One Pot Synthesis of Indene through Copper(I)-catalyzed Three-components Coupling and Cyclization Reaction

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General Remarks:

Column chromatography was carried out on silica gel. ^{1}H NMR spectra were recorded on 400 MHz in $CDCl_3$ and ^{13}C NMR spectra were recorded on 100 MHz in $CDCl_3$ using TMS as internal standard. IR spectra were recorded on a FT-IR spectrometer and only major peaks are reported in cm^{-1}. Melting points were determined on a microscopic apparatus and were uncorrected. All new compounds were further characterized by element analysis; Copies of their ^{1}H NMR and ^{13}C NMR spectra are provided. Unless otherwise stated, all amines were purchased from commercial suppliers and used without further purification.

Starting Materials:

Diethyl (2-iodophenyl)malonate was prepared according to the literature[1]

Diethyl (2-iodobenzyl)malonate and Dimethyl (2-iodobenzyl)malonate were prepared according to the literature [2]

References

(1) D. H. Zhang, E. K. Yum, Z. Liu and R. C. Larock, *Org. Lett*., 2005, **7**, 4963.

(2) H. P. Bi, L. N. Guo, X. H. Duan, F. R. Gou and Y. M. Liang, *Org. Lett.*, 2007, **9**, 397.

Typical procedure for the preparation of propargylic trimethylsilane

Diethyl2-(2-(2-(trimethylsilyl)entynyl)phenyl)malonate

To a solution of diethyl (2-iodophenyl)malonate (1.81 g, 5.0 mmol) and ethynyltrimethylsiane (0.58 g, 6 mmol) in Et_2NH (20.0 mL) was added $Pd(PPh_3)_4$ (57.5mg, 0.5 mol %). The mixture was stirred for 5 min and CuI (9.5mg, 1 mol %) was added. The resulting mixture was then stirring under an argon atmosphere at room temperature for 3 h. The ammonium salt was removed by filtration. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica get to afford 1.53 g (92 %) as oil;

Diethyl 2-(2-(2-(trimethylsilyl)entynyl)benzyl)malonate

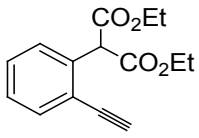
The was prepared by the same method. But employing Diethyl (2-iodobenzyl)malonate (1.88 g, 5.0 mmol) and (0.58 g, 6 mmol) for 3 h afforded 1.54 g (89 %) as oil;

Dimethyl 2-(2-(2-(trimethylsilyl)entynyl)benzyl)malonate

The was prepared by the same method. But employing Dimethyl (2-iodobenzyl)malonate (0.72 g, 2.0 mmol) and (0.17 g, 2.4 mmol) for 3 h afforded 0.54 g (90 %) as oil.

Typical procedure for the preparation of 1a-c.

To a solution of Diethyl 2-(2-(2-(trimethylsilyl)entynyl)phenyl)malonate (0.66 g, 2.0 mmol) in THF (10 mL) was added TBAF at -78°C (0.76g, 2.4 mmol). After stirring for 10 min the reaction mixture was diluted with CH_2Cl_2. The CH_2Cl_2 solution was washed with water, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by column chromatography on silica gel to afford the corresponding product **1a** 0.44g (85 %) as oil.



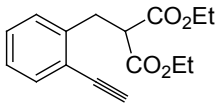
1a

^{1}HNMR (400 MHz, $CDCl_3$) δ 7.52-7.55 (m, 2H), 7.37-7.39 (m, 1H), 7.27-7.32 (m, 1H), 5.33 (s, 1H), 4.23-4.26 (m, 4H), 3.25 (s, 1H), 1.26-1.27 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

167.9, 135.2, 132.7, 129.1, 128.7, 127.9, 122.6, 82.2, 81.9, 61.9, 55.5, 13.9; IR (neat, cm^{-1}): 2956, 2252, 1631, 1309, 1248, 1146, 1045; Anal. Calcd for $C_{15}H_{16}O_4$: C 69.22; H 6.20 Found: C 69.08; H 6.33.

Diethyl 2-(2-entynylbenzyl)malonate

The **1b** was prepared by the above method, but employing diethyl 2-(2-(3-hydroxyprop-1-ynyl)benzyl)malonate (0.58 g, 2.0 mmol) and methyl chloroformate afforded **1b** 0.61 g (87 %) as oil.

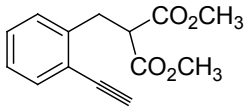


1b

^{1}HNMR (400 MHz, $CDCl_3$) δ 7.46-7.48 (d, J = 7.2 Hz, 1H), 7.18-7.20 (m, 2H), 4.12-4.18 (m, 4H), 3.87-3.91 (t, J = 7.6Hz, 1H), 3.37-3.39 (d, J = 7.6 Hz, 2H), 3.32 (s, 1H), 1.15-1.18 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 140.2, 132.9, 129.7, 128.8, 126.7, 121.8, 81.8, 81.5, 61.3, 52.1, 33.4, 13.9; IR (neat, cm^{-1}): 2923, 2167, 1676, 1331, 1234, 1167, 1045; Anal. Calcd for C_{22} $H_{31}O_4$: C 70.06; H 6.61. Found: C 70.08; H 6.63.

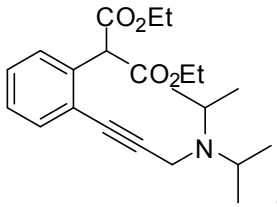
Dimethyl 2-(2-entynylbenzyl) malonate

The **1c** was prepared by the above method, but employing Dimethyl 2-(2-(2-(trimethylsilyl)entynyl)benzyl)malonate (0.58 g, 2.0 mmol) and methyl chloroformate afforded **1c** 0.61 g (87 %) as oil.



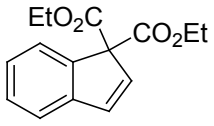
1c

^{1}HNMR (400 MHz, $CDCl_3$) δ 7.46-7.48 (m, 1H), 7.17-7.28 (m, 3H), 3.91-3.95 (t, J = 7.6Hz, 1H), 3.69 (s, 6H), 3.38-3.40 (d, J = 7.6 Hz, 2H), 3.33 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 140.6, 133.1, 129.7, 128.9, 126.8, 121.8, 81.9, 81.4, 52.4, 51.8, 33.5; IR (neat, cm^{-1}): 2956, 2223, 1667, 1354, 1268, 1123; Anal. Calcd for $C_{14}H_{14}O_4$: C 68.28; H 5.73. Found: C 68.25; H 5.78.



4a

^{1}HNMR (400 MHz, $CDCl_3$) δ 7.41-7.52 (m, 1H), 7.23-7.33 (m, 3H), 5.35 (s, 1H), 4.15-4.28 (m, 4H), 3.70 (s, 2H), 3.23-3.29 (m, 2H), 1.24-1.28 (t, J = 7.2 Hz, 6H), 1.14-1.16 (d, J = 6.8 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 134.4, 132.1, 128.0, 127.8, 124.2, 94.1, 81.2, 61.7, 55.4, 48.4, 34.7, 20.7, 14.0; IR (neat, cm^{-1}): 3437, 2982, 2232, 1671, 1301, 1228, 1154, 1032; Anal. Calcd for C_{22} $H_{31}NO_4$: C 70.75; H 8.37; N 3.75. Found: C 70.77; H 8.35; N 3.68. HRMS (ESI) Calcd for C_{22} $H_{31}NO_4$: M+H = 374.2345. Found: 374.2326.



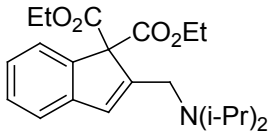
6a

^{1}HNMR (400 MHz, $CDCl_3$) δ 7.64-7.62 (d, *J* = 7.2 Hz, 1H), 7.17-7.26 (m, 3H), 6.82-6.84 (d, *J* =

5.6 Hz, 1H), 6.49-6.50 (d, *J* = 5.6 Hz, 1H), 4.10-4.18 (m, 4H), 1.16-1.22 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 143.6, 139.8, 134.7, 133.4, 128.6, 126.3, 125.4, 121.5, 70.4, 62.12, 13.9; IR (neat, cm^{-1}): 2986, 1671, 1301, 1228, 1154, 1032; Anal. Calcd for $C_{15}H_{16}O_4$: C 69.22; H 6.20. Found: C 69.25; H 6.31. HRMS (ESI) Calcd for $C_{15}H_{16}O_4$: M+H = 261.1144. Found: 261.1121.

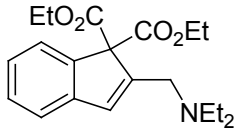
General procedure for the preparation of indenes or dihydronaphthalene (5)

A mixture of (**1**, 0.20 mmol), paraformaldehyde (**2**, 0.40 mmol), amine (**3**, 0.04 mol), CuI (1.9mg, 5.0 mol %), 0.2g 4 Å MS, THF (3.0 mL) was placed under argon atmosphere in a 10 mL flask. The resulting mixture was then heated at 60°C. When the reaction was considered the first step complete as determined by TLC analysis, added *t*-BuOLi (19.2 mg, 0.24mmol), when the reaction was considered the complete as determined by TLC analysis, the reaction mixture was allowed to cool to room temperature. The reaction mixture was concentrated under reduced pressure and the residue was purified by chromatography on silica gel to afford the corresponding 2-substituted indenes **5a**.



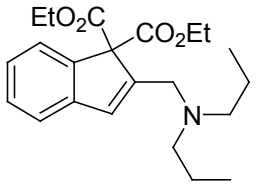
5aa

5aa: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 59mg (79 %) of the indicated compound as oil: 1HNMR (400 MHz, CDCl3) δ 7.49-7.51 (d, J = 7.2 Hz, 1H), 7.14-7.20 (m, 2H), 7.05-7.18 (m, 1H), 6.19 (s, 1H), 4.09-4.19 (m, 4H), 3.441-3.448 (d, J = 2 Hz, 2H), 3.00-3.03 (t, J = 6.8 Hz, 2H), 1.15-1.18 (t, J = 7.2 Hz, 6H), 0.91-0.96 (d, J = 6.8 Hz, 12H); 13C NMR (100 MHz, CDCl3) δ 169.2, 140.1, 131.8, 130.0, 128.4, 126.8, 122.3, 96.7, 81.8, 61.6, 58.6, 52.5, 33.9, 24.2, 13.9; IR (neat, cm-1): 3437, 2982, 1732, 1371, 1301, 1228, 1154, 1032; Anal. Calcd for $C_{22}H_{31}NO_4$: C 70.75; H 8.37; N 3.75. Found: C 70.78; H 8.33; N 3.69. HRMS (ESI) Calcd for $C_{22}H_{31}NO_4$: M+H = 374.2351. Found: 374.2326.



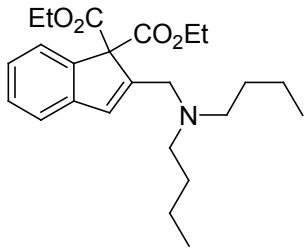
5ab

5ab: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 48.3 mg (70 %) of the indicated compound as oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.51 (d, *J* = 7.2 Hz, 1H), 7.10-7.21 (m, 3H), 6.82 (s, 1H), 4.09-4.15 (m, 4H), 3.414-3.418 (d, *J* = 1.6 Hz, 2H), 2.48-2.53 (q, *J* = 7.2 Hz, 4H), 1.27-1.21 (t, *J* = 7.2 Hz, 6H), 1.06-1.01 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 146.2, 144.1, 141.4, 131.6, 128.5, 125.3, 124.8, 120.5, 70.7, 61.8, 52.3, 47.2, 13.9, 11.9; IR (neat, cm^{-1}): 3424, 2972, 1731, 1464, 1234, 1050; Anal. Calcd for $C_{20}H_{27}NO_4$: C 69.54; H 7.88; N 4.05. Found: C 69.48; H 7.84; N 3.96. HRMS (ESI) Calcd for $C_{20}H_{27}NO_{44}$: M+Li = 352.1568. Found: 352.2095.



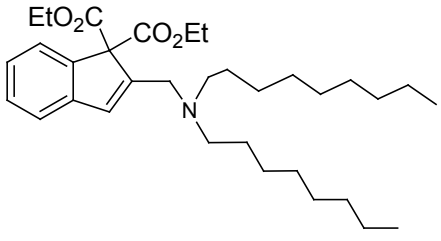
5ac

5ac: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 52.3 mg (52 %) of the indicated compound as oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56-7.58 (m, 1H), 7.14-7.29 (m, 3H), 6.90 (s, 1H), 4.15-4.23 (m, 4H), 3.45 (s, 2H), 2.41-2.45 (t, J = 7.6 Hz, 4H), 1.40-1.50 (m, 4H), 1.18-1.27 (m, 6H), 0.85-0.89 (t, J = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 144.2, 140.9, 139.6, 131.4, 128.5, 125.3, 124.8, 120.8, 70.7, 61.8, 56.5, 53.3, 13.9, 11.9; IR (neat, cm^{-1}): 3434, 2981, 1726, 1459, 1239, 1047; Anal. Calcd for $C_{22}H_{31}NO_4$: C 70.75; H 8.37; N 3.75.
Found: C 70.79; H 8.35; N 3.70. HRMS (ESI) Calcd for $C_{22}H_{31}NO_4$: M+H = 374.2350. Found: 374.2326.



5ad

5ad: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 54.5mg (68 %) of the indicated compound as oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.59 (d, J = 7.2 Hz, 1H), 7.19-7.31 (m, 3H), 6.93 (s, 1H), 4.19-4.23 (m, 4H), 3.47 (d, J = 1.6 Hz, 2H), 1.36-1.48 (m, 4H), 1.27-1.34 (m, 4H), 1.21-1.25 (m, 6H), 0.90-0.94 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 146.5, 144.2, 141.0, 131.2, 128.5, 125.32, 124.8, 120.8, 70.8, 61.8, 54.3, 53.3, 29.5, 20.6, 14.1, 13.9; IR (neat, cm^{-1}): 3434, 2972, 1731, 1464, 1234, 1050; Anal. Calcd for $C_{24}H_{35}NO_4$: C 71.79; H 8.79; N 3.49. Found: C 71.81; H 8.77; N 3.45. HRMS (ESI) Calcd for $C_{24}H_{35}NO_4$: M+H = 402.1717. Found: 402.2639.

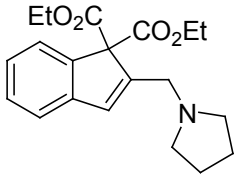


5ae

5ae: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 86.4 mg (82 %) of the indicated compound as oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58-7.60 (d, J = 7.2 Hz, 1H), 7.23-7.30 (m, 2H), 7.14-7.18 (m, 1H), 6.91 (s, 1H), 4.12-4.22 (m, 4H), 3.45-3.46 (d, J = 1.6 Hz, 2H), 2.45-2.48 (t, J = 7.6 Hz , 4H), 1.46 (s, 4H), 1.19-1.28 (m, 26H), 0.85-0.89 (t, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 146.5, 144.2, 141.0, 131.2, 128.5, 125.32, 124.8, 120.7, 70.8, 61.8, 54.5, 53.3, 31.8, 29.6, 29.3, 27.5, 27.3, 22.6, 14.0, 13.9; IR (neat, cm^{-1}): 3451,

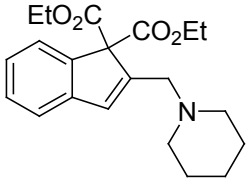
2980,

1736, 1468, 1254, 1038; Anal. Calcd for $C_{33}H_{55}NO_4$: C 75.10; H 10.12; N 2.65. Found: C 75.12; H 10.06; N 2.63. HRMS (ESI) Calcd for $C_{33}H_{55}NO_4$: M+H = 528.4073. Found: 528.4047.



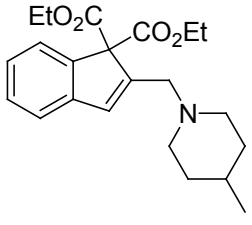
5af

5af: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 54.8 mg (80 %) of the indicated compound as oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.61 (d, J = 8.0 Hz, 1H), 7.24-7.32 (m, 2H), 7.17-7.21 (m, 1H), 6.88 (s, 1H), 4.15-4.23 (m, 4H), 3.59 (s, 2H), 2.60-2.63 (t, J = 6.4 Hz, 4H), 1.78-1.81 (m, 4H), 1.22-1.30 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 145.2, 144.0, 140.9, 131.7, 128.5, 125.5, 124.9, 120.9, 71.0, 61.8, 54.5, 54.4, 23.7, 13.9; IR (neat, cm^{-1}): 3402, 2964, 1731, 1463, 1234, 1050; Anal. Calcd for $C_{20}H_{25}NO_4$: C 69.95; H 7.34; N 4.08. Found: C 69.86; H 7.38; N 3.99. HRMS (ESI) Calcd for $C_{20}H_{25}NO_4$: M+H = 344.1837. Found: 344.1856.



5ag

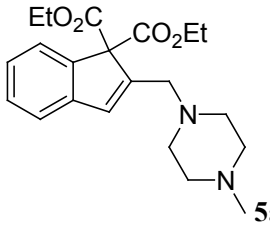
5ag: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 53.6 mg (81%) of the indicated compound as oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.60 (d, J = 7.6 Hz, 1H), 7.25-7.31 (m, 2H), 7.16-7.20 (m, 1H), 6.85 (s, 1H), 4.16-4.23 (m, 4H), 3.39 (s, 2H), 2.46 (s, 4H), 1.56-1.60 (m, 4H), 1.44-1.45 (d, J = 4.4 Hz, 1H), 1.22-1.26 (t, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 144.5, 143.9, 141.1, 132.1, 128.5, 125.5, 124.8, 120.8, 70.8, 61.9, 57.6, 55.0, 26.1, 24.4, 13.9; IR (neat, cm^{-1}): 3431, 2934, 1731, 1465, 1236, 1049; Anal. Calcd for $C_{21}H_{27}NO_4$: C 70.56; H 7.61; N 3.92. Found: C 70.36; H 7.67; N 3.78. HRMS (ESI) Calcd for $C_{21}H_{27}NO_4$: M+H = 358.2033. Found: 358.2013.



5ah

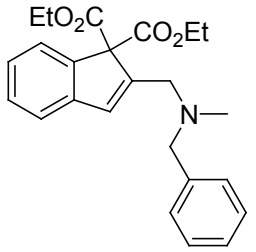
5ah: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 52.7 mg (71 %) of the indicated compound as oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.60 (d, J = 7.6 Hz, 1H), 7.23-7.30 (m, 2H), 7.16-7.20 (m, 1H), 6.85 (s, 1H), 4.15-4.23 (m, 4H), 3.996-3.999 (d, J = 1.2 Hz, 2H), 2.95-2.96 (d, J = 11.6 Hz, 2H), 1.94-2.00 (m, 2H), 1.59-1.62 (d, J = 12.8 Hz, 2H), 1.27-1.38 (m, 1H), 1.18-1.28 (m, 7H), 0.90-0.93 (t, J = 5.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 144.6, 143.9, 141.1, 132.1, 128.5, 125.4, 124.8, 120.8, 70.8, 61.8, 57.3, 54.3, 34.6, 30.8,

21.9, 13.9; IR (neat, cm^{-1}): 3432, 2936, 1732, 1464, 1237, 1047; Anal. Calcd for $C_{22}H_{29}NO_4$: C 71.13; H 7.83;
N 3.77. Found: C 71.16; H 7.87; N 3.79. HRMS (ESI) Calcd for $C_{22}H_{29}NO_4$: M+H = 372.2154. Found: 372.2169.



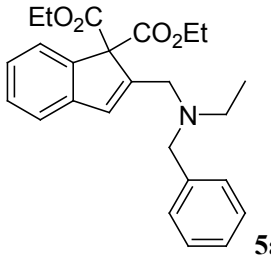
5ai

5ai: The reaction mixture was chromatographed using 1:1 CH_3OH/EtOAc to afford 53.6 mg (82 %) of the indicated compound as oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.53 (d, J = 7.6 Hz, 1H), 7.12-7.22 (m, 3H), 6.78 (s, 1H), 4.11-4.13 (m, 4H), 3.385-3.389 (d, J = 1.6 Hz, 2H), 2.52 (s, 8H), 1.19-1.15 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 143.7, 143.6, 141.0, 132.4, 128.5, 125.6, 124.8, 120.9, 70.8, 61.9, 56.6, 55.2, 53.0, 45.9, 13.9; IR (neat, cm^{-1}): 3435, 2939, 1738, 1465, 1238, 1056; Anal. Calcd for $C_{21}H_{28}N_2O_4$: C 69.72; H 7.58; N 7.52. Found: C 69.75; H 7.62; N 7.49. HRMS (ESI) Calcd for $C_{21}H_{28}N_2O_4$: M+H = 373.2123. Found: 373.2122.



5aj

5aj: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 48.7 mg (62 %) of the indicated compound as oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.53 (d, J = 7.6 Hz, 1H), 7.19-7.38 (m, 8H), 7.00 (s, 1H), 4.10-4.20 (m, 4H), 3.60-3.62 (d, J = 10.4 Hz, 2H), 3.48-3.52 (m, 2H), 2.24 (s, 3H), 1.18-1.21 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 145.1, 143.9, 141.0, 139.5, 132.0, 128.7, 128.6, 125.5, 124.8, 120.9, 70.8, 62.3, 61.9, 56.3, 42.5, 13.9; IR (neat, cm^{-1}): 3435, 2939, 1738, 1465, 1238, 1042; Anal. Calcd for $C_{24}H_{27}NO_4$: C 72.36; H 6.92; N 3.56. Found: C 72.38; H 7.01; N 3.58. HRMS (ESI) Calcd for $C_{24}H_{27}NO_4$: M+H = 394.2041. Found: 394.2013.

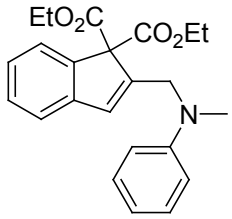


5ak

5ak: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 52.1 mg (64 %) of the indicated compound as oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.53 (d, J = 7.6 Hz,

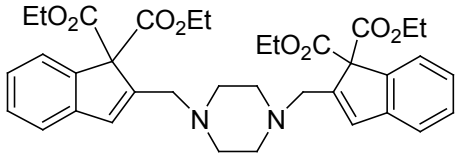
1H), 7.19-7.38 (m, 8H), 7.00 (s, 1H), 4.08-4.18 (m, 4H), 3.67-3.62 (s, 2H), 3.51-3.50 (d, J = 1.6 Hz,

2H), 2.55-2.60 (q, J = 7.2 Hz, 4H), 1.16-1.20 (t, J = 7.2 Hz, 6H), 1.06-1.10 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 145.1, 143.9, 141.0, 139.5, 132.0, 128.7, 128.6, 125.5, 124.8, 120.9, 70.8, 62.3, 61.9, 56.3, 42.5, 13.9; IR (neat, cm^{-1}): 3435, 2939, 1738, 1465, 1238, 1047; Anal. Calcd for $C_{25}H_{29}NO_4$: C 73.68; H 7.17; N 3.44. Found: C 73.36; H 7.18; N 3.45. HRMS (ESI) Calcd for $C_{25}H_{29}NO_4$: M+H = 408.2187. Found: 408.2169



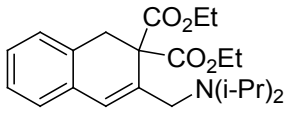
5al

5al: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 34.1 mg (45 %) of the indicated compound as oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62-7.64 (d, J = 7.6 Hz, 1H), 7.15-7.28 (m, 8H), 7.76-7.78 (m, 2H), 6.58 (s, 1H), 3.44-3.45 (d, J = 1.6 Hz, 2H), 4.13-4.11 (m, 4H), 3.07 (s, 3H), 1.27-1.30 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 143.4, 143.1, 140.9, 131.3, 129.1, 128.7, 125.6, 125.0, 121.0, 116.2, 111.7, 70.4, 62.34, 52.2, 38.5, 13.9; IR (neat, cm^{-1}): 3453, 2949, 1756, 1467, 1055; Anal. Calcd for $C_{23}H_{25}NO_4$: C 72.80; H 6.64; N 3.69. Found: C 72.86; H 6.67; N 3.68. HRMS (ESI) Calcd for $C_{23}H_{25}NO_{44}$: M+Na = 402.2660. Found: 402.1676



5am

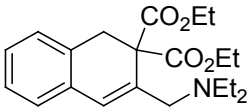
5am: The reaction mixture was chromatographed using EtOAc to afford 53.6 mg (56 %) of the indicated compound as a solid: mp 146-148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.61 (d, J = 7.6 Hz, 2H), 7.17-7.31 (m, 6H), 6.85 (s, 2H), 4.16-4.23(m, 8H), 3.45 (s, 4H), 2.56 (s, 8H), 1.19-1.15 (t, J = 7.2 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) 168.0, 144.0, 143.8, 141.0, 132.4, 128.5, 125.6, 124.9, 120.9, 70.8, 61.9, 56.8, 13.9; IR (neat, cm^{-1}): 3435, 2939, 1738, 1465, 1238, 1047; Anal. Calcd for $C_{36}H_{42}N_2O_8$: C 68.55; H 6.71; N 4.44. Found: C 68.48; H 6.67; N 4.47. HRMS (ESI) Calcd for $C_{36}H_{42}N_2O_8$: M+H = 631.3061. Found: 631.3014.



5ba

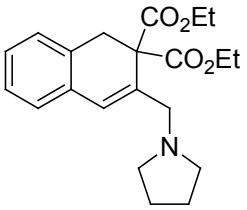
5ba: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 53.4 mg (69 %) of the indicated compound as oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.53 (d, J = 7.6 Hz, 1H), 7.12-7.22 (m, 3H), 6.78 (s, 1H), 4.13-4.11 (m, 4H), 3.385-3.389 (d, J = 1.6 Hz, 2H), 2.52 (s, 8H), 1.19-1.15 (t, J = 7.2 Hz, 6H), 1.02-1.03 (d, J = 6.8 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) 170.8, 137.9, 133.1, 132.1, 127.1, 126.9, 126.8, 126.0, 125.0, 61.5, 58.7, 48.0, 47.5, 20.7, 14.0; IR (neat, cm^{-1}): 3432, 2923, 1743, 1463, 1248, 1056; Anal. Calcd for $C_{23}H_{33}NO_4$: C 71.29; H 8.58;

N 3.61. Found: C 71.36; H 8.57; N 3.68. HRMS (ESI) Calcd for $C_{23}H_{33}NO_4$: M+H = 388.2514. Found: 388.2482.



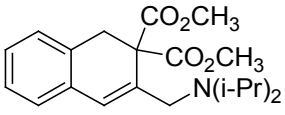
5bb

5bb: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 36.6 mg (51 %) of the indicated compound as oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07-7.26 (m, 4H), 6.71 (s, 1H), 4.06-4.22 (m, 4H), 3.45 (s, 2H), 3.30-3.33 (d, *J* = 1.6Hz, 2H), 2.53-2.60 (m, 4H), 1.19-1.23 (t, *J* = 7.2 Hz, 6H), 0.99 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 139.6, 132.4, 130.6, 128.5, 128.2, 127.2, 126.8, 126.1, 61.4, 57.9, 46.03, 36.2, 14.0, 13.9, 10.9; IR (neat, cm^{-1}): 3436, 2949, 1768, 1467, 1238, 1087; Anal. Calcd for $C_{21}H_{29}NO_4$: C 70.17; H 8.13; N 3.90. Found: C 70.16; H 8.17; N 3.98. HRMS (ESI) Calcd for $C_{21}H_{29}NO_4$: M+H = 360.2197. Found: 360.2169.



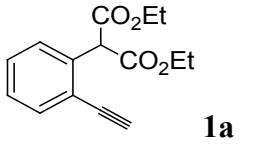
5be

5be: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 41.4 mg (56 %) of the indicated compound as oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07-7.16 (m, 4H), 6.04 (s, 1H), 4.06-4.20 (m, 4H), 3.46 (s, 2H), 3.39 (s, 2H), 2.49 (s, 4H), 1.75 (s, 4H), 1.20-1.24 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 132.7, 132.5, 127.3, 127.2, 126.9, 126.8, 61.51, 59.6, 57.7, 53.8, 36.1, 23.9, 23.7, 13.9; IR (neat, cm^{-1}): 3454, 2980, 1743, 1455, 1239, 1043; Anal. Calcd for $C_{21}H_{27}NO_4$: C 70.56; H 7.61; N 3.92. Found: C 70.36; H 7.67; N 3.78. HRMS (ESI) Calcd for $C_{21}H_{27}NO_4$: M+H = 358.2037. Found: 358.2013.



5ca

5ca: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 53.4 mg (69 %) of the indicated compound as oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06-7.16 (m, 4H), 6.97 (s, 1H), 3.74 (s, 6H), 3.45 (s, 2H), 3.27-3.28 (d, *J* = 1.6 Hz, 2H), 3.05-3.12 (m, 2H), 1.01-1.03 (d, *J* = 6.8 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) 171.4, 137.6, 132.9, 131.9, 127.1, 127.0, 126.1, 125.5, 58.6, 48.5, 47.6, 36.5, 20.7; IR (neat, cm^{-1}): 3435, 2939, 1738, 1465, 1238, 1047; Anal. Calcd for $C_{21}H_{29}NO_4$: C 70.17; H 8.13; N 3.90. Found: C 70.26; H 8.17; N 3.98. HRMS (ESI) Calcd for $C_{21}H_{29}NO_4$: M+H = 360.2190. Found: 360.2169.



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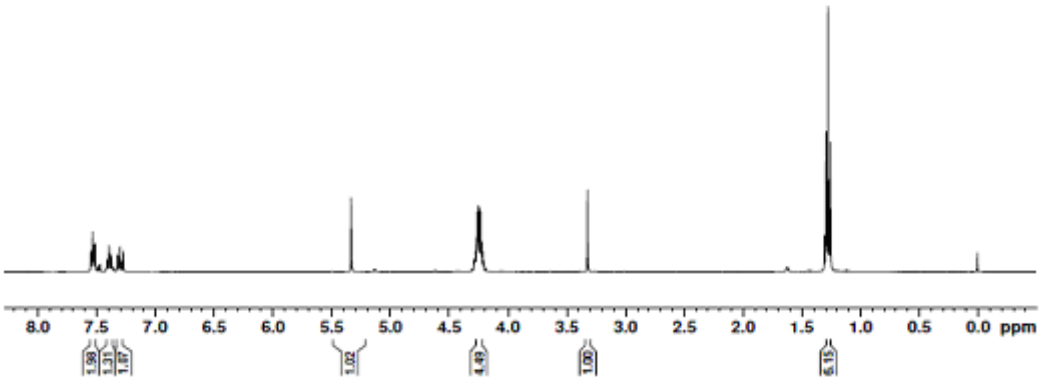

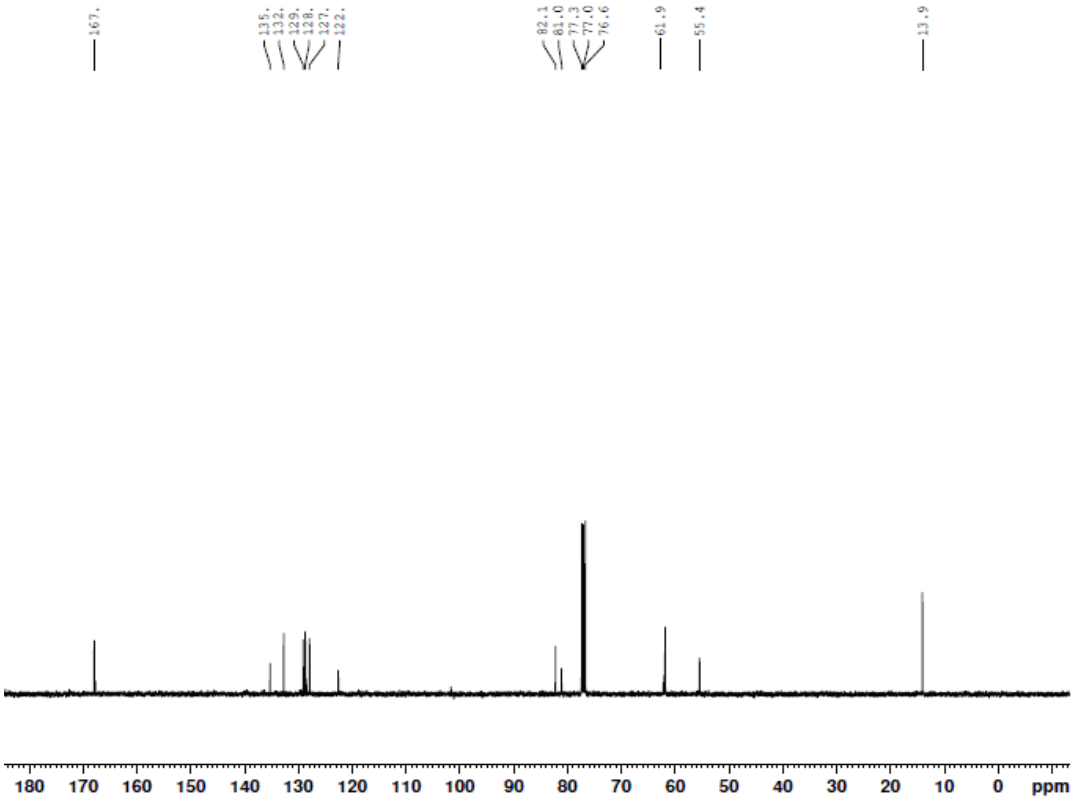

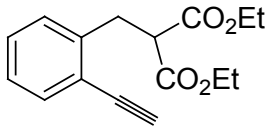

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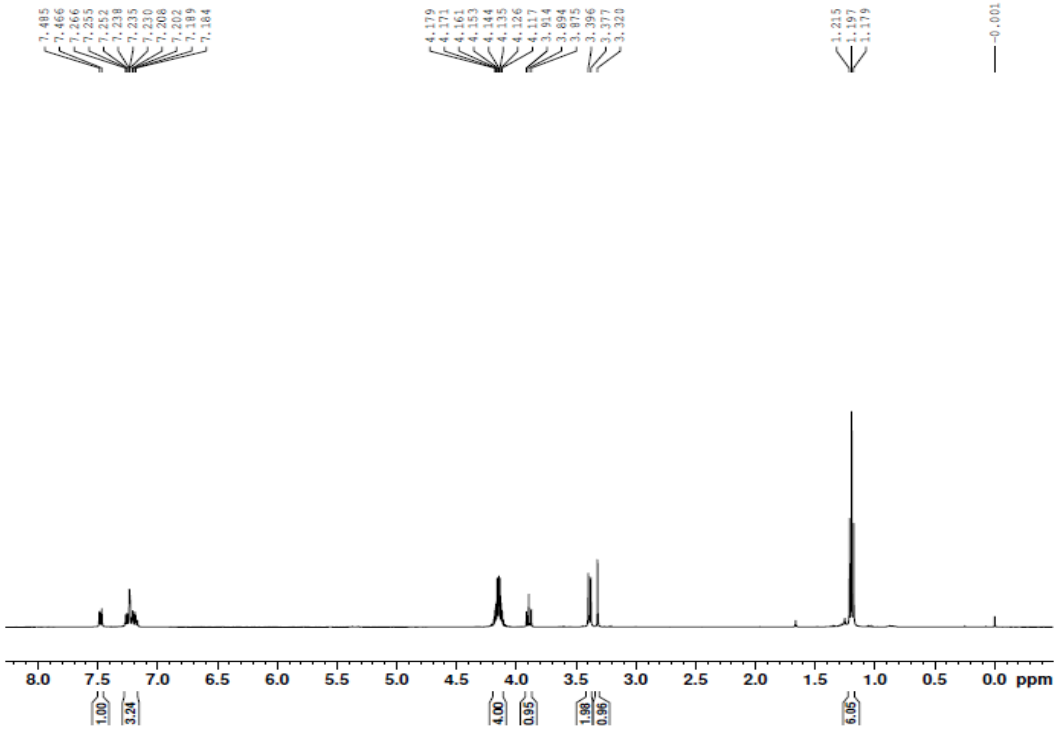

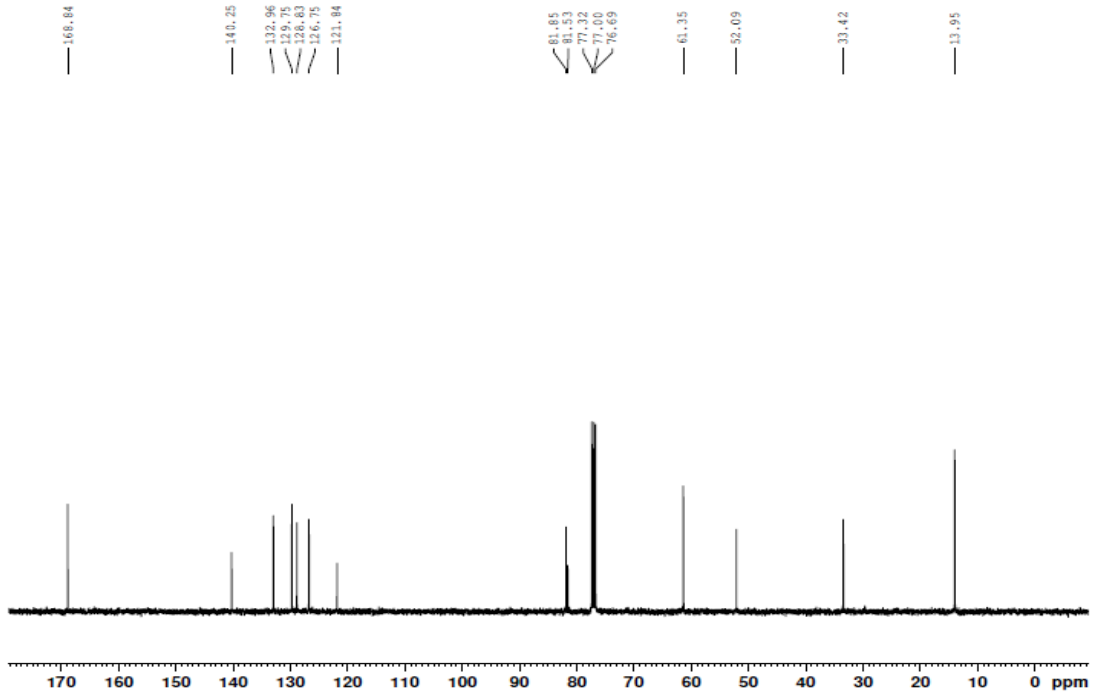

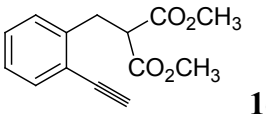

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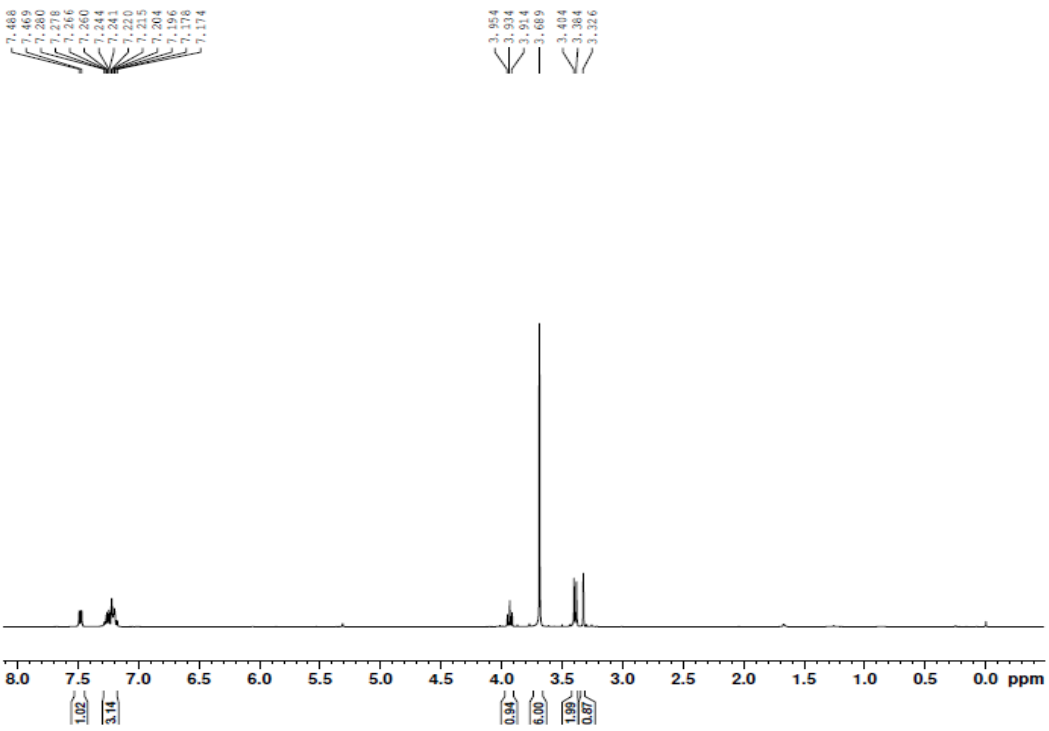

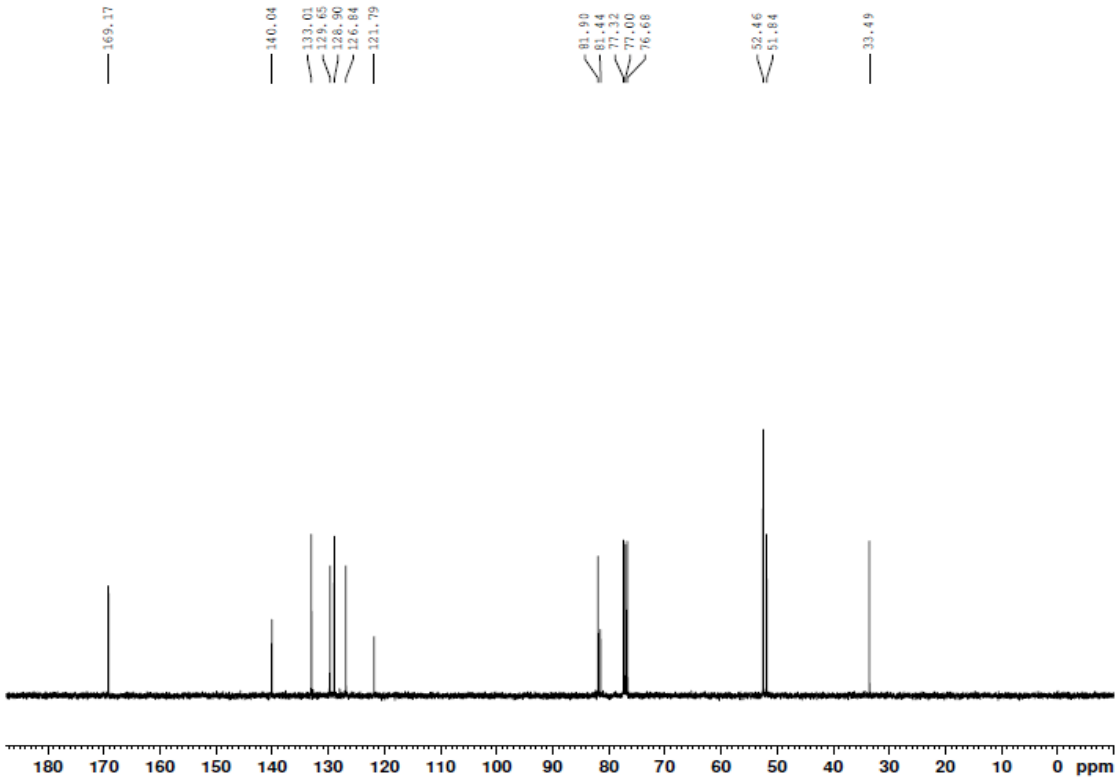

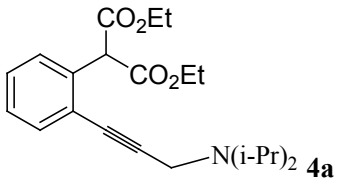

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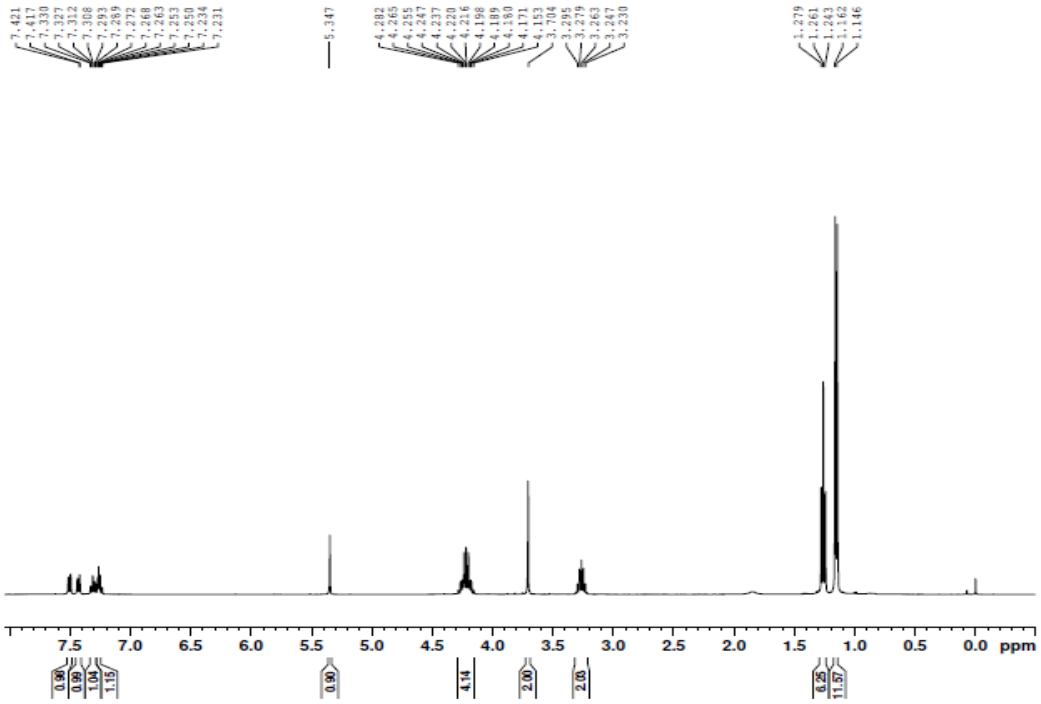

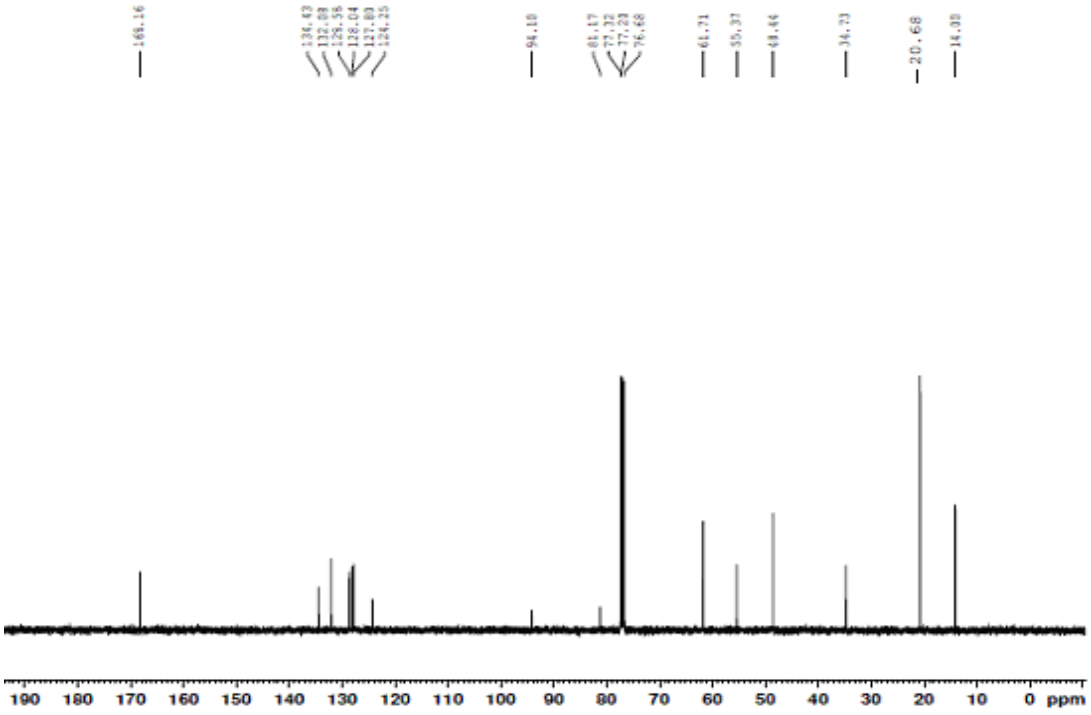

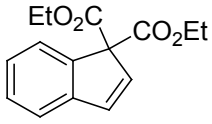

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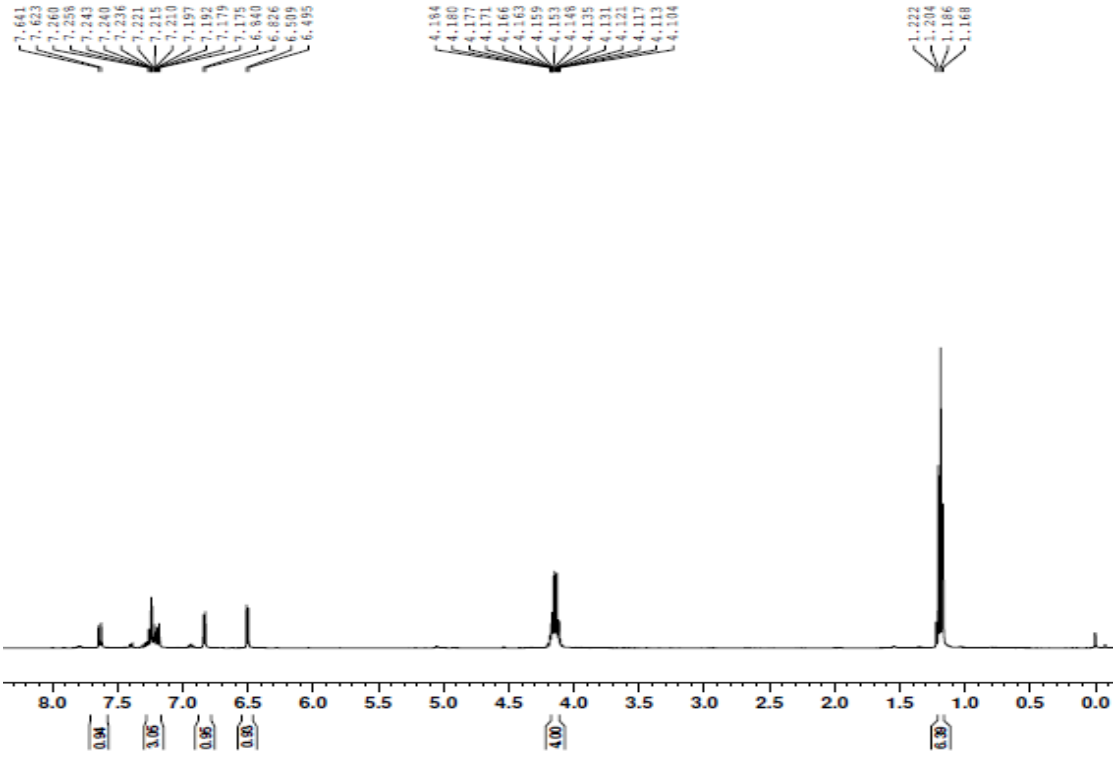

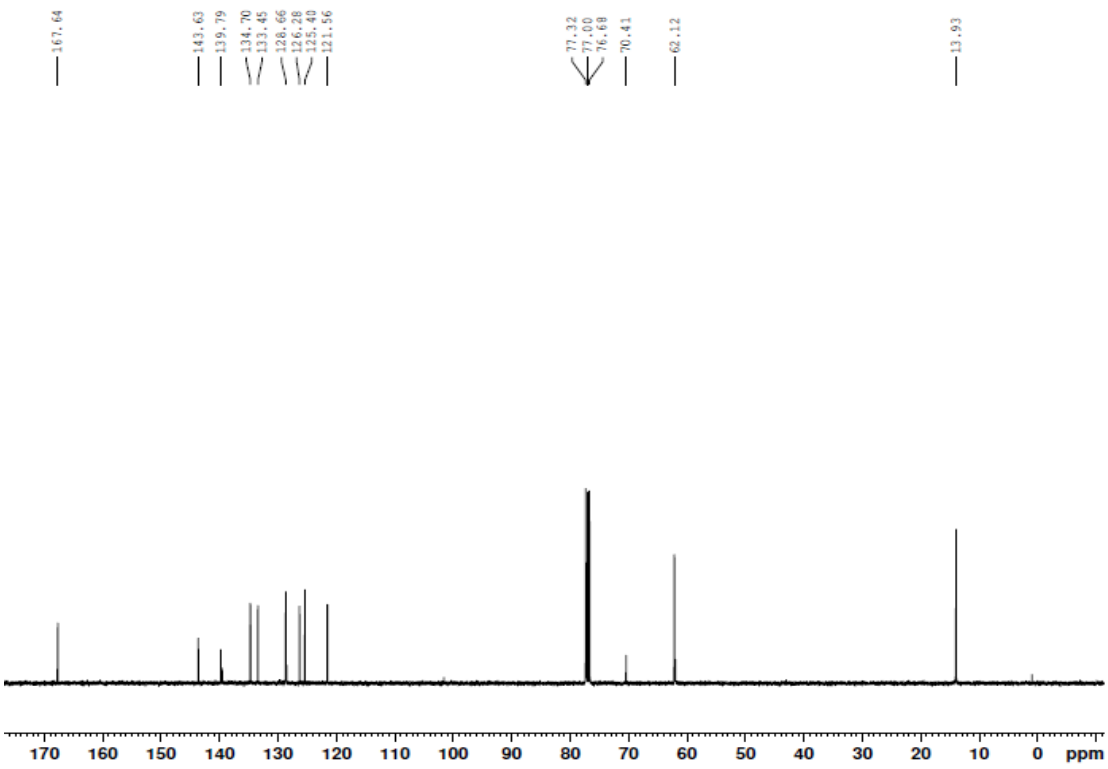

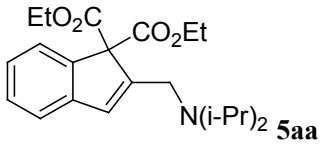

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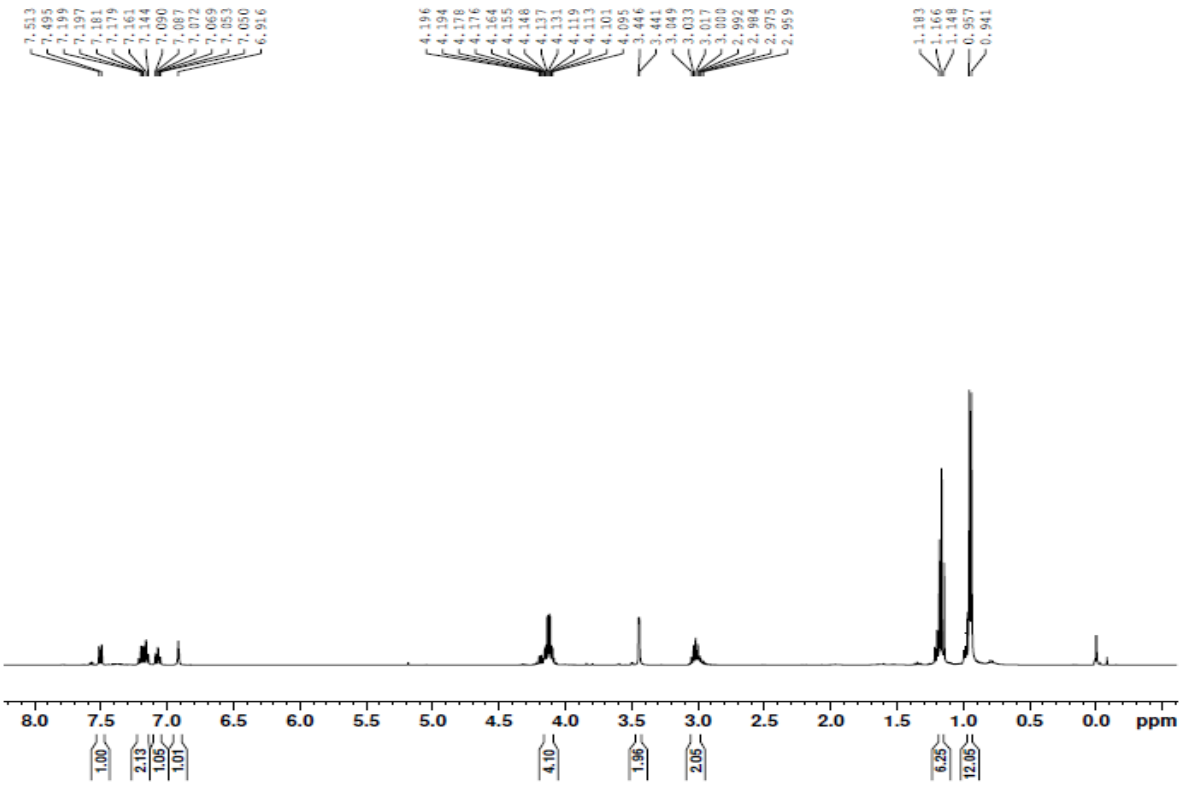

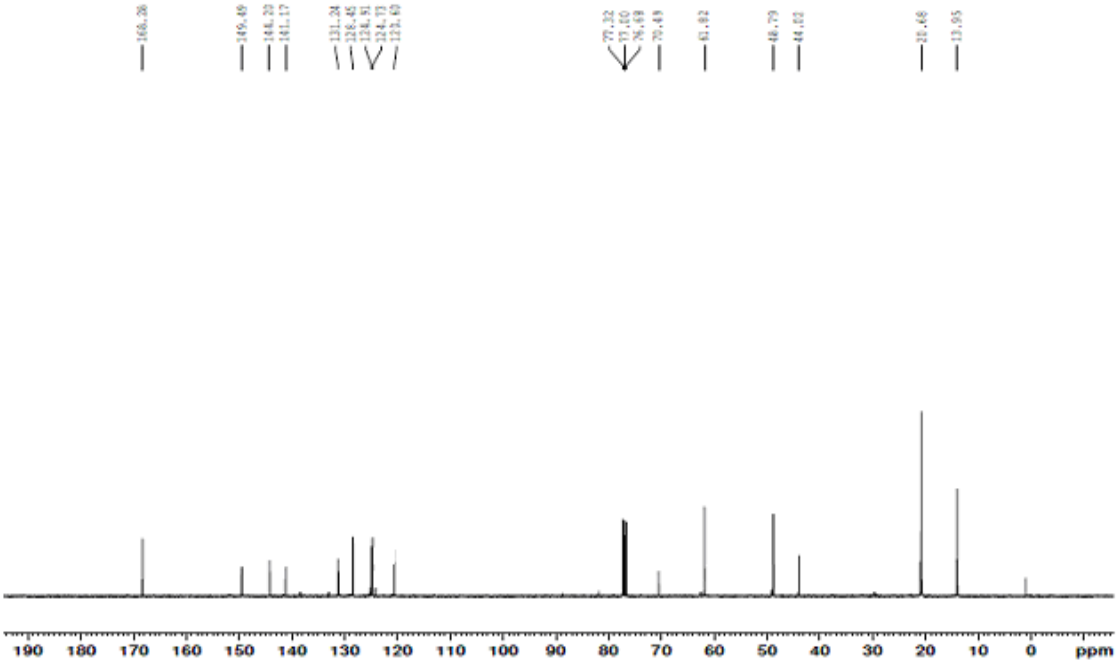

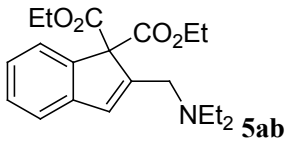

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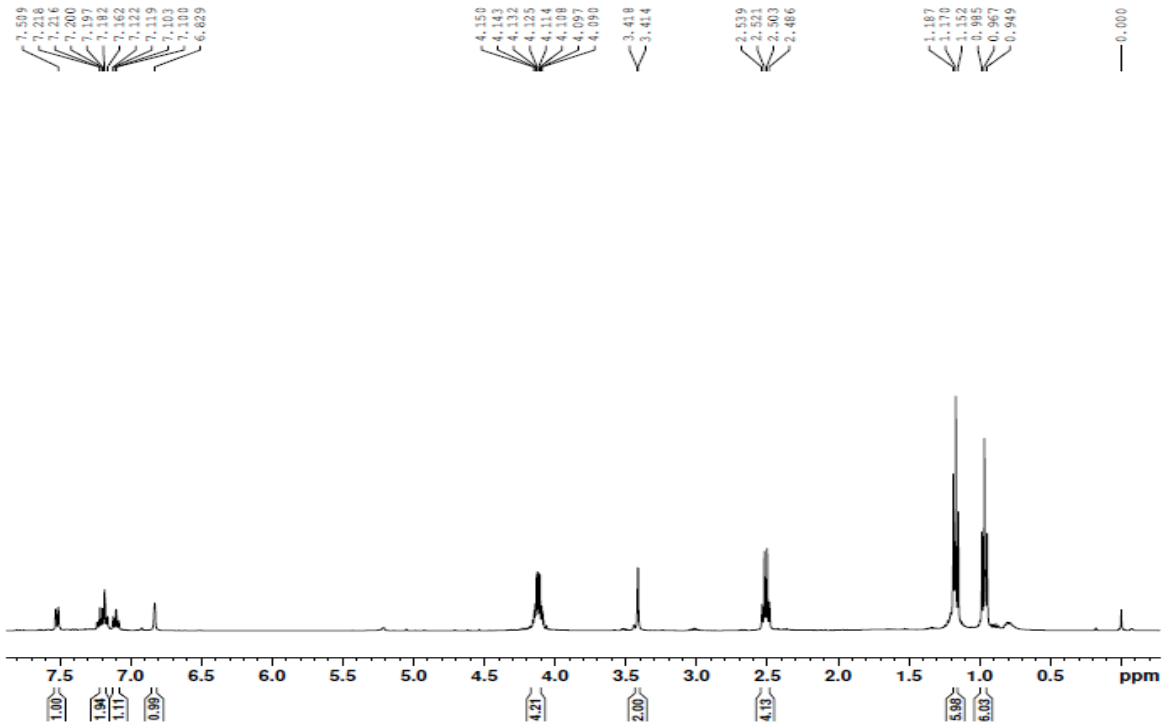

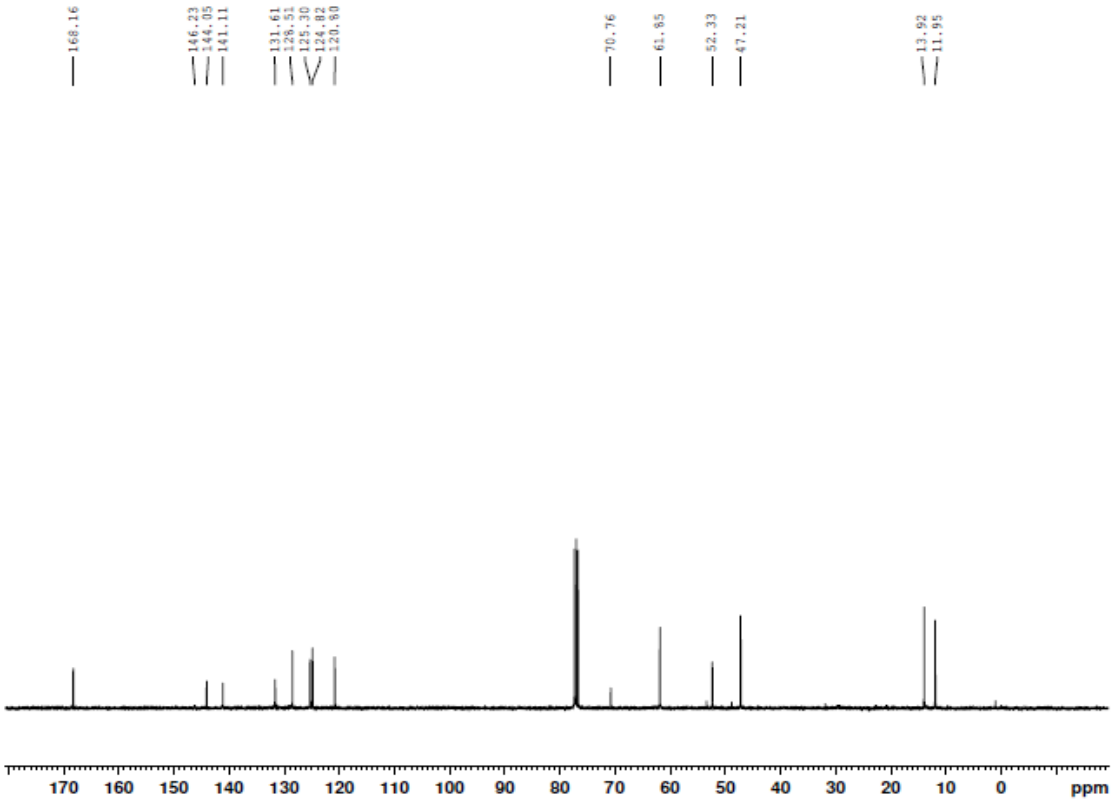

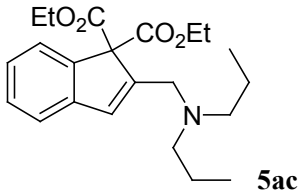

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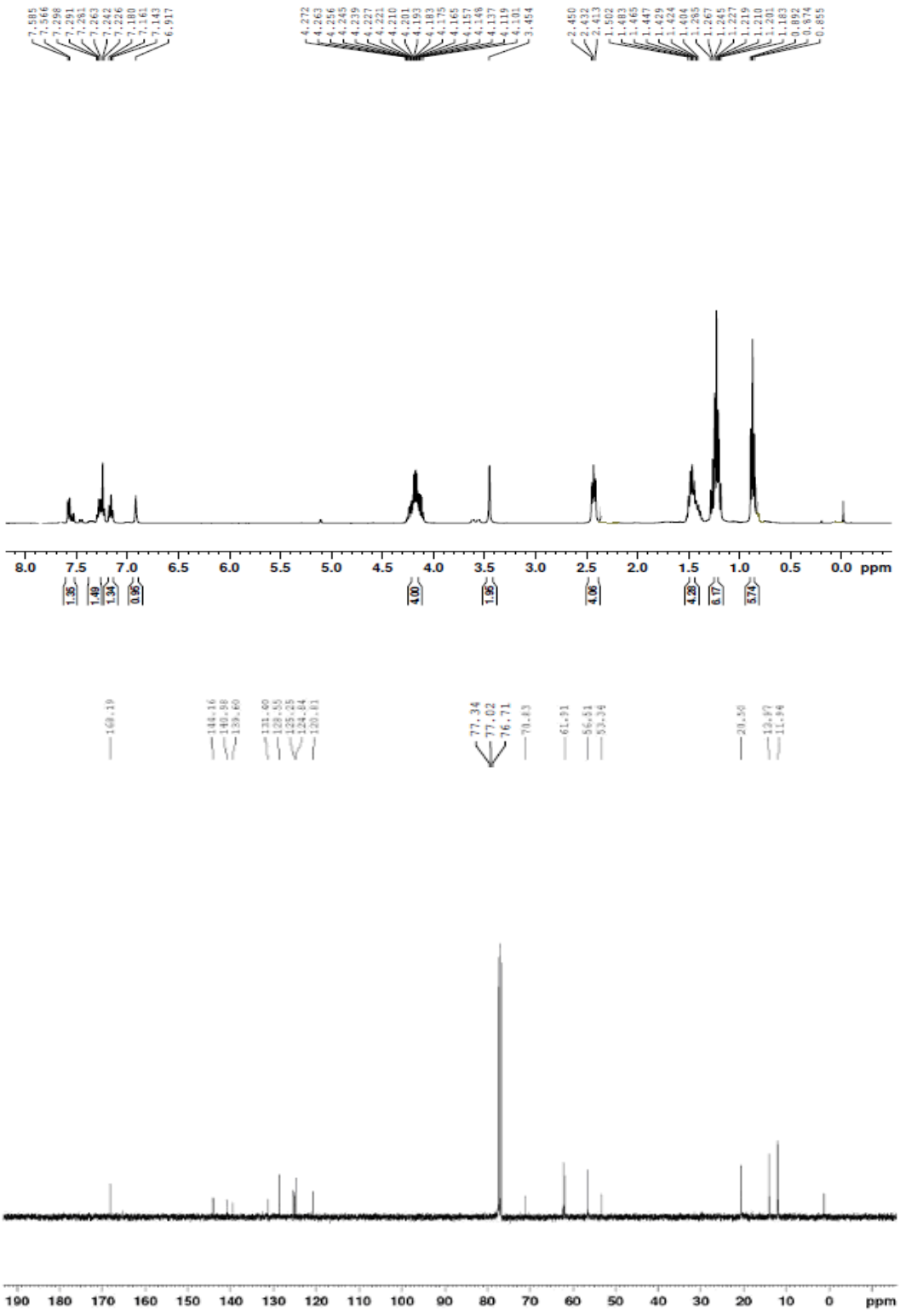

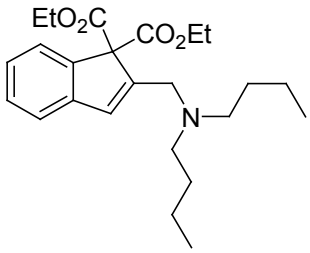

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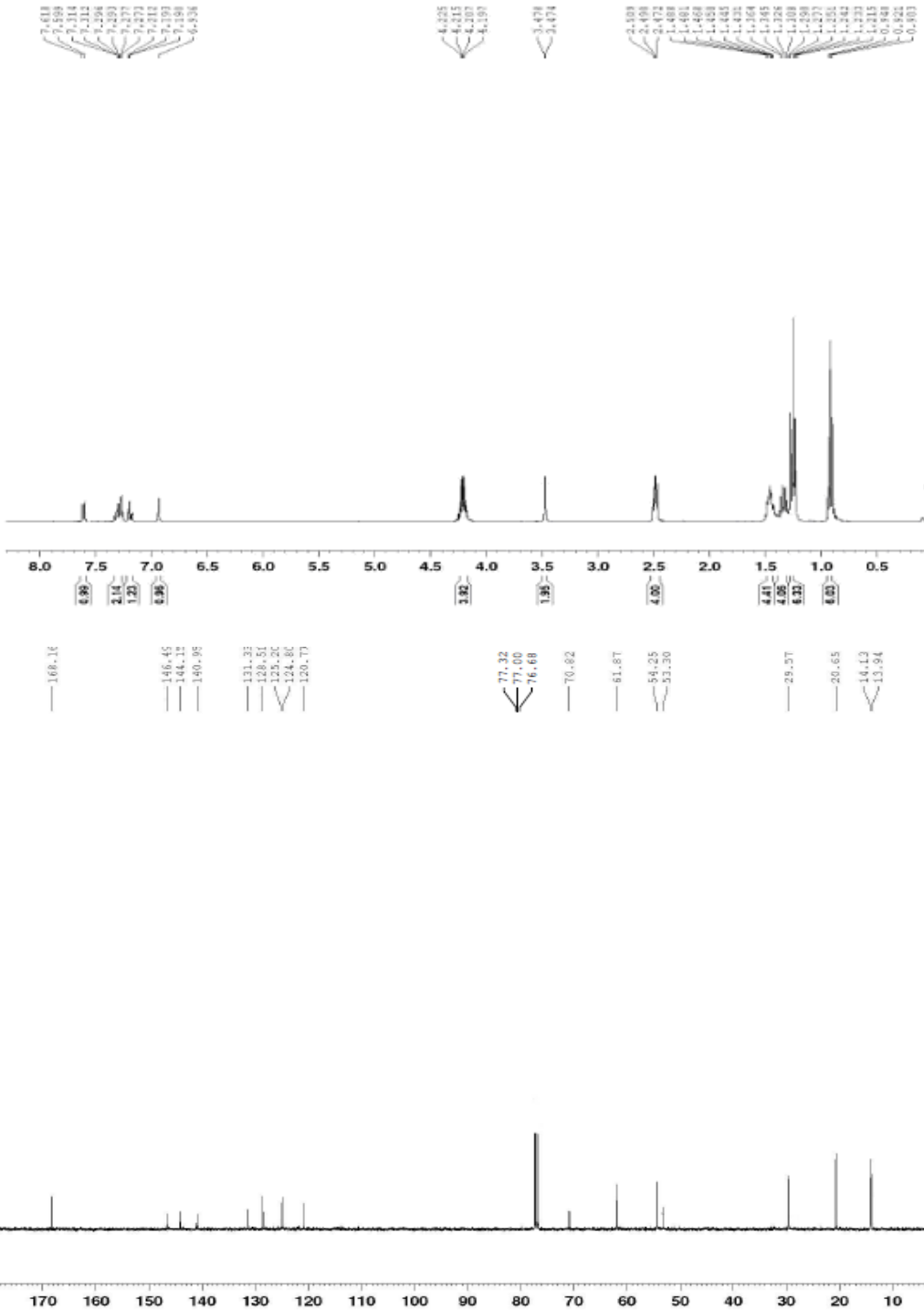

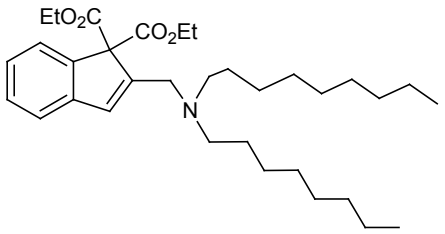

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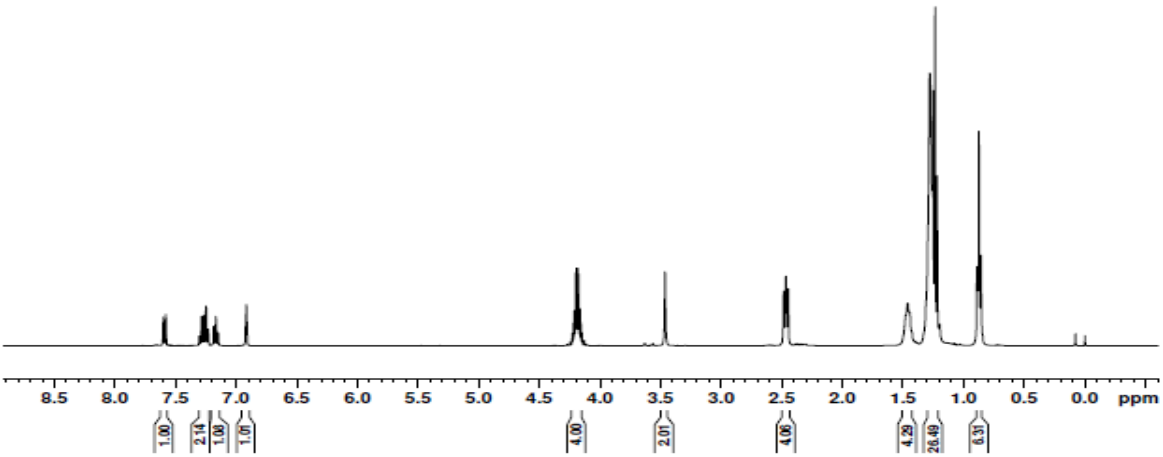

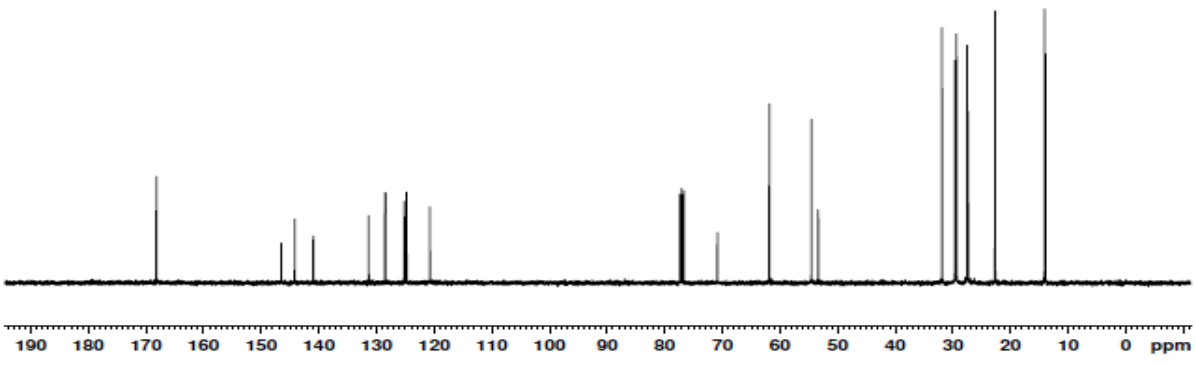

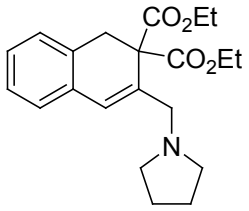

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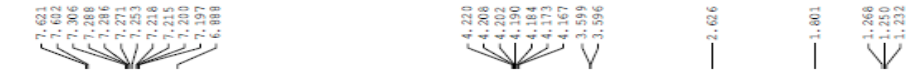

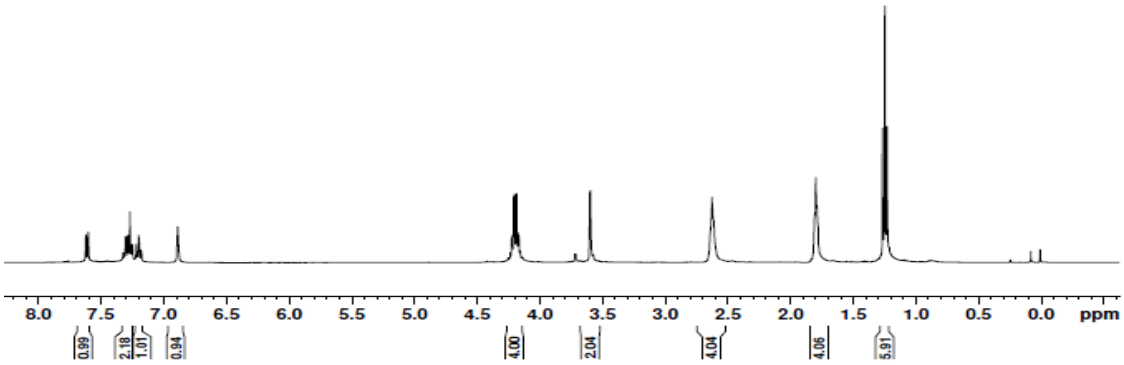

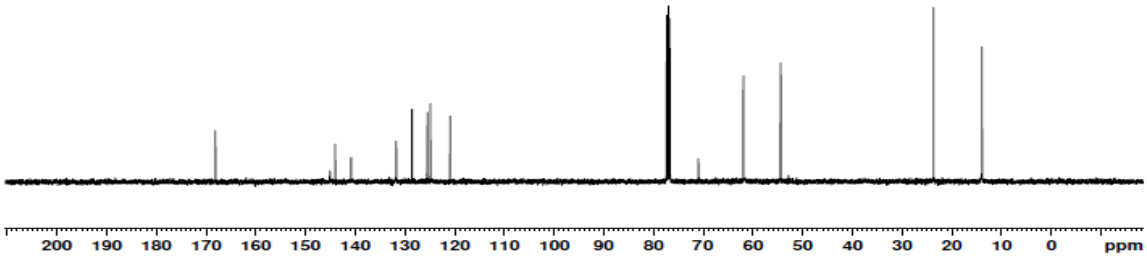

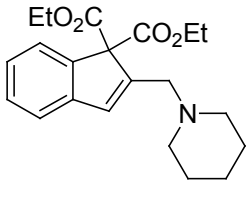

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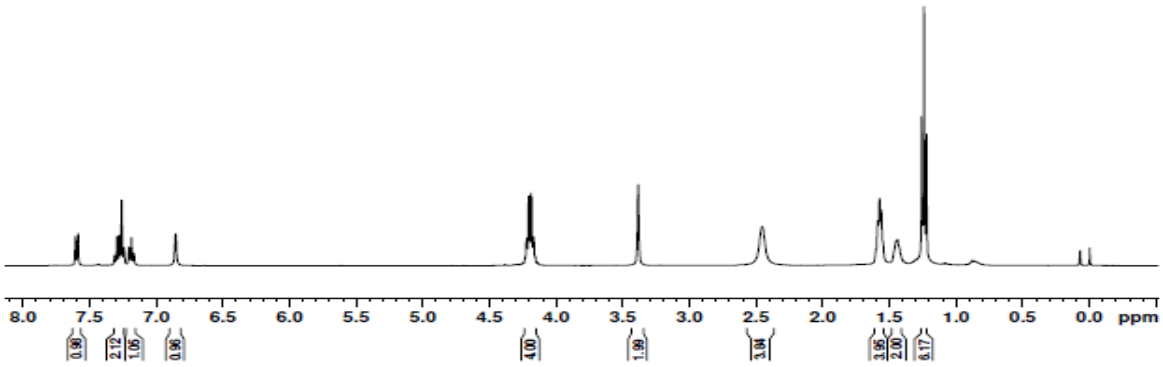

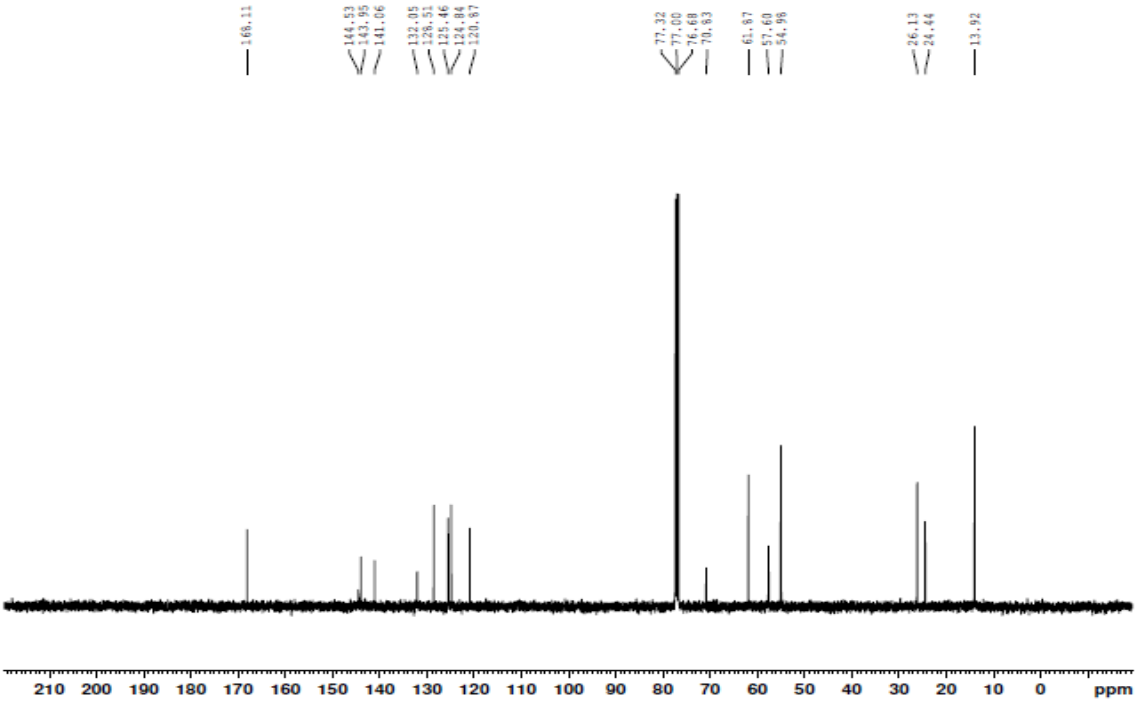

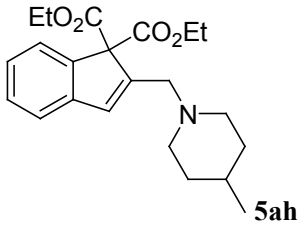

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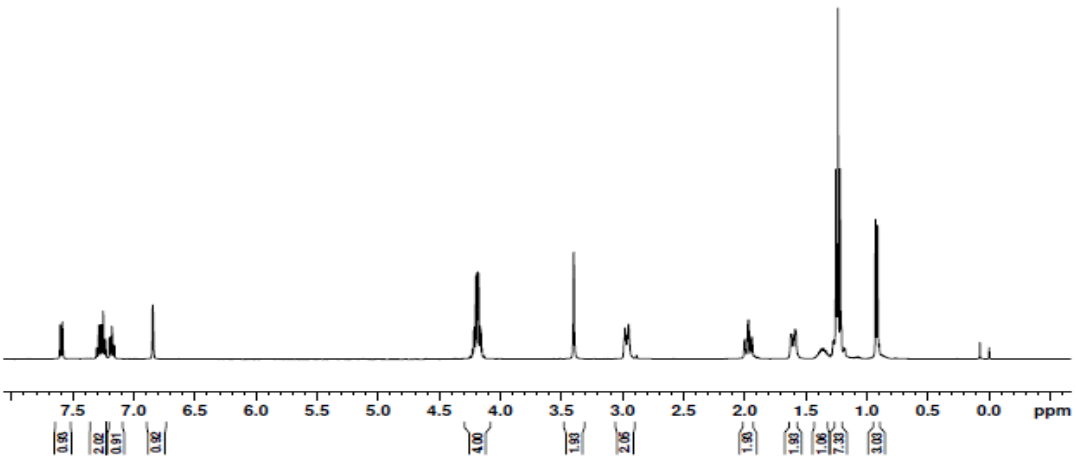

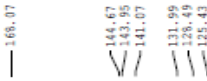

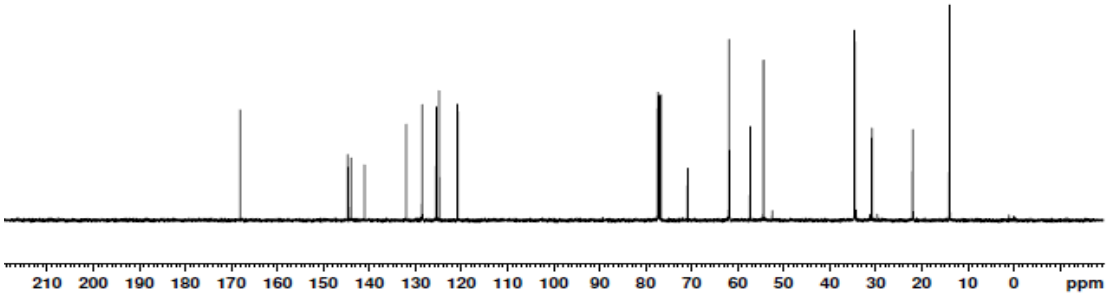

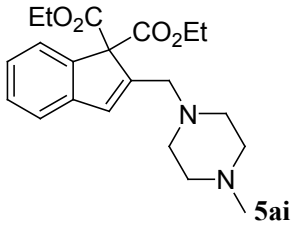

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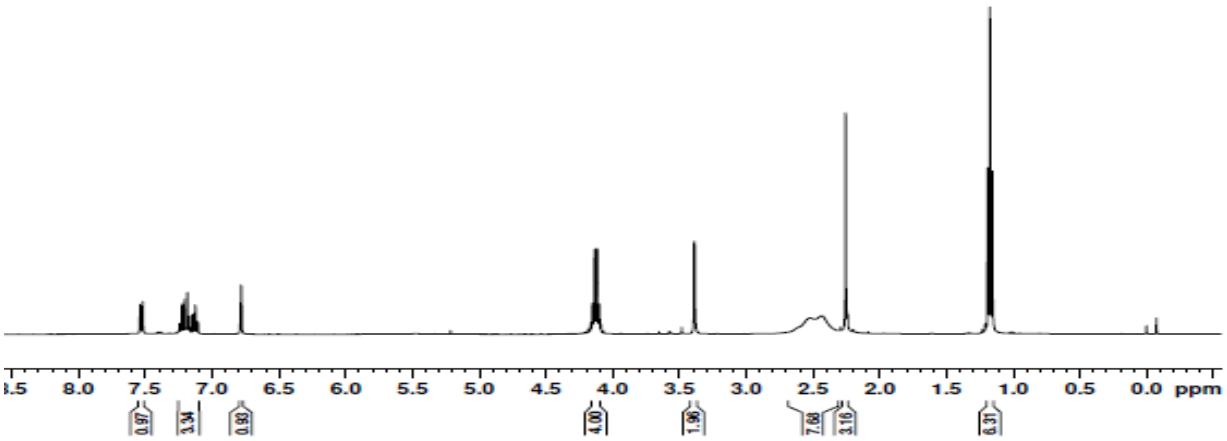

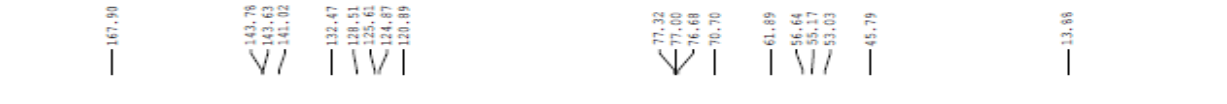

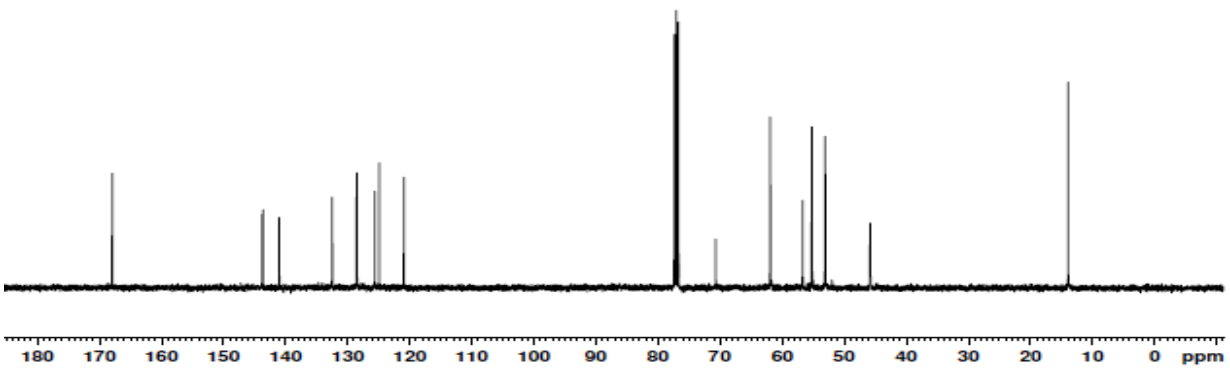

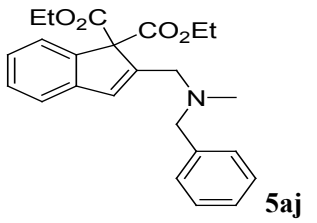

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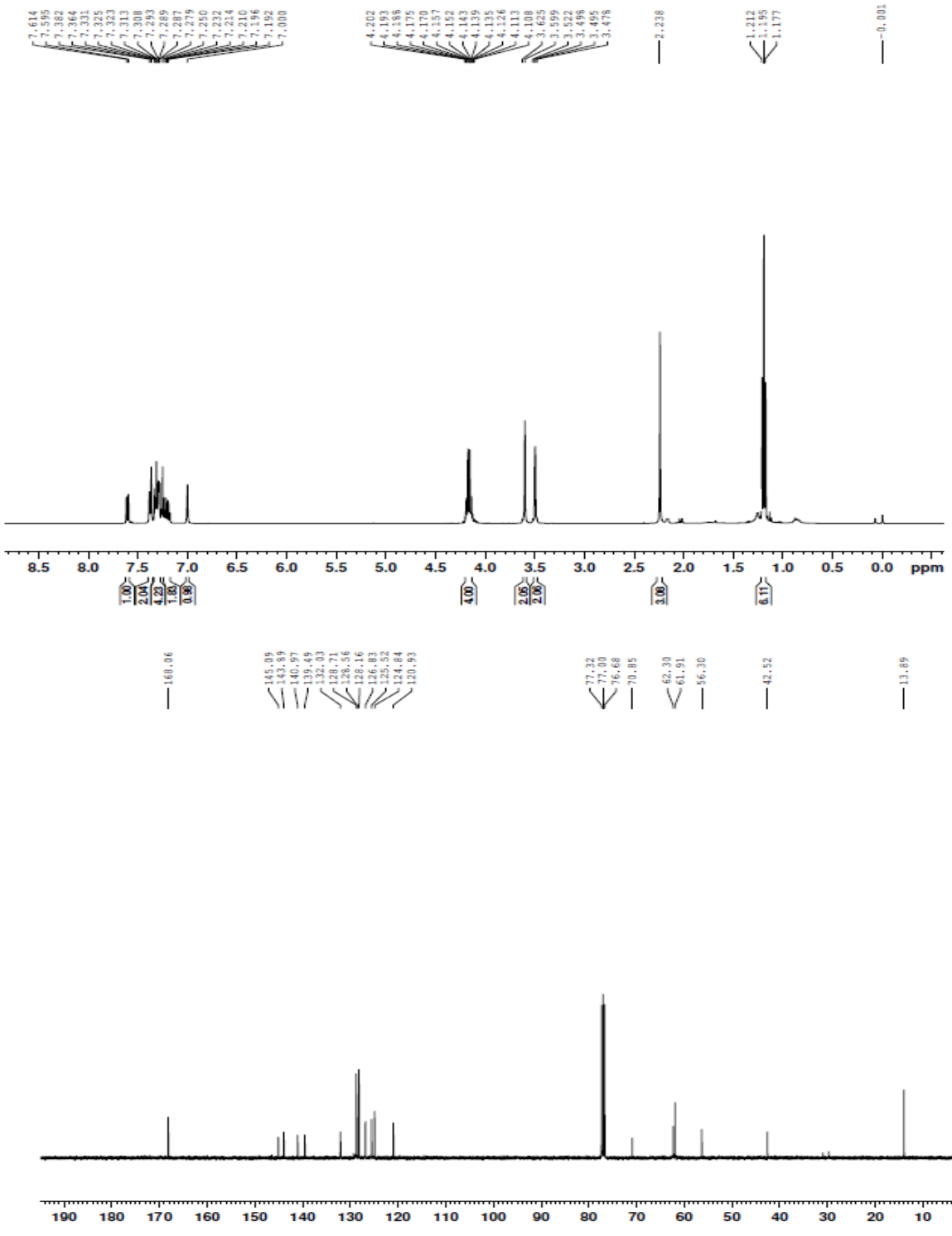

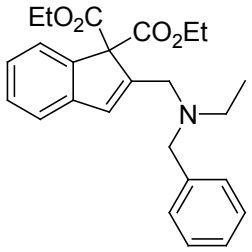

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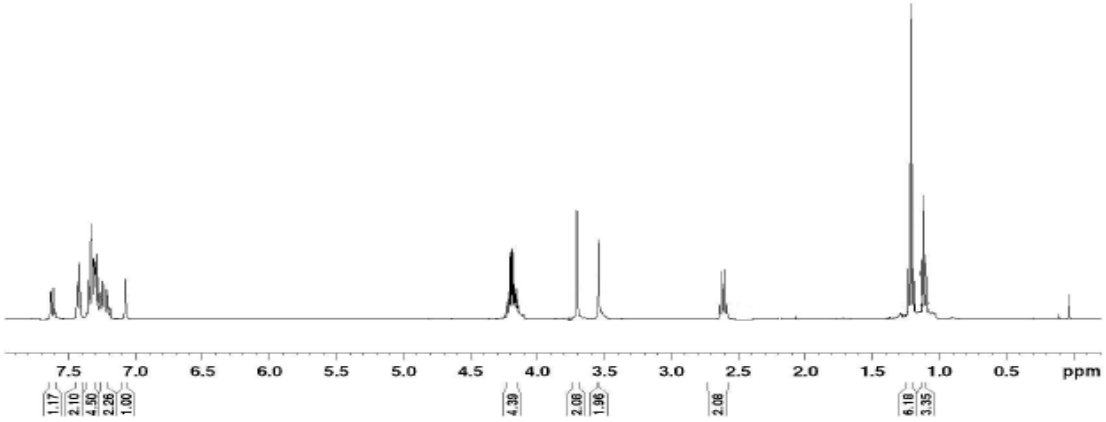

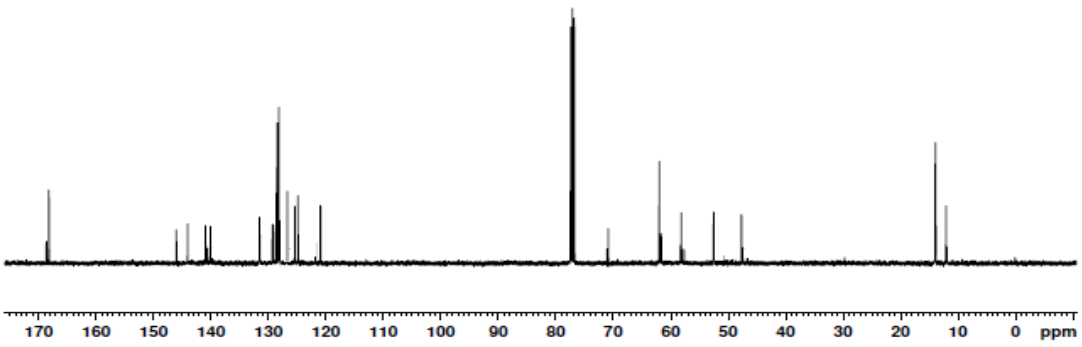

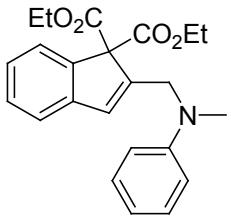

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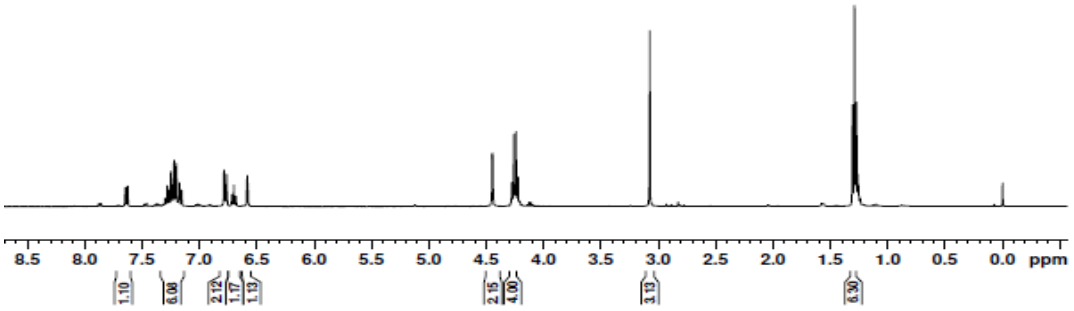

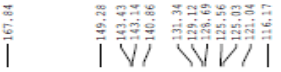

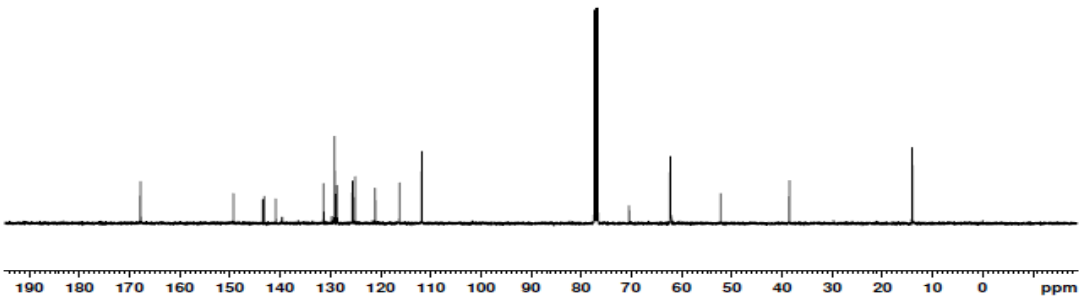

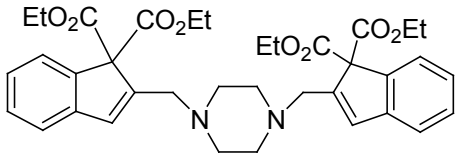

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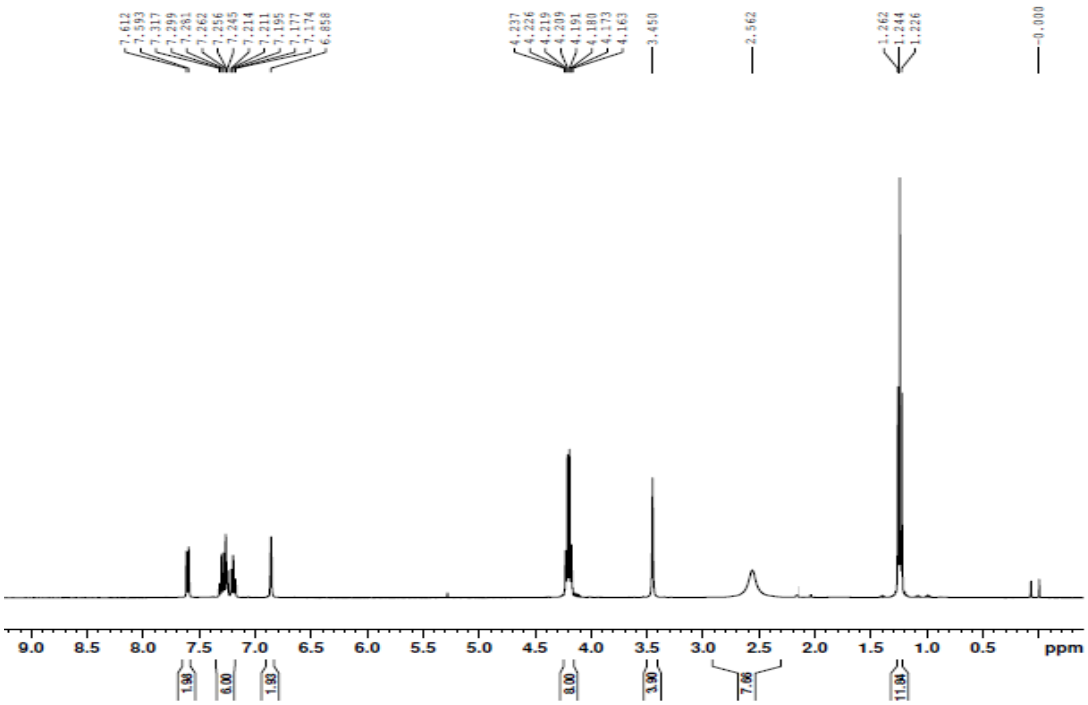

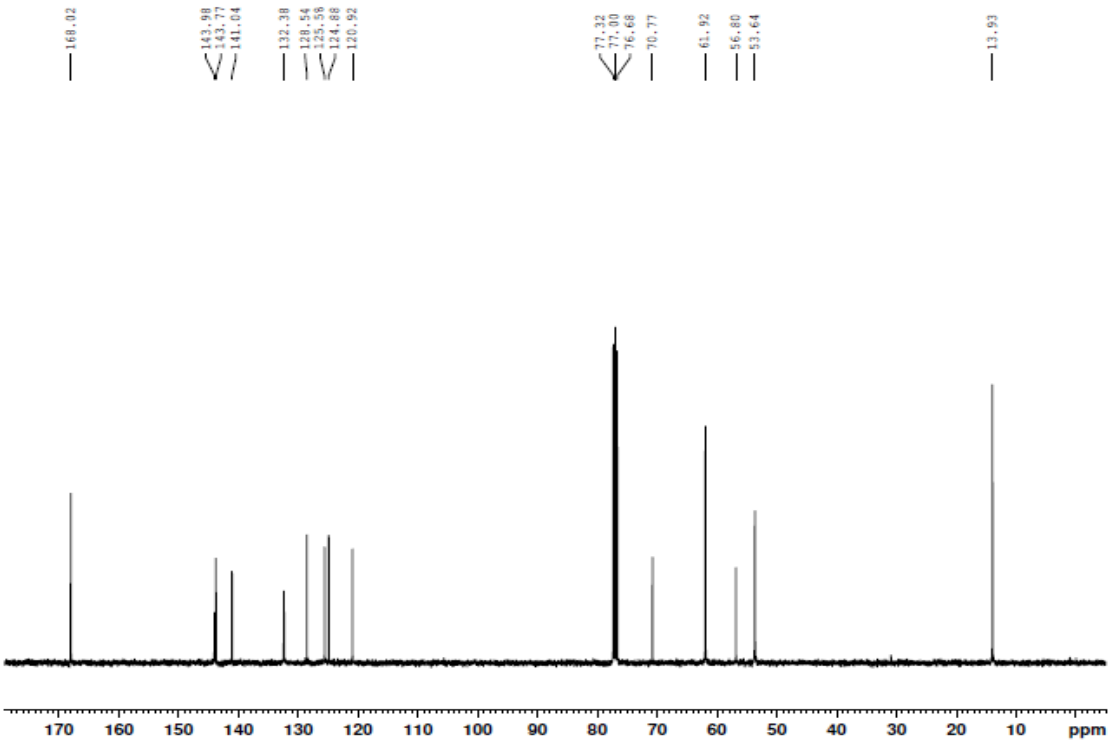

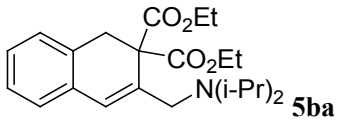

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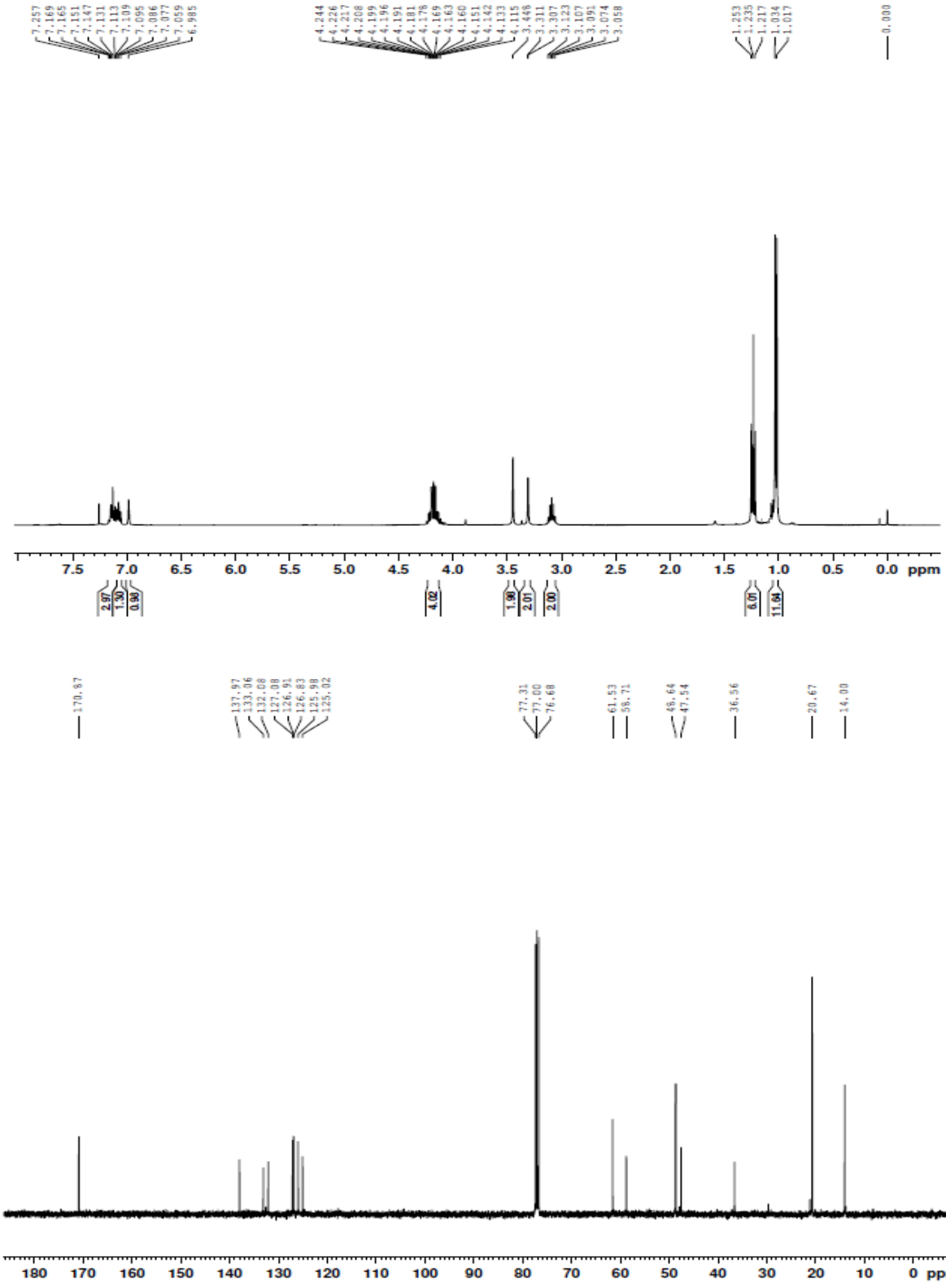

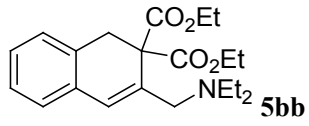

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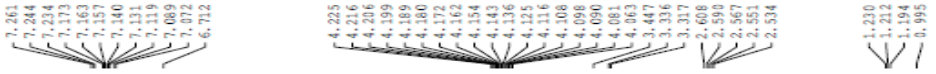

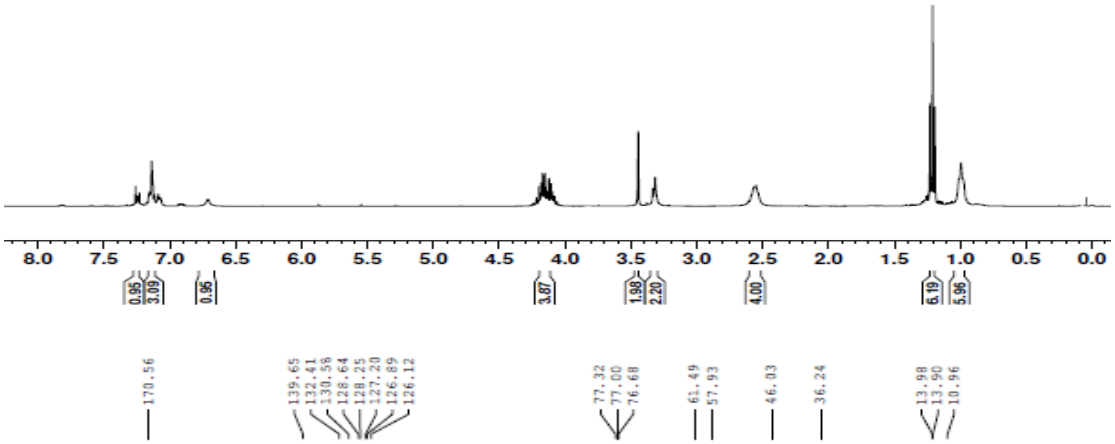

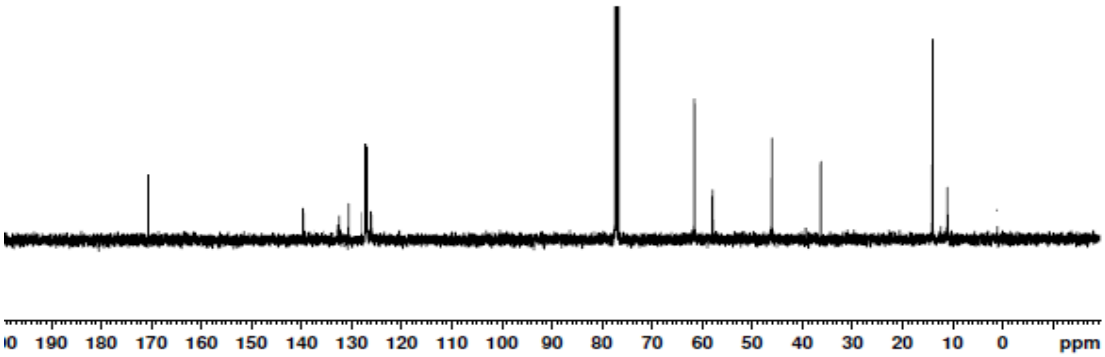

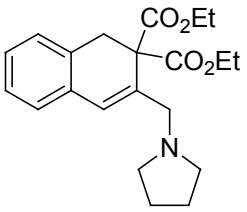

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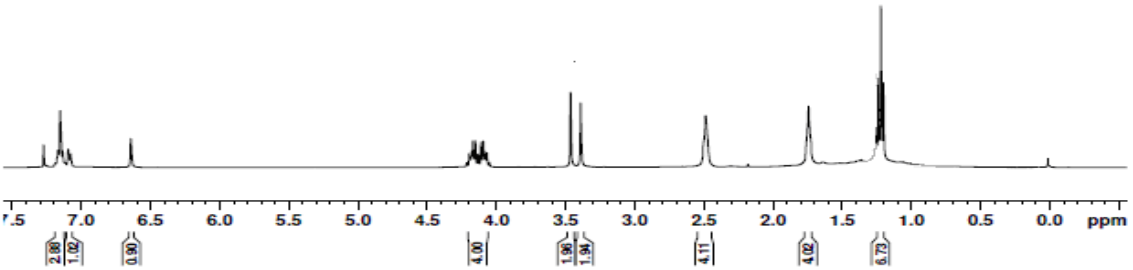

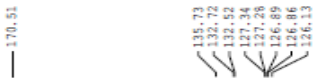

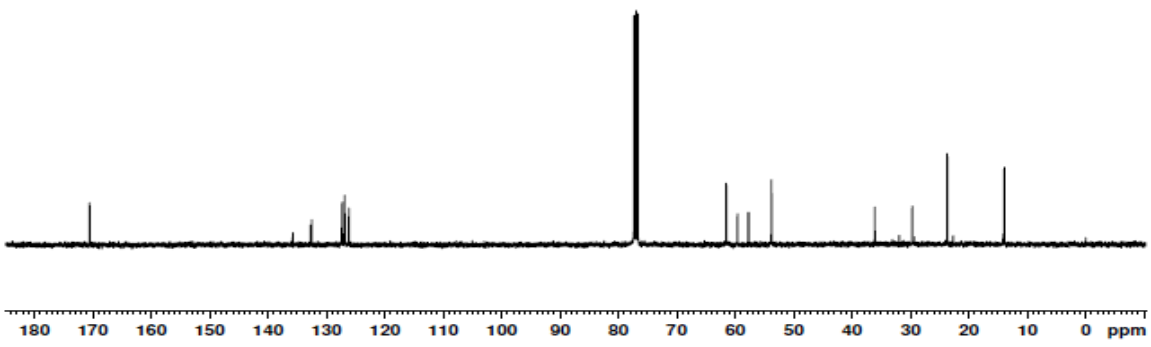

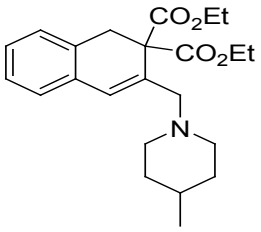

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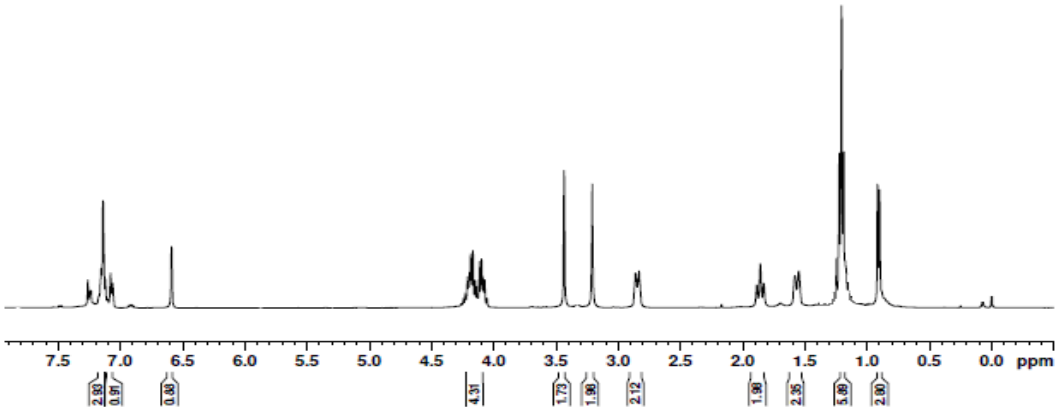

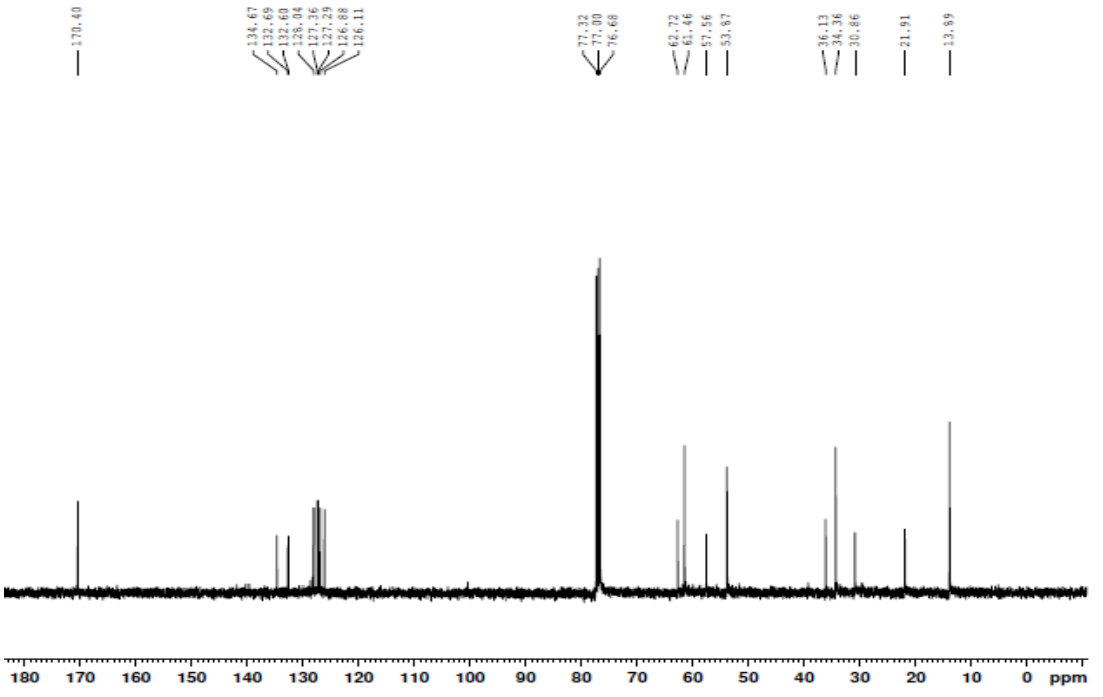

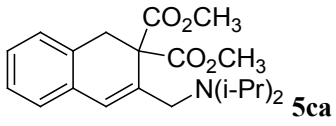

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