 245:

1H NMR (600 MHz, CDCl3) δ 8.24 (dd, J = 8.4, 2.4 Hz, 1H), 8.06 (d, J = 1.8 Hz, 1H), 7.83 (d, J = 8.4 Hz, 1H), 6.97 (dd, J = 17.4, 11.4 Hz, 1H), 5.92 (d, J = 17.4 Hz, 1H), 5.75 (d, J = 10.8 Hz, 1H); 13C NMR (150 MHz, CDCl3) δ 147.4, 145.9, 137.5, 127.8, 127.5, 123.2, 122.9, 118.5 (q, Jc-F = 319 Hz), 117.7; IR (ATR) 3118, 1528, 1425, 1346, 1210, 1132 cm-1; HRMS (ESI) calcd for C9H7NO5F3S (M+H+) 297.9997; found 297.9994.

2-Ethenyl-5-nitrophenyl trifluoromethanesulfonate (245) and 4-bromo-3-ethenyl-nitrobenzene (246). Cross coupling of 222 (85.9 mg, 0.25 mmol) with ethenyltributyltin (98.2 mg, 0.31 mmol) in the presence of LiCl (32.2 mg, 0.76 mmol) and Pd(PPh3)2Cl2 (3.6 mg, 0.005 mmol) in DMF (1.5 mL) was performed as described for 207 under Conditions B. Work up and chromatography (hexanes/EtOAc, 97:3) gave, in order of elution, 246 (3.8 mg, 0.02 mmol, 7%) as an off-white solid, 222 (27.0 mg, 0.08 mmol, 31%) and 245 (22.4 mg, 0.08 mmol, 31%). Analytical data for 246: mp = 38-40 °C; 1H NMR (400 MHz, CDCl3) δ 8.38 (d, J = 2.8 Hz, 1H), 7.96 (dd, J = 8.8, 2.8 Hz, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.05 (dd, J = 17.2, 10.8 Hz, 1H), 5.88 (d, J = 17.2 Hz, 1H), 5.56 (d, J = 10.8 Hz, 1H); 13C NMR (100 MHz, CDCl3) δ 147.4, 139.0, 134.1, 133.9, 130.3, 123.1, 121.5, 119.7; IR (ATR) 3099, 2926, 1525, 1341, 1030 cm-1; HRMS (ESI) calcd for C8H6NNaO2Br (M+Na+) 251.9454; found 251.9452.

2-Ethenyl-5-nitrophenyl trifluoromethanesulfonate (245) A solution of 222 (162 mg, 0.463 mmol) in dioxane (2 mL) was treated with ethenyltributyltin (191 mg, 0.602 mmol) in the presence of PdCl2(PPh3)2 (13.0 mg, 0.019 mmol), was performed as described for 206 as described under Conditions C (100 °C, 24 h). Work up and purification, gave after chromatography SiO2/K2CO3 (10% K2CO3, hexanes/EtOAc, 19:1) 245 (122 mg, 0.412 mmol, 89%) as a pale yellow oil. 1H NMR (600 MHz, CDCl3) δ 8.24 (dd, J =
8.4, 2.4 Hz, 1H), 8.17 (d, J = 1.8 Hz, 1H), 7.83 (d, J = 8.4 Hz, 1H), 6.97 (dd, J = 17.4, 11.4 Hz, 1H), 6.05 (d, J = 17.4 Hz, 1H), 5.75 (d, J = 10.8 Hz, 1H); 13C NMR (150 MHz, CDCl3) δ 147.4, 145.9, 137.5, 127.8, 127.5, 123.2, 122.9, 118.5 (q, JCF = 319 Hz), 117.7; IR (ATR) 1526, 1425, 1345, 1209, 1134, 944, 836 cm⁻¹; HRMS (ESI) calcd for C₉H₆NNaO₃Fᵢ₅S (M+Na⁺) 319.9811; found 319.9812.

3-Ethenyl-6-trifluoromethanesulfonate-nitrobenzene (241), 3-Ethenyl-6-hydroxy-1-nitrobenzene (248), and 2,5-Diethenyl-1-nitrobenzene (230). Cross coupling of 4-iodo-6-nitrophenyl trifluoromethanesulfonate (247)¹⁸⁹ (102 mg, 0.26 mmol) with ethenyltributyltin (106 mg, 0.33 mmol) in the presence of in the presence of PPh₃ (5.8 mg, 0.02 mmol) and Pd(dba)₂ (3.5 mg, 0.006 mmol) in dioxane (1.5 mL) was performed as described for 206 under Conditions A. Work up and chromatography (hexanes/EtOAc, 97:3) gave, in order of elution, a mixture of 248 and 230 (8.2 mg; 5.8 mg, 0.035 mmol, 14% of 248 and 2.4 mg, 0.014 mmol, 5% of 230, calculated from 1H NMR spectrum) followed by 241 (29.5 mg, 0.099 mmol, 38%) as a yellow oil.

3-Ethenyl-6-trifluoromethanesulfonate-nitrobenzene (241), 3-Iodo-6-ethenyl-nitrobenzene (249) and 5-Iodo-2-hydroxynitrobenzene. Cross coupling of 247 (116 mg, 0.29 mmol) with ethenyltributyltin (120 mg, 0.38 mmol) in the presence of LiCl (39.7 mg, 0.94 mmol) and Pd(PPh₃)₂Cl₂ (4.1 mg, 0.006 mmol) in DMF (1.5 mL) was performed as described for 207 under Conditions B. Work up and chromatography (hexanes/EtOAc, 97:3) gave in order of elution, 249 (3.2 mg, 0.01 mmol, 4%) as a brown oil, 5-iodo-2-hydroxynitrobenzene (8.7 mg, 0.03 mmol, 14%), and a mixture of 241 and 247 (67.1 mg; 43.7 mg, 0.147 mmol, 50% of 241 and 23.3 mg, 0.059 mmol, 20% of 247, calculated from 1H NMR spectrum). Analytical data for 249: 1H NMR (600 MHz, CDCl₃) δ 8.25 (d, J = 1.8 Hz, 1H), 7.89 (dd, J = 7.8, 1.8 Hz, 1H), 7.35 (d, J = 7.8 Hz, 1H), 7.09 (dd, J = 17.4, 11.4 Hz, 1H), 5.76 (d, J = 167.4 Hz, 1H), 5.52 (d, J = 11.4 Hz, 1H); 13C NMR (150 MHz, CDCl₃) δ 148.0, 141.9, 133.0, 132.8, 131.6, 129.8, 119.7, 91.8; IR (ATR) 3094, 2925, 1519, 1341, 1261, 1086 cm⁻¹; HRMS (ESI) calcd for C₈H₆NNaO₃I (M+Na⁺) 297.9335; found 297.9333.

3-Ethenyl-6-trifluoromethanesulfonate-nitrobenzene (241) and 2,5-Diethenyl-1-nitrobenzene (230). Cross coupling of 247 (205 mg, 0.517 mmol) with ethenyltributyltin (213 mg, 0.671 mmol) in the presence of PdCl₂(PPh₃)₂ (7.3 mg, 0.010 mmol) in dioxane (2 mL) was performed as described for 206 under Conditions C (100 °C, 24 h). Work up and purification gave after chromatography SiO₂/K₂CO₃ (10% K₂CO₃, hexanes/EtOAc, 19:1), in order of elution, 230 (10.0 mg, 0.057 mmol, 8%) and 241 (133 mg, 0.449 mmol, 87%) as faint yellow oil.
3-Bromo-6-trifluoromethanesulfonate acetophenone (253). To a solution of 1-hydroxy-5-bromoacetophenone (381 mg, 1.77 mmol) in CH₂Cl₂ (10 mL) at 0 °C was added pyridine (275 µL, 3.41 mmol) and Tf₂O (325 µL, 1.92 mmol). The mixture was removed from the cold bath and allowed to stir at ambient temperature for 1 h. The resulting mixture was filtered through a small plug of silica gel and the solvent was removed under reduced pressure from the filtrate to give 253 (590 mg, 1.70 mmol, 96%) as a pale orange oil. The compound was used as such without further purification.

1H NMR (400 MHz, CDCl₃) δ 7.90 (d, J = 2.8 Hz, 1H), 7.70 (dd, J = 8.8 Hz, 2.8 Hz, 1H), 7.22 (d, J = 8.8 Hz, 1H), 2.62 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ 195.1, 145.5, 136.4, 133.5, 133.4, 124.3, 122.0, 118.4 (d, J_C-F = 213 Hz) 29.2; IR (ATR) 1701, 1424, 1202, 1133, 879, 796 cm⁻¹; HRMS (ESI) calcd for C₉H₇BrO₄F₃S (M+H⁺) 348.9175; found 348.9177.

3-Ethenyl-6-trifluoromethanesulfonate acetophenone (254). Cross coupling of 253 (101 mg, 0.29 mmol) with ethenyltributyltin (116 mg, 0.007 mmol) in dioxane (1.5 mL) was performed as described for 206 under Conditions A. Work up and chromatography (hexanes/EtOAc, 9:1) gave 254 (11.6 mg, 0.04 mmol, 14%) as a colorless oil.

1H NMR (600 MHz, CDCl₃) δ 7.78 (d, J = 2.4 Hz, 1H), 7.60 (dd, J = 8.4, 2.4 Hz, 1H), 7.30 (d, J = 9.0 Hz, 1H), 6.73 (dd, J = 17.4, 10.8 Hz, 1H), 5.63 (dd, J = 17.4 Hz, 1H), 5.44 (d, J = 10.8 Hz, 1H), 2.65 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ 196.5, 145.8, 138.1, 134.2, 132.2, 130.7, 128.3, 122.8, 118.5 (q, J_C-F = 319 Hz), 117.2, 29.4; IR (ATR) 3096, 1698, 1421, 1202, 1134 cm⁻¹; HRMS (ESI) calcd for C₁₁H₁₀F₃O₄S (M+H⁺) 295.0252; found 295.0249.

6-Ethenyl-3-bromoacetophenone (255). Cross coupling of 253 (112 mg, 0.32 mmol) with ethenyltributyltin (116 mg, 0.017 mmol) in DMF (1.5 mL) was performed as described for 207 under Conditions B. Work up and chromatography (hexanes/EtOAc, 8:2) gave 255 (42.6 mg, 0.19 mmol, 58%) as a colorless oil.

1H NMR (600 MHz, CDCl₃) δ 7.72 (d, J = 1.8 Hz, 1H), 7.56 (dd, J = 8.4, 2.4 Hz, 1H), 7.42 (d, J = 8.4 Hz, 1H), 7.09 (dd, J = 17.4, 10.8 Hz, 1H), 5.63 (dd, J = 17.4, 1.2 Hz, 1H), 5.37 (dd, J = 11.4, 1.2 Hz, 1H), 2.56 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ 200.5, 138.9, 136.3, 134.7, 134.4, 131.3, 129.1, 121.1, 117.4, 29.8; IR (ATR) 3088, 1686, 1472, 1355, 1235, 830 cm⁻¹; HRMS (ESI) calcd for C₁₀H₁₀BrO (M+H⁺) 224.9915; found 224.9914.

3-Ethenyl-6-trifluoromethanesulfonate acetophenone (254). Cross coupling of 253 (70.2 mg, 0.202 mmol) with ethenyltributyltin (83.4 mg, 0.007 mmol) in dioxane (0.6 mL) was performed as described for 206 under Conditions C (100 °C, 24 h). Work
up and purification gave after chromatography SiO$_2$/K$_2$CO$_3$ (10% K$_2$CO$_3$, hexanes/EtOAc, 19:1) 254 (33.8 mg, 0.115 mmol, 57%).

**3-Ethenyl-4-trifluoromethanesulfonate-1-methoxybenzene (251).** Cross coupling of 3-bromo-4-trifluoromethanesulfonate-1-methoxybenzene (250)$^{191}$ (106 mg, 0.32 mmol) with ethenyltributyltin (126 mg, 0.40 mmol) in the presence of in the presence of PPh$_3$ (7.0 mg, 0.03 mmol) and Pd(dba)$_2$ (3.7 mg, 0.006 mmol) in dioxane (1.5 mL) was performed as described for 206 under Conditions A. Work up and chromatography (hexanes/EtOAc, 19:1) gave 251 (29.6 mg, 0.10 mmol, 33%) as a colorless oil. $^1$H NMR $\delta$ 7.18 (d, $J = 9.0$ Hz, 1H), 7.09 (d, $J = 3.0$ Hz, 1H), 6.89 (dd, $J = 17.4$, 11.4 Hz, 1H), 6.84 (dd, $J = 9.0$, 3.0 Hz, 1H), 5.83 (d, $J = 18.0$ Hz, 1H), 5.49 (d, $J = 11.4$ Hz, 1H), 3.84 (s, 1H); $^{13}$C NMR $\delta$ 158.9, 140.5, 132.1, 129.1, 122.6, 118.6, 118.3 (q, $J^{C-F} = 319$ Hz), 114.5, 111.6, 55.7; IR (ATR) 2968, 1485, 1419, 1206, 1137, 868 cm$^{-1}$; HRMS (ESI) calcd for C$_{10}$H$_8$F$_3$O$_4$S (M-H) 281.0095; found 281.0100.

**3-Ethenyl-4-trifluoromethanesulfonate-1-methoxybenzene (251) and 3-Bromo-4-ethenylanisole (252).**$^{192}$ Cross coupling of 250 (103 mg, 0.31 mmol) with ethenyltributyltin (119 mg, 0.38 mmol) in the presence of LiCl (38.9 mg, 0.92 mmol) and Pd(PPh$_3$)$_2$Cl$_2$ (4.5 mg, 0.006 mmol) in DMF (2 mL) was performed as described for 207 under Conditions B. Work up and chromatography (hexanes/EtOAc, 9:1) gave, in order of elution, 251 (26.3 mg, 0.12 mmol, 39%) as a faint orange oil and 252 (3.3 mg, 0.01 mmol, 4%). Spectral data for 252 were in accordance with literature values.
4-Bromo-2,3-dinitrophenol (257). To a solution of 256 (730 mg, 2.24 mmol) in THF (8 mL) and H₂O (0.5 mL) in an ACE Glass pressure tube was added NaOH (1.04 g, 26.1 mmol). The pressure tube was sealed with a Teflon screw cap and the solution was heated at 80 °C (18 h). The resulting brown solution was diluted with H₂O (25 mL), acidified with HCl, and extracted with EtOAc (3x30 mL). The combined organic layers were dried (MgSO₄), filtered, and solvents removed from the filtrate under reduced pressure. The crude brown oil was purified by chromatography (hexanes/EtOAc, 7:3 with 5% AcOH) to afford 257 (554 mg, 2.11 mmol, 94%) as a yellow solid. mp=59-61 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.55 (d, J = 8.4 Hz, 1H), 7.20 (d, J = 8.8 Hz, 1H); ¹³C NMR (150 MHz, DMSO-d₆) δ 151.3, 143.8, 137.6, 132.4, 123.1, 101.9; IR (ATR) 3391, 1566, 1535, 1456, 1374 cm⁻¹; HRMS (ESI) calcd for C₆H₃BrN₂O₅ (M-H⁺) 260.9147, found 260.9148.

4-Bromo-2,3-dinitrophenyltrifluoromethanesulfonate (258). To an ice-cooled solution of 257 (1003 mg, 3.812 mmol) in CH₂Cl₂ (10 mL) under a nitrogen atmosphere was added pyridine (933 µL, 11.441 mmol) followed by addition of trifluoromethanesulfonic anhydride (Tf₂O, 834 µL, 4.957 mmol) and the solution was stirred while warming to ambient temperature over 30 minutes. Solvents were removed under reduced pressure and the crude product was purified by chromatography (hexane/EtOAc, 7:3) to afford 258 (1229 mg, 3.111 mmol, 82%) as a colorless viscous oil. mp=59-60 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.06 (d, J =9.2 Hz, 1H), 7.59 (d, J =9.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 144.9, 139.8, 138.3, 137.4, 126.3, 118.3 (q, J_C-F =319 Hz), 115.1, ¹⁹F NMR (376.10 MHz, CDCl₃) δ -72.6; IR (ATR) 1547, 1436, 1350, 1222, 1130 cm⁻¹; HRMS (ESI) calcd for C₇H₃BrF₃N₂O₇S (M+H⁺) 394.8796 (M+Na=416.8616), found

4-Bromo-2,5-dinitrophenol (262) and 4-bromo-2,3-dinitrophenol (257). 4-Bromo-3-nitrophenol (259) (5.0 g, 22.94 mmol) was added to concentrated nitric acid (130 mL) and the solution was stirred at ambient temperature for 1 h whereby yellow solid started separating out. The mixture was quenched with ice-cold water (100 mL) and allowed to cool to ambient temperature. The mixture was diluted with EtOAc (180 mL) and the organic layer was washed with ice-cold water (100 mLx5). The organic layer was dried (MgSO₄), filtered and was concentrated under reduced pressure. The crude was purified by chromatography (Hexane/EtOAc, 95:5, then, 8:2 acidified with few drops of AcOH) to give, in order of elution, 262 (2.25 g, 8.56 mmol, 37%) and 257 (3.06 g, 11.62 mmol, 51%) both as a yellow solid. Analytica data for 262: mp=113-114 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.50 (s, 1H), 8.49 (s, 1H), 7.58 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 154.4, 154.1, 134.8, 131.1, 117.0, 103.0; IR (ATR) 3286, 1538, 1254 cm⁻¹; HRMS (ESI) calculated for C₆H₄BrN₂O₃ (M+H⁺) 262.9304, found
4-Iodo-2,5-dinitrophenol (263)\(^{218}\) and 4-iolo-2,3-dinitrophenol (261). 4-Iodo-3-nitrophenol (260) (5.0 g, 18.87 mmol) was added to concentrated nitric acid (HNO\(_3\), 100 mL) and the solution was stirred at ambient temperature for 1 h whereby yellow solid started separating out. The mixture was quenched with ice-cold water (150 mL) and allowed to cool to ambient temperature. The mixture was diluted with EtOAc (150 mL) and the organic layer was washed with ice-cold water (100 mLx5). The organic layer was dried (MgSO\(_4\)), filtered and was concentrated under reduced pressure. The crude was purified by chromatography (Hexane/DCM, 7:3, acidified with few drops of AcOH) to give, in order of elution, 263 (1.79 g, 5.77 mmol, 31%) and 261 (2.90 g, 9.36 mmol, 50%) both as a yellow solid. Analytical data for 261: mp=139-140 \(^\circ\)C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 11.25 (br, s, 1H), 7.72 (d, \(J=9.2\) Hz, 1H), 6.98 (d, \(J=8.8\) Hz, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)/DMSO-d\(_6\)) \(\delta\) 151.8, 147.7, 142.5, 132.5, 122.6, 72.8; IR (ATR) 3237, 1544, 1433, 1215, 1137 cm\(^{-1}\); HRMS (ESI) calculated for C\(_6\)H\(_4\)IN\(_2\)O\(_5\) (M+H\(^+\)) 310.9165, found.

4-Iodo-2,3-dinitrophenyltrifluoromethanesulfonate (264). Treatment of 261 (1.923 g, 6.203 mmol) with Tf\(_2\)O (1.40 mL, 8.32 mmol) in CH\(_2\)Cl\(_2\) (20 mL) in the presence of pyridine (1.50 mL, 18.39 mmol) under a nitrogen atmosphere, as described for 258 (0 °C -rt, 30 mins.), gave after solvent removal and chromatography (Hexane/EtOAc, 7:3), 264 (2.523 g, 5.707 mmol, 92%) as a yellow solid. mp=61-62 \(^\circ\)C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.26 (d, \(J=8.8\) Hz, 1H), 7.42 (d, \(J=8.8\) Hz, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 148.5, 144.5, 140.7, 137.2, 126.3, 118.3 (q, \(J_{C-F}=319\) Hz), 86.8; \(^{19}\)F NMR (376.10 MHz, CDCl\(_3\)) \(\delta\) -72.5; IR (ATR) 1546, 1435, 1349, 1213, 1131 cm\(^{-1}\); HRMS (ESI) calculated for C\(_7\)H\(_3\)F\(_3\)IN\(_2\)O\(_7\)S (M+H\(^+\)) 442.8658 (M+Na=464.8477), found.

4-Bromo-2,5-dinitrophenyltrifluoromethanesulfonate (265). Treatment of a solution of 262 (1.500 g, 5.705 mmol) with TfO (1.25 mL, 7.416 mmol) in CH\(_2\)Cl\(_2\) in the presence of pyridine (1.50 mL, 17.114 mmol) under a nitrogen atmosphere, as described for 258 (0 °C -rt, 30 mins.) gave after solvent removal and chromatography (Hexane/EtOAc, 9:1), 265 (1.803 g, 4.564 mmol, 80%) as a white solid. mp=62-63 \(^\circ\)C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.54 (s, 1H), 7.94 (s, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 151.1, 142.8, 142.6, 133.1, 121.7, 118.4 (q, J\(_{C-F}=320\) Hz), 115.1; \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) -72.5; IR (ATR) 1539, 1426, 1353, 1231, 1141 cm\(^{-1}\); HRMS (ESI) calculated for C\(_7\)H\(_3\)BrF\(_3\)N\(_2\)O\(_7\)S (M+H\(^+\)) 394.8796 (M+Na=416.8616), found.

4-Iodo-2,5-dinitrophenyltrifluoromethanesulfonate (266). Treatment of 263 (1.389 g, 4.480 mmol) with Tf\(_2\)O (0.98 mL, 5.82 mmol) in CH\(_2\)Cl\(_2\) (16 mL) in the presence of pyridine (1.10 mL, 13.44 mmol) under a nitrogen atmosphere, as described for 258 (0 °C -rt, 25 mins.), gave after solvent removal and chromatography (Hexane/EtOAc, 95:5), 266 (1.596 g, 3.610 mmol, 81%) as a yellow oil. mp=60-61 \(^\circ\)C;
1H NMR (400 MHz, CDCl₃) δ 8.77 (s, 1H), 7.92 (s, 1H); 13C NMR (100 MHz, CDCl₃) δ 155.4, 142.5, 141.2, 139.6, 121.2, 118.4 (q, J_C-F=319 Hz), 85.8; 19F NMR (376.10 MHz, CDCl₃) δ -72.4; IR (ATR) 1532, 1434, 1336, 1195, 1132 cm⁻¹; HRMS (ESI) calcd for C₇H₅F₃N₂O₇S (M+H⁺) 442.8658 (M+Na=464.8477), found

5-Bromo-2,4-dinitrophenol (270) and 3-bromo-2,6-dinitrophenol (271). Treatment of a solution of 5-bromo-2-nitrophenol (268) (579 mg, 2.658 mmol) in DCM (2 mL) with NaN₃ (271 mg, 3.190 mmol) in concentrated H₂SO₄ (5 mL) at 0 °C, as described for 274 and 275 (10 h), gave, after work up and chromatography (Hexane/EtOAc, 9:1), a mixture of 270 and 271 (693 mg, 2.634 mmol, 99%) as a yellow oil. 1H NMR (400 MHz, CDCl₃) δ 10.93 (s, 1H), 10.82 (s, 1H), 8.82 (s, 1H), 8.14 (d, J=9.2 Hz, 1H), 7.63 (s, 1H), 7.35 (d, J=9.2 Hz, 1H); IR (ATR) 3233, 1542, 1236, 854 cm⁻¹; HRMS (ESI) calcd for, found

5-Bromo-2,5-dinitrophenyltrifluoromethanesulfonate (204) and 3-bromo-2,6-dinitrophenyltrifluoromethanesulfonate (273). Treatment of the mixture of 270 and 271 (1.700 g, 6.465 mmol) with Tf₂O (1.41 mL, 8.40 mmol) in CH₂Cl₂ (18 mL) in the presence of triethylamine (Et₃N, 2.34 mL, 16.81 mmol) under a nitrogen atmosphere, as described for 258 (0 °C -rt, 1 h), gave, in order of elution, after solvent removal and chromatography (Hexane/EtOAc, 9:1), 204 (1.458 g, 3.691 mmol, 57%) as a yellow oil and 273 (409 mg, 1.034 mmol, 16%) as a white solid. Analytical data for 273: mp=93-94 °C; 1H NMR (400 MHz, CDCl₃) δ 10.90 (s, 1H), 10.82 (s, 1H), 8.14 (d, J=9.2 Hz, 1H), 7.63 (s, 1H), 7.35 (d, J=9.2 Hz, 1H); IR (ATR) 3233, 1542, 1236, 854 cm⁻¹; HRMS (ESI) calcd for, found

5-Iodo-2,4-dinitrophenol (274)²¹⁵ and 3-Iodo-2,6-dinitrophenol (275). To an ice-cooled solution of NaN₃ (648 mg, 7.629 mmol) in concentrated H₂SO₄ (13 mL) was added drop wise the solution of 5-iodo-2-nitrophenol (269) (1.264 g, 4.768 mmol) in DCM (5 mL). The resulting solution was maintained at 0 °C overnight (10 h). The solution was quenched with ice-cold water and allowed to cool to ambient temperature. The solution was extracted in EtOAc (3X30 mL), dried (MgSO₄), filtered and was concentrated under reduced pressure. The crude oil was purified by chromatography (Hexane/DCM, 7:3, acidified with AcOH) to give a mixture of 274 and 275 (1.168 g, 3.768 mmol, 79%) as a yellow oil. Analytical data for 274 and 275 from the mixture: 1H NMR (600 MHz, CDCl₃) δ 10.94 (s, 1H), 10.74 (s, 1H), 8.79 (s, 1H), 7.79 (s, 1H), 7.95 (d, J=9.0 Hz, 1H), 7.57 (d, J=9.0 Hz, 1H); 13C NMR (150 MHz, CDCl₃) δ 155.9, 147.0, 146.9, 144.3, 134.1, 133.9, 132.2, 130.2, 126.2, 122.6, 97.2, 96.9; IR (ATR) 3276, 1538, 1239, 835 cm⁻¹; HRMS (ESI) calcd for, found

173
5-Iodo-2,5-dinitrophenyltrifluoromethanesulfonate (276) and 3-iodo-2,6-dinitrophenyltrifluoromethanesulfonate (277). Treatment of the mixture of 274 and 275 (1.167 g, 3.764 mmol) with Tf₂O (0.86 mL, 5.08 mmol) in CH₂Cl₂ (12 mL) in the presence of triethylamine (Et₃N, 1.40 mL, 9.79 mmol) under a nitrogen atmosphere, as described for 258 (0 °C -rt, 30 mins.), gave, in order of elution, after solvent removal and chromatography (Hexane/EtOAc, 9:1), 276 (1.035 g, 2.341 mmol, 62%) as a yellow oil and 277 (466 mg, 1.054 mmol, 28%) as a white solid. Analytical data for 276: 1H NMR (400 MHz, CDCl₃) δ 8.68 (s, 1H), 8.16 (s, 1H); 151.5, 142.1, 140.9, 138.0, 123.2, 118.4 (q, JZF = 319.5 Hz), 94.3; 19F NMR (MHz, CDCl₃) δ -72.4; IR (ATR) 1527, 1433, 1343, 1197, 837 cm⁻¹; HRMS (ESI) calcd for, found

Analytical data for 277: mp=121-122 °C; 1H NMR (400 MHz, CDCl₃) δ 8.18 (d, J=8.4 Hz, 1H), 7.98 (d, J=9.0 Hz, 1H); 13C NMR (100 MHz, CDCl₃) δ 149.6, 142.2, 140.3, 133.0, 127.8, 118.1 (q, JZF = 319.5 Hz), 94.3; 19F NMR (376.10 MHz, CDCl₃) δ -71.9; IR (ATR) 1532, 1436, 1352, 1216, 897 cm⁻¹; HRMS (ESI) calcd for, found

2-Bromo-3,6-dinitrophenol (279) and 2-Bromo-3,4-dinitrophenol (280). To an ice-cooled solution of NaNO₃ (869 mg, 10.23 mmol) in concentrated H₂SO₄ (20 mL) was added drop wise the solution of 2-bromo-3-nitrophenol (278) (1.716 g, 7.872 mmol) in DCM/MeOH (5/5 mL). The resulting solution was maintained at 0 °C 3 h and then was allowed to warm to ambient temperature over a period of 1 h. The solution was quenched with ice-cold water and allowed to cool to ambient temperature. The solution was extracted in EtOAc (3X20 mL), dried (MgSO₄), filtered and was concentrated under reduced pressure. The crude oil was purified by chromatography (Hexane/EtOAc, 9:1, then, 7:3, acidified with AcOH) to give, in order of elution, 279 (1.263 g, 4.802 mmol, 61%) and 280 (213 g, 0.811 mmol, 10%) both as a yellow solid.

Analytical data for 279: mp=92-93 °C; 1H NMR (600 MHz, CDCl₃) δ 11.43 (s, 1H), 8.29 (d, J=9.0 Hz, 1H), 7.31 (d, J=9.0 Hz, 1H); 13C NMR (100 MHz, CDCl₃) δ 155.4, 153.6, 134.7, 125.2, 114.7, 107.0; IR (ATR) 3239, 1536, 1445, 1141, 816 cm⁻¹; HRMS (ESI) calcd for C₆H₄BrN₂O₅ (M+H⁺) 262.9304 (M+Na=284.9123), found

Analytical data for 280: mp=149 °C (decomposition); 1H NMR (400 MHz, CDCl₃) δ 8.25 (d, J=9.2 Hz, 1H), 7.28 (d, J=9.2 Hz, 1H), 6.55 (br, s, 1H); 13C NMR (100 MHz, CDCl₃/DMSO-d₆) δ 161.8, 146.2, 130.9, 125.9, 115.8, 103.6; IR (ATR) 3234, 1553, 1313, 1091 cm⁻¹; HRMS (ESI) calcd for C₆H₄BrN₂O₅ (M+H⁺) 262.9304 (M+Na=284.9123), found

2-Bromo-3,6-dinitrophenyltrifluoromethanesulfonate (281). Treatment of a solution of 279 (1.2360 g, 4.700 mmol) with Tf₂O (1.12 mL, 6.657 mmol) in CH₂Cl₂ (15 mL) in the presence of Et₃N (1.70 mL,
12.220 mmol) under a nitrogen atmosphere, as described for 258 (0 °C -rt, 30 min), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3), 281 (1.6934 g, 4.286 mmol, 91%) as a white solid. mp=108-109 °C; 1H NMR (600 MHz, CDCl3) δ 8.20 (d, J=9.0 Hz, 1H), 7.93 (d, J=9.0 Hz, 1H); 13C NMR (150 MHz, CDCl3) δ 153.7, 144.7, 140.7, 126.0, 124.2, 118.3 (q, JCF=319.5 Hz), 113.3; 19F NMR (MHz, CDCl3) δ -72.3; IR (ATR) 1544, 1434, 1351, 1214, 1131 cm⁻¹; HRMS (ESI) calcd for C7H3BrF3N2O7 (M+H⁺) 394.8796 (M+Na=416.8616), found.

1,4-Diethenyl-2,3-dinitrobenzene (285). To a yellow mixture of 2,3-dinitro-1,4-dibromobenzene 256 (538.3 mg, 1.652 mmol) and PdCl2(PPh3)2 in 1,4-dioxane (4 mL) at ambient temperature under a nitrogen atmosphere was added a solution of ethenyl tributyltin (282) (1153 mg, 3.634 mmol) in 1,4-dioxane (1 mL) via syringe. The resulting solution was heated at reflux (100 °C, 21 h). The solvent was removed at reduced pressure and the crude product was purified by chromatography (10% K2CO3-SiO2, hexane/EtOAc, 95:5) to give 285 (245.1 mg, 1.113 mmol, 67%) as a yellow solid. mp=113-114 °C; 1H NMR (400 MHz, CDCl3) δ 7.77 (s, 2H), 6.74 (dd, J=17.2, 11.2 Hz, 2H), 5.93 (d, J=17.2 Hz, 2H), 5.64 (d, J=11.2 Hz, 2H); 13C NMR (100 MHz, CDCl3) δ 142.0, 131.4, 129.2, 128.4, 122.1; IR (ATR) 1525, 1478, 1352, 975, 934, 848 cm⁻¹; HRMS (ESI) calcd for C10H8N2O4Na (M+Na⁺) 243.0382, found 243.0375.

2,3-Dinitro-1,4-di(1-propen-1-yl)benzene (286). To a solution of 256 (106 mg, 0.327 mmol), PdCl2(PPh3)2 (4.7 mg, 0.01 mmol) and PPh3 (3.4 mg, 0.01 mmol) in dioxane (3 mL), under a nitrogen atmosphere, was added the solution of 1-propen-1-yl tributyltin (283) (282 mg, 0.852 mmol) in dioxane (1 mL) via syringe. The solution was heated at reflux (100 °C, 24 h). The solvent was removed under reduced pressure and the residue was purified by chromatography (10% K2CO3-SiO2, hexane/EtOAc, 9:1) to afford 286 (69.0 mg, 0.278 mmol, 85%, ~2:1 trans-cis/trans-trans mixture) as a yellow solid. mp=125-127 °C; 1H NMR (400 MHz, CDCl3) δ 7.69 (d, J= 8.3 Hz, 1H), 7.64 (s, 1H), 7.50 (s, 1H), 7.45 (d, J = 8.3 Hz, 1H), 6.47 – 6.33 (m, 6H), 6.06 (ddq, J = 11.5, 9.7, 7.2 Hz, 2H), 1.94 (m, 6H), 1.78 (dd, J = 7.0, 1.6 Hz, 3H), 1.76 (dd, J = 7.0, 1.6 Hz, 3H); 13C NMR (150 MHz, DMSO-d6) δ 141.8, 141.7, 140.5, 140.4, 135.8, 135.6, 133.8, 133.7, 133.5, 133.4, 130.4, 130.2, 129.9, 129.9, 129.8, 129.8, 121.7, 121.7, 121.5, 18.7, 14.3; IR (ATR) 3041, 2954, 1649, 1528, 1358, 859, 820 cm⁻¹; HRMS (ESI) calcd for C12H12N2O3Na (M+Na⁺) 271.0689, found 271.0688.

2,3-Dinitro-1,4-di(1-propen-2-yl)benzene (287). To a solution of 256 (352 mg, 1.082 mmol) and PdCl2(PPh3)2 (30.4 mg, 0.043 mmol) in 1,4-dioxane (3 mL), stirred for 5 min under a nitrogen atmosphere, was added the solution of isopropenyltributyltin (284) (824 mg, 2.488 mmol) in dioxane (1mL) via a syringe. The solution was heated at reflux (100 °C) for 24 h. The solvent was removed under
reduced pressure and the resulting crude was purified by chromatography (10% K$_2$CO$_3$-SiO$_2$, hexane/EtOAc, 95:5) to afford 287 (189 mg, 0.761 mmol, 70%) as a white solid. mp=138-139 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.45 (s, 2H), 5.27 (s, 2H), 5.02 (s, 2H), 2.10 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 141.9, 139.2, 137.4, 131.5, 118.1, 23.1; IR (ATR) 3094, 2973, 1643, 1543, 1526, 1355, 911, 847 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{13}$N$_2$O$_4$ (M+H$^+$) 249.0875 (M+Na=271.0695), found xxxxxxxx.

1,5-Diethenyl-2,4-dinitrobenzene (289). Treatment of a solution of 288 (500 mg, 1.535 mmol) with 282 (1.071 g, 3.38 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (43.1 mg, 0.061 mmol) in dioxane (6.5 mL), as described for 285 (90 °C, 24 h), gave after solvent removal and chromatography (Hexane/EtOAc, 95:5) 289 (247 mg, 1.121 mmol, 73%) as a white solid. mp=60-61 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 8.65 (s, 1H), 7.83 (s, 1H), 7.27 (dd, $J$=17.2, 10.8 Hz, 2H), 5.90 (d, $J$=17.2 Hz, 2H), 5.70 (d, $J$=11.2 Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 145.6, 137.9, 131.2, 129.1, 122.4, 121.6; IR (ATR) 1578, 1517, 1340, 940, 907 cm$^{-1}$; HRMS (ESI) calcd for C$_{10}$H$_9$N$_2$O$_4$ (M+H$^+$) 221.0562 (M+Na=243.0382), found

2,4-Dinitro-1,5-di(1-propen-1-yl)benzene (290). Treatment of a solution of 288 (136.1 mg, 0.418 mmol) with 283 (360 mg, 1.086 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (5.9 mg, 0.008 mmol) and PPh$_3$ (4.4 mg, 0.017 mmol) in dioxane (4 mL), as described for 285 (90 °C, 24 h), gave after solvent removal and chromatography (Hexane/EtOAc, 95:5) 290 (96.7 mg, 0.390 mmol, 93%) as a yellow solid. mp=98-99 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 8.75 (s, 1H), 8.65 (s, 1H), 8.56 (s, 1H), 7.73 (s, 1H), 7.57 (s, 1H), 7.39 (s, 1H), 6.99-6.93 (m, 2H), 6.78-6.74 (m, 2H), 6.46-6.35 (m, 2H), 6.13-6.04 (m, 2H), 2.02-1.99 (m, 6H), 1.79 (dd, $J$=7.2, 2.0 Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 145.9, 145.5, 144.7, 144.5, 137.6, 137.2, 137.0, 136.9, 135.9, 135.6, 135.4, 131.8, 131.3, 131.2, 128.4, 125.2, 125.0, 124.9, 124.7, 121.8, 121.7, 121.6, 19.1, 19.0, 14.5, 14.5; IR (ATR) 1537, 1352, 1277, 938 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{13}$N$_2$O$_4$ (M+H$^+$) 249.0875 (M+Na=271.0695), found

2,4-Dinitro-1,5-di(1-propen-2-yl)benzene (291). Treatment of a solution of 288 (175.6 mg, 0.539 mmol) with 284 (464 mg, 1.401 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (15.1 mg, 0.022 mmol) and PPh$_3$ (11.3 mg, 0.043 mmol) in dioxane (5 mL), as described for 285 (90 °C, 24 h), gave after solvent removal and
chromatography (Hexane/EtOAc, 9:1) 291 (116.5 mg, 0.469 mmol, 87%) as a white solid. mp=69-70 °C; 
^1^H NMR (400 MHz, CDCl₃) δ 8.45 (s, 1H), 7.31 (s, 1H), 5.28 (s, 2H), 5.02 (s, 2H), 2.11 (s, 6H); ^13^C NMR (100 MHz, CDCl₃) δ 146.3, 143.3, 141.1, 133.0, 120.6, 117.1, 22.9; IR (ATR) 1584, 1525, 1344, 908, 734 cm⁻¹; HRMS (ESI) calcd for C₁₂H₁₃N₂O₄ (M+H⁺) 249.0875 (M+Na=271.0695), found

1,4-Diethenyl-2,5-dinitrobenzene (292). To a solution of 266 (310.3 mg, 0.740 mmol) in DMF (5 mL) under nitrogen atmosphere were added BHT (18.4 mg, 0.084 mmol), PdCl₂(PPh₃)₂ (9.9 mg, 0.014 mmol), LiCl (95.3 mg, 2.248 mmol) and 282 (534.2 mg, 1.685 mmol) respectively. The reaction mixture was stirred at ambient temperature for 27 h. EtOAc (20 mL) was added and the mixture was washed with water (6X15 mL). The organic layer was dried (MgSO₄), filtered and the solvent was evaporated under reduced pressure. The resulting residue was purified by chromatography (Hexane/EtOAc, 98:2) to give 292 (82 mg, 0.372 mmol, 53%) as a yellow solid. mp=148-149 °C; ^1^H NMR (400 MHz, CDCl₃) δ 8.14 (s, 2H), 7.09 (dd, J=17.2, 11.2 Hz, 2H), 5.90 (d, J=17.6 Hz, 2H), 5.65 (d, J=11.2 Hz, 2H); ^13^C NMR (100 MHz, CDCl₃) δ 149.3, 133.0, 129.9, 124.3, 121.6; IR (ATR) 1518, 1348, 1283, 937 cm⁻¹; HRMS (ESI) calcd for C₁₀H₉N₂O₄ (M+H⁺) 221.0562 (M+Na=243.0382), found

2,5-Dinitro-1,4-di(1-propen-1-yl)benzene (293). A mixture of 266 (397.6 mg, 0.899 mmol) and 283 (774.3 mg, 2.338 mmol) in DMF (6 mL) in the presence of PdCl₂(PPh₃)₂ (25.3 mg, 0.036 mmol), BHT (21.8 mg, 0.099 mmol) and LiCl (137.3 mg, 3.239 mmol) was stirred at 65 °C for 14 h. After cooling to ambient temperature, the solution was diluted with EtOAc (15 mL) and was washed with water (7x10 mL). The resulting crude was purified by chromatography (10% K₂CO₃ silica gel, Hexane/EtOAc, 97:3) to give 293 (89.1 mg, 0.359 mmol, 40%) as a yellow solid. mp=114-115 °C; ^1^H NMR (600 MHz, CDCl₃) δ 8.14 (s, 1H), 8.01 (s, 1H), 7.95 (s, 1H), 7.82 (s, 1H), 6.78 (dq, J=16.8, 1.2 Hz, 1H), 6.74 (dq, J=15.6, 1.8 Hz, 1H), 6.64 (dq, J=11.4, 1.8 Hz, 1H), 6.61 (dq, J=11.4, 1.8 Hz, 1H), 6.46-6.36 (m, 2H), 6.11-6.02 (m, 2H), 1.99 (dd, J=6.6, 1.8 Hz, 3H), 1.97 (dd, J=6.6, 1.8 Hz, 3H), 1.81 (dd, J=7.2, 1.8 Hz, 3H), 1.79 (dd, J=7.2, 1.8 Hz, 3H); ^13^C NMR (100 MHz, CDCl₃) δ 150.0, 149.6, 148.9, 148.4, 134.6, 134.2, 132.5, 131.9, 131.8, 131.6, 131.2, 127.6, 127.5, 124.0, 123.9, 123.8, 123.5, 123.5, 18.9, 18.9, 14.5, 14.5; IR (ATR) 1519, 1350, 1270, 963 cm⁻¹; HRMS (ESI) calcd for C₁₀H₉N₂O₄ (M+H⁺) 221.0562 (M+Na=243.0382), found

2,5-Dinitro-1,4-di(1-propen-1-yl)benzene (293). Treatment of a solution of 266 (213 mg, 0.482 mmol) with 283 (416.5 mg, 1.258 mmol) in the presence of PdCl₂(PPh₃)₂ (6.8 mg, 0.010 mmol), PPh₃ (5.2 mg, 0.020 mmol), BHT (12.6 mg, 0.057 mmol) and LiCl (73.5 mg, 1.734 mmol) in dioxane (2.5 mL), as
described for 285 (100 °C, 24 h), gave after solvent removal and chromatography (Hexane/EtOAc, 9:1) 293 (62.2 mg, 0.251 mmol, 52%) as a yellow solid.

2,5-Dinitro-1,4-di(1-propen-1-yl)benzene (293). Treatment of a solution of 265 (313.1 mg, 0.793 mmol) with 283 (685 mg, 2.069 mmol) in the presence of PdCl₂(PPh₃)₂ (11.1 mg, 0.016 mmol), PPh₃ (8.3 mg, 0.032 mmol), BHT (20.9 mg, 0.0595 mmol) and LiCl (121.6 mg, 2.855 mmol) in dioxane (3 mL), as described for 285 (100 °C, 24 h), gave after solvent removal and chromatography (Hexane/EtOAc, 9:1) 293 (62.2 mg, 0.251 mmol, 52%) as a yellow solid.

2,5-Dinitro-1,4-di(1-propen-2-yl)benzene (294). Treatment of a solution of 266 (239.2 mg, 0.541 mmol) with 284 (466 mg, 1.407 mmol) in the presence of PdCl₂(PPh₃)₂ (7.6 mg, 0.011 mmol), PPh₃ (5.7 mg, 0.022 mmol), BHT (11.9 mg, 0.054 mmol), and LiCl (78 mg, 1.840 mmol) in dioxane (5 mL), as described for 285 (100 °C, 30 h), gave after solvent removal and chromatography (Hexane/EtOAc, 95:5) 294 (124 mg, 0.500 mmol, 63%) as a yellow solid.

1,2-Diethenyl-3,6-dinitrobenzene (295) Treatment of a solution of 288 (103 mg, 0.261 mmol) with 282 (206.6 mg, 0.652 mmol) in the presence of PdCl₂(PPh₃)₂ (3.7 mg, 0.005 mmol), PPh₃ (2.7 mg, 0.010 mmol), BHT (6.9 mg, 0.031 mmol) and LiCl (39.8 mg, 0.940 mmol) in dioxane (1.5 mL), as described for 285 (100 °C, 24 h), gave after solvent removal and chromatography (Hexane/EtOAc, 9:1) 295 (21.2 mg, 0.096 mmol, 37%) as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.71 (s, 2H), 6.73 (dd, J=18.0, 11.6 Hz, 2H), 5.60 (dd, J=11.2, 0.4 Hz, 2H), 5.41 (dd, J=18.0, 0.8 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 151.0, 133.6, 129.6, 123.3, 122.8; IR (ATR) 1523, 1350, 804, 726 cm⁻¹; HRMS (ESI) calcd for C₁₀H₉N₂O₄ (M+H⁺) 249.0875 (M+Na=271.0695), found
3,6-Dinitro-1,3-di(1-propen-1-yl)benzene (296) Treatment of a solution of 288 (482.2 mg, 1.221 mmol) with 283 (1.0104 g, 3.051 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (17.1 mg, 0.024 mmol), PPh$_3$ (12.7 mg, 0.048 mmol), BHT (32.3 mg, 0.147 mmol) and LiCl (186.2 mg, 4.396 mmol) in dioxane (4 mL), as described for 285 (100 °C, 20 h), gave after solvent removal and chromatography (Hexane/EtOAc, 9:1) 296 (143.6 mg, 0.578 mmol, 47%) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.80 (s, 1H), 7.71 (8.8 Hz, 1H), 7.63 (d, $J$=8.8 Hz, 1H), 7.56 (s, 1H), 6.36 - 6.28 (m, 4H), 5.96 - 5.77 (m, 4H), 1.85 (dd, $J$=6.8, 1.6 Hz, 3H), 1.82 (dd, $J$=6.8, 2.0 Hz, 3H), 1.43 (dd, $J$=6.8, 1.6 Hz, 3H), 1.41 (dd, $J$=7.2, 1.6 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 151.6, 151.3, 151.3, 151.2, 135.0, 134.5, 133.8, 133.8, 133.3, 133.0, 131.3, 131.3, 122.9, 122.8, 122.6, 122.5, 122.3, 122.1, 121.9, 18.9, 18.9, 14.5, 14.4; IR (ATR) 1528, 1350, 959, 826 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{13}$N$_2$O$_4$ (M+H$^+$) 249.0875 (M+Na=271.0695), found.

3,6-Dinitro-1,2-di-(1-propen-2-yl)benzene (297) Treatment of a solution of 288 (400.1 mg, 1.013 mmol) with 32 (831.6 g, 2.512 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (14.2 mg, 0.020 mmol), PPh$_3$ (11 mg, 0.042 mmol), BHT (26.8 mg, 0.122 mmol) and LiCl (154.4 mg, 3.642 mmol) in dioxane (4 mL), as described for 285 (100 °C, 20 h), gave after solvent removal and chromatography (Hexane/EtOAc, 9:1) 297 (121.2 mg, 0.488 mmol, 48%) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.75 (s, 2H), 5.30 (s, 2H), 4.92 (s, 2H), 2.11 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 151.1, 139.1, 138.7, 122.8, 118.7, 24.1; IR (ATR) 1531, 1348, 912, 735 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{13}$N$_2$O$_4$ (M+H$^+$) 249.0875 (M+Na=271.0695), found.

1,3-Diethenyl-2,6-dinitrobenzene (298). Treatment of a solution of 273 (463 mg, 1.172 mmol) with 282 (929 mg, 2.930 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (32.9 mg, 0.047 mmol), PPh$_3$ (24.6 mg, 0.094 mmol), BHT (28.4 mg, 0.129 mmol), and LiCl (159 mg, 3.75 mmol) in dioxane (8 mL), as described for 285 (90 °C, 24 h), gave after solvent removal and chromatography (Hexane/DCM, 95:5, then 9:1), 298 (82.6 mg, 0.375 mmol, 32%) as a yellow oil. $^1$H NMR (600 MHz, CDCl$_3$) δ 8.08 (d, $J$=8.4 Hz, 1H), 7.71 (d, $J$=9.0 Hz, 1H), 6.89 (dd, $J$=17.4, 10.8 Hz, 1H), 6.61 (dd, $J$=17.4, 11.4 Hz, 1H), 6.50 (d, $J$=17.4 Hz, 1H), 5.69 (d, $J$=10.8 Hz, 1H), 5.56 (d, $J$=12.0 Hz, 1H), 5.46 (d, $J$=18.0 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 149.7, 146.9, 134.2, 128.1, 127.3, 127.2, 126.0, 125.5, 123.4, 122.3; IR (ATR) 1516, 1346, 937, 914 cm$^{-1}$; HRMS (ESI) calcd for C$_{10}$H$_9$N$_2$O$_4$ (M+H$^+$) 221.0562 (M+Na=243.0382), found.

Scheme 7.12 Selective coupling of 258 with 282. Treatment of a solution of 258 (203.2 mg, 0.514 mmol) with 282 (196.2 mg, 0.619 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (7.2 mg, 0.010 mmol), PPh$_3$ (5.4 mg, 0.021 mmol), and BHT (10 mg, 0.045 mmol) in dioxane (4 mL), as described for 285 (100 °C, 24 h), gave, in order of elution, after solvent removal and chromatography (Hexane/DCM, 95:5, then 9:1),
inseparable mixtures of 285 and 4-bromo-1-ethenyl-2,3-dinitrobenzene (285 + 299, 22.7 mg) as a white solid and 258 and 300 (258 + 300, 69.8 mg) as a colorless oil.

4-Ethenyl-2,3-Dinitrophenyltrifluoromethanesulfonate (300). Treatment of a solution of 264 (884.1 mg, 2.000 mmol) with 282 (761 mg, 2.400 mmol) in the presence of PdCl₂(PPh₃)₂ (28.1 mg, 0.040 mmol), PPh₃ (21 mg, 0.080 mmol), and BHT (44 mg, 0.200 mmol) in dioxane (8 mL), as described for 285 (98 °C, 24 h), gave in order of elution, after solvent removal and chromatography (Hexane/EtOAc, 9:1) 285 (8.8 mg, 0.040 mmol, 2%) and 300 (444 mg, 1.297 mmol, 65%) both as a white solid. mp=58-59 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.93 (d, J=8.8 Hz, 1H), 7.65 (d, J=8.8 Hz, 1H), 6.75 (dd, J=17.2, 10.8 Hz, 1H), 5.97 (d, J=17.6 Hz, 1H), 5.76 (d, J=10.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 142.3, 139.5, 136.9, 132.6, 131.2, 127.4, 118.3 (q, J_C-F=319 Hz); ¹⁹F NMR (376.10 MHz, CDCl₃) δ -72.7; IR (ATR) 1521, 1421, 1326, 1200, 1132 cm⁻¹; HRMS (ESI) calcd for C₉H₆F₃N₂O₇ (M+H⁺) 342.9848 (M+Na=364.9667), found.

2,3-Dinitro-4-(1-propen-1-yl)phenyltrifluoromethanesulfonate (301). Treatment of a solution of 264 (720 mg, 1.629 mmol) with 283 (663 mg, 2.003 mmol) in the presence of PdCl₂(PPh₃)₂ (22.8 mg, 0.032 mmol), PPh₃ (17.1 mg, 0.065 mmol), and BHT (35 mg, 0.159 mmol) in dioxane (6 mL), as described for 285 (100 °C, 24 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 9:1) 301 (370.2 mg, 1.039 mmol, 64%) as a yellow solid. mp=64-65 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.84 (d, J=9.0 Hz, 1H), 7.67 (d, J=8.8 Hz, 1H), 7.64 (d, J=8.8 Hz, 1H), 7.58 (d, J=9.0 Hz, 1H), 6.54 – 6.37 (m, 3H), 6.18 (dq, J=11.6, 7.2 Hz, 1H), 1.99 (d, J=5.1 Hz, 3H), 1.79 (dd, J=7.2, 1.8 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 143.1, 141.6, 138.8, 138.6, 137.9, 136.9, 136.8, 135.4, 135.2, 133.0, 132.6, 131.3, 125.4, 125.2, 121.1, 120.6, 118.3 (q, J_C-F=319 Hz, 2C), 18.9, 14.5; IR (ATR) 1547, 1436, 1350, 1233, 1137 cm⁻¹; HRMS (ESI) calcd for C₁₀H₁₀F₃N₂O₇S (M+H⁺) 357.0004 (M+Na=378.9824), found.

2,3-Dinitro-4-(1-propen-2-yl)phenyltrifluoromethanesulfonate (302). Treatment of a solution of 264 (923.1 mg, 2.088 mmol) with 284 (830 mg, 2.506 mmol) in the presence of PdCl₂(PPh₃)₂ (29.3 mg, 0.042 mmol), PPh₃ (21.9 mg, 0.083 mmol), and BHT (46 mg, 0.209 mmol) in dioxane (10 mL), as described for 285 (98 °C, 24 h), gave, in order of elution, after solvent removal and chromatography (Hexane/EtOAc, 9:1) 302 (479 mg, 1.344 mmol, 64%) both as a white solid. mp=69-70 °C; ¹H NMR (600 MHz, CDCl₃) δ 7.67 (d, J=8.4 Hz, 1H), 7.63 (d, J=8.4 Hz, 1H), 5.34 (s, 1H), 5.08 (s, 1H), 2.12 (s, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 142.8, 139.2, 138.9, 138.1, 136.6, 133.7, 125.3, 119.5, 118.3 (q, J_C-F=319.5 Hz); IR (ATR) 1544, 1429, 1219, 1135, 834 cm⁻¹; HRMS (ESI) calcd for C₁₀H₈F₃N₂O₇S (M+H⁺) 357.0004 (M+Na=378.9824), found.
Ethyl 4-(trifluoromethylsulfonyloxy)-2,3-dinitrophenylprop-2-enoate (303). Treatment of a solution of 264 (367.8 mg, 0.832 mmol) with ethyl 2-tributylstannyl-2-propenoate (369 mg, 0.948 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (11.7 mg, 0.017 mmol), PPh$_3$ (8.7 mg, 0.033 mmol), and BHT (20.2 mg, 0.092 mmol) in dioxane (4 mL), as described for 285 (98 °C, 23 h), gave, after solvent removal and chromatography (Hexane/DCM, 6:4) 303 (170.7 mg, 0.412 mmol, 50%) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.73 (d, $J=8.8$ Hz, 1H), 7.67 (d, $J=8.8$ Hz, 1H), 6.73 (s, 1H), 6.05 (s, 1H), 4.23 (quartet, $J=7.2$ Hz, 2H), 1.27 (t, $J=7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 163.1, 142.5, 140.1, 137.6, 135.8, 134.8, 133.2, 131.8, 125.9, 119.9, 116.7, 62.3, 13.8; $^{19}$F NMR (376.10 MHz, CDCl$_3$) $\delta$ -72.3; IR (ATR) 1716, 1552, 1212, 1131, 832 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{10}$F$_3$N$_2$O$_9$S (M+H$^+$) 415.0059 (M+Na=436.9879), found

5-Ethenyl-2,4-Dinitrophenyltrifluoromethanesulfonate (205). Treatment of a solution of 276 (112.2 mg, 0.254 mmol) with 282 (98 mg, 0.309 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (3.6 mg, 0.005 mmol), PPh$_3$ (2.7 mg, 0.010 mmol), and BHT (6.7 mg, 0.030 mmol) in dioxane (2 mL), as described for 285 (98 °C, 32 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 95:5) 205 (30 mg, 0.088 mmol, 35%) as a faint yellow oil. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 8.80 (s, 1H), 7.74 (s, 1H), 7.26 (dd, $J=17.4$, 10.8 Hz, 1H), 6.02 (d, $J=16.8$ Hz, 1H), 5.87 (d, $J=10.8$ Hz, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 145.3, 143.5, 140.6, 139.6, 129.7, 124.9, 124.3, 123.9, 118.5 (q, $J_{C-F}=213$ Hz); $^{19}$F NMR (MHz, CDCl$_3$) $\delta$ -72.8; IR (ATR) 1536, 1434, 1338, 1210, 1131 cm$^{-1}$; HRMS (ESI) calcd for C$_9$H$_6$F$_3$N$_2$O$_7$S (M+H$^+$) 342.9848 (M+Na=364.9667), found

2,4-Dinitro-5-(1-propen-1-yl)phenyl trifluoromethanesulfonate (305). Treatment of a solution of 204 (703.2 mg, 1.780 mmol) with 283 (766 mg, 2.314 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (25 mg, 0.036 mmol), PPh$_3$ (18.7 mg, 0.071 mmol), and BHT (43.1 mg, 0.196 mmol) in dioxane (8 mL), as described for 285 (90 °C, 24 h), gave, in order of elution, after solvent removal and chromatography (Hexane/EtOAc, 95:5) 290 (52.6 mg, 0.212 mmol, 12%) as a yellow solid and 305 (476.3 mg, 1.337 mmol, 75%) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.85 (s, 1H), 8.75 (s, 1H), 7.64 (s, 1H), 7.51 (s, 1H), 6.95 (dq, $J=15.6$, 2.0 Hz, 1H), 6.76 (dq, $J=12.0$, 2.0 Hz, 1H), 6.54 (dq, $J=15.6$, 6.8 Hz, 1H), 6.24 (dq, $J=12.0$, 7.2 Hz, 1H), 2.06 (dd, $J=6.8$, 1.6 Hz, 3H), 1.84 (dd, $J=7.2$, 2.0 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 146.1, 144.8, 143.3, 142.9, 140.6, 140.2, 139.4, 139.1, 138.6, 134.4, 127.6, 123.9, 123.7, 123.5, 123.1, 118.5 (q, $J_{C-F}=320$ Hz), 118.4 (q, $J_{C-F}=319$ Hz); $^{19}$F NMR (376.10 MHz, CDCl$_3$) $\delta$ -73.0, -72.9; IR (ATR) 1534, 1434, 1339, 1210, 1131 cm$^{-1}$; HRMS (ESI) calcd for C$_{10}$H$_8$F$_3$N$_2$O$_2$S (M+H$^+$) 357.0004 (M+Na=378.9824), found
2,4-Dinitro-5-(1-propen-2-yl)trifluoromethanesulfonate (306). Treatment of a solution of 276 (312.7 mg, 0.707 mmol) with 284 (284 mg, 0.858 mmol) in the presence of PdCl₂(PPh₃)₂ (9.9 mg, 0.014 mmol), PPh₃ (7.4 mg, 0.028 mmol), and BHT (17.1 mg, 0.078 mmol) in dioxane (3 mL), as described for 285 (90 °C, 23 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 97:3), in order of elution, 291 (9.9 mg, 0.040 mmol, 6%) as a white solid and 306 (129 mg, 0.362 mmol, 51%) as a colorless oil. 

1H NMR (400 MHz, CDCl₃) δ 8.70 (s, 1H), 7.44 (s, 1H), 5.38 (s, with further fine splitting, 1H), 5.11 (s, 1H), 2.12 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ 146.3, 146.3, 143.1, 139.8, 139.6, 126.7, 123.2, 118.9, 118.5 (q, J_C-F =320 Hz); 19F NMR (376.10 MHz, CDCl₃) δ -72.6; IR (ATR) 1539, 1435, 1340, 1213, 1131 cm⁻¹; HRMS (ESI) calcd for C₁₀H₈F₃N₂O₇S (M+H⁺) 357.0004 (M+Na=378.9824), found.

4-Ethenyl-2,5-dinitrophenyltrifluoromethanesulfonate (307). Treatment of a solution of 266 (782.4 mg, 1.770 mmol) with 282 (670.5 mg, 2.114 mmol) in the presence of PdCl₂(PPh₃)₂ (24.8 mg, 0.035 mmol), PPh₃ (18.6 mg, 0.071 mmol), and BHT (39 mg, 0.177 mmol) in dioxane (10 mL), as described for 285 (80 °C, 24 h), gave, in order of elution, after solvent removal and chromatography (Hexane/EtOAc, 98:2, then 95:5) 292 (12.2 mg, 0.055 mmol, 3%) as a yellow solid and 307 (463.3 mg, 1.354 mmol, 76%) as yellow oil. 

1H NMR (600 MHz, CDCl₃) δ 8.41 (s, 1H), 8.00 (s, 1H), 7.13 (dd, J=17.4, 10.8 Hz, 1H), 6.01 (d, J=17.4 Hz, 1H), 5.78 (d, J=10.8 Hz, 1H); 13C NMR (150 MHz, CDCl₃) δ 149.0, 143.5, 139.7, 134.5, 129.0, 126.7, 123.7, 120.8, 118.4 (q, J_C-F =213 Hz); 19F NMR ( MHz, CDCl₃) δ -72.9; IR (ATR) 1553, 1437, 1342, 1213, 1130 cm⁻¹; HRMS (ESI) calcd for C₉H₆F₃N₂O₇S (M+H⁺) 342.9848 (M+Na=364.9667), found.

2,5-Dinitro-4-(1-propen-1-yl)phenyltrifluoromethanesulfonate (308). Treatment of a solution of 266 (723 mg, 1.636 mmol) with 283 (763.2 mg, 2.305 mmol) in the presence of PdCl₂(PPh₃)₂ (23 mg, 0.033 mmol), and PPh₃ (17.2 mg, 0.065 mmol) in dioxane (7 mL), as described for 285 (90 °C, 24 h), gave, in order of elution, after solvent removal and chromatography (Hexane/EtOAc, 98:2) 293 (29.6 mg, 0.119 mmol, 7%) as a yellow solid and 308 (406.9 mg, 1.142 mmol, 70%) as yellow oil. 

1H NMR (400 MHz, CDCl₃) δ 8.34 (s, 1H), 8.17 (s, 1H), 8.06 (s, 1H), 7.94 (s, 1H), 6.84 (dq, J = 15.6, 1.6 Hz, 1H), 6.72 – 6.62 (m, 1H), 6.52 (dq, J = 15.6, 6.8 Hz, 1H), 6.20 (dq, J = 11.6, 7.2 Hz, 1H), 2.03 (dd, J = 6.4, 1.6 Hz, 3H), 1.83 (dd, J = 7.2, 1.8 Hz, 3H); 13C NMR (100 MHz, CDCl₃) δ 150.0, 148.5, 143.3, 142.9, 139.3, 138.8, 137.6, 134.6, 133.9, 133.6, 129.8, 126.4, 122.8, 122.4, 120.8, 120.7, 118.4 (q, J_C-F =319 Hz); 19F NMR (376.10 MHz, CDCl₃) δ -72.6, -72.6; IR (ATR) 1532, 1336, 1202, 1123 cm⁻¹; HRMS (ESI) calcd for C₁₀H₈F₃N₂O₇S (M+H⁺) 357.0004 (M+Na=378.9824), found.
2-Ethenyl-3,6-dinitrophenyltrifluoromethanesulfonate (309). Treatment of a solution of 281 (987.8 mg, 2.500 mmol) with 282 (961.1 mg, 3.031 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (35.1 mg, 0.050 mmol), PPh$_3$ (26.2 mg, 0.100 mmol) and BHT (66.1 mg, 0.300 mmol) in dioxane (7 mL), as described for 285 (98 °C, 24 h), gave, in order of elution, after solvent removal and chromatography (Hexane/EtOAc, 95:5) 295 (55.6 mg, 0.253 mmol, 10%) as a yellow oil and 309 (301.2 mg, 0.880 mmol, 35%) as a faint yellow solid. mp=61-62 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.11 (d, $J=8.8$ Hz, 1H), 7.98 (d, $J=8.8$ Hz, 1H), 6.77 (dd, $J=17.6$, 11.6 Hz, 1H), 5.90 (d, $J=11.6$ Hz, 1H), 7.75 (d, $J=18.0$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 151.5, 144.8, 139.4, 131.1, 127.2, 125.4, 124.6, 123.8, 118.2 (q, $J_{C-F}=319$ Hz); $^{19}$F NMR (MHz, CDCl$_3$) $\delta$ -73.0; IR (ATR) 1548, 1341, 1207, 1129, 971 cm$^{-1}$; HRMS (ESI) calcd for C$_{9}$H$_{6}$F$_{3}$N$_{2}$O$_{7}$S (M+H$^+$) 342.9848 (M+Na=364.9667), found

3,6-dinitro-2-(1-propen-1-yl)phenyltrifluoromethanesulfonate (310). Treatment of a solution of 281 (1.2523 g, 3.170 mmol) with 283 (1.2500 g, 3.775 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (44.5 mg, 0.063 mmol), PPh$_3$ (33.3 mg, 0.127 mmol) and BHT (83.8 mg, 0.300 mmol) in dioxane (10 mL), as described for 285 (100 °C, 25 h), gave, in order of elution, after solvent removal and chromatography (Hexane/EtOAc, 96:4) 296 (48.8 mg, 0.197 mmol, 6%) and 310 (509.3 mg, 1.430 mmol, 45%) both as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.12 (d, $J=8.8$ Hz, 1H), 8.04 (d, $J=8.8$ Hz, 1H), 8.03 (d, $J=8.8$ Hz, 1H), 7.91 (d, $J=8.8$ Hz, 1H), 6.44-6.39 (m, 2H), 6.30-6.19 (m, 2H), 1.97 (dd, $J=6.8$, 2.0 Hz, 3H), 1.63 (dd, $J=6.8$, 1.6 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 152.0, 151.6, 144.6, 140.3, 139.6, 139.4, 136.4, 130.9, 129.9, 125.4, 124.7, 124.0, 123.6, 118.1 (q, $J_{C-F}=320$ Hz), 118.1 (q, $J_{C-F}=319$ Hz), 117.7, 117.2, 19.0, 15.1; $^{19}$F NMR (MHz, CDCl$_3$) $\delta$ -73.4, -73.5; IR (ATR) 1557, 1423, 1347, 1203, 839 cm$^{-1}$; HRMS (ESI) calcd for C$_{10}$H$_{8}$F$_{3}$N$_{2}$O$_{7}$S (M+H$^+$) 357.0004 (M+Na=378.9824), found

3,6-Dinitro-2-(1-propen-2-yl)phenyltrifluoromethanesulfonate (311). Treatment of a solution of 281 (1.5178 g, 3.842 mmol) with 284 (1.5100 g, 4.560 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (53.9 mg, 0.077 mmol), PPh$_3$ (40.3 mg, 0.154 mmol) and BHT (101.6 mg, 0.461 mmol) in dioxane (10 mL), as described for 285 (100 °C, 25 h), gave, in order of elution, after solvent removal and chromatography (Hexane/EtOAc, 96:4) 297 (32.9 mg, 0.133 mmol, 3%) as a yellow oil and 311 (698 mg, 1.959 mmol, 51%) as a white solid. mp=94-95 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.08 (d, $J=8.8$ Hz, 1H), 7.89 (d, $J=8.8$ Hz, 1H), 5.34 (s, 1H), 5.18 (s, 1H), 2.19 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 152.1, 144.5, 139.0, 135.6, 134.5, 125.4, 123.5, 122.7, 118.1 (q, $J_{C-F}=319$ Hz), 22.4; $^{19}$F NMR (MHz, CDCl$_3$) $\delta$ -72.8; IR (ATR) 1548, 1419, 1336, 1197, 837 cm$^{-1}$; HRMS (ESI) calcd for C$_{10}$H$_{8}$F$_{3}$N$_{2}$O$_{7}$S (M+H$^+$) 357.0004 (M+Na=378.9824), found
3-Ethenyl-2,6-dinitrophenyltrifluoromethanesulfonate (312). Treatment of a solution of 273 (803.2 mg, 2.033 mmol) with 282 (762 mg, 2.403 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (28.5 mg, 0.041 mmol), PPh$_3$ (21.3 mg, 0.081 mmol) and BHT (44.7 mg, 0.203 mmol) in dioxane (6 mL), as described for 282 (98 °C, 24 h), gave, in order of elution, after solvent removal and chromatography (Hexane/EtOAc, 9:1) an inseparable mixture of 298 and 3-bromo-2,6-dinitrobenzene (80.2 mg) as a colorless oil and 312 (305.2 mg, 0.892 mmol, 44%) as white solid. mp=72-73 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.26 (d, $J$=8.8 Hz, 1H), 7.87 (d, $J$=8.8 Hz, 1H), 6.66 (dd, $J$=17.2, 11.2 Hz, 1H), 6.10 (d, $J$=17.2 Hz, 1H), 5.82 (d, $J$=10.8 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 143.0, 140.7, 137.8, 133.5, 127.6, 127.4, 126.7, 125.6, 118.1 (q, $J$$_{CF}$=320 Hz); $^{19}$F NMR (376.10 MHz, CDCl$_3$) $\delta$ -72.3; IR (ATR) 1546, 1435, 1349, 1209, 1132 cm$^{-1}$; HRMS (ESI) calcd for C$_9$H$_6$F$_3$N$_2$O$_7$S (M+H$^+$) 342.9848 (M+Na=364.9667), found

2,6-Dinitro-3-(1-propen-2-yl)phenyltrifluoromethanesulfonate (313). Treatment of a solution of 273 (1.126 g, 2.850 mmol) with 284 (1.213 g, 3.663 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (40 mg, 0.057 mmol), PPh$_3$ (29.9 mg, 0.114 mmol) and BHT (62.8 mg, 0.285 mmol) in dioxane (7 mL), as described for 285 (100 °C, 22 h), gave, in order of elution, after solvent removal and chromatography (Hexane/EtOAc, 96:4), an inseparable mixture of decoupling and C-OTf coupling products along with unknown impurities (125.3 mg) and 313 (459 mg, 1.288 mmol, 45%) both as a yellow oil. Analytical data for 313: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.07 (d, $J$= 8.6 Hz, 1H), 7.44 (d, $J$= 8.6 Hz, 1H), 5.19 (s, 1H), 4.95 (s, 1H), 1.94 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.4, 143.4, 140.7, 138.2, 133.1, 129.6, 127.5, 119.7, 118.1 (q, $J$$_{CF}$=319 Hz), 22.5; $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -72.6; IR (ATR) 1546, 1454, 1353, 1216, 1139 cm$^{-1}$; HRMS (ESI) calcd for C$_{10}$H$_8$F$_3$N$_2$O$_7$S (M+H$^+$) 357.0004 (M+Na=378.9824), found

4-Chloro-2,3-Dinitro-1-ethenylbenzene (314). Reaction of 300 (260 mg, 0.760 mmol) with 284 (317 mg, 0.957 mmol) in DMF (3 mL) in the presence of PdCl$_2$(PPh$_3$)$_2$ (10.6 mg, 0.015 mmol), BHT (18.4 mg, 0.084 mmol), and LiCl (103.4 mg, 2.440 mmol), as described for 292 (rt, 16 h), gave, after work up and chromatography (Hexane/EtOAc, 95:5, then 9:1) 314 (109.3 mg, 0.478 mmol, 63%) as a white solid. mp=100-101 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.77 (d, $J$ =6.0 Hz, 1H), 7.68 (d, $J$=6.0 Hz, 1H), 6.72 (dd, $J$=17.2, 10.8 Hz, 1H), 5.93 (d, $J$=17.2 Hz, 1H), 5.67 (d, $J$=11.2 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 142.5, 142.2, 133.3, 131.4, 129.8, 128.0, 126.3, 122.9; IR (ATR) 1548, 1546, 1454, 1353, 1216, 1139 cm$^{-1}$; HRMS (ESI) calcd for C$_8$H$_6$ClN$_2$O$_4$ (M+H$^+$) 357.0004 (M+Na=378.9824), found

4-Chloro-2,5-Dinitro-1-ethenylbenzene (315). Reaction of 307 (158.3 mg, 0.463 mmol) with 284 (188.4 mg, 0.569 mmol) in DMF (2 mL) in the presence of PdCl$_2$(PPh$_3$)$_2$ (6.4 mg, 0.009 mmol), BHT (12.2 mg, 0.056 mmol), and LiCl (57 mg, 1.345 mmol), as described for 292 (rt, 21 h), gave, after work up and
chromatography (Hexane/EtOAc, 98:2) 315 (56 mg, 0.245 mmol, 53%) as a white solid. \( \text{mp}=102-103 \, ^{\circ}\text{C} \); \(^1\text{H NMR}\) (400 MHz, CDCl\(_3\)) \( \delta \) 8.09 (s, 2H), 7.08 (dd, \( J=17.2, 10.8 \, \text{Hz}, \, 1\text{H} \)), 5.90 (d, \( J=17.2 \, \text{Hz}, \, 1\text{H} \)), 5.69 (d, \( J=11.2 \, \text{Hz}, \, 1\text{H} \)); \(^{13}\text{C NMR}\) (100 MHz, CDCl\(_3\)) \( \delta \) 149.9, 148.4, 133.1, 129.5, 127.8, 126.4, 125.1, 122.4; IR (ATR) 1547, 1524, 1347, 1274, 851 \text{cm}^{-1}; HRMS (ESI) calcd for C\(_8\)H\(_6\)ClN\(_2\)O\(_4\) (M+H\(^+\)) 229.0016 (M+Na=250.9836), found.

1-Ethenyl-2,5-dinitro-4-(1-propen-2-yl)benzene (316) Treatment of a solution of 315 (95 mg, 0.416 mmol) with 284 (206 mg, 0.623 mmol) in the presence of PdCl\(_2\)(PPh\(_3\))\(_2\) (5.8 mg, 0.008 mmol), PPh\(_3\) (8.7 mg, 0.033 mmol), and BHT (11 mg, 0.050 mmol) in dioxane (4 mL), as described for 285 (90 \text{o}^\circ\text{C}, 24 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 98:2) 316 (76.9 mg, 0.328 mmol, 79%) as a faint yellow solid. \( \text{mp}=89-90 \, ^{\circ}\text{C} \); \(^1\text{H NMR}\) (400 MHz, CDCl\(_3\)) \( \delta \) 8.04 (s, 1H), 7.86 (s, 1H), 7.09 (dd, \( J=17.2, 10.8 \, \text{Hz}, \, 1\text{H} \)), 5.88 (d, \( J=17.2 \, \text{Hz}, \, 1\text{H} \)), 5.64 (d, \( J=11.2 \, \text{Hz}, \, 1\text{H} \)), 5.29 (s, with further fine splitting, 1H), 5.05 (s, with further fine splitting, 1H); 2.10 (dd, \( J=1.2, 0.8 \, \text{Hz}, \, 3\text{H} \)); \(^{13}\text{C NMR}\) (100 MHz, CDCl\(_3\)) \( \delta \) 150.2, 148.7, 140.1, 138.5, 133.0, 130.0, 126.4, 123.8, 121.5, 117.7, 22.8; IR (ATR) 1528, 1350, 912, 853 \text{cm}^{-1}; HRMS (ESI) calcd for C\(_{11}\)H\(_{11}\)N\(_2\)O\(_4\) (M+H\(^+\)) 235.0719 (M+Na=257.0537), found.

1-Ethenyl-2,3-dinitro-4-(1-propen-1-yl)benzene (317). Treatment of a solution of 300 (203.5 mg, 0.595 mmol) with 283 (256 mg, 0.773 mmol) in the presence of PdCl\(_2\)(PPh\(_3\))\(_2\) (8.3 mg, 0.012 mmol), PPh\(_3\) (6.2 mg, 0.024 mmol), BHT (15.7 mg, 0.071 mmol) and LiCl (95.8 mg, 2.260 mmol) in dioxane (6 mL), as described for 285 (98 \text{o}^\circ\text{C}, 30 h), gave after solvent removal and chromatography (Hexane/EtOAc, 85:15) 317 (91.2 mg, 0.389 mmol, 65%) as a faint yellow solid. \( \text{mp}=95-97 \, ^{\circ}\text{C} \); \(^1\text{H NMR}\) (400 MHz, CDCl\(_3\)) \( \delta \) 7.77 (d, \( J=8.4 \, \text{Hz}, \, 1\text{H} \)), 7.71 (s, 2H), 7.52 (d, \( J=8.0 \, \text{Hz}, \, 1\text{H} \)), 6.70 (dd, \( J=17.2, 11.2 \, \text{Hz}, \, 1\text{H} \)), 6.68 (dd, \( J=17.2, 11.2 \, \text{Hz}, \, 1\text{H} \)), 6.49-6.35 (m, 3H), 6.07 (dq, \( J=14.0, 6.8 \, \text{Hz}, \, 1\text{H} \)), 5.93 (d, \( J=10.4 \, \text{Hz}, \, 1\text{H} \)), 5.88 (d, \( J=10.4 \, \text{Hz}, \, 1\text{H} \)), 5.61 (d, \( J=10.4 \, \text{Hz}, \, 1\text{H} \)), 5.58 (d, \( J=11.2 \, \text{Hz}, \, 1\text{H} \)), 1.93 (dd, \( J=6.0, 0.8 \, \text{Hz}, \, 3\text{H} \)), 1.76 (dd, \( J=7.2, 2.0 \, \text{Hz}, \, 3\text{H} \)); \(^{13}\text{C NMR}\) (100 MHz, CDCl\(_3\)) \( \delta \) 142.7, 142.0, 141.9, 141.4, 135.2, 133.6, 133.2, 131.6, 131.4, 130.7, 130.2, 129.1, 128.8, 128.7, 128.4, 128.4, 122.3, 121.9, 121.8, 121.5, 18.9, 14.6; IR (ATR) 1533, 1436, 1437, 1216, 1128, 902 \text{cm}^{-1}; HRMS (ESI) calcd for C\(_{11}\)H\(_{11}\)N\(_2\)O\(_4\) (M+H\(^+\)) 235.0719 (M+Na=257.0537), found.

1-Ethenyl-2,3-dinitro-4-(1-propen-2-yl)benzene (318). Treatment of a solution of 300 (189.3 mg, 0.553 mmol) with 284 (234.4 mg, 0.708 mmol) in the presence of PdCl\(_2\)(PPh\(_3\))\(_2\) (7.8 mg, 0.011 mmol), PPh\(_3\) (5.8 mg, 0.022 mmol), BHT (14.6 mg, 0.066 mmol) and LiCl (89.1 mg, 2.102 mmol) in dioxane (4.5 mL), as described for 285 (100 \text{o}^\circ\text{C}, 28 h), gave after solvent removal and chromatography (Hexane/EtOAc, 9:1) 318 (83.2 mg, 0.355 mmol, 64%) as a white solid. \( \text{mp}=99-100 \, ^{\circ}\text{C} \); \(^1\text{H NMR}\) (400...
MHz, CDCl$_3$) $\delta$ 7.75 (d, $J$=8.4 Hz, 1H), 7.48 (d, $J$=8.4 Hz, 1H), 6.72 (dd, $J$=17.2, 10.8 Hz, 1H), 5.91 (d, $J$=17.2 Hz, 1H), 5.62 (d, $J$=11.2 Hz, 1H), 5.25 (s, with further fine splitting, 1H), 5.02 (s, with further fine splitting, 1H), 2.09 (dd, $J$=1.6, 1.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 142.2, 141.6, 139.2, 137.8, 131.8, 131.0, 129.0, 128.4, 122.0, 118.1, 22.9IR (ATR) 1536, 1302, 1169, 803 cm$^{-1}$; HRMS (ESI) calcd for C$_{11}$H$_{11}$N$_2$O$_4$ (M+H$^+$) 235.0719 (M+Na=257.0537), found

2,3-Dinitro-4-(1-propen-1-yl)-1-(1-propen-2-yl)benzene (319). Treatment of a solution of 302 (199.8 mg, 0.561 mmol) with 283 (232.2 mg, 0.701 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (7.8 mg, 0.011 mmol), BHT (13.6 mg, 0.062 mmol), and LiCl (76.1 mg, 1.795 mmol) in DMF (2.5 mL), as described for 292 (rt, 18 h), gave after work up and chromatography (Hexane/EtOAc, 95:5) 319 (63 mg, 0.254 mmol, 45%) as a white solid. mp=62-63$^\circ$C; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.67 (d, $J$=7.8 Hz, 1H), 7.48 (d, $J$=8.4 Hz, 1H), 7.45 (d, $J$=7.8 Hz, 1H), 7.40 (d, $J$=8.4 Hz, 1H), 6.42-6.38 (m, 3H), 6.07 (dq, $J$=14.4, 7.2 Hz, 1H), 5.26 (s, 1H), 5.24 (s, 1H), 5.03 (s, 1H), 5.01 (s, 1H), 2.11 (s, 3H), 2.09 (s, 3H), 1.94 (dd, $J$=4.8, 2.4 Hz, 3H), 1.77 (dd, $J$=7.2, 1.8 Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 142.5, 142.3, 142.2, 141.3, 139.3, 139.3, 137.1, 136.8, 134.9, 133.4, 132.9, 131.5, 131.3, 131.3, 131.0, 128.9, 122.4, 121.9, 118.1, 117.9, 23.1, 23.0, 18.9, 14.6; IR (ATR) 1547, 1409, 1326, 1174, 837 cm$^{-1}$; HRMS (ESI) calcd for C$_{11}$H$_{11}$N$_2$O$_4$ (M+H$^+$) 235.0719 (M+Na=257.0538), found

Ethyl 4-(ethenyl-2,3-dinitrophenyl)prop-2-enoate (320). Treatment of a solution of 300 (403.2 mg, 1.178 mmol) with ethyl 2-tributylstannyl-2-propenoate (531.2 mg, 1.365 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (16.5 mg, 0.023 mmol), PPh$_3$ (12.4 mg, 0.047 mmol), BHT (31 mg, 0.141 mmol) and LiCl (179.8 mg, 4.242 mmol) in dioxane (4 mL), as described for 285 (100 $^\circ$C, 24 h), gave after solvent removal and chromatography (Hexane/EtOAc, 9:1) 320 (174.5 mg, 0.597 mmol, 51%) as a colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.84 (d, $J$=8.40 Hz, 1H), 7.50 (d, $J$=8.4 Hz, 1H), 6.67 (dd, $J$=17.2, 11.2 Hz, 1H), 6.64 (s, 1H), 5.98 (s, 1H), 5.95 (d, $J$=17.2 Hz, 1H), 5.64 (d, $J$=11.2 Hz, 1H), 4.19 (quartet, $J$=7.2 Hz, 2H), 1.24 (t, $J$=7.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 163.6, 142.5, 142.3, 142.2, 141.3, 139.3, 137.1, 136.8, 134.9, 133.4, 132.9, 131.5, 131.3, 131.3, 131.0, 128.9, 122.4, 121.9, 118.1, 117.9, 23.1, 23.0, 18.9, 14.6; IR (ATR) 1703, 1523, 1363, 1156, 802 cm$^{-1}$; HRMS (ESI) calcd for C$_{13}$H$_{13}$N$_2$O$_6$ (M+H$^+$) 293.0774 (M+Na=315.0593), found

Ethyl 2,3-dinitro-4-(1-propen-1-yl)phenylprop-2-enoate (321). Treatment of a solution of 301 (360.1 mg, 1.011 mmol) with ethyl 2-tributylstannyl-2-propenoate (444.6 mg, 1.142 mmol) in the presence of PdCl$_2$(PPh$_3$)$_2$ (14.2 mg, 0.020 mmol), PPh$_3$ (10.6 mg, 0.040 mmol), BHT (22.1 mg, 0.100 mmol) and LiCl (150 mg, 3.539 mmol) in dioxane (4 mL), as described for 285 (100 $^\circ$C, 24 h), gave after solvent removal and chromatography (Hexane/EtOAc, 9:1) 321 (157.9 mg, 0.516 mmol, 51%) as a faint yellow oil. $^1$H
NMR (600 MHz, CDCl₃) δ 7.75 (d, J = 8.4 Hz, 1H), 7.57 (d, J = 8.4 Hz, 1H), 7.48 (d, J = 8.4 Hz, 1H), 7.43 (d, J = 8.4 Hz, 1H), 6.66 (s, 1H), 6.63 (s, 1H), 6.46 (dq, J = 15.6, 6.6 Hz, 1H), 6.40 – 6.35 (m, 2H), 6.11 (dq, J = 11.6, 7.2 Hz, 1H), 5.99 (s, 1H), 5.95 (s, 1H), 4.21 (dq, J = 8.0, 7.2 Hz, 4H), 1.95 (dd, J = 6.6, 1.2 Hz, 4H), 1.79 (dd, J = 7.2, 1.8 Hz, 3H), 1.26 (t, J = 7.2 Hz, 3H), 1.25 (t, J = 7.2 Hz, 3H); 13C NMR (150 MHz, CDCl₃) δ 163.7, 143.5, 142.1, 141.9, 141.9, 137.0, 137.0, 135.6, 134.1, 133.8, 133.0, 132.7, 132.4, 132.1, 131.6, 131.2, 130.5, 129.8, 122.1, 121.5, 62.0, 62.0, 19.0, 14.6, 13.9, 13.9; IR (ATR) 1708, 1547, 1355, 1207, 1097 cm⁻¹; HRMS (ESI) calcd for C₁₄H₁₅N₂O₆ (M+H⁺) 307.0930 (M+Na=329.0750), found

**Ethyl 2,3-dinitro-4-(1-propen-1-yl)phenylprop-2-enenate (321).** Treatment of a solution of 303 (100.3 mg, 0.242 mmol) with 283 (104 mg, 0.314 mmol) in the presence of PdCl₂(PPh₃)₂ (3.4 mg, 0.005 mmol), PPh₃ (2.5 mg, 0.010 mmol), BHT (5.3 mg, 0.024 mmol), and LiCl (36.9 mg, 0.871 mmol) in dioxane (2 mL), as described for 285 (100 °C, 26 h), gave after solvent removal and chromatography (Hexane/EtOAc, 7:3) 321 (32.1 mg, 0.105 mmol, 43%) as a faint yellow oil.

**Ethyl 4-(1-propen-2-yl,2,3-dinitrophenyl)prop-2-enenate (322).** Treatment of a solution of 302 (465.5 mg, 1.307 mmol) with ethyl 2-tributylstannyl-2-propenoate (661 mg, 1.698 mmol) in the presence of PdCl₂(PPh₃)₂ (18.3 mg, 0.026 mmol), PPh₃ (13.7 mg, 0.052 mmol), BHT (34.5 mg, 0.157 mmol), and LiCl (199.4 mg, 4.704 mmol) in dioxane (4 mL), as described for 285 (100 °C, 24 h), gave after solvent removal and chromatography (Hexane/DCM, 6:4) 322 (218.2 mg, 1.058 mmol, 55%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.53 (d, J = 8.0 Hz, 1H), 7.48 (d, J = 8.0 Hz, 1H), 6.63 (s, 1H), 5.97 (s, 1H), 5.27 (s, with further fine splitting, 1H), 5.02 (s, with further fine splitting, 1H), 4.20 (quartet, J = 7.2 Hz, 2H), 2.09 (s, 3H), 1.25 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 146.4, 145.6, 143.7, 141.3, 137.5, 131.0, 131.2, 117.0, 802 cm⁻¹; HRMS (ESI) calcd for C₁₄H₁₅N₂O₆ (M+H⁺) 307.0930 (M+Na=329.0750), found

**1-Ethenyl-2,4-dinitro-5-(1-propen-2-yl)benzene (323).** Treatment of a solution of 205 (310.3 mg, 0.907 mmol) with 284 (381.3 mg, 1.152 mmol) in the presence of PdCl₂(PPh₃)₂ (12.7 mg, 0.018 mmol), PPh₃ (9.5 mg, 0.036 mmol), BHT (23.9 mg, 0.108 mmol) and LiCl (130.7 mg, 3.084 mmol) in dioxane (6 mL), as described for 285 (90 °C, 24 h), gave after solvent removal and chromatography (Hexane/EtOAc, 98:2) 323 (135.2 mg, 0.577 mmol, 64%) as a faint yellow oil. ¹H NMR (600 MHz, CDCl₃) δ 8.53 (s, 1H), 7.58 (s, 1H), 7.23 (dd, J = 17.4, 11.4 Hz, 1H), 5.89 (d, J = 17.4 Hz, 1H), 5.67 (d, J = 11.4 Hz, 1H), 5.29 (s, with further fine splitting, 1H), 5.03 (s, with further fine splitting, 1H), 2.11 (s, with further fine splitting, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 146.4, 145.6, 143.7, 141.3, 137.5, 131.0, 131.2, 117.0, 22.9;
IR (ATR) 1582, 1522, 1344, 1265, 911, 733 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{11}H_{11}N_2O_4\) (M+H\(^+\)) 235.0719 (M+Na=257.0538), found

\[\text{2,4-Dinitro-5-(1-propen-1-yl)-1-(1-propen-2-yl)benzene (324). Treatment of a solution of 305 (404.4 mg, 1.135 mmol) with 284 (473.6 mg, 1.430 mmol) in the presence of PdCl}_2(PPh\(_3\))\(_2\) (15.9 mg, 0.023 mmol), PPh\(_3\) (11.9 mg, 0.045 mmol), BHT (25 mg, 0.114 mmol) and LiCl (154 mg, 3.633 mmol) in dioxane (8 mL), as described for 285 (80 °C, 24 h), gave after solvent removal and chromatography (Hexane/EtOAc, 97:3) 324 (203.2 mg, 0.819 mmol, 72%) as a faint yellow oil. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 8.57 (s, 1H), 8.48 (s, 1H), 7.54 (s, 1H), 7.36 (s, 1H), 6.91 (dq, \(J=15.6, 1.8\) Hz, 1H), 6.73 (dq, \(J=11.4, 1.8\) Hz, 1H), 6.45 (dq, \(J=15.6, 6.6\) Hz, 1H), 6.08 (dq, \(J=11.6, 7.2\) Hz, 1H), 5.27 (s, with further fine splitting, 1H), 5.25 (s, with further fine splitting, 1H), 5.01 (s, with further fine splitting, 1H), 4.99 (s, with further fine splitting, 1H), 2.10 (s, 3H), 2.09 (s, 3H), 1.99 (dd, \(J=3.0, 1.2\) Hz, 3H), 1.78 (dd, \(J=7.2, 1.8\) Hz, 3H); \(^1\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 146.2, 145.8, 145.4, 145.2, 143.4, 143.0, 141.6, 141.2, 137.6, 137.0, 136.0, 134.3, 131.7, 130.7, 124.7, 124.4, 121.2, 121.1, 116.9, 116.6, 22.9, 22.8, 19.0, 14.5; IR (ATR) 1579, 1517, 1339, 909, 832 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{12}H_{13}N_2O_4\) (M+H\(^+\)) 249.0875 (M+Na=271.0695), found

\[\text{1-Ethenyl-2,5-dinitro-4-(1-propen-1-yl)benzene (325). Treatment of a solution of 307 (302.7 mg, 0.885 mmol) 283 (369.5 mg, 1.116 mmol) in the presence of PdCl}_2(PPh\(_3\))\(_2\) (12.4 mg, 0.018 mmol), PPh\(_3\) (9.3 mg, 0.035 mmol), BHT (23.4 mg, 0.106 mmol) and LiCl (142.6 mg, 3.364 mmol) in dioxane (4 mL), as described for 285 (100 °C, 30 h), gave after solvent removal and chromatography (Hexane/DCM, 9:1) 325 (132.6 mg, 0.566 mmol, 64%) as a yellow solid. mp=111-113 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.19 (s, 1H), 8.08 (s, 1H), 8.06 (s, 1H), 7.90 (s, 1H), 7.10 (dd, \(J=17.2, 10.8\) Hz, 1H), 7.07 (dd, \(J=17.2, 10.8\) Hz, 1H), 6.77 (dq, \(J=15.6, 1.2\) Hz, 1H), 6.64 (dq, \(J=11.6, 1.6\) Hz, 1H), 6.43 (dq, \(J=15.2, 6.8\) Hz, 1H), 6.08 (dq, \(J=14.4, 7.2\) Hz, 1H), 5.90 (d, \(J=16.8\) Hz, 1H), 5.86 (d, \(J=17.2\) Hz, 1H), 5.65 (d, \(J=10.8, 5.61\) (d, \(J=11.2\) Hz, 1H), 1.98 (dd, \(J=6.8, 1.6\) Hz, 3H), 1.80 (dd, \(J=7.2, 2.0\) Hz, 3H); \(^1\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 150.1, 149.2, 149.0, 148.7, 148.7, 134.8, 133.0, 132.4, 132.3, 132.0, 131.8, 130.0, 127.6, 124.2, 124.1, 124.0, 123.7, 123.4, 121.4, 121.0, 18.9, 14.5; IR (ATR) 1538, 1520, 1351, 1275, 938 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{12}H_{13}N_2O_4\) (M+H\(^+\)) 249.0875 (M+Na=271.0695), found

(325). Treatment of a solution of 307 (325.9 mg, 0.952 mmol) with 283 (387.8 mg, 1.171 mmol) in the presence of PdCl\(_2(PPh_3)_2\) (13.4 mg, 0.019 mmol), BHT (23 mg, 0.105 mmol) and LiCl (129.1 mg, 3.046 mmol) in DMF (4 mL), as described for 292 (rt, 21 h), gave after work up and chromatography
(Hexane/EtOAc, 98:2) 325 (37 mg, 0.158 mmol, 17%) as a yellow solid and 315 (13.4 mg, 0.059 mmol, 6%) as a white solid.

2,5-Dinitro-4-(1-propen-1-yl)-1-(1-propen-2-yl)benzene (326). Treatment of a solution of 308 (362.2 mg, 1.017 mmol) with 284 (424.2 mg, 1.281 mmol) in the presence of PdCl₂(PPh₃)₂ (14.3 mg, 0.020 mmol), BHT (26.9 mg, 0.122 mmol) and LiCl (176.8 mg, 4.171 mmol) in DMF (7 mL), as described for 292 (rt, 21 h), gave after work up and chromatography (Hexane/EtOAc, 98:2) 326 (66.3 mg, 0.267 mmol, 26%) as a yellow oil. 

1H NMR (600 MHz, CDCl₃) δ 7.99 (s, 1H), 7.90 (s, 1H), 7.80 (s, 1H), 7.78 (s, 1H), 6.76 (dq, J=15.6, 1.2 Hz, 1H), 6.62 (dq, J=11.4, 1.2 Hz, 1H), 6.41 (dq, J=15.6, 2.4 Hz, 1H), 6.07 (dq, J=14.4, 7.2 Hz, 1H), 5.28 (s, with further splitting, 1H), 5.26 (s, with further splitting, 1H), 5.06 (s, with further splitting, 1H), 5.03 (s, with further splitting, 1H), 2.11 (s, with further splitting, 3H), 2.08 (s, with further splitting, 3H), 1.97 (dd, J=6.6, 1.8 Hz, 3H), 1.80 (dd, J=7.2, 1.8 Hz, 3H); 13C NMR (100 MHz, CDCl₃) δ 150.0, 149.5, 148.4, 140.2, 137.9, 137.4, 134.7, 133.0, 132.3, 131.8, 127.1, 126.4, 126.3, 123.7, 123.6, 123.4, 117.6, 117.4, 22.8, 22.8, 18.9, 14.4; IR (ATR) 1540, 1345, 1265, 733 cm⁻¹; HRMS (ESI) calcd for C₁₂H₁₃N₂O₄ (M+H⁺) 249.0875 (M+Na=271.0695), found

1-Ethenyl-3,6-dinitro-2-(1-propen-1-yl)benzene (327). Treatment of a solution of 309 (301 mg, 0.880 mmol) with 283 (363.7 mg, 1.098 mmol) in the presence of PdCl₂(PPh₃)₂ (12.9 mg, 0.018 mmol), PPh₃ (9.2 mg, 0.035 mmol), BHT (22.3 mg, 0.101 mmol) and LiCl (135.6 mg, 3.199 mmol) in dioxane (3 mL), as described for 285 (100 °C, 30 h), gave after solvent removal and chromatography (Hexane/EtOAc, 97:3) 327 (130 mg, 0.555 mmol, 63%) as a yellow oil. 

1H NMR (400 MHz, CDCl₃) δ 7.78 (d, J=8.8 Hz, 1H), 7.70 (d, J=8.8 Hz, 1H), 7.63 (s, 2H), 6.69 (dd, J=17.6, 11.6 Hz, 1H), 6.67 (dd, J=17.6, 11.6 Hz, 1H), 6.38-6.34 (m, 2H), 5.98-5.80 (m, 2H), 5.57 (d, J=11.6 Hz, 1H), 5.50 (d, J=11.6 Hz, 1H), 5.38 (d, J=17.6 Hz, 2H), 1.85 (dd, J=6.8, 1.6 Hz, 3H), 1.42 (dd, J=6.8, 1.6 Hz, 3H); 13C NMR (100 MHz, CDCl₃) δ 151.3, 151.2, 151.0, 135.6, 134.1, 133.5, 133.3, 133.1, 131.7, 129.8, 129.4, 122.8, 122.7, 122.7, 122.6, 122.3, 122.0, 18.9, 14.6; IR (ATR) 1531, 1351, 906, 726 cm⁻¹; HRMS (ESI) calecd for C₁₁H₁₁N₂O₄ (M+H⁺) 235.0719 (M+Na=257.0538), found

1-Ethenyl-3,6-dinitro-2-(1-propen-2-yl)benzene (328). Treatment of a solution of 309 (211.8 mg, 0.619 mmol) with 284 (276.7 mg, 0.836 mmol) in the presence of PdCl₂(PPh₃)₂ (8.7 mg, 0.012 mmol), PPh₃ (6.5 mg, 0.025 mmol), BHT (16.4 mg, 0.074 mmol) and LiCl (95 mg, 2.241 mmol) in dioxane (2.5 mL), as described for 285 (100 °C, 30 h), gave after solvent removal and chromatography (Hexane/EtOAc, 95:5) 328 (93 mg, 0.397 mmol, 64%) as a yellow oil. 

1H NMR (400 MHz, CDCl₃) δ 7.74 (d, J=8.8 Hz, 1H), 7.70 (d, J=8.8 Hz, 1H), 6.75 (dd, J=18.0, 11.6 Hz, 1H), 5.53 (d, J=11.6 Hz, 1H), 5.44 (d, J=18.0 Hz,
1H), 5.26 (s, with further fine splitting, 1H), 4.90 (s, with further fine splitting, 1H), 2.05 (s, with further fine splitting, 3H) \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 151.0, 150.8, 139.2, 139.0, 132.9, 128.8, 122.8, 122.7, 118.2, 23.2; IR (ATR) 1531, 1349, 804, 726 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{11}\)H\(_{11}\)N\(_2\)O\(_4\) (M+H\(^+\)) 235.0719 (M+Na=257.0538), found

3,6-Dinitro-1-((1-propen-1-yl)-2-(1-propen-2-yl)benzene (329). Treatment of a solution of 311 (303.1 mg, 0.851 mmol) with 283 (366.3 mg, 1.106 mmol) in the presence of PdCl\(_2\)(PPh\(_3\))\(_2\) (11.9 mg, 0.017 mmol), PPh\(_3\) (8.9 mg, 0.034 mmol), BHT (22.5 mg, 0.102 mmol) and LiCl (129.9 mg, 3.064 mmol) in dioxane (3 mL), as described for 285 (100 °C, 30 h), gave after solvent removal and chromatography (Hexane/EtOAc, 97:3) 329 (106 mg, 0.427 mmol, 50%) as a yellow oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.77 (s, 2H), 7.67 (d, J=8.8 Hz, 1H), 7.63 (d, J=8.8 Hz, 1H), 6.41-6.34 (m, 2H), 5.95-5.85 (m, 2H), 5.25-5.24 (m, 1H), 5.18-5.16 (m, 1H), 4.88-4.87 (m, 1H), 4.82 (m, 1H), 2.05-2.04 (m, 6H), 1.83 (dd, J=6.4, 1.6 Hz, 3H), 1.42 (dd, J=6.8, 1.6 Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 151.7, 151.3, 150.9, 150.8, 139.9, 139.7, 139.5, 138.9, 134.8, 132.6, 132.6, 131.6, 122.8, 122.6, 122.5, 122.1, 122.0, 121.9, 117.9, 116.8, 23.0, 22.8, 18.9, 14.6; IR (ATR) 1537, 1435, 1341, 1216, 1332, 793 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{12}\)H\(_{13}\)N\(_2\)O\(_4\) (M+H\(^+\)) 249.0875 (M+Na=271.0695), found

3-Ethynyl-2,6-dinitro-1-(1-propen-2-yl)benzene (330). Treatment of a solution of 313 (415.8 mg, 0.1167 mmol) with 282 (666.2 mg, 2.101 mmol) in the presence of PdCl\(_2\)(PPh\(_3\))\(_2\) (16.4 mg, 0.023 mmol), PPh\(_3\) (12.2 mg, 0.047 mmol), BHT (25.7 mg, 0.117 mmol) and LiCl (178 mg, 4.199 mmol) in dioxane (3.5 mL), as described for 285 (100 °C, 24 h), gave after solvent removal and chromatography (Hexane/DCM, 95:5) 330 (122.7 mg, 0.524 mmol, 45%) as a yellow oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.05 (d, J=8.4 Hz, 1H), 7.41 (d, J=8.4 Hz, 1H), 6.90 (dd, J=17.8, 11.6 Hz, 1H), 5.55 (dd, J=11.6, 0.5 Hz, 1H), 5.44 (dd, J=17.8, 0.5 Hz, 1H), 5.31 (s, 1H), 5.07 (s, 1H), 2.10 (d, J=0.4 Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 149.7, 146.8, 140.9, 138.8, 128.7, 127.3, 127.1, 125.2, 122.2, 118.7, 23.2; IR (ATR) 1546, 1387, 1178, 837 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{11}\)H\(_{11}\)N\(_2\)O\(_4\) (M+H\(^+\)) 235.0719 (M+Na=257.0538), found

1-Ethynyl-2,6-dinitro-3-(1-propen-2-yl)benzene (331). Treatment of a solution of 312 (293.1 mg, 0.856 mmol) with 284 (357.2 mg, 1.079 mmol) in the presence of PdCl\(_2\)(PPh\(_3\))\(_2\) (12 mg, 0.017 mmol), PPh\(_3\) (9 mg, 0.034 mmol), BHT (18.8 mg, 0.086 mmol) and LiCl (130.7 mg, 3.083 mmol) in dioxane (4 mL), as described for 285 (100 °C, 24 h), gave after solvent removal and chromatography (Hexane/DCM, 85:15) 331 (54.8 mg, 0.234 mmol, 27%) as a colorless oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.10 (d, J=8.4 Hz, 1H), 7.46 (d, J=8.4 Hz, 1H), 6.60 (dd, J=17.2, 11.2 Hz, 1H), 6.00 (d, J=17.2 Hz, 1H), 5.68 (d, J=11.2 Hz, 1H), 5.64 (d, J=11.2 Hz, 1H), 4.88-4.87 (m, 1H), 4.82 (m, 1H), 2.05-2.04 (m, 6H), 1.83 (dd, J=6.4, 1.6 Hz, 3H), 1.42 (dd, J=6.8, 1.6 Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 151.0, 150.8, 139.2, 139.0, 132.9, 128.8, 122.8, 122.7, 118.2, 23.2; IR (ATR) 1531, 1349, 804, 726 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{11}\)H\(_{11}\)N\(_2\)O\(_4\) (M+H\(^+\)) 235.0719 (M+Na=257.0538), found
2.11 (dd, J=1.6, 1.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 149.8, 146.7, 136.8, 134.2, 132.0, 128.4, 125.9, 125.8, 123.3, 118.7, 23.3; IR (ATR) 1546, 1397, 1179, 836 cm$^{-1}$; HRMS (ESI) calcd for C$_{11}$H$_{11}$N$_2$O$_4$ (M+H$^+$) 235.0719 (M+Na=257.0538), found

1H,6H-Pyrrolo[2,3-g]indole (336). A solution of 285 (35.2 mg, 0.160 mmol), palladium (II) acetate (Pd(OAc)$_2$, 2.9 mg, 0.013 mmol), and 1,10-phenanthroline (2.4 mg, 0.013 mmol) was prepared in anhydrous N,N-dimethylformamide (DMF, 2 mL) in a threaded ACE glass pressure tube. The tube was fitted with a pressure head, the solution was saturated with carbon monoxide (four cycles of 6 atm of CO). The reaction mixture was stirred at 120 $^\circ$C for 93 h. The solution was concentrated under reduced pressure at 80 $^\circ$C and the resulting crude was purified by chromatography (Hexane/EtOAc, 7:3) to give 336 (17.5 mg, 0.112 mmol, 70%) as a white solid. mp=199-200 $^\circ$C (decomposition); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.43 (s, 2H), 6.88 (br, s, 2H), 6.79 (t, J=2.8 Hz, 2H), 6.64 (dd, J=3.2, 2.0 Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 123.1, 121.9, 121.7, 113.8, 103.2; IR (ATR) 3353, 1516, 1135, 1053, 754 cm$^{-1}$; HRMS (ESI) calcd for C$_{10}$H$_9$N$_2$O (M+H$^+$) 157.0766 (M+Na=179.0585), found

1H,6H-Pyrrolo[3,2-g]indole (336). Reaction of a solution of 285 (14.1 mg, 0.064 mmol), bis(dibenzylideneacetone)palladium (0) (Pd=dba)$_2$, 3.8 mg, 0.007 mmol), and triphenylphosphine (6.8 mg, 0.026 mmol) in DMF (1.2 mL), as described for 336 above (pCO = 6 atm, 120 $^\circ$C, 126 h), gave after solvent removal and chromatography (Hexane/EtOAc, 7:3) 336 (6.4 mg, 0.041 mmol, 64%) as a white solid.

6-Ethenyl-7-nitroindole (337). Reaction of a solution of 285 (27.8 mg, 0.126 mmol), Pd(OAc)$_2$ (2.8 mg, 0.012 mmol), and 1,3-bis(diphenylphosphino)propane (dppp, 5.2 mg, 0.013 mmol) in DMF (1.5 mL), as described for 336 (pCO = 6 atm, 120 $^\circ$C, 94 h), gave after solvent removal and chromatography (Hexane/EtOAc, 7:3) 337 (11.4 mg, 0.061 mmol, 48%) as a yellow solid. mp=90-91 $^\circ$C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.93 (br, s, 1H), 7.87 (d, J=8.0 Hz, 1H), 7.56 (dd, J=17.2, 11.2 Hz, 1H), 7.37 (dd, J=2.8, 0.4 Hz, 1H), 7.33 (d, J=8.4 Hz, 1H), 6.67 (dd, J=3.2, 2.0 Hz, 1H), 5.72 (dd, J=17.2, 1.2 Hz, 1H), 5.49 (dd, J=10.8, 0.8 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 135.2, 135.2, 131.5, 130.9, 130.0, 127.6, 126.6, 120.7, 117.9, 103.9; IR (ATR) 3407, 1330, 1265, 1092 cm$^{-1}$; HRMS (ESI) calcd for C$_{10}$H$_9$N$_2$O$_2$ (M+H$^+$) 189.0664 (M+Na=211.0483), found
2,5-Dimethyl-1H,6H-pyrrolo[2,3-g]indole (338). Reaction of a solution of 286 (45.5 mg, 0.183 mmol), Pd(OAc)$_2$ (4.1 mg, 0.018 mmol), and 1,10-phen (3.3 mg, 0.018 mmol) in DMF (1.5 mL), as described for 336 (pCO = 6 atm, 120 °C, 144 h), gave after solvent removal and chromatography (Hexane/EtOAc, 7:3) 338 (22.6 mg, 0.119 mmol, 67%) as a white solid. mp=209 °C (decomposition); $^1$H NMR (400 MHz, CDCl$_3$) δ 7.24 (s, 2H), 7.11 (br, s, 2H), 6.25 (dd, $J$ = 2.0, 1.2 Hz, 2H), 2.27 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 131.9, 123.9, 121.7, 112.6, 101.5, 13.5; IR (ATR) 3354, 1547, 1432, 1333, 1234 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{13}$N$_2$ (M+H$^+$) 185.1079, found

2-Methyl-7-nitro-(1-propen-1-yl)indole (339). Reaction of a solution of 286 (46.7 mg, 0.188 mmol), Pd(OAc)$_2$ (4.2 mg, 0.019 mmol), and dppp (7.8 mg, 0.019 mmol) in DMF (2 mL), as described for 336 (pCO = 6 atm, 120 °C, 57 h), gave, in order of elution, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 339 (28.1 mg, 0.130 mmol, 69%) as a yellow solid and 338 (3.1 mg, 0.017 mmol, 9%) as a white solid. mp=116-117 °C; $^1$H NMR (600 MHz, CDCl$_3$) δ 9.72 (br, s, 1H), 9.63 (br, s, 1H), 7.70 (d, $J$ = 8.4 Hz, 1H), 7.66 (d, $J$ = 7.8 Hz, 1H), 7.23 (d, $J$ = 18.6 Hz, 1H), 7.20 (d, $J$ = 8.4 Hz, 1H), 7.02 (d, $J$ = 7.8 Hz, 1H), 6.96 (d, $J$ = 11.4 Hz, 1H), 6.33 (dd, $J$ = 1.2 Hz, 1H), 6.30 (d, $J$ = 1.2 Hz, 1H), 6.18 (dq, $J$ = 15.6, 6.6 Hz, 1H), 5.91 (dq, $J$ = 14.4, 7.2 Hz, 1H), 2.52 (s, 3H), 2.50 (s, 3H), 1.98 (dd, $J$ = 6.6, 1.2 Hz, 3H), 1.75 (dd, $J$ = 7.2, 1.8 Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 137.7, 137.4, 131.4, 131.3, 131.3, 130.5, 130.4, 130.3, 129.8, 129.1, 128.9, 128.8, 126.5, 126.2, 125.7, 123.2, 120.5, 101.5, 101.4, 18.9, 14.5, 13.7; IR (ATR) 3399, 1507, 1333, 1217, 764 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{13}$N$_2$O$_2$ (M+H$^+$) 217.0977, found

2,5-Dimethyl-1H,6H-pyrrolo[3,2-g]indole (338). Reaction of a solution of 286 (42.7 mg, 0.172 mmol), Pd(OAc)$_2$ (9.9 mg, 0.017 mmol), and dppp (7.1 mg, 0.017 mmol) in DMF (1.5 mL), as described for 336 (pCO = 6 atm, 120 °C, 48 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 85:15) 338 (11.4 mg, 0.062 mmol, 36%) as a white solid.

3,6-Dimethyl-1H,6H-pyrrolo[2,3-g]indole (340). Reaction of a solution of 287 (29.2 mg, 0.118 mmol), Pd(OAc)$_2$ (2.6 mg, 0.012 mmol), and 1,10-phen (2.6 mg, 0.014 mmol) in DMF (1.5 mL), as described for 336 (pCO = 6 atm, 120 °C, 98 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 340 (11.7 mg, 0.061 mmol, 54%) as a white solid. mp=245 °C (decomposition); $^1$H NMR (400 MHz, Acetone-d$_6$) δ 9.73 (br, s, 2H), 7.19 (s, 2H), 6.92 (m, 2H), 2.32 (d, $J$ = 1.2 Hz, 6H); $^{13}$C NMR (100 MHz, Acetone-d$_6$) δ 124.9, 124.3, 119.5, 112.4, 111.4, 10.3; IR (ATR) 3367, 1548, 1433, 1323, 1232 cm$^{-1}$; HRMS (ESI) calcd for C$_{13}$H$_{13}$N$_2$ (M+H$^+$) 185.1079, found
3,6-Dimethyl-1\textit{H},6\textit{H}-\textit{pyrrolo}[3,2-\textit{g}]\textit{indole} (340). Reaction of a solution of 287 (39.6 mg, 0.160 mmol), Pd(dba)$_2$ (9.2 mg, 0.016 mmol), dppp (6.6 mg, 0.016 mmol), and 1,10-phen (5.7 mg, 0.032 mmol) in DMF (1.5 mL), as described for 336 (pCO = 6 atm, 120 °C, 110 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 340 (19.6 mg, 0.106 mmol, 67%) as a white solid.

3,6-Dimethyl-1\textit{H},6\textit{H}-\textit{pyrrolo}[3,2-\textit{g}]\textit{indole} (340). Reaction of a solution of 287 (34.6 mg, 0.139 mmol), Pd(dba)$_2$ (8 mg, 0.014 mmol), and PPh$_3$ (14.7 mg, 0.056 mmol) in DMF (1.5 mL), as described for 336 (pCO = 6 atm, 120 °C, 60 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 340 (15.8 mg, 0.086 mmol, 62%) as a white solid.

3-Methyl-7-nitro-(1-propen-2-yl)\textit{indole} (341). Reaction of a solution of 287 (21.3 mg, 0.086 mmol), Pd(OAc)$_2$ (1.3 mg, 0.006 mmol), and dppp (2.5 mg, 0.006 mmol) in DMF (1 mL), as described for 336 (pCO = 6 atm, 120 °C, 72 h), gave, in order of elution, after solvent removal and chromatography (Hexane/EtOAc, 9:1) 341 (14.5 mg, 0.067 mmol, 78%) as a yellow oil) and 340 (2.6 mg, 0.014 mmol, 16%) as a white solid. Analytical data for 341: mp=179 °C (decomposition); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.62 (br, s, 1H), 7.78 (d, J=7.6 Hz, 1H), 7.12 (s, with further fine splitting, 1H), 7.01 (d, J=7.6 Hz, 1H), 5.19 (s, with further fine splitting, 1H), 4.93 (s, with further fine splitting, 1H), 2.35 (s, with further fine splitting, 3H), 2.13 (s, with further fine splitting, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 145.4, 136.7, 131.1, 130.3, 125.5, 123.8, 121.7, 113.7, 112.9, 23.7, 9.4; IR (ATR) 3330, 1493, 1301, 1268, 1096, 894 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{13}$N$_2$O$_2$ (M+H$^+$) 217.0977, found

3,6-Dimethyl-1\textit{H},6\textit{H}-\textit{pyrrolo}[3,2-\textit{g}]\textit{indole} (342). Reaction of a solution of 317 (56 mg, 0.239 mmol), Pd(OAc)$_2$ (4.3 mg, 0.019 mmol), and 1,10-phen (3.5 mg, 0.019 mmol) in DMF (3 mL), as described for 336 (pCO = 6 atm, 120 °C, 100 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 342 (25.7 mg, 0.151 mmol, 63%) as a white solid. mp=179 °C (decomposition); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.38 (d, J=8.4 Hz, 1H), 7.32 (d, J=8.4 Hz, 1H), 6.67 (br, s, 1H), 6.65-6.63 (m, 1H), 6.59-6.58 (m, 1H), 6.55 (br, s, 1H), 6.32-6.31 (m, 1H), 2.33 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 145.4, 136.7, 131.1, 130.3, 122.6, 121.7, 121.6, 121.5, 113.3, 113.1, 102.9, 101.3, 13.5; IR (ATR) 3356, 1532, 1473, 1302, 1272 cm$^{-1}$; HRMS (ESI) calcd for

3,6-Dimethyl-1\textit{H},6\textit{H}-\textit{pyrrolo}[3,2-\textit{g}]\textit{indole} (342). Reaction of a solution of 317 (31 mg, 0.132 mmol), Pd(OAc)$_2$ (1.5 mg, 0.007 mmol), and PPh$_3$ (6.9 mg, 0.026 mmol) in DMF (1.5 mL), as described for 336 (pCO = 6 atm, 120 °C, 31 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3), 342 (5.7 mg, 0.033 mmol, 25%) as a white solid.
3,6-Dimethyl-1H,6H-pyrrolo[3,2-g]indole (343). Reaction of a solution of 318 (52.3 mg, 0.223 mmol), Pd(OAc)$_2$ (3 mg, 0.013 mmol), and 1,10-phen (2.4 mg, 0.013 mmol) in DMF (3 mL), as described for 336 (pCO = 6 atm, 120 °C, 98 h), gave, after solvent removal and chromatography (Hexane/DCM, 3:7) 343 (24.5 mg, 0.144 mmol, 65%) as a white solid. mp=181 °C (decomposition); $^1$H NMR (400 MHz, CDCl$_3$) δ 7.43 (d, $J=8.4$ Hz, 1H), 7.35 (d, $J=8.4$ Hz, 1H), 6.74-6.73 (m, 1H), 6.63 (m, 2H), 6.55 (s, 1H), 6.45 (br, s, 1H), 2.42 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 123.4, 123.1, 121.9, 121.9, 121.7, 119.4, 113.1, 112.3, 112.0, 103.0, 10.0; IR (ATR) 3380, 1548, 1403, 1375, 1205 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{13}$_N$_2$O (M+H$^+$) 185.1979, found 3,6-Dimethyl-1H,6H-pyrrolo[3,2-g]indole (344). Reaction of a solution of 319 (41.3 mg, 0.166 mmol), Pd(OAc)$_2$ (2.7 mg, 0.012 mmol), and 1,10-phen (2.1 mg, 0.012 mmol) in DMF (2 mL), as described for 336 (pCO = 6 atm, 120 °C, 100 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 8:2) 344 (20.6 mg, 0.112 mmol, 67%) as a white solid. mp=210 °C (decomposition); $^1$H NMR (400 MHz, CDCl$_3$/DMSO-d$_6$) δ 10.36 (br, s, 1H), 9.92 (br, s, 1H), 7.01 (s, 2H), 6.87-6.86 (m, 1H), 6.10-6.09 (m, 1H), 2.41 (d, $J=0.8$ Hz, 3H), 2.25 (d, $J=0.8$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$/DMSO-d$_6$) δ 130.5, 123.4, 122.5, 122.5, 122.2, 118.3, 111.2, 110.5, 110.2, 100.3, 13.3, 9.9; IR (ATR) 3396, 1601, 1406, 1343, 1263 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{13}$N$_2$ (M+H$^+$) 185.1979, found 3,6-Dimethyl-1H,6H-pyrrolo[3,2-g]indole (345). Reaction of a solution of 320 (79.8 mg, 0.273 mmol), Pd(OAc)$_2$ (3.7 mg, 0.016 mmol), and 1,10-phen (3 mg, 0.017 mmol) in DMF (3 mL), as described for 336 (pCO = 6 atm, 120 °C, 109 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 6:4) 345 (42.1 mg, 0.184 mmol, 68%) as a white solid. mp=199 °C (decomposition); $^1$H NMR (400 MHz, DMSO-d$_6$) δ 11.45 (br, s, 1H), 10.68 (br, s, 1H), 7.94 (d, $J=2.8$ Hz, 1H), 7.68 (d, $J=8.4$ Hz, 1H), 7.35 (d, J=8.8 Hz, 1H), 7.27 (t, J=2.8 Hz, 1H), 6.51 (dd, J=2.8, 2.0 Hz, 1H), 4.29 (quartet, J=7.2 Hz, 2H), 1.34 (t, J=7.2 Hz, 3H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 164.8, 128.7, 123.6, 123.0, 122.3, 122.3, 120.6, 114.8, 112.5, 108.0, 102.5, 58.8, 14.5; IR (ATR) 3325, 1642, 1433, 1175 cm$^{-1}$; HRMS (ESI) calcd for C$_{13}$H$_{13}$N$_2$O$_2$ (M+H$^+$) 229.0977, found 3,6-Dimethyl-1H,6H-pyrrolo[3,2-g]indole (346). Reaction of a solution of 321 (59.2 mg, 0.193 mmol), Pd(OAc)$_2$ (3.1 mg, 0.014 mmol), and 1,10-phen (2.5 mg, 0.014 mmol) in DMF (3 mL), as described for 336 (pCO = 6 atm, 120 °C, 108 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 1:1) 346 (34.2 mg, 0.141 mmol, 73%) as a white solid. mp=235 °C (decomposition); $^1$H NMR (400 MHz, DMSO-d$_6$) δ 11.16 (br, s, 1H), 10.56 (br, s, 1H), 7.89 (d, J=3.2 Hz, 1H), 7.61 (d, J=8.4 Hz, 1H), 7.22 (d, J=8.4 Hz, 1H), 6.19 (s, with further fine splitting, 1H), 4.28 (quartet, J=7.2 Hz, 2H), 2.44 (s, 3H), 1.34 (t,
J=7.2 Hz, 3H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 164.8, 131.9, 128.7, 124.3, 122.6, 122.0, 120.2, 114.1, 112.1, 107.9, 100.6, 58.8, 14.5, 13.4; IR (ATR) 3343, 1651, 1403, 1313, 1170, 803 cm$^{-1}$; HRMS (ESI) calcd for C$_{14}$H$_{15}$N$_2$O$_2$ (M+H$^+$) 243.1134, found

3,6-Dimethyl-1H,6H-pyrrolo[3,2-g]indole (347). A solution of 322 (85.3 mg, 0.279 mmol), Pd(OAc)$_2$ (3.2 mg, 0.014 mmol), and 1,10-phen (2.5 mg, 0.014 mmol) in DMF (3 mL) was stirred under CO (pCO = 6 atm) at 120 °C for 110 h. After cooling to ambient temperature, pressure was released and the reaction mixture was diluted with EtOAc (30 mL). The organic layer was washed with brine (6x10 mL), dried (MgSO$_4$) and was filtered. The filtrate was concentrated and the resulting crude was purified by chromatography (Hexane/EtOAc, 1:1) to give 347 (50.2 mg, 0.207 mmol, 74%) as a white solid. mp=233 °C (decomposition); $^1$H NMR (400 MHz, DMSO-d$_6$) δ 11.43 (br, s, 1H), 10.33 (br, s, 1H), 7.93 (d, $J$=2.8 Hz, 1H), 7.68 (d, $J$=8.4 Hz, 1H), 7.29 (d, $J$=8.4 Hz, 1H), 7.04 (s, with further fine splitting, 1H), 4.28 (quartet, $J$=7.2 Hz, 2H), 2.29 (s, 3H), 1.34 (t, $J$=7.2 Hz, 3H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 164.8, 128.7, 123.8, 123.0, 122.5, 120.8, 119.8, 113.0, 111.8, 110.7, 107.9, 58.8, 14.5, 9.9; IR (ATR) 3350, 1644, 1428, 1184, 1133 cm$^{-1}$; HRMS (ESI) calcd for C$_{14}$H$_{15}$N$_2$O$_2$ (M+H$^+$) 243.1134, found

2-Methyl-6-nitro-5-(1-propen-1-yl)indole (348). Reaction of a solution of 290 (35.9 mg, 0.145 mmol), Pd(OAc)$_2$ (2.3 mg, 0.010 mmol), and 1,10-phen (1.8 mg, 0.010 mmol) in DMF (1.5 mL), as described for 336 (pCO = 6 atm, 120 °C, 46 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 85:15) 348 (11.6 mg, 0.054 mmol, 37%) as a yellow solid. mp=118-119 °C; $^1$H NMR (400 MHz, CDC$_3$) δ 8.29 (s, 1H), 8.22 (s, 1H), 8.15 (s, 1H), 8.03 (s, 1H), 7.56 (s, 1H), 7.37 (s, 1H), 7.03 – 6.94 (m, 1H), 6.87 – 6.81 (m, 1H), 6.30-6.27 (m, 2H), 6.09 (dq, $J$ = 15.6, 6.8 Hz, 1H), 5.86 (dq, $J$ = 11.6, 7.2 Hz, 1H), 2.51 (d, $J$ = 0.8 Hz, 3H), 2.49 (d, $J$ = 0.8 Hz, 3H), 1.93 (dd, $J$ = 6.8, 2.0 Hz, 3H), 1.74 (dd, $J$ = 7.2, 2.0 Hz, 3H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 143.4, 143.3, 141.3, 141.0, 133.6, 133.5, 132.9, 132.4, 128.3, 126.6, 125.1, 124.8, 122.9, 120.8, 117.9, 108.1, 107.7, 100.5, 100.4, 18.5, 14.1, 13.7, 13.6; IR (ATR) 3353, 1490, 1437, 1297 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{13}$N$_2$O$_2$ (M+H$^+$) 217.0977, found

3,6-Dimethyl-1H,6H-pyrrolo[3,2-g]indole (348). Reaction of a solution of 290 (35.6 mg, 0.143 mmol), Pd(dba)$_2$ (6.6 mg, 0.010 mmol), and PPh$_3$ (12 mg, 0.046 mmol) in DMF (1.5 mL), as described for 336 (pCO = 6 atm, 120 °C, 92 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 348 (19.9 mg, 0.092 mmol, 64%) as a yellow solid.
3,6-Dimethyl-1H,6H-pyrrolo[3,2-g]indole (349). Reaction of a solution of 291 (45.6 mg, 0.184 mmol), Pd(dba)$_2$ (5.3 mg, 0.009 mmol), dppp (3.8 mg, 0.009 mmol), and 1,10-phen (3.3 mg, 0.018 mmol) in DMF (2 mL), as described for 347 (pCO = 6 atm, 120 °C, 82 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 349 (18.1 mg, 0.098 mmol, 53%) as a white solid. mp=200 °C (decomposition); $^1$H NMR (400 MHz, CDCl$_3$) δ 7.65 (s, 1H), 7.57 (br, s, 2H), 7.19 (s, 1H), 6.93 (s, 2H), 2.41 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 135.2, 124.7, 121.1, 111.0, 106.7, 90.9, 10.0; IR (ATR) 3329, 1474, 1301, 1092 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{13}$N$_2$ (M+H$^+$) 185.1079, found

3-Methyl-6-nitro-5-(1-propen-2-yl)indole (350). Reaction of a solution of 291 (56.5 mg, 0.228 mmol), Pd(OAc)$_2$ (3.1 mg, 0.014 mmol), and 1,10-phen (2.5 mg, 0.014 mmol) in DMF (2 mL), as described for 336 (pCO = 6 atm, 120 °C, 50 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 350 (9.7 mg, 0.045 mmol, 20%) as a yellow solid. mp=117-118 °C; $^1$H NMR (600 MHz, CDCl$_3$) δ 8.29 (br, s, 1H), 8.08 (s, 1H), $^{13}$C NMR (150 MHz, CDCl$_3$) δ 145.2, 143.2, 133.7, 131.6, 131.2, 127.4, 120.0, 114.0, 112.7, 108.5, 24.1, 9.5; IR (ATR) 3335, 1206, 1100, 896 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{13}$N$_2$O$_2$ (M+H$^+$) 217.0977, found

3,6-Dimethyl-1H,6H-pyrrolo[3,2-g]indole (351). Reaction of a solution of 292 (29.3 mg, 0.133 mmol), Pd(OAc)$_2$ (2.1 mg, 0.009 mmol), and 1,10-phen (1.7 mg, 0.009 mmol) in DMF (1 mL), as described for 336 (pCO = 6 atm, 120 °C, 48 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 351 (12.5 mg, 0.080 mmol, 60%) as a white solid. mp=239 °C (decomposition); $^1$H NMR (600 MHz, CDCl$_3$) δ 7.91 (br, s, 2H), 7.58 (s, 2H), $^{13}$C NMR (100 MHz, CDCl$_3$) δ 133.2, 126.0, 125.0, 101.4, 100.0; IR (ATR) 3336, 1156, 1053, 756 cm$^{-1}$; HRMS (ESI) calcd for C$_{10}$H$_9$N$_2$ (M+H$^+$) 157.0766, found

3,6-Dimethyl-1H,6H-pyrrolo[3,2-g]indole (XX). Reaction of a solution of 292 (29.3 mg, 0.133 mmol), Pd(dba)$_2$ (4.6 mg, 0.008 mmol), and PPh$_3$ (8.5 mg, 0.032 mmol) in DMF (1 mL), as described for 336 (pCO = 6 atm, 120 °C, 64 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) XX (14 mg, 0.074 mmol, 56%) as a yellow solid. $^1$H NMR (400 MHz, CDCl$_3$) δ 7$^{13}$C NMR (100 MHz, CDCl$_3$) δ 71; IR (ATR) cm$^{-1}$; HRMS (ESI) calcd for 196
2-Methyl-5-nitro-6-(1-propen-1-yl)indole (352). Reaction of a solution of 293 (39 mg, 0.157 mmol), Pd(OAc)$_2$ (2.5 mg, 0.011 mmol), and 1,10-phen (2 mg, 0.011 mmol) in DMF (2 mL), as described for 336 (pCO = 6 atm, 120 °C, 49 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 352 (10.5 mg, 0.049 mmol, 31%) as a yellow solid. mp=111-112 °C; $^1$H NMR (600 MHz, CDCl$_3$) δ 8.31 (s, 1H), 8.18 (s, 1H), 8.18 (br, s, 1H), 8.15 (br, s, 1H), 7.32 (s, 1H), 7.15 (s, 1H), 6.97 (d, $J$=15.6 Hz, 1H), 6.84 (d, $J$=11.4 Hz, 1H), 6.07 (dq, $J$=15.6, 6.0 Hz, 1H), 5.85 (dq, $J$=11.4, 6.6 Hz, 1H), 2.48 (s, 3H), 2.47 (s, 3H), 1.93 (d, $J$=6.6 Hz, 3H), 1.72 (d, $J$=6.6 Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 142.3, 142.0, 138.8, 138.7, 138.5, 138.0, 128.5, 128.2, 127.8, 127.8, 127.4, 127.4, 126.1, 126.1, 117.6, 117.2, 112.4, 109.2, 102.1, 102.0, 18.6, 14.3, 13.8; IR (ATR) 3321, 1462, 1285, 823 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{13}$N$_2$O$_2$ (M+H$^+$) 217.0977, found

3,6-Dimethyl-1H,6H-pyrrolo[3,2-g]indole (352). Reaction of a solution of 293 (45.6 mg, 0.184 mmol), Pd(dba)$_2$ (6.4 mg, 0.011 mmol), and PPh$_3$ (11.6 mg, 0.044 mmol) in DMF (1.5 mL), as described for 336 (pCO = 6 atm, 120 °C, 72 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 352 (39.7 mg, 0.184 mmol, 100%) as a yellow solid.

3-Methyl-5-nitro-6-(1-propen-2-yl)indole (353). Reaction of a solution of 294 (45.2 mg, 0.182 mmol), Pd(dba)$_2$ (6.3 mg, 0.011 mmol), and PPh$_3$ (11.5 mg, 0.044 mmol) in DMF (2 mL), as described for 347 (pCO = 6 atm, 120 °C, 72 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 9:1) 353 (28.7 mg, 0.133 mmol, 73%) as a yellow solid. mp=114-115 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 8.34 (br, s, 1H), 8.30 (s, 1H), 7.20 (s, 1H), 7.10 (s, 1H), 5.14 (s, 1H), 4.95 (s, 1H), 2.34 (s, 3H), 2.11 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 145.1, 141.5, 138.1, 133.9, 126.8, 124.7, 117.0, 114.0, 113.8, 112.2, 9.5; IR (ATR) 3337, 1208, 1113, 836 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{13}$N$_2$O$_2$ (M+H$^+$) 185.1079, found

3,6-Dimethyl-1H,6H-pyrrolo[3,2-g]indole (YY). Reaction of a solution of 294 (24.9 mg, 0.100 mmol), Pd(dba)$_2$ (3.5 mg, 0.006 mmol), and PPh$_3$ (6.3 mg, 0.024 mmol) in DMF (1.5 mL), as described for 336 (pCO = 6 atm, 120 °C, 68 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) YY (4.8 mg, 0.026 mmol, 26%) as a white solid. mp=214 °C (decomposition); $^1$H NMR (400 MHz, CDCl$_3$/DMSO-d$_6$) δ 9.88 (br, s, 2H), 7.25 (s, 2H), 6.91 (s, 2H), 2.25 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$/DMSO-d$_6$) δ 132.9, 125.9, 122.2, 107.6, 97.4, 9.8; IR (ATR) 3315, 1476, 1300, 1175 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{13}$N$_2$O (M+H$^+$) 185.1079, found

4-Ethenyl-5-nitroindole(354). A solution of 295 (81.4 mg, 0.370 mmol), Pd(OAc)$_2$ (4.2 mg, 0.018 mmol), and 1,10-phen (3.4 mg, 0.019 mmol) in DMF (3 mL) was stirred under CO (pCO = 6 atm) at 120
°C for 120 h. After cooling to ambient temperature, pressure was released and the reaction mixture was concentrated under reduced pressure via bulb-to-bulb distillation. The resulting crude was purified by chromatography (Hexane/EtOAc, 7:3) to give 354 (30.1 mg, 0.160 mmol, 43%) as a yellow solid. mp=143-144 °C; 1H NMR (400 MHz, CDCl3/DMSO-d6) δ 11.35 (br, s, 1H), 7.77 (d, J=9.2 Hz, 1H), 7.33 (d, J=5.6, 2.8 Hz, 1H), 7.20 (dd, J=17.6, 11.2 Hz, 1H), 6.72-6.71 (m, 1H), 5.66 (dd, J=17.6, 1.6 Hz, 1H), 5.60 (dd, J=11.6, 1.6 Hz, 1H); 13C NMR (100 MHz, CDCl3/DMSO-d6) δ 139.4, 137.9, 132.4, 127.8, 127.5, 126.0, 119.3, 117.5, 110.4, 103.4; IR (ATR) 3323, 1311, 929, 739 cm⁻¹; HRMS (ESI) calcd for C10H9N2O4 (M+H⁺) 189.0664, found (354). Reaction of a solution of 295 (71.1 mg, 0.323 mmol), Pd(dba)2 (9.5 mg, 0.016 mmol), and PPh3 (16.9 mg, 0.065 mmol) in DMF (2.5 mL), as described for 354 (pCO = 6 atm, 120 °C, 110 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 354 (41.1 mg, 0.218 mmol, 68%) as a yellow solid.

2-Methyl-5-nitro-4-(1-propen-1-yl)indole(355). Reaction of a solution of 296 (70.4 mg, 0.284 mmol), Pd(OAc)2 (3.3 mg, 0.015 mmol), and 1,10-phen (2.7 mg, 0.015 mmol) in DMF (3 mL), as described for 336 (pCO = 6 atm, 120 °C, 70 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 355 (45.3 mg, 0.209 mmol, 74%) as a yellow solid. mp=101-103 °C; 1H NMR (600 MHz, CDCl3) δ 8.34 (br, s, 2H), 7.93 (d, J=9.0 Hz, 1H), 7.82 (d, J=9.0 Hz, 1H), 7.22 (d, J=9.0 Hz, 1H), 6.50-6.49 (m, 1H), 6.24-6.18 (m, 2H), 5.97 (d, J=13.8, 1.8 Hz, 1H), 2.47 (m, 6H), 2.01 (dd, J=7.2, 1.8 Hz, 3H), 1.50 (dd, J=6.6, 1.8 Hz, 3H); 13C NMR (150 MHz, CDCl3) δ 141.1, 140.6, 138.1, 137.9, 137.7, 137.7, 132.0, 128.5, 128.0, 127.9, 127.8, 126.8, 126.4, 125.4, 118.3, 118.3, 108.9, 108.7, 103.1, 102.9, 19.0, 15.1, 13.8, 13.7; IR (ATR) 3351, 1508, 1316, 1172 cm⁻¹; HRMS (ESI) calcd for C12H13N2O2 (M+H⁺) 217.0977, found (355). Reaction of a solution of 296 (34.5 mg, 0.139 mmol), Pd(dba)2 (4 mg, 0.007 mmol), and PPh3 (7.3 mg, 0.028 mmol) in DMF (2 mL), as described for 336 (pCO = 6 atm, 120 °C, 72 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 8:2) 355 (20.9 mg, 0.097 mmol, 70%) as a yellow solid.

3-Methyl-5-nitro-4-(1-propen-2-yl)indole(356). Reaction of a solution of 297 (80.3 mg, 0.323 mmol), Pd(OAc)2 (3.7 mg, 0.016 mmol), and 1,10-phen (3.0 mg, 0.017 mmol) in DMF (3 mL), as described for 354 (pCO = 6 atm, 120 °C, 100 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 356 (60.3 mg, 0.279 mmol, 86%) as a yellow solid. mp=98-99 °C; 1H NMR (400 MHz, CDCl3) δ 8.43 (br, s, 1H), 7.84 (d, J=8.8 Hz, 1H), 7.28 (d, J=8.8 Hz, 1H), 7.09-7.08 (m, 1H), 5.32-5.30 (m, 1H), 4.91-
4.90 (m, 1H), 2.38 (d, J=0.8 Hz, 3H), 2.30-2.29 (m, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 141.3, 140.9, 138.6, 134.3, 125.2, 124.8, 118.7, 115.1, 114.8, 110.0, 25.3, 11.6; IR (ATR) 3369, 1406, 799 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{12}\)H\(_{13}\)N\(_2\)O\(_2\) (M+H\(^+\)) 217.0977, found 356.

Reaction of a solution of 297 (57.7 mg, 0.232 mmol), Pd(dba)\(_2\) (6.7 mg, 0.012 mmol), dppp (4.8 mg, 0.012 mmol), and 1,10-phen (4.2 mg, 0.023 mmol) in DMF (2.5 mL), as described for 354 (pCO = 6 atm, 120 °C, 91 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 356 (25.7 mg, 0.119 mmol, 51%) as a yellow solid.

5-Nitro-4-(1-propen-1-yl)indole (357) and 4-ethenyl-2-methyl-5-nitroindole (358). Reaction of a solution of 327 (75.2 mg, 0.321 mmol), Pd(dba)\(_2\) (11.1 mg, 0.019 mmol), dppp (7.9 mg, 0.019 mmol), and 1,10-phen (6.9 mg, 0.038 mmol) in DMF (3 mL), as described for 336 (pCO = 6 atm, 120 °C, 74 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 85:15) an inseparable mixture of 357 and 358 (28.9 mg, 0.143 mmol, 45%, 357/358, 1:1) as a yellow oil.

5-Nitro-4-(1-propen-2-yl)indole (359) and 4-ethenyl-3-methyl-5-nitroindole (360). Reaction of a solution of 328 (83.9 mg, 0.358 mmol), Pd(OAc)\(_2\) (4.8 mg, 0.021 mmol), and 1,10-phen (3.9 mg, 0.022 mmol) in DMF (3 mL), as described for 336 (pCO = 6 atm, 120 °C, 96 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 8:2) an inseparable mixture of 359 and 360 (51 mg, 0.252 mmol, 70%, 359/360, 1:1) as a yellow oil.

5-Nitro-3-methyl-4-(1-propen-1-yl)indole (361) and 5-nitro-2-methyl-4-(1-propen-2-yl)indole (362). Reaction of a solution of 329 (81.5 mg, 0.328 mmol), Pd(OAc)\(_2\) (5.2 mg, 0.023 mmol), and 1,10-phen (4.2 mg, 0.023 mmol) in DMF (3 mL), as described for 336 (pCO = 6 atm, 120 °C, 122 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 8:2) an inseparable mixture of 361 and 362 (54.6 mg, 0.253 mmol, 77%, 361/362, 1:1) as a yellow oil.

3,6-Dimethyl-1\(H\),6\(H\)-pyrrolo[3,2-g]indole (363) and (364). Reaction of a solution of 298 (78.5 mg, 0.357 mmol), Pd(OAc)\(_2\) (4.8 mg, 0.021 mmol), and 1,10-phen (3.9 mg, 0.022 mmol) in DMF (3 mL), as described for 336 (pCO = 6 atm, 120 °C, 101 h), gave, in order of elution, after solvent removal and chromatography (Hexane/DCM, 1:1) 364 (13.7 mg, 0.073 mmol, 20%) as a yellow solid and 363 (28 mg, 0.179 mmol, 50%) as a white solid. Analytical data for 363: mp=138-139 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)/DMSO-d\(_6\)) \(\delta\) 11.06 (br, s, 1H), 10.89 (br, s, 1H), 7.22 (d, \(J\) = 8.8 Hz, 1H), 7.13 (t, \(J\) = 2.8 Hz, 1H), 7.07 (d, \(J\) = 8.8 Hz, 1H), 7.05 (t, \(J\)=2.8 Hz, 1H), 6.62 (t, \(J\) = 2.4 Hz, 1H), 6.40 (dd, \(J\) = 2.8, 2.0 Hz, 1H).
$^{13}$C NMR (100 MHz, CDCl$_3$/DMSO-d$_6$) δ 132.4, 128.6, 121.6, 120.0, 119.6, 114.2, 113.4, 104.9, 101.9, 97.9; IR (ATR) 3426, 3363, 1389, 718 cm$^{-1}$; C$_{10}$H$_9$N$_2$ (M+H$^+$) 157.0766, found cm$^{-1}$; HRMS (ESI) calcd for Analytical data for 364: mp=97-98 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 8.58 (br, s, 1H), 7.59 (d, $J$=8.4 Hz, 1H), 7.43 (d, $J$=8.4 Hz, 1H), 7.38 (t, $J$=2.4 Hz, 1H), 7.25 (dd, $J$=17.2, 10.8 Hz, 1H), 6.92 (s, with further fine splitting, 1H), 5.73 (d, $J$=17.2 Hz, 1H), 5.43 (d, $J$=10.8 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 140.0, 136.8, 133.3, 127.7, 126.5, 122.2, 121.4, 117.0, 116.0, 102.6; IR (ATR) 3461, 1520, 1264, 731 cm$^{-1}$; HRMS (ESI) calcd for C$_{10}$H$_9$N$_2$O$_2$ (M+H$^+$) 189.0664, found

7-Ethenyl-6-nitroindole (364). Reaction of a solution of 298 (45.6 mg, 0.207 mmol), Pd(db)$_2$ (7.1 mg, 0.012 mmol), and PPh$_3$ (13 mg, 0.050 mmol) in DMF (2 mL), as described for 354 (pCO = 6 atm, 120 °C, 126 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 364 (19.2 mg, 0.102 mmol, 49%) as a yellow solid.

5-Ethenyl-3-methyl-4-nitroindole (365). Reaction of a solution of 331 (49.1 mg, 0.210 mmol), Pd(OAc)$_2$ (2.4 mg, 0.011 mmol), and 1,10-phen (1.9 mg, 0.011 mmol) in DMF (2.5 mL), as described for 354 (pCO = 6 atm, 120 °C, 71 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 365 (31 mg, 0.153 mmol, 73%) as a yellow sticky oil. mp=64-65 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 8.23 (br, s, 1H), 7.41 (s, 2H), 7.04 (m, 1H), 6.81 (dd, $J$=17.2, 10.8 Hz, 1H), 5.77 (dd, $J$=17.2, 0.8 Hz, 1H), 5.38 (dd, $J$=10.8, 0.8 Hz, 1H), 2.18 (d, $J$=0.8 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 142.1, 137.6, 130.4, 125.1, 121.5, 119.4, 118.6, 116.8, 113.7, 110.4, 9.8; IR (ATR) 3392, 1504, 1331, 807 cm$^{-1}$; HRMS (ESI) calcd for C$_{11}$H$_{11}$N$_2$O$_2$ (M+H$^+$) 203.0821, found

4-Nitro-5-(1-propen-2-yl)indole (366). Reaction of a solution of 330 (57.8 mg, 0.247 mmol), Pd(OAc)$_2$ (4.4 mg, 0.020 mmol), and 1,10-phen (3.6 mg, 0.020 mmol) in DMF (2 mL), as described for 354 (pCO = 6 atm, 120 °C, 108 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 366 (30.3 mg, 0.150 mmol, 61%) as a yellow solid. mp=100-101 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 8.69 (s, 1H), 7.56 (d, $J$ = 8.4 Hz, 1H), 7.39 (s, 1H), 7.10 (d, $J$ = 8.4 Hz, 1H), 6.89 (s, 1H), 5.17 (s, 1H), 4.95 (s, 1H), 2.15 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 143.8, 139.7, 136.4, 132.2, 127.9, 123.3, 122.0, 115.5, 114.7, 101.9, 23.8; IR (ATR) 3387, 1488, 1333, 814 cm$^{-1}$; HRMS (ESI) calcd for C$_{11}$H$_{11}$N$_2$O$_2$ (M+H$^+$) 203.0821, found

4-Nitro-5-(1-propen-2-yl)indole (366) and pyrroloindole (367). Reaction of a solution of 330 (62.8 mg, 0.268 mmol), Pd(db)$_2$ (9.3 mg, 0.016 mmol), dppp (6.6 mg, 0.016 mmol) and 1,10-phen (5.8 mg, 0.032 mmol) in DMF (2 mL), as described for 354 (pCO = 6 atm, 120 °C, 72 h), gave, after solvent removal and
chromatography (Hexane/EtOAc, 8:2) an inseparable mixture of 366 and 367 (27.5 mg, 367 nearly 8% of the mixture) as a yellow oil.

1-Acetoxy-2-methyl-5-nitro-6-(1-propen-1-yl)indole (368). A solution of 352 (35.6 mg, 0.165 mmol), acetic anhydride ((CH₃CO)₂O, (0.6 mL, 6.347 mmol), 4-dimethylaminopyridine (77 mg, 0.630 mmol), and Et₃N (0.7 mL, 5.019 mmol) in 1,2-dichloroethane (DCE, 2 mL) was stirred at 75 °C under a nitrogen atmosphere for 18 h. After cooling to ambient temperature, the mixture was diluted with water and was extracted in EtOAc (2x10 mL). The organic layer was dried (MgSO₄), filtered and was concentrated under reduced pressure. The resulting crude was purified by chromatography (Hexane/EtOAc, 8:2) to give 368 (42.4 mg, 0.164 mmol, 100%) as a yellow oil. ¹H NMR (600 MHz, CDCl₃) δ 8.29 (s, 1H), 8.16 (s, 1H), 8.08 (s, 1H), 8.03 (s, 1H), 6.94 (dd, J = 15.5, 1.7 Hz, 1H), 6.82 (dd, J = 11.5, 1.5 Hz, 1H), 6.47 (d, J = 0.8 Hz, 1H), 6.43 (d, J = 0.8 Hz, 1H), 6.21 (dq, J = 15.3, 6.6 Hz, 1H), 5.93 (dq, J = 11.4, 7.1 Hz, 1H), 2.74 (d, J = 3.5 Hz, 6H), 2.67 (dd, J = 8.3, 1.0 Hz, 6H), 1.95 (dd, J = 6.7, 1.7 Hz, 3H), 1.78 (dd, J = 7.1, 1.8 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 170.04, 170.0, 144.4, 143.9, 139.9, 139.7, 139.0, 138.4, 129.8, 129.6, 128.2, 128.1, 128.0, 127.6, 127.5, 127.3, 118.0, 116.4, 116.1, 114.9, 109.7, 109.6, 27.2, 27.2, 18.7, 17.6, 17.6, 14.3; IR (ATR) 1710, 1510, 1365, 1295 cm⁻¹; HRMS (ESI) calcd for C₁₄H₁₅N₂O₃ (M+H⁺) 259.1083, found 2-Methyl-5-nitro-6-(1-propen-1-yl)indole (352). Reaction of a solution of 368 (33.4 mg, 0.129 mmol), Pd(dba)₂ (3.7 mg, 0.006 mmol), dppp (2.7 mg, 0.007 mmol), and 1,10-phen (2.3 mg, 0.013 mmol) in DMF (2 mL), as described for 354 (pCO = 6 atm, 120 °C, 36 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 352 (11 mg, 0.051 mmol, 39%) as a yellow solid. mp=189-190 °C; ¹H NMR (600 MHz, CDCl₃) δ 8.49 (d, J = 9.1 Hz, 1H), 7.87 (d, J = 9.1 Hz, 1H), 7.29 (s, 1H), 5.33 (s, 1H), 4.91 (s, 1H), 2.62 (s, 3H), 2.35 (s, 3H), 2.26 (s, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 168.3, 144.3, 140.1, 138.0, 132.8, 128.3, 125.5, 121.1, 119.4, 116.6, 115.5, 25.5, 23.9, 11.9; IR (ATR) 1718, 1533, 1371, 1303 cm⁻¹;

1-Acetoxy-2-methyl-5-nitro-4-(1-propen-2-yl)indole (369). Treatment of a solution of 356 (50 mg, 0.231 mmol) with (CH₃CO)₂O (0.84 mL, 8.996 mmol) in the presence of Et₃N (0.98 mL, 7.030 mmol), and DMAP (108 mg, 0.883 mmol) in DCE (3 mL) under nitrogen atmosphere, as described for 368 (75 °C, 18 h), gave after work up and chromatography (Hexane/EtOAc, 8:2) 369 (56.3 mg, 0.218 mmol, 94%) as a white solid. mp=189-190 °C; ¹H NMR (600 MHz, CDCl₃) δ 8.49 (d, J = 9.1 Hz, 1H), 7.87 (d, J = 9.1 Hz, 1H), 7.29 (s, 1H), 5.33 (s, 1H), 4.91 (s, 1H), 2.62 (s, 3H), 2.35 (s, 3H), 2.26 (s, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 168.3, 144.3, 140.1, 138.0, 132.8, 128.3, 125.5, 121.1, 119.4, 116.6, 115.5, 25.5, 23.9, 11.9; IR (ATR) 1718, 1533, 1371, 1303 cm⁻¹;

3-Methyl-5-nitro-4-(1-propen-2-yl)indole (356). Reaction of a solution of 369 (27.5 mg, 0.106 mmol), Pd(dba)₂ (3.1 mg, 0.005 mmol), dppp (2.2 mg, 0.005 mmol), and 1,10-phen (1.9 mg, 0.011 mmol) in
DMF (2 mL), as described for 354 (pCO = 6 atm, 120 °C, 48 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) a mixture of 356 and the pyrroloindole (7.2 mg).

**3-Methyl-5-nitro-4-(1-propen-2-yl)-1-tosyliindole (370).** To a slurry of NaH (60%, 84.5 mg, 2.112 mmol) in DMF (2 mL) at 0 °C under a nitrogen atmosphere was added the solution of 356 (228.3 mg, 1.056 mmol) in DMF (2 mL) via a syringe and the red solution was allowed to stir for 20 min. A solution of p-toluenesulfonyl chloride (TsCl, 241.6 mg, 1.267 mmol) in DMF (2 mL) was added drop wise via a syringe at the same temperature. The orange solution was allowed to warm to ambient temperature. After 8 h, the reaction mixture was quenched with saturated solution of NaHCO₃ and diluted with EtOAc (20 mL). The organic layer was washed with water (6X10 mL), dried (MgSO₄) and filtered. The filtrate was concentrated under reduced pressure and purified by chromatography (Hexane/EtOAc, 8:2) to afford 370 (306 mg, 0.826 mmol, 78%) as a white solid. mp=154-155 °C; ¹H NMR (600 MHz, CDCl₃) δ 8.00 (d, J = 9.1 Hz, 1H), 7.85 (d, J = 9.1 Hz, 1H), 7.80 (d, J = 8.3 Hz, 2H), 7.47 (s, 1H), 7.27 (d, J = 8.2 Hz, 2H), 5.29 (s, 1H), 4.85 (s, 1H), 2.35 (s, 3H), 2.32 (s, 3H), 2.21 (s, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 145.5, 144.0, 139.7, 136.9, 134.7, 133.4, 130.0, 128.4, 126.8, 126.2, 120.3, 119.3, 116.5, 112.3, 25.24, 21.44, 11.63; IR (ATR) 1518, 1341, 1176, 906 cm⁻¹;

(371). Reaction of a solution of 370 (53.6 mg, 0.145 mmol), Pd(dba)₂ (4.3 mg, 0.008 mmol), dppp (3.2 mg, 0.008 mmol), and 1,10-phen (2.7 mg, 0.015 mmol) in DMF (2 mL), as described for 336 (pCO=6 atm, 120 °C, 48 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 371 (43.2 mg, 0.128 mmol, 88%) as an off white solid. mp=147-148 °C; ¹H NMR (600 MHz, CDCl₃) δ 8.07 (s, 1H), 7.88 (d, J = 8.9 Hz, 1H), 7.68 (d, J = 8.1 Hz, 2H), 7.35 (s, 1H), 7.22 (d, J = 8.9 Hz, 1H), 7.07 (d, J = 8.0 Hz, 2H), 6.92 (s, 1H), 2.51 (s, 3H), 2.49 (s, 3H), 2.21 (s, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 144.3, 135.3, 133.9, 130.6, 129.5, 126.5, 124.3, 123.1, 122.9, 120.3, 118.8, 111.1, 108.9, 108.5, 21.34, 14.97, 14.89; IR (ATR) 3417, 1353, 1165, 1087 cm⁻¹;

(372). Treatment of 350 (119.6 mg, 0.553 mmol) with TsCl (137 mg, 0.719 mmol) in DMF (4 mL) in the presence of NaH (60%, 44.3 mg, 1.108 mmol), as described for 370 (0 °C -ambient temperature, 8 h), gave after work up and chromatography 372 (158.2 mg, 0.427 mmol, 77%) as a white solid. mp=177-178 °C; ¹H NMR (600 MHz, CDCl₃) δ 8.57 (s, 1H), 7.79 (d, J = 8.3 Hz, 2H), 7.53 (s, 1H), 7.36 (s, 1H), 7.26 (d, J = 8.3 Hz, 2H), 5.16 (s, 1H), 4.92 (s, 1H), 2.36 (s, 3H), 2.28 (d, J = 0.7 Hz, 3H), 2.09 (s, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 145.5, 145.1, 143.6, 134.7, 134.6, 134.3, 132.7, 130.1, 127.6, 126.7, 120.7, 118.2, 114.9, 110.2, 23.6, 21.5, 9.4; IR (ATR) 1516, 1370, 1175, 906 cm⁻¹;
Treatment of 348 (58.3 mg, 0.270 mmol) with TsCl (66.9 mg, 0.351 mmol) in DMF (3 mL) in the presence of NaH (60%, 21.6 mg, 0.540 mmol), as described for 370 (0 °C-ambient temperature, 8 h), gave after work up and chromatography 373 (69.4 mg, 0.187 mmol, 69%) as a faint yellow solid. mp=181-182 °C; 1H NMR (400 MHz, CDCl3) δ 8.89 (s, 1H), 8.76 (s, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.70 (d, J = 8.4 Hz, 2H), 7.49 (s, 1H), 7.30 (d, J = 11.2 Hz, 1H), 7.27 – 7.23 (m, 3H), 6.88 (dd, J = 15.5, 1.4 Hz, 1H), 6.75 (dd, J = 11.4, 1.1 Hz, 1H), 6.39 (s, 1H), 6.36 (s, 1H), 6.18 – 6.08 (m, 1H), 5.89 (dq, J = 11.5, 7.0 Hz, 1H), 2.64 (s, 3H), 2.62 (s, 3H), 2.38 (s, 3H), 2.37 (s, 3H), 1.92 (dd, J = 6.6, 1.6 Hz, 3H), 1.71 (dd, J = 7.0, 1.7 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ 145.6, 145.5, 144.7, 144.2, 142.8, 142.8, 135.5, 134.5, 134.4, 133.3, 132.8, 130.2, 130.2, 129.3, 129.6, 128.1, 127.5, 127.2, 126.9, 126.6, 126.5, 122.2, 119.1, 111.5, 111.2, 108.9, 108.8, 21.6, 18.7, 15.8, 14.3; IR (ATR) 1518, 1341, 1175, 1096, 811 cm⁻¹;

(374). Treatment of 353 (159.2 mg, 0.736 mmol) with TsCl (168.4 mg, 0.883 mmol) in DMF (4 mL) in the presence of NaH (60%, 58.8 mg, 1.472 mmol), as described for 370 (0 °C-ambient temperature, 8 h), gave after work up and chromatography 374 (197.5 mg, 0.533 mmol, 72%) as a white solid. mp=169-170 °C; 1H NMR (600 MHz, CDCl3) δ 8.05 (s, 1H), 7.89 (s, 1H), 7.77 (d, J = 8.3 Hz, 2H), 7.44 (s, 1H), 7.26 (d, J = 8.2 Hz, 2H), 5.21 (s, 1H), 4.95 (s, 1H), 2.36 (s, 3H), 2.12 (s, 3H); 13C NMR (150 MHz, CDCl3) δ 145.5, 144.3, 143.5, 136.6, 135.8, 134.7, 130.4, 130.0, 126.7, 125.7, 118.7, 116.3, 115.3, 114.7, 23.6, 21.5, 9.4; IR (ATR) 1513, 1338, 1175, 905, 726 cm⁻¹;

(375). Treatment of 352 (127 mg, 0.587 mmol) with TsCl (146.5 mg, 0.768 mmol) in DMF (4 mL) in the presence of NaH (60%, 47.2 mg, 1.180 mmol), as described for 370 (0 °C-ambient temperature, 8 h), gave after work up and chromatography (Hexane/EtOAc, 9:1), 375 (154.7 mg, 0.418 mmol, 71%) as a faint yellow oil. 1H NMR (600 MHz, CDCl3) δ 8.32 (s, 1H), 8.11 (d, J = 11.8 Hz, 2H), 7.95 (s, 1H), 6.43 (s, 1H), 6.38 (s, 1H), 6.26 (dq, J = 13.3, 6.7 Hz, 1H), 5.94 (dq, J = 14.1, 7.0 Hz, 1H), 2.63 (s, 3H), 2.60 (s, 3H), 2.37 (s, 6H), 1.97 (d, J = 5.8 Hz, 3H), 1.78 (dd, J = 6.8, 0.9 Hz, 3H); 13C NMR (150 MHz, CDCl3) δ 145.5, 145.5, 144.7, 144.3, 140.7, 140.6, 139.0, 138.4, 135.7, 130.1, 130.1, 129.4, 128.1, 127.9, 127.8, 127.2, 127.0, 126.4, 126.3, 116.8, 116.6, 116.4, 113.3, 109.1, 109.1, 21.5, 18.7, 15.7, 14.3; IR (ATR) 1521, 1342, 1165, 1096, 843 cm⁻¹;

(376). Treatment of 354 (41.6 mg, 0.221 mmol) with TsCl (50.6 mg, 0.265 mmol) in DMF (4 mL) in the presence of NaH (60%, 10.6 mg, 0.442 mmol), as described for 370 (0 °C-ambient temperature, 12 h), gave after work up and chromatography (Hexane/EtOAc, 9:1) 376 (58.5 mg, 0.171 mmol, 77%) as a
white solid. mp=148-149 °C; \(^1^H\) NMR (600 MHz, CDCl\(_3\)) \(\delta\) 8.03 – 7.96 (m, 2H), 7.79 (d, \(J = 8.3\) Hz, 2H), 7.71 (d, \(J = 3.7\) Hz, 1H), 7.28 (d, \(J = 8.1\) Hz, 2H), 7.17 (dd, \(J = 17.6, 11.4\) Hz, 1H), 6.94 (d, \(J = 3.7\) Hz, 1H), 5.69 (d, \(J = 11.4\) Hz, 1H), 5.58 (d, \(J = 17.7\) Hz, 1H), 2.37 (s, 3H); \(^{13}C\) NMR (150 MHz, CDCl\(_3\)) \(\delta\) 145.8, 143.1, 136.7, 134.6, 131.3, 130.2, 130.0, 128.9, 128.6, 126.9, 121.4, 120.9, 112.5, 109.3, 21.6; IR (ATR) 1513, 1374, 1168, 823 cm\(^{-1}\);

(377). Treatment of 355 (128.7 mg, 0.595 mmol) with TsCl (147.5 mg, 0.774 mmol) in DMF (5 mL) in the presence of NaH (60%, 47.6 mg, 1.190 mmol), as described for 370 (0 °C-ambient temperature, 10 h), gave after work up and chromatography (Hexane/EtOAc, 8:2), 377 (174.4 mg, 0.471 mmol, 79%) as a yellow oil. \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.17 (d, \(J = 9.2\) Hz, 1H), 8.11 (d, \(J = 9.2\) Hz, 1H), 7.98 (d, \(J = 9.2\) Hz, 1H), 7.86 (d, \(J = 9.2\) Hz, 1H), 7.70 (dd, \(J = 8.2, 1.1\) Hz, 1H), 6.60 (s, 1H), 6.00 (ddq, \(J = 20.8, 11.5, 6.8\) Hz, 2H), 2.62 (s, 6H), 2.36 (d, \(J = 2.7\) Hz, 6H), 1.95 (dd, \(J = 6.6, 1.6\) Hz, 3H), 1.42 (dd, \(J = 7.0, 1.6\) Hz, 3H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 145.5, 145.5, 143.7, 143.1, 139.9, 139.6, 138.6, 138.2, 135.6, 135.5, 133.3, 130.1, 130.0, 129.3, 129.1, 128.9, 127.0, 126.3, 126.3, 125.9, 124.7, 123.8, 120.0, 119.9, 113.0, 112.6, 109.7, 109.6, 21.4, 18.8, 15.6, 14.9; IR (ATR) 1518, 1365, 1176, 1095, 810 cm\(^{-1}\);

(378). Treatment of 366 (50.8 mg, 0.251 mmol) with TsCl (57.4 mg, 0.301 mmol) in DMF (4 mL) in the presence of NaH (60%, 20 mg, 0.502 mmol), as described for 370 (0 °C-ambient temperature, 8 h), gave after work up and chromatography (Hexane/EtOAc, 9:1), 378 (69 mg, 0.194 mmol, 77%) as a white solid. mp=128-129 °C; \(^1^H\) NMR (600 MHz, CDCl\(_3\)) \(\delta\) 8.14 (d, \(J = 8.5\) Hz, 1H), 7.78 (d, \(J = 8.3\) Hz, 2H), 7.25 (d, \(J = 3.7\) Hz, 1H), 7.24 (d, \(J = 8.5\) Hz, 1H), 6.94 (d, \(J = 3.6\) Hz, 1H), 5.17 (s, 1H), 4.92 (s, 1H), 2.36 (s, 3H); \(^{13}C\) NMR (150 MHz, CDCl\(_3\)) \(\delta\) 145.7, 142.4, 140.4, 134.7, 134.4, 130.2, 129.3, 126.9, 126.0, 124.9, 117.1, 115.8, 106.9, 23.5, 21.6; IR (ATR) 1512, 1373, 1161, 1128, 662 cm\(^{-1}\);

(379). Treatment of 337 (39.8 mg, 0.211 mmol) with TsCl (52.4 mg, 0.275 mmol) in DMF (3 mL) in the presence of NaH (60%, 16.9 mg, 0.422 mmol), as described for 370 (0 °C-ambient temperature, 10 h), gave after work up and chromatography (Hexane/EtOAc, 8:2) 379 (58.2 mg, 0.170 mmol, 81%) as a colorless oil. \(^1^H\) NMR (600 MHz, CDCl\(_3\)) \(\delta\) 7.72-7.70 (m, 3H), 7.60 (d, \(J = 8.3\) Hz, 1H), 7.48 (d, \(J = 8.3\) Hz, 1H), 7.25 (d, \(J = 8.5\) Hz, 2H), 6.74 (d, \(J = 3.7\) Hz, 1H), 6.70 (dd, \(J = 16.8, 10.8\) Hz, 1H), 5.80 (d, \(J = 17.2\) Hz, 1H), 5.45 (d, \(J = 11.0\) Hz, 1H), 2.36 (s, 3H); \(^{13}C\) NMR (150 MHz, CDCl\(_3\)) \(\delta\) 145.3, 137.6, 134.8, 133.8, 130.8, 130.2, 129.7, 127.0, 127.0, 123.9, 123.6, 121.8, 119.6, 109.4, 21.6; IR (ATR) 1593, 1514, 1344, 1161, 662 cm\(^{-1}\);
(380). Reaction of a solution of 372 (76.4 mg, 0.206 mmol), Pd(dba)$_2$ (7.1 mg, 0.012 mmol), dppe (5.1 mg, 0.012 mmol), and 1,10-phen (4.5 mg, 0.025 mmol) in DMF (2 mL), as described for 336 (pCO=6 atm, 120 °C, 24 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3), 380 (55.4 mg, 0.164 mmol, 79%) as an off white solid. mp=143-144 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.98 (s, 1H), 7.94 (s, 1H), 7.68 (d, $J$= 8.3 Hz, 2H), 7.49 (s, 1H), 7.22 (d, $J$= 0.8 Hz, 1H), 7.08 (d, $J$= 8.1 Hz, 2H), 6.98 (s, 1H), 2.33 (s, 3H), 2.28 (d, $J$= 0.6 Hz, 3H), 2.23 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.2, 135.4, 135.0, 133.0, 129.5, 126.8, 126.6, 126.3, 122.6, 122.1, 119.6, 111.0, 107.9, 95.9, 21.4, 10.0, 9.8; IR (ATR) 3417, 1444, 1353, 1165, 1087 cm$^{-1}$;

(381). Reaction of a solution of 373 (41.1 mg, 0.111 mmol), Pd(dba)$_2$ (3.8 mg, 0.007 mmol), dppe (2.7 mg, 0.007 mmol), and 1,10-phen (2.4 mg, 0.013 mmol) in DMF (2 mL), as described for 336 (pCO=6 atm, 120 °C, 24 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 8:2) 381 (26.4 mg, 0.078 mmol, 70%) as an off white solid. mp=153 °C (dec.); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.11 (s, 1H), 7.88 (s, 1H), 7.59 (d, $J$= 8.5 Hz, 2H), 7.41 (s, 1H), 7.11 (d, $J$= 8.0 Hz, 2H), 6.35 (s, 1H), 6.19 (dt, $J$= 1.9, 0.9 Hz, 1H), 2.57 (d, $J$= 1.2 Hz, 3H), 2.44 (d, $J$= 0.9 Hz, 3H), 2.28 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.2, 136.2, 136.1, 136.0, 134.7, 134.0, 129.6, 127.0, 126.1, 124.7, 110.7, 109.0, 99.5, 96.5, 21.5, 16.1, 13.9; IR (ATR) 3418, 1353, 1165, 1086 cm$^{-1}$;

(382). Reaction of a solution of 374 (61.2 mg, 0.165 mmol), Pd(dba)$_2$ (6.7 mg, 0.012 mmol), dppe (4.8 mg, 0.012 mmol), and 1,10-phen (4.2 mg, 0.023 mmol) in DMF (2 mL), as described for 336 (pCO=6 atm, 120 °C, 24 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 382 (49.4 mg, 0.146 mmol, 88%) as an off white solid. mp=143-144 °C (dec.); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.12 (s, 1H), 7.78 (s, 1H), 7.70 (d, $J$= 8.3 Hz, 2H), 7.23 (d, $J$= 1.0 Hz, 1H), 7.19 (s, 1H), 7.07 (d, $J$= 8.2 Hz, 2H), 6.97 (s, 1H), 2.38 (s, 3H), 2.22 (s, 3H), 2.20 (d, $J$= 0.8 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.2, 136.2, 136.1, 136.0, 134.7, 134.0, 129.6, 127.0, 126.1, 124.7, 110.7, 109.0, 99.5, 96.5, 21.5, 16.1, 13.9; IR (ATR) 3418, 1353, 1165, 1086 cm$^{-1}$;

(383). Reaction of a solution of 375 (58.2 mg, 0.157 mmol), Pd(dba)$_2$ (6.3 mg, 0.011 mmol), dppe (4.5 mg, 0.011 mmol), and 1,10-phen (4 mg, 0.022 mmol) in DMF (2 mL), as described for 336 (pCO=6 atm, 120 °C, 25 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 8:2) 383 (40.5 mg, 0.120 mmol, 76%) as a faint yellow oil. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 8.28 (s, 1H), 7.71 (s, 1H), 7.62 (d, $J$= 8.0 Hz, 2H), 7.11 (s, 1H), 7.08 (d, $J$= 8.0 Hz, 2H), 6.31 (s, 1H), 6.28 (s, 1H), 2.61 (s, 3H), 2.41 (s, 3H), 2.25 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 144.1, 136.7, 136.2, 136.1, 134.2, 133.0, 129.5, 127.3, 126.1, 125.8, 110.4, 104.7, 100.5, 99.6, 21.4, 16.2, 13.8; IR (ATR) 3436, 1359, 1166 cm$^{-1}$;
(384). Reaction of a solution of 376 (52.5 mg, 0.153 mmol), Pd(dba)$_2$ (5.3 mg, 0.010 mmol), dppp (3.8 mg, 0.010 mmol), and 1,10-phen (3.3 mg, 0.018 mmol) in DMF (2 mL), as described for 336 (pCO=6 atm, 120 °C, 25 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3), 384 (42.4 mg, 0.137 mmol, 89%) as a faint yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.32 (s, 1H), 7.87 (d, $J$ = 9.0 Hz, 1H), 7.72 (d, $J$ = 8.4 Hz, 2H), 7.59 (d, $J$ = 3.6 Hz, 1H), 7.30 (d, $J$ = 9.0 Hz, 1H), 7.18 (t, $J$ = 2.8 Hz, 1H), 7.11 (d, $J$ = 8.4 Hz, 2H), 6.90 (d, $J$ = 3.4 Hz, 1H), 6.70 – 6.64 (m, 1H), 2.24 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 144.6, 135.3, 132.1, 129.6, 129.5, 126.6, 125.3, 123.9, 123.2, 120.2, 108.7, 108.4, 108.0, 100.8, 21.4; IR (ATR) 3401, 1348, 1160, 1102 cm$^{-1}$; 

(385). Reaction of a solution of 377 (85.4 mg, 0.230 mmol), Pd(dba)$_2$ (8.0 mg, 0.014 mmol), dppp (5.7 mg, 0.014 mmol), and 1,10-phen (5.0 mg, 0.028 mmol) in DMF (2.5 mL), as described for 336 (pCO=6 atm, 120 °C, 26 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 8:2), 385 (60.4 mg, 0.178 mmol, 77%) as an off white solid. mp=134-135 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.98 (d, $J$ = 9.1 Hz, 1H), 7.98 (s, 1H), 7.62 (d, $J$ = 8.2 Hz, 2H), 7.15 (d, $J$ = 9.0 Hz, 1H), 7.10 (d, $J$ = 8.2 Hz, 2H), 6.56 (s, 1H), 6.31 (s, 1H), 2.66 (s, 3H), 2.42 (s, 3H), 2.27 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 144.2, 136.3, 136.0, 134.8, 132.5, 131.5, 129.6, 126.0, 121.4, 120.4, 108.9, 108.5, 106.9, 98.7, 21.4, 16.1, 13.7; IR (ATR) 3401, 1348, 1160, 1102 cm$^{-1}$; 

(386). Reaction of a solution of 378 (59.9 mg, 0.168 mmol), Pd(dba)$_2$ (4.9 mg, 0.010 mmol), dppp (3.5 mg, 0.010 mmol), and 1,10-phen (3.1 mg, 0.20 mmol) in DMF (2 mL), as described for 336 (pCO=6 atm, 120 °C, 26 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 8:2), 386 (47.6 mg, 0.147 mmol, 87%) as an off white solid. mp=137 °C (dec.); $^1$H NMR (400 MHz, CDCl$_3$) δ 8.17 (s, 1H), 7.83 (d, $J$ = 8.8 Hz, 1H), 7.76 (d, $J$ = 8.2 Hz, 2H), 7.57 (d, $J$ = 3.6 Hz, 1H), 7.50 (d, $J$ = 8.8 Hz, 1H), 7.14 (d, $J$ = 8.1 Hz, 2H), 6.90 (s, 1H), 6.77 (d, $J$ = 3.5 Hz, 1H), 2.35 (s, 3H), 2.27 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 144.7, 135.1, 131.7, 129.7, 128.5, 126.7, 124.8, 123.7, 119.8, 116.0, 115.9, 112.5, 106.1, 105.3, 21.4, 9.8; IR (ATR) 3415, 1353, 1165, 1087 cm$^{-1}$; 

(379). Reaction of a solution of 379 (52.7 mg, 0.154 mmol), Pd(dba)$_2$ (5.3 mg, 0.010 mmol), dppp (3.8 mg, 0.010 mmol), and 1,10-phen (3.3 mg, 0.018 mmol) in DMF (3 mL), as described for 336 (pCO=6 atm, 120 °C, 36 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 379 (37.1 mg, 0.108 mmol, 70%) as a colorless oil.
(379). Reaction of a solution of 379 (31 mg, 0.091 mmol), Pd(OAc)$_2$ (2.1 mg, 0.009 mmol) and 1,10-phen (1.7 mg, 0.009 mmol) in DMF (2 mL), as described for 354 (pCO=6 atm, 120 °C, 50 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) 379 (30.2 mg, 0.088 mmol, 82%) as a colorless oil.
References and Footnotes


6. For a recent extensive review of indoles isolated from marine organisms, see: Netz, N.; Opatz, T. Mar. Drugs 2015, 13, 4814-4914.


41. Compound 14 has been described in a patent but only a very cursory ¹H NMR was reported. Piotrowski, D. W.; Rogers, B. N.; McWhorter, W. W., Jr.; Walker, D. P.; Corbett, J. W.; Groppi, V. E., Jr.; Rudmann, D. G. PCT Int. Appl. WO 2003093250 [CAN139:395938].
42. The compound is commercially available however it was prepared in two steps from 4-bromopyrimidine according to: Maji, A.; Hazra, A.; Maiti, D. *Org. Lett.* **2014**, *16*, 4524-4527.


54. TMB = 2,4,6-trimethylbenzoate; TMphenanthroline = 3,4,7,8-tetramethylphenanthroline.


76. For a very recent example and references to previously reported reactions, see: Guo, T.; Han, S.-L.; Liu, Y.-C.; Liu, Y.; Liu, H.-M. Tetrahedron Lett. 2016, 57, 1097-1099.


93. One carbon resonance was missing in the spectrum.

94. Compound 6 is commercially available however, it was prepared for this study according to: Hughes, I.; Raphael, R. A. *Tetrahedron Lett.* **1994**, *24*, 1441-1444.


96. Compound 17 is commercially available however, it was prepared for this study according to: Coffman, K. C.; Palazzo, T. A.; Hartley, T. P.; Fettinger, J. C.; Tantillo, D. J.; Kurth, M. J. *Org. Lett.* **2013**, *15*, 2062-2065.


100. The chromatography was performed using silica gel/K$_2$CO$_3$ (10% K$_2$CO$_3$).


133. Compound 12 is known but only the 1H NMR was reported. Chen Y. I.; Helberg, K.; Guarino, K.; et al. *J. Antibiot.* 1991, 44, 870-884.


135. NaH (80%) in mineral oil without removal of oil was used in all experiments. The amount of NaH shown in each experimental procedure represents the mass of NaH and not the total mass of NaH plus mineral oil.


141. This catalyst system was used as a convenient substitute for 1.5% Pd₂(dba)₃-3.0% P(t-Bu)₃, since Pd₂(dba)₃ and Pd(P(t-Bu)₃)₂ are more easily handled and stored.


151. It has been shown that an increase in temperature from ambient to 70 °C resulted in erosion of C-OTf versus C-Br selectivity in Suzuki couplings. Wang, B., Sun, H.-X.; Sun, Z.-H. Eur. J. Org. Chem. 2009, 3688-3692.


173. We were unable to obtain a HRMS of this compound.
182. Commercially available.
190. The compound has been prepared previously but no analytical data were reported. Murugesan, N.; Tellew, J. E.; Macor, J. E.; Gu, Z. U.S. Pat Appl. (2002) US 20020143024.


Figure 1.2 $^1$H and $^{13}$C NMR of compound 2
Figure 1.3 $^1$H and $^{13}$C NMR of compound 3
Figure 1.4 $^1$H and $^{13}$C NMR of compound 4
Figure 1.5 $^1$H and $^{13}$C NMR of compound 6
Figure 1.6 $^1\text{H}$ and $^{13}\text{C}$ NMR of compound 7
Figure 1.7 $^1$H and $^{13}$C NMR of compound 8
Figure 1.8 $^1$H and $^{13}$C NMR of Alocasin A
Figure 1.9 $^1$H and $^{13}$C NMR of compound 11
Figure 1.10 $^1$H and $^{13}$C NMR of compound 12
Figure 1.11 $^1$H and $^{13}$C NMR of compound 13
Figure 1.12 $^1$H and $^{13}$C NMR of compound 14
Figure 1.13 $^1$H and $^{13}$C NMR of scalaridine A
Figure 1.14 $^1$H and $^{13}$C NMR of compound 16
Figure 1.15 $^1$H and $^{13}$C NMR of compound 17
Figure 1.16 $^1$H and $^{13}$C NMR of compound 18
Figure 1.17 $^1$H and $^{13}$C NMR of compound 19
Figure 1.18 \( ^1H \) and \( ^13C \) NMR of compound 20
Figure 1.19 $^1$H and $^{13}$C NMR of compound 21
Figure 1.20 $^1$H and $^{13}$C NMR of compound 22
Figure 1.21 $^1$H and $^{13}$C NMR of hyrtinadine A
Figure 1.22 $^1$H and $^{13}$C NMR of compound 24
Figure 1.23 $^1$H and $^{13}$C NMR of compound 25
Figure 1.24 $^1$H and $^{13}$C NMR of compound 26
Figure 1.25 $^1$H and $^{13}$C NMR of hyrtinadine B
Figure 2.2 $^1$H and $^{13}$C NMR of compound 28
Figure 2.3 $^1$H and $^{13}$C NMR of compound 29
Figure 2.4 $^1$H and $^{13}$C NMR of compound 30
Figure 2.5 $^1$H and $^{13}$C NMR of compound 32
Figure 2.6 $^1$H and $^{13}$C NMR of compound 34
Figure 2.7 $^1$H and $^{13}$C NMR of compound 35
Figure 2.8 $^1$H and $^{13}$C NMR of compound 36
Figure 2.9 $^1$H and $^{13}$C NMR of compound 37
Figure 2.10 $^1$H and $^{13}$C NMR of compound 38
Figure 2.11 $^1$H and $^{13}$C NMR of compound 39
Figure 2.12 $^1$H and $^{13}$C NMR of compound 40
Figure 2.13 $^1$H and $^{13}$C NMR of compound 41
Figure 2.14 $^1$H and $^{13}$C NMR of compound 42
Figure 2.15 $^1$H and $^{13}$C NMR of compound 43
Figure 2.16 $^1$H and $^{13}$C NMR of compound 48
Figure 2.17 $^1$H and $^{13}$C NMR of compound 49
Figure 2.18 $^1$H and $^{13}$C NMR of compound 50
Figure 2.19 $^1$H and $^{13}$C NMR of compound 51
Figure 2.20 $^1$H and $^{13}$C NMR of compound 52
Figure 2.21 $^1$H and $^{13}$C NMR of compound 53
Figure 2.22 $^1$H and $^{13}$C NMR of compound 54
Figure 2.23 $^1$H and $^{13}$C NMR of compound 55
Figure 2.24 $^1$H and $^{13}$C NMR of compound 56
Figure 2.25 $^1$H and $^{13}$C NMR of compound 57
Figure 2.26 $^1$H and $^{13}$C NMR of compound 58
Figure 2.27 $^1$H and $^{13}$C NMR of compound 59
Figure 2.28 \(^1\)H and \(^{13}\)C NMR of compound 60
Figure 2.29 $^1$H and $^{13}$C NMR of compound 62
Figure 2.30 $^1$H and $^{13}$C NMR of compound 63
Figure 2.31 $^1$H and $^{13}$C NMR of compound 64
Figure 2.32 $^1$H and $^{13}$C NMR of compound 66
Figure 2.33 $^1$H and $^{13}$C NMR of compound 67
Figure 2.34 $^1$H and $^{13}$C NMR of compound 68
Figure 2.35 $^1$H and $^{13}$C NMR of compound 69
Figure 2.35 $^1$H and $^{13}$C NMR of compound 71
Figure 2.37 $^1$H and $^{13}$C NMR of compound 72
Figure 2.38 $^1$H and $^{13}$C NMR of compound 73
Figure 2.39 $^1$H and $^{13}$C NMR of compound 74
Figure 2.40 $^1$H and $^{13}$C NMR of compound 75
Figure 2.41 $^1$H and $^{13}$C NMR of compound 76
Figure 2.42 $^1$H and $^{13}$C NMR of compound 77
Figure 2.43 $^1$H and $^{13}$C NMR of compound 78
Figure 2.44 $^1$H and $^{13}$C NMR of compound 81
Figure 2.45 $^1$H and $^{13}$C NMR of compound 82
Figure 2.46 $^1$H and $^{13}$C NMR of compound 88
Figure 2.47 $^1$H and $^{13}$C NMR of compound 89
Figure 2.48 $^1$H and $^{13}$C NMR of compound 90
Figure 2.49 $^1$H and $^{13}$C NMR of compound 91
Figure 2.50 $^1$H and $^{13}$C NMR of compound 92
Figure 2.51 $^1$H and $^{13}$C NMR of compound 93
Figure 2.52 $^1$H and $^{13}$C NMR of compound 94
Figure 2.53 $^1$H and $^{13}$C NMR of compound 95
Figure 2.54 $^1$H and $^{13}$C NMR of compound 96
Figure 2.55 $^1$H and $^{13}$C NMR of compound 97
Figure 2.56 $^1$H and $^{13}$C NMR of compound 99
Figure 2.57 $^1$H and $^{13}$C NMR of compound 100
Figure 2.58 $^1$H and $^{13}$C NMR of compound 101
Figure 2.59 $^1$H and $^{13}$C NMR of compound 102
Figure 3.2 $^1$H and $^{13}$C NMR of compound 113
Figure 3.3 $^1$H and $^{13}$C NMR of compound 114
Figure 3.4 $^1$H and $^{13}$C NMR of compound 115
Figure 3.5 $^1$H and $^{13}$C NMR of compound 116
Figure 3.7 $^1$H and $^{13}$C NMR of compound 103
Figure 3.8 $^1$H and $^{13}$C NMR of compound 105
Figure 3.9 $^1$H and $^{13}$C NMR of compound 118
Figure 3.10 $^1$H and $^{13}$C NMR of compound 119
Figure 3.11 $^1$H and $^{13}$C NMR of compound 120
Figure 3.12 $^1$H and $^{13}$C NMR of compound 104
Figure 3.13 $^1$H and $^{13}$C NMR of compound 121
Figure 4.1 $^1$H and $^{13}$C NMR of compound 124
Figure 4.2 $^1$H and $^{13}$C NMR of compound 125
Figure 4.3 $^1$H and $^{13}$C NMR of compound 125
Figure 4.4 $^1$H and $^{13}$C NMR of compound 128
Figure 4.5 $^1$H and $^{13}$C NMR of compound 129
Figure 4.6 $^1$H and $^{13}$C NMR of compound 130
Figure 4.7 $^1$H and $^{13}$C NMR of compound 132
Figure 4.8 $^1$H and $^{13}$C NMR of compound 133
Figure 4.9 $^1$H and $^{13}$C NMR of compound 134
Figure 4.10 $^1$H and $^{13}$C NMR of compound 135
Figure 4.11 $^1$H and $^{13}$C NMR of compound 136
Figure 4.12 $^1$H and $^{13}$C NMR of compound 137
Figure 4.13 $^1$H and $^{13}$C NMR of compound 139
Figure 4.14 $^1$H and $^{13}$C NMR of compound 140
Figure 4.15 $^1$H and $^{13}$C NMR of compound 141
Figure 4.16 $^1$H and $^{13}$C NMR of compound 143
Figure 4.17 $^1$H and $^{13}$C NMR of compound 145
Figure 4.18 $^1$H and $^{13}$C NMR of compound 146
Figure 4.19 $^1$H and $^{13}$C NMR of compound 148
Figure 4.20 $^1$H and $^{13}$C NMR of compound 149
Figure 4.21 $^1$H and $^{13}$C NMR of compound 150
Figure 4.22 $^1$H and $^{13}$C NMR of compound 151
Figure 4.23 $^1$H and $^{13}$C NMR of compound 152
Figure 4.24 $^1$H and $^{13}$C NMR of compound 153
Figure 4.25 $^1$H and $^{13}$C NMR of compound 154
Figure 4.26 $^1$H and $^{13}$C NMR of compound 155
Figure 4.27 $^1$H and $^{13}$C NMR of compound 156
Figure 4.28 $^1$H and $^{13}$C NMR of compound 158
Figure 4.29 $^1$H and $^{13}$C NMR of compound 159
Figure 4.30 $^1$H and $^{13}$C NMR of compound 160
Figure 4.31 $^1$H and $^{13}$C NMR of compound 161
Figure 4.32 $^1$H and $^{13}$C NMR of compound 162
Figure 4.33 $^1$H and $^{13}$C NMR of compound 163
Figure 4.34 $^1$H and $^{13}$C NMR of compound 164
Figure 4.35 $^1$H and $^{13}$C NMR of compound 165
Figure 4.36 $^1$H and $^{13}$C NMR of compound 166
Figure 4.37 $^1$H and $^{13}$C NMR of compound 167
Figure 4.38 $^1$H and $^{13}$C NMR of compound 169
Figure 4.39 $^1$H and $^{13}$C NMR of compound 171
Figure 4.40 $^1$H and $^{13}$C NMR of compound 172
Figure 4.41 $^1$H and $^{13}$C NMR of compound 173
Figure 4.42 $^1$H and $^{13}$C NMR of compound 174
Figure 4.43 $^1$H and $^{13}$C NMR of compound 175
Figure 4.44 $^1$H and $^{13}$C NMR of compound 176
Figure 4.45 $^1$H and $^{13}$C NMR of compound 177
Figure 4.46 $^1$H and $^{13}$C NMR of compound 178
Figure 4.47 $^1$H and $^{13}$C NMR of compound 179
Figure 4.48 $^1$H and $^{13}$C NMR of compound 180
Figure 4.49 $^1$H and $^{13}$C NMR of compound 181
Figure 4.50 $^1$H and $^{13}$C NMR of compound 182
Figure 4.51 $^1$H and $^{13}$C NMR of 4-carbomethoxy-N-methyl-N-(2-methyl-1-propen-1-yl)-2-nitroaniline
Figure 4.52 $^1$H and $^{13}$C NMR of 2,4-dinitro-$N$-methyl-$N$-(2-methyl-1-propen-1-yl)aniline
Figure 4.53 $^1$H and $^{13}$C NMR of 5-chloro-N-(2-methyl-1-propen-1-yl)-2-nitroaniline
Figure 5.1 $^1$H and $^{13}$C NMR of compound 190
Figure 5.2 $^1$H and $^{13}$C NMR of compound 191
Figure 5.3 $^1$H and $^{13}$C NMR of compound 192
Figure 5.4 $^1$H and $^{13}$C NMR of compound 193
Figure 5.5 $^1$H and $^{13}$C NMR of compound 195
Figure 5.6 $^1$H and $^{13}$C NMR of compound 196
Figure 5.7 $^1$H and $^{13}$C NMR of compound 197
Figure 5.8 $^1$H and $^{13}$C NMR of compound 198
Figure 5.9 $^1$H and $^{13}$C NMR of compound 199
Figure 5.10 $^1$H and $^{13}$C NMR of compound 200
Figure 5.1 $^1$H and $^{13}$C NMR of compound 201
Figure 6.2 $^1$H of compound 204
Figure 6.3 $^{13}$C and $^{19}$F NMR of compound 204
Figure 6.4 $^1$H NMR of compound 205
Figure 6.5 $^{13}$C and $^{19}$F NMR of compound 205
Figure 6.6 $^1$H and $^{13}$C NMR of compound 211
Figure 6.7 $^1$H and $^{13}$C NMR of compound 215
Figure 6.8 $^1$H of compound 216
Figure 6.9 $^{13}$C and $^{19}$F NMR of compound 216
Figure 6.10 $^1$H of compound 217
Figure 6.11 $^{13}$C and $^{19}$F NMR of compound 217
Figure 6.12 $^1$H and $^{13}$C NMR of compound 219
Figure 6.13 $^1$H and $^{13}$C NMR of compound 222
Figure 6.14 $^1$H and $^{13}$C NMR of compound 224
Figure 6.15 \(^1\)H and \(^{13}\)C NMR of compound 225
Figure 6.16 $^1$H and $^{13}$C NMR of compound 226
Figure 6.17 $^1$H and $^{13}$C NMR of compound 227
Figure 6.18 $^1$H of a mixture of compounds 226 and 228
Figure 6.19 \(^1\)H and \(^{13}\)C NMR of compound 229
Figure 6.20 $^1$H and $^{13}$C NMR of compound 232
Figure 6.21 $^1$H and $^{13}$C NMR of compound 233
Figure 6.22 $^1$H and $^{13}$C NMR of compound 234
Figure 6.23 $^1$H and $^{13}$C NMR of compound 235
Figure 6.24 $^1$H and $^{13}$C NMR of compound 237
Figure 6.25 $^1$H and $^{13}$C NMR of compound 238
Figure 6.26 $^1$H and $^{13}$C NMR of compound 239
Figure 6.27 $^1$H and $^{13}$C NMR of compound 240
Figure 6.28 $^1$H and $^{13}$C NMR of compound 241
Figure 6.29 $^1$H and $^{13}$C NMR of compound 242
Figure 6.30 $^1$H and $^{13}$C NMR of compound 243
Figure 6.31 $^1$H and $^{13}$C NMR of compound 245
Figure 6.32 $^1$H and $^{13}$C NMR of compound 246
Figure 6.33 $^1$H and $^{13}$C NMR of compound 249
Figure 6.34 $^1$H and $^{13}$C NMR of compound 253
Figure 6.35 $^1$H and $^{13}$C NMR of compound 254
Figure 6.36 $^1$H and $^{13}$C NMR of compound 255
Figure 7.2 $^1$H and $^{13}$C NMR of compound 257
Figure 7.3 $^1$H of compound 258
Figure 7.4 $^{13}$C and $^{19}$F NMR of compound 258
Figure 7.5 $^1$H and $^{13}$C NMR of compound 261
Figure 7.6 $^1$H and $^{13}$C NMR of compound 262
Figure 7.7 $^1$H NMR of compound 264
Figure 7.8 $^{13}$C and $^{19}$F NMR of compound 264
Figure 7.9 $^1$H NMR of compound 265
Figure 7.10 $^{13}$C and $^{19}$F NMR of compound 265
Figure 7.11 $^1$H NMR of compound 266
Figure 7.12 $^{13}$C and $^{19}$F NMR of compound 266
Figure 7.13 $^1$H NMR of a mixture of 270 and 271
Figure 7.14 $^1$H NMR of compound 273
Figure 7.15 $^{13}$C and $^{19}$F NMR of compound 273
Figure 7.16 $^1$H and $^{13}$C NMR of a mixture of 274 and 275
Figure 7.17 $^1$H NMR of compound 276
Figure 7.18 $^{13}$C and $^{19}$F NMR of compound 276
Figure 7.19 $^1$H NMR of compound 277
Figure 7.20 $^{13}$C and $^{19}$F NMR of compound 277
Figure 7.21 $^1$H and $^{13}$C NMR of compound 279
Figure 7.22 $^1$H and $^{13}$C NMR of compound 280
Figure 7.23 $^1$H NMR of compound 281
Figure 7.24 $^{13}$C and $^{19}$F NMR of compound 281
Figure 7.25 $^1$H and $^{13}$C NMR of compound 285
Figure 7.26 $^1$H and $^{13}$C NMR of compound 286
Figure 7.27 $^1$H and $^{13}$C NMR of compound 287
Figure 7.28 $^1$H and $^{13}$C NMR of compound 289
Figure 7.29 $^1$H and $^{13}$C NMR of compound 290
Figure 7.30 $^1$H and $^{13}$C NMR of compound 291
Figure 7.31 $^1$H and $^{13}$C NMR of compound 292
Figure 7.32 $^1\text{H}$ and $^{13}\text{C}$ NMR of compound 293
Figure 7.33 $^1$H and $^{13}$C NMR of compound 294
Figure 7.34 $^1$H and $^{13}$C NMR of compound 295
Figure 7.35 $^1$H and $^{13}$C NMR of compound 296
Figure 7.36 $^1$H and $^{13}$C NMR of compound 297
Figure 7.37 $^1$H and $^{13}$C NMR of compound 298
Figure 7.38 $^1$H NMR of compound 300
Figure 7.39 $^{13}$C and $^{19}$F NMR of compound 300
Figure 7.40 $^1$H NMR of compound 301
Figure 7.41 $^{13}$C and $^{19}$F NMR of compound 300
Figure 7.42 $^1$H and $^{13}$C NMR of compound 302
Figure 7.43 $^1$H NMR of compound 303
Figure 7.44 $^{13}$C and $^{19}$F NMR of compound 303
Figure 7.45 ¹H NMR of compound 305
Figure 7.46 $^{13}$C and $^{19}$F NMR of compound 305
Figure 7.47 $^1$H NMR of compound 306
Figure 7.48 $^{13}$C and $^{19}$F NMR of compound 306
Figure 7.49 $^1$H NMR of compound 307
Figure 7.50 $^{13}$C and $^{19}$F NMR of compound 307
Figure 7.51 $^1$HNMR of compound 308
Figure 7.52 $^{13}$C and $^{19}$F NMR of compound 308
Figure 7.53 $^1$H NMR of compound 309
Figure 7.54 $^{13}$C and $^{19}$F NMR of compound 309
Figure 7.55 $^1$H NMR of compound 310
Figure 7.56 $^{13}$C and $^{19}$F NMR of compound 310
Figure 7.57 $^1$H NMR of compound 311
Figure 7.58 $^{13}$C and $^{19}$F NMR of compound 311
Figure 7.59 $^1$H NMR of compound 312
Figure 7.60 $^{13}$C and $^{19}$F NMR of compound 312
Figure 7.61 $^1$H NMR of compound 313
Figure 7.62 $^{13}$C and $^{19}$F NMR of compound 313
Figure 7.63 $^1$H and $^{13}$C NMR of compound 314
Figure 7.64 $^1$H and $^{13}$C NMR of compound 315
Figure 7.65 $^1$H and $^{13}$C NMR of compound 316
Figure 7.66 $^1$H and $^{13}$C NMR of compound 317
Figure 7.67 $^1$H and $^{13}$C NMR of compound 318
Figure 7.68 $^1$H and $^{13}$C NMR of compound 319
Figure 7.69 $^1$H and $^{13}$C NMR of compound 320
Figure 7.70 $^1$H and $^{13}$C NMR of compound 321
Figure 7.71 $^1$H and $^{13}$C NMR of compound 322
Figure 7.72 $^1$H and $^{13}$C NMR of compound 323
Figure 7.73 $^1$H and $^{13}$C NMR of compound 324
Figure 7.74 $^1$H and $^{13}$C NMR of compound 325
Figure 7.75 $^1$H and $^{13}$C NMR of compound 326
**Figure 7.76** $^1$H and $^{13}$C NMR of compound 327
Figure 7.77 $^1$H and $^{13}$C NMR of compound 328
Figure 7.78 $^1$H and $^{13}$C NMR of compound 329
Figure 7.79 $^1$H and $^{13}$C NMR of compound 330
Figure 7.80 $^1$H and $^{13}$C NMR of compound 331
Figure 7.81 $^1$H and $^{13}$C NMR of compound 336
Figure 7.82 $^1$H and $^{13}$C NMR of compound 337
Figure 7.83 $^1$H and $^{13}$C NMR of compound 338
Figure 7.84 $^1$H and $^{13}$C NMR of compound 339
Figure 7.85 $^1$H and $^{13}$C NMR of compound 340
Figure 7.86 $^1$H and $^{13}$C NMR of compound 341
Figure 7.87 $^1$H and $^{13}$C NMR of compound 342
Figure 7.88 $^1$H and $^{13}$C NMR of compound 343
Figure 7.89 $^1$H and $^{13}$C NMR of compound 344
Figure 7.90 \(^1\)H and \(^{13}\)C NMR of compound 345
Figure 7.91 $^1$H and $^{13}$C NMR of compound 346
Figure 7.92 $^1$H and $^{13}$C NMR of compound 347
Figure 7.93 $^1$H and $^{13}$C NMR of compound 348
Figure 7.94 $^1$H and $^{13}$C NMR of compound 349
Figure 7.95 $^1$H and $^{13}$C NMR of compound 350
Figure 7.96 $^1$H and $^{13}$C NMR of compound 351
Figure 7.97 $^1$H and $^{13}$C NMR of compound 352
Figure 7.98 $^1$H and $^{13}$C NMR of compound 353
Figure 7.99 $^1$H and $^{13}$C NMR
Figure 7.100 $^1$H and $^{13}$C NMR of compound 354
Figure 7.101 $^1$H and $^{13}$C NMR of compound 355
Figure 7.102 $^1$H and $^{13}$C NMR of compound 356
Figure 7.103 $^1$H and $^{13}$C NMR of compound 363
Figure 7.104 $^1$H and $^{13}$C NMR of compound 364
Figure 7.105 $^1$H and $^{13}$C NMR of compound 365
Figure 7.106 $^1$H and $^{13}$C NMR of compound 366
Figure 7.107 $^1$H and $^{13}$C NMR of compound 368
Figure 7.108 $^1$H and $^{13}$C NMR of compound 369
Figure 7.109 $^1$H and $^{13}$C NMR of compound 370
Figure 7.110 $^1$H and $^{13}$C NMR of compound 371
Figure 7.111 $^1$H and $^{13}$C NMR of compound 372
Figure 7.112 $^1$H and $^{13}$C NMR of compound 373
Figure 7.113 $^1$H and $^{13}$C NMR of compound 374
Figure 7.114 $^1$H and $^{13}$C NMR of compound 375
Figure 7.115 $^1$H and $^{13}$C NMR of compound 376
Figure 7.116 $^1$H and $^{13}$C NMR of compound 377
Figure 7.117 $^1$H and $^{13}$C NMR of compound 378
Figure 7.118 $^1$H and $^{13}$C NMR of compound 379
Figure 7.119 $^1$H and $^{13}$C NMR of compound 380
Figure 7.120 $^1$H and $^{13}$C NMR of compound 381
Figure 7.121 $^1$H and $^{13}$C NMR of compound 382
Figure 7.122 $^1$H and $^{13}$C NMR of compound 383
Figure 7.123 $^1$H and $^{13}$C NMR of compound 384
Figure 7.124 $^1$H and $^{13}$C NMR of compound 385
Figure 7.125 $^1$H and $^{13}$C NMR of compound 386
Synthesis of indoles, biindoles, indole alkaloids, pyrroloindoles, and benzimidazoles from aromatic nitro compounds and a study of the chemoselectivity in the Kosugi-Migita-Stille coupling

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Dissertation submitted to the Eberly College of Arts and Sciences at West Virginia University in partial fulfillment of the requirements for the degree of

Doctor of Philosophy in Chemistry

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