Application of 1,2,3-Triazole in Gold Catalysis and Photoredox Catalysis

Rong Cai

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Application of 1, 2, 3-Triazole in Gold Catalysis and Photoredox Catalysis

Rong Cai

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

Doctor of Philosophy in Organic Chemistry

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Morgantown, West Virginia 2016

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Abstract

Application of 1, 2, 3-Triazole in Gold Catalysis and Photoredox Catalysis
Rong Cai

Homogeneous gold catalysis has envisioned a rapid development during the past decade due to the remarkable efficiency of Au(I) in alkyne and allene activation. Air and thermally stable triazapentalene zwitterion compounds (TAPZ) were prepared through Au(I)-catalyzed triazole-alkyne 5-endo-dig cyclization. While effective gold catalyst turnover was achieved, the stability of these new 10-π-electron bicyclic structures was also significantly improved through the introduction of electron-withdrawing groups, which allowed the further application of these fluorescent dyes in cell imaging.

Silver salts are generally used for the activation of LAuCl through Cl⁻ removal, and they are assumed to be innocent in Au(I) catalysis. For the first time, experimental evidences from XPS and ³¹P NMR were obtained to confirm that the combination of Ag⁺ cation with [L-Au]⁺ resulted in the formation of different complexes in solution. Cationic gold was proved to be inactive without the presence of silver salts and it could be re-activated by the addition of silver salts in several precedent reactions. This study revealed a long-overlooked “silver effect” and initiated a mechanistic reconsideration in gold catalysis.

Compared with Au(I) catalysis, redox gold catalysis is far less developed due to the relatively high oxidation potential of Au(I)/Au(III). With the assistance of bpy ligand, gold-catalyzed sp-sp² and sp²-sp² cross-coupling reactions are accomplished with aryldiazonium salts as the coupling partner. The gold(I) species were oxidized to gold(III) by diazonium without any external oxidants. Monitoring the reaction with NMR and ESI-MS provided strong evidence for the nitrogen extrusion as the key step followed by Au(III) reductive elimination. To further extend the scope of the gold redox chemistry with aryldiazonium salts, gold-catalyzed Sandmeyer reactions were investigated using different nucleophiles, forming C-Br, C-S and C-P bonds in high yields and selectivity.

Despite the high efficiency of gold catalysts, their application for large-scale synthesis is limited due to the high catalyst cost. A recyclable triazole-gold catalyst, which dramatically decreases the catalyst cost, is prepared using porous polymer as the support ligand. This unique catalyst is successfully applied into previously challenging transformations with good efficiency and recyclability.

Visible light photocatalysis is an efficient and green method that can convert the energy from visible light to chemical energy. One challenge to accomplish the catalytic cycle is the matching of redox potential between the substrate and the photocatalyst. With the easily tunable triazole ligands, N-2-Aryl chelated triazole-Ir(III) complexes with various substituents were prepared. These Ir(III) complexes were tested in photoredox catalysis with different reactivities related with their tunable photoredox potentials.
Dedicated to

My Dear Parents
&
Grandparents
Acknowledgment

I would like to express my deepest gratitude to my supervisor, Prof. Xiaodong Michael Shi, for his guidance during my PhD studies. He is the one who led me to the door of organic chemistry and guided me through the jungle of obstacles. His enthusiasm, diligence, persistence and broad knowledge in chemistry have always inspired me. Not only has he taught me how to become a better chemist, but also he has never hesitated to offer me advise and support whenever they are needed throughout my graduate life. Without him, I would have never got this far.

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TABLE OF CONTENT

Abstract ........................................................................................................................................ii
Dedication ..................................................................................................................................iii
Acknowledgements ........................................................................................................................iv
Table of Contents ........................................................................................................................vi
List of Scheme ............................................................................................................................viii
List of Table ..................................................................................................................................x
List of Figure ...............................................................................................................................xi

Chapter 1. Gold-Catalyzed Synthesis of Triazapentalene Zwitterions ............. 1
1.1 Introduction ............................................................................................................................... 1
   1.1.1 Homogeneous gold(I) catalysis ......................................................................................... 1
   1.1.2 Triazole-gold(I) catalyst with improved stability .............................................................. 3
   1.1.3 Acid-stable vinyl-gold complexes ............................................................................... 4
1.2 Catalytic cyclization of propargyl triazole ................................................................. 5
1.3 Triazapentalenes as biocompatible fluorophores ...................................................... 8
   1.3.1 Triazapentalenes from cascade click chemistry ............................................................ 8
   1.3.2 Triazapentalenes with improved stability ........................................................................ 9
   1.3.3 Fluorescence investigation of selected triazapentalenes .......................................... 10
1.4 Conclusion ............................................................................................................................... 13
1.5 Contribution ............................................................................................................................ 14

Chapter 2. “Silver Effect” in Gold(I) Catalysis ...................................................... 17
2.1 Introduction ............................................................................................................................... 17
2.2 Gold(I)-catalyzed propargyl ester hydration .............................................................. 18
2.3 “Silver effect” in alkyne hydration ...................................................................................... 20
2.4 Revision of gold(I)-catalyzed reactions ........................................................................... 25
   2.4.1 Different types of gold(I) catalysis .............................................................................. 25
   2.4.2 Celite filtration ............................................................................................................ 28
   2.4.3 Other activation factors in gold(I) catalysis ............................................................... 29
2.5 Conclusion ............................................................................................................................... 31
2. 6 Contribution .................................................................................................................. 31

Chapter 3. Gold-Catalyzed Cross-Coupling with Aryldiazonium Salts .......................... 34
3. 1 Introduction...................................................................................................................... 34
3. 2 Cross-coupling of alkyne and aryldiazonium ............................................................... 38
3. 3 Reactions of diazonium salts with gold complexes ...................................................... 42
3. 4 Cross-coupling of aryl boronic acid and diazonium ...................................................... 46
3. 6 Mechanistic investigation ............................................................................................ 48
3. 7 Gold-catalyzed C-X formation with aryldiazonium ...................................................... 52
   3.7.1 Catalytic Sandmeyer reaction .................................................................................. 52
   3.7.2 Gold-catalyzed C-S and C-P bond formation ......................................................... 54
3. 8 Conclusion .................................................................................................................... 58
3. 9 Contribution .................................................................................................................. 59

Chapter 4. Porous Polymer-Supported Heterogeneous Gold(I) Catalysis ....................... 64
4. 1 Introduction .................................................................................................................... 64
   4.1.1 Heterogeneous gold(I) catalysis ............................................................................. 64
   4.1.2 Porous polymer for transition-metal catalysts ....................................................... 66
4. 2 Porous polymer-supported triazole-gold catalyst ....................................................... 66
   4.2.1 Improved stability of Pol-TA-Au ........................................................................... 66
   4.2.2 Combining Lewis acid with Pol-TA-Au ................................................................. 70
4. 3 Conclusion .................................................................................................................... 71
4. 4 Contribution .................................................................................................................. 72

Chapter 5. N-2-Aryl-1,2,3-Triazole as Ligands for Iridium Photocatalysts .................... 74
5. 1 Introduction .................................................................................................................... 74
   5.1.1 Visible light photoredox catalysis ......................................................................... 74
   5.1.2 Iridium photocatalysts utilizing triazole ligands ...................................................... 77
5. 2 NAT-based iridium complexes as photocatalysts ......................................................... 79
5. 3 Conclusion .................................................................................................................... 84
5. 4 Contribution .................................................................................................................. 84

Appendix ............................................................................................................................... 87

Experimental Details ........................................................................................................... 88
List of Schemes

Scheme 1. Relativistic effect of gold ................................................................. 1
Scheme 2. Nucleophilic addition to gold-activated alkynes .............................. 2
Scheme 3. Examples for nucleophilic addition to gold-activated alkynes .... 3
Scheme 4. Triazole-gold catalyst for intermolecular alkyne hydroamination .... 4
Scheme 5. Formation of acid-stable vinyl-gold complexes ......................... 5
Scheme 6. Proposed strategy for gold turnover ............................................. 6
Scheme 7. Triazapentalene synthesis from click-cyclization-aromatization ..... 8
Scheme 8. Preparation of EWG-free TAPZ through decarboxylation .......... 9
Scheme 9. Will silver influence gold catalysis? ........................................... 17
Scheme 10. Proposed asymmetric synthesis of α-hydroxyl methyl ketone .... 18
Scheme 11. Refining gold catalysis based on the reactivity ......................... 25
Scheme 12. Purely Au-catalyzed reactions ......................................................... 26
Scheme 13. Au-Ag bimetallic catalysis ................................................................. 26
Scheme 14. Ag-assisted Au catalysis ................................................................. 27
Scheme 15. Ag-promoted reactions ................................................................. 28
Scheme 16. Gold catalysis using Tf₂N⁻ as the activation factor ..................... 30
Scheme 17. Representative examples of redox gold catalysis ....................... 34
Scheme 18. Combining gold catalysis with photocatalysis ......................... 35
Scheme 19. Selected examples of gold(I) oxidative addition to C-X bonds .... 36
Scheme 20. Examples for reductive elimination from gold(III) ..................... 37
Scheme 21. Oxidative cross-coupling of terminal alkynes ......................... 39
Scheme 22. Summary of reaction between diazonium and gold complexes .... 45
Scheme 23. Radical trapping experiment ............................................................. 49
Scheme 24. Proposed mechanism of gold-catalyzed C-C cross-coupling .... 51
Scheme 25. Literature precedence of solid-supported gold catalysts .......... 65
Scheme 27. Representative hydration reactions with Pol-TA-Au ............... 69
Scheme 28. Chemoselectivity of Pol-TA-Au ......................................................... 69
Scheme 29. Hydroamination of alkyne with Pol-TA-Au ........................................... 70
Scheme 30. Examples for Pol-TA-Au catalyzed challenging reactions ........... 71
Scheme 31. The photochemistry of Ru(bpy)$_3^{2+}$ .......................................................... 75
Scheme 32. Selected example of photoredox catalysis ................................................. 76
Scheme 33. The ligand effect in photocatalysis............................................................... 77
Scheme 34. C-Aryl-Ir(III) complex with 1,2,3-triazole ligands ......................... 78
Scheme 35. Proposed new N-Aryl-Ir(III) complexes .................................................. 79
Scheme 36. Synthetic route for NAT-Ir(III) complexes ............................................. 79
Scheme 37. TA-Ir as effective photocatalysts................................................................. 83
List of Tables

Table 1. Optimization of reaction conditions for TAPZ synthesis ....................... 6
Table 2. Reaction substrate scope for TAPZ synthesis .................................... 7
Table 3. Fluorescence properties of selected TAPZs ......................................... 11
Table 4. Fluorescence properties of diester TAPZs ........................................... 12
Table 5. Optimization of conditions for propargyl ester hydration ...................... 19
Table 6. Substrate scope for propargyl ester hydration .................................... 20
Table 7. Silver effect in propargyl ester hydration ........................................... 21
Table 8. Silver effect in IPr-Au catalyzed alkyne hydration ................................ 24
Table 9. Comparison of celite filtration and acid activation ............................... 29
Table 10. Gold-catalyzed C(sp)-C(sp²) coupling without external oxidants ......... 39
Table 11. Condition optimization for gold-catalyzed C(sp)-C(sp²) coupling ........... 40
Table 12. Substrate scope for gold-catalyzed C(sp)-C(sp²) coupling ................. 42
Table 13. Condition optimization for gold-catalyzed C(sp²)-C(sp²) coupling ...... 46
Table 14. Substrate scope for gold-catalyzed C(sp²)-C(sp²) coupling ............... 47
Table 15. Gold-catalyzed C-Br bond formation .............................................. 53
Table 16. Substrate scope for gold-catalyzed C-Br bond formation ................. 54
Table 17. Gold-catalyzed C-S bond formation ............................................... 55
Table 18. Substrate scope for gold-catalyzed C-S bond formation .................... 56
Table 19. Gold-catalyzed C-P bond formation .............................................. 57
Table 20. Substrate scope for gold-catalyzed C-P bond formation ................. 58
Table 21. Redox potential of selected iridium complexes ............................... 81
Table 22. Redox potential of selected iridium complexes with tapy ligand ......... 83
List of Figures

Figure 1. X-ray crystal structure of TAZ-Au-IPr........................................................5
Figure 2. Stability comparison of different triazapentalenes ...............................9
Figure 3. Emission spectra of TAPZs with different substitutes ..................10
Figure 4. X-ray crystal structures and emission spectra for selected TAPZs ....11
Figure 5. Selected images of cells incubated with 10µM TAPZs ..............13
Figure 6. X-ray crystal structure of [IPr-Au-TA]+OTf complex ..................21
Figure 7. XPS spectra of the (PPh₃)AuCl/AgSbF₆ mixture after filtration......22
Figure 8. ³¹P NMR of different Au(I) samples ..................................................23
Figure 9. ³¹P NMR comparison of different Au(I) catalysts .......................29
Figure 10. Reaction between diazonium and Ph₃PAuNTf₂..........................43
Figure 11. Reaction between diazonium and gold acetylide.....................44
Figure 12. Reaction between diazonium and aryl gold complex..............44
Figure 13. Monitoring the catalytic C(sp)-C(sp²) coupling..........................48
Figure 14. ESI-MS spectra of reaction mixture between diazonium and alkyne 49
Figure 15. Explore the reaction intermediate with ESI-MS spectra ...........48
Figure 16. Teles hydration reaction with Pol-TA-Au ..................................68
Figure 17. UV-Vis and fluorescence comparison.......................................80
Figure 18. Fluorescence comparison of different substituent ..................81
Chapter 1. Gold-Catalyzed Synthesis of Triazapentalene Zwitterions

1.1 Introduction

1.1.1 Homogeneous gold(I) catalysis

Homogeneous gold catalysis has been considered as one of the most important developments in organic synthesis during the last decade.\(^1\) One reason for the vast development is the unique reactivity of gold as a strong alkynophilic Lewis acid.\(^2\) In 2007, Toste reported “the relativistic effect in homogeneous gold catalysis”, which provided some theoretical insights into the observed reactivity of gold catalysts ([Scheme 1]).\(^3\) Because of the relativistic contraction of 6s orbital, the gold-ligand bond is strengthened. The contracted 6s orbital also provides better shielding effect for the electrons in the 5d orbital, leading to the expansion of 5d. Since the electrons in 5d orbital are more dispersed, gold is a stronger Lewis acid compared with silver (non-relativistic). For the same reason, gold(I) is retarded for oxidative addition, which allows ambient conditions for gold catalysis without the need for inert-gas protection.

Scheme 1. Relativistic effect of gold

[Diagram showing relativistic effect of gold with annotations]

\(^1\) Toste, Nature, 2007
One typical reaction mode for Au(I) is the activation of $\pi$-systems towards nucleophiles (Scheme 2). For most cases, the nucleophiles attack the gold-activated alkyne from the trans position to Au, forming a vinyl-gold intermediate. The product is then formed from proto-deauration of the vinyl-gold. As a highly reactive intermediate in Au(I) catalysis, the vinyl-gold species could also be trapped by other electrophiles, or following a carbenoid-like reaction route through backbonding from gold.

Scheme 2. Nucleophilic addition to gold-activated alkynes

In 1998, Teles reported the addition of alcohols to alkynes using a cationic phosphine-Au(I) catalyst with very high reactivity (TOF up to 1500 h$^{-1}$). He was also the first one who used acid to activate the homogeneous Au(I) catalyst. For the reaction of diphenylacetylene (Scheme 3A), an initial dominance of Z-isomer was observed ($Z:E = 8:1$), suggesting the trans-addition of methanol to alkyne. The final $Z:E$ selectivity decreased, possibly due to isomerization through the corresponding acetal. Hydroamination with terminal alkynes have also been achieved using gold catalyst with an acid promoter (Scheme 3B). Another example of gold-catalyzed nucleophilic addition to alkynes is the Conia-ene reaction (Scheme 3C), which incorporated an enolate as the nucleophile for the intramolecular cycloaddition. Cationic gold(I) catalyst could promote this reaction with high efficiency at room temperature (Conia-ene reactions usually require high temperature for the thermal cyclization).
After the discovery of these early examples, homogeneous gold(I) catalysts have been rapidly developed for various transformations that involving activation of π-systems and applied into complex molecular synthesis.¹²

### 1.1.2 Triazole-gold(I) catalyst with improved stability

Despite the remarkable efficiency of homogeneous Au(I) catalysts, one big challenge is the poor stability of cationic gold(I) complexes (L-Au⁺), especially at elevated temperatures. Among the reported ligands, N-heterocyclic carbenes (NHCs) has been observed to give improved catalyst stability.¹³ Compared with other counteranions for L-Au⁺, such as OTf⁻, SbF₆⁻, and BF₄⁻, NTf₂⁻ as the counteranion for L-Au⁺ also helped increase catalyst stability through a dynamic Au-N coordination.¹⁴

Our group has focused on the investigation of 1,2,3-triazoles and their coordination with transition metals.¹⁵ The electron-deficient nature of triazoles has made them less attractive as ligands for transition metals.¹⁶ However, since the coordinating lone pair electrons on nitrogen are not conjugated with π electrons, 1,2,3-triazole appears to be a good σ-donor. The three adjacent nitrogen atoms also increase the electron density on the nitrogen side, which could further increase the σ-donating ability. Meanwhile, the electronic deficiency makes triazole a potential π-acceptor for metal backbonding. Based on the unique properties of 1,2,3-triazole, it is a feasible consideration to employ 1,2,3-triazole as a ligand to enhance the stability of Au(I) catalysts.
In 2009, our group successfully developed triazole-gold complexes (TA-Au) as an effective catalyst for alkyne hydroamination with improved thermal stability (Scheme 4).\textsuperscript{17} Compared with triazole-gold catalyst, other gold(I) catalysts decomposed before reaction completion. By the $\textit{in situ}$ activation of TA-Au by an acid promoter, the desired imine was formed in high yields, which highlighted the good balance between reactivity and stability of TA-Au complexes.

\textbf{Scheme 4. Triazole-gold catalyst for intermolecular alkyne hydroamination}

1.1.3 Acid-stable vinyl-gold complexes

As mentioned in section 1.1.1 (Scheme 2), the vinyl-gold species is a critical intermediate in gold-catalyzed alkyne activation. However, the study of vinyl-gold complexes is often more difficult due to the high reactivity of vinyl-Au complexes, such as easy proto-deauration.\textsuperscript{18} To trap this intermediate, we postulate that with 1,2,3-triazole as a stabilizing ligand for gold catalyst, isolation of the desired vinyl-gold complex may be feasible.

Our group discovered the gold-catalyzed nucleophilic addition of triazole to alkenes, forming the corresponding vinyl triazoles in good yields.\textsuperscript{19} However, an intramolecular addition of triazole to alkyne did not give the desired product. Instead, a vinyl-Au complex was formed when propargyl triazole was treated with a stoichiometric amount of cationic gold catalyst (Scheme 5). This complex was successfully isolated in high yield. Unlike other reported organo-Au complexes, this vinyl-Au complex is stable toward air, moisture, and even survives upon treatment with HOTf for more than 12 h.\textsuperscript{20}
Scheme 5. Formation of acid-stable vinyl-gold complexes

Considering that triazolium (TAZ) is a neutral ligand with a C-binding site, it is similar to the well-known N-heterocyclic carbene (NHC) ligands. To understand the reactivity of TAZ-Au complex 3, we prepared the corresponding NHC-gold complex. The crystal structure is shown in Figure 1.

Figure 1. X-ray crystal structure of TAZ-Au-IPr

As shown in the crystal structure, the TAZ ligand bound to Au in a similar fashion as IPr ligand, giving almost identical C-Au bond lengths. This result suggests the possibility for applying this TAZ as a ligand to stabilize gold catalysts similar to the well-explored IPr ligand.

1. 2 Catalytic cyclization of propargyl triazole

One challenge for efficient synthesis of TAZ ligand is the poor gold catalyst turnover due to the formation of a stable C-Au bond in complex 3. Considering that protonation in TAZ complexes occurred on ring A instead of the C-Au bond, we postulated that the introduction of an electron-withdrawing group (EWG) on ring A may reduce the basicity of the corresponding carbanion, which will “redirect” the protonation to the C-Au bond, leading to gold catalyst turnover.
through protodeauration. As the result, the proposed triazapentalene zwitterions (TAPZ) synthesis could be achieved with catalytic amount of gold (Scheme 6).

Scheme 6. Proposed strategy for gold turnover

To verify our hypothesis, triazole-alkyne 4a was prepared and charged with [Au] catalyst (1% PPh₃AuCl/AgOTf). As expected, TAPZ 5a was successfully prepared in good yield (91%) and its structure was confirmed by X-ray crystallography. Further screening (Table 1) revealed elevated temperature (60 °C) in DCE as the optimal conditions, giving 5a in excellent isolated yield (96%) with only 0.5% catalyst loading.

Table 1. Optimization of reaction conditions for TAPZ synthesis

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Loading (%)</th>
<th>Solvn[9]</th>
<th>Temp (°C)</th>
<th>Time (h)</th>
<th>Convn (%)</th>
<th>Yield (%)[c]</th>
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<td>91</td>
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<tr>
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<td>72</td>
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<tr>
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<td>&gt;98</td>
<td>94</td>
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<tr>
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<td>48</td>
<td>69</td>
<td>64</td>
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<td>&gt;98</td>
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<td>48</td>
<td>79</td>
<td>77$^{[d]}$</td>
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</table>

$^a$ General reaction conditions: 4a (0.5 mmol), catalyst (0.2-1.0 mol%) in 5 mL solvent, the reactions were monitored by TLC, rt-60°C; $^b$ DCE: 1,2-dichloroethane; $^c$ NMR yields of 5a with 1,3,5-trimethoxybenzene as internal standard; $^d$ Isolated yield; $^e$ TA = N-methyl-benzotriazole.

With the optimal conditions in hand, various N-2-alkynyl-triazoles were prepared to explore the reaction substrate scope. Some representative substrates are summarized in Table 2.

Table 2. Reaction substrate scope for TAPZ synthesis $^a$

![Diagram of reaction substrate scope for TAPZ synthesis]

<table>
<thead>
<tr>
<th>R$^1$</th>
<th>R$^2$</th>
<th>R$^3$</th>
<th>EWG</th>
<th>Reaction conditions</th>
<th>Isolated yield</th>
<th>NMR yield</th>
<th>TA</th>
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<tr>
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<td>Ph</td>
<td>CH$_3$</td>
<td>5a</td>
<td>R = CH$_3$, 96%;</td>
<td>96%</td>
<td>96%</td>
<td></td>
</tr>
<tr>
<td>n-C$_4$H$_9$</td>
<td>n-C$<em>5$H$</em>{11}$</td>
<td>5b</td>
<td>R = n-C$_4$H$_9$, 95%;</td>
<td>95%</td>
<td>95%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>5d</td>
<td>R = H, 1% cat., 5%</td>
<td>1% cat., 24 h, 11%;</td>
<td>11%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ph</td>
<td>5e</td>
<td>R = Ph, 81%;</td>
<td>81%;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-F-Ph</td>
<td>5f</td>
<td>R = p-F-Ph, 78%;</td>
<td>78%;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-OMe-Ph</td>
<td>5g</td>
<td>R = p-OMe-Ph, 75%;</td>
<td>75%;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tol</td>
<td>5h</td>
<td>R = Tol, 93%;</td>
<td>93%;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>o-F-Ph</td>
<td>5i</td>
<td>R = o-F-Ph, 98%;</td>
<td>98%;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-Cl-Ph</td>
<td>5j</td>
<td>R = p-Cl-Ph, 92%;</td>
<td>92%;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-naphthalenyl</td>
<td>5k</td>
<td>R = 2-naphthalenyl, 91%;</td>
<td>91%;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ph</td>
<td>5m</td>
<td>R = OMe, 68%;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Standard reaction condition: 4 (0.5 mmol), AuPPh$_3$Cl/AgSbF$_6$ (0.5 mol%) in DCE (5 mL), the reactions were monitored by TLC (3-24 h), 60 °C; $^b$ Isolated yield.

As shown in Table 2, this reaction tolerates a large group of substrates. Both alkyl (5a-5c) and aryl (5l) groups are suitable for the alkyne terminal, giving the corresponding TAPZ in excellent yields. The terminal alkyne (5d) is problematic due to the slow reaction rate and eventual gold catalyst decomposition (after long reaction time). This is likely caused by the unfavored anti-Markovnikov addition to the alkyne. In addition, an ester can also be used as the EWG (5m) to
promote the gold turnover (though with lower yields), which further extended the scope of TAPZ with this method.

1.3 Triazapentalenes as biocompatible fluorophores

Fluorescent probes have been recognized as powerful tools for chemistry and biology research.\textsuperscript{22} Various systems of small organic fluorophores have been widely utilized in cell labeling and recognition.\textsuperscript{23} Despite the rapid development in this field, many of the reported systems involve large conjugated structures, which are often associated with some limitations, including difficult synthesis, small Stokes shift and/or poor water solubility.\textsuperscript{24} Thus, the development of new organic fluorophores with tunable emission wavelengths is of great interest for chemical, medicinal and biological research.

1.3.1 Triazapentalenes from cascade click chemistry

In 2011, Namba and Tanino prepared similar TAPZ via cascade click-cyclization-aromatization (\textbf{Scheme 7}).\textsuperscript{25} One interesting observation from their work was the strong fluorescence emission in the visible light region with $\lambda_{\text{max}}$ between 380 nm to 560 nm. However, these TAPZs also indicated modest to poor stability especially under acidic conditions, which made them less practical as fluorescent dyes in biological systems. Meanwhile, the reported synthetic route is only suitable for terminal alkynes (necessary for click chemistry) and involves a highly reactive di-triflate moiety, which significantly limits the substrate scope and makes these novel fluorophores less attractive.

\textbf{Scheme 7. Triazapentalene synthesis from click-cyclization-aromatization}
1.3.2 Triazapentalenes with improved stability

Compared with the synthesis using click chemistry, our gold-catalyzed approach allows effective syntheses of TAPZ derivatives with various substituents at C-4, C-5, C-6 and C-8 positions, which provides a good opportunity to construct a TAPZ library for the fluorescence evaluation. Notably, the EWG-free TAPZ (reported by Namba and Tanino),\textsuperscript{25} although much less stable, can also be prepared using this method through a simple decarboxylation as shown in Scheme 8.

Scheme 8. Preparation of EWG-free TAPZ through decarboxylation

As discussed in the previous section, another concern for the mono-substituted TAPZs is their poor stability. For example, dissolving 7 in untreated CDCl\textsubscript{3} caused an immediate color change from light yellow to green, probably due to the protonation by trace amount of acid in CDCl\textsubscript{3}.

Figure 2. Stability comparison of different triazapentalenes
To quantize the decomposition, we monitored the TAPZ solution with $^1$H NMR over time. The C-4, C-5 di-substituted TAPZs prepared using our method indicated significantly improved stability, giving almost no decomposition under the identical conditions over two weeks (Figure 2). The significantly improved stability of the di-substituted TAPZs makes further investigation and application feasible.

1.3.3 Fluorescence investigation of selected triazapentalenes

With the ability to prepare various new TAPZ derivatives, we turned our attention toward evaluating TAPZ fluorescence activities. As shown in Figure 3A and 3B, the fluorescence emission of ketone and ester TAPZs can be easily tuned by substituent on ring B. Interestingly, with p-nitrophenyl group on C-8 position, a red shift was observed (emission $\lambda_{\text{max}}$: 5p = 594 nm, 5s = 587 nm) and the fluorescence intensity was also increased. Compared with nitro group, cyano group (5q and 5t) showed a different trend in fluorescence.

Figure 3. Emission spectra of TAPZs with different substitutes

However, the fluorescence intensities of these newly developed TAPZs are quite low with quantum yields less than 1% (Table 3). Compared with ketone (5o-q) and mono-ester (5r-m), the diester derivative (6a) exhibited a much stronger emission. Furthermore, the yield and stability of these TAPZs is also improved.
Table 3. Fluorescence properties of selected TAPZs

<table>
<thead>
<tr>
<th>TAPZ</th>
<th>yield</th>
<th>ɛ_max</th>
<th>ɛ_{ex}/nm</th>
<th>ɛ_{em}/nm</th>
<th>Stocks</th>
<th>Stocks</th>
<th>φ_F</th>
</tr>
</thead>
<tbody>
<tr>
<td>5a: R = H</td>
<td>71%</td>
<td>0.163</td>
<td>358</td>
<td>454</td>
<td>96</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>5p: R = NO₂</td>
<td>74%</td>
<td>0.274</td>
<td>472</td>
<td>594</td>
<td>122</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>5q: R = CN</td>
<td>58%</td>
<td>0.285</td>
<td>432</td>
<td>592</td>
<td>160</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>5r: R = H</td>
<td>56%</td>
<td>0.222</td>
<td>372</td>
<td>450</td>
<td>78</td>
<td>0.14^d</td>
<td></td>
</tr>
<tr>
<td>5s: R = NO₂</td>
<td>70%</td>
<td>0.241</td>
<td>454</td>
<td>587</td>
<td>133</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>5t: R = CN</td>
<td>53%</td>
<td>0.429</td>
<td>408</td>
<td>486</td>
<td>30</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>5m: R = Ph</td>
<td>68%</td>
<td>0.231</td>
<td>372</td>
<td>450</td>
<td>78</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>6a: R = COOMe</td>
<td>91%</td>
<td>0.181</td>
<td>366</td>
<td>488</td>
<td>122</td>
<td>0.14^d</td>
<td></td>
</tr>
</tbody>
</table>

All data obtained at room temperature, 10⁻⁵ M solution in DCM; b measured in 10⁻⁶ M DCM solution; c extinction coefficient in 10⁻⁵ M⁻¹ cm⁻¹; d quantum yields were measured with quinine sulfate as reference (Φ=0.60 in 0.1 N H₂SO₄); e isolated yields.

To understand the substituent effect on fluorescence properties, crystal structures of several representative TAPZs were determined (Figure 4).

Figure 4. X-ray crystal structures and emission spectra for selected TAPZs

As revealed by the X-ray structural analyses, switching ketone to an ester group led to better conjugation between carbonyl and TAPZ ring A, which is likely...
caused by the reduced steric repulsion of the smaller ester group. Since ring A is electron rich (negative charged), a second EWG in the diester TAPZ will help improve the stability and likely enhance fluorescence emission.

Considering that the diester TAPZ gave the strongest emission, a small library of diester derivatives were prepared to further evaluate this new class of fluorophores. Their fluorescence properties are summarized in Table 4.

Table 4. Fluorescence properties of diester TAPZs

<table>
<thead>
<tr>
<th></th>
<th>6b R=CN</th>
<th>6c R=COOMe</th>
<th>6d R=F</th>
<th>6a R=H</th>
<th>6e R=OMe</th>
<th>6f</th>
<th>6g</th>
</tr>
</thead>
<tbody>
<tr>
<td>λ&lt;sub&gt;em&lt;/sub&gt;/nm</td>
<td>467nm</td>
<td>476nm</td>
<td>488nm</td>
<td>488nm</td>
<td>504nm</td>
<td>479nm</td>
<td>488nm</td>
</tr>
<tr>
<td>λ&lt;sub&gt;ex&lt;/sub&gt;/nm</td>
<td>394</td>
<td>388</td>
<td>364</td>
<td>366</td>
<td>365</td>
<td>364</td>
<td>362</td>
</tr>
<tr>
<td>Stocks shift /nm</td>
<td>72</td>
<td>88</td>
<td>124</td>
<td>122</td>
<td>139</td>
<td>114</td>
<td>126</td>
</tr>
<tr>
<td>ε&lt;sub&gt;max&lt;/sub&gt;</td>
<td>0.373</td>
<td>0.331</td>
<td>0.171</td>
<td>0.181</td>
<td>0.192</td>
<td>0.256</td>
<td>0.184</td>
</tr>
<tr>
<td>Φ&lt;sub&gt;F&lt;/sub&gt;</td>
<td>0.01</td>
<td>0.04</td>
<td>0.17</td>
<td>0.14</td>
<td>0.16</td>
<td>0.02</td>
<td>0.10</td>
</tr>
<tr>
<td>yield</td>
<td>80%</td>
<td>88%</td>
<td>96%</td>
<td>91%</td>
<td>31%</td>
<td>82%</td>
<td>90%</td>
</tr>
</tbody>
</table>

<sup>a</sup> All data obtained at room temperature, 10<sup>-6</sup> M DCM solution; <sup>b</sup> extinction coefficient in 10<sup>5</sup>M<sup>-1</sup>cm<sup>-1</sup>; <sup>c</sup> quantum yields were measured with quinine sulfate as reference (Φ=0.60 in 0.1N H<sub>2</sub>SO<sub>4</sub>); <sup>d</sup> isolated yields.

As shown in Table 3 and 4, these new 4,5-disubstituted TAPZ fluorescent dyes gave tunable emission with λ<sub>max</sub> between 450 nm to 590 nm. The Stokes shifts ranged from 38nm to 160nm. For the diester TAPZs, electron-withdrawing groups such as CN (6b, 6g) and COOMe (6c) caused lower quantum yield, whereas the TAPZ with p-fluorophenyl on C-8 gave a stronger emission. Red shift was observed by incorporating strong electron-donating groups (EDGs) on the positively charged B-ring (R = CN, λ<sub>max</sub> = 467 nm; R = OMe, λ<sub>max</sub> = 504 nm).
Introducing a strong electron-withdrawing nitro (NO$_2$) group led to less than 10% yield of TAPZ with low fluorescence activity. This is totally opposite to the ketone (5p) and mono-ester (5s) for which higher yield and stronger emission were observed. Clearly, the overall TAPZ emission relies on substituents on both rings.

Although these di-substituted TAPZs are much more stable than the mono-substituted TAPZs, their overall stability followed the general trend as diester > mono-ester > ketone. These dyes also tolerate various environments, from CH$_2$Cl$_2$ to more polar solvents like DMSO and water, which enables us to test the feasibility of using TAPZs in cell imaging. After incubating the cells with selected TAPZ solutions for 10 minutes, the illumination of the cells was observed under a fluorescence microscope (Figure 5). This result suggested promising future applications of these TAPZs as new biocompatible fluorescence probes.

**Figure 5. Selected images of cells incubated with 10µM TAPZs**

A1) and C1): bright-field view of HEK-293t cells incubated with 10µM 6a or 5s in 1% DMSO/media solution, scale bar = 50µm; A2) and C2): fluorescence images of the same cells; B1) and D1): bright-field view of A549 cells incubated with 10µM 6a or 5s in 1% DMSO/media solution, scale bar = 100µm; B2) and D2): fluorescence images of the same cells.

**1.4 Conclusion**

In summary, we report the investigation of gold catalyzed triazole-alkyne 5-endo-dig cyclization for the synthesis of stable triazapentalene zwitterions (TAPZs). Through the introduction of electron-withdrawing groups, the electron
density distribution on the triazapentalene was altered, which resulted in effective
gold catalyst turnover. Good to excellent yields of desired TAPZs were achieved
in most of the cases. In addition, the resulting ester modified TAPZs gave
excellent fluorescence, with tuneable optical properties. The cell imaging
highlighted great potential of this new class of TAPZs as new biocompatible
probes and the unique advantage of the gold catalyzed cyclization.

1.5 Contribution

Dr. Dawei Wang was the first investigator of this gold-catalyzed cyclization.
He developed the optimal conditions and synthesized part of the substrates.
Rong Cai developed TAPZs with esters as EWG and investigated fluorescence
properties as well as cell imaging. Dr. Yunfeng Chen developed the acid-stable
vinyl-gold complexes. Dr. Wuming Yan provided help on the iron-catalyzed
propargylation of triazole for the substrate synthesis. Natalie Geise and Sripadh
Sharma helped with substrate preparation. Dr. Huiyuan Li provided help on the
bio-related experiments. Dr. Jeffrey Petersen performed the X-ray
crystallographic analyses.

Part of this project is published on Chem. Commun., 2014, 50, 7303-7305.

References:
1 For selected recent reviews on homogeneous gold catalysis, see: a) Furstner, A.;
4 Selected examples, see: a) Fukuda, Y.; Ultimoto, K. J. Org. Chem. 1991, 56, 3729; b)


Chapter 2. “Silver Effect” in Gold(I) Catalysis

2.1 Introduction

It has been generally accepted that the [L-Au]⁺ was the actual catalyst toward alkyne and alkene activation in homogeneous Au(I) promoted reactions. Currently, the dominant approach for the [L-Au]⁺ preparation was through the treatment of L-Au-Cl with corresponding silver salts to abstract chloride. Since AgCl was not involved in the reaction, it has been assumed that removing or keeping the AgCl salts in the reaction mixtures should not make a difference, giving “identical” results. Although it has been reported in a few cases that the presence of silver would help the reactivity of gold catalysts, it is still widely accepted that all these reactions were catalyzed by gold cation as long as silver salt itself could not catalyze the reaction.

Scheme 9. Will silver influence gold catalysis?

However, based on our experimental evidences, gold catalysis was not simply activated by the [L-Au]⁺ as previously assumed. In some reactions, the Ag-free [L-Au]⁺ catalysts showed absolutely no reactivity. With the clear experimental support described in this work, this long overlooked “silver effect” should lead to serious reconsideration for the reported and yet to be reported results. More importantly, these results raise a more significant question regarding the true nature of the catalytically active gold species.
2.2 Gold(I)-catalyzed propargyl ester hydration

The “silver effect” was discovered during the exploration of triazole-gold (TA-Au) catalyzed reactions. Considering the importance of the α-hydroxyl methyl ketone in medicinal chemistry and the readily availability of enantiomeric pure propargyl alcohols, our initial attempt was to investigate the possibility of direct alkyne hydration to form ketone with retention of stereochemistry at the hydroxy position (Scheme 10A). However, after screening a series of Au(I) complexes, no catalysts, including TA-Au, promoted this reaction effectively even at 80 °C. It is well known that terminal propargyl ester could undergo 1,2-migration with gold catalyst, forming the oxonium cation (Scheme 10B). Therefore, it is possible to reach the desired α-hydroxy methyl ketone through water trapping of the oxonium cation. To explore this, propargyl ester 1a was prepared to react with different gold catalysts under various conditions.

Scheme 10. Proposed asymmetric synthesis of α-hydroxyl methyl ketone

As shown in Table 5, both TA-Au-1 and TA-Au-2 could effectively promote this reaction. Screening of the conditions revealed acetone as the optimal solvent, giving the desired α-acetate-ketone in nearly quantitative yield (1% loading). It should be noted that the [PPh₃-Au]⁺ and [IPr-Au]⁺ complexes did NOT promote this reaction at all (Table 5, entries 1-3) and most of the starting material 1a was recovered. This result highlighted the advantage of the triazole-gold catalyst: simple modification resulted in high efficiency and new reactivity.
Table 5. Optimization of conditions for propargyl ester hydration

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[(PPh₃)Au]⁺ TfO⁻</td>
<td>dioxane</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>[(PPh₃)Au]⁺ SbF₆⁻</td>
<td>dioxane</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>[(IPr)Au]⁺ SbF₆⁻</td>
<td>dioxane</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>TA-Au-1</td>
<td>dioxane</td>
<td>12</td>
<td>87</td>
</tr>
<tr>
<td>5</td>
<td>TA-Au-2</td>
<td>dioxane</td>
<td>12</td>
<td>85</td>
</tr>
<tr>
<td>6</td>
<td>TA-Au-1</td>
<td>DCM</td>
<td>12</td>
<td>32</td>
</tr>
<tr>
<td>7</td>
<td>TA-Au-1</td>
<td>THF</td>
<td>12</td>
<td>&lt;5</td>
</tr>
<tr>
<td>8</td>
<td>TA-Au-1</td>
<td>MeOH</td>
<td>12</td>
<td>24</td>
</tr>
<tr>
<td>9</td>
<td>TA-Au-1</td>
<td>DMF</td>
<td>12</td>
<td>&lt;5</td>
</tr>
<tr>
<td>10</td>
<td>TA-Au-1</td>
<td>CH₃NO₂</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>11</td>
<td>TA-Au-1</td>
<td>CH₃CN</td>
<td>4</td>
<td>89</td>
</tr>
<tr>
<td>12</td>
<td>TA-Au-1</td>
<td>acetone</td>
<td>4</td>
<td>99 (96)</td>
</tr>
</tbody>
</table>

General reaction conditions: 8a (0.5 mmol), catalyst (0.2-1.0 mol%) in 5 mL solvent, the reactions were monitored by TLC, rt-60°C; DCE: 1,2-dichloroethane; NMR yields of 9a with 1,3,5-trimethoxybenzene as internal standard; Isolated yield; TA = N-methyl-benzotriazole.

With the optimal conditions in hand, the reaction substrate scope was explored (Table 6). While we were excited about this result that TA-Au offered new reactivity over [L-Au]⁺, Sahoo and co-workers reported the same transformation using the PPh₃AuCl/AgSbF₆ mixtures. This result was shocking because we have observed that the [L-Au]⁺ could not promote this reaction (Table 5, entries 1-3). These conflicting results were significant and need to be further investigated.
Table 6. Substrate scope for propargyl ester hydration $^{a,b}$

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Yield</th>
<th>Chirality</th>
</tr>
</thead>
<tbody>
<tr>
<td>9a</td>
<td>96%</td>
<td>Excellent</td>
</tr>
<tr>
<td>9b</td>
<td>98%</td>
<td>8a, 91% ee</td>
</tr>
<tr>
<td>9c</td>
<td>94%</td>
<td>8b, 93% ee</td>
</tr>
<tr>
<td>9d</td>
<td>91%</td>
<td></td>
</tr>
<tr>
<td>9e</td>
<td>93%</td>
<td></td>
</tr>
<tr>
<td>9f</td>
<td>90%</td>
<td></td>
</tr>
<tr>
<td>9g</td>
<td>95%</td>
<td></td>
</tr>
<tr>
<td>9h</td>
<td>93%</td>
<td></td>
</tr>
<tr>
<td>9i</td>
<td>91%</td>
<td></td>
</tr>
<tr>
<td>9j</td>
<td>90%</td>
<td></td>
</tr>
</tbody>
</table>

$^{a}$General reaction condition: 8 (0.25 mmol, 1.0 equiv.) and TA-Au-1 (1.0 mol%) in acetone (2.5 mL), H$_2$O (3.0 equiv.). Reactions were monitored by TLC (4-10 h), rt. $^{b}$Isolated yields.

2.3 “Silver effect” in alkyne hydration

To understand the different reactivity that we observed for propargyl ester hydration using the same catalytic system (PPh$_3$AuCl/AgSbF$_6$), the direct comparison of the gold catalyst with or without AgCl presence was then carried out. As shown in Table 6, under the optimal conditions reported by Sahoo (entry 2), none of the tested silver salts could catalyze the reaction, with mostly 8a recovered. The [(PPh$_3$)Au]$^+$A$^-$, which was prepared from celite filtration of the PPh$_3$AuCl/Ag$^+$A$^-$ mixtures, also did not promote this reaction (entry 3). However, when the mixtures of PPh$_3$AuCl and Ag$^+$A$^-$ were used directly without filtration to remove AgCl, the reaction worked as reported, but with complete racemization (entries 4, 5). Careful degassing and N$_2$ protection helped to avoid the racemization (entry 6). Interestingly, the mixture of [(PPh$_3$)Au]$^+$TfO$^-$ (inactive complex obtained from the filtration through celite) and AgSbF$_6$ could promote
this reaction effectively (entry 7), which suggested that the combination of these gold and silver complexes was necessary for the catalytic reactivity.

Table 7. Silver effect in propargyl ester hydration

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1% TA-Au-1</td>
<td>5</td>
<td>87</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>10% AgOTf, AgSbF6 or AgBF4</td>
<td>12</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>2% [(PPh3)Au]+ A- (A- = TfO-, SbF6-, BF4-)</td>
<td>12</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>2% (PPh3)AuCl/AgOTf</td>
<td>12</td>
<td>90</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>2% (PPh3)AuCl/AgSbF6</td>
<td>8</td>
<td>97</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>2% (PPh3)AuCl/AgOTf (with N2 protection)</td>
<td>5</td>
<td>92</td>
<td>90</td>
</tr>
<tr>
<td>7</td>
<td>2% [(PPh3)Au]+ SbF6- + 2% AgSbF6</td>
<td>12</td>
<td>91</td>
<td>-</td>
</tr>
</tbody>
</table>

* General reaction condition: 1a (1.0 equiv.) and cat. in 2.5 mL dioxane/water (H2O, 3.0 equiv.), rt. reactions were monitored by TLC. b NMR yields.

Notably, filtration through celite is a practical procedure used in our group during the preparation of the TA-Au complexes. In general, silver salts could decompose to silver nanoparticle or Ag2O precipitate over time, and this process is accelerated in the presence of AgX, forming a dark purple solution over time. Filtration through celite allows the majority of [L-Au]+ A- to go through and removes most of the silver salts that can pass through regular filter paper.

Figure 6. X-ray crystal structure of [IPr-Au-TA]+OTf complex
This procedure has no influence on the counteranion and worked for various ligands. For example, Figure 6 shows the crystal structure of [(IPr)Au-triazole]^+TfO^−, which was prepared from the celite filtration of triazole and (IPr)AuCl/AgOTf mixture, giving the desired [IPr-Au-TA]^+OTf complex in 92% yield.

To verify the difference between celite filtration and paper filtration, X-ray photoelectron spectroscopy (XPS) was applied (Figure 7).

Figure 7. XPS spectra of the (PPh₃)AuCl/AgSbF₆ mixture after filtration

As shown in the XPS spectra, gold was observed in both filtrates. The binding energies (Au 4f₇/2, 85.5 ev; Au 4f₅/2 89.2 ev) suggested the presence of Au(I) cation after celite filtration. The silver signal was observed in the filtrate when the mixture of (PPh₃)AuCl and AgSbF₆ is filtered through regular filter paper (Figure 7A: Ag 3d₅/₂, 368.7 ev; Ag 3d₃/₂, 374.7 ev). Interestingly, the filtrate obtained after celite filtration did not contain any silver (Figure 7B), even when excess amounts of silver salt was added (Au:Ag = 1:1.5). These results indicated that the filtrate from celite contained only [(PPh₃)Au]^+ and no detectable amount of Ag^+. Similar results were observed with the (IPr)AuCl/AgSbF₆ system. These XPS results supported the observation that the presence of Ag^+ influenced the gold cation reactivity.
Meanwhile, for PR₃-Au-X complexes, ³¹P NMR could help to evaluate the electronic nature of the gold cation in solution. In general, more cationic gold complexes would give the up-field shift ³¹P signals (Figure 8A). The chemical shift of [PPh₃Au]⁺TfO⁻ (after celite filtration) is 27.1 ppm whereas it is 33.8 ppm for PPh₃AuCl, suggesting the formation of cationic [PPh₃Au]⁺ species. However, the (PPh₃)AuCl/AgOTf (with no filtration) give a different chemical shift at 28.1 ppm (Figure 8A, b). Although this ³¹P NMR data supports the formation of a new complex, the true structure of this species has not been determined at this time.

Figure 8. ³¹P NMR of different Au(I) samples

Since the purpose of AgOTf is to remove the chloride anion from PPh₃AuCl, it is anticipated that more AgOTf should lead to an upfielded chemical shift of the ³¹P signal due to the formation of more cationic gold (Figure 8B, entry 1 to 4). After a stoichiometric amount of AgOTf is added, no further chemical shift change is observed even with the addition of excess AgOTf (Figure 8B, entry 4 and 5). Notably, different chemical shifts are observed after filtering the sample through celite to remove the silver. Addition of AgOTf to the solution of [(PPh₃)Au]⁺OTf gave a slow conversion back to the species corresponding to the ³¹P signal at 28.1 ppm (the gold species prior to filtration). The gold species generated is independent of the amount of AgOTf added: both 0.5 eq and 1.0 eq of AgOTf shifted the ³¹P signal from 27.1 ppm to 28.1 ppm. No change in the chemical shift is observed while AgCl is added to the silver-free [(PPh₃)Au]⁺TfO⁻ solution, which suggests that the influence is from the Ag⁺ instead of AgCl. This
discovery is critical since it will lead to a revision of the current assumed mechanism of homogenous gold(I) catalysis, because the actual catalyst may not be simply a cationic gold species.

The reaction of the gold-catalyzed propargyl ester hydration shown above is a good example that highlighted the importance of the silver effect (i.e., [(PPh₃)Au]⁺TfO⁻ alone does not promote the reaction unless silver salt was added). One concern is that the presence of silver may help the hydration of the oxzonium cation intermediate, which plays an important role in promoting the overall reaction. However, the reaction with TA-Au, which did not contain silver, led to effective transformation with a faster reaction rate, suggesting that hydration of the oxzonium cation is fast and silver is not required in this step.

To ensure that this “silver effect” did not only occur in propargyl ester hydration, we extended the investigation to more general alkyne hydration reactions. It has been reported by Nolan and coworkers that (IPr)AuCl/AgSbF₆ was the optimal catalyst to promote challenging internal alkyne hydration.³⁰

Table 8. Silver effect in IPr-Au catalyzed alkyne hydration

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Time / h</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2% [(IPr)Au]Cl/AgSbF₆, no filtration</td>
<td>2</td>
<td>97%</td>
</tr>
<tr>
<td>2</td>
<td>5% [(IPr)Au]⁺SbF₆⁻</td>
<td>24</td>
<td>0%</td>
</tr>
<tr>
<td>3</td>
<td>5% AgSbF₆</td>
<td>24</td>
<td>0%</td>
</tr>
<tr>
<td>4</td>
<td>2% [(IPr)Au]⁺SbF₆⁻ + 2% AgSbF₆</td>
<td>12</td>
<td>95%</td>
</tr>
<tr>
<td>5</td>
<td>2% [(IPr)Au]⁺SbF₆⁻ + 1% AgSbF₆</td>
<td>24</td>
<td>88%</td>
</tr>
<tr>
<td>6</td>
<td>2% [(IPr)Au]⁺SbF₆⁻ + 0.5% AgSbF₆</td>
<td>24</td>
<td>67%</td>
</tr>
</tbody>
</table>

As shown in Table 8, excellent yield of the ketone 11a was obtained when (IPr)AuCl/AgSbF₆ mixtures was used without filtration. When 10a was charged with [IPr-Au]⁺ (the same catalyst mixture after celite filtration), no reaction occurred even with increased catalyst loading (5 mol%) and prolonged reaction time (entry 2). In contrast, the addition of 2% AgSbF₆ reactivated the catalyst, giving ketone 11a in excellent yield though with longer reaction time (entry 4).
Notably, silver salts alone could not promote this reaction (entry 3). Reducing the amounts of silver salts caused the slower reaction rate. When a 0.25 equivalent of silver (relative to gold) was used (entry 6), the reaction could not reach complete conversion (around 25% starting materials recovered under identical conditions). These results demonstrate again that the combination of \([L\text{-Au}]^+\) and \(Ag^+\) was the actual active catalysts for these transformations, which revised the previous assumption regarding homogeneous gold(I) catalysis.

2. 4 Revision of gold(I)-catalyzed reactions

The discovery of “silver effect” led to a revision of previously reported gold-catalyzed reactions. Based on the different reactivity of gold, we divided gold catalysis into three categories (Scheme 11).

Scheme 11. Refining gold catalysis based on the reactivity

2.4.1 Different types of gold(I) catalysis

*Type I. Purely Au catalysis*

Purely Au catalysis refers to the type of reactions promoted by \([L\text{-Au}]^+\) with competitive or even better reactivity than the \([L\text{-Au}]^+/Ag^+\) mixtures. Among the 14 reported reactions we screened, only two examples belong to this category that are promoted by Ag-free \([L\text{-Au}]^+\) without losing reactivity (compared with Au/Ag mixture).

The first example was the Hashmi phenol synthesis, where gold promoted furan-yne rearrangement to phenol through the formation of gold carbene intermediates (Scheme 12A).\(^{31}\) Our investigation revealed similar reactivity of the Ag-free Au catalyst (filtration through celite) compared with the mixture of Au
and Ag. Similar results were obtained in the gold catalyzed oxidative coupling reaction between vinyl gold and boronic acid shown in Scheme 12B, which was originally reported by Zhang and co-workers.32

Scheme 12. Purely Au-catalyzed reactions

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A)</td>
<td><img src="image" alt="reaction" /></td>
<td>[XPhos-Au]⁺⁻TI₂N⁻</td>
</tr>
<tr>
<td></td>
<td>2.5% [cat.]</td>
<td>CH₂Cl₂, rt, 3 h</td>
</tr>
<tr>
<td>B)</td>
<td><img src="image" alt="reaction" /></td>
<td>[PPh₃Au]⁺⁻TI₂N⁻</td>
</tr>
</tbody>
</table>

Type II. Au-Ag bimetallic catalysis

Au-Ag bi-metallic catalysis includes reactions that are promoted exclusively by the mixture of Au and Ag. Neither Au nor Ag could catalyze these reactions alone. Besides the alkyne hydration shown in Table 7 and Table 8, four more transformations were identified with the same catalytic pattern (Scheme 13).33

Scheme 13. Au-Ag bimetallic catalysis

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A)</td>
<td><img src="image" alt="reaction" /></td>
<td>[PPh₃Au]⁺⁻SbF₆⁻</td>
<td>5% AgSbF₆</td>
</tr>
<tr>
<td>B)</td>
<td><img src="image" alt="reaction" /></td>
<td>[PPh₃Au]⁺⁻SbF₆⁻</td>
<td>5% AgSbF₆</td>
</tr>
<tr>
<td>C)</td>
<td><img src="image" alt="reaction" /></td>
<td>[PPh₃Au]⁺⁻SbF₆⁻</td>
<td>10% AgSbF₆</td>
</tr>
<tr>
<td>D)</td>
<td><img src="image" alt="reaction" /></td>
<td>[PPh₃Au]⁺⁻BF₄⁻</td>
<td>5% AgBF₄</td>
</tr>
</tbody>
</table>
Again, these transformations were all previously assumed as gold catalysis since silver salts could not promote these reactions at all. However, based on our investigation, purely cationic gold catalysts could not promote these reactions. Addition of the silver salts (AgCl could not activate the gold) resulted in reactivation of the gold catalysts, though longer reaction times were needed.

**Type III. Ag-assisted Au catalysis**

The type III gold catalysis, on the other hand, combines the transformations that promoted by either gold or silver or the combination of both metals.

**Scheme 14. Ag-assisted Au catalysis**

As shown in Scheme 14, although pure gold could promote these reactions, the combination of gold and silver gave better results. In addition, these reactions could not be promoted by silver.

Notably, two other reactions were also identified that could be promoted by both gold and silver. However, gold/silver mixture or even gold alone gave better performance than simply silver (Scheme 15). Furthermore, in the α-bromo-enone synthesis, the E/Z selectivity was altered when the combination of gold and silver catalysts was used.
Scheme 15. Ag-promoted reactions

<table>
<thead>
<tr>
<th>Scheme</th>
<th>Reaction</th>
<th>Conditions</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>A)</td>
<td><img src="image" alt="Reaction A" /></td>
<td>2% [Au] cat.</td>
<td><img src="image" alt="Products A" /></td>
</tr>
<tr>
<td>B)</td>
<td><img src="image" alt="Reaction B" /></td>
<td>2% [Au] cat.</td>
<td><img src="image" alt="Products B" /></td>
</tr>
</tbody>
</table>

**2.4.2 Celite filtration**

The results shown above clearly suggest that silver salts have a great influence in gold catalysis. In 2009, Gagné and co-workers reported Au-Ag dinuclear resting states in the catalytic cycle in their mechanistic investigation of gold-catalyzed allene hydroarylation, which was consistent with this “silver-effect”.

As described in section 2.3, celite filtration allows [L-Au]⁺A⁻ to pass through and removes most of the silver salts without altering the counteranion (NTf₂⁻, TfO⁻, SbF₆⁻ or BF₄⁻). One concern about celite filtration is whether it can deactivate the gold catalysts. Although sequential addition of silver salts to the celite filtrates resulted in reactivation of the catalyst, the influence from celite filtration was still unclear.

Another general strategy for the preparation of [L-Au]⁺ is the acid activation of L-Au-Me or L-Au-Ph (formation of methane or benzene). This process was extremely sensitive to solvents, which made the silver salt activation of L-Au-Cl a better practical choice. For example, addition of TfOH to PPh₃-Au-Me in CH₂Cl₂, CH₂NO₂ or CH₃CN caused immediate catalyst decomposition, forming gold nano particles or a gold mirror. Therefore, it is very difficult to directly compare the reactivity difference of [L-Au]⁺ formed from PPh₃-Au-Me/TfOH or from celite filtration of PPh₃-AuCl/AgOTf. Fortunately, through screening, dioxane was identified as one optimal solvent with much slower catalyst decomposition using the acid activation approach, which allowed the parallel comparison of the propargyl acetate hydration for the claimed “silver effect”.

28
Table 9. Comparison of celite filtration and acid activation

As shown in Table 9, the [PPh₃Au]⁺TfO⁻ obtained from PPh₃AuMe/TfOH gave the exactly same results as observed with celite filtration. Without the addition of AgOTf, [PPh₃Au]⁺TfO⁻ indicated no reactivity, which provided an unambiguous evidence for the observed “silver effect” in gold catalysis.

2.4.3 Other activation factors in gold(I) catalysis

While the silver influence on gold catalysis was unexpected and influential, the reactivity offered by triazole-gold (TA-Au) catalyst suggested that silver salts were not the only “activation factor” for gold. Interestingly, the two purely gold-catalyzed reactions shown in Scheme 13 both contained a coordinating Tf₂N⁻ anion. In general, The L-Au-NTf₂ complexes were different than the gold catalysts [L-Au]⁺X⁻ formed with non-coordinated counter anions, such as TfO⁻.

Figure 9. ³¹P NMR comparison of different Au(I) catalysts
As indicated by $^{31}$P NMR (Figure 9), the $^{31}$P chemical shift of PPh$_3$-Au-NTf$_2$ ($\delta$ 31.1 ppm) is between [PPh$_3$Au]$^+$TfO$^-$ (\(\delta\) 27.1 ppm) and PPh$_3$AuCl ($\delta$ 33.8 ppm). The PPh$_3$-Au-NTf$_2$ complex has a similar chemical shift as TA-Au ($\delta$ 30.8 ppm), suggesting the coordination of Tf$_2$N$^-$ anion with [PPh$_3$-Au]$^+$, which is also supported by crystal structure.\(^{37}\)

The silver-free TA-Au effectively promoted the hydration of 8, suggesting that other coordination ligands, such as 1,2,3-triazoles, could serve as potential “activation factors” for gold catalysts.

Scheme 16. Gold catalysis using Tf$_2$N$^-$ as the activation factor

<table>
<thead>
<tr>
<th></th>
<th>L-Au$^+$</th>
<th>L-Au-NTf$_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A)</td>
<td>[PPh$_3$-Au]$^+$ TIO(-)</td>
<td>PPh$_3$-Au-NTf$_2$</td>
</tr>
<tr>
<td></td>
<td>10 h, 0% yield</td>
<td>6 h, 93% yield</td>
</tr>
<tr>
<td>(B)</td>
<td>[IPr-Au]$^+$ TIO(-)</td>
<td>IPr-Au-NTf$_2$</td>
</tr>
<tr>
<td></td>
<td>24 h, 0% yield</td>
<td>8 h, 88% yield</td>
</tr>
<tr>
<td>(C)</td>
<td>[PPh$_3$-Au]$^+$ TIO(-)</td>
<td>PPh$_3$-Au-NTf$_2$</td>
</tr>
<tr>
<td></td>
<td>4 h, 0% yield</td>
<td>1 h, 89% yield</td>
</tr>
<tr>
<td>(D)</td>
<td>[PPh$_3$-Au]$^+$ TIO(-)</td>
<td>PPh$_3$-Au-NTf$_2$</td>
</tr>
<tr>
<td></td>
<td>8 h, 0% yield</td>
<td>6 h, 80% yield</td>
</tr>
<tr>
<td>(E)</td>
<td>[PPh$_3$-Au]$^+$ TIO(-) + 5% AgNTf$_2$</td>
<td>PPh$_3$-Au-NTf$_2$</td>
</tr>
<tr>
<td></td>
<td>0.5 h, 51% yield</td>
<td></td>
</tr>
</tbody>
</table>

To investigate the influence from Tf$_2$N$^-$, silver-free PPh$_3$-AuNTf$_2$ and IPr-Au-NTf$_2$ were prepared with celite filtration (confirmed by XPS). Using these silver-free catalysts, several Au-Ag bi-metallic catalysed reactions were re-evaluated (Scheme 16). Indeed, the silver-free L-Au-NTf$_2$ indicated good reactivity toward these transformations that were not promoted by [L-Au]$^+$TfO$^-$. This is interesting due to the fact that a coordinating anionic ligand enhanced the reactivity despite reducing the cationic nature of the gold catalyst. Notably, for the intermolecular cyclopropanation reaction (Scheme 16E), the combination of [Ph$_3$P-Au]$^+$TfO$^-$ and
AgNTf\textsubscript{2} showed improved reactivity compared with Ph\textsubscript{3}P-Au-NTf\textsubscript{2}, which once again demonstrated the enhanced reactivity of the gold catalytic system in the presence of silver salt.

Overall, the revision of previously reported gold-catalyzed reactions confirmed the unexpected observations that gold catalysis was greatly influenced by the presence of silver salts.

2. 5 Conclusion

Considering the tremendous efforts that have been put into homogeneous gold catalysis, better understanding of the reaction mechanism is crucial to further advance this research field. With the non-coordination anions (TfO\textsuperscript{-}, SbF\textsubscript{6}\textsuperscript{-} and BF\textsubscript{4}\textsuperscript{-}), purely cationic gold complexes [L-Au]\textsuperscript{+} was less active or even inactive in most of the tested reactions without the presence of silver salts. Addition of AgCl salts did not activate gold catalysts in all tested cases, which ruled out the formation of [Ag-Cl-Au]\textsuperscript{+} as the actual catalyst. The relatively broad scope of the reactions tested in this work confirmed the widely overlooked influence of silver ion in contemporary gold catalytic systems. Although the exact complexes formed from cationic gold and silver salts are not certain at this moment, this discovery initiated a revision of gold catalysis.

2. 6 Contribution

Dr. Dawei Wang investigated the proparyl ester hydration, discovered the “silver effect” in gold catalysis and evaluated various gold-catalyzed reactions. Rong Cai further evaluated the influence from celite filtration and the activation factors in gold catalysis. Sripadhr Sharma, James Jirak, and Sravan K. Thummanapelli helped with substrates preparation. Dr. Novruz G. Akhmedov provided help with NMR studies. Dr. Hui Zhang and Dr. Xingbo Liu did the XPS analysis of the gold complexes. Dr. Jeffrey Petersen performed the X-ray crystallographic analyses.
This project is published on *J. Am. Chem. Soc.* **2012**, 134, 9012-9019.

**References:**


Chapter 3. Gold-Catalyzed Cross-Coupling with Aryldiazonium Salts

3.1 Introduction

Homogeneous gold catalysis has grown rapidly during the past decade. Within this enduring field, the π-activation mode has gained far more attention than redox gold catalysis.\(^\text{38}\) This reluctance is likely due to concerns regarding the high redox potential between Au(I) and Au(III).\(^\text{39}\) The “seal of hesitation” was clearly broken in the past few years with some breakthrough examples.\(^\text{40}\)

For example, Zhang reported the propargyl ester rearrangement and sequential coupling with boronic acid using Selectfluor as the oxidant.\(^\text{41}\) Russell also developed the arene cross-coupling with PhI(OAc)\(_2\) (PIDA) as the oxidant (Scheme 17).\(^\text{42}\) In these representative cases, strong oxidants were required to operate the Au(I)/Au(III) catalytic cycle.

Scheme 17. Representative examples of redox gold catalysis

More recently, Glorius and Toste groups demonstrated that the Au(I)/Au(III) catalytic cycle could be alternatively accessed through the combination of a photocatalyst and a radical precursor, such as aryldiazonium salts (Scheme 18).\(^\text{43}\) As proposed by the authors, the oxidation of gold catalyst was achieved through initial combination of aryl radical to gold (I) species and sequential single electron transfer from the resulting gold(II) intermediate to the photocatalyst.
As mentioned in Section 1.1.1, because of the relativistic effect, Au(I) possesses more dispersed 5d electrons, which retards the rate of oxidative addition.\(^3\) Compared with the isoelectronic Pd(0) complexes, which undergo oxidative addition with aryl halide easily, Au(I) shows far less reactivity for this classic type of organometallic reactions. Only limited examples of Au(I) oxidative addition has been reported (Scheme 19).\(^{44}\)

In the 1970s, Kochi, Schmidbaur, and Puddephatt discovered that phosphine gold(I) methyl complex could react with methyl iodide slowly under room temperature, generating phosphine gold(I) iodide and ethane (Scheme 19A).\(^{45}\) The gold(III) intermediate likely formed through a S\(_{N}\)2-type addition of gold(I) to methyl iodide, which is common among late transition metals. More recently, Toste reported a photo-initiated oxidative addition of CF\(_3\)I to aryl gold(I) complexes (Scheme 19B).\(^{46}\) Detailed mechanistic studies suggested a radical chain reaction starting from the photoinitiated excitation of CF\(_3\)I. The resulting gold(III) complex is stable towards air, water, and even column purification.

In 2014, Amgoune and Bourissou reported a strategy using phosphine-chelated aryl halide to direct the gold(I) center close to the C-X bond through phosphine coordination, which led to a facile intramolecular oxidative addition of C-I or C-Br bonds (Scheme 19C).\(^{47}\) This is the first example for the C(sp\(^2\))-X oxidative addition to a single gold center. The activation barrier determined by NMR (confirmed by DFT calculations) is 10-15 kcal/mol lower than the predicted activation barrier of a similar intermolecular oxidative addition.
Later, the same group reported another example using a specially designed carborane diphosphine (DPCb) ligand to trigger the oxidative addition to gold(I). This DPCb ligand is one rare example that could chelate gold(I) with a small bite angles (100°, usually 180° for two-coordinated gold(I) complexes), which facilitates gold(I) to undergo oxidative addition of aryl iodides under mild conditions with broad substrate scope. Although the studies of gold(III) reductive elimination is limited compared with oxidative addition, there is clear evidence that gold(III) undergoes efficient reductive elimination. Not until the recent development of well-characterized

---

**Scheme 19. Selected examples of gold(I) oxidative addition to C-X bonds**

**A) S_{n}2-type oxidative addition**

\[
\text{Ph}_{3}P\text{-Au-CH}_{3} + \text{H}_{3}C\text{-I} \rightarrow \text{Ph}_{3}P\text{-Au-CH}_{3} \text{I} \text{Ph}_{3}P\text{-Au-CH}_{3} \rightarrow \text{Ph}_{3}P\text{-Au-CH}_{3} + \text{H}_{3}C\text{-CH}_{3}
\]

Kochi, Schmidbaur, 1972
Puddephatt, 1973

**B) Radical chain mechanism**

\[
\text{CF}_{3} \rightarrow \text{[CF}_{3}]^{+} \rightarrow \text{[CF}_{3}]^{+} \text{I}^{\ominus} \rightarrow \text{[CF}_{3}]^{+} \rightarrow \text{Cy}_{3}P\text{-Au-Ar} \text{CF}_{3}
\]

Toste, 2014

**C) Phosphine-directed oxidative addition**

\[
\begin{align*}
\text{X} \text{PPh}_{2} & \xrightarrow{a \text{ AuI}} \text{X} \text{PPh}_{2} \\
\text{X} = \text{I or Br} & \xrightarrow{b \text{ DMSAuBr}} \text{X} \text{PPh}_{2}
\end{align*}
\]

Bourissou, 2014

**D) Bending turns on reactivity**

\[
\begin{align*}
\text{PrN} \text{NPr} \text{NPr} \text{NPr} \text{NPr} \text{NPr} \text{NPr} & \xrightarrow{\text{Ar-I}} \text{DCM rt} \\
\text{PrN} \text{NPr} \text{NPr} \text{NPr} \text{NPr} \text{NPr} \text{NPr} & \xrightarrow{\text{Ar-I}} \text{DCM rt}
\end{align*}
\]

Bourissou, 2014
gold(III) complexes through oxidative addition, that significant progress in mechanistic understanding of gold(III) reductive elimination has been achieved.

Early kinetic studies suggested that dissociation of phosphine ligand form four-coordinate gold complexes to generate a Y-shape (or T-shape) intermediate is the rate-determining step for reductive elimination of C(sp³)-C(sp³) and C(sp³)-C(sp²). In accordance with the dissociative mechanism, less coordinating phosphine ligands enhance the reductive elimination reaction rate.

Recently, the Toste group reported more detailed mechanistic studies on gold(III) reductive elimination (Scheme 20).

Scheme 20. Examples for reductive elimination from gold(III)

A) Exceptionally fast C-C reductive elimination

\[
\begin{align*}
\text{Ph}_3\text{P}^+\text{Au}^-\text{Cl}^- & \quad \text{Ar}^- = 4\text{-fluorophenyl} \\
-52 ^\circ C, \text{CD}_2\text{Cl}_2 & \quad k_1 = 1.5 \times 10^{-4} \text{ s}^{-1} \\
\text{PPh}_3^- & \quad k_2 = 0.019 \text{ s}^{-1} \text{ M}^{-1}
\end{align*}
\]

B) C-X and C-CF₃ reductive elimination

\[
\begin{align*}
\text{F}_3\text{C}^-\text{Au}^-\text{Ar}^- & \quad \text{rt} \quad k_3 > 0.22 \text{ s}^{-1} \quad \text{faster R.E.} \\
\text{Ar}^-\text{CF}_3^- & \quad k_2 = 0.019 \text{ s}^{-1} \\
\text{PPh}_3^- & \quad \text{Ar}^-\text{CF}_3^- + \text{Ph}_3^+\text{AuCF}_3
\end{align*}
\]

C) C-P reductive elimination

\[
\begin{align*}
\text{Cl}^-\text{Au}^-\text{Cl}^- & \quad \text{AgSbF}_6^- - \text{AgCl} \\
-78 ^\circ C & \quad 78 ^\circ C \quad \text{to} -20 ^\circ C \\
\text{Ar}^- & \quad -78 ^\circ C \quad \text{Au n.p.} \\
\text{R}_3\text{P}^- & \quad \text{R}_3\text{P}^-\text{Ar}^- \\
\text{Toste, 2014, 2016} & \quad \text{Toste, 2013}
\end{align*}
\]

The C(sp³)-C(sp³) bond reductive elimination is among the fastest C-C coupling reactions catalyzed by transition metals (Scheme 20A). Interestingly, the reaction is accelerated by addition of excess PPh₃ ligand, which is opposite to that observed for C(sp³)-C(sp³). The gold(III) complex possibly undergoes associative ligand exchange with excess PPh₃, generating a cationic bis-PPh₃-biaryl gold complex, which rapidly eliminates the biaryl product. Without excess
PPh₃, the square-planar gold(III) complex could generate biaryl directly through reductive elimination.

The other three examples all follow dissociative mechanism (Scheme 20B, 20C).⁵² The four-coordinated Au(III) complexes, in these cases, are very stable and do not decompose under room temperature. At elevated temperature, the phosphine ligand dissociates to generate the reactive Y-shaped intermediate, which will reductively eliminate to form carbon-halide bonds, with a reaction rate I > Br > Cl (C-F bond formation is not observed). By extract the halides out from the initial gold(III) complex using a silver salt, a different Y-shaped intermediate is formed and undergoes rapid reductive elimination within seconds, forming C-CF₃ or C-P bonds.

Although the scope for redox gold catalysis is still limited, the unique properties of Au(I), such as efficient π-activation and non-parallel reactivity with other group 10 metals, makes redox gold chemistry very attractive. Based on the different reaction pathways of Au(I) and Pd(0) toward oxidative addition, redox gold chemistry will not become an alternative of palladium chemistry but rather a irreplaceable supplement. Recent progress in this field has certainly enriched gold catalysis regarding elementary organometallic reactions, while further mechanistic investigation and new transformation discovery remain challenging.

### 3.2 Cross-coupling of alkyne and aryldiazonium

Our group recently disclosed a gold-catalyzed cross-coupling between aromatic and aliphatic terminal alkynes, which was achieved through the selective formation of gold acetylide intermediates.⁵³ With the aid of a strong oxidant (PIDA) and phenanthroline ligand, rapid reductive elimination of Au(III) intermediate led to facile and selective diyne formation (Scheme 21). Encouraged by this success and inspired by previous works from Glorius and Toste (Scheme 18), we were intrigued by the possibility of sp-sp² cross-coupling using aryldiazonium salts as the coupling partner under mild photocatalytic conditions.⁵⁴
Scheme 21. Oxidative cross-coupling of terminal alkynes

To test this hypothesis, alkyne 1a and diazonium salt 2a were selected as the model substrates and charged into the “dual” photoredox and gold catalysis conditions.

Table 10. Gold-catalyzed C(sp)-C(sp²) coupling without external oxidants

<table>
<thead>
<tr>
<th>Entry</th>
<th>Variations from above conditions</th>
<th>Conc. (M)</th>
<th>Convn (%)</th>
<th>Yield (%)</th>
<th>14aa</th>
<th>15a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No Change</td>
<td>0.2</td>
<td>46</td>
<td>41</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>No Na₂CO₃</td>
<td>0.2</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>No Ph₃PAuNTf₂</td>
<td>0.2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>No Ru(bpy)₃(PF₆)₂</td>
<td>0.2</td>
<td>44</td>
<td>41</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>No light</td>
<td>0.2</td>
<td>40</td>
<td>36</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>PdCl₂ (5%) as the catalyst</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>PdCl₂ (5%) and Ph₃PAuNTf₂ (5%) as the catalyst</td>
<td>0.5</td>
<td>86</td>
<td>56</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Pd(OAc)₂ (5%) as the catalyst</td>
<td>0.5</td>
<td>83</td>
<td>13</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Pd(OAc)₂ (5%) and Ph₃PAuNTf₂ (5%) as the catalyst</td>
<td>0.5</td>
<td>100</td>
<td>62</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

a Reaction conditions: 12a (0.1mmol), 13a (0.12mmol), catalysts and additives in acetonitrile (ACN), rt, 10h; b Less than 1% of 13a homo-coupling product 4,4’-difluorobiphenyl (16a) was detected; c Determined by 1H-NMR using p-xylene as the internal standard; d Determined by 19F-NMR using benzotrifluoride as the internal standard.

As shown in Table 10 (entry 2), reaction of 12a and 13a in the presence of both photocatalyst and gold catalyst gave no desired coupling products (low conversion of 12a). Considering that the formation of gold acetylide could be critical, a base (Na₂CO₃) was added to assist the alkyne deprotonation. As expected, the cross-coupling product 14aa was formed, though in modest yield.
In the control experiments (entries 3-5), almost identical kinetics and yields were observed under standard or dark conditions in the absence of photocatalyst, which negated the involvement of a photocatalytic process. This result was exciting since it implied that the diazonium salt alone, in this reaction, might be fully capable of oxidizing the active gold(I) species to gold(III).

It has been reported that trace amount of Pd(II) in gold salts might contribute to Sonogashira-type coupling. To rule out this possibility, PdCl$_2$ was tested as the catalyst either by itself or combined with gold. The negative results obtained from the studies (Table 10, entries 6-9) confirmed this reaction as a gold-catalyzed process.

**Table 11. Condition optimization for gold-catalyzed C(sp)-C(sp$^2$) coupling $^a, b$**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (%)</th>
<th>Additive (equiv)</th>
<th>Time (h)</th>
<th>Conc. (M)</th>
<th>Convn (%)</th>
<th>Yield (%)</th>
<th>14aa</th>
<th>15a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph$_3$PAuNTf$_2$ (5)</td>
<td>-</td>
<td>20</td>
<td>0.2</td>
<td>0</td>
<td>0</td>
<td>14aa</td>
<td>15a</td>
</tr>
<tr>
<td>2</td>
<td>Ph$_3$PAuNTf$_2$ (5)</td>
<td>Na$_2$CO$_3$ (2)</td>
<td>20</td>
<td>0.2</td>
<td>44</td>
<td>41</td>
<td>14aa</td>
<td>15a</td>
</tr>
<tr>
<td>3</td>
<td>Ph$_3$PAuNTf$_2$ (5)</td>
<td>bpy (2)</td>
<td>20</td>
<td>0.2</td>
<td>73</td>
<td>60</td>
<td>14aa</td>
<td>15a</td>
</tr>
<tr>
<td>4</td>
<td>Ph$_3$PAuNTf$_2$ (5)</td>
<td>bpy (2)</td>
<td>8</td>
<td>0.5</td>
<td>100</td>
<td>83</td>
<td>14aa</td>
<td>15a</td>
</tr>
<tr>
<td>5</td>
<td>Ph$_3$PAuNTf$_2$ (5)</td>
<td>Na$_2$CO$_3$ (2), bpy (0.2)</td>
<td>6</td>
<td>0.5</td>
<td>100</td>
<td>94</td>
<td>14aa</td>
<td>15a</td>
</tr>
<tr>
<td>6</td>
<td>Ph$_3$PAuNTf$_2$ (5)</td>
<td>Na$_2$CO$_3$ (2), bpy (0.2)</td>
<td>10</td>
<td>0.5</td>
<td>53</td>
<td>40</td>
<td>14aa</td>
<td>15a</td>
</tr>
<tr>
<td>7</td>
<td>Ph$_3$PAuNTf$_2$ (5)</td>
<td>Li$_2$CO$_3$ (2), bpy (0.2)</td>
<td>6</td>
<td>0.5</td>
<td>50</td>
<td>39</td>
<td>14aa</td>
<td>15a</td>
</tr>
<tr>
<td>8</td>
<td>Ph$_3$PAuNTf$_2$ (5)</td>
<td>K$_2$CO$_3$ (2), bpy (0.2)</td>
<td>6</td>
<td>0.5</td>
<td>64</td>
<td>62</td>
<td>14aa</td>
<td>15a</td>
</tr>
<tr>
<td>9</td>
<td>Ph$_3$PAuOAc (5)</td>
<td>Na$_2$CO$_3$ (2), bpy (0.2)</td>
<td>6</td>
<td>0.5</td>
<td>100</td>
<td>88</td>
<td>14aa</td>
<td>15a</td>
</tr>
<tr>
<td>10</td>
<td>Ph$_3$PAu(TA)OTf (5)$^e$</td>
<td>Na$_2$CO$_3$ (2), bpy (0.2)</td>
<td>6</td>
<td>0.5</td>
<td>100</td>
<td>88</td>
<td>14aa</td>
<td>15a</td>
</tr>
<tr>
<td>11</td>
<td>Ph$_3$PAuCl (5)</td>
<td>Na$_2$CO$_3$ (2), bpy (0.2)</td>
<td>12</td>
<td>0.5</td>
<td>30</td>
<td>27</td>
<td>14aa</td>
<td>15a</td>
</tr>
<tr>
<td>12</td>
<td>Et$_3$PAuNTf$_2$ (5)</td>
<td>Na$_2$CO$_3$ (2), bpy (0.2)</td>
<td>12</td>
<td>0.5</td>
<td>59</td>
<td>44</td>
<td>14aa</td>
<td>15a</td>
</tr>
<tr>
<td>13</td>
<td>(ArO)$_2$PAuNTf$_2$ (5)$^f$</td>
<td>Na$_2$CO$_3$ (2), bpy (0.2)</td>
<td>12</td>
<td>0.5</td>
<td>42</td>
<td>40</td>
<td>14aa</td>
<td>15a</td>
</tr>
</tbody>
</table>

$^a$ Reaction conditions: 12a (0.1mmol), 13a (0.12mmol), catalysts and additives in acetonitrile (ACN), rt; $^b$ Less than 1% of 13a homo-coupling product 4,4'-difluorobiphenyl (16a) was detected; $^c$ Determined by $^1$H-NMR using p-xylene as the internal standard; $^d$ Determined by $^{19}$F-NMR using benzotriﬂuoride as the internal standard.
To optimize the reaction conditions, various additives and catalysts were tested (Table 11). An organic base 2, 2'-bipyridine (bpy) gave better yield (60%) among all tested organic and inorganic bases (entry 3). We reasoned that the bpy additive served both as a base and an ancillary ligand. Complete consumption of 12a (14aa in 83% yield, entry 4) was achieved by simply increasing the reaction concentration. The combination of Na₂CO₃ as the base and bpy as the ligand gave the best result with 14aa obtained in 94% yield (entry 5). Reducing the catalyst loading led to lower conversion likely due to gold decomposition (entry 6). Other inorganic bases proved to be less effective compared with Na₂CO₃. Screening of the gold catalysts revealed that cationic [Ph₃PAu]⁺X⁻ gave optimal yields regardless of the counteranion (entry 9, 10). The more electron-rich PEt₃ ligand (entry 12) and electron-poor phosphite ligand (entry 13) are both less efficient in this reaction. A neutral gold(I) complex Ph₃PAuCl could catalyze this cross coupling but with a much lower conversion and yield, which is probably due to its difficulty in forming a gold acetylide intermediate compared to the cationic gold catalysts.

With the optimized conditions in hand, we explored the reaction scope (Table 12). Electron-deficient diazonium 14aa (4 h) reacted faster than 14ab (6 h). On the contrary, electron-rich diazonium 14ac reacted slower (8 h). Ortho-substituted phenyldiazonium salts gave lower conversion and yield (<30%), which hinted at the steric sensitivity of this reaction. Various terminal alkynes (both aliphatic and aromatic) with different functional groups such as hydroxyl (14a), ester (14e), heterocycles (14g, 14h) and estrone derivative (14o) were well tolerated under this mild and efficient condition. The high reactivity of p-methoxyphenyl acetylene (14l) resulted in a messy reaction with the desired product isolated in only 36% yield (16% alkyne homo-coupling product detected with NMR). In general, aliphatic alkynes reacted faster than aromatic alkynes, suggesting that the gold oxidation likely occurred after the formation of gold acetylide since aliphatic gold acetylides are more electron-rich.
Table 12. Substrate scope for gold-catalyzed C(sp)-C(sp²) coupling

<table>
<thead>
<tr>
<th>R¹</th>
<th>R²</th>
<th>Product Structure</th>
<th>Isolated Yields (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>Me</td>
<td>14aa</td>
<td>92%</td>
</tr>
<tr>
<td>H</td>
<td>Me</td>
<td>14ab</td>
<td>88%</td>
</tr>
<tr>
<td>OMe</td>
<td>Me</td>
<td>14ac</td>
<td>86%</td>
</tr>
<tr>
<td>Me</td>
<td>Me</td>
<td>14ad</td>
<td>89%</td>
</tr>
<tr>
<td>Br</td>
<td>Me</td>
<td>14ae</td>
<td>89%</td>
</tr>
<tr>
<td>t-Bu</td>
<td>Me</td>
<td>14af</td>
<td>87%</td>
</tr>
<tr>
<td>CF₃</td>
<td>Me</td>
<td>14ag</td>
<td>80%</td>
</tr>
<tr>
<td>N</td>
<td>Ph</td>
<td>14ah</td>
<td>71%</td>
</tr>
<tr>
<td>F</td>
<td>Me</td>
<td>14ai</td>
<td>89%</td>
</tr>
<tr>
<td>OMe</td>
<td>Me</td>
<td>14aj</td>
<td>66%</td>
</tr>
<tr>
<td>Br</td>
<td>Me</td>
<td>14ak</td>
<td>89%</td>
</tr>
<tr>
<td>t-Bu</td>
<td>Me</td>
<td>14al</td>
<td>87%</td>
</tr>
<tr>
<td>CF₃</td>
<td>Me</td>
<td>14am</td>
<td>80%</td>
</tr>
<tr>
<td>N</td>
<td>Ph</td>
<td>14an</td>
<td>88%</td>
</tr>
</tbody>
</table>

*a* Reaction condition: 12 (0.4mmol), 13 (0.48mmol), Ph₃PAuNTf₂ (0.02 mmol), bpy (0.08 mmol) and Na₂CO₃ (0.8mmol) in 0.8 mL ACN, rt; b: Isolated yields; c: 10% of Ph₃PAuNTf₂ was used; d: 3 eq. of 13a was used.

3. 3 Reactions of diazonium salts with gold complexes

To study the reaction mechanism, different types of gold complexes were prepared and treated with diazonium salts. The cationic gold catalyst Ph₃PAuNTf₂ did not react with diazonium salts without bpy. No decomposition of both diazonium 13a and gold catalyst was observed even after 18 hours (Figure 10: a-b). With the addition of bpy in a parallel NMR tube, the [Ph₃PAu(bpy)]⁺ complex (³¹P NMR: δ31.6 ppm) was formed instantly (Figure 10: c). Interestingly, this gold complex decomposed during the reaction with ArN₂⁺, forming phosphonium M overtime through reductive elimination of the corresponding Au(III) complex (Figure 10: d-e). After complete conversion of [Ph₃PAu(bpy)]⁺,
diazonium 13a was no longer being consumed, which refuted the possibility of M to be an active species.

Figure 10. Reaction between diazonium and Ph₃PAuNTf₂

\[
\text{Ph}_3\text{PAuNTf}_2 + \text{N}_2\text{BF}_4^- 13a (10 \text{ eq.}) \xrightarrow{\text{bpy (2 eq.) CD₃CN}} \text{PPh}_3\text{BF}_4^- \]

\[
\begin{align*}
\text{31P-NMR} \\
a. & \text{no bpy, no reaction} & t = 0 & \text{PPh}_3\text{AuNTf}_2 + 13a (10 \text{ eq.}) \\
b. & \text{formation of } [\text{Ph}_3\text{PAu(bpy)}]^+ & t = 18 \text{ h} & \text{PPh}_3\text{AuNTf}_2 + \text{bpy (2 eq.)} + 13a (10 \text{ eq.}) \\
c. & \text{M} & t = 2 \text{ h} & \text{PPh}_3\text{Au(bpy)} + 13a (10 \text{ eq.}) \\
d. & \text{M} & t = 8 \text{ h} & \text{PPh}_3\text{Au(bpy)} + 13a (10 \text{ eq.}) \\
\end{align*}
\]

It is known that cationic Au(I) complexes can react rapidly with terminal alkynes to form gold acetylides, especially under basic conditions. To prove that the gold acetylide was the reaction intermediate, complex 17a was prepared and treated with diazonium 13b (1.1 eq.).

As shown in Figure 11A, without bpy, gold acetylide 17a decomposed overtime with only 22% of the cross-coupling product 15r formed (no further conversion after 4 h). The formation of gold mirror and [(Ph₃P)₂Au]⁺ (31P NMR: δ 44.9 ppm) was observed within 1 h. Impressively, with the addition of bpy, 15r was formed instantly and the reaction was completed in a nearly quantitative yield (Figure 11B). After reaction was complete, the [Ph₃PAu(bpy)]⁺ complex was confirmed as the final gold species (small amount of [Ph₃P-Ar]⁺ M was formed after reaction completion from the reaction between excess 13b and [Ph₃PAu(bpy)]⁺).
Figure 11. Reaction between diazonium and gold acetylide

Figure 12. Reaction between diazonium and aryl gold complex

Compared to the C(sp)-C(sp²) coupling (Figure 11), the C(sp²)-C(sp²) coupling with aryl gold complex is much faster (Figure 12). Rapid gas evolution was observed almost simultaneously with the addition of diazonium salt to the mixture of 17b and bpy in CD₃CN.
Similar to the C(sp)-C(sp\(^2\)) coupling, addition of bpy was critical for the reaction outcome. In the absence of bpy, a gold mirror was observed within 10 min. When bpy was present (Figure 12B), the [\(\text{Ph}_3\text{PAu(bpy)}\)]\(^+\) (\(\delta\) 31.6 ppm) was the major species in the \(^{31}\text{P}\) NMR from the beginning of the reaction, suggesting that the reductive elimination of the biaryl product from the Au(III) intermediate is very rapid, which is in accordance with previous report from Toste. Phosphonium M [\(\text{Ph}_3\text{P-Ar}\)]\(^+\) was also generated, though in a trace amount. One issue for the C(sp)-C(sp\(^2\)) coupling is the formation of C(sp\(^2\))-C(sp\(^2\)) homo-coupling product, possibly formed from transmetallation of aryl gold(I) \(17b\) with the corresponding gold(III)-aryl intermediate (generated from reaction of gold(I) with diazonium) and sequential reductive elimination. The presence of bpy helped to suppress homo-coupling pathway, which facilitated the formation of cross-coupling product. At this point, the role of bpy in the overall reaction is unclear.

The reaction with \(\text{Ph}_3\text{PAuMe}\) was quite sluggish both with and without bpy. In the absence of bpy, the gold complex \(\text{Ph}_3\text{PAuMe}\) (terrible solubility in CD\(_3\)CN) slowly decomposed to yield gold mirror with the formation of small amount of unidentified mixture. Although no gold mirror was observed in the presence of bpy, the reaction was also slow and yielded a messy mixture. The desired product (p-xylene) was not detected by \(^1\text{H}\) NMR.

**Scheme 22. Summary of reaction between diazonium and gold complexes**
These NMR experiments provided important mechanistic insights. First, the Ph$_3$PAuNTf$_2$ catalyst alone could not promote diazoniun decomposition (Scheme 22A). The addition of bpy is crucial in assisting the nitrogen extrusion. However, the gold acetylide species reacted with diazonium without bpy, generating the cross-coupling products, though in low yield. In the presence of bpy, a significantly faster reaction rate was observed (Scheme 22B). Considering the fact that M ([Ph$_3$P-Ar]$^+$) was only formed after reaction completion, it is clear that the oxidation of Au(I) preferred to occur on gold acetylide rather than [Ph$_3$PAu(bpy)]$^+$. This discovery was rather exciting since it suggested that [Ph$_3$P-Au-R] complexes were more feasible than cationic gold in diazonium promoted gold oxidation. By forming the [Ph$_3$P-Au-R] intermediate in situ, similar cross-coupling reactions with different R group could be achieved under proper conditions.

3. 4 Cross-coupling of aryl boronic acid and diazonium

According to literature, aryl boronic acids can react with Au(I) under basic conditions to form the corresponding aryl gold complexes. Thus, it is reasonable to envision a catalytic sp$^2$-sp$^2$ cross-coupling between aryl boronic acid and diazonium salts.

Table 13. Condition optimization for gold-catalyzed C(sp$^2$)-C(sp$^2$) coupling$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (%)</th>
<th>Ligand (20%)</th>
<th>Convn (%)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph$_3$PAuNTf$_2$ (5)</td>
<td>bpy</td>
<td>90</td>
<td>38</td>
</tr>
<tr>
<td>2</td>
<td>Ph$_3$PAu(TA)OTf (5)$^d$</td>
<td>bpy</td>
<td>86</td>
<td>64</td>
</tr>
<tr>
<td>3</td>
<td>Ph$_3$PAu(TAa) (5)$^e$</td>
<td>bpy</td>
<td>76</td>
<td>47</td>
</tr>
<tr>
<td>4</td>
<td>(ArO)$_3$PAu(TA)OTf (5)$^f$</td>
<td>bpy</td>
<td>80</td>
<td>33</td>
</tr>
<tr>
<td>5</td>
<td>Et$_3$PAu(TA)OTf (5)</td>
<td>bpy</td>
<td>68</td>
<td>10</td>
</tr>
</tbody>
</table>
Under previously optimized conditions (Table 13, entry 1), the desired cross-coupling product 18 was successfully obtained. However, the yield is much lower (around 40%), presumably due to fast catalyst decomposition. Applying the more stable triazole-gold complex Ph₃PAu(TA)OTf developed by our group, higher yields approaching 65% were observed (entry 2). Changing the phosphine ligand did not help improve the reaction performance (entry 4-6). The full conversion of starting material was obtained by an increase in the catalyst loading to 10% (entry 7). The bpy ligand is still the optimal choice among all tested chelating ligands (entry 8, 9).

Under this new condition, various substituted aryl boronic acids and diazonium salts were tested. Overall, good to excellent yields were obtained for most of the tested substrates (Table 14). Considering the importance of C-C bond formation in organic synthesis, this new approach in redox gold catalysis is of great interest since it offers an alternative strategy for cross-coupling.

Table 14. Substrate scope for gold-catalyzed C(sp²)-C(sp²) coupling

<table>
<thead>
<tr>
<th>R¹</th>
<th>R²</th>
<th>Ar¹</th>
<th>Ar²</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me</td>
<td>Me</td>
<td>4-F</td>
<td>4-F</td>
<td>18a</td>
<td>91%</td>
</tr>
<tr>
<td>H</td>
<td>Me</td>
<td>4-F</td>
<td>4-F</td>
<td>18b</td>
<td>90%</td>
</tr>
<tr>
<td>4-Br</td>
<td>H</td>
<td>4-F</td>
<td>4-F</td>
<td>18c</td>
<td>76%</td>
</tr>
<tr>
<td>4-Ph</td>
<td>H</td>
<td>4-F</td>
<td>4-F</td>
<td>18d</td>
<td>72%</td>
</tr>
<tr>
<td>4-COO Me</td>
<td>H</td>
<td>4-F</td>
<td>4-F</td>
<td>18e</td>
<td>63%</td>
</tr>
<tr>
<td>2,4-di-F</td>
<td>Me</td>
<td>4-F</td>
<td>4-F</td>
<td>18f</td>
<td>81%</td>
</tr>
<tr>
<td>4-OH</td>
<td>4-OMe</td>
<td>4-OMe</td>
<td>4-OMe</td>
<td>18g</td>
<td>62%</td>
</tr>
<tr>
<td>4-OH</td>
<td>4-OMe</td>
<td>4-OMe</td>
<td>4-OMe</td>
<td>18h</td>
<td>42%</td>
</tr>
</tbody>
</table>
Reaction condition: $^{19}$ (0.4mmol), $^{13}$ (0.48mmol), Ph$_3$PAu(TA)OTf (0.04 mmol), bpy (0.08 mmol) and Na$_2$CO$_3$ (0.8mmol) in 0.8 mL ACN, rt; $^{b}$ NMR yields.

3.6 Mechanistic investigation

After study of the stoichiometric reactions using NMR, the catalytic reaction between alkyne and diazonium was investigated as well. Based on $^{31}$P NMR data, the [Ph$_3$PAu(bpy)]$^+$ complex ($\delta$ 31.6 ppm) was the major gold species detected during the reaction. As the reaction proceeded toward completion, this [Ph$_3$PAu(bpy)]$^+$ complex started to accumulate. After the reaction was complete (7 h), phosphonium M ([Ph$_3$P-Ar]$^+$) started to form. No induction period was observed for this reaction, suggesting that the formation of catalytically active intermediate was very rapid.

Figure 13. Monitoring the catalytic C(sp)-C(sp$^2$) coupling

To verify whether the reaction proceeded through a radical mechanism, diazonium salt $^{13c}$ was prepared and charged into the optimal conditions. As shown in Scheme 23, the reaction of $^{13c}$ with $^{12a}$ was quite sluggish with only 25% of the desired coupling product $^{20a}$ formed. The radical trapping product 3-methyl-dihydrobenzofuran was not detected, but a cyclized byproduct $^{20b}$,
generated from two molecule diazonium salt 13c, was isolated and characterized by NMR and HR-MS. The mechanism of 20b formation is still unclear to this point. It is highly likely that the aryl radical formation is not a key step in this cross-coupling reaction but it cannot be ruled out from possible reaction pathways.

Scheme 23. Radical trapping experiment

Figure 14. ESI-MS spectra of reaction mixture between diazonium and alkyne
To further shed light on the reaction mechanism, we utilized the electrospray ionization mass spectrometry (ESI-MS) studies to detect possible intermediates. As shown in Figure 14, aryldiazenido gold complexes 21 were observed at m/z 713, 701 and 689 respectively for the three different alkynes. The intensities of 21 were quite low compared with other gold complexes ([Ph₃PAu(bpy)]⁺ and σ,π-acetylide gold complex) in the reaction mixture. In fact, the intensity of 21 decreased as the reaction proceeded (almost not detectable after 2 h), which suggested 21 as an active reaction intermediate. The MS/MS fragment analysis confirmed the composition of 21 (see details in the experimental section).

**Figure 15. Explore the reaction intermediate with ESI-MS spectra**

In order to trap plausible intermediates, compound 13d was prepared. Under the standard conditions, very low intensity of the coupling product 20c was detected with crude NMR and ESI-MS. Analyzing the reaction mixture with ESI-MS after 10 min revealed the formation of a major ion with m/z 744.1. With the
help from MS/MS fragment analysis, structure 22 was proposed as the gold(III) intermediate.

It was highly likely that the potential coordination from pyridyl group with gold restricted the reductive elimination of 22. However, without the presence of bpy, a dominant gold cation was detected with m/z 772.2, which is tentatively assigned as the aryldiazenido gold complex 21d based on the MS/MS analysis. Although the exact reason is uncertain at this moment, the presence of bpy clearly assisted the nitrogen extrusion, which was a crucial step for the overall transformation.

Based on the above-discussed experimental results, a simplified mechanism was proposed as shown in Scheme 2. Both $^{31}$P-NMR and ESI-MS confirmed the formation of the more stable gold complex $[\text{Ph}_3\text{PAu(bpy)}]^+$ by the addition of bpy. Based on current evidence, the diazonium oxidation occurred preferentially on either aryl gold or gold acetylide, forming intermediate A. The bpy-assisted nitrogen extrusion followed by rapid Au(III) reductive elimination gave the desired coupling product and regenerated the Au(I) catalyst. Certainly, it is interesting to uncover how L-Au-R reacts with the diazonium to form A and understand the exact function of bpy.

Scheme 24. Proposed mechanism of gold-catalyzed C-C cross-coupling
3. 7 Gold-catalyzed C-X formation with aryldiazonium

Although redox gold catalysis has attracted much attention during recent years, most of the reported systems are focused on C-C bond formation. There are very few successful examples regarding C-heteroatom (C-X) coupling. One problem in gold-catalyzed C-X bond formation is the fast C-C homo-coupling (via transmetallation and reductive elimination). Thus, to achieve this challenging C-X coupling, lowering the activation energy is crucial to avoid undesired homo-coupling. To develop an effective system for C-X formation under mild conditions, we investigated the diazonium-promoted gold oxidation conditions and applied that chemistry in catalytic Sandmeyer reactions toward C-Br, C-S and C-P bond syntheses.

3.7.1 Catalytic Sandmeyer reaction

Conversion of ArN$_2^+$ to ArBr or ArCl is usually achieved using stoichiometric amount of CuBr or CuCl under standard Sandmeyer conditions. Successful examples of catalytic Sandmeyer reaction are rare. Initiated by our previous investigation on the reaction between gold and diazonium salts, Ph$_3$PAuNTf$_2$ and bpy were charged into the mixture of diazonium and NaBr. To our delight, aryl bromide product was successfully obtained in 63% yield. Different from previous C-C cross-coupling reactions, the bpy ligand did not help with the reaction performance in this case (Table 15, entry 6, 7).

Through screening, the less reactive Ph$_3$PAuCl catalyst is revealed to give the optimal result (entry 1). Without the gold catalyst, the only product observed is fluorobenzene formed from diazonium decomposition (Table 15, entry 2). Only trace amount of aryl chloride was detected by GC-MS when using LiCl as the nucleophile source (entry 3). This is consistence with the recent study reported by Toste and coworkers, in which the reductive elimination rate is suggested as I > Br > Cl through the evaluation of different Au(III)-X bond dissociation energies. Changing the solvent to acetone led to 100% conversion but with majorly homo-coupling product, possibly generated from radical process (entry 4). Lowering gold loading to 3 mol% gave a similar result (80%). A further decrease of
catalyst loading to 1 mol% led to poor yield. To the best of our knowledge, this is the first example of catalytic Sandmeyer reaction using only the gold catalyst.

Table 15. Gold-catalyzed C-Br formation $^{a,b}$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Variations from above conditions</th>
<th>Time (h)</th>
<th>Convn (%)</th>
<th>Yield (%)</th>
<th>23a</th>
<th>24a</th>
<th>25a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>5</td>
<td>100</td>
<td>81</td>
<td>7</td>
<td>&lt;5</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>without Ph$_3$PAuCl</td>
<td>12</td>
<td>50</td>
<td>&lt;10</td>
<td>trace</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>LiCl instead of LiBr</td>
<td>12</td>
<td>70</td>
<td>&lt;5</td>
<td>trace</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>acetone instead of ACN</td>
<td>12</td>
<td>100</td>
<td>11</td>
<td>37</td>
<td>&lt;5</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Ph$_3$PAuNTf$_2$ instead of Ph$_3$PAuCl</td>
<td>12</td>
<td>100</td>
<td>68</td>
<td>10</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Ph$_3$PAuNTf$_2$ with 20 mol% bpy</td>
<td>5</td>
<td>100</td>
<td>63</td>
<td>8</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>with 3 mol% Ph$_3$PAuCl</td>
<td>12</td>
<td>100</td>
<td>80</td>
<td>7</td>
<td>&lt;5</td>
<td></td>
</tr>
</tbody>
</table>

$a$ Reaction conditions: 13a (0.1 mmol), LiBr (0.3 mmol), cat. Au (5 mol%) in acetonitrile (ACN), 50 $^\circ$C; $^b$ $^{19}$F NMR yield with benzotrifluoride as the internal standard.

With the optimal conditions in hand, the reaction substrate scope was explored. As shown in Table 16, excellent substrate compatibility was found with the gold-catalyzed conditions. Diazonium with EWGs and EDGs all furnished the products in good yields (23a-23g). Notably, aryl iodide is also compatible in this catalytic system (23e), highlighting the orthogonal reactivity of Au catalyst over Pd, Cu, and Ni, for which oxidative addition could occur with aryl iodide. Carbonyl groups (23h, 23i, 23j), benzodioxo (23k), azobenzene (23q) are all well tolerated in this reaction. Hetero-aromatic diazonium salts, such as pyridines (23m, 23n) and indole (23p) also worked well in this reaction. Moreover, this reaction proceeded with high efficiency and selectivity with α, β-unsaturated ester (23s) and p-acetylide aryl diazonium (23r) to give the corresponding products. To further evaluate the synthetic utility and generality of this reaction, coumarin derivative (23l) and estrone derivative (23t) were tested under the reaction...
conditions. The desired products were achieved with good yields, highlighting the potential application of this catalytic system for complex molecular synthesis.

### Table 16. Substrate scope for gold-catalyzed C-Br bond formation

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Isolated yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>23a</td>
<td>82%</td>
</tr>
<tr>
<td>23b</td>
<td>79%</td>
</tr>
<tr>
<td>23c</td>
<td>88%</td>
</tr>
<tr>
<td>23d</td>
<td>71%</td>
</tr>
<tr>
<td>23e</td>
<td>73%</td>
</tr>
<tr>
<td>23f</td>
<td>81%</td>
</tr>
<tr>
<td>23g</td>
<td>80%</td>
</tr>
</tbody>
</table>

"a" Reaction conditions: 13 (0.2 mmol), LiBr (0.6 mmol), PPh₃AuCl (3 mol%) in acetonitrile (ACN), 50 °C, 5h; "b" Isolated yield; "c" determined by ¹⁹F-NMR with benzotrifluoride as the internal standard; "d" determined by GC-Mass using decane as the internal standard.

### 3.7.2 Gold-catalyzed C-S and C-P bond formation

Encouraged by the success of gold-catalyzed C-Br bond formation, we turned our attention to the synthesis of C-S and C-P bonds. Unlike C-Br bond, which can be alternatively prepared using stoichiometric amount of CuBr, thiolst and phosphonates are not valid nucleophiles under Sandmeyer conditions due to the coordination of sulfur or phosphine with Cu cation, which could potentially quench catalyst reactivity.

Thiols are good nucleophiles and can react with arenediazonium through SₙAr mechanism with the assistance of a base, especially for acidic thiophenols. However, one side reaction of diazonium decomposition is the
formation of Ar-H. This side reaction turned to be even more severe when using proton-containing nucleophiles (NuH). Therefore, reaction of cysteine derivative 26a with diazonium 13a gave only Ar-H 24a (23%) as the product (Table 17, entry 1). Addition of base could produce thioether 27a in 37% yield, along with 55% of 24a (entry 2). Using stoichiometric Cu(OAc)₂ did not improve the reaction performance (31%, entry 3).

Interestingly, with PPh₃AuCl as the catalyst, the desired thioether 27a was obtained even without base (49% yield). These results suggested that with the help of thiol nucleophile, PPh₃AuCl could be an effective catalyst for diazonium decomposition. With the aid from base, this challenging C-S coupling was achieved in 86% yield with only 3 mol% gold catalyst loading. Based on the reaction kinetics, the C-S bond formation was dramatically improved with gold catalyst. Without catalyst, C-S coupling product 7a has nearly same kinetics with byproduct 4a; with the gold catalyst, the formation of 7a is accelerated while less than 10% 4a was formed.

Table 17. Gold-catalyzed C-S bond formation

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol%)</th>
<th>Base (eq.)</th>
<th>Time (h)</th>
<th>Conv. (%)</th>
<th>Yield (%)</th>
<th>27a</th>
<th>24a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
<td>None</td>
<td>24</td>
<td>30</td>
<td>0</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>None</td>
<td>Na₂CO₃ (2)</td>
<td>10</td>
<td>100</td>
<td>37</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Cu(OAc)₂ (100)</td>
<td>Na₂CO₃ (2)</td>
<td>10</td>
<td>100</td>
<td>31</td>
<td>65</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>PPh₃AuCl (5)</td>
<td>None</td>
<td>10</td>
<td>55</td>
<td>49</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>PPh₃AuCl (5)</td>
<td>Na₂CO₃ (2)</td>
<td>3</td>
<td>100</td>
<td>87</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>PPh₃AuCl (3)</td>
<td>Na₂CO₃ (2)</td>
<td>3</td>
<td>100</td>
<td>86</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>PPh₃AuCl (1)</td>
<td>Na₂CO₃ (2)</td>
<td>7</td>
<td>100</td>
<td>53</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>

*Reaction conditions: 13a (0.2 mmol), 26a (0.1 mmol), cat. Au (5 mol%) and Na₂CO₃ (0.2 mmol) in acetonitrile (ACN), 50 °C.*

**F NMR yield with benzotrifluoride as internal standard.**
With the optimal conditions, various cysteine derivatives were successfully prepared in good yields (Table 18). Both electron-rich and electron-deficient diazonium salts were suitable for this transformation with excellent yields. Diazonium with iodide substituent is also tolerated in this reaction (27e), which could be a potential synthetic handle for further functionalization. Heterocycles, including various substituted pyridines (27j-27l) and benzothiazole (27m), gave the desired products efficiently with this catalytic system. Acetylide (27n) and α, β-unsaturated ester (27o) also reacted with good yields. Notably, sulfur containing molecules, as an important class of compounds for both chemical and biological research, are challenging to construct through traditional cross-coupling strategies because of the potential coordination between sulfur and transition metal catalysts. Our catalytic system thus provided an efficient and easy way to achieve these bioactive amino acids.

Table 18. Substrate scope for gold-catalyzed C-S bond formation

<table>
<thead>
<tr>
<th>Reaction conditions</th>
<th>R = F, 87%, 27a; OMe, 66%, 27b; Me, 91%, 27c; H, 90%, 27d; CF₃, 83%, 27e; I, 87%, 27f; Br, 90%, 27g</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R = Me, 27h, 70%; Ph, 27l, 72%</td>
</tr>
<tr>
<td></td>
<td>R' = NHBoc COOMe, NHBoc COOR, NHBoc COOR' (27j, 67%, 27k, 78%, 27l, 75%, 27m, 72%, 27n, 80%, 27o, 76%, 27p, 78%, 27q, 78%)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>a Reaction conditions, C-S formation: 13 (0.4 mmol), 26 (0.2 mmol), PPh₃AuCl (3 mol%) and Na₂CO₃ (0.4 mmol) in acetonitrile (ACN), rt, 3h; b isolated yield; c determined by ¹H-NMR using 1,3,5-trimethoxybenzene as the internal standard with E/Z selectivity 1:1.</td>
</tr>
</tbody>
</table>

Another application using this methodology is the preparation of arylphosphonate. Compared with sulfur, this C-P bond formation is more challenging, since H-phosphonate is much less nucleophilic. Thus, the C-P bond formation with diazonium cannot be achieved through either SₕAr or Cu-
promoted Sandmeyer reactions. Recently, Toste reported the application of photocatalyst in gold-catalyzed oxidative coupling to achieve this C-P bond formation.\(^{71}\) Based on the results discussed above, we were wondering whether this challenging C-P bond formation could be achieve with our newly discovered nucleophile-promoted gold redox catalysis under mild conditions.

As shown in Table 19, no arylphosphonate (28a) was obtained with copper acetate or without a catalyst (entry 1-3). In contrast, the product 28a could be achieved with 5% PPh\(_3\)AuCl (entry 4), although with low yield (25%) due to the poor nucleophilicity of phosphonate. Addition of Na\(_2\)CO\(_3\) did not improve the yield of the coupling but promoted the Ar-H formation. The combination of PPh\(_3\)AuNTf\(_2\) and bpy in the presence of Na\(_2\)CO\(_3\) (previously reported C-C bond cross-coupling conditions) also failed to increase the yield. Considering that nucleophilic ligand is crucial in this gold redox catalysis, we focused our attention of additives to other pyridine derivatives. Through screening, 3-Cl-pyridine was identified to give the optimal result. With the addition of 2 eq. 3-Cl-pyridine, PPh\(_3\)AuCl could effectively catalyze this C-P bond coupling, giving the desired product 28a with 83% isolated yield in 5h. In contrast, with PPh\(_3\)AuNTf\(_2\), the major product was the diaza compound 29a.\(^{72}\)

Table 19. Gold-catalyzed C-P bond formation\(^{a,b}\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol%)</th>
<th>Additives (eq.)</th>
<th>Time (h)</th>
<th>Conv. (%)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
<td>None</td>
<td>10</td>
<td>50</td>
<td>0 0 31</td>
</tr>
<tr>
<td>2</td>
<td>None</td>
<td>Na(_2)CO(_3) (2)</td>
<td>10</td>
<td>100</td>
<td>0 0 70</td>
</tr>
<tr>
<td>3</td>
<td>Cu(OAc)(_2) (100)</td>
<td>Na(_2)CO(_3) (2)</td>
<td>10</td>
<td>100</td>
<td>0 0 75</td>
</tr>
<tr>
<td>4</td>
<td>PPh(_3)AuCl (5)</td>
<td>None</td>
<td>10</td>
<td>50</td>
<td>25 0 13</td>
</tr>
<tr>
<td>5</td>
<td>PPh(_3)AuCl (5)</td>
<td>Na(_2)CO(_3) (2)</td>
<td>10</td>
<td>100</td>
<td>11 0 38</td>
</tr>
<tr>
<td>6</td>
<td>PPh(_3)AuNTf(_2) (5)</td>
<td>bpy (0.2), Na(_2)CO(_3) (2)</td>
<td>10</td>
<td>100</td>
<td>&lt;5 11 53</td>
</tr>
<tr>
<td>7</td>
<td>PPh(_3)AuCl (5)(^c)</td>
<td>3-Cl-py (2)</td>
<td>5</td>
<td>100</td>
<td>83 0 7</td>
</tr>
</tbody>
</table>
Similar to the C-Br and C-S bond coupling, broad substrate scope is obtained in the C-P bond formation reactions (Table 20). Aryl phosphonates with electron-rich (28b, 28c) and electron-deficient (28a, 28d-28h) substituents could be generated with good yields. Halogen-substituted groups (28a, 28e, 28f) were all tolerated. Alkyne (28i), α,β-unsaturated ester (28j) and azobenzene (28k) also gave good results, suggesting potential synthetic application of this methodology.

Table 20. Substrate scope for gold-catalyzed C-P bond formation

<table>
<thead>
<tr>
<th>R</th>
<th>Ph</th>
<th>PPh₃AuNTf₂ (5)</th>
<th>3-Cl-py (2)</th>
<th>5</th>
<th>100</th>
<th>0</th>
<th>71</th>
<th>22</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>83%</td>
<td>28a</td>
<td>68%</td>
<td>87%</td>
<td>28c</td>
<td>77%</td>
<td>74%</td>
<td>28f</td>
</tr>
<tr>
<td>OMe</td>
<td>28b</td>
<td>66%</td>
<td>28b</td>
<td>28c</td>
<td>28d</td>
<td>28e</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Me</td>
<td>87%</td>
<td>87%</td>
<td>28c</td>
<td>28d</td>
<td>28e</td>
<td>28f</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>51%</td>
<td>28d</td>
<td>28e</td>
<td>28f</td>
<td>28f</td>
<td>28f</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Br</td>
<td>77%</td>
<td>28e</td>
<td>28f</td>
<td>28f</td>
<td>28f</td>
<td>28f</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cl</td>
<td>74%</td>
<td>28f</td>
<td>28f</td>
<td>28f</td>
<td>28f</td>
<td>28f</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3.8 Conclusion

In summary, we discovered a novel gold-catalyzed cross-coupling strategy using aryldiazonium salts as the oxidant. By forming an alkyne or aryl gold complex in situ, oxidation of Au(I) to Au(III) was achieved without strong oxidants or photocatalysts. Preliminary studies revealed the importance of the bpy ligand in assisting nitrogen extrusion, which appeared to be a key step in this
transformation. This strategy offers a new effective cross-coupling approach together with insight about gold redox catalysis.

The reaction between gold and diazonium is further applied to C-Br, C-S, and C-P bond formation reactions through gold redox catalysis. Other than the previously reported bpy ligand, nucleophiles played a crucial role in the gold-promoted diazonium decomposition. Various C-X coupling could be achieved with excellent yields and broad substrate scope simply using Ph₃PAuCl as the catalyst (no need for external oxidant).

3.9 Contribution

For the C-C cross-coupling reaction (sections 3.1 to 3.6), Rong Cai discovered and investigated this redox gold catalysis. Mei Lu and Prof. Hao Chen helped with the ESI-MS studies. Ellen Y. Aguilera helped with substrate preparation. Yumeng Xi helped with manuscript preparation. Dr. Novruz G. Akhmedov provided help with 2D-NMR studies. Dr. Jeffrey L. Petersen carried out the X-ray crystallographic analyses.

For the C-X coupling (section 3.7), Dr. Haihui Peng discovered the developed these reactions. Rong Cai helped with substrate preparation and mechanistic investigations.

The C-C cross-coupling is published on Angew. Chem. Int. Ed. 2015, 54, 8772-8776. The manuscript for C-X coupling is in preparation.

References:


56 There are two precedent examples regarding the cross-coupling of aryldiazonium salts and alkyne: a) Fabrizi, G.; Goggiamani, A.; Sferrazza, A.; Cacchi, S. *Angew. Chem. Int. Ed.* **2010**, 49, 4067; b) Panda, B.; Sarkar, T. K. *Chem. Commun.* **2010**, 46, 3131. In both cases, the reductive elimination occurred on the Pd center. To the best of our knowledge, there is no literature precedence regarding the diazonium salt cross-coupling purely catalyzed by gold.


The monitored quantitative rate constant for \( sp^2 \)-C-C coupling is \((1.5 \pm 0.1) \times 10^{-4}\) S\(^{-1}\) (\(k_{\text{obs}}\), -52 °C), see reference 51; the homo-coupling product was generated from transmetallation between Au(III) and Au(I) intermediate followed by reductive elimination, see reference 40f.


He, Y.; Wu, H.; Toste, F. D. *Chem. Sci.* 2015, 6, 1194.

Chapter 4. Porous Polymer-Supported Heterogeneous Gold(I) Catalysis

4.1 Introduction

As we discussed in the previous sections, homogeneous gold catalysis has experienced a big leap during the past decade. As a carbophilic Lewis acid, cationic gold(I) catalyst facilitated various C-C and C-heteroatom bond formation through the activation of alkynes, allenes and alkenes under mild conditions. While being highly efficient, cationic gold(I) complexes usually suffer from poor stability, especially at elevated temperatures or in the presence of the substrate. The high cost of gold catalysts also prevented their application in large-scale syntheses and industrial processes.

4.1.1 Heterogeneous gold(I) catalysis

The development of solid-phase chemistry has led to great advancements in the field of heterogeneous catalysis. Compared with expensive homogeneous transition-metal catalysts, solid-supported heterogeneous catalysts are much more economically appealing due to easy separation of product from support and effective catalyst recycling protocols (catalyst dependent). The easy separation and good recyclability could significantly reduce the cost of the overall process, as well as simplify the handling and purification. Despite decades of advancements in the field of solid-phase catalysis, immobilization of the transition metal catalysts to a solid-supported ligand can cause problems, such as: 1) low reactivity due to limited access to the active catalytic site; 2) undesired interaction between the solid support and the metal complex or the reaction substrate; 3) leaching of metal catalyst due to weak linkage between the metal and the solid support; 4) substrate induced catalyst deactivation. Considering these limitations, the key to designing heterogeneous transition-metal catalysts relies on the
development and synthesis of suitable solid supports for transition metals and transition metal complexes.

Although solid-supported gold nanoparticles has been extensively investigated, there are only limited examples regarding heterogeneous gold(I) catalysis. In 2011, a polystyrene-supported gold(I) catalyst was reported by Yu and co-workers using triazole-functionalized polystyrene resin as the ligand for PPh$_3$Au$.^77$ Although this catalyst showed good reactivity towards enyne cyclization, it suffered from gold leaching each cycle, possibly because of the dynamic coordination between Au and triazole ligand (Scheme 25A). Later, the same group developed another gold catalyst using a polystyrene-supported phosphine ligand (Scheme 25B).$^78$ Compared with triazole, phosphine ligands coordinate stronger with gold. However, the activation of this gold catalyst required stoichiometric amount of silver salt as simple R$_3$PAuCl is usually not active for alkyne activation. The AgCl generated in this process cannot be removed from the polymer gold catalyst and may influence the catalyst reactivity.

**Scheme 25. Literature precedence of solid-supported gold catalysts**

In 2015, the Toste group reported the synthesis of a heterogeneous gold catalyst by absorbing cationic gold onto mesoporous silica via hydrogen bonding.$^79$ Because of the surface acidity of silica, the protodeauration of this catalyst is greatly accelerated. Using a chiral bisphosphine ligand, the regio- and enantioselectivity for lactonization of allenoic acid are significantly improved for the heterogeneous catalyst (81% ee) compared with the homogeneous analogue (0% ee). At the same time, the mesoporous structure of the silica support also helped to enhance the enantioselectivity (50% ee for nonmesoporous silica).
4.1.2 Porous polymer for transition-metal catalysts

Mesoporous supported materials are usually applied in heterogeneous catalysts because of their high surface area and easily accessible pores, which could help to enhance both the reactivity and selectivity of the catalysts. Among different mesoporous polymer ligands, porous organic polymers (POPs) exhibited excellent performance as the ligand supports for transition metal catalysts.\(^\text{80}\) Because of the stable covalent bond linkage, these POPs are very robust toward acidic/basic conditions and high temperature (normally higher than 300 °C), which make them more feasible as ligands for heterogeneous catalysis compared to metal-organic frameworks (MOFs) or covalent-organic frameworks (COFs) (reversible linkage, sensitive to acid/base).\(^\text{81}\) Moreover, POP ligands possess hierarchical porosity that could enhance the catalytic reactivity and substrate diffusion, as well as lead to different reactivity compared with homogeneous catalysts.\(^\text{82}\) At the same time, the high surface area and good solvent swellability also benefit the overall performance of transition-metal catalysts using POP ligands.\(^\text{83}\)

In 2014, a porous organic polymer ligand of \(\text{PPh}_3\) (POL-PPh\(_3\)) has been reported to facilitate hydroformylation of olefins using the corresponding Rh catalyst.\(^\text{84}\) Excellent activity and selectivity are achieved with this heterogeneous catalyst and are further improved using POL-dppe ligand.\(^\text{85}\)

Based on the broad application of phosphine ligands in gold catalysts, the POL-PPh\(_3\) ligand could be a good starting point to investigate heterogeneous gold(I) catalysts.

4. 2 Porous polymer-supported triazole-gold catalyst

4.2.1 Improved stability of Pol-TA-Au

As we mentioned in Scheme 25B, silver salt is usually involved in the activation of \(\text{R}_3\text{PAuCl}\). During this activation protocol, a celite filtration is used to remove any insoluble Ag-salts leading to differential Au-catalyst reactivity. When considering the development of a polymer-supported Au-catalyst (presumably
using a polymer based phosphine to bind to L-Au-Cl precursor), removing silver salts via celite filtration (following \( \text{R}_3\text{PAuCl} \) activation) would be challenging due to the insolubility of many solid support catalysts in organic solvents and water. With that being said, we had set our eyes on developing a new heterogeneous catalyst synthesis that avoids the use of Ag-salts for chloride abstraction. This could be performed using a ligand exchange method whereby the generation of a more strongly binding X-type ligand could displace the chloride. Luckily, our group has developed syntheses toward the introduction of anionic triazole ligands to Au(I)-complexes, followed by acidification to the corresponding L-type triazole ligand. This would also be especially efficacious due to our previous discovery of triazole-gold (TA-Au) complex as a thermally more stable and chemoselective cationic gold catalyst, which selectively activate alkynes over allenes.\(^{86}\) Intrigued by the unique reactivity and easy synthesis of TA-Au, we put our effort into the development an efficient synthesis of a heterogeneous triazole-gold catalyst.

**Scheme 26. Synthesis of Pol-TA-Au**

As shown in **Scheme 26**, Pol-TA-Au was successfully prepared with high yields. The POL-PPPh\(_3\) could be easily synthesized from solvothermal polymerization of vinyl-functionalized PPh\(_3\). The corresponding Ar\(_3\)PAuCl was obtained by reacting POL-PPPh\(_3\) with DMSAuCl. Using anionic triazole to exchange out the chloride ligand, a neutral gold complex Pol-TAA-Au could be generated. This complex is catalytically inactive due to the difficult ligand
exchange required between the substrate and X-type triazole ligand. With the addition of an acid, this Pol-TAA-Au complex could be easily activated to the cationic Pol-TA-Au.

With this heterogeneous catalyst in hand, we explored the reactivity of it using Teles hydration as a model reaction. Under the same conditions, homogeneous TA-Au decomposed after 2 h, generating the hydration product in 78% yield (Figure 16A). Although the reaction with Pol-TA-Au is initially slower than TA-Au, it could give a 95% yield because of the much better stability of the gold catalyst. By increasing the concentration of the starting material, the reaction is greatly accelerated and completed within 1 h. The Pol-TAA-Au without acid activation is not able to catalyze this reaction. Treating the Pol-TAA-Au with a weaker acid (such as TFA) prior to the reaction could activate the catalyst but with a much slower reaction rate.

Figure 16. Teles hydration reaction with Pol-TA-Au

After separating the heterogeneous catalyst Pol-TA-Au from the reaction mixture by centrifuge and charging it into another portion of starting material, a slower reaction was observed (Figure 16B). We reasoned the decreased reactivity from either catalyst decomposition due to the loss of triazole ligand, or...
the difficulty in triazole ligand dissociation due to the loss of HOTf. With this hypothesis, we treated the catalyst with either triazole or triflic acid after first cycle of the hydration reaction. To our delight, the catalyst was re-activated by triflic acid, promoting the reaction in a same efficiency as the first cycle. The catalyst treated with triazole ligand did not show any improvement on the reactivity, suggesting that the triazole ligand had not leached from polymer catalyst. This Pol-TA-Au catalyst has been recovered and recycled for more than 5 times without any loss of reactivity by using triflic acid to reactivate the catalyst between each cycle.

**Scheme 27. Representative hydration reactions with Pol-TA-Au**

Hydration reactions of other alkynes were also tested with Pol-TA-Au catalyst. With the less reactive internal alkyne, excellent yield was achieved at a higher temperature (Scheme 27A). Monitoring the reaction revealed that methanol was a non-innocent solvent in this reaction, which formed the vinyl ether intermediate through nucleophilic addition to the alkyne and help to accelerate the hydration. Propargyl acetates also gave good yields (Scheme 27B). For the internal propargyl alcohol (Scheme 27C) and acetate (Scheme 27D), the corresponding enones were produced with excellent yields.

**Scheme 28. Chemoselectivity of Pol-TA-Au**
Other than increased thermal stability, this Pol-TA-Au catalyst also presented good chemoselectivity in the 3,3-rearrangement of propargyl esters (Scheme 28). Similar to the homogeneous TA-Au catalyst, only allene was observed as the product with the Pol-TA-Au catalyst in a dry solvent.

Despite the excellent reactivity for hydration reactions, this Pol-TA-Au catalyst showed much lower reactivity for other gold-catalyzed nucleophilic addition to alkyne with weaker nucleophiles such as sulfinic acid, and 1,3-diketone. It is worth noting that the homogeneous TA-Au analogue gave lower yields or even no desired product for these reactions.

4.2.2 Combining Lewis acid with Pol-TA-Au

Our group reported that the addition of a Lewis acid could increase the reactivity of TA-Au catalysts. By coordination with the Lewis acid, triazole ligand became easier to dissociate from cationic gold, making the gold catalyst more reactive for alkyne activation through the associative ligand exchange. With this strategy, several challenging reactions were achieved with different TA-Au-catalysts. To test whether the Lewis acid strategy is effective for Pol-TA-Au catalyst, hydroamination reaction of alkynes was investigated.

Scheme 29. Hydroamination of alkyne with Pol-TA-Au

As shown in Scheme 29, the addition of either a Brønsted acid or a Lewis acid enhanced the catalyst’s performance. With 2 mol% Lewis acid Ga(OTf)₃, the desired imine product was observed in 82% yield with only 1 mol% gold catalyst loading. Other Lewis acids could also help to increase the reactivity of gold catalyst but gave lower yields.

Combining Lewis acids with gold catalysis, Nakamura reaction and vinyl sulfone formation have been developed by our group using either XPhosAu(TA)OTf or BrettPhosAu(TA)OTf as the catalyst precursor (Scheme 30).
The steric hindered XPhos or BrettPhos ligands could help increase the stability of the catalytically active gold catalyst enabling the execution of several challenging reactions.

**Scheme 30. Examples for Pol-TA-Au catalyzed challenging reactions**

Additionally, the reactions outlined above (Scheme 30) were also successfully achieved with the heterogeneous Pol-TA-Au catalyst. As a comparison, the homogeneous Ph₃PAu(TA)OTf does not catalyze the C-S bond formation and gives a much lower yield for Nakamura reaction. Another heterogeneous catalyst prepared from polystyrene resin supported PPh₃ failed to give the desired products.

Compared with expensive XPhos or BrettPhos ligands, the POL-PPh₃ ligand is much cheaper and easily accessible. Meanwhile, Pol-TA-Au could be efficiently recycled by centrifuge and applied to the next cycle without any loss of reactivity.

**4. 3 Conclusion**

In summary, we synthesized and developed a heterogeneous triazole-gold catalyst using a porous polymer as the support. This Pol-TA-Au catalyst showed increased thermal stability and good chemoselectivity compared with the
homogeneous TA-Au catalyst. More importantly, this heterogeneous catalyst was successfully applied to challenging transformations that were previously achieved with expensive phosphine ligands, which further highlighted the potential application of Pol-TA-Au in large-scale synthesis and flow reactions. At this time, further studies need to be performed to answer several important structural and functional aspects of this newly designed system.

4. 4 Contribution

Rong Cai developed this heterogeneous gold catalyst and investigated its reactivity. Dr. Qi Sun helped with polymer preparation and preformed characterization of the polymers. Ying He helped with substrate preparation.

The manuscript of this project is in preparation.

References:


Chapter 5. N-2-Aryl-1,2,3-Triazole as Ligands for Iridium Photocatalysts

5.1 Introduction

5.1.1 Visible light photoredox catalysis

As early as the 19th century, Dr. Ciamician proposed a pioneer idea about photochemistry.\(^{91}\) He envisioned the future of artificial photosynthesis as a green and renewable process in chemical industry, by which the solar energy could be converted to chemical energy. One challenge for the application of sunlight in photochemical reactions in organic synthesis is that most of the organic molecules have poor absorption of visible light. Usually, the high-energy ultraviolet light, which is not abundant in solar light, is required for organic synthesis using photochemistry.\(^{92}\) Although visible-light photochemistry is limited for organic molecules, many organometallic compounds have strong absorption in the visible light region, such as \(\text{Ru(bpy)}_3^{2+}\) and \([\text{Ir(ppy)}_2(\text{bpy})]\)^+. While being stable in the ground state, these complexes could be easily activated by visible light to the photoexcited state, which could provide electrochemical potential to facilitate redox reactions.\(^{93}\)

Using \(\text{Ru(bpy)}_3^{2+}\) as an example, upon irradiation with visible light, one electron from a metal \(t_{2g}\) orbital is excited to the \(\pi^*\) orbital of the ligand through a metal to ligand charge transfer (MLCT) and rapid intersystem crossing (Scheme 31).\(^{94}\) The resulted triplet excited state has a relatively long lifetime because that the decay to the singlet ground state is spin-forbidden. This photoexcited state is both a much better oxidant and better reductant compared with the ground state based on the reduction potentials. For example, the reduction potential of the excited state \(E_{1/2}^{\text{III/II}} = -0.81\) V vs SCE, which suggested that the excited-state *\(\text{Ru(bpy)}_3^{2+}\) is easier to be oxidized (tend to donate electrons) compared with the ground-state \(\text{Ru(bpy)}_3^{2+}\) \((E_{1/2}^{\text{III/II}} = +1.29\) V vs SCE). Similarly, the reduction
potential $E_{1/2}^{\text{II/II}} = +0.77$ V, which suggested that $^*\text{Ru(bpy)}_3^{2+}$ is easier to be reduced than $\text{Ru(bpy)}_3^{2+}$ ($E_{1/2}^{\text{II/II}} = -1.33$ V vs SCE). This could also be rationalized from the molecular orbital diagram. In the triplet excited state, the high-energy electron in the $\pi^*$ orbital is much easier to lose, while the low-energy vacant in the $t_{2g}$ orbital is much easier to accept an electron.

Scheme 31. The photochemistry of $\text{Ru(bpy)}_3^{2+}$

Based on the unique “dual” property of the photoexcited state, $\text{Ru(II)}^*$ can undergo either an oxidative quenching by losing one electron to an electron acceptor, or an reductive quenching by accepting one electron from an electron donor. The resulting $\text{Ru(III)}$ from oxidative quenching serves as a strong oxidant ($E_{1/2}^{\text{III/II}} = +1.29$ V vs SCE), while $\text{Ru(II)}$ from reductive quenching serves as a strong reductant ($E_{1/2}^{\text{II/II}} = -1.33$ V vs SCE).

The first application of photoredox catalysis in organic synthesis is a $\text{Ru(bpy)}_3\text{Cl}_2$ catalyzed Pschorr reaction reported in 1984 for the synthesis of phenanthrene from diazonium salt. Very few examples have been reported since then. It was not until the year 2008 that visible-light photoredox catalysis started to catch attention from chemists and be explosively explored.

In 2008, Yoon and coworkers reported a visible-light photocatalyzed [2+2] cycloaddition reaction using $\text{Ru(bpy)}_3\text{Cl}_2$ as the catalyst (Scheme 32A). This reaction proceeded through a reductive quenching mechanism by using DIPEA.
to reduce the photoexcited Ru(II)*. The resulting Ru(I) could reduce enone to a radical anion, which then induced the cyclization. The same group later developed an oxidative quenching condition for electron-rich substrates using methyl viologen as the oxidative quencher.

Scheme 32. Selected example of photoredox catalysis

A) [2+2] cycloaddition

\[
\begin{align*}
\text{Ph} & \text{O} \\
\text{H} & \text{O} \\
\text{Ph} & \text{O}
\end{align*}
\]

\[
\begin{align*}
\text{Ph} & \text{O} \\
\text{H} & \text{O} \\
\text{Ph} & \text{O}
\end{align*}
\]

5 mol% Ru(bpy)₃Cl₂, 2 eq. i-Pr₂NEt, 2 eq. LiBF₄, ACN, visible light

89% yield, > 10:1 d.r.

Yoon, 2008

B) Enantioselective α-alkylation of aldehydes

\[
\begin{align*}
\text{R} & \text{O} \\
\text{Br} & \text{O}
\end{align*}
\]

Ru(bpy)₃Cl₂ (0.5 mol%), visible light, DMF, 2,6-lutidine

organocatalyst (20 mol%)

\[
\begin{align*}
\text{R} & \text{O} \\
\text{Br} & \text{O}
\end{align*}
\]

organocatalyst

Stephenson, 2010

C) Aza-Henry reaction

\[
\begin{align*}
\text{N} & \text{Ph} \\
\text{N} & \text{Ph}
\end{align*}
\]

1% Ir(ppy)₂(dtbbpy)PF₆, MeNO₂, hv, rt

\[
\begin{align*}
\text{N} & \text{Ph} \\
\text{N} & \text{Ph}
\end{align*}
\]

Stephenson, 2010

In the same year, MacMillan and his coworkers reported an enantioselective α-alkylation reaction of aldehyde through the combination of photoredox catalysis and organocatalysis (Scheme 32B). In this case, the enamine intermediate could serve as a reductive quencher to initiate the photocatalytic cycle.

Another pioneer example in visible light photoredox catalysis is an oxidative aza-Henry reaction developed by Stephenson in 2010. An iminium cation was generated from tetrahydroisoquinoline by reductive quenching of the photocatalyst followed by single electron oxidation. A sequential nucleophilic addition to the iminium cation yielded the product. Later on, other groups extensively studied the aza-Henry reactions employing various nucleophiles such as vinyl ether, phosphonate, acetone, alkynes etc.

One big challenge in order to operate a photoredox catalytic cycle is to find a suitable photocatalyst, for which the redox potential could match with the substrates. As we know, the redox potential of transition metal photocatalysts is
highly dependent on the ligands. Using a more electron-deficient ligand could effectively increase the reduction potential \( E_{1/2}(M^+/M) \), making \( M^+ \) a stronger oxidant, which could be applied into more challenging substrates that are more reluctant towards oxidation. At the same time, the reduction potential \( E_{1/2}(M^*/M^-) \) could also be increased, making \( M^+ \) a better oxidant as well. For instance, when 2,2'-bipyrazine (bpz) is used as the ligand for Ru(II) instead of bpy ligand, the \( E_{1/2}(M^*/M^-) \) is increased (+1.45 V compared with +0.77 V for Ru(bpy)_3), making Ru(II)* a much better oxidant that is sufficient to oxidize the dienophile (+1.1 V) in this [4+2] cycloaddition reaction (Scheme 33).^103

**Scheme 33. The ligand effect in photocatalysis**

The rapid development of visible light photocatalysis led to a strong need for new catalysts with potentially new reactivity, especially with controllable photoredox potentials.

### 5.1.2 Iridium photocatalysts utilizing triazole ligands

Cationic Ir(III) polyimine complexes have been widely applied in various areas,^104 including live cell imaging,^105 electroluminescent materials,^106 and water oxidation.^107 Recently, \([\text{Ir}(ppy)_2(bpy)]^+\) and \([\text{Ir}(ppy)_2(dtbbpy)]^+\) have gained tremendous attention as efficient photocatalysts in promoting organic transformations.\(^108\) Instead of the 2-phenylpyridine (ppy) ligand, a more electron-deficient ligand dF(CF_3)ppy (3,5-difluoro-2-[5-(trifluoromethyl)-2-pyridinyl] phenyl) is more widely applied because of the stronger redox potential of the excited state \( E_{1/2}^{III/II} = +1.21 \text{ V} \) for \([\text{Ir}(dF(CF_3)ppy)_2(dtbbpy)]^+\) (dtbbpy = 4,4'-bis(tert-butyl)-2,2'-bipyridine) compared with the ppy complex \([\text{Ir}(ppy)_2(dtbbpy)]^+\) \( (E_{1/2}^{III/II} = +0.66 \text{ V})\).
After the discovery of “click chemistry”, 1,2,3-triazole (TA) became one of the most important heterocycles in chemical research. During the past several years, our group has been working on developing new synthetic methods toward triazole functionalization while investigating the coordination ability of various triazole derivatives. Inspired by recent success on Ir(III)-promoted photocatalysis, we became interested in studying triazole, an electron-deficient ligand, for the binding ability with Ir(III) and hope to develop a new class of photoactive complexes with the potential to further extend the reaction scope of photocatalysis.

In 2009, Schubert and co-workers reported the first triazole coordinated Ir(III) complexes using N1-substituted 1,2,3-triazole as the C^N ligand (bis-chelating C^N ligand). Later, De Cola and co-workers reported the electroluminescent properties of similar Ir(III) complexes (Scheme 34A). Although these and other pioneering work revealed good coordination ability of TA ligands with Ir(III), no photocatalytic reactivity has been reported. More importantly, as mentioned by Schubert, only C-aryl-TA chelated Ir(III) complexes could be produced. The attempts to form N-aryl-TA chelating complexes were unsuccessful due to either poor complex stability or the formation of unidentified byproducts.

Scheme 34. C-Aryl-Ir(III) complex with 1,2,3-triazole ligands

(A) C-Aryl TA-Ir complexes reported by Schubert

(B) Strong substituent influence at N-aryl position revealed from fluorescence emission
Among various triazole derivatives, one particularly interesting compound is the fluorescence active N-2-aryl triazoles (NATs). As revealed by the crystal structures, the N-2-aryl group holds a perfect co-planar conformation with the triazole ring, resulting in a strong fluorescence emission, whereas the N-1-isomer exhibits no emission.\textsuperscript{113} Moreover, substitution on the N-2-aryl group exhibited strong influence on fluorescence emission wavelengths (Scheme 34B).

Based on these results, we postulated that NAT may be used as the C^N ligand to prepare novel N-aryl-chelated Ir(III) complexes, by providing specific coordination sites as well as easily tunable functional groups (Scheme 35).\textsuperscript{114} At the same time, N-pyridine-triazole (tapy) could serve as the N^N ligand to further diversify the proposed Ir(III) complexes.

Scheme 35. Proposed new N-Aryl-Ir(III) complexes

5. 2 NAT-based iridium complexes as photocatalysts

To test our hypothesis, NATs were prepared and used for Ir(III) complex formation. The general synthetic route is summarized in Scheme 36.\textsuperscript{115}
As expected, treating NAT 30 with IrCl₃·xH₂O gave the corresponding chloro-bridged iridium(III) dimer 31 in excellent yields (generally > 80%). Subsequent reaction with bpy ligand gave the corresponding NAT-Ir(III) complex (C-1). Notably, unlike N-1-aryl triazoles, the N-2-aryl triazoles indicated strong coordination ability, forming stable Ir(III) complexes, which could be purified by column chromatography without decomposition. With this synthetic method, various TA-Ir complexes were prepared. Good to excellent yields were obtained in most cases, which warranted further applications of N-2-aryl triazoles as the C^N ligand for iridium photocatalysts.

Similar to Ru(bpy)₃²⁺, the general mechanism of photocatalysis with iridium is initiated from the promotion of Ir(III) to excited-state Ir(III)* by visible light, followed by oxidative or reductive quenching through single-electron transfer. The resulting Ir(IV) or Ir(II) will be reduced or oxidized to regenerate the ground state Ir(III). The redox potential for each step is crucial for an operable catalytic cycle. Compared to ppy ligand, N-phenyl-triazole (pta) is more electron-deficient. Thus, higher oxidation potentials of the corresponding iridium complexes are expected. To evaluate the photophysical properties of these new TA-Ir complexes, UV-Vis absorption and fluorescence emission were tested. Compared with Ir[(ppy)₂(bpy)]PF₆, the TA-Ir cationic complexes [Ir(pta)₂(bpy)]PF₆ indicated better absorption of blue light and stronger fluorescence emission in the visible light region (Figure 17).

Figure 17. UV-Vis and fluorescence comparison of TA-Ir
The fluorescence spectra of TA-Ir complexes with different substituents are compared (Figure 18). Introducing an EWG at the R¹ position showed a blue shift while EDG showed a red shift. Variation at the R² position did not have much influence on the emission wavelength.

Figure 18. Fluorescence comparison of different substituened TA-Ir

![Fluorescence comparison of different substituened TA-Ir](image)

Other than photophysical properties, the redox potential of these iridium complexes are measured with cyclic voltammetry. The results are summarized in Table 21.

Table 21. Redox potential of selected iridium complexes a, b

<table>
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<tr>
<th></th>
<th>R¹</th>
<th>R²</th>
<th>λ_{em} (nm)</th>
<th>Φ</th>
<th>Φ² (ns)</th>
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<td>558</td>
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<td>18</td>
<td>+1.25</td>
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a S1 = [Ir((ppy)₂(bpy))PF₆]; All potentials are given vs saturated calomel electrode (SCE). Measurements were performed at room temperature in acetonitrile using an internal standard Fc/Fc⁻ redox couple (0.40V vs. SCE); b PF₆⁻ is the counter anion; c The quantum yields were calculated relative to Ru(bpy)₃(PF₆)_2 (Φ=0.062 in ACN); d Excited-state lifetime.
The data in Table 21 revealed a clear substituent effect on the Ir\(^{4+/3+}\) reduction potential. First, with more electron-deficient pta ligand, C-1a gave higher reduction potential E\(_{1/2}(\text{Ir}^{4+/3+}) = +1.54\) V (vs SCE) than [Ir(ppy)\(_2\)(bpy)]PF\(_6\) (S1, +1.28 V). The introduction of electron withdrawing groups (such as F, C-1b) at R\(^1\) position (N-2 aryl) further increased the E\(_{1/2}(\text{Ir}^{4+/3+})\) to +1.67 V. In contrast, complex C-1c (with electron-donating OMe) gave lower E\(_{1/2}(\text{Ir}^{4+/3+})\) (+1.37 V), which was still higher than ppy complex S1. A similar trend was also observed in the reduction potential E\(_{1/2}(\text{Ir}^{3+/2+})\), though with a smaller variation. Substitution at R\(^2\) position indicated little influence to the redox potential (eg. C-1b, +1.67 V vs C-1d, +1.66 V), suggesting that the electronic effect influence from the ring that is directly touching the metal center is much more important. Similarly, introducing EWG at R\(^1\) position (C-1b) helped to increase the excited-state lifetime and quantum yield while introducing EDG (C-1c) impaired the excited-state lifetime and quantum yield.

The reduction potential E\(_{1/2}(\text{Ir}^{3+/2+})\) of all tested C-1 TA-Ir complexes were almost the same even with different C\(^^\text{N}\) ligands. To fully elucidate the ligand effect on redox potential, we prepared triazole-pyridine (tapy)\(^{116}\) as a new type of N\(^^\text{N}\) ligands to coordinate with Ir cations. The reaction between the chloro-bridged iridium dimer 2a and N-2-tapy gave messy mixtures with no desired complex isolated. Interestingly, a much cleaner reaction was obtained with N-1-tapy. Although growing a single crystal is unsuccessful at this moment, the TA-Ir complexes with N-1-tapy as an N\(^^\text{N}\) ligand have been successfully prepared and characterized by \(^1\text{H}, \(^{13}\text{C}, \(^{19}\text{F NMR and HRMS. The fluorescence emission and redox potentials of these complexes were then determined as shown in Table 22.}\)

Interestingly, compared to complex S1 (with ppy N\(^^\text{N}\) ligand), complex C-2 (with tapy N\(^^\text{N}\) ligand) resulted in a clear change of E\(_{1/2}(\text{Ir}^{3+/2+})\) reduction potential, from -1.38 V to -1.48 V, similar to complex S2 (with dtbbpy N\(^^\text{N}\) ligand). Notably, the E\(_{1/2}(\text{Ir}^{3+/2+})\) reduction potential remained almost the same when changing the C\(^^\text{N}\) ligand to pta. These [Ir(pta)\(_2\)(tapy)]\(^+\) complexes are even stronger oxidants compared with [Ir(pta)\(_2\)(bpy)]\(^+\). These results highlighted the excellent viability of these new triazole based Ir photocatalysts: using pta as the C\(^^\text{N}\) ligand to adjust
the Ir$^{4+/3+}$ oxidation potential while using tapy as the N^N ligand to tune the Ir$^{3+/2+}$ reduction potential.

Table 22. Redox potential of selected iridium complexes with tapy ligand $^a, b$

<table>
<thead>
<tr>
<th></th>
<th>R$^1$</th>
<th>$\lambda_{em}$ (nm)</th>
<th>$\Phi^c$</th>
<th>$\tau^d$ (ns)</th>
<th>$E_{1/2}$ (V)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(Ir$^{4+/3+}$)</td>
</tr>
<tr>
<td>S1</td>
<td>-</td>
<td>566</td>
<td></td>
<td></td>
<td>+1.28</td>
</tr>
<tr>
<td>S2</td>
<td>-</td>
<td>560</td>
<td>0.20</td>
<td>175</td>
<td>+1.25</td>
</tr>
<tr>
<td>C-2</td>
<td>-</td>
<td>546</td>
<td>0.12</td>
<td>110</td>
<td>+1.37</td>
</tr>
<tr>
<td>C-3a</td>
<td>H</td>
<td>462, 486</td>
<td>0.06</td>
<td>217</td>
<td>+1.61</td>
</tr>
<tr>
<td>C-3b</td>
<td>F</td>
<td>458, 482</td>
<td>0.07</td>
<td>375</td>
<td>+1.75</td>
</tr>
<tr>
<td>C-3c</td>
<td>OMe</td>
<td>508</td>
<td>0.01</td>
<td>108</td>
<td>+1.37</td>
</tr>
</tbody>
</table>

$^a$ S1 = [Ir[(ppy)$_2$(bpy)]PF$_6$; S2 = [Ir[(ppy)$_2$(dtbbpy)]PF$_6$; $^b, c, d$ Same conditions as Table 21 applied.

Two typical photocatalytic reactions$^{117}$ were performed to prove the feasibility of these new TA-Ir complexes. Although the reactions are slower, good yields were obtained as shown in Scheme 37.

Scheme 37. TA-Ir as effective photocatalysts
5. 3 Conclusion

In summary, we synthesized and characterized N-2-aryl-1,2,3-triazole-Ir(III) complexes (TA-Ir). A series of complexes with different substituents have been prepared and their photophysical properties were evaluated. With the electron-deficient triazole ligands, TA-Ir complexes are stronger oxidants compared with the commonly used [Ir(pta)₂(bpy)]⁺. Tunable redox potentials were achieved through varying substituents on either the pta C^N ligand or the tapy N^N ligand, which indicated promising future of these new photocatalysts. Other functional groups could be installed to further modify these types of complexes to improve their photophysical and photocatalytic properties.

5. 4 Contribution

Rong Cai developed, characterized these cationic TA-Ir complexes and applied them in photocatalysis. Dr. Wuming Yan initiated this project and developed part of the synthetic methods. Matthew G. Bologna helped with ligand preparation. Kaushalya de Silva and Dr. Harry O. Finklea helped with cyclic voltammetry measurements. Zhao Ma helped with manuscript preparation. Dr. Jeffrey L. Petersen performed the X-ray structural analyses.

This project is published on Org. Chem. Front. 2015, 2, 141-144.

References:

91 Ciamician, G. Science 1912, 36, 385.


Appendix

Publications during Ph.D. research at West Virginia University:


Experimental Details

Application of 1, 2, 3-Triazole in Gold Catalysis and Photoredox Catalysis

Rong Cai
# TABLE OF CONTENT

Chapter S1. Gold-Catalyzed Synthesis of Triazapentalene Zwitterions .......................... S1
  S1.1 General Methods and materials .............................................................................. S1
  S1.2 Compounds Characterization ................................................................................. S2
  S1.3 ORTEP Drawing of the Crystal Structures ............................................................. S10
  S1.4 Stability test ........................................................................................................... S14
  S1.5 UV-Vis Spectra and Fluorescence Spectra ............................................................... S16

Chapter S2. “Silver Effect” in Gold(I) Catalysis ............................................................... S30
  S2.1 General Methods and materials .............................................................................. S30
  S2.2 Compounds Characterization ................................................................................. S31
  S2.3 ORTEP Drawing of the Crystal Structures for IPr-TA-Au .................................. S35
  S2.4 $^{31}$P NMR comparison between different gold catalyst ........................................ S35
  S2.5 HPLC data for chirality retention .......................................................................... S36

Chapter S3. Gold-Catalyzed Cross-Coupling with Aryldiazonium Salts ....................... S39
  S3.1 General Methods and materials .............................................................................. S39
  S3.2 General procedures ............................................................................................... S39
  S3.3 Mechanistic studies .............................................................................................. S43
  S3.4 Compounds characterization ................................................................................ S57

Chapter S4. Porous Polymer-Supported Heterogeneous Gold(I) Catalysis .................. S78
  S4.1 General Methods and materials .............................................................................. S78
  S4.2 XPS analysis .......................................................................................................... S80
  S4.3 Compounds Characterization ................................................................................ S82

Chapter S5. N-2-Aryl-1,2,3-Triazole as ligand for Iridium Photocatalyst ....................... S84
  S5.1 General Methods and materials .............................................................................. S84
  S5.2 Compounds characterization ................................................................................ S87
  S5.3 ORTEP Drawing of the Crystal Structures ............................................................. S93
  S5.4 UV-Vis Spectra and Fluorescence Spectra .............................................................. S95
  S5.5 Cyclic Voltammetry ............................................................................................... S105
  S5.5 Excited-state lifetime ............................................................................................ S111
  NMR Spectra ................................................................................................................ S125
Chapter S1. Gold-Catalyzed Synthesis of Triazapentalene Zwitterions

S1.1 General Methods and Materials

All of the reactions dealing with air and/or moisture-sensitive reactions were carried out under an atmosphere of nitrogen using oven/flame-dried glassware and standard syringe/septa techniques. Unless otherwise noted, all commercial reagents and solvents were obtained from the commercial provider and used without further purification. \(^1\)H NMR and \(^{13}\)C NMR spectra were recorded on Varian 600 MHz or Agilent 400 MHz spectrometer. Chemical shifts were reported relative to internal tetramethylsilane (δ 0.00 ppm) or CDCl\(_3\) (δ 7.26 ppm) for \(^1\)H NMR and CDCl\(_3\) (δ 77.0 ppm) for \(^{13}\)C NMR. Flash column chromatography was performed on 230-430 mesh silica gel. Analytical thin layer chromatography was performed with precoated glass baked plates (250µ) and visualized by fluorescence and by charring after treatment with potassium permanganate stain. HRMS were recorded on LTQ-FUHRA spectrometer.

The UV-Vis spectra were obtained with a Shimadzu UV-1800 UV spectrophotometer in 10 mm path length quartz cuvettes with 1×10\(^{-6}\)M TAPZ solutions in freshly distilled methylene chloride (DCM). The fluorescence spectra were obtained in 10 mm path length quartz cuvettes using Shimadzu RF-5301 PC spectrofluorophotometer with 1×10\(^{-5}\)M (for 5m-5t) or 1×10\(^{-6}\)M (for 6a-6g) TAPZ solutions in DCM.

The fluorescence quantum yields of TAPZs (\(\Phi_x\)) were calculated based on equation (1) using quinine sulfate in 0.1N H\(_2\)SO\(_4\) solution (\(\Phi = 0.55\))\(^{[1]}\) as a standard. The absorption of TAPZs and standard was less than 0.05 (1×10\(^{-6}\)M solution).

\[
\Phi_x = \frac{n_x^2}{n_{std}^2} \cdot \frac{1 - 10^{-Abs_{x}}}{1 - 10^{-Abs_{std}}} \cdot \frac{I_x}{I_{std}} \cdot \Phi_{std}
\]

\(\Phi\) is the quantum yield, \(I\) is integrated emission intensity, \(Abs\) is the absorption at the excitation wavelength, and \(n\) is the refractive index of pure solvents (\(n_x=1.424, n_{std}=1.333\)); ‘std’ stands for reference standard samples, ‘x’ stands for samples.

All the cells were grown in BioNano Research Facility in West Virginia University. The HEK 293t cells were cultured in complete medium (Dulbecco’s modified Eagle’s Medium, supplemented with 10% fetal bovine serum (FBS), 1% penicillin-streptomycin) at 37 °C in atmosphere containing 5% CO\(_2\). The A549 cells were cultured in complete medium (Kaighn’s Modification of Ham’s F-12 Medium, supplemented with 10% fetal bovine serum (FBS), 1% penicillin-streptomycin) at 37 °C in atmosphere containing 5% CO\(_2\). The cell images were taken with a Leica DMI6000 B Inverted Fluorescent Microscope.

For microscopic observation, HEK-293t cells or A549 cells were seeded onto coverslips in 6-well plates at 1×10\(^5\)cells/well (4 mL cell suspensions per well), and allowed to attach overnight at 37°C in atmosphere containing 5% CO\(_2\). Cells were then treated with 10µM TAPZ in 1% DMSO/media for 30 min. After TAPZ solutions were aspirated, the cells were washed with PBS for three times. Then the cells were incubated with 1.5 mL/well

---

3.7% paraformaldehyde for another 10 min. After washing the cells with PBS three times, the coverslips were placed on glass microscope slides with 20µL Prolong® Gold Antifade reagent. The slides were left in a 4°C refrigerator overnight and observed under a Leica DMI6000 B Inverted Fluorescent Microscope. Cells incubated with 5s were examined under fluorescent microscope at 365nm excitation wavelength while cells incubated with 6a were excited at 470nm.

Substrates 4 were synthesized according to the literature as below:

Representative procedure for the preparation of triazapentalene

\[
\begin{align*}
\text{O} & \quad \text{PPh}_3\text{AuCl} / \text{AgSbF}_6 \\
\text{DCE, 60°C} & \quad 0.5\% \text{PPh}_3\text{AuCl}/\text{AgSbF}_6 \\
\text{4a} & \quad \text{5a}
\end{align*}
\]

To a solution of PPh$_3$AuCl (1.24 mg, 0.0025 mol) in DCE (1 mL), AgSbF$_6$ (0.86 mg, 0.0025 mmol) was added at RT. The mixture was stirred for 2 min at RT and added 4a (150 mg, 0.50 mmol) dissolved in another 4 mL DCE. The reaction mixture was stirred at 60°C and monitored by TLC. After the reaction was completed (4 h), the solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (ethyl acetate/hexane = 1 : 5, V/V) to give 5a (96% yield) as a yellow solid. The product was further purified by recrystallization from ethanol.

Procedure for the preparation of triazapentalene 6 from 5m:

\[
\begin{align*}
\text{O} & \quad \text{LiOH (1 M aq), 60°C} \\
\text{THF:MeOH = 1:1} & \quad \text{6 h} \\
\text{5m} & \quad \text{7m}
\end{align*}
\]

To a solution of 5m (222 mg, 0.87 mmol) in THF:MeOH (10 mL:10 mL), 10 mL 1M LiOH (aq.) was added. The reaction mixture was stirred at 70°C for 8 h. After the reaction was completed, the solution was extracted with methylene chloride for four times. The combined organic layer was dried over anhydrous MgSO$_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (pre-washed with triethylamine, ethyl acetate/hexane = 1 : 10, V/V) to give 6 (76% yield) as a yellow solid.

S1.2 Compounds Characterization
5a: $^1$H NMR (600 MHz, CDCl$_3$): δ 7.62 (d, $J = 2.4$ Hz, 1H), 7.46-7.48 (m, 2H), 7.11-7.19 (m, 4H), 7.02-7.05 (m, 4H), 6.47-6.48 (m, 1H), 2.79 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): δ 179.7, 154.8, 139.0, 131.1, 130.9, 129.7, 129.4, 128.5, 127.6, 127.5, 122.7, 113.6, 109.6, 108.2, 14.1; HRMS Calculated for [C$_{19}$H$_{15}$N$_3$O+Na]$^+$: 324.1113, Found: 324.1121.

5b: $^1$H NMR (600 MHz, CDCl$_3$): δ 7.64 (d, $J = 2.1$ Hz, 1H), 7.46-7.48 (m, 2H), 7.10-7.19 (m, 4H), 7.01-7.05 (m, 4H), 6.51 (d, $J = 3.0$ Hz, 1H), 3.29 (t, $J = 7.5$ Hz, 2H), 1.66 (quin, $J = 7.7$ Hz, 2H), 1.37 (sex, $J = 7.4$ Hz, 2H), 0.91 (t, $J = 7.5$ Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): δ 179.6, 154.9, 139.1, 131.1, 130.9, 129.6, 129.3, 128.4, 127.5, 127.4, 127.3, 113.7, 108.4, 108.2, 30.5, 27.1, 22.0, 13.9; HRMS Calculated for [C$_{22}$H$_{21}$N$_3$O+H]$^+$: 344.1763, Found: 344.1764.

5c: $^1$H NMR (600 MHz, CDCl$_3$): δ 7.64 (m, 1H), 7.47 (d, $J = 8.4$ Hz, 2H), 7.15-7.19 (m, 3H), 7.10-7.13 (t, $J = 7.2$ Hz, 1H), 7.01-7.04 (t, $J = 7.8$ Hz, 4H), 6.51 (m, 1H), 3.28 (t, $J = 7.8$ Hz, 2H), 1.62 (quin, $J = 7.5$ Hz, 2H), 1.26-1.39 (m, 4H), 0.85 (t, $J = 6.9$ Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): δ 179.6, 154.8, 139.1, 131.0, 130.8, 129.6, 129.3, 128.4, 127.5, 127.4, 127.3, 113.7, 108.3, 108.2, 31.0, 28.0, 27.3, 22.4, 13.9; HRMS Calculated for [C$_{23}$H$_{23}$N$_3$O+H]$^+$: 358.1919, Found: 358.1912.

5d: $^1$H NMR (600 MHz, CDCl$_3$): δ 8.44 (d, $J = 3.0$ Hz, 1H), 7.70 (d, $J = 3.0$ Hz, 1H), 7.32-7.34 (m, 2H), 7.19-7.23 (m, 4H), 7.09 (t, $J = 7.2$ Hz, 2H), 7.04 (t, $J = 7.2$ Hz, 2H), 6.81 (d, $J = 3.0$ Hz, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$): δ 180.8, 153.8, 138.5, 130.4, 129.7, 128.9, 128.6, 127.8, 127.5, 113.0, 111.9, 111.8, 109.0, 108.2, 108.1; HRMS Calculated for [C$_{18}$H$_{13}$N$_3$O+H]$^+$: 288.1137, Found: 288.1125.
5e: $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 8.18 (d, $J = 8.4$ Hz, 2H), 7.49 (d, $J = 7.2$ Hz, 2H), 7.46 (t, $J = 7.2$ Hz, 2H), 7.31 (t, $J = 7.5$ Hz, 1H), 7.23 (d, $J = 6.6$ Hz, 2H), 7.18 (t, $J = 7.5$ Hz, 1H), 7.13 (t, $J = 7.5$ Hz, 1H), 7.05 (q, $J = 8.4$ Hz, 4H), 6.83 (s, 1H), 3.30 (t, $J = 7.8$ Hz, 2H), 1.65 (quin, $J = 7.6$ Hz, 2H), 1.43 (sex, $J = 7.6$ Hz, 2H), 0.93 (t, $J = 7.5$ Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 179.7, 154.5, 139.2, 131.2, 130.9, 129.9, 129.4, 128.8, 128.5, 127.7, 127.6, 127.5, 127.47, 127.46, 125.2, 121.6, 113.5, 105.7, 30.3, 27.1, 22.0, 13.9; HRMS Calculated for [C$_{28}$H$_{25}$N$_3$O$^+$H]: 420.2076, Found: 420.2081.

5f: $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 8.16-8.19 (m, 2H), 7.50 (d, $J = 7.8$ Hz, 2H), 7.13-7.23 (m, 6H), 7.03-7.08 (m, 4H), 6.78 (s, 1H), 3.30 (t, $J = 7.8$ Hz, 2H), 1.64 (quin, $J = 7.6$ Hz, 2H), 1.44 (sex, $J = 7.6$ Hz, 2H), 0.93 (t, $J = 7.5$ Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 179.7, 162.1 (d, $J = 247.1$ Hz), 154.6, 139.1, 131.1 (d, $J = 24.6$ Hz), 129.9, 129.4, 127.6, 127.5, 127.4, 127.1 (d, $J = 7.7$ Hz), 123.9, 120.7, 116.0, 115.8, 113.5, 105.5, 30.4, 27.1, 22.1, 13.9; HRMS Calculated for [C$_{28}$H$_{24}$FN$_3$O$^+$H]: 438.1982, Found: 438.1997.

5g: $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 8.12 (d, $J = 9.0$ Hz, 2H), 7.48 (d, $J = 8.4$ Hz, 2H), 7.22 (d, $J = 7.2$ Hz, 2H), 7.17 (t, $J = 7.5$ Hz, 1H), 7.13 (d, $J = 7.5$ Hz, 1H), 6.99-7.06 (m, 6H), 6.74 (s, 1H), 3.84 (s, 3H), 3.30 (t, $J = 7.5$ Hz, 2H), 1.64 (quin, $J = 7.6$ Hz, 2H), 1.43 (sex, $J = 7.6$ Hz, 2H), 0.92 (t, $J = 7.5$ Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 179.4, 159.3, 154.7, 139.4, 131.4, 130.8, 129.9, 129.4, 128.4, 127.6, 127.5, 127.4, 126.9, 121.9, 120.4, 114.3, 113.5, 105.0, 55.3, 30.4, 27.1, 22.1, 13.9; HRMS Calculated for [C$_{29}$H$_{27}$N$_3$O$_2$+H]: 450.2182, Found: 450.2173.

5h: $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.59 (d, $J = 3.0$ Hz, 1H), 7.47 (d, $J = 7.8$ Hz, 2H), 7.19 (t, $J = 7.5$ Hz, 1H), 7.02-7.04 (m, 4H), 6.83 (d, $J = 7.8$ Hz, 2H), 6.45 (d, $J = 2.4$ Hz, 1H), 2.77 (s, 3H), 2.21 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 179.6, 154.7, 139.0, 138.3, 130.7, 129.4, 129.3, 128.2, 128.0, 127.3, 122.5, 113.4, 109.4, 108.1, 21.1, 14.1; HRMS Calculated for [C$_{20}$H$_{17}$N$_3$O$^+$Na]: 338.1269, Found: 338.1272.
5i: $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.61-7.62 (m, 1H), 7.48 (d, $J$ = 7.2 Hz, 2H), 7.20 (t, $J$ = 7.2 Hz, 1H), 7.08-7.16 (m, 2H), 7.02 (t, $J$ = 7.8 Hz, 2H), 6.91 (t, $J$ = 7.5 Hz, 1H), 6.66 (t, $J$ = 8.7 Hz, 1H), 6.46 (s, 1H), 2.79 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 179.6, 158.5 (d, $J$ = 247.7 Hz), 148.6, 138.5, 131.1, 130.8 (d, $J$ = 8.3 Hz), 130.6, 128.8, 126.9, 123.3 (d, $J$ = 3.2 Hz), 122.5, 119.5 (d, $J$ = 14.7 Hz), 114.9 (d, $J$ = 21.3 Hz), 113.9, 109.4 (d, $J$ = 7.2 Hz), 108.4, 13.8; HRMS Calculated for [C$_{19}$H$_{14}$FN$_3$O+H]$^+$: 320.1199, Found: 320.1206.

5j: $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.61 (d, $J$ = 3.0 Hz, 1H), 7.44-7.46 (m, 2H), 7.24-7.26 (m, 1H), 7.06-7.08 (m, 4H), 7.00-7.02 (m, 2H), 6.47-6.48 (m, 1H), 2.78 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 179.6, 153.5, 138.9, 134.7, 131.2, 130.9, 129.6, 129.4, 127.7, 122.9, 113.5, 109.7, 108.4, 14.1; HRMS Calculated for [C$_{19}$H$_{14}$ClN$_3$O+H]$^+$: 336.0904, Found: 336.0912.

5k: $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.85 (d, $J$ = 7.8 Hz, 1H), 7.63-7.65 (m, 2H), 7.23 (dd, $J$ = 7.8 Hz, 1.2 Hz, 1H), 7.18 (dd, $J$ = 7.8 Hz, 1.2 Hz, 2H), 7.13 (t, $J$ = 7.8 Hz, 1H), 6.85 (t, $J$ = 7.5 Hz, 1H), 6.61 (t, $J$ = 7.8 Hz, 2H), 6.48-6.49 (m, 1H), 2.83 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 180.1, 153.2, 138.6, 132.8, 131.9, 130.3, 129.1, 128.8, 128.4, 128.1, 127.7, 126.4, 126.3, 125.6, 125.1, 124.2, 122.8, 115.1, 109.4, 108.6, 14.0; HRMS Calculated for [C$_{23}$H$_{21}$N$_3$O+H]$^+$: 352.1450, Found: 352.1461.

5l: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.26 (dd, $J$ = 8.0 Hz, 1.2 Hz, 2H), 7.51 (tt, $J$ = 9.2 Hz, 1.6Hz, 4H), 7.35-7.43 (m, 4H), 7.27-7.34 (m, 4H), 7.17-7.23 (m, 2H), 7.17 (s, 1H), 7.03-7.12 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 178.9, 153.8, 138.8, 131.2, 131.0, 130.0, 129.4, 129.3, 128.9, 128.6, 128.2, 128.0, 127.6, 127.5, 127.4, 127.3, 125.4, 124.7, 122.3, 113.5, 107.1; HRMS Calculated for [C$_{30}$H$_{21}$N$_3$O]$^+$: 439.1685, Found: 439.1680.
5m: $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 8.22 (d, $J = 8.4$ Hz, 2H), 7.97-7.99 (m, 2H), 7.48-7.51 (m, 7H), 7.46 (t, $J = 8.4$ Hz, 2H), 7.40 (t, $J = 5.4$ Hz, 1H), 7.34 (t, $J = 7.8$ Hz, 1H), 7.03 (s, 1H), 3.29 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 158.5, 154.6, 130.8, 130.6, 130.3, 129.6, 128.9, 128.0, 127.8, 127.7, 127.6, 127.2, 125.1, 123.9, 121.5, 106.9, 102.4, 50.4; HRMS Calculated for [C$_{25}$H$_{19}$N$_3$O$_2$]$^+$: 393.1477, Found: 393.1475.

5n: $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.70 (m, 2H), 7.54 (d, $J = 3.0$ Hz, 1H), 7.43 (m, 3H), 6.39 (d, $J = 3.0$ Hz, 1H), 3.68 (s, 3H), 2.76 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 159.5, 154.6, 131.2, 129.9, 129.2, 127.7, 121.1, 109.3, 107.2, 102.2, 50.6, 14.0; HRMS Calculated for [C$_{14}$H$_{13}$N$_3$O$_2$]+H$^+$: 256.1086, Found: 256.1092.

7m: $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 8.27 (d, $J = 7.2$ Hz, 2H), 7.94 (d, $J = 7.2$ Hz, 2H), 7.86 (s, 1H), 7.65 (d, $J = 7.2$ Hz, 2H), 7.45-7.51 (m, 6H), 7.38 (t, $J = 7.2$ Hz, 1H), 7.28 (q, $J = 7.8$ Hz, 2H), 7.19 (s, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 148.1, 131.3, 129.8, 129.2, 128.8, 128.7, 128.6, 126.4, 126.2, 126.1, 123.8, 123.8, 117.9, 116.0, 103.4, 94.2; HRMS Calculated for [C$_{23}$H$_{17}$N$_3$]+: 336.1495, Found: 336.1498.

7n: (known compound, See: Namba, K.; Osawa, A.; Ishizaka, S.; Kitamura, N.; Tanino K. J. Am. Chem. Soc. 2011, 133, 11466-11469.) $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.79 (d, $J = 7.8$ Hz, 2H), 7.39-7.43 (m, 3H), 7.34 (t, $J = 7.2$ Hz, 1H), 7.16 (br s, 1H), 6.34 (d, $J = 2.4$ Hz, 1H), 2.42 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 147.7, 131.8, 128.7, 128.2, 125.8, 109.8, 107.3, 102.2, 90.3, 11.2.
5o: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.26 (d, $J = 7.6$ Hz, 2H), 7.50 (t, $J = 8.0$ Hz, 2H), 7.29-7.42 (m, 10H), 7.20 (t, $J = 7.6$ Hz, 1H), 7.16 (s, 1H), 7.11 (t, $J = 7.6$ Hz, 2H), 6.85 (d, $J = 8.4$ Hz, 2H), 2.23 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 179.0, 153.5, 141.8, 136.1, 131.1, 130.0, 129.5, 129.3, 128.9, 128.5, 128.3, 128.1, 127.9, 127.6, 127.5, 127.4, 127.3, 125.3, 124.3, 122.0, 113.3, 107.0, 21.4; HRMS Calculated for [C$_{31}$H$_{23}$N$_3$O]$: 453.1841$, Found: 453.1837.

\[
\begin{array}{c}
\text{Ph} \\
\text{N} \\
\text{N} \\
\text{Ph} \\
\text{Tol} \\
\text{O} \\
\text{Ph}
\end{array}
\]

5p: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.44 (d, $J = 9.2$ Hz, 2H), 8.35 (d, $J = 8.8$ Hz, 2H), 7.43 (d, $J = 8.0$ Hz, 2H), 7.38-7.40 (m, 5H), 7.23-7.36 (m, 3H), 7.27 (s, 1H), 7.19 (t, $J = 7.6$ Hz, 2H), 6.89 (d, $J = 8.0$ Hz, 2H), 2.25 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 179.8, 153.1, 146.1, 142.6, 135.5, 133.6, 130.5, 129.9, 129.6, 128.9, 128.8, 128.6, 128.5, 127.9, 127.6, 127.3, 124.9, 124.5, 124.5, 119.1, 113.6, 108.2, 21.5; HRMS Calculated for [C$_{31}$H$_{22}$N$_4$O$_3$]: 498.1692$, Found: 498.1688.

\[
\begin{array}{c}
\text{Ph} \\
\text{N} \\
\text{N} \\
\text{Ph} \\
\text{Tol} \\
\text{CN}
\end{array}
\]

5q: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.38 (d, $J = 8.8$ Hz, 2H), 7.77 (d, $J = 8.4$ Hz, 2H), 7.43 (d, $J = 8.0$ Hz, 2H), 7.22-7.39 (m, 8H), 7.22 (s, 1H), 7.16 (t, $J = 7.6$ Hz, 2H), 6.89 (d, $J = 7.6$ Hz, 2H), 2.25 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 179.6, 153.2, 142.5, 135.6, 132.7, 131.7, 130.6, 129.9, 129.6, 128.9, 128.8, 128.4, 127.8, 127.6, 127.3, 125.0, 124.4, 119.4, 118.9, 113.5, 110.3, 107.8, 21.5; HRMS Calculated for [C$_{32}$H$_{22}$N$_4$O]: 478.1794$, Found: 478.1790.

\[
\begin{array}{c}
\text{MeO} \\
\text{Ph} \\
\text{N} \\
\text{N} \\
\text{Ph} \\
\text{Ph}
\end{array}
\]

5r: $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 8.23 (dd, $J = 8.4$, 1.2 Hz, 2H), 7.98 (dd, $J = 7.8$, 1.8 Hz, 2H), 7.44-7.52 (m, 9H), 7.27 (s, 1H), 7.39 (tt, $J = 7.2$, 1.2 Hz, 1H), 7.35 (tt, $J = 7.2$, 1.2 Hz, 1H), 7.05 (s, 3H), 3.86 (q, $J = 7.2$ Hz, 2H), 0.73 (d, $J = 7.2$ Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 158.3, 154.7, 130.8, 130.7, 130.4, 129.6, 128.9, 128.0, 127.9, 127.7, 127.7, 126.8, 125.1, 123.7, 121.6, 106.9, 102.7, 59.9, 13.5; HRMS Calculated for [C$_{26}$H$_{21}$N$_3$O$_2$]: 407.1634$, Found: 407.1630.
5s: $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 8.40 (d, $J = 9.0$ Hz, 2H), 8.35 (d, $J = 8.4$ Hz, 2H), 7.97-7.98 (m, 2H), 7.43-7.52 (m, 8H), 7.17 (s, 1H), 3.87 (q, $J = 7.2$ Hz, 2H), 0.75 (d, $J = 7.2$ Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 158.0, 154.4, 146.0, 133.7, 130.3, 130.2, 130.1, 130.0, 128.5, 128.1, 127.9, 127.0, 124.7, 124.3, 118.8, 108.2, 104.0, 60.4, 13.4; HRMS Calculated for [C$_{26}$H$_{20}$N$_4$O$_4$]$^+$: 452.1485, Found: 452.1484.

5t: $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 8.35 (d, $J = 8.4$ Hz, 2H), 7.95-7.97 (m, 2H), 7.76 (d, $J = 9.0$ Hz, 2H), 7.42-7.51 (m, 8H), 7.12 (s, 1H), 3.86 (q, $J = 7.2$ Hz, 2H), 0.74 (d, $J = 7.2$ Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 158.1, 154.4, 132.7, 131.8, 130.4, 130.3, 130.2, 129.8, 128.4, 128.0, 127.9, 126.9, 124.8, 124.1, 119.1, 119.0, 110.1, 107.8, 103.7, 60.3, 13.4; HRMS Calculated for [C$_{27}$H$_{20}$N$_4$O$_2$]$^+$: 432.1586, Found: 432.1585.

6a: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.13 (d, $J = 7.2$ Hz, 2H), 7.49 (t, $J = 7.2$ Hz, 2H), 7.39-7.45 (m, 5H), 7.34 (t, $J = 7.2$ Hz, 1H), 7.05 (s, 1H), 4.03 (s, 3H), 3.50 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 161.7, 157.4, 144.6, 129.5, 128.9, 128.5, 128.1, 127.8, 127.6, 126.9, 125.1, 123.8, 122.0, 108.2, 103.8, 53.1, 51.3; HRMS Calculated for [C$_{21}$H$_{17}$N$_3$O$_4$]$^+$: 375.1219, Found: 375.1218.

6b: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.28 (d, $J = 8.4$ Hz, 2H), 7.77 (d, $J = 8.4$ Hz, 2H), 7.40-7.48 (m, 5H), 7.16 (s, 1H), 4.05 (s, 3H), 3.52 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 161.3, 157.2, 144.2, 132.7, 131.1, 129.1, 128.9, 127.9, 127.9, 125.0, 124.1, 119.5, 118.8, 110.7, 109.1, 105.0, 53.3, 51.7; HRMS Calculated for [C$_{22}$H$_{16}$N$_4$O$_4$]$^+$: 400.1172, Found: 400.1171.
6c: $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 8.22 (d, $J = 8.4$ Hz, 2H), 8.14 (d, $J = 8.4$ Hz, 2H), 7.41-7.46 (m, 5H), 7.14 (s, 1H), 4.05 (s, 3H), 3.94 (s, 3H), 3.91 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 166.5, 161.5, 157.3, 144.4, 131.1, 130.2, 129.3, 129.0, 128.7, 127.9, 127.8, 124.6, 124.0, 120.6, 109.0, 104.5, 53.2, 52.2, 51.5; HRMS Calculated for [C$_{23}$H$_{19}$N$_3$O$_6$]$^+$: 433.1274, Found: 433.1274.

6d: $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 8.11-8.14 (m, 2H), 7.40-7.45 (m, 5H), 7.18 (t, $J = 8.4$ Hz, 2H), 7.00 (s, 1H), 4.03 (s, 3H), 3.51 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 162.3 (d, $J = 247.2$ Hz), 161.7, 157.4, 144.6, 129.5, 128.6, 127.8 (d, $J = 26.4$ Hz), 127.1 (d, $J = 7.9$ Hz), 123.8, 123.3, 123.1, 119.7, 114.4, 107.5, 103.9, 53.2, 51.3; HRMS Calculated for [C$_{21}$H$_{16}$FN$_3$O$_4$]$^+$: 393.1125, Found: 393.1124.

6e: $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 8.07 (d, $J = 9.0$ Hz, 2H), 7.40-7.45 (m, 5H), 7.02 (d, $J = 9.0$ Hz, 2H), 6.96 (s, 1H), 4.03 (s, 3H), 3.86 (s, 3H), 3.50 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 161.9, 159.5, 157.5, 144.8, 129.7, 128.4, 127.9, 127.6, 126.8, 123.8, 119.7, 114.4, 107.5, 103.5, 55.3, 53.1, 51.2; HRMS Calculated for [C$_{22}$H$_{19}$N$_3$O$_5$]$^+$: 405.1325, Found: 405.1324.

6f: $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 8.07 (d, $J = 7.8$ Hz, 2H), 7.46 (t, $J = 7.8$ Hz, 2H), 7.33 (t, $J = 7.8$ Hz, 1H), 6.77 (s, 1H), 4.01 (s, 3H), 3.85 (s, 3H), 3.25 (t, $J = 7.8$ Hz, 2H), 1.67 (quin, $J = 7.8$ Hz, 2H), 1.43 (sex, $J = 7.8$ Hz, 2H), 0.96 (t, $J = 7.8$ Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 162.3, 158.2, 145.2, 128.8, 127.9, 127.2, 126.1, 125.1, 121.4, 106.6, 102.9, 53.1, 51.6, 30.9, 26.3, 22.1, 13.9; HRMS Calculated for [C$_{19}$H$_{21}$N$_3$O$_4$]$^+$: 355.1532, Found: 355.1530.
$^6g$: $^1H$ NMR (600 MHz, CDCl$_3$): $\delta$ 8.14 (d, $J = 7.8$ Hz, 2H), 7.53 (d, $J = 8.4$ Hz, 2H), 7.50 (d, $J = 8.4$ Hz, 2H), 7.40 (t, $J = 7.5$ Hz, 1H), 7.15 (s, 1H), 4.05 (s, 3H), 3.68 (s, 3H);
$^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 161.5, 157.4, 144.9, 133.6, 131.4, 129.1, 128.7, 128.1, 126.5, 125.4, 123.0, 121.7, 118.6, 111.7, 108.7, 104.4, 53.3, 51.8; HRMS Calculated for [C$_{22}$H$_{16}$N$_4$O$_4$]$^+$: 400.1172, Found: 400.1171.

S1.3 ORTEP Drawing of the Crystal Structures

ORTEP Drawing of the Crystal Structures for compound 3

Perspective view of the molecular structure of Au(C$_{27}$H$_{36}$N$_2$)(C$_{12}$H$_{11}$N$_3$)$^+$ cation (molecule 1) with the atom labeling scheme. The thermal ellipsoids are scaled to 30% probability. CCDC number: 855874
ORTEP Drawing of the Crystal Structures for compound 5a

Perspective view of the molecular structure of C_{19}H_{15}N_3O with the atom labeling scheme. The thermal ellipsoids are scaled to enclose 30% probability. CCDC number: 855875

ORTEP Drawing of the Crystal Structures for compound 5l

Perspective view of the molecular structure of C_{30}H_{21}N_3O with the atom labeling scheme provided for the non-hydrogen atoms. The thermal ellipsoids are scaled to enclose 30% probability. CCDC number: 987461
Perspective view of the molecular structure of \( \text{C}_{23}\text{H}_{23}\text{N}_3\text{O}_2 \) with the atom labeling scheme provided for the non-hydrogen atoms. The thermal ellipsoids are scaled to enclose 30% probability. CCDC number: 987462
ORTEP Drawing of the Crystal Structures for compound 6f

Perspective view of the molecular structure of C₁₉H₂₁N₃O₄ with the atom labeling scheme provided for the non-hydrogen atoms. The thermal ellipsoids are scaled to enclose 30% probability. CCDC number: 987463
S1.4 Stability test

The samples were prepared with 0.1 mmol compounds dissolved in 0.5 mL CDCl₃ with ca. 0.3 equiv. 1,3,5-trimethoxybenzene as an internal standard. H-NMR spectra were monitored over two weeks.
S1.5 UV-Vis Spectra and Fluorescence Spectra

![UV-Vis Spectra](image1)

![Fluorescence Spectra](image2)
**Abs.**

![Absorption Spectrum](image)

**Fluorescence Intensity**

![Fluorescence Spectrum](image)

**Wavelength (nm)**

![Chemical Structure](image)
**Absorption Spectrum**

- **Wavelength (nm)**: 250 to 600
- **Absorption (Abs.)**

**Emission Spectrum**

- **Wavelength (nm)**: 250 to 700
- **Fluorescence Intensity**
- **Excitation (black line)**
- **Emission (red line)**

化学结构式:

- **MeO**
- **Ph**
- **OMe**
Chapter S2. “Silver Effect” in Gold(I) Catalysis

S2.1 General Methods and materials

All of the reactions dealing with air and/or moisture-sensitive reactions were carried out under an atmosphere of nitrogen using oven/flame-dried glassware and standard syringe/septa techniques. Unless otherwise noted, all commercial reagents and solvents were obtained from the commercial provider and used without further purification. \(^1\)H NMR and \(^{13}\)C NMR spectra were recorded on Varian 600 MHz spectrometers. Chemical shifts were reported relative to internal tetramethylsilane (δ 0.00 ppm) or CDCl₃ (δ 7.26 ppm) for \(^1\)H NMR, CDCl₃ (δ 77.0 ppm) for \(^{13}\)C NMR and H₃PO₄ (85%) (δ 0.00 ppm) for \(^{31}\)P NMR. Flash column chromatography was performed on 230-430 mesh silica gel. Analytical thin layer chromatography was performed with precoated glass baked plates (250µ) and visualized by fluorescence and by charring after treatment with potassium permanganate stain. The X-ray photoelectron spectroscopy (XPS, Physical Electronics VersaProbe 5000) measurements were conducted with Al Kα radiation (1486.71 eV), the binding energy scale was calibrated by a C 1s peak at 284.8 eV.

Substrates 8 were synthesized according to the literature as below:

Representative procedure for the preparation of 9a

\[
\begin{align*}
8a & \xrightarrow{[Au] \text{ rt}} 9a
\end{align*}
\]

To a solution of 8a (44 mg, 0.25 mmol) in acetone (2.5 mL, 0.1 M), was added Au(I) catalyst (1.8 mg, 0.0025 mol, 1.0 mol%) and H₂O (0.75 mmol, 3.0 equiv.) at RT under nitrogen. The reaction mixture was stirred at RT and monitored by TLC. After the reaction was completed (5 h), the solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (ethyl acetate/hexane = 1 : 20, V/V) to give 9a (96% yield) as a colorless oil.
S2.2 Compounds Characterization

2-oxo-1-phenylpropyl acetate (9a): 96% yield, $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.38-7.42 (m, 5H), 5.98 (s, 1H), 2.19 (s, 3H), 2.11 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 201.6, 170.2, 133.2, 129.3, 129.0, 128.0, 80.9, 26.1, 20.7.

1-(3-nitrophenyl)-2-oxopropyl acetate (9b): 98% yield, $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 8.30-8.31 (m, 1H), 8.25 (dq, $J = 8.4, 1.2$ Hz, 1H), 7.78 (d, $J = 6.6$ Hz, 1H), 7.62 (d, $J = 8.1$ Hz, 1H), 6.08 (s, 1H), 2.45 (s, 3H), 2.20 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 201.1, 169.8, 148.5, 135.5, 133.6, 130.0, 124.1, 122.6, 79.5, 26.1, 20.5.

3-oxo-1-phenylbutan-2-yl acetate (9c): 94% yield, $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.20-7.32 (m 5H), 5.21 (q, $J = 3.3$ Hz, 1H), 3.10 (dd, $J = 13.8, 4.8$ Hz, 1H), 3.00 (dd, $J = 13.8, 8.4$ Hz, 1H), 2.08 (s, 3H), 2.07 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 205.3, 170.3, 135.8, 129.2, 128.5, 126.9, 79.0, 36.6, 26.8, 20.5.

2-oxohexan-3-yl acetate (9d): 91% yield, $^1$H NMR (600 MHz, CDCl$_3$): 4.99 (dd, $J = 8.4, 4.8$ Hz, 1H), 2.16 (s, 3H), 2.15 (s, 3H), 1.68-1.76 (m, 2H), 1.39-1.46 (m, 2H), 0.95 (t, $J = 7.5$ Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 205.4, 170.6, 78.5, 32.2, 26.0, 20.6, 18.5, 13.6.

1-acetylcyclohexyl acetate (9e): 93% yield, $^1$H NMR (600 MHz, CDCl$_3$): 2.13 (s, 3H), 2.09 (s, 3H), 2.02-2.05 (m, 2H), 1.62-1.69 (m, 5H), 1.49-1.56 (m, 2H), 1.24-1.29 (m, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 207.2, 170.2, 85.2, 30.8, 24.9, 23.6, 21.2, 21.0.
1-(4-fluorophenyl)-2-oxopropyl acetate (9f): 90% yield, $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.38-7.42 (m, 2H), 7.08-7.12 (m 2H), 5.96 (s, 1H), 2.19 (s, 3H), 2.12 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 201.5, 170.1, 162.4 (d, $J = 247.5$ Hz), 129.9 (d, $J = 8.1$ Hz), 129.1 (d, $J = 3.3$ Hz), 116.1 (d, $J = 21.3$ Hz), 80.0, 26.1, 20.6.

1-(4-methoxyphenyl)-2-oxopropyl acetate (9g): 95% yield, $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.32 (dt, $J = 8.4$, 2.4 Hz, 2H), 6.92 (dt, $J = 9.0$, 2.7 Hz, 2H), 5.93 (s, 1H), 3.82 (s, 3H), 2.17 (s, 3H), 2.10 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 201.8, 170.3, 160.4, 129.6, 125.0, 114.5, 80.4, 55.3, 26.1, 20.7.

1-(methyl-4-benzoate)-2-oxopropyl acetate (9h): 93% yield, $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 8.07 (d, $J = 8.4$ Hz, 2H), 7.50 (d, $J = 8.4$ Hz, 2H), 6.02 (s, 1H), 3.93 (s, 3H), 2.22 (s, 3H), 2.13 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 201.2, 170.0, 166.4, 137.9, 131.0, 130.2, 127.8, 80.4, 52.3, 26.0, 20.6.

1-(4-chlorophenyl)-2-oxopropyl acetate (9i): 91% yield, $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.34-7.40 (m, 4H), 5.94 (s, 1H), 2.19 (s, 3H), 2.12 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 201.3, 170.1, 135.4, 131.7, 129.3, 129.2, 80.7, 26.1, 20.6.

(E)-4-oxo-1-phenylpent-1-en-3-yl acetate (9j): 87% yield, $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.39-7.40 (m, 2H), 7.28-7.36 (m, 3H), 6.81 (d, $J = 16.2$ Hz, 1H), 6.16 (dd, $J = 16.2$, 7.8 Hz, 1H), 5.94 (dd, $J = 7.8$, 1.2 Hz, 1H), 2.23 (s, 3H), 2.20 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 202.3, 170.1, 136.3, 135.5, 128.7, 126.8, 120.5, 79.8, 26.1, 20.7.
1,2-diphenylethananone (11a): $^1$H NMR (600 MHz, CDCl$_3$): δ 8.00-8.02 (m, 2H), 7.53-7.56 (m, 1H), 7.45 (d, $J = 7.8$ Hz, 2H), 7.32 (d, $J = 7.5$ Hz, 2H), 7.24-7.27 (m, 3H), 4.28 (s, 2H). $^{13}$C NMR (150 MHz, CDCl$_3$): δ 197.6, 136.6, 134.5, 133.1, 129.4, 128.6, 128.6, 128.5, 126.9, 45.5.

(E)-1,2-diphenylhept-1-en-3-one (Scheme 12B): (known compound, See: Zhang, G.; Peng, Y.; Cui, L.; Zhang, L. Angew. Chem. Int. Ed. 2009, 48, 3112-3115.) $^1$H NMR (600 MHz, CDCl$_3$): 7.62 (s, 1H), 7.43 – 7.39 (m, 3H), 7.22 – 7.12 (m, 5H), 7.03 (d, $J = 6.0$ Hz, 2H), 2.55 (t, $J = 7.8$ Hz, 2H), 1.61 – 1.58 (m, 2H), 1.33 – 1.26 (m, 2H), 0.87 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): δ 201.8, 140.8, 137.7, 137.1, 134.7, 130.8, 129.6, 129.0, 128.2, 127.8, 13.9.

4-ethyl-2-methylcyclopenta-1,4-dienyl acetate (Scheme 13A): (See: Zhang, L.; Wang, S. J. Am. Chem. Soc. 2006, 128, 1442-1443.) $^1$H NMR (600 MHz, CDCl$_3$): δ 5.95 (s, 1H), 2.81 (s, 2H), 2.33 (q, $J = 7.2$ Hz, 2H), 2.22 (s, 3H), 1.82 (s, 3H), 1.11 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$): δ 169.1, 147.8, 145.6, 122.5, 121.5, 43.4, 24.0, 20.7, 13.2, 11.3.

methyl 1-acetylcyclopent-2-enecarboxylate (Scheme 13B): (See: Staben, S.T.; Kennedy-Smith, J.J.; Toste, F.D. Angew. Chem. Int. Ed. 2004, 43, 5350-5352.) $^1$H NMR (600 MHz, CDCl$_3$): δ 6.03 (td, $J = 5.4$, 2.4 Hz, 1H), 5.86 (td, $J = 5.4$, 1.8 Hz, 1H), 3.74 (s, 3H), 2.35–2.51 (m, 4H), 2.18 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$): δ 203.8, 172.3, 136.4, 128.7, 73.5, 52.6, 31.9, 30.1, 26.4.

3-phenylbicyclo[3.1.0]hex-2-ene (Scheme 13D): (See: Luzung, M.R.; Markham, J.P.; Toste, F.D. J. Am. Chem. Soc. 2004, 126, 10858-10859.) $^1$H NMR (600 MHz, CDCl$_3$): δ 7.38 (d, $J = 7.8$ Hz, 2H), 7.30 (t, $J = 7.8$ Hz, 2H), 7.21(t, $J = 7.8$ Hz, 1H), 6.42 (d, $J = 1.8$ Hz, 1H), 3.02 (dd, $J = 16.8$, 7.2 Hz, 1H), 2.75 (d, $J = 16.8$ Hz, 1H), 1.98-1.94 (m, 1H), 1.76-1.72 (m, 1H), 0.97-0.93 (m, 1H), 0.11-0.09 (m, 1H). $^{13}$C NMR (150 MHz, CDCl$_3$): δ 139.7, 136.6, 129.6, 128.2, 126.7, 125.1, 36.3, 24.1, 17.6, 15.4.
(E)-1-phenylhept-1-en-3-one (Scheme 14A): (known compound, See: Wang, D.; Zhang, Y.; Harris, A.; Gautam, L. N. S.; Shi, X. Adv. Syn. Cat. 2011, 353, 2584-2588.) ^1^H NMR (600 MHz, CDCl$_3$): δ 7.53-7.56 (m, 3H), 7.38-7.40 (m, 3H), 6.73 (t, $J = 16.2$ Hz, 1H), 2.66 (t, $J = 7.5$ Hz, 2H), 1.66 (quintet, $J = 7.5$ Hz, 2H), 1.37 (sextet, $J = 7.4$ Hz, 2H), 0.94 (t, $J = 7.5$ Hz, 3H); ^1^C NMR (150 MHz, CDCl$_3$): δ 200.8, 142.5, 134.8, 130.6, 129.1, 128.4, 126.5, 40.9, 26.7, 22.7, 14.1.

1,2-dihydro-2-methylnaphtho[2,1-b]furan (Scheme 14D): (known compound, See: Reich, N.W.; Yang, C.G.; Shi, Z.; He, C. Synlett. 2006, 8, 1278-1280.) ^1^H NMR (600 MHz, CDCl$_3$): δ 7.77 (d, $J = 8.4$ Hz, 1H), 7.64 (d, $J = 8.4$ Hz, 1H), 7.53 (d, $J = 8.4$ Hz, 1H), 7.43 (t, $J = 7.2$ Hz, 1H), 7.27 (t, $J = 7.2$ Hz, 1H), 7.07 (d, $J = 9.0$ Hz, 1H), 5.12-5.07 (m, 1H), 3.56 (dd, $J = 15.6$, 9.6 Hz, 1H), 3.04 (dd, $J = 15.0$, 7.2 Hz, 1H), 1.52 (d, $J = 6.6$ Hz, 3H). ^1^C NMR (150 MHz, CDCl$_3$): δ 156.9, 130.9, 129.1, 128.9, 128.7, 126.5, 122.6, 118.3, 112.1, 80.2, 35.9, 22.1.

(Z)-2-bromo-1-phenylhept-1-en-3-one (Scheme 15B-Z): (known compound, See: Wang, D.; Ye, X.; Shi, X. Org. Lett. 2010, 12, 2088-2091.) ^1^H NMR (600 MHz, CDCl$_3$): δ 8.03 (s, 1H), 7.84-7.86 (m, 2H), 7.42-7.44 (m, 2H), 2.93 (t, $J = 7.5$ Hz, 2H), 1.69 (quintet, $J = 7.5$ Hz, 2H), 1.40 (sextet, $J = 7.4$ Hz, 2H), 0.96 (t, $J = 7.5$ Hz, 3H); ^1^C NMR (150 MHz, CDCl$_3$): δ 195.6, 138.8, 133.9, 130.4, 130.2, 128.4, 123.2, 38.8, 26.8, 22.3, 13.9.

(E)-2-bromo-1-phenylhept-1-en-3-one (Scheme 15B-E): (known compound, See: Wang, D.; Ye, X.; Shi, X. Org. Lett. 2010, 12, 2088-2091.) ^1^H NMR (600 MHz, CDCl$_3$): δ 7.32-7.33 (m, 3H), 7.25 (s, 1H), 7.21-7.23 (m, 2H), 2.53 (t, $J = 7.5$ Hz, 2H), 1.55 (quintet, $J = 7.5$ Hz, 2H), 1.23 (sextet, $J = 7.4$ Hz, 2H), 0.83 (t, $J = 7.5$ Hz, 3H); ^1^C NMR (150 MHz, CDCl$_3$): δ 201.0, 136.0, 134.7, 128.9, 128.7, 128.2, 120.4, 41.0, 26.0, 22.0, 13.7.
S2.3 ORTEP Drawing of the Crystal Structures for IPr-TA-Au

Perspective view of the molecular structure of the [Au(C_{27}H_{36}N_2)(C_6H_3N_3)]^+ cation with the atom labeling scheme. The thermal ellipsoids are scaled to enclose 30% probability. CCDC number: 855876

S2.4 $^{31}$P NMR comparison between different gold catalyst

![NMR spectrum](image)
S2.5 HPLC data for chirality retention

1: 254 nm, 4 nm Results

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1: 254 nm, 4 nm Results

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### Spectrum Max Plot Results

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### Spectrum Max Plot Results

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Chapter S3. Gold-Catalyzed Cross-Coupling with Aryldiazonium Salts

S3.1 General Methods and materials

All of the reactions dealing with air and/or moisture-sensitive reactions were carried out under an atmosphere of nitrogen using oven/flame-dried glassware and standard syringe/septa techniques. Unless otherwise noted, all commercial reagents and solvents were obtained from the commercial provider and used without further purification. $^1$H NMR and $^{13}$C NMR spectra were recorded on Varian 600 MHz or Agilent 400 MHz spectrometer. Chemical shifts were reported relative to internal tetramethylsilane ($\delta$ 0.00 ppm) for $^1$H NMR and CDCl$_3$ ($\delta$ 77.0 ppm) for $^{13}$C NMR. Flash column chromatography was performed on 230-430 mesh silica gel. Analytical thin layer chromatography was performed with precoated glass baked plates (250µ) and visualized by UV lamp. ESI-MS spectra for products were recorded on Thermo Scientific Q-exactive spectrometer in West Virginia University BioNano Research Facility. The X-ray crystal structure was acquired with a Bruker AXS D8 Venture X-ray diffractometer.

ESI-MS spectra for monitoring reaction mixtures were collected in Ohio University using a Waters Xevo QTof mass spectrometer (Milford, MA, USA) in the positive ion mode. The samples were infused with a flow rate of 2 µL/min and spray voltage of 5 kV.

S3.2 General procedures

A. Preparation of aryldiazonium salts:

\[
\begin{align*}
\text{R} & \quad \text{NH}_2 \quad \xrightarrow{\text{NaNO}_2, 50\% \text{HBF}_4} \quad \text{R} \quad \text{N}^+ \text{N}^+ \quad \text{BF}_4^- \\
&
\end{align*}
\]

The preparation aryldiazonium salts is adapted from literature report.$^2$ The aniline 1 (10 mmol) was added to a mixture of 50% fluoroboric acid (3 mL) and distilled water (3 mL) in ice bath. To this solution, an ice-cold solution of sodium nitrite (704 mg, 10.2 mmol) in distilled water (3 mL) was added. After stirring for 30 mins, the precipitate was collected on a hirsch funnel and washed with small amount of ice-cold distilled water. The solid was dissolved in acetone and precipitated with slow addition of ethyl ether. White crystalline solids were obtained after repeat this trituration two to three times. Yields of the aryldiazonium salts 2 are ranged from 65% to 92%.

B. Condition optimization of sp-sp$^2$ coupling:

The gold catalyst and additives were added to 0.2 mL freshly distilled acetonitrile (or other solvents) in a 1-dram vial. To this solution was added the alkyne 12a (0.1 mmol, 8.4 mg) and the diazonium salt 13a (0.12 mmol, 25.6 mg). The conversions of 12a and yields of 15a were determined by $^1$H-NMR using p-xylene as the standard. The yields of 14aa, 16a, and 16a’ were determined by $^{19}$F-NMR using trifluorotoluene as the standard.

a. Effects of different bases

The gold catalyst and additives were added to freshly distilled acetonitrile (ACN) in a 1-dram vial. To this solution was added the alkyne 12a (0.1 mmol, 8.4 mg) and the diazonium salt 13a (0.12 mmol, 25.6 mg).

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<th>Conc. (M)</th>
<th>Conv. (%)</th>
<th>Yield (%)</th>
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<th>15a</th>
<th>16a</th>
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b. Effects of different solvents

The gold catalyst and additives were added to 0.5 mL solvent in a 1-dram vial. To this solution was added the alkyne 12a (0.1 mmol, 8.4 mg) and the diazonium salt 13a (0.12 mmol, 25.6 mg). The mixture was stirred under room temperature for 20 hrs.
### c. Effects of gold catalysts

The gold catalyst (0.005 mmol), Na₂CO₃ (0.2 mmol, 21.2 mg), and 2,2'-bipyridine (bpy, 0.02 mmol, 3.1 mg) were added to 0.2 mL freshly distilled ACN in a 1-dram vial. To this solution was added the alkyne 12a (0.1 mmol, 8.4 mg) and the diazonium salt 13a (0.12 mmol, 25.6 mg). The mixture was stirred under room temperature for 12 hrs.

### d. Effects of other metal catalysts

The catalysts and additives were added to freshly distilled ACN in a 1-dram vial. To this solution was added the alkyne 12a (0.1 mmol, 8.4 mg) and the diazonium salt 13a (0.12 mmol, 25.6 mg). The mixture was stirred under room temperature for 10 hrs.

---

#### Table 1: Effects of gold catalysts

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**a** TA=1-methylbenzotriazole; **b** Ar=2,4-di-tert-butyl-phenyl.

### Table 2: Effects of other metal catalysts

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<td>Ru(bpy)₃(PF₆)₂ (2.5)</td>
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<th>Conc. (M)</th>
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<td>8</td>
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<td>0.5</td>
<td>83</td>
<td>13</td>
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<td>9</td>
<td>Pd(OAc)₂ (5), Ph₃PAuNTf₂ (5)</td>
<td>bpy</td>
<td>10</td>
<td>0.5</td>
<td>100</td>
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C. Gold-catalyzed cross coupling of alkynes and aryl diazonium salts:

\[
\begin{array}{c}
\text{R}^1 \equiv + \text{N} \equiv \text{BF}_4^- \\
\text{R}^2
\end{array}
\]

The gold catalyst Ph₃PAuNTf₂ (14.8 mg, 0.02 mmol), bpy (12.4 mg, 0.08 mmol) and sodium carbonate (84.8 mg, 0.8 mmol) were added to 0.8 mL freshly distilled acetonitrile in a 1-dram vial. To this solution was added the alkyne 12 (0.4 mmol) and the diazonium salt 13 (0.48 mmol). The mixture was stirred under room temp for 4 to 15 hrs. Upon reaction completion, the solvent was removed under reduce pressure and the residue was purified by flash chromatography on silica gel using hexanes or hexanes/ethyl acetate.

D. Condition optimization of sp²-sp² coupling:

The gold catalyst, boronic acid 7a and additives were added to 0.2 mL freshly distilled acetonitrile in a 1-dram vial. To this solution was added the diazonium salt 2a (0.2 mmol, 42.0 mg). The conversions and yields were determined by ¹⁹F-NMR using trifluorotoluene as the standard.

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<td>5</td>
<td>86</td>
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<td>4</td>
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<td>69</td>
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<td>Ph₃PAu(TA)OTf (10)</td>
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<td>100</td>
<td>86 8 0</td>
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</table>

Entries: 1-9. TA=1-methylbenzotriazole; TAA = benzotriazole anion; Ar=2,4-di-tert-butyl-phenyl.

E. Gold-catalyzed cross coupling of boronic acids and aryl diazonium salts:

The gold catalyst Ph₃PAu(TA)OTf (14.8 mg, 0.04 mmol), bpy (12.4 mg, 0.08 mmol), sodium carbonate (84.8 mg, 0.8 mmol) and boronic acid 19 (0.4 mmol) were added to 0.8 mL freshly distilled acetonitrile in a 1-dram vial. To this solution was added the
diazonium salt 13 (0.48 mmol). The mixture was stirred under room temp for 2 to 10 hrs. Upon reaction completion, the solvent was removed under reduce pressure and the residue was purified by flash chromatography on silica gel using hexanes.

**F. Gold-catalyzed C-Br bond formation:**

In a dried glass tube, 13 (0.2 mmol), PPh₃AuCl (0.010 mmol, 5 mol %) and LiBr (0.6 mmol, 3 equiv) were dissolved in CH₃CN (0.5 mL). The reaction mixture was stirred at 50 °C for 5 h. After the reaction completed, the product was purified by column chromatography.

**G. Gold-catalyzed C-S bond formation:**

In a dried glass tube, 13 (0.4 mmol, 2 equiv), PPh₃AuCl (0.010 mmol, 5 mol %), Na₂CO₃ (2 equiv) and 26 (0.2 mmol, 1 equiv) were dissolved in CH₃CN (0.5 mL). The reaction mixture was stirred at room temperature for 3 h. After the reaction completed, the product was purified by column chromatography.

**H. Gold-catalyzed C-P bond formation:**

In a dried glass tube, 13 (0.4 mmol, 2 equiv), PPh₃AuCl (0.010 mmol, 5 mol %), diethyl phosphite (0.2 mmol, 1 equiv) and 3-Cl-Py (0.4 mmol, 1 equiv) were dissolved in CH₃CN (0.5 mL). The reaction mixture was stirred at 50 °C for 8 h. After the reaction completed, the product was purified by column chromatography.

**S3.3 Mechanistic studies**

**A. The reaction of diazonium salts with gold complexes**

**a. Reaction with Ph₃PAuNTf₂**

Three NMR tubes were labeled as A, B and C. The gold catalyst Ph₃PAuNTf₂ (7.4 mg, 0.01 mmol) was dissolved in 0.4 mL CD₃CN in tube A. The gold catalyst Ph₃PAuNTf₂ (7.4 mg, 0.01 mmol), and bpy (3.1 mg, 0.02 mmol) were added to 0.4 mL CD₃CN in tube
The gold catalyst Ph$_3$PAuCl (4.9 mg, 0.01 mmol) and Ru(bpy)$_3$(PF$_6$)$_2$ (0.6 mg, 0.001 mmol) were added to 0.4 mL CD$_3$CN in tube C (C was used as reference regarding the formation of the phosphonium salt) $^3$.

The diazonium salt 13a (10 eq.) was added to the three NMR tubes separately. Tube C was placed under blue LED light. The reactions were monitored by $^1$H-NMR and $^{31}$P-NMR. The D$_2$O solution of phosphoric acid in a seal tube was used as the standard for $^{31}$P-NMR.

For tube A (without bpy present), no reaction was observed after addition of 13a for 18 h. After 18 h, 10 eq. of the alkyne 12a was added, still without any reaction.

For tube B (with 2 eq. bpy), the in-situ formed [Ph$_3$PAu(bpy)]$^+$ ($^{31}$P NMR: $\delta$ 31.6 ppm) reacted with the diazonium salt and generated a new species M. The gold catalyst reached full conversion within 8 h to M with 10% consumption of the diazonium salt 2a (10 eq. relevant to gold catalyst).

After comparison the NMR with tube C, which is a method reported by the Toste group $^2$ to generate phosphonium, we were able to conclude the formation of phosphonium M by simply reacting Ph$_3$PAuNTf$_2$ with diazonium salt with bpy present. However, adding 10 eq. of the alkyne 12a after 18 h did not form the cross-coupling product. This suggested that the phosphonium is not an active species in this transformation.

b. Reaction with gold acetylide

\[
\text{AuPh}_3 + \text{17a} \quad \xrightarrow{\text{CD}_3\text{CN, rt, 4 h}} \quad \text{Me} + \text{13b (1.1 eq.)} \quad \xrightarrow{\text{CD}_3\text{CN, rt, 4 h}} \quad \text{F} + \text{N}_2\text{BF}_4^- \quad \xrightarrow{\text{14r}} \quad \text{Fluorene} \quad \text{Me}
\]

A. no bpy: 22%
B. 2 eq. bpy: 98%

Figure S2. The NMR spectra for the reaction between Ph₃PAuNTf₂ and 13a (2 eq. bpy)

Figure S3. The NMR spectra for the phosphonium M
The synthesis of gold acetylide 17a was adapted from literature report.\textsuperscript{4} \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): $\delta$ 7.58-7.43 (m, 17H), 6.94 (t, $J = 8.8$ Hz, 2H); \textsuperscript{31}P NMR (162 MHz, CDCl\textsubscript{3}): $\delta$ 42.2; \textsuperscript{19}F NMR (376 MHz, CDCl\textsubscript{3}): $\delta$ -114.3 (m, 1F).

Two NMR tubes were labeled as A and B. The gold acetylide 17a (17.4 mg, 0.03 mmol) was added to 0.4 mL CD\textsubscript{3}CN in tube A. The gold acetylide 17a (17.4 mg, 0.03 mmol) and bpy (9.4 mg, 0.06 mmol) were added to 0.4 mL CD\textsubscript{3}CN in tube B.

The diazonium salt 13b (6.8 mg, 0.033 mmol) was added to the two NMR tubes separately. The reactions were monitored by $^1$H-NMR, $^{19}$F-NMR and $^{31}$P-NMR. A D\textsubscript{2}O solution of phosphoric acid in a seal tube was used as the standard for $^{31}$P-NMR. Trifluorotoluene was used as the internal standard for $^{19}$F-NMR and p-xylene was used as the internal standard for $^1$H-NMR. The yields of the product were calculated based on both the $^{19}$F-NMR and the $^1$H-NMR.

\textbf{Figure S4.} NMR spectra for the reaction between gold acetylide 17a and 13a (no bpy)

Figure S4. NMR spectra for the reaction between gold acetylide 17a and 13a (no bpy)

Figure S5. NMR spectra for the reaction between gold acetylide 6a and 2a (2 eq. bpy)
The gold acetylide 6a is poorly soluble in CD$_3$CN. However, it dissolved gradually as the reaction proceeded. Gold mirror formation was observed in tube A within 1 h, whereas no decomposition of the gold complex was observed in tube B during the reaction. This is most likely due to the stabilization of cation gold complex and/or reaction intermediate by the bpy ligand. The bpy also contributed to the nitrogen extrusion based on the results in the previous section (III. A. 1), which might explain the much higher yield and reaction rate we observed in tube B compared to tube A.

In tube A, an unidentified intermediate I was observed from the beginning of the reaction. However, this intermediate is almost invisible in tube B (with 2 eq. bpy present, only trace amount was observed in the very beginning of the reaction). If our hypothesis is correct, this intermediate I should be the adduct between diazonium and gold acetylide, for which the nitrogen extrusion was a problem without the help from bpy.

In tube B, the gold acetylide 6a was fully converted to [Ph$_3$PAu(bpy)]$^+$ in 4 h with almost quantitative yield of the product 3r. Upon reaction completion, phosphonium M was generated by the reaction between [Ph$_3$PAu(bpy)]$^+$ with excess diazonium salt 2b.

c. Reaction with aryl gold
The aryl gold complex 6b was synthesized based on previous report.\(^5\)

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.62-7.43 (m, 17H), 7.01 (ddd, \(J = 10.0, 8.6, 1.3\) Hz, 2H);

\(^{31}\)P NMR (162 MHz, CDCl\(_3\)): \(\delta\) 43.5;

\(^{19}\)F NMR (376 MHz, CDCl\(_3\)): \(\delta\) -117.3 (m, 1F).

Two NMR tubes were labeled as A and B. The aryl gold complex 17b (16.6 mg, 0.03 mmol) was added to 0.4 mL CD\(_3\)CN in tube A. The aryl gold complex 17b (16.6 mg, 0.03 mmol) and bpy (9.4 mg, 0.06 mmol) were added to 0.4 mL CD\(_3\)CN in tube B.

The diazonium salt 13b (6.8 mg, 0.033 mmol) was added to the two NMR tubes separately. The reactions were monitored by \(^1\)H-NMR, \(^{19}\)F-NMR and \(^{31}\)P-NMR. The D\(_2\)O solution of phosphoric acid in a seal tube was used as the standard for \(^{31}\)P-NMR. Trifluorotoluene was used as the internal standard for \(^{19}\)F-NMR and p-xylene was used as the internal standard for \(^1\)H-NMR. The yields of the product were calculated based on both the \(^{19}\)F-NMR and the \(^1\)H-NMR.

Similar to the gold acetylide, the aryl gold 17b is poorly soluble in CD\(_3\)CN. However, it dissolved gradually as the reaction proceeded. Gold mirror formation was observed in tube A within 10 min, whereas no decomposition of the gold complex was observed in tube B during the reaction. Much higher yield and reaction rate were observed in tube B compared to tube A.

Compared to the reaction with gold acetylide, the reaction of diazonium salt with aryl gold complex seemed to suffer from the homo-coupling especially without bpy present (tube A). When bpy presented (tube B), the [Ph\(_3\)PAu(bpy)]\(^+\) (\(\delta\) 31.6 ppm) was the major species in the \(^{31}\)P NMR from the beginning of the reaction, suggesting the rapid reductive elimination from the Au(III) intermediate. Phosphonium M was also generated in the early stage of the reaction, which is consistent with the formation of [Ph\(_3\)PAu(bpy)]\(^+\). Although the homo-coupling is suppressed with bpy present, it still was a problem that caused the lower yield of the cross-coupling product.

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Figure S6. NMR spectra for the reaction between aryl gold 17b and 13a (no bpy)
Two NMR tubes were labeled as A and B. The alkyl gold 17c (14.2 mg, 0.03 mmol) was added to 0.4 mL CD$_3$CN in tube A. The gold acetylide 17b (14.2 mg, 0.03 mmol) and bpy (9.4 mg, 0.06 mmol) were added to 0.4 mL CD$_3$CN in tube B. The diazonium salt 13b (6.8 mg, 0.033 mmol) was added to the two NMR tubes separately. The reactions...
were monitored by $^1$H-NMR and $^{31}$P-NMR. The D$_2$O solution of phosphoric acid in a seal tube was used as the standard for $^{31}$P-NMR. 1,3,5-tribromobenzene was used as the internal standard for $^1$H-NMR.

The reaction with Ph$_3$PAuMe was quite sluggish both with and without bpy. The alkyl gold Ph$_3$PAuMe showed very terrible solubility in CD$_3$CN. In tube A, the gold complex slowly decomposed to yield gold mirror with small amount of unidentified mixture formed. Although no gold mirror was observed in tube B, the reaction was also slow and messy. The desired product (p-xylene) was not detected by $^1$H-NMR.

**B. Monitoring the catalytic sp-sp$^2$ coupling**

![Chemical diagram](image)

The alkyne 12a (0.2 mmol, 16.8 mg), bpy (0.4 mmol, 62.4 mg) and the diazonium salt 13a (0.22 mmol, 46.2 mg) were dissolved in 0.4 mL CD$_3$CN in a NMR tube. To this solution was added the gold catalyst Ph$_3$PAuNTf$_2$ (7.4 mg, 0.01 mmol). The reactions were monitored by $^1$H-NMR and $^{31}$P-NMR. The D$_2$O solution of phosphoric acid in a seal tube was used as the standard for $^{31}$P-NMR. The conversions of 12a and yields of 14aa were determined by $^1$H-NMR using p-xylene as the standard.

Based on the $^{31}$P-NMR, the [Ph$_3$Au(bpy)]$^+$ ($\delta$ 31.6 ppm) was the major species detected during the reaction. As the reaction proceeded toward completion, the [Ph$_3$Au(bpy)]$^+$ started to accumulate. After the reaction was completed (7 h), the phosphonium M formed. No induction period was observed for this reaction based on the $^1$H-NMR.

![Figure S8](image)

**Figure S8.** Reaction kinetics for the catalytic sp-sp$^2$ cross-coupling
C. Radical trapping experiment

To test whether this gold catalyzed cross-coupling was a radical process, diazonium salt 13c was synthesized from the corresponding aniline, which was synthesized according to literature report.\(^6\) The diazonium 13c was then was reacted with alkyne 12a under the optimized conditions.

The cross-coupling product 20a was successfully isolated in 25% yield with 37% of alkyne 12a consumed. This was consistent with the lower yield observed with \textit{ortho}-substituted phenyldiazonium salts. The radical trapping product was not detected.

However, a cyclized byproduct 20b, generated from two molecule diazonium salt 13c, was isolated and characterized by NMR and HR-MS. The mechanism of the formation of 20b is still unclear to this point. But it is highly likely that the aryl radical formation is not a key step in this cross-coupling reaction.

D. Exploring the reaction intermediates with ESI-MS

ESI-MS spectra were collected using a Waters Xevo QTof mass spectrometer (Milford, MA, USA) in the positive ion mode. The samples were infused with a flow rate of 2 μL/min and sprayed at a high voltage of 5 kV.

The reactions were prepared using the same method as the in the general procedures. After 10 minutes, the reaction mixtures were tested with the ESI-MS.

The adducts 21 from gold acetylides and the diazonium were successfully observed at m/z 713, 701 and 689 respectively for the three different alkynes (Fig. 10). However, the intensities of 21 were quite low compared with other gold complexes in the reaction mixture. In fact, the intensity of 21 decreased as the reaction proceeded (almost not detectable after 2 h). The MS/MS spectra confirmed the composition of 21 (Fig. 11).
Figure S10. ESI-MS spectra of 10 min reaction mixture of 13a with different alkynes

Figure S11. MS/MS spectra of mass-selected ions: a) m/z 713, b) m/z 701 and c) m/z 689
In order to trap the reaction intermediate, diazonium salt 13d was synthesized and tested under the same conditions. In the absence of bpy, a similar gold acetylide/diazonium adduct 21b was observed at m/z 772, though with a much higher intensity. However, with 2 eq. bpy added, high abundance of Au(III) intermediate ion (after nitrogen extrusion) was detected at m/z 744, indicating that bpy helped to accelerate the nitrogen extrusion, which is consistent with the NMR data described in section III.A1. The MS/MS fragmentation of the intermediate ion m/z 744 (Fig. 13b) confirmed the composition of this Au(III) intermediate. The cross-coupling product was detected in low intensity with both the ESI-MS (m/z 286) and crude NMR. It is possible that the coordination of pyridyl with Au(III) intermediate inhibited the reductive elimination.

Figure S12. ESI-MS spectra of reaction mixture between diazonium 13d and alkyne 12b
Figure S13. MS/MS spectra of mass-selected ions at a) m/z 772.2 and b) m/z 744.2

S3.4 Compounds characterization

14aa: Yellow liquid (92% yield).
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.40-7.35 (dd, $J = 9.2$, 5.6 Hz, 2H), 7.00-6.95 (t, $J = 8.4$ Hz, 2H), 2.57 (br. s, 1H), 1.61 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 162.36 (d, $J = 248.1$ Hz), 133.43 (d, $J = 7.8$ Hz), 118.74, 115.42 (d, $J = 22.0$ Hz), 93.46, 81.01, 65.51, 31.36; $^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ -112.1 (m, 1F).
ESI-MS calculated for [C$_{11}$H$_{12}$FO]$^+$: 179.0867, found: 179.0872.

14ab: Yellow liquid (88% yield).
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.43-7.40 (m, 2H), 7.31-7.28 (m, 3H), 2.10 (br s, 1H), 1.62 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 131.61, 128.21, 122.70, 93.75, 82.12, 65.61, 31.48.
ESI-MS calculated for [C$_{11}$H$_{13}$O]$^+$: 161.0961, found: 161.0968.
**14ac:** Yellow liquid (86% yield).

$^1$H NMR (400 MHz, CDCl$_3$): δ 7.34 (d, $J = 8.9$ Hz, 2H), 6.82 (d, $J = 8.8$ Hz, 2H), 3.80 (s, 3H), 2.13 (br. s, 1H), 1.61 (s, 6H);

$^{13}$C NMR (100 MHz, CDCl$_3$): δ 159.50, 133.03, 114.80, 113.83, 92.38, 81.96, 65.61, 55.23, 31.55.

ESI-MS calculated for [C$_{12}$H$_{15}$O$_2$]$^+$: 191.1067, found: 191.1075.

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**14ad:** Yellow liquid (88% yield).

$^1$H NMR (400 MHz, CDCl$_3$): δ 7.30 (d, $J = 8.1$ Hz, 2H), 7.10 (d, $J = 7.8$ Hz, 2H), 2.33 (s, 3H), 2.12 (br. s, 1H), 1.61 (s, 6H);

$^{13}$C NMR (100 MHz, CDCl$_3$): δ 159.49, 133.02, 114.79, 113.82, 92.36, 81.95, 65.60, 55.22, 31.54.

ESI-MS calculated for [C$_{12}$H$_{15}$O]$^+$: 175.1117, found: 175.1125.

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**14ae:** Yellow liquid (89% yield).

$^1$H NMR (400 MHz, CDCl$_3$): δ 7.43 (d, $J = 8.4$ Hz, 2H), 7.27 (d, $J = 8.4$ Hz, 2H), 2.06 (br. s, 1H), 1.61 (s, 6H);

$^{13}$C NMR (100 MHz, CDCl$_3$): δ 133.06, 131.49, 122.46, 121.68, 94.86, 81.11, 65.62, 31.39.

ESI-MS calculated for [C$_{11}$H$_{12}$BrO]$^+$: 239.0066, found: 239.0074.

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**14af:** Yellow liquid (87% yield).

$^1$H NMR (400 MHz, CDCl$_3$): δ 7.36 (d, $J = 8.1$ Hz, 2H), 7.32 (d, $J = 8.4$ Hz, 2H), 2.23 (br. s, 1H), 1.62 (s, 6H), 1.31 (s, 9H);

$^{13}$C NMR (100 MHz, CDCl$_3$): δ 151.41, 131.30, 125.18, 119.66, 93.12, 82.16, 65.59, 34.69, 31.52, 31.13.

ESI-MS calculated for [C$_{15}$H$_{21}$O]$^+$: 217.1587, found: 217.1595.

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**14ag:** Yellow liquid (80% yield).

$^1$H NMR (400 MHz, CDCl$_3$): δ 7.53 (d, $J = 8.5$ Hz, 2H), 7.49 (d, $J = 8.7$ Hz, 2H), 2.51 (br. s, 1H), 1.63 (s, 6H);

$^{13}$C NMR (100 MHz, CDCl$_3$): δ 131.79, 129.94 (q, $J = 32.5$ Hz), 126.55, 125.09 (q, $J = 3.8$ Hz), 123.83 (q, $J = 270.8$ Hz), 96.21, 80.81, 65.55, 31.26.
\textsuperscript{19}F NMR (376 MHz, CDCl\textsubscript{3}): δ -62.9 (s, 3F).
ESI-MS calculated for [C\textsubscript{12}H\textsubscript{12}F\textsubscript{3}O]\textsuperscript{+}: 229.0835, found: 229.0843.

\textbf{14ah}: Yellow liquid (70\% yield).
\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): δ 7.68 (s, 1H), 7.62 (d, \(J = 7.8\) Hz, 1H), 7.57 (d, \(J = 7.5\) Hz, 1H), 7.42 (t, \(J = 7.8\) Hz, 1H), 2.33 (br. s, 1H), 1.62 (s, 6H);
\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): δ 135.66, 134.90, 131.38, 129.13, 124.36, 117.94, 112.66, 96.28, 79.78, 65.47, 31.24.
ESI-MS calculated for [C\textsubscript{12}H\textsubscript{12}NO]\textsuperscript{+}: 186.0913, found: 186.0920.

\textbf{14ai}: Yellow liquid (89\% yield).
\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): δ 7.24 (td, \(J = 7.9, 5.8\) Hz, 1H), 7.18 (d, \(J = 7.7\) Hz, 1H), 7.12-7.08 (m, 1H), 7.02-6.97 (m, 1H), 2.47 (br. s, 1H), 1.61 (s, 6H);
\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): δ 163.23 (d, \(J = 244.7\) Hz), 129.74 (d, \(J = 8.4\) Hz), 127.44 (d, \(J = 2.9\) Hz), 124.51, 118.37 (d, \(J = 22.7\) Hz), 115.50 (d, \(J = 20.9\) Hz), 94.71, 80.91, 65.50, 31.31.
\textsuperscript{19}F NMR (376 MHz, CDCl\textsubscript{3}): δ -113.1 (m, 1F).
ESI-MS calculated for [C\textsubscript{11}H\textsubscript{12}FO]\textsuperscript{+}: 179.0867, found: 179.0875.

\textbf{14aj}: Yellow liquid (66\% yield).
\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): δ 7.20 (t, \(J = 8.0\) Hz, 1H), 7.01 (d, \(J = 7.6\) Hz, 1H), 6.94 (t, \(J = 1.9\) Hz, 1H), 6.86 (dd, \(J = 8.3, 2.6\) Hz, 1H), 3.79 (s, 3H), 2.07 (s, 1H), 1.62 (s, 6H);
\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): δ 159.24, 129.29, 124.15, 123.70, 116.39, 114.91, 93.54, 82.04, 65.60, 55.22, 31.47.
ESI-MS calculated for [C\textsubscript{12}H\textsubscript{15}O\textsubscript{2}]\textsuperscript{+}: 191.1067, found: 191.1074.

n-Bu ——— Ph 

\textbf{14b}: Colorless liquid (88\% yield).
\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): δ 7.40-7.38 (m, 2H), 7.29-7.25 (m, 3H), 2.41 (t, \(J = 7.0\) Hz, 2H), 1.63-1.56 (m, 2H), 1.48 (dq, \(J = 14.9, 7.3\) Hz, 2H), 0.95 (t, \(J = 7.3\) Hz, 3H);
\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): δ 131.51, 128.14, 127.41, 124.09, 90.38, 80.53, 30.85, 22.01, 19.09, 13.63.
ESI-MS calculated for [C\textsubscript{12}H\textsubscript{15}]\textsuperscript{+}: 159.1168, found: 159.1176.
$14c$: Colorless liquid (68% yield).
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.40-7.37 (m, 2H), 7.29-7.24 (m, 3H), 2.58 (tt, $J = 8.8$, 4.2 Hz, 1H), 1.90-1.85 (m, 2H), 1.79-1.72 (m, 2H), 1.58-1.49 (m, 3H), 1.40-1.30 (m, 3H);
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 131.55, 128.11, 127.36, 124.12, 94.44, 80.49, 32.72, 29.66, 25.93, 24.90.
ESI-MS calculated for [C$_{14}$H$_{17}$]$^+$: 185.1325, found: 185.1332.

$14d$: Colorless liquid (81% yield).
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.39-7.35 (m, 2H), 7.27-7.23 (m, 3H), 1.48-1.41 (m, 1H), 0.88-0.83 (m, 2H), 0.82-0.78 (m, 2H);
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 131.58, 128.13, 127.41, 123.90, 93.38, 75.74, 8.58, 0.15.
ESI-MS calculated for [C$_{11}$H$_{11}$]$^+$: 143.0855, found: 143.0862.

$14e$: Yellow liquid (58% yield).
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.58 (d, $J = 8.3$ Hz, 2H), 7.45 (t, $J = 7.5$ Hz, 1H), 7.37 (t, $J = 7.9$ Hz, 2H), 3.84 (s, 3H);
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 154.44, 132.97, 130.65, 128.55, 119.50, 86.47, 80.33, 52.77.
ESI-MS calculated for [C$_{10}$H$_9$O$_2$]$^+$: 161.0597, found: 161.0603.

$14f$: Colorless liquid (63% yield).
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.43-7.40 (m, 2H), 7.31-7.26 (m, 3H), 6.21 (tt, $J = 4.0$, 2.0 Hz, 1H), 2.25-2.20 (m, 2H), 2.17-2.12 (m, 2H), 1.71-1.59 (m, 4H);
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 135.15, 131.42, 128.19, 127.69, 123.76, 120.71, 91.24, 86.75, 29.24, 25.77, 22.35, 21.53.
ESI-MS calculated for [C$_{14}$H$_{15}$]$^+$: 183.1168, found: 183.1176.

$14g$: Light brown solid (73% yield).
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.77 (s, 1H), 8.54 (d, $J = 4.8$ Hz, 1H), 7.80 (dd, $J = 7.7$,
0.6 Hz, 1H), 7.56-7.53 (m, 2H), 7.37-7.35 (m, 3H), 7.26 (dd, \( J = 7.8, 4.9 \) Hz, 1H);

\[^{13}\text{C}\text{ NMR (100 MHz, CDCl}_3\): \delta \ 152.18, 148.48, 138.33, 131.62, 128.74, 128.38, 122.95, 122.45, 120.40, 92.58, 85.88.}

ESI-MS calculated for \([\text{C}_{13}\text{H}_{10}\text{N}]^+\): 180.0808, found: 180.0815.

14h: Light yellow solid (64% yield).

\(^1\text{H NMR (400 MHz, CDCl}_3\): \delta \ 7.53-7.50 (m, 3H), 7.36-7.32 (m, 3H), 7.30 (dd, \( J = 5.0, 3.0 \) Hz, 1H), 7.20 (dd, \( J = 5.0, 1.2 \) Hz, 1H);

\[^{13}\text{C}\text{ NMR (100 MHz, CDCl}_3\): \delta \ 131.50, 129.85, 128.56, 128.31, 128.18, 125.33, 123.18, 122.28, 88.85, 84.48.}

ESI-MS calculated for \([\text{C}_{12}\text{H}_9\text{S}]^+\): 185.0419, found: 185.0425.

14i: Yellow liquid (44% yield).

\(^1\text{H NMR (400 MHz, CDCl}_3\): \delta \ 7.44 (dd, \( J = 8.9, 5.4 \) Hz, 4H), 7.01 (t, \( J = 8.8 \) Hz, 4H), 4.52 (s, 4H);

\[^{13}\text{C}\text{ NMR (100 MHz, CDCl}_3\): \delta \ 162.64 (d, \( J = 248.3 \) Hz), 133.73 (d, \( J = 8.3 \) Hz), 118.52 (d, \( J = 3.6 \) Hz), 115.60 (d, \( J = 22.0 \) Hz), 85.76, 84.03, 57.43.}

\(^{19}\text{F NMR (376 MHz, CDCl}_3\): \delta \ -110.5 (m, 1F).

ESI-MS calculated for \([\text{C}_{18}\text{H}_{13}\text{F}_2\text{O}]^+\): 283.0929, found: 283.0940.

14j: White solid (80% yield).

\(^1\text{H NMR (400 MHz, CDCl}_3\): \delta \ 7.55-7.52 (m, 2H), 7.38-7.33 (m, 3H);

\[^{13}\text{C}\text{ NMR (100 MHz, CDCl}_3\): \delta \ 131.58, 128.32, 128.23, 123.26, 89.36.}

ESI-MS calculated for \([\text{C}_{14}\text{H}_{11}]^+\): 179.0855, found: 179.0865.

14k: White solid (85% yield).

\(^1\text{H NMR (400 MHz, CDCl}_3\): \delta \ 7.54-7.49 (m, 4H), 7.36-7.33 (m, 3H), 7.04 (t, \( J = 8.8 \) Hz, 2H);

\[^{13}\text{C}\text{ NMR (100 MHz, CDCl}_3\): \delta \ 162.48 (d, \( J = 248.2 \) Hz), 133.45 (d, \( J = 8.3 \) Hz), 131.53, 128.35, 128.31, 123.08, 119.36 (d, \( J = 3.5 \) Hz), 115.62 (d, \( J = 21.9 \) Hz), 89.02, 88.27.}

\(^{19}\text{F NMR (376 MHz, CDCl}_3\): \delta \ -111.0 (m, 1F).

ESI-MS calculated for \([\text{C}_{14}\text{H}_{10}\text{F}]^+\): 197.0761, found: 197.0771.
**14l:** Light yellow solid (36% yield).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.52-7.50 (m, 2H), 7.47 (d, $J = 8.8$ Hz, 2H), 7.36-7.30 (m, 3H), 6.88 (d, $J = 8.8$ Hz, 2H), 3.83 (s, 3H);

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 159.60, 133.03, 131.43, 128.28, 127.91, 123.59, 113.98, 89.34, 88.05, 55.30.

ESI-MS calculated for [C$_{15}$H$_{13}$O]$^+$: 209.0961, found: 209.0970.

**14m:** Colorless liquid (78% yield).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.53-7.51 (m, 2H), 7.45 (d, $J = 7.9$ Hz, 2H), 7.36-7.31 (m, 3H), 7.18 (d, $J = 7.9$ Hz, 2H), 2.66 (q, $J = 7.6$ Hz, 2H), 1.24 (t, $J = 7.3$ Hz, 3H);

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 144.66, 131.57, 131.53, 128.28, 128.04, 127.89, 123.49, 120.41, 89.57, 88.69, 28.83, 15.34.

ESI-MS calculated for [C$_{16}$H$_{15}$]$^+$: 207.1168, found: 207.1178.

**14n:** White solid (90% yield).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.65-7.59 (m, 4H), 7.56-7.54 (m, 2H), 7.37 (t, $J = 3.2$ Hz, 3H);

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 131.78, 131.73, 129.88 (q, $J = 32.6$ Hz), 128.81, 128.43, 127.12, 125.25 (q, $J = 3.8$ Hz), 123.44 (q, $J = 271.7$ Hz), 122.56, 91.75, 87.96.

$^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ -62.8 (s, 3F).

ESI-MS calculated for [C$_{15}$H$_{10}$F$_3$]$^+$: 247.0729, found: 247.0733.

**14o:** White solid (65% yield).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.53-7.50 (m, 2H), 7.36-7.28 (m, 5H), 7.26 (s, 1H), 2.91 (dd, $J = 8.8$, 4.0 Hz, 2H), 2.51 (dd, $J = 18.7$, 8.6 Hz, 1H), 2.45-2.40 (m, 1H), 2.32 (td, $J = 10.6$, 4.0 Hz, 1H), 2.20-1.96 (m, 4H), 1.69-1.41 (m, 6H), 0.92 (s, 3H);

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 220.65, 162.18, 140.24, 136.59, 132.02, 131.53, 128.91, 128.29, 128.06, 125.37, 123.44, 120.56, 89.46, 88.74, 50.50, 47.93, 44.46, 37.97, 35.82, 31.55, 29.10, 26.34, 25.58, 21.57, 13.83.

ESI-MS calculated for [C$_{26}$H$_{27}$O]$^+$: 355.2056, found: 355.2072.

**14p:** Colorless liquid (82% yield).

Me

Ph

MeO

O

**14q:** MeO

Ph

Et

**14m:** Colorless liquid (78% yield).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.53-7.51 (m, 2H), 7.45 (d, $J = 7.9$ Hz, 2H), 7.36-7.31 (m, 3H), 7.18 (d, $J = 7.9$ Hz, 2H), 2.66 (q, $J = 7.6$ Hz, 2H), 1.24 (t, $J = 7.3$ Hz, 3H);

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 144.66, 131.57, 131.53, 128.28, 128.04, 127.89, 123.49, 120.41, 89.57, 88.69, 28.83, 15.34.

ESI-MS calculated for [C$_{16}$H$_{15}$]$^+$: 207.1168, found: 207.1178.
\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.54-7.51 (m, 2H), 7.37-7.32 (m, 5H), 7.23 (d, \(J = 7.6\) Hz, 1H), 7.15 (d, \(J = 7.7\) Hz, 1H), 2.35 (s, 3H);
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 137.96, 132.15, 131.56, 129.13, 128.65, 128.29, 128.20, 128.13, 123.35, 123.04, 89.55, 89.02, 21.20.
ESI-MS calculated for \([\text{C}_{15}\text{H}_{13}]^+\): 193.1012, found: 193.1021.

\(14\)q: Colorless liquid (81% yield).
\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.55-7.52 (m, 2H), 7.38-7.34 (m, 3H), 7.32-7.30 (m, 2H), 7.23 (dddd, \(J = 9.5, 2.6, 1.1, 0.8\) Hz, 1H), 7.07-7.01 (m, 1H);
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 162.38 (d, \(J = 245.2\) Hz), 131.65, 129.87 (d, \(J = 8.8\) Hz), 128.56, 128.37, 127.46 (d, \(J = 3.1\) Hz), 125.12 (d, \(J = 9.3\) Hz), 122.77, 118.33 (d, \(J = 22.8\) Hz), 115.54 (d, \(J = 21.2\) Hz), 90.24, 88.07.
\(^{19}\)F NMR (376 MHz, CDCl\(_3\)): \(\delta\) -113.0 (m, 1F).
ESI-MS calculated for \([\text{C}_{14}\text{H}_{10}\text{F}]^+\): 197.0761, found: 197.0771.

\(18a\): White solid (91% yield).
\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.52-7.45 (m, 1H), 7.10 (t, \(J = 8.8\) Hz, 1H), 6.97 (d, \(J = 8.8\) Hz, 1H);
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 162.08 (d, \(J = 244.4\) Hz), 159.10, 136.96 (d, \(J = 3.1\) Hz), 132.83, 128.20 (d, \(J = 8.2\) Hz), 128.02, 115.51 (d, \(J = 21.3\) Hz), 114.24, 55.35.
\(^{19}\)F NMR (376 MHz, CDCl\(_3\)): \(\delta\) -116.8 (m, 1F).
ESI-MS calculated for \([\text{C}_{13}\text{H}_{12}\text{FO}]^+\): 203.0867, found: 203.0875.

\(18b\): White solid (90% yield).
\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.56-7.52 (m, 4H), 7.41 (t, \(J = 7.6\) Hz, 2H), 7.32-7.28 (m, 1H), 6.98 (d, \(J = 8.9\) Hz, 2H), 3.85 (s, 3H);
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 159.40, 139.73, 132.49, 131.77, 128.70, 128.14, 126.72, 126.63, 114.19, 55.36.
ESI-MS calculated for \([\text{C}_{13}\text{H}_{13}\text{O}]^+\): 185.0961, found: 185.0969.

\(18c\): White solid (76% yield).
\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.53 (d, \(J = 8.7\) Hz, 2H), 7.48 (d, \(J = 8.9\) Hz, 2H), 7.41 (d, \(J = 8.7\) Hz, 2H), 6.97 (d, \(J = 8.9\) Hz, 2H), 3.85 (s, 3H);
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 159.40, 139.73, 132.49, 131.77, 128.28, 127.97, 120.77, 114.32, 55.36.
ESI-MS calculated for \([\text{C}_{13}\text{H}_{12}\text{BrO}]^+\): 263.0066, found: 263.0076.
18d: White solid (72% yield).
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.67-7.62 (m, 6H), 7.58 (d, $J$ = 8.9 Hz, 2H), 7.45 (t, $J$ = 7.6 Hz, 2H), 7.35 (tt, $J$ = 7.4, 1.6 Hz, 1H), 7.00 (d, $J$ = 8.8 Hz, 2H), 3.86 (s, 3H);
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 167.01, 159.81, 145.17, 132.37, 130.07, 128.32, 126.42, 114.34, 55.34, 52.03.
ESI-MS calculated for [C$_{19}$H$_{17}$O]$^+$: 261.1274, found: 261.1281.

18e: White solid (63% yield).
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.43 (dd, $J$ = 8.7, 1.7 Hz, 2H), 7.36 (td, $J$ = 8.7, 6.5 Hz, 1H), 6.98 (d, $J$ = 8.8 Hz, 2H), 6.95-6.86 (m, 2H), 3.85 (s, 3H);
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 161.90 (dd, $J$ = 246.9, 11.5 Hz), 159.64 (dd, $J$ = 248.6, 11.6 Hz), 159.25, 131.11 (dd, $J$ = 9.3, 4.8 Hz), 130.00 (d, $J$ = 2.9 Hz), 127.34 (d, $J$ = 1.2 Hz), 124.98 (dd, $J$ = 13.8, 4.0 Hz), 113.99, 111.42 (dd, $J$ = 21.2, 3.8 Hz), 104.28 (dd, $J$ = 25.2, 27.2 Hz), 55.32.
$^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ -112.4 (dt, $J$ = 15.4, 7.8 Hz), -113.9 (dd, $J$ = 17.7, 8.7 Hz).
ESI-MS calculated for [C$_{13}$H$_{11}$F$_3$O]$^+$: 221.0772, found: 221.0783.

18f: White solid (81% yield).
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.82-7.79 (m, 1H), 7.75-7.73 (m, 1H), 7.64 (d, $J$ = 8.9 Hz, 2H), 7.42 (d, $J$ = 0.7 Hz, 1H), 7.35-7.26 (m, 2H), 6.96 (d, $J$ = 8.9 Hz, 2H), 3.86 (s, 3H);
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 159.78, 144.12, 140.86, 139.16, 127.73, 127.04, 124.41, 123.91, 123.22, 122.15, 118.18, 114.34, 55.38.
ESI-MS calculated for [C$_{13}$H$_{13}$OS]$^+$: 241.0682, found: 241.0692.

18g: White solid (62% yield).
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.82-7.79 (m, 1H), 7.75-7.73 (m, 1H), 7.64 (d, $J$ = 8.9 Hz, 2H), 7.42 (d, $J$ = 0.7 Hz, 1H), 7.35-7.26 (m, 2H), 6.96 (d, $J$ = 8.9 Hz, 2H), 3.86 (s, 3H);
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 159.78, 144.12, 140.86, 139.16, 127.73, 127.04, 124.41, 123.91, 123.22, 122.15, 118.18, 114.34, 55.38.
ESI-MS calculated for [C$_{13}$H$_{13}$OS]$^+$: 241.0682, found: 241.0692.
**18h**: White solid (42% yield).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.53 (d, $J = 8.9$ Hz, 2H), 7.38-7.33 (m, 3H), 6.94 (d, $J = 8.9$ Hz, 2H), 3.84 (s, 3H);

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 158.86, 142.00, 128.74, 127.54, 126.23, 126.03, 118.91, 114.17, 55.33.

ESI-MS calculated for [C$_{11}$H$_{11}$OS]$^+$: 191.0525, found: 191.0534.

**18i**: White solid (83% yield), previously reported (Döbele, M.; Vanderheiden, S.; Jung, N.; Bräse, S. Angew. Chem. Int. Ed. 2010, 49, 5986).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.52 (dd, $J = 8.9, 5.4$ Hz, 2H), 7.43 (d, $J = 8.2$ Hz, 2H), 7.23 (dd, $J = 7.7, 0.7$ Hz, 2H), 7.10 (t, $J = 8.8$ Hz, 2H), 2.39 (s, 3H);

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 162.27 (d, $J = 246.0$ Hz), 137.36, 137.24 (d, $J = 3.1$ Hz), 137.00, 129.50, 128.43 (d, $J = 8.2$ Hz), 126.82, 115.50 (d, $J = 21.3$ Hz), 21.04.

$^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ -116.4 (m, 1F).


$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.57 (d, $J = 7.5$ Hz, 2H), 7.48 (t, $J = 7.9$ Hz, 2H), 7.42 (t, $J = 7.7$ Hz, 2H), 7.32 (t, $J = 7.3$ Hz, 1H), 7.25 (d, $J = 8.0$ Hz, 2H), 2.39 (s, 3H);

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 141.14, 138.34, 136.98, 129.45, 129.40, 128.68, 126.97, 126.94, 21.08.

**18k**: White solid (72% yield), previously reported (Lü, B.; Fu, C.; Ma, S. Tetrahedron Lett. 2010, 51, 1284).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.51 (d, $J = 8.8$ Hz, 2H), 7.44 (d, $J = 8.2$ Hz, 2H), 7.22 (d, $J = 7.8$ Hz, 2H), 6.96 (d, $J = 8.8$ Hz, 2H), 3.84 (s, 3H), 2.38 (s, 3H);

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 158.90, 137.94, 136.31, 133.72, 129.45, 129.40, 128.68, 126.97, 126.94, 21.08.

**18l**: White solid (93% yield), reported previously (Cheng, K.; Wang, C.; Ding, Y.; Song, Q.; Qi, C.; Zhang, X.-M. J. Org. Chem. 2011, 76, 9261).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.47 (d, $J = 8.2$ Hz, 2H), 7.38-7.34 (m, 2H), 7.29-7.24 (m, 3H), 7.03-6.98 (m, 1H), 2.40 (s, 3H);

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 163.11 (d, $J = 243.8$ Hz), 143.42 (d, $J = 7.6$ Hz), 137.68,
137.03, 130.20 (d, J = 8.4 Hz), 129.57, 126.89, 122.50 (d, J = 2.9 Hz), 113.75 (d, J = 21.5 Hz), 113.69 (d, J = 21.0 Hz), 21.09.

$^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ -113.4 (m, 1F).

19a: Yellow liquid (68% yield brsm).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.38 (dd, J = 7.6, 1.7 Hz, 1H), 7.27-7.22 (m, 1H), 6.91-6.84 (m, 2H), 6.07 (ddt, J = 17.2, 10.6, 4.8 Hz, 1H), 5.52 (dq, J = 17.2, 1.7 Hz, 1H), 5.29 (dq, J = 10.6, 1.6 Hz, 1H), 4.58 (dt, J = 4.8, 1.7 Hz, 2H), 2.17 (br s, 1H), 1.63 (s, 6H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 159.08, 133.43, 132.98, 132.96, 129.55, 120.65, 116.95, 112.53, 112.42, 97.99, 78.41, 69.11, 65.73, 31.50.

ESI-MS calculated for [C$_{14}$H$_{17}$O$_2$]$^+$: 217.1223, found: 217.1231.

19b: Yellow liquid (23% yield).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.38 (d, J = 1.0 Hz, 1H), 7.33 (dd, J = 8.0, 1.7 Hz, 1H), 7.28-7.26 (m, 1H), 7.17 (d, J = 0.6 Hz, 1H), 7.06 (d, J = 8.4 Hz, 1H), 6.98 (t, J = 7.6 Hz, 1H), 6.89 (t, J = 7.4 Hz, 1H), 6.85 (t, J = 6.8 Hz, 1H), 6.11 (ddt, J = 17.3, 10.5, 5.2 Hz, 1H), 5.45 (dq, J = 17.3, 1.6 Hz, 1H), 5.32 (dq, J = 10.6, 1.4 Hz, 1H), 4.79-4.74 (m, 3H), 4.53 (ddd, J = 17.6, 11.4, 6.1 Hz, 2H), 4.31 (dd, J = 13.2, 8.7 Hz, 1H), 4.17-4.10 (m, 1H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 160.17, 155.04, 141.85, 133.00, 131.82, 128.62, 128.30, 124.83, 120.92, 120.49, 117.85, 117.28, 114.36, 109.65, 75.29, 73.13, 69.99, 41.18.

ESI-MS calculated for [C$_{18}$H$_{19}$N$_2$O$_2$]$^+$: 295.1441, found: 295.1434.

Compounds 23a to 23g are commercially available and volatile compounds. 23h,$^{[7]}$ 23i,$^{[8]}$ 23j,$^{[9]}$ 23k,$^{[10]}$ 23m,$^{[11]}$ 23n,$^{[12]}$ 23o,$^{[13]}$ 23p,$^{[14]}$ 23r,$^{[15]}$ 23s,$^{[16]}$ 28a, 28c,$^{[17]}$ 28d, 28e,$^{[18]}

17 He, Y.; Wu, H.; Toste, F. D. Chem. Sci., 2015, 6, 1194.
28g,\textsuperscript{[19]} and 28h\textsuperscript{[20]} were reported in literature.

![Chemical structure](image)

23a: CAS: 460-00-4, GC-MS: 174.0, 95.1, 87.1, 75.1, 68.1, 50.1.

![Chemical structure](image)

23b: CAS: 104-92-7, GC-MS: 187.8, 170.8, 142.9, 118.9, 92.0, 77.0, 63.0.

![Chemical structure](image)

23c: CAS: 106-38-7, GC-MS: 169.9, 91.0, 65.0.

![Chemical structure](image)

23d: CAS: 402-43-7, GC-MS: 223.8, 204.8, 173.8, 144.9, 125.0, 95.0, 75.0.

![Chemical structure](image)

23e: CAS: 589-87-7, GC-MS: 281.6, 154.8, 140.9, 126.8, 75.0.

![Chemical structure](image)

23f: CAS: 106-37-6, GC-MS: 235.7, 154.8, 117.9, 75.0.

![Chemical structure](image)

23g: CAS: 108-86-1, GC-MS: 155.8, 77.0, 51.0.

![Chemical structure](image)

23h: \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): $\delta$ 7.82 (dt, $J$ = 1.6, 8.4 Hz, 2H), 7.61 (dt, $J$ = 1.6, 8.8 Hz, 2H), 2.61 (s, 3H).

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): $\delta$ 197.0, 135.8, 131.9, 129.8, 128.3, 26.5.


$23i$: $^1H$ NMR (400 MHz, CDCl$_3$): δ 7.77 (d, $J = 7.2$ Hz, 2H), 7.67 (dt, $J = 2.0$, 8.8 Hz, 2H), 7.61 (m, 3H), 7.49 (t, $J = 7.6$ Hz, 2H).

$^{13}C$ NMR (100 MHz, CDCl$_3$): δ 195.6, 137.1, 136.3, 132.6, 131.6, 131.5, 129.9, 128.4, 127.5.

$23j$: $^1H$ NMR (400 MHz, CDCl$_3$): δ 7.81 (dd, $J = 1.2$, 8.4 Hz, 2H), 7.63 (m, 2H), 7.45 (m, 3H), 7.35 (m, 2H).

$^{13}C$ NMR (100 MHz, CDCl$_3$): δ 195.9, 140.7, 136.1, 133.8, 133.2, 131.2, 130.3, 129.0, 128.7, 127.2, 119.5.

$23k$: $^1H$ NMR (400 MHz, CDCl$_3$): δ 7.04 (s, 1H), 7.03 (s, 1H), 6.04 (s, 2H), 2.61 (s, 3H).

$^{13}C$ NMR (100 MHz, CDCl$_3$): δ 199.4, 150.3, 147.3, 134.2, 113.8, 109.8, 102.4, 33.8, 30.2.

$23l$: $^1H$ NMR (400 MHz, CDCl$_3$): δ 7.45 (m, 3H), 6.29 (q, $J = 1.6$ Hz, 1H), 2.38 (q, $J = 1.6$ Hz, 3H).

$^{13}C$ NMR (100 MHz, CDCl$_3$): δ 159.9, 153.7, 151.8, 127.5, 125.6, 125.5, 120.1, 118.9, 115.2, 18.5.

HRMS: m/z (ESI) Calculated for [M+H]$^+$ 238.9708, Found 238.9688.

$23m$: $^1H$ NMR (400 MHz, CDCl$_3$): δ 9.13 (d, $J = 2.0$ Hz, 1H), 8.84 (d, $J = 2.0$ Hz, 1H), 8.43 (d, $J = 2.0$ Hz, 1H), 3.97 (s, 3H).

$^{13}C$ NMR (100 MHz, CDCl$_3$): δ 164.5, 154.5, 148.8, 139.5, 127.3, 120.6, 52.7.
23n: \( ^1\text{H NMR (400 MHz, DMSO-}d_6\text{)}: \delta 8.30\ (d, J = 2.4\ Hz, 1H), 8.27\ (d, J = 2.4\ Hz, 1H), 3.88\ (s, 3H). \)

23o: \( ^1\text{H NMR (500 MHz, CDCl}_3\text{)}: \delta 7.99\ (d, J = 7.0\ Hz, 1H), 7.81\ (dd, J = 1.5, 8.5\ Hz, 1H), 7.47\ (dt, J = 1.0, 8.5\ Hz, 1H), 7.42\ (dt, J = 1.5, 8.0\ Hz, 1H). \)

\( ^{13}\text{C NMR (125 MHz, CDCl}_3\text{)}: \delta 152.3, 138.9, 137.3, 126.6, 125.7, 122.8, 120.9. \)

23p: \( ^1\text{H NMR (500 MHz, CDCl}_3\text{)}: \delta 8.20\ (d, J = 2.0\ Hz, 1H), 8.04\ (d, J = 3.0\ Hz, 1H), 7.53\ (dd, J = 2.0, 9.0\ Hz, 1H), 7.47\ (dd, J = 1.0, 7.0\ Hz, 1H), 7.40\ (d, J = 8.0\ Hz, 1H), 7.26\ (m, 2H), 4.34\ (q, J = 7.5\ Hz, 2H), 1.4\ (t, J = 7.5\ Hz, 3H). \)

\( ^{13}\text{C NMR (125 MHz, CDCl}_3\text{)}: \delta 140.2, 138.5, 128.2, 126.3, 124.7, 123.1, 121.9, 120.6, 119.2, 111.5, 109.9, 108.7, 37.7, 13.7. \)

23q: \( ^1\text{H NMR (400 MHz, CDCl}_3\text{)}: \delta 7.55\ (s, 1H), 7.59\ (m, 3H), 7.31\ (m, 2H), 7.23\ (m, 1H), 2.69\ (s, 3H), 2.46\ (s, 3H). \)

\( ^{13}\text{C NMR (100 MHz, CDCl}_3\text{)}: \delta 152.0, 150.6, 138.8, 138.3, 133.0, 131.4, 131.2, 127.6, 126.5, 125.3, 121.4, 115.4, 23.1, 17.6. \)


23r: \( ^1\text{H NMR (500 MHz, CDCl}_3\text{)}: \delta 7.52\ (d, J = 8.0\ Hz, 2H), 7.41\ (d, J = 8.0\ Hz, 2H), 0.33\ (s, 9H). \)

\( ^{13}\text{C NMR (125 MHz, CDCl}_3\text{)}: \delta 133.4, 131.5, 122.7, 122.1, 103.8, 95.6, 29.7, -0.1. \)

23s: \( ^1\text{H NMR (500 MHz, CDCl}_3\text{)}: \delta 8.20\ (d, J = 2.0\ Hz, 1H), 8.04\ (d, J = 3.0\ Hz, 1H), \)
7.61 (d, \( J = 16.0 \) Hz, 1H), 7.52 (d, \( J = 8.0 \) Hz, 2H), 7.38 (d, \( J = 8.0 \) Hz, 2H), 6.42 (d, \( J = 16.0 \) Hz, 1H), 4.26 (q, \( J = 7.5 \) Hz, 2H), 1.33 (t, \( J = 7.5 \) Hz, 3H).

\(^{13}\text{C} \) NMR (125 MHz, CDCl\(_3\)): \( \delta \) 166.7, 143.2, 133.4, 132.1, 129.4, 124.4, 119.0, 60.6, 14.3.

23t: \(^1\text{H} \) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.94 (dd, \( J = 2.0, 6.4 \) Hz, 2H), 7.53 (dd, \( J = 2.0, 6.4 \) Hz, 2H), 7.23 (d, \( J = 8.4 \) Hz, 1H), 6.88 (dd, \( J = 2.8, 8.4 \) Hz, 1H), 6.84 (d, \( J = 2.8 \) Hz, 1H), 2.83 (dd, \( J = 4.4 \) Hz, 2H), 2.42 (d, \( J = 8.4 \) Hz, 1H), 2.32 (m, 2H), 2.20 (m, 1H), 1.97 (m, 4H), 1.41 (m, 6H), 0.83 (s, 3H).

\(^{13}\text{C} \) NMR (100 MHz, CDCl\(_3\)): \( \delta \) 220.5, 164.5, 148.5, 138.0, 137.5, 131.7, 131.5, 131.4, 128.5, 126.4, 121.4, 118.6, 50.4, 47.9, 44.2, 38.0, 35.9, 31.5, 29.4, 26.3, 25.7, 21.6, 13.8.

HRMS: m/z (ESI) Calculated for [M+H]\(^+\) 453.1065, Found 453.1061.

27a: \(^1\text{H} \) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.39 (dd, \( J = 5.6, 9.2 \) Hz, 2H), 6.96 (t, \( J = 8.8 \) Hz, 2H), 5.35 (d, \( J = 7.6 \) Hz, 1H), 4.50 (m, 1H), 3.53 (s, 3H), 3.27 (m, 2H), 1.38 (s, 9H).

\(^{13}\text{C} \) NMR (100 MHz, CDCl\(_3\)): \( \delta \) 170.9, 162.1 (d, \( J = 246.0 \) Hz), 154.8, 133.9 (dd, \( J = 8.0, 13.2 \) Hz), 129.6, 116.0 (d, \( J = 21.7 \) Hz), 80.0, 53.2, 52.2 (d, \( J = 12.2 \) Hz), 38.1, 28.1 (d, \( J = 6.8 \) Hz).

HRMS: m/z (ESI) Calculated for [M+Na]\(^+\) 352.0995, Found 352.0983.

27b: \(^1\text{H} \) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.39 (dt, \( J = 2.0, 7.2 \) Hz, 2H), 6.83 (dt, \( J = 2.0, 7.2 \) Hz, 2H), 5.35 (d, \( J = 6.0 \) Hz, 1H), 4.50 (m, 1H), 3.78 (s, 3H), 3.54 (s, 3H), 3.25 (d, \( J = 4.0 \) Hz, 2H), 1.42 (s, 9H).

\(^{13}\text{C} \) NMR (125 MHz, CDCl\(_3\)): \( \delta \) 171.1, 159.4, 154.9, 134.4, 124.7, 114.6, 79.9, 55.2, 53.1, 52.2, 38.7, 28.2.

HRMS: m/z (ESI) Calculated for [M+Na]\(^+\) 364.1195, Found 364.1185.

27c: \(^1\text{H} \) NMR (500 MHz, CDCl\(_3\)): \( \delta \) 7.31 (d, \( J = 8.0 \) Hz, 2H), 7.09 (d, \( J = 8.0 \) Hz, 2H), 5.37 (d, \( J = 7.0 \) Hz, 1H), 4.53 (m, 1H), 3.54 (s, 3H), 3.31 (d, \( J = 5.0 \) Hz, 2H), 2.31 (s, 3H),
1.41 (s, 9H).

$^{13}$C NMR (125 MHz, CDCl$_3$): δ 171.0, 154.9, 137.1, 131.6, 130.8, 129.7, 79.9, 53.2, 52.2, 37.7, 28.1, 20.9.


![Chemical Structure](image)

$^{27d}$: $^1$H NMR (500 MHz, CDCl$_3$): δ 7.41 (d, $J = 8.0$ Hz, 2H), 7.28 (t, $J = 8.0$ Hz, 2H), 7.21 (t, $J = 7.5$ Hz, 1H), 5.39 (d, $J = 7.0$ Hz, 1H), 4.56 (m, 1H), 3.53 (s, 3H), 3.37 (m, 2H), 1.42 (s, 9H).

$^{13}$C NMR (125 MHz, CDCl$_3$): δ 171.0, 154.9, 134.7, 131.0, 129.0, 127.0, 80.1, 53.2, 52.3, 37.2, 28.2.


![Chemical Structure](image)

$^{27e}$: $^1$H NMR (400 MHz, CDCl$_3$): δ 7.52 (d, $J = 8.4$ Hz, 2H), 7.46 (d, $J = 8.4$ Hz, 2H), 5.34 (d, $J = 6.4$ Hz, 1H), 4.56 (m, 1H), 3.59 (s, 3H), 3.35 (m, 2H), 1.41 (s, 9H).

$^{13}$C NMR (125 MHz, CDCl$_3$): δ 170.7, 154.9, 140.5, 129.3, 128.5 (q, $J = 26.2$ Hz), 125.7, (d, $J = 2.7$ Hz), 124.0 (q, $J = 216.3$ Hz), 80.3, 53.3, 52.5, 36.0, 28.2.


![Chemical Structure](image)

$^{27f}$: $^1$H NMR (400 MHz, CDCl$_3$): δ 7.60 (dd, $J = 2.0$, 6.8 Hz, 2H), 7.14 (dt, $J = 1.6$, 6.8 Hz, 2H), 5.29 (d, $J = 8.0$ Hz, 1H), 4.57 (m, 1H), 3.60 (s, 3H), 3.37 (m, 2H), 1.42 (s, 9H).

$^{13}$C NMR (125 MHz, CDCl$_3$): δ 170.8, 154.8, 138.0, 132.5, 92.1, 80.2, 53.3, 52.5, 37.0, 28.2.


![Chemical Structure](image)

$^{27g}$: $^1$H NMR (500 MHz, CDCl$_3$): δ 7.40 (dt, $J = 2.5$, 9.0 Hz, 2H), 7.27 (dt, $J = 2.0$, 8.5 Hz, 2H), 5.35 (d, $J = 7.5$ Hz, 1H), 4.56 (m, 1H), 3.59 (s, 3H), 3.35 (m, 2H), 1.41 (s, 9H).

$^{13}$C NMR (125 MHz, CDCl$_3$): δ 170.8, 154.8, 134.0, 132.4, 132.0, 120.9, 80.1, 53.2, 52.4, 37.1, 28.2.

**27h:** $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.87 (d, $J = 8.5$ Hz, 2H), 7.40 (d, $J = 8.5$ Hz, 2H), 5.32 (d, $J = 7.5$ Hz, 1H), 4.57 (m, 1H), 3.56 (s, 3H), 3.37 (m, 2H), 2.57 (s, 3H), 1.41 (s, 9H).
$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 197.0, 170.7, 154.9, 142.4, 134.7, 128.8, 128.1, 80.3, 53.2, 52.6, 35.4, 28.2, 26.5.

**27i:** $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.76 (d, $J = 7.6$ Hz, 2H), 7.73 (d, $J = 8.4$ Hz, 2H), 7.59 (t, $J = 7.6$ Hz, 1H), 7.49 (d, $J = 7.6$ Hz, 2H), 7.43 (d, $J = 8.4$ Hz, 2H), 5.41 (d, $J = 6.8$ Hz, 1H), 4.65 (m, 1H), 3.66 (s, 3H), 3.47 (m, 2H), 1.43 (s, 9H).
$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 195.6, 170.8, 154.9, 141.6, 137.5, 135.0, 132.4, 130.6, 129.8, 128.3, 127.9, 80.3, 53.2, 52.5, 35.4, 28.2.

**27j:** $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 6.97 (d, $J = 2.0$ Hz, 1H), 6.92 (dd, $J = 2.0$, 6.4 Hz, 1H), 6.78 (d, $J = 6.8$ Hz, 1H), 5.34 (d, $J = 5.6$ Hz, 1H), 4.51 (m, 1H), 4.23 (s, 4H), 3.61 (s, 3H), 3.26 (m, 2H), 1.42 (s, 9H).
$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 171.1, 154.9, 143.6, 143.4, 125.8, 121.4, 117.8, 79.9, 64.3, 64.2, 53.2, 52.3, 38.4, 28.2.

**27k:** $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 9.05 (s, 1H), 8.76 (d, $J = 1.5$ Hz, 1H), 8.31 (s, 1H), 5.39 (d, $J = 7.5$ Hz, 1H), 4.60 (m, 1H), 3.96 (s, 3H), 3.64 (s, 3H), 3.46 (m, 2H), 1.41 (s, 9H).
$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 170.6, 165.1, 154.6, 148.7, 138.6, 132.7, 126.1, 80.4, 53.2, 52.6, 36.9, 28.2.
**27l:** $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.53 (s, 1H), 7.65 (dd, $J = 1.6$, 7.6 Hz, 1H), 7.10 (d, $J = 8.4$ Hz, 1H), 5.38 (d, $J = 6.8$ Hz, 1H), 4.53 (m, 1H), 3.60 (s, 3H), 3.33 (m, 2H), 2.53 (s, 3H), 1.41 (s, 9H).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 170.6, 157.4, 154.8, 151.8, 139.8, 128.2, 123.4, 80.1, 53.2, 37.8, 28.2, 23.9.


**27m:** $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.17 (dd, $J = 1.6$, 7.6 Hz, 1H), 7.10 (d, $J = 8.4$ Hz, 1H), 5.38 (d, $J = 6.8$ Hz, 1H), 4.53 (m, 1H), 3.60 (s, 3H), 3.33 (m, 2H), 2.53 (s, 3H), 1.41 (s, 9H).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 170.8, 159.8, 154.8, 149.6, 145.9, 123.9, 106.9, 80.3, 54.7, 53.3, 52.5, 38.9, 28.2.


**27n:** $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.87 (d, $J = 8.0$ Hz, 1H), 7.75 (d, $J = 8.0$ Hz, 1H), 7.42 (t, $J = 7.5$ Hz, 1H), 7.31 (t, $J = 7.5$ Hz, 1H), 6.19 (d, $J = 7.5$ Hz, 1H), 4.75 (dd, $J = 5.5$, 12.0 Hz, 1H), 3.82 (d, $J = 5.0$ Hz, 2H), 3.73 (s, 3H), 1.41 (s, 9H).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 170.9, 152.7, 135.5, 127.1, 126.2, 124.6, 121.6, 121.0, 111.8, 80.0, 53.9, 52.7, 35.4, 28.2.


**27o:** $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.35 (d, $J = 8.5$ Hz, 2H), 7.29 (d, $J = 8.0$ Hz, 2H), 5.32 (d, $J = 7.5$ Hz, 1H), 4.57 (m, 1H), 3.56 (s, 3H), 3.37 (m, 2H), 1.41 (s, 9H), 0.23 (s, 9H).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 170.8, 154.9, 135.8, 132.3, 129.8, 121.5, 104.4, 95.1, 80.2, 53.2, 52.4, 36.6, 28.2, -0.1.

**27p:** $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.68 (d, $J = 16.5$ Hz, 1H), 7.58 (s, 4H), 6.47 (d, $J = 16.5$ Hz, 1H), 5.53 (d, $J = 7.5$ Hz, 1H), 4.76 (m, 1H), 4.27 (q, $J = 7.0$ Hz, 2H), 3.96 (m, 2H), 3.73 (s, 3H), 1.42 (s, 9H), 1.34 (t, $J = 7.5$ Hz, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 170.9, 166.6, 154.9, 152.1, 143.2, 135.8, 128.8, 122.0, 119.4, 80.1, 60.6, 53.2, 52.6, 36.7, 28.2, 14.2.


**Z-27q:** $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.62 (d, $J = 15.5$ Hz, 1H), 7.43 (d, $J = 8.5$ Hz, 2H), 7.37 (d, $J = 8.0$ Hz, 2H), 6.40 (d, $J = 15.5$ Hz, 1H), 5.38 (d, $J = 7.5$ Hz, 1H), 4.60 (m, 1H), 4.26 (q, $J = 7.0$ Hz, 2H), 3.60 (s, 3H), 3.41 (m, 2H), 1.41 (s, 9H), 1.34 (t, $J = 7.0$ Hz, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 170.7, 166.8, 154.8, 152.1, 143.5, 132.6, 129.8, 128.4, 118.1, 80.0, 60.5, 53.2, 52.4, 36.2, 28.2, 14.2.


**E-27q:** $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.73 (s, 1H), 7.72 (d, $J = 8.0$ Hz, 1H), 7.60 (d, $J = 8.4$ Hz, 1H), 7.46 (d, $J = 8.0$ Hz, 1H), 7.35 (m, 2H), 7.24 (m, 1H), 5.38 (d, $J = 7.6$ Hz, 1H), 4.65 (m, 1H), 3.63 (s, 3H), 3.45 (m, 2H), 2.71 (s, 3H), 2.47 (s, 3H), 1.43 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 170.9, 154.9, 151.2, 150.7, 138.7, 138.0, 131.2, 130.8, 129.2, 129.1, 126.3, 124.4, 121.0, 115.3, 80.2, 53.2, 52.5, 35.8, 29.6, 28.2, 20.6, 17.4.


**28a:** $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.83 (ddd, $J = 5.6$, 8.4, 13.6 Hz, 2H), 7.15 (ddd, $J = 3.2$, 9.2 Hz, 2H), 4.12 (m, 4H), 1.33 (t, $J = 7.2$ Hz, 6H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 165.3 (d, $J = 199.3$ Hz), 134.3 (t, $J = 9.1$ Hz), 124.4 (d, $J = 150.7$ Hz), 115.8 (dd, $J = 12.9$, 16.6 Hz), 62.1 (d, $J = 3.8$ Hz), 16.2 (d, $J = 4.9$ Hz).
28b: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.75 (dd, $J = 8.8$, 12.4 Hz, 2H), 6.97 (dd, $J = 3.6$, 8.8 Hz, 2H), 4.09 (m, 4H), 3.85 (s, 3H), 1.31 (t, $J = 6.8$ Hz, 6H).
$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 162.8, 133.8 (d, $J = 11.4$ Hz), 119.5 (d, $J = 193.6$ Hz), 114.0 (d, $J = 15.6$ Hz), 61.9 (d, $J = 5.2$ Hz), 53.3, 16.3 (d, $J = 6.6$ Hz).
HRMS: m/z (ESI) Calculated for [M+H]$^+$ 245.0943, Found 245.0931.

28c: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.70 (dd, $J = 8.0$, 13.0 Hz, 2H), 7.27 (dd, $J = 3.5$, 8.0 Hz, 2H), 4.10 (m, 4H), 2.40 (s, 3H), 1.31 (t, $J = 7.0$ Hz, 6H).
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 142.9 (d, $J = 2.3$ Hz), 131.8 (t, $J = 7.9$ Hz), 129.2 (d, $J = 12.1$ Hz), 124.9 (d, $J = 155.0$ Hz), 61.9 (d, $J = 4.2$ Hz), 21.6, 16.3 (d, $J = 5.3$ Hz).

28d: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.83 (dd, $J = 3.6$, 8.4 Hz, 2H), 7.52 (dd, $J = 8.0$, 12.8 Hz, 2H), 4.11 (m, 4H), 1.32 (t, $J = 7.2$ Hz, 6H).
$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 137.7 (d, $J = 15.2$ Hz), 133.1 (d, $J = 10.4$ Hz), 128.0 (d, $J = 188.8$ Hz), 100.1 (d, $J = 3.9$ Hz), 62.3 (d, $J = 5.3$ Hz), 16.3 (d, $J = 6.2$ Hz).

28e: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.65 (m, 4H), 4.12 (m, 4H), 1.32 (t, $J = 7.2$ Hz, 6H).
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 133.2 (d, $J = 8.3$ Hz), 131.7 (d, $J = 12.1$ Hz), 127.5 (d, $J = 3.1$ Hz), 127.4 (d, $J = 151.9$ Hz), 62.2 (d, $J = 4.2$ Hz), 16.2 (d, $J = 5.4$ Hz).

28f: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.75 (dd, $J = 8.4$, 13.2 Hz, 2H), 7.45 (dd, $J = 3.6$, 8.4 Hz, 2H), 4.11 (m, 4H), 1.32 (t, $J = 7.2$ Hz, 6H).
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 138.9 (d, $J = 3.0$ Hz), 133.1 (d, $J = 8.7$ Hz), 128.8 (d, $J = 12.5$ Hz), 126.9 (d, $J = 151.8$ Hz), 62.2 (d, $J = 4.2$ Hz), 16.2 (d, $J = 5.4$ Hz).
**28g**: $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.94 (dd, $J = 8.0$, 12.8 Hz, 1H), 7.85 (m, 1H), 7.81 (m, 3H), 7.63 (m, 2H), 7.51 (m, 2H), 4.15 (m, 4H), 1.36 (t, $J = 7.2$ Hz, 6H).

**28h**: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.75 (dd, $J = 8.4$, 13.2 Hz, 2H), 7.45 (dd, $J = 3.6$, 8.4 Hz, 2H), 4.11 (m, 4H), 1.32 (t, $J = 7.2$ Hz, 6H).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 138.9 (d, $J = 3.0$ Hz), 133.1 (d, $J = 8.7$ Hz), 128.8 (d, $J = 12.5$ Hz), 126.9 (d, $J = 151.8$ Hz), 62.2 (d, $J = 4.2$ Hz), 16.2 (d, $J = 5.4$ Hz).

**28i**: $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.74 (dd, $J = 8.5$, 13.5 Hz, 2H), 7.54 (dd, $J = 3.5$, 8.5 Hz, 2H), 4.10 (m, 4H), 1.32 (t, $J = 7.2$ Hz, 6H), 0.25 (s, 9H).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 131.8 (d, $J = 14.6$ Hz), 131.5 (d, $J = 9.9$ Hz), 128.2 (d, $J = 188.3$ Hz), 127.3 (d, $J = 3.3$ Hz), 103.8, 97.4, 62.2 (d, $J = 5.3$ Hz), 16.3 (d, $J = 6.7$ Hz), 14.3.

HRMS: m/z (ESI) Calculated for [M+H]$^+$ 311.1232, Found 311.1220.

**28j**: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.83 (dd, $J = 8.0$, 12.8 Hz, 2H), 7.78 (d, $J = 16.0$ Hz, 1H), 7.60 (dd, $J = 3.6$, 8.0 Hz, 2H), 6.51 (d, $J = 16.0$ Hz, 1H), 4.28 (q, $J = 7.2$ Hz, 2H), 4.13 (m, 4H), 1.35 (t, $J = 7.2$ Hz, 3H), 1.33 (t, $J = 7.2$ Hz, 6H).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 166.5, 143.1, 138.2 (d, $J = 3.3$ Hz), 132.3 (d, $J = 10.0$ Hz), 127.8 (d, $J = 15.2$ Hz), 120.7, 130.1 (d, $J = 187.9$ Hz), 62.3 (d, $J = 5.6$ Hz), 60.8, 16.3 (d, $J = 6.6$ Hz), 14.3.

HRMS: m/z (ESI) Calculated for [M+H]$^+$ 313.1205, Found 313.1200.
**(E)-28k**: $^1$H NMR (500 MHz, CDCl$_3$): δ 8.07 (dd, $J = 8.5, 13.5$ Hz, 1H), 7.76 (m, 2H), 7.76 (d, $J = 8.0$ Hz, 1H), 7.38 (m, 2H), 7.27 (dt, $J = 2.0, 8.0$ Hz, 1H), 4.16 (m, 4H), 2.74 (s, 3H), 2.69 (s, 3H), 1.36 (t, $J = 6.5$ Hz, 6H).

$^{13}$C NMR (125 MHz, CDCl$_3$): δ 155.0 (d, $J = 4.3$ Hz), 150.7, 143.1, 138.7, 135.0 (d, $J = 13.6$ Hz), 130.2 (d, $J = 188.6$ Hz), 131.4, 126.4, 125.4 (d, $J = 19.5$ Hz), 119.4 (d, $J = 19.0$ Hz), 115.4, 62.0 (d, $J = 6.6$ Hz), 21.3 (d, $J = 4.2$ Hz), 17.6, 16.3 (d, $J = 7.8$ Hz).

HRMS: m/z (ESI) Calculated for [M+H]$^+$ 347.1525, Found 347.1510.

**(Z)-28k**: $^1$H NMR (500 MHz, CDCl$_3$): δ 7.72 (dd, $J = 8.0, 13.5$ Hz, 1H), 7.18 (d, $J = 8.0$ Hz, 1H), 7.06 (t, $J = 7.5$ Hz, 1H), 6.91 (t, $J = 8.0$ Hz, 1H), 6.83 (dd, $J = 1.5, 5.0$ Hz, 1H), 6.54 (dt, $J = 2.5, 7.5$ Hz, 1H), 6.19 (d, $J = 8.0$ Hz, 1H), 4.09 (m, 4H), 2.49 (s, 3H), 2.33 (s, 3H), 1.30 (t, $J = 6.5$ Hz, 6H).

$^{13}$C NMR (125 MHz, CDCl$_3$): δ 156.5 (d, $J = 4.3$ Hz), 152.8, 143.2, 141.4, 134.3 (d, $J = 13.6$ Hz), 131.1 (d, $J = 188.6$ Hz), 128.2, 127.7, 125.9, 123.1 (d, $J = 19.0$ Hz), 117.1, 115.8 (d, $J = 19.5$ Hz), 62.0 (d, $J = 6.6$ Hz), 21.2 (d, $J = 4.2$ Hz), 17.5, 16.2 (d, $J = 7.8$ Hz).

HRMS: m/z (ESI) Calculated for [M+H]$^+$ 347.1525, Found 347.1510.
Chapter S4. Porous Polymer-Supported Heterogeneous Gold(I) Catalysis

S4.1 General Methods and materials

All of the reactions dealing with air and/or moisture-sensitive reactions were carried out under an atmosphere of nitrogen using oven/flame-dried glassware and standard syringe/septa techniques. Unless otherwise noted, all commercial reagents and solvents were obtained from the commercial provider and used without further purification. $^1$H NMR and $^{13}$C NMR spectra were recorded on Varian 600 MHz or Agilent 400 MHz spectrometer. Chemical shifts were reported relative to internal tetramethylsilane ($\delta$ 0.00 ppm) or CDCl$_3$ ($\delta$ 7.26 ppm) for $^1$H NMR, CDCl$_3$ ($\delta$ 77.0 ppm) for $^{13}$C NMR. Flash column chromatography was performed on 230-430 mesh silica gel. Analytical thin layer chromatography was performed with precoated glass baked plates (250µ) and visualized by UV lamp. The X-ray photoelectron spectroscopy (XPS, Physical Electronics VersaProbe 5000) measurements were conducted with Al Kα radiation (1486.71 eV), the binding energy scale was calibrated by a C 1s peak at 284.8 eV.

The yields of hydration reactions and hydroamination reactions were obtained by Gas Chromatography (Agilent 7890B GC) using bromobenzene as the internal standard. The yields of other reactions were calculated from NMR data using p-xylene as the internal standard.

Procedure for the preparation of the solid support ligand Pol-PPh$_3$

Prior to reaction, 4-bromo-vinylbenzene was purified by vacuum distillation to give a colorless liquid. In a flame-dried 500 mL round-bottom flask, 3 g Mg was dried under vacuum with a heat gun. After the addition of 200 mL anhydrous THF, 0.5 mL 1,2-dibromoethane was added to initiate the Grignard reaction. After the solution is cooled down, 18.31 g 4-bromo-vinylbenzene was added slowly at 0 °C and stirred for 3 h at room temperature. This solution was cooled in an ice bath and a solution of 3.66 g PCl$_3$ in 20 mL THF was added over 2 h via a syringe pump. After stirring for another 2 h at rt, 50 mL of saturated NH$_4$Cl aqueous solution was added to quench the reaction. The organic layer was separated and the aqueous layer was extracted with hexanes. The combined organic layer was dried with MgSO$_4$ and filtered through a short silica column. The solvent was removed under reduced pressure. After recrystallization from MeOH, 7.93 g trivinyl-functionalized PPh$_3$ (3V-PPh$_3$) was obtained as a white solid (88% yield).

Pol-PPh$_3$ was synthesized from polymerization of 3V-PPh$_3$ under solvothermal conditions. Generally, 1.0 g of 3V-PPh$_3$ was dissolved in 10 mL of THF, followed by the addition of 20 mg of azobisisobutyronitrile (AIBN). This clear solution was transferred
into an autoclave at 100 °C for 12 h. After evaporation of THF under vacuum, the white solid was DCM and acetone and dried under vacuum at 80 °C over night.

**Procedure for the preparation of the heterogeneous gold catalyst Pol-TA-Au**

Dimethyl sulfide gold chloride (DMSAuCl, 173 mg) was dissolved in 50 mL methylene chloride (DCM). To this solution, 1 g Pol-PPh₃ (mol ratio of P:Au = 5:1) was added and stirred for 10 h. The solid was isolated by vacuum filtration and washed with DCM. After drying under vacuum, the solid was dispersed in 50 mL methanol. To this mixture was added a solution of 140 mg benzotriazole (2 eq. based on the mol of Au) and 47 mg NaOH (2 eq. based on the mol of Au). After stirring for 12 h, Pol-TAA-Au was isolated by vacuum filtration and washed with methanol, water and acetone. To a suspension of Pol-TAA-Au in 50 mL MeOH, a 0.5 M HOTf in methanol solution (2.3 mL, 2 eq. based on the mol of Au) was added. After stirring for 12 h, the Pol-TA-Au catalyst was isolated by vacuum filtration, washed with methanol and dried under vacuum.

**Procedure for Pol-TA-Au catalyzed hydration reactions**

The starting alkynes (0.2 mmol) are dissolved in 0.4 mL methanol (with 5% water) in a 2-mL centrifuge tube. To this solution, 8 mg of the Pol-TA-Au catalyst was added (1 mol%). The mixture was stirred at 60 °C (80 °C for internal alkynes) and checked with GC for completion. After reaction was completed, the products were isolated by centrifuge. The heterogeneous catalyst (precipitated in the bottom of the vial) was treated with 2 eq. of 0.1 M HOTf/MeOH solution for 10 mins and washed with MeOH three times. The same catalyst could be reused for the next batch of starting material without loss of reactivity.

**Procedure for Pol-TA-Au catalyzed hydroamination reaction**

The aniline (0.2 mmol) was dissolved in 0.4 mL dry Toluene in a 2-mL centrifuge tube. To this solution was added 0.4 mmol alkyne, 8 mg Pol-TA-Au (1 mol%), and 1.5 mg
Zn(OTf)_2 (2 mol%). This mixture was heated at 80 °C and checked with GC for completion. After reaction was completed, the products were isolated by centrifuge. The heterogeneous catalyst (precipitated in the bottom of the vial) was washed with toluene three times. The same catalyst could be reused for the next batch of starting material.

The other reactions were performed using previously reported methods:

S4.2 XPS analysis

Pol-PPh_3

Pol-PPh_3-Au-Cl
Pol-PPh₃-Au-TA
S4.3 Compounds Characterization

The following substrates are same as some substrates in S2.2. Other substrates have been reported previously.

2-oxo-1-phenylpropyl acetate (9a): 96% yield, $^1$H NMR (600 MHz, CDCl₃): $\delta$ 7.38-7.42 (m, 5H), 5.98 (s, 1H), 2.19 (s, 3H), 2.11 (s, 3H); $^{13}$C NMR (150 MHz, CDCl₃): $\delta$ 201.6, 170.2, 133.2, 129.3, 129.0, 128.0, 80.9, 26.1, 20.7.

1,2-diphenylethanone (11a): $^1$H NMR (600 MHz, CDCl₃): $\delta$ 8.00-8.02 (m, 2H), 7.53-7.56 (m, 1H), 7.45 (d, $J$ = 7.8 Hz, 2H), 7.32 (d, $J$ = 7.5 Hz, 2H), 7.24-7.27 (m, 3H), 4.28 (s, 2H). $^{13}$C NMR (150 MHz, CDCl₃): $\delta$ 197.6, 136.6, 134.5, 133.1, 129.4, 128.6, 128.6, 128.5, 126.9, 45.5.
3-phenylbicyclo[3.1.0]hex-2-ene (Scheme 13D): (See: Luzung, M.R.; Markham, J.P.; Toste, F.D. *J. Am. Chem. Soc.* 2004, 126, 10858-10859.) $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.38 (d, $J = 7.8$ Hz, 2H), 7.30 (t, $J = 7.8$ Hz, 2H), 7.21(t, $J = 7.8$ Hz, 1H), 6.42 (d, $J = 1.8$ Hz, 1H), 3.02 (dd, $J = 16.8, 7.2$ Hz, 1H), 2.75 (d, $J = 16.8$ Hz, 1H), 1.98-1.94 (m, 1H), 1.76-1.72 (m, 1H), 0.97-0.93 (m, 1H), 0.11-0.09 (m, 1H). $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 139.7, 136.6, 129.6, 128.2, 126.7, 125.1, 36.3, 24.1, 17.6, 15.4.

(E)-1-phenylhept-1-en-3-one (Scheme 14A): (known compound, See: Wang, D.; Zhang, Y.; Harris, A.; Gautam, L. N. S.; Shi, X. *Adv. Syn. Cat.* 2011, 353, 2584-2588.) $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.53-7.56 (m, 3H), 7.38-7.40 (m, 3H), 6.73 (t, $J = 16.2$ Hz, 1H), 2.66 (t, $J = 7.5$ Hz, 2H), 1.66 (quintet, $J = 7.5$ Hz, 2H), 1.37 (sextet, $J = 7.4$ Hz, 2H), 0.94 (t, $J = 7.5$ Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 200.8, 142.5, 134.8, 130.6, 129.1, 128.4, 126.5, 40.9, 26.7, 22.7, 14.1.
Chapter S5. N-2-Aryl-1,2,3-Triazole as ligand for Iridium Photocatalyst

S5.1 General Methods and materials

All of the reactions dealing with air and/or moisture-sensitive reactions were carried out under an atmosphere of nitrogen using oven/flame-dried glassware and standard syringe/septa techniques. Unless otherwise noted, all commercial reagents and solvents were obtained from the commercial provider and used without further purification. $^1$H NMR and $^{13}$C NMR spectra were recorded on Varian 600 MHz or Agilent 400 MHz spectrometer. Chemical shifts were reported relative to internal tetramethylsilane ($\delta$ 0.00 ppm) or CD$_3$CN ($\delta$ 1.94 ppm) for $^1$H NMR and CD$_3$CN ($\delta$ 1.39 ppm) for $^{13}$C NMR. Flash column chromatography was performed on 230-430 mesh silica gel. Analytical thin layer chromatography was performed with precoated glass baked plates (250µ) and visualized by UV lamp. ESI-MS were recorded on Thermo Scientific Q-exactive spectrometer.

The UV-Vis spectra were obtained with a Shimadzu UV-1800 UV spectrophotometer in 10 mm path length quartz cuvettes with $1\times10^{-5}$M Iridium complex solutions in freshly distilled acetonitrile (ACN). The fluorescence spectra were obtained in 10 mm path length quartz cuvettes using Shimadzu RF-5301 PC spectrofluorophotometer with $1\times10^{-5}$M Iridium complex solutions in ACN.

The fluorescence quantum yields of iridium complexes ($\Phi_x$) were calculated based on equation (1) using Ru(bpy)$_3$(PF$_6$)$_2$ in ACN ($\Phi = 0.094$)$^{21}$ as a standard. All the samples were tested with $1\times10^{-5}$M ACN solutions under argon protection.

$$\Phi_x = \frac{n_x^2}{n_{std}^2} \cdot \frac{1 - 10^{-Abs_{std}}}{1 - 10^{-Abs_x}} \cdot \frac{I_x}{I_{std}} \cdot \Phi_{std}$$  \hspace{1cm} (1)

$\Phi$ is the quantum yield, $I$ is integrated emission intensity, $Abs$ is the absorption at the excitation wavelength (370nm), and $n$ is the refractive index of pure solvents ($n_x = n_{std}$ in this case); ‘std’ stands for reference standard samples, ‘x’ stands for samples.

The excited-state lifetime were measured on a Horiba Fluorolog-3 spectrofluorometer with a NanoLED-370nm as the light source. The samples were prepared in ACN ($1\times10^{-5}$M solutions) and tested in 10 mm path length quartz cuvettes. A highly diluted colloidal silica solution (0.01% dilution of LUDOX AS-40 colloidal silica using deionized water) was used to get the prompt spectra. All samples were tested under same conditions.

The cyclic voltammetry measurements were conducted on a WaveNow USB potentiostat in a three-compartment cell at 0.1 V/s scan rate using 1 mM Iridium complex solutions in freshly distilled acetonitrile with 0.1 M tetrabutylammonium hexafluorophosphate as the

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supporting electrolyte. A platinum wire was used as the working electrode and a folded platinum plate was used as the counter electrode. A silver wire was used as the quasi-reference electrode. Potentials were calibrated using Fe⁺/Fc redox couple (0.40V in ACN) after each experiment and reported vs. SCE.

The N-2-aryl triazoles were synthesized according to the literature reported previously. The photocatalytic reactions were performed under same conditions as previous literature reports.

**General procedure for the preparation of [pta]Ir(µ-Cl)]₂:**

The preparation [pta]Ir(µ-Cl)]₂ is adapted from literature report. The pta ligand 30 (2.5 mmol), IrCl₃·xH₂O (353 mg, 1 mmol) in 32 mL 2-ethoxyethanol/water (3:1) was refluxed at 140 °C under nitrogen or argon atmosphere for 24 h. After cooled to room temperature, the yellow precipitate was isolated by filtration and washed with water and ethanol and allowed to air dry. The yellow solid was used for the next step without further purification. Yields of the µ-dichloro-bridged iridium(III) dimer 31 are ranged from 53% to 95% (31a: 63%, 31b: 92%, 31c: 53%, 31d: 78%, 31e: 87%, 31f: 89%, 31g: 95%).

**Procedure for the preparation of N-1b:**

The procedure is adapted from literature report. The µ-dichloro-bridged iridium(III) dimer 31b (424 mg, 0.3 mmol), sodium carbonate (350 mg, 3.3 mmol) and the N^N

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ligand 2-picolinamide (96 mg, 0.78 mmol) was suspended in 22 mL 2-ethoxyethanol. The reaction mixture was stirred at 140 °C for 20 h under nitrogen atmosphere. After the reaction was cooled to room temperature, 150 mL ethyl acetate was added. The solution was extracted with water three times. The organic layer was dried over Na2SO4 and concentrated under reduced pressure. The solid was then purified by flash chromatography on silica gel using ethyl acetate and recrystallized from ether / hexane to yield N-1b in 75% yield.

General procedure for the preparation of [(pta)2Ir(ppy)]PF6:27:

The µ-dichloro-bridged iridium(III) dimer 31 (0.15 mmol) and the N^N ligand 2,2’-bispyridine (58 mg, 0.375 mmol) was suspended in 10 mL 1,2-ethanediol. The reaction mixture was stirred at 120 °C for 20 h under nitrogen or argon atmosphere. After the reaction was cooled to room temperature, 150 mL distilled water was added. The solution was extracted with ethyl ether three times to remove the excess bpy. Ammonium hexafluorophosphate solution (1 g in 10 mL water) was added to the aqueous layer to yield a yellow precipitate. The solution was then heated at 70 °C for 10 min. After cooled to room temperature, the yellow precipitate was filtrated and further purified by flash chromatography on silica gel using 10% DCM / acetone eluent. After the column, the solid was re-dissolved in minimum amount of methanol and precipitated again using NH4PF6 (1 g in 10 mL water). The yellow precipitate was filtered and washed with water and then recrystallized from minimum amount of hot acetonitrile for further experiments.

General procedure for the preparation of [(pta)2Ir(tapy)]PF6:

The µ-dichloro-bridged iridium(III) dimer 31 (0.15 mmol) and the N^N ligand tapy (83

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mg, 0.375 mmol) was suspended in 10 mL 1,2-ethanediol. The reaction mixture was stirred at 120 °C for 20 h under nitrogen or argon atmosphere. After the reaction was cooled to room temperature, 150 mL distilled water was added, followed by ammonium hexafluorophosphate solution (1 g in 10 mL water) to yield a yellow precipitate. The precipitate was filtered and further purified by flash chromatography on silica gel using 10% acetone/DCM eluent. After the column, the solid was re-dissolved in minimum amount of methanol and precipitated again using NH₄PF₆ (1 g in 10 mL water). The precipitate was filtered and washed with water and then recrystallized from minimum amount of hot acetonitrile for further experiments.

S5.2 Compounds characterization

C-1a: Yellow Solid (79% yield). ¹H NMR (400 MHz, CD₃CN): δ 8.58 (d, J = 8.2 Hz, 2H), 8.22-8.16 (m, 4H), 7.88 (dd, J = 8.1, 1.5 Hz, 4H), 7.84 (s, 2H), 7.80 (dd, J = 8.0, 1.2 Hz, 2H), 7.57 (ddd, J = 7.6, 5.5, 1.1 Hz, 2H), 7.51-7.45 (m, 6H), 7.19 (td, J = 7.7, 1.1 Hz, 2H), 7.00 (td, J = 7.5, 1.3 Hz, 2H), 6.52 (dd, J = 7.5, 1.2 Hz, 2H); ¹³C NMR (100 MHz, CD₃CN): δ 157.57, 152.88, 150.26, 142.34, 141.07, 133.72, 132.51, 130.81, 130.64, 130.26, 129.65, 129.57, 129.44, 127.01, 125.64, 125.24, 115.46. ESI-MS calculated for [C₃₈H₂₈IrN₈]⁺: 789.2066, found: 789.2047.

C-1b: Yellow Solid (85% yield). ¹H NMR (400 MHz, CD₃CN): δ 8.57 (d, J = 8.2 Hz, 2H), 8.24-8.18 (m, 4H), 7.88-7.83 (m, 6H), 7.80 (s, 2H), 7.59 (ddd, J = 7.6, 5.5, 1.3 Hz, 2H), 7.51-7.43 (m, 6H), 6.98 (td, J = 8.8, 2.6 Hz, 2H), 6.22 (dd, J = 8.8, 2.6 Hz, 2H); ¹³C NMR (100 MHz, CD₃CN): δ 163.01 (d, J = 248.1 Hz), 157.48, 153.12, 150.33, 141.07, 133.72, 132.51, 130.81, 130.64, 130.26, 129.65, 129.57, 129.44, 127.01, 125.64, 125.24, 115.46. ESI-MS calculated for [C₃₈H₂₆F₂IrN₈]⁺: 825.1878, found: 825.1861.
**C-1c:** Yellow Solid (68% yield). $^1$H NMR (400 MHz, CD$_3$CN): $\delta$ 8.55 (d, $J = 8.2$ Hz, 2H), 8.23-8.18 (m, 4H), 7.85 (dd, $J = 8.1$, 1.6 Hz, 4H), 7.75 (d, $J = 9.1$ Hz, 2H), 7.74 (s, 2H), 7.58 (dd, $J = 7.7$, 5.5, 1.2 Hz, 2H), 7.50-7.41 (m, 6H), 6.77 (dd, $J = 8.8$, 2.6 Hz, 2H), 5.91 (d, $J = 2.6$ Hz, 2H), 3.63 (s, 6H); $^{13}$C NMR (100 MHz, CD$_3$CN): $\delta$ 160.70, 157.54, 153.00, 149.67, 141.05, 136.24, 132.81, 131.68, 130.66, 130.24, 129.67, 129.42, 126.91, 125.56, 118.95, 116.72, 109.51, 55.96. ESI-MS calculated for [C$_{40}$H$_{32}$Ir$_8$N$_8$O$_2$]$^+$: 849.2277, found: 849.2262.

![C-1c structure](image)

**C-1d:** Synthesized from one-Pot sequential reactions without isolating the $\mu$-dichloro-bridged iridium(III) dimer. Yellow Solid (62% yield over two steps). $^1$H NMR (400 MHz, CD$_3$CN): $\delta$ 8.56 (d, $J = 8.1$ Hz, 2H), 8.24-8.17 (m, 4H), 7.91-7.86 (m, 4H), 7.84 (dd, $J = 8.8$, 4.8 Hz, 2H), 7.76 (s, 2H), 7.59 (dd, $J = 7.7$, 5.5, 1.2 Hz, 2H), 7.26-7.20 (m, 4H), 6.98 (td, $J = 8.8$, 2.7 Hz, 2H), 6.21 (dd, $J = 8.8$, 2.6 Hz, 2H); $^{13}$C NMR (100 MHz, CD$_3$CN): $\delta$ 164.49 (d, $J = 246.0$ Hz), 163.03 (d, $J = 248.1$ Hz), 157.47, 153.13, 149.44, 141.34, 138.83, 133.35 (d, $J = 6.0$ Hz), 132.53, 129.55, 129.29 (d, $J = 8.5$ Hz), 126.00 (d, $J = 2.9$ Hz), 125.70, 120.13 (d, $J = 20.5$ Hz), 117.20 (d, $J = 22.1$ Hz), 117.24 (d, $J = 9.2$ Hz), 112.02 (d, $J = 24.7$ Hz); $^{19}$F NMR (376 MHz, CD$_3$CN): -73.92 (d, $J = 706.0$ Hz, 6F), -113.59 (m, 2F), -114.77 (m, 2F). ESI-MS calculated for [C$_{38}$H$_{24}$F$_4$Ir$_8$N$_8$]$:^+$ 861.1689, found: 861.1670.

![C-1d structure](image)
C-1e: Yellow Solid (55% yield). $^1$H NMR (400 MHz, CD$_3$CN): $\delta$ 8.56 (d, $J = 8.1$ Hz, 2H), 8.23-8.18 (m, 4H), 7.89-7.84 (m, 4H), 7.74 (d, $J = 8.7$ Hz, 2H), 7.71 (s, 2H), 7.58 (ddd, $J = 7.7$, 5.5, 1.2 Hz, 2H), 7.25-7.19 (m, 4H), 6.76 (dd, $J = 8.8$, 2.6 Hz, 2H), 5.90 (d, $J = 2.6$ Hz, 2H), 3.63 (s, 6H); $^{13}$C NMR (100 MHz, CD$_3$CN): $\delta$ 164.36 (d, $J = 246.0$ Hz), 160.72, 157.53, 152.98, 148.78, 141.08, 136.19, 132.77, 131.55, 129.42, 129.12 (d, $J = 8.4$ Hz), 126.19 (d, $J = 3.0$ Hz), 125.57, 118.99, 117.16 (d, $J = 22.0$ Hz), 116.72, 109.47, 55.96; $^{19}$F NMR (376 MHz, CD$_3$CN): -73.84 (d, $J = 706.2$ Hz, 6F), -113.93 (m, 2F). ESI-MS calculated for [C$_{40}$H$_{30}$F$_{2}$IrN$_{8}$O$_{2}$]$^+$: 885.2089, found: 885.2078.

C-1f: Yellow Solid (56% yield). $^1$H NMR (400 MHz, CD$_3$CN): $\delta$ 8.56 (d, $J = 8.1$ Hz, 2H), 8.23-8.17 (m, 4H), 7.83-7.77 (m, 6H), 7.69 (s, 2H), 7.58 (ddd, $J = 7.7$, 5.5, 1.2 Hz, 2H), 7.04-7.00 (m, 4H), 6.97 (td, $J = 8.8$, 2.7 Hz, 2H), 6.19 (dd, $J = 8.8$, 2.6 Hz, 2H), 3.82 (s, 6H); $^{13}$C NMR (100 MHz, CD$_3$CN): $\delta$ 162.89 (d, $J = 247.6$ Hz), 162.00, 157.47, 153.09, 150.30, 141.28, 138.98, 133.29 (d, $J = 6.0$ Hz), 131.96, 129.53, 128.57, 125.68, 121.90, 120.06 (d, $J = 20.4$ Hz), 117.02 (d, $J = 9.1$ Hz), 115.62, 111.91 (d, $J = 24.5$ Hz), 56.21; $^{19}$F NMR (376 MHz, CD$_3$CN): -73.87 (d, $J = 705.7$ Hz, 6F), -115.13 (m, 2F). ESI-MS calculated for [C$_{40}$H$_{30}$F$_{2}$IrN$_{8}$O$_{2}$]$^+$: 885.2089, found: 885.2076.
**C-1g**: Yellow Solid (38% yield). $^1$H NMR (400 MHz, CD$_3$CN): $\delta$ 8.55 (d, $J = 8.1$ Hz, 2H), 8.22-8.17 (m, 4H), 7.79-7.75 (m, 4H), 7.72 (d, $J = 8.7$ Hz, 2H), 7.64 (s, 2H), 7.59-7.56 (m, 2H), 7.03-6.99 (m, 4H), 6.76 (dd, $J = 8.8$, 2.6 Hz, 2H), 5.89 (d, $J = 2.6$ Hz, 2H), 3.82 (s, 6H), 3.62 (s, 6H); $^{13}$C NMR (100 MHz, CD$_3$CN): $\delta$ 161.84, 160.55, 157.53, 152.96, 149.65, 141.00, 136.34, 132.70, 130.96, 129.39, 128.41, 125.54, 122.11, 118.96, 116.51, 115.59, 109.37, 56.19, 55.94. ESI-MS calculated for [C$_{42}$H$_{36}$IrN$_8$O$_2$]$^+$: 909.2489, found: 909.2478.

**C-2**: Yellow Solid (40% yield). $^1$H NMR (600 MHz, CD$_3$CN): $\delta$ 8.42 (d, $J = 8.4$ Hz, 1H), 8.26 (td, $J = 8.0$, 1.6 Hz, 1H), 8.09-8.07 (m, 2H), 8.05 (s, 1H), 7.95 (ddd, $J = 4.6$, 3.2, 1.6 Hz, 2H), 7.90-7.88 (m, 3H), 7.82-7.80 (m, 3H), 7.73 (dd, $J = 5.8$, 0.7 Hz, 1H), 7.54-7.49 (m, 4H), 7.10-7.04 (m, 4H), 6.93 (dt, $J = 14.5$, 7.3, 1.3 Hz, 2H), 6.28 (dd, $J = 21.6$, 7.7 Hz, 2H); $^{13}$C NMR (150 MHz, CD$_3$CN): $\delta$ 168.48, 167.95, 153.69, 150.83, 150.18, 149.39, 148.19, 145.52, 145.21, 145.19, 143.13, 140.05, 139.98, 136.93, 132.94, 132.38, 131.81, 131.47, 131.03, 130.42, 128.56, 127.76, 127.61, 126.00, 125.74, 124.78, 124.67, 124.12, 123.92, 121.01, 120.97, 115.87. ESI-MS calculated for [C$_{35}$H$_{28}$IrN$_6$]$^+$: 723.1843, found: 723.1858.
C-3a: Light yellow Solid (85% yield). $^1$H NMR (400 MHz, CD$_3$CN): $\delta$ 8.46 (d, $J = 8.4$ Hz, 1H), 8.33 (ddd, $J = 8.4$, 7.6, 1.6 Hz, 1H), 8.25 (s, 1H), 8.13 (s, 1H), 8.01-7.87 (m, 4H), 7.92-7.90 (m, 4H), 7.82 (d, $J = 7.9$ Hz, 2H), 7.58-7.44 (m, 10H), 7.02 (ddd, $J = 10.6$, 7.5, 1.3 Hz, 2H), 6.52 (dd, $J = 7.6$, 5.1 Hz, 2H); $^{13}$C NMR (100 MHz, CD$_3$CN): $\delta$ 153.49, 151.48, 150.37, 150.20, 149.76, 143.74, 142.50, 142.24, 138.52, 134.05, 133.56, 133.35, 133.33, 131.88, 130.91, 130.88, 130.51, 130.55, 130.33, 129.64, 129.59, 129.56, 129.44, 128.57, 127.72, 127.69, 127.47, 127.02, 126.98, 125.79, 125.56, 124.70, 115.77, 115.59, 115.37. ESI-MS calculated for [C$_{41}$H$_{30}$IrN$_{10}$]$^+$: 855.2284, found: 855.2269.

C-3b: Light yellow Solid (71% yield). $^1$H NMR (400 MHz, CD$_3$CN): $\delta$ 8.46 (ddd, $J = 8.4$, 1.2, 0.8 Hz, 1H), 8.34 (ddd, $J = 8.4$, 7.6, 1.6 Hz, 1H), 8.32 (s, 1H), 8.10 (s, 1H), 8.03-7.99 (m, 3H), 7.95 (s, 1H), 7.91-7.88 (m, 4H), 7.86 (dd, $J = 8.8$, 4.9 Hz, 2H), 7.59-7.44 (m, 10H), 7.02 (ddd, $J = 8.8$, 6.0, 2.7 Hz, 2H), 6.23 (ddd, $J = 8.8$, 4.3, 2.6 Hz, 2H); $^{13}$C NMR (100 MHz, CD$_3$CN): $\delta$ 162.80 (d, $J = 248.1$ Hz), 162.64 (d, $J = 247.9$ Hz), 153.59, 151.71, 150.44, 149.61, 144.02, 139.10, 139.08, 138.80, 133.45 (d, $J = 3.6$ Hz), 131.95, 130.94 (d, $J = 2.1$ Hz), 130.55, 130.33, 130.31, 130.26, 130.19, 129.48, 129.45, 128.49, 127.71, 127.54, 127.34, 127.28, 127.06, 127.02, 120.56 (d, $J = 21.0$ Hz), 120.12 (d, $J = 21.1$ Hz), 117.36 (d, $J = 9.3$ Hz), 117.05 (d, $J = 9.3$ Hz), 115.84, 112.57 (d, $J = 19.4$ Hz), 112.32 (d, $J = 19.4$ Hz); $^{19}$F NMR (376 MHz, CD$_3$CN): -73.92 (d, $J = 705.9$ Hz, 6F), -114.50 (m, 1F), -115.05 (m, 1F). ESI-MS calculated for [C$_{41}$H$_{30}$F$_2$IrN$_{10}$]$^+$: 891.2096, found: 891.2083.

C-3c: Light yellow Solid (44% yield). $^1$H NMR (400 MHz, CD$_3$CN): $\delta$ 8.45 (dd, $J = 8.3$, 0.6 Hz, 1H), 8.33 (td, $J = 8.0$, 1.5 Hz, 1H), 8.29 (s, 1H), 8.06-8.00 (m, 3H), 8.05 (s, 1H), 7.90 (s, 1H), 7.90-7.87 (m, 4H), 7.76 (d, $J = 8.7$ Hz, 2H), 7.59-7.42 (m, 10H), 6.80 (ddd,
$J = 8.7, 6.2, 2.6 \text{ Hz}, 2\text{H}$), 5.91 (dd, $J = 2.2 \text{ Hz}, 2\text{H}$), 3.64 (2s, 6H).; $^{13}\text{C}$ NMR (100 MHz, CD$_3$CN): δ 160.58, 160.30, 153.47, 151.58, 149.76, 149.71, 149.60, 143.76, 138.54, 136.40, 136.08, 132.50, 132.46, 131.90, 130.74, 130.72, 130.52, 130.31, 130.29, 129.78, 129.66, 129.63, 128.57, 127.72, 127.43, 126.92, 126.88, 126.83, 119.37, 118.81, 116.86, 116.56, 115.74, 110.01, 109.82, 56.02, 55.97. ESI-MS calculated for [C$_{43}$H$_{34}$IrN$_{10}$O$_2$]$^+$: 915.2495, found: 915.2481.
Perspective view of the molecular structure of Ir(N$_3$C$_{14}$H$_9$F)$_2$(C$_6$H$_5$N$_2$O) with the atom labeling scheme. The thermal ellipsoids are scaled to 30% probability. CCDC number: 1012360
Perspective view of the molecular structure of [Ir(bpy)(C_{14}H_{8}N_{3}F_{2})_{2}]PF_{6} with the atom labeling scheme. The thermal ellipsoids are scaled to enclose 30% probability. CCDC number: 1010939
S5.4 UV-Vis Spectra and Fluorescence Spectra
\[ \epsilon (\text{M} \cdot \text{cm}^{-1}) \]

- 220 250 300 350 400 450 500

- Intensity

- 400 450 500 550 600 650 700

C-1a \((R^1=H, R^2=H)\)
C-1b \((R^1=H, R^2=H)\)
C-1c \((R^1=OMe, R^2=H)\)

C-2

C-3a \((R^1=H, R^2=H)\)
C-3b \((R^1=F, R^2=H)\)
C-3c \((R^1=OMe, R^2=H)\)
Normalized Absorption

Normalized Emission Intensity

wavelength (nm)

Normalized Absorption

Normalized Emission Intensity

wavelength (nm)
Normalized Absorption vs. wavelength (nm)

Normalized Emission Intensity vs. wavelength (nm)

C-1c

C-1d

PF₆⁻
S5.5 Cyclic Voltammetry

**S1**

**S2**
S5.5 Excited-state lifetime

All the samples are tested under same conditions as described above (Section I). The sample solutions were degassed with nitrogen bubbles for 20 mins, capped with rubber septum and sealed with Parafilm, followed by protection with nitrogen using freeze/thaw techniques prior to the measurement. For parallel comparison, we tested two literature reported samples under our conditions: [(ppy)$_2$Ir(dtbbpy)]PF$_6$ (experimental: 175 ns, literature: 557 ns) and Ru(bpy)$_3$(PF$_6$)$_2$ (experimental: 382 ns, literature: 1100 ns). Complexes C-3a, C-3b and C-3c were fitted with two exponentials while all the other complexes were fitted with one exponential using DAS6.
Calculated using 1 exponential

The initial parameters are:

- **Shift Value**: 0 ch; 0 sec
- **Shift Limit**: 40 ch; 1.75583E-08 sec
- **T1 Estimate**: 299.4264 ch; 1.314355E-07 sec
- **A Free**
- **B1 Free**

- **Prompt and decay LO**: 193 ch; 8.471879E-08 sec
- **Prompt and decay HI**: 2695 ch; 1.18299E-06 sec

**Background on prompt = 1 (manual)**

**Time calibration**: 4.389575E-10 sec/ch

The fitted parameters are:

- **Hi reduced to**: 2655 ch

- **SHIFT**: 0.503097 ch; 2.208382E-10 sec S.Dev = 1.189053E-11 sec
- **T1**: 397.7953 ch; 1.746152E-07 sec S.Dev = 2.967923E-10 sec
- **A**: 14.67546 S.Dev = 0.1670179
- **B1**: 0.3065412 [100.00 Rel.Ampl] [1.00 Alpha] S.Dev = 3.783242E-04
- **Average Life Time**: 1.746152E-07 sec

**CHISQ**: 1.017701 [2459 degrees of freedom]
The initial parameters are:

- Shift Value = 0 ch; 0 sec
- Shift Limit = 40 ch; 3.51166E-08 sec
- T1 Estimate = 307.987 ch; 2.703864E-07 sec
- A Free
- B1 Free

Prompt and decay LO = 85 ch; 7.462277E-08 sec
Prompt and decay HI = 2703 ch; 2.373004E-06 sec

Background on prompt = 1 (manual)
Time calibration = 8.77915E-10 sec/ch

The fitted parameters are:

Hi reduced to: 2663 ch

- SHIFT = 0.3908297 ch; 3.431153E-10 sec S.Dev = 2.258932E-11 sec
- T1 = 434.98 ch; 3.818755E-07 sec S.Dev = 8.897758E-10 sec
- A = 97.82068 S.Dev = 0.3045523
- B1 = 0.470622 [ 100.00 Rel.Ampl][ 1.00 Alpha] S.Dev = 6.445636E-04

Average Life Time = 3.818755E-07 sec
CHISQ = 1.06252 [ 2575 degrees of freedom ]
Calculated using 1 exponential

The initial parameters are:

- Shift Value = 0 ch; 0 sec
- Shift Limit = 40 ch; 3.51166E-08 sec
- T1 Estimate = 292.838 ch; 2.570869E-07 sec
- A Free
- B1 Free

Prompt and decay LO = 57 ch; 5.004115E-08 sec
Prompt and decay HI = 2647 ch; 2.323841E-06 sec

Background on prompt = 1 (manual)
Time calibration = 8.77915E-10 sec/ch

The fitted parameters are:

- Hi reduced to: 2607 ch
- SHIFT = 0.5974014 ch; 5.244676E-10 sec S.Dev = 1.119862E-11 sec
- T1 = 302.9154 ch; 2.65934E-07 sec S.Dev = 3.112539E-10 sec
- A = 41.43258 S.Dev = 0.2173026
- B1 = 0.5112242 [100.00 Rel.Ampl][1.00 Alpha] S.Dev = 4.446301E-04

Average Life Time = 2.65934E-07 sec
CHISQ = 1.099121 [2547 degrees of freedom]
Calculated using 1 exponential

The initial parameters are:

Shift Value = 0 ch; 0 sec
Shift Limit = 40 ch; 3.51166E-08 sec
T1 Estimate = 372.2305 ch; 3.267867E-07 sec

A Free
B1 Free

Prompt and decay LO = 37 ch; 3.248285E-08 sec
Prompt and decay HI = 2671 ch; 2.344911E-06 sec

Background on prompt = 1 (manual)
Time calibration = 8.77915E-10 sec/ch

The fitted parameters are:

Hi reduced to: 2631 ch

SHIFT = 0.5086936 ch; 4.465898E-10 sec S.Dev = 1.235969E-11 sec
T1 = 407.7457 ch; 3.57966E-07 sec S.Dev = 4.258433E-10 sec
A = 47.75816

B1 = 0.4984699 [ 100.00 Rel.Ampl][ 1.00 Alpha] S.Dev = 3.910421E-04
Average Life Time = 3.57966E-07 sec

CHISQ = 1.135972 [ 2591 degrees of freedom ]
Calculated using 1 exponential

The initial parameters are:

Shift Value = 0 \text{ ch; } 0 \text{ sec}
Shift Limit = 40 \text{ ch; } 4.389575 \times 10^{-9} \text{ sec}
T1 Estimate = 169.1614 \text{ ch; } 1.856367 \times 10^{-8} \text{ sec}
A Free
B1 Free
Prompt and decay LO = 812 \text{ ch; } 8.910837 \times 10^{-8} \text{ sec}
Prompt and decay HI = 2683 \text{ ch; } 2.944307 \times 10^{-7} \text{ sec}
Background on prompt = 1 (manual)
Time calibration = 1.097394 \times 10^{-10} \text{ sec/ch}

The fitted parameters are:

Hi reduced to: 2643 ch
SHIFT = 0.453698 \text{ ch; } 4.978853 \times 10^{-11} \text{ sec} \quad \text{S.Dev} = 8.439614 \times 10^{-12} \text{ sec}
T1 = 275.3003 \text{ ch; } 3.021128 \times 10^{-8} \text{ sec} \quad \text{S.Dev} = 9.846059 \times 10^{-11} \text{ sec}
A = 37.60783 \quad \text{S.Dev} = 0.2243803
B1 = 8.788235 \times 10^{-2} \quad \text{[100.00 Rel.Ampl][1.00 Alpha]} \quad \text{S.Dev} = 2.024839 \times 10^{-4}
Average Life Time = 3.021128 \times 10^{-8} \text{ sec}
CHISQ = 0.933201 \quad \text{[1828 degrees of freedom]}

Chi.Sq. = 0.933201
Calculated using 1 exponential

The initial parameters are:

- Shift Value = 0 ch; 0 sec
- Shift Limit = 40 ch; 3.51166E-08 sec
- T1 Estimate = 287.6757 ch; 2.52548E-07 sec
- A Free
- B1 Free

Prompt and decay LO = 69 ch; 6.05761E-08 sec
Prompt and decay HI = 2687 ch; 2.358958E-06 sec

Background on prompt = 1 (manual)
Time calibration = 8.77915E-10 sec/ch

The fitted parameters are:

Hi reduced to: 2647 ch

- SHIFT = 0.4703841 ch; 4.129572E-10 sec S.Dev = 1.27369E-11 sec
- T1 = 308.0277 ch; 2.704222E-07 sec S.Dev = 3.395406E-10 sec
- A = 52.95856 S.Dev = 0.2339391
- B1 = 0.5000985 [100.00 Rel.Ampl][1.00 Alpha] S.Dev = 4.39496E-04
- Average Life Time = 2.704222E-07 sec
- CHISQ = 1.131363 [2575 degrees of freedom]
Calculated using 1 exponential

The initial parameters are:

- Shift Value = 0 \text{ ch} ; \ 0 \text{ sec}
- Shift Limit = 40 \text{ ch} ; \ 4.389575 \times 10^{-9} \text{ sec}
- T1 Estimate = 269.9332 \text{ ch} ; \ 2.96223 \times 10^{-8} \text{ sec}
- A Free
- B1 Free
- Prompt and decay LO = 817 \text{ ch} ; \ 8.965706 \times 10^{-8} \text{ sec}
- Prompt and decay HI = 2727 \text{ ch} ; \ 2.992593 \times 10^{-7} \text{ sec}
- Background on prompt = 1 (manual)
- Time calibration = 1.097394 \times 10^{-10} \text{ sec/ch}

The fitted parameters are:

- Hi reduced to: 2687 \text{ ch}
- SHIFT = 9.247364 \times 10^{-3} \text{ ch} ; \ 1.0148 \times 10^{-12} \text{ sec} \ S.Dev = 9.412315 \times 10^{-12} \text{ sec}
- T1 = 288.3633 \text{ ch} ; \ 3.164481 \times 10^{-8} \text{ sec} \ S.Dev = 1.262334 \times 10^{-10} \text{ sec}
- A = 56.06471 \ S.Dev = 0.260014
- B1 = 8.461874 \times 10^{-2} [ 100.00 \text{ Rel.Ampl} ] [ 1.00 \text{ Alpha} ] \ S.Dev = 2.07085 \times 10^{-4}
- Average Life Time = 3.164481 \times 10^{-8} \text{ sec}
- CHISQ = 0.9649003 \ [ 1867 \text{ degrees of freedom} ]
Calculated using 1 exponential

The initial parameters are:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shift Value</td>
<td>0 ch; 0 sec</td>
</tr>
<tr>
<td>Shift Limit</td>
<td>40 ch; 1.75583E-08 sec</td>
</tr>
<tr>
<td>T1 Estimate</td>
<td>297.8851 ch; 1.307589E-07 sec</td>
</tr>
<tr>
<td>A Free</td>
<td></td>
</tr>
<tr>
<td>B1 Free</td>
<td></td>
</tr>
<tr>
<td>Prompt and decay LO</td>
<td>201 ch; 8.823045E-08 sec</td>
</tr>
<tr>
<td>Prompt and decay HI</td>
<td>2675 ch; 1.174211E-06 sec</td>
</tr>
<tr>
<td>Background on prompt</td>
<td>1 (manual)</td>
</tr>
<tr>
<td>Time calibration</td>
<td>4.389575E-10 sec/ch</td>
</tr>
</tbody>
</table>

The fitted parameters are:

<table>
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<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hi reduced to</td>
<td>2635 ch</td>
</tr>
<tr>
<td>SHIFT</td>
<td>0.3860314 ch; 1.694514E-10 sec S.Dev = 8.379197E-12 sec</td>
</tr>
<tr>
<td>T1</td>
<td>330.7628 ch; 1.715283E-07 sec S.Dev = 2.22235E-10 sec</td>
</tr>
<tr>
<td>A</td>
<td>82.85342      S.Dev = 0.3409277</td>
</tr>
<tr>
<td>B1</td>
<td>0.2904978 [ 100.00 Rel.Ampl] [ 1.00 Alpha] S.Dev = 2.399315E-04</td>
</tr>
<tr>
<td>Average Life Time</td>
<td>1.715283E-07 sec</td>
</tr>
<tr>
<td>CHISQ</td>
<td>1.082008 [ 2431 degrees of freedom ]</td>
</tr>
</tbody>
</table>
Calculated using 1 exponential

The initial parameters are:

Shift Value = 0      ch;          0         sec
Shift Limit = 40     ch;          4.389575E-09  sec
T1 Estimate = 117.7722 ch;        1.292425E-08  sec

A Free
B1 Free

Prompt and decay LO = 835    ch;  9.163237E-08  sec
Prompt and decay HI = 2659   ch;  2.91797E-07    sec

Background on prompt = 1  (manual)
Time calibration = 1.097394E-10 sec/ch

The fitted parameters are:

Hi reduced to: 2619 ch

SHIFT = -1.511307    ch;        -1.658498E-10 sec  S.Dev = 1.129568E-11  sec
T1    = 164.2944     ch;        1.802956E-08  sec  S.Dev = 8.000964E-11  sec
A     = 43.13564

B1    = 0.1359902    [ 100.00 Rel.Ampl][ 1.00 Alpha] S.Dev = 4.017249E-04

Average Life Time = 1.802956E-08  sec

CHISQ = 1.046326   [ 1781 degrees of freedom ]
Calculated using 1 exponential

The initial parameters are:

- Shift Value = 0 ch; 0 sec
- Shift Limit = 40 ch; 8.77915E-09 sec
- T1 Estimate = 387.4972 ch; 8.504739E-08 sec
- A Free
- B1 Free
- Prompt and decay LO = 409 ch; 8.976681E-08 sec
- Prompt and decay HI = 2691 ch; 5.906173E-07 sec
- Background on prompt = 1 (manual)
- Time calibration = 2.194787E-10 sec/ch

The fitted parameters are:

- Hi reduced to: 2651 ch
- SHIFT = 0.3212092 ch; 7.049859E-11 sec  S.Dev = 9.764486E-12 sec
- T1 = 501.614 ch; 1.100936E-07 sec  S.Dev = 3.117276E-10 sec
- A = 84.2297 S.Dev = 0.392129
- B1 = 0.1542881 [ 100.00 Rel.Ampl][ 1.00 Alpha] S.Dev = 2.143631E-04
- Average Life Time = 1.100936E-07 sec
- CHISQ = 1.018662  [ 2239 degrees of freedom ]
The initial parameters are:

- Shift Value = 0 ch; 0 sec
- Shift Limit = 40 ch; 1.75583E-08 sec
- T1 Estimate = 150.4275 ch; 6.603126E-08 sec
- T2 Estimate = 601.7099 ch; 2.64125E-07 sec

A Free
B1 Free
B2 Free

Prompt and decay LO = 205 ch; 8.998629E-08 sec
Prompt and decay HI = 3518 ch; 1.544252E-06 sec

Background on prompt = 1 (manual)
Time calibration = 4.389575E-10 sec/ch

The fitted parameters are:

Hi reduced to: 3478 ch

- SHIFT = 9.356263E-02 ch; 4.107002E-11 sec S.Dev = 7.121309E-12 sec
- T1 = 6.639951 ch; 2.914656E-09 sec S.Dev = 9.402936E-11 sec
- T2 = 516.1541 ch; 2.265697E-07 sec S.Dev = 4.253594E-10 sec
- A = 77.17587 S.Dev = 0.2509782
- B1 = 0.2414948 [ 2.24 Rel.Ampl] [ 0.64 Alpha] S.Dev = 2.503661E-03
- B2 = 0.135377 [ 97.76 Rel.Ampl] [ 0.36 Alpha] S.Dev = 1.506701E-04
- Average Life Time = 8.325431E-08 sec
- CHISQ = 1.143413 [ 3268 degrees of freedom]
Calculating using 2 exponentials

The initial parameters are:

- **Shift Value**: 0 ch; 0 sec
- **Shift Limit**: 40 ch; 3.51166E-08 sec
- **T1 Estimate**: 106.7029 ch; 9.367609E-08 sec
- **T2 Estimate**: 426.8117 ch; 3.747044E-07 sec

**A Free**

- **B1 Free**: [0.3673247; 0.60 Alpha] S.Dev = 1.066362E-02
- **B2 Free**: [0.2421349; 0.40 Alpha] S.Dev = 5.042904E-04

**Prompt and decay**

- **LO**: 2 ch; 1.75583E-09 sec
- **HI**: 4096 ch; 3.59594E-06 sec

**Background on prompt**: 1 (manual)

**Time calibration**: 8.77915E-10 sec/ch

The fitted parameters are:

- **Hi reduced to**: 4056 ch
- **SHIFT**: 0.1195633 ch; 1.049664E-10 sec
- **S.Dev**: 2.888147E-11 sec
- **T1**: 3.303561 ch; 2.900246E-09 sec
- **S.Dev**: 2.73716E-10 sec
- **T2**: 438.8091 ch; 3.852371E-07 sec
- **S.Dev**: 1.334552E-09 sec
- **A**: 129.7937
- **S.Dev**: 0.2192968
- **B1**: 0.3673247 [1.13 Rel.Ampl] [0.60 Alpha]
- **S.Dev**: 1.066362E-02
- **B2**: 0.2421349 [0.87 Rel.Ampl] [0.40 Alpha]
- **S.Dev**: 5.042904E-04

**Average Life Time**: 1.548005E-07 sec

**CHISQ**: 1.035399 [4050 degrees of freedom]
C-3c

Calculated using 2 exponentials

The initial parameters are:

- **Shift Value**: 0 ch; 0 sec
- **Shift Limit**: 40 ch; 8.77915E-09 sec
- **T1 Estimate**: 321.9654 ch; 7.066456E-08 sec
- **T2 Estimate**: 1287.861 ch; 2.826582E-07 sec
- **Prompt and decay LO**: 381 ch; 8.36214E-08 sec
- **Prompt and decay HI**: 3401 ch; 7.464472E-07 sec
- **Background on prompt**: 1 (manual)
- **Time calibration**: 2.194787E-10 sec/ch

The fitted parameters are:

- **Hi reduced to**: 3361 ch
  - **SHIFT**: -0.1458581 ch; -3.201274E-11 sec, **S.Dev**: 1.377985E-11 sec
  - **T1**: 10.5551 ch; 2.31662E-09 sec, **S.Dev**: 1.14752E-10 sec
  - **T2**: 540.5867 ch; 1.186473E-07 sec, **S.Dev**: 7.761685E-10 sec
  - **A**: 103.4928, **S.Dev**: 0.2637861
  - **B1**: 6.355906E-02 [3.13 Rel.Ampl][0.62 Alpha], **S.Dev**: 1.31891E-03
  - **B2**: 3.844109E-02 [96.87 Rel.Ampl][0.38 Alpha], **S.Dev**: 1.240731E-04
  - **Average Life Time**: 4.615849E-08 sec
  - **CHISQ**: 1.074417 [2975 degrees of freedom]
NMR Spectra

Application of 1, 2, 3-Triazole in Gold Catalysis and Photoredox Catalysis

Rong Cai
Chapter S1. Gold-Catalyzed Synthesis of Triazapentalene Zwitterions
$5b$
Ph

\[ \text{5g} \]

\[ \text{p-OMe-Ph} \]
Ph
O
CH₃
p-Cl-Ph

5j
$\text{MeO}$
$\text{N}$
$\text{N}$
$\text{CH}_3$

$5n$
S155
S162
Chapter S2. “Silver Effect” in Gold(I) Catalysis

\[
\ce{Ph\text{OAc}}
\]
OAc

Ph

O

10  9  8  7  6  5  4  3  2  1  0 ppm
Chapter S3. Gold-Catalyzed Cross-Coupling with Aryldiazonium Salts
S232
n-Bu — Ph
n-Bu — Ph
MeO

=Ph
MeO – \( \text{Ar} \) – Ph
Et\(-\text{C}=-\text{Ph}\)
S281
Ph

Br

O
OEt

O

S

COOMe

NHBOc
Chapter S5. N-2-Aryl-1,2,3-Triazole as ligand for Iridium Photocatalyst
S389
S408