Silanol – a Traceless Directing Group for Pd-Catalyzed *o*-Alkenylation of Phenols

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Supporting Information

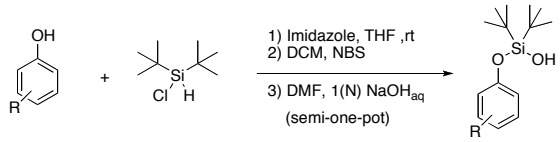
Content

General Information

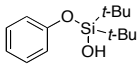
GC/MS analysis was performed on a Hewlett Packard Model 6890 GC interfaced to a Hewlett Packard Model 5973 mass selective detector (15 m x 0.25 mm capillary column, HP-5MS). Column chromatography was carried out employing Silicycle Silica-P flash silica gel (40-63 μm). Precoated silica gel plates F-254 were used for thin-layer analytical chromatography. NMR spectra were recorded on Bruker Avance DRX-500 (500 MHz) or DPX-400 (400 MHz) instrument. LRMS and HRMS analyses were performed on Micromass 70 VSE mass spectrometer. All manipulations with transition metal catalysts were conducted in oven-dried glassware under inert atmosphere using a combination of glovebox and standard Schlenk techniques. Anhydrous solvents purchased from Aldrich were additionally purified on PureSolv PS-400-4 by Innovative Technology, Inc. purification system and/or stored over calcium hydride. (+)Menthyl(O_2C)-Leu-OH was prepared according to a known procedure.[1] All other starting materials were purchased from Strem Chemicals, Aldrich, Gelest Inc., or Alfa Aesar.

[1] Shi, B.-F.; Maugel, N.; Zhang, Y.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2008**, *47*, 4882.

Part I. Preparation of Silanols in Semi-one-pot.[2]

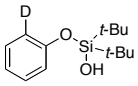


To a stirred mixture of imidazole (749 mg, 5 mmol) and THF (40 ml), di-*t*-butylchlorosilane (938.6 mg, 5.25 mmol) was added at rt under argon atmosphere. To this mixture, phenol (5 mmol) in 10 mL of THF was added. The mixture was stirred until completion of the reaction by GCMS. To this mixture, hexane (50 ml) was added and filtered. The filtrate was then evaporated by rotary evaporator under reduced pressure. To this crude mixture, 50 ml hexane was added and filtered again, and evaporated to give the pure compound. To this compound, 25 ml DCM was added and NBS (981 mg, 1.1 equiv.) was added slowly. After monitoring by GCMS, DMF (1.25 ml) and 1(N) aqueous NaOH (1.25 ml) was added and stirred at rt. Upon completion (judged by GCMS), the mixture was evaporated by rotary evaporator under reduced pressure. Water (50 ml) was added and extracted with ether, dried over Na_2SO_4 and evaporated. The residue was purified by silica gel column chromatography (eluent: hexanes/EtOAc or hexanes/Et_2O) to give the silanols.



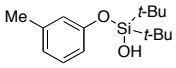
1a: (86%, eluent: 3% EtOAc in hexanes)

^{1}H NMR (500 MHz, $CHCl_3$): δ ppm 7.24 (dd, *J* = 8.6, 7.4 Hz, 2H), 7.02-7.00 (m, 2H), 6.95 (t, *J* = 7.3 Hz, 1H), 2.26 (s, 1H), 1.09 (s, 18H).
^{13}C NMR (101 MHz, $CHCl_3$): δ ppm 155.7, 129.4, 121.2, 119.8, 27.4, 20.6.
HRMS (EI) calcd. for $C_{14}H_{24}O_2Si$ $[M]^+$: 252.15456. Found: 252.15375.



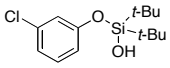
1a-*d*: (86%, eluent: 3% EtOAc in hexanes)

^{1}H NMR (500 MHz, $CHCl_3$): δ ppm 7.17 - 7.32 (m, 2 H), 7.02 (d, *J*=7.70 Hz, 1 H), 6.88 - 6.98 (m, 1 H), 2.29 (s, 1 H), 1.10 (s, 18 H);
^{13}C NMR (126 MHz, $CHCl_3$): δ ppm 155.7, 134.3, 129.4, 129.3, 121.2, 119.8, 27.4, 20.6.
HRMS (EI) calcd. for $C_{14}H_{23}O_2SiD$ $[M]^+$: 253.16084. Found: 253.16166.



1b: (67%, eluent: 3% Et_2O in hexanes)

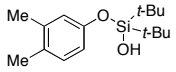
^{1}H NMR (500 MHz, $CHCl_3$): δ ppm 7.12 (t, *J*=7.52 Hz, 1 H), 6.80 - 6.86 (m, 2 H), 6.77 (d, *J*=6.97 Hz, 1 H), 2.31 (s, 3 H), 2.24 (s, 1 H), 1.09 (s, 18 H);
^{13}C NMR (126 MHz, $CHCl_3$): δ ppm 155.6, 139.4, 129.1, 122.1, 120.5, 116.7, 27.4, 26.0, 20.6.
HRMS (EI) calcd. for $C_{15}H_{26}O_2Si$ $[M]^+$: 266.17021. Found: 266.17120.



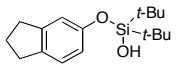
1d: (59%, eluent: 1% Et_2O in hexanes)

^{1}H NMR (500 MHz, $CHCl_3$): δ ppm 7.14 (t, *J*=8.07 Hz, 1 H), 7.03 (t, *J*=2.20 Hz, 1 H), 6.94 (d, *J*=8.07 Hz, 1 H), 6.91 (dd, *J*=8.80, 1.83 Hz, 1 H), 2.37 (s, 1 H), 1.08 (s, 18 H);
^{13}C NMR (126 MHz, $CHCl_3$) δ ppm 156.5, 134.5, 130.1, 121.5, 120.2, 118.1, 27.3, 20.6.
HRMS (EI) calcd. for $C_{14}H_{23}O_2SiCl$ $[M]^+$: 286.11559. Found: 286.11535.

[2] For stepwise procedure, see: Petit, M.; Chouraqui, G.; Aubert, C.; Malacria, M. *Org. Lett.* **2003**, *5*, 2037.

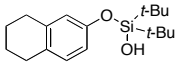


1e: (76%, eluent: 2% Et_2O in hexanes)
^{1}H NMR (500 MHz, $CHCl_3$): δ ppm 6.98 (d, *J*=8.07 Hz, 1 H), 6.79 (d, *J*=2.20 Hz, 1 H), 6.74 (dd, *J*=8.44, 2.57 Hz, 1 H), 2.21 - 2.23 (m, 4 H), 2.19 (s, 3 H), 1.09 (s, 18 H);
^{13}C NMR (126 MHz, $CHCl_3$): δ ppm 153.6, 137.6, 130.2, 129.1, 120.9, 116.8, 27.4, 20.6, 19.9, 18.8.
HRMS (EI) calcd. for $C_{16}H_{28}O_2Si$ $[M]^+$: 280.18586. Found: 280.18684.



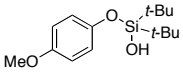
1f: (68%, eluent: 2% Et_2O in hexanes)

^{1}H NMR (500 MHz, $CHCl_3$): δ ppm 7.07 (d, *J*=8.07 Hz, 1 H), 6.88 (d, *J*=1.83 Hz, 1 H), 6.78 (dd, *J*=8.07, 2.57 Hz, 1 H), 2.74 - 2.94 (m, 4 H), 2.25 (s, 1 H), 1.94 - 2.13 (m, 2 H), 1.10 (s, 18 H);
^{13}C NMR (126 MHz, $CHCl_3$): δ ppm 154.2, 145.6, 136.6, 124.6, 117.4, 115.7, 32.1, 27.4, 26.0, 25.8, 20.6.
HRMS (EI) calcd. for $C_{17}H_{28}O_2Si$ $[M]^+$: 292.18586. Found: 292.18685.



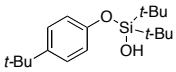
1g: (65%, eluent: 2% Et_2O in hexanes)

^{1}H NMR (500 MHz, $CHCl_3$): δ ppm 6.93 (d, *J*=8.44 Hz, 1 H), 6.76 (dd, *J*=8.07, 2.57 Hz, 1 H), 6.72 (d, *J*=2.20 Hz, 1 H), 2.63 - 2.81 (m, 4 H), 2.28 (s, 1 H), 1.70 - 1.87 (m, 4 H), 1.10 (s, 18 H);
^{13}C NMR (126 MHz, $CHCl_3$) δ ppm 153.2, 138.1, 129.8, 119.7, 117.1, 29.6, 28.7, 27.4, 23.5, 23.2, 20.6.
HRMS (EI) calcd. for $C_{18}H_{30}O_2Si$ $[M]^+$: 306.20151. Found: 306.20234.



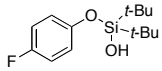
1h: (82%, eluent: 2% Et_2O in hexanes)

^{1}H NMR (500 MHz, $CHCl_3$): δ ppm 6.92 (d, *J*=9.17 Hz, 2 H), 6.77 (d, *J*=9.17 Hz, 2 H), 3.76 (s, 3 H), 2.27 (s, 1 H), 1.07 (s, 18 H);
^{13}C NMR (126 MHz, $CHCl_3$): δ ppm 154.0, 149.5, 120.2, 114.5, 55.7, 27.4, 20.6.
HRMS (EI) calcd. for $C_{15}H_{26}O_3Si$ $[M]^+$: 282.16513. Found: 282.16617.



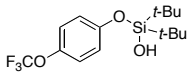
1i: (81%, eluent: 2% Et_2O in hexanes)

^{1}H NMR (500 MHz, $CHCl_3$): δ ppm 7.24 (d, *J*=8.80 Hz, 2 H), 6.92 (d, *J*=8.80 Hz, 2 H), 2.23 (s, 1 H), 1.30 (s, 9 H), 1.09 (s, 18 H);
^{13}C NMR (126 MHz, $CHCl_3$): δ ppm 153.2, 143.8, 126.1, 119.1, 34.1, 31.6, 27.4, 20.6.
HRMS (EI) calcd. for $C_{18}H_{32}O_2Si$ $[M]^+$: 308.21716. Found: 308.21783.



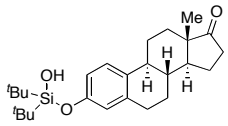
1j: (66%, eluent: 2% Et_2O in hexanes)

^{1}H NMR (500 MHz, $CHCl_3$): δ ppm 6.57 - 7.16 (m, 4 H), 2.30 (s, 1 H), 1.08 (s, 18 H);
^{13}C NMR (126 MHz, $CHCl_3$): δ ppm 157.4 (d, *J*=238.6 Hz), 151.7, 120.7, 115.7 (d, *J*=22.2 Hz),, 27.4, 20.6.
HRMS (EI) calcd. for $C_{14}H_{23}O_2SiF$ $[M]^+$: 270.14514. Found: 270.14621.



1k: (25%, eluent: 3% Et_2O in hexanes)

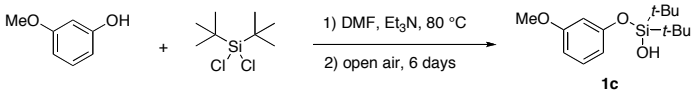
^{1}H NMR (500 MHz, $CHCl_3$): δ ppm 7.08 (d, *J*=9.17 Hz, 2 H), 6.92 - 7.03 (m, 2 H), 2.30 (s, 1 H), 1.08 (s, 18 H);
^{13}C NMR (126 MHz, $CHCl_3$): δ ppm 155.4, 143.1, 133.8, 122.2, 120.5, 27.3, 20.6.
HRMS (EI) calcd. for $C_{15}H_{23}O_3SiF_3$ $[M]^+$: 336.13687. Found: 336.13729.



7: (99%, eluent: 15% Et_2O in hexanes)

^{1}H NMR (500 MHz, $CHCl_3$): δ ppm 7.13 (d, *J*=8.80 Hz, 1 H), 6.80 (dd, *J*=8.44, 2.20 Hz, 1 H), 6.73 (d, *J*=2.20 Hz, 1 H), 2.78 - 2.94 (m, 2 H), 2.50 (dd, *J*=18.89, 8.62 Hz, 1 H), 2.32 - 2.42 (m, 1 H), 2.20 - 2.30 (m, 1 H), 1.84 - 2.19 (m, 4 H), 1.32 - 1.71 (m, 6 H), 1.08 (s, 18 H), 0.91 (s, 3 H);
^{13}C NMR (126 MHz, $CHCl_3$): δ ppm 221.0, 153.6, 137.6, 132.5, 126.2, 119.7, 117.2, 50.5, 48.0, 44.1, 38.4, 35.9, 31.6, 29.5, 27.4, 26.6, 25.9, 21.6, 20.6, 13.9.
HRMS (EI) calcd. for $C_{26}H_{40}O_3Si$ $[M]^+$: 428.27468. Found: 428.27393.

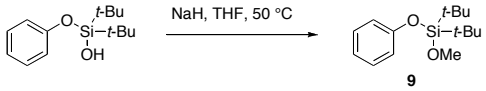
Preparation of Silanol 1c:



1c

To a stirred mixture of 3-methoxyphenol (620.7 mg, 5 mmol), DMF (40 ml), Et_3N (5 ml), di-*t*-butylchlorosilane (1.9 g, 9 mmol) was added at rt under argon atmosphere. The mixture was heated at 80 ^{o}C for 24 h. After completion, (judged by GCMS) left it 6 days at open air. Water (50 ml) was added and extracted with ether, dried over Na_2SO_4 and evaporated under reduced pressure. After column chromatographic separation (eluent: 3% Et_2O in hexanes), it gave the silanol **1c** in 53% yield as colorless oil.
^{1}H NMR (500 MHz, $CHCl_3$): δ ppm 7.12 (t, *J*=8.25 Hz, 1 H), 6.62 (dd, *J*=8.07, 2.20 Hz, 1 H), 6.58 (t, *J*=2.38 Hz, 1 H), 6.52 (dd, *J*=7.89, 2.02 Hz, 1 H), 3.78 (s, 3 H), 2.40 (s, 1 H), 1.08 (s, 18 H);
^{13}C NMR (126 MHz, $CHCl_3$): δ ppm 160.7, 156.9, 129.7, 112.4, 106.8, 106.1, 55.2, 27.4, 20.6.
HRMS (EI) calcd. for $C_{15}H_{26}O_3Si$ $[M]^+$: 282.16513. Found: 282.16638.

Preparation of 9:

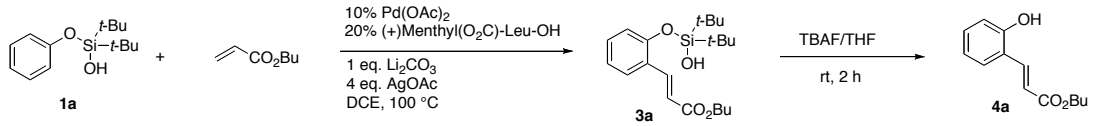


9

In a glovebox, 5 mL Weaton microreactor was charged with silanol **1a** and THF (1 ml). NaH (96 mg, 2 equiv.) was added slowly. After 5 min stirring at rt, iodomethane (6 equiv.) was added. The microreactor was capped with Teflon pressure cap and placed into pre-heated aluminum block at 50 ^{o}C. The reaction mixture was stirred for 12 h (as judged by GCMS analysis). After completion, filtered and evaporated under reduced pressure and chromatographic separation with silica gel (eluent: hexanes) gave **9** (388 mg) in 73% yield as colorless oil.
^{1}H NMR (500 MHz, $CHCl_3$): δ ppm 7.25 (d, *J*=8.44 Hz, 2 H), 6.92 - 7.04 (m, 3 H), 3.77 (s, 3 H), 1.09 (s, 18 H);
^{13}C NMR (126 MHz, $CHCl_3$): δ ppm 129.4, 121.1, 119.8, 52.7, 27.8, 21.4.
HRMS (EI) calcd. for $C_{15}H_{26}O_2Si$ $[M]^+$: 266.17021. Found: 266.17124.

Part II: Preparation of *ortho*-alkenylated phenols.

A: Stepwise approach.

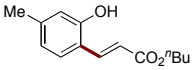


An oven dried 2.5 ml Wheaton V-vial, containing a stirring bar, was charged with silanol **1a** (0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), Li_2CO_3 (14.8 mg, 0.2 mmol), AgOAc (133.8 mg, 0.8 mmol), and (+)Menthyl(O_2C)-Leu-OH (12.6 mg, 0.04 mmol) under N_2 atmosphere. Butyl acrylate (0.4 mmol, 2 equiv) and dry DCE (2 ml) were added via syringes and the reaction vessel was capped with pressure screw cap. The reaction mixture was heated at 100 °C for 24 h. The resulting mixture was cooled down to room temperature and filtered through a celite plug with the aid of EtOAc. The filtrate was concentrated under a reduced pressure. ^{1}H NMR analysis of the crude mixture showed 78% yield of **3a** using CH_2Br_2 as internal standard. The rough purification of the crude mixture by column chromatography on a silica gel (eluent: hexanes/EtOAc = 10/1) afforded the product **3a** (65.3 mg, impure). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.15 (d, *J*=16.2 Hz, 1H), 7.53 (d, *J*=7.8 Hz, 1H), 7.22-7.23 (m, 2H), 6.92-6.96 (m, 1H), 6.39 (d, *J*=16.3 Hz, 1H), 4.18 (t, *J*=6.6 Hz, 2H), 2.86 (br. s., 1H), 1.62-1.69 (m, 2H), 1.38-1.477 (m, 2H), 1.08 (s, 18H), 0.95 (t, *J*=7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 167.4, 155.0, 140.0, 131.3, 127.1, 121.4, 119.9, 118.4, 117.8, 64.3, 30.7, 27.5, 20.7, 19.2, 13.8. To a solution of **3a** (65.3 mg, impure) in THF (1 ml), TBAF (0.34 ml, 1.0 M solution in THF) was added via syringe at room temperature. The reaction mixture was stirred for 2 h. Upon completion of the reaction, the mixture was washed with water, extracted with diethyl ether, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on a silica gel (eluent: hexanes/EtOAc = 5/1) affording the product **4a**[3] (31.9 mg, 84%). ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.05 (d, *J*=16.32 Hz, 1 H), 7.47 (dd, *J*=7.79, 1.56 Hz, 1 H), 7.24 (td, *J*=7.70, 1.65 Hz, 1 H), 6.92 (td, *J*=7.52, 0.92 Hz, 1 H), 6.86 (dd, *J*=8.07, 0.92 Hz, 1 H), 6.72 (s, 1 H), 6.66 (d, *J*=16.32 Hz, 1 H), 4.24 (t, *J*=6.79 Hz, 2 H), 1.67 - 1.74 (m, 2 H), 1.39 - 1.50 (m, 2 H), 0.97 (t, *J*=7.43 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 168.6, 155.4, 140.6, 131.4, 129.2, 121.8, 120.7, 118.5, 116.4, 64.6, 30.8, 19.2, 13.8; HRMS (EI) calcd. for $C_{13}H_{16}O_3$ $[M]^+$: 220.10995. Found: 220.11082.

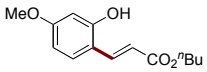
B: Semi-one-pot approach for preparation of *ortho*-alkenylated phenols.

General procedure: An oven dried 2.5 ml Wheaton V-vial, containing a stirring bar, was charged with phenol-derived silanols (0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), Li_2CO_3 (14.8 mg, 0.2 mmol), AgOAc (133.8 mg, 0.8 mmol), and (+)Menthyl(O_2C)-Leu-OH (12.6 mg, 0.04 mmol) under N_2 atmosphere. Alkene (0.4 mmol, 2 equiv) and dry DCE (2 ml) were added via syringes and the reaction vessel was capped with pressure screw cap. The reaction mixture was heated at 100 – 120 °C for 24 h. The resulting mixture was cooled down to room temperature and filtered through a celite plug with the aid of EtOAc. The filtrate was concentrated under a reduced pressure. The residue was added with THF (1 ml) and TBAF (0.4 ml, 2 equiv). The reaction mixture was stirred at room temperature for 2 h. Upon completion, the mixture was washed with water, extracted with diethyl ether, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on a silica gel (eluent: hexanes/EtOAc = 3/1 – 8/1) affording the corresponding *ortho*-alkenylated product.

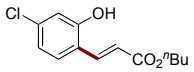
[3] Peng, Y.; Chen, J.; Ding, J.; Liu, M.; Gao, W.; Wu, H. *Synthesis* **2011**, *2*, 213.



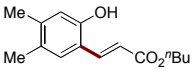
4b: (94%)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.02 (d, *J*=16.14 Hz, 1 H), 7.35 (d, *J*=7.89 Hz, 1 H), 6.93 (br. s., 1 H), 6.72 (d, *J*=8.07 Hz, 1 H), 6.69 (s, 1 H), 6.63 (d, *J*=16.14 Hz, 1 H), 4.24 (t, *J*=6.69 Hz, 2 H), 2.30 (s, 3 H), 1.66 - 1.77 (m, 2 H), 1.39 - 1.51 (m, 2 H), 0.97 (t, *J*=7.34 Hz, 3 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 168.9, 155.5, 142.3, 140.8, 129.2, 121.7, 119.0, 117.3, 117.0, 64.5, 30.8, 21.4, 19.2, 13.7.
HRMS (EI) calcd. for $C_{14}H_{18}O_3$ $[M]^+$: 234.12560. Found: 234.12522.



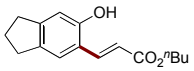
4c: (97%)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.00 (d, *J*=16.14 Hz, 1 H), 7.44 (br. s., 1 H), 7.39 (d, *J*=8.62 Hz, 1 H), 6.56 (d, *J*=15.96 Hz, 1 H), 6.48 (dd, *J*=8.62, 2.38 Hz, 1 H), 6.43 (d, *J*=2.38 Hz, 1 H), 4.23 (t, *J*=6.69 Hz, 2 H), 3.79 (s, 3 H), 1.66 - 1.74 (m, 2 H), 1.40 - 1.49 (m, 2 H), 0.96 (t, *J*=7.43 Hz, 3 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 169.2, 162.5, 157.2, 140.7, 130.5, 115.5, 115.0, 107.0, 101.9, 64.5, 55.4, 30.8, 19.2, 13.7.
HRMS (EI) calcd. for $C_{14}H_{18}O_4$ $[M]^+$: 250.12051. Found: 250.12011.



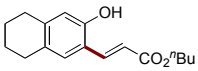
4d: (53% NMR yield; analytic pure sample was obtained by Kugelrohr distillation)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.00 (d, *J*=16.14 Hz, 1 H), 7.96 (br. s., 1 H), 7.38 (d, *J*=8.25 Hz, 1 H), 6.92 (d, *J*=2.02 Hz, 1 H), 6.89 (dd, *J*=8.25, 2.02 Hz, 1 H), 6.66 (d, *J*=16.32 Hz, 1 H), 4.26 (t, *J*=6.69 Hz, 2 H), 1.67 - 1.76 (m, 2 H), 1.40 - 1.50 (m, 2 H), 0.98 (t, *J*=7.43 Hz, 3 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 169.1, 156.3, 140.0, 136.7, 130.0, 120.9, 120.5, 118.3, 116.7, 65.0, 30.7, 19.2, 13.7.
HRMS (EI) calcd. for $C_{13}H_{15}O_3Cl$ $[M]^+$: 254.07098. Found: 254.07005.



4e: (97%)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.99 (d, *J*=16.14 Hz, 1 H), 7.21 (s, 1 H), 6.68 (br. s., 1 H), 6.66 (s, 1 H), 6.61 (d, *J*=16.14 Hz, 1 H), 4.23 (t, *J*=6.69 Hz, 2 H), 2.20 (s, 3 H), 2.17 (s, 3 H), 1.64 - 1.77 (m, 2 H), 1.40 - 1.51 (m, 2 H), 0.97 (t, *J*=7.43 Hz, 3 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 168.8, 153.6, 140.8, 129.9, 128.6, 119.1, 117.7, 117.1, 64.5, 30.8, 19.8, 19.2, 18.7, 13.7.
HRMS (EI) calcd. for $C_{15}H_{20}O_3$ $[M]^+$: 248.14125. Found: 248.14197.

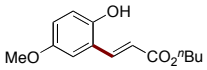


4f: (88% NMR yield, analytic pure sample was obtained by preparative HPLC)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.03 (d, *J*=16.14 Hz, 1 H), 7.32 (s, 1 H), 6.72 (s, 1 H), 6.55 (d, *J*=16.14 Hz, 1 H), 6.14 (s, 1 H), 4.22 (t, *J*=6.69 Hz, 2 H), 2.78 - 2.92 (m, 4 H), 2.00 - 2.13 (m, 2 H), 1.67 - 1.71 (m, 2 H), 1.33 - 1.54 (m, 2 H), 0.97 (t, *J*=7.34 Hz, 3 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 168.5, 154.1, 148.8, 140.7, 136.6, 124.0, 119.7, 117.0, 112.3, 64.4, 33.2, 31.8, 30.8, 25.7, 19.2, 13.8.
HRMS (EI) calcd. for $C_{16}H_{20}O_3$ $[M]^+$: 260.14125. Found: 260.14061.

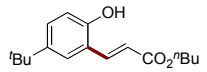


4g: (97%)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.96 (d, *J*=15.96 Hz, 1 H), 7.16 (s, 1 H),

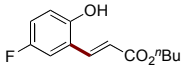
6.59 (d, *J*=16.14 Hz, 1 H), 6.55 (s, 1 H), 6.22 (s, 1 H), 4.22 (t, *J*=6.69 Hz, 2 H), 2.63 - 2.75 (m, 4 H), 1.74 - 1.83 (m, 4 H), 1.64 - 1.73 (m, 2 H), 1.37 - 1.51 (m, 2 H), 0.97 (t, *J*=7.43 Hz, 3 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 168.5, 153.0, 141.3, 140.6, 129.6, 129.5, 119.5, 117.5, 116.3, 64.4, 30.8, 29.5, 28.4, 23.3, 22.9, 19.2, 13.7.
HRMS (EI) calcd. for $C_{17}H_{22}O_3$ $[M]^+$: 274.15690. Found: 274.15736.



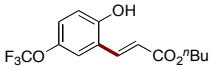
4h: (81%)
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.99 (d, *J*=16.08 Hz, 1 H), 6.98 (d, *J*=2.78 Hz, 1 H), 6.81 - 6.86 (m, 1 H), 6.74 - 6.79 (m, 1 H), 6.56 (d, *J*=16.08 Hz, 1 H), 5.84 (br. s., 1 H), 4.23 (t, *J*=6.72 Hz, 2 H), 3.78 (s, 3 H), 1.64 - 1.75 (m, 2 H), 1.38 - 1.50 (m, 2 H), 0.96 (t, *J*=7.38 Hz, 3 H)
^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 168.0, 153.6, 149.2, 140.0, 122.1, 118.8, 117.9, 117.4, 112.5, 64.6, 55.8, 30.8, 19.2, 13.8.
HRMS (EI) calcd. for $C_{14}H_{18}O_4$ $[M]^+$: 250.12051. Found: 250.12182.



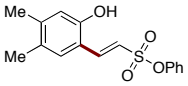
4i: (89%)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.97 (d, *J*=16.14 Hz, 1 H), 7.46 (d, *J*=2.38 Hz, 1 H), 7.24 - 7.30 (m, 1 H), 6.77 (d, *J*=8.44 Hz, 1 H), 6.62 (d, *J*=16.14 Hz, 1 H), 5.74 (br. s., 1 H), 4.23 (t, *J*=6.69 Hz, 2 H), 1.66 - 1.75 (m, 2 H), 1.40 - 1.51 (m, 2 H), 1.30 (s, 9 H), 0.97 (t, *J*=7.34 Hz, 3 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 168.0, 152.7, 143.7, 140.5, 128.5, 126.0, 121.0, 118.7, 116.0, 64.4, 34.1, 31.4, 30.8, 19.2, 13.7.
HRMS (EI) calcd. for $C_{17}H_{24}O_3$ $[M]^+$: 276.17255. Found: 276.17304.



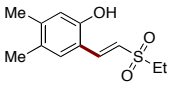
4j: (58% NMR yield, analytic pure sample was obtained by preparative HPLC)
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.98 (dd, *J*=16.23, 0.83 Hz, 1 H), 7.17 (dd, *J*=9.17, 2.93 Hz, 1 H), 6.95 (ddd, *J*=8.80, 7.79, 3.03 Hz, 1 H), 6.80 (dd, *J*=8.89, 4.49 Hz, 1 H), 6.57 (d, *J*=16.14 Hz, 1 H), 6.43 (s, 1 H), 4.24 (t, *J*=6.69 Hz, 2 H), 1.67 - 1.76 (m, 2 H), 1.39 - 1.50 (m, 2 H), 0.97 (t, *J*=7.34 Hz, 3 H).
^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 168.0, 156.9 (d, *J*=238.8 Hz), 151.3, 139.2, 122.7 (d, *J*=7.4 Hz), 119.5, 118.0 (d, *J*=23.6 Hz), 117.3 (d, *J*=8.1 Hz), 114.4 (d, *J*=23.6 Hz), 64.8, 30.7, 19.2, 13.8.
HRMS (EI) calcd. for $C_{13}H_{15}O_3F$ $[M]^+$: 238.10053. Found: 238.10119.



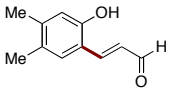
4k: (52% NMR yield, analytic pure sample was obtained by preparative HPLC)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.96 (d, *J*=16.14 Hz, 1 H), 7.33 (d, *J*=2.75 Hz, 1 H), 7.11 (dd, *J*=8.71, 2.11 Hz, 1 H), 6.85 (d, *J*=8.80 Hz, 1 H), 6.62 (d, *J*=16.14 Hz, 1 H), 6.57 (s, 1 H), 4.25 (t, *J*=6.69 Hz, 2 H), 1.66 - 1.75 (m, 2 H), 1.40 - 1.50 (m, 2 H), 0.97 (t, *J*=7.43 Hz, 3 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 168.6, 154.1, 142.4, 139.5, 124.2, 122.6, 121.4, 119.6, 121.0 (q, *J*=256.2 Hz), 117.3, 65.0, 30.7, 19.2, 13.7.
HRMS (EI) calcd. for $C_{14}H_{15}O_4F_3$ $[M]^+$: 304.09225. Found: 304.09207.



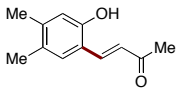
4l: (96%)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.56 (d, *J*=15.59 Hz, 1 H), 7.33 - 7.38 (m, 2 H), 7.24 - 7.30 (m, 3 H), 7.16 (d, *J*=15.59 Hz, 1 H), 7.06 (s, 1 H), 6.61 (s, 1 H), 5.56 (br. s., 1 H), 2.22 (s, 3 H), 2.17 (s, 3 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 153.7, 149.7, 142.5, 142.4, 132.3, 129.7, 129.4, 127.0, 122.5, 120.3, 117.7, 116.5, 19.9, 18.6.
HRMS (EI) calcd. for $C_{16}H_{16}O_4S$ $[M]^+$: 304.07693. Found: 304.07703.



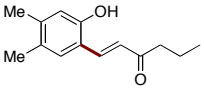
4m: (87% NMR yield, analytic pure sample was obtained by preparative HPLC)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.65 (d, *J*=15.41 Hz, 1 H), 7.23 (s, 1 H), 7.17 (d, *J*=15.41 Hz, 1 H), 7.09 (s, 1 H), 6.70 (s, 1 H), 3.09 (q, *J*=7.52 Hz, 2 H), 2.20 (s, 3 H), 2.16 (s, 3 H), 1.38 (t, *J*=7.43 Hz, 3 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 154.4, 142.2, 142.1, 132.2, 128.8, 122.8, 117.8, 116.7, 49.7, 19.9, 18.6, 7.3.
HRMS (EI) calcd. for $C_{12}H_{16}O_3S$ $[M]^+$: 240.08202. Found: 240.08318.



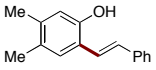
4n: (70%, 20% Boc-Val-OH as the ligand, 4 equiv acrolein, 110 ºC)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 9.62 (d, *J*=8.07 Hz, 1 H), 7.72 (d, *J*=15.96 Hz, 1 H), 7.22 (s, 1 H), 7.04 (dd, *J*=15.86, 8.16 Hz, 1 H), 6.91 (s, 1 H), 6.71 (s, 1 H), 2.24 (s, 3 H), 2.20 (s, 3 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 195.9, 154.0, 150.3, 142.6, 130.9, 129.0, 128.1, 118.7, 117.8, 20.0, 18.7.
HRMS (EI) calcd. for $C_{11}H_{12}O_2$ $[M]^+$: 176.08373. Found: 176.08424.



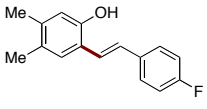
4o: (67%, 20% Boc-Val-OH as the ligand, 4 equiv 3-buten-2-one, 110 ºC)
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.79 (d, *J*=16.37 Hz, 1 H), 7.28 (s, 1 H), 7.21 (s, 1 H), 7.04 (d, *J*=16.37 Hz, 1 H), 6.73 (s, 1 H), 2.42 (s, 3 H), 2.22 (s, 3 H), 2.18 (s, 3 H).
^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 201.3, 154.2, 141.6, 141.3, 130.6, 128.7, 126.8, 118.8, 117.8, 26.6, 20.0, 18.8.
HRMS (EI) calcd. for $C_{12}H_{14}O_2$ $[M]^+$: 190.09938. Found: 190.10015.



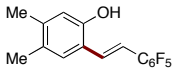
4p: (69%, 20% Boc-Val-OH as the ligand, 4 equiv 1-hexen-3-one, 110 ºC)
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.85 (d, *J*=16.37 Hz, 1 H), 7.23 (s, 1 H), 6.95 (d, *J*=16.37 Hz, 1 H), 6.78 (s, 1 H), 6.70 (s, 1 H), 2.68 (t, *J*=7.45 Hz, 2 H), 2.22 (s, 3 H), 2.18 (s, 3 H), 1.66-1.78 (m, 2 H), 0.99 (t, *J*=7.45 Hz, 3 H).
^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 202.9, 153.9, 141.3, 139.3, 130.1, 128.8, 125.8, 119.0, 117.8, 42.0, 20.0, 18.8, 18.2, 14.0.
HRMS (EI) calcd. for $C_{14}H_{18}O_2$ $[M]^+$: 218.13068. Found: 218.13202.



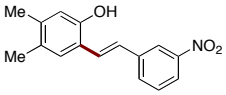
4q: (64% NMR yield, analytic pure sample was obtained by Kugelrohr distillation)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.52 (d, *J*=7.34 Hz, 2 H), 7.28 - 7.38 (m, 4 H), 7.22 - 7.27 (m, 1 H), 7.08 (d, *J*=16.51 Hz, 1 H), 6.62 (s, 1 H), 4.76 (s, 1 H), 2.22 (s, 6 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 151.0, 137.9, 137.4, 129.0, 128.6, 128.1, 127.3, 126.4, 123.1, 121.8, 117.3, 19.6, 18.9.
HRMS (EI) calcd. for $C_{16}H_{16}O$ $[M]^+$: 224.12012. Found: 224.11907.



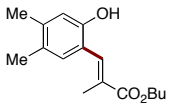
4r: (79%)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.48 (dd, *J*=8.53, 5.59 Hz, 2 H), 7.27 (s, 1 H), 7.23 (d, *J*=16.32 Hz, 1 H), 7.00 - 7.08 (m, 3 H), 6.61 (s, 1 H), 4.76 (s, 1 H), 2.22 (s, 6 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 162.2 (d, *J*=246.9 Hz), 150.9, 137.5, 134.1, 129.0, 128.0, 127.8 (d, *J*=8.3 Hz), 127.7, 122.9, 121.7, 117.3, 115.5 (d, *J*=21.3 Hz), 19.6, 18.8.
HRMS (EI) calcd. for $C_{16}H_{15}OF$ $[M]^+$: 242.11070. Found: 242.11164.



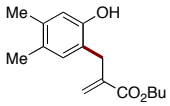
4s: (83%)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.63 (d, *J*=16.87 Hz, 1 H), 7.27 (s, 1 H), 6.98 (d, *J*=16.87 Hz, 1 H), 6.59 (s, 1 H), 4.85 (s, 1 H), 2.23 (s, 6 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 151.5, 143.2 - 146.6 (m), 139.0, 138.6 - 140.7 (m), 136.5 - 138.6 (m), 132.0 (t, *J*=7.9 Hz), 129.3, 128.3, 121.1, 117.4, 112.9 - 113.3 (m), 112.4, 19.7, 18.8.
HRMS (EI) calcd. for $C_{16}H_{11}OF_5$ $[M]^+$: 314.07302. Found: 314.07253.



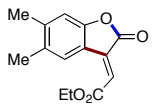
4t: (66%)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.34 (t, *J*=2.02 Hz, 1 H), 8.05 (ddd, *J*=8.16, 2.29, 0.92 Hz, 1 H), 7.78 (d, *J*=7.70 Hz, 1 H), 7.48 (t, *J*=7.89 Hz, 1 H), 7.46 (d, *J*=16.51 Hz, 1 H), 7.29 (s, 1 H), 7.13 (d, *J*=16.32 Hz, 1 H), 6.61 (s, 1 H), 4.94 (s, 1 H), 2.22 (s, 6 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 151.3, 148.7, 139.9, 138.5, 132.1, 129.4, 129.2, 128.3, 126.4, 125.9, 121.6, 120.9, 120.8, 117.4, 19.7, 18.8.
HRMS (EI) calcd. for $C_{16}H_{15}O_3N$ $[M]^+$: 269.10520. Found: 269.10508.



4u: (45% NMR yield, analytic pure sample was obtained by three columns of chromatography)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.69 (s, 1 H), 6.97 (s, 1 H), 6.69 (s, 1 H), 4.95 (s, 1 H), 4.22 (t, *J*=6.69 Hz, 2 H), 2.23 (s, 3 H), 2.19 (s, 3 H), 2.02 (d, *J*=1.28 Hz, 3 H), 1.67 - 1.77 (m, 2 H), 1.40 - 1.49 (m, 2 H), 0.97 (t, *J*=7.34 Hz, 3 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 168.5, 151.3, 138.7, 133.7, 130.5, 130.0, 128.4, 119.9, 117.0, 64.8, 30.8, 19.8, 19.3, 18.8, 14.3, 13.8.
HRMS (EI) calcd. for $C_{16}H_{22}O_3$ $[M]^+$: 262.15690. Found: 262.15727.

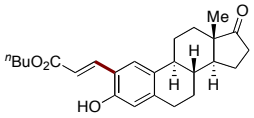


4v: (39% nmr yield, analytic sample still has impurities)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.42 (s, 1 H), 6.86 (s, 1 H), 6.73 (s, 1 H), 6.20 (d, *J*=1.10 Hz, 1 H), 5.83 (d, *J*=1.10 Hz, 1 H), 4.16 (t, *J*=6.69 Hz, 2 H), 3.51 (s, 2 H), 2.18 (s, 3 H), 2.16 (s, 3 H), 1.61 - 1.68 (m, 2 H), 1.34 - 1.42 (m, 2 H), 0.93 (t, *J*=7.43 Hz, 3 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 169.1, 152.0, 139.8, 136.7, 131.4, 128.7, 126.7, 122.6, 118.8, 65.6, 32.7, 30.5, 19.4, 19.1, 18.7, 13.7.
HRMS (EI) calcd. for $C_{16}H_{22}O_3$ $[M]^+$: 262.15690. Found: 262.15753.



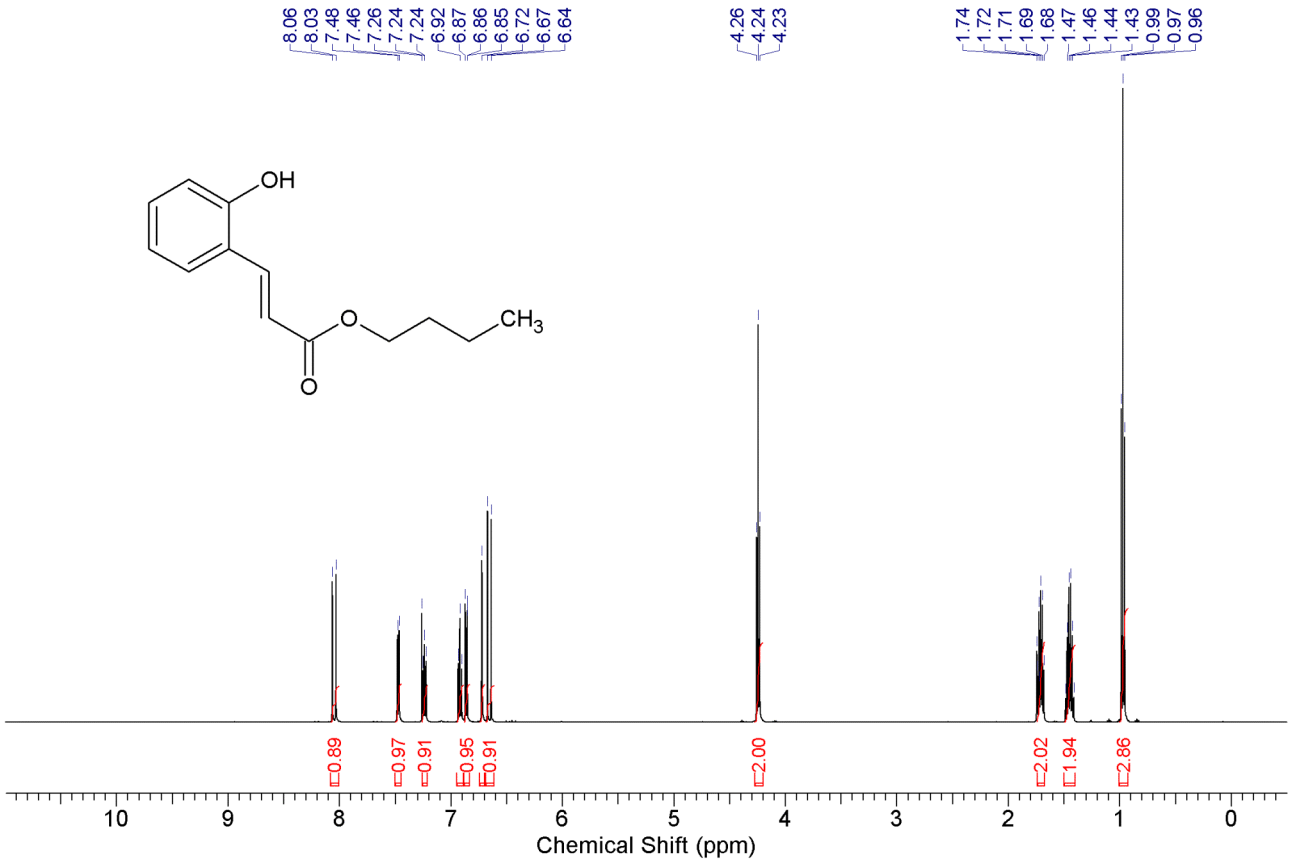
6: (58%)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.96 (s, 1 H), 7.12 (s, 1 H), 6.82 (s, 1 H), 4.45 (q, *J*=7.15 Hz, 2 H), 2.34 (s, 3 H), 2.31 (s, 3 H), 1.43 (t, *J*=7.15 Hz, 3

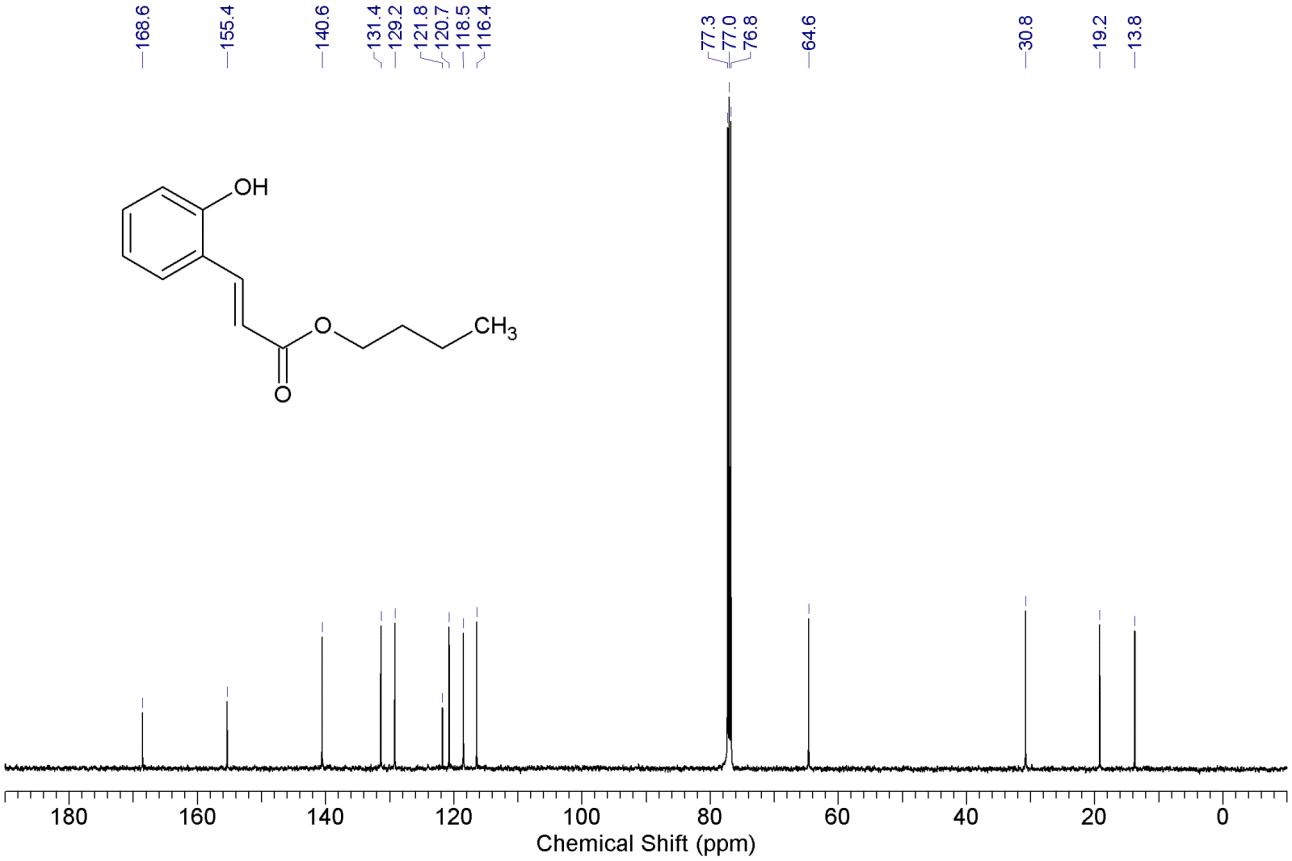
H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 164.0, 160.6, 152.7, 142.7, 142.6, 133.5, 126.7, 117.8, 117.6, 113.6, 62.4, 20.2, 19.5, 14.1.
HRMS (EI) calcd. for $C_{14}H_{14}O_4$ $[M]^+$: 246.08921. Found: 246.09001.



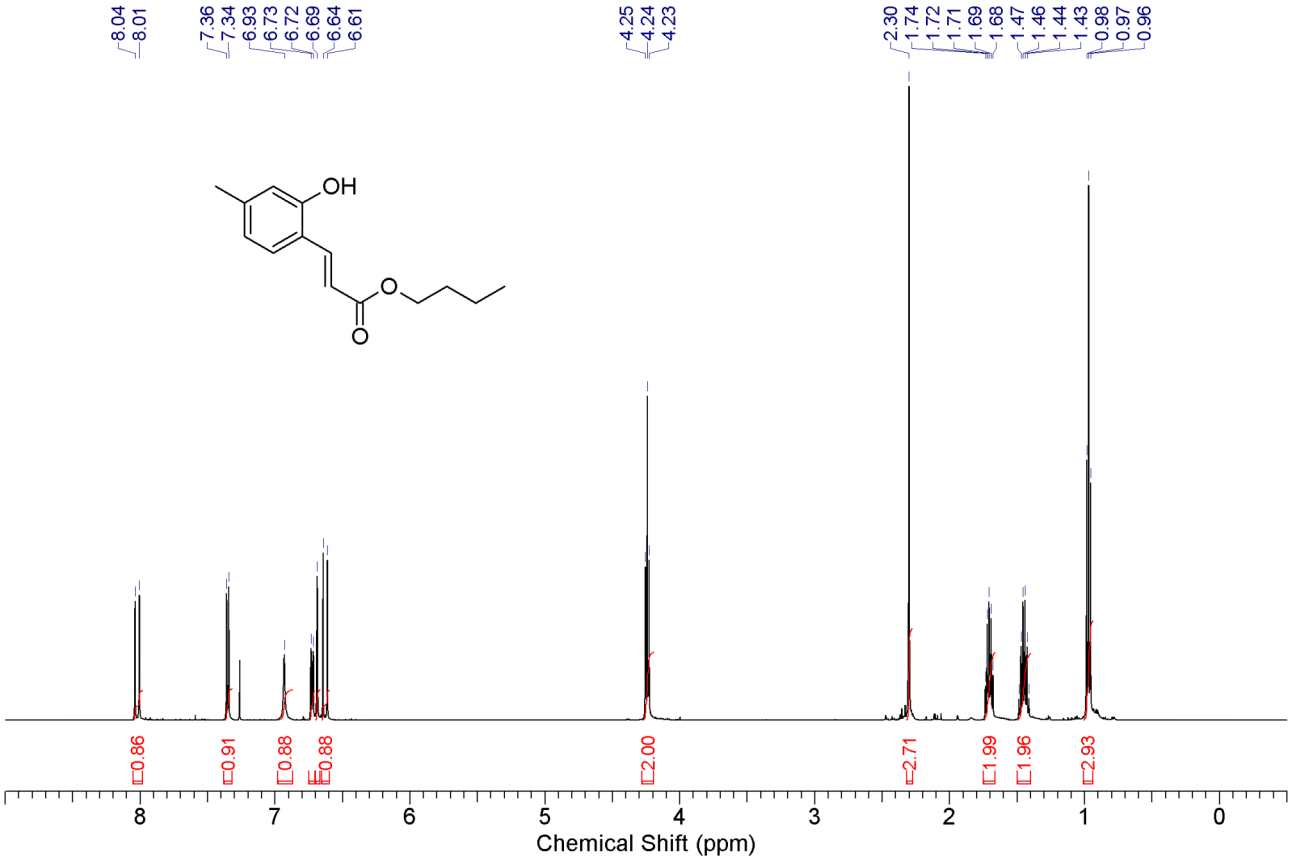
8: (89%)
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.97 (d, *J*=16.14 Hz, 1 H), 7.36 (s, 1 H), 6.95 (br. s., 1 H), 6.61 (s, 1 H), 6.62 (d, *J*=15.96 Hz, 1 H), 4.22 (t, *J*=6.69 Hz, 2 H), 2.85 (dd, *J*=8.71, 3.94 Hz, 2 H), 2.52 (dd, *J*=19.26, 8.44 Hz, 1 H), 2.39 - 2.46 (m, 1 H), 2.19 - 2.27 (m, 1 H), 2.11 - 2.18 (m, 1 H), 1.94 - 2.09 (m, 3 H), 1.66 - 1.74 (m, 2 H), 1.59 - 1.65 (m, 1 H), 1.48 - 1.58 (m, 4 H), 1.38 - 1.47 (m, 3 H), 0.96 (t, *J*=7.34 Hz, 3 H), 0.92 (s, 3 H).
^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 221.3, 168.6, 153.6, 141.0, 140.8, 132.1, 126.2, 119.4, 117.4, 116.3, 64.5, 50.4, 48.0, 43.7, 38.2, 35.9, 31.5, 30.8, 29.4, 26.4, 25.9, 21.6, 19.2, 13.9, 13.8.
HRMS (EI) calcd. for $C_{25}H_{32}O_4$ $[M]^+$: 396.23006. Found: 396.23176.

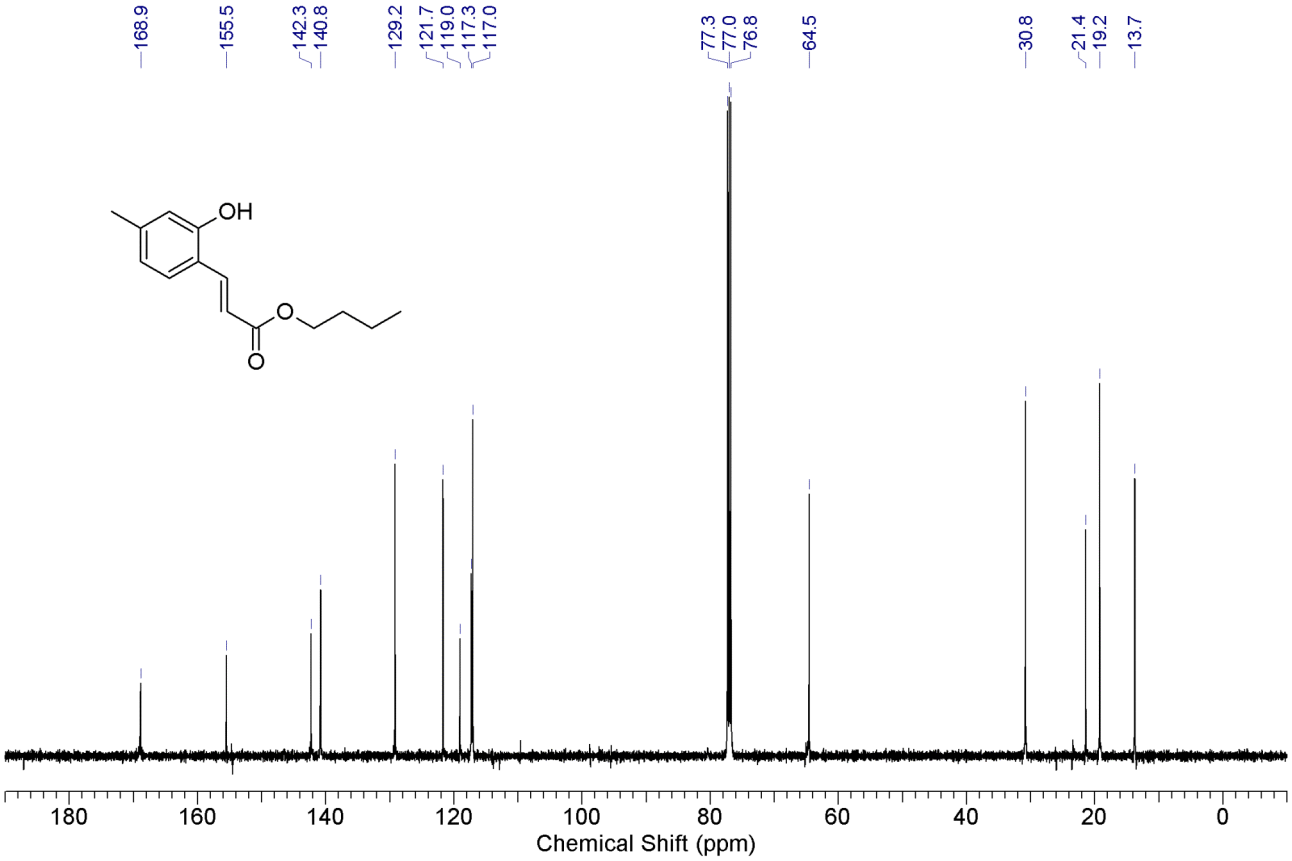
4a


8.06
8.03
7.48
7.46
7.26
7.24
7.24
6.92
6.87
6.86
6.85
6.72
6.67
6.64
4.26
4.24
4.23
1.74
1.72
1.71
1.69
1.68
1.47
1.46
1.44
1.43
0.99
0.97
0.96
OH
O
O
CH3
0.89
0.97
0.91
0.95
0.91
2.00
2.02
1.94
2.86
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

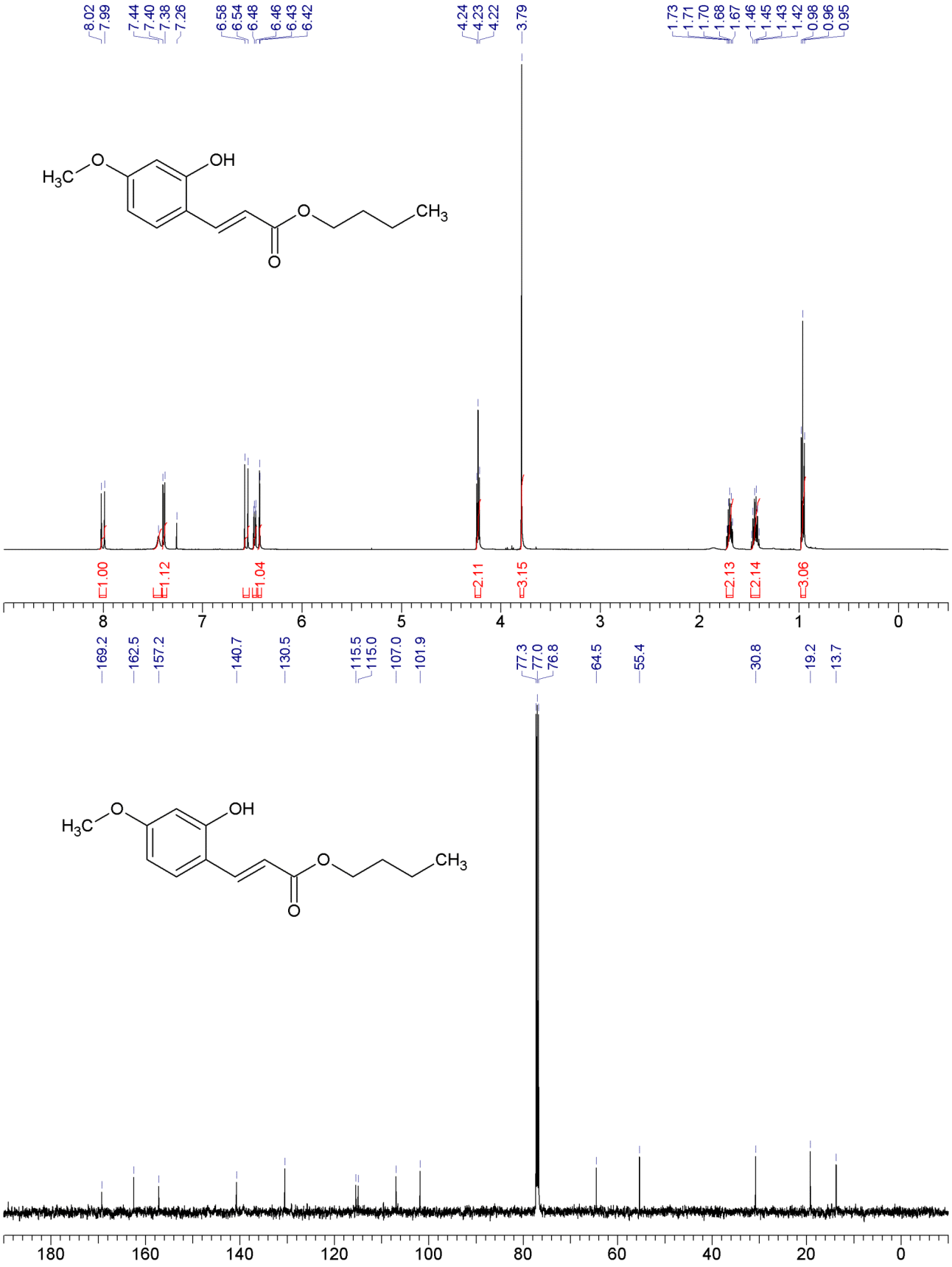

168.6
155.4
140.6
131.4
129.2
121.8
120.7
118.5
116.4
77.3
77.0
76.8
64.6
30.8
19.2
13.8
OH
O
O
CH3
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

4b

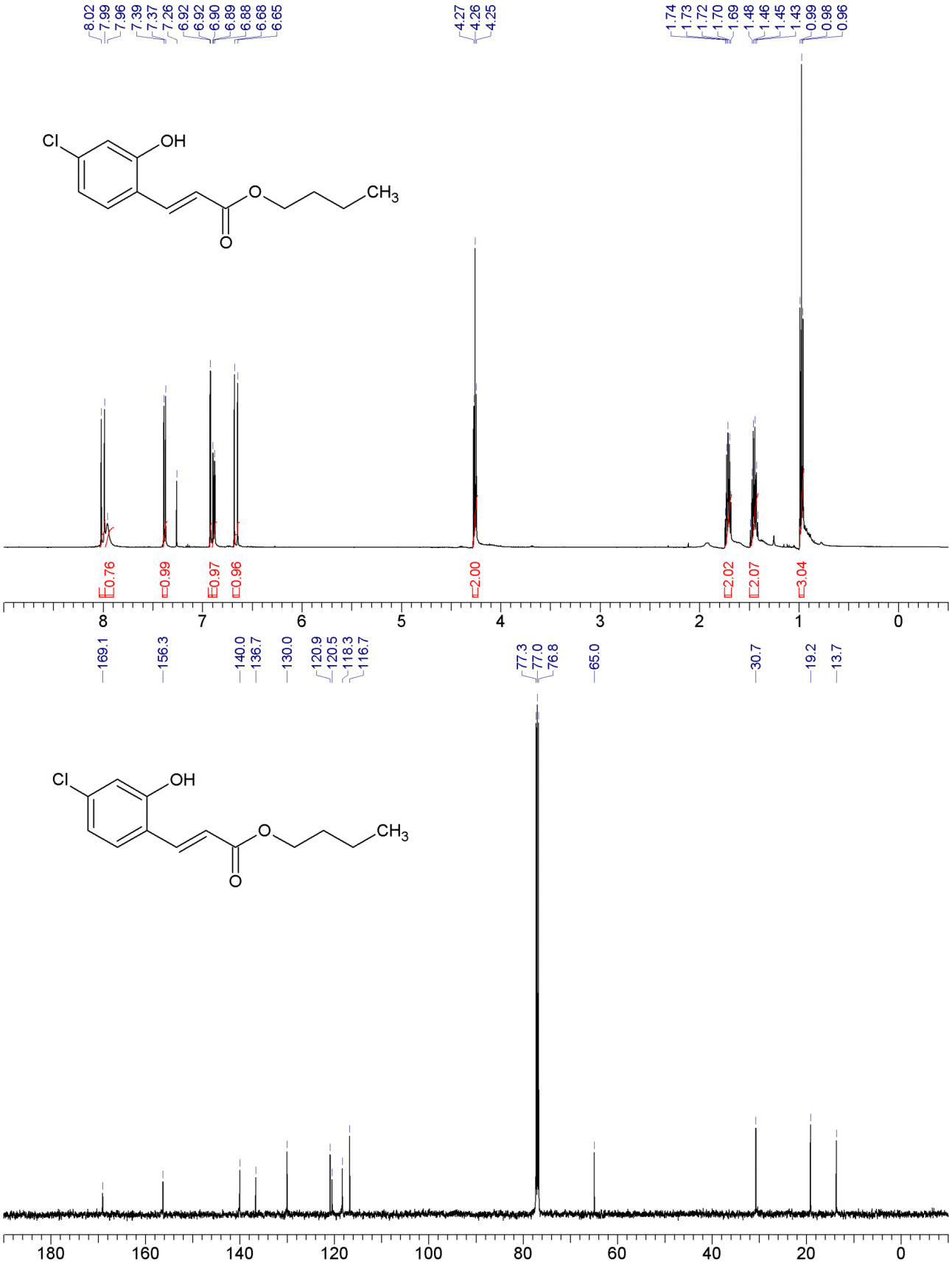

8.04
8.01
7.36
7.34
6.93
6.73
6.72
6.69
6.64
6.61
4.25
4.24
4.23
2.30
1.74
1.72
1.71
1.69
1.68
1.47
1.46
1.44
1.43
0.98
0.97
0.96
OH
O
O
0.86
0.91
0.88
0.88
2.00
2.71
1.99
1.96
2.93
Chemical Shift (ppm)


168.9
155.5
142.3
140.8
129.2
121.7
119.0
117.3
117.0
77.3
77.0
76.8
64.5
30.8
21.4
19.2
13.7
OH
O
O
Chemical Shift (ppm)

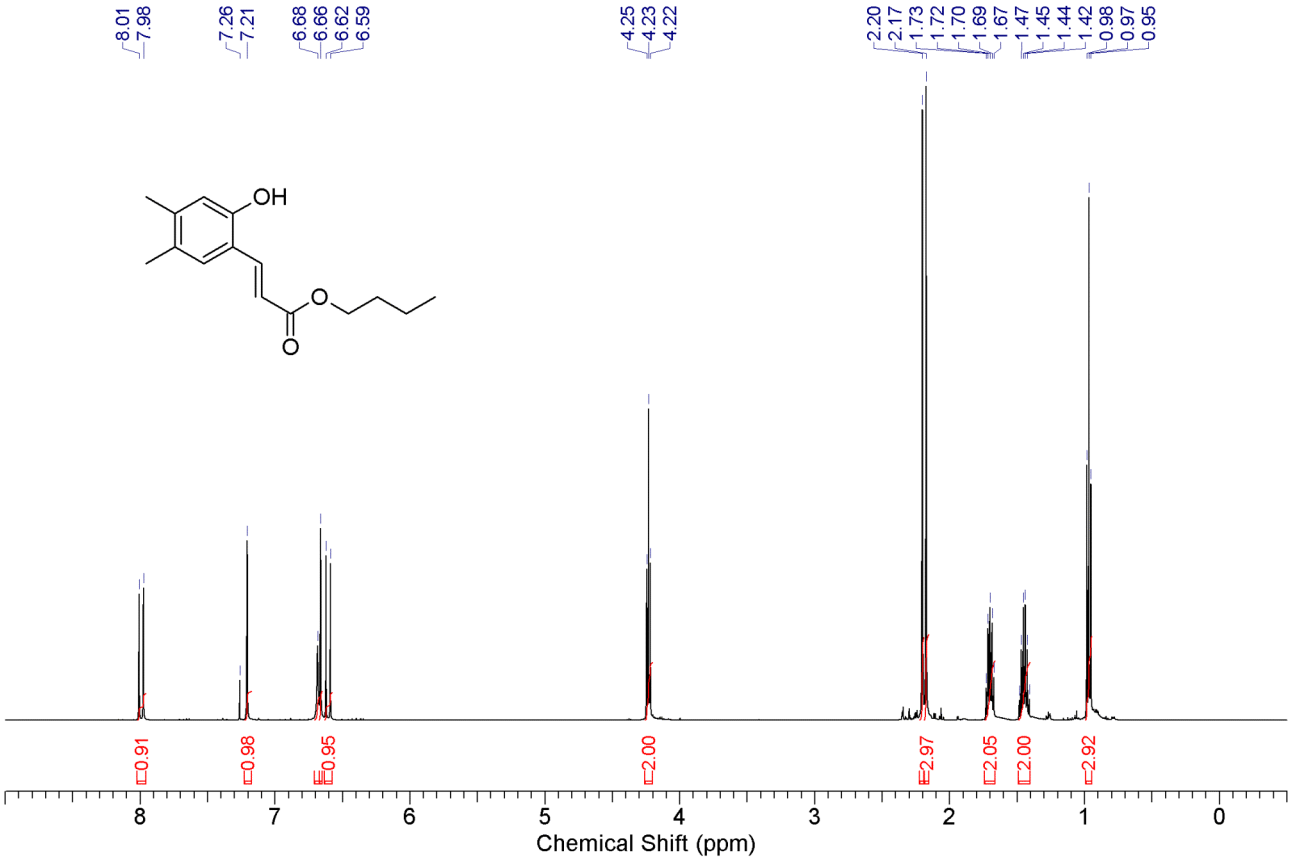
4c

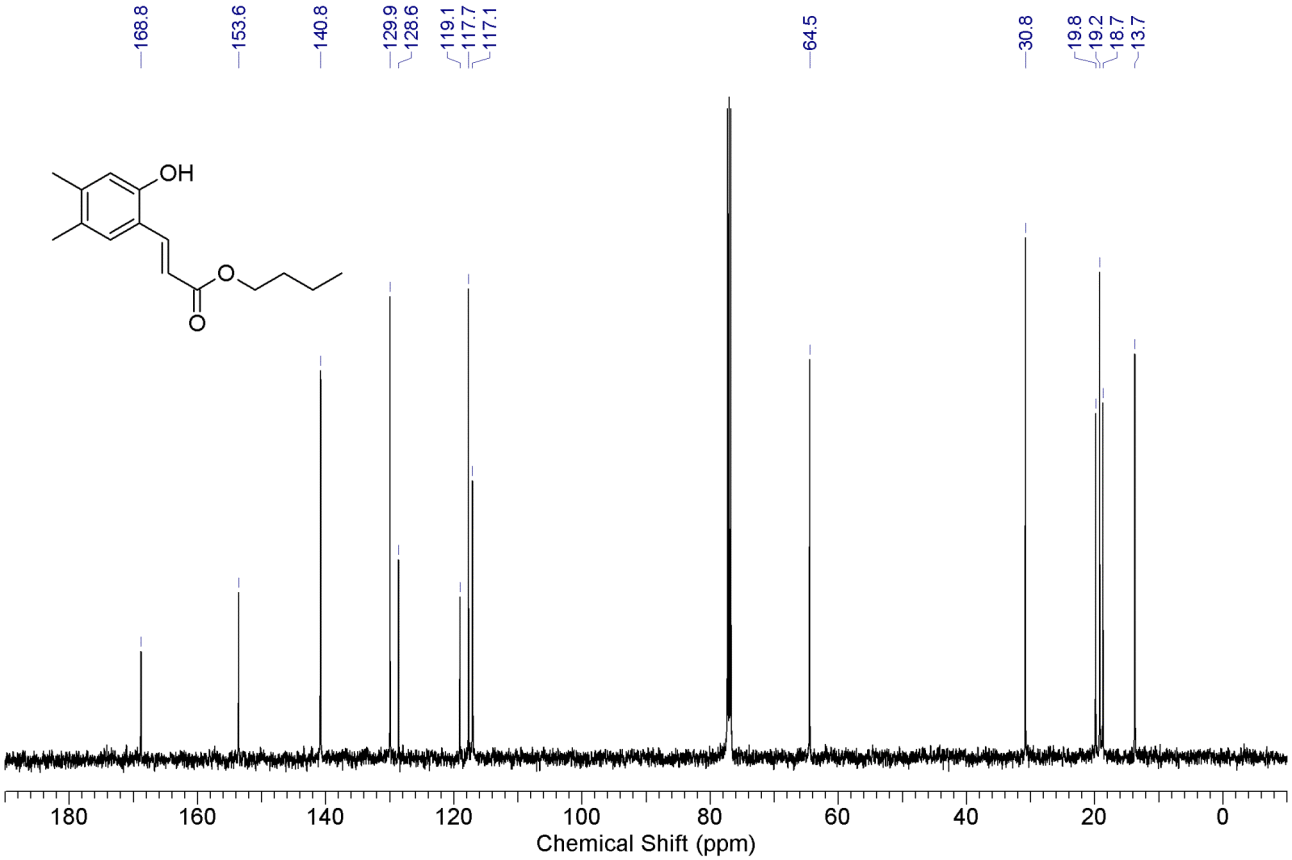

8.02
7.99
7.44
7.40
7.38
7.26
6.58
6.54
6.48
6.46
6.43
6.42
4.24
4.23
4.22
3.79
1.73
1.71
1.70
1.68
1.67
1.46
1.45
1.43
1.42
0.98
0.96
0.95
H3C
O
OH
O
O
CH3
1.00
1.12
1.04
2.11
3.15
2.13
2.14
3.06
169.2
162.5
157.2
140.7
130.5
115.5
115.0
107.0
101.9
77.3
77.0
76.8
64.5
55.4
30.8
19.2
13.7

4d

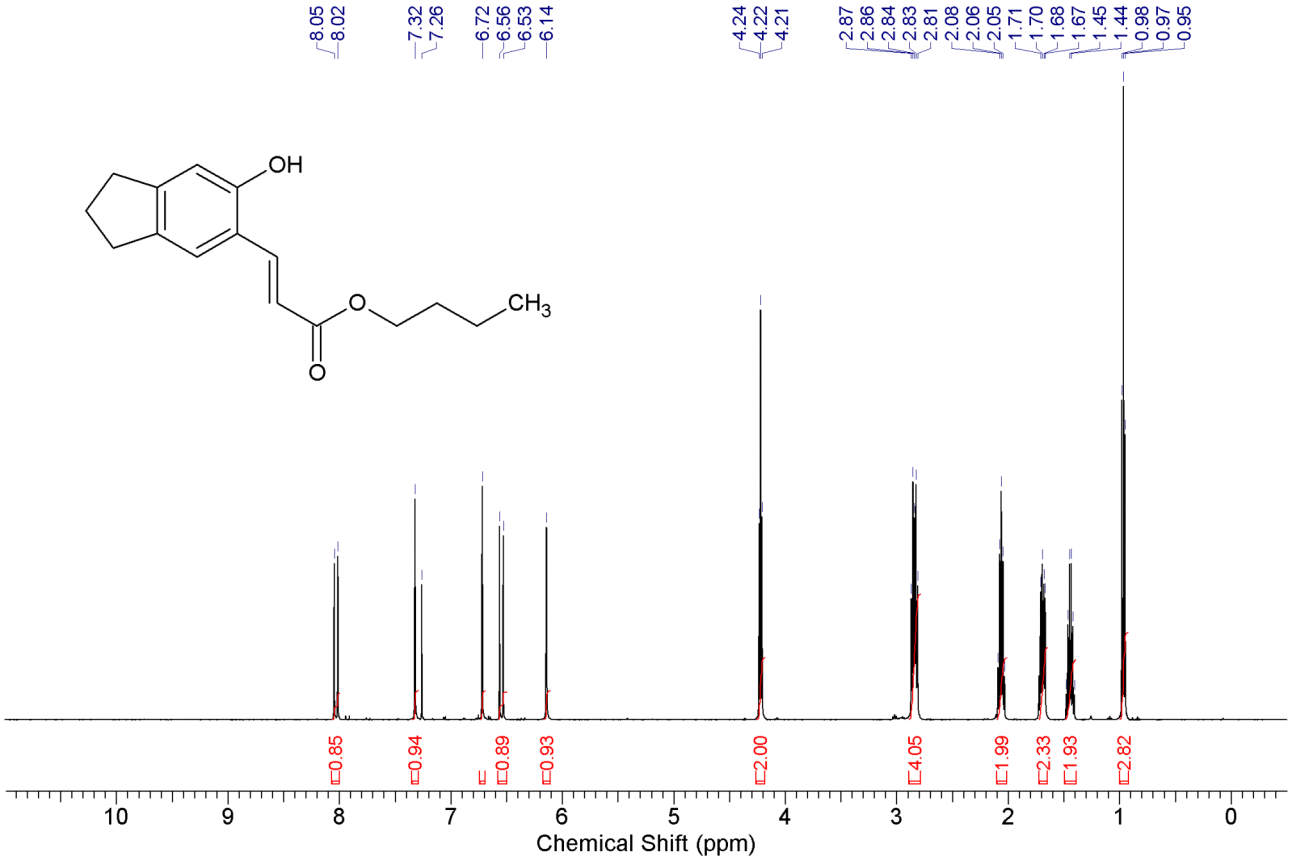

8.02
7.99
7.96
7.39
7.37
7.26
6.92
6.92
6.90
6.89
6.88
6.68
6.65
4.27
4.26
4.25
1.74
1.73
1.72
1.70
1.69
1.48
1.46
1.45
1.43
0.99
0.98
0.96
Cl
OH
O
O
CH3
0.76
0.99
0.97
0.96
2.00
2.02
2.07
3.04
8
7
6
5
4
3
2
1
0
169.1
156.3
140.0
136.7
130.0
120.9
120.5
118.3
116.7
77.3
77.0
76.8
65.0
30.7
19.2
13.7
Cl
OH
O
O
CH3
180
160
140
120
100
80
60
40
20
0

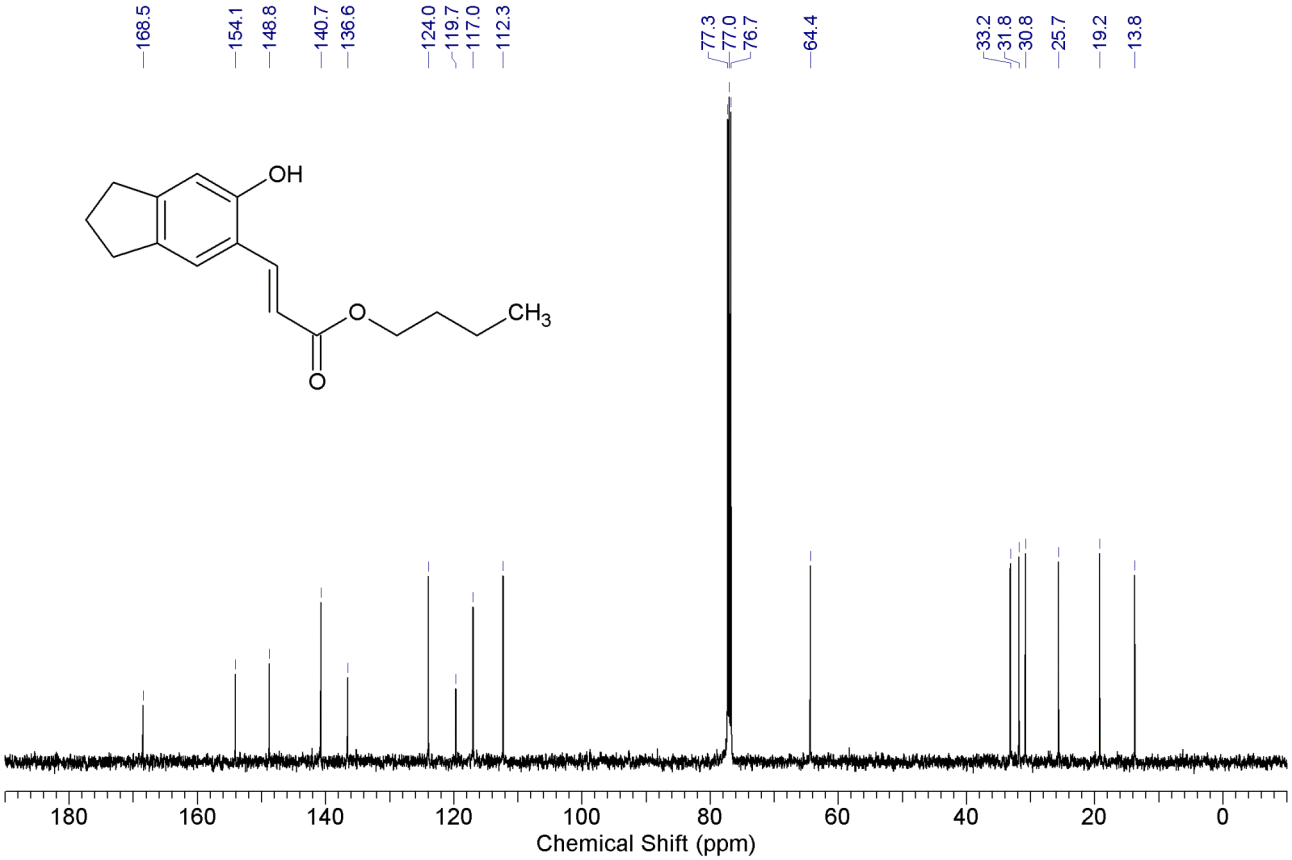
4e


8.01
7.98
7.26
7.21
6.68
6.66
6.62
6.59
4.25
4.23
4.22
2.20
2.17
1.73
1.72
1.70
1.69
1.67
1.47
1.45
1.44
1.42
0.98
0.97
0.95
OH
O
O
0.91
0.98
0.95
2.00
2.97
2.05
2.00
2.92
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

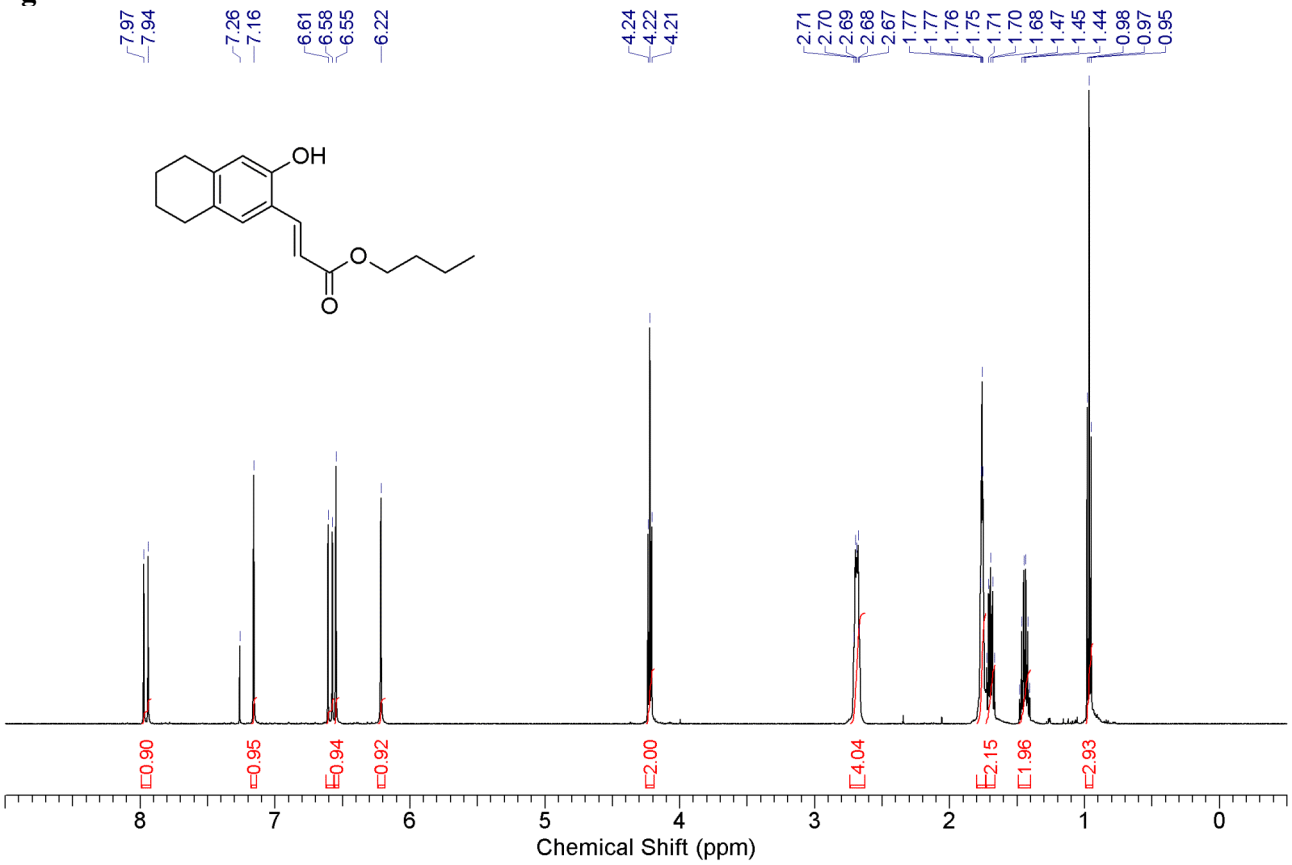

168.8
153.6
140.8
129.9
128.6
119.1
117.7
117.1
64.5
30.8
19.8
19.2
18.7
13.7
OH
O
O
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

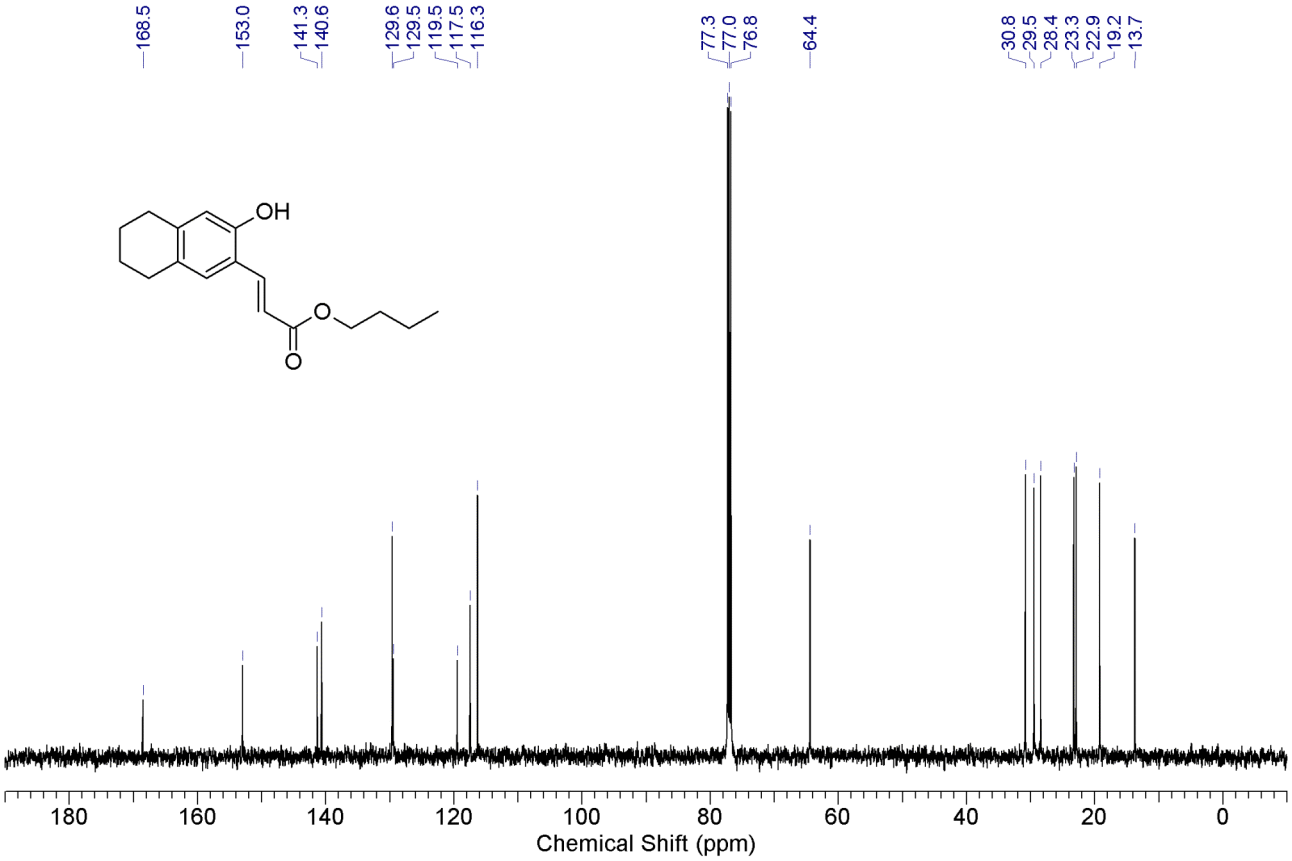
4f


8.05
8.02
7.32
7.26
6.72
6.56
6.53
6.14
4.24
4.22
4.21
2.87
2.86
2.84
2.83
2.81
2.08
2.06
2.05
1.71
1.70
1.68
1.67
1.45
1.44
0.98
0.97
0.95
OH
O
CH3
O
0.85
0.94
0.89
0.93
2.00
4.05
1.99
2.33
1.93
2.82
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

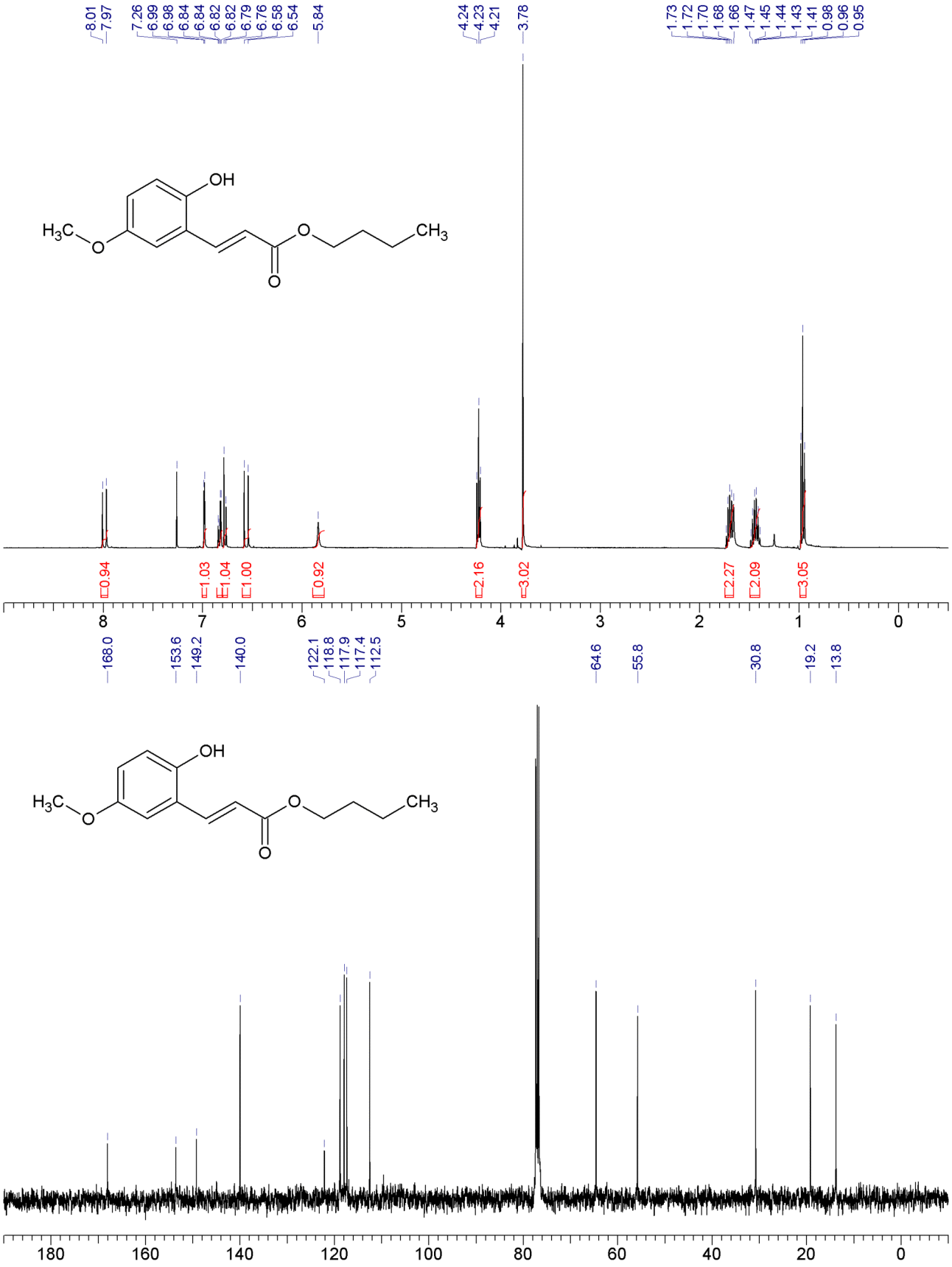

168.5
154.1
148.8
140.7
136.6
124.0
119.7
117.0
112.3
77.3
77.0
76.7
64.4
33.2
31.8
30.8
25.7
19.2
13.8
OH
O
CH3
O
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

4g


7.97
7.94
7.26
7.16
6.61
6.58
6.55
6.22
4.24
4.22
4.21
2.71
2.70
2.69
2.68
2.67
1.77
1.77
1.76
1.75
1.71
1.70
1.68
1.47
1.45
1.44
0.98
0.97
0.95
OH
O
O
0.90
0.95
0.94
0.92
2.00
4.04
2.15
1.96
2.93
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


168.5
153.0
141.3
140.6
129.6
129.5
119.5
117.5
116.3
77.3
77.0
76.8
64.4
30.8
29.5
28.4
23.3
22.9
19.2
13.7
OH
O
O
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

4h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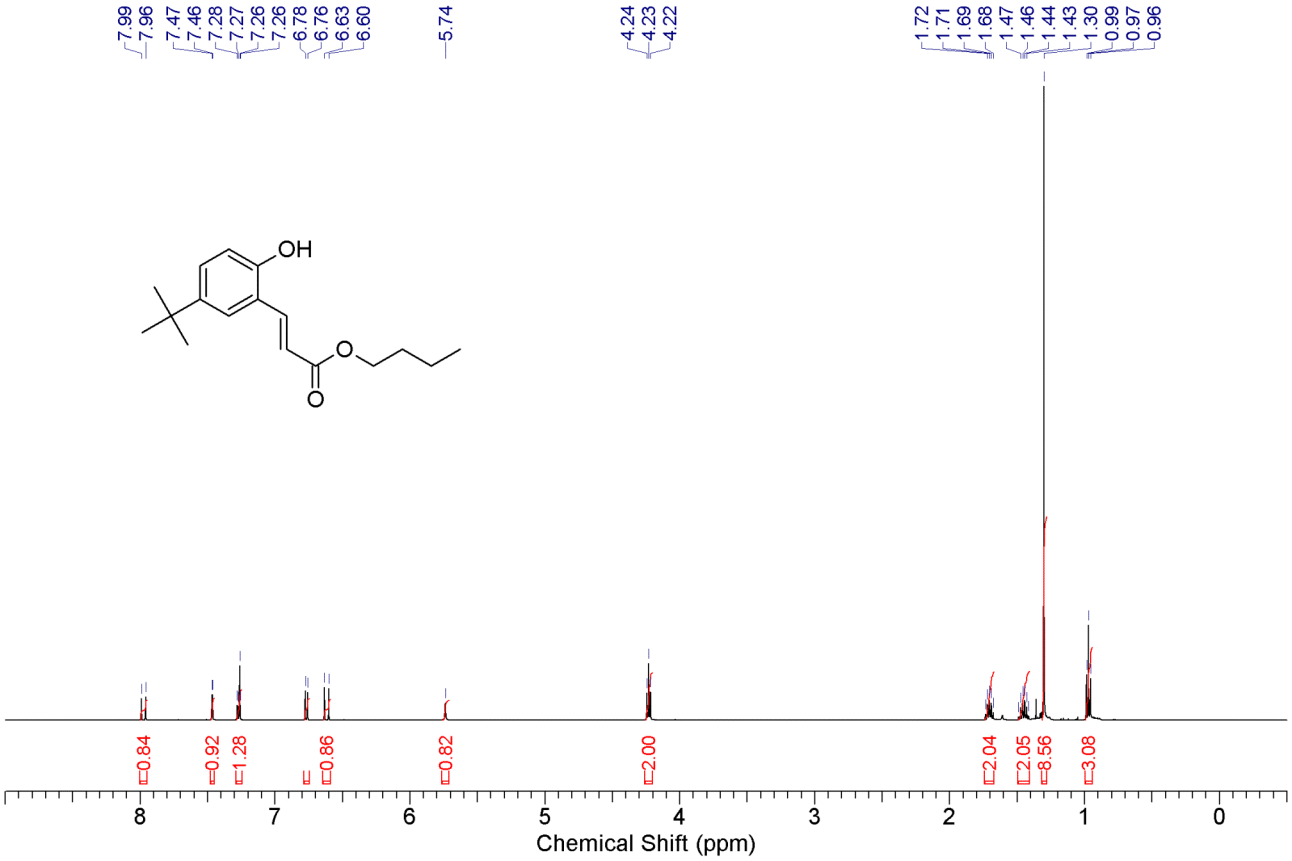
7.97
7.26
6.99
6.98
6.84
6.84
6.82
6.82
6.79
6.76
6.58
6.54
5.84
4.24
4.23
4.21
3.78
1.73
1.72
1.70
1.68
1.66
1.47
1.45
1.44
1.43
1.41
0.98
0.96
0.95
OH
H3C
O
O
O
CH3
0.94
1.03
1.04
1.00
0.92
2.16
3.02
2.27
2.09
3.05
8
7
6
5
4
3
2
1
0
168.0
153.6
149.2
140.0
122.1
118.8
117.9
117.4
112.5
64.6
55.8
30.8
19.2
13.8
OH
H3C
O
O
O
CH3
180
160
140
120
100
80
60
40
20
0

4i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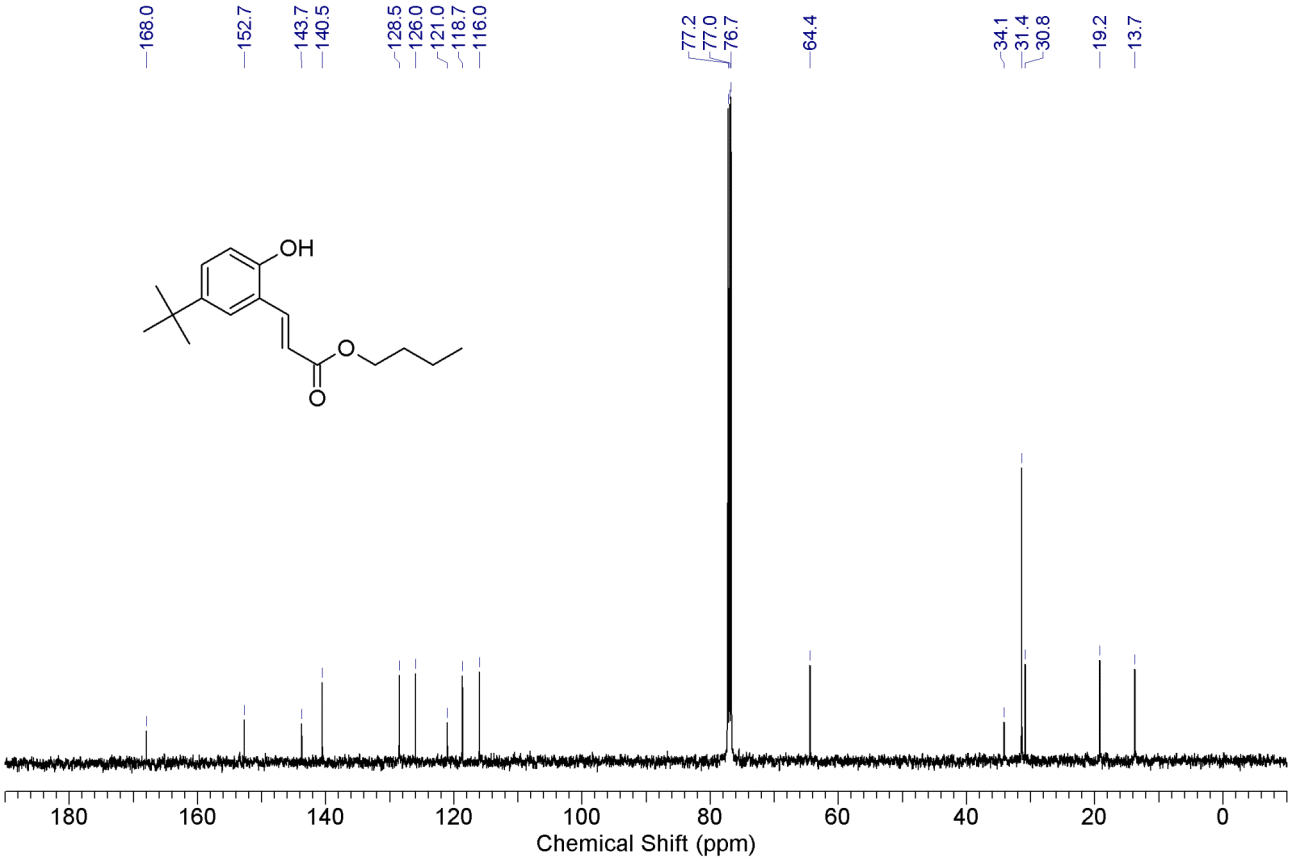
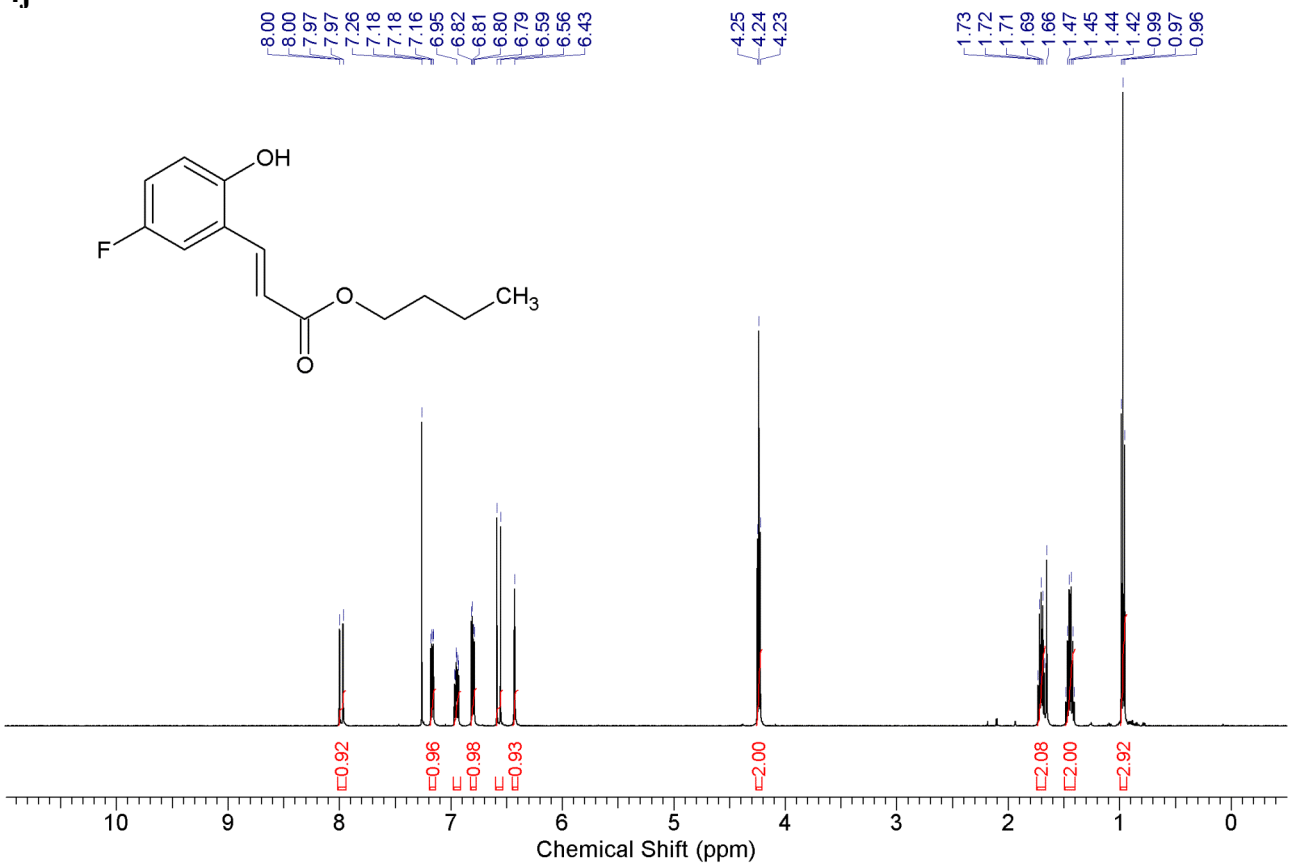
7.96
7.47
7.46
7.28
7.27
7.26
6.78
6.76
6.63
6.60
5.74
4.24
4.23
4.22
1.72
1.71
1.69
1.68
1.47
1.46
1.44
1.43
1.30
0.99
0.97
0.96
OH
O
O
0.84
0.92
1.28
0.86
0.82
2.00
2.04
2.05
8.56
3.08
Chemical Shift (ppm)


168.0
152.7
143.7
140.5
128.5
126.0
121.0
118.7
116.0
77.2
77.0
76.7
64.4
34.1
31.4
30.8
19.2
13.7
OH
O
O
Chemical Shift (ppm)

4j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8.00
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7.26
7.18
7.18
7.16
6.95
6.82
6.81
6.80
6.79
6.59
6.56
6.43
4.25
4.24
4.23
1.73
1.72
1.71
1.69
1.66
1.47
1.45
1.44
1.42
0.99
0.97
0.96
OH
F
O
O
CH3
I=0.92
I=0.96
I=0.98
I=0.93
I=2.00
I=2.08
I=2.00
I=2.92
10
9
8
7
6
5
4
3
2
1
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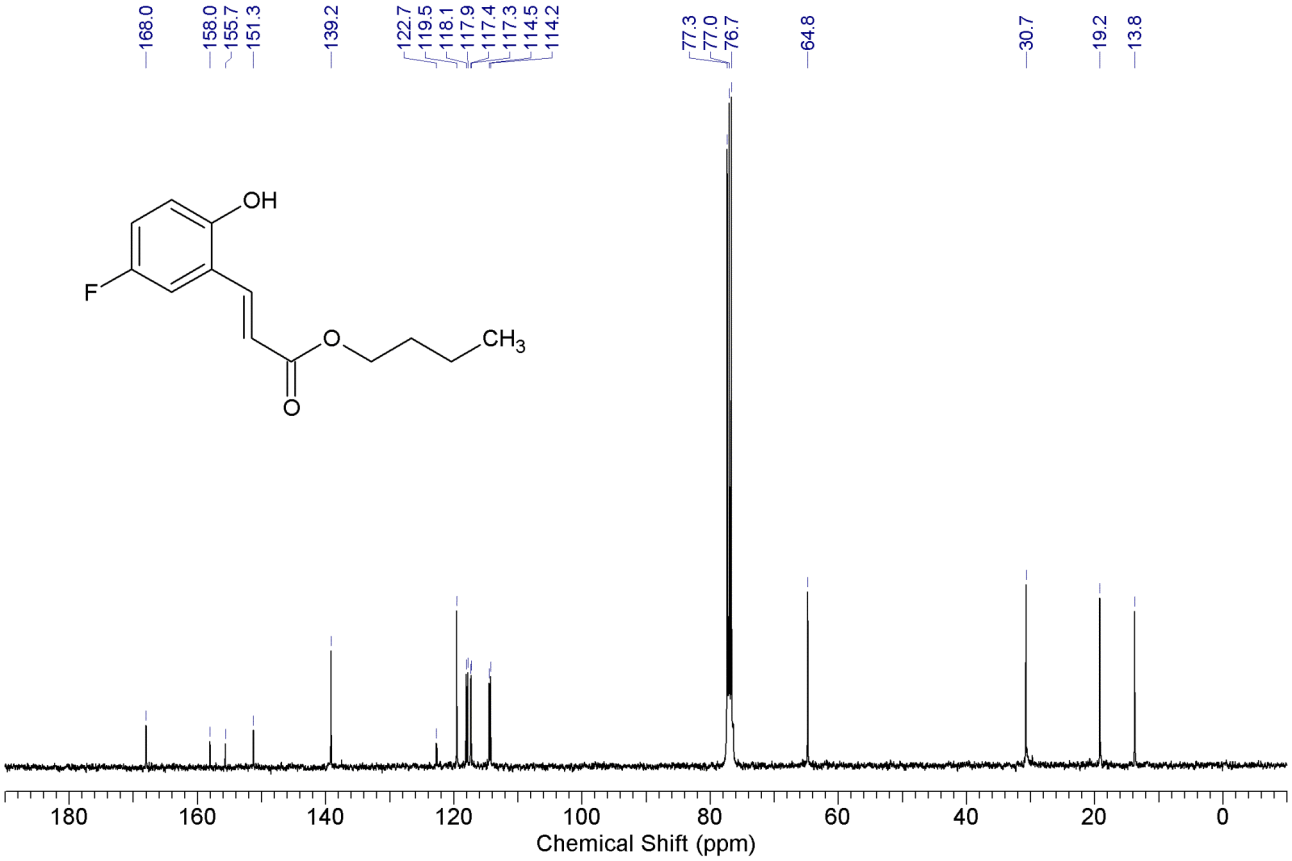
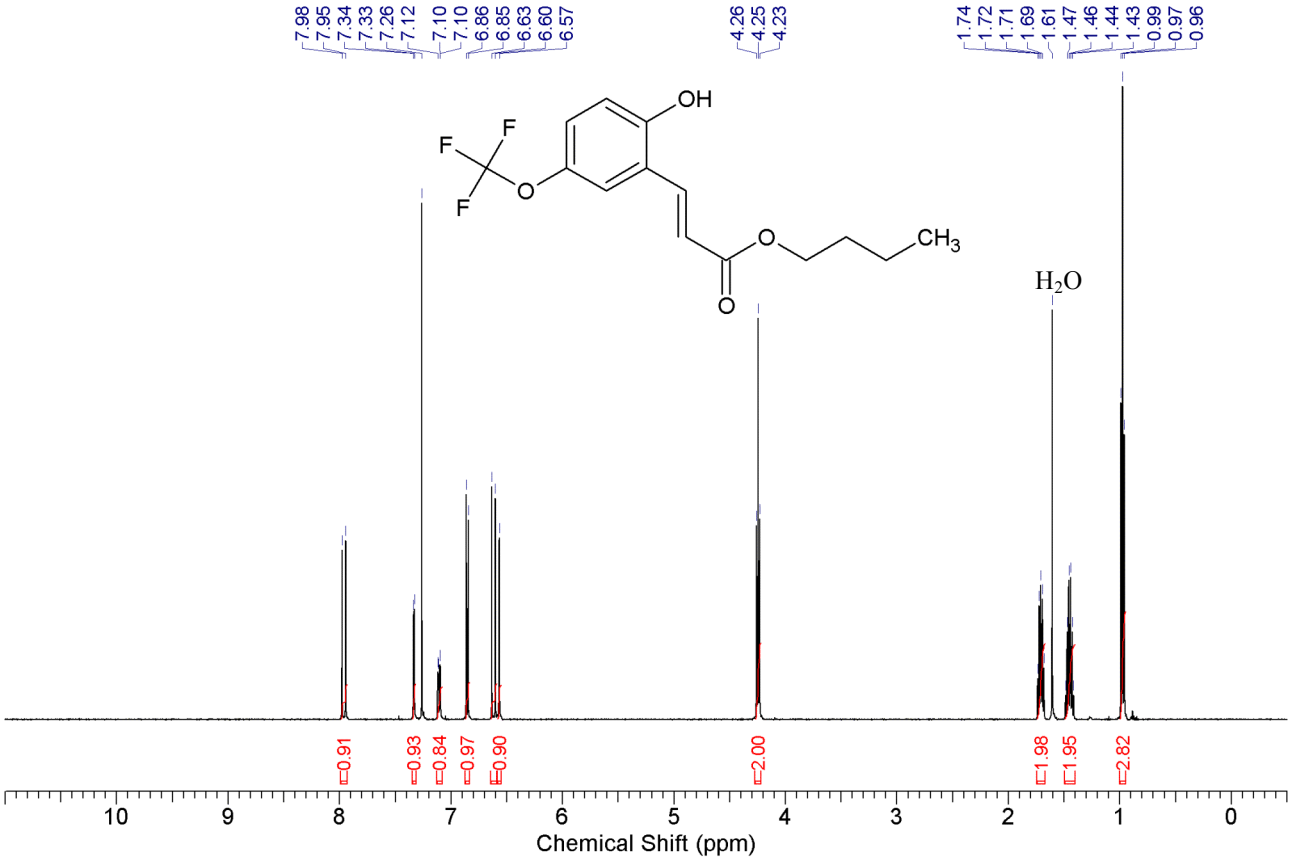
Chemical Shift (ppm)


168.0
158.0
155.7
151.3
139.2
122.7
119.5
118.1
117.9
117.4
117.3
114.5
114.2
77.3
77.0
76.7
64.8
30.7
19.2
13.8
OH
F
O
O
CH3
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

4k


7.98
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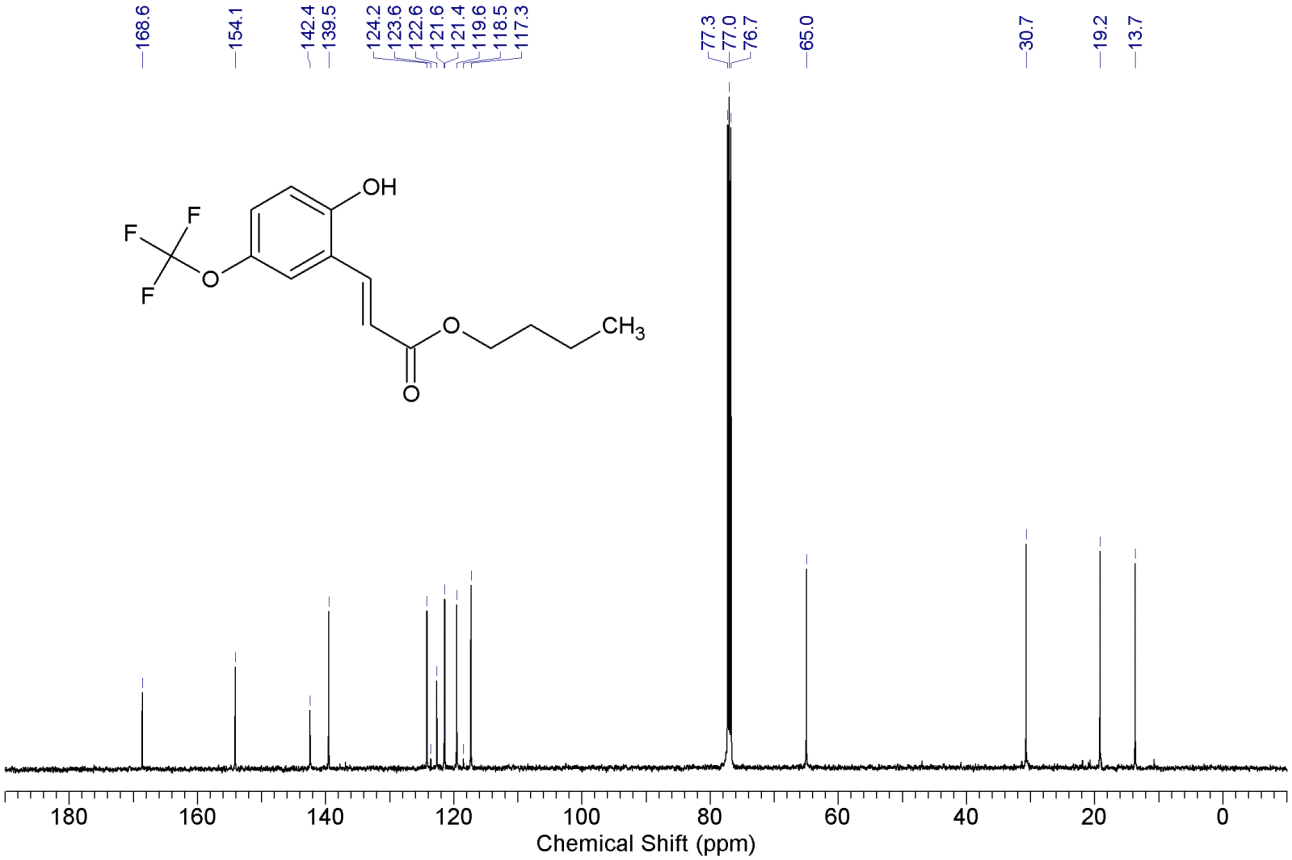
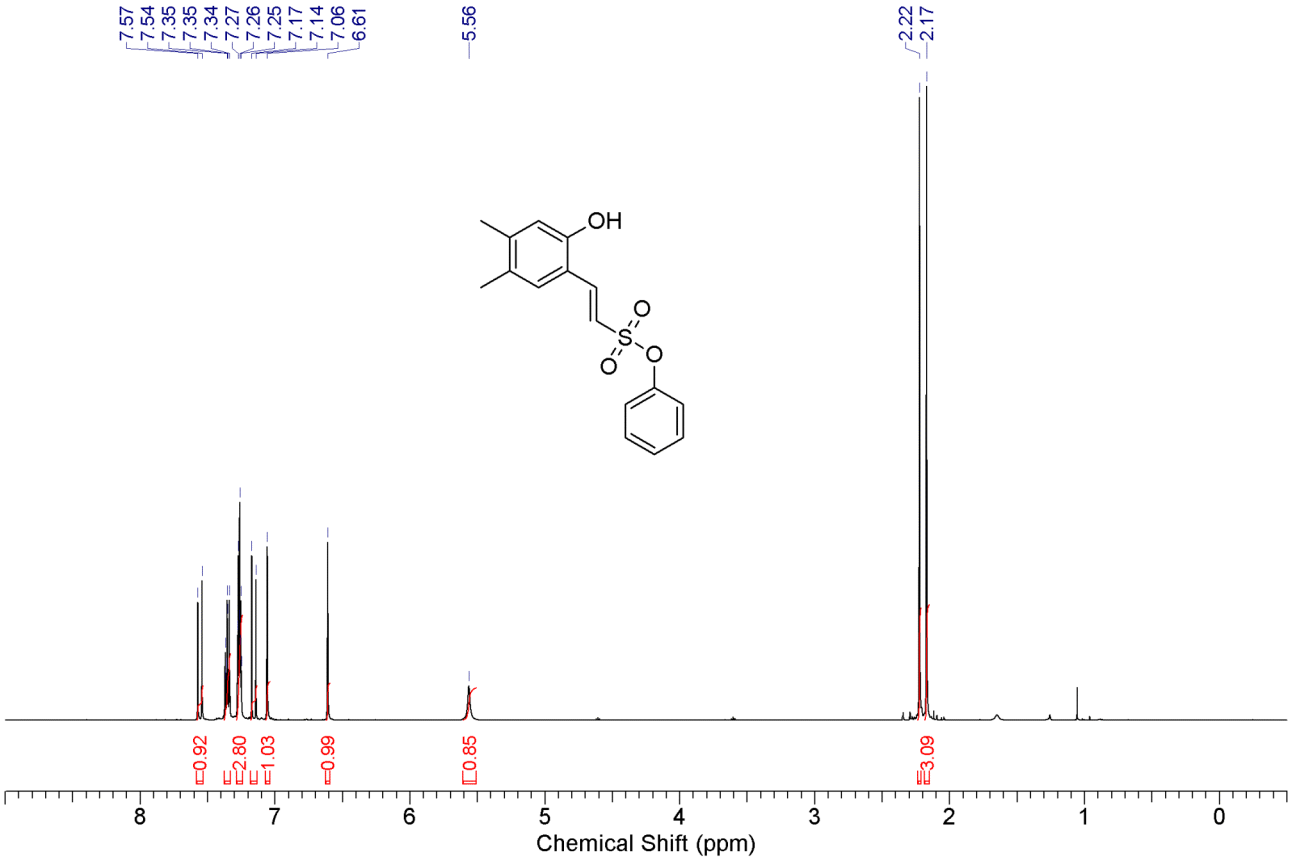
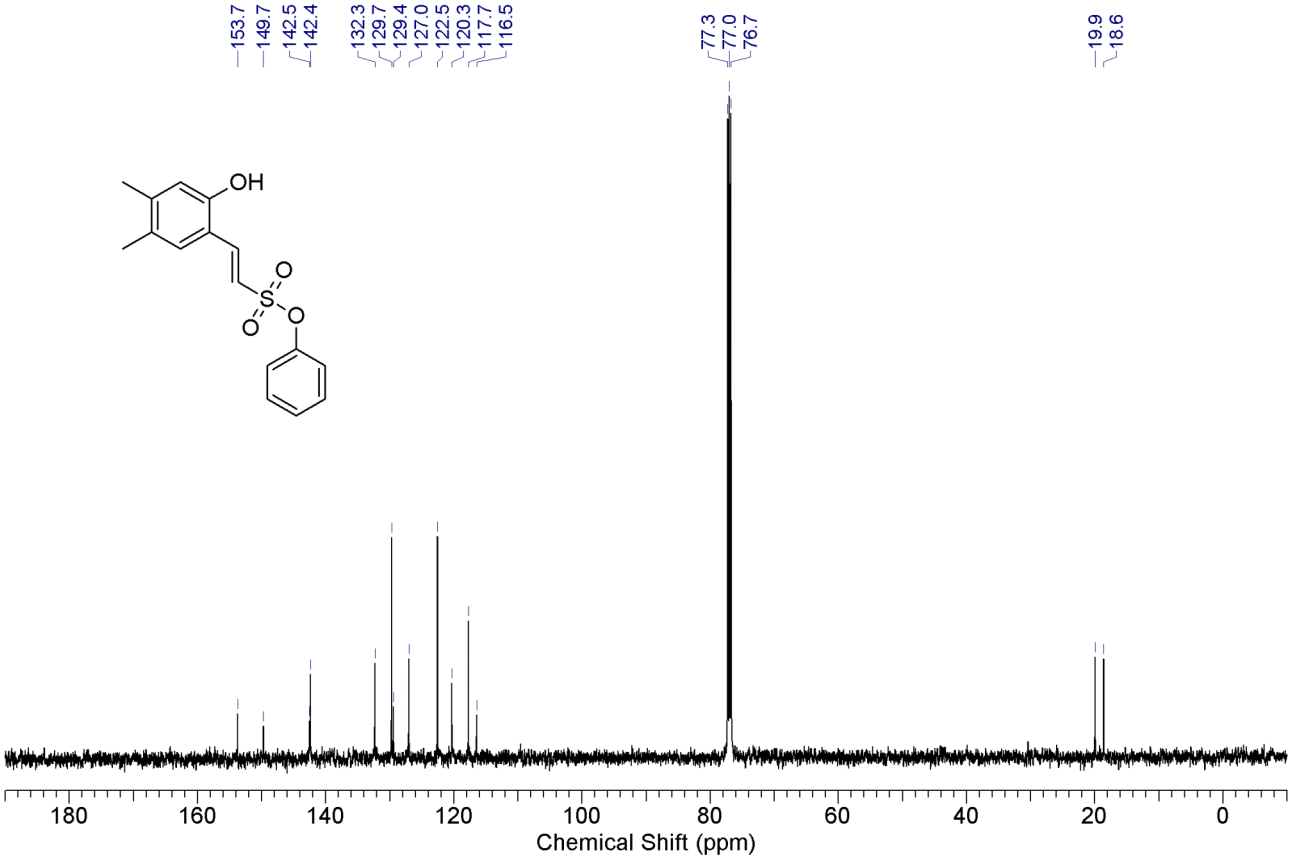
7.33
7.26
7.12
7.10
7.10
6.86
6.85
6.63
6.60
6.57
4.26
4.25
4.23
1.74
1.72
1.71
1.69
1.61
1.47
1.46
1.44
1.43
0.99
0.97
0.96
OH
F
F
F
O
O
O
CH3
H2O
0.91
0.93
0.84
0.97
0.90
2.00
1.98
1.95
2.82
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

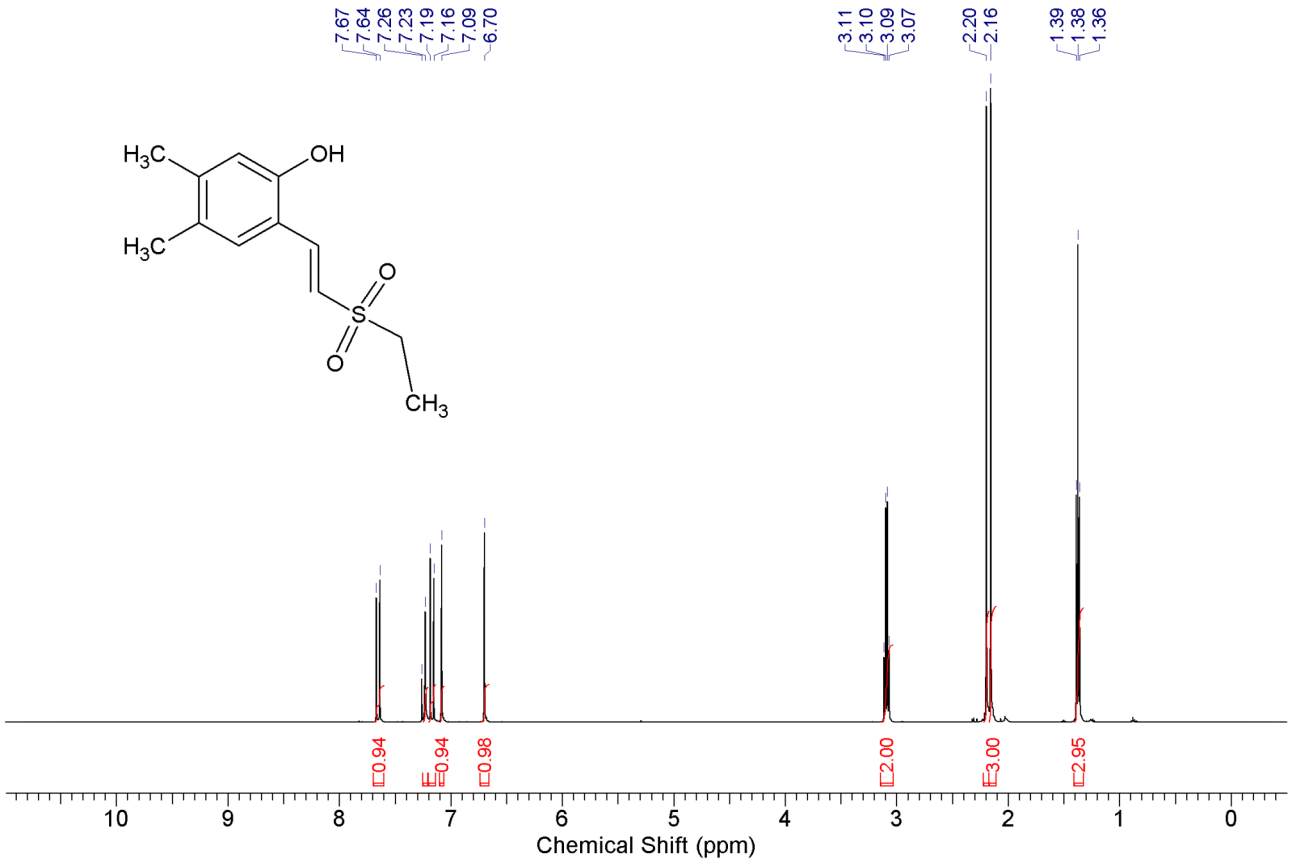

168.6
154.1
142.4
139.5
124.2
123.6
122.6
121.6
121.4
119.6
118.5
117.3
77.3
77.0
76.7
65.0
30.7
19.2
13.7
OH
F
F
F
O
O
O
CH3
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

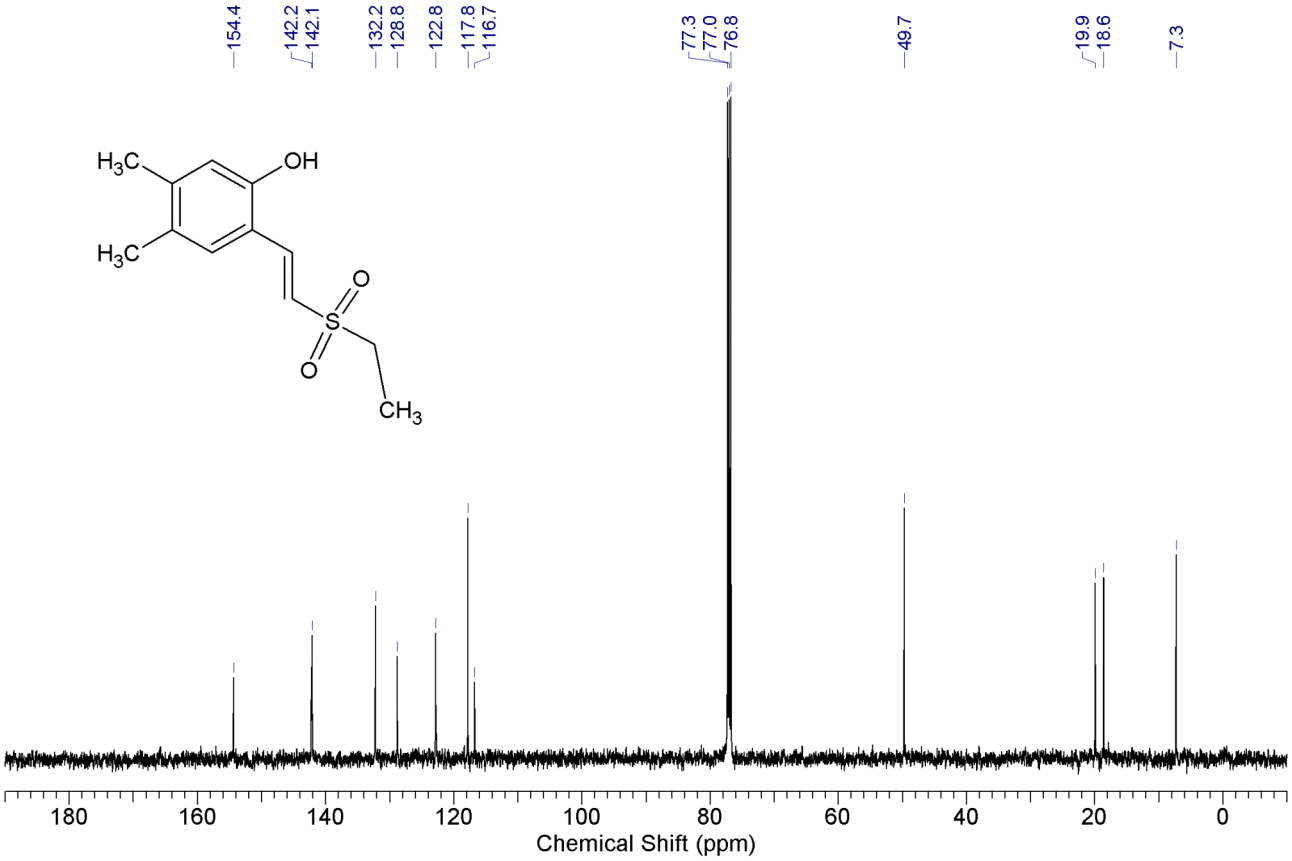
4l


7.57
7.54
7.35
7.35
7.34
7.27
7.26
7.25
7.17
7.14
7.06
6.61
5.56
2.22
2.17
OH
O
S
O
O
O
1.00
2.80
1.03
0.99
0.85
3.09
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

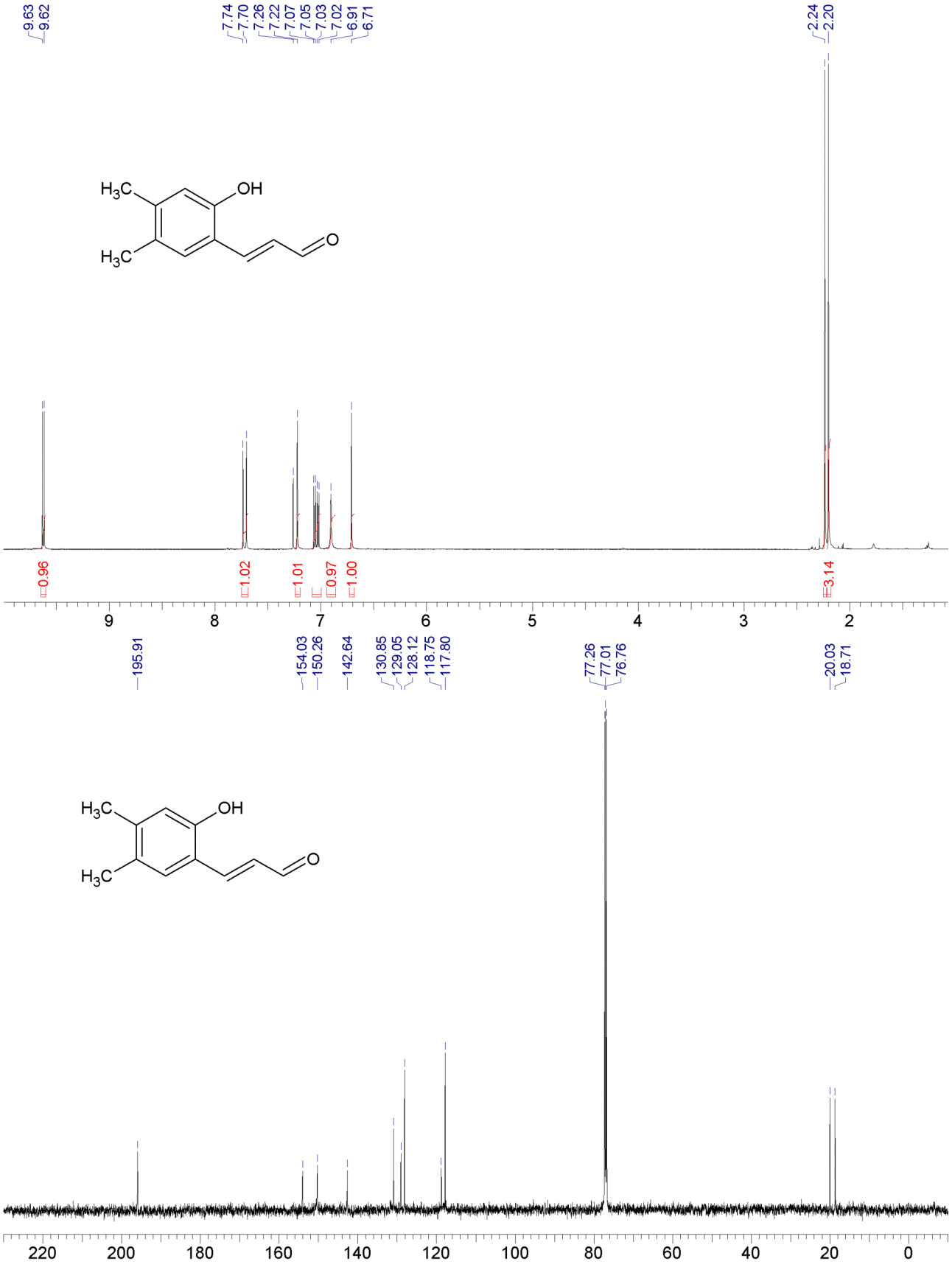

153.7
149.7
142.5
142.4
132.3
129.7
129.4
127.0
122.5
120.3
117.7
116.5
77.3
77.0
76.7
19.9
18.6
OH
O
S
O
O
O
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

4m

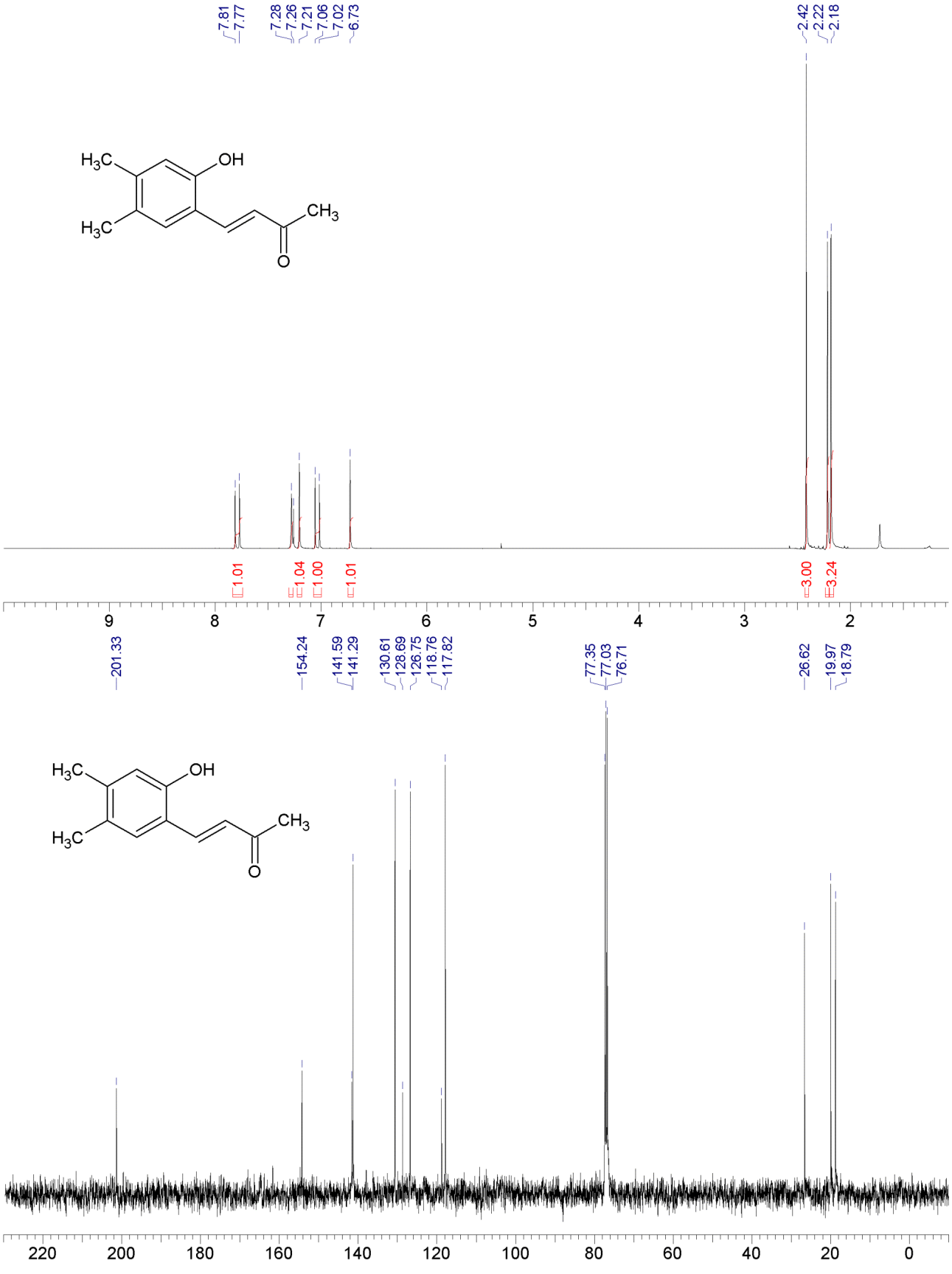

7.67
7.64
7.26
7.23
7.19
7.16
7.09
6.70
3.11
3.10
3.09
3.07
2.20
2.16
1.39
1.38
1.36
H3C
OH
H3C
O
S
O
CH3
0.94
0.94
0.98
2.00
3.00
2.95
Chemical Shift (ppm)


154.4
142.2
142.1
132.2
128.8
122.8
117.8
116.7
77.3
77.0
76.8
49.7
19.9
18.6
7.3
H3C
OH
H3C
O
S
O
CH3
Chemical Shift (ppm)

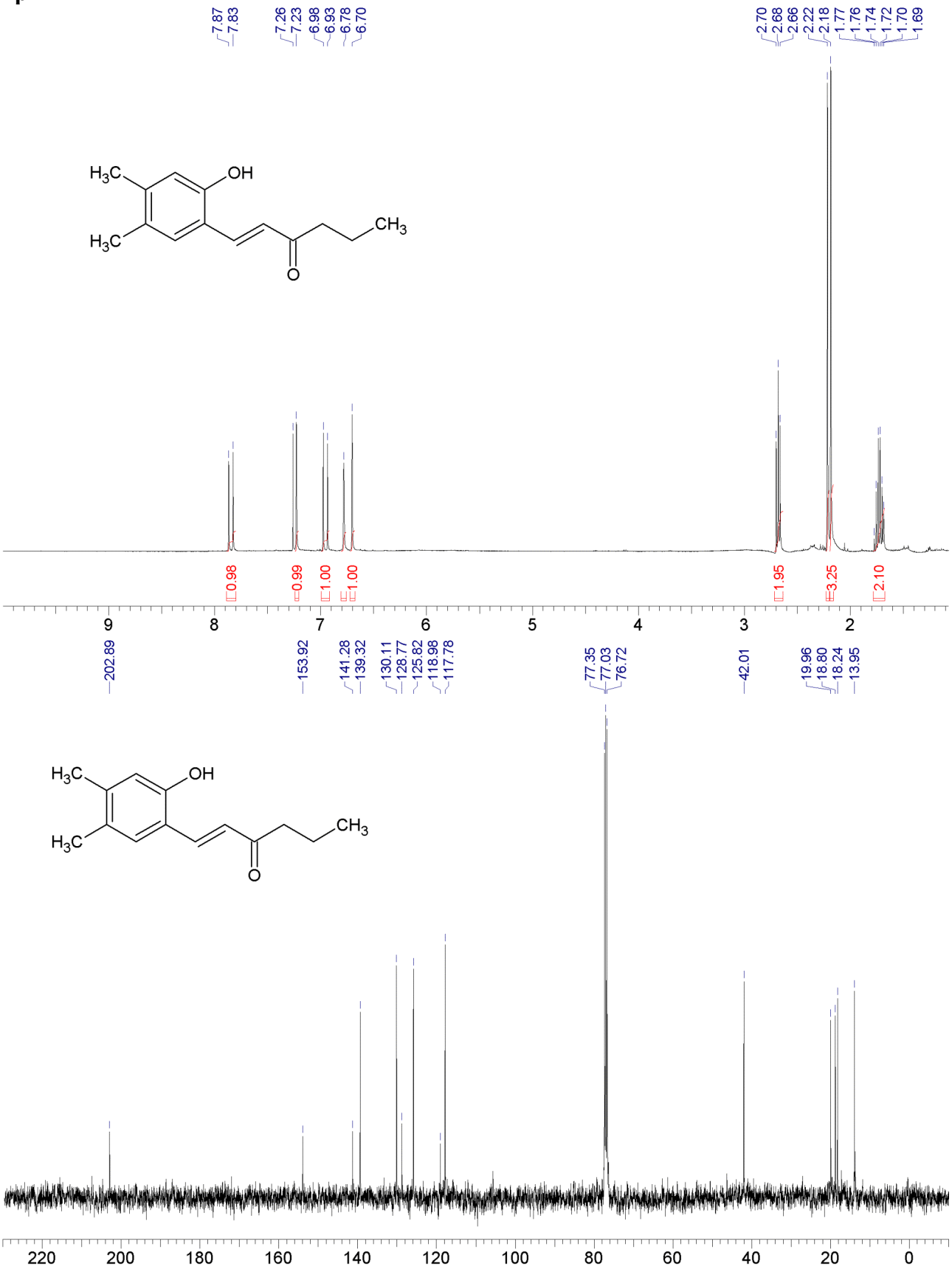
4n


9.63
9.62
7.74
7.70
7.26
7.22
7.07
7.05
7.03
7.02
6.91
6.71
2.24
2.20
H3C
OH
H3C
O
0.96
1.02
1.01
0.97
1.00
3.14
9
8
7
6
5
4
3
2
195.91
154.03
150.26
142.64
130.85
129.05
128.12
118.75
117.80
77.26
77.01
76.76
20.03
18.71
H3C
OH
H3C
O
220
200
180
160
140
120
100
80
60
40
20
0

4o


7.81
7.77
7.28
7.26
7.21
7.06
7.02
6.73
2.42
2.22
2.18
H3C
OH
H3C
CH3
O
1.01
1.04
1.00
1.01
3.00
3.24
9
8
7
6
5
4
3
2
201.33
154.24
141.59
141.29
130.61
128.69
126.75
118.76
117.82
77.35
77.03
76.71
26.62
19.97
18.79
H3C
OH
H3C
CH3
O
220
200
180
160
140
120
100
80
60
40
20
0

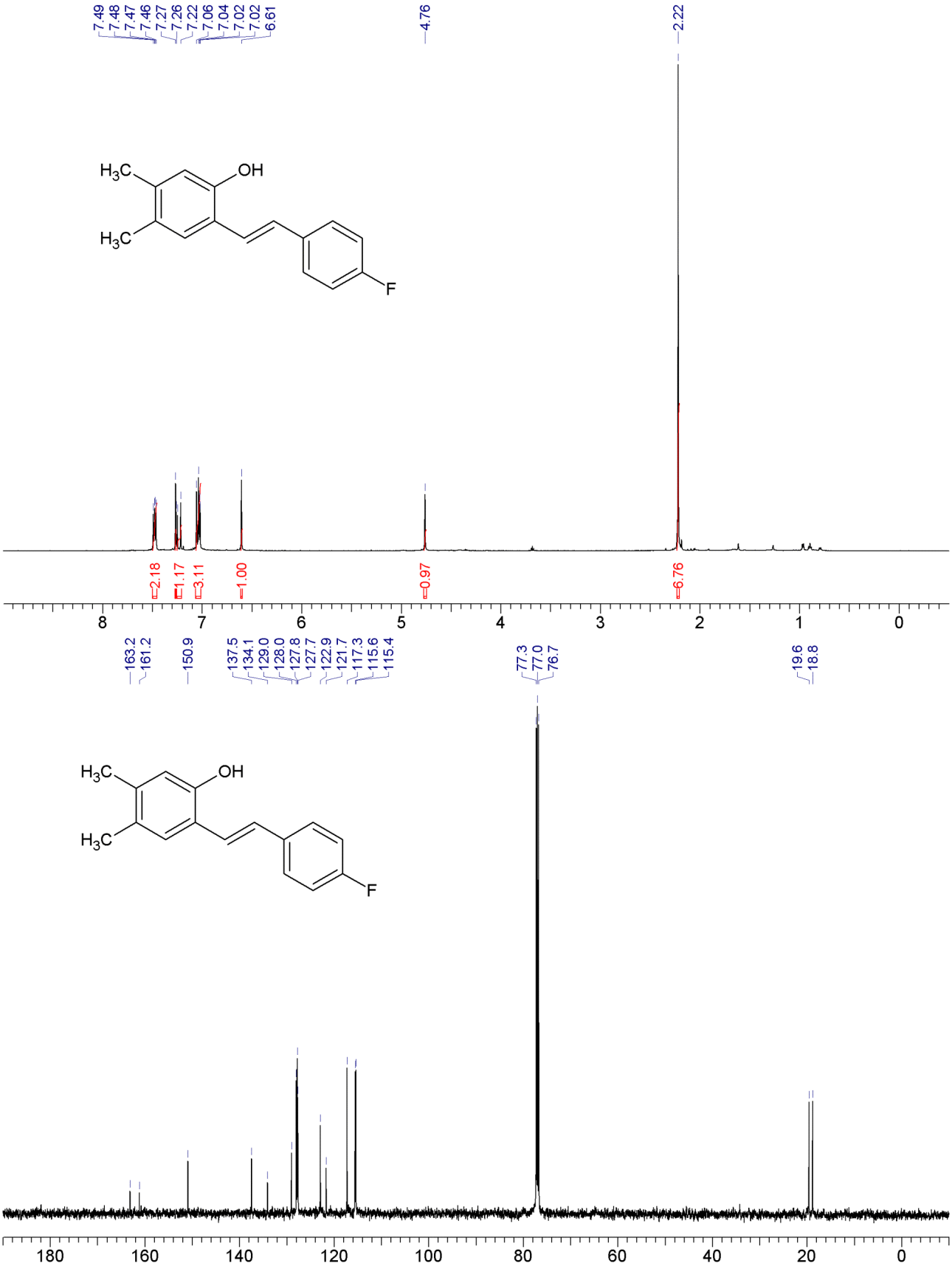
4p


7.87
7.83
7.26
7.23
6.98
6.93
6.78
6.70
2.70
2.68
2.66
2.22
2.18
1.77
1.76
1.74
1.72
1.70
1.69
H3C
OH
H3C
CH3
O
0.98
0.99
1.00
1.00
1.95
3.25
2.10
9
8
7
6
5
4
3
2
202.89
153.92
141.28
139.32
130.11
128.77
125.82
118.98
117.78
77.35
77.03
76.72
42.01
19.96
18.80
18.24
13.95
220
200
180
160
140
120
100
80
60
40
20
0

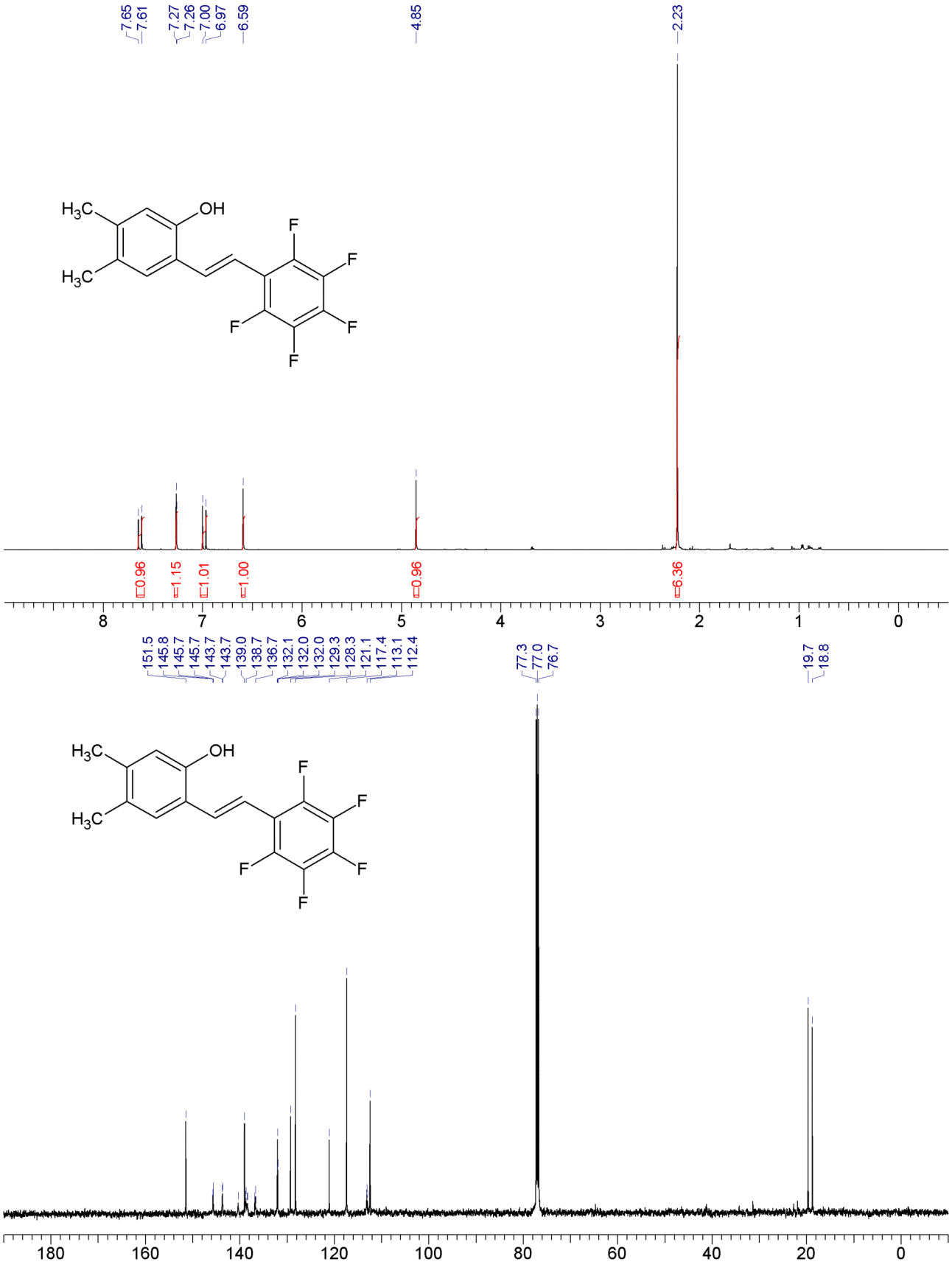
4q


7.53
7.52
7.37
7.35
7.34
7.30
7.29
7.26
7.10
7.06
6.62
4.76
2.22
H3C
OH
H3C
1.99
1.27
1.00
0.88
0.84
5.98
9
8
7
6
5
4
3
2
150.96
137.86
137.45
128.98
128.60
128.08
127.33
126.40
123.09
121.82
117.27
77.26
77.00
76.75
19.61
18.85
H3C
OH
H3C
220
200
180
160
140
120
100
80
60
40
20
0

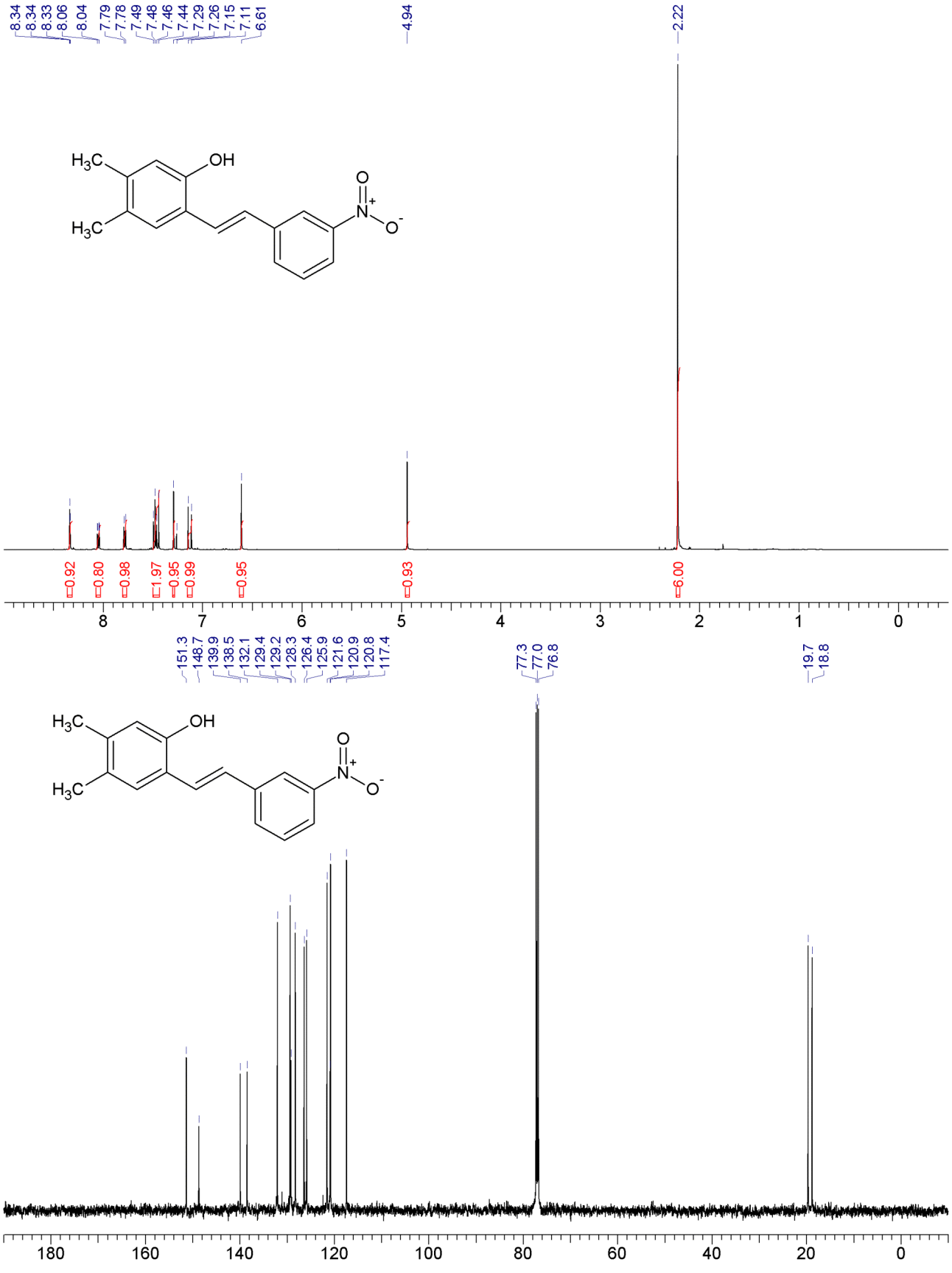
4r


7.49
7.48
7.47
7.46
7.27
7.26
7.22
7.06
7.04
7.02
7.02
6.61
4.76
2.22
H3C
OH
H3C
F
2.18
1.17
3.11
1.00
0.97
6.76
8
7
6
5
4
3
2
1
0
163.2
161.2
150.9
137.5
134.1
129.0
128.0
127.8
127.7
122.9
121.7
117.3
115.6
115.4
77.3
77.0
76.7
19.6
18.8
H3C
OH
H3C
F
180
160
140
120
100
80
60
40
20
0

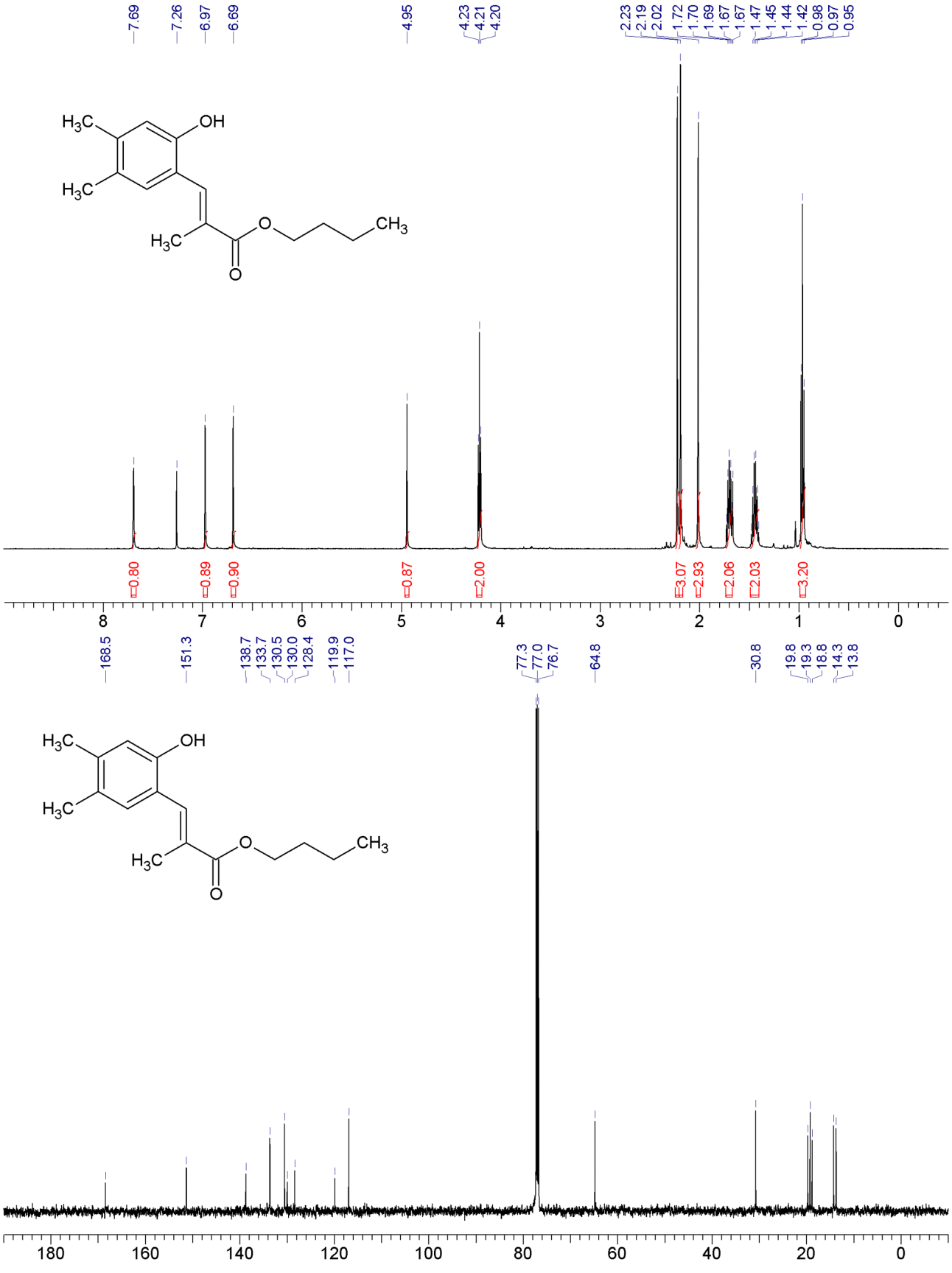
4s


7.65
7.61
7.27
7.26
7.00
6.97
6.59
4.85
2.23
H3C
OH
H3C
F
F
F
F
F
0.96
1.15
1.01
1.00
0.96
6.36
8
7
6
5
4
3
2
1
0
151.5
145.8
145.7
145.7
143.7
143.7
139.0
138.7
136.7
132.1
132.0
132.0
129.3
128.3
121.1
117.4
113.1
112.4
77.3
77.0
76.7
19.7
18.8
H3C
OH
H3C
F
F
F
F
F
180
160
140
120
100
80
60
40
20
0

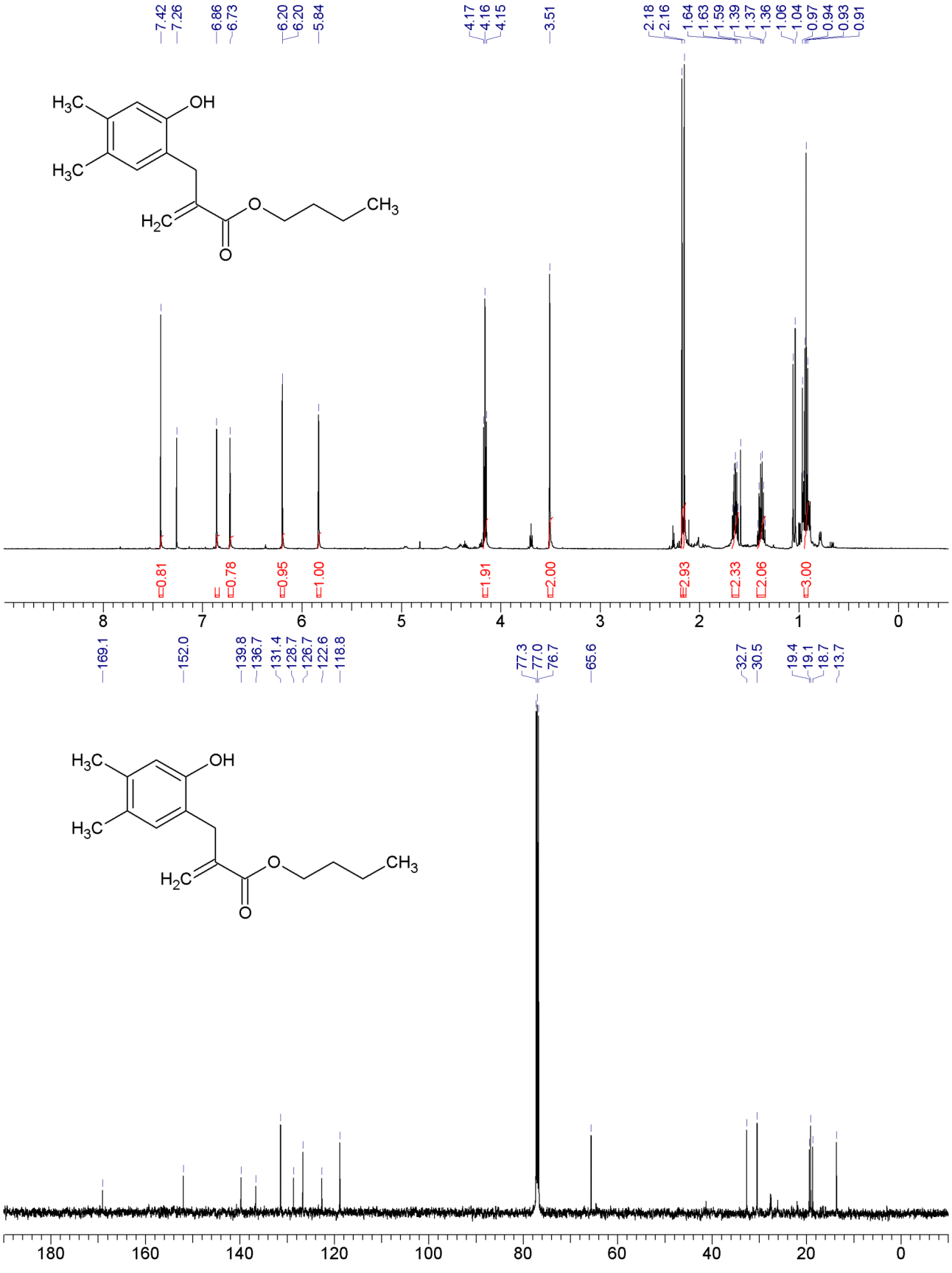
4t


8.34
8.34
8.33
8.06
8.04
7.79
7.78
7.49
7.48
7.46
7.44
7.29
7.26
7.15
7.11
6.61
4.94
2.22
H3C
OH
H3C
O
N+
O-
0.92
0.80
0.98
1.97
0.95
0.99
0.95
0.93
6.00
8
7
6
5
4
3
2
1
0
151.3
148.7
139.9
138.5
132.1
129.4
129.2
128.3
126.4
125.9
121.6
120.9
120.8
117.4
77.3
77.0
76.8
19.7
18.8
H3C
OH
H3C
O
N+
O-
180
160
140
120
100
80
60
40
20
0

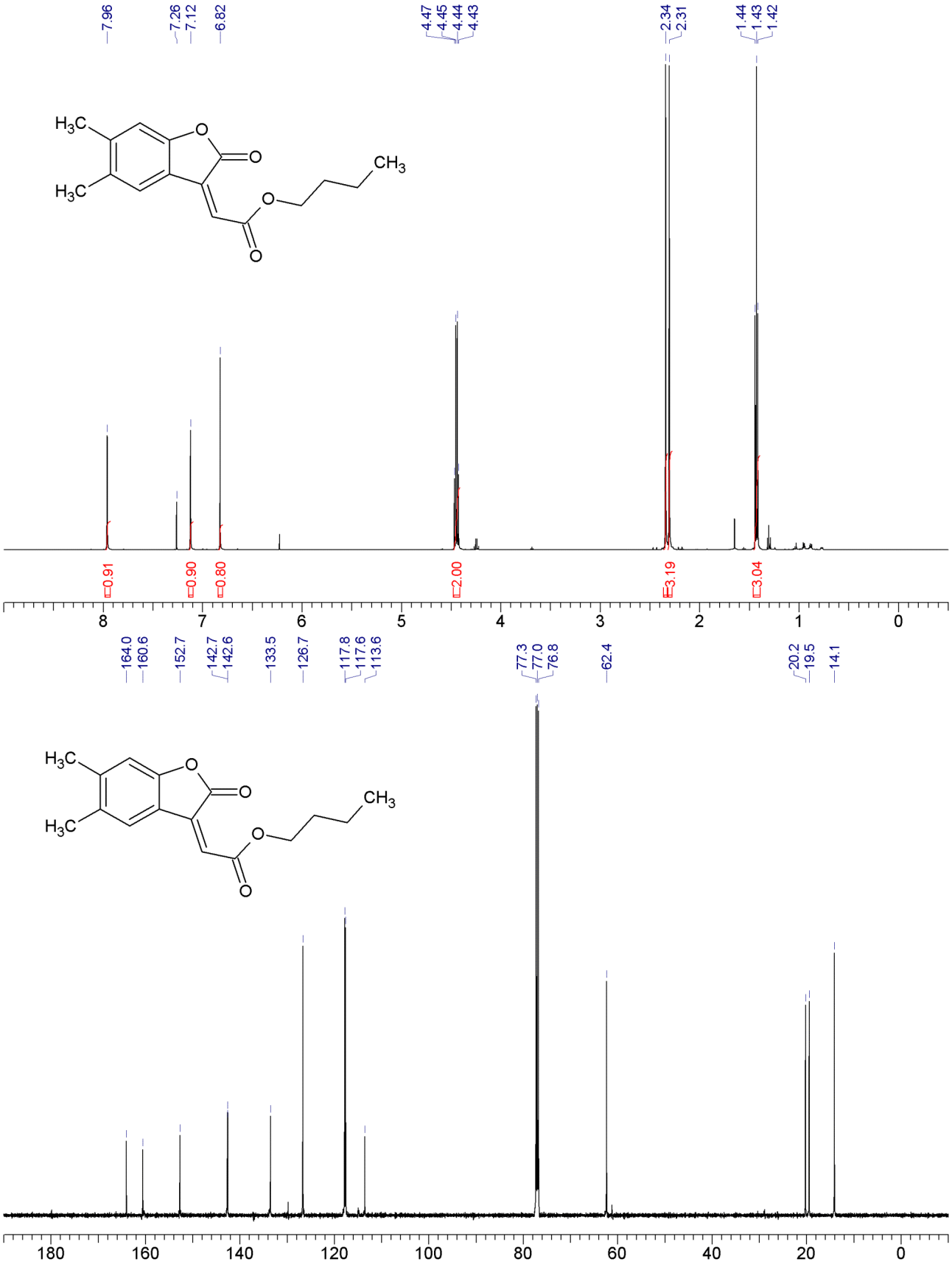
4u


7.69
7.26
6.97
6.69
4.95
4.23
4.21
4.20
2.23
2.19
2.02
1.72
1.70
1.69
1.67
1.67
1.47
1.45
1.44
1.42
0.98
0.97
0.95
H3C
OH
H3C
H3C
O
CH3
O
0.80
0.89
0.90
0.87
2.00
3.07
2.93
2.06
2.03
3.20
168.5
151.3
138.7
133.7
130.5
130.0
128.4
119.9
117.0
77.3
77.0
76.7
64.8
30.8
19.8
19.3
18.8
14.3
13.8

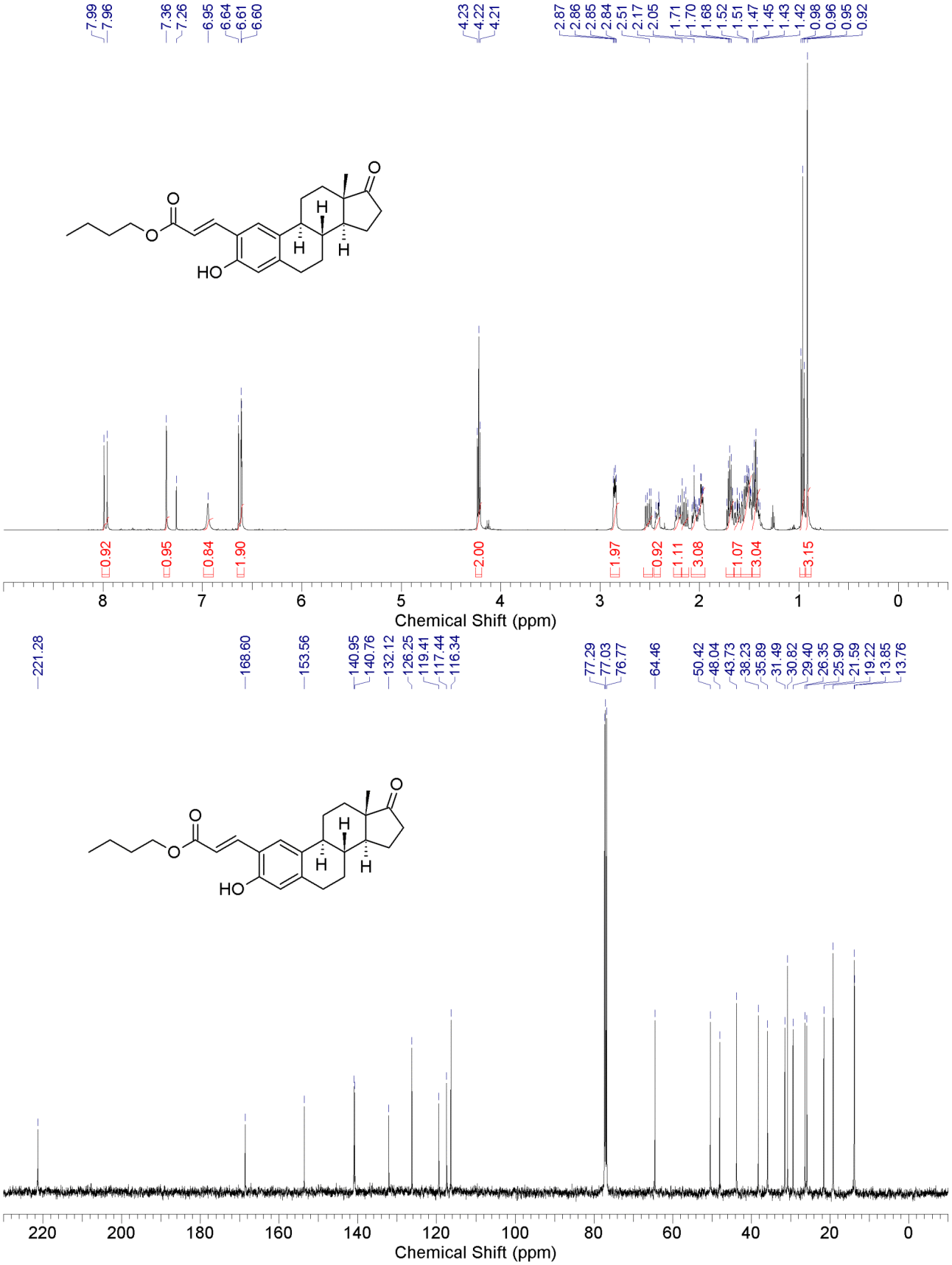
4v


7.42
7.26
6.86
6.73
6.20
6.20
5.84
4.17
4.16
4.15
3.51
2.18
2.16
1.64
1.63
1.59
1.39
1.37
1.36
1.06
1.04
0.97
0.94
0.93
0.91
H3C
OH
H3C
H2C
O
O
CH3
0.81
0.78
0.95
1.00
1.91
2.00
2.93
2.33
2.06
3.00
8
7
6
5
4
3
2
1
0
169.1
152.0
139.8
136.7
131.4
128.7
126.7
122.6
118.8
77.3
77.0
76.7
65.6
32.7
30.5
19.4
19.1
18.7
13.7
180
160
140
120
100
80
60
40
20
0

6


7.96
7.26
7.12
6.82
4.47
4.45
4.44
4.43
2.34
2.31
1.44
1.43
1.42
0.91
0.90
0.80
2.00
3.19
3.04
H3C
H3C
O
O
O
O
CH3
8
7
6
5
4
3
2
1
0
164.0
160.6
152.7
142.7
142.6
133.5
126.7
117.8
117.6
113.6
77.3
77.0
76.8
62.4
20.2
19.5
14.1
180
160
140
120
100
80
60
40
20
0

8


7.99
7.96
7.36
7.26
6.95
6.64
6.61
6.60
4.23
4.22
4.21
2.87
2.86
2.85
2.84
2.51
2.17
2.05
1.71
1.70
1.68
1.52
1.51
1.47
1.45
1.43
1.42
0.98
0.96
0.95
0.92
O
O
O
H
H
H
HO
0.92
0.95
0.84
1.90
2.00
1.97
0.92
1.11
3.08
1.07
3.04
3.15
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)
221.28
168.60
153.56
140.95
140.76
132.12
126.25
119.41
117.44
116.34
77.29
77.03
76.77
64.46
50.42
48.04
43.73
38.23
35.89
31.49
30.82
29.40
26.35
25.90
21.59
19.22
13.85
13.76
220
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)