Organocatalytic Synthesis of Optically Active β-Branched α-Amino Esters via Asymmetric Biomimetic Transamination

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Supporting Information

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General Methods. All commercially available reagents were used without further purification. All dry solvents were freshly distilled under nitrogen from appropriate drying agents before use. Toluene, benzene, tetrahydrofuran, and ethyl ether were distilled from sodium-benzophenone. Dichloromethane, 1,2-dichloroethane, and acetonitrile were distilled from CaH_2. *N*,*N*-Dimethylformamide was dried over 4 Å molecular sieves (activated at 180 ^oC under vacuum over 8 h). Column chromatography was performed on silica gel (200-300 mesh). ^1H NMR spectra were recorded on a 400 MHz NMR spectrometer and ^{13}C NMR spectra were recorded on a 100 MHz NMR spectrometer. IR spectra were recorded on a FT-IR spectrometer. Melting points were uncorrected. Catalysts **C1**-**C3** were prepared according to the reported procedures.[1,2] *t*-Butyl β,β'-disubstituted α-keto esters were generally prepared from the corresponding ketones by olefination with ethyl 2-[(*t*-butyldimethylsilyl)oxy]-2-(diethoxyphosphoryl)acetate,[3] hydrolysis of the resulting α-siloxy α,β-unsaturated esters to keto acids,[3-5] and subsequent esterification with isobutene.[6] α-Keto esters **4i** was prepared from **4h** by ring-closing metathesis (RCM) using Grubbs second-generation ruthenium catalyst.[7]

(1) X. Xiao, Y. Xie, C. Su, M. Liu and Y. Shi, *J. Am. Chem. Soc.*, 2011, **133**, 12914.

(2) X. Xiao, M. Liu, C. Rong, F. Xue, S. Li, Y. Xie and Y. Shi, *Org. Lett.*, 2012, **14**, 5270.

(3) S. He, Z. Lai, D. X. Yang, Q. Hong, M. Reibarkh, R. P. Nargund and W. K. Hagmann, *Tetrahedron Lett.*, 2010, **51**, 4361.

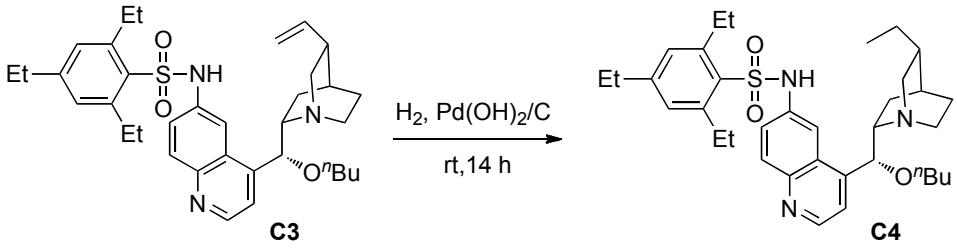
(4) C. H. Senanayake, K. Fang, P. Grover, R. P. Bakale, C. P. Vandenbossche and S. A. Wald, *Tetrahedron Lett.*, 1999, **40**, 819.

(5) R. M. Archer, S. F. Royer, W. Mahy, C. L. Winn, M. J. Danson and S. D. Bull, *Chem. Eur. J.*, 2013, **19**, 2895.

(6) H. Molines, M. H. Massoudi, D. Cantacuzene and C. Wakselman, *Synthesis*, 1983, 322.

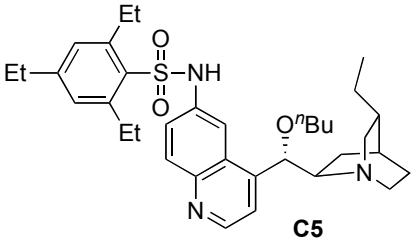
(7) H. Hu, J. A. Faraldos and R. M. Coates, *J. Am. Chem. Soc.*, 2009, **131**, 11998.

Preparation of Catalyst C4



To a solution of compound **C3** (1.770 g, 3.0 mmol) in MeOH (30.0 mL) was added $Pd(OH)_2/C$ (20%) (0.300 g).[1] The reaction mixture was stirred at room temperature under hydrogen (1 atm) for 14 h, filtered through Celite, washed with EtOAc, concentrated, and purified by flash column chromatography (silica gel, packed with EtOAc containing 1% Et_3N) (eluent: EtOAc/MeOH = 40/1) to give compound **C4** as a yellow solid (1.699 g, 96% yield). mp. 87-88 ^oC; $[\alpha]^{20}_D$ = -83.7 (*c* 0.73, $CHCl_3$); IR (film) 3239, 1622, 1457, 1154 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.70 (br s, 1H), 8.73 (d, *J* = 4.4 Hz, 1H), 7.93 (d, *J* = 8.8 Hz, 1H), 7.84 (s, 1H), 7.55 (d, *J* = 8.8 Hz, 1H), 7.37 (d, *J* = 4.4 Hz, 1H), 6.95 (s, 2H), 5.20-5.00 (m, 1H), 3.41-2.88 (m, 9H), 2.69-2.52 (m, 3H), 2.44-2.34 (m, 1H), 1.81-1.68 (m, 3H), 1.53-1.40 (m, 3H), 1.40-1.31 (m, 3H), 1.30-1.07 (m, 12H), 0.83-0.72 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.9, 148.3, 145.9, 145.8, 145.7, 137.7, 134.2, 131.4, 129.2, 127.4, 124.1, 118.9, 113.2, 79.6, 69.2, 60.3, 58.6, 43.7, 37.3, 32.1, 28.5, 28.4, 28.1, 27.6, 25.4, 22.2, 19.4, 16.7, 14.9, 14.0, 12.1; HRMS Calcd for $C_{35}H_{50}N_3O_3S$ (M+H): 592.3567; Found: 592.3566.

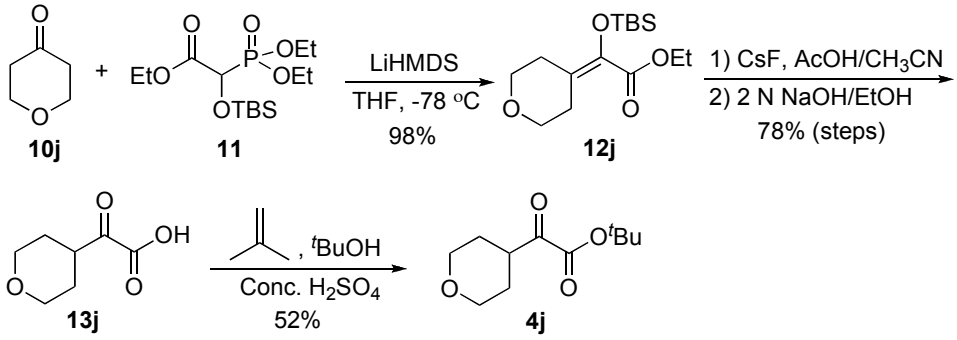
(1) G. Sabitha, S. Nayak, M. Bhikshapathi, M. Chittapragada and J. S. Yadav, *Synthesis*, 2011, **22**, 3661.



Prepared in a manner similar to **C4**. light yellow solid; mp. 86-87 ^oC; $[\alpha]^{20}_D$ =

+184.2 (*c* 0.84, $CHCl_3$); IR (film) 3239, 1489, 1457, 1154 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, *J* = 4.4 Hz, 1H), 7.94 (d, *J* = 9.2 Hz, 1H), 7.78 (s, 1H), 7.49 (dd, *J* = 9.2, 2.0 Hz, 1H), 7.35 (d, *J* = 4.4 Hz, 1H), 7.05-6.98 (m, 1H), 6.96 (s, 2H), 5.05 (s, 1H), 3.21-3.00 (m, 7H), 2.99-2.79 (m, 3H), 2.79-2.68 (m, 1H), 2.63-2.53 (m, 2H), 2.02-1.91 (m, 1H), 1.72-1.67 (m, 1H), 1.53-1.41 (m, 7H), 1.36-1.17 (m, 12H), 0.94-0.81 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.1, 148.4, 146.0, 145.9, 145.7, 137.3, 134.0, 131.4, 129.2, 127.0, 124.9, 119.0, 114.6, 80.4, 69.3, 60.0, 51.0, 50.2, 37.3, 32.2, 28.54, 28.49, 27.0, 26.2, 25.2, 21.5, 19.5, 16.8, 14.9, 14.0, 12.1. HRMS Calcd for $C_{35}H_{50}N_3O_3S$ (M+H): 592.3567; Found: 592.3571.

Representative procedures for the preparation of β,β'-disubstituted α-keto esters



To a solution of phosphonate **11**[1] (38.990 g, 110.0 mmol) in THF (100.0 mL) was added a solution of LiHMDS (1 M solution in THF) (110.0 mL, 110.0 mmol) at -78 °C under N_2.[1] After the reaction mixture was stirred at -78 °C for 30 min, a solution of ketone **10j** (10.011 g, 100.0 mmol) in THF (10.0 mL) was added dropwise over 10 min. The reaction mixture was stirred at -78 °C for 30 min, warmed to room temperature overnight, quenched with saturated aqueous NH_4Cl solution (100.0 mL), extracted with CH_2Cl_2 (3 x 100.0 mL), washed with brine (100.0 mL), dried over $MgSO_4$, filtered, concentrated, and purified by flash column chromatography (silica gel, eluent: petroleum ether/EtOAc = 10/1) to afford ester **12j** as a light yellow oil (29.446 g, 98%). IR (film) 1712, 1280, 1216, 1097 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.21 (q, *J* = 7.2 Hz, 2H), 3.71 (t, , *J* = 5.6 Hz, 2H), 3.67 (t, *J* = 5.6 Hz, 2H), 2.76 (t, *J* = 5.6 Hz, 2H), 2.45 (t, *J* = 5.6 Hz, 2H), 1.33 (t, *J* = 7.2 Hz, 3H), 0.95 (s, 9H), 0.10

(s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 134.9, 129.8, 68.7, 68.2, 60.8, 29.9, 29.4, 25.9, 18.5, 14.4, -4.3; HRMS Calcd for $C_{15}H_{28}NaO_4Si$ (M+Na): 323.1649; Found: 323.1654.

(1) S. He, Z. Lai, D. X. Yang, Q. Hong, M. Reibarkh, R. P. Nargund and W. K. Hagmann, *Tetrahedron Lett*., 2010, **51**, 4361.

To a solution of ester **12j** (29.446 g, 98.0 mmol) and acetic acid (28.0 mL, 490.0 mmol) in CH_3CN (100.0 mL) was added solid cesium fluoride (29.772 g, 196.0 mmol) in one portion at 0 °C.[1] Upon stirring at 0 °C for 30 min and room temperature for 24 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (100.0 mL), extracted with EtOAc (3 x 100.0 mL), washed with saturated aqueous $NaHCO_3$ (100.0 mL), and concentrated to give a yellow oil, which was subsequently dissolved in EtOH (200.0 mL), followed by the addition of aqueous 2 N NaOH (100.0 mL).[2] Upon stirring at room temperature for 17 h, the reaction mixture was diluted with water, washed with n-hexane (3 x 50.0 mL), acidified with concentrated HCl to pH = 2, extracted with CH_2Cl_2 (3 x 50.0 mL), washed with brine (50.0 mL), dried over $MgSO_4$, filtered, concentrated, and purified by flash column chromatography (silica gel, eluent: petroleum ether/EtOAc = 10/1 to 0/1) to give α-keto acid **13j** as a white solid (12.010 g, 78% yield). mp. 88-90 °C; IR (film) 3421, 1723, 1273, 1081 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.06 (ddd, *J* = 11.6, 3.6, 2.4 Hz, 2H), 3.54 (td, *J* = 11.6, 2.4 Hz, 2H), 3.46 (tt, *J* = 11.2, 4.0 Hz, 1H), 1.92-1.84 (m, 2H), 1.79-1.67 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.4, 161.0, 66.9, 42.5, 27.3; HRMS Calcd for $C_7H_9O_4$ (M-H): 157.0495; Found: 157.0493.

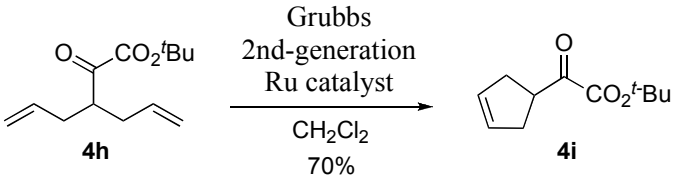
(1) R. M. Archer, S. F. Royer, W. Mahy, C. L. Winn, M. J. Danson and S. D. Bull, *Chem. Eur. J.*, 2013, *19*, 2895.

(2) C. H. Senanayake, K. Fang, P. Grover, R. P. Bakale, C. P. Vandenbossche and S. A. Wald, *Tetrahedron Lett.*, 1999, **40**, 819.

To a screw capped pyrex heavy-walled pressure bottle containing a solution of α-keto acid **13j** (12.012 g, 76.0 mmol), *t*-butanol (12.0 mL), and Et_2O (5.0 mL) at -40 °C, were

added concentrated sulfuric acid (3.0 mL) and liquid isobutene (70.0 mL), respectively.[1] Upon stirring at room temperature for 48 h, the reaction mixture was cooled to -20 ^{o}C, quenched with saturated aqueous $NaHCO_3$ (70.0 mL), extracted with EtOAc (3 x 100.0 mL), washed with brine (100.0 mL), dried over $MgSO_4$, filtered, concentrated, and purified by flash column chromatography (silica gel, eluent: petroleum ether/EtOAc = 40/1 to 10/1) to give α-keto ester **4j** as a yellow oil (8.424 g, 52% yield). IR (film) 1721, 1371, 1113, 1019 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.40-3.95 (m, 2H), 3.48 (td, *J* = 11.2, 1.6 Hz, 2H), 3.24-3.14 (m, 1H), 1.85-1.77 (m, 2H), 1.75-1.62 (m, 2H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.6, 161.2, 84.4, 67.0, 43.4, 27.9, 27.3; HRMS Calcd for $C_{11}H_{18}NaO_4$ (M+Na): 237.1097; Found: 237.1104.

(1) H. Molines, M. H. Massoudi, D. Cantacuzene and C. Wakselman, *Synthesis*, 1983, 322.



A mixture of *t*-butyl 3-allyl-2-oxohex-5-enoate (**4h**) (1.262 g, 5.6 mmol) and Grubbs 2nd-generation Ru catalyst (0.153 g, 0.18 mmol) in dry CH_2Cl_2 (60.0 mL) was stirred at room temperature under N_2 for 18 h,[1] concentrated, and purified by flash column chromatography (silica gel, eluent: petroleum ether/EtOAc = 20/1) to give α-keto ester **4i** as a light yellow oil (0.766 g, 70% yield); IR (film) 1722, 1370, 1161 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.62 (br s, 2H), 3.84-3.71 (m, 1H), 2.68-2.62 (m, 4H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.3, 161.5, 128.8, 84.1, 45.3, 34.6, 28.0; HRMS Calcd for $C_{11}H_{17}O_3$ (M+H): 197.1172; Found: 197.1174.

(1) H. Hu, J. A. Faraldos and R. M. Coates, *J. Am. Chem. Soc.*, 2009, **131**, 11998.

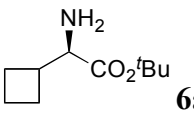
Representative procedure for transamination of β-branched α-keto esters (Table 2, entry 3)

To a well-dried Schlenk tube charged with 4 Å molecular sieves (0.25 g), 4-CNPhCH_2NH_2 (0.198 g, 1.50 mmol), and catalyst **C4** (0.0296 g, 0.050 mmol) under N_2 at room temperature was added a solution of α-keto ester **4c** (0.106 g, 0.50 mmol) in dry toluene (5.0 mL). Upon stirring at 80 °C for 72 h, the reaction mixture was filtered through a short plug of silica gel to remove molecular sieves, washed with EtOAc (containing 1% MeOH), and concentrated. The resulting residue was dissolved in THF (7.5 mL), followed by the addition of aqueous 2 N HCl (7.5 mL). Upon stirring at room temperature for 1 h, the resulting mixture was diluted with water (50 mL) and washed with diethyl ether (3 x 10.0 mL). The organic phase was extracted with 1 N HCl (10.0 mL). The aqueous phases were combined, brought to pH = 8 with solid $NaHCO_3$, extracted with CH_2Cl_2 (3 x 30.0 mL), dried over $MgSO_4$, filtered, concentrated, and purified by flash column chromatography (silica gel, eluent: EtOAc/CH_3OH = 40/1) to give α-amino ester **6c** as a yellow oil (0.087 g, 82% yield, 94% ee).

Representative procedure for the preparation of *N*-benzoyl derivative of amino ester for the determination of the enantiomeric excess

To a solution of **6c** (0.021 g, 0.10 mmol) in CH_2Cl_2 (1.0 mL) were added Et_3N (0.018 g, 0.18 mmol) and BzCl (0.021 g, 0.15 mmol). The reaction mixture was stirred at room temperature for 30 min and purified by flash column chromatography (silica gel, eluent: petroleum ether/EtOAc = 10/1) to afford *N*-benzoyl amino ester **14c** as a white solid (0.029 g, 90% yield). The sample was subjected to chiral HPLC (Chiralcel OD-H column) to determine the enantiomeric excess.

Table 2, entry 1

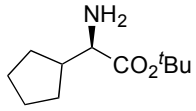


6a

Yellow oil; $[\alpha]^{20}_D$ = -31.8 (*c* 0.77, $CHCl_3$) (87% ee); IR (film) 3384, 1727, 1595, 1260, 1154 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.20 (d, *J* = 8.4 Hz, 1H), 2.51-2.37 (m, 1H),

2.10-1.91 (m, 3H), 1.90-1.72 (m, 3H), 1.71-1.55 (m, 2H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 81.0, 59.6, 40.3, 28.3, 25.5, 25.4, 18.1; HRMS Calcd for $C_{10}H_{20}NO_2$ (M+H): 186.1489; Found: 186.1484.

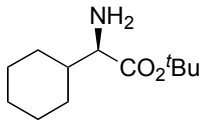
Table 2, entry 2



6b

Yellow oil; $[\alpha]^{20}_D$ = -11.0 (*c* 0.84, $CHCl_3$) (94% ee); IR (film) 3377, 1727, 1367, 1152 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.17 (d, *J* = 7.2 Hz, 1H), 2.12-1.99 (m, 1H), 1.76-1.48 (m, 8H), 1.46 (s, 9H), 1.42-1.28 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 80.9, 59.1, 44.6, 29.4, 28.5, 28.3, 25.8, 25.6; HRMS Calcd for $C_{11}H_{22}NO_2$ (M+H): 200.1645; Found: 200.1642.

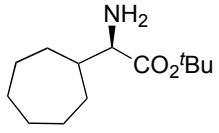
Table 2, entry 3



6c

Yellow oil; $[\alpha]^{20}_D$ = -22.8 (*c* 0.87, $CHCl_3$) (94% ee); IR (film) 3384, 1727, 1367, 1152 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.12 (d, *J* = 4.4 Hz, 1H), 1.79-1.69 (m, 2H), 1.68-1.54 (m, 4H), 1.51-1.35 (m, 2H), 1.45 (s, 9H), 1.31-1.00 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 81.0, 60.3, 42.5, 29.9, 28.3, 28.0, 26.52, 26.51, 26.4; HRMS Calcd for $C_{12}H_{24}NO_2$ (M+H): 214.1802; Found: 214. 1803.

Table 2, entry 4

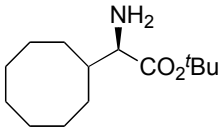


6d

Yellow oil; $[\alpha]^{20}_D$ = -23.9 (*c* 1.08, $CHCl_3$) (94% ee); IR (film) 3457, 1738, 1366, 1229 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.22 (d, *J* = 4.4 Hz, 1H), 1.88-1.79 (m, 1H), 1.75-1.63 (m, 3H), 1.63-1.53 (m, 3H), 1.52-1.28 (m, 8H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$)

δ 175.2, 81.0, 60.9, 43.7, 31.9, 29.1, 28.5, 28.3, 28.1, 27.4, 27.2; HRMS Calcd for $C_{13}H_{26}NO_2$ (M+H): 228.1958; Found: 228.1960.

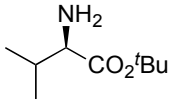
Table 2, entry 5



6e

Yellow oil; $[\alpha]^{20}_D$ = -20.2 (*c* 1.16, $CHCl_3$) (95% ee); IR (film) 3381, 1725, 1275, 1154 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.18 (d, *J* = 4.8 Hz, 1H), 1.98-1.88 (m, 1H), 1.75-1.64 (m, 2H), 1.63-1.53 (m, 4H), 1.52-1.25 (m, 10H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 80.9, 61.4, 41.3, 31.3, 28.3, 27.9, 26.9, 26.8, 26.4, 25.8; HRMS Calcd for $C_{14}H_{28}NO_2$ (M+H): 242.2115; Found: 242.2112.

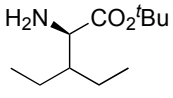
Table 2, entry 6



6f

Yellow oil; $[\alpha]^{20}_D$ = -14.2 (*c* 0.63, $CHCl_3$) (92% ee); IR (film) 3403, 1736, 1366, 1218 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.16 (d, *J* = 4.4 Hz, 1H), 2.05-1.93 (m, 1H), 1.67 (br s, 2H), 1.45 (s, 9H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.0, 81.0, 60.4, 32.3, 28.3, 19.5, 17.2; HRMS Calcd for $C_9H_{20}NO_2$ (M+H): 174.1489; Found: 174.1484.

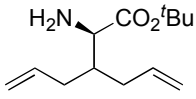
Table 2, entry 7



6g

Yellow oil; $[\alpha]^{20}_D$ = -23.6 (*c* 0.84, $CHCl_3$) (91% ee); IR (film) 3386, 1727, 1368, 1154 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.40 (d, *J* = 4.0 Hz, 1H), 1.63-1.20 (m, 7H), 1.46 (s, 9H), 0.94 (t, *J* = 7.2 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 80.9, 56.4, 45.5, 28.2, 23.1, 22.1, 12.1, 12.0; HRMS Calcd for $C_{11}H_{24}NO_2$ (M+H): 202.1802; Found: 202.1799.

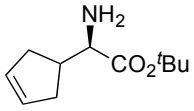
Table 2, entry 8



6h

Yellow oil; $[\alpha]^{20}_D$ = -33.8 (*c* 1.00, $CHCl_3$) (92% ee); IR (film) 3384, 1727, 1367, 1217 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.85-5.70 (m, 2H), 5.12-4.98 (m, 4H), 3.41 (d, *J* = 3.6 Hz, 1H), 2.18-1.98 (m, 4H), 1.97-1.89 (m, 1H), 1.46 (s, 9H), 1.40 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 137.1, 137.0, 116.9, 116.8, 81.2, 56.3, 41.9, 35.1, 33.9, 28.3; HRMS Calcd for $C_{13}H_{24}NO_2$ (M+H): 226.1802; Found: 226.1803.

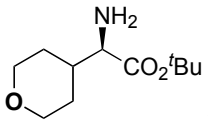
Table 2, entry 9



6i

Yellow oil; $[\alpha]^{20}_D$ = -4.9 (*c* 1.24, $CHCl_3$) (92% ee); IR (film) 3462, 1736, 1366, 1218 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.65 (br s, 2H), 3.28 (d, *J* = 6.8 Hz, 1H), 2.63-2.52 (m, 1H), 2.48-2.35 (m, 2H), 2.31-2.18 (m, 2H), 1.52 (br s, 2H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8, 129.9, 129.7, 80.9, 58.7, 41.4, 35.7, 34.6, 28.1; HRMS Calcd for $C_{11}H_{20}NO_2$ (M+H): 198.1489; Found: 198.1485.

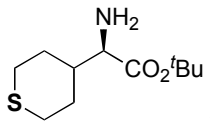
Table 2, entry 10



6j

Yellow oil; $[\alpha]^{20}_D$ = -23.5 (*c* 0.77, $CHCl_3$) (91% ee); IR (film) 3383, 1726, 1367, 1152 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.03-3.95 (m, 2H), 3.41-3.31 (m, 2H), 3.14 (d, *J* = 6.0 Hz, 1H), 1.87-1.75 (m, 1H), 1.63-1.38 (m, 6H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 81.4, 68.2, 68.0, 59.7, 39.9, 29.6, 28.4, 28.3; HRMS Calcd for $C_{11}H_{22}NO_3$ (M+H): 216.1594; Found: 216.1595.

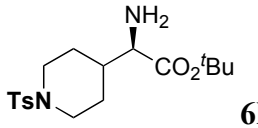
Table 2, entry 11



6k

Yellow oil; $[\alpha]^{20}_{D}$ = -21.2 (*c* 0.91, $CHCl_3$) (93% ee); IR (film) 3464, 1735, 1366, 1218 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.14 (d, *J* = 4.4 Hz, 1H), 2.73-2.57 (m, 4H), 1.96-1.87 (m, 2H), 1.70-1.47 (m, 5H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 81.4, 60.2, 42.1, 31.0, 29.4, 28.98, 28.97, 28.3; HRMS Calcd for $C_{11}H_{22}NO_2S$ (M+H): 232.1366; Found: 232.1366.

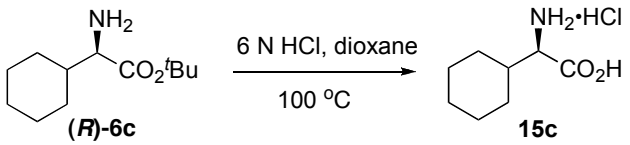
Table 2, entry 12



6l

Yellow oil; $[\alpha]^{20}_{D}$ = -10.4 (*c* 1.05, $CHCl_3$) (90% ee); IR (film) 3453, 1737, 1366, 1217 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 3.87-3.77 (m, 2H), 3.14-2.99 (m, 1H), 2.42 (s, 3H), 2.27-2.15 (m, 2H), 1.76-1.68 (m, 1H), 1.66-1.47 (m, 6H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 143.6, 133.3, 129.8, 127.9, 81.6, 59.1, 46.5, 46.4, 40.0, 28.3, 27.0, 21.7; HRMS Calcd for $C_{18}H_{28}N_2NaO_4S$ (M+Na): 391.1662; Found: 391.1671.

The determination of the absolute configuration of α-amino ester 6c

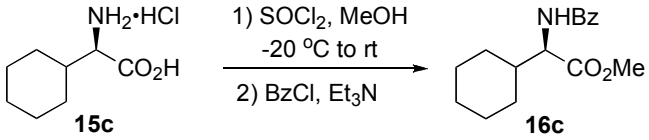


A solution of α-amino ester (*R*)-**6c** (0.107 g, 0.50 mmol) (94% ee) in 6 N HCl (7.5 mL) and dioxane (2.5 mL) was stirred at 100 °C for 12 h.[1] The reaction mixture was cooled to room temperature, washed with Et_2O (3 x 5.0 mL), and concentrated to give amino acid hydrochloride **15c** as a white solid (0.096 g, 99% yield). decomp. 257 °C; $[\alpha]^{20}_{D}$ = -24.9 (*c* 0.88, 1.5 N HCl) [lit.[2] $[\alpha]^{20}_{D}$ = -33.5 (1.5 N HCl)]; IR (film) 3331, 1736, 1366, 1217,

1153 cm^{-1}; ^1H NMR (400 MHz, MeOD) δ 3.81 (d, *J* = 4.0 Hz, 1H), 2.00-1.90 (m, 1H), 1.89-1.78 (m, 3H), 1.77-1.65 (m, 2H), 1.41-1.10 (m, 5H); ^{13}C NMR (100 MHz, MeOD) δ 171.2, 59.0, 40.2, 29.5, 29.3, 27.0, 26.9, 26.7; HRMS Calcd for $C_8H_{16}NO_2$ (M-Cl): 158.1176; Found: 158.1172.

(1) T. Ooi, D. Kato, K. Inamura, K. Ohmatsu and K. Maruoka, *Org. Lett.*, 2007, **9**, 3945.

(2) C. Toniolo, G. M. Bonora and S. Salardi, *Int. J. Biol. Macromol*., 1981, **3**, 377.



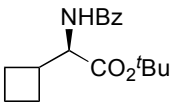
15c **16c**

To a solution of amino acid hydrochloride **15c** (0.058 g, 0.30 mmol) in MeOH (2.0 mL) was added $SOCl_2$ (0.642 g, 5.4 mmol) dropwise at -20 °C. The reaction mixture was stirred at room temperature overnight, concentrated, and dissolved in CH_2Cl_2 (1.0 mL), followed by the addition of Et_3N (0.091 g, 0.90 mmol) and BzCl (0.063 g, 0.45 mmol) successively. Upon stirring at room temperature for 30 min, the reaction mixture was purified by flash column chromatography (silica gel, eluent: petroleum ether/EtOAc = 10/1 to 5/1) to afford *N*-benzoyl amino ester **16c** as a white solid (0.064 g, 78% yield). The sample was subjected to chiral HPLC (Chiralcel OD-H column) to determine the enantiomeric excess. mp. 123-124 °C; $[\alpha]^{20}_D$ = -40.2 (*c* 0.99, $CHCl_3$) (94% ee); IR (film) 3330, 1740, 1365, 1217 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.6 Hz, 2H), 7.55-7.49 (m, 1H), 7.48-7.42 (m, 2H), 6.62 (d, *J* = 8.0 Hz, 1H), 4.81-4.75 (m, 1H), 3.78 (s, 3H), 1.95-1.86 (m, 1H), 1.81-1.62 (m, 5H), 1.32-1.06 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 167.3, 134.3, 131.9, 128.8, 127.2, 57.3, 52.4, 41.5, 29.7, 28.6, 26.1; HRMS Calcd for $C_{16}H_{22}NO_3$ (M+H): 276.1594; Found: 276.1597.

T. Ooi, D. Kato, K. Inamura, K. Ohmatsu and K. Maruoka, *Org. Lett.*, 2007, **9**, 3945.

The chromatograms for determination of enantioselectivity

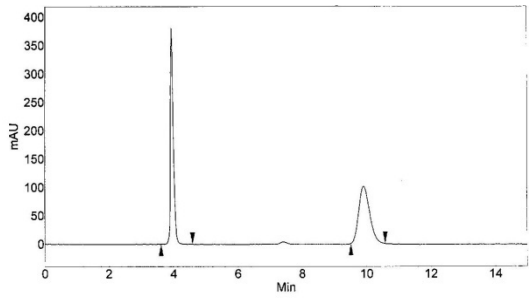
Table 2, entry 1



14a

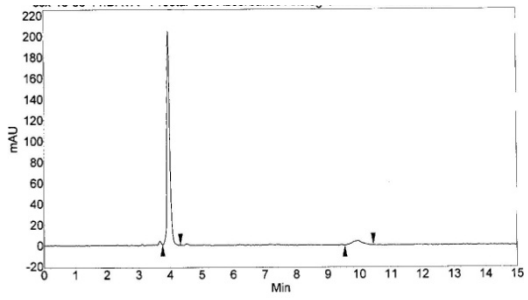
HPLC Condition: Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (85/15); **Flow rate:** 1.0 mL/min; **Detection:** UV226 nm.

Racemic



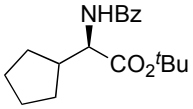
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	3.95	50.043	3.60	4.58
2	9.91	49.957	9.51	10.58
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
2	3.96	93.589	3.76	4.32
1	9.93	6.411	9.55	10.44
Total		100.000		

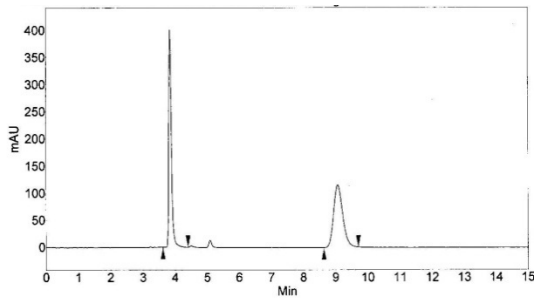
Table 2, entry 2



14b

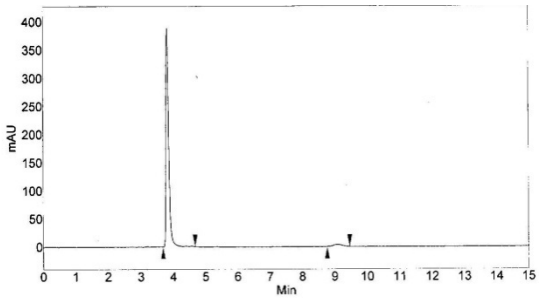
HPLC Condition: Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (85/15); **Flow rate:** 1.0 mL/min; **Detection:** UV226 nm.

Racemic



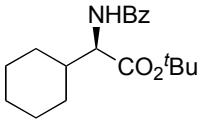
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	3.84	49.842	3.62	4.40
2	9.07	50.158	8.64	9.71
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	3.83	96.834	3.68	4.67
2	9.09	3.166	8.77	9.46
Total		100.000		

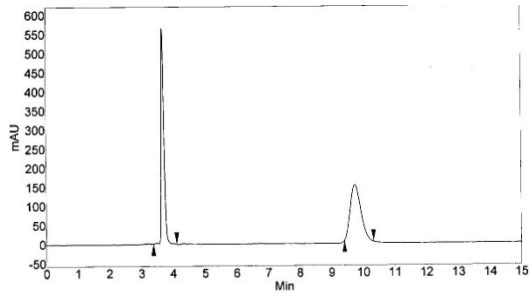
Table 2, entry 3



14c

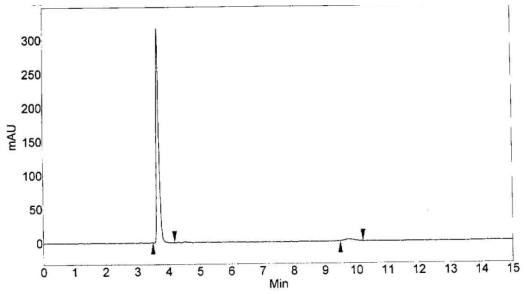
HPLC Condition: Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (85/15); **Flow rate:** 1.0 mL/min; **Detection:** UV226 nm.

Racemic



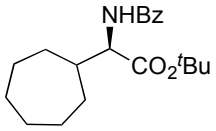
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	3.67	49.822	3.37	4.10
2	9.75	50.178	9.41	10.33
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	3.67	97.100	3.50	4.18
2	9.77	2.900	9.49	10.22
Total		100.000		

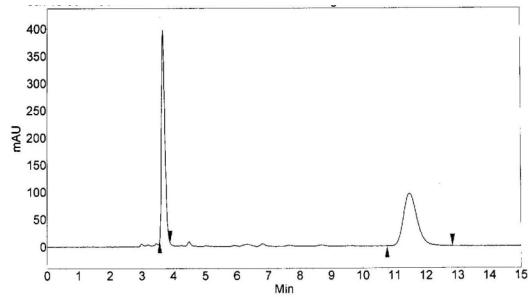
Table 2, entry 4



14d

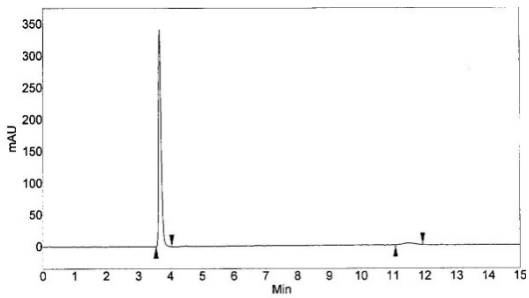
HPLC Condition: Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (85/15); **Flow rate:** 1.0 mL/min; **Detection:** UV226 nm.

Racemic



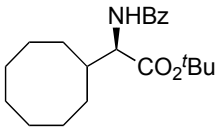
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
2	3.67	50.052	3.56	3.88
1	11.48	49.948	10.77	12.83
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
2	3.68	96.938	3.54	4.04
1	11.51	3.062	11.08	11.94
Total		100.000		

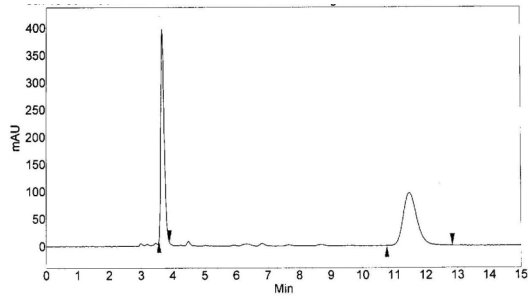
Table 2, entry 5



14e

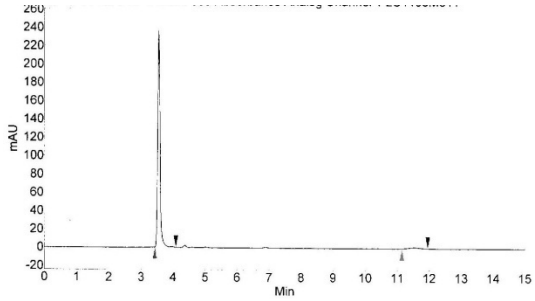
HPLC Condition: Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (85/15); **Flow rate:** 1.0 mL/min; **Detection:** UV226 nm.

Racemic



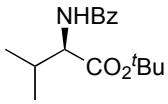
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
2	3.67	50.052	3.56	3.88
1	11.48	49.948	10.77	12.83
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	3.55	97.629	3.44	4.09
2	11.53	2.371	11.15	11.95
Total		100.000		

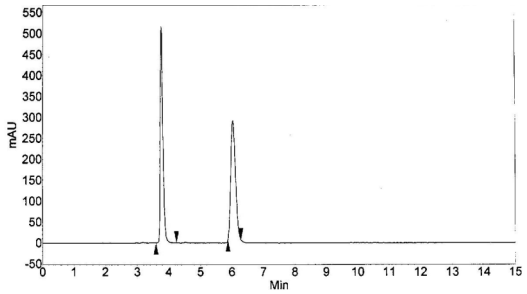
Table 2, entry 6



14f

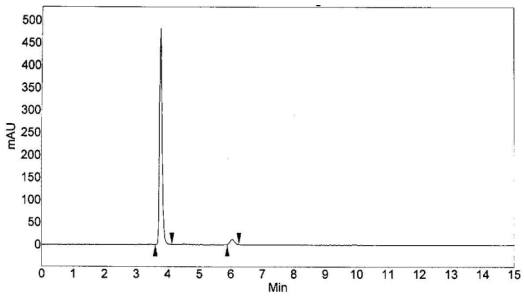
HPLC Condition: Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (85/15); **Flow rate:** 1.0 mL/min; **Detection:** UV226 nm.

Racemic



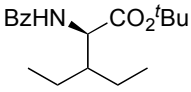
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	3.77	49.802	3.59	4.24
2	6.04	50.198	5.87	6.28
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	3.77	96.033	3.61	4.13
2	6.04	3.967	5.88	6.25
Total		100.000		

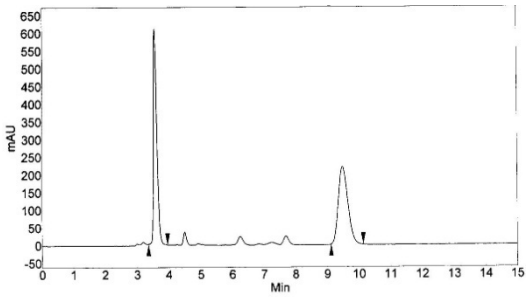
Table 2, entry 7



14g

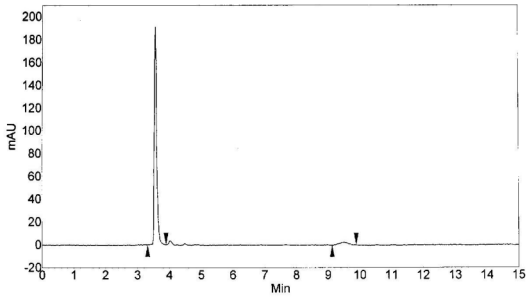
HPLC Condition: **Column:** Chiralcel OD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (85/15); **Flow rate:** 1.0 mL/min; **Detection:** UV226 nm.

Racemic



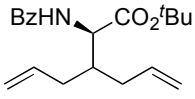
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	3.57	49.988	3.35	3.95
2	9.49	50.012	9.12	10.14
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	3.57	95.302	3.32	3.90
2	9.51	4.698	9.13	9.89
Total		100.000		

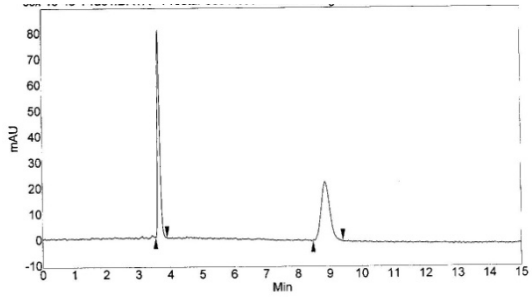
Table 2, entry 8



14h

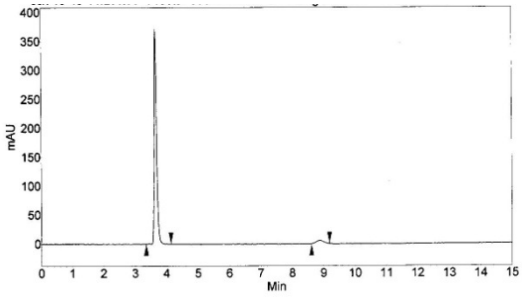
HPLC Condition: **Column:** Chiralcel OD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (85/15); **Flow rate:** 1.0 mL/min; **Detection:** UV226 nm.

Racemic



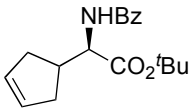
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	3.65	49.930	3.54	3.89
2	8.87	50.070	8.48	9.42
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	3.65	95.756	3.35	4.14
2	8.88	4.244	8.62	9.18
Total		100.000		

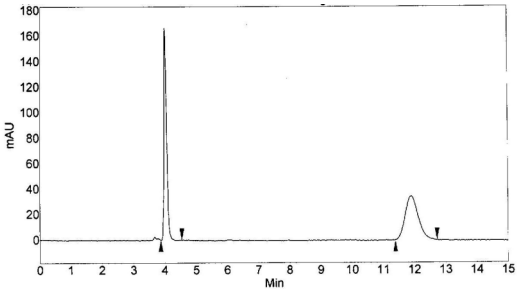
Table 2, entry 9



14i

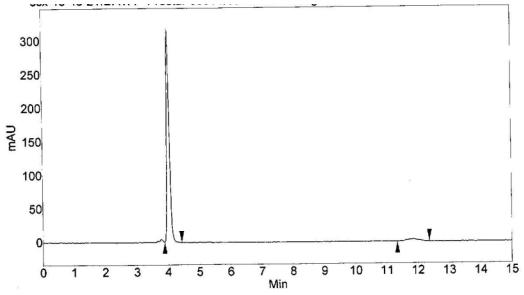
HPLC Condition: Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (85/15); **Flow rate:** 1.0 mL/min; **Detection:** UV226 nm.

Racemic



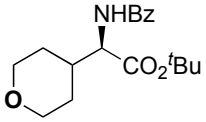
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	4.01	49.945	3.87	4.54
2	11.91	50.055	11.39	12.73
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	4.01	95.802	3.88	4.43
2	11.85	4.198	11.34	12.36
Total		100.000		

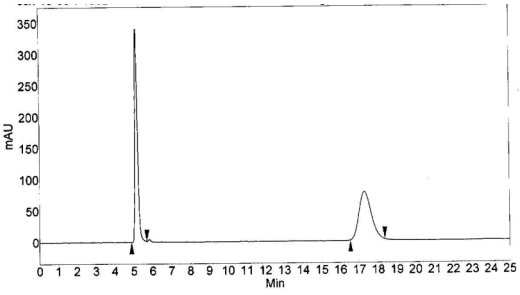
Table 2, entry 10



14j

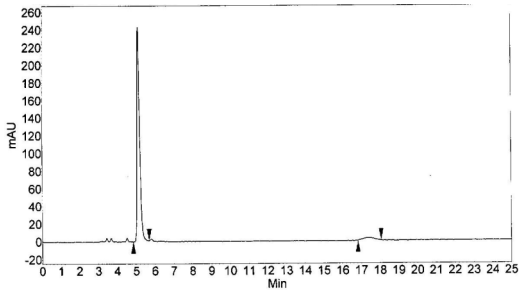
HPLC Condition: Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (85/15); **Flow rate:** 1.0 mL/min; **Detection:** UV226 nm.

Racemic



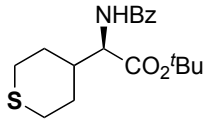
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	5.15	49.976	4.88	5.68
2	17.29	50.024	16.54	18.37
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	5.13	95.501	4.85	5.68
2	17.44	4.499	16.82	18.06
Total		100.000		

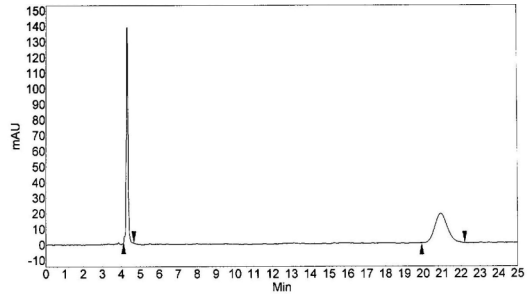
Table 2, entry 11



14k

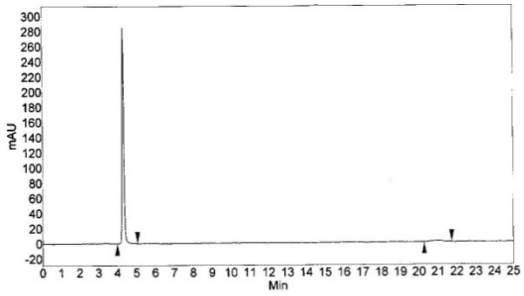
HPLC Condition: Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (85/15); **Flow rate:** 1.0 mL/min; **Detection:** UV226 nm.

Racemic



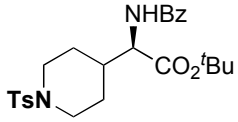
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	4.32	49.953	4.13	4.67
2	20.93	50.047	19.92	22.19
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	4.29	96.272	4.00	5.06
2	21.04	3.728	20.28	21.72
Total		100.000		

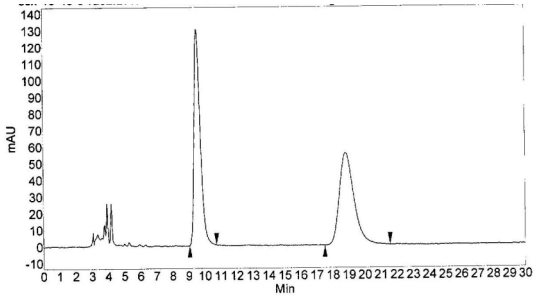
Table 2, entry 12



14l

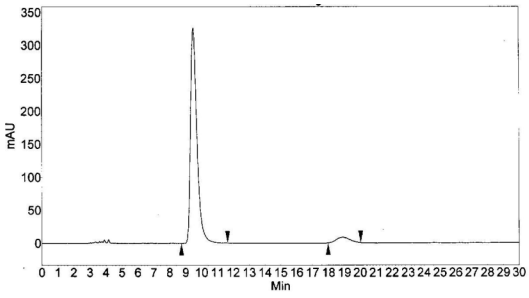
HPLC Condition: Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (85/15); **Flow rate:** 1.0 mL/min; **Detection:** UV226 nm.

Racemic

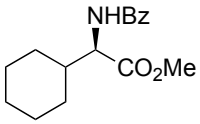


Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
2	9.55	50.088	9.06	10.73
1	18.83	49.912	17.51	21.57
Total		100.000		

Chiral



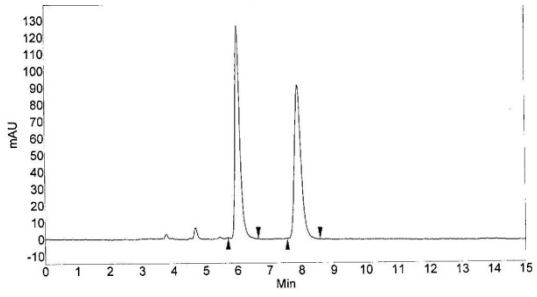
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	9.49	94.924	8.73	11.64
2	18.93	5.076	17.99	20.03
Total		100.000		



16c

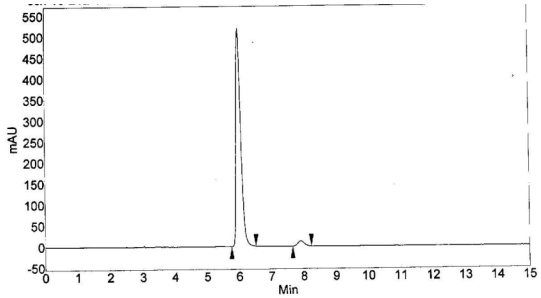
HPLC Condition: **Column:** Chiralcel OD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (90/10); **Flow rate:** 1.0 mL/min; **Detection:** UV226 nm.

Racemic



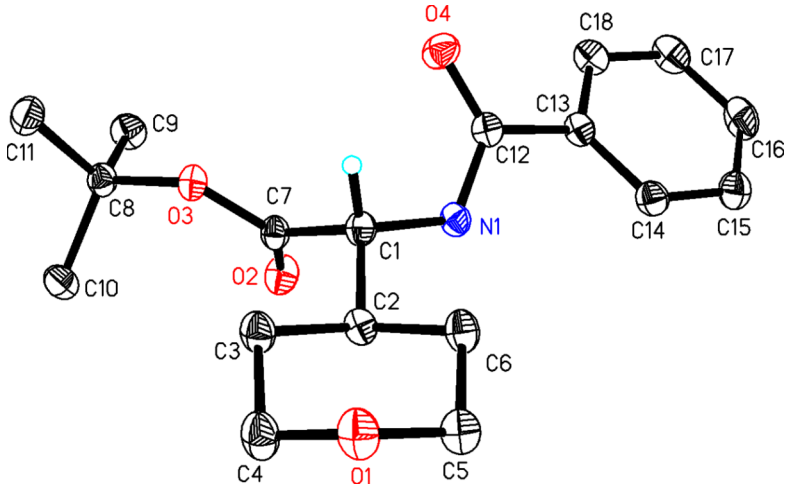
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
2	6.00	50.173	5.70	6.64
1	7.88	49.827	7.55	8.58
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
2	5.99	96.889	5.76	6.51
1	7.91	3.111	7.65	8.23
Total		100.000		

The X-ray structure of compound 14j



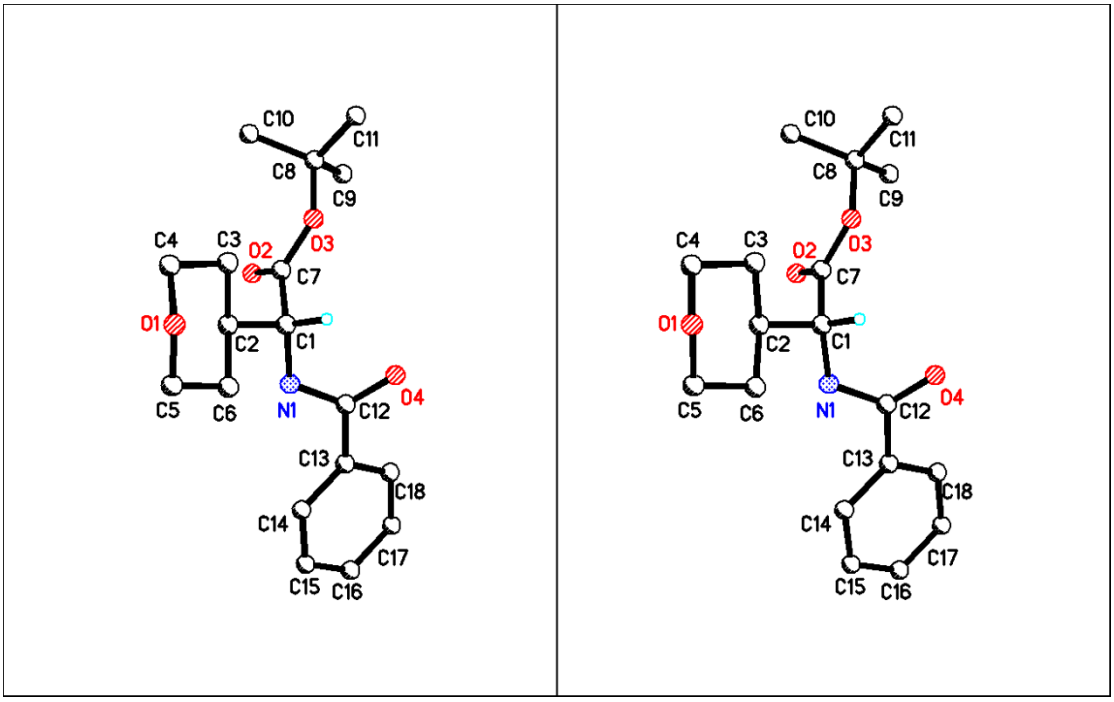


Table 1. Crystal data and structure refinement for **14j**.

Identification code	14j	
Empirical formula	C18 H25 N O4	
Formula weight	319.39	
Temperature	173.1500 K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 5.5701(4) Å	a= 90°.
	b = 9.0120(6) Å	b= 90°.
	c = 33.683(2) Å	g = 90°.
Volume	1690.8(2) $Å^3$	
Z	4	
Density (calculated)	1.255 Mg/m^3	
Absorption coefficient	0.088 mm^{-1}	
F(000)	688	
Crystal size	0.34 x 0.14 x 0.1 mm^3	
Theta range for data collection	3.311 to 27.479°.	
Index ranges	-7<=h<=7, -11<=k<=11, -43<=l<=42	
Reflections collected	20256	
Independent reflections	3875 [R(int) = 0.0705]	
Completeness to theta = 26.000°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.0000 and 0.5829	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3875 / 0 / 211	
Goodness-of-fit on F^2	1.116	
Final R indices [I>2sigma(I)]	R1 = 0.0531, wR2 = 0.1152	
R indices (all data)	R1 = 0.0671, wR2 = 0.1257	
Absolute structure parameter	0.2(7)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.185 and -0.264 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **14j**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O1	-2088(4)	3181(3)	7456(1)	43(1)
O2	1300(4)	6221(2)	5964(1)	40(1)
O3	3951(4)	6378(2)	6474(1)	31(1)
O4	5572(4)	2806(3)	5965(1)	42(1)
N1	1579(4)	3120(3)	6052(1)	31(1)
C1	1924(5)	4102(3)	6389(1)	30(1)
C2	-207(5)	4024(3)	6679(1)	30(1)
C3	297(6)	4894(4)	7061(1)	37(1)
C4	-1746(7)	4697(4)	7354(1)	45(1)
C5	-2697(6)	2339(4)	7114(1)	39(1)
C6	-781(6)	2419(3)	6792(1)	35(1)
C7	2338(5)	5680(3)	6244(1)	30(1)
C8	4615(5)	7952(3)	6407(1)	31(1)
C9	5759(6)	8119(4)	6000(1)	41(1)
C10	2463(6)	8948(3)	6461(1)	39(1)
C11	6409(6)	8208(4)	6737(1)	41(1)
C12	3488(6)	2531(3)	5861(1)	31(1)
C13	2973(5)	1501(3)	5525(1)	31(1)
C14	876(6)	675(3)	5504(1)	37(1)
C15	543(7)	-337(4)	5195(1)	46(1)
C16	2263(8)	-487(4)	4905(1)	51(1)
C17	4332(7)	354(4)	4920(1)	45(1)
C18	4706(6)	1341(4)	5229(1)	37(1)

Table 3. Bond lengths [Å] and angles [°] for **14j**.

O1-C4	1.421(4)
O1-C5	1.422(4)
O2-C7	1.209(3)
O3-C7	1.343(3)
O3-C8	1.484(3)
O4-C12	1.238(4)
N1-C1	1.454(3)
N1-C12	1.351(4)
C1-C2	1.539(4)
C1-C7	1.521(4)
C2-C3	1.531(4)
C2-C6	1.529(4)
C3-C4	1.518(5)
C5-C6	1.521(4)
C8-C9	1.520(4)
C8-C10	1.509(4)
C8-C11	1.513(4)
C12-C13	1.491(4)
C13-C14	1.387(4)
C13-C18	1.396(4)
C14-C15	1.396(4)
C15-C16	1.374(5)
C16-C17	1.380(5)
C17-C18	1.385(4)
C4-O1-C5	110.5(2)
C7-O3-C8	121.8(2)
C12-N1-C1	120.5(2)
N1-C1-C2	111.5(2)
N1-C1-C7	109.7(2)
C7-C1-C2	111.3(2)
C3-C2-C1	111.6(2)
C6-C2-C1	111.3(2)
C6-C2-C3	108.2(2)
C4-C3-C2	110.4(3)
O1-C4-C3	111.7(3)

O1-C5-C6	112.5(3)
C5-C6-C2	111.7(2)
O2-C7-O3	125.5(3)
O2-C7-C1	123.7(3)
O3-C7-C1	110.7(2)
O3-C8-C9	109.7(2)
O3-C8-C10	110.7(2)
O3-C8-C11	101.4(2)
C10-C8-C9	112.5(3)
C11-C8-C9	111.8(3)
O4-C12-N1	121.6(3)
O4-C12-C13	121.4(3)
N1-C12-C13	117.0(3)
C14-C13-C12	122.4(3)
C14-C13-C18	119.3(3)
C18-C13-C12	118.3(3)
C13-C14-C15	120.1(3)
C16-C15-C14	120.0(3)
C15-C16-C17	120.2(3)
C16-C17-C18	120.3(3)
C17-C18-C13	120.0(3)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **14j**. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + \ldots + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O1	61(2)	43(1)	25(1)	-1(1)	6(1)	-5(1)
O2	50(1)	39(1)	33(1)	5(1)	-9(1)	-5(1)
O3	37(1)	27(1)	30(1)	-1(1)	-3(1)	-4(1)
O4	35(1)	55(1)	35(1)	-10(1)	0(1)	-4(1)
N1	35(1)	33(1)	24(1)	-6(1)	0(1)	-1(1)
C1	34(2)	31(1)	24(1)	-1(1)	-2(1)	-1(1)
C2	37(2)	30(1)	23(1)	1(1)	-2(1)	2(1)
C3	45(2)	37(2)	28(1)	-5(1)	3(1)	-3(2)
C4	60(2)	40(2)	34(2)	-6(1)	11(2)	-8(2)
C5	49(2)	38(2)	31(1)	2(1)	0(1)	-2(2)
C6	49(2)	31(2)	26(1)	-1(1)	0(1)	-2(1)
C7	36(2)	29(1)	25(1)	-3(1)	1(1)	-2(1)
C8	35(2)	26(1)	33(1)	0(1)	3(1)	-4(1)
C9	43(2)	42(2)	38(2)	2(1)	11(2)	-2(2)
C10	41(2)	34(2)	42(2)	-1(1)	7(1)	4(1)
C11	41(2)	40(2)	43(2)	-4(1)	-2(2)	-7(2)
C12	37(2)	31(2)	24(1)	1(1)	2(1)	0(1)
C13	39(2)	32(2)	22(1)	-2(1)	0(1)	2(1)
C14	41(2)	37(2)	32(2)	-3(1)	2(1)	1(1)
C15	50(2)	41(2)	47(2)	-11(2)	-4(2)	-3(2)
C16	70(2)	46(2)	37(2)	-17(2)	-8(2)	6(2)
C17	58(2)	50(2)	28(2)	-5(1)	4(2)	9(2)
C18	44(2)	42(2)	26(1)	1(1)	4(1)	4(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **14j**.

	x	y	z	U(eq)
H1	150	2913	5973	37
H1A	3368	3780	6531	35
H2	-1620	4455	6550	36
H3A	1782	4545	7179	44
H3B	485	5938	6999	44
H4A	-1403	5261	7593	54
H4B	-3214	5085	7239	54
H5A	-4203	2702	7007	47
H5B	-2927	1311	7190	47
H6A	-1332	1889	6559	42
H6B	669	1938	6887	42
H9A	7046	7418	5973	61
H9B	6377	9108	5971	61
H9C	4576	7938	5798	61
H10A	1298	8736	6259	58
H10B	2955	9966	6441	58
H10C	1766	8776	6717	58
H11A	5636	8065	6989	62
H11B	7015	9203	6721	62
H11C	7712	7518	6711	62
H14	-308	795	5696	44
H15	-845	-910	5185	55
H16	2033	-1157	4699	61
H17	5480	258	4721	54
H18	6112	1896	5239	45

Table 6. Torsion angles [°] for **14j**.

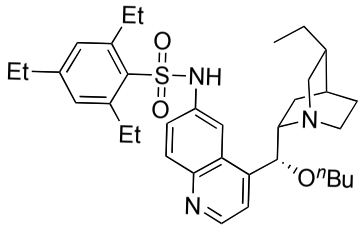
O1-C5-C6-C2	-54.8(3)
O4-C12-C13-C14	151.3(3)
O4-C12-C13-C18	-26.8(4)
N1-C1-C2-C3	172.4(2)
N1-C1-C2-C6	51.4(3)
N1-C1-C7-O2	38.2(4)
N1-C1-C7-O3	-143.3(2)
N1-C12-C13-C14	-27.1(4)
N1-C12-C13-C18	154.8(3)
C1-N1-C12-O4	-0.1(4)
C1-N1-C12-C13	178.3(2)
C1-C2-C3-C4	-175.5(3)
C1-C2-C6-C5	173.7(2)
C2-C1-C7-O2	-85.7(3)
C2-C1-C7-O3	92.8(3)
C2-C3-C4-O1	59.4(4)
C3-C2-C6-C5	50.7(3)
C4-O1-C5-C6	59.0(3)
C5-O1-C4-C3	-61.5(4)
C6-C2-C3-C4	-52.8(3)
C7-O3-C8-C9	-62.4(3)
C7-O3-C8-C10	62.3(3)
C7-O3-C8-C11	179.3(2)
C7-C1-C2-C3	-64.7(3)
C7-C1-C2-C6	174.3(2)
C8-O3-C7-O2	0.9(4)
C8-O3-C7-C1	-177.6(2)
C12-N1-C1-C2	-151.5(3)
C12-N1-C1-C7	84.6(3)
C12-C13-C14-C15	-176.3(3)
C12-C13-C18-C17	177.6(3)
C13-C14-C15-C16	-1.8(5)
C14-C13-C18-C17	-0.6(5)
C14-C15-C16-C17	0.4(5)
C15-C16-C17-C18	0.9(5)
C16-C17-C18-C13	-0.8(5)

C18-C13-C14-C15	1.8(5)

Symmetry transformations used to generate equivalent atoms:

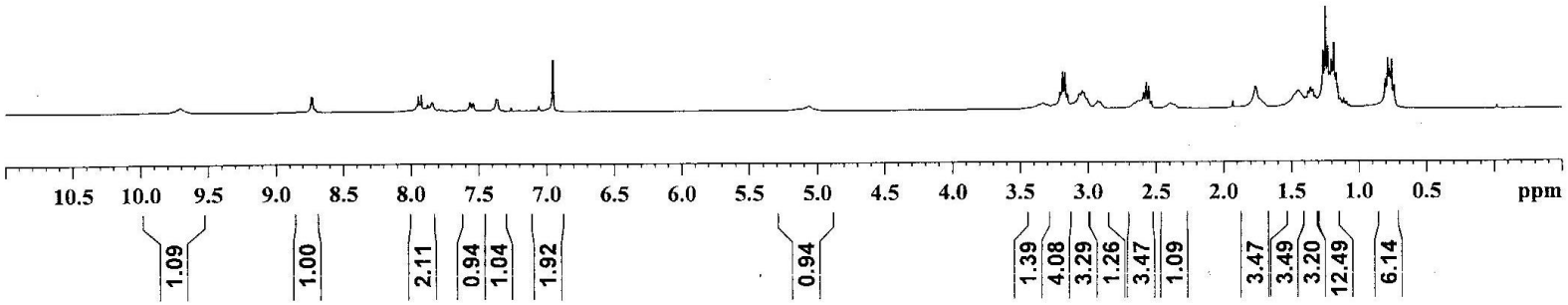
Table 7. Hydrogen bonds for **14j** [Å and °].

D-H…A	d(D-H)	d(H…A)	d(D…A)	<(DHA)



C4

(mixture of rotamers)

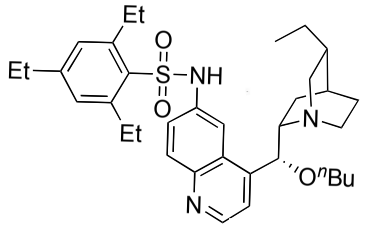


148.869
148.343
145.918
145.792
145.692
137.680
134.172
131.393
129.177
127.353
124.072
118.947
113.235

79.591
77.549
77.231
76.913
69.213

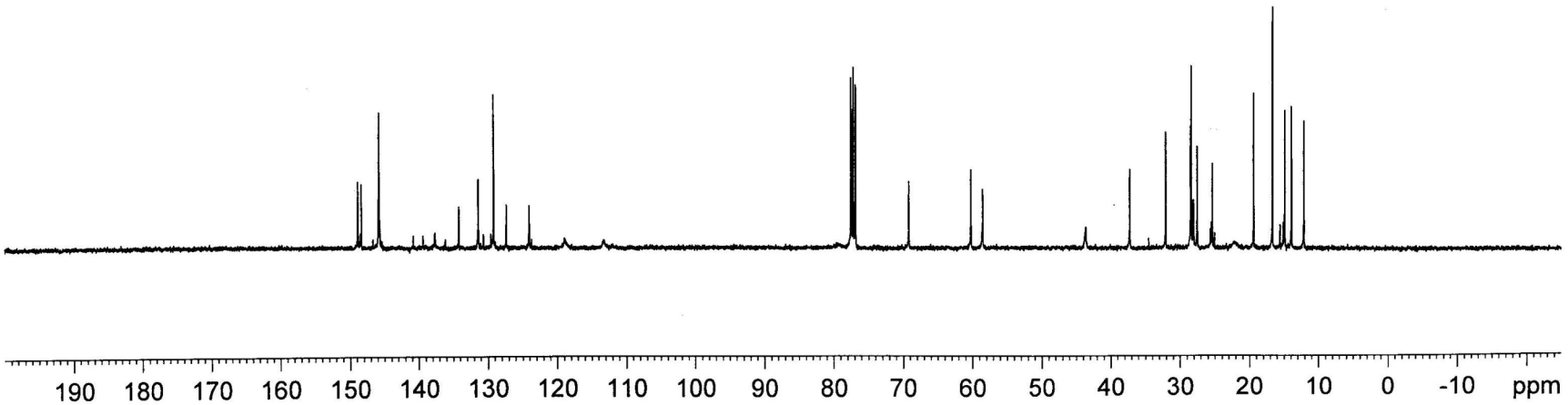
60.271
58.558

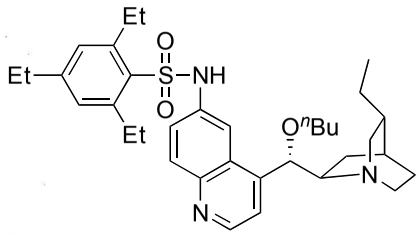
43.668
37.300
32.111
28.531
28.422
28.126
27.584
25.412
22.208
19.446
16.715
14.928
13.960
12.144



C4

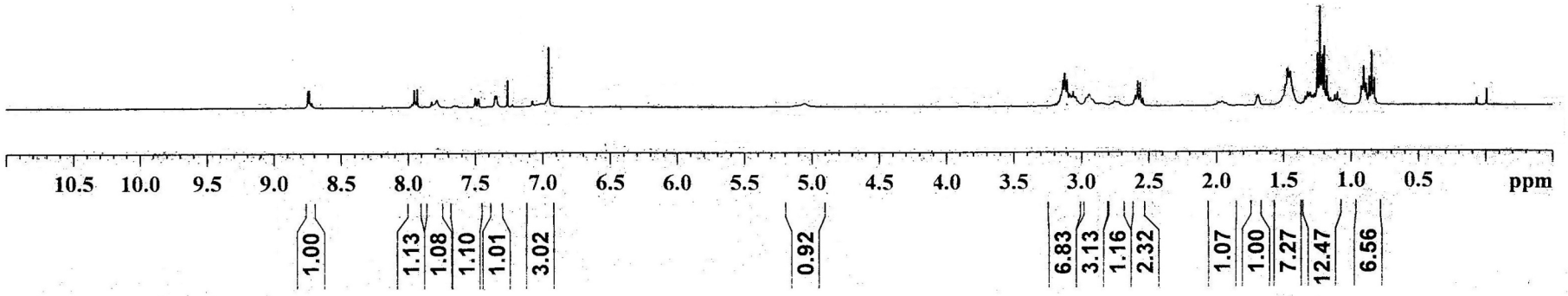
(mixture of rotamers)

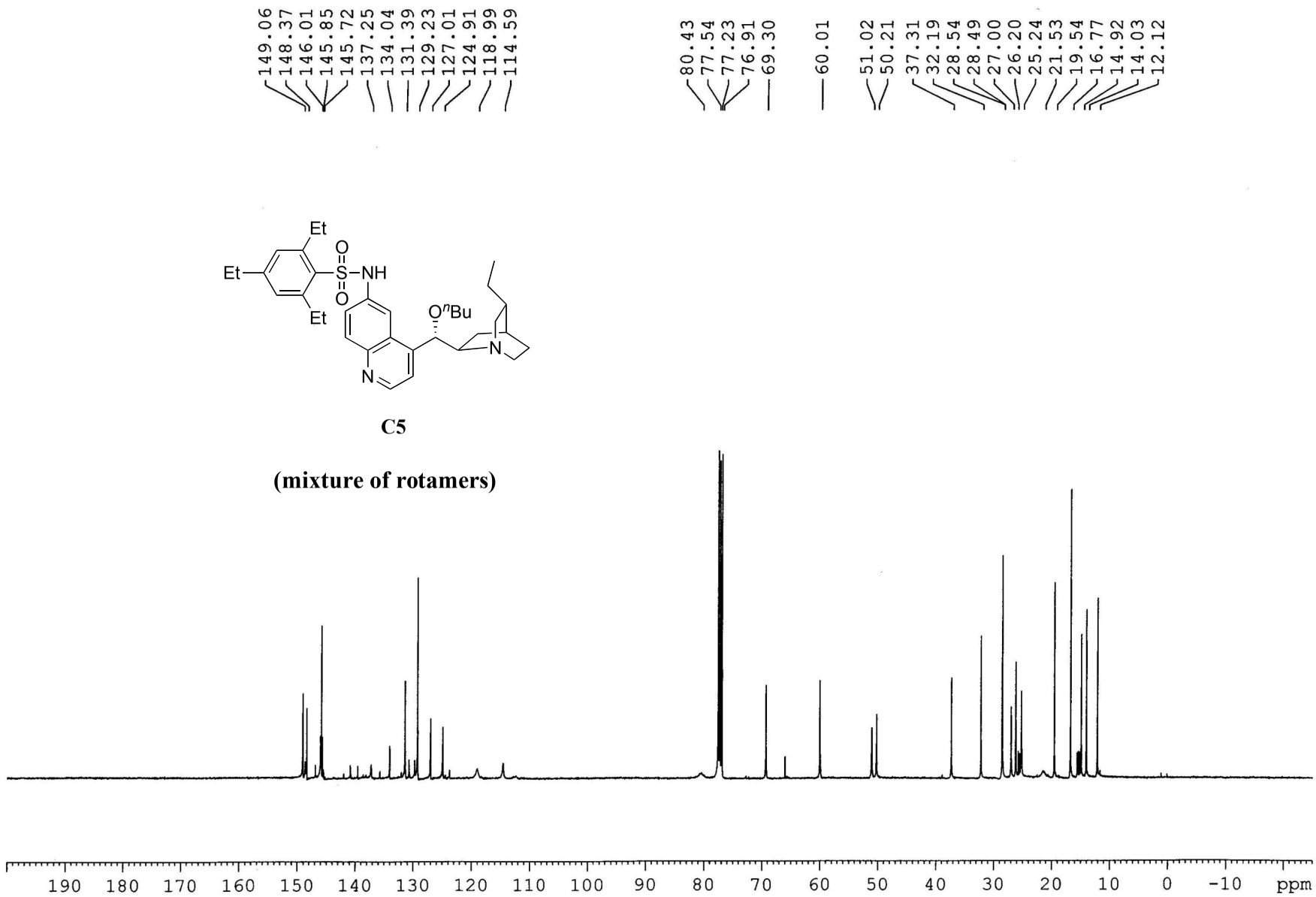




C5

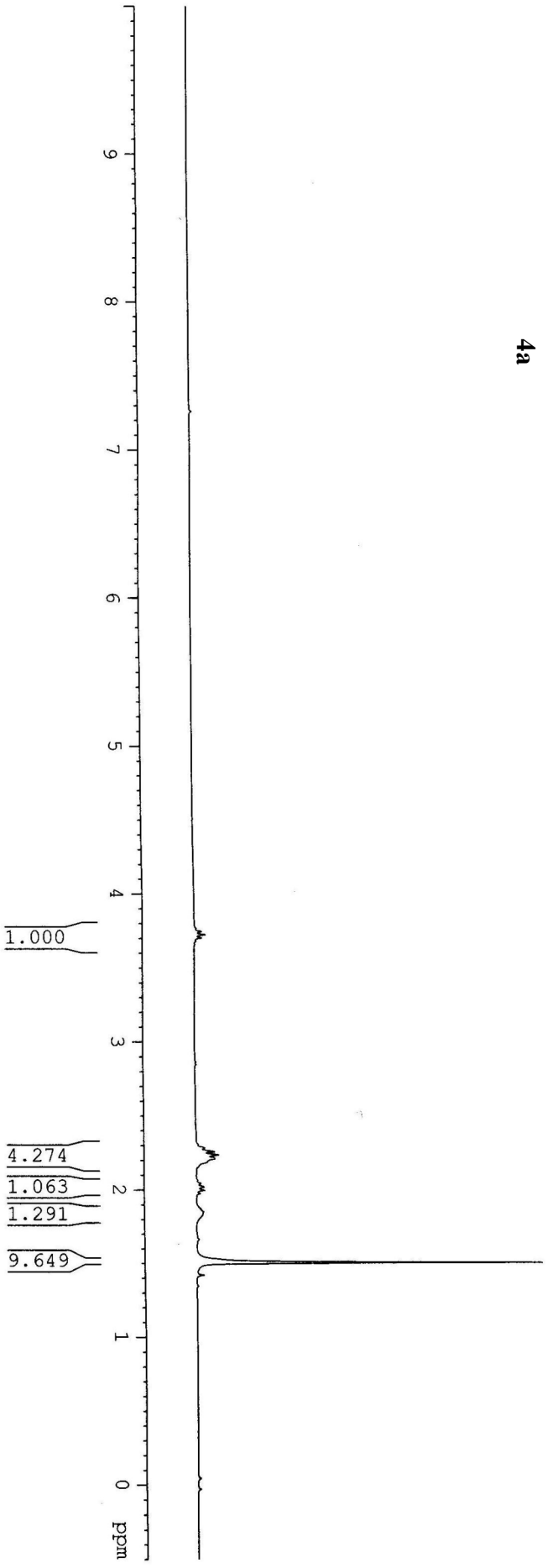
(mixture of rotamers)

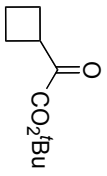




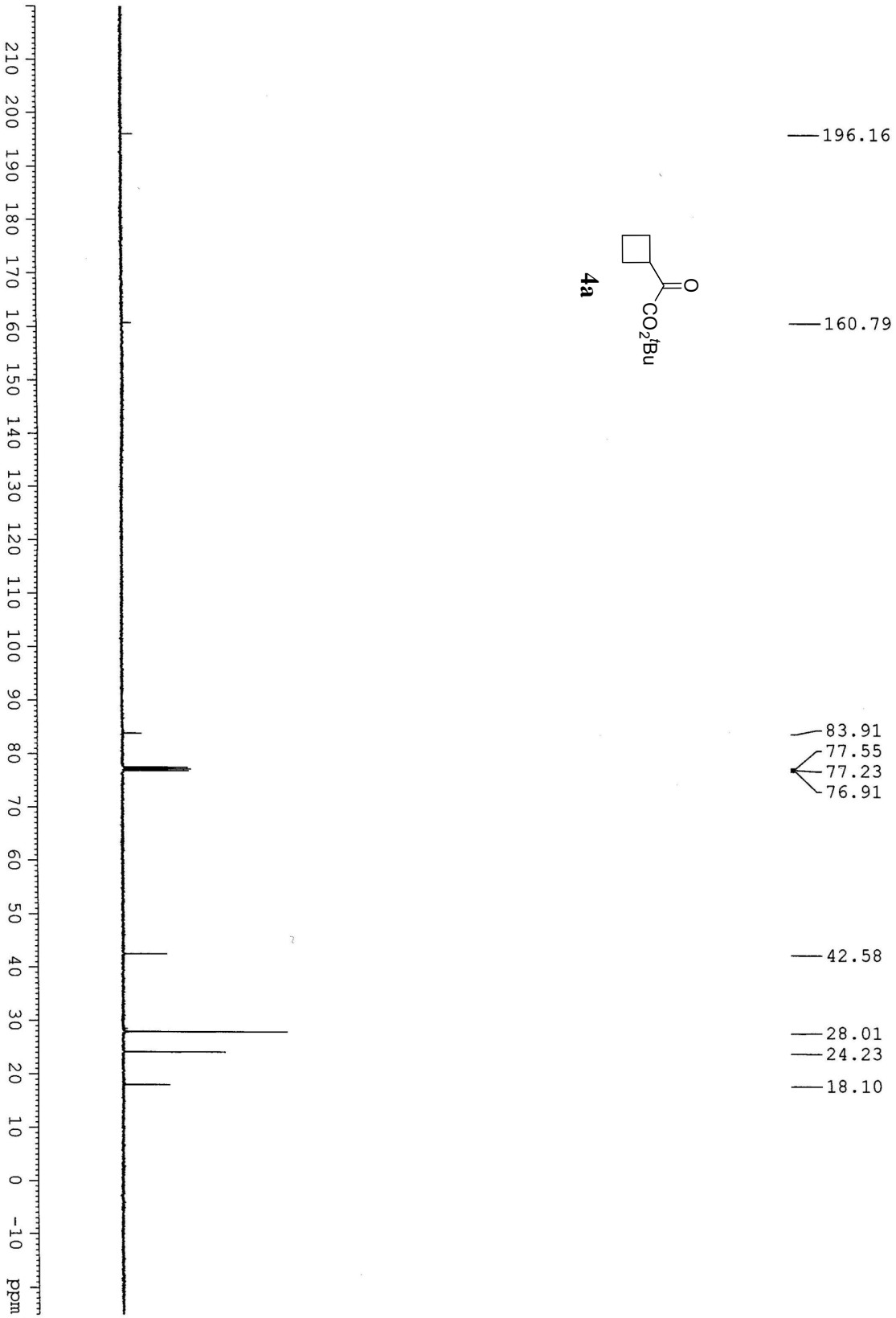
C5

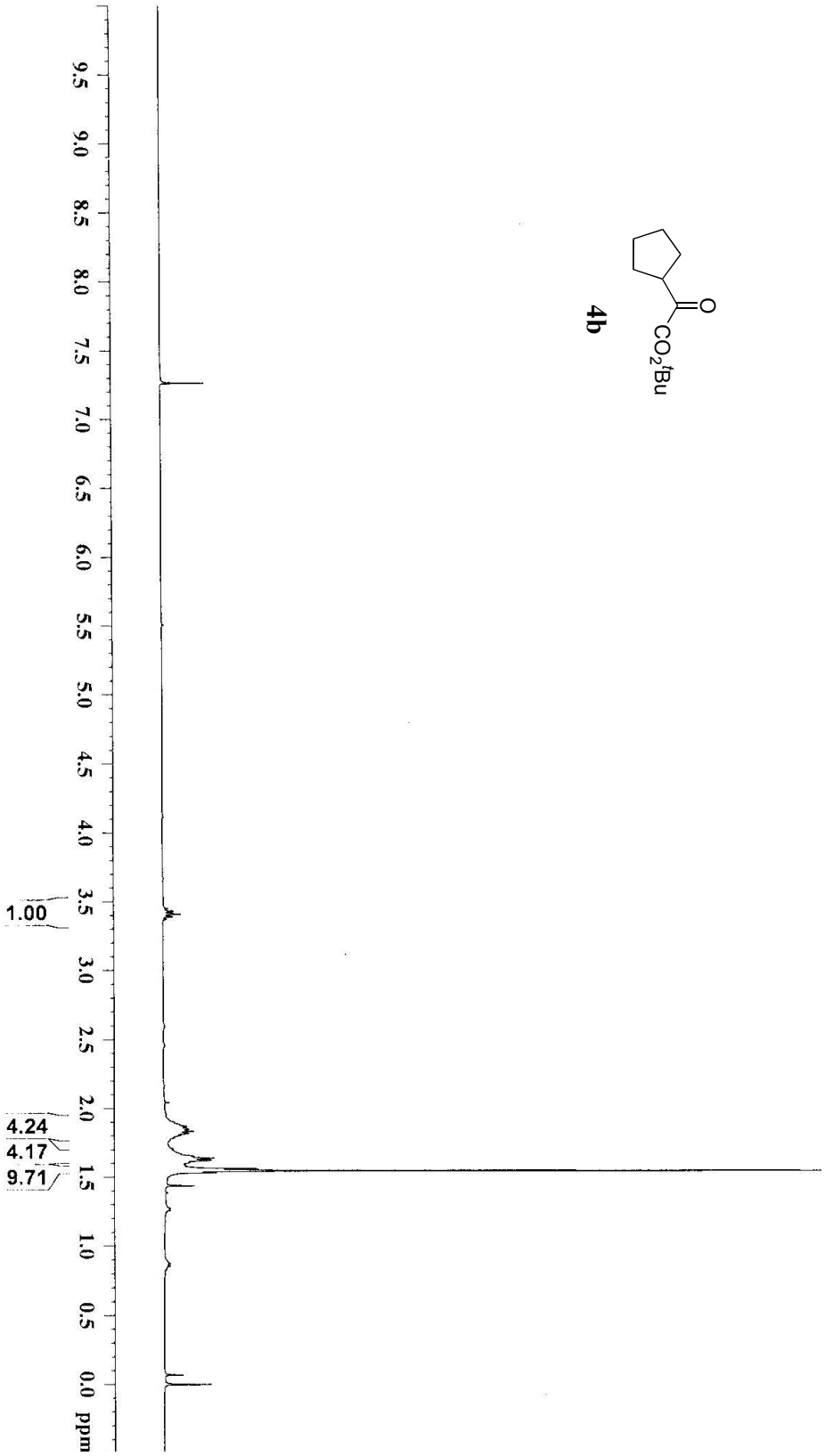
(mixture of rotamers)





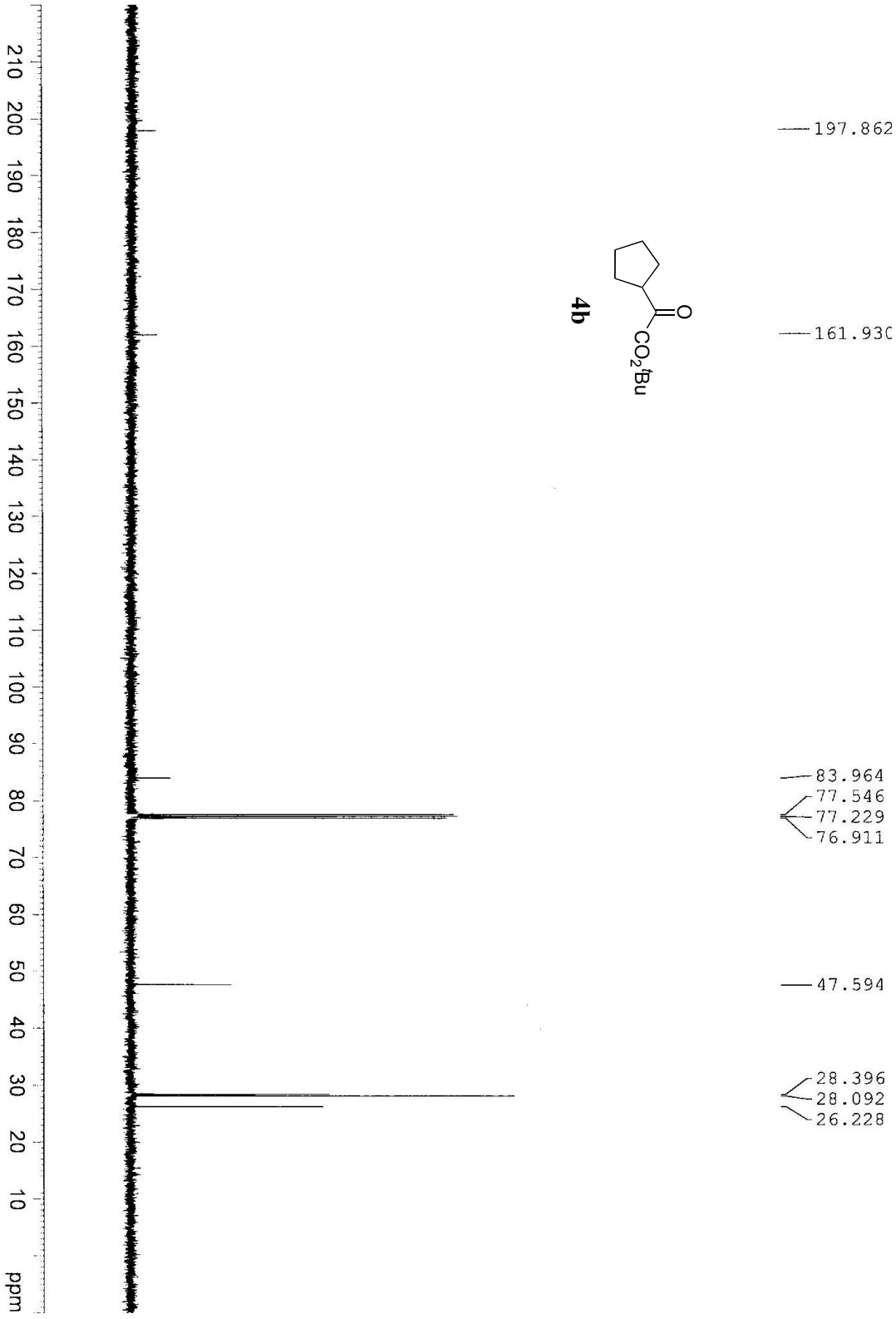
4a


196.16
160.79
83.91
77.55
77.23
76.91
42.58
28.01
24.23
18.10
O
CO2tBu
4a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 ppm

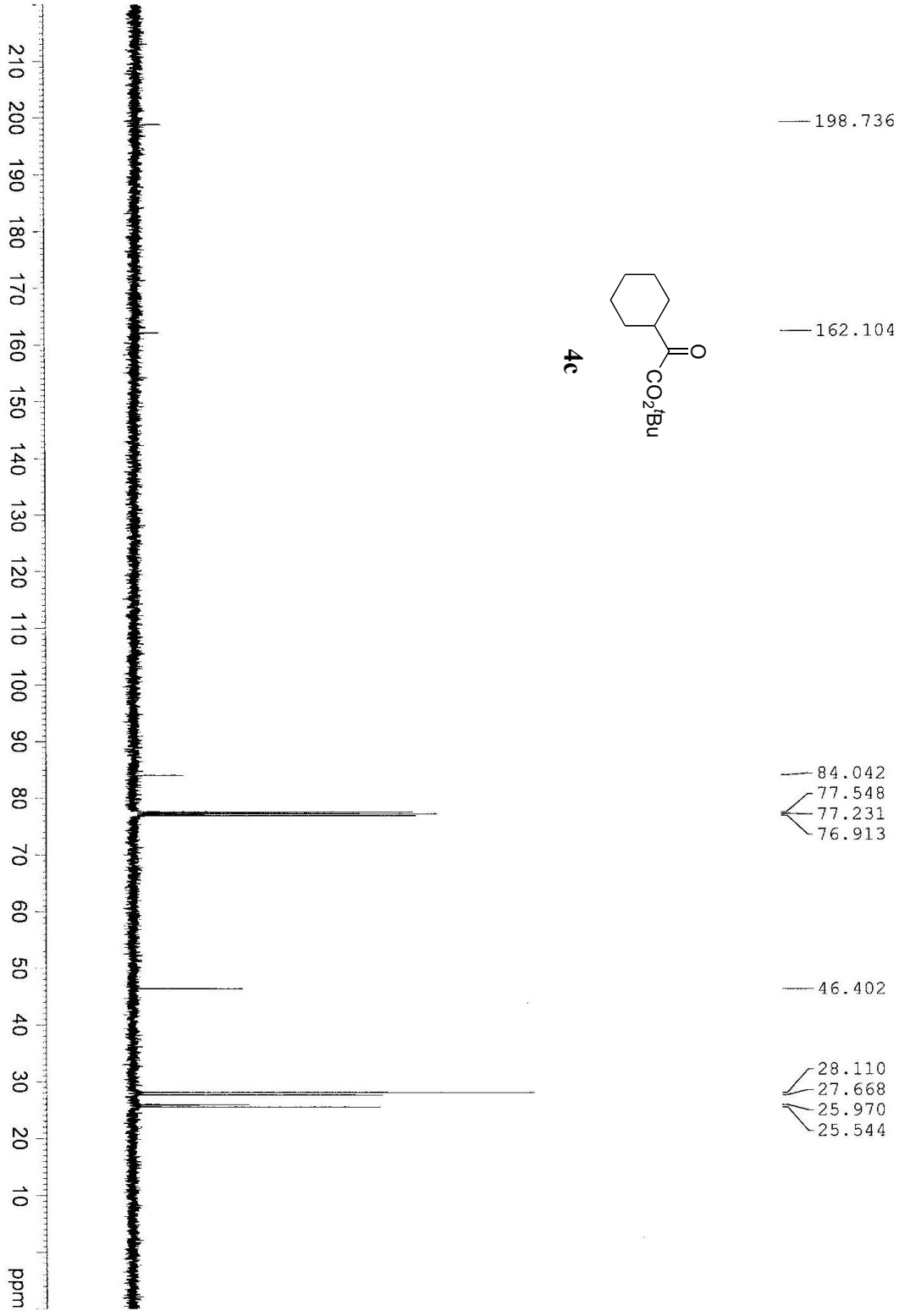

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
4.24
4.17
9.71

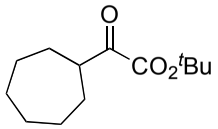
O
CO2tBu

4b

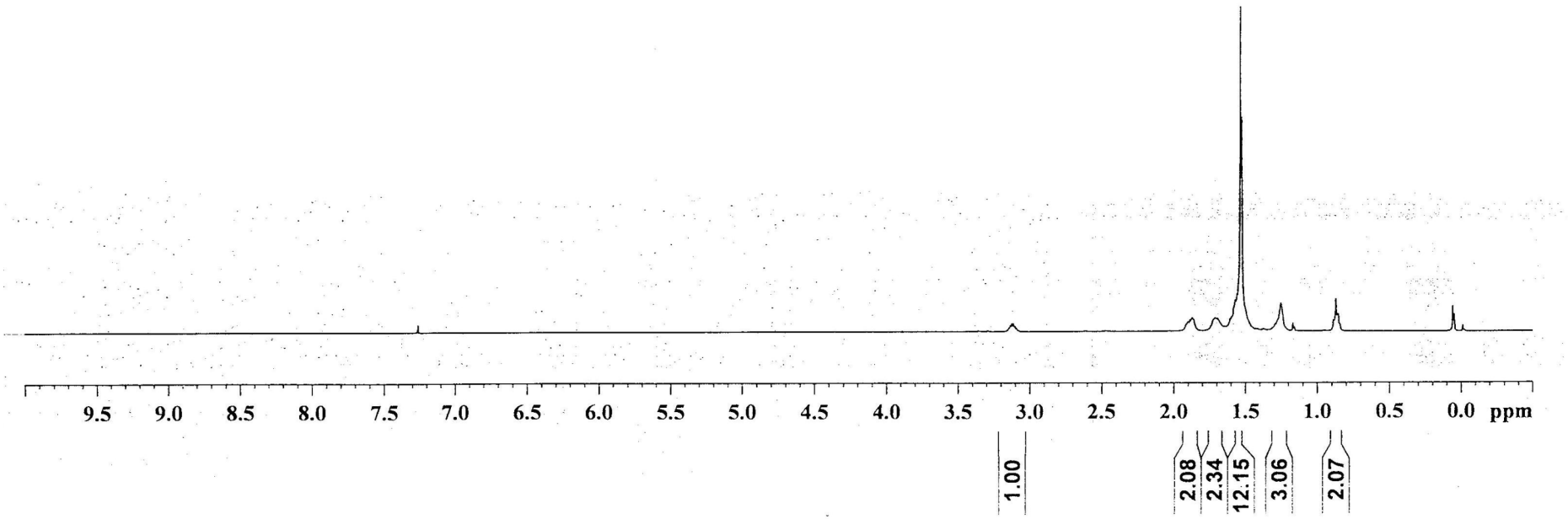

197.862
161.930
83.964
77.546
77.229
76.911
47.594
28.396
28.092
26.228
4b
O
CO2tBu
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

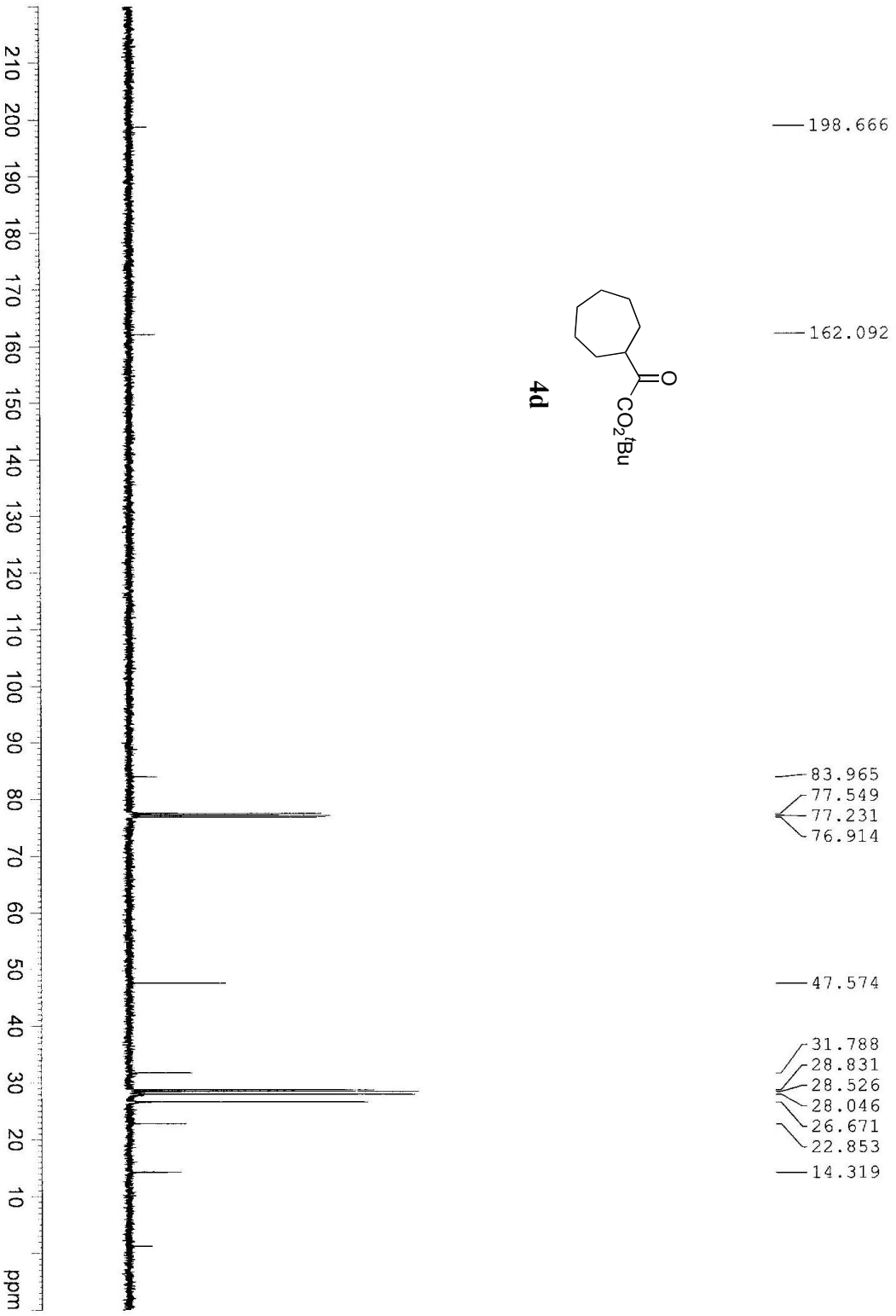
4c
O
CO2tBu
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
2.05
2.05
1.30
9.12
5.55

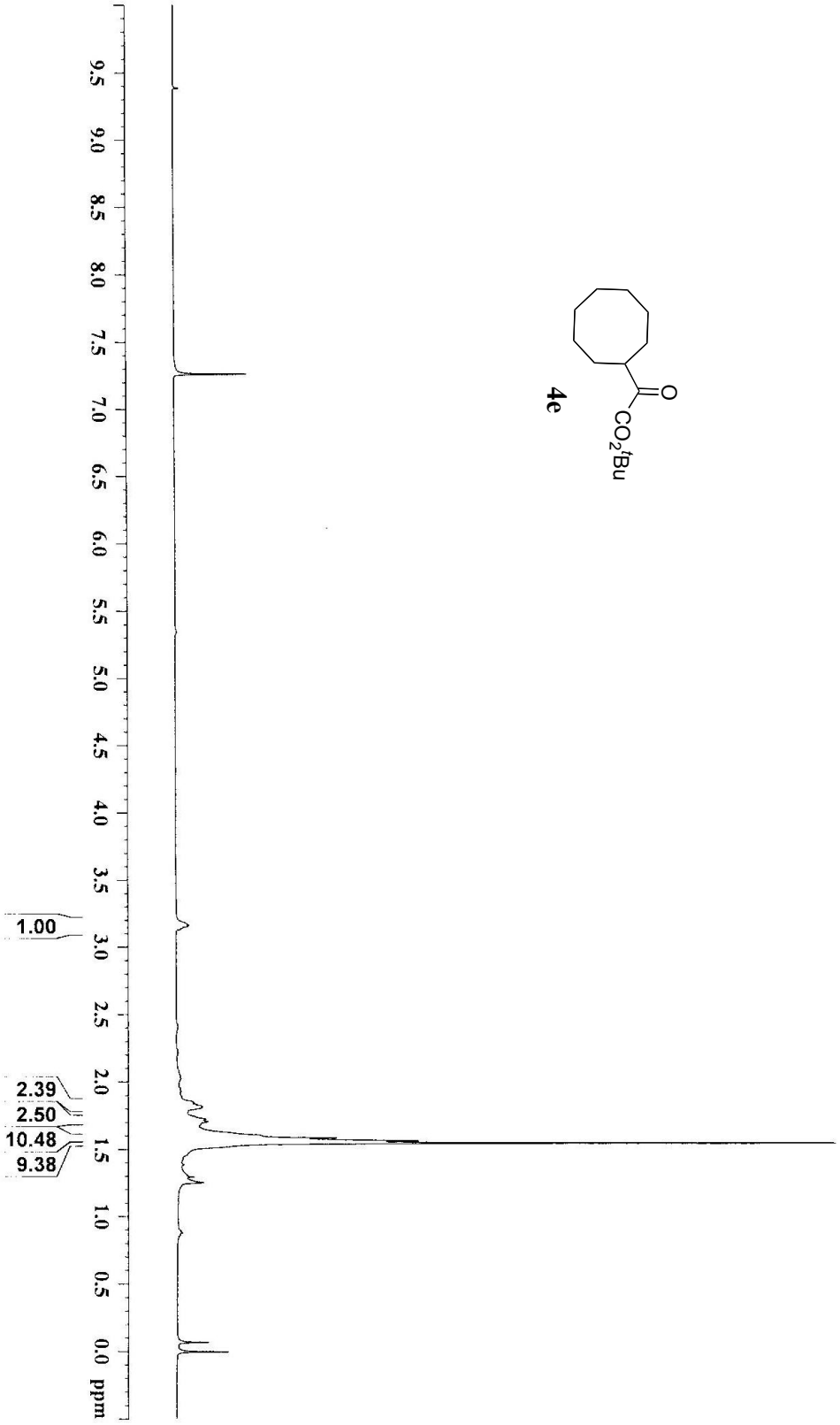

198.736
162.104
84.042
77.548
77.231
76.913
46.402
28.110
27.668
25.970
25.544
4c
O
CO2tBu
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

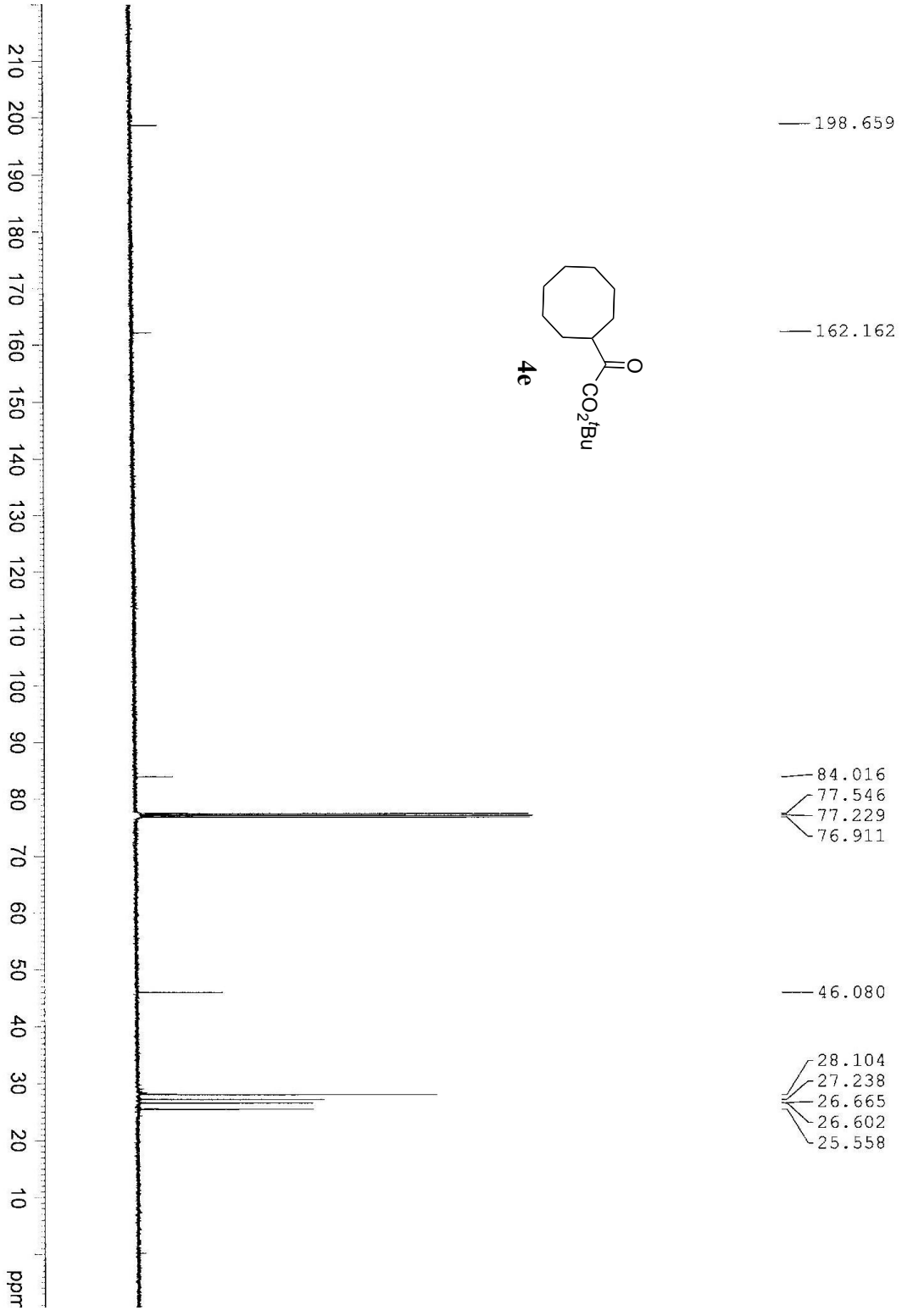

O
CO2tBu

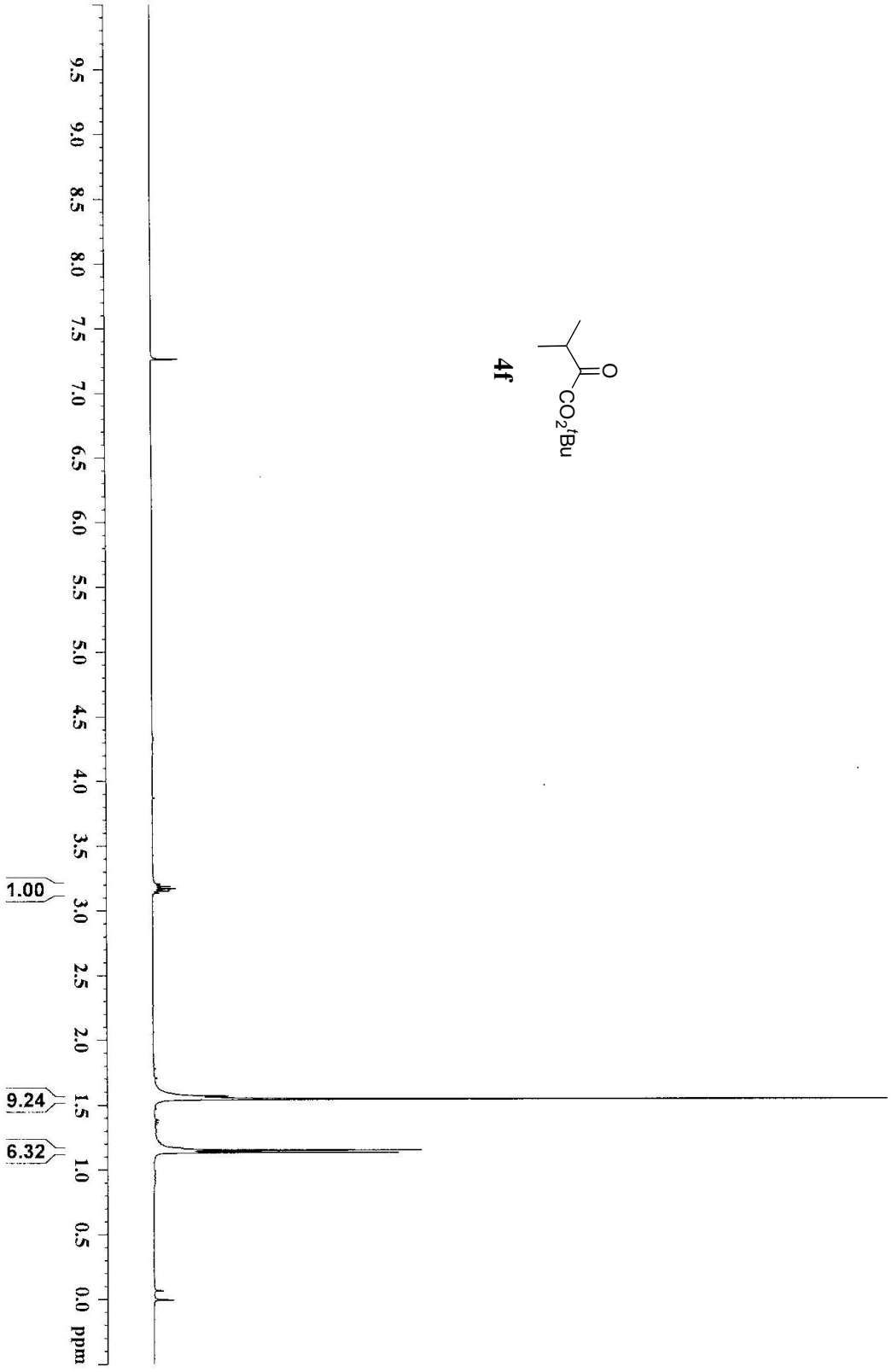
4d


9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
2.08
2.34
12.15
3.06
2.07

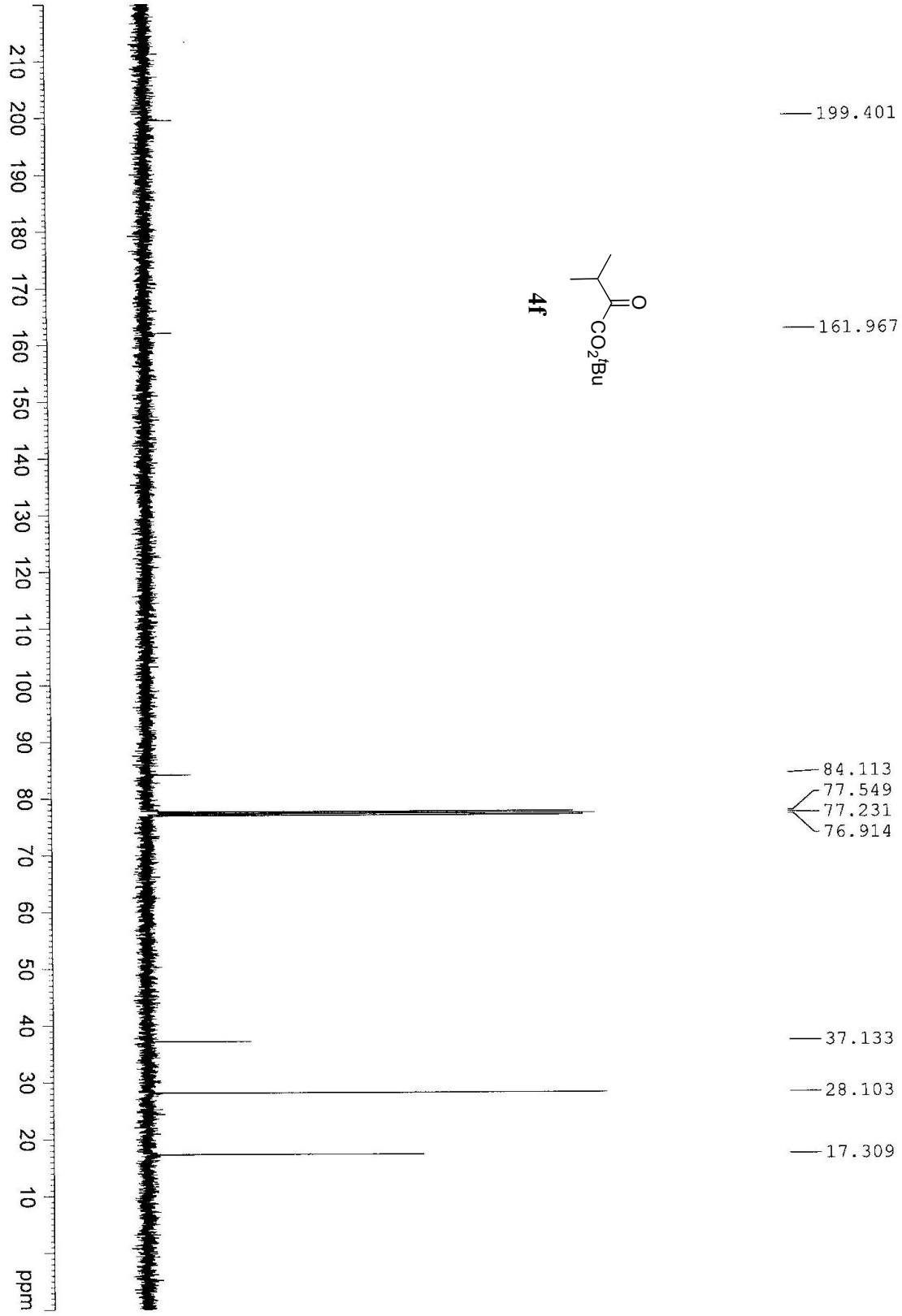

198.666
162.092
83.965
77.549
77.231
76.914
47.574
31.788
28.831
28.526
28.046
26.671
22.853
14.319
O
CO2tBu
4d
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

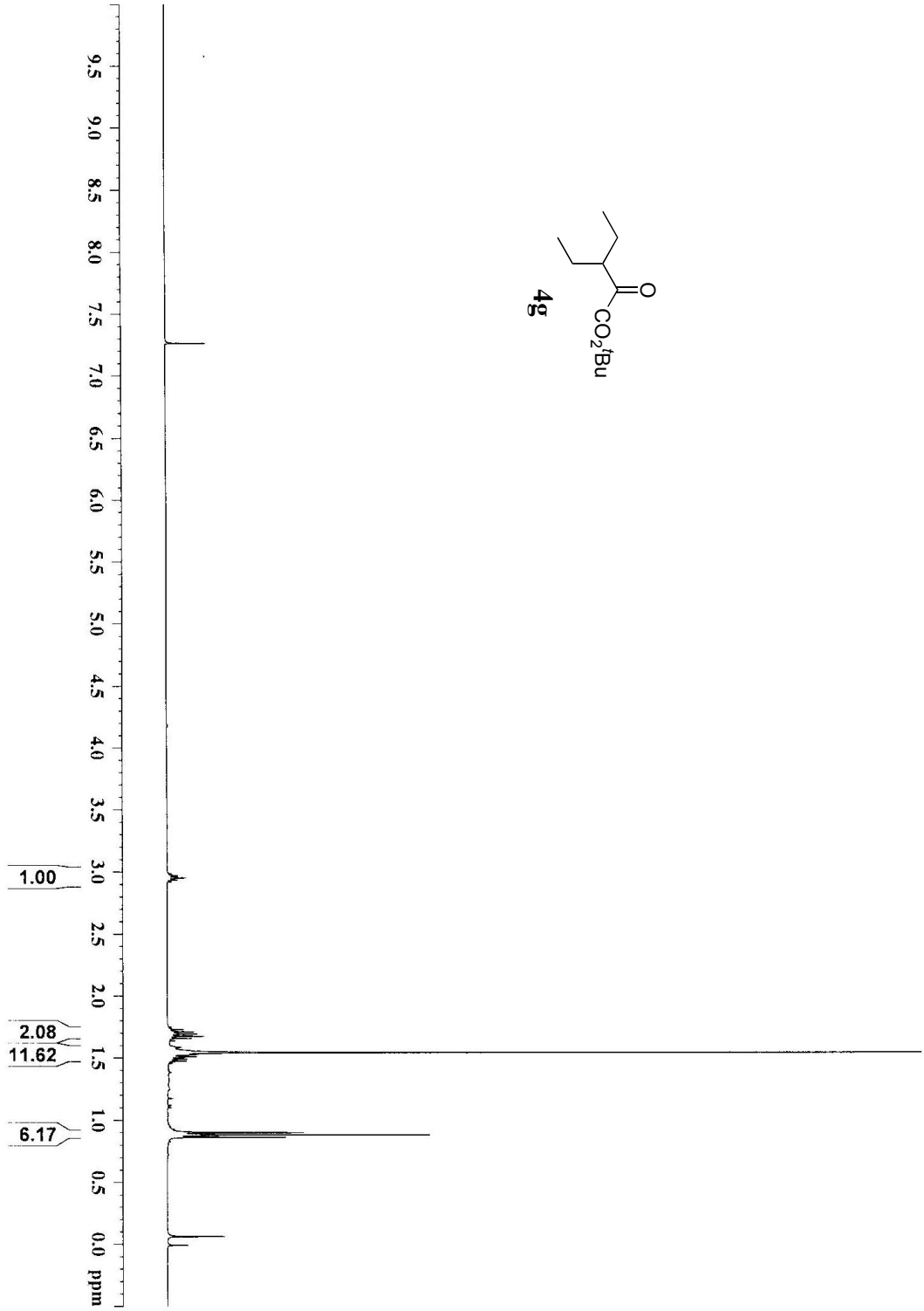

4e
O
CO2tBu
1.00
2.39
2.50
10.48
9.38
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

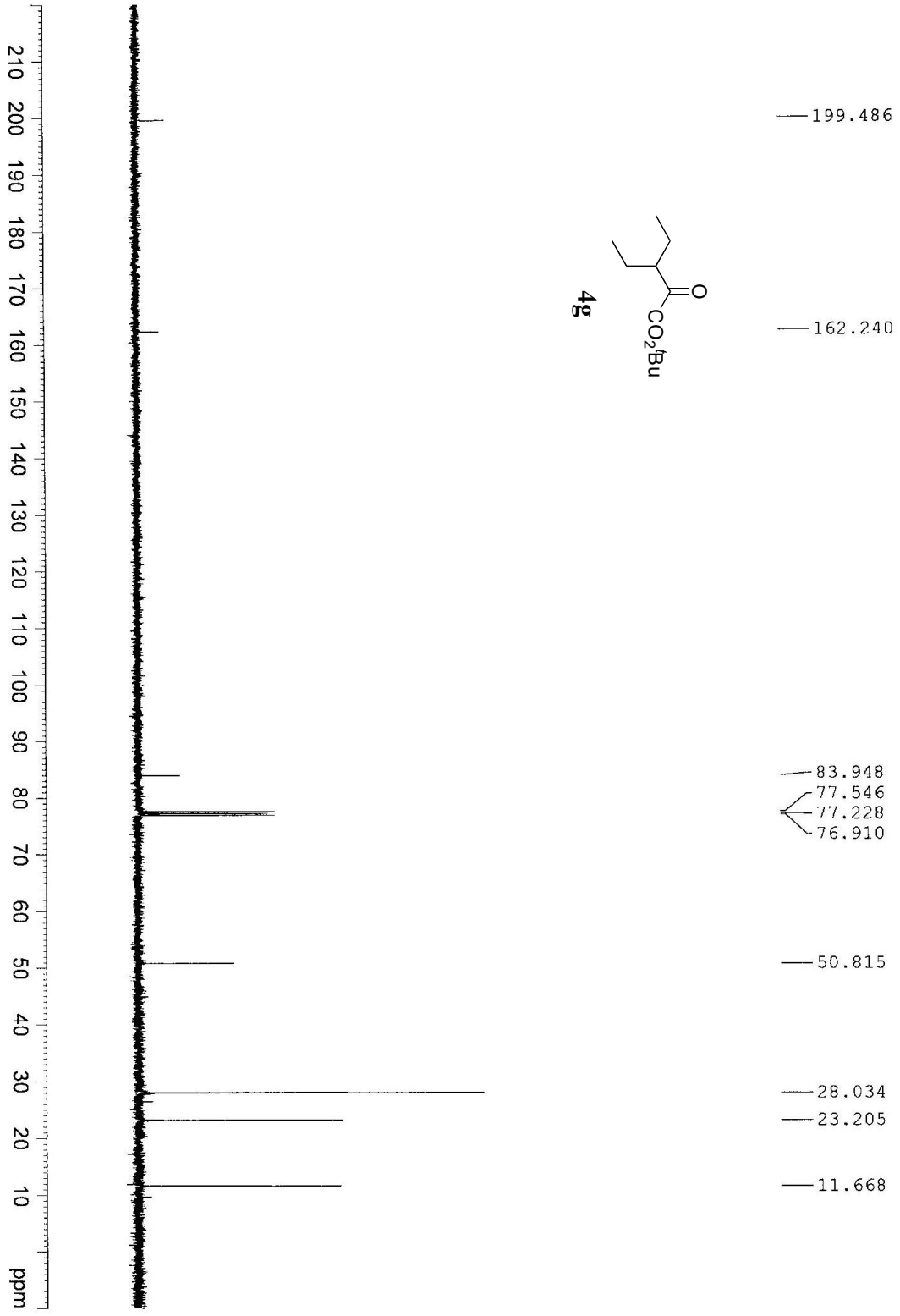

198.659
162.162
84.016
77.546
77.229
76.911
46.080
28.104
27.238
26.665
26.602
25.558
O
CO2tBu
4e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

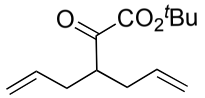

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
9.24
6.32

4f

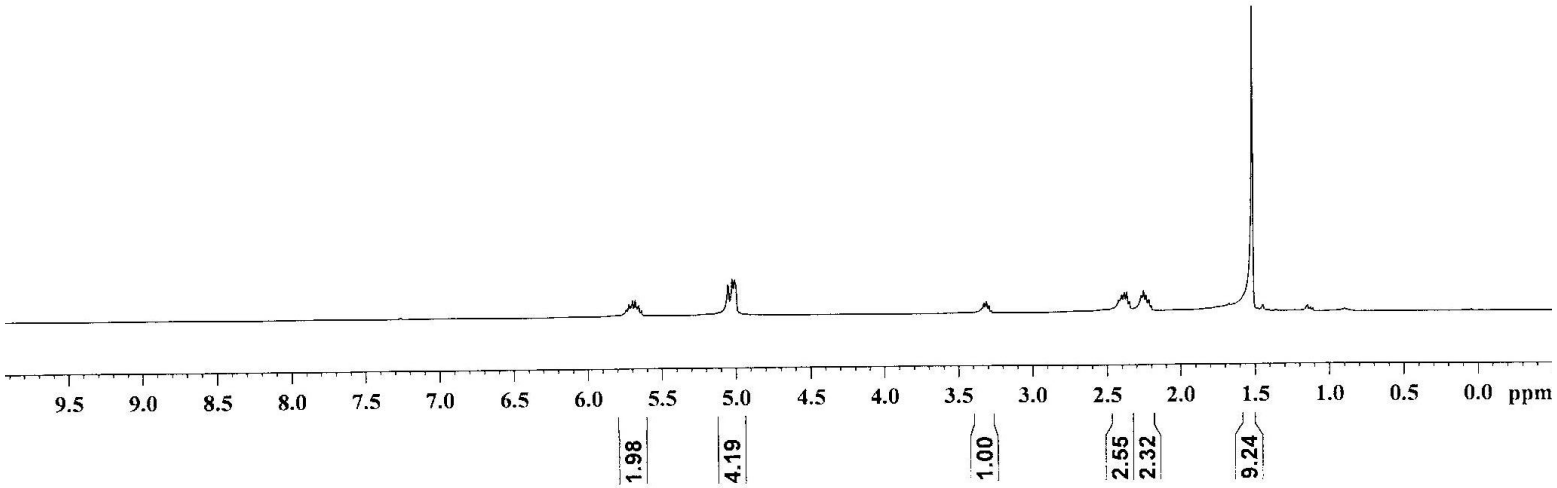

199.401
161.967
84.113
77.549
77.231
76.914
37.133
28.103
17.309
4f
O
CO2tBu
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

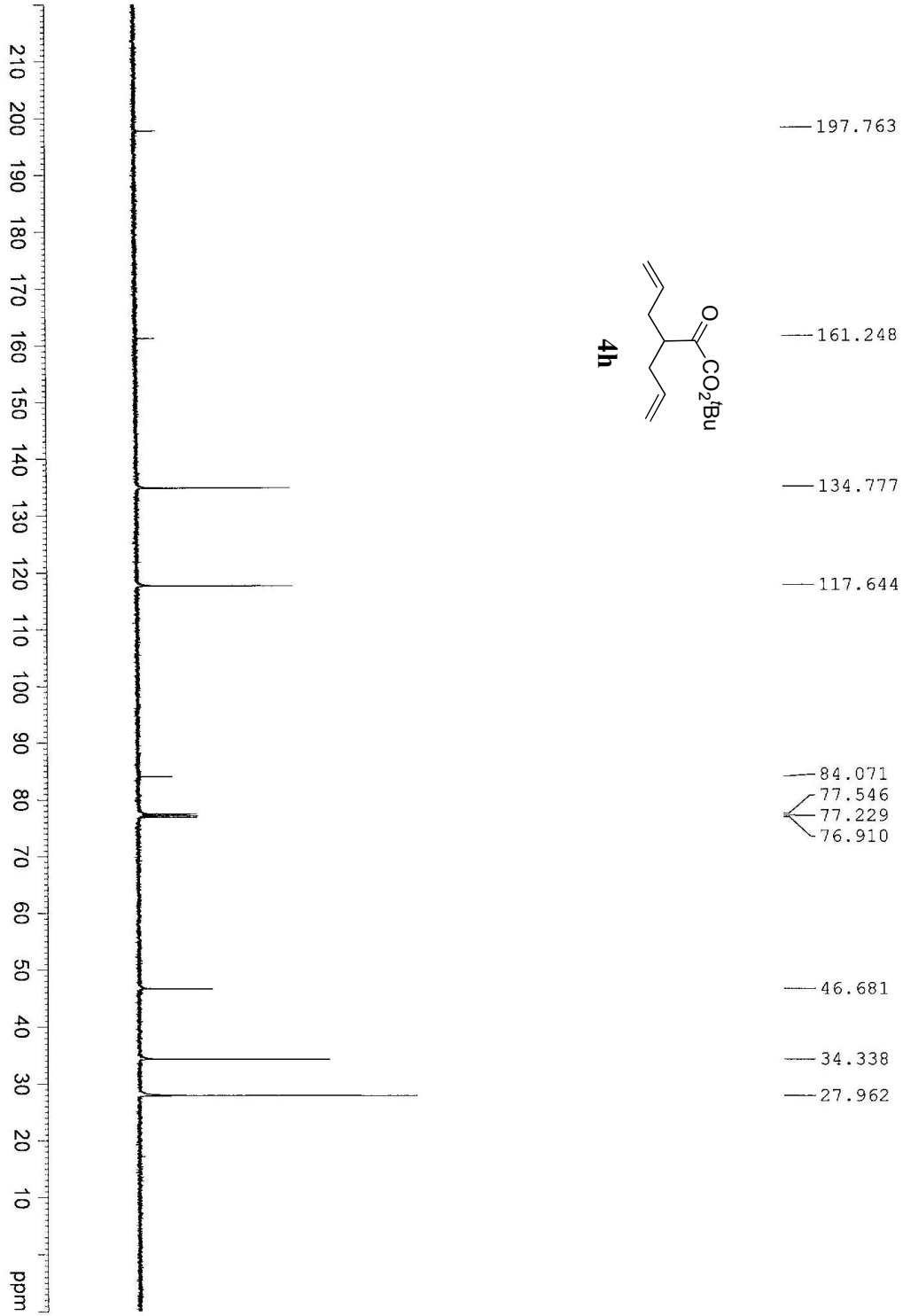

4g
O
CO2tBu
1.00
2.08
11.62
6.17
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

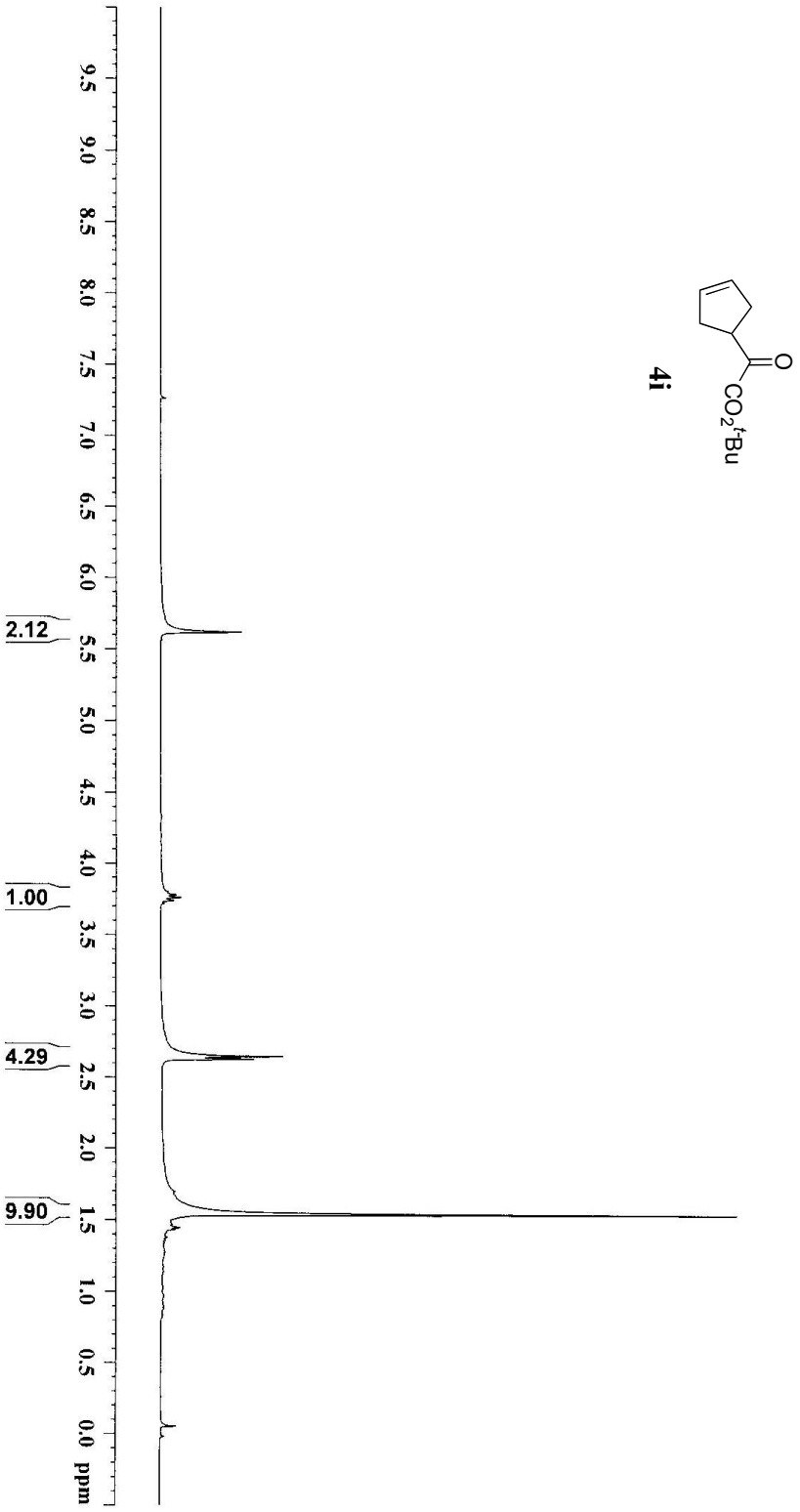

199.486
162.240
83.948
77.546
77.228
76.910
50.815
28.034
23.205
11.668
4g
O
CO2tBu
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


O
CO2tBu

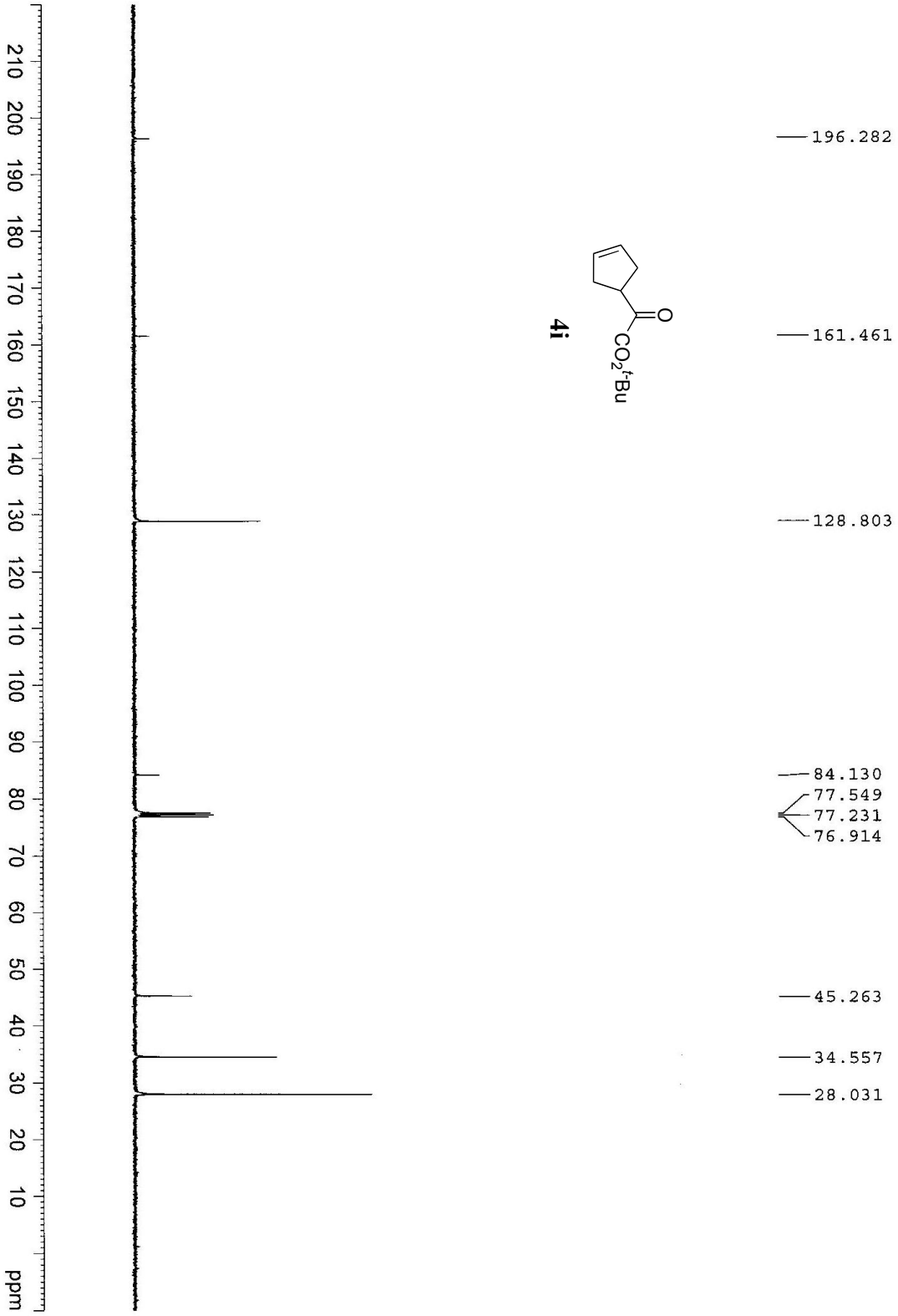
4h


9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0 ppm
1.98
4.19
1.00
2.55
2.32
9.24

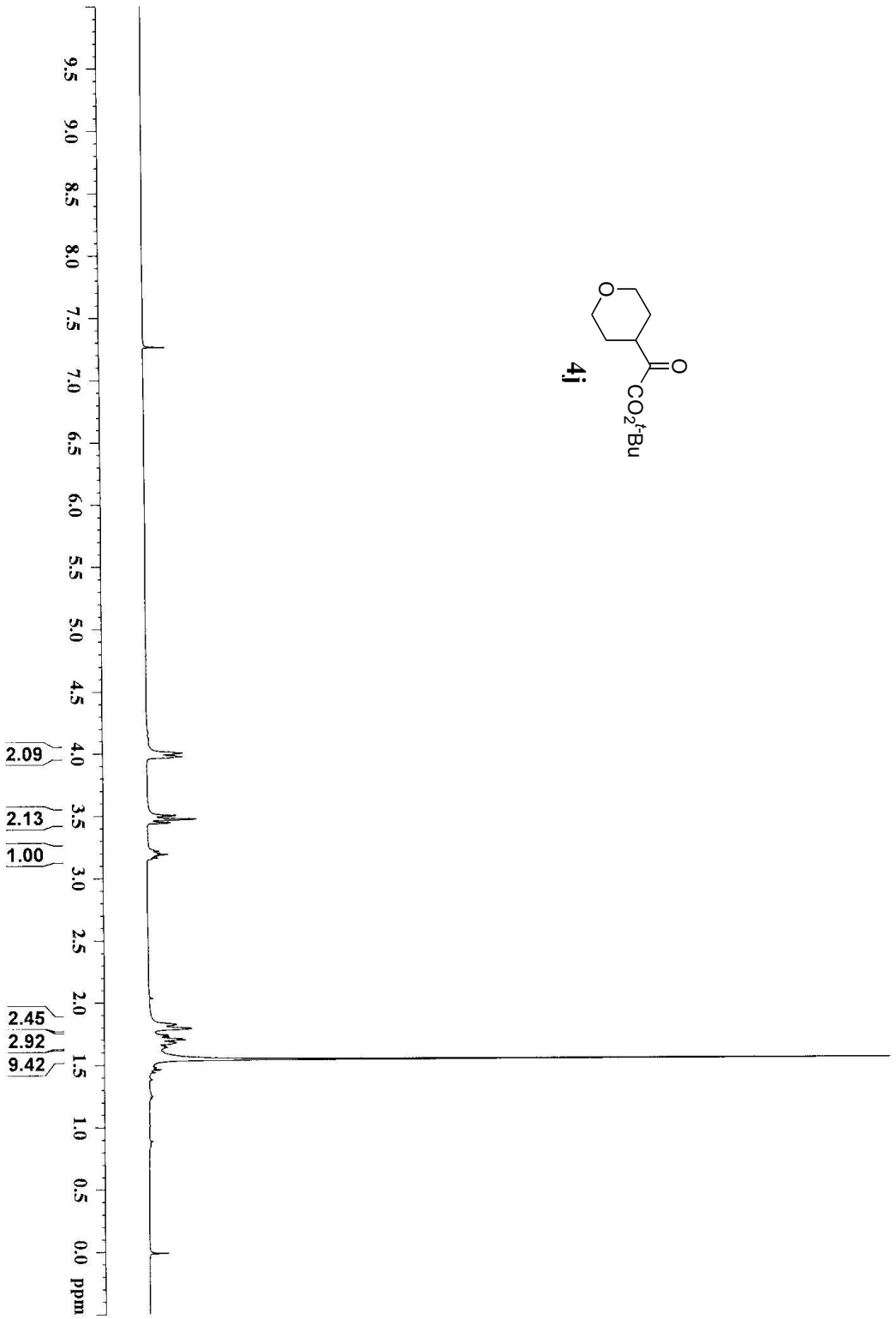

197.763
161.248
134.777
117.644
84.071
77.546
77.229
76.910
46.681
34.338
27.962
4h
O
CO2tBu
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.12
1.00
4.29
9.90
O
CO2tBu

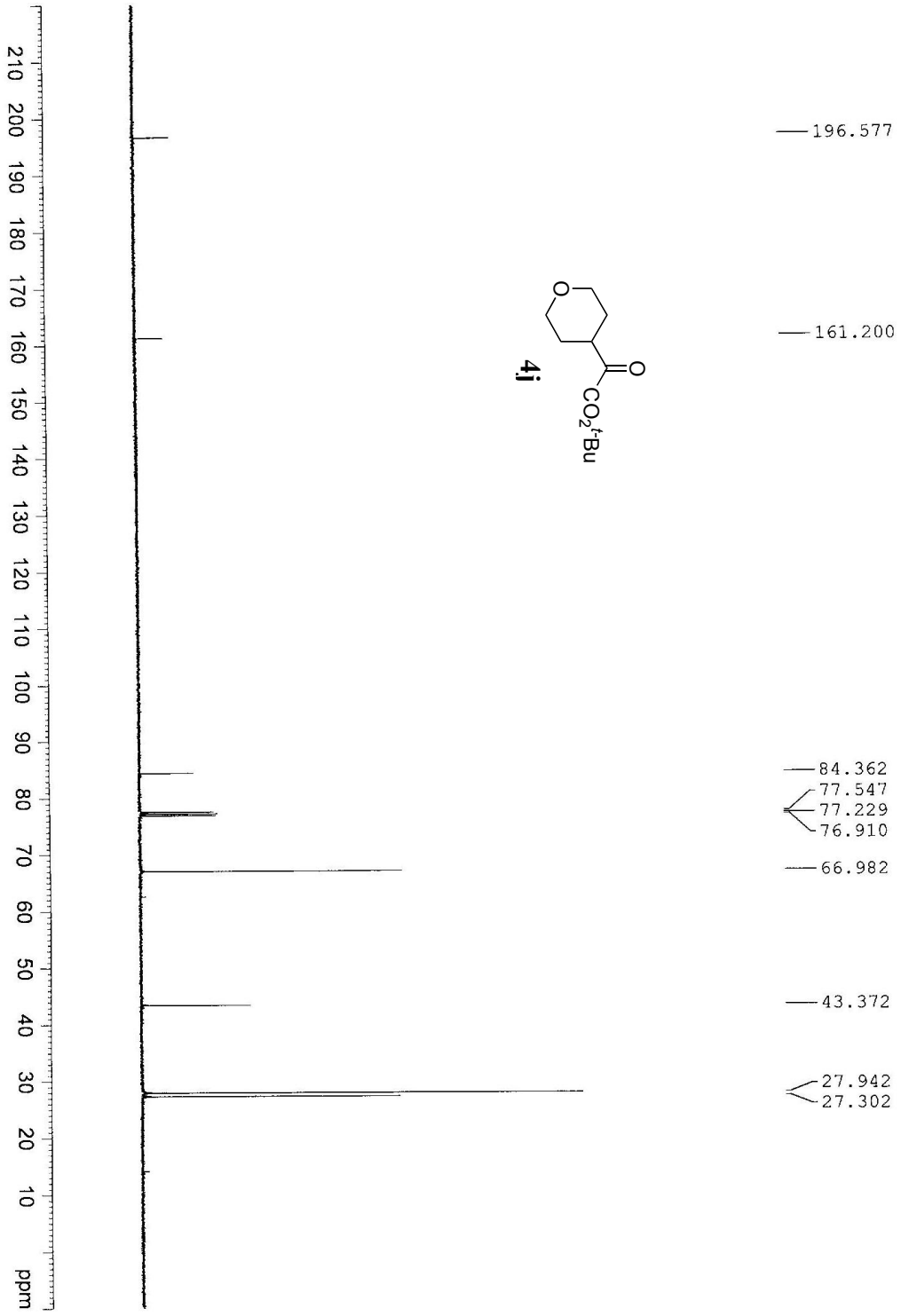
4i

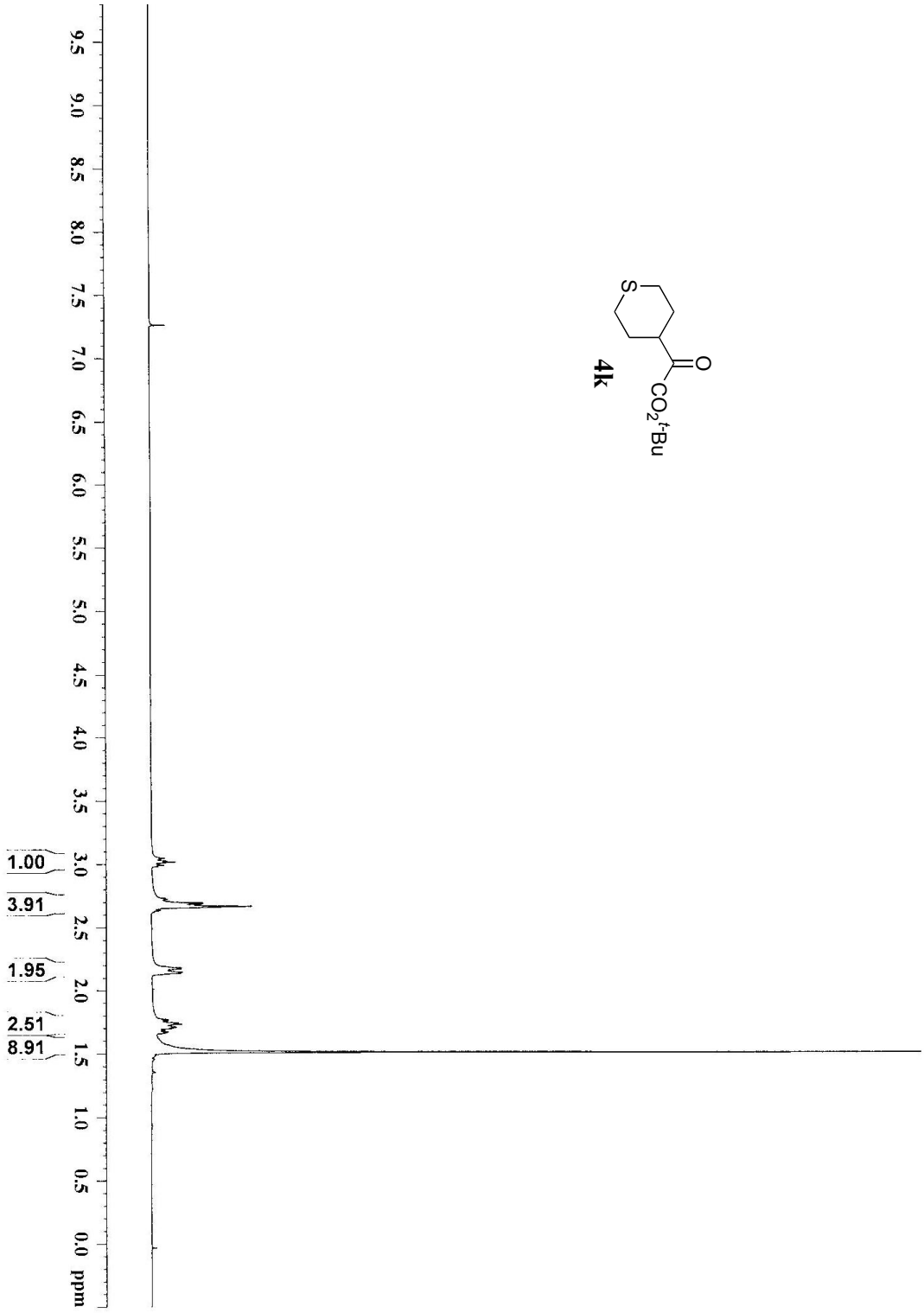

196.282
161.461
128.803
84.130
77.549
77.231
76.914
45.263
34.557
28.031
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
O
CO2t-Bu

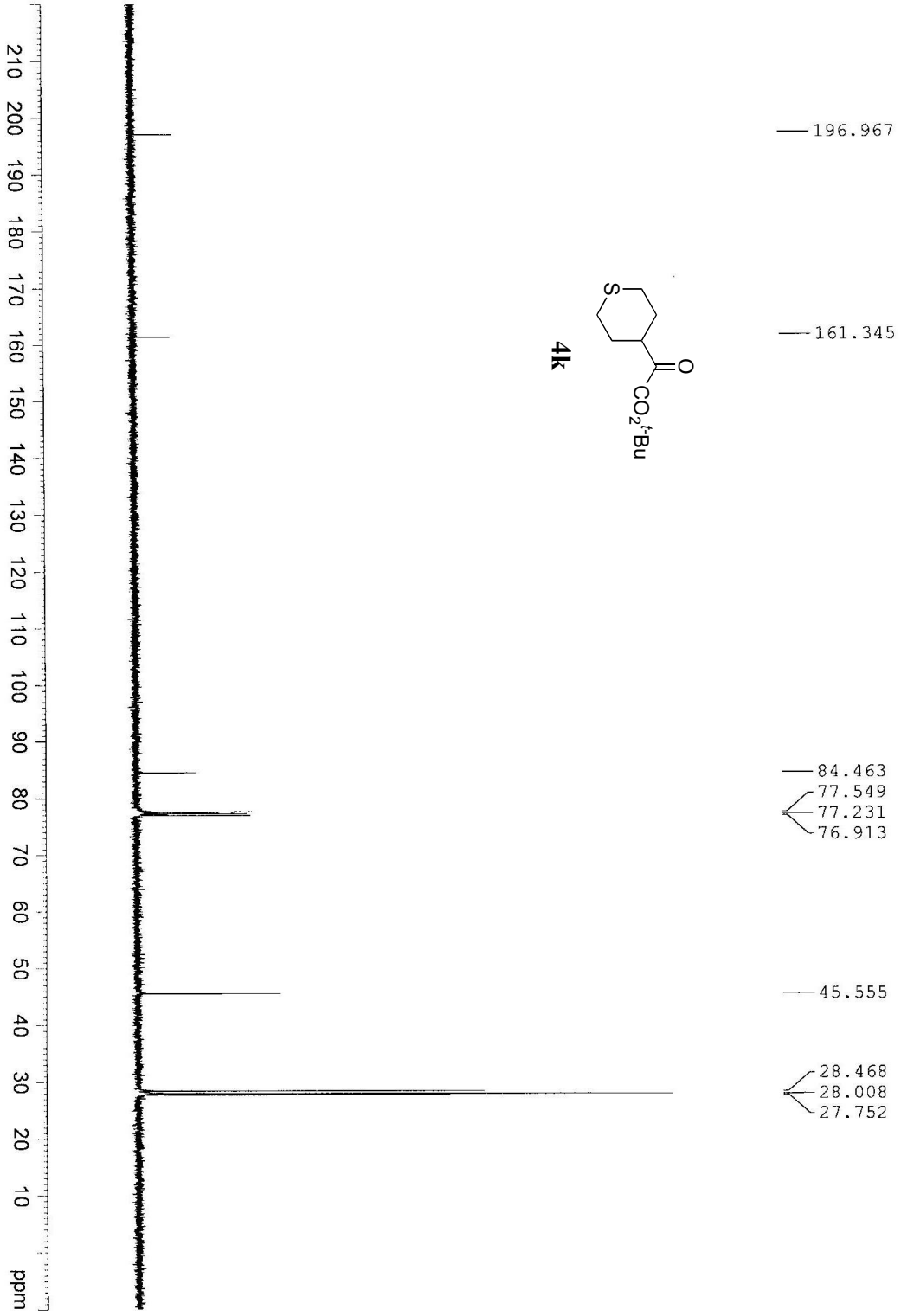
4i

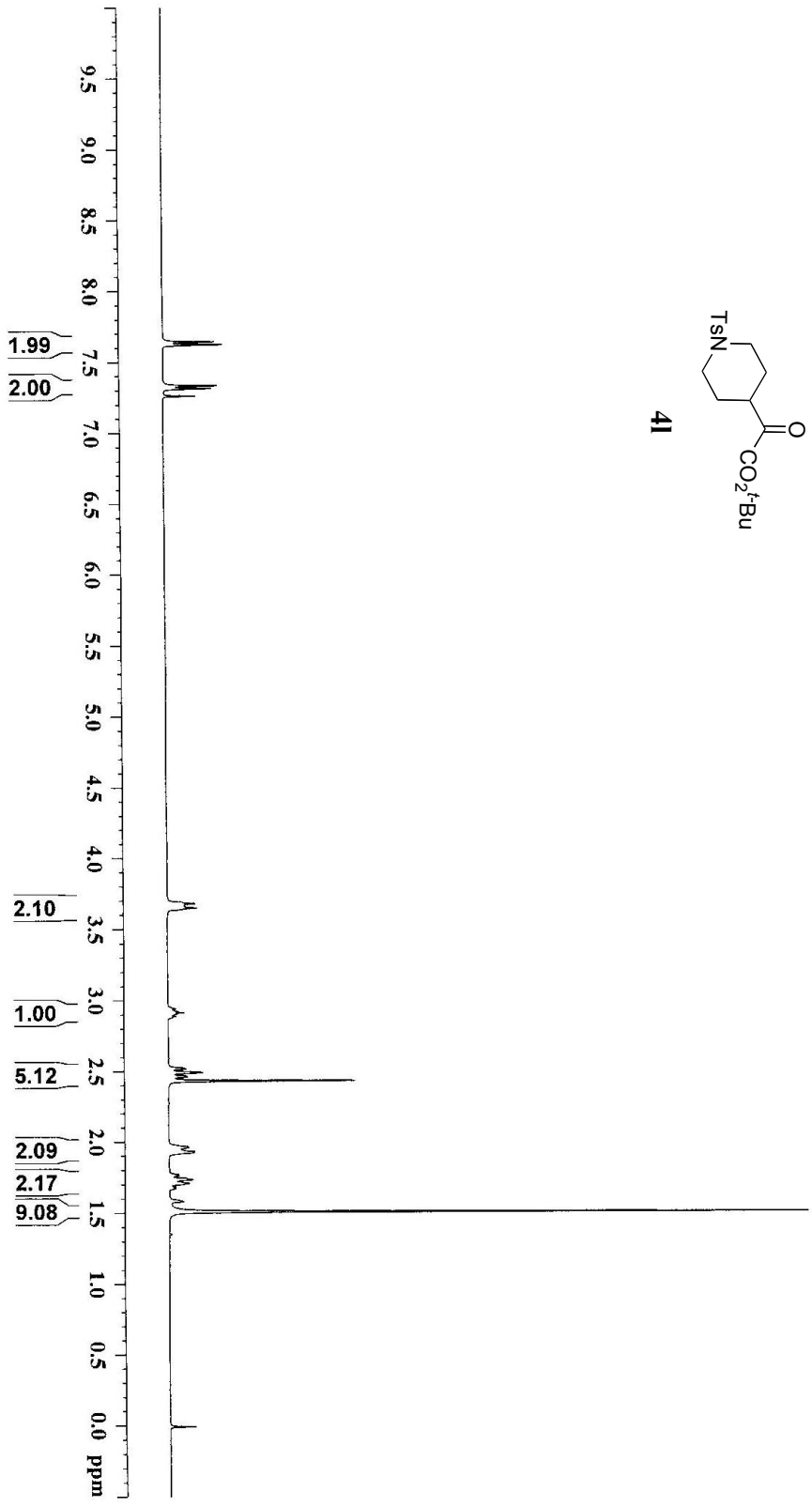

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.09
2.13
1.00
2.45
2.92
9.42
O
O
CO2tBu

4j


196.577
161.200
84.362
77.547
77.229
76.910
66.982
43.372
27.942
27.302
4i
O
O
CO2t-Bu
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


S
O
CO2t-Bu
4k
1.00
3.91
1.95
2.51
8.91
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


196.967
161.345
84.463
77.549
77.231
76.913
45.555
28.468
28.008
27.752
4k
S
O
CO2t-Bu
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


TsN
O
CO2t-Bu
41
1.99
2.00
2.10
1.00
5.12
2.09
2.17
9.08
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

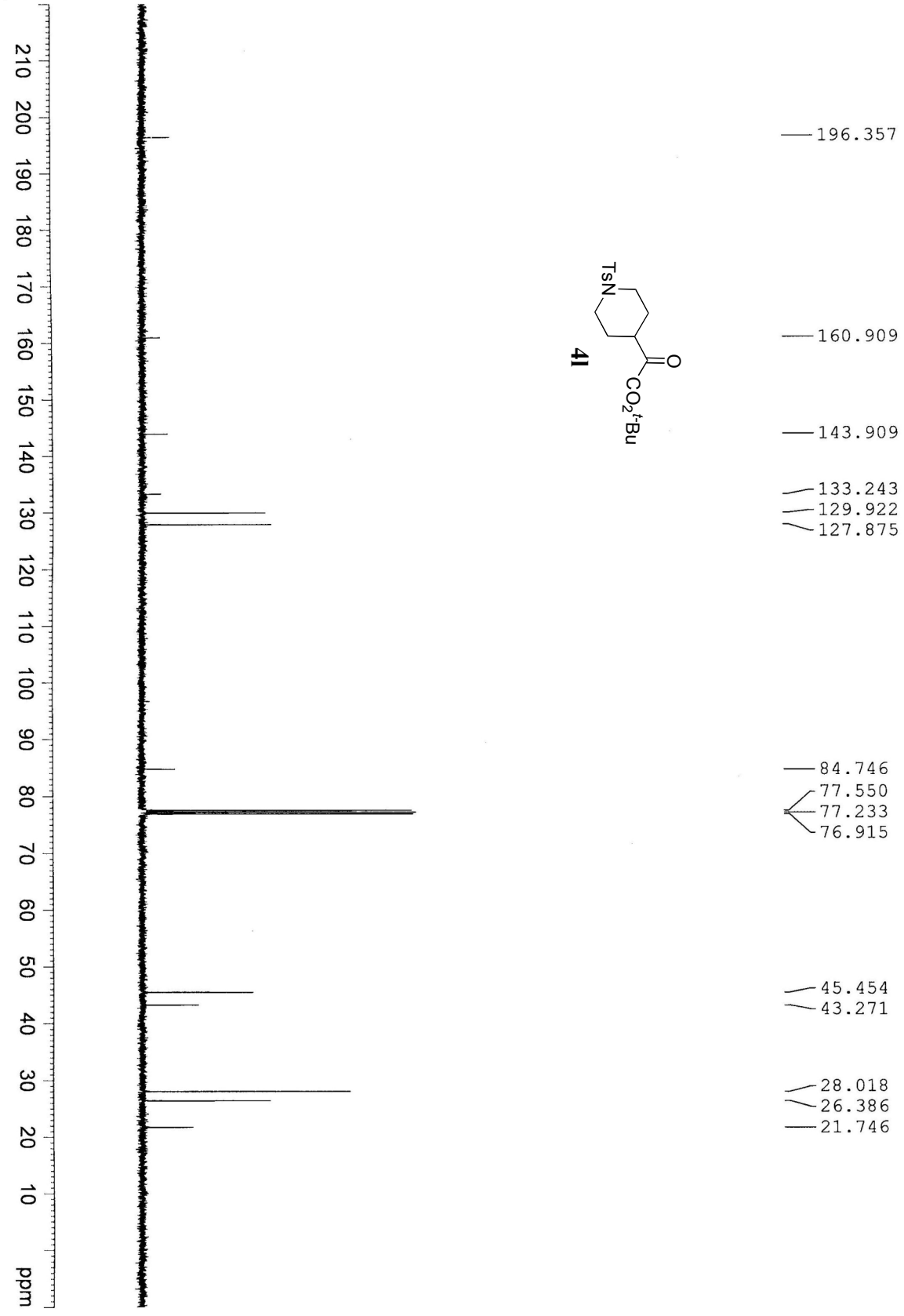
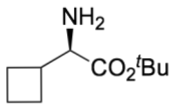

TsN
O
CO2tBu
41
196.357
160.909
143.909
133.243
129.922
127.875
84.746
77.550
77.233
76.915
45.454
43.271
28.018
26.386
21.746
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Table 2, entry 1



6a

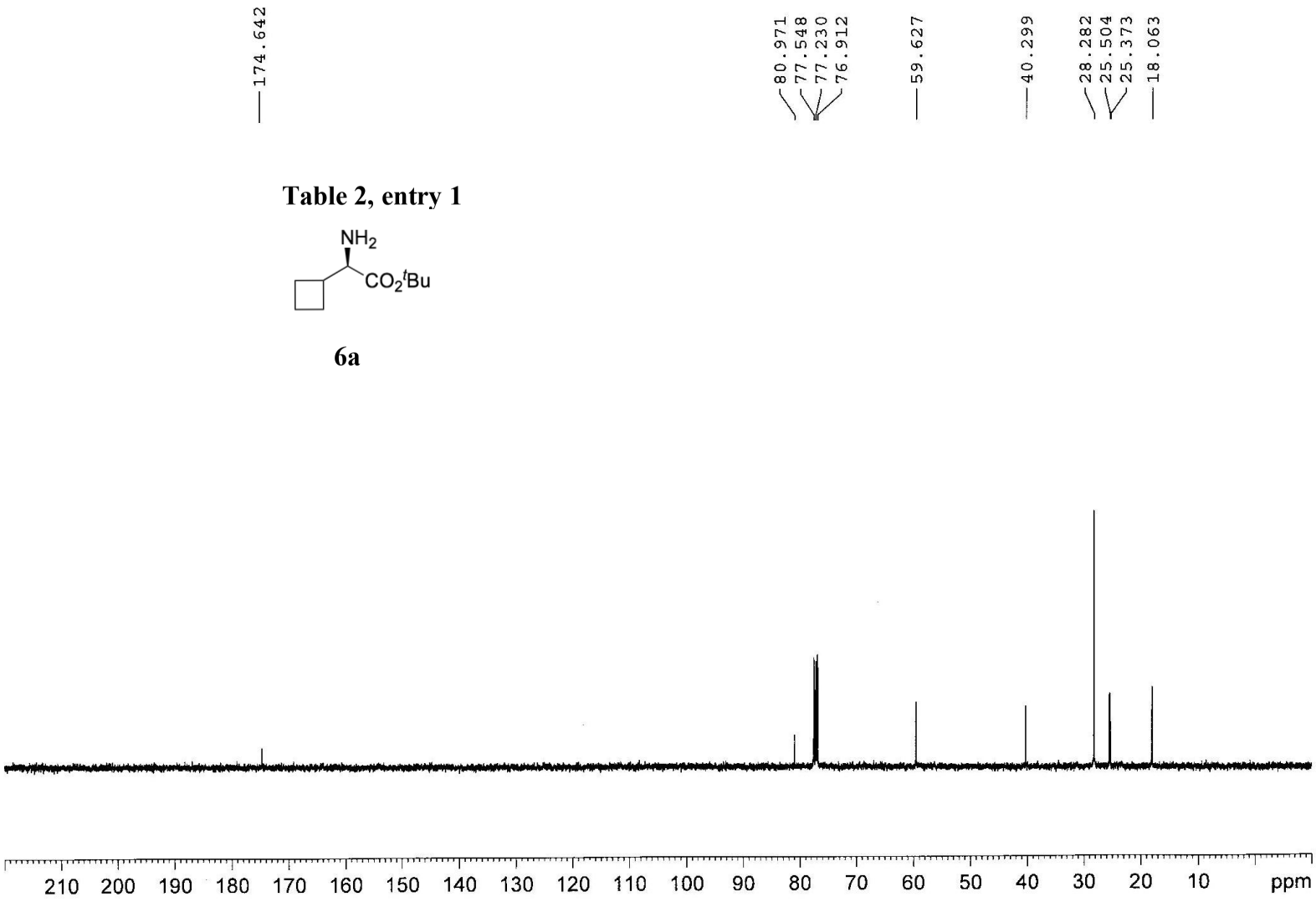
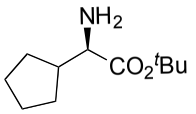

174.642
80.971
77.548
77.230
76.912
59.627
40.299
28.282
25.504
25.373
18.063
Table 2, entry 1
NH2
CO2tBu
6a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Table 2, entry 2



6b

175.427

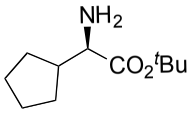
80.942
77.551
77.233
76.915

59.142

44.635

29.439
28.539
28.287
25.808
25.569

Table 2, entry 2



6b

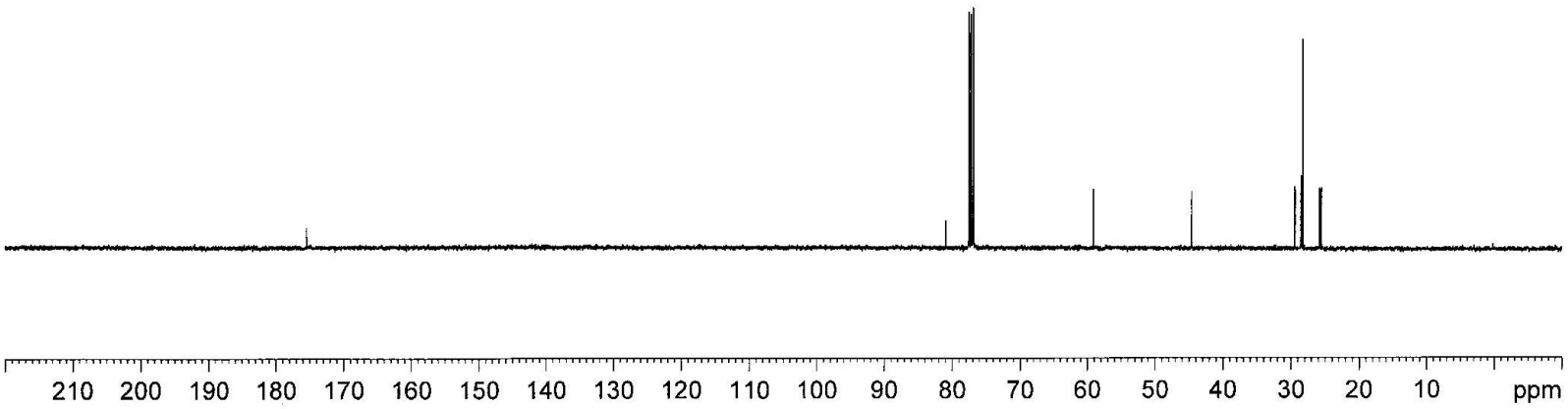
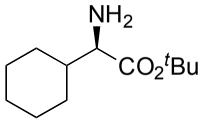


Table 2, entry 3



6c

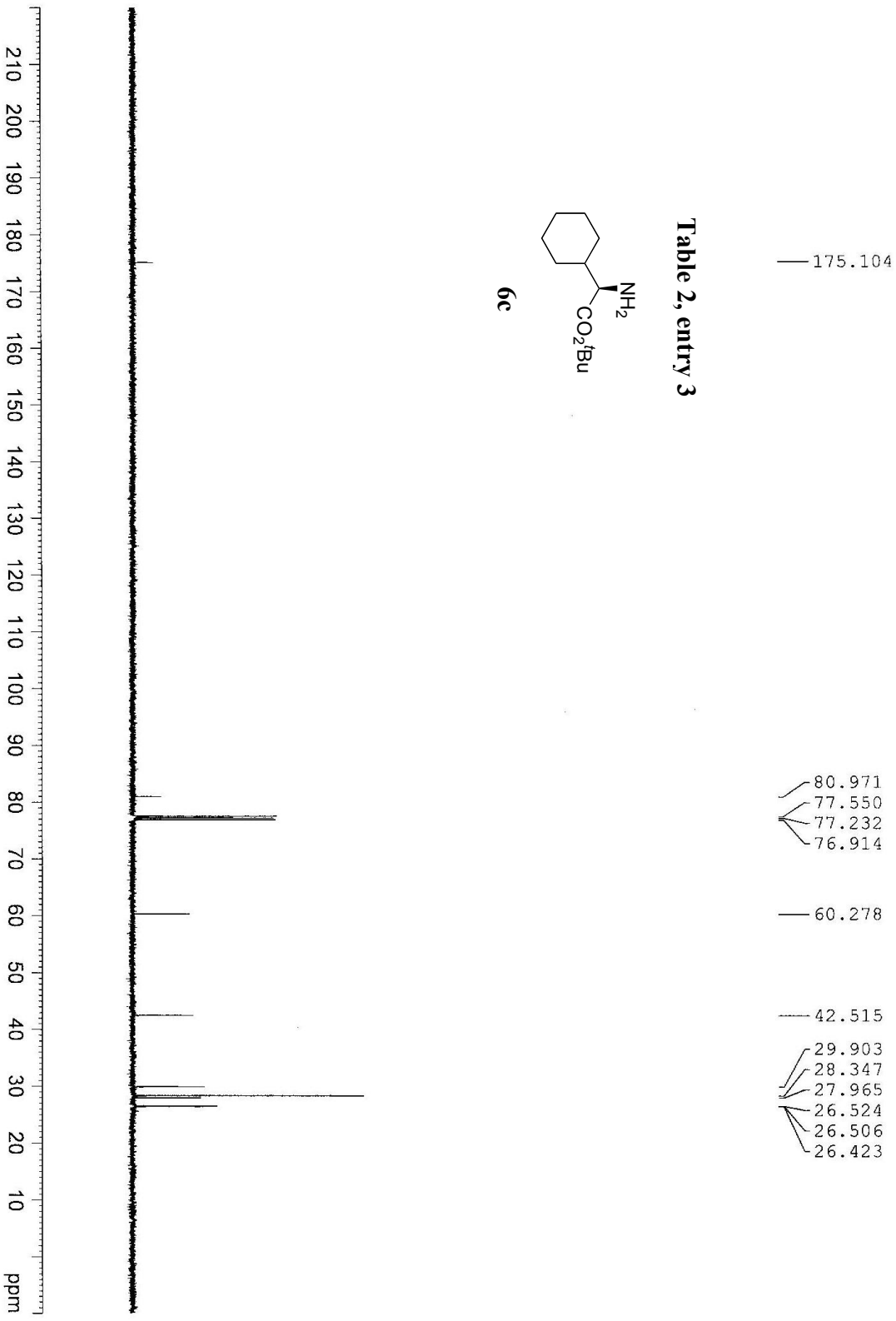
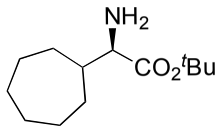


Table 2, entry 3
6c
NH2
CO2tBu
175.104
80.971
77.550
77.232
76.914
60.278
42.515
29.903
28.347
27.965
26.524
26.506
26.423
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Table 2, entry 4

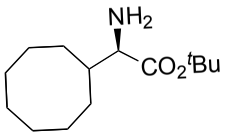


6d

Table 2, entry 4

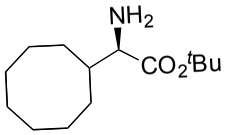
6d

Table 2, entry 5



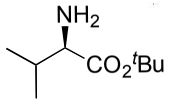
6e

Table 2, entry 5



6e

Table 2, entry 6



6f

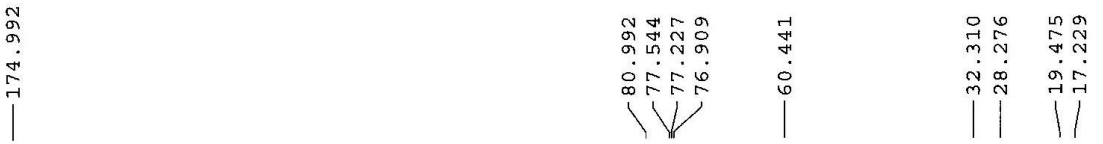
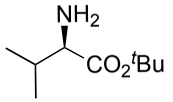


Table 2, entry 6



6f

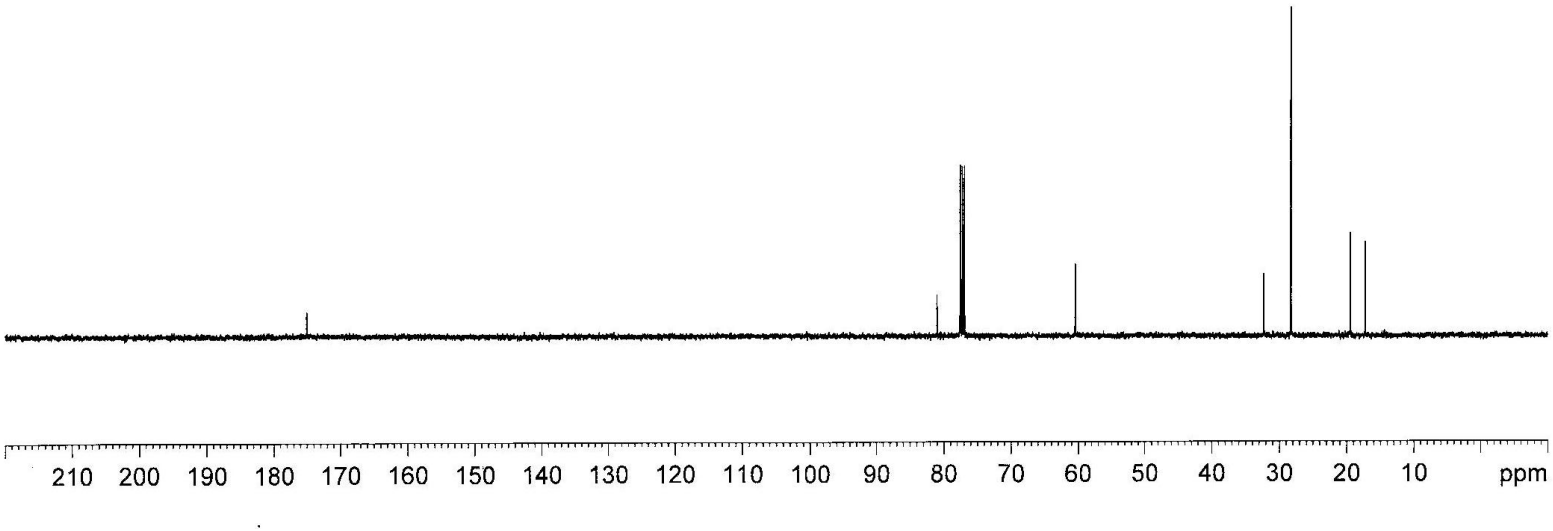
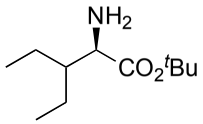


Table 2, entry 7



6g

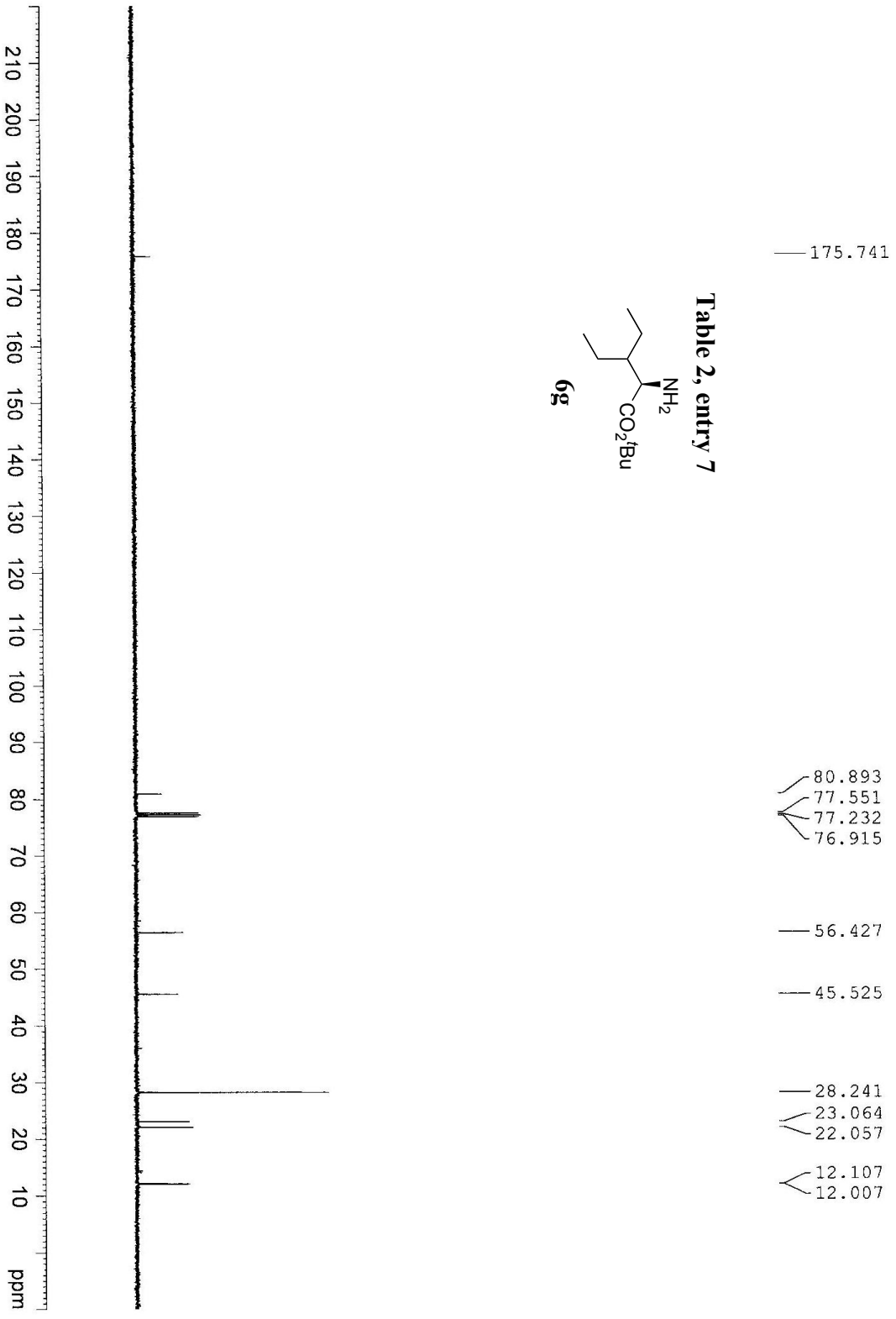
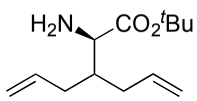


Table 2, entry 7
6g
NH2
CO2tBu
175.741
80.893
77.551
77.232
76.915
56.427
45.525
28.241
23.064
22.057
12.107
12.007
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

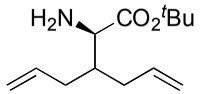
Table 2, entry 8



6h

175.242
137.132
136.980
116.892
116.841
81.220
77.547
77.230
76.912
56.304
41.865
35.129
33.901
28.300

Table 2, entry 8



6h

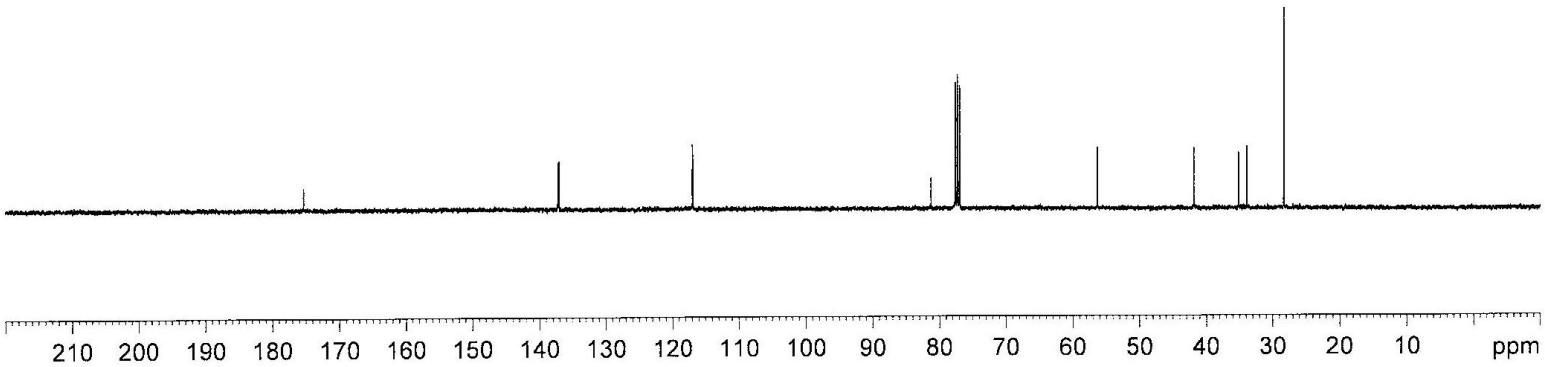
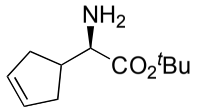


Table 2, entry 9



6i

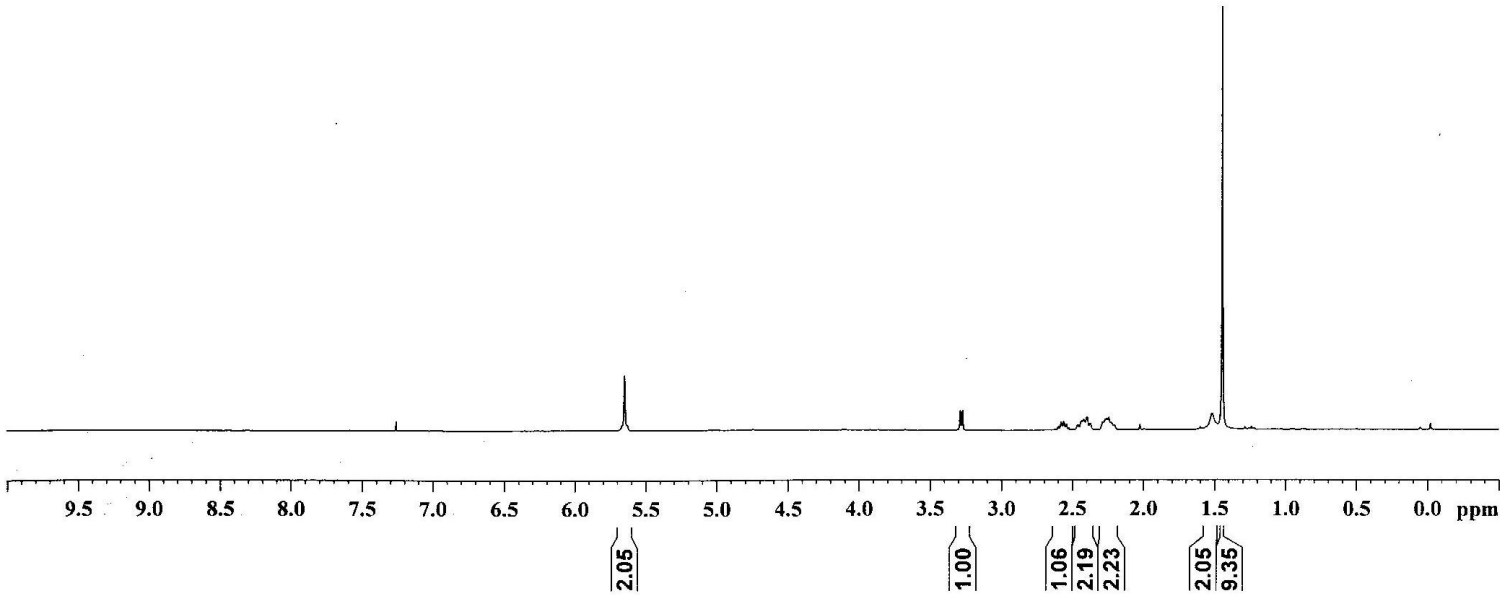
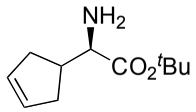


Table 2, entry 9



6i

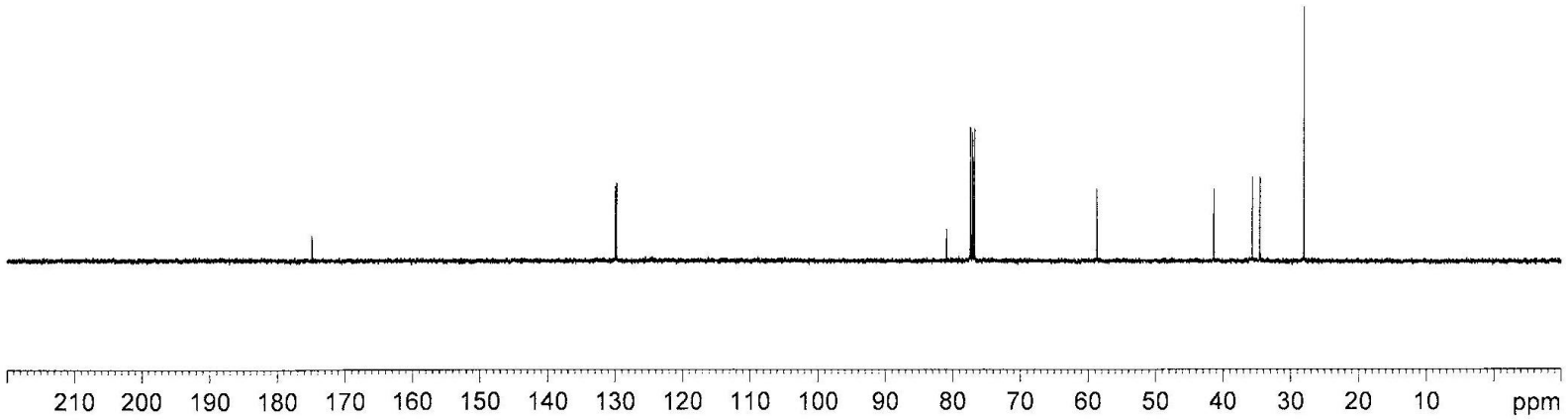
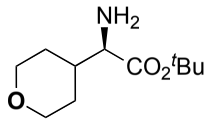


Table 2, entry 10

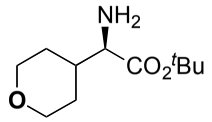


6j

174.582

81.404
77.550
77.232
76.915
68.151
68.018
59.736
39.888
29.619
28.389
28.328

Table 2, entry 10



6j

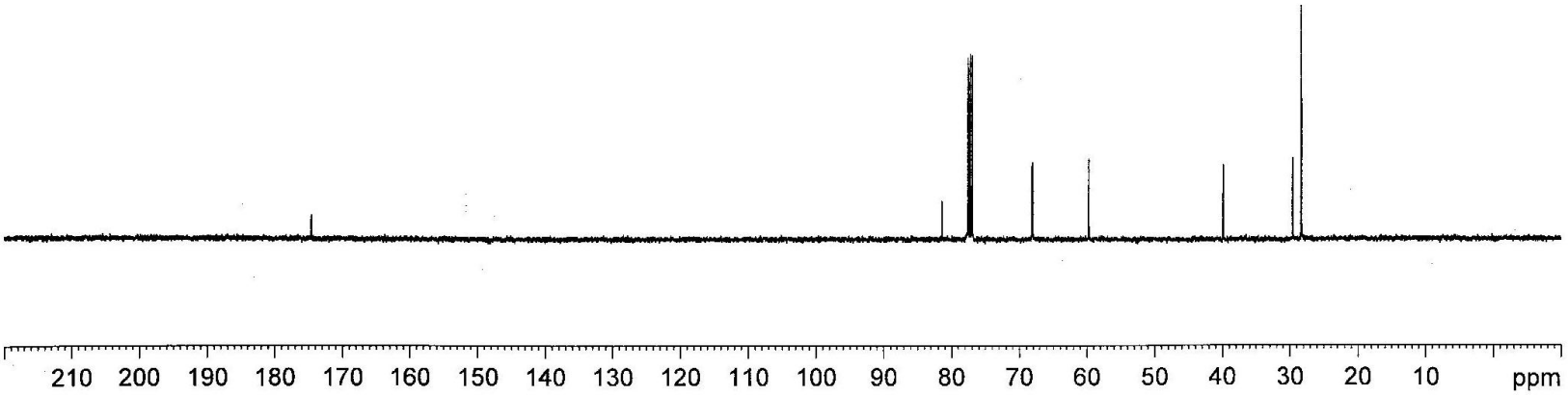
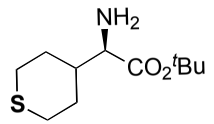
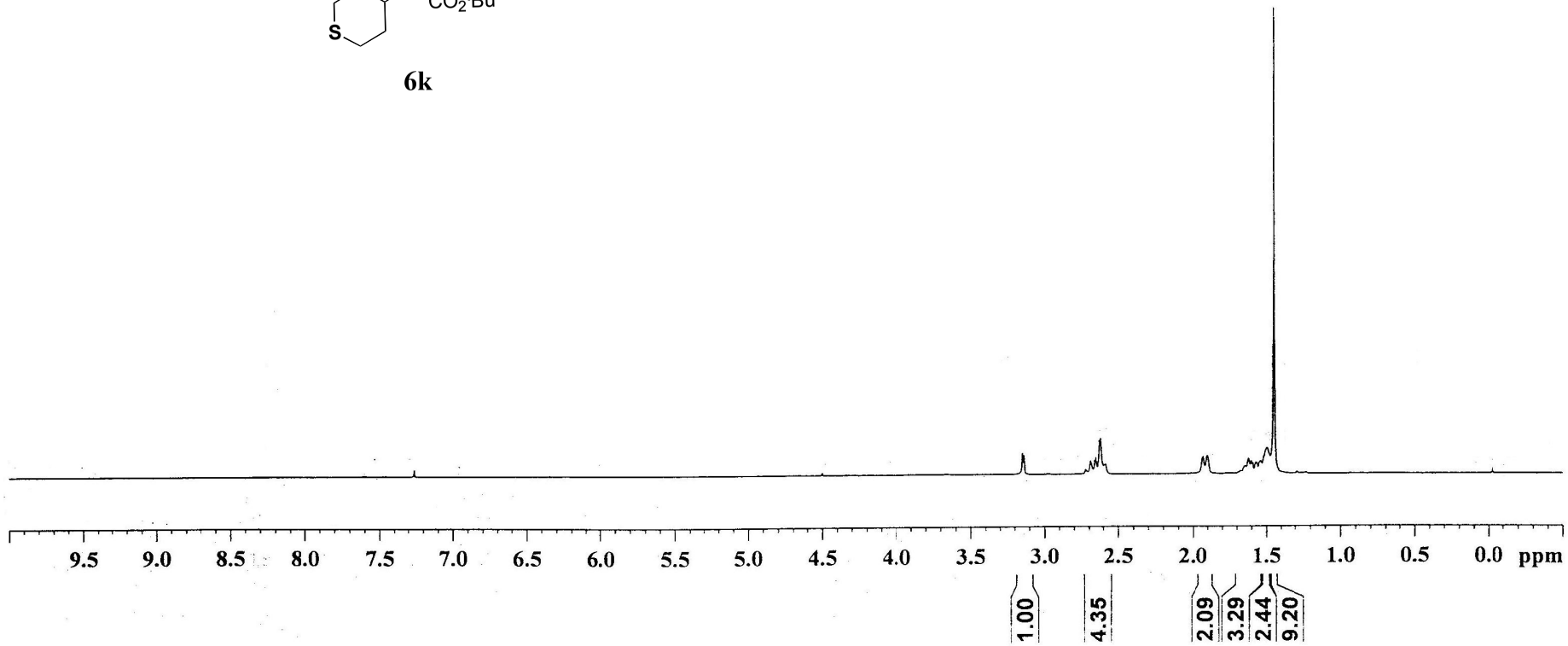


Table 2, entry 11



6k



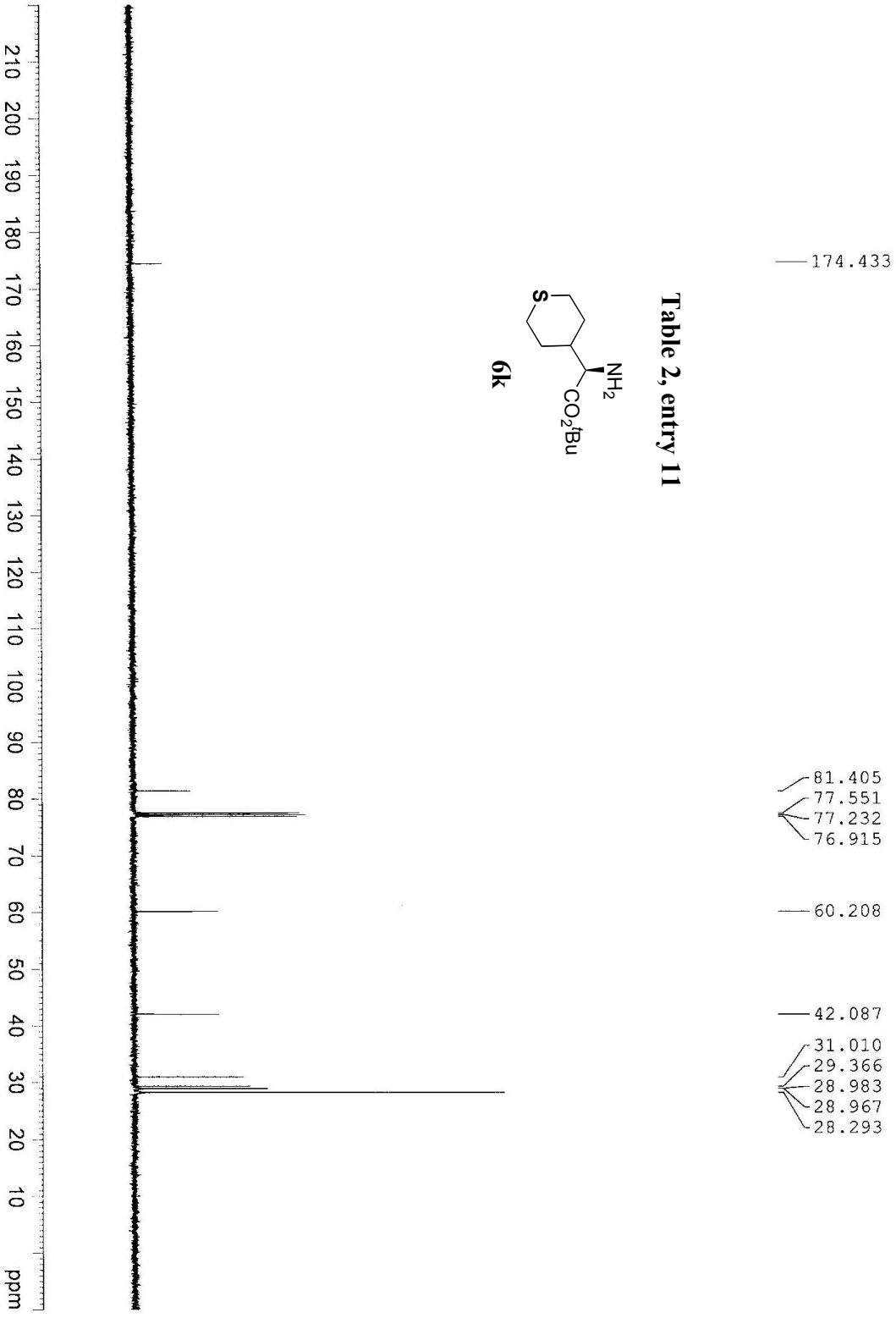
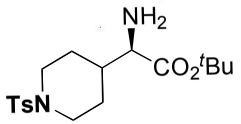


Table 2, entry 11
6k
NH2
CO2tBu
S
174.433
81.405
77.551
77.232
76.915
60.208
42.087
31.010
29.366
28.983
28.967
28.293
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

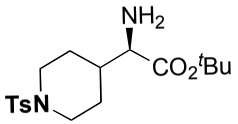
Table 2, entry 12



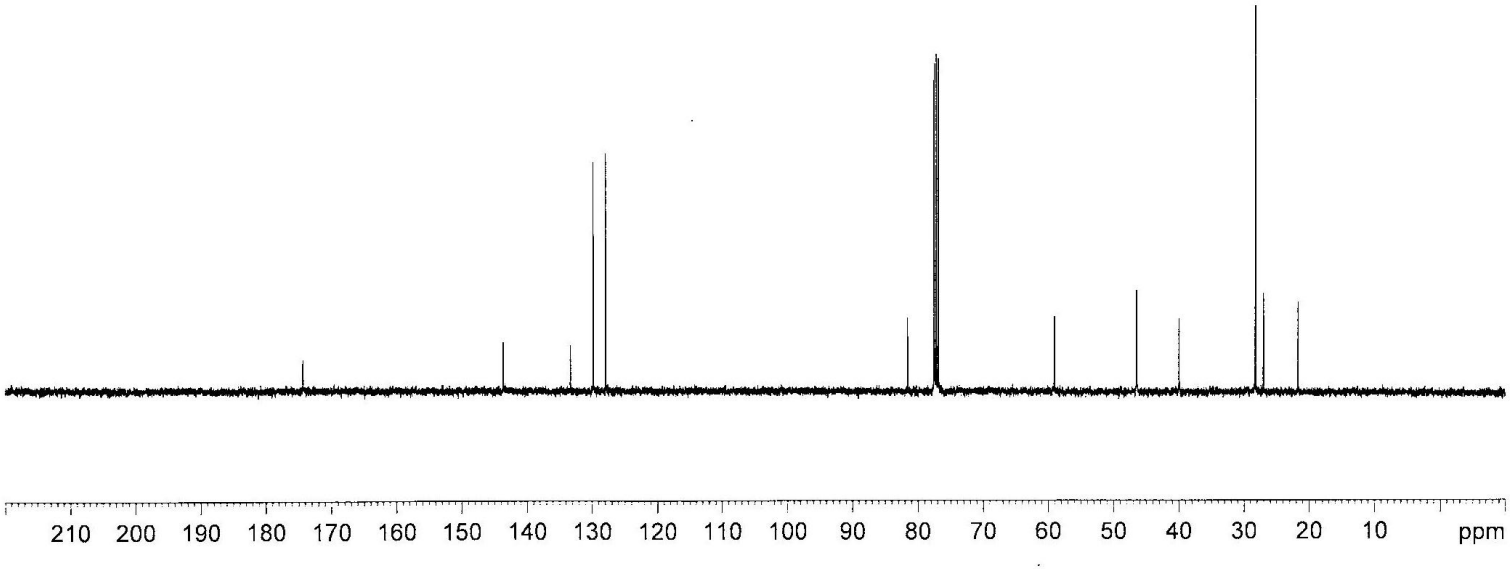
6l

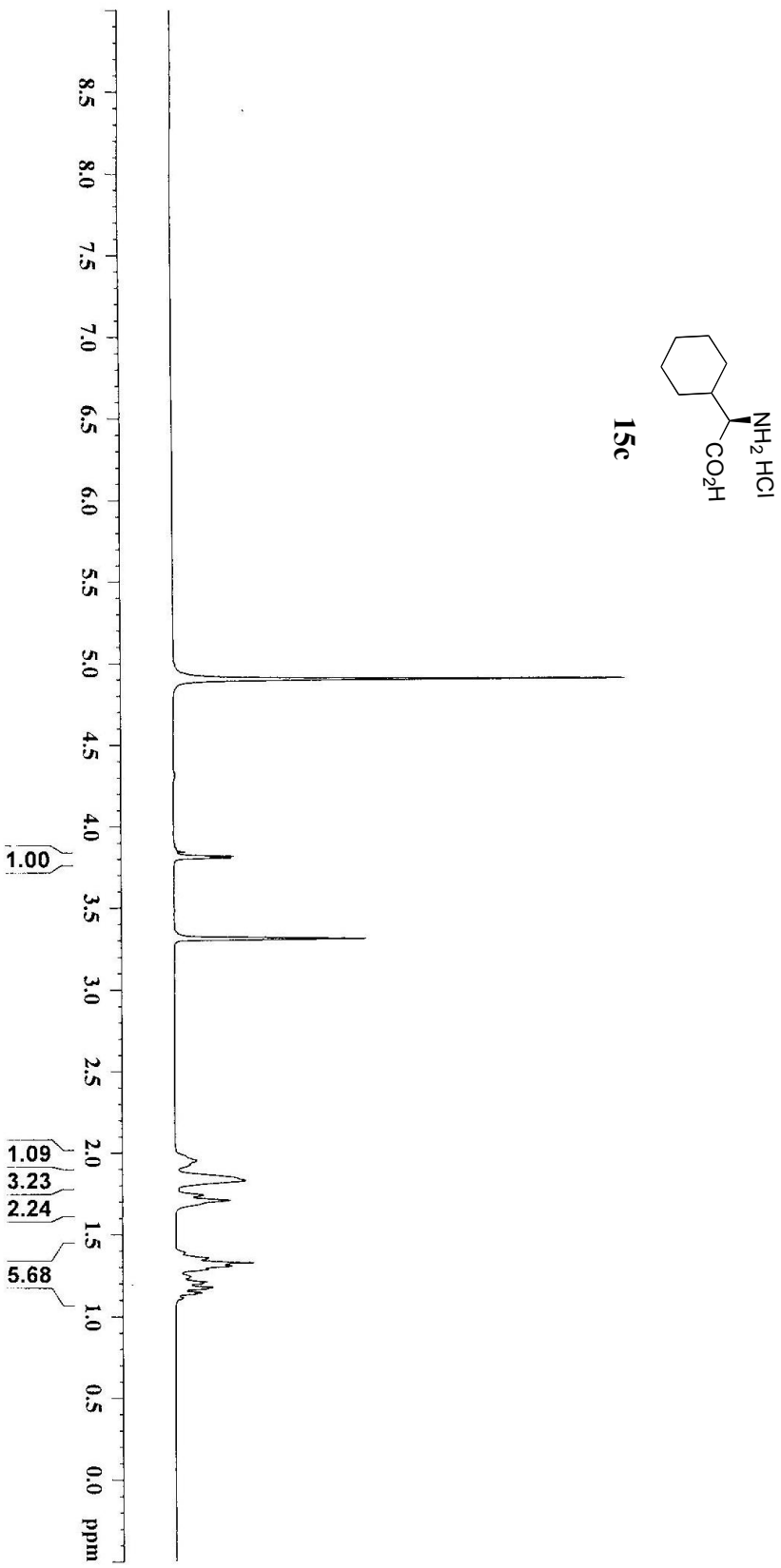
174.318
143.634
133.294
129.780
127.898
81.589
77.546
77.228
76.910
59.079
46.488
46.427
39.974
28.260
27.018
21.708

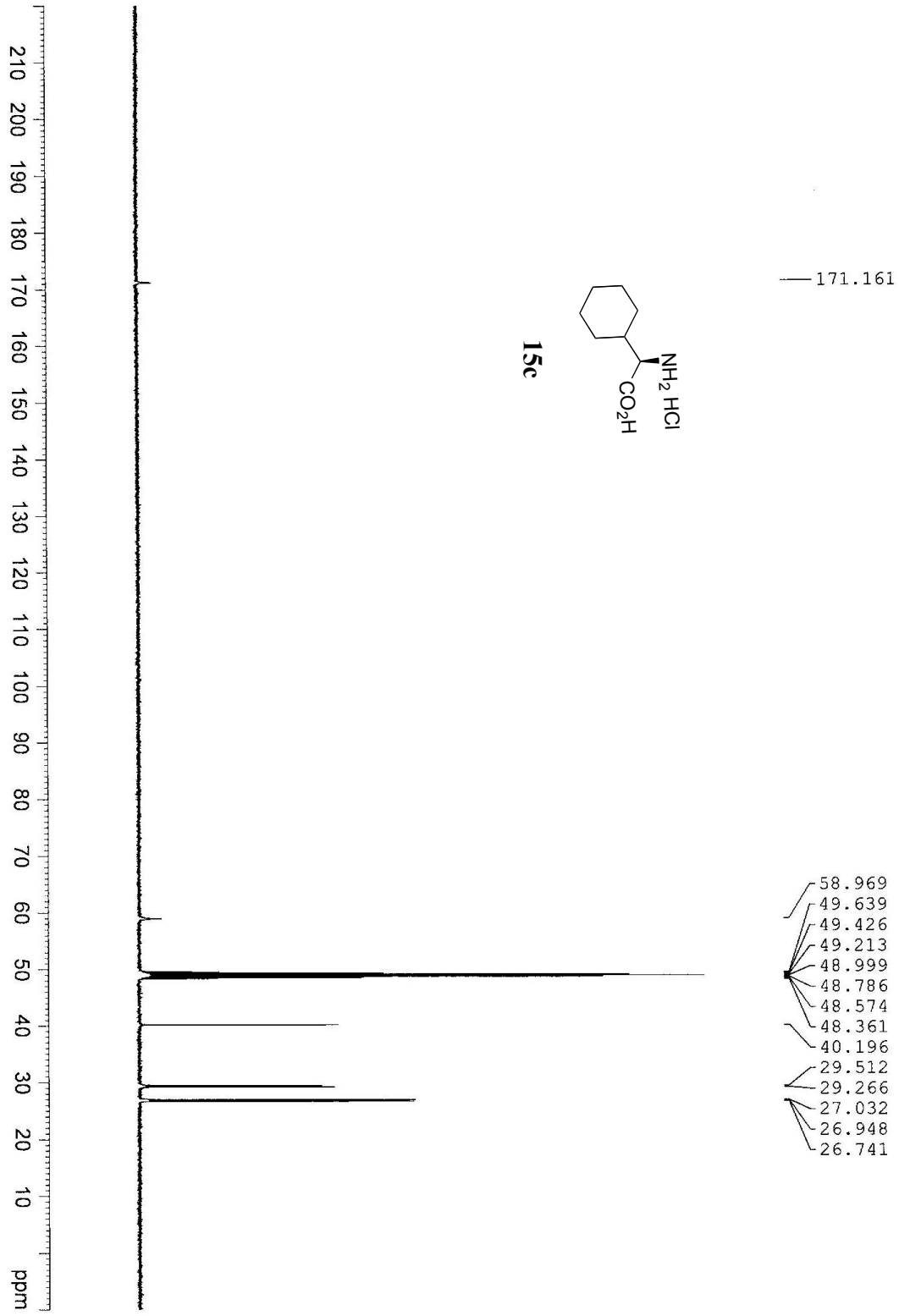
Table 2, entry 12



6l

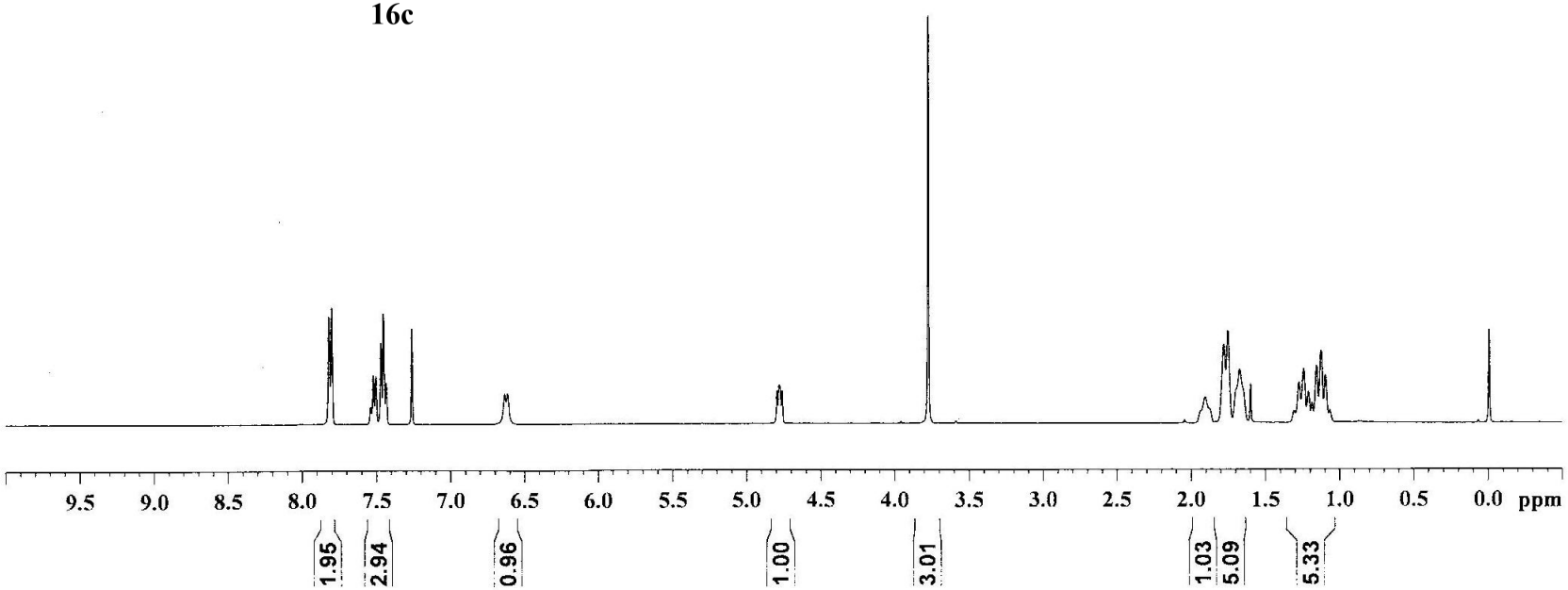


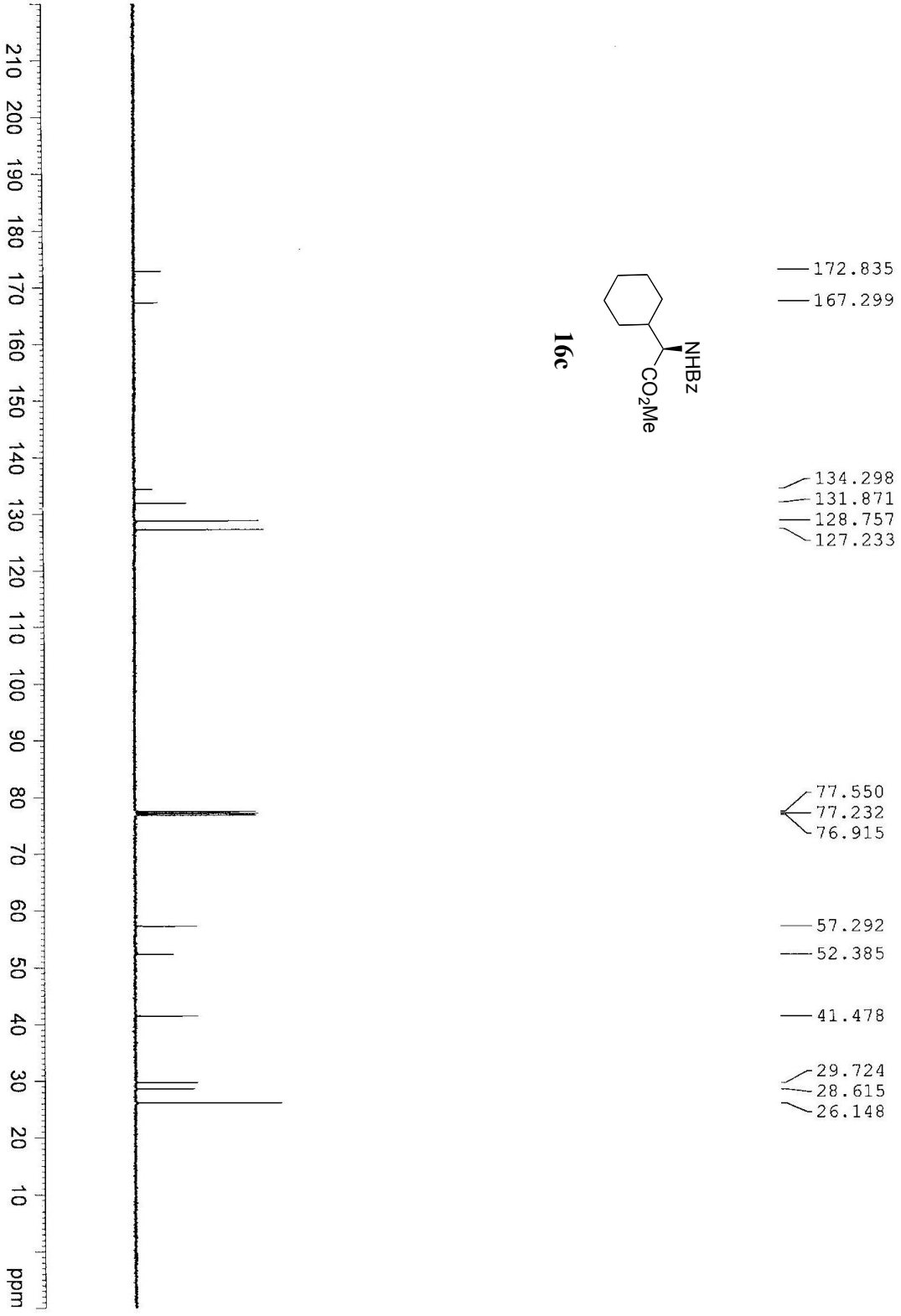

NH2 HCl
CO2H
15c
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.09
3.23
2.24
5.68


171.161
58.969
49.639
49.426
49.213
48.999
48.786
48.574
48.361
40.196
29.512
29.266
27.032
26.948
26.741
NH2 HCl
CO2H
15c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


NHBz
CO2Me

16c


9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.95
2.94
0.96
1.00
3.01
1.03
5.09
5.33


16c
NHBz
CO2Me
172.835
167.299
134.298
131.871
128.757
127.233
77.550
77.232
76.915
57.292
52.385
41.478
29.724
28.615
26.148
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm