Co-catalyzed atom transfer radical addition of bromodifluoroacetamides, expanding the scope of radical difluoroalkylation

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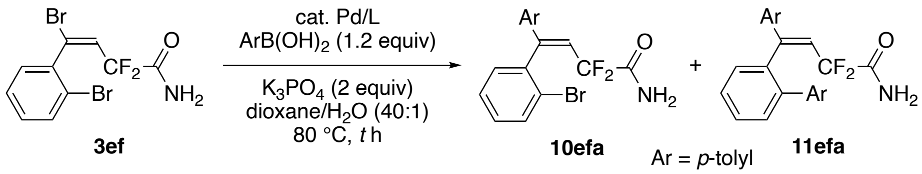
Supporting Information

General Information. All air- and moisture sensitive reactions were performed under an argon atmosphere in dried glassware. Analytical thin layer chromatography was performed using 0.25 mm silica gel plate (Merck TLC Silica gel 60 F_{254}). Column chromatography was performed on silica gel (Cica silica gel 60N) with eluents specified below. NMR spectra were recorded for samples in $CDCl_3$ solutions at 25 °C. ^{1}H NMR chemical shifts are reported in terms of chemical shift (δ, ppm) relative to the singlet at δ 7.26 ppm for chloroform. ^{13}C NMR spectra were fully decoupled and are reported in terms of chemical shift (δ, ppm) relative to the triplet at δ 77.0 ppm for $CDCl_3$. ^{19}F NMR spectra are reported in terms of chemical shift (δ, ppm) relative to the singlet at δ −63.7 ppm for α,α,α-trifluorotoluene as an external standard. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; m, multiplet; br, broad. Coupling constants are reported in Hz. High resolution mass spectra (HRMS) were obtained on a DART-TOF or ESI-TOF mass spectrometer. $CoBr_2$, dppbz, Zn, and solvents were purchased and used as received. Bromodifluoroacetamides were previously reported.[1] Alkyne **3h**, diene **4d**, enyne **4e**, and *N*,*N*-diallylbromodifluoroacetamide **6** were prepared according to the literature.[2]

Table S1. Suzuki–Miyaura coupling of **3ef** with *p*-tolylboronic acid.

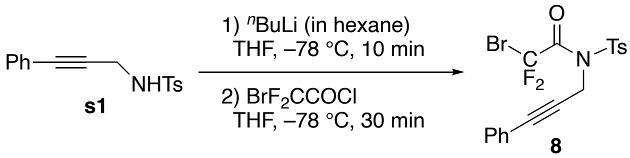


Pd (mol%)	L (mol%)	*t*	Conv./%	**10efa** yield/%	**10efa**:**11efa**
$PdCl_2(PPh_3)_2$ (10)	–	5	100	65[a]	7:1
$Pd_2(dba)_3$ (2.5)	SPhos (5)	7	81	40[a]	1.6:1
$Pd_2(dba)_3$ (2.5)	XPhos (5)	3	100	50[a]	5:1
$Pd_2(dba)_3$ (2.5)	PCy_3 (5)	7	62	18[a]	1:0
$Pd_2(dba)_3$ (2.5)	P(*p*-$F_3CC_6H_4)_3$ (5)	3	100	86	21:1

[a] Yields estimated by the ^{1}H NMR analysis of crude reaction mixtures.

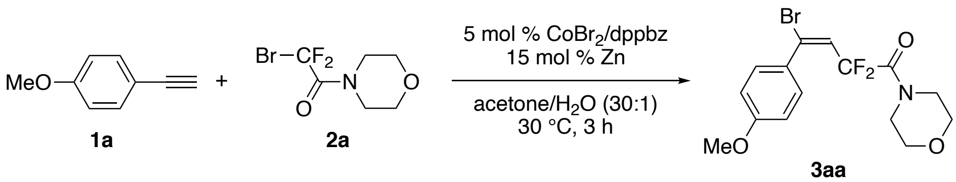
[1] Y. Yamamoto, E. Kuroyanagi, H. Suzuki, T. Yasui, *Adv. Synth. Catal.* **2021**, in press.
[2] (a) H. Wang, S. Qiu, S. Wang, H. Zhai, *ACS Catal.* **2018**, *8*, 11960-11965. (b) Y. Yamamoto, Y. Nakagai, K. Itoh, *Chem. Eur. J.* **2004**, *10*, 231-236. (c) S. Y. Kim, Y. K. Chung, *J. Org. Chem.* **2010**, *75*, 1281-1284. (d) H. Nagashima, Y. Isono, S. Iwamatsu, *J. Org. Chem.* **2001**, *66*, 315-319.

Synthesis of 2-bromo-2,2-difluoro-*N*-tosyl-*N*-propargylacetamide 8



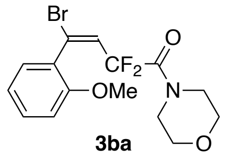
To a solution of *N*-propargyltosylamide **s1** (284.56 mg, 0.997 mmol) in dry THF (4 mL) was added ^{n}BuLi (15 w/w% in hexane, 640 µL, 1.02 mmol) at –78 °C, and the solution was stirred for 10 min. To this solution was added BrF_2CCOCl (246.32 mg, 1.274 mmol) at –78 °C, and the solution was stirred for 30 min. The reaction was quenched by adding sat. aq. NH_4Cl (15 mL), and aqueous phase was extracted with AcOEt (3×10 mL). The combined organic extract was washed with brine (15 mL), and dried over anhydrous Na_2SO_4. The solvents were evaporated *in vacuo*, and the obtained crude product was purified by recrystallization (hexane/AcOEt) to afford **8** (310.4 mg, 70%) as a colorless solid (mp 122.6–124.7 °C): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 8.07 (d, 2H, J = 8.4 Hz), 7.41–7.31 (m, 5H), 7.29 (d, 2H, J = 8.0 Hz), 5.07 (s, 2H), 2.43 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 157.4 (t, $^2J_{CF}$ = 29.6 Hz), 146.0, 134.0, 131.7, 130.0, 129.4, 129.0, 128.4, 121.6, 109.6 (t, $^1J_{CF}$ = 315.2 Hz), 85.4, 82.5, 37.6 (t, $^4J_{CF}$ = 4.3 Hz), 21.7; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –57.4 (s, 2F); HRMS (DART) Because of methanolysis of **8**, the molecular ion peak of **s1** was observed. *m/z* $[M+NH_4]^+$ calcd for $C_{16}H_{19}N_2O_2S$ 304.1161, found 304.1171.

Atom Transfer Radical Addition of Bromodifluoroacetamides to Alkynes



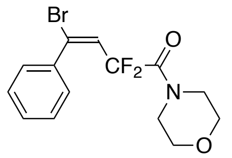
Representative procedure – Synthesis of 3aa: A solution of $CoBr_2$ (4.0 mg, 0.018 mmol) and dppbz (7.0 mg, 0.012 mmol) in acetone/H_2O (30:1, 0.3 mL) was stirred for 5 min at room temperature under an Ar atmosphere. Subsequently, alkyne **1a** (37.5 mg, 0.284 mmol), amide **2a** (110.7 mg, 0.454 mmol), Zn powder (3.3 mg, 0.050 mmol), and acetone/H_2O (30:1, 0.3 mL) were added to this solution and the solution was degassed at –80 °C. The reaction mixture was stirred for 3 h at 30 °C under an Ar atmosphere. The reaction was quenched by adding AcOEt (10 mL) and the crude mixture was passed through a short column (SiO_2, eluent AcOEt). The combined organic extract was washed with brine (10 mL), dried over anhydrous Na_2SO_4. The solvents were evaporated *in vacuo,* and the obtained crude product was purified by silica gel column chromatography (hexane) to afford **3aa** (86.2 mg, 81%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.36 (d, 2H, J = 8.8 Hz), 6.86 (d, 2H, J = 8.8 Hz), 6.56 (t, 1H, J = 11.2 Hz), 3.82 (s, 3H), 3.62 (t, 2H, J = 4.8 Hz), 3.57 (t, 2H, J = 5.0 Hz), 3.48 (t, 2H, J = 4.6 Hz), 3.35 (t, 2H, J = 4.8 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C): δ 160.8, 160.3 (t, $^2J_{CF}$ = 29.1 Hz), 133.1 (t, $^3J_{CF}$ = 9.5 Hz), 130.3, 129.0, 124.5 (t, $^2J_{CF}$ = 27.7 Hz), 113.3, 113.0 (t, $^1J_{CF}$ = 247.9 Hz), 66.3, 66.2, 55.2, 46.5, 42.9; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –88.8 (s, 2F); IR ($CHCl_3$) 1676 (C=O) cm^{-1}; HRMS (DART) m/z $[M+NH_4]^+$ calcd for $C_{15}H_{20}BrF_2N_2O_3$ 393.0625, found 393.0634.

Analytical data for 3ba: 88.6 mg, 77%; colorless oil; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.35 (ddd, 1H, J = 8.8, 7.2, 1.6 Hz), 7.22 (dd, 1H, J = 8.0, 1.6 Hz), 6.95 (td, 1H, J = 7.6, 0.8 Hz), 6.89 (d, 1H, J = 8.4 Hz), 6.63 (t, 1H, J = 11.0 Hz), 3.88 (s, 3H), 3.62 (t, 4H, J = 4.8 Hz), 3.51 (t, 2H, J = 4.6 Hz), 3.38 (br s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C): δ 160.3 (t, $^2J_{CF}$ = 29.6 Hz), 155.9, 131.4, 130.0, 129.2 (t, $^3J_{CF}$ = 9.6 Hz), 126.7 (t, $^2J_{CF}$ = 26.7 Hz), 125.8, 120.1, 112.9 (t, $^1J_{CF}$ = 248.4 Hz), 110.9, 66.3, 55.6, 46.4, 42.9; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –91.7 (d, 2F, J = 103.8 Hz); IR ($CHCl_3$) 1676 (C=O) cm^{-1}; HRMS (DART) m/z $[M+NH_4]^+$ calcd for $C_{15}H_{20}BrF_2N_2O_3$ 393.0625, found 393.0641.

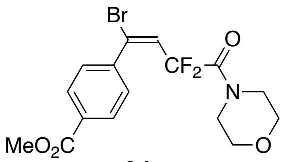


3ba

Analytical data for 3ca: 85.2 mg, 80%; colorless solid (mp 66.8–69.8 °C); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.42–7.34 (m, 5H), 6.65 (t, 1H, J = 11.4 Hz), 3.62–3.57 (m, 4H), 3.49 (t, 2H, J = 4.6 Hz), 3.36 (t, 2H, J = 4.6 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C): δ 160.2 (t, $^2J_{CF}$ = 29.1 Hz), 137.0, 132.6 (t, $^3J_{CF}$ = 9.6 Hz), 129.9, 128.4, 128.0, 125.3 (t, $^2J_{CF}$ = 27.2 Hz), 113.1 (t, $^1J_{CF}$ = 248.9 Hz), 66.3, 66.2, 46.4, 43.0; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –89.3 (s, 2F); IR ($CHCl_3$) 1671 (C=O) cm^{-1}; HRMS (DART) m/z $[M+H]^+$ calcd for $C_{14}H_{15}BrF_2NO_2$ 346.0254, found 346.0252.

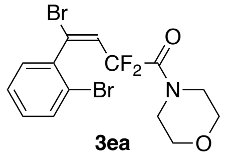


Analytical data for 3da: 82.5 mg, 68%; colorless solid (mp 91.7–94.1 °C; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 8.03 (d, 2H, J = 8.8 Hz), 7.46 (d, 2H, J = 8.0 Hz), 6.73 (t, 1H, J = 12.2 Hz), 3.93 (s, 3H), 3.63 (t, 2H, J = 4.8 Hz), 3.61 (t, 2H, J = 4.8 Hz), 3.51 (t, 2H, J = 4.4 Hz), 3.45 (t, 2H, J = 4.8 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C): δ 166.1, 160.3 (t, $^2J_{CF}$ = 29.1 Hz), 141.7, 131.0, 130.7 (t, $^3J_{CF}$ = 8.2 Hz), 129.2, 128.3, 126.1 (t, $^2J_{CF}$ = 26.3 Hz), 113.4 (t, $^1J_{CF}$ = 251.3 Hz), 66.3, 52.2, 46.3 (t, $^4J_{CF}$ = 4.8 Hz), 43.1; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –90.2 (s, 2F); IR ($CHCl_3$) 1722 (C=O), 1669 (C=O) cm^{-1}; HRMS (DART) m/z $[M+NH_4]^+$ calcd for $C_{16}H_{20}BrF_2N_2O_4$ 421.0575, found 421.0586.



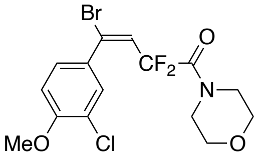
3da

Analytical data for 3ea: 107.7 mg, 82%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.59 (d, 1H, J = 8.4 Hz), 7.36–7.29 (m, 2H), 7.22 (ddd, 1H, J = 8.0, 6.4, 2.8 Hz), 6.75 (t, 1H, J = 12.2 Hz), 3.78–3.46 (m, 8H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 160.4 (t, $^{2}J_{CF}$ = 29.1 Hz), 138.2, 132.8, 130.7, 130.1 (t, $^{3}J_{CF}$ = 8.1 Hz), 129.9, 127.2 (t, $^{2}J_{CF}$ = 24.8 Hz), 127.1, 121.5, 113.3 (t, $^{1}J_{CF}$ = 252.7 Hz), 66.5, 66.4, 46.3 (t, $^{4}J_{CF}$ = 5.2 Hz), 43.2; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –92.2 (d, 1F, J = 288.8 Hz), –93.2 (d, 1F, J = 288.8 Hz); IR ($CHCl_3$) 1671 (C=O) cm^{-1}; HRMS (DART) m/z $[M+NH_4]^+$ calcd for $C_{14}H_{17}Br_2F_2N_2O_2$ 440.9625, found 440.9606.



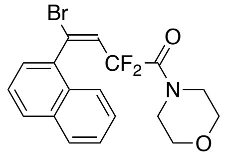
3ea

Analytical data for 3fa: 93.3 mg, 75%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.42 (d, 1H, J = 2.0 Hz), 7.29 (d, 1H, J = 8.8, 2.0 Hz), 6.88 (d, 1H, J = 8.8 Hz), 6.62 (t, 1H, J = 11.6 Hz), 3.92 (s, 3H), 3.63 (t, 4H, J = 4.8 Hz), 3.52 (t, 2H, J = 4.6 Hz), 3.44 (t, 2H, J = 4.6 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 160.3 (t, $^{2}J_{CF}$ = 29.1 Hz), 156.0, 131.0 (t, $^{3}J_{CF}$ = 9.6 Hz), 130.13, 130.07, 128.6, 125.5 (t, $^{2}J_{CF}$ = 26.7 Hz), 122.0, 113.2 (t, $^{1}J_{CF}$ = 249.3 Hz), 111.0, 66.33, 66.28, 56.1, 46.5 (t, $^{4}J_{CF}$ = 3.8 Hz), 43.1; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –89.6 (s, 2F); IR ($CHCl_3$) 1671 (C=O) cm^{-1}; HRMS (DART) m/z $[M+H]^+$ calcd for $C_{15}H_{16}BrClF_2NO_3$ 409.9970, found 409.9979.



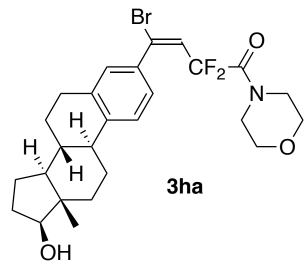
3fa

Analytical data for 3ga: 98.9 mg, 80%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 8.01 (d, 1H, J = 8.4 Hz), 7.88 (dd, 2H, J = 6.8, 2.4 Hz), 7.60 (dd, 1H, J = 8.0, 6.8, 1.2 Hz), 7.53 (ddd, 1H, J = 8.0, 6.8, 1.2 Hz), 7.48–7.42 (m, 2H), 6.95 (t, 1H, J = 11.2 Hz), 3.58–3.32 (m, 7H), 3.01–2.94 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 160.2 (t, $^{2}J_{CF}$ = 29.6 Hz), 134.3, 133.2, 130.6 (t, $^{3}J_{CF}$ = 8.6 Hz), 130.1, 129.5, 128.4, 128.1 (t, $^{2}J_{CF}$ = 25.8 Hz), 126.6, 126.5, 126.3, 125.0, 124.9, 113.4 (t, $^{1}J_{CF}$ = 251.3 Hz), 66.32, 66.26, 46.3 (t, $^{4}J_{CF}$ = 4.8 Hz), 42.9; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –91.3 (s, 2F); IR ($CHCl_3$) 1670 (C=O) cm^{-1}; HRMS (DART) m/z $[M+NH_4]^+$ calcd for $C_{18}H_{20}BrF_2N_2O_2$ 413.0676, found 413.0662.



3ga

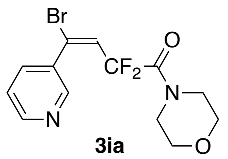
Analytical data for 3ha: 83.1 mg, 65%; colorless paste; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.27 (d, 1H, J = 8.0 Hz), 7.17 (d, 1H, J = 8.0 Hz), 7.09 (s, 1H), 6.58 (t, 1H, J = 11.2 Hz), 3.73 (br s, 1H), 3.60 (t, 2H, J = 4.6 Hz), 3.56 (t, 2H, J = 5.0 Hz), 3.47 (t, 2H, J = 4.2 Hz), 3.33 (t, 2H, J = 4.6 Hz), 2.86 (dd, 2H, J = 8.8, 4.0 Hz), 2.36–2.28 (m, 1H), 2.23 (td, 1H, J = 11.0, 3.6 Hz), 2.17–2.08 (m, 1H), 2.00–



3ha

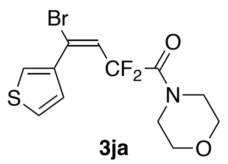
1.88 (m, 2H), 1.75–1.67 ‘m, 1H), 1.55–1.15 (m, 8H), 0.78 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C): δ 160.3 (t, $^2J_{CF}$ = 29.6 Hz), 142.6, 136.5, 134.0, 133.3 (t, $^3J_{CF}$ = 9.5 Hz), 128.9, 125.6, 124.9, 124.5 (t, $^2J_{CF}$ = 27.2 Hz), 113.0 (t, $^1J_{CF}$ = 247.9 Hz), 81.6, 66.3, 66.2, 50.0, 46.4, 44.3, 43.04, 42.89, 38.2, 36.5, 30.4, 29.2, 26.9, 25.9, 23.0, 11.0; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –89.1 (s, 2F); IR ($CHCl_3$) 2926 (OH), 1672 (C=O) cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{26}H_{32}BrF_2NNaO_3$ 546.1431, found 546.1415.

Analytical data for 3ia: 76.9 mg, 73%; colorless oil; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 8.63 (d, 1H, *J* = 2.0 Hz), 8.59 (dd, 1H, *J* = 4.8, 1.6 Hz), 7.71 (dt, 1H, *J* = 7.6, 2.0 Hz), 7.31 (dd, 1H, *J* = 8.0, 4.8 Hz), 6.81 (t, 1H, *J* = 12.6 Hz), 3.66 (t, 2H, *J* = 4.8 Hz), 3.62 (t, 2H, *J* = 4.6 Hz), 3.55 (t, 2H, *J* = 4.8 Hz), 3.51 (t, 2H, *J* = 4.8 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C): δ 160.3 (t, $^2J_{CF}$ = 29.1 Hz), 150.4, 148.5, 135.7, 133.9, 128.3 (t, $^3J_{CF}$ = 7.7 Hz), 127.0 (t, $^2J_{CF}$ = 25.3 Hz), 122.7, 113.5 (t, $^1J_{CF}$ = 252.7 Hz), 66.4, 46.3 (t, $^4J_{CF}$ = 5.2 Hz), 43.3; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –90.2 (s, 2F); IR ($CHCl_3$) 1668 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{13}H_{14}BrF_2N_2O_2$ 347.0207, found 347.0194.



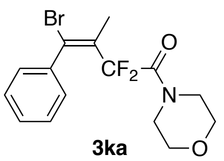
3ia

Analytical data for 3ja: 45.6 mg, 42%; colorless solid (mp 104.2–107.0 °C); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.54 (dd, 1H, *J* = 3.6, 1.6 Hz), 7.31 (dd, 1H, *J* = 4.8, 2.8 Hz), 7.18 (dd, 1H, *J* = 4.8, 1.6 Hz), 6.58 (t, 1H, *J* = 11.2 Hz), 3.62 (t, 2H, *J* = 4.8 Hz), 3.57 (t, 2H, *J* = 4.8 Hz), 3.50 (t, 2H, *J* = 4.6 Hz), 3.40 (t, 2H, *J* = 4.8 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C): δ 160.2 (t, $^2J_{CF}$ = 29.6 Hz), 136.3, 128.2, 127.9, 127.1 (t, $^3J_{CF}$ = 10.0 Hz), 125.8, 125.3 (t, $^2J_{CF}$ = 28.2 Hz), 113.0 (t, $^1J_{CF}$ = 247.4 Hz), 66.4, 66.2, 46.7, 43.1; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –88.9 (s, 2F); IR ($CHCl_3$) 1676 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{12}H_{13}BrF_2NO_2S$ 351.9818, found 351.9814.



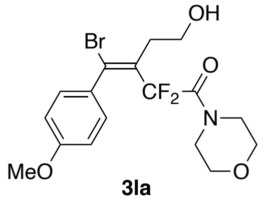
3ja

Analytical data for 3ka: 89.4 mg, 82%; colorless oil; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.36–7.27 (m, 5H), 3.60 (t, 2H, *J* = 4.8 Hz), 3.57 (t, 2H, *J* = 4.8 Hz), 3.37 (t, 2H, *J* = 4.6 Hz), 3.30 (t, 2H, *J* = 4.8 Hz), 2.19 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C): δ 160.5 (t, $^2J_{CF}$ = 30.0 Hz), 139.0, 130.5 (t, $^2J_{CF}$ = 23.3 Hz), 129.3 (t, $^3J_{CF}$ = 7.7 Hz), 129.1, 128.6, 127.9, 114.8 (t, $^1J_{CF}$ = 252.7 Hz), 66.3, 66.2, 46.2, 42.8, 19.9; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –91.5 (s, 2F); IR ($CHCl_3$) 1682 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{15}H_{17}BrF_2NO_2$ 360.0411, found 360.0431.



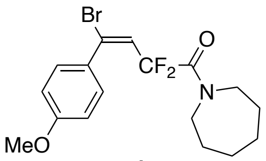
3ka

Analytical data for 3la: 56.4 mg, 45%; colorless solid (mp 131.1–133.9 °C); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.22 (d, 2H, J = 8.8 Hz), 6.83 (d, 2H, J = 8.4 Hz), 3.91 (q, 2H, J = 6.4 Hz), 3.81 (s, 3H), 3.59 (t, 2H, J = 4.8 Hz), 3.52 (t, 2H, J = 4.6 Hz), 3.43 (t, 2H, J = 4.6 Hz), 3.38 (t, 2H, J = 4.8 Hz), 2.95 (t, 2H, J = 6.4 Hz), 2.61 (t, 1H, J = 6.6 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 161.4 (t, $^{2}J_{CF}$ = 30.5 Hz), 160.0, 132.2 (t, $^{3}J_{CF}$ = 7.2 Hz), 132.0 (t, $^{2}J_{CF}$ = 23.8 Hz), 131.6, 130.2, 115.5 (t, $^{1}J_{CF}$ = 255.1 Hz), 113.2, 66.4, 66.3, 60.3, 55.3, 46.4 (t, $^{4}J_{CF}$ = 4.8 Hz), 43.3, 36.9; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –89.6 (s, 2F); IR ($CHCl_3$) 3480 (OH), 1656 (C=O) cm^{-1}; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{17}H_{20}BrF_2NNaO_4$ 442.0442, found 442.0433.



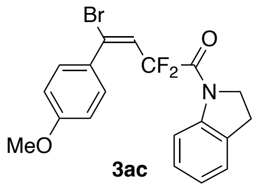
3la

Analytical data for 3ab: 94.4 mg, 80%; pale-yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.35 (d, 2H, J = 8.8 Hz), 6.85 (d, 2H, J = 8.8 Hz), 6.58 (t, 1H, J = 11.4 Hz), 3.82 (s, 3H), 3.43 (t, 2H, J = 6.2 Hz), 3.24 (t, 2H, J = 5.6 Hz), 1.70–1.58 (m, 4H), 1.54–1.47 (m, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 161.4 (t, $^{2}J_{CF}$ = 29.1 Hz), 160.5, 132.3 (t, $^{3}J_{CF}$ = 9.6 Hz), 130.2, 129.5, 125.2 (t, $^{2}J_{CF}$ = 27.7 Hz), 113.4 (t, $^{1}J_{CF}$ = 248.9 Hz), 113.2, 55.2, 47.8, 29.3, 27.3, 26.1, 25.7; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –89.4 (s, 2F); IR ($CHCl_3$) 1660 (C=O) cm^{-1}; HRMS (DART) m/z $[M+H]^+$ calcd for $C_{17}H_{21}BrF_2NO_2$ 388.0724, found 388.0745.



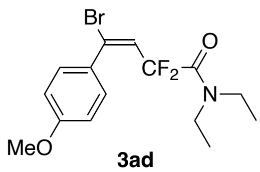
3ab

Analytical data for 3ac: 104.7 mg, 83%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.92 (d, 1H, J = 8.0 Hz), 7.32 (d, 2H, J = 8.8 Hz), 7.21–7.15 (m, 2H), 7.07 (td, 1H, J = 7.4, 0.8 Hz), 6.77 (d, 2H, J = 8.8 Hz), 6.63 (t, 1H, J = 11.4 Hz), 4.11 (t, 2H, J = 8.2 Hz), 3.75 (s, 3H), 3.13 (t, 2H, J = 8.4 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 160.6, 159.6 (t, $^{2}J_{CF}$ = 30.0 Hz), 142.2, 133.2 (t, $^{3}J_{CF}$ = 9.6 Hz), 131.3, 129.9, 129.4, 127.3, 125.0, 124.50 (t, $^{2}J_{CF}$ = 27.2 Hz), 117.7, 113.3, 113.1 (t, $^{1}J_{CF}$ = 249.8 Hz), 55.2, 47.8 (t, $^{4}J_{CF}$ = 5.3 Hz), 28.5; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –93.0 (s, 2F); IR ($CHCl_3$) 1673 (C=O) cm^{-1}; HRMS (DART) m/z $[M+NH_4]^+$ calcd for $C_{19}H_{20}BrF_2N_2O_2$ 425.0676, found 425.0654.



3ac

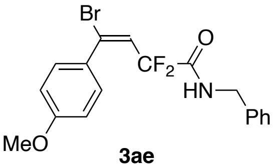
Analytical data for 3ad: 98.1 mg, 89%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.36 (d, 2H, J = 8.8 Hz), 6.84 (d, 2H, J = 8.4 Hz), 6.59 (t, 1H, J = 11.6 Hz), 3.82 (s, 3H), 3.33 (q, 2H, J = 7.2 Hz), 3.21 (q, 2H, J = 7.2 Hz), 1.12 (t, 3H, J = 7.2 Hz), 0.96 (t, 3H, J = 7.2 Hz);



3ad

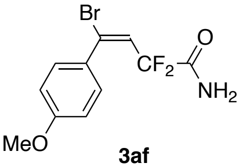
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C): δ 161.2 (t, $^2J_{CF}$ = 29.6 Hz), 160.6, 132.4 (t, $^3J_{CF}$ = 9.1 Hz), 130.3, 129.5, 125.1 (t, $^2J_{CF}$ = 26.7 Hz), 113.4 (t, $^1J_{CF}$ = 249.3 Hz), 113.2, 55.2, 42.0 (t, $^4J_{CF}$ = 4.3 Hz), 41.3, 13.8, 12.1; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –89.6 (s, 2F); IR ($CHCl_3$) 1661 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{15}H_{19}BrF_2NO_2$ 362.0567, found 362.0560.

Analytical data for 3ae: 93.1 mg, 78%; colorless solid (mp 101.1–102.1 °C); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.37–7.30 (m, 3H), 7.32 (d, 2H, *J* = 8.4 Hz), 7.17 (d, 2H, *J* = 6.4 Hz), 6.80 (d, 2H, *J* = 8.4 Hz), 6.53 (t, 1H, *J* = 12.2 Hz), 6.22 (br s, 1H), 4.28 (d, 2H, *J* = 5.6 Hz), 3.80 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C): δ 162.8 (t, $^2J_{CF}$ = 29.6 Hz), 160.4, 136.3, 133.8 (t, $^3J_{CF}$ = 8.6 Hz), 130.0, 129.9, 128.8, 127.9, 127.8, 124.4 (t, $^2J_{CF}$ = 26.7 Hz), 113.3, 112.6 (t, $^1J_{CF}$ = 251.3 Hz), 55.2, 43.6; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –95.6 (s, 2F); IR ($CHCl_3$) 3439 (NH), 1706 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{18}H_{20}BrF_2N_2O_2$ 413.0676, found 413.0662.



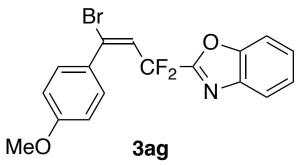
3ae

Analytical data for 3af: 82.5 mg, 89%; colorless solid (mp 77.1–78.3 °C); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.36 (d, 2H, *J* = 8.4 Hz), 6.87 (d, 2H, *J* = 8.8 Hz), 6.50 (t, 1H, *J* = 12.4 Hz), 5.93 (br s, 1H), 5.40 (br s, 1H), 3.83 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C): δ 165.5 (t, $^2J_{CF}$ = 30.5 Hz), 160.6, 134.2 (t, $^3J_{CF}$ = 8.1 Hz), 130.1, 129.9, 123.7 (t, $^2J_{CF}$ = 26.2 Hz), 113.4, 112.3 (t, $^1J_{CF}$ = 251.3 Hz), 55.3; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –95.6 (s, 2F); IR ($CHCl_3$) 3524 (NH), 3407 (NH), 1727 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{11}H_{14}BrF_2N_2O_2$ 323.0207, found 323.0219.



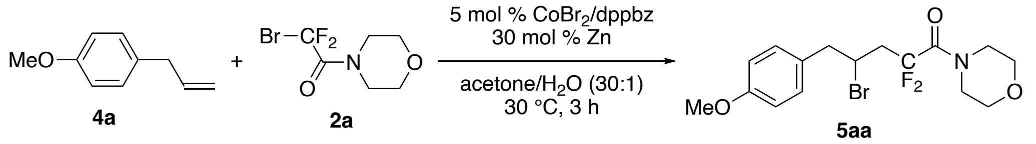
3af

Analytical data for 3ag: 96.5 mg, 83%; colorless oil; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.70 (dd, 1H, *J* = 7.6, 1,.2 Hz), 7.48 (d, 1H, *J* = 7.2 Hz), 7.40 (td, 1H, *J* = 7.6, 1.6 Hz), 7.36 (td, 1H, *J* = 7.6, 1.2 Hz), 7.22 (d, 2H, *J* = 8.8 Hz), 6.80 (t, 1H, *J* = 10.2 Hz), 6.61 (d, 2H, *J* = 8.8 Hz), 3.65 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C): δ 160.3, 156.7 (t, $^2J_{CF}$ = 33.9 Hz), 150.3, 139.7, 134.8 (t, $^3J_{CF}$ = 10.0 Hz), 129.7, 129.2, 126.7, 125.1, 125.0 (t, $^2J_{CF}$ = 28.6 Hz), 121.0, 113.1, 112.0 (t, $^1J_{CF}$ = 239.3 Hz), 111.1, 55.1; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –87.6 (s, 2F); HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{17}H_{13}BrF_2NO_2$ 380.0098, found 380.0111.



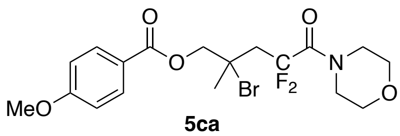
3ag

Atom Transfer Radical Addition of Bromodifluoroacetamides to Alkenes

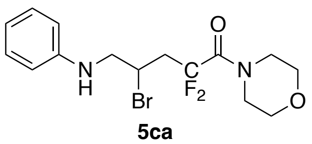


Representative procedure – Synthesis of 5aa: In a similar manner with the representative procedure for the reaction of terminal alkynes, the reaction of terminal alkene **4a** (45.00 mg, 0.304 mmol) with amide **2a** (110.6 mg, 0.453 mmol) was performed using $CoBr_2$ (3.00 mg, 0.0137 mmol), dppbz (6.91 mg, 0.0155 mmol), and Zn powder (5.70 mg, 0.087 mmol) in acetone/H_2O (30:1, 0.6 mL) at 30 °C under an Ar atmosphere for 3 h. Purification by silica gel column chromatography (hexane/AcOEt 100:0~8:1) to afford **5aa** (91.3 mg, 77%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.15 (d, 2H, J = 8.4 Hz), 6.86 (d, 2H, J = 8.8 Hz), 4.48–4.40 (m, 1H), 3.80 (s, 3H), 3.74–3.61 (m, 8H), 3.21 (dd, 1H, J = 14.4, 6.4 Hz), 3.15 (dd, 1H, J = 14.4, 8.0 Hz), 2.95–2.73 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 161.3 (t, $^2J_{CF}$ = 28.6 Hz), 158.6, 130.3, 129.6, 118.2 (t, $^1J_{CF}$ = 255.6 Hz), 113.8, 66.60, 66.56, 55.1, 46.4 (t, $^3J_{CF}$ = 6.2 Hz), 46.2, 45.0, 43.4, 42.5 (t, $^2J_{CF}$ = 21.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –98.4 (dd, 1F, J = 300.4, 22.9 Hz), –99.8 (dd, 1F, J = 277.5, 22.9 Hz); IR ($CHCl_3$) 1666 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{16}H_{24}BrF_2N_2O_3$ 409.0938, found 409.0922.

Analytical data for 5ba: 94.1 mg, 69% (including trace amounts of *N*-(difluoroacetyl)morpholine); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 8.03 (d, 2H, J = 9.2 Hz), 6.95 (d, 2H, J = 8.4 Hz), 4.57 (d, 1H, J = 12.0 Hz), 4.53 (d, 1H, J = 12.0 Hz), 3.87 (s, 3H), 3.76–3.57 (m, 8H), 3.24–2.98 (m, 2H), 2.01 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 165.2, 163.6, 161.3 (t, $^2J_{CF}$ = 28.6 Hz), 131.7, 121.7, 118.3 (t, $^1J_{CF}$ = 256.5 Hz), 113.7, 71.7, 66.5, 59.0, 55.4, 46.5 (t, $^3J_{CF}$ = 6.2 Hz), 44.5 (t, $^2J_{CF}$ = 21.0 Hz), 43.4, 29.2; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –97.7 (dd, 1F, J = 277.5, 22.9 Hz), –98.6 (dd, 1F, J = 277.1, 22.9 Hz); IR ($CHCl_3$) 1714 (C=O), 1667 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{18}H_{26}BrF_2N_2O_5$ 469.0973, found 469.0986.

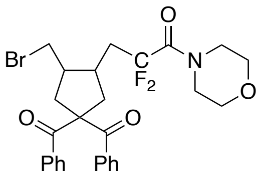


Analytical data for 5ca: 46.9 mg, 40%; colorless paste; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.23–7.17 (m, 2H), 6.76 (t, 1H, J = 7.2 Hz), 6.68–6.63 (m, 2H), 4.50 (quint, 1H, J = 6.2 Hz), 4.17 (br s, 1H), 3.76–3.61 (m, 9H), 3.47 (dd, 1H, J = 12.8, 7.2 Hz), 3.06–2.80 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 161.1 (t, $^2J_{CF}$ =



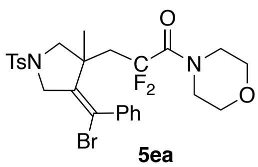
28.6 Hz), 146.8, 129.4, 118.4 (t, $^{1}J_{CF}$ = 252.7 Hz), 118.3, 113.2, 66.64, 66.57, 50.8, 46.4 (t, $^{3}J_{CF}$ = 6.2 Hz), 45.3 (t, $^{4}J_{CF}$ = 3.4 Hz), 43.4, 41.3 (t, $^{2}J_{CF}$ = 22.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –97.8 (dd, 1F, *J* = 300.4, 34.6 Hz), –99.9 (dd, 1F, *J* = 300.4, 34.6 Hz); IR ($CHCl_3$) 1666 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{15}H_{20}BrF_2N_2O_2$ 377.0676, found 377.0698.

Analytical data for 5da: 122.1 mg, 74% (14:1); colorless paste; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.80–7.75 (m, 4H), 7.43–7.37 (m, 2H), 7.29 (t, 4H, *J* = 7.8 Hz), 3.77–3.67 (m, 8H), 3.66–3.60 (m, 1H), 3.51 (dd, 1H, *J* = 10.0, 4.8 Hz), 3.31 (t, 1H, *J* = 9.8 Hz), 2.85 (dd, 1H, *J* = 12.8, 6.0 Hz), 2.77 (d, 1H, *J* = 5.6 Hz), 2.72–2.58 (m, 2H), 2.53 (dd, 1H, *J* = 12.8, 8.8 Hz), 2.50–2.10 (m, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, 25 °C): δ 198.3, 197.5, 161.6 (t, $^{2}J_{CF}$ = 29.1 Hz), 135.4, 135.0, 133.14, 133.09, 129.19, 129.16, 128.5, 119.3 (t, $^{1}J_{CF}$ = 254.1 Hz), 68.0, 66.66, 66,57, 46.4 (t, $^{3}J_{CF}$ = 5.8 Hz), 45.7, 43.3, 39.3, 38.3, 36.3, 33.4 (t, $^{2}J_{CF}$ = 22.4 Hz), 33.3; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –98.7 (d, 1F, *J* = 300.4 Hz), –100.7 (d, 1F, *J* = 300.4 Hz); IR ($CHCl_3$) 1665 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{27}H_{29}BrF_2NO_4$ 550.1228, found 550.1253.



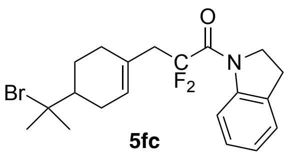
5da

Analytical data for 5ea: 67.1 mg, 50%; colorless paste; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.74 (d, 2H, *J* = 8.4 Hz), 7.39 (d, 2H, *J* = 8.4 Hz), 7.36–7.32 (m, 3H), 7.25–7.21 (m, 2H), 3.96 (d, 1H, *J* = 14.8 Hz), 3.91 (d, 1H, *J* = 15.6 Hz), 3.75–3.55 (m, 8H), 3.42 (d, 1H, *J* = 9.6 Hz), 3.11 (d, 1H, *J* = 9.6 Hz), 2.48 (s, 3H), 2.32–2.02 (m, 2H), 1.08 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, 25 °C): δ 161.5 (t, $^{2}J_{CF}$ = 29.1 Hz), 143.9, 139.0, 131.4, 129.8, 129.0, 128.7, 128.5, 128.0, 118.9 (t, $^{1}J_{CF}$ = 255.1 Hz), 117.0, 66.5, 60.34, 60.29, 56.0, 46.4 (t, $^{3}J_{CF}$ = 6.2 Hz), 45.1, 43.4, 40.7 (t, $^{2}J_{CF}$ = 21.5 Hz), 24.6, 21.6; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –96.7 (d, 1F, *J* = 288.8 Hz), –97.8 (d, 1F, *J* = 288.8 Hz); IR ($CHCl_3$) 1666 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{26}H_{30}BrF_2N_2O_4S$ 586.1051, found 5869.1040.



5ea

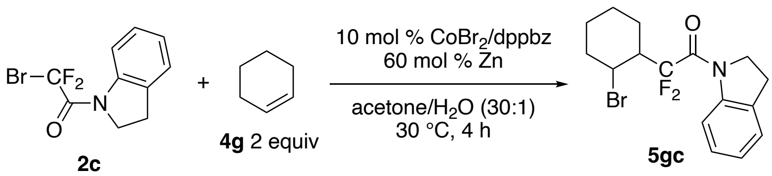
Analytical data for 5fc: 41.3 mg, 33% (containing **5fc'**); colorless solid (mp 141.1–142.8 °C); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 8.21 (d, 1H, *J* = 8.4 Hz), 7.26–7.21 (m, 2H), 7.10 (t, 1H, *J* = 7.2 Hz), 5.69−5.64 (m, 1H), 4.33 (t, 2H, *J* = 8.4 Hz), 3.20 (t, 2H, *J* = 8.4 Hz), 2.98 (t, 2H, *J* = 18.6 Hz), 2.34–2.18 (m, 3H), 2.11–1.96 (m, 2H), 1.80 (s, 3H), 1.74 (s, 3H), 1.71–1.61 (m, 1H), 1.43 (qd, 1H, *J* = 12.0, 6.0 Hz); $^{13}C\{^{1}H\}$ NMR



5fc

(100 MHz, $CDCl_3$, 25 °C): δ 161.5 (t, $^2J_{CF}$ = 30.6 Hz), 142.6, 131.6, 128.9, 127.5, 125.0, 124.6, 118.4 (t, $^1J_{CF}$ = 279.3 Hz), 117.9, 72.8, 48.0 (t, $^4J_{CF}$ = 7.6 Hz), 46.9, 41.5 (t, $^2J_{CF}$ = 23.4 Hz), 32.4, 31.7, 30.5, 28.7, 28.5, 25.9; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –102.4 (d, 1F, J = 22.9 Hz), –102.5 (d, 1F, J = 35.0 Hz); IR ($CHCl_3$) 1669 (C=O) cm^{-1}; HRMS (DART) m/z $[M+H]^+$ calcd for $C_{20}H_{25}BrF_2NO$ 412.1088, found 412.1063.

The ^1H and ^{13}C NMR signals of **5fc'** are obscure because of extensive overlaps with those of **5fc**. The methyl groups of the isopropyl substituent were observed as a pair of doublet peaks [δ 1.08 (d, 3H, J = 6.4 Hz) and 1.05 (d, 3H, J = 6.4 Hz)] in the ^1H NMR spectrum and a pair of singlet peaks (δ 18.8 and 18.4 ppm) in the ^{13}C NMR spectrum. The vinyl proton was observed as a multiplet peak at δ 5.58 ppm. In addition, three singlet peaks of Csp^3 were observed at δ 39.7, 39.4, and 35.3 ppm.

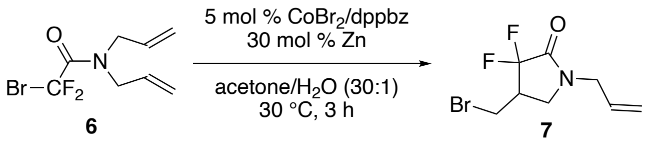


Synthesis of 5gc: In a similar manner with the representative procedure for the reaction of terminal alkynes, the reaction of cyclohexene **4g** (40.6 mg, 0.414 mmol) with amide **2c** (44.4 mg, 0.201 mmol) was performed using $CoBr_2$ (4.00 mg, 0.0183 mmol), dppbz (9.20 mg, 0.0206 mmol), and Zn powder (7.66 mg, 0.117 mmol) in acetone/H_2O (30:1, 0.45 mL) at 30 °C under an Ar atmosphere for 4 h. Purification by silica gel column chromatography (hexane/AcOEt 100:0~90:1) to afford **5gc** as diastereomers. The minor diastereomer was further purified by recrystallization ($CHCl_3$/hexane).

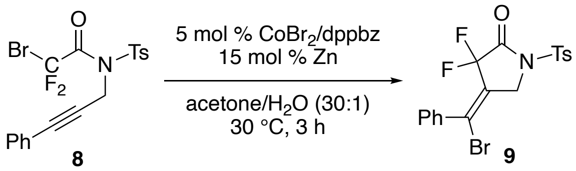
Analytical data for major isomer of 5gc: 19.9 mg, 28%; colorless oil; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 8.24 (d, 1H, J = 8.4 Hz), 7.26–7.21 (m, 2H), 7.10 (t, 1H, J = 7.2 Hz), 4.40–4.34 (m, 2H), 4.30 (td, 1H, J = 9.6, 4.4 Hz), 3.21 (t, 2H, J = 8.2 Hz), 3.02 (sextd, 1H, J = 9.6, 4.0 Hz), 2.40–2.30 (m, 1H), 2.20–2.14 (m, 1H), 2.00–1.44 (m, 3H), 1.62–1.51 (m, 1H), 1.48–1.38 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C): δ 161.6 (t, $^2J_{CF}$ = 29.6 Hz), 142.9, 131.6, 127.5, 125.0, 124.6, 118.6 (dd, $^1J_{CF}$ = 261.2, 254.5 Hz), 118.1, 49.1 (t, $^4J_{CF}$ = 3.8 Hz), 48.24 (t, $^2J_{CF}$ = 21.5 Hz), 48.23 (t, $^3J_{CF}$ = 5.7 Hz), 37.6, 28.7, 25.01, 24.97, 23.9; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –102.0 (d, 1F, J = 277.1 Hz), –110.3 (d, 1F, J = 277.5 Hz); IR ($CHCl_3$) 1665 (C=O) cm^{-1}; HRMS (DART) m/z $[M+H]^+$ calcd for $C_{16}H_{19}BrF_2NO$ 358.0618, found 358.0620.

Analytical data for minor isomer of 5gc: 15.0 mg, 21%; colorless solid (mp 125.2–126.8 °C); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 8.21 (d, 1H, J = 7.6 Hz), 7.26–7.21 (m, 2H), 7.11 (t, 1H, J = 7.2 Hz), 4.86–4.82 (m, 1H), 4.48–4.29 (m, 2H), 3.20 (t, 2H, J = 8.2 Hz), 2.91–2.78 (m, 1H), 2.21–2.13 (m, 1H), 1.98–1.79 (m, 4H), 1.65–1.58 (m, 1H), 1.50–1.36 (m, 1H), 1.34–1.22 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C): δ 161.0 (t, $^2J_{CF}$ = 30.5 Hz), 142.7, 131.9, 127.5, 125.2, 124.7, 118.2 (t, $^1J_{CF}$ = 258.9 Hz), 118.0, 50.2 (dd, $^3J_{CF}$ = 4.8, 2.8 Hz), 48.19 (t, $^3J_{CF}$ = 8.6 Hz), 45.5 (dd, $^2J_{CF}$ = 22.9, 20.0 Hz), 35.5, 28.7, 25.0, 20.8 (t, $^4J_{CF}$ = 3.3 H), 20.5; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –108.1 (d, 1F, J = 300.4 Hz), –110.3 (d, 1F, J = 277.1 Hz); IR ($CHCl_3$) 1663 (C=O) cm^{-1}; HRMS (DART) m/z $[M+H]^+$ calcd for $C_{16}H_{19}BrF_2NO$ 358.0618, found 358.0643.

Intramolecular ATRA



Synthesis of lactam 7: In a similar manner with the representative procedure for the reaction of terminal alkenes, the reaction of amide **6** (77.7 mg, 0.306 mmol) was performed using $CoBr_2$ (3.50 mg, 0.0160 mmol), dppbz (6.70 mg, 0.0150 mmol), and Zn powder (6.70 mg, 0.102 mmol) in acetone/H_2O (30:1, 0.6 mL) at 30 °C under an Ar atmosphere for 3 h. Purification by silica gel column chromatography (hexane/AcOEt 50:0~6:1) to afford **7** (55.9 mg, 72%) as a colorless oil. The following spectral data were in good accordance with those reported:[2d] ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 5.73 (ddt, 1H, J = 16.8, 10.0, 6.4 Hz), 5.32 (d, 1H, J = 10.0 Hz), 5.28 (d, 1H, J = 16.8 Hz), 3.99 (t, 1H, J = 6.4 Hz), 3.69 (dd, 2H, J = 10.8, 4.8 Hz), 3.61 (ddd, 1H, J = 10.0, 7.6, 2.0 Hz), 3.39 (t, 1H, J = 10.4 Hz), 3.21 (ddd, 1H, J = 9.6, 6.8, 2.0 Hz), 3.07–2.91 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C): δ 162.4 (t, $^2J_{CF}$ = 30.0 Hz), 130.1, 120.0, 116.1 (dd, $^1J_{CF}$ = 255.5, 250.7 Hz), 46.8 (d, $^3J_{CF}$ = 5.8 Hz), 45.9, 42.3 (dd, $^2J_{CF}$ = 21.9, 20.0 Hz), 25.9 (d, $^3J_{CF}$ = 10.5 H), 20.5.

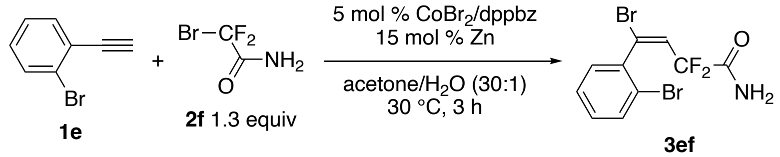


Synthesis of lactam 9: In a similar manner with the representative procedure for the reaction of terminal alkenes, the reaction of amide **8** (132.6 mg, 0.300 mmol) was performed using $CoBr_2$ (3.00 mg, 0.0137 mmol), dppbz (6.93 mg, 0.0155 mmol), and Zn powder (5.72 mg, 0.0876 mmol) in acetone/H_2O (30:1, 0.9 mL) at 30 °C under an Ar atmosphere for 3 h. Purification by silica gel column chromatography (hexane/AcOEt 20:0~2:1) to afford **9** (86.89 g, 66%) as a colorless solid (mp 139.2–141.7 °C): ^1H NMR

(400 MHz, $CDCl_3$, 25 °C): δ 8.01 (d, 2H, J = 8.8 Hz), 7.46–7.35 (m, 7H), 4.56 (s, 2H), 2.48 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C): δ 160.6 (t, $^2J_{CF}$ = 31.9 Hz), 146.7, 136.4, 135.7, 133.4, 130.5, 130.1, 128.4, 128.2, 123.4 (t, $^3J_{CF}$ = 18.6 Hz), 109.6 (t, $^1J_{CF}$ = 252.2 Hz), 49.7, 21.7; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –95.5 (s, 2F); IR ($CHCl_3$) 1769 (C=O) cm^{-1}; HRMS (DART) m/z $[M+NH_4]^+$ calcd for $C_{18}H_{18}BrF_2N_2O_3S$ 462.0163, found 462.0144.

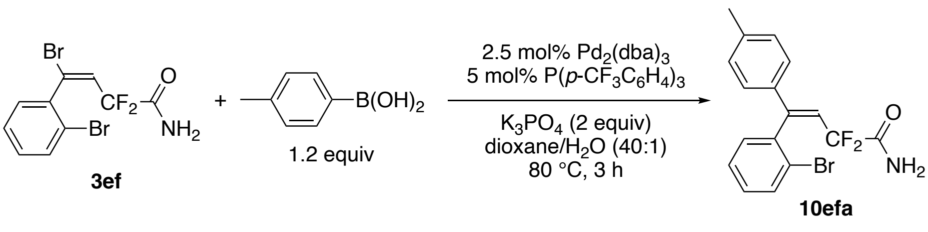
Synthetic Applications

Reaction of (*o*-bromophenyl)acetylene 1e with bromodifluoroacetamide 2f



According to the representative procedure, the reaction of (*o*-bromophenyl)acetylene **1e** (56.2 mg, 0.31 mmol) with bromodifluoroacetamide **2f** (70.0 mg, 0.40 mmol) was performed using $CoBr_2$ (4.0 mg, 0.018 mmol) and dppbz (7.1 mg, 0.016 mmol) in acetone/H_2O (30:1, 0.6 mL) at room temperature under an Ar atmosphere for 3 h. Purification by silica gel column chromatography (hexane/AcOEt 20:1~3:1) to afford **3ef** (98.1 mg, 89%) as a colorless solid (mp 53.1–55.3 °C): ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.60 (d, 1H, J = 7.6 Hz), 7.36–7.32 (m, 2H), 7.23 (ddd, 1H, J = 7.6, 6.0, 3.2 Hz), 6.63 (dd, 1H, J = 13.6, 11.2 Hz), 5.94 (br s, 1H), 5.48 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 165.2 (t, $^2J_{CF}$ = 30.1 Hz), 138.3, 132.8, 131.0 (t, $^3J_{CF}$ = 8.1 Hz), 130.8, 129.7, 127.2, 126.3 (t, $^2J_{CF}$ = 25.8 Hz), 121.6, 111.9 (t, $^1J_{CF}$ = 252.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –98.2 (d, 1F, J = 265.8 Hz), –101.8 (d, 1F, J = 254.2 Hz); IR ($CHCl_3$) 1727 (C=O) cm^{-1}; HRMS (DART) m/z $[M+NH_4]^+$ calcd for $C_{10}H_{11}Br_2F_2N_2O$ 370.9206, found 370.9233.

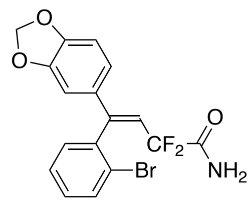
Suzuki–Miyaura coupling of ATRA products



Representative procedure – Synthesis of 10efa: A solution of **3ef** (84.9 mg, 0.24 mmol), *p*-tolylboronic acid (39.7 mg, 0.29 mmol), $Pd_2(dba)_3$ (5.9 mg, 0.0064 mmol), $P(p\text{-}CF_3C_6H_4)_3$ (6.6 mg, 0.014 mmol), and K_3PO_4 (112.3 mg, 0.53 mmol) in dioxane/H_2O

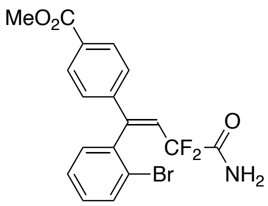
(40:1, 2.3 mL) was degassed at −78 °C and then stirred at 80 °C under an Ar atmosphere for 3 h. After cooling to room temperature, the reaction mixture was diluted with H_2O (10 mL) and was extracted with AcOEt (3×7 mL). The combined organic extract was washed with brine (10 mL), dried over anhydrous Na_2SO_4. The solvents were evaporated *in vacuo,* and the obtained crude product was purified by silica gel column chromatography (hexane/AcOEt 10:1~7:1) to afford **10efa** (75.1 mg, 86%) as a colorless solid (mp 64.7–66.5 °C): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.60 (dd, 1H, J = 8.0, 0.8 Hz), 7.37 (td, 1H, J = 7.6, 1.2 Hz), 7.31 (dd, 1H, J = 7.6, 2.0 Hz), 7.25 (td, 1H, J = 7.6, 2.0 Hz), 7.16 (d, 2H, J = 8.8 Hz), 7.12 (d, 2H, J = 8.0 Hz), 6.45 (dd, 1H, J = 14.4, 12.8 Hz), 5.90 (br s, 1H), 5.37 (br s, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 166.3 (t, $^2J_{CF}$ = 31.0 Hz), 148.9 (t, $^3J_{CF}$ = 7.2 Hz), 139.3, 138.2, 135.1, 132.7, 131.3, 129.6, 129.2, 126.9, 126.8, 123.2, 118.4 (t, $^2J_{CF}$ = 25.8 Hz), 113.5 (t, $^1J_{CF}$ = 248.9 Hz), 21.2; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –95.9 (d, 1F, J = 265.8 Hz), –98.5 (d, 1F, J = 265.8 Hz); IR ($CHCl_3$) 1724 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{17}H_{18}BrF_2N_2O$ 383.0571, found 383.0587.

Analytical data for 10efb: 69.3 mg, 76%; colorless solid (mp 85.0–87.2 °C): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.60 (dd, 1H, J = 8.4, 0.8 Hz), 7.37 (td, 1H, J = 7.2, 0.8 Hz), 7.31–7.23 (m, 2H), 6.80 (d, 1H, J = 2.0 Hz), 6.73 (d, 1H, J = 8.4 Hz), 6.69 (dd, 1H, J = 8.4, 2.0 Hz), 6.36 (dd, 1H, J = 14.0, 12.4 Hz), 5.98 (d, 1H, J = 1.2 Hz), 5.97 (d, 1H, J = 1.6 Hz), 5.89 (br s, 1H), 5.33 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 165.7 (t, $^2J_{CF}$ = 31.0 Hz), 148.6, 148.5, 148.1, 138.3, 132.8, 132.4, 131.4, 129.7, 126.8, 123.3, 121.8, 118.0 (t, $^2J_{CF}$ = 25.8 Hz), 113.5 (t, $^1J_{CF}$ = 249.4 Hz), 108.2, 107.1, 101.5; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –95.7 (d, 1F, J = 277.5 Hz), –98.3 (d, 1F, J = 265.8 Hz); IR ($CHCl_3$) 1724 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{17}H_{16}BrF_2N_2O_3$ 413.0312, found 413.0306.



10efb

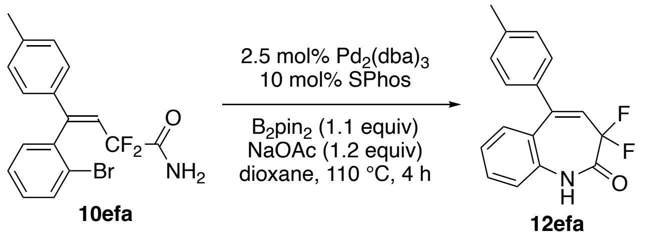
Analytical data for 10efc: 80.2 mg, 77% (including trace amounts of **7efc**); yellow paste: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.98 (d, 2H, J = 8.8 Hz), 7.62 (dd, 1H, J = 8.0, 0.8 Hz), 7.41 (td, 1H, J = 8.0, 0.8 Hz), 7.36–7.33 (m, 1H), 7.34 (d, 2H, J = 8.8 Hz), 7.29 (td, 1H, J = 8.0, 1.6 Hz), 6.55 (dd, 1H, J = 13.6, 12.4 Hz), 5.93 (br s, 1H), 5.39 (br s, 1H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 166.5, 165.9 (t, $^2J_{CF}$ = 30.1 Hz), 148.2 (t, $^3J_{CF}$ = 7.2 Hz), 142.4, 137.5, 132.9, 131.3, 130.5, 130.0, 129.7, 127.1, 126.9, 121.4 (t, $^2J_{CF}$ = 25.3 Hz), 113.2 (t, $^1J_{CF}$ = 249.6 Hz), 52.2; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –96.5 (d, 1F, J = 265.8 Hz), –98.9 (dd, 1F, J = 265.6, 23.3



10efc

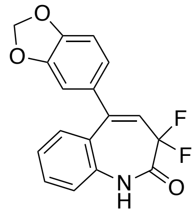
Hz); IR ($CHCl_3$) 1722 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{18}H_{18}BrF_2N_2O_3$ 427.0469, found 427.0459.

Intramolecular C–N coupling of alkenyldifluoroacetamides 6



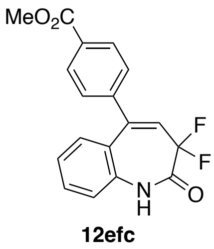
Representative procedure – Synthesis of 12efa: To a solution of **10efa** (55.7 mg, 0.30 mmol), B_2pin_2 (45.2 mg, 0.18 mmol), $Pd_2(dba)_3$ (3.6 mg, 0.0039 mmol), SPhos (6.4 mg, 0.016 mmol), and NaOAc (14.8 mg, 0.18 mmol) in dioxane (0.4 mL) was degassed at −78 °C and then stirred at 110 °C under an Ar atmosphere for 4 h. The reaction mixture was degassed at −78 °C and then stirred at 40 °C for 3 hours. After cooling to room temperature, the reaction mixture was diluted with H_2O (10 mL) and was extracted with AcOEt (3×7 mL). The combined organic extract was washed with brine (10 mL), dried over anhydrous Na_2SO_4. The solvents were evaporated *in vacuo,* and the obtained crude product was purified by silica gel column chromatography (hexane/AcOEt 20:1~10:1) to afford **12efa** (33.2 mg, 77%) as a colorless solid (mp 191.8–193.2 °C): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 8.58 (br s, 1H), 7.42 (td, 1H, *J* = 7.6, 1.6 Hz), 7.24–7.17 (m, 6H), 7.13 (td, 1H, *J* = 7.6, 1.6 Hz), 6.18 (t, 1H, *J* = 11.0 Hz), 240 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 164.6 (t, $^2J_{CF}$ = 34.4 Hz), 147.8 (t, $^3J_{CF}$ = 10.5 Hz), 139.4, 137.2, 135.2, 131.5, 130.2, 129.2, 129.1, 128.6, 124.3, 121.5, 120.7 (t, $^2J_{CF}$ = 28.6 Hz), 111.8 (t, $^1J_{CF}$ = 245.1 Hz), 21.2; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –108.0 (s, 2F); IR ($CHCl_3$) 1708 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{17}H_{17}F_2N_2O$ 303.1309, found 303.1313.

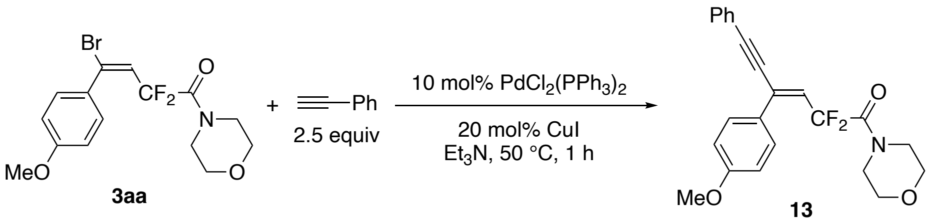
Analytical data for 12efb: 21.5 mg, 69%; colorless solid (mp 188.1–190.2 °C): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 8.13 (br s, 1H), 7.42 (td, 1H, *J* = 7.8, 2.0 Hz), 7.27–7.24 (m, 1H), 7.18–7.13 (m, 2H), 6.83 (d, 2H, *J* = 1.2 Hz), 6.74 (s, 1H), 6.15 (t, 1H, *J* = 10.8 Hz), 6.02 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 164.4 (t, $^2J_{CF}$ = 34.8 Hz), 148.6, 147.8, 147.3 (t, $^3J_{CF}$ = 10.5 Hz), 135.1, 134.1, 131.6, 130.3, 128.5, 124.4, 123.4, 121.4, 120.6 (t, $^2J_{CF}$ = 29.1 Hz), 111.8 (t, $^1J_{CF}$ = 245.1 Hz), 109.5, 108.3, 101.5; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –108.1 (s, 2F); IR ($CHCl_3$) 1714 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{17}H_{15}F_2N_2O_3$ 333.1051, found 333.1063.



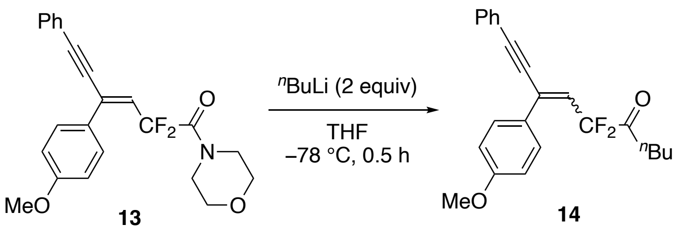
12efb

Analytical data for 12efc: 19.9 mg, 60%; colorless solid (mp 2004.9–206.3 °C): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 8.25 (br s, 1H), 8.07 (d, 2H, J = 8.0 Hz), 7.45 (ddd, 1H, J = 8.0, 6.4, 2.0 Hz), 7.39 (d, 2H, J = 8.8 Hz), 7.22–7.11 (m, 3H), 6.26 (t, 1H, J = 10.6 Hz), 3.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 166.5, 164.2 (t, $^{2}J_{CF}$ = 34.3 Hz), 146.9 (t, $^{3}J_{CF}$ = 10.0 Hz), 144.4, 135.2, 131.3, 130.9, 130.6, 129.8, 129.2, 127.9, 124.6, 122.5 (t, $^{2}J_{CF}$ = 29.6 Hz), 121.6, 111.5 (t, $^{1}J_{CF}$ = 245.1 Hz), 52.3; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –108.2 (s, 2F); IR ($CHCl_3$) 1719 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{18}H_{14}F_2NO_3$ 330.0942, found 330.09248.





Sonogashira coupling of 3aa: A solution of **3aa** (75.9 mg, 0.20 mmol), phenylacetylene acid (55 μL, 0.5 mmol), $PdCl_2(PPh_3)_2$ (14.5 mg, 0.021 mmol), and CuI (7.6 mg, 0.040 mmol) in Et_3N (2.0 mL) was degassed at −78 °C and then stirred at 50 °C under an Ar atmosphere for 1 h. After cooling to room temperature, the solvents were evaporated *in vacuo,* and the obtained crude product was purified by silica gel column chromatography (hexane/AcOEt 10:1~4:1) to afford **13** (72.3 mg, 90%) as a brown oil: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.48–7.42 (m, 4H), 7.38–7.31 (m, 3H), 6.90 (d, 2H, J = 8.4 Hz), 6.36 (t, 1H, J = 12.4 Hz), 3.83 (s, 3H), 3.60 (br t, 2H, J = 4.6 Hz), 3.52 (br t, 2H, J = 4.8 Hz), 3.47 (br t, 2H, J = 4.6 Hz), 3.30 (br t, 2H, J = 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 160.6 (t, $^{2}J_{CF}$ = 30.5 Hz), 160.4, 132.4 (t, $^{3}J_{CF}$ = 9.5 Hz), 131.7, 130.3, 129.0, 128.3, 127.2, 125.8 (t, $^{2}J_{CF}$ = 27.7 Hz), 122.1, 113.38 (t, $^{1}J_{CF}$ = 243.6 Hz), 113.35, 93.0, 89.4, 66.3, 66.1, 55.2, 46.6, 42.8; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –87.5 (s, 2F); IR ($CHCl_3$) 2205 (C≡C), 1680 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{23}H_{22}F_2NO_3$ 398.1568, found 398.1548.



Synthesis of ketone 14: To a solution of amide **13** (68.0 mg, 0.171 mmol) in dry THF (2 mL) was added dropwise ^{n}BuLi (1.6 M in hexane, 212 μL, 0.34 mmol) at –78 °C under an argon atmosphere. The mixture was stirred at this temperature for 30 min. The reaction was quenched by adding sat. aq. NH_4Cl (10 mL). The aqueous phase was extracted with ether (3×10 mL). The combined organic extract was washed with brine (10 mL) and dried over anhydrous Na_2SO_4. The solvents were evaporated *in vacuo*, and the obtained crude product was purified by silica gel column chromatography (hexane/AcOEt, 80:1~70:1) to afford **14** (36.8 mg, 58%, *E*/*Z* = 12:1) as a yellow oil: data for major stereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.47–7.43 (m, 2H), 7.39 (d, 2H, *J* = 8.8 Hz), 7.36–7.29 (m, 3H), 6.89 (d, 2H, *J* = 8.8 Hz), 6.28 (t, 1H, *J* = 13.4 Hz), 3.83 (3H, s), 2.43 (t, 2H, *J* = 7.2 Hz), 1.40 (quint, 2H, *J* = 7.5 Hz), 1.20 (sext, 2H, *J* = 7.4 Hz), 0.85 (t, 3H, *J* = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 199.1 (t, $^2J_{CF}$ = 30.6 Hz), 160.3, 133.7 (t, $^3J_{CF}$ = 9.1 Hz), 131.8, 130.2, 129.0, 128.4, 128.1, 125.5 (t, $^2J_{CF}$ = 26.7 Hz), 122.3, 114.1 (t, $^1J_{CF}$ = 247.4 Hz), 113.5, 93.1, 89.5, 55.3, 36.3, 24.7, 21.9, 13.7; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ –95.2 (s, 2F); IR ($CHCl_3$) 2206 (C≡C), 1743 (C=O) cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{23}H_{23}F_2O_2$ 369.1666, found 369.1688.

Single Crystal X-ray Diffraction Study

A single crystal of **12efa**, which was obtained by recrystallization from toluene, was mounted on a glass fiber, and diffraction data were collected in θ ranges specified in Table S2 at 123 K on a Rigaku R-AXIS Rapid diffractomter with graphite monochromatized Cu-Kα radiation (λ = 1.54187 Å). The Lorenz polarization absorption correction was applied. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were refined using the riding model. Final refinement details are compiled in Table S2. The supplementary crystallographic data for this paper (CCDC 2149781) can also be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk).

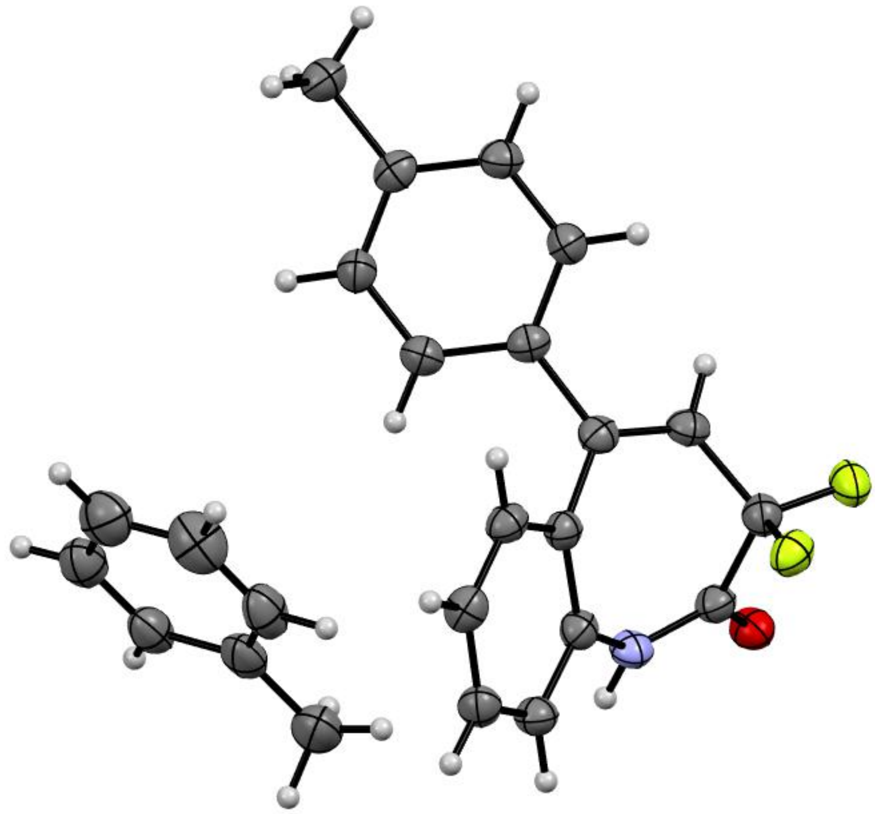


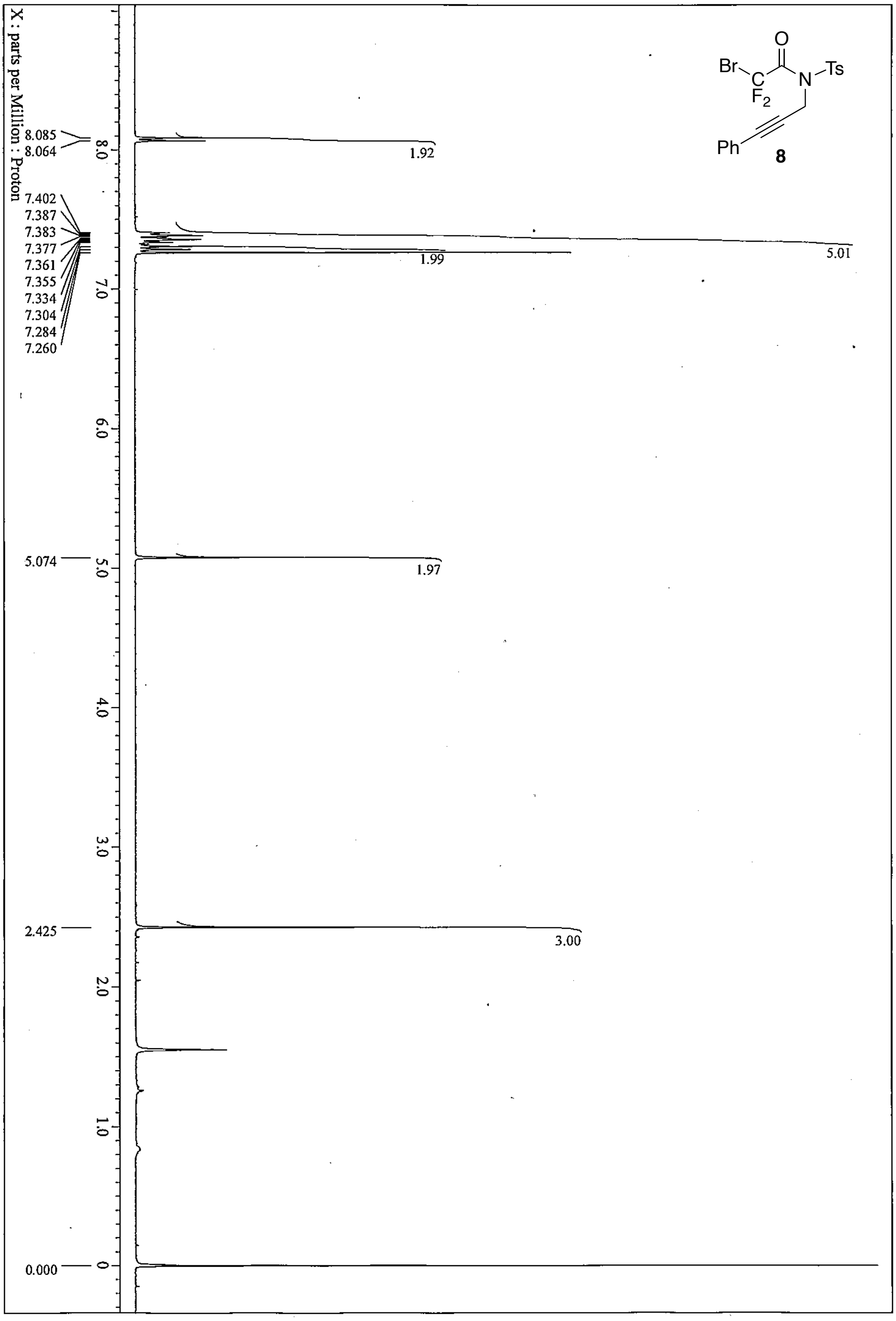
Figure S1. ORTEP drawing of **12efa**•MePh. Ellipsoids are shown at the 50% probability level.

Table S2. Selected crystallographic data and collection parameters for **12efa**•MePh.

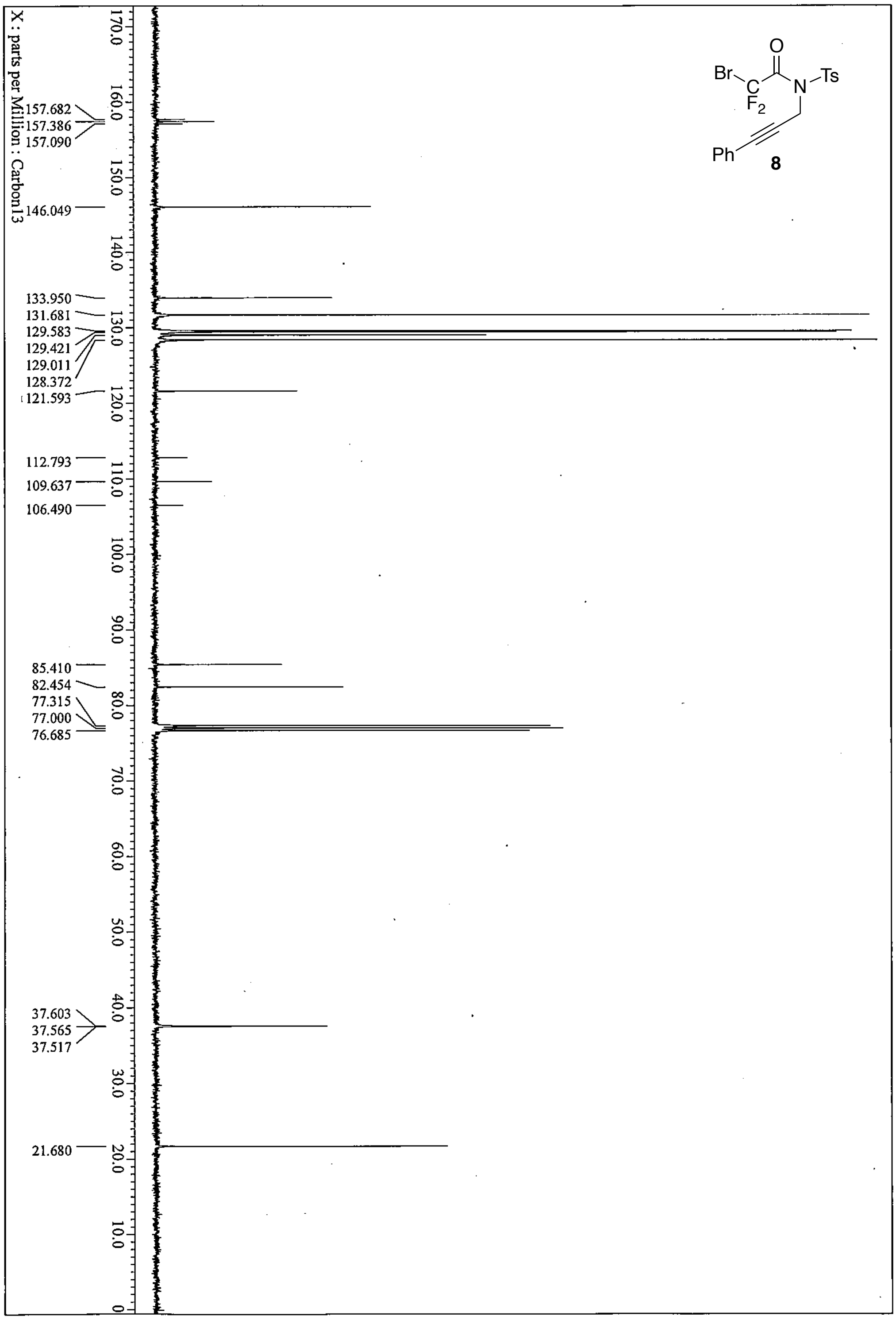
formula	$C_{24}H_{21}F_2NO$
fw	377.43
crystal system	monoclinic
space group	$P2_1/n$ (#14)
a, Å	10.2403(5)
b, Å	15.5996(8)
c, Å	12.3812(6)
β, deg	102.080(7)
volume, $Å^3$	1934.01(17)
Z	4
D (calcd), Mg m^{-3}	1.296
μ, cm^{-1}	7.544
F(000)	792.00
crystal size, mm	0.20 x 0.20 x 0.20
maximum 2θ, deg	136.5
reflections collected	21888
independent reflections [*R*(int)]	3537 [R(int) = 0.0390]
max. and min. transmission	0.860/0.669
data / restraints / parameters	3537 / 0 / 253
goodness-of-fit on F^2	1.054
R_1 [$I > 2\sigma(I)$]	0.0481
R, wR_2 (all data)	0.0519, 0.1243
Weighting scheme	$R_1 = \Sigma\|\|Fo\| - \|Fc\|\|/\Sigma\|Fo\|$
	$wR_2 = [\Sigma(w(Fo^2 - Fc^2)^2)/\Sigma w(Fo^2)^2]^{1/2}$
largest diff. peak and hole, e $Å^{-3}$	0.40 and -0.40

NMR Charts

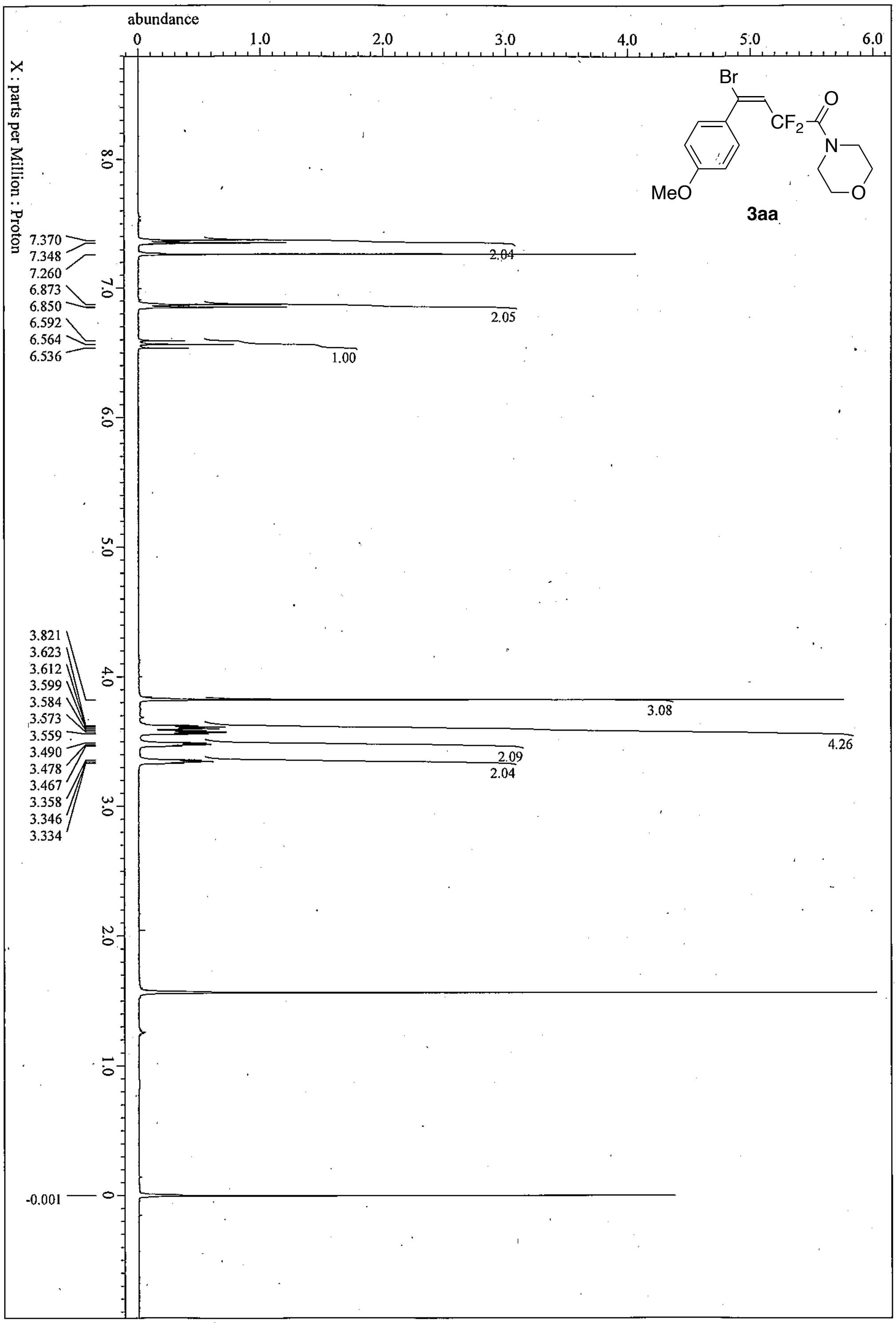
8: ^{1}H NMR (400 MHz, $CDCl_3$)



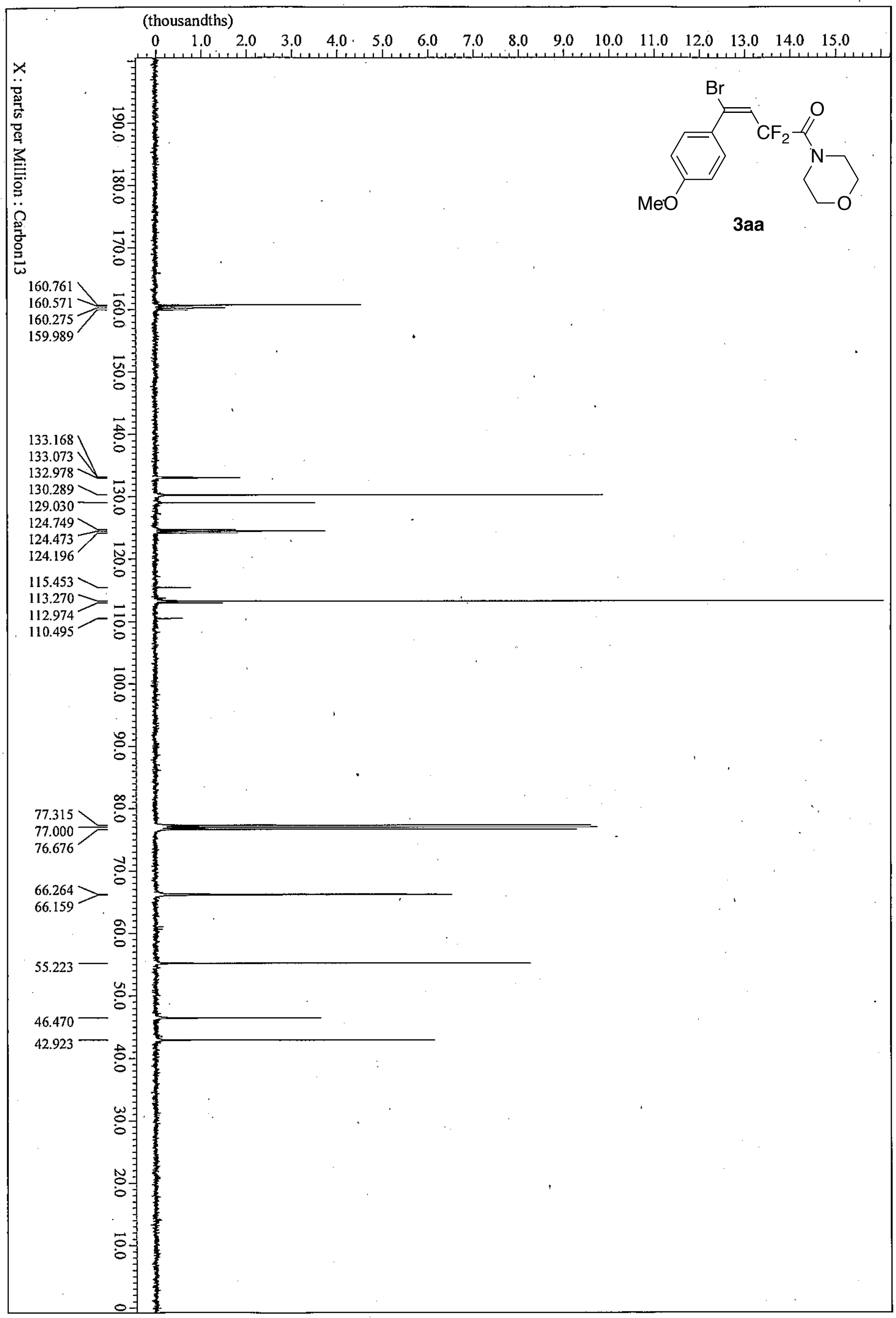
8: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



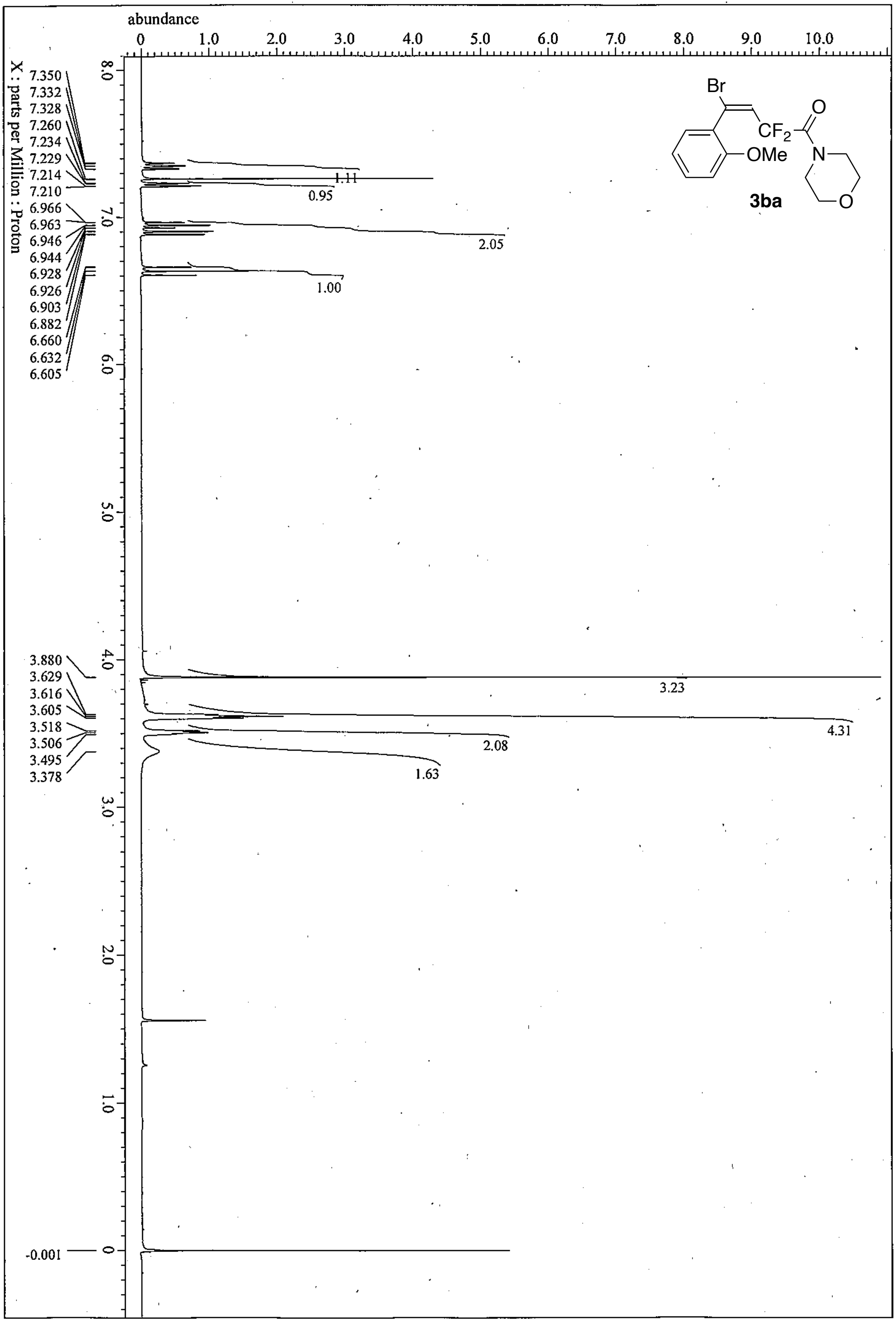
3aa: ^{1}H NMR (400 MHz, $CDCl_3$)



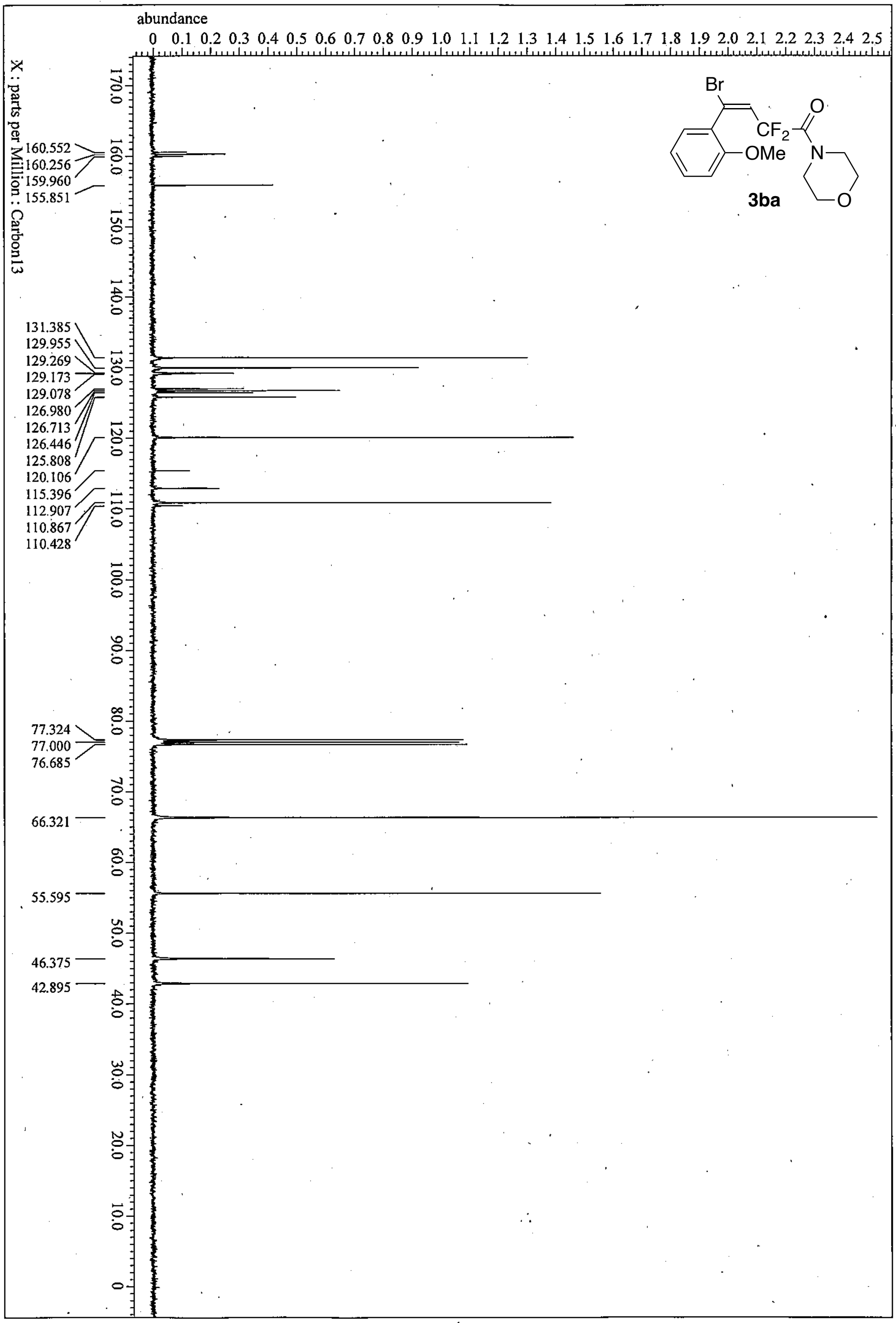
3aa: $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)



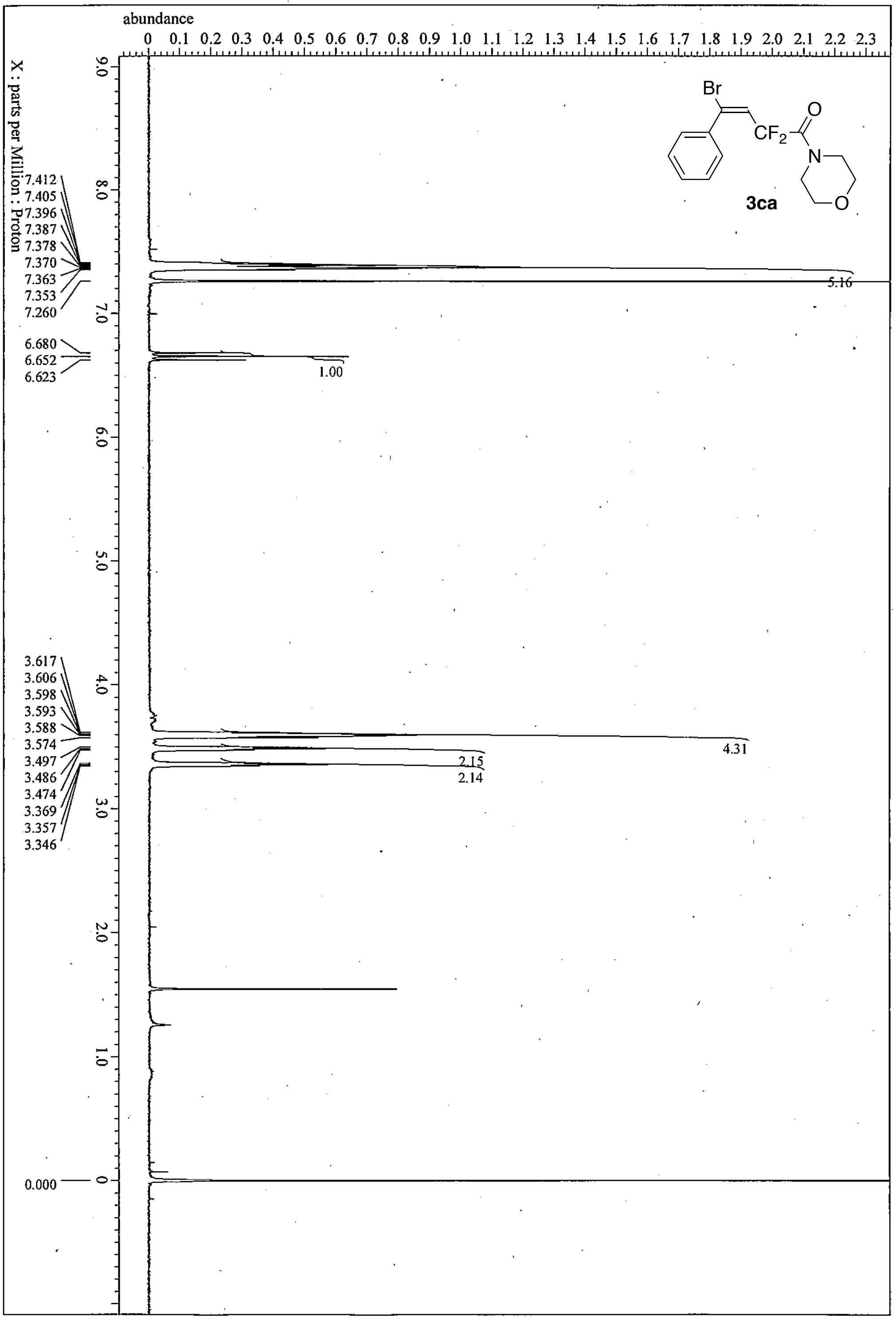
3ba: ^{1}H NMR (400 MHz, $CDCl_3$)



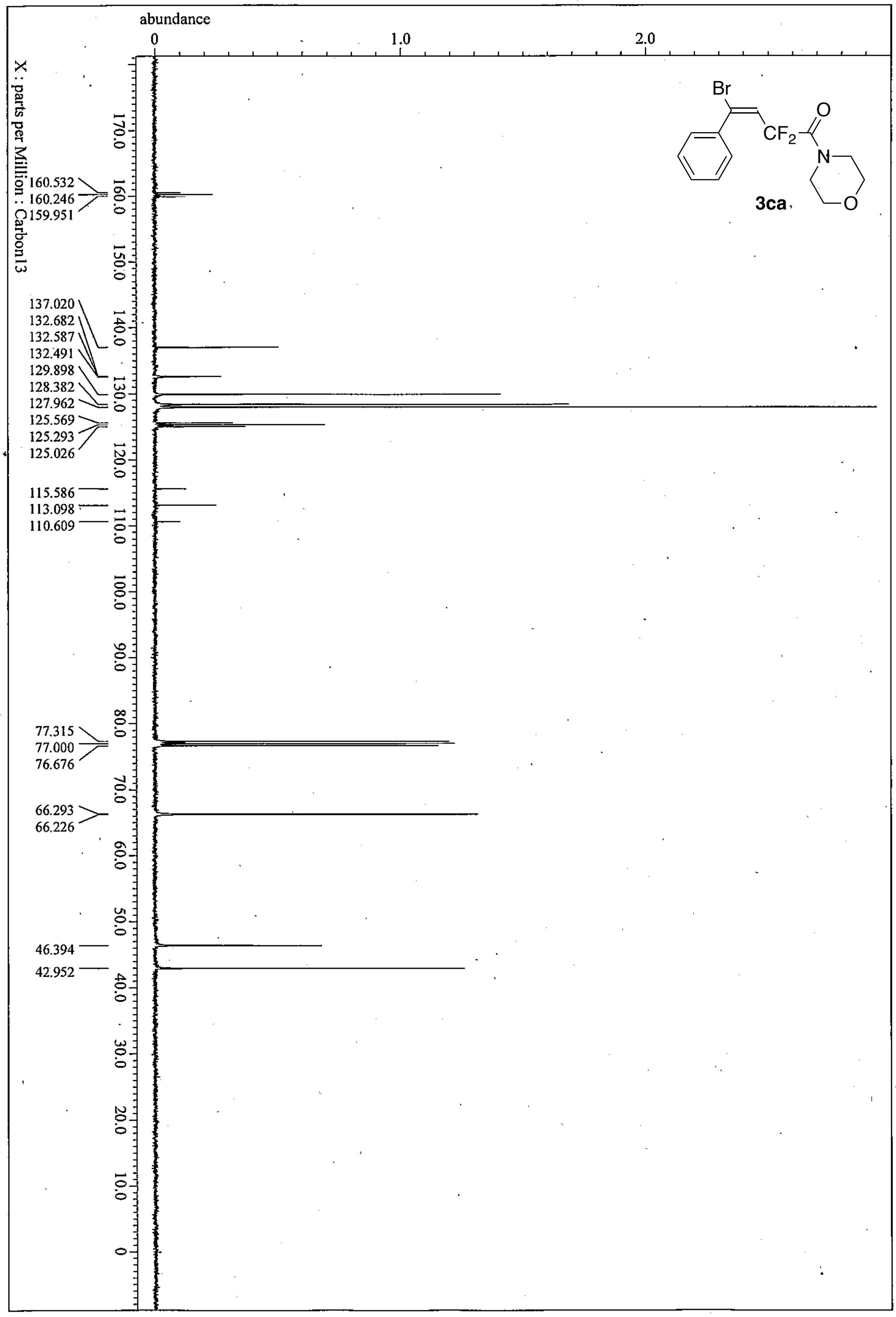
3ba: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



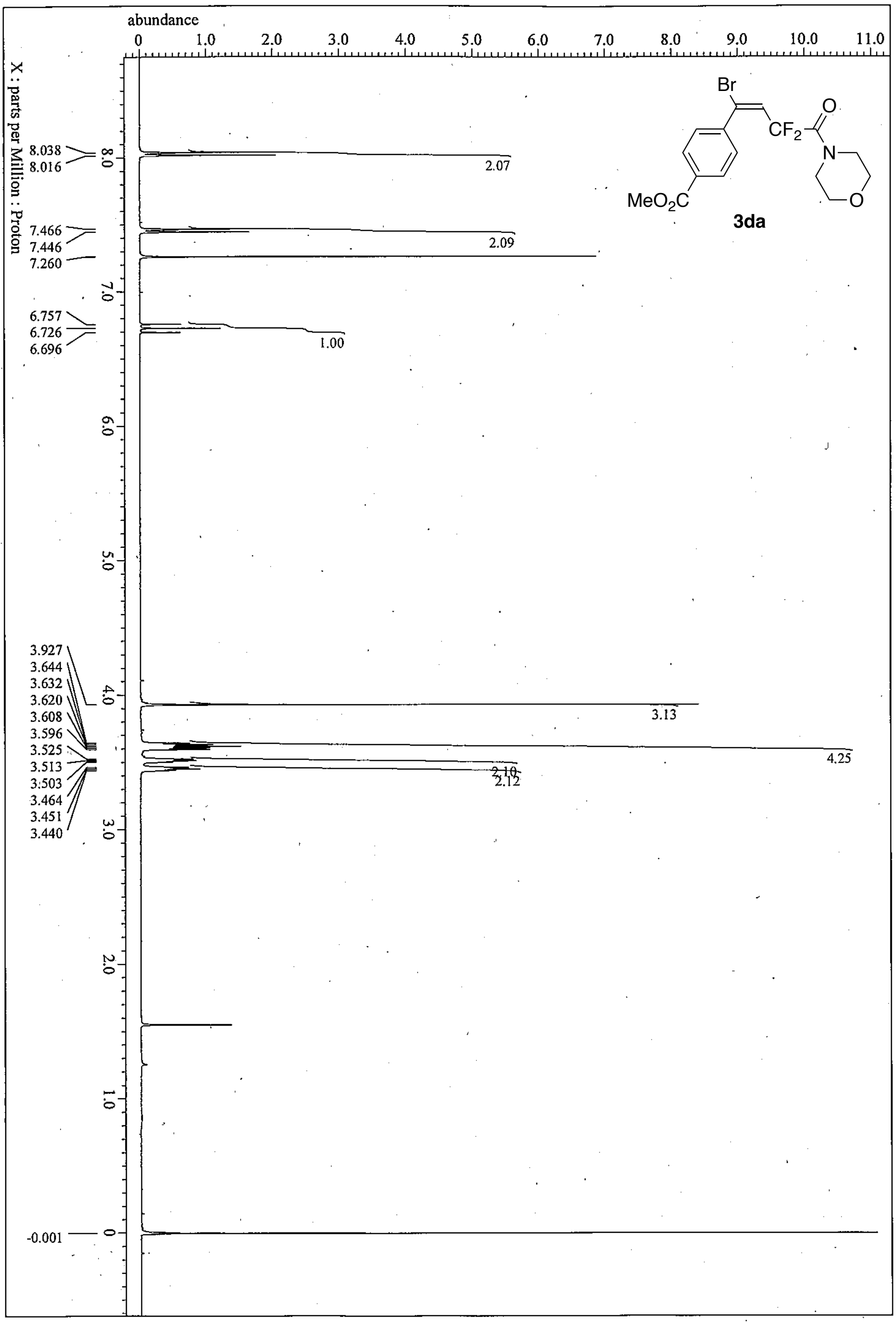
3ca: ^{1}H NMR (400 MHz, $CDCl_3$)



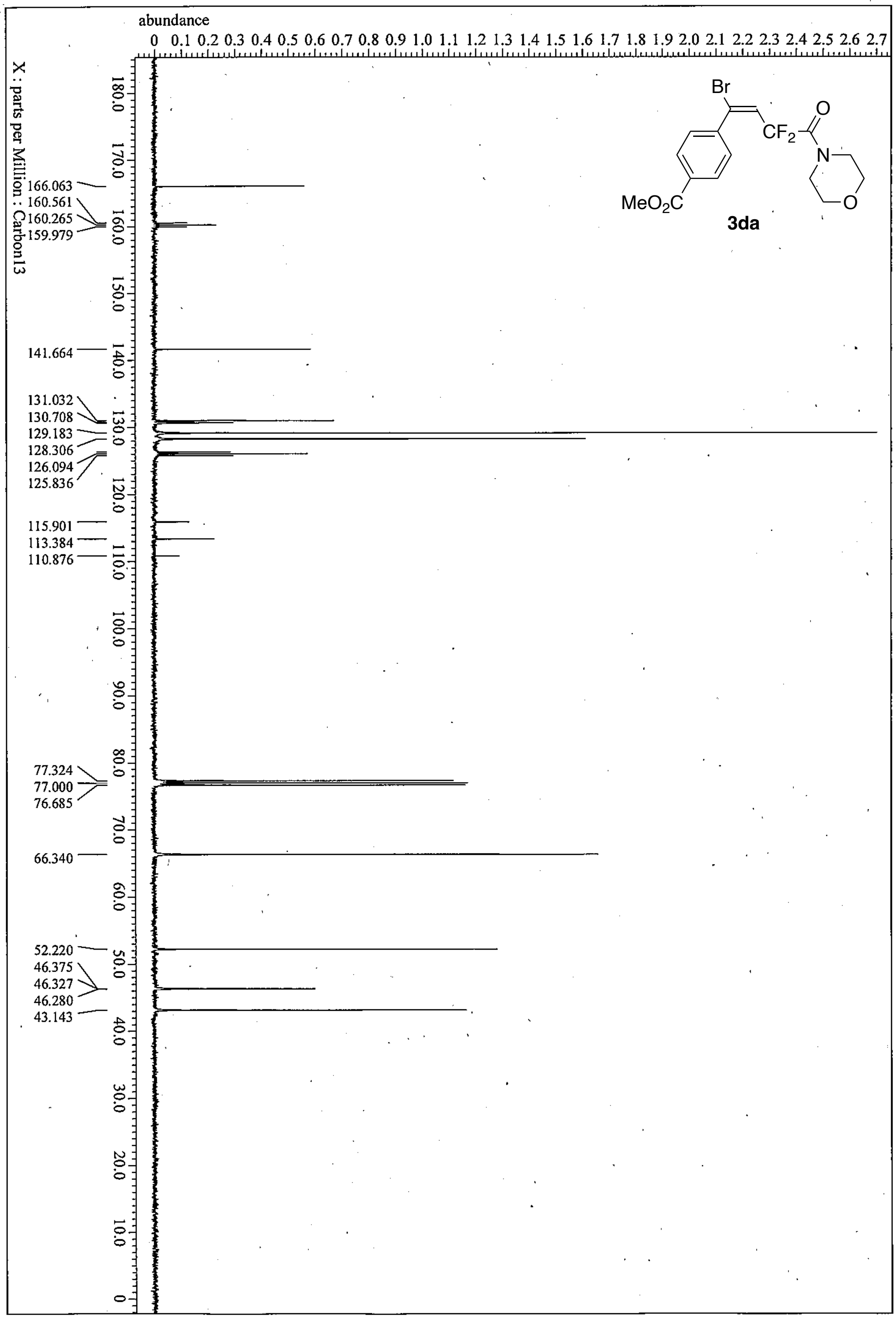
3ca: $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)



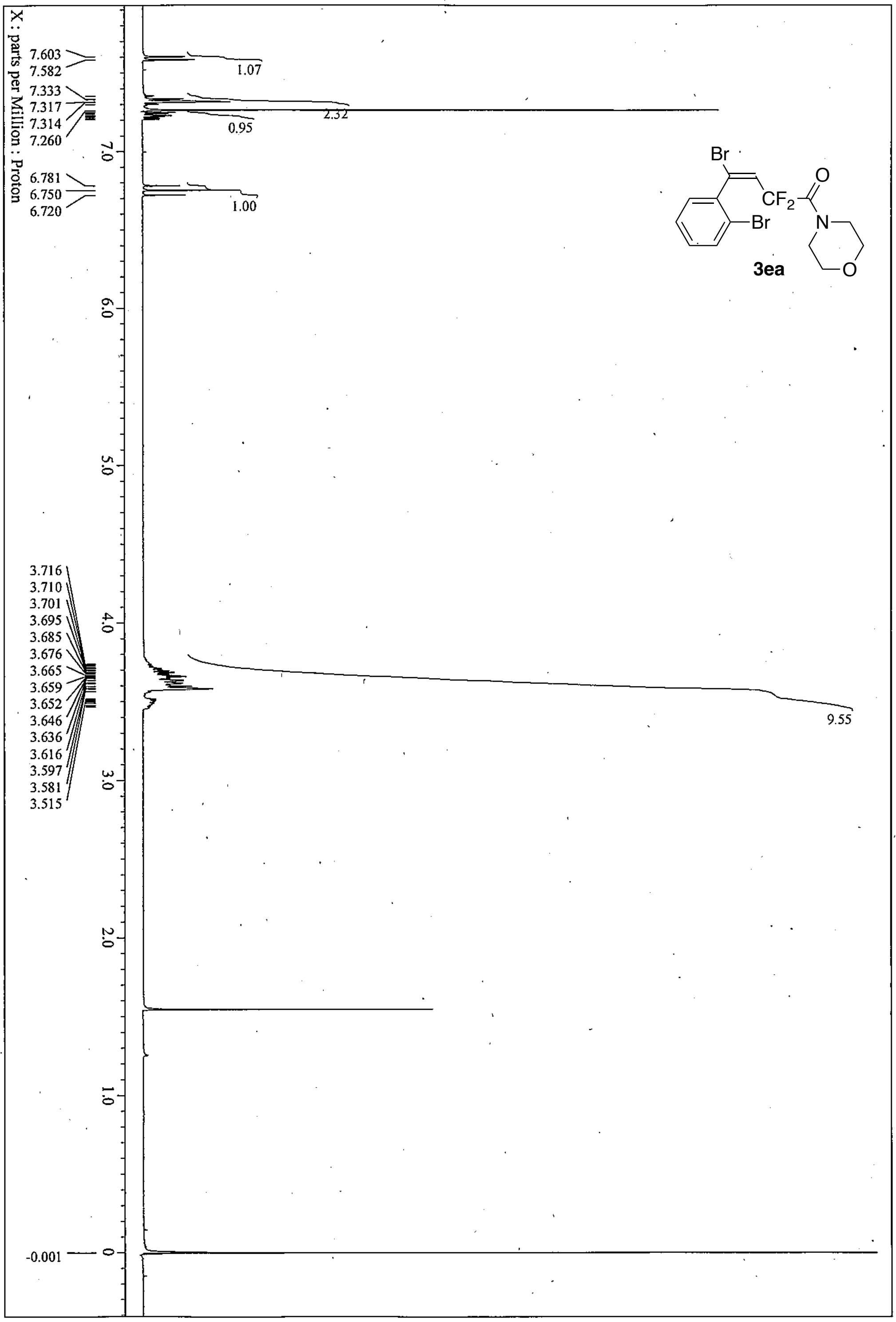
3da: ^{1}H NMR (400 MHz, $CDCl_3$)



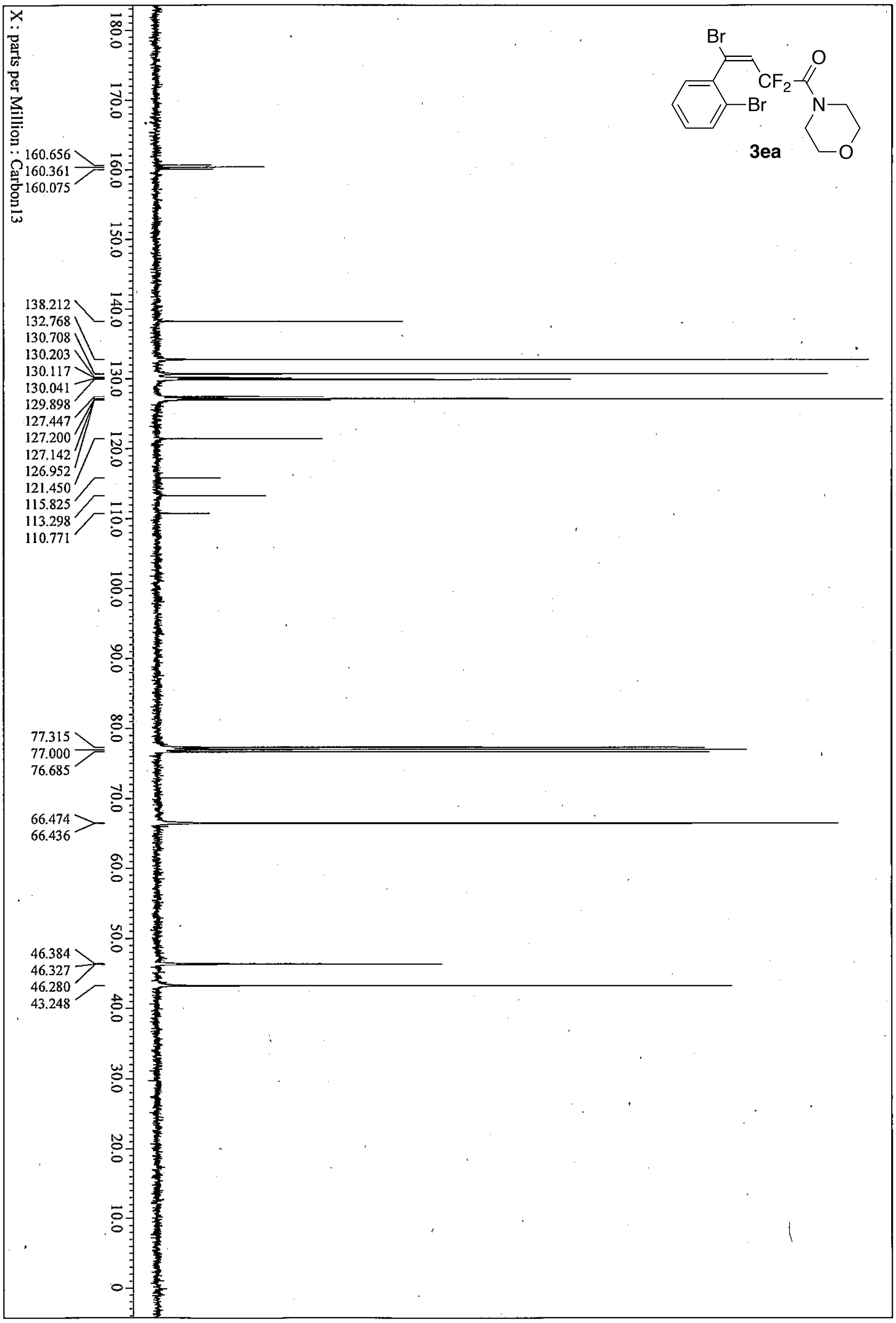
3da: $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)



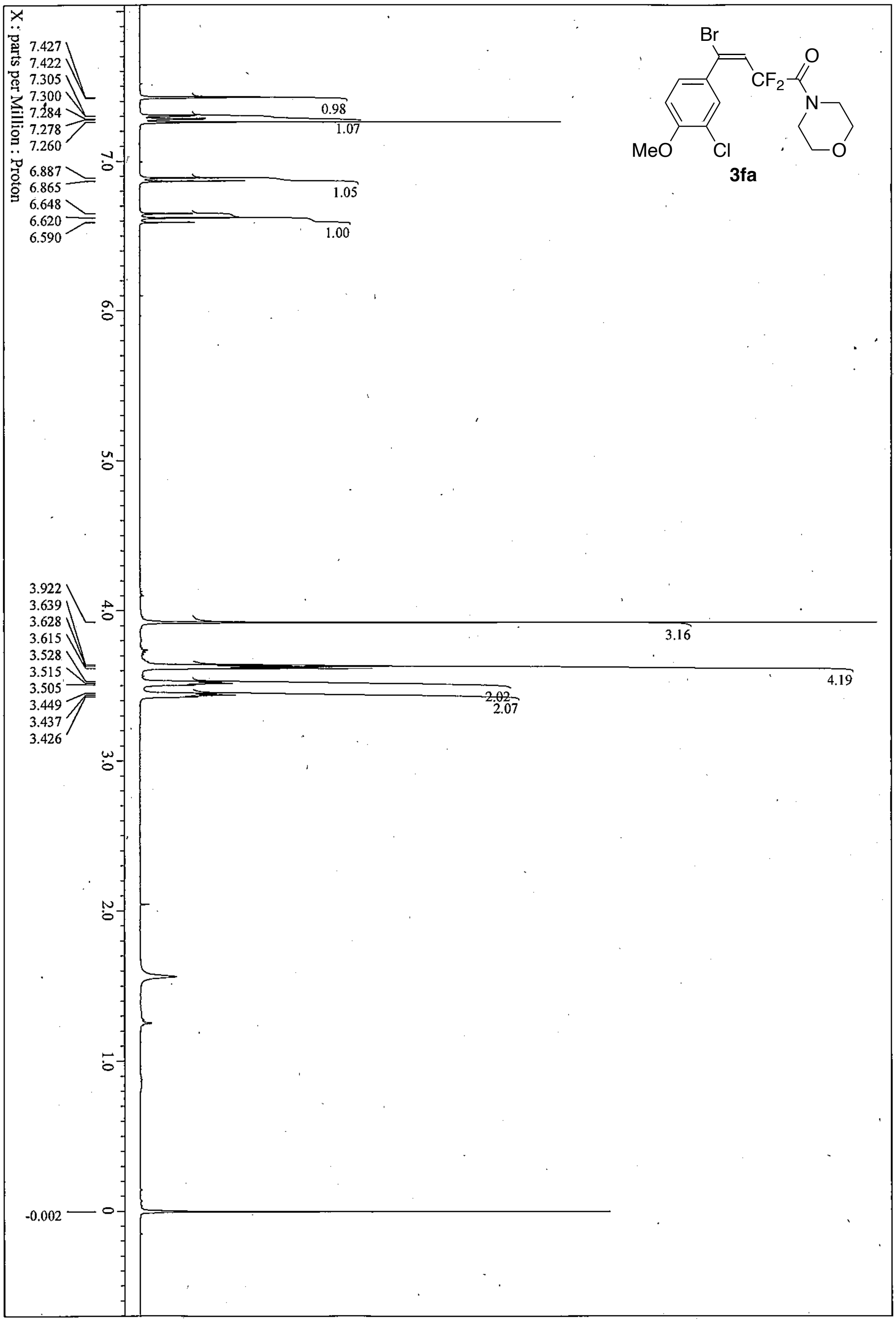
3ea: ^{1}H NMR (400 MHz, $CDCl_3$)



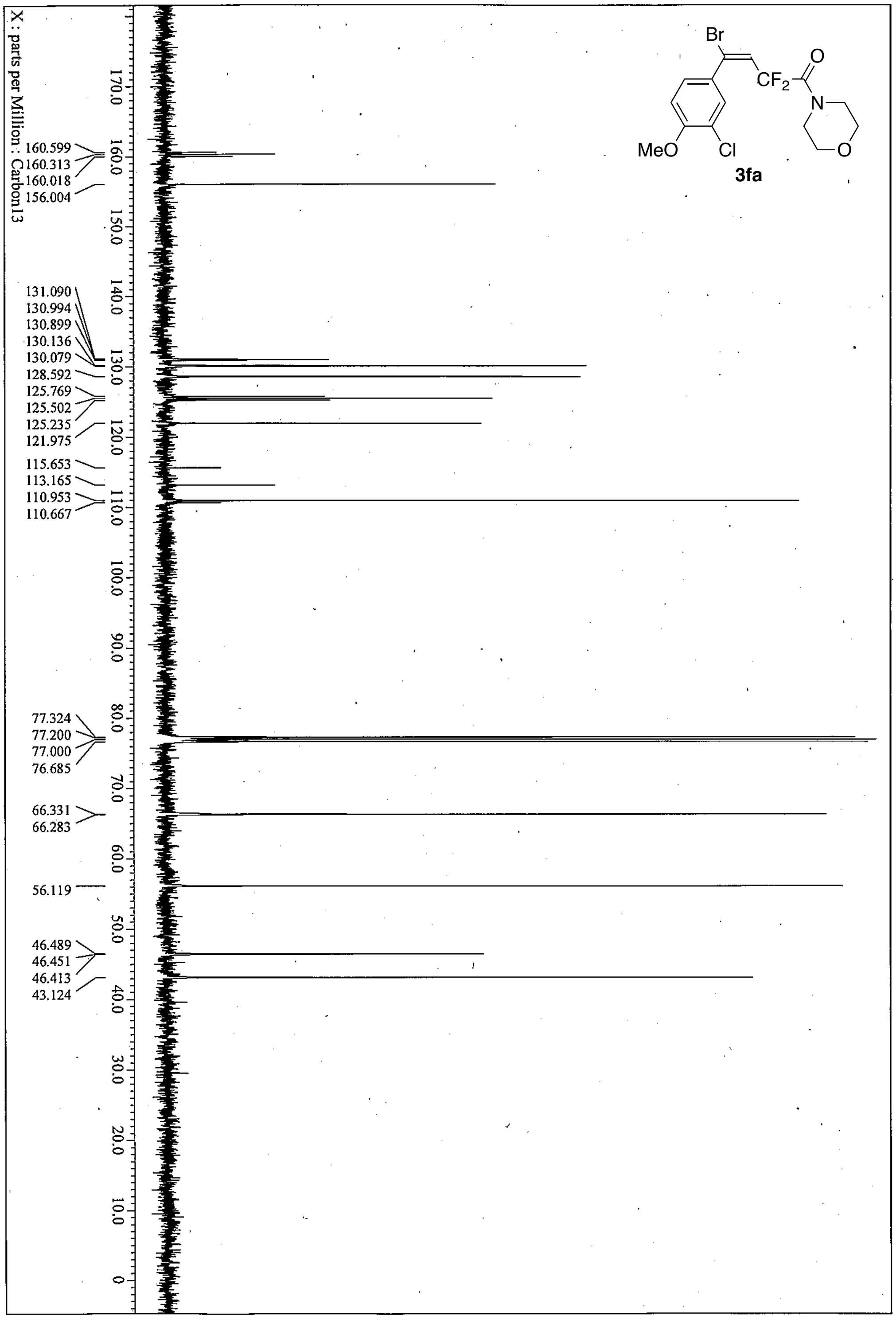
3ea: $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)



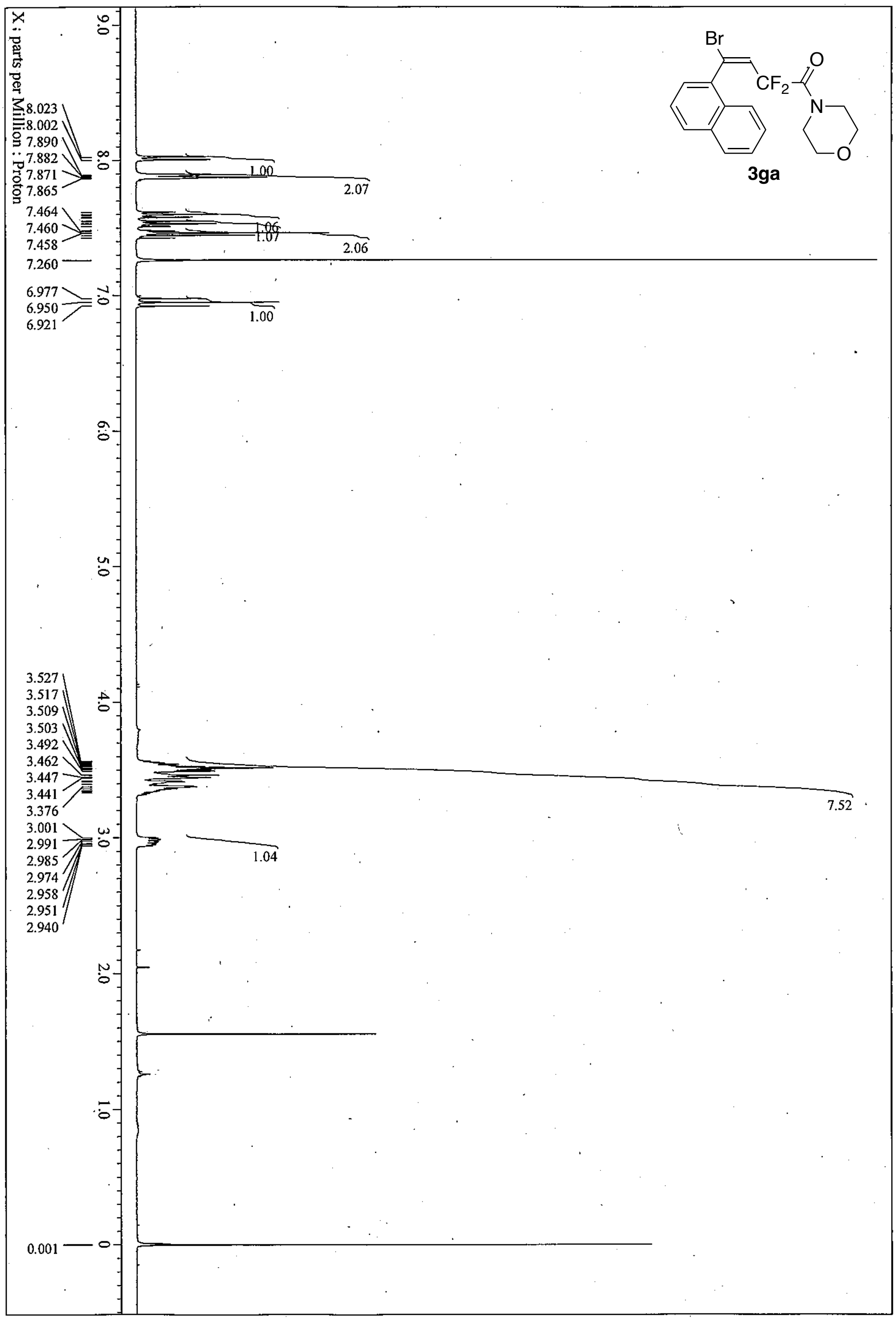
3fa: ^1H NMR (400 MHz, $CDCl_3$)



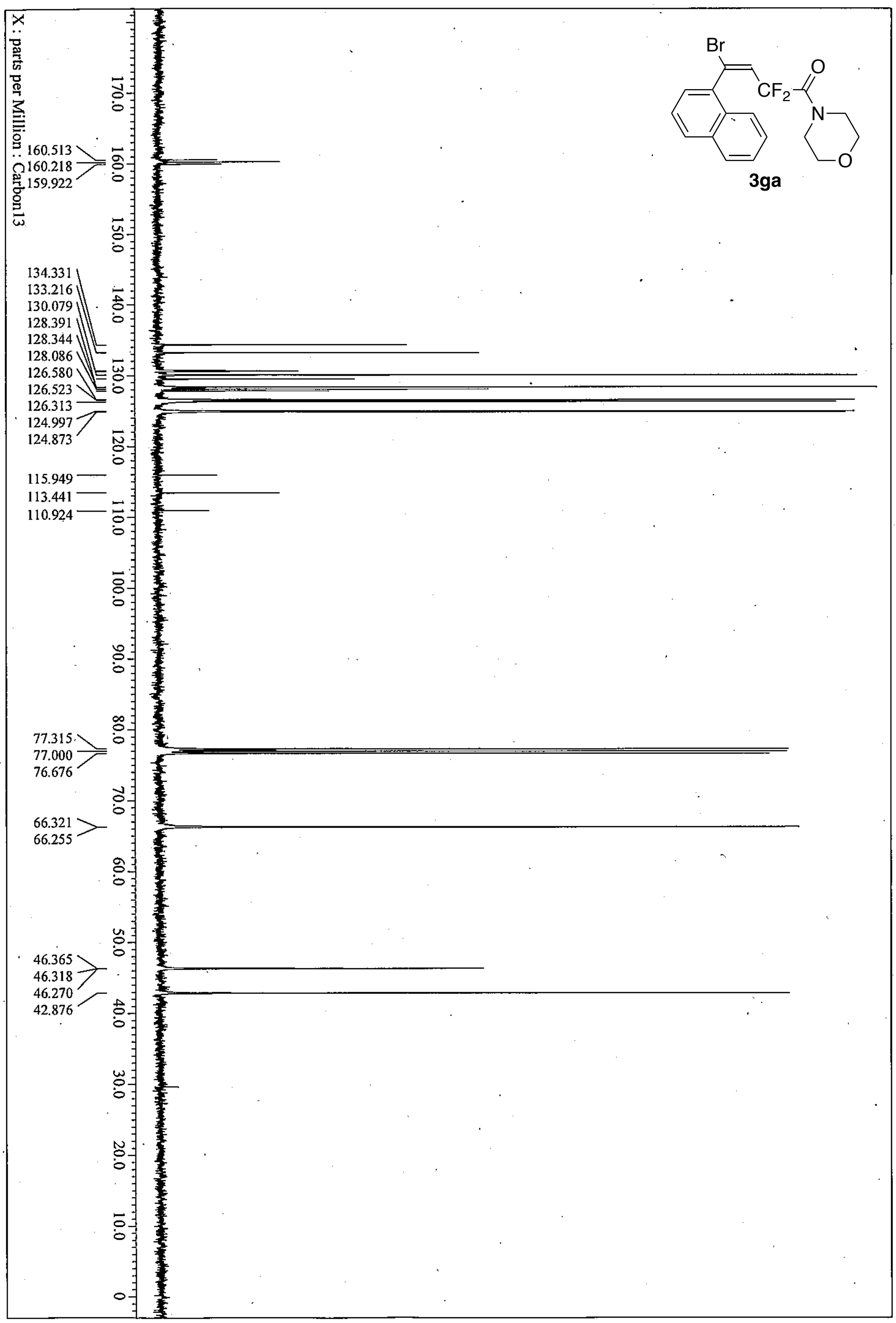
3fa: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



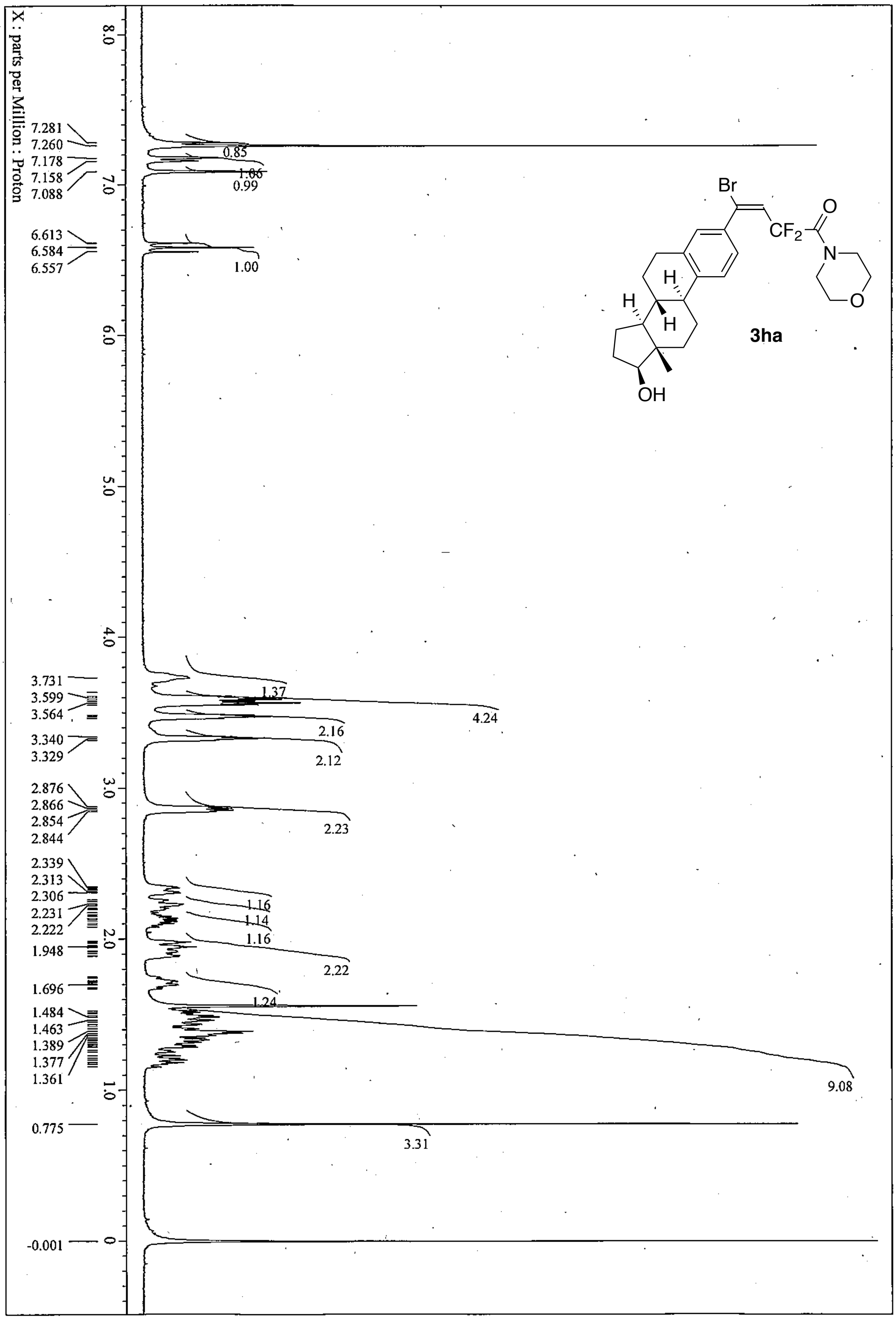
3ga: ^{1}H NMR (400 MHz, $CDCl_3$)



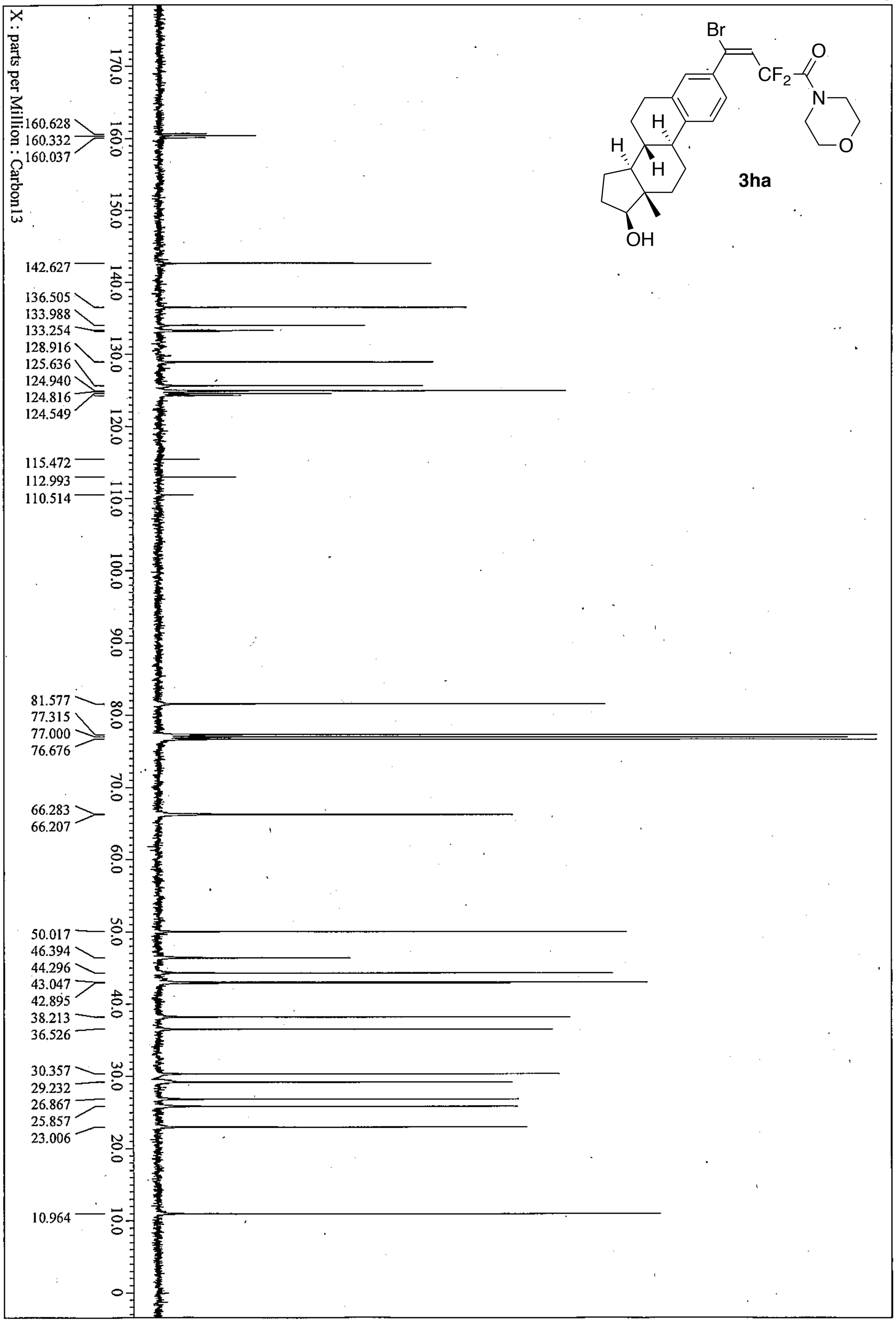
3ga: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



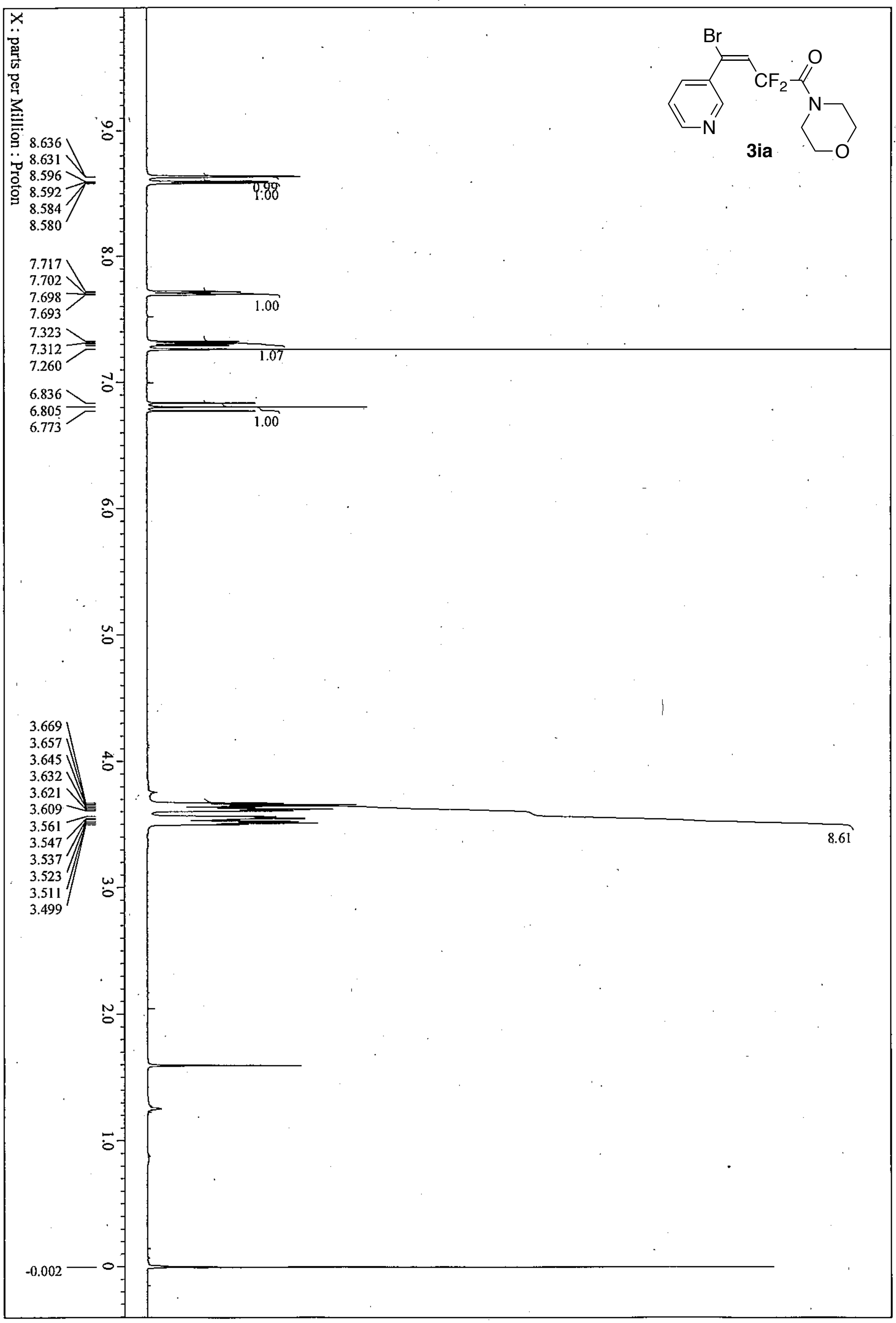
3ha: ^{1}H NMR (400 MHz, $CDCl_3$)



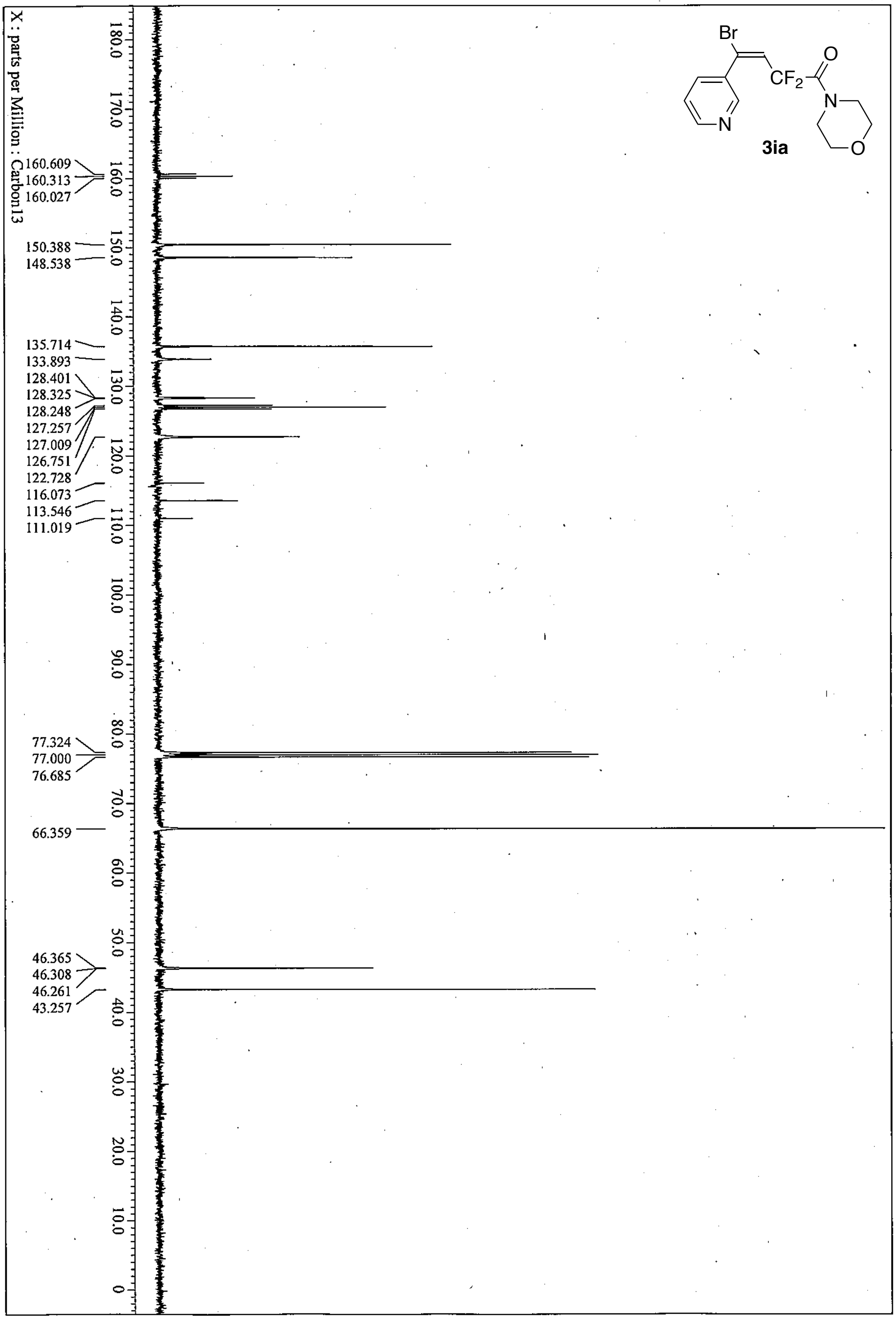
3ha: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



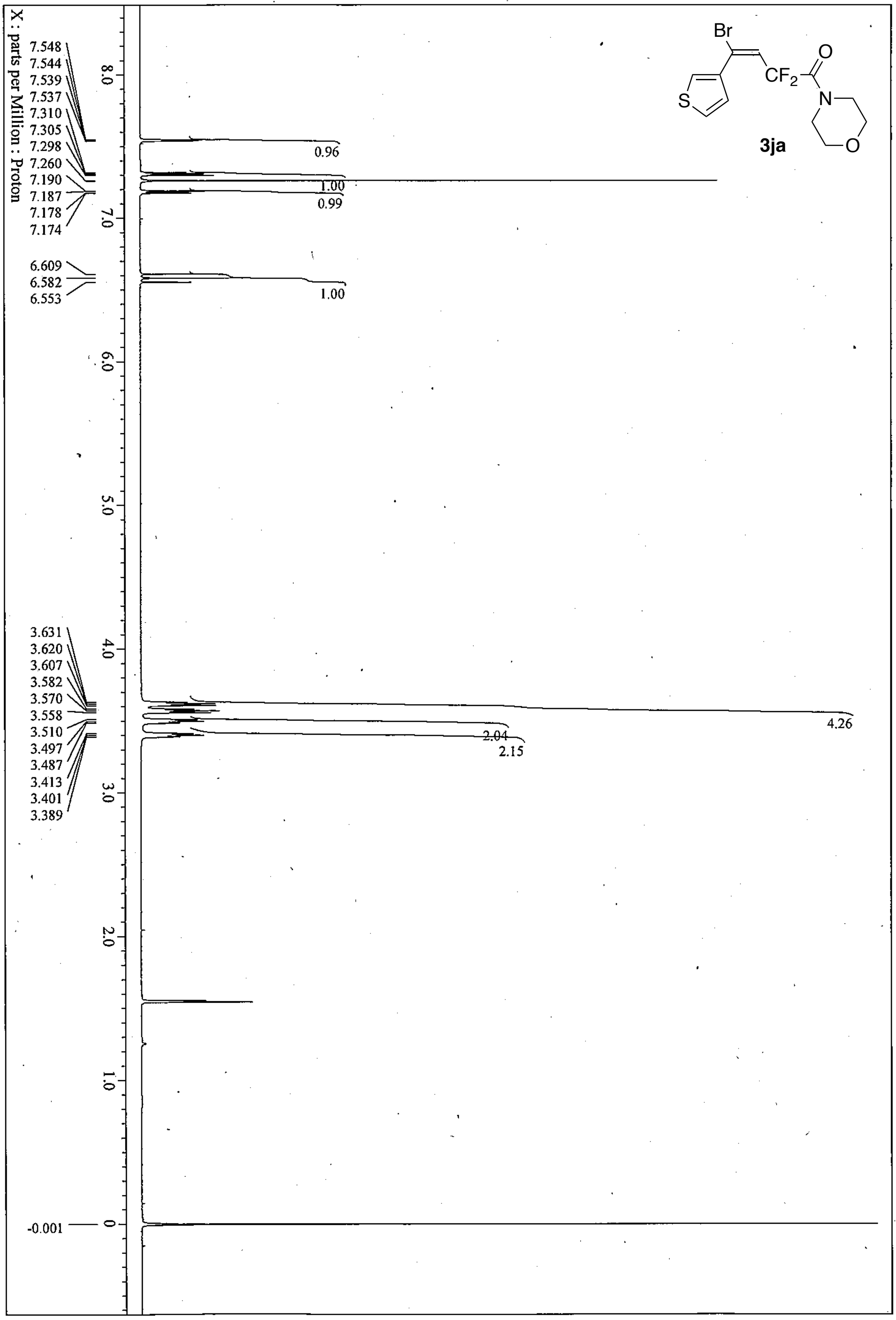
3ia: ^{1}H NMR (400 MHz, $CDCl_3$)



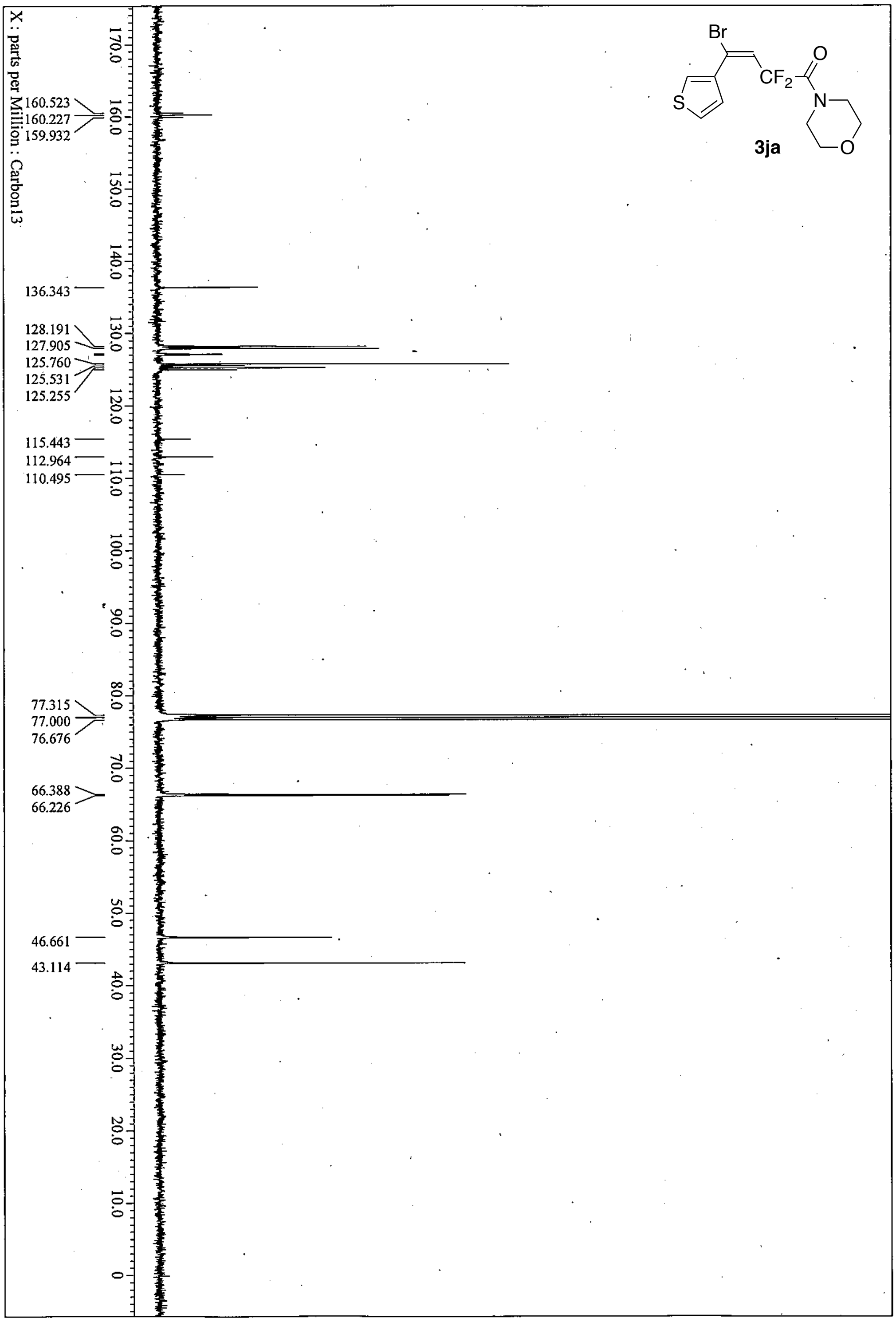
3ia: $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)



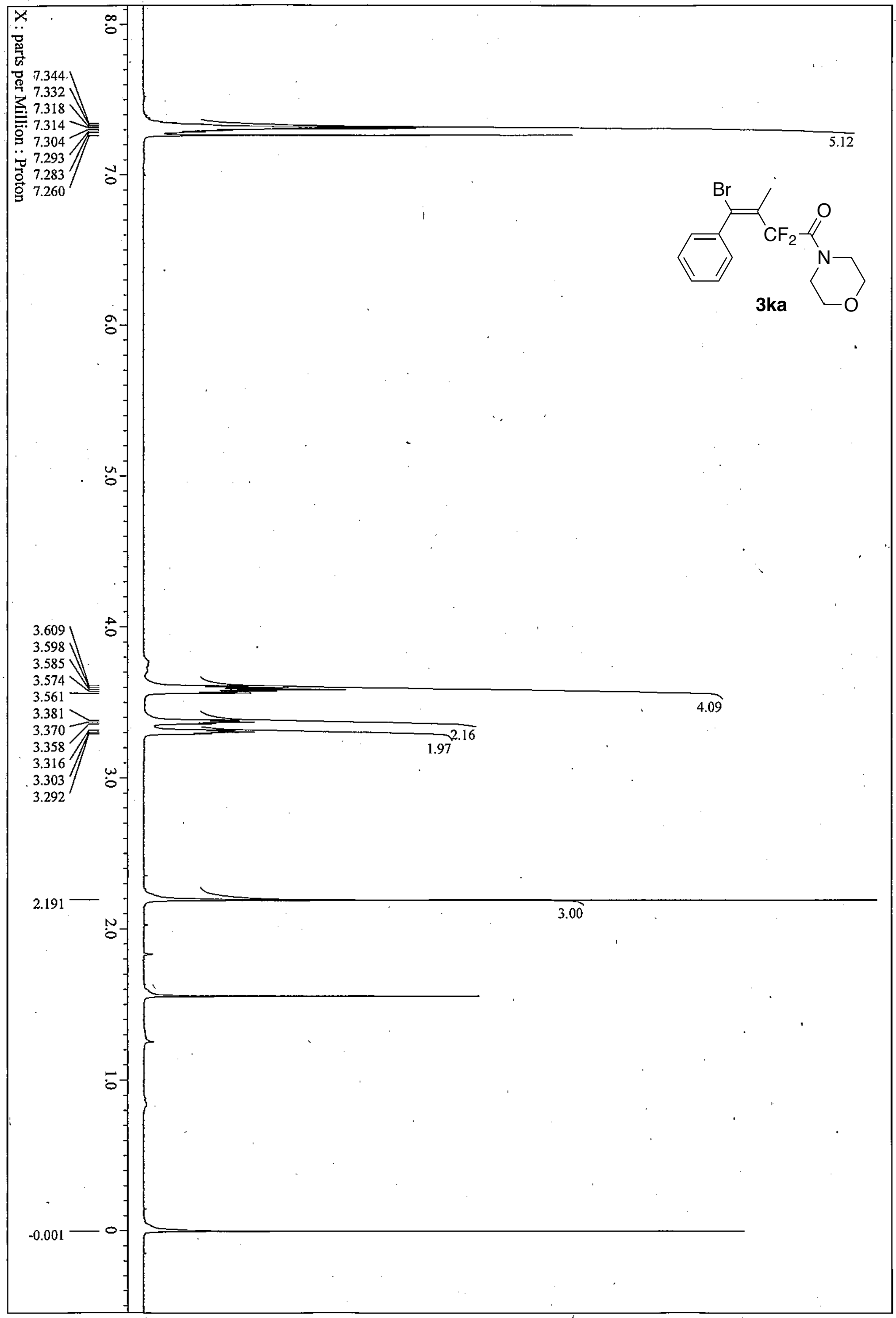
3ja: ^{1}H NMR (400 MHz, $CDCl_3$)



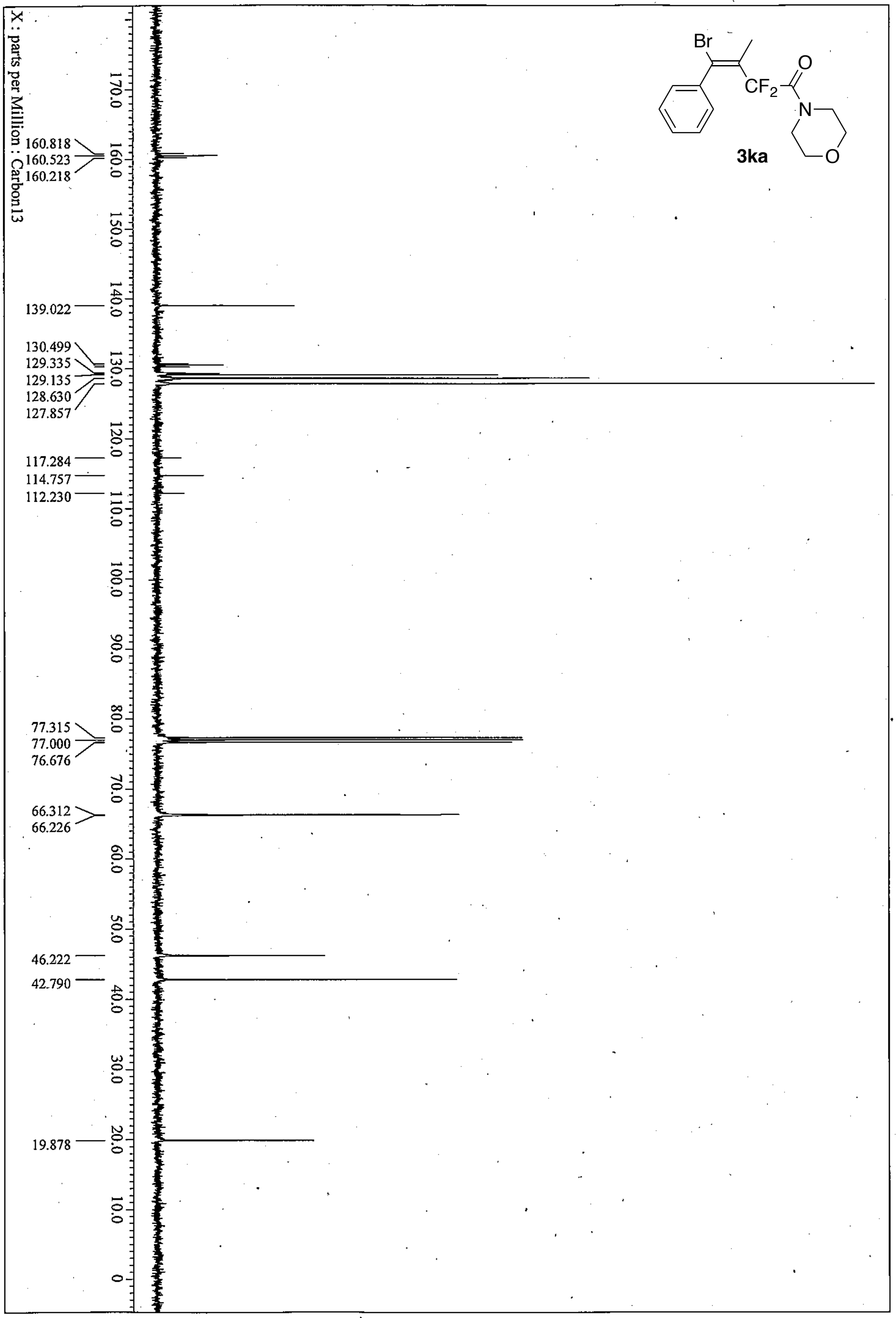
3ja: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



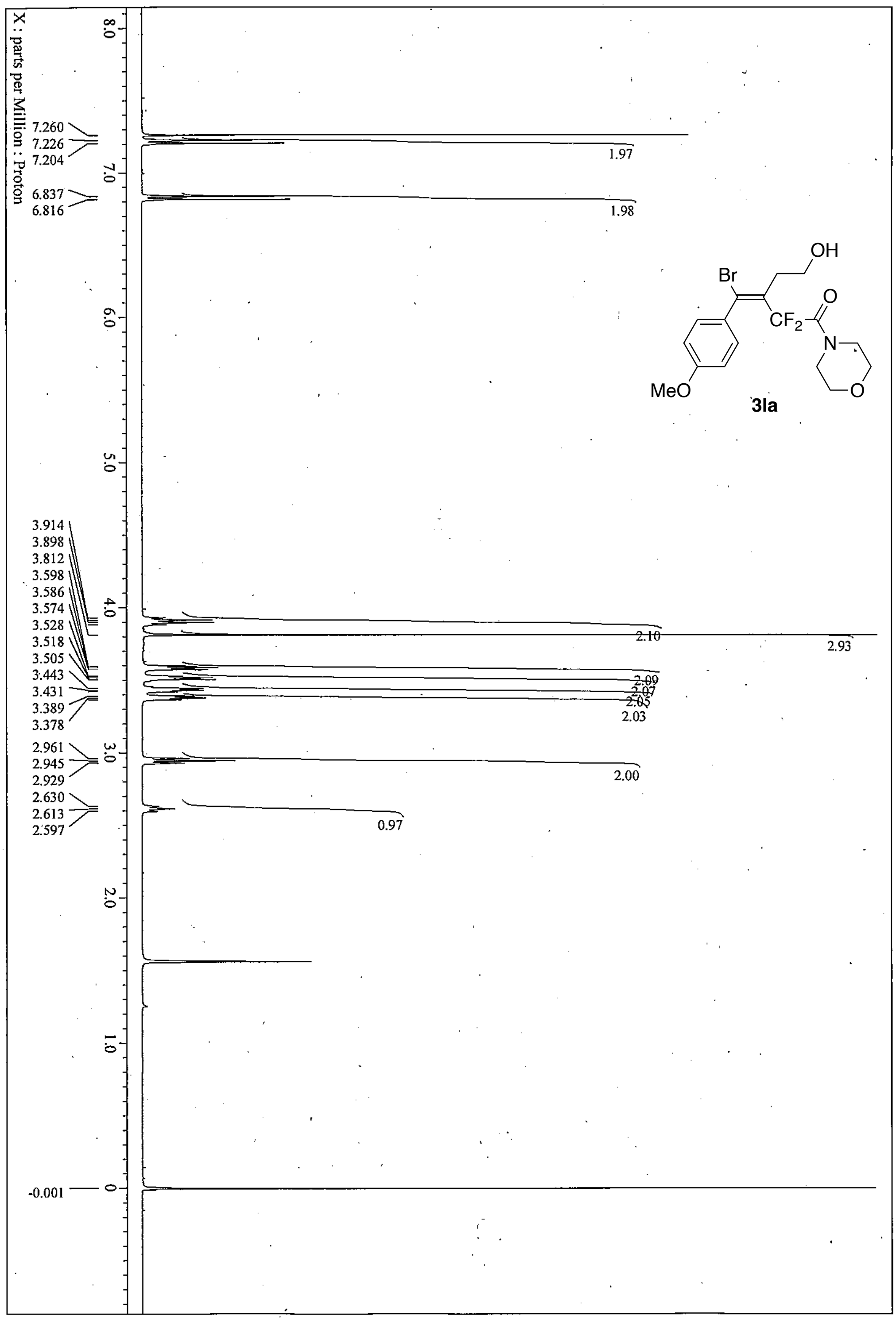
3ka: ^{1}H NMR (400 MHz, $CDCl_3$)



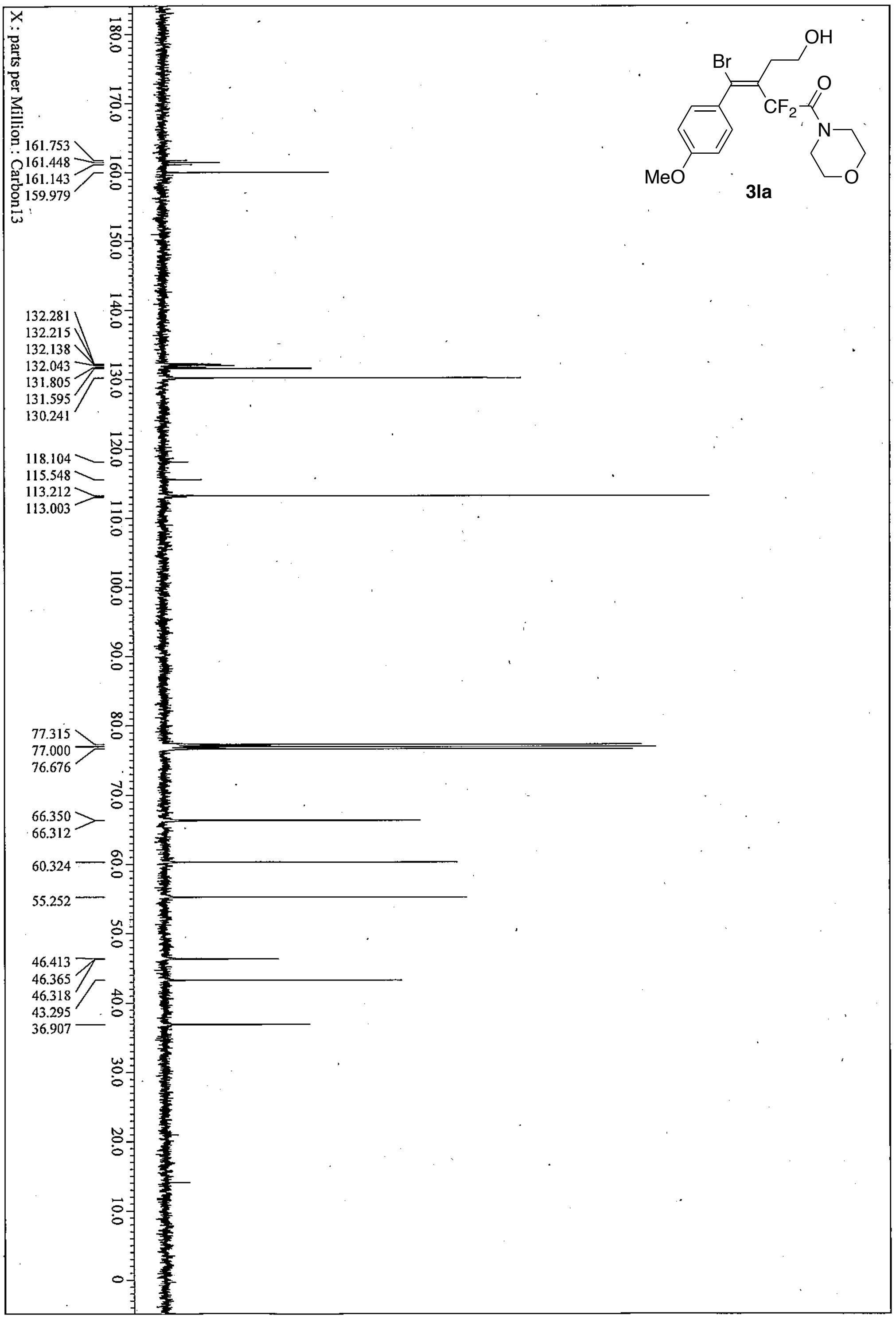
3ka: $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)



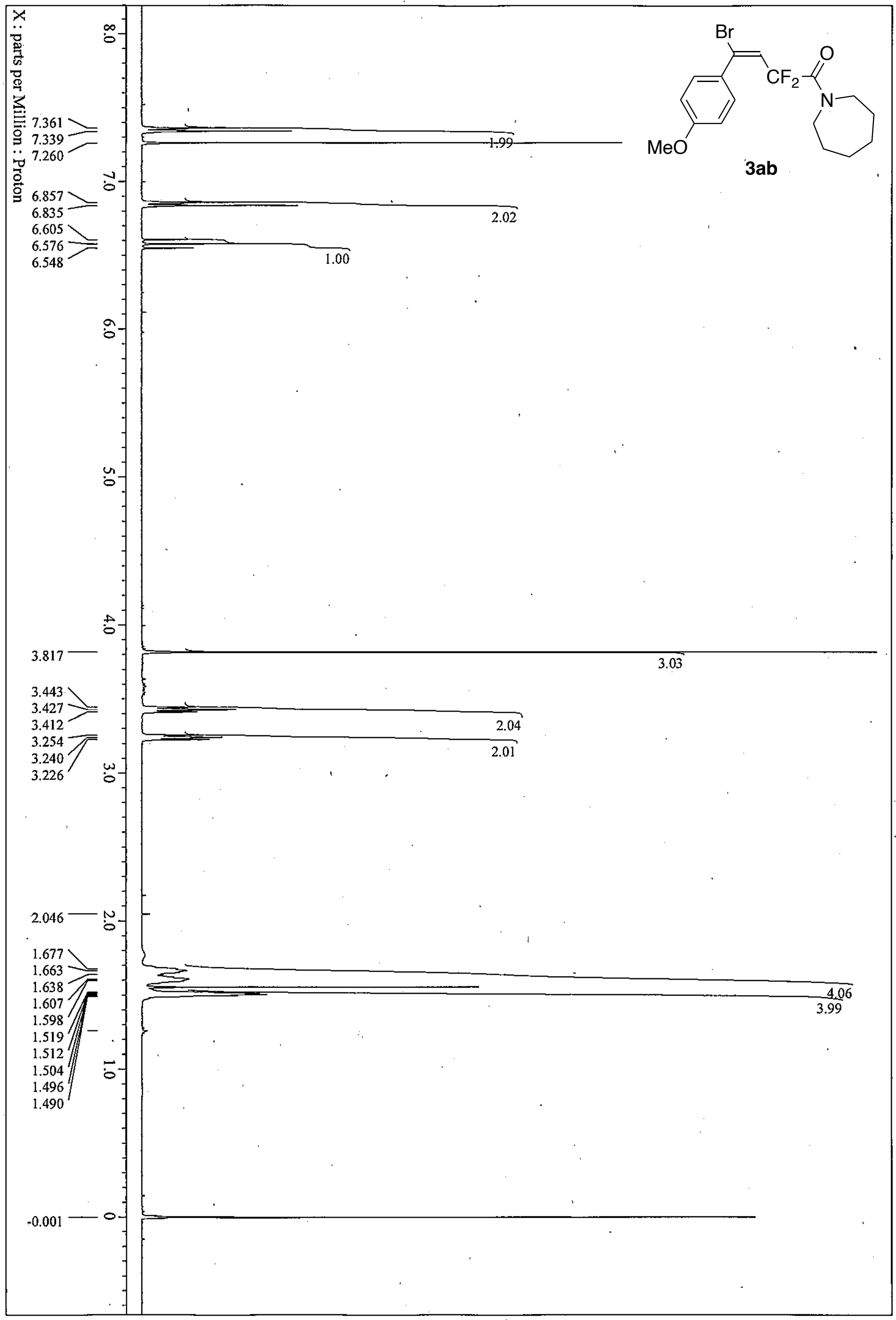
3la: ^{1}H NMR (400 MHz, $CDCl_3$)



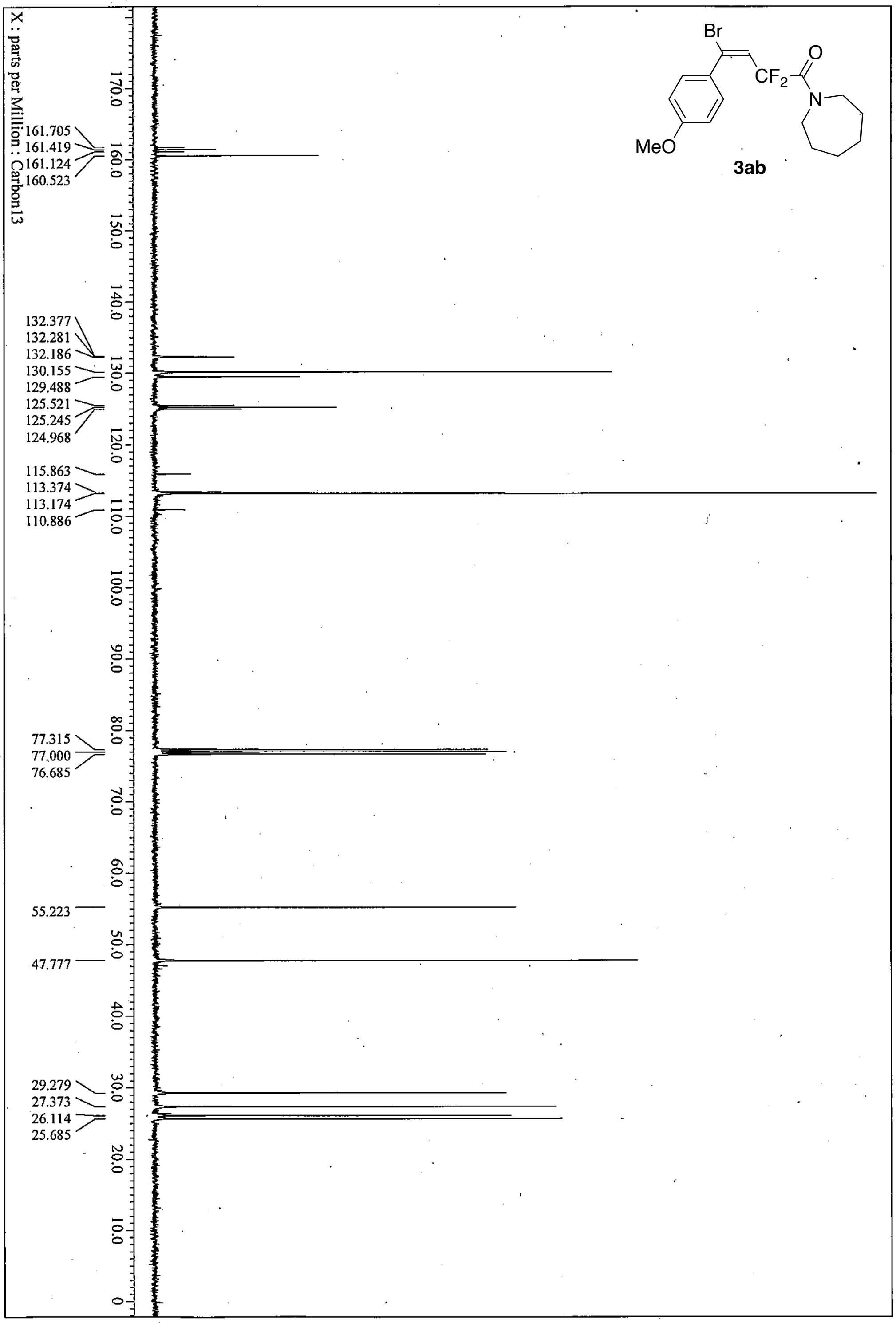
3la: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



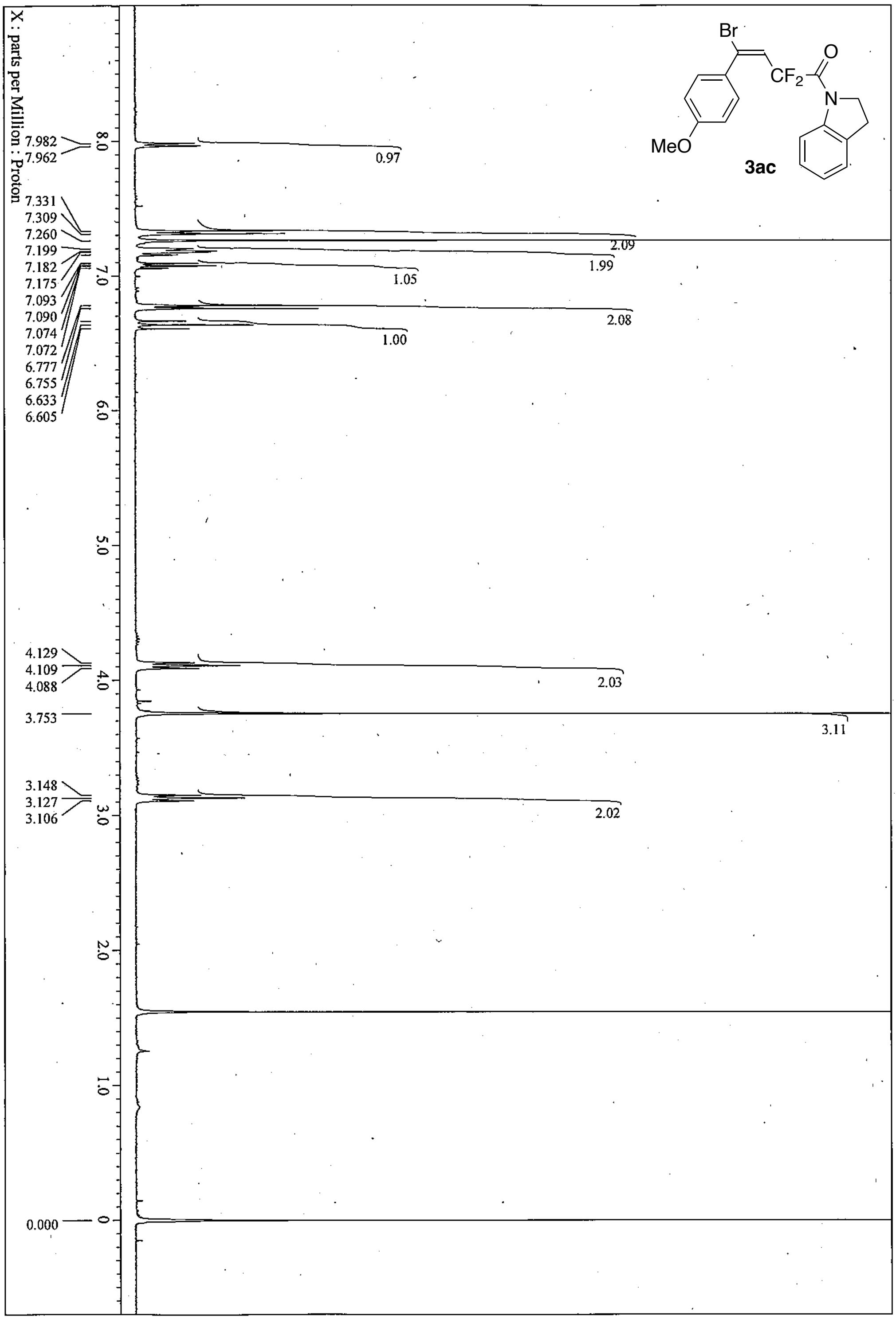
3ab: ^{1}H NMR (400 MHz, $CDCl_3$)



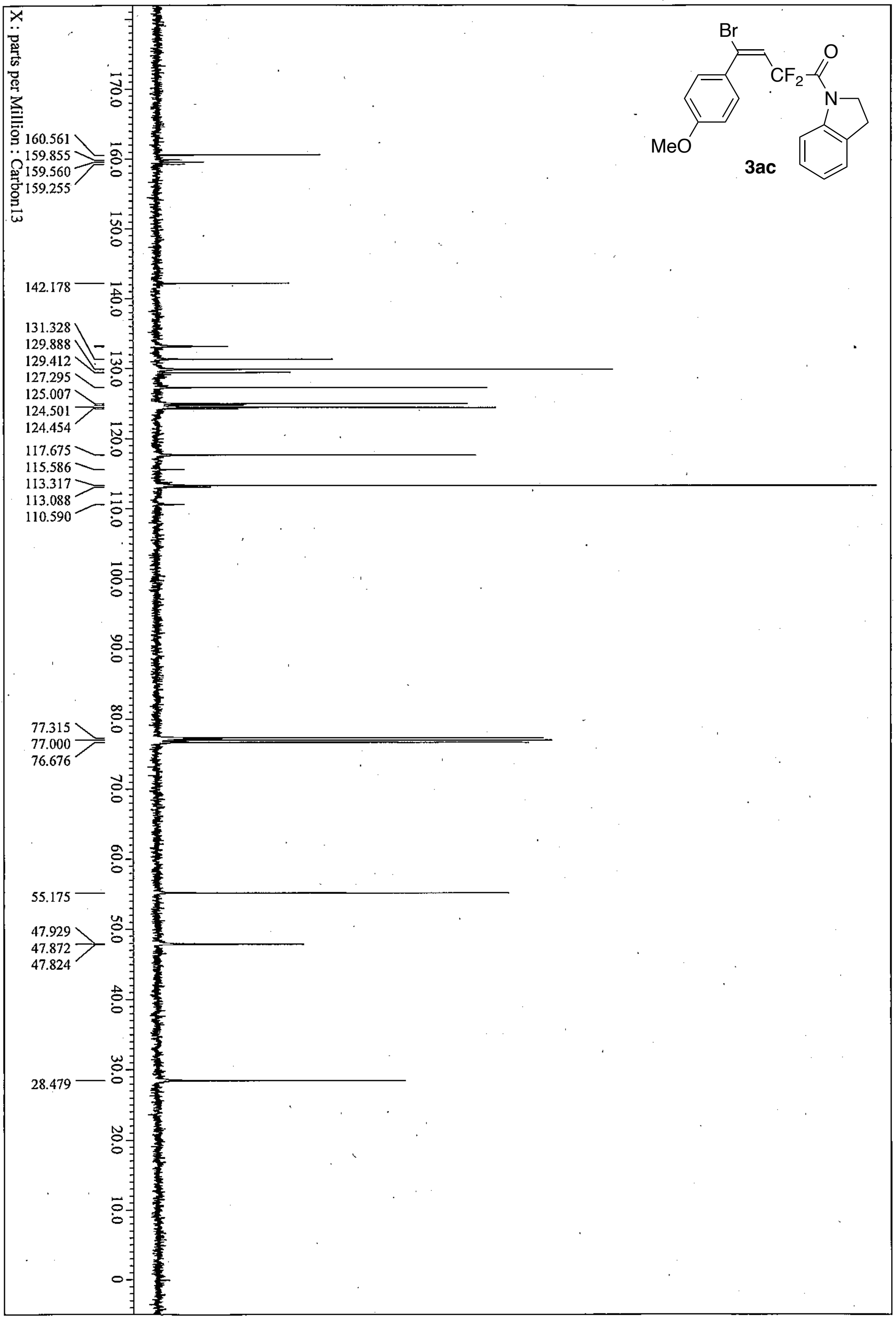
3ab: $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)



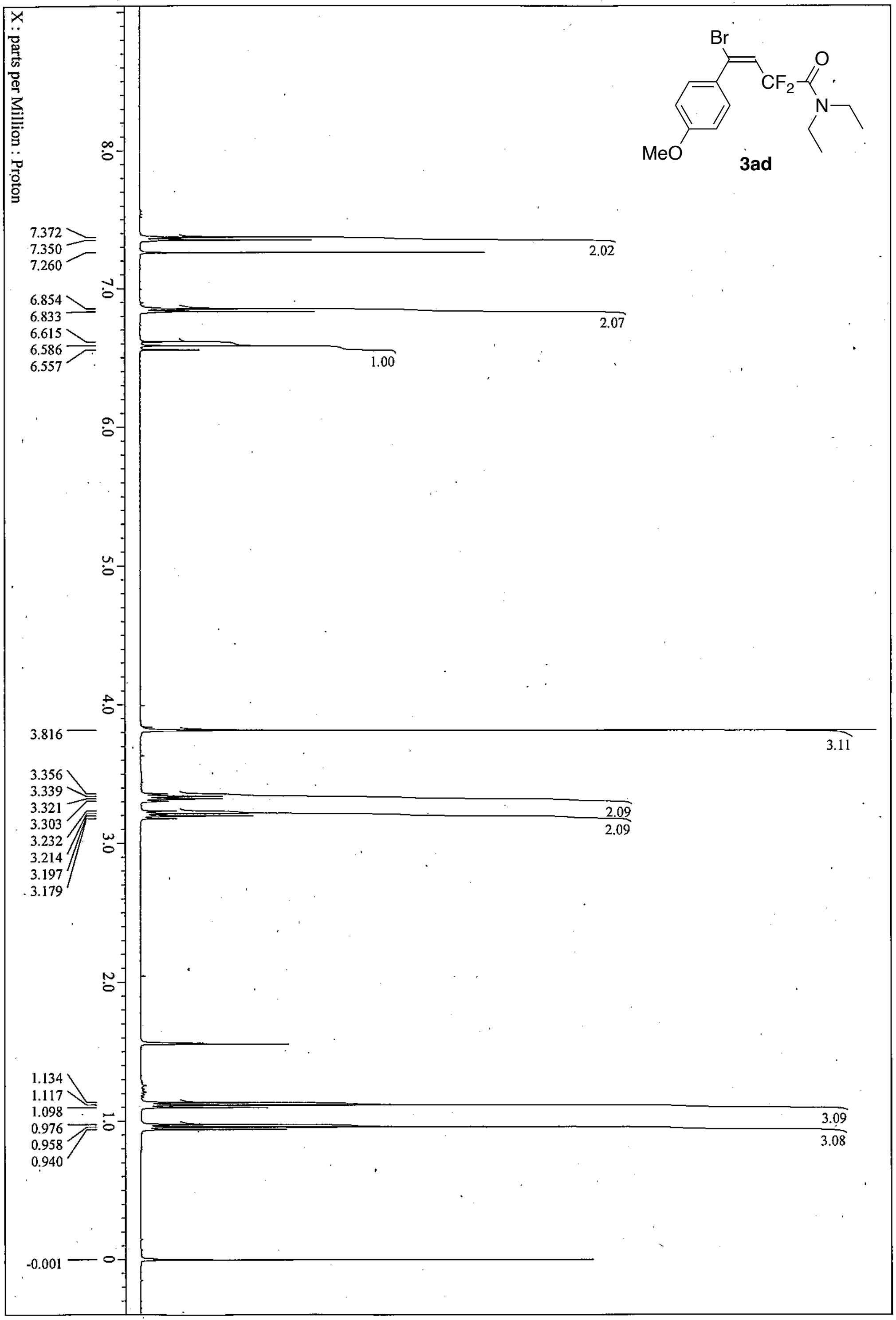
3ac: ^{1}H NMR (400 MHz, CDCl$_3$)



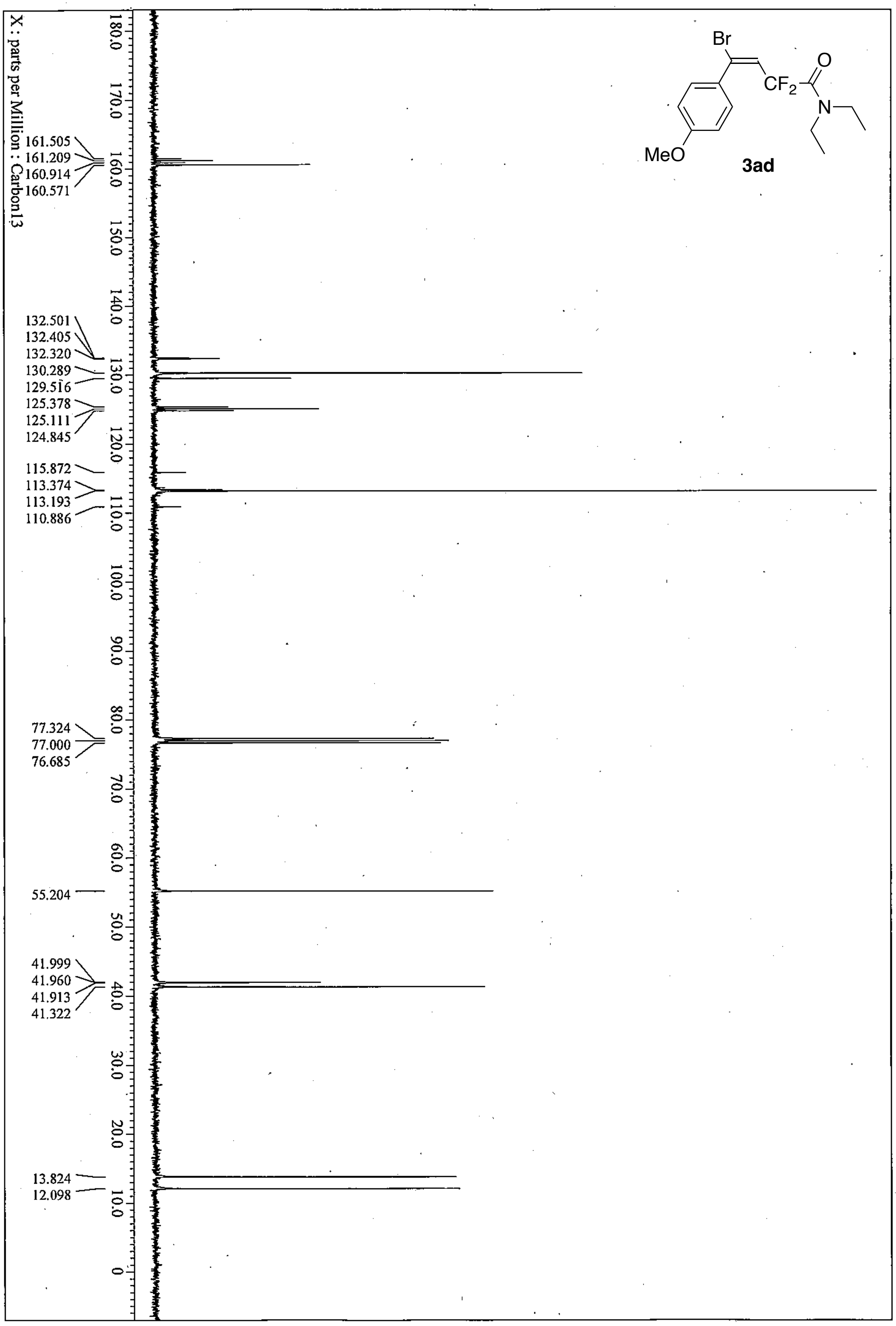
3ac: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



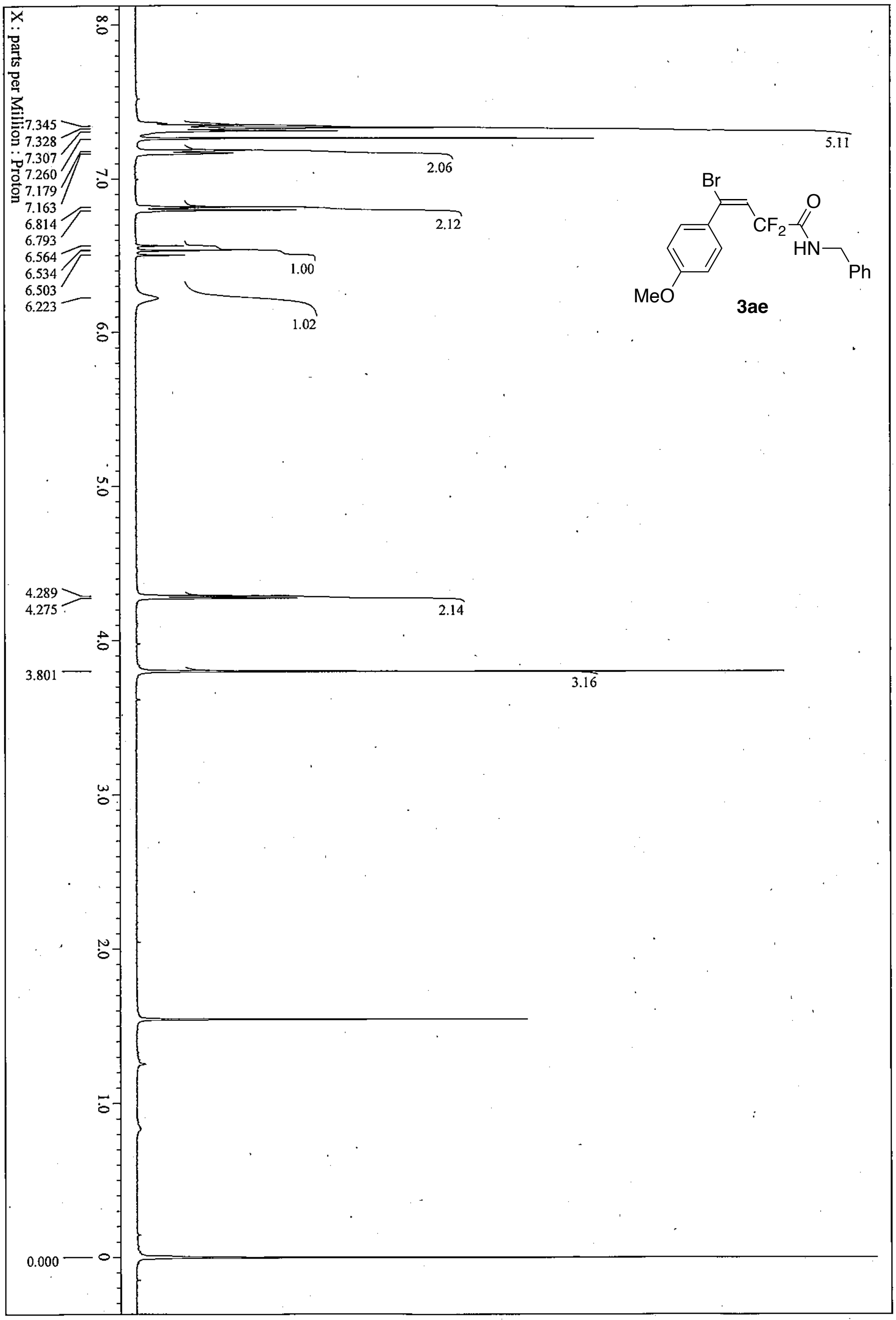
3ad: ^{1}H NMR (400 MHz, $CDCl_3$)



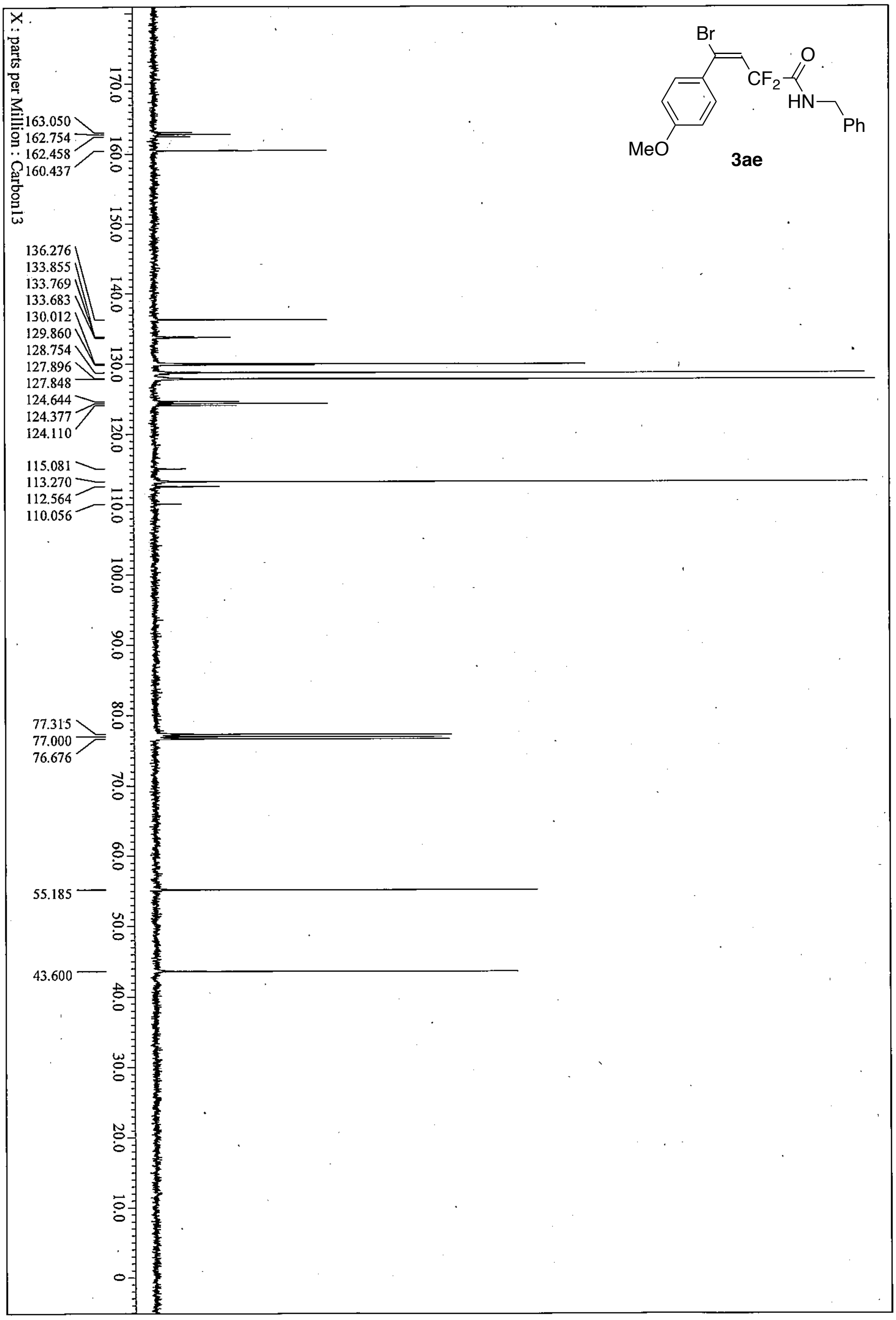
3ad: $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)



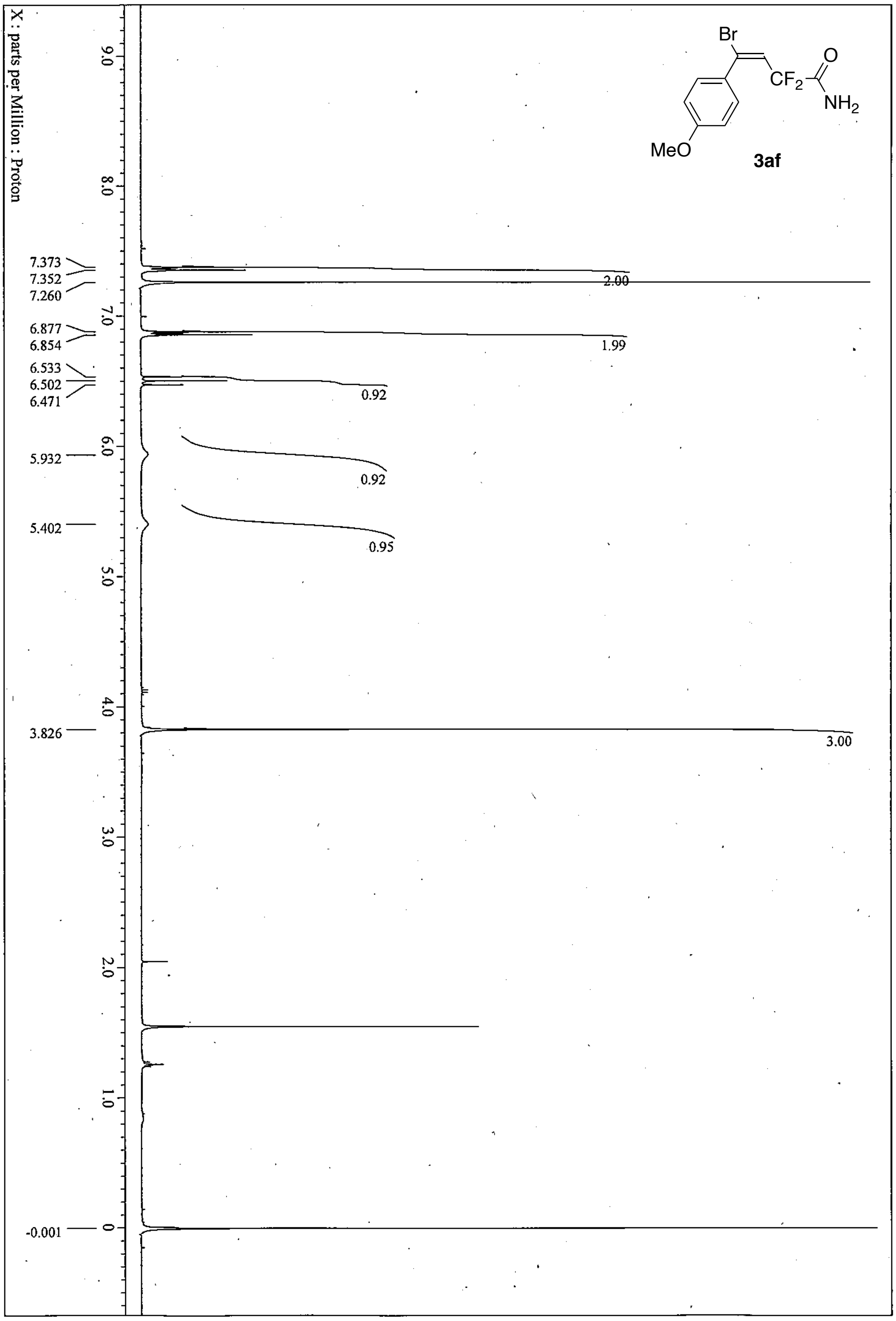
3ae: ^{1}H NMR (400 MHz, $CDCl_3$)



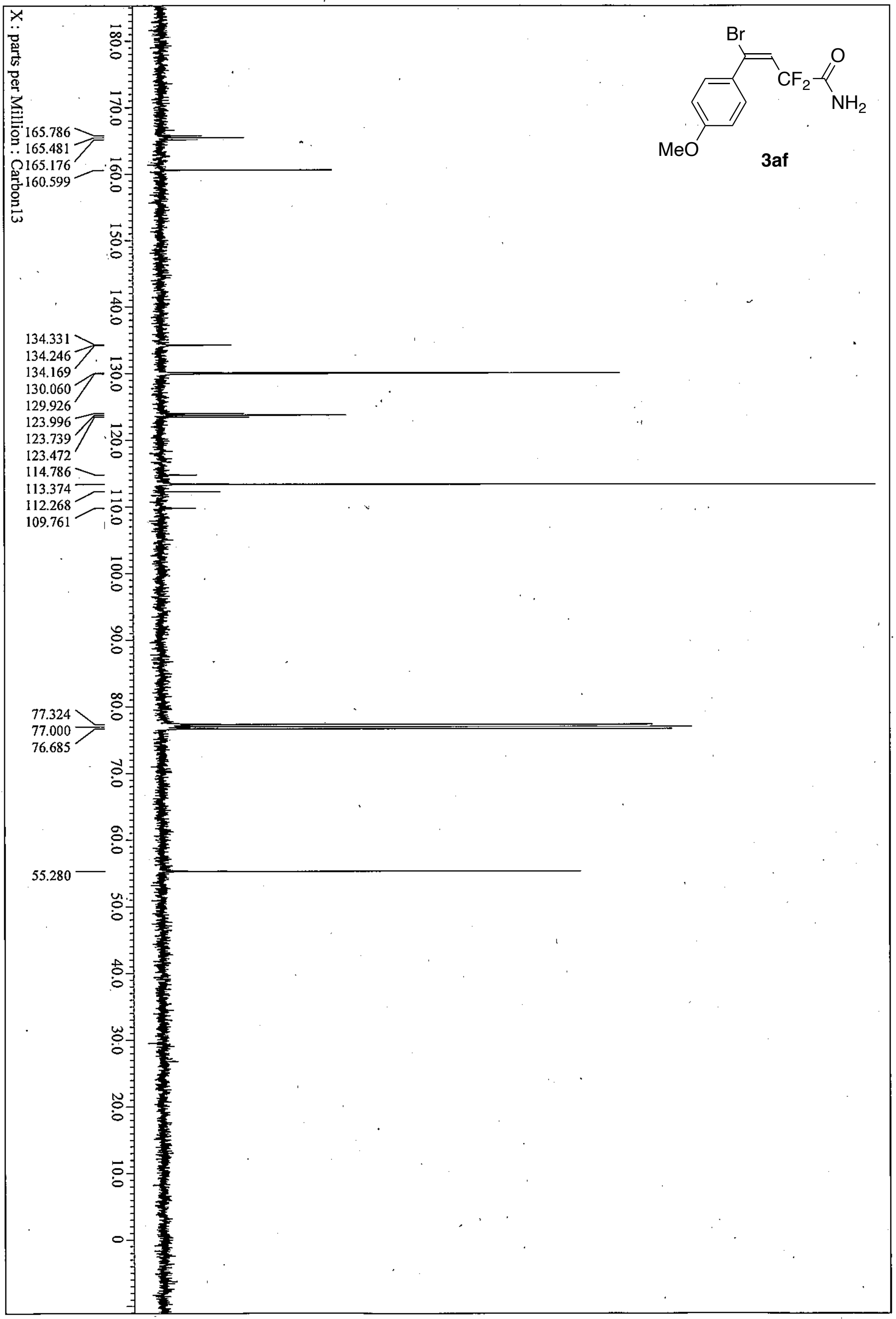
3ae: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



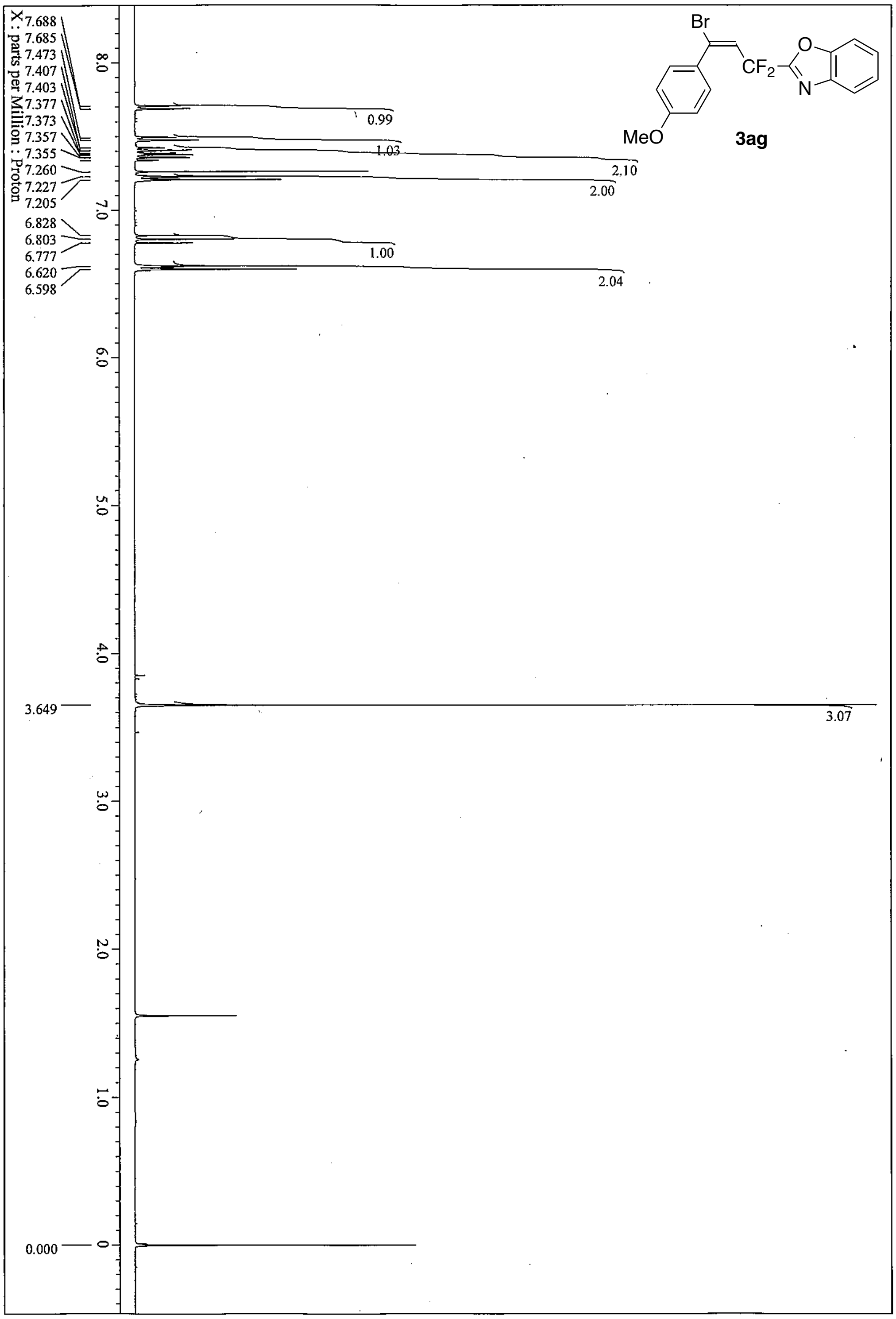
3af: ^{1}H NMR (400 MHz, $CDCl_3$)



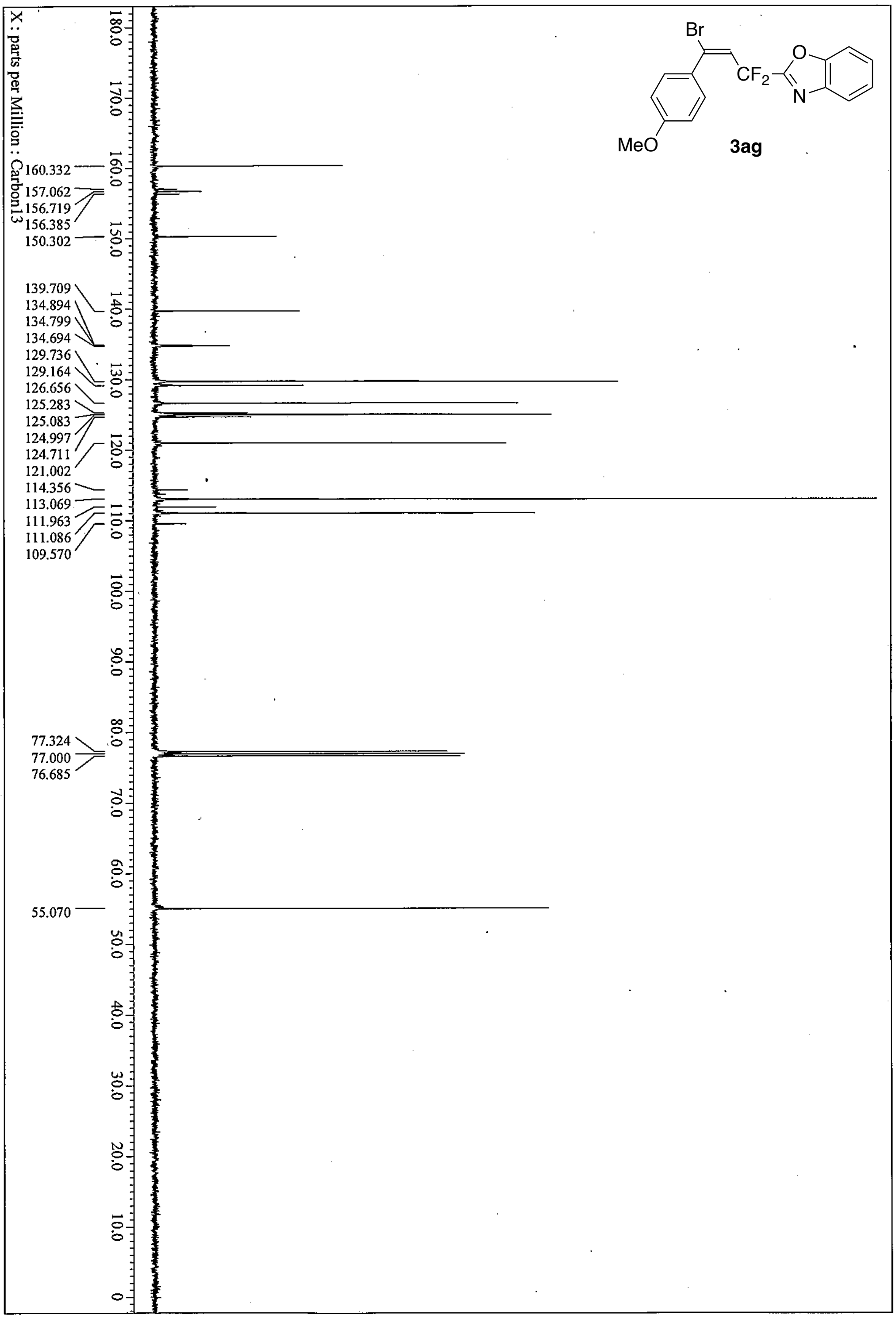
3af: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



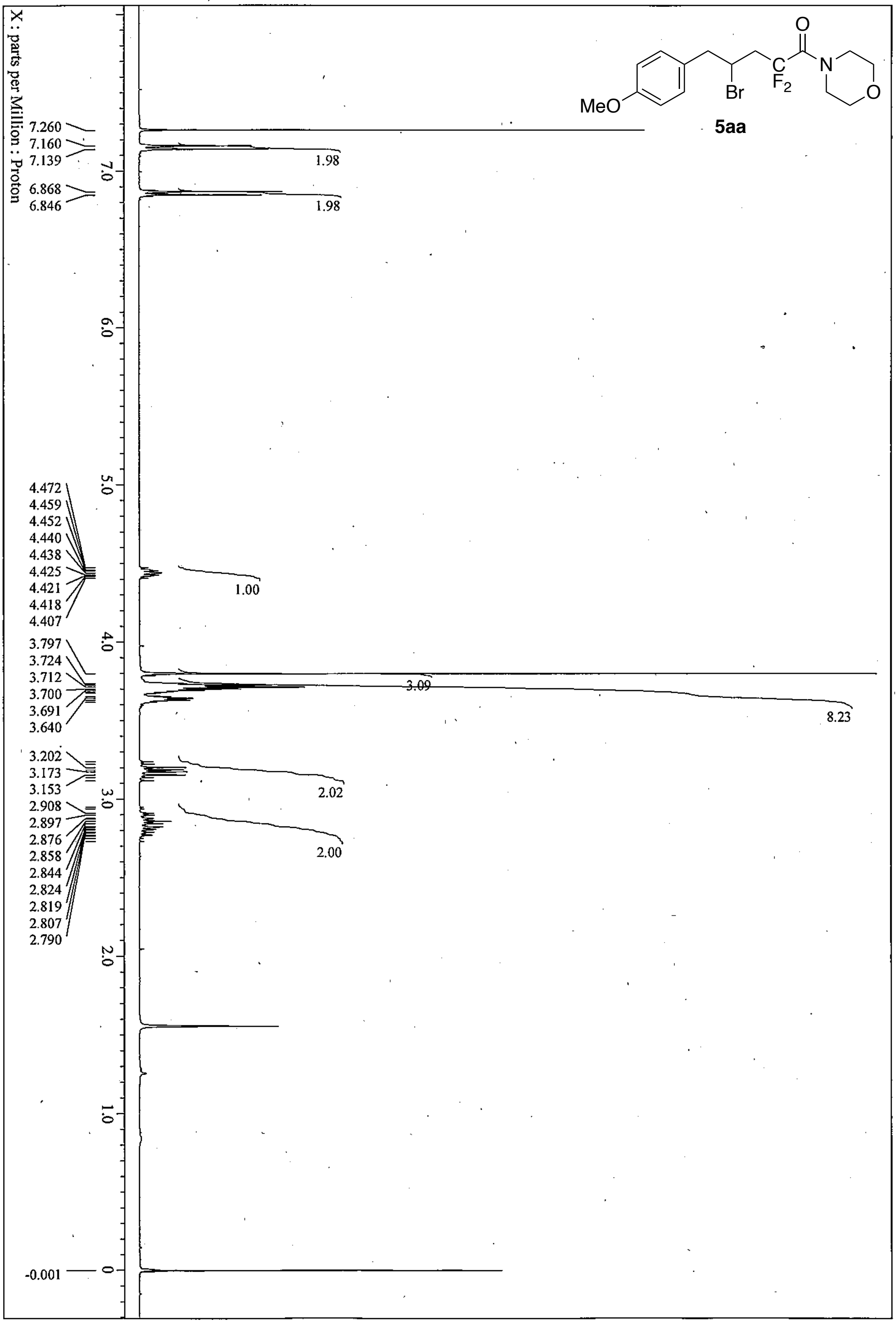
3ag: ^{1}H NMR (400 MHz, $CDCl_3$)



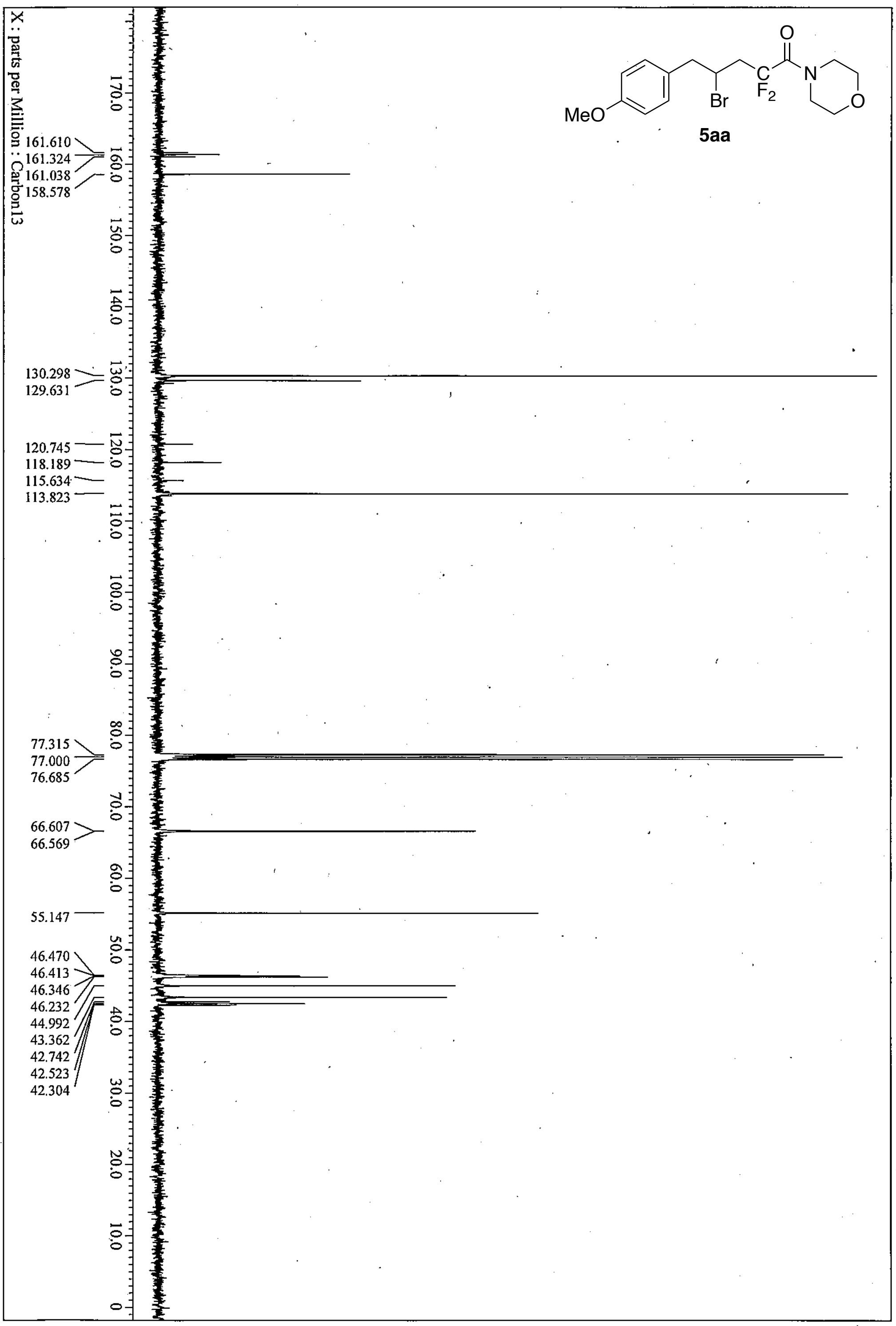
3ag: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



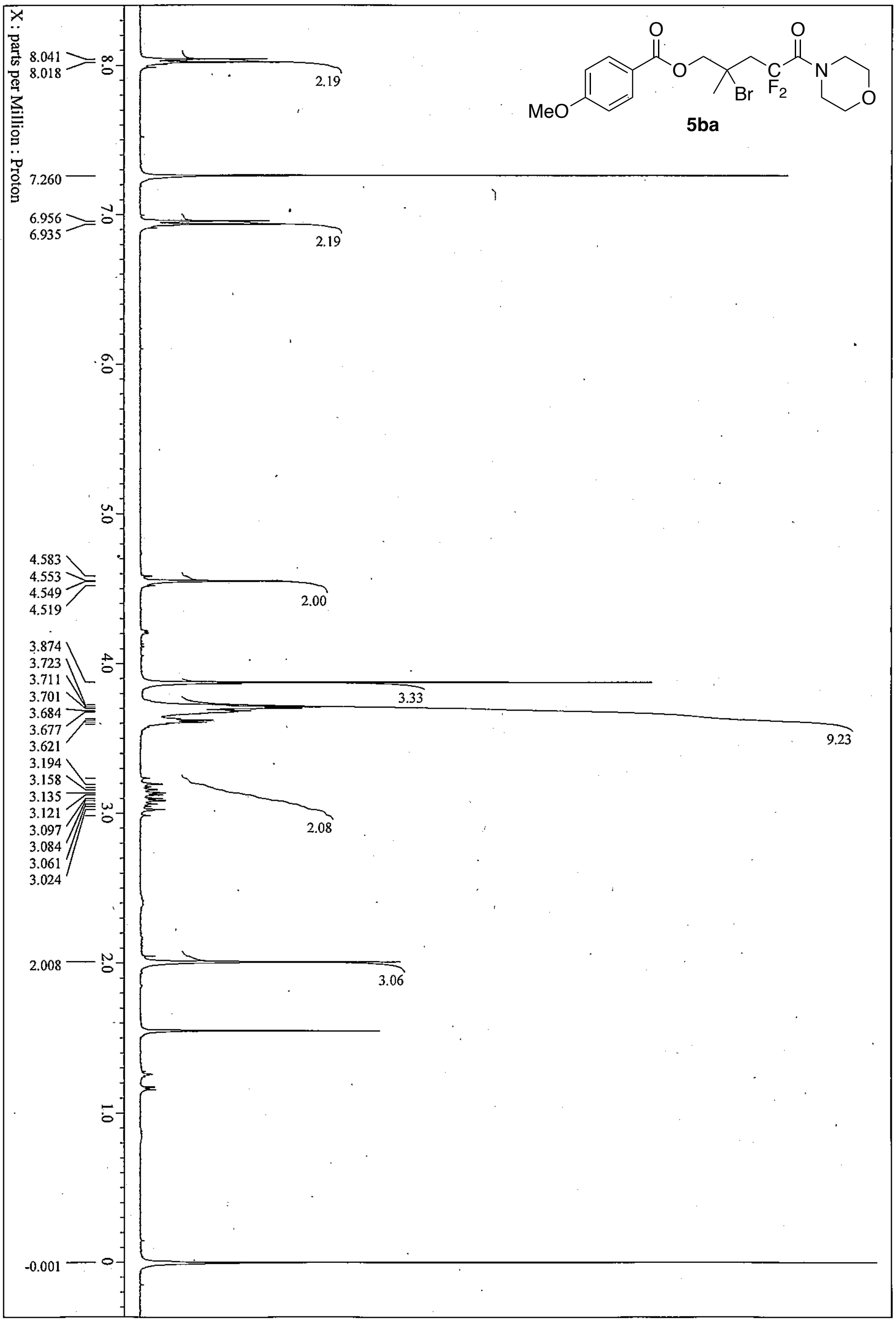
5aa: ^1H NMR (400 MHz, $CDCl_3$)



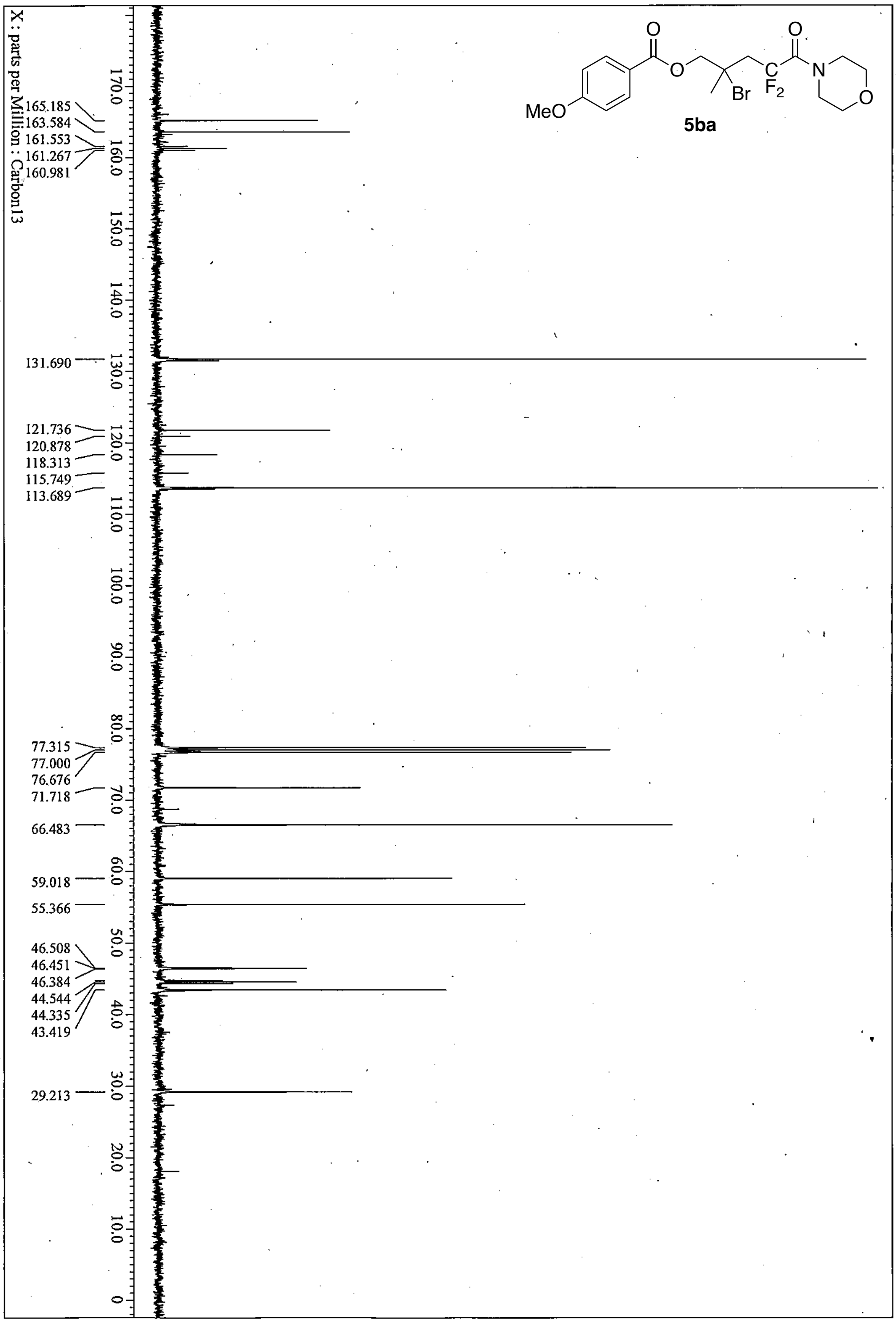
5aa: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



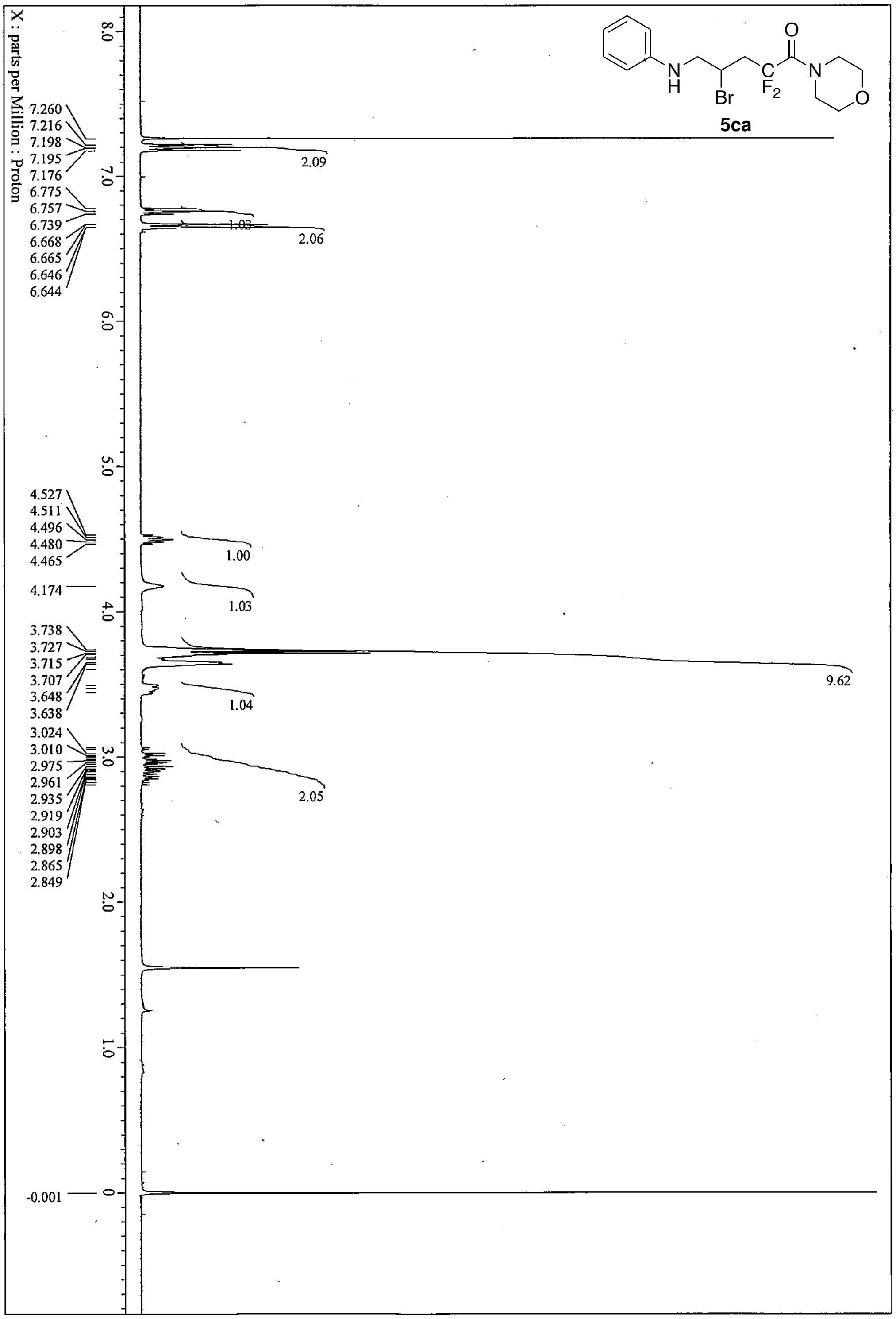
5ba: ^{1}H NMR (400 MHz, $CDCl_3$)



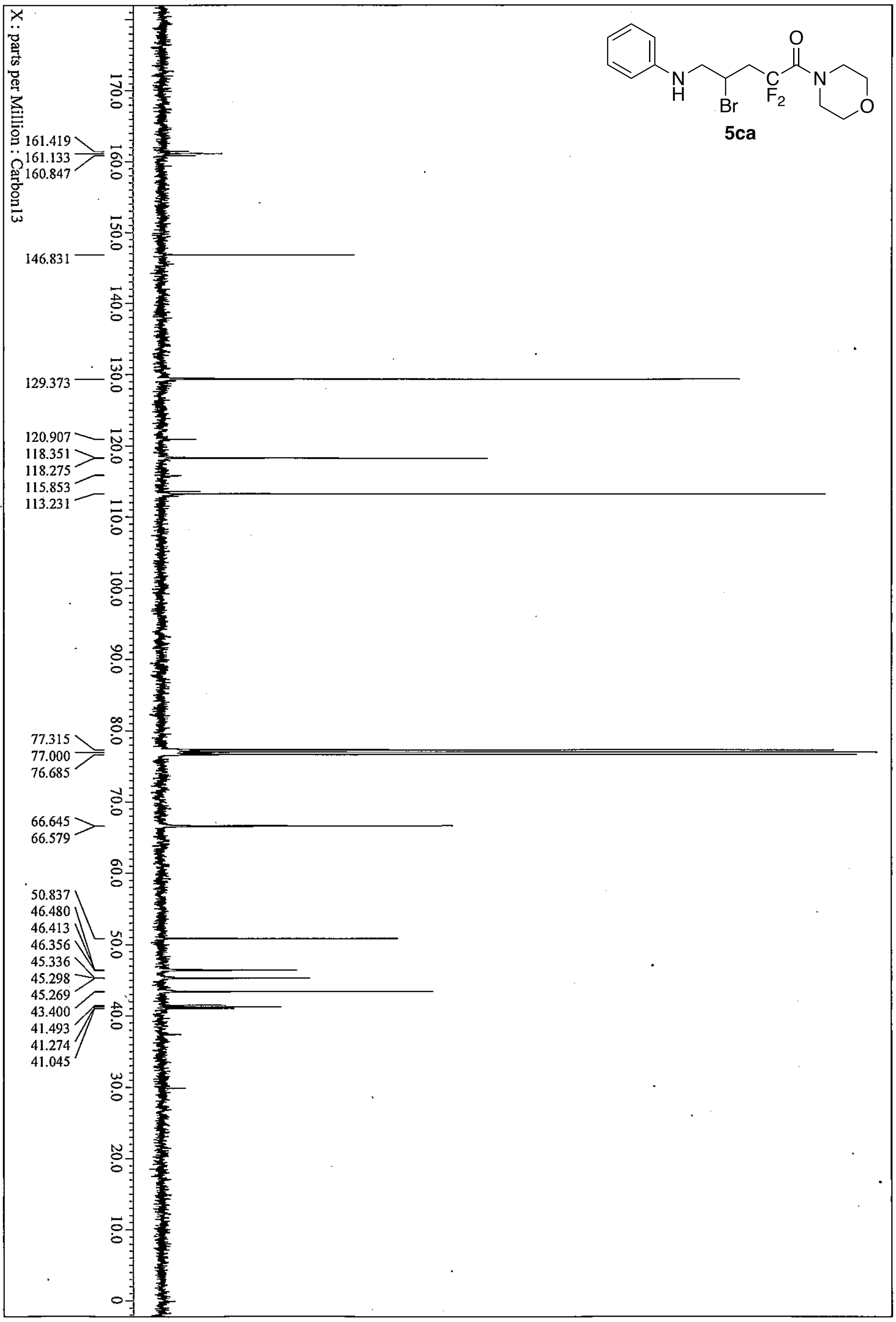
5ba: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



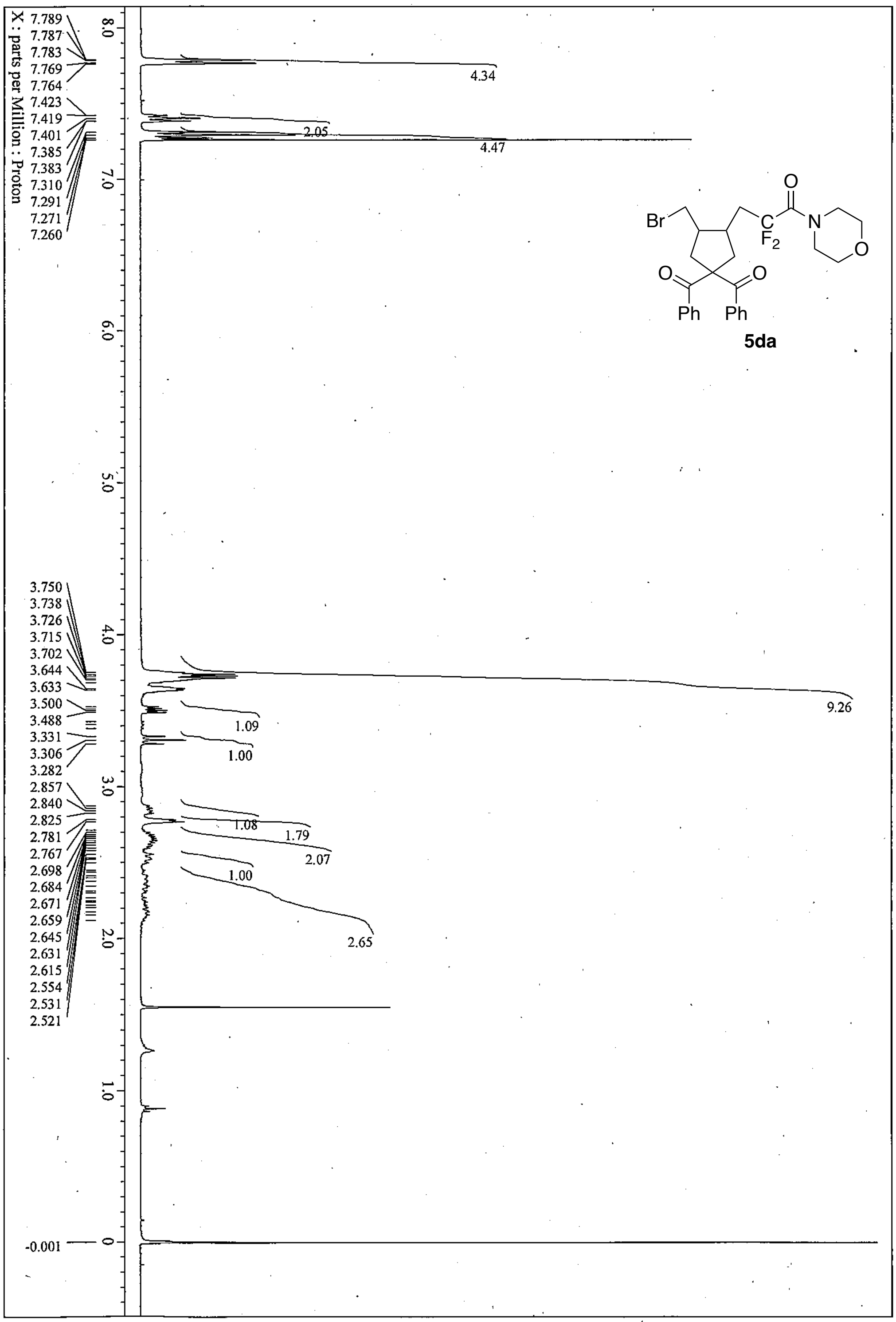
5ca: ^{1}H NMR (400 MHz, $CDCl_3$)



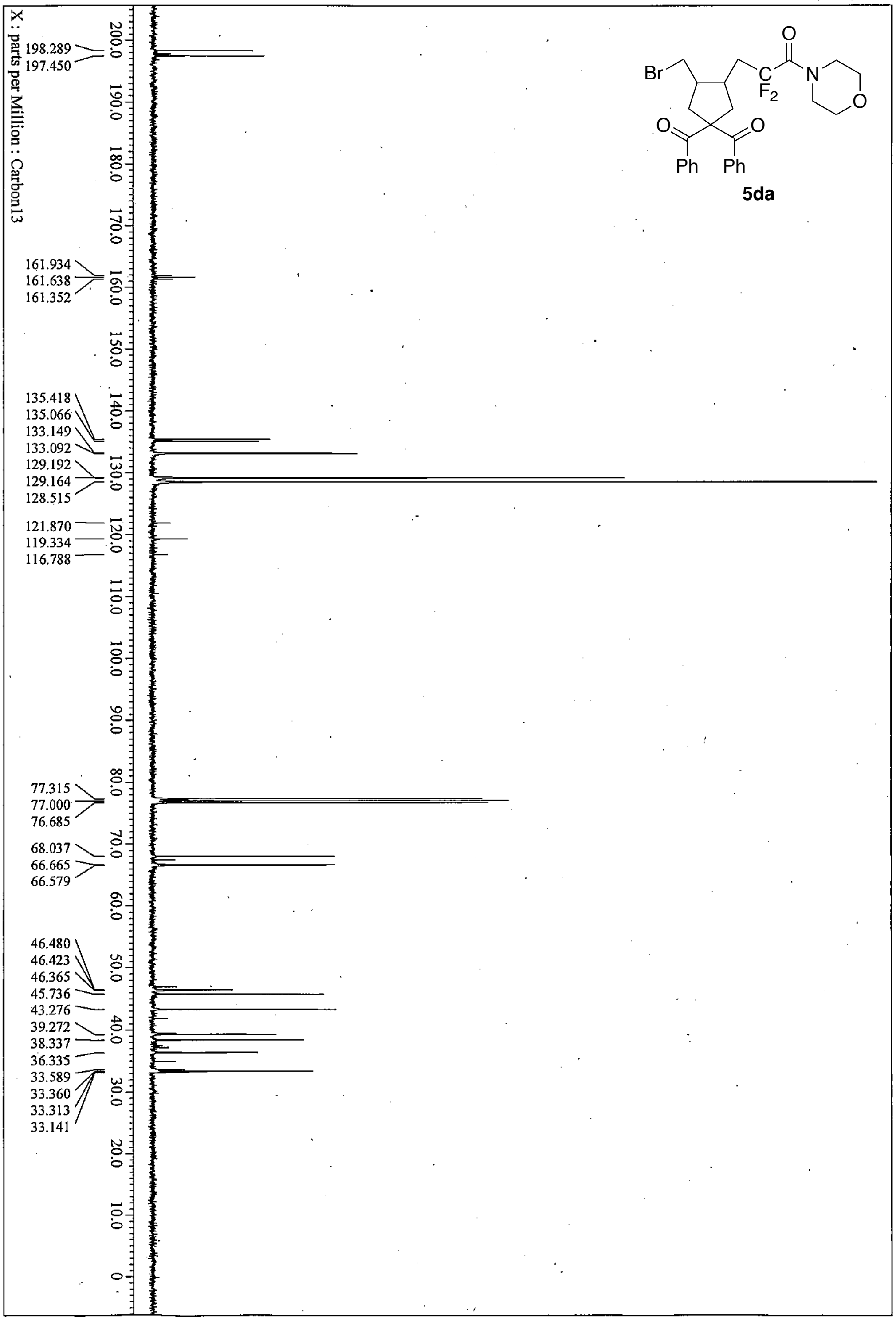
5ca: ^{1}H NMR (400 MHz, $CDCl_3$)



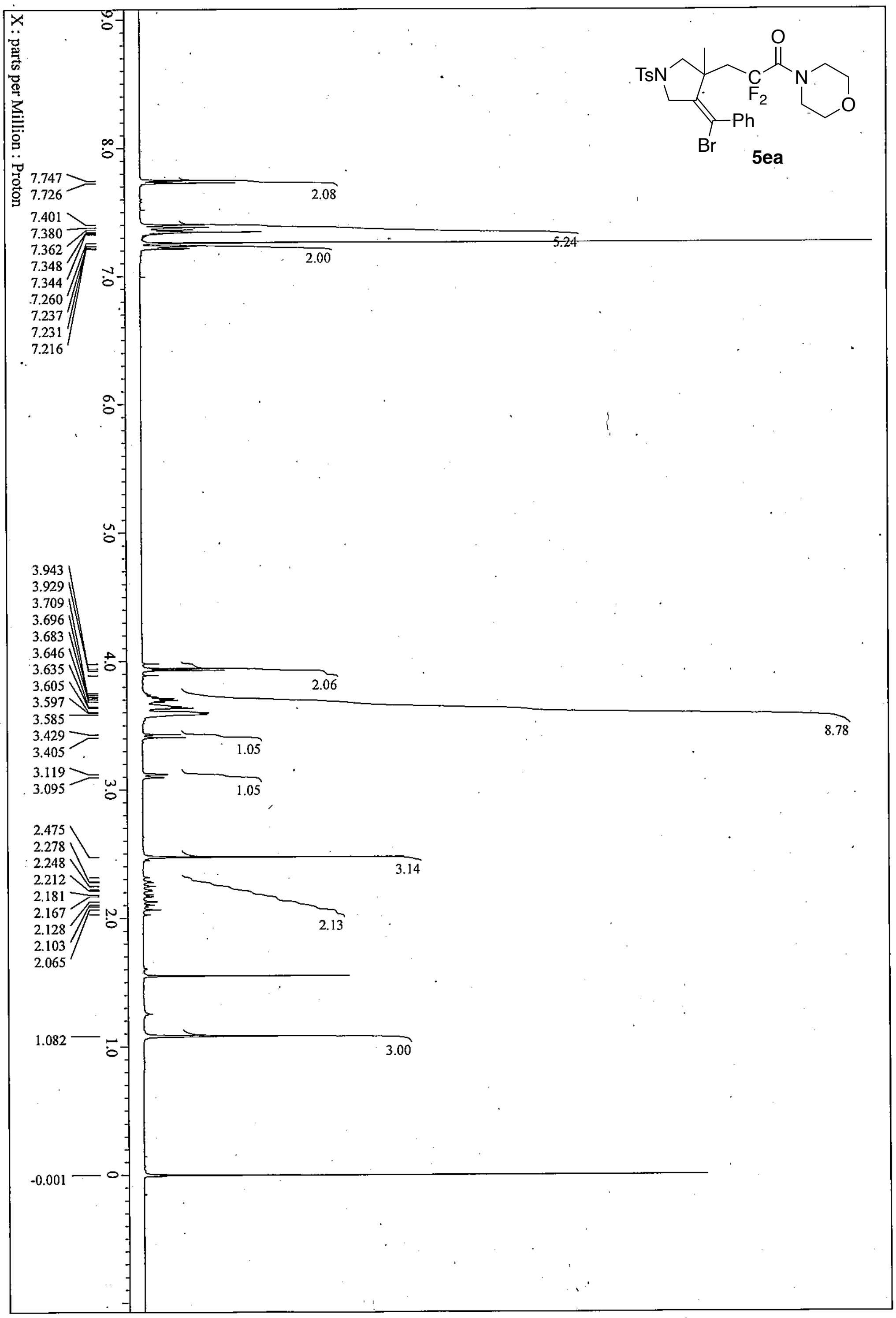
5da: ^{1}H NMR (400 MHz, $CDCl_3$)



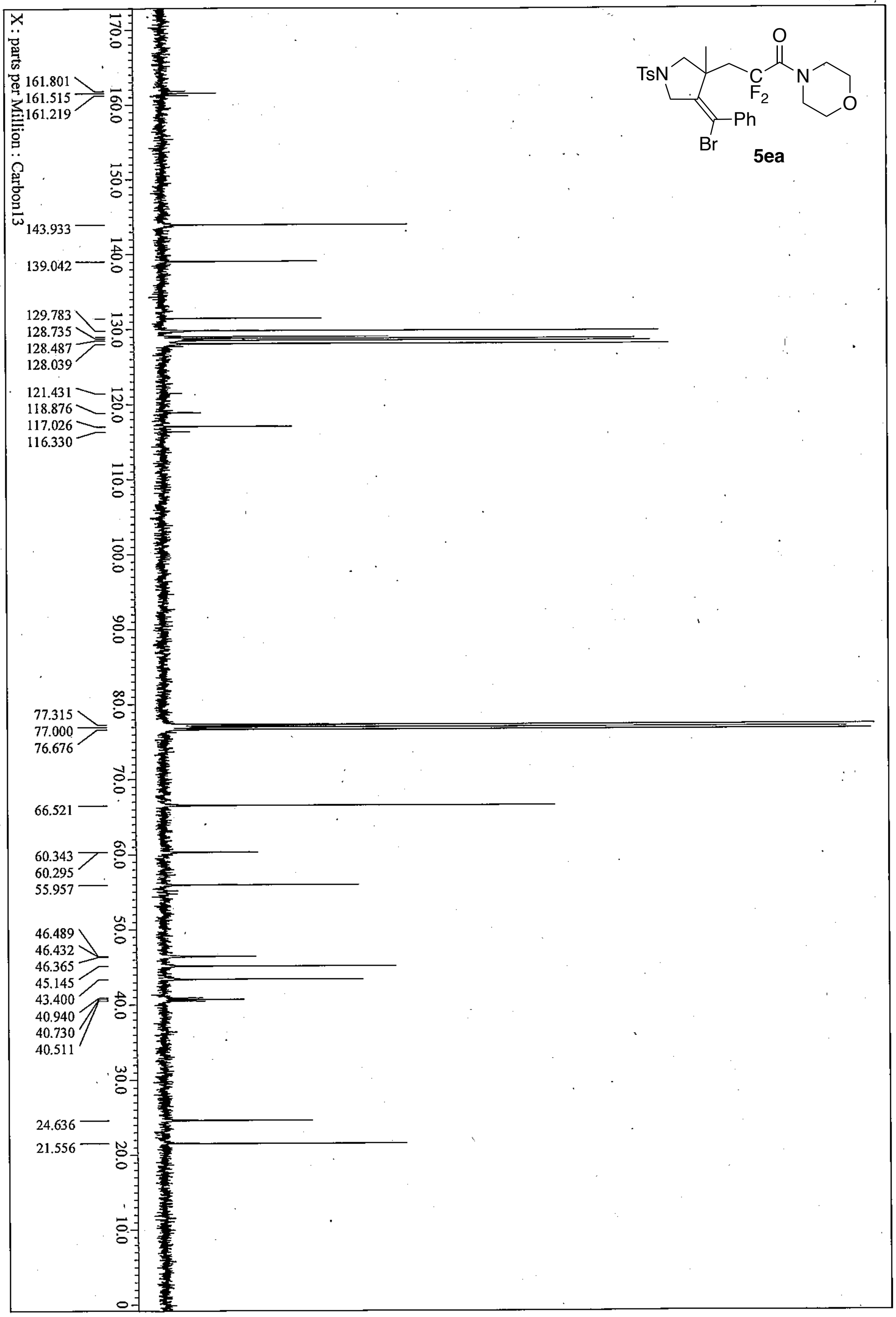
5da: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



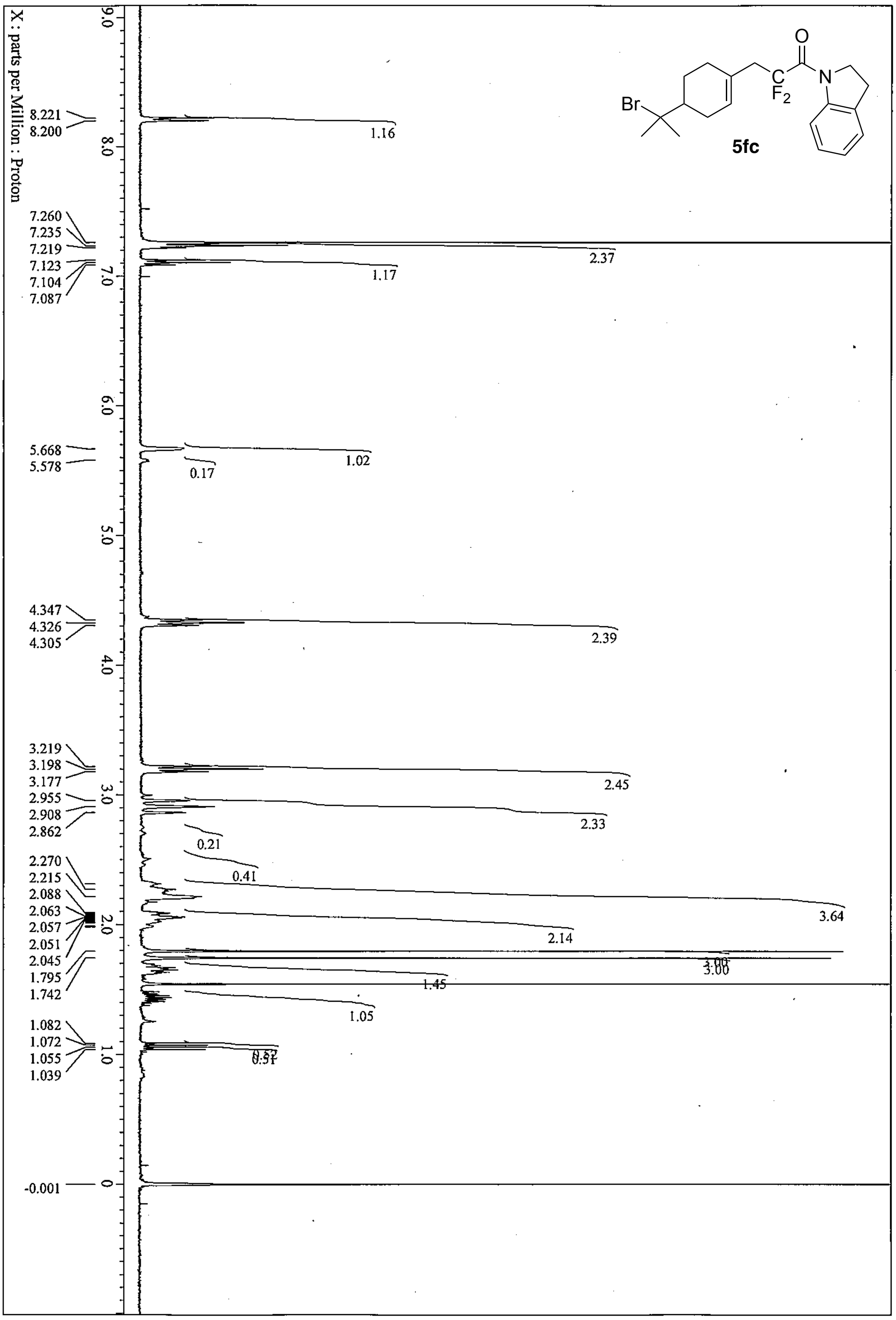
5ea: ^{1}H NMR (400 MHz, $CDCl_3$)



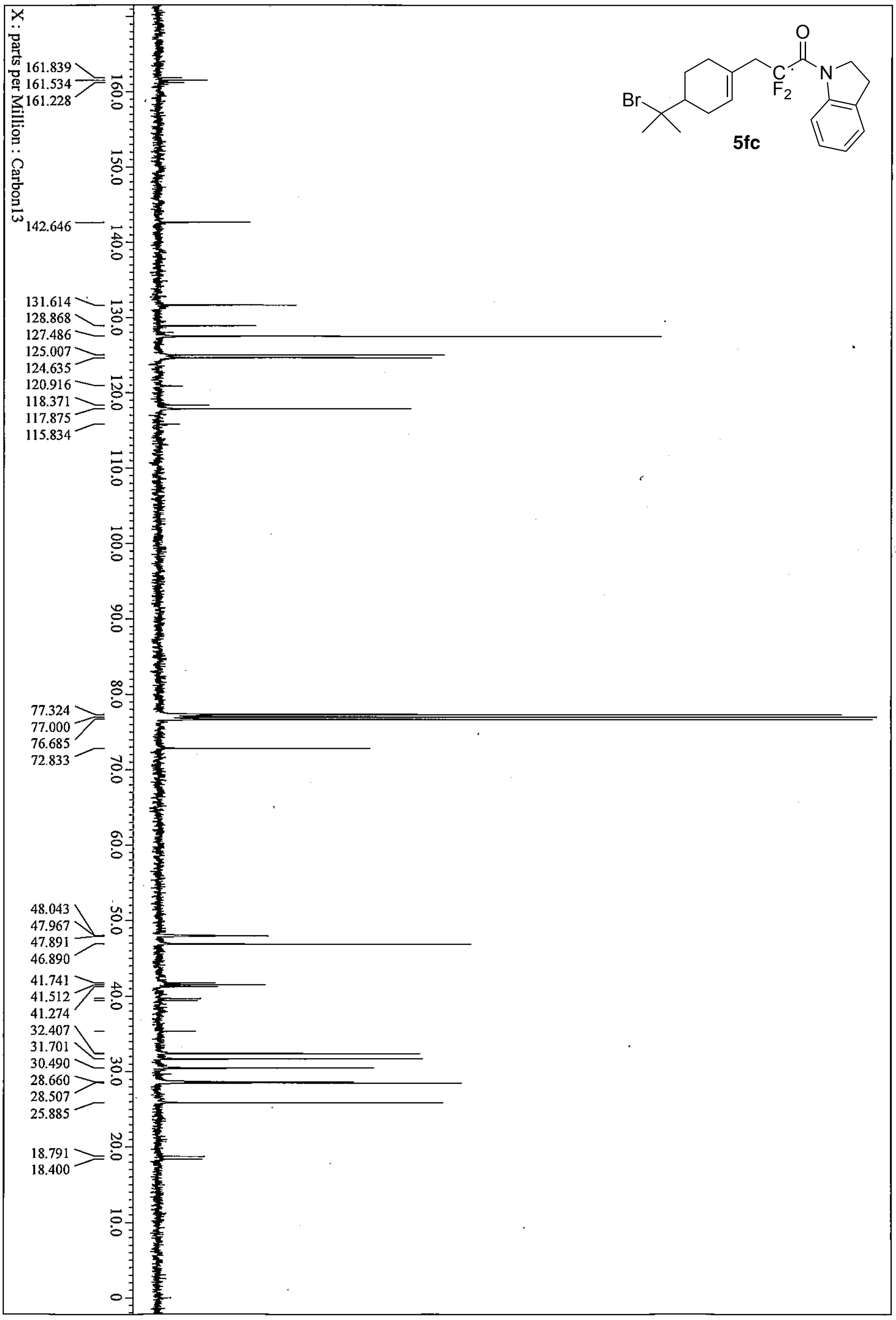
5ea: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



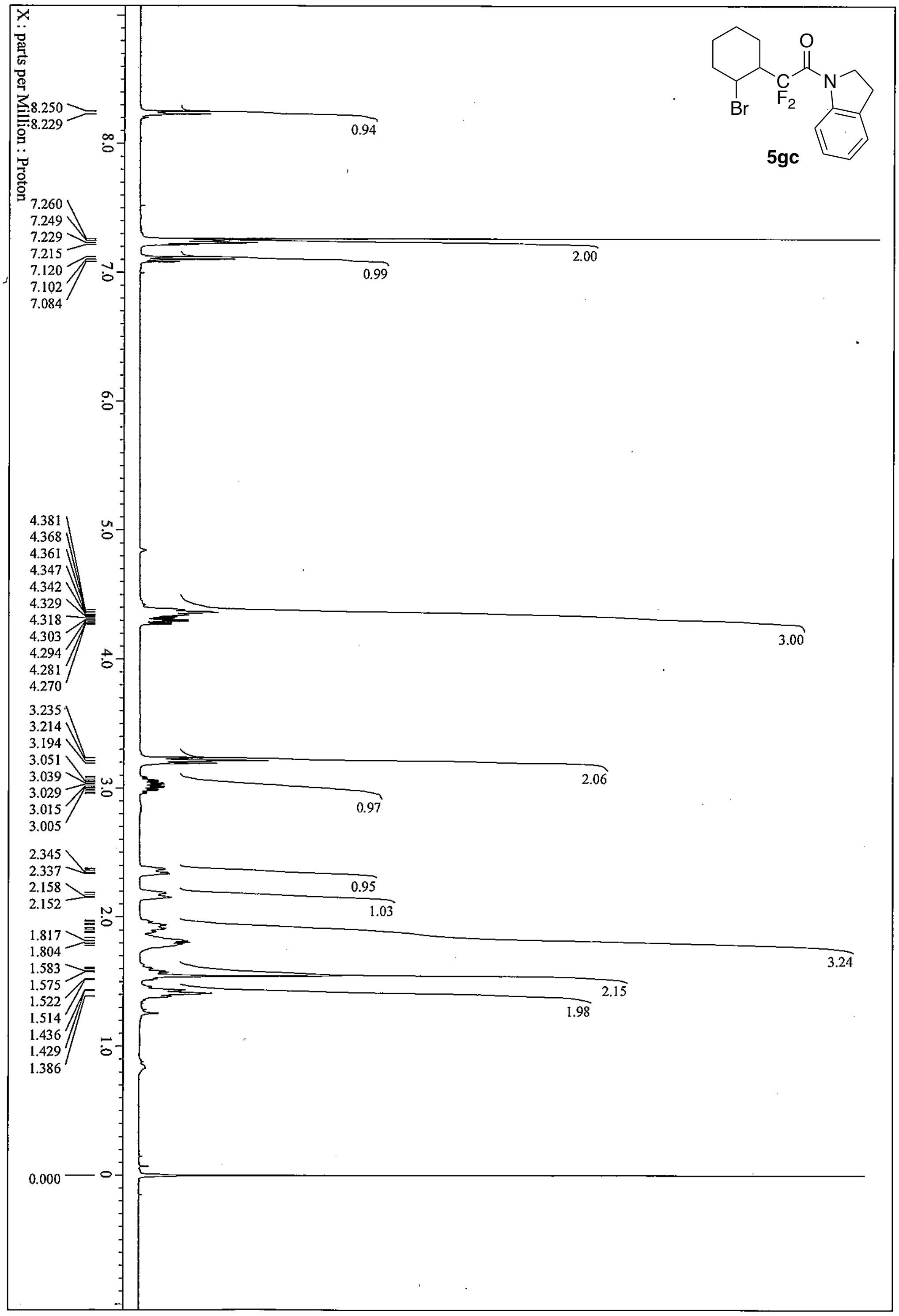
5fc (+ 5fc'): ^{1}H NMR (400 MHz, $CDCl_3$)



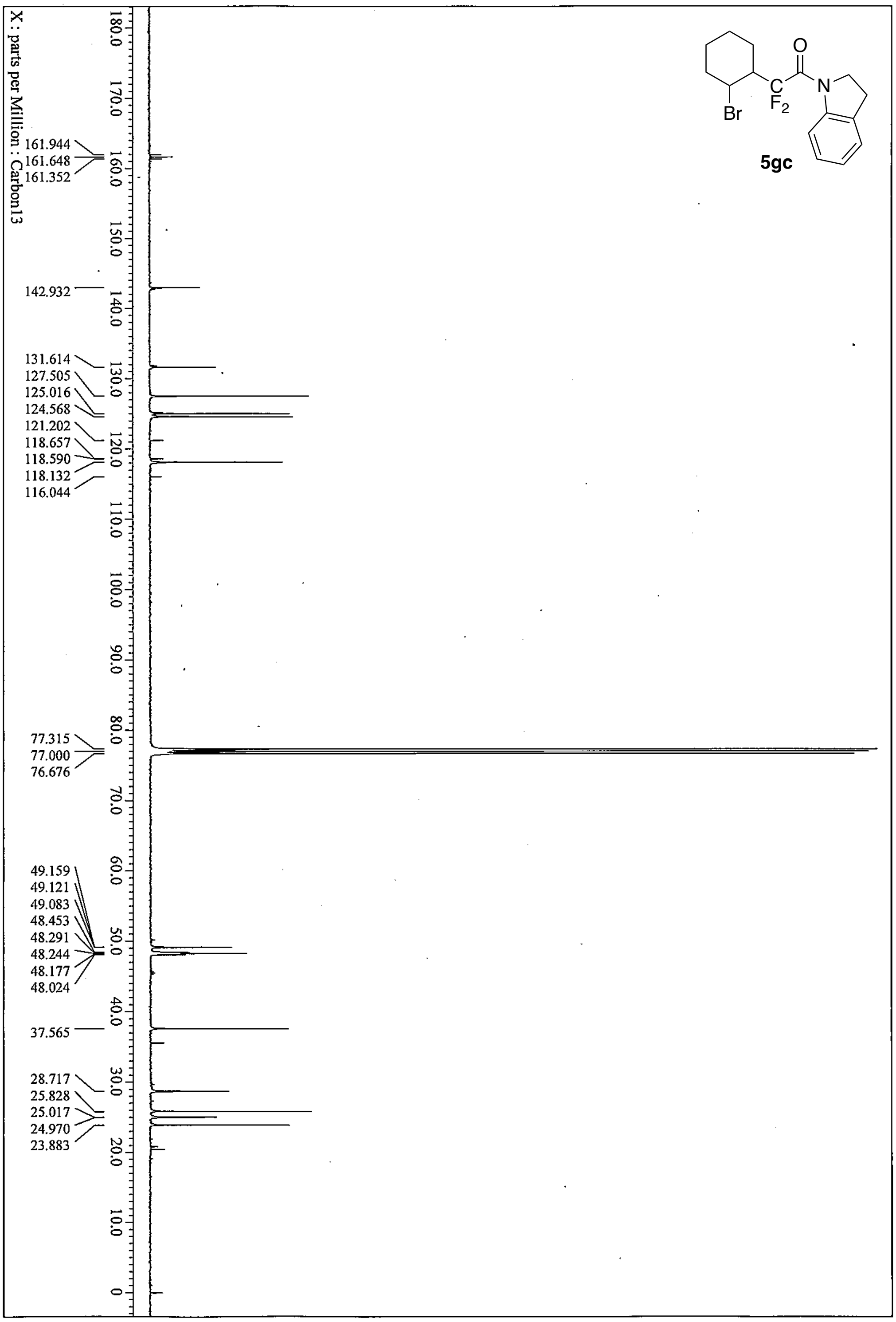
5fc (+ 5fc'): $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)



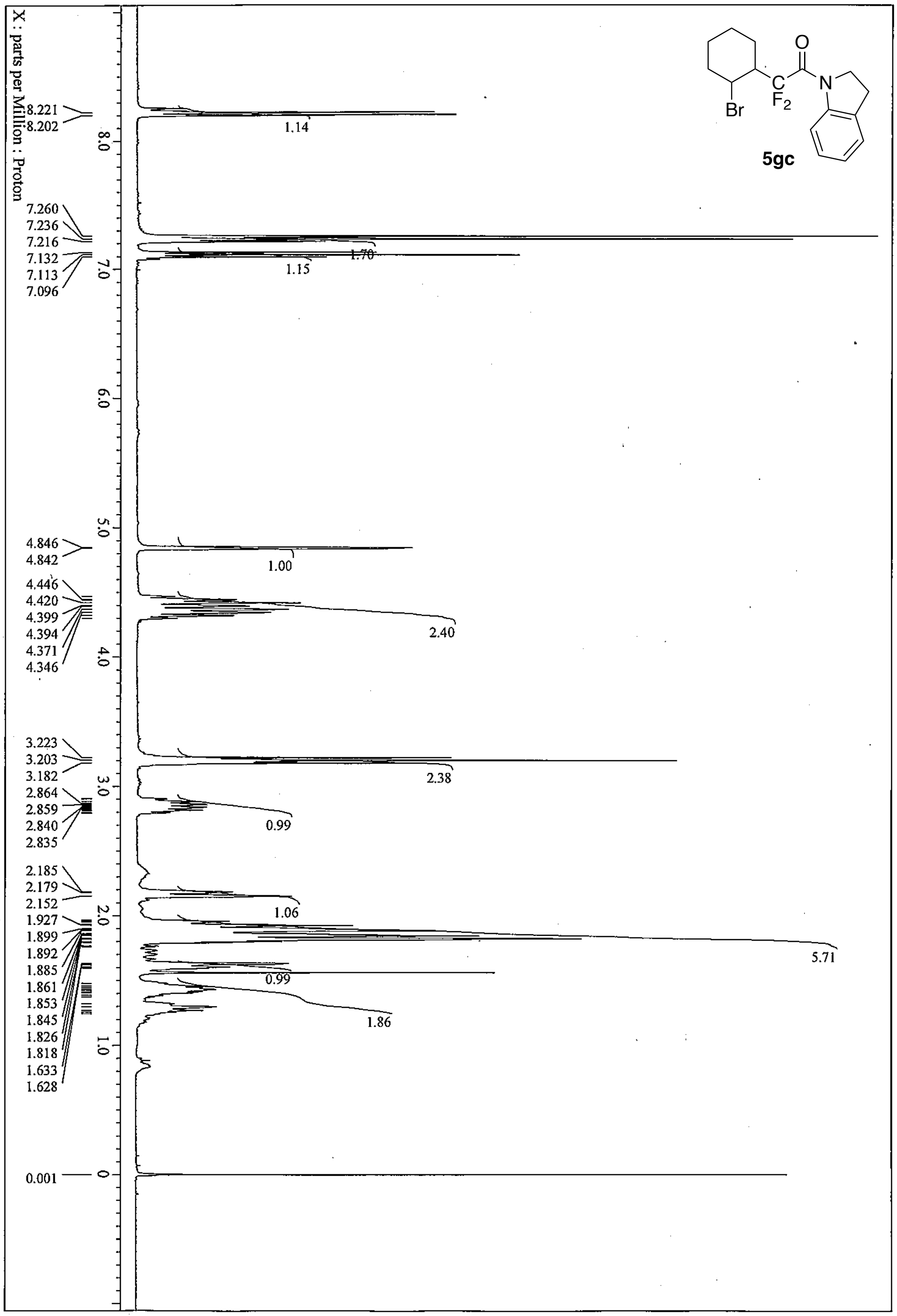
5gc major: ^{1}H NMR (400 MHz, $CDCl_3$)



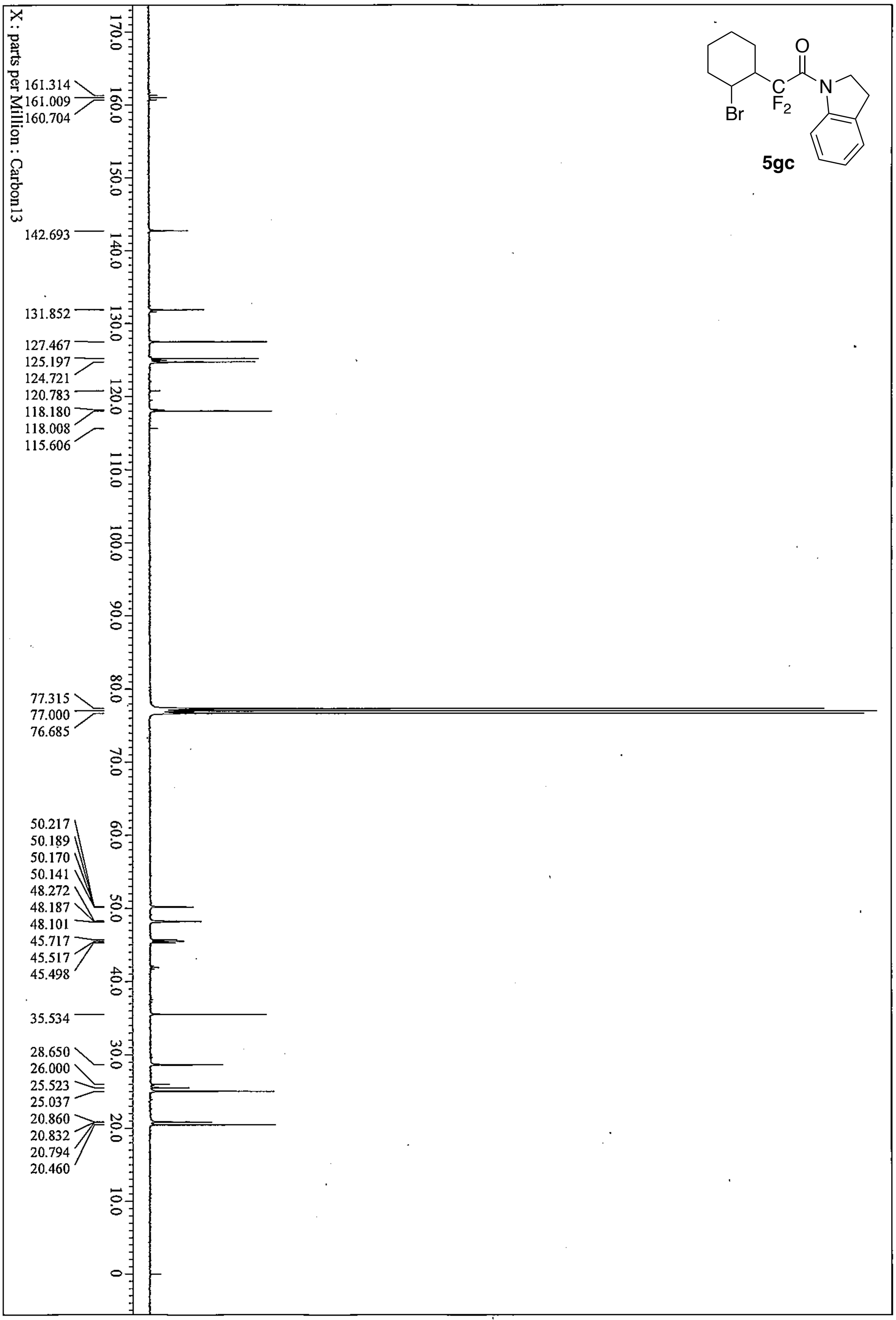
5gc major: $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)



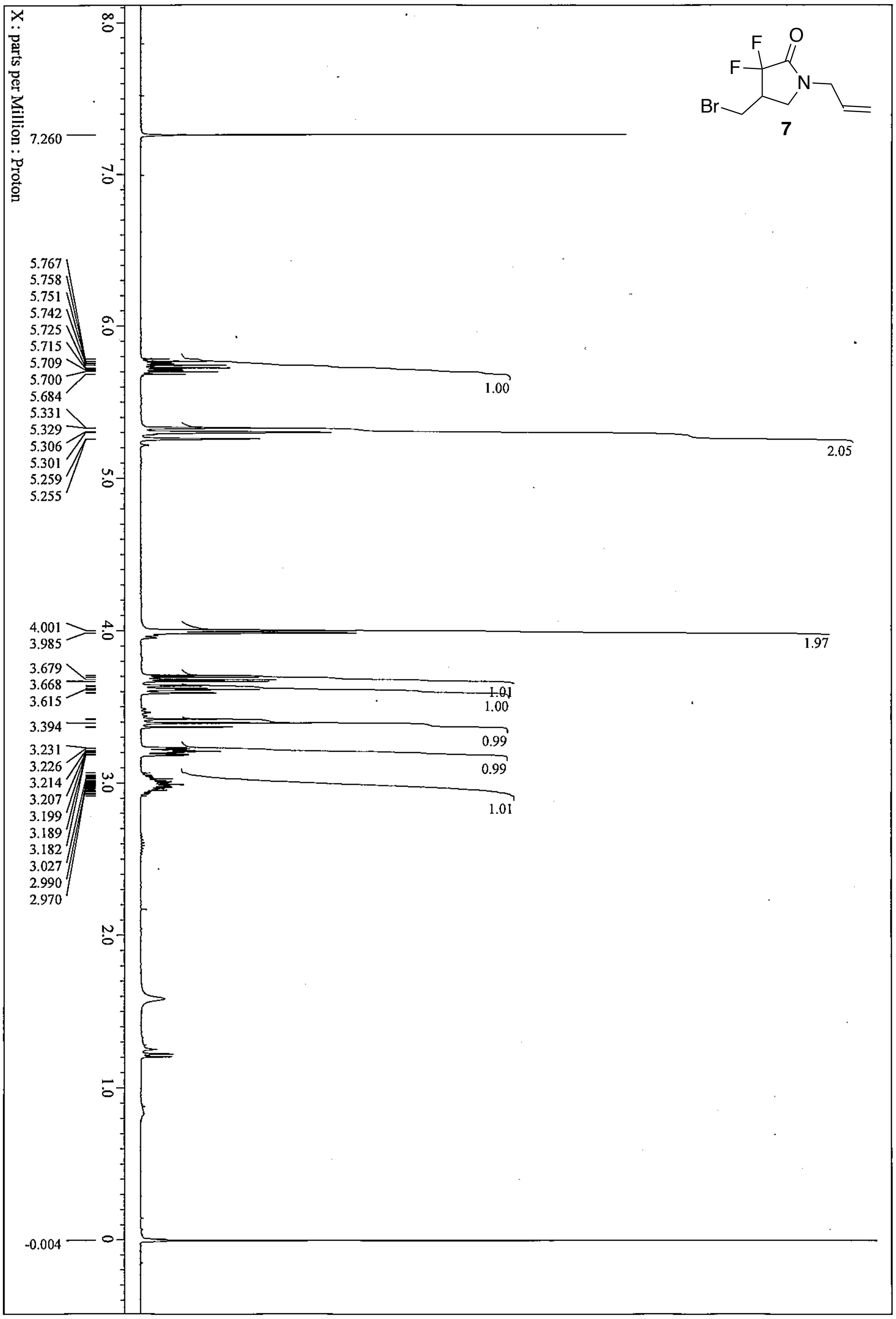
5gc minor: ^{1}H NMR (400 MHz, $CDCl_3$)



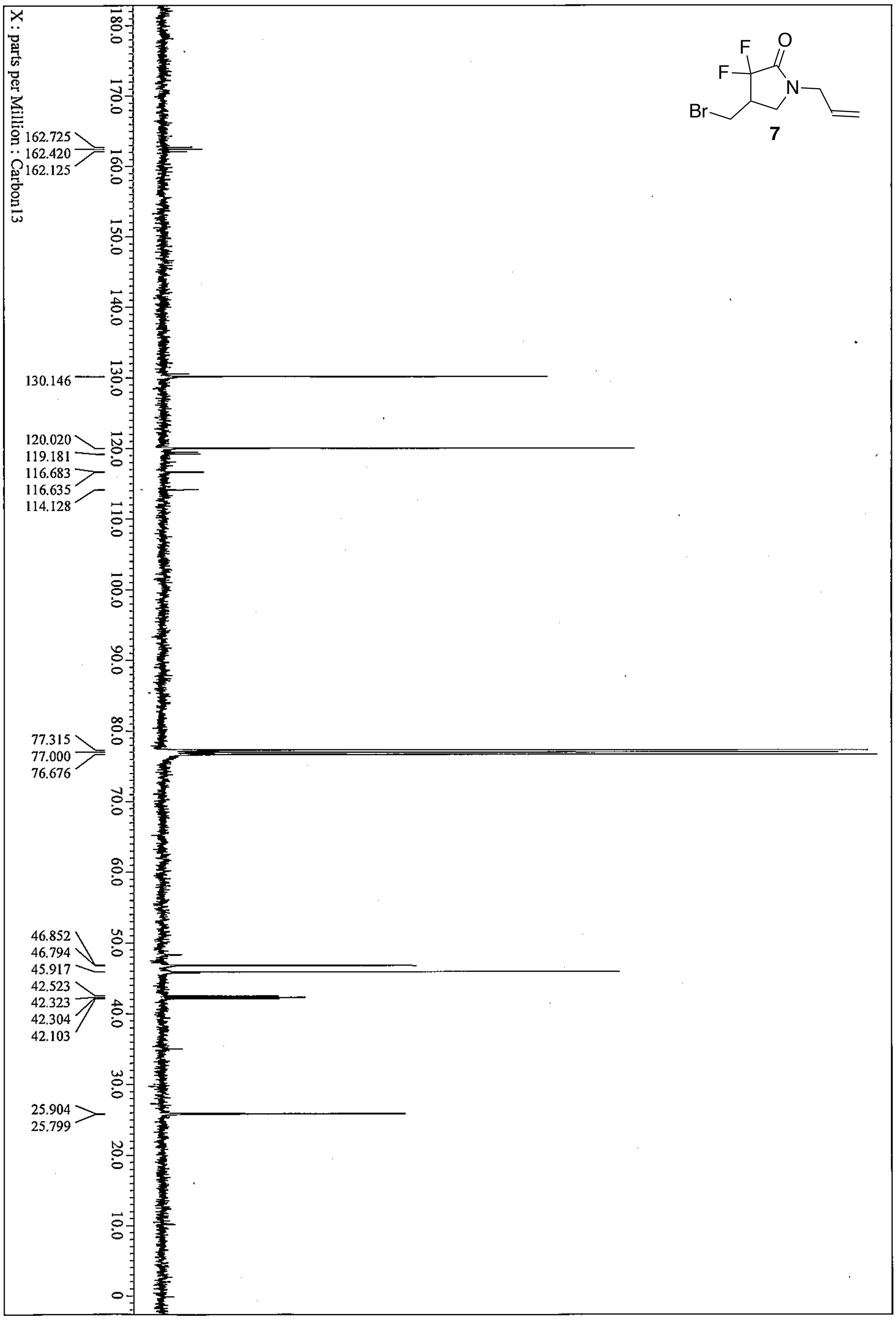
5gc minor: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



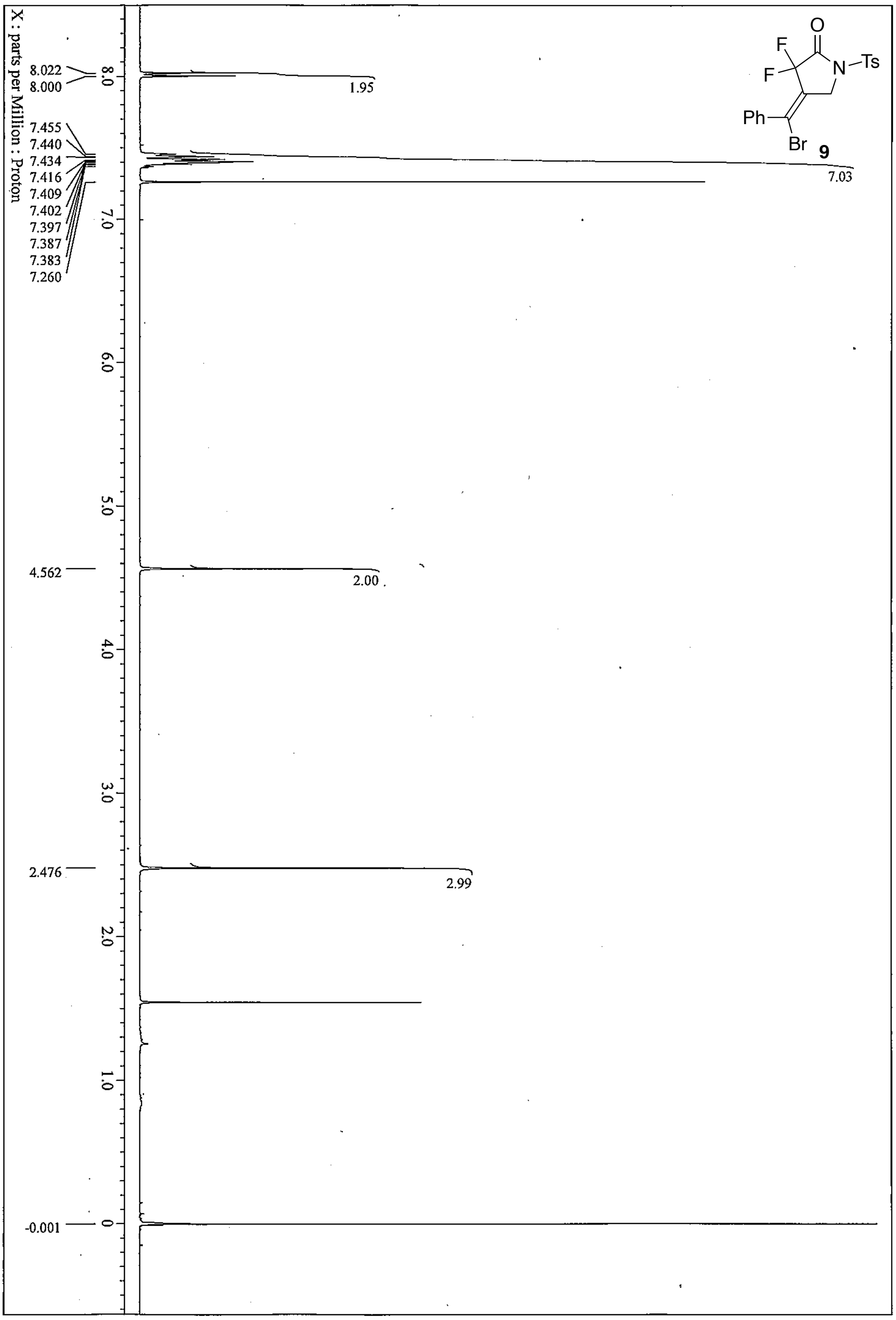
7: ^{1}H NMR (400 MHz, $CDCl_3$)



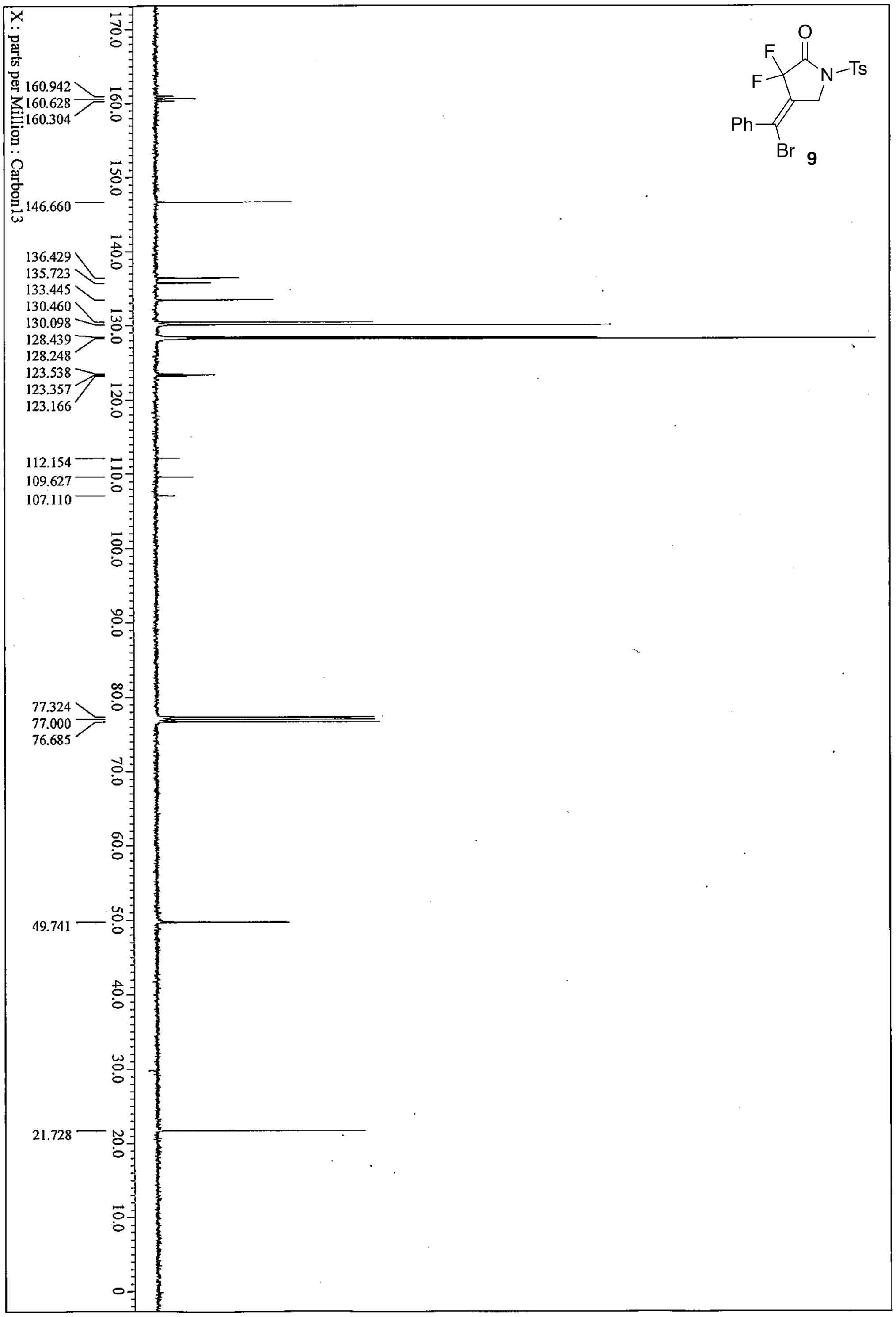
7: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



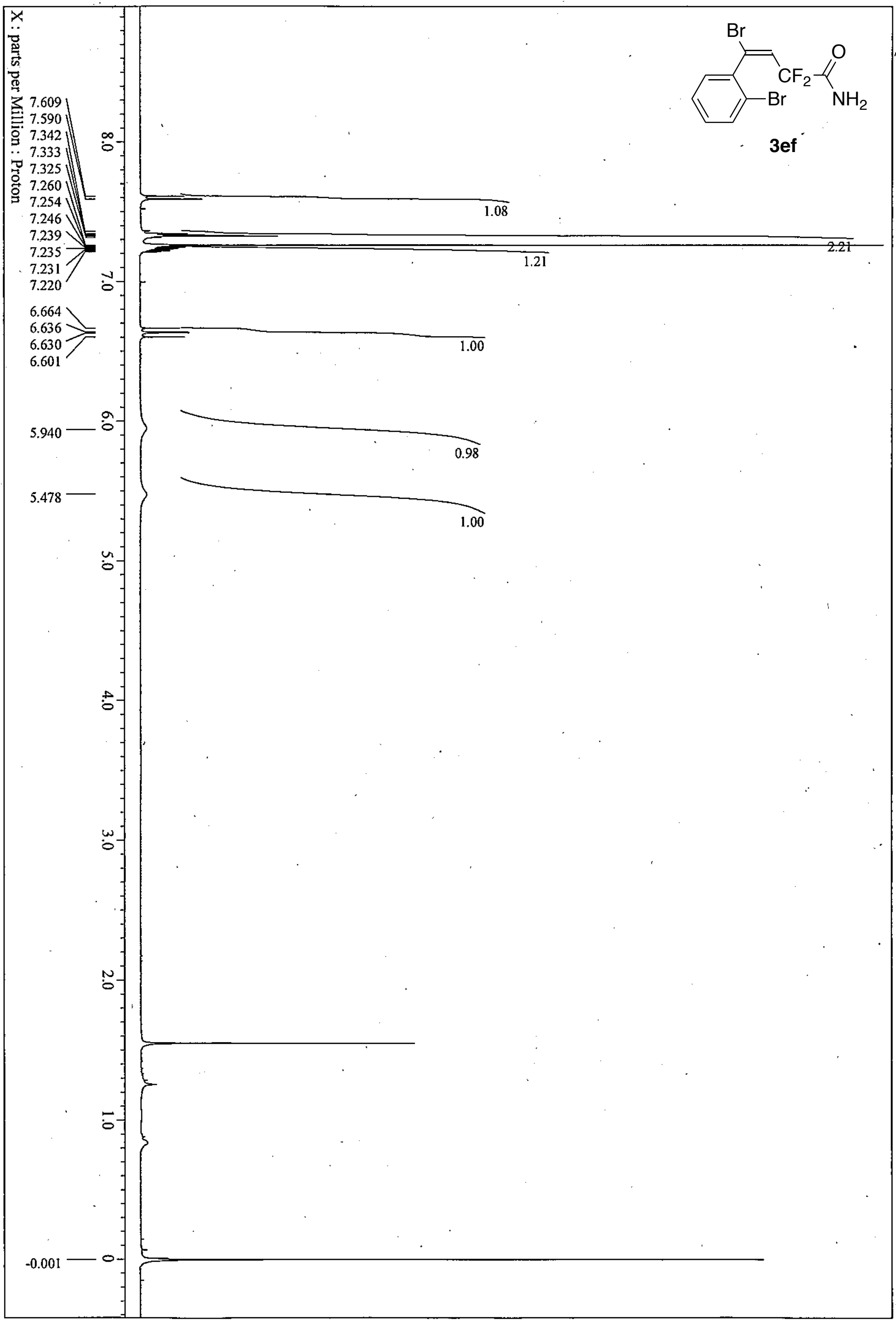
9: ^{1}H NMR (400 MHz, $CDCl_3$)



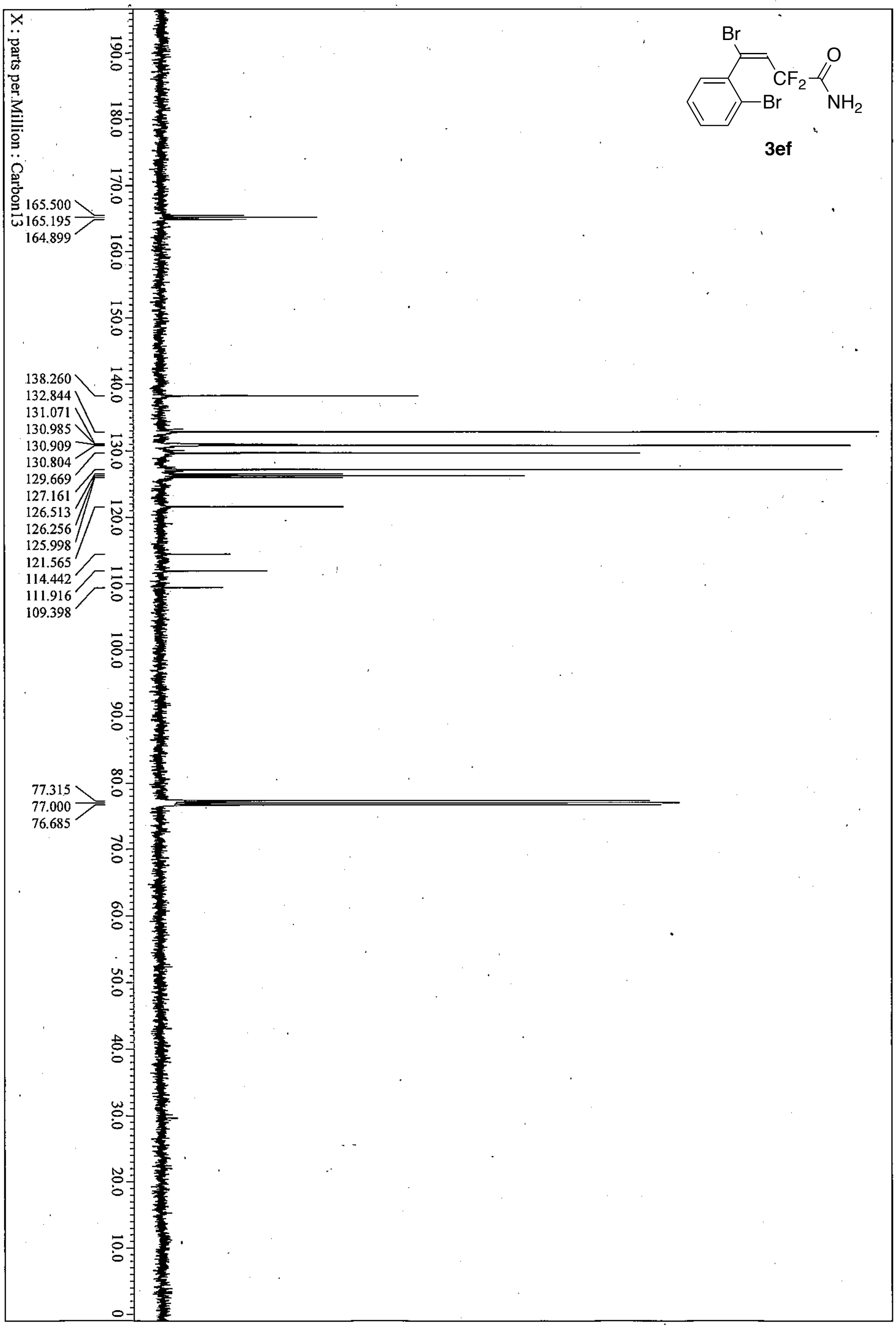
9: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



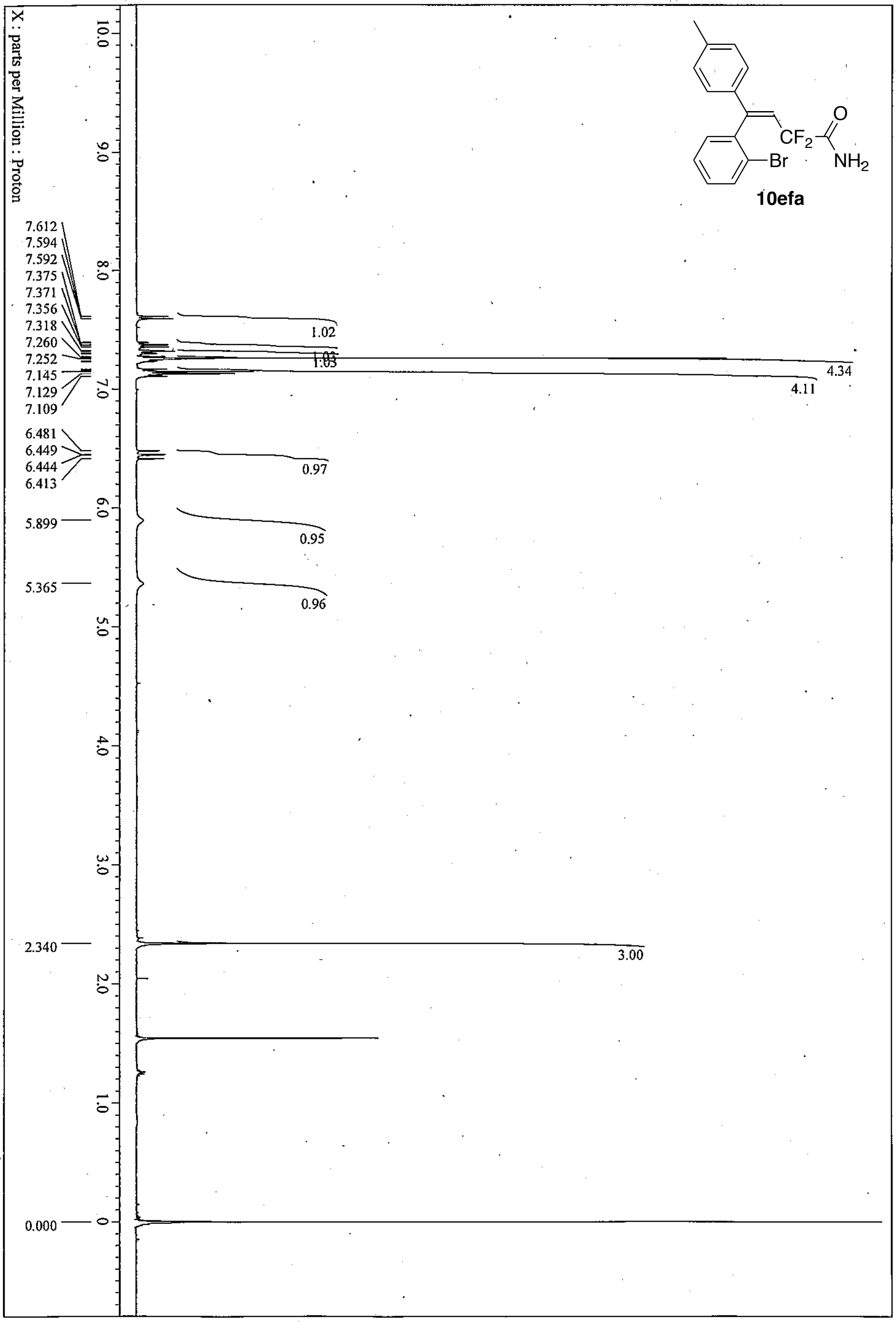
3ef: ^{1}H NMR (400 MHz, CDCl$_3$)



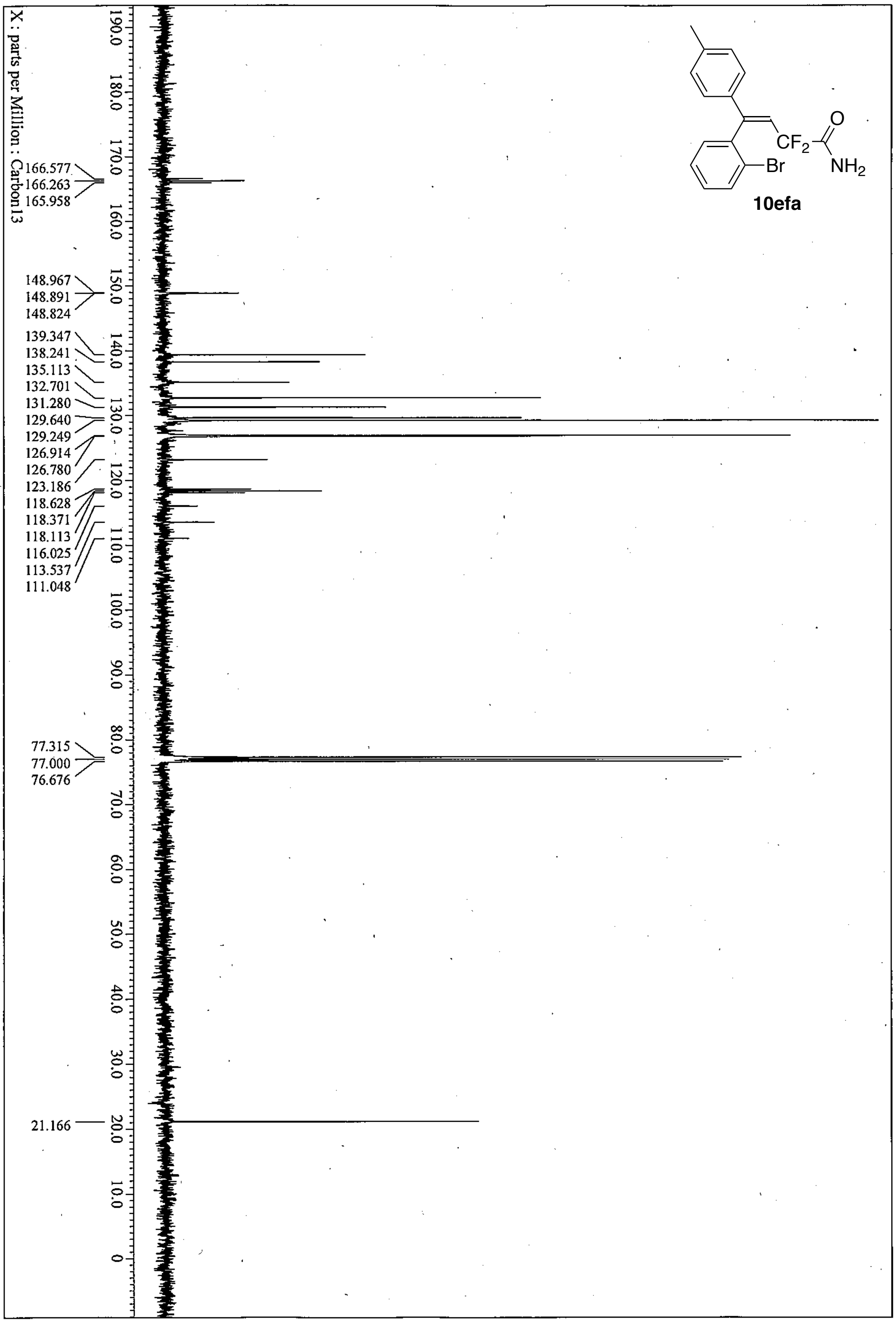
3ef: $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)



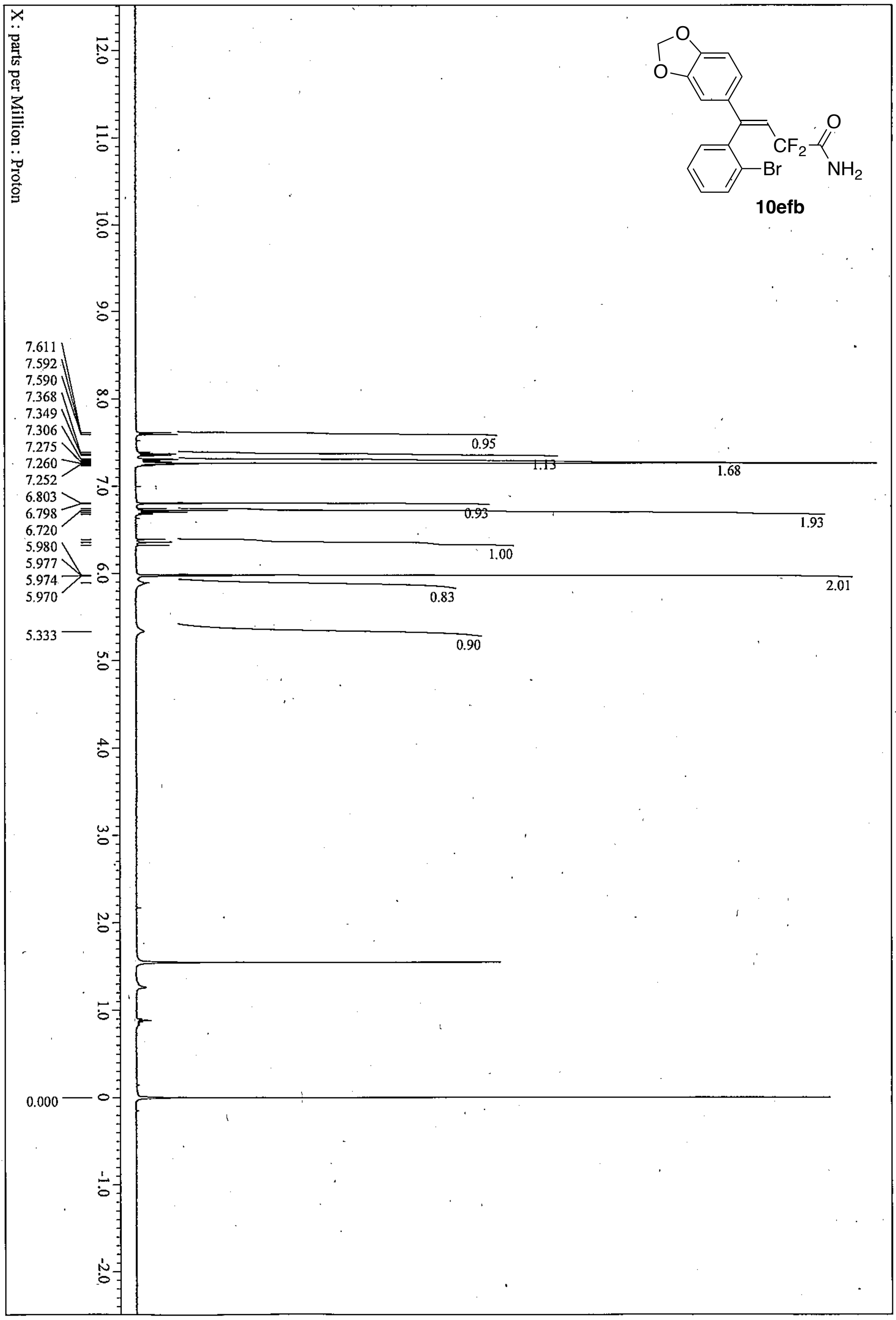
10efa: ^{1}H NMR (400 MHz, $CDCl_3$)



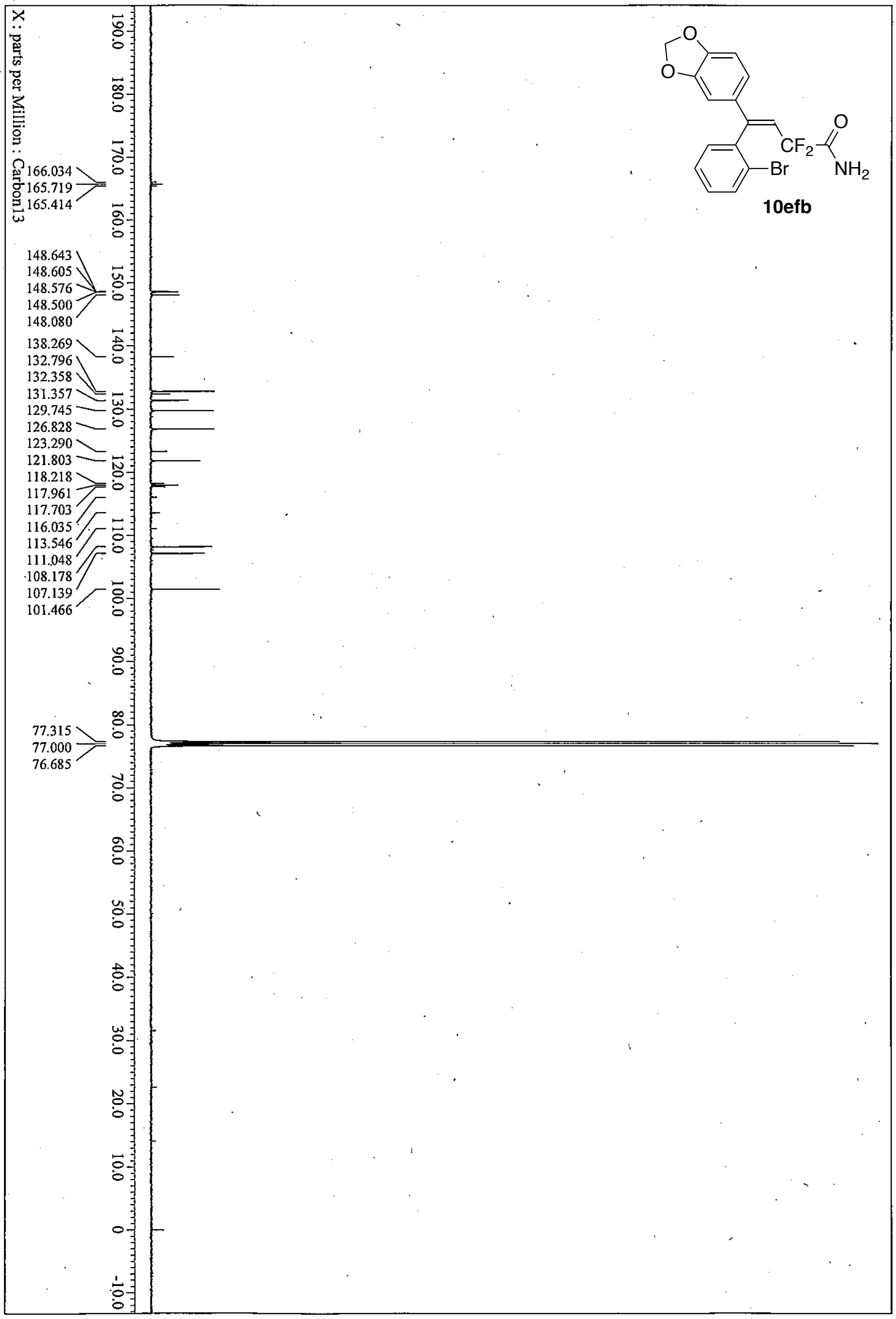
10efa: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



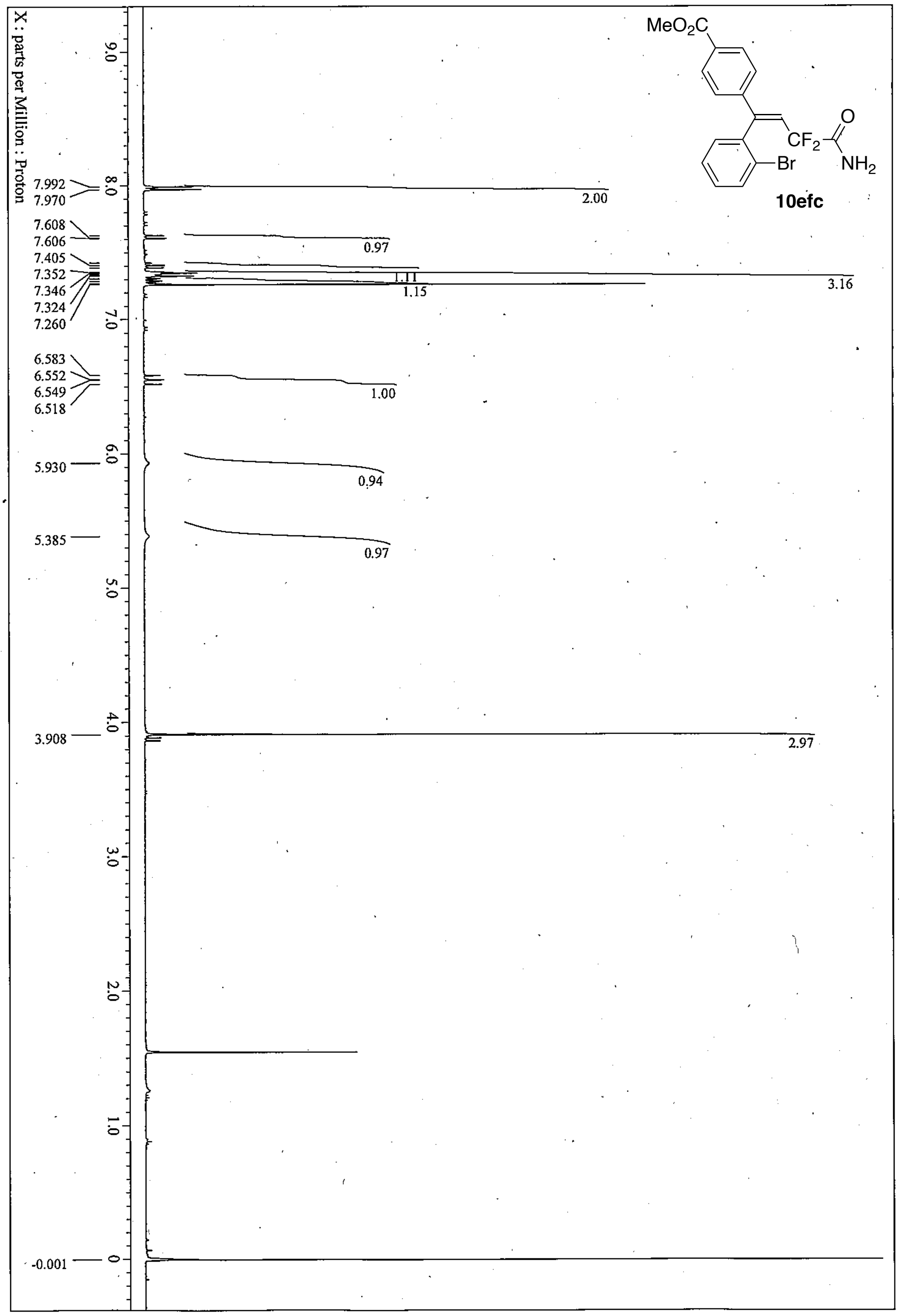
10efb: ^{1}H NMR (400 MHz, $CDCl_3$)



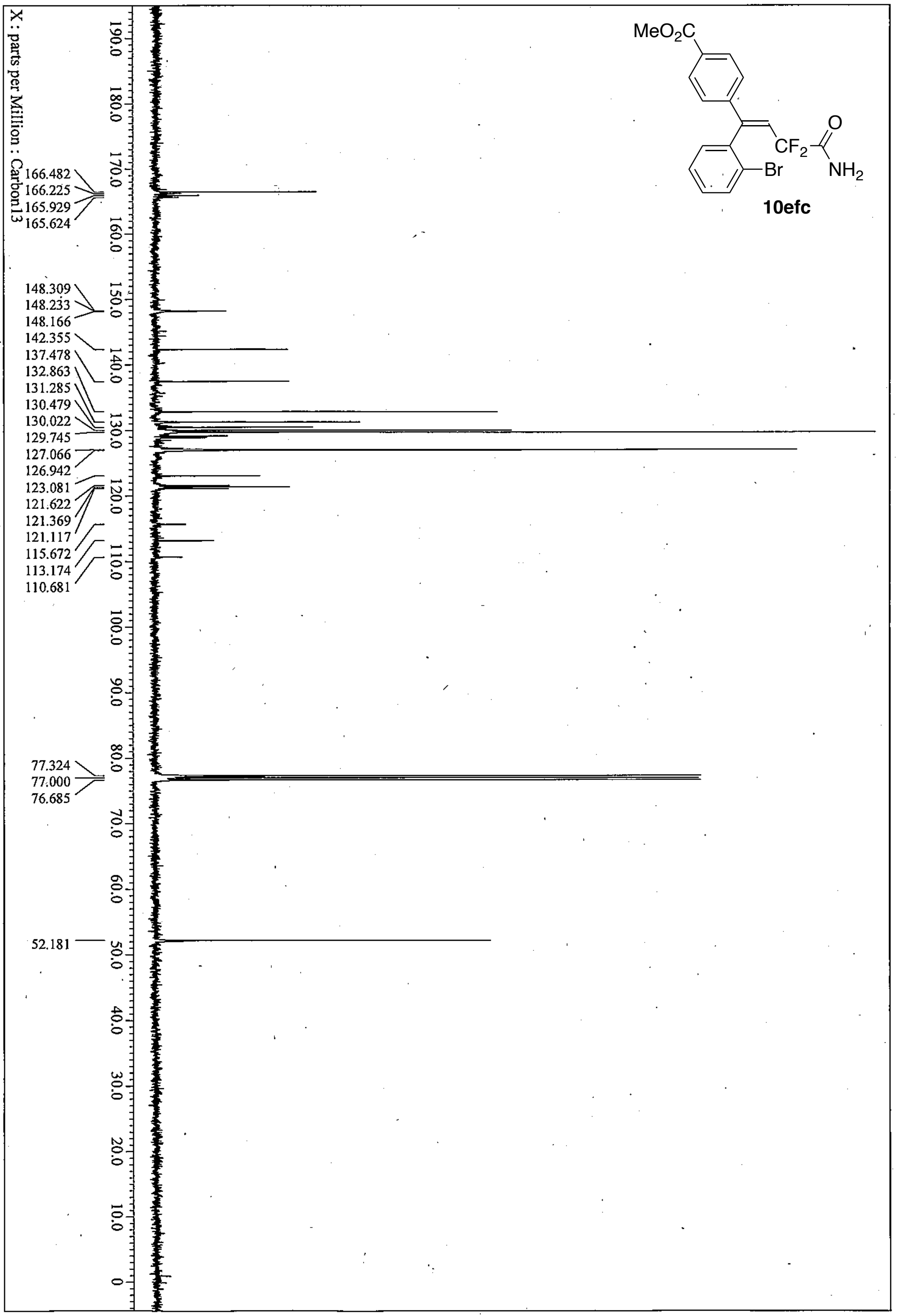
10efb: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



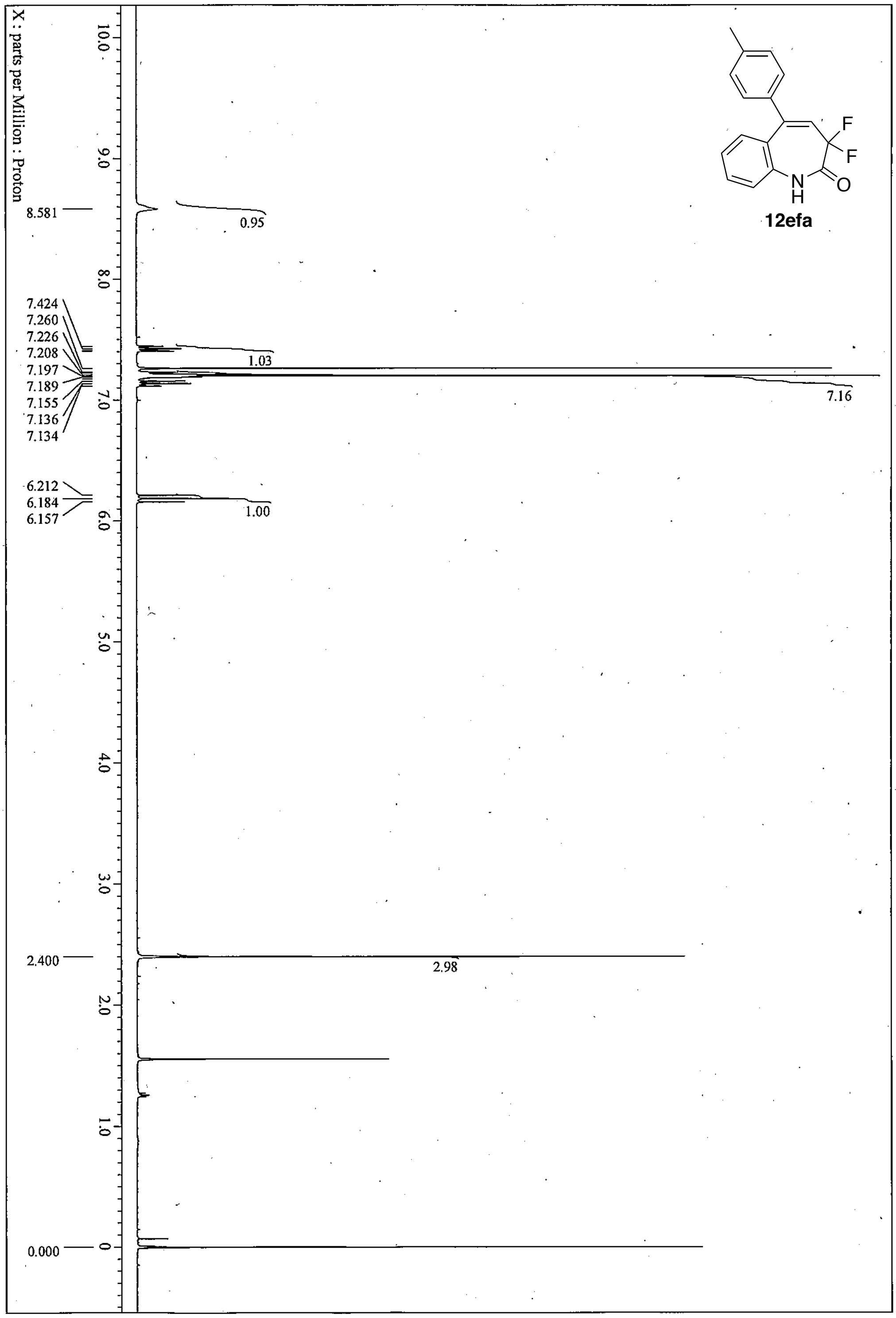
10efc: ^{1}H NMR (400 MHz, $CDCl_3$)



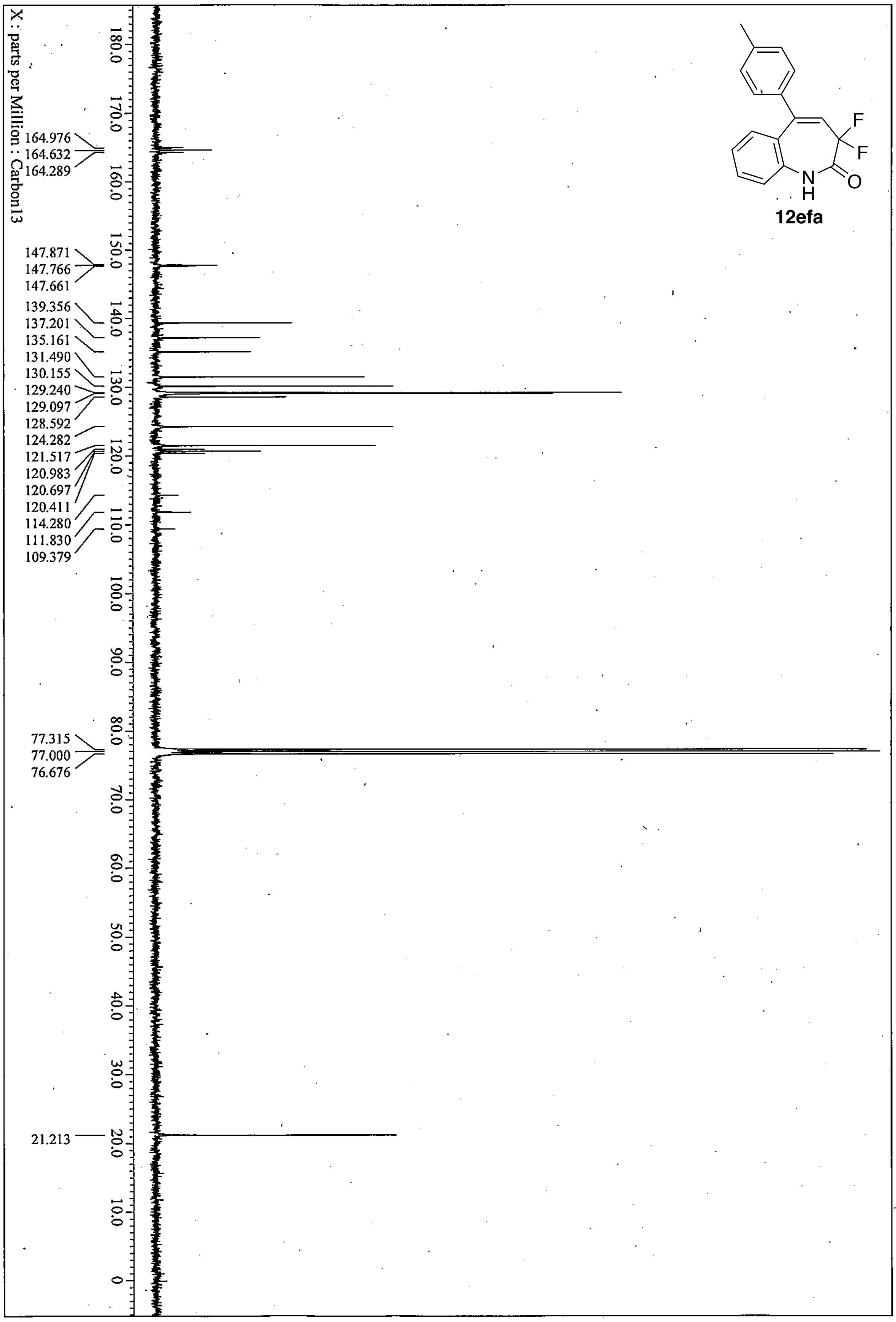
10efc: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



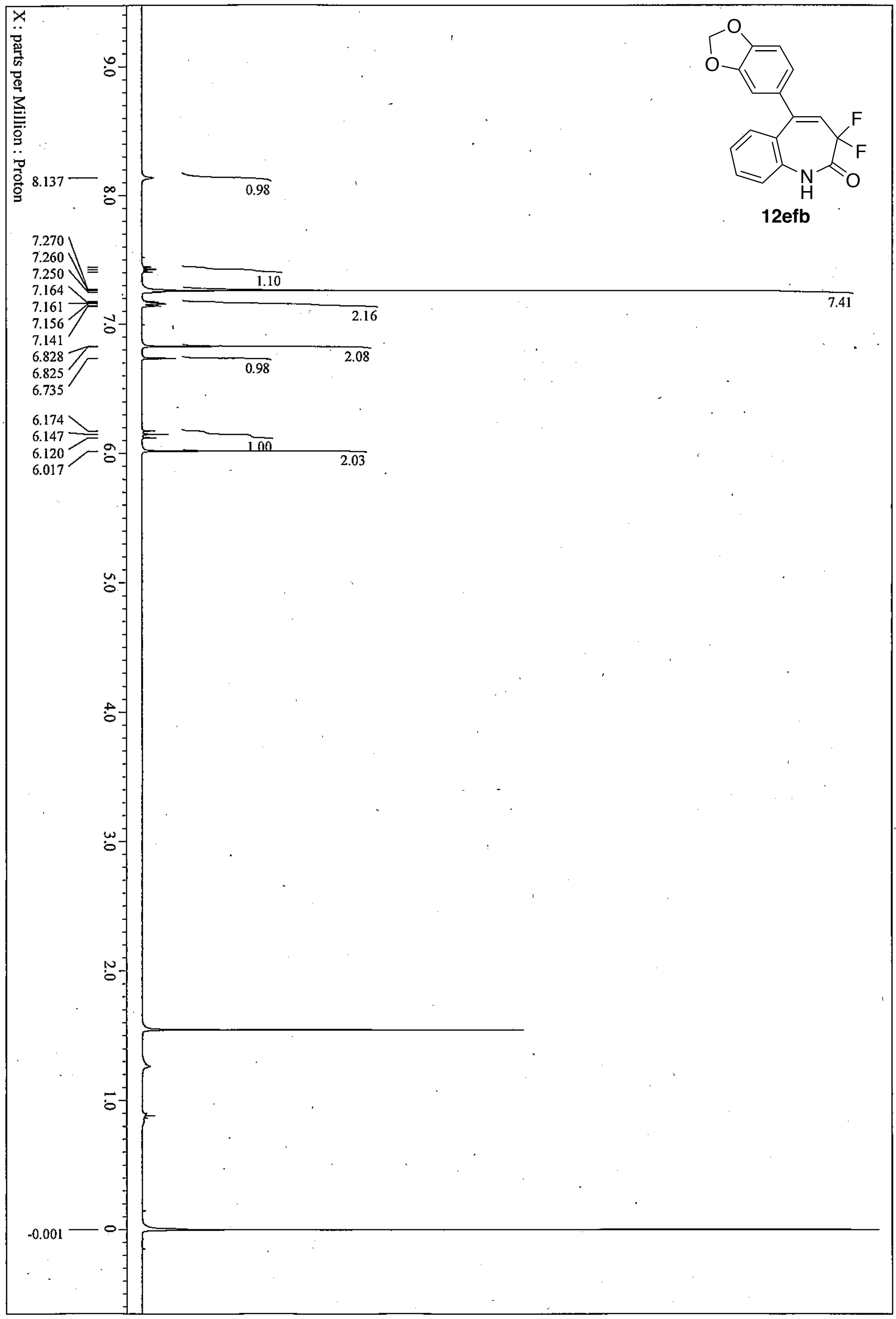
12efa: ^{1}H NMR (400 MHz, CDCl$_3$)



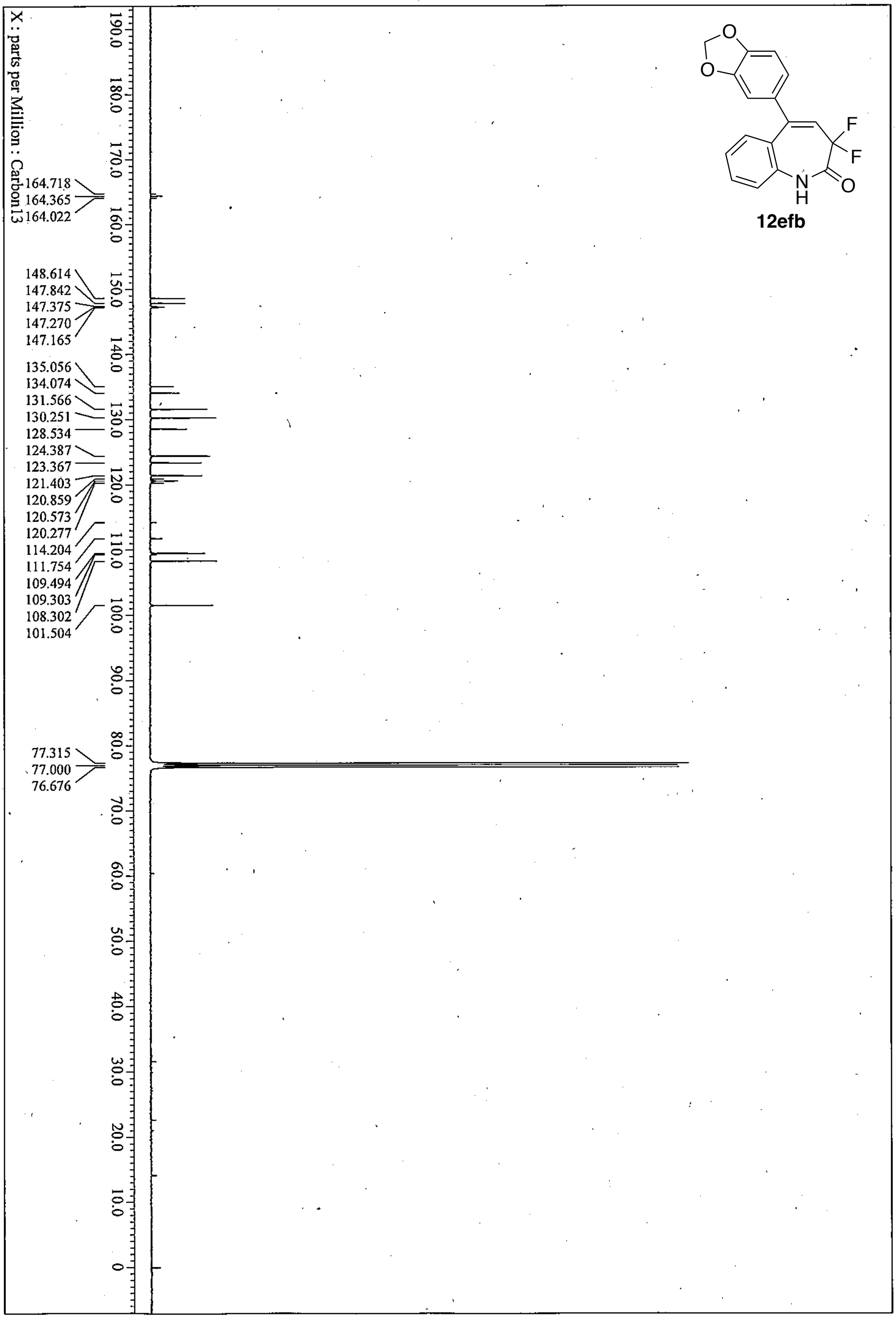
12efa: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



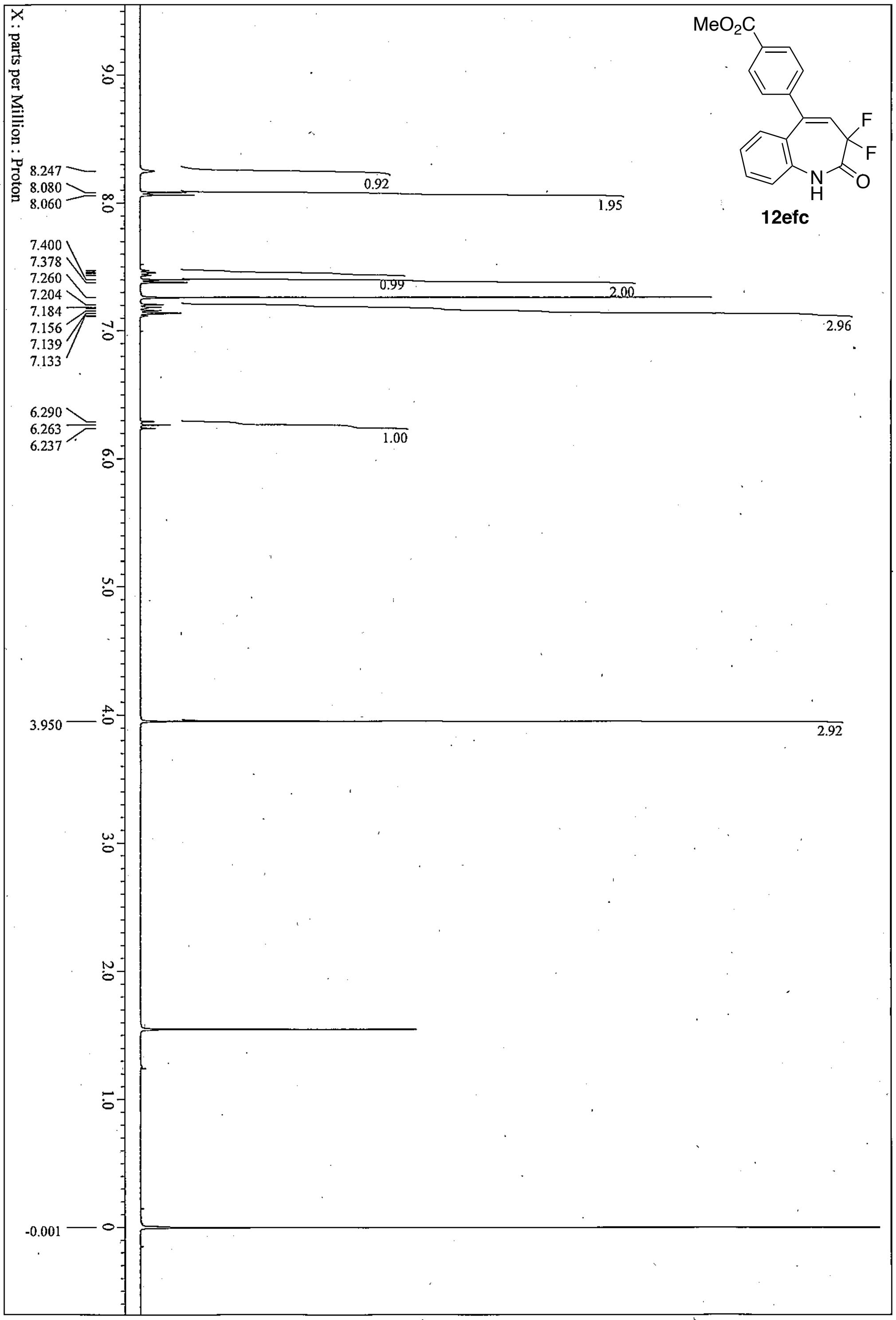
12efb: ^{1}H NMR (400 MHz, $CDCl_3$)



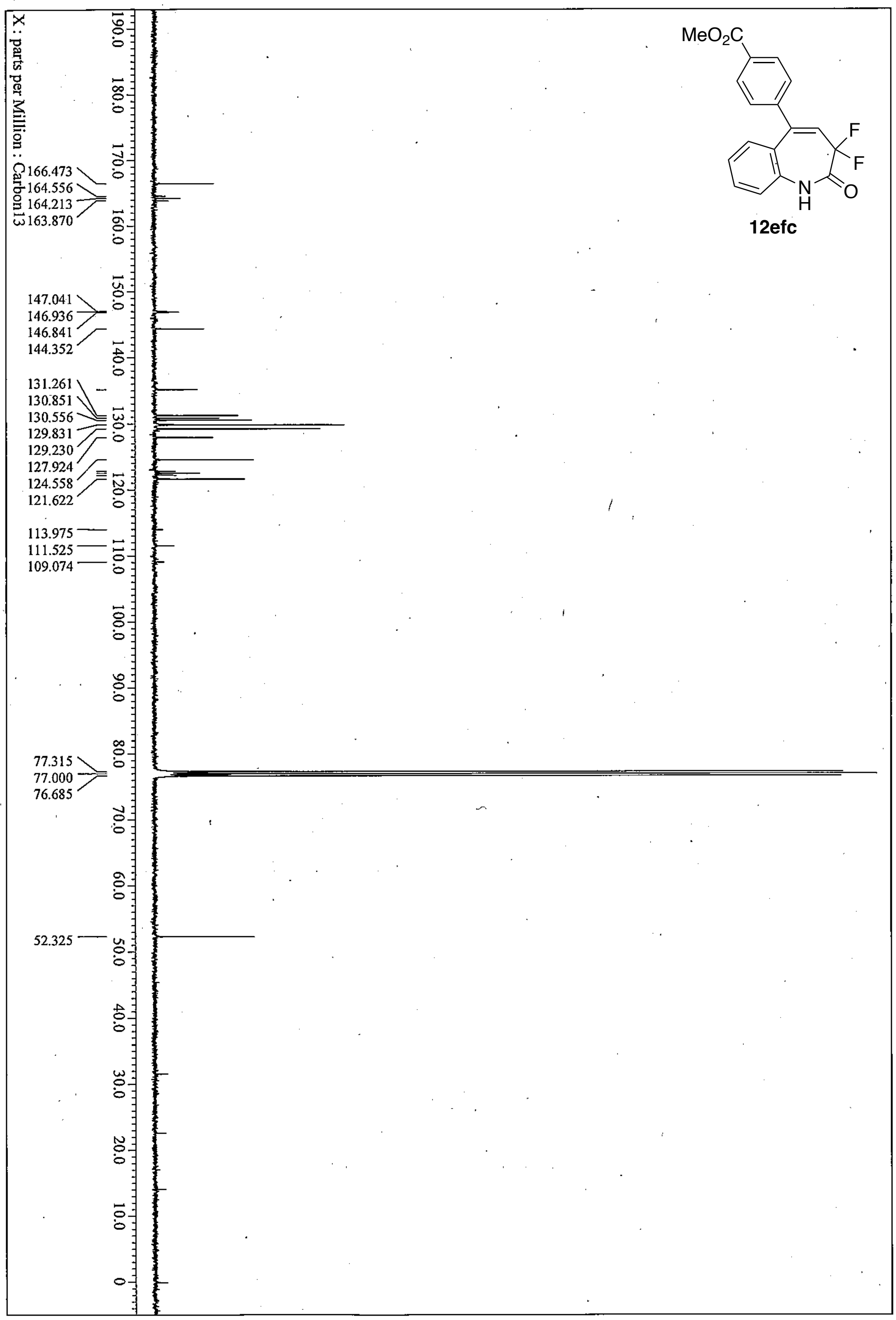
12efb: $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)



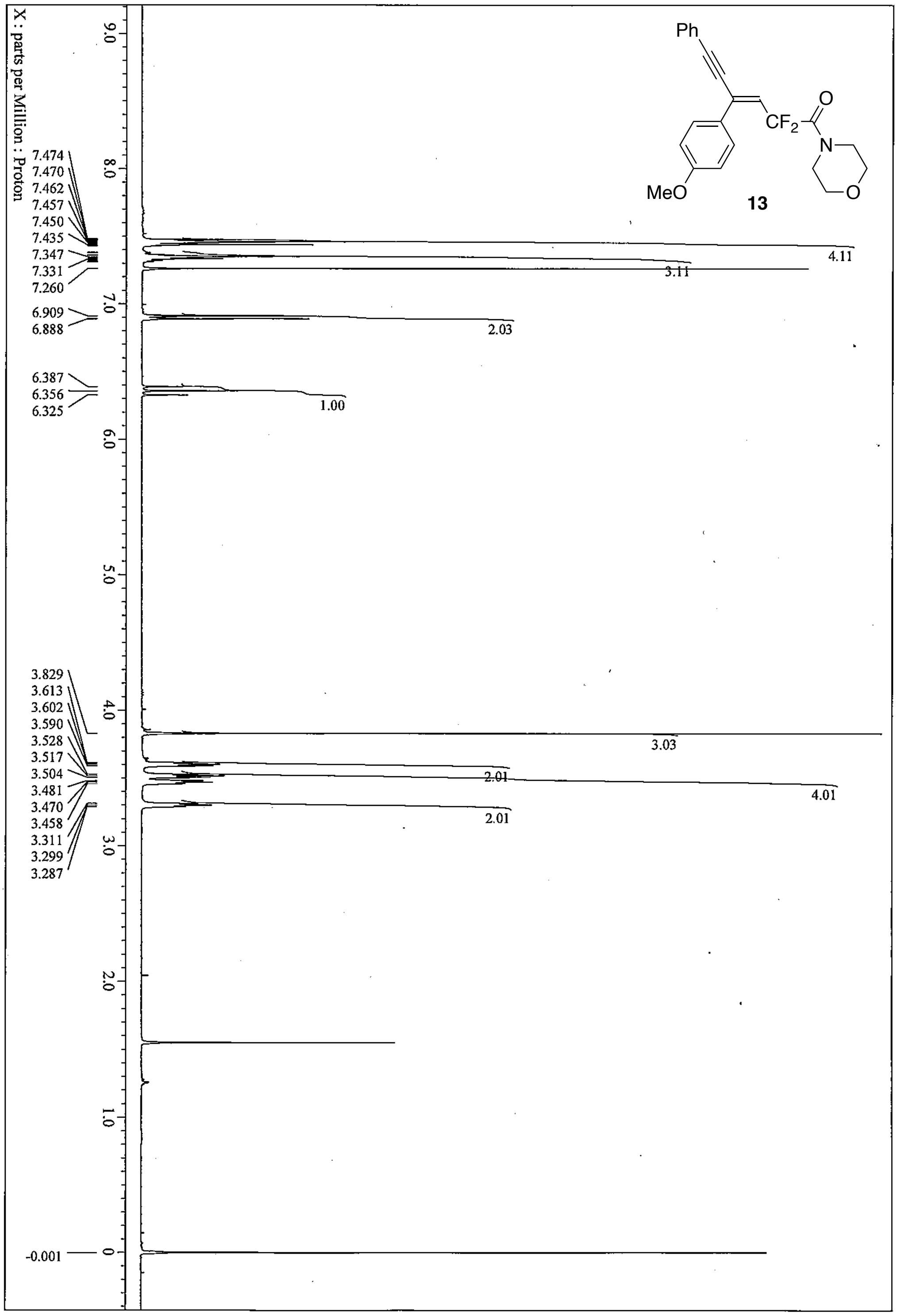
12efc: ^{1}H NMR (400 MHz, $CDCl_3$)



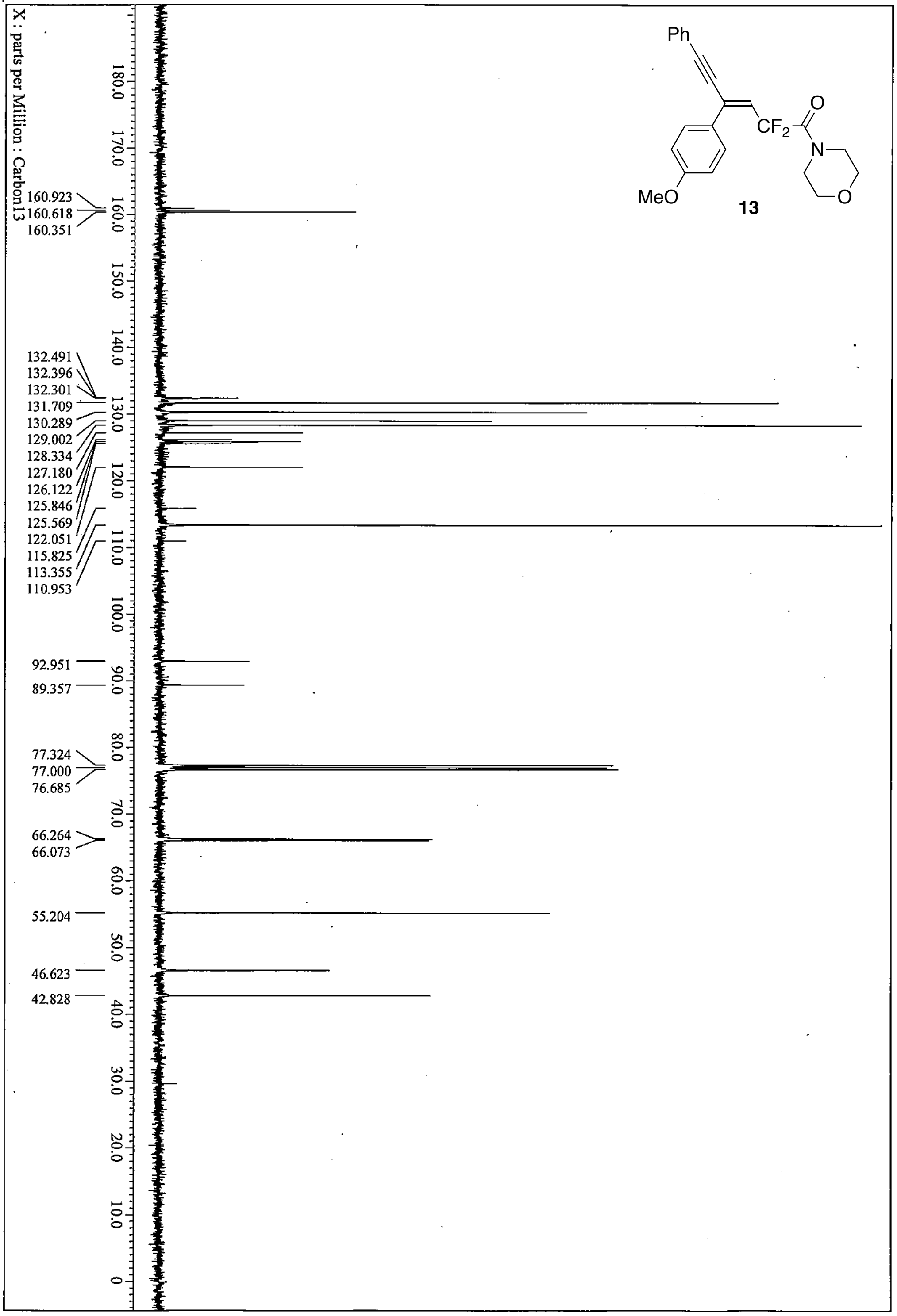
12efc: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



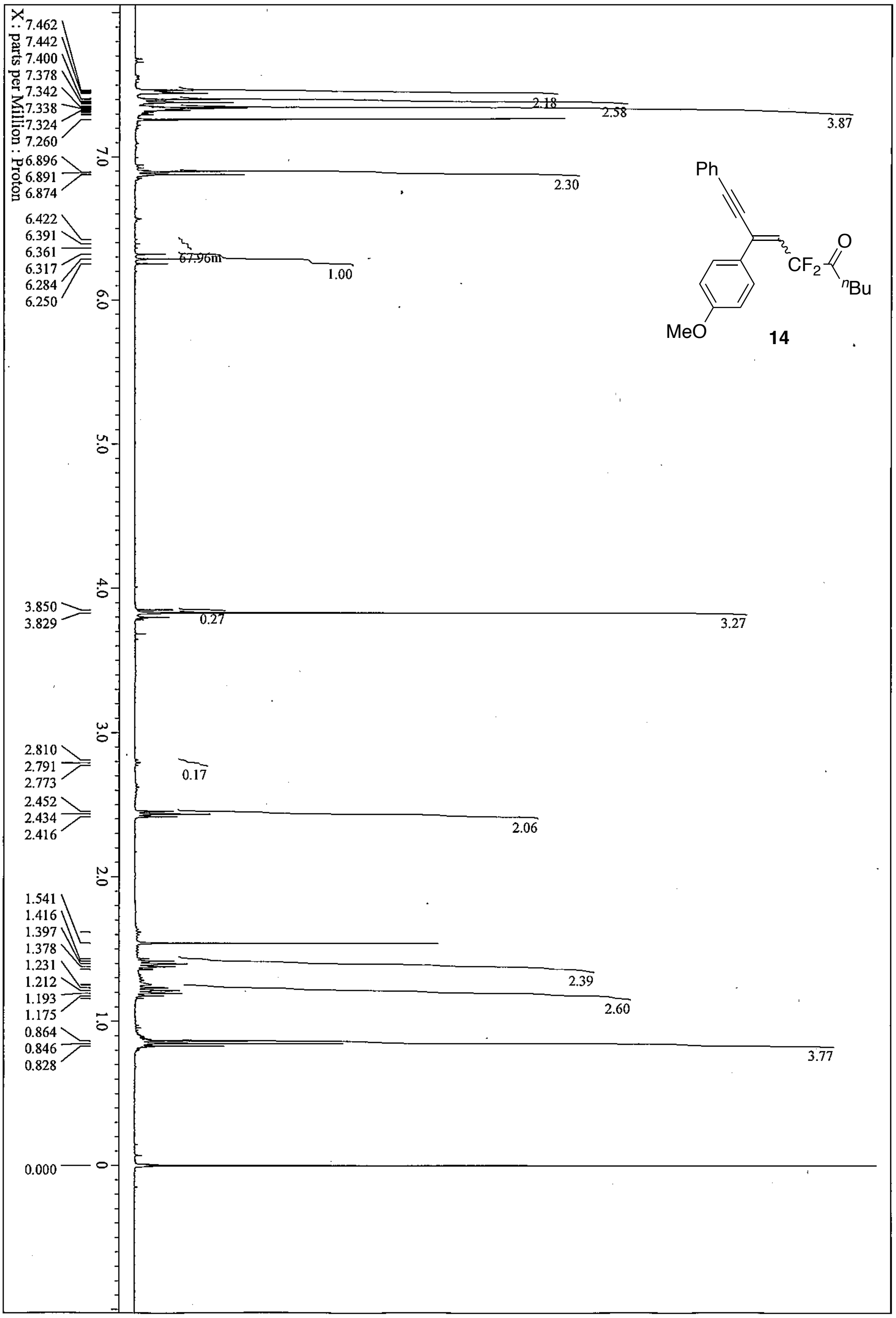
13: ^{1}H NMR (400 MHz, $CDCl_3$)



13: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



14: ^{1}H NMR (400 MHz, $CDCl_3$)



14: $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)