Supporting Information

For

Pd(II)-Catalyzed *Ortho*- or *Meta*-C–H Olefination of Phenol Derivatives

Hui-Xiong Dai,[†] Gang Li,[†] Xing-Guo Zhang,[†] Antonia F. Stepan,[‡] Jin-Quan Yu*,[†]

[†]Department of Chemistry, The Scripps Research Institute, 10550 N. Torrey Pines Road, La Jolla, California 92037, United States; [‡]Neuroscience Medicinal Chemistry, Pfizer Global Research and Development, Groton, Connecticut 06340, United States

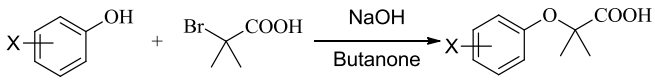
Contents:

1. General Information:

All commercial reagents were purchased from Sigma-Aldrich, Fluka, Alfa Aesar, TCI, Oakwood, and Acros of the highest purity grade. They were used without further purification unless specified. Palladium acetate, silver acetate was purchased from Sigma-Aldrich. The amino acid ligands were bought from Novabiochem, Bachem and Sigma-Aldrich. 2,2'-azanediyldibenzonitrile was prepared by literature methods.[1] ^{1}H and ^{13}C NMR spectra were recorded on Bruker AV 400, Varian Inova 400 (400 MHz and 100 MHz, respectively), Bruker DRX 500 (500 MHz and 125 MHz, respectively) and Bruker DRX 600 (600 MHz and 150 MHz, respectively) instruments. The peaks were internally referenced to TMS (0.00 ppm) or residual undeuterated solvent signal. The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad. High resolution mass spectra were recorded at the Center for Mass Spectrometry, The Scripps Research Institute.

2. Experimental Section

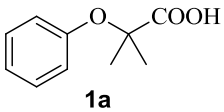
2.1 Preparation of substrates 1a-1r.[2]



1a-1r

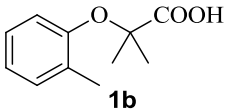
Phenol (1.88 g, 20 mmol) was dissolved in methyl ethyl ketone (40 mL), and NaOH pellets (4.0 g, 100 mmol, 5 equiv) were added. The mixture was heated to 50 °C and stirred at 50 °C for 2 h. A solution of α-bromoisobutyric acid (6.01 g, 36 mmol, 1.8 equiv) in methyl ethyl ketone (15 mL) was added to the resultant suspension over 8 h. The reaction mixture was stirred at 50 °C for an additional 3 h. Water (20 mL) was added, and the reaction mixture was held at room temperature overnight. Methyl ethyl ketone was removed by vacuum distillation. The resultant solution was washed with EtOAc (50 mL). The pH of the aqueous phase was adjusted to 6.5 with 3 N HCl before $NaHSO_3$ (4.16 g, 40 mmol) was added to the reaction mixture. The resultant mixture was stirred at room temperature overnight. The mixture was acidified with 3 N HCl to pH 1.6 and extracted with EtOAc (30 mL × 3). The combined organic extract was washed with brine, dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by a silica

gel packed flash chromatography column, using ethyl acetate/hexane as the eluent. The product **1a** was obtained as a white amorphous solid (2.92 g, 81% yield).



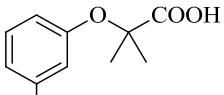
1a

1a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.25 (m, 2H), 7.08-7.05 (m, 1H), 6.96-6.93 (m, 2H), 1.61 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.85, 154.43, 129.25, 79.46, 25.09; HRMS (ESI-TOF) *m/z* Calcd for $C_{10}H_{13}O_3$ $(M+H)^+$: 181.0859, found: 181.0860.



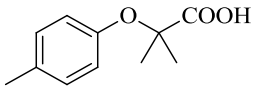
1b

1b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.09 (br, 1H), 7.16 (d, *J* = 7.2 Hz, 1H), 7.08 (t, *J* = 8.0 Hz, 1H), 6.93 (t, *J* = 7.2 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 2.24 (s, 3H), 1.62 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.17, 153.15, 131.14, 129.94, 126.33, 122.40, 117.65, 79.11, 25.19, 16.73; HRMS (ESI-TOF) *m/z* Calcd for $C_{11}H_{15}O_3$ $(M+H)^+$: 195.1016, found: 195.1025.



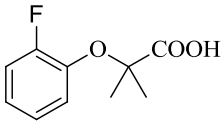
1c

1c: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (t, *J* = 8.0 Hz, 1H), 6.89 (d, *J* = 7.2 Hz, 1H), 6.77 (s, 1H), 6.75 (t, *J* = 8.0 Hz, 1H), 2.32 (s, 3H), 1.60 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.40, 154.28, 139.45, 128.96, 124.12, 117.31, 79.49, 25.07, 21.40; HRMS (ESI-TOF) *m/z* Calcd for $C_{11}H_{15}O_3$ $(M+H)^+$: 195.1016, found: 195.1023.



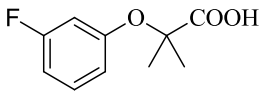
1d

1d: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 2.30 (s, 3H), 1.58 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.53, 152.15, 132.77, 129.74, 120.65, 79.43, 25.03, 20.60; HRMS (ESI-TOF) *m/z* Calcd for $C_{11}H_{15}O_3$ $(M+H)^+$: 195.1016, found: 195.1012.



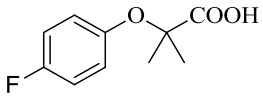
1e

1e: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14-7.02 (m, 4H), 1.61 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.42, 156.52 (d, *J* = 45.1 Hz), 142.03 (d, *J* = 1.2 Hz), 124.60 (d, *J* = 7.2 Hz), 124.18 (d, *J* = 3.8 Hz), 123.76 (d, *J* = 2.1 Hz), 116.56 (d, *J* = 19.6 Hz), 81.5, 24.63; HRMS (ESI-TOF) *m/z* Calcd for $C_{10}H_{12}FO_3$ $(M+H)^+$: 199.0765, found: 199.0769.



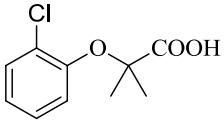
1f

1f: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24-7.18 (m, 1H), 6.77-6.64 (m, 3H), 1.64 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.57, 163.14 (d, *J* = 244.9 Hz), 156.11 (d, *J* = 10.5 Hz), 129.96 (d, *J* = 9.8 Hz), 115.41 (d, *J* = 3.0 Hz), 109.74 (d, *J* = 21.1 Hz), 107.65 (d, *J* = 23.8 Hz), 79.49, 25.15; HRMS (ESI-TOF) *m/z* Calcd for $C_{10}H_{12}FO_3$ $(M+H)^+$: 199.0765, found: 199.0769.



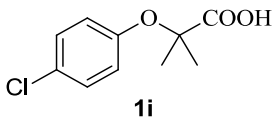
1g

1g: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.98-6.90 (m, 4H), 1.58 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.72, 158.82 (d, *J* = 239.9 Hz), 150.51 (d, *J* = 2.9 Hz), 122.44 (d, *J* = 8.1 Hz), 115.72 (d, *J* = 23.0 Hz), 79.84, 25.04; HRMS (ESI-TOF) *m/z* Calcd for $C_{10}H_{12}FO_3$ $(M+H)^+$: 199.0765, found: 199.0771.



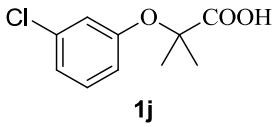
1h

1h: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.0 Hz, 1H), 7.19 (t, *J* = 8.0 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 7.03 (t, *J* = 8.0 Hz, 1H), 1.65 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.43, 150.60, 130.51, 127.47, 127.45, 124.40, 121.59, 81.52, 24.81; HRMS (ESI-TOF) *m/z* Calcd for $C_{10}H_{12}ClO_3$ $(M+H)^+$: 215.0469, found: 215.0471.



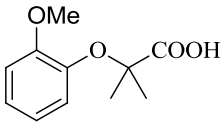
1i

1i: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 9.2 Hz, 2H), 6.87 (d, *J* = 9.2 Hz, 2H), 1.61 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.55, 153.29, 129.24, 128.17, 121.66, 79.57, 25.10; HRMS (ESI-TOF) *m/z* Calcd for $C_{10}H_{12}ClO_3$ $(M+H)^+$: 215.0469, found: 215.0459.



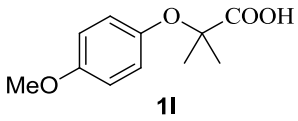
1j

1j: ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.34 (br, 1H), 7.18 (t, *J* = 8.0 Hz, 1H), 7.02 (d, *J* = 8.0 Hz, 1H), 6.95 (s, 1H), 6.81 (d, *J* = 8.4 Hz, 1H), 1.63 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.60, 155.58, 134.56, 129.96, 123.05, 120.60, 118.01, 79.53, 25.15; HRMS (ESI-TOF) *m/z* Calcd for $C_{10}H_{12}ClO_3$ $(M+H)^+$: 215.0469, found: 215.0469.



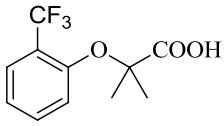
1k

1k: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (t, *J* = 6.8 Hz, 1H), 7.02 (d, *J* = 9.2 Hz, 1H), 6.95-6.88 (m, 2H), 3.86 (s, 3H), 1.53 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.63, 152.26, 142.69, 125.05, 123.32, 120.89, 111.81, 81.77, 55.49, 24.67; HRMS (ESI-TOF) *m/z* Calcd for $C_{11}H_{15}O_4$ $(M+H)^+$: 211.0965, found: 211.0960.



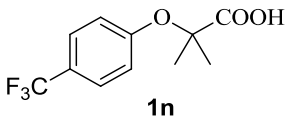
1l

1l: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.92 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 9.2 Hz, 2H), 3.77 (s, 3H), 1.55 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.77, 155.83, 147.77, 122.72, 114.25, 80.03, 55.51, 24.93; HRMS (ESI-TOF) *m/z* Calcd for $C_{11}H_{15}O_4$ $(M+H)^+$: 211.0965, found: 211.0966.



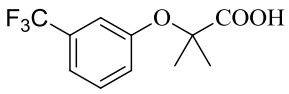
1m

1m: ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.24 (br, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 1.67 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.91, 153.30, 132.59, 127.27 (q, *J* = 5.2 Hz), 123.49 (q, *J* = 270.7 Hz), 121.96 (q, *J* = 29.9 Hz), 121.72, 118.35, 79.92, 24.91; HRMS (ESI-TOF) *m/z* Calcd for $C_{11}H_{12}F_3O_3$ $(M+H)^+$: 249.0733, found: 249.0730.



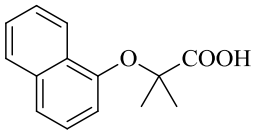
1n

1n: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 1.67 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.54, 158.02, 127.06 (q, *J* = 2.2 Hz), 124.86 (q, *J* = 31.3 Hz), 124.56 (q, *J* = 269.9 Hz), 118.97, 79.26, 25.22; HRMS (ESI-TOF) *m/z* Calcd for $C_{11}H_{12}F_3O_3$ $(M+H)^+$: 249.0733, found: 249.0742.



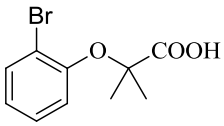
1o

1o: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (t, *J* = 8.0 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.19 (s, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 1.65 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.31, 155.08, 131.84 (q, *J* = 32.7 Hz), 129.80, 123.72 (q, *J* = 270.6 Hz), 122.78, 119.43 (q, *J* =3.8 Hz), 117.06 (q, *J* = 3.7 Hz), 79.61, 25.06; HRMS (ESI-TOF) *m/z* Calcd for $C_{11}H_{12}F_3O_3$ $(M+H)^+$: 249.0733, found: 249.0744.



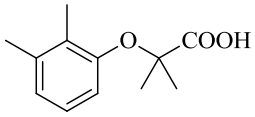
1p

1p: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26-8.22 (m, 1H), 7.81-7.78 (m, 1H), 7.53-7.46 (m, 3H), 7.33 (t, *J* = 8.0 Hz, 1H), 6.87 (d, *J* = 7.6 Hz, 1H), 1.74 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.46, 150.78, 134.84, 127.62, 127.60, 126.39, 126.38, 125.59, 125.33, 122.25, 111.77, 79.58, 25.14; HRMS (ESI-TOF) *m/z* Calcd for $C_{14}H_{15}O_3$ $(M+H)^+$: 231.1016, found: 231.1005.



1q

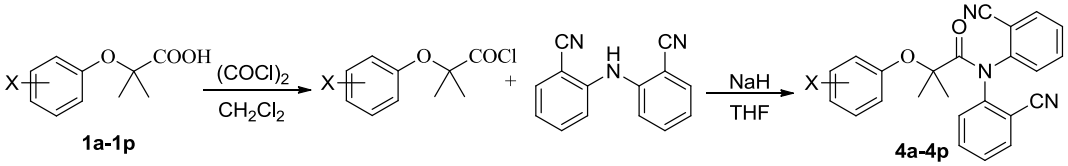
1q: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.0 Hz, 1H), 7.21 (t, *J* = 8.4 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 6.93 (t, *J* = 8.4 Hz, 1H), 1.66 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.33, 151.84, 133.46, 128.07, 124.31, 120.60, 116.74, 80.97, 24.86; HRMS (ESI-TOF) *m/z* Calcd for $C_{10}H_{12}BrO_3$ $(M+H)^+$: 258.9964, found: 258.9966.



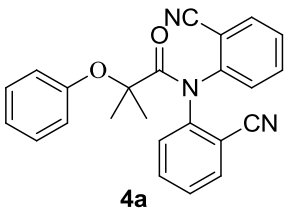
1r

1r: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (br, 1H), 6.97 (t, *J* = 8.0 Hz, 1H), 6.85 (d, *J* = 7.2 Hz, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 2.26 (s, 3H), 2.16 (s, 3H), 1.60 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.78, 152.82, 138.39, 128.65, 125.34, 124.22, 115.69, 79.29, 25.12, 20.23, 12.51; HRMS (ESI-TOF) *m/z* Calcd for $C_{12}H_{17}O_3$ $(M+H)^+$: 209.1172, found: 209.1181.

2.2 Preparation of substrates 4a-4p.[3]

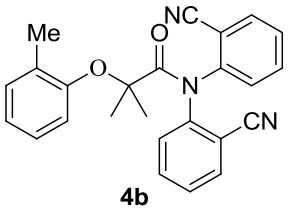


To a cooled solution of 2,2'-azanediyldibenzonitrile (1.15g, 5.25 mmol, 1.05 equiv.) in THF (10 mL) was added NaH (60% in mineral oil, 220 mg, 5.5 mmol, 1.10 equiv.) in two portions at 0 °C. After the bubbling had subsided, acid chloride (5.0 mmol, 1.00 equiv.), prepared from the corresponding carboxylic acid and oxalyl chloride, was added dropwise to the reaction mixture at 0 °C. After stirred overnight, the reaction was diluted with EtOAc and quenched with water. The solution was extracted with EtOAc three times. The combined organic extract was washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the crude product by a silica gel packed flash chromatography column using hexanes/EtOAc as the eluent yielded the amide (**4a**-**4p**).



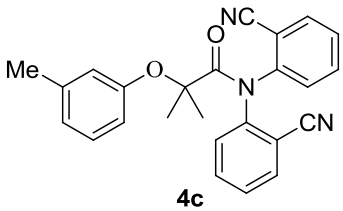
4a

4a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.56 (m, 6H), 7.39 (br, 2H), 7.17 (t, *J* = 8.0 Hz, 2H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.65 (d, *J* = 7.6 Hz, 2H), 1.68 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.61, 152.87, 145.67, 133.76, 129.05, 128.09, 123.79, 122.61, 117.32, 113.19, 83.72, 26.46, 25.79; HRMS (ESI-TOF) *m/z* Calcd for $C_{24}H_{20}N_3O_2$ $(M+H)^+$: 382.1550, found: 382.1556.



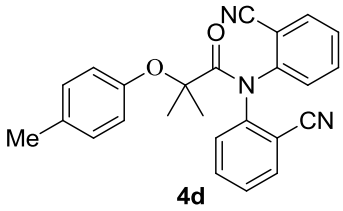
4b

4b: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64-7.49 (m, 6H), 7.36 (br, 2H), 7.09 (t, *J* = 7.8 Hz, 1H), 7.05 (t, *J* = 7.2 Hz, 1H), 6.93-6.89 (m, 2H), 1.90 (s, 3H), 1.74 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.90, 151.70, 144.17, 133.91, 133.84, 133.58, 130.94, 130.26, 128.08, 126.40, 122.74, 122.71, 119.97, 118.49, 117.26, 116.56, 112.80, 103.23, 99.55, 82.81, 27.01, 16.70; HRMS (ESI-TOF) *m/z* Calcd for $C_{25}H_{22}N_3O_2$ $(M+H)^+$: 396.1706, found: 396.1723.



4c

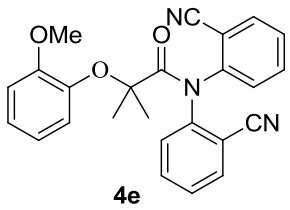
4c: 1H NMR (600 MHz, $CDCl_3$) δ 7.94-7.47 (m, 6H), 7.36 (s, 2H), 7.04 (t, *J* = 7.8 Hz, 1H), 6.84 (d, *J* = 7.7 Hz, 1H), 6.48 (s, 1H), 6.42 (dd, J_1 = 8.1, J_2 = 2.4 Hz, 1H), 2.26 (s, 3H), 1.68 (s, 6H); 13C NMR (150 MHz, $CDCl_3$) δ 174.7, 152.8, 145.6, 139.1, 134.1, 133.7, 133.3, 129.7, 129.0, 128.6, 128.0, 124.5, 123.1, 119.4, 117.3, 113.0, 83.5, 26.7, 25.7, 21.3; HRMS (ESI-TOF) *m/z* Calcd for $C_{25}H_{22}N_3O_2$ $(M+H)^+$: 396.1706, found: 396.1698.



4d

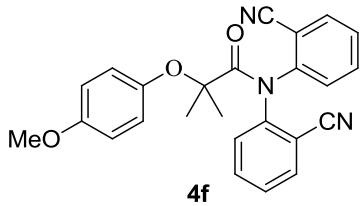
4d: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76-7.51 (m, 6H), 7.36 (br, 2H), 6.96 (d, *J* = 7.8 Hz, 2H), 6.52 (d, *J* = 7.8 Hz, 2H), 2.26 (s, 3H), 1.66 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$)

δ 174.69, 150.35, 145.79, 133.74, 133.42, 129.51, 128.05, 122.68, 118.49, 117.34, 83.68, 26.48, 25.55, 20.65; HRMS (ESI-TOF) *m/z* Calcd for $C_{25}H_{22}N_3O_2$ $(M+H)^+$: 396.1706, found: 396.1725.



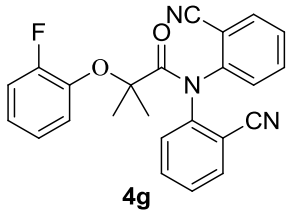
4e

4e: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84-7.58 (m, 6H), 7.35 (br, 2H), 7.04-7.00 (m, 1H), 6.82-6.78 (m, 3H), 3.71 (s, 3H), 1.63 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.68, 153.14, 145.49, 141.93, 127.85, 124.79, 124.74, 120.28, 112.90, 84.50, 55.13, 26.34, 25.55; HRMS (ESI-TOF) *m/z* Calcd for $C_{25}H_{22}N_3O_3$ $(M+H)^+$: 412.1656, found: 412.1661.



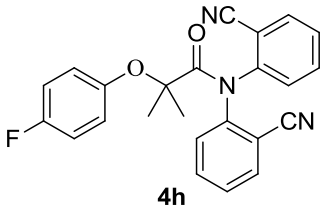
4f

4f: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75-7.56 (m, 6H), 7.36 (br, 2H), 6.69 (d, *J* = 9.0 Hz, 2H), 6.55 (d, *J* = 9.6 Hz, 2H), 3.73 (s, 3H), 1.63 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.67, 156.05, 145.91, 133.70, 128.02, 123.99, 117.34, 113.95, 83.86, 55.45, 26.35, 25.34; HRMS (ESI-TOF) *m/z* Calcd for $C_{25}H_{22}N_3O_3$ $(M+H)^+$: 412.1656, found: 412.1645.



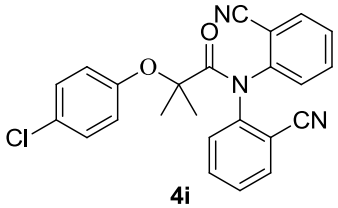
4g

4g: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81-7.58 (m, 6H), 7.37 (br, 2H), 7.02-6.92 (m, 4H), 1.69 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.15, 156.01 (d, *J* = 246.8 Hz), 145.65, 139.94 (d, *J* = 11.7 Hz), 133.68, 128.08, 126.09, 125.18 (d, *J* = 7.2 Hz), 124.02 (d, *J* = 3.6 Hz), 117.23, 116.55 (d, *J* = 19.5 Hz), 113.10, 85.47, 26.30, 25.32; HRMS (ESI-TOF) *m/z* Calcd for $C_{24}H_{19}FN_3O_2$ $(M+H)^+$: 400.1456, found: 400.1466.



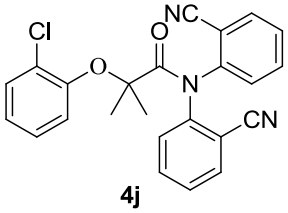
4h

4h: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.58 (m, 6H), 7.37 (br, 2H), 6.88-6.83 (m, 2H), 6.62-6.58 (m, 2H), 1.65 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.29, 159.14 (d, *J* = 241.1 Hz), 148.34 (d, *J* = 2.7 Hz), 145.64, 134.31, 133.71, 133.39, 129.38, 128.70, 128.15, 124.14 (d, *J* = 8.3 Hz), 117.22, 115.53 (d, *J* = 22.9 Hz), 113.23, 112.60, 83.94, 26.32, 25.33; HRMS (ESI-TOF) *m/z* Calcd for $C_{24}H_{19}FN_3O_2$ $(M+H)^+$: 400.1456, found: 400.1446.



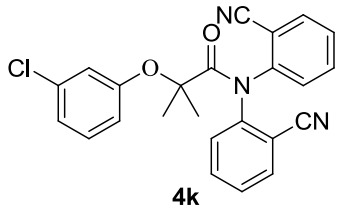
4i

4i: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86-7.36 (m, 8H), 7.14 (d, J = 8.4 Hz, 2H), 6.60 (d, J = 9.0 Hz, 2H), 1.69 (s, 3H), 1.66 (S, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.20, 151.19, 145.33, 134.23, 133.68, 133.37, 129.46, 129.01, 128.27, 128.00, 123.92, 117.13, 113.00, 112.53, 83.87, 26.36, 25.51; HRMS (ESI-TOF) *m/z* Calcd for $C_{24}H_{19}ClN_3O_2$ $(M+H)^+$: 416.1160, found: 416.1178.



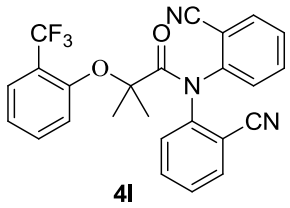
4j

4j: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76-7.51 (m, 6H), 7.39 (br, 2H), 7.26 (d, *J* = 8.4 Hz, 1H), 7.18 (t, *J* = 8.4 Hz, 1H), 7.12 (d, *J* = 7.8 Hz, 1H), 6.98 (t, *J* = 7.8 Hz, 1H), 1.77 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.31, 149.26, 145.13, 144.18, 134.13, 133.78, 133.31, 130.33, 129.01, 128.44, 127.91, 127.29, 127.07, 124.10, 122.81, 117.22, 112.56, 84.57, 27.13, 26.45; HRMS (ESI-TOF) *m/z* Calcd for $C_{24}H_{19}ClN_3O_2$ $(M+H)^+$: 416.1160, found: 416.1173.



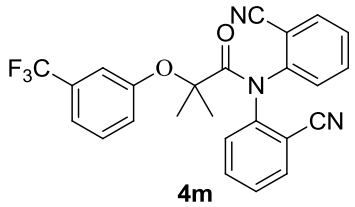
4k

4k: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71-7.58 (m, 6H), 7.41-7.36 (m, 2H), 7.12 (t, *J* = 8.0 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.63 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1H), 6.56 (t, *J* = 2.0 Hz, 1H), 1.70 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.09, 153.53, 145.36, 134.31, 134.21, 133.79, 133.47, 129.85, 129.63, 128.78, 128.37, 128.04, 124.11, 122.83, 120.66, 117.19, 113.08, 112.68, 84.16, 26.52, 25.65; HRMS (ESI-TOF) *m/z* Calcd for $C_{24}H_{19}ClN_3O_2$ $(M+H)^+$: 416.1160, found: 416.1150.



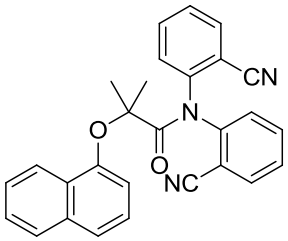
4l

4l: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91-7.28 (m, 11H), 7.08 (t, *J* = 7.5 Hz, 1H), 1.78 (s, 3H), 1.77 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.49, 151.94, 134.03, 132.91, 126.84 (q, *J* = 5.1 Hz), 123.14 (q, *J* = 270.9 Hz), 121.87, 121.42 (q, *J* = 30.0 Hz), 120.36, 82.54, 27.50, 27.00; HRMS (ESI-TOF) *m/z* Calcd for $C_{25}H_{19}FN_3O_2$ $(M+H)^+$: 450.1424, found: 450.1435.



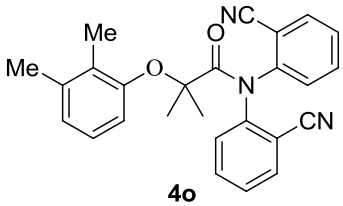
4m

4m: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75-7.60 (m, 6H), 7.40-7.26 (m, 4H), 7.00-6.97 (m, 1H), 6.65 (s, 1H), 1.73 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.99, 153.14, 145.44, 133.82, 131.59 (q, *J* = 33.0 Hz), 129.79, 128.29, 125.48, 123.52 (q, *J* = 270.7 Hz), 120.48 (q, *J* = 3.6 Hz), 119.28 (q, *J* = 3.6 Hz), 117.20, 84.30, 26.54, 25.81; HRMS (ESI-TOF) *m/z* Calcd for $C_{25}H_{19}FN_3O_2$ $(M+H)^+$: 450.1424, found: 450.1414.



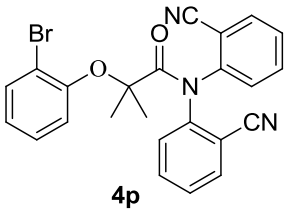
4n

4n: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78-7.34 (m, 12H), 7.27-7.10 (m, 2H), 7.07 (d, *J* = 7.8 Hz, 1H), 1.86 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.68, 149.27, 134.52, 133.85, 127.79, 127.41, 126.14, 125.58, 125.24, 122.54, 122.41, 117.27, 114.06, 83.04, 27.18, 27.05; HRMS (ESI-TOF) *m/z* Calcd for $C_{28}H_{22}N_3O_2$ $(M+H)^+$: 432.1706, found: 432.1695.



4o

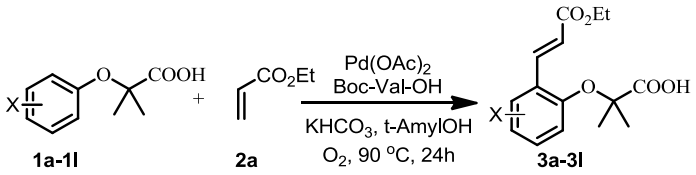
4o: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76-7.46 (m, 6H), 7.39-7.29 (m, 2H), 6.96 (t, *J* = 7.8 Hz, 1H), 6.84 (d, *J* = 7.2 Hz, 1H), 6.69 (d, *J* = 7.8 Hz, 1H), 2.19 (s, 3H), 1.88 (s, 3H), 1.70 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.92, 151.17, 144.08, 138.19, 134.10, 133.92, 133.79, 133.54, 132.89, 130.29, 129.43, 128.24, 127.87, 125.24, 124.57, 122.69, 118.40, 118.32, 117.24, 116.59, 112.77, 83.17, 26.83, 26.53, 20.25, 12.81; HRMS (ESI-TOF) *m/z* Calcd for $C_{26}H_{24}N_3O_2$ $(M+H)^+$: 410.1863, found: 410.1863.



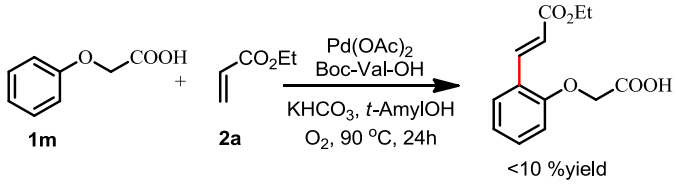
4p

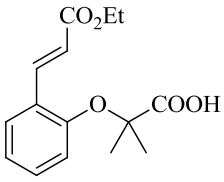
4p: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.55 (m, 6H), 7.44 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1H), 7.40-7.35 (m, 2H), 7.26-7.22 (m, 1H), 7.18 (dd, J_1 = 8.4 Hz, J_2 = 1.6 Hz, 1H), 6.89 (dt, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1H), 1.79 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.35, 150.63, 133.88, 133.57, 133.45, 128.11, 124.14, 121.75, 117.26, 116.15, 112.61, 84.10, 27.27, 27.15; HRMS (ESI-TOF) *m/z* Calcd for $C_{24}H_{19}BrN_3O_2$ $(M+H)^+$: 460.0655, found: 460.0659.

2.3 Typical procedures for Pd(II)-catalyzed *ortho*-olefination of phenol derivatives.

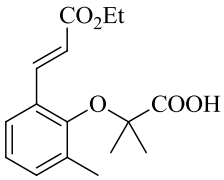


A 50 mL Schlenk-type tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with acid **1** (0.20 mmol, 1.0 equiv.), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol, 5 mol %), Boc-Val-OH (4.3 mg, 0.020 mmol, 10 mol %), $KHCO_3$ (40 mg, 0.40 mmol, 2.0 equiv.), ethyl acrylate **2a** (0.40 mmol, 2.0 equiv.), and *t*-AmylOH (2.0 mL). The reaction tube was evacuated and backfilled with O_2 (5-times, balloon) and heated to 90 °C for 24 hours under vigorous stirring. The reaction vessel was then cooled to 0 °C in an ice bath. A 2.0 N HCl solution (5 mL) was then added, and the mixture was extracted with EtOAc (3 × 20 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting residue was purified by preparative TLC using hexanes/EtOAc as the eluent to afford the product (**3a**-**3l**).



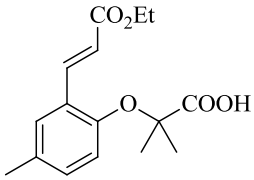


3a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 16.4 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.28 (t, *J* = 8.8 Hz, 1H), 7.04 (t, *J* = 7.6 Hz, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.47 (d, *J* = 16.4 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 1.67 (s, 6H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.47, 167.27, 153.75, 139.85, 130.82, 128.31, 126.74, 122.70, 118.96, 118.29, 80.23, 60.48, 25.21, 14.29; HRMS (ESI-TOF) *m/z* Calcd for $C_{15}H_{19}O_5$ $(M+H)^+$: 279.1227, found: 279.1225.



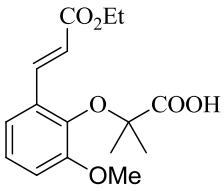
3b

3b: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 (d, *J* = 16.2 Hz, 1H), 7.41 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.22 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.07 (t, *J* = 7.8 Hz, 1H), 6.35 (d, *J* = 16.2 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 2.28 (s, 3H), 1.49 (s, 6H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.70, 167.13, 152.59, 141.15, 133.71, 133.11, 130.79, 124.86, 124.74, 119.03, 82.42, 60.61, 25.05, 17.83, 14.25; HRMS (ESI-TOF) *m/z* Calcd for $C_{16}H_{21}O_5$ $(M+H)^+$: 293.1383, found: 293.1390.



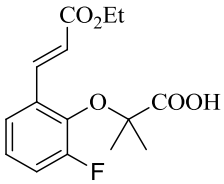
3c

3c: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (d, *J* = 16.2 Hz, 1H), 7.36 (s, 1H), 7.06 (d, *J* = 7.2 Hz, 1H), 6.79 (d, *J* = 7.2 Hz, 1H), 6.45 (d, *J* = 16.2 Hz, 1H), 4.25 (q, *J* = 7.2 Hz, 2H), 2.29 (s, 3H), 1.63 (s, 6H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.03, 167.48, 151.69, 140.08, 132.08, 131.54, 128.51, 126.53, 118.56, 118.52, 79.90, 60.45, 25.16, 20.55, 14.27; HRMS (ESI-TOF) *m/z* Calcd for $C_{16}H_{21}O_5$ $(M+H)^+$: 293.1383, found: 293.1381.



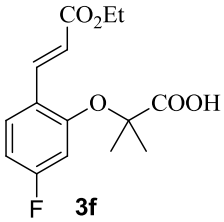
3d

3d: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 16.0 Hz, 1H), 7.22 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H), 7.15 (t, *J* = 8.4 Hz, 1H), 6.95 (dd, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 1H), 6.41 (d, *J* = 16.4 Hz, 1H), 4.28 (q, *J* = 7.2 Hz, 2H), 3.89 (s, 3H), 1.51 (s, 6H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.13, 166.57, 153.00, 142.12, 139.24, 131.03, 125.47, 120.25, 119.07, 112.75, 83.90, 60.65, 55.62, 24.84, 14.28; HRMS (ESI-TOF) *m/z* Calcd for $C_{16}H_{21}O_6$ $(M+H)^+$: 309.1333, found: 309.1332.



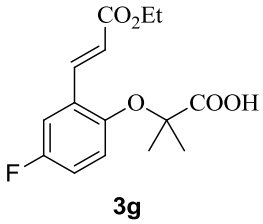
3e

3e: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 16.0 Hz, 1H), 7.38-7.35 (m, 1H), 7.15-7.06 (m, 2H), 6.45 (d, *J* = 16.0 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 1.59 (s, 6H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.17, 166.72, 155.92 (d, *J* = 244.5 Hz), 140.88 (d, *J* = 12.7 Hz), 138.57 (d, *J* = 3.4 Hz), 131.68 (d, *J* = 2.2 Hz), 124.77 (d, *J* = 8.1 Hz), 122.63 (d, *J* = 3.2 Hz), 120.51, 117.84 (d, *J* = 20.4 Hz), 82.66, 60.69, 24.92, 24.89, 14.24; HRMS (ESI-TOF) *m/z* Calcd for $C_{15}H_{18}FO_5$ $(M+H)^+$: 297.1133, found: 297.1126.



3f

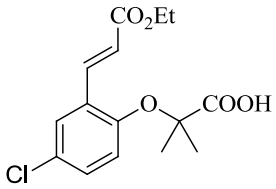
3f: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 (d, *J* = 16.8 Hz, 1H), 7.22-7.17 (m, 1H), 6.79-6.74 (m, 2H), 6.64 (d, *J* = 8.4 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 1.70 (s, 6H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 178.53, 167.82, 162.52 (d, *J* = 252.7 Hz), 155.22 (d, *J* = 6.5 Hz), 133.57, 130.38 (d, *J* = 11.4 Hz), 122.88 (d, *J* = 11.5 Hz), 115.12 (d, *J* = 13.1 Hz), 112.96 (d, *J* = 3.0 Hz), 109.73 (d, *J* = 22.8 Hz), 80.18, 60.58, 25.18, 14.26; HRMS (ESI-TOF) *m/z* Calcd for $C_{15}H_{18}FO_5$ $(M+H)^+$: 297.1133, found: 297.1133.



3g

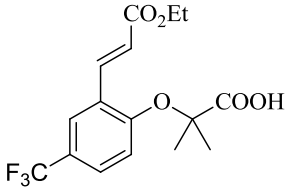
3g: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 16.4 Hz, 1H), 7.28-7.22 (m, 1H), 6.99-6.92 (m, 2H), 6.43 (d, *J* = 16.0 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 1.63 (s, 6H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.45, 166.98, 158.11 (d, *J* = 241.1 Hz), 149.90, 138.79 (d, *J* = 2.2 Hz), 128.76 (d, *J* = 7.7 Hz), 120.60 (d, *J* = 8.3 Hz), 120.01, 117.41 (d, *J* = 23.1 Hz), 113.82

(d, J = 23.3 Hz), 80.83, 60.97, 25.15, 14.24; HRMS (ESI-TOF) *m/z* Calcd for $C_{15}H_{18}FO_5$ $(M+H)^+$: 297.1133, found: 297.1132.



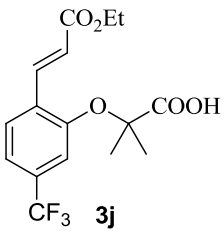
3h

3h: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (d, J =16.2 Hz, 1H), 7.53 (d, J = 2.4 Hz, 1H), 7.23 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 6.83 (d, J = 8.4 Hz, 1H), 6.45 (d, J = 16.2 Hz, 1H), 4.27 (q, J = 7.2 Hz, 2H), 1.66 (s, 6H), 1.33 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.90, 166.89, 152.25, 138.39, 130.40, 128.35, 127.96, 127.80, 120.19, 119.56, 80.21, 60.65, 25.16, 14.26; HRMS (ESI-TOF) *m/z* Calcd for $C_{15}H_{18}ClO_5$ $(M+H)^+$: 313.0837, found: 313.0836.



3i

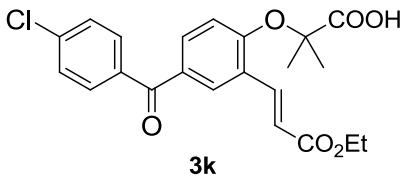
3i: ^{1}H NMR (400 MHz, CD_3OD) δ 8.00 (d, J = 16.2 Hz, 1H), 7.88 (s, 1H), 7.58 (d, J = 9.2 Hz, 1H), 7.00 (d, J = 8.8 Hz, 1H), 6.63 (d, J = 16.2 Hz, 1H), 4.26 (q, J = 7.1 Hz, 2H), 1.71 (s, 6H), 1.33 (t, J = 7.1 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 178.5, 167.1, 156.2, 138.6, 127.4, 126.3, 125.6 (q, $J_{C\text{-}F}$ = 3.5 Hz), 124.3 (q, $J_{C\text{-}F}$ = 33.1 Hz), 123.8 (q, $J_{C\text{-}F}$ = 271.8 Hz), 120.4, 116.9, 80.2, 60.8, 25.3, 14.2; HRMS (ESI-TOF) *m/z* Calcd for $C_{16}H_{18}F_3O_5(M+H)^+$: 347.1101, found: 347.1098.



3j

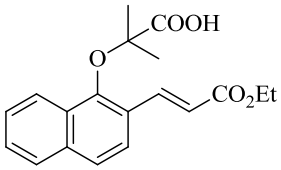
3j: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (d, J =16.2 Hz, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.28 (d, J = 8.4 Hz, 1H), 7.09 (s, 1H), 6.53 (d, J = 16.2 Hz, 1H), 4.27 (q, J = 7.2 Hz, 2H), 1.69 (s, 6H), 1.34 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 178.66, 166.94, 153.88, 138.52, 132.26 (q, J

= 32.6 Hz), 129.94, 128.69, 123.41 (q, *J* = 271.1 Hz), 121.16, 119.08 (q, *J* = 3.6 Hz), 114.77, 80.47, 60.79, 25.22, 14.23; HRMS (ESI-TOF) *m/z* Calcd for $C_{16}H_{18}F_3O_5(M+H)^+$: 347.1101, found: 347.1108.



3k

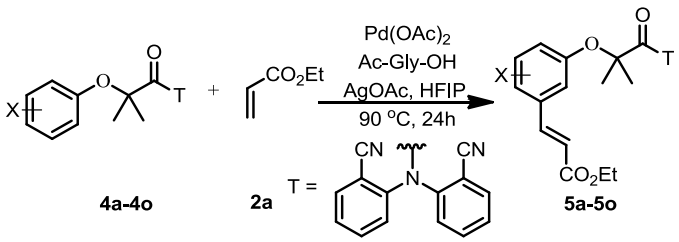
3k: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03-7.98 (m, 2H), 7.75-7.69 (m, 3H), 7.47 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 1H), 6.49 (d, *J* = 16.0 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 1.76 (s, 6H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.05, 177.65, 167.09, 157.46, 138.91, 138.81, 135.73, 132.70, 131.20, 130.94, 130.60, 128.74, 125.52, 120.30, 115.96, 80.01, 60.69, 25.35, 14.27; HRMS (ESI-TOF) *m/z* Calcd for $C_{22}H_{22}ClO_6$ $(M+H)^+$: 417.1099, found: 417.1087.



3l

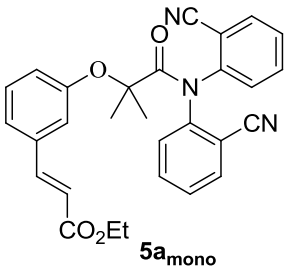
3l: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.28 (d, *J* =16.2 Hz, 1H), 8.17-8.15 (m, 1H), 7.83-7.81 (m, 1H), 7.67-7.63 (m, 2H), 7.54-7.52 (m, 2H), 6.48 (d, *J* = 15.6 Hz, 1H), 4.29 (q, *J* = 7.2 Hz, 2H), 1.54 (s, 6H), 1.35 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.89, 167.17, 150.68, 140.42, 135.46, 130.71, 127.98, 127.43, 126.80, 126.21, 125.48, 123.71, 122.97, 118.91, 84.21, 60.69, 25.12, 14.30; HRMS (ESI-TOF) *m/z* Calcd for $C_{19}H_{21}O_5$ $(M+H)^+$: 329.1383, found: 329.1380.

2.4 Typical procedures for Pd(II)-catalyzed *meta*-olefination of phenol derivatives.



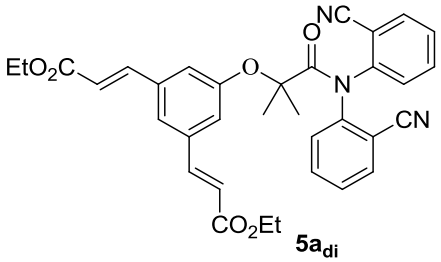
4a-4o **2a** **5a-5o**

A 35 mL sealed tube (with a Teflon cap) equipped with a magnetic stir bar was charged with amide **4** (0.10 mmol, 1.0 equiv.), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol, 10 mol %), Ac-Gly-OH (2.4 mg, 0.020 mmol, 20 mol %) and AgOAc (50 mg, 0.30 mmol, 3.0 equiv.). HFIP (0.60 mL) was added to the mixture, followed by ethyl acrylate **2a** (2.0 equiv.) and then another 1.0 mL of HFIP. The tube was then capped and submerged into a pre-heated 90 °C oil bath. The reaction was stirred for 24 h and cooled down to room temperature. The crude reaction mixture was diluted with EtOAc (2 mL) and filtered through a short pad of Celite. The sealed tube and Celite pad were washed with an additional 15 mL of EtOAc. The filtrate was concentrated *in vacuo*, and the resulting residue was purified by preparative TLC using hexanes/EtOAc as the eluent. The positional selectivity was determined by ^{1}H NMR analysis of the unpurified reaction mixture.



5a$_{mono}$

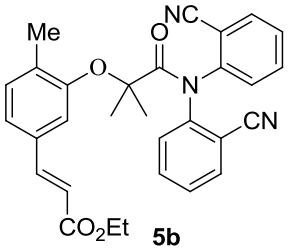
5a$_{mono}$: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83-7.56 (m, 6H), 7.55 (d, *J* =16.2 Hz, 1H), 7.38 (br, 2H), 7.23-7.20 (m, 2H), 6.76-6.73 (m, 1H), 6.71 (s, 1H), 6.34 (d, *J* =16.2 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 1.71 (s, 6H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.27, 166.74, 153.30, 145.51, 143.77, 135.63, 133.77, 129.55, 129.08, 127.99, 124.15, 123.55, 121.72, 118.86, 117.21, 83.93, 60.55, 26.65, 25.73, 14.28; HRMS (ESI-TOF) *m/z* Calcd for $C_{29}H_{26}N_3O_4$ $(M+H)^+$: 480.1918, found: 480.1930.



5a$_{di}$

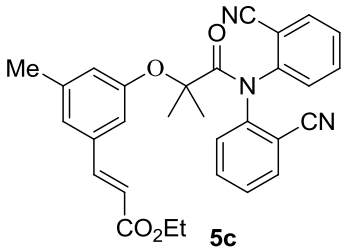
5a$_{di}$: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85-7.61 (m, 6H), 7.56 (d, *J* =15.6 Hz, 2H), 7.40 (br, 2H), 7.35 (s, 1H), 6.79 (s, 2H), 6.38 (d, *J* =15.6 Hz, 2H), 4.28 (q, *J* = 7.2 Hz, 4H), 1.72 (s, 6H), 1.35 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.00, 166.49, 153.84, 145.46, 142.94, 136.23,

133.82, 123.17, 122.92, 119.88, 117.21, 84.22, 60.69, 26.67, 25.83, 14.27; HRMS (ESI-TOF) *m/z* Calcd for $C_{34}H_{32}N_3O_6$ $(M+H)^+$: 578.2286, found: 578.2284.



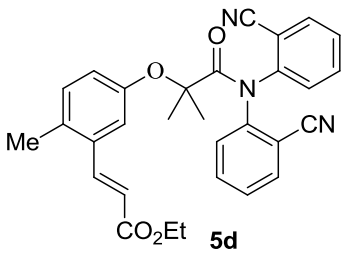
5b

5b: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86-7.45 (m, 8H), 7.38 (br, 2H), 7.13 (dd, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 1H), 7.08 (d, *J* = 7.8 Hz, 1H), 6.98 (d, *J* = 1.8 Hz, 1H), 6.36 (d, *J* = 16.2 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 1.96 (s, 3H), 1.74 (s, 6H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.51, 167.03, 151.92, 144.14, 133.83, 133.34, 133.04, 131.41, 122.56, 119.80, 117.83, 117.18, 112.82, 83.40, 60.41, 27.04, 26.75, 16.90, 14.30; HRMS (ESI-TOF) *m/z* Calcd for $C_{30}H_{28}N_3O_4$ $(M+H)^+$: 494.2074, found: 494.2071.



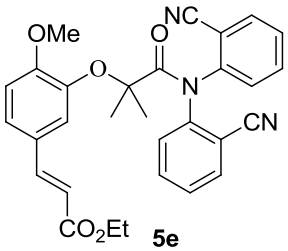
5c

5c: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86-7.59 (m, 6H), 7.51 (d, *J* = 15.6 Hz, 1H), 7.38 (br, 2H), 7.02 (s, 1H), 6.60 (s, 1H), 6.49 (s, 1H), 6.31 (d, *J* = 15.6 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 2.29 (s, 3H), 1.70 (s, 6H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.33, 166.81, 153.22, 145.42, 144.00, 139.69, 135.23, 133.74, 128.18, 124.74, 124.30, 118.54, 117.20, 83.67, 60.47, 26.80, 25.79, 21.22, 14.27; HRMS (ESI-TOF) *m/z* Calcd for $C_{30}H_{28}N_3O_4$ $(M+H)^+$: 494.2074, found: 494.2078.



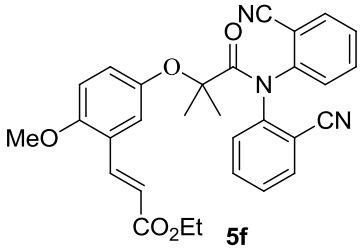
5d

5d: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 (d, *J* = 16.2 Hz, 1H), 7.80-7.52 (m, 6H), 7.38 (br, 2H), 7.02 (d, *J* = 7.8 Hz, 1H), 6.68 (d, *J* = 2.4 Hz, 1H), 6.64 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 6.19 (d, *J* = 15.6 Hz, 1H), 4.28 (q, *J* = 7.2 Hz, 2H), 2.34 (s, 3H), 1.68 (s, 6H), 1.35 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.37, 166.99, 150.99, 150.11, 145.73, 141.61, 139.77, 134.07, 133.76, 133.29, 132.69, 131.74, 131.33, 128.15, 126.83, 124.39, 121.28, 121.03, 120.37, 119.72, 118.31, 117.25, 83.92, 60.55, 26.42, 25.60, 19.00, 14.30; HRMS (ESI-TOF) *m/z* Calcd for $C_{30}H_{28}N_3O_4$ $(M+H)^+$: 494.2074, found: 494.2068.



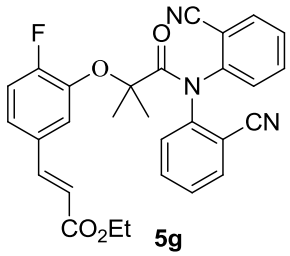
5e

5e: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90-7.51 (m, 7H), 7.35 (br, 2H), 7.20 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 6.95 (dd, *J* = 2.4 Hz, 1H), 6.81 (d, *J* = 8.4 Hz, 1H), 6.24 (d, *J* = 16.2 Hz, 1H), 4.25 (q, *J* = 7.2 Hz, 2H), 3.77 (s, 3H), 1.64 (s, 6H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.41, 167.09, 155.10, 145.56, 143.68, 142.16, 133.66, 127.91, 127.08, 125.71, 124.62, 123.90, 123.47, 120.61, 117.22, 116.32, 112.98, 112.05, 84.96, 60.33, 55.27, 26.43, 25.39, 14.30; HRMS (ESI-TOF) *m/z* Calcd for $C_{30}H_{28}N_3O_5$ $(M+H)^+$: 510.2023, found: 510.2016.



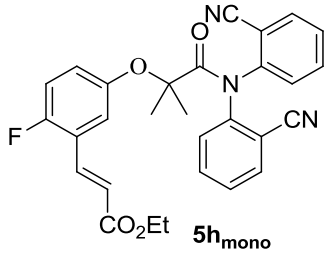
5f

5f: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89-7.53 (m, 7H), 7.38 (br, 2H), 6.72 (s, 2H), 6.23 (s, 1H), 6.37 (d, *J* = 16.2 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 3.82 (s, 3H), 1.65 (s, 6H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.41, 167.19, 154.90, 145.74, 139.19, 133.71, 129.50, 128.11, 125.79, 123.67, 122.91, 120.79, 119.23, 117.27, 111.44, 84.01, 60.38, 55.72, 26.26, 25.34, 14.31; HRMS (ESI-TOF) *m/z* Calcd for $C_{30}H_{28}N_3O_5$ $(M+H)^+$: 510.2023, found: 510.2015.



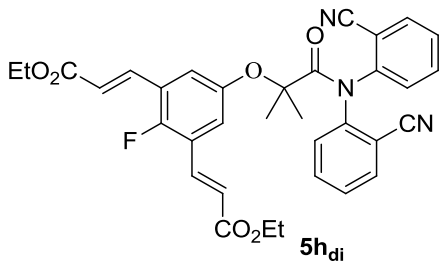
5g

5g: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93-7.59 (m, 6H), 7.54 (d, *J* = 15.6 Hz, 1H), 7.38 (br, 2H), 7.21-7.18 (m, 1H), 7.06 (d, *J* = 6.6 Hz, 1H), 6.99 (t, *J* = 3.0 Hz, 1H), 6.31 (d, *J* = 16.2 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 1.70 (s, 6H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.79, 166.63, 157.04 (d, *J* = 252.2 Hz), 145.56, 142.67 (d, *J* = 1.4 Hz), 140.31 (d, *J* = 12.5 Hz), 133.68, 131.05 (d, *J* = 3.6 Hz), 128.17, 125.38 (d, *J* = 1.7 Hz), 125.19 (d, *J* = 7.5 Hz), 118.71 (d, *J* = 2.3 Hz), 117.21, 117.09 (d, *J* = 20.4 Hz), 85.84, 60.58, 26.28, 25.29, 14.27; HRMS (ESI-TOF) *m/z* Calcd for $C_{29}H_{25}FN_3O_4$ $(M+H)^+$: 498.1824, found: 498.1818.



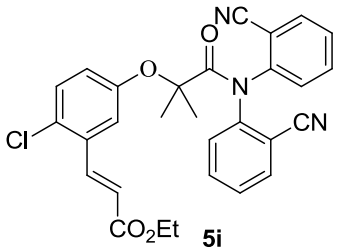
5h$_{mono}$

5h$_{mono}$: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80-7.55 (m, 7H), 7.39 (br, 2H), 6.94-6.91 (m, 1H), 6.71-6.68 (m, 2H), 6.41 (d, *J* = 16.2 Hz, 1H), 4.28 (q, *J* = 7.2 Hz, 2H), 1.67 (s, 6H), 1.35 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.09, 166.56, 157.78 (d, *J* = 249.8 Hz), 158.62, 156.95, 148.71 (d, *J* = 2.7 Hz), 145.65, 136.51 (d, *J* = 2.3 Hz), 133.78, 128.24, 125.84 (d, *J* = 8.6 Hz), 122.90 (d, *J* =13.7 Hz), 122.57 (d, *J* = 3.2 Hz), 121.35 (d, *J* = 6.6 Hz), 117.24, 116.57 (d, *J* = 23.6 Hz), 84.28, 60.70, 26.47, 25.50, 14.27; HRMS (ESI-TOF) *m/z* Calcd for $C_{29}H_{25}FN_3O_4$ $(M+H)^+$: 498.1824, found: 498.1817.



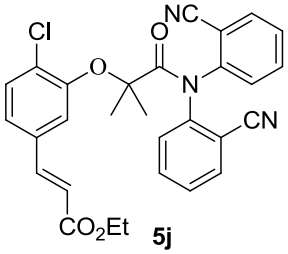
5h$_{di}$

5h$_{di}$: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95-7.60 (m, 8H), 7.41 (br, 2H), 6.79 (s, 1H), 6.78 (s, 1H), 6.43 (d, *J* = 16.2 Hz, 2H), 4.29 (q, *J* = 7.2 Hz, 4H), 1.69 (s, 6H), 1.35 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.88, 166.32, 156.08 (d, *J* = 256.8 Hz), 148.74 (d, *J* = 2.9 Hz), 145.63, 135.79 (d, *J* = 3.5 Hz), 133.84, 128.33, 123.91 (d, *J* = 5.3 Hz), 123.85 (d, *J* = 5.6 Hz), 122.19 (d, *J* = 5.9 Hz), 117.23, 84.53, 60.84, 26.60, 25.56, 14.28; HRMS (ESI-TOF) *m/z* Calcd for $C_{34}H_{31}FN_3O_6$ $(M+H)^+$: 596.2191, found: 596.2178.



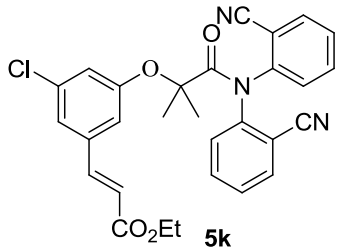
5i

5i: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 (d, *J* = 15.6 Hz, 1H), 7.82-7.50 (m, 6H), 7.39 (br, 2H), 7.24 (d, *J* = 8.4 Hz, 1H), 6.76 (d, *J* = 3.0 Hz, 1H), 6.70 (dd, J_1 = 8.4 Hz, J_2 = 3.0 Hz, 1H), 6.27 (d, *J* = 15.6 Hz, 1H), 4.29 (q, *J* = 7.2 Hz, 2H), 1.69 (s, 6H), 1.36 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.98, 166.25, 151.69, 145.55, 139.76, 133.82, 133.43, 130.63, 129.95, 128.30, 125.23, 121.44, 121.35, 117.23, 84.32, 60.77, 26.53, 25.70, 14.29; HRMS (ESI-TOF) *m/z* Calcd for $C_{29}H_{25}ClN_3O_4$ $(M+H)^+$: 514.1528, found: 514.1530.



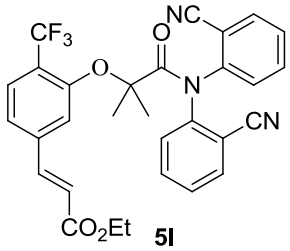
5j

5j: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81-7.48 (m, 7H), 7.38 (br, 2H), 7.28 (d, *J* = 8.4 Hz, 1H), 7.23 (d, *J* = 1.8 Hz, 1H), 7.16 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 6.41 (d, *J* = 16.2 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 1.77 (s, 6H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.01, 166.58, 149.64, 142.74, 133.77, 133.76, 133.74, 130.68, 129.25, 123.55, 122.30, 119.47, 117.17, 112.65, 85.11, 60.55, 27.19, 26.35, 14.24; HRMS (ESI-TOF) *m/z* Calcd for $C_{29}H_{25}ClN_3O_4$ $(M+H)^+$: 514.1528, found: 514.1521.



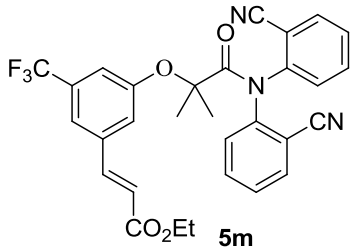
5k

5k: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83-7.53 (m, 6H), 7.49 (d, *J* = 15.6 Hz, 1H), 7.42-7.35 (m, 2H), 7.20 (t, *J* = 1.8 Hz, 1H), 6.67 (t, *J* = 1.8 Hz, 1H), 6.63 (t, *J* = 1.8 Hz, 1H), 6.35 (d, *J* = 15.6 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 1.72 (s, 6H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.82, 166.36, 154.00, 145.42, 142.33, 136.75, 134.97, 133.84, 128.34, 124.01, 123.39, 120.36, 120.09, 117.19, 84.54, 60.75, 26.64, 25.76, 14.27; HRMS (ESI-TOF) *m/z* Calcd for $C_{29}H_{25}ClN_3O_4$ $(M+H)^+$: 514.1528, found: 514.1519.



5l

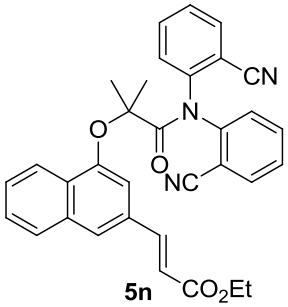
5l: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84-7.45 (m, 9H), 7.38 (br, 2H), 7.26 (d, *J* = 7.8 Hz, 1H), 6.58 (d, *J* = 16.2 Hz, 1H), 4.28 (q, *J* = 7.2 Hz, 2H), 1.79 (s, 6H), 1.35 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.21, 166.42, 152.33, 142.43, 139.28, 134.04, 133.29, 130.60, 128.88, 128.11, 127.29 (q, *J* = 4.9 Hz), 125.55, 124.19 (q, *J* = 288.2 Hz), 123.73, 122.64 (q, *J* = 30.3 Hz), 121.92, 121.62, 121.04, 119.95, 83.02, 60.68, 27.65, 26.77, 14.26; HRMS (ESI-TOF) *m/z* Calcd for $C_{30}H_{25}F_3N_3O_4$ $(M+H)^+$: 548.1792, found: 548.1785.



5m

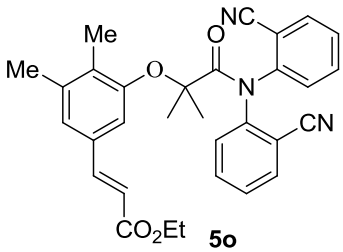
5m: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89-7.60 (m, 6H), 7.58 (d, *J* = 15.6 Hz, 1H), 7.45 (s, 1H), 7.43-7.40 (m, 2H), 7.02 (s, 1H), 6.71 (s, 1H), 6.43 (d, *J* = 16.2 Hz, 1H), 4.28 (q, *J* = 7.2 Hz, 2H), 1.75 (s, 6H), 1.35 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.69, 166.21, 153.76,

145.40, 142.08, 136.69, 133.86, 132.27 (q, *J* = 32.4 Hz), 129.78, 128.37, 124.44, 123.18 (q, *J* = 271.4 Hz), 120.91, 120.45 (q, *J* = 3.8 Hz), 119.86 (q, *J* = 3.6 Hz), 117.16, 84.64, 60.82, 26.70, 25.91, 14.25; HRMS (ESI-TOF) *m/z* Calcd for $C_{30}H_{25}F_3N_3O_4$ $(M+H)^+$: 548.1792, found: 548.1779.



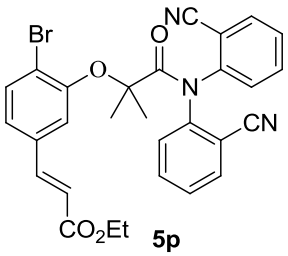
5n

5n: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82-7.12 (m, 15H), 6.50 (d, *J* = 16.2 Hz, 1H), 4.29 (q, *J* = 7.2 Hz, 2H), 1.85 (s, 6H), 1.35 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.39, 167.01, 149.93, 144.34, 134.32, 133.87, 131.96, 129.16, 128.18, 127.06, 126.72, 124.95, 122.77, 118.81, 117.19, 112.76, 112.07, 83.79, 60.52, 27.20, 26.82, 14.34; HRMS (ESI-TOF) *m/z* Calcd for $C_{33}H_{28}N_3O_4$ $(M+H)^+$: 530.2074, found: 530.2062.



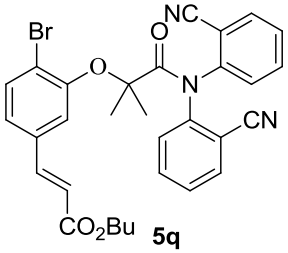
5o

5o: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82-7.45 (m, 7H), 7.37 (br, 2H), 7.04 (s, 1H), 6.76 (s, 1H), 6.33 (d, *J* = 16.2 Hz, 1H), 4.25 (q, *J* = 7.2 Hz, 2H), 2.22 (s, 3H), 1.94 (s, 3H), 1.70 (s, 6H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.59, 167.09, 151.51, 145.22, 144.33, 138.79, 136.89, 133.83, 132.70, 131.80, 128.01, 126.91, 124.44, 124.00, 118.33, 117.56, 117.21, 112.85, 83.84, 60.40, 26.87, 26.40, 20.31, 14.32, 13.30; HRMS (ESI-TOF) *m/z* Calcd for $C_{31}H_{30}N_3O_4$ $(M+H)^+$: 508.2231, found: 508.2224.



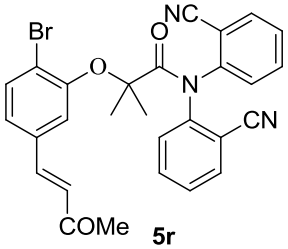
5p

5p: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83-7.50 (m, 7H), 7.46 (d, *J* = 8.4 Hz), 7.39 (br, 2H), 7.26 (d, *J* = 1.8 Hz, 1H), 7.08 (dd, J_1 = 8.4 Hz, J_2 = 1.8 Hz, 1H), 6.45 (d, *J* = 15.6 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 1.80 (s, 6H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.04, 166.64, 150.99, 142.88, 134.82, 133.85, 133.79, 123.42, 121.16, 119.62, 118.43, 117.20, 112.59, 84.59, 60.57, 27.42, 26.79, 14.27; HRMS (ESI-TOF) *m/z* Calcd for $C_{29}H_{25}BrN_3O_4$ $(M+H)^+$: 558.1023, found: 558.1005.



5q

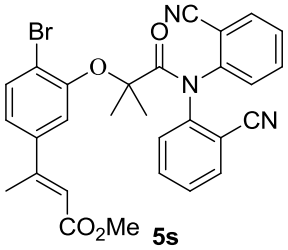
5q: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84-7.49 (m, 7H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.39 (br, 2H), 7.26 (s, 1H), 7.09 (dd, J_1 = 8.4 Hz, J_2 = 1.8 Hz, 1H), 6.44 (d, *J* = 16.2 Hz, 1H), 4.21 (t, *J* = 6.6 Hz, 2H), 1.80 (s, 6H), 1.72-1.67 (m, 2H), 1.47-1.43 (m, 2H), 0.97 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.06, 166.76, 151.00, 142.86, 134.86, 133.87, 133.80, 123.40, 121.22, 119.65, 118.44, 117.22, 112.62, 84.62, 64.52, 30.70, 27.46, 26.76, 19.16, 13.75; HRMS (ESI-TOF) *m/z* Calcd for $C_{31}H_{29}BrN_3O_4$ $(M+H)^+$: 586.1336, found: 586.1320.



5r

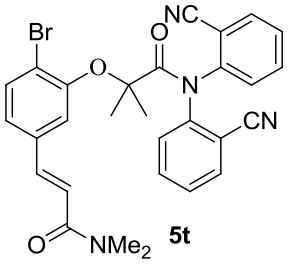
5r: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86-7.49 (m, 7H), 7.44 (s, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.39 (br, 2H), 7.12 (dd, J_1 = 8.4 Hz, J_2 = 1.8 Hz, 1H), 6.73 (d, *J* = 16.8 Hz, 1H), 2.41 (s, 3H), 1.84 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.87, 174.62, 151.02, 142.21, 135.00, 133.86, 133.76,

128.36, 122.69, 121.21, 117.92, 84.07, 27.68, 27.32, 26.86; HRMS (ESI-TOF) *m/z* Calcd for $C_{28}H_{23}BrN_3O_3$ $(M+H)^+$: 528.0917, found: 528.0904.



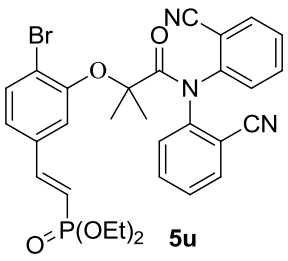
5s

5s: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77-7.51 (m, 6H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.41-7.37 (m, 2H), 7.11 (d, *J* = 2.0 Hz, 1H), 7.02 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1H), 6.10 (d, *J* = 1.6 Hz, 1H), 3.75 (s, 3H), 2.53 (d, *J* = 1.6 Hz, 3H), 1.78 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.06, 166.95, 154.01, 150.71, 142.41, 133.90, 133.44, 128.32, 122.38, 120.31, 117.63, 117.50, 117.19, 112.74, 84.91, 51.21, 27.37, 26.58, 17.89; HRMS (ESI-TOF) *m/z* Calcd for $C_{29}H_{25}BrN_3O_4$ $(M+H)^+$: 558.1023, found: 558.1023.



5t

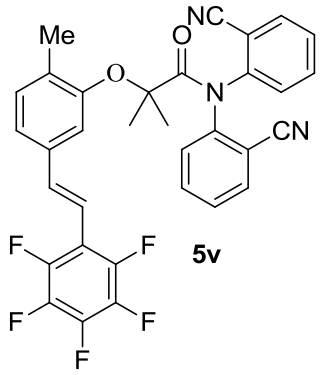
5t: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84-7.46 (m, 7H), 7.45-7.34 (m, 4H), 7.07 (d, *J* = 12.0 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 3.19 (s, 3H), 3.06 (s, 3H), 1.81 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.85, 166.57, 150.96, 140.26, 135.84, 133.51, 124.99, 120.08, 119.40, 117.82, 84.54, 37.51, 35.96, 28.48, 26.73; HRMS (ESI-TOF) *m/z* Calcd for $C_{29}H_{26}BrN_4O_3$ $(M+H)^+$: 557.1183, found: 557.1168.



5u

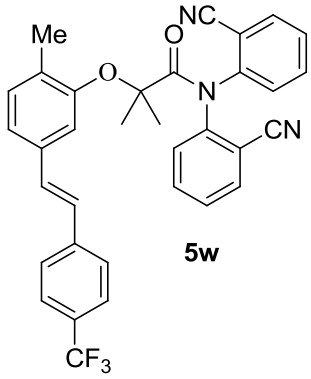
5u: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88-7.48 (m, 6H), 7.47-7.35 (m, 4H), 7.31 (s, 1H), 7.05 (dd, J_1 = 8.4 Hz, J_2 = 1.8 Hz, 1H), 6.35 (t, *J* = 17.4 Hz, 1H), 4.17-4.12 (m, 4H), 1.80 (s, 6H), 1.36 (t, *J*

= 7.2 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.22, 150.98, 146.77, 135.32, 135.16, 133.76, 133.67, 123.35, 120.61, 118.42, 117.14, 116.21, 114.96, 84.48, 61.95, 27.84, 26.64, 16.34; HRMS (ESI-TOF) *m/z* Calcd for $C_{30}H_{30}BrN_3O_5P$ $(M+H)^+$: 622.1101, found: 622.1090.



5v

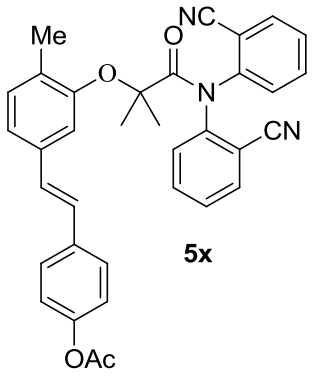
5v: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84-7.49 (m, 6H), 7.45-7.33 (m, 3H), 7.15 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 7.05 (s, 1H), 6.91 (d, *J* = 16.8 Hz, 1H), 1.92 (s, 3H), 1.77 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.9, 152.0, 145.6 (br), 144.8 (brm), 143.9 (br), 140.4 (br), 138.6 (brm), 136.8, 135.2, 133.9, 133.1, 131.5, 131.3, 130.4 (brm), 128.2 (br), 120.9, 118.9, 117.2, 112.8, 112.4, 112.4, 83.1, 27.6, 26.9, 16.7; HRMS (ESI-TOF) *m/z* Calcd for $C_{33}H_{23}F_5N_3O_2$ $(M+H)^+$: 588.1705, found: 588.1733.



5w

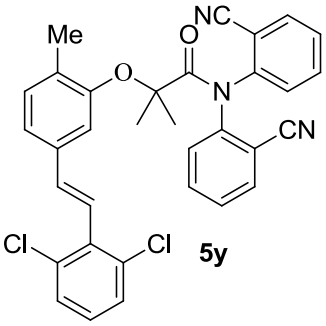
5w: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87-7.30 (brm, 13H), 7.22 (d, *J* = 16.5 Hz, 1H), 7.15 (s, 1H), 7.10 (d, *J* = 16.6 Hz, 1H), 7.03 (d, *J* = 7.8 Hz, 1H), 1.87 (s, 3H), 1.81 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 175.0, 152.1, 144.7 (brm), 141.0, 135.3, 133.8, 133.0 (br), 131.1, 130.8, 130.2, 128.2 (br), 126.7, 126.6, 126.1 (q, *J* =270.6 Hz,), 125.5, 123.4, 120.6, 118.3, 117.3 (br), 112.7

(br), 82.8, 27.7, 27.2, 16.6; HRMS (ESI-TOF) *m/z* Calcd for $C_{34}H_{27}F_3N_3O_2$ $(M+H)^+$: 566.2050, found: 566.2070.



5x

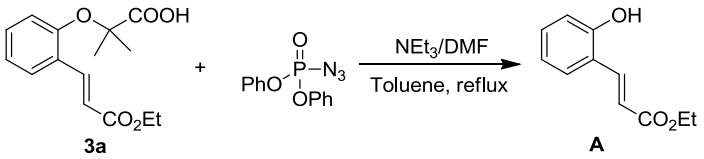
5x: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85-7.30 (m, 10H), 7.11 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.09 – 7.03 (m, 5H), 7.02 (d, *J* = 7.6 Hz, 1H), 2.31 (s, 4H), 1.89 (s, 3H), 1.79 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.9, 169.5, 151.9, 149.9, 144.8, 135.8, 135.2, 133.8, 133.0, 131.1, 130.4, 129.8, 128.5, 128.1, 127.4, 127.2, 121.7, 120.5, 118.3, 117.3, 112.8, 82.9, 77.2, 77.0, 76.8, 27.2, 21.1, 16.6; HRMS (ESI-TOF) *m/z* Calcd for $C_{35}H_{30}N_3O_4$ $(M+H)^+$: 556.2231, found: 556.2238.



5y

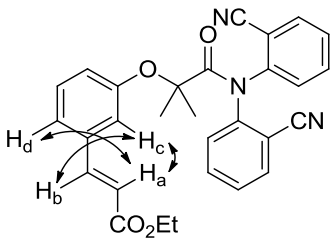
5y: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80-7.49 (brm, 6H), 7.45-7.30 (brm, 4H), 7.20-7.06 (m, 4H), 7.01 (d, *J* = 16.6 Hz, 1H), 6.93 (s, 1H), 1.99 (s, 3H), 1.76 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.7, 151.9, 136.5, 135.4, 134.6, 133.8, 131.3, 131.2, 128.5, 128.2, 127.9, 122.2, 121.2, 119.1, 117.2, 113.0, 83.5, 26.9, 16.8; HRMS (ESI-TOF) *m/z* Calcd for $C_{33}H_{26}Cl_2N_3O_2$ $(M+H)^+$: 566.1396, found: 566.1396.

2.5 Procedure for removal of template.[4]

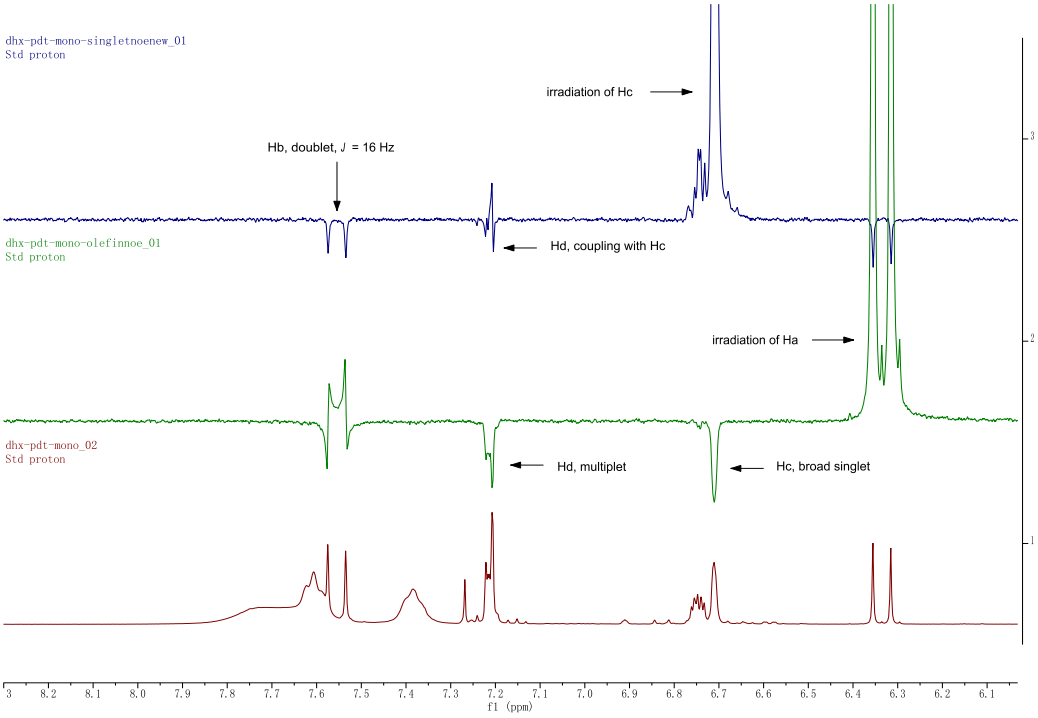


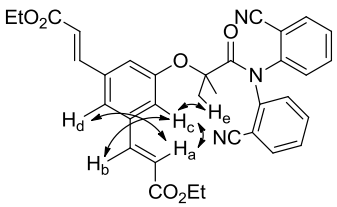
To a 50 mL of flask, **3a** (111.2 mg, 0.4 mmol) was dissolved in anhydrous toluene (5 mL) and DMF (0.5 mL), then Et_3N (46.4 mg, 0.4 mmol) and DPPA (110 mg, 0.4 mmol) were added and the mixture was refluxed for 3h. 30 mL of water was added and continue to reflux for 2h. After the mixture cool to room temperature, the solution was acidified with 2N HCl solution (5 mL) and extracted with EtOAc(3 x 5 mL). The combined organic phases were washed with brine, dried over anhydrous $MgSO_4$ and evaporated. The residue was purified via column chromatography on silica with hexane and EtOAc (10:1) as eluents to afford product **A**[5] in 71% yield (54.3 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05 (d, *J* = 16.2 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.26–7.21 (m, 1H), 6.93–6.85 (m, 2H), 6.80 (br, 1H), 6.65 (d, *J* = 16.2 Hz, 1H), 4.30 (q, *J* = 7.2 Hz, 2H), 1.35 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (600 MHz, $CDCl_3$) δ: 169.3, 158.3, 141.5, 132.2, 130.1, 122.6, 121.5, 119.2, 117.3, 61.6, 15.2.

2.6 Determination of regioselectivity (1D selective NOESY).

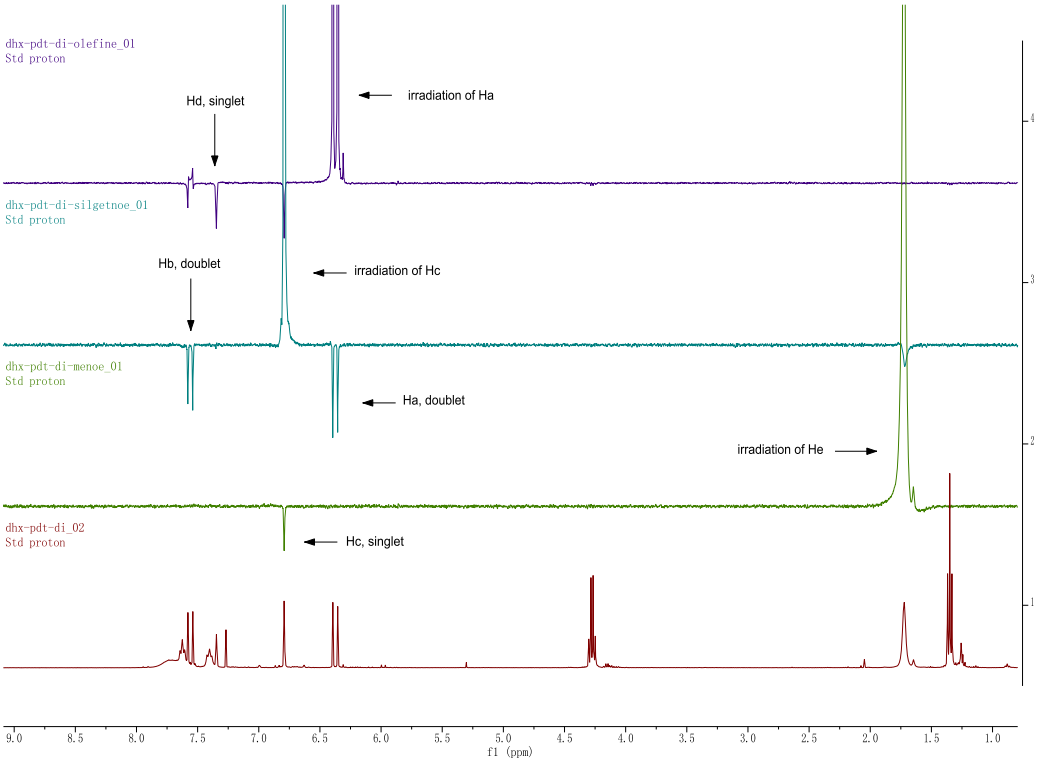


5a$_{mono}$



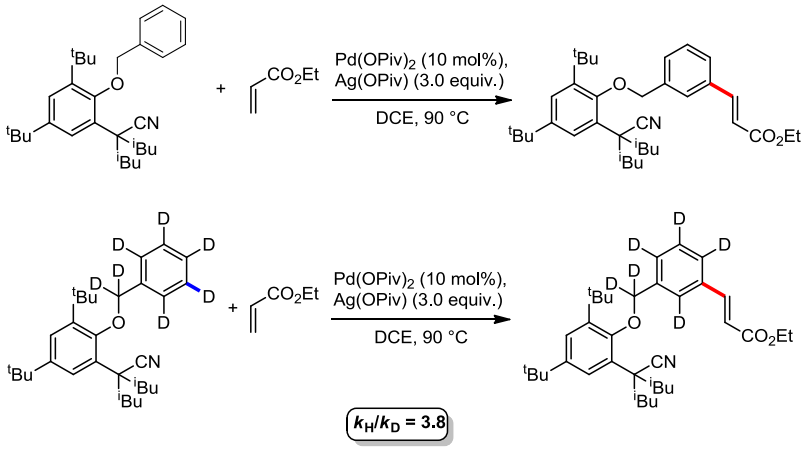

EtO2C
NC
O
O
N
Hd
Hc
He
NC
Ha
Hb
CO2Et

5a$_{di}$


dhx-pdt-di-olefine_01
Std proton
Hd, singlet
irradiation of Ha
dhx-pdt-di-silgetnoe_01
Std proton
Hb, doublet
irradiation of Hc
dhx-pdt-di-menoe_01
Std proton
Ha, doublet
irradiation of He
dhx-pdt-di_02
Std proton
Hc, singlet
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

2.7 Isotope effect

Following the experimental procedure reported previously,[3] we have measured the kinetic isotope effects with an analogous substrate. The significant isotope effect observed (k_H/K_D = 3.8) suggests that the nitrile directed *meta*-C–H olefination involves C–H cleavage as the rate-determining step.



3. References

(1) Gorvin, J. H. *J. Chem.Soc., Perkin Trans.1*, **1988**, 1331.

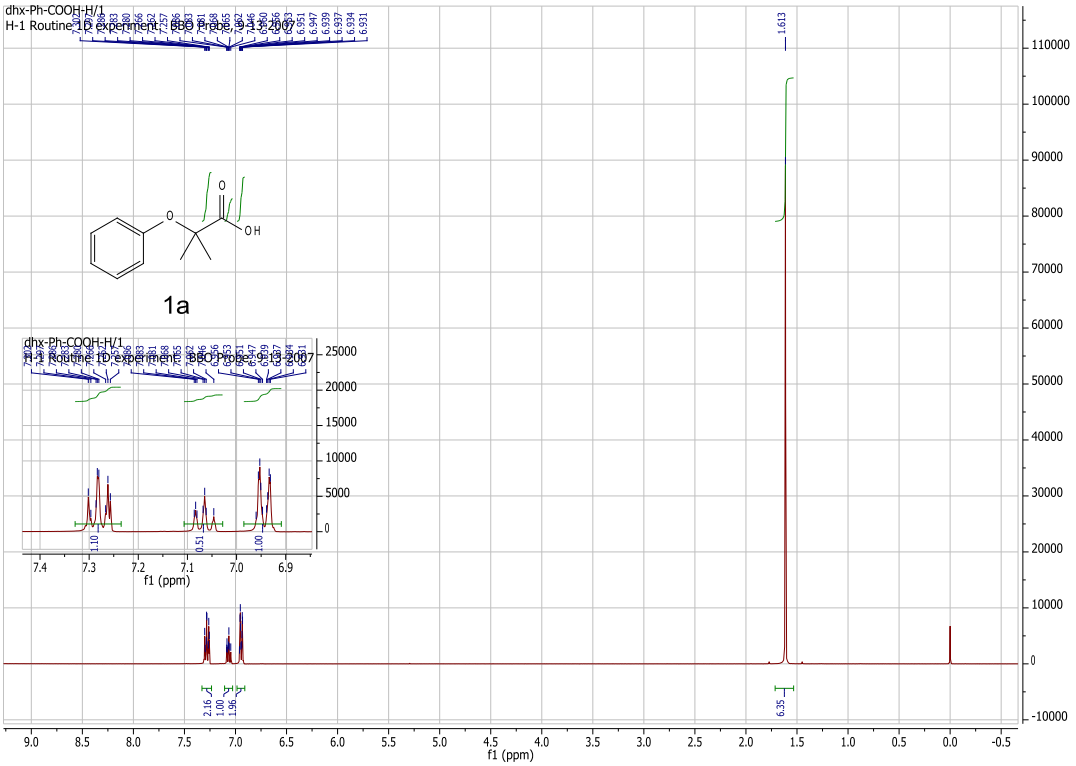
(2) Oh, L. M.; H. Wang, Shilcrat, S. C.; Herrmann, R. E.; Patience, D. B.; Spoors, P. G.; Sisko, J. *Org. Process Res. Dev.* **2007**, *11*, 1032.

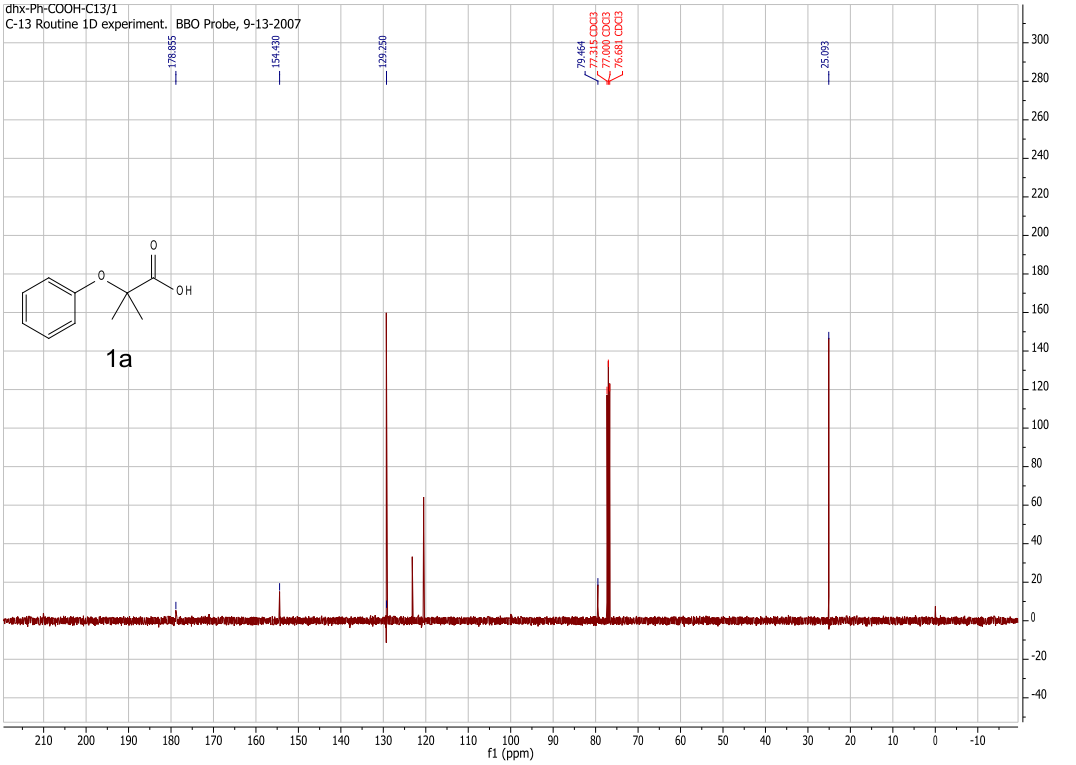
(3) Leow, D.; Li, G.; Mei, T.-S. Yu, J.-Q. *Nature* **2012**, *486*, 518.

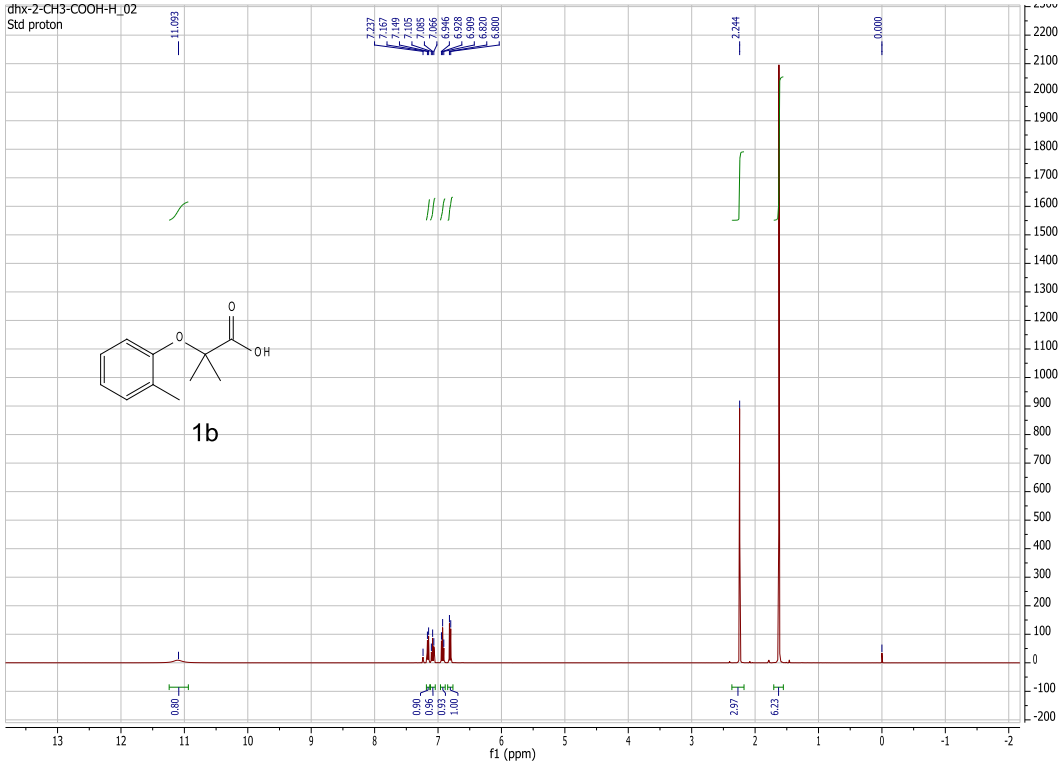
(4) Mirk, D.; Waldvogel, S. R. *Tetrahedron Lett.* **2004**, *45*, 7911.

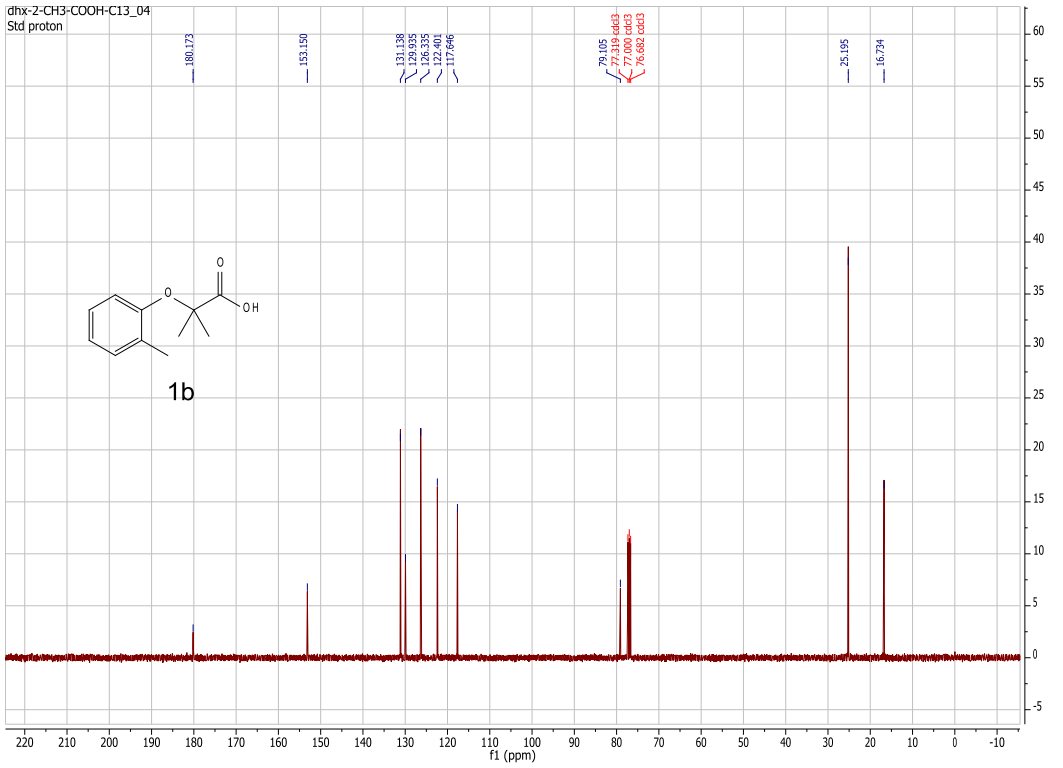
(5) Park, J. O.; Youn, S. W. *Org. Lett.* **2010**, *12*, 2258.

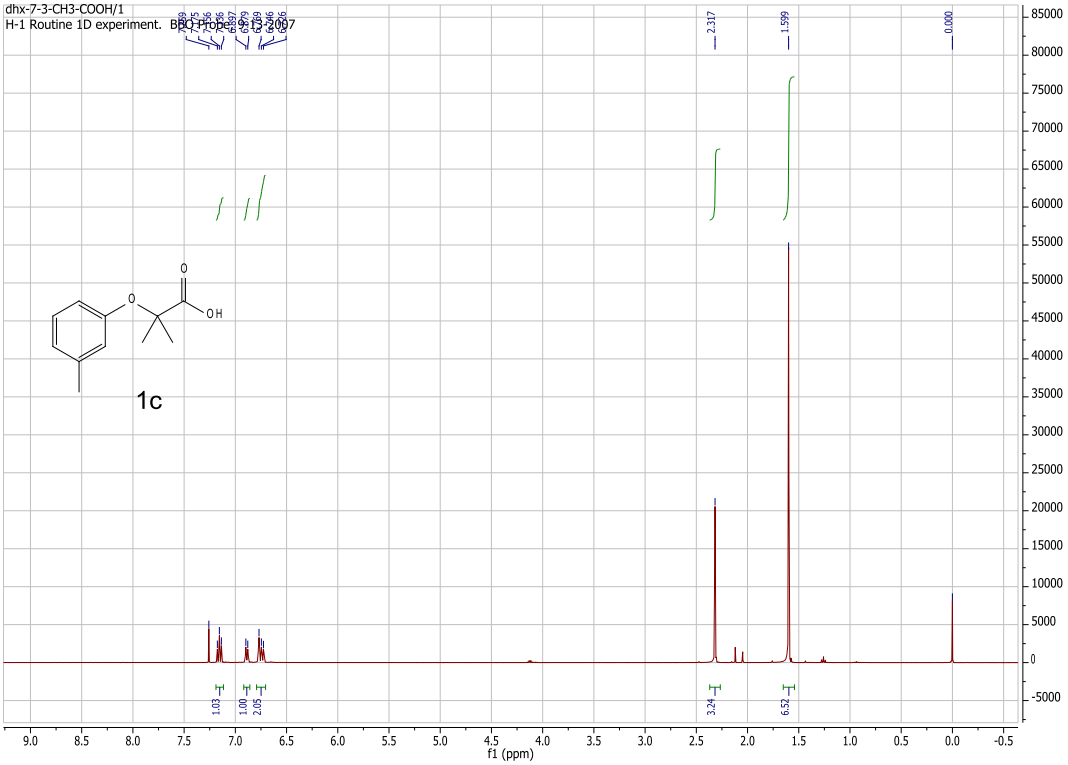
4. NMR Spectra for New Compounds

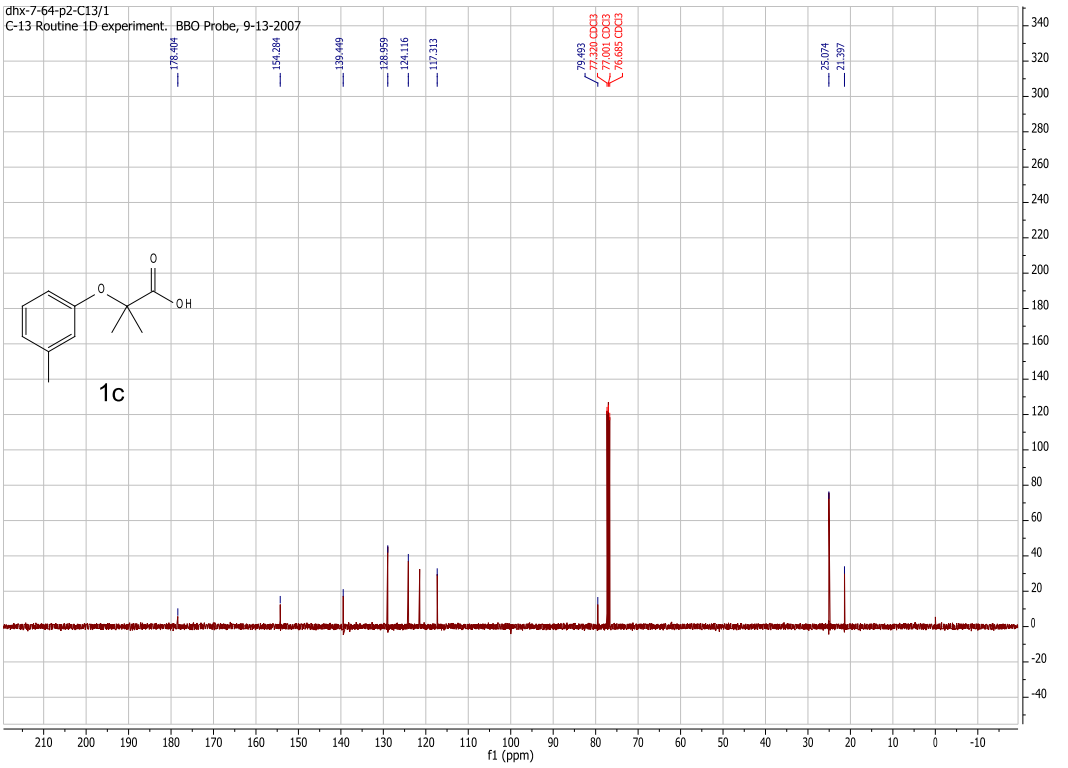


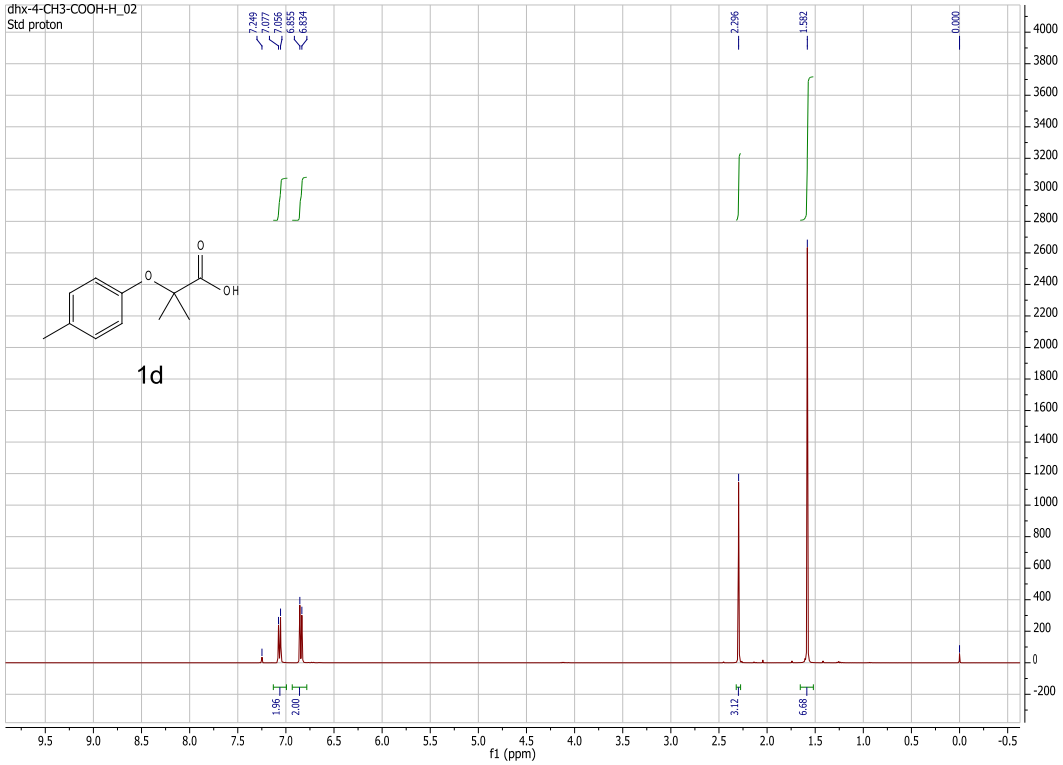


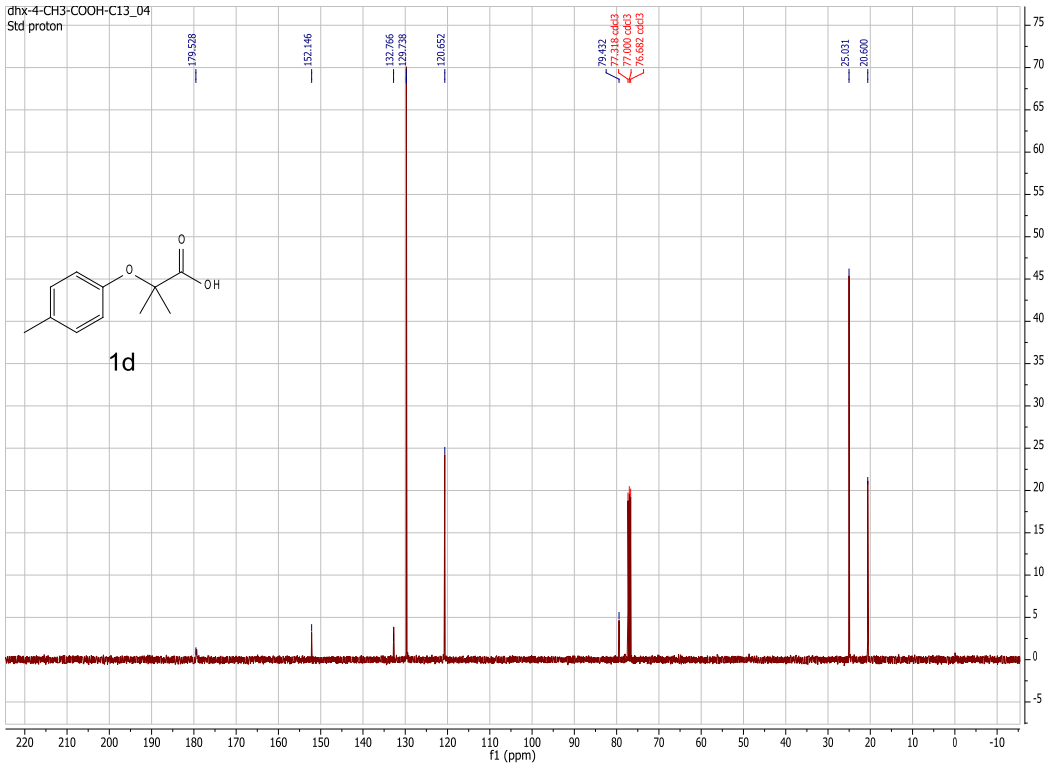

dhx-2-CH3-COOH-H_02
Std proton
11.093
7.237
7.167
7.149
7.105
7.085
6.946
6.928
6.909
6.820
6.800
2.244
0.000
OH
1b
0.80
0.91
0.96
0.93
1.00
2.97
6.23
f1 (ppm)

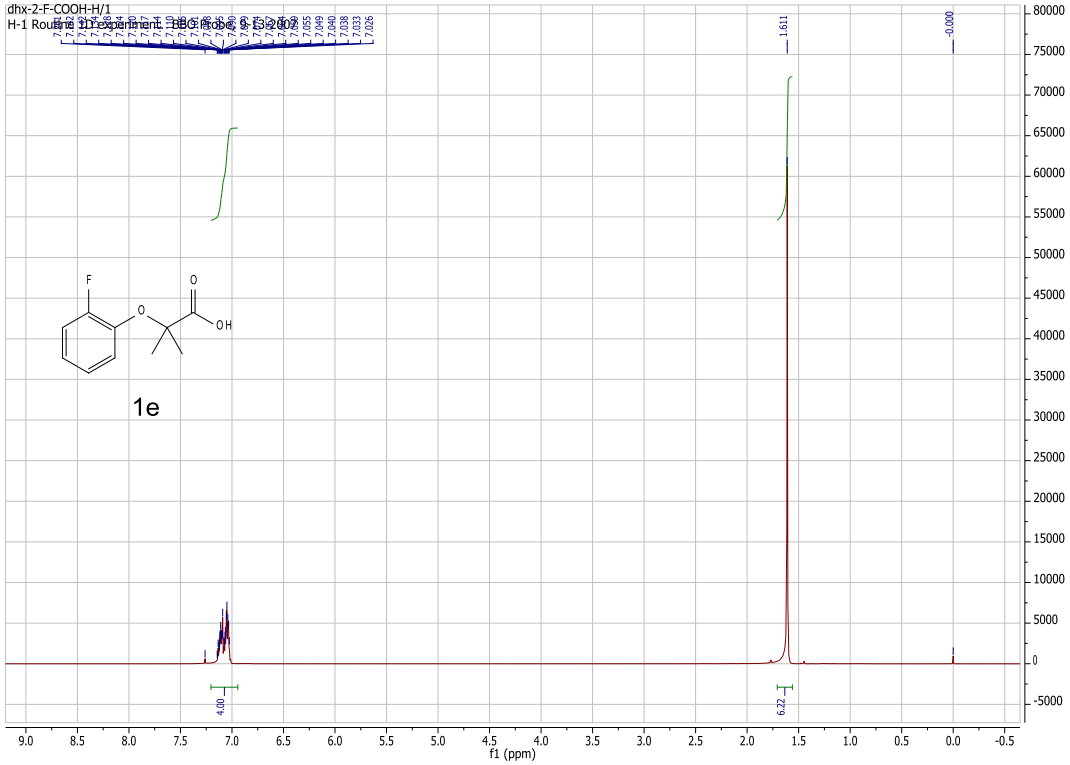

dhx-2-CH3-COOH-C13_04
Std proton
180.173
153.150
131.138
129.935
126.335
122.401
117.646
79.105
77.319 cdcl3
77.000 cdcl3
76.682 cdcl3
25.195
16.734
OH
1b
f1 (ppm)

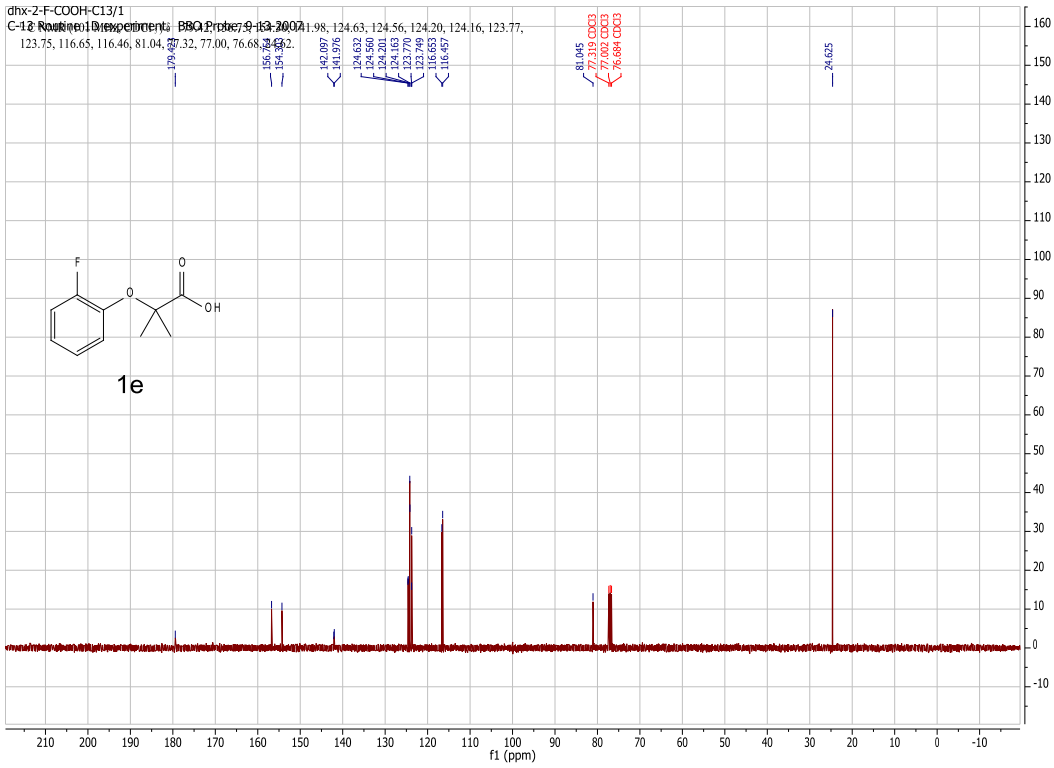

dhx-7-3-CH3-COOH/1
H-1 Routine 1D experiment. BBO Probe, 9-13-2007
2.317
1.599
0.000
1.03
1.00
2.05
3.24
6.52
1c
f1 (ppm)

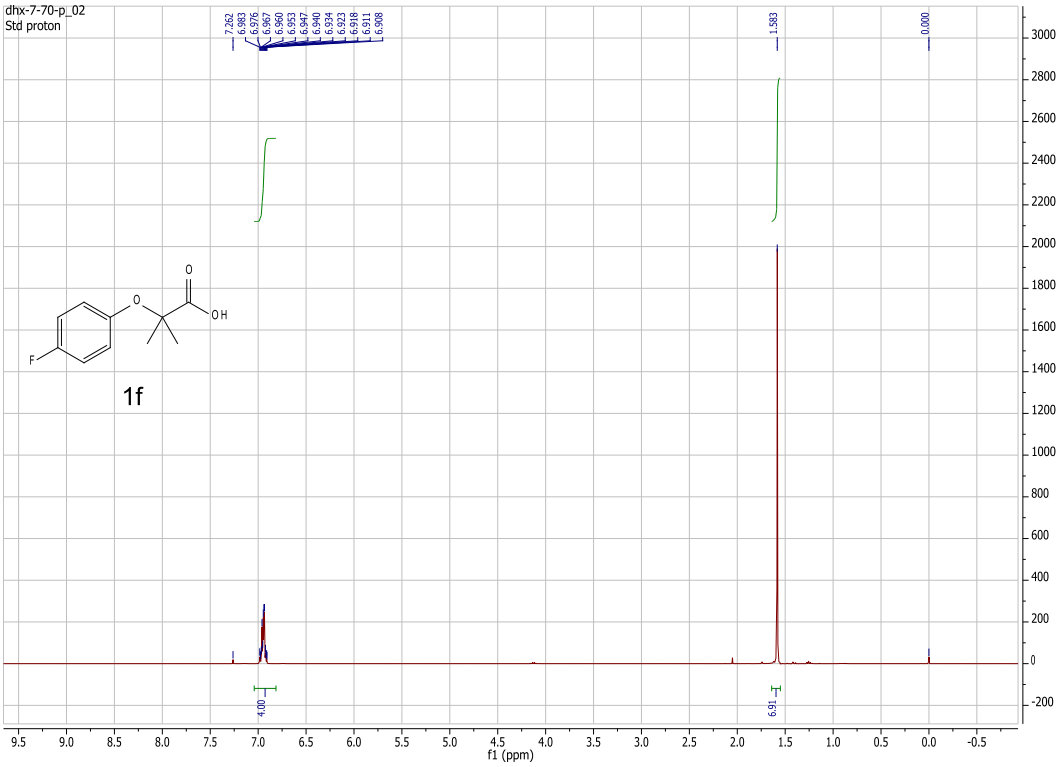

dhx-7-64-p2-C13/1
C-13 Routine 1D experiment. BBO Probe, 9-13-2007
178.404
154.284
139.449
128.959
124.116
117.313
79.493
77.320 CDCl3
77.001 CDCl3
76.685 CDCl3
25.074
21.397
1c
f1 (ppm)

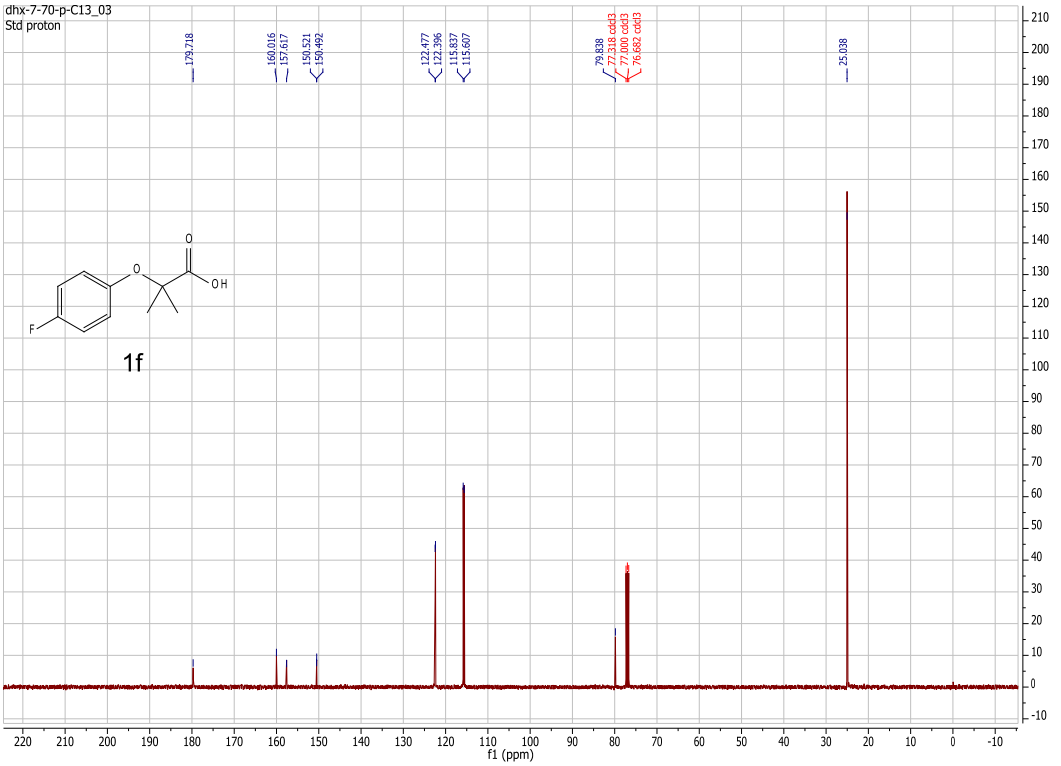

dhx-4-CH3-COOH-H_02
Std proton
7.249
7.077
7.057
6.855
6.834
2.296
1.582
0.000
1.96
2.00
3.12
6.68
f1 (ppm)
1d

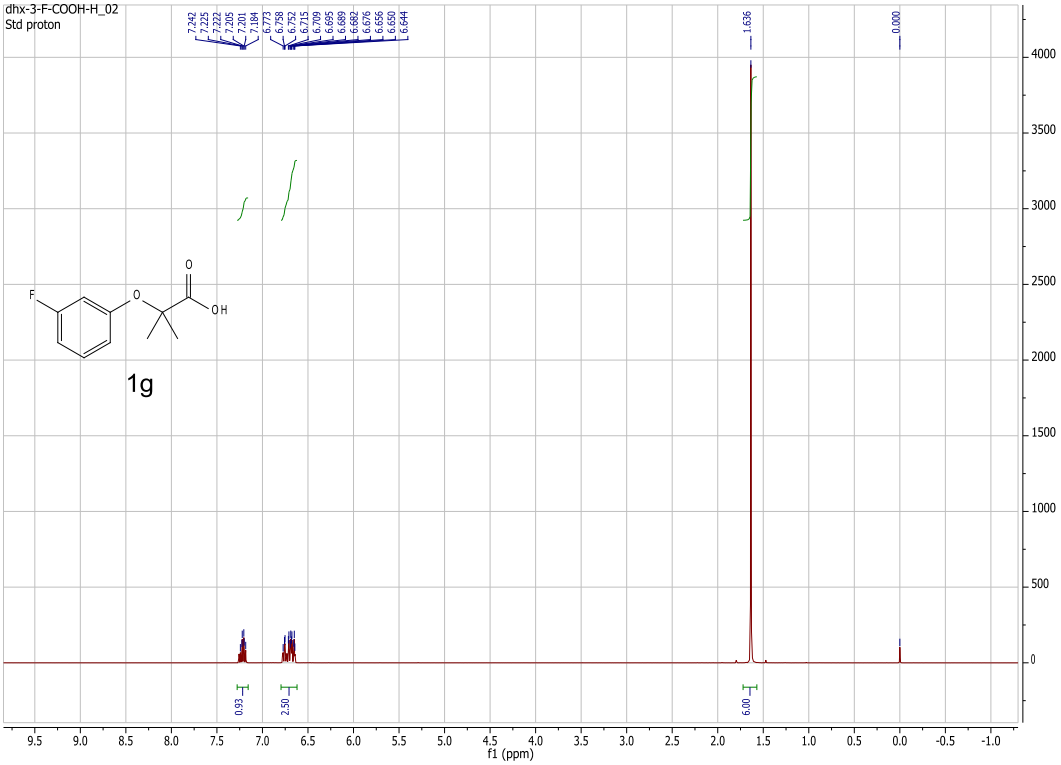

dhx-4-CH3-COOH-C13_04
Std proton
179.528
152.146
132.766
129.738
120.652
79.432
77.316 cdcl3
77.000 cdcl3
76.682 cdcl3
25.031
20.600
f1 (ppm)
1d

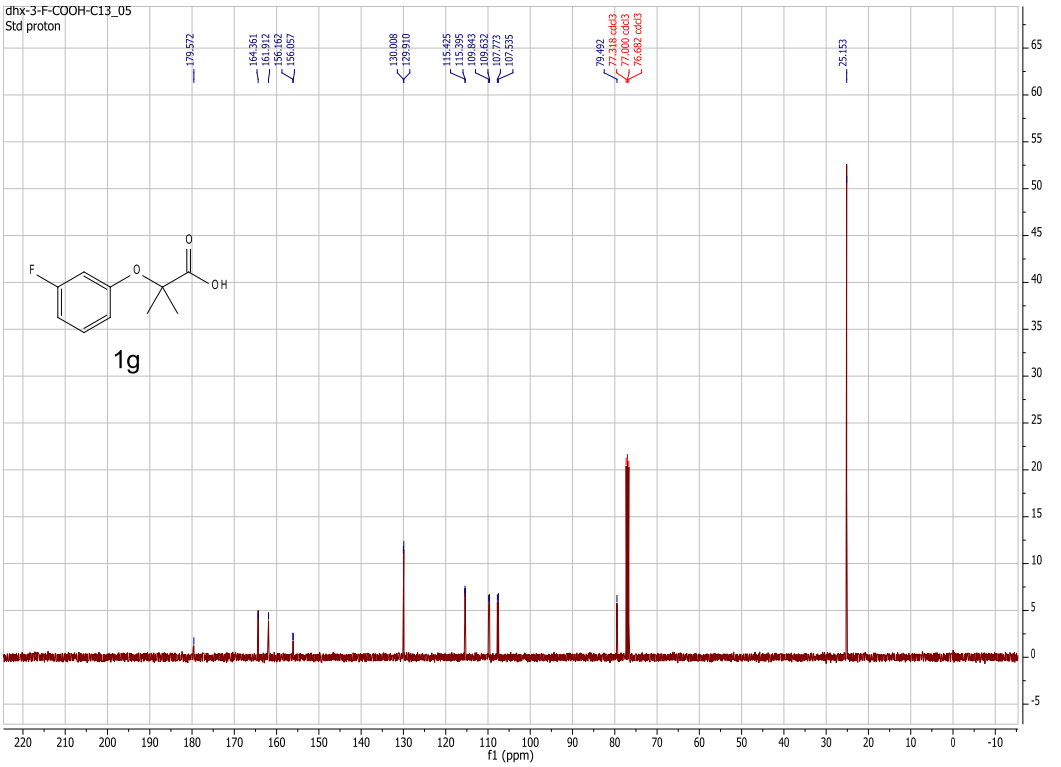

dhx-2-F-COOH-H/1
1e
f1 (ppm)

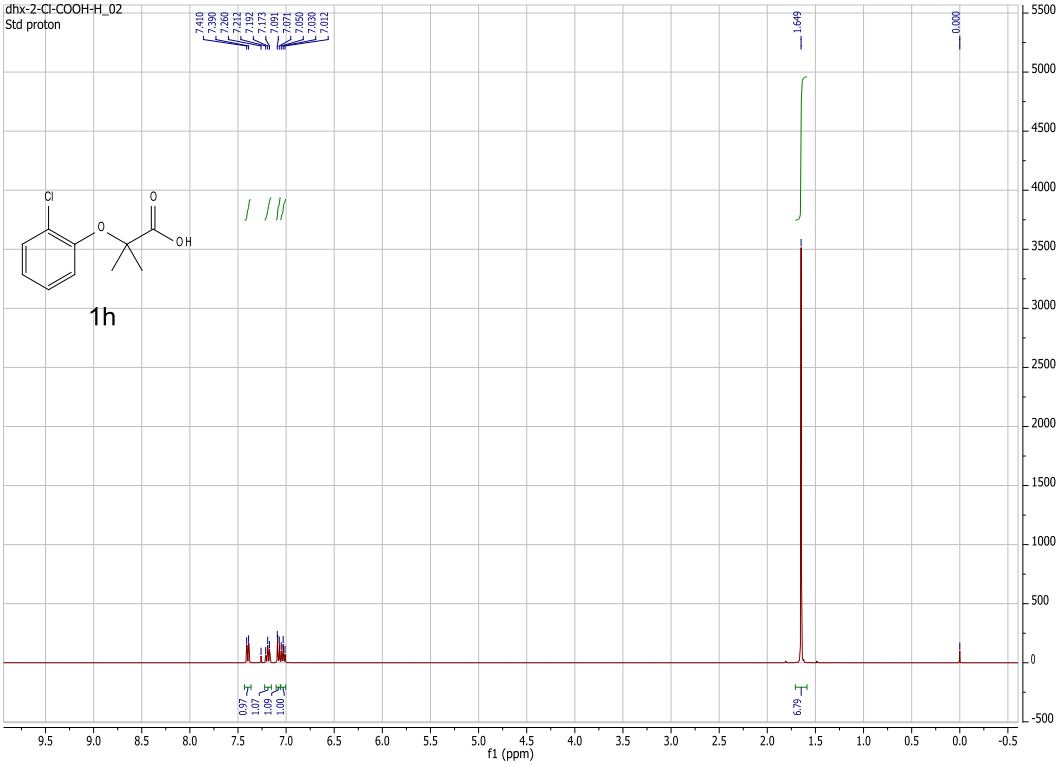

dhx-2-F-COOH-C13/1
1e
f1 (ppm)

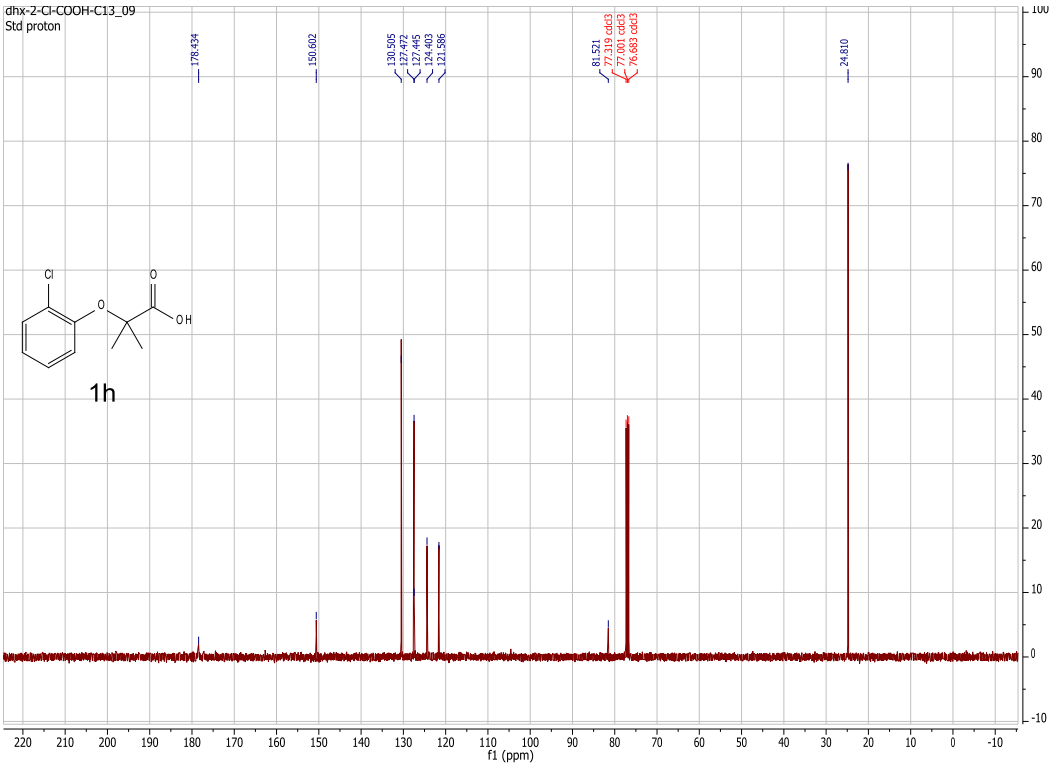

dhx-7-70-p_02
Std proton
7.262
6.983
6.976
6.967
6.960
6.953
6.947
6.940
6.934
6.923
6.918
6.911
6.908
1.583
0.000
4.00
6.91
f1 (ppm)
1f

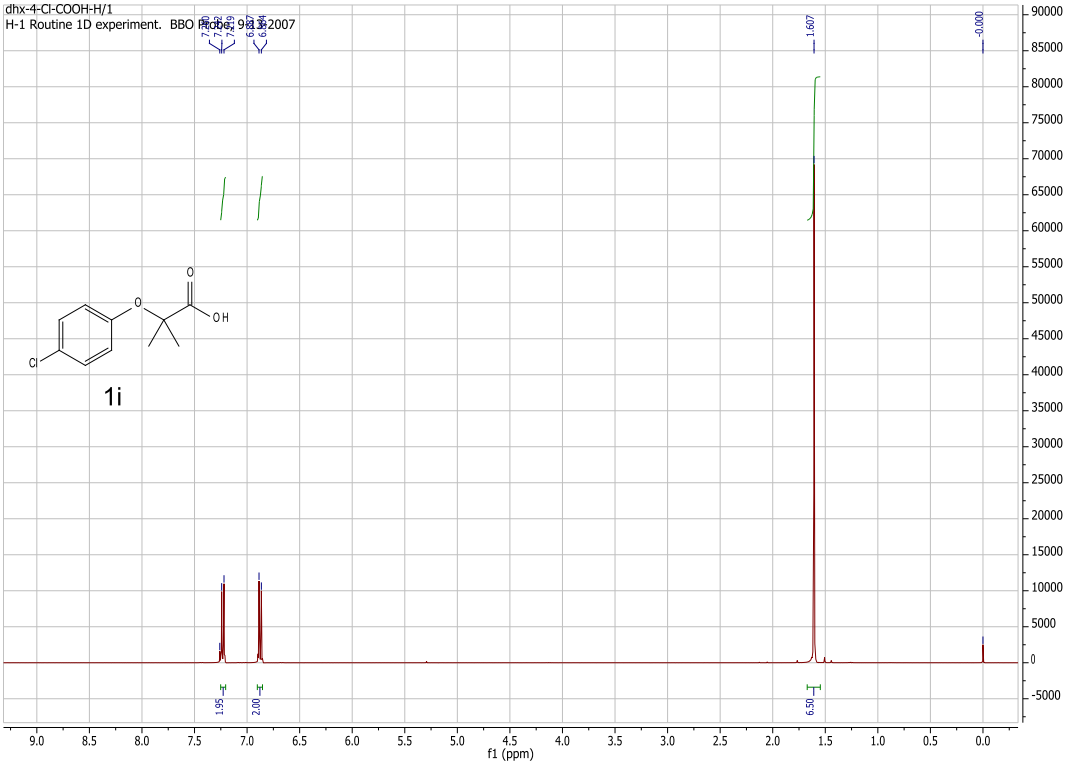

dhx-7-70-p-C13_03
Std proton
179.718
160.016
157.617
150.521
150.492
122.477
122.396
115.837
115.607
79.838
77.318 cdcl3
77.000 cdcl3
76.682 cdcl3
25.038
f1 (ppm)
1f

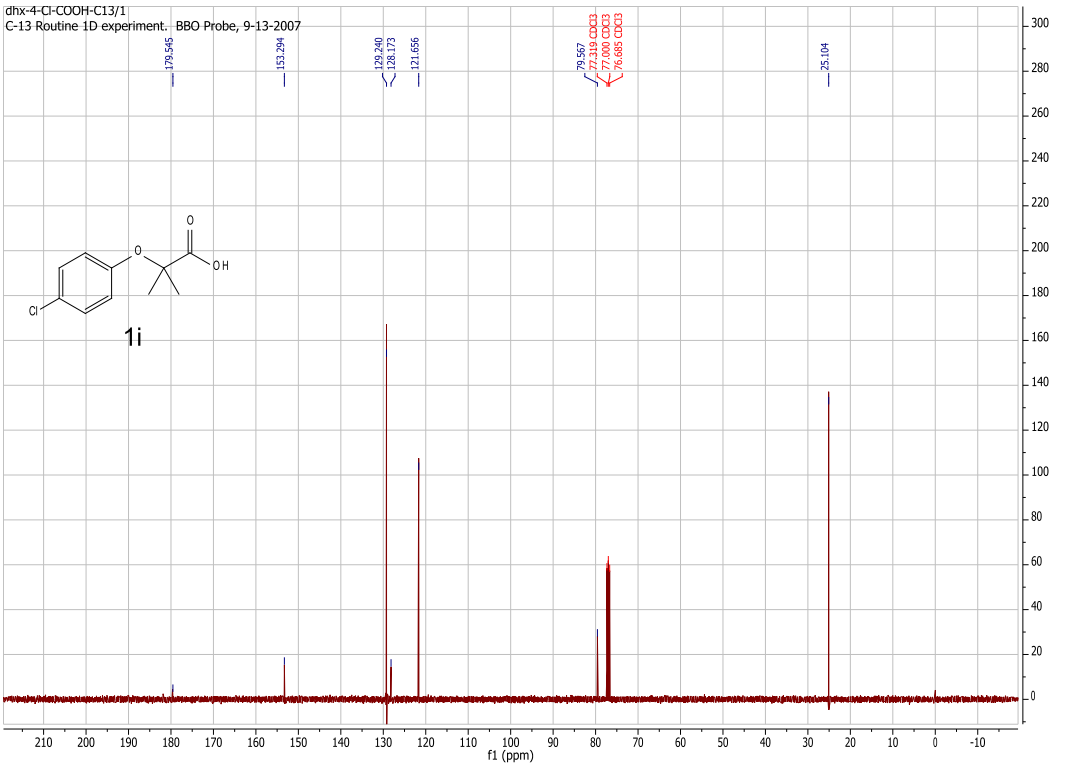

dhx-3-F-COOH-H_02
Std proton
1g
f1 (ppm)

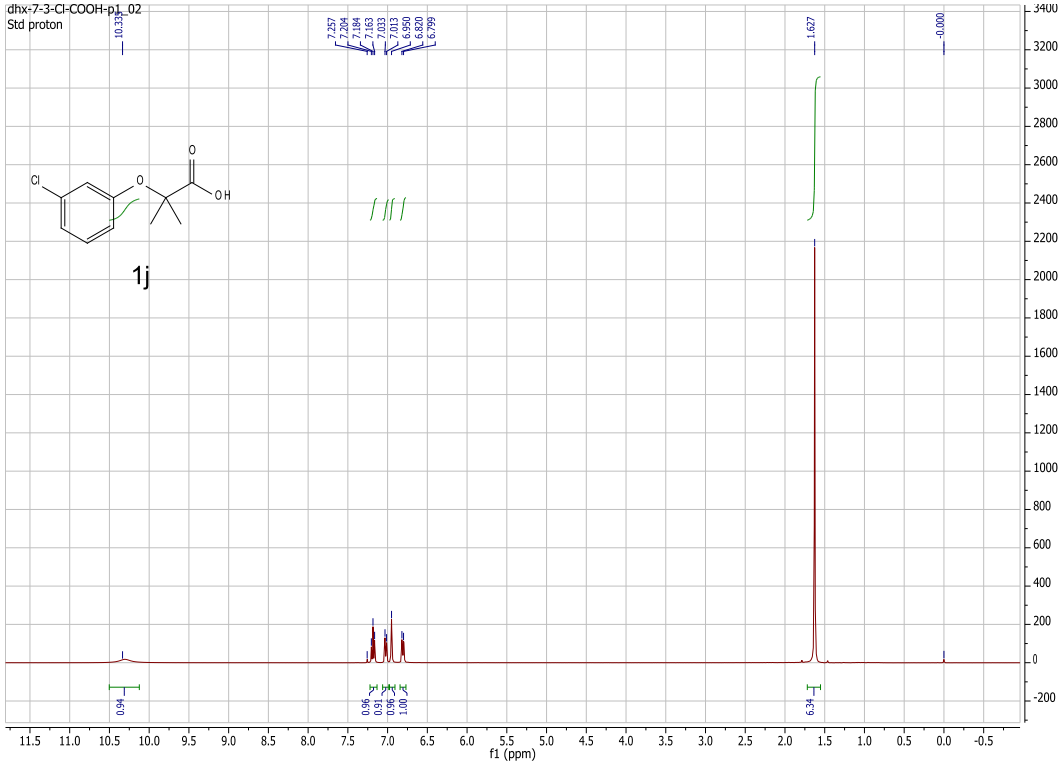

dhx-3-F-COOH-C13_05
Std proton
1g
f1 (ppm)

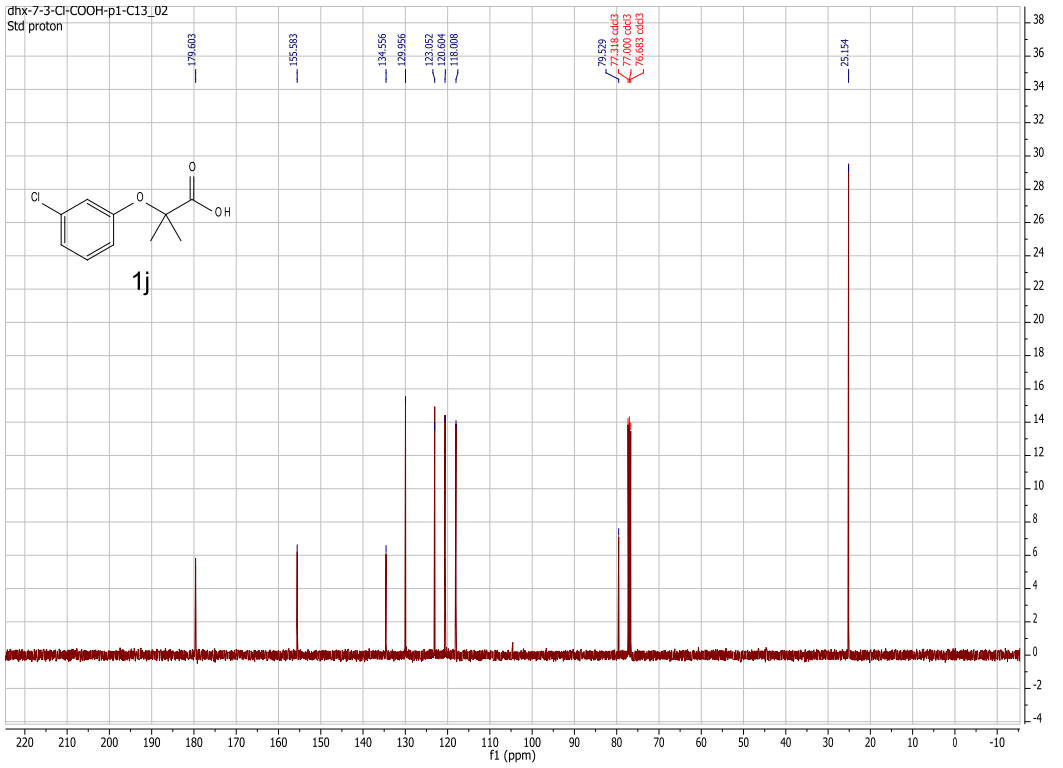

dhx-2-Cl-COOH-H_02
Std proton
7.410
7.390
7.260
7.212
7.192
7.173
7.091
7.071
7.050
7.030
7.012
1.649
0.000
Cl
O
O
OH
1h
0.97
1.07
1.09
1.00
6.79
f1 (ppm)


dhx-2-Cl-COOH-C13_09
Std proton
178.434
150.602
130.505
127.472
124.745
124.403
121.586
81.521
77.319 cdcl3
77.001 cdcl3
76.683 cdcl3
24.810
Cl
O
O
OH
1h
f1 (ppm)


dhx-4-Cl-COOH-H/1
H-1 Routine 1D experiment. BBO Probe, 9-13-2007
1.607
0.000
1.95
2.00
6.50
f1 (ppm)
1i


dhx-4-Cl-COOH-C13/1
C-13 Routine 1D experiment. BBO Probe, 9-13-2007
179.545
153.294
129.240
128.173
121.656
79.567
77.319 CDCl3
77.000 CDCl3
76.685 CDCl3
25.104
f1 (ppm)
1i


dhx-7-3-Cl-COOH-p1_02
Std proton
10.333
7.257
7.204
7.184
7.163
7.033
7.013
6.950
6.930
6.799
1.627
-0.000
Cl
O
O
OH
1j
0.94
0.96
0.94
1.98
1.00
6.34
f1 (ppm)


dhx-7-3-Cl-COOH-p1-C13_02
Std proton
179.603
155.583
134.556
129.956
123.052
120.604
118.008
79.529
77.318 cdcl3
77.000 cdcl3
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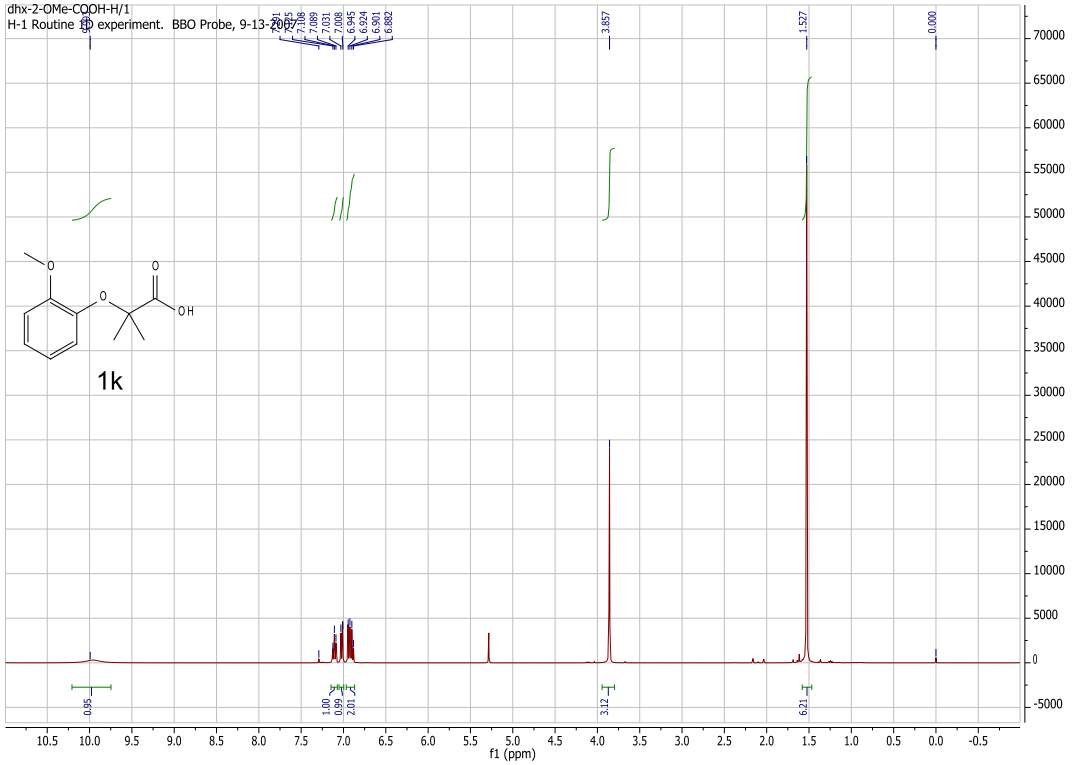
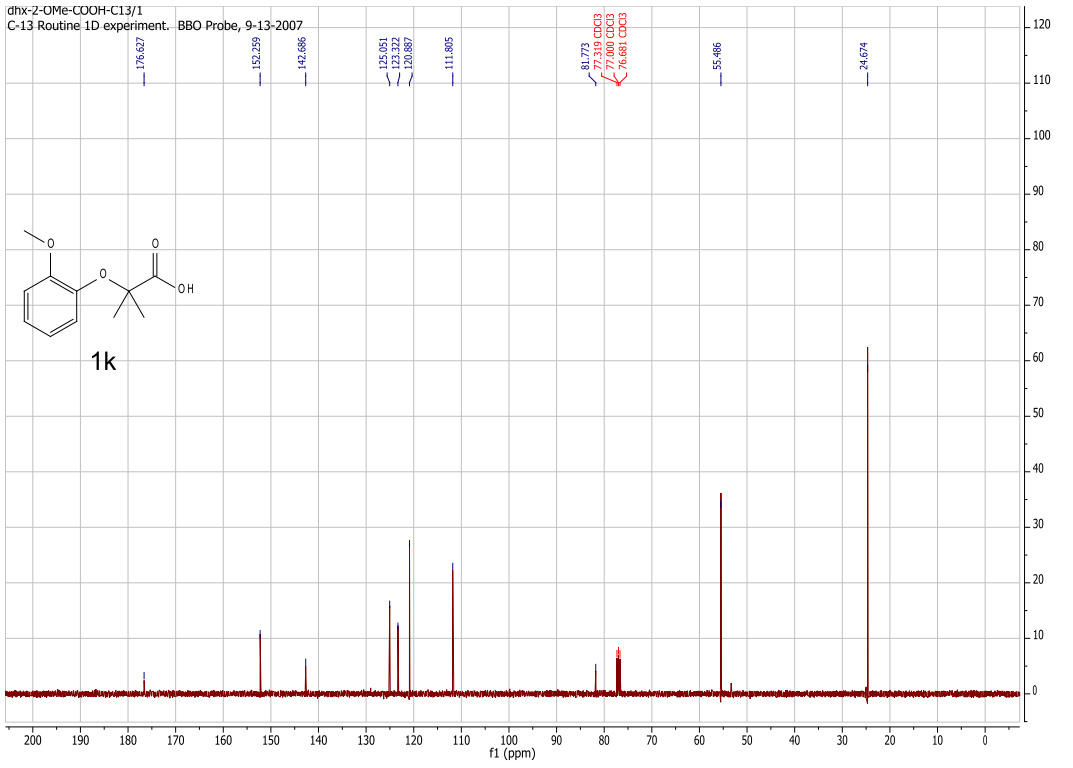
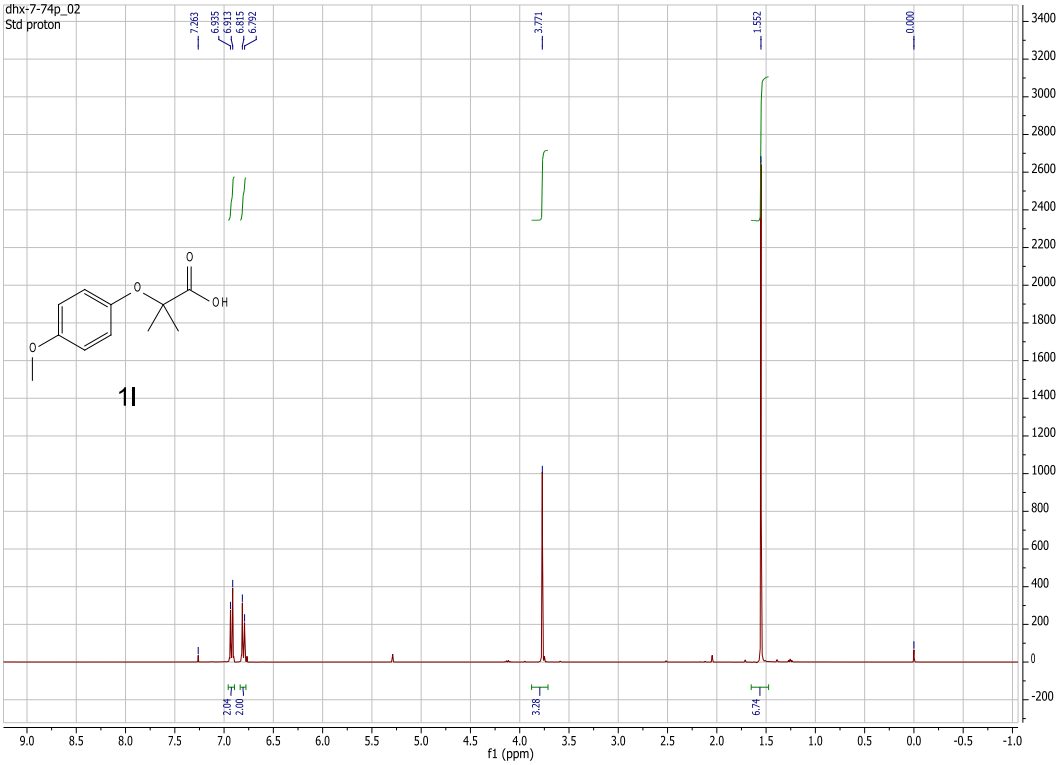
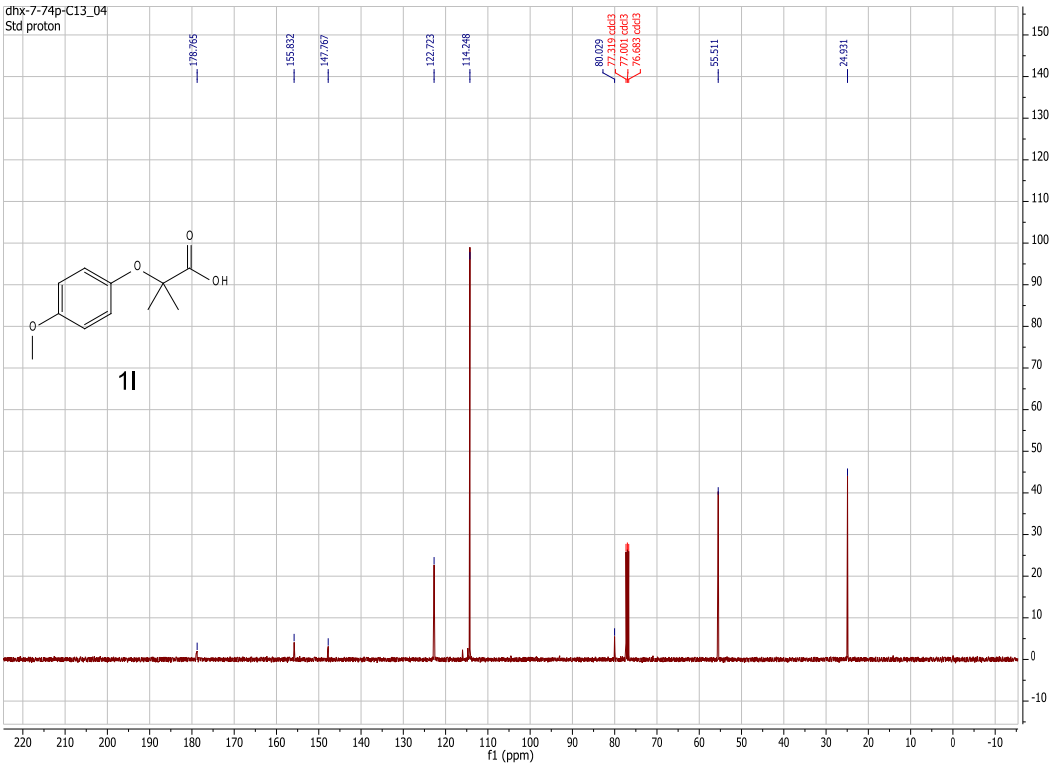
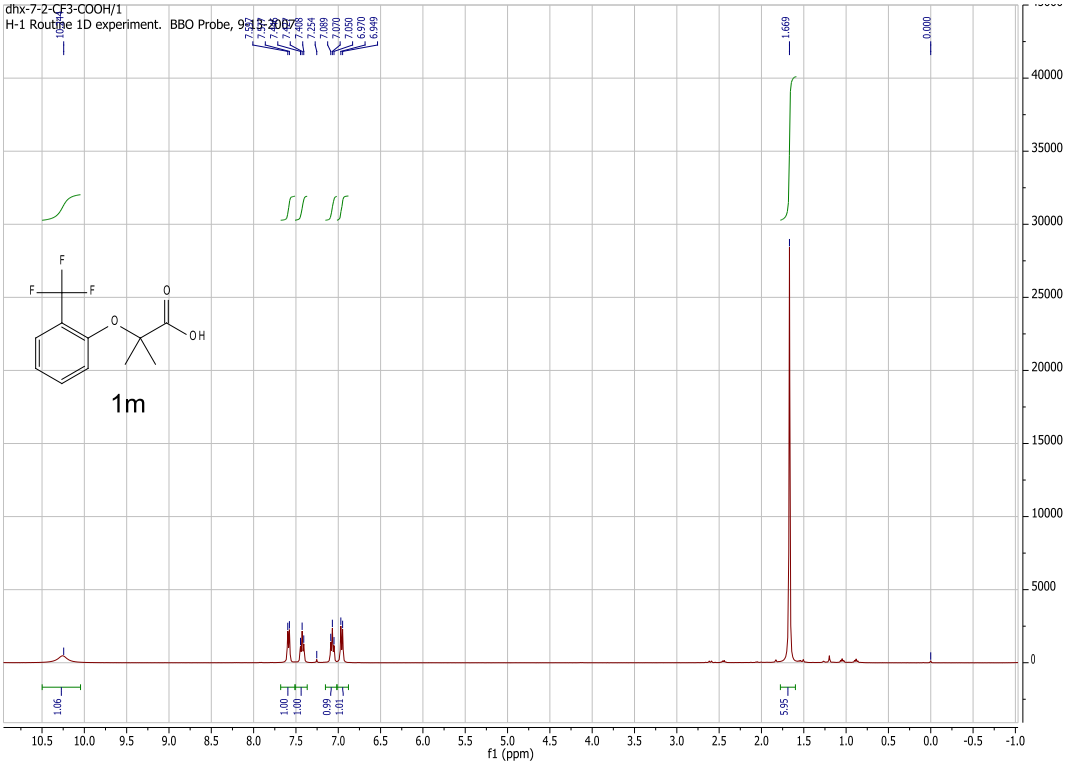
25.154
Cl
O
O
OH
1j
f1 (ppm)

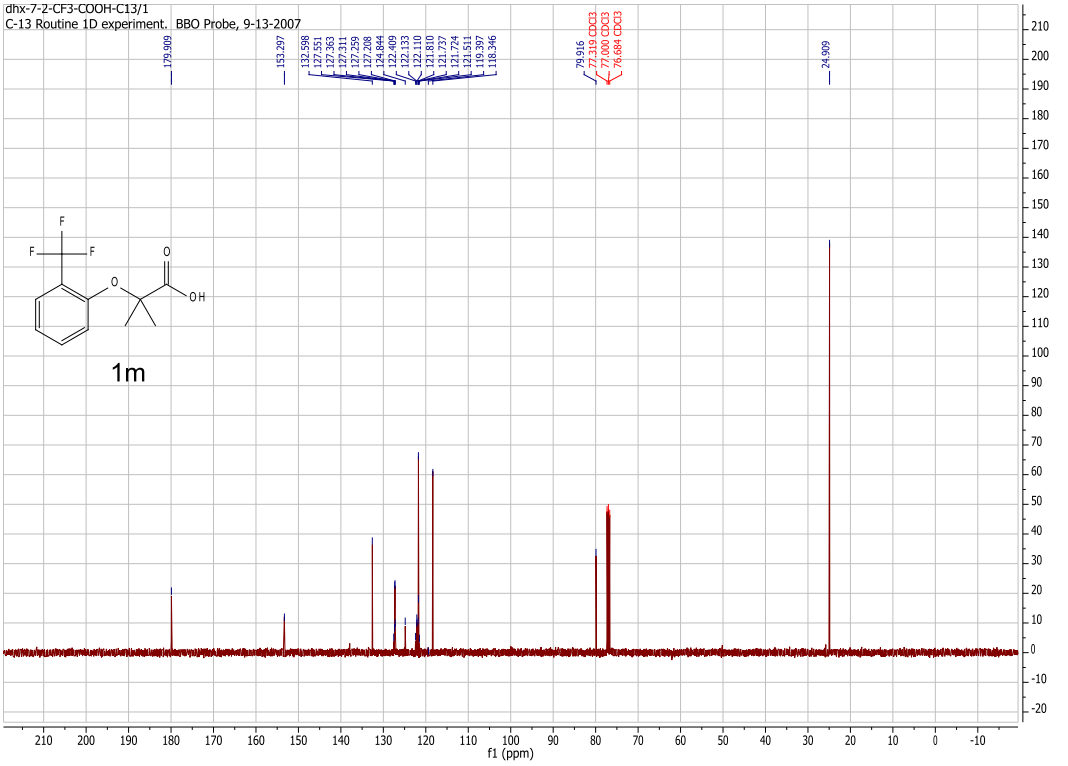

dhx-2-OMe-COOH-H/1
H-1 Routine 1D experiment. BBO Probe, 9-13-2007
7.201
7.125
7.108
7.089
7.031
7.008
6.945
6.924
6.901
6.882
3.857
1.527
0.000
1k
f1 (ppm)

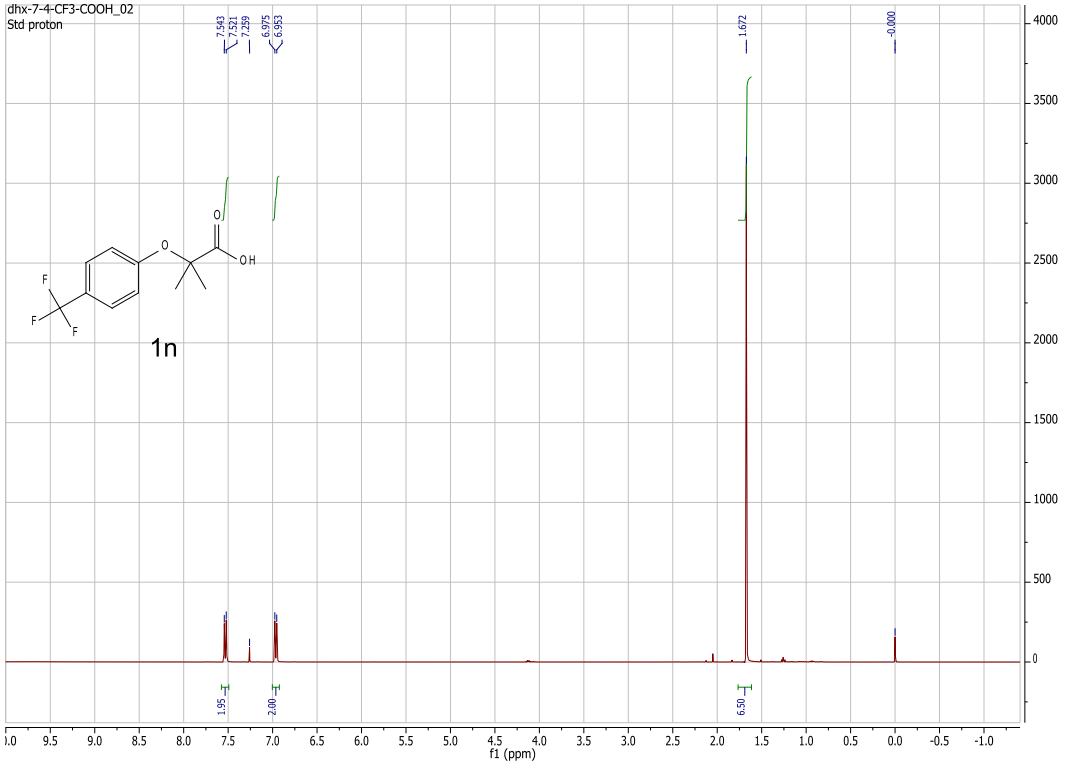

dhx-2-OMe-COOH-C13/1
C-13 Routine 1D experiment. BBO Probe, 9-13-2007
176.627
152.259
142.686
125.051
123.322
120.887
111.805
81.773
77.319 CDCl3
77.000 CDCl3
76.681 CDCl3
55.486
24.674
1k
f1 (ppm)

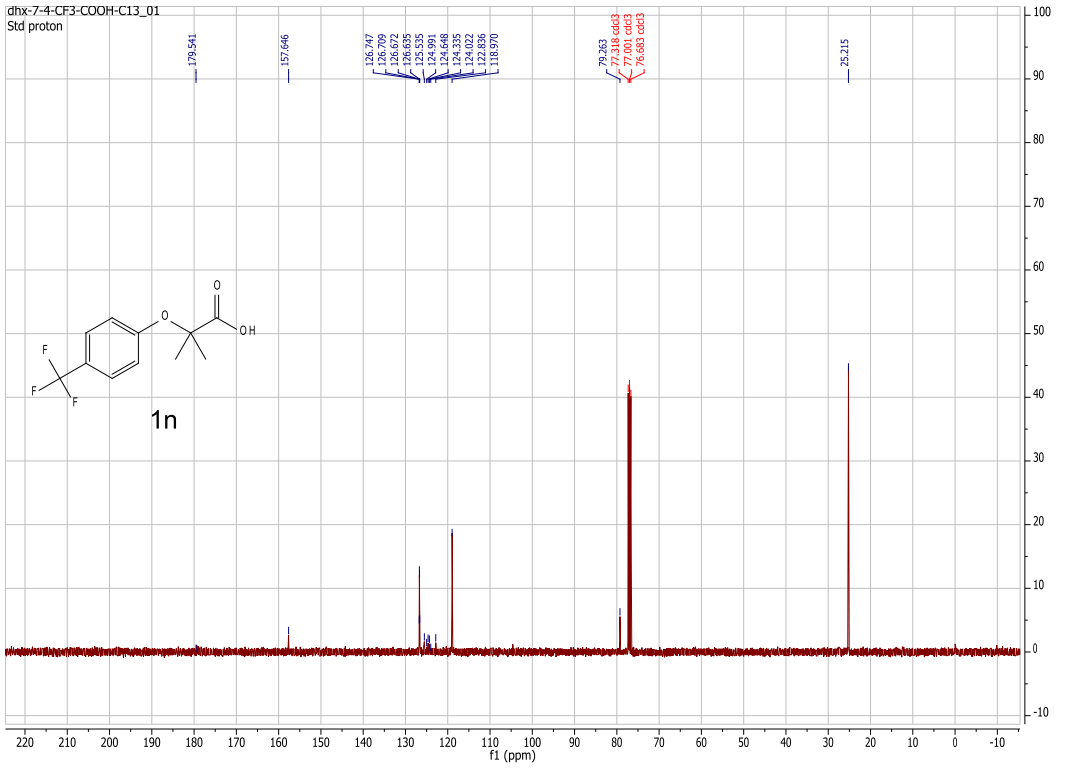

dhx-7-74p_02
Std proton
7.263
6.935
6.913
6.815
6.792
3.771
1.552
0.000
2.04
2.00
3.28
6.74
f1 (ppm)
1l

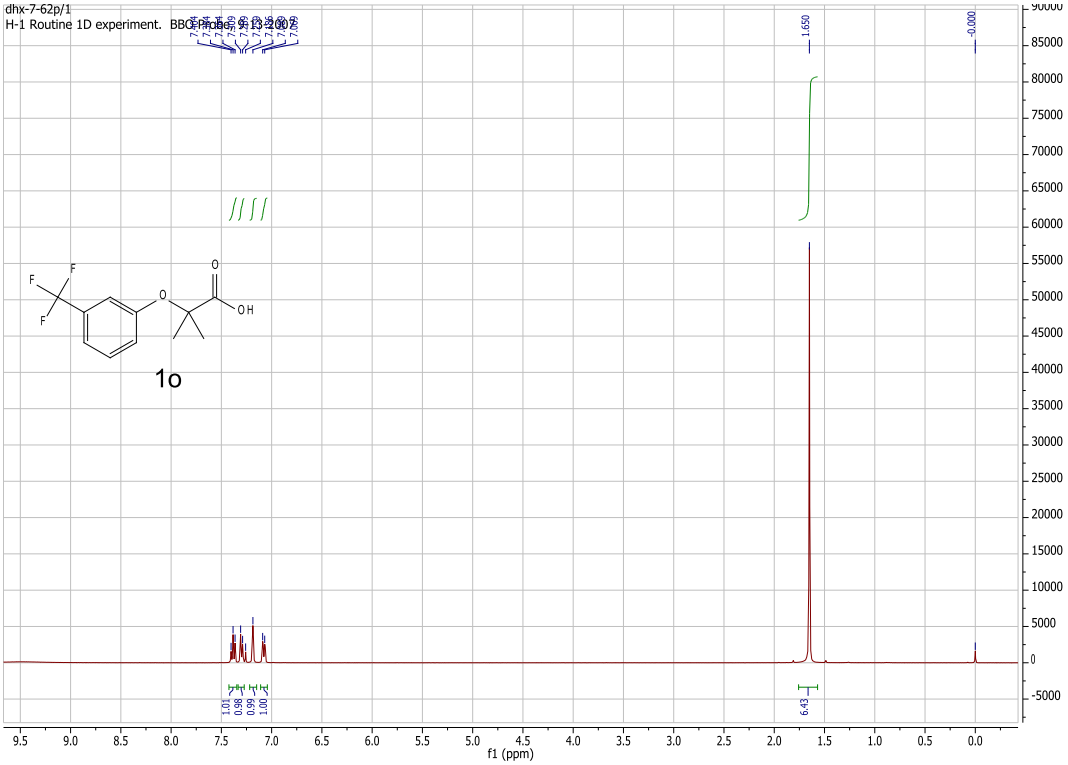

dhx-7-74p-C13_04
Std proton
178.765
155.832
147.767
122.723
114.248
80.029
77.319 cdcl3
77.001 cdcl3
76.683 cdcl3
55.511
24.931
f1 (ppm)
1l

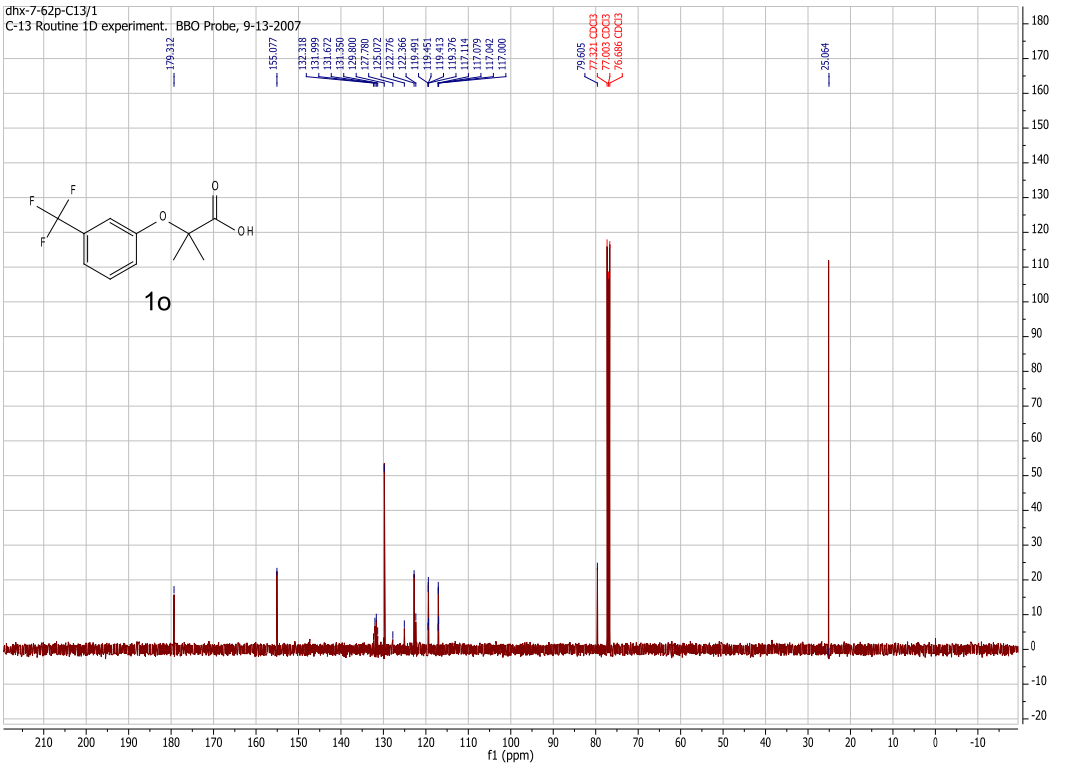

dhx-7-2-CF3-COOH/1
H-1 Routine 1D experiment. BBO Probe, 9-13-2007
1m
f1 (ppm)

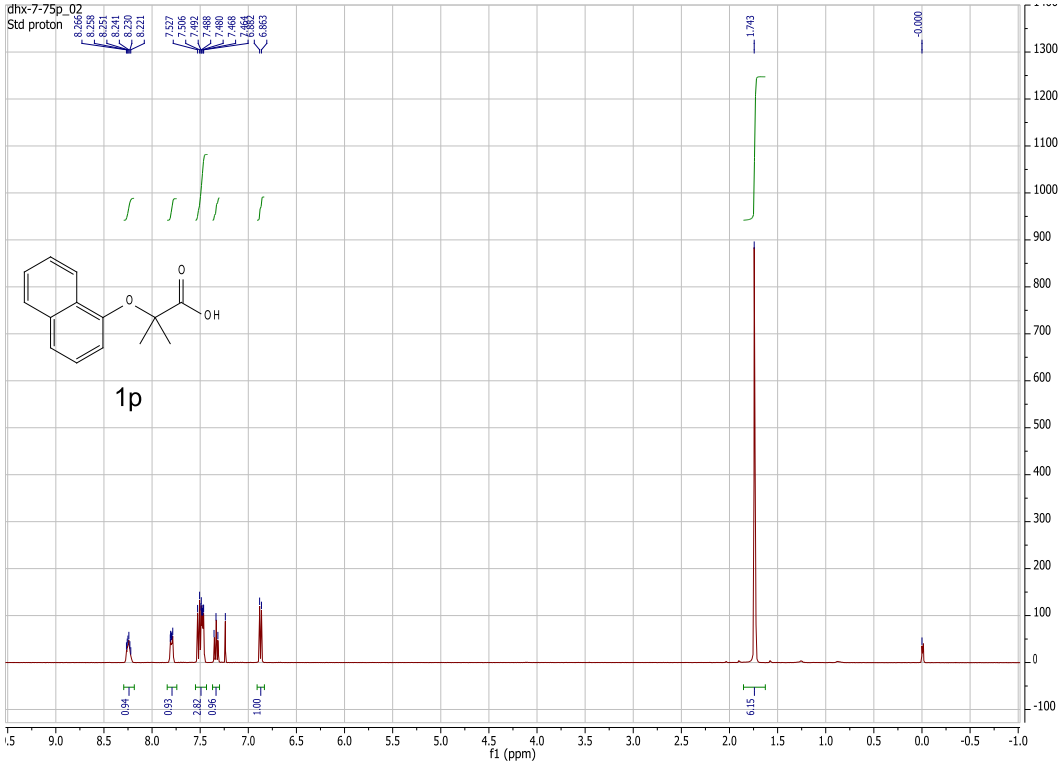

dhx-7-2-CF3-COOH-C13/1
C-13 Routine 1D experiment. BBO Probe, 9-13-2007
1m
f1 (ppm)

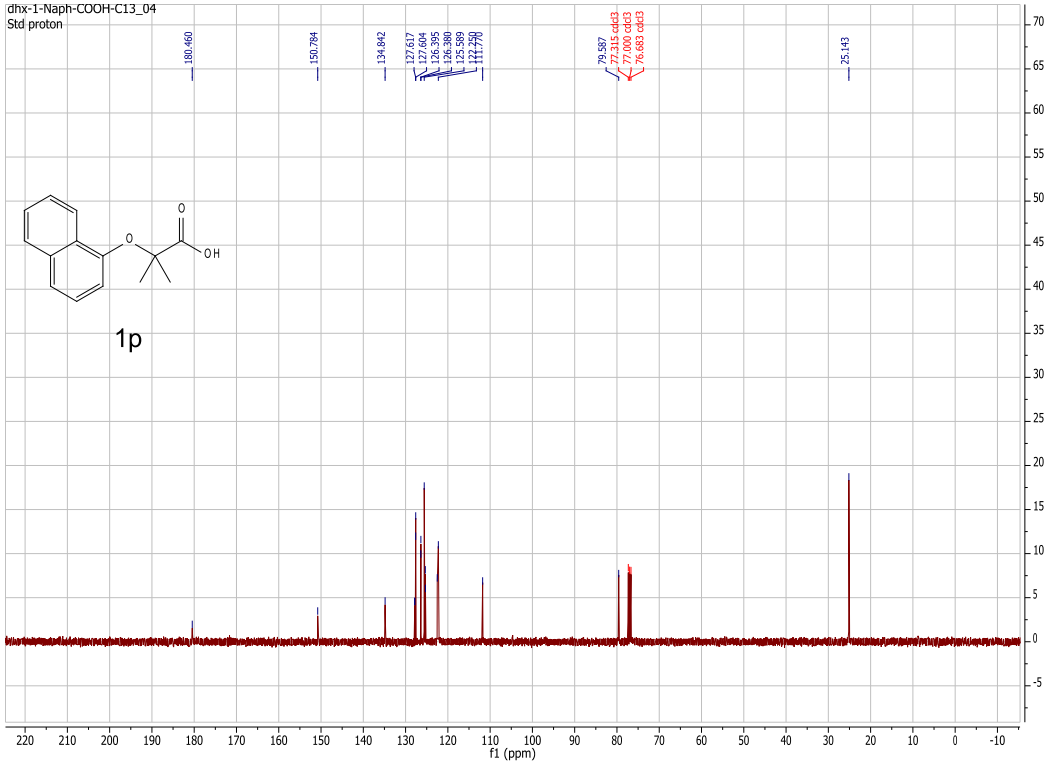

dhx-7-4-CF3-COOH_02
Std proton
7.543
7.521
7.259
6.975
6.953
1.672
-0.000
1n
1.95
2.00
6.50
f1 (ppm)

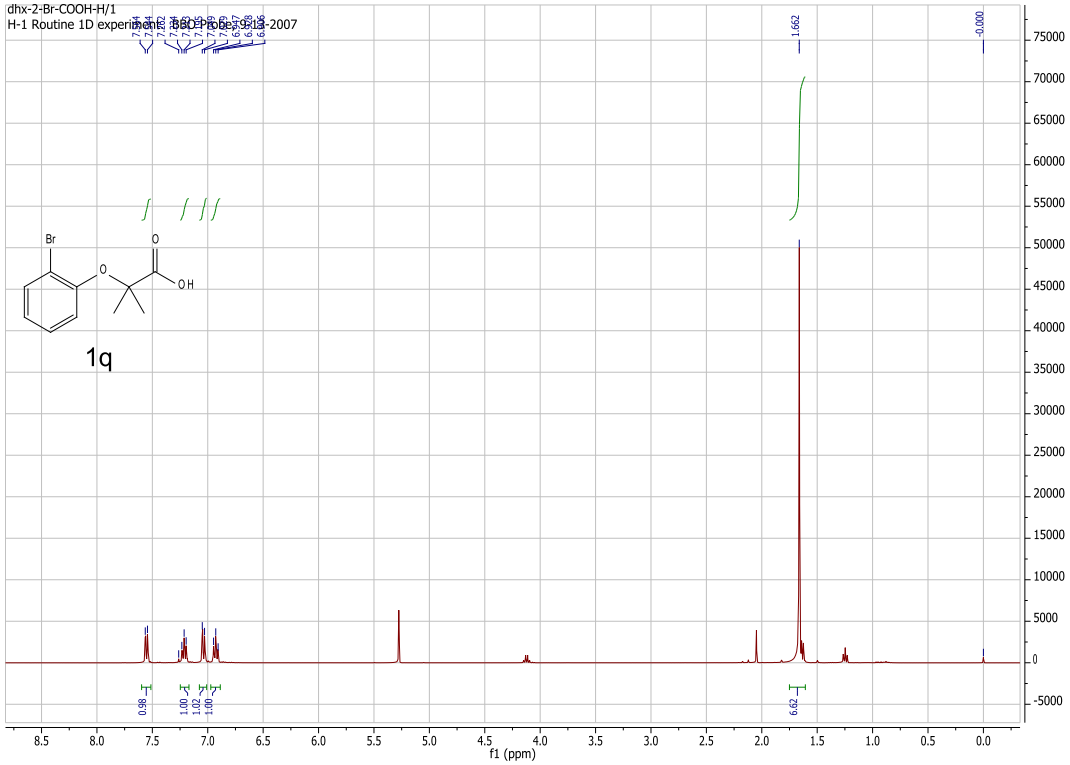

dhx-7-4-CF3-COOH-C13_01
Std proton
179.541
157.646
126.747
126.709
126.672
126.635
125.555
125.501
124.648
124.335
124.022
122.836
118.970
79.263
77.318 cdcl3
77.000 cdcl3
76.683 cdcl3
25.215
1n
f1 (ppm)

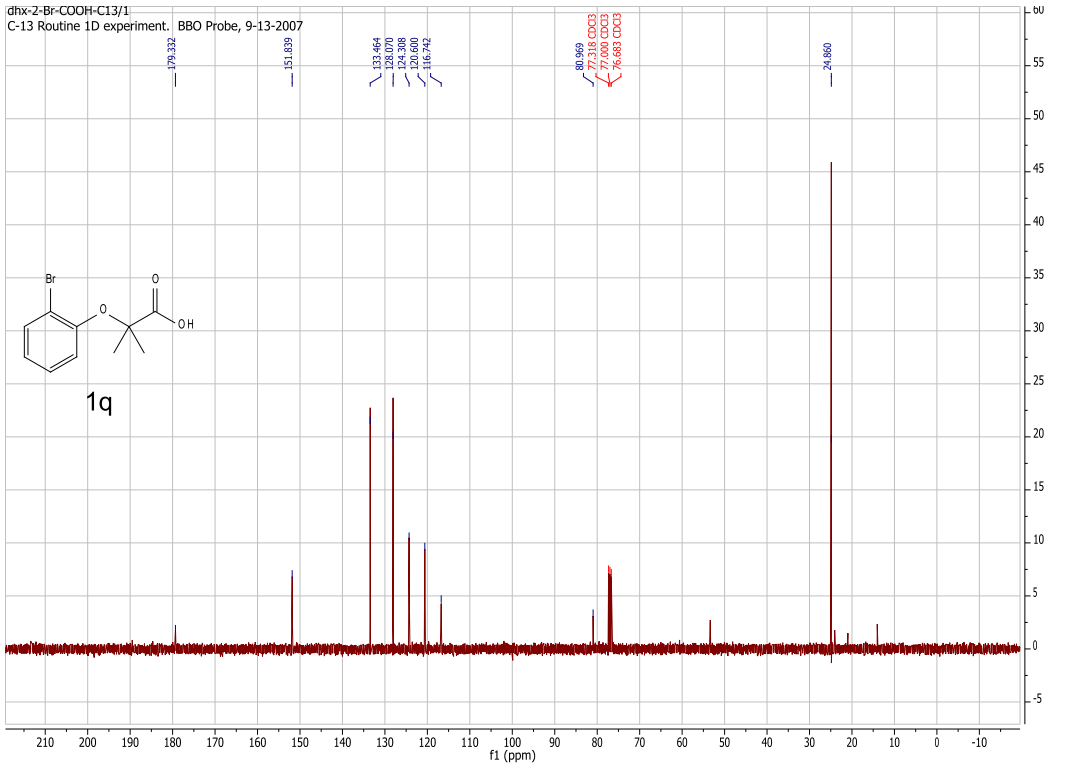

dhx-7-62p/1
H-1 Routine 1D experiment. BBO Probe, 9-13-2007
1.650
0.000
1.01
0.98
0.99
1.00
6.43
f1 (ppm)
1o

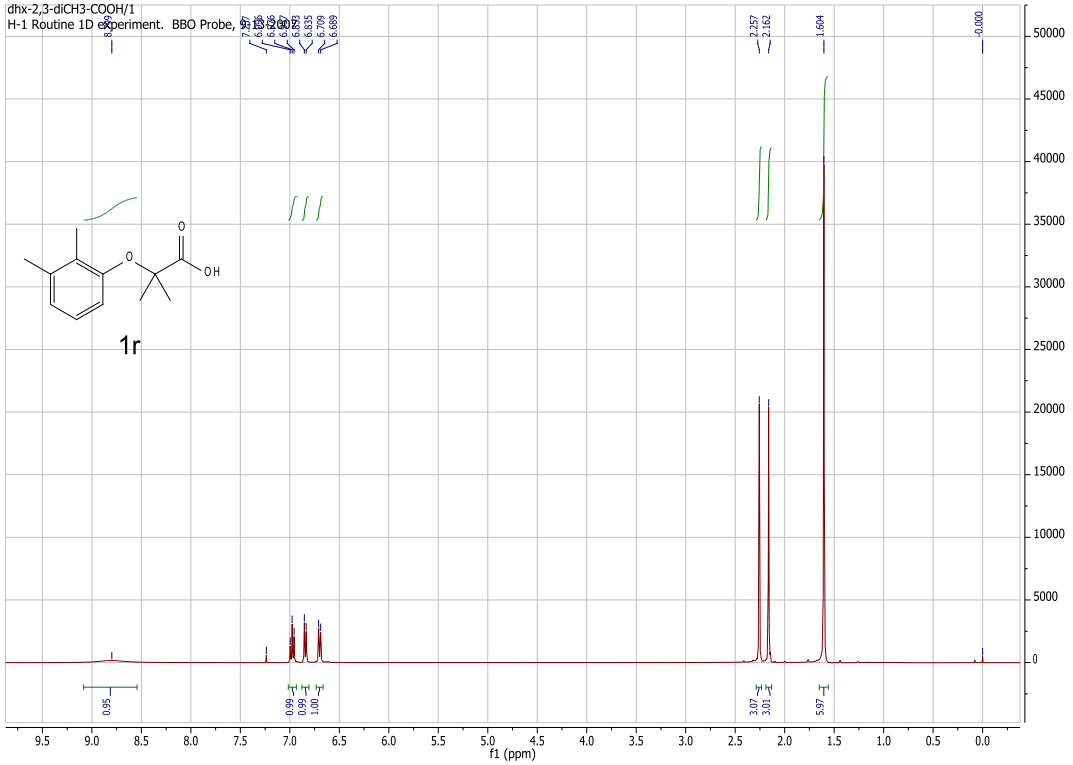

dhx-7-62p-C13/1
C-13 Routine 1D experiment. BBO Probe, 9-13-2007
179.312
155.077
132.318
131.999
131.672
131.350
129.800
127.780
125.072
122.776
121.365
119.491
119.451
119.413
119.376
117.114
117.079
117.042
117.000
79.605
77.321 CDCl3
77.003 CDCl3
76.686 CDCl3
25.064
f1 (ppm)
1o

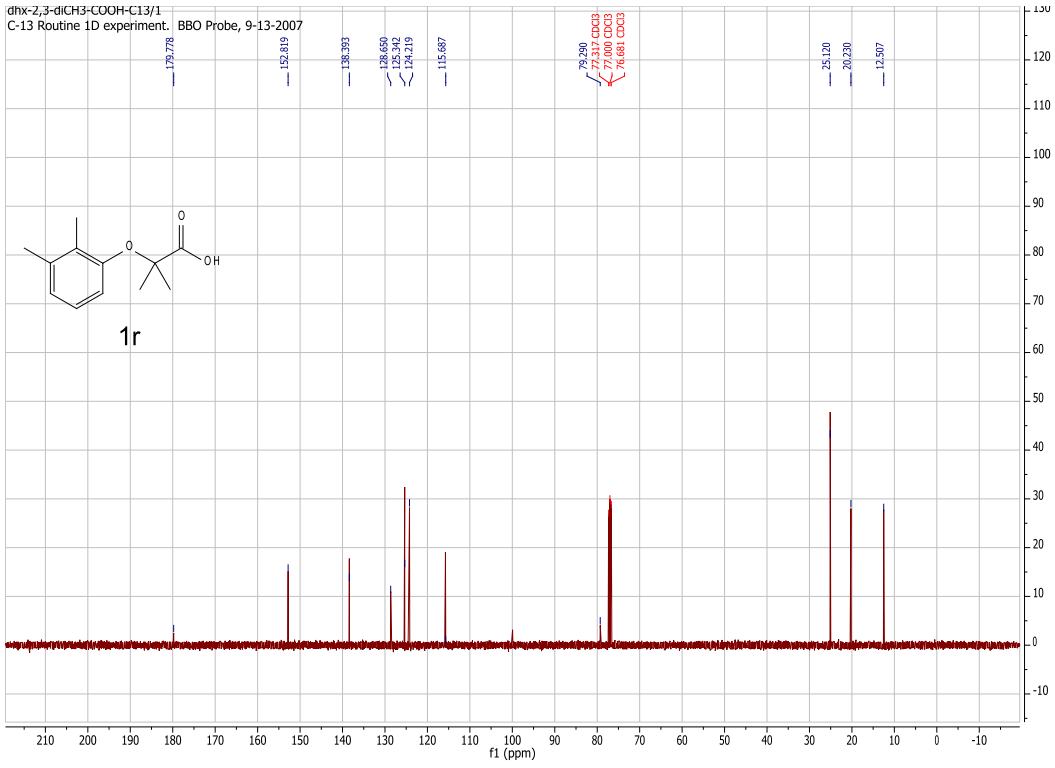

dhx-7-75p_02
Std proton
1p
f1 (ppm)

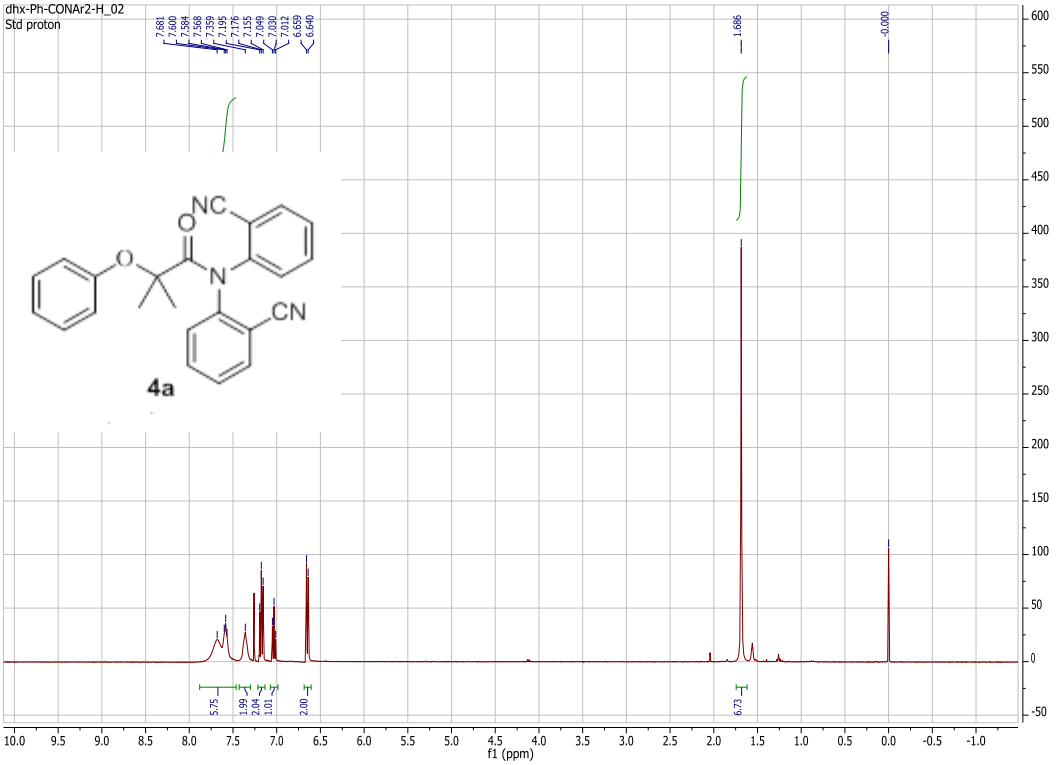

dhx-1-Naph-COOH-C13_04
Std proton
1p
f1 (ppm)

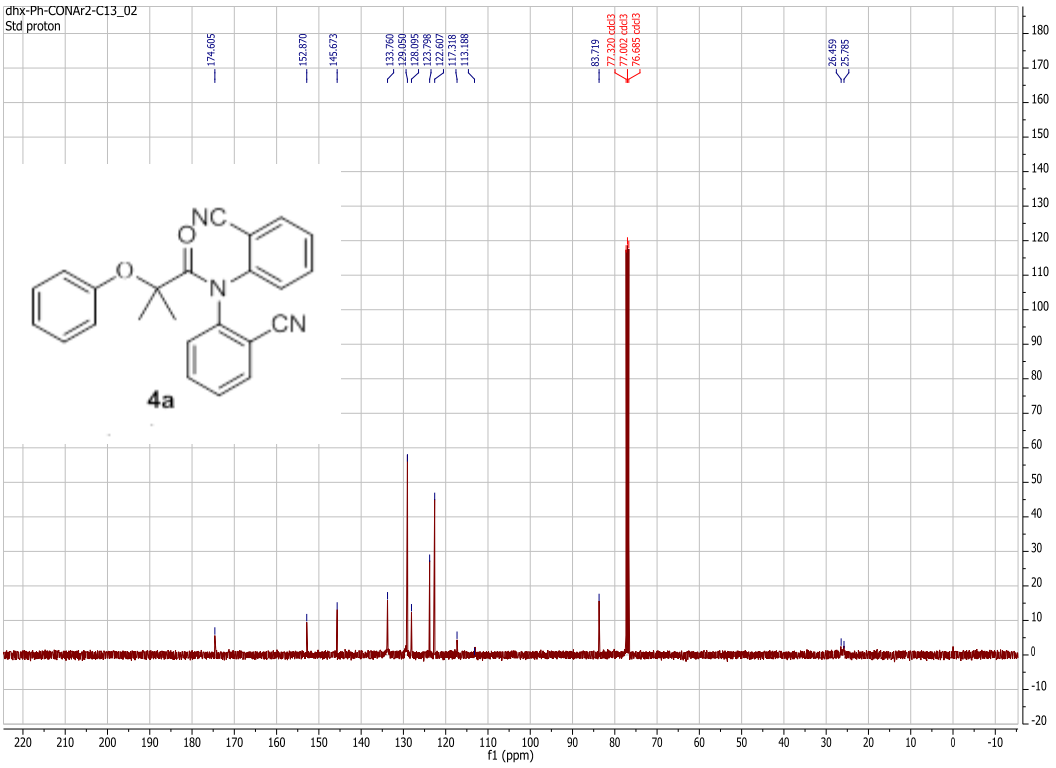

dhx-2-Br-COOH-H/1
H-1 Routine 1D experiment, BBO Probe, 9-13-2007
1.662
0.000
Br
O
O
O H
1q
0.98
1.00
1.02
1.00
6.62
f1 (ppm)

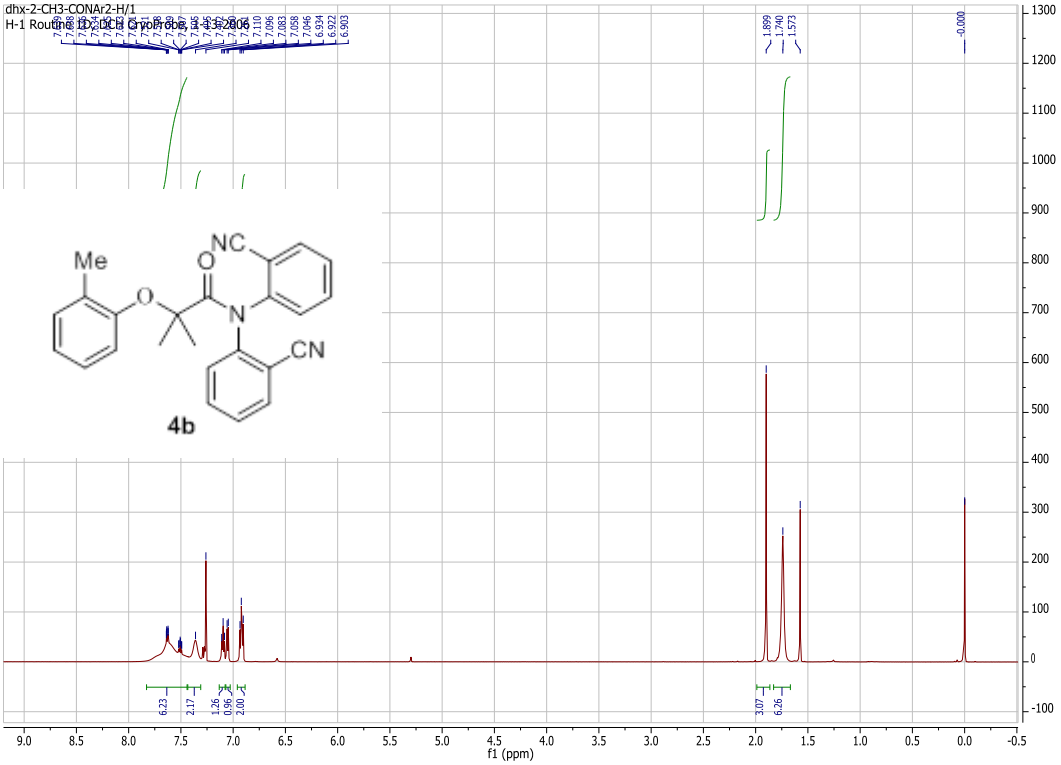

dhx-2-Br-COOH-C13/1
C-13 Routine 1D experiment, BBO Probe, 9-13-2007
179.332
151.839
133.464
129.070
124.308
120.600
116.742
80.969
77.318 CDCl3
77.000 CDCl3
76.683 CDCl3
24.860
Br
O
O
O H
1q
f1 (ppm)

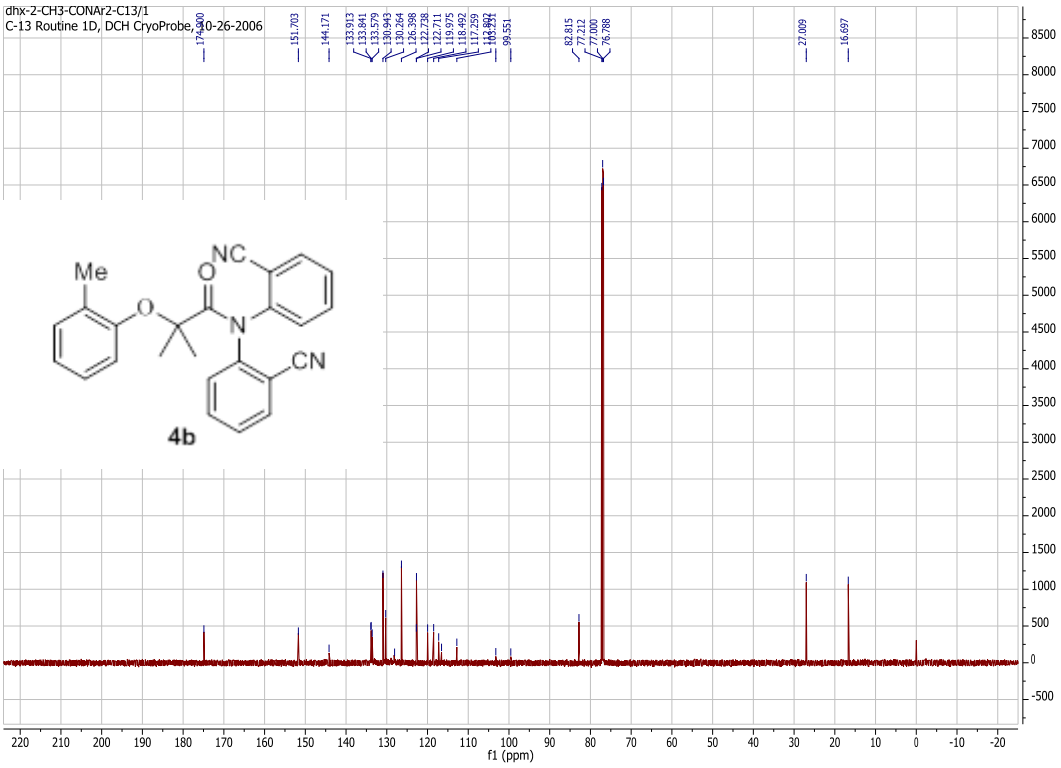

dhx-2,3-diCH3-COOH/1
H-1 Routine 1D experiment. BBO Probe, 9-13-2007
2.257
2.162
1.604
0.000
1r
f1 (ppm)

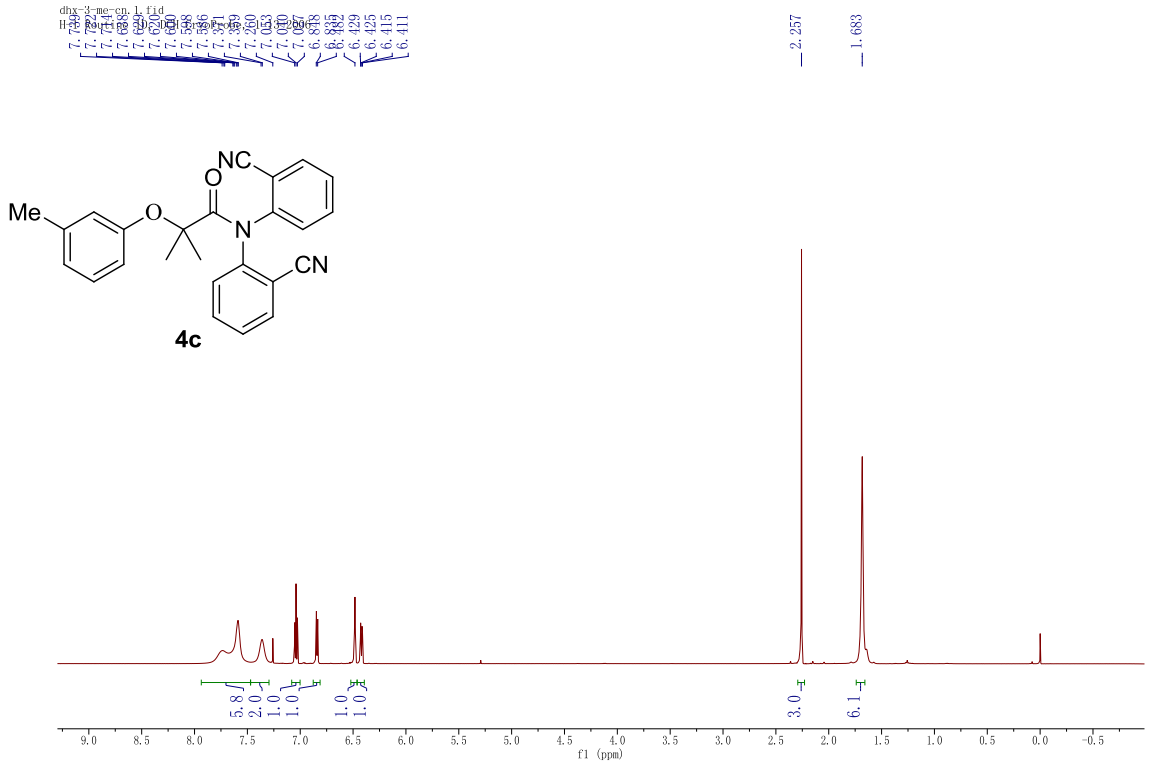

dhx-2,3-diCH3-COOH-C13/1
C-13 Routine 1D experiment. BBO Probe, 9-13-2007
179.778
152.819
138.393
128.650
125.342
124.219
115.687
79.290
77.317 CDCl3
77.000 CDCl3
76.681 CDCl3
25.120
20.230
12.507
1r
f1 (ppm)

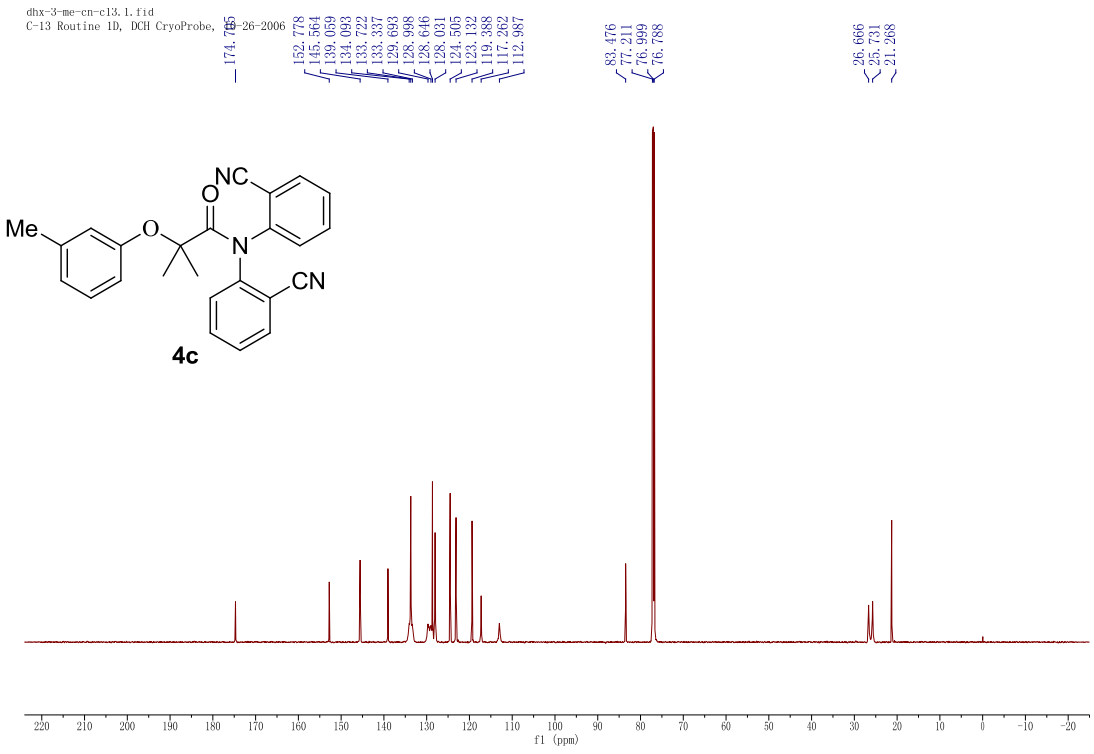

dhx-Ph-CONAr2-H_02
Std proton
7.681
7.600
7.584
7.568
7.359
7.195
7.176
7.155
7.049
7.030
7.012
6.659
6.640
1.686
0.000
NC
O
N
O
CN
4a
5.75
1.99
2.04
1.01
2.00
6.73
f1 (ppm)

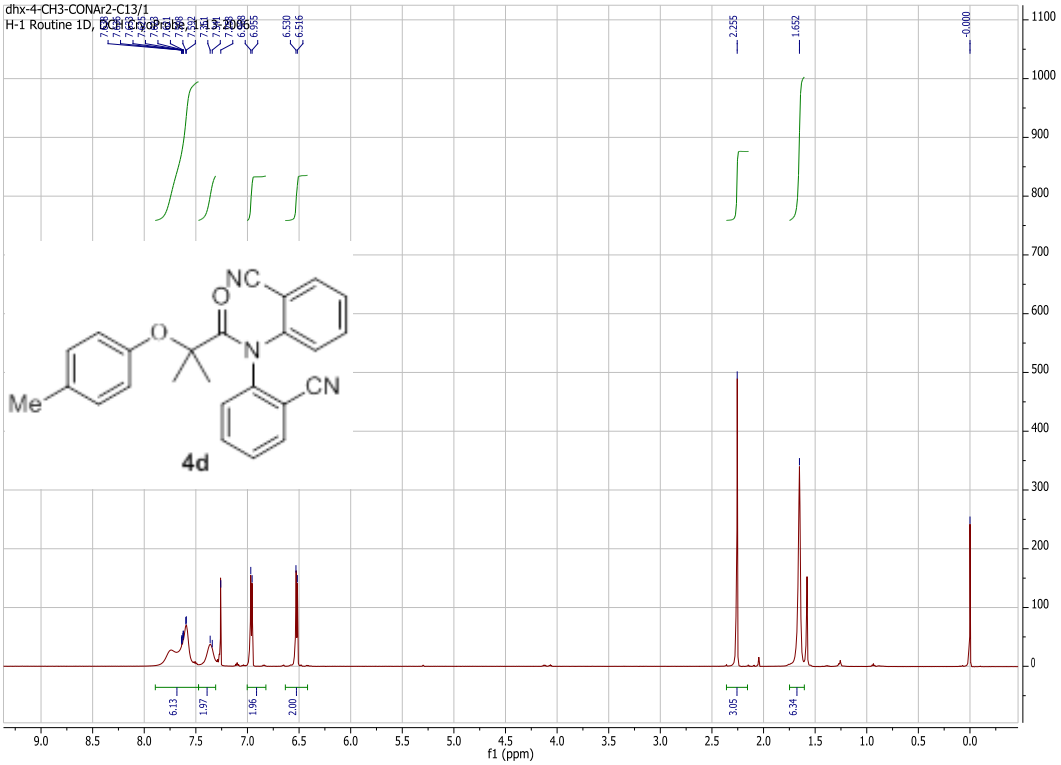

dhx-Ph-CONAr2-C13_02
Std proton
174.605
152.870
145.673
133.760
129.045
128.095
123.798
122.607
117.318
113.188
83.719
77.320 cdcl3
77.002 cdcl3
76.685 cdcl3
26.459
25.785
NC
O
N
O
CN
4a
f1 (ppm)

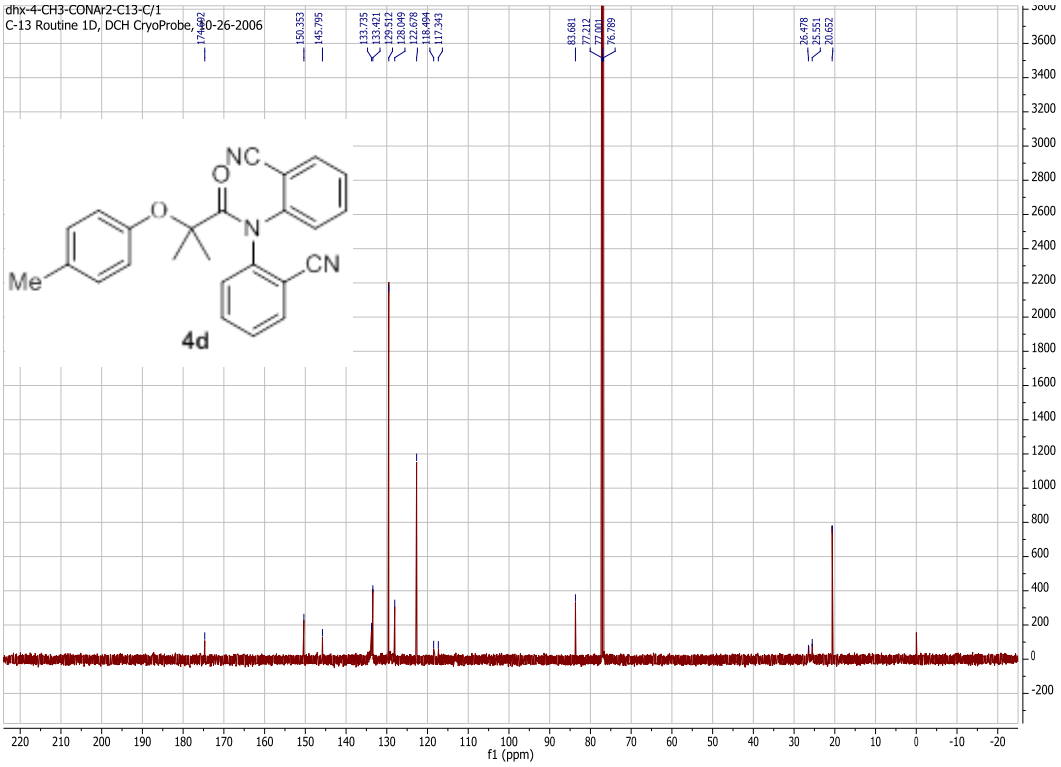

dhx-2-CH3-CONAr2-H/1
H-1 Routine 1D, DCH CryoProbe, 4-13-2006
Me
O
NC
O
N
CN
4b
f1 (ppm)

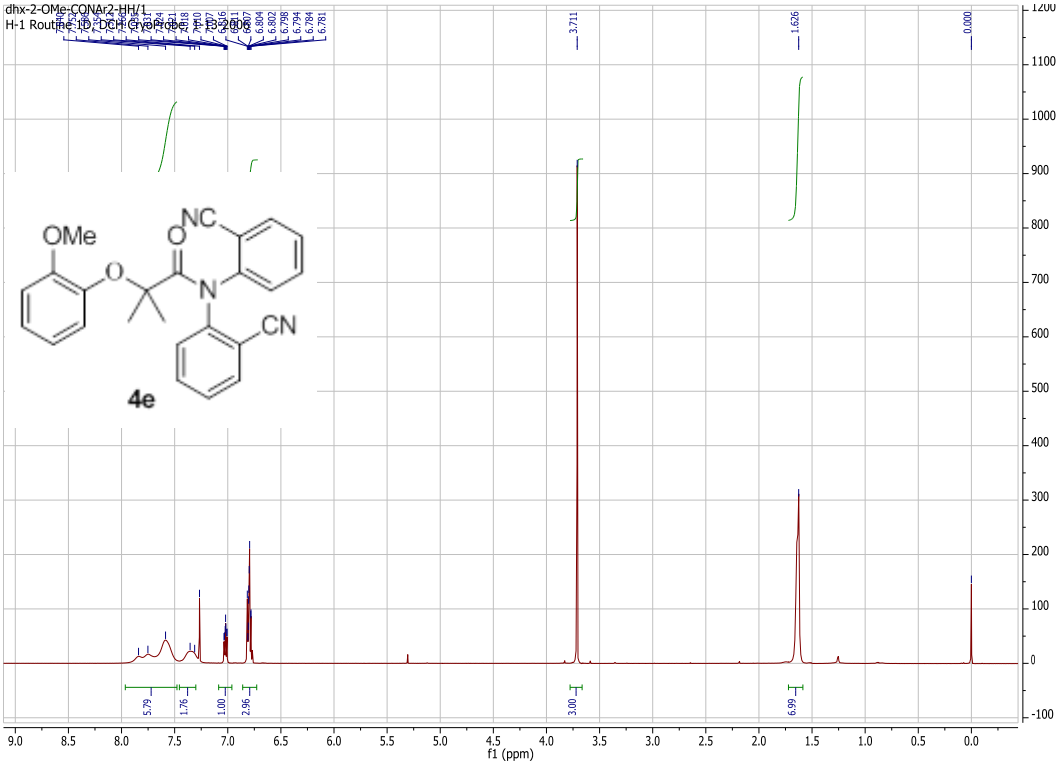

dhx-2-CH3-CONAr2-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
Me
O
NC
O
N
CN
4b
f1 (ppm)

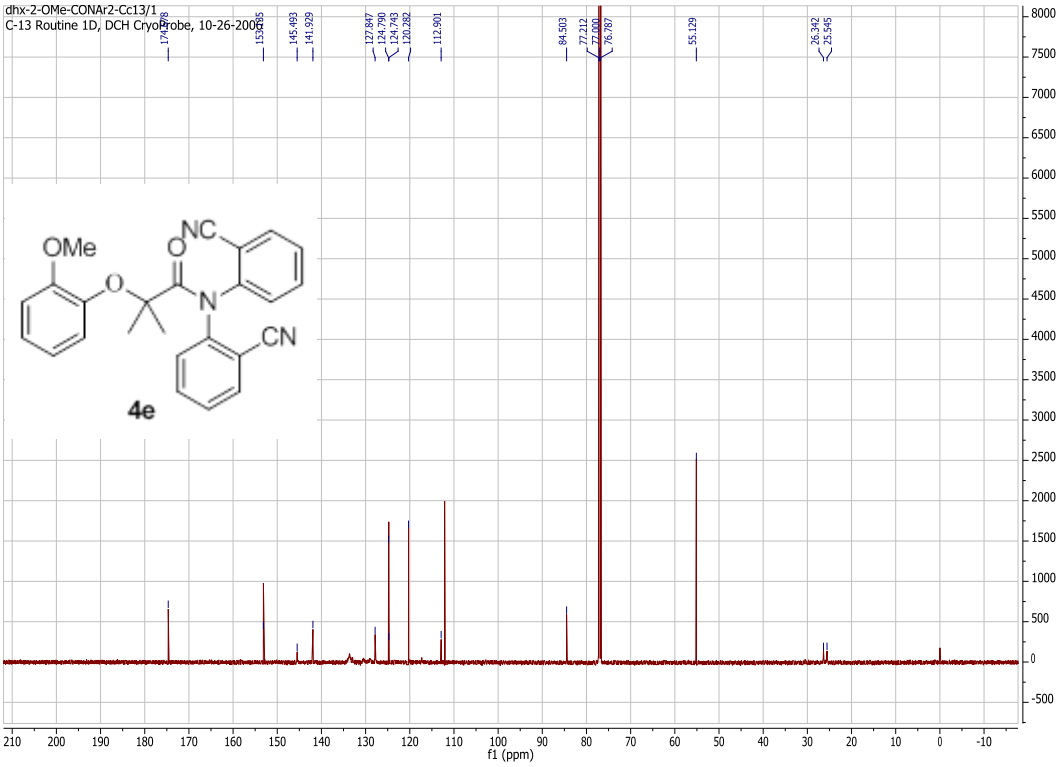

dhx-3-me-cn_1.fid
NC
O
N
Me
O
CN
4c
2.257
1.683
5.8
2.0
1.0
1.0
1.0
1.0
3.0
6.1
f1 (ppm)

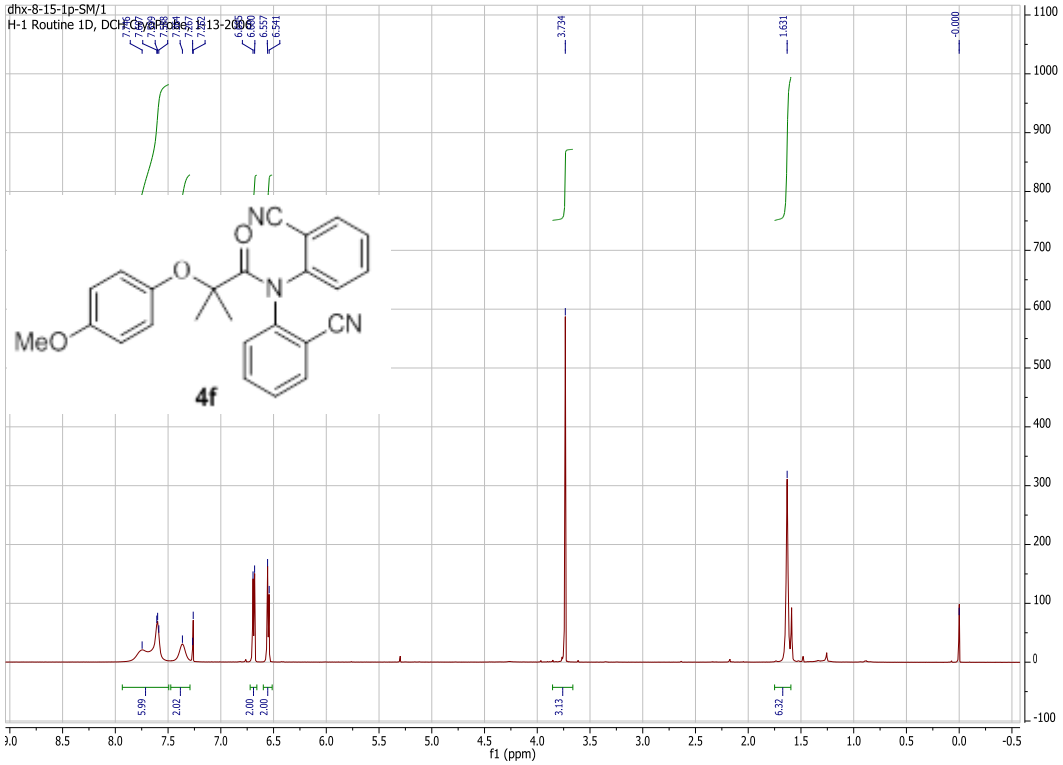

dhx-3-me-cn-c13_1.fid
C-13 Routine 1D, DCH CryoProbe, 12-26-2006
174.785
152.778
145.564
139.059
134.093
133.722
133.337
129.693
128.998
128.646
128.031
124.505
123.132
119.388
117.262
112.987
83.476
77.211
76.999
76.788
26.666
25.731
21.268
NC
O
N
Me
O
CN
4c
f1 (ppm)

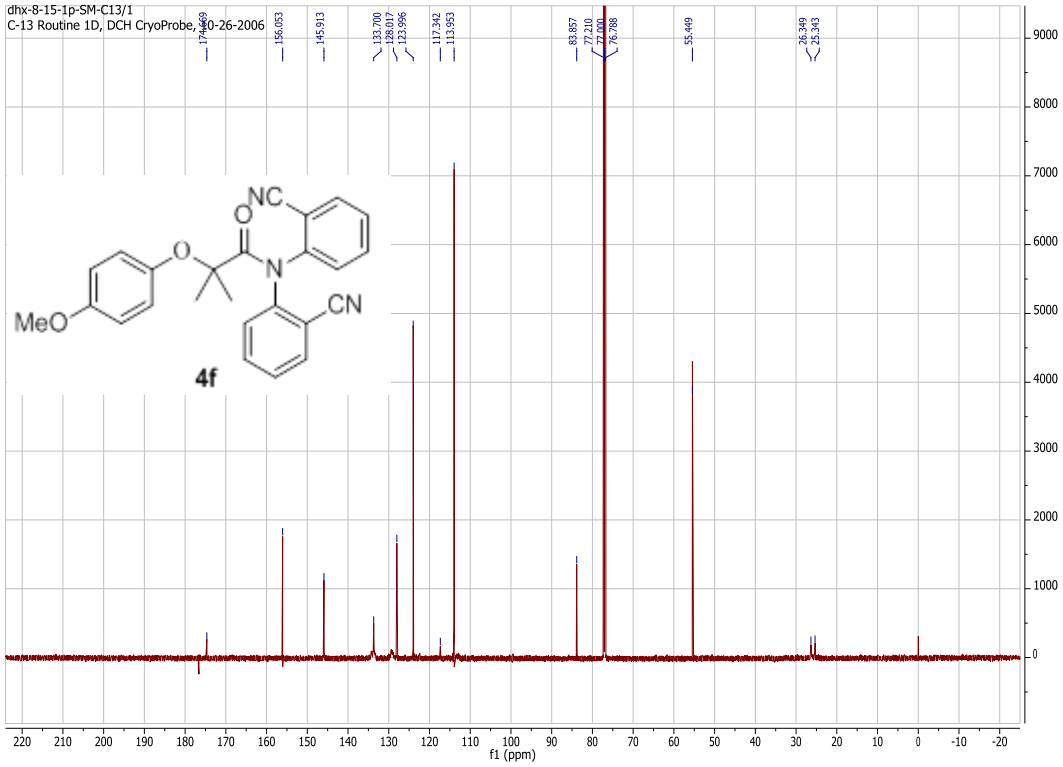

dhx-4-CH3-CONAr2-C13/1
H-1 Routine 1D, DCH CryoProbe, 10-26-2006
6.530
6.516
6.955
2.255
1.652
0.000
NC
O
N
O
CN
Me
4d
6.13
1.97
1.96
2.00
3.05
6.34
f1 (ppm)

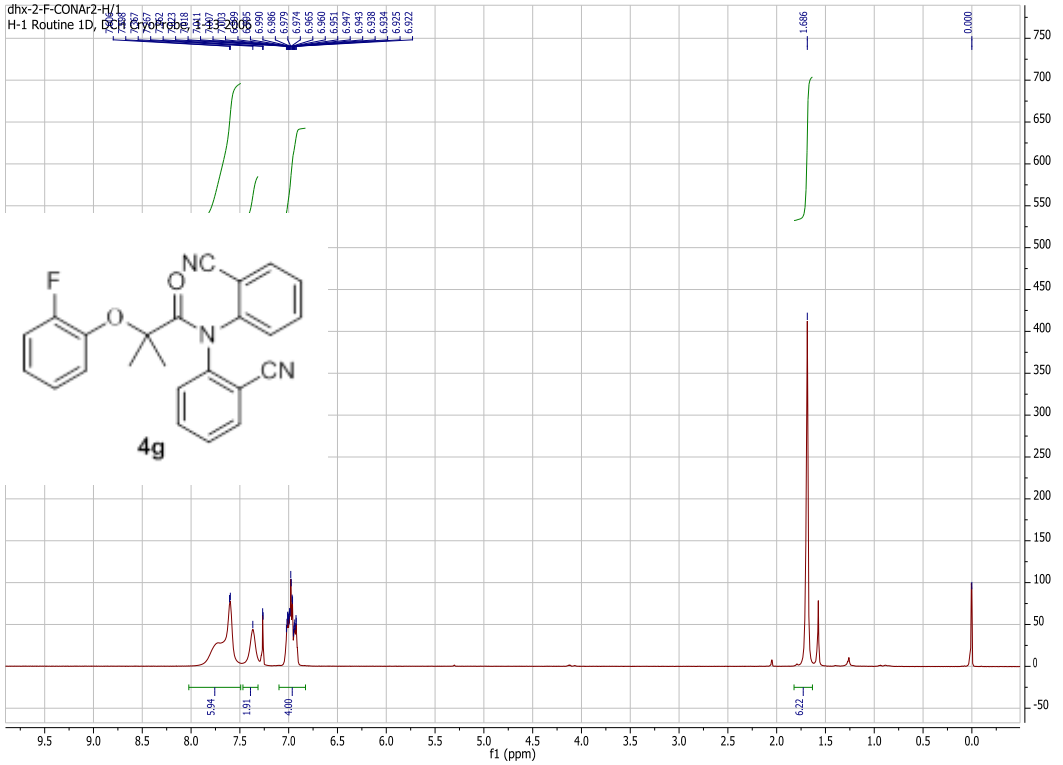

dhx-4-CH3-CONAr2-C13-C/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
174.692
150.353
145.795
133.735
133.421
128.957
128.049
122.678
118.494
117.343
83.681
77.212
77.000
76.789
26.478
25.551
20.652
NC
O
N
O
CN
Me
4d
f1 (ppm)

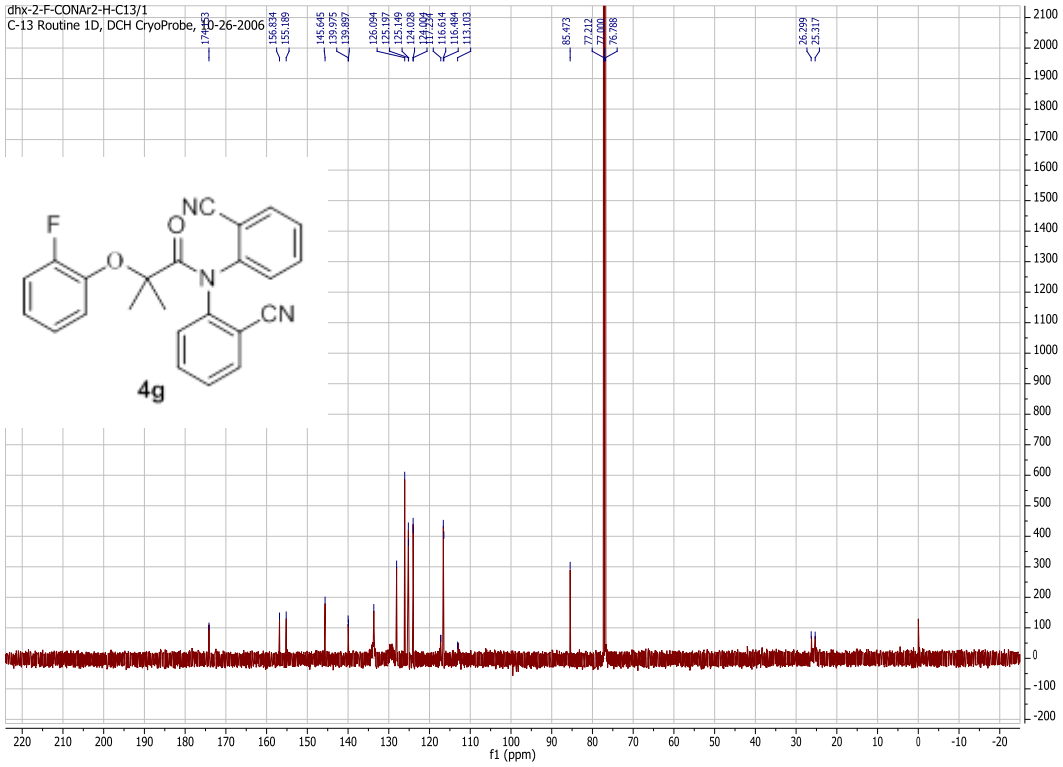

dhx-2-OMe-CONAr2-HH/1
H-1 Routine 1D, DCH CryoProbe, 10-26-2006
OMe
O
NC
O
N
CN
4e
3.711
1.626
0.000
5.79
1.76
1.00
2.96
3.00
6.99
f1 (ppm)

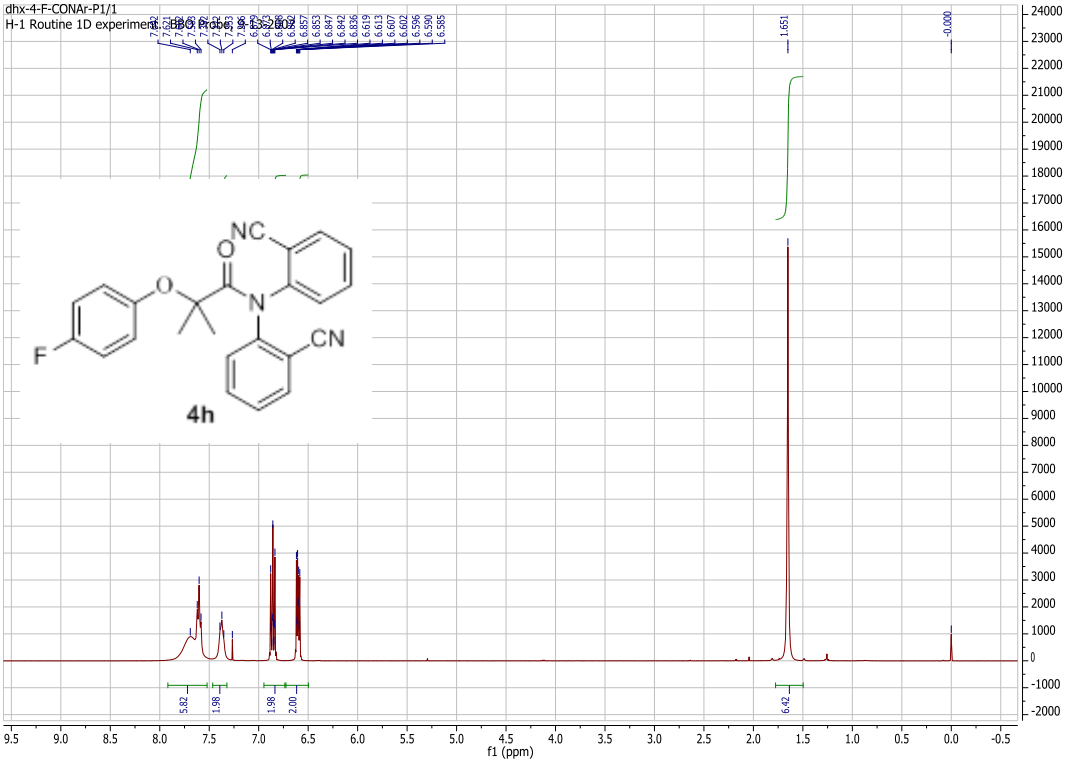

dhx-2-OMe-CONAr2-Cc13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
OMe
O
NC
O
N
CN
4e
176.978
159.605
145.493
141.929
127.847
124.790
124.743
120.282
112.901
84.503
77.212
77.000
76.787
55.129
26.342
25.545
f1 (ppm)

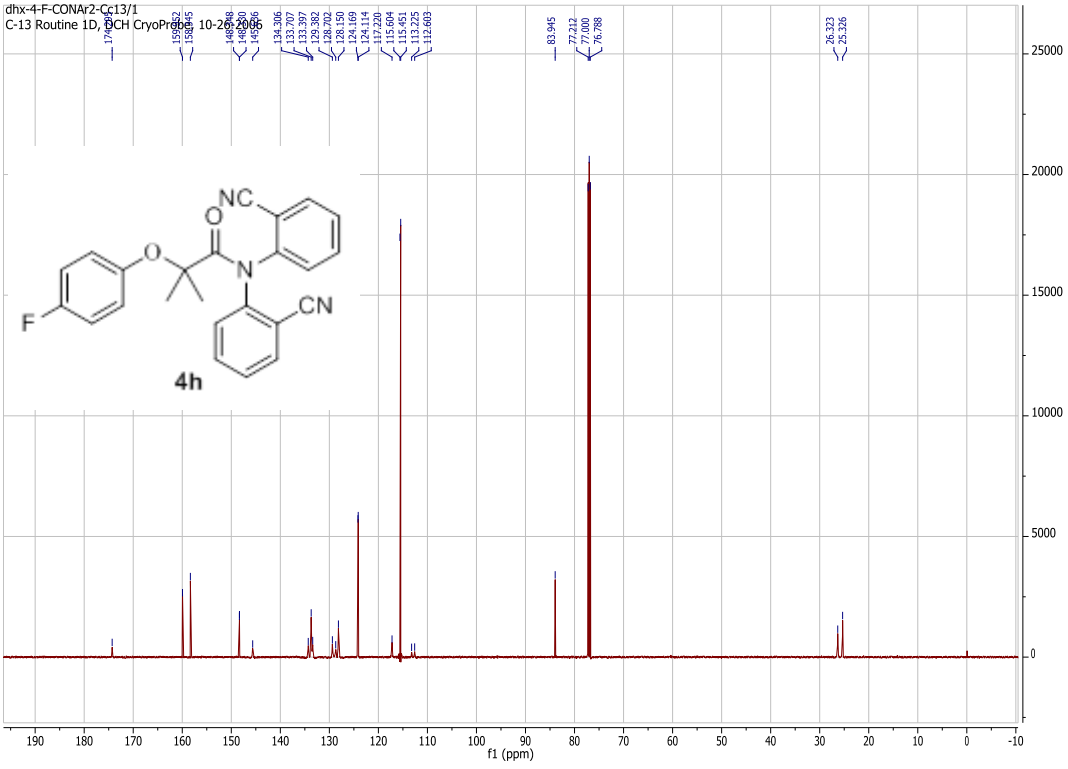

dhx-8-15-1p-SM/1
H-1 Routine 1D, DCH CryoProbe, 10-13-2006
3.734
1.631
0.000
5.99
2.02
2.00
2.00
3.13
6.32
NC
O
N
O
MeO
CN
4f
f1 (ppm)

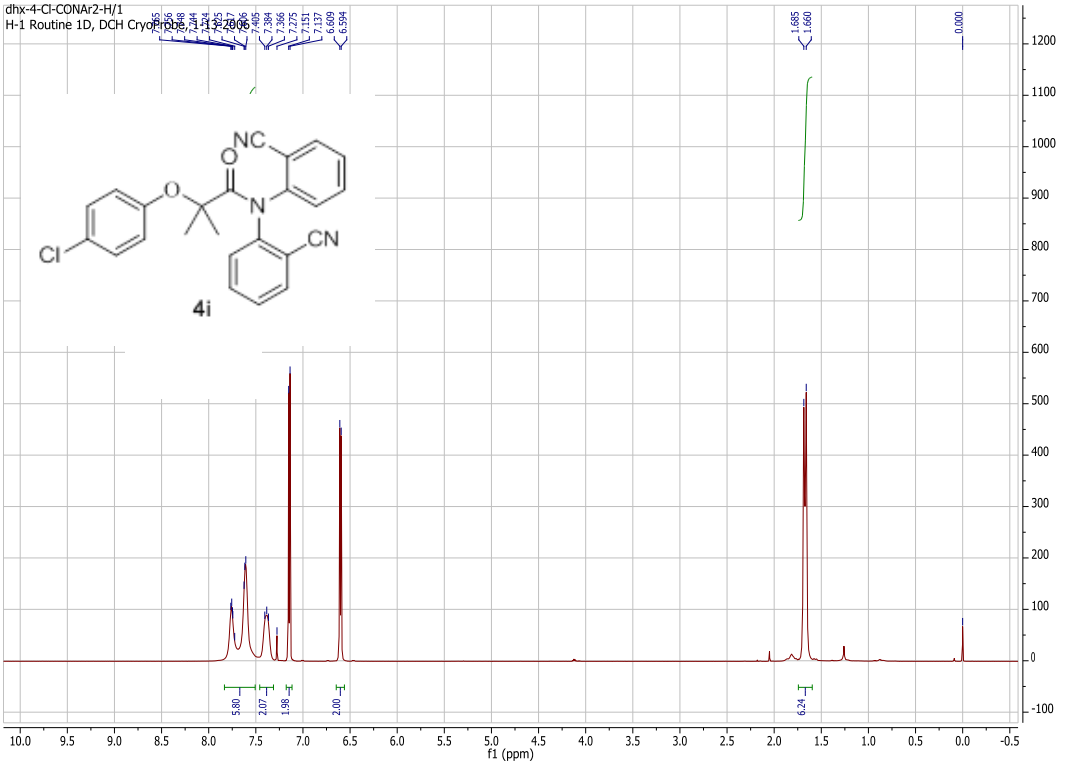

dhx-8-15-1p-SM-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
174.669
156.053
145.913
133.700
128.017
123.996
117.342
113.953
83.857
77.210
77.000
76.788
55.449
26.349
25.343
NC
O
N
O
MeO
CN
4f
f1 (ppm)

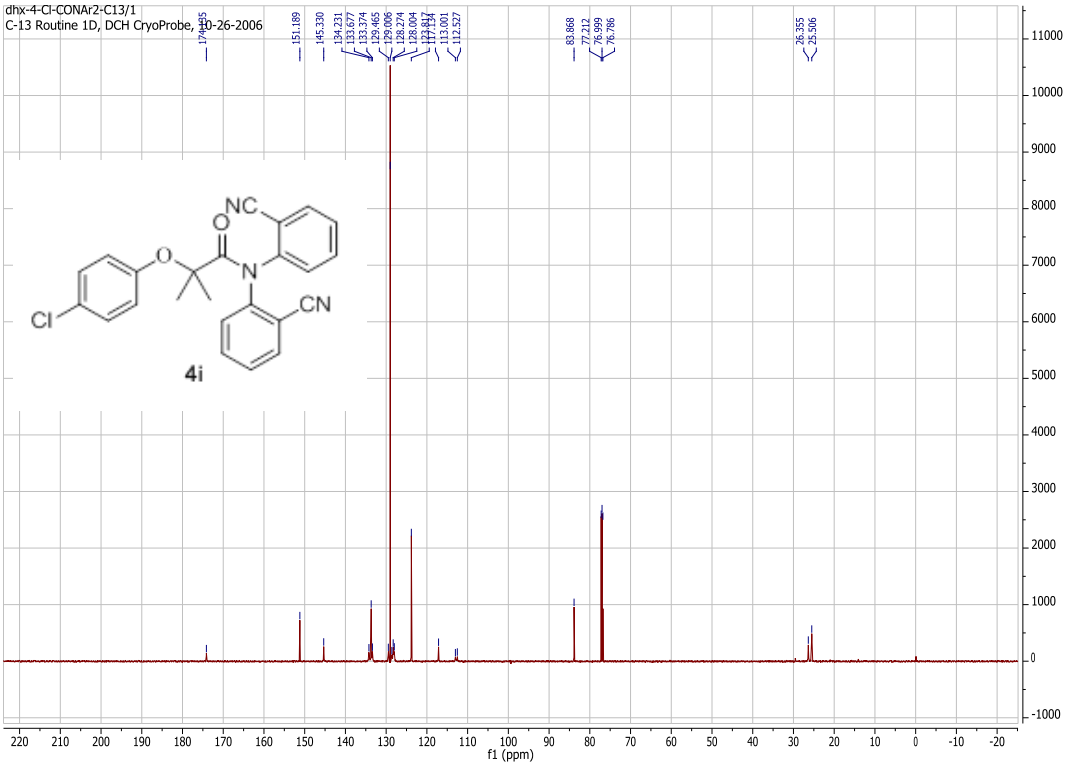

dhx-2-F-CONAr2-H/1
H-1 Routine 1D, DCH CryoProbe, 1-23-2006
F
O
NC
O
N
CN
4g
1.686
0.000
5.94
1.91
4.00
6.22
f1 (ppm)

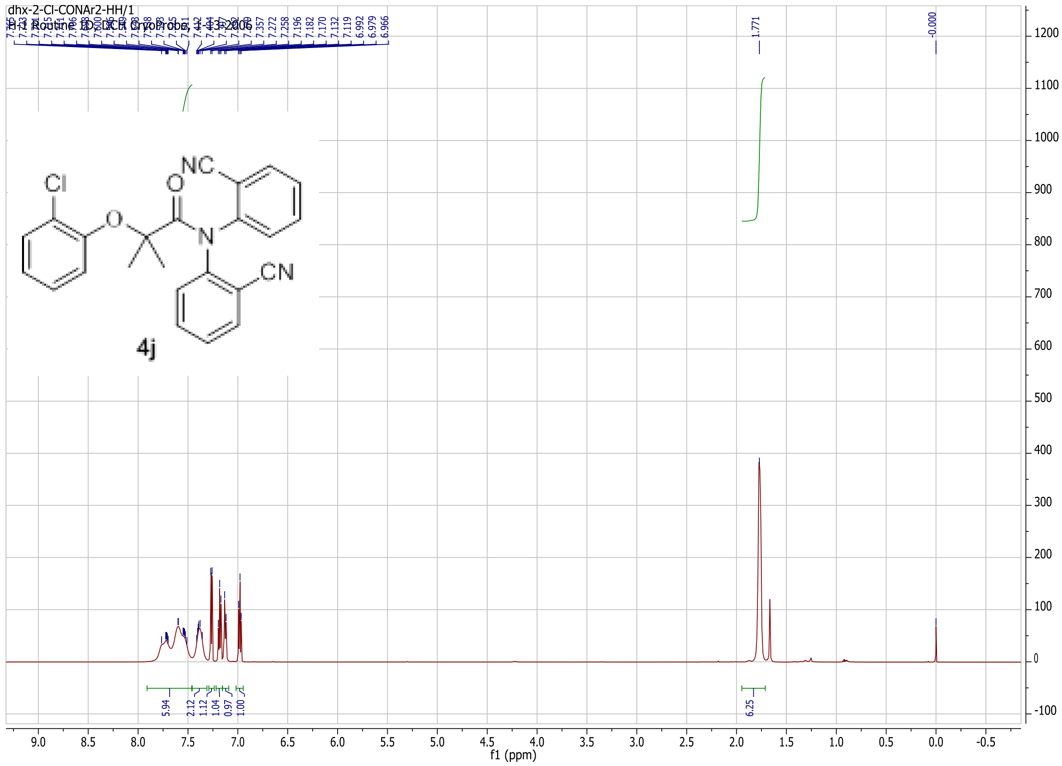

dhx-2-F-CONAr2-H-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
F
O
NC
O
N
CN
4g
174.453
156.834
155.189
145.645
139.975
139.897
126.094
125.197
125.149
124.028
116.614
116.484
113.103
85.473
77.212
76.788
26.299
25.317
f1 (ppm)

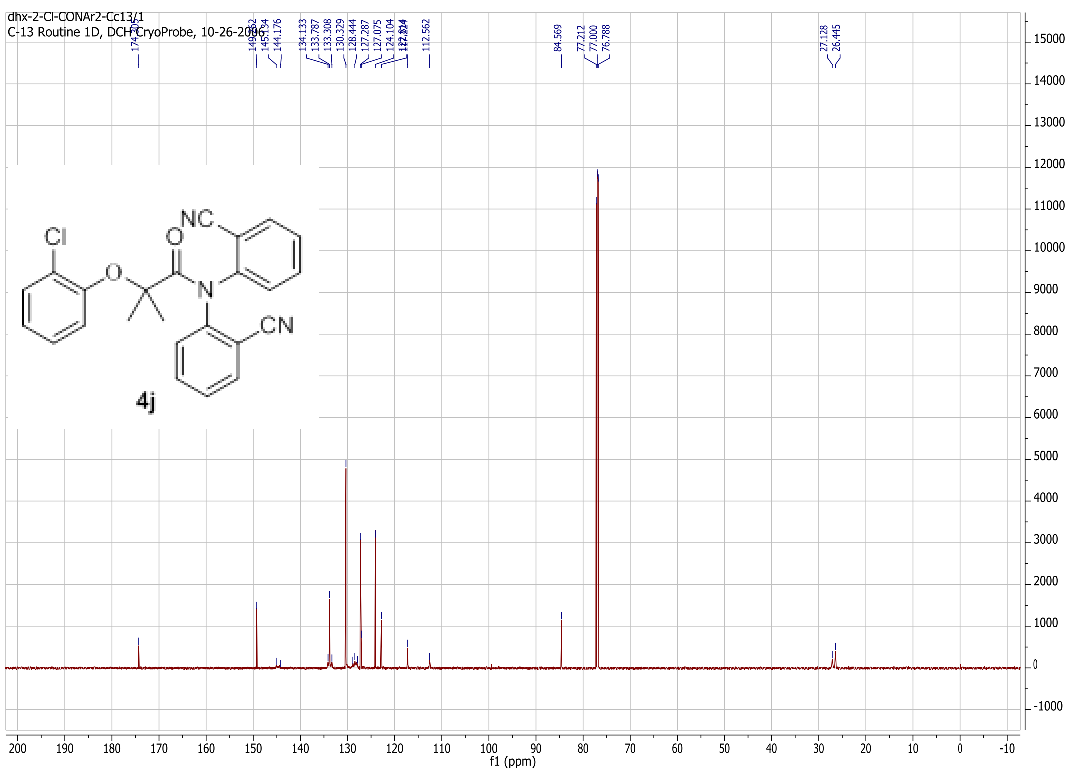

dhx-4-F-CONAr-P1/1
H-1 Routine 1D experiment, CBBO Probe, 4-15-2008
1.651
-0.000
5.82
1.98
1.98
2.00
6.42
f1 (ppm)
4h

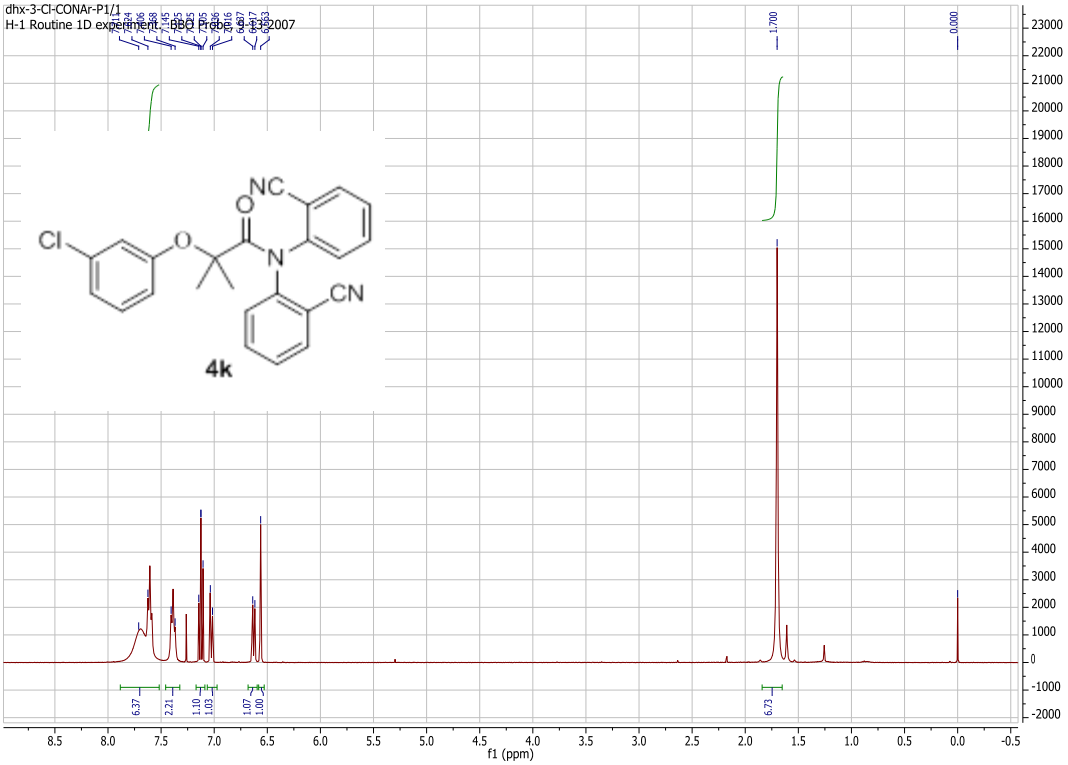

dhx-4-F-CONAr2-Cc13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
83.945
77.212
77.000
76.788
26.323
25.326
f1 (ppm)
4h

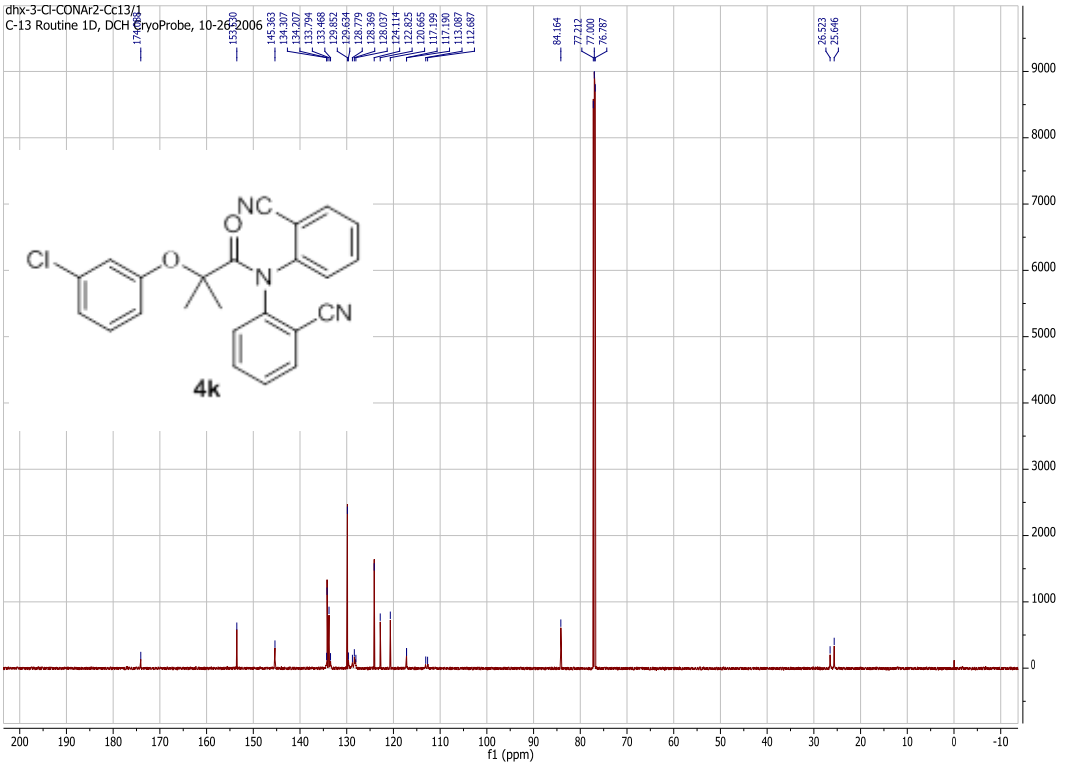

dhx-4-Cl-CONAr2-H/1
H-1 Routine 1D, DCH CryoProbe, 11-13-2006
7.405
7.384
7.366
7.275
7.151
7.137
6.609
6.594
1.685
1.660
0.000
NC
O
O
N
Cl
CN
4i
5.80
2.07
1.98
2.00
6.24
f1 (ppm)

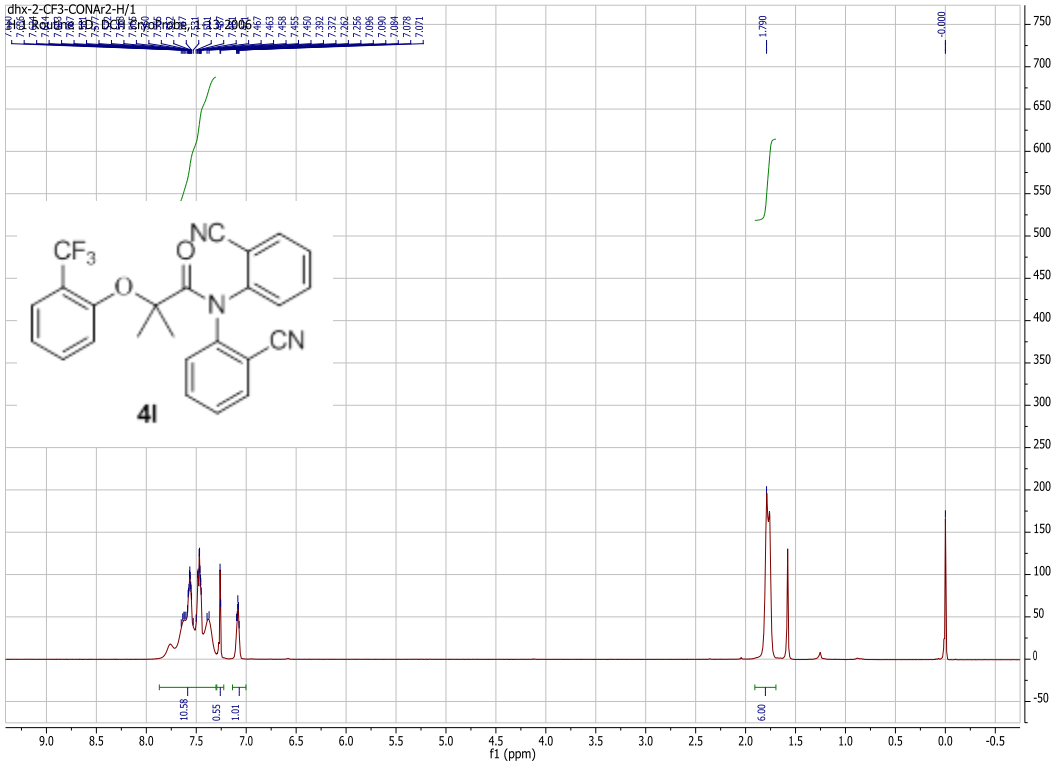

dhx-4-Cl-CONAr2-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
174.435
151.189
145.330
134.231
133.677
133.374
129.465
129.096
128.274
128.004
123.847
123.634
113.001
112.527
83.868
77.212
76.999
76.786
26.355
25.506
NC
O
O
N
Cl
CN
4i
f1 (ppm)

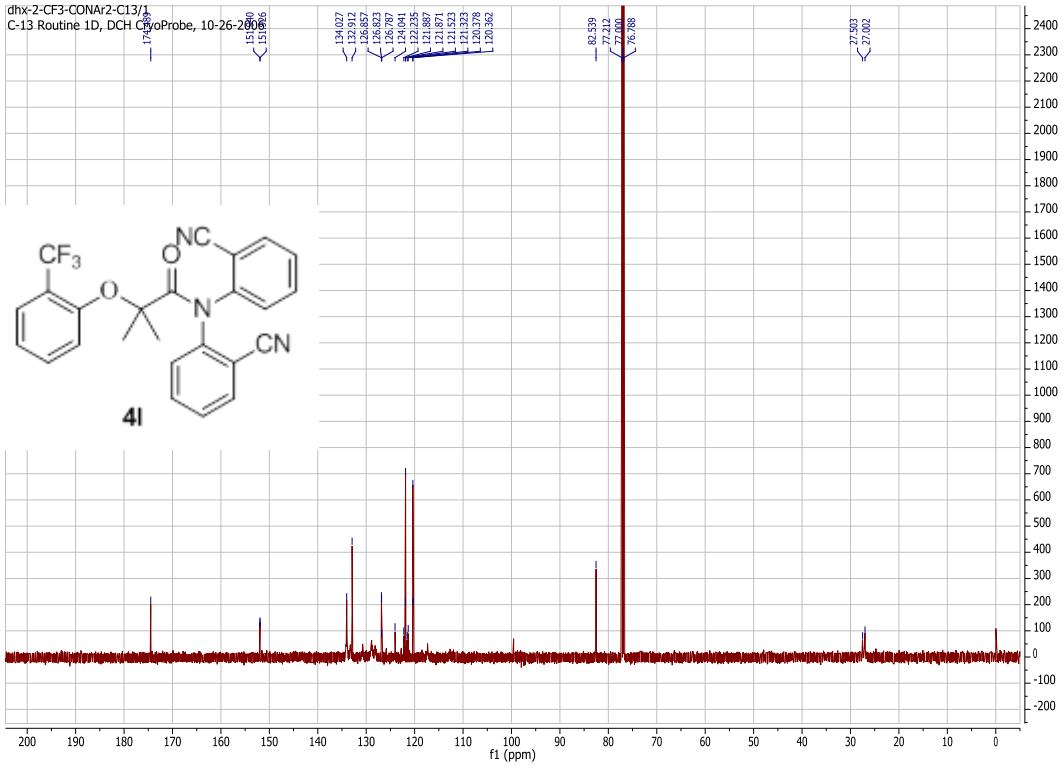

dhx-2-Cl-CONAr2-HH/1
1.771
-0.000
5.94
2.12
1.12
1.04
0.97
1.00
6.25
4j
f1 (ppm)

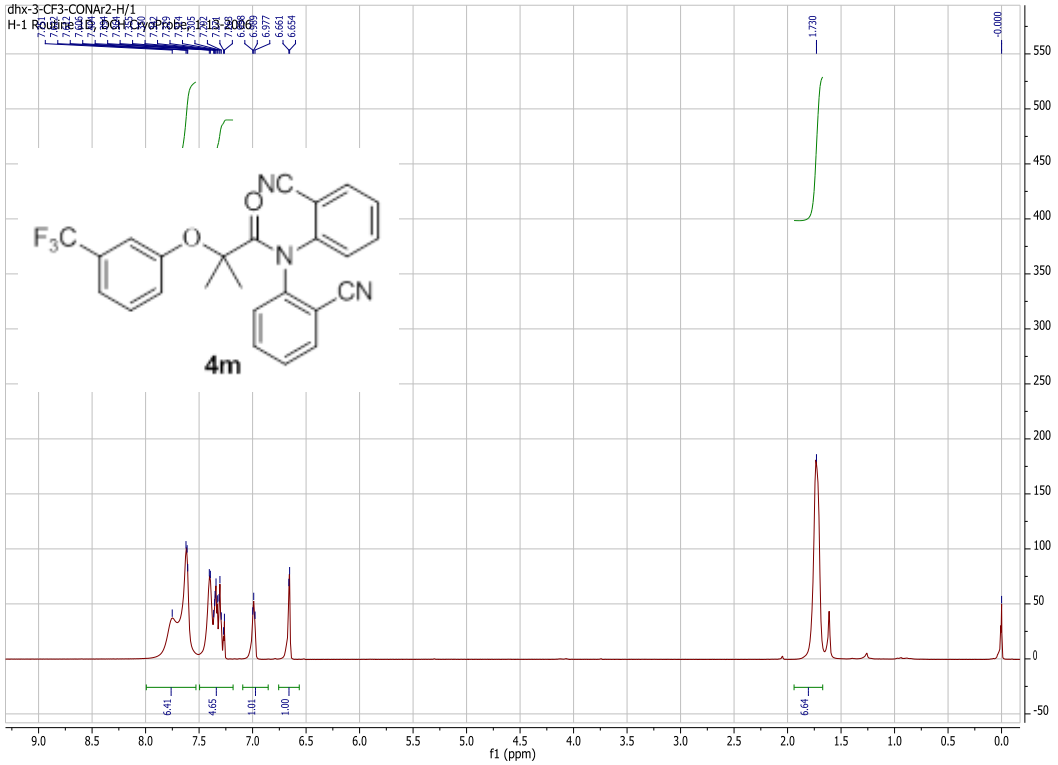

dhx-2-Cl-CONAr2-Cc13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
144.176
134.133
133.787
133.308
130.329
128.444
127.287
127.075
124.104
112.562
84.569
77.212
77.000
76.788
27.128
26.445
4j
f1 (ppm)

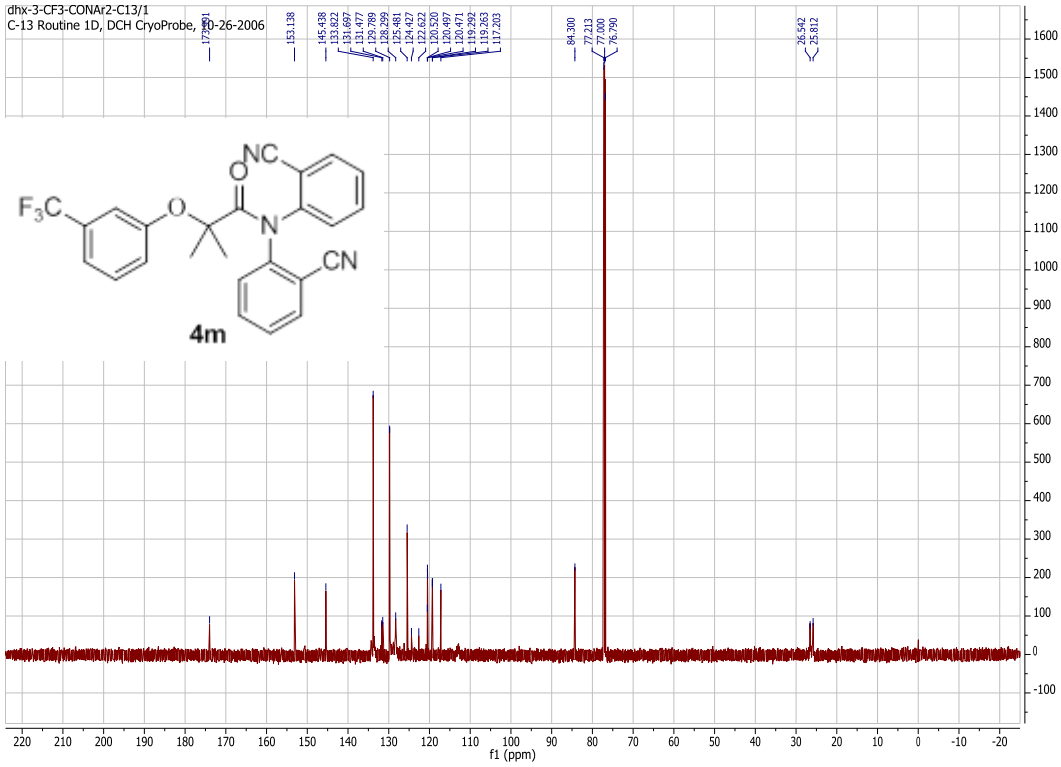

dhx-3-Cl-CONAr-P1/1
H-1 Routine 1D experiment, BBO Probe, 9-13-2007
1.700
0.000
NC
O
Cl
O
N
CN
4k
6.37
2.21
1.10
1.03
1.07
1.00
6.73
f1 (ppm)

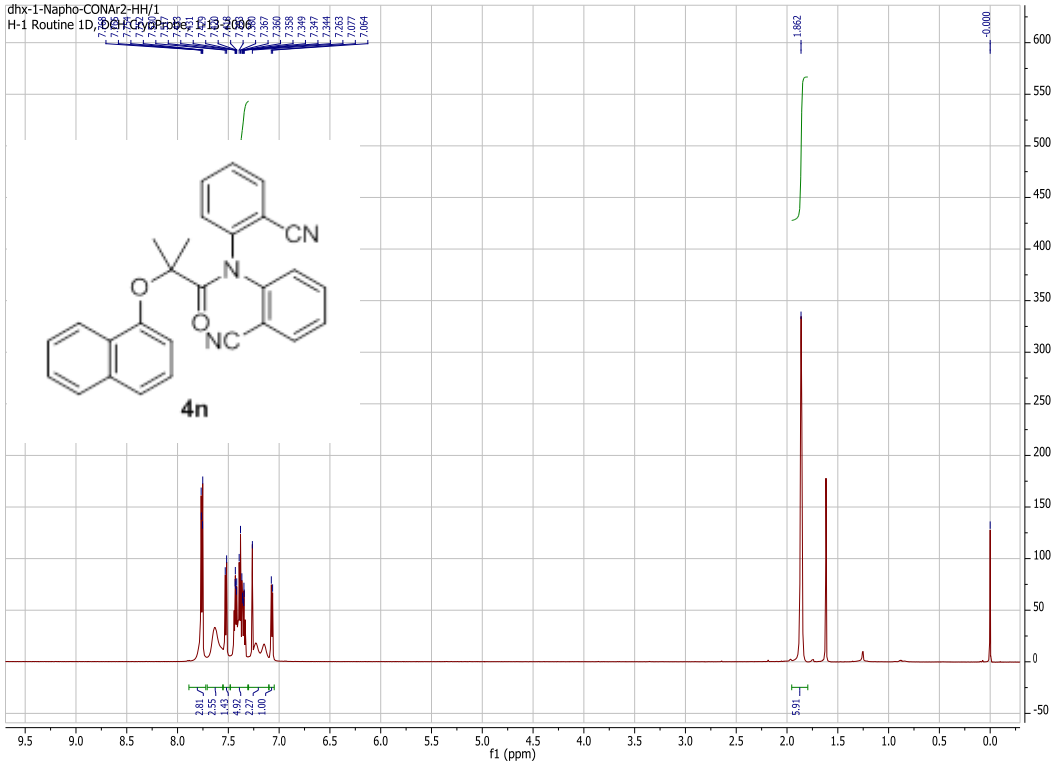

dhx-3-Cl-CONAr2-Cc13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
145.363
134.307
134.207
133.794
133.468
129.832
128.694
128.779
128.369
128.037
124.114
122.825
120.665
117.199
117.080
113.087
112.687
84.164
77.212
77.000
76.787
26.523
25.646
NC
O
Cl
O
N
CN
4k
f1 (ppm)

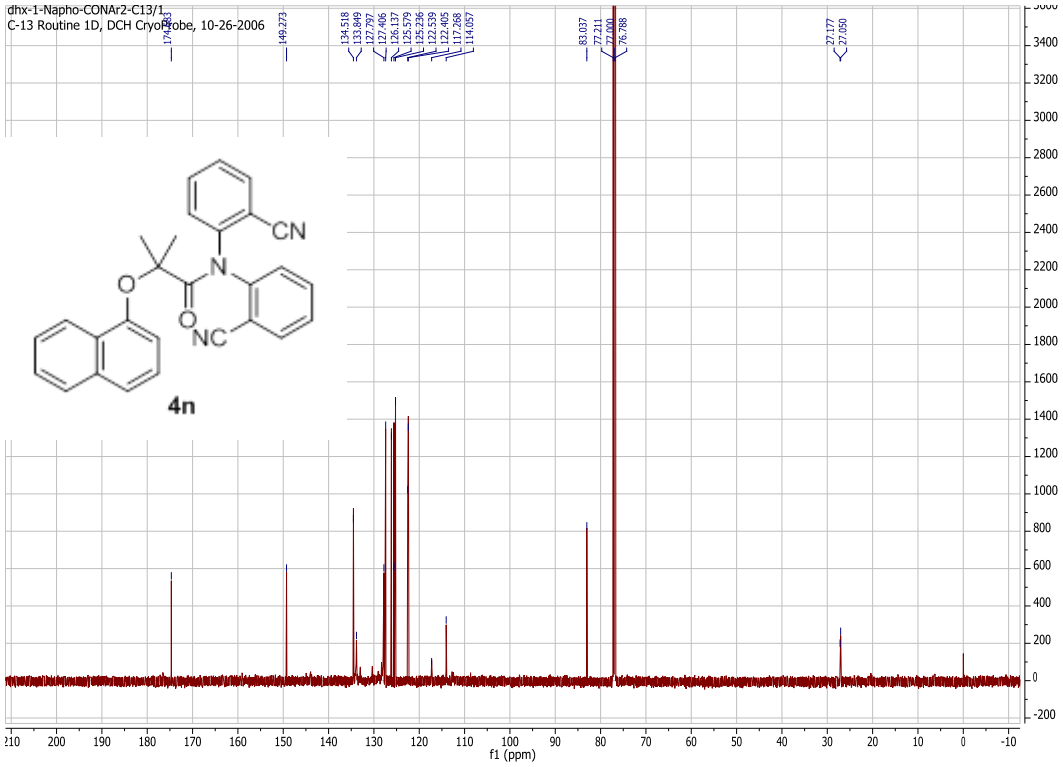

dhx-2-CF3-CONAr2-H/1
H-1 Routine 1D, DCH cryoProbe, 10-26-2006
CF3
O
NC
O
N
CN
4l
1.790
0.000
10.58
0.55
1.01
6.00
f1 (ppm)

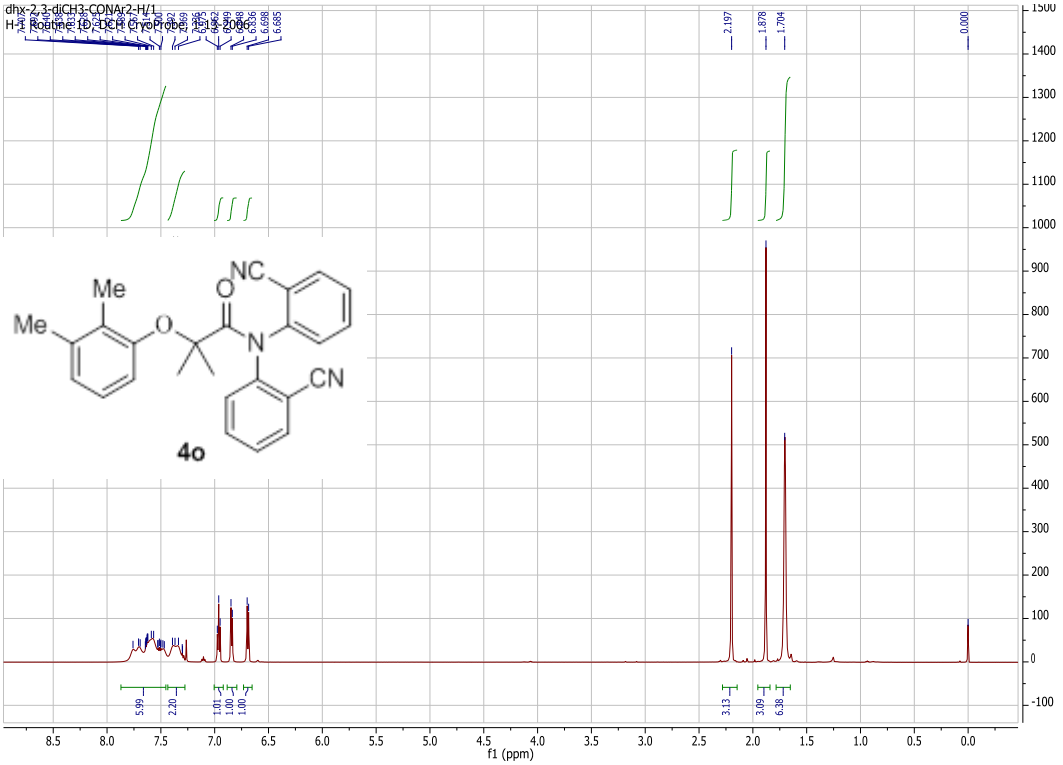

dhx-2-CF3-CONAr2-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
CF3
O
NC
O
N
CN
4l
82.539
77.212
77.000
76.788
27.503
27.002
f1 (ppm)

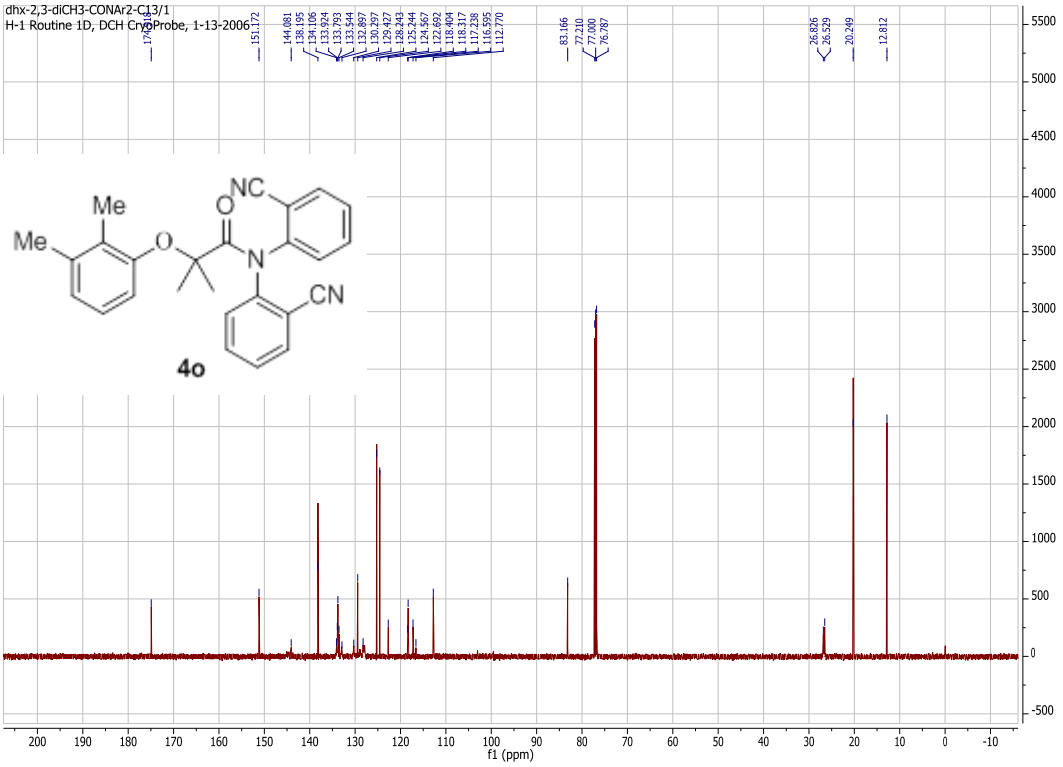

dhx-3-CF3-CONAr2-H/1
H-1 Routine 1D, DCH CryoProbe, 11-13-2006
NC
O
N
F3C
O
CN
4m
1.720
0.000
6.41
4.65
1.01
1.00
6.64
f1 (ppm)

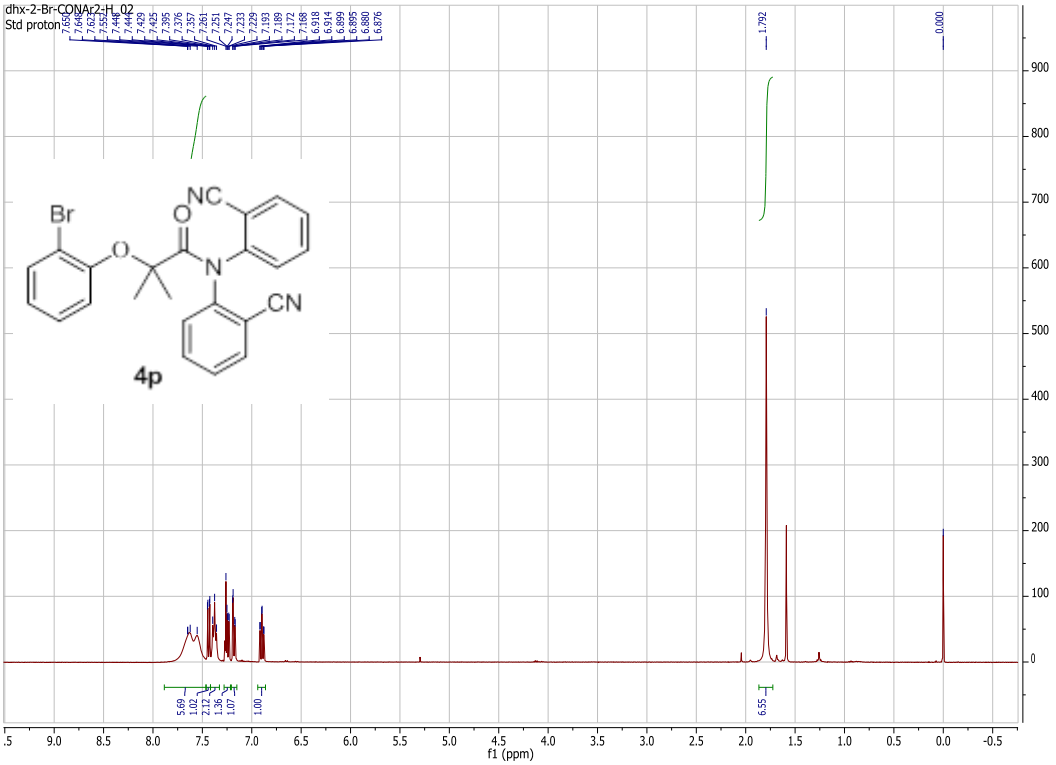

dhx-3-CF3-CONAr2-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
153.138
145.438
131.477
129.789
128.299
125.481
124.427
122.622
84.300
77.213
76.790
26.542
25.812
NC
O
N
F3C
O
CN
4m
f1 (ppm)

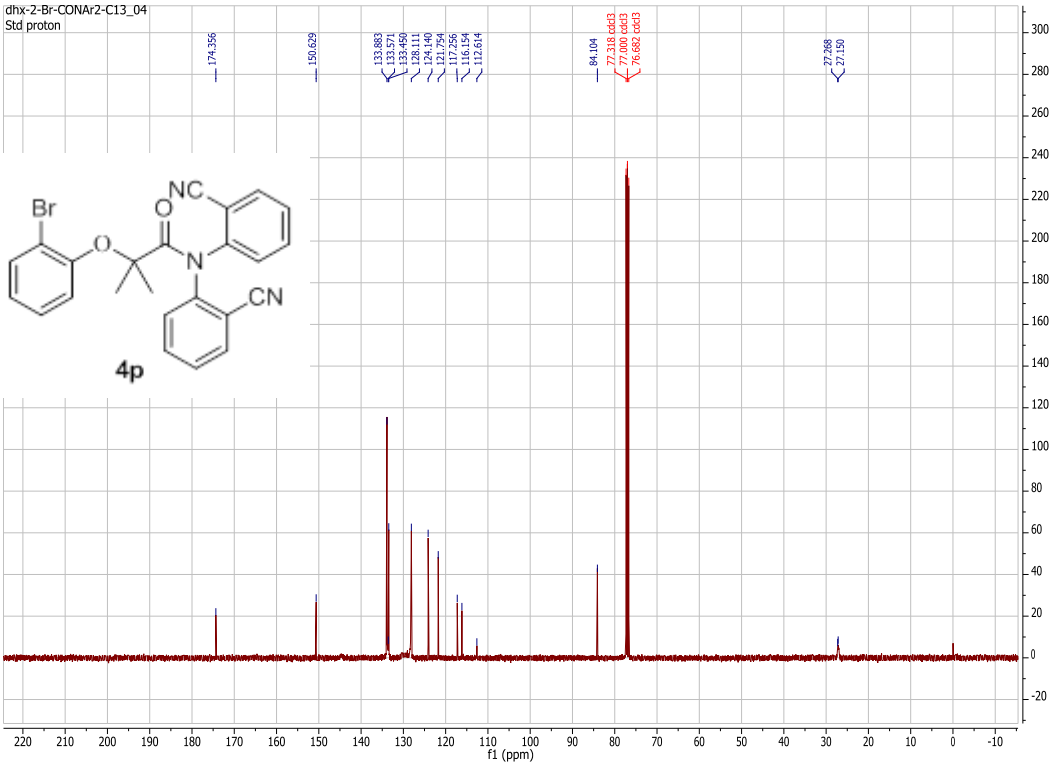

dhx-1-Napho-CONAr2-HH/1
H-1 Routine 1D, DCH CryoProbe, 1-13-2006
CN
O
N
O
NC
4n
f1 (ppm)

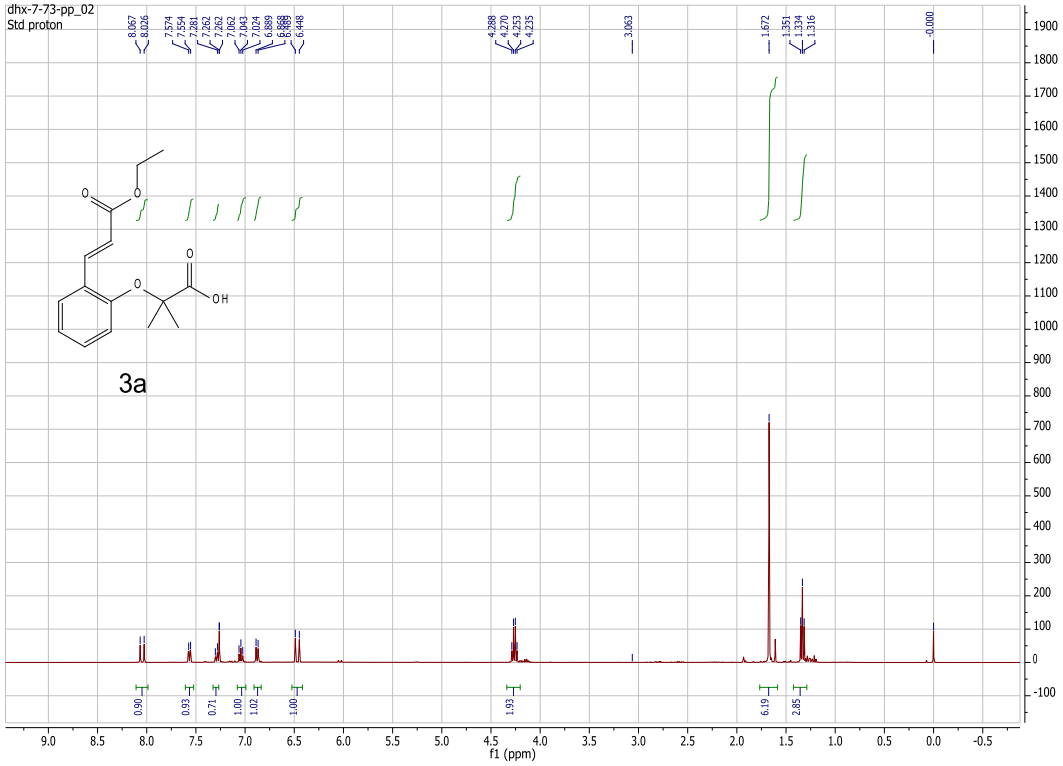

dhx-1-Napho-CONAr2-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
CN
O
N
O
NC
4n
f1 (ppm)

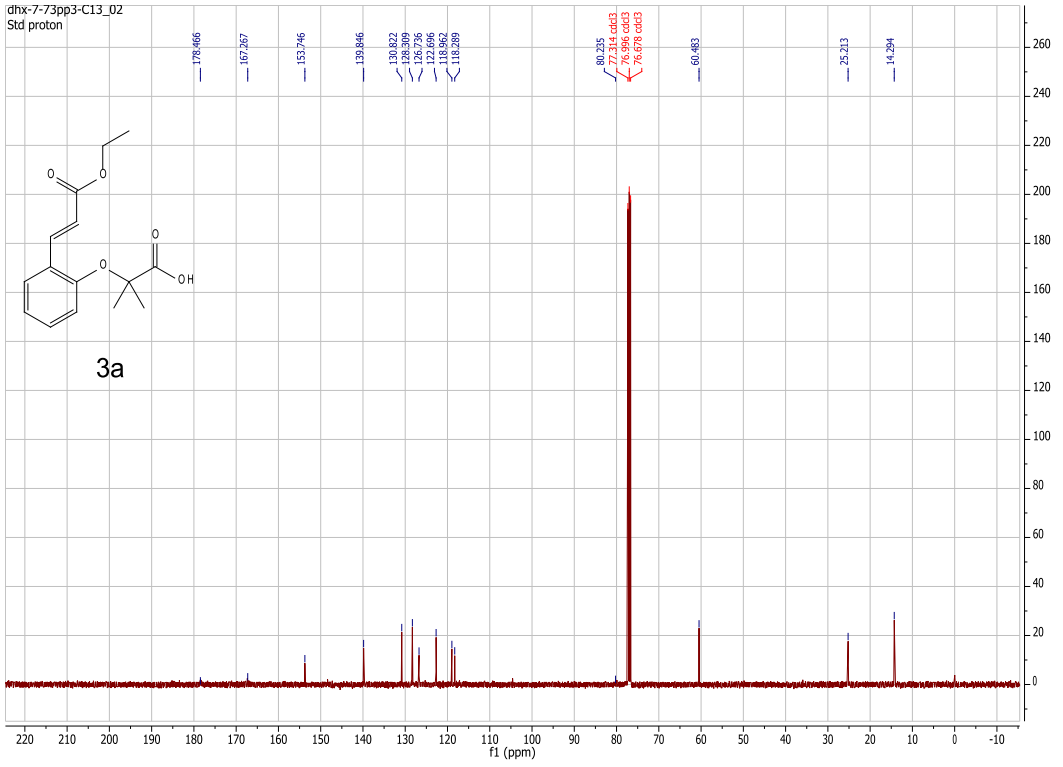

dhx-2,3-diCH3-CONAr2-H/1
H-1 Routine 1D, DCH CryoProbe, 1-13-2006
2.197
1.878
1.704
0.000
Me
Me
O
NC
O
N
CN
4o
5.99
2.20
1.01
1.00
1.00
3.13
3.09
6.38
f1 (ppm)

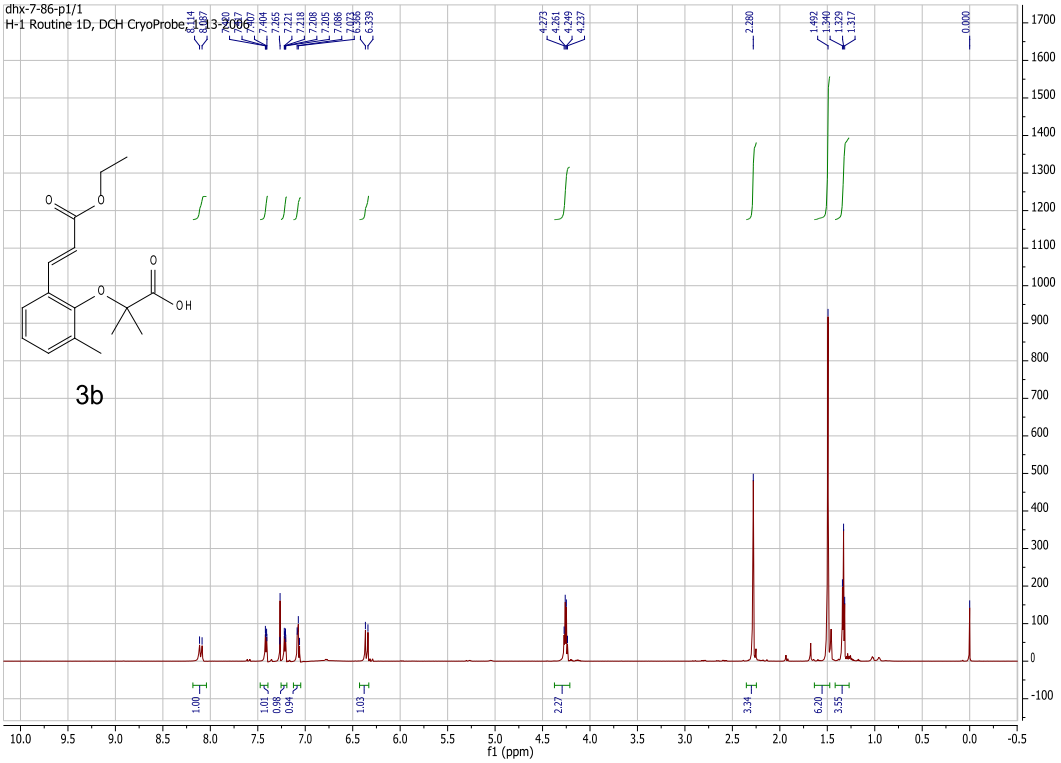

dhx-2,3-diCH3-CONAr2-C13/1
H-1 Routine 1D, DCH CryoProbe, 1-13-2006
151.172
144.081
138.195
134.106
133.924
133.793
133.544
132.857
129.427
128.243
125.244
124.567
122.692
118.404
118.317
117.238
115.595
112.770
83.166
77.210
77.000
76.787
26.826
26.529
20.249
12.812
Me
Me
O
NC
O
N
CN
4o
f1 (ppm)

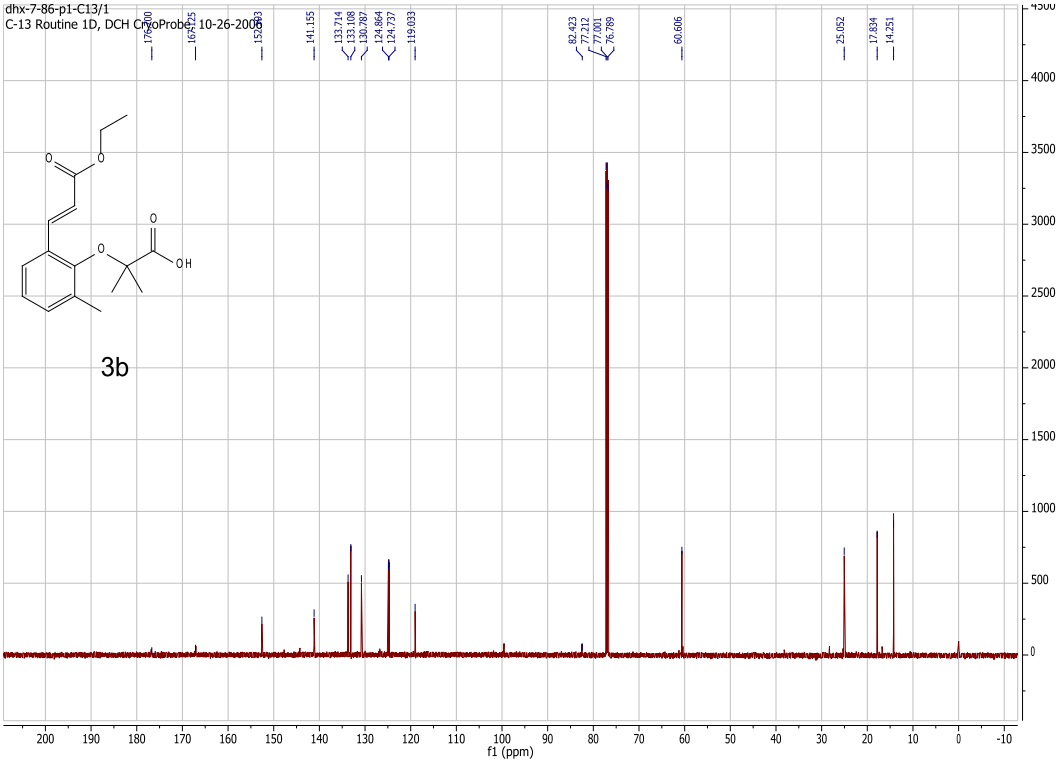

dhx-2-Br-CONAr2-H_02
Std proton
Br
O
NC
O
N
CN
4p
f1 (ppm)

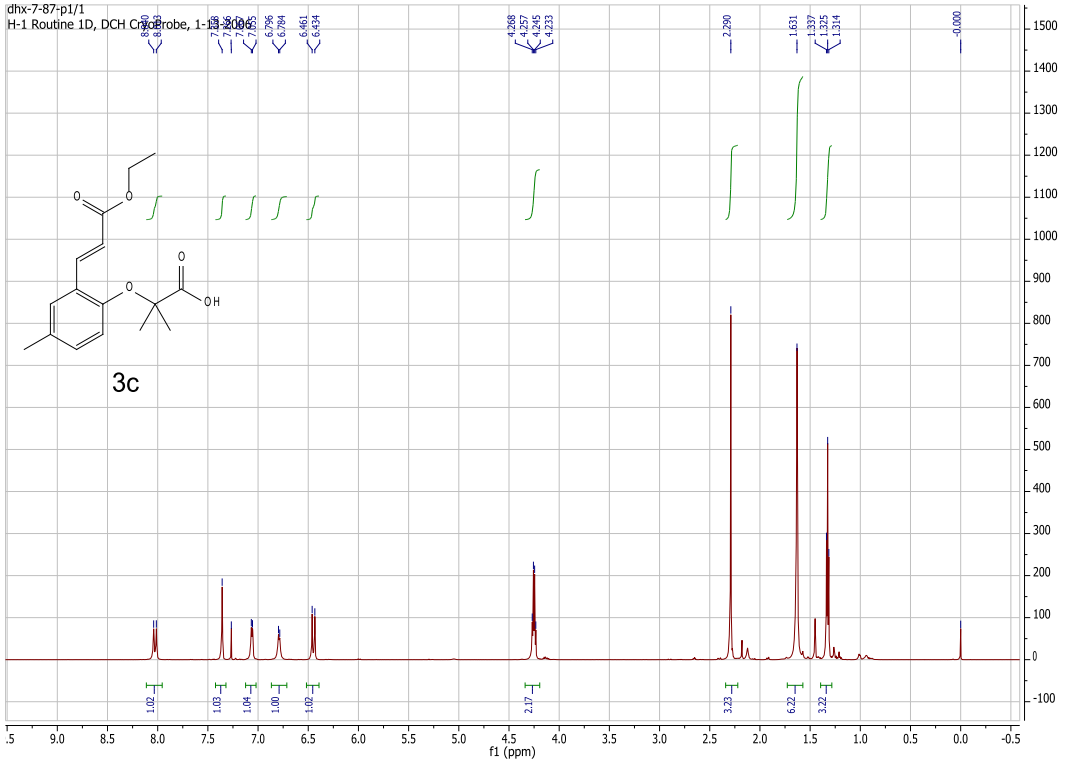

dhx-2-Br-CONAr2-C13_04
Std proton
Br
O
NC
O
N
CN
4p
f1 (ppm)

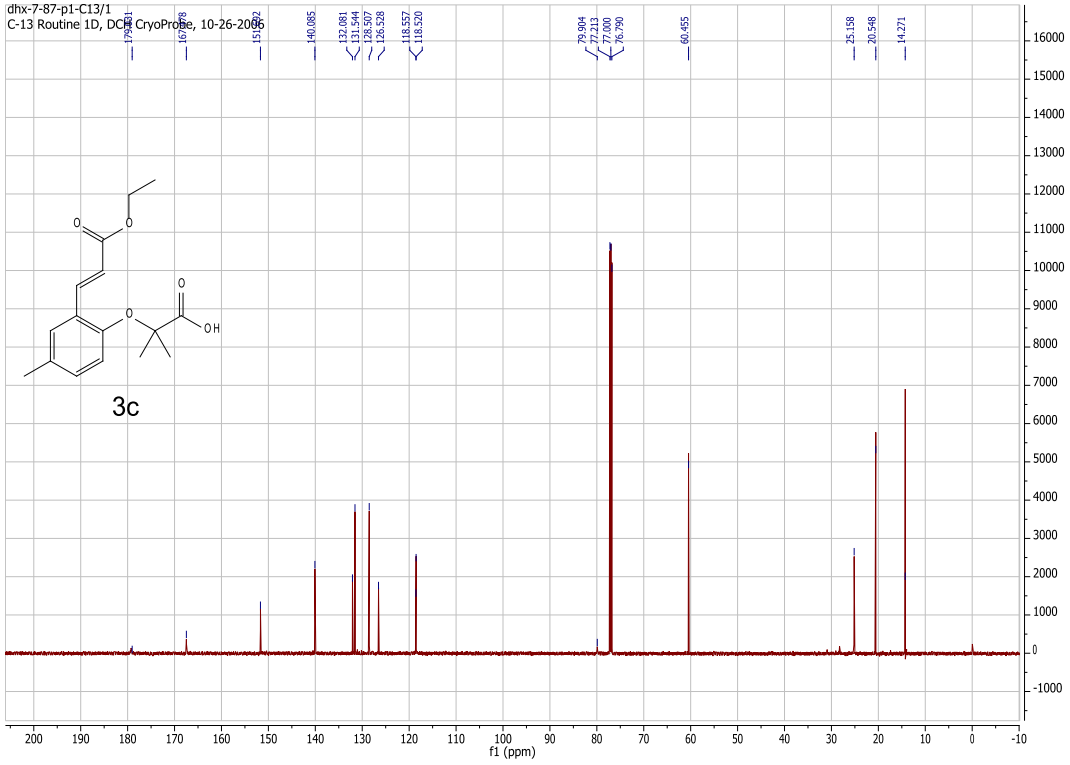

dhx-7-73-pp_02
Std proton
3a
f1 (ppm)

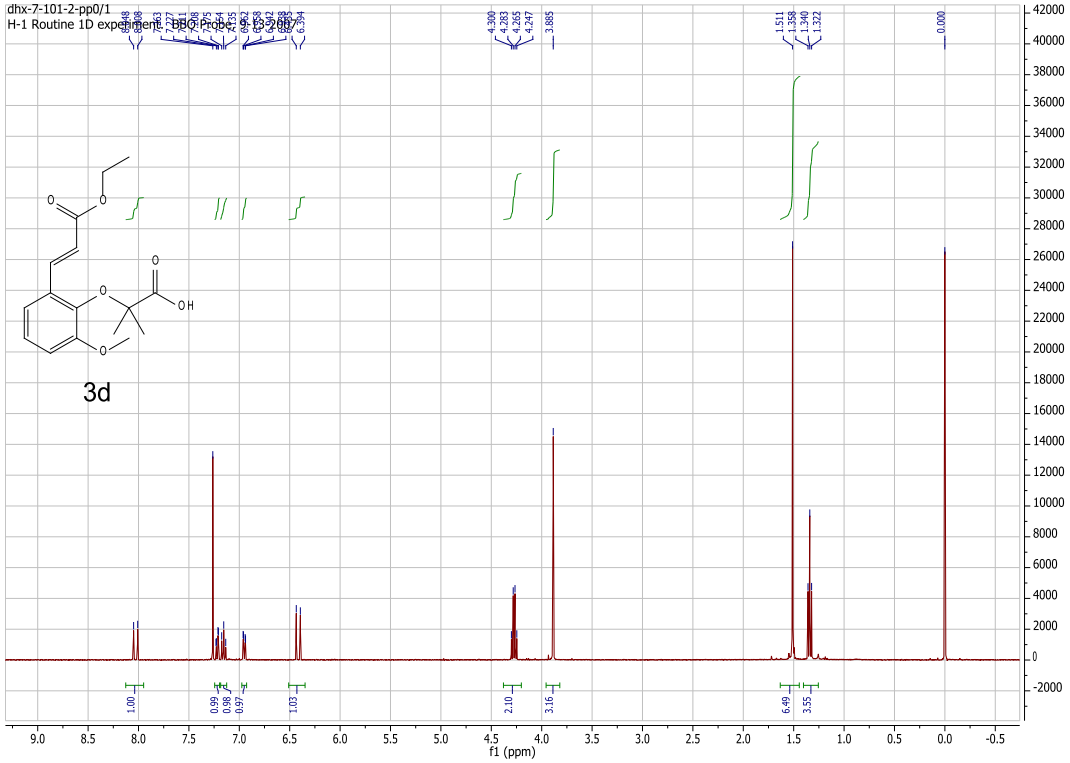

dhx-7-73pp3-C13_02
Std proton
3a
f1 (ppm)

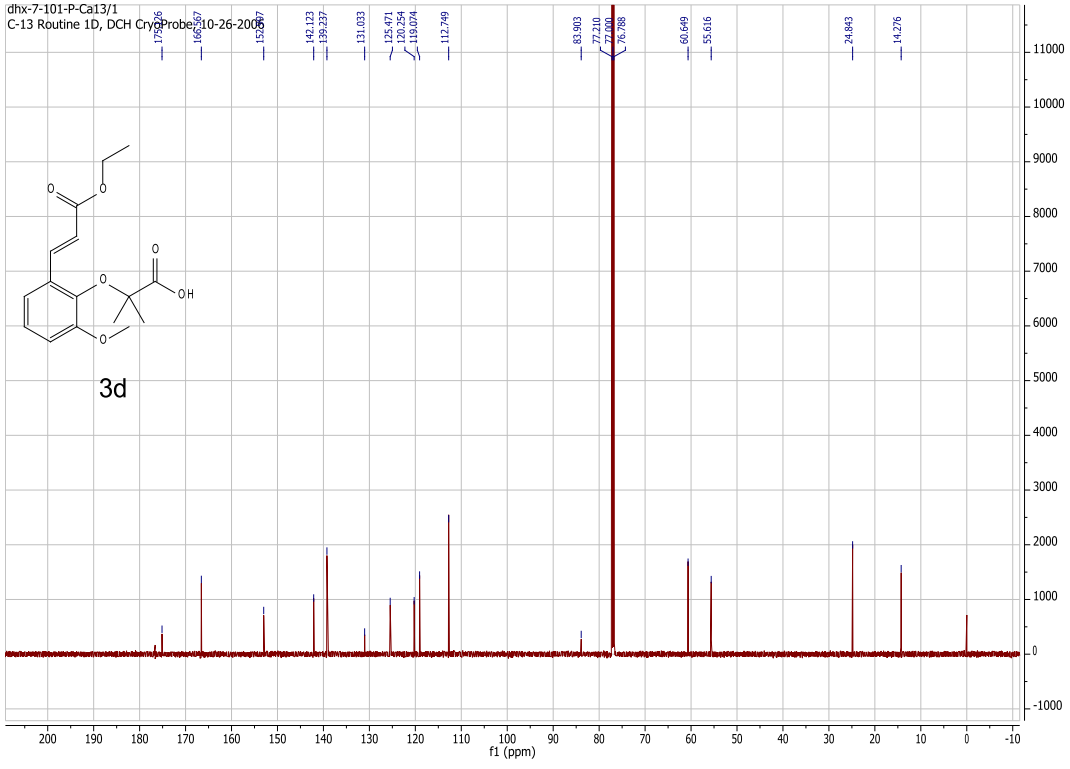

dhx-7-86-p1/1
H-1 Routine 1D, DCH CryoProbe, 10-26-2006
3b
f1 (ppm)

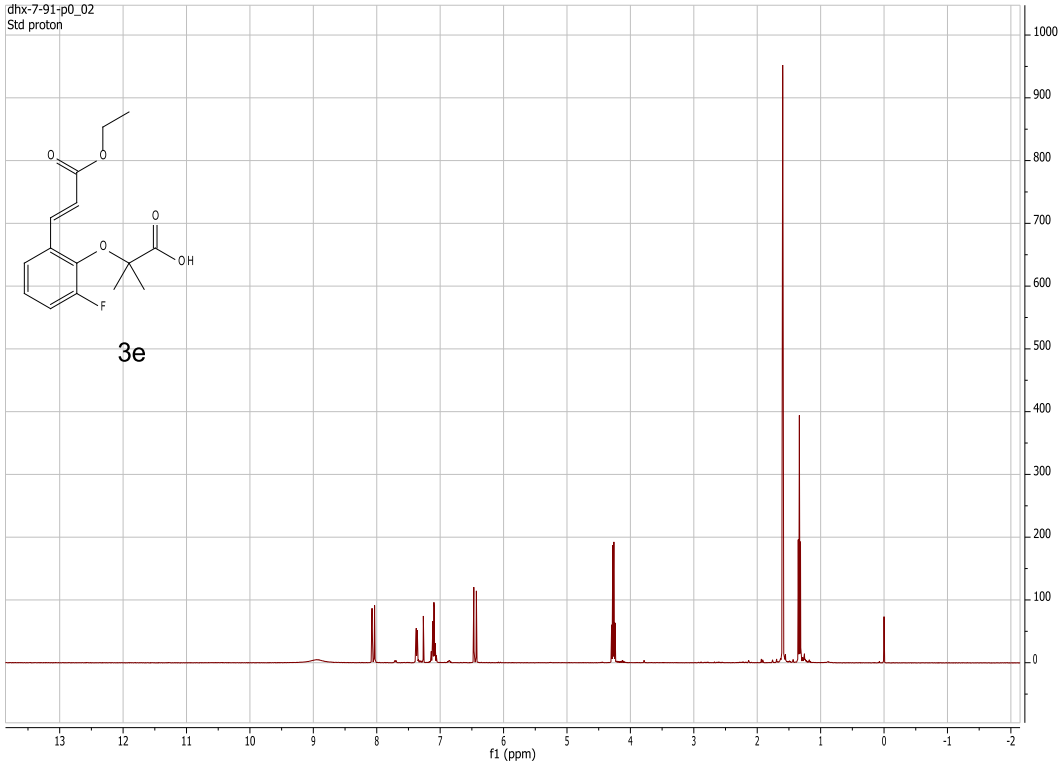

dhx-7-86-p1-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
3b
f1 (ppm)

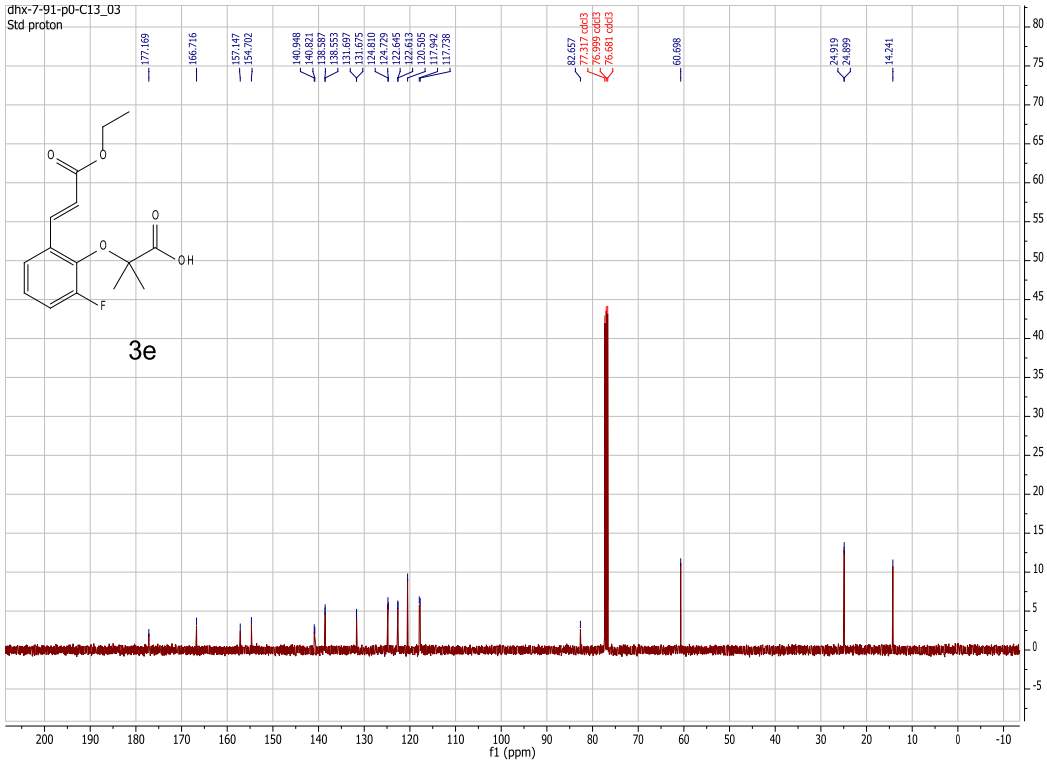

dhx-7-87-p1/1
H-1 Routine 1D, DCH CryoProbe, 1-18-2006
3c
f1 (ppm)

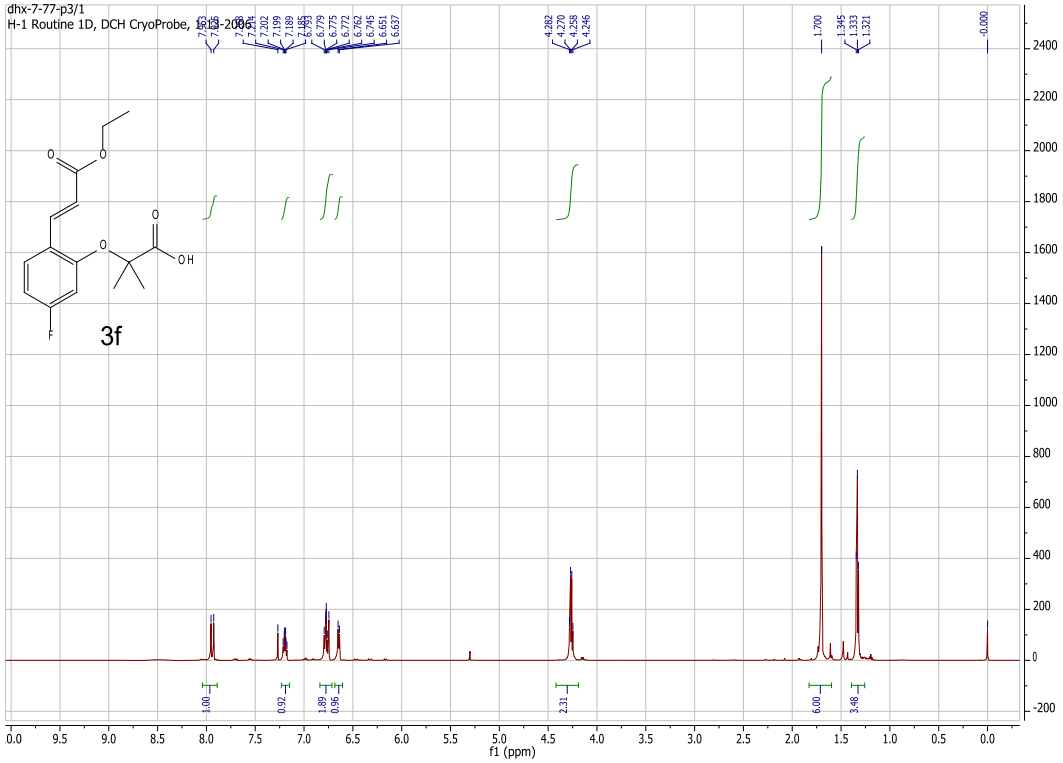

dhx-7-87-p1-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
3c
f1 (ppm)

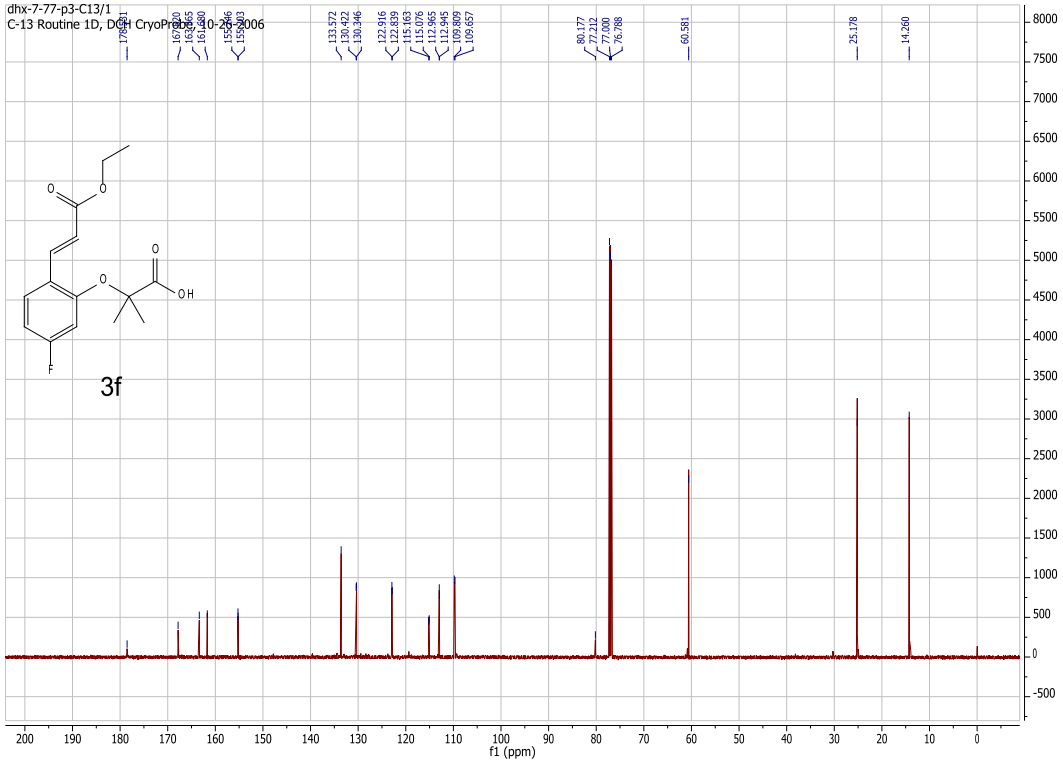

dhx-7-101-2-pp0/1
H-1 Routine 1D experiment, DBO Probe, CDCl3-200
3d
f1 (ppm)

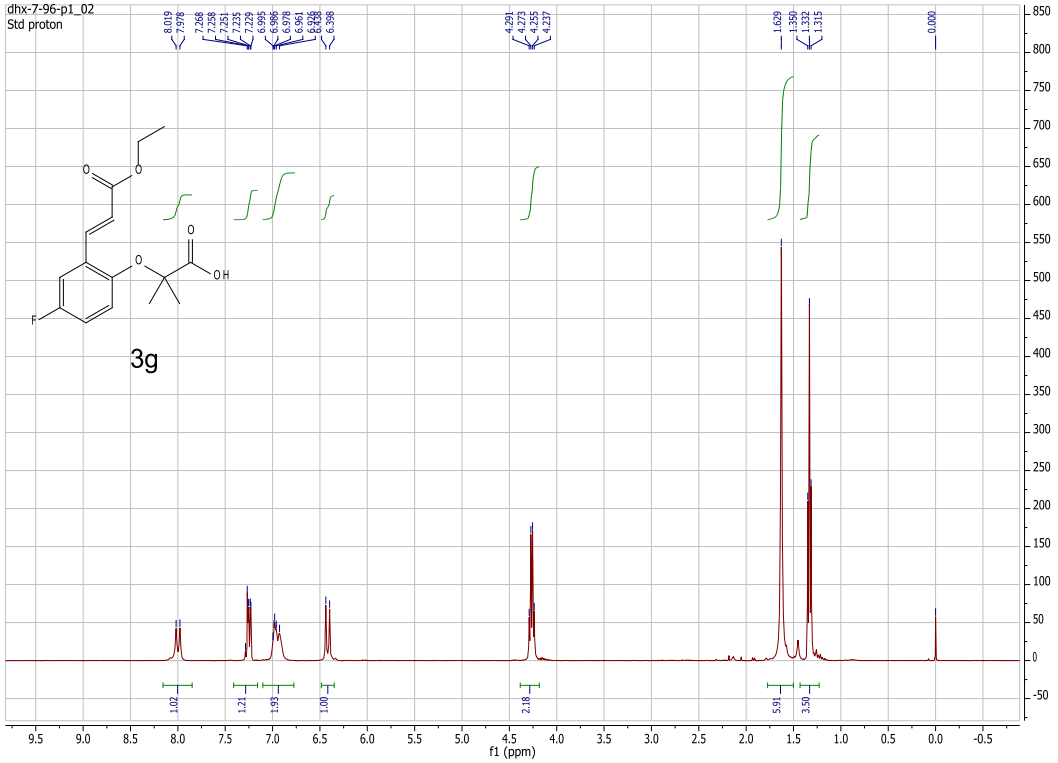

dhx-7-101-P-Ca13/1
C-13 Routine 1D, DCH CryoProbe-10-26-2006
3d
f1 (ppm)

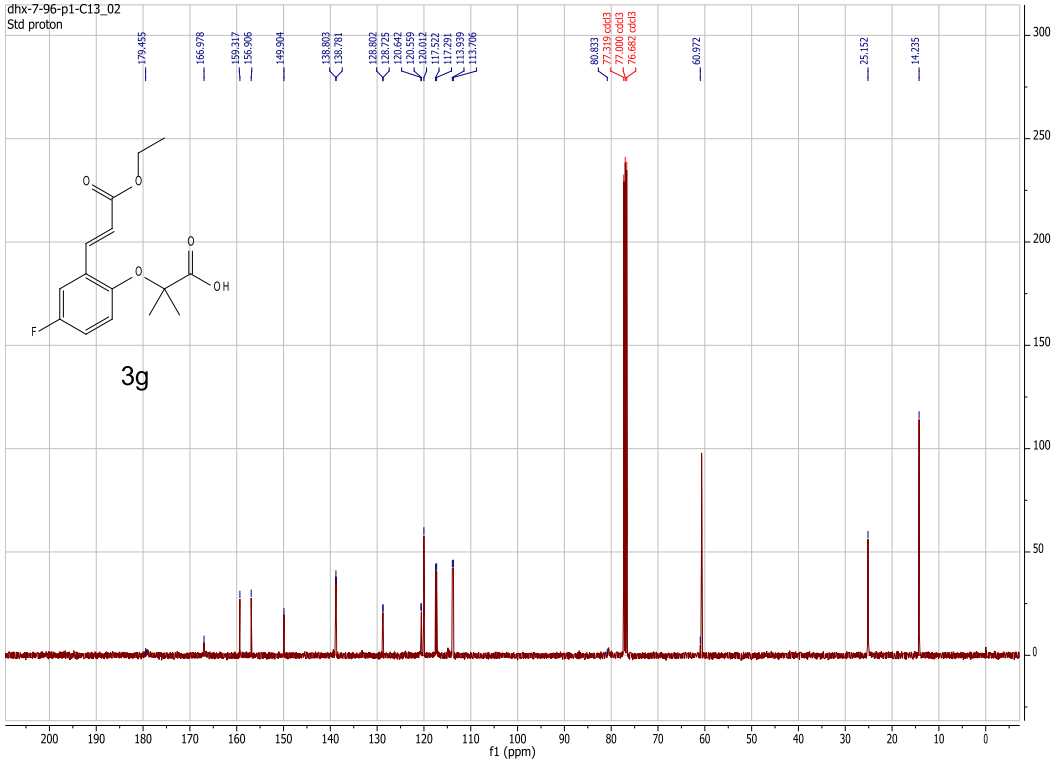

dhx-7-91-p0_02
Std proton
3e
f1 (ppm)

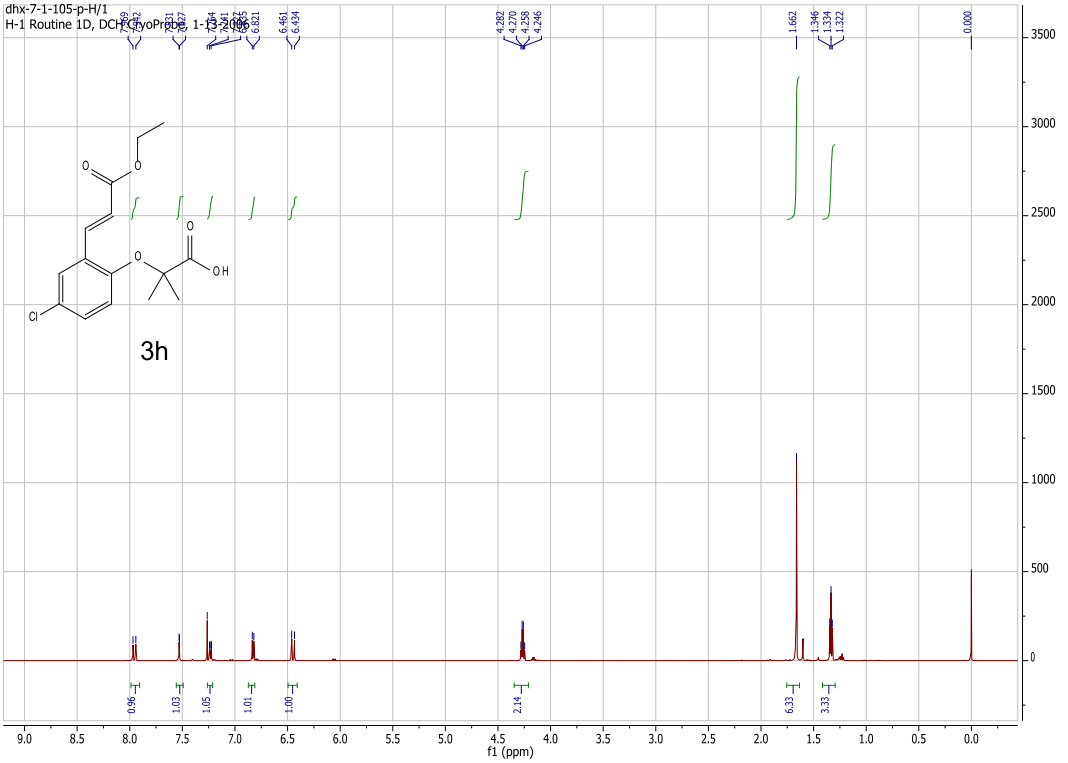

dhx-7-91-p0-C13_03
Std proton
177.169
166.716
157.147
154.702
140.948
140.821
138.557
138.553
131.697
131.675
124.810
124.729
122.645
122.613
120.505
117.942
117.738
82.657
77.317 cdcl3
76.999 cdcl3
76.681 cdcl3
60.698
24.919
24.899
14.241
3e
f1 (ppm)

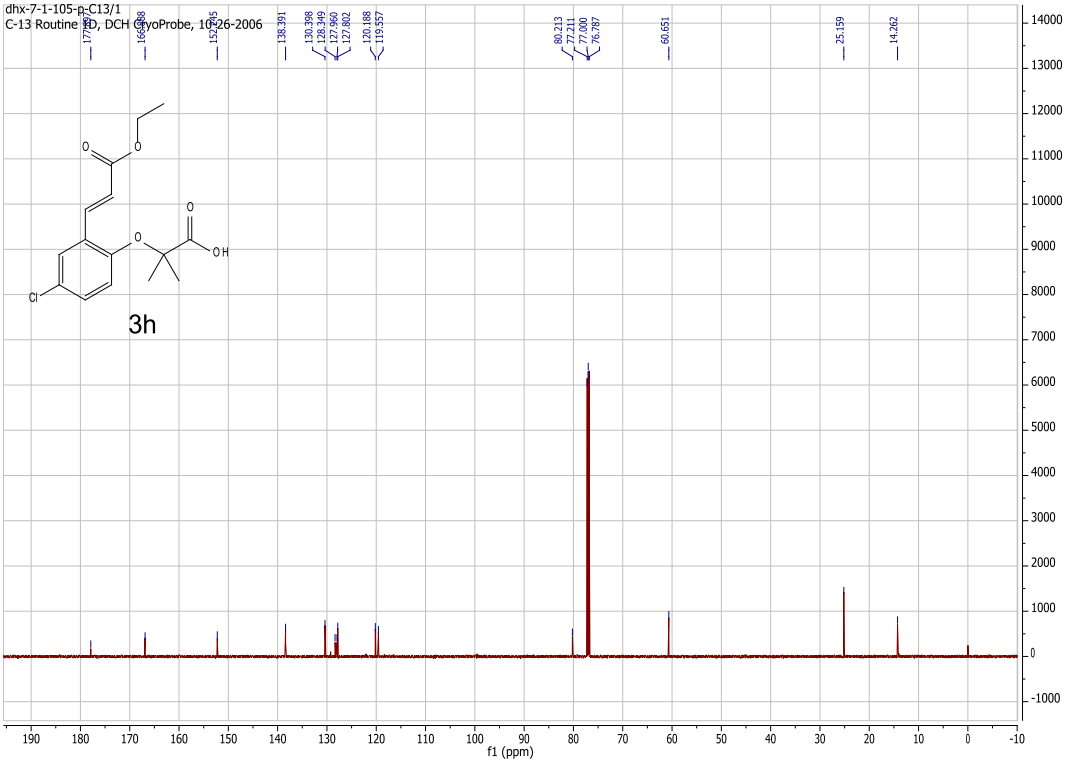

dhx-7-77-p3/1
H-1 Routine 1D, DCH CryoProbe, 10-25-2006
3f
f1 (ppm)

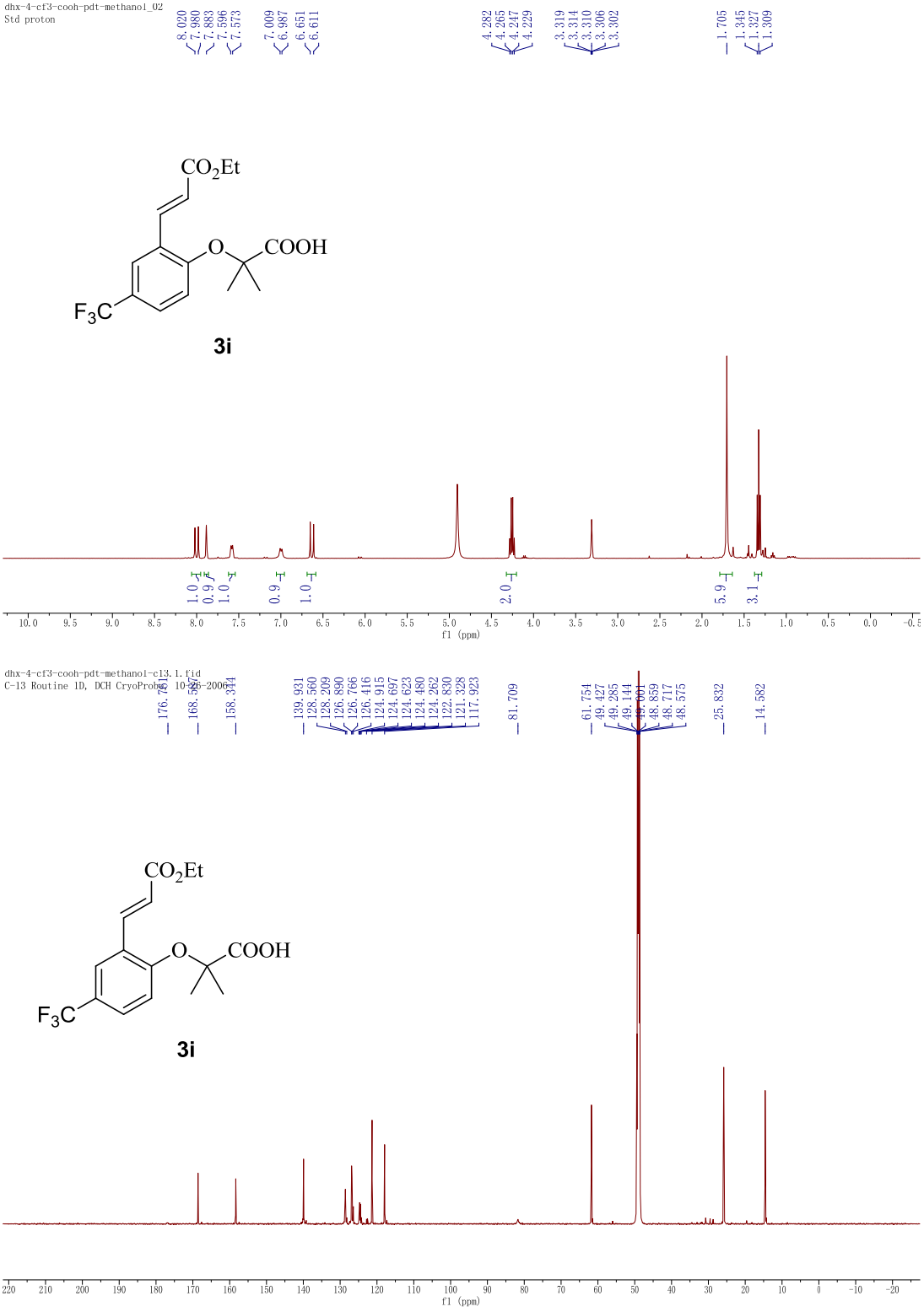

dhx-7-77-p3-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-25-2006
3f
f1 (ppm)

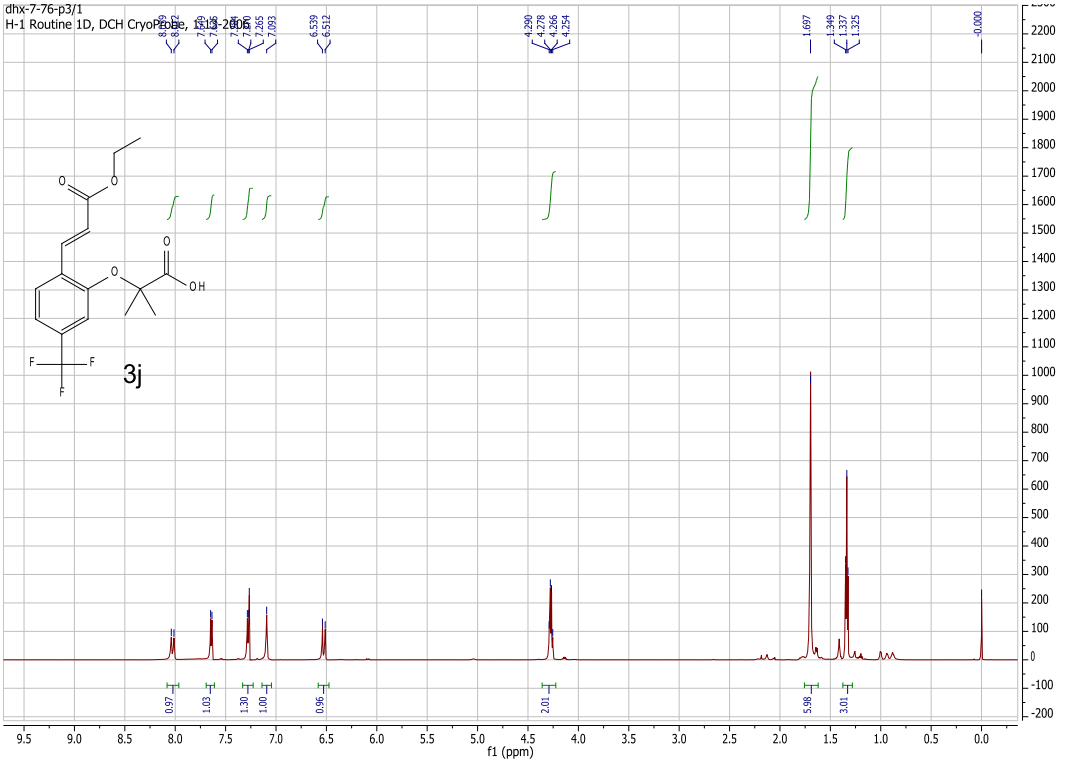

dhx-7-96-p1_02
Std proton
8.019
7.978
7.268
7.258
7.251
7.235
7.229
6.995
6.986
6.978
6.961
6.428
6.398
4.291
4.273
4.255
4.237
1.629
1.350
1.332
1.315
0.000
3g
1.02
1.21
1.93
1.00
2.18
5.91
3.50
f1 (ppm)

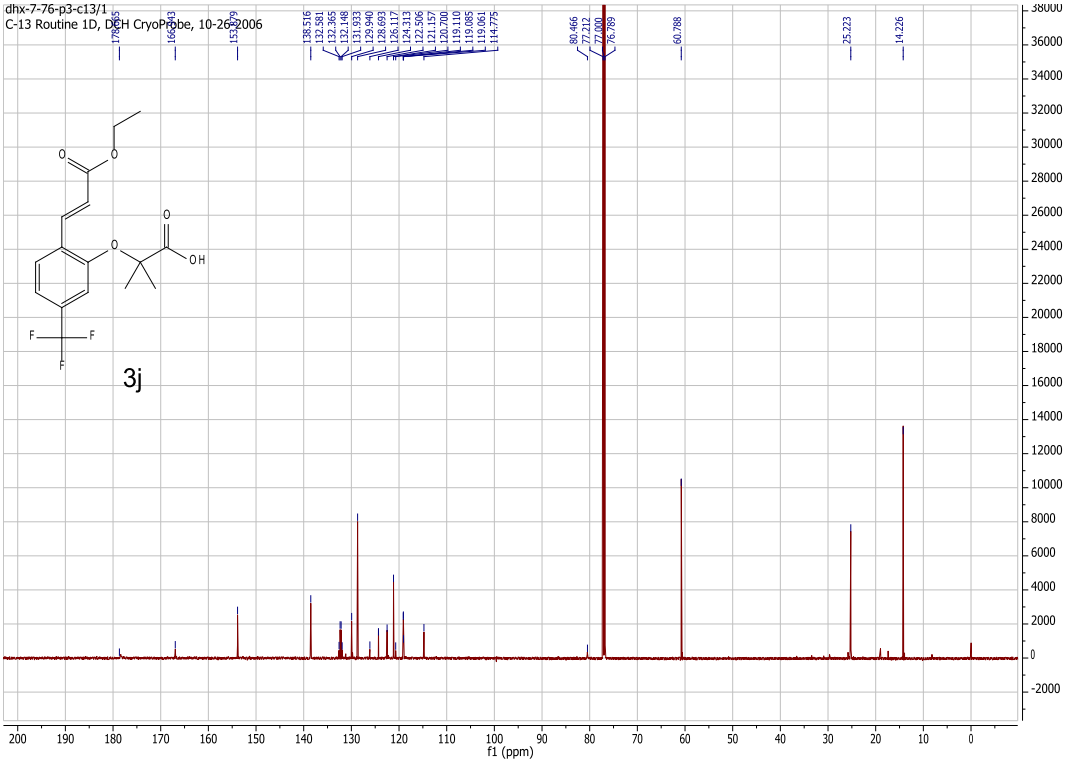

dhx-7-96-p1-C13_02
Std proton
179.455
166.978
159.317
156.906
149.904
138.803
138.781
128.802
128.725
120.642
120.559
120.012
117.522
117.291
113.598
113.706
80.833
77.319 cdcl3
77.000 cdcl3
76.682 cdcl3
60.972
25.152
14.235
3g
f1 (ppm)

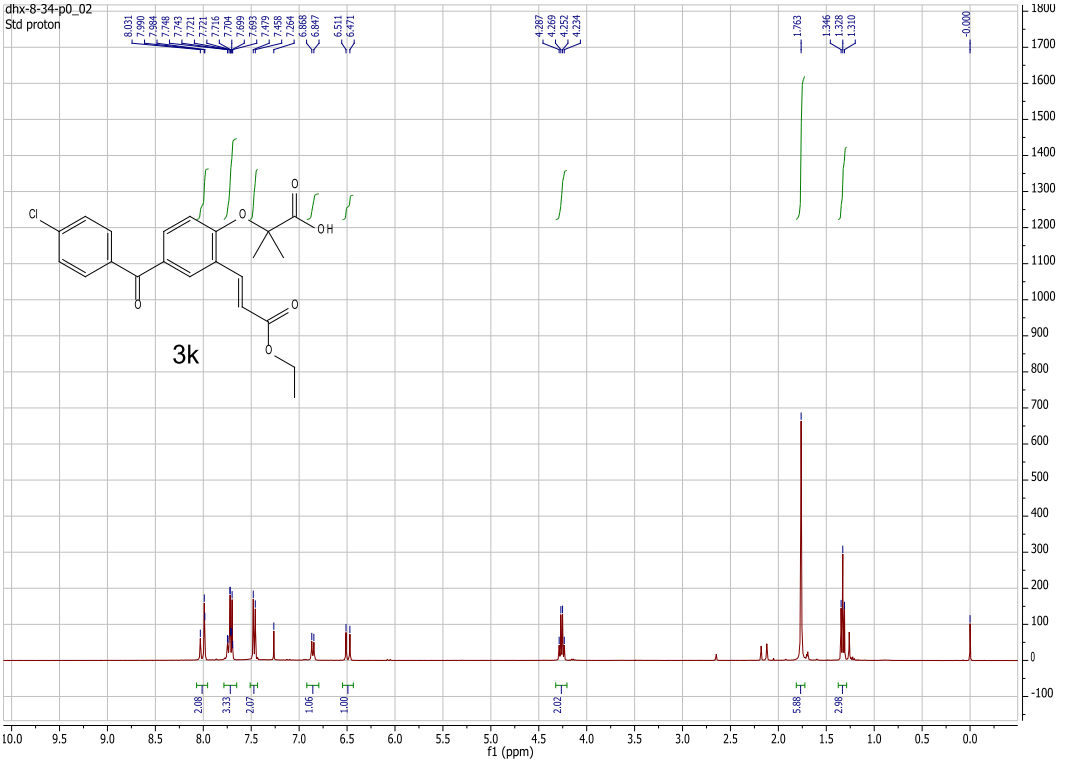

dhx-7-1-105-p-H/1
H-1 Routine 1D, DCH CryoProbe, 1-13-2006
3h
f1 (ppm)

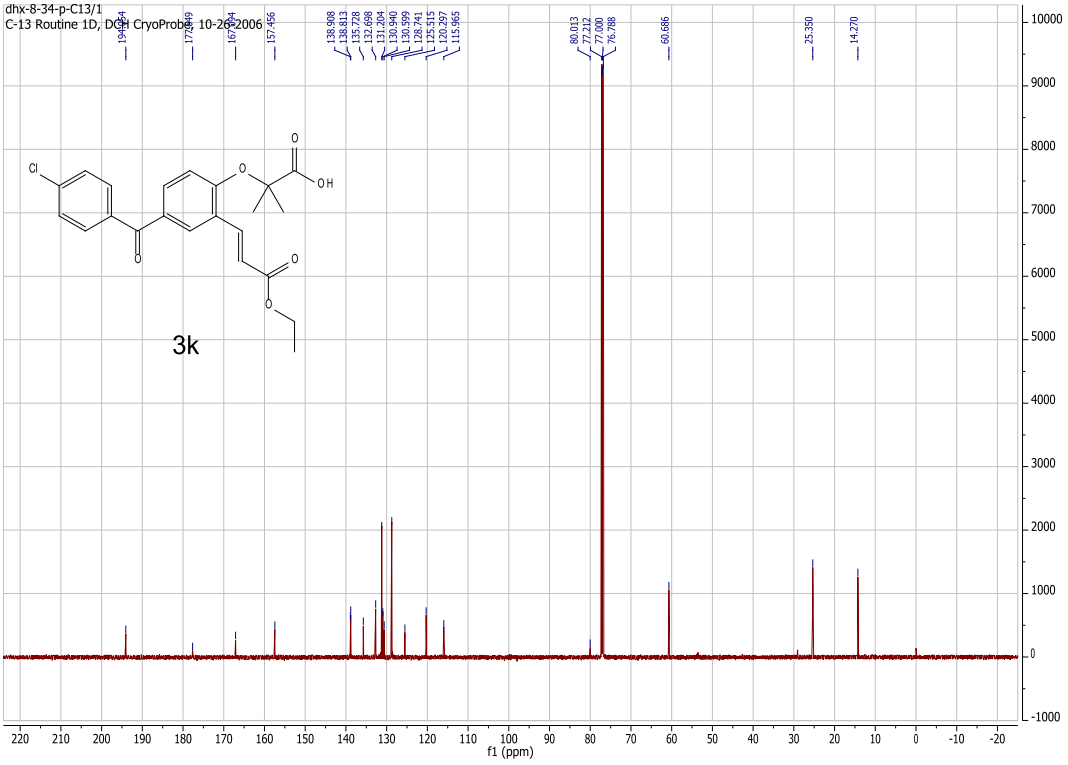

dhx-7-1-105-p-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
3h
f1 (ppm)

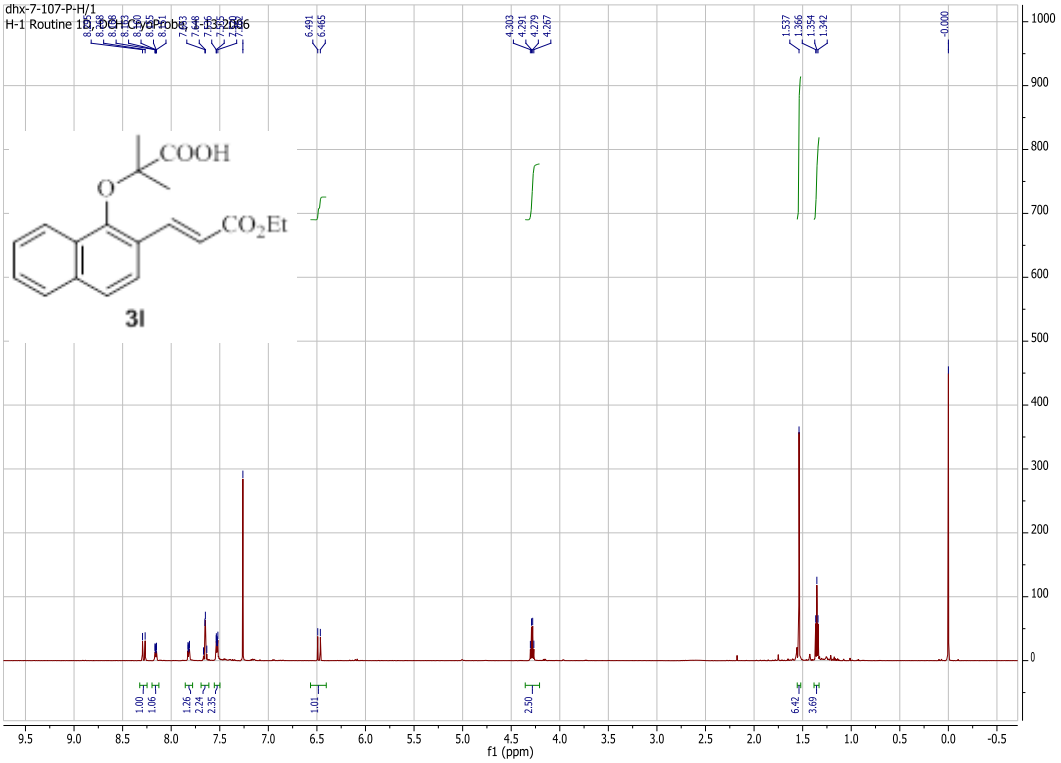

dhx-4-cf3-cooh-pdt-methanol_02
Std proton
8.020
7.980
7.883
7.596
7.573
7.009
6.987
6.651
6.611
4.282
4.265
4.247
4.229
3.319
3.314
3.310
3.306
3.302
1.705
1.345
1.327
1.309
CO2Et
O
COOH
F3C
3i
1.0
0.9
1.0
0.9
1.0
2.0
5.9
3.1
f1 (ppm)
dhx-4-cf3-cooh-pdt-methanol-c13.1.fid
C-13 Routine 1D, DCH CryoProbe 10-26-2009
176.761
168.887
158.374
139.931
128.560
128.209
126.890
126.766
126.416
124.915
124.697
124.623
124.480
124.262
122.830
121.328
117.923
81.709
61.754
49.427
49.285
49.144
49.001
48.859
48.717
48.575
25.832
14.582
CO2Et
O
COOH
F3C
3i
f1 (ppm)

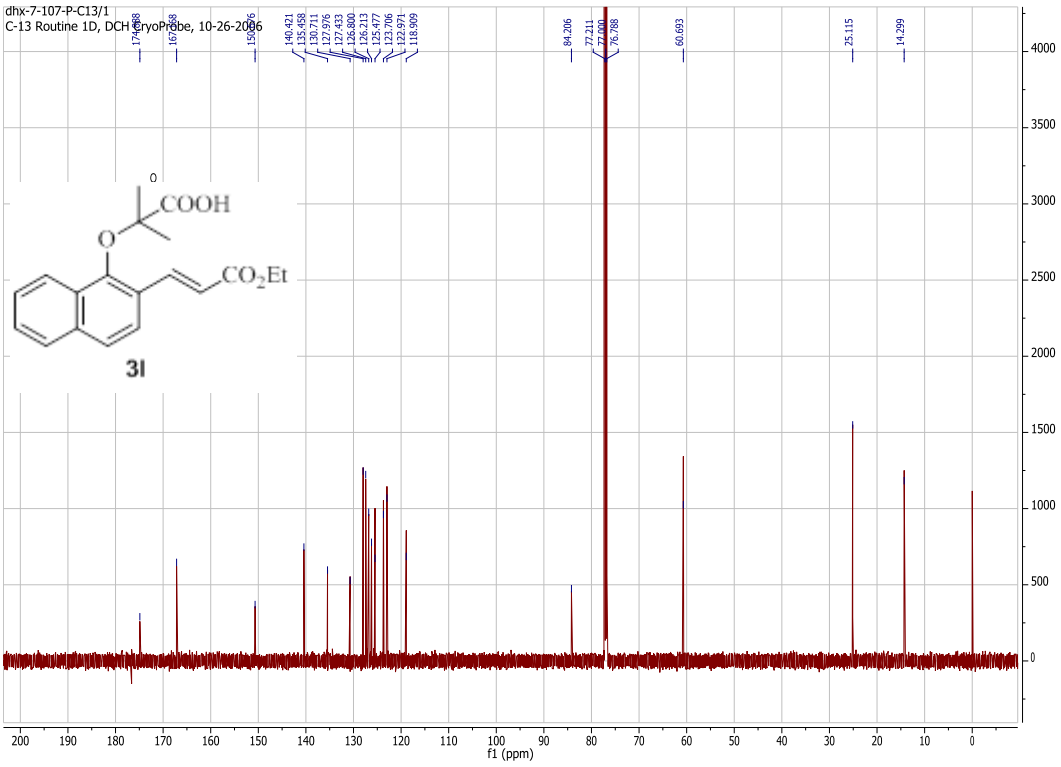

dhx-7-76-p3/1
H-1 Routine 1D, DCH CryoProbe, 11-13-2006
3j
f1 (ppm)

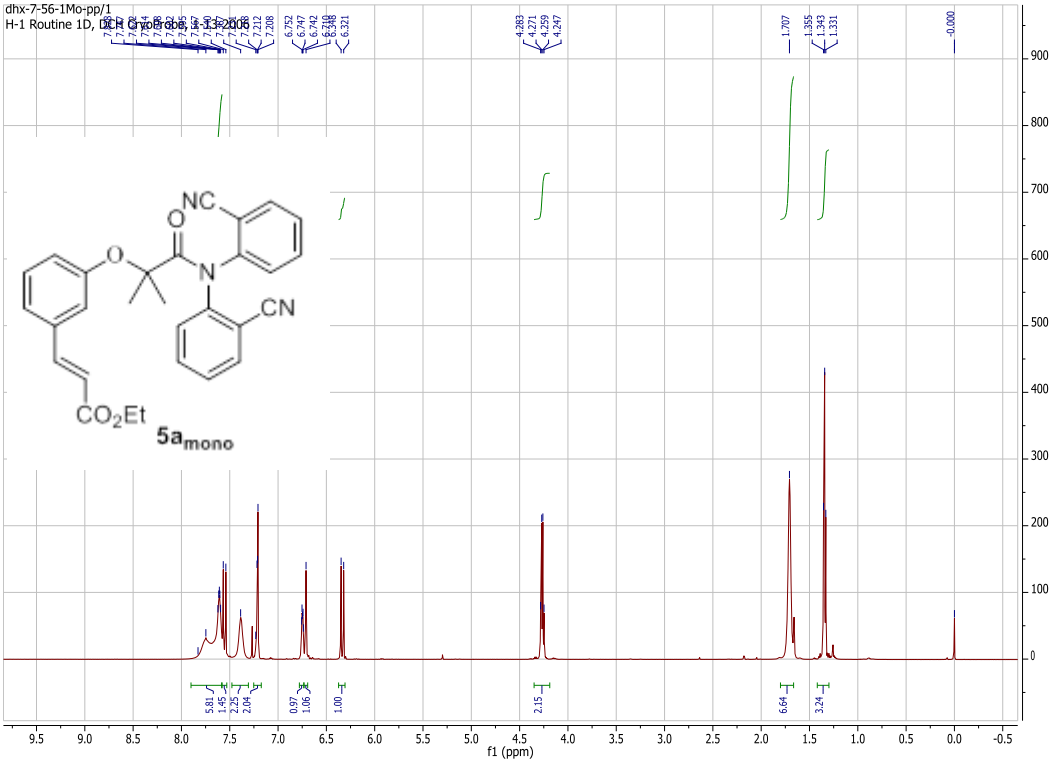

dhx-7-76-p3-c13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
3j
f1 (ppm)

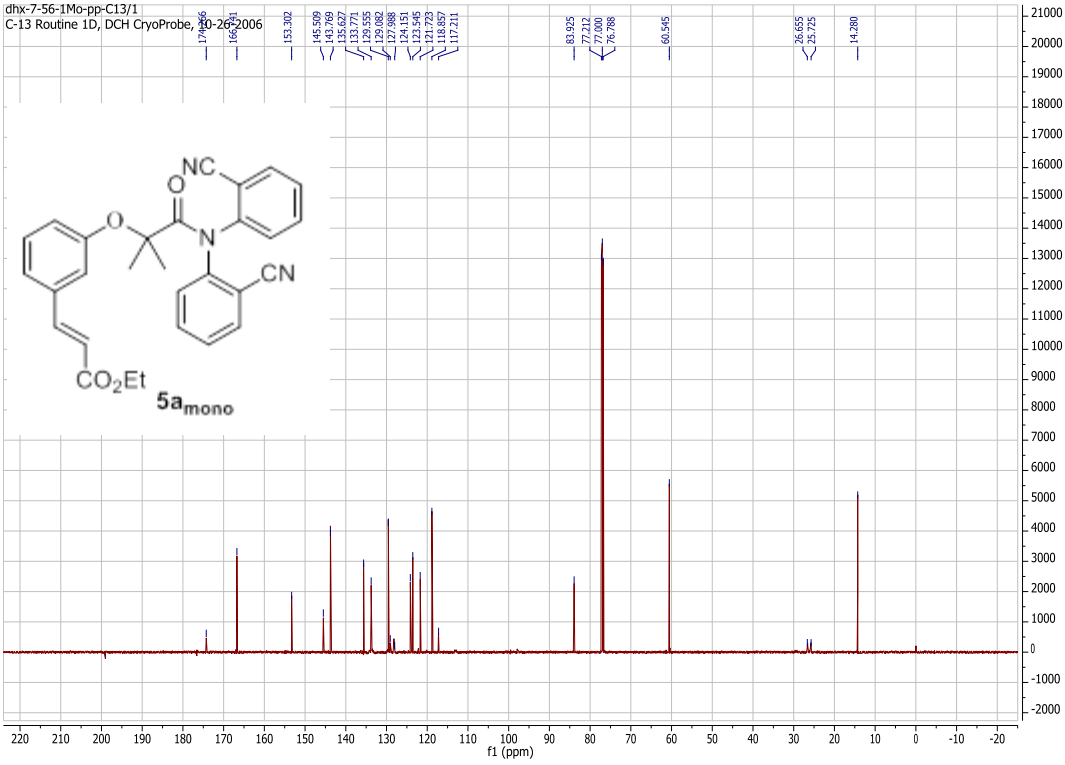

dhx-8-34-p0_02
Std proton
3k
f1 (ppm)

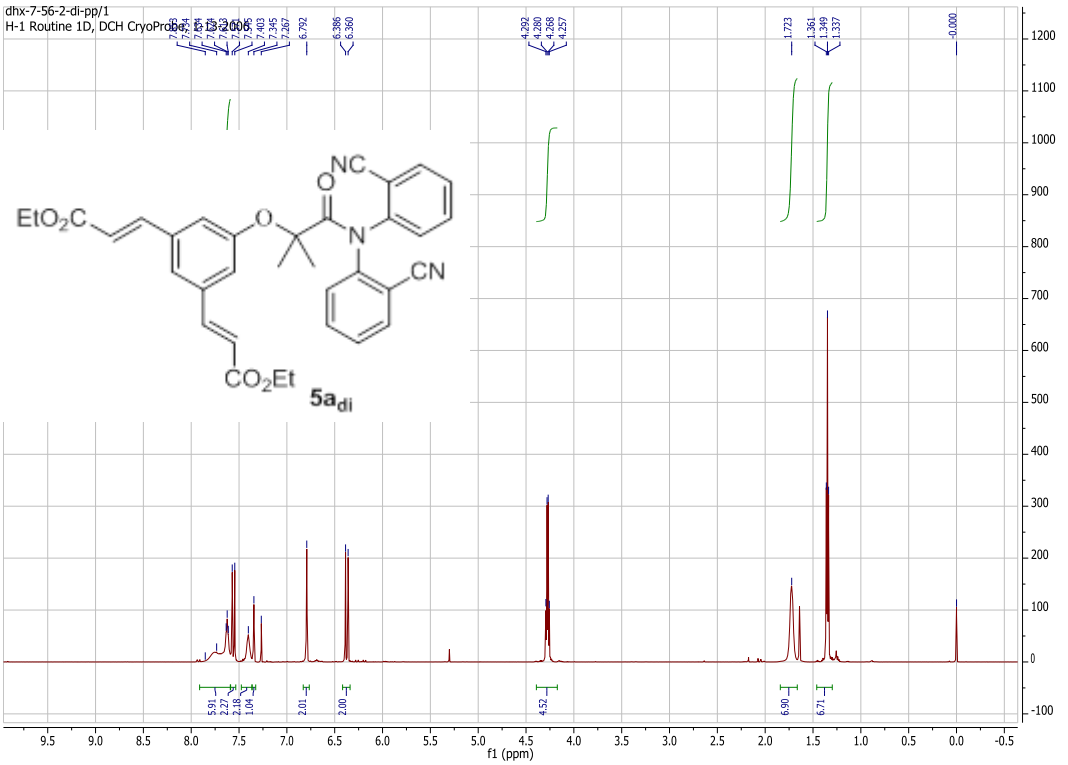

dhx-8-34-p-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
3k
f1 (ppm)

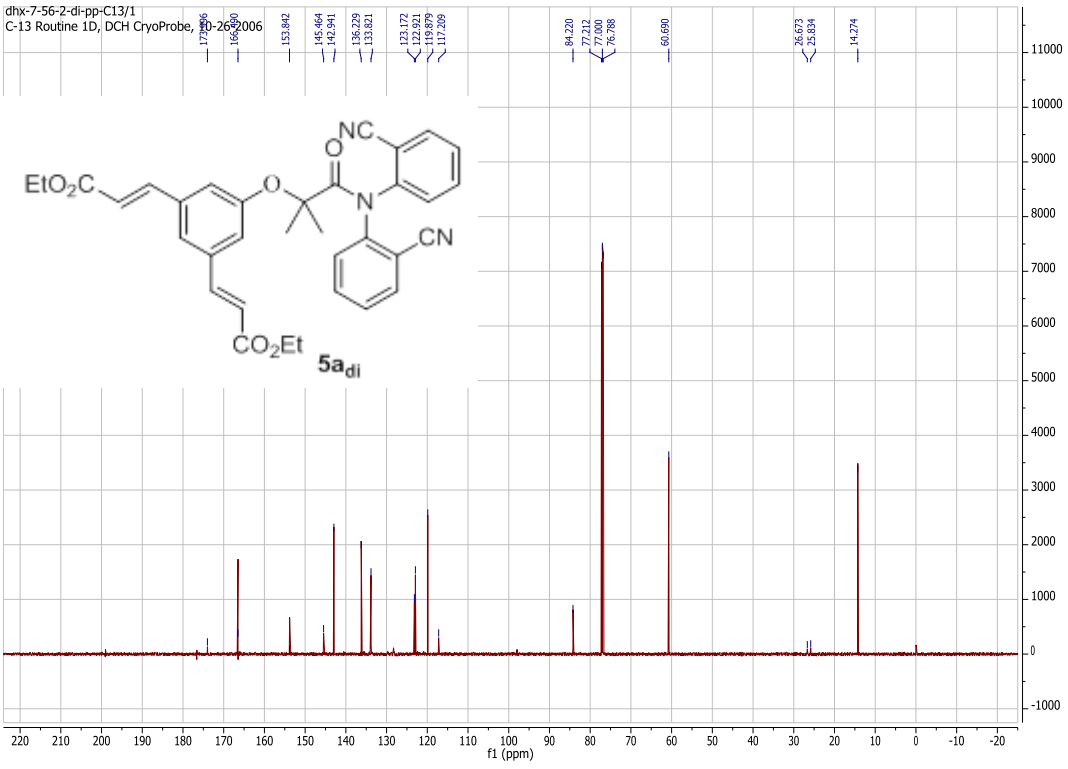

dhx-7-107-P-H/1
H-1 Routine 1D, DCH-CryoProbe, 11-13-2006
COOH
O
CO2Et
3l
f1 (ppm)

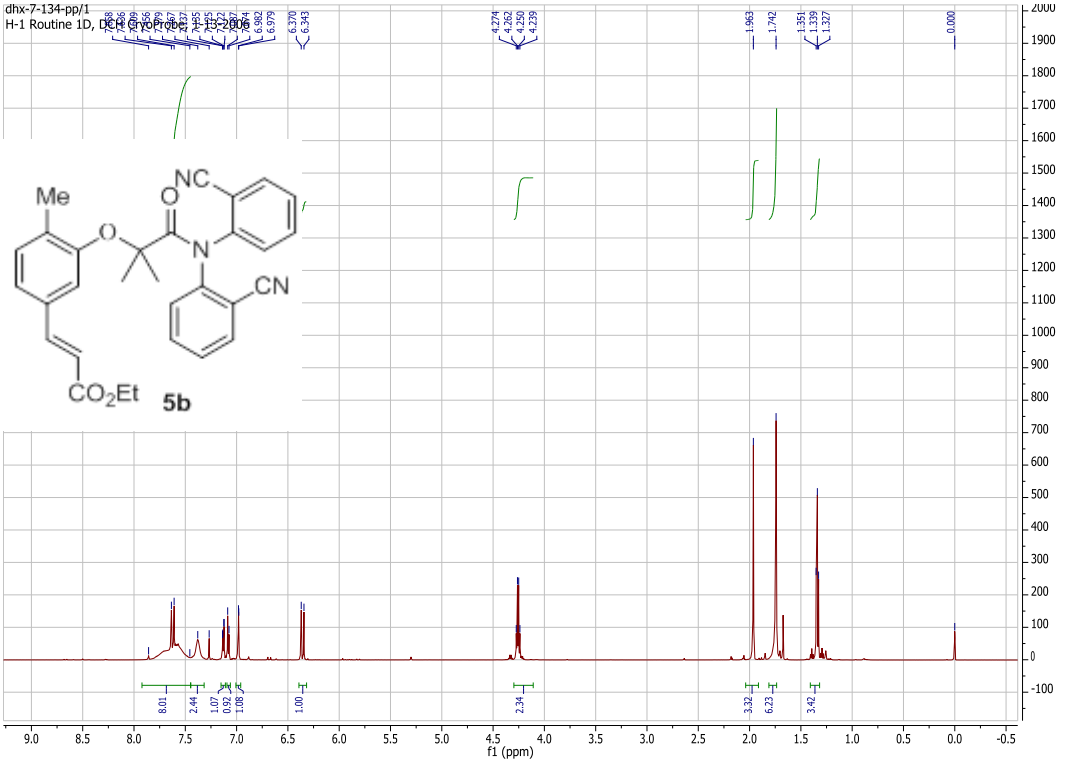

dhx-7-107-P-C13/1
C-13 Routine 1D, DCH-CryoProbe, 10-26-2006
COOH
O
CO2Et
3l
f1 (ppm)

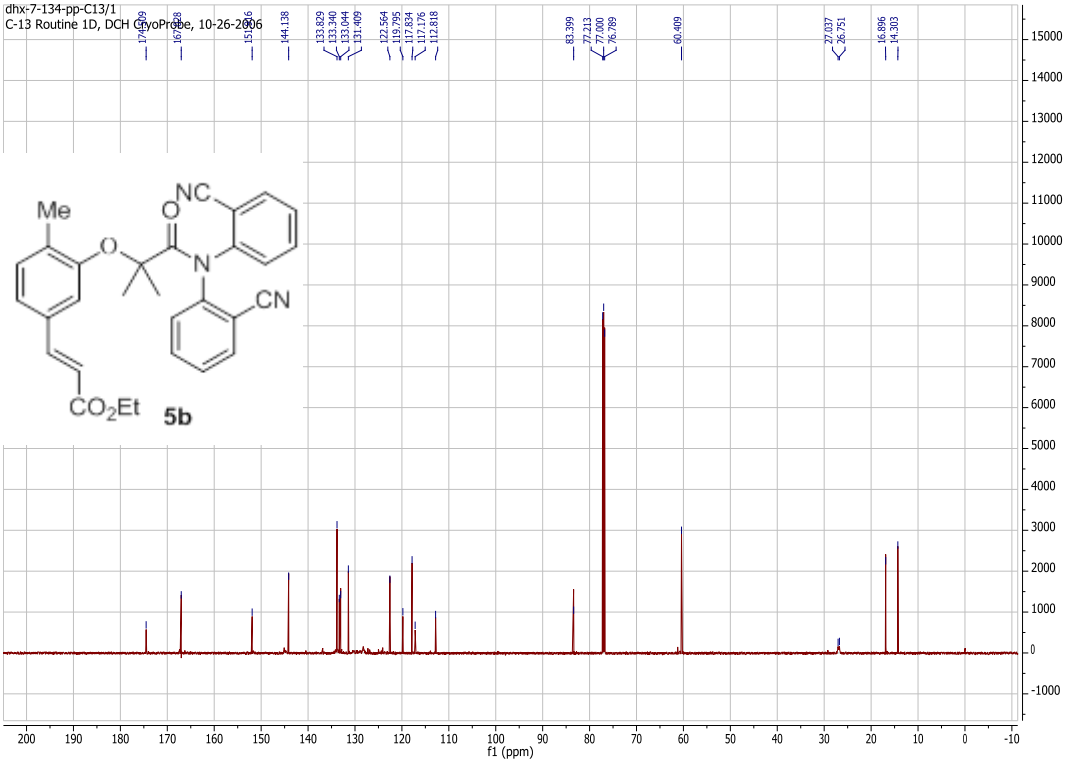

dhx-7-56-1Mo-pp/1
H-1 Routine 1D, DCH CryoProbe, 11-2006
NC
O
O
N
CN
CO2Et
5amono
f1 (ppm)

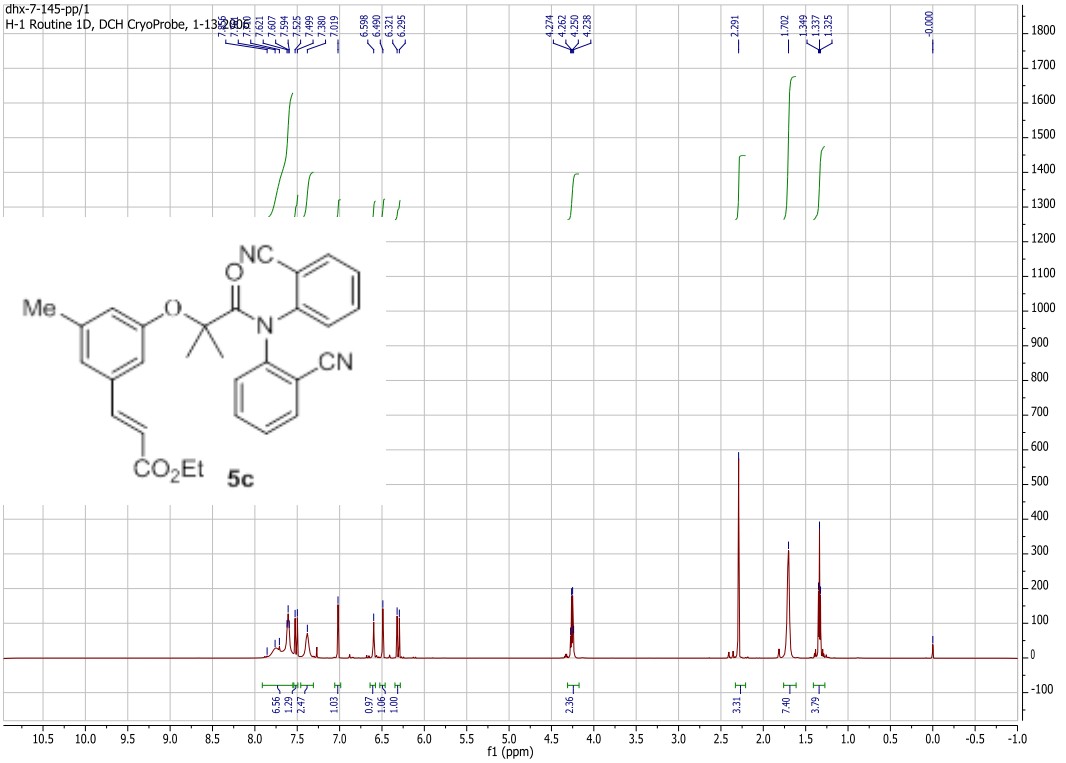

dhx-7-56-1Mo-pp-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
NC
O
O
N
CN
CO2Et
5amono
f1 (ppm)

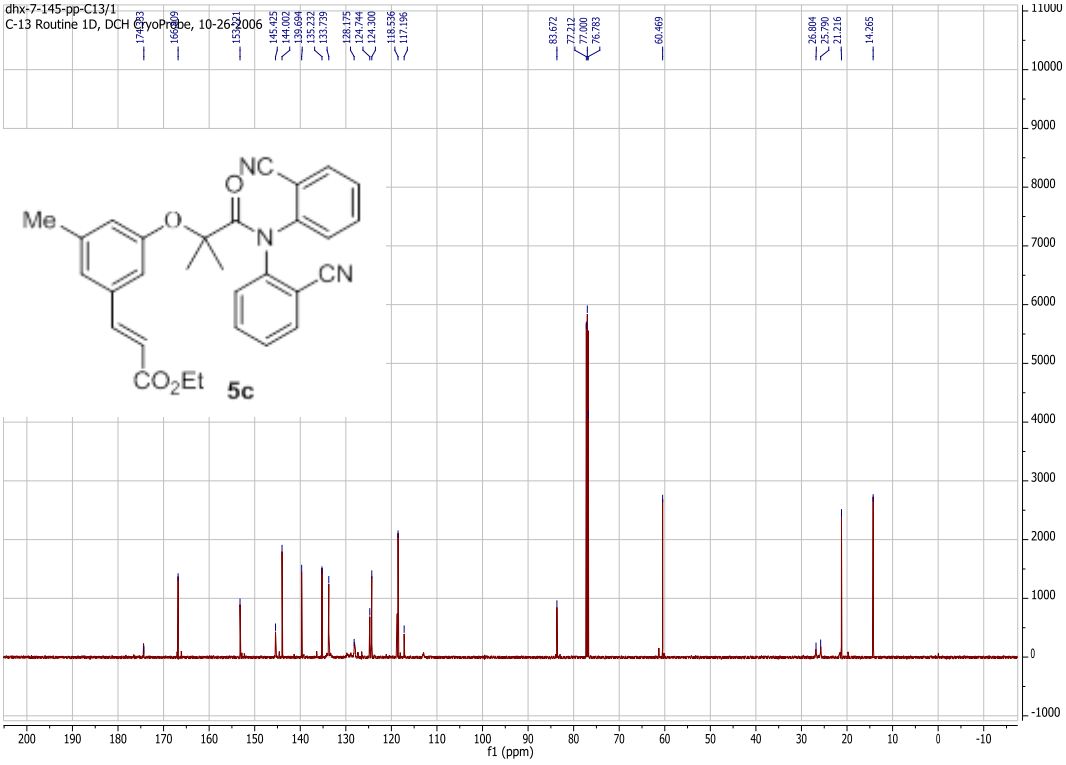

dhx-7-56-2-di-pp/1
H-1 Routine 1D, DCH CryoProbe, 10-26-2006
EtO2C
O
NC
N
CN
CO2Et
5adi
f1 (ppm)

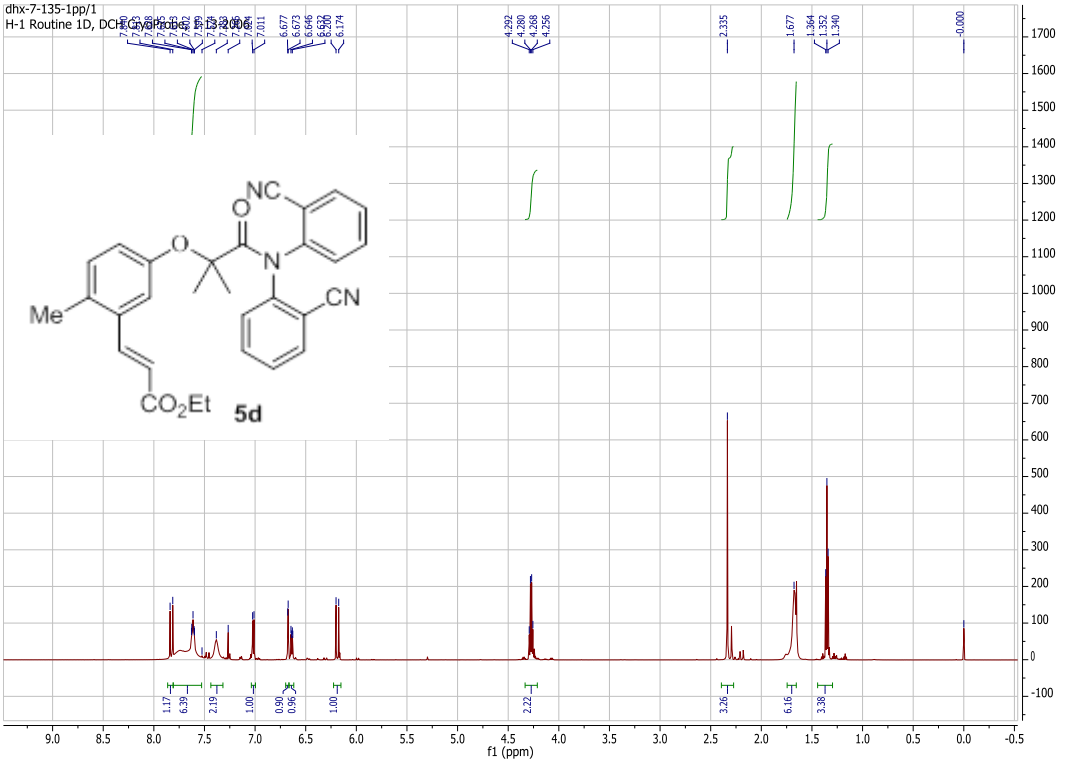

dhx-7-56-2-di-pp-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
EtO2C
O
NC
N
CN
CO2Et
5adi
f1 (ppm)

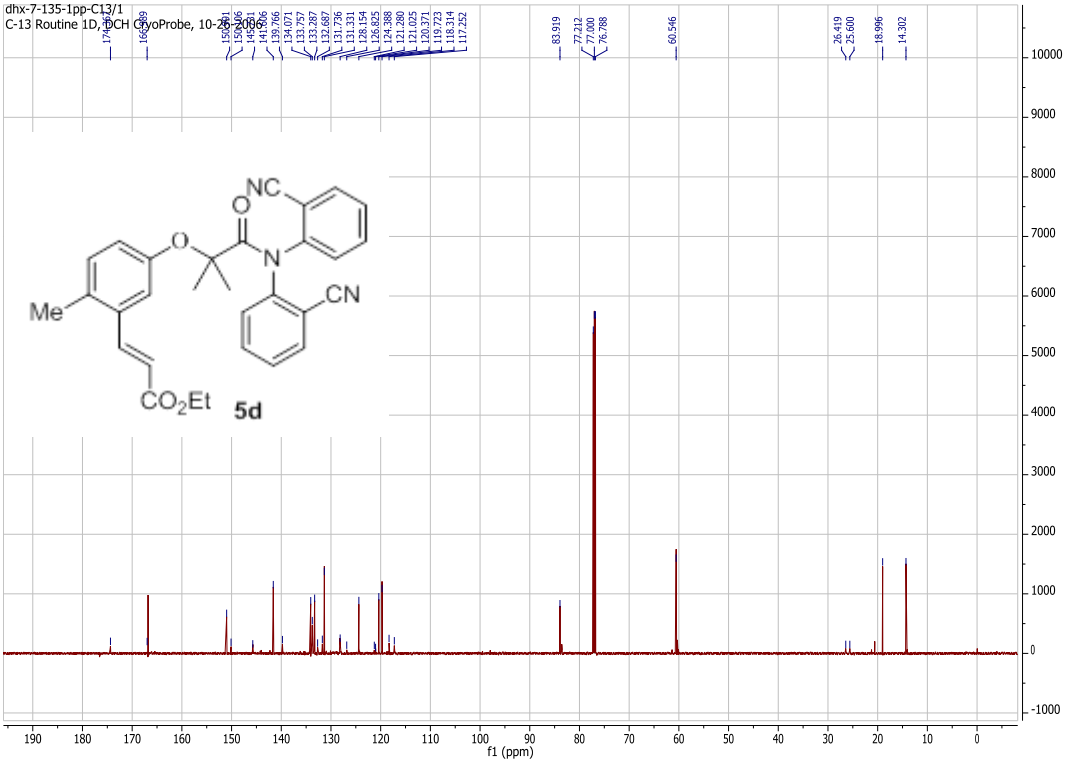

dhx-7-134-pp/1
H-1 Routine 1D, DCH CryoProbe, 7-13-2006
Me
O
NC
O
N
CN
CO2Et
5b
f1 (ppm)

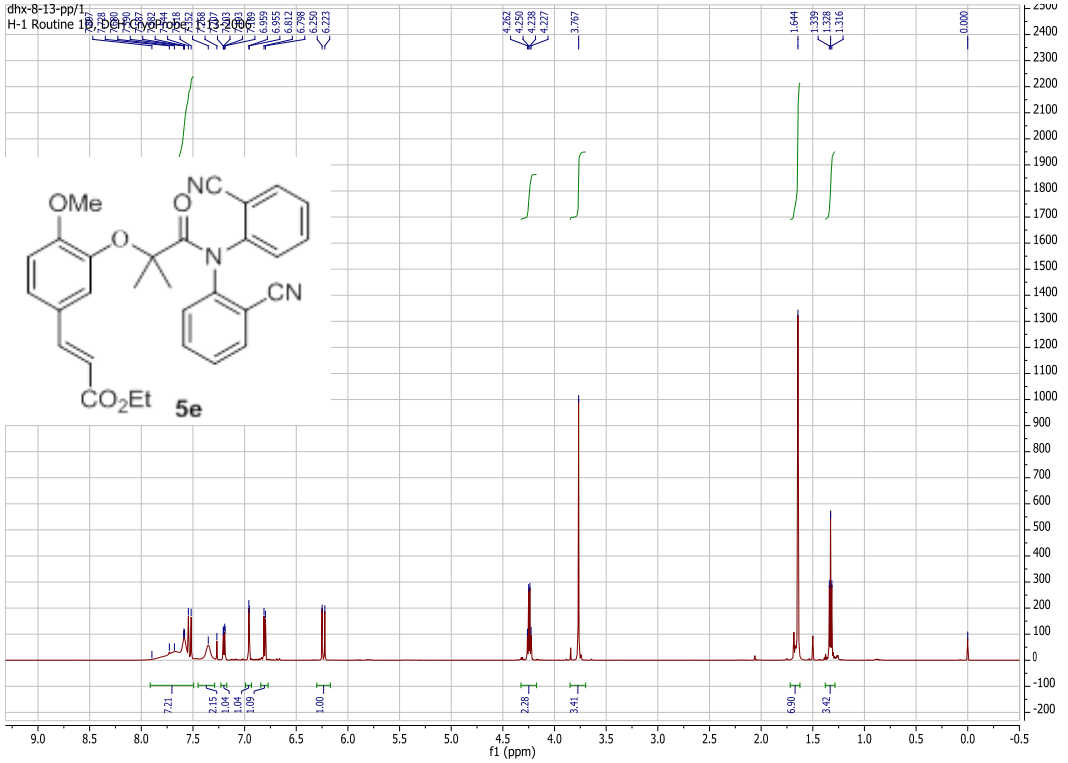

dhx-7-134-pp-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
Me
O
NC
O
N
CN
CO2Et
5b
f1 (ppm)

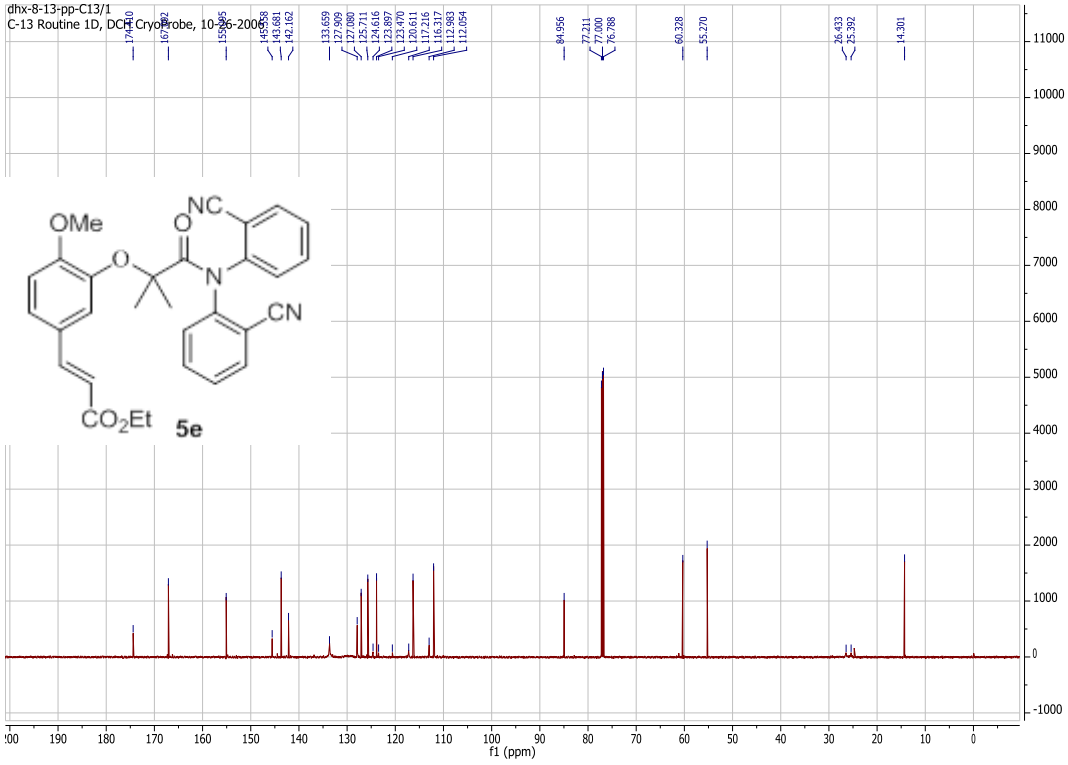

dhx-7-145-pp/1
H-1 Routine 1D, DCH CryoProbe, 1-13-2006
Me
O
NC
O
N
CN
CO2Et
5c
f1 (ppm)

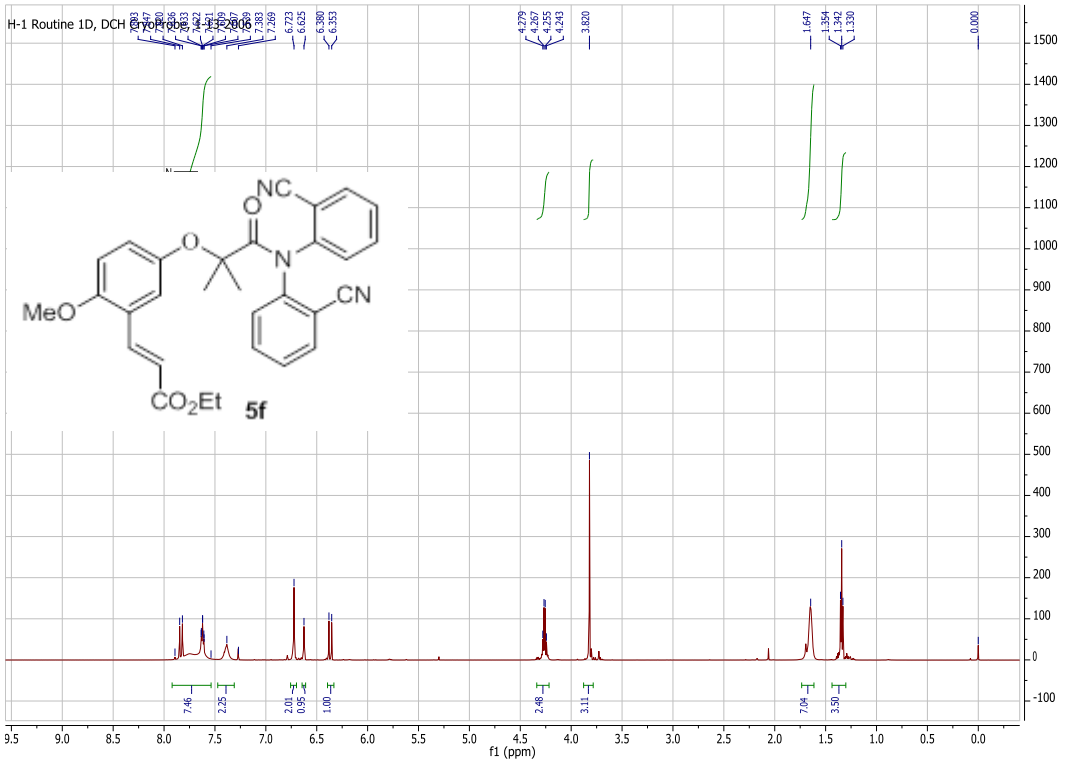

dhx-7-145-pp-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
Me
O
NC
O
N
CN
CO2Et
5c
f1 (ppm)

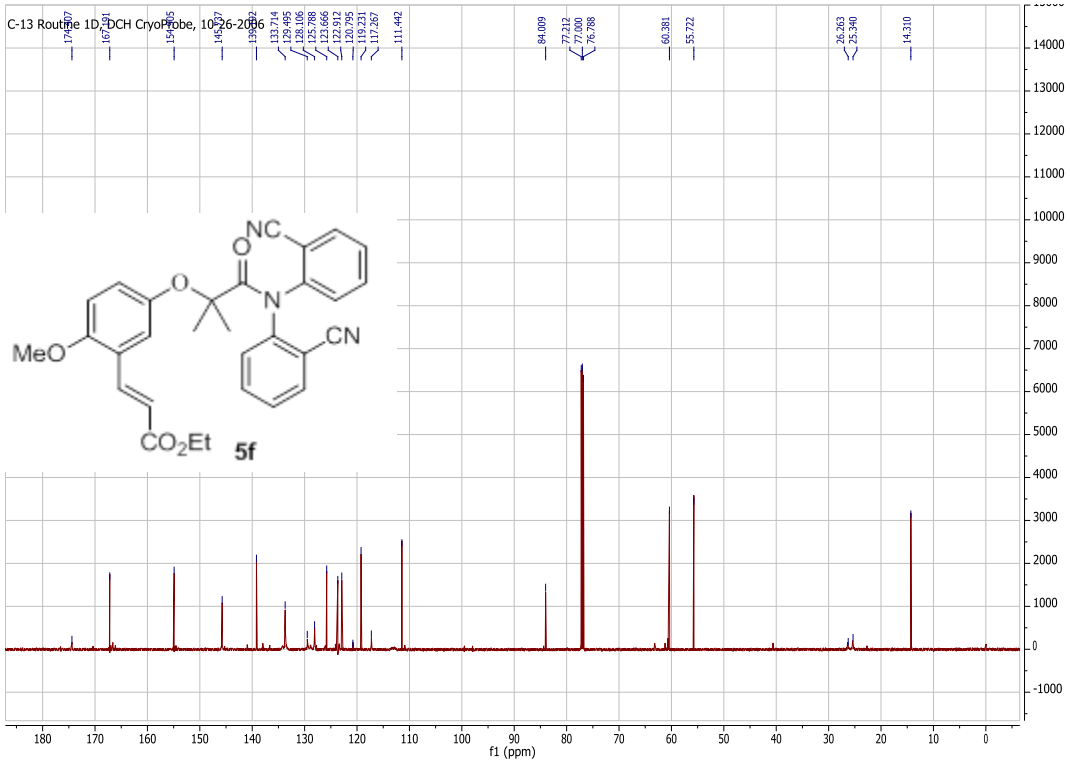

dhx-7-135-1pp/1
H-1 Routine 1D, DCH CryoProbe, 12-20-2006
NC
O
N
O
Me
CN
CO2Et
5d
f1 (ppm)

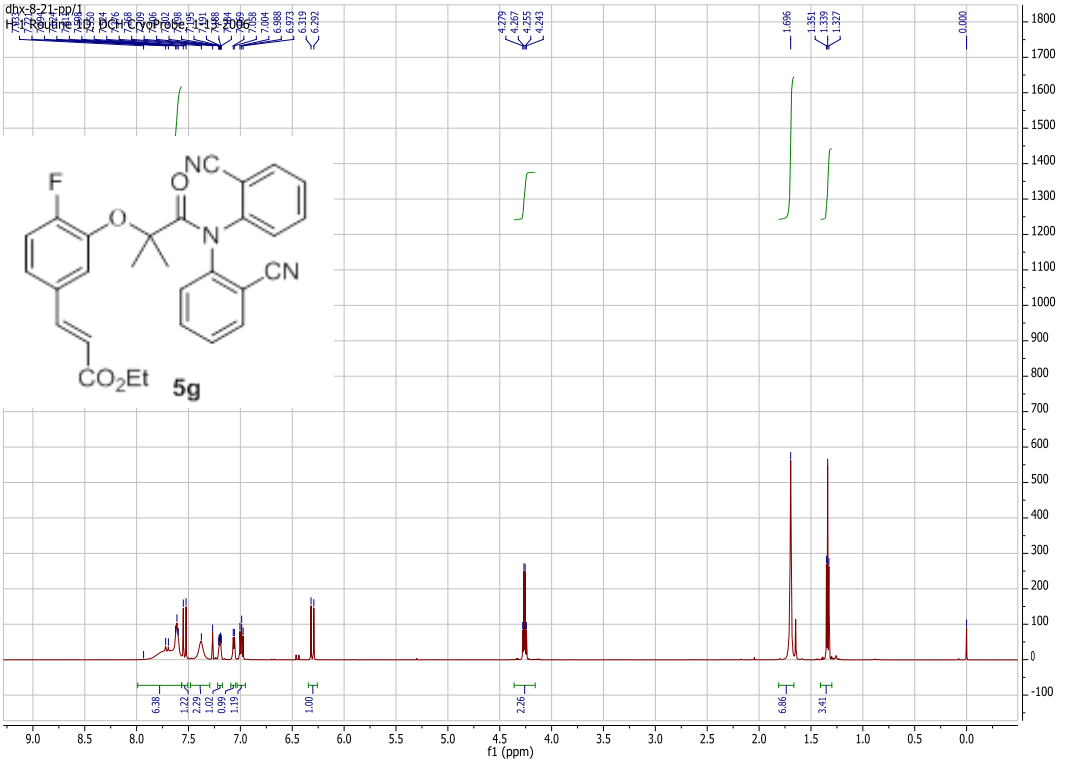

dhx-7-135-1pp-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
NC
O
N
O
Me
CN
CO2Et
5d
f1 (ppm)

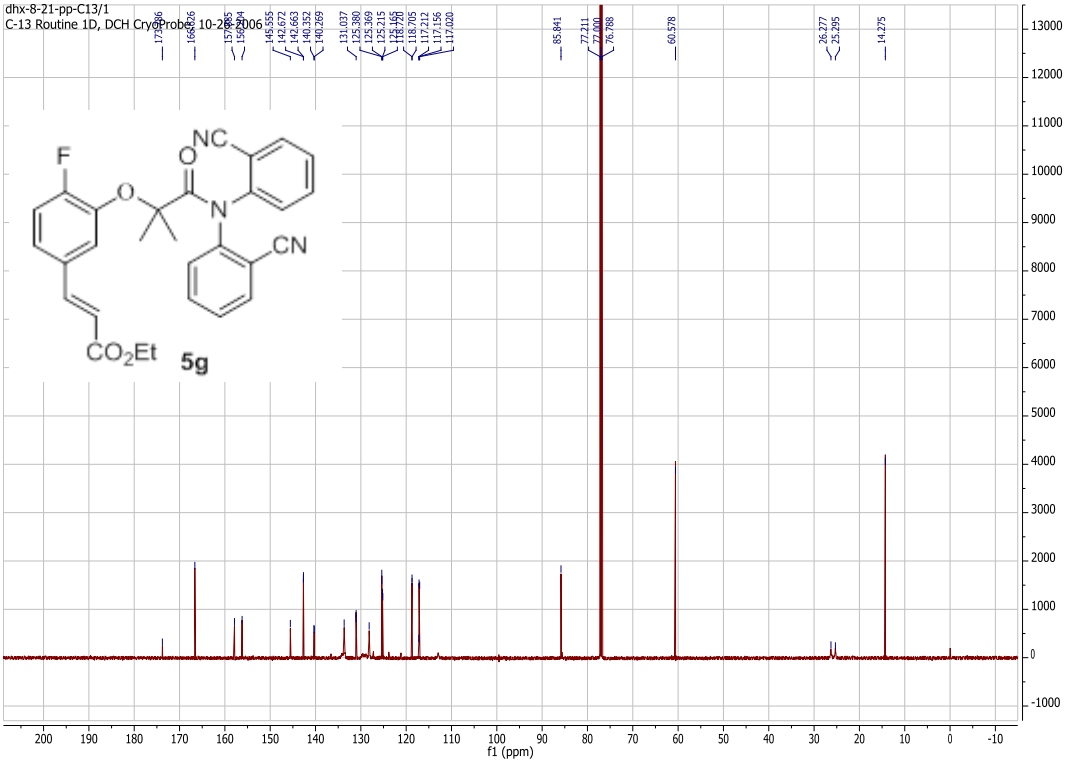

dhx-8-13-pp/1
H-1 Routine 1D, DCM CryoProbe, 7-13-2006
OMe
O
NC
O
N
CN
CO2Et
5e
f1 (ppm)

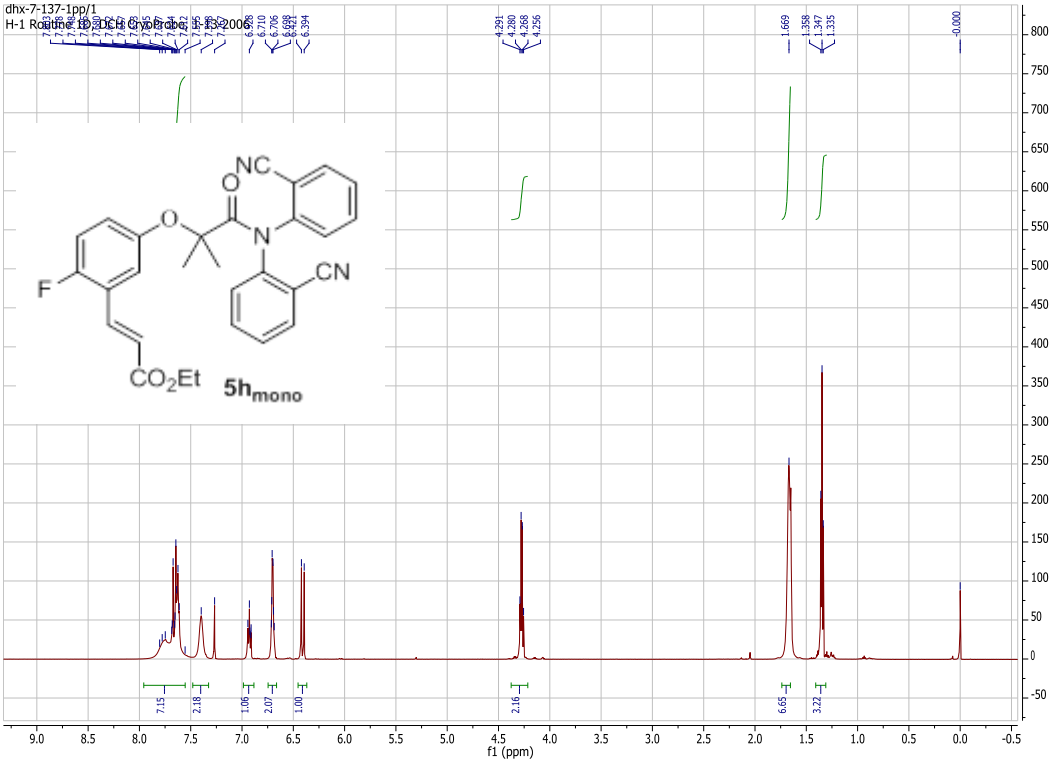

dhx-8-13-pp-C13/1
C-13 Routine 1D, DCM CryoProbe, 10-26-2006
OMe
O
NC
O
N
CN
CO2Et
5e
f1 (ppm)

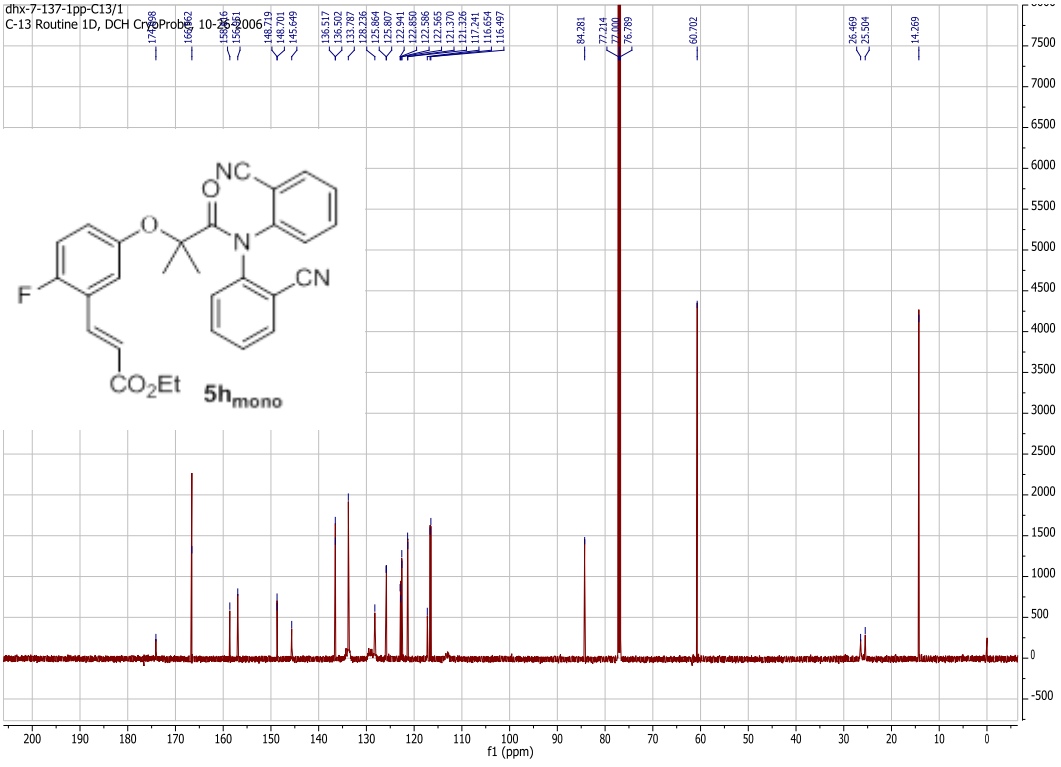

H-1 Routine 1D, DCH CryoProbe, 1-23-2006
NC
O
N
O
MeO
CN
CO2Et
5f
f1 (ppm)

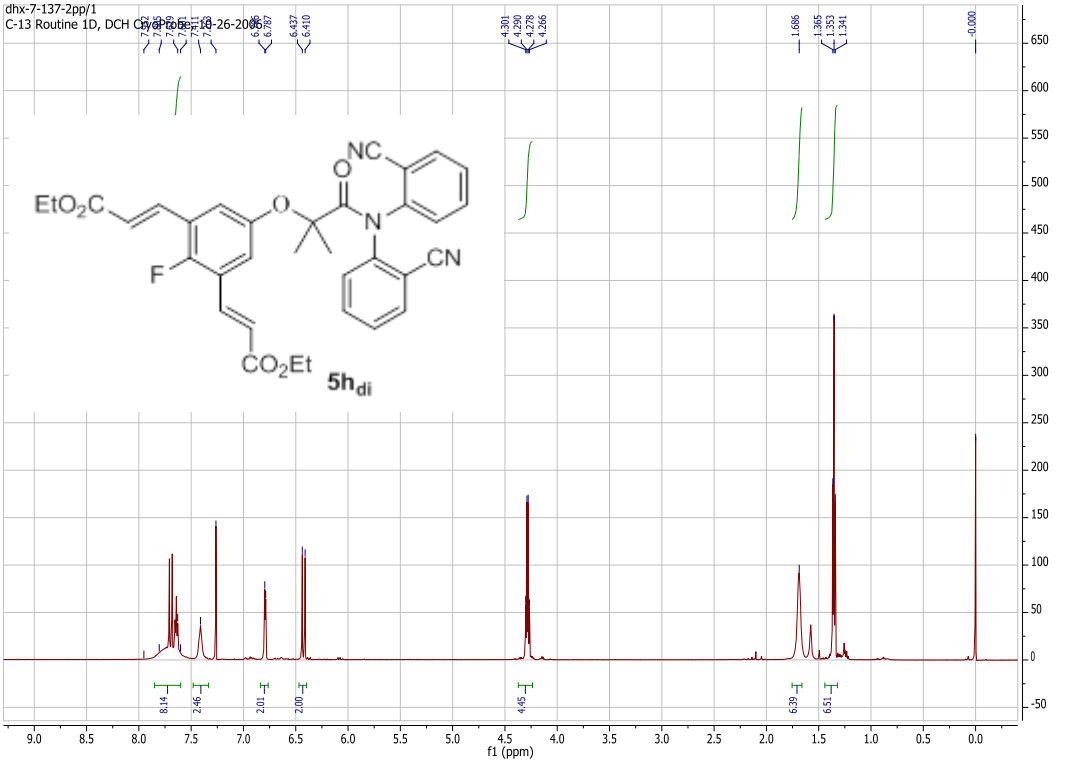

C-13 Routine 1D, DCH CryoProbe, 10-26-2006
NC
O
N
O
MeO
CN
CO2Et
5f
f1 (ppm)

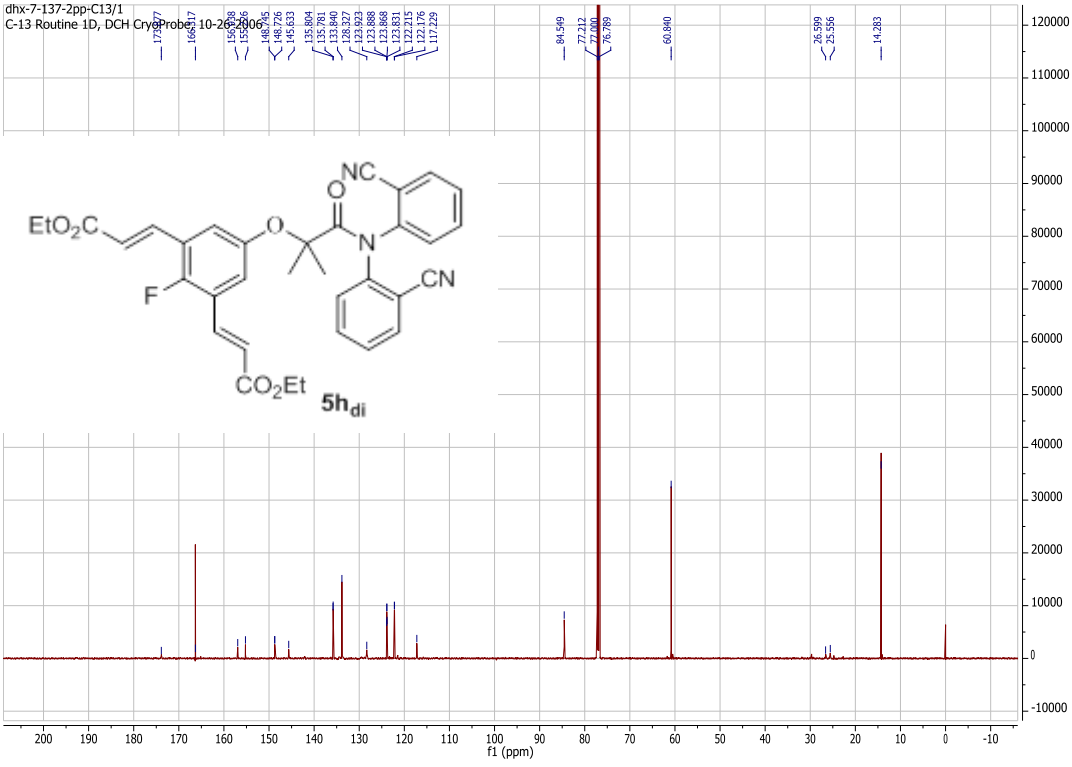

dhx-8-21-pp/1
H-1 Routine 1D, DCH CryoProbe, 1-11-2006
F
O
NC
O
N
CN
CO2Et
5g
f1 (ppm)

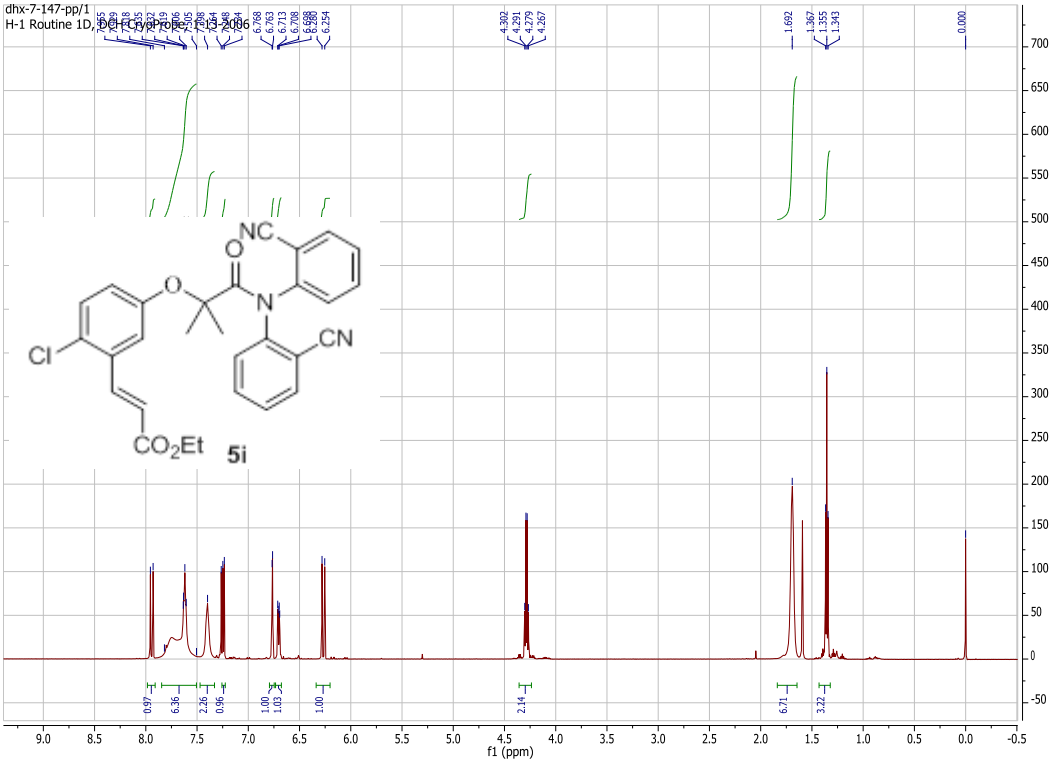

dhx-8-21-pp-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
F
O
NC
O
N
CN
CO2Et
5g
f1 (ppm)

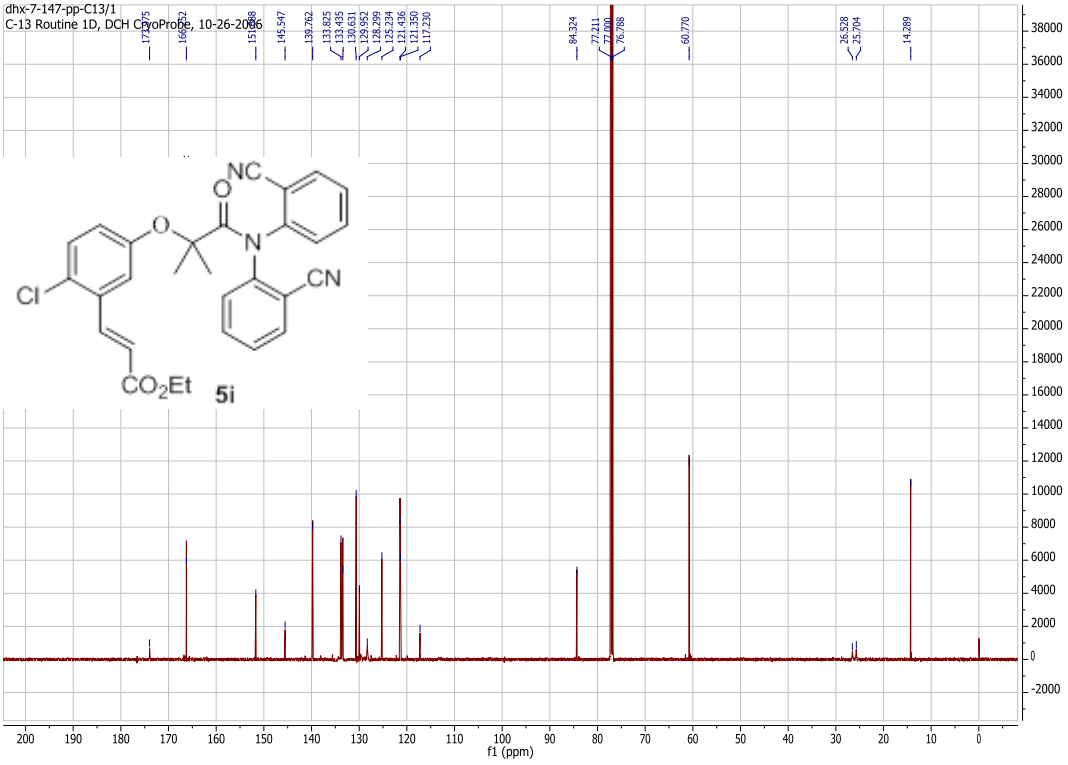

dhx-7-137-1pp/1
H-1 Routine 1D, DCH CryoProbe, 10-26-2006
NC
O
N
O
F
CN
CO2Et
5hmono
f1 (ppm)

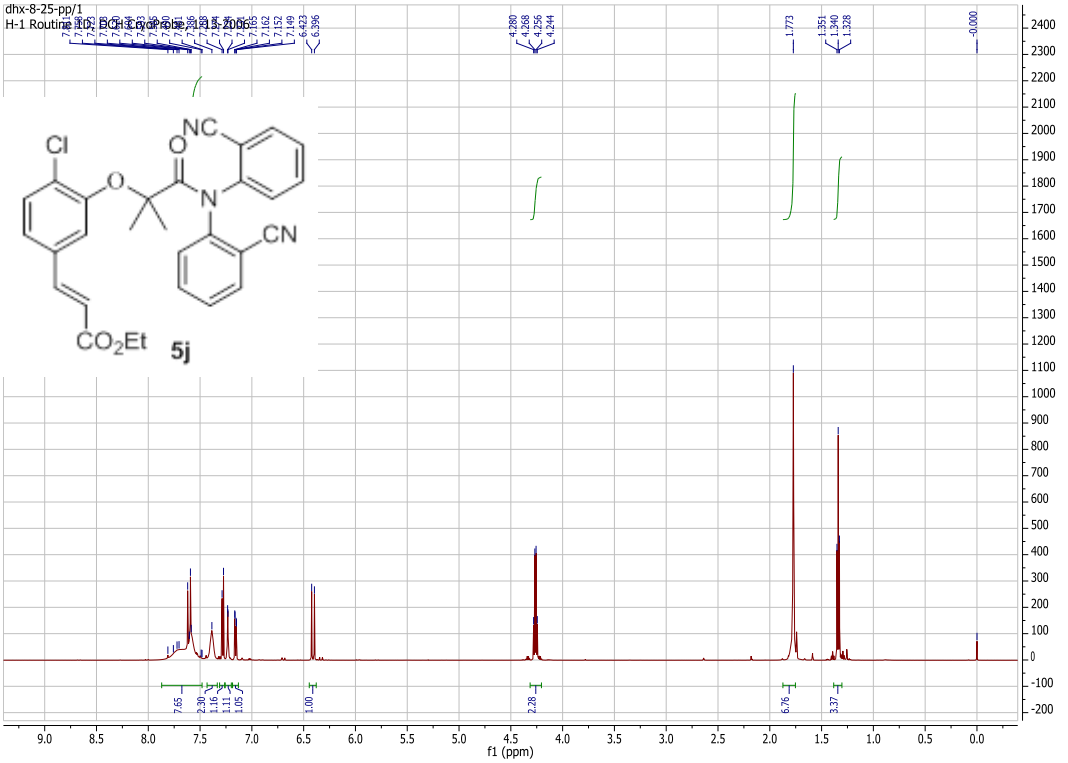

dhx-7-137-1pp-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
NC
O
N
O
F
CN
CO2Et
5hmono
f1 (ppm)

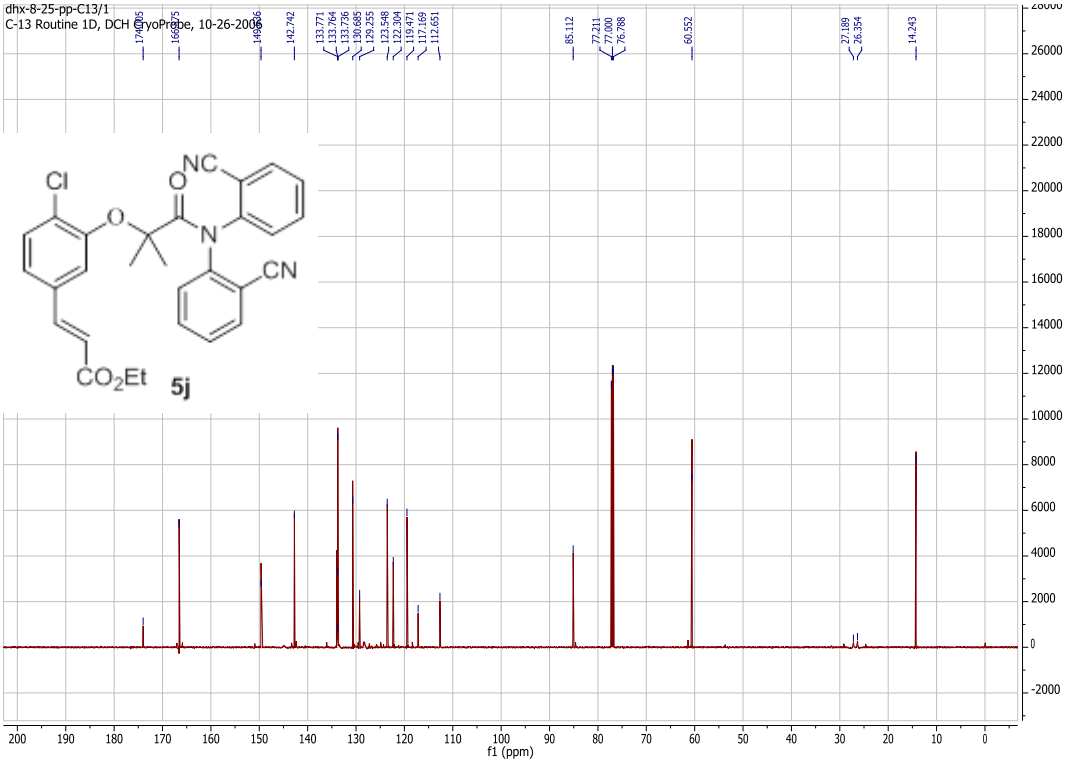

dhx-7-137-2pp/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
NC
O
EtO2C
O
N
CN
F
CO2Et
5hdi
f1 (ppm)

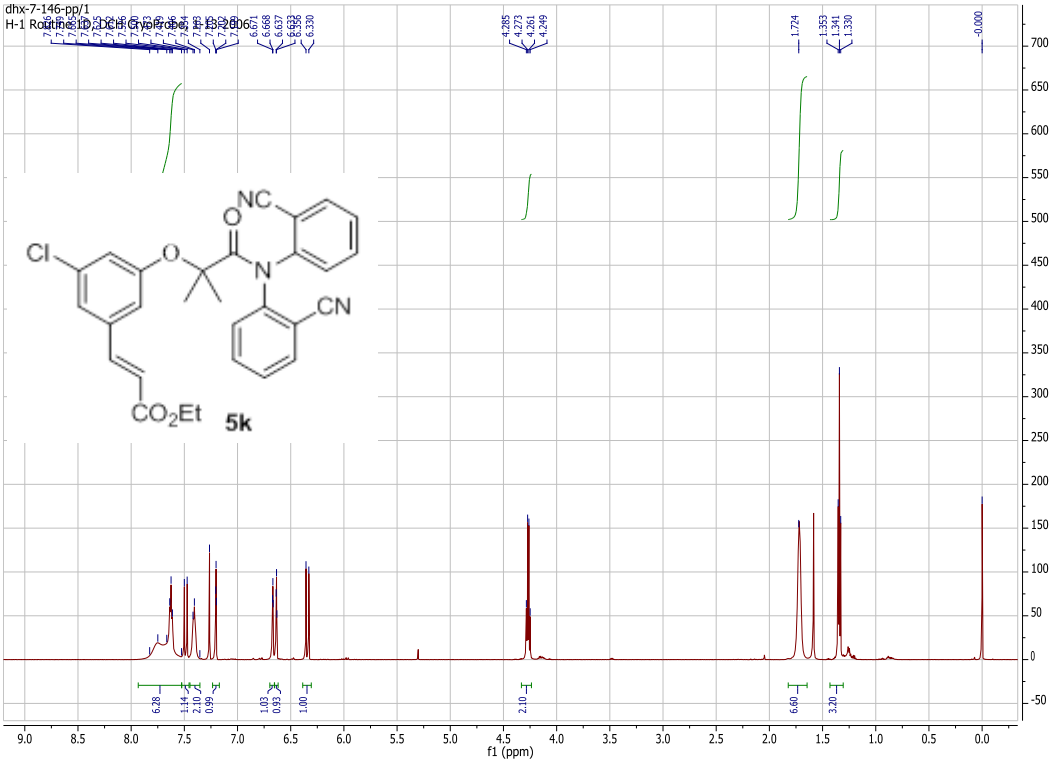

dhx-7-137-2pp-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
NC
O
EtO2C
O
N
CN
F
CO2Et
5hdi
f1 (ppm)

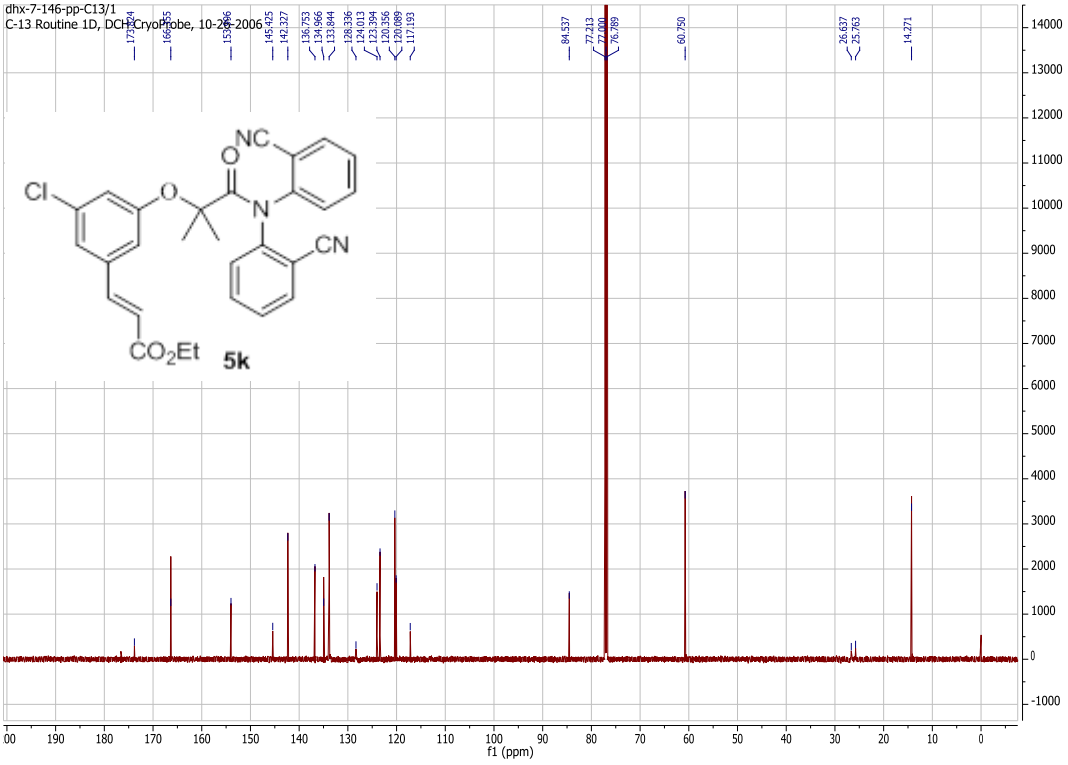

dhx-7-147-pp/1
H-1 Routine 1D, DCH CryoProbe, 1-13-2006
NC
O
O
N
CN
Cl
CO2Et
5i
f1 (ppm)

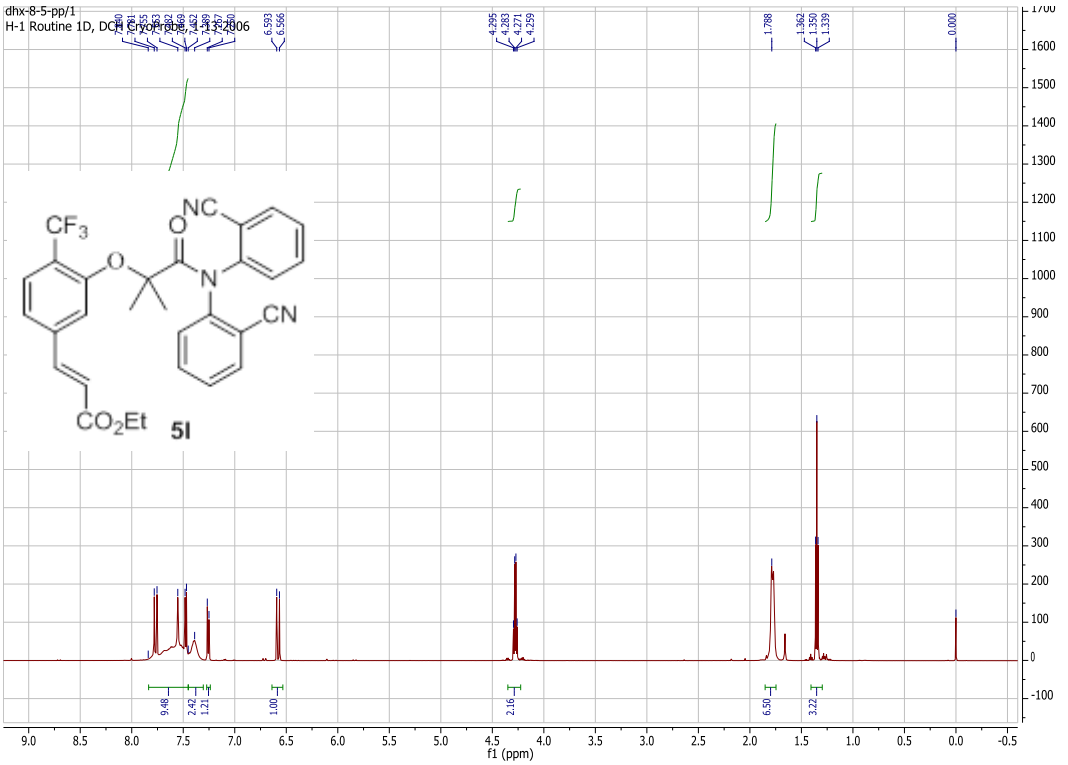

dhx-7-147-pp-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
NC
O
O
N
CN
Cl
CO2Et
5i
f1 (ppm)

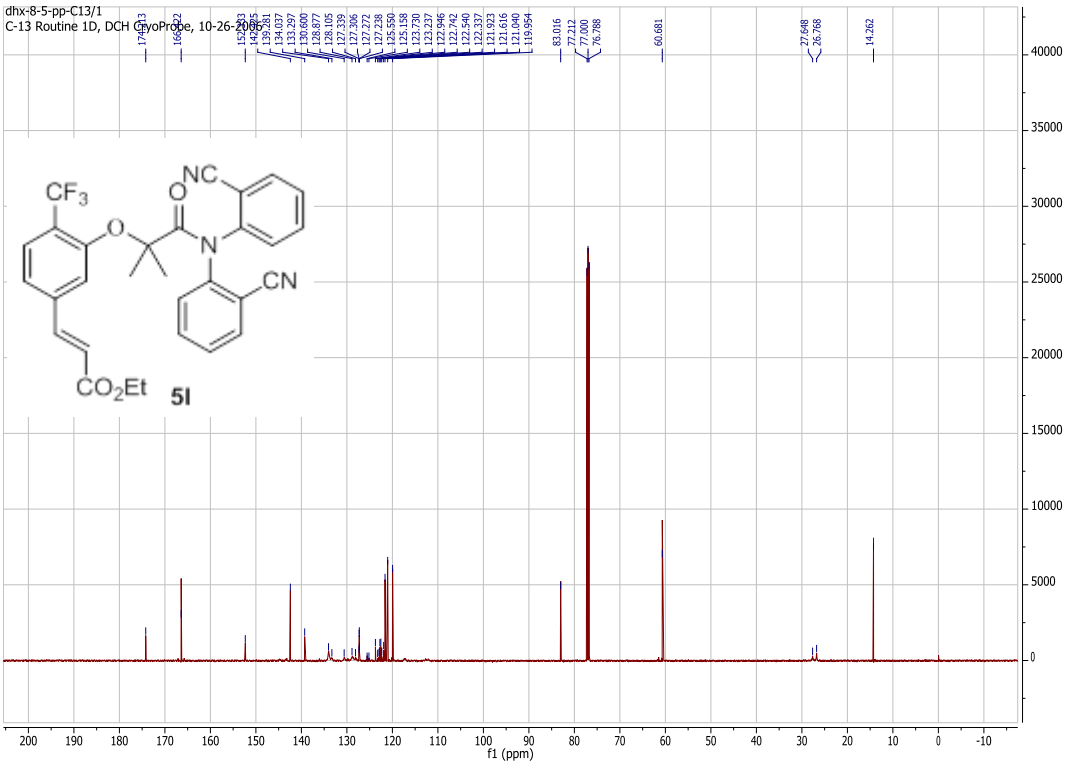

dhx-8-25-pp/1
H-1 Routine 1D, DCH CryoProbe, 2015 2006
Cl
O
NC
O
N
CN
CO2Et
5j
f1 (ppm)

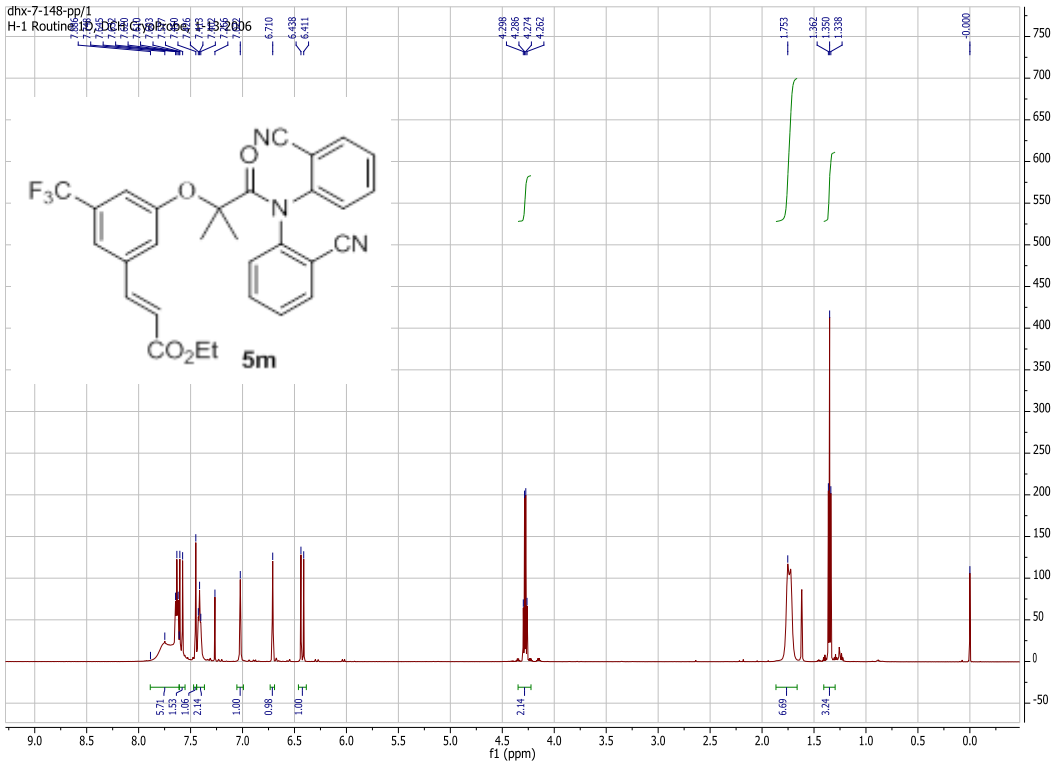

dhx-8-25-pp-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
Cl
O
NC
O
N
CN
CO2Et
5j
f1 (ppm)

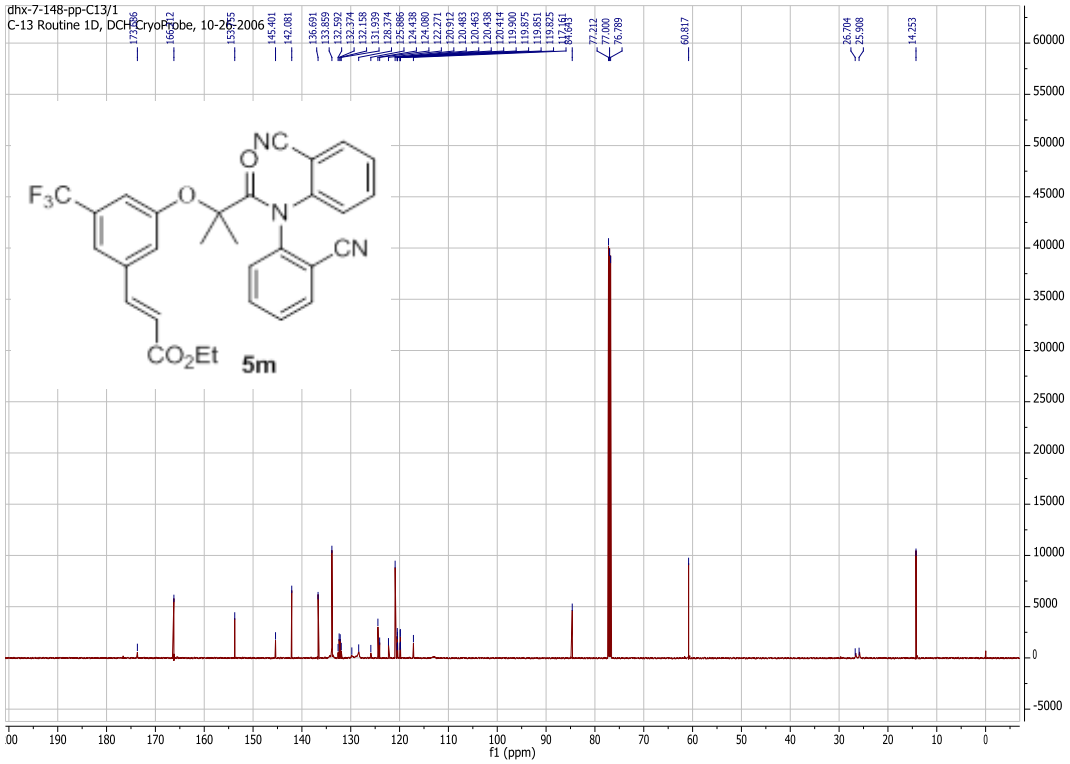

dhx-7-146-pp/1
H-1 Routine 1D, DCM, CryoProbe, 10-26-2006
NC
O
Cl
O
N
CN
CO2Et
5k
f1 (ppm)


dhx-7-146-pp-C13/1
C-13 Routine 1D, DCM, CryoProbe, 10-26-2006
NC
O
Cl
O
N
CN
CO2Et
5k
f1 (ppm)

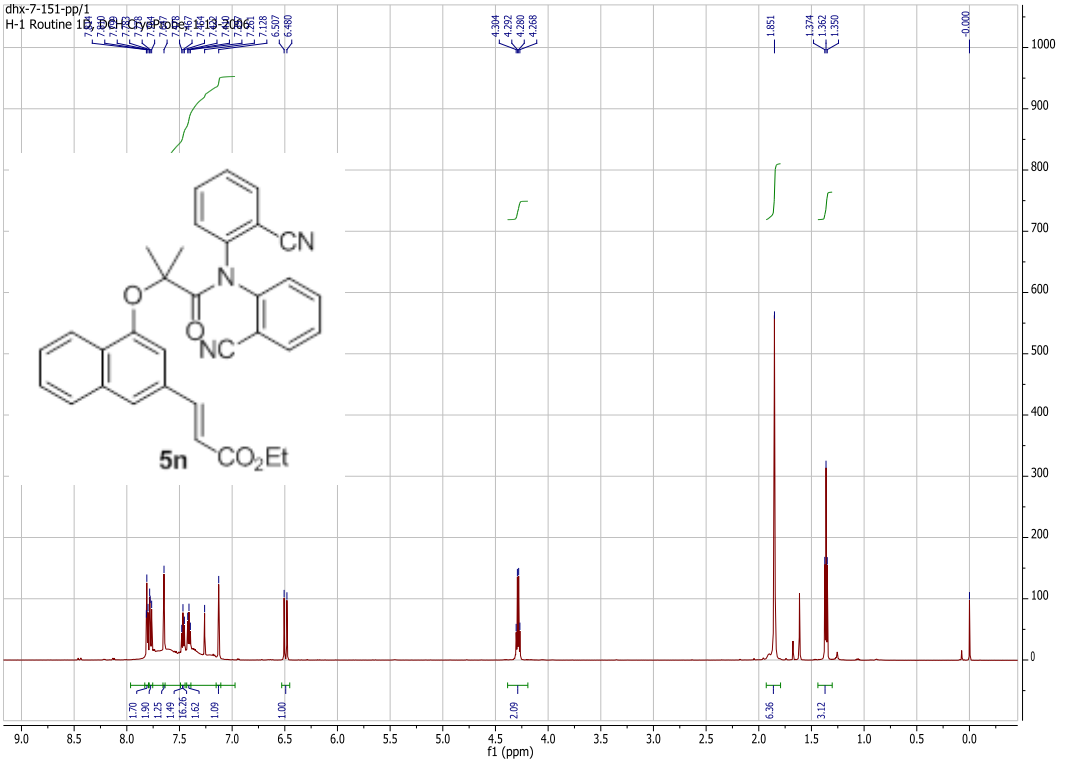

dhx-8-5-pp/1
H-1 Routine 1D, DCH CryoProbe, 4-13-2006
CF3
O
NC
O
N
CN
CO2Et
5l
f1 (ppm)

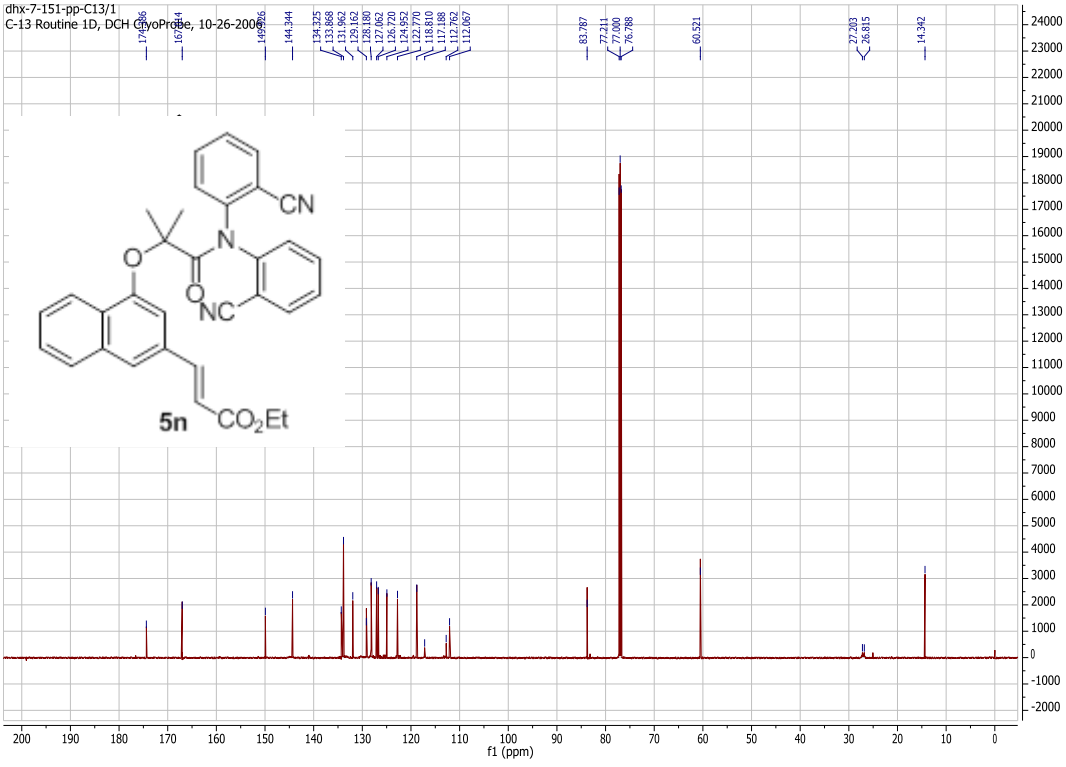

dhx-8-5-pp-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
CF3
O
NC
O
N
CN
CO2Et
5l
f1 (ppm)

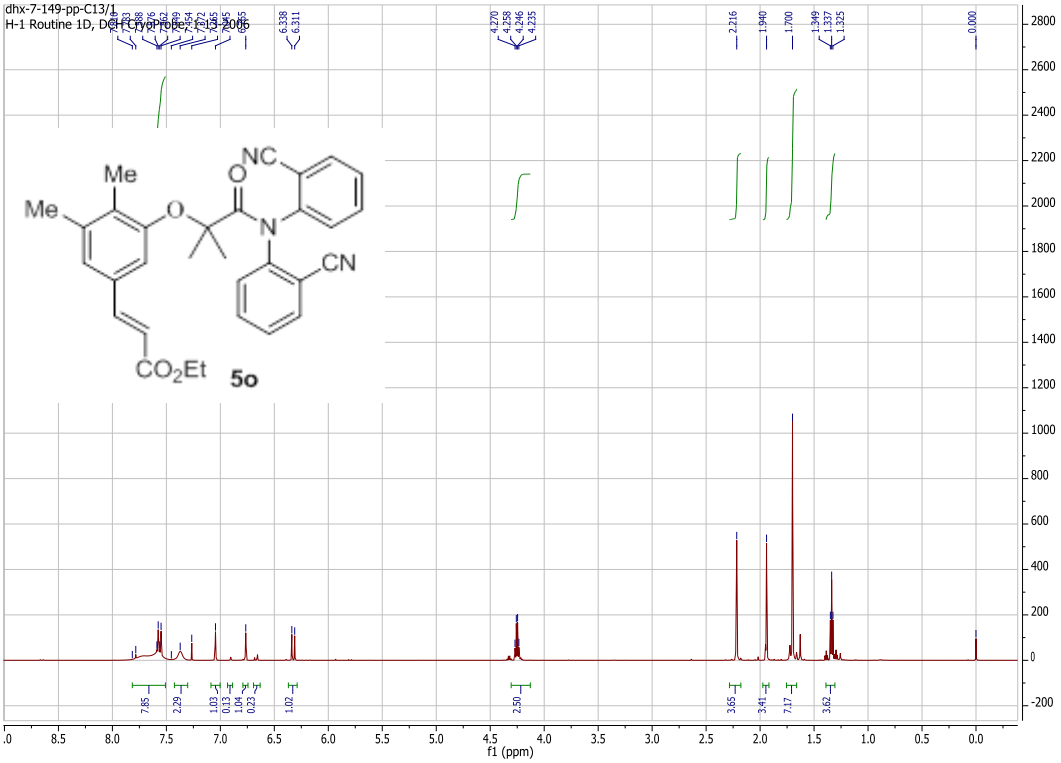

dhx-7-148-pp/1
H-1 Routine 1D, DCH CryoProbe, 10-2-2006
NC
O
F3C
O
N
CN
CO2Et
5m
f1 (ppm)

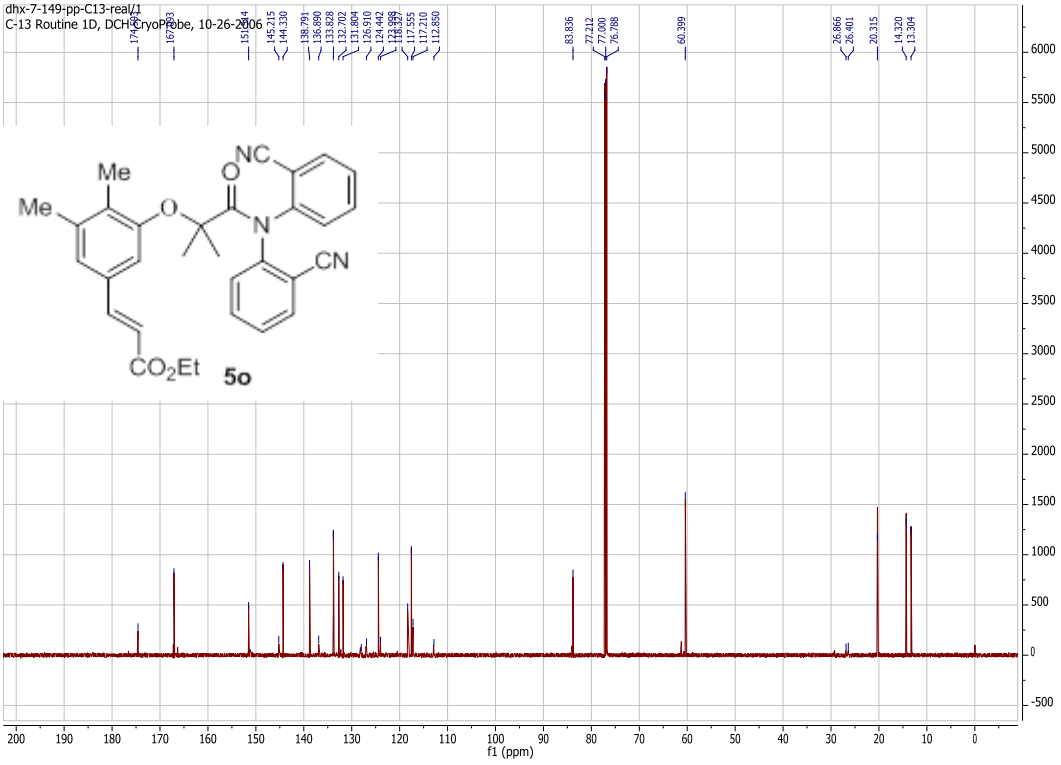

dhx-7-148-pp-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
NC
O
F3C
O
N
CN
CO2Et
5m
f1 (ppm)

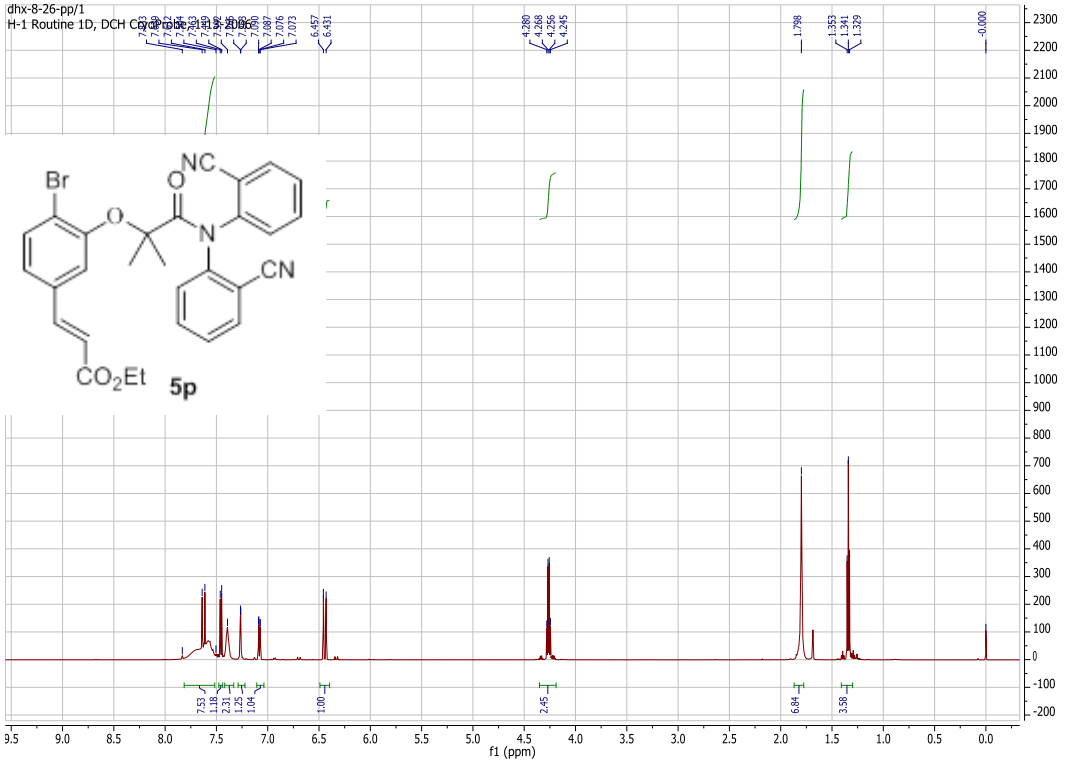
5m

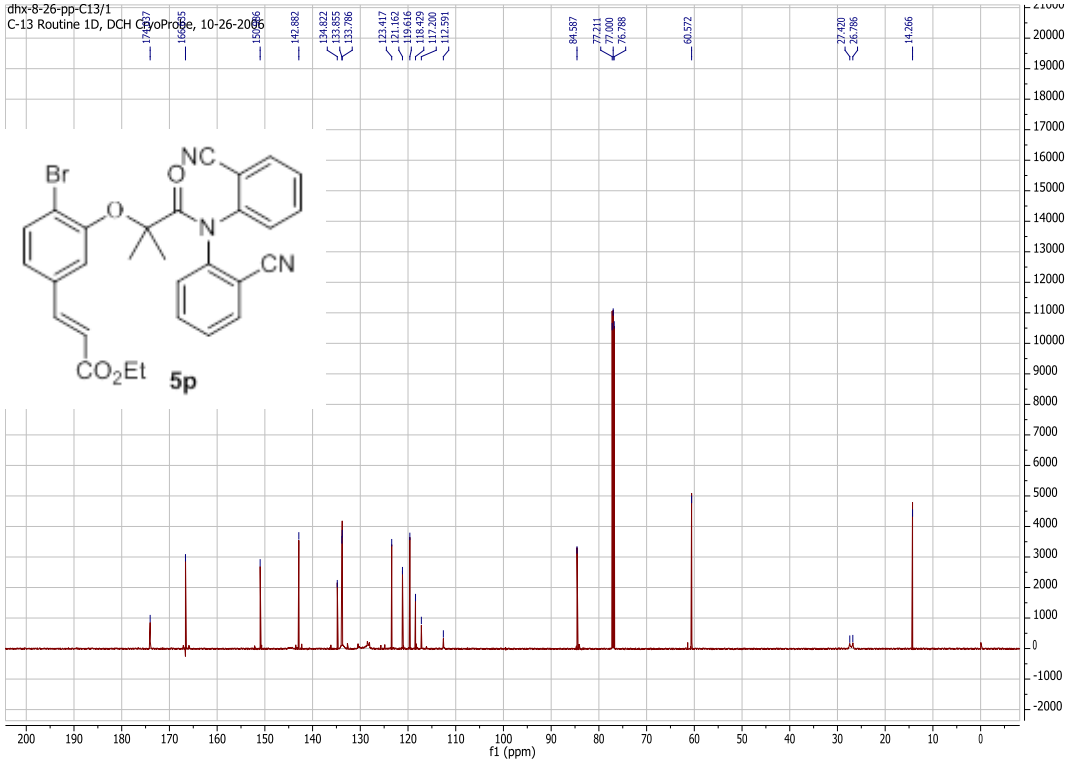

dhx-7-151-pp/1
H-1 Routine 1D, DCH CryoProbe, 10-26-2006
CN
N
O
O
NC
5n
CO2Et
f1 (ppm)

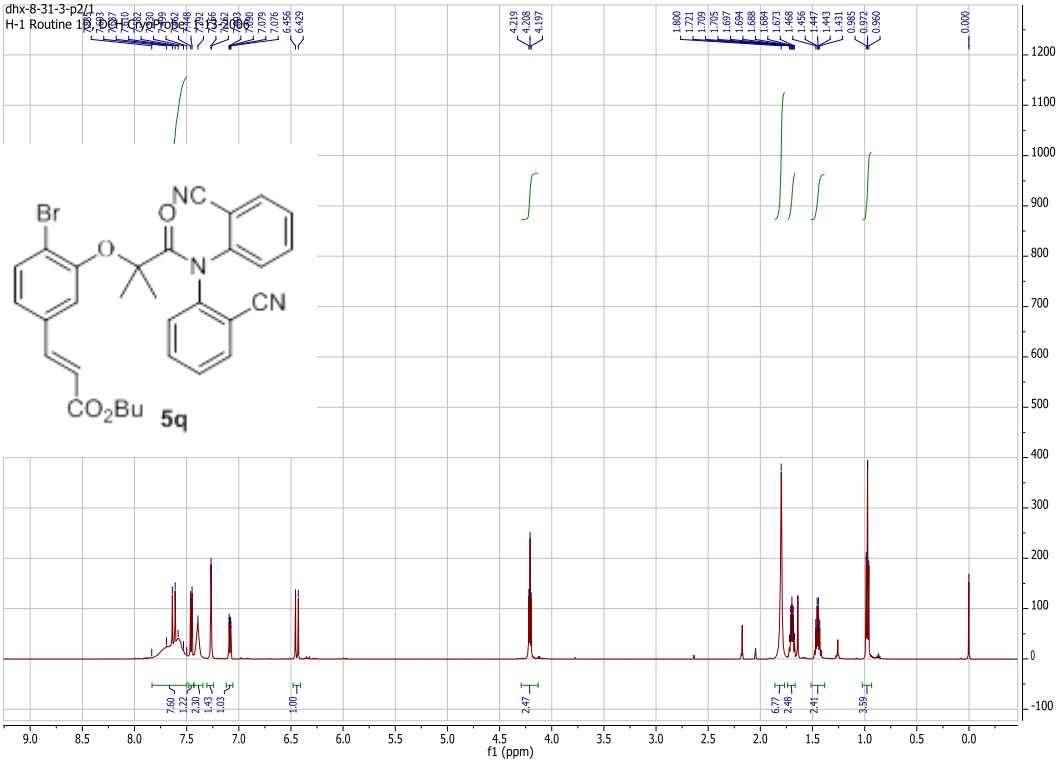

dhx-7-151-pp-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
CN
N
O
O
NC
5n
CO2Et
f1 (ppm)

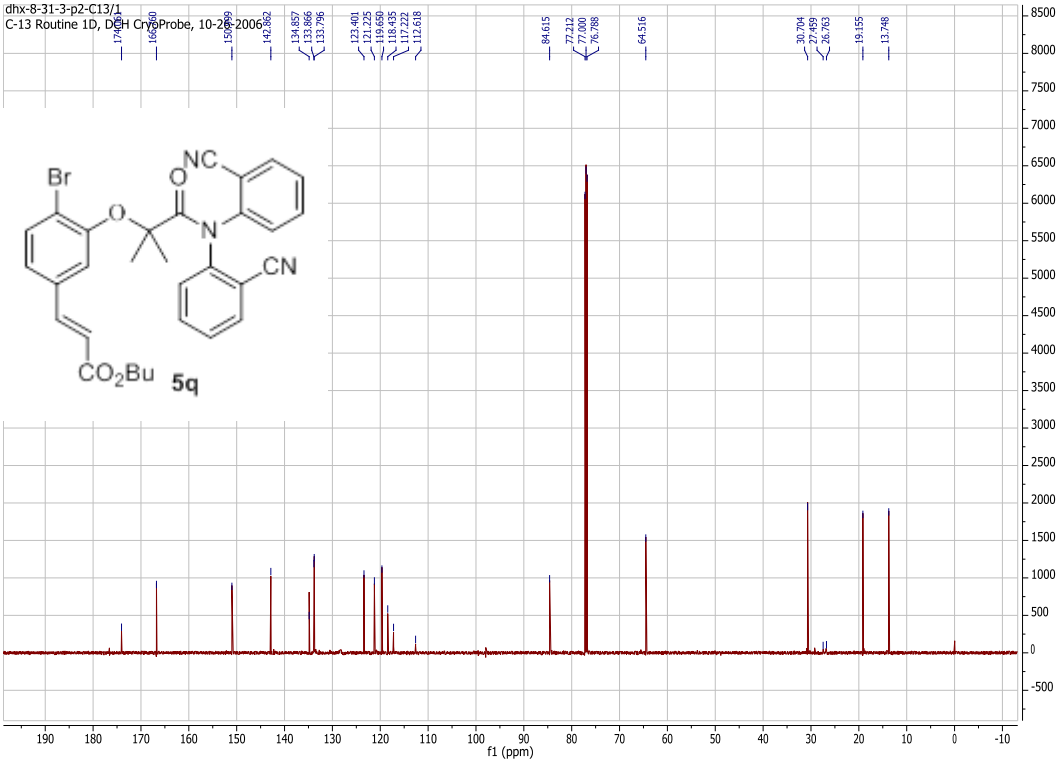

dhx-7-149-pp-C13/1
H-1 Routine 1D, DCH-CryoProbe, 7-13-2006
Me
Me
O
NC
O
N
CN
CO2Et
5o
f1 (ppm)

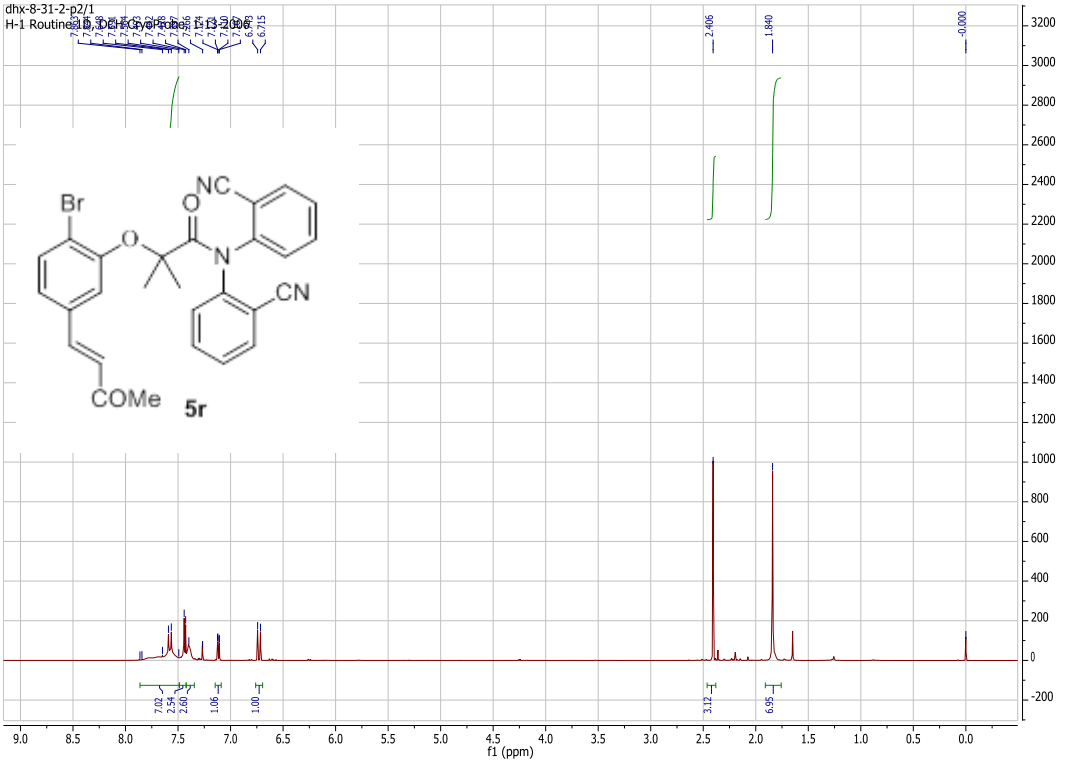

dhx-7-149-pp-C13-real/1
C-13 Routine 1D, DCH-CryoProbe, 10-26-2006
Me
Me
O
NC
O
N
CN
CO2Et
5o
f1 (ppm)

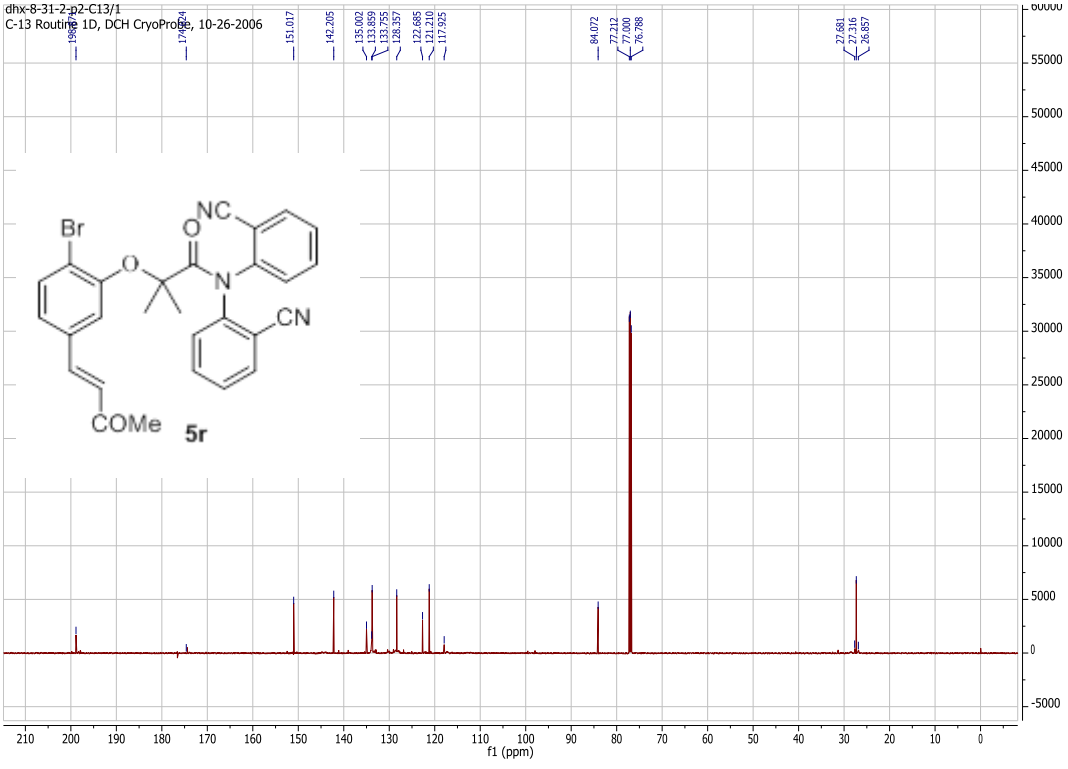

dhx-8-26-pp/1
H-1 Routine 1D, DCH CryoProbe, 10-26-2006
Br
O
NC
O
N
CN
CO2Et
5p
f1 (ppm)

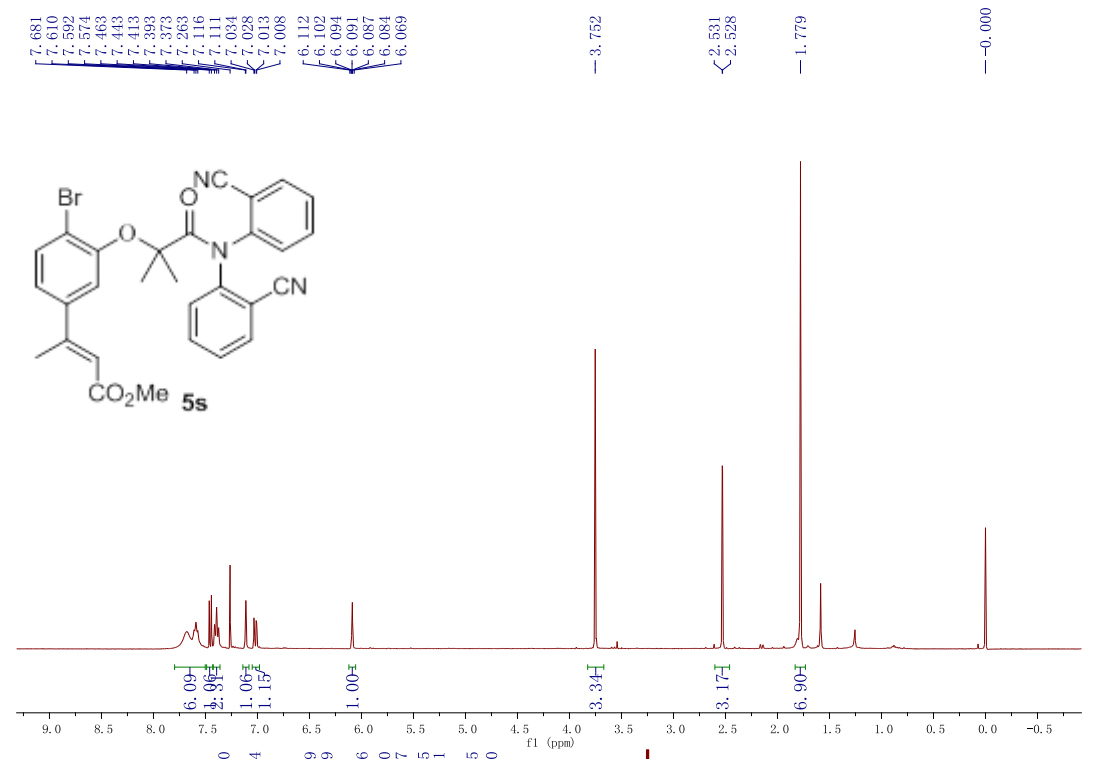

dhx-8-26-pp-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
Br
O
NC
O
N
CN
CO2Et
5p
f1 (ppm)

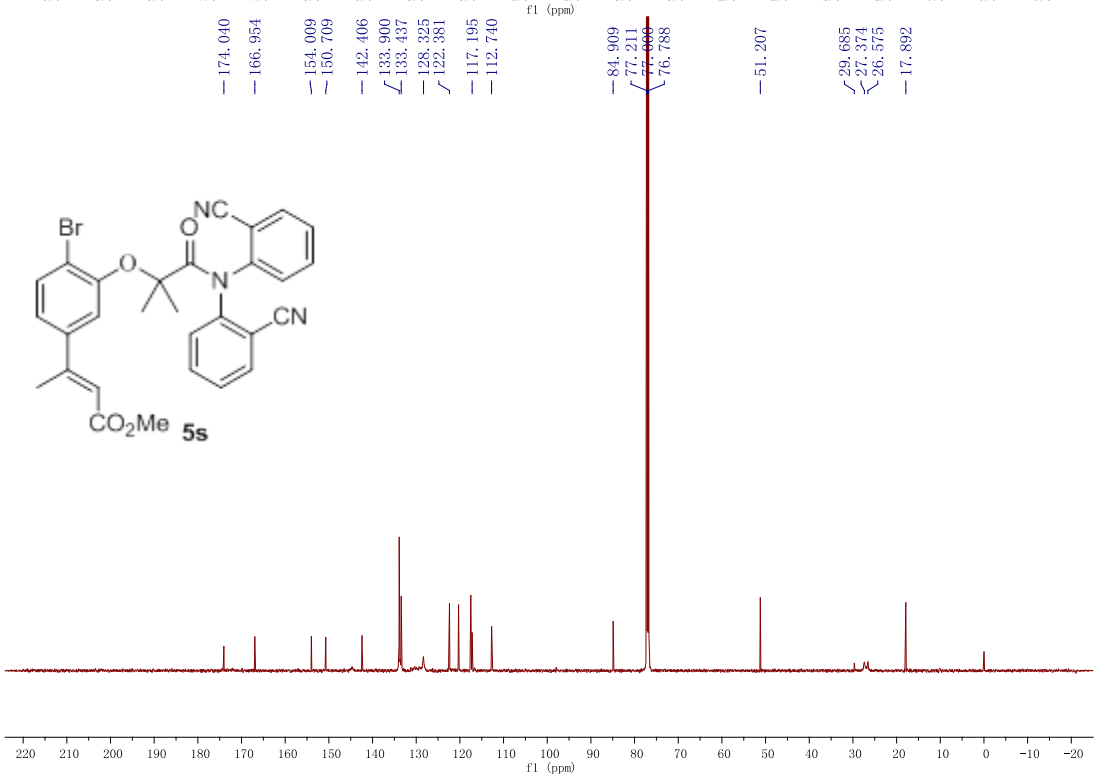

dhx-8-31-3-p2/1
H-1 Routine 1D, DCH CryoProbe, 1-13-2006
Br
O
NC
O
N
CN
CO2Bu
5q
f1 (ppm)

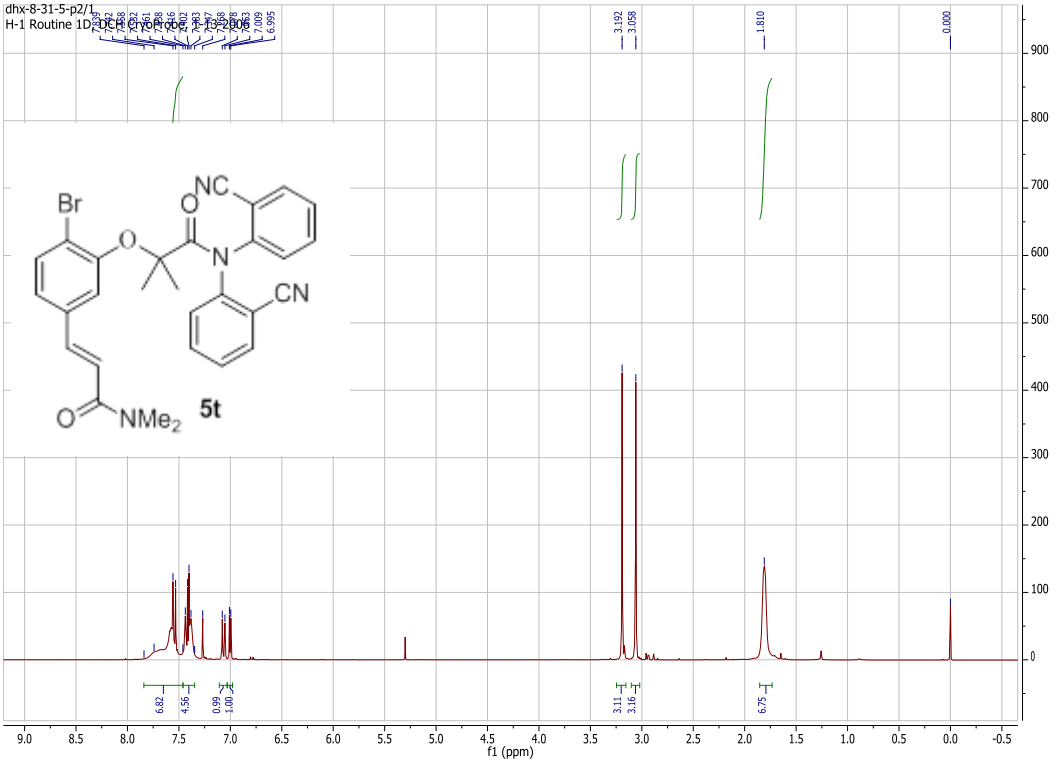

dhx-8-31-3-p2-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-2-2006
Br
O
NC
O
N
CN
CO2Bu
5q
f1 (ppm)

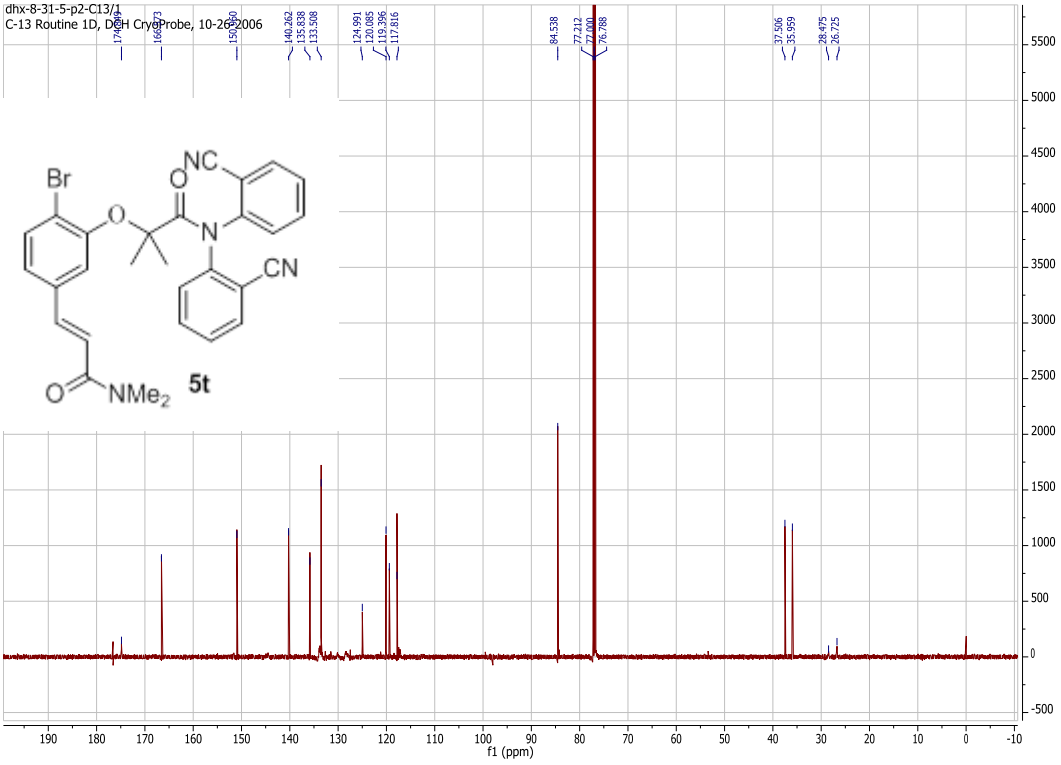

dhx-8-31-2-p2/1
H-1 Routine 1D, DCH CryoProbe, 1-13-2006
Br
O
NC
O
N
CN
COMe
5r
2.406
1.840
-0.000
7.02
2.54
2.60
1.06
1.00
3.12
6.95
f1 (ppm)

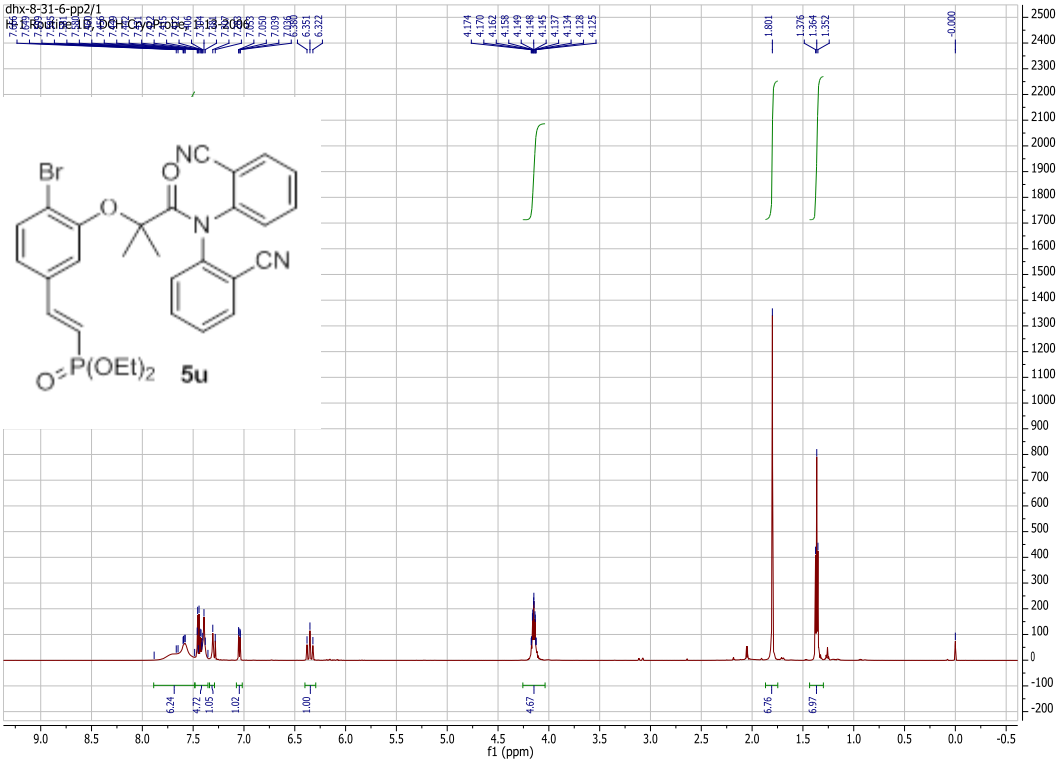

dhx-8-31-2-p2-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
151.017
142.205
135.002
133.859
133.755
128.357
122.685
121.210
117.925
84.072
77.212
77.000
76.788
27.681
27.316
26.857
Br
O
NC
O
N
CN
COMe
5r
f1 (ppm)

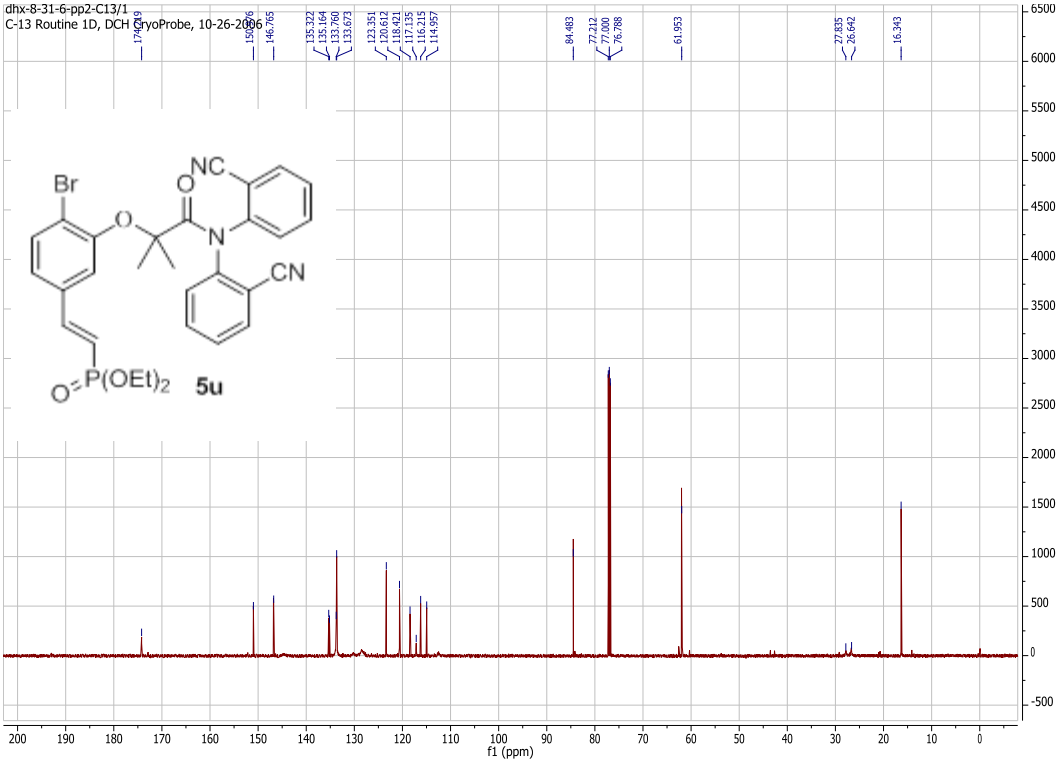

7.681
7.610
7.592
7.574
7.463
7.443
7.413
7.393
7.373
7.263
7.116
7.111
7.034
7.028
7.013
7.008
6.112
6.102
6.094
6.091
6.087
6.084
6.069
3.752
2.531
2.528
1.779
0.000
Br
O
NC
O
N
CN
CO2Me
5s
6.09
1.06
1.06
1.15
1.00
3.34
3.17
6.90
f1 (ppm)

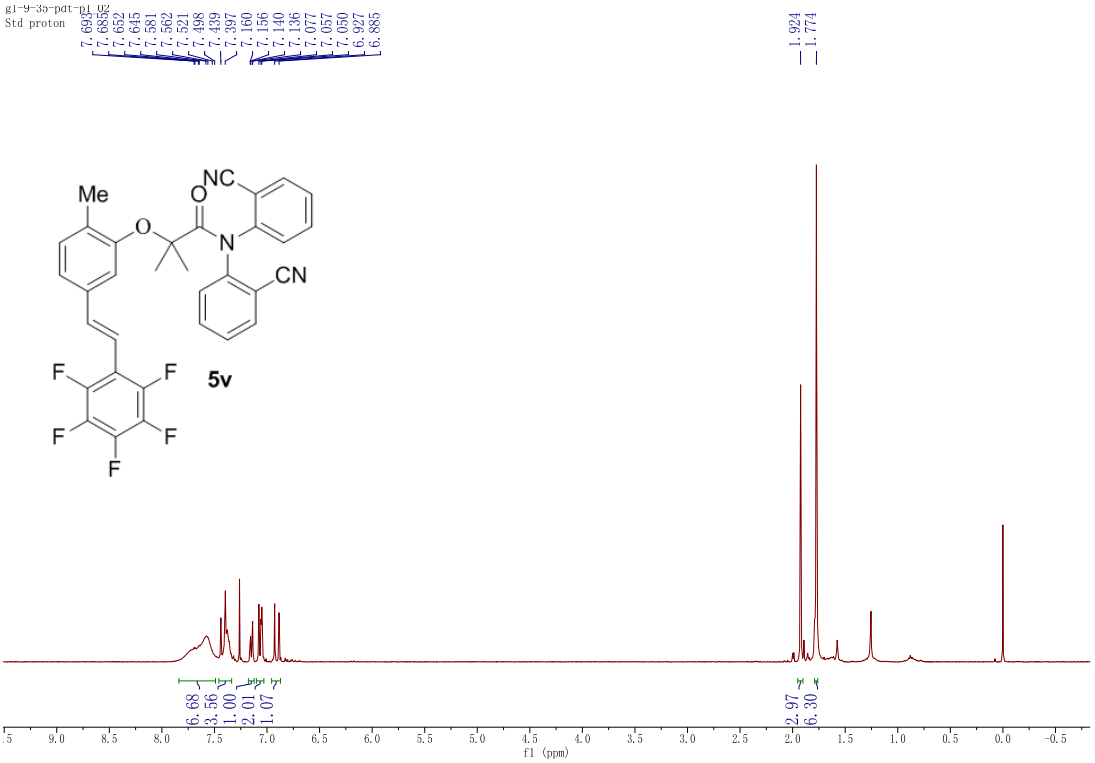

174.040
166.954
154.009
150.709
142.406
133.900
133.437
128.325
122.381
117.195
112.740
84.909
77.211
77.000
76.788
51.207
29.685
27.374
26.575
17.892
Br
O
NC
O
N
CN
CO2Me
5s
f1 (ppm)

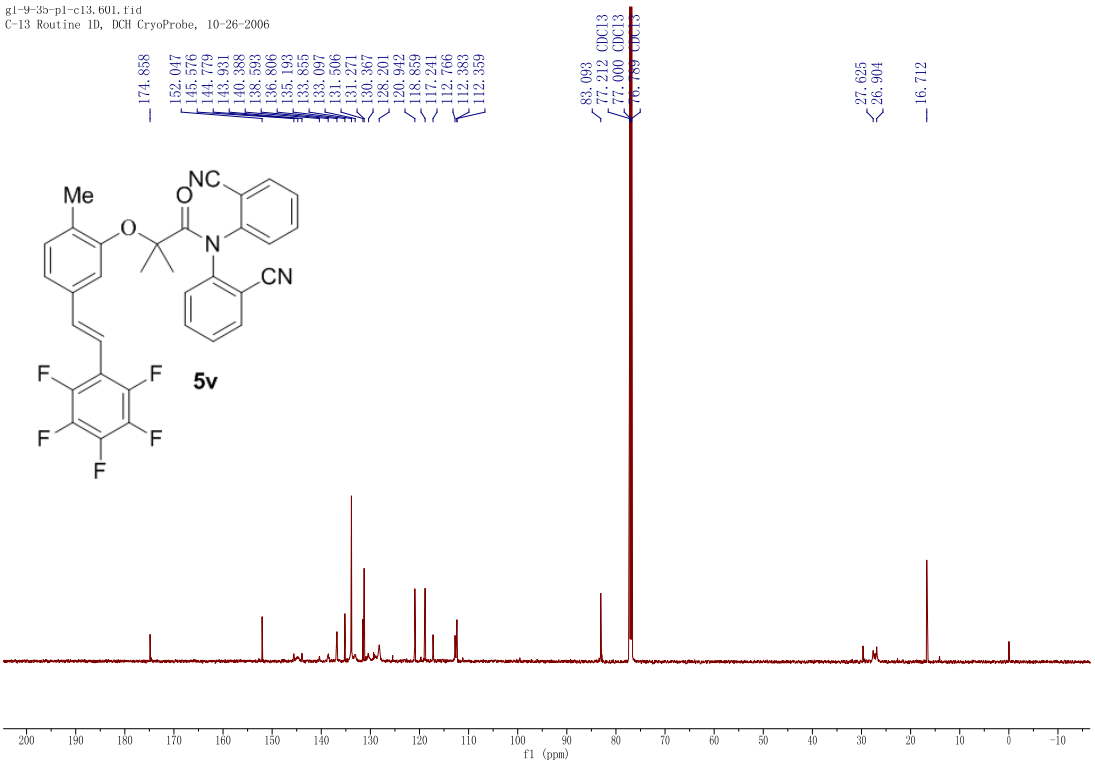

dhx-8-31-5-p2/1
H-1 Routine 1D, DCH CryoProbe, 1-10-2006
Br
O
NC
O
N
CN
O
NMe2
5t
f1 (ppm)

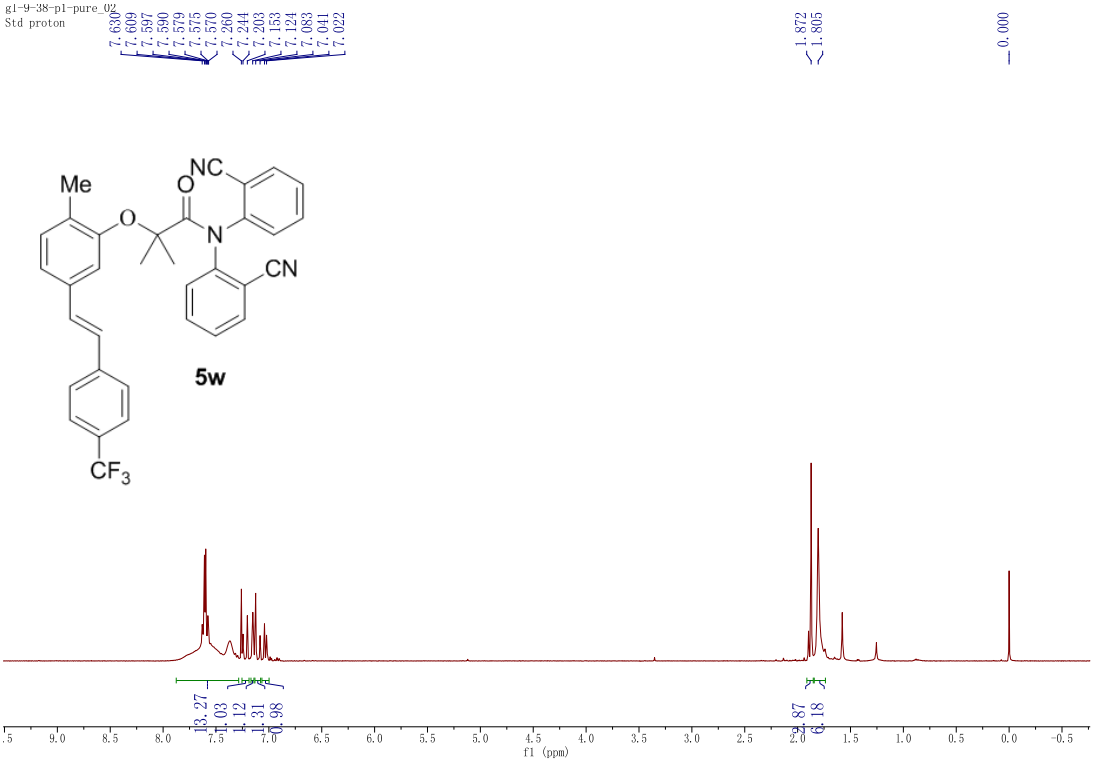

dhx-8-31-5-p2-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
Br
O
NC
O
N
CN
O
NMe2
5t
f1 (ppm)

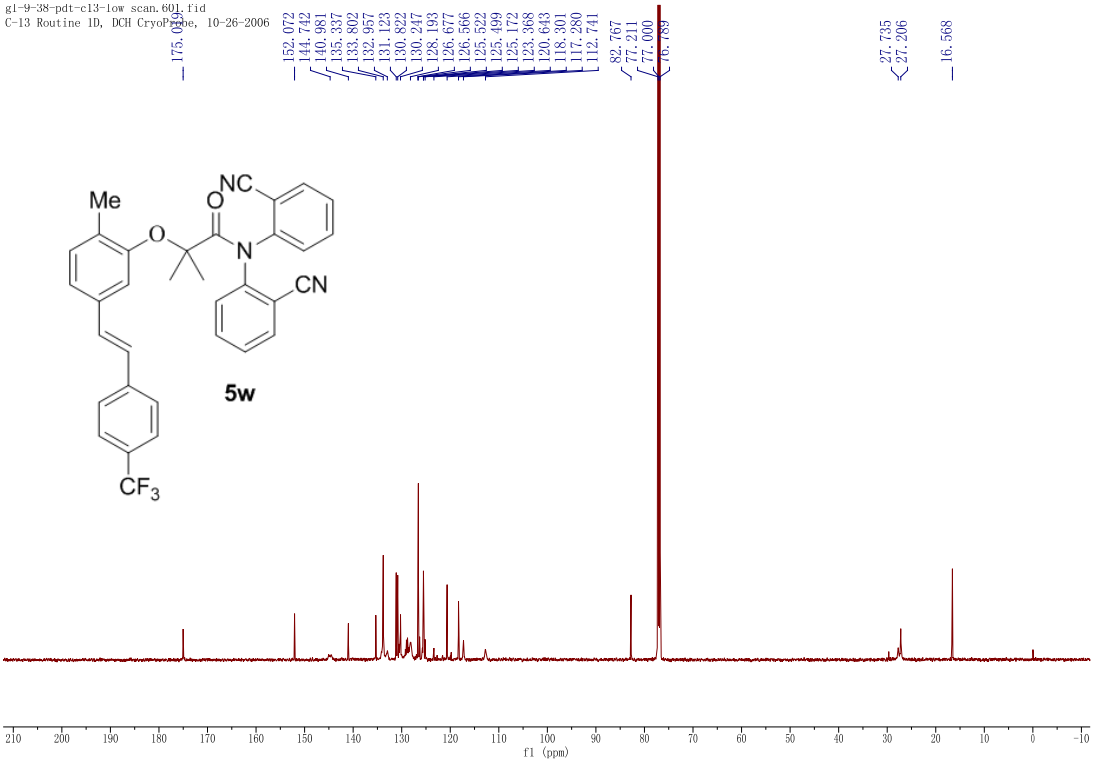

dhx-8-31-6-pp2/1
Br
O
NC
O
N
CN
O=P(OEt)2
5u
f1 (ppm)

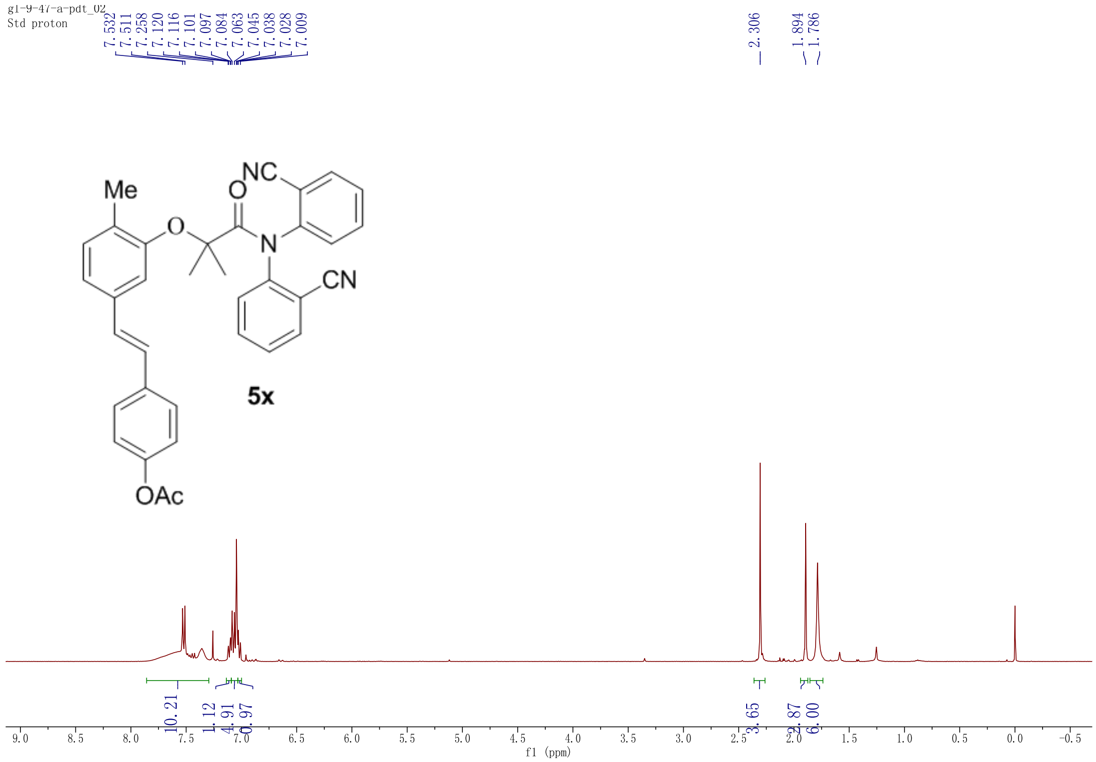

dhx-8-31-6-pp2-C13/1
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
Br
O
NC
O
N
CN
O=P(OEt)2
5u
f1 (ppm)

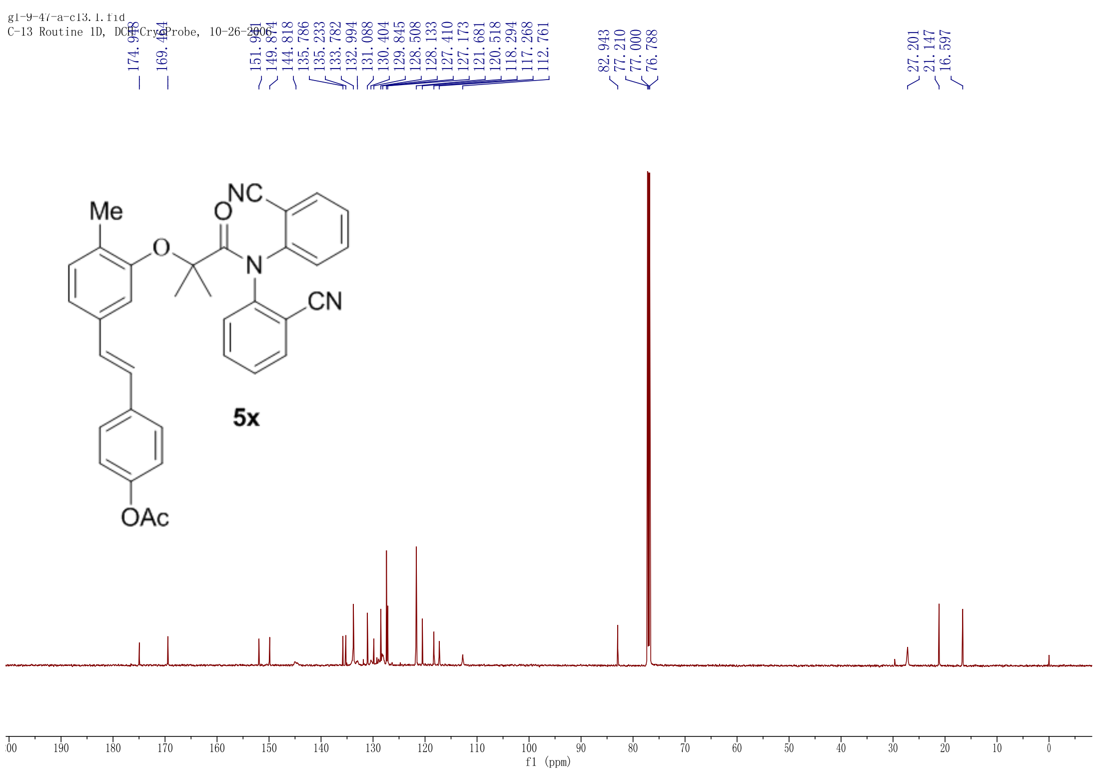

gl-9-35-pdt-p1 02
Std proton
7.693
7.685
7.652
7.645
7.581
7.562
7.521
7.498
7.439
7.397
7.160
7.156
7.140
7.136
7.077
7.057
7.050
6.927
6.885
1.924
1.774
Me
O
NC
O
N
CN
F
F
F
F
F
5v
6.68
3.56
1.00
2.01
1.07
2.97
6.30
f1 (ppm)

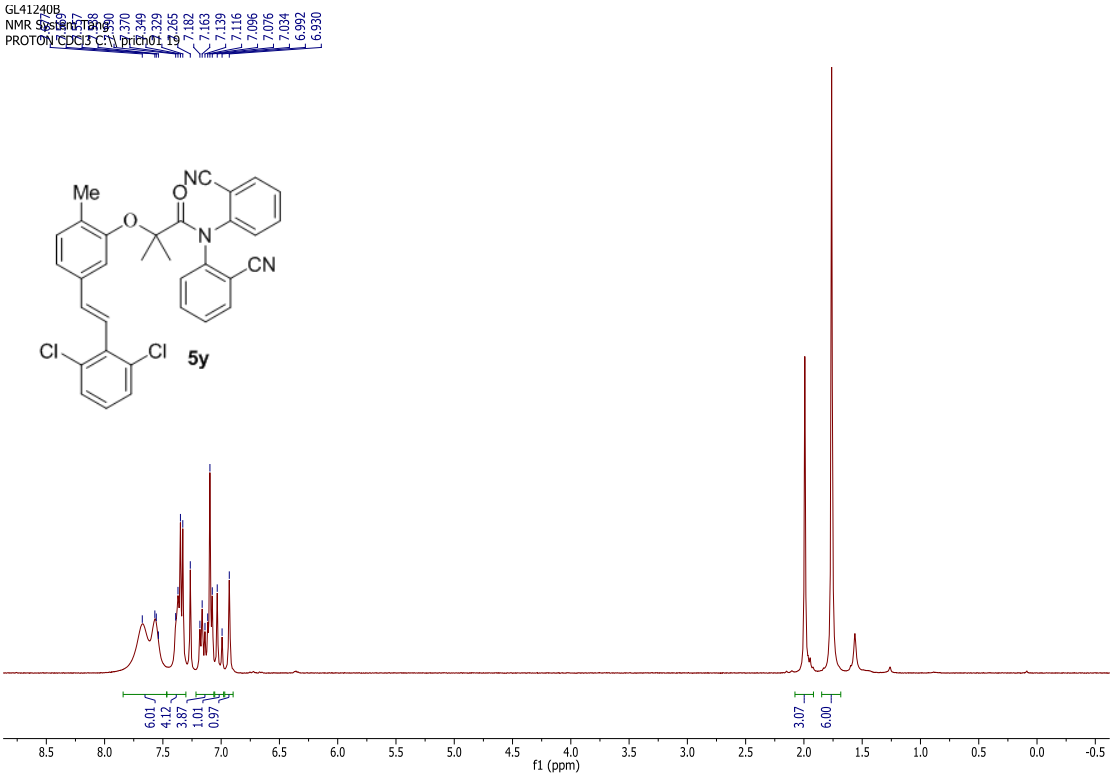

gl-9-35-p1-c13.601.fid
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
174.858
152.047
145.576
144.779
143.931
140.388
138.593
136.806
135.193
133.855
133.097
131.506
131.271
130.367
128.201
120.942
118.859
117.241
112.766
112.383
112.359
83.093
77.212 CDCl3
77.000 CDCl3
76.789 CDCl3
27.625
26.904
16.712
Me
O
NC
O
N
CN
F
F
F
F
F
5v
f1 (ppm)

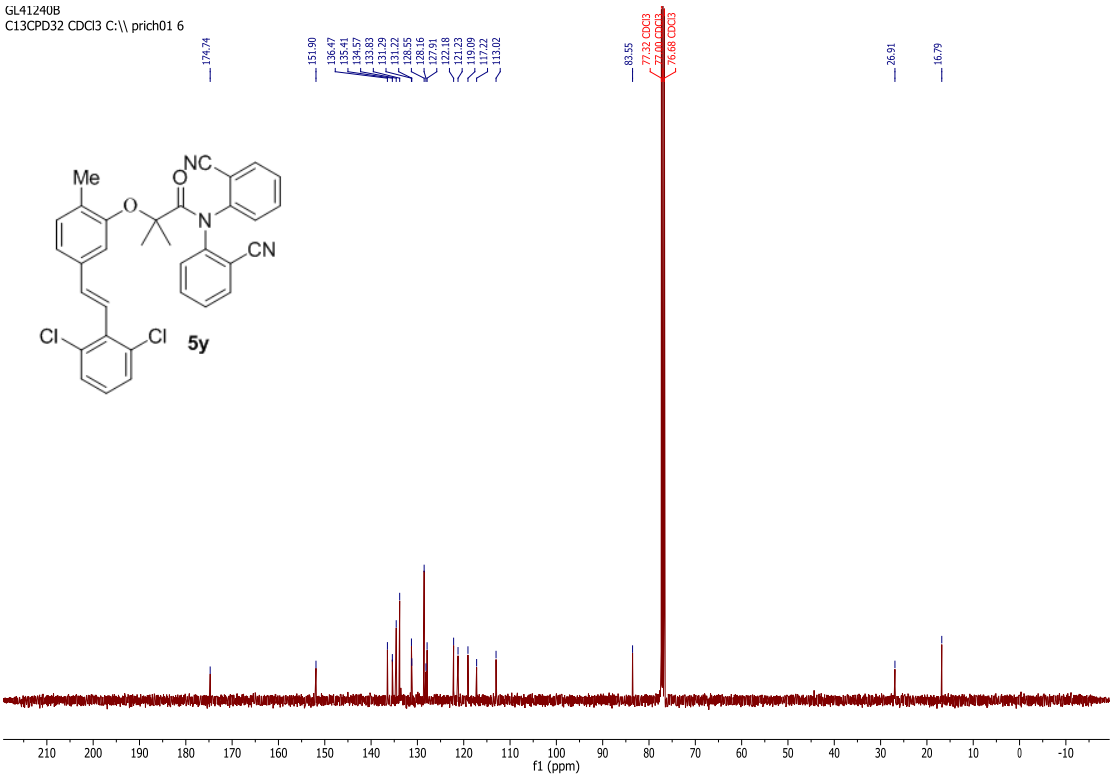

g1-9-38-p1-pure_02
Std proton
7.630
7.609
7.597
7.590
7.579
7.575
7.570
7.260
7.244
7.203
7.153
7.124
7.083
7.041
7.022
1.872
1.805
0.000
Me
O
NC
O
N
CN
5w
CF3
13.27
1.03
1.12
1.31
0.98
2.87
6.18
f1 (ppm)


g1-9-38-pdt-c13-low scan.601.fid
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
175.090
152.072
144.742
140.981
135.337
133.802
132.957
131.123
130.822
130.247
128.193
126.677
126.566
125.522
125.499
125.172
123.368
120.643
118.301
117.280
112.741
82.767
77.211
77.000
76.789
27.735
27.206
16.568
Me
O
NC
O
N
CN
5w
CF3
f1 (ppm)


gl-9-47-a-pdt_02
Std proton
7.532
7.511
7.258
7.120
7.116
7.101
7.097
7.084
7.063
7.045
7.038
7.028
7.009
2.306
1.894
1.786
Me
O
O
NC
N
CN
5x
OAc
10.21
1.12
4.91
0.97
3.65
2.87
6.00
f1 (ppm)


gl-9-47-a-c13.1.fid
C-13 Routine 1D, DCH CryoProbe, 10-26-2006
174.978
169.464
151.931
149.874
144.818
135.786
135.233
133.782
132.994
131.088
130.404
129.845
128.508
128.133
127.410
127.173
121.681
120.518
118.294
117.268
112.761
82.943
77.210
77.000
76.788
27.201
21.147
16.597
Me
O
O
NC
N
CN
5x
OAc
f1 (ppm)


GL41240B
NMR System: Tang
PROTON CDCl3 C:\\ prich01 19
Me
O
NC
N
CN
Cl
Cl
5y
6.01
4.12
3.87
1.01
0.97
3.07
6.00
f1 (ppm)


GL41240B
C13CPD32 CDCl3 C:\\ prich01 6
174.74
151.90
136.47
135.41
134.57
133.83
131.29
131.22
128.55
128.16
127.91
122.18
121.23
119.09
117.22
113.02
83.55
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
26.91
16.79
Me
O
NC
N
CN
Cl
Cl
5y
f1 (ppm)