

ESI for

## **Synergetic catalysis of Se and Cu allowing diethoxylation of halomethylene ketones using O<sub>2</sub> as the mild oxidant**

Zhicheng Cao,<sup>ab</sup> Xin Deng,<sup>a</sup> Chao Chen,<sup>a</sup> Yonghong Liu,<sup>\*a</sup> Lei Yu,<sup>\*a</sup> and Xuefeng Jiang<sup>\*b</sup>

<sup>a</sup> School of Chemistry and Chemical Engineering, Yangzhou University, Yangzhou, Jiangsu 225002, China. E-mails: [yhliu@yzu.edu.cn](mailto:yhliu@yzu.edu.cn) (Y. Liu), [yulei@yzu.edu.cn](mailto:yulei@yzu.edu.cn) (L. Yu).

<sup>b</sup> Shanghai Key Laboratory of Green Chemistry and Chemical Process, Department of Chemistry, East China Normal University, Shanghai 200062, China. E-mail: [xfjiang@chem.ecnu.edu.cn](mailto:xfjiang@chem.ecnu.edu.cn).

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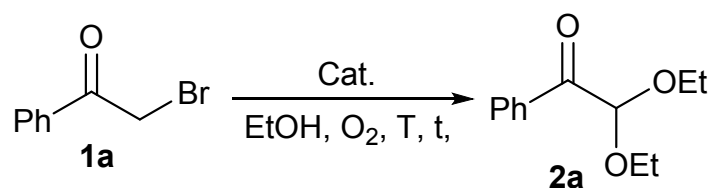
## 1. Experimental details

**General:** Reagents were purchased from Sinopharm Chemical Reagent and Energy Chemical with their purities more than 98% and were directly used as received. Solvents were analytical pure (AR) and directly used without any special treatment. Melting points were measured by WRS-2A digital instrument. IR spectra were determined on Bruker Tensor 27 Infrared spectrometer. NMR spectra were recorded on a Bruker Avance 400 instrument (400 MHz for  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR) using  $\text{CDCl}_3$  as the solvent and  $\text{Me}_4\text{Si}$  as the internal standard. Chemical shifts for  $^1\text{H}$  NMR were referred to internal  $\text{Me}_4\text{Si}$  (0 ppm) and  $J$ -values were shown in Hz. Mass spectra were determined on a Thermo Trace DSQ II or a Shimadzu GCMS-QP2010 Ultra spectrometer (EI). Elemental analysis was performed on an Elementar Vario EL cube instrument.

**General procedure for the synthesis of  $\alpha$ -carbonyl acetals:** To a 100 mL reaction tube, a piece of magnetic bar, 1 mmol of bromomethylene ketone **1**, 5 mol% of  $\text{PhSe(O)OH}$  (vs. **1**), 2 mol% of  $\text{Cu(OAc)}_2\cdot\text{H}_2\text{O}$  (vs. **1**) and 3 mL of EtOH were added. The tube was then charged with  $\text{O}_2$  and sealed. After being magnetically stirred at 100  $^\circ\text{C}$  for 24 h, the solvent was removed by evaporation under reduced pressure on a rotary evaporator. The residue was separated by preparative thin-layer chromatography (silica plate with eluent petroleum ether/EtOAc = 40/1) to afford the related product **2**.

**Synthesis of **2a** at kilogram scale:** To a 10 L reaction kettle equipped with water condenser, 1.2 kg of **1a** (10 mol), 94.5 g of  $\text{PhSe(O)OH}$ , 40 g of  $\text{Cu(OAc)}_2\cdot\text{H}_2\text{O}$  and 3 L EtOH were added. Oxygen was then introduced into the system via pipe below the liquid level of the system at the velocity of 0.9-1.0  $\text{cm}^3/\text{s}$ . The reaction system was mechanically stirred (500-550 rpm) and heated to reflux for 48 h. Excess EtOH in the system was evaporated and recycled, while the residue was then separated via distillation under reduced pressure (130-136  $^\circ\text{C}/10$  mmHg) to give 1.58 kg of **2a** (in ca 76% yield).

## 2. Detailed conditional optimizations

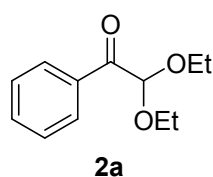
**Table S1** Condition optimizations<sup>a</sup>

Entry	Cat. (%) <sup>b</sup>	T/°C; t/h	<b>2a</b> / % <sup>c</sup>
1	PhSe(O)OH (5)	130; 48	25 <sup>d</sup>
2	Cu(OAc) <sub>2</sub> (2)	130; 24	32 <sup>d</sup>
3	PhSe(O)OH (2), Cu(OAc) <sub>2</sub> (2)	130; 7	57 <sup>d</sup>
4	PhSe(O)OH (5), Cu(OAc) <sub>2</sub> (2)	130; 7	76
5	PhSe(O)OH (10), Cu(OAc) <sub>2</sub> (2)	130; 7	78
6	PhSe(O)OH (5), Cu(OAc) <sub>2</sub> (2)	100; 7	50 <sup>d</sup>
7	PhSe(O)OH (5), Cu(OAc) <sub>2</sub> (2)	100; 16	71 <sup>d</sup>
8	PhSe(O)OH (5), Cu(OAc) <sub>2</sub> (2)	100; 24	84
9	PhSe(O)OH (5), Cu(OAc) <sub>2</sub> (2)	100; 32	80
10	PhSe(O)OH (5), Cu(OAc) <sub>2</sub> (2)	90; 24	76 <sup>d</sup>
11	PhSe(O)OH (5), Cu(OAc) <sub>2</sub> (2)	90; 30	80 <sup>d</sup>
12	PhSe(O)OH (5), Cu(OAc) <sub>2</sub> (2)	80; 24	71 <sup>d</sup>
13	PhSe(O)OH (5), Cu(OAc) <sub>2</sub> (2)	70; 24	63 <sup>d</sup>
14	PhSe(O)OH (5), Cu(OAc) <sub>2</sub> (2)	60; 24	45 <sup>d</sup>
15	3,5-(CF <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> Se(O)OH (5), Cu(OAc) <sub>2</sub> (2)	100; 24	76
16	4-MeOC <sub>6</sub> H <sub>4</sub> Se(O)OH (5), Cu(OAc) <sub>2</sub> (2)	100; 24	58 <sup>d</sup>
17	(PhSe) <sub>2</sub> (2.5), Cu(OAc) <sub>2</sub> (2)	100; 24	78
18	(PhSe) <sub>2</sub> (5), Cu(OAc) <sub>2</sub> (2)	100; 24	81
19	Se powder (5), Cu(OAc) <sub>2</sub> (2)	100; 24	38 <sup>d</sup>
20	SeO <sub>2</sub> (5), Cu(OAc) <sub>2</sub> (2)	100; 24	48 <sup>d</sup>
21	Na <sub>2</sub> SeO <sub>3</sub> (5), Cu(OAc) <sub>2</sub> (2)	100; 24	45 <sup>d</sup>
22	PhSe(O)OH (5), CuCl <sub>2</sub> (2)	100; 24	76
23	PhSe(O)OH (5), CuBr <sub>2</sub> (2)	100; 24	74
24	PhSe(O)OH (5), CuBr (2)	100; 24	79
25	PhSe(O)OH (5), CuO (2)	100; 24	70 <sup>d</sup>

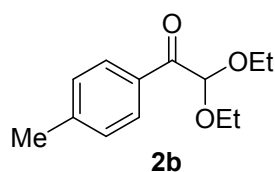
26	PhSe(O)OH (5), Cu <sub>2</sub> O (2)	100; 24	67 <sup>d</sup>
27	PhSe(O)OH (5), Cu powder (2)	100; 24	36 <sup>d</sup>

<sup>a</sup> 1 mmol of **1a** and 3 mL of alcohol were employed; The reaction was performed in a sealed tube. <sup>b</sup> Catalyst molar ratios based on **1a** amount inside the parentheses. <sup>c</sup> Isolated yield based on **1a**. <sup>d</sup> Reaction uncompleted.

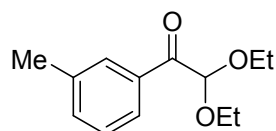
### 3. Characterization data of the products



**2,2-Diethoxy-1-phenylethan-1-one (2a):** Oil, 84% yield, 174.9 mg; IR (film): 3060, 2977, 2929, 2882, 1685, 1625, 1596, 1467, 1386, 1294, 1115, 1060 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, TMS, ppm): δ 8.09 (d, *J* = 8.4 Hz, 2H), 7.47 (t, *J* = 7.9 Hz, 1H), 7.36 (t, *J* = 7.8 Hz, 2H), 5.20 (s, 1H), 3.75–3.64 (m, 2H), 3.63–3.53 (m, 2H), 1.17 (t, *J* = 7.7 Hz, 6H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, TMS, ppm): δ 193.88, 133.73, 133.34, 129.63, 128.24, 102.44, 63.15, 15.12; MS (EI, 70 eV) *m/z* (%) 208 (26) [M<sup>+</sup>], 105 (100); Known compound.<sup>1</sup>

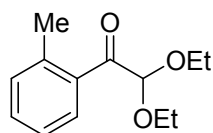


**2,2-Diethoxy-1-(*p*-tolyl)ethen-1-one (2b):** Oil, 81% yield, 180.0 mg; IR (film): 3034, 2980, 2930, 2883, 1686, 1608, 1572, 1446, 1311, 1293, 1114, 1064 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, TMS, ppm): δ 7.77 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 8.0 Hz, 2H), 4.97 (s, 1H), 3.45 (dt, *J* = 14.3, 7.1 Hz, 2H), 3.35 (p, *J* = 7.1 Hz, 2H), 2.09 (s, 3H), 0.94 (t, *J* = 7.1 Hz, 6H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, TMS, ppm): δ 193.69, 144.40, 131.26, 129.83, 129.08, 102.23, 63.03, 21.77, 15.22; MS (EI, 70 eV) *m/z* (%) 222 (21) [M<sup>+</sup>], 119 (100); Known compound.<sup>1</sup>



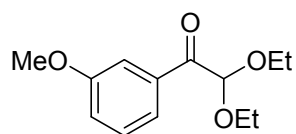
**2c**

**2,2-Diethoxy-1-(*m*-tolyl)ethanone (2c):** Oil; 83% yield, 184.5 mg; IR (KBr film): 3035, 2978, 2928, 2883, 1693, 1595, 1447, 1381, 1292, 1255, 1120, 1062, 903, 794, 737, 652, 490  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , TMS, ppm):  $\delta$  7.87 (s, 1H), 7.89 (d,  $J = 8.0$  Hz, 1H), 7.32–7.24 (m, 2H), 5.23 (s, 1H), 3.71–3.54 (m, 4H), 2.33 (s, 3H), 1.17 (t,  $J = 8.0$  Hz, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , TMS, ppm):  $\delta$  194.18, 138.16, 134.32, 133.86, 130.00, 128.26, 126.98, 101.99, 63.01, 21.38, 15.23; MS (EI, 70 eV)  $m/z$  (%) 222 (20) [ $\text{M}^+$ ], 119 (100); Known compound.<sup>1</sup>



**2d**

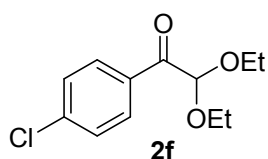
**2,2-Diethoxy-1-(*o*-tolyl)ethanone (2d):** Oil; 84%, 186.7 mg; IR (film): 3065, 2975, 2927, 1697, 1600, 1570, 1452, 1381, 1294, 1226, 1114, 1062, 911, 735, 647, 476  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , TMS, ppm):  $\delta$  7.92 (d,  $J = 8.0$  Hz, 1H), 7.32 (dd,  $J_1 = 4.0$  Hz,  $J_2 = 8.0$  Hz, 1H), 7.20–7.17 (m, 2H), 5.15 (s, 1H), 3.71–3.54 (m, 4H), 2.45 (s, 3H), 1.16 (t,  $J = 6.0$  Hz, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , TMS, ppm):  $\delta$  197.34, 139.83, 134.16, 131.85, 130.15, 125.33, 102.31, 63.07, 21.48, 15.21; MS (EI, 70 eV)  $m/z$  (%) 222 (18) [ $\text{M}^+$ ], 119 (100); Known compound.<sup>1</sup>



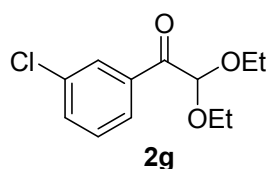
**2e**

**2,2-Diethoxy-1-(3-methoxyphenyl)ethanone (2e):** Oil, 50% yield, 119.1 mg; IR (film): 3077, 2976, 2933, 2883, 1688, 1596, 1582, 1486, 1432, 1324, 1288, 1115, 1060  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , TMS, ppm):  $\delta$  7.71 (d,  $J = 8.0$  Hz, 1H), 7.59 (s, 1H), 7.29 (dd,  $J_1 = 8.0$  Hz,  $J_2 = 8.0$  Hz, 1H), 7.05 (d,  $J = 8.0$  Hz, 1H), 5.22 (s, 1H), 3.78 (s, 3H), 3.73–3.51 (m, 4H), 1.18 (t,  $J = 8.0$  Hz, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , TMS,

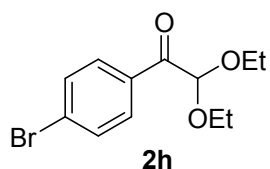
ppm):  $\delta$  193.83, 159.55, 135.07, 129.39, 122.48, 120.23, 113.59, 102.11, 63.11, 55.44, 15.25; MS (EI, 70 eV)  $m/z$  (%) 238 (9) [ $M^+$ ], 135 (100); Known compound.<sup>1</sup>



**2,2-Diethoxy-1-(4-chlorophenyl)ethan-1-one (2f):** Oil, 80%, 194.2 mg; IR (KBr film): 3075, 2980, 2932, 2884, 1694, 1590, 1570, 1489, 1402, 1288, 1118, 1092, 1063, 1016  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , TMS, ppm):  $\delta$  8.10 (d,  $J = 8.0$  Hz, 2H), 7.40 (d,  $J = 8.0$  Hz, 2H), 5.15 (s, 1H), 3.78–3.57 (m, 4H), 1.21 (d,  $J = 8.0$  Hz, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , TMS, ppm):  $\delta$  193.05, 139.90, 131.92, 131.34, 128.65, 103.20, 63.59, 15.19; MS (EI, 70 eV)  $m/z$  (%) 242 (8) [ $M^+$ ], 139 (100); Known compound.<sup>1</sup>

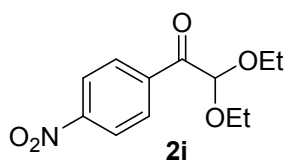


**2,2-Diethoxy-1-(3-chlorophenyl)ethan-1-one (2g):** Oil, 83%, 201.4 mg; IR (KBr film): 3070, 2981, 2929, 2884, 1688, 1590, 1572, 1485, 1403, 1289, 1114, 1092, 1065, 1011  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , TMS, ppm):  $\delta$  8.05 (s, 1H), 7.98 (d,  $J = 7.9$  Hz, 1H), 7.43 (d,  $J = 8.0$  Hz, 1H), 7.29 (t,  $J = 7.9$  Hz, 1H), 5.10 (s, 1H), 3.74–3.66 (m, 2H), 3.61–3.51 (m, 2H), 1.16 (t,  $J = 7.1$  Hz, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , TMS, ppm):  $\delta$  192.68, 135.14, 134.39, 133.17, 129.65, 127.91, 102.92, 63.51, 15.09; MS (EI, 70 eV)  $m/z$  (%) 242 (8) [ $M^+$ ], 139 (100); Known compound.<sup>1</sup>

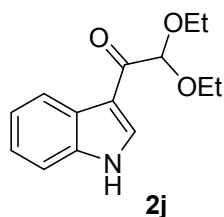


**1-(4-Bromophenyl)-2,2-diethoxyethanone (2h):** Oil, 80%, 229.8 mg; IR (KBr film): 2978, 2931, 2883, 1693, 1586, 1484, 1400, 1287, 1118, 1071, 1012  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , TMS, ppm):  $\delta$  8.02 (d,  $J = 8.4$  Hz, 2H), 7.56 (d,  $J = 8.4$  Hz, 2H), 5.14 (s, 1H), 3.81–3.68 (m, 2H), 3.67–3.55 (m, 2H), 1.22 (t,  $J = 7.1$  Hz, 6H).  $^{13}\text{C}$  NMR (100

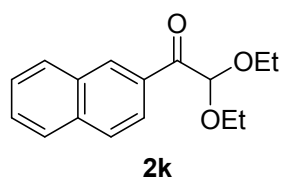
MHz, CDCl<sub>3</sub>, TMS, ppm):  $\delta$  193.19, 131.60, 131.38, 130.38, 128.70, 103.14, 63.55, 15.16; MS (EI, 70 eV) m/z (%) 286 (5) [M<sup>+</sup>], 183 (100); Known compound.<sup>1</sup>



**2,2-Diethoxy-1-(4-nitrophenyl)ethan-1-one (2i):** Oil, 69%, 174.7 mg; IR (KBr film): 3108, 3075, 3050, 2978, 2939, 2902, 1701, 1603, 1526, 1480, 1371, 1345, 1278, 1115, 1053, 1014 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, TMS, ppm):  $\delta$  8.29 (d, *J* = 8.6 Hz, 2H), 8.22 (d, *J* = 8.6 Hz, 2H), 5.10 (s, 1H), 3.82–3.72 (m, 2H), 3.65–3.56 (m, 2H), 1.20 (t, *J* = 7.1 Hz, 6H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, TMS, ppm):  $\delta$  192.72, 150.38, 138.08, 131.09, 123.36, 103.85, 64.19, 15.19; MS (EI, 70 eV) m/z (%) 253 (11) [M<sup>+</sup>], 105 (100); Known compound.<sup>1</sup>



**2,2-Diethoxy-1-(1H-indol-3-yl)ethenone (2j):** Yellow solid, m. p.: 131-132 °C, 56%, 138.4 mg; IR (KBr film): 3423, 3197, 2978, 2888, 1635, 1513, 1416, 1305, 1246, 1160, 1105, 1058, 956, 914, 805, 753, 634, 592, 523 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, TMS, ppm):  $\delta$  9.08 (s, 1H), 8.43 (d, *J* = 8.0 Hz, 1H), 8.34 (d, *J* = 3.0 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.31–7.25 (m, 2H), 5.12 (s, 1H), 3.84–3.58 (m, 4H), 1.24 (t, *J* = 8.0 Hz, 6H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, TMS, ppm):  $\delta$  190.94, 135.77, 134.33, 126.32, 123.69, 122.79, 122.41, 113.46, 111.37, 103.44, 62.89, 15.24; MS (EI, 70 eV) m/z (%) 247 (10) [M<sup>+</sup>], 116 (100); Anal. Calcd for C<sub>14</sub>H<sub>17</sub>NO<sub>3</sub>: C, 68.00; H, 6.93. Found: C, 68.05; H, 6.88.



**2,2-Diethoxy-1-(naphthalen-2-yl)ethan-1-one (2k):** Oil; 57%, 147.2 mg; IR (KBr film): 3070, 2980, 2932, 2889, 1689, 1598, 1580, 1449, 1396, 1285, 1229, 1117, 1063  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , TMS, ppm):  $\delta$  8.77 (s, 1H), 8.14 (dd,  $J = 8.6, 1.6$  Hz, 1H), 7.96 (d,  $J = 8.1$  Hz, 1H), 7.84 (t,  $J = 8.8$  Hz, 2H), 7.61–7.49 (m, 2H), 5.40 (s, 1H), 3.82–3.55 (m, 4H), 1.25 (t,  $J = 7.1$  Hz, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , TMS, ppm):  $\delta$  194.09, 135.81, 132.45, 132.02, 131.08, 129.92, 128.64, 128.09, 127.72, 126.57, 124.94, 102.56, 63.22, 15.25; MS (EI, 70 eV)  $m/z$  (%) 258 (16) [ $\text{M}^+$ ], 155 (100); Known compound.<sup>1</sup>

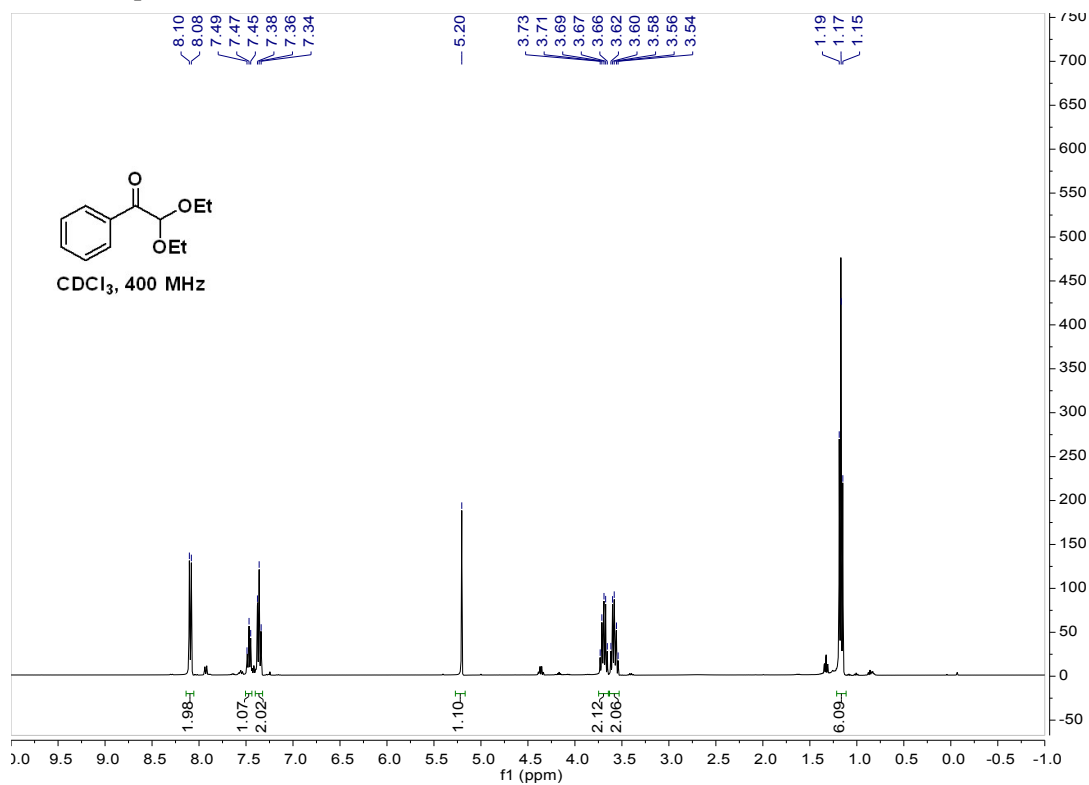
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1. C. Chen, Z. Cao, X. Zhang, Y. Li, L. Yu and X. Jiang, *Chin. J. Chem.*, 2020, **38**, 1045.

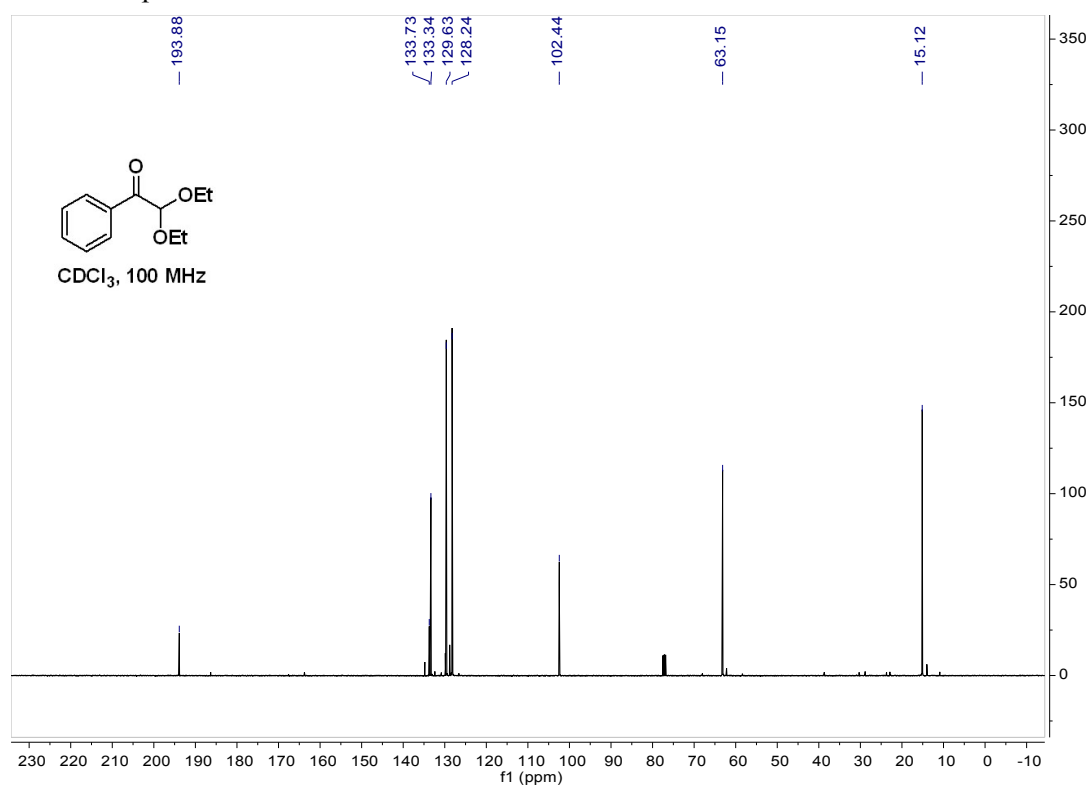


## 4. NMR spectra of products

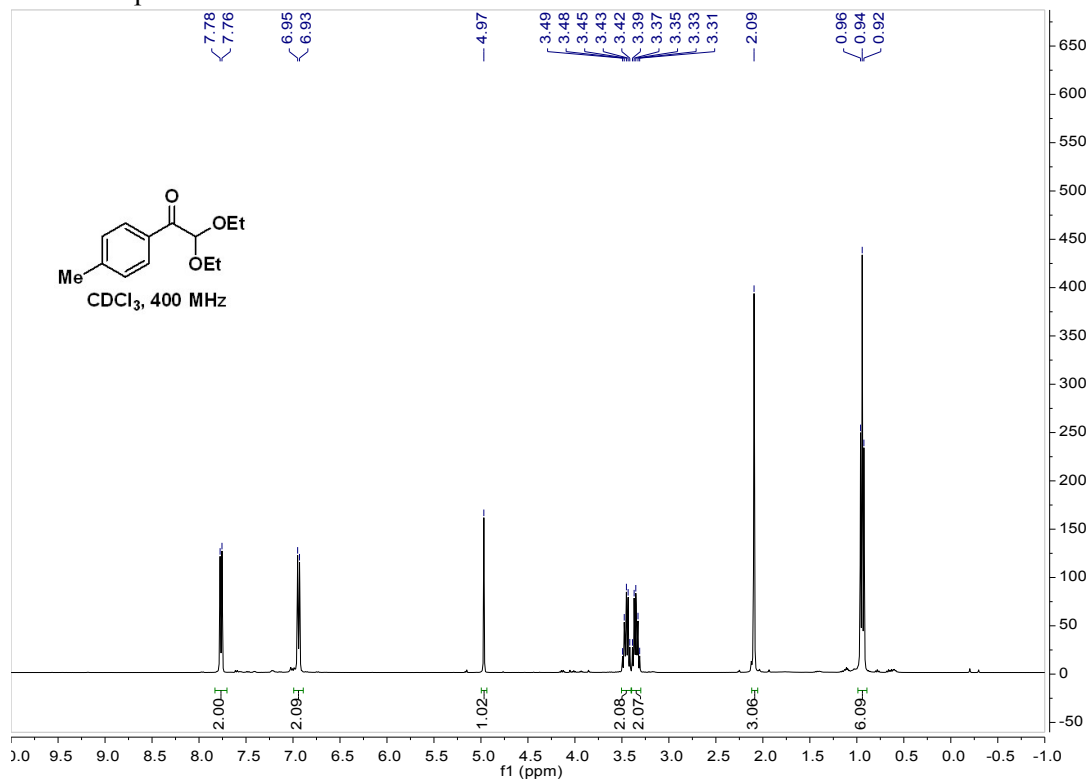
$^1\text{H}$  NMR spectrum of **2a**



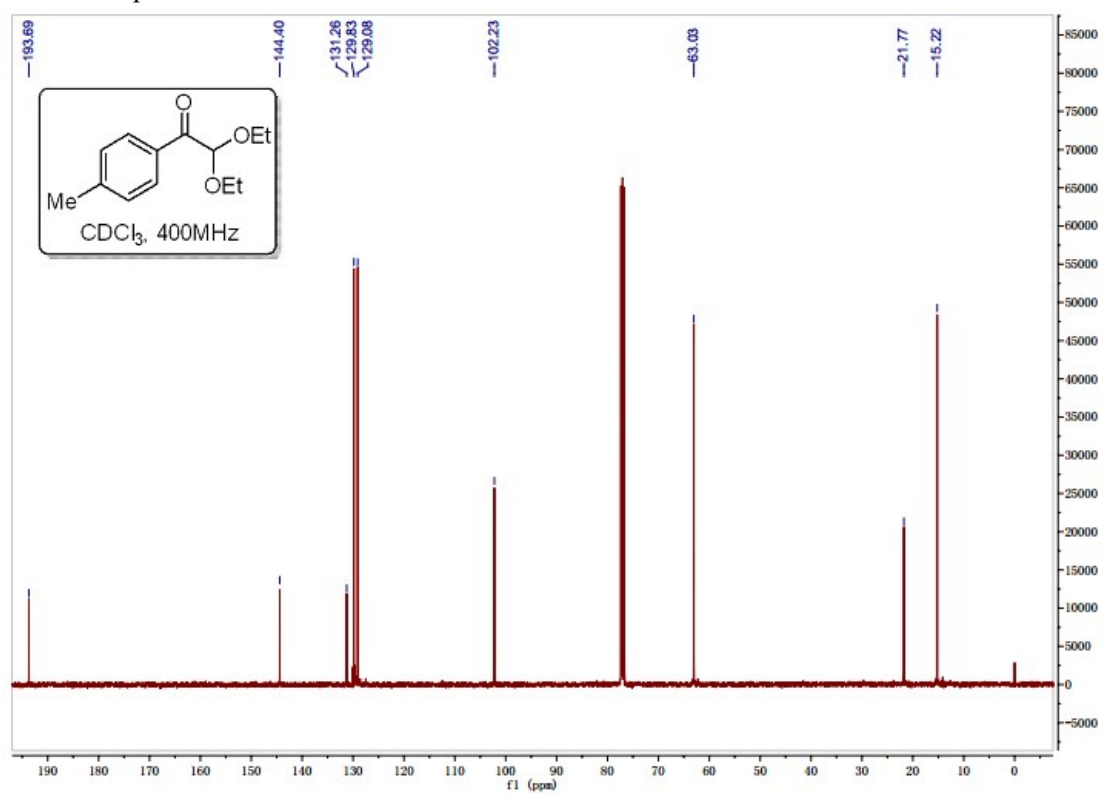
$^{13}\text{C}$  NMR spectrum of **2a**



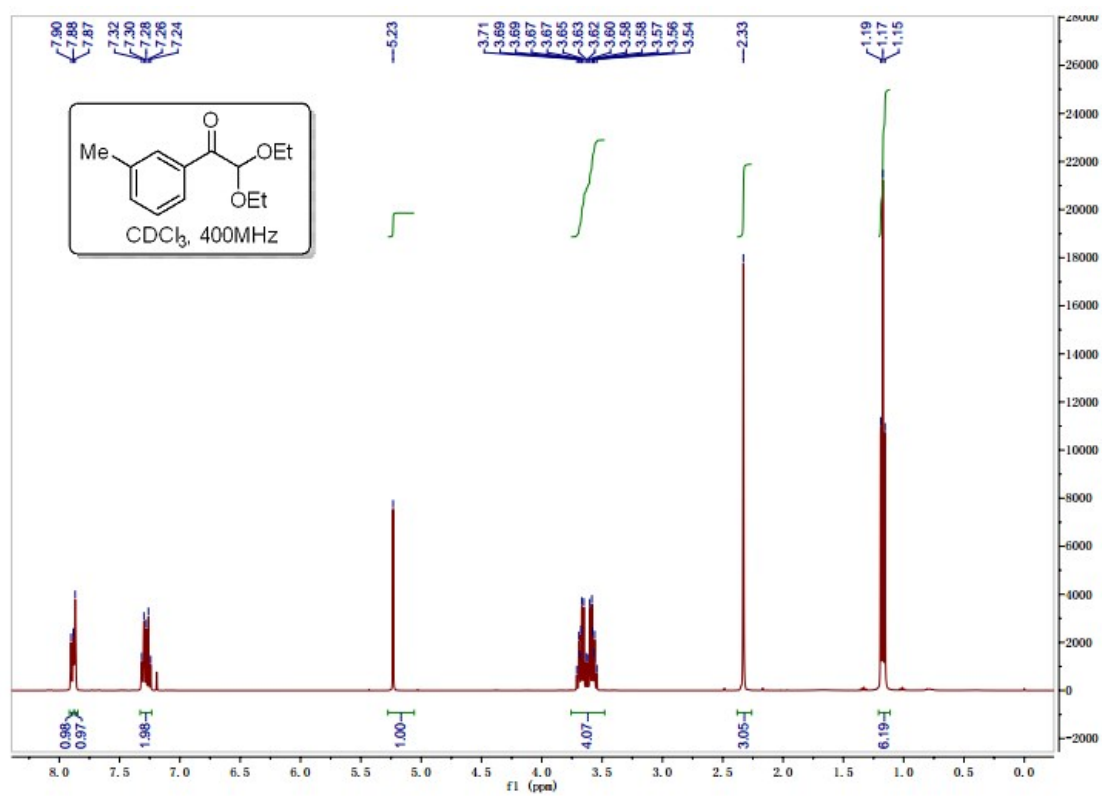
<sup>1</sup>H NMR spectrum of **2b**



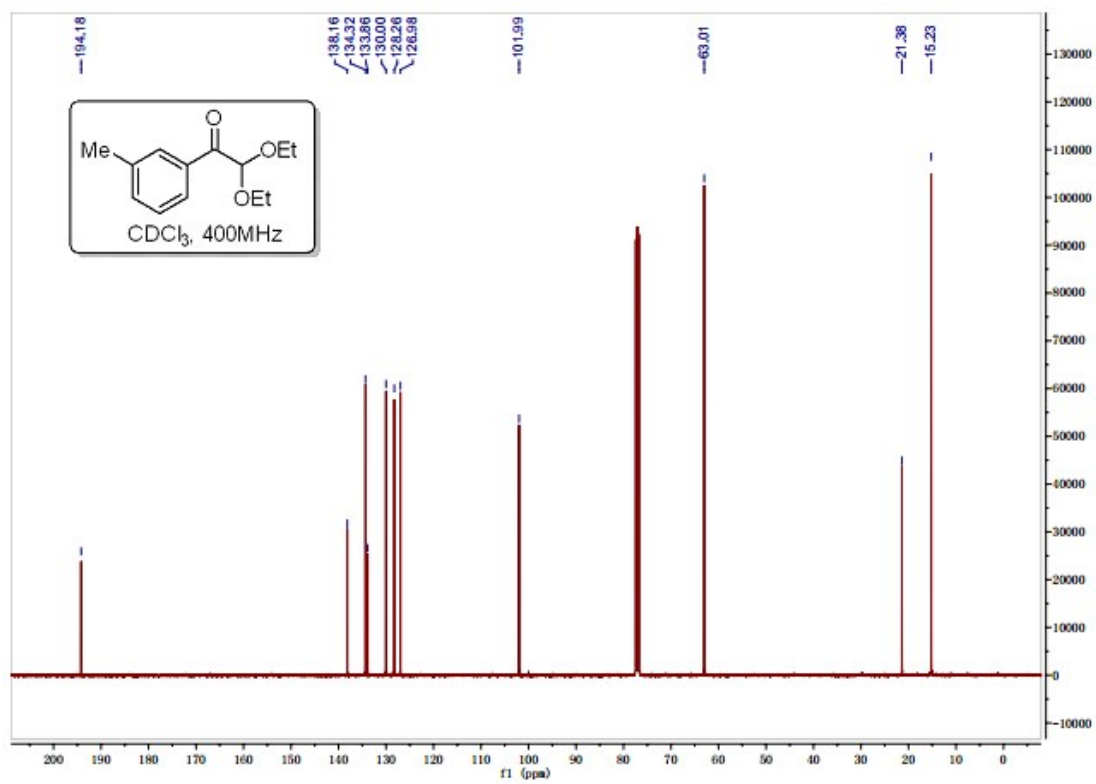
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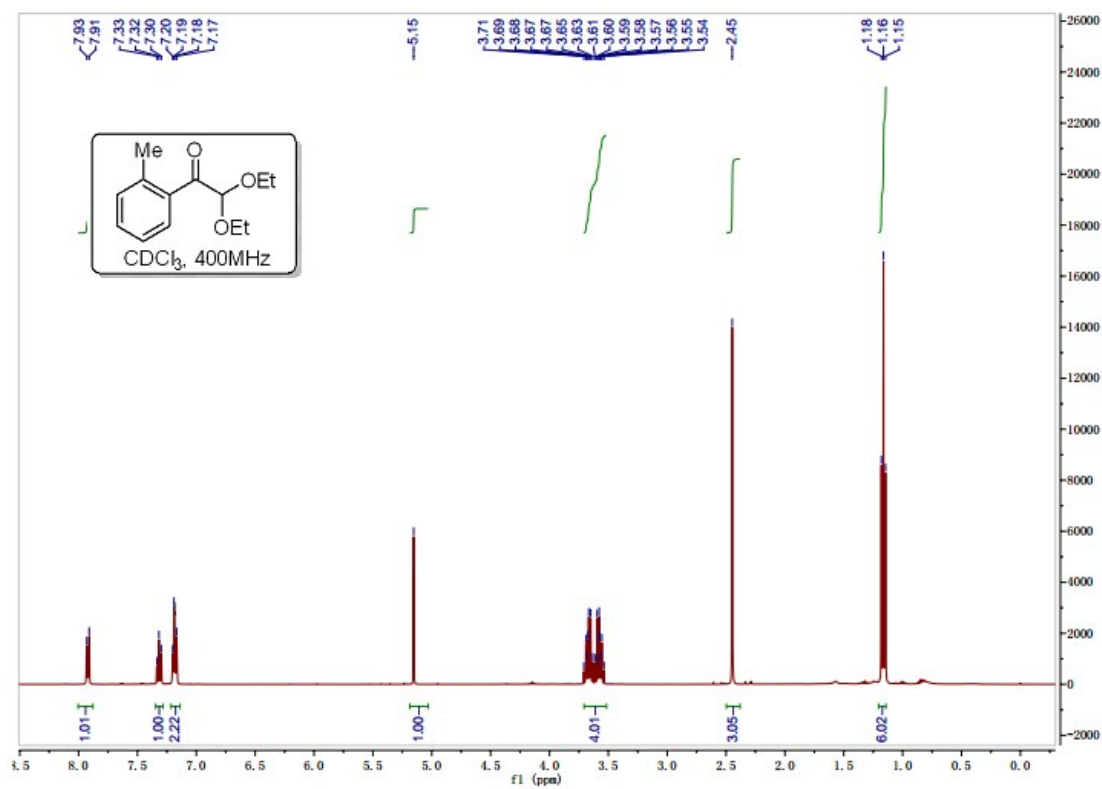
$^1\text{H}$  NMR spectrum of **2c**



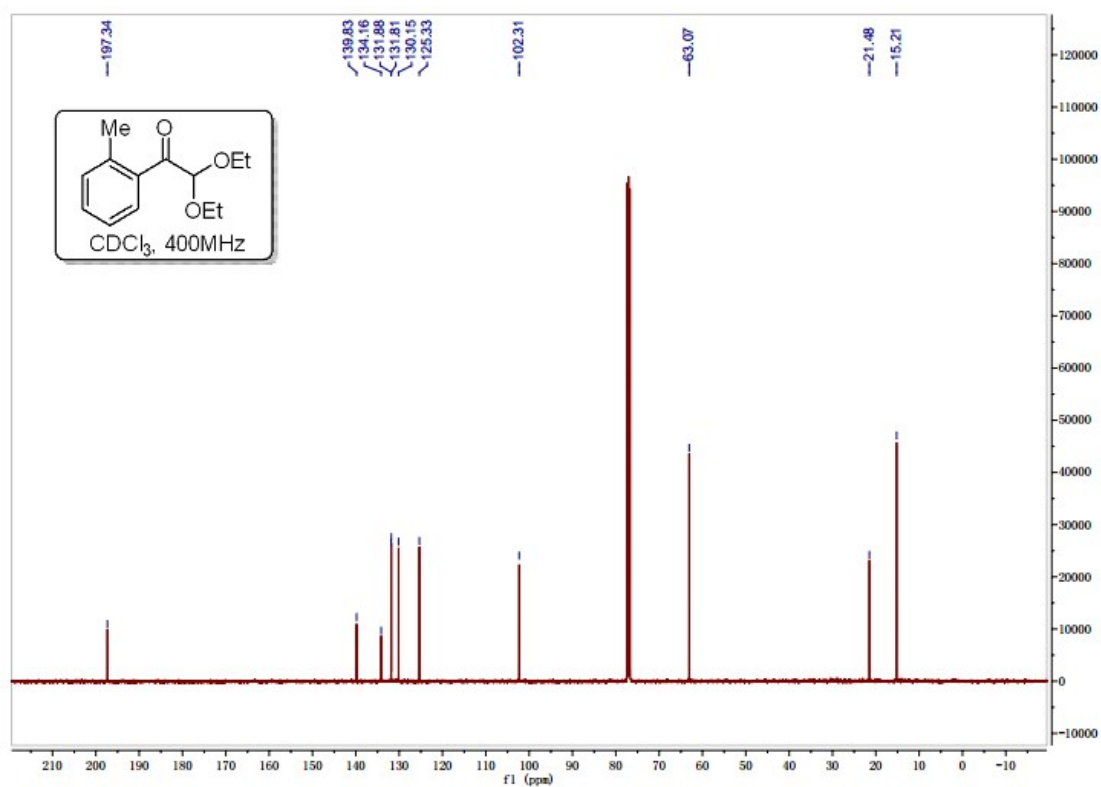
$^{13}\text{C}$  NMR spectrum of **2c**



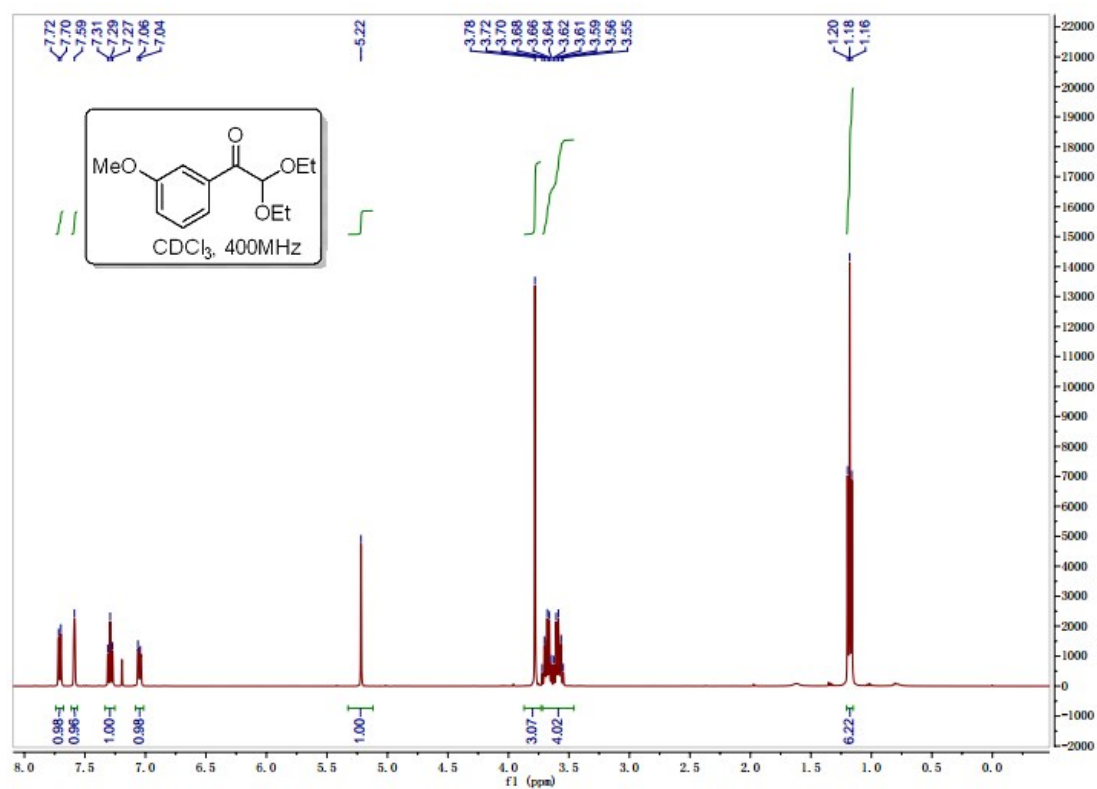
<sup>1</sup>H NMR spectrum of **2d**



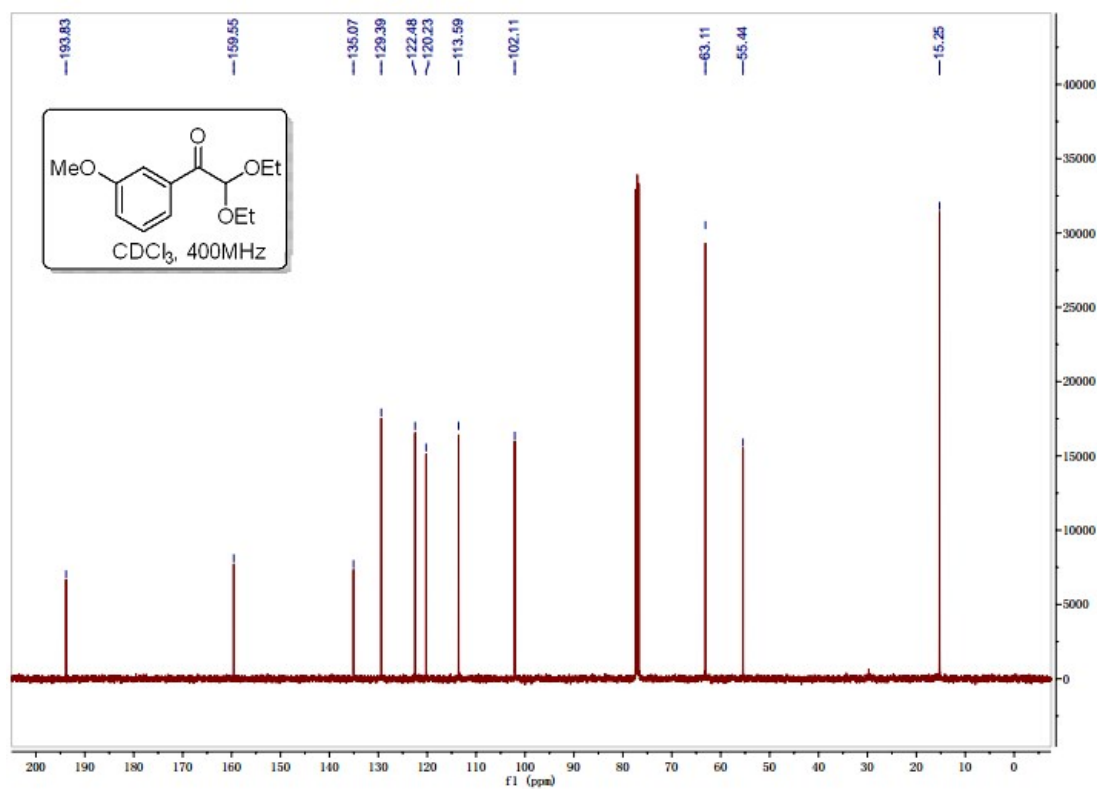
<sup>13</sup>C NMR spectrum of **2d**



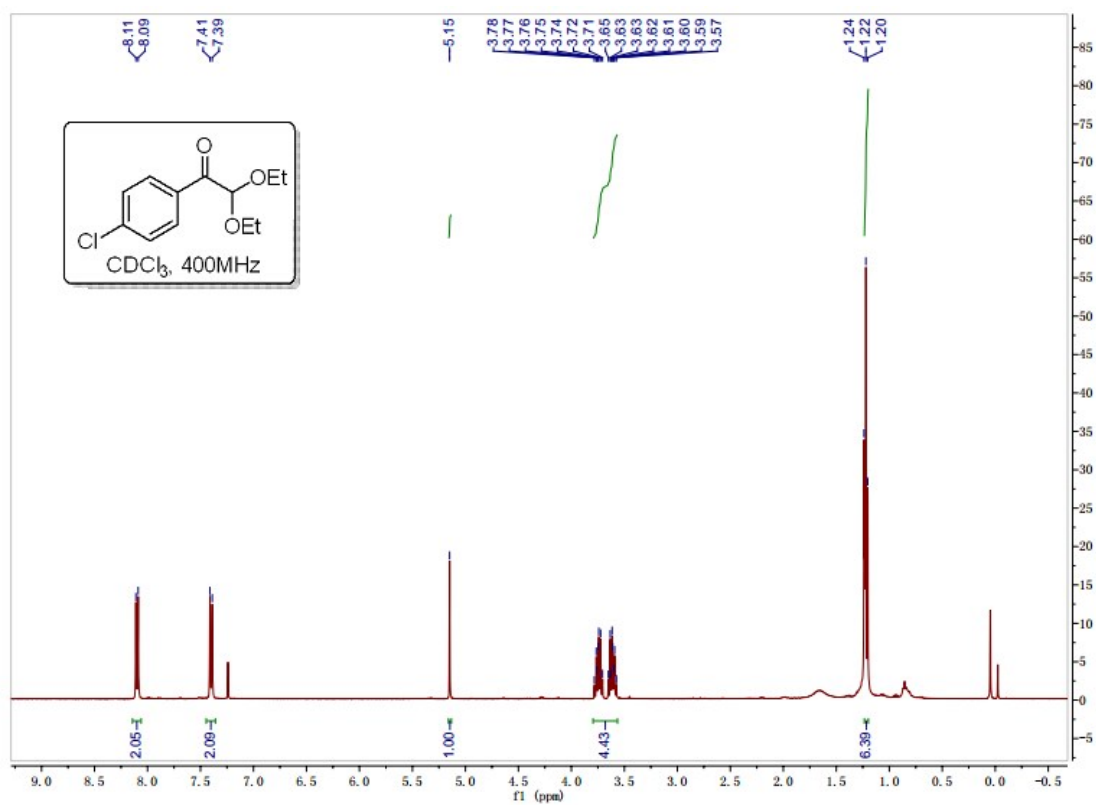
$^1\text{H}$  NMR spectrum of **2e**



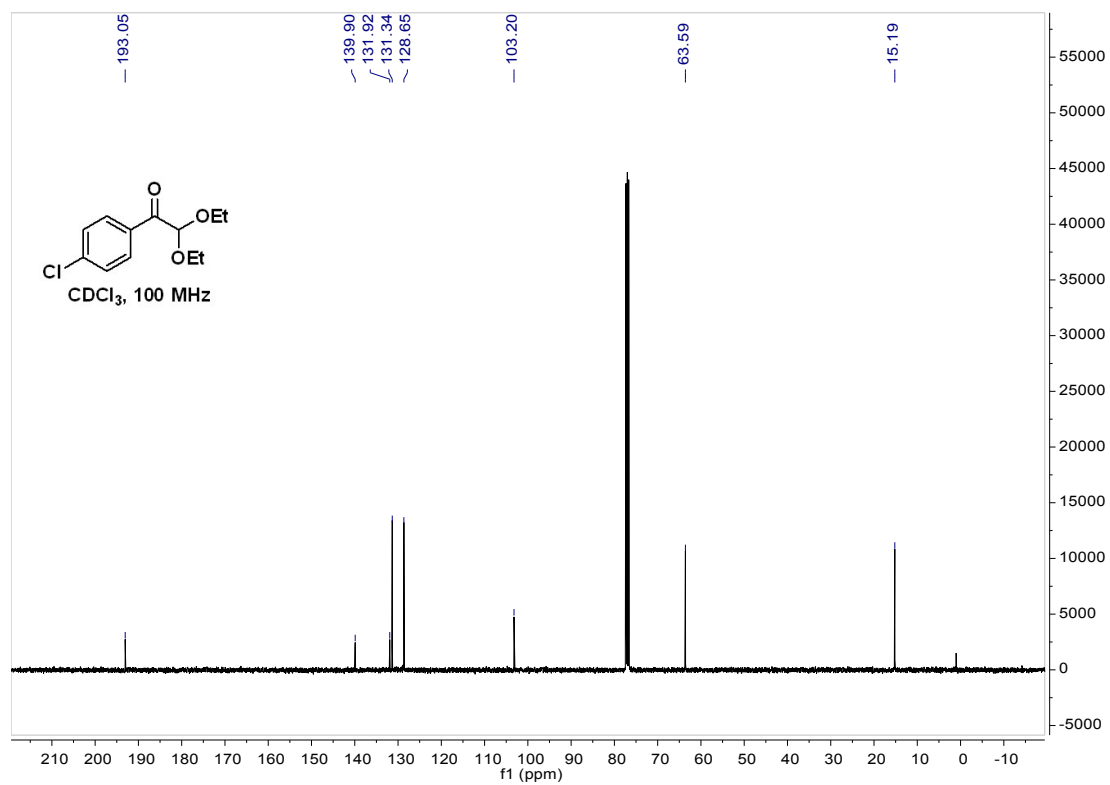
$^{13}\text{C}$  NMR spectrum of **2e**



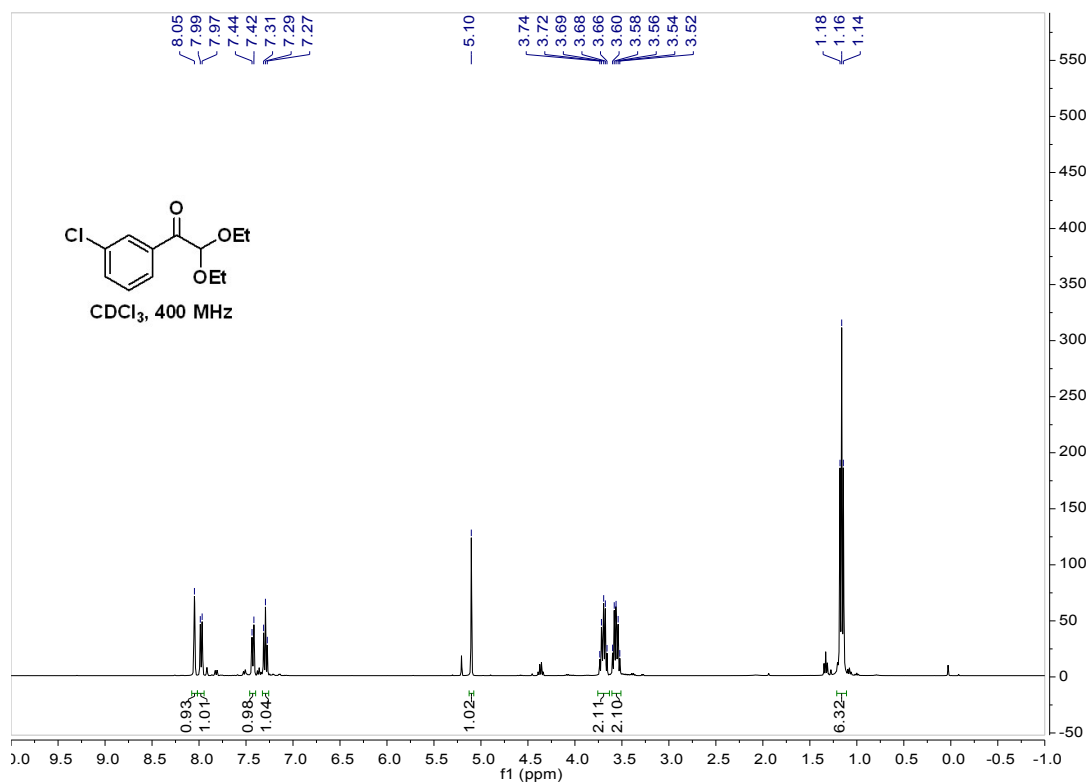
$^1\text{H}$  NMR spectrum of **2f**



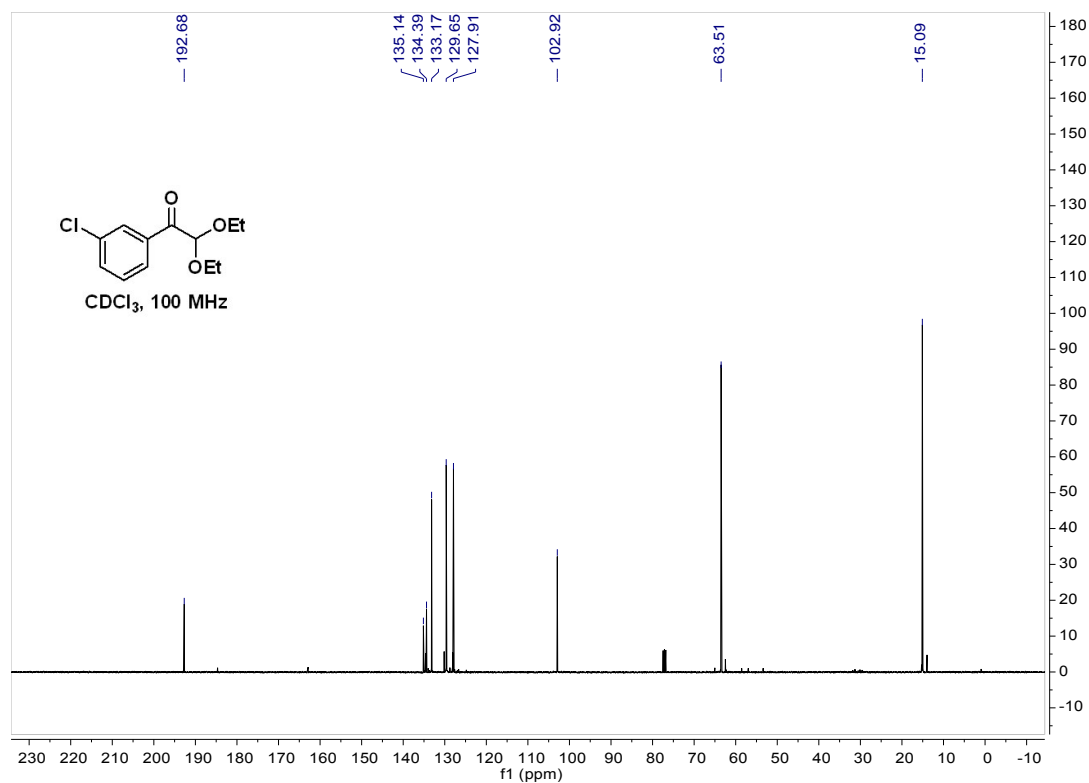
$^{13}\text{C}$  NMR spectrum of **2f**



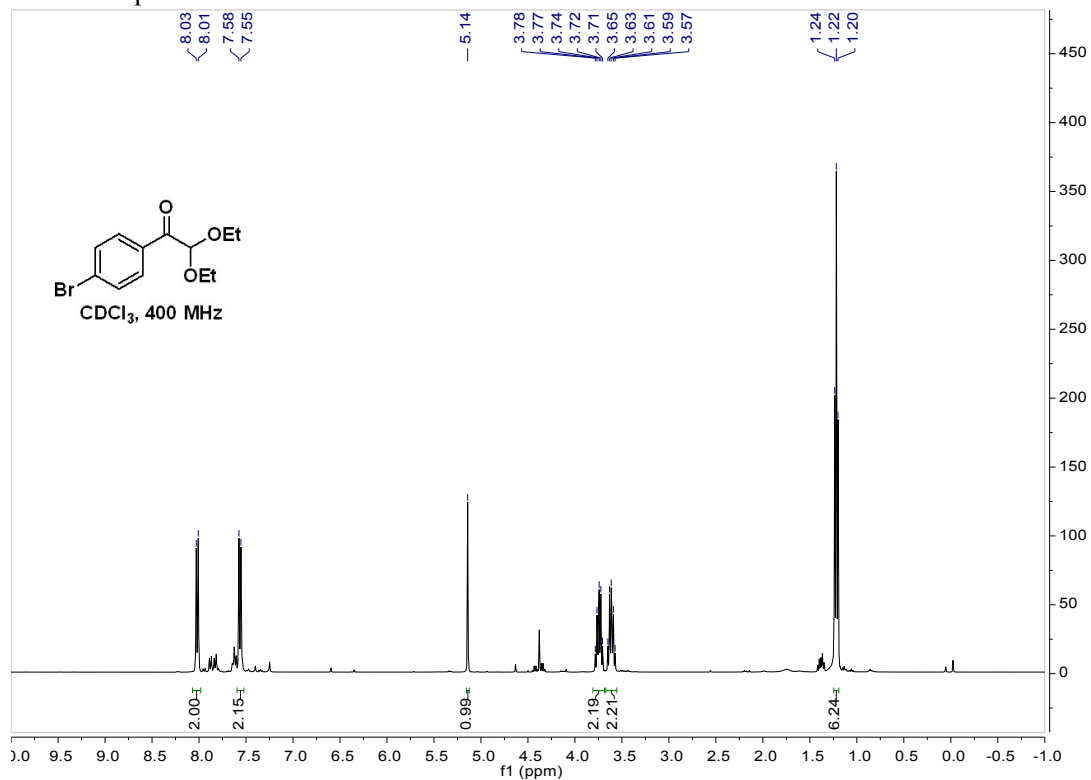
<sup>1</sup>H NMR spectrum of **2g**



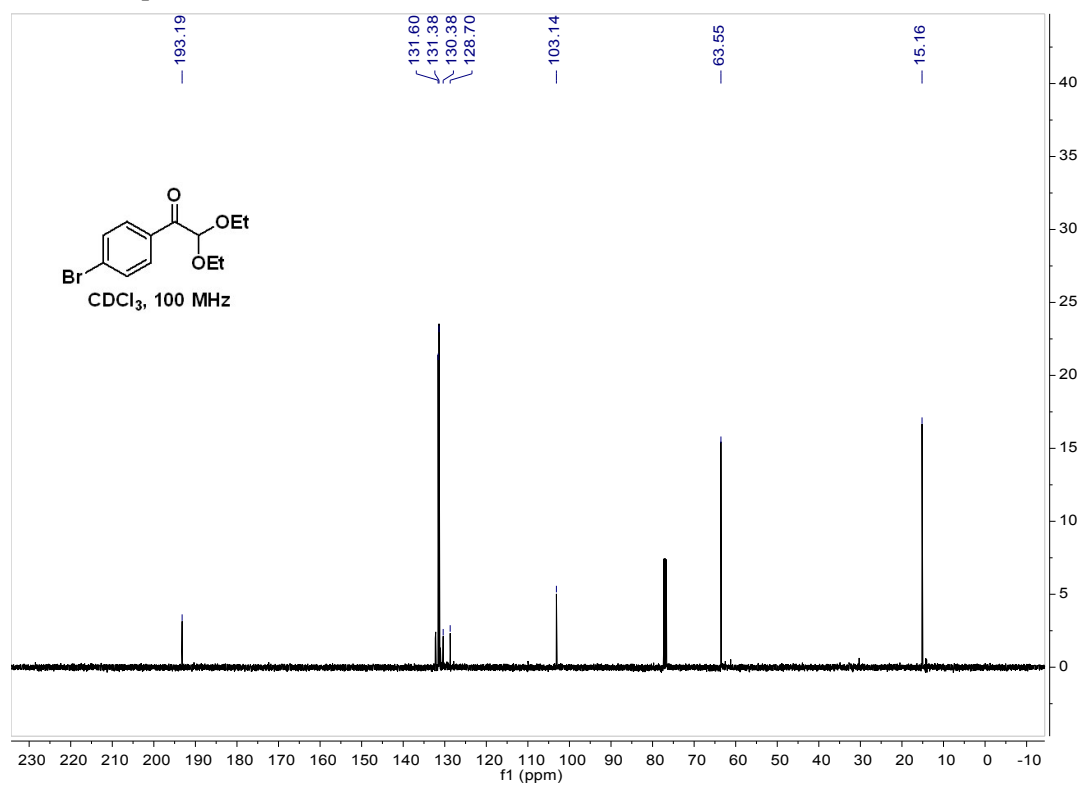
<sup>13</sup>C NMR spectrum of **2g**



<sup>1</sup>H NMR spectrum of **2h**

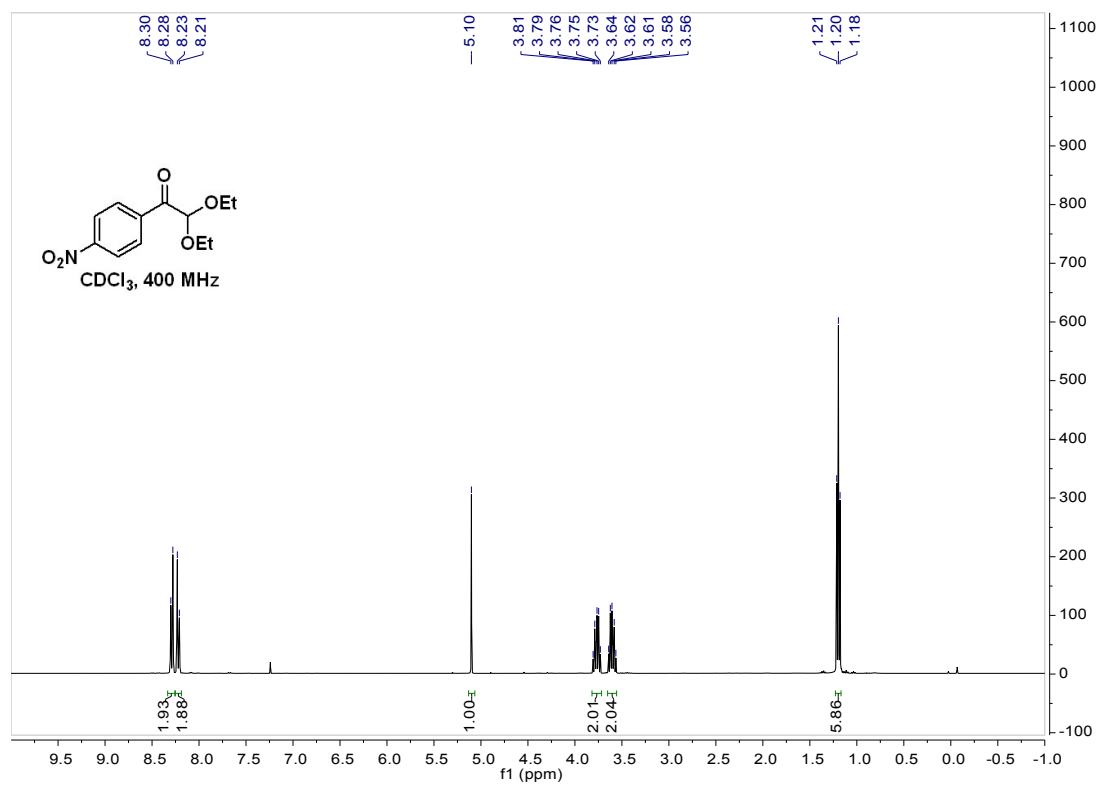


<sup>13</sup>C NMR spectrum of **2h**

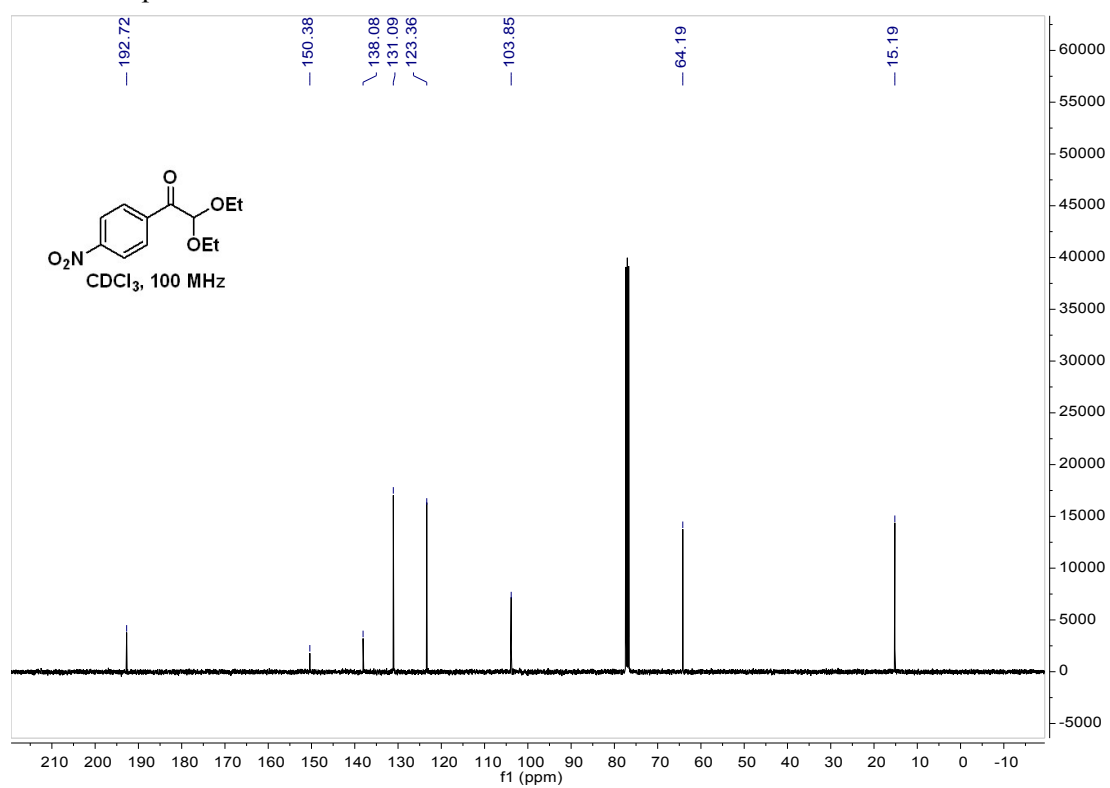




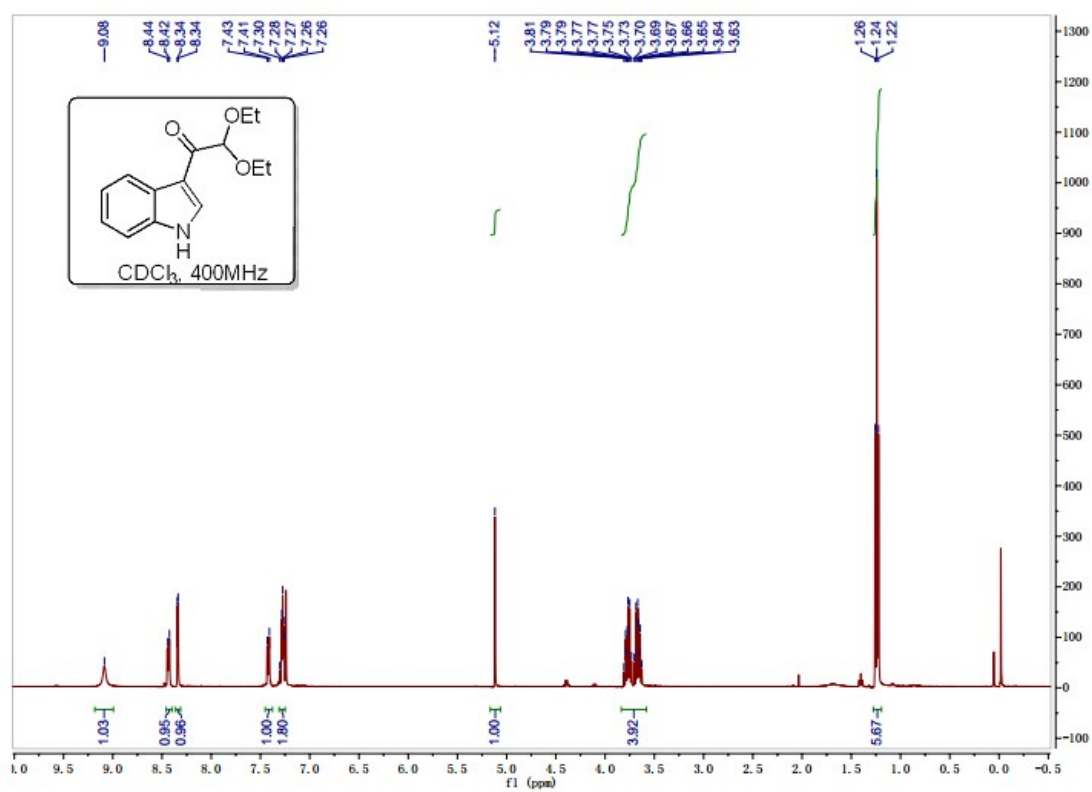
### <sup>1</sup>H NMR spectrum of **2i**



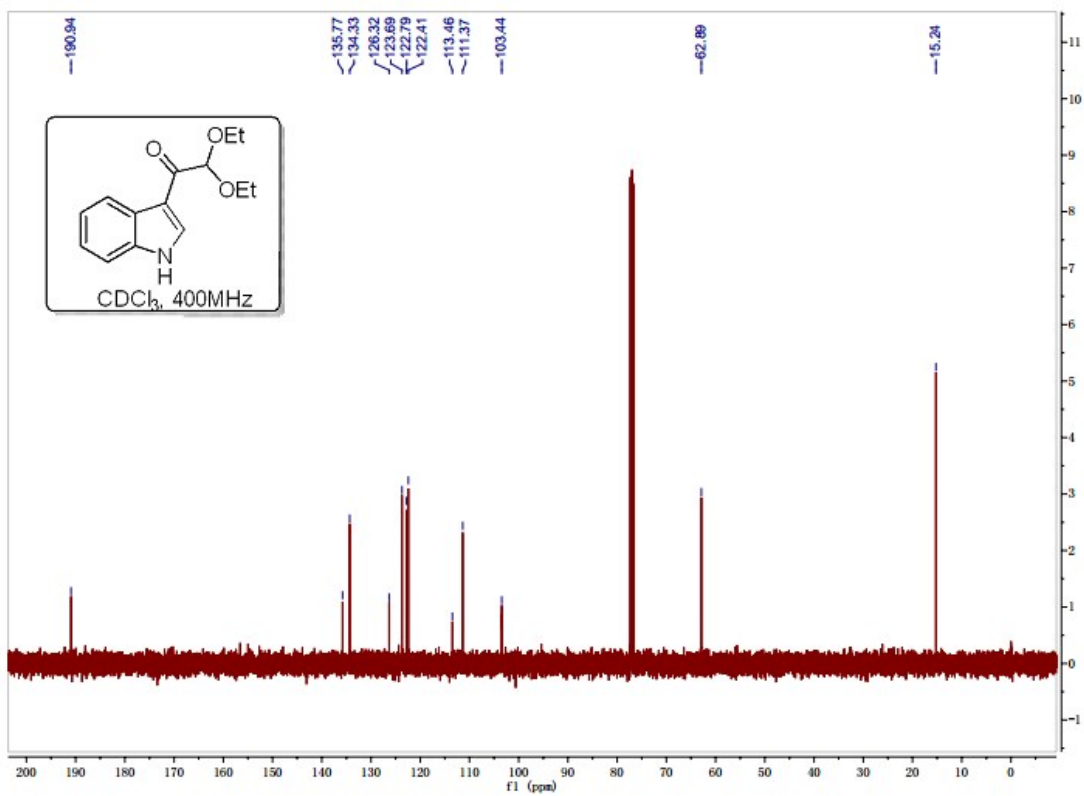
### <sup>13</sup>C NMR spectrum of **2i**



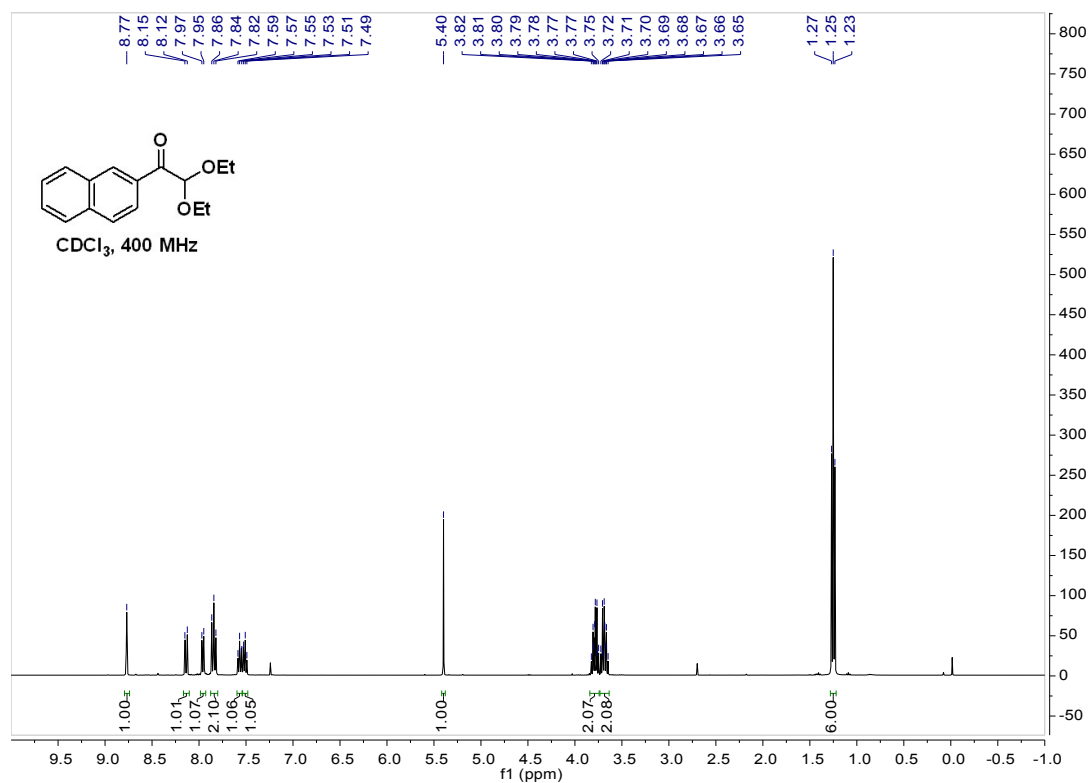
$^1\text{H}$  NMR spectrum of **2j**



$^{13}\text{C}$  NMR spectrum of **2j**



<sup>1</sup>H NMR spectrum of **2k**



<sup>13</sup>C NMR spectrum of **2k**

