Electronic Supplementary Information (ESI)

For

"S_N2 *vs* E2 on quaternary centres: an application to the synthesis of enantiopure $\beta^{2,2}$-amino acids"

submitted to ***Chemical Communications*** by:
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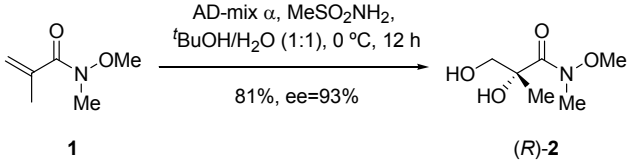
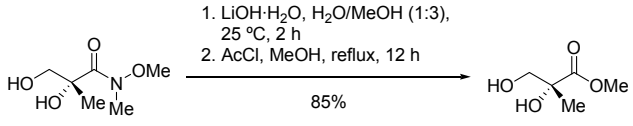
1. (*R*)-2,3-Dihydroxy-*N*-methoxy-2,*N*-dimethylpropionamide. (*R*)-2.



1 (*R*)-**2**

A round-bottomed flask was charged with *tert*-butyl alcohol (80 mL), H_2O (80 mL), AD-mix-α (21.7 g) and methanesulfonamide (1.50 g). The mixture was stirred at 25ºC until both phases are clear, and then cooled to 0ºC, whereupon the inorganic salts partially precipitated. Olefin **1** (2.00 g, 15.5 mmol) was added and the heterogeneous slurry was vigorously stirred at 0ºC for 12 h. The reaction was quenched at 0ºC by addition of sodium sulphite (23.20 g) and then stirred for 1 h. The reaction mixture was extracted with ethyl acetate (3×30 mL) and then dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexane/ethyl acetate, 3:7) to give compound (*R*)-**2** as a colourless oil (2.05 g, 12.5 mmol); yield: 81%. $[\alpha]^{25}_D$ =+4.7 (*c* 1.80, MeOH); ^{1}H NMR ($CDCl_3$): δ 1.38 (s, 3H, CH_3), 3.31 (s, 3H, NCH_3), 3.63 (d, 1H, *J*=11.4 Hz, CH_2OH), 3.76 (s, 3H, $NOCH_3$), 3.93 (d, 1H, *J*=11.4 Hz, CH_2OH); ^{13}C NMR ($CDCl_3$): δ 21.8 (CH_3), 34.0 (NCH_3), 61.4 ($NOCH_3$), 68.0 (CH_2OH), 76.2 (*C*OH(CH_3)), 174.8 (CON); ESI$^+$ (*m*/*z*) = 164. Anal. calcd. for $C_6H_{13}NO_4$: C, 44.16; H, 8.03; N, 8.58. Found: C, 44.01; H, 8.00; N, 8.56.

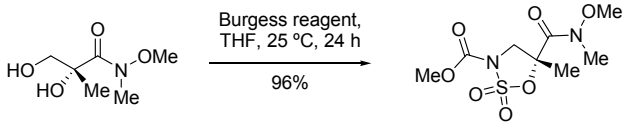
2. Methyl (*R*)-2,3-dihydroxy-2-methylpropanoate. (*R*)-3.



(*R*)-**2** (*R*)-**3**

To a solution of compound (*R*)-**2** (8.60 g, 52.7 mmol) in H_2O/MeOH (1:3, 120 mL), LiOH·H_2O (11.1 g, 264 mmol) was added and the mixture was stirred at room temperature for 2 h. The *N*,*O*-dimethylhydroxylamine formed in the reaction and MeOH were removed and the mixture was acidified with conc. HCl to pH 1-2. After removing the solvent, the white solid was dissolved in HCl/MeOH, previously prepared by dropwise addition of AcCl (30 mL) to a pre-cooled MeOH (120 mL) at 0ºC, and the mixture was heated under reflux for 12 h. The mixture was concentrated and the residue partitioned between H_2O (50 mL) and $CHCl_3$/isopropanol (3:1, 100 mL). The aqueous layer was successively washed with $CHCl_3$/isopropanol (4×100 mL), dried (Na_2SO_4), concentrated and the crude product was purified by column chromatography (hexane/ethyl acetate, 3:7) to give (*R*)-**3** as a Colourless oil (5.98 g, 44.6 mmol); yield: 85%. $[\alpha]_D^{25}$=–1.0 (c 2.66, MeOH). ^{1}H NMR ($CDCl_3$): δ 1.35 (s, 3H, CH_3), 3.57 (d, 1H, *J*=11.2 Hz, CH_2), 3.80 (d, 1H, *J*=11.2 Hz, CH_2), 3.81 (s, 3H, CO_2CH_3). ^{13}C NMR ($CDCl_3$): δ 21.9 (CH_3), 53.1 (CO_2CH_3), 68.3 (CH_2), 75.6 (*C*OH(CH_3)), 176.1 (CO_2CH_3) ; ESI$^+$ (*m*/*z*) =135. Anal. calcd for $C_5H_{10}O_4$: C, 44.77; H, 7.51. Found: C, 44.61; H, 7.45.

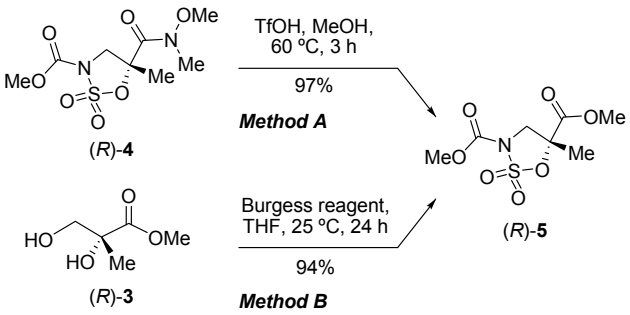
3. Methyl (*R*)-5-(methoxymethylcarbamoyl)-5-methyl-2,2-dioxo-2λ^6-[1,2,3]oxathiazolidine-3-carboxylate. (*R*)-4.



(*R*)-**2** (*R*)-**4**

Diol (*R*)-**2** (3.00 g, 18.4 mmol) was dissolved in THF (50 mL) and Burgess reagent (11.0 g, 46.0 mmol) was added. The resultant solution was stirred at 25ºC for 24 h, concentrated and then purified by column chromatography ($CHCl_3$/ethyl acetate, 9.5:0.5) to give (*R*)-**4** as a white solid (5.00 g, 17.7 mmol); yield: 96%. Mp: 97 ºC. $[\alpha]^{25}_D$ = –67.3 (*c* 0.92, MeOH); ^{1}H NMR ($CDCl_3$): δ 1.84 (s, 3H, CH_3), 3.25 (s, 3H, NCH_3), 3.78 (s, 3H, $NOCH_3$), 3.83 (d, 1H, *J*=10.4 Hz, CH_2N), 3.90 (s, 3H, OCH_3), 4.81 (d, 1H, *J*=10.4 Hz, CH_2N); ^{13}C NMR ($CDCl_3$): δ 21.9 (CH_3), 33.3 (NCH_3), 53.5 (CH_2N), 54.7 ($NOCH_3$), 61.5 (OCH_3), 85.3 (*C*O(CH_3)), 150.0 (NCO_2), 166.2 (CON); ESI$^+$ (*m*/*z*) = 283. Anal. calcd. for $C_8H_{14}N_2O_7S$: C, 34.04; H, 5.00; N, 9.92. Found: C, 34.30; H, 4.98; N, 9.96.

4. Dimethyl (*R*)-5-methyl-2,2-dioxo-2λ^6-[1,2,3]oxathiazolidine-3,5-dicarboxylate. (*R*)-5.

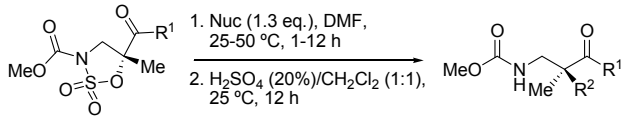


(*R*)-**4** (*R*)-**3** (*R*)-**5**

Method A: To a solution of (*R*)-**4** (2.50 g, 8.9 mmol) in MeOH, TfOH (6.65 g, 44.3 mmol) was added. After stirring for 3 h at 60ºC, the mixture was cooled to 25ºC, neutralized with saturated $NaHCO_3$ and then concentrated. Finally, the crude product was purified by column chromatography (hexane/ethyl acetate, 6:4) to give (*R*)-**5** as a white solid (2.19 g, 8.6 mmol); yield: 97%.

Method B: Diol (*R*)-**3** (0.71 g, 5.3 mmol) was dissolved in THF (60 mL) and Burgess reagent (2.59 g, 13.2 mmol) was added. The resultant solution was stirred at 25ºC for 24 h, concentrated and then purified by column chromatography (hexane/ethyl acetate, 6:4) to give (*R*)-**5** as a white solid (1.27 g, 5.0 mmol); yield: 94%. $[\alpha]^{25}_D$ = –45.0 (*c* 1.00, MeOH); ^{1}H NMR ($CDCl_3$): δ 1.82 (s, 3H, CH_3), 3.88 (s, 3H, OCH_3), 3.91 (d, 1H, *J*=10.3 Hz, CH_2N), 3.92 (s, 3H, OCH_3), 4.58 (d, 1H, *J*=10.3 Hz, CH_2N); ^{13}C NMR ($CDCl_3$): δ 22.8 (CH_3), 53.1 (CH_2N), 53.9 (OCH_3), 54.8 (OCH_3), 83.4 (*C*O(CH_3)), 149.9 (NCO_2), 168.3 (CO_2CH_3); ESI$^+$ (*m*/*z*) = 254. Anal. calcd. for $C_7H_{11}NO_7S$: C, 33.20; H, 4.38; N, 5.53. Found: C, 33.60; H, 4.39; N, 5.51.

5. General procedure for the ring opening of sulfamidates (*R*)-4 and (*R*)-5.



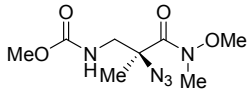
(*R*)-**4** or (*R*)-**5**

(*S*)-**6** to (*S*)-**9**, (*R*)-**10**

(*R*)-**4**: R^1 = N(OMe)Me
(*R*)-**5**: R^1 = OMe

The sulfamidate (1.0 eq.) and nucleophile (1.3 eq.) were heated in DMF at 25-50ºC for 1-12 h, when consumption of sulfamidate was observed by TLC. The solution was then cooled, the solvent removed and the residue solved into a mixture of 20% H_2SO_4/CH_2Cl_2 (1:1) and stirred for 12 h to hydrolize the sulfamic acid intermediate. The desired S_N2 products were isolated after extraction with EtOAc and purification by column chromatography.

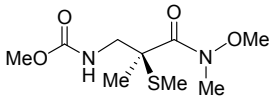
5.1. Methyl (*S*)-2-azido-2-(methoxymethylcarbamoyl)propylcarbamate. (*S*)-6.



(*S*)-**6**

Colourless oil; yield: 86%. $[\alpha]^{25}_D$ = –78.5 (*c* 1.01, MeOH); ^{1}H NMR ($CDCl_3$): δ 1.55 (s, 3H, CH_3), 3.21 (s, 3H, NCH_3), 3.51-3.57 (m, 2H, CH_2N), 3.66 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 5.31 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 18.2 (CH_3), 33.3 (NCH_3), 47.9 (CH_2N), 52.1 (OCH_3), 60.7 (OCH_3), 66.5 ($CN_3(CH_3)$), 157.2 (NCO_2), 170.9 (CON); ESI$^+$ (*m*/*z*) = 246. Anal. calcd. for $C_8H_{15}N_5O_4$: C, 39.18; H, 6.17; N, 28.56. Found: C, 38.90; H, 6.15; N, 28.51.

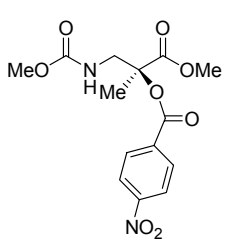
5.2. Methyl (*S*)-2-(methoxymethylcarbamoyl)-2-(methylsulfanyl)propylcarbamate. (*S*)-7.



(*S*)-**7**

Colourless oil; yield: 93%. $[\alpha]^{25}_D$ = –3.5 (*c* 1.0, MeOH); ^{1}H NMR ($CDCl_3$): δ 1.56 (s, 3H, CH_3), 2.04 (s, 3H, SCH_3), 3.25 (s, 3H, NCH_3), 3.51-3.66 (m, 2H, CH_2N), 3.65 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 5.25-5.35 (m, 1H NH); ^{13}C NMR ($CDCl_3$): δ 12.2 (SCH_3), 20.0 (CH_3), 34.0 (NCH_3), 48.3 (CH_2N), 52.0 (OCH_3), 60.7 (OCH_3), 68.1 ($C(SCH_3)CH_3$), 157.4 (NCO_2), 172.4 (CON); ESI$^+$ (*m*/*z*) = 251. Anal. calcd. for $C_9H_{18}N_2O_4S$: C, 43.18; H, 7.25; N, 11.19. Found: C, 42.90; H, 7.23; N, 11.16.

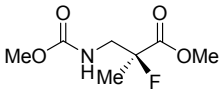
5.3. Methyl (*S*)-2-(methoxycarbonylaminomethyl)-2-(4'-nitrobenzoyloxy)propanoate. (*S*)-8.



(*S*)-**8**

Colourless oil; yield: 99%. $[\alpha]^{25}_D$ = +11.6 (*c* 0.99, MeOH); ^{1}H NMR ($CDCl_3$): δ 1.78 (s, 3H, CH_3), 3.18 (s, 3H, CH_3O), 3.51-3.68 (m, 5H, CH_2N, CH_3O), 5.38 (br s, 1H, NH), 8.20-8.32 (m, 4H, Arom.); ^{13}C NMR ($CDCl_3$): δ 20.3 (CH_3), 46.6 (CH_2N), 52.5 (OCH_3), 52.9 (OCH_3), 81.3 ($CO(CH_3)$), 123.6, 131.0, 135.0, 150.8 (Arom.), 157.2 (NCO_2), 163.6, 170.7 ($2CO_2$); ESI$^+$ (*m*/*z*) = 341. Anal. calcd. for $C_{14}H_{16}N_2O_8$: C, 49.41; H, 4.74; N, 8.23. Found: C, 49.57; H, 4.77; N, 8.38.

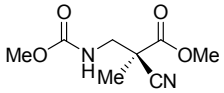
5.4. Methyl (*S*)-2-fluoro-2-(methoxycarbonylaminomethyl)-2-methylpropanoate. (*S*)-9.



(*S*)-**9**

Colourless oil; yield: 97%. $[\alpha]^{25}_D$ = +13.9 (*c* 0.99, MeOH); ^{1}H NMR ($CDCl_3$): δ 1.55 (d, 3H, $J_{H,F}$ = 21.6 Hz, CH_3), 3.42-3.75 (m, 2H, CH_2N), 3.65 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 5.08 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 20.8 (d, $J_{C,F}$ =23.2 Hz, CH_3), 47.1 (d, $J_{C,F}$ = 22.3 Hz, CH_2N), 52.5 (OCH_3), 52.9 (OCH_3), 94.4 (d, $J_{C,F}$ = 183.9 Hz, $CF(CH_3)$), 157.0 (NCO_2), 170.8 (d, $J_{C,F}$ = 25.5 Hz, CO_2CH_3); ESI$^+$ (*m*/*z*) = 194. Anal. calcd. for $C_7H_{12}FNO_4$: C, 43.52; H, 6.26; N, 7.25. Found: C, 43.60; H, 6.35; N, 7.17.

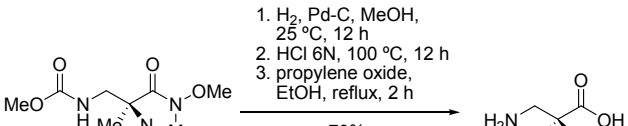
5.5. Methyl (*R*)-2-cyano-2-(methoxycarbonylaminomethyl)-2-methylpropanoate. (*R*)-10.



(*R*)-**10**

Colourless oil; yield: 96%. $[\alpha]^{25}_D$ = –8.2 (*c* 1.57, MeOH); ^{1}H NMR ($CDCl_3$): δ 1.57 (s, 3H, CH_3), 3.55-3.77 (m, 5H, CH_2 + NCO_2CH_3), 3.81 (s, 3H, CO_2CH_3), 5.37 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 20.4 (CH_3), 45.0 (CCH_3), 46.7 (CH_2), 52.5 (NCO_2CH_3), 53.7 (CO_2CH_3), 118.5 (CN), 156.9 (NCO), 168.4 (CO); ESI$^+$ (*m*/*z*) = 200. Anal. calcd. for $C_8H_{12}N_2O_4$: C, 48.00; H, 6.04; N, 13.99. Found: C, 48.60; H, 6.10; N, 13.87.

6. (*S*)-2,3-Diamino-2-methylpropionic acid. (*S*)-11.

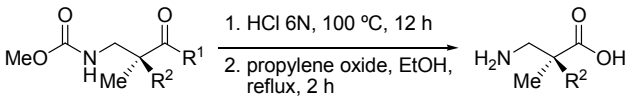


(*S*)-**6** (*S*)-**11**

To a solution of (*S*)-**6** (2.00 g, 8.16 mmol) in MeOH (40 mL), palladium on carbon (1:5 catalyst/substrate by weight) was added and the resulting suspension was stirred at 25ºC for 12 h. The catalyst was removed by filtration and the solvent was evaporated to give the corresponding amine. To this compound, an aqueous solution of 6N HCl (20 mL) was added and the mixture was heated under reflux for 12 h. The solvent was removed to give (*S*)-**11** as hydrochloride derivative (white solid). This compound was dissolved in EtOH/propylene oxide (3:1, 4 mL) and the mixture was heated under reflux for 2 h. After this time, (*S*)-**11**

partially precipitated as a white solid (330 mg). The filtrate was concentrated and the residue was dissolved in H_2O and eluted through a C_{18} reverse-phase Sep-pak cartridge to give, after removal of the H_2O, 344 mg of (*S*)-**11** as a white solid; total amount (674 mg, 5.70 mmol); yield: 70%. $[\alpha]^{25}_D$ = +3.2 (*c* 0.93, H_2O); ^{1}H NMR (D_2O): δ 1.54 (s, 3H, CH_3), 3.26 (d, 1H, *J*=13.2 Hz, CH_2N), 3.36 (d, 1H, *J*=13.2 Hz, CH_2N); ^{13}C NMR (D_2O): δ 22.6 (CH_3), 45.7 (CH_2N), 59.5 ($CNH_2(CH_3)$), 176.3 (CO_2H); ESI$^+$ (*m*/*z*) = 119. Anal. calcd. for $C_4H_{10}N_2O_2$: C, 40.67; H, 8.53; N, 23.71. Found: C, 40.21; H, 8.52; N, 23.66.

7. General procedure for the synthesis of β-amino acids (*S*)-12 to (*S*)-14.

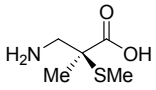


(*S*)-**7** to (*S*)-**9** (*S*)-**12** to (*S*)-**14**

(*S*)-**7**: R^1 = N(OMe)Me
(*S*)-**8**, (*S*)-**9**: R^1 = OMe

Compound (*S*)-**7**, (*S*)-**8** or (*S*)-**9** (1.0 eq.) was suspended in an aqueous solution of 6N HCl (15 mL) and the mixture was heated under reflux for 12 h. The solvent was removed to give the corresponding hydrochloride as a white solid. The treatment of this mixture with ethanol/propylene oxide gave the desired β-amino acid as a white solid.

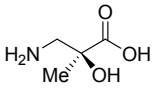
7.1. (*S*)-3-Amino-2-methyl-2-methylsulfanylpropionic acid. (*S*)-12.



(*S*)-**12**

Yield: 81%. $[\alpha]^{25}_D$ = –2.6 (*c* 0.97, H_2O); ^{1}H NMR (D_2O): δ 1.48 (s, 3H, CH_3), 2.06 (s, 3H, SCH_3), 3.22-3.35 (m, 2H, CH_2N); ^{13}C NMR (D_2O): δ 11.7 (SCH_3), 22.0 (CH_3), 44.9 (CH_2N), 51.6 ($CSCH_3(CH_3)$), 178.1 (CO_2H); ESI$^+$ (*m*/*z*) = 150. Anal. calcd. for $C_5H_{11}NO_2S$: C, 40.25; H, 7.43; N, 9.39. Found: C, 40.12; H, 7.42; N, 9.37.

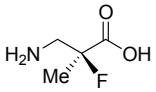
7.2. (*S*)-3-Amino-2-hydroxy-2-methylpropionic acid. (*S*)-13.



(*S*)-**13**

Yield: 85%. $[\alpha]^{25}_D$ = +2.8 (*c* 1.01, H_2O); ^{1}H NMR (D_2O): δ 1.51 (s, 3H, CH_3), 3.21 (d, 1H, *J* = 13.2 Hz, CH_2N), 3.38 (d, 1H, *J* = 13.2 Hz, CH_2N); ^{13}C NMR (D_2O): δ 23.6 (CH_3), 46.7 (CH_2N), 72.9 ($COH(CH_3)$), 179.4 (CO_2H); ESI$^+$ (*m*/*z*) = 120. Anal. calcd. for $C_4H_9NO_3$: C, 40.33; H, 7.62; N, 11.76. Found: C, 40.24; H, 7.64; N, 11.69.

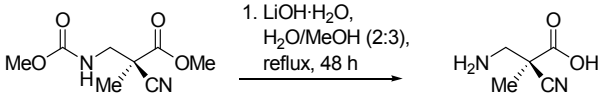
7.3. (*S*)-3-Amino-2-fluoro-2-methylpropionic acid. (*S*)-14.



(*S*)-**14**

Yield: 83%. $[\alpha]^{25}_D$ = –1.4 (*c* 1.00, H_2O); ^{1}H NMR (D_2O): δ 1.54 (d, 3H, $J_{H,F}$ = 21.9 Hz, CH_3), 3.22-3.52 (m, 2H, CH_2N); ^{13}C NMR (D_2O): δ 23.5 (d, $J_{C,F}$ = 23.7 Hz, CH_3), 47.5 (d, $J_{C,F}$ = 23.8 Hz, CH_2N), 96.1 (d, $J_{C,F}$ = 181.3 Hz, $CF(CH_3)$), 178.2 (d, $J_{C,F}$ = 20.9 Hz, CO_2H); ESI$^+$ (*m*/*z*) = 122. Anal. calcd. for $C_4H_8FNO_2$: C, 39.67; H, 6.66; N, 11.57. Found: C, 39.48; H, 6.64; N, 11.55.

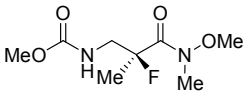
8. (*R*)-2-(Aminomethyl)-2-cyanopropanoic acid. (*R*)-15.



(*R*)-**10** (*R*)-**15**

To a solution of compound (*R*)-**10** (0.16 g, 0.80 mmol) in H_2O/MeOH (2:3, 10 mL), LiOH·H_2O (0.34 g, 8.00 mmol) was added and the mixture was stirred at reflux for 48 h. This mixture was cooled, H_2O was added (20 mL) and the resulting solution was treated with Dowex® H^+ until pH=7. After filtering, the solution was evaporated to give a white solid (0.10 g, 98%), corresponding to β-amino acid (*R*)-**15**. Another exhaustive purification was developed involving the treatment of a solution of the amino acid (10 mL of H_2O) with an aqueous solution of 0.5 N HCl (until pH 1–2). This aqueous solution was washed with ethyl acetate (2×15 mL), the solvent was eliminated and the residue was solved in a mixture of ethanol/propylene oxide (3:1, 2 mL). After refluxing this mixture for 2 h and filtering the solid, the desired β-amino acid (*R*)-**15** was obtianed as a white solid (0.03 g, 29%). The filtrate was concentrated and the residue was dissolved in H_2O and eluted through a C_{18} reverse-phase Sep-pak cartridge to give, after removal of the H_2O, 0.04 g (36%) of (*R*)-**15** as a white solid. Overall yield of this exhaustive purification: 65%. $[\alpha]^{25}_D$ = –5.5 (*c* 1.06, H_2O); ^{1}H NMR (D_2O): δ 1.52–1.70 (m, 3H, CH_3), 3.35–3.43 (m, 2H, CH_2); ^{13}C NMR (D_2O): δ 23.8 (CH_3), 46.5 (CH_2), 47.6 (CCH_3), 123.0 (CN), 179.9 (CO_2H); ESI$^+$ (*m*/*z*) = 128. Anal. calcd. for $C_5H_8N_2O_2$: C, 46.87; H, 6.29; N, 21.86. Found: C, 46.56; H, 6.21; N, 21.99.

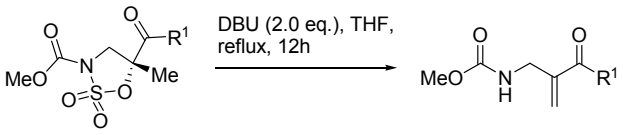
9. Methyl (*S*)-2-Fluoro-2-(methoxymethylcarbamoyl)propylcarbamate. (*S*)-16.



(*S*)-**16**

Following the general procedure for the ring opening of sulfamidates, the treatment of (*R*)-**4** with the nucleophile NBu_4F gave a mixture of compounds (*S*)-**16** (32%) and **17** (68%). Data for (*S*)-**16**: $[\alpha]^{25}_D$ = –12.2 (*c* 1.01, MeOH); ^{1}H NMR ($CDCl_3$): δ 1.59 (d, 3H, $J_{H,F}$ = 21.9 Hz, CH_3), 3.21 (s, 3H, NCH_3), 3.52-3.72 (m, 8H, CH_2N, $2OCH_3$), 5.23 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 20.3 (d, $J_{C,F}$ = 23.0 Hz, CH_3), 47.2 (d, $J_{C,F}$ = 24.9 Hz, CH_2N), 52.2 (OCH_3), 61.5 (OCH_3), 96.1 (d, $J_{C,F}$ = 187.4 Hz, $CF(CH_3)$), 157.2 (NCO_2), 170.1 (CON); ESI$^+$ (*m*/*z*) = 223. Anal. calcd. for $C_8H_{15}FN_2O_4$: C, 43.24; H, 6.80; N, 12.61. Found: C, 43.03; H, 6.78; N, 12.58.

10. General procedure for the synthesis of 17 and 18.



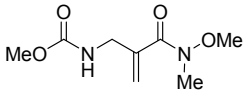
(*R*)-**4** or (*R*)-**5** **17** or **18**

(*R*)-**4**: R^1 = N(OMe)Me
(*R*)-**5**: R^1 = OMe

17: R^1 = N(OMe)Me
18: R^1 = OMe

Sulfamidate (*R*)-**4** or (*R*)-**5** (1.0 eq.) was dissolved in THF and DBU (2.0 eq.) was added. After heating under reflux for 12 h, the mixture was washed with 0.5N HCl. Then, the aqueous phase was extracted with ethyl acetate and concentrated. The crude product was purified by column chromatography (hexane/ethyl acetate, 3:2) to give **17** or **18**.

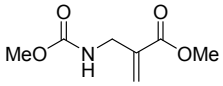
10.1. *N*-Methoxy-*N*-methyl 2-(methoxycarbonylaminomethyl)acrylamide. 17.



17

Colourless oil, yield: 88%. ^{1}H NMR ($CDCl_3$): δ 3.22 (s, 3H, NCH_3), 3.55-3.70 (m, 6H, $2OCH_3$), 3.99 (d, 2H, J = 6.0 Hz, CH_2N), 5.29 (br s, 1H, NH), 5.49 (br s, 1H, CH_2=C), 5.53 (br s, 1H, CH_2=C); ^{13}C NMR ($CDCl_3$): δ 33.4 (NCH_3), 43.6 (CH_2N), 52.1 (OCH_3), 61.2 (OCH_3), 118.8 (*C*H_2=C), 140.4 (CH_2=*C*), 156.9 (NCO_2), 168.9 (CON); ESI$^+$ (*m*/*z*) = 203. Anal. calcd. for $C_8H_{14}N_2O_4$: C, 47.52; H, 6.98; N, 13.85. Found: C, 47.35; H, 6.96; N, 13.85.

10.2. Methyl 2-(methoxycarbonylaminomethyl)acrylate. 18.



18

Colourless oil, yield: 80%. ^{1}H NMR ($CDCl_3$): δ 3.66 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 4.00 (d, 2H, J = 6.3 Hz, CH_2N), 5.16 (br s, 1H, CH_2N), 5.82 (s, 1H, CH_2=C), 6.26 (s, 1H, CH_2=C); ^{13}C NMR ($CDCl_3$): δ 42.2 (CH_2N), 52.0 (OCH_3), 52.2 (OCH_3), 126.9 (*C*H_2=C), 136.8 (CH_2=*C*), 156.8 (NCO_2), 166.6 (COO); ESI$^+$ (*m*/*z*) = 174. Anal. calcd. for $C_7H_{11}NO_4$: C, 48.55; H, 6.40; N, 8.09. Found: C, 48.32; H, 6.41; N, 8.06.

11. General Procedures.

Unless otherwise stated, all starting materials were obtained from commercial suppliers and used without further purification. Melting points are uncorrected. All manipulations involving air-sensitive reagents were carried out under a dry argon atmosphere using standard Schlenk techniques. Solvents were purified according to standard procedures. Analytical TLC was performed using Polychrom SI F_{254} plates. Column chromatography was performed using Kieselgel 60 (230–400 mesh). Organic solutions were dried over anhydrous Na_2SO_4 and, when necessary, concentrated under reduced pressure using a rotary evaporator. NMR spectra were recorded at 300 MHz (^{1}H) and at 75 MHz (^{13}C) and are reported in ppm downfield from TMS. Microanalyses were carried out on a CE Instruments EA-1110 analyser and were in good agreement with the calculated values. Mass spectra were obtained by electrospray ionization (ESI).

12. Determination of the absolute configuration and the enantiomeric purity of β-amino acids.

In the case of known amino acids (*S*)-**11** and (*S*)-**13**, both the absolute configuration and the enantiomeric purity were determined by comparison of the optical rotations with literature values.

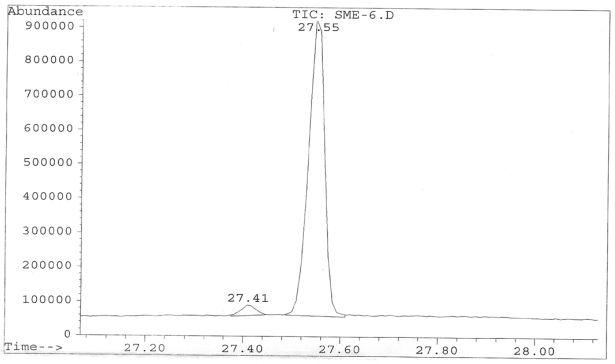
Amino acid	[α]	[α]lit.	Reference
(*S*)-**11**	+3.2	+4.1	*J. Org. Chem.* 1993, **58**, 5918.
(*S*)-**13**	+2.8	+2.9	*Tetrahedron: Asymmetry* 2004, **15**, 131.

In this context, it is important to highlight that in a recent work (*Tetrahedron: Asymmetry* 2004, **15**, 131), the authors have unequivocally established the absolute configuration of β-amino acid (*S*)-**11** and its enantiomer (*R*)-**11** (both obtained by other different synthetic procedures) as well as their enantiomeric purity by transformation in some diastereomeric derivatives, which were analyzed by X-ray diffraction and NMR experiments.

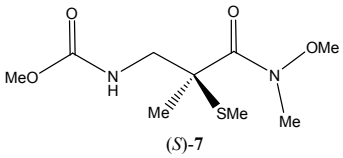
The absolute configuration for the rest of the amino acids synthesized was assigned by applying the same model: creation of the stereogenic centre in the AD reaction followed by total inversion of the configuration in the S_N2 reaction.

A GC/MS system of a gas chromatograph combined with a mass spectrometer (Hewlett-Packard G1800B GCD Plus) was used with α- or γ-DEX^{TM} – 120 fused silica capillary columns (30 m × 0.25 mm × 0.25 μm) in order to determine the enantiomeric purity of β-amino acid precursors (*S*)-**7** and (*S*)-**9**. Conditions as follows: GC/MS injector and detector temperatures were 225 °C, flow rate 1.00 mL min^{-1}, split mode. Injection volume, 2.0 μL of a solution of about 15 mg mL^{-1} of the mixture in dichloromethane. Helium was used as the carrier gas. The MS were determined at 70 eV. Scanning speed was 0.84 scan sec^{-1} from *m/z* 33 to 450. Oven temperature for (*S*)-**9** was isocratic 125 °C using α-DEX^{TM} capillary column. In the case of (*S*)-**7**, the temperature program for the column oven was 150 °C for 23.5 min, a linear ramp to 220 ºC at 20 ºC/min and an 8 min held, using γ-DEX^{TM} capillary column. Unfortunately, the enantiomeric purity of the β-amino acid precursor (*R*)-**10** could not be measured by this method since in all conditions tested we did not get the separation. Alternatively, the enantiomeric purity of the sulfamidate (*R*)-**5** was determined as follows: the temperature program for the column oven was 90 °C for 97 min, a linear ramp to 140 ºC at 20 ºC/min and a 15 min held, using α-DEX^{TM} capillary column. Figure ESI-1 shows the chromatograms and the corresponding area percent reports, indicating the enantiomeric excess for each compound (approx. 93%).

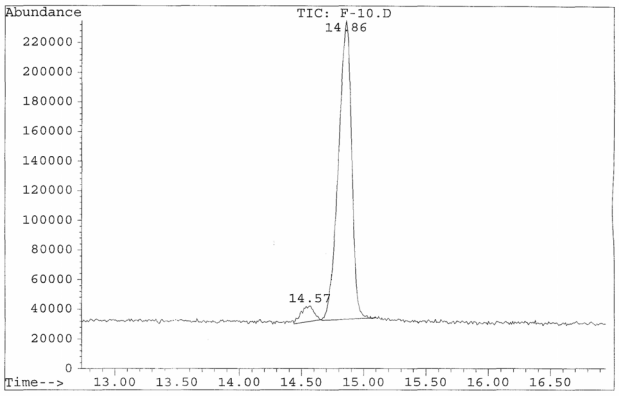
Figure ESI-1. Chromatograms and area percent reports corresponding to compounds (*S*)-**7,** (*S*)-**9** and (*R*)-**5**.



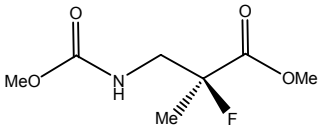
Retention Time	Area	Area %	Ratio %	Type	Width
Total Ion Chromatogram					
27.411	656045	3.160	3.263	M	0.035
27.550	20104033	96.840	100.000	M	0.038



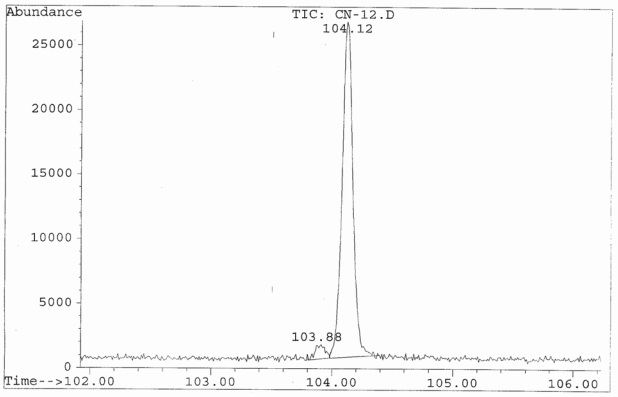
(*S*)-**7**



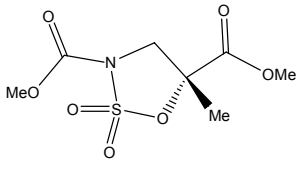
Retention Time	Area	Area %	Ratio %	Type	Width
Total Ion Chromatogram					
14.571	731538	4.578	4.798	M	0.119
14.858	15246635	95.422	100.000	M	0.125



(*S*)-**9**



Retention Time	Area	Area %	Ratio %	Type	Width
Total Ion Chromatogram					
103.879	63614	3.788	3.937	M	0.095
104.119	1615924	96.212	100.000	M	0.103



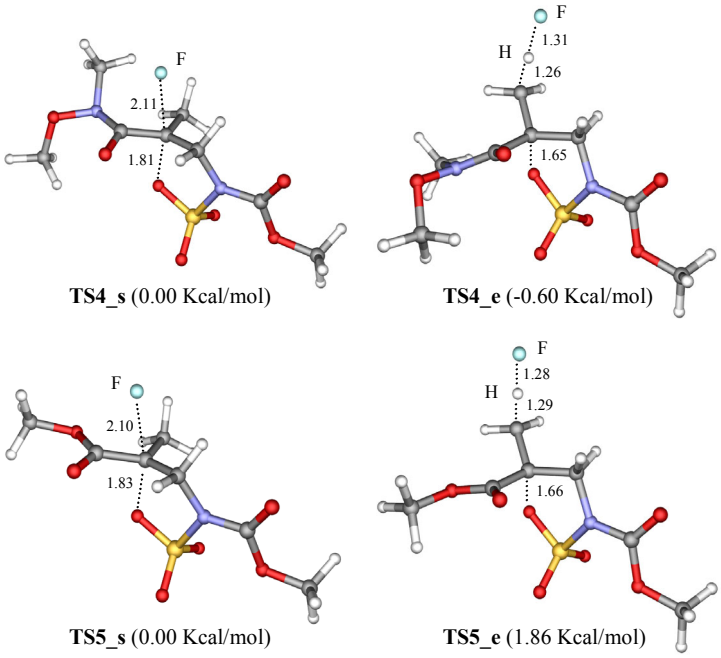
(*R*)-**5**

Table ESI-1. Calculated energies, entropies, Gibbs free energies and lowest frequencies of the reactants and transition structures (B3LYP/6-31+G(d) optimized geometries).

	E_0(B3LYP/6-31+G(d)) (a.u.)[a]	Lowest freq. (cm^{-1})	S (cal mol^{-1} K^{-1})	G_{298} (B3LYP/6-31+G(d)) (a.u.)	E_{basis} (B3LYP/6-311++G(2d,p)) (a.u.)
F^-	-99.8596977	-	34.768	-99.8738567	-99.8886932
4	-1347.4476052	26.02	147.835	-1347.252726	-1347.7711283
5	-1252.8459231	27.75	135.836	-1252.692234	-1253.1447859
TS4_s	-1447.3535115	389.87i	151.946	-1447.159968	-1447.7088730
TS4_e	-1447.3464824	469.04i	157.026	-1447.159567	-1447.7031930
TS5_s	-1352.7573902	392.17i	140.372	-1352.605239	-1353.0876126
TS5_e	-1352.7461679	606.13i	144.025	-1352.600266	-1353.0783935

[a] 1 a.u. = 627.5 kcal mol^{-1}

Figure ESI-2. TS calculated with (*R*)-**4** and (*R*)-**5** and fluoride anion. Distances are given in Å. In brackets the relative energies calculated at theB3LYP/6-311++G(2d,p)//B3LYP/6-31+G(d) level.



TS4_s (0.00 Kcal/mol) **TS4_e** (-0.60 Kcal/mol)

TS5_s (0.00 Kcal/mol) **TS5_e** (1.86 Kcal/mol)

B3LYP/6-31+G (d) geometries

4

C	-0.83766	-1.05243	0.87373	C -3.14684	-0.66486	-1.18654
C	0.48915	-0.66648	1.54931	O -3.55490	1.38472	-0.12324
O	-0.43406	-1.55266	-0.44223	C 2.50566	0.53156	0.71370
C	-1.54324	-2.20035	1.59212	C -2.97772	2.61117	-0.60490
C	-1.78164	0.19126	0.81027	O 2.89719	0.78073	1.83512
N	1.30394	-0.12268	0.46142	O 3.12438	0.84223	-0.43342
S	0.88552	-0.78349	-1.06743	C 4.39318	1.51594	-0.30540
N	-2.64829	0.32132	-0.23734	H 0.33559	0.09872	2.30862
O	-1.71079	1.01399	1.71718	H 0.96800	-1.54902	1.98935
O	1.81272	-1.81372	-1.50223	H -2.46972	-2.47823	1.08170
O	0.46586	0.26459	-1.98177	H -1.79227	-1.88613	2.61117

H	-0.88931	-3.07634	1.63483
H	-4.14037	-1.00805	-0.87327
H	-2.45937	-1.50378	-1.25333
H	-3.22486	-0.19652	-2.17199
H	-3.79498	3.33459	-0.55666
H	-2.63431	2.49666	-1.63944
H	-2.15570	2.92884	0.04225
H	4.26083	2.47017	0.20977
H	5.09757	0.88980	0.24732
H	4.73251	1.67076	-1.32906

5

C	0.000000	0.000000	0.000000
N	0.000000	0.000000	1.462214
S	1.584761	0.000000	2.139120
O	2.283366	0.040935	0.648138
C	1.385428	0.550559	-0.377021
C	-1.164263	-0.208128	2.189006
O	-0.909980	-0.210799	3.504289
C	-2.044306	-0.430543	4.367136
O	1.935067	-1.274110	2.738567
O	1.817950	1.246266	2.848283
C	1.898326	0.022808	-1.714875
C	1.386204	2.097792	-0.399806
O	0.408016	2.750725	-0.699556
O	2.591605	2.597697	-0.128604
C	2.700040	4.038484	-0.131730
O	-2.249666	-0.355840	1.663669
H	-0.799472	0.642539	-0.369509
H	-0.129223	-1.016906	-0.387469
H	2.901537	0.407203	-1.917295
H	1.226461	0.342478	-2.518876
H	1.934988	-1.070176	-1.692156
H	3.739856	4.245026	0.118939
H	2.028241	4.462015	0.618318
H	2.448053	4.432946	-1.119272
H	-2.781931	0.363076	4.226932
H	-2.497950	-1.401094	4.152750
H	-1.636437	-0.407657	5.377140

TS4_s

C	0.000000	0.000000	0.000000
C	0.000000	0.000000	1.513247
C	1.355059	0.000000	2.209324
N	1.990180	1.319484	2.027728
C	3.340117	1.456033	2.214410
O	3.730171	2.750006	2.122060
C	5.126771	2.986385	2.308685
C	-1.169211	-0.451802	2.390022
O	-1.117612	-0.323658	3.599581
N	-2.397855	-0.696342	1.720766
C	-2.557742	-1.795128	0.771712
O	-3.477353	-0.821363	2.645018
C	-3.971821	0.468051	2.994465
S	0.873056	2.657436	1.880252
O	-0.379286	1.757172	1.740034
O	1.185017	3.375480	0.639129
O	0.858312	3.432061	3.123657
O	4.108473	0.528221	2.427664
F	0.106007	-2.105999	1.646786
H	0.270954	-0.998079	-0.349335
H	-0.977331	0.288398	-0.393095
H	0.736722	0.721158	-0.365823
H	-4.826210	0.273810	3.651373
H	-4.300680	1.015740	2.100744
H	-3.216070	1.049038	3.532941
H	1.990753	-0.756741	1.754887
H	1.219995	-0.227181	3.267834
H	5.248021	4.066347	2.207436
H	5.714883	2.461756	1.549173
H	5.447177	2.656152	3.301689
H	-2.694436	-2.738477	1.314980
H	-1.662388	-1.893541	0.166849
H	-3.436107	-1.592963	0.148342

TS4_e

S	0.000000	0.000000	0.000000
O	0.000000	0.000000	1.587072
C	1.509191	0.000000	2.244415
C	2.236728	-0.852073	1.206347
N	1.640132	-0.550143	-0.103782
C	1.488231	-0.601297	3.579221
C	1.983627	1.473793	2.197517
N	1.144805	2.433179	2.707181
C	-0.080062	2.324664	3.474761
C	2.274399	-0.879085	-1.276950
O	3.367799	-1.413603	-1.340577
O	-0.922943	-1.020725	-0.495867
O	-0.098743	1.352384	-0.548872
O	3.063054	1.762521	1.695046
O	1.530210	-0.528890	-2.352267
C	2.101198	-0.849093	-3.625039
O	1.674564	3.729960	2.778318
C	1.554163	4.397257	1.513182
F	3.852753	-1.330792	4.286289
H	1.059296	0.037435	4.354397
H	0.992571	-1.577997	3.568008
H	3.296289	-0.598429	1.194278
H	2.117943	-1.911247	1.452910
H	-0.789723	3.076985	3.111771
H	0.116781	2.501439	4.540422
H	-0.515829	1.339223	3.333275
H	3.056468	-0.333187	-3.758968
H	2.257374	-1.928044	-3.717820
H	1.371516	-0.503046	-4.358772
H	1.925102	5.409847	1.697455
H	0.506475	4.432151	1.188900
H	2.167579	3.899504	0.757876
H	2.673286	-0.887464	3.914844

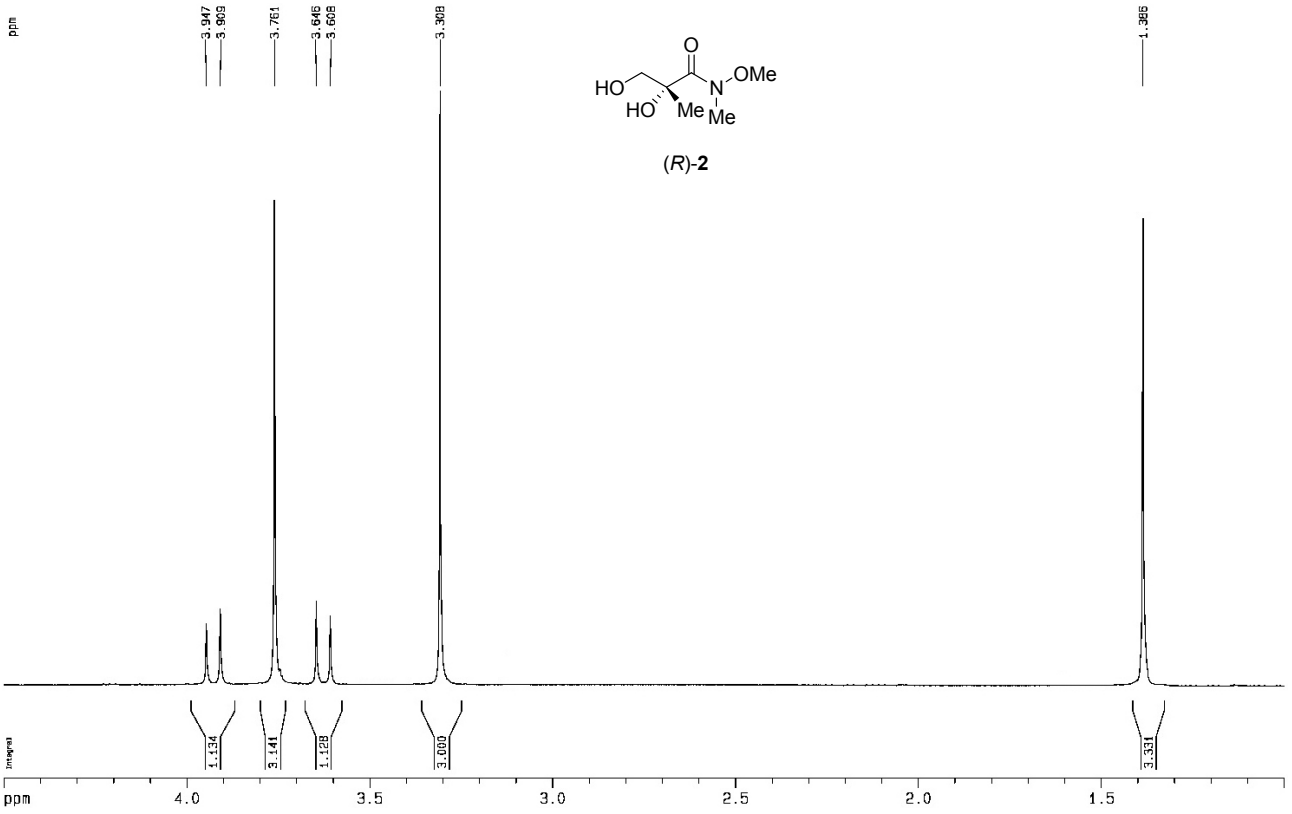
TS5_s

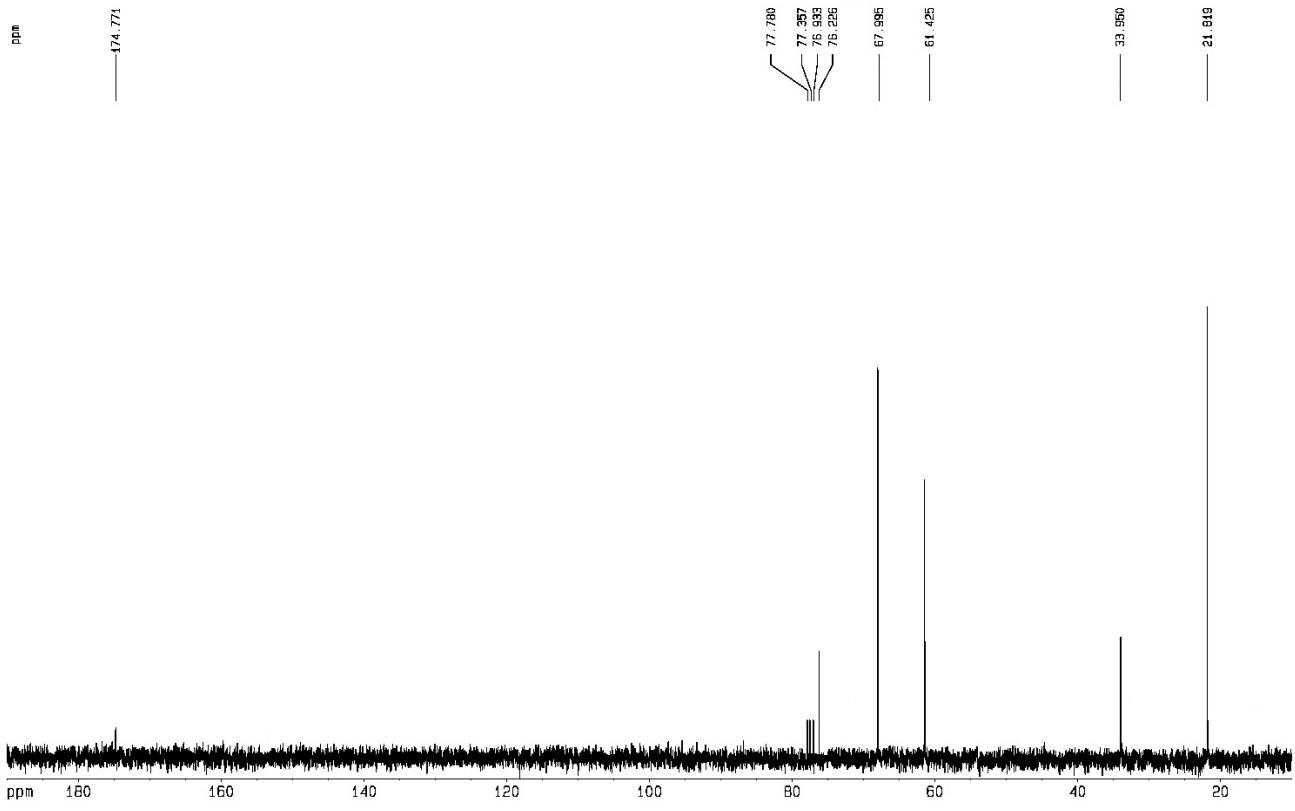
C	0.000000	0.000000	0.000000
C	0.000000	0.000000	1.506153
C	1.351977	0.000000	2.180813
O	1.255229	0.107851	3.528192
C	2.501794	0.150888	4.220109
C	-1.235049	0.511397	2.235183
N	-2.320458	-0.476906	2.088511
S	-1.776611	-2.139614	2.011887
O	-2.004714	-2.786260	3.308588
C	-3.618249	-0.096470	2.305770
O	-3.979488	1.054676	2.509895
O	-4.465251	-1.152067	2.253733
C	-5.843821	-0.846644	2.471379

O	2.393939	-0.249305	1.604096
O	-0.288882	-1.771229	1.802597
O	-2.375067	-2.764443	0.828542
F	0.701561	1.978387	1.676771
H	0.207903	1.020690	-0.328351
H	0.782048	-0.663929	-0.372817
H	-0.971135	-0.329070	-0.380987
H	-1.553973	1.445629	1.778211
H	-1.009747	0.691800	3.286756
H	-6.362279	-1.803996	2.394283
H	-6.211960	-0.149089	1.712601
H	-5.993135	-0.408949	3.463374
H	2.245756	0.235518	5.278758
H	3.084560	1.019791	3.897146
H	3.080755	-0.760590	4.038413

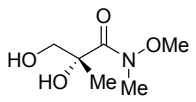
TS5_e

N	0.000000	0.000000	0.000000
S	0.000000	0.000000	1.741964
O	1.576050	0.000000	1.844932
C	2.349489	0.394123	0.424421
C	1.337968	-0.135763	-0.587754
O	-0.542961	-1.263176	2.244342
O	-0.589031	1.248921	2.223132
C	3.663858	-0.219659	0.360527
C	2.380468	1.923916	0.477776
O	1.780171	2.649984	-0.287437
C	-1.126580	-0.086725	-0.777671
O	-2.250803	0.019439	-0.032474
C	-3.480818	-0.066950	-0.757925
O	3.166323	2.375680	1.472059
C	3.264696	3.802624	1.578366
O	-1.115410	-0.238150	-1.988774
F	4.684224	0.360875	-1.927165
H	1.390322	0.444153	-1.509815
H	1.558181	-1.184811	-0.808968
H	4.354152	0.162046	1.115079
H	3.611819	-1.312818	0.377228
H	-3.550920	0.738620	-1.494810
H	-3.561865	-1.031329	-1.268562
H	-4.262869	0.034010	-0.003696
H	3.929147	3.983329	2.424953
H	2.278515	4.239536	1.761343
H	3.684754	4.224257	0.660561
H	4.166713	0.088175	-0.785360

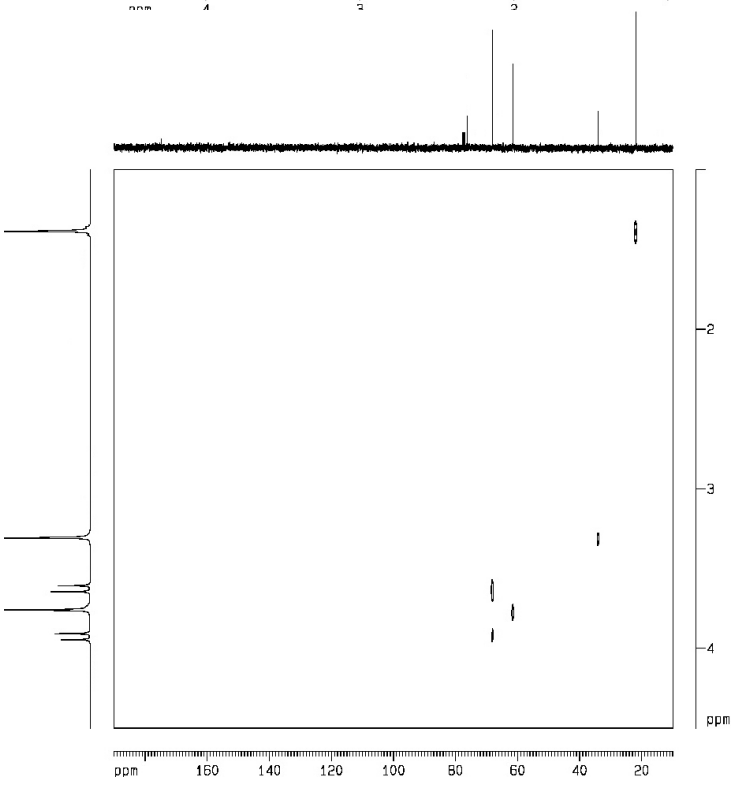

3.947
3.909
3.761
3.646
3.608
3.369
1.365
1.134
3.141
1.128
3.000
3.331
ppm
4.0
3.5
3.0
2.5
2.0
1.5

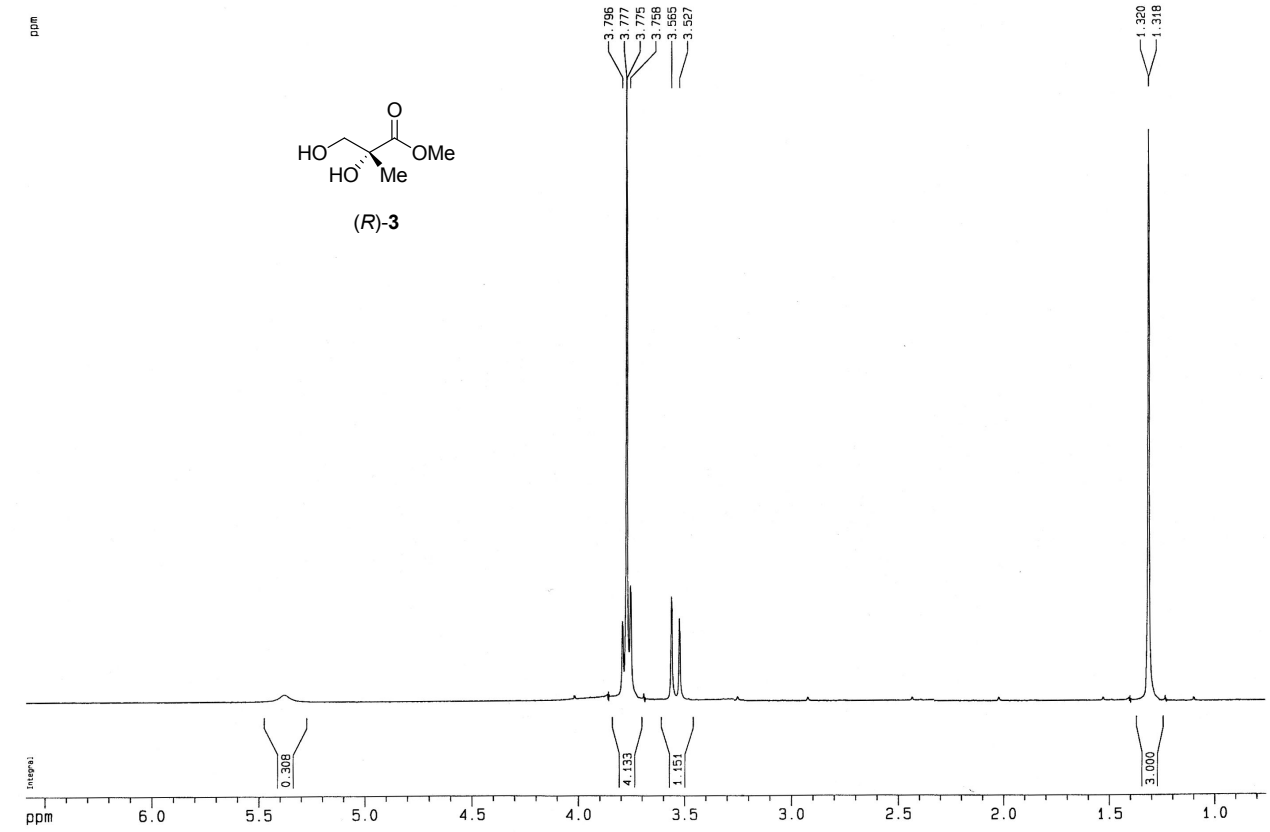

174.771
77.780
77.357
75.933
76.226
67.995
61.425
33.950
21.819
ppm
180
160
140
120
100
80
60
40
20

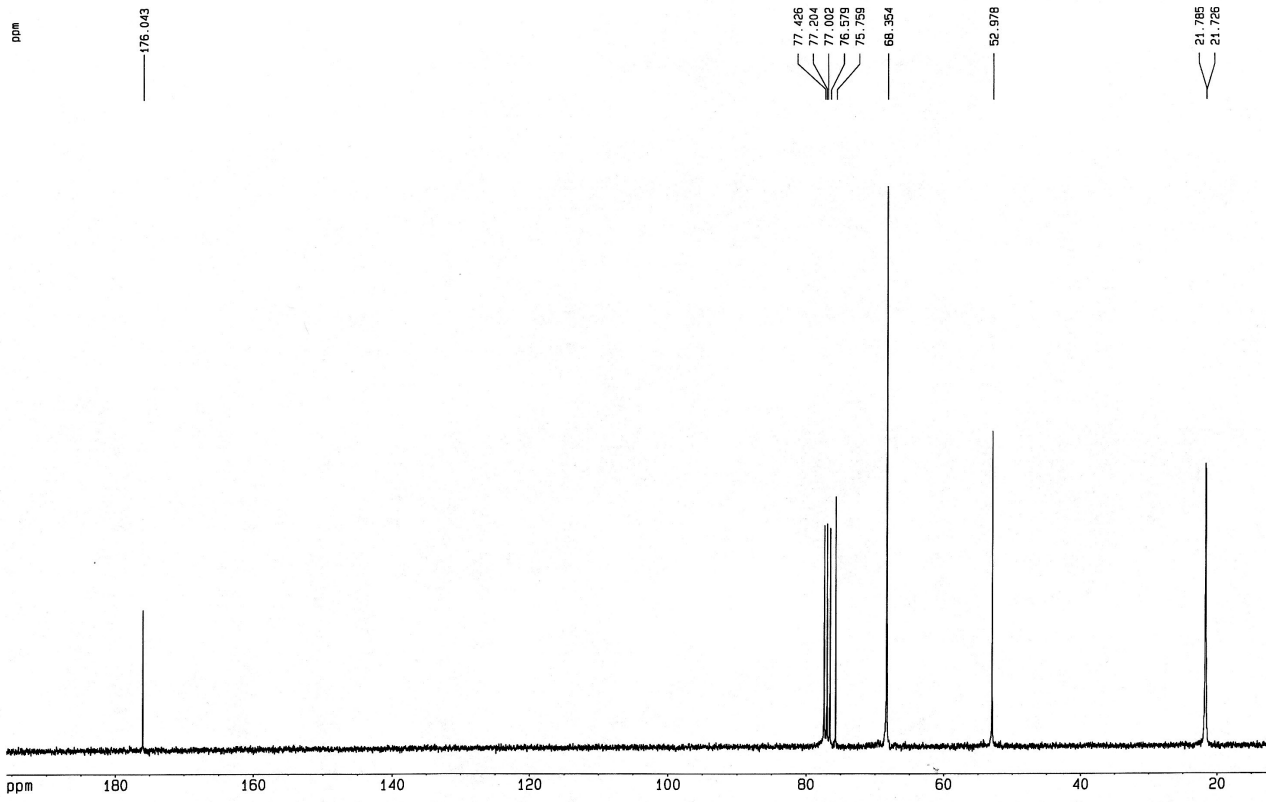
(*R*)-**2**

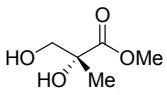


(*R*)-**2**

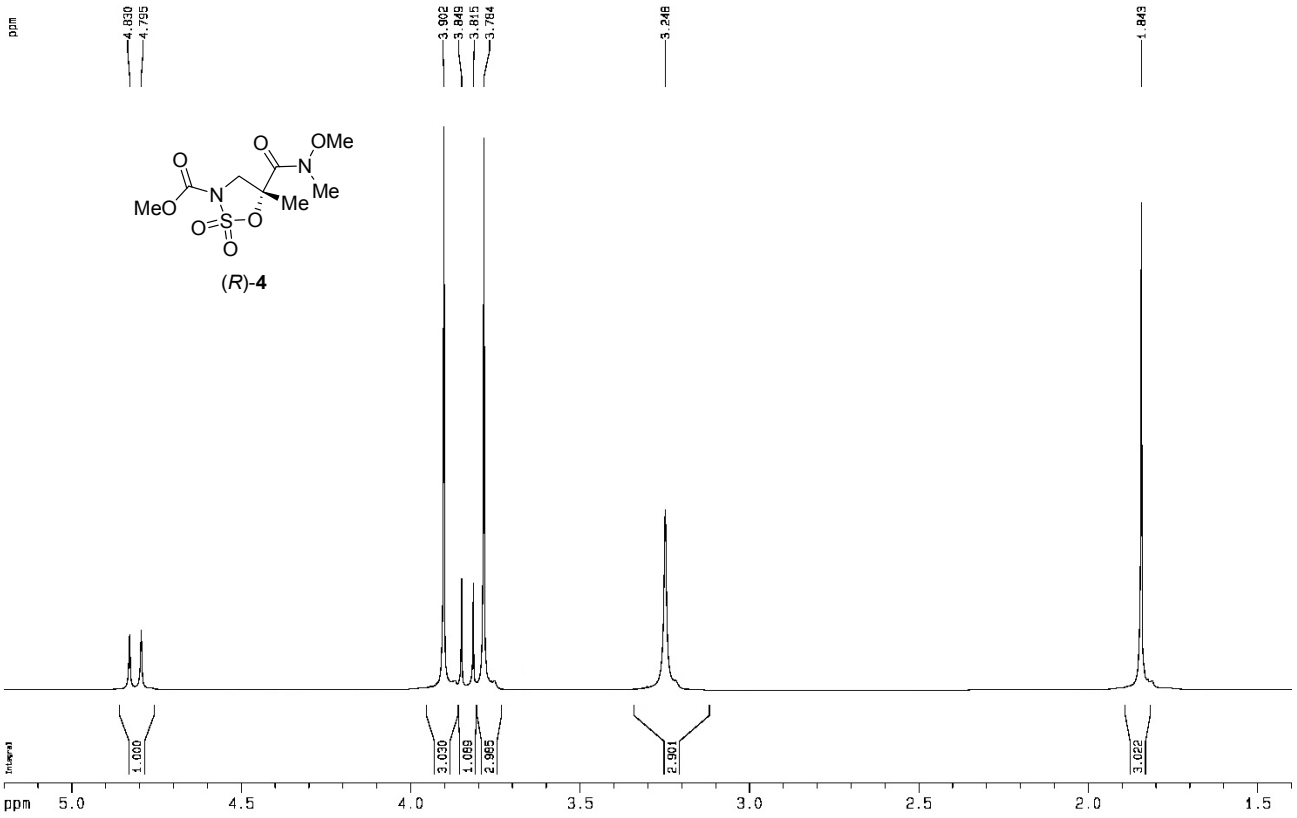



ppm
3.796
3.777
3.775
3.758
3.565
3.527
1.320
1.318
HO
OMe
HO
Me
O
(R)-3
Integral
0.308
4.133
1.151
3.000
ppm
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0

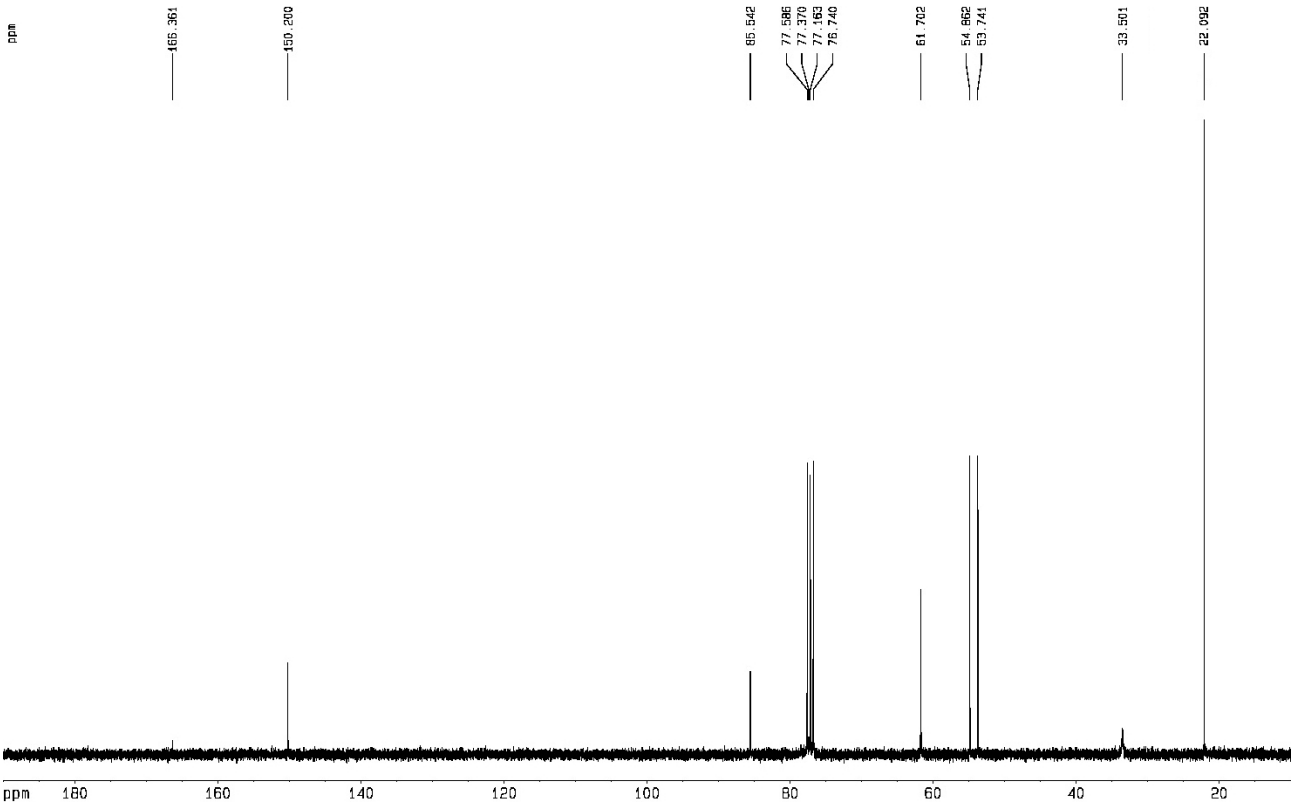

ppm
176.043
77.426
77.204
77.002
76.579
75.759
68.354
52.978
21.785
21.726
ppm
180
160
140
120
100
80
60
40
20

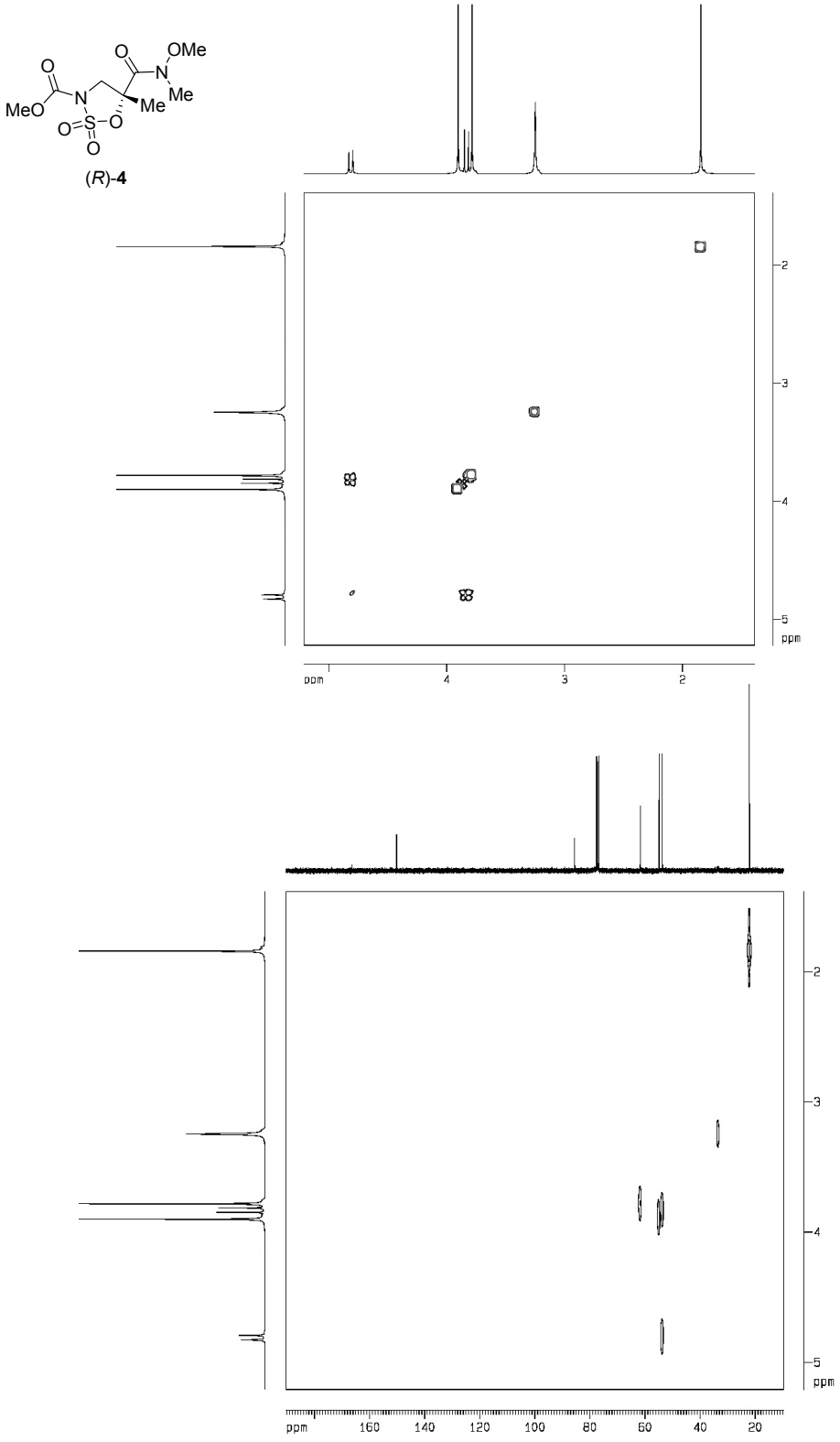


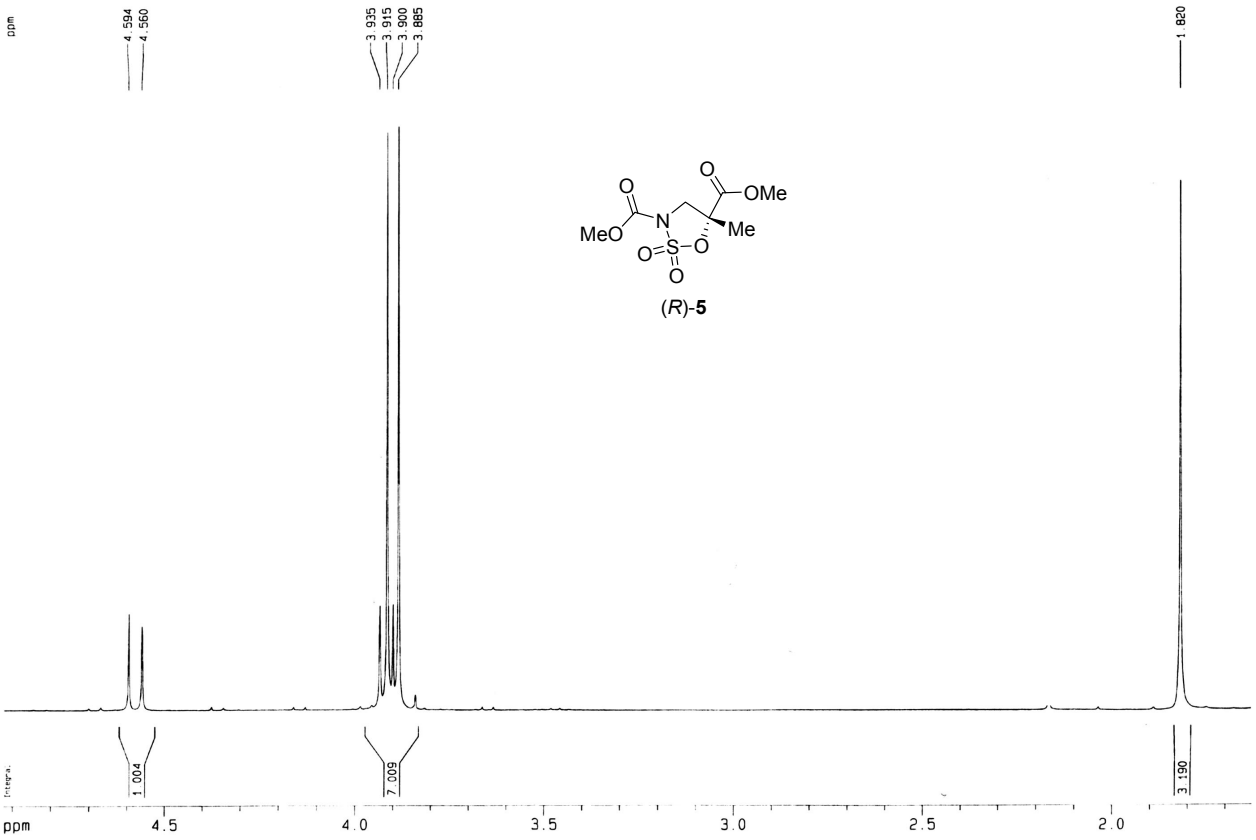
(*R*)-**3**


ppm
4.830
4.795
3.902
3.849
3.815
3.784
3.248
1.843
Integral
1.000
3.030
1.069
2.965
2.901
3.022
ppm 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5

(*R*)-**4**

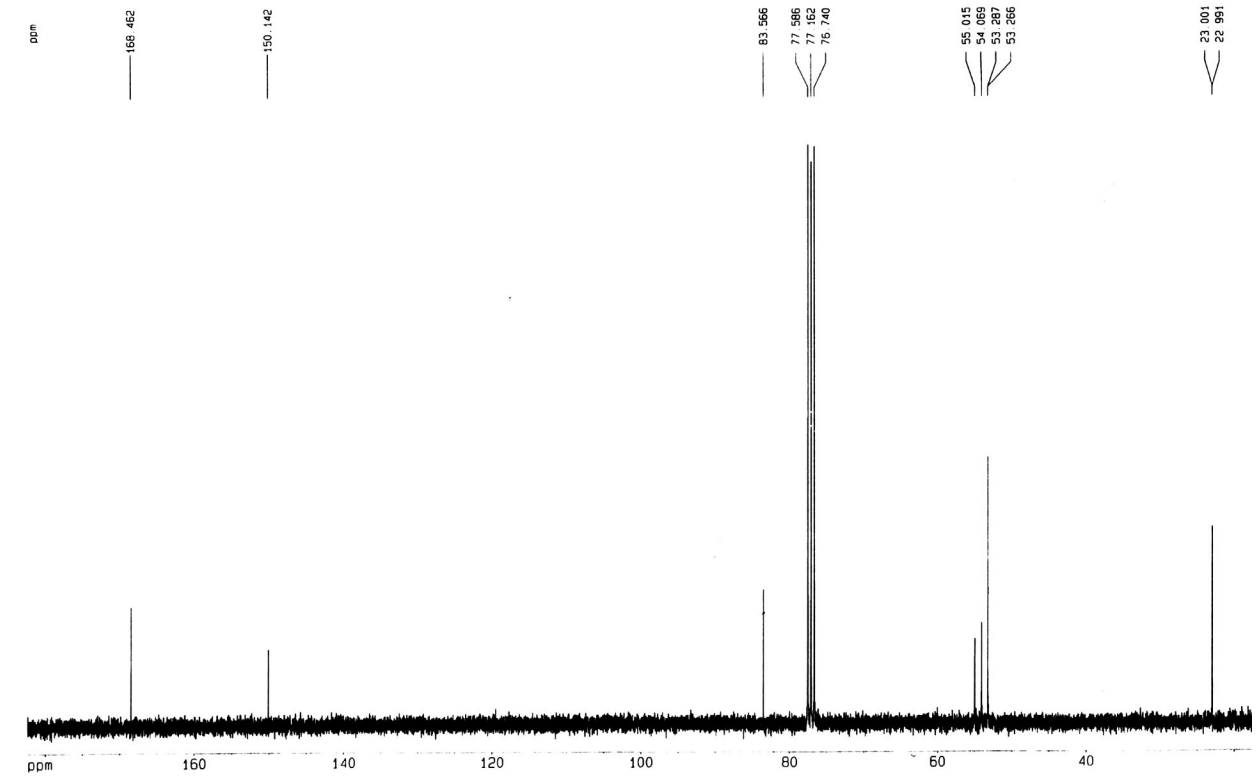

ppm
165.361
150.200
85.542
77.586
77.370
77.163
76.740
61.702
54.862
53.741
33.501
22.092
ppm 180 160 140 120 100 80 60 40 20

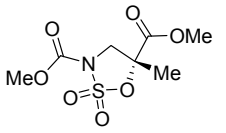

(R)-4
ppm
ppm
ppm
ppm


ppm
4.594
4.560
3.935
3.915
3.900
3.885
1.820
1.004
7.009
3.190
4.5
4.0
3.5
3.0
2.5
2.0

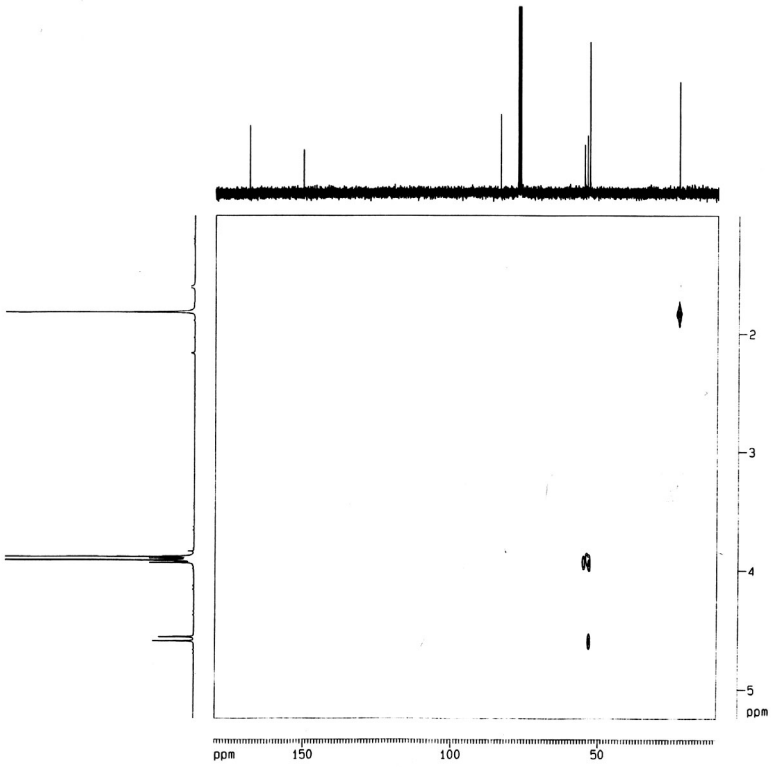
O
OMe
MeO
N
Me
O
S
O
O

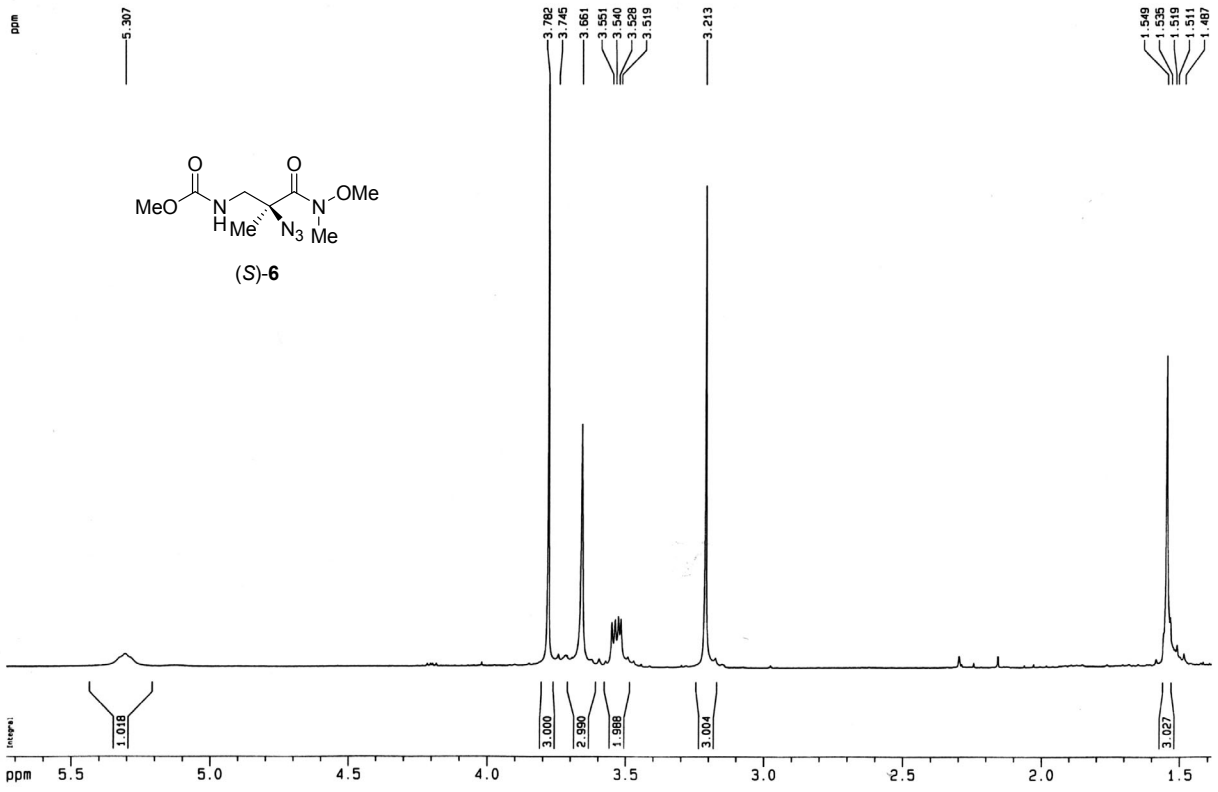
(*R*)-**5**


ppm
166.462
150.142
83.566
77.586
77.162
76.740
55.015
54.069
53.287
53.266
23.001
22.991
160
140
120
100
80
60
40



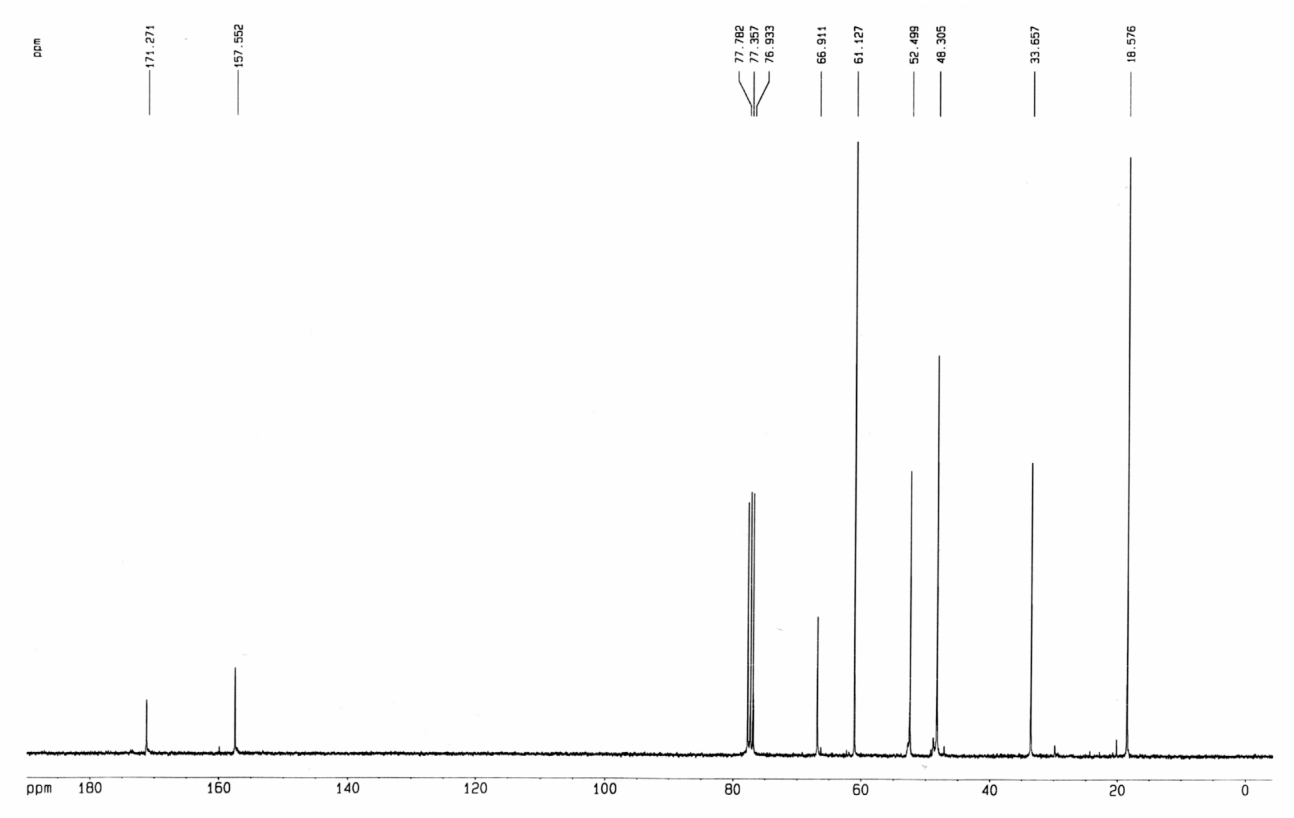
(*R*)-**5**

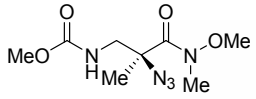



ppm
5.307
3.782
3.745
3.661
3.551
3.540
3.528
3.519
3.213
1.549
1.535
1.519
1.511
1.487
Integral
1.018
3.000
2.990
1.988
3.004
3.027
ppm 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5

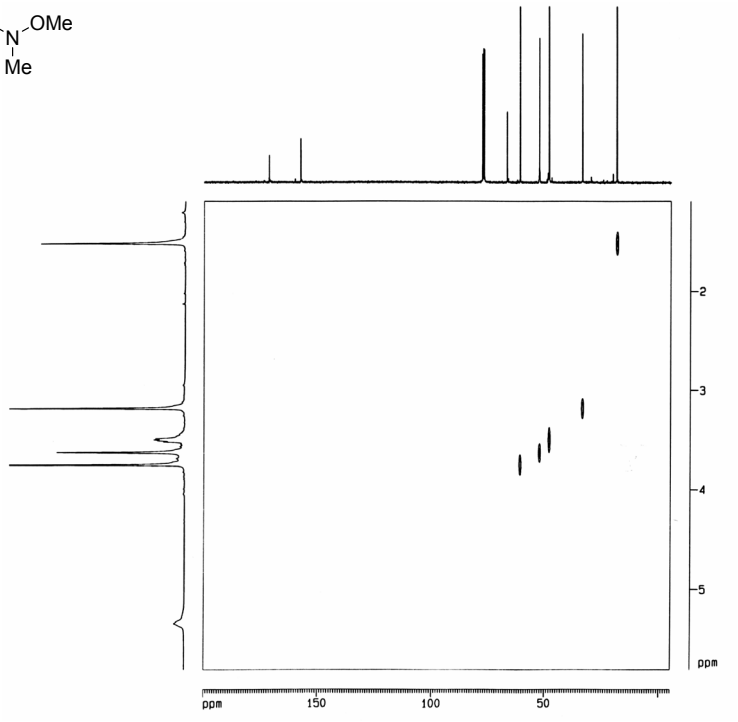
MeO
O
N
H
Me
N3
Me
O
N
OMe
Me

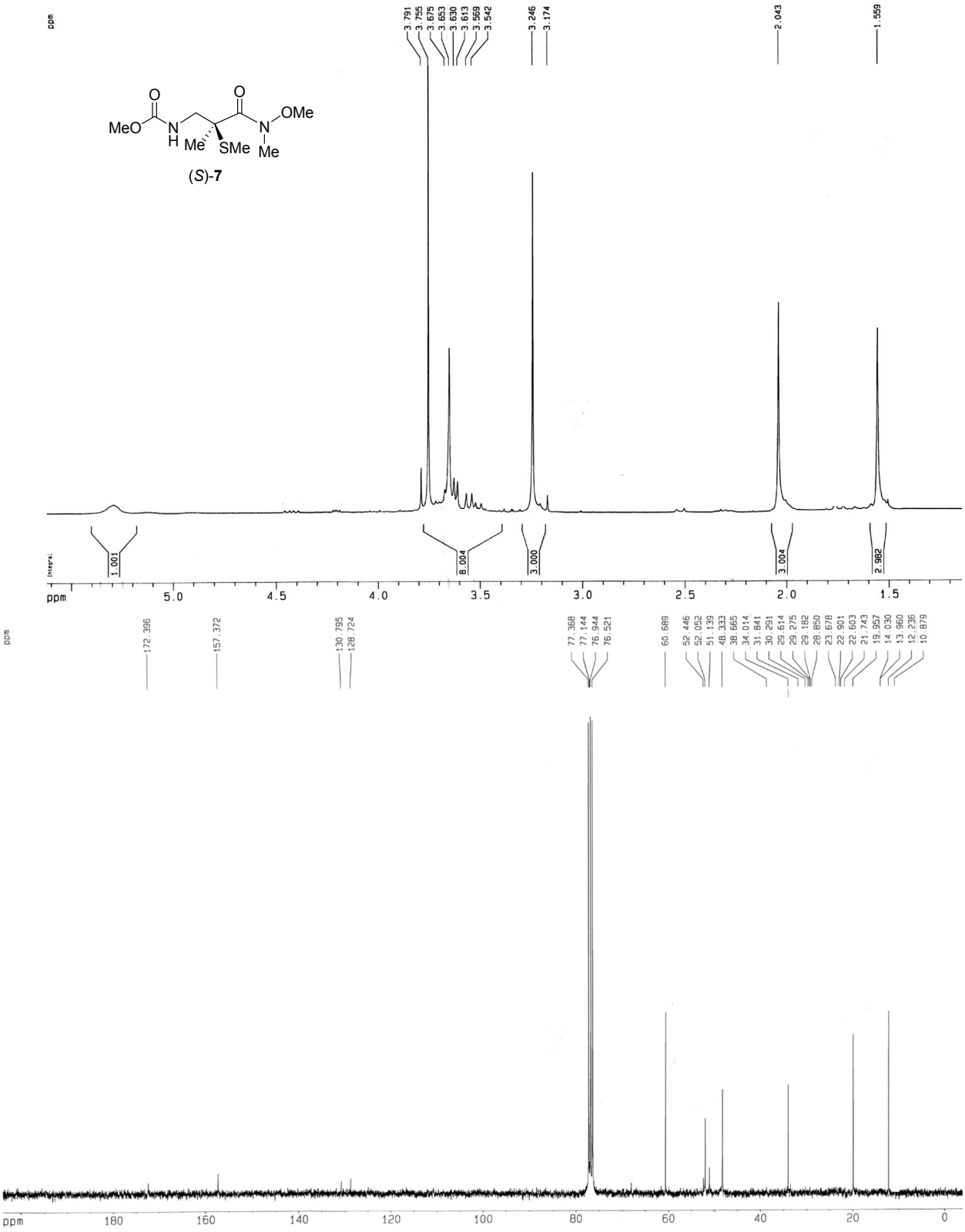
(*S*)-**6**

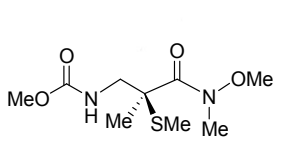

ppm
171.271
157.552
77.782
77.357
76.933
66.911
61.127
52.499
48.305
33.657
18.576
ppm 180 160 140 120 100 80 60 40 20 0



(*S*)-**6**

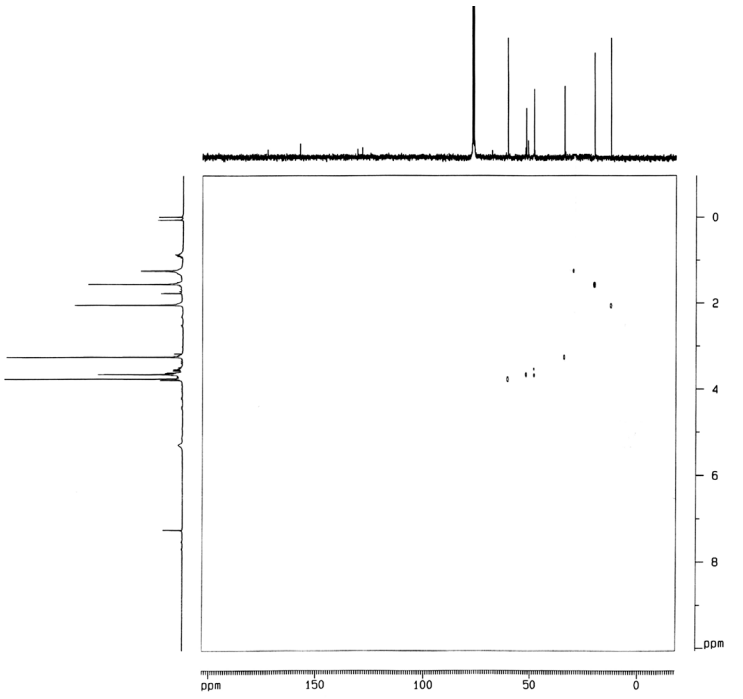


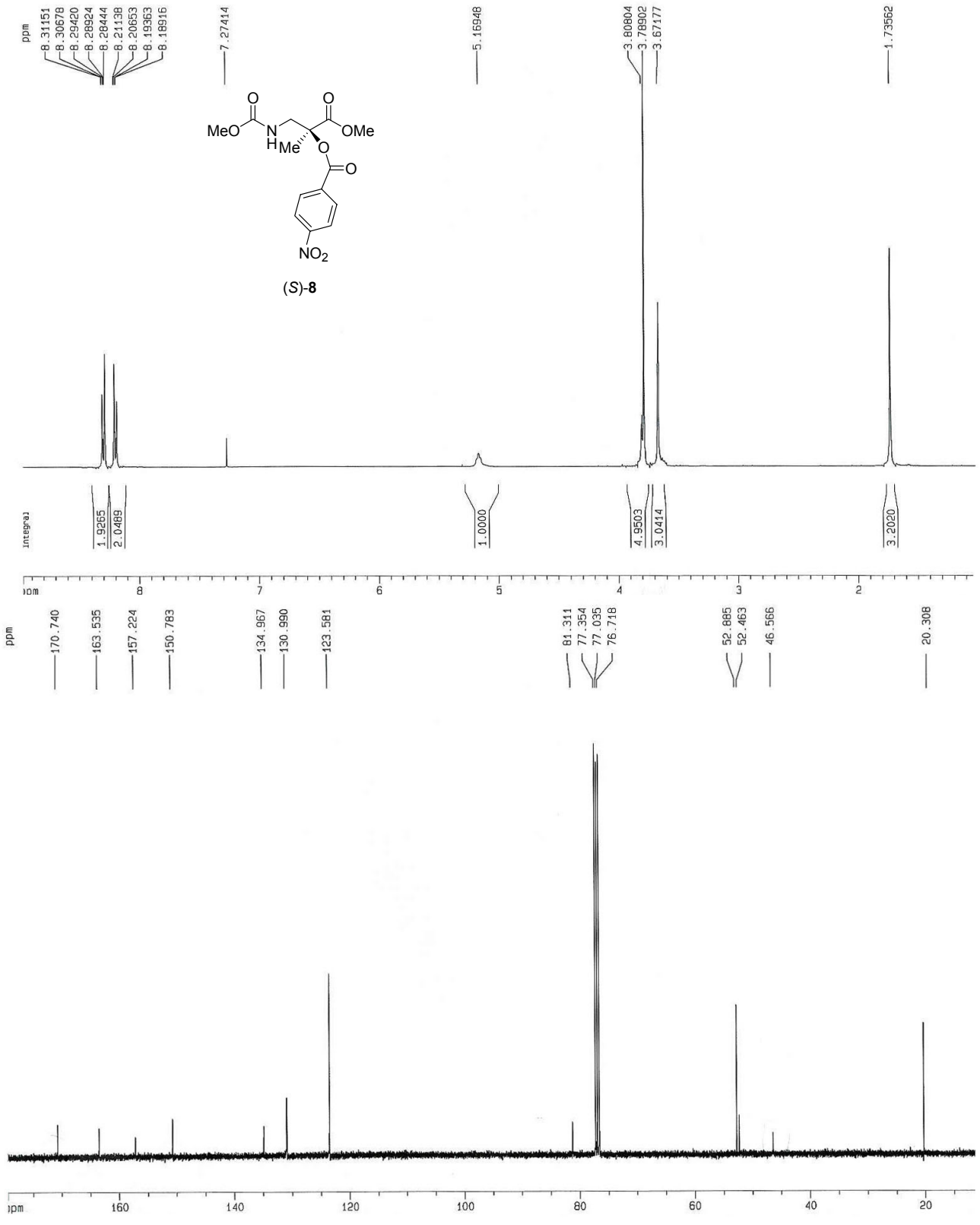

(S)-7
3.791
3.755
3.675
3.653
3.630
3.613
3.569
3.542
3.246
3.174
2.043
1.559
1.001
8.004
3.000
3.004
2.982
ppm
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
172.396
157.372
130.795
128.724
77.368
77.144
76.944
76.521
60.689
52.446
52.052
51.139
48.333
38.665
34.014
31.841
30.291
29.614
29.275
29.182
28.850
23.678
22.901
22.603
21.743
19.957
14.030
13.960
12.236
10.879
180
160
140
120
100
80
60
40
20
0

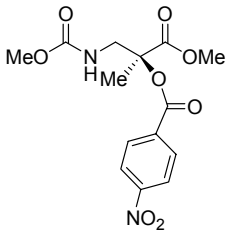

O
O
MeO
N
H
Me
SMe
N
OMe
Me

(*S*)-**7**

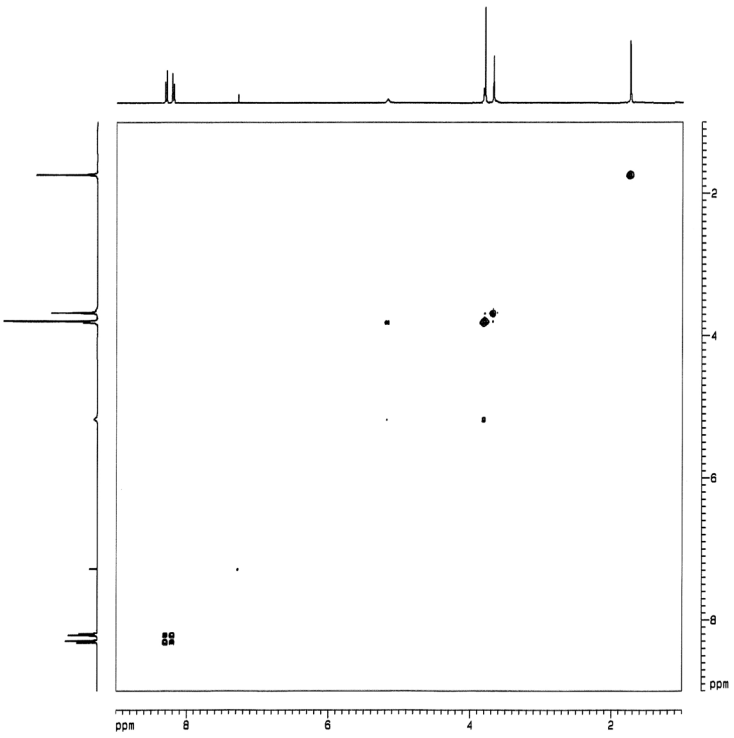
2
3
4
5
ppm
ppm
5
4
3
2

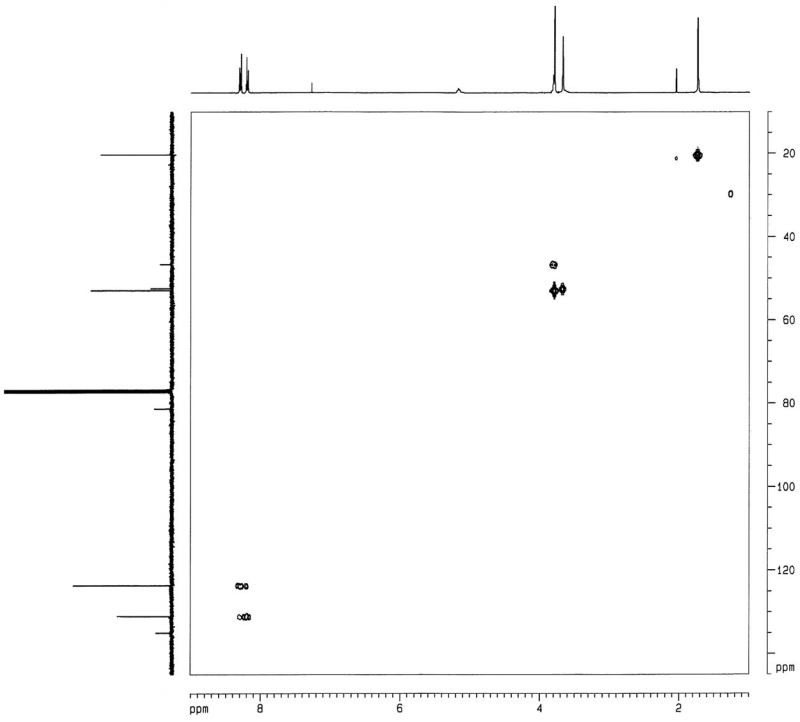

0
2
4
6
8
ppm
ppm
150
100
50
0

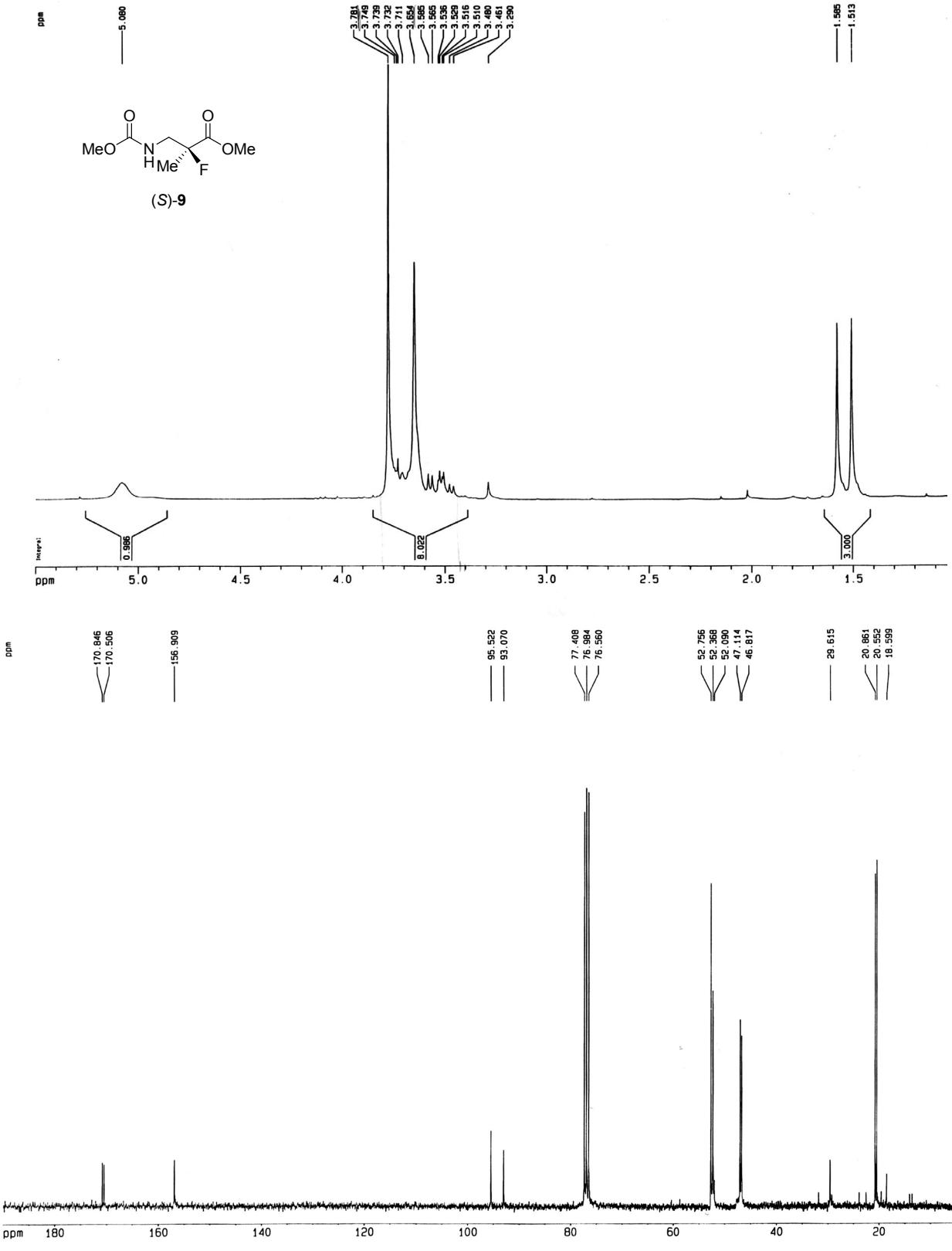

ppm
8.31151
8.30678
8.29420
8.28924
8.28444
8.21138
8.20653
8.19363
8.18916
7.27414
5.16948
3.80804
3.78902
3.67177
1.73562
MeO
N
H
Me
O
O
O
OMe
O
NO2
(S)-8
Integral
1.9265
2.0489
1.0000
4.9503
3.0414
3.2020
ppm
8
7
6
5
4
3
2
ppm
170.740
163.535
157.224
150.783
134.967
130.990
123.581
81.311
77.354
77.035
76.718
52.885
52.463
46.566
20.308
ppm
160
140
120
100
80
60
40
20

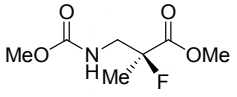

O
O
MeO
N
H
Me
OMe
O
O
NO2

(*S*)-**8**

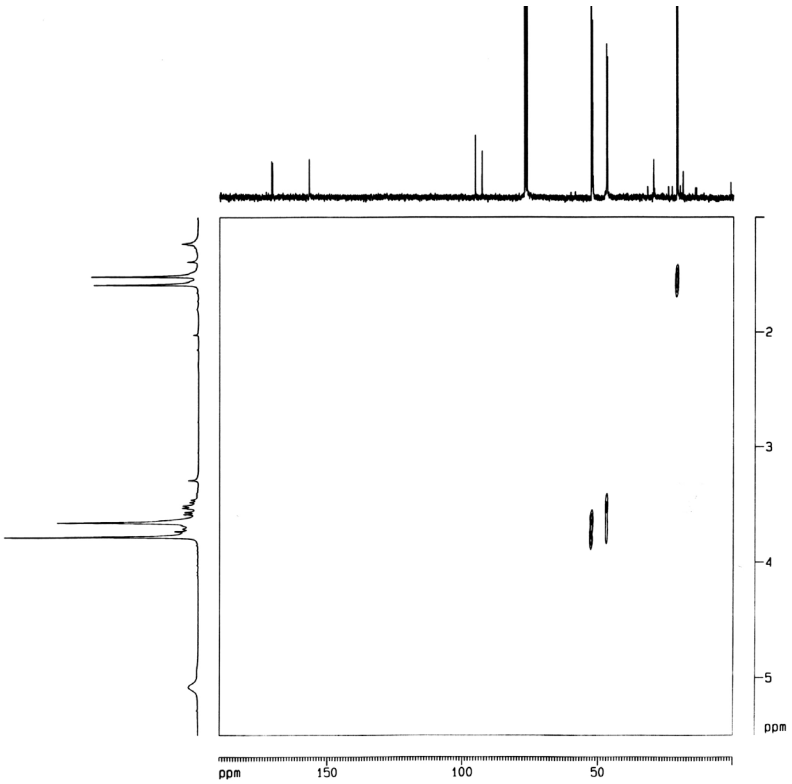

2
4
6
8
ppm
ppm
8
6
4
2

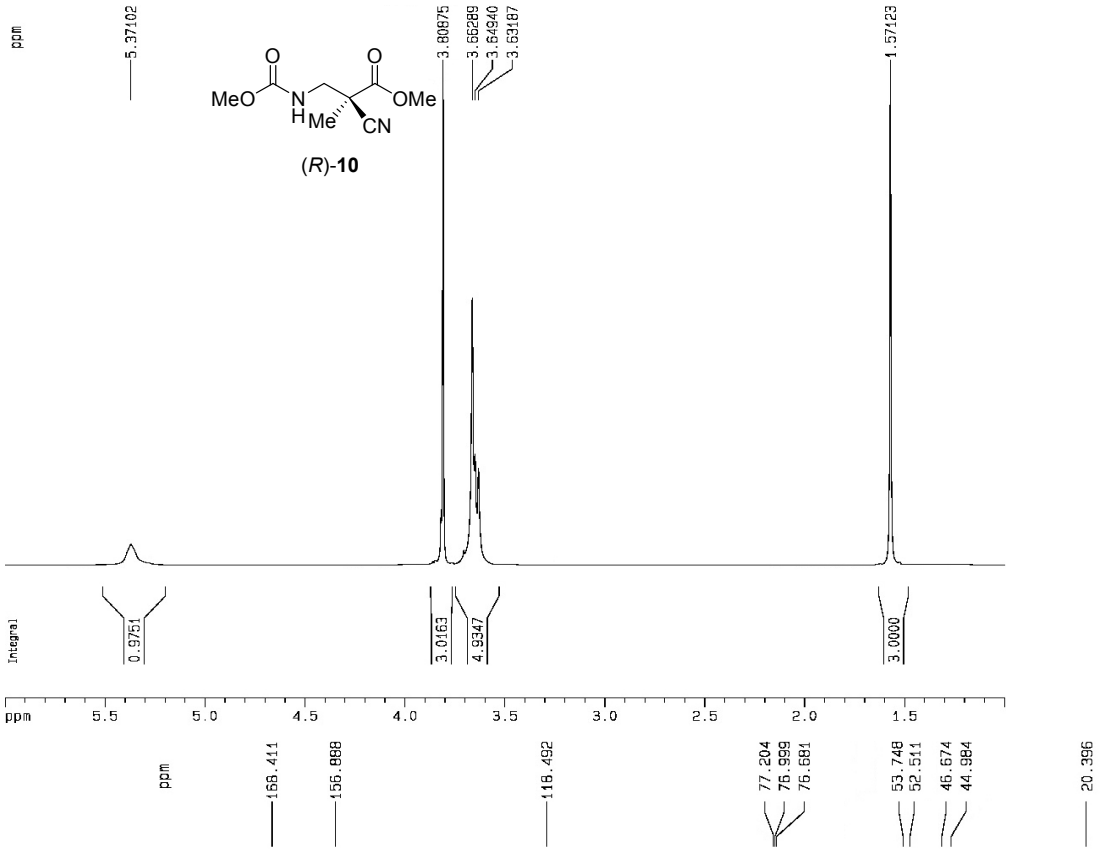

20
40
60
80
100
120
ppm
ppm
8
6
4
2


ppm
5.060
3.781
3.749
3.739
3.732
3.711
3.654
3.585
3.565
3.536
3.529
3.516
3.510
3.480
3.451
3.290
1.585
1.513
MeO
OMe
Me
F
(S)-9
Integral
0.986
8.022
3.000
ppm
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
170.846
170.506
156.909
95.522
93.070
77.408
76.984
76.560
52.756
52.368
52.090
47.114
46.817
29.615
20.861
20.552
18.599
ppm
180
160
140
120
100
80
60
40
20

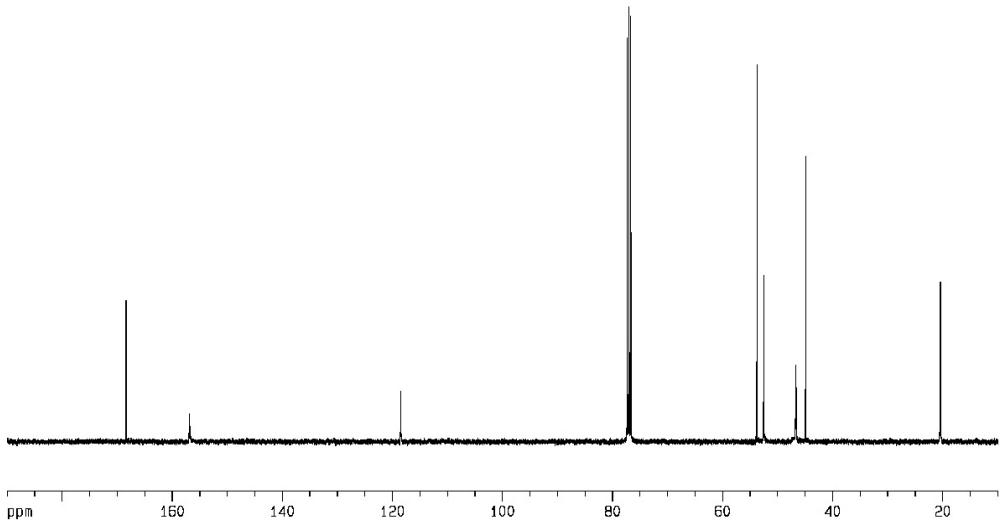


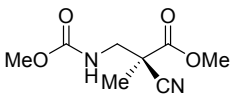
(*S*)-**9**



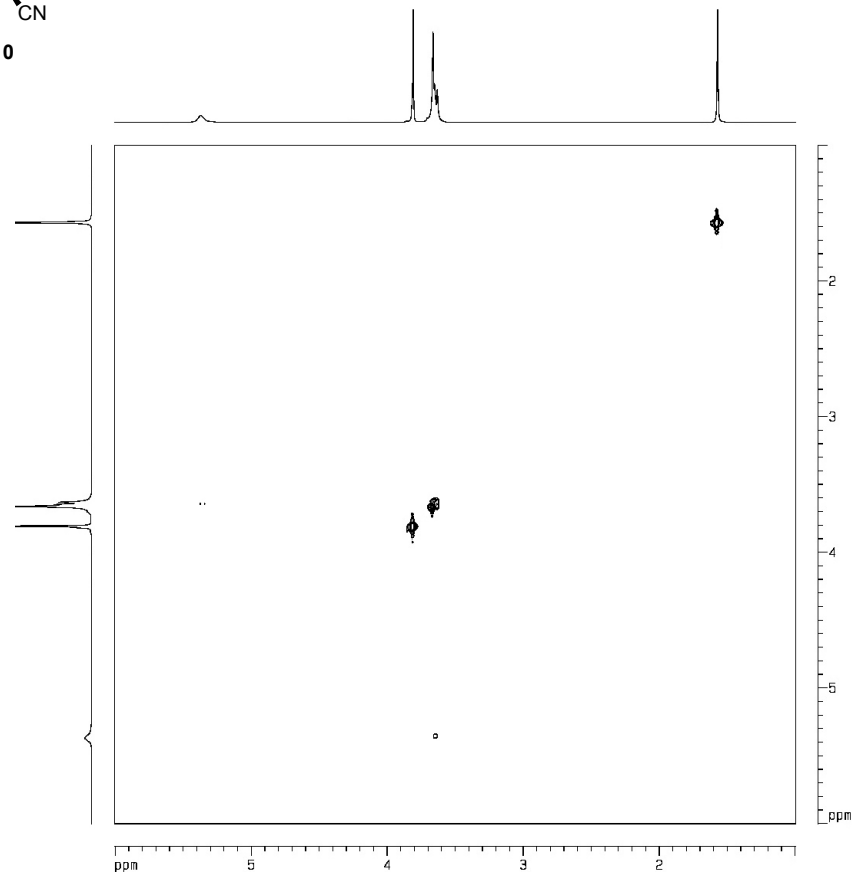

ppm
5.37102
3.80875
3.66288
3.64940
3.63187
1.57123
MeO
O
N
H
Me
O
OMe
CN
(R)-10
Integral
0.9751
3.0163
4.9347
3.0000
ppm
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5

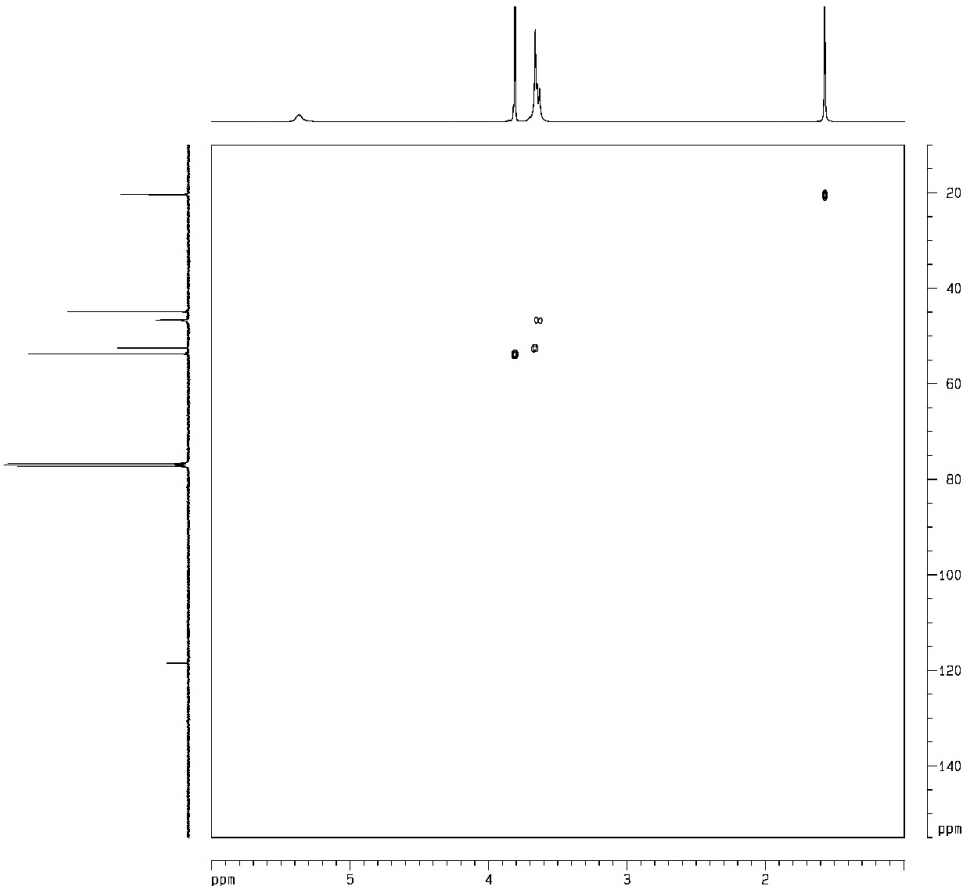
ppm
168.411
156.888
118.492
77.204
75.999
75.681
53.748
52.511
46.674
44.984
20.396

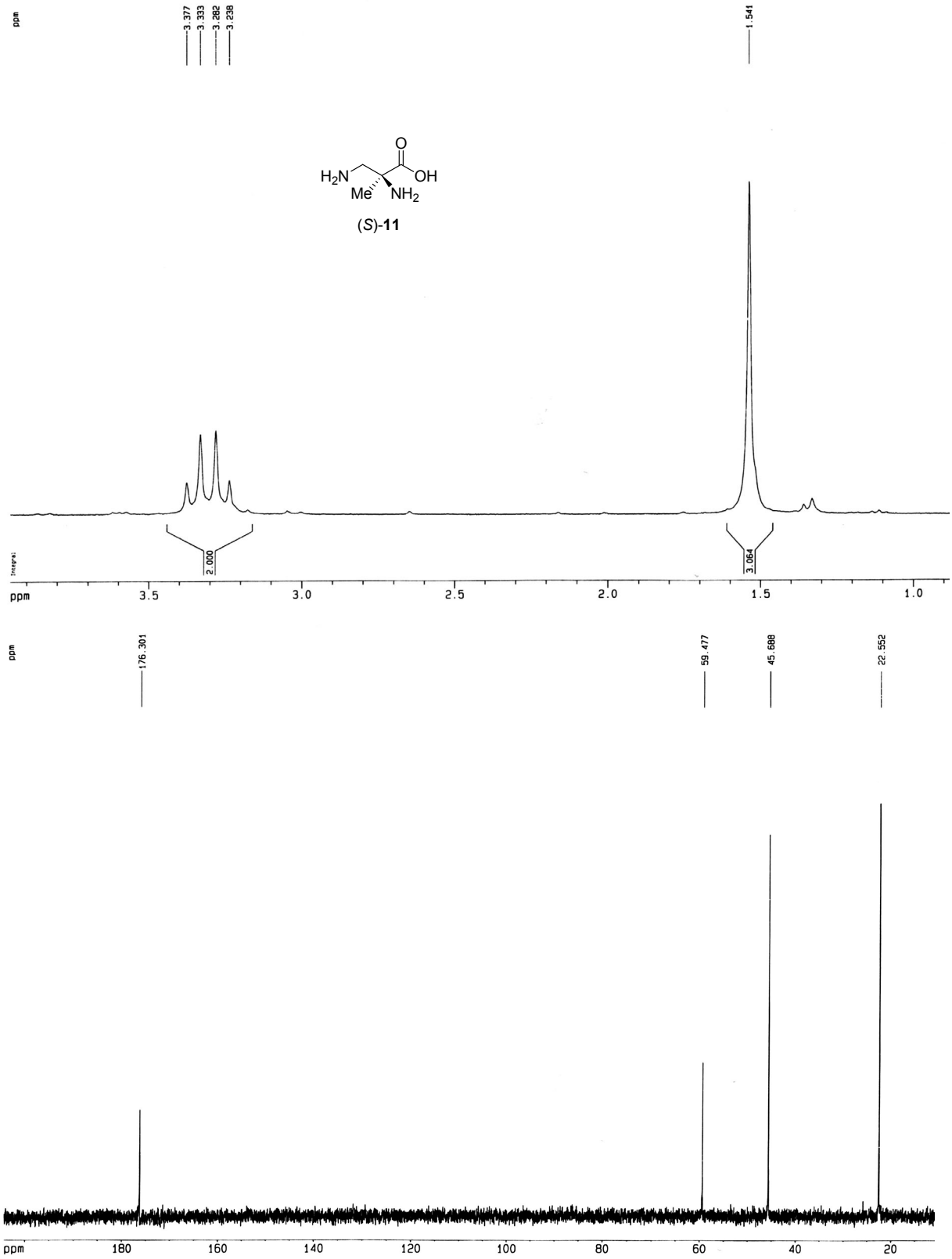

ppm
160
140
120
100
80
60
40
20


O
O
MeO
N
H
Me
OMe
CN

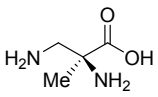
(*R*)-**10**


2
3
4
5
ppm
ppm
5
4
3
2

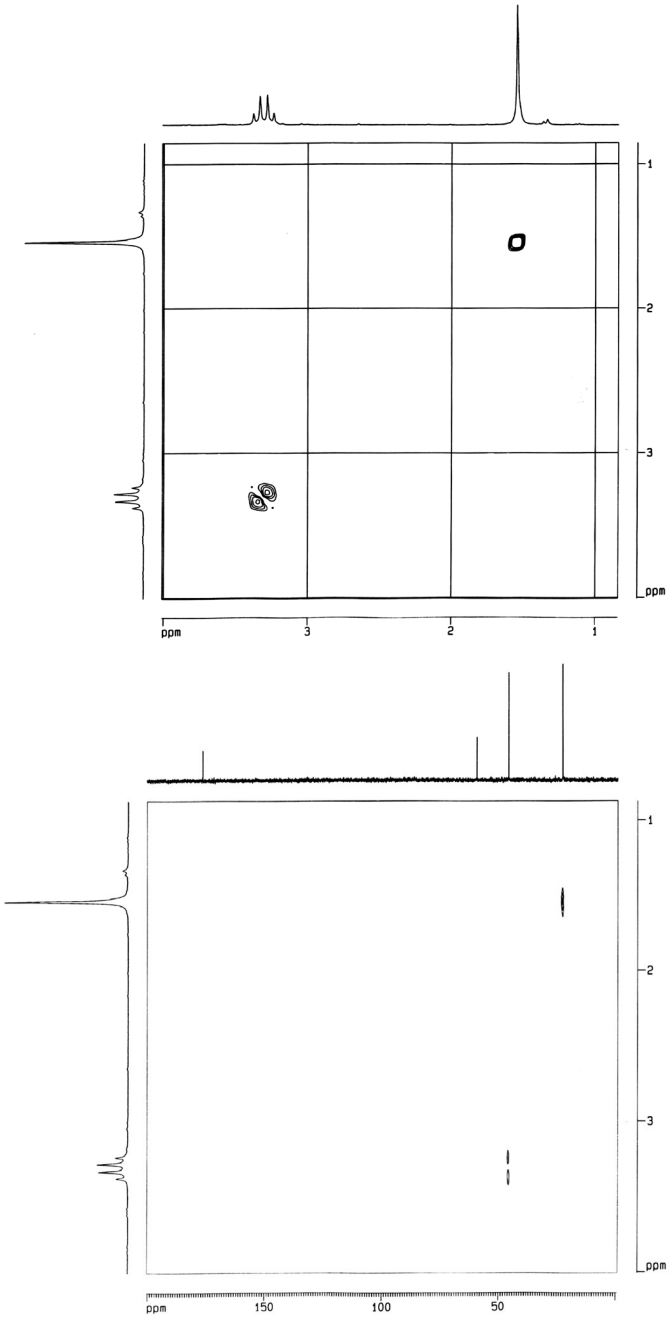

20
40
60
80
100
120
140
ppm
ppm
5
4
3
2

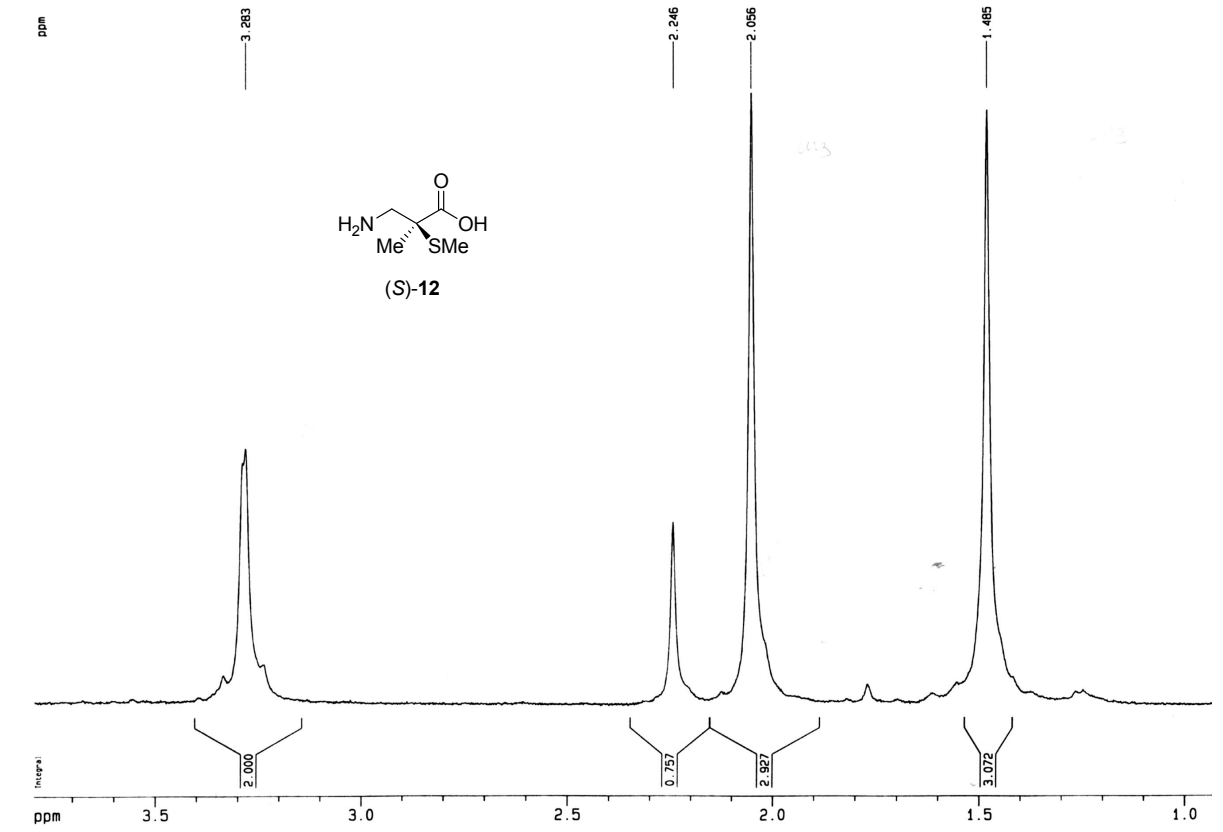

ppm
3.377
3.333
3.282
3.238
1.541
O
OH
H_2N
Me
NH_2
2.000
3.064
ppm
3.5
3.0
2.5
2.0
1.5
1.0
ppm
176.301
59.477
45.688
22.552
ppm
180
160
140
120
100
80
60
40
20

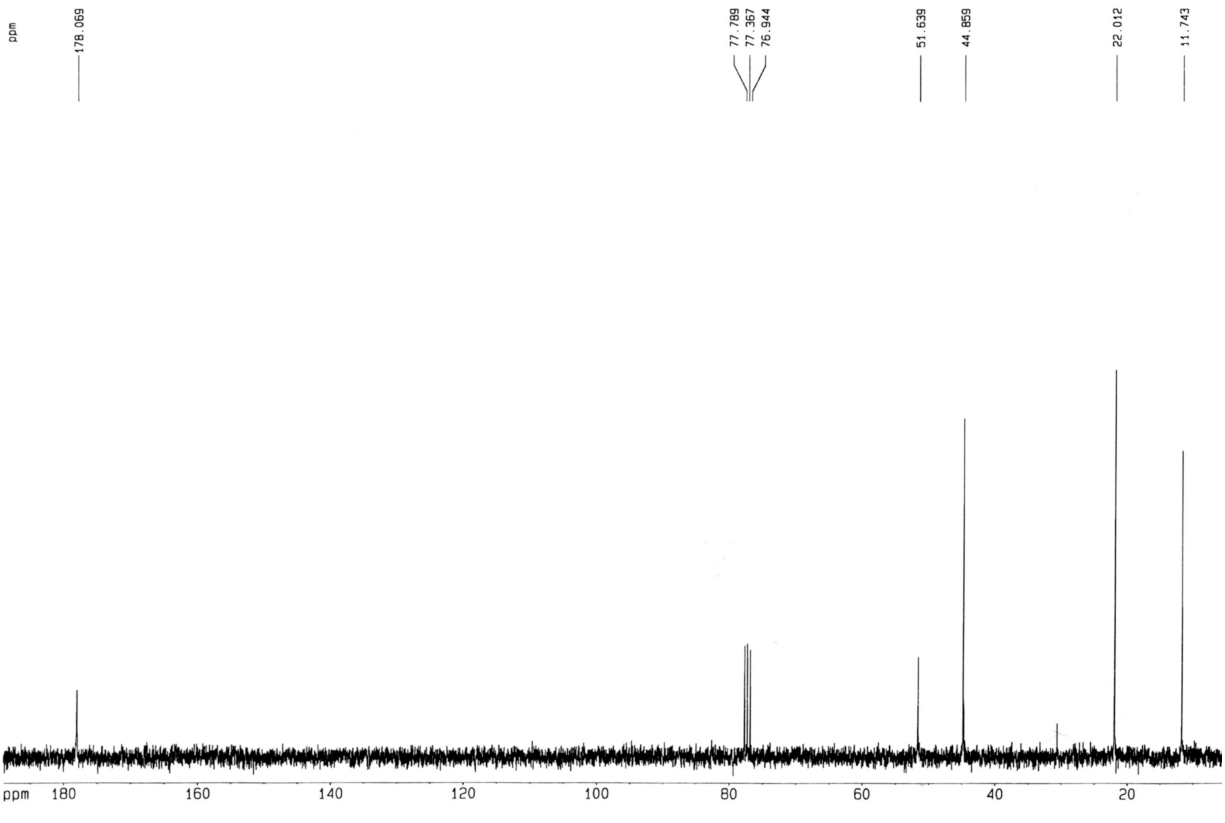
(*S*)-**11**

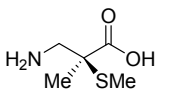


(*S*)-**11**

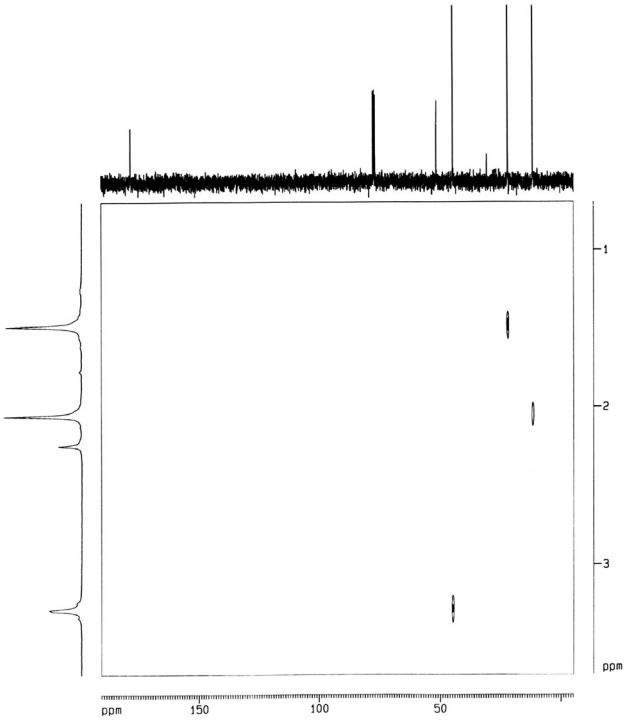


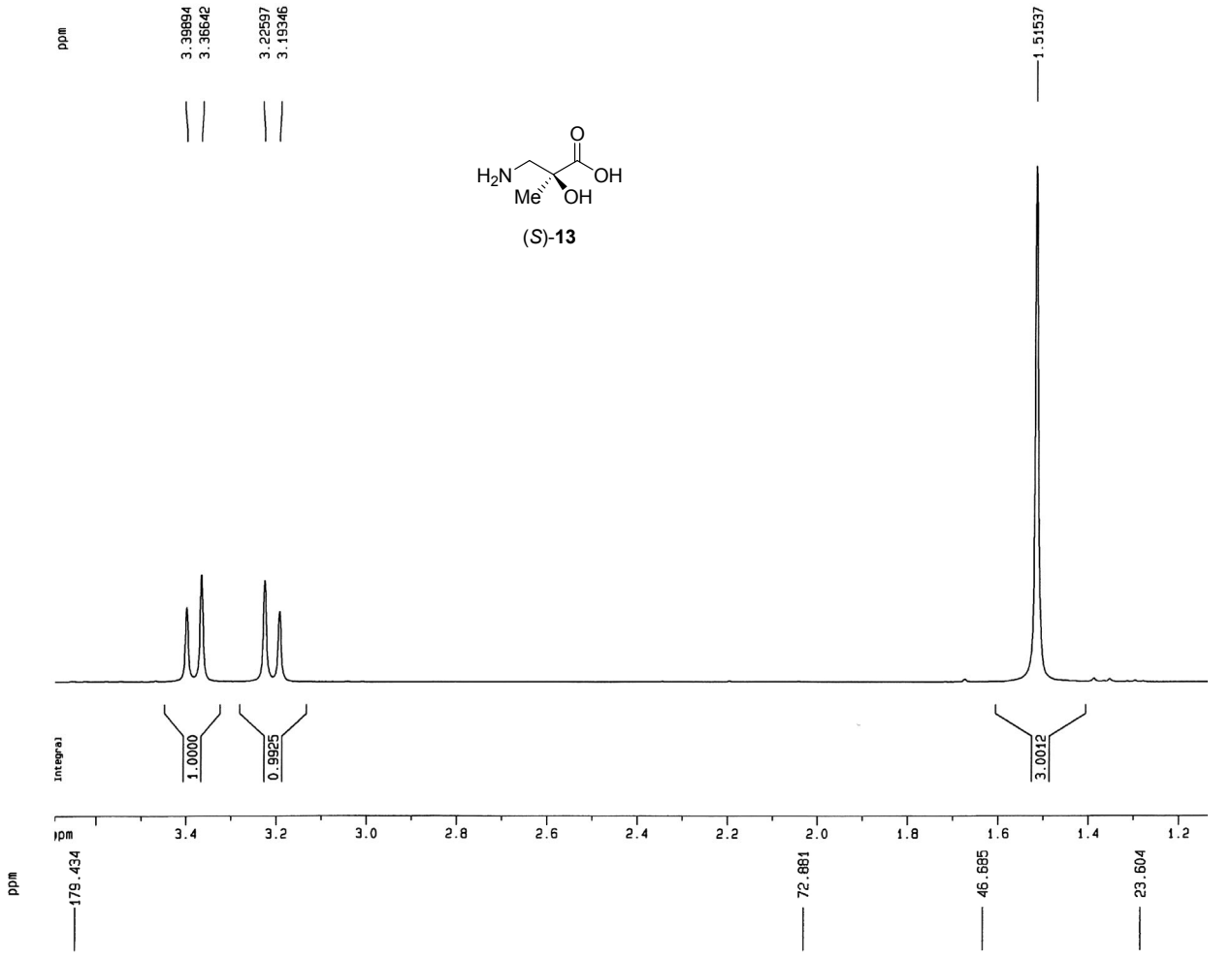

ppm
3.283
2.246
2.056
1.485
O
H2N
OH
Me
SMe
(S)-12
Integral
2.000
0.757
2.927
3.072
ppm
3.5
3.0
2.5
2.0
1.5
1.0

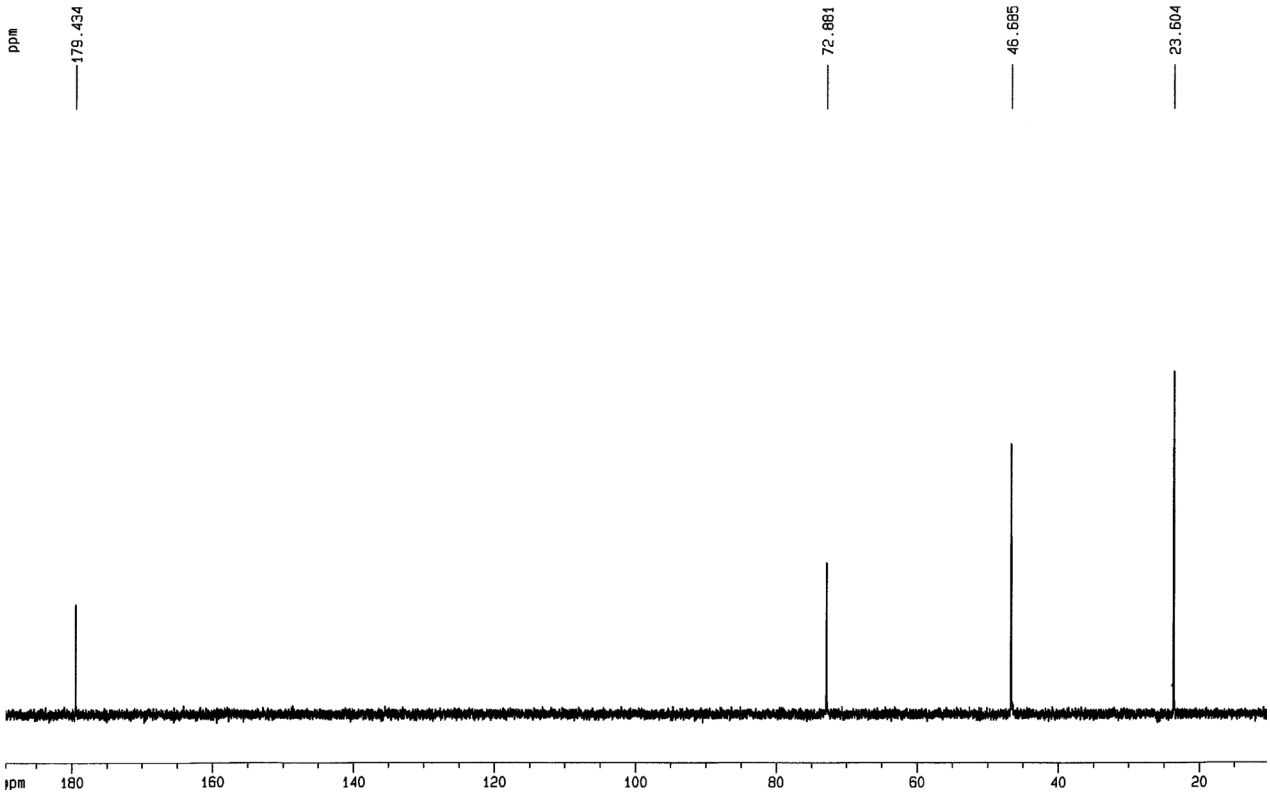

ppm
178.069
77.789
77.367
76.944
51.639
44.859
22.012
11.743
ppm
180
160
140
120
100
80
60
40
20

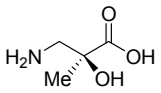


(*S*)-**12**

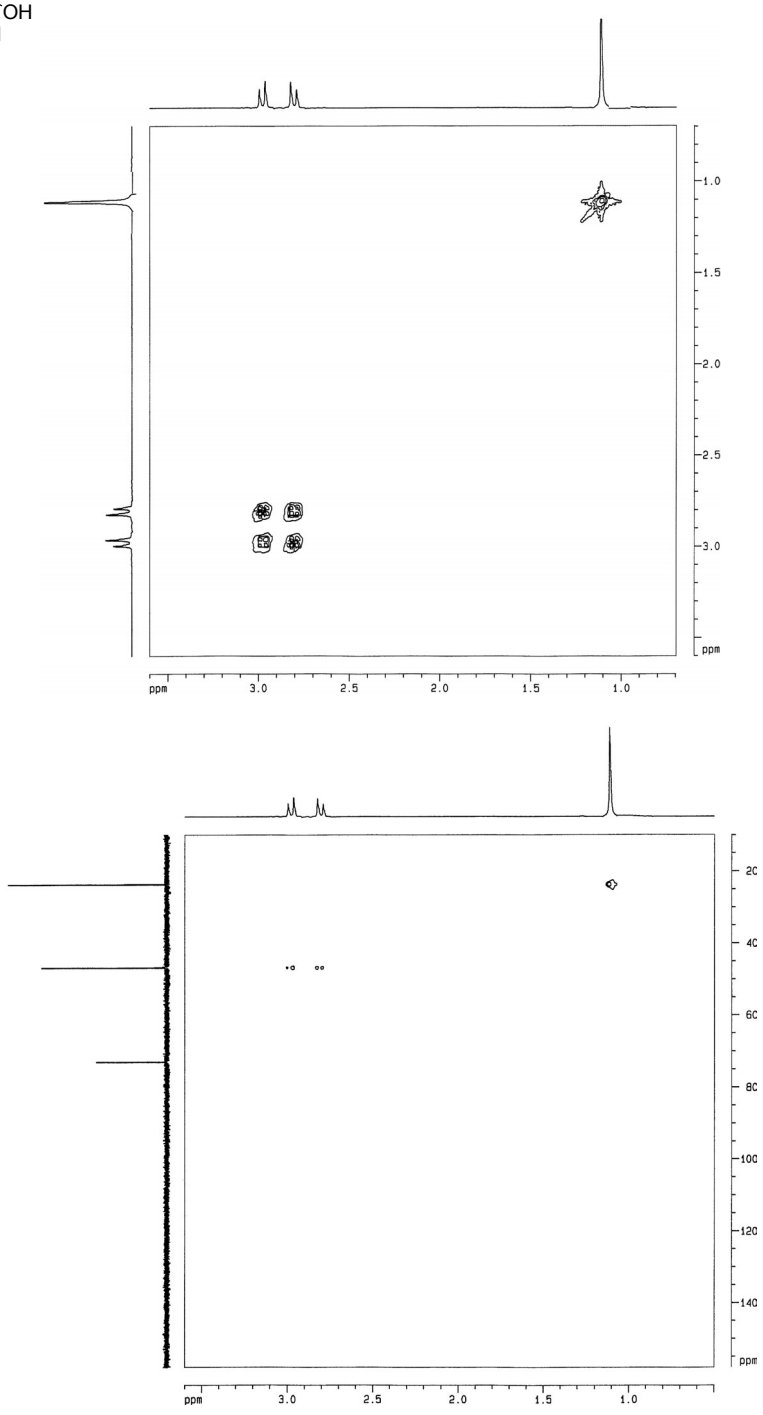


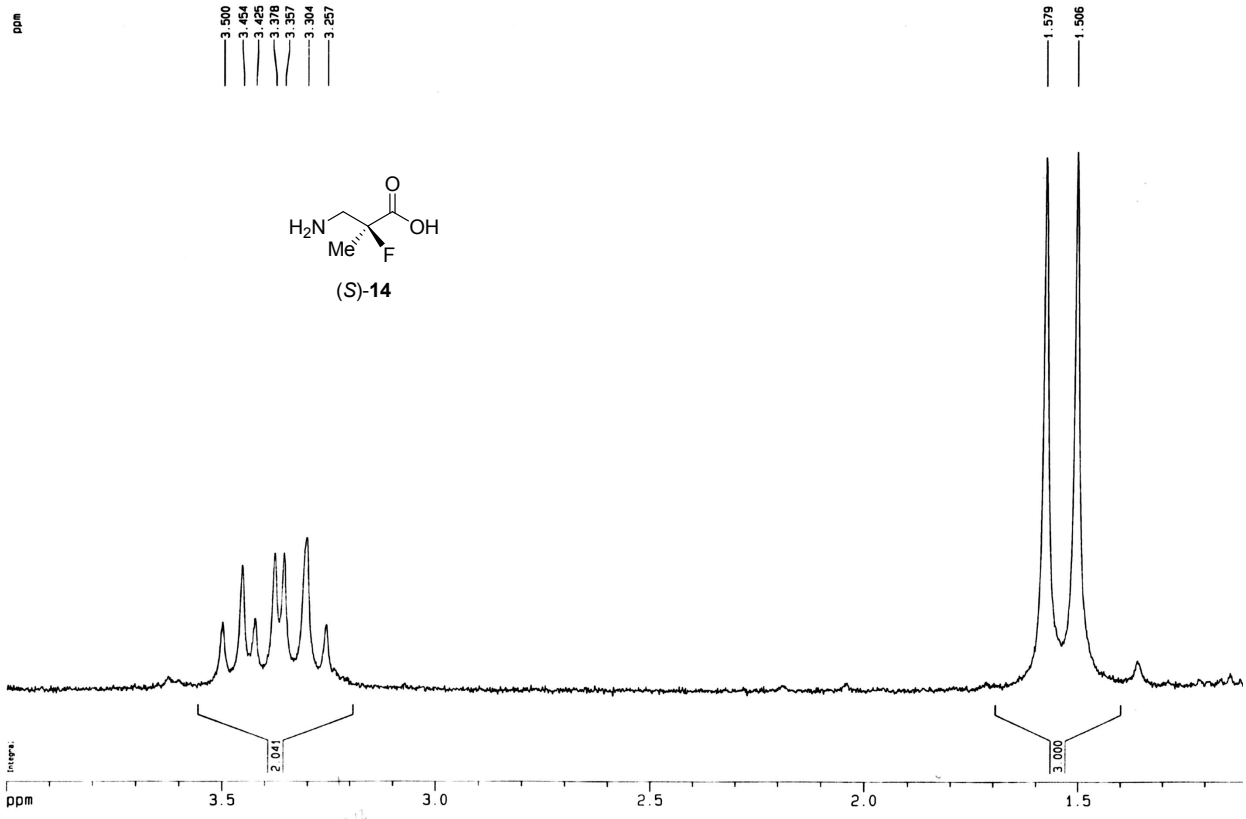

ppm
3.39894
3.36642
3.22597
3.19346
1.51537
O
OH
H_2N
Me
OH
(S)-13
Integral
1.0000
0.9925
3.0012
ppm
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2


ppm
179.434
72.881
46.685
23.604
ppm
180
160
140
120
100
80
60
40
20

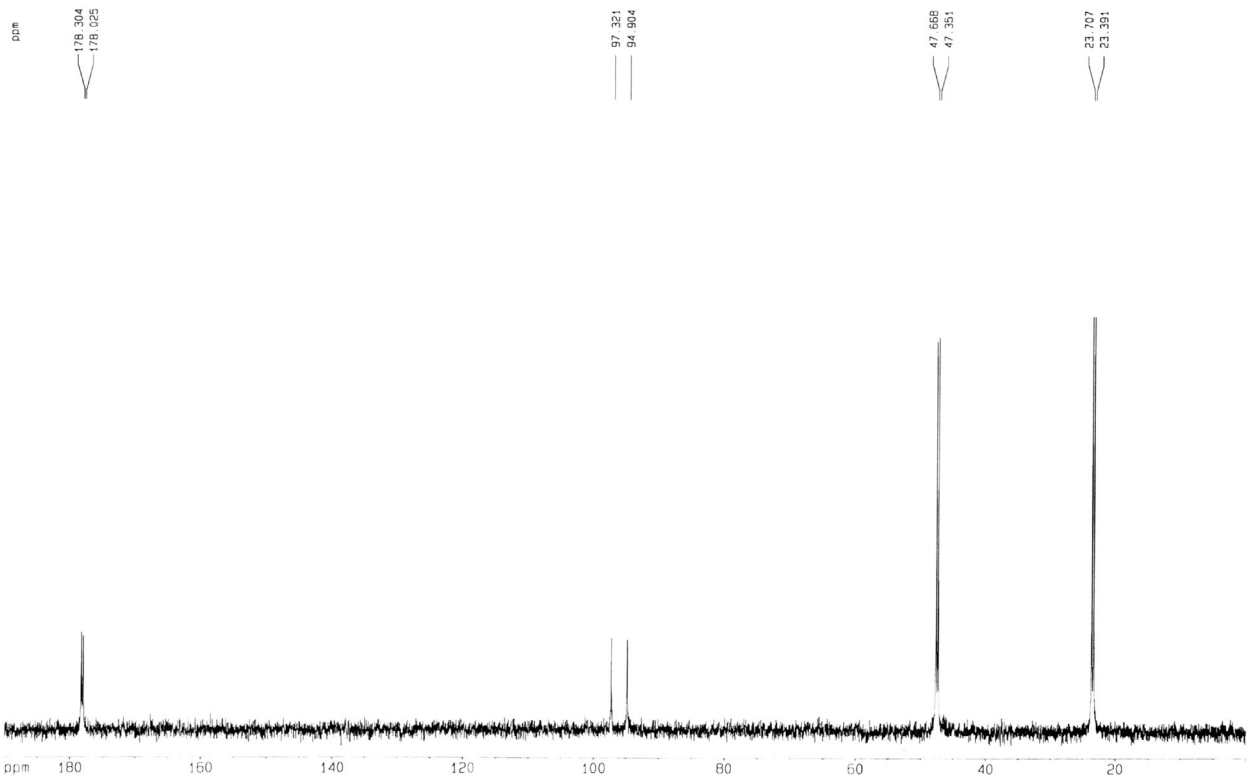

O
H2N
OH
Me
OH

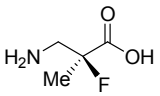
(*S*)-**13**


1.0
1.5
2.0
2.5
3.0
ppm
ppm
3.0
2.5
2.0
1.5
1.0
20
40
60
80
100
120
140
ppm
ppm
3.0
2.5
2.0
1.5
1.0

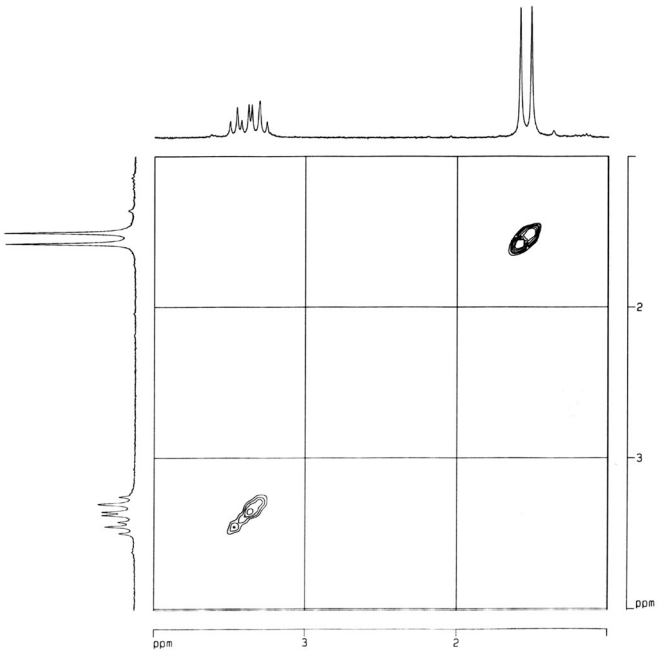

ppm
3.500
3.454
3.425
3.378
3.357
3.304
3.257
1.579
1.506
O
OH
H2N
Me
F
2.041
3.000
ppm
3.5
3.0
2.5
2.0
1.5

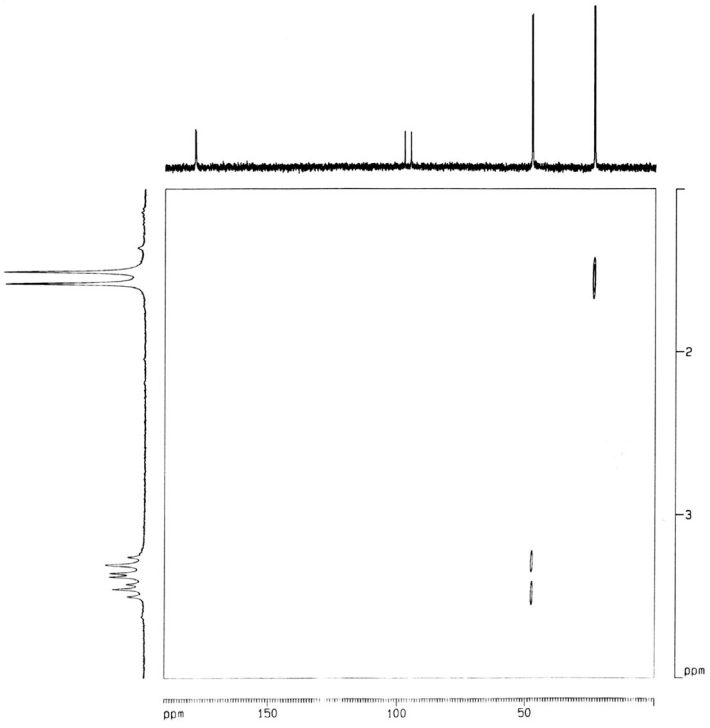
(*S*)-**14**

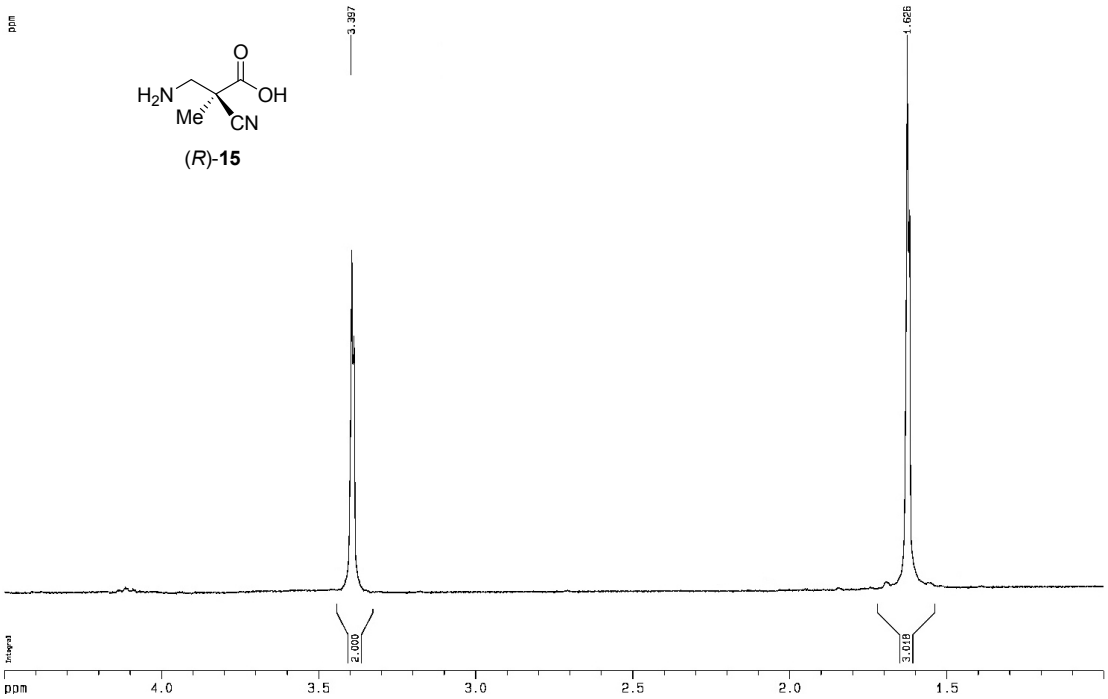

ppm
178.304
178.025
97.321
94.904
47.668
47.351
23.707
23.391
ppm
180
160
140
120
100
80
60
40
20



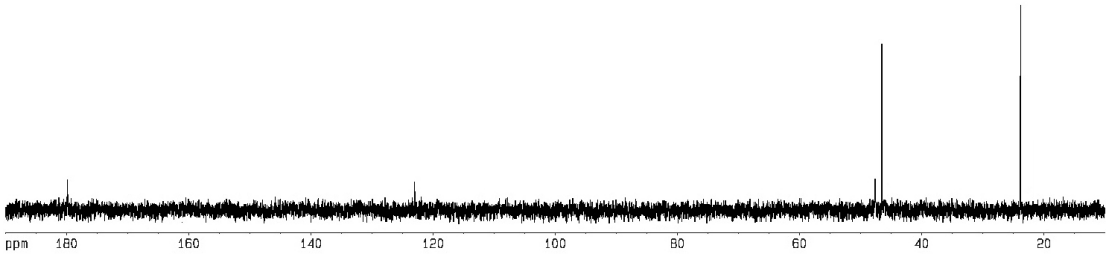
(*S*)-**14**

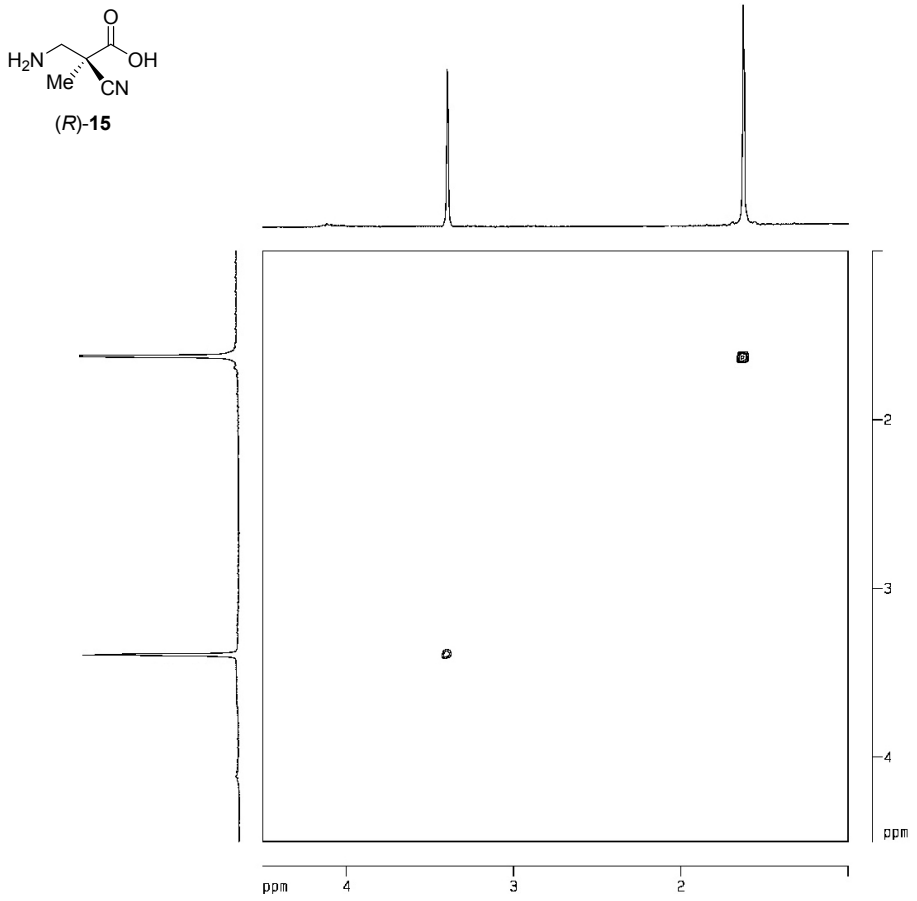


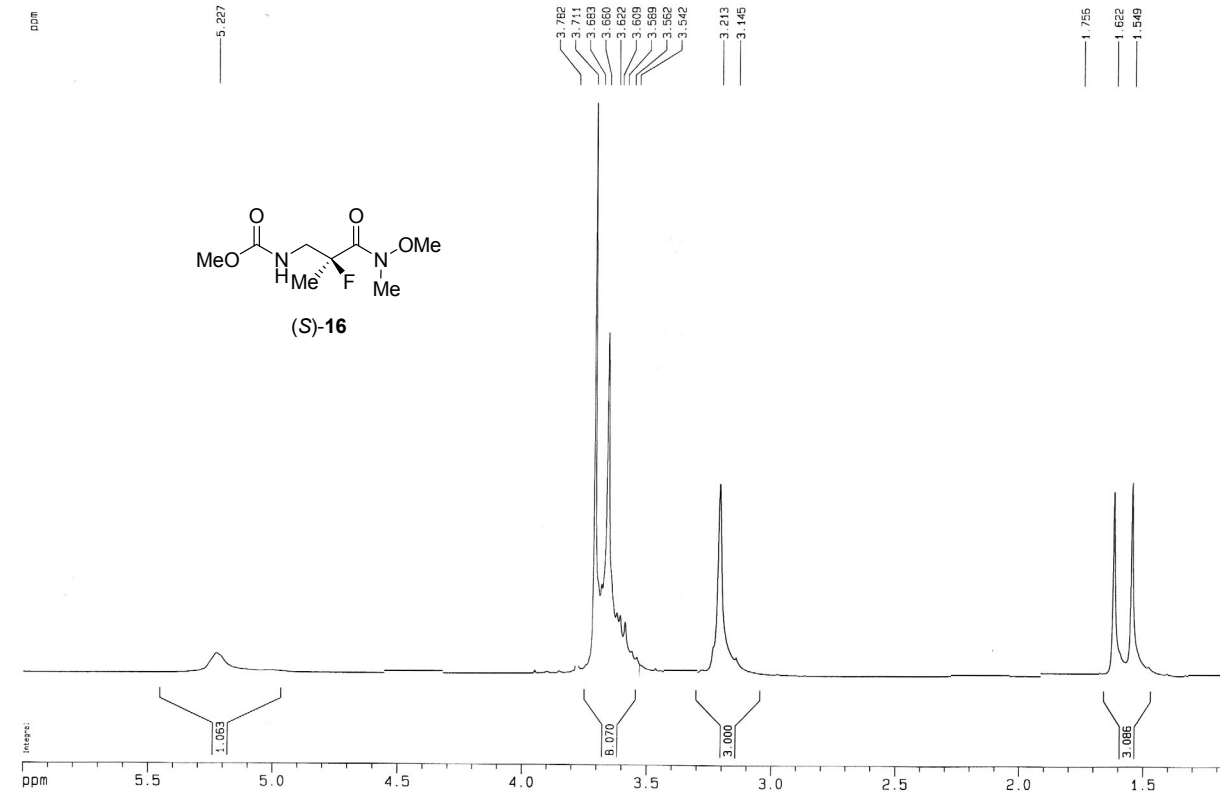


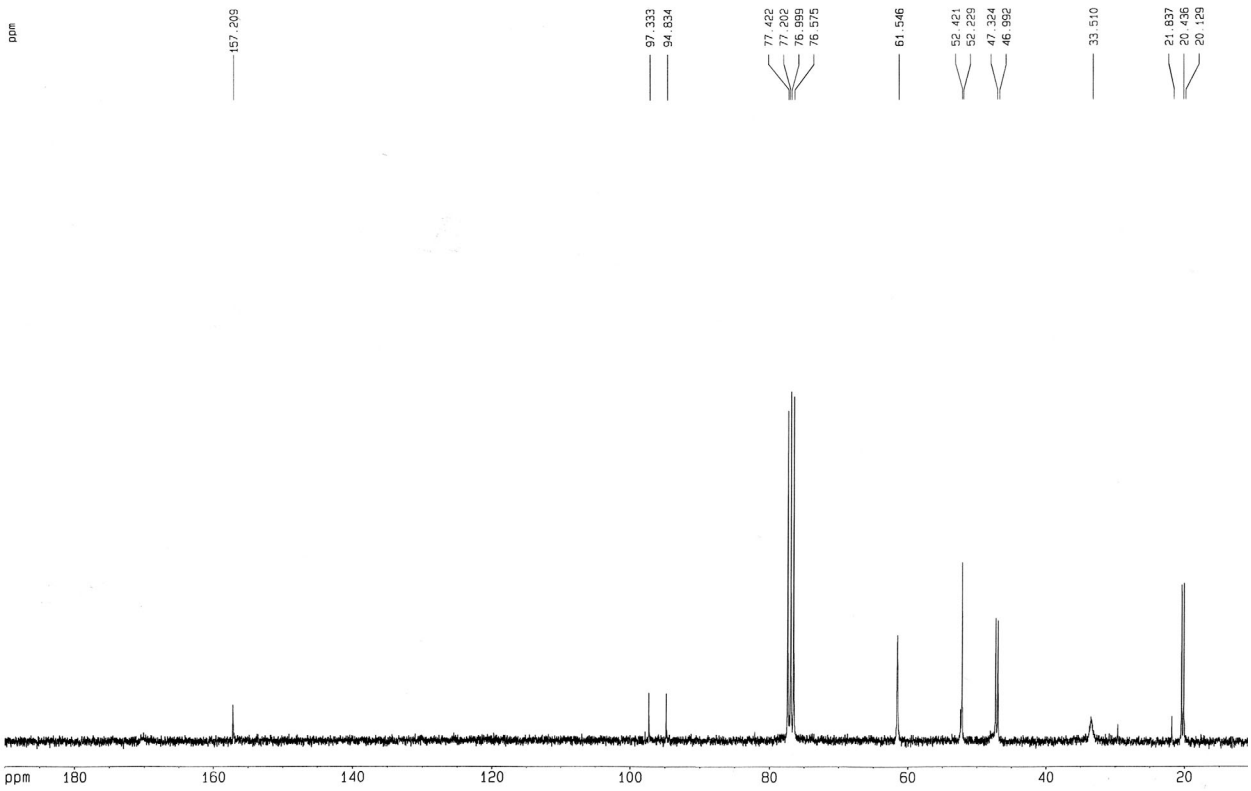

ppm
3.397
1.626
O
H2N
OH
Me
CN
(R)-15
2.000
3.018
ppm
4.0
3.5
3.0
2.5
2.0
1.5

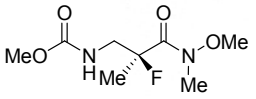

ppm
179.856
123.005
47.561
45.514
23.812


ppm
180
160
140
120
100
80
60
40
20

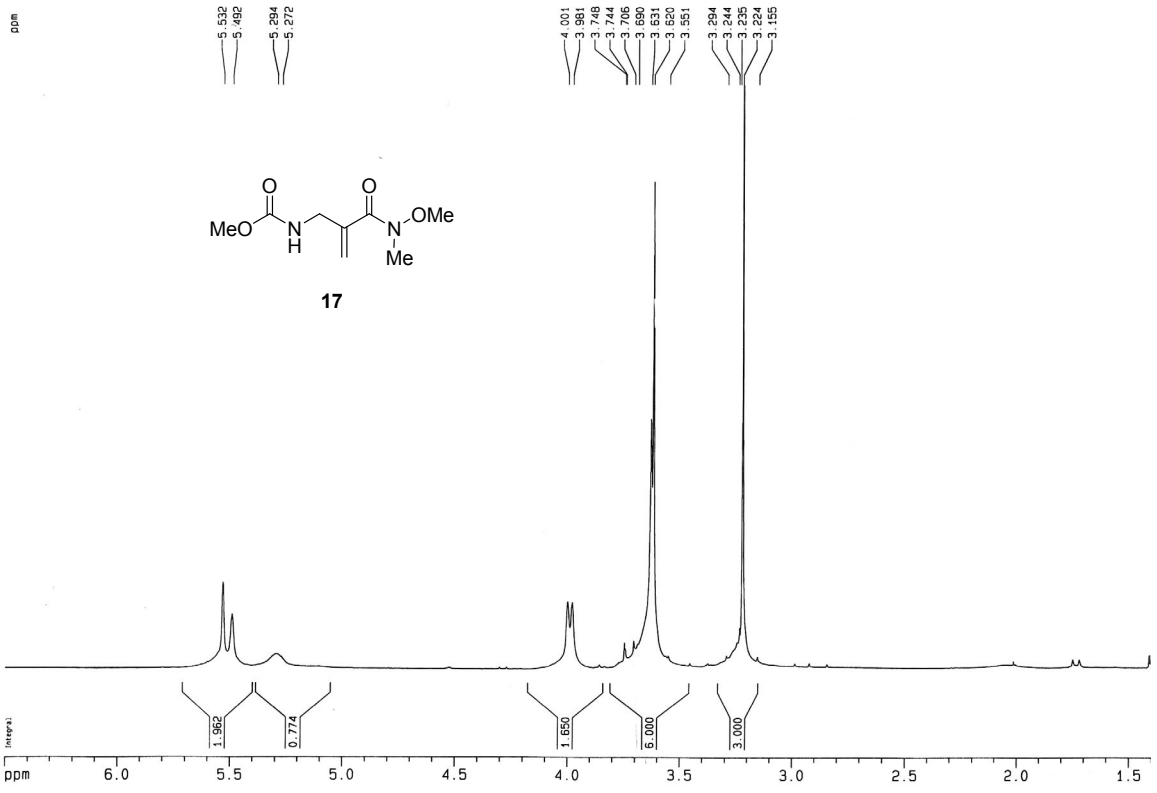

O
H2N
OH
Me
CN
(R)-15
2
3
4
ppm
ppm
4
3
2

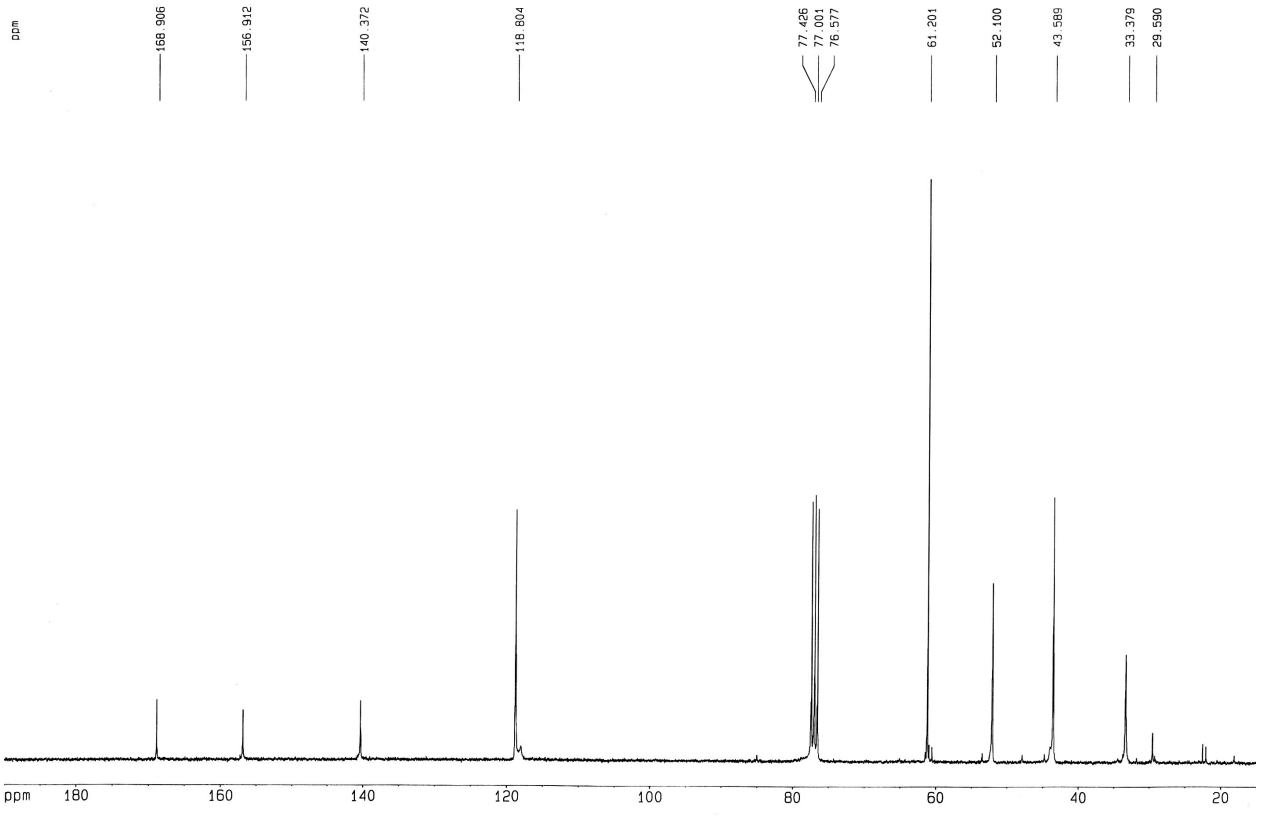

ppm
5.227
3.782
3.711
3.683
3.650
3.622
3.609
3.589
3.562
3.542
3.213
3.145
1.755
1.622
1.549
MeO
N
H
Me
O
F
O
N
OMe
Me
(S)-16
Integral
1.063
8.070
3.000
3.086
ppm
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5

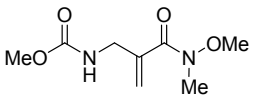

ppm
157.209
97.333
94.834
77.422
77.202
76.999
76.575
61.546
52.421
52.229
47.324
46.992
33.510
21.837
20.436
20.129
ppm
180
160
140
120
100
80
60
40
20



(*S*)-**16**


ppm
5.532
5.492
5.294
5.272
4.001
3.981
3.748
3.744
3.706
3.690
3.631
3.620
3.551
3.294
3.244
3.235
3.224
3.155
MeO
O
N
H
O
N
OMe
Me
17
Integral
1.962
0.774
1.650
6.000
3.000
ppm
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5


ppm
168.906
156.912
140.372
118.804
77.426
77.001
76.577
61.201
52.100
43.589
33.379
29.590
ppm
180
160
140
120
100
80
60
40
20



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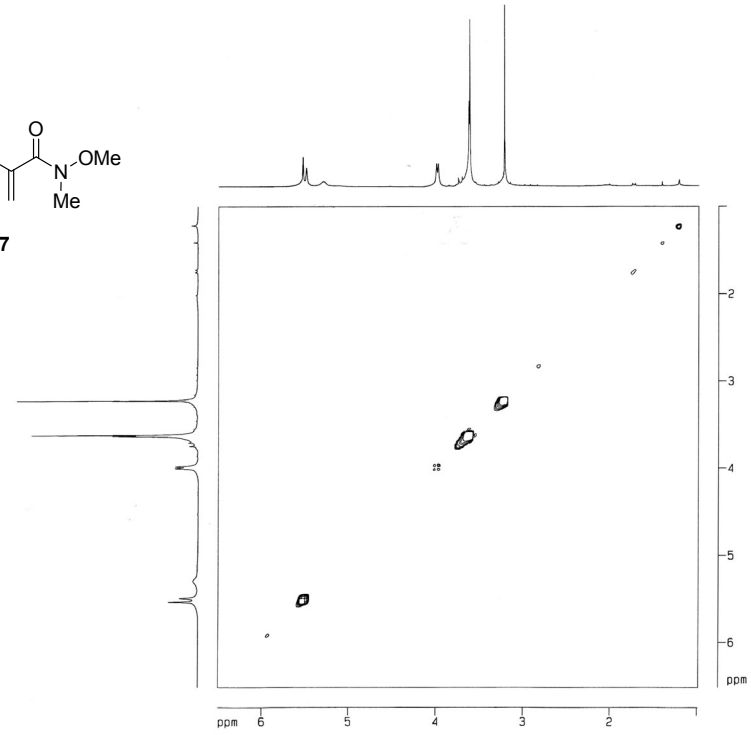
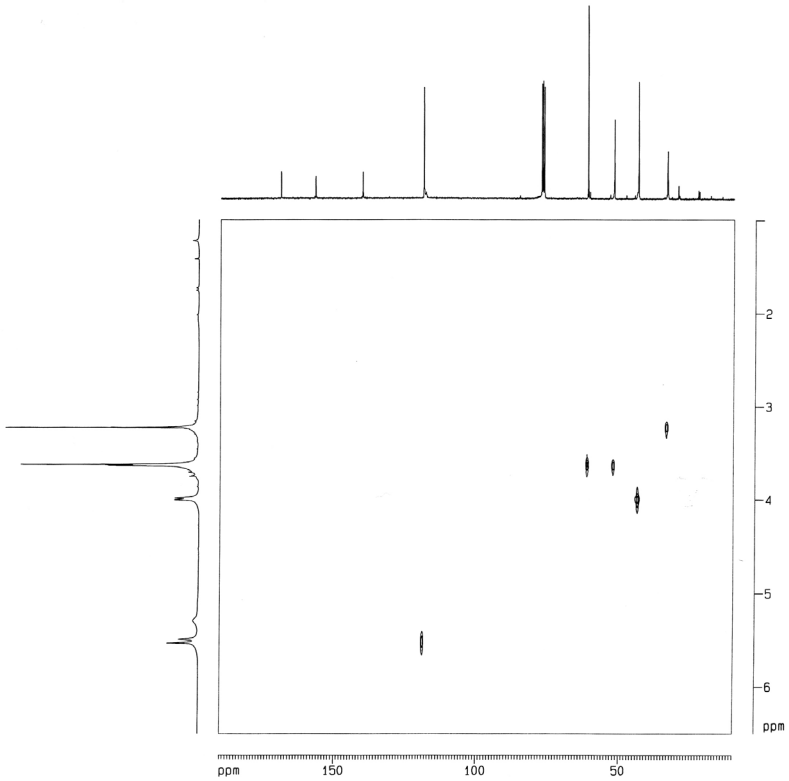
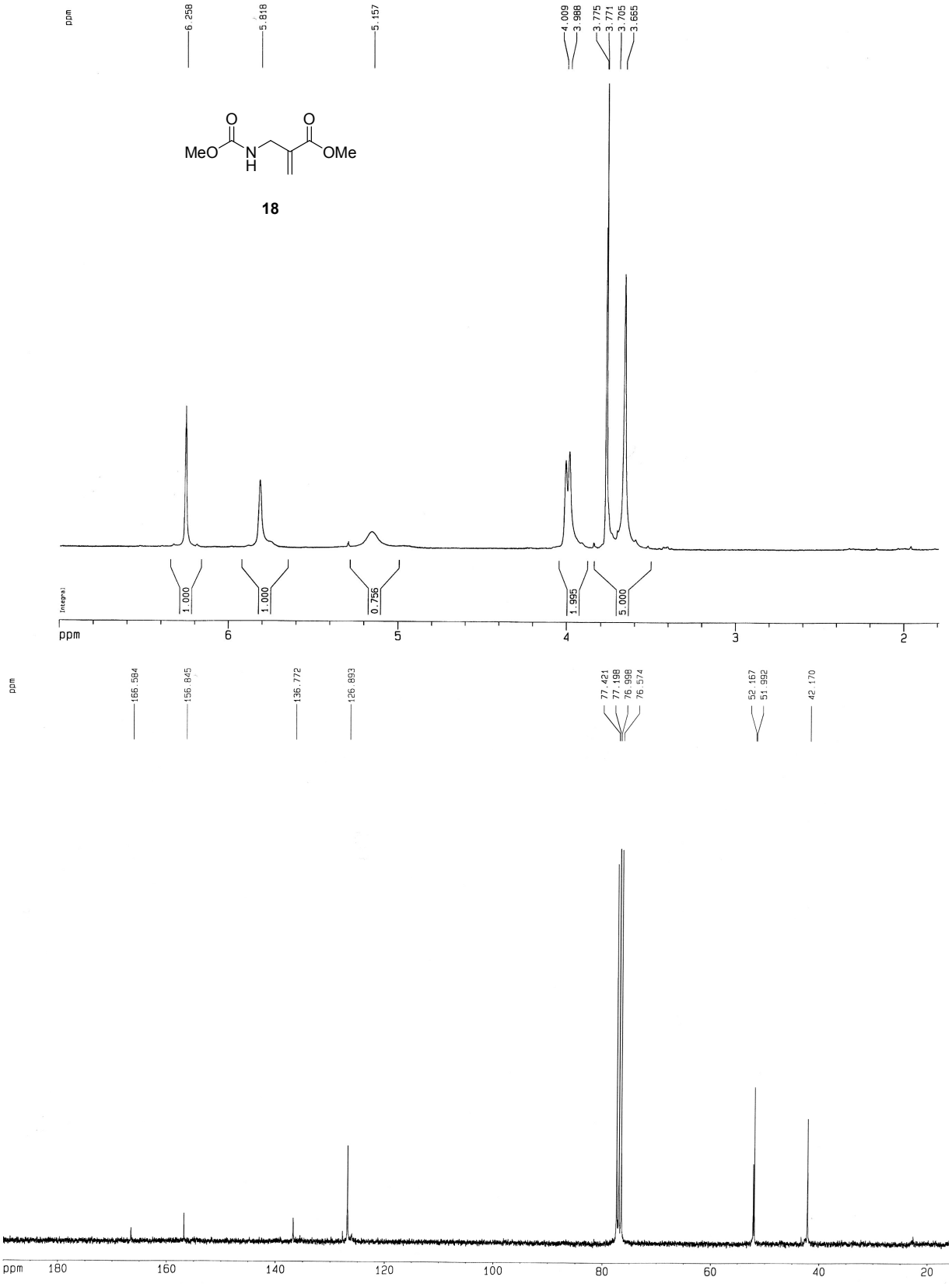
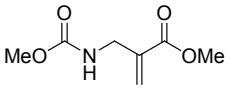





ppm
6.258
5.818
5.157
4.009
3.988
3.775
3.771
3.705
3.665
MeO
O
N
H
O
OMe
18
Integral
1.000
1.000
0.756
1.995
5.000
ppm
6
5
4
3
2
ppm
166.584
156.845
136.772
126.893
77.421
77.198
76.998
76.574
52.167
51.992
42.170
ppm
180
160
140
120
100
80
60
40
20



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