

Supporting Information

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# Efficient Synthesis of *O*-*tert*-Propargylic Oximes via Nicholas Reaction

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## Supporting Information

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## 1. General information

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on JEOL JNM-ECS400 (400 MHz for  $^1\text{H}$  and 100 MHz for  $^{13}\text{C}$ ) spectrometer. Chemical shifts are reported in ppm relative to  $\text{CHCl}_3$  (for  $^1\text{H}$ ,  $\delta$  7.26), and  $\text{CDCl}_3$  (for  $^{13}\text{C}$ ,  $\delta$  77.00).  $^1\text{H}$  NMR data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sext = sextet, br = broad, m = multiplet) and coupling constants (Hz). Infrared (IR) spectra were recorded on a JASCO FT/IR- 4100 spectrometer. High-resolution mass spectra analysis was performed on a Bruker Daltonics APEX III FT-ICR-MS spectrometer and Bruker Daltonics solariX FT-ICR-MS spectrometer at Research and Analytical Center for Giant Molecules, Graduate School of Science, Tohoku University. Melting point (Mp) was measured by METTLER TOLEDO MP70. Flash column chromatography was performed on silica gel 60N (Merck 40-63  $\mu\text{m}$  or Kanto 40-50  $\mu\text{m}$ ). Analytical thin layer chromatography (TLC) was performed on Merck pre-coated TLC plates (silica gel 60 F254).

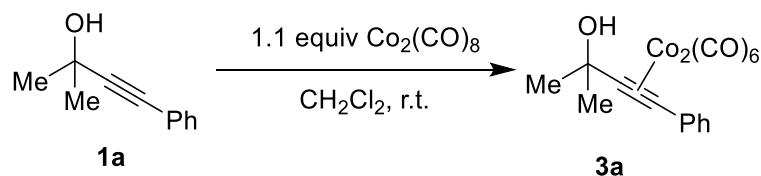
### Materials

Acetone, hexane,  $\text{CH}_3\text{CN}$ , 1,4-dioxane, 1,2-dichloroethane, and methanol were purchased from FUJIFILM Wako Pure Chemical Corporation.  $\text{CH}_2\text{Cl}_2$  was purchased from KANTO CHEMICAL CO., INC.  $\text{Co}_2(\text{CO})_8$ ,  $\text{BF}_3\cdot\text{OEt}_2$ , and CAN were purchased from TCI. These reagents were used as received.  $[\text{Cu}(\text{cod})]_2$  and  $(\text{PPh}_3)\text{AuNTf}_2$  were prepared according to reported procedures.<sup>1,2</sup>  $\text{CDCl}_3$  was purchased from MERCK. All air- and moisture-sensitive manipulations were performed under argon atmosphere using oven-dried glassware, including glovebox techniques.

1. Chi, K, M.; Shin, H.-K.; Hampden-Smith, M. J.; Duesler, E. N.; Kostas, T. T. *Polyhedron* **1991**, *10*, 2293.
2. Mézailles, N.; Ricard, L.; Gagosz, F. *Org. Lett.*, **2005**, *7*, 4133.

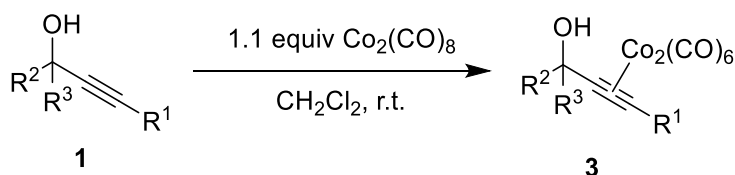
## 2. Ligation of the propargylic alcohol **1** with $\text{Co}_2(\text{CO})_8$

General procedure for ligation of the propargylic alcohol **1a** with  $\text{Co}_2(\text{CO})_8$ .



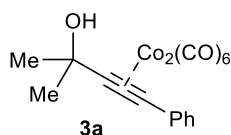
To a suspension of  $\text{Co}_2(\text{CO})_8$  (5.6 g, 16.5 mmol) in  $\text{CH}_2\text{Cl}_2$  (150 mL) in a 300 mL three-neck flask was added **1a** (15 mmol) at room temperature. The mixture was stirred at room temperature for 3 h. After solvents were removed in vacuo, the crude product was purified by silica-gel column chromatography using hexane/ $\text{CH}_2\text{Cl}_2$  (1:2) as eluent to afford **3a** (6.18g, 14 mmol, 93% yield).

Table S1. Ligation of the propargylic alcohol **1** with  $\text{Co}_2(\text{CO})_8$ <sup>a</sup>



entry	<b>1</b>	R <sup>1</sup>	R <sup>2</sup> , R <sup>3</sup>	<b>3</b> (Yield, %) <sup>b</sup>
1	<b>1a</b>	Ph	Me, Me	<b>3a</b> (93)
2	<b>1b</b>	Ph	Ph, Me	<b>3b</b> (69)
3	<b>1c</b>	Ph	Ph, Ph	<b>3c</b> (quant.)
4	<b>1d</b>	Ph	-(CH <sub>2</sub> ) <sub>3</sub> -	<b>3d</b> (93)
5	<b>1e</b>	Ph	-(CH <sub>2</sub> ) <sub>4</sub> -	<b>3e</b> (97)
6	<b>1f</b>	Ph	-(CH <sub>2</sub> ) <sub>5</sub> -	<b>3f</b> (93)
7	<b>1g</b>	4-MeOC <sub>6</sub> H <sub>4</sub>	Me, Me	<b>3g</b> (96)
8	<b>1h</b>	4-F <sub>3</sub> CC <sub>6</sub> H <sub>4</sub>	Me, Me	<b>3h</b> (88)
9	<b>1i</b>	<i>n</i> -Hex	Me, Me	<b>3i</b> (88)
10	<b>1j</b>	Me <sub>3</sub> Si	Me, Me	<b>3j</b> (70)

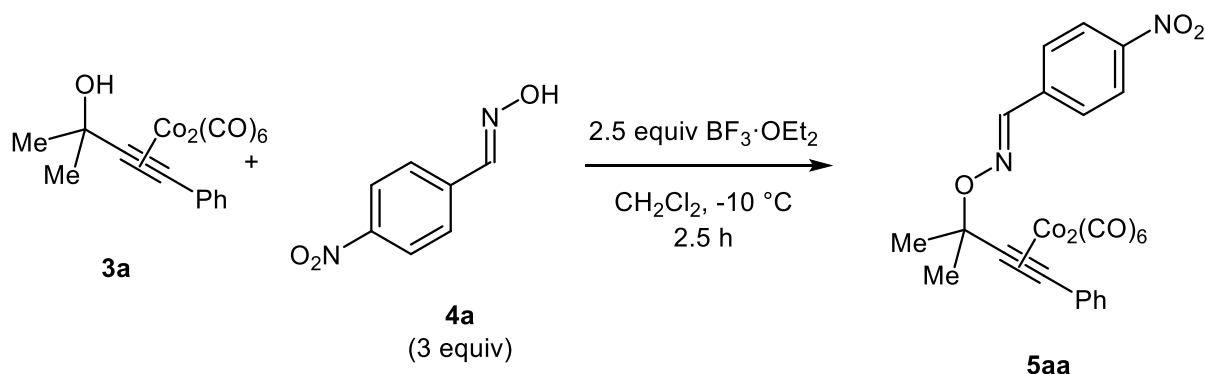
<sup>a</sup> The reactions of **1** was carried out in the presence of  $\text{Co}_2(\text{CO})_8$  (1.1 mmol) at room temperature for 2.5 h. <sup>b</sup> Isolated yields.



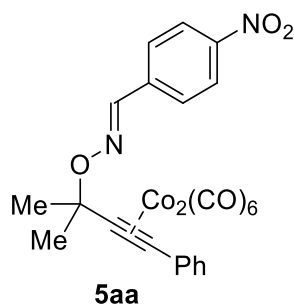
**3a.** Reaction time: 2.5 h. 6.18 g (13.9 mol, 93% yield). Black solid. Melting point: 72.6 °C  $R_f$  = 0.68 [hexane/EtOAc = 4:1 (v/v)]. <sup>1</sup>H NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.61 (m, 2H), 7.35 (m, 3H), 1.72 (s, 6H). <sup>13</sup>C NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.6, 164.7, 137.7, 129.7, 128.8, 127.8, 107.0, 96.1, 91.7, 73.4, 32.4. IR (neat) 3606, 3535, 3082, 2988, 2933, 2475, 2089, 2041, 2001, 1606, 1573, 1482, 1459, 1443, 1377, 1362, 1312,

1231, 1153, 1106, 1073, 1030, 998, 954, 918, 828, 761, 736, 691, 672, 621  $\text{cm}^{-1}$ . HRMS (ESI) calcd. for  $\text{C}_{17}\text{H}_{12}\text{Co}_2\text{O}_7$  ( $\text{M}+\text{Na}$ )<sup>+</sup> 468.9139, found 468.9139.

### 3. General procedure for Nicholas reaction between alkyne-cobalt complex **3** and oximes **4**.



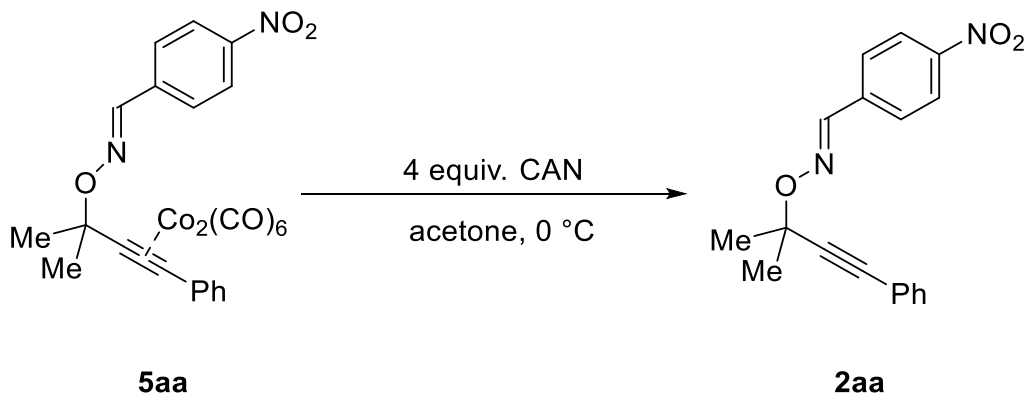
To a mixture of **3a** (6.18 g, 13.9 mmol) and the oxime **4a** (6.94 g, 41.8 mmol) in  $\text{CH}_2\text{Cl}_2$  (140 mL) was added  $\text{BF}_3\cdot\text{OEt}_2$  (4.42 mL, 35.2 mmol) dropwise at  $-10\text{ }^\circ\text{C}$ . After stirring at  $-10\text{ }^\circ\text{C}$  for 2.5 h, the reaction was quenched with aqueous  $\text{NaHCO}_3$  solution and the mixture was extracted with  $\text{CH}_2\text{Cl}_2$ . The organic layer was washed with water and brine and dried over anhydrous sodium sulfate. After solvents were removed in vacuo, the residue was purified by silica gel column chromatography using hexane/ethyl acetate (5/1) as eluent to obtain **5aa** (7.57 g, 12.7 mmol, 91% yield).



**5aa**. Reaction time: 2.5 h. Yield: 7.57 g (12.7 mmol, 91% yield). Black solid. Melting point:  $137.7\text{ }^\circ\text{C}$   $R_f = 0.67$  [hexane/EtOAc = 4:1 (v/v)].  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.19-8.15 (m, 2H), 8.11-8.10 (m, 1H), 7.58-7.54 (m, 4H), 7.36-7.34 (m, 3H), 1.875 (s, 1H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.6, 148.0, 138.6, 138.3, 129.7, 128.8, 127.5, 123.9, 102.5, 92.6, 83.7, 46.2, 29.2. IR (neat) 3428, 3413, 3370, 3359, 2989, 2937, 2376, 2362, 2347, 2334, 2323, 2090, 2051, 2021, 1601, 1587, 1523, 1482, 1442, 1377, 1345, 1140, 1109, 962, 852, 795, 762, 691  $\text{cm}^{-1}$ . HRMS (ESI) calcd. for  $\text{C}_{24}\text{H}_{16}\text{Co}_2\text{N}_2\text{O}_9$  ( $\text{M}+\text{Na}$ ) $^+$  616.9412, found 616.9412.

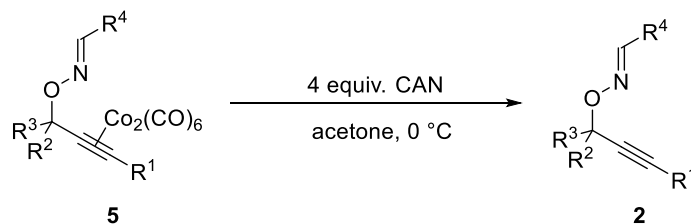
## 4. Deprotection of 5

General procedure for decomplexation of **5aa**;



To **5aa** (4.87 g, 8.16 mmol) in acetone (81.6 mL) in 200 mL round-bottom flask was added CAN (17.9 g, 32.6 mmol) at 0 °C. After stirring at 0 °C for 5 h, the reaction was quenched with water and the mixture was extracted with ether. The organic layer was washed with water and brine and dried over Na<sub>2</sub>SO<sub>4</sub>. After removing solvents in vacuo, the residue was purified by silica gel column chromatography using hexane/ethyl acetate (10/1) as eluent to obtain **2aa** (2.52 g, 8.16 mmol, quant) in an analytically pure form.

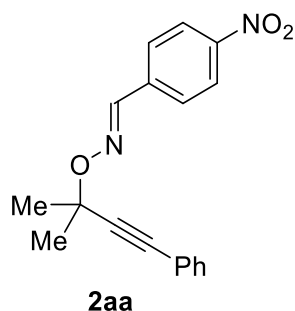
**Table S2. Decomplexation of 5<sup>a</sup>**



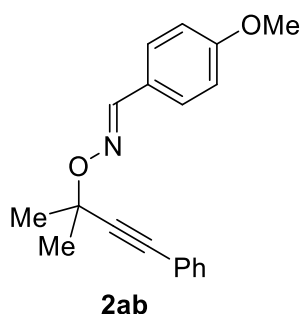
entry	<b>5</b>	R <sup>1</sup>	R <sup>2</sup> ,R <sup>3</sup>	R <sup>4</sup>	time / h	<b>2</b> (yield, %) <sup>b</sup>
1	<b>5aa</b>	Ph	Me, Me	<i>p</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	5	<b>2aa</b> (quant.)
2	<b>5ab</b>	Ph	Me, Me	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	0.67	<b>2ab</b> (30)
3	<b>5ac</b>	Ph	Me, Me	Cy	0.25	<1
4	<b>5ba</b>	Ph	Ph, Me	<i>p</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	1	<b>2ba</b> (83)
5	<b>5ca</b>	Ph	Ph, Ph	<i>p</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	11	<b>2ca</b> (77)
6	<b>5da</b>	Ph	-(CH <sub>2</sub> ) <sub>3</sub> -	<i>p</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	2	<b>2da</b> (77)
7	<b>5ea</b>	Ph	-(CH <sub>2</sub> ) <sub>4</sub> -	<i>p</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	2	<b>2ea</b> (56)
8	<b>5fa</b>	Ph	-(CH <sub>2</sub> ) <sub>5</sub> -	<i>p</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	2.5	<b>2fa</b> (78)
9 <sup>c</sup>	<b>5ga</b>	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	Me, Me	<i>p</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	0.33	<b>2ga</b> (25)
10	<b>5ha</b>	4-F <sub>3</sub> CC <sub>6</sub> H <sub>4</sub>	Me, Me	<i>p</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	1	<b>2ha</b> (58)
11	<b>5ia</b>	Me <sub>3</sub> Si	Me, Me	<i>p</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	5	<b>2ia</b> (66)
12	<b>5ja</b>	<i>n</i> -Hex	Me, Me	<i>p</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	12	<b>2ja</b> (91)

<sup>a</sup> The reactions of **5** (1.0 mmol) was carried out in the presence of cerium ammonium nitrate (CAN, 4.0 mmol) in acetone (10 mL) at 0 °C for 0.25-12 h. <sup>b</sup> Isolated yield in parentheses. <sup>c</sup> 2 equivalent of CAN was used.

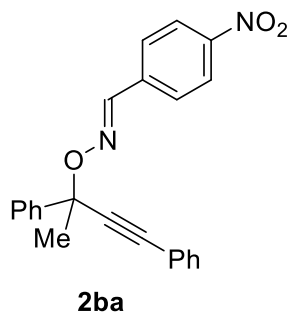
## 5. Analytical Data of 2



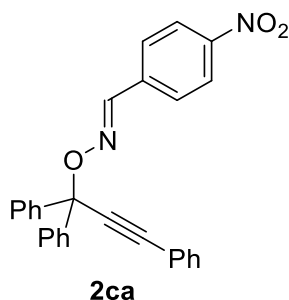
**(E)-4-Nitrobenzaldehyde O-(2-methyl-4-phenylbut-3-yn-2-yl) oxime (2aa).** Reaction time: 5 h. 4.01 g (13.0 mmol, 85% yield for 3 steps). Yellow oil.  $R_f = 0.50$  [hexane/EtOAc = 10:1 (v/v)].  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.25-8.23 (d,  $J = 8.7$  Hz, 2H), 8.17 (s, 1H), 7.82-7.80 (d,  $J = 8.7$  Hz, 2H), 7.45-7.43 (m, 2H), 7.31-7.29 (m, 3H), 1.74 (s, 6H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  148.3, 147.6, 138.4, 131.8, 128.4, 128.2, 127.8, 123.9, 122.6, 90.5, 84.9, 83.8, 77.9, 35.1, 14.0. IR (neat) 2997, 2949, 1598, 1589, 1519, 1491, 1443, 1421, 1409, 1341, 1305, 1245, 1215, 1174, 1154, 1102, 1070, 1028, 1013, 947, 851, 795, 757, 690, 642, 622  $\text{cm}^{-1}$ . HRMS (ESI) calcd. for  $\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_3$  ( $\text{M}+\text{Na}$ ) $^+$  331.1053, found 331.1053.



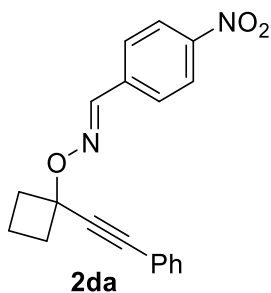
**(E)-4-Methoxybenzaldehyde O-(2-methyl-4-phenylbut-3-yn-2-yl) oxime (2ab).** Reaction time: 40 min. 51.7 mg (0.176 mmol, 15% yield for 3 steps). Colorless oil.  $R_f = 0.68$  [hexane/EtOAc = 4:1 (v/v)].  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.07 (s, 1H), 7.60-7.57 (d,  $J = 9.2$  Hz, 2H), 7.46-7.42 (m, 2H), 7.29-7.25 (m, 3H), 6.90-6.88 (d,  $J = 8.7$  Hz, 2H), 3.82 (s, 3H), 1.75 (s, 6H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  162.7, 160.8, 148.2, 131.8, 128.6, 128.1, 128.1, 125.4, 123.0, 114.0, 92.3, 83.3, 75.1, 55.3, 28.2. IR (neat) 2985, 2934, 2837, 1606, 1573, 1513, 1489, 1463, 1442, 1419, 1377, 1359, 1288, 1249, 1171, 1149, 1109, 1070, 1031, 1011, 961, 859, 831, 756, 722, 691, 642, 613  $\text{cm}^{-1}$ . HRMS (ESI) calcd. for  $\text{C}_{19}\text{H}_{19}\text{NO}_2$  ( $\text{M}+\text{Na}$ ) $^+$  316.1308, found 316.1308.



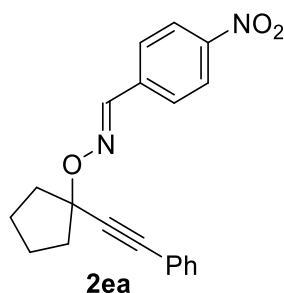
**(E)-4-Nitrobenzaldehyde O-(2,4-diphenylbut-3-yn-2-yl) oxime (2ba).** Reaction time: 1 h. 0.282 g (0.761 mmol, 76% yield for 3 steps). Colorless solid. Melting point: 107.8 °C.  $R_f = 0.41$  [hexane/EtOAc = 10:1 (v/v)].  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.23-8.16 (m, 3H), 8.7.72-7.70 (m, 4H), 7.51-7.33 (m, 8H), 2.03 (s, 3H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  148.2, 147.1, 142.6, 138.4, 131.8, 128.5, 128.3, 128.0, 127.8, 126.1, 123.8, 122.5, 90.1, 86.7, 80.9, 30.1. IR (neat) 3060, 2991, 2353, 1615, 1598, 1519, 1491, 1445, 1408, 1342, 1315, 1296, 1276, 1224, 1178, 1155, 1141, 1109, 1067, 1028, 955, 854, 831, 789, 758, 691, 643, 625  $\text{cm}^{-1}$ . HRMS (ESI) calcd. for  $\text{C}_{23}\text{H}_{18}\text{N}_2\text{O}_3$  ( $\text{M}+\text{Na}$ ) $^+$  393.1210, found 393.1210.



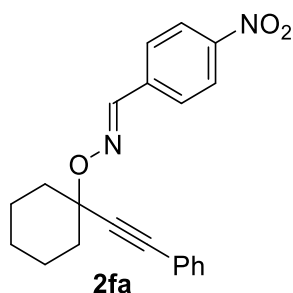
**(E)-4-Nitrobenzaldehyde O-(1,1,3-triphenylprop-2-yn-1-yl) oxime (2ca).** Reaction time: 11 h. 2.93 g (6.77 mmol, 77% yield for 3 steps). Yellow solid. Melting point: 109.1 °C.  $R_f = 0.23$  [hexane/EtOAc = 10:1 (v/v)].  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.37 (s, 1H), 8.19-8.17 (d,  $J = 8.2$  Hz, 2H), 7.73-7.71 (d,  $J = 8.2$  Hz, 2H), 7.65-7.64 (d,  $J = 7.8$  Hz, 4H), 7.54-7.53 (m, 2H), 7.40-7.30 (m, 9H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  148.3, 147.8, 142.3, 138.2, 131.8, 129.0, 128.7, 128.3, 128.2, 128.0, 127.9, 127.2, 123.8, 89.7, 88.8, 85.4. IR (neat) 3060, 3033, 2934, 2851, 2447, 2227, 1952, 1883, 1808, 1769, 1659, 1598, 1519, 1490, 1449, 1408, 1382, 1341, 1315, 1297, 1267, 1212, 1182, 1109, 1050, 1031, 951, 926, 876, 844  $\text{cm}^{-1}$ . HRMS (ESI) calcd. for  $\text{C}_{28}\text{H}_{20}\text{N}_2\text{O}_3$  ( $\text{M}+\text{Na}$ ) $^+$  455.1366, found 455.1366.



**(E)-4-Nitrobenzaldehyde O-(1-(phenylethynyl)cyclobutyl) oxime (2da).** Reaction time: 2 h. 0.748 g (2.33 mmol, 44% yield for 3 steps). Yellow solid. Melting point: 50.1 °C.  $R_f = 0.5$  [hexane/EtOAc = 10:1 (v/v)].  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.25-8.23 (d,  $J = 8.2$  Hz, 3H), 7.82-7.80 (d,  $J = 8.2$  Hz, 2H), 7.47-7.46 (m, 2H), 7.45-7.43 (m, 2H), 7.31 (m, 3H), 2.63-2.59 (t,  $J = 7.8$  Hz, 4H), 2.08-2.01 (m, 2H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  148.2, 146.4, 138.8, 137.7, 128.3, 128.2, 127.7, 124.0, 123.6, 122.7, 91.5, 83.8, 76.4, 75.8, 28.2. IR (neat) 2988, 2936, 1597, 1589, 1519, 1490, 1443, 1409, 1379, 1340, 1312, 1287, 1199, 1188, 1175, 1146, 1109, 1070, 1011, 962, 864, 846, 800, 757, 690, 634, 612  $\text{cm}^{-1}$ . HRMS (ESI) calcd. for  $\text{C}_{19}\text{H}_{16}\text{N}_2\text{O}_3(\text{M}+\text{Na})^+$  343.1053, found 343.1053.

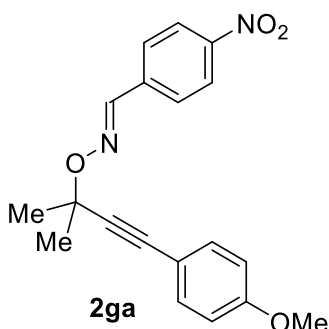


**(E)-4-Nitrobenzaldehyde O-[1-(phenylethynyl)cyclopentyl] oxime.** Reaction time: 2 h. 0.323 g (0.966 mmol, 20% yield for 3 steps). Yellow solid. Melting point: 60.1 °C.  $R_f = 0.53$  [hexane/EtOAc = 10:1 (v/v)].  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.24-8.22 (d,  $J = 8.2$ , 2H), 8.17 (s, 1H), 7.82-7.80 (d,  $J = 8.2$  Hz, 2H), 7.44-7.42 (m, 2H), 7.30-7.28 (m, 3H), 2.43-2.39 (m, 2H), 2.15-2.05 (m, 2H), 1.84-1.78 (m, 4H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  148.2, 146.9, 138.7, 131.7, 128.1, 127.7, 123.9, 122.8, 91.0, 86.0, 84.4, 39.4, 31.5, 23.8, 22.6, 14.1. IR (neat) 2968, 2873, 1614, 1598, 1588, 1519, 1490, 1442, 1409, 1341, 1313, 1297, 1274, 1212, 1191, 1109, 1070, 1013, 978, 954, 850, 795, 757, 690, 649, 623  $\text{cm}^{-1}$ . HRMS (ESI) calcd. for  $\text{C}_{20}\text{H}_{18}\text{N}_2\text{O}_3(\text{M}+\text{Na})^+$  357.1210, found 357.1210.

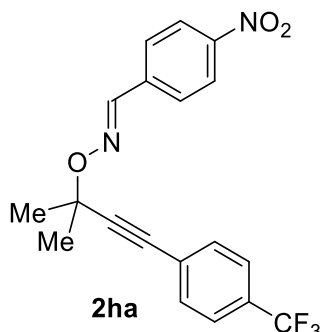


**(E)-4-Nitrobenzaldehyde O-[1-(phenylethynyl)cyclohexyl] oxime (2fa).** Reaction time: 2.5 h. 0.471 g (1.35 mmol, 42% yield for 3 steps). Yellow oil.  $R_f = 0.33$  [hexane/EtOAc = 10:1 (v/v)].  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.25-8.22 (d,  $J = 8.7$  Hz, 2H), 8.20 (s, 1H), 7.81-7.80 (d,  $J = 8.7$  Hz, 2H), 7.47-7.43 (m, 2H), 7.31-7.28 (m, 3H), 2.19-2.15 (m, 2H), 1.94-1.88 (m, 2H), 1.77-1.60 (m, 5H), 1.43-1.33 (m, 1H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  148.1, 146.4, 138.8, 131.7, 128.2, 128.2, 127.6, 123.9, 122.8, 90.8, 85.6, 79.6, 60.4, 36.6, 25.3, 22.8, 14.2. IR (neat) 2934, 2858, 1598, 1588, 1519, 1490, 1444, 1310, 1107, 1046, 1028,

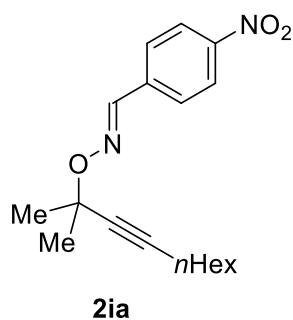
961, 936, 904, 851, 835, 791, 755, 690, 605  $\text{cm}^{-1}$ . HRMS (ESI) calcd. for  $\text{C}_{21}\text{H}_{20}\text{N}_2\text{O}_3$  ( $\text{M}+\text{Na}$ ) $^+$  371.1366, found 371.1366.



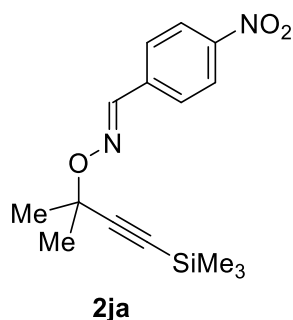
**(E)-4-Nitrobenzaldehyde O-[4-(4-methoxyphenyl)-2-methylbut-3-yn-2-yl] oxime (2ga).** Reaction time: 20 min. 20.1 mg (0.0594 mmol, 7.8% yield for 3 steps). Gray solid. Melting point: 64.4  $^{\circ}\text{C}$ .  $R_f$  = 0.38 [hexane/EtOAc = 5:1 (v/v)].  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.23-8.16 (m, 3H), 7.8 (s, 2H), 7.38 (s, 2H), 6.82 (m, 2H), 3.80 (s, 3H), 1.74 (s, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  159.5, 148.2, 146.3, 138.8, 133.2, 127.6, 123.9, 114.7, 113.8, 90.0, 83.7, 83.8, 76.4, 55.2, 28.3. IR (neat) 3076, 3043, 2987, 2935, 2839, 2546, 2373, 2353, 2323, 2223, 2052, 2020, 1889, 1605, 1570, 1509, 1465, 1442, 1410, 1379, 1341, 1283, 1249, 1200, 1171, 1146, 1108, 1031, 1011, 963, 865, 849, 833, 810, 769, 750, 691, 632, 610  $\text{cm}^{-1}$ . HRMS (ESI) calcd. for  $\text{C}_{19}\text{H}_{18}\text{N}_2\text{O}_4$  ( $\text{M}+\text{Na}$ ) $^+$  361.1159, found 361.1159.



**(E)-4-Nitrobenzaldehyde O-[2-methyl-4-(4-(trifluoromethyl)phenyl)but-3-yn-2-yl] oxime (2ha).** Reaction time: 1 h. 43.5 mg (0.116 mmol, 51% yield for 3 steps). Colorless solid. Melting point: 87.6  $^{\circ}\text{C}$ .  $R_f$  = 0.45 [hexane/EtOAc = 5:1 (v/v)].  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.26-8.24 (d,  $J$  = 8.7 Hz, 2H), 8.18 (s, 1H), 7.82-7.80 (d,  $J$  = 9.2 Hz, 2H), 7.58-7.52 (dd,  $J$  = 9.2, 8.7 Hz, 4H), 1.76 (s, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  148.3, 146.7, 138.6, 132.0, 127.7, 126.5, 125.1, 125.1, 124.0, 122.5, 82.4, 76.2, 28.0. IR (neat) 3274, 3081, 2991, 2937, 2856, 2370, 2357, 2345, 2333, 2323, 1769, 1680, 1615, 1590, 1521, 1437, 1406, 1381, 1342, 1323, 1287, 1167, 1149, 1127, 1106, 1066, 1016, 964, 865, 845, 809, 765, 750, 691, 633, 613  $\text{cm}^{-1}$ . HRMS (ESI) calcd. for  $\text{C}_{19}\text{H}_{15}\text{F}_3\text{N}_2\text{O}_3$  ( $\text{M}+\text{Na}$ ) $^+$  399.0927, found 399.0927.



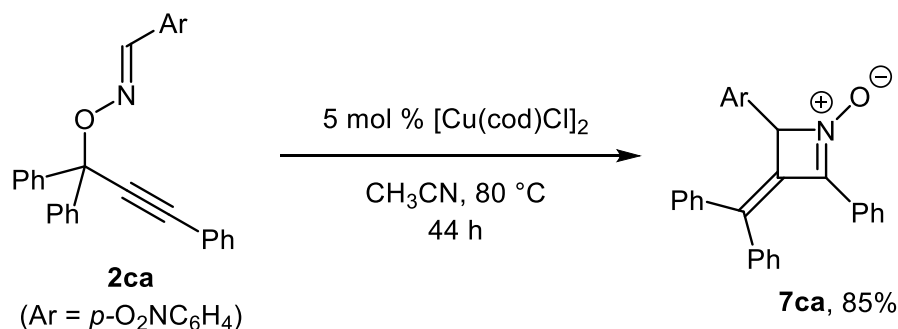
**(E)-4-Nitrobenzaldehyde O-(2-methyldec-3-yn-2-yl) oxime (2ia).** Reaction time: 5 h. 57.4 mg (0.181 mmol, 75% yield for 3 steps). Brown oil.  $R_f = 0.55$  [hexane/EtOAc = 10:1 (v/v)].  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.24-8.22 (d,  $J = 7.3$  Hz, 2H), 8.13 (s, 1H), 7.79-7.77 (d,  $J = 8.7$  Hz, 2H), 1.62 (s, 6H), 1.50-1.25 (m, 10H), 0.856 (m, 3H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  148.2, 146.1, 138.9, 138.8, 127.6, 127.5, 124.0, 123.9, 120.3, 84.6, 83.4, 82.6, 76.2, 31.3, 28.5, 28.4, 22.5, 18.7, 14.0. IR (neat) 2985, 2956, 2933, 2858, 2369, 2357, 2322, 2243, 2089, 2049, 2024, 1588, 1523, 1466, 1379, 1343, 1297, 1261, 1199, 1148, 1108, 965, 854, 795, 750, 691, 613  $\text{cm}^{-1}$ . HRMS (ESI) calcd. for  $(\text{M}+\text{Na})^+$  339.1679, found 339.1679.



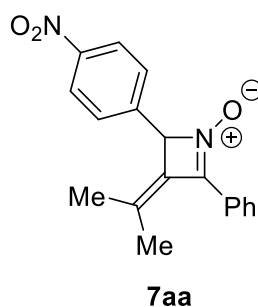
**(E)-4-Nitrobenzaldehyde O-[2-methyl-4-(trimethylsilyl)but-3-yn-2-yl] oxime (2ja).** Reaction time: 12 h. 58.8 mg (0.193 mmol, 38% yield for 3 steps). Orange solid. Melting point: 51.6  $^{\circ}\text{C}$ .  $R_f = 0.36$  [hexane/EtOAc = 10:1 (v/v)].  $^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.24-8.23 (d,  $J = 8.9$  Hz, 2H), 8.13 (s, 1H), 7.79-7.78 (d,  $J = 8.9$  Hz, 2H), 1.64 (s, 6H), 0.17 (s, 9H).  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  148.2, 146.3, 138.8, 127.6, 123.9, 107.8, 88.1, 76.1, 28.1, -0.09. IR (neat) 3747, 3649, 2360, 2337, 1919, 1869, 1844, 1828, 1793, 1772, 1733, 1716, 1699, 1684, 1651, 1558, 1541, 1522, 1458, 1419, 1396, 1342  $\text{cm}^{-1}$ . HRMS (FD) calcd. for  $\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}_3\text{Si}$   $(\text{M}+\text{Na})^+$  304.1243, found 304.1240.

## 6. Transformations of *O*-*tert*-propargylic oximes **2** using $\pi$ -Lewis acidic catalysts.

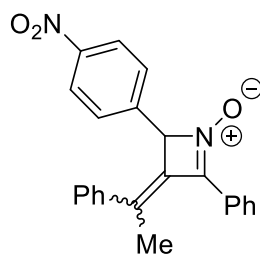
### 1) Cu- and Au-catalyzed reactions of **2ca**.



To a mixture of [Cu(cod)Cl]<sub>2</sub> (4.14 mg, 0.0100 mmol) and oxime **2ca** (86.5 mg, 0.200 mmol) in a vial was added CH<sub>3</sub>CN (0.4 mL) under argon atmosphere and the mixture was stirred at 80 °C for 44 h. The reaction mixture was passed through a pad of silica gel with ethyl acetate. After removing solvents in vacuo, the residue was purified by flash column chromatography using hexane/EtOAc (4/1) as eluent to give **7ca** (73.2 mg, 85%)



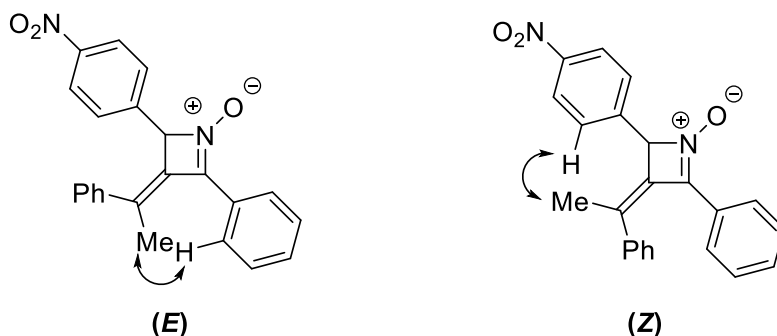
**2-(4-Nitrophenyl)-4-phenyl-3-(propan-2-ylidene)-2,3-dihydroazete 1-oxide. (7aa).** Reaction time: 26 h. 18.4 mg (0.0597 mmol, 30% yield). Colorless oil.  $R_f$  = 0.48 [hexane/EtOAc = 5:1 (v/v)]. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.30-8.28 (d,  $J$  = 8.2 Hz, 2H), 7.92-7.90 (d,  $J$  = 6.4 Hz, 2H), 7.65-7.63 (d,  $J$  = 8.2 Hz, 2H), 7.50-7.48 (m, 3H), 5.84 (s, 1H), 2.03 (s, 3H), 1.61 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  150.8, 148.5, 139.6, 130.3, 129.4, 128.6, 128.0, 126.2, 124.2, 124.2, 123.7, 83.2, 21.7, 21.3. IR (neat) 3108, 3059, 2978, 2913, 2855, 2728, 2370, 2357, 2349, 2320, 1711, 1602, 1575, 1546, 1521, 1492, 1447, 1400, 1345, 1316, 1275, 1232, 1199, 1182, 1132, 1109, 1086, 1066, 1032, 1008, 1086, 1066, 1032, 1008, 995, 918, 854, 832, 795, 759, 736, 708, 695, 620 cm<sup>-1</sup>. HRMS (ESI) calcd. for C<sub>18</sub>H<sub>16</sub>N<sub>2</sub>O<sub>3</sub> (M+Na)<sup>+</sup> 331.1053, found 331.1053.



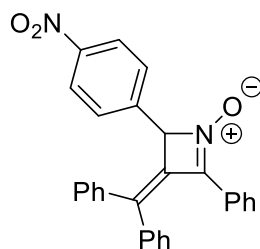
**7ba**

**(E)-2-(4-Nitrophenyl)-4-phenyl-3-(1-phenylethylidene)-2,3-dihydroazete 1-oxide (7ba).** Reaction time: 45 h. 63.7 mg (0.172 mmol, 86% yield). Yellow solid. Melting point: 104.4 °C.  $R_f = 0.27$  [hexane/EtOAc = 5:1 (v/v)].  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ , E+Z mixture)  $\delta$  8.35-8.33 (d,  $J = 6.9$  Hz, 2H for Z isomer), 8.02-7.97 (m, 4H for E isomer), 7.75-7.73 (d,  $J = 6.9$  Hz, 2H for Z isomer), 7.57-7.51 (m, 2H), 7.35-7.28, 7.22-7.20, 7.16-7.12 (m, 7H), 6.06 (s, 1H for E isomer), 6.02 (s, 1H for Z isomer), 2.35 (s, 3H for E isomer), 1.977 (s, 3H for Z isomer).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  151.6, 148.0, 139.3, 138.7, 138.6, 132.5, 130.4, 130.1, 129.4, 128.7, 128.5, 128.2, 128.2, 127.8, 127.5, 125.4, 123.6, 84.0. IR (neat) 3080, 3060, 3030, 2925, 2855, 2376, 2356, 2324, 2054, 1687, 1601, 1576, 1522, 1492, 1444, 1402, 1346, 1317, 1273, 1220, 1181, 1108, 1050, 1016, 990, 916, 857, 832, 791, 766, 733, 697, 635, 620  $\text{cm}^{-1}$ . HRMS (ESI) calcd. for  $\text{C}_{23}\text{H}_{18}\text{N}_2\text{O}_3$  ( $\text{M}+\text{Na}$ ) $^+$  393.1210, found 393.1210.

The stereochemistry at the olefin moiety of **7ba** was determined by NOE experiments.



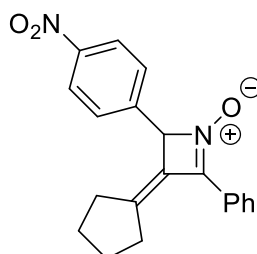
**E : Z = 44 : 56**



**7ca**

**3-(Diphenylmethylene)-2-(4-nitrophenyl)-4-phenyl-2,3-dihydroazete 1-oxide (7ca).** Reaction time: 45 h. 73.2 mg (0.169 mmol, 85% yield). Yellow solid. Melting point: 101.8 °C.  $R_f = 0.33$  [hexane/EtOAc = 5:1 (v/v)].  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.07-8.05 (d,  $J = 8.7$  Hz, 2H), 7.35-7.29 (m,

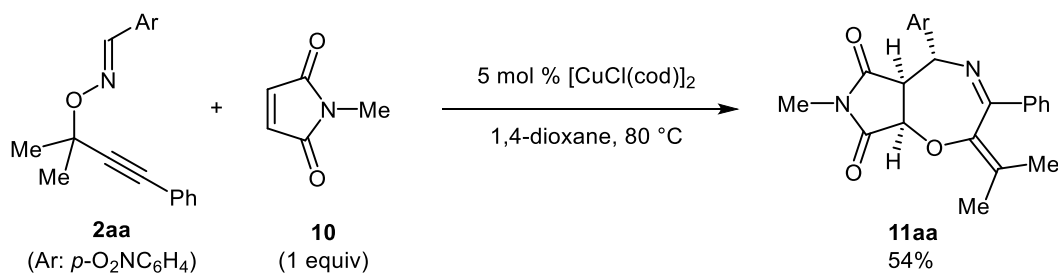
6H), 7.24-7.17 (m, 9H), 7.09-7.07 (m, 2H), 6.29 (s, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  151.6, 148.0, 139.3, 130.7, 138.6, 132.5, 130.4, 130.1, 129.4, 128.7, 128.5, 128.2, 128.2, 127.8, 127.5, 125.4, 123.6, 84.0. IR (neat) 3058, 1666, 1603, 1576, 1523, 1490, 1442, 1405, 1345, 1317, 1274, 1172, 1109, 1071, 1032, 1015, 856, 833, 754, 768, 696, 732, 661, 620  $\text{cm}^{-1}$ . HRMS (ESI) calcd. for  $\text{C}_{28}\text{H}_{20}\text{N}_2\text{O}_3(\text{M}+\text{Na})^+$  455.1366, found 455.1366.



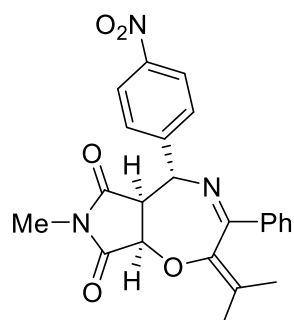
**7ea**

**3-Cyclopentylidene-2-(4-nitrophenyl)-4-phenyl-2,3-dihydroazete 1-oxide (7ea).** Reaction time: 17 h. Yield: 32.8 mg (0.0981 mmol, 49% yield). Yellow solid. Melting point: 169.4  $^{\circ}\text{C}$ .  $R_f$  = 0.46 [hexane/EtOAc = 5:1 (v/v)].  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.28-8.26 (d,  $J$  = 8.2 Hz, 2H), 8.12-8.10 (d,  $J$  = 6.7 Hz, 2H), 7.63-7.61 (d,  $J$  = 8.2 Hz, 2H), 7.50-7.48 (m, 3H), 5.82 (s, 1H), 2.69 (s, 2H), 2.27-1.66 (m, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  151.0, 148.4, 139.6, 134.5, 130.4, 129.3, 128.7, 127.2, 126.3, 124.1, 120.9, 83.5, 32.9, 32.0, 27.1, 26.0. IR (neat) 2958, 2870, 2369, 2351, 2324, 1715, 1602, 1576, 1543, 1522, 1491, 1448, 1401, 1346, 1317, 1273, 1215, 1183, 1108, 1015, 850, 832, 794, 766, 706, 691, 619  $\text{cm}^{-1}$ . HRMS (ESI) calcd. for  $\text{C}_{20}\text{H}_{18}\text{N}_2\text{O}_3(\text{M}+\text{Na})^+$  357.1210, found 357.1209

## 2) Cu-catalyzed reaction between **2aa** and *N*-methylmaleimide **10**.



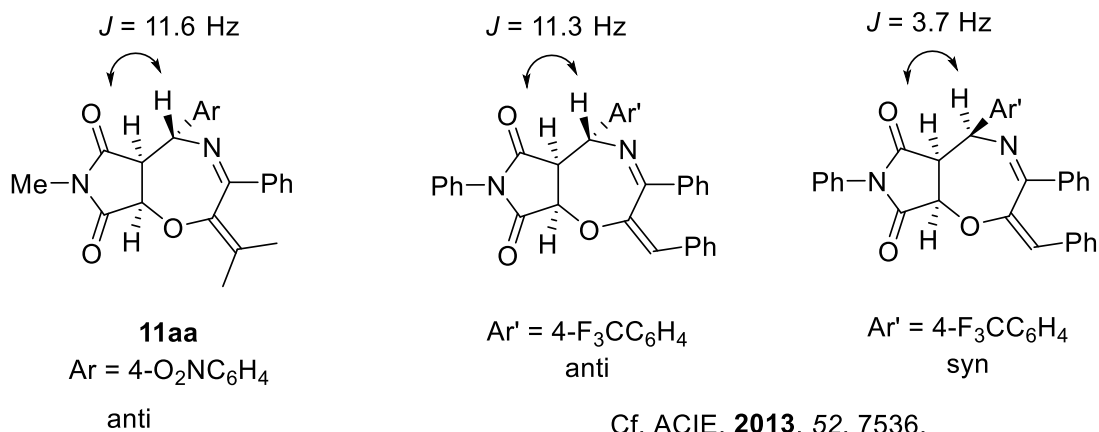
To a mixture of  $[\text{CuCl}(\text{cod})]_2$  (4.14 mg, 0.0100 mmol) and *N*-phenylmaleimide **2c** (22.0 mg, 0.200 mmol) in 1,4-dioxane (0.2 mL) in a pressure vial was added **1a** (61.2 mg, 0.2 mmol) under argon atmosphere. After stirring the mixture at 30  $^{\circ}\text{C}$  for 16 h, the reaction mixture was passed through a short pad of silica gel with EtOAc (50 mL). After removing the solvents in vacuo, the crude product was purified using flash column chromatography with hexane/EtOAc (5:1) as eluents to afford pure **11aa** (45.2 mg, 0.108 mmol, 54% yield).



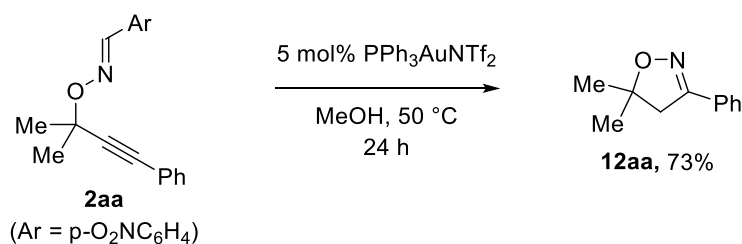
**11aa**

**(5*R*\*,5*aS*\*,8*aR*\*)-7-Methyl-5-(4-nitrophenyl)-3-phenyl-2-(propan-2-ylidene)-2,5,5*a*,8*a*-tetrahydro-6*H*-pyrrolo[3,4-*f*][1,4]oxazepine-6,8(7*H*)-dione (11aa).** Reaction time: 24 h. 45.2 mg (0.108 mmol, 54% yield). Colorless solid. Melting point: 219.2 °C.  $R_f = 0.52$  [hexane/EtOAc = 2:1 (v/v)].  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.32-8.30 (d,  $J = 8.2$  Hz, 2H), 7.88-7.86 (d,  $J = 8.7$  Hz, 2H), 7.79-7.77 (d,  $J = 6.9$  Hz, 2H), 7.48-7.40 (m, 3H), 5.04-5.01 (d,  $J = 11.5$  Hz, 1H), 4.59-4.58 (m, 1H), 3.40-3.37 (m, 1H), 3.02 (s, 3H), 1.87 (s, 3H), 1.32 (s, 3H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  173.60, 171.44, 147.98, 147.51, 140.47, 138.54, 134.17, 130.99, 129.81, 128.73, 128.16, 123.42, 120.09, 73.85, 73.43, 61.78, 50.34, 25.08, 20.87, 17.37. IR (neat) 2917, 2372, 2357, 2318, 1792, 1715, 1593, 1571, 1521, 1491, 1436, 1383, 1346, 1283, 1239, 1166, 1133, 1065, 1024, 981, 849, 795, 725, 699, 647  $\text{cm}^{-1}$ . HRMS (ESI) calcd. for  $\text{C}_{23}\text{H}_{21}\text{N}_3\text{O}_5(\text{M}+\text{Na})^+$  442.1373, found 442.1374

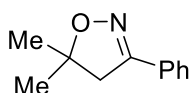
The anti-configuration of **11aa** was determined by comparison of the coupling constant to related compounds.



### 3) Au-catalyzed reactions of **2** in MeOH.

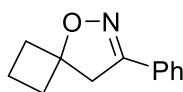


To a mixture of **2aa** (61.7 mg, 0.200 mmol) and  $\text{PPh}_3\text{AuNTf}_2$  (7.39 mg, 0.0100 mmol) in a vial was added methanol (0.4 mL) under argon atmosphere. The mixture was stirred at 50 °C for 24 hr. After complete consumption of **2aa** monitored by TLC, the mixture was passed through a pad of silica gel with ethyl acetate (50 mL). After removing solvents in vacuo, the residue was purified by silica gel column chromatography using hexane/ethyl acetate (5/1) as eluent to afford **12aa** (25.6 mg, 0.146 mmol, 73% yield) in an analytically pure form.



**12aa**

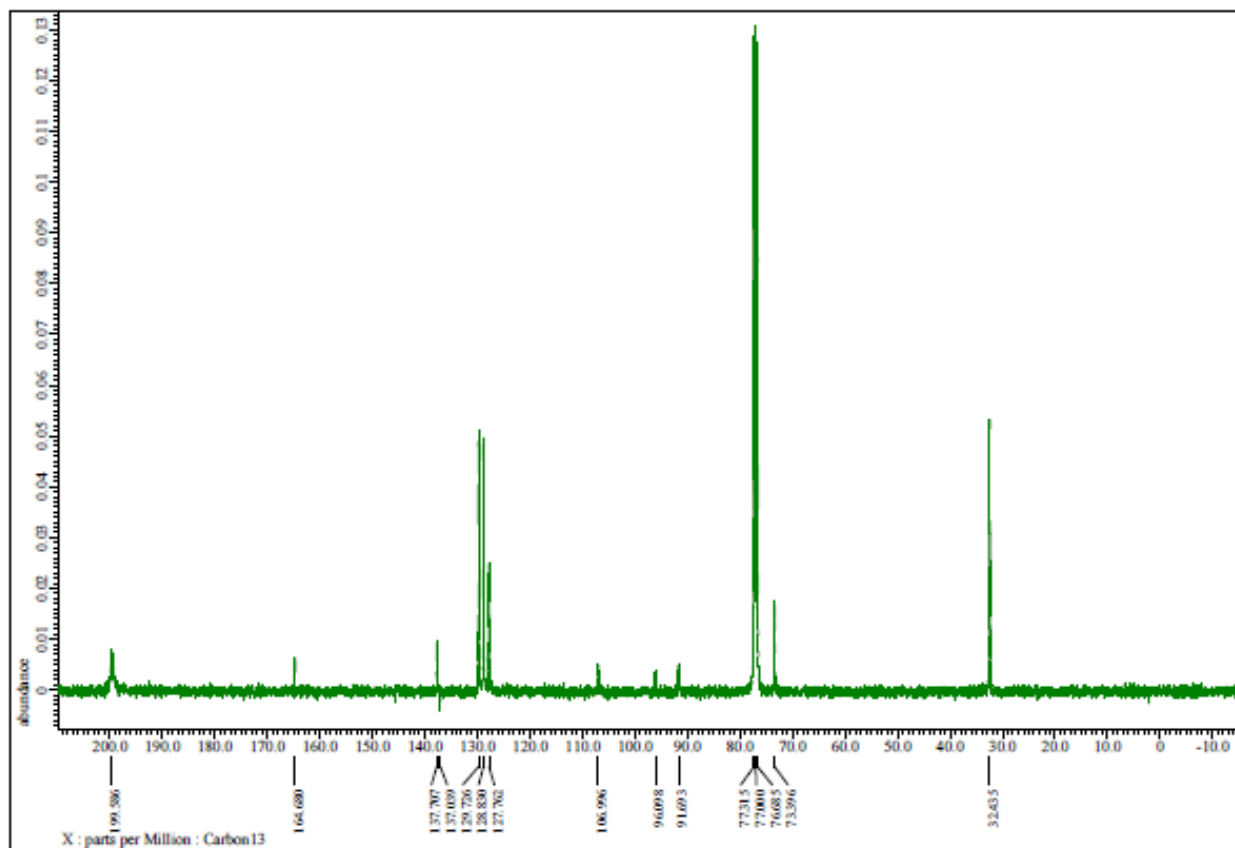
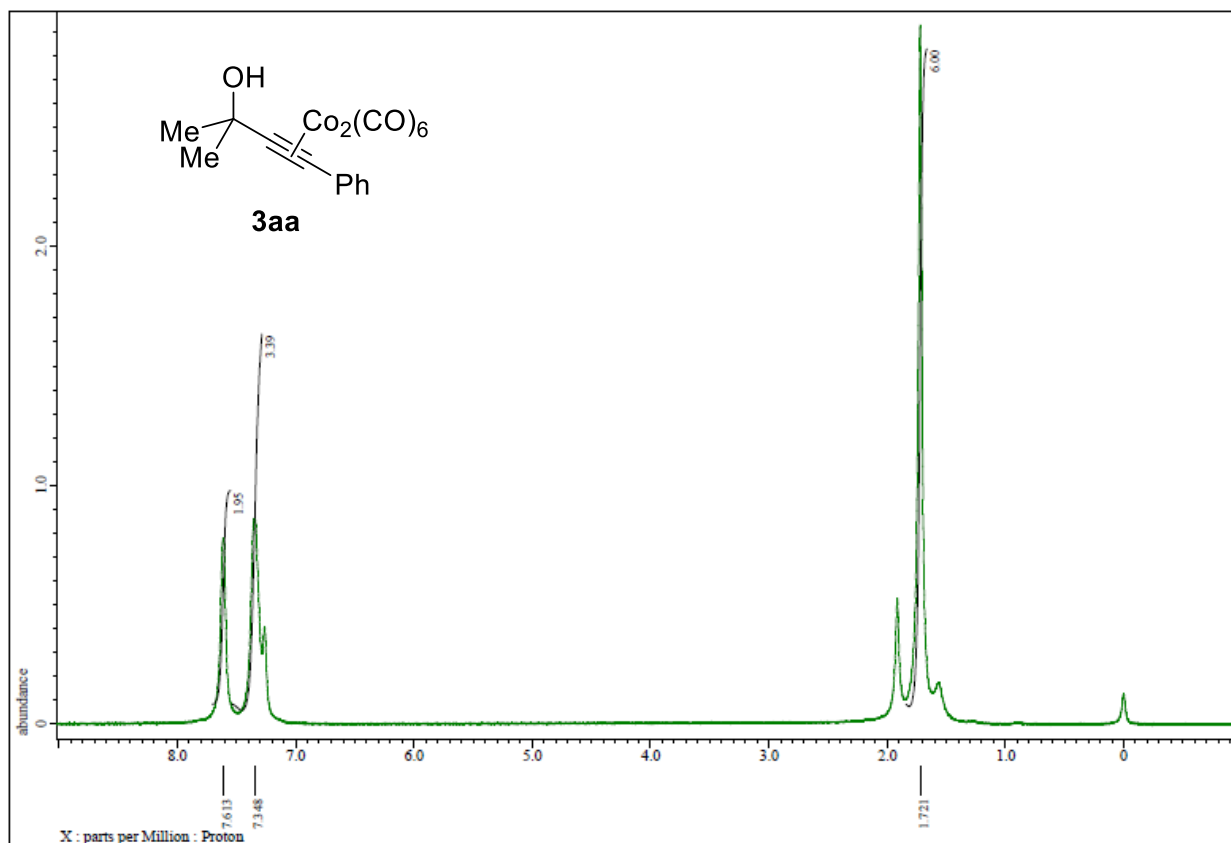
**5,5-Dimethyl-3-phenyl-4,5-dihydroisoxazole (12aa).** Reaction time: 24 h. 25.6 mg (0.146 mmol, 73% yield). Colorless solid. Melting point: 59.3 °C.  $R_f = 0.48$  [hexane/EtOAc = 5:1 (v/v)].  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.65 (m, 2H), 7.39 (m, 3H), 3.10 (s, 2H), 1.49 (s, 6H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  156.3, 130.2, 129.7, 128.6, 126.4, 126.0, 84.9, 46.7, 27.3. IR (neat) 2979, 1592, 1563, 1497, 1446, 1433, 1370, 1361, 1316, 1257, 1228, 1150, 1079, 920, 831, 793, 766, 699, 614  $\text{cm}^{-1}$ . HRMS (ESI) calcd. for  $\text{C}_{11}\text{H}_{13}\text{NO}$  ( $\text{M}+\text{Na}$ ) $^+$  198.0889, found 198.0889



**12da**

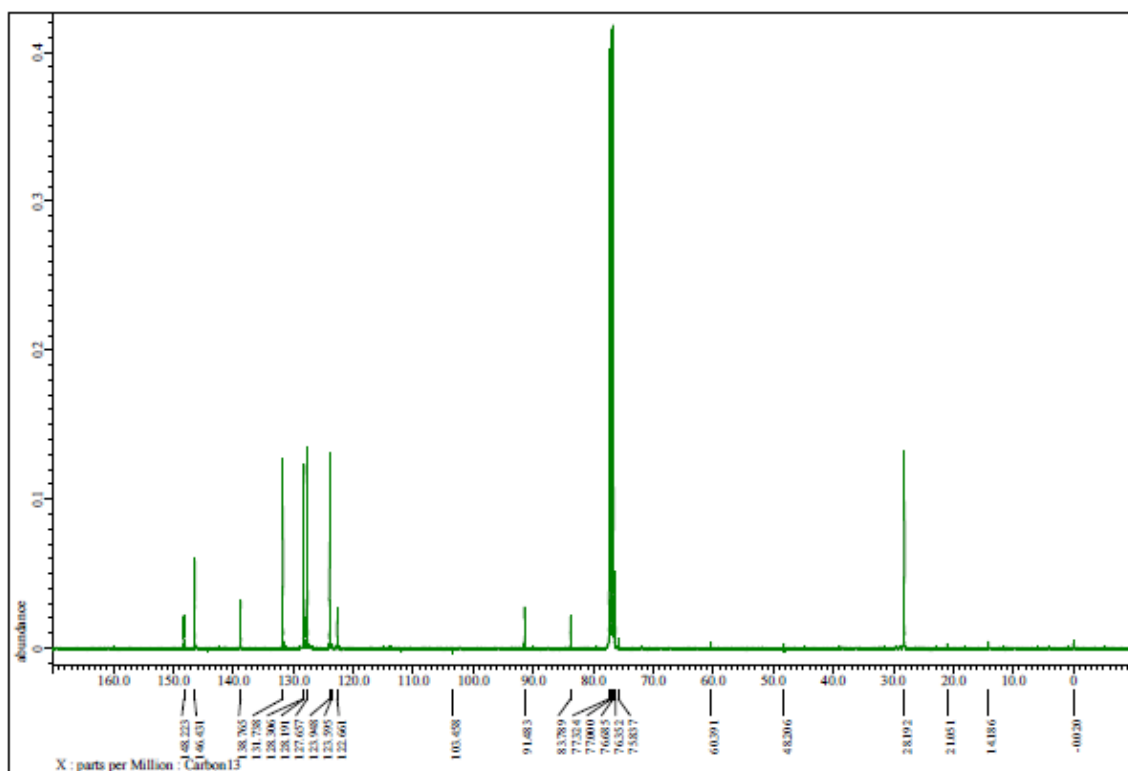
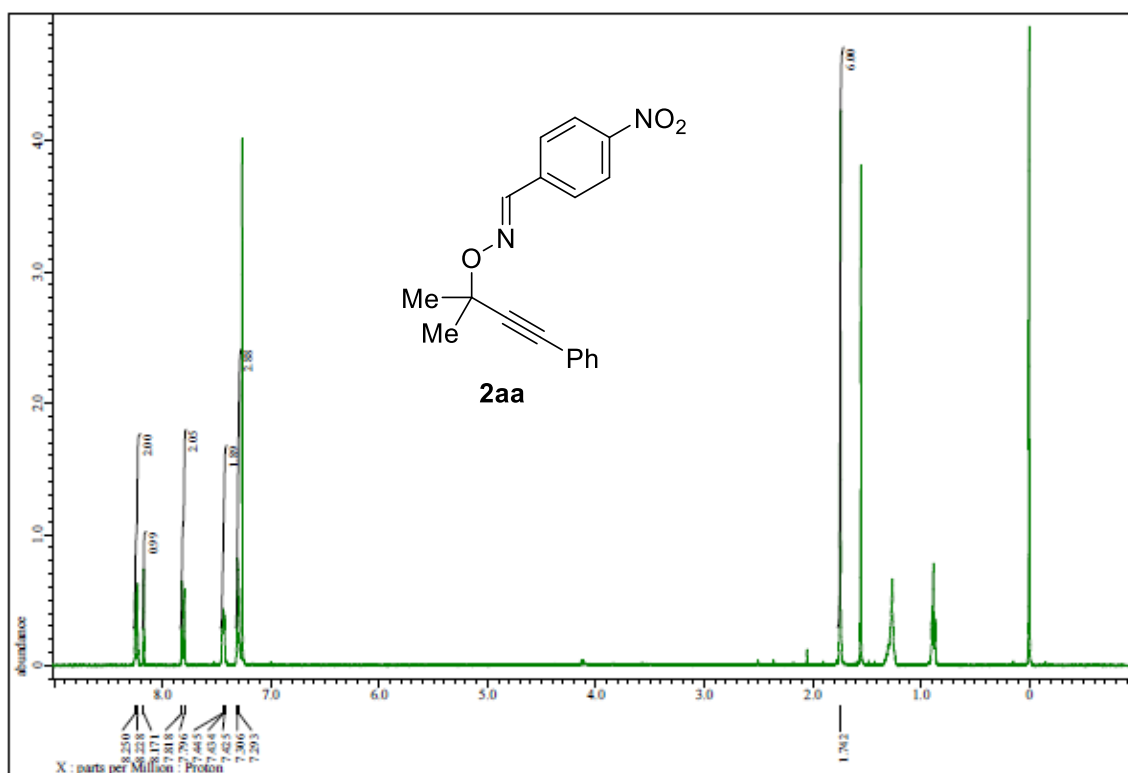
**7-Phenyl-5-oxa-6-azaspiro[3.4]oct-6-ene (12da).** Reaction time: 24 h. 30.3 mg (0.162 mmol, 81% yield). Colorless solid. Melting point: 95.3 °C.  $R_f = 0.48$  [hexane/EtOAc = 10:1 (v/v)].  $^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.67-7.64 (m, 2H), 7.41-7.37 (m, 3H), 3.41-3.40 (s, 2H), 2.60-2.54 (m, 2H), 2.24-2.21 (m, 2H), 1.87-1.84 (m, 1H), 1.67-1.63 (m, 1H).  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  156.7, 129.9, 129.9, 128.6, 126.5, 86.0, 45.6, 36.6, 12.5. IR (neat) 3649, 2360, 2341, 1869, 1845, 1829, 1793, 1771, 1734, 1716, 1699, 1684, 1670, 1653, 1635, 1617, 1576, 1558, 1541, 1521, 1507, 1497, 1489, 1473  $\text{cm}^{-1}$ . HRMS (FD) calcd. for  $\text{C}_{12}\text{H}_{13}\text{NO}$  ( $\text{M}+\text{Na}$ ) $^+$  187.0997, found 187.0996.

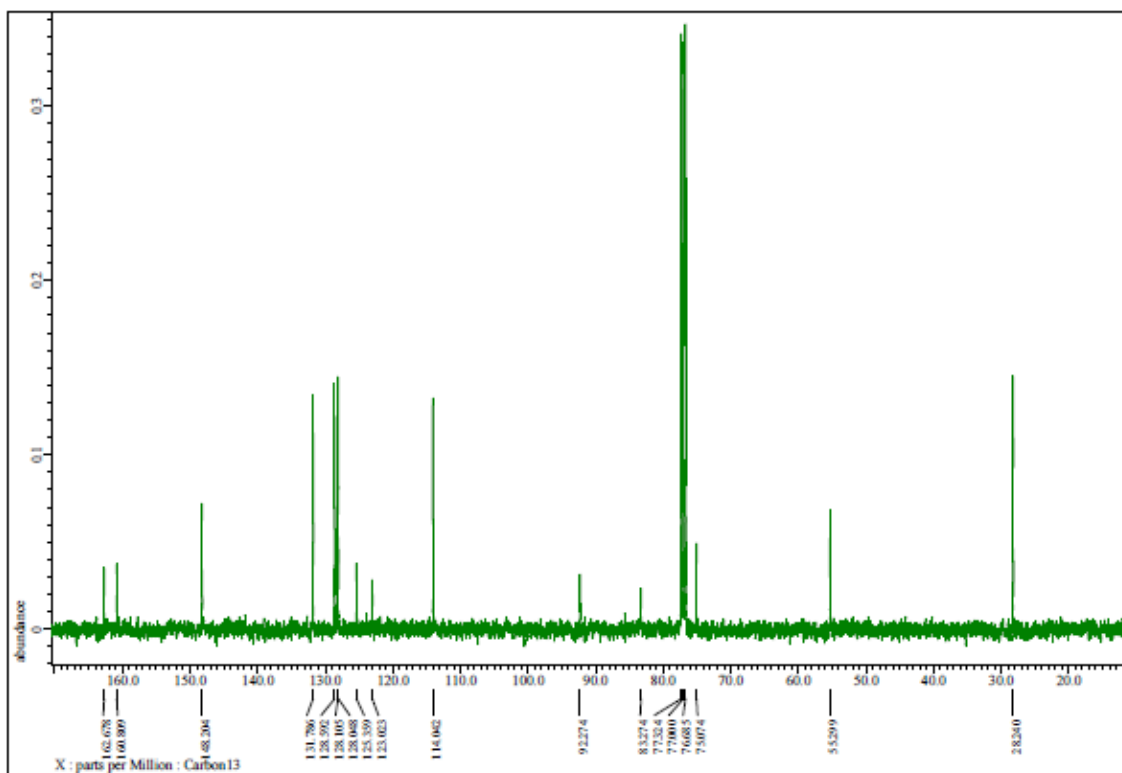
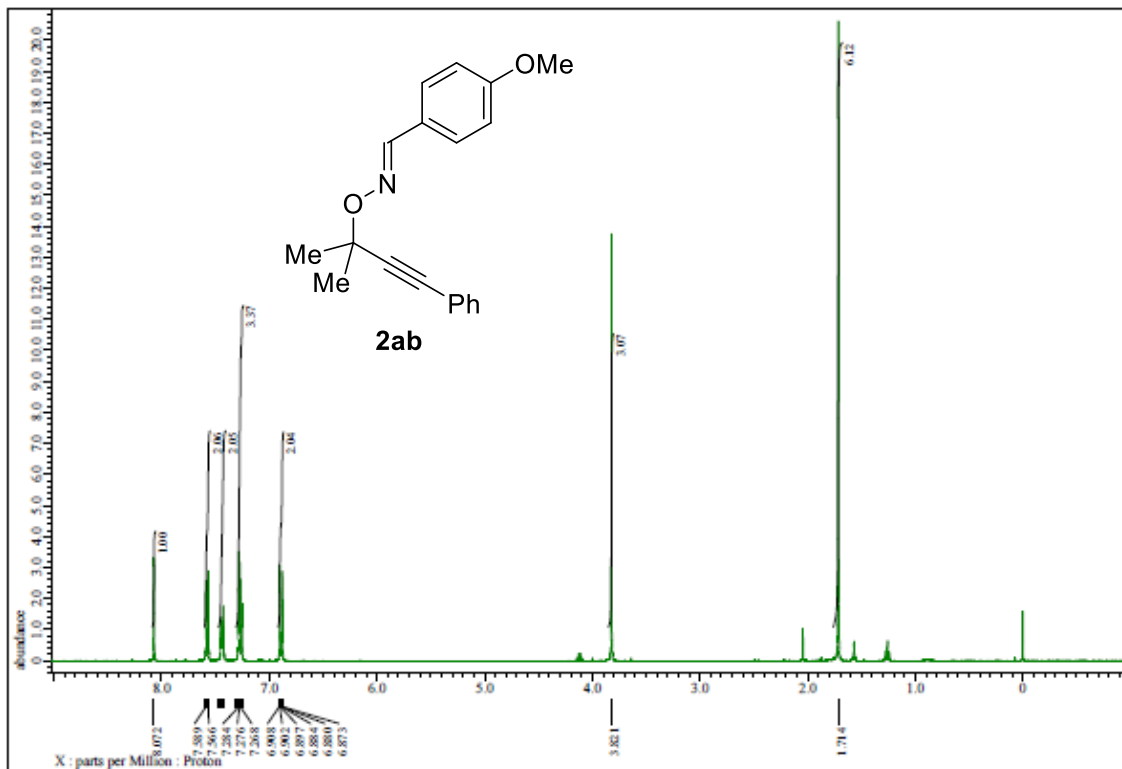
## 7. NMR charts of **3aa** and **5aa**

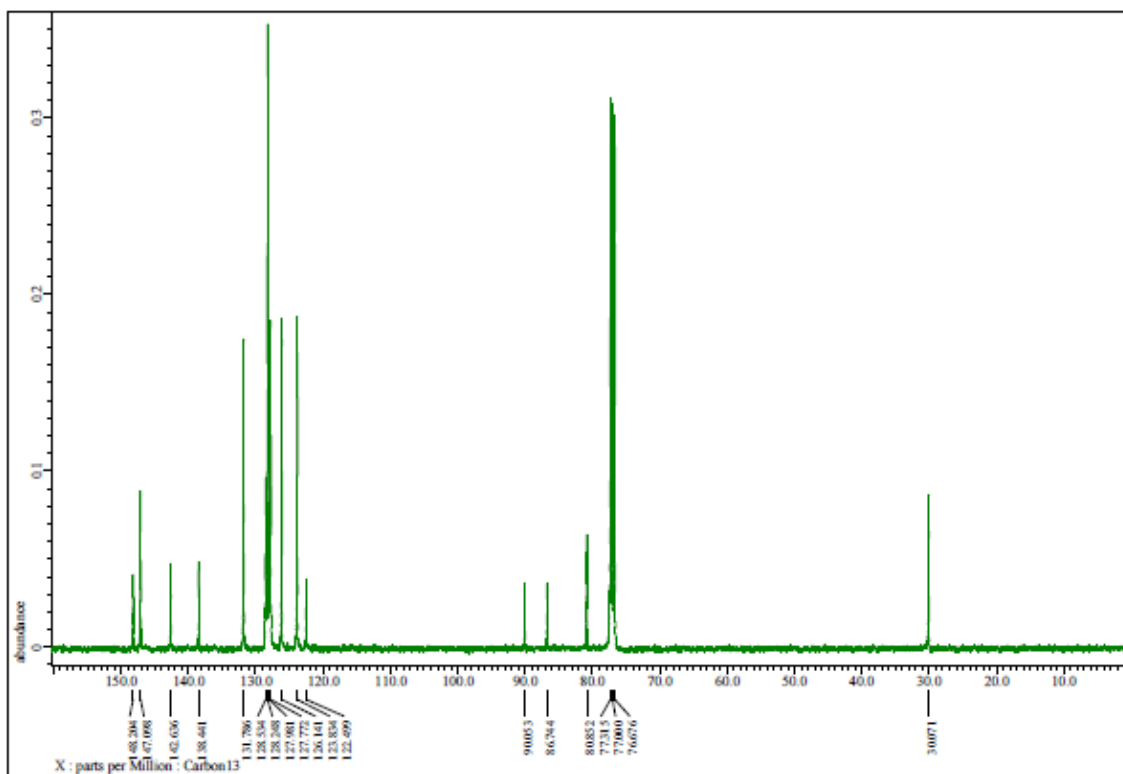
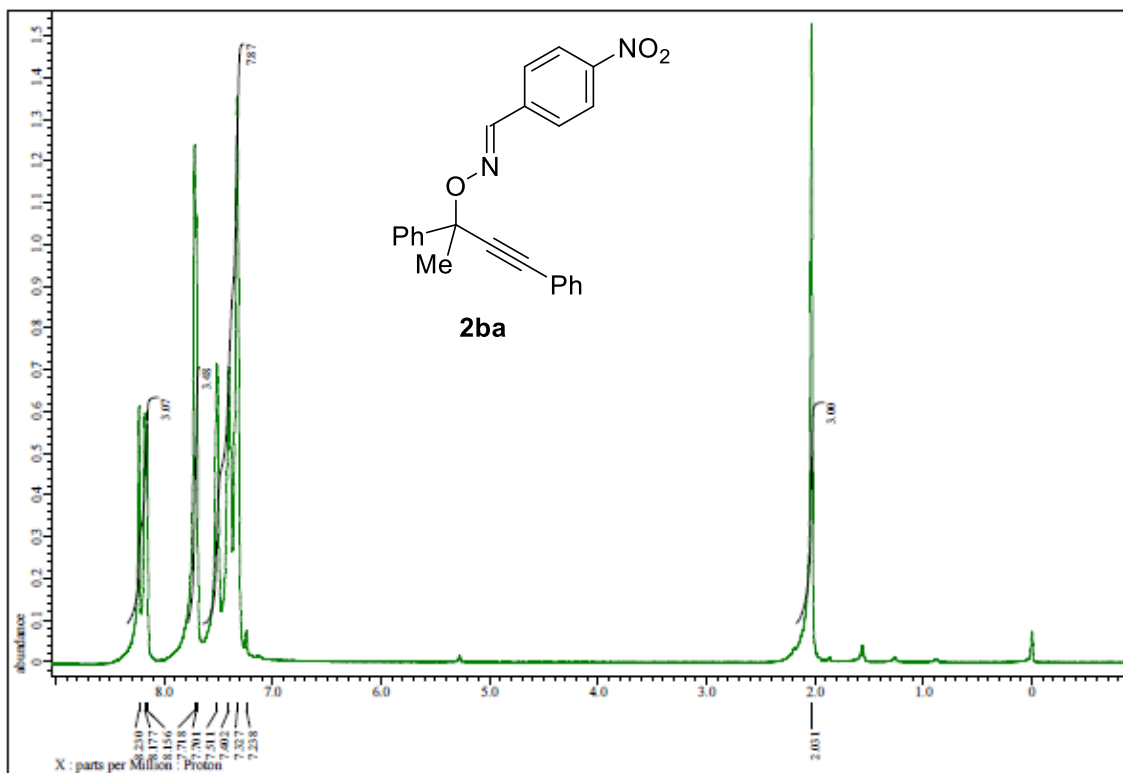


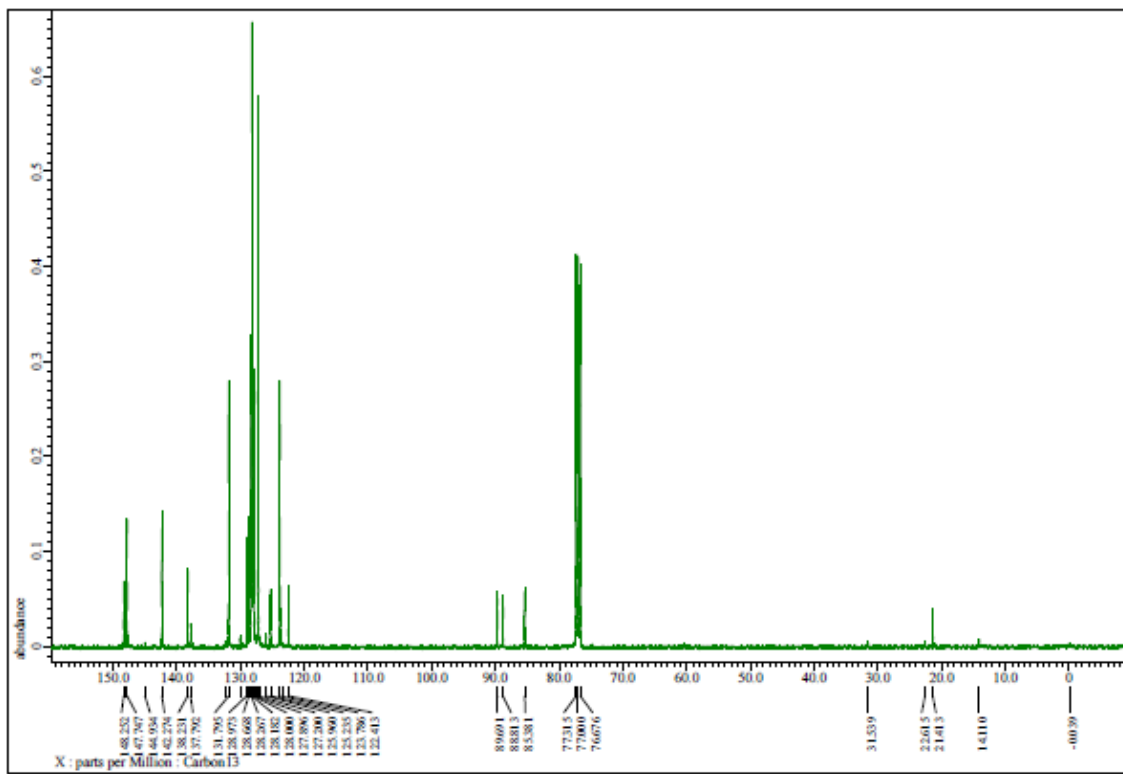
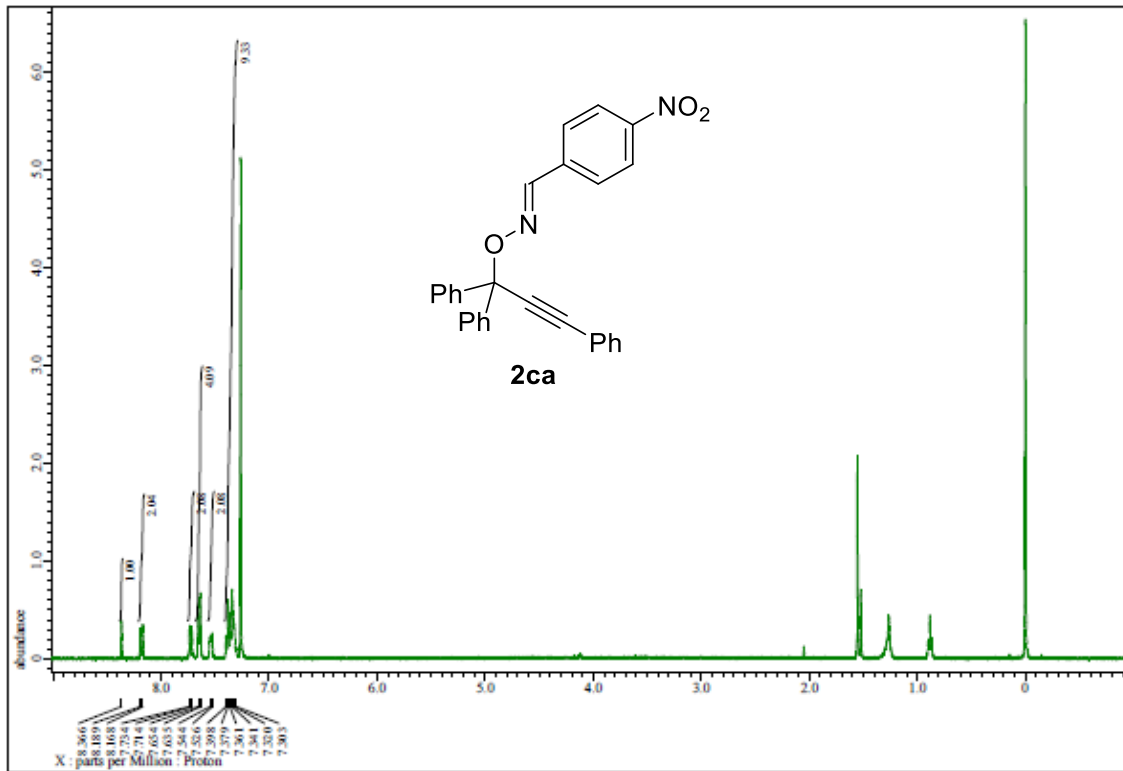


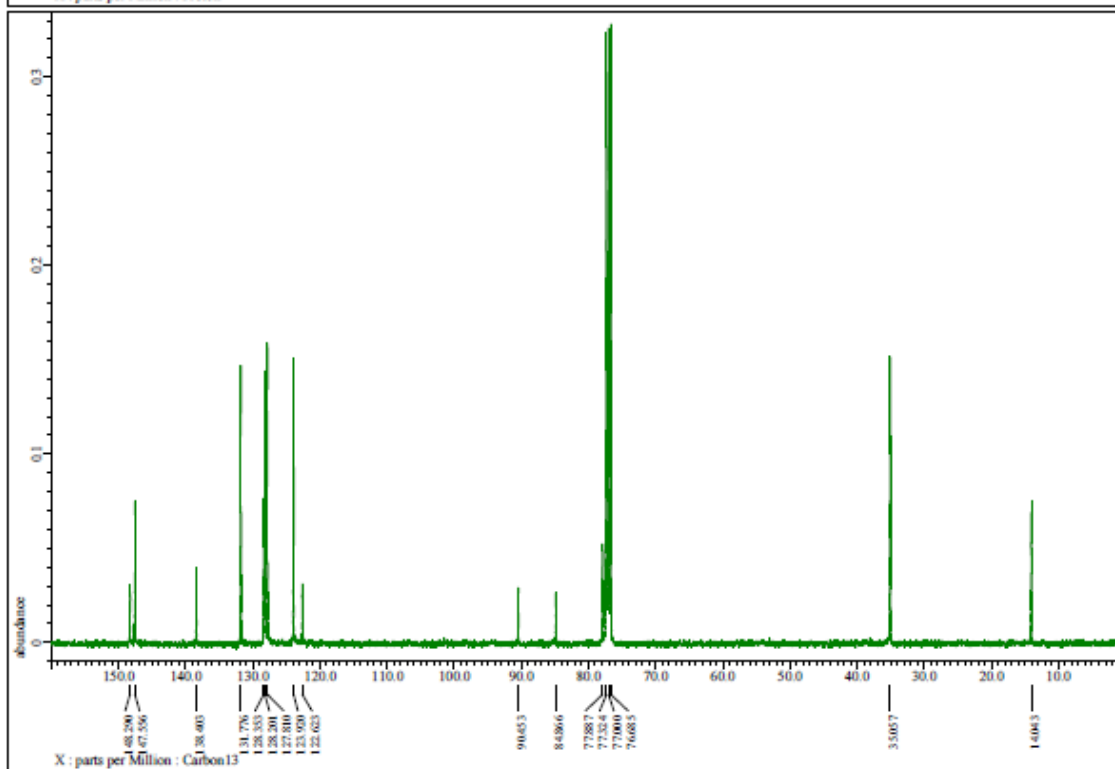
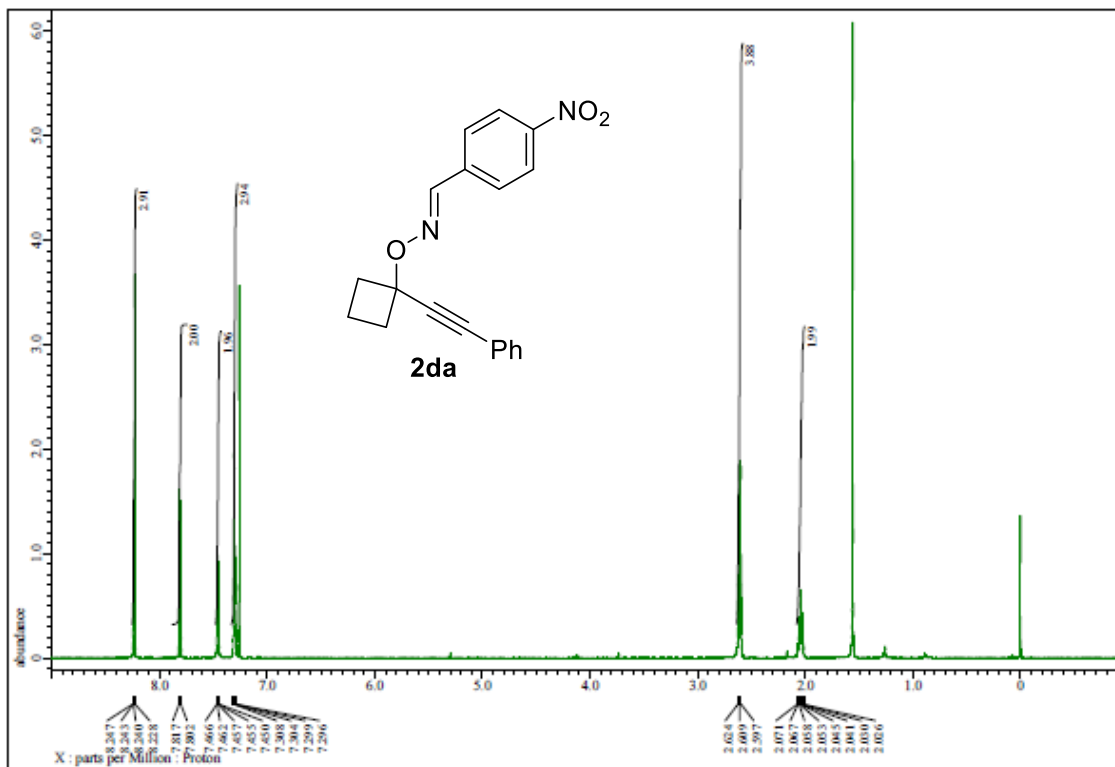
## 8. NMR charts of 2



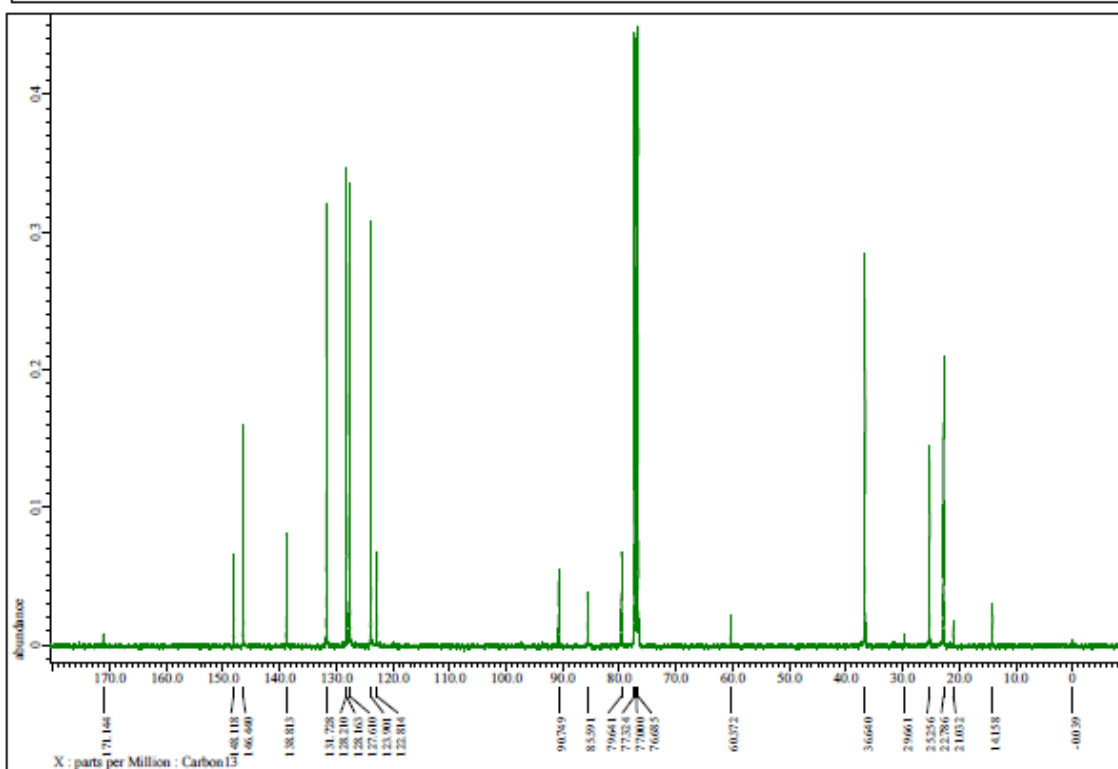
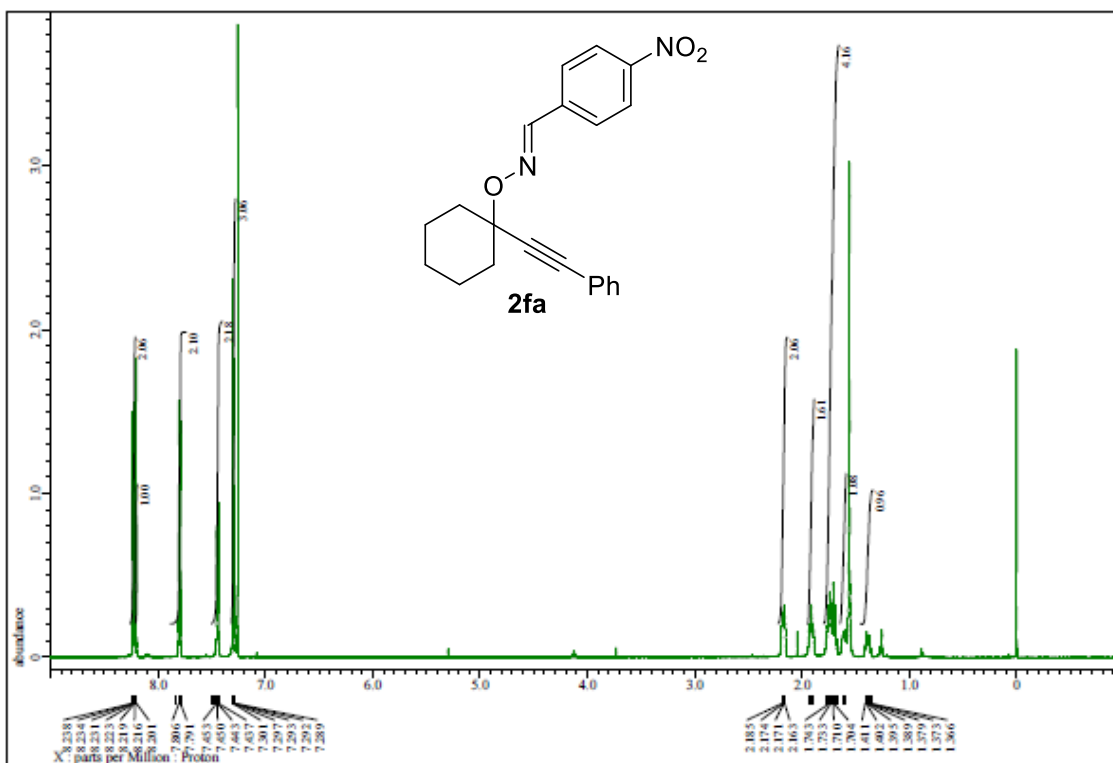


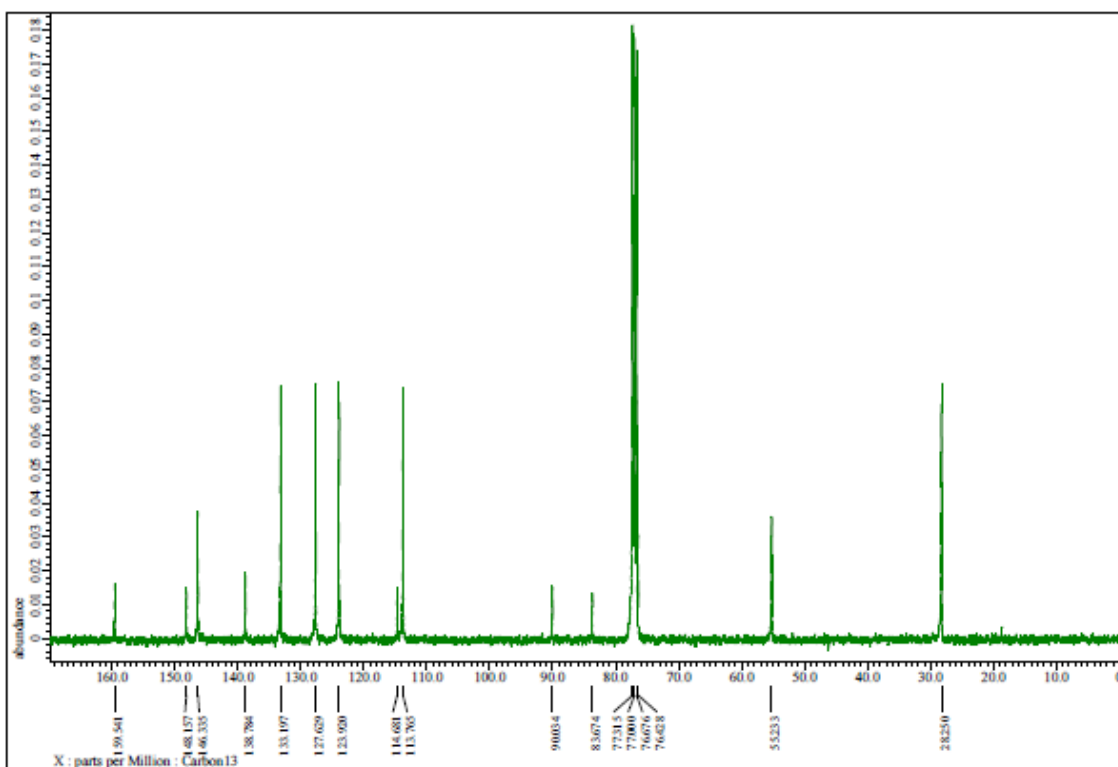
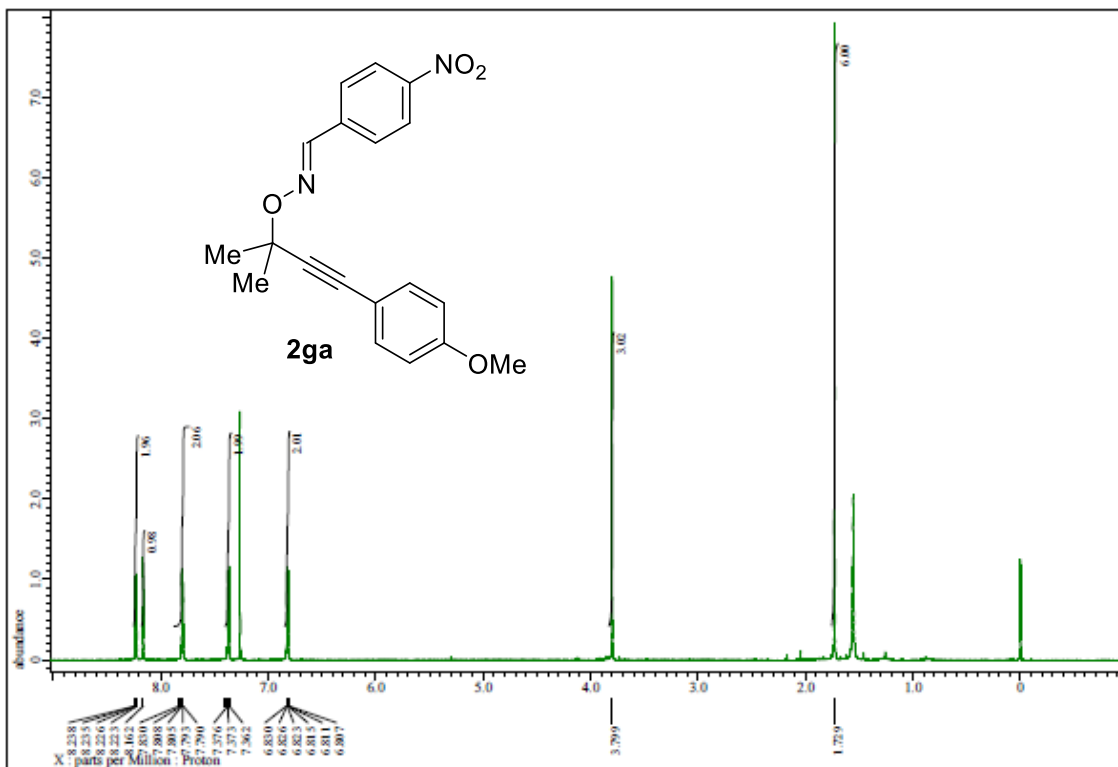


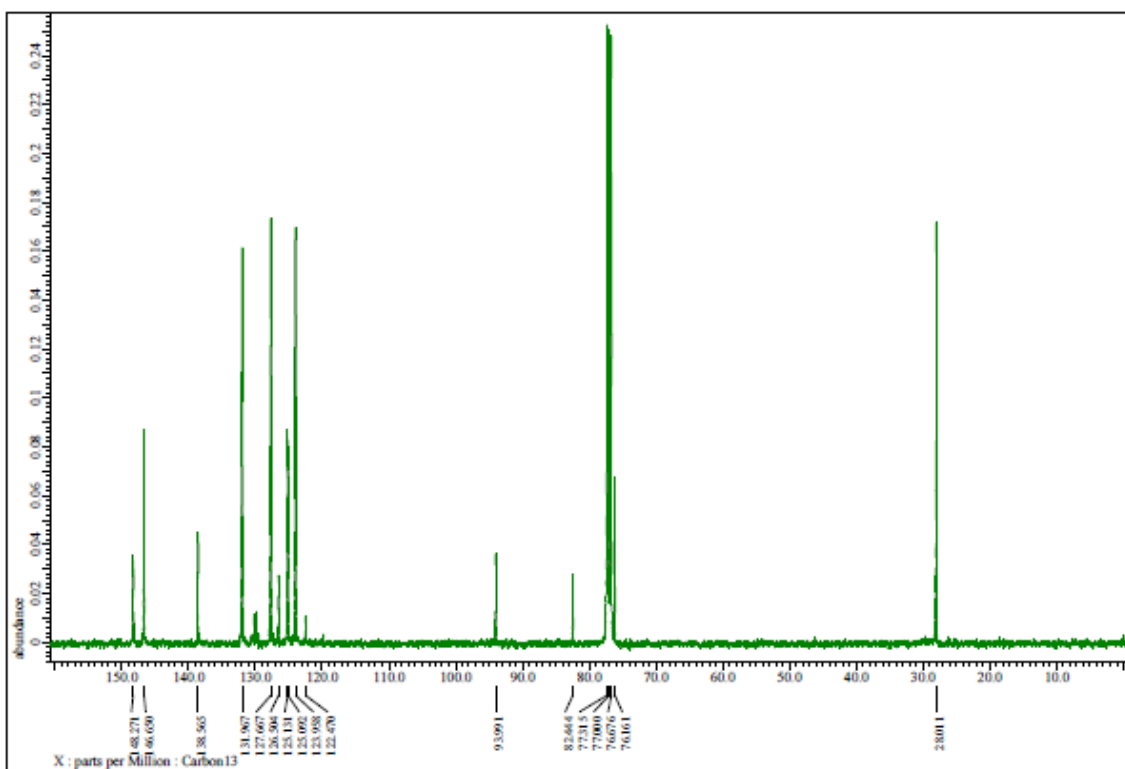
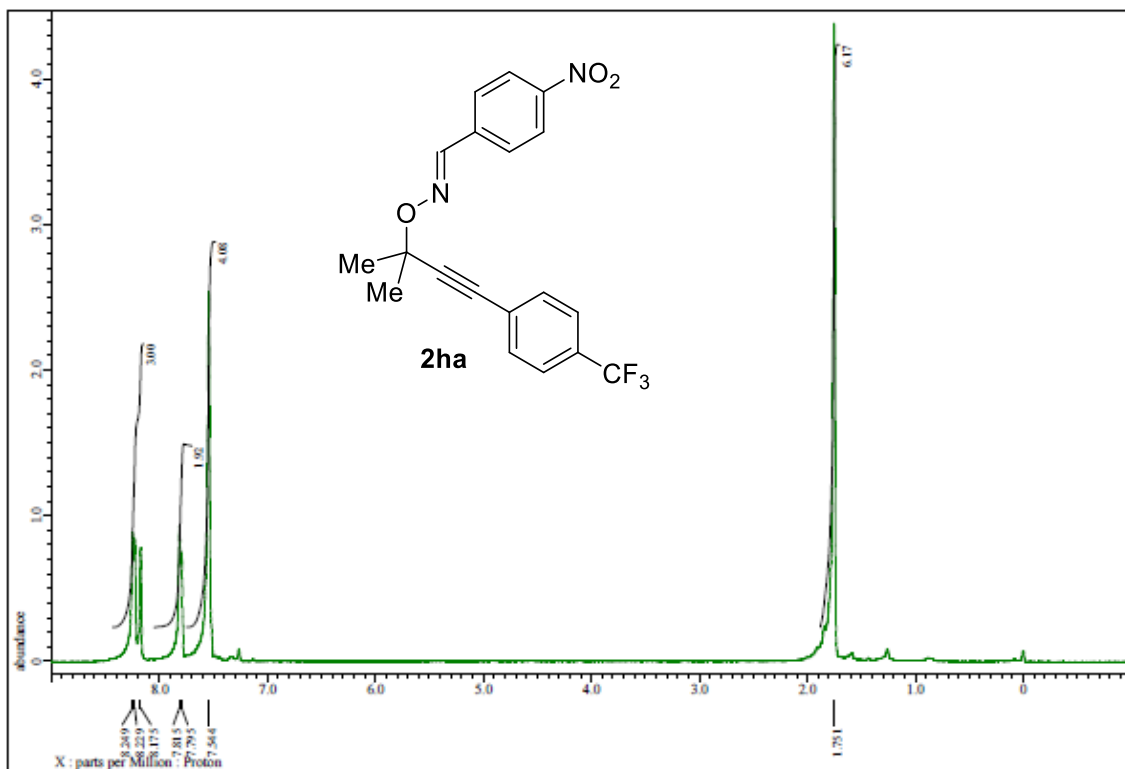


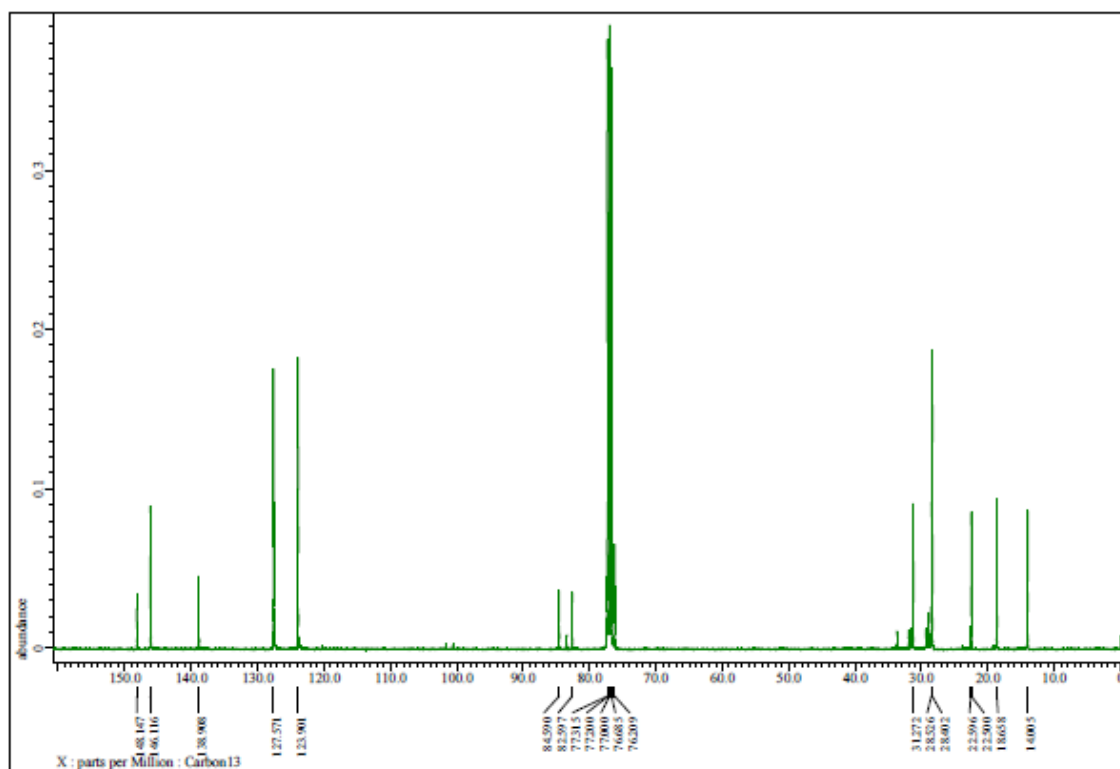
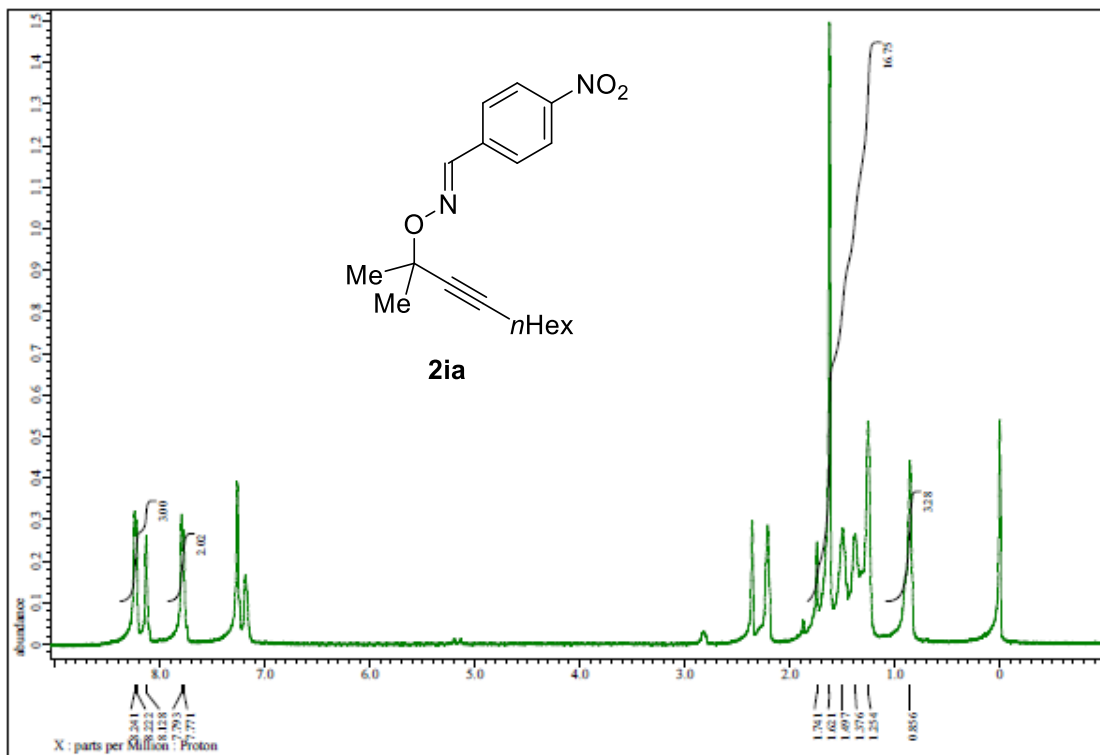


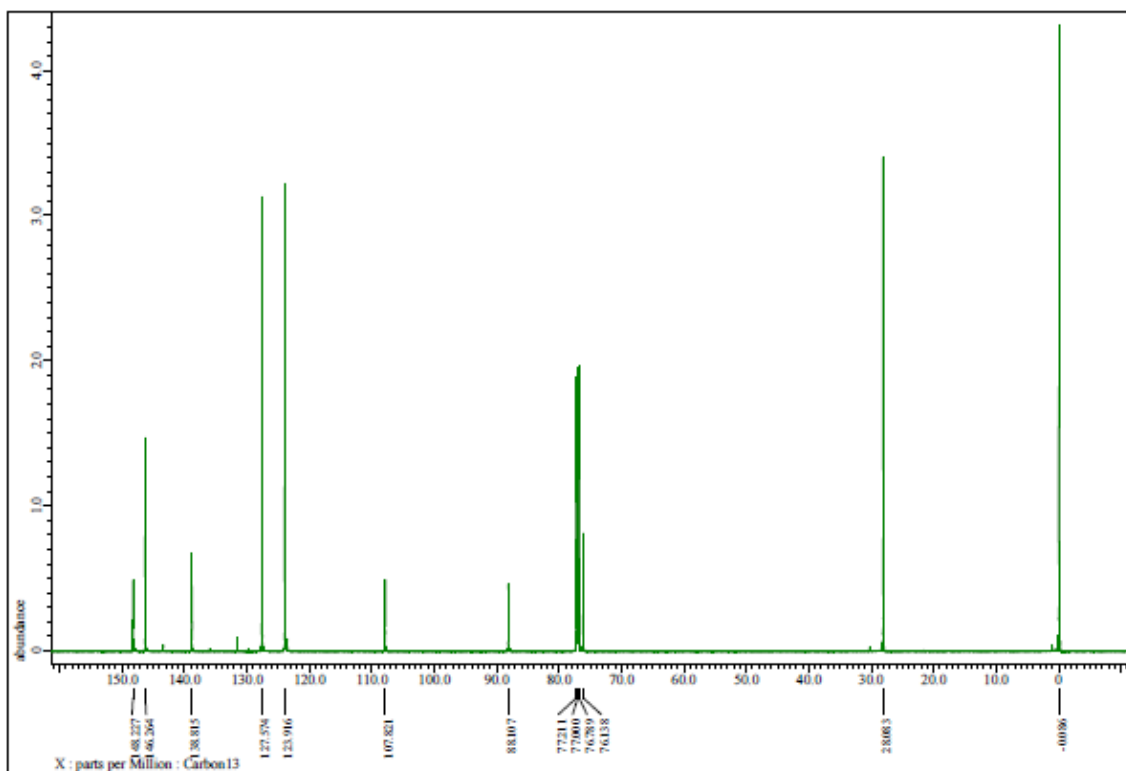
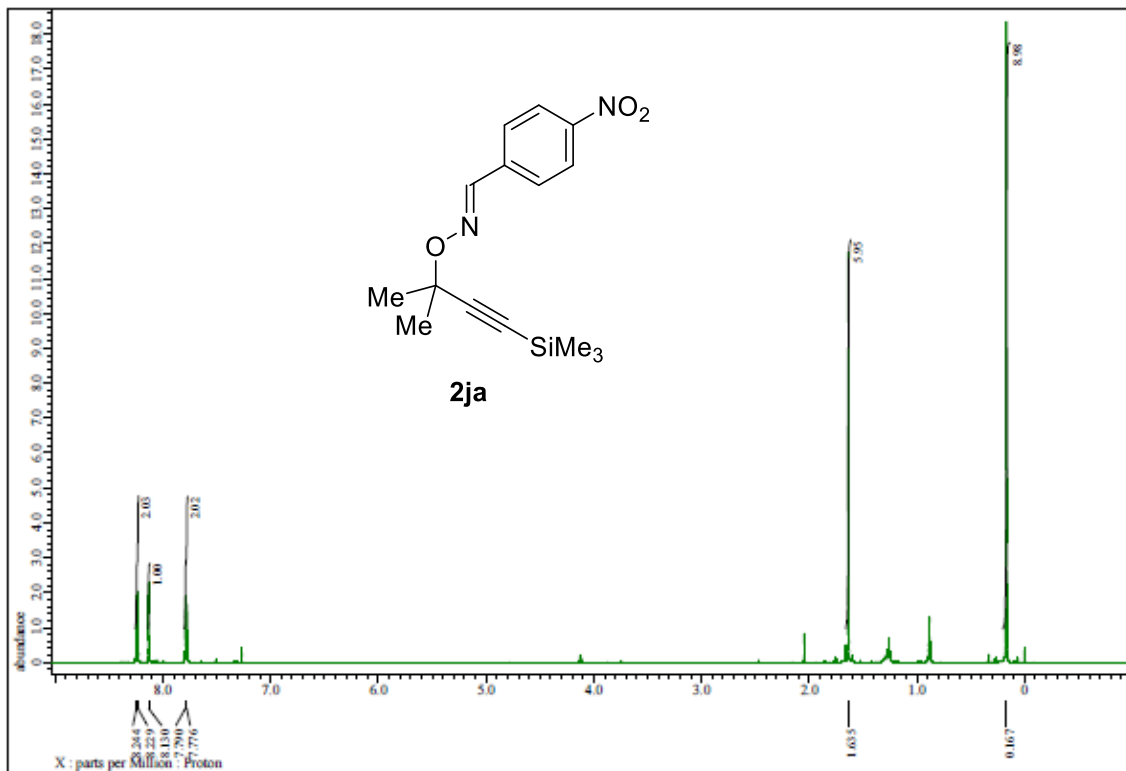












9. NMR charts of 7, 11, and 12

