Supporting Information

for

"A Convenient Enantioselective Synthesis of (*S*)-α-Trifluoromethylisoserine"

submitted to ***The Journal of Organic Chemistry*** as a ***NOTE*** by:

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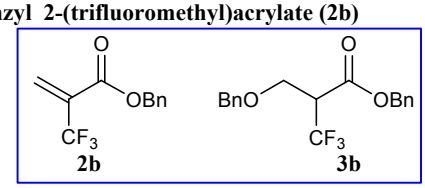
CONTENTS

Experimental procedures and a full listing of ^{1}H, ^{13}C NMR and ^{19}F NMR data, completed with peak assignments for all new compounds

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 or 400 MHz (^{1}H), at 75 or 100 MHz (^{13}C) and 282 MHz (^{19}F) and are reported in ppm downfield from TMS; coupling constants (*J*) in Hz. Microanalyses were carried out on a elemental analyser and were in good agreement with the calculated values. Mass spectra were obtained by electrospray ionization (ESI).

Benzyl 2-(trifluoromethyl)acrylate (2b)

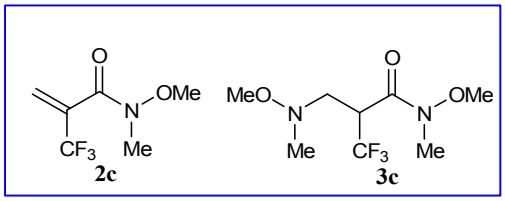


2-(Trifluoromethyl)acrylic acid **2a** (989 mg, 7.06 mmol), 2-chloro-1-methylpyridinium iodide (2.19 g, 8.31 mmol) and triethylamine (TEA) (2.40 mL, 16.61 mmol) were dissolved in CH_2Cl_2 (50 mL) at RT. Furthermore, benzylic alcohol (0.86 mL) was added and the mixture was stirred for 16 h at reflux. The solution was then evaporated and the reaction crude was purified by flash column chromatography (hexane/CH_2Cl_2, 8:2) to give compound **2b** (540 mg, 34%) as a colorless liquid and the racemic sideproduct benzyl 3-(benzyloxy)-2-(trifluoromethyl)propanoate **3b** (18%).

Compound **3b**: ESI+ (*m*/*z*) = 339.3. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 3.52 (m, 1H); 3.86 (dd, 1H, J = 4.8 Hz, J = 9.5); 3.92-3.99 (m, 1H); 4.51 (s, 2H); 5.19-5.28 (m, 2H); 7.22-7.37 (m, 10H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 51.1 (q, $^{2}J_{CF}$ = 27.2); 65.4 (q, $^{3}J_{CF}$ = 2.9); 67.6; 73.5; 123.6 (q, $^{1}J_{CF}$ = 280.2); 127.6; 127.9; 128.1; 128.4; 128.6; 134.9; 131.1; 165.8 (q, $^{3}J_{CF}$ = 3.2, CO). Anal. Calcd. for $C_{18}H_{17}F_3O_3$: C, 63.90; H, 5.06. Found: C, 64.01; H, 5.13.

Compound **2b**: ESI+ (*m*/*z*) = 231.2. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.30 (s, 2H); 6.45 (d, 1H, J = 1.1); 6.75 (d, 1H, J = 1.7); 7.31-7.42 (m, 5H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 67.4; 121.3 (q, $^{1}J_{CF}$ = 271.1); 128.0; 128.5; 128.7; 131.5 (q, $^{2}J_{CF}$ = 32.0, *C*CF_3); 132.9 (q, $^{3}J_{CF}$ = 2.5); 135.0; 161.1. **^{19}F NMR** (282 MHz, $CDCl_3$): δ −64.4 (s). Anal. Calcd. for $C_{11}H_9F_3O_2$: C, 57.40; H, 3.94. Found: C, 57.56; H, 3.83.

2-(Trifluoromethyl)-*N*-methoxy-*N*-methylacrylamide (2c)

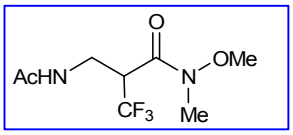


A solution of *N*,*O*-dimethylhydroxylamine (933 mg, 9.37 mmol), freshly prepared by slow addition of DIEA over the corresponding hydrochloride suspended in CH_2Cl_2 (50 mL) at 0 ºC, was added to a solution of acid **2a** (1.12 g, 7.83 mmol) in CH_2Cl_2 at −40 ºC. Then DCC (1.95 g, 9.37 mmol) was added and the mixture was stirred at 0 ºC for 16 h. The suspension was filtered and the evaporated residue was treated with cold hexane. The resulting suspension was filtered again and concentrated to obtain a reaction crude that was purified by flash column chromatography (hexane/ethyl acetate, 8.5:1.5) to give compound **2c** (1.21 g, 83%) as a colorless liquid and the racemic sideproduct 3-(*N*-methoxy-*N*-methylamino)-2-(trifluoromethyl)-*N*-methoxy-*N*-methylpropanamide **3c** (8%).

Compound **3c**: ESI+ (*m*/*z*) = 245.3. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.58 (s, 3H); 2.92 (dd, 1H, J = 2.9 Hz, J = 12.9); 3.23-3.34 (m, 4H); 3.45 (s, 3H); 3.76 (s, 3H) 4.15-4.30 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 32.3; 42.8 (q, $^{2}J_{CF}$ = 26.1); 44.9; 56.7; 59.4; 61.4; 124.5 (q, $^{1}J_{CF}$ = 280.3); 167.2. Anal. Calcd. for $C_8H_{15}F_3N_2O_3$: C, 39.35; H, 6.19; N, 11.47. Found: C, 39.48; H, 6.23; N, 11.32.

Compound **2c**: ESI+ (*m*/*z*) = 184.1. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 3.27 (s, 3H); 3.63 (s, 3H); 5.97 (s, 1H); 6.13 (s, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ 32.7; 61.2; 121.4 (q, $^{1}J_{CF}$ = 271.9); 125.1 (q, $^{3}J_{CF}$ = 2.5); 134.4 (q, $^{2}J_{CF}$ = 32.6); 163.3. **^{19}F NMR** (282 MHz, $CDCl_3$): δ −64.4 (s). Anal. Calcd. for $C_6H_8F_3NO_2$: C, 39.35; H, 4.40; N, 7.65 Found: C, 39.51; H, 4.32; N, 7.69.

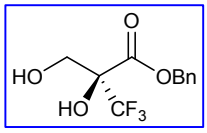
Sharpless asymmetric aminohydroxylation of olefin 2c:
3-Acetamido-2-(trifluoromethyl)-*N*-methoxy-*N*-methylpropanamide (3d)



A round-bottomed flask was charged with H_2O (2 mL), $LiOH{\cdot}H_2O$ (28 mg, 0.67 mmol) and $K_2OsO_4{\cdot}2H_2O$ (10 mg) to give a clear pink solution. $(DHQD)_2PHAL$ (25 mg) and *tert*-butyl alcohol (4 mL) were added and the mixture was stirred at 25 ºC until both phases were clear. H_2O (4 mL) was then added and the mixture cooled to 0 ºC for 30 min. Olefin **2c** (120 mg, 0.66 mmol) and *N*-bromoacetamide (99 mg, 0.73 mmol) were added in a single portion. The color mixture became dark green at this point, and was stirred at 0 ºC for 24 h, whereupon its color slowly turned into red. The reaction was quenched by addition of sodium sulphite (325 mg, 2.58 mmol) and then stirred at 25 ºC for 1 h. The reaction mixture was extracted with ethyl acetate (3×10 mL) and then dried

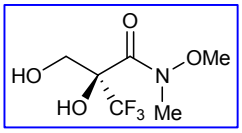
(Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexane/ethyl acetate, 4:6) to give, in the place of aminohydroxylation products, racemic compound **3d** (coming from the Michel addition of acetamide on olefin **2c**) and dihydroxylation product (10% of **4c**) in a 90/10 ratio. Compound **3d**: (colorless oil, 134 mg, 84%). $[\alpha]^{24}_D$ (*c* 1.00, $CHCl_3$) = 0.0. ESI+ (*m*/*z*) = 243.2. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.98 (s, 3H); 3.25 (s, 3H); 3.49-3.62 (m, 1H); 3.72 (s, 3H); 3.76-3.88 (m, 1H); 4.17-4.33 (m, 1H), 6.60 (br s, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 22.7; 32.0; 36.5; 43.8 (q, $^2J_{CF}$ = 25.8); 61.6; 124.1 (q, $^1J_{CF}$ = 279.1); 168.2; 170.9. Anal. Calcd. for $C_8H_{13}F_3N_2O_3$: C, 39.67; H, 5.41; N, 11.57. Found: C, 39.78; H, 5.45; N, 11.42.

Benzyl (*S*)-2-(trifluoromethyl)-2,3-dihydroxypropanoate [(*S*)-4b, 66% ee**]***



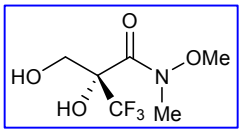
A round-bottomed flask was charged with *tert*-butyl alcohol (12 mL), H_2O (12 mL), AD-mix-β (3.31 g), $K_2OsO_4{\cdot}2H_2O$ (40 mg), $(DHQD)_2PHAL$ (94 mg) and methanesulfonamide (232 mg, 2.37 mmol). The mixture was stirred at 25 ºC until both phases are clear, and then cooled to 0 ºC, whereupon the inorganic salts partially precipitated. Olefin **2b** (540 mg, 2.37 mmol) was added and the heterogeneous slurry was vigorously stirred at 0 ºC for 24 h. The reaction was quenched by addition of sodium sulphite (3.56 g) and then stirred for 1 h. The reaction mixture was extracted with ethyl acetate (3×60 mL) and then dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexane/ethyl acetate, 8:2) to give compound (*S*)-**4b** (543 mg, 87%, 66% ee)* as a colorless oil. ESI+ (*m*/*z*) = 265.3. $[\alpha]^{24}_D$ (*c* 2.21, $CHCl_3$) = −14.5. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.97 (br s, 1H); 3.87 (d, 1H, *J* = 11.7); 4.07 (d, 1H, *J* = 11.7); 4.53 (br s, 1H); 5.26-5.35 (m, 2H); 7.33-7.38 (m, 5H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 62.2; 69.3; 78.6 (q, $^2J_{CF}$ = 28.3); 122.5 (q, $^1J_{CF}$ = 284.5); 127.0; 128.0; 128.7; 131.4; 168.2. **^{19}F NMR** (282 MHz, $CDCl_3$): δ −76.5 (s). Anal. Calcd. for $C_{11}H_{11}F_3O_4$: C, 50.01; H, 4.20. Found: C, 49.87; H, 4.31.

(*S*)-2-(Trifluoromethyl)-2,3-dihydroxy-*N*-methoxy-*N*-methylpropanamide [(*S*)-4c, 90% ee**]***



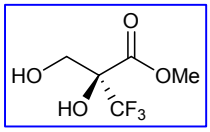
A round-bottomed flask was charged with *tert*-butyl alcohol (27 mL), H_2O (27 mL), AD-mix-β (7.51 g), $K_2OsO_4{\cdot}2H_2O$ (90 mg), $(DHQD)_2PHAL$ (213 mg) and methanesulfonamide (526 mg, 5.37 mmol). The mixture was stirred at 25 ºC until both phases are clear, and then cooled to 0 ºC, whereupon the inorganic salts partially precipitated. Olefin **2c** (983 mg, 5.37 mmol) was added and the heterogeneous slurry was vigorously stirred at 0 ºC for 24 h. The reaction was quenched by addition of sodium sulphite (8.06 g) and then stirred for 1 h. The reaction mixture was extracted with ethyl acetate (3×100 mL) and then dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexane/ethyl acetate, 7:3) to give compound (*S*)-**4c** (1.05 mg, 90%, 90% ee)* as a colorless oil. $[\alpha]^{24}_D$ (*c* 1.28, $CHCl_3$) = −28.9. ESI+ (*m*/*z*) = 218.1. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.60 (br s, 1H); 3.36 (s, 3H); 3.77 (s, 3H); 3.93 (d, 1H, *J* = 11.8); 4.25 (d, 1H, *J* = 11.8); 5.24 (s, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 34.1; 61.1; 62.2 (q, $^3J_{CF}$ = 1.6); 79.1 (q, $^2J_{CF}$ = 28.4); 122.9 (q, $^1J_{CF}$ = 284.6); 165.7. **^{19}F NMR** (282 MHz, $CDCl_3$): δ −75.2 (s). Anal. Calcd. for $C_6H_{10}F_3NO_4$: C, 33.19; H, 4.64; N, 6.45. Found: C, 33.02; H, 4.76; N, 6.36.

(*R*)-2-(Trifluoromethyl)-2,3-dihydroxy-*N*-methoxy-*N*-methylpropanamide [(*R*)-4c, 90% ee**]***



The same protocol using AD-mix-α and the proper amount of $(DQD)_2PHAL$ lead to (*R*)-diol. $[\alpha]^{24}_D$ (*c* 0.87, $CHCl_3$) = +29.2.

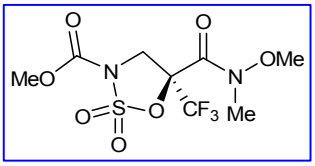
Methyl (*S*)-2-(trifluoromethyl)-2,3-dihydroxypropanoate [(*S*)-4d]



To a solution of compound (*S*)-**4c** (624 mg, 2.87 mmol) in H_2O/MeOH (1:3, 20 mL), $LiOH{\cdot}H_2O$ (603 mg, 14.35 mmol) was added and the mixture was stirred at 25 ºC 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, prepared by dropwise addition of AcCl (15 mL) to MeOH (60 mL) at 0 ºC, and the mixture was heated under reflux for 12 h. The mixture was concentrated and the residue partitioned between H_2O (20 mL) and $CHCl_3$/isopropanol (3:1, 30 mL). The aqueous layer was successively washed with $CHCl_3$/isopropanol (4×30 mL), dried (Na_2SO_4), concentrated and the crude product was purified by column chromatography (hexane/ethyl acetate, 7:3) to give (*S*)-**4d** (458 mg, 85%) as a colorless oil. $[\alpha]^{24}_D$ (*c* 1.45, MeOH) = −13.7. ESI+ (*m*/*z*) = 189.0. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 2.68 (br s, 1H); 3.90 (d, 1H, *J* = 11.7); 3.93 (s, 3H); 4.06 (d, 1H, *J* = 11.7); 4.36 (s, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ 54.5; 62.2 (q, $^3J_{CF}$ = 1.7); 78.5 (q, $^2J_{CF}$ = 28.5); 122.4 (q, $^1J_{CF}$ = 284.3); 168.8. **^{19}F NMR** (282 MHz, $CDCl_3$): δ −75.8 (s). Anal. Calcd. for $C_5H_7F_3O_4$: C, 31.93; H, 3.75. Found: C, 32.08; H, 3.80.

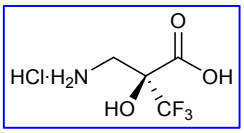
* Enantiomeric excess (ee) of the resulting diols were measured by GC-MS using a chiral capilar column (β-DEX™) as stationary phase, and obtained cromatograms are shown in other section (page S31).

Methyl (*S*)-5-(methoxymethylcarbamoyl)-5-(trifluoromethyl)-2,2-dioxo-2λ^6-[1,2,3]oxathiazolidine-3-carboxylate [(*S*)-5]



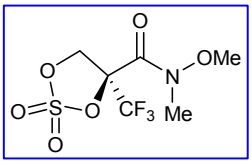
Diol (*S*)-**4c** (168 mg, 0.77 mmol) was dissolved in THF (60 mL) and Burgess reagent (461 mg, 1.93 mmol) was added. The resulting solution was stirred at reflux for 1 h, concentrated and then purified by column chromatography (hexane/ethyl acetate, 7:3) to give (*S*)-**5** (132 mg, 51%) as a colorless oil. $[\alpha]^{24}_D$ (*c* 1.41, MeOH) = +6.8. ESI+ (*m*/*z*) = 337.3. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 3.31 (s, 3H); 3.78 (s, 3H); 3.94 (s, 3H); 4.38 (d, 1H, *J* = 11.6); 4.78 (d, 1H, *J* = 11.0). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 33.8; 44.0; 55.2; 61.9; 81.2 (q, $^2J_{CF}$ = 33.3); 121.2 (q, $^1J_{CF}$ = 284.7); 149.2; 160.1. **^{19}F NMR** (282 MHz, $CDCl_3$): δ −76.2 (s). Anal. Calcd. for $C_8H_{11}F_3N_2O_7S$: C, 28.58; H, 3.30; N, 8.33; S, 9.54. Found: C, 28.33; H, 3.21; N, 8.49; S, 9.78.

(*S*)-3-Amino-2-(trifluoromethyl)-2-hydroxypropanoic acid hydrochloride or (*S*)-2-(trifluoromethyl)isoserine hydrochloride [(*S*)-1·HCl]



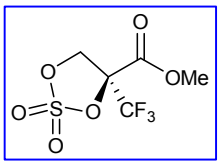
Sulfamidate (*S*)-**5** (63 mg, 0.19 mmol) was treated with an aqueous solution of 6N HCl (2 mL) at reflux for 12 h. The solvent was removed to give (*S*)-**1** as hydrochloride derivative (white solid). The *N*,*O*-dimethylhydroxylamine hydrochloride formed in the reaction was removed by suspending and filtrating the mixture in absolute ethanol. Further purification was achieved eluting the resulting mixture through a C_{18} reverse-phase Sep-pak cartridge with water and evaporating the solvent (36 mg, 90%). $[\alpha]^{24}_D$ (*c* 0.95, H_2O) = −16.8. ESI+ (*m*/*z*) = 174.2. **^{1}H NMR** (300 MHz, D_2O): δ 3.36-3.54 (m, 2H). **^{13}C NMR** (75 MHz, D_2O): δ 42.1; 76.3 (q, $^2J_{CF}$ = 29.6); 124.3 (q, $^1J_{CF}$ = 284.6); 169.7. **^{19}F NMR** (282 MHz, D_2O): δ −75.4 (s).

(*S*)-4-(Trifluoromethyl)-2,2-dioxo-2λ^6-[1,3,2]dioxathiolane-4-carboxylic acid *N*-methoxy-*N*-methylamide [(*S*)-6c]



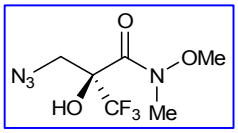
Diol (*S*)-**4c** (610 mg, 2.81 mmol) was dissolved in CH_2Cl_2 (20 mL), and TEA (1.7 mL, 12.36 mmol) and SO_2Cl_2 (0.47 mL, 5.61 mmol) were added dropwise at −20 ºC. The resulting solution was stirred for 1 h, concentrated and then purified by column chromatography (hexane/ethyl acetate, 4:1) to give (*S*)-**6c** (637 mg, 81%) as a colorless liquid. $[\alpha]^{24}_D$ (*c* 1.12, $CHCl_3$) = −17.0. ESI+ (*m*/*z*) = 280.0. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 3.31 (s, 3H); 3.79 (s, 3H); 4.96 (d, 1H, *J* = 10.4); 5.13 (d, 1H, *J* = 10.4). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 33.5; 62.2; 70.1; 84.0 (q, $^2J_{CF}$ = 33.8); 121.1 (q, $^1J_{CF}$ = 284.7); 160.2. **^{19}F NMR** (282 MHz, $CDCl_3$): δ −76.6 (s). Anal. Calcd. for $C_6H_8F_3NO_6S$: C, 25.81; H, 2.89; N, 5.02; S, 11.48. Found: C, 25.68; H, 2.98; N, 5.09; S, 11.36.

Methyl (*S*)-4-(trifluoromethyl)-2,2-dioxo-2λ^6-[1,3,2]dioxathiolane-4-carboxylate [(*S*)-6d]



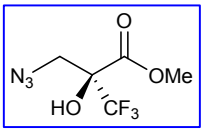
Diol (*S*)-**4c** (225 mg, 1.20 mmol) was dissolved in CH_2Cl_2 (15 mL) and DIEA (0.75 mL, 5.96 mmol) and SO_2Cl_2 (0.20 mL, 2.39 mmol) were added dropwise at −20 ºC. The resulting solution was stirred for 1 h, concentrated and then purified by column chromatography (hexane/ethyl acetate, 4:1) to give (*S*)-**6d** (234 mg, 78%) as a colorless liquid. $[\alpha]^{24}_D$ (*c* 1.84, $CHCl_3$) = −0.9. ESI+ (*m*/*z*) = 251.2. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.00 (s, 3H); 4.95 (d, 1H, *J* = 10.2); 5.04 (d, 1H, *J* = 10.2). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 55.1; 68.8 (q, $^3J_{CF}$ = 1.6); 82.2 (q, $^2J_{CF}$ = 34.0); 120.5 (q, $^1J_{CF}$ = 283.6); 161.9. **^{19}F NMR** (282 MHz, $CDCl_3$): δ −77.4 (s). Anal. Calcd. for $C_5H_5F_3O_6S$: C, 24.01; H, 2.01; S, 12.82. Found: C, 24.16; H, 1.97; S, 12.73.

(*S*)-3-Azido-2-(trifluoromethyl)-2-hydroxy-*N*-methoxy-*N*-methylpropanamide [(*S*)-7c]



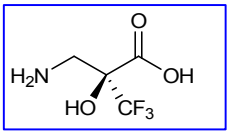
Compound (*S*)-**6c** (560 mg, 2.00 mmol) and NaN_3 (391 mg, 6.02 mmol) were heated in DMF (10 mL) at 70 ºC for 12 h, when consumption of sulfite was observed by GC/MS. The solution was then cooled, concentrated and the residue was partitioned between H_2SO_4 20% (10 mL) and CH_2Cl_2 (20 mL). The aqueous layer was successively extracted with CH_2Cl_2 (2×20 mL), dried over Na_2SO_4, concentrated and the crude product chromatographed (hexane/ethyl acetate, 9:1) to give the β-azido-α-alcohol (*S*)-**7c** (480 mg, 99%) as a colorless liquid. $[\alpha]^{24}_D$ (*c* 1.9, $CHCl_3$) = −73.8. ESI+ (*m*/*z*) = 243.2. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 3.35 (s, 3H); 3.72 (d, 1H, *J* = 12.6); 3.73 (s, 3H); 3.86 (d, 1H, *J* = 12.6); 5.28 (s, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 34.0; 51.6; 61.0; 79.0 (q, $^2J_{CF}$ = 29.1); 122.5 (q, $^1J_{CF}$ = 284.8); 165.0. **^{19}F NMR** (282 MHz, $CDCl_3$): δ −76.0 (s). Anal. Calcd. for $C_6H_9F_3N_4O_3$: C, 29.76; H, 3.75; N, 23.14. Found: C, 29.92; H, 3.65; N, 23.34.

(*S*)-Methyl 3-azido-2-(trifluoromethyl)-2-hydroxypropanoate [(*S*)-7d]



Compound (*S*)-**6d** (160 mg, 0.64 mmol) and NaN_3 (125 mg, 1.92 mmol) were heated in DMF (5 mL) at 70 ºC for 12 h, when consumption of sulfite was observed by GC/MS. The solution was then cooled, concentrated and the residue was partitioned between H_2SO_4 20% (10 mL) and CH_2Cl_2 (20 mL). The aqueous layer was successively extracted with CH_2Cl_2 (2×15 mL), dried over Na_2SO_4, concentrated and the crude product chromatographed (hexane/ethyl acetate, 9:1) to give the β-azido-α-alcohol (*S*)-**7d** (123 mg, 90%) as a colorless liquid. $[\alpha]^{24}_D$ (*c* 1.0, $CHCl_3$) = −48.5. ESI+ (*m*/*z*) = 214.1. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 3.64 (d, 1H, *J* = 12.8); 3.73 (d, 1H, *J* = 12.8); 3.96 (s, 3H); 4.15 (s, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 51.7; 54.8; 78.2 (q, $^2J_{CF}$ = 29.2); 122.2 (q, $^1J_{CF}$ = 285.0); 168.1. **^{19}F NMR** (282 MHz, $CDCl_3$): δ −75.9 (s). Anal. Calcd. for $C_5H_6F_3N_3O_3$: C, 28.18; H, 2.84; N, 19.72. Found: C, 28.31; H, 2.99; N, 19.56.

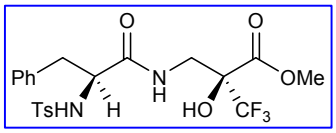
(*S*)-3-Amino-2-(trifluoromethyl)-2-hydroxypropanoic acid or (*S*)-2-(trifluoromethyl)isoserine [(*S*)-1]



Method A: To a solution of compound (*S*)-**7c** (128 mg, 0.53 mmol) in H_2O/MeOH (1:3, 10 mL) was added LiOH·H_2O (111 mg, 2.64 mmol) with the resulting mixture stirred at 25 ºC for 2 h. The *N*,*O*-dimethylhydroxylamine formed in the reaction along with MeOH was removed and the mixture acidified with conc. HCl to pH 1–2. The solvent was removed and the residue partitioned between H_2O (10 mL) and ethyl acetate (20 mL). The aqueous layer was successively extracted with ethyl acetate (2×20 mL), dried over Na_2SO_4 and concentrated. The obtained acid was dissolved in MeOH (5 mL) after which palladium on carbon (1:5, catalyst/substrate by weight) was added. The resulting suspension was stirred at 25 ºC for 48 h. Then, H_2O (5 ml) was added, the catalyst was removed by filtration and the solvent evaporated to give the corresponding amino acid (*S*)-**1** (87 mg, 95%) as a white solid.

Method B: Compound (*S*)-**7d** (67 mg, 0.31 mmol) was treated with an aqueous solution of 6N HCl (5 mL) at 60 ºC for 12 h. The solvent was removed and the residue partitioned between H_2O (10 mL) and ethyl acetate (20 mL). The aqueous layer was successively extracted with ethyl acetate (2×20 mL), dried over Na_2SO_4 and concentrated. The acid obtained was dissolved in methanol (5 mL) after which palladium on carbon (1:5, catalyst/substrate by weight) was added. The resulting suspension was stirred at 25 ºC for 48 h. Then, H_2O (5 mL) was added, the catalyst was removed by filtration and the solvent evaporated to give the corresponding amino acid (*S*)-**1** (47 mg, 87%) as a white solid. $[\alpha]^{24}_D$ (*c* 1.0, H_2O) = −24.1. ESI+ (*m*/*z*) = 174.2. **^{1}H NMR** (400 MHz, D_2O): δ 3.39-3.51 (m, 2H); **^{13}C NMR** (100 MHz, D_2O): δ 40.8; 74.8 (q, $^2J_{CF}$ = 28.0); 123.7 (q, $^1J_{CF}$ = 283.3); 169.9. **^{19}F NMR** (282 MHz, D_2O): δ −75.4 (s). Anal. Calcd. for $C_4H_6F_3NO_3$: C, 27.76; H, 3.49; N, 8.09. Found: C, 27.89; H, 3.57; N, 7.98.

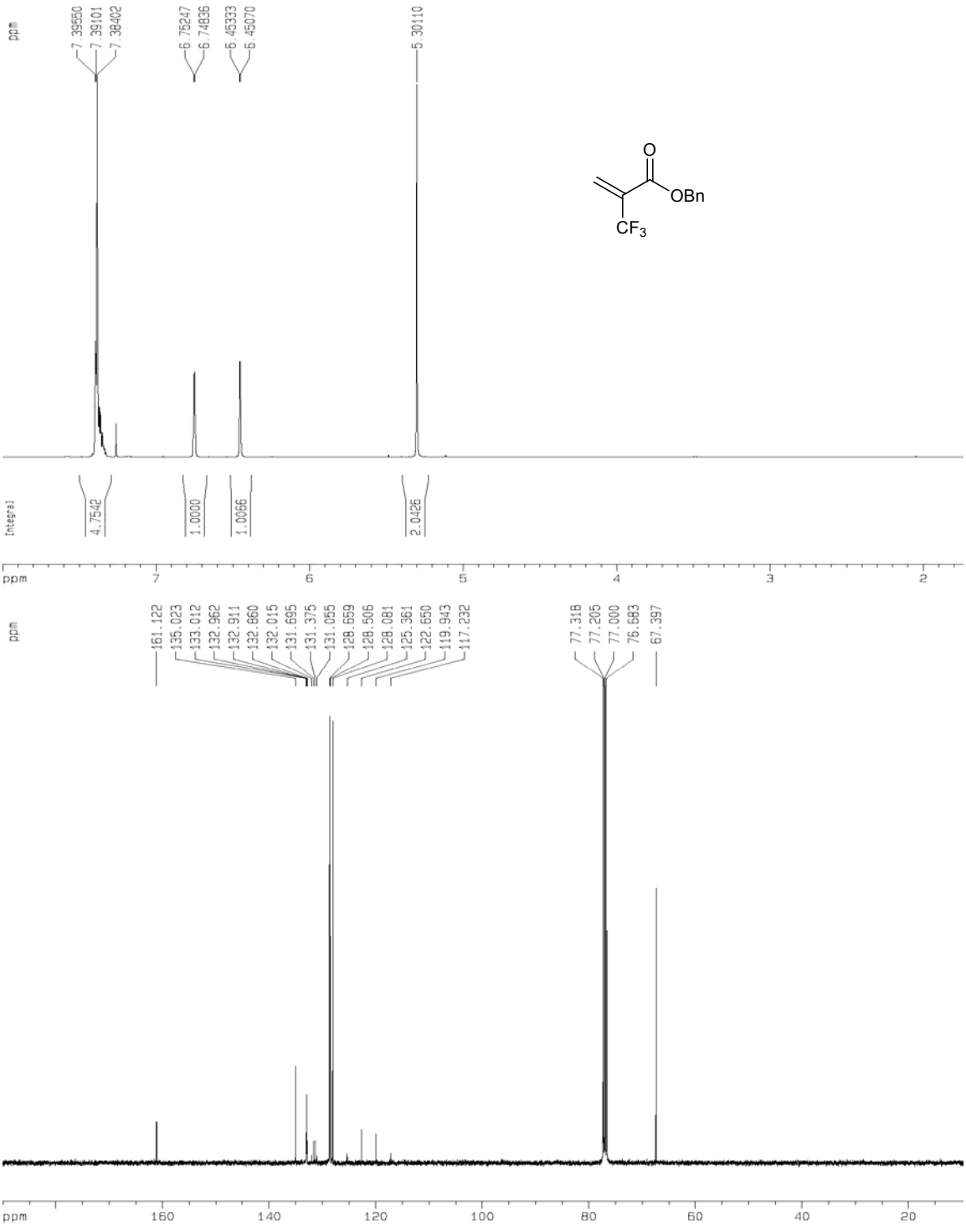
(*S*)-*N*-(Tosyl)phenylalaninyl (*S*)-2-(trifluoromethyl)isoserine methyl ester [(*S*,*S*)-8]

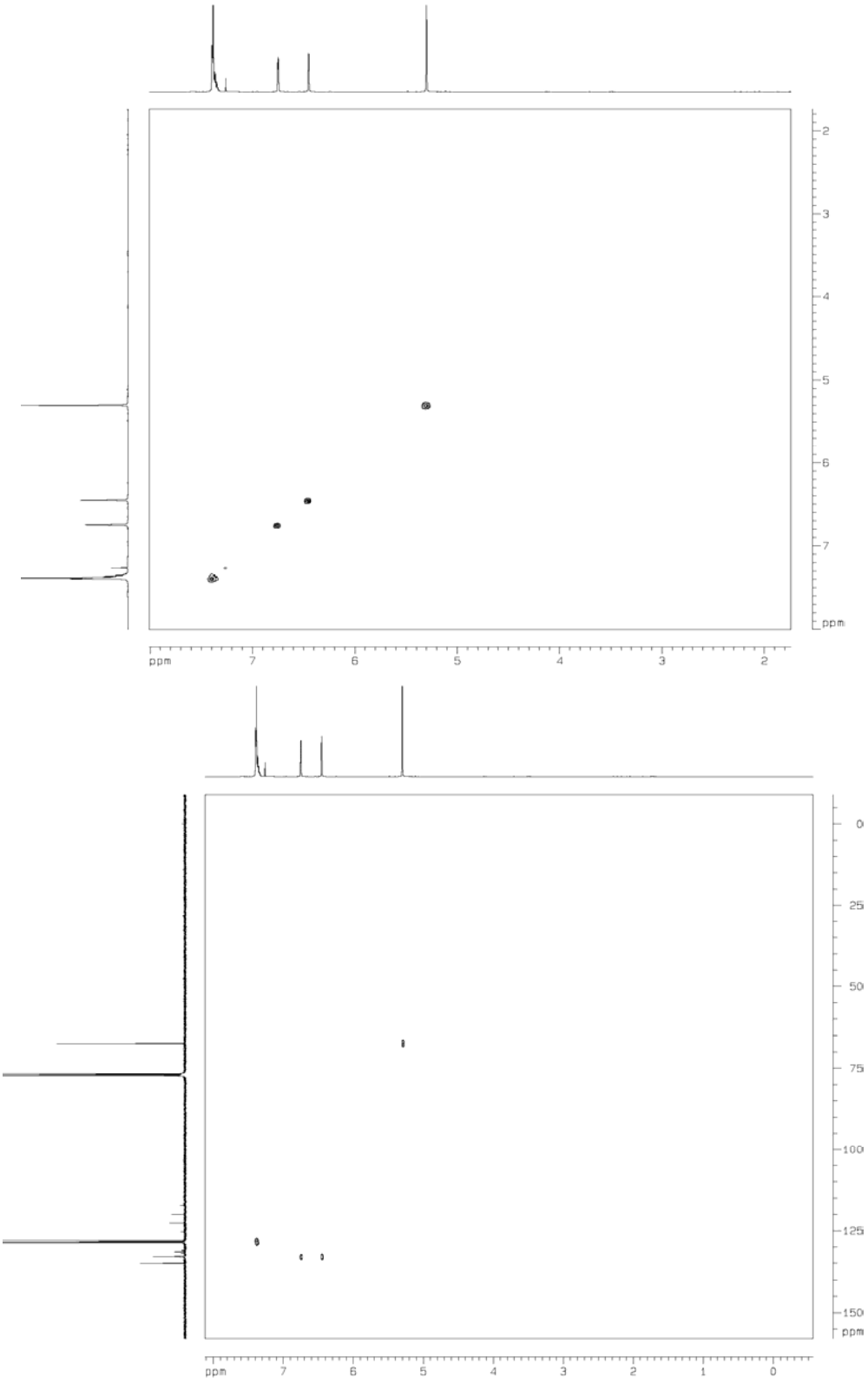


Amino acid (*S*)-**1** (48 mg, 0.28 mmol) was dissolved in HCl/MeOH, prepared by dropwise addition of AcCl (4 mL) to MeOH (16 mL) at 0 ºC, and the mixture was heated under reflux for 10 h. The solvent was evaporated and the resulting hydrochloride was exhaustively dried before being suspended in CH_2Cl_2 (10 mL) under an argon atmosphere. *N*-(tosyl)phenylalaninyl chloride (124 mg, 0.36 mmol) and DIEA (146 µL, 0.84 mmol) were added and the mixture was stirred at 25 ºC for 14 h. The reaction was quenched with 0.5N HCl (2 mL), and the aqueous layer was extracted with ethyl acetate (2×15 mL), dried over Na_2SO_4, concentrated, and the crude product chromatographed (hexane/ethyl acetate, 6:4) to give dipeptide (*S*,*S*)-**8** (120 mg, 88%) as a white solid (mp = 124-126 °C). $[\alpha]^{24}_D$ (*c* 1.27, $CHCl_3$) = −29.0. ESI+ (*m*/*z*) = 489.5. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.42 (s, 3H); 2.75 (dd, 1H, *J* = 14.1, *J* = 8.7); 2.99 (dd, 1H, *J* = 14.1, *J* = 5.2); 3.53 (dd, 1H, *J* = 14.0, *J* = 4.9); 3.84 (td, 1H, *J* = 8.6, *J* = 5.7); 3.89 (s, 3H); 4.18 (dd, 1H, *J* = 14.0, *J* = 7.9), 4.71 (br s, 1H); 5.23 (d, 1H, *J* = 6.3); 6.84-6.90 (m, 2H); 7.04 (dd, 1H, *J* = 7.4, *J* = 5.0); 7.09-7.18 (m, 5H); 7.40-7.47 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 21.5; 37.9; 41.3; 54.4; 58.0; 73.3 (q, $^2J_{CF}$ = 28.9); 122.6 (q, $^1J_{CF}$ = 286.5); 125.3; 126.7; 126.9; 127.2; 128.9; 129.8; 135.1; 143.9; 168.4; 171.8. **^{19}F NMR** (282 MHz, $CDCl_3$): δ −77.5 (s). Anal. Calcd. for $C_{21}H_{23}F_3N_2O_6S$: C, 51.63; H, 4.75; N, 5.73; S, 6.56. Found: C, 51.39; H, 4.87; N, 5.81; S, 6.45.

^{1}H and ^{13}C NMR spectra for compounds as well as ^{1}H-^{1}H and ^{1}H-^{13}C correlations for all new compounds

Benzyl 2-(trifluoromethyl)acrylate (2b)

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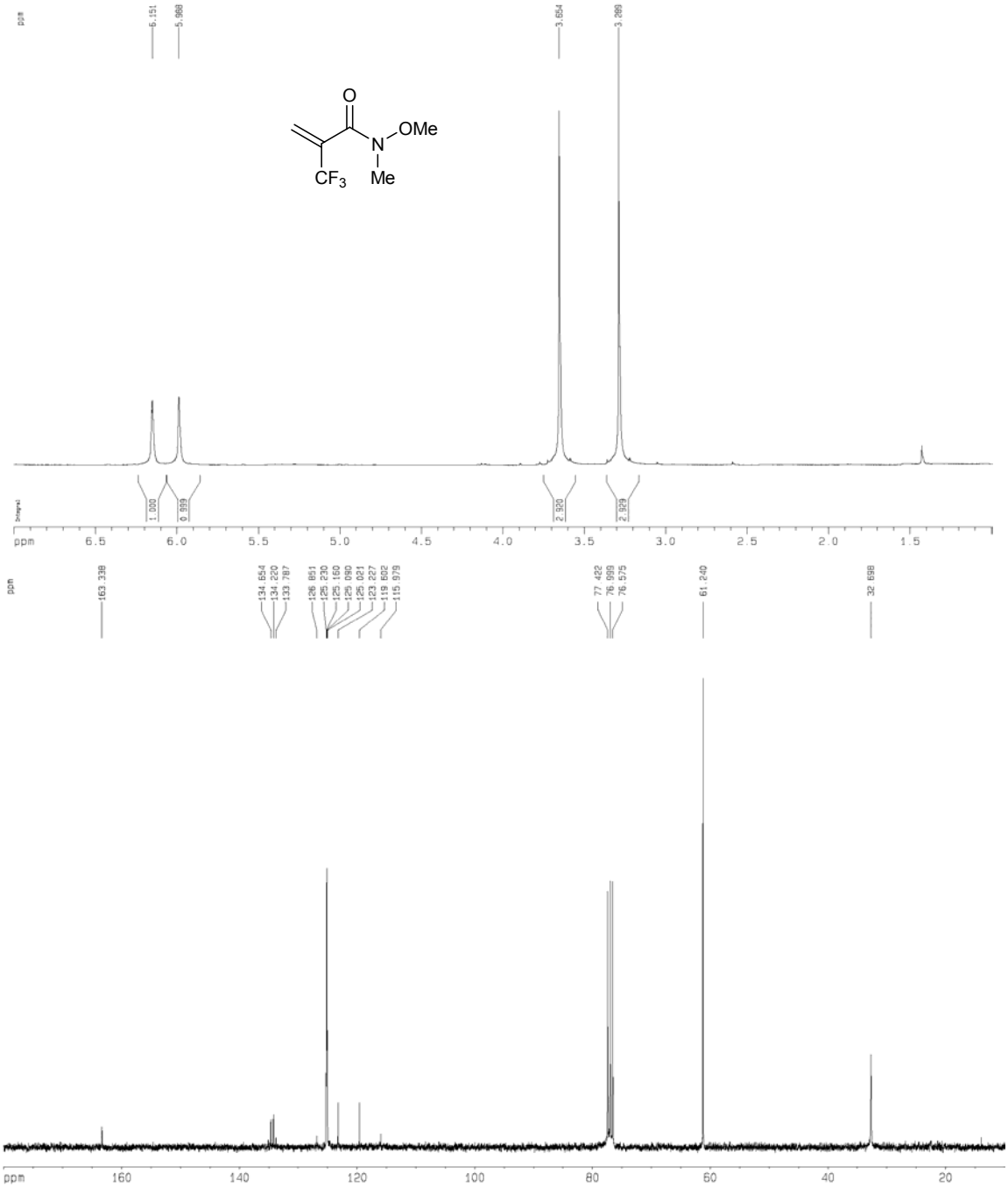
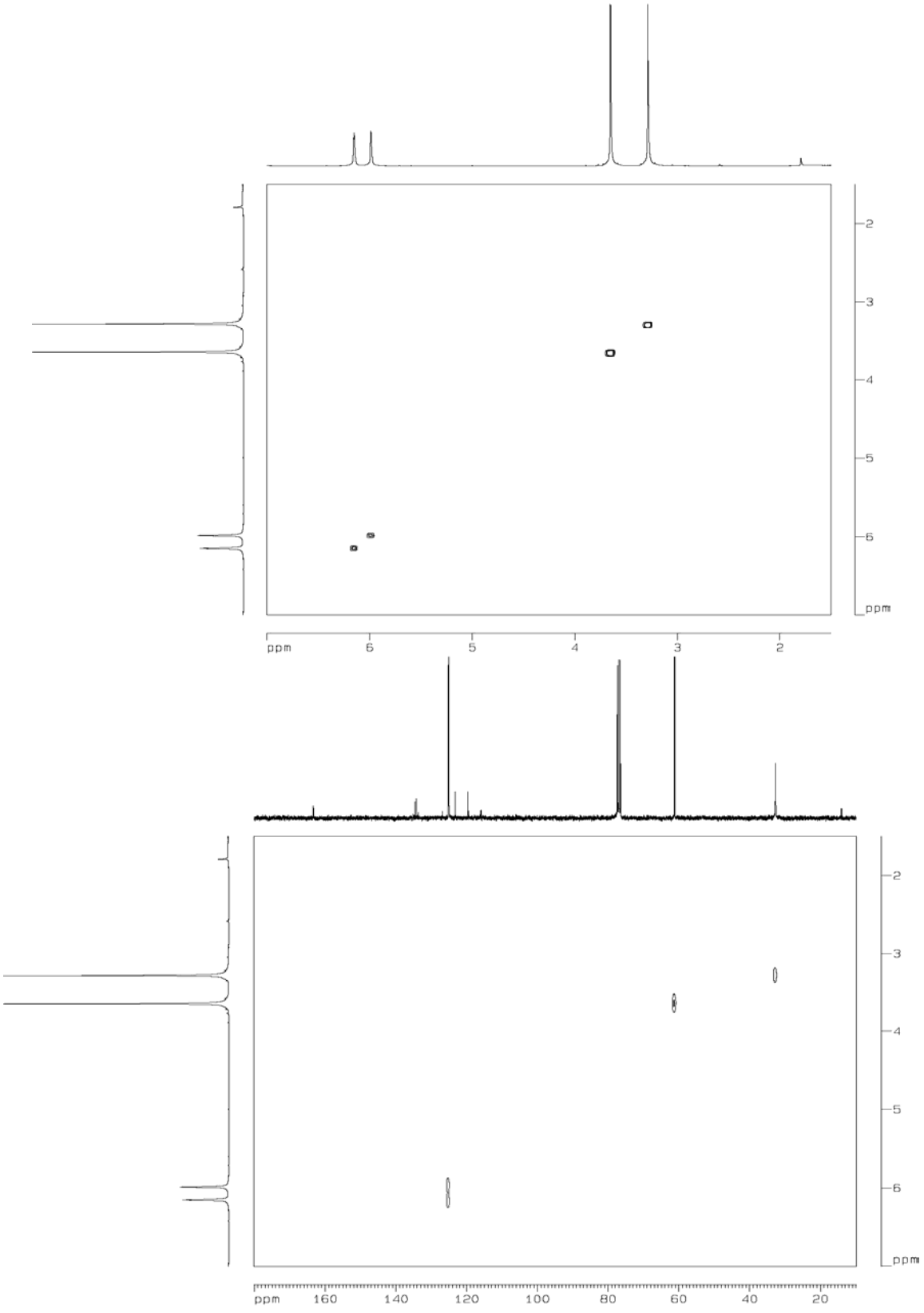
2-(Trifluoromethyl)-*N*-methoxy-*N*-methylacrylamide (2c)

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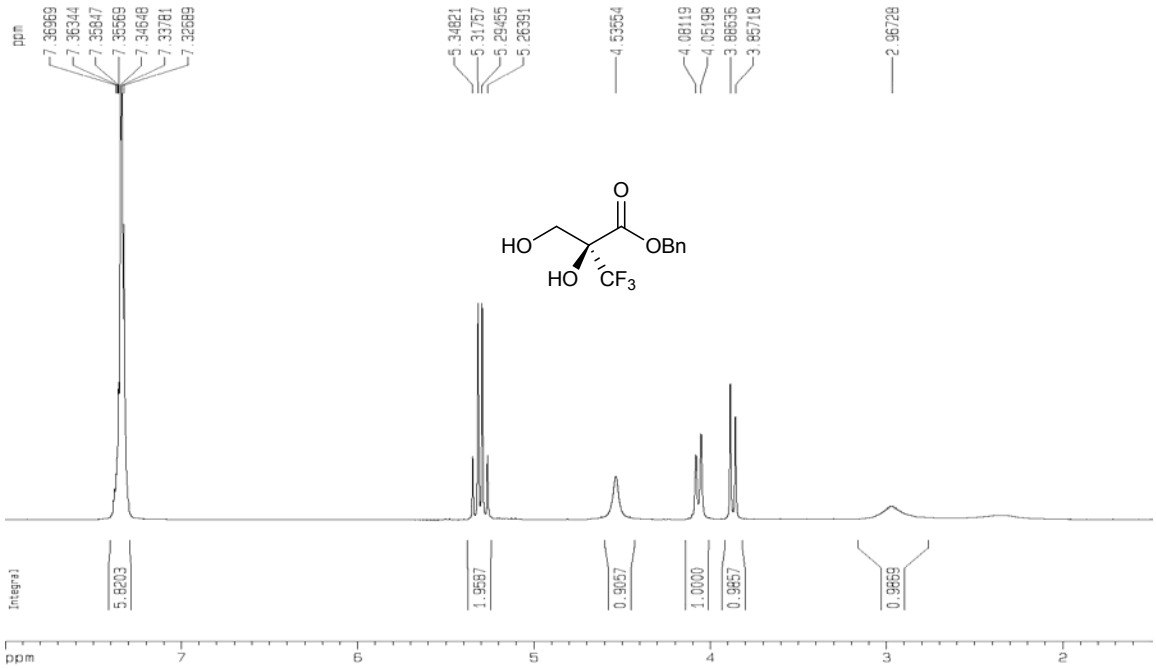
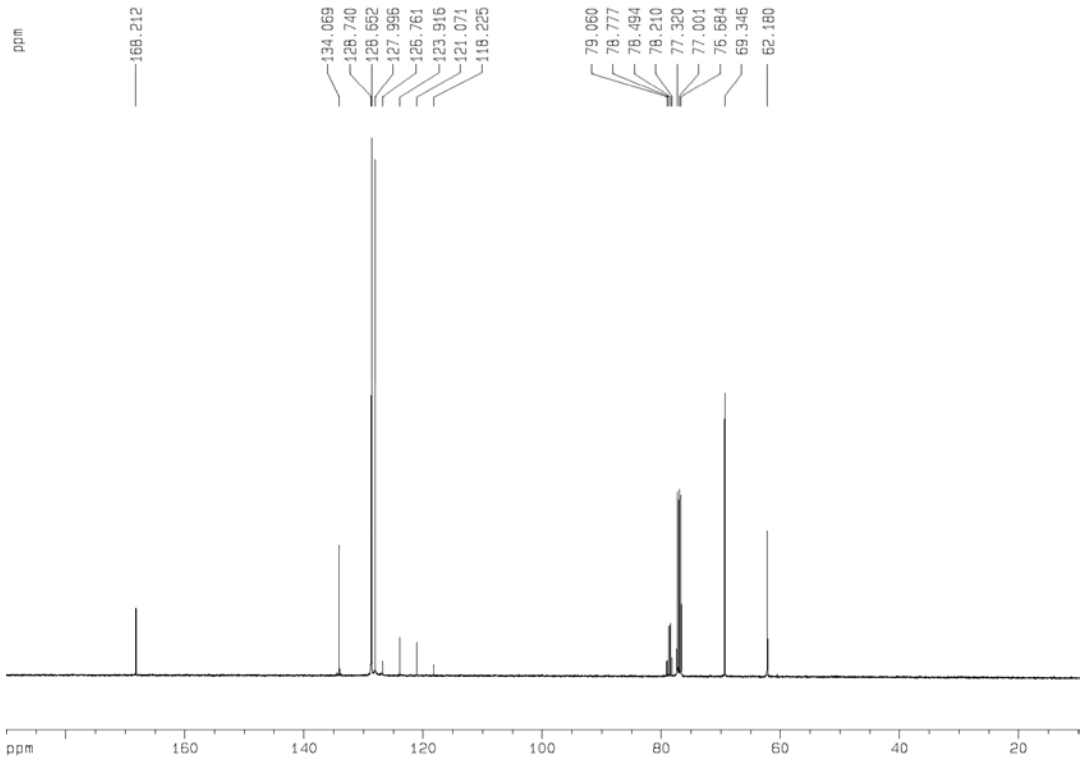
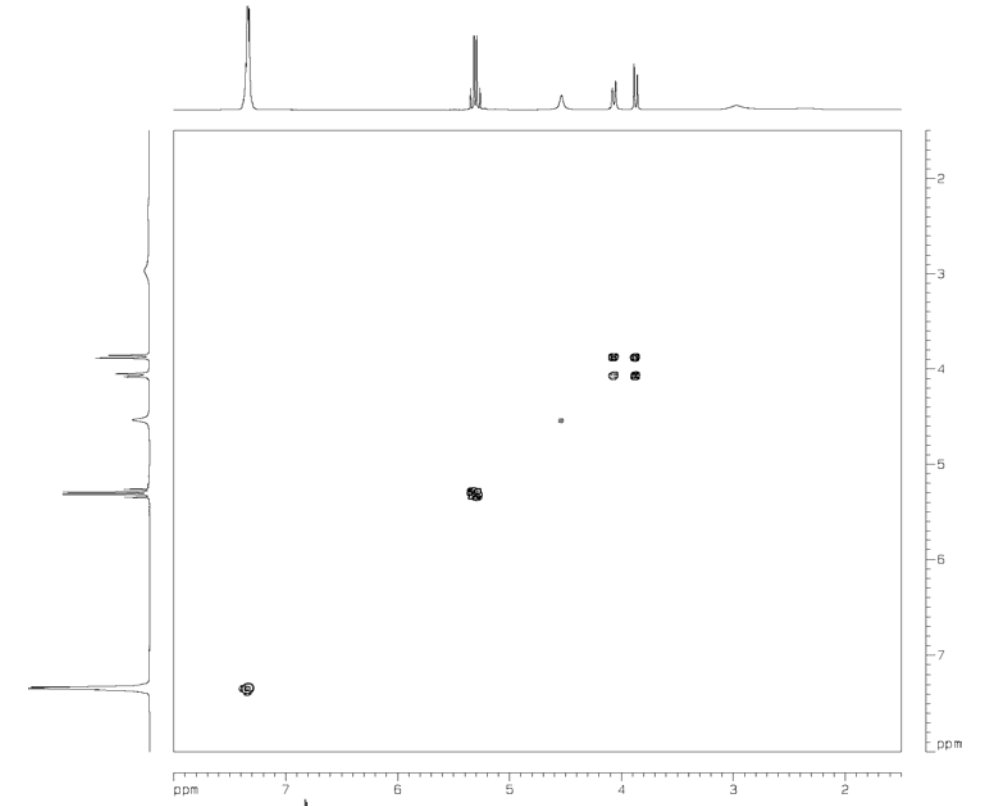
Benzyl (*S*)-2-(trifluoromethyl)-2,3-dihydroxy-propanoate

[(*S*)–4b]



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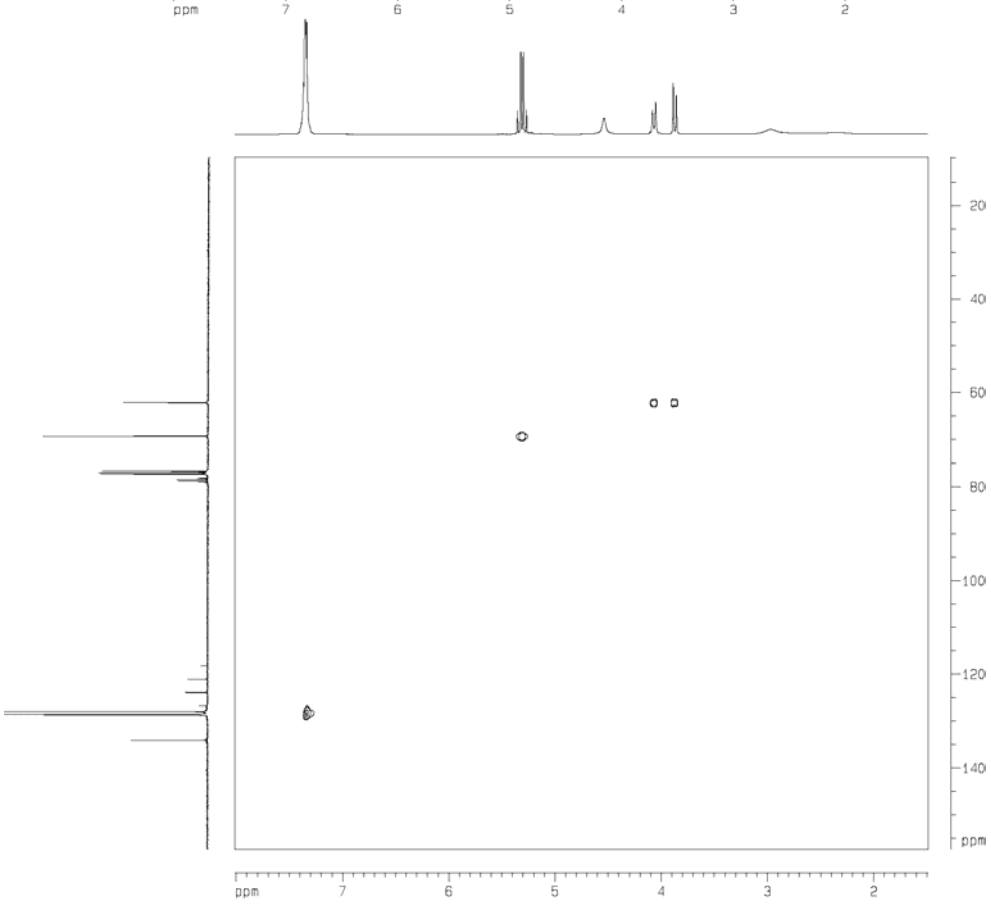
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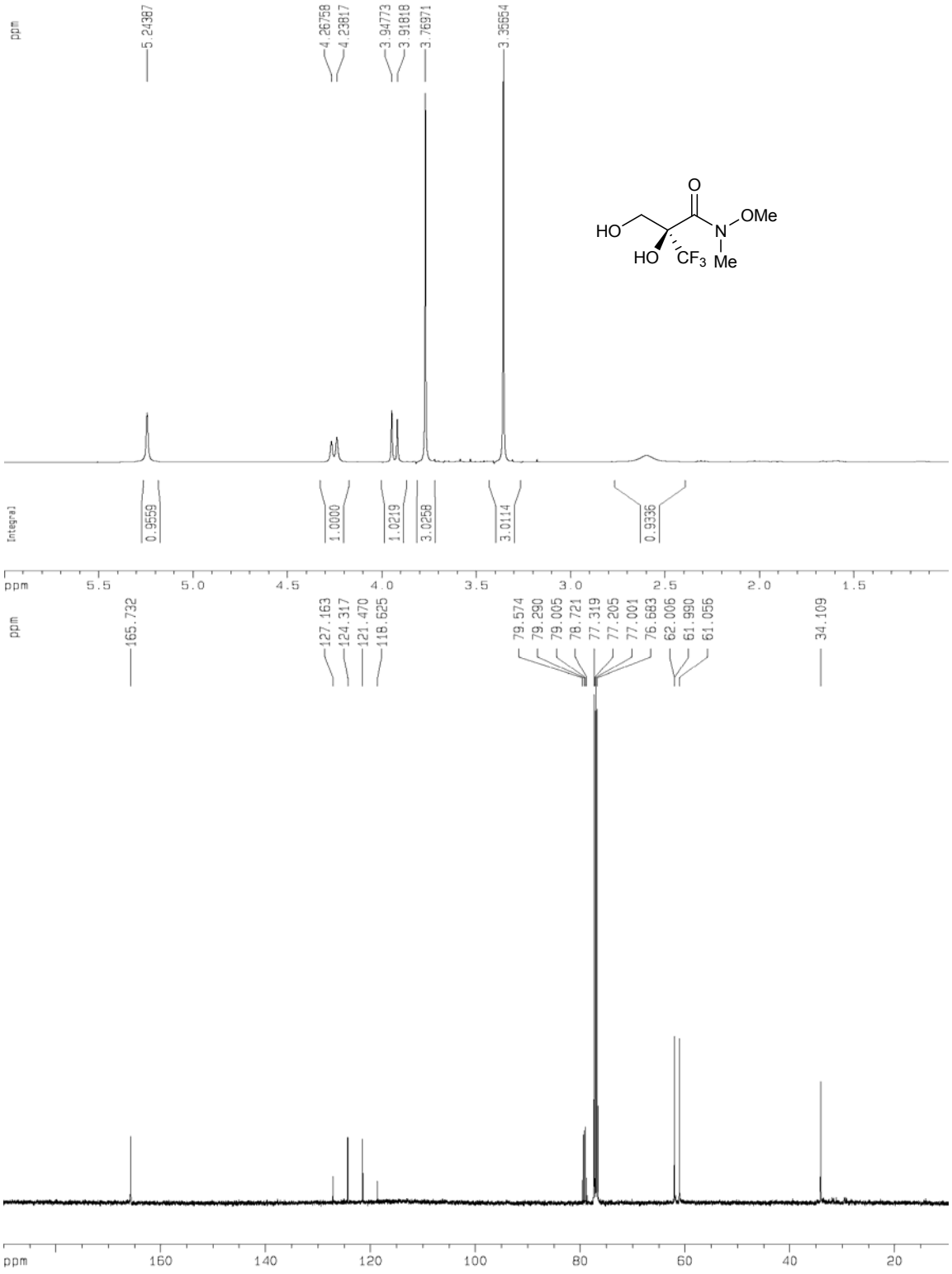
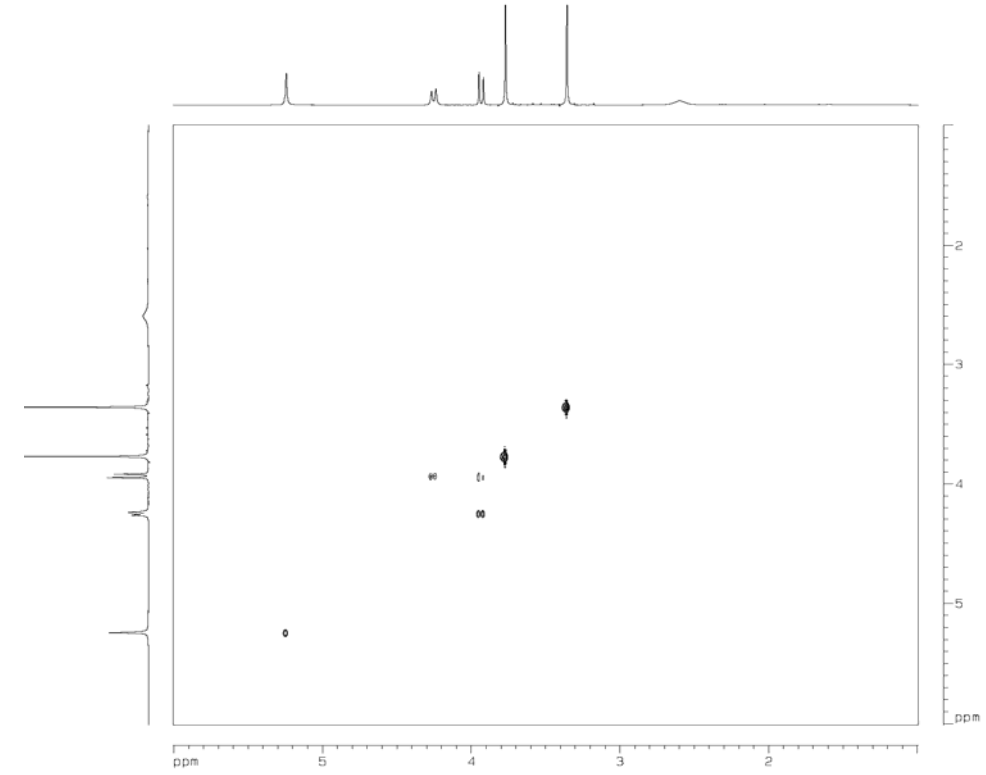
(*S*)-2-(Trifluoromethyl)-2,3-dihydroxy-*N*-methoxy-*N*-methylpropanamide [(*S*)-4c]

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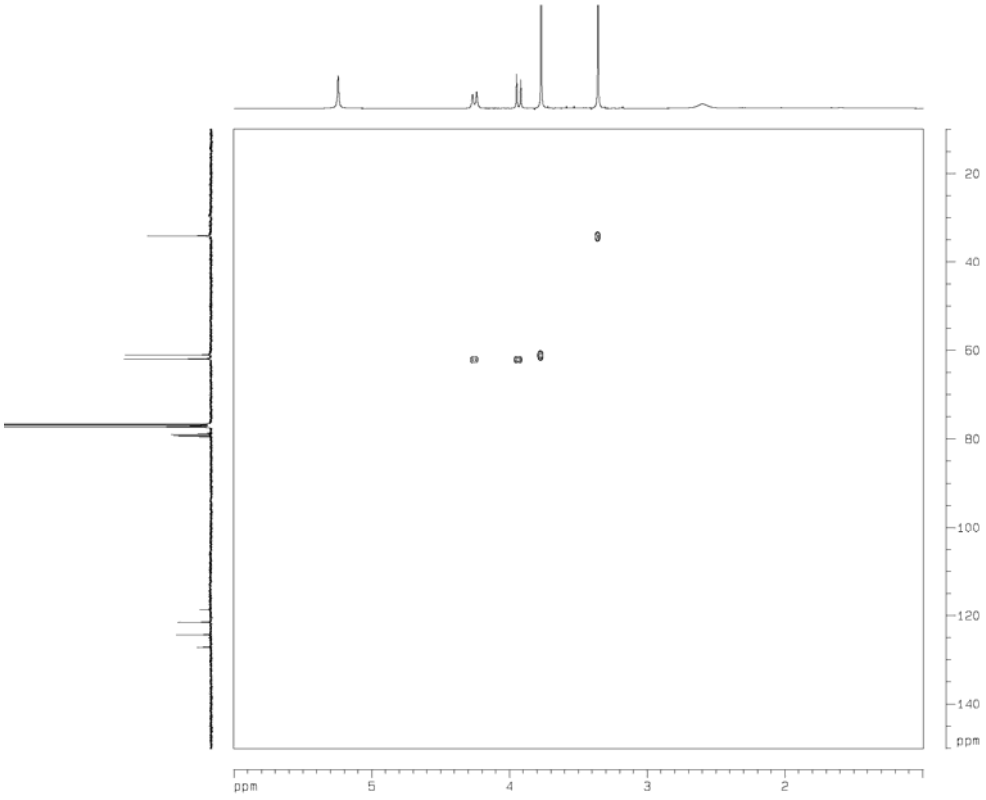
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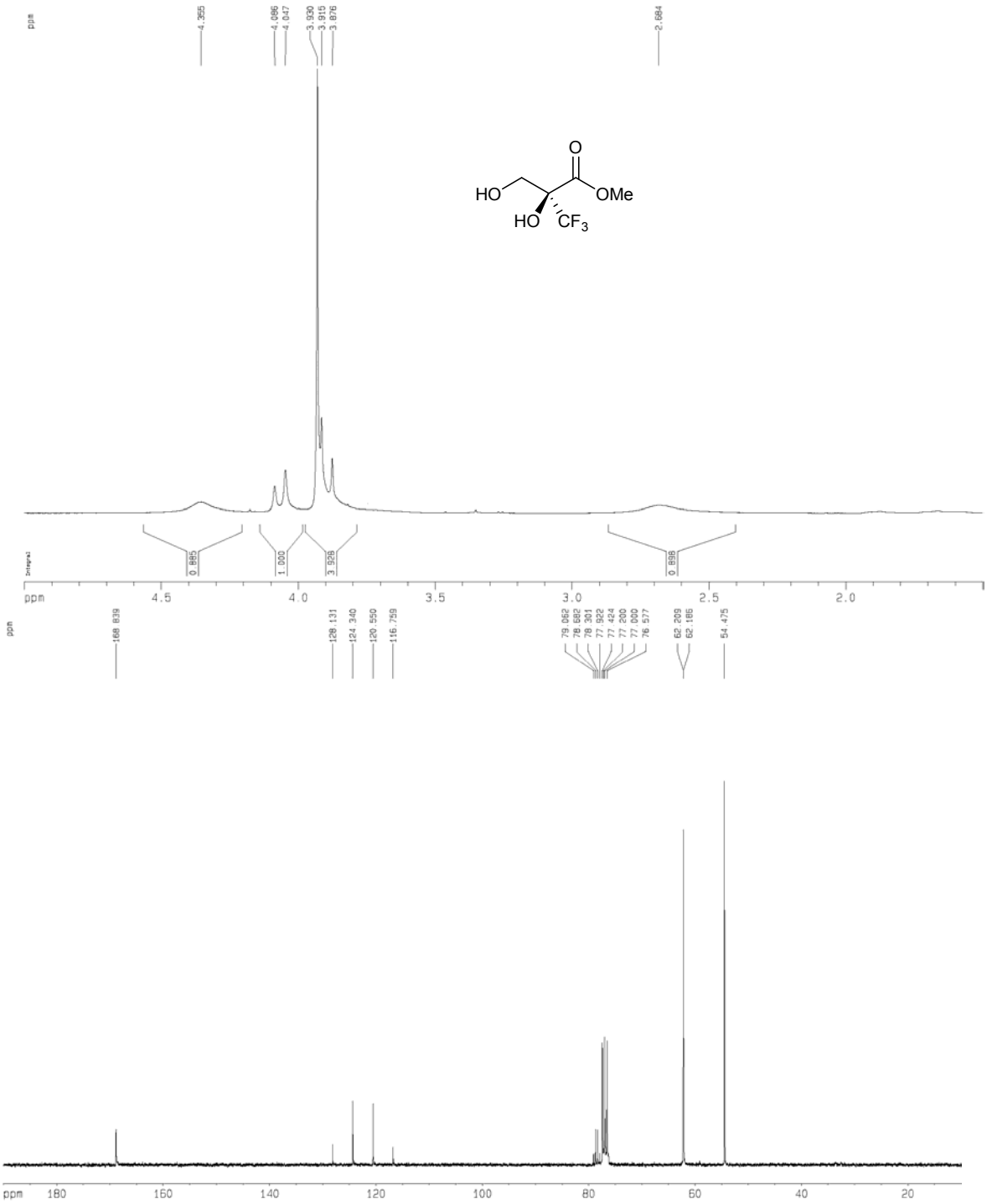
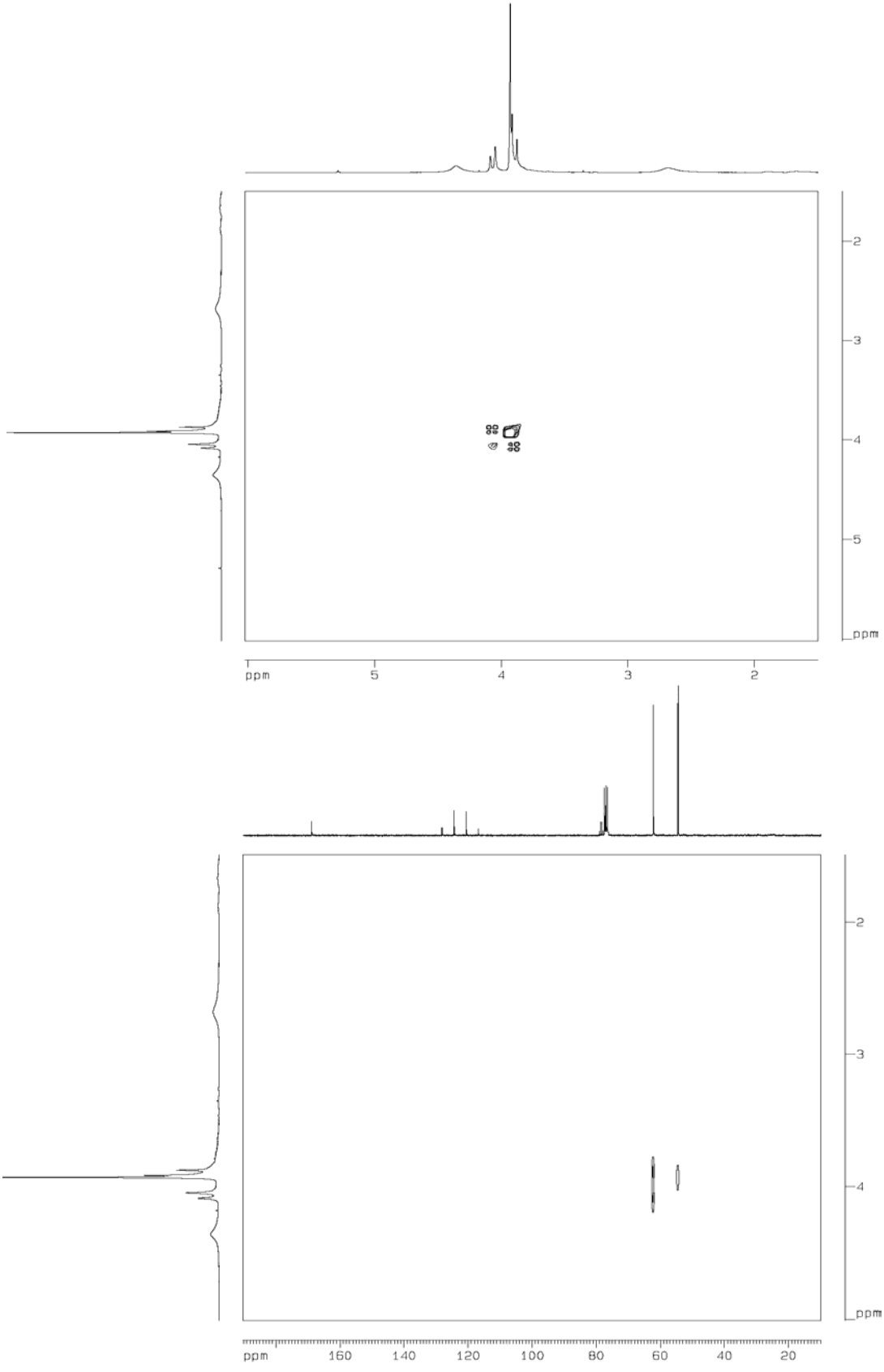
Methyl (*S*)-2-(trifluoromethyl)-2,3-dihydroxypropanoate [(*S*)-4d]

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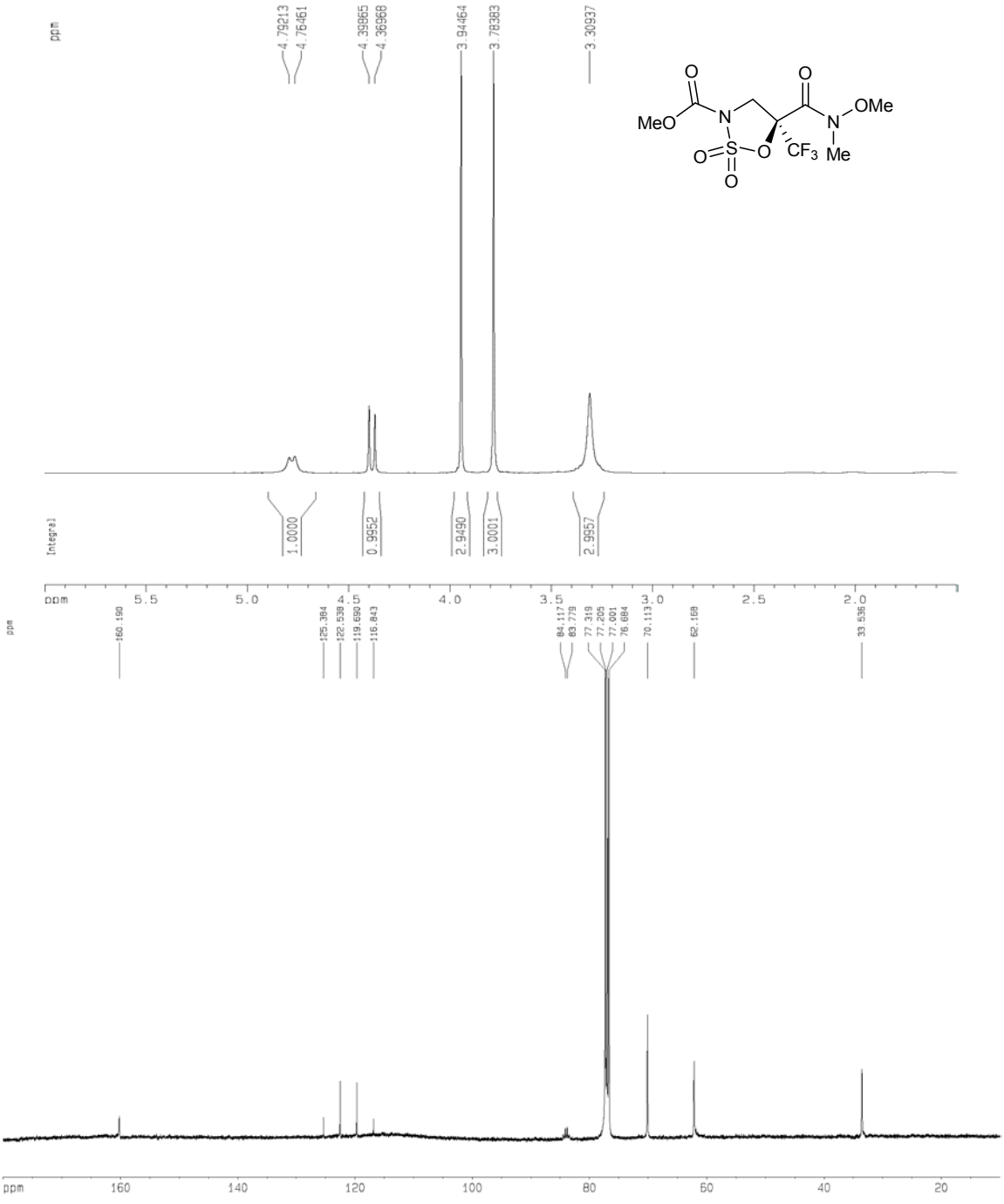
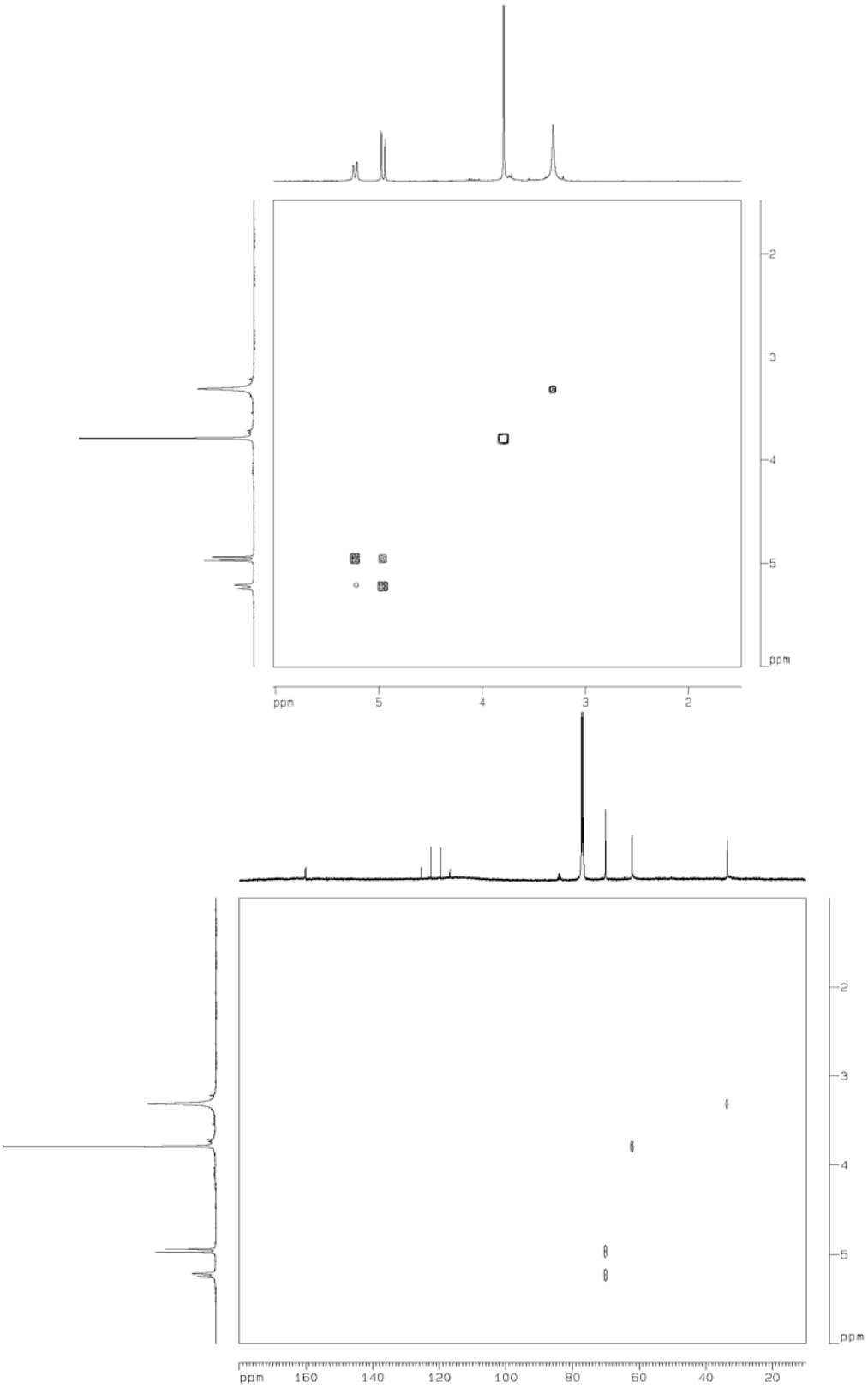
Methyl (*S*)-5-(methoxymethylcarbamoyl)-5-(trifluoromethyl)-2,2-dioxo-2λ^6-[1,2,3]oxathiazolidine-3-carboxylate [(*S*)-5]

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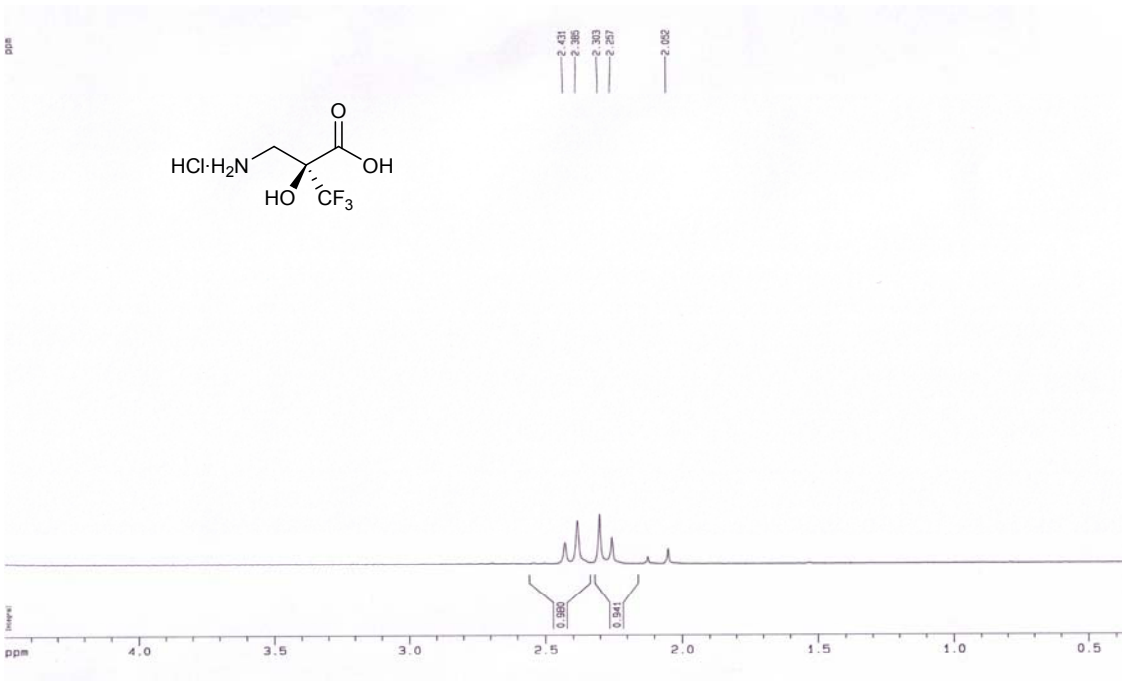
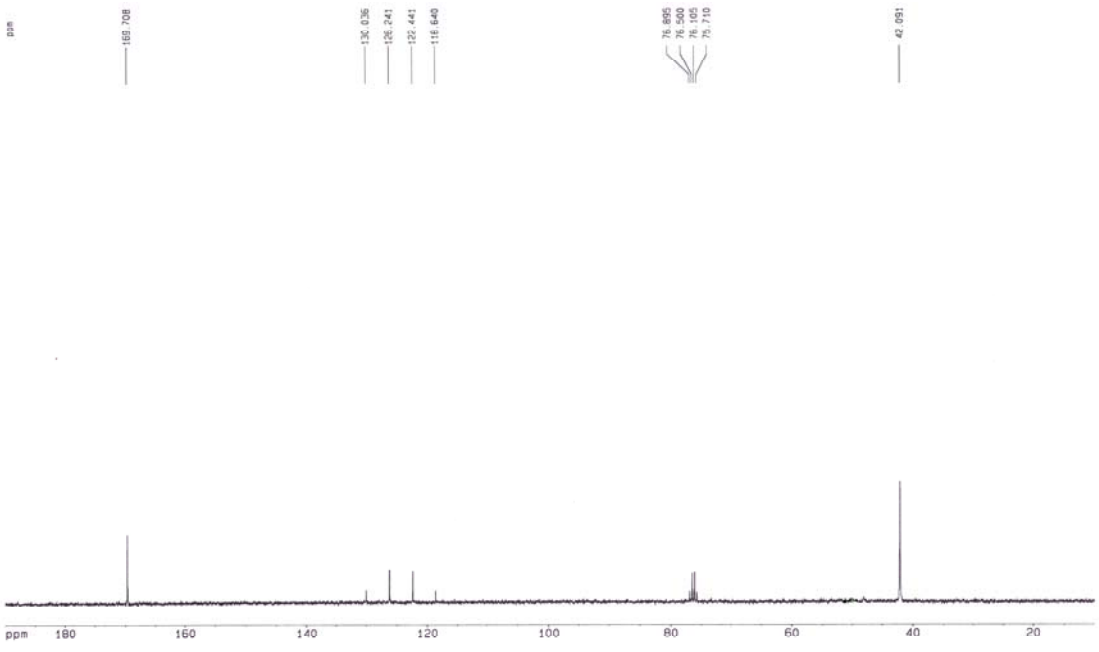
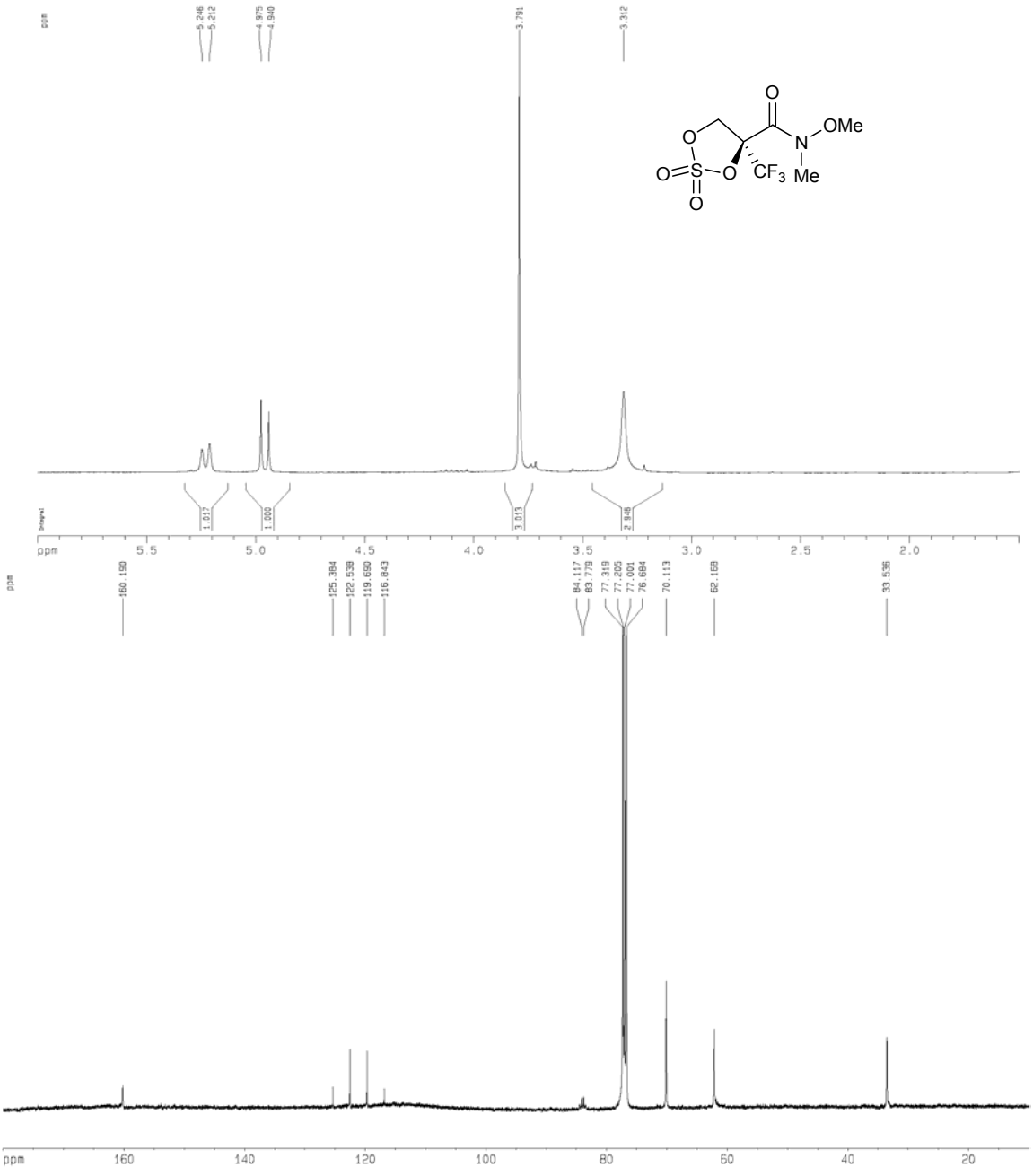
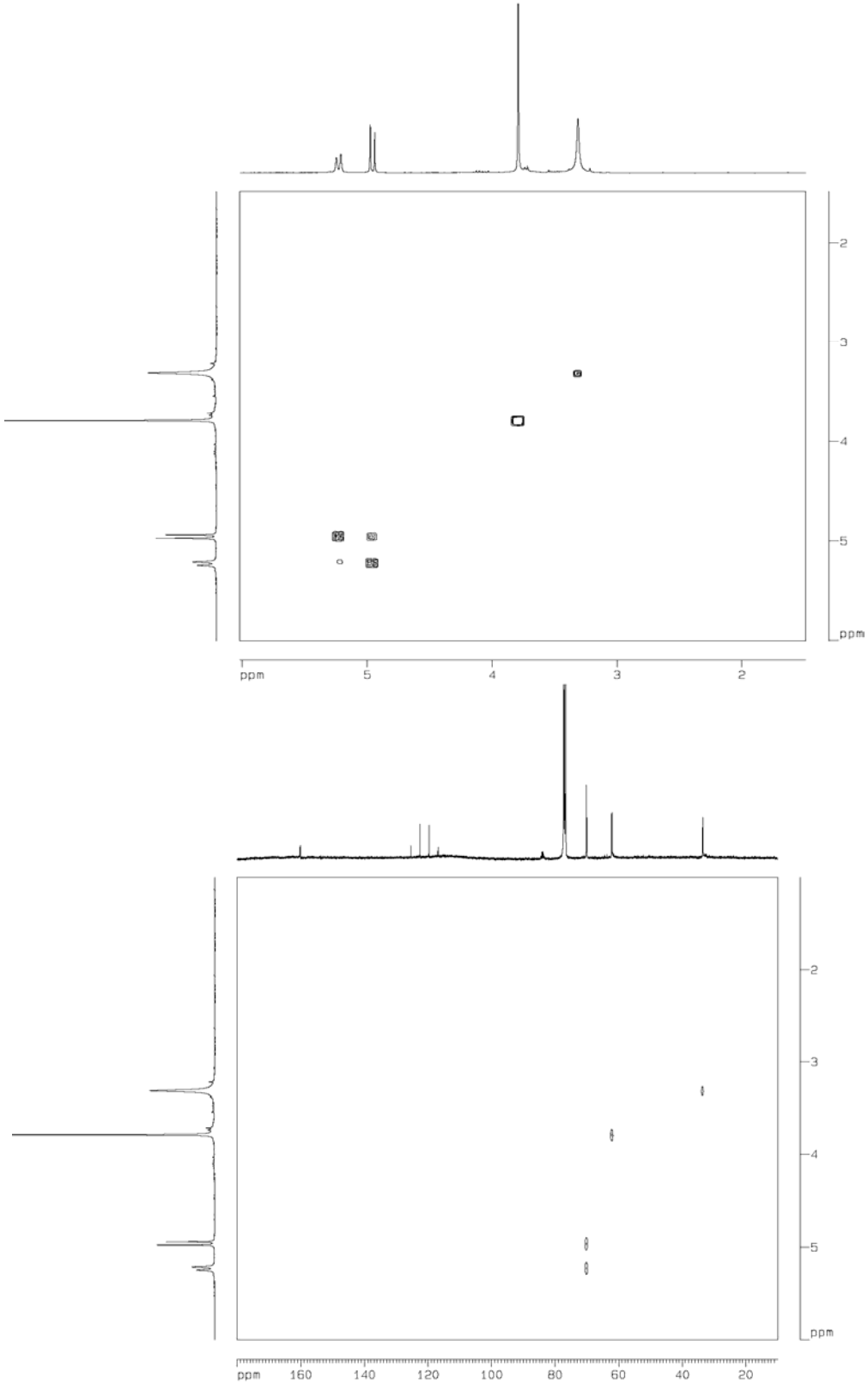
(*S*)-2-(Trifluoromethyl)isoserine hydrochloride [(*S*)-1·HCl]





(*S*)-4-(Trifluoromethyl)-2,2-dioxo-2λ^6-[1,3,2]dioxathiolane-4-carboxylic acid *N*-methoxy-*N*-methylamide [(*S*)-6c]

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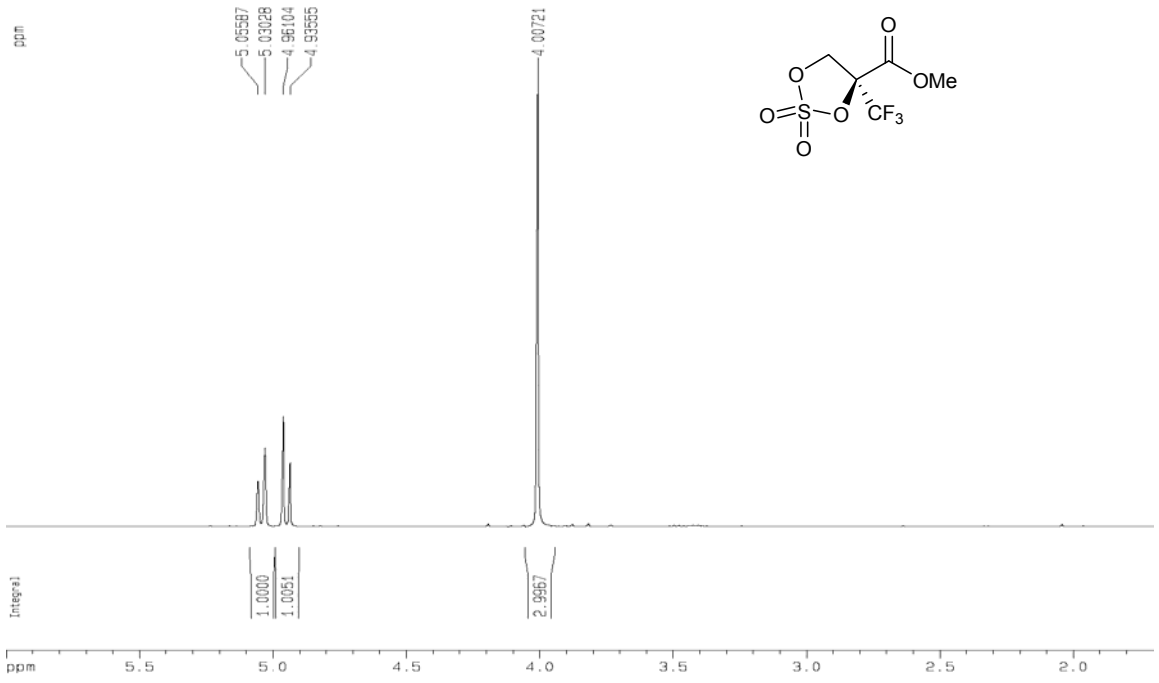
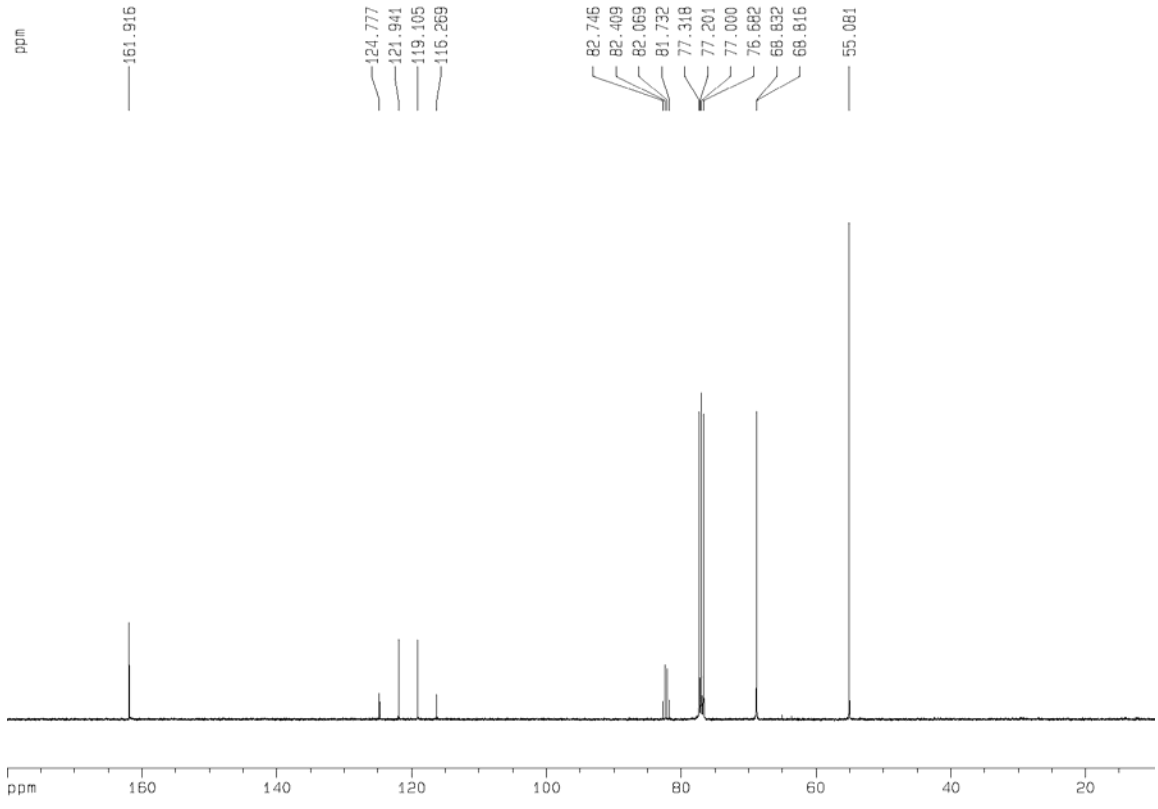
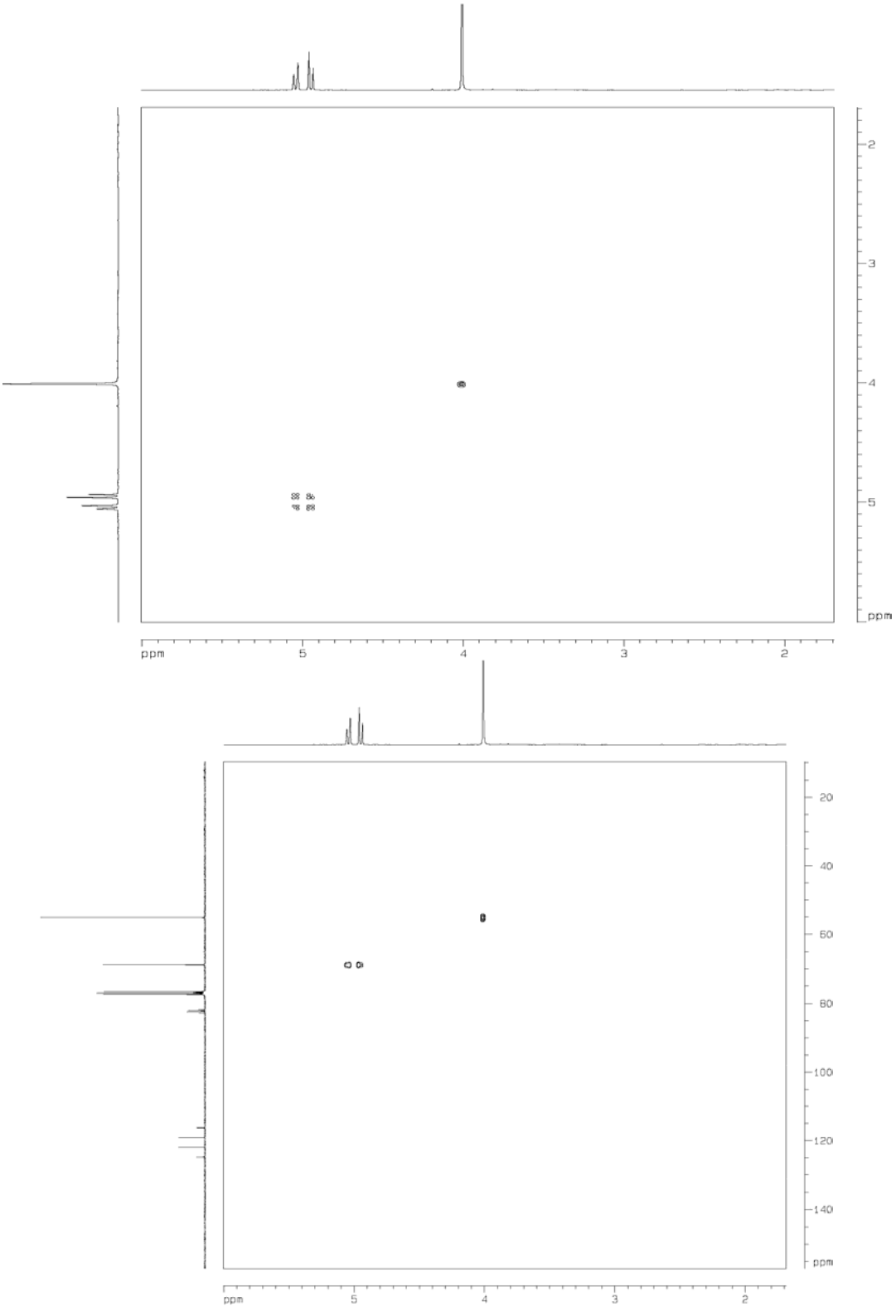
Methyl (*S*)-4-(trifluoromethyl)-2,2-dioxo-2λ^6-[1,3,2]dioxathiolane-4-carboxylate

[(*S*)-6d]



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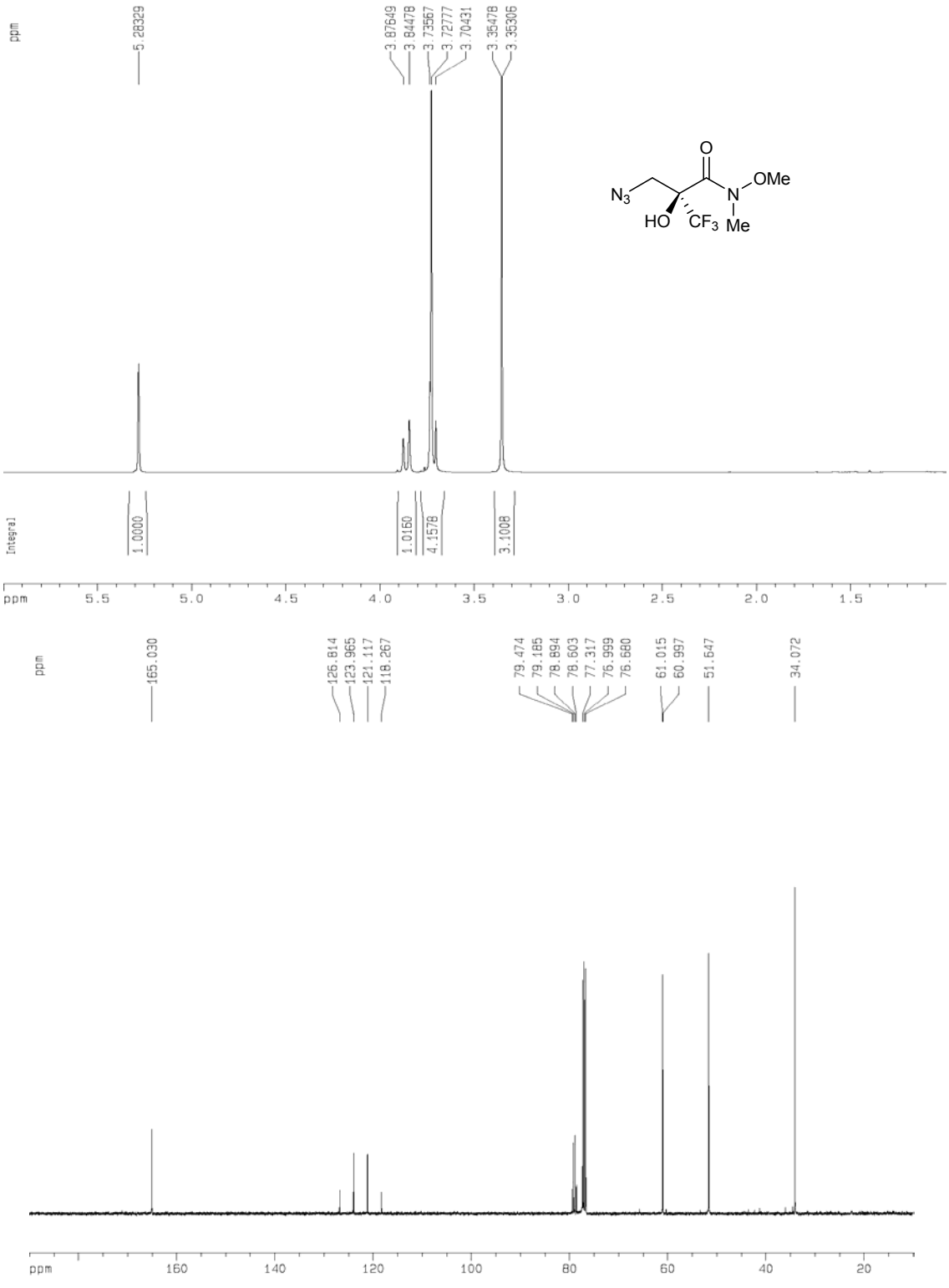
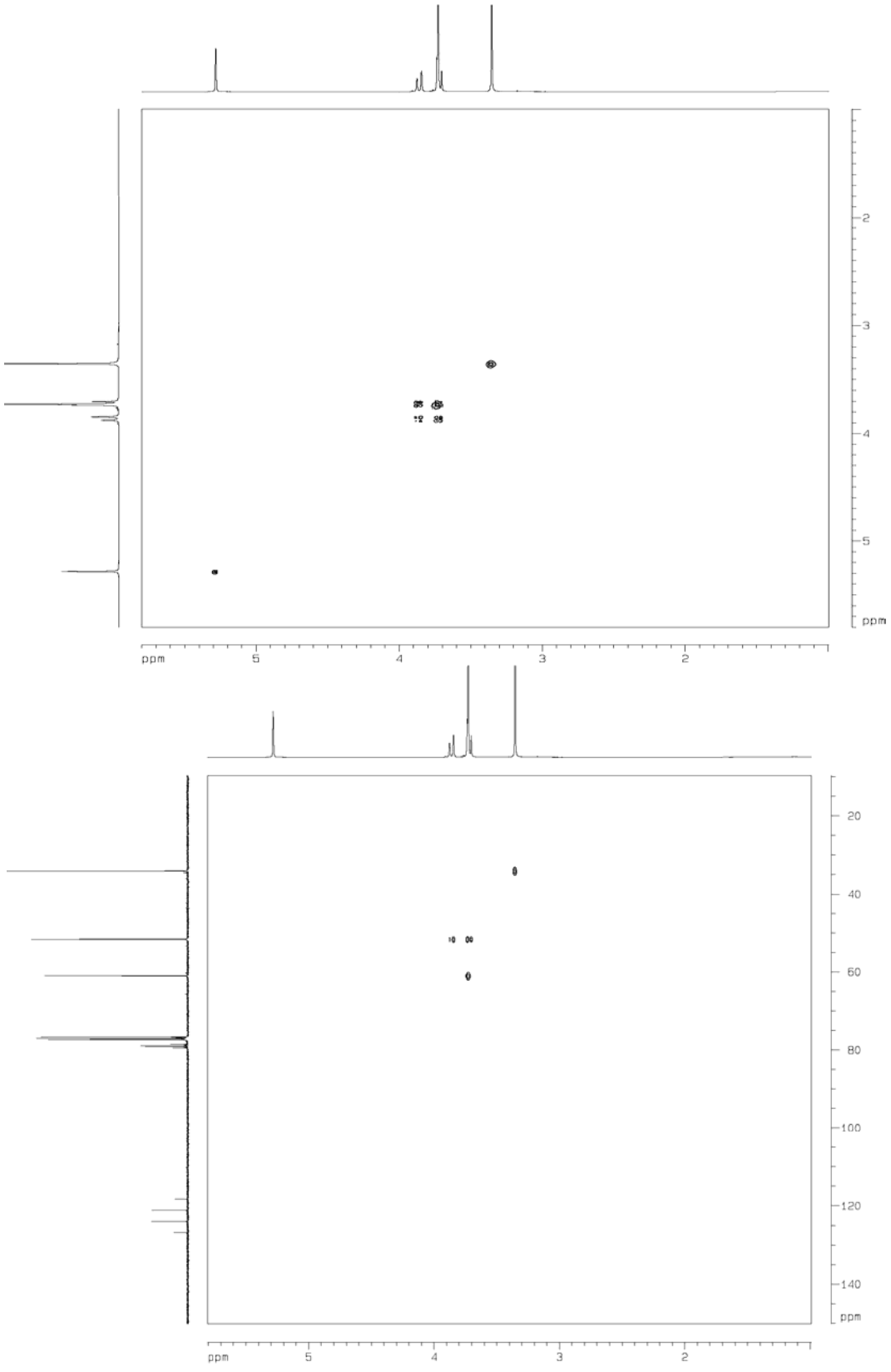
(*S*)-3-Azido-2-(trifluoromethyl)-2-hydroxy-*N*-methoxy-*N*-methylpropanamide

[(*S*)-7c]

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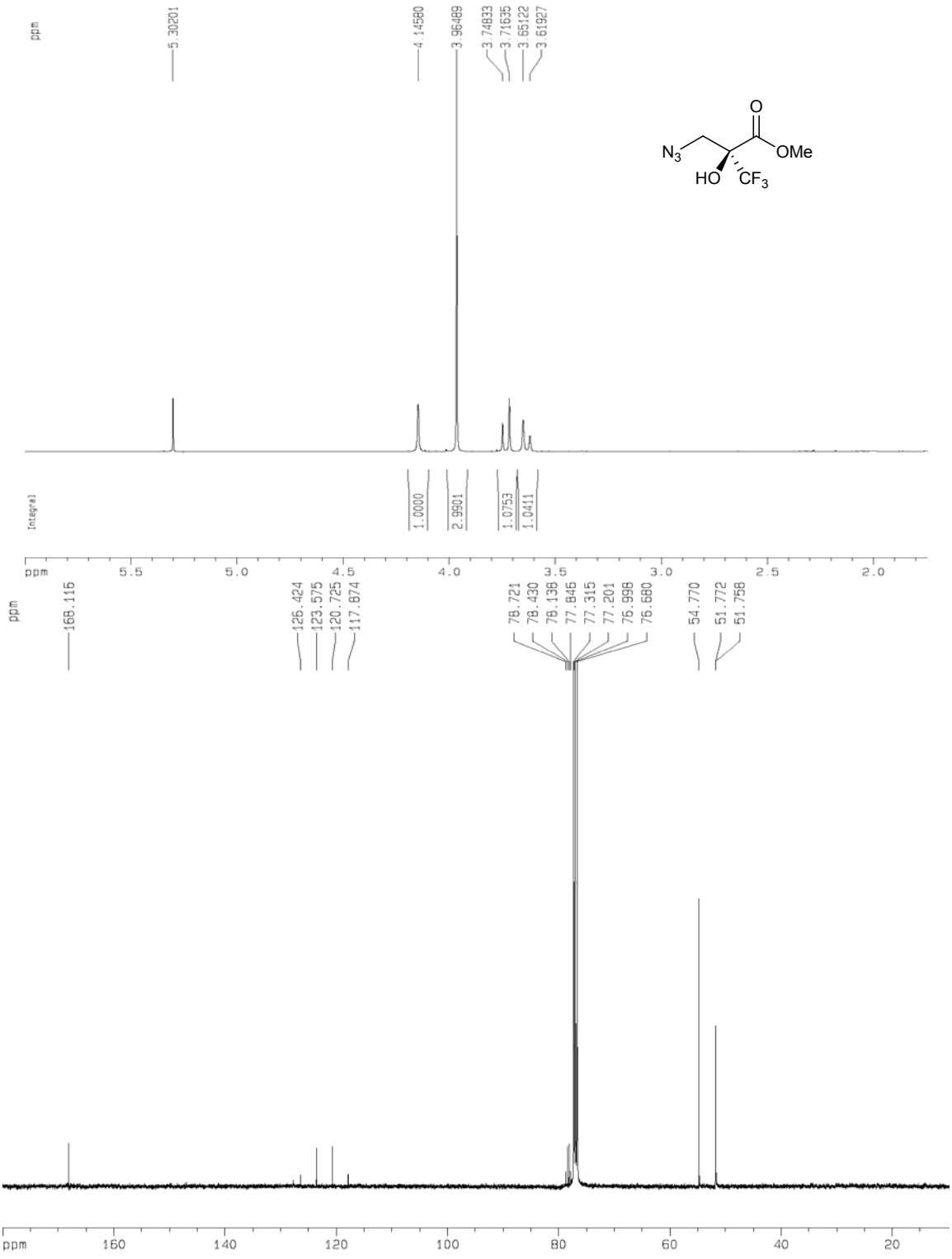
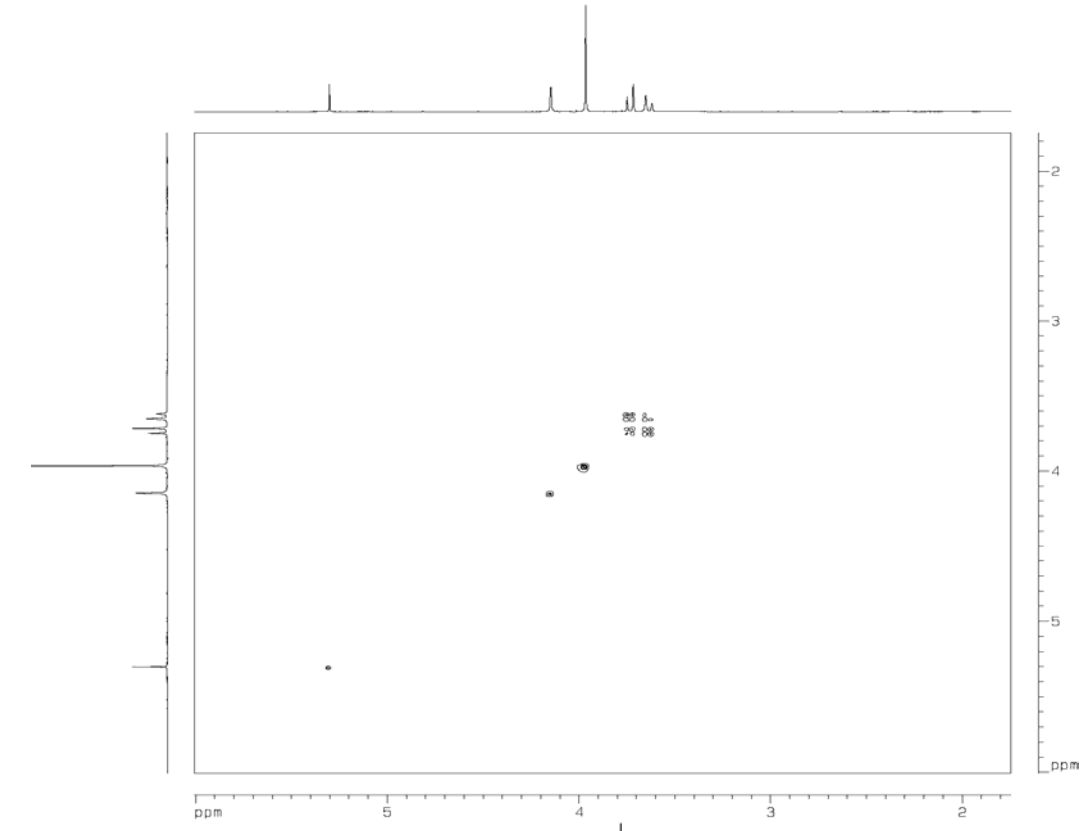
(*S*)-Methyl 3-azido-2-(trifluoromethyl)-2-hydroxypropanoate [(*S*)-7d]

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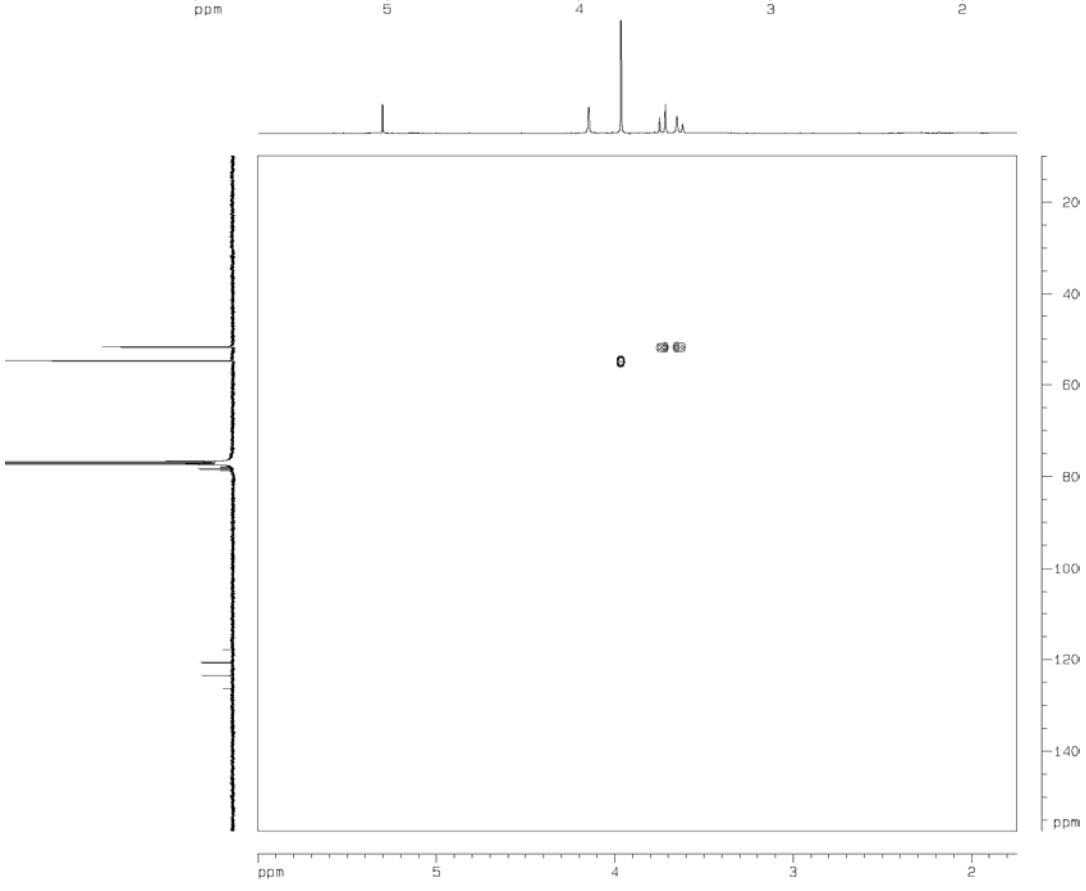
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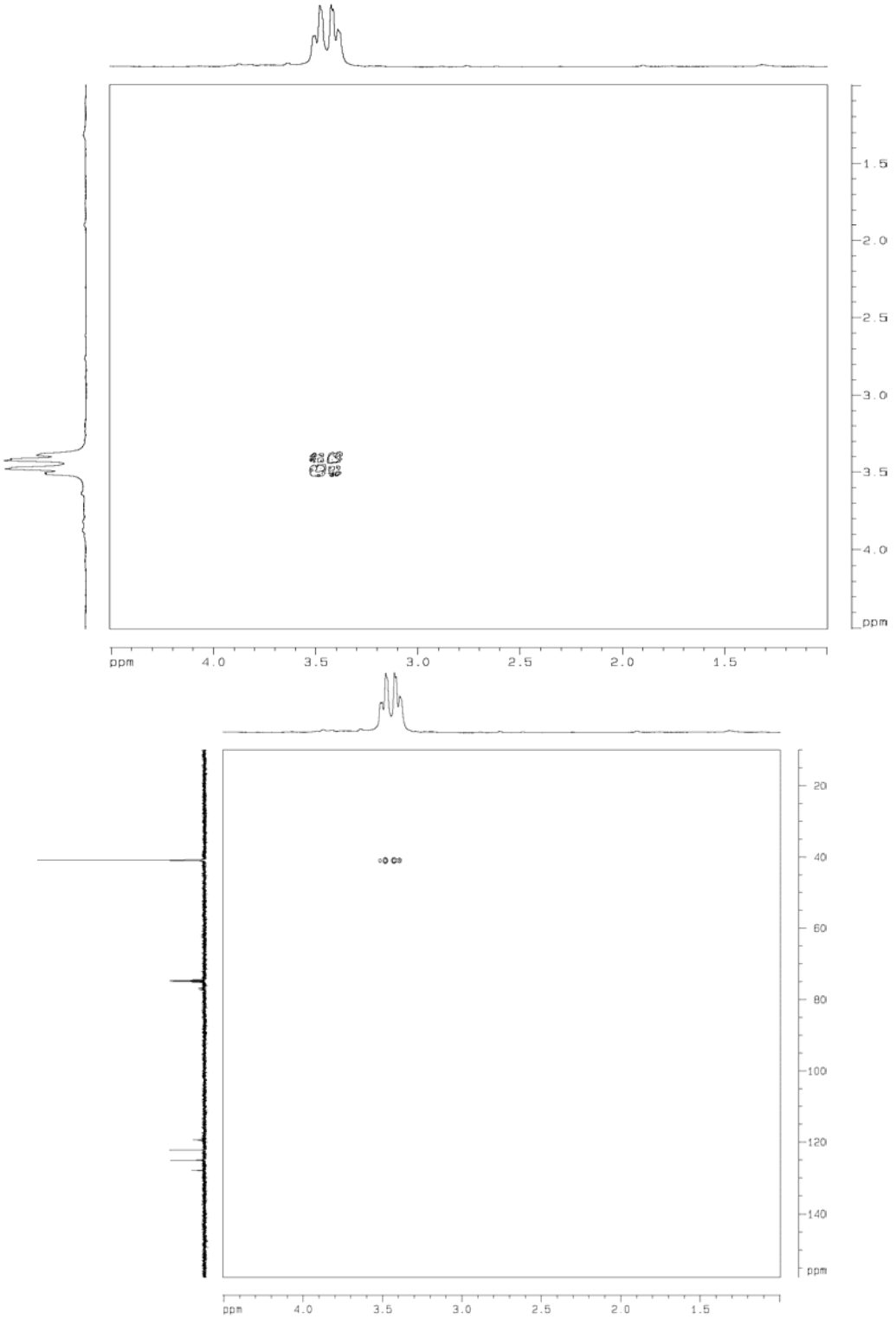
(*S*)-2-(Trifluoromethyl)isoserine [(*S*)-1]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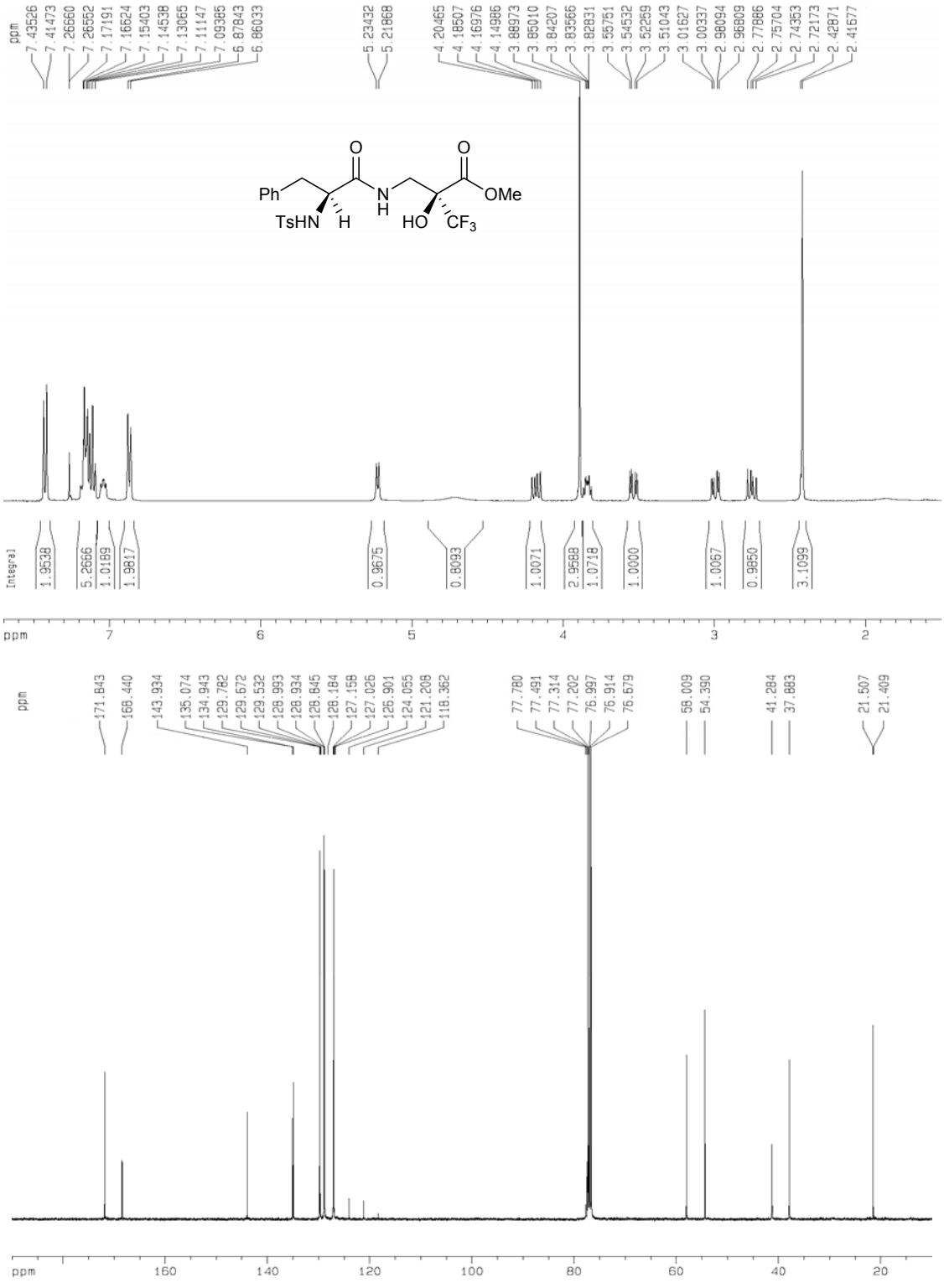
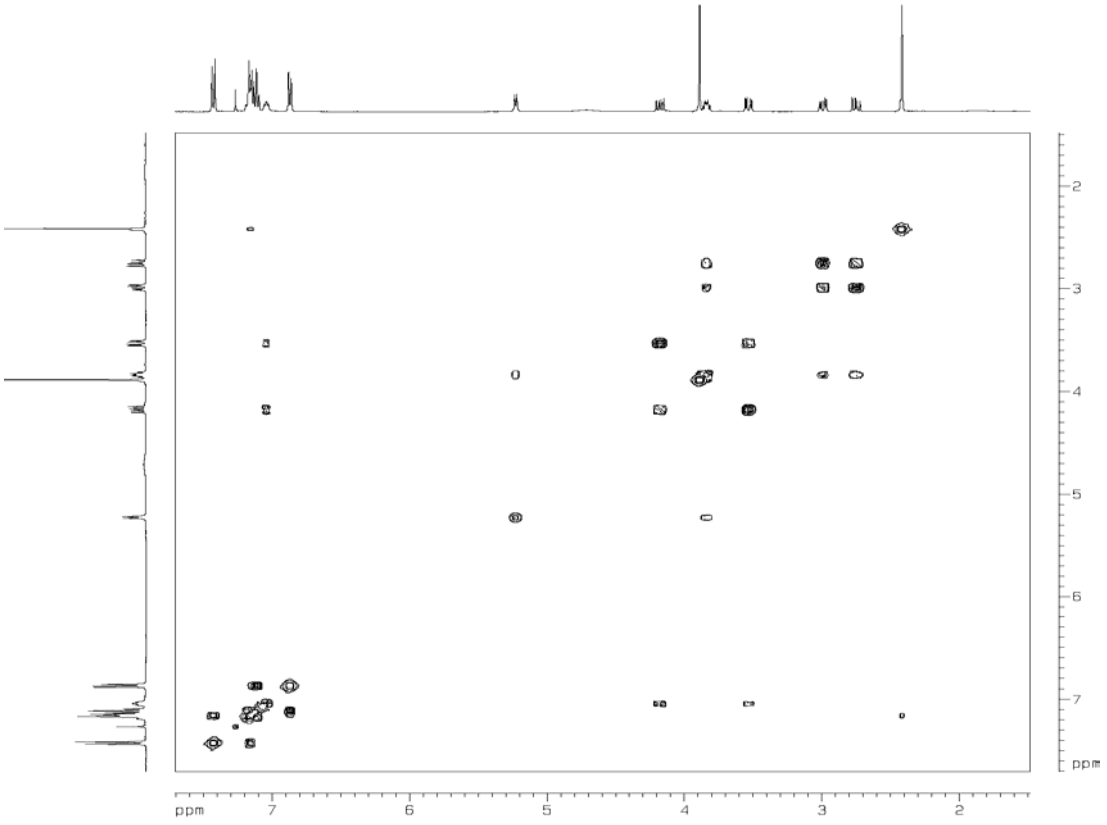
(*S*)-*N*-(Tosyl)phenylalaninyl (*S*)-2-(trifluoromethyl)isoserine methyl ester [(*S*,*S*)-8]

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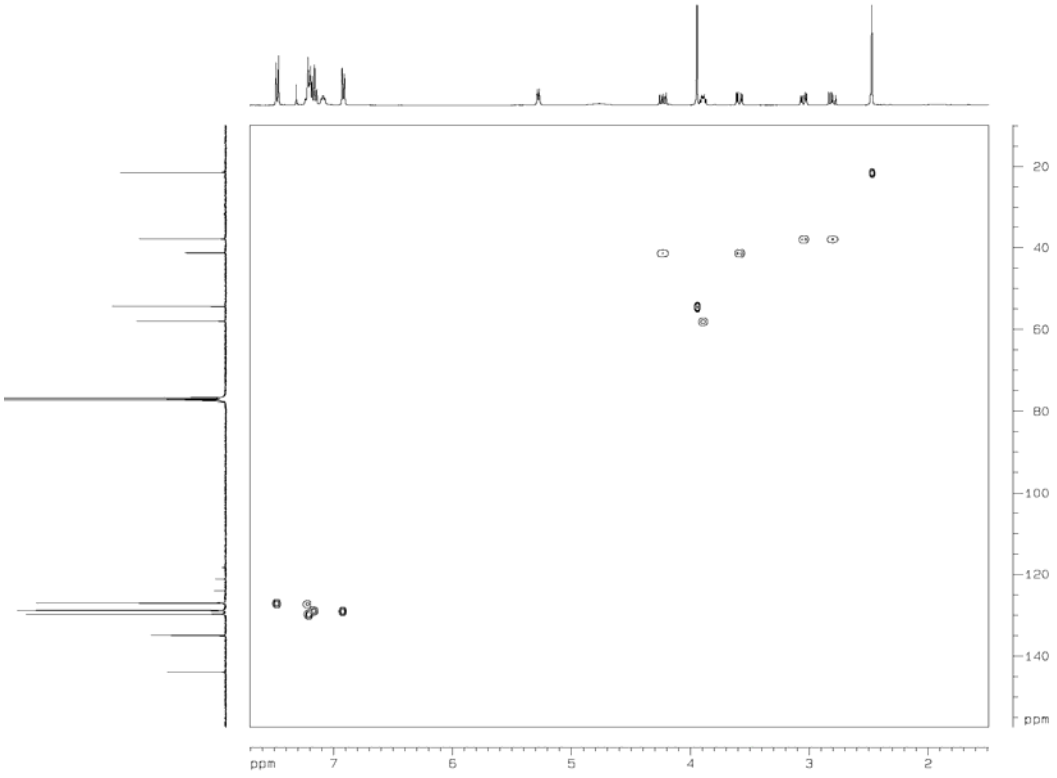
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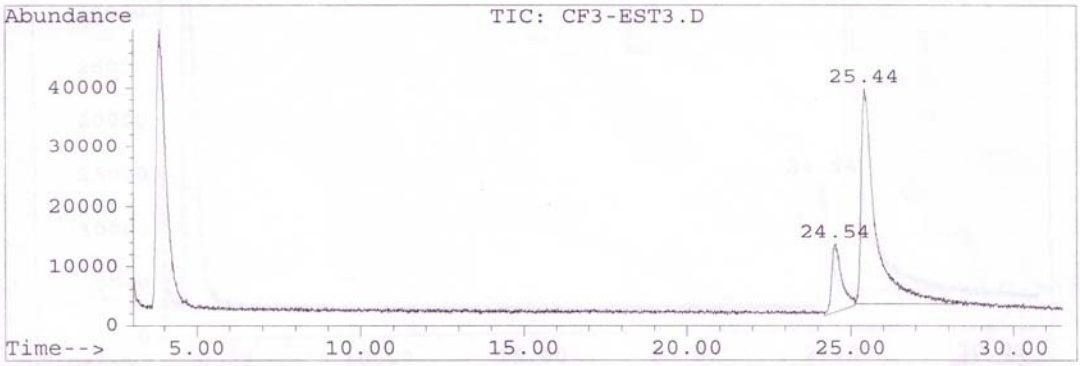
40
60
80
100
120
140
ppm
ppm
7
6
5
4
3
2

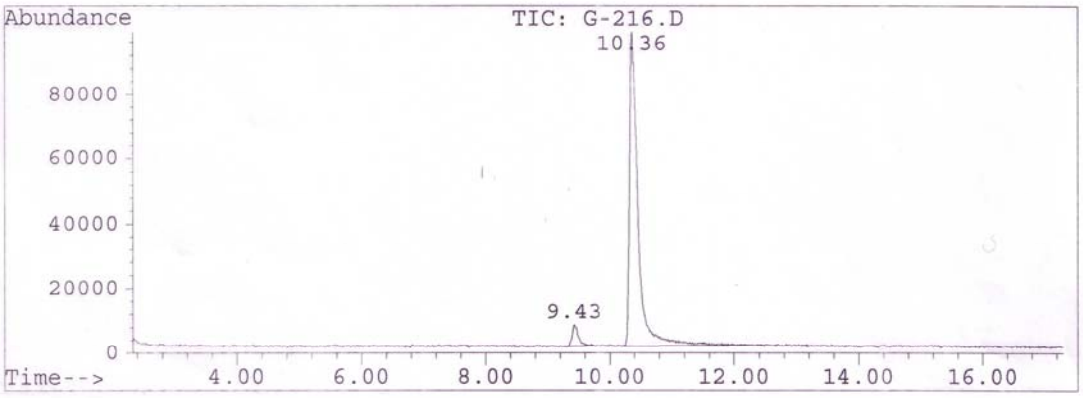
Enantiomeric excess for Sharpless asymmetric dihydroxylation determinted by GC-MS

For compound **4b**. β-DEX™ column (30 m × 0.25mm × 0.25 μm); T= 110 ˚C isotherm. Tdet. = Tinlet = 225 ˚C;



Retention Time	Area	Area %	Ratio %	Type	Width
Total Ion Chromatogram					
24.543	2458357	17.810	21.670	M	0.354
25.438	11344621	82.190	100.000	M	0.521

For compound **4c**. β-DEX™ column (30 m × 0.25mm × 0.25 μm); T= 110 ˚C isotherm. Tdet. = Tinlet = 225 ˚C;



Retention Time	Area	Area %	Ratio %	Type	Width
Total Ion Chromatogram					
9.431	488109	4.899	5.151	M	0.120
10.359	9475779	95.101	100.000	M	0.163

Computational energy data and the coordinates for structures

Computational Details

In order to understand the behavior of this kind of fluorinated cyclic sulfates in the ring-opening reaction with the azide ion, we performed a theoretical study.

All ground state and transition state (TS) geometries were located using hybrid density functional theory (B3LYP)[1] and the 6-31+G(d) basis implemented in Gaussian 98.[2] All the TS geometries were fully optimized and characterized by frequency analysis. In all cases single-point energy calculations at the B3LYP/6-311++G(2d,p) level were carried out on the B3LYP/6-31+G(d) geometries. Furthermore, solvent effects were taken into account through single point energy calculations with the Isodensity Polarized Surface Continuum Model (IPCM) method,[3] as implemented in Gaussian 98, at the B3LYP/6-31+G(d) level, using the dielectric permittivity of dimethylformamide (38.25), which was the solvent used in the experiments.

Two competitive S_N2 pathways were examined; azide attack at the "free" (**f**) secondary position and at the "hindered" (**h**) quaternary position. Each TS was located in the two possible carbonyl conformations, namely *syn* (**s**) and *anti* (**a**) with regard to the trifluoromethyl group. This leads to four possible TS for each sulfate and these are denoted as **TSc-d_af**, **TSc-d_ah**, **TSc-d_sf** and **TSc-d_sh**, respectively. Several geometrical features of the minimum energy TS are shown in Figure SI-1 and the energetic results are gathered in Table SI-1.

Only Gibbs free energies are used for the discussion on the relative stabilities of the TS considered. These energies were obtained using the following correction formula:

$$\Delta\Delta G^{\ddagger} = \Delta\Delta E_{basis} + \Delta\Delta G_{298} + \Delta\Delta G_{solv}$$

where $\Delta\Delta E_{basis}$ is the relative energy at the B3LYP/6-311++G(2d,p)//B3LYP/6-31+G(d) level, $\Delta\Delta G_{298}$ represents the thermal and entropic corrections at 298 K, calculated at the B3LYP/6-31+G(d) level, and

[1] Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 1372–1377.
[2] *Gaussian* 98, Revision A.11, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, P. Salvador, J. J. Dannenberg, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, and J. A. Pople, Gaussian, Inc., Pittsburgh PA, 2001.
[3] Foresman, J. B.; Keith, T. A.; Wiberg, K. B.; Snoonian, J.; Frisch, M. J. *J. Phys. Chem.* **1996**, *100*, 16098–16104.

$\Delta\Delta G_{solv}$ is the solvation correction (relative solvation free energies), calculated at the IPCM/B3LYP/6-31+G(d) level.

As far as substrates (*S*)-**6c** and (*S*)-**6d** are concerned, the TS obtained for the S_N2 reaction on "free" position (**TSc_sf** and **TSd_sf**, respectively) were considerably lower in energy (4.82 Kcal/mol and 5.94 Kcal/mol more stable) than that resulting from the nucleophilic attack on "hinderend" position (**TSc_ah** and **TSd_ah**, respectively). This situation is in agreement with the experimentally observed regioselectivity.

NOTE: Stereochemistry is ignored for simplicity

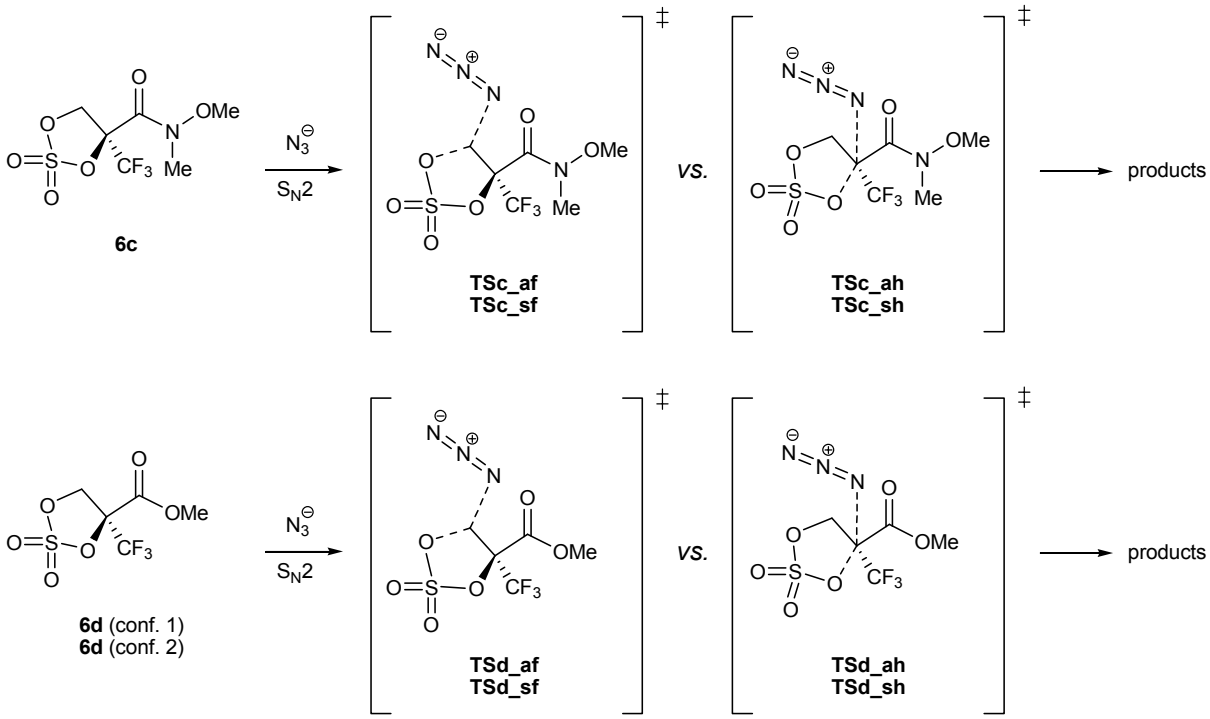
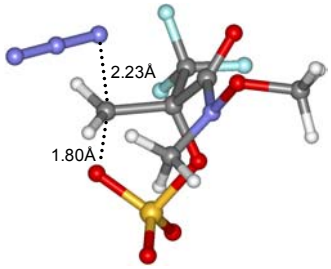


Table SI-1. Calculated energies, entropies, Gibbs free energies and lowest frequencies of the reactants and transition structures (B3LYP/6-31+G(d) optimized geometries).

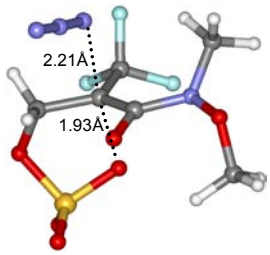
	E_0(B3LYP/6-31+G(d)) (a.u.)[a]	Lowest freq. (cm^{-1})	S (cal mol^{-1} K^{-1})	G_{298} (B3LYP/6-31+G(d)) (a.u.)	E_{IPCM}(B3LYP/6-31+G(d)) (a.u.)	E_{basis} (B3LYP/6-311++G(2d,p)) (a.u.)
N_3^-	-164,244683	618.7	43.6	-164.252070	-164.345127	-164.289798
6c	-1437.1553473	32.2	133.9	-1437.035306	-1437.1743712	-1437.5113275
6d (cf. 1)	-1342,5517623	32.2	122.3	-1342.473141	-1342.5694346	-1342.8829437
6d (cf. 2)	-1342,5493817	22.0	122.9	-1342.471180	-1342.5677627	-1342.8806749
TSc_sf	-1601,4116550	483.7i	151.1	-1601.286744	-1601,4904122	-1601,8122998
TSc_sh	-1601,3999335	370.9i	148.9	-1601.273693	-1601,4774615	-1601,8007655
TSc_af	-1601,4058438	504.6i	151.2	-1601.281087	-1601,4820702	-1601,8059319
TSc_ah	-1601,4008135	393.7i	147.3	-1601.273987	-1601,4849121	-1601,8011866
TSd_sf	-1506,8152859	500.0i	139.1	-1506.731503	-1506,8948209	-1507,1906104
TSd_sh	-1506,8035882	376.0i	137.3	-1506.718721	-1506,8816253	-1507,1791442
TSd_af	-1506,8128216	502.1i	139.8	-1506.729427	-1506,8898273	-1507,1880992
TSd_ah	-1506,8023411	380.4i	137.7	-1506.717742	-1506,8860671	-1507,1777738

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

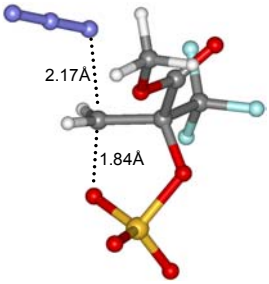
Figure SI-1. Minimum energy TS calculated with **6c** and **6d** and azide anion. Relative energies shown in brackets were obtained by using the following above-mentioned correction formula: $\Delta\Delta G^{\ddagger} = \Delta\Delta E_{basis} + \Delta\Delta G_{298} + \Delta\Delta G_{solv}$



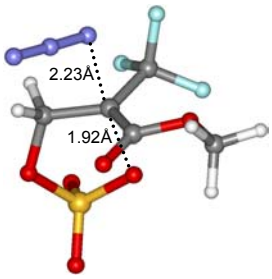
TSc_sf (0.00 Kcal/mol)



TSc_ah (4.82 Kcal/mol)



TSd_sf (0.00 Kcal/mol)



TSd_ah (5.94 Kcal/mol)

B3LYP/6-31+G (d) geometries

Azide anion

N	1.112410	0.411590	0.000000
N	0.000000	0.000350	0.000000
N	-1.112410	-0.411940	0.000000

6c

C	-0.249348	0.539788	0.256074
C	-1.070221	0.238613	1.539050
O	-1.445023	-1.147288	1.403911
S	-1.866648	-1.436260	-0.149281
O	-0.826467	-0.275398	-0.770402
O	-3.225998	-1.011431	-0.412905
O	-1.386917	-2.745795	-0.527276
C	-0.438290	2.016818	-0.166068
C	1.266016	0.229153	0.521788
N	2.015740	-0.323958	-0.474101
C	1.859319	-0.281568	-1.925444
O	1.689935	0.434805	1.651694
O	3.367492	-0.496800	-0.144647
C	3.580725	-1.739225	0.548952
H	-0.452700	0.321680	2.430008
H	-1.967648	0.859291	1.602978
H	4.664688	-1.800178	0.668235
H	3.219273	-2.583253	-0.049717
H	3.096704	-1.721839	1.529268
H	2.490283	0.514940	-2.334444
H	0.820991	-0.109645	-2.192387
H	2.178683	-1.243945	-2.334220
F	0.315980	2.327047	-1.240943
F	-1.721218	2.274739	-0.476139
F	-0.080035	2.834281	0.843566

6d (conform. 1)

O	-1.587311	0.390378	1.399010
S	-2.134380	0.404885	-0.151922
O	-0.634097	0.066509	-0.810504
C	0.318341	-0.283578	0.190038
C	-0.485244	-0.529920	1.493573
O	-3.003763	-0.726256	-0.402554
O	-2.514535	1.756073	-0.490140
C	1.026827	-1.577452	-0.280266
C	1.363651	0.845979	0.397774
O	1.427149	1.667320	-0.640354
C	2.387872	2.746647	-0.540734
O	2.026749	0.914223	1.409799
H	0.088676	-0.261249	2.378211
H	-0.857842	-1.556001	1.554544
H	2.282149	3.303083	-1.470698
H	3.395511	2.337438	-0.438530
H	2.151469	3.374131	0.321415
F	1.814962	-2.053880	0.707924
F	1.797955	-1.353555	-1.358973
F	0.132405	-2.529410	-0.593236

6d (conform. 2)

O	0.816722	-0.035063	-0.872817
C	-0.278500	0.121206	0.021676
C	0.256469	-0.192103	1.457914
O	1.678446	-0.010175	1.384547
S	2.184817	-0.562430	-0.077741
C	-1.421350	-0.833737	-0.403067
O	-2.307168	-0.951042	0.596385
C	-3.458944	-1.789623	0.330487
C	-0.729234	1.601556	-0.104742
O	2.190939	-2.012684	-0.081767
O	3.314189	0.219060	-0.514592
O	-1.482191	-1.379971	-1.473355
H	0.024860	-1.219887	1.746494
H	-0.117974	0.504420	2.206627
H	-4.053424	-1.752199	1.242308
H	-3.133621	-2.809565	0.114063
H	-4.018052	-1.390520	-0.518590
F	-1.735027	1.867616	0.759882
F	-1.167204	1.870942	-1.345546
F	0.284786	2.437200	0.178123

TSc_sf

C	0.416136	1.368897	0.212189
C	0.250098	-0.145417	0.440840
C	-1.224372	-0.695066	0.346750
O	-1.740904	-1.225081	1.312263
O	1.009677	-0.875227	-0.528542
S	2.270984	-0.001036	-1.258517
O	3.519337	-0.693767	-0.961395
O	2.089776	1.306356	-0.456057
C	0.824607	-0.531938	1.845351
O	1.871705	0.123077	-2.664027
N	-1.796800	-0.734186	-0.909702
C	-1.555015	0.151812	-2.039863
O	-3.152978	-1.119121	-0.883488
C	-3.268927	-2.539672	-0.991825
H	0.702811	2.003834	1.033230
H	-0.003096	1.825457	-0.667134
H	-2.017595	1.134285	-1.884175
H	-2.000947	-0.318020	-2.920311
H	-0.485521	0.245301	-2.224637
H	-4.346038	-2.730047	-1.022219
H	-2.827342	-3.032314	-0.120238
H	-2.798538	-2.901897	-1.915791
N	-1.598033	1.878439	1.010025
N	-1.878984	2.897400	0.436116
N	-2.145591	3.890002	-0.126707
F	0.169068	0.060296	2.856888
F	0.814388	-1.864391	2.039956
F	2.121912	-0.141816	1.943016

TSc_sh

O	-1.375566	-0.510478	-0.926914
S	-2.464329	-1.042950	0.034469
O	-1.538910	-1.018706	1.417740
C	-0.539648	0.022474	1.447977
C	-0.068015	0.522293	0.061292
C	1.061058	-0.028178	-0.802657
O	1.461955	0.625299	-1.753084
C	-0.602161	1.918647	-0.443375
O	-3.585274	-0.118015	0.208669
O	-2.768177	-2.456199	-0.192355
N	1.677024	-1.207785	-0.396440
C	1.016175	-2.432572	0.043080
H	-0.926813	0.872485	2.007040
H	0.286138	-0.429951	1.992729
H	0.706900	-3.022663	-0.828593
H	0.135069	-2.212845	0.639001
H	1.727547	-3.005525	0.643966
N	1.511863	1.557146	1.270178
N	2.211957	0.796069	1.884355
N	2.894799	0.069443	2.495364
O	2.742366	-1.580488	-1.247023
C	3.941547	-0.881230	-0.890308
H	4.718487	-1.333705	-1.514027
H	4.167903	-1.021059	0.172323
H	3.851031	0.184569	-1.122685
F	0.321312	2.886334	-0.509389
F	-1.567104	2.356441	0.410594
F	-1.159916	1.856322	-1.664292

TSc_af

C	0.587536	1.470032	-0.196936
C	0.215221	0.051316	0.262198
C	-1.060021	-0.389224	-0.569933

O	-0.925292	-0.367332	-1.777121
O	1.180409	-0.924681	-0.137058
S	2.658768	-0.317413	-0.725068
O	3.698440	-0.904428	0.119572
O	2.396632	1.168658	-0.416615
C	0.244852	-0.044205	1.819424
O	2.688171	-0.630410	-2.152375
N	-2.111549	-1.060097	0.054908
C	-2.929656	-0.505756	1.130229
H	0.804573	2.247941	0.513963
H	0.432511	1.704779	-1.237730
H	-3.301708	-1.324439	1.753860
H	-3.770763	0.039998	0.687174
H	-2.356789	0.196109	1.725011
N	-1.444336	2.118169	0.112809
N	-1.690528	2.941568	-0.734057
N	-1.931173	3.748045	-1.540998
O	-3.008763	-1.637813	-0.882991
C	-2.500937	-2.886660	-1.355596
H	-3.291858	-3.280277	-2.000991
H	-2.319502	-3.573267	-0.518790
H	-1.584939	-2.744414	-1.937561
F	-0.496636	0.890636	2.457915
F	1.507998	0.118114	2.266594
F	-0.176634	-1.256148	2.253703

TSc_ah

C	0.115442	-1.321995	-1.330755
C	-0.020119	-0.557157	0.020984
C	-1.017170	0.554250	0.340914
N	-1.900814	0.973649	-0.661409
O	-2.629344	2.128545	-0.276667
C	-1.842976	3.304771	-0.484444
C	0.861532	-1.056747	1.178877
O	2.254796	-0.755459	1.003170
S	2.523013	0.723062	0.292850
O	2.500609	1.760748	1.325795
O	1.253057	0.748831	-0.604736
O	3.754903	0.560080	-0.479112
O	-0.893404	1.154411	1.394483
C	-2.838765	0.092102	-1.349369
N	-1.641281	-1.823840	0.831626
N	-1.918100	-1.621831	1.992514
N	-2.215243	-1.466633	3.106619
H	0.816283	-2.143425	1.236254
H	0.492975	-0.601771	2.098885
H	-3.771351	0.040611	-0.773212
H	-2.437501	-0.913150	-1.425562
H	-3.042281	0.494834	-2.346369
H	-2.513728	4.132126	-0.233572
H	-1.525318	3.377099	-1.532101
H	-0.971922	3.317462	0.177381
F	-0.717230	-2.377482	-1.479135
F	1.361433	-1.828948	-1.449134
F	-0.106416	-0.523656	-2.397672

TSd_sf

C	-0.147133	-0.279958	-1.230629
C	0.070378	0.418340	0.123314
O	1.180958	-0.135552	0.834270
S	2.179685	-1.175953	-0.064729
O	1.582505	-0.865401	-1.450396
C	0.399234	1.929453	-0.063754
C	-1.141830	0.226278	1.070573
O	-1.647120	1.100257	1.736768
O	-1.452109	-1.075769	1.141474
C	-2.549582	-1.413287	2.003816
O	1.883867	-2.528093	0.410034
O	3.540787	-0.673495	0.103264
N	-2.212375	0.375960	-1.351300
N	-2.889795	-0.601735	-1.541488
N	-3.552700	-1.547248	-1.723748
H	-0.087742	0.274906	-2.150266
H	-0.557442	-1.276832	-1.224860
H	-2.658635	-2.494326	1.916382
H	-3.458375	-0.907571	1.667761
H	-2.322888	-1.124763	3.034455
F	-0.624137	2.638237	-0.567477
F	0.770721	2.500151	1.099076
F	1.441940	2.072108	-0.922186

TSd_sh

C	-0.062334	1.926395	0.281859
C	-0.300743	0.409719	-0.026146
C	0.116335	-0.165216	-1.396364
O	1.169402	-1.137165	-1.304314
S	2.314608	-0.739519	-0.174435
O	3.265231	0.195563	-0.783479
C	-1.080168	-0.391121	0.984883
O	-1.484366	0.026402	2.048453
O	-1.222909	-1.657966	0.553318
C	-1.928682	-2.540194	1.436865
O	2.832454	-2.011592	0.326279
O	1.360404	-0.042623	0.834006
N	-2.347301	0.781606	-0.860296
N	-2.834958	-0.181142	-1.394894
N	-3.319575	-1.101550	-1.926672
H	0.421461	0.657432	-2.047233
H	-0.696390	-0.722753	-1.851696
H	-1.958885	-3.498628	0.917853
H	-1.393525	-2.628640	2.386767
H	-2.940840	-2.168110	1.618210
F	-1.113904	2.735266	0.076586
F	0.319152	2.132194	1.553988
F	0.930208	2.386114	-0.523975

TSd_af

C	0.047046	1.225377	-0.244043
C	-0.077490	-0.284195	0.053503
C	0.066427	-1.127069	-1.249016
C	0.937511	-0.653681	1.176100
O	1.889234	-1.495738	0.762930
C	3.040621	-1.582161	1.618469
O	-1.348603	-0.614834	0.594621
S	-2.574312	0.548252	0.373874
O	-2.841495	1.100580	1.701539
O	0.823224	-0.216511	2.294488
O	-3.665985	-0.142014	-0.309950
O	-1.778884	1.496197	-0.541406
N	2.198805	1.214518	0.020076
N	2.836869	2.100642	-0.481881
N	3.502223	2.942297	-0.946710
H	0.253210	1.582359	-1.238970
H	0.079282	1.896165	0.597622
H	3.723864	-2.265170	1.112069
H	2.763818	-1.964491	2.604506
H	3.483380	-0.586236	1.707846
F	-0.920879	-0.817702	-2.121640
F	1.231270	-0.924780	-1.895457
F	-0.041997	-2.449512	-0.988827

TSd_ah

C	-0.246557	1.749915	-0.289038
C	-0.293526	0.183601	-0.210606
C	0.331123	-0.657145	-1.340674
O	1.502173	-1.381609	-0.930708
S	2.438824	-0.555359	0.155896
O	3.314512	0.359166	-0.583827
C	-1.086033	-0.536931	0.845657
O	-1.154668	-1.747125	0.904932
O	-1.662274	0.303000	1.724747
C	-2.435593	-0.328576	2.753282

O	3.069236	-1.572245	0.994631
O	1.285320	0.190644	0.883495
N	-2.249355	0.097695	-1.274592
N	-2.589155	-1.015868	-1.591132
N	-2.935863	-2.080989	-1.914476
H	0.570183	-0.004733	-2.183275
H	-0.352241	-1.443238	-1.649510
H	-2.809698	0.488125	3.372698
H	-3.264688	-0.891720	2.314492
H	-1.808450	-1.004852	3.341346
F	-1.344503	2.350018	-0.778732
F	-0.030091	2.320166	0.912495
F	0.776089	2.113868	-1.103381