Supporting Information

for

Eight-Step Enantioselective Total Synthesis of (−)-Cycloclavine

Stephanie R. McCabe and Peter Wipf*

Department of Chemistry, University of Pittsburgh, Pittsburgh, PA 15260, U.S.A.

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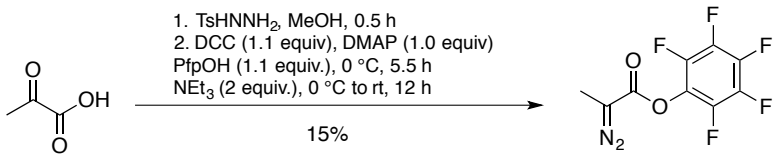
General Comments

All glassware was dried in an oven at 140 °C for at least 2 h prior to use. All air and moisture-sensitive reactions were performed under a dry N_2 atmosphere. Reactions carried out at 0 °C employed an ice bath and reactions carried out at -78 °C employed a dry ice/ acetone bath. THF and Et_2O were distilled over sodium/benzophenone ketyl, Et_3N, CH_2Cl_2 and toluene were distilled from CaH_2. All other materials were obtained from commercial sources and used as received. Microwave reactions were performed in a monowave microwave synthesis reactor. Infrared spectra were obtained from neat solids or oils on ATR FT-IR spectrometers. Melting points were determined in open capillary tubes and are uncorrected. High- resolution mass spectra were obtained on a Q-TOF MS or an Thermo Scientific Exactive Orbitrap LC-MS. ^{1}H spectra were obtained at 300 MHz, 400 MHz, 500, 600 or 700 MHz NMR in $CDCl_3$ unless otherwise specified. ^{13}C NMR spectra were obtained at 100, 125, or 150 MHz using a proton-decoupled pulse observed peak. Chemical shifts (δ) are reported in parts per million with the residual solvent peak used as an internal standard δ $^{1}H/^{13}C$ (Solvent); 7.26/77.16 ($CDCl_3$); 7.16/128.06 (C_6D_6) and 5.32/54.00 (CD_2Cl_2) and are tabulated as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), and coupling constant(s), number of protons. Reactions were monitored by thin layer chromatography analysis (pre-coated silica gel 60 F254 plates, 250 μm layer thickness) and visualization was accomplished with a $KMnO_4$ solution (1.50 g of $KMnO_4$, 10 g of K_2CO_3, and 1.25 mL of 10% NaOH in 200 mL of H_2O) when needed. Flash chromatography was performed using SiO_2 (40-63 μm). Optical rotations were measured on a polarimeter equipped with a sodium lamp. Specific rotation values were calculated using the equation:

$$[\alpha]_{\lambda}^{T} = (100 \cdot \alpha)/(l \cdot c)$$

Where [α] represents the specific rotation of the sample in ($10^{-1} \cdot deg \cdot cm^2 \cdot g^{-1}$), *T* indicates ambient temperature in °C, λ indicates wavelength (*D* is used to indicate the sodium line, λ = 589 nm), α indicates the measured optical rotation, *l* indicates the path length in decimeters and *c* indicates the concentration in g/100 mL. Enantiomeric excesses were determined by analytical supercritical fluid chromatography (SFC) using a ChiralPak IC

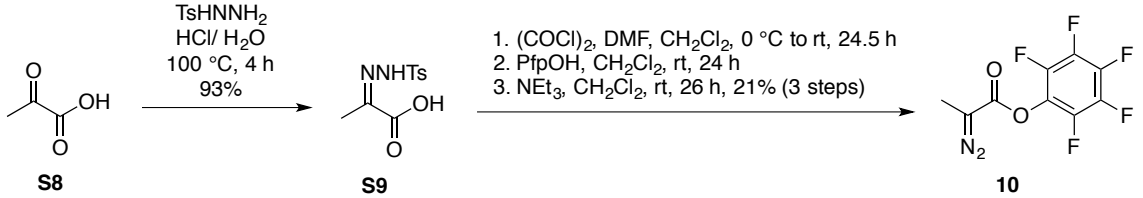
column.



10

Perfluorophenyl 2-diazopropanoate (10). Prepared using a modified protocol originally reported by Maruoka *et al.*[1] A solution of *p*-toluenesulfonyl hydrazide (10.7 g, 56.2 mmol) in MeOH (30 mL) was treated with pyruvic acid (3.95 mL, 56.2 mmol). The resulting clear and colorless solution was stirred at room temperature for 0.5 h then concentrated to deliver 2-(2-tosylhydrazono)propanoic acid as a white foam which was immediately dissolved in CH_2Cl_2 (580 mL), cooled to 0 °C and treated sequentially with DCC (13.9 g, 61.8 mmol) and DMAP (6.87 g, 56.2 mmol). The resulting mixture was stirred at 0 °C for 30 min then treated with pentafluorophenol (11.4 g, 61.8 mmol) in CH_2Cl_2 (5 mL). The reaction was allowed to stir at 0 °C for 5 h then treated with triethylamine (15.9 mL, 112 mmol) and the resulting yellow, heterogenous solution was stirred for 12 h while warming slowly to room temperature. The mixture was filtered through a pad of Florisil washing with CH_2Cl_2 and the filtrate was carefully concentrated under reduced pressure. The crude residue was purified by chromatography on SiO_2 (0-2% Et_2O/hexanes) to deliver **10** (2.21 g, 8.29 mmol, 15%) as a yellow oil: IR (ATR) 2940, 2094, 1721, 1655, 1515, 1474, 1338, 1297, 1147, 1055, 992, 713 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 1.20 (s, 3 H).

An alternate, higher yielding synthesis of perfluorophenyl 2-diazopropanoate (**10**):

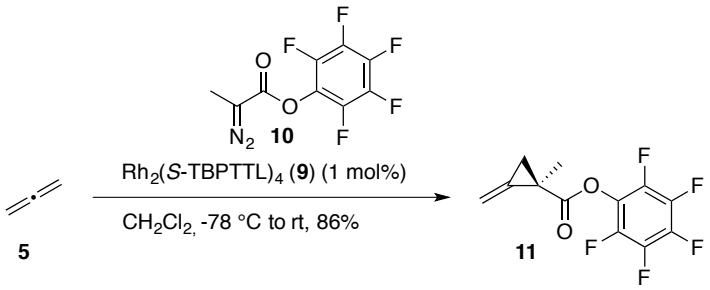


S8 **S9** **10**

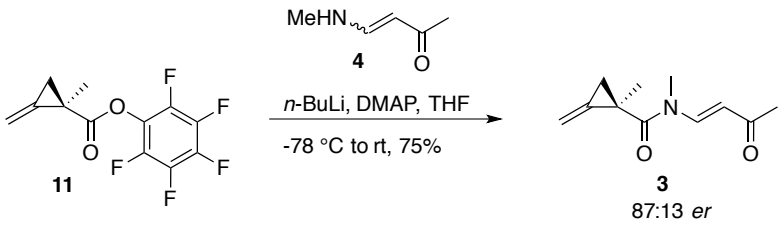
2-(2-Tosylhydrazono)propanoic acid (S9). A solution of *p*-toluenesulfonyl hydrazide (5.00 g, 26.3 mmol) in H_2O (25 mL) was treated sequentially with 2.5M HCl (12.5 mL)

and pyruvic acid (2.24 mL, 31.6 mmol) and the resulting heterogenous mixture heated at 100 °C for 4 h. The reaction was cooled to room temperature and the white precipitate collected by vacuum filtration, washing with cold H_2O (3x) and dried under high vacuum to deliver 2-(2-tosylhydrazono)propanoic acid **S9** (6.29 g, 93%) as a white solid. Mp 158.4-159.6 °C; IR (ATR) 3546, 3215, 2930, 1690, 1596, 1340, 1166, 1121, 1083, 907, 786 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 12.8 (bs, 1 H), 11.1 (s, 1 H), 7.76 (d, J = 8.4 Hz, 2 H), 7.41 (d, J = 8.0 Hz, 2 H), 2.38 (s, 3 H), 1.93 (s, 3 H); ^{13}C NMR (100 MHz, DMSO-d_6); δ 165.2, 145.3, 143.8, 136.0, 129.7, 127.4, 21.0, 13.1; HRMS (LCMS ESI^+) *m/z* calcd for $C_{10}H_{13}N_2O_4S$ 257.0591, found 257.0587.

Perfluorophenyl 2-diazopropanoate (10). A suspension of 2-(2-tosylhydrazono)propanoic acid **S9** (8.00 g, 31.2 mmol) in CH_2Cl_2 (336 mL) under an atmosphere of argon (balloon) was cooled to 0 °C and treated sequentially with oxalyl chloride (4.10 mL, 46.8 mmol) and DMF (0.0121 mL, 0.156 mmol) upon the addition of which gas evolution occurred. The resulting suspension was stirred at 0 °C warming to room temperature over 24.5 h during which time the white solid gradually went into solution becoming clear and pale yellow. The reaction was then treated dropwise with a solution of pentafluorophenol (8.62 g, 46.8 mmol) in CH_2Cl_2 (13 mL) and the resulting clear and pale yellow solution let stir at room temperature for 24 h. The reaction was then treated with NEt_3 (8.87 mL, 62.4 mmol) during the addition of which a white gas evolved and the solution became orange/ yellow in colour. The resulting orange solution was allowed to stir at room temperature for 26 h then filtered through a pad of florosil (washing with CH_2Cl_2) and concentrated. The crude oil was purified by chromatography on SiO_2 (0-1% Et_2O/hexanes) to deliver diazopropanoate **10** (1.76 g, 21%) as a yellow oil. ^1H NMR (300 MHz, C_6D_6) δ 1.21 (s, 3 H).



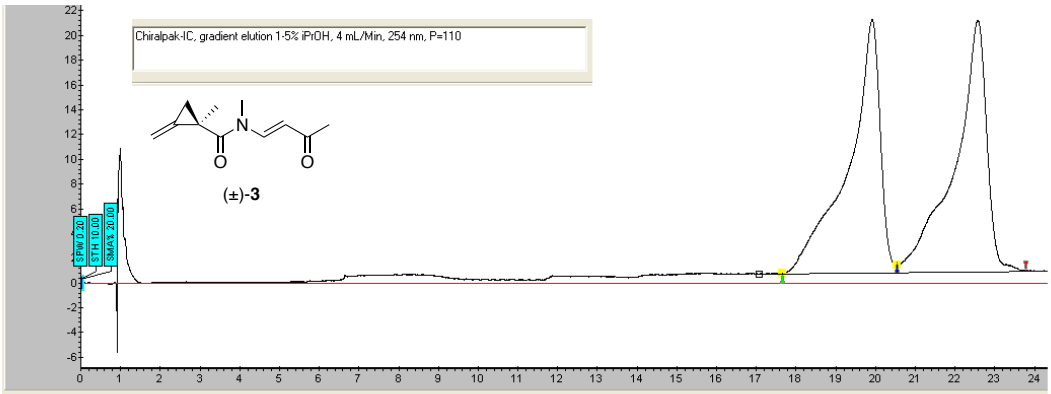
Perfluorophenyl (*R*)-1-methyl-2-methylenecyclopropane-1-carboxylate (11). An oven-dried three-neck flask fitted with a nitrogen inlet, a dry-ice condenser, and septum was charged with Rh_2(*S*-TBPTTL)$_4$ (**9**)[2] (0.236 g, 0.0939 mmol) and CH_2Cl_2 (51 mL) and the resulting green solution was cooled to -78°C and treated dropwise with an excess of condensed allene gas (**5**, 2.23 g, 55.7 mmol). A solution of perfluorophenyl 2-diazopropanoate (**10**, 2.50 g, 9.39 mmol) in anhydrous CH_2Cl_2 (9.0 mL) was then added slowly *via* syringe pump at a rate of ca. 1 mL/h, allowing the solution to run down the side of the flask into the reaction mixture. After the addition was complete, the mixture was allowed to stir at -78 °C for 1 h before warming to room temperature. The solution was concentrated and the resulting green residue was purified by chromatography on SiO_2 (gradient elution 0-1% Et_2O/hexanes) to deliver methylenecyclopropane **11** (2.24 g, 8.05 mmol, 86%) as a clear and pale yellow oil: $[\alpha]_D^{18}$ -2.9 (*c* 5.1, $CHCl_3$); IR (ATR) 2985, 2939, 1770, 1655, 1517, 1459, 1283, 1070, 1028, 993 cm^{-1}; ^1H NMR (400 MHz, CD_2Cl_2) δ 5.64 (t, *J* = 2.8 Hz, 1 H), 5.56 (t, *J* = 2.2 Hz, 1 H), 2.30 (dt, *J* = 9.2, 2.5 Hz, 1 H), 1.63 (dt, *J* = 9.2, 2.4 Hz, 1 H), 1.51 (s, 3 H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 170.4, 143.2-143.0 (m), 141.3-141.0 (m), 140.7-140.5 (m), 139.9-139.5 (m), 137.4-137.0 (m), 136.8, 126.2-125.8 (m), 104.5, 23.2, 20.6, 18.8; DEPT-135 (100 MHz, CD_2Cl_2) δ 104.5 (CH_2), 20.6 (CH_2), 18.8 (CH_3); ^{19}F NMR (471 MHz, CD_2Cl_2) δ -153.9 (m, 2 F), -59.4 (t, J_F = 21.2 Hz, 1 F), -163.5 to -163.6 (m, 2 F); HRMS (APCI+) *m/z* calcd for $C_{12}H_8O_2F_5$ (M+H) 279.04390, found 279.04312.



(*R*,*E*)-*N*,1-Dimethyl-2-methylene-*N*-(3-oxobut-1-en-1-yl)cyclopropane-1-carboxamide (3). An oven-dried flask charged with vinylogous amide **4**[3] (0.700 g, 7.06 mmol) was evacuated and backfilled with nitrogen (3x). Freshly distilled THF (24 mL) was added and the resulting solution was cooled to -78 °C and treated dropwise with *n*-BuLi (3.24 mL, 2.29 M solution in hexanes, 7.42 mmol). The resulting clear, pale yellow solution was stirred for 5 min at -78 °C, then treated with a solution of ester **11** (2.06 g, 7.41 mmol) in THF (4 mL). The resulting bright yellow solution was treated with DMAP (0.0862 g, 0.706 mmol) and stirred for 10 min at -78 °C. The cold bath was removed and the reaction mixture was allowed to stir, warming to room temperature. The reaction was quenched with sat. $NaHCO_3$. After addition of EtOAc, the aqueous layer was extracted with EtOAc (3x) and the combined organic layers were dried (Na_2SO_4) and concentrated. The crude product was purified by chromatography on SiO_2 (10-15% EtOAc/hexanes) to deliver **3** (1.03 g, 5.32 mmol, 75%) as a clear, pale yellow oil: $[\alpha]_D^{18}$ +251.5 (*c* 2.2, $CHCl_3$); IR (ATR) 2968, 2932, 1680, 1615, 1578, 1516, 1355, 1262, 1247, 1072, 968 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 13.6 Hz, 1 H), 5.73-5.69 (m, 2 H), 5.53 (ap. s, 1 H), 3.15 (s, 3 H), 2.29 (s, 3 H), 1.79 (dt, *J* = 9.6, 2.2 Hz, 1 H), 1.49 (s, 3 H), 1.32 (dt, *J* = 9.6, 2.2 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.9, 172.4, 142.9, 134.9, 108.4, 104.9, 30.9, 28.9, 24.9, 21.8, 15.9; HRMS $(ESI)^+$ *m/z* calcd for $C_{11}H_{16}O_2N$ (M+H) 194.1176, found 194.1174.

SFC conditions: Chiralpak-IC column (250 x 4.6 mm), gradient elution: 1% *i*PrOH (hold for 5 min), 2% *i*PrOH (hold for 5 min), 3% *i*PrOH (hold for 6 min), 4% *i*PrOH (hold for 3 min), 4.50% *i*PrOH (hold for 2 min), 5% *i*PrOH (hold for 3 min), 4 mL/min, 254 nM, P=110 (BAR).

Racemic standard:



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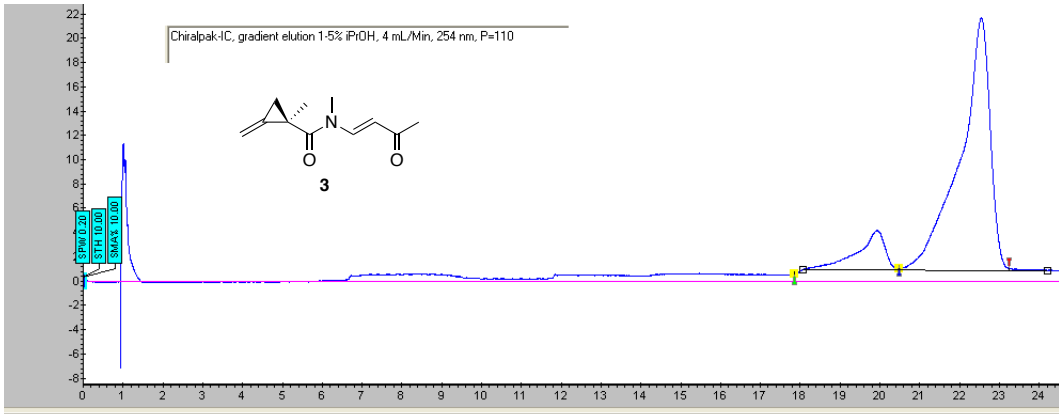
1	UNKNOWN	17.65	19.92	20.54	0.00	49.89	20.5	19.0	49.894
2	UNKNOWN	20.54	22.57	23.78	0.00	50.11	20.3	19.0	50.106
Total						100.00	40.8	38.0	100.000

Enantiomeric excess of vinylogous amide **3**:



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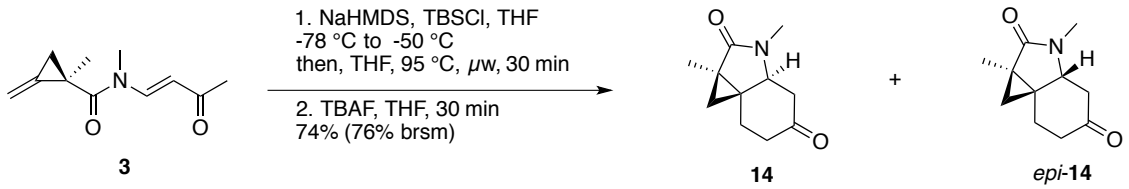
1	UNKNOWN	17.85	19.93	20.48	0.00	12.53	3.2	2.6	12.531
2	UNKNOWN	20.48	22.55	23.24	0.00	87.47	20.8	18.1	87.469
Total						100.00	24.0	20.7	100.000



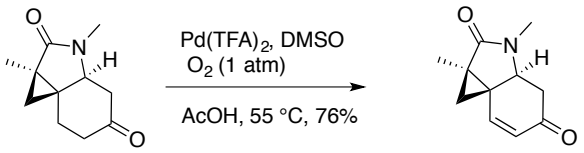
(1a*R*,3a*S*,7a*S*)-1a,3-Dimethylhexahydro-2*H*-cyclopropa[*c*]indole-2,5(3*H*)-dione (14) and (1a*R*,3a*R*,7a*S*)-1a,3-dimethylhexahydro-2*H*-cyclopropa[*c*]indole-2,5(3*H*)-dione (*epi*-14). An oven-dried flask was charged with NaHMDS (0.611 g, 3.17 mmol) followed by anhydrous THF (31.5 mL) under an atmosphere of nitrogen. The resulting clear,

colourless solution was stirred for 15 min at room temperature, cooled to -78 °C and stirred for a further 15 min prior to treatment with a solution of vinylogous amide **3** (0.556 g, 2.88 mmol) in THF (6.0 mL) that was added slowly via syringe pump at a rate of ca. 2 mL/h. During the slow addition of the amide, the solution changes color from clear pale yellow, to clear and gold to clear and deep orange. The resulting clear, orange solution was allowed to stir for 1 h while warming to -50 °C, cooled to -78 °C and treated dropwise with a solution of TBSCl (0.526 g, 3.45 mmol) in THF (11.5 mL) over a period of 5 min. The solution was allowed to stir for 5 min at -78 °C before the cold bath was removed and the solution allowed to reach room temperature. ^{1}H NMR analysis of an aliquot ($CDCl_3$) indicated formation of the desired TBS enol ether. The reaction mixture was concentrated under reduced pressure to obtain crude enol ether **12** as an orange gel, which was immediately taken up in THF (8.4 mL) and heated under microwave irradiation in a sealed vial at 95 °C for 30 min (3 x 2.8 mL batches). The combined batches were concentrated to deliver a mixture of crude enol ethers, which were taken up in THF (29 mL), treated dropwise with TBAF (2.88 mL, 1 M solution in THF, 2.88 mmol) and allowed to stir at room temperature for 30 min. The reaction mixture was filtered through a pad of Celite and concentrated. The resulting residue was purified by chromatography on SiO_2 (gradient elution: 20% EtOAc/hexanes to elute recovered vinylogous amide **3**, then 50-70% EtOAc/hexanes to elute ketone **14** and then 90-100% EtOAc/hexanes to elute *epi*-**14**) to deliver recovered vinylogous amide **3** (0.0153 g) as a yellow oil along with *trans*-ketone **14** (0.339 g, 1.75 mmol, 61%, (63% brsm)) as a yellow crystalline solid and *cis*-ketone *epi*-**14** (0.0711 g, 0.368 mmol, 13% (13% brsm)) as a yellow oil.

***trans*-Ketone 14**: $[\alpha]_D^{19}$ +97.1 (*c* 0.17, $CHCl_3$); Mp 95.5-98.4 °C; IR (ATR) 2955, 1706, 1676, 1414, 1395, 1359, 1292, 1230, 1123, 1072, 1042, 865 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.40 (dd, *J* = 13.1, 4.1 Hz, 1 H), 2.80 (ddd, *J* = 13.5, 4.1, 1.4 Hz, 1 H), 2.72-2.66 (m, 4 H), 2.53 (ddd, *J* = 15.4, 12.1, 7.3 Hz, 1 H), 2.35 (ap. t, *J* = 13.4 Hz, 1 H), 2.18-2.08 (m, 1 H), 1.72 (ddd, *J* = 13.2, 7.2, 1.8 Hz, 1 H), 1.38 (s, 3 H), 0.95 (d, *J* = 3.6 Hz, 1 H), 0.66 (d, *J* = 3.9 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.6, 178.9, 60.1, 45.1, 41.5, 31.8, 30.7, 27.2, 25.8, 22.7, 11.0; HRMS (LCMS-ESI) *m/z* calcd for $C_{11}H_{16}O_2N$ (M+H) 194.1176, found 194.1175.

A single X-ray crystal was obtained for racemic (±)-**14**. Ketone (±)-**14** was obtained as an oil which solidified at -20 °C to provide crystals of sufficient quality for X-ray analysis. The X-ray structure of **14** (CCDC 1499046) has been deposited with the Cambridge Crystallographic Data Centre (http://www.ccdc.cam.ac.uk/).

***cis*-Ketone *epi*-14**: $[\alpha]_D^{18}$ -9.1 (*c* 1, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) δ 3.73 (ap. t, *J* = 6.6 Hz, 1 H), 2.83 (dd, *J* =15.0, 6.3 Hz, 1 H), 2.72 (s, 3 H), 2.55-2.25 (m, 4 H), 1.82 (dt, *J* = 13.8, 5.1 Hz, 1 H), 1.34 (s, 3 H), 0.92 (d, *J* = 4.5 Hz, 1 H), 0.84 (d, *J* = 4.5 Hz, 1 H). The experimental ^{1}H NMR was identical to the literature-reported spectral data.[4]

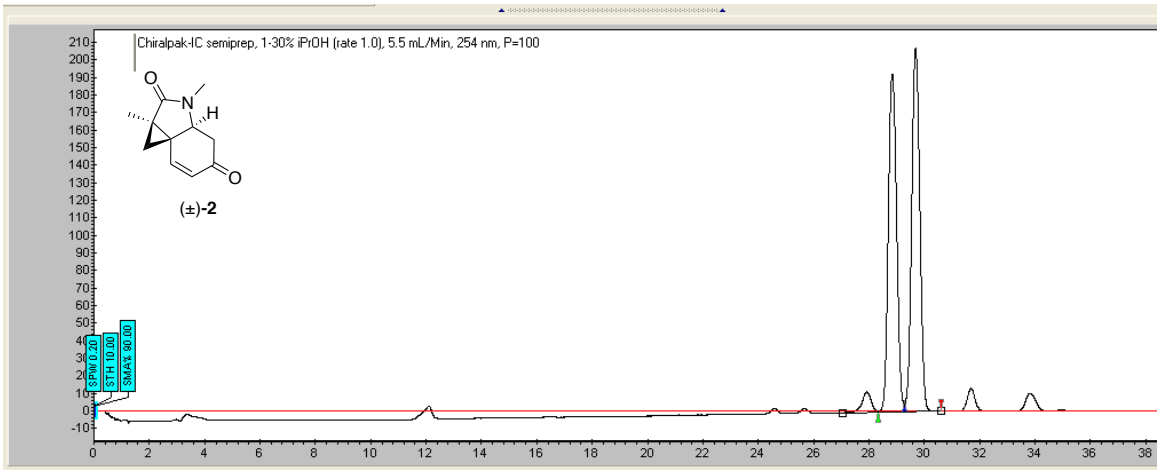


14 **2**

(1a*R*,3a*S*,7a*R*)-1a,3-Dimethyl-1,1a,3a,4-tetrahydro-2*H*-cyclopropa[*c*]indole-2,5(3*H*)-dione (2). A solution of $Pd(TFA)_2$ (0.00940 g, 0.0274 mmol) and DMSO (3.90 µL, 0.0549 mmol) in AcOH (2.74 mL) was heated at 55 °C under an atmosphere of O_2 (balloon) to pre-activate the catalyst system. After 19.5 h, ketone **14** (0.106 g, 0.549 mmol) was added and the reaction was allowed to stir at 55 °C under an atmosphere of O_2 (balloon). Additional $Pd(TFA)_2$ was added at 48 h (4.7 mg) and 72 h (4.7 mg) after the addition of the ketone in order to drive the reaction to completion. After 5 d, ^{1}H NMR of an aliquot ($CDCl_3$) showed that the conversion was complete and the reaction mixture was concentrated and purified by chromatography on SiO_2 (3-5% acetone/CH_2Cl_2) to deliver enone **2** (0.0796 g, 0.416 mmol, 76%) as a cream crystalline solid. Protocol for the enantiomeric enrichment by recrystallization: Enone **2** (0.0610 g, 0.319 mmol) was dissolved in a 15:1 mixture of boiling MTBE: 1,2-dichloroethane (*c* 0.08 M) and allowed to cool to room temperature prior to the addition of a seed crystal. The resulting solution was allowed to stand overnight at -20 °C during which time white needle-shaped crystals formed. The mother liquor was removed via pipette transfer and the crystals were washed with MTBE (2x) and placed under vacuum to remove trace solvents. The first recrystallization provided crystals of 100% *ee,* the second recrystallization provided

crystals of >99% *ee* and the third recrystallization provided crystals of 92% *ee*. Three rounds of recrystallization delivered enone **2** (29.7 mg, 56% of theoretical maximum yield) as white, needle-shaped crystals. Only samples with *ee* >96% were carried on in the subsequent reaction. The *ee* of the combined material was >99% *ee* by SFC analysis: $[\alpha]_D^{16}$ -110.1 (*c* 1.1, $CHCl_3$); Mp 131.7-134.1 °C; IR (ATR) 2966, 2929, 1683, 1664, 1618, 1585, 1452, 1389, 1235, 1071, 796 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.97 (d, *J* = 9.5 Hz, 1 H), 6.14 (d, *J* = 9.5 Hz, 1 H), 3.81 (dd, *J* = 13.8, 3.8 Hz, 1 H), 2.90 (dd, *J* = 15.5, 4.0 Hz, 1 H), 2.71 (s, 3 H), 2.44 (dd, *J* = 15.8, 14.3 Hz, 1 H), 1.46 (s, 3 H), 1.33 (d, *J* = 4.0 Hz, 1 H), 0.86 (d, *J* = 4.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.0, 177.8, 148.4, 131.4, 58.6, 41.9, 32.9, 32.1, 27.3, 23.5, 10.9; HRMS $(ESI)^+$ *m/z* calcd for $C_{11}H_{14}O_2N$ (M+H) 192.1019, found 192.1017. SFC analysis: Chiralpak-IC semiprep column (250 x 10 mm), gradient elution: 1-30% *i*PrOH (rate 1.0), 5.5 mL/min, 254 nM, P=100 (BAR).

Racemic standard:



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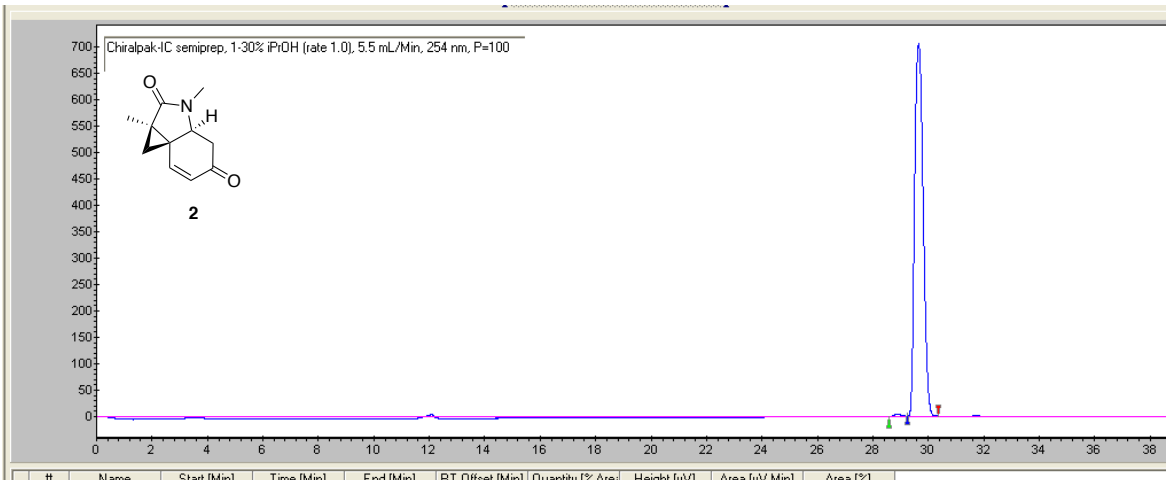
1	UNKNOWN	28.32	28.84	29.27	0.00	48.67	192.8	66.9	48.670
2	UNKNOWN	29.27	29.68	30.62	0.00	51.33	207.0	70.6	51.330
Total						100.00	399.9	137.5	100.000

Enantiomeric excess of enantioenriched enone **2** after recrystallization:



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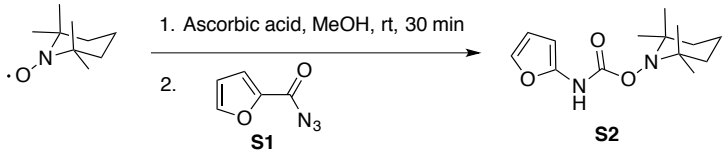
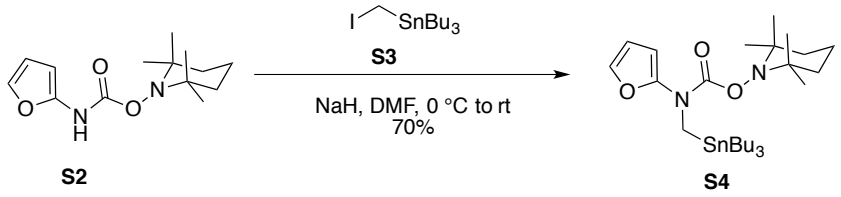
1	UNKNOWN	28.57	28.88	29.22	0.00	0.48	3.8	1.2	0.477
2	UNKNOWN	29.22	29.65	30.35	0.00	99.52	706.5	252.0	99.523
Total						100.00	710.3	253.2	100.000



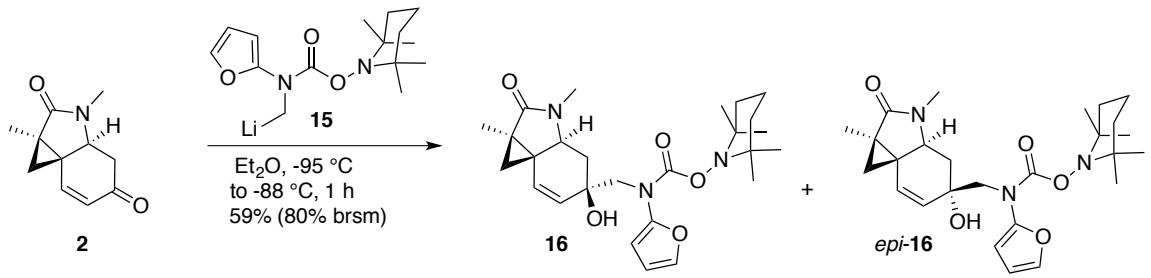
2,2,6,6-Tetramethylpiperidin-1-ol. A solution of TEMPO (2.00 g, 96% pure, 12.3 mmol) in deoxygenated MeOH (104 mL) was treated with ascorbic acid (2.60 g, 14.8 mmol) upon the addition of which the solution immediately changed colour from clear and orange to a clear pale yellow solution. The solution was allowed to stir for 30 min, then concentrated under reduced pressure. The resulting residue was diluted with deoxygenated Et_2O (60 mL) and water (60 mL) and transferred to a separatory funnel. The aqueous phase was further extracted with deoxygenated Et_2O (4 x 30 mL) and the combined organic layers were dried ($MgSO_4$) under nitrogen, filtered and concentrated to deliver crude 2,2,6,6-tetramethylpiperidin-1-ol (1.55 g, 80% crude yield), which was carried on without further purification.

2,2,6,6-Tetramethylpiperidin-1-yl furan-2-ylcarbamate (S2). A solution of acyl azide **S1**[5] (0.800 g, 5.84 mmol) in PhMe (45 mL) was heated at reflux for 1 h then cooled to room temperature. IR analysis of the reaction mixture indicated isocyanate formation (ν_{NCO} 2265 cm^{-1}). The reaction mixture was then treated with a solution of 2,2,6,6-tetramethylpiperidin-1-ol (1.55 g, 9.86 mmol) in PhMe (12 mL). The resulting

orange/brown solution was stirred for 1 h and concentrated. The residue was purified by chromatography on SiO_2 (0-4% EtOAc/hexanes) to deliver TEMPO-carbamate **S2** (1.35 g, 5.08 mmol, 87%) as a white solid: Mp 101.4-102.8 °C; IR (ATR) 3256, 2936, 2924, 2921, 1715, 1620, 1506, 1439, 1379, 1251, 1154, 1010, 719 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.00 (bs, 1 H), 7.10 (d, J = 1.0 Hz, 1 H), 6.38 (dd, J = 3.3, 2.3 Hz, 1 H), 6.17 (d, J = 3.0 Hz, 1 H), 1.71-1.55 (m, 5 H), 1.48-1.44 (m, 1 H), 1.26 (s, 6 H), 1.19 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.6, 144.9, 136.4, 111.7, 95.6, 61.5, 39.9, 31.7, 20.9, 16.9; HRMS (ESI+) *m/z* calcd for $C_{14}H_{23}O_3N_2$ (M+H) 267.17032, found 267.17137.



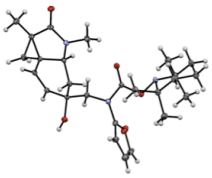
2,2,6,6-Tetramethylpiperidin-1-yl furan-2-yl((tributylstannyl)methyl)carbamate (S4). A solution of furan **S2** (0.150 g, 0.563 mmol) in DMF (0.9 mL) was cooled to 0 °C and treated with NaH (0.0270 g, 60% dispersion in mineral oil, 0.675 mmol). The resulting solution was stirred at 0 °C for 0.5 h then treated with (iodomethyl)tributyltin **S3**[6] (0.255 g, 0.591 mmol). The resulting brown solution was stirred for 1 h while warming to room temperature, diluted with Et_2O and quenched with sat. $NH_4Cl_{(aq)}$. The aqueous layer was extracted with Et_2O (2x) and the combined organic layers were dried (Na_2SO_4) and concentrated. The resulting residue was purified by chromatography on SiO_2 (gradient elution 0-3% EtOAc/hexanes) to deliver stannane **S4** (0.223 g, 0.392 mmol, 70%) as a clear, pale yellow oil: IR (ATR) 2947, 2926, 2926, 2869, 1728, 1609, 1502, 1430, 1377, 1349, 1185, 1072, 986 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 6.90 (dd, J = 2.0, 0.80 Hz, 1 H), 6.05 (dd, J = 3.2, 2.0 Hz, 1 H), 5.93 (bs, 1 H), 3.35 (s, 2 H, $^2J^{117/119}$Sn-^{1}H = 27.6 Hz), 1.69-1.54 (m, 9 H), 1.44-1.35 (m, 7 H), 1.33 (s, 6 H), 1.27-1.23 (m, 2 H), 1.09-1.05 (m, 6 H), 0.97-0.94 (m, 15 H); ^{13}C NMR (100 MHz, C_6D_6) δ 157.2, 151.1, 138.8, 111.3, 101.5, 60.4, 39.4, 36.7, 32.0, 29.6 ($J^{117/119}$Sn-^{13}C = 20 Hz), 27.9 ($J^{117/119}$Sn-^{13}C = 57 Hz), 20.6, 17.2, 14.0, 11.0 ($^1J^{119}$Sn-^{13}C = 334 Hz, $^1J^{117}$Sn-^{13}C = 319 Hz); HRMS (ESI+) *m/z* calcd for $C_{27}H_{51}O_3N_2Sn$ (M+H) 571.29162, found 571.28963.



Allylic alcohols 16 and *epi*-16. An oven-dried 2-neck flask equipped with a septum fitted with a nitrogen inlet and a stopper was charged with stannane **S4** (0.107 g, 0.188 mmol) and evacuated under high vacuum, then backfilled with nitrogen (3x). The stopper was exchanged for a thermocouple thermometer under a positive flow of nitrogen, and anhydrous Et_2O (0.60 mL) was added. The clear, colorless solution was cooled to -74 °C (Et_2O/dry ice), stirred for 10 min, then treated dropwise with *n*-BuLi (0.0753 mL, 2.5 M solution in hexanes, 0.188 mmol) during the slow addition of which the temperature increased to -71.4 °C. The resulting clear and colourless solution was stirred at -73 °C for 15 min then cooled to -94 °C ($N_{2(l)}$/ Et_2O) over a period of 10 min and treated dropwise with a solution of enone **2** (0.0300 g, 0.157 mmol) in THF/Et_2O (1:1 , 600 μL). During this addition the temperature rose to -88 °C and the solution became clear yellow. The mixture was stirred for 1 h while the internal temperature was kept between -89 to -95 °C. The solution was then allowed to warm slowly to -75 °C over 20 min, diluted with EtOAc (0.50 mL) and quenched with sat. $NH_4Cl_{(aq)}$ (1.0 mL), keeping the internal temperature below -50 °C. The cold bath was removed and the reaction mixture was warmed to room temperature. The aqueous layer was extracted with EtOAc (3x). The combined organic layers were dried (Na_2SO_4) and concentrated. The resulting residue was purified by chromatography on SiO_2 (5-10% acetone/CH_2Cl_2) to deliver recovered starting material **2** (7.8 mg) as a white solid along with allylic alcohols **16** (0.0260 g, 0.0551 mmol, 35% (48% brsm)) and *epi*-**16** (0.0176 g, 0.0373 mmol, 24% (32% brsm)) as a white foams.

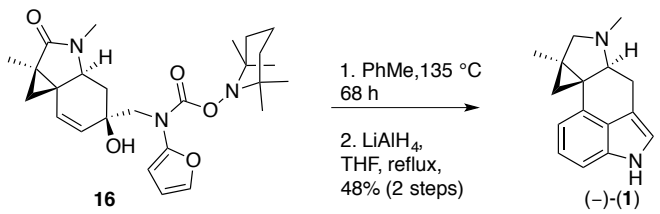
Allylic alcohol 16: $[\alpha]_D^{17}$ -26.1 (*c* 1.1, $CHCl_3$); IR (ATR) 3415, 2932, 1736, 1676, 1614, 1504, 1380, 1365, 1287, 1124, 915, 730 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 6.81 (dd, *J* = 2.0, 0.8 Hz, 1 H), 5.99 (dd, *J* = 3.2, 2.4 Hz, 1 H), 5.90 (dd, 3.2, 0.8 Hz, 1 H), 5.43 (dd, *J* = 9.8, 0.6 Hz, 1 H), 5.36 (d, *J* = 9.6 Hz, 1 H), 3.76 (d, *J* = 14.8 Hz, 1 H), 3.54 (d, *J* = 14.0 Hz, 1 H), 3.37 (s, 1 H), 2.98 (dd, *J* = 13.2, 2.4 Hz, 1 H), 2.54 (s, 3 H), 2.42

(dd, J = 12.0, 0.8 Hz, 1 H), 1.68 (ap. t, J = 12.2 Hz, 1 H), 1.58-1.55 (m, 2 H), 1.31 (s, 3 H), 1.27-1.23 (m, 9 H), 1.08-1.05 (m, 1 H), 0.93 (s, 3 H), 0.92 (s, 3 H), 0.75 (d, J = 3.6 Hz, 1 H), 0.23 (d, J = 3.6 Hz, 1 H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 179.2, 159.0, 148.9, 139.5, 132.3, 128.8, 111.5, 103.1, 75.1, 60.9, 60.8, 59.5, 58.2, 39.1 (2C), 35.8, 32.4, 32.1, 31.9, 31.7, 27.2, 24.6, 20.5 (2C), 16.9, 10.8; HRMS (LCMS ESI+) *m/z* calcd for $C_{26}H_{38}O_5N_3$ (M+H) 472.2806, found 472.2807.



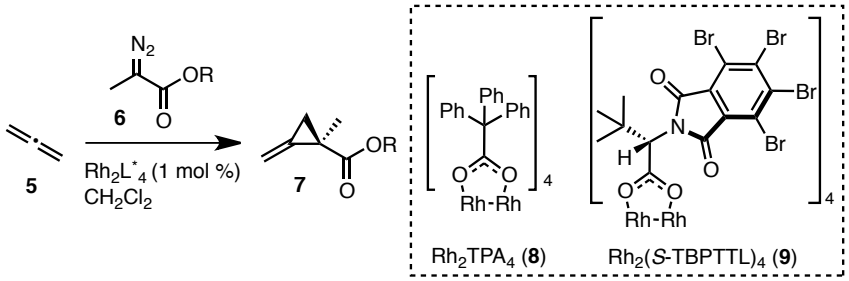
The relative configuration of allylic alcohol **16** was established through a combination of X-ray and ^{1}H NMR data (see SI figures **7**-**10**). An X-ray crystal structure of (±)-**16** confirmed the assigned relative configuration. Crystals were grown by slow evaporation at room temperature from a mixture of Et_2O/hexanes (1:1): Mp 91.4-94.3 °C. The X-ray structure of **16** (CCDC 1499047) has been deposited with the Cambridge Crystallographic Data Centre (http://www.ccdc.cam.ac.uk/).

Allylic alcohol *epi*-16: $[\alpha]_D^{17}$ -3.8 (*c* 1.0, $CHCl_3$); IR (ATR) 3413, 2932, 1744, 1677, 1611, 1504, 1451, 1381, 1364, 1287, 1177, 924, 736 cm^{-1}; ^{1}H NMR (400 MHz, C_6D_6) δ 6.86 (dd, J = 2.0, 0.8 Hz, 1 H), 6.03 (dd, J = 3.2, 2.0 Hz, 1 H), 5.87 (dd, J = 3.2, 0.8 Hz, 1 H), 5.66 (dd, J = 9.8, 0.6 Hz, 1 H), 5.48 (d, J = 10.0 Hz, 1 H), 3.84, 3.80 (ABq, J = 14.4 Hz, 2 H), 3.53 (dd, J = 12.6, 2.6 Hz, 1 H), 3.48 (bs, 1 H), 2.47 (s, 3 H), 2.12 (ddd, J = 12.0, 2.8, 1.2 Hz, 1 H), 1.66-1.55 (m, 3 H), 1.33-1.28 (m, 12 H), 1.13-1.07 (m, 1 H), 0.93 (ap. s, 6 H), 0.78 (d, J = 3.6 Hz, 1 H), 0.25 (d, J = 3.6 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.5, 158.8, 148.7, 139.6, 131.0, 129.6, 111.4, 103.4, 74.0, 61.0, 60.9, 60.8, 57.1, 39.1 (2 C), 37.2, 32.3, 31.9, 31.8, 31.7, 27.2, 23.6, 20.5 (2 C), 17.0, 10.8; HRMS (LCMS ESI+) *m/z* calcd for $C_{26}H_{38}O_5N_3$ (M+H) 472.2806, found 472.2803.



(−)-Cycloclavine ((−)-(1)). A solution of tertiary alcohol **16** (0.0140 g, 0.0297 mmol) in dry degassed PhMe (2.0 mL) was heated at 135 °C in a sealed tube for 68 h. The reaction mixture was filtered through a pad of SiO_2 washing with EtOAc and concentrated. The crude indole was dissolved in anhydrous THF (0.4 mL), treated with $LiAlH_4$ (0.24 mL, 1.0 M solution in Et_2O, 0.240 mmol) and stirred at reflux (66 °C) in a sealed tube overnight. The reaction mixture was cooled to 0 °C and diluted with Et_2O (1 mL), then treated successively with H_2O (9 μL), 15% NaOH (9 μL) and H_2O (27 μL). The suspension was stirred for 15 min while warming to room temperature, then treated with $MgSO_4$ and stirred for a further 15 min. The mixture was filtered through a pad of Celite and concentrated. The crude product was purified by chromatography on SiO_2 (20% acetone/ $CHCl_3$) to deliver **(−)-(1)** (0.0034 g, 0.0143 mmol, 48%, 2 steps) as a white solid: $[\alpha]_D^{20}$ -58.9 (*c* 0.23, $CHCl_3$); IR (ATR) 3413, 2930, 2879, 1591, 1443 1322, 1165, 1093, 738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (bs, 1 H), 7.14 (dd, *J* = 8.0, 0.8 Hz, 1 H), 7.09 (dd, *J* = 8.0, 6.8 Hz, 1 H), 6.90 (ap. t, *J* = 1.6 Hz, 1 H), 6.82 (dd, *J* = 6.8, 0.4 Hz, 1 H), 3.17-3.11 (m, 2 H), 2.78 (dd, *J* = 11.6, 4.0 Hz, 1 H), 2.63-2.57 (m, 1 H), 2.40 (d, *J* = 8.4 Hz, 1 H), 2.36 (s, 3 H), 1.69 (s, 3 H), 1.60 (d, *J* = 3.6 Hz, 1 H), 0.45 (d, *J* = 3.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.6, 133.7, 128.8, 123.1, 118.2, 113.5, 110.5, 108.1, 69.8, 65.8, 40.1, 34.5, 27.9, 25.1, 24.4, 16.6; HRMS (LCMS ESI+) *m/z* calcd for $C_{16}H_{19}N_2$ (M+H) 239.1543, found 239.1541.

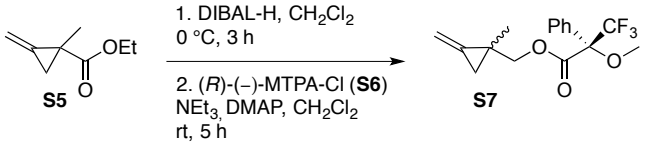
Table S1. Table 1. Optimization of Catalytic Allene Cyclopropanation.



Entry	R	Catalyst	T (°C)	Yield (%)	*er*
1	Et	**8**	-78	88	50:50[a]
2	*t*-Bu	**9**	-78	51	91:9[a]
3	*t*-Bu	**9**	-98 to -80	47	93:7[a]
4	Su[b]	**9**	-78 to rt	27	77:23[a]
5	Pcp[c]	**9**	-78	74[f](84)[g]	77:23[a,e]
6	Pfp[d]	**9**	-78	86	87:13

[a] Approximate enantiomeric ratios determined by ^{1}H NMR analysis of diastereomeric Mosher ester derivatives [b]succinimide; [c]pentachlorophenyl; [d]pentafluorophenyl; [e]crystallization provided enrichment of the mother liquor up to 90:10 *er*; [f] reaction on 0.2 mmol scale; [g]reaction on 9 mmol scale.

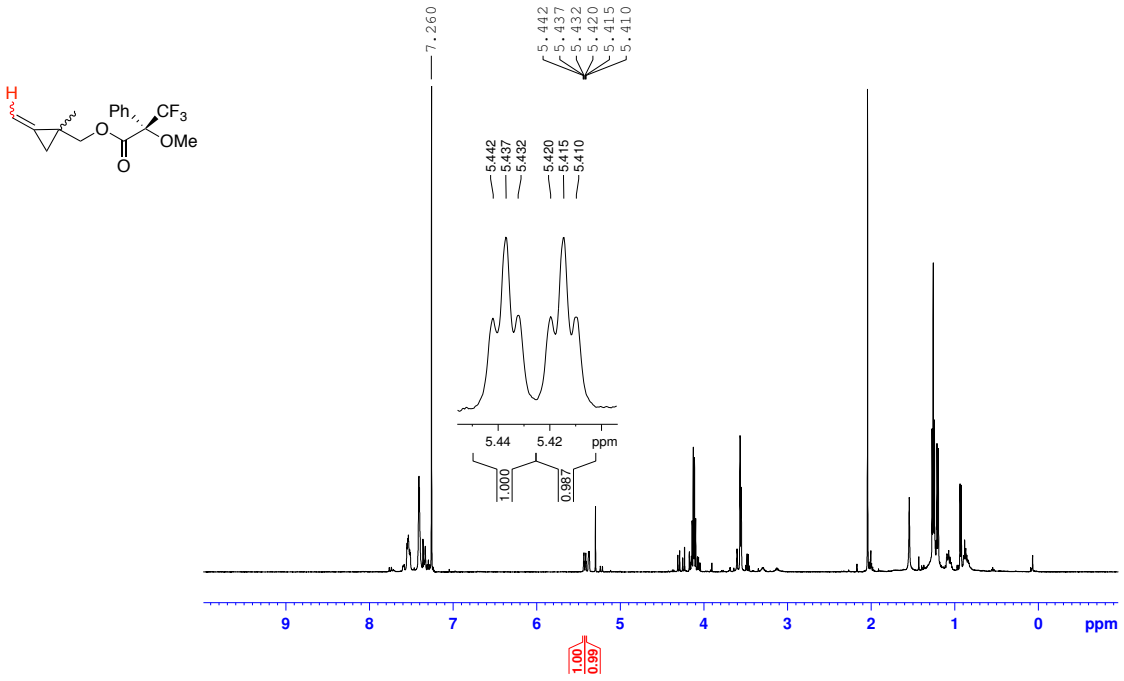
Mosher-acid chloride derivatization, representative procedure:



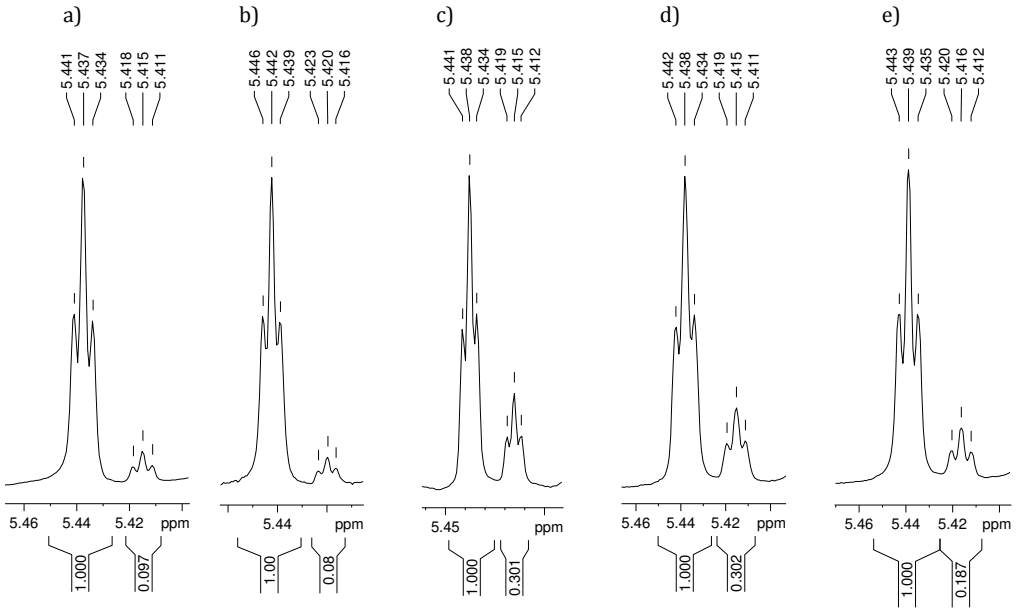
Mosher Acid derivative (S7). A solution of ethyl 1-methyl-2-methylenecyclopropane-1-carboxylate (**S5**) (0.0200 g, 0.143 mmol) in CH_2Cl_2 (1 mL) was cooled to 0 °C, treated with DIBAL-H (0.385 mL, 1 M solution in hexanes, 0.385 mmol) and stirred at 0 °C for 3 h. The reaction mixture was treated successively with H_2O (15 μL), 15% NaOH (15 μL) and H_2O (39 μL), dried ($MgSO_4$) and filtered through a pad of Celite washing with EtOAc and concentrated. A solution of crude alcohol in CH_2Cl_2 (1.1 mL) under an inert atmosphere was treated sequentially with a solution of (*R*)-(−)-MTPA-Cl (**S6**)[7] (0.0278, 0.110 mmol) in CH_2Cl_2 (0.5 mL), anhydrous NEt_3 (0.0234 mL, 0.165 mmol) and DMAP

(0.000700 g, 0.00573 mmol). The resulting clear and colorless solution was stirred at room temperature for 5 h after which time TLC analysis indicated complete consumption of the alcohol starting material. The reaction was filtered through a small pad of Florisil (washing with 30% Et_2O/ hexanes) and concentrated. ^1H NMR analysis of the crude reaction mixture showed a 1: 1 mixture of diastereomers.

Racemic standard (entry 1) (500 MHz, $CDCl_3$):

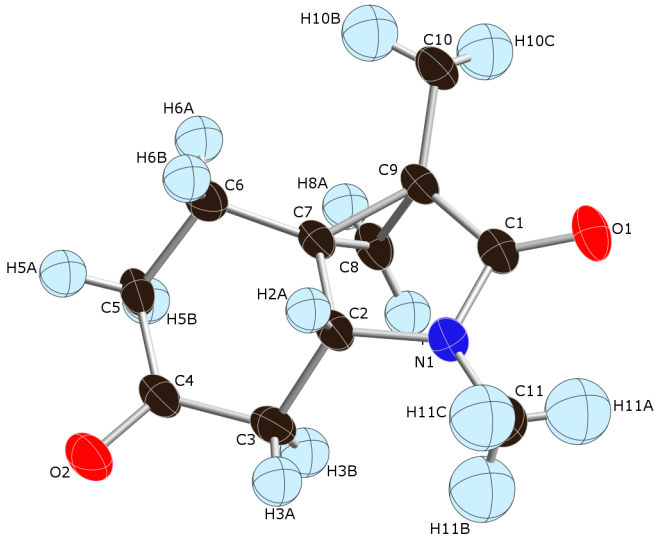


Enantioenriched ester derivatives. a) *t*-butyl derivative (entry 2, 700 MHz, $CDCl_3$); (b) *t*-butyl derivative (entry 3, 700 MHz, $CDCl_3$); (c) succinimide derivative (entry 4, 700 MHz, $CDCl_3$); (d) pentachlorophenyl derivative (entry 5, 600 MHz, $CDCl_3$); pentafluorophenyl derivative (entry 6, 600 MHz, $CDCl_3$).



X-ray structural information for **14**.

ORTEP Plot:



A specimen of $C_{11}H_{15}NO_2$ was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a Bruker Apex II CCD system equipped with a Cu IMuS micro-focus (λ = 1.54178 Å).
The total exposure time was 7.31 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 6297 reflections to a maximum θ angle of 68.22° (0.83 Å resolution), of which 1762 were independent (average redundancy 3.574, completeness = 96.9%, R_{int} = 3.94%) and 1639 (93.02%) were greater than $2\sigma(F^2)$. The final cell constants of a = 6.8166(4) Å, b = 10.8726(6) Å, c = 13.4701(9) Å, β = 91.661(4)°, volume = 997.91(10) $Å^3$, are based upon the refinement of the XYZ-centroids of 3600 reflections above 20 σ(I) with 10.45° < 2θ < 136.6°. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.734. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.7200 and 0.8980.

The final anisotropic full-matrix least-squares refinement on F^2 with 127 variables converged at R1 = 11.09%, for the observed data and wR2 = 28.61% for all data. The goodness-of-fit was 3.255. The largest peak in the final difference electron density synthesis was 0.650 $e^-/Å^3$ and the largest hole was -0.432 $e^-/Å^3$ with an RMS deviation of 0.126 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.286 g/cm^3 and F(000), 416 e^-.

Table 1. Sample and crystal data for Ketone 14.

Identification code	Ketone 14	
Chemical formula	$C_{11}H_{15}NO_2$	
Formula weight	193.24	
Temperature	150(2) K	
Wavelength	1.54178 Å	
Crystal system	monoclinic	
Space group	P 1 21/n 1	
Unit cell dimensions	a = 6.8166(4) Å	α = 90°
	b = 10.8726(6) Å	β = 91.661(4)°
	c = 13.4701(9) Å	γ = 90°
Volume	997.91(10) $Å^3$	
Z	4	
Density (calculated)	1.286 g/cm^3	
Absorption coefficient	0.713 mm^{-1}	
F(000)	416	

Table 2. Data collection and structure refinement for Ketone 14.

Diffractometer	Bruker Apex II CCD
Radiation source	IMuS micro-focus, Cu
Theta range for data collection	5.23 to 68.22°
Index ranges	-7<=h<=8, -12<=k<=13, -15<=l<=16
Reflections collected	6297
Independent reflections	1762 [R(int) = 0.0394]
Coverage of independent reflections	96.9%
Absorption correction	multi-scan
Max. and min. transmission	0.8980 and 0.7200
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-2013 (Sheldrick, 2013)
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	1762 / 0 / 127
Goodness-of-fit on F^2	3.255
Final R indices	1639 data; I>2σ(I) R1 = 0.1109, wR2 = 0.2851
	all data R1 = 0.1135, wR2 = 0.2861
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0680P)^2]$ where $P=(F_o^2+2F_c^2)/3$

Largest diff. peak and hole	0.650 and -0.432 eÅ^{-3}
R.M.S. deviation from mean	0.126 eÅ^{-3}

Table 3. Atomic coordinates and equivalent isotropic atomic displacement parameters (Å^2) for Ketone 14.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
O1	0.0224(4)	0.9844(2)	0.7226(2)	0.0381(7)
O2	0.9272(4)	0.6922(3)	0.6518(2)	0.0512(9)
N1	0.3009(4)	0.9050(3)	0.6553(2)	0.0315(7)
C1	0.1848(5)	0.9371(3)	0.7317(2)	0.0292(8)
C2	0.4996(5)	0.8724(3)	0.6886(2)	0.0291(8)
C3	0.5962(6)	0.7631(3)	0.6392(2)	0.0348(9)
C4	0.7842(5)	0.7290(3)	0.6951(3)	0.0331(9)
C5	0.7852(5)	0.7314(3)	0.8077(3)	0.0319(8)
C6	0.6745(5)	0.8406(3)	0.8527(2)	0.0324(8)
C7	0.4814(5)	0.8480(3)	0.7981(2)	0.0263(8)
C8	0.3199(5)	0.7594(3)	0.8246(3)	0.0302(8)
C9	0.2853(5)	0.8985(3)	0.8271(2)	0.0270(8)
C10	0.2416(6)	0.9656(3)	0.9212(3)	0.0361(9)
C11	0.2457(7)	0.9283(4)	0.5531(3)	0.0498(11)

Table 4. Bond lengths (Å) for Ketone 14.

O1-C1	1.224(4)	O2-C4	1.218(5)
N1-C1	1.362(4)	N1-C11	1.439(5)
N1-C2	1.459(5)	C1-C9	1.499(5)
C2-C7	1.507(4)	C2-C3	1.521(4)
C2-H2A	1.0	C3-C4	1.513(5)
C3-H3A	0.99	C3-H3B	0.99
C4-C5	1.516(5)	C5-C6	1.540(4)
C5-H5A	0.99	C5-H5B	0.99
C6-C7	1.491(5)	C6-H6A	0.99
C6-H6B	0.99	C7-C8	1.514(4)
C7-C9	1.507(4)	C8-C9	1.531(4)

C8-H8A	0.99	C8-H8B	0.99
C9-C10	1.500(4)	C10-H10A	0.98
C10-H10B	0.98	C10-H10C	0.98
C11-H11A	0.98	C11-H11B	0.98
C11-H11C	0.98		

Table 5. Bond angles (°) for Ketone 14.

C1-N1-C11	122.5(3)	C1-N1-C2	112.6(3)
C11-N1-C2	123.5(3)	O1-C1-N1	125.2(3)
O1-C1-C9	126.4(3)	N1-C1-C9	108.4(3)
N1-C2-C7	104.0(2)	N1-C2-C3	117.7(3)
C7-C2-C3	109.8(3)	N1-C2-H2A	108.3
C7-C2-H2A	108.3	C3-C2-H2A	108.3
C2-C3-C4	110.1(3)	C2-C3-H3A	109.6
C4-C3-H3A	109.6	C2-C3-H3B	109.6
C4-C3-H3B	109.6	H3A-C3-H3B	108.1
O2-C4-C5	120.3(4)	O2-C4-C3	121.3(3)
C5-C4-C3	118.2(3)	C4-C5-C6	114.7(3)
C4-C5-H5A	108.6	C6-C5-H5A	108.6
C4-C5-H5B	108.6	C6-C5-H5B	108.6
H5A-C5-H5B	107.6	C7-C6-C5	106.4(3)
C7-C6-H6A	110.4	C5-C6-H6A	110.4
C7-C6-H6B	110.4	C5-C6-H6B	110.4
H6A-C6-H6B	108.6	C6-C7-C8	119.1(3)
C6-C7-C2	113.3(3)	C8-C7-C2	115.1(3)
C6-C7-C9	132.0(3)	C8-C7-C9	60.9(2)
C2-C7-C9	106.8(3)	C7-C8-C9	59.34(19)
C7-C8-H8A	117.8	C9-C8-H8A	117.8
C7-C8-H8B	117.8	C9-C8-H8B	117.8
H8A-C8-H8B	115.0	C1-C9-C10	119.4(3)
C1-C9-C7	105.4(2)	C10-C9-C7	126.6(3)
C1-C9-C8	109.0(3)	C10-C9-C8	122.2(3)
C7-C9-C8	59.8(2)	C9-C10-H10A	109.5
C9-C10-H10B	109.5	H10A-C10-H10B	109.5

C9-C10-H10C	109.5	H10A-C10-H10C	109.5
H10B-C10-H10C	109.5	N1-C11-H11A	109.5
N1-C11-H11B	109.5	H11A-C11-H11B	109.5
N1-C11-H11C	109.5	H11A-C11-H11C	109.5
H11B-C11-H11C	109.5		

Table 6. Anisotropic atomic displacement parameters (Å^2) for Ketone 14.

The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O1	0.0285(13)	0.0263(13)	0.0595(16)	0.0047(9)	0.0047(11)	0.0067(9)
O2	0.0309(16)	0.0590(18)	0.0644(18)	-0.0273(14)	0.0112(13)	0.0050(12)
N1	0.0289(16)	0.0321(14)	0.0336(14)	0.0020(10)	0.0033(11)	0.0035(11)
C1	0.0275(17)	0.0176(14)	0.0429(18)	-0.0003(11)	0.0059(13)	-0.0020(12)
C2	0.0250(17)	0.0277(16)	0.0350(16)	-0.0030(11)	0.0059(12)	0.0020(12)
C3	0.035(2)	0.0364(18)	0.0336(16)	-0.0076(12)	0.0091(14)	0.0029(13)
C4	0.0255(18)	0.0251(15)	0.0491(19)	-0.0113(12)	0.0095(14)	-0.0026(12)
C5	0.0208(17)	0.0279(16)	0.0471(19)	-0.0030(12)	0.0025(13)	0.0029(12)
C6	0.0275(18)	0.0332(17)	0.0369(16)	-0.0056(12)	0.0051(13)	-0.0010(12)
C7	0.0227(17)	0.0230(15)	0.0336(15)	-0.0033(10)	0.0064(12)	0.0015(11)
C8	0.0236(17)	0.0238(16)	0.0437(17)	0.0017(11)	0.0068(13)	-0.0003(11)
C9	0.0232(17)	0.0240(15)	0.0341(16)	-0.0016(11)	0.0076(12)	0.0021(11)
C10	0.0364(19)	0.0353(18)	0.0371(17)	-0.0047(13)	0.0118(14)	0.0058(13)
C11	0.050(3)	0.059(3)	0.040(2)	0.0046(16)	0.0004(17)	0.0117(19)

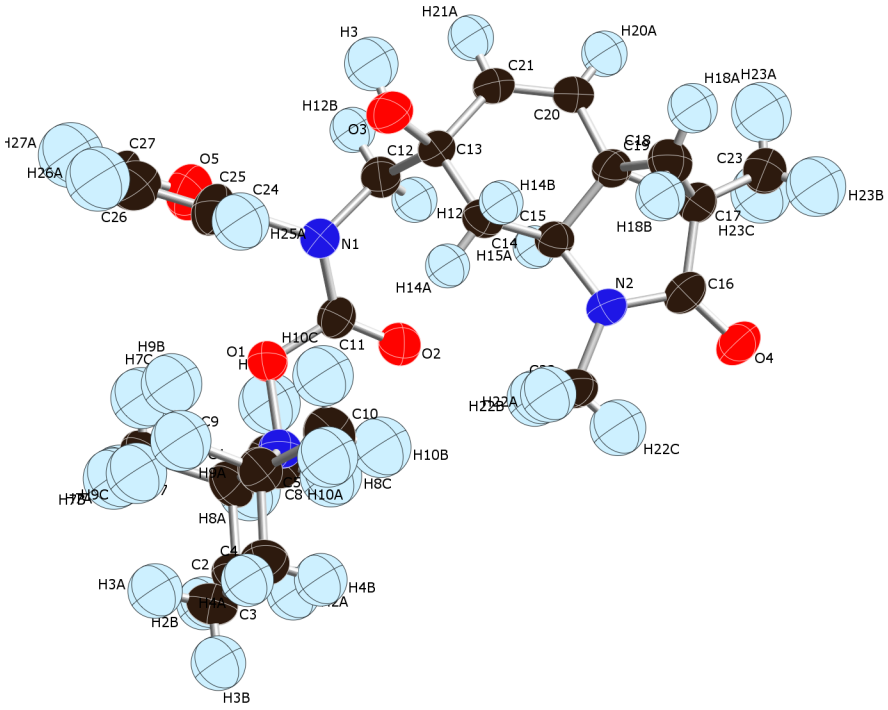
Table 7. Hydrogen atomic coordinates and isotropic atomic displacement parameters (Å^2) for Ketone 14.

	x/a	y/b	z/c	U(eq)
H2A	0.5857	0.9460	0.6804	0.035
H3A	0.6255	0.7840	0.5697	0.042
H3B	0.5053	0.6921	0.6384	0.042
H5A	0.9231	0.7335	0.8328	0.038
H5B	0.7259	0.6540	0.8314	0.038
H6A	0.6552	0.8270	0.9244	0.039
H6B	0.7494	0.9178	0.8444	0.039

	x/a	y/b	z/c	U(eq)
H8A	0.3327	0.7155	0.8889	0.036
H8B	0.2555	0.7118	0.7702	0.036
H10A	0.2236	1.0533	0.9068	0.054
H10B	0.3512	0.9550	0.9691	0.054
H10C	0.1215	0.9324	0.9491	0.054
H11A	0.1059	0.9489	0.5480	0.075
H11B	0.2707	0.8546	0.5134	0.075
H11C	0.3231	0.9971	0.5282	0.075

X-ray structural information for **16**.

ORTEP Plot:



A specimen of $C_{26}H_{37}N_3O_5$, approximate dimensions 0.070 mm x 0.160 mm x 0.190 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a Bruker Apex II CCD system equipped with a Cu IMuS micro-focus (λ = 1.54178 Å).

Table 1: Data collection details for allylic alcohol 16.

Axis	dx/mm	2θ/°	ω/°	φ/°	χ/°	Width/°	Frames	Time/s	Wavelength/Å	Voltage/kV	Current/mA	Temperature/K
Omega	40.174	102.90	-81.10	-144.95	54.65	0.50	376	10.00	1.54184	45	0.7	230
Omega	40.174	103.19	-80.81	-76.57	54.65	0.50	376	10.00	1.54184	45	0.7	230
Omega	40.174	-57.76	-241.76	-117.09	54.65	0.50	376	10.00	1.54184	45	0.7	230
Omeg	40.17	103.3	-	-	54.6	0.50	376	10.00	1.54184	45	0.7	230

Axis	dx/mm	2θ/°	ω/°	φ/°	χ/°	Width/°	Frames	Time/s	Wavelength/Å	Voltage/kV	Current/mA	Temperature/K
a	4	7	80.63	246.29	5							
Phi	40.174	43.16	-140.84	-60.00	54.65	0.50	416	10.00	1.54184	45	0.7	230
Omega	40.174	105.18	-78.82	7.25	54.65	0.50	376	10.00	1.54184	45	0.7	230
Phi	40.174	-18.13	-14.13	-103.50	54.65	0.50	446	10.00	1.54184	45	0.7	230
Omega	40.174	-104.39	-288.39	-115.56	54.65	0.50	376	10.00	1.54184	45	0.7	230
Omega	40.174	-66.41	-117.59	110.67	54.65	0.50	376	10.00	1.54184	45	0.7	230

A total of 3494 frames were collected. The total exposure time was 9.71 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 14241 reflections to a maximum θ angle of 68.50° (0.83 Å resolution), of which 4735 were independent (average redundancy 3.008, completeness = 98.8%, R_{int} = 10.06%, R_{sig} = 12.98%) and 2672 (56.43%) were greater than $2\sigma(F^2)$. The final cell constants of a = 9.0643(13) Å, b = 19.525(3) Å, c = 15.1889(18) Å, β = 104.307(11)°, volume = 2604.8(6) $Å^3$, are based upon the refinement of the XYZ-centroids of 1486 reflections above 20 σ(I) with 7.522° < 2θ < 134.2°. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.600. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.8820 and 0.9540.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 1 21/c 1, with Z = 4 for the formula unit, $C_{26}H_{37}N_3O_5$. The final anisotropic full-matrix least-squares refinement on F^2 with 317 variables converged at R1 = 9.22%, for the observed data and wR2 = 22.52% for all data. The goodness-of-fit was 1.152. The largest peak in the final difference electron density synthesis was 0.544 $e^-/Å^3$ and the largest hole was -0.279 $e^-/Å^3$ with an RMS deviation of 0.113 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.203 g/cm^3 and F(000), 1016 e^-.

Table 2. Sample and crystal data for allylic alcohol 16.

Identification code	Allylic alcohol 16

Chemical formula	$C_{26}H_{37}N_3O_5$	
Formula weight	471.58 g/mol	
Temperature	229(2) K	
Wavelength	1.54178 Å	
Crystal size	0.070 x 0.160 x 0.190 mm	
Crystal system	monoclinic	
Space group	P 1 21/c 1	
Unit cell dimensions	a = 9.0643(13) Å	α = 90°
	b = 19.525(3) Å	β = 104.307(11)°
	c = 15.1889(18) Å	γ = 90°
Volume	2604.8(6) $Å^3$	
Z	4	
Density (calculated)	1.203 g/cm^3	
Absorption coefficient	0.676 mm^{-1}	
F(000)	1016	

Table 3. Data collection and structure refinement for allylic alcohol 16.

Diffractometer	Bruker Apex II CCD
Radiation source	IMuS micro-focus, Cu
Theta range for data collection	3.76 to 68.50°
Index ranges	-10<=h<=10, -23<=k<=22, -16<=l<=18
Reflections collected	14241
Independent reflections	4735 [R(int) = 0.1006]
Coverage of independent reflections	98.8%
Absorption correction	multi-scan
Max. and min. transmission	0.9540 and 0.8820
Structure solution technique	direct methods
Structure solution program	SHELXL-2014/6 (Sheldrick, 2014)
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-2014/6 (Sheldrick, 2014)
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	4735 / 0 / 317
Goodness-of-fit on F^2	1.152
Δ/σ_{max}	0.444

Final R indices	2672 data; I>2σ(I)	R1 = 0.0922, wR2 = 0.1973
	all data	R1 = 0.1407, wR2 = 0.2252
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0680P)^2]$ where $P=(F_o^2+2F_c^2)/3$	
Largest diff. peak and hole	0.544 and -0.279 eÅ^{-3}	
R.M.S. deviation from mean	0.113 eÅ^{-3}	

Table 4. Atomic coordinates and equivalent isotropic atomic displacement parameters (Å^2) for allylic alcohol 16.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
O1	0.3718(3)	0.71375(13)	0.52526(16)	0.0516(6)
N1	0.5116(3)	0.64695(15)	0.63095(19)	0.0496(7)
C1	0.2265(5)	0.81229(19)	0.4733(3)	0.0568(9)
O2	0.2715(3)	0.67526(13)	0.64034(17)	0.0552(6)
N2	0.1017(3)	0.51393(16)	0.7153(2)	0.0502(7)
C2	0.0738(5)	0.8347(2)	0.4110(3)	0.0678(11)
O3	0.6186(3)	0.50353(15)	0.67015(19)	0.0611(7)
C3	0.0408(5)	0.8023(2)	0.3182(3)	0.0720(12)
O4	0.9160(3)	0.48706(15)	0.78893(18)	0.0625(7)
C4	0.0416(5)	0.7250(2)	0.3283(3)	0.0668(11)
O5	0.7218(4)	0.7042(2)	0.6037(3)	0.0996(12)
C5	0.1922(4)	0.69733(19)	0.3868(3)	0.0559(9)
N3	0.2205(3)	0.73570(14)	0.47447(19)	0.0482(7)
C7	0.3604(5)	0.8431(2)	0.4429(3)	0.0720(12)
C8	0.2333(6)	0.8356(2)	0.5698(3)	0.0736(12)
C9	0.3164(5)	0.7003(2)	0.3358(3)	0.0704(11)
C10	0.1692(5)	0.6225(2)	0.4119(3)	0.0710(12)
C11	0.3728(4)	0.67788(17)	0.6028(2)	0.0458(8)
C12	0.5498(4)	0.61392(19)	0.7211(2)	0.0490(8)
C13	0.5255(4)	0.53573(18)	0.7206(2)	0.0454(8)
C14	0.3612(4)	0.51508(18)	0.6747(2)	0.0466(8)
C15	0.2649(4)	0.52448(17)	0.7410(2)	0.0439(8)

	x/a	y/b	z/c	U(eq)
C16	0.0485(4)	0.48754(19)	0.7840(2)	0.0496(9)
C17	0.1795(4)	0.45581(19)	0.8527(2)	0.0504(8)
C18	0.2570(5)	0.40365(19)	0.8060(3)	0.0590(10)
C19	0.3184(4)	0.47538(17)	0.8191(2)	0.0463(8)
C20	0.4791(4)	0.48566(19)	0.8650(2)	0.0496(8)
C21	0.5722(4)	0.51259(19)	0.8194(2)	0.0501(9)
C22	0.0055(4)	0.5512(2)	0.6400(3)	0.0603(10)
C23	0.1694(5)	0.4478(2)	0.9491(3)	0.0688(11)
C24	0.6214(4)	0.6528(2)	0.5824(3)	0.0621(11)
C25	0.6469(5)	0.6171(3)	0.5111(3)	0.0795(13)
C26	0.7654(6)	0.6461(4)	0.4848(4)	0.0994(18)
C27	0.8131(5)	0.6977(4)	0.5412(4)	0.102(2)

Table 5. Bond lengths (Å) for allylic alcohol 16.

O1-C11	1.368(4)	O1-N3	1.462(4)
N1-C11	1.366(5)	N1-C24	1.383(5)
N1-C12	1.476(4)	C1-N3	1.497(5)
C1-C8	1.521(6)	C1-C7	1.525(6)
C1-C2	1.534(6)	O2-C11	1.196(4)
N2-C16	1.354(5)	N2-C15	1.448(4)
N2-C22	1.452(5)	C2-C3	1.505(6)
C2-H2A	0.98	C2-H2B	0.98
O3-C13	1.419(4)	O3-H3	0.87(5)
C3-C4	1.517(6)	C3-H3A	0.98
C3-H3B	0.98	O4-C16	1.222(4)
C4-C5	1.531(6)	C4-H4A	0.98
C4-H4B	0.98	O5-C24	1.339(6)
O5-C27	1.412(7)	C5-N3	1.494(5)
C5-C9	1.517(6)	C5-C10	1.538(6)
C7-H7A	0.97	C7-H7B	0.97
C7-H7C	0.97	C8-H8A	0.97
C8-H8B	0.97	C8-H8C	0.97
C9-H9A	0.97	C9-H9B	0.97

C9-H9C	0.97	C10-H10A	0.97
C10-H10B	0.97	C10-H10C	0.97
C12-C13	1.542(5)	C12-H12A	0.98
C12-H12B	0.98	C13-C21	1.524(5)
C13-C14	1.534(5)	C14-C15	1.497(5)
C14-H14A	0.98	C14-H14B	0.98
C15-C19	1.509(5)	C15-H15A	0.99
C16-C17	1.506(5)	C17-C23	1.497(5)
C17-C18	1.509(5)	C17-C19	1.519(5)
C18-C19	1.502(5)	C18-H18A	0.98
C18-H18B	0.98	C19-C20	1.465(5)
C20-C21	1.326(5)	C20-H20A	0.94
C21-H21A	0.94	C22-H22A	0.97
C22-H22B	0.97	C22-H22C	0.97
C23-H23A	0.97	C23-H23B	0.97
C23-H23C	0.97	C24-C25	1.354(7)
C25-C26	1.358(7)	C25-H25A	0.94
C26-C27	1.324(9)	C26-H26A	0.94
C27-H27A	0.94		

Table 6. Bond angles (°) for allylic alcohol 16.

C11-O1-N3	114.2(2)	C11-N1-C24	121.7(3)
C11-N1-C12	118.1(3)	C24-N1-C12	119.8(3)
N3-C1-C8	106.3(3)	N3-C1-C7	115.6(3)
C8-C1-C7	109.1(3)	N3-C1-C2	105.2(3)
C8-C1-C2	109.0(4)	C7-C1-C2	111.4(3)
C16-N2-C15	112.4(3)	C16-N2-C22	122.6(3)
C15-N2-C22	121.0(3)	C3-C2-C1	113.5(4)
C3-C2-H2A	108.9	C1-C2-H2A	108.9
C3-C2-H2B	108.9	C1-C2-H2B	108.9
H2A-C2-H2B	107.7	C13-O3-H3	120.(3)
C2-C3-C4	109.2(3)	C2-C3-H3A	109.9
C4-C3-H3A	109.8	C2-C3-H3B	109.8
C4-C3-H3B	109.8	H3A-C3-H3B	108.3

C3-C4-C5	113.0(3)	C3-C4-H4A	109.0
C5-C4-H4A	109.0	C3-C4-H4B	109.0
C5-C4-H4B	109.0	H4A-C4-H4B	107.8
C24-O5-C27	104.2(5)	N3-C5-C9	116.8(3)
N3-C5-C4	105.8(3)	C9-C5-C4	111.0(4)
N3-C5-C10	105.0(3)	C9-C5-C10	109.0(3)
C4-C5-C10	108.8(3)	O1-N3-C1	105.5(2)
O1-N3-C5	104.8(3)	C1-N3-C5	119.3(3)
C1-C7-H7A	109.5	C1-C7-H7B	109.5
H7A-C7-H7B	109.5	C1-C7-H7C	109.5
H7A-C7-H7C	109.5	H7B-C7-H7C	109.5
C1-C8-H8A	109.5	C1-C8-H8B	109.5
H8A-C8-H8B	109.5	C1-C8-H8C	109.5
H8A-C8-H8C	109.5	H8B-C8-H8C	109.5
C5-C9-H9A	109.5	C5-C9-H9B	109.5
H9A-C9-H9B	109.5	C5-C9-H9C	109.5
H9A-C9-H9C	109.5	H9B-C9-H9C	109.5
C5-C10-H10A	109.5	C5-C10-H10B	109.5
H10A-C10-H10B	109.5	C5-C10-H10C	109.5
H10A-C10-H10C	109.5	H10B-C10-H10C	109.5
O2-C11-O1	126.2(3)	O2-C11-N1	126.0(3)
O1-C11-N1	107.8(3)	N1-C12-C13	115.3(3)
N1-C12-H12A	108.5	C13-C12-H12A	108.5
N1-C12-H12B	108.5	C13-C12-H12B	108.5
H12A-C12-H12B	107.5	O3-C13-C21	110.0(3)
O3-C13-C14	106.2(3)	C21-C13-C14	111.8(3)
O3-C13-C12	109.8(3)	C21-C13-C12	106.5(3)
C14-C13-C12	112.6(3)	C15-C14-C13	108.9(3)
C15-C14-H14A	109.9	C13-C14-H14A	109.9
C15-C14-H14B	109.9	C13-C14-H14B	109.9
H14A-C14-H14B	108.3	N2-C15-C14	121.9(3)
N2-C15-C19	103.2(3)	C14-C15-C19	108.9(3)
N2-C15-H15A	107.4	C14-C15-H15A	107.4
C19-C15-H15A	107.4	O4-C16-N2	126.3(3)

O4-C16-C17	125.0(3)	N2-C16-C17	108.7(3)
C23-C17-C16	119.4(3)	C23-C17-C18	122.5(3)
C16-C17-C18	109.3(3)	C23-C17-C19	127.7(3)
C16-C17-C19	103.9(3)	C18-C17-C19	59.5(2)
C19-C18-C17	60.6(2)	C19-C18-H18A	117.7
C17-C18-H18A	117.7	C19-C18-H18B	117.7
C17-C18-H18B	117.7	H18A-C18-H18B	114.8
C20-C19-C18	118.9(3)	C20-C19-C15	112.1(3)
C18-C19-C15	116.9(3)	C20-C19-C17	133.1(3)
C18-C19-C17	59.9(2)	C15-C19-C17	107.0(3)
C21-C20-C19	119.4(3)	C21-C20-H20A	120.3
C19-C20-H20A	120.3	C20-C21-C13	125.0(3)
C20-C21-H21A	117.5	C13-C21-H21A	117.5
N2-C22-H22A	109.5	N2-C22-H22B	109.5
H22A-C22-H22B	109.5	N2-C22-H22C	109.5
H22A-C22-H22C	109.5	H22B-C22-H22C	109.5
C17-C23-H23A	109.5	C17-C23-H23B	109.5
H23A-C23-H23B	109.5	C17-C23-H23C	109.5
H23A-C23-H23C	109.5	H23B-C23-H23C	109.5
O5-C24-C25	109.8(4)	O5-C24-N1	117.9(4)
C25-C24-N1	132.2(4)	C26-C25-C24	108.9(6)
C26-C25-H25A	125.5	C24-C25-H25A	125.5
C27-C26-C25	106.4(5)	C27-C26-H26A	126.8
C25-C26-H26A	126.8	C26-C27-O5	110.5(4)
C26-C27-H27A	124.7	O5-C27-H27A	124.7

Table 7. Anisotropic atomic displacement parameters ($Å^2$) for allylic alcohol 16.

The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O1	0.0494(13)	0.0528(15)	0.0509(14)	0.0085(10)	0.0090(11)	0.0004(11)
N1	0.0460(16)	0.0529(18)	0.0498(17)	0.0047(13)	0.0115(13)	-0.0013(13)
C1	0.072(2)	0.041(2)	0.054(2)	0.0015(15)	0.0103(18)	-0.0050(18)
O2	0.0563(15)	0.0517(15)	0.0601(15)	0.0054(11)	0.0191(12)	0.0061(11)

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
N2	0.0383(14)	0.0550(18)	0.0546(18)	0.0060(13)	0.0064(13)	0.0002(13)
C2	0.075(3)	0.047(2)	0.076(3)	0.0079(18)	0.008(2)	0.0086(19)
O3	0.0521(15)	0.0726(19)	0.0608(17)	0.0011(13)	0.0184(13)	0.0117(13)
C3	0.074(3)	0.071(3)	0.064(3)	0.015(2)	0.004(2)	0.003(2)
O4	0.0415(14)	0.082(2)	0.0639(17)	-0.0004(13)	0.0131(12)	-0.0044(12)
C4	0.069(3)	0.066(3)	0.058(2)	-0.0028(19)	0.0009(19)	-0.007(2)
O5	0.078(2)	0.121(3)	0.094(2)	0.024(2)	0.0105(18)	-0.035(2)
C5	0.063(2)	0.049(2)	0.053(2)	-0.0044(15)	0.0083(17)	-0.0076(17)
N3	0.0487(16)	0.0405(16)	0.0515(17)	0.0004(12)	0.0051(13)	-0.0008(12)
C7	0.083(3)	0.057(3)	0.070(3)	0.0068(19)	0.010(2)	-0.018(2)
C8	0.097(3)	0.048(2)	0.071(3)	-0.0113(18)	0.011(2)	-0.003(2)
C9	0.084(3)	0.072(3)	0.055(2)	-0.0025(19)	0.018(2)	0.002(2)
C10	0.091(3)	0.046(2)	0.073(3)	-0.0142(18)	0.014(2)	-0.009(2)
C11	0.0458(18)	0.0427(19)	0.050(2)	-0.0045(15)	0.0144(16)	-0.0033(15)
C12	0.0461(18)	0.055(2)	0.0433(19)	0.0024(15)	0.0070(15)	-0.0037(16)
C13	0.0383(16)	0.051(2)	0.0484(19)	0.0062(15)	0.0136(14)	0.0035(15)
C14	0.0480(18)	0.0424(18)	0.0468(19)	0.0012(14)	0.0069(15)	0.0019(15)
C15	0.0391(16)	0.0395(18)	0.0505(19)	0.0024(14)	0.0060(14)	-0.0005(14)
C16	0.0396(19)	0.053(2)	0.056(2)	-0.0105(16)	0.0111(15)	-0.0069(15)
C17	0.0439(18)	0.052(2)	0.054(2)	0.0026(15)	0.0101(15)	-0.0044(16)
C18	0.063(2)	0.044(2)	0.067(2)	0.0049(16)	0.0109(18)	-0.0031(17)
C19	0.0432(17)	0.0421(19)	0.053(2)	0.0015(14)	0.0109(15)	0.0011(14)
C20	0.0441(18)	0.054(2)	0.049(2)	0.0071(15)	0.0078(15)	0.0064(16)
C21	0.0385(17)	0.060(2)	0.049(2)	0.0057(16)	0.0053(15)	0.0041(16)
C22	0.0469(19)	0.064(3)	0.062(2)	0.0065(18)	-0.0016(17)	-0.0004(17)
C23	0.061(2)	0.082(3)	0.063(3)	0.013(2)	0.0139(19)	-0.010(2)
C24	0.0425(19)	0.076(3)	0.066(3)	0.027(2)	0.0112(18)	-0.0012(19)
C25	0.071(3)	0.104(4)	0.074(3)	0.019(3)	0.039(2)	0.014(3)
C26	0.072(3)	0.142(6)	0.088(4)	0.028(4)	0.026(3)	0.011(3)
C27	0.048(2)	0.149(6)	0.111(4)	0.057(4)	0.024(3)	-0.023(3)

Table 8. Hydrogen atomic coordinates and isotropic atomic displacement parameters ($Å^2$) for allylic alcohol 16.

	x/a	y/b	z/c	U(eq)
H2A	-0.0081	0.8228	0.4400	0.081
H2B	0.0740	0.8846	0.4042	0.081
H3	0.715(6)	0.498(3)	0.694(3)	0.083(15)
H3A	0.1181	0.8162	0.2867	0.086
H3B	-0.0588	0.8175	0.2821	0.086
H4A	0.0219	0.7040	0.2679	0.08
H4B	-0.0412	0.7115	0.3558	0.08
H7A	0.3642	0.8921	0.4540	0.108
H7B	0.3479	0.8346	0.3786	0.108
H7C	0.4544	0.8223	0.4769	0.108
H8A	0.2218	0.8849	0.5708	0.11
H8B	0.3307	0.8227	0.6094	0.11
H8C	0.1519	0.8139	0.5908	0.11
H9A	0.3026	0.6630	0.2922	0.106
H9B	0.4151	0.6959	0.3785	0.106
H9C	0.3110	0.7437	0.3041	0.106
H10A	0.1255	0.5966	0.3571	0.106
H10B	0.1009	0.6209	0.4520	0.106
H10C	0.2666	0.6027	0.4424	0.106
H12A	0.4879	0.6350	0.7584	0.059
H12B	0.6568	0.6236	0.7504	0.059
H14A	0.3220	0.5435	0.6209	0.056
H14B	0.3581	0.4671	0.6554	0.056
H15A	0.2833	0.5715	0.7658	0.053
H18A	0.3161	0.3674	0.8435	0.071
H18B	0.2043	0.3895	0.7444	0.071
H20A	0.5159	0.4733	0.9263	0.06
H21A	0.6750	0.5178	0.8504	0.06
H22A	0.0136	0.5309	0.5831	0.09
H22B	0.0381	0.5987	0.6422	0.09
H22C	-0.0994	0.5491	0.6443	0.09
H23A	0.2653	0.4304	0.9856	0.103
H23B	0.0883	0.4160	0.9515	0.103

	x/a	y/b	z/c	U(eq)
H23C	0.1481	0.4920	0.9726	0.103
H25A	0.5916	0.5786	0.4843	0.095
H26A	0.8055	0.6322	0.4362	0.119
H27A	0.8963	0.7261	0.5398	0.122

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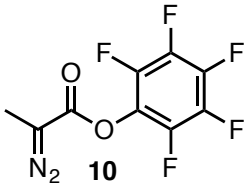
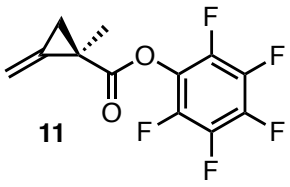
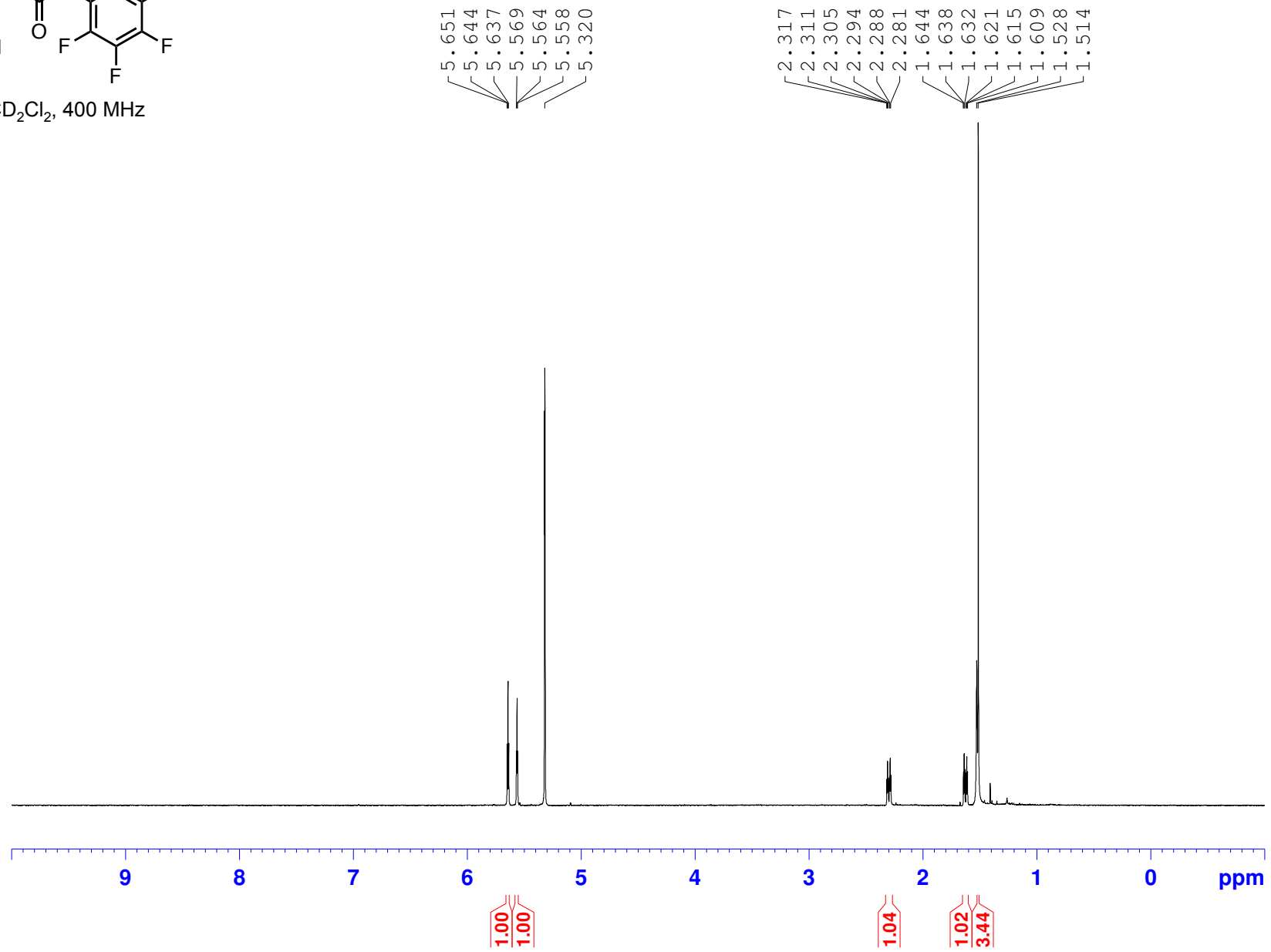


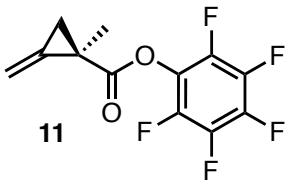
10

C_6D_6, 300 MHz



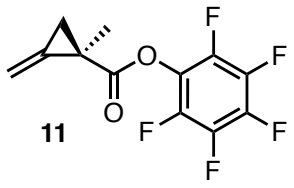
CD_2Cl_2, 400 MHz



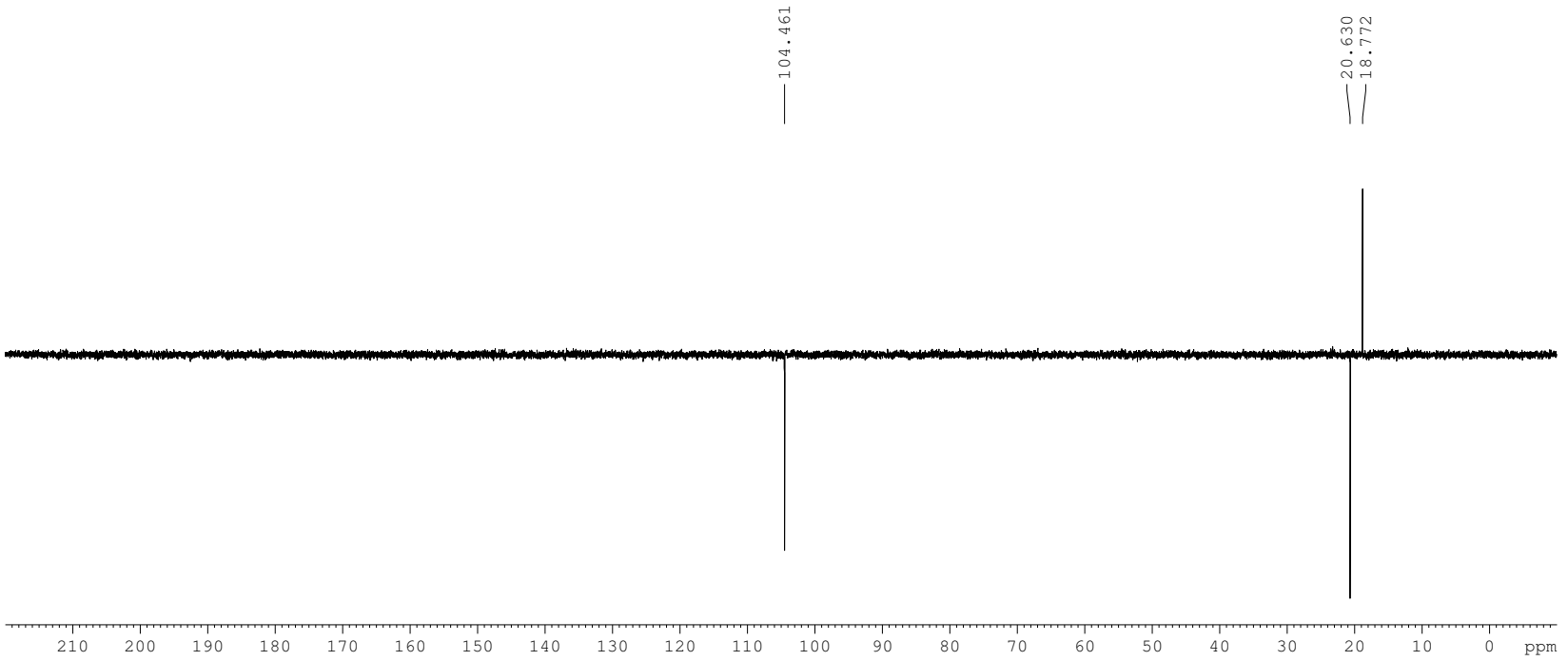


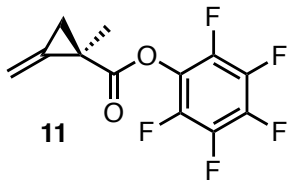
11

CD_2Cl_2, 100 MHz



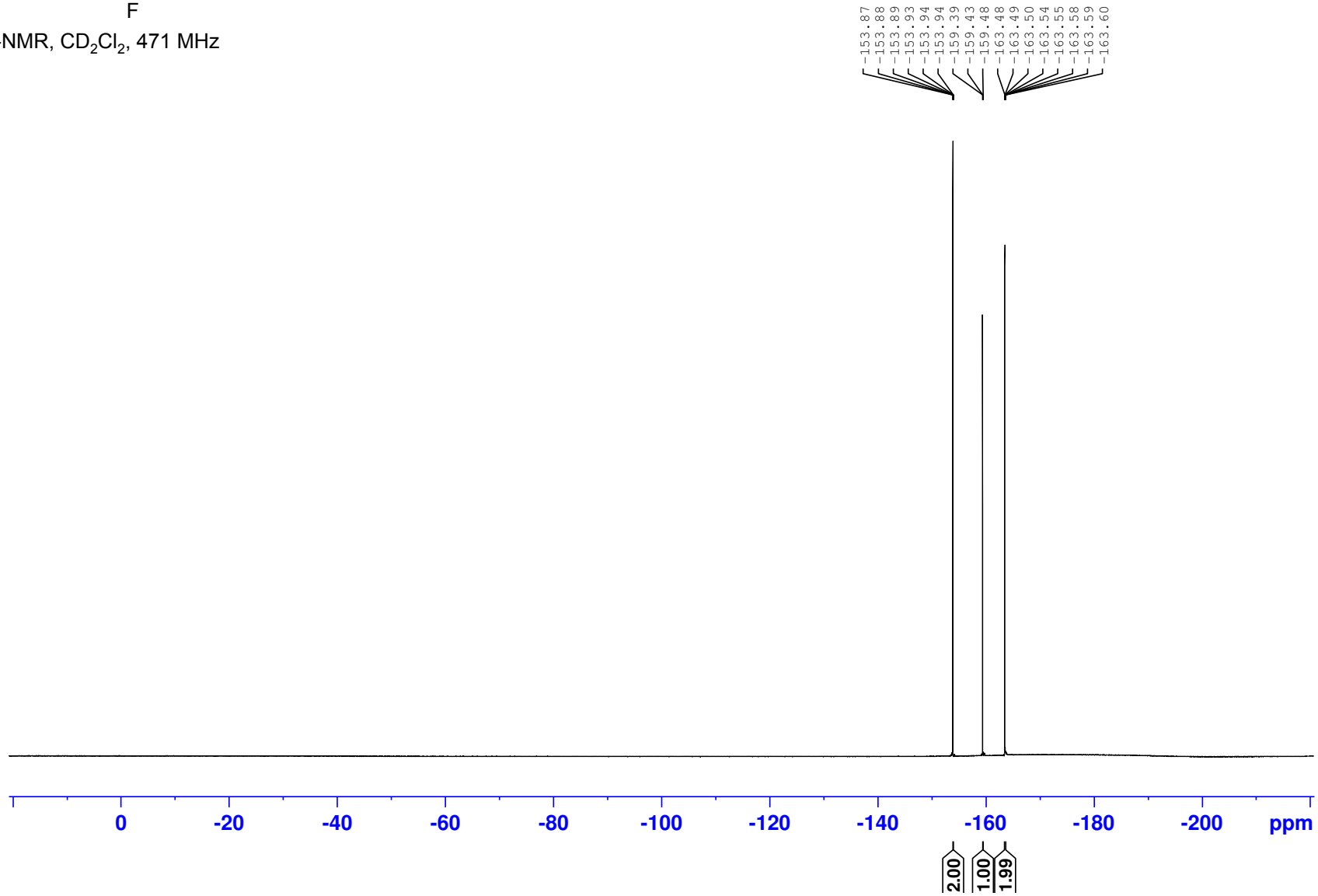
DEPT-135, CD_2Cl_2, 100 MHz

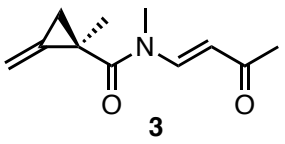




11

^{19}F-NMR, CD_2Cl_2, 471 MHz

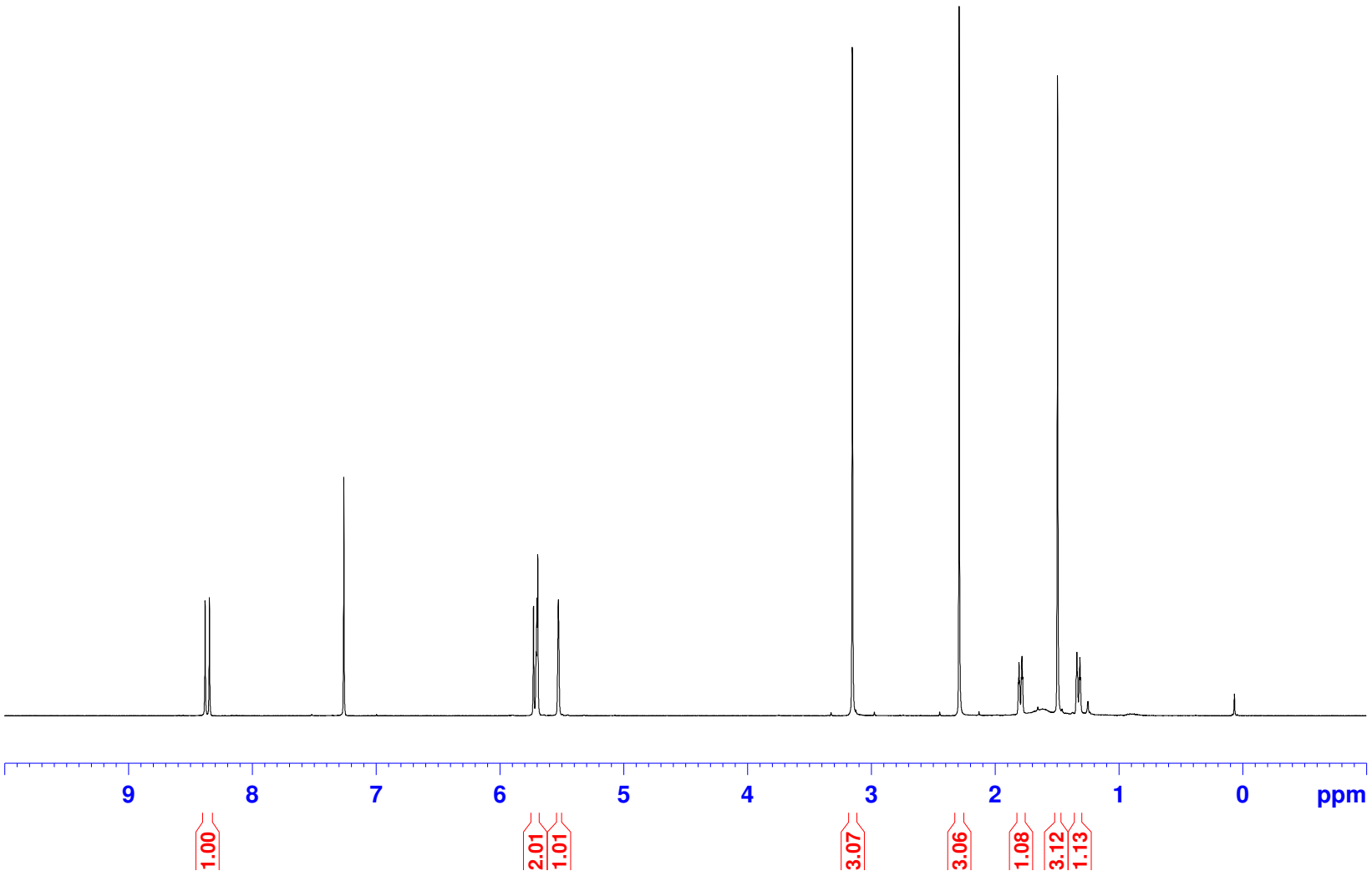


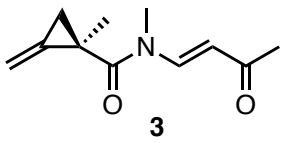


3

$CDCl_3$, 400 MHz

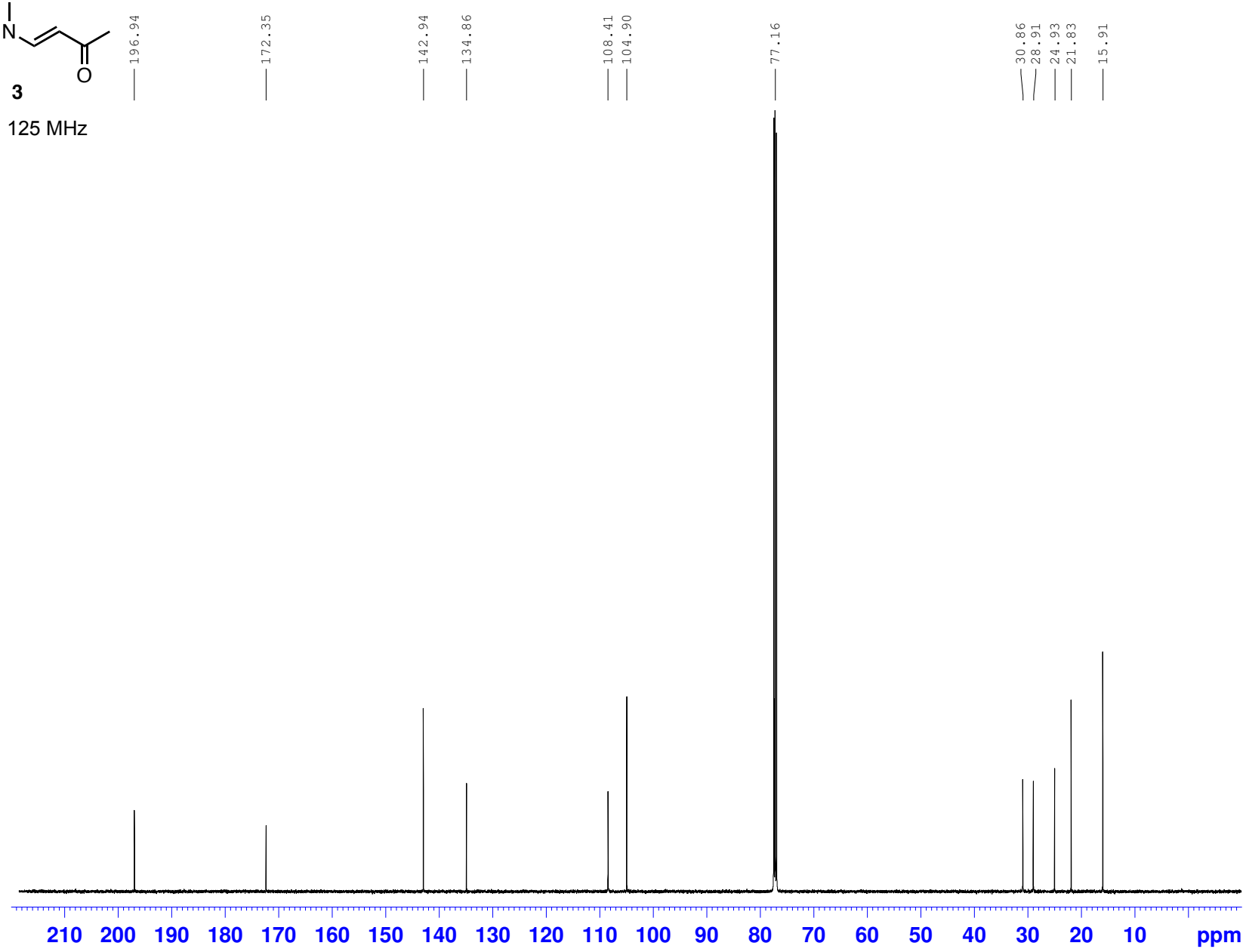
8.380
8.346
7.260
5.728
5.707
5.700
5.693
5.527
3.152
2.289
1.811
1.805
1.800
1.787
1.781
1.776
1.494
1.343
1.338
1.332
1.319
1.314
1.308

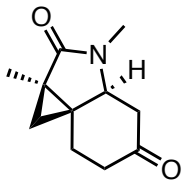




3

$CDCl_3$, 125 MHz

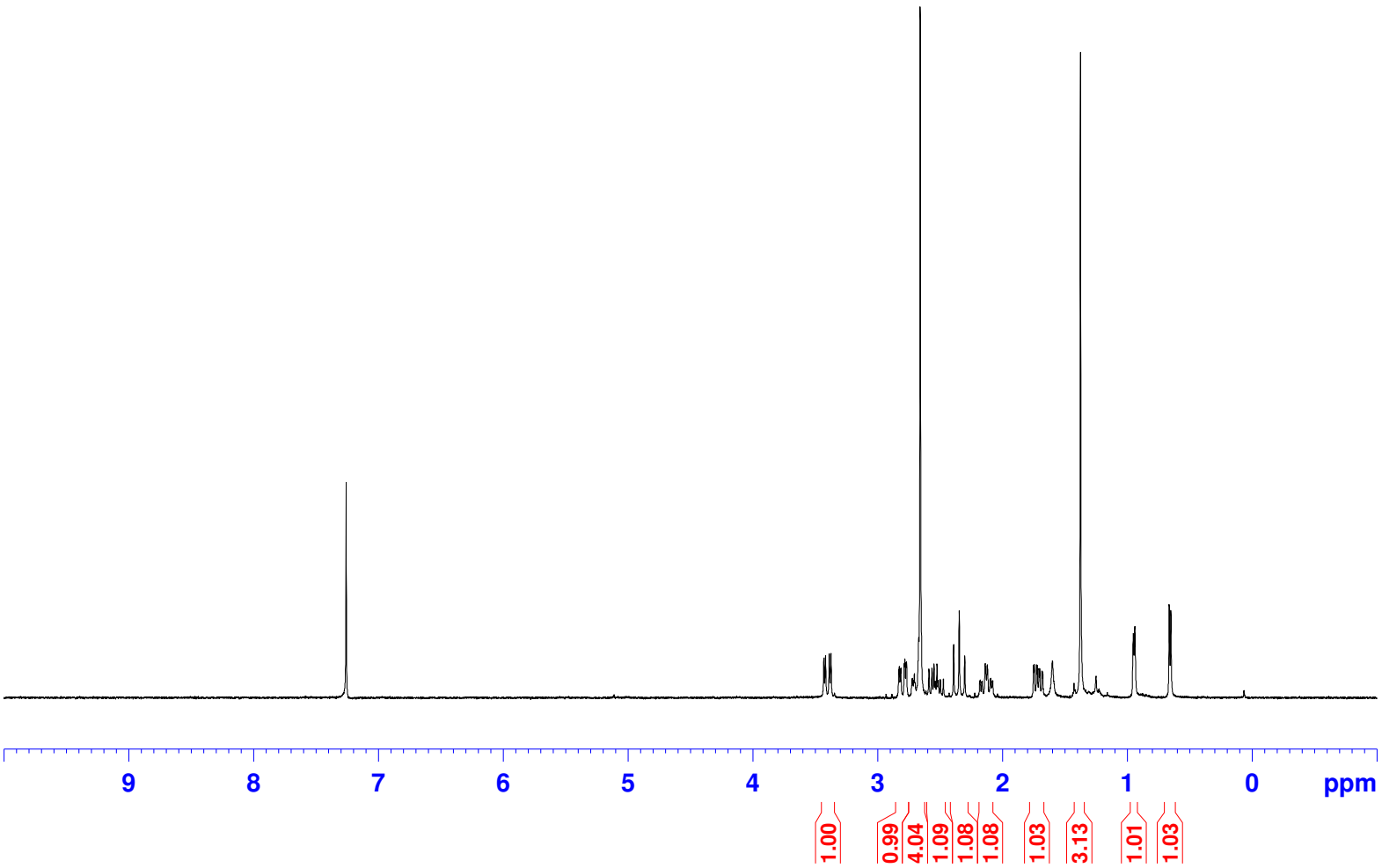


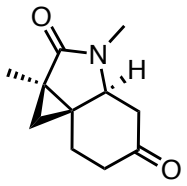


14

$CDCl_3$, 300 MHz

7.260
3.432
3.419
3.389
3.375
2.832
2.828
2.819
2.814
2.787
2.783
2.774
2.769
2.724
2.712
2.707
2.660
2.590
2.566
2.550
2.539
2.526
2.515
2.499
2.474
2.392
2.347
2.303
2.179
2.167
2.162
2.139
2.122
2.100
2.095
2.082
2.078
1.752
1.746
1.728
1.722
1.708
1.702
1.684
1.678
1.601
1.376
0.952
0.940
0.664
0.651





14

$CDCl_3$, 100 MHz

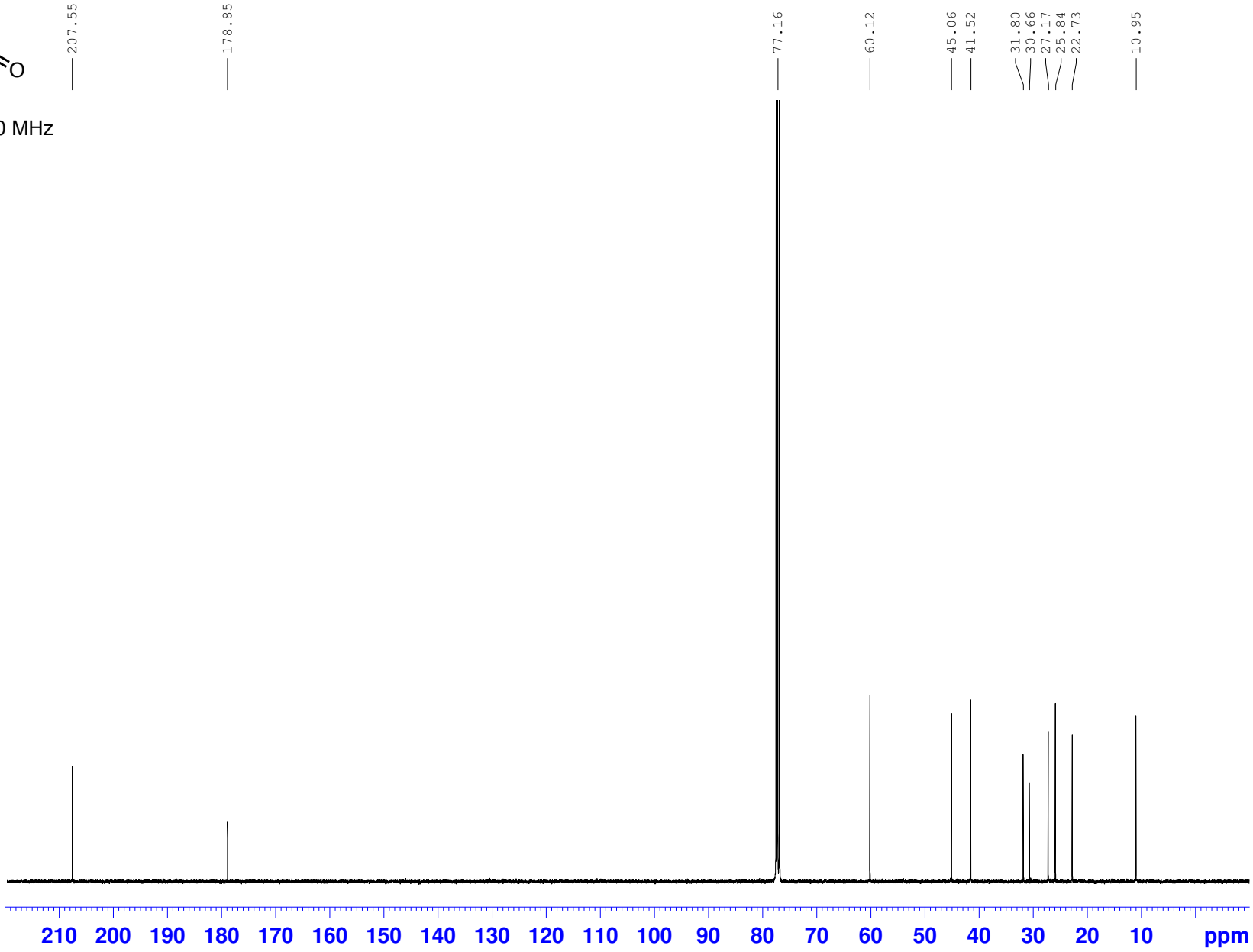


Figure 1. ketone **14**, HSQC ($CDCl_3$, 500 MHz)

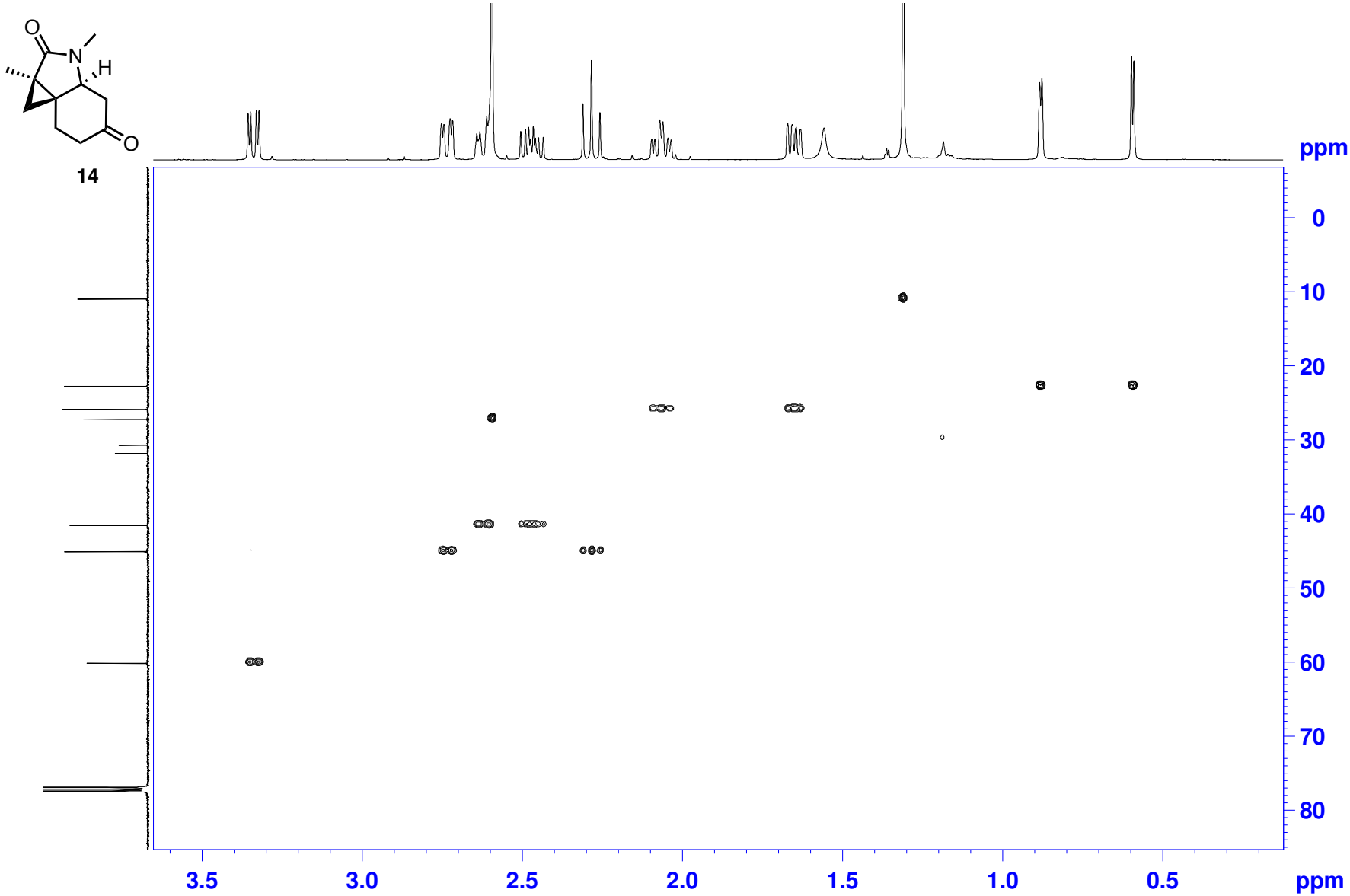
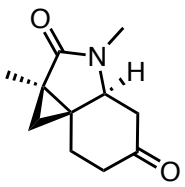
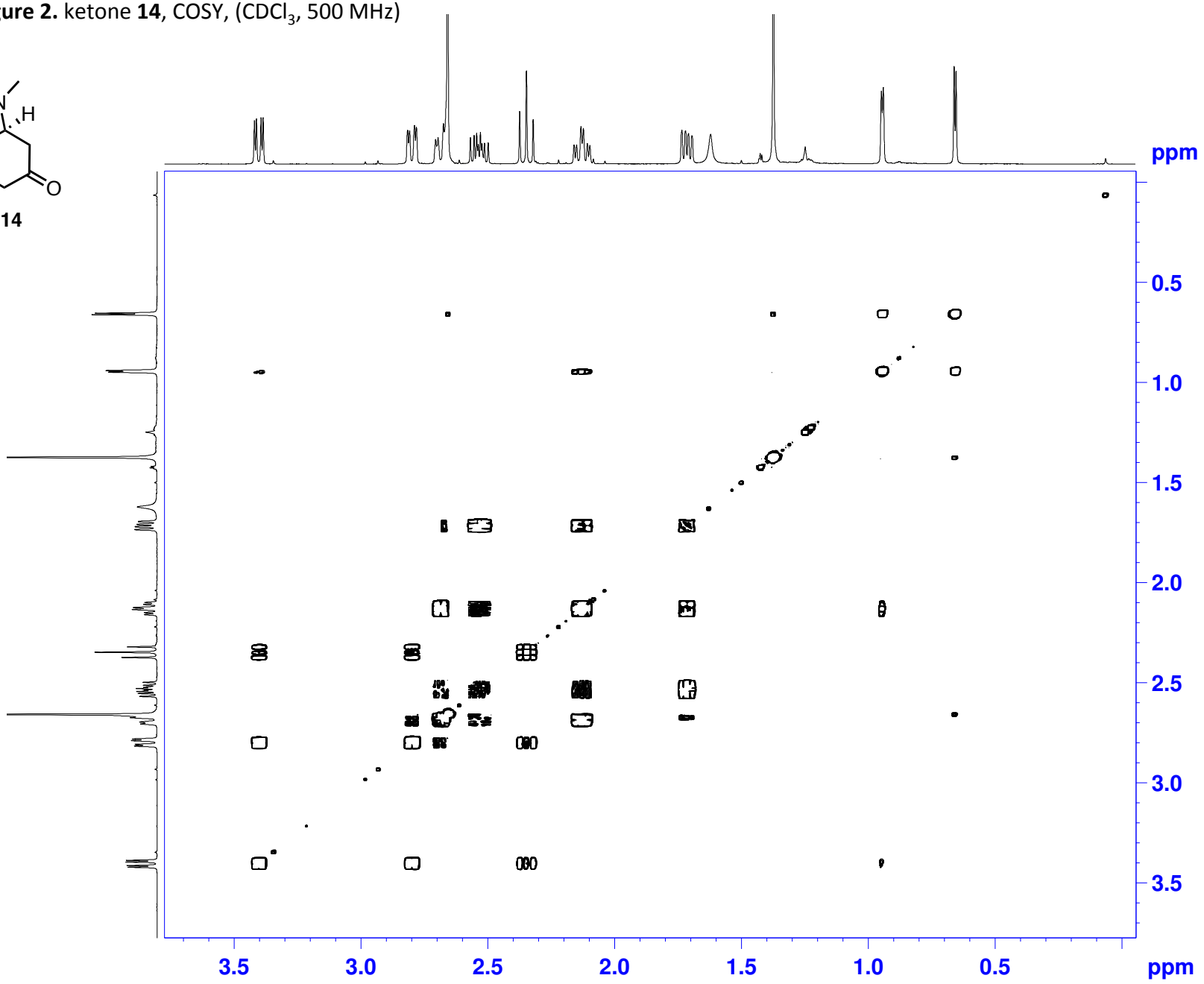
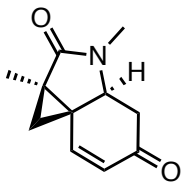


Figure 2. ketone **14**, COSY, ($CDCl_3$, 500 MHz)



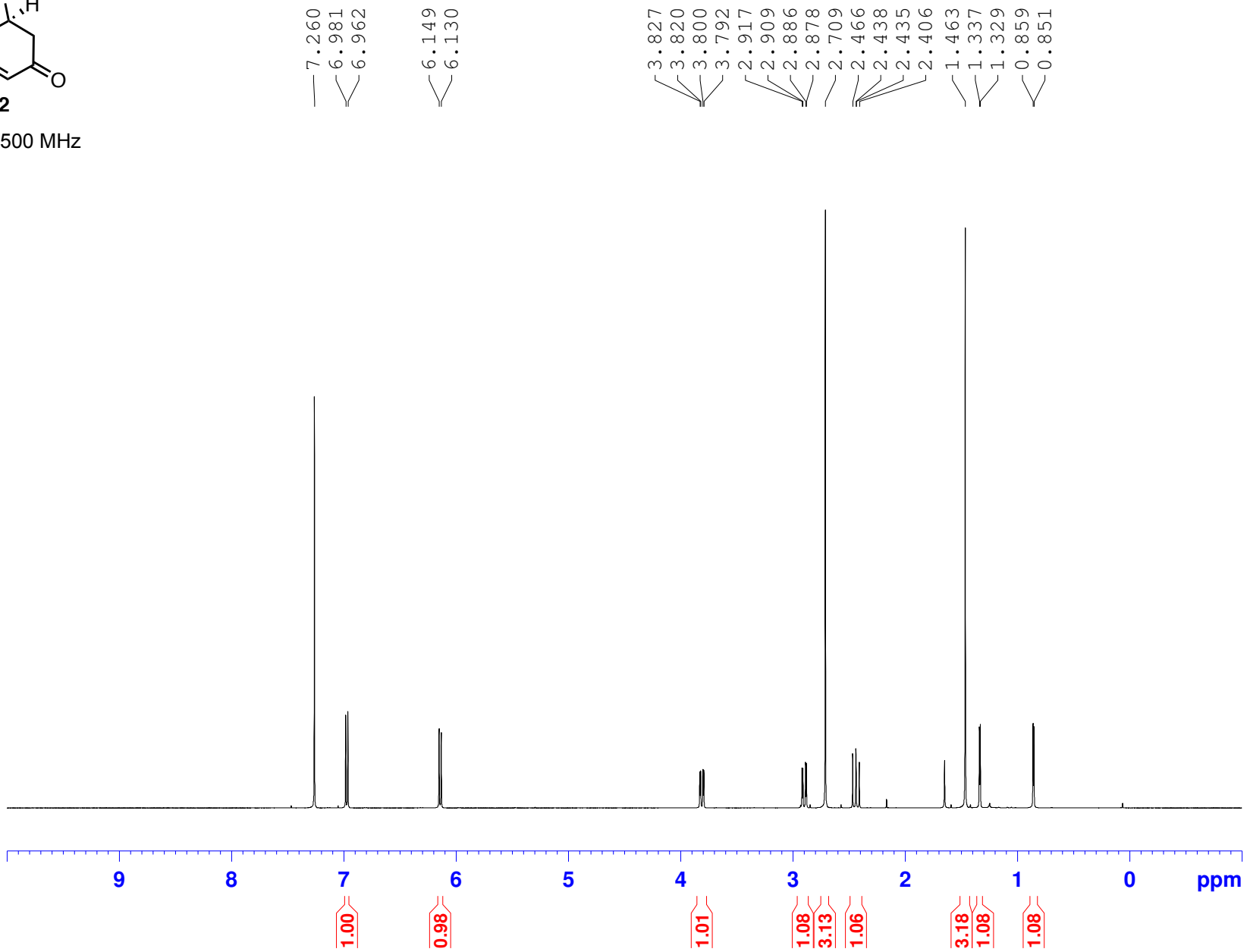
14

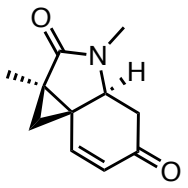




2

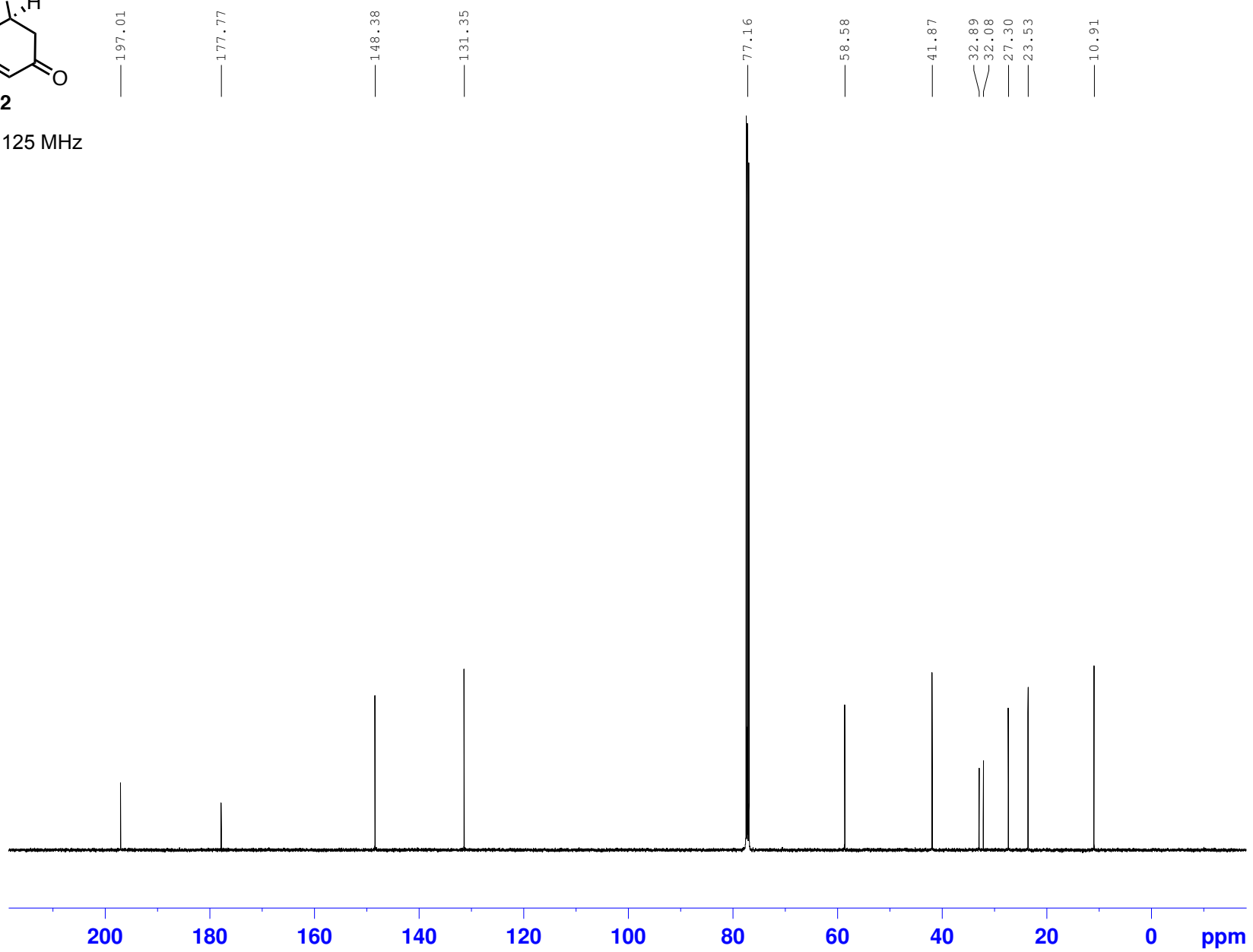
$CDCl_3$, 500 MHz

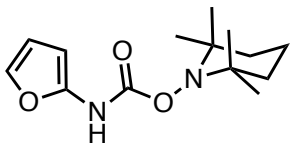




2

$CDCl_3$, 125 MHz





S2

$CDCl_3$, 500 MHz

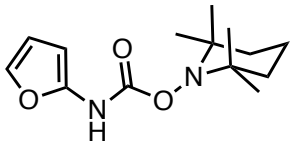
9.003

7.260
7.097
7.095
6.385
6.380
6.378
6.374
6.175
6.169

1.707
1.681
1.676
1.655
1.650
1.623
1.596
1.570
1.549
1.484
1.477
1.470
1.464
1.458
1.451
1.445
1.438
1.264
1.190

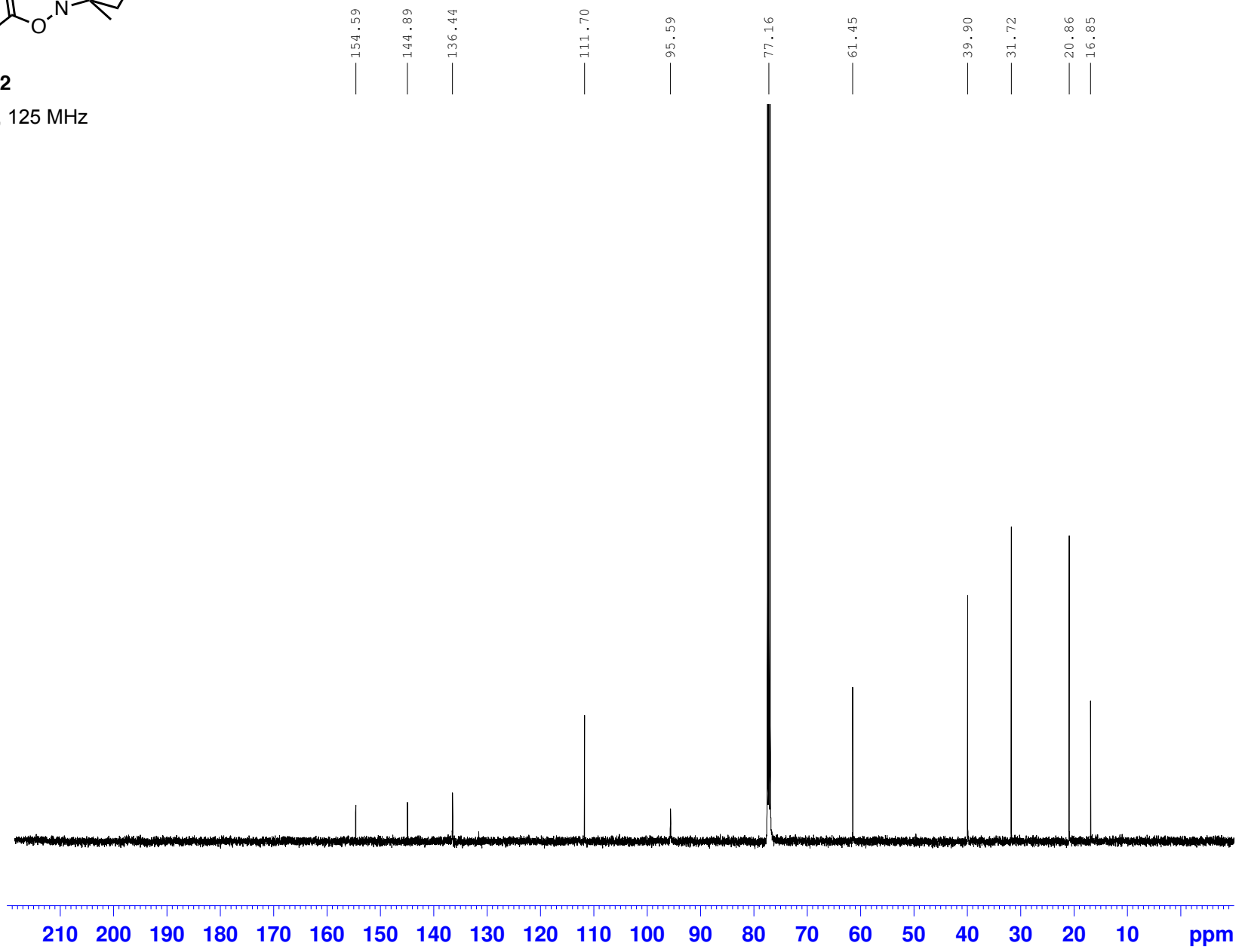
9 8 7 6 5 4 3 2 1 0 ppm

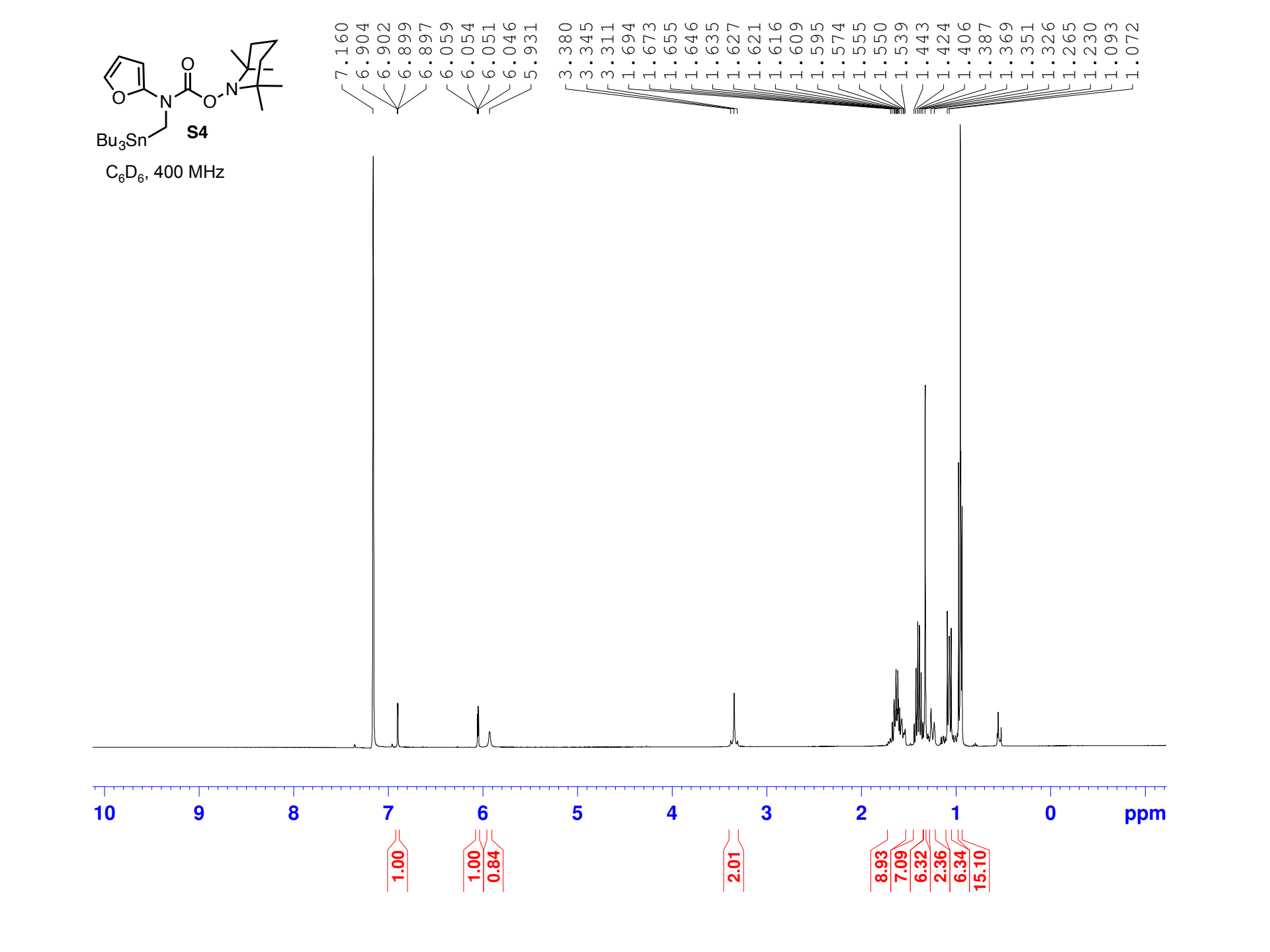
0.93 1.00 1.04 1.00 5.40 1.17 6.16 6.35

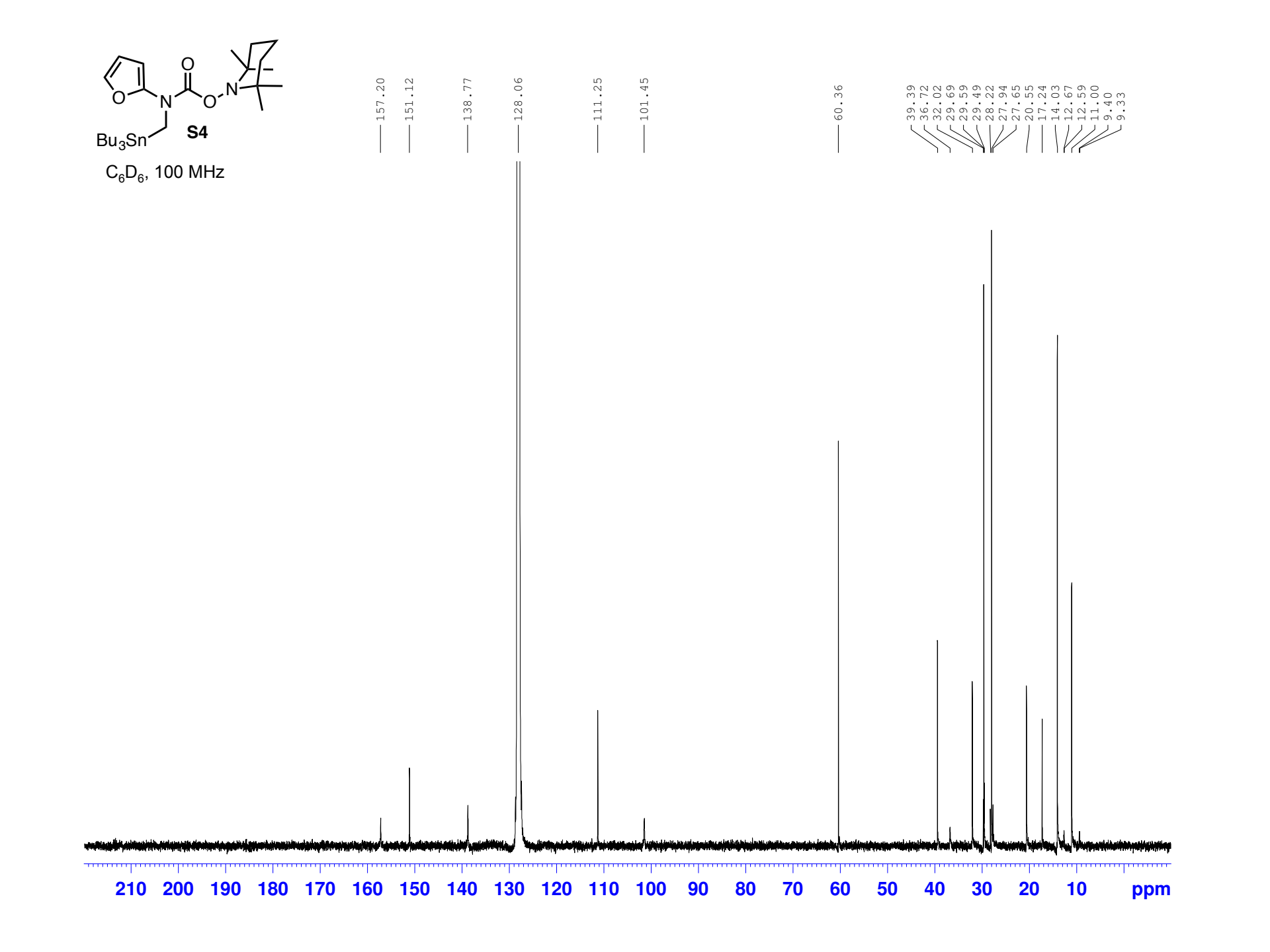


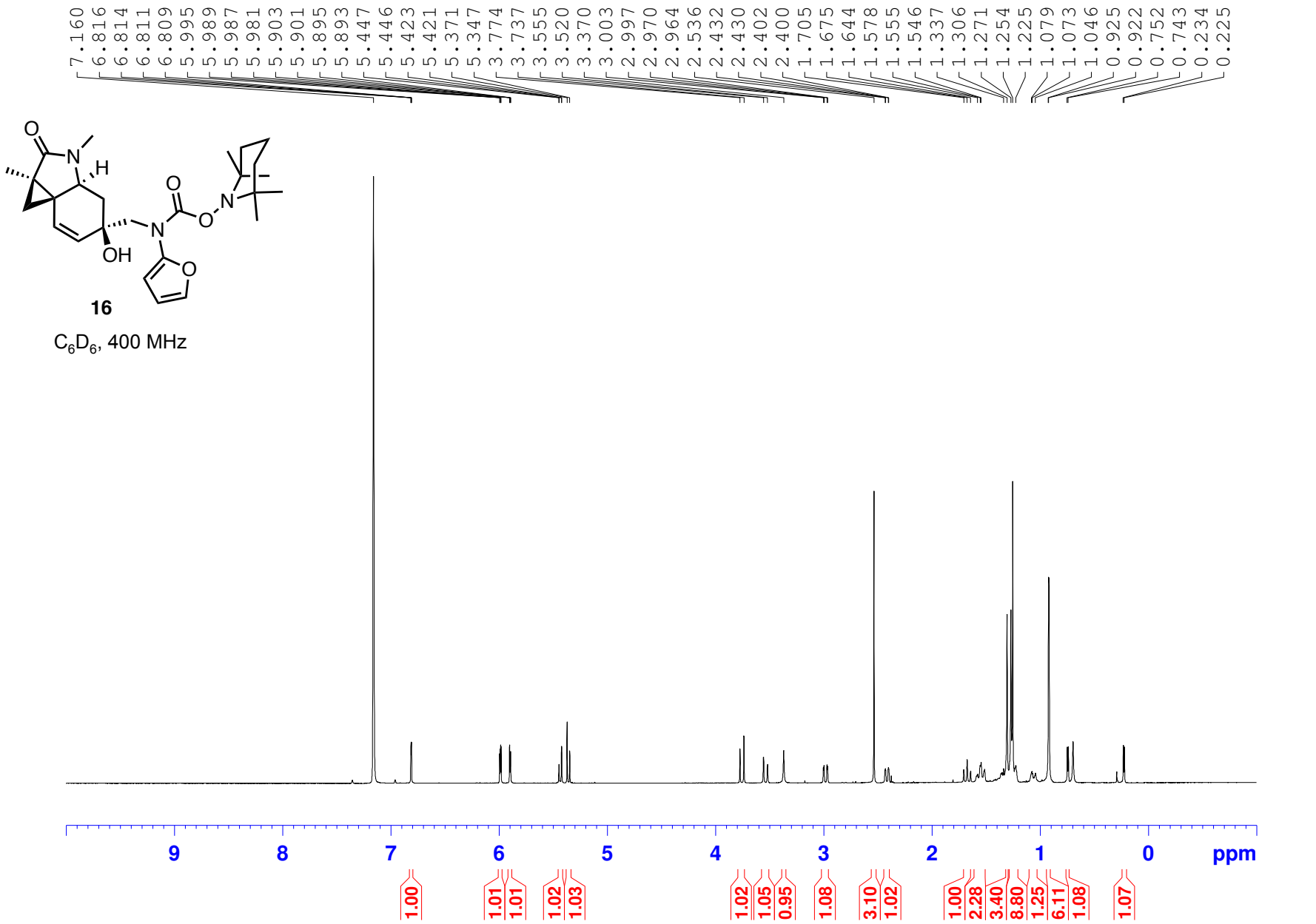
S2

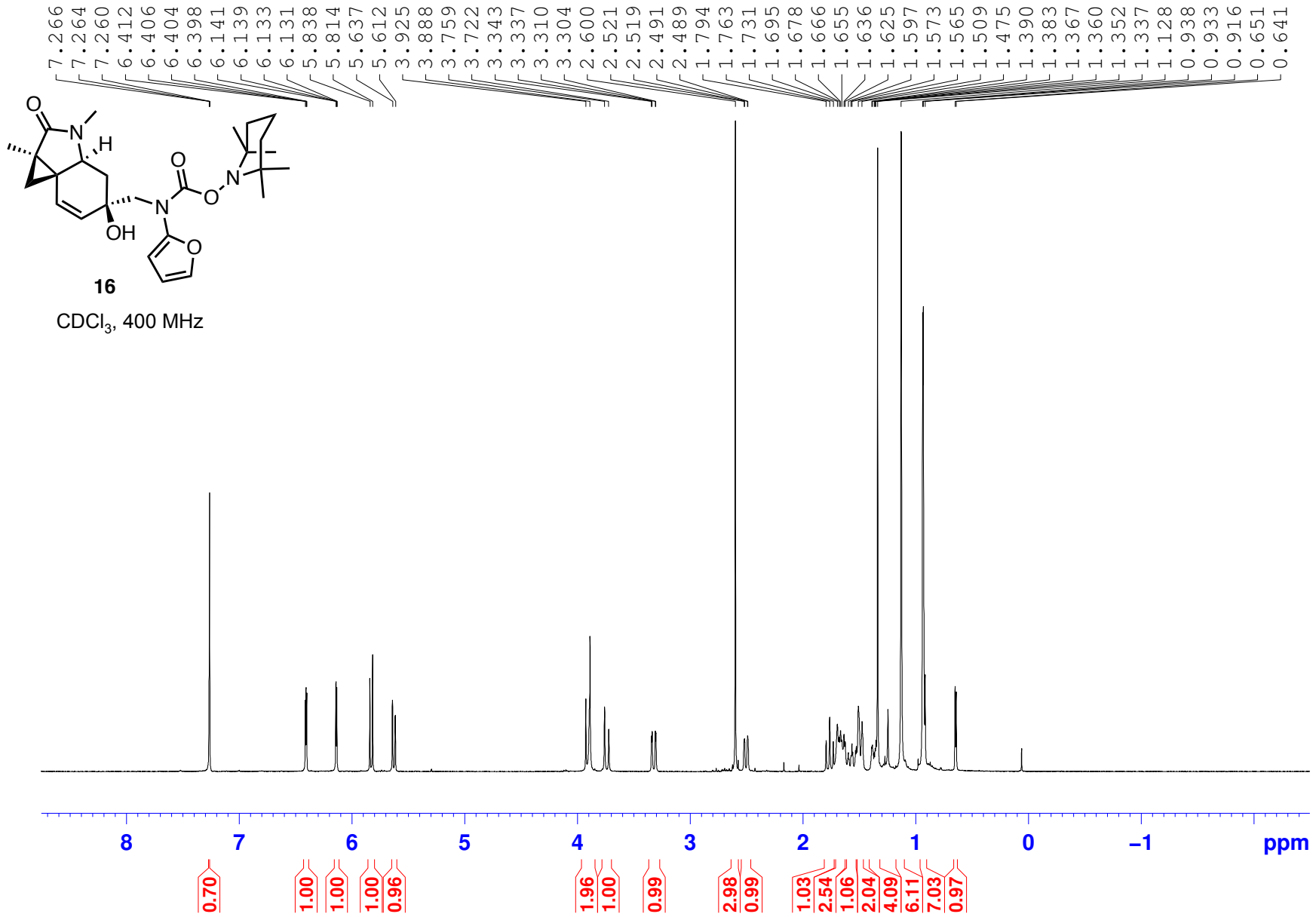
$CDCl_3$, 125 MHz




S4
Bu3Sn
C6D6, 400 MHz
7.160
6.904
6.902
6.899
6.897
6.059
6.054
6.051
6.046
5.931
3.380
3.345
3.311
1.694
1.673
1.655
1.646
1.635
1.627
1.621
1.616
1.609
1.595
1.574
1.555
1.550
1.539
1.443
1.424
1.406
1.387
1.369
1.351
1.326
1.265
1.230
1.093
1.072
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.00
0.84
2.01
8.93
7.09
6.32
2.36
6.34
15.10

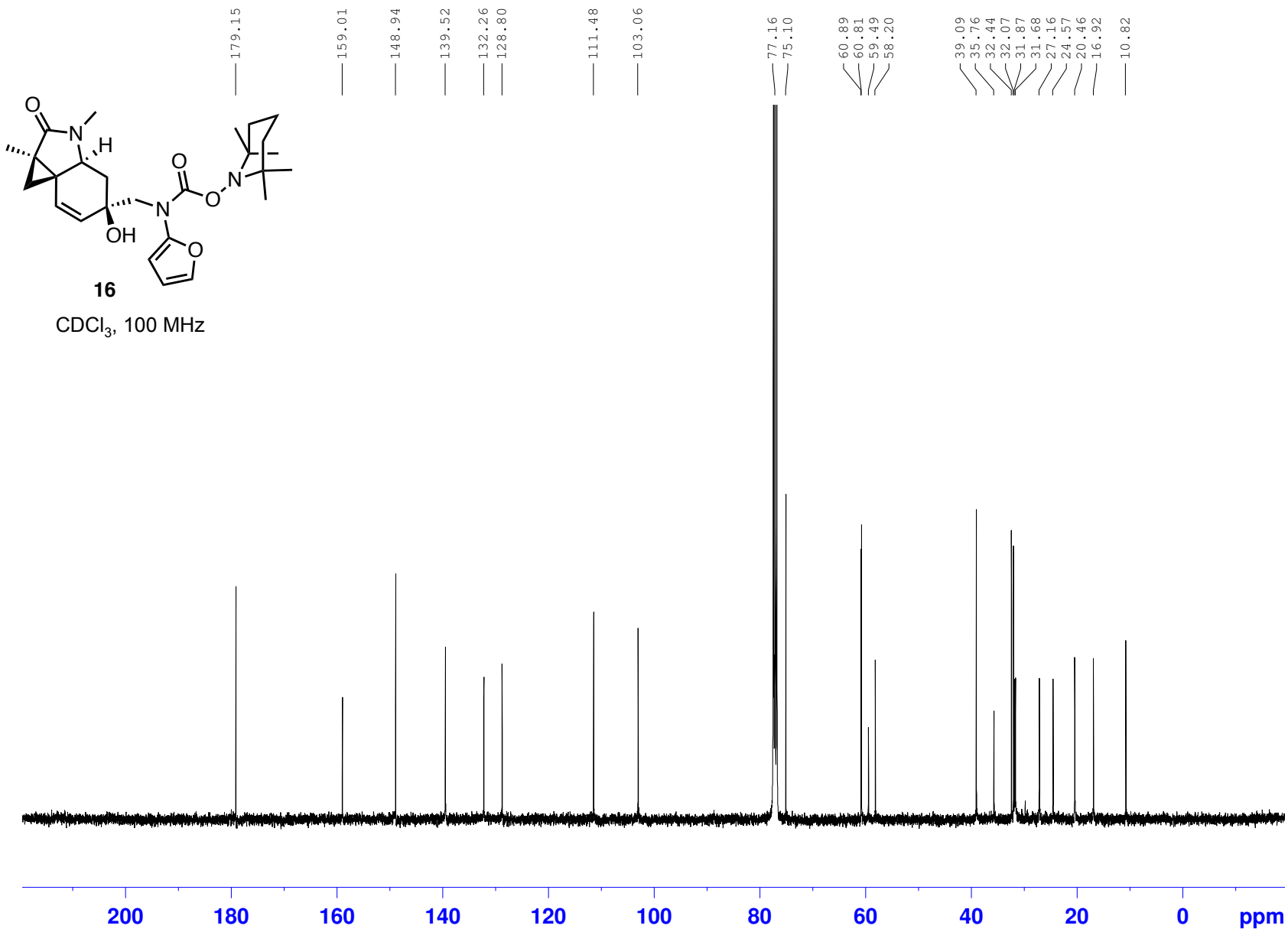

S4
Bu_3Sn
C_6D_6, 100 MHz
157.20
151.12
138.77
128.06
111.25
101.45
60.36
39.39
36.72
32.02
29.69
29.59
29.49
28.22
27.94
27.65
20.55
17.24
14.03
12.67
12.59
11.00
9.40
9.33
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.160
6.816
6.814
6.811
6.809
5.995
5.989
5.987
5.981
5.903
5.901
5.895
5.893
5.447
5.446
5.423
5.421
5.371
5.347
3.774
3.737
3.555
3.520
3.370
3.003
2.997
2.970
2.964
2.536
2.432
2.430
2.402
2.400
1.705
1.675
1.644
1.578
1.555
1.546
1.337
1.306
1.271
1.254
1.225
1.079
1.073
1.046
0.925
0.922
0.752
0.743
0.234
0.225
O
N
H
O
O
N
N
O
OH
16
C6D6, 400 MHz
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.01
1.01
1.02
1.03
1.02
1.05
0.95
1.08
3.10
1.02
1.00
2.28
3.40
8.80
1.25
6.11
1.08
1.07



16

$CDCl_3$, 400 MHz



16

$CDCl_3$, 100 MHz

Figure 3. HSQC, **16** ($CDCl_3$, 400 MHz)

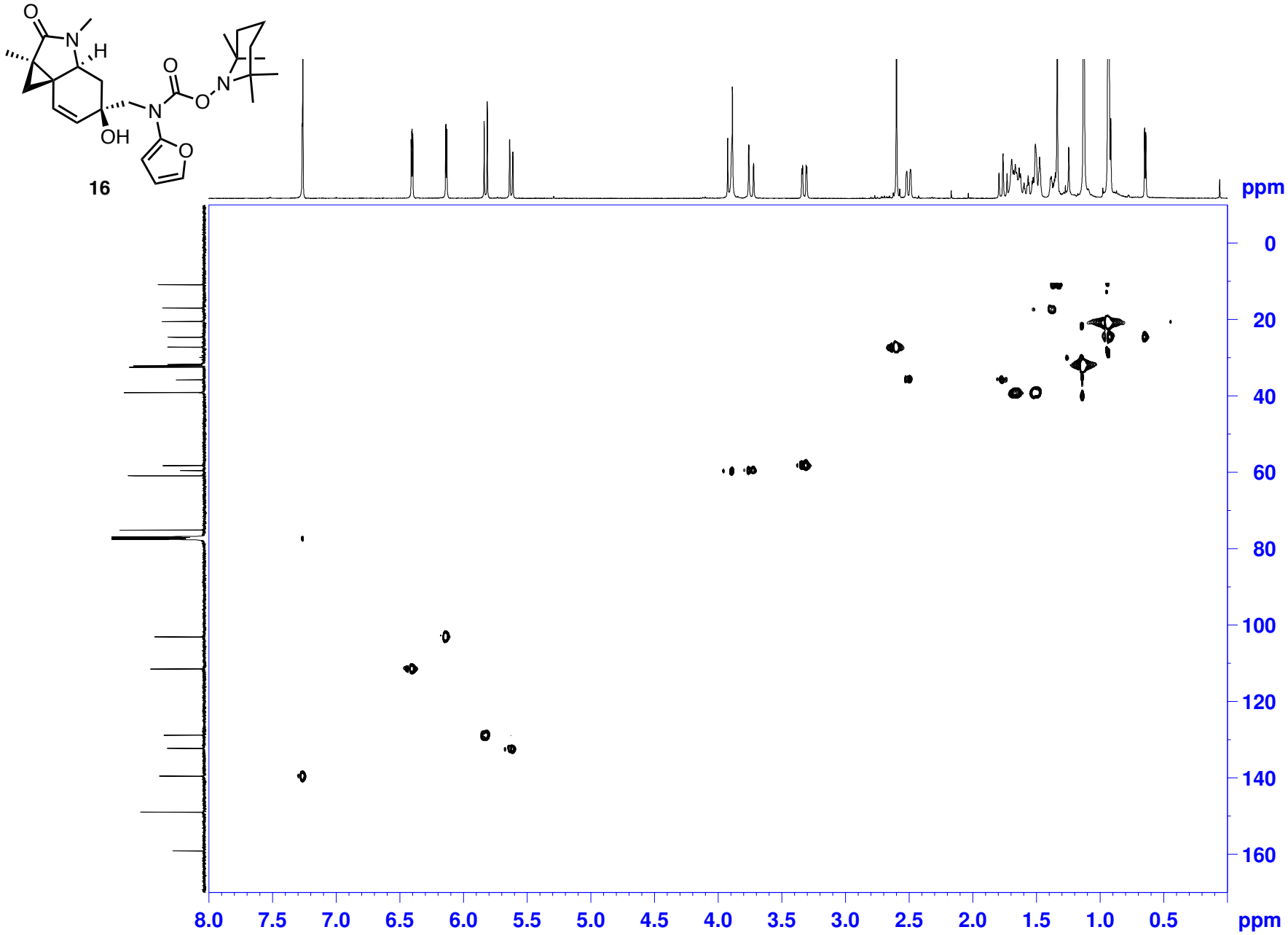
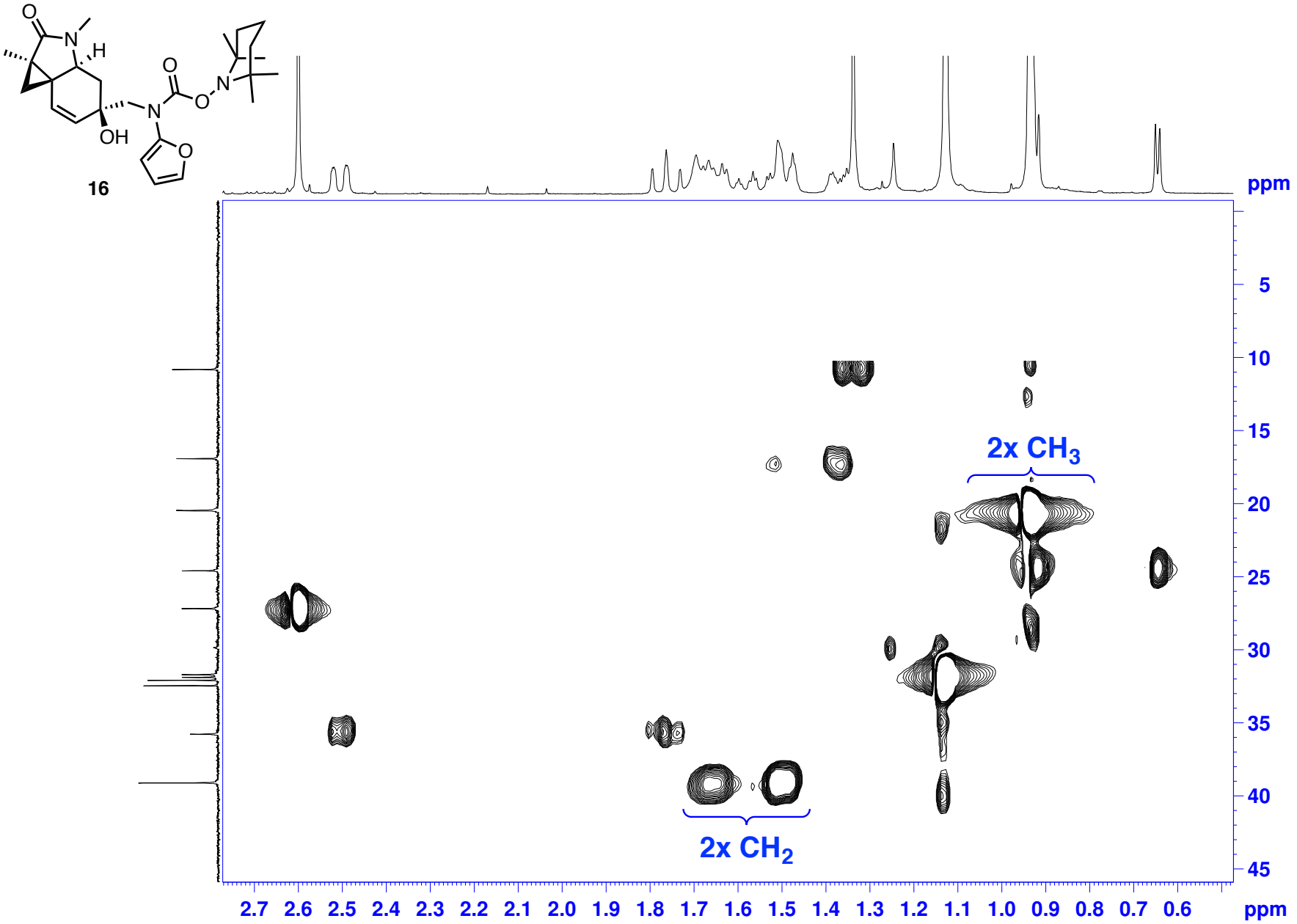
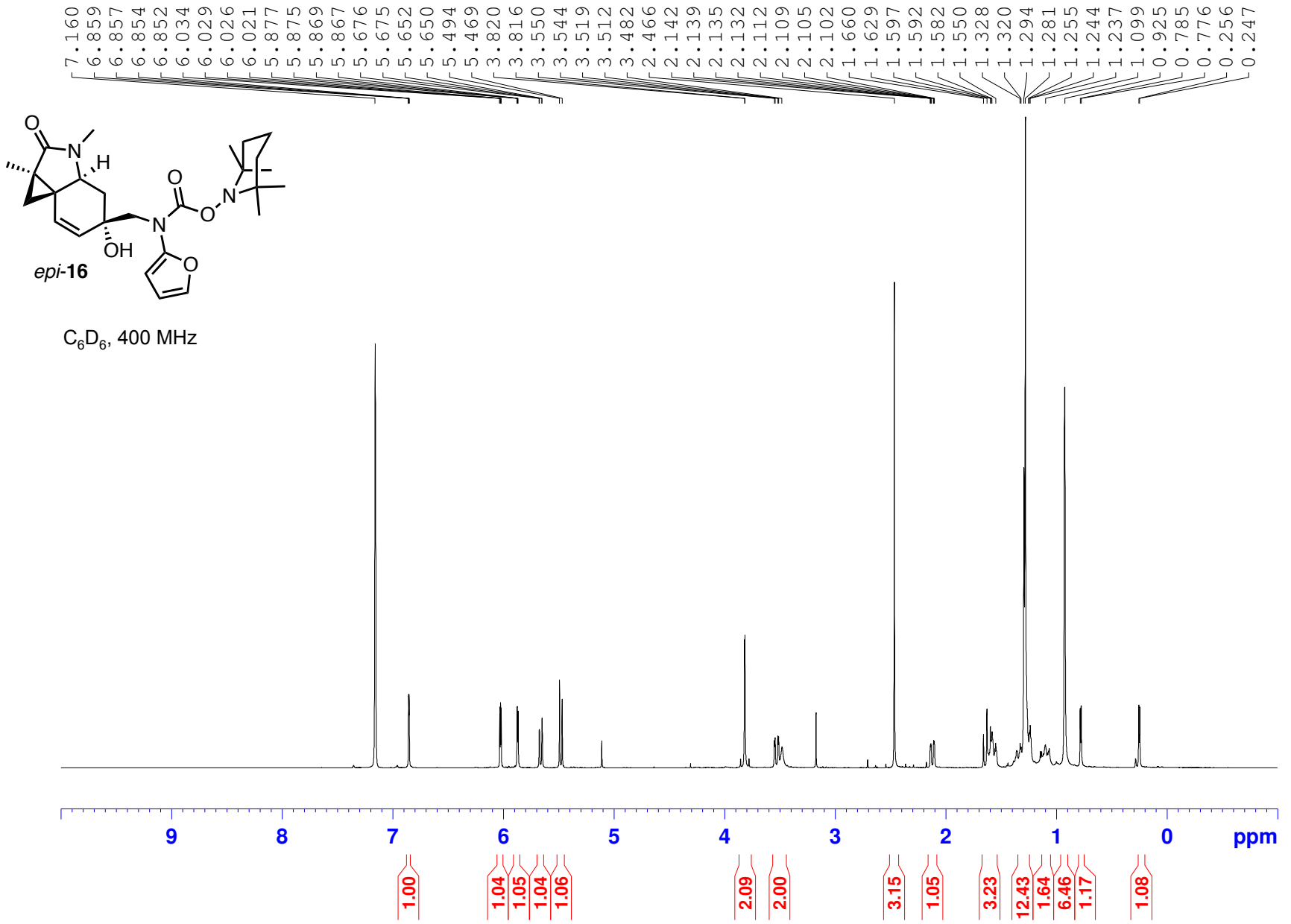
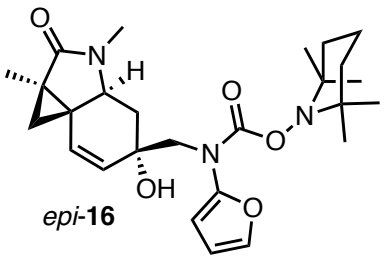


Figure 4. HSQC – magnified, **16** ($CDCl_3$, 400 MHz)

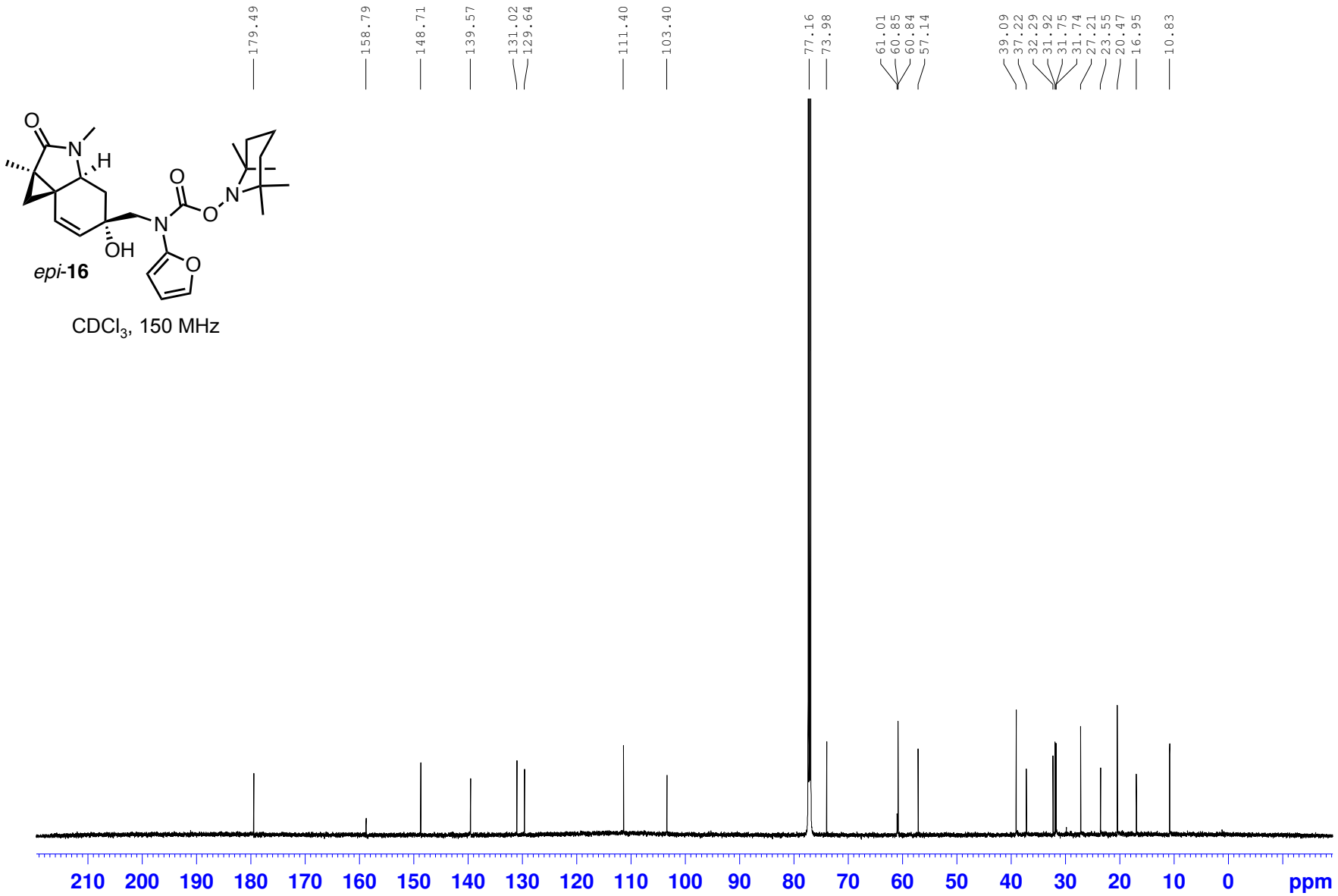



7.160
6.859
6.857
6.854
6.852
6.034
6.029
6.026
6.021
5.877
5.875
5.869
5.867
5.676
5.675
5.652
5.650
5.494
5.469
3.820
3.816
3.550
3.544
3.519
3.512
3.482
3.466
2.142
2.139
2.135
2.132
2.112
2.109
2.105
2.102
1.660
1.629
1.597
1.592
1.582
1.550
1.328
1.320
1.294
1.281
1.255
1.244
1.237
1.099
0.925
0.785
0.776
0.256
0.247
O
N
H
O
O
N
N
O
OH
O
epi-16
C6D6, 400 MHz
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.04
1.05
1.04
1.06
2.09
2.00
3.15
1.05
3.23
12.43
1.64
6.46
1.17
1.08



epi-**16**

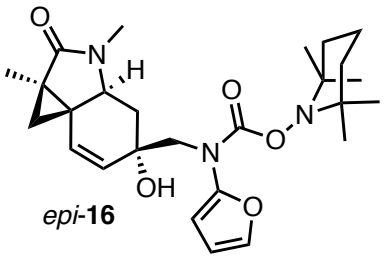
$CDCl_3$, 600 MHz



epi-**16**

$CDCl_3$, 150 MHz

Figure 5. HSQC, *epi*-**16** ($CDCl_3$, 600 MHz)



epi-**16**

Figure 6. HSQC - magnified, *epi*-**16** ($CDCl_3$, 600 MHz)

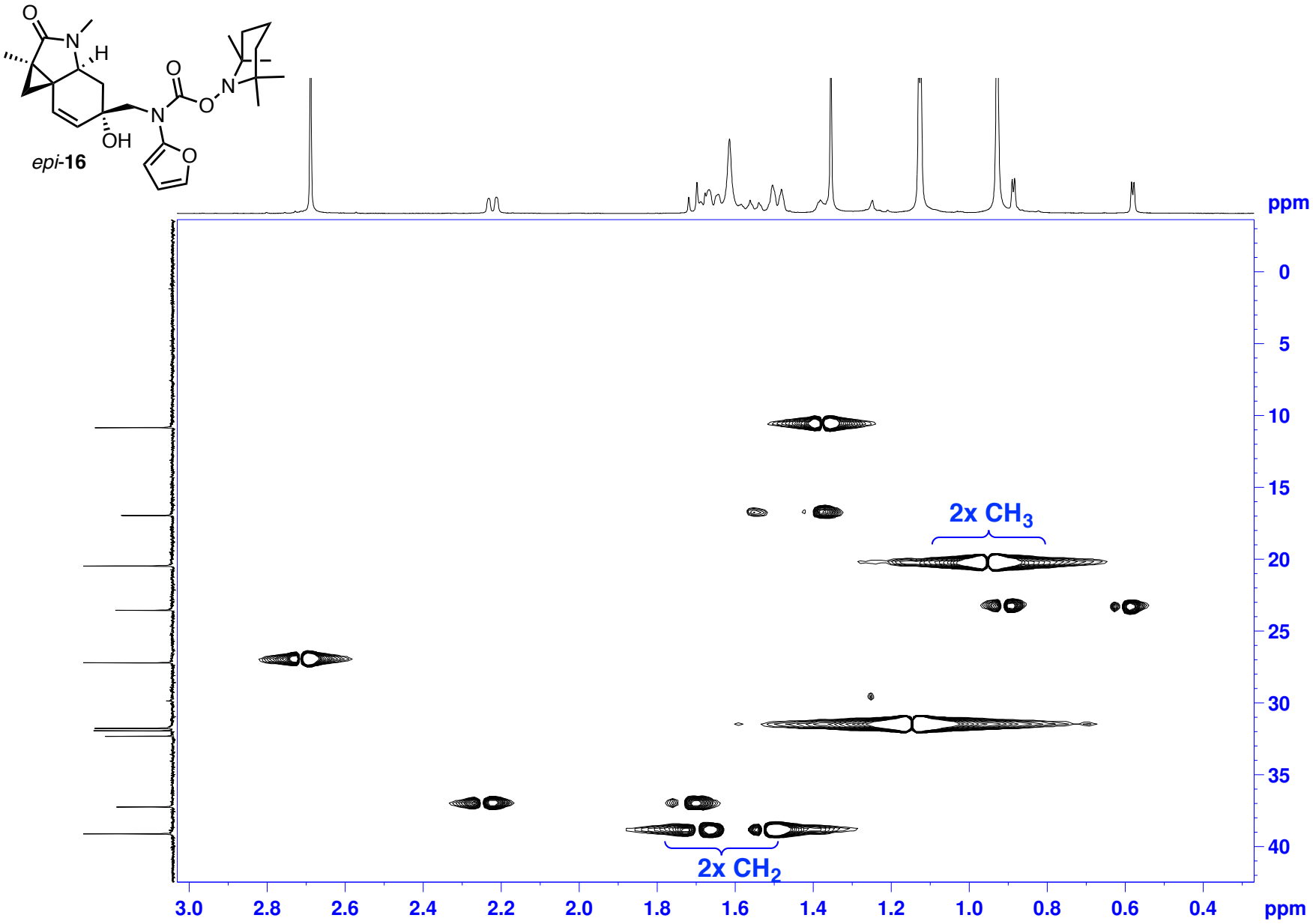


Figure 7. Key ROESY correlations in **16** ($CDCl_3$, 500 MHz)

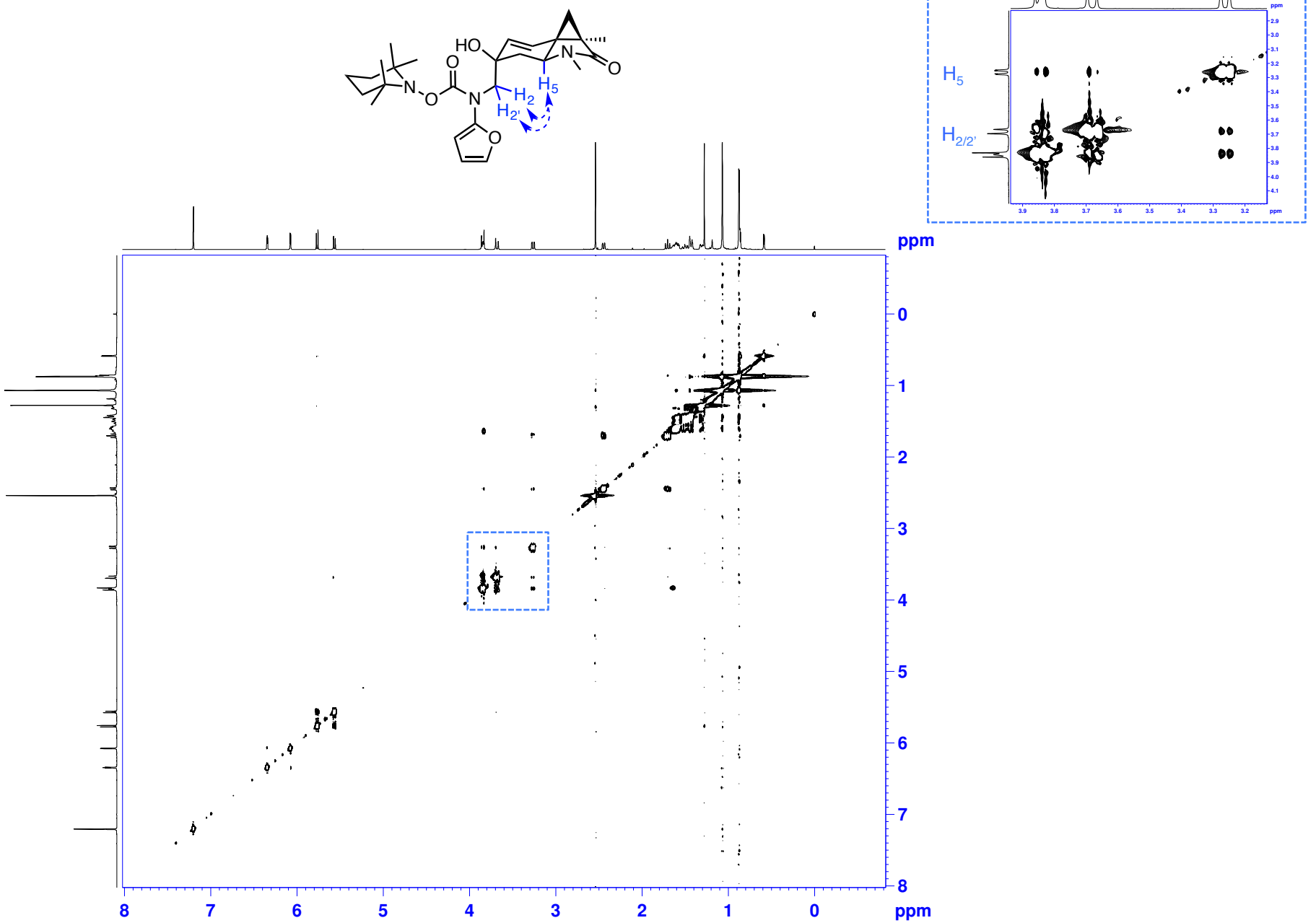


Figure 8. Lack of key ROESY correlations in *epi*-**16** ($CDCl_3$, 600 MHz)

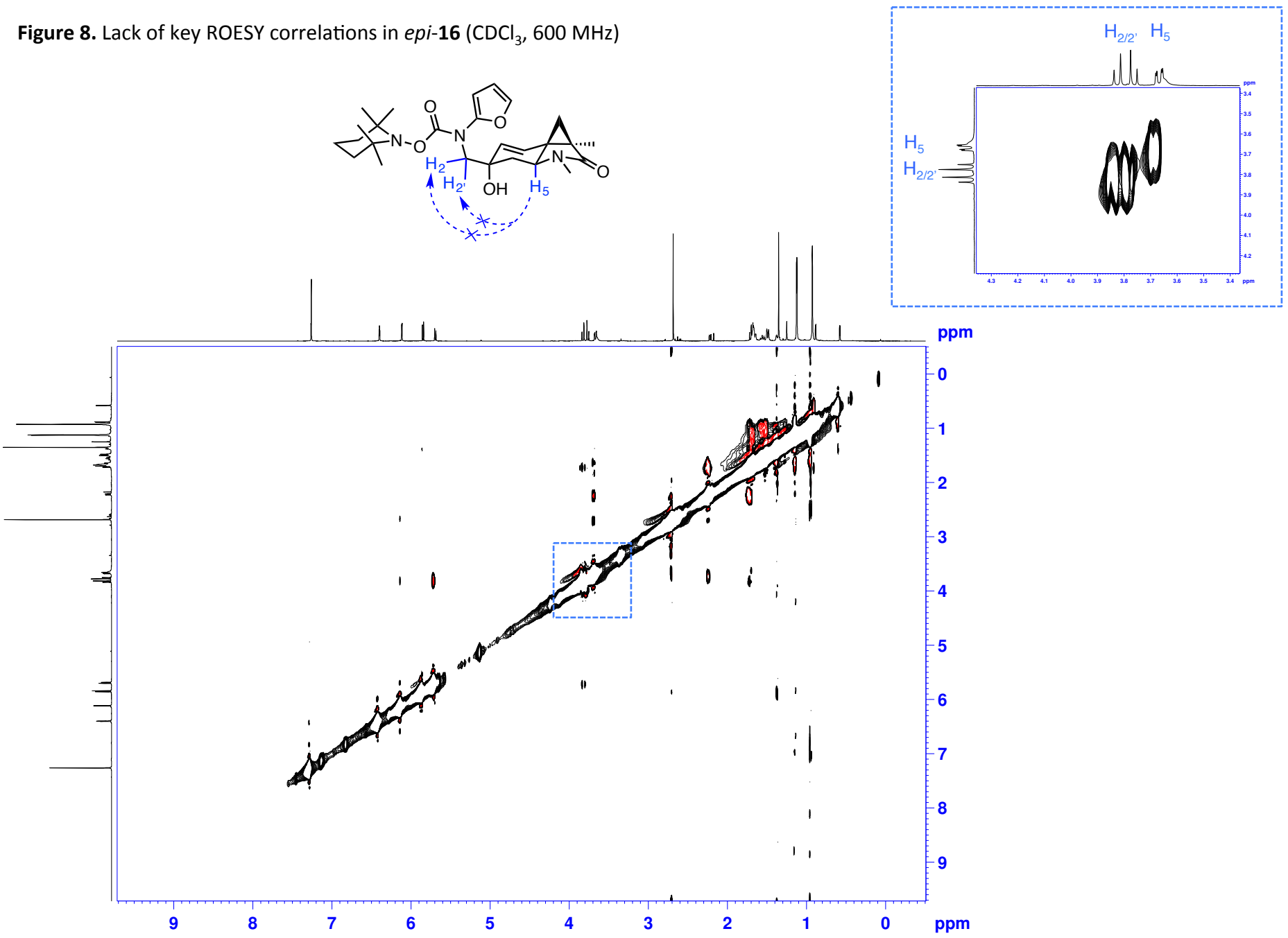


Figure 9. Key 1D-NOE correlations in **16** ($CDCl_3$, 600 MHz)

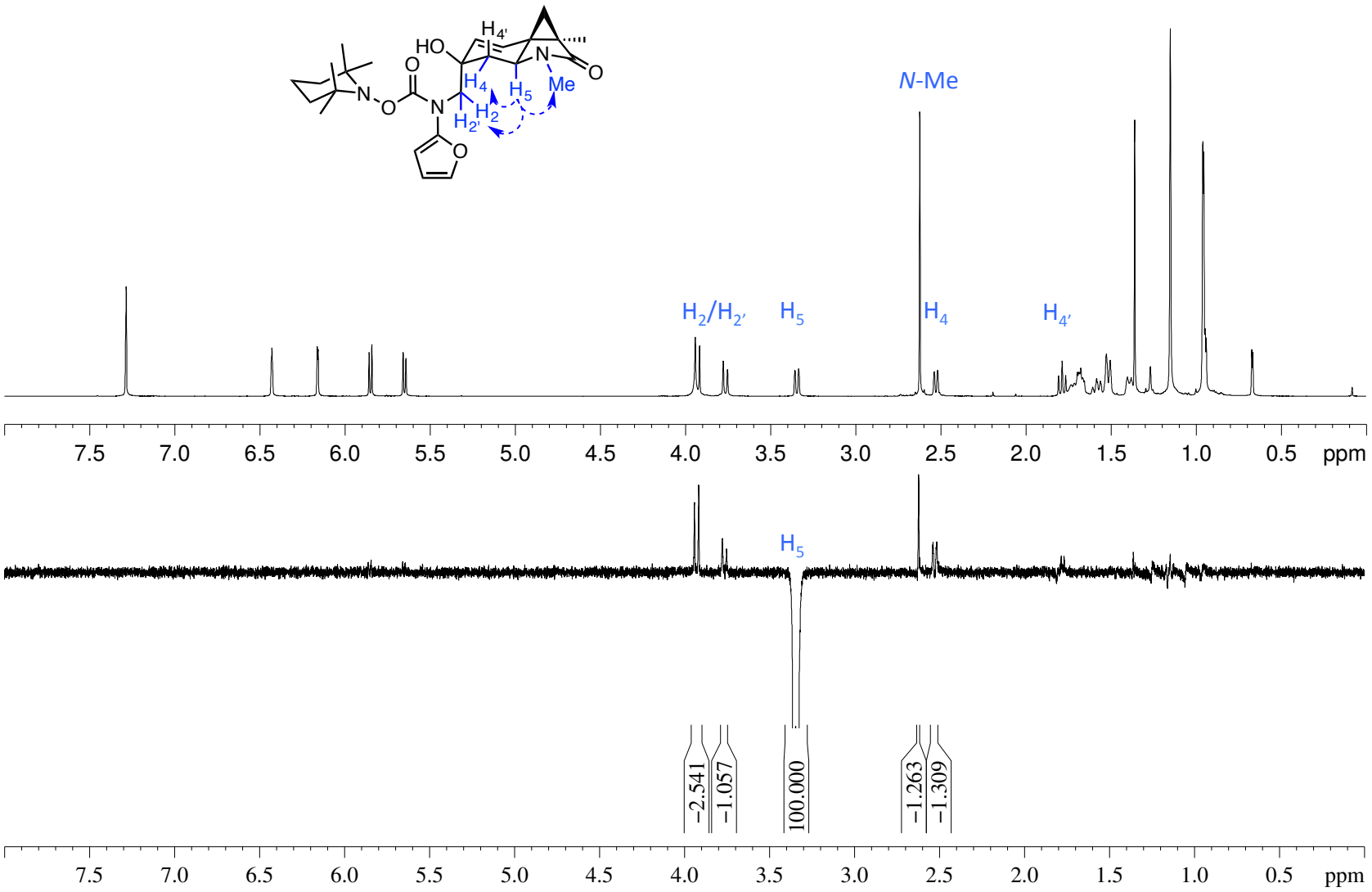
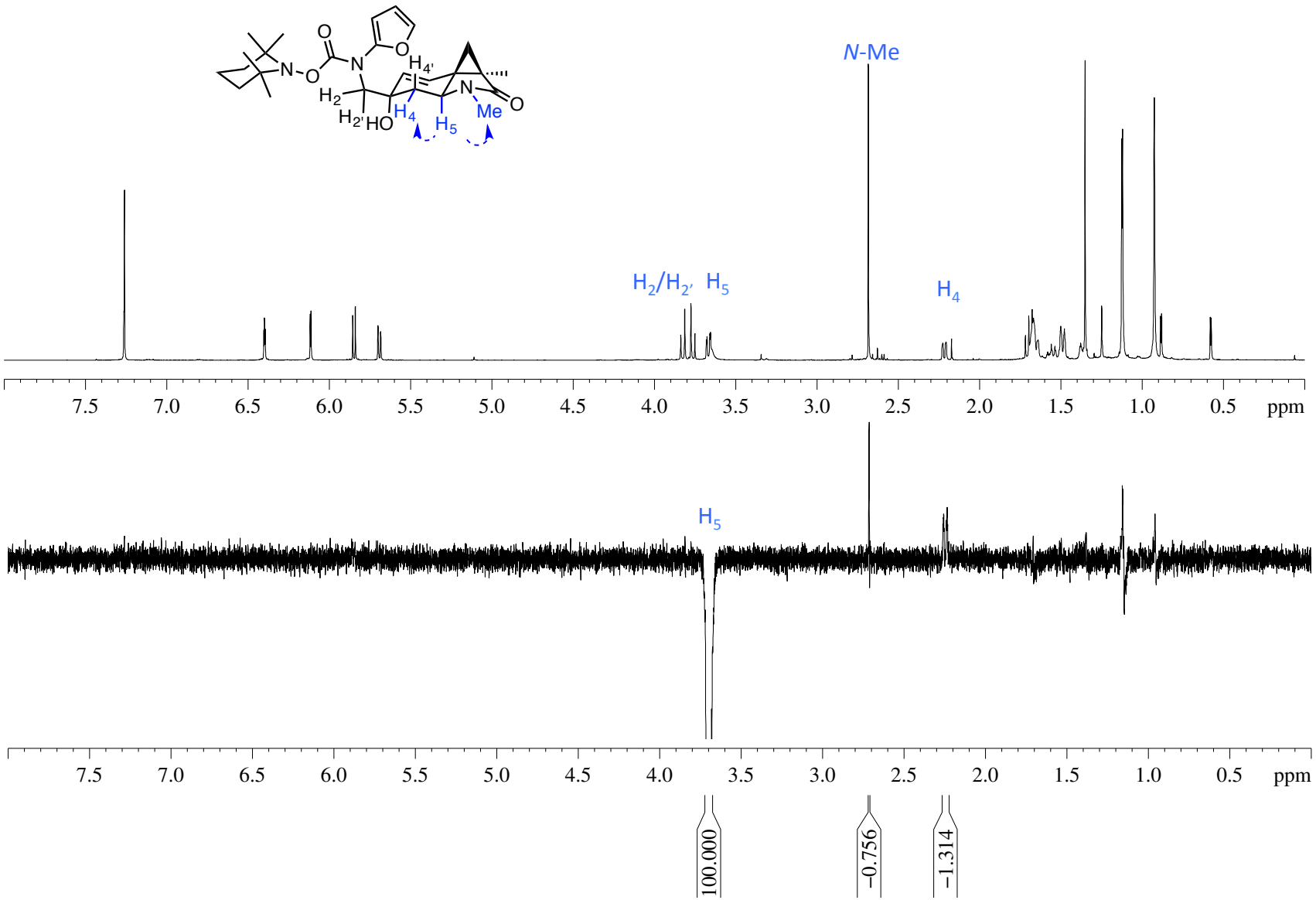
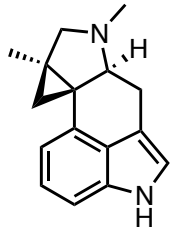


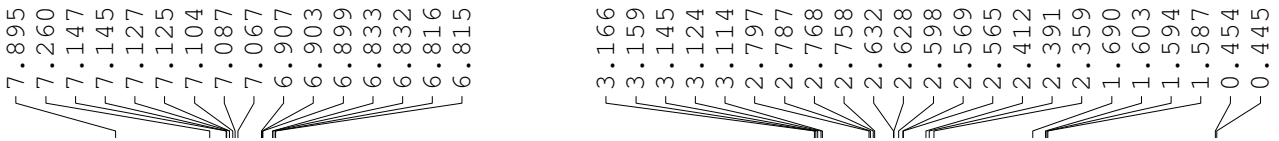
Figure 10. Key 1D-NOE correlations in *epi*-**16** ($CDCl_3$, 600 MHz)

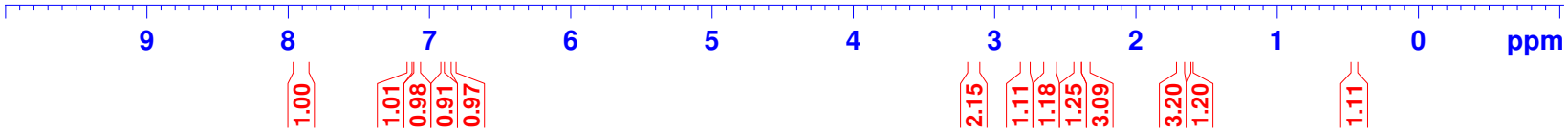


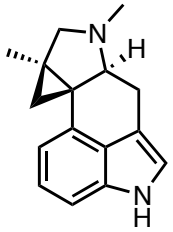


(–)-(**1**)

$CDCl_3$, 400 MHz







(–)-(**1**)

$CDCl_3$, 100 MHz