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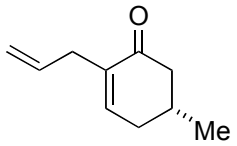
Supporting Information

69451 Weinheim, Germany

Total Synthesis of (+)-Fawcettimine

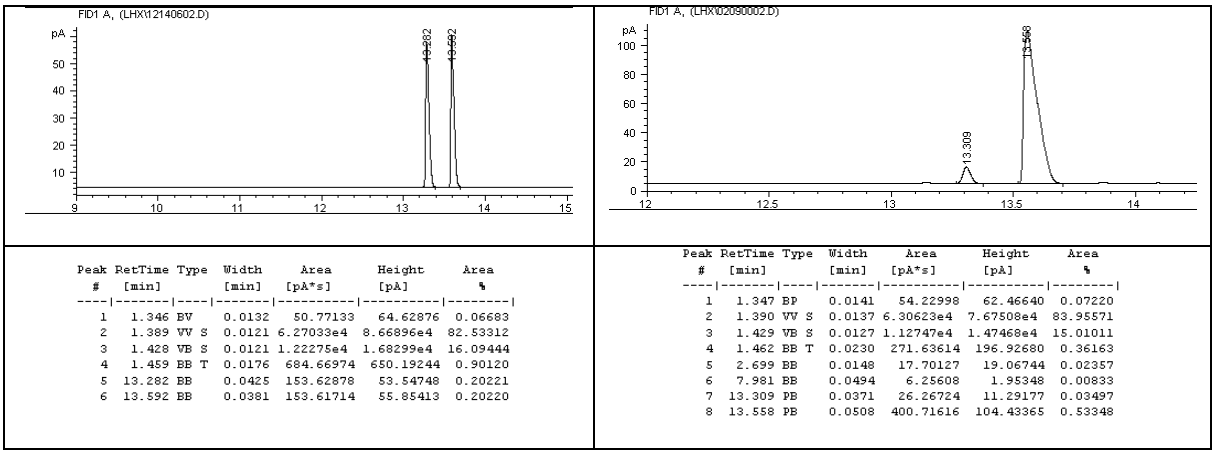
*Xin Linghu, Joshua J. Kennedy-Smith, and F. Dean Toste**

General Information. Unless otherwise noted all commercial materials were used without purification. Small-scale reactions (< 4 mL) were carried out in Fisher Scientific disposable scintillation vials. Reactions that required an inert atmosphere were carried out under a blanket nitrogen with glassware, stir bars, and needles that were oven dried prior to use at 175 °C. Diethyl ether (Et_2O), methylene chloride (CH_2Cl_2), tetrahydrofuran (THF), and toluene were dried according to the method of Grubbs[1] as modified by Bergman.[2] Carbontetrachloride (CCl_4), dimethylformamide (DMF), dimethylsulfoxide (DMSO), and pyridine were purchased from Aldrich in Sure-Seal bottles. Benzene was distilled prior to use from calcium hydride. *t*BuOH was purchased from EM Science. Solutions of *n*-butyllithium (*n*BuLi) were titrated prior to use in THF using 2,6-di-*tert*-butyl-4-methyl-phenol (BHT) with 1,10-phenanthroline as an indicator. TLC analysis of reaction mixtures was performed on Merck silica gel 60 F254 TLC plates. Chromatography was carried out on Merck 60 silica gel (32-63 μm). ^{1}H and ^{13}C NMR spectra were recorded with Bruker AV-300, AVB-400, and AVQ-400 spectrometers and referenced to $CDCl_3$ (^{1}H NMR: $CDCl_3$ at 7.26 ppm and ^{13}C NMR: $CDCl_3$ at 77.0 ppm). ^{1}H NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sep = septet, m = multiplet), coupling constants (Hz), and integration. Mass spectral and analytical data were obtained via the Micro-Mass/Analytical Facility operated by the College of Chemistry, University of California, Berkeley. Optical rotations were determined using a Perkin-Elmer polarimeter equipped with a sodium lamp and they are reported as follows: $[\alpha]^{rt}_D$ (c in g per 100 mL, solvent). The ee was determined by GC analysis on an Astec G-TA chiral stationary phase.



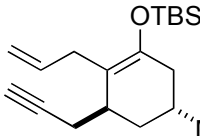
10c

(*R*)-(–)-(10c). The title compound was prepared following the Jørgensen's procedure[3]: In a 250 mL round-bottom flash equipped with a magnetic stirring bar, *β*-ketoester **17**[4] (15.8 g, 80 mmol) was added to a mixture of catalyst **19**[5] (5 g, 8.0 mmol) and crotonaldehyde **18** (10 mL, 120 mmol). The stirring was maintained at 0 °C for 72 h. To the reaction was added toluene (50 mL) and *p*-TSA (3.2 g, 17 mmol), and the resulting solution was stirred at 80 °C for 16 h. The crude reaction mixture was directly charged on silica gel and subjected to flash chromatograph (11:1 *n*-pentane/ Et_2O) to give (-)-enone **10c** (8.6 g, 72%, 88% ee) as a pale yellow liquid. Analytical data for title compound: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.69 (m, 1H), 5.81 (m, 1H), 5.02 (m, 2H), 2.94 (d, J = 6.6, 2H), 2.55-2.37 (m, 2H), 2.30-1.97 (m, 3H), 1.05 (d, J = 6.3, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 199.24, 145.08, 137.71, 135.85, 116.21, 46.55, 34.38, 33.28, 30.62, 21.20; For ^{1}H NMR and ^{13}C NMR spectra, see the Appendix; HRMS (EI) calc. for $[C_{10}H_{14}O]^+$ 150.1045, found 150.1042; The ee was determined by GC analysis on an Astec G-TA chiral stationary phase (T_1 = 70 °C; T_2 = 100 °C, rate = 10 °C/min; T_3 = 100 °C, time = 8 min; T_4 = 150 °C, rate = 10 °C/min, time = 15 min; τ_{minor} = 13.3 min, τ_{major} = 13.6 min); $[\alpha]^{rt}_D$ = -64.8 (c = 1.2, $CHCl_3$). GC data for racemic and 88% ee shown below.

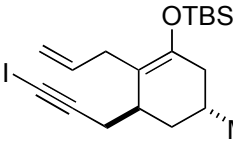


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	1.346	BV	0.0132	50.77133	64.62876	0.06683
2	1.389	VV S	0.0121	6.27033e4	8.66896e4	82.53312
3	1.428	VB S	0.0121	1.22275e4	1.68299e4	16.09444
4	1.459	BB T	0.0176	684.66974	650.19244	0.90120
5	13.282	BB	0.0425	153.62878	53.54748	0.20221
6	13.592	BB	0.0381	153.61714	55.85413	0.20220

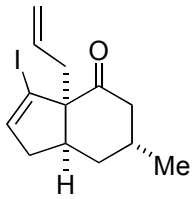
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	1.347	BP	0.0141	54.22998	62.46640	0.07220
2	1.390	VV S	0.0137	6.30623e4	7.67508e4	83.95571
3	1.429	VB S	0.0127	1.12747e4	1.47468e4	15.01011
4	1.462	BB T	0.0230	271.63614	196.92680	0.36163
5	2.699	BB	0.0148	17.70127	19.06744	0.02357
6	7.981	BB	0.0494	6.25608	1.95348	0.00833
7	13.309	PB	0.0371	26.26724	11.29177	0.03497
8	13.558	PB	0.0508	400.71616	104.43365	0.53348



To a stirred solution of enone **10c** (9.4 g, 62 mmol) and allenyl stannane **12** (24 g, 74 mmol) in CH_2Cl_2 (50 mL) at -78 °C was added TBSOTf (17 mL, 74 mmol) dropwise over 5 min. The reaction mixture was stirred for 4 h at which point it was placed in a 0 °C bath and quenched with sat. $NaHCO_3$ (150 mL). The reaction mixture was diluted with Et_2O (500 mL), and then washed with sat. $NaHCO_3$, H_2O, and brine. The organic layer was separated and dried with Na_2SO_4 before being concentrated *in vacuo* and flash chromatographed (120:1:1 hexanes/Et_2O/Et_3N) to give the silyl enol ether (16.3 g, 86%) as a clear oil. Analytical data for title compound: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.73 (m, 1H), 4.98 (m, 2H), 3.14 (dd, J = 15.2, 4.8, 1H), 2.55 (dd, J = 15.2, 7.6, 1H), 2.45-2.32 (m, 2H), 2.11-1.85 (m, 5H), 1.72 (dd, J = 16.0, 10.4, 1H), 1.25 (dt, J = 12.4, 5.2, 1H), 0.98 (d, J = 6.4, 3H), 0.94 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 145.40, 136.93, 114.86, 114.58, 84.27, 68.72, 38.96, 35.93, 34.67, 32.36, 25.82, 24.71, 22.59, 21.77, 18.19, -3.52, -3.72; For ^{1}H NMR and ^{13}C NMR spectra, see the Appendix; HRMS (EI) calc. for $[C_{19}H_{32}OSi]^+$ 304.2222, found 304.2224; $[\alpha]^{rt}_D$ = +67.0 (c = 0.47, $CHCl_3$).

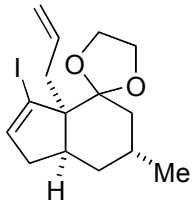


To a rapidly stirred solution of the silyl enol ether (3.9 g, 13 mmol) in DMF (150 mL) in the dark and at 0 °C was added NIS (3.6 g, 16 mmol), quickly followed by finely ground $AgNO_3$ (2.7 g, 16 mmol). The reaction mixture was kept in the dark and stirred for 4 h at which point it was diluted with 1:1 Et_2O / hexanes (150 mL) and quenched with sat. $Na_2S_2O_3$ (100 mL). The thick brown reaction mixture was filtered over celite to remove the succinimide salts and then extracted with 1:1 Et_2O/hexanes (3 x 100 mL). The organic layers were combined and washed with H_2O and brine and subsequently dried with Na_2SO_4 before being concentrated *in vacuo* and chromatographed (100:1:1 hexanes/Et_2O/Et_3N) to give the iodoalkyne (5.2 g, 95%) as a clear oil. Analytical data for title compound: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.70 (m, 1H), 4.98 (m, 2H), 3.13 (dd, J = 15.2, 5.6, 1H), 2.56 (m, 2H), 2.40-2.21 (m, 2H), 2.08 (dd, J = 16.8, 5.2, 1H), 1.95-1.79 (m, 2H), 1.71 (dd, J = 16.8, 9.6, 1H), 1.25 (dt, J = 12.0, 5.2, 1H), 0.98 (d, J = 6.8, 3H), 0.93 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 145.50, 136.91, 114.91, 114.35, 94.40, 38.90, 36.07, 34.90, 32.37, 25.82, 25.03, 24.75, 21.75, 18.19, -3.51, -3.69, 1 C unresolved; For ^{1}H NMR and ^{13}C NMR spectra, see the Appendix; HRMS (EI) calc. for $[C_{19}H_{31}IOSi]^+$ 430.1189, found 430.1179; $[\alpha]^{rt}_D$ = +19.7 (c = 1.3, $CHCl_3$).

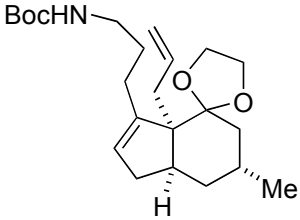


15c

(–)-(15c). To a rapidly stirred solution of the iodoalkyne (1.57 g, 3.7 mmol) in CH_2Cl_2 (20 mL) was added MeOH (2 mL), followed by $AuCl(PPh_3)$ (183 mg, 0.37 mmol), and $AgBF_4$ (72 mg, 0.37 mmol). The reaction mixture was then placed in a preheated 40 °C oil bath and stirred for 10 min, it was then cooled and filtered over celite to remove gold black. The filtrate was concentrated *in vacuo*, and chromatographed directly (18:1 hexanes/EtOAc) to give vinyliodide **15c** (1.02 g, 85%) as a pale yellow liquid. Analytical data for title compound: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.37 (t, J = 2.4, 1H), 5.66 (m, 1H), 5.10 (m, 2H), 2.69 (m, 1H), 2.62-2.46 (m, 2H), 2.44-2.31 (m, 2H), 2.25-2.10 (m, 2H), 1.97 (dd, J = 16.0, 9.2, 1H), 1.69 (m, 1H), 1.45 (m, 1H), 0.97 (d, J = 6.8, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 212.00, 143.39, 133.37, 118.76, 98.43, 65.80, 46.62, 40.59, 40.28, 38.88, 36.55, 26.86, 21.93; For ^{1}H NMR and ^{13}C NMR spectra, see the Appendix; HRMS (EI) calc. for $[C_{13}H_{17}IO]^+$ 316.0324, found 316.0326; $[\alpha]^{rt}_D$ = -78.5 (c = 1.1, CH_2Cl_2).



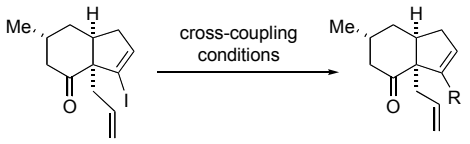
To a solution of dienone **15c** (1.0 g, 3.2 mmol) and ethylene glycol (4 g, 63 mmol) in benzene was added *p*-TSA (120 mg, 0.64 mmol). The reaction was refluxed with the Dean-Stark trap for 12 h, The reaction mixture was cooled and diluted with Et_2O (100 mL), and then washed with sat. $NaHCO_3$, H_2O, and brine. The organic layer was separated and dried with Na_2SO_4 before being concentrated *in vacuo* to give clean ketal as a clear oil without further purification. Analytical data for title compound: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.45 (s, 1H), 5.69 (ddd, J = 4.4, 10.0, 16.8, 1H), 5.10 (m, 2H), 4.11-3.91 (m, 3H), 3.79 (q, J = 6.8, 1H), 2.86 (m, 1H), 2.45 (m, 1H), 2.32-2.20 (m, 2H), 2.07 (dd, J = 3.2, 8.0, 1H), 1.89 (m, 1H), 1.61 (m, 1H), 1.49 (ddd, J = 2.0, 3.2, 12.8, 1H), 1.26 (t, J = 12.8, 1H), 1.17 (dd, J = 6.0, 12.8, 1H), 0.91 (d, J = 6.4, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.03, 135.18, 117.54, 112.10, 99.56, 65.70, 63.52, 57.88, 40.19, 40.10, 38.05, 36.17, 32.93, 25.16, 21.86; For ^{1}H NMR and ^{13}C NMR spectra, see the Appendix.



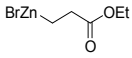
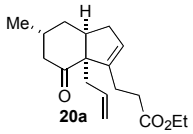
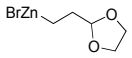
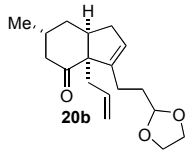
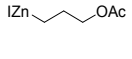
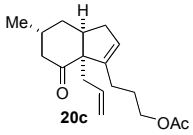
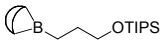
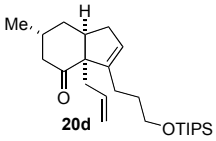
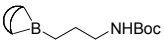
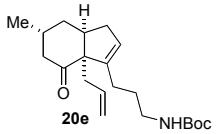
To a solution of allyl-carbamic acid tert-butyl ester (754 mg, 4.8 mmol) in THF (10 mL) was added a solution of 9-BBN (0.5 M in THF, 13 mL, 6.4 mmol) at 25 °C. After stirring for 4 h at the same temperature, the resulting solution was treated with degassed water (2 mL) and transferred to a mixture of ketal intermediate from the last step (1.2 g, 3.2 mmol), [1,1'-bis(diphenylphosphino)-ferrocene]palladiumdichloride (131 mg, 0.16 mmol, 5 mol%), triphenylarsine (49 mg, 0.16 mmol, 5 mol%) and cesium carbonate (1.5 g, 4.8 mmol) and DMF (30 mL). After stirring at 25 °C for 12 h, the mixture turned to a dark brown solution and was poured to a sat. NH_4Cl solution (100 mL) and diluted with Et_2O (150 mL). The organic layer was separated, washed with water (100 mL × 2) and brine, dried with Na_2SO_4, concentrated *in vacuo*, and flash chromatographed directly (8:1 hexanes/EtOAc) to give the

diene as a pale yellow liquid. Analytical data for title compound: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 5.55 (m, 2H), 5.01 (d, *J* = 15.9, 1H), 4.96 (d, *J* = 9.3, 1H), 4.65 (br s, 1H), 3.90-3.60 (m, 4H), 3.09 (q, *J* = 6.3, 2H), 2.68 (dd, *J* = 6.3, 14.7, 1H), 2.40-2.03 (m, 3H), 2.01-1.40 (m, 8H), 1.39 (s, 9H), 1.15 (t, *J* = 12.3, 2H), 0.88 (d, *J* = 6.3, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 155.81, 144.74, 135.97, 126.39, 116.62, 112.65, 78.77, 70.68, 64.62, 62.73, 56.21, 41.92, 38.94, 35.53, 34.61, 32.96, 31.95, 28.30, 26.35, 25.03, 21.89; For ^{1}H NMR and ^{13}C NMR spectra, see the Appendix.

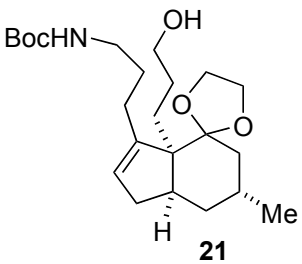
Table 1. Cross-coupling Reaction of Vinyl Iodide Intermediate **15c**.



15c **20a-e**

entry	coupling reagent	conditions	product	yield
1		I	 **20a**	96%
2		I	 **20b**	89%
3		I	 **20c**	59%
4		II	 **20d**	88%
5		II	 **20e**	86%

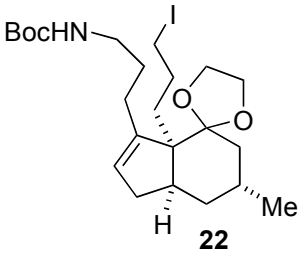
Conditions: (I) **15c** (1 equiv), organozinc reagent (2 equiv), and $Cl_2Pd(PPh_3)_2$ (0.1 equiv) in THF at 25 °C for 3 h; (II) **15c** (1 equiv), organoboron reagent (2 equiv), $Cl_2Pd(dppf)$ (0.05 equiv), $AsPh_3$ (0.05 equiv), and Cs_2CO_3 (1.5 equiv) in DMF at 25 °C for 4 h.



21

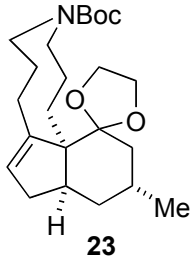
(–)-21. To a solution of impure diene (3.2 mmol) in THF (50 mL) was added a solution of 9-BBN (0.5 M in THF, 13 mL, 6.4 mmol) at 25 °C. The reaction mixture was then placed in a 60 °C oil bath and stirred for 12 h. After cooling to 25 °C, to the resulting solution was added 3 M NaOH solution (5 mL) and H_2O_2 (30 wt%, 5 mL) dropwise and the reaction was then stirred at 25 °C for 4 h. To the resulting solution was added Et_2O (200 mL) and a sat. NH_4Cl solution (100 mL). The organic layer

was separated, washed with a sat. NH_4Cl solution (100 mL × 2) and brine, dried with Na_2SO_4, concentrated *in vacuo*, and flash chromatographed directly (1.3:1 hexanes/EtOAc) to give alcohol **21** (960 mg, 74% over 3 steps from **15c**) as a white solid. Analytical data for title compound: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.57 (s, 1H), 4.68 (br. s, 1H), 3.88-3.60 (m, 6H), 3.12 (q, J = 6.4, 2H), 2.30 (br. q, J = 8.8, 1H), 2.16 (br. t, J = 9.6, 1H), 2.04 (m, 1H), 1.95-1.80 (m, 4H), 1.80-1.46 (m, 7H), 1.43 (s, 9H), 1.20 (m, 2H), 0.89 (d, J = 6.8, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.98, 144.90, 126.67, 113.06, 79.03, 64.66, 63.60, 62.75, 56.76, 41.56, 40.64, 38.92, 35.74, 33.34, 28.40, 28.20, 27.81, 25.96, 25.44, 25.07, 22.14; For ^{1}H NMR and ^{13}C NMR spectra, see the Appendix; HRMS (EI) calc. for $[C_{23}H_{39}NO_5]^+$ 409.2828, found 409.2829; $[\alpha]^{rt}_D$ = -4.8 (c = 1.0, $CHCl_3$).



22

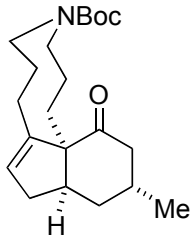
(–)-(22). To a solution of PPh_3 (891 mg, 3.4 mmol) in CH_2Cl_2 (15 mL) was added I_2 (864 mg, 3.4 mmol) and imidazole (292 mg, 4.3 mmol) at 25 °C. The resulting solution was stirred for 10 min, before a solution of alcohol **19** (715 mg 1.7 mmol) in CH_2Cl_2 (5 mL) was added. The reaction mixture was then stirred at the same temperature for 1 h. The reaction was quenched by 5% of $Na_2S_2O_3$ solution (5 mL) and diluted with Et_2O (100 mL). The organic layer was separated, washed with brine, dried with Na_2SO_4, concentrated *in vacuo*, and flash chromatographed (4:1 hexanes/EtOAc) to give iodide **22** (855 mg, 97%) as a clear oil. Analytical data for title compound: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.54 (s, 1H), 4.61 (br. s, 1H), 3.91-3.78 (m, 2H), 3.75 (q, J = 7.2, 1H), 3.64 (q, J = 6.8, 1H), 3.15 (t, J = 6.8, 2H), 3.11 (q, J = 6.4, 2H), 2.22 (br. q, J = 7.6, 1H), 2.16 (m, 1H), 2.04 (m, 1H), 1.95-1.78 (m, 4H), 1.77-1.57 (m, 4H), 1.57-1.45 (m, 3H), 1.41 (s, 9H), 1.16 (t, J = 12.0, 2H), 0.86 (d, J = 6.8, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.82, 144.69, 126.70, 112.73, 78.86, 64.62, 62.74, 56.62, 41.73, 40.63, 38.86, 35.70, 33.30, 30.67, 29.24, 28.37, 27.78, 26.07, 24.93, 22.09, 7.70; For ^{1}H NMR and ^{13}C NMR spectra, see the Appendix; HRMS (EI) calc. for $[C_{23}H_{38}INO_4]^+$ 519.1846, found 519.1846; $[\alpha]^{rt}_D$ = -2.4 (c = 2.0, $CHCl_3$).



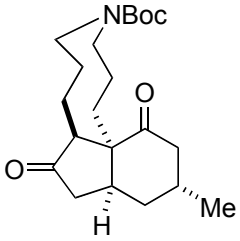
23

(–)-(23). To a solution of iodide **22** (840 mg, 1.6 mmol) in THF (150 mL, 0.01 M) was added *t*-BuOK (360 mg, 3.2 mmol) in one portion at 25 °C. The resulting solution was stirred at the same temperature for 0.5 h. The reaction was quenched by sat. NH_4Cl solution (50 mL) and extracted with Et_2O (200 mL × 3). The organic layer was combined, washed with brine, dried with Na_2SO_4, concentrated *in vacuo*, and flash chromatographed (5:1 hexanes/EtOAc) to give **23** (385 mg, 62%) as a clear oil and elimination byproduct (122 mg, 20%). Analytical data for title compound: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 5.63 (s, 1H), 3.91-3.70 (m, 4H), 3.68-3.34 (m, 1H), 3.33-3.10 (m, 1H), 3.06-2.78 (m, 2H), 2.35-1.50 (m, 14H), 1.42 (s, 9H), 1.20 (m, 2H), 0.87 (d, J = 6.6, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$ some peaks doubled due to amide conformational isomers) δ 156.84, 156.25, 145.74, 128.31, 113.28, 78.88, 78.81, 64.62, 64.53, 62.82, 57.65, 49.03, 48.64, 45.52, 44.67, 41.11, 40.89, 38.87, 38.59, 36.54, 33.83, 33.65, 28.49, 27.88, 26.93, 25.16, 24.94, 24.77, 23.66, 22.62, 22.53, 22.32, 21.63; For ^{1}H NMR and ^{13}C NMR

spectra, see the Appendix; HRMS (EI) calc. for $[C_{23}H_{37}NO_4]^+$ 391.2723, found 391.2729; $[\alpha]^{rt}_D$ = -29.4 (c = 0.5, $CHCl_3$).

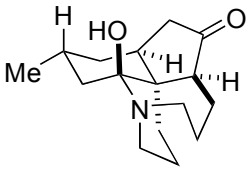


To a solution of **23** (360 mg, 0.92 mmol) in acetone/H_2O (10:1, 20 mL) was added pyridinium *p*-toluenesulfonate (PPTS) (38 mg, 0.15 mmol) at 25 °C. The resulting solution was refluxed for 3 h. After cooling to 25 °C, the reaction was concentrated *in vacuo*, and flash chromatographed directly (5:1 hexanes/EtOAc) to give the enone as a clear oil. Analytical data for title compound: **^{1}H NMR** (400 MHz, $CDCl_3$ some peaks doubled and/or broadened due to amide conformational isomers) δ 5.63 and 5.61 (s, 1H), 3.49-3.22 (m, 1H), 3.20-2.85 (m, 3H), 2.70-2.44 (m, 1H), 2.44-2.21 (m, 2H), 2.20-1.70 (m, 7H), 1.70-1.15 (m, 6H), 1.38 (s, 9H), 0.88 and 0.86(d, *J* = 6.8, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$ some peaks doubled due to amide conformational isomers) δ 215.63, 215.38, 156.24, 155.70, 144.07, 143.55, 129.50, 128.96, 78.92, 78.82, 65.68, 65.53, 50.29, 49.53, 47.50, 46.60, 43.37, 42.48, 38.96, 37.79, 37.40, 36.29, 31.83, 29.66, 28.41, 27.05, 26.33, 26.05, 25.71, 25.47 24.22, 22.29, 22.24, 21.70, 21.00; For ^{1}H NMR and ^{13}C NMR spectra, see the Appendix; HRMS (EI) calc. for $[C_{21}H_{33}NO_3]H^+$ 348.2539, found 348.2535; $[\alpha]^{rt}_D$ = -143 (c = 0.2, $CHCl_3$).



24

(+)-(24). To a solution of enone from the last step (285 mg, 0.82 mmol) in THF (15 mL) was added a solution of BH_3·THF (1.0 M in THF, 8.2 mL, 8.2 mmol) at 25 °C. The reaction mixture was then placed in a 55 °C oil bath and stirred for 4 h. After cooling to 25 °C, to the resulting solution was added 3 M NaOH solution (3 mL) and H_2O_2 (30 wt%, 3 mL) dropwise and the reaction was then stirred at 25 °C for 4 h. To the resulting solution was added Et_2O (200 mL) and a sat. NH_4Cl solution (50 mL). The organic layer was separated, washed with a sat. NH_4Cl solution (100 mL × 2) and brine, dried with Na_2SO_4, concentrated *in vacu* to give diol as a white foam which was carried on to the next step without further purification. To a solution of crude diol in CH_2Cl_2 (5 mL) was added Dess-Martin periodinane (1.7 g, 4.1 mmol) at 25 °C. The resulting solution was refluxed for 0.5 h. The reaction was quenched by 5% of $Na_2S_2O_3$ solution (5 mL) and sat. $NaHCO_3$ solution (5 mL) and diluted with Et_2O (50 mL). The organic layer was separated, washed with sat. $NaHCO_3$ and brine, dried with Na_2SO_4, concentrated *in vacuo*, and flash chromatographed (3:1 hexanes/EtOAc) to give diketone **24** (268 mg, 84% from **23** over 3 steps, ~10:1 d.r.) as a clear oil. Analytical data for title compound: **^{1}H NMR** (400 MHz, $CDCl_3$ for the major diastereomer) δ 3.75-3.55 (m, 2H), 2.91-2.77 (m, 2H), 2.41-1.51 (m, 17H), 1.40 (s, 9H), 1.05 (d, *J* = 6.8, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$ for the major diastereomer) δ 215.12, 214.61, 156.57, 79.68, 59.88, 50.10, 49.45, 46.83, 42.15, 38.24, 31.48, 31.15, 30.91, 28.45, 28.35, 25.46, 22.24, 22.11, 21.60; For ^{1}H NMR and ^{13}C NMR spectra, see the Appendix; HRMS (EI) calc. for $[C_{21}H_{33}NO_4]H^+$ 364.2488, found 364.2480; $[\alpha]^{rt}_D$ = +74 (c = 1.8, $CHCl_3$).

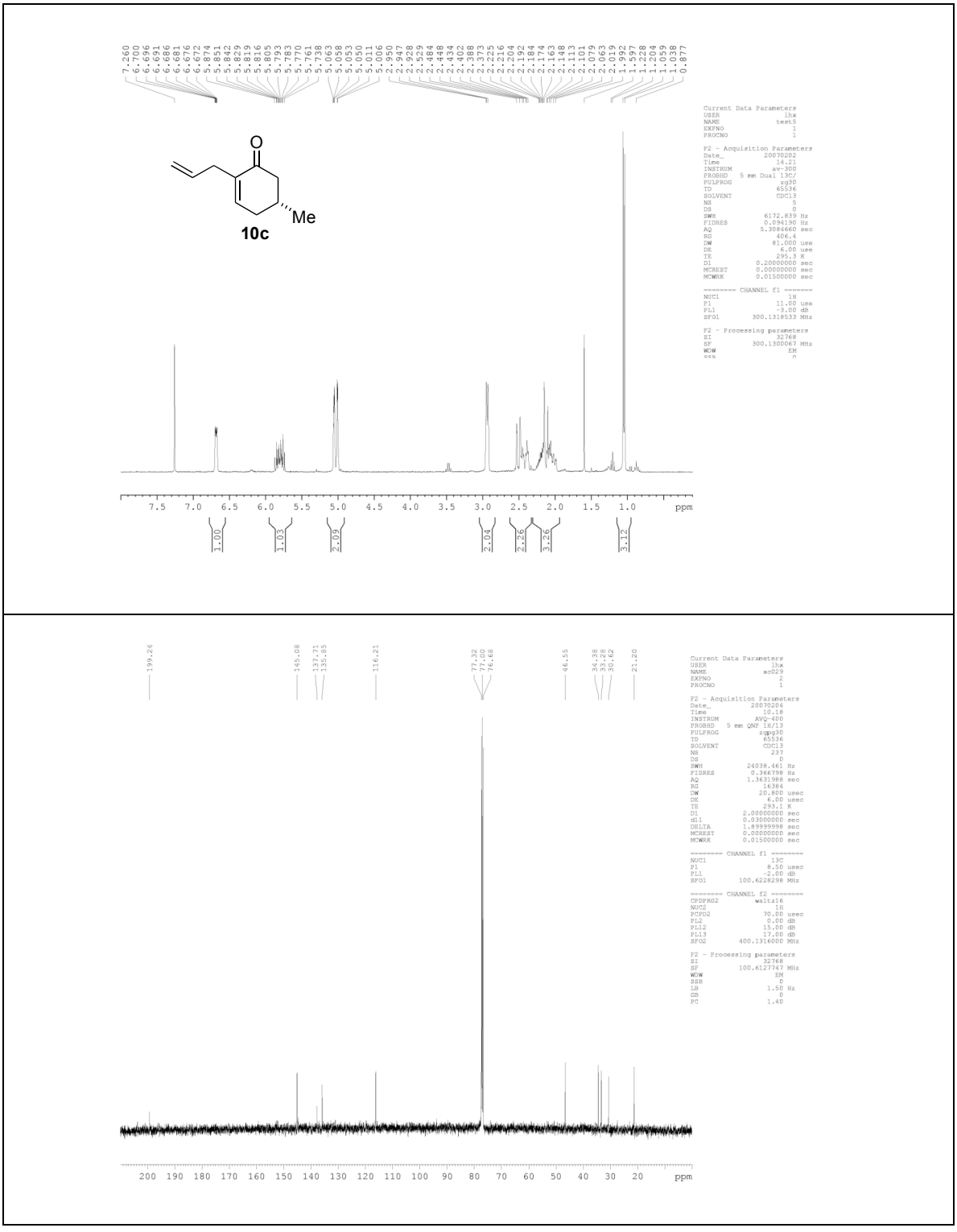


(+)-fawcettimine **1**

(+)-fawcettimine (1). To a solution of **24** (170mg, 0.47 mmol) in CH_2Cl_2 (10 mL) was added 1 mL of trifluoroacetic acid (TFA) at 0 °C. The reaction was then warmed to 25 °C and stirred for 2 h. The reaction was quenched by sat. $NaHCO_3$ solution (20 mL) and extracted with $CHCl_3$ (50 mL × 3). The organic layer was combined, washed with sat. $NaHCO_3$ (50 mL × 3) and brine, dried with Na_2SO_4. After standing in solution for 24 h, solvent was removed *in vacuo* to give **1** (102 mg, 83%) as a white foam. Analytical data for title compound: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.20 (br. s, 1H), 3.53 (ddd, *J* = 4.0, 9.6, 14.4, 1H), 3.25 (dt, *J* = 4.0, 14.0, 1H), 2.89 (dd, *J* = 4.8, 14.4, 1H), 2.71 (ddd, *J* = 4.0, 4.8, 14.4, 1H), 2.59 (dd, *J* = 13.6, 17.6, 1H), 2.28-1.75 (m, 10H), 1.65-1.42 (m, 5H), 1.36 (dt, *J* = 6.0, 14.0, 1H), 0.93 (d, *J* = 6.4, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 219.29, 59.85, 53.61, 49.86, 47.95, 43.14, 42.80, 41.62, 35.01, 31.71, 27.69, 27.43, 23.57, 21.67, 21.49; For ^{1}H NMR and ^{13}C NMR spectra, see the Appendix; HRMS (EI) calc. for $[C_{16}H_{25}NO_2]H^+$ 264.1964, found 264.1959; $[\alpha]^{rt}_D$ = +89 (c = 0.55, MeOH), (natural product: $[\alpha]^{rt}_D$ = +91 (c = 0.66, MeOH))[6]. The hydrobromide salt was prepared by treating **1** with HBr and recrystallizing from acetone/Et_2O. Analytical data for (+)-fawcettimine hydrobromide: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.47 (br. s, 1H), 6.99 (br. s, 1H), 4.01 (dt, *J* = 4.0, 9.6, 1H), 3.53 (dt, *J* = 4.0, 14.4, 1H), 3.18 (dd, *J* = 4.0, 14.4, 1H), 3.00 (m, 1H), 2.66 (br. d, *J* = 13.2, 1H), 2.62 (br. d, *J* = 12.4, 1H), 2.41-2.21 (m, 4H), 2.21-2.02 (m, 5H), 2.00-1.80 (m, 3H), 1.71 (br. d, *J* = 13.6, 1H), 1.58 (br. d, *J* = 13.2, 1H), 1.44 (dt, *J* = 4.8, 13.6, 1H), 1.00 (d, *J* = 6.4, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 216.22, 95.97, 58.92, 55.28, 51.12, 47.53, 43.07, 40.99, 39.76, 33.27, 31.08, 26.53, 23.83, 23.71, 21.28, 18.89; For ^{1}H NMR and ^{13}C NMR spectra, see the Appendix; $[\alpha]^{rt}_D$ = +100 (c = 0.7, $CHCl_3$). Both fawcettimine and fawcettimine hydrobromide had spectra identical with literature.[7]

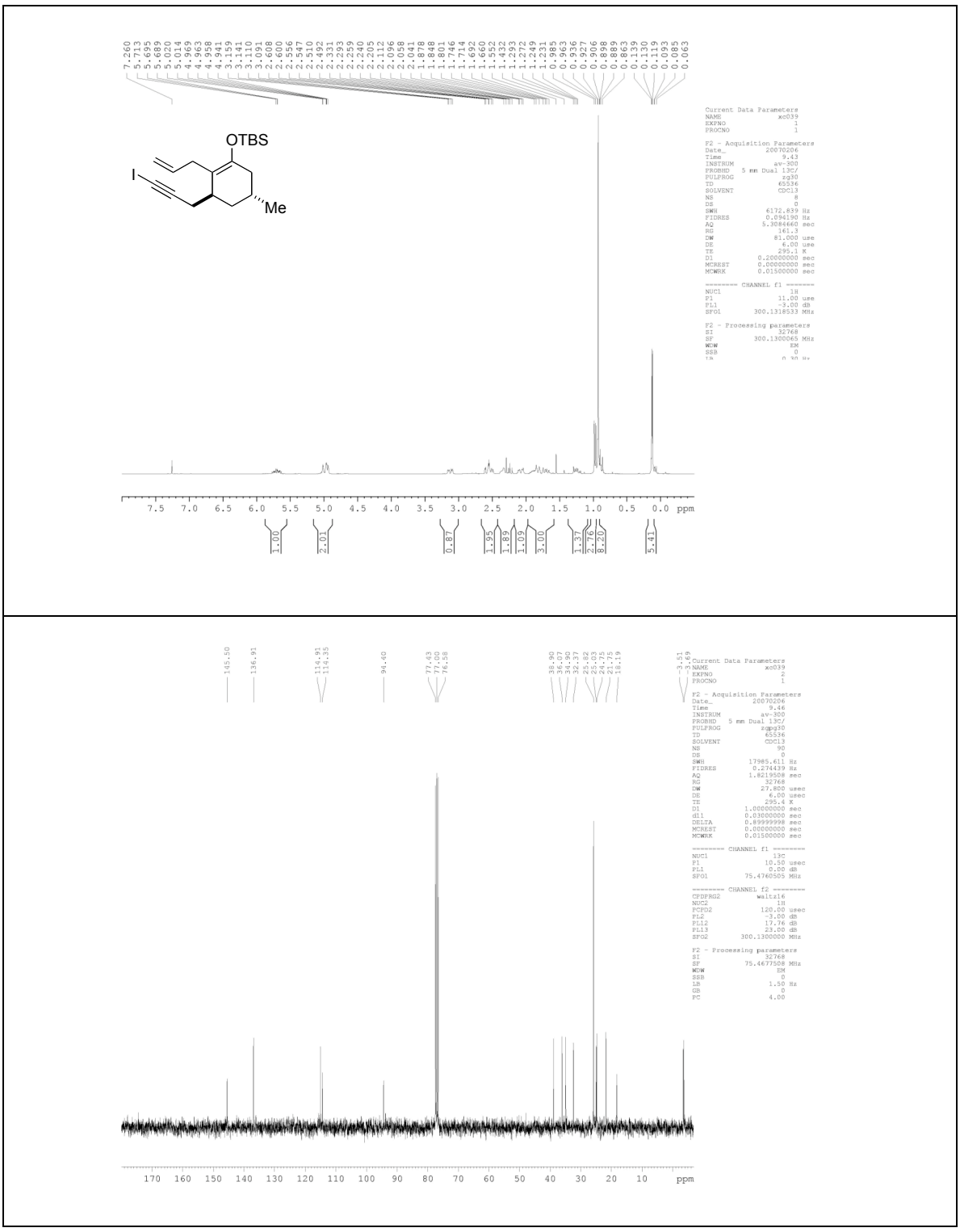
[1] A. B. Pangborn, M. A. Giardello, R. H. Grubbs, R. K. Rosen, F. J. Timmers, *Organometallics* **1996**, *15*, 1518.
[2] P. J. Alaimo, D. W. Peters, J. Arnold, R. G. Bergman, *J. Chem. Ed.* **2001**, *78*, 64.
[3] A. Carlone, M. Marigo, C. North, A. Landa, K. A. Jorgensen, *Chem. Commun.* **2006**, 4928.
[4] H. Graalfs, R. Frohlich, C. Wolff, J. Mattay, *Eur. J. Org. Chem.* **1999**, 1057.
[5] M. Marigo, T. C. Wabnitz, D. Fielenbach, K. A. Jorgensen, *Angew. Chem., Int. Ed.* **2005**, *44*, 794.
[6] D. Zhu *unpublished result*
[7] C. H. Heathcock, T. A. Blumenkopf, K. M. Smith, *J. Org. Chem.* **1989**, *54*, 1548.

^{1}H and ^{13}C NMR spectra for **10c**

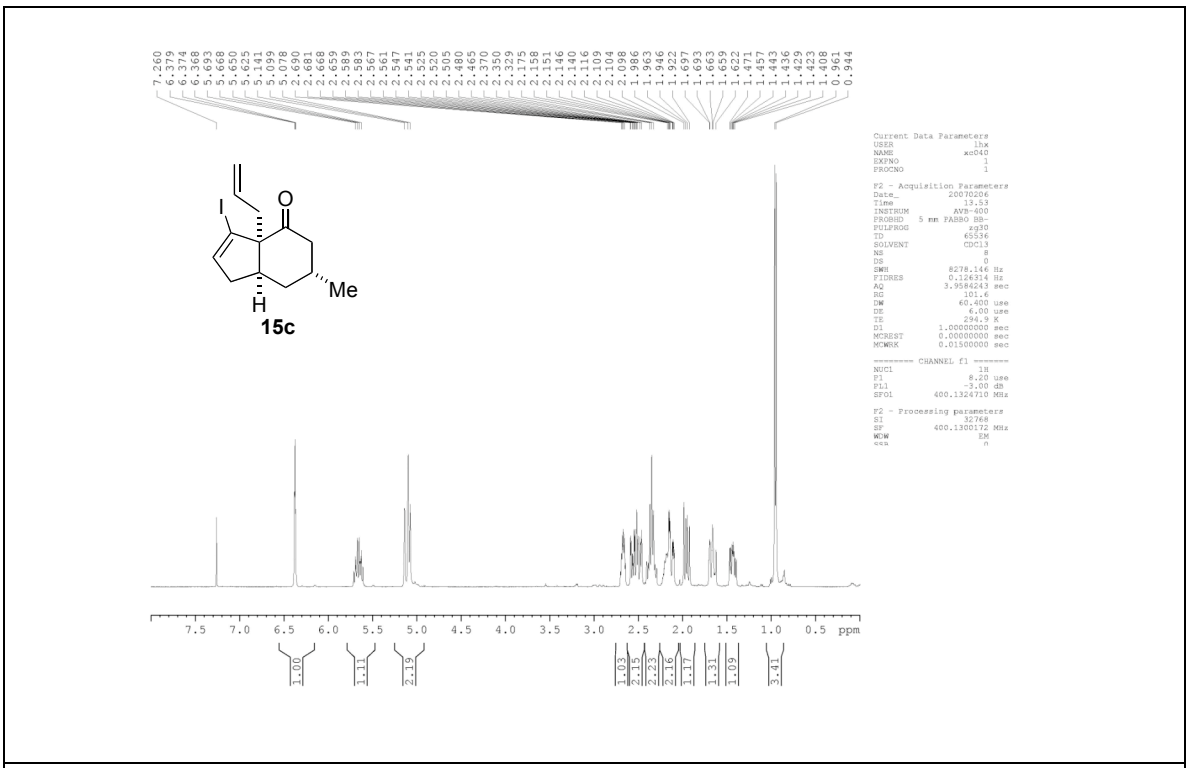


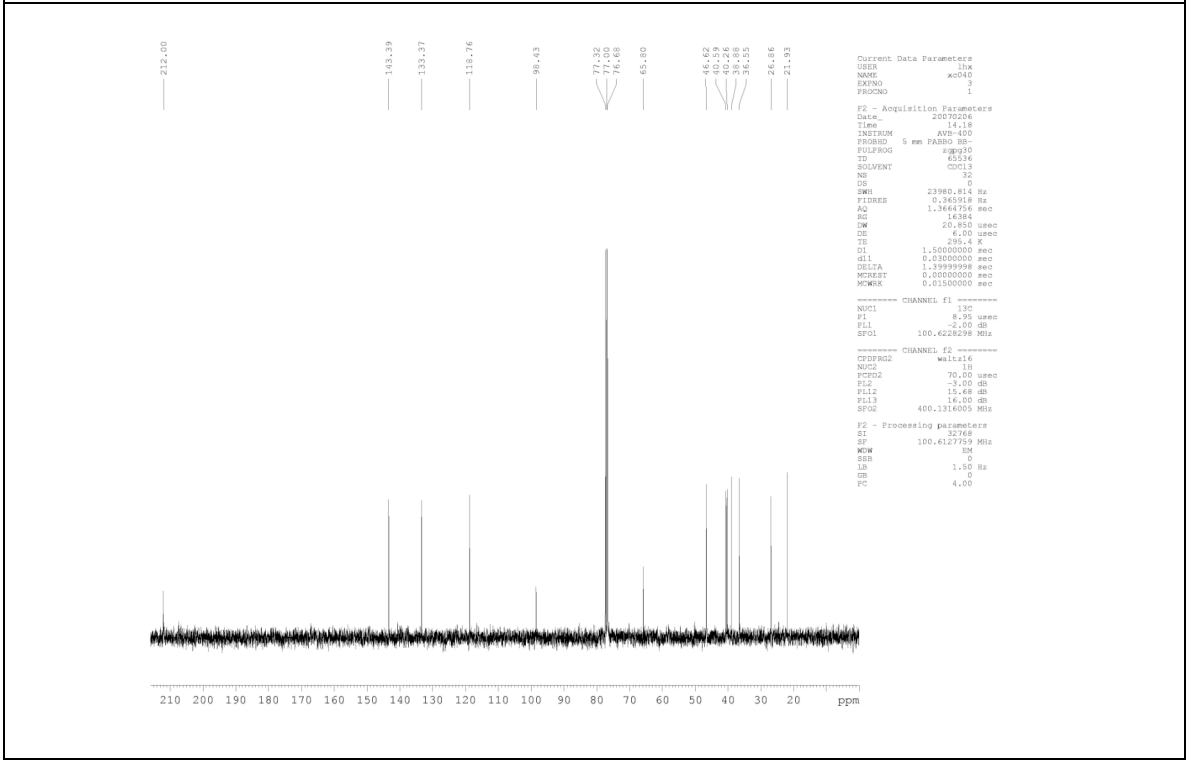
^{1}H and ^{13}C NMR spectra for silyl enol ether

^{1}H and ^{13}C NMR spectra for iodoalkyne

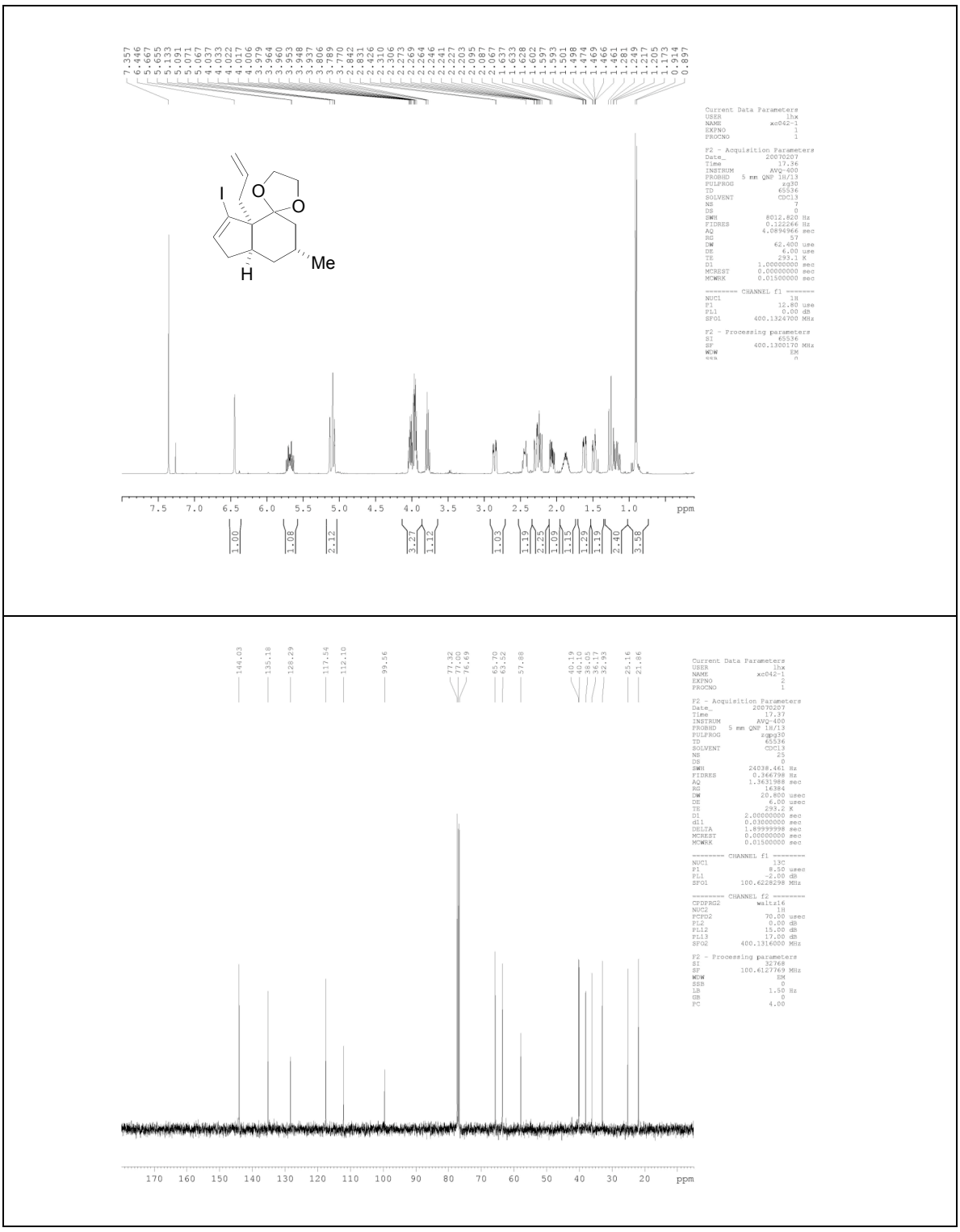


^{1}H and ^{13}C NMR spectra for **15c**

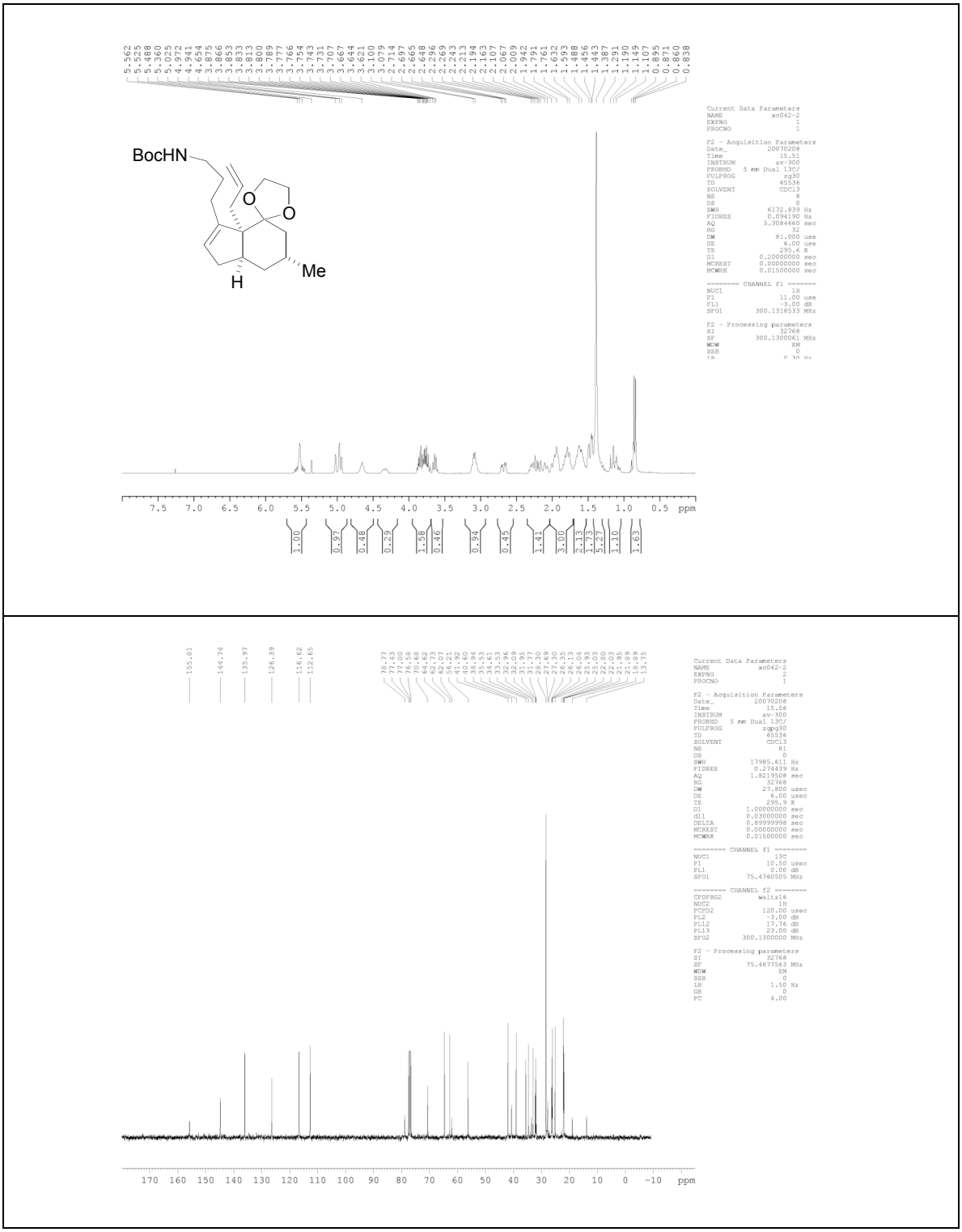




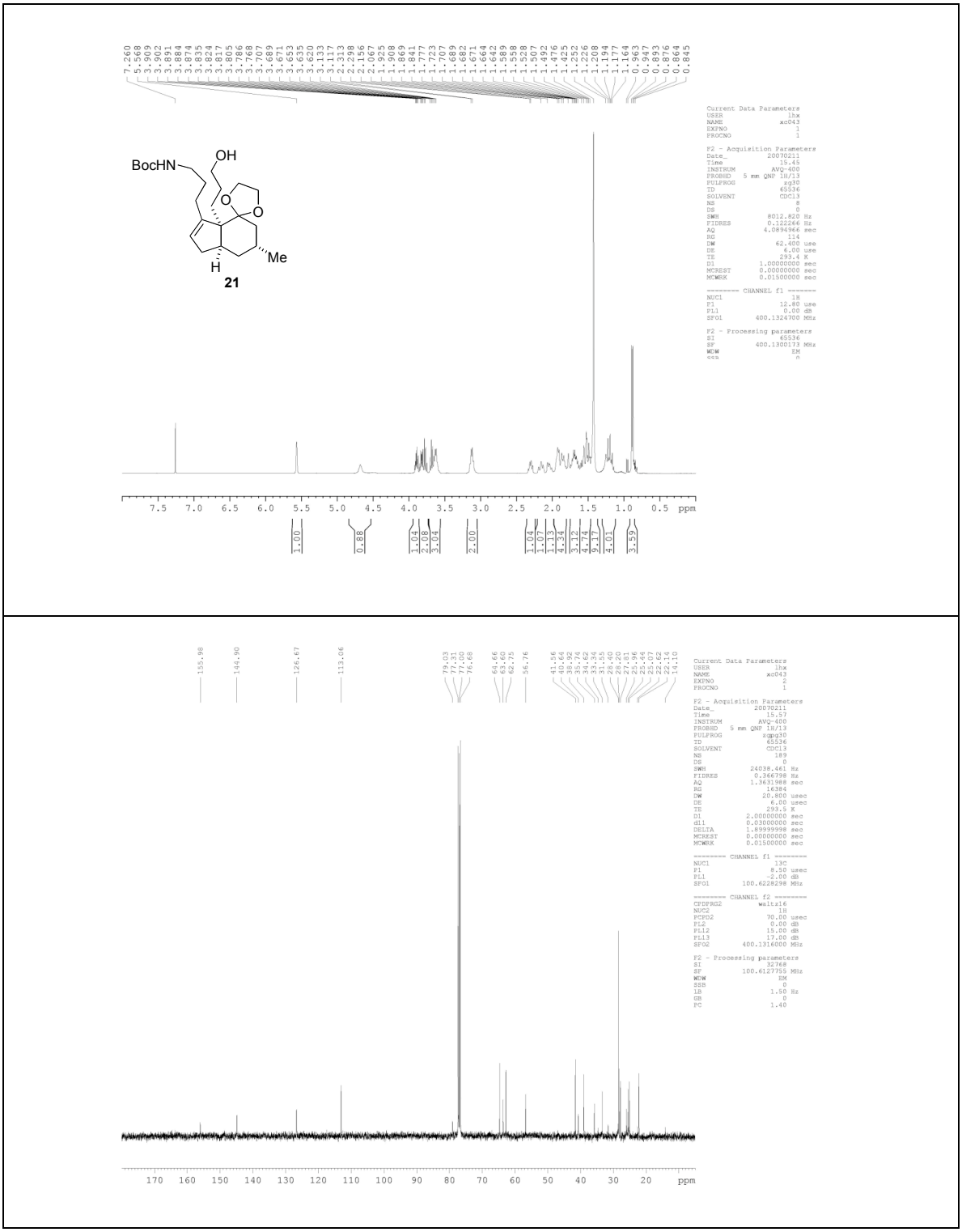
^{1}H and ^{13}C NMR spectra for **ketal** (contains trace benzene)



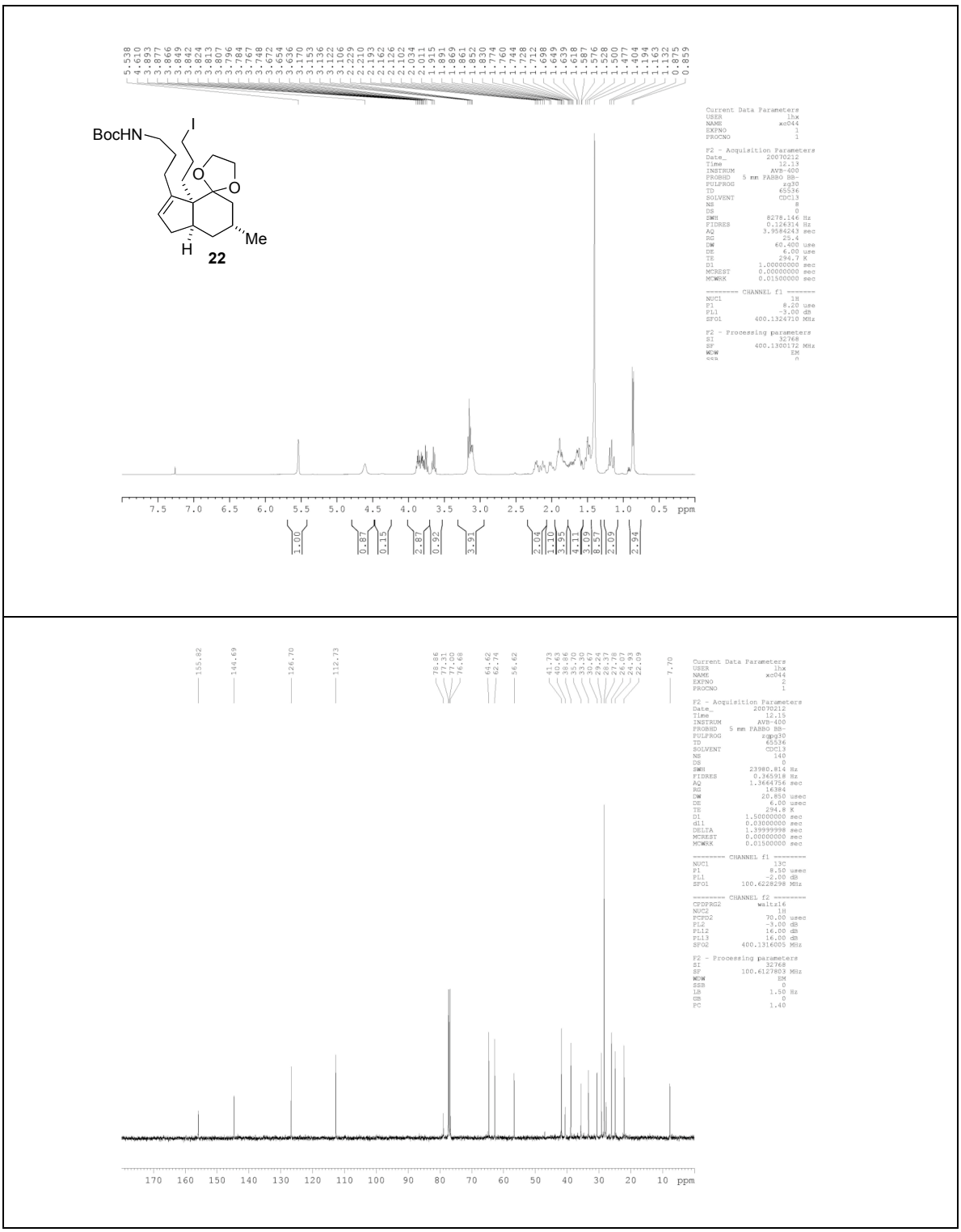
^{1}H and ^{13}C NMR spectra for **diene**



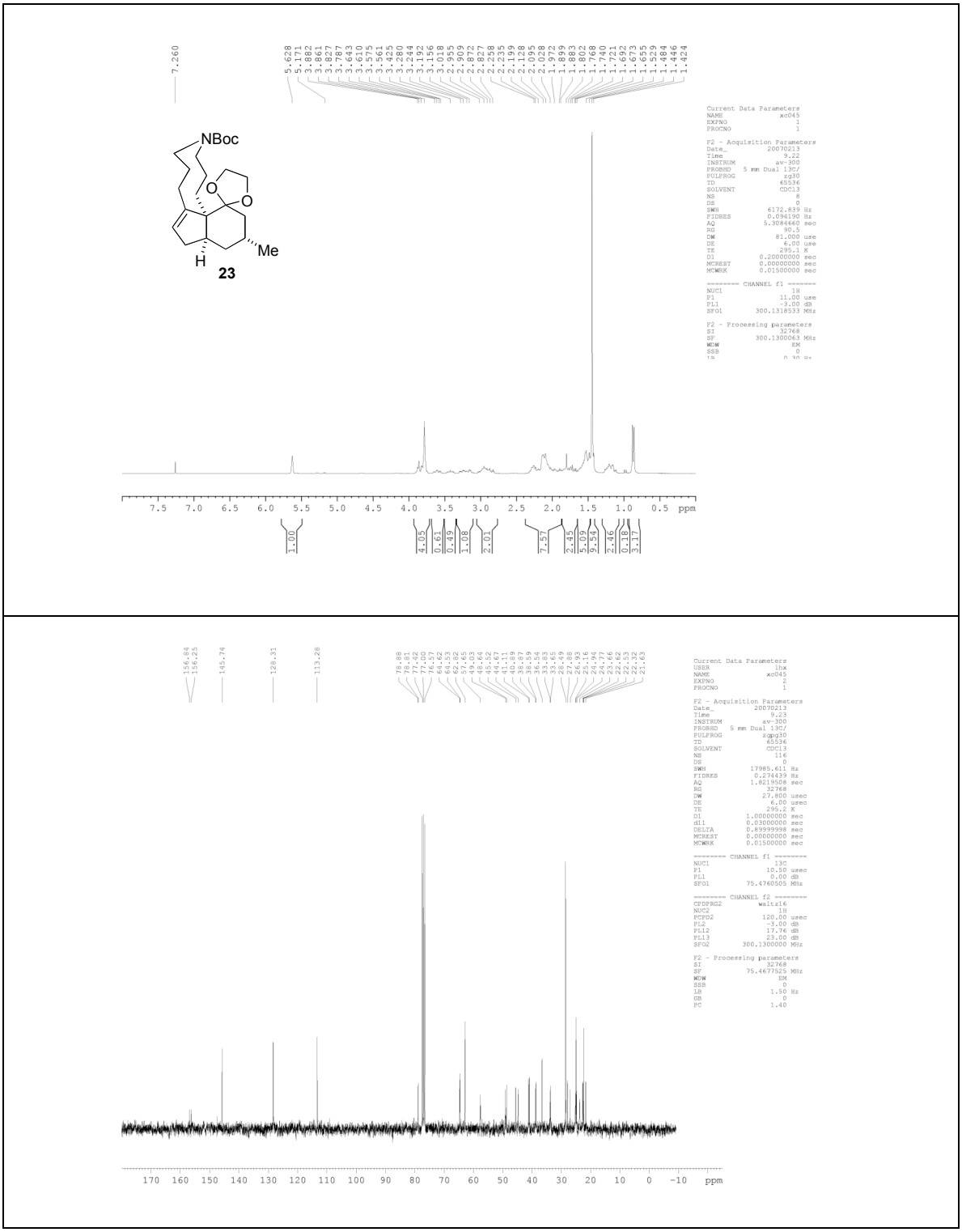
^{1}H and ^{13}C NMR spectra for **21**



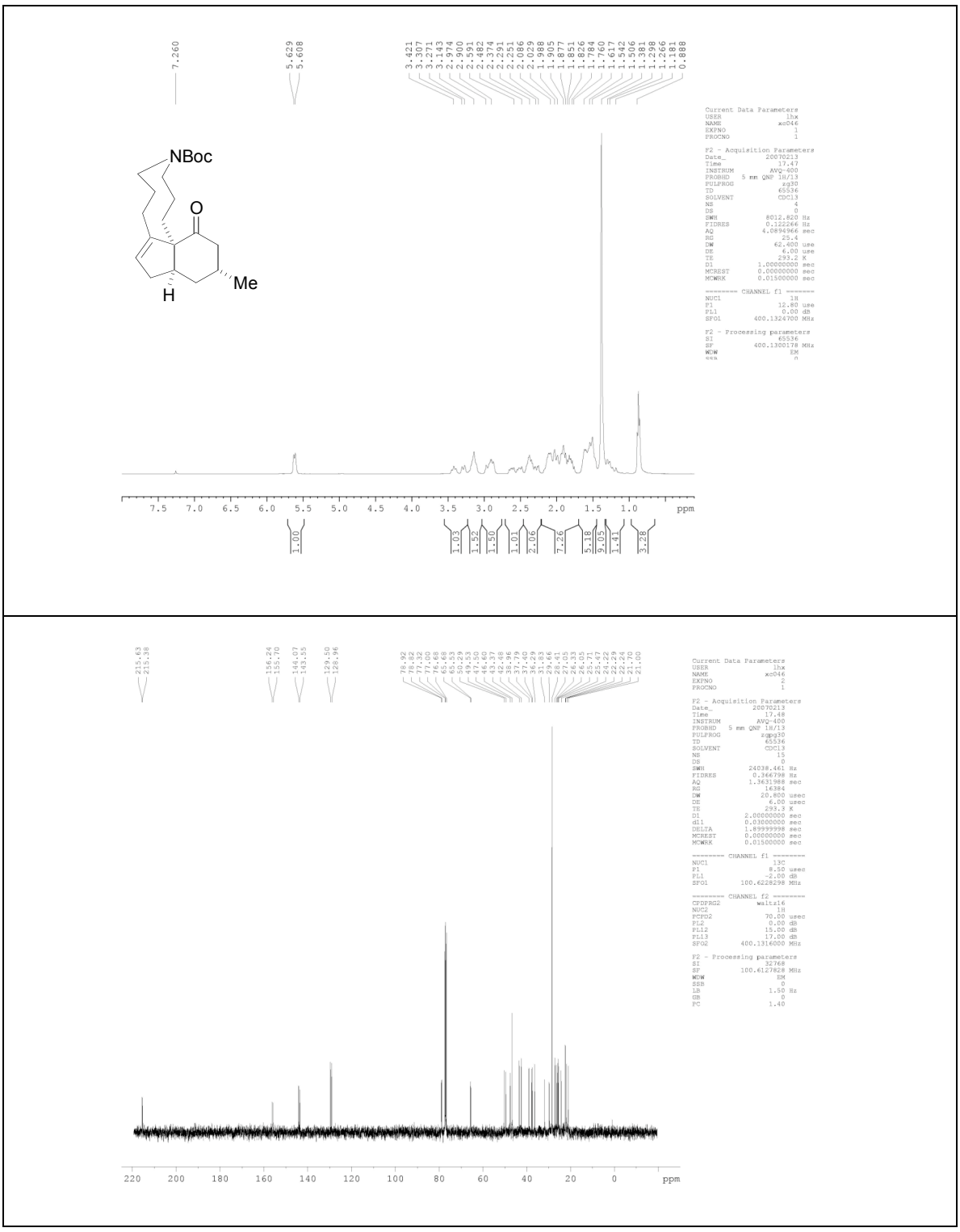
^{1}H and ^{13}C NMR spectra for **22**



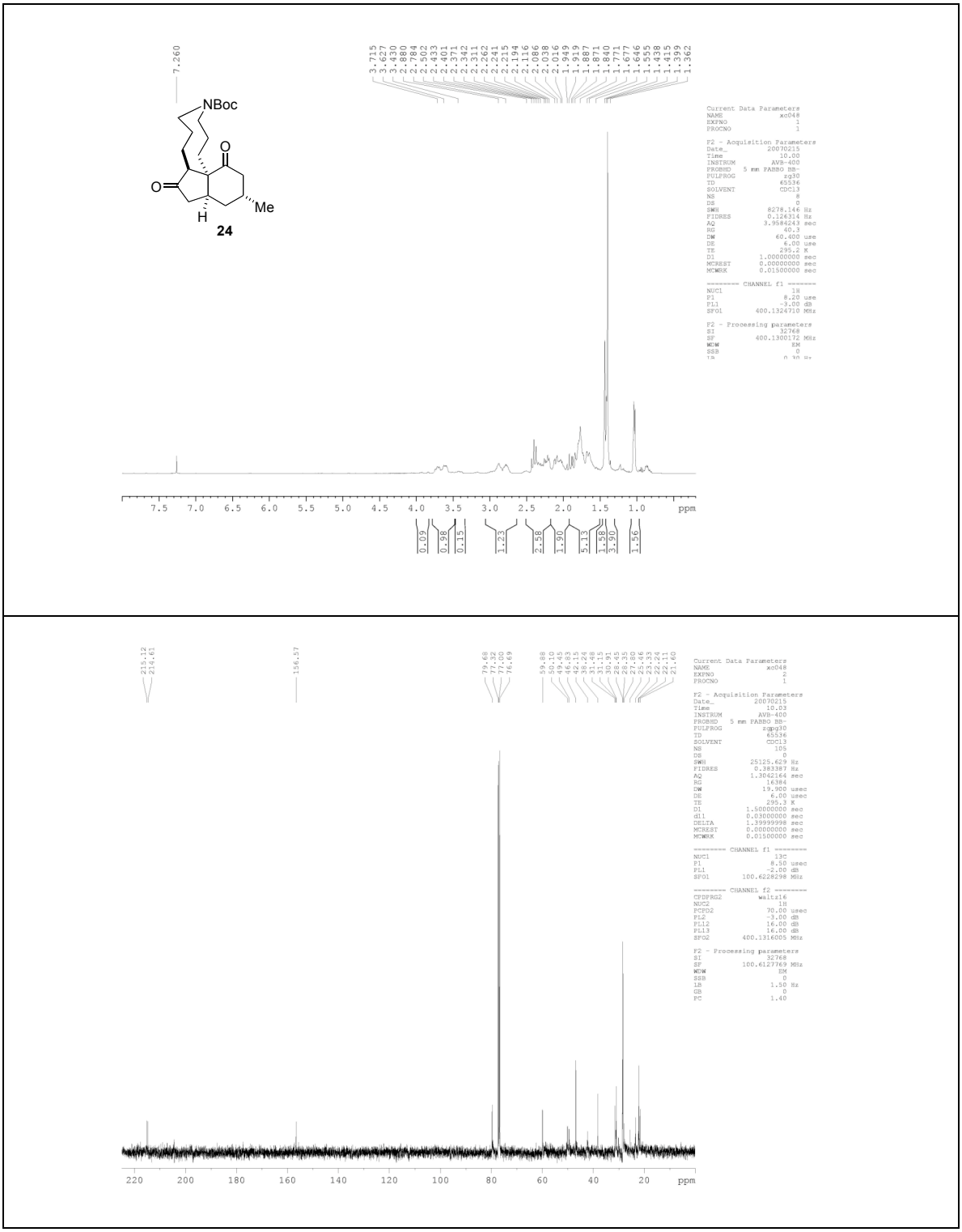
^{1}H and ^{13}C NMR spectra for **23**



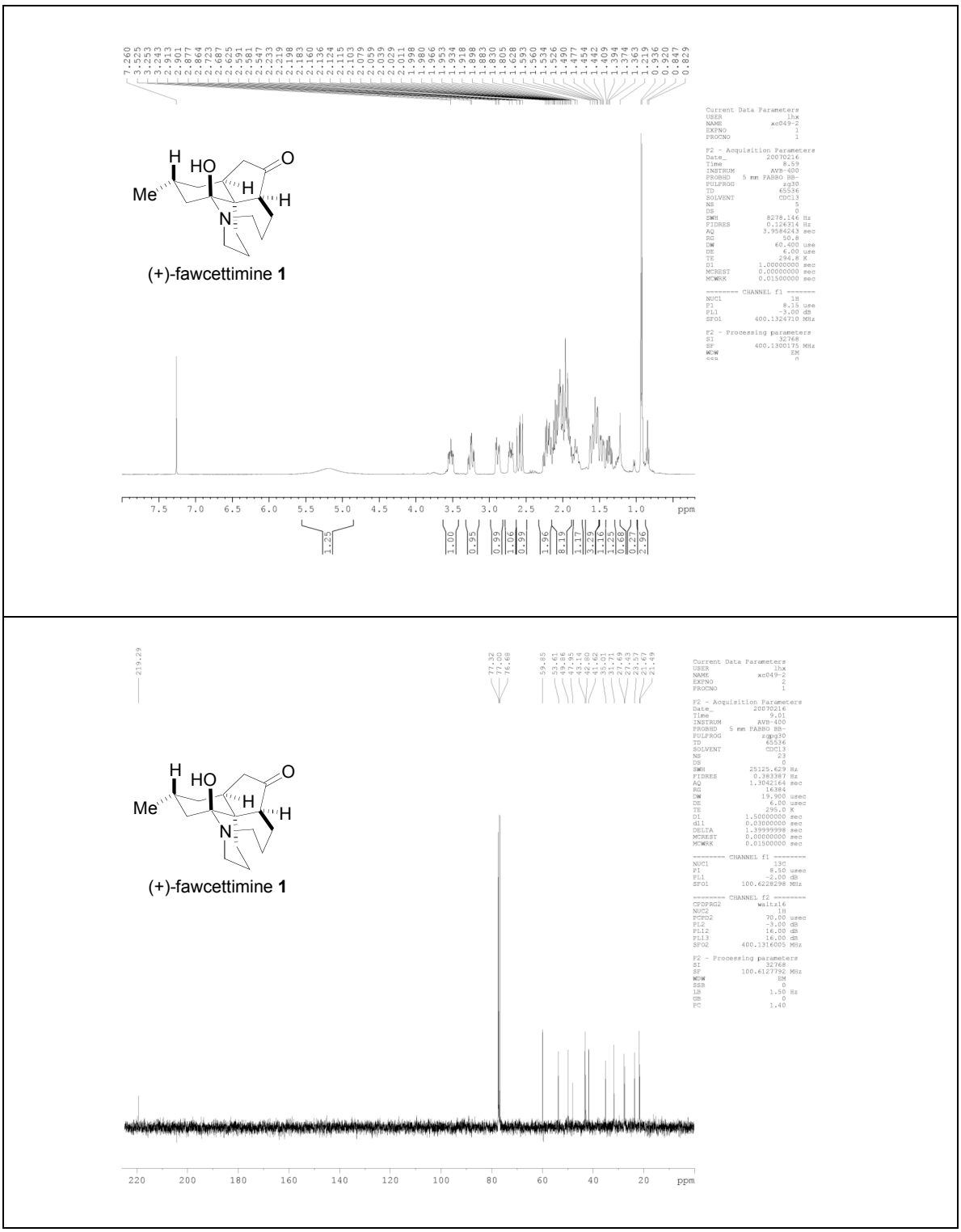
^{1}H and ^{13}C NMR spectra for **enone**



^{1}H and ^{13}C NMR spectra for **24**



^{1}H and ^{13}C NMR spectra for (+)-fawcettimine **1**



^{1}H and ^{13}C NMR spectra for fawcettimine hydrobromide