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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

Nurul Hoda Ansari

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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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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

Nurul Hoda Ansari

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-1*H*-indole, 2,2',6,6'-tetrabromo-3,3'-bi-1*H*-indole and 2,2',5,5',6,6'-hexabromo-3,3'-bi-1*H*-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 bromophenyl- 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

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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,¹ dragmacidins,² topsentins (spongetins),^{1c-e,3} nortopsentins⁴ and rhopaladins.⁵ These metabolites possess diverse bioactivities such as cytotoxic,^{1f,g,2d,3a,4} antiviral,^{1g,2b,4} antifungal,⁷ antibacterial⁷ and antiplasmodial⁸ 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).⁹ 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.¹⁰ and scalaridine A and hyrtinadine B isolated from the marine sponge *Scalarispongia* sp.¹¹ 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),¹² 3,5-dibromopyridine (scalaridine A, Scheme 1.2)¹³ and 2-iodo-5-bromopyrimidine (hyrtinadine A, Scheme 1.3)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).¹⁵ Synthesis of hyrtinadine B has not been reported to date.

Scheme 1.1 Sperry's synthesis of alocasin A

Scheme 1.2 Sperry's synthesis of scalaridine A

Scheme 1.3 Tasch's synthesis of hyrtinadine A

Scheme 1.4 Mosquera's synthesis of scalaridine A

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.¹⁶ A number of naturally occurring indole alkaloids have been synthesized including tjipanazoles,¹⁷ murrayaquinone,¹⁸ bauerine A,¹⁹ carbazole alkaloids,²⁰ mushroom metabolites,²¹ and the tetracyclic alkaloid ht-13-B²² 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 α -regioselective palladium catalyzed hydrostannylation of *ortho*-substituted arylalkynes reported by Alami et al²³ gave rise to the expected vinylstannane **4** in excellent yield.²⁴ Palladium catalyzed reactions of halopyrazines²⁵ including Sonogashira,²⁶ Suzuki-Miyaura,²⁷ Negishi,²⁸ and Kosugi-Migita-Stille²⁹ 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(dibenzylideneacetone)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-H₂ (10% Pd, pH₂=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).

Scheme 1.5 Synthesis of alocasin A

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,³³ 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-substitution³⁴ have been observed in palladium catalyzed cross couplings using 1-trimethylstannyl-1-phenylethene and 2- and 3-bromopyridines (Scheme 1.6).³⁵

Scheme 1.6 Attempted cross coupling of **4** with 3,5-dibromopyridine (**9**)

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. Hydrostannylation of ethyne-substituted heterocycles are relatively rare in the literature. A single example of a copper catalyzed, α -regioselective hydrostannylation, of 2-ethynylpyridine using hexamethylditin was reported by Yoshida et al.³² A palladium catalyzed hydrostannylation of an *N*-protected 3-ethynylindole also gave exclusively α -stannylated product.³⁶ In contrast, palladium catalyzed hydrostannylation of 2-ethynylpyridine with an ionic liquid supported stannane was shown to be relatively unselective having an α/β -ratio of 38:62.³⁷

In our case, palladium catalyzed hydrostannylation of 3,5-diethynylpyridine (**10**) gratifyingly furnished **11** with exclusive α -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 debenzoylation afforded scalaridine A. Synthetic scalaridine A was spectroscopically and thermally identical to sample obtained from natural sources (^1H NMR, ^{13}C NMR, IR, HRMS, mp). Starting from **10**, the overall yield was 13% in four synthetic transformations (Scheme 1.7).

Scheme 1.7 Synthesis of scalaridine A

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.³⁸ 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 ¹H NMR wherein a doublet resonance at δ 8.65 ppm integrating to two protons and a triplet at δ 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).³

Scheme 1.8 Attempted cross coupling of **4** with 2,5-dibromopyrimidine (**15**)

Here as well the reductive cyclization precursor was prepared by Kosugi-Migita-Stille coupling by reversing the polarity of the coupling partners. Double Sonogashira coupling⁴⁰ 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 debenzylolation proceeded eventually to give hyrtinadine A. The spectroscopic data (^1H 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).

Scheme 1.9 Synthesis of hyrtinadine A

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).

Scheme 1.10 Synthesis of hyrtinadine B

1.C Conclusion

Expedient synthetic routes to four naturally occurring indole alkaloids, allocasin 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 hydrostannylations of heteroarylethynes indicates that an *ortho*-substituent is not a requirement for high α -regioselectivity when ethynyl substituted heterocycles are used.

Chapter 2 Double palladium catalyzed reductive cyclizations. Synthesis of 2,2'-, 2,3'-, and 3,3'-bi-1*H*-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. Cadogan⁴³ and Sundberg⁴⁴ 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.⁴⁵ 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-1*H*-indole (**38**). The cyclization precursor, 1,4-bis(2-nitrophenyl)-1,3-butadiene (**33**), was prepared following the procedure of Lowinger et al⁴⁶ 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 system, in the presence of carbon monoxide ($p\text{CO}=6$ 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 gold⁴⁹ and base⁵⁰ catalyzed cyclization of the

diamine corresponding to **33**, Cadogan-Sunderberg type cyclizations using triphenylphosphine⁵¹ or triphenylphosphite,⁵² and double Madelung cyclization.⁵³ Pertinent to the current methodology, Cenini et al. reported a Pd(TMB)₂-TMphenanthroline⁵⁴ 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%).⁵⁵ A related reaction has also been described by Davies et al. using a palladium catalyzed route without any experimental details or yields.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-nitrocinnamaldehyde (**32**) in the presence of a base. 5-Bromo-2-nitrocinnamaldehyde, 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-1*H*-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-1*H*-indoles

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

^aIsolated yield of pure product after chromatography. ^bMixtures of *EE/ZZ* isomers obtained for **35-37**.

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

After the successful synthesis of 2,2'-bi-1*H*-indoles, double cyclization of 2,3-bis(2-nitrophenyl)-1,3-butadienes to give 3,3'-bi-1*H*-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(carboxyloxy)-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-1*H*-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)ethenyltin 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-1*H*-indoles

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

^aIsolated yield of product after chromatography. ^bPdCl₂(PPh₃)₂ used. ^cCuCl used.

As an example of pyridine-linked biindole, 4,4'-diaz-3,3'-bi-1*H*-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'-diaz-3,3'-bi-1*H*-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**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 SiO₂/K₂CO₃ stationary phase as described by Harrowven et al.⁷² Double reductive cyclization smoothly converted **67** to the desired 3,3'-biindole in quantitative yield (Scheme 2.3).⁷³

The parent cyclization precursor **71** was prepared in moderate yield by the treatment of the Wittig salt with 2-(2-nitrophenyl)-2-propenal (**70**)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-1*H*-indoles (**75-78**) in 61-72% yields. The results are summarized in Table 2.3.

Table 2.3 Synthesis of 2,3'-bi-1*H*-indoles

Phosphane	Aldehyde	Diene ^a	2,3'-Bi-1 <i>H</i> -indole ^a
27 (R=H)	70	71 (R=H, 41%)	75 (R=H, 61%)
29 (R=3-OMe)	70	72 (R=3-OMe, 38%)	76 (R=7-OMe, 72%)
30 (R=4-Br)	70	73 (R=4-Br, 21%)	77 (R=6-Br, 66%)
69 (R=5-Br)	70	74 (R=5-Br, 22%)	78 (R=5-Br, 67%)

^aIsolated yield of pure product after chromatography

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**)⁷⁹ to the palladium catalyzed reductive cyclization conditions for 56 h did not furnish the double cyclization product indolo[3,2-*b*]indole (**80**)⁸⁰ but gave two isomeric tetracyclic compounds indolo[1,2-*c*]quinazolin-6(5*H*)-one (**81**) and 5,11-dihydro-6*H*-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.⁸¹ 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**.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.⁸³ 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).⁸⁴

Scheme 2.4 Reductive cyclization of **79**

Scheme 2.5 Reductive cyclization of **84**⁸⁴

The formation of indolo[1,2-*c*]quinazolin-6(5*H*)-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(5*H*)-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).

Scheme 2.6 Reductive cyclization of **88**

Scheme 2.7 Reductive cyclization of **91**

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-iodo-2-nitrobenzene in good yield.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 triphenylphosphine⁸⁶ or triethyl phosphite⁸⁷ 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,⁸⁸ photochemical cyclizations of indole-2-carboxylic acid arylamides,⁸⁹ and 3-(2-azidophenyl)-*N*-phenylacrylamides,⁹⁰ oxidative cyclizations of 3-arylindole-2-carboxamides,⁹¹ and a platinum catalyzed reduction of ethyl 3-(2-nitrophenyl)-1*H*-indole-2-carboxylates.⁹²

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-1*H*-indoles

3.A Introduction

Halogen and/ or sulfur containing 3,3'-bi-1*H*-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-1*H*-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-1*H*-indole (**104**) was later isolated from the same species.¹¹⁰ More recently was isolated 2,2',5,5',6,6'-hexabromo-3,3'-bi-1*H*-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 brongniartii*. The only example of a 3,3'-bi-1*H*-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-1*H*-indoles

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).¹¹³ For instance, reductive cyclization of 2,3-bis(2-nitrophenyl)-1,3-butadiene (**52**) gave the parent 3,3'-bi-1*H*-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

3.B Results and Discussion

Biindole **120** has previously been prepared by a palladium catalyzed oxidative dimerization of 5-bromoindole (Scheme 3.2),⁶⁷ reductive cyclization⁷³ and a two-step procedure employing a nucleophilic addition of 5-bromoindole to 5-bromoisatine followed by borane reduction of the intermediate (Scheme 3.3).¹¹⁴

Scheme 3.2 Palladium catalyzed oxidative dimerization of 5-bromoindole

Scheme 3.3 Two common routes to **16**

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 trimethylsilylethyne 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 α -selectivity (Scheme 3.4). No trace of the β -isomer was observed by ¹H NMR of the crude reaction mixture.^{23b} 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-1*H*-indole **111**. The ¹H NMR and ¹³C 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 (CCl_4) 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-1*H*-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-1*H*-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-SiO₂ in dichloromethane gave 2,6-dibromo-3-cyanomethylindole (81%), 2,5-dibromo-3-cyanomethylindole (3%), and 2,4-dibromo-3-cyanomethylindole (5%).¹¹⁶ 3-Methylindole afforded selectively 2,6-dibromo-3-methylindole using NBS-SiO₂ in dichloromethane¹¹⁷ 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-1*H*-indole **56**

3.C Conclusion

The naturally occurring polybrominated indoles 2,2',5,5'-tetrabromo-3,3'-bi-1*H*-indole, 2,2',6,6'-tetrabromo-3,3'-bi-1*H*-indole, and 2,2',5,5',6,6'-hexabromo-3,3'-bi-1*H*-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-nitrobenzeneamines and organic halides in the presence of a base and by Popov and Kryshalyuk for the formation of 2-substituted *N*-hydroxybenzimidazoles from 2-nitrobenzeneamines (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-protozoa¹²⁷ and anti-HIV activities.^{123d}

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

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 ¹H 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 ¹H 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

Entry	Eq. NaH	Eq. MeI	Solvent	Alkoxybenzimidazoles ^a		
1 ^b	1.05	1.05	DMSO	128^c	--	--
2 ^d	1.05	2.10	DMSO	128 (1%)	--	130 (34%)
3 ^e	1.05	3.17	DMSO	128 (3%)	--	130 (30%)
4	2.10	1.05	DMSO	128 (2%)	129 tr.	130 (74%)
5	2.10	2.10	DMSO	128 (5%)	129 (17%)	130 (56%)
6	2.10	3.16	DMSO	128 (7%)	129 (18%)	130 (46%)
7	3.15	3.15	DMSO	128^c	129 (69%)	130^c
8	3.75	3.33	DMSO	128 (5%)	129 (64%)	130 (2%)
9	5.0	5.0	DMSO	128^c	129 (65%)	--
10	3.74	3.20	DMF	128 (21%)	129 (8%)	--
11	3.75	3.32	NMP	128^c	129 (2%)	--
12	3.74	3.20	MeCN	128 (65%)	129 (13%)	--

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

Based on the results from table 4.1, we devised two set 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 2*H*-*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 2*H*-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

		Condition A	Alkoxybenzimidazoles ^b

Entry	Enamine	Time/Temp ^a	% Yield	% Yield	% Yield	Σ (%) ^c
1	127 (R=4-OMe)	1 h-0 °C	128 ^d	129 (71)		71
2	127	2 min-rt		129 (71)		71
3	127	9 h-rt	128 ^d	129 (69)		69
4	131 (R=4-Cl)	1 h-0 °C		132 (86)		86
5	131	1 h-rt		132 (94)		94
6	133 (R=4-Br)	1 h-0 °C	134 ^d	135 (78)		78
7	133	4 min-rt	134 ^d	135 (93)		93
8	136 (R=4-F)	1 h-rt		137 (75)		75
9	138 (R=4-Me)	1 h-0 °C	139 (28)	140 (52)	141 (5)	85
10	138	1 h-rt	139 (27)	140 (68)		95
11	122 (R=H)	1 h-0 °C	124 (5)	125 (57)	126 (15)	77
12	122	1 h-rt	124 (31)	125 (34)		65
13	142 (R=4-CO ₂ Me)	10 min-rt ^f				-
14	142	24 h-rt	143 (74)			74
15	23 (R=4-NO ₂)	1 h-0 °C ^g				-
16	144	24 h-rt				-
17	145 (R=5-OMe)	1 h-rt ⁱ				-

18	145 ⁱ	24 h-rt	146 (51)			51
19	147 (R=5-Cl)	6 min-rt ^k	149 (9)			9
20	147	1 h-0 °C	148 (56)	149 (27)		83
21	147	1 h-rt	148 (52)	149 (31)		83
22	150 (R=5-Br)	10 min-rt	151 (67)	152 (28)		95
23	150	1 h-rt	151 (55)	152 (29)		84
24	153 (R=5-Me)	1 h-0 °C	154 (21)	155 (22)	156 (20)	63
25	153	10 min-rt	154 (31)	155 (26)		57
	157 (R=4-OMe)		158	159		
26	157	1 h-0 °C	128 ^d	158 (78)		78
27	157	2 min-rt	128 ^d	158 (84)	159 (11) ^l	95
	160 (R=Br)		134	161	162	
28	160	1 h-0 °C	134 (22)	161 (22)	162 (13)	57
29	160	38 min-rt	134 (92)			92

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.

b. Isolated yields of pure products after chromatography unless stated as ~%. The ~% are yields calculated from ¹H NMR spectrum of an inseparable mixture.

c. Total yield of benzimidazoles isolated

d. Trace amount of the compound was observed in the ¹H NMR of the crude reaction mixture.

e. Trace amount of **138** was observed in the ¹H NMR spectrum.

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.

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.

h. No product or unreacted **144** was observed.

i. 5-Methoxy-2-nitro-*N*-methylaniline¹²⁸ 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 ¹H 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-carbomethoxy- 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 2*H*-*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 2*H*-*N*-methoxybenzimidazoles.

Table 4.3 Base-mediated synthesis of benzimidazoles under Condition B

Alkoxybenzimidazoles ^b					
Entry ^a	Enamine	% Yield	% Yield	% Yield	Σ (%) ^c
1	122 (R=H)			126 (55) ^d	55
2	123 (R=4-OMe)	128 (2)		130 (74)	76
3	131 (R=4-Cl)		132 (20)	163 (59)	79
4	133 (R=4-Br)		135 (22)	164 (68)	90
5	136 (R=4-F)		137 (15)	165 (56)	72
6	138 (R=4-Me)	139 (11)		141 (45)	55
7	142 (R=4-CO ₂ Me) ^e				-

8	142 ⁱ	143 (73)		73
9	145 (R=5-OMe) ^g			-
10	145 ^f	146 (64)		64
11	147 (R=5-Cl)	149 (15)	166 (55)	70
12	140 (R=5-Br)	152 (16)	167 (63)	79
13	153 (R=5-Me)		156 (61)	61

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

15	160 (R=4-Br)	134 (22)	162 (52)	74

- 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.
- Isolated yields of pure products after chromatography unless otherwise stated. The % yields are calculated from the ¹H NMR spectrum of an inseparable mixture.
- Total yield of benzimidazoles.
- Trace amount of **124** was observed in the ¹H NMR spectrum.
- A nearly 3:1 mixture of 4-carbomethoxy-*N*-methyl-*N*-(2-methyl-1-propen-1-yl)-2-nitroaniline and **142** was observed in the ¹H NMR spectrum of the crude reaction mixture.
- The base substrate mixture was stirred for 24 h before addition of MeI.
- Neither product nor starting material was observed.

The formation of 2*H*-*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

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^{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**

Entry	Time/Temp ^a	Electrophile (R-X)	Alkoxybenzimidazoles ^b			Σ (%) ^c
1	1 h-0 °C	Bn-Br		171 (38%)	172 (29%)	67%
2	2 min-rt	Bn-Br		171 (19%)	172 (50%)	69%
3	1 h-0 °C	Allyl bromide	173 (5%)	174 (14%)	175 (31%)	50%
4	1 min-rt	Allyl bromide		174 (59%)		59%
5	2 min-rt	CH ₂ I ₂		176 (40%)		40%
6	1 min-rt	Propargyl bromide	177 (6%)		178 (47%)	53%
7	1 h-0 °C	3-Bromo-1-butyne	179 (9%)		180 (41%)	50%
8	2 min-rt	3-Bromo-1-butyne			180 (66%)	66%

a. 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.

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

c. 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.¹²⁹ In the preparation of indazole-*N*-oxide from azomethine ylides, Nyerges et al proposed 1,7-electrocyclization.^{130,131} 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.¹³²

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-2*H*-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

In the course of our investigation for suitable reaction conditions, we found that the reaction can be tailored to give *N*-alkoxy-2*H*-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 1*H*-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 2*H*- *N*-alkoxybenzimidazole was reported (Scheme 5.2).

Scheme 5.2 Gardiner's synthesis of *N*-methoxybenzimidazole

The objective of this work was to develop short and efficient synthetic routes to 2*H*-*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.¹³⁴ 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 2*H*-*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

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

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**

Entry	Enamine ^a	Electrophile	Benzimidazole ^b
1	<p style="text-align: center;">127</p>	Benzyl bromide	193 (82%)
2		Allyl bromide	194 (100%)
3		2-Methyl-3-bromopropene	195 (90%)
4		Propargyl bromide	196 (15%)
5		3-Bromo-1-butyne	197 (12%)
6		Acetyl chloride	198 (54%)
7		1-Bromoheptane	199 (16%)
8		1-Iodobutane	200 (15%)
9		2-Iodopropane	201 (8%)

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.¹³⁸ For example, treatment of **202** with vinyltin in the presence of Pd(PPh₃)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 PdCl₂(PPh₃)₂ and LiCl in DMF at 24 °C.^{139,140} 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 PhBu₃Sn in the presence of Pd₂(dba)₃-Pd(*t*-Bu)₃¹⁴¹ and CsF in dioxane at ambient temperature gave exclusive C-Cl coupling products.^{142,143} 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 reports¹⁴⁴⁻¹⁴⁹ 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.¹⁵⁰

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.^{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 ¹H 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 ¹H 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 ¹H, ¹⁹F and ¹³C NMRs. A very indicative quartet (*J*=320 Hz) in the ¹³C NMR and a resonance at -72.9 Hz in the ¹⁹F NMR confirmed the product to be **205**; the expected C-OTf coupling product was not observed.

Scheme 6.1 Preparation and Kosugi-Migita-Stille coupling of **204**

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, PPh₃, 1,4-dioxane, ethenyltributyltin, reflux
2. Conditions B: PdCl₂(PPh₃)₂, LiCl, ethenyltributyltin, DMF, 24 °C
3. Conditions C: PdCl₂(PPh₃)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 Stille 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 ¹H NMR of the crude reaction mixture (Table 6.1). When the reaction was repeated, in our hands only product **206** was detected in the ¹H NMR of the crude reaction mixture (600 MHz, Table 6.1, entry 2). The palladium catalyst, Pd(PPh₃)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 PPh₃ gave the same exclusive selectivity as Pd(PPh₃)₄ (entry 3). So, this catalyst system (Pd(dba)₂ and PPh₃) was used as a substitute for Pd(PPh₃)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).¹⁵¹ 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.¹⁵² 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

Entry	Conditions ^a	Product (s) & ratio ^b		Yield ^c

1 ^d	Pd(PPh ₃) ₄ , 1,4-dioxane, reflux	33	1	77%
2	Pd(PPh ₃) ₄ , 1,4-dioxane, reflux	>30	1	
3	Pd(dba) ₂ , 4 PPh ₃ , 1,4-dioxane, reflux	>30	1	30%
4	PdCl ₂ (PPh ₃) ₂ , 1,4-dioxane, reflux	>30	1	90%
5 ^d	PdCl ₂ (PPh ₃) ₂ , LiCl, DMF, 24 °C	0	100	77%
6	PdCl ₂ (PPh ₃) ₂ , LiCl, DMF, 24 °C	1	6.7	
7 ^d	PdCl ₂ (PPh ₃) ₂ , LiCl, DMF, 70 °C	1	5	45% ^e
8 ^d	PdCl ₂ (PPh ₃) ₂ , LiCl, 1,4-dioxane, reflux	1	6	75% ^e

9	Pd(dba) ₂ , 4 PPh ₃ , 1,4-dioxane, reflux	>30	1	5%
10	PdCl ₂ (PPh ₃) ₂ , LiCl, DMF, 24 °C	1	5.9

11	Pd(dba) ₂ , 4 PPh ₃ , 1,4-dioxane, reflux	30	1 ^f	34% ^g
12	PdCl ₂ (PPh ₃) ₂ , 1,4-dioxane, reflux ^{h,i}	30	1	47%
13	PdCl ₂ (PPh ₃) ₂ , LiCl, DMF, 24 °C	1	6.3 ^j	K
14 ^l	PdCl ₂ (dppp), LiCl, DMF 25 °C ^m	0	100	25%

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 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 ¹H NMR spectrum. g) Isolated as a mixture with **203**. Yield calculated from ¹H 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 ¹H NMR spectrum. K) Product **212** was not isolated. l) See reference 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.¹⁵¹ On the other hand, reaction of **202** with 4-MeC₆H₄SnBu₃ in the presence of PdCl₂(PPh₃)₂, PPh₃, and CuBr in refluxing dioxane afforded C-Br coupling product exclusively.¹³⁹ For Suzuki-Miyaura couplings with aryl/alkenylboronic acids, the C-Br bond generally undergoes selective coupling regardless of electron density of the substrate and regardless of the palladium based catalyst used.^{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 site¹⁵⁷ or at the least hindered but more electron rich site.¹⁵⁸ Oh-e, Miyaura and Suzuki established the order of reactivity as I>Br>OTf for Suzuki-Miyaura couplings with 9-BBN reagent.¹⁵⁹ Fu and coworkers have shown that the chemoselectivity could be changed depending on the ligand system and the type of the reaction solvents.¹⁴³ Similarly, Sonogashira coupling of **202** and **203** with phenylethyne gave exclusive coupling at C-Br bond in the presence of 10 mol% of ZnCl₂ at ambient temperature¹⁶⁰ whereas the same reaction gave only C-OTf coupling product when trimethylsilylethyne was used as a coupling partner in the presence of CuI.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.^{152,162} Negishi coupling of **207** with organozinc reagents gave C-OTf coupling product in the presence of PdCl₂(dppp)¹⁵², [Pd₂(dba)₃]-dppb¹⁶³. In contrast, coupling of **202** with Me₂Zn gave C-Br coupling product using Pd(OAc)₂-AsPPh₃ and a 3:1 ratio of C-Br to C-OTf coupling products when PdCl₂(dppe)₂ was used.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 ethenyltributyltin. Under Conditions A, a combination of relatively air stable $\text{Pd}(\text{dba})_2$ and PPh_3 , a substitute for $\text{Pd}(\text{PPh}_3)_4$ 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 $\text{PdCl}_2(\text{PPh}_3)_2$ 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 $\text{PdCl}_2(\text{PPh}_3)_2$ 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 ^1H 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 ^1H 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

Entry	Substrate	C-Br coupling product	C-OTf coupling product	Additional product(s)	
1-A ^a		223 (36%)			(^b)
1-B ^c	213 (~27%)	223 (20%)	224 (38%)		(~12%)
1-C	213	223 (77%)			
1-D ^e	213 (75%)				
1-E ^f	213	223 (19%)	224 (49%)	225 (10%)	(11%)
1-F ^g	213	223 (91%)			
2-A		226 (82%)		227 (9%)	
2-B	214	226 (~9%) ^h	228 (~37%) ^h	227 (15%)	
2-C	214	226 (68%)			
2-D ⁱ	213	226 (68%)		227 (4%)	
3-A		229 (68%)		230 (2%)	
3-B	215 (17%) ⁱ	229 (~23%) ⁱ	231 (36%)	230 (3%)	
3-C	215	229 (81%)		230 (3%)	
3-D ⁱ	215	229 (74%)		230 (2%)	
4-A		232 (60%)	233 (3%)	234 (30%)	
4-B	216		233 (61%)	234 (trace)	
4-C	216	232 (68%)	233 (1%)	234 (23%)

5-A ^j	217 (9%)	235 (24%)	236 (~5%) ^k	225 (~5%) ^k	(7%)
5-B ^l	217 (5%)		236 (43%)		(12%)
5-C	217	235 (66%)	236 (~4%) ^k	225 (~8%) ^k

6-A ^m	218 (7%)	237 (22%)			(7%)
6-B ⁿ	218 (8%)		238 (57%)		(16%)
6-C ^o	218	237 (94%)

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

8-A ^p	220	241 (~41%) ^q			
8-B	220		242 (78%)		
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%)		

10-C	222	245 (89%)
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Details of the reaction Conditions A-C

A) Pd(dba)₂ (2 mol%), PPh₃ (8 mol%), 1,4-dioxane, reflux

B) PdCl₂(PPh₃)₂ (2 mol%), LiCl (300 mol%), DMF, ambient temperature

C) PdCl₂(PPh₃)₂ (2 mol%), 1,4-dioxane, reflux

a) A ratio of 1:2 was observed for **213/223** in the ¹H 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 ¹H NMR of the crude reaction mixture. d) A mixture of **213** and 2-bromo-3-nitrophenol was obtained from the ¹H NMR of the mixture. e) PdCl₂(dppp)₂ (2 mol%), LiCl (300 mol%), DMF, ambient temperature used for the reaction. f) PdCl₂(dppp)₂ (2 mol%), DMF, ambient temperature was used for the reaction. g) Pd(PPh₃)₄ (2 mol%), toluene, reflux condition used for the reaction. h) An inseparable mixture of **226** and **228** was obtained; yield calculated from ¹H NMR of the crude reaction mixture. i) An inseparable mixture of **215** and **229** was obtained; yield calculated from the ¹H 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 ¹H NMR of the crude reaction mixture. l) A ratio of 1:6.67 for compounds **217/236** was observed by ¹H NMR of the crude reaction mixture. m) A ratio of 1:2.58 for compounds **218/237** was observed by ¹H NMR of the crude reaction mixture. n) A ratio of 1:5 for compounds **218/239** was observed by ¹H 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 ¹H 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.¹⁶⁵ 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.¹⁶⁶ 4-Cyanobromobenzene has been reported to be 326 times more reactive than the bromobenzene.¹⁶⁷ Stille couplings of usually unreactive aryl fluorides have also been reported.^{168,169}

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.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 $\text{Pd}_2(\text{dba})_3$ 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.^{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 ^1H NMR spectrum of the crude reaction mixtures.

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

6.C Conclusion

The chemoselectivity of Kosugi-Migita-Stille couplings of all isomeric permutations of bromophenyl 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 ^1H 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.¹⁹³ Among other representative examples of pyrroloindole containing natural products include terreusinone A,^{194,195} and indolo[3,2-*b*]carbazole.¹⁹⁶⁻¹⁹⁸ Terreusinone A possesses significant UV-A protecting properties.¹⁹⁵

Figure 7.1 Isomeric pyrroloindoles

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

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

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

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

1*H*,5*H*-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 synthesis¹⁹⁹ intramolecular cyclization of a bis-(β -aminoethyl)-hydroquinone derivative in presence of water.²⁰⁰ The second general methodology includes a double Reissert indole synthesis^{201,202} and a double Batcho-Leimgruber²⁰³ Shannon *et al.* prepared pyrrolo[3,2-*f*]- and -[2,3-*f*]-indoles through the Montmorillonite K-10 clay catalyzed Vilsmeier formylation of pyrrole.²⁰⁴

Scheme 7.1 Vilsmeier formylation route to pyrroloindoles

Samsoniya *et al.* reported numerous methods to prepare pyrroloindoles.^{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.

Scheme 7.2 Samsoniya et al synthesis of pyrroloindoles

Although the second methodology by Samsoniya 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

While the palladium-catalyzed aerobic oxidative bicyclization route to the preparation of pyrroloindoles from *N*-aryl imines reported by Yoshikai et al²⁰⁷ 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

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-acetylamine 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

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-1*H*-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

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 ($\text{Pd}(\text{dba})_2$, 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 ($\text{Pd}(\text{OAc})_2$, dppp, 1,10-phen) which improved the yield, but this was again not very satisfactory (Table 7.1, entry 2). Although a combination of $\text{Pd}(\text{dba})_2$ 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 ($\text{Pd}(\text{OAc})_2$, 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

285

$\xrightarrow[\text{Time}]{\text{Conditions}}$
 CO (6 atm), 120 °C

336

337

Entry	Conditions	Time (h)	336 % Yield	337 % Yield	Σ (%)
1.	Pd(dba) ₂ , dppp, 1,10-phen	89	23	-	23
2.	Pd(OAc) ₂ , dppp, 1,10-phen	100	35	-	35
3.	Pd(dba) ₂ , PPh ₃	126	64	-	64
4.	Pd(OAc) ₂ , PPh ₃	126	-	54	54
5.	Pd(OAc) ₂ , dppp	36	9	49	58
6.	Pd(OAc) ₂ , 1,10-phen	48	41	-	48
7.	Pd(OAc)₂, 1,10-phen	90	70	-	70

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 1*H*,8*H*-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**)²¹⁰ 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**)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

A selective oxidative iodination of 2,5-dinitrophenol (**267**)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.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**).

Nitration of 5-iodo-2-nitrophenol (**269**)²¹⁴ with sodium nitrate in sulfuric acid afforded 5-iodo-2,4-dinitrophenol (**274**)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 dinitrobromophenols **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

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** **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**),²⁰⁹ 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 $\text{PdCl}_2(\text{PPh}_3)_2$ and/or PPh_3 in 1,4-dioxane at 90-100 °C and the results are summarized in Table 7.2.

Table 7.2 Synthesis of cyclization precursor by double Kosugi-Migita-Stille coupling

Entry	Aryl-Br/OTf	Tin reagent	Product

1	256	282 (R=R'=H)	285 (R=R'=H, 67%)
2	256	283 (R=H, R'=Me)	286 (R=H, R'=Me, 85%)
3	256	284 (R=Me, R'=H)	287 (R=Me, R'=H, 70%)

4	288	282	289 (R=R'=H, 73%)
5	288	283	290 (R=H, R'=Me, 93%)
6	288	284	291 (R=Me, R'=H, 87%)

7	266	282	292 (R=R'=H, 60%)
8	266	283	293 (R=H, R'=Me, 52%)
9	266	284	294 (R=Me, R'=H, 54%)

10	288	282	295 (R=R'=H, 34%)

11	288	283	296 (R=H, R'=Me, 48%)
12	288	284	297 (R=Me, R'=H, 47%)

13	273	282	298 (R=R'=H, 32%)

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.

Entry	Aryl-Br/I/Cl/OTf	Tin reagent	Products	
1		282	300 (65%)	285 (2%)
2		283	301 (64%)	
3		284	302 (64%)	287 (2%)
4			303 (50%)	
5		282	205 (35%)	
6		283	305 (75%)	290 (12%)

7		284
	276		306 (51%)	291 (6%)
8		282
	266		307 (76%)	292 (4%)
9		283
	266		308 (70%)	293 (7%)
10		282
	281		309 (35%)	295 (10%)
11		283
	281		310 (45%)	296 (6%)
12		284
	281		311 (51%)	297 (3%)
12		284

13	273	282	312 (42%)

	273	284	313 (45%)

The second alkene was thought to be readily introduced by an aryl triflate – organotin cross coupling using the conditions described by Echavarren and Stille ($\text{PdCl}_2(\text{PPh}_3)_2$, LiCl , DMF, RT). However attempted coupling of **300** and **307** resulted only in a replacement of the triflate 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 triflate 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 triflates 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 7.4 Synthesis of unsymmetrical cyclization precursors

Entry	Aryl-Br/I/Cl/OTf	Tin reagent	Product
1	300	283	317 (66%)
2	300	284	318 (64%)
3	302	283	319 (45%)
4	300	Bu₃Sn	320 (51%)
5	301	Bu₃Sn	321 (51%)
6	303	283	321 (43%)

7	302	284	322 (55%)
8	205	284	323 (64%)
9	305	284	324 (73%)
10	307	283	325 (64%)
11	308	284	326 (65%)
12	309	283	327 (63%)

13	309	284	328 (64%)
14	311	283	329 (50%)
15	313	282	330 (45%)
16	312	284	331 (27%)

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**²¹⁶ was converted to aryl iodide **333** via reaction of the corresponding diazonium salt with potassium iodide (Scheme 7.15). Employing Mundla's methodology²¹⁷ 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.

Scheme 7.15 Alternative route to **330** **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 ($\text{Pd}(\text{OAc})_2$, 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 1*H*,8*H*-pyrrolo[3,2-*g*]indoles (Type A)

Entry	Substrate	Reaction conditions	Pyrroloindole	Indole

1	286	Pd(OAc) ₂ -phen	338 (67%)	
2	286	Pd(OAc) ₂ -dppp	338 (9%)	339 (69%)
3	286	Pd(OAc) ₂ - dppp-phen	338 (36%)

4	287	Pd(OAc) ₂ -phen	340 (54%)	
5	287	Pd(dba) ₂ -dppp- phen	340 (67%)	
6	287	Pd(dba) ₂ -PPh ₃	340 (62%)	
7	287	Pd(dba) ₂ -dppp	340 (16%)	341 (78%)

8	317	Pd(OAc) ₂ -phen	342 (63%)	
9	317	Pd(OAc) ₂ -PPh ₃	342 (25%)

10	318	$\text{Pd}(\text{OAc})_2\text{-phen}$	343 (64%)

11	319	$\text{Pd}(\text{OAc})_2\text{-phen}$	344 (67%)

12	320	$\text{Pd}(\text{OAc})_2\text{-phen}$	345 (68%)

13	321	$\text{Pd}(\text{OAc})_2\text{-phen}$	346 (73%)

14	322	$\text{Pd}(\text{OAc})_2\text{-phen}$	347 (74%)

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 $\text{Pd}(\text{OAc})_2\text{-1,10-phen}$ 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 $\text{Pd}(\text{dba})_2\text{-dppp-1,10-phen}$; 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 $\text{Pd}(\text{dba})_2\text{-dppp-1,10-phen}$, 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 $\text{Pd}(\text{dba})_2\text{-PPh}_3$ 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 be seen, 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 dialkenyldinitrobenzenes went on smoothly to give rise to indoles in high isolated yields after chromatography. Completely different observations were noticed when the unsymmetrically substituted dialkenyldinitrobenzenes 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 7.6 Attempted synthesis of pyrroloindoles (Type B-E)

Entr y	Substrate	Conditions	Pyrroloindole	Indole
1	289	Pd(OAc) ₂ , phen		
2	290	Pd(OAc) ₂ , phen		348 (37%)
3	290	Pd(dba) ₂ , PPh ₃		348 (64%)
4	291	Pd(dba) ₂ , dppp, phen	349 (56%)	350 (78%)
5	291	Pd(dba) ₂ , dppp	349 (16%)	350 (20%)
6	291	Pd(dba) ₂ , phen		350 (85%)
7	291	Pd(dba) ₂ , PPh ₃		
8	292	Pd(OAc) ₂ , phen	351 (60%)

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 ,	356 (86%)

		phen	
17	297	Pd(OAc) ₂ , dppp, phen	356 (51%)
18	297	Pd(OAc) ₂ , PPh ₃	356 (84%)

19	327	Pd(OAc) ₂ , dppp, phen	357 + 358 (46%, 1:1)

20	328	Pd(OAc) ₂ , phen	359 + 360 (70%, 1:1)

21	329	Pd(OAc) ₂ , phen	361 + 362 (77%, 1:1)

22	298	Pd(OAc) ₂ , phen	363 (50%) 364 (20%)

23	298	Pd(OAc) ₂ , PPh ₃		364 (49%)

24	331	Pd(OAc) ₂ , phen		365 (73%)

25	330	Pd(OAc) ₂ , phen		366 (61%)
26	330	Pd(dba) ₂ , dppp, phen	367 (minor product)	366 (major product)

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-PPh₃ -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-PPh₃ -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 7.7 Synthesis of *N*-tosylated indoles

Entry	Indole	Reaction conditions	<i>N</i> -Tosyl indole
1	 350		 372 (77%)
2	 348		 373 (69%)
3	 353		 374 (72%)
4	 352		 375 (71%)
5	 354		 376 (77%)
6	 355	NaH, TsCl, DMF, 0 °C-rt	 377 (79%)

7	366	378 (77%)
8	337	379 (80%)

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)

Entry	<i>N</i> -Tosyl indole	Reaction conditions	Pyrroloindole
1	372	Pd(dba) ₂ , dppp, 1,10-phen	380 (79%)
2	373	CO (6 atm), DMF, 120 °C	381 (70%)

3	374	382 (88%)
4	375	383 (76%)
5	376	384 (89%)
6	377	385 (77%)
7	378	386 (87%)
8	379	379 (70%)

7.E Conclusion Palladium catalyzed, carbon monoxide mediated, double reductive *N*-heterocyclization of dialkenyldinitrobenzenes 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-Benzoyloxy-2-nitrophenyl)-1-trimethylsilylethyne (2). 5-Benzoyloxy-2-nitro-1-bromobenzene⁴¹ (**1**) (3.91 g, 12.7 mmol) was dissolved in toluene (10 mL) and triethylamine (NEt₃, 40 mL) whereby bis(triphenylphosphine)palladium 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, *J*=9.2 Hz, 1H), 7.43-7.36 (m, 5H), 7.18 (d, *J*=2.8 Hz, 1H), 6.97 (dd, *J*=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-Benzoyloxy-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, *J*=9.2 Hz, 1H), 7.45-7.35 (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) δ 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 $\text{C}_{15}\text{H}_{12}\text{NO}_3$ ($\text{M}+\text{H}^+$) 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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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_2O (3x30 mL) and brine (30 mL). The organic layer was dried (MgSO_4), filtered, and the solvent was 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. ^1H NMR (400 MHz, CDCl_3) δ 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, $J=2.0$ 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) δ 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 $\text{C}_{27}\text{H}_{40}\text{NO}_3\text{Sn}$ ($\text{M}+\text{H}^+$) 546.2030, found 546.2025.

2,5-Di(1-(5-benzyloxy-2-nitrophenyl)-1-ethenyl)pyrazine (6) and 2,3-di(5-benzyloxy-2-nitrophenyl)-1,3-butadiene (7). To a solution of 2,5-dibromopyrazine (**5**) (100 mg, 0.420 mmol) and **4** (458 mg, 0.841 mmol) in dry DMF (2 mL) was added bis(dibenzylideneacetone)palladium ($\text{Pd}(\text{dba})_2$, 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 $^\circ\text{C}$ for 41 h. EtOAc (25 mL) was added and the mixture was washed with H_2O (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 $\text{SiO}_2/\text{K}_2\text{CO}_3$ (10% K_2CO_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 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{34}\text{H}_{27}\text{N}_4\text{O}_6$ ($\text{M}+\text{H}^+$) 587.1931, found 587.1925. Analytical data for **7**: mp=158-160 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{30}\text{H}_{25}\text{N}_2\text{O}_6$ ($\text{M}+\text{H}^+$) 509.1713, found 509.1715.

5,5'-Dibenzyloxy-3,3'-(2,5-pyrazindiyl)bis-1(*H*)-indole (8). To a solution of **5** (114 mg, 0.194 mmol) in dry DMF (2 mL), in a treaded 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 $\text{Pd}(\text{dba})_2$ (8 mg, 0.014 mmol). The tube was fitted 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_2O (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 yellow powder. mp=264-265 °C; ^1H NMR (400 MHz, acetone- d_6) δ 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) δ 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 $\text{C}_{34}\text{H}_{26}\text{N}_4\text{O}_2$ ($\text{M}+\text{H}^+$) 523.2134, found 523.2116.

Alocasin A. To a solution of **8** (41 mg, 0.078 mmol) in EtOH (2 mL), in a treaded pressure tube, was added Pd/C (10%-Pd, 18 mg, 0.017 mmol). The tube was fitted 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 faint yellow solid. mp=244-245 °C (lit. mp=243-244 °C);⁹ ^1H NMR (400 MHz, CD_3OD) δ 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_3OD) δ 152.8, 148.4, 141.4, 133.6, 127.3, 126.6, 113.8, 113.3, 113.2, 106.1; IR (ATR) 3298, 2927, 1551, 1466, 1154 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_2$ ($\text{M}+\text{H}^+$) 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 $\text{Pd}(\text{dba})_2$ (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 $\text{SiO}_2/\text{K}_2\text{CO}_3$ (10% K_2CO_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 Bu₃SnH (1.03 mg, 3.59 mmol) in the presence of PdCl₂(PPh₃)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. ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₃₃H₆₂NSn (M+H⁺) 712.2926, found 712.2929.

2-Iodo-4-benzyloxy-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 K₂CO₃ (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 (MgSO₄), 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 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.97 (d, *J*=9.2 Hz, 1H), 7.63 (d, *J*=2.8 Hz, 1H), 7.45-7.36 (m, 5H), 7.00 (dd, *J*=8.8, 2.8 Hz, 1H), 5.12 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₁₃H₁₁INO₃ (M+H⁺) 355.9784, found 355.9785.

3,5-Di(5-benzyloxy-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), PPh₃ (111 mg, 0.423 mmol) and CuI (403 mg, 2.11 mmol) in DMF (6 mL), as described for **5** (120 °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. ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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, 1509, 1332, 1224 cm⁻¹; HRMS (ESI) calcd for C₃₅H₂₈N₃O₆ (M+H⁺) 586.1978, found 586.1979.

3,5-Bis(5-benzyloxy-3-indolyl)pyridine (14). Treatment of a solution of **13** (176 mg, 0.300 mmol) in the presence of Pd₂(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 °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. ¹H NMR (400 MHz, CDCl₃) δ 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 $\text{C}_{35}\text{H}_{28}\text{N}_3\text{O}_2$ ($\text{M}+\text{H}^+$) 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), scalaridine A (45 mg, 0.13 mmol, 79%) as yellow solid. mp=321 °C dec. (lit. mp = 319-329 °C dec.); ^{13}H NMR (400 MHz, $\text{DMSO}-d_6$) 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, $\text{DMSO}-d_6$) δ 151.6, 143.7, 132.0, 131.3, 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 $\text{C}_{21}\text{H}_{16}\text{N}_3\text{O}_2$ ($\text{M}+\text{H}^+$) 342.1243, found 342.1240.

(5-Benzyloxy-2-nitrophenyl)ethene (16), 2,3-di(5-benzyloxy-2-nitrophenyl)-1,3-butadiene (7), 1-(5-benzyloxy-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 $\text{Pd}(\text{dba})_2$ (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 $\text{SiO}_2/\text{K}_2\text{CO}_3$ (10% K_2CO_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; ^1H 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} .

Analytical data for **17**: ^1H NMR (400 MHz, CDCl_3) δ 8.65 (d, $J=5.2$ Hz, 1H), 8.18 (d, $J=8.8$ Hz, 1H), 7.46-7.35 (m, 5H), 7.10 (t, $J=5.2$ Hz, 1H), 7.07 (d, $J=2.8$ Hz, 1H), 7.04 (dd, $J=8.8$, 2.8 Hz, 1H), 6.86 (d, $J=1.2$ Hz, 1H), 5.78 (d, $J=1.2$ Hz, 1H), 5.17 (s, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 163.9, 162.6, 156.9, 146.9, 141.6, 138.2, 135.5, 128.7, 128.5, 127.6, 127.0, 122.4, 119.2, 118.4, 113.9, 70.6; IR (ATR) 1583, 1567, 1554, 1506, 1336, 1249, 758, 698 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{16}\text{N}_3\text{O}_3$ ($\text{M}+\text{H}^+$) 334.1192, found 334.1190.

2,5-Di(2-trimethylsilyl-1-ethynyl)pyrimidine (18). A solution of **15** (2.25 g, 9.49 mmol), $\text{PdCl}_2(\text{PPh}_3)_2$ (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 N₂ for 5 min. Triethylamine (25 mL) and a solution of trimethylsilylethyne (2.52 g, 25.6 mmol) in NEt₃ (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 Et₂O (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; ¹H NMR (400 MHz, CDCl₃) δ 8.72 (s, 2H), 0.29 (s, 9H), 0.27 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₄H₂₁N₂Si₂ (M+H⁺) 273.1243, found 273.1240.

2,5-Diethynylpyrimidine (19). A heterogeneous mixture of **18** (744 mg, 2.94 mmol), K₂CO₃ (2.43 g, 17.6 mmol) in MeOH/Et₂O (1:2, 15 mL) was stirred at ambient temperature under an N₂ 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; ¹H NMR (400 MHz, CDCl₃) δ 8.79 (s, 2H), 3.49 (s, 1H), 3.26 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) 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 C₈H₅N₂ (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 PdCl₂(PPh₃)₂ (169 mg, 0.241 mmol) under an atmosphere of N₂. The mixture was stirred at ambient temperature for 5 min followed by slow addition of Bu₃SnH (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. ¹H NMR (400 MHz, CDCl₃) 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 (d_{hex}, *J*=7.2, 3.2 Hz, 12H), 1.04-0.84 (m, 30H); ¹³C NMR (100 MHz, CDCl₃) δ 166.7, 154.4, 153.9, 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 C₃₂H₆₁N₂Sn₂ (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 Pd₂(dba)₃ (56 mg, 0.061 mmol), PPh₃ (65 mg, 0.25 mmol) and CuI (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. ^1H NMR (400 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{34}\text{H}_{27}\text{N}_4\text{O}_6$ ($\text{M}+\text{H}^+$) 587.1931, found 587.1934.

3-[2-(5-benzyloxy-1H-indol-3-yl)-5-pyrimidinyl]-5-benzyloxy-1H-indole (22). Treatment of a solution of **21** (141 mg, 0.240 mmol) in the presence of tris(dibenzylideneacetone)dipalladium ($\text{Pd}_2(\text{dba})_3$, 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 $^\circ\text{C}$, 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 $^\circ\text{C}$; ^1H NMR (400 MHz, DMSO-d_6) δ 11.54 (br, s, 1H), 11.46 (br, s, 1H), 9.09 (s, 2H), 8.26 (s, 1H), 8.19 (s, 1H), 7.88 (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) δ 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, 127.6, 127.6, 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 $\text{C}_{34}\text{H}_{27}\text{N}_4\text{O}_2$ ($\text{M}+\text{H}^+$) 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 $^\circ\text{C}$, 14 h) gave after work up and chromatography (EtOAc/hexanes, 9:1) hyrtinandine A (32 mg, 0.093 mmol, 87%) as a white solid. mp=290-291 $^\circ\text{C}$ (lit. mp = 296 $^\circ\text{C}$); ^1H NMR (400 MHz, DMSO-d_6) δ 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) δ 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 $\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_2$ ($\text{M}+\text{H}^+$) 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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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. ^1H NMR (600 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{18}\text{H}_{33}\text{N}_2\text{Sn}(\text{M}+\text{H}^+)$ 397.1666, found 397.1666.

1-(5-Benzoyloxy-2-nitrophenyl)-1-(4-pyrimidyl)ethene (25). To mixture of **12** (584 mg, 1.64 mmol), PPh_3 (66 mg, 0.25 mmol), CuI (241 mg, 1.26 mmol) and Pd_2dba_3 (58 mg, 0.063 mmol) in DMF (5 mL) at ambient under an atmosphere of N_2 , was added a solution of **24** (500 mg, 1.26 mmol) in DMF (1 mL). The resulting brown reaction mixture was heated at 120 $^\circ\text{C}$ 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 MgSO_4 , 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 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) 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); ^{13}C NMR (100 MHz, CDCl_3) 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 $\text{C}_{19}\text{H}_{16}\text{N}_3\text{O}_3(\text{M}+\text{H}^+)$ 334.1192, found 334.1190.

5-Benzoyloxy-3-(4-pyrimidyl)indole (26). Treatment of a solution of **25** (200 mg, 0.600 mmol) in the presence of $\text{Pd}_2(\text{dba})_3$ (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 $^\circ\text{C}$, 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 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) 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); ^{13}C NMR (100 MHz, CDCl_3) 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 $\text{C}_{19}\text{H}_{16}\text{N}_3\text{O}(\text{M}+\text{H}^+)$ 302.1293, found 302.1291.

Hyrtinadine 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 H_2 , 60 $^\circ\text{C}$, 6 h) gave after work up and chromatography (EtOAc) hyrtinadine B (53 mg, 0.251 mmol, 84%) as a white solid. mp=289-290 $^\circ\text{C}$; ^1H NMR (400 MHz, CD_3OD) 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); ^{13}C NMR (100 MHz, CD_3OD) 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 $\text{C}_{12}\text{H}_{10}\text{N}_3\text{O}(\text{M}+\text{H}^+)$ 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*^{CP}=4.5 Hz), 136.4 (d, *J*^{CP}=6.0 Hz), 135.4 (d, *J*^{CP}=3.0 Hz), 135.1 (d, *J*^{CP}=3.0 Hz), 133.8 (d, *J*^{CP}=10.5 Hz), 131.3 (d, *J*^{CP}=3.0 Hz), 130.0 (d, *J*^{CP}=13.5 Hz), 124.9 (d, *J*^{CP}=3.0 Hz), 123.5 (d, *J*^{CP}=9.0 Hz), 117.9 (d, *J*^{CP}=85.5 Hz), 25.9 (d, *J*^{CP}=51.0 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 151.4 (d, *J*^{CP}=2.2 Hz), 140.9 (d, *J*^{CP}=6.9 Hz), 135.3 (d, *J*^{CP}=3.4 Hz), 133.9 (d, *J*^{CP}=10.2 Hz), 132.1 (d, *J*^{CP}=3.4 Hz), 130.2 (d, *J*^{CP}=12.6 Hz), 123.1 (d, *J*^{CP}=4.6 Hz), 121.8 (d, *J*^{CP}=7.9 Hz), 117.1 (d, *J*^{CP}=84.6 Hz), 114.3 (d, *J*^{CP}=2.2 Hz), 57.0, 25.3 (d, *J*^{CP}=49.2 Hz); IR (ATR) 1536, 1433, 1281, 1108, 685 cm⁻¹; HRMS (ESI, negative ion mode) calcd for C₂₆H₂₃BrNO₃P (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 148.8 (d, *J*^{CP}=6.1 Hz), 137.3 (d, *J*^{CP}=3.0 Hz), 135.3 (d, *J*^{CP}=3.0 Hz), 133.9 (d, *J*^{CP}=10.6 Hz), 130.3 (d, *J*^{CP}=12.1 Hz), 128.4 (d, *J*^{CP}=2.3 Hz), 123.1 (d, *J*^{CP}=8.4 Hz), 122.6 (d, *J*^{CP}=4.5 Hz), 117.4, 116.6, 26.4 (d, *J*^{CP}=49.3 Hz); IR (ATR) 1521, 1367, 1346, 1284, 1066, 852 cm⁻¹; HRMS (ESI) calcd for C₂₅H₂₀Br₂NO₂P (M-Br) 476.0415, found 476.0416.

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 CHCl_3 (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, CDCl_3) 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); ^{13}C NMR (150 MHz, CDCl_3) 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 $\text{C}_9\text{H}_6\text{BrNO}_3$ (M^-) 254.9531, found 254.9530.

Analytical data for **43**: mp=110-119 °C; ^1H NMR (600 MHz, CDCl_3) δ 9.68 (d, $J=7.8$ Hz, 1H), 7.92 (d, $J=8.4$ Hz, 1H), 7.84 (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); ^{13}C NMR (150 MHz, CDCl_3) 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 $\text{C}_{11}\text{H}_8\text{BrNO}_3$ (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 (MgSO_4), 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, CDCl_3) 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); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) 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, 130.2, 129.7, 128.9, 128.4, 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 $\text{C}_{16}\text{H}_{12}\text{ClN}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 331.0485, found 331.0480.

EE/ZE-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/ZE*=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 C₁₇H₁₅N₂O₅ (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;⁹³ IR (ATR) 3027, 1520, 1347, 1217, 748 cm⁻¹; HRMS (ESI) calcd for C₁₆H₁₂BrN₂O₄ (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, CDCl₃) δ 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); ¹³C NMR (150 MHz, DMSO-d₆) δ 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, 128.1, 128.0, 127.8, 126.5, 126.4, 126.4, 126.3, 121.9, 121.7; IR (ATR) 3381, 1589, 1517, 1335, 748 cm⁻¹; HRMS (ESI, negative ion mode) calcd for C₁₆H₁₀Br₂N₂O₄ (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 (MgSO₄), filtered, and the solvent was removed under reduced pressure. The resulting crude product was purified by chromatography (hexane/EtOAc, 19:1) 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** (6 atm CO, 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; ¹H NMR (400 MHz, Acetone-d₆) δ 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); ¹³C NMR (100 MHz, Acetone-d₆) δ 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 C₁₆H₁₂ClN₂ (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; ¹H NMR (400 MHz, Acetone-d₆) δ 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); ¹³C NMR (100 MHz, Acetone-d₆) δ 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 $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}$ ($\text{M}+\text{H}^+$) 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 $\text{Pd}(\text{dba})_2$ (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 $^\circ\text{C}$, 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 $^\circ\text{C}$; ^1H NMR (400 MHz, Acetone- d_6) 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); ^{13}C NMR (100 MHz, Acetone- d_6) 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 $\text{C}_{16}\text{H}_{12}\text{BrN}_2$ ($\text{M}+\text{H}^+$) 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 $\text{Pd}(\text{dba})_2$ (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 $^\circ\text{C}$, 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 $^\circ\text{C}$; ^1H NMR (600 MHz, $\text{CDCl}_3/\text{DMSO}-\text{d}_6$) 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); ^{13}C NMR (150 MHz, $\text{CDCl}_3/\text{DMSO}-\text{d}_6$) 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 $\text{C}_{16}\text{H}_{11}\text{Br}_2\text{N}_2$ ($\text{M}+\text{H}^+$) 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 $\text{PdCl}_2(\text{PPh}_3)_2$ (119 mg, 0.170 mmol) and 1-ethynyl-2-nitrobenzene (**44**)⁹⁶ (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, 95:5) gave **48** (707 mg, 1.61 mmol, 95%) as a pale green oil. ^1H NMR (600 MHz, CDCl_3) 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); ^{13}C NMR (150 MHz, CDCl_3) 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 $\text{C}_{20}\text{H}_{34}\text{NO}_2^{120}\text{Sn}$ ($\text{M}+\text{H}^+$) 440.1606, found 440.1607.

Tributyl(1-(5-benzyloxy-2-nitrophenyl)ethenyl)tin (4). Treatment of **3**⁵⁸ (1.30 g, 5.15 mmol) in dry THF (15 mL) with tributyltin hydride (2.30 g, 7.90 mmol) in the presence of $\text{PdCl}_2(\text{PPh}_3)_2$ (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. ^1H NMR (400 MHz, CDCl_3) δ 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, $J=2.0$ 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) δ 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 $\text{C}_{27}\text{H}_{40}\text{NO}_3\text{Sn}$ ($\text{M}+\text{H}^+$) 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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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. ^1H NMR (400 MHz, CDCl_3) δ 7.99 (d, $J=2.0$ Hz, 1H), 7.48 (dd, $J=8.4, 2.4$ 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) δ 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 $\text{C}_{20}\text{H}_{32}\text{ClNO}_2\text{Sn}$ (M^-) 473.1144, found 473.1188.

Tributyl(1-(4-carbomethoxy-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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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. ^1H NMR (400 MHz, CDCl_3) δ 8.63 (d, $J=1.6$ Hz, 1H), 8.15 (dd, $J=7.6, 1.6$ 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) δ 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 $\text{C}_{22}\text{H}_{35}\text{N}_2\text{O}_4\text{Sn}$ (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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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. ^1H NMR (400 MHz, CDCl_3) δ 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).⁵⁸ 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 C₁₆H₁₂N₂NaO₄ (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, 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 C₃₀H₂₅N₂O₆ (M+H⁺) 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 $\text{C}_{16}\text{H}_{10}\text{Cl}_2\text{N}_2\text{O}_4$ (M^-) 364.0018, found 364.0048.

2,3-Di(4-carbomethoxy-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 chromatography¹⁰⁰ (hexane/EtOAc, 9:1), **54** (306 mg, 0.742 mmol, 92%) as a white solid. mp=187-188 °C; ^1H NMR (400 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{20}\text{H}_{16}\text{N}_2\text{O}_8$ (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 chromatography¹⁰⁰ (hexane/EtOAc, 9:1) **55** (37.1 mg, 0.104 mmol, 98%) as a white solid. mp=163.5-164 °C; ^1H NMR (400 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{18}\text{H}_{17}\text{N}_2\text{O}_6$ ($\text{M}+\text{H}^+$) 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 $\text{Pd}(\text{OAc})_2$ (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 $\text{Pd}(\text{dba})_2$ (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; ^1H NMR (400 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{30}\text{H}_{24}\text{N}_2\text{O}_2$ (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 $\text{Pd}(\text{dba})_2$ (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-d₆) 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-d₆) 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 C₁₆H₁₁Cl₂N₂ (M+H⁺) 301.0299, found 301.0292.

6,6'-Carbomethoxy-3,3'-Bi-1*H*-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, CDCl₃/DMSO-d₆) 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, CDCl₃/DMSO-d₆) δ 167.1, 135.5, 129.2, 125.7, 122.3, 119.5, 118.9, 113.6, 109.5, 51.4; IR (ATR) 3305, 1689, 1436, 1319, 1227 cm⁻¹; HRMS (ESI) calcd for C₂₀H₁₇N₂O₄ (M+H⁺) 349.1188, found 349.1182.

6,6'-Dimethoxy-3,3'-Bi-1*H*-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-d₆) 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-d₆) 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 C₁₈H₁₇N₂O₂ (M+H⁺) 293.1290, found 293.1284.

Tributyl(1-(3-nitro-2-pyridyl)ethenyl)tin (62). Treatment of a solution of **61**¹⁰² (100 mg, 0.675 mmol) in THF (2 mL) with tributyltin hydride (295 mg, 1.01 mmol) in the presence of PdCl₂(PPh₃)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, CDCl₃) 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), 1.30-1.25 (m, 6H), 1.00-0.83 (m, 15H); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₉H₃₃N₂O₂¹²⁰Sn (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, CDCl₃) 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, CDCl₃) 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 C₁₄H₁₁N₄O₄ (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-d₆) 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-d₆) 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 C₁₄H₁₁N₄ (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**)¹⁰³ (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 (MgSO₄), 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, CDCl₃) 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, CDCl₃) 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 C₉H₉BrNO₃ (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(PPh₃)₄ (143 mg, 0.124 mmol) in DMF (3 mL) was added, under a N₂ 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 (MgSO₄), filtered, and the filtrate was concentrated under reduced pressure. The resulting brown oil was purified by chromatography¹⁰⁰ (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, CDCl₃) 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); ^{13}C NMR (100 MHz, CDCl_3) 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 $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}_5$ ($\text{M}+\text{H}^+$) 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 $\text{Pd}_2(\text{dba})_3$ (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-d_6) 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); ^{13}C NMR (100 MHz, DMSO-d_6) 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 $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}$ ($\text{M}+\text{H}^+$) 263.1184, found 263.1180.

[(5-Bromo-2-nitrophenyl)methyl] triphenylphosphonium bromide (69).¹⁰⁴ Treatment of 5-bromo-2-nitrobenzyl bromide (486 mg, 1.65 mmol) with PPh_3 (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-d_6) 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); ^{13}C NMR (150 MHz, DMSO-d_6) δ 147.3 (d, $J^{\text{CP}}=5.7$ Hz), 136.3 (d, $J^{\text{CP}}=10.3$ Hz), 136.3, 135.4, 134.0 (d, $J^{\text{CP}}=10.3$ Hz), 133.3, 127.9 (d, $J^{\text{CP}}=4.5$ Hz), 127.8, 125.9 (d, $J^{\text{CP}}=9.1$ Hz), 116.9 (d, $J^{\text{CP}}=85.8$ Hz), 26.6 (d, $J^{\text{CP}}=49.2$ Hz); IR 1519, 1330, 1109, 884, 754 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{25}\text{H}_{20}\text{Br}_2\text{NO}_2\text{P}$ ($\text{M}-\text{Br}$) 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**¹⁰⁵ (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, CDCl_3) 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, CDCl_3) 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,

$J=16.0$ Hz, 1H), 5.59 (s, 1H), 5.30 (s, 1H); ^{13}C NMR (150 MHz, CDCl_3) δ 148.6, 147.8, 147.6, 146.9, 144.6, 142.0, 135.4, 134.4, 134.2, 133.2, 133.1, 132.5, 132.4, 132.3, 132.1, 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, 120.2; IR (ATR) 1568, 1514, 1339, 912, 786 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{13}\text{N}_2\text{O}_4$ ($\text{M}+\text{H}^+$) 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. ^1H NMR (400 MHz, CDCl_3) δ 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) δ 150.2, 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, 833, 756, 721, 690 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}_5$ ($\text{M}+\text{H}^+$) 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 $^{\circ}\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 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), 6.74 (d, $J=12.0$ Hz, 1H), 6.60 (d, $J=12.4$ Hz, 1H), 5.54 (s, 1H), 5.25 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 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 $\text{C}_{16}\text{H}_{11}\text{BrN}_2\text{O}_4$ (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 $^{\circ}\text{C}$; ^1H NMR (600 MHz, CDCl_3) δ 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) δ 147.7, 145.6, 141.8, 135.1, 135.1, 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 $\text{C}_{16}\text{H}_{11}\text{BrN}_2\text{O}_4$ (M^-) 373.9902, found 373.9898.

2,3'-Bi-1*H*-indole (75). Treatment of a solution of **71** (200 mg, 0.675 mmol) in the presence of $\text{Pd}(\text{dba})_2$ (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 $^\circ\text{C}$; ^1H NMR (600 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{16}\text{H}_{13}\text{N}_2$ ($\text{M}+\text{H}^+$) 233.1078, found 233.1073.

7-Methoxy-2,3'-Bi-1*H*-indole (76). Reaction of a solution of **72** (46 mg, 0.14 mmol) in the presence of $\text{Pd}(\text{dba})_2$ (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 $^\circ\text{C}$, 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. ^1H NMR (600 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}$ ($\text{M}+\text{H}^+$) 263.1184, found 263.1182.

6-Bromo-2,3'-Bi-1*H*-indole (77). Reaction of a solution of **73** (50 mg, 0.133 mmol) in the presence of $\text{Pd}(\text{dba})_2$ (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 $^\circ\text{C}$, 43 h), gave after work up and chromatography (hexane/EtOAc, 7:3) **77** (27.4 mg, 0.088 mmol, 66%) as a white solid. mp=205-206 $^\circ\text{C}$; ^1H NMR (400 MHz, $\text{CDCl}_3/\text{DMSO}-d_6$) δ 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, $\text{CDCl}_3/\text{DMSO}-d_6$) δ 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 $\text{C}_{16}\text{H}_{12}\text{BrN}_2$ ($\text{M}+\text{H}^+$) 311.0184, found 311.0183.

5-Bromo-2,3'-Bi-1*H*-indole (78). Reaction of a solution of **74** (121 mg, 0.323 mmol) in the presence of $\text{Pd}(\text{dba})_2$ (13 mg, 0.023 mmol), dppp (9.4 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 $^\circ\text{C}$, 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 C₁₆H₁₂BrN₂ (M+H⁺) 311.0184, found 311.0182.

Indolo[1,2-*c*]quinazolin-6(5*H*)-one (81**)⁸⁷ and 5,11-Dihydro-6*H*-Indolo[3,2-*c*] quinolin-6-one (**82**).¹⁰⁶**

Treatment of a solution of *trans*-2,2'-di(2-nitrophenyl)ethene (**79**)¹⁰⁷ (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 C₁₅H₁₁N₂O (M+H⁺) 235.0871, found 235.0868.

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 C₁₄H₉ClNO₂ (M⁻) 304.0251, found 304.0272.

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(dba)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; ¹H 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); ¹³C 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 C₁₅H₁₀ClN₂O (M+H⁺) 269.0482, found 269.0475.

Analytic data for **90**: mp=182-183 °C; ¹H 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); ¹³C 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 C₁₄H₉ClN₂ (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: ¹H NMR (600 MHz, CDCl₃) 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: ¹H NMR (600 MHz, CDCl₃) 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; ¹³C NMR (150 MHz, CDCl₃) 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 C₁₅H₁₃N₂O₅ (M+H⁺) 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-6*H*-indolo[3,2-*c*]quinolin-6-one (94). Reaction of **91** (439 mg, 1.46 mmol) in the presence of Pd(dba)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, CDCl_3) 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); ^{13}C NMR (100 MHz, DMSO-d_6) 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 $\text{C}_{15}\text{H}_{13}\text{N}_2\text{O}_3$ ($\text{M}+\text{H}^+$) 269.0926, found 269.0919.

Analytic data for **93**: mp=158-160 °C; ^1H NMR (600 MHz, $\text{CDCl}_3/\text{DMSO-d}_6$) 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); ^{13}C NMR (150 MHz, $\text{CDCl}_3/\text{DMSO-d}_6$) 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 $\text{C}_{15}\text{H}_{13}\text{N}_2\text{O}_3$ ($\text{M}+\text{H}^+$) 269.0926, found 269.0919.

Analytic data for **94**: mp=355-360 °C; ^1H NMR (600 MHz, DMSO-d_6) 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); ^{13}C NMR (100 MHz, DMSO-d_6) 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 $\text{C}_{16}\text{H}_{13}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 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), $\text{PdCl}_2(\text{PPh}_3)_2$ (67 mg, 0.095 mmol), PPh_3 (50 mg, 0.190 mmol) and CuI (271 mg, 1.43 mmol). The reaction was stirred at ambient temperature for 24 h. Et_2O (30 mL) was added and the organic phase was washed with NH_4OH (10%-aqueous, 3x30 mL), H_2O (30 mL), and brine (30 mL). The organic phase was dried (MgSO_4), 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, CDCl_3) 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); ^{13}C NMR (150 MHz, CDCl_3) 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 $\text{C}_{14}\text{H}_{10}\text{N}_2\text{NaO}_4$ ($\text{M}+\text{Na}^+$) 293.0538, found 293.0534.

Indolo[2,3-*b*]indole (96) and 6H-Indolo[2,3-*c*]quinolin-6-one (97).¹⁰⁸ 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 °C; ¹H 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); ¹³C 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 C₁₄H₁₁N₂ (M+H⁺) 207.0922, found 207.0917.

Analytical data for **97**: mp 312-314 °C; ¹H 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); ¹³C NMR (150 MHz, DMSO-*d*₆) δ 155.7, 138.8, 134.9, 127.6, 125.9, 125.7, 123.0, 122.3, 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 C₁₅H₁₁N₂O (M+H⁺) 235.0871, found 235.0867.

1-(5-Benzyloxy-2-nitrophenyl)-2-(4-methoxy-2-nitrophenyl)ethene (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(PPh₃)₄ (124 mg, 0.108 mmol) and **4** (1.10 g, 2.01 mmol). The mixture was stirred at 50 °C under N₂ for 8 h. After cooling to ambient temperature, the crude mixture was diluted with EtOAc (35 mL), washed with H₂O (3x35 mL) and brine (2x35 mL). The organic layer was dried (MgSO₄), filtered, and the solvents were removed under reduced pressure. The residue was purified by chromatography on SiO₂/K₂CO₃ (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 °C; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₂₂H₁₉N₂O₆ (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-*d*₆) 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-*d*₆) 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-*d*₆) 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-*d*₆) 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-*d*₆) 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-*d*₆) 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-trimethylsilylethyne (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 ($\text{PdCl}_2(\text{PPh}_3)_2$, 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_3N , 16 mL). After stirring the mixture for 5 minutes, the solution of trimethylsilylethyne (1.40 g, 13.4 mmol) in Et_3N (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. ^1H 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 $\text{C}_{11}\text{H}_{13}\text{BrNO}_2\text{Si}$ ($\text{M}+\text{H}^+$) 297.9899, found 297.9883.

1-(5-Bromo-2-nitrophenyl)ethyne (114). A heterogeneous mixture of **113** (2.56 g, 8.58 mmol) and K_2CO_3 (2.37 g, 17.2 mmol) in MeOH/ Et_2O (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 $^\circ\text{C}$; ^1H 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 $\text{C}_8\text{H}_5\text{BrNO}_2$ ($\text{M}+\text{H}^+$) 225.9504, found 225.9502.

Tributyl(1-(5-bromo-2-nitrophenyl)ethenyl)tin (115). Tributyltin hydride (1.98 g, 6.79 mmol) was added drop wise, at ambient temperature, to a solution of $\text{PdCl}_2(\text{PPh}_3)_2$ (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. ^1H 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, 1522, 1339, 878 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{33}\text{BrNO}_2\text{Sn}$ ($\text{M}+\text{H}^+$) 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 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) affording **116** (223 mg, 0.491 mmol, 56%) as a white solid. mp=235 °C (decomposed); ¹H NMR (600 MHz, CDCl₃) δ 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); ¹H NMR (100 MHz, CDCl₃) δ 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 C₁₆H₁₁Br₂N₂O₄ (M+H⁺) 452.9085, found 452.9068.

5,5'-Dibromo-3,3'-bi-1*H*-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 (MgSO₄), 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. ¹H NMR (600 MHz, DMSO-d₆) δ 11.42 (br s, 1H), d, *J*=1.8 Hz, 1H), 7.74 (d, *J*=2.4 Hz, 1H), 7.42 (d, *J*=8.4 Hz, 1H), 7.25 (dd, *J*=9.0, 1.8 Hz, 1H); ¹H NMR (100 MHz, DMSO-d₆) δ 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-1*H*-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. ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₁₆H₈Br₄N₂ (M⁺) 547.7380, found 547.7359.

2,2',5,5',6,6'-Hexabromo-3,3'-bi-1*H*-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-1*H*-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

CO). 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-1*H*-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-1*H*-indole (105) and 2,2',5,6,6'-pentabromo-3,3'-bi-1*H*-indole (121). Treatment of **120** (76.1 mg, 0.195 mmol) with NBS (174 mg, 0.978 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, **121** (40.3 mg, 0.064 mmol, 33%) and **105** (64.9 mg, 0.098 mmol, 47%) both as a colorless oil. Analytical data for **121**: ¹H NMR (400 MHz, CDCl₃) δ 8.41 (br s, 1H), 8.40 (s, 1H), 7.68 (s, 1H), 7.59 (s, 1H), 7.55 (d, *J*=1.2 Hz, 1H), 7.24 (dd, *J*=8.4, 1.6 Hz, 1H), 7.18 (d, *J*=8.4 Hz, 1H); ¹³C NMR (400 MHz, CDCl₃) δ 136.6, 135.5, 128.6, 126.7, 124.1, 123.8, 120.7, 118.0, 116.4, 116.2, 115.3, 113.5, 111.7, 110.3, 108.4, 108.3; IR (ATR) 3411, 1433, 1372, 1303, 805 cm⁻¹; HRMS (ESI) calcd for C₁₆H₈Br₅N₂ (M+H⁺) 622.6604, found 622.6589.

2,2',6,6'-Tetrabromo-3,3'-bi-1*H*-indole (104) and 2,2',5,6,6'-Pentabromo-3,3'-bi-1*H*-indole (121). Compound **56** (40.1 mg, 0.173 mmol) was treated with NBS (123 mg, 0.690 mmol) in THF/CH₂Cl₂ (1:1, 3 mL), as described for **103** (70 °C, 15 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',5,6,6'-Pentabromo-3,3'-bi-1*H*-indole (121) and 2,2',5,5',6,6'-Hexabromo-3,3'-bi-1*H*-indole (105). Compound **56** (32.2 mg, 0.139 mmol) was treated with NBS (126 mg, 0.708 mmol) in

THF/CH₂Cl₂ (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-1*H*-indole (105). Compound **56** (40.8 mg, 0.176 mmol) was treated with NBS (250 mg, 1.40 mmol) in THF/CH₂Cl₂ (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, 1560, 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*=8.8, 2.8 Hz, 1H), 7.27-7.22 (ddd, *J*=9.6, 6.4, 2.4 Hz, 1H), 7.02 (dd, *J*=9.6, 4.8 Hz, 1H), 6.21 (d, with further fine splitting *J*=9.6 Hz, 1H), 1.81 (s, 3H), 1.78 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 153.0 (d, *J*^{C-F}=239.0 Hz), 138.6 (d, *J*^{C-F}=1.0 Hz), 130.5 (d, *J*^{C-F}=8.0 Hz), 124.9 (d, *J*^{C-F}=24 Hz), 119.2, 118.2, 115.7 (d, *J*^{C-F}=8.0 Hz), 111.8 (d, *J*^{C-F}=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 C₁₅H₁₄BrN₂O₂ (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.

Table 4.2, Entry 11

1-Methoxybenzimidazole (124),¹³³ 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**)¹³⁴ (160 mg, 0.833 mmol) and sodium hydride¹³⁵ (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*=8.0 Hz, 1H), 7.34 (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 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), 7.26 (td, *J*=7.2, 1.2 Hz, 1H), 4.20 (s, 3H), 3.19 (s, 3H), 1.80 (s, 6H); 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 $\text{C}_9\text{H}_{11}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 179.0820, found 179.0814.

1,6-Dimethoxy-2-(2-methoxy-2-propyl)benzimidazole (129). Pale yellow oil; ^1H NMR (400 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{13}\text{H}_{19}\text{N}_2\text{O}_3$ ($\text{M}+\text{H}^+$) 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 $^\circ\text{C}$; ^1H NMR δ 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 δ 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 $\text{C}_{12}\text{H}_{17}\text{N}_2\text{O}_3$ ($\text{M}+\text{H}^+$) 237.1239, found 237.1229.

6-Chloro-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (132). Orange solid; mp=66-67 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 7.62 (d, $J=8.4$ Hz, 1H), 7.41 (d, $J=1.6$ Hz, 1H), 7.19 (dd, $J=8.4, 1.6$ Hz, 1H), 4.16 (s, 3H), 3.16 (s, 3H), 1.76 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 152.4, 135.5, 132.1, 129.4, 123.1, 121.4, 108.4, 74.5, 65.5, 51.3, 24.8; IR (ATR) 2944, 1677, 1496, 1340, 1268, 1228 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{12}\text{H}_{16}\text{ClN}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 255.0900, found 255.0893.

6-Bromo-1-methoxybenzimidazole (134). White solid; mp=46-47 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 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) δ 138.3, 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 $\text{C}_8\text{H}_8\text{BrN}_2\text{O}$ ($\text{M}+\text{H}^+$) 226.9820, found 226.9814.

6-Bromo-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (135). Orange oil; ^1H NMR (600 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{12}\text{H}_{16}\text{BrN}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 299.0395, found 299.0390.

6-Fluoro-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (137). Pale yellow oil; ^1H NMR (400 MHz, CDCl_3) δ 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),

4.13 (s, 3H), 3.14 (s, 3H), 1.73 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.9 (d, $J^{\text{C-F}}=241.0$ Hz), 152.2 (d, $J^{\text{C-F}}=3.0$ Hz), 133.2, 131.5 (d, $J^{\text{C-F}}=13.0$ Hz), 121.4 (d, $J^{\text{C-F}}=10.0$ Hz), 110.8 (d, $J^{\text{C-F}}=25.0$ Hz), 95.0 (d, $J^{\text{C-F}}=28.0$ Hz), 74.4, 65.2, 51.3, 24.7; IR (ATR) 1486, 1448, 1172, 1067, 965, 811 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{12}\text{H}_{16}\text{FN}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 239.1196, found 239.1191.

1-Methoxy-6-methylbenzimidazole (139). Colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 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) δ 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 $\text{C}_9\text{H}_{11}\text{N}_2\text{O}$ ($\text{M}+\text{H}^+$) 163.0871, found 163.0867.

1-Methoxy-2-(2-methoxy-2-propyl)-6-methylbenzimidazole (140). Colorless oil; ^1H NMR (600 MHz, CDCl_3) δ 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), 2.48 (s, 3H), 1.76 (s, 6H); ^{13}C NMR (150 MHz, CDCl_3) δ 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 $\text{C}_{13}\text{H}_{19}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 235.1446, found 235.1441.

2-(2-Hydroxy-2-propyl)-1-methoxy-6-methylbenzimidazole (141). White solid; mp=99-100 $^\circ\text{C}$; ^1H NMR (600 MHz, CDCl_3) δ 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 (100 MHz, CDCl_3) δ 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 $\text{C}_{12}\text{H}_{17}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 221.1290, found 221.1285.

Methyl 1-methoxybenzimidazole-6-carboxylate (143). White solid; mp=126-127 $^\circ\text{C}$; ^1H NMR (600 MHz, CDCl_3) δ 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) δ 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, 1280, 1226 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{10}\text{H}_{11}\text{N}_2\text{O}_3$ ($\text{M}+\text{H}^+$) 207.0769, found 207.0763.

1,5-Dimethoxybenzimidazole (146). Colorless oil; ^1H NMR (600 MHz, CDCl_3) δ 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) δ 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 $\text{C}_9\text{H}_{11}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 179.0820, found 179.0820.

5-Chloro-1-methoxybenzimidazole (148). Yellow oil; ^1H NMR (600 MHz, CDCl_3) δ 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) δ 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 $\text{C}_8\text{H}_7\text{ClN}_2\text{O}$ ($\text{M}+\text{Na}^+$) 205.0144, found 205.0139.

5-Chloro-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (149). Yellow oil; ^1H NMR (600 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{12}\text{H}_{16}\text{ClN}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 255.0900, found 255.0901.

5-Bromo-1-methoxybenzimidazole (151). Faint yellow oil; ^1H NMR (400 MHz, CDCl_3) δ 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) δ 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 $\text{C}_8\text{H}_8\text{BrN}_2\text{O}$ ($\text{M}+\text{H}^+$) 226.9820, found 226.9815.

5-Bromo-1-methoxy-2-(2-methoxy-2-propyl)benzimidazole (152). Red oil; ^1H NMR (400 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{12}\text{H}_{16}\text{BrN}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 299.0395, found 299.0376.

1-Methoxy-5-methylbenzimidazole (154). Orange oil; ^1H NMR (600 MHz, CDCl_3) δ 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) δ 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 $\text{C}_9\text{H}_{11}\text{N}_2\text{O}$ ($\text{M}+\text{H}^+$) 163.0871, found 163.0866.

1-Methoxy-5-methyl-2-(2-methoxy-2-propyl)benzimidazole (155). Orange oil; ^1H NMR (400 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{13}\text{H}_{19}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 235.1446, found 235.1439.

1-Methoxy-(2-hydroxy-2-propyl)-5-methylbenzimidazole (156). White solid; mp=99-100 °C; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₁₂H₁₇N₂O₂ (M+H⁺) 221.1290, found 221.1285.

6-Bromo-1-methoxy-(1-methoxy-1-phenylethyl)benzimidazole (161). Orange oil; ¹H NMR (400 MHz, CDCl₃) δ 7.67 (dd, *J*=8.8, 0.4 Hz, 1H), 7.51 (d, *J*=1.6 Hz, 1H), 7.38 (dd, *J*=8.8, 1.6 Hz, 1H), 7.42-7.40 (m, 2H), 7.35-7.24 (m, 3H), 3.53 (s, 3H), 3.29 (s, 3H), 2.04 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 152.1, 144.0, 136.1, 128.2, 127.4, 125.9, 125.2, 122.0, 117.0, 111.6, 110.0, 78.3, 64.8, 51.4, 25.0; IR (ATR) 1437, 1373, 1245, 1185, 981, 792 cm⁻¹; HRMS (ESI) calcd for C₁₇H₁₈N₂O₂ (M+H⁺) 361.0551, found 361.0549.

6-Bromo-(1-hydroxy-1-phenylethyl)-1-methoxybenzimidazole (162). Colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 7.65 (d, *J*=8.4 Hz, 1H), 7.50 (d, *J*=1.6 Hz, 1H), 7.48-7.46 (m, 2H), 7.39 (dd, *J*=8.4, 1.6 Hz, 1H), 7.38-7.27 (m, 3H), 3.90 (br s, 1H), 3.39 (s, 3H), 2.08 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₁₆H₁₆N₂O₂ (M+H⁺) 347.0395, found 347.0395.

1,6-Dimethoxy-2-(1-methoxycyclohexyl)benzimidazole (158). Colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (150 MHz, CDCl₃) δ 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 C₁₆H₂₃N₂O₃ (M+H⁺) 291.1708, found 291.1701.

1,6-Dimethoxy-2-(1-hydroxycyclohexyl)benzimidazole (159). White solid; mp=132-133 °C; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₁₅H₂₁N₂O₃ (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⁺) 241.0744, found 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, 731cm⁻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); ^{13}C NMR (100 MHz, CDCl_3) 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 $\text{C}_{22}\text{H}_{21}\text{N}_2\text{O}_3$ ($\text{M}+\text{H}^+$) 361.1552, found 361.1548.

1-Benzyloxy-2-(2-benzyloxy-2-propyl)-6-methoxybenzimidazole (171). Orange oil; ^1H NMR (400 MHz, CDCl_3) δ 7.64 (d, $J=8.8$ Hz, 1H), 7.38-7.20 (m, 10H), 6.87 (dd, $J=8.8$, 2.4 Hz, 1H), 6.66 (d, $J=2.8$ Hz, 1H), 5.18 (s, 2H), 4.48 (s, 2H), 3.78 (s, 3H), 1.93 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) 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 $\text{C}_{25}\text{H}_{27}\text{N}_2\text{O}_3$ ($\text{M}+\text{H}^+$) 403.2022, found 403.2014.

1-Benzyloxy-2-(2-hydroxyl-2-propyl)-6-methoxybenzimidazole (172). White solid; mp=118-119 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) 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); ^{13}C NMR (100 MHz, CDCl_3) 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 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{21}\text{N}_2\text{O}_3$ ($\text{M}+\text{H}^+$) 313.1552, found 313.1547.

1-(2-Propen-1-yloxy)-6-methoxybenzimidazole (173). Pale yellow oil; ^1H NMR (400 MHz, CDCl_3) δ 7.88 (s, 1H), 7.61 (dd, $J=9.6$, 1.2 Hz, 1H), 6.90-6.87 (m, 2H), 6.07 (ddt, $J=17.2$, 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); ^{13}C NMR (100 MHz, CDCl_3) 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, 1224, 1061, 932, 815 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{11}\text{H}_{13}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 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, CDCl_3) 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, 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); ^{13}C NMR (100 MHz, CDCl_3) 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 $\text{C}_{17}\text{H}_{23}\text{N}_2\text{O}_3$ ($\text{M}+\text{H}^+$) 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; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₁₄H₁₉N₂O₃ (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; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₁₂H₁₅N₂O₃ (M+H⁺) 235.1082, found 235.1077.

6-Methoxy-1-(2-propyn-1-yloxy)benzimidazole (177). Pale yellow oil; ¹H NMR (400 MHz, CDCl₃) δ 8.03 (s, 1H), 7.62 (d, *J*=8.8 Hz, 1H), 6.92 (d, *J*=2.0 Hz, 1H), 6.90 (dd, *J*=8.8, 2.4 Hz, 1H), 4.86 (d, *J*=2.4 Hz, 2H), 3.85 (s, 3H), 2.68 (t, *J*=2.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 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, 1238, 1021; HRMS (ESI) calcd for C₁₁H₁₁N₂O₂ (M+H⁺) 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.); ¹H NMR (600 MHz, CDCl₃) δ 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); ¹³C NMR (150 MHz, CDCl₃) δ 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 C₁₄H₁₆N₂O₃ (M+Na⁺) 283.1058, found 283.1042.

1-(3-Butyn-2-yloxy)-6-methoxybenzimidazole (179). Colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₁₂H₁₃N₂O₃ (M+H⁺) 217.0977, found 217.0968.

1-(3-Butyn-2-yloxy)-2-(2-hydroxy-2-propyl)-6-methoxybenzimidazole (180). White solid; mp=131-132 °C; ^1H NMR (400 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{15}\text{H}_{19}\text{N}_2\text{O}_3$ ($\text{M}+\text{H}^+$) 275.1396, found 275.1391.

1-Acetoxy-2-(2-acetoxy-2-propyl)-6-methoxybenzimidazole (181). Yellow oil; ^1H NMR (600 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{15}\text{H}_{19}\text{N}_2\text{O}_5$ ($\text{M}+\text{H}^+$) 307.1294, found 307.1275.

1-Acetoxy-2-(1-propen-2-yl)-6-methoxybenzimidazole (182). Pale yellow oil; ^1H NMR (600 MHz, CDCl_3) δ 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), 2.40 (s, 3H), 2.27 (dd, $J=1.8$, 1.2 Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 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 $\text{C}_{13}\text{H}_{15}\text{N}_2\text{O}_3$ ($\text{M}+\text{H}^+$) 247.1083, found 247.1066.

2,4-Dinitro-*N*-methyl-*N*-(2-methyl-1-propen-1-yl)benzenamine. Red oil; ^1H NMR (400 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{11}\text{H}_{14}\text{N}_3\text{O}_4$ ($\text{M}+\text{H}^+$) 252.0984, found 252.0980.

Methyl 4-*N*-methyl-*N*-(2-methyl-1-propen-1-yl)amino-3-nitrobenzoate. Red oil; ^1H NMR (600 MHz, CDCl_3) δ 8.27 (d, $J=1.8$ Hz, 1H), 7.96 (dd, $J=9.0$, 2.4 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) δ 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 $\text{C}_{13}\text{H}_{17}\text{N}_2\text{O}_4$ ($\text{M}+\text{H}^+$) 265.1188, found 265.1171.

5-Chloro-2-nitro-*N*-methyl-*N*-(2-methyl-1-propen-1-yl)benzenamine. Yellow oil; ^1H NMR (600 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{11}\text{H}_{14}\text{ClN}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 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 ^1H 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 μ L, 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 (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** (28.4 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 See Table 4.3, Entry 1

Table 4.1, Entry 5

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 $^\circ\text{C}$ and MeI (71 μ L, 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 (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, **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 $^\circ\text{C}$ and MeI (62 μ L, 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 (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, **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 μ L, 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 μ L, 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 μ L, 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 μ L, 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 μ L, 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 μ L, 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 (5x15 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** (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 (4x10 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 **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 (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 4.2, 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 (5x15 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 **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 μ L, 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 μ L, 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 μ L, 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 μ L, 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 μ L, 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 μ L, 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, **125** (62.6 mg, 0.284 mmol, 34%) and **124** (37.8 mg, 0.255 mmol, 31%) 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 μ L, 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 (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 **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 μ L, 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 (MgSO_4), 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 μ L, 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 (MgSO_4), 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 μ L, 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 μ L, 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 μ L, 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 °C and MeI (205 μ L, 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

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 μ L, 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 μ L, 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 μ L, 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 μ L, 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 μ L, 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 μ L,

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 μ L, 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 μ L, 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 μ L, 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 ^1H 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. 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-Benzyloxy-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-Benzyloxy-2-(2-benzyloxy-2-propyl)-6-methoxybenzimidazole (171) and 1-Benzyloxy-2-(2-hydroxyl-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 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) 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 μ L, 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 (MgSO₄), 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-butyne (135 μ L, 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 (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, 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-butyne (261 μ L, 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; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 151.1, 150.7, 141.4, 139.1, 136.1, 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 C₁₆H₁₇N₂O₃ (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

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-yl)benzenamine (**131**)¹³⁴ (75 mg, 0.331 mmol) with MeI (62 μ L, 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 **1234** (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-yl)benzenamine (**133**)¹³⁶ (136.2 mg, 0.502 mmol) with MeI (94 μ L, 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-yl)benzenamine (**136**)¹³⁶ (118.1 mg, 0.562 mmol) with MeI (75 μ L, 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, *J*^{C-F}=10 Hz, 1C), 111.3 (d, *J*^{C-F}=25 Hz, 1C), 95.1 (d, *J*^{C-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-yl)benzenamine (**12**)¹³⁶ (77.2 mg, 0.347 mmol) with MeI (65 μ L, 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).¹³⁶ Reaction of a solution of 5-methyl-2-nitro-*N*-(2-methyl-1-propen-1-yl)benzenamine (**153**)¹³⁶ (183 mg, 0.887 mmol) with MeI (166 μ L, 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).¹³⁶ Reaction of a solution of 5-chloro-2-nitro-*N*-(2-methyl-1-propen-1-yl)benzenamine (**147**)¹³⁴ (197.9 mg, 0.873 mmol) with MeI (163 μ L, 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).¹³⁶ Reaction of a solution of 5-bromo-2-nitro-*N*-(2-methyl-1-propen-1-yl)benzenamine (**150**)¹³⁶ (86.9 mg, 0.321 mmol) with MeI (60 μ L, 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).¹³⁶ Reaction of a solution of 4-methoxy-2-nitro-*N*-(cyclohexylmethylene)benzenamine (**157**)¹³⁴ (339.5 mg, 1.295 mmol) with MeI (258 μ L, 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 μ L, 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 μ L, 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-Benzyloxy-6-methoxybenzimidazole (193). Reaction of a solution of **127** (109.7 mg, 0.494 mmol) with benzyl bromide (BnBr, 152 μ L, 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. ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₁₅H₁₅N₂O₂ (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 μ L, 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 μ L, 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. ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₁₂H₁₅N₂O₂ (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 μL, 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. ¹H NMR (400 MHz, CDCl₃) δ 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*=9.2, 2.4 Hz, 1H), 5.69 (d, *J*=6.4 Hz, 2H), 3.87 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₁₁H₁₁N₂O₂ (M+H⁺) 208.0820, found 208.0811.

1-(1,2-Butadien-1-yloxy)-6-methoxybenzimidazole (197). Reaction of a solution of **127** (222.2 mg, 1.000 mmol) with 3-bromo-1-butyne (181 μL, 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. ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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, 1234, 1061, 816 cm⁻¹; HRMS (ESI) calcd for C₁₂H₁₃N₂O₂ (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 μL, 1.236 mmol) in *t*-BuOH (10 mL) in the presence of *t*-BuOK (263.2 mg, 2.346 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, ¹H NMR (400 MHz, DMSO-*d*₆) δ 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); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 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 C₁₀H₁₀N₂O₃ (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 μ L, 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. ^1H NMR (400 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{15}\text{H}_{23}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 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 μ L, 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. ^1H NMR (400 MHz, CDCl_3) δ 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), 4.29 (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) δ 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 $\text{C}_{12}\text{H}_{17}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 221.1290, found 221.1280.

6-methoxy-1-(2-methylethyloxy)benzimidazole (201). Reaction of a solution of **127** (143.6 mg, 0.646 mmol) with 2-iodopropane (136 μ L, 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. ^1H NMR (400 MHz, CDCl_3) δ 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) δ 157.2, 138.2, 133.9, 131.2, 121.4, 112.0, 92.0, 81.3, 55.8, 21.0; IR (neat) 1625, 1497, 1105, 817 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{11}\text{H}_{15}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 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, *J*^{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, *J*^{C-F} = 319 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ -72.9; IR (ATR) 1614, 1590, 1539, 1437, 1345, 1223, 1134 cm⁻¹.¹⁷³

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, *J*^{C-F} = 319 Hz), 114.6; IR (ATR) 3103, 1541, 1428, 1208, 1132 cm⁻¹; HRMS (ESI) calcd for C₇H₃BrNNaO₅F₃S (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, CDCl_3) δ 7.74-7.72 (m, 1H), 7.50-7.49 (m, 2H); ^{13}C NMR (150 MHz, CDCl_3) δ 140.6, 133.4, 132.1, 121.6, 119.4, 117.3 (q, $J^{C-F} = 319$ Hz), 115.2; ^{19}F NMR (376 MHz, CDCl_3) δ -73.2; IR (ATR) 3099, 1538, 1434, 1360, 1219, 1132 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_7\text{H}_3\text{BrNNaO}_5\text{F}_3\text{S}$ ($\text{M}+\text{Na}^+$) 371.8765; found 371.8767.

2-Bromo-6-nitrophenyl trifluoromethanesulfonate (217). Treatment of 2-bromo-6-nitrophenol¹⁷⁶ (189 mg, 0.87 mmol) in CH_2Cl_2 (5 mL) with pyridine (150 μL , 1.85 mmol) and Tf_2O (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, CDCl_3) 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); ^{13}C NMR (150 MHz, CDCl_3) δ 143.6, 139.4, 139.1, 129.3, 125.6, 119.0, 118.4 (q, $J^{C-F} = 319$ Hz); ^{19}F NMR (376 MHz, CDCl_3) δ -73.2; IR (ATR) 3093, 1588, 1540, 1431, 1347, 1207 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_7\text{H}_3\text{BrNNaO}_5\text{F}_3\text{S}$ ($\text{M}+\text{Na}^+$) 371.8765; found 371.8761.

3-Bromo-5-nitrophenyl trifluoromethanesulfonate (219) Treatment of 3-bromo-5-nitrophenol¹⁷⁷ (329 mg, 1.51 mmol) in CH_2Cl_2 (10 mL) with pyridine (250 μL , 3.10 mmol) and Tf_2O (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, CDCl_3) 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); ^{13}C NMR (150 MHz, CDCl_3) δ 149.2, 130.8, 126.8, 123.8, 118.6 (q, $J^{C-F} = 319$ Hz), 116.1; IR (ATR) 3097, 1732, 1542, 1427, 1344, 1210, 1134 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_7\text{H}_3\text{BrNNaO}_5\text{F}_3\text{S}$ ($\text{M}+\text{Na}^+$) 371.8765; found 371.8764.

4-Bromo-2-nitrophenyl trifluoromethanesulfonate (220).¹⁶⁴ Treatment of 4-bromo-3-nitrophenol¹⁷⁸ (353 mg, 1.60 mmol) in CH_2Cl_2 (5 mL) with pyridine (260 μL , 3.22 mmol) and Tf_2O (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, CDCl_3) 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); ^{13}C NMR (150 MHz, CDCl_3) δ 141.9, 140.5, 138.2, 129.7, 125.6, 122.3, 118.5 (q, $J^{C-F} = 319$ Hz); IR (ATR) 3105, 1540, 1431, 1207, 1131 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_7\text{H}_3\text{BrNNaO}_5\text{F}_3\text{S}$ ($\text{M}+\text{Na}^+$) 371.8765; found 371.8764.

2-Bromo-5-nitrophenyl trifluoromethanesulfonate (222). Treatment of 2-bromo-5-nitrophenol¹⁷⁹ (119 mg, 0.55 mmol) in CH_2Cl_2 (5 mL) with pyridine (90 μL , 1.12 mmol) and Tf_2O (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, CDCl_3) 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); ^{13}C NMR (100 MHz, CDCl_3) δ 147.6, 146.9, 135.2, 124.0, 123.9, 118.5 (q, $J^{C-F} = 320$ Hz), 118.3; IR

(ATR) 3104, 1534, 1431, 1348, 1211, 1134 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_7\text{H}_3\text{BrNNaO}_5\text{F}_3\text{S}$ ($\text{M}+\text{Na}^+$) 371.8765; found 371.8764.

Conditions A

4-Ethenylphenyl trifluoromethanesulfonate (206).¹³⁸ To a solution of PPh_3 (7.5 mg, 0.029 mmol) and $\text{Pd}(\text{dba})_2$ (4.3 mg, 0.007 mmol) in dioxane (1.5 mL), stirred for 5 min under an atmosphere of N_2 , was added 4-bromophenyl trifluoromethanesulphonate (**202**)¹³⁸ (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 NH_4OH (10% aqueous, 3 x 20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried (MgSO_4), 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, CDCl_3) of the crude reaction mixture.

Conditions B

4-Ethenylphenyl trifluoromethanesulfonate (206) and 4-ethenyl-1-bromobenzene (207).¹³⁸ To a solution of LiCl (45.5 mg, 1.07 mmol) and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (4.7 mg, 0.007 mmol) in DMF (1.5 mL), under an atmosphere of N_2 , 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 NH_4OH (10% aqueous, 3 x 20 mL) and brine (20 mL). The organic phase was dried (MgSO_4), 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 $\text{PdCl}_2(\text{PPh}_3)_2$ (4.3 mg, 0.007 mmol) in dioxane (4 mL), stirred for 5 min under an atmosphere of N_2 , 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 $\text{SiO}_2/\text{K}_2\text{CO}_3$ (10% K_2CO_3 , 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, CDCl_3) of the crude reaction mixture.

2-Ethenylphenyl trifluoromethanesulfonate (209).¹⁸⁰ Cross coupling of 2-bromophenyl trifluoromethanesulphonate (**208**)¹⁸¹ (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 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).¹⁸² 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).¹⁸² 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 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).¹⁸³ Cross coupling of 2-bromo-3-nitrophenyl trifluoromethanesulfonate (**213**)¹⁸³ (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-nitrophenol¹⁸² (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, CDCl_3) 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); ^{13}C NMR (100 MHz, CDCl_3) 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 $\text{C}_{10}\text{H}_{10}\text{NO}_2$ ($\text{M}+\text{H}^+$) 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 $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (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 $^\circ\text{C}$, 24 h). Work up and chromatography on $\text{SiO}_2/\text{K}_2\text{CO}_3$ (10% K_2CO_3 , hexanes/EtOAc, 98:2) gave **223** (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**)¹⁸⁴ (67.6 mg, 0.19 mmol) with ethenyltributyltin (72.8 mg, 0.23 mmol) in the presence of PPh_3 (4.5 mg, 0.02 mmol) and $\text{Pd}(\text{dba})_2$ (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, CDCl_3) 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); ^{13}C NMR (150 MHz, CDCl_3) δ 151.7, 146.6, 136.4, 131.0, 127.0, 121.4, 121.3, 121.0, 118.6 (q, $J^{C-F} = 319$ Hz); IR (ATR) 3118, 1530, 1424, 1350, 1207, 1131 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_9\text{H}_6\text{NNaO}_5\text{F}_3\text{S}$ ($\text{M}+\text{Na}^+$) 319.9811; found 319.9809.

Analytical data for **227**: ^1H NMR (400 MHz, CDCl_3) 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) δ 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 $\text{C}_{10}\text{H}_{10}\text{NO}_2$ ($\text{M}+\text{H}^+$) 176.0711, found 176.0709.

3-Ethenyl-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 $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (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 ^1H 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: ^1H NMR (600 MHz, CDCl_3) δ 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) δ 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 $\text{C}_8\text{H}_6\text{NNaO}_2\text{Br}$ ($\text{M}+\text{Na}^+$) 249.9474; found

4-Ethenyl-3-nitrophenyl trifluoromethanesulfonate (229) and 2,5-diethenyl-nitrobenzene (230).¹⁸⁵ 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 $\text{Pd}(\text{dba})_2$ (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**: ^1H NMR (600 MHz, CDCl_3) δ 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) δ 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 $\text{C}_9\text{H}_6\text{NNaO}_5\text{F}_3\text{S}$ ($\text{M}+\text{Na}^+$) 319.9811; found 319.9810.

4-Ethenyl-3-nitrophenyl trifluoromethanesulfonate (229), 2,5-diethenyl-nitrobenzene (230), and 2-bromo-5-ethenyl-nitrobenzene (231).¹⁸⁶ 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 $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (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-Ethenyl-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 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* = 8.4, 1.2 Hz, 1H), 6.68 (dd, *J* = 17.6, 11.2 Hz, 1H), 5.91 (d, *J* = 17.2 Hz, 1H), 5.61 (d, *J* = 11.2 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 142.0, 140.2, 133.1, 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 C₉H₆NNaO₅F₃S (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-Ethenyl-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 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).¹⁸⁷ 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**)¹⁶⁴ (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 $\text{Pd}(\text{dba})_2$ (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-nitrophenol¹⁷⁶ (5.2 mg, 0.02 mmol, 7%). The mixture was repurified by chromatographed (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**: ^1H 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 (100 MHz, CDCl_3) δ 149.9, 147.2, 132.7, 127.2, 124.0, 122.9, 122.6, 121.7, 118.5 (q, $J^{C-F} = 319$ Hz); IR (ATR) 3107, 1536, 1424, 1347, 1209, 1134 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_9\text{H}_6\text{NNaO}_5\text{F}_3\text{S}$ ($\text{M}+\text{Na}^+$) 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 $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (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**: ^1H 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, 1520, 1342, 1116, 1035 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_8\text{H}_6\text{NNaO}_2\text{Br}$ ($\text{M}+\text{Na}^+$) 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 $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (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 $^\circ\text{C}$, 24 h). Work up and purification gave after chromatography on $\text{SiO}_2/\text{K}_2\text{CO}_3$ (10% K_2CO_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 in the presence of (6.4 mg, 0.02 mmol) and $\text{Pd}(\text{dba})_2$ (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**: ^1H

NMR (400 MHz, CDCl_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_3) δ 149.4, 149.2, 141.7, 133.2, 124.6, 120.6, 119.8, 118.6 (q, $J^{\text{C-F}} = 319$ Hz), 115.6; IR (ATR) 3103, 1540, 1425, 1348, 1213, 1132 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_9\text{H}_7\text{NO}_5\text{F}_3\text{S}$ ($\text{M}+\text{H}^+$) 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 $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (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 $^\circ\text{C}$; ^1H NMR (600 MHz, CDCl_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_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 $\text{C}_8\text{H}_6\text{NNaO}_2\text{Br}$ ($\text{M}+\text{Na}^+$) 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 $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (4.3 mg, 0.006 mmol) in 1,4-dioxane (1 mL) was performed as described for **206** as described under Conditions C (100 $^\circ\text{C}$, 24 h). Work up and purification gave after chromatography on $\text{SiO}_2/\text{K}_2\text{CO}_3$ (10% K_2CO_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 in the presence of (6.8 mg, 0.03 mmol) and $\text{Pd}(\text{dba})_2$ (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, 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 ^1H 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 $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (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 $^\circ\text{C}$; ^1H 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 (d, $J = 10.8$ Hz, 1H); ^{13}C NMR (150 MHz, CDCl_3) δ 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 $\text{C}_8\text{H}_6\text{NNaO}_2\text{Br}$ ($\text{M}+\text{Na}^+$) 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 $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (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 $^\circ\text{C}$, 26 h). Work up and purification gave after chromatography on $\text{SiO}_2/\text{K}_2\text{CO}_3$ (10% K_2CO_3 , hexanes/EtOAc, 98:2) gave **241** (54.5 mg, 0.311 mmol, 89%). Analytical data for **241**: ^1H NMR (600 MHz, CDCl_3) δ d, $J=2.4$ Hz, 1H), 7.72 (dd, $J=8.4, 1.8$ Hz, 1H), 7.41 (d, $J=9.0$ Hz, 1H), 6.74 (dd, $J=17.4, 10.8$ Hz, 1H), 5.92 (d, $J=17.4$ Hz, 1H), 5.55 (d, $J=10.8$ Hz, 1H); ^{13}C NMR (150 MHz, CDCl_3) δ 141.6, 140.2, 139.2, 133.1, 132.2, 124.3, 123.8, 119.1, 118.5 (q, $J^{C-F} = 319$ Hz), IR (ATR) 3117, 1581, 1519, 1431, 1343, 1207 cm^{-1} ; HRMS (ESI) calculated for $\text{C}_9\text{H}_7\text{F}_3\text{NO}_5\text{S}$ ($\text{M}+\text{H}^+$) 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 in the presence of (6.0 mg, 0.02 mmol) and $\text{Pd}(\text{dba})_2$ (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**: ^1H NMR (600 MHz, CDCl_3) δ 8.15 (d, $J = 8.4$ Hz, 1H), 7.55 (dd, $J = 9.0, 1.8$ Hz, 1H), 7.41 (d, $J = 1.2$ Hz, 1H), 6.75 (dd, $J = 17.4, 10.8$ Hz, 1H), 5.97 (d, $J = 17.4$ Hz, 1H), 5.63 (d, $J = 10.8$ Hz, 1H); ^{13}C NMR (150 MHz, CDCl_3) δ 145.3, 141.9, 139.9, 133.3, 127.1, 126.3, 121.7, 120.9, 118.5 (q, $J^{C-F} = 318$ Hz); IR (ATR) 3114, 1587, 1529, 1429, 1341, 1209 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_9\text{H}_7\text{NO}_5\text{F}_3\text{S}$ ($\text{M}+\text{H}^+$) 297.9997; found 297.9995.

3-Ethenyl-6-nitrophenyl trifluoromethanesulfonate (243) and 4-Bromo-2-ethenyl-nitrobenzene (244).¹⁸⁸ 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 $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (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 $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (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 $\text{SiO}_2/\text{K}_2\text{CO}_3$ (10% K_2CO_3 , 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 in the presence of PPh_3 (5.0 mg, 0.02 mmol) and $\text{Pd}(\text{dba})_2$ (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, CDCl_3) 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); ^{13}C NMR (150 MHz, CDCl_3) δ 147.4, 145.9, 137.5, 127.8, 127.5, 123.2, 122.9, 118.5 (q, $J^{\text{C-F}} = 319$ Hz), 117.7; IR (ATR) 3118, 1528, 1425, 1346, 1210, 1132 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_9\text{H}_7\text{NO}_5\text{F}_3\text{S}$ ($\text{M}+\text{H}^+$) 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 $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (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, CDCl_3) 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); ^{13}C NMR (100 MHz, CDCl_3) 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 $\text{C}_8\text{H}_6\text{NNaO}_2\text{Br}$ ($\text{M}+\text{Na}^+$) 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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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 $\text{SiO}_2/\text{K}_2\text{CO}_3$ (10% K_2CO_3 , hexanes/EtOAc, 19:1) **245** (122 mg, 0.412 mmol, 89%) as a pale yellow oil. ^1H NMR (600 MHz, CDCl_3) 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); ^{13}C NMR (150 MHz, CDCl_3) δ 147.4, 145.9, 137.5, 127.8, 127.5, 123.2, 122.9, 118.5 (q, $J^{\text{C-F}} = 319$ Hz), 117.7; IR (ATR) 1526, 1425, 1345, 1209, 1134, 944, 836 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_9\text{H}_6\text{NNaO}_5\text{F}_3\text{S}$ ($\text{M}+\text{Na}^+$) 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 PPh_3 (5.8 mg, 0.02 mmol) and $\text{Pd}(\text{dba})_2$ (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 $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (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, CDCl_3) 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); ^{13}C NMR (150 MHz, CDCl_3) 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 $\text{C}_8\text{H}_6\text{NNaO}_2\text{I}$ ($\text{M}+\text{Na}^+$) 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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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 $\text{SiO}_2/\text{K}_2\text{CO}_3$ (10% K_2CO_3 , 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).¹⁹⁰ To a solution of 1-hydroxy-5-bromoacetophenone¹⁸² (381 mg, 1.77 mmol) in CH₂Cl₂ (10 mL) at 0 °C was added pyridine (275 μ L, 3.41 mmol) and Tf₂O (325 μ L, 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, 0.37 mmol) in the presence of PPh₃ (6.4 mg, 0.02 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 **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), 5.83 (d, *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 (129 mg, 0.41 mmol) in the presence of LiCl (43.5 mg, 1.03 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, 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, 0.263 mmol) in the presence of PdCl₂(PPh₃)₂ (3.0 mg, 0.004 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 SiO₂/K₂CO₃ (10% K₂CO₃, 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 PPh₃ (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, 9:1) gave **251** (29.6 mg, 0.10 mmol, 33%) as a colorless oil. ¹H NMR δ 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); ¹³C NMR δ 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 C₁₀H₈F₃O₄S (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(PPh₃)₂Cl₂ (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 C₆H₃N₂O₅Br (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. Analytical 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 C₆H₄BrN₂O₅ (M+H⁺) 262.9304, found

4-Iodo-2,5-dinitrophenol (263)²¹⁸ and **4-iodo-2,3-dinitrophenol (261)**. 4-Iodo-3-nitrophenol (**260**) (5.0 g, 18.87 mmol) was added to concentrated nitric acid (HNO₃, 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 (MgSO₄), 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 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.25 (br, s, 1H), 7.72 (d, *J*=9.2 Hz, 1H), 6.98 (d, *J*=8.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃/DMSO-d₆) δ 151.8, 147.7, 142.5, 132.5, 122.6, 72.8; IR (ATR) 3237, 1544, 1433, 1215, 1137 cm⁻¹; HRMS (ESI) calcd for C₆H₄IN₂O₅ (M+H⁺) 310.9165, found

4-Iodo-2,3-dinitrophenyltrifluoromethanesulfonate (264). Treatment of **261** (1.923 g, 6.203 mmol) with Tf₂O (1.40 mL, 8.32 mmol) in CH₂Cl₂ (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 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.26 (d, *J*=8.8 Hz, 1H), 7.42 (d, *J*=8.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 148.5, 144.5, 140.7, 137.2, 126.3, 118.3 (q, *J*^{C-F}=319 Hz), 86.8; ¹⁹F NMR (376.10 MHz, CDCl₃) δ -72.5; IR (ATR) 1546, 1435, 1349, 1213, 1131 cm⁻¹; HRMS (ESI) calculated for C₇H₃F₃IN₂O₇S (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 Tf₂O (1.25 mL, 7.416 mmol) in CH₂Cl₂ in the presence of pyridine (1.40 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 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.54 (s, 1H), 7.94 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 152.0, 142.8, 140.3, 133.1, 121.7, 118.4 (q, *J*^{C-F}=320 Hz), 115.1; ¹⁹F NMR (376 MHz, CDCl₃) δ -72.5; IR (ATR) 1539, 1426, 1353, 1231, 1141 cm⁻¹; HRMS (ESI) calcd for C₇H₃BrF₃N₂O₇S (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 Tf₂O (0.98 mL, 5.82 mmol) in CH₂Cl₂ (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 °C;

^1H NMR (400 MHz, CDCl_3) δ 8.77 (s, 1H), 7.92 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 155.4, 142.5, 141.2, 139.6, 121.2, 118.4 (q, $J^{\text{C-F}}=319$ Hz), 85.8; ^{19}F NMR (376.10 MHz, CDCl_3) δ -72.4; IR (ATR) 1532, 1434, 1336, 1195, 1132 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_7\text{H}_3\text{F}_3\text{IN}_2\text{O}_7\text{S}$ ($\text{M}+\text{H}^+$) 442.8658 ($\text{M}+\text{Na}=464.8477$), 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 NaNO_3 (271 mg, 3.190 mmol) in concentrated H_2SO_4 (5 mL) at 0 $^\circ\text{C}$, 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, CDCl_3) 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 Tf_2O (1.41 mL, 8.40 mmol) in CH_2Cl_2 (18 mL) in the presence of triethylamine (Et_3N , 2.34 mL, 16.81 mmol) under a nitrogen atmosphere, as described for **258** (0 $^\circ\text{C}$ -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 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 8.18 (d, $J=8.8$ Hz, 1H), 7.95 (d, $J=9.2$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 145.8, 141.4, 134.0, 133.9, 127.7, 121.4, 118.1 (q, $J^{\text{C-F}}=320$ Hz); ^{19}F NMR (376.10 MHz, CDCl_3) δ -71.8 IR (ATR) 1534, 1437, 1350, 1218, 1131 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 NaNO_3 (648 mg, 7.629 mmol) in concentrated H_2SO_4 (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 $^\circ\text{C}$ 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 (MgSO_4), 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, CDCl_3) 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); ^{13}C NMR (150 MHz, CDCl_3) 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

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 TiF_4 (0.86 mL, 5.08 mmol) in CH_2Cl_2 (12 mL) in the presence of triethylamine (Et_3N , 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, CDCl_3) δ 8.68 (s, 1H), 8.16 (s, 1H); 151.5, 142.1, 140.9, 138.0, 123.2, 118.4 (q, $J^{\text{C-F}}$ =319.5 Hz), 94.3; ^{19}F NMR (MHz, CDCl_3) 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, CDCl_3) δ 8.18 (d, J =8.4 Hz, 1H), 7.98 (d, J =9.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 149.6, 142.2, 140.3, 133.0, 127.8, 118.1 (q, $J^{\text{C-F}}$ =319.5 Hz), 94.3; ^{19}F NMR (376.10 MHz, CDCl_3) 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 NaNO_3 (869 mg, 10.23 mmol) in concentrated H_2SO_4 (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 (MgSO_4), 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, CDCl_3) δ 11.43 (s, 1H), 8.29 (d, J =9.0 Hz, 1H), 7.31 (d, J =9.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) 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 $\text{C}_6\text{H}_4\text{BrN}_2\text{O}_5$ ($\text{M}+\text{H}^+$) 262.9304 ($\text{M}+\text{Na}$ =284.9123), found

Analytical data for 280: mp=149 °C (decomposition); ^1H NMR (400 MHz, CDCl_3) δ 8.25 (d, J =9.2 Hz, 1H), 7.28 (d, J =9.2 Hz, 1H), 6.55 (br, s, 1H); ^{13}C NMR (100 MHz, $\text{CDCl}_3/\text{DMSO}-d_6$) 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 $\text{C}_6\text{H}_4\text{BrN}_2\text{O}_5$ ($\text{M}+\text{H}^+$) 262.9304 ($\text{M}+\text{Na}$ =284.9123), found

2-Bromo-3,6-dinitrophenyltrifluoromethanesulfonate (281). Treatment of a solution of **279** (1.2360 g, 4.700 mmol) with TiF_4 (1.12 mL, 6.657 mmol) in CH_2Cl_2 (15 mL) in the presence of Et_3N (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, *J*^{C-F}=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 C₇H₃BrF₃N₂O₇S (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 a syringe. The solution was heated at reflux (100 °C, 24 h). The solvent was removed under reduced pressure and the resulting 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 C₁₂H₁₂N₂O₄Na (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 isopropenytributyltin (**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% $\text{K}_2\text{CO}_3\text{-SiO}_2$, hexane/EtOAc, 95:5) to afford **287** (189 mg, 0.761 mmol, 70%) as a white solid. mp=138-139 °C; ^1H 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 $\text{C}_{12}\text{H}_{13}\text{N}_2\text{O}_4$ ($\text{M}+\text{H}^+$) 249.0875 ($\text{M}+\text{Na}=271.0695$), found xxxxxxxxxx.

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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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; ^1H 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 $\text{C}_{10}\text{H}_9\text{N}_2\text{O}_4$ ($\text{M}+\text{H}^+$) 221.0562 ($\text{M}+\text{Na}=243.0382$), 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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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; ^1H 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 $\text{C}_{12}\text{H}_{13}\text{N}_2\text{O}_4$ ($\text{M}+\text{H}^+$) 249.0875 ($\text{M}+\text{Na}=271.0695$), found

2,4-Dinitro-1,5-di(1-propen-1-yl)benzene (290). Treatment of a solution of **204** (400.3 mg, 1.013 mmol) with **283** (772 mg, 2.331 mmol) in the presence of $\text{PdCl}_2(\text{PPh}_3)_2$ (28.3 mg, 0.040 mmol), BHT (20.1 mg, 0.091 mmol) and LiCl (133.1 mg, 3.140 mmol) in dioxane (3 mL), as described for **285** (90 °C, 23 h), gave after solvent removal and chromatography (Hexane/EtOAc, 95:5) **290** (104.2 mg, 0.420 mmol, 41%) as a yellow solid.

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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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; ¹H 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); ¹³C 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; ¹H 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); ¹³C 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; ¹H 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); ¹³C NMR (100 MHz, CDCl₃) δ 150.0, 149.6, 148.9, 148.4, 134.6, 134.2, 132.5, 131.9, 131.8, 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 C₁₂H₁₃N₂O₄ (M+H⁺) 249.0875 (M+Na=271.0695), 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, 95:5) **293** (124 mg, 0.500 mmol, 63%) 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** (71.9 mg, 0.290 mmol, 54%) as a white solid. mp=118-119 °C; ¹H NMR (600 MHz, CDCl₃) δ 7.77 (s, 2H), 5.29 (s, with further fine splitting, 2H), 5.05 (s, with further fine splitting, 2H), 2.11 (dd, *J*=2.4, 1.2 Hz, 6H); ¹³C NMR (150 MHz, CDCl₃) δ 149.6, 140.1, 138.5, 125.9, 117.6, 22.85; IR (ATR) 1533, 1350, 905, 847 cm⁻¹; HRMS (ESI) calcd for C₁₂H₁₃N₂O₄ (M+H⁺) 249.0875 (M+Na=271.0695), found

2,5-Dinitro-1,4-di(1-propen-2-yl)benzene (294). Treatment of a solution of **265** (203.4 mg, 0.515 mmol) with **284** (445 mg, 1.344 mmol) in the presence of PdCl₂(PPh₃)₂ (7.3 mg, 0.010 mmol), PPh₃ (5.4 mg, 0.021 mmol), BHT (13.2 mg, 0.060 mmol) and LiCl (78.6 mg, 1.854 mmol) in dioxane (2 mL), as described for **285** (100 °C, 26 h), gave after solvent removal and chromatography (Hexane/EtOAc, 97:3) **294** (81.9 mg, 0.330 mmol, 64%) as a white 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⁺) 221.0562 (M+Na=243.0382), 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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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. ^1H 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, 122.5, 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 $\text{C}_{12}\text{H}_{13}\text{N}_2\text{O}_4$ ($\text{M}+\text{H}^+$) 249.0875 ($\text{M}+\text{Na}$ =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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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. ^1H 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 $\text{C}_{12}\text{H}_{13}\text{N}_2\text{O}_4$ ($\text{M}+\text{H}^+$) 249.0875 ($\text{M}+\text{Na}$ =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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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/EtOAc, 95:5) **298** (82.6 mg, 0.375 mmol, 32%) as a yellow oil. ^1H 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 $\text{C}_{10}\text{H}_9\text{N}_2\text{O}_4$ ($\text{M}+\text{H}^+$) 221.0562 ($\text{M}+\text{Na}$ =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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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 C₉H₆F₃N₂O₇S (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 C₁₀H₈F₃N₂O₇S (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) **287** (15.4 mg, 0.062 mmol, 2%) and **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 PdCl₂(PPh₃)₂ (11.7 mg, 0.017 mmol), PPh₃ (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. ¹H NMR (400 MHz, CDCl₃) δ 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, 7.2 Hz, 2H), 1.27 (t, *J*=7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 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; ¹⁹F NMR (376.10 MHz, CDCl₃) δ -72.3; IR (ATR) 1716, 1552, 1212, 1131, 832 cm⁻¹; HRMS (ESI) calcd for C₁₂H₁₀F₃N₂O₉S (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 PdCl₂(PPh₃)₂ (3.6 mg, 0.005 mmol), PPh₃ (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. ¹H NMR (600 MHz, CDCl₃) δ 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); ¹³C NMR (150 MHz, CDCl₃) δ 145.3, 143.5, 140.6, 139.6, 129.7, 124.9, 124.3, 123.9, 118.5 (q, *J*^{C-F}=213 Hz); ¹⁹F NMR (MHz, CDCl₃) δ -72.8; IR (ATR) 1536, 1434, 1338, 1210, 1131 cm⁻¹; HRMS (ESI) calcd for C₉H₆F₃N₂O₇S (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 PdCl₂(PPh₃)₂ (25 mg, 0.036 mmol), PPh₃ (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. ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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, 123.7, 123.5, 123.1, 118.5 (q, *J*^{C-F}=320 Hz), 118.4 (q, *J*^{C-F}=319 Hz); ¹⁹F NMR (376.10 MHz, CDCl₃) δ -73.0, -72.9; IR (ATR) 1534, 1434, 1339, 1215, 1131 cm⁻¹; HRMS (ESI) calcd for C₁₀H₈F₃N₂O₇S (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 $\text{PdCl}_2(\text{PPh}_3)_2$ (9.9 mg, 0.014 mmol), PPh_3 (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, CDCl_3) 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); ^{13}C NMR (100 MHz, CDCl_3) δ 146.3, 146.3, 143.1, 139.8, 139.6, 126.7, 123.2, 118.9, 118.5 (q, $J^{\text{C-F}}$ =320 Hz); ^{19}F NMR (376.10 MHz, CDCl_3) δ -72.6; IR (ATR) 1539, 1435, 1340, 1213, 1131 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{10}\text{H}_8\text{F}_3\text{N}_2\text{O}_7\text{S}$ ($\text{M}+\text{H}^+$) 357.0004 ($\text{M}+\text{Na}$ =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 $\text{PdCl}_2(\text{PPh}_3)_2$ (24.8 mg, 0.035 mmol), PPh_3 (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, CDCl_3) 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); ^{13}C NMR (150 MHz, CDCl_3) δ 149.0, 143.5, 139.7, 134.5, 129.0, 126.7, 123.7, 120.8, 118.4 (q, $J^{\text{C-F}}$ =213 Hz); ^{19}F NMR (MHz, CDCl_3) δ -72.9; IR (ATR) 1553, 1437, 1342, 1213, 1130 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_9\text{H}_6\text{F}_3\text{N}_2\text{O}_7\text{S}$ ($\text{M}+\text{H}^+$) 342.9848 ($\text{M}+\text{Na}$ =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 $\text{PdCl}_2(\text{PPh}_3)_2$ (23 mg, 0.033 mmol), and PPh_3 (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, CDCl_3) 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); ^{13}C NMR (100 MHz, CDCl_3) 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, $J^{\text{C-F}}$ =319 Hz); ^{19}F NMR (376.10 MHz, CDCl_3) δ -72.6, -72.6; IR (ATR) 1532, 1336, 1202, 1123 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{10}\text{H}_8\text{F}_3\text{N}_2\text{O}_7\text{S}$ ($\text{M}+\text{H}^+$) 357.0004 ($\text{M}+\text{Na}$ =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 PdCl₂(PPh₃)₂ (35.1 mg, 0.050 mmol), PPh₃ (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; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 151.5, 144.8, 139.4, 131.1, 127.2, 125.4, 124.6, 123.8, 118.2 (q, *J*^{C-F}=319 Hz); ¹⁹F NMR (MHz, CDCl₃) δ -73.0; IR (ATR) 1548, 1341, 1207, 1129, 971 cm⁻¹; HRMS (ESI) calcd for C₉H₆F₃N₂O₇S (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 PdCl₂(PPh₃)₂ (44.5 mg, 0.063 mmol), PPh₃ (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. ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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; ¹⁹F NMR (MHz, CDCl₃) δ -73.4, -73.5; IR (ATR) 1557, 1423, 1347, 1203, 839 cm⁻¹; HRMS (ESI) calcd for C₁₀H₈F₃N₂O₇S (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 PdCl₂(PPh₃)₂ (53.9 mg, 0.077 mmol), PPh₃ (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; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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; ¹⁹F NMR (MHz, CDCl₃) δ -72.8; IR (ATR) 1548, 1419, 1336, 1197, 837 cm⁻¹; HRMS (ESI) calcd for C₁₀H₈F₃N₂O₇S (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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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; ^1H NMR (400 MHz, CDCl_3) δ 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) δ 143.0, 140.7, 137.8, 133.5, 127.6, 127.4, 126.7, 125.6, 118.1 (q, $J^{\text{C-F}}$ =320 Hz); ^{19}F NMR (376.10 MHz, CDCl_3) δ -72.3; IR (ATR) 1546, 1435, 1349, 1209, 1132 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_9\text{H}_6\text{F}_3\text{N}_2\text{O}_7\text{S}$ ($\text{M}+\text{H}^+$) 342.9848 ($\text{M}+\text{Na}$ =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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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**: ^1H NMR (400 MHz, CDCl_3) δ 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) δ 144.4, 143.4, 140.7, 138.2, 133.1, 129.6, 127.5, 119.7, 118.1 (q, $J^{\text{C-F}}$ =319 Hz), 22.5; ^{19}F NMR (376 MHz, CDCl_3) δ -72.6; IR (ATR) 1546, 1454, 1353, 1216, 1139 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{10}\text{H}_8\text{F}_3\text{N}_2\text{O}_7\text{S}$ ($\text{M}+\text{H}^+$) 357.0004 ($\text{M}+\text{Na}$ =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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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; ^1H NMR (400 MHz, CDCl_3) δ 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) δ 142.5, 142.2, 133.3, 131.4, 129.8, 128.0, 126.3, 122.9; IR (ATR) 1548, 1354, 947, 841 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_8\text{H}_6\text{ClN}_2\text{O}_4$ ($\text{M}+\text{H}^+$) 229.0016 ($\text{M}+\text{Na}$ =250.9836), 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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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. mp=102-103 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.09 (s, 2H), 7.08 (dd, *J*=17.2, 10.8 Hz, 1H), 5.90 (d, *J*=17.2 Hz, 1H), 5.69 (d, *J*=11.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 149.9, 148.4, 133.1, 129.5, 127.8, 126.4, 125.1, 122.4; IR (ATR) 1547, 1524, 1347, 1274, 851 cm⁻¹; HRMS (ESI) calcd for C₈H₆ClN₂O₄ (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 PdCl₂(PPh₃)₂ (5.8 mg, 0.008 mmol), PPh₃ (8.7 mg, 0.033 mmol), and BHT (11 mg, 0.050 mmol) in dioxane (4 mL), as described for **285** (90 °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. mp=89-90 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.04 (s, 1H), 7.86 (s, 1H), 7.09 (dd, *J*=17.2, 10.8 Hz, 1H), 5.88 (d, *J*=17.2 Hz, 1H), 5.64 (d, *J*=11.2 Hz, 1H), 5.29 (s, with further fine splitting, 1H), 5.05 (s, with further fine splitting, 1H); 2.10 (dd, *J*=1.2, 0.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 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 cm⁻¹; HRMS (ESI) calcd for C₁₁H₁₁N₂O₄ (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 PdCl₂(PPh₃)₂ (8.3 mg, 0.012 mmol), PPh₃ (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 °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. mp=95-97 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.77 (d, *J*=8.4 Hz, 1H), 7.71 (s, 2H), 7.52 (d, *J*=8.0 Hz, 1H), 6.70 (dd, *J*=17.2, 11.2 Hz, 1H), 6.68 (dd, *J*=17.2, 11.2 Hz, 1H), 6.49-6.35 (m, 3H), 6.07 (dq, *J*=14.0, 6.8 Hz, 1H), 5.93 (d, *J*=10.4 Hz, 1H), 5.88 (d, *J*=10.4 Hz, 1H), 5.61 (d, *J*=10.4 Hz, 1H), 5.58 (d, *J*=11.2 Hz, 1H), 1.93 (dd, *J*=6.0, 0.8 Hz, 3H), 1.76 (dd, *J*=7.2, 2.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 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, 1347, 1216, 1128, 902 cm⁻¹; HRMS (ESI) calcd for C₁₁H₁₁N₂O₄ (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 PdCl₂(PPh₃)₂ (7.8 mg, 0.011 mmol), PPh₃ (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 °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. mp=99-100 °C; ¹H NMR (400

MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 142.2, 141.6, 139.2, 137.8, 131.8, 131.0, 129.0, 128.4, 122.0, 118.1, 22.9; IR (ATR) 1536, 1302, 1169, 803 cm⁻¹; HRMS (ESI) calcd for C₁₁H₁₁N₂O₄ (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 PdCl₂(PPh₃)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 °C; ¹H NMR (600 MHz, CDCl₃) δ 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); ¹³C NMR (150 MHz, CDCl₃) δ 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 C₁₁H₁₁N₂O₄ (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 PdCl₂(PPh₃)₂ (16.5 mg, 0.023 mmol), PPh₃ (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 °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. ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 163.6, 142.5, 141.8, 136.8, 133.3, 132.3, 132.0, 130.6, 129.9, 127.9, 122.6, 61.9, 13.8; IR (ATR) 1703, 1523, 1363, 1156, 802 cm⁻¹; HRMS (ESI) calcd for C₁₃H₁₃N₂O₆ (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 PdCl₂(PPh₃)₂ (14.2 mg, 0.020 mmol), PPh₃ (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 °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. ¹H

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, 130.3, 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-enoate (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-enoate (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 163.6, 142.7, 141.5, 138.8, 138.4, 136.8, 133.1, 132.5, 131.8, 130.6, 118.3, 61.9, 23.1, 13.8; IR (ATR) 1650, 1534, 1372, 1169, 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, 131.0, 122.4, 121.2, 117.0, 22.9;

IR (ATR) 1582, 1522, 1344, 1265, 911, 733 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{11}\text{H}_{11}\text{N}_2\text{O}_4$ ($\text{M}+\text{H}^+$) 235.0719 ($\text{M}+\text{Na}=257.0538$), found

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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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. ^1H NMR (600 MHz, CDCl_3) δ 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); ^{13}C NMR (100 MHz, CDCl_3) δ 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 $\text{C}_{12}\text{H}_{13}\text{N}_2\text{O}_4$ ($\text{M}+\text{H}^+$) 249.0875 ($\text{M}+\text{Na}=271.0695$), found

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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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; ^1H NMR (400 MHz, CDCl_3) δ 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); ^{13}C NMR (100 MHz, CDCl_3) δ 150.1, 149.2, 149.0, 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 $\text{C}_{11}\text{H}_{11}\text{N}_2\text{O}_4$ ($\text{M}+\text{H}^+$) 235.0719 ($\text{M}+\text{Na}=257.0538$), 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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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 $\text{PdCl}_2(\text{PPh}_3)_2$ (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, CDCl_3) 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); ^{13}C NMR (100 MHz, CDCl_3) 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 $\text{C}_{12}\text{H}_{13}\text{N}_2\text{O}_4$ ($\text{M}+\text{H}^+$) 249.0875 ($\text{M}+\text{Na}=271.0695$), 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 $\text{PdCl}_2(\text{PPh}_3)_2$ (12.9 mg, 0.018 mmol), PPh_3 (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 $^\circ\text{C}$, 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, CDCl_3) 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); ^{13}C NMR (100 MHz, CDCl_3) 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, 122.8, 122.7, 122.7, 122.6, 122.3, 122.0, 18.9, 14.6; IR (ATR) 1531, 1351, 906, 726 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{11}\text{H}_{11}\text{N}_2\text{O}_4$ ($\text{M}+\text{H}^+$) 235.0719 ($\text{M}+\text{Na}=257.0538$), 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 $\text{PdCl}_2(\text{PPh}_3)_2$ (8.7 mg, 0.012 mmol), PPh_3 (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 $^\circ\text{C}$, 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, CDCl_3) 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) ¹³C NMR (100 MHz, CDCl₃) δ 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 C₁₁H₁₁N₂O₄ (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 PdCl₂(PPh₃)₂ (11.9 mg, 0.017 mmol), PPh₃ (8.9 mg, 0.034 mmol), BHT (22.5 mg, 0.102 mmol) and LiCl (1299 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. ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₁₂H₁₃N₂O₄ (M+H⁺) 249.0875 (M+Na=271.0695), found

3-Ethenyl-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 PdCl₂(PPh₃)₂ (16.4 mg, 0.023 mmol), PPh₃ (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. ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₁₁H₁₁N₂O₄ (M+H⁺) 235.0719 (M+Na=257.0538), found

1-Ethenyl-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 PdCl₂(PPh₃)₂ (12 mg, 0.017 mmol), PPh₃ (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. ¹H NMR (400 MHz, CDCl₃) δ 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),

2.11 (dd, $J=1.6, 1.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 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 $\text{C}_{11}\text{H}_{11}\text{N}_2\text{O}_4$ ($\text{M}+\text{H}^+$) 235.0719 ($\text{M}+\text{Na}=257.0538$), found

1H,6H-Pyrrolo[2,3-*g*]indole (336). A solution of **285** (35.2 mg, 0.160 mmol), palladium (II) acetate ($\text{Pd}(\text{OAc})_2$, 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 °C for 93 h. The solution was concentrated under reduced pressure at 80 °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 °C (decomposition); ^1H NMR (400 MHz, CDCl_3) δ 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) δ 123.1, 121.9, 121.7, 113.8, 103.2; IR (ATR) 3353, 1516, 1135, 1053, 754 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{10}\text{H}_9\text{N}_2$ ($\text{M}+\text{H}^+$) 157.0766 ($\text{M}+\text{Na}=179.0585$), 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) ($\text{Pd}(\text{dba})_2$, 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 °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), $\text{Pd}(\text{OAc})_2$ (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 °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 °C; ^1H NMR (400 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{10}\text{H}_9\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 189.0664 ($\text{M}+\text{Na}=211.0483$), 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); ¹H NMR (400 MHz, CDCl₃) δ 7.24 (s, 2H), 7.11 (br, s, 2H), 6.25 (dd, *J*=2.0, 1.2 Hz, 2H), 2.27 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₂H₁₃N₂ (M+H⁺) 185.1079, found

2-Methyl-7-nitro-6-(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; ¹H NMR (600 MHz, CDCl₃) 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 (d, *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); ¹³C NMR (150 MHz, CDCl₃) 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 C₁₂H₁₃N₂O₂ (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); ¹H NMR (400 MHz, Acetone-d₆) δ 9.73 (br, s, 2H), 7.19 (s, 2H), 6.92 (m, 2H), 2.32 (d, *J*=1.2 Hz, 6H); ¹³C NMR (100 MHz, Acetone-d₆) 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 C₁₂H₁₃N₂ (M+H⁺) 185.1079, found

3,6-Dimethyl-1*H*,6*H*-pyrrolo[3,2-*g*]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*H*,6*H*-pyrrolo[3,2-*g*]indole (340). Reaction of a solution of **287** (34.6 mg, 0.139 mmol), Pd(dba)₂ (8 mg, 0.014 mmol), and PPh₃ (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** (15.8mg, 0.086 mmol, 62%) as a white solid.

3-Methyl-7-nitro-6-(1-propen-2-yl)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); ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₁₂H₁₃N₂O₂ (M+H⁺) 217.0977, found

3,6-Dimethyl-1*H*,6*H*-pyrrolo[3,2-*g*]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); ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 132.5, 124.0, 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*H*,6*H*-pyrrolo[3,2-*g*]indole (342). Reaction of a solution of **317** (31 mg, 0.132 mmol), Pd(OAc)₂ (1.5 mg, 0.007 mmol), and PPh₃ (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-1*H*,6*H*-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); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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

3,6-Dimethyl-1*H*,6*H*-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); ¹H NMR (400 MHz, CDCl₃/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); ¹³C NMR (100 MHz, CDCl₃/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 C₁₂H₁₃N₂ (M+H⁺) 185.1979, found

3,6-Dimethyl-1*H*,6*H*-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); ¹H 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); ¹³C 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 C₁₃H₁₃N₂O₂ (M+H⁺) 229.0977, found

3,6-Dimethyl-1*H*,6*H*-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); ¹H 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 $\text{C}_{14}\text{H}_{15}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 243.1134, found

3,6-Dimethyl-1*H*,6*H*-pyrrolo[3,2-*g*]indole (347). A solution of **322** (85.3 mg, 0.279 mmol), $\text{Pd}(\text{OAc})_2$ (3.2 mg, 0.014 mmol), and 1,10-phen (2.5 mg, 0.014 mmol) in DMF (3 mL) was stirred under CO ($p_{\text{CO}} = 6$ atm) at 120 $^\circ\text{C}$ 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 $^\circ\text{C}$ (decomposition); ^1H 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 $\text{C}_{14}\text{H}_{15}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 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), $\text{Pd}(\text{OAc})_2$ (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** ($p_{\text{CO}} = 6$ atm, 120 $^\circ\text{C}$, 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 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_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 $\text{C}_{12}\text{H}_{13}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 217.0977, found

3,6-Dimethyl-1*H*,6*H*-pyrrolo[3,2-*g*]indole (348). Reaction of a solution of **290** (35.6 mg, 0.143 mmol), $\text{Pd}(\text{dba})_2$ (6.6 mg, 0.010 mmol), and PPh_3 (12 mg, 0.046 mmol) in DMF (1.5 mL), as described for **336** ($p_{\text{CO}} = 6$ atm, 120 $^\circ\text{C}$, 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-1*H*,6*H*-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); ¹H NMR (400 MHz, CDCl₃) δ 7.65 (s, 1H), 7.57 (br, s, 2H), 7.19 (s, 1H), 6.93 (s, 2H), 2.41 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₂H₁₃N₂ (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; ¹H NMR (600 MHz, CDCl₃) δ 8.29 (br, s, 1H), 8.08 (s, 1H), ¹³C NMR (150 MHz, CDCl₃) 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 C₁₂H₁₃N₂O₂ (M+H⁺) 217.0977, found

3,6-Dimethyl-1*H*,6*H*-pyrrolo[3,2-*g*]indole (350). Reaction of a solution of **291** (51.7 mg, 0.208 mmol), Pd(dba)₂ (7.1 mg, 0.012 mmol), and PPh₃ (13.1 mg, 0.050 mmol) in DMF (2 mL), as described for **336** (pCO = 6 atm, 120 °C, 121 h), gave, after solvent removal and chromatography (Hexane/EtOAc, 7:3) **350** (38.1 mg, 0.176 mmol, 85%) as a yellow solid.

3,6-Dimethyl-1*H*,6*H*-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); ¹H NMR (600 MHz, CDCl₃) δ 7.91 (br, s, 2H), 7.58 (s, 2H), ¹³C NMR (100 MHz, CDCl₃) δ 133.2, 126.0, 125.0, 101.4, 100.0; IR (ATR) 3336, 1156, 1053, 756 cm⁻¹; HRMS (ESI) calcd for C₁₀H₉N₂ (M+H⁺) 157.0766, found

3,6-Dimethyl-1*H*,6*H*-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 PPh₃ (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. ¹H NMR (400 MHz, CDCl₃) δ 7 ¹³C NMR (100 MHz, CDCl₃) δ 1IR (ATR) cm⁻¹; HRMS (ESI) calcd for

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; ¹H NMR (600 MHz, CDCl₃) 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), 6.34 (s, 1H), 6.29 (s, 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); ¹³C NMR (150 MHz, CDCl₃) 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 C₁₂H₁₃N₂O₂ (M+H⁺) 217.0977, found

3,6-Dimethyl-1*H*,6*H*-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 PPh₃ (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 PPh₃ (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; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ 145.1, 141.5, 138.1, 133.9, 126.8, 124.7, 117.0, 114.0, 113.8, 112.2, 23.8, 9.5; IR (ATR) 3337, 1208, 1113, 836 cm⁻¹; HRMS (ESI) calcd for C₁₂H₁₃N₂O₂ (M+H⁺) 217.0977, found

3,6-Dimethyl-1*H*,6*H*-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 PPh₃ (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); ¹H NMR (400 MHz, CDCl₃/DMSO-*d*₆) δ 9.88 (br, s, 2H), 7.25 (s, 2H), 6.91 (s, 2H), 2.25 (s, 3H); ¹³C NMR (100 MHz, CDCl₃/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 C₁₂H₁₃N₂ (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=9.2 Hz, 1H), 7.32 (dd, 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), 7.16 (d, J=9.0 Hz, 1H), 6.98 (dq, J=16.2, 1.8 Hz, 1H), 6.85 (dq, J=11.4, 1.8 Hz, 1H), 6.50-6.49 (m, 1H), 6.24-6.18 (m, 2H), 5.97 (dq, J=13.8, 7.2 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) δ 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 $\text{C}_{12}\text{H}_{13}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 217.0977, found

(356). Reaction of a solution of **297** (57.7 mg, 0.232 mmol), $\text{Pd}(\text{dba})_2$ (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** ($p\text{CO} = 6$ atm, 120 $^\circ\text{C}$, 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), $\text{Pd}(\text{dba})_2$ (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** ($p\text{CO} = 6$ atm, 120 $^\circ\text{C}$, 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), $\text{Pd}(\text{OAc})_2$ (4.8 mg, 0.021 mmol), and 1,10-phen (3.9 mg, 0.022 mmol) in DMF (3 mL), as described for **336** ($p\text{CO} = 6$ atm, 120 $^\circ\text{C}$, 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), $\text{Pd}(\text{OAc})_2$ (5.2 mg, 0.023 mmol), and 1,10-phen (4.2 mg, 0.023 mmol) in DMF (3 mL), as described for **336** ($p\text{CO} = 6$ atm, 120 $^\circ\text{C}$, 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), $\text{Pd}(\text{OAc})_2$ (4.8 mg, 0.021 mmol), and 1,10-phen (3.9 mg, 0.022 mmol) in DMF (3 mL), as described for **336** ($p\text{CO} = 6$ atm, 120 $^\circ\text{C}$, 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 $^\circ\text{C}$; ^1H NMR (400 MHz, $\text{CDCl}_3/\text{DMSO}-d_6$) δ 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, $\text{CDCl}_3/\text{DMSO}-d_6$) 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} ; $\text{C}_{10}\text{H}_9\text{N}_2$ ($\text{M}+\text{H}^+$) 157.0766, found cm^{-1} ; HRMS (ESI) calcd for Analytical data for **364**: mp=97-98 $^\circ\text{C}$; ^1H 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 $\text{C}_{10}\text{H}_9\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 189.0664, found

7-Ethenyl-6-nitroindole (364). Reaction of a solution of **298** (45.6 mg, 0.207 mmol), $\text{Pd}(\text{dba})_2$ (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 $^\circ\text{C}$, 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), $\text{Pd}(\text{OAc})_2$ (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 $^\circ\text{C}$, 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 $^\circ\text{C}$; ^1H 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 $\text{C}_{11}\text{H}_{11}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 203.0821, found

4-Nitro-5-(1-propen-2-yl)indole (366). Reaction of a solution of **330** (57.8 mg, 0.247 mmol), $\text{Pd}(\text{OAc})_2$ (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 $^\circ\text{C}$, 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 $^\circ\text{C}$; ^1H 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 $\text{C}_{11}\text{H}_{11}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$) 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), $\text{Pd}(\text{dba})_2$ (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 $^\circ\text{C}$, 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.

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-tosylindole (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, 728 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;

(373). 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), 2.27 (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), 7.67 (dd, *J* = 8.2, 3.2 Hz, 4H), 7.26 (d, *J* = 7.8 Hz, 4H), 6.91 (d, *J* = 15.4 Hz, 1H), 6.80 (d, *J* = 11.5 Hz, 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 ; ^1H NMR (600 MHz, CDCl_3) δ 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) δ 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/EoOAc, 8:2), **377** (174.4 mg, 0.471 mmol, 79%) as a yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 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, 5.5 Hz, 3H), 7.26 (dd, J = 8.1, 4.1 Hz, 3H), 6.82 (dd, J = 15.9, 1.5 Hz, 1H), 6.71 (dd, J = 11.4, 1.1 Hz, 1H), 6.60 (s, 1H), 6.34 (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) δ 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 ; ^1H NMR (600 MHz, CDCl_3) δ 8.14 (d, J = 8.5 Hz, 1H), 7.78 (d, J = 8.3 Hz, 2H), 7.72 (d, J = 3.7 Hz, 1H), 7.27 (d, J = 8.4 Hz, 2H), 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), 2.10 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 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. ^1H NMR (600 MHz, CDCl_3) δ 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) δ 145.3, 137.6, 134.8, 133.8, 130.8, 130.2, 129.7, 127.2, 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), dppp (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 ; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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), dppp (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.) ; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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), dppp (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=179-180 °C ; ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 144.1, 135.1, 134.3, 131.0, 129.5, 129.1, 127.4, 126.6, 123.1, 119.1, 111.5, 103.0, 99.8, 21.4, 9.9, 9.9; IR (ATR) 3436, 1349, 1166, 734 cm⁻¹;

(383). Reaction of a solution of **375** (58.2 mg, 0.157 mmol), Pd(dba)₂ (6.3 mg, 0.011 mmol), dppp (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. ¹H NMR (600 MHz, CDCl₃) δ 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); ¹³C NMR (150 MHz, CDCl₃) δ 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. ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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, 777 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; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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.); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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

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Figure 1.2 ¹H and ¹³C NMR of compound **2**

Figure 1.3 ¹H and ¹³C NMR of compound **3**

Figure 1.4 ¹H and ¹³C NMR of compound **4**

Figure 1.5 ¹H and ¹³C NMR of compound 6

Figure 1.6 ¹H and ¹³C NMR of compound **7**

Figure 1.7 ¹H and ¹³C NMR of compound **8**

Figure 1.8 ^1H and ^{13}C NMR of Alocasin A

Figure 1.9 ^1H and ^{13}C NMR of compound **11**

Figure 1.10 ¹H and ¹³C NMR of compound **12**

Figure 1.11 ¹H and ¹³C NMR of compound **13**

Figure 1.12 ¹H and ¹³C NMR of compound **14**

Figure 1.13 ¹H and ¹³C NMR of scalaridine A

Figure 1.14 ¹H and ¹³C NMR of compound **16**

Figure 1.15 ¹H and ¹³C NMR of compound **17**

Figure 1.16 ¹H and ¹³C NMR of compound **18**

Figure 1.17 ¹H and ¹³C NMR of compound **19**

Figure 1.18 ^1H and ^{13}C NMR of compound **20**

Figure 1.19 ¹H and ¹³C NMR of compound 21

Figure 1.20 ¹H and ¹³C NMR of compound 22

Figure 1.21 ¹H and ¹³C NMR of hyrtinadine A

Figure 1.22 ¹H and ¹³C NMR of compound **24**

Figure 1.23 ^1H and ^{13}C NMR of compound **25**

Figure 1.24 ¹H and ¹³C NMR of compound 26

Figure 1.25 ¹H and ¹³C NMR of hyrtinadine B

Figure 2.2 ¹H and ¹³C NMR of compound **28**

Figure 2.3 ¹H and ¹³C NMR of compound **29**

Figure 2.4 ¹H and ¹³C NMR of compound **30**

Figure 2.5 ¹H and ¹³C NMR of compound 32

Figure 2.6 ¹H and ¹³C NMR of compound 34

Figure 2.7 ¹H and ¹³C NMR of compound **35**

Figure 2.8 ¹H and ¹³C NMR of compound **36**

Figure 2.9 ^1H and ^{13}C NMR of compound **37**

Figure 2.10 ^1H and ^{13}C NMR of compound **38**

Figure 2.11 ¹H and ¹³C NMR of compound **39**

Figure 2.12 ¹H and ¹³C NMR of compound **40**

Figure 2.13 ¹H and ¹³C NMR of compound **41**

Figure 2.14 ¹H and ¹³C NMR of compound **42**

Figure 2.15 ¹H and ¹³C NMR of compound **43**

Figure 2.16 ¹H and ¹³C NMR of compound **48**

Figure 2.17 ¹H and ¹³C NMR of compound **49**

Figure 2.18 ¹H and ¹³C NMR of compound **50**

Figure 2.19 ¹H and ¹³C NMR of compound **51**

Figure 2.20 ¹H and ¹³C NMR of compound **52**

Figure 2.21 ¹H and ¹³C NMR of compound **53**

Figure 2.22 ^1H and ^{13}C NMR of compound **54**

Figure 2.23 ^1H and ^{13}C NMR of compound **55**

Figure 2.24 ¹H and ¹³C NMR of compound 56

Figure 2.25 ¹H and ¹³C NMR of compound **57**

Figure 2.26 ¹H and ¹³C NMR of compound **58**

Figure 2.27 ¹H and ¹³C NMR of compound 59

Figure 2.28 ¹H and ¹³C NMR of compound **60**

Figure 2.29 ¹H and ¹³C NMR of compound **62**

Figure 2.30 ^1H and ^{13}C NMR of compound **63**

Figure 2.31 ^1H and ^{13}C NMR of compound **64**

Figure 2.32 ¹H and ¹³C NMR of compound 66

Figure 2.33 ¹H and ¹³C NMR of compound **67**

Figure 2.34 ^1H and ^{13}C NMR of compound **68**

Figure 2.35 ¹H and ¹³C NMR of compound **69**

Figure 2.35 ¹H and ¹³C NMR of compound **71**

Figure 2.37 ¹H and ¹³C NMR of compound **72**

Figure 2.38 ¹H and ¹³C NMR of compound **73**

Figure 2.39 ¹H and ¹³C NMR of compound **74**

Figure 2.40 ¹H and ¹³C NMR of compound **75**

Figure 2.41 ¹H and ¹³C NMR of compound 76

Figure 2.42 ¹H and ¹³C NMR of compound 77

Figure 2.43 ¹H and ¹³C NMR of compound **78**

Figure 2.44 ¹H and ¹³C NMR of compound **81**

Figure 2.45 ¹H and ¹³C NMR of compound 82

Figure 2.46 ¹H and ¹³C NMR of compound **88**

Figure 2.47 ¹H and ¹³C NMR of compound 89

Figure 2.48 ¹H and ¹³C NMR of compound **90**

Figure 2.49 ¹H and ¹³C NMR of compound **91**

Figure 2.50 ^1H and ^{13}C NMR of compound **92**

Figure 2.51 ¹H and ¹³C NMR of compound **93**

Figure 2.52 ¹H and ¹³C NMR of compound 94

Figure 2.53 ^1H and ^{13}C NMR of compound **95**

Figure 2.54 ¹H and ¹³C NMR of compound **96**

Figure 2.55 ¹H and ¹³C NMR of compound 97

Figure 2.56 ¹H and ¹³C NMR of compound **99**

Figure 2.57 ^1H and ^{13}C NMR of compound 100

Figure 2.58 ¹H and ¹³C NMR of compound 101

Figure 2.59 ¹H and ¹³C NMR of compound **102**

Figure 3.2 ^1H and ^{13}C NMR of compound **113**

Figure 3.3 ¹H and ¹³C NMR of compound **114**

Figure 3.4 ¹H and ¹³C NMR of compound **115**

Figure 3.5 ¹H and ¹³C NMR of compound 116

Figure 3.6 ¹H and ¹³C NMR of compound **111**

Figure 3.7 ¹H and ¹³C NMR of compound **103**

Figure 3.8 ¹H and ¹³C NMR of compound **105**

Figure 3.9 ¹H and ¹³C NMR of compound **118**

Figure 3.10 ¹H and ¹³C NMR of compound **119**

Figure 3.11 ¹H and ¹³C NMR of compound **120**

Figure 3.12 ¹H and ¹³C NMR of compound **104**

Figure 3.13 ¹H and ¹³C NMR of compound **121**

Figure 4.1 ^1H and ^{13}C NMR of compound **124**

Figure 4.2 ¹H and ¹³C NMR of compound **125**

Figure 4.3 ^1H and ^{13}C NMR of compound **125**

Figure 4.4 ¹H and ¹³C NMR of compound **128**

Figure 4.5 ^1H and ^{13}C NMR of compound **129**

Figure 4.6 ¹H and ¹³C NMR of compound **130**

Figure 4.7 ^1H and ^{13}C NMR of compound **132**

Figure 4.8 ¹H and ¹³C NMR of compound **133**

Figure 4.9 ¹H and ¹³C NMR of compound **134**

Figure 4.10 ^1H and ^{13}C NMR of compound **135**

Figure 4.11 ^1H and ^{13}C NMR of compound **136**

Figure 4.12 ^1H and ^{13}C NMR of compound **137**

Figure 4.13 ^1H and ^{13}C NMR of compound **139**

Figure 4.14 ^1H and ^{13}C NMR of compound **140**

Figure 4.15 ^1H and ^{13}C NMR of compound **141**

Figure 4.16 ¹H and ¹³C NMR of compound **143**

Figure 4.17 ¹H and ¹³C NMR of compound **145**

Figure 4.18 ^1H and ^{13}C NMR of compound **146**

Figure 4.19 ¹H and ¹³C NMR of compound **148**

Figure 4.20 ^1H and ^{13}C NMR of compound **149**

Figure 4.21 ¹H and ¹³C NMR of compound **150**

Figure 4.22 ¹H and ¹³C NMR of compound **151**

Figure 4.23 ^1H and ^{13}C NMR of compound **152**

Figure 4.24 ¹H and ¹³C NMR of compound **153**

Figure 4.25 ¹H and ¹³C NMR of compound **154**

Figure 4.26 ^1H and ^{13}C NMR of compound **155**

Figure 4.27 ^1H and ^{13}C NMR of compound **156**

Figure 4.28 ^1H and ^{13}C NMR of compound **158**

Figure 4.29 ^1H and ^{13}C NMR of compound **159**

Figure 4.30 ¹H and ¹³C NMR of compound **160**

Figure 4.31 ¹H and ¹³C NMR of compound **161**

Figure 4.32 ^1H and ^{13}C NMR of compound **162**

Figure 4.33 ¹H and ¹³C NMR of compound **163**

Figure 4.34 ^1H and ^{13}C NMR of compound **164**

Figure 4.35 ^1H and ^{13}C NMR of compound **165**

Figure 4.36 ¹H and ¹³C NMR of compound **166**

Figure 4.37 ¹H and ¹³C NMR of compound **167**

Figure 4.38 ¹H and ¹³C NMR of compound **169**

Figure 4.39 ¹H and ¹³C NMR of compound **171**

Figure 4.40 ¹H and ¹³C NMR of compound **172**

Figure 4.41 ^1H and ^{13}C NMR of compound **173**

Figure 4.42 ^1H and ^{13}C NMR of compound **174**

Figure 4.43 ^1H and ^{13}C NMR of compound **175**

Figure 4.44 ¹H and ¹³C NMR of compound **176**

Figure 4.45 ¹H and ¹³C NMR of compound **177**

Figure 4.46 ^1H and ^{13}C NMR of compound **178**

Figure 4.47 ¹H and ¹³C NMR of compound **179**

Figure 4.48 ¹H and ¹³C NMR of compound **180**

Figure 4.49 ^1H and ^{13}C NMR of compound **181**

Figure 4.50 ^1H and ^{13}C NMR of compound **182**

Figure 4.51 ¹H and ¹³C NMR of 4-carbomethoxy-*N*-methyl-*N*-(2-methyl-1-propen-1-yl)-2-nitroaniline

Figure 4.52 ¹H and ¹³C NMR of 2,4-dinitro-*N*-methyl-*N*-(2-methyl-1-propen-1-yl)aniline

Figure 4.53 ¹H and ¹³C NMR of 5-chloro-*N*-(2-methyl-1-propen-1-yl)-2-nitroaniline

Figure 5.1 ¹H and ¹³C NMR of compound **190**

Figure 5.2 ¹H and ¹³C NMR of compound **191**

Figure 5.3 ¹H and ¹³C NMR of compound **192**

Figure 5.4 ^1H and ^{13}C NMR of compound **193**

Figure 5.5 ¹H and ¹³C NMR of compound **195**

Figure 5.6 ¹H and ¹³C NMR of compound **196**

Figure 5.7 ^1H and ^{13}C NMR of compound **197**

Figure 5.8 ¹H and ¹³C NMR of compound **198**

Figure 5.9 ¹H and ¹³C NMR of compound **199**

Figure 5.10 ¹H and ¹³C NMR of compound **200**

Figure 5.11 ^1H and ^{13}C NMR of compound **201**

Figure 6.2 ¹H of compound **204**

Figure 6.3 ¹³C and ¹⁹F NMR of compound **204**

Figure 6.4 ¹H NMR of compound **205**

Figure 6.5 ¹³C and ¹⁹F NMR of compound **205**

Figure 6.6 ¹H and ¹³C NMR of compound **211**

Figure 6.7 ¹H and ¹³C NMR of compound **215**

Figure 6.8 ¹H of compound **216**

Figure 6.9 ^{13}C and ^{19}F NMR of compound **216**

Figure 6.10 ¹H of compound **217**

Figure 6.11 ¹³C and ¹⁹F NMR of compound **217**

Figure 6.12 ¹H and ¹³C NMR of compound **219**

Figure 6.13 ¹H and ¹³C NMR of compound **222**

Figure 6.14 ¹H and ¹³C NMR of compound **224**

Figure 6.15 ¹H and ¹³C NMR of compound **225**

Figure 6.16 ¹H and ¹³C NMR of compound **226**

Figure 6.17 ¹H and ¹³C NMR of compound **227**

Figure 6.18 ¹H of a mixture of compounds **226** and **228**

Figure 6.19 ¹H and ¹³C NMR of compound **229**

Figure 6.20 ¹H and ¹³C NMR of compound **232**

Figure 6.21 ¹H and ¹³C NMR of compound **233**

Figure 6.22 ^1H and ^{13}C NMR of compound **234**

Figure 6.23 ¹H and ¹³C NMR of compound **235**

Figure 6.24 ¹H and ¹³C NMR of compound 237

Figure 6.25 ¹H and ¹³C NMR of compound **238**

Figure 6.26 ¹H and ¹³C NMR of compound **239**

Figure 6.27 ¹H and ¹³C NMR of compound **240**

Figure 6.28 ¹H and ¹³C NMR of compound **241**

Figure 6.29 ¹H and ¹³C NMR of compound **242**

Figure 6.30 ¹H and ¹³C NMR of compound **243**

Figure 6.31 ¹H and ¹³C NMR of compound **245**

Figure 6.32 ¹H and ¹³C NMR of compound **246**

Figure 6.33 ¹H and ¹³C NMR of compound 249

Figure 6.34 ^1H and ^{13}C NMR of compound **253**

Figure 6.35 ^1H and ^{13}C NMR of compound **254**

Figure 6.36 ¹H and ¹³C NMR of compound **255**

Figure 7.2 ¹H and ¹³C NMR of compound **257**

Figure 7.3 ¹H of compound **258**

Figure 7.4 ¹³C and ¹⁹F NMR of compound **258**

Figure 7.5 ¹H and ¹³C NMR of compound 261

Figure 7.6 ^1H and ^{13}C NMR of compound **262**

Figure 7.7 ¹H NMR of compound **264**

Figure 7.8 ¹³C and ¹⁹F NMR of compound 264

Figure 7.9 ^1H NMR of compound **265**

Figure 7.10 ^{13}C and ^{19}F NMR of compound **265**

Figure 7.11 ^1H NMR of compound **266**

Figure 7.12 ^{13}C and ^{19}F NMR of compound **266**

Figure 7.13 ^1H NMR of a mixture of **270** and **271**

Figure 7.14 ¹H NMR of compound **273**

Figure 7.15 ¹³C and ¹⁹F NMR of compound **273**

Figure 7.16 ¹H and ¹³C NMR of a mixture of **274** and **275**

Figure 7.17 ^1H NMR of compound **276**

Figure 7.18 ¹³C and ¹⁹F NMR of compound **276**

Figure 7.19 ¹H NMR of compound **277**

Figure 7.20 ^{13}C and ^{19}F NMR of compound **277**

Figure 7.21 ¹H and ¹³C NMR of compound 279

Figure 7.22 ¹H and ¹³C NMR of compound **280**

Figure 7.23 ^1H NMR of compound **281**

Figure 7.24 ¹³C and ¹⁹F NMR of compound **281**

Figure 7.25 ¹H and ¹³C NMR of compound **285**

Figure 7.26 ^1H and ^{13}C NMR of compound **286**

Figure 7.27 ¹H and ¹³C NMR of compound **287**

Figure 7.28 ¹H and ¹³C NMR of compound **289**

Figure 7.29 ^1H and ^{13}C NMR of compound **290**

Figure 7.30 ^1H and ^{13}C NMR of compound **291**

Figure 7.31 ^1H and ^{13}C NMR of compound **292**

Figure 7.32 ¹H and ¹³C NMR of compound **293**

Figure 7.33 ^1H and ^{13}C NMR of compound **294**

Figure 7.34 ^1H and ^{13}C NMR of compound **295**

Figure 7.35 ^1H and ^{13}C NMR of compound **296**

Figure 7.36 ^1H and ^{13}C NMR of compound **297**

Figure 7.37 ¹H and ¹³C NMR of compound **298**

Figure 7.38 ^1H NMR of compound **300**

Figure 7.39 ¹³C and ¹⁹F NMR of compound **300**

Figure 7.40 ¹H NMR of compound **301**

Figure 7.41 ¹³C and ¹⁹F NMR of compound **300**

Figure 7.42 ^1H and ^{13}C NMR of compound **302**

Figure 7.43 ¹H NMR of compound **303**

Figure 7.44 ¹³C and ¹⁹F 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 ¹H NMR of compound **306**

Figure 7.48 ¹³C and ¹⁹F NMR of compound **306**

Figure 7.49 ¹H NMR of compound **307**

Figure 7.50 ¹³C and ¹⁹F NMR of compound **307**

Figure 7.51 ¹H NMR of compound **308**

Figure 7.52 ¹³C and ¹⁹F NMR of compound **308**

Figure 7.53 ^1H NMR of compound **309**

Figure 7.54 ¹³C and ¹⁹F NMR of compound **309**

Figure 7.55 ^1H NMR of compound **310**

Figure 7.56 ^{13}C and ^{19}F NMR of compound **310**

Figure 7.57 ¹H NMR of compound **311**

Figure 7.58 ¹³C and ¹⁹F NMR of compound **311**

Figure 7.59 ¹H NMR of compound **312**

Figure 7.60 ^{13}C and ^{19}F NMR of compound **312**

Figure 7.61 ¹H NMR of compound **313**

Figure 7.62 ¹³C and ¹⁹F NMR of compound **313**

Figure 7.63 ¹H and ¹³C NMR of compound **314**

Figure 7.64 ^1H and ^{13}C NMR of compound **315**

Figure 7.65 ¹H and ¹³C NMR of compound **316**

Figure 7.66 ^1H and ^{13}C NMR of compound **317**

Figure 7.67 ^1H and ^{13}C NMR of compound **318**

Figure 7.68 ^1H and ^{13}C NMR of compound **319**

Figure 7.69 ^1H and ^{13}C NMR of compound **320**

Figure 7.70 ^1H and ^{13}C NMR of compound **321**

Figure 7.71 ^1H and ^{13}C NMR of compound **322**

Figure 7.72 ^1H and ^{13}C NMR of compound **323**

Figure 7.73 ¹H and ¹³C NMR of compound **324**

Figure 7.74 ^1H and ^{13}C NMR of compound **325**

Figure 7.75 ¹H and ¹³C NMR of compound **326**

Figure 7.76 ^1H and ^{13}C NMR of compound **327**

Figure 7.77 ^1H and ^{13}C NMR of compound **328**

Figure 7.78 ¹H and ¹³C NMR of compound **329**

Figure 7.79 ^1H and ^{13}C NMR of compound **330**

Figure 7.80 ¹H and ¹³C NMR of compound **331**

Figure 7.81 ^1H and ^{13}C NMR of compound **336**

Figure 7.82 ¹H and ¹³C NMR of compound 337

Figure 7.83 ^1H and ^{13}C NMR of compound **338**

Figure 7.84 ^1H and ^{13}C NMR of compound **339**

Figure 7.85 ¹H and ¹³C NMR of compound **340**

Figure 7.86 ^1H and ^{13}C NMR of compound **341**

Figure 7.87 ^1H and ^{13}C NMR of compound **342**

Figure 7.88 ^1H and ^{13}C NMR of compound **343**

Figure 7.89 ¹H and ¹³C NMR of compound 344

Figure 7.90 ^1H and ^{13}C NMR of compound **345**

Figure 7.91 ¹H and ¹³C NMR of compound **346**

Figure 7.92 ¹H and ¹³C NMR of compound 347

Figure 7.93 ¹H and ¹³C NMR of compound 348

Figure 7.94 ^1H and ^{13}C NMR of compound **349**

Figure 7.95 ^1H and ^{13}C NMR of compound **350**

Figure 7.96 ^1H and ^{13}C NMR of compound **351**

Figure 7.97 ¹H and ¹³C NMR of compound **352**

Figure 7.98 ^1H and ^{13}C NMR of compound **353**

Figure 7.99 ¹H and ¹³C NMR

Figure 7.100 ¹H and ¹³C NMR of compound **354**

Figure 7.101 ¹H and ¹³C NMR of compound **355**

Figure 7.102 ^1H and ^{13}C NMR of compound **356**

Figure 7.103 ¹H and ¹³C NMR of compound **363**

Figure 7.104 ¹H and ¹³C NMR of compound **364**

Figure 7.105 ^1H and ^{13}C NMR of compound **365**

Figure 7.106 ^1H and ^{13}C NMR of compound **366**

Figure 7.107 ^1H and ^{13}C NMR of compound **368**

Figure 7.108 ^1H and ^{13}C NMR of compound **369**

Figure 7.109 ¹H and ¹³C NMR of compound **370**

Figure 7.110 ^1H and ^{13}C NMR of compound **371**

Figure 7.111 ¹H and ¹³C NMR of compound **372**

Figure 7.112 ¹H and ¹³C NMR of compound **373**

Figure 7.113 ¹H and ¹³C NMR of compound **374**

Figure 7.114 ¹H and ¹³C NMR of compound **375**

Figure 7.115 ^1H and ^{13}C NMR of compound **376**

Figure 7.116 ^1H and ^{13}C NMR of compound **377**

Figure 7.117 ¹H and ¹³C NMR of compound **378**

Figure 7.118 ^1H and ^{13}C NMR of compound **379**

Figure 7.119 ^1H and ^{13}C NMR of compound **380**

Figure 7.120 ¹H and ¹³C NMR of compound **381**

Figure 7.121 ^1H and ^{13}C NMR of compound **382**

Figure 7.122 ^1H and ^{13}C NMR of compound **383**

Figure 7.123 ^1H and ^{13}C NMR of compound **384**

Figure 7.124 ^1H and ^{13}C NMR of compound **385**

Figure 7.125 ¹H and ¹³C 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**

Nurul Hoda Ansari

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