Supporting Information

Functionally Diverse Nucleophilic Trapping of Iminium Intermediates Generated Utilizing Visible Light

David B. Freeman, Laura Furst, Allison G. Condie and Corey R. J. Stephenson

Department of Chemistry, Boston University
590 Commonwealth Ave.
Boston, MA, 02215

Table of Contents

General Information:

All chemicals were purchased from Sigma-Aldrich and were used as received unless otherwise stated. Solvents including *N,N*-dimethylformamide (DMF), tetrahydrofuran (THF), acetonitrile (CH_3CN), toluene, benzene, and dichloromethane were purchased from Fischer Scientific and further dried using Glass Contour Solvent System by SG Waters USA LLC. Unless stated differently, all reactions were performed under inert atmosphere (Argon) and previously dried using common anhydrous techniques. Reactions were monitored by TLC and visualized by a dual short wave/long wave UV lamp and stained with I_2. All compounds were purified via flash column chromatography using 230–400 mesh silica gel. NMR spectra were recorded on Varian Unity Plus 400 and Varian Mercury 400 spectrometers. Chemical shifts for ^1H NMR were reported as δ, parts per million, relative to the signal of $CHCl_3$ at 7.26(s) ppm or DMF at 8.03 (s), 2.92(p), and 2.75(p) ppm. Chemical shifts for ^{13}C NMR were reported as δ, parts per million, relative to the center line signal of the $CDCl_3$ triplet at 77.0 ppm. Proton and carbon assignments were established using spectral data of similar compounds. The abbreviations s, br. s, d, dd, br. d, ddd, t, q, br. q, p, m, and br. m stand for the resonance multiplicity singlet, broad singlet, doublet, doublet of doublets, broad doublet, doublet of doublet of doublets, triplet, quartet, broad quartet, pentet, multiplet and broad multiplet, respectively. IR spectra were recorded on an Avatar 360 FT-IR spectrometer. Mass spectra were recorded in the Mass Spectrometry Facility at the Department of Chemistry of Boston University in Boston, MA on a Waters Q-Tof API-US with ESI high resolution mass spectrometer. Concentration refers to removal of solvent under reduced pressure (house vacuum at ca. 20 mmHg). 1,2,3,4-Tetrahydroisoquinoline derivatives[1] and 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline[2] were prepared according to published literature procedures.

Reaction Apparatus:

Photocatalyzed reactions were carried out under visible light irradiation by a 30 cm, 1W blue LED strip (available from http://www.creativelightings.com, λ_{max} = 435 nm) surrounding the reaction vessel.

---

[1] (a) Kwong, F. Y.; Klapars, A.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 581. (b) Li, Z.; Li, C.-J. *J. Am. Chem. Soc.* **2005**, *127*, 6968.

[2] Okano, K.; Tokuyama, H.; Fukuyama, T. *J. Am. Chem. Soc.* **2006**, *128*, 7136.

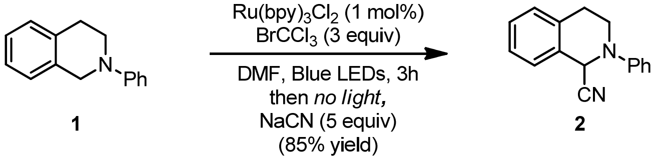
General Procedure:

A 10 ml round bottom flask was equipped with a rubber septum and magnetic stir bar and was charged with *N*-phenyl-1,2,3,4-tetrahydroisoquinoline (0.244 mmol, 1.0 equiv), $Ru(bpy)_3Cl_2$ (0.002 mmol, 0.01 equiv), and DMF (1.0 mL). The flask was degassed (3x freeze/pump/thaw) before $BrCCl_3$ (0.731 mmol, 3.0 equiv) was added. The mixture was then irradiated by a 1 W blue LED 30 cm strip under an atmosphere of argon for 3h. After the starting material was consumed as indicated by TLC, the blue LED was removed and the nucleophile (1.218 mmol, 5.0 equiv) was added. The reaction was covered with aluminum foil and stirred at room temperature. After approximately 12h, the reaction was poured into a separatory funnel containing 75 mL of a saturated solution of $NaHCO_3$ and 25 mL of EtOAc. The layers were separated and the aqueous layer was extracted with EtOAc (2 x 25 mL). The combined organic layers were washed with brine (25 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography in the indicated solvent mixture to afford the desired product.

Data for Compounds Afforded by Photoredox Catalysis:

Cyanation, (*Table 1, entry 5*)

2-Phenyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (**2**)[3]:



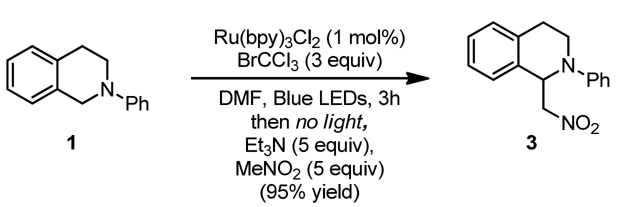
According to the general procedure, **1** (51.0 mg, 0.244 mmol, 1.0 equiv), Ru(bpy)$_3$Cl$_2$ (2.0 mg, 0.002 mmol, 0.01 equiv), and BrCCl$_3$ (72.0 µL, 0.731 mmol, 3.0 equiv) in DMF (1.0 mL) were irradiated with 1W blue LED lights until starting material was consumed as indicated by TLC. The reaction vessel was covered with aluminum foil before NaCN (60.0 mg, 1.218 mmol, 5.0 equiv) was added. After workup, the crude oil was purified via silica gel chromatography (EtOAc/hexanes 1:39) to afford **2** in 85% yield.

R$_f$ (EtOAc/hexane 1:39): 0.15;

^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.27 (dd, *J* = 7.6, 8.8 Hz, 2 H), 7.23–7.14 (m, 4 H), 6.99 (d, *J* = 7.6 Hz, 2 H), 6.93 (t, *J* = 7.2 Hz, 1 H), 5.43 (s, 1 H), 3.68 (dddd, *J* = 1.2, 3.4, 6.0, 12.4 Hz, 1 H), 3.39 (ddd, *J* = 4.0, 10.8, 12.4 Hz, 1 H), 3.07 (ddd, *J* = 6.0, 10.8, 16.4 Hz, 1 H), 2.87 (dt, *J* = 3.2, 16 Hz, 1 H).

aza-Henry, (*Table 2, entry 1*)

1-(Nitromethyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (**4**)[4]:



According to the general procedure, **1** (51.0 mg, 0.244 mmol, 1.0 equiv), Ru(bpy)$_3$Cl$_2$ (2.0 mg, 0.002 mmol, 0.01 equiv), and BrCCl$_3$ (72.0 µL, 0.731 mmol, 3.0 equiv) in DMF (1.0 mL) were irradiated with 1W blue LED lights until starting material was consumed as indicated by TLC.

---

[3] (a) Murahashi, S.-I.; Komiya, N.; Terai, H.; Nakae, T. *J. Am. Chem. Soc.* **2003**, *125*, 15312. (b) Li, Z.; Li, C.-J. *Eur. J. Org. Chem.* **2005**, *15*, 3173. (c) Li, Z.; Bohle, S.; Li, C.-J. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 8928.

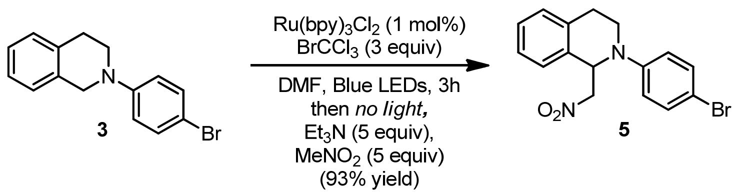
[4] (a) Condie, A. G.; González-Gómez, J. C.; Stephenson, C. R. J. *J. Am. Chem. Soc.* **2010**, *132*, 1464. (b) Li, Z.; Li, C-J. *J. Am. Chem. Soc.* **2005**, *127*, 6968.

The reaction vessel was covered with aluminum foil before Et_3N (0.17 mL, 1.218 mmol, 5.0 equiv) and $MeNO_2$ (66.0 µL, 1.218 mmol, 5.0 equiv) were added. The crude mixture was dissolved in a minimal amount of dichloromethane (approx. 0.5 mL) followed by excess diethyl ether (approx. 3.0 mL). A precipitate was observed and the heterogeneous mixture was filtered quickly over a plug of plug of silica that was washed heavily with diethyl ether. Concentration of the filtrate provided aza-Henry product **4** in 95% yield.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.16–7.03 (m, 5 H), 6.98 (d, *J* = 6.8 Hz, 1 H), 6.83 (d, *J* = 8.0 Hz, 2 H), 6.70 (t, *J* = 7.4 Hz, 1 H), 5.40 (dd, *J* = 7.6, 6.9 Hz, 1 H), 4.72 (dd, *J* = 11.8, 7.6 Hz, 1 H), 4.41 (dd, *J* = 11.8, 6.9 Hz, 1 H), 3.54–3.44 (m, 2 H), 2.94 (ddd, *J* = 16.1, 8.5, 5.6 Hz, 1 H), 2.65 (ddd, *J* = 16.1, 5.1, 4.9 Hz, 1 H).

aza-Henry, (*Table 2, entry 2*)

2-(4-Bromophenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (**5**)[2a,5]:



According to the general procedure, **3** (50.0 mg, 0.174 mmol, 1.0 equiv), $Ru(bpy)_3Cl_2$ (1.5 mg, 0.002 mmol, 0.01 equiv), and $BrCCl_3$ (51.0 µL, 0.521 mmol, 3.0 equiv) in DMF (1.0 mL) were irradiated with 1W blue LED lights until starting material was consumed as indicated by TLC. The reaction vessel was covered with aluminum foil before Et_3N (120.0 µL, 0.868 mmol, 5.0 equiv) and $MeNO_2$ (46.0 µL, 0.868 mmol, 5.0 equiv) were added. The crude mixture was dissolved in a minimal amount of dichloromethane (approx. 0.5 mL) followed by excess diethyl ether (approx. 3.0 mL). A precipitate was observed and the heterogeneous mixture was filtered quickly over a plug of plug of silica that was washed heavily with diethyl ether. Concentration of the filtrate provided aza-Henry product **5** in 93% yield.

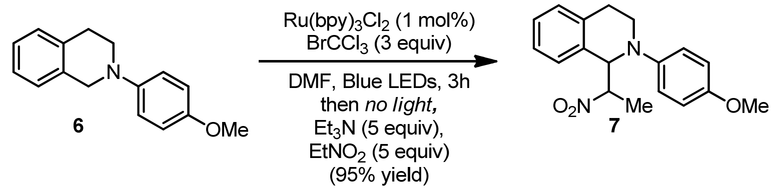
^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.23 (d, *J* = 8.8 Hz, 2 H), 7.17–7.07 (m, 3 H), 7.02 (d, *J* = 7.5 Hz, 1 H), 6.74 (d, *J* = 8.8 Hz, 2 H), 5.38 (dd, *J* = 7.5, 7.0 Hz, 1 H), 4.74 (dd, *J* = 11.9, 7.5 Hz, 1 H), 4.47 (dd, *J* = 11.9, 7.0 Hz, 1 H), 3.59–3.47 (m, 2 H), 2.97 (ddd, *J* = 16.2, 8.5, 6.0 Hz, 1 H), 2.70 (ddd, *J* = 16.2, 4.8, 4.8 Hz, 1 H).

---

[5] Shu, X.-Z.; Xia, X.-F.; Yang, Y.-F. Ji, K.-G.; Liu, X.-Y.; Liang, Y.-M. *J. Org. Chem.* **2009**, *74*, 7464.

aza-Henry, (*Table 2, entry 3*)

2-(4-Methoxyphenyl)-1-(1-nitroethyl)-1,2,3,4-tetrahydroisoquinoline (**7**)[2]:

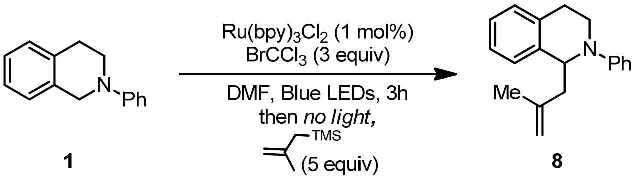


According to the general procedure, **6** (100.0 mg, 0.418 mmol, 1.0 equiv), Ru(bpy)$_3$Cl$_2$ (3.0 mg, 0.004 mmol, 0.01 equiv), and BrCCl$_3$ (120.0 µL, 1.254 mmol, 3.0 equiv) in DMF (1.7 mL) were irradiated with 1W blue LED lights until starting material was consumed as indicated by TLC. The reaction vessel was covered with aluminum foil before Et$_3$N (290.0 µL, 2.089 mmol, 5.0 equiv) and EtNO$_2$ (150.0 µL, 2.089 mmol, 5.0 equiv) were added. The crude mixture was dissolved in a minimal amount of dichloromethane (approx. 0.5 mL) followed by excess diethyl ether (approx. 3.0 mL). A precipitate was observed and the heterogeneous mixture was filtered quickly over a plug of plug of silica that was washed heavily with diethyl ether. Concentration of the filtrate provided aza-Henry product **7** in 95% yield as a ~ 2:1 inseparable mixture of diastereomers.

^{1}H NMR (CDCl$_3$, 500 MHz) δ 7.30–7.10 (m, 6 H), 7.02–6.99 (m, 2 H), 6.84–6.81 (m, 2 H), 5.26 (d, *J* = 7.7 Hz, 1 H), 5.24 (d, *J* = 7.7 Hz, 1 H), 5.05 (dq, *J* = 7.7, 7.0 Hz, 1 H), 4.89 (dq, *J* = 7.7, 6.5 Hz, 1 H), 3.84 (ddd, *J* = 13.3, 7.5, 5.5 Hz, 2 H), 3.62–3.55 (m, 2 H), 3.09–3.03 (m, 1 H), 2.95–2.85 (m, 1 H), 1.70 (d, *J* = 6.5 Hz, 3 H), 1.55 (d, *J* = 7.0 Hz, 3 H).

Allylation, (*Table 2, entry 4*)

1-(2-Methylallyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (**8**)[6]:



According to the general procedure, **1** (53.0 mg, 0.253 mmol, 1.0 equiv), Ru(bpy)$_3$Cl$_2$ (2.0 mg, 0.002 mmol, 0.01 equiv), and BrCCl$_3$ (75.0 µL, 0.760 mmol, 3.0 equiv) in DMF (1.0 mL) were irradiated with 1W blue LED lights until starting material was consumed as indicated by TLC. The reaction vessel was covered with aluminum foil before methallyltrimethylsilane (220 µL,

---

[6] Boess, E.; Sureshkumar, D.; Sud, A.; Wirtz, C.; Farès, C.; Klussmann, M. *J. Am. Chem. Soc.* **2011**, *133*, 8106.

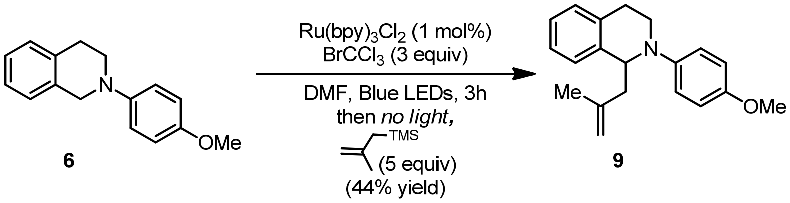
1.266 mmol, 5.0 equiv) was added. After workup, the crude oil was purified via silica gel chromatography (EtOAc/hexanes 1:39) to afford **8** in 85% yield.

R$_f$ (EtOAc/hexane 1:39): 0.15;

^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.42–7.38 (t, J = 8.8 Hz, 2 H), 7.31–7.24 (m, 4 H), 7.08 (d, J = 8.4 Hz, 2 H), 6.92–6.88 (t, J = 7.2 Hz, 1 H), 5.02 (t, J = 7.2 Hz, 1 H), 4.98 (s, 1 H), 4.84 (s, 1 H), 3.81–3.78 (dd, J = 5.2, 6.8, 2 H), 3.19 (dt, J = 7.6, 16 Hz, 1 H), 3.00 (dt, J = 4.2, 16 Hz, 1 H), 2.86 (dd, J = 6.8, 13.6 Hz, 1 H), 2.57 (dd, J = 7.2, 14 Hz, 1 H), 1.96 (s, 3H).

Allylation, (*Table 2, entry 5*)

2-(4-Methoxyphenyl)-1-(2-methylallyl)-1,2,3,4-tetrahydroisoquinoline (**9**)[5]:



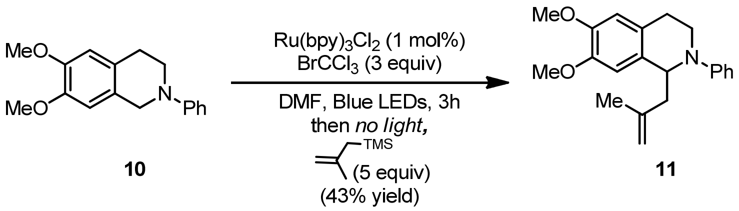
According to the general procedure, **6** (50.0 mg, 0.209 mmol, 1.0 equiv), Ru(bpy)$_3$Cl$_2$ (2.0 mg, 0.002 mmol, 0.01 equiv), and BrCCl$_3$ (62.0 μL, 0.627 mmol, 3.0 equiv) in DMF (0.85 mL) were irradiated with 1W blue LED lights until starting material was consumed as indicated by TLC. The reaction vessel was covered with aluminum foil before methallyltrimethylsilane (180 μL, 1.045 mmol, 5.0 equiv) was added. After workup, the crude oil was purified via silica gel chromatography (EtOAc/hexanes 1:99) to afford **9** in 44% yield.

R$_f$ (EtOAc/hexane 1:99): 0.15;

^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.17–7.10 (m, 4 H), 6.55 (d, J = 9 Hz, 2 H), 6.82 (d, J = 9.2 Hz, 2 H), 4.82 (s, 1 H), 4.70 (t, J = 7.1 Hz, 1 H), 4.68 (s, 1 H), 3.76 (s, 3 H), 3.61–3.57 (m, 2 H), 2.99 (ddd, J = 6.8, 9.0, 16.0 Hz, 1 H), 2.74 (dt, J = 4.1, 16.2 Hz, 1 H), 2.65 (dd, J = 7.2, 13.9 Hz, 1 H), 2.41 (dd, J = 6.7, 13.9 Hz, 1 H), 1.78 (s, 3 H).

Allylation, (*Table 2, entry 6*)

6,7-Dimethoxy-1-(2-methylallyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (**11**):



According to the general procedure, **10** (54.0 mg, 0.200 mmol, 1.0 equiv), Ru(bpy)$_3$Cl$_2$ (2.0 mg, 0.002 mmol, 0.01 equiv), and BrCCl$_3$ (59.0 µL, 0.760 mmol, 3.0 equiv) in DMF (0.8 mL) were irradiated with 1W blue LED lights until starting material was consumed as indicated by TLC. The reaction vessel was covered with aluminum foil before methallyltrimethylsilane (176 µL, 1.00 mmol, 5.0 equiv) was added. After workup, the crude oil was purified via silica gel chromatography (EtOAc/hexanes 1:19) to afford **11** in 43% yield as a colorless oil.

R_f (EtOAc/hexane 1:19): 0.15;

IR (neat): ν_{max} 3069, 2933, 2849, 2834, 1598, 1598, 1516, 1502, 1464, 1452, 1388, 1353, 1247, 1230, 1211, 1110, 1032 cm^{-1};

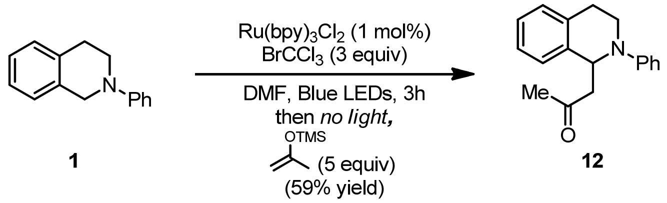
^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.22 (t, *J* = 7.6 Hz, 2 H), 6.91 (d, *J* = 8.4 Hz, 2 H), 6.74 (t, *J* = 7.2 Hz, 1 H), 6.60 (s, 2 H), 4.82 (s, 1 H), 4.77 (t, *J* = 7.0 Hz, 1 H), 4.70 (s, 1 H), 3.85 (s, 6 H), 3.69–3.63 (m, 1 H), 3.58 (ddd, *J* = 4.5, 9.6, 13.9 Hz, 1 H), 2.95 (ddd, *J* = 4.8, 8.6, 15.6 Hz, 1 H), 2.70 (dt, *J* = 4.3, 16.0 Hz, 1 H), 2.65 (dd, *J* = 6.7, 13.5 Hz, 1 H), 2.40 (dd, *J* = 7.0, 13.7 Hz, 1 H), 1.80 (s, 3 H);

^{13}C NMR (CDCl$_3$, 100 MHz): δ 149.7, 147.5, 146.8, 143.2, 141.7, 130.5, 129.2, 126.6, 117.6, 114.8, 113.4, 111.3, 110.6, 57.8, 55.9, 55.8, 44.4, 41.5, 26.4, 23.0;

HRMS (ESI) *m/z* calculated for $C_{21}H_{26}NO_2^+$ ([M+1]$^+$) 324.1964, found 324.1961.

Mannich, (*Table 2, entry 7*)

1-(2-Phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (**12**)[7]:



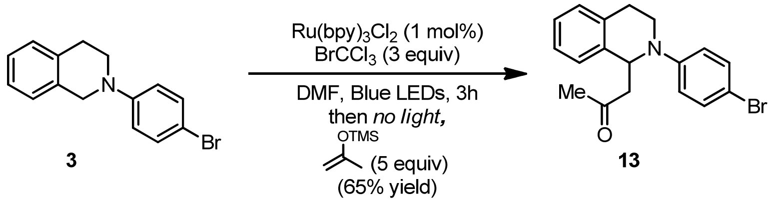
According to the general procedure, **1** (52.0 mg, 0.249 mmol, 1.0 equiv), Ru(bpy)$_3$Cl$_2$ (2.0 mg, 0.002 mmol, 0.01 equiv), and BrCCl$_3$ (74.0 µL, 0.568 mmol, 3.0 equiv) in DMF (1.0 mL) were irradiated with 1W blue LED lights until starting material was consumed as indicated by TLC. The reaction vessel was covered with aluminum foil before acetone trimethylsilylenol ether (124.0 µL, 0.745 mmol, 3.0 equiv) was added. After workup, the crude oil was purified via silica gel chromatography (EtOAc/hexanes 1:19) to afford **12** in 59% yield.

R$_f$ (EtOAc/hexane 1:19): 0.15;

^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.27 (t, J = 7.8 Hz, 2 H), 7.21–7.40 (m, 4 H), 6.96 (d, J = 8.2 Hz, 2 H), 6.80 (t, J = 7.3 Hz, 1 H), 5.43 (t, J = 6.3 Hz, 1 H), 3.67 (ddd, J = 5.1, 5.1, 12.2 Hz, 1 H), 3.55 (ddd, J = 4.5, 9, 13.1 Hz, 1 H), 3.11–3.05 (m, 1 H), 2.87–2.81 (m, 1 H), 2.09 (s, 3 H).

Mannich, (*Table 2, entry 8*)

1-(2-(4-Bromophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (**13**)[4b]:



According to the general procedure, **3** (52.0 mg, 0.180 mmol, 1.0 equiv), Ru(bpy)$_3$Cl$_2$ (1.0 mg, 0.002 mmol, 0.01 equiv), and BrCCl$_3$ (53.0 µL, 0.541 mmol, 3.0 equiv) in DMF (0.75 mL) were irradiated with 1W blue LED lights until starting material was consumed as indicated by TLC. The reaction vessel was covered with aluminum foil before acetone trimethylsilylenol ether (90.0 µL, 0.541 mmol, 3.0 equiv) was added. After workup, the crude oil was purified via silica gel chromatography (EtOAc/hexanes 1:19) to afford **13** in 65% yield.

---

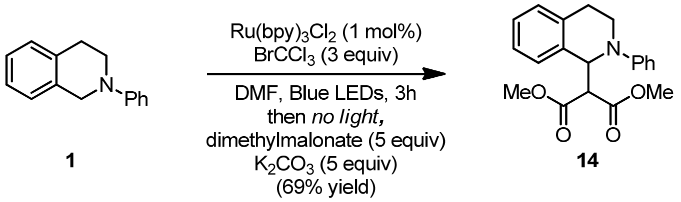
[7] (a) Shen, Y.; Li, M.; Wang, S.; Zhan, T.; Tan, Z.; Guo, C.-C. *Chem. Comm.* **2009**, *8*, 953. (b) Rueping, M.; Vila, C.; Koenigs, R. M.; Poscharny, K.; Fabry, D. C. *Chem. Comm.* **2011**, *47*, 2360.

R_f (EtOAc/hexane 1:19): 0.15;

^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.23 (d, J = 8.8 Hz, 2 H), 7.11–7.04 (m, 4 H), 6.72 (d, J = 8.8 Hz, 2 H), 5.26 (t, J = 6.4 Hz, 1 H), 3.51 (ddd, J = 5.2, 12.4, 12.4 Hz, 1 H), 3.42 (ddd, J = 4.4, 8.4, 13.2 Hz, 1 H), 2.95 (m, 2 H), 2.74 (m, 2 H), 2.00 (s, 3 H).

Mannich, (*Table 2, entry 9*)

Dimethyl 2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)malonate (**14**)[1b,3]:



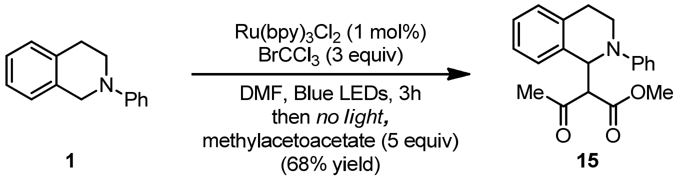
According to the general procedure, **1** (64.0 mg, 0.306 mmol, 1.0 equiv), Ru(bpy)$_3$Cl$_2$ (2.0 mg, 0.003 mmol, 0.01 equiv), and BrCCl$_3$ (91.0 μL, 0.917 mmol, 3.0 equiv) in DMF (1.0 mL) were irradiated with 1W blue LED lights until starting material was consumed as indicated by TLC. The reaction vessel was covered with aluminum foil before dimethylmalonate (171 μL, 1.529 mmol, 5.0 equiv) and K$_2$CO$_3$ (211.0 mg, 1.529 mmol, 5 equiv) were added. After workup, the crude oil was rapidly purified via silica gel chromatography (EtOAc/hexanes 1:39) to afford **14** in 69% yield.

R_f (EtOAc/hexane 1:39): 0.2;

^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.26–7.10 (m, 6 H), 7.00 (d, J = 8.0 Hz, 2 H), 6.78 (t, J = 7.2 Hz, 1 H), 5.73 (d, J = 9.2 Hz, 1 H), 3.97 (d, J = 9.2 Hz, 1 H), 3.74–3.61 (m, 2 H), 3.67 (s, 3 H), 3.56 (s, 3 H), 3.08 (ddd, J = 6.4, 8.8, 16.0 Hz, 1 H), 2.89 (dt, J = 5.2, 16.4 Hz, 1 H).

Mannich, (*Table 2, entry 10*)

Methyl 3-oxo-2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)butanoate (**15**)[3]:



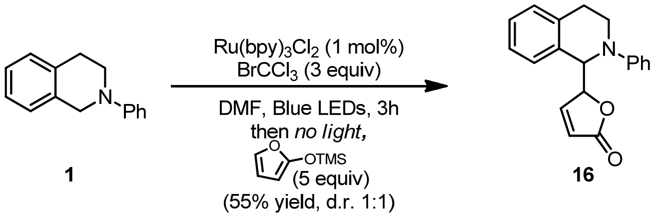
According to the general procedure, **1** (52.0 mg, 0.248 mmol, 1.0 equiv), Ru(bpy)$_3$Cl$_2$ (2.0 mg, 0.002 mmol, 0.01 equiv), and BrCCl$_3$ (73.0 μL, 0.745 mmol, 3.0 equiv) in DMF (1.0 mL) were irradiated with 1W blue LED lights until starting material was consumed as indicated by TLC. The reaction vessel was covered with aluminum foil before methylacetoacetate (130.0 μL, 1.242 mmol, 5.0 equiv) was added. Upon workup, the crude oil was rapidly purified via silica gel chromatography (EtOAc/hexanes 1:39) to afford **15** in 68% yield as a ~ 3:2 inseparable mixture of diastereomers.

R*f* (EtOAc/hexane 1:39): 0.2;

^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.24–7.08 (m, 12 H), 6.97 (dd, *J* = 7.1, 7.8 Hz, 4 H), 6.84 (dd, *J* = 6.4, 7.1 Hz, 1 H), 6.76 (dd, *J* = 6.3, 7.4 Hz, 1 H), 5.75 (d, *J* = 9.6 Hz, 1 H), 5.61 (d, *J* = 9.7 Hz, 1 H), 4.17 (d, *J* = 9.3 Hz, 1 H), 4.01 (d, *J* = 9.0 Hz, 1 H), 3.75–3.58 (m, 7 H), 3.53 (s, 3 H), 3.11–3.04 (m, 1 H), 2.97–2.86 (m, 2 H), 2.70–2.67 (m, 1 H), 2.17 (s, 3 H), 2.11 (s, 3 H).

Allylation, (*Equation 1*)

5-(2-Phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)furan-2(5H)-one (**16**)[8]:



According to the general procedure, **1** (54.0 mg, 0.258 mmol, 1.0 equiv), Ru(bpy)$_3$Cl$_2$ (2.0 mg, 0.002 mmol, 0.01 equiv), and BrCCl$_3$ (77.0 μL, 0.774 mmol, 3.0 equiv) in DMF (1.0 mL) were irradiated with 1W blue LED lights until starting material was consumed as indicated by TLC. The reaction vessel was covered with aluminum foil before siloxy furan (81.0 mg, 0.516 mmol, 2.0 equiv) was added. After workup, the crude oil was purified via silica gel chromatography (EtOAc/hexanes 1:4) to afford **16** in 55% yield as a 1:1 mixture of inseparable diastereomers.

R*f* (EtOAc/hexane 1:3): 0.25;

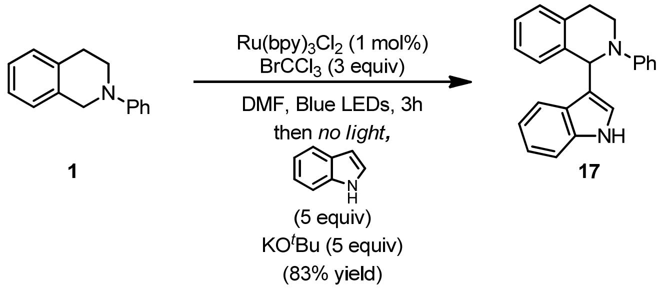
^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.53 (d, *J* = 5.6 Hz, 1 H), 7.39 (d, *J* = 5.6 Hz, 1 H), 7.33–7.16 (m, 10 H), 7.00 (d, *J* = 8.4 Hz, 2 H), 6.90 (d, *J* = 8.4 Hz, 2 H), 6.84 (dd, *J* = 7.2, 14.4 Hz, 2 H), 6.13 (dd, *J* = 1.6, 5.6 Hz, 1 H), 5.93 (dd, *J* = 1.6, 5.6 Hz, 1 H), 5.45 (dd, *J* = 2.0, 2.0 Hz, 1 H), 5.35 (d, *J* = 6.4 Hz, 1 H), 5.18 (d, *J* = 4.4 Hz, 1 H), 4.92 (d, *J* = 6.0 Hz, 1 H), 3.79 (ddd, *J* = 5.6, 5.6, 11.6 Hz, 1 H), 3.69–3.56 (m, 2 H), 3.45 (ddd, *J* = 5.2, 8.0, 12.8 Hz, 1 H), 3.10–2.91 (m, 4 H).

---

[8] Catino, A. J.; Nichols, J. M.; Nettles, B. J.; Doyle, M. P. *J. Am. Chem. Soc.* **2006**, *128*, 5648.

Indolation, (*Equation 2*)

1-(1H-Indol-3-yl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (**17**)[1c,2b,9]:



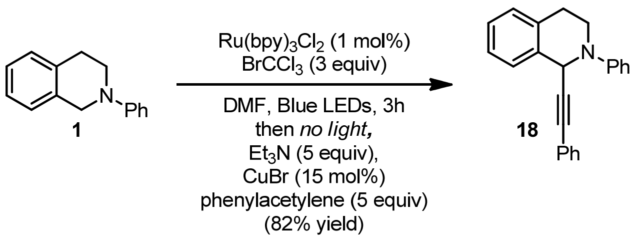
According to the general procedure, **1** (52.0 mg, 0.249 mmol, 1.0 equiv), Ru(bpy)$_3$Cl$_2$ (2.0 mg, 0.002 mmol, 0.01 equiv), and BrCCl$_3$ (74.0 µL, 0.745 mmol, 3.0 equiv) in DMF (1.0 mL) were irradiated with 1W blue LED lights until starting material was consumed as indicated by TLC. The reaction vessel was covered with aluminum foil before indole (145.0 mg, 1.242 mmol, 5.0 equiv) and KO^{t}Bu (139.0 mg, 1.242 mmol, 5.0 equiv) were added successively. After workup, the crude solid was purified via silica gel chromatography (benzene/hexanes 13:7) to afford **17** in 83% yield.

R$_f$ (benzene/hexane 13:7): 0.15;

^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.90 (bs, 1 H), 7.58 (d, *J* = 8.0 Hz, 1 H), 7.32–7.23 (m, 6 H), 7.22–7.16 (m, 5 H), 7.07–7.03 (m, 4 H), 6.81 (t, *J* = 7.2 Hz, 1 H), 6.62 (d, *J* = 2.0 Hz, 1 H), 6.20 (s, 1 H), 3.65 (d, *J* = 7.6 Hz, 1 H), 3.64 (d, *J* = 8.0 Hz, 1 H), 3.09 (ddd, *J* = 7.6, 7.6, 15.6 Hz, 1 H), 2.83 (dt, *J* = 4.4, 16.4 Hz, 1 H).

Alkynylation, (*Figure 2*)

2-Phenyl-1-(phenylethynyl)-1,2,3,4-tetrahydroisoquinoline (**18**)[2b,7b,7c,10]:



---

[9] (a) Liu, P.; Zhou, C.-Y.; Xiang, S.; Che, C.-M. *Chem. Comm.* **2010**, *46*, 2739. (b) Chu, L. ; Qing, F.-L. *Chem. Comm.* **2010**, *46*, 6285. (c) Ghobrial, M.; Harhammer, K.; Mihovilovic, M. D.; Schnürch, M. *Chem. Comm.* **2010**, *46*, 8836.

[10] Li, Z.; Li, C.-J. *Org. Lett.* **2004**, *6*, 4997.

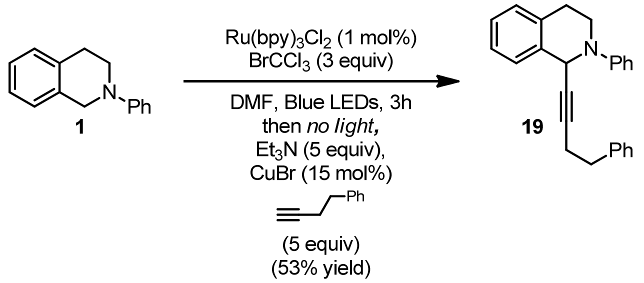
According to the general procedure, **1** (53.0 mg, 0.253 mmol, 1.0 equiv), Ru(bpy)$_3$Cl$_2$ (2.0 mg, 0.002 mmol, 0.01 equiv), and BrCCl$_3$ (75.0 µL, 0.760 mmol, 3.0 equiv) in DMF (1.0 mL) were irradiated with 1W blue LED lights until starting material was consumed as indicated by TLC. The reaction vessel was covered with aluminum foil before Et$_3$N (176.0 µL, 1.266 mmol, 5.0 equiv), CuBr (5.5 mg, 0.038 mmol, 0.15 equiv), and phenylacetylene (140.0 µL, 1.266 mmol, 5.0 equiv) were added successively. After workup, the crude oil was purified via silica gel chromatography (EtOAc/hexanes 1:39) to afford **18** in 82% yield.

R$_f$ (EtOAc/hexane 1:39): 0.25;

^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.29–7.19 (m, 5 H), 7.16–7.09 (m, 6 H), 7.04 (d, J = 8.0 Hz, 2 H), 6.80 (t, J = 7.6 Hz, 1 H), 5.56 (s, 1 H), 3.66 (ddd, J = 3.6, 6.0, 12.0 Hz, 1 H), 3.58 (ddd, J = 4.0, 10.0, 12.4 Hz, 1 H), 3.05 (ddd, J = 6.0, 10.0, 16.0 Hz, 1 H), 2.88 (dt, J = 4.0, 16.4 Hz, 1 H)

Alkynylation, (*Figure 2*)

2-Phenyl-1-(4-phenylbut-1-yn-1-yl)-1,2,3,4-tetrahydroisoquinoline (**19**):



According to the general procedure, **1** (60.0 mg, 0.287 mmol, 1.0 equiv), Ru(bpy)$_3$Cl$_2$ (2.0 mg, 0.003 mmol, 0.01 equiv), and BrCCl$_3$ (85.0 µL, 0.860 mmol, 3.0 equiv) in DMF (1.1 mL) were irradiated with 1W blue LED lights until starting material was consumed as indicated by TLC. The reaction vessel was covered with aluminum foil before Et$_3$N (200.0 µL, 1.433 mmol, 5.0 equiv), CuBr (6.0 mg, 0.043 mmol, 0.15 equiv), and 4-phenyl butyne (200.0 µL, 1.433 mmol, 5.0 equiv) were added successively. After workup, the crude oil was purified via silica gel chromatography (Et$_2$O/pentane 1:199) to afford **19** in 53% yield.

R$_f$ (Et$_2$O/pentane 1:99): 0.2;

IR (neat): ν_{max} 3061, 3025, 2923, 2835, 1597, 1502, 1453, 1428, 1377, 1342, 1288, 1224, 1202, 1153, 1032, 938 cm^{-1};

^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.32 (t, J = 8.2 Hz, 2 H), 7.28–7.17 (m, 7 H), 7.07 (d, J = 6.1 Hz, 2 H), 7.06 (t, J = 8.0 Hz, 2 H), 6.89 (t, J = 7.2 Hz, 1 H), 5.41 (s, 1 H), 3.71–3.66 (m, 1 H), 3.53

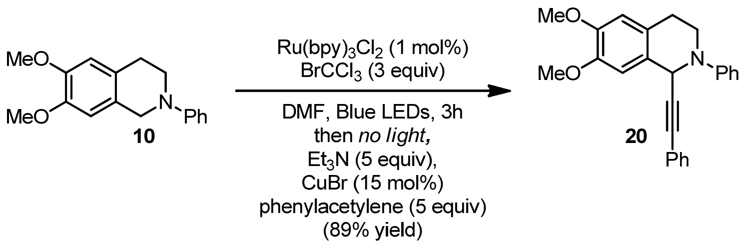
(ddd, *J* = 4.3, 10.6, 12.4 Hz, 1 H), 3.09 (ddd, *J* = 5.9, 10.4, 16.3 Hz, 1 H), 2.90 (dt, *J* = 3.7, 16.1 Hz, 1 H), 2.70 (t, *J* = 7.4 Hz, 2 H), 2.41 (dt, *J* = 1.8, 7.2 Hz, 2 H);

^{13}C NMR ($CDCl_3$, 125 MHz): δ 149.7, 140.8, 136.2, 134.4, 129.2, 129.0, 128.7, 128.4, 127.5, 127.2, 126.3, 126.2, 119.4, 116.5, 84.6, 80.2, 51.7, 43.3, 35.2, 29.0, 21.2;

HRMS (ESI) *m/z* calculated for $C_{25}H_{24}N^+$ ($[M+1]^+$) 338.1909, found 338.1915.

Alkynylation, (*Figure 2*)

6,7-Dimethoxy-2-phenyl-1-(phenylethynyl)-1,2,3,4-tetrahydroisoquinoline (**20**):



According to the general procedure, **10** (66.0 mg, 0.245 mmol, 1.0 equiv), $Ru(bpy)_3Cl_2$ (2.0 mg, 0.002 mmol, 0.01 equiv), and $BrCCl_3$ (72.5 µL, 0.735 mmol, 3.0 equiv) in DMF (1.0 mL) were irradiated with 1W blue LED lights until starting material was consumed as indicated by TLC. The reaction vessel was covered with aluminum foil before Et_3N (170.0 µL, 1.225 mmol, 5.0 equiv), CuBr (5.3 mg, 0.037 mmol, 0.15 equiv), and phenylacetylene (130.0 µL, 1.225 mmol, 5.0 equiv) were added successively. After workup, the crude oil was purified via silica gel chromatography (EtOAc/hexanes 1:19 → 1:9) to afford **20** in 89% yield as a brownish-yellow solid.

R_f (EtOAc/hexane 1:19): 0.15;

IR (neat): ν_{max} 3060, 3001, 2993, 2834, 2253, 1598, 1517, 1502, 1490, 1463, 1443, 1408, 1376, 1266, 1248, 1214, 1157, 1116, 1070, 1027 cm^{-1};

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37–7.33 (m, 4 H), 7.26–7.25 (m, 2 H), 7.15 (d, *J* = 8 Hz, 2 H), 6.92 (t, *J* = 7.2 Hz, 1 H), 6.90 (s, 1 H), 6.69 (s, 1 H), 5.61 (s, 1 H), 3.93 (s, 3 H), 3.90 (s, 3 H), 3.82–3.77 (m, 1 H), 3.68 (ddd, *J* = 3.9, 10.9, 10.9 Hz, 1 H), 3.10 (ddd, *J* = 5.8, 10.7, 16.0 Hz, 1 H), 2.88 (dt, *J* = 3.1, 15.8 Hz, 1 H);

^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.6, 148.3, 147.6, 131.8, 129.2, 128.1, 128.0, 127.1, 126.4, 123.0, 119.7, 116.9, 111.4, 110.1, 88.7, 84.7, 56.1, 55.9, 52.1, 43.4, 28.5;

HRMS (ESI) *m/z* calculated for $C_{25}H_{24}NO_2^+$ ($[M+1]^+$) 370.1807, found 370.1807.

$\mathrm{pK_a}$ Approximation Calculations:

The following was extrapolated from known derivations[11,12]:

$$\mathrm{pKa}_{(\mathrm{RH}+\cdot)\mathrm{sol}} = \left\{\frac{(\Delta G^{\circ}{}_{\mathrm{BDE(RH)g}} - 37.6)}{1.36}\right\} - \left\{\frac{E^{\circ\prime}{}_{(\mathrm{RH})}}{0.0592}\right\}$$

$$\mathrm{pKa}_{(\mathrm{RH}+\cdot)\mathrm{sol}} = \left\{\frac{(\mathrm{BDE} - 37.6)}{1.36}\right\} - \left\{\frac{\mathrm{E1/2(+)ox}}{0.0592}\right\}$$

$T = 300$ K
$\Delta G^{\circ}{}_{\mathrm{f(H)g}} = 203.2$ KJ/mol
$\Delta G^{\circ}{}_{\mathrm{tr(H+)MeCN}}$ = (transfer of proton from water to solvent) 46.0 KJ/mol
F = Faraday's constant ($9.6485\mathrm{x}10^{4}$ C/mol)
R = Gas constant (8.3145 V*C/mol*K)
$E^{\circ\prime}{}_{(\mathrm{RH})}$ = Formal potential for oxidation in V vs. SCE

$\mathrm{pK_a}$ approximation for α-C–H amino radical cations of tertiary amines ($\mathrm{Et_3N}$ used as a representative example)[13,14]:

$$\mathrm{pKa}_{(\mathrm{RH}+\cdot)\mathrm{sol}} = \left\{\frac{(90.7 - 37.6)}{1.36}\right\} - \left\{\frac{+0.73}{0.0592}\right\}$$

$$\mathrm{pKa}_{(\mathrm{RH}+\cdot)\mathrm{sol}} = 26.7$$

BDE ($\mathrm{Et_3N}$) = 90.7 kcal/mol
$E^{\circ\prime}(\mathrm{Et_3N})$ = E1/2(+)ox = +0.73 V

---

[11] (a) Nicholas, M. de P.; Arnold, D. R. *Can. J. Chem.* **1982**, *60*, 2165. (b) Nelsen, S. P.; Ippoliti, J. T. *J. Am. Chem. Soc.* **1986**, *108*, 4879. (c) Xu, W.; Mariano, P. S. *J. Am. Chem. Soc.* **1991**, *113*, 1431. (d) Zhang, X.; Bordwell, F. G. *J. Org. Chem.* **1992**, *57*, 4163.

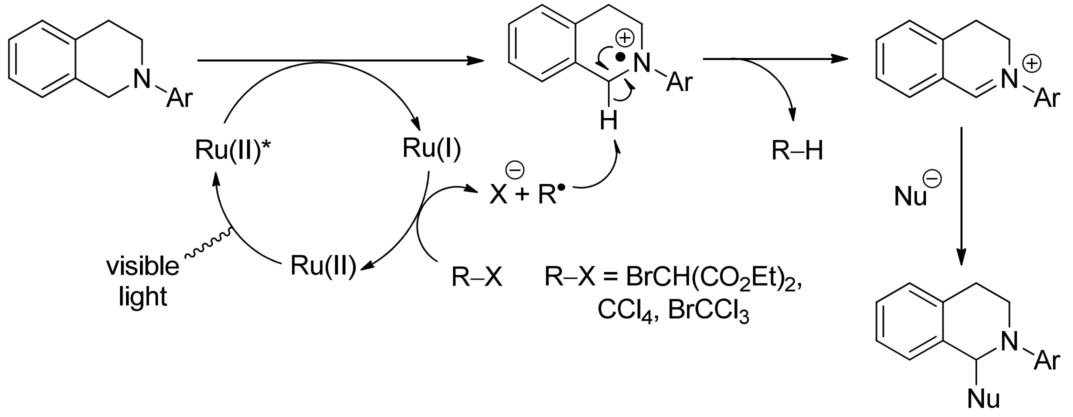
[12] Calculations adjusted to kcal/mol.

[13] BDE for α-C–H of $\mathrm{Et_3N}$: Dombrowski, G. W.; Dinnocenzo, J. P.; Farid, S.; Goodman, J. L.; Gould, I. R. *J. Org. Chem.* **1991**, *64*, 427.

[14] Formal potential for oxidation in V vs. SCE for $\mathrm{Et_3N}$ see: Lindsay Smith, J. R.; Masheder, D. *J. Chem. Soc., Perkin Trans. 2*, **1976**, 47.

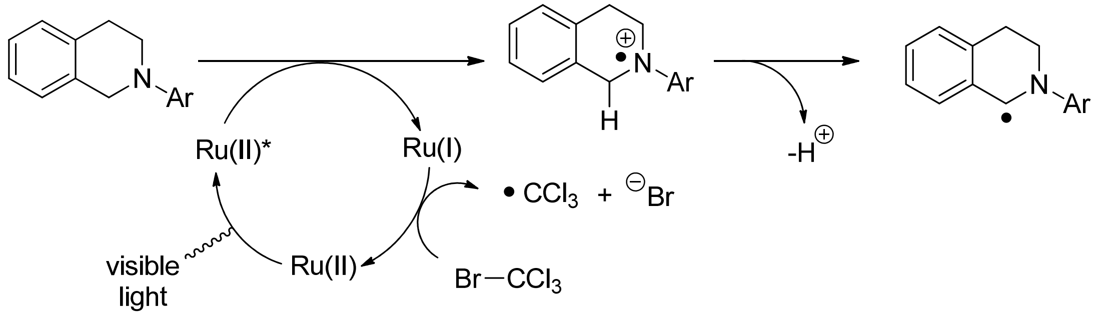
Proposed Mechanisms

Hypothesis 1

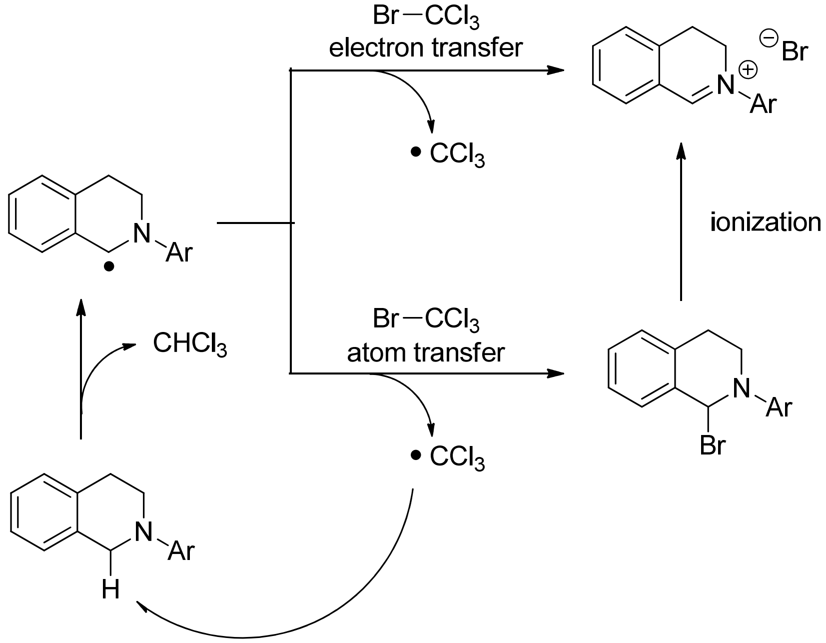


Hypothesis 2

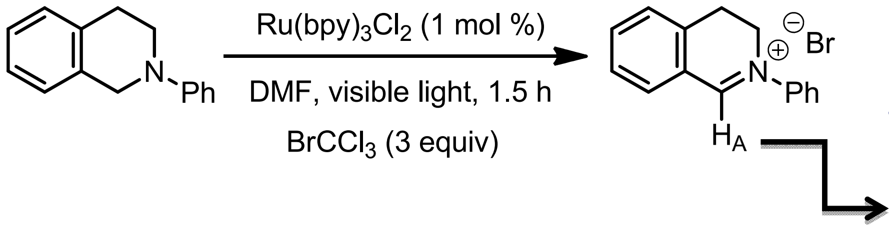
Initiation

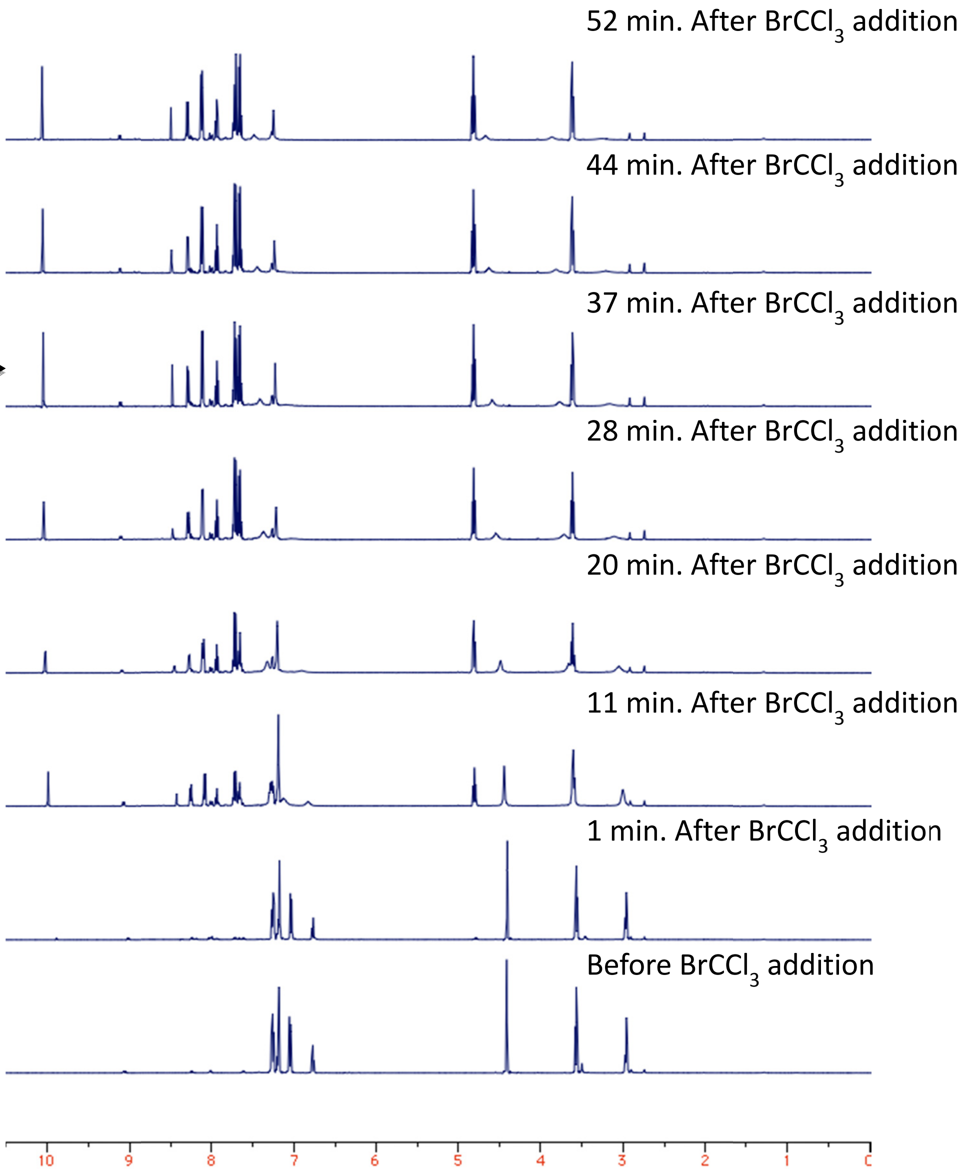


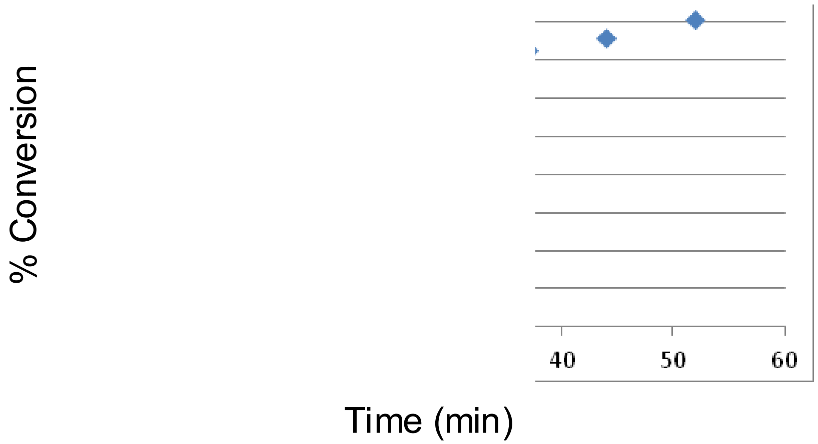
Propagation



NMR Experiments for Iminium Ion and Chloroform Formation:

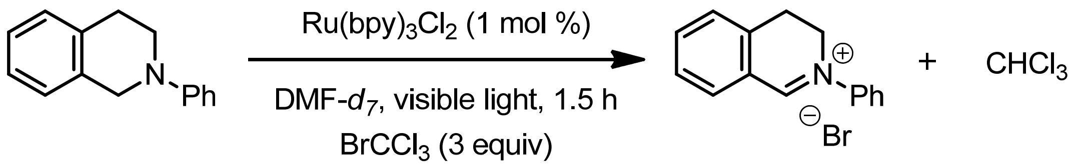


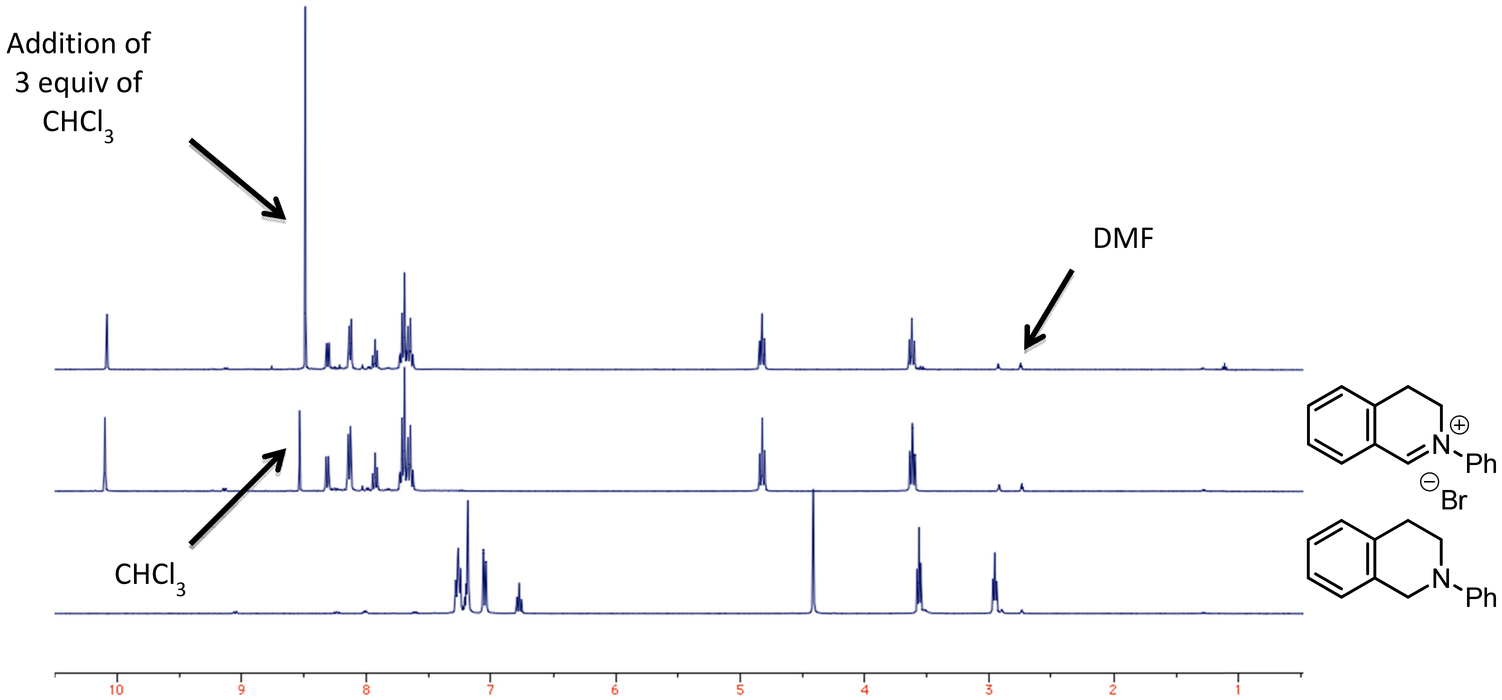




Interestingly, during the course of our reaction screening, we observed a significant difference in reaction time associated with the formation of the product as compared to our previous studies. TLC analysis indicated the consumption of starting material within three hours to form the putative iminium ion. To better understand the rate of consumption of the starting material we monitored the reaction via ^{1}H NMR (S16). Initial addition of bromotrichloromethane ($BrCCl_3$) to an NMR tube containing tetrahydroisoquinoline 1 and $Ru(bpy)_3Cl_2$ (1 mol%) in DMF-d_7 without blue LED irradiation displayed little change in the spectrum. However, once the reaction was exposed to light for 10 minutes, we observed approximately 40% conversion to the corresponding iminium ion as indicated by the singlet at 10.1 ppm. Continual monitoring of the reaction under light irradiation revealed 85% conversion to the iminium ion after one hour. Upon further inspection of the spectral data, we discovered that the singlet at 8.5 ppm corresponds to chloroform generated from the reduction of $BrCCl_3$. This observation provides additional evidence for our proposed mechanistic role of bromotrichloromethane in the catalytic cycle.

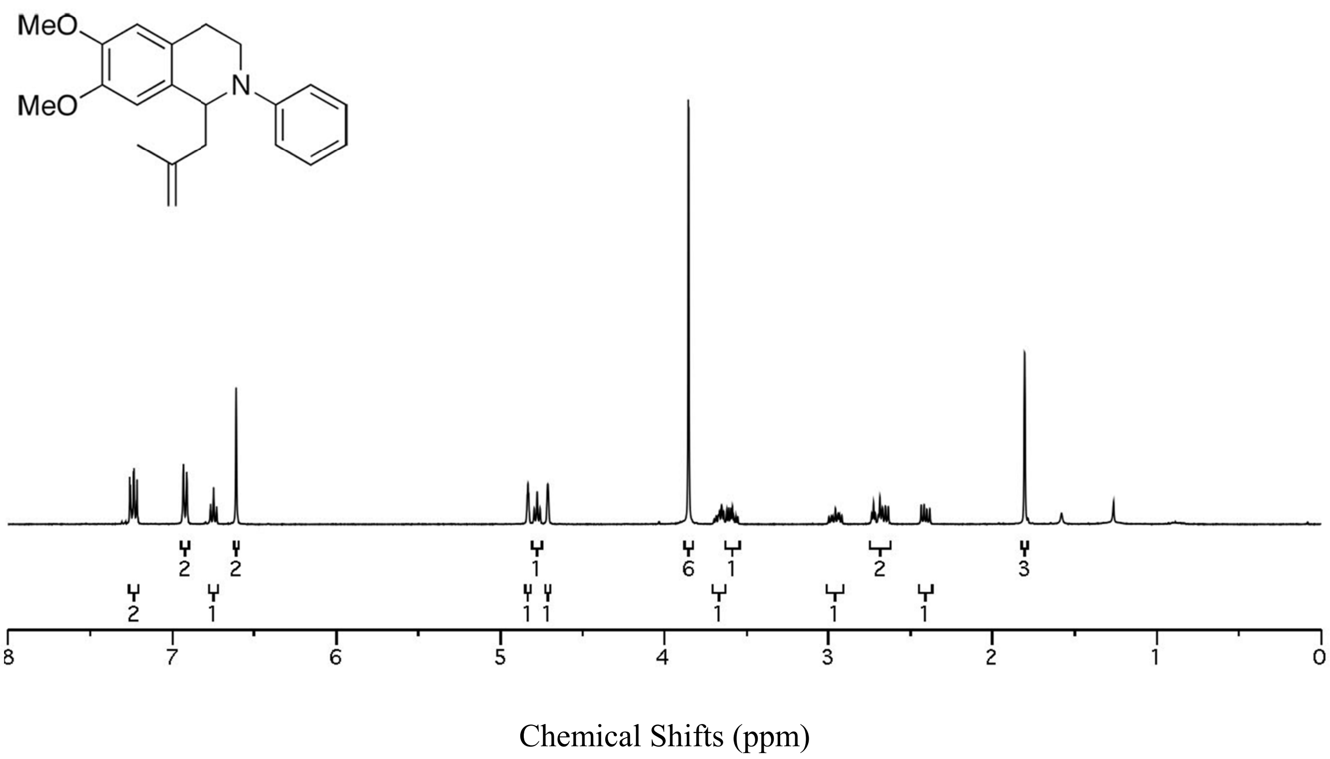
Evidence of catalyst turnover from external oxidants:



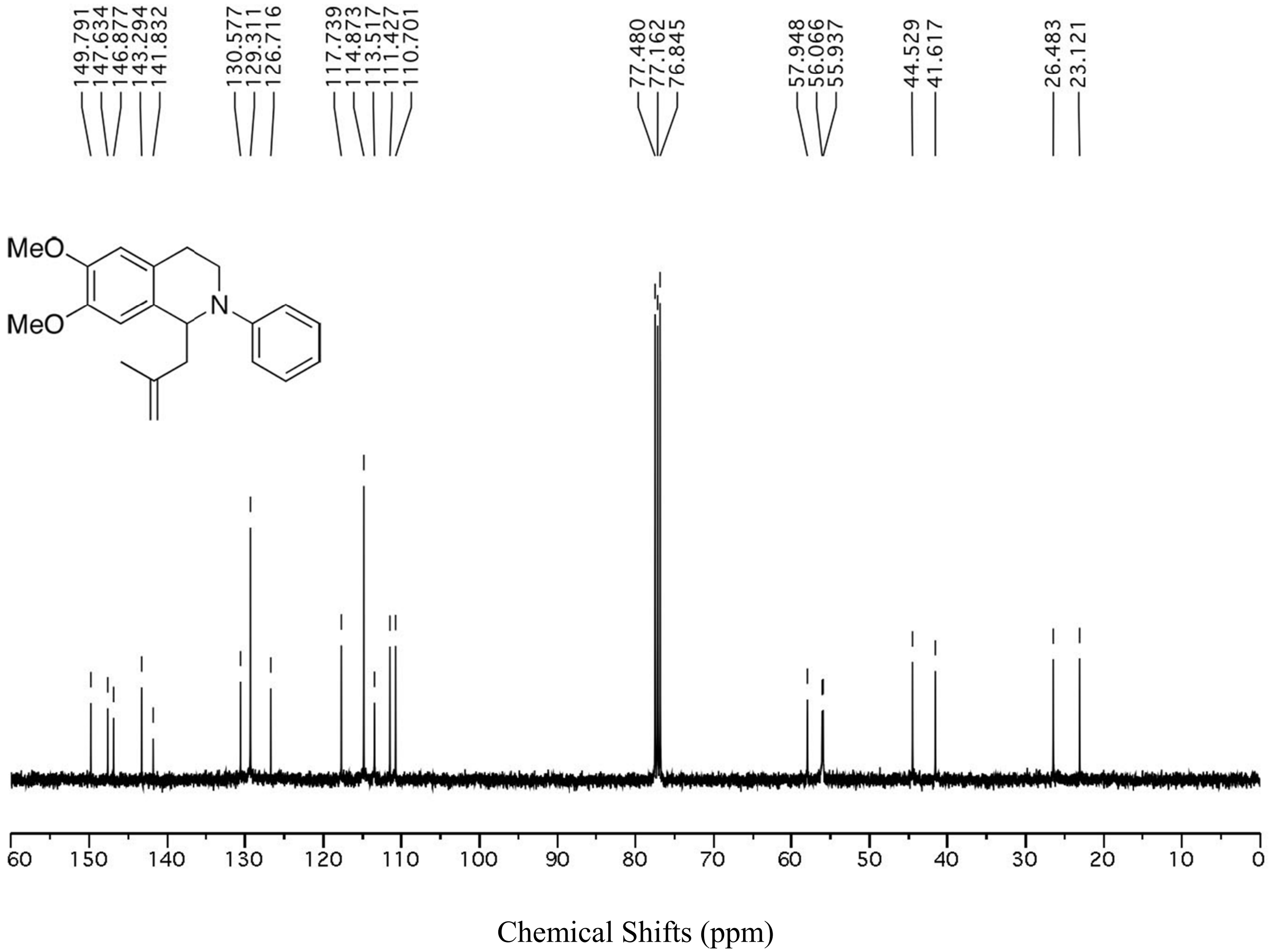


^{1}H and ^{13}C Spectra for All New Compounds:

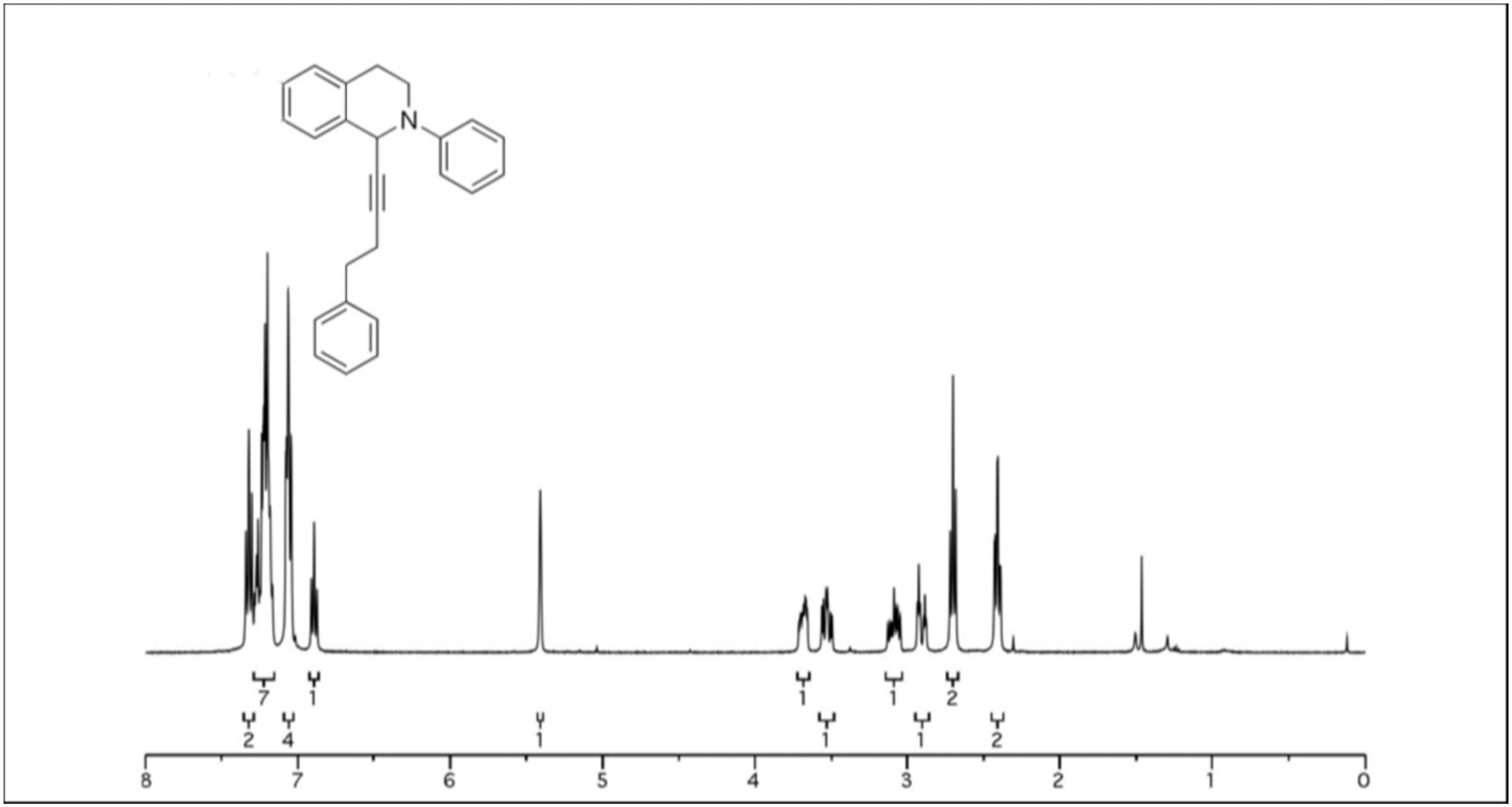
Compound **11** ^{1}H NMR Spectrum



Compound **11** ^{13}C NMR Spectrum

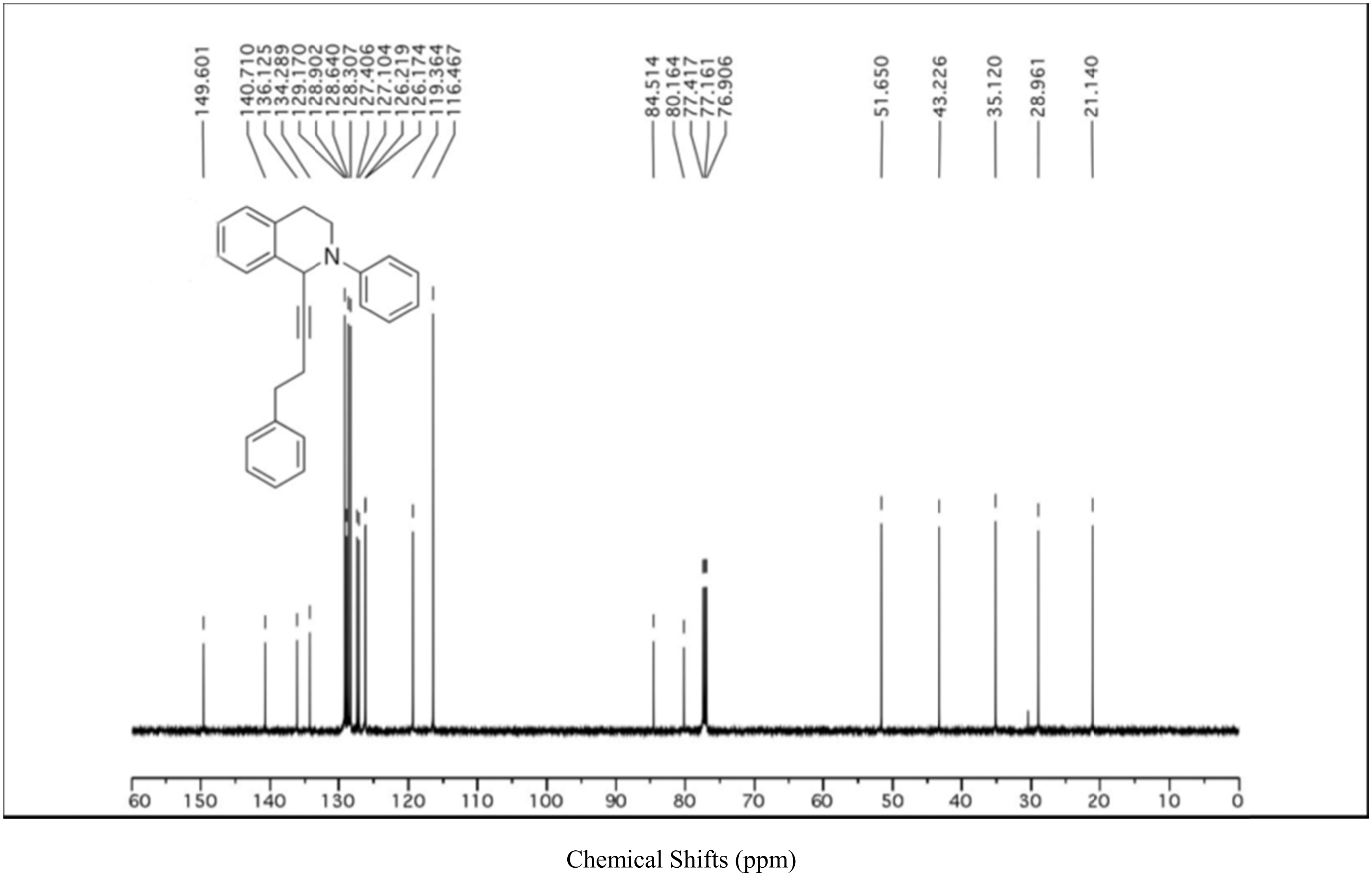


Compound **19** ^{1}H NMR Spectrum

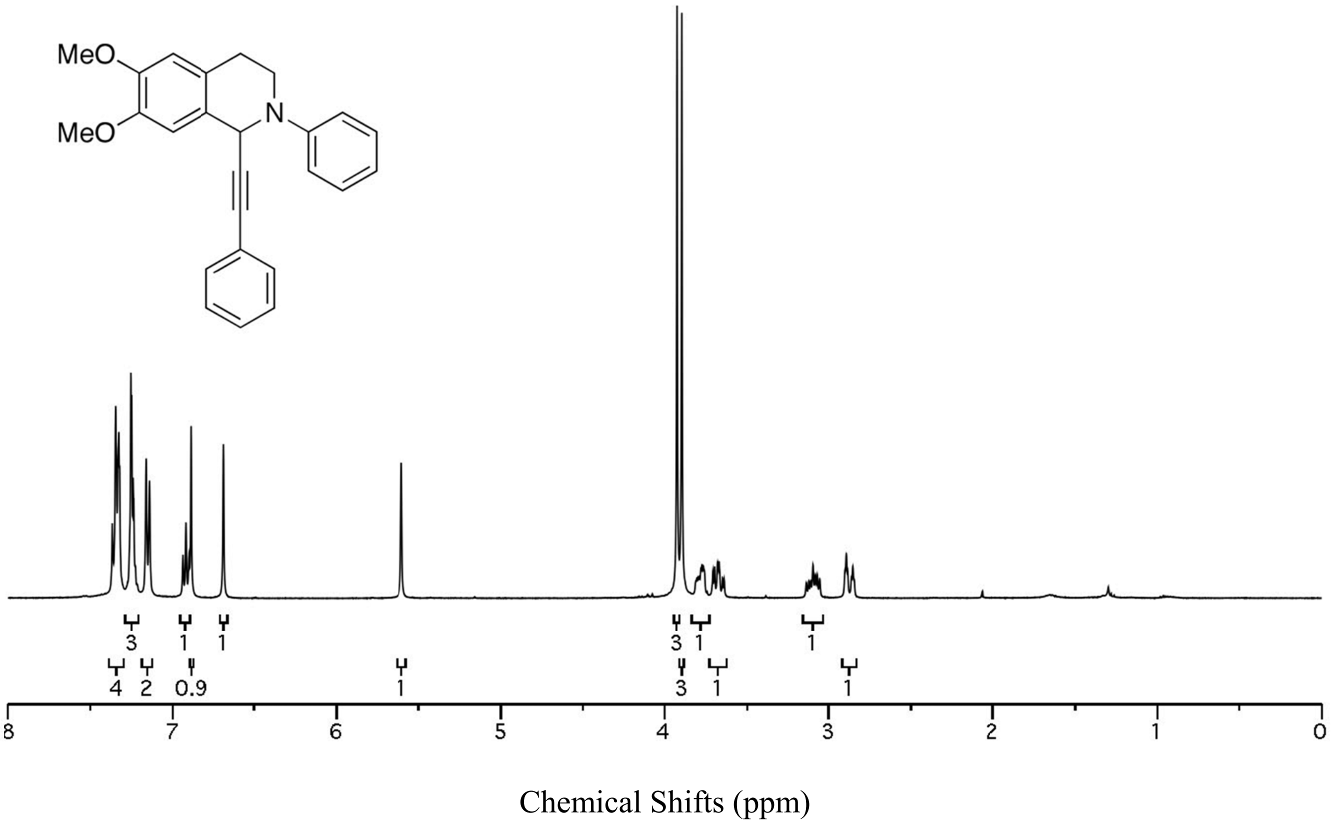


Chemical Shifts (ppm)

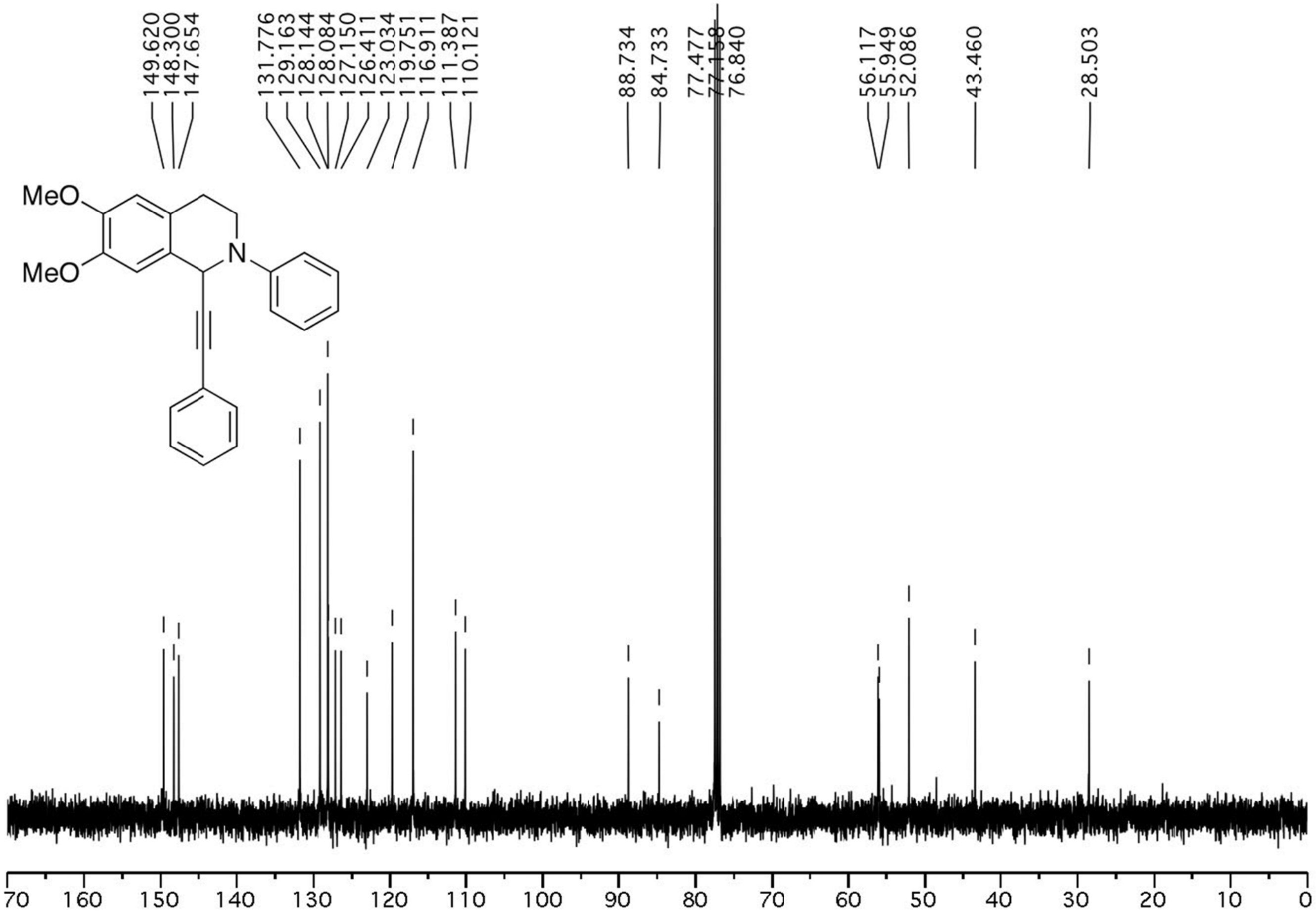
Compound **19** ^{13}C NMR Spectrum



Compound **20** ^{1}H NMR Spectrum



Compound **20** ^{13}C NMR Spectrum



Chemical Shifts (ppm)