From *N*-Triisopropylsilyl Pyrrole to an Optically Active C-4 Substituted Pyroglutamic Acid: Total Synthesis of Penmacric Acid

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Electronic Supporting Information

Tools, Reagents, Solvents and Procedures

Reactions were performed using oven-dried glassware under an atmosphere of dry argon. They were monitored by thin layer chromatography (TLC) using commercial aluminium-backed silica gel plates (Merck, Kieselgel 60 PF_{254}). TLC spots were viewed under ultraviolet light and by heating the plate after treatment with an appropriate revelatory ($KMnO_4$, TTC, phosphomolybdic acid, ninhydrine).

Solvents and reagents: Tetrahydrofuran was refluxed over sodium-benzophenone and then distilled. Dichloromethane was dried by refluxing over CaH_2 and then distilled. Methanol was refluxed over magnesium turnings and then distilled. Triethylamine and 2,6-lutidine were refluxed over KOH and then distilled. Trichloroacetyl chloride and benzoyl chloride were distilled over $CaCl_2$. Trifluoroacetic acid was refluxed in the presence of trifluoroacetic anhydride and then distilled. Unless otherwise noted, all reagent-grade chemicals and solvents were used as supplied (analytical or HPLC grade) without prior purification.

Purifications by column chromatography were performed using Kieselgel 60 silica (40-60 mesh).

Melting points were obtained on a Büchi B35 apparatus and are uncorrected.

Optical rotations were determined with a Perkin-Elmer 341 polarimeter operating at the sodium D-line with a water-jacketed 10 cm cell. Specific rotations are reported in 10^{-1} deg cm^2 g^{-1} and concentrations in g per 100 mL.

Circular dichroisms were recorded on a JASCO J-810 spectropolarimeter.

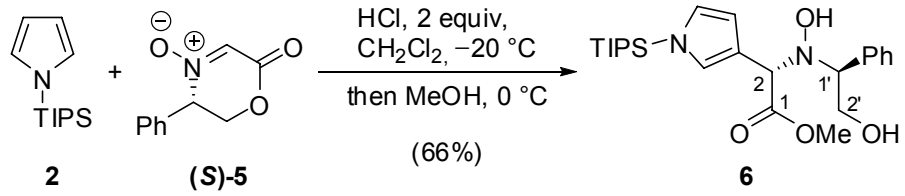
Infrared spectra (IR) were recorded on a Nicolet Impact-400 Fourier transform infrared spectrometer (FTIR) either as thin films on NaCl plates (thin film) or KBr discs (KBr disc), as stated. The data are reported in reciprocal centimetres (cm^{-1}).

^{1}H NMR Spectra (300 or 400 MHz) and **^{13}C NMR spectra** (75 or 100 MHz) were recorded on either a Bruker Advance300 or Advance400 spectrometers in the deuterated solvent as stated. The field was locked by external referencing to the relevant deuteron resonance. Chemical shifts are given in ppm (δ) and were referenced to the internal solvent signal or to TMS used as an internal standard. When ambiguous, proton and carbon assignments were

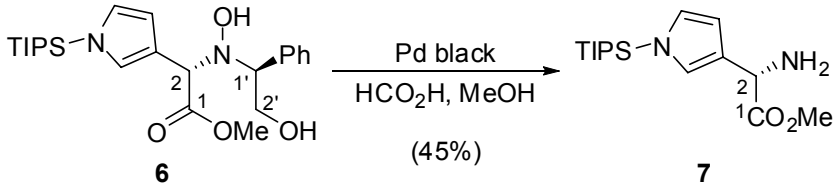
established using COSY, HMQC and/or DEPT experiments. Multiplicities are declared as follows: *s* (singlet), *br s* (broad singlet), *d* (doublet), *t* (triplet), *dd* (doublet of doublet), *ddd* (doublet of doublet of doublet), *dt* (doublet of triplet), *m* (multiplet). Coupling constants *J* are given in Hertz.

Low Resolution Mass Spectra (LRMS) were recorded on a Bruker Esquire 3000 plus (ESI) or a ThermoFinnigan PolarisQ ion-trap spectrometer, using DCI (ammonia/isobutane 63/37). **Accurate Mass measurements (HRMS)** were recorded on an Orbitrap apparatus (ESI) in the "Structure et Fonction de Molécules Bioactives" laboratory, Paris, France.

Elemental analysis were performed Service d'Analyse Elémentaire du Département de Chimie Moléculaire, Grenoble, France.

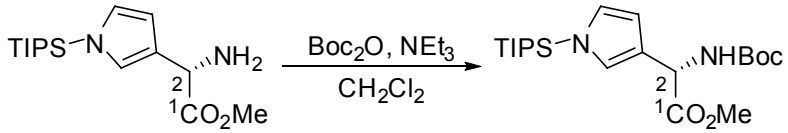


(*S*)-[Hydroxy-((*R*)-2-hydroxy-1-phenylethyl)amino]-(1-triisopropylsilanyl-1*H*-pyrrol-3-yl)acetic acid methyl ester (6). To a stirred solution of nitrone **(*S*)-5** (0.96 g, 5.02 mmol) in anhydrous CH_2Cl_2 (25 mL) at −40 °C was added HCl (5.0 mL, 2.0 N in Et_2O, 10.0 mmol) and *N*-TIPS-pyrrole **2** (1.23 g, 5.51 mmol). The resulting mixture was slowly warmed to −20 °C and then stirred at this temperature for 12 hours where'upon anhydrous MeOH (25 mL) was added. It was then allowed to run at 0 °C for 24 hours. The mixture was then treated with a saturated aqueous $NaHCO_3$ solution until pH 8-9. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash chromatography on silica gel (eluent: pentane/EtOAc, 9/1 to 7/3) to afford pure *N*-hydroxylamine **6** (1.48 g, 66%) as a pale pink solid; mp 50-51 °C; $[\alpha]_D^{20}$ +119.3 (*c* 1.00 in $CHCl_3$); ν_{MAX}/cm^{-1} (KBr disc) 3550-3350 (broad, OH × 2), 1752 (CO); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.09-1.13 (18H, m, $((CH_3)_2CH)_3Si$), 1.38-1.50 (3H, m, $((CH_3)_2CH)_3Si$), 3.54-3.58 (1H, m, C(2')H_2), 3.63 (3H, s, OCH_3), 4.00 (1H, dd, J = 9.7 and 3.8 Hz, C(1')*H*), 4.23 (1H, br s, O*H*), 4.33-4.38 (1H, m, C(2')H_2), 4.39 (1H, s, C(2)*H*), 6.42 (1H, dd, J = 2.4 and 1.2 Hz, pyrr*H*), 6.57 (1H, s, O*H*), 6.70 (1H, s, pyrr*H*), 6.76 (1H, t, J = 2.4 Hz, pyrr*H*), 7.30-7.32 (5H, m, Ar*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 11.7 ($((CH_3)_2CH)_3Si$), 17.8 ($((CH_3)_2CH)_3Si$), 52.2 (OCH_3), 63.4 (*C*(2')H_2), 66.6 (*C*(2)H), 67.6 (*C*(1')H), 110.5 (pyrr*C*H), 117.8 (pyrr*C*), 124.5 (pyrr*C*H), 124.9 (pyrr*C*H), 127.8 (Ar*C*H), 127.9 (Ar*C*H), 130.2 (Ar*C*H), 140.2 (Ar*C*), 174.0 (*C*=O); *m*/*z* (DCI, NH_3-isobutane) 447 ($[M+H]^+$), 431, 399, 294 (100%); Elemental analysis, calcd (%) for $C_{24}H_{38}N_2O_4Si$: C, 64.54; H, 8.58; N, 6.28. Found: C, 64.36; H, 8.73; N, 6.38.



6 **7**

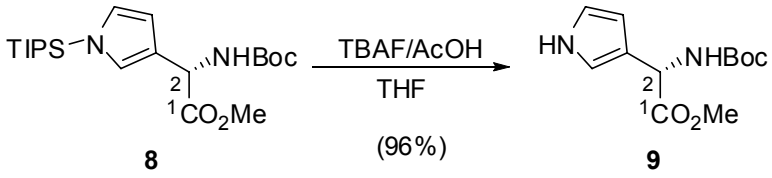
(*S*)-Amino-(1-triisopropylsilanyl-1*H*-pyrrol-3-yl)acetic acid methyl ester (7). To a stirred solution of hydroxylamine **6** (466 mg, 1.04 mmol) in anhydrous MeOH/formic acid (36 mL) was added palladium black (0.63 g, 6.00 mmol). The resulting mixture was stirred for 1 hour. It was then filtered through celite pad and methanol was removed under vaccum. The residue was then dissolved in CH_2Cl_2 and $NaHCO_3$ was added. After filtration, the solvent was removed *in vacuo*. The crude product was purified by flash chromatography on silica gel (eluent: pentane/EtOAc, 1/1 to 0/1) to afford α-amino methyl ester **7** (144 mg, 0.46 mmol, 45%) as a yellow oil: $[\alpha]_D^{20}$ +59.0 (*c* 1.00 in $CHCl_3$); ν_{MAX}/cm^{-1} (thin film) 3388 (NH_2), 1740 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.11 (18H, app. d, $J = 7.6$ Hz, $((CH_3)_2CH)_3Si$), 1.35-1.50 (3H, m, $((CH_3)_2CH)_3Si$), 1.85 (2H, br s, NH_2), 3.72 (3H, s, OCH_3), 4.60 (1H, s, C(2)*H*), 6.27-6.28 (1H, m, pyrr*H*), 6.70-6.71 (1H, m, pyrr*H*), 6.74 (1H, s, pyrr*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 11.6 ($((CH_3)_2CH)_3Si$), 17.7 ($((CH_3)_2CH)_3Si$), 52.0 (OCH_3), 52.7 (*C*(2)H), 108.8 (pyrr*C*H), 121.4 (pyrr*C*H), 124.5 (pyrr*C*H), 125.0 (pyrr*C*), 175.5 (*C*=O); *m*/*z* (DCI, NH_3-isobutane) 294 ($[M+H-NH_3]^+$) (100%); Elemental analysis, calcd (%) for $C_{16}H_{30}N_2O_2Si$: C, 61.90; H, 9.74; N, 9.03. Found: C, 61.85; H, 9.50; N, 9.14.



7 **8**

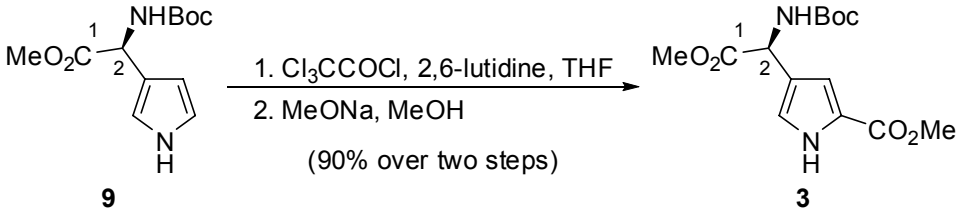
(*S*)-*tert*-Butoxycarbonylamino-(1-triisopropylsilanyl-1*H*-pyrrol-3-yl)acetic acid methyl ester (8). To a stirred solution of α-amino methyl ester **7** (1.60 g, 5.15 mmol) in anhydrous CH_2Cl_2 (20 mL) at 0 °C was added anhydrous NEt_3 (0.90 mL, 6.38 mmol) and Boc_2O (1.28 g, 5.86 mmol). The resulting mixture was warmed to room temperature and stirred for 2 hours. Water was then added and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash

chromatography on silica gel (eluent: pentane/EtOAc, 9/1 to 7/3) to afford α-amino methyl ester **8** (1.84 g, 4.48 mmol, 87%) as a yellow oil: $[\alpha]_D^{20}$ +71.9 (*c* 1.00 in $CHCl_3$); ν_{MAX}/cm^{-1} (thin film) 3450-3350 (broad, NH), 1756 (CO), 1718 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.07 (18H, d, *J* = 7.4 Hz, $((CH_3)_2CH)_3Si$), 1.36-1.45 (12H, m, $((CH_3)_2CH)_3Si$ and $C(CH_3)_3$), 3.73 (3H, s, OCH_3), 5.18-5.28 (2H, m, C(2)*H* and N*H*), 6.24 (1H, dd, *J* = 2.7 and 1.5 Hz, pyrr*H*), 6.68-6.70 (1H, m, pyrr*H*), 6.72-6.73 (1H, m, pyrr*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 11.5 ($((CH_3)_2CH)_3Si$), 17.7 ($((CH_3)_2CH)_3Si$), 28.3 ($C(CH_3)_3$), 51.8 (*C*(2)H), 52.2 (OCH_3), 79.7 ($C(CH_3)_3$), 109.1 (pyrr*C*H), 120.7 (pyrr*C*), 122.3 (pyrr*C*H), 124.8 (pyrr*C*H), 155.1 (*C*=O), 172.6 (*C*=O); *m*/*z* (DCI, NH_3-isobutane) 409 ($[M-H]^-$, 100%), 335; Elemental analysis, calcd (%) for $C_{21}H_{38}N_2O_4Si$: C, 61.43; H, 9.33; N, 6.83. Found: C, 61.65; H, 9.41; N, 6.62.



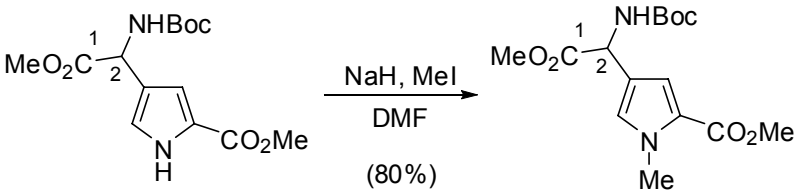
8 **9**

(*S*)-*tert*-Butoxycarbonylamino-(1*H*-pyrrol-3-yl)acetic acid methyl ester (9). To a stirred solution of *N*-TIPS-pyrrole **8** (1.76 g, 4.28 mmol) in anhydrous THF (43 mL) was added acetic acid (1.50 mL, 25.7 mmol). TBAF (9.80 mL, 1.0 M solution in THF, 9.80 mmol) was then added dropwise and the mixture was stirred at room temperature for 15 minutes. The mixture was then treated with a saturated aqueous NH_4Cl solution. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The crude product was purified by flash chromatography on silica gel (eluent: pentane/EtOAc, 9/1 to 1/1) to afford α-amino methyl ester **9** (1.05 g, 4.13 mmol, 96%) as a brown oil: $[\alpha]_D^{20}$ +83.3 (*c* 0.90 in $CHCl_3$); ν_{MAX}/cm^{-1} (thin film) 3400-3250 (broad, NH), 1752 (CO), 1697 (CO); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.45 (9H, s, $C(CH_3)_3$), 3.74 (3H, s, OCH_3), 4.91-5.30 (2H, m, C(2)*H* and N*H*), 6.20 (1H, dd, *J* = 4.2 and 2.6 Hz, pyrr*H*), 6.74 (1H, dd, *J* = 4.9 and 2.6 Hz, pyrr*H*), 6.79-6.80 (1H, m, pyrr*H*), 8.25 (1H, br s, N*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 28.3 ($C(CH_3)_3$), 51.7 (*C*(2)H), 52.3 (OCH_3), 79.9 ($C(CH_3)_3$), 107.0 (pyrr*C*H), 116.3 (pyrr*C*H), 118.6 (pyrr*C*H), 118.8 (pyrr*C*), 155.1 (*C*=O), 172.6 (*C*=O); *m*/*z* (DCI, NH_3-isobutane) 255 ($[M+H]^+$), 216, 155 (100%); HRMS (ESI^+) $C_{12}H_{18}N_2O_4Na$ ($[M+Na]^+$) requires 277.11588 found 277.11585.



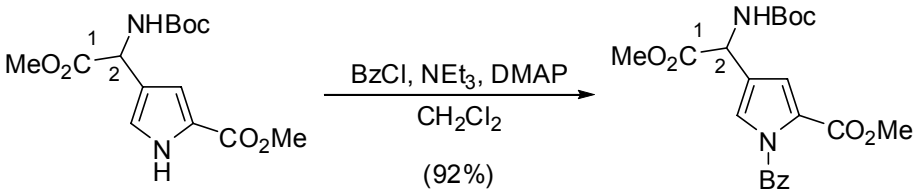
9 **3**

4-[(*S*)-*tert*-Butoxycarbonylamino-methoxycarbonyl-methyl]-1*H*-pyrrole-2-carboxylic acid methyl ester (3). To a stirred solution of compound **9** (1.03 g, 4.05 mmol) in anhydrous THF (32 mL) at 0 °C was added 2,6-lutidine (1.20 mL, 10.3 mmol). Freshly distilled trichloroacetyl chloride (1.20 mL, 10.3 mmol) was added dropwise and the mixture was allowed to warm to room temperature. After being stirred for 12 hours, the reaction mixture was quenched with water. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution, brine, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The resulting crude product was dissolved in anhydrous MeOH (81 mL) and placed at 0 °C. Sodium methoxide (1.00 g, 18.5 mmol) was added and the mixture was stirred at 0 °C for 15 minutes. It was then acidified with 3.0 N aqueous HCl to pH 3-4. After removal of the solvent under reduced pressure, the residue was dissolved in CH_2Cl_2. Water was added and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The crude product was purified by flash chromatography on silica gel (eluent: pentane/EtOAc, 9/1 to 7/3) to afford **3** (1.14 g, 90% over two steps) as a white solid: mp 40-41 °C; $[\alpha]_D^{20}$ +86.8 (*c* 1.00 in $CHCl_3$); ν_{MAX}/cm^{-1} (KBr disc) 3400-3200 (broad, NH), 1735 (CO), 1693 (CO); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.44 (9H, s, C(C*H*$_3$)$_3$), 3.76 (3H, s, OC*H*$_3$), 3.84 (3H, s, OC*H*$_3$), 5.11-5.33 (2H, m, C(2)*H* and N*H*), 6.86-6.87 (1H, m, pyrr*H*), 6.96-6.97 (1H, m, pyrr*H*), 9.07 (1H, br s, N*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 28.2 (C(*C*H$_3$)$_3$), 51.3 (*C*(2)H), 51.5 (O*C*H$_3$), 52.5 (O*C*H$_3$), 80.1 (*C*(CH$_3$)$_3$), 113.4 (pyrr*C*H), 121.3 (pyrr*C*), 121.4 (pyrr*C*H), 123.0 (pyrr*C*), 155.0 (*C*=O), 161.4 (*C*=O), 171.2 (*C*=O); *m*/*z* (DCI, NH_3/isobutane) 313 ([M+H]$^+$), 274, 213, 196 (100%); Elemental analysis, calcd (%) for $C_{14}H_{20}N_2O_6$: C, 53.84; H, 6.46; N, 8.97. Found: C, 53.95; H, 6.73; N, 8.98.



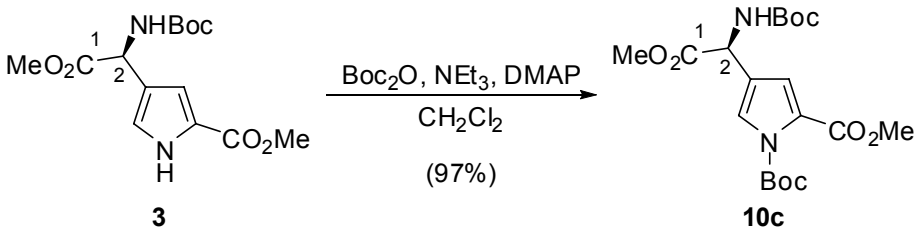
3 **10a**

***rac*-4-(*tert*-Butoxycarbonylamino-methoxycarbonyl-methyl-1-methyl-1*H*-pyrrole-2-carboxylic acid methyl ester (10a).** To a stirred solution of pyrrole **3** (78 mg, 0.25 mmol) in anhydrous DMF (4.2 mL) at 0 °C was added sodium hydride (60% dispersion in mineral oil, 11 mg, 0.27 mmol). The mixture was stirred 15 minutes at room temperature, where'upon iodomethane (17 µL, 0.27 mmol) was added at 0 °C. The resulting mixture was allowed to warm slowly to room temperature, and stirred for 12 hours. Water was added and the aqueous layer was extracted three times with Et_2O. The combined organic layers were washed with water, brine, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (eluent: pentane/EtOAc, 9/1 to 1/1) to afford *N*-methyl-pyrrole **10a** (65 mg, 0.20 mmol, 80%) as a yellow oil: ν_{MAX}/cm^{-1} (thin film) 3500-3300 (broad, NH), 1752 (CO), 1710 (broad, CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.44-1.46 (9H, m, C(C*H*$_3$)$_3$), 3.75 (3H, s, OC*H*$_3$), 3.80 (3H, s, OC*H*$_3$), 3.88 (3H, s, NC*H*$_3$), 4.94-5.31 (2H, m, C(2)*H* and N*H*), 6.81 (1H, s, pyrr*H*), 6.89 (1H, s, pyrr*H*); δ_C (100 MHz; $CDCl_3$; Me_4Si) 28.3 (C(*C*H$_3$)$_3$), 36.9 (N*C*H$_3$), 51.1 (O*C*H$_3$), 51.1 (*C*(2)H), 52.6 (O*C*H$_3$), 80.1 (*C*(CH$_3$)$_3$), 115.7 (pyrr*C*H), 118.7 (pyrr*C*), 122.8 (pyrr*C*), 127.6 (pyrr*C*), 154.9 (*C*=O), 161.3 (*C*=O), 171.8 (*C*=O); *m*/*z* (DCI, NH_3/isobutane) 327 ($[M+H]^+$), 288, 210 (100%); Elemental analysis, calcd (%) for $C_{15}H_{22}N_2O_6$: C, 55.21; H, 6.80; N, 8.59. Found: C, 54.78; H, 6.87; N, 8.43.



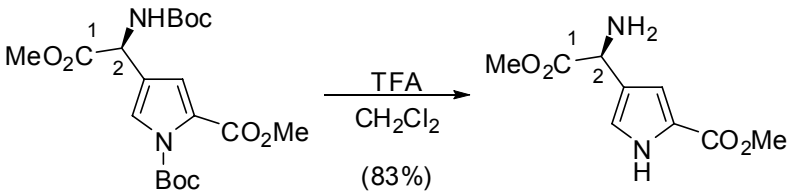
3 **10b**

***rac*-1-Benzoyl-4-(*tert*-butoxycarbonylamino-methoxycarbonyl-methyl)-1*H*-pyrrole-2-carboxylic acid methyl ester (10b).** To a stirred solution of pyrrole **3** (78 mg, 0.25 mmol) in anhydrous CH_2Cl_2 (2.5 mL) at 0 °C was added NEt_3 (70 μL, 0.50 mmol), DMAP (3 mg, 0.02 mmol) and freshly distilled benzoyl chloride (43 μL, 0.37 mmol). The temperature was allowed to warm to room temperature, and stirred for 3 hours. Water was added and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with saturated aqueous $NaHCO_3$, brine, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (eluent: pentane/EtOAc, 9/1 to 7/1) to afford *N*-benzoyl-pyrrole **10b** (96 mg, 0.23 mmol, 92%) as a yellow oil: ν_{MAX}/cm^{-1} (thin film) 3500-3300 (broad, NH), 1714 (broad, CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.45 (9H, s, C(C*H*$_3$)$_3$), 3.59 (3H, s, OC*H*$_3$), 3.79 (3H, s, OC*H*$_3$), 5.30-5.42 (2H, m, C(2)*H* and N*H*), 7.04-7.05 (1H, m, pyrr*H*), 7.23 (1H, s, pyrr*H*), 7.46-7.51 (2H, m, Ar*H*), 7.60-7.65 (1H, m, Ar*H*), 7.73-7.75 (2H, m, Ar*H*); δ_C (100 MHz; $CDCl_3$; Me_4Si) 28.2 (C(*C*H$_3$)$_3$), 50.9 (*C*(2)H), 51.7 (O*C*H$_3$), 52.8 (O*C*H$_3$), 80.4 (*C*(CH$_3$)$_3$), 119.3 (pyrr*C*H), 121.9 (pyrr*C*), 125.3 (pyrr*C*H), 126.5 (pyrr*C*), 128.7 (Ar*C*H), 129.9 (Ar*C*H), 132.9 (Ar*C*), 133.8 (Ar*C*H), 154.8 (*C*=O), 160.3 (*C*=O), 168.0 (*C*=O), 171.0 (*C*=O); *m*/*z* (DCI, NH_3/isobutane) 434 ($[M+NH_4]^+$), 417 ($[M+H]^+$), 378, 361 (100%); Elemental analysis, calcd (%) for $C_{21}H_{24}N_2O_7$: C, 60.57; H, 5.81; N, 6.73. Found: C, 60.35; H, 5.93; N, 6.72.



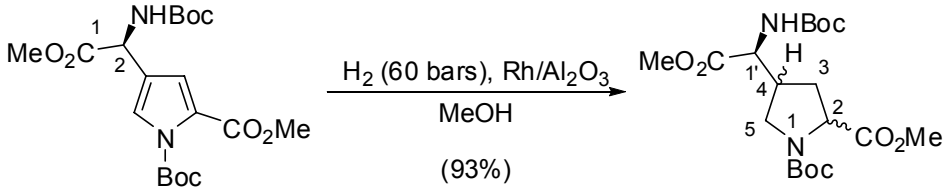
3 **10c**

4-[(*S*)-*tert*-Butoxycarbonylamino-methoxycarbonyl-methyl]-pyrrole-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-methyl ester (10c). To a stirred solution of pyrrole **3** (1.08 g, 3.46 mmol) in anhydrous CH_2Cl_2 (28 mL) at 0 °C was added anhydrous NEt_3 (1.00 mL, 7.17 mmol), DMAP (35 mg, 0.35 mmol) and Boc_2O (1.13 g, 5.18 mmol). The resulting mixture was stirred at 0 °C for 1 hour. Water was then added and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with water, brine, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (eluent: pentane/EtOAc, 9/1 to 7/3) to afford *N*-Boc-pyrrole **10c** (1.39 g, 3.37 mmol, 97%) as a yellow oil: $[\alpha]_D^{20}$ +66.5 (*c* 1.00 in $CHCl_3$); ν_{MAX}/cm^{-1} (thin film) 3400-3250 (broad, NH), 1753 (CO), 1727 (broad, CO), 1702 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.44 (9H, s, C(C*H*$_3$)$_3$), 1.57 (9H, s, C(C*H*$_3$)$_3$), 3.76 (3H, s, OC*H*$_3$), 3.83 (3H, s, OC*H*$_3$), 5.27-5.41 (2H, m, C(2)*H* and N*H*), 6.80 (1H, d, *J* = 2.1 Hz, pyrr*H*), 6.72 (1H, d, *J* = 2.1 Hz, pyrr*H*); δ_C (75 MHz; $CDCl_3$; Me_4Si) 27.6 (C(*C*H$_3$)$_3$), 28.2 (C(*C*H$_3$)$_3$), 50.9 (*C*(2)H), 51.9 (O*C*H$_3$), 52.7 (O*C*H$_3$), 80.3 (*C*(CH$_3$)$_3$), 85.2 (*C*(CH$_3$)$_3$), 118.7 (pyrr*C*H), 121.3 (pyrr*C*), 124.1 (pyrr*C*H), 125.7 (pyrr*C*), 147.8 (*C*=O), 154.8 (*C*=O), 160.8 (*C*=O), 171.0 (*C*=O); *m*/*z* (DCI, NH_3/isobutane) 413 ($[M+H]^+$), 313, 274, 213, 196 (100%); Elemental analysis, calcd (%) for $C_{19}H_{28}N_2O_8$: C, 55.34; H, 6.85; N, 6.80. Found: C, 55.74; H, 7.13; N, 6.62.



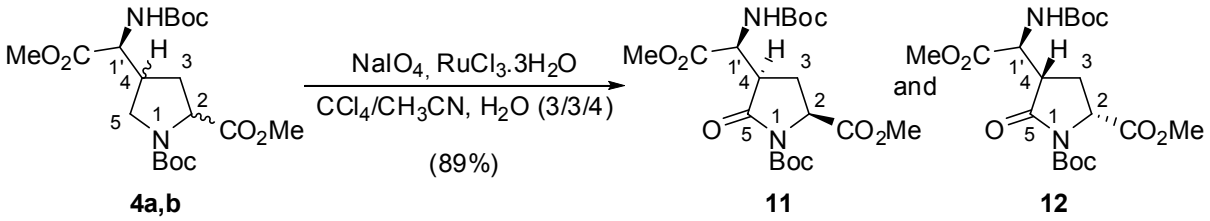
10c **10d**

4-[(*S*)-Amino-methoxycarbonyl-methyl]-1*H*-pyrrole-2-carboxylic acid methyl ester (10d). To a stirred solution of pyrrole **10c** (124 mg, 0.31 mmol) in anhydrous CH_2Cl_2 (3.1 mL) at 0 °C was added anhydrous TFA (460 μL, 6.21 mmol). After being stirred for 2 hours at this temperature, solvents were evaporated under reduced pressure. The crude product was purified by flash chromatography on silica gel (eluent: EtOAc/MeOH, 1/0 to 9/1) to afford pyrrole **10d** (55 mg, 0.26 mmol, 83%) as a yellow oil. The enantiomeric ratio was determined by ^{1}H NMR spectrum in the presence of the chiral shift reagent, europium (III) tris-[3-heptafluoropropylhydroxymethylene)-(+)-camphorate] Eu(hfc)$_3$, and was 98:2. $[\alpha]_D^{20}$ +65.6 (*c* 1.00 in $CHCl_3$); ν_{MAX}/cm^{-1} (thin film) 3369 (NH_2), 1718 (CO), 1702 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.89 (2H, br s, N*H*$_2$), 3.74 (3H, s, OC*H*$_3$), 3.84 (3H, s, OC*H*$_3$), 4.59 (1H, s, C(2)*H*), 6.90-6.91 (1H, m, pyrr*H*), 6.97-6.98 (1H, m, pyrr*H*), 9.41 (1H, br s, N*H*); δ_C (100 MHz; $CDCl_3$; Me_4Si) 51.5 (*C*(2)H), 52.3 (O*C*H$_3$), 52.4 (O*C*H$_3$), 113.2 (pyrr*C*H), 120.1 (pyrr*C*H), 122.9 (pyrr*C*), 125.0 (pyrr*C*), 161.4 (*C*=O), 174.9 (*C*=O); *m*/*z* (ESI$^+$) 235 ([M+Na]$^+$), 213 ([M+H]$^+$); HRMS (ESI$^+$) $C_9H_{12}N_2O_4Na$ ([M+Na]$^+$) requires 235.06893, found 235.06876.



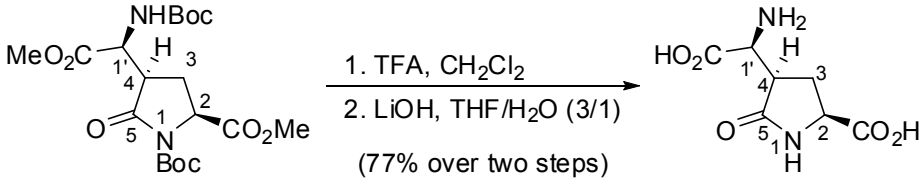
10c **4a,b**

(2*S*,4*S*)-4-[(*S*)-*tert*-Butoxycarbonylamino-methoxycarbonyl-methyl]-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-methyl ester (4a) and (2*R*,4*R*)-4-[(*S*)-*tert*-butoxycarbonylamino-methoxycarbonyl-methyl]-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-methyl ester (4b). To a stirred solution of pyrrole **10c** (1.00 g, 2.42 mmol) in anhydrous MeOH (12 mL) in pressure vessel, was added rhodium on alumina (200 mg, 5% in weight, 0.05 mmol). The reactor was magnetically stirred and the reaction was carried out under a pressure of 60 bars of hydrogen. After being stirred 2 hours, the mixture was filtered through a celite pad and the solvent was removed under reduced pressure. The product ratio was determined by ^{13}C NMR of the crude mixture. The residue was purified by flash chromatography on silica gel (eluent: pentane/EtOAc, 9/1 to 1/1) to afford pyrrolidine **4a,b** in a mixture of diastereoisomers (0.94 g, 2.26 mmol, 93%, dr = 1:1) as a white foam: ν_{MAX}/cm^{-1} (KBr disc) 3500-3300 (broad, NH), 1743 (CO), 1706 (broad, CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.24-1.45 (m, 18H, 2 × C(C*H*$_3$)$_3$), 1.76-1.88 (1H, m, 1H of C(3)*H*$_2$), 2.27-2.58 (2H, m, 1H of C(3)*H*$_2$ and C(4)*H*), 3.21-3.30 (1H, m, 1H of C(5)*H*$_2$), 3.54-3.77 (7H, m, 1H of C(5)*H*$_2$ and 2 × OC*H*$_3$), 4.16-4.29 (2H, m, C(2)*H* and C(1')*H*), 5.11-5.17 (1H, m, N*H*); δ_C (100 MHz; $CDCl_3$; Me_4Si) 28.2 and 28.3 (C(*C*H$_3$)), 31.7 and 34.5 (*C*(3)H$_2$), 40.4 and 41.1 (*C*(4)H), 48.0 and 48.6 (*C*(5)H$_2$), 52.0 and 52.5 (O*C*H$_3$), 53.8 and 54.3 (*C*(1')H), 58.3 and 59.1 (*C*(2)H), 80.3 (*C*(CH$_3$)$_3$), 153.3 and 155.4 (*C*=O), 171.8 and 173.0 (*C*=O); *m*/*z* (DCI, NH_3/isobutane) 434 ([M+NH_4]$^+$), 317 (100%); Elemental analysis, calcd (%) for $C_{19}H_{32}N_2O_8$: C, 54.80; H, 7.75; N, 6.73. Found: C, 54.79; H, 7.90; N, 6.76.



(2*S*,4*R*)-4-[(*S*)-*tert*-Butoxycarbonylamino-methoxycarbonyl-methyl]-5-oxo-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-methyl ester (11) and (2*R*,4*S*)-4-[(*S*)-*tert*-butoxycarbonylamino-methoxycarbonyl-methyl]-5-oxo-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-methyl ester (12). To a stirred solution of pyrrolidines **4a,b** (500 mg, 1.20 mmol) in a mixture of CCl_4, CH_3CN and H_2O (3/3/4, 24 mL) at 0 °C were sequentially added $NaIO_4$ (1.30 g, 6.06 mmol) and $RuCl_3,3H_2O$ (50 mg, 0.24 mmol). The resulting mixture was slowly warmed to room temperature and then stirred at this temperature for 36 hours. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were dried over anhydrous $MgSO_4$, filtered through a celite pad and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (eluent: pentane/EtOAc, 9/1 to 1/1) to afford pyrrolidinone **11** (*cis-syn*) (230 mg, 44%) as a white solid and pyrrolidinone **12** (*cis-anti*) (233 mg, 45%) as a white solid. **Data for compound 11** (*cis-syn*): mp 69-70 °C; $[\alpha]_D^{20}$ +15.1 (*c* 1.00 in $CHCl_3$); ν_{MAX}/cm^{-1} (KBr disc) 3500-3300 (broad, NH), 1798 (CO), 1748 (CO), 1714 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.44 (9H, s, C(CH_3)$_3$), 1.46 (9H, s, C(CH_3)$_3$), 1.93 (1H, ddd, *J* = 13.3, 10.9 and 8.9 Hz, 1H of C(3)H_2), 2.55 (1H, ddd, *J* = 13.2, 9.7 and 8.2 Hz, 1H of C(3)H_2), 3.48 (1H, dt, *J* = 10.8, and 3.0 Hz, C(4)*H*), 3.76 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 4.50 (1H, dd, *J* = 10.7 and 8.5 Hz, C(2)*H*), 4.53 (1H, d, *J* = 8.9 Hz, C(1')*H*), 5.29 (1H, d, *J* = 8.7 Hz, N*H*); δ_C (100 MHz; $CDCl_3$; Me_4Si) 24.3 (*C*(3)H_2), 27.7 (C(*C*H_3)$_3$), 28.1 (C(*C*H_3)$_3$), 45.7 (*C*(4)H), 52.4 (2 × O*C*H_3), 52.8 (*C*(1')H), 57.1 (*C*(2)H), 80.3 (*C*(CH$_3$)$_3$), 84.0 (*C*(CH$_3$)$_3$), 148.7 (*C*=O), 156.1 (*C*=O), 170.3 (*C*=O), 171.1 (*C*=O), 171.8 (*C*=O); *m*/*z* (DCI, NH_3/isobutane) 448 ([M+NH_4]$^+$), 376, 331, 231 (100%); Elemental analysis, calcd (%) for $C_{19}H_{30}N_2O_9$: C, 53.02; H, 7.03; N, 6.51. Found: C, 52.67; H, 7.18; N, 6.34; **Data for compound 12** (*cis-anti*): mp 50-51 °C; $[\alpha]_D^{20}$ +14.1 (*c* 1.00 in $CHCl_3$); ν_{MAX}/cm^{-1} (KBr disc) 3500-3300 (broad, NH), 1790 (CO), 1752 (broad, CO), 1718 (CO); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.44 (9H, s, C(CH_3)$_3$), 1.49 (9H, s, C(CH_3)$_3$), 2.06-2.16 (1H, m, 1H of C(3)H_2), 2.49-2.60 (1H, m, 1H of C(3)H_2), 3.07 (1H, dt, *J* = 9.9 and 4.1 Hz, C(4)*H*), 3.76 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 4.52 (1H, dd, *J* = 8.8 and 7.7 Hz, C(2)*H*), 4.57 (1H, dd, *J* = 8.7

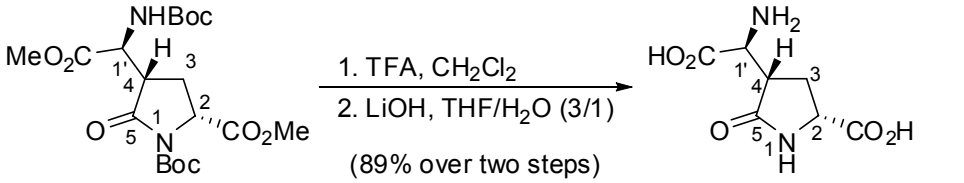
and 4.2 Hz, C(1')*H*), 5.64 (1H, br s, N*H*); δ_C (100 MHz; $CDCl_3$; Me_4Si) 24.0 (*C*(3)H_2), 27.8 (C(*C*H_3)$_3$), 28.1 (C(*C*H_3)$_3$), 45.4 (*C*(4)H), 52.5 (O*C*H_3), 52.6 (O*C*H_3), 52.9 (*C*(1')H), 57.0 (*C*(2)H), 80.3 (*C*(CH$_3$)$_3$), 84.0 (*C*(CH$_3$)$_3$), 148.9 (*C*=O), 155.2 (*C*=O), 170.5 (*C*=O), 171.3 (*C*=O), 172.1 (*C*=O); *m*/*z* (DCI, NH_3/isobutane) 448 ([M+NH_4]$^+$), 376, 331, 231 (100%); Elemental analysis, calcd (%) for $C_{19}H_{30}N_2O_9$: C, 53.02; H, 7.03; N, 6.51. Found: C, 52.73; H, 7.09; N, 6.23.



11 Penmacric acid (**1**)

(2*S*,4*R*)-4-[(*S*)-Amino-carboxy-methyl]-5-oxo-pyrrolidine-2-carboxylic acid; Penmacric acid (1). To a stirred solution of pyrrolidinone **11** (186 mg, 0.43 mmol) in anhydrous CH_2Cl_2 (4.3 mL) at 0 °C was added anhydrous trifluoroacetic acid (640 µL, 8.64 mmol). After being stirred for 2 hours at this temperature, solvents were evaporated under reduced pressure. The resulting crude product was dissolved in a THF/H_2O mixture (3/1, 21 mL) at 0 °C. Lithium hydroxide monohydrate (72 mg, 1.72 mmol) was added and the resulting mixture was stirred for 2 hours at this temperature. It was then acidified with 0.2 N aqueous HCl to pH 3. After removal of the solvent *in vacuo*, the residue was passed through a column of Dowex 50W-X8 ion exchange resin (H^+ form), eluted with water and then 0.5 N aqueous ammonia. Lyophilization afforded penmacric acid **1** (67 mg, 77% over two steps) as a white hygroscopic solid: mp 194-195 °C; $[\alpha]_D^{20}$ +33.6 (*c* 0.070 in 0.1 N HCl), lit.[1] $[\alpha]_D^{20}$ +35 (*c* 0.070 in 0.1 N HCl); ν_{MAX}/cm^{-1} (KBr disc) 3600-2800 (broad, NH, NH_2 and OH), 1689 (broad, CO); δ_H (300 MHz; D_2O) 1.96 (1H, dd, *J* = 22.2 and 10.8 Hz, 1H of C(3)*H*$_2$), 2.75 (1H, ddd, *J* = 13.1, 8.5 and 8.4 Hz, 1H of C(3)*H*$_2$), 3.10 (1H, dd, *J* = 18.1 and 8.4 Hz, C(4)*H*), 3.94 (1H, d, *J* = 7.3 Hz, C(1')*H*), 4.21 (1H, t, *J* = 8.3 Hz, C(2)*H*); δ_C (100 MHz; D_2O) 29.3 (*C*(3)H_2), 41.7 (*C*(4)H), 55.0 (*C*(1')H), 56.1 (*C*(2)H), 172.0 (*C*=O), 177.7 (*C*=O), 178.9 (*C*=O); *m*/*z* (ESI$^+$) 225 ([M+Na]$^+$), 203 ([M+H]$^+$); HRMS (ESI$^+$) $C_7H_{11}N_2O_5$ ([M+H]$^+$) requires 203.06625 found 203.06563.

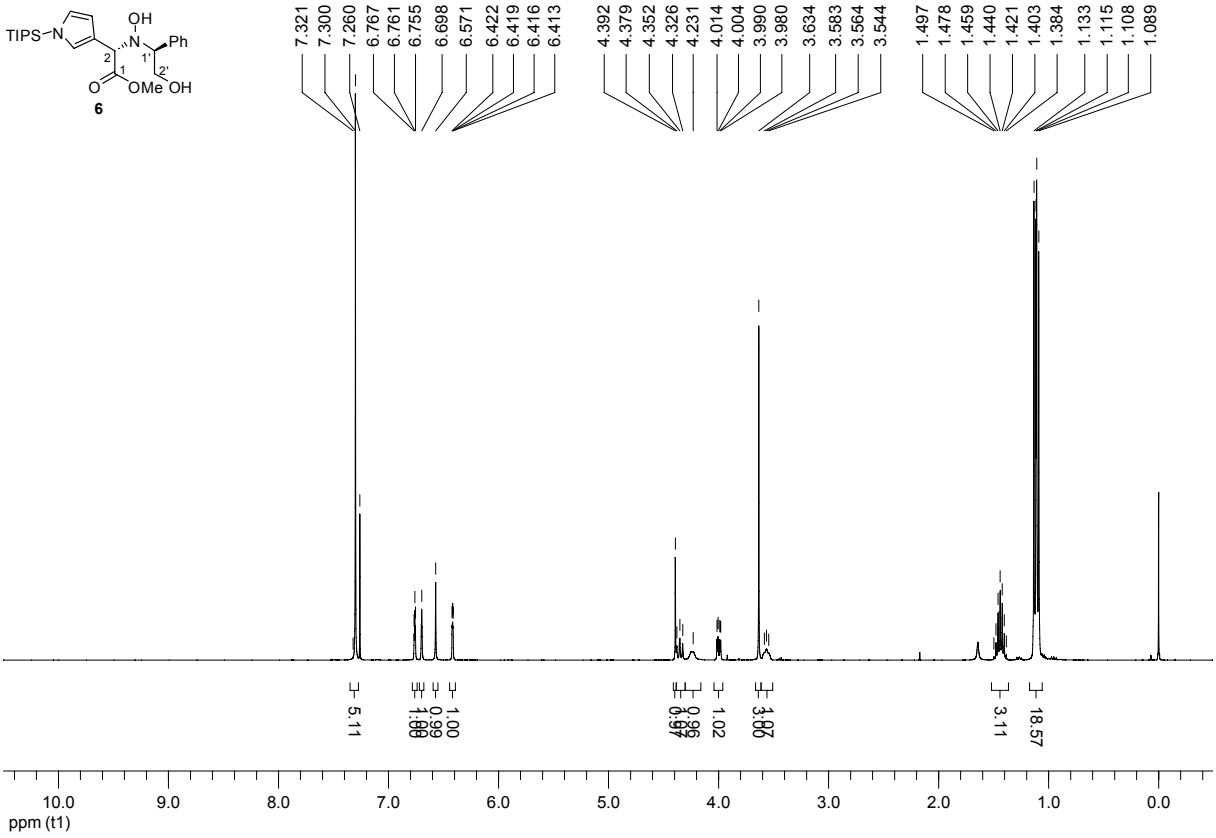
[1] Welter, A.; Jadot, J.; Dardenne, G.; Marlier, M.; Casimir, J. *Phytochemistry* **1975**, *14*, 1347-1350.



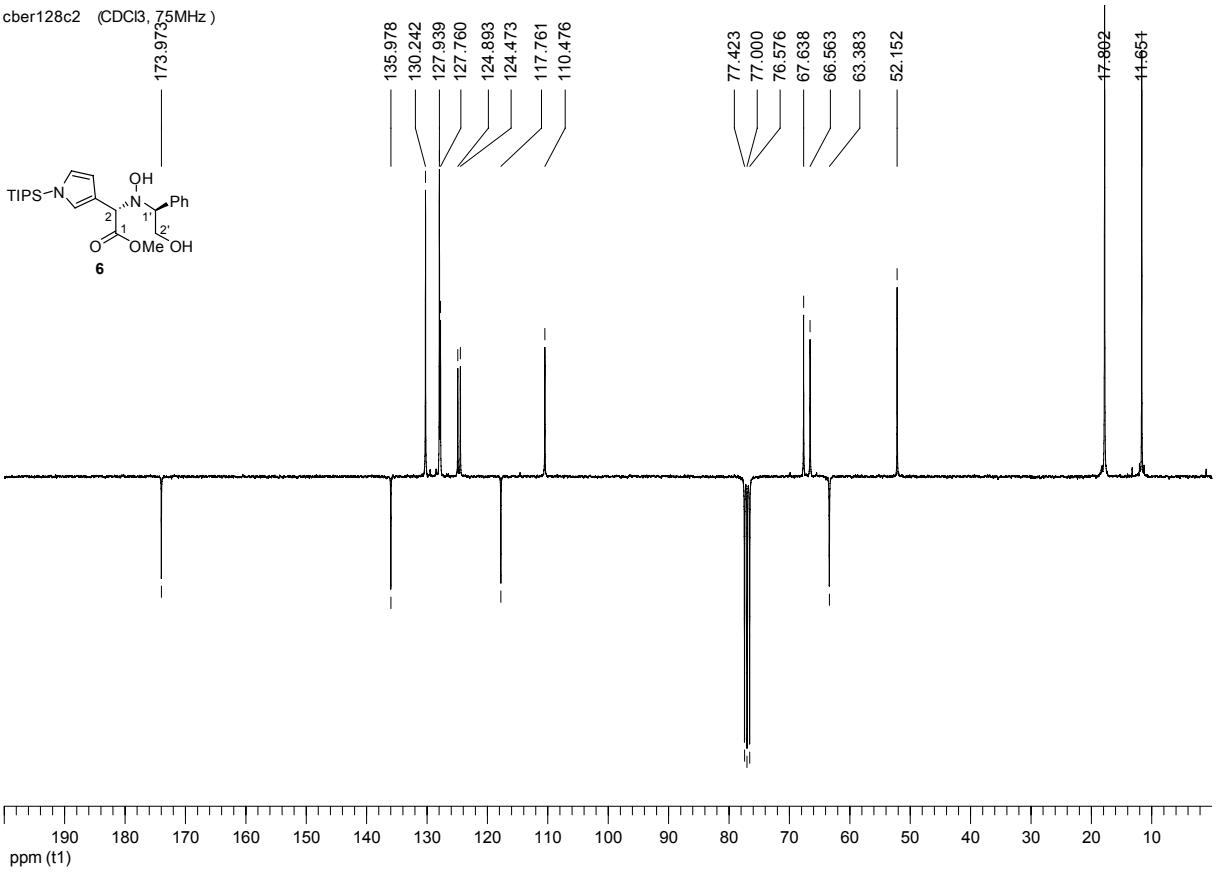
12 3,5-di-*epi*-Penmacric acid (**13**)

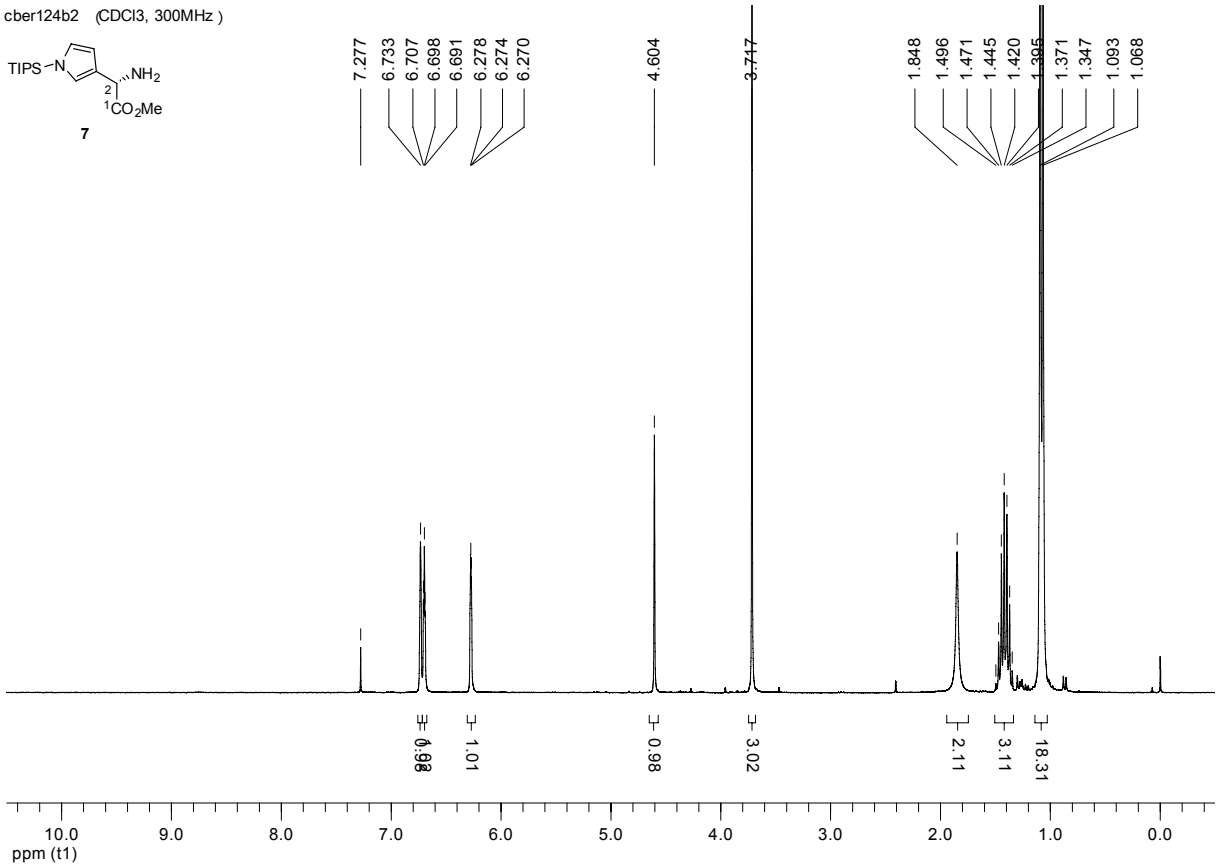
(2*R*,4*S*)-4-[(*S*)-Amino-carboxy-methyl]-5-oxo-pyrrolidine-2-carboxylic acid (13). The same procedure applied to pyrrolidinone **12** (220 mg, 0.51 mmol) afforded penmacric acid's stereoisomer **13** (91 mg, 89% over two steps) as a white hygroscopic solid: mp 137-138 °C (decomp.); $[\alpha]_D^{20}$ +32.4 (*c* 0.50 in 0.1N HCl); ν_{MAX}/cm^{-1} (KBr disc) 3600-2800 (broad, NH, NH_2 and OH), 1680 (broad, CO); δ_H (300 MHz; D_2O) 1.93 (1H, ddd, *J* = 13.5, 10.0 and 8.4 Hz, 1H of C(3)H_2), 2.65 (1H, ddd, *J* = 14.1, 11.4 and 8.8 Hz, 1H of C(3)H_2), 3.47 (1H, dt, *J* = 10.0 and 3.3 Hz, C(4)*H*), 4.19 (1H, d, *J* = 3.0 Hz, C(1')*H*), 4.24 (1H, t, *J* = 8.1 Hz, C(2)*H*); δ_C (100 MHz; D_2O) 25.9 (*C*(3)H_2), 42.7 (*C*(4)H), 52.8 (*C*(1')H), 56.0 (*C*(2)H), 172.6 (*C*=O), 177.2 (*C*=O), 179.2 (*C*=O); *m*/*z* (ESI^+) 225 ($[M+Na]^+$), 203 ($[M+H]^+$); HRMS (ESI^+) $C_7H_{11}N_2O_5$ ($[M+H]^+$) requires 203.06625 found 203.06561.

cber88d4 (CDCl3, 400MHz)



cber128c2 (CDCl3, 75MHz)

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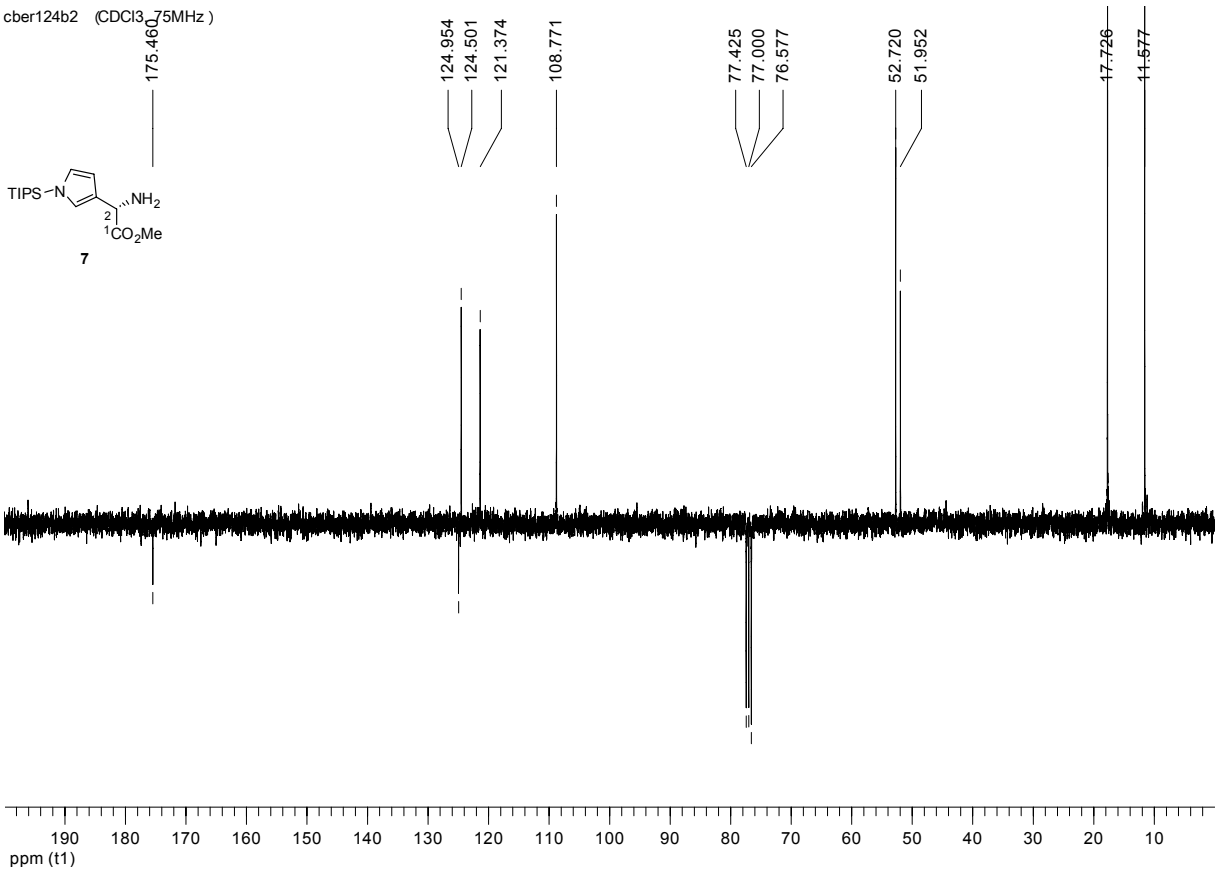
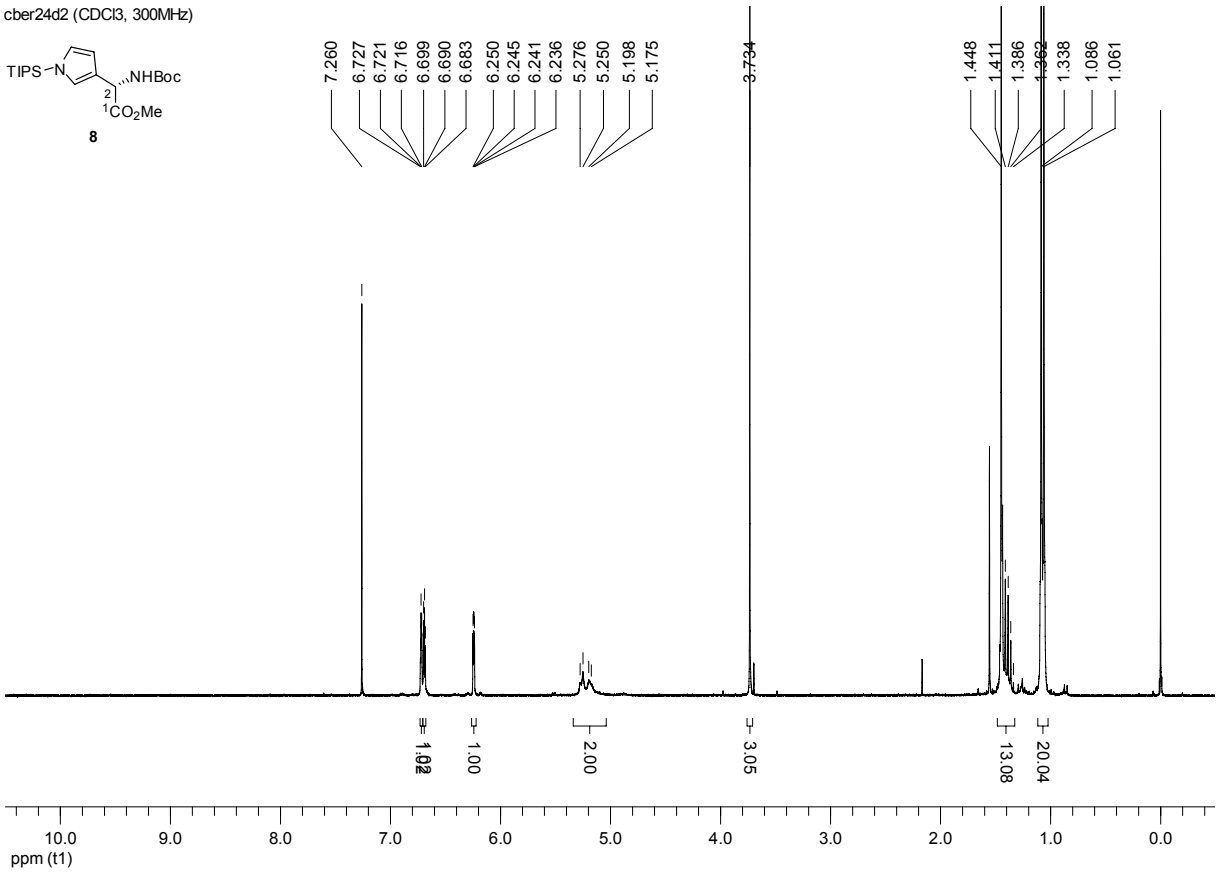
TIPS
NH2
CO2Me
7
7.277
6.733
6.707
6.698
6.691
6.278
6.274
6.270
4.604
3.717
1.848
1.496
1.471
1.445
1.420
1.395
1.371
1.347
1.093
1.068
1.01
0.98
3.02
2.11
3.11
18.31
ppm (t1)


cber124b2 (CDCl3, 75MHz)
175.460
124.954
124.501
121.374
108.771
77.425
77.000
76.577
52.720
51.952
17.726
11.577
TIPS
NH2
CO2Me
7
ppm (t1)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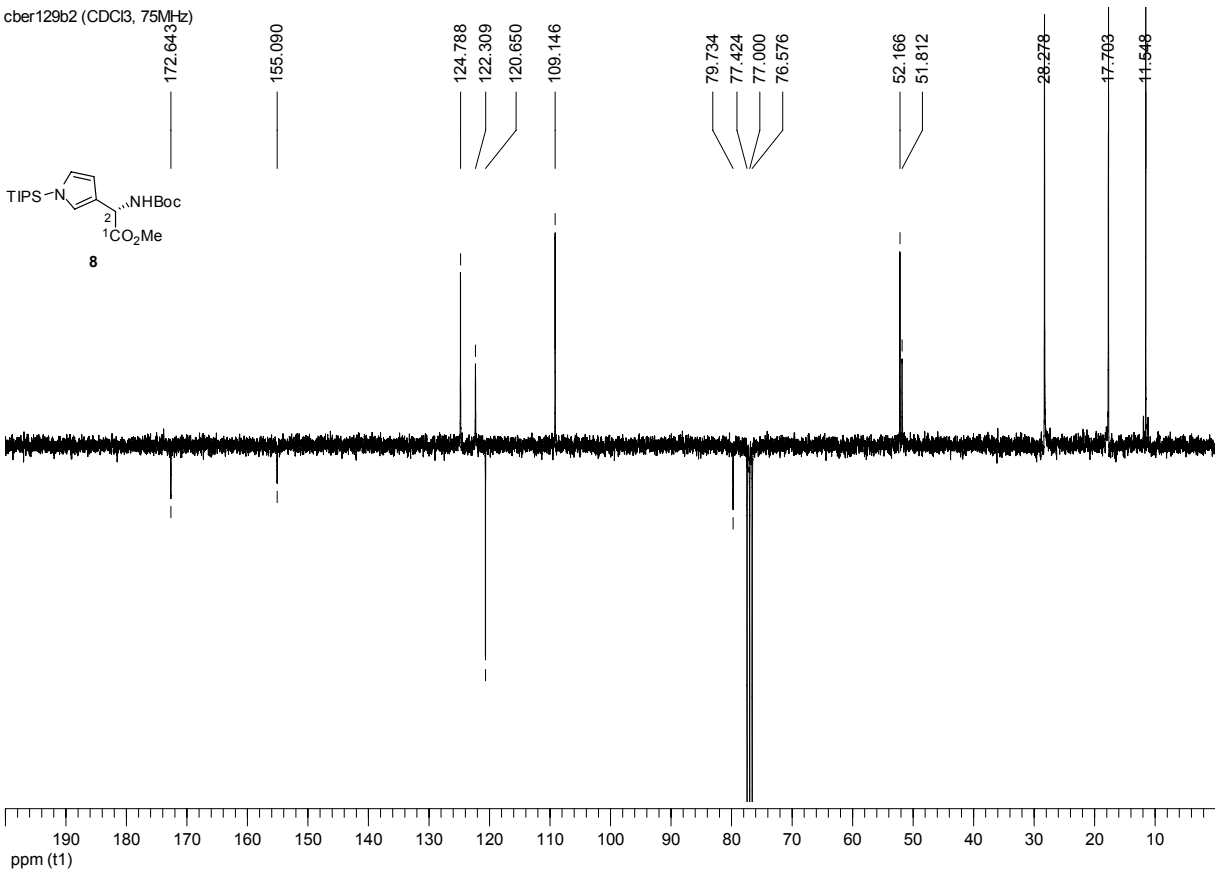
TIPS
NHBoc
2
1CO2Me
8
7.260
6.727
6.721
6.716
6.699
6.690
6.683
6.250
6.245
6.241
6.236
5.276
5.250
5.198
5.175
3.734
1.448
1.411
1.386
1.362
1.338
1.086
1.061
1.02
1.00
2.00
3.05
13.08
20.04
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)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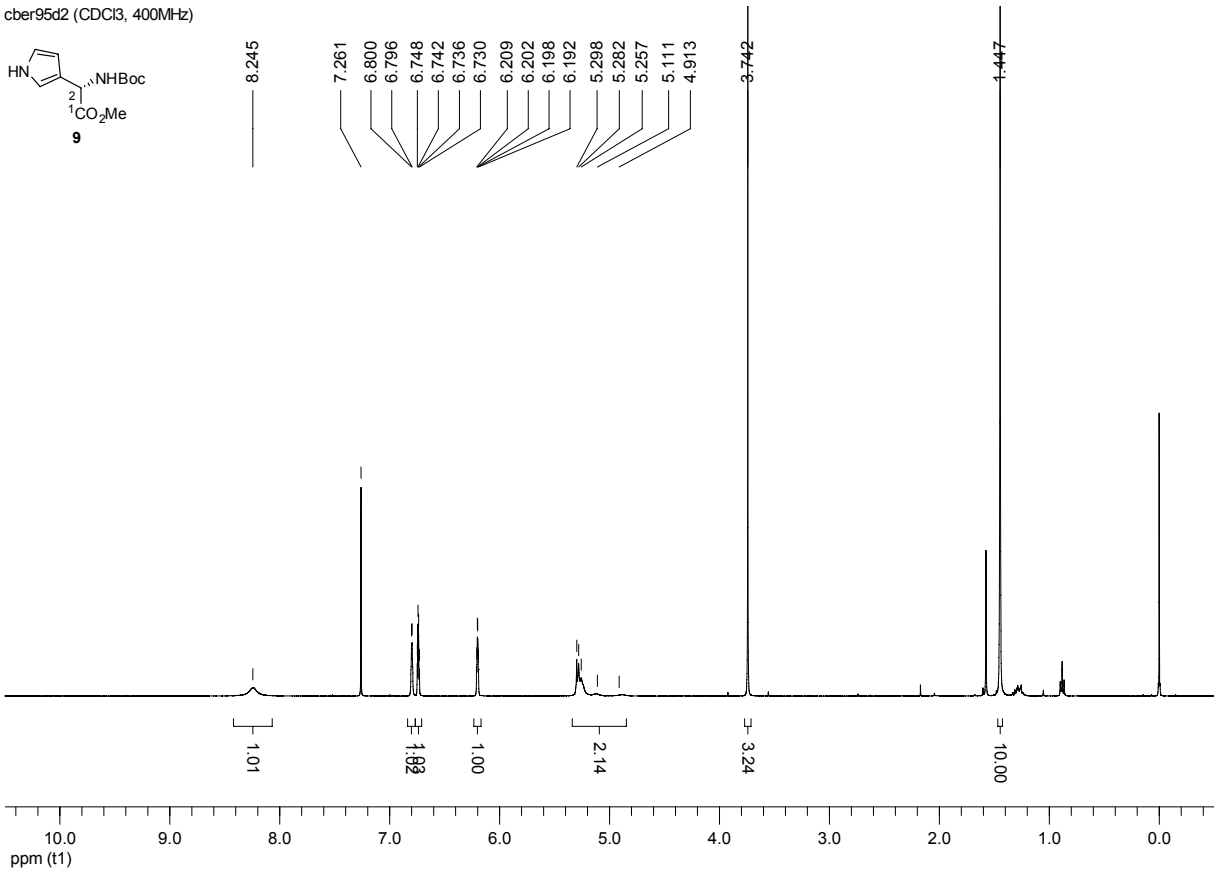
172.643
155.090
124.788
122.309
120.650
109.146
79.734
77.424
77.000
76.576
52.166
51.812
28.278
17.703
11.548
TIPS
NHBoc
2
1CO2Me
8
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)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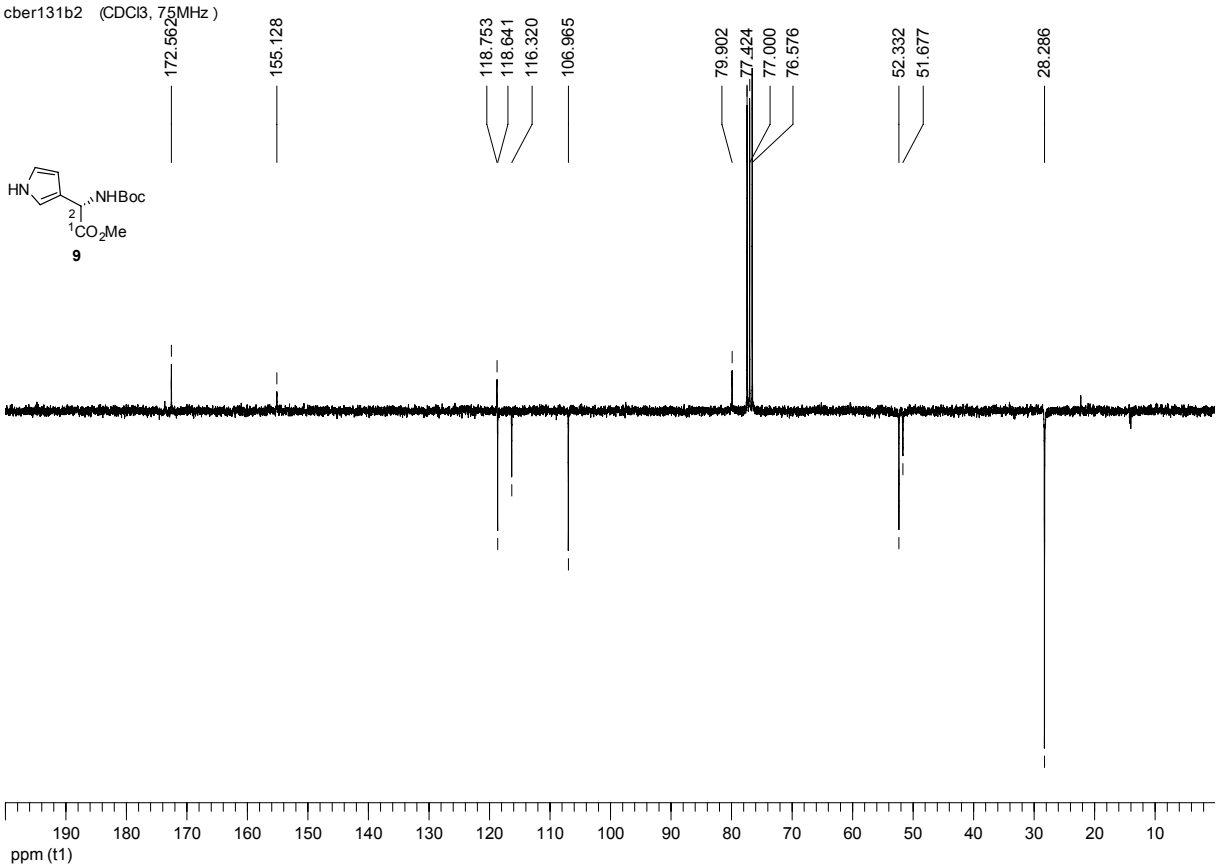
HN
NHBoc
2
1CO2Me
9
8.245
7.261
6.800
6.796
6.748
6.742
6.736
6.730
6.209
6.202
6.198
6.192
5.298
5.282
5.257
5.111
4.913
3.742
1.447
1.01
1.03
1.00
2.14
3.24
10.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)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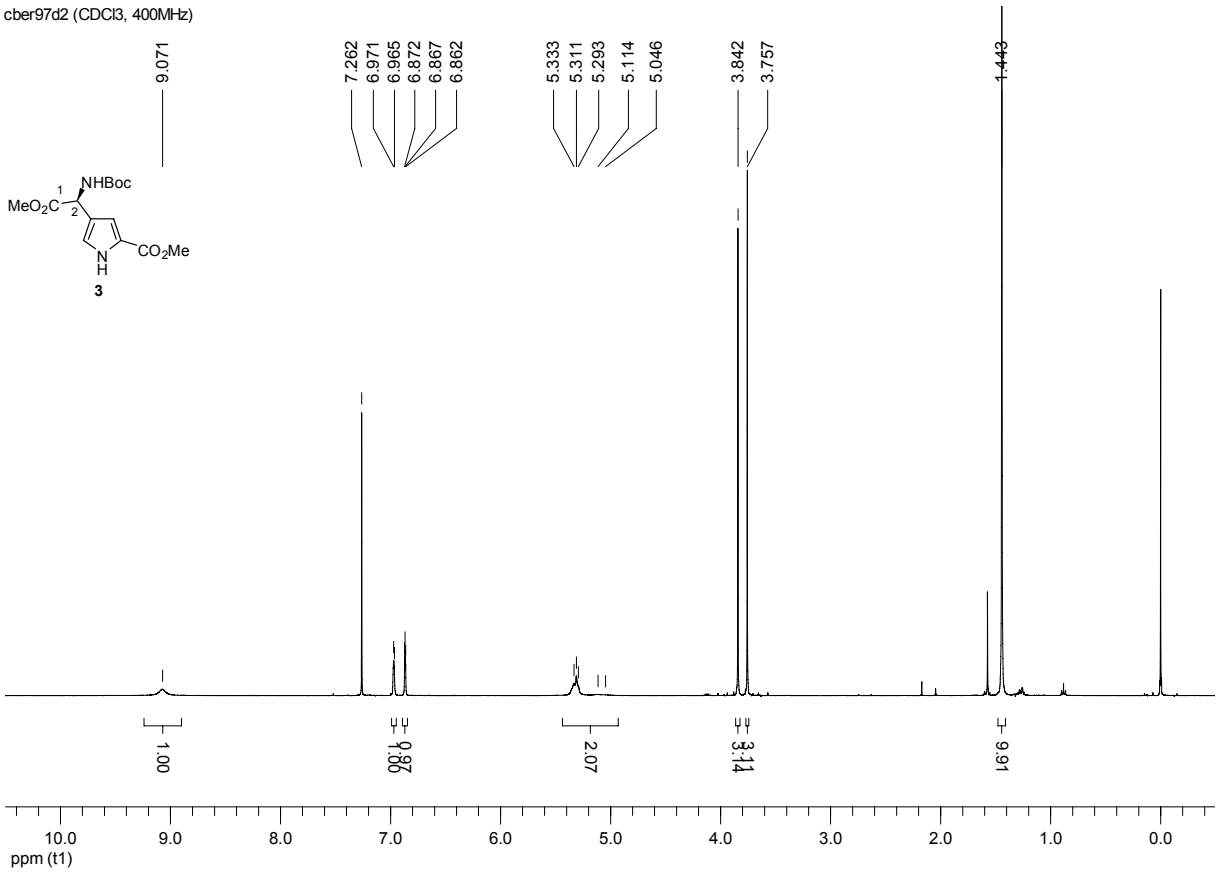
172.562
155.128
118.753
118.641
116.320
106.965
79.902
77.424
77.000
76.576
52.332
51.677
28.286
HN
NHBoc
2
1CO2Me
9
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)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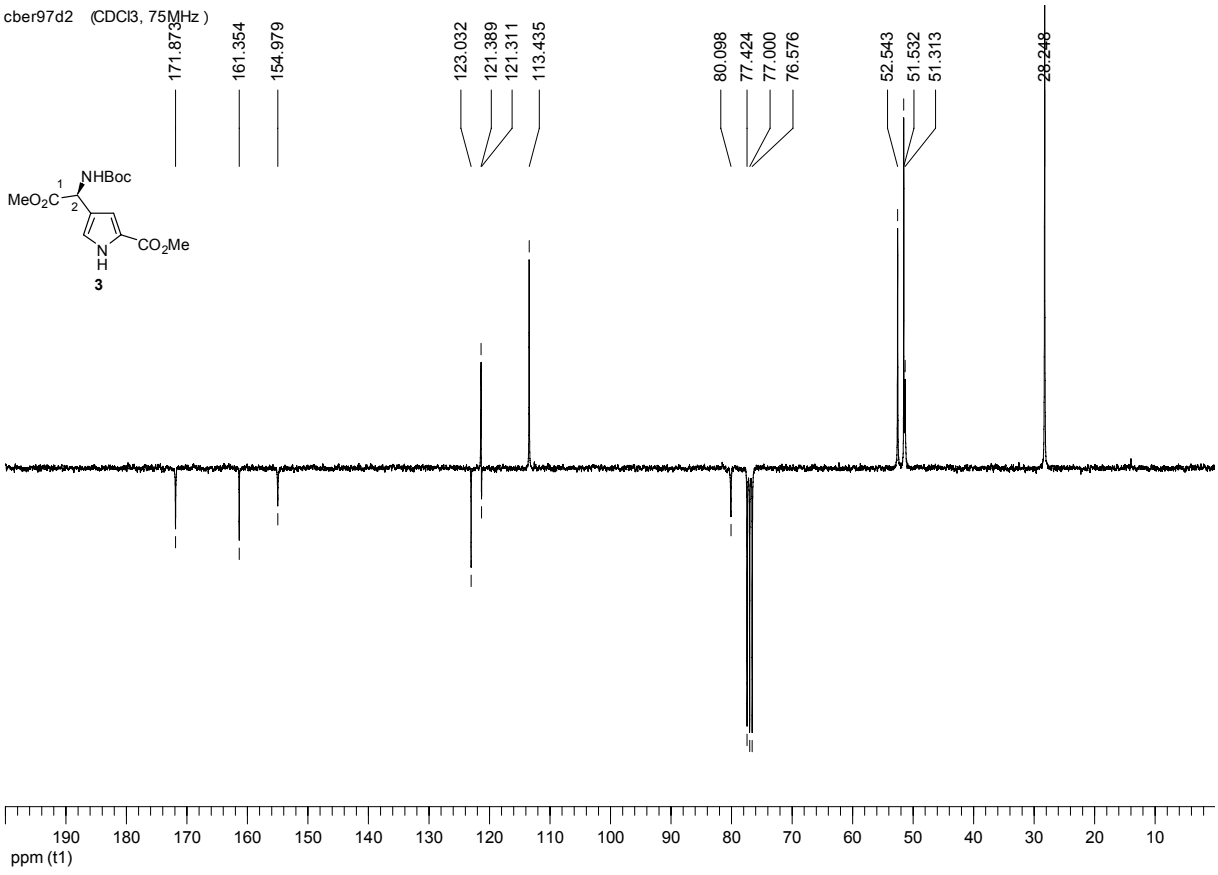
9.071
7.262
6.971
6.965
6.872
6.867
6.862
5.333
5.311
5.293
5.114
5.046
3.842
3.757
1.443
NHBoc
MeO2C
CO2Me
N
H
3
1.00
1.80
2.07
3.14
9.91
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)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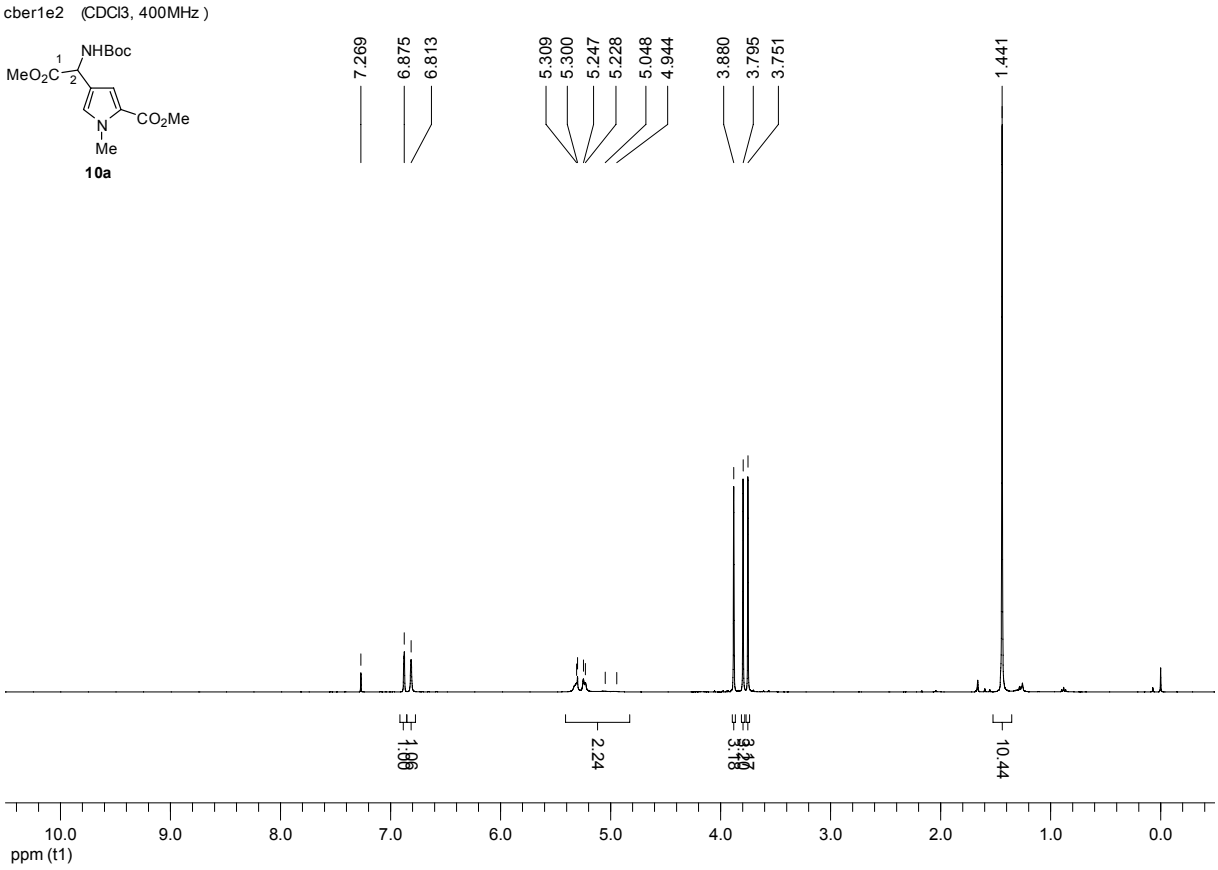
161.354
154.979
123.032
121.389
121.311
113.435
80.098
77.424
77.000
76.576
52.543
51.532
51.313
28.248
NHBoc
MeO2C
CO2Me
N
H
3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)


cber1e2 (CDCl3, 400MHz)
NHBoc
MeO2C
CO2Me
N
Me
10a
7.269
6.875
6.813
5.309
5.300
5.247
5.228
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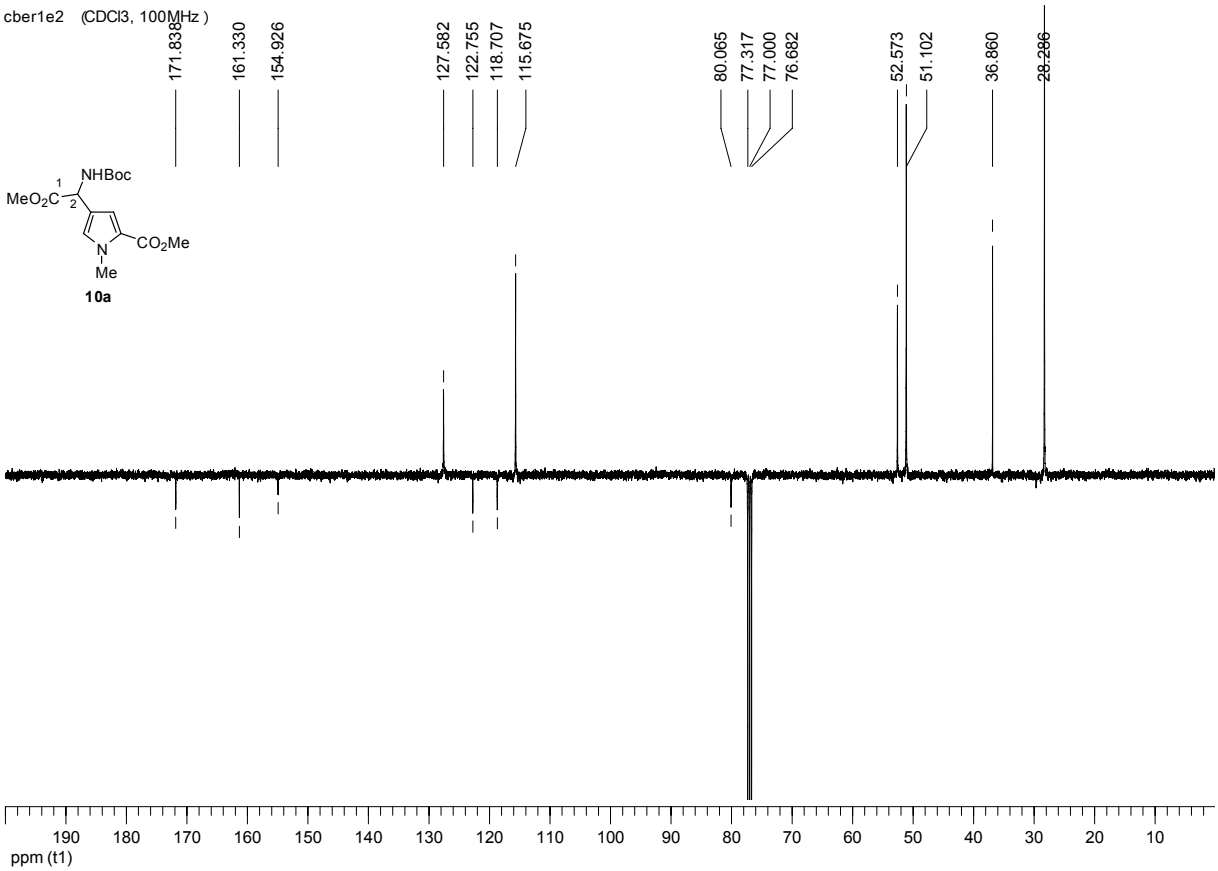
3.751
1.441
1.00
2.24
10.44
ppm (t1)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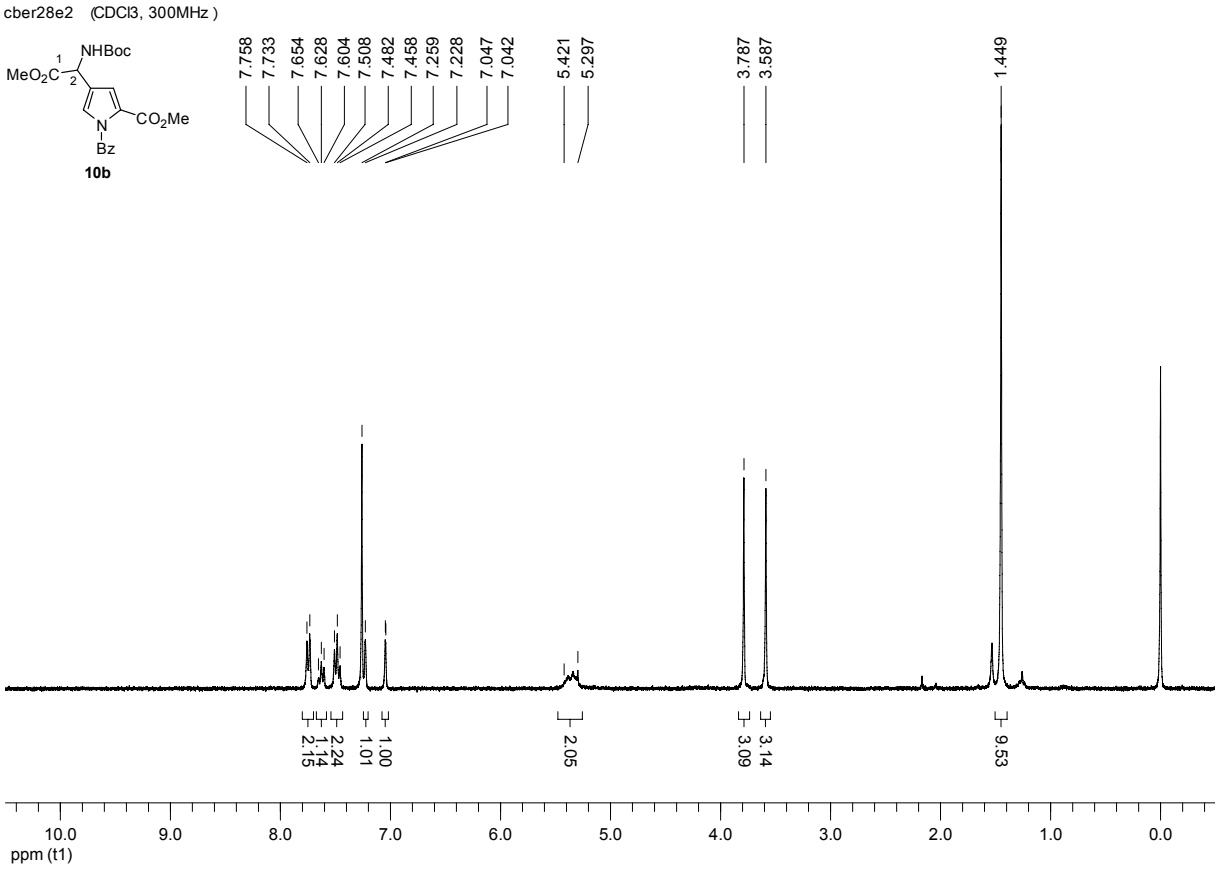
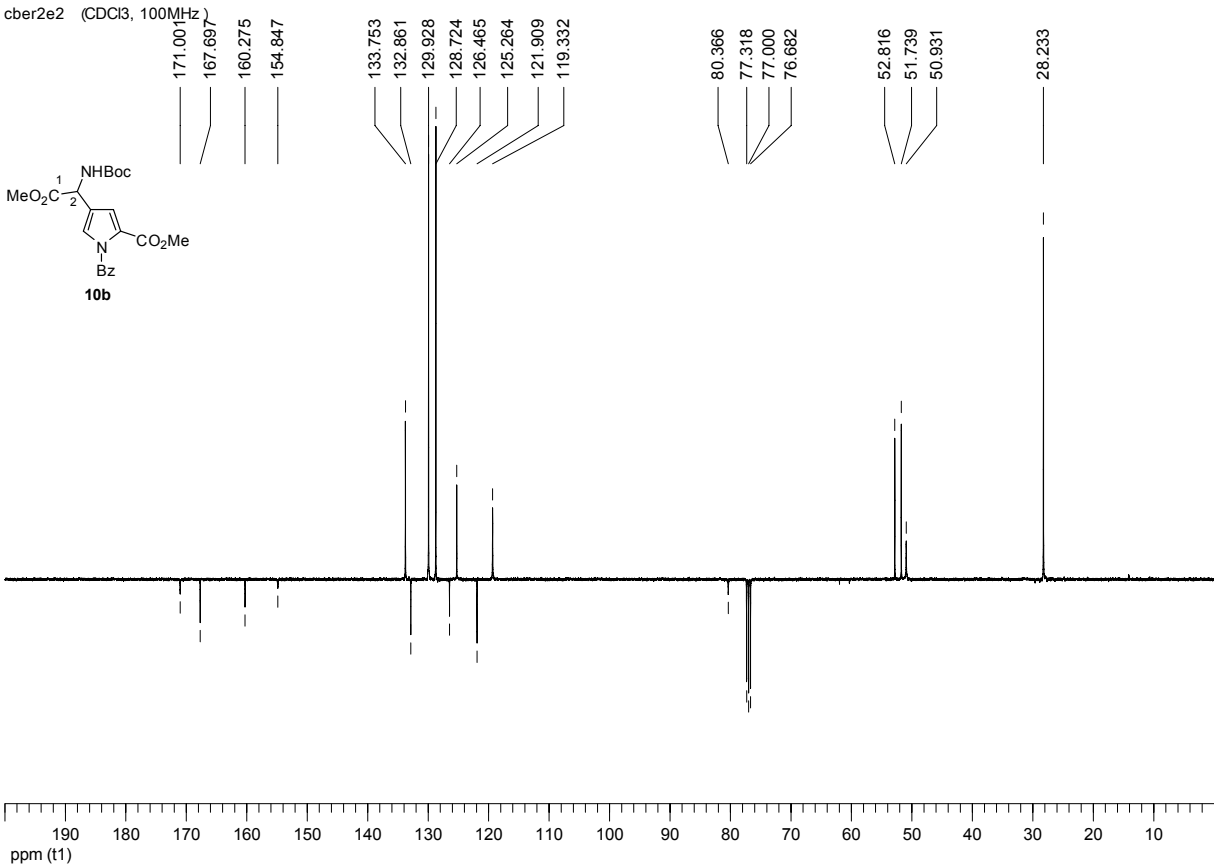
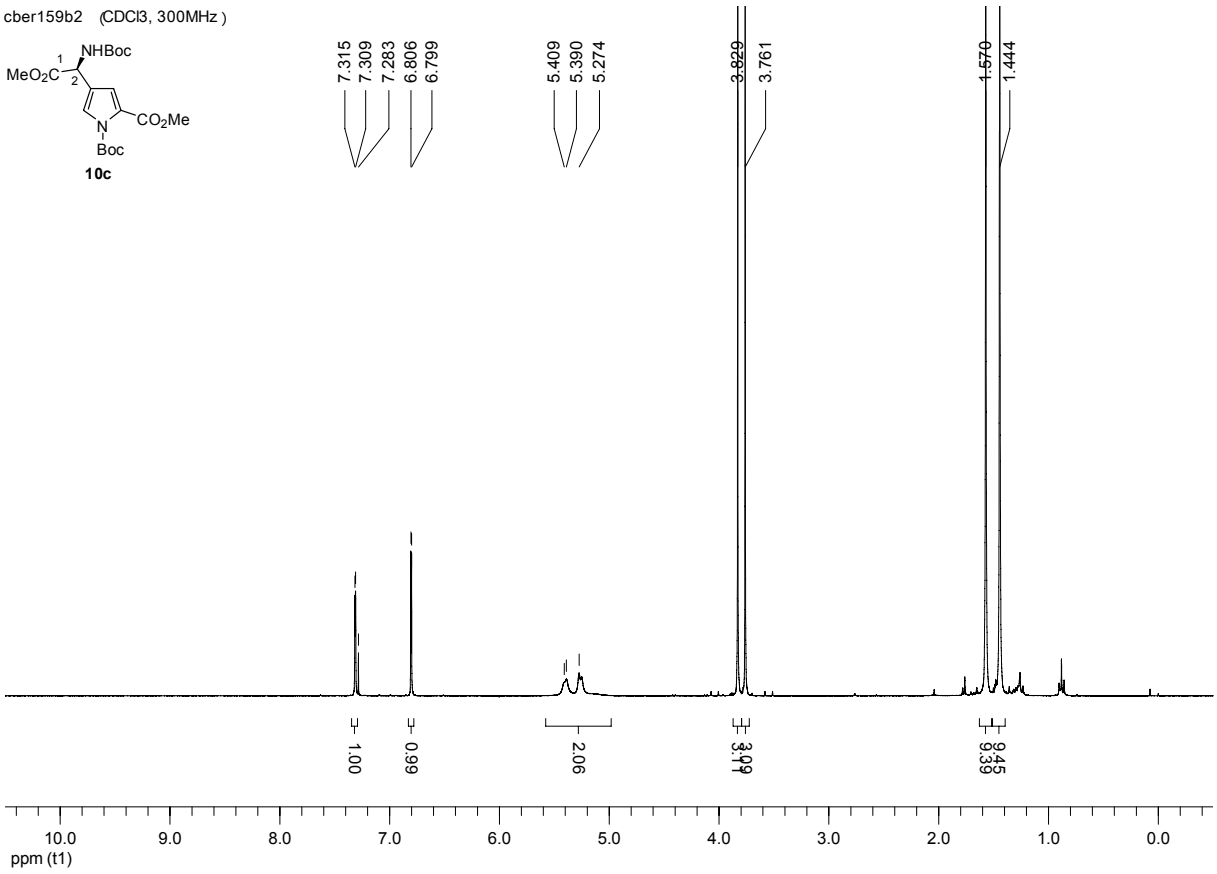
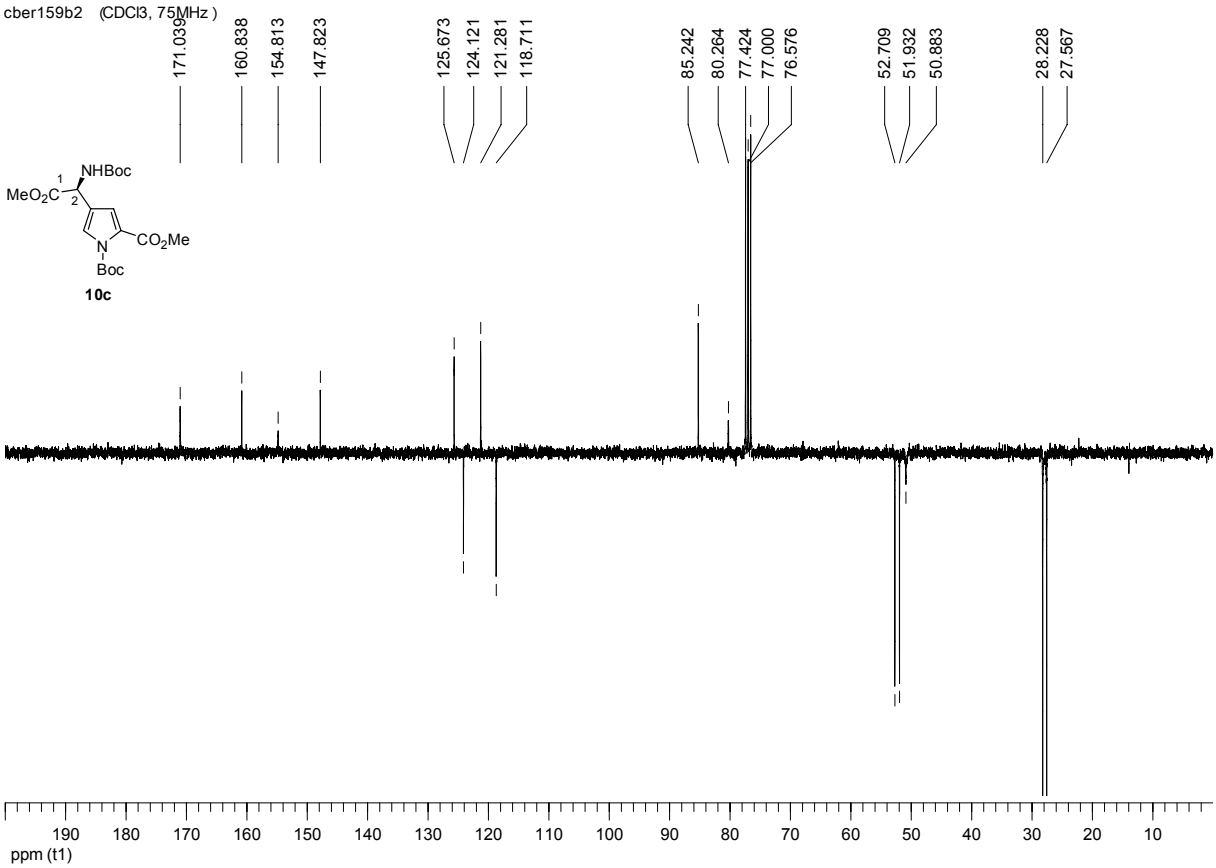
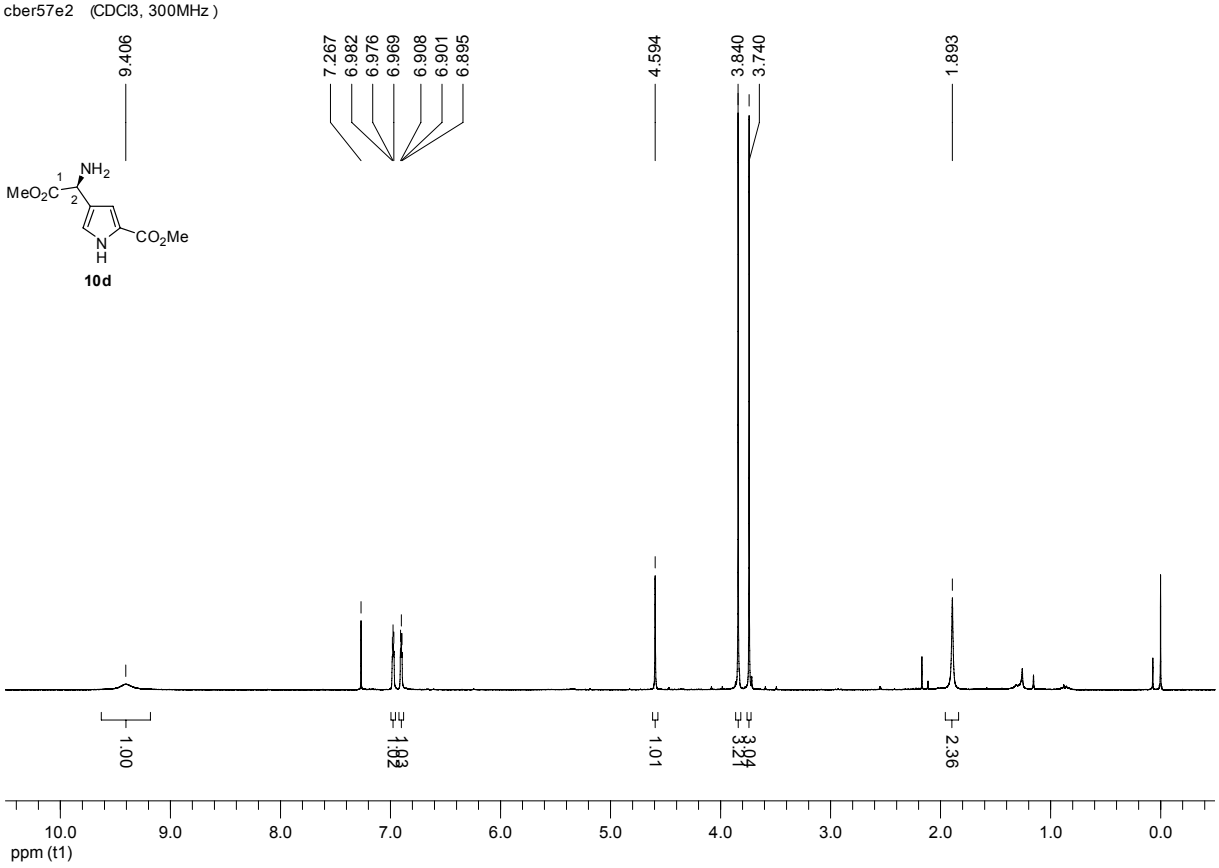
154.926
127.582
122.755
118.707
115.675
80.065
77.317
77.000
76.682
52.573
51.102
36.860
28.286
NHBoc
MeO2C
CO2Me
N
Me
10a
ppm (t1)

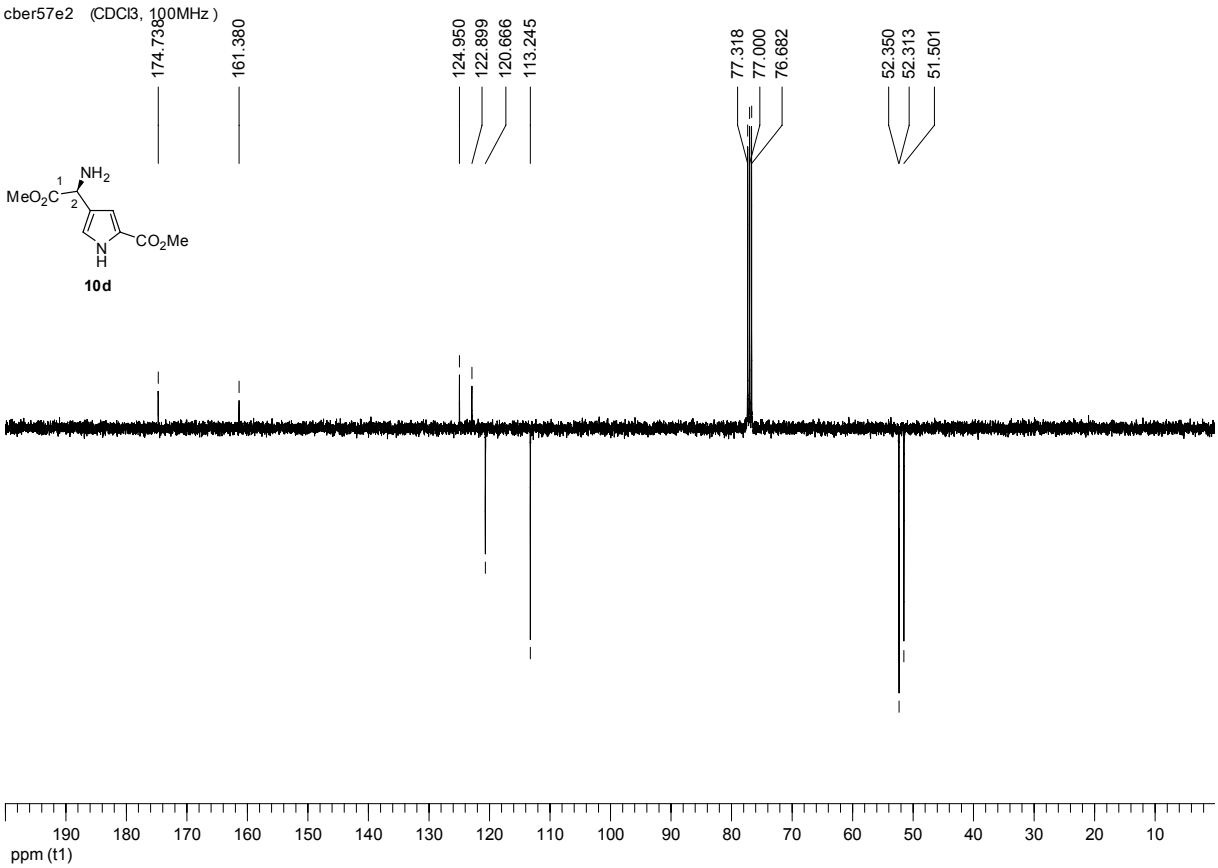

cber28e2 (CDCl3, 300MHz)
NHBoc
MeO2C
CO2Me
N
Bz
10b
7.758
7.733
7.654
7.628
7.604
7.508
7.482
7.458
7.259
7.228
7.047
7.042
5.421
5.297
3.787
3.587
1.449
2.15
1.14
2.24
1.01
1.00
2.05
3.09
3.14
9.53
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

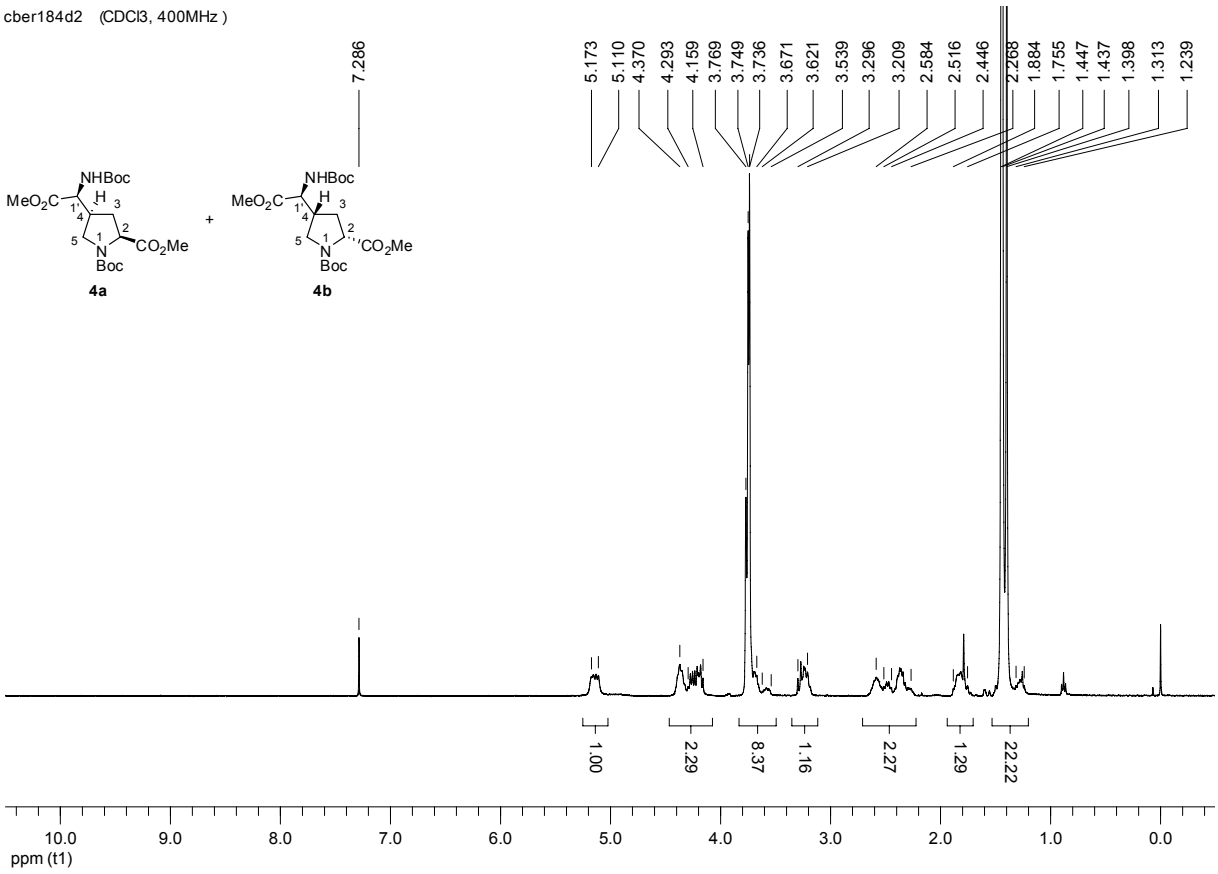

cber2e2 (CDCl3, 100MHz)
NHBoc
MeO2C
CO2Me
N
Bz
10b
171.001
167.697
160.275
154.847
133.753
132.861
129.928
128.724
126.465
125.264
121.909
119.332
80.366
77.318
77.000
76.682
52.816
51.739
50.931
28.233
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)

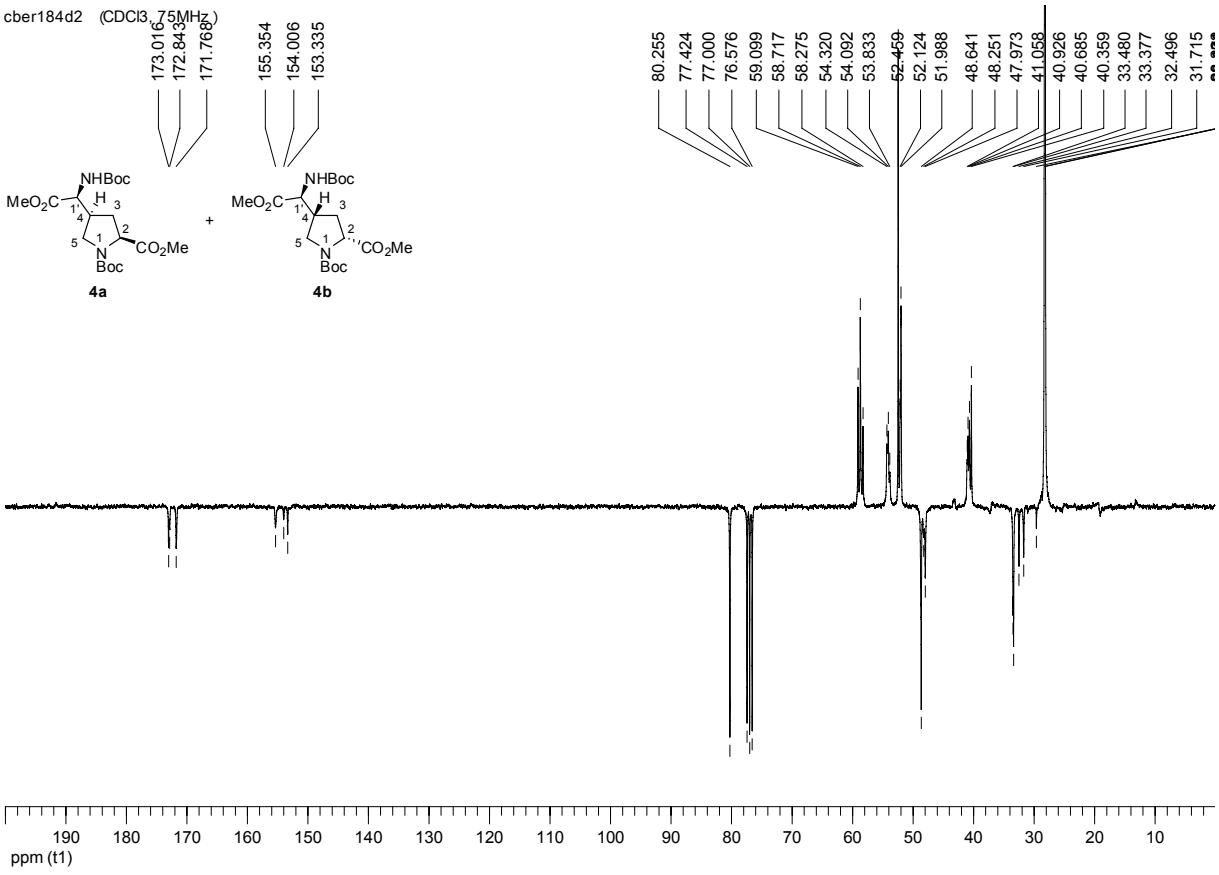

cber159b2 (CDCl3, 300MHz)
NHBoc
MeO2C
CO2Me
N
Boc
10c
7.315
7.309
7.283
6.806
6.799
5.409
5.390
5.274
3.829
3.761
1.570
1.444
1.00
0.99
2.06
3.01
3.09
9.45
6.39
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

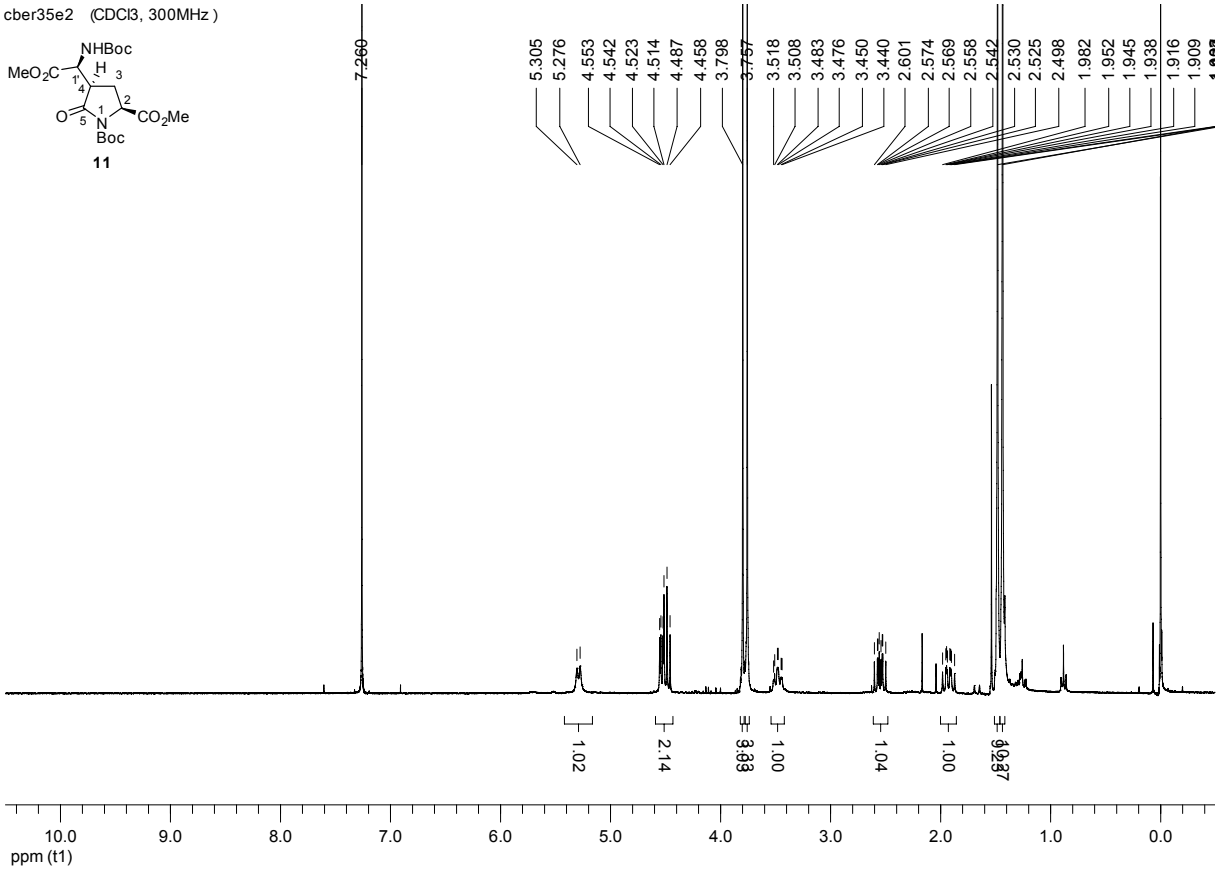

cber159b2 (CDCl3, 75MHz)
171.039
160.838
154.813
147.823
125.673
124.121
121.281
118.711
85.242
80.264
77.424
77.000
76.576
52.709
51.932
50.883
28.228
27.567
NHBoc
MeO2C
CO2Me
N
Boc
10c
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)

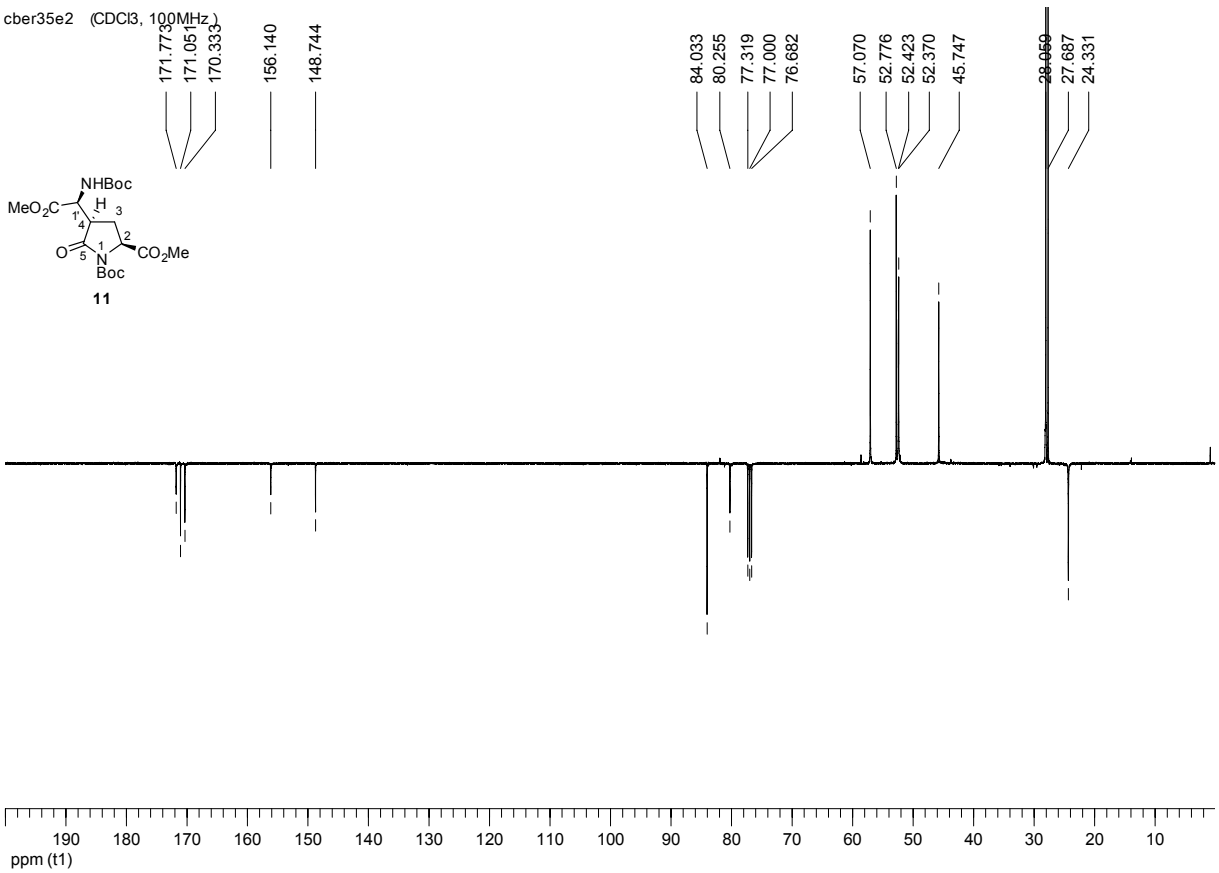

cber57e2 (CDCl3, 300MHz)
9.406
7.267
6.982
6.976
6.969
6.908
6.901
6.895
4.594
3.840
3.740
1.893
NH2
MeO2C
CO2Me
N
H
10d
1.00
1.01
2.36
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

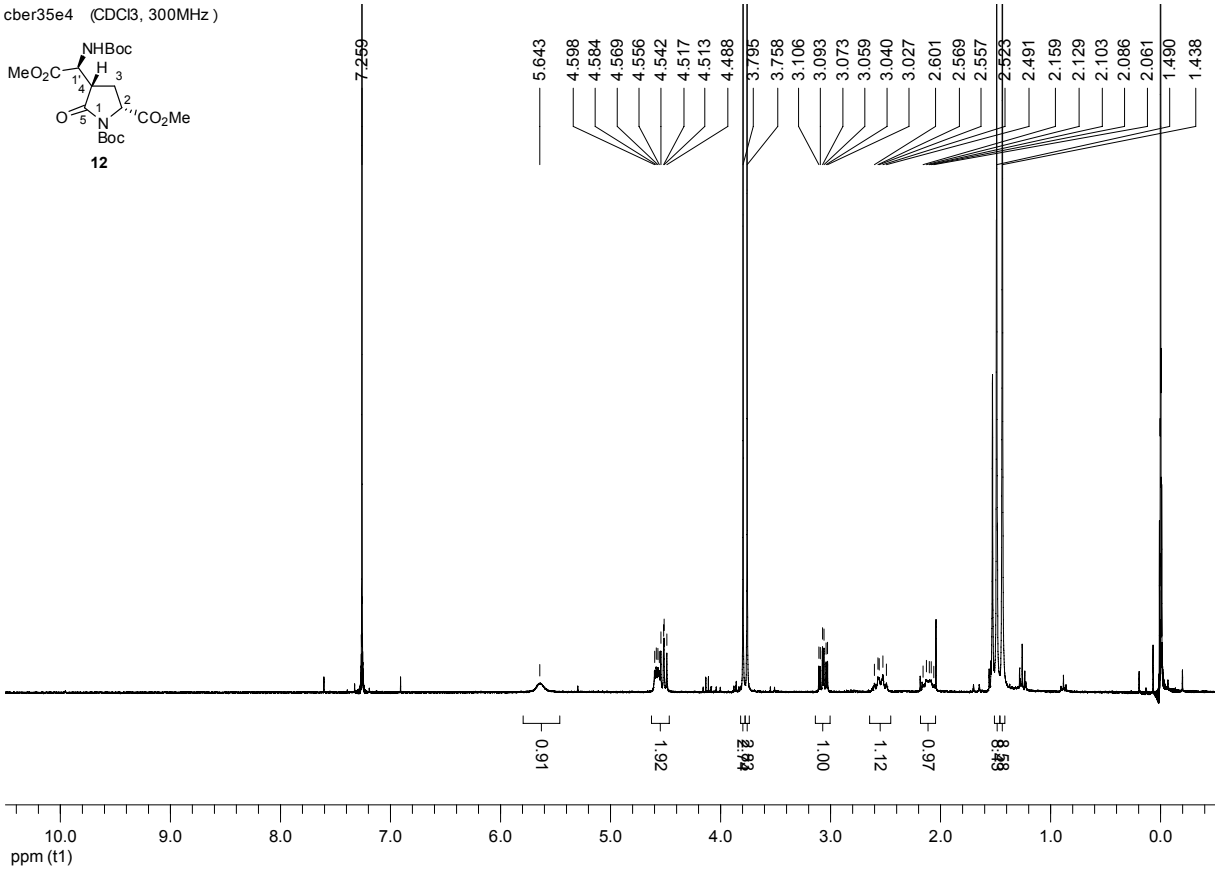

cber57e2 (CDCl3, 100MHz)
174.738
161.380
124.950
122.899
120.666
113.245
77.318
77.000
76.682
52.350
52.313
51.501
NH2
MeO2C
CO2Me
N
H
10d
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)

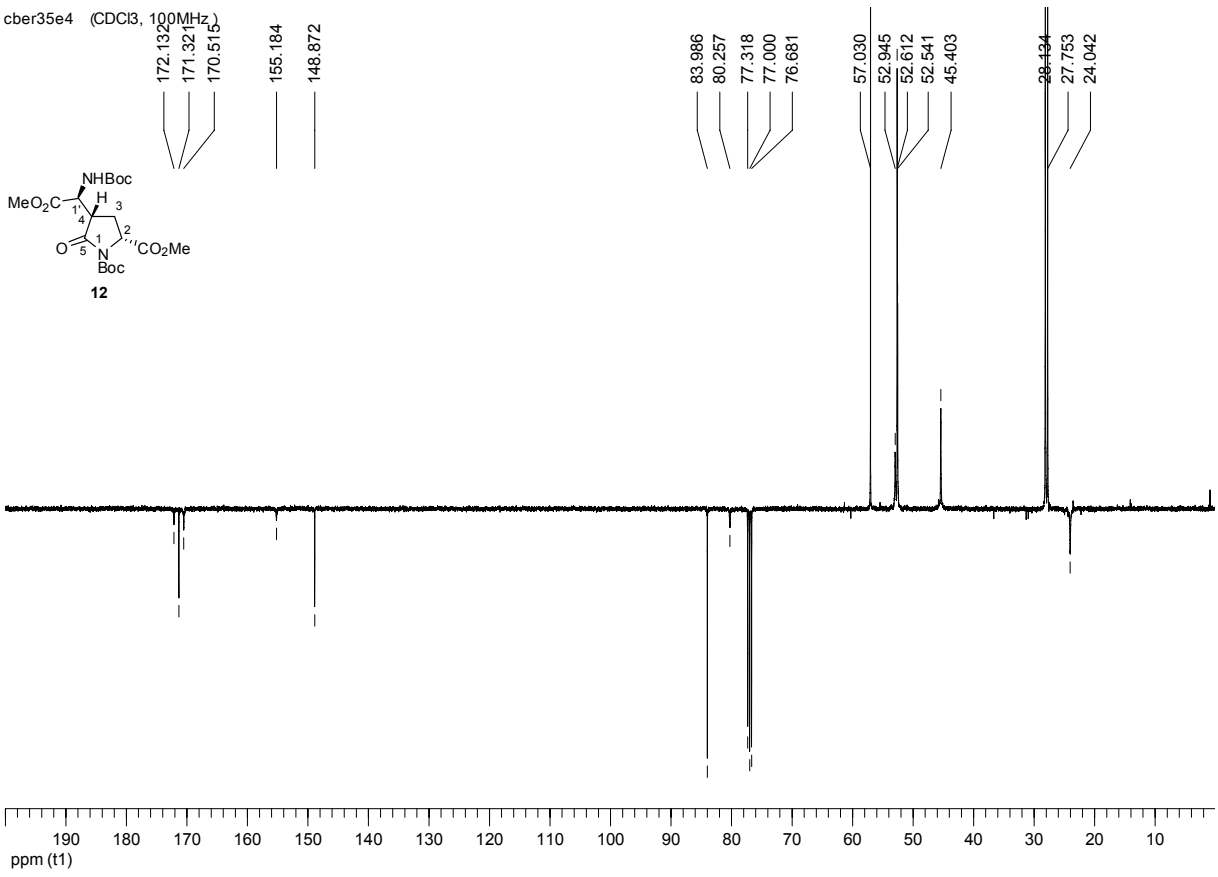

cber184d2 (CDCl3, 400MHz)
7.286
5.173
5.110
4.370
4.293
4.159
3.769
3.749
3.736
3.671
3.621
3.539
3.296
3.209
2.584
2.516
2.446
2.268
1.884
1.755
1.447
1.437
1.398
1.313
1.239
NHBoc
MeO2C
CO2Me
Boc
4a
4b
1.00
2.29
8.37
1.16
2.27
1.29
2.22
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

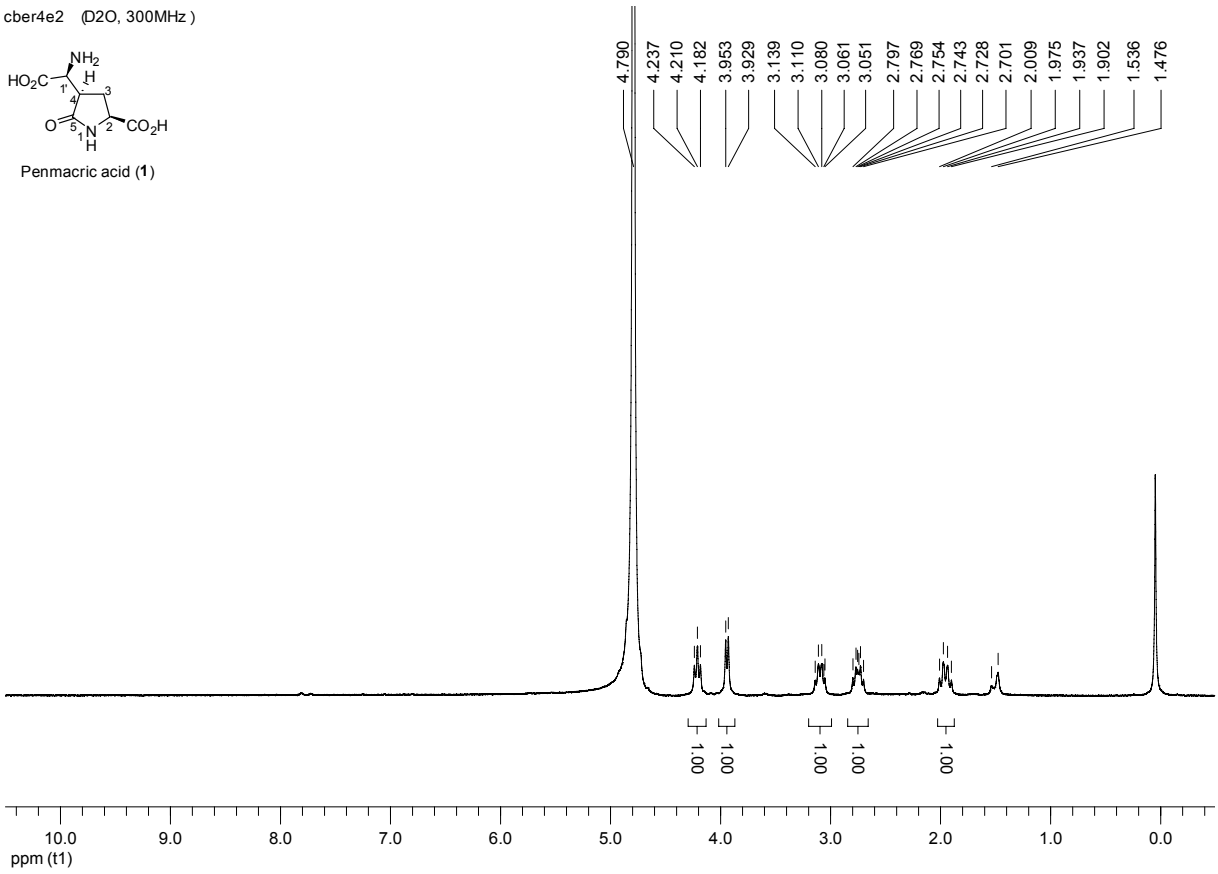

cber184d2 (CDCl3, 75MHz)
173.016
172.843
171.765
155.354
154.006
153.335
80.255
77.424
77.000
76.576
59.099
58.717
58.275
54.320
54.092
53.833
52.459
52.124
51.988
48.641
48.251
47.973
41.058
40.926
40.685
40.359
33.480
33.377
32.496
31.715
NHBoc
MeO2C
CO2Me
Boc
4a
4b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)

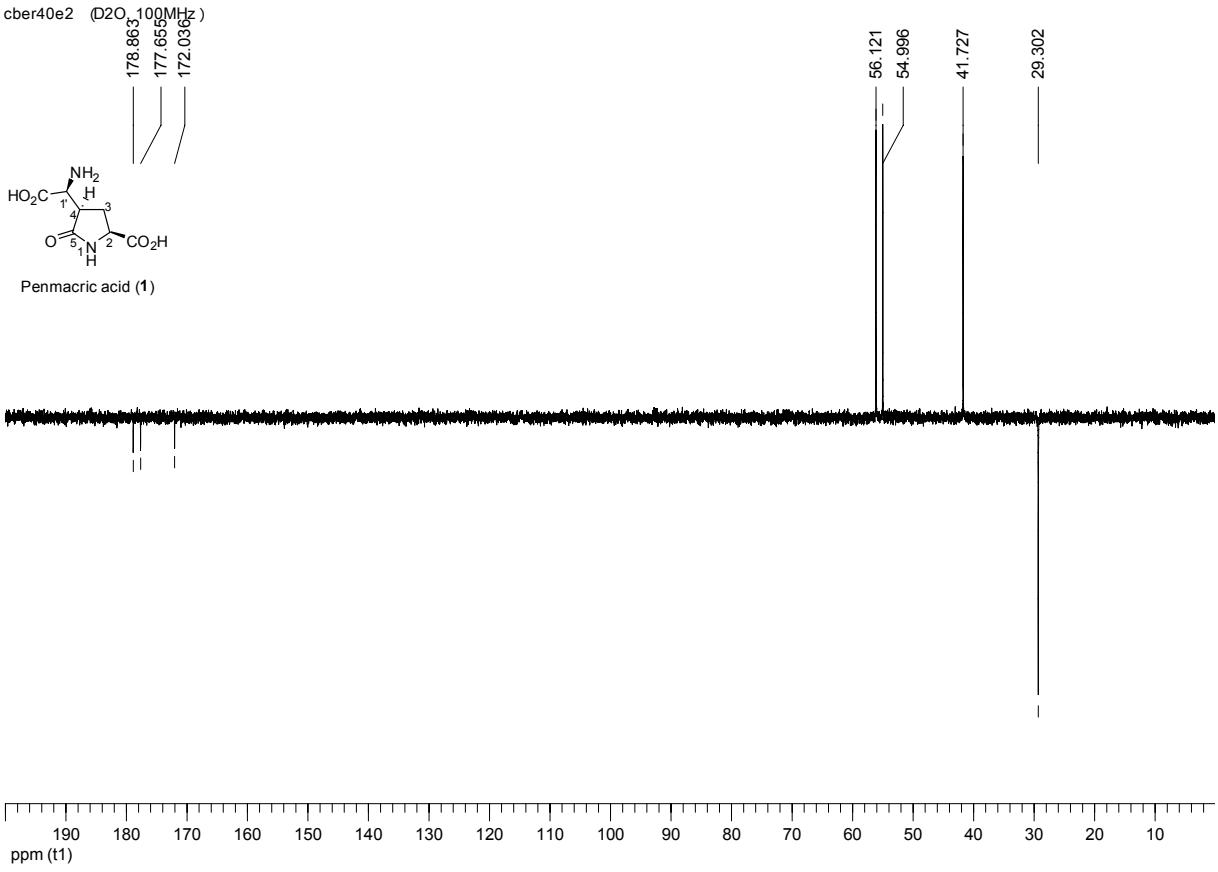

cber35e2 (CDCl3, 300MHz)
NHBoc
MeO2C
H
CO2Me
Boc
11
7.260
5.305
5.276
4.553
4.542
4.523
4.514
4.487
4.458
3.798
3.787
3.518
3.508
3.483
3.476
3.450
3.440
2.601
2.574
2.569
2.558
2.542
2.530
2.525
2.498
1.982
1.952
1.945
1.938
1.916
1.909
1.02
2.14
3.03
1.00
1.04
1.00
10.37
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

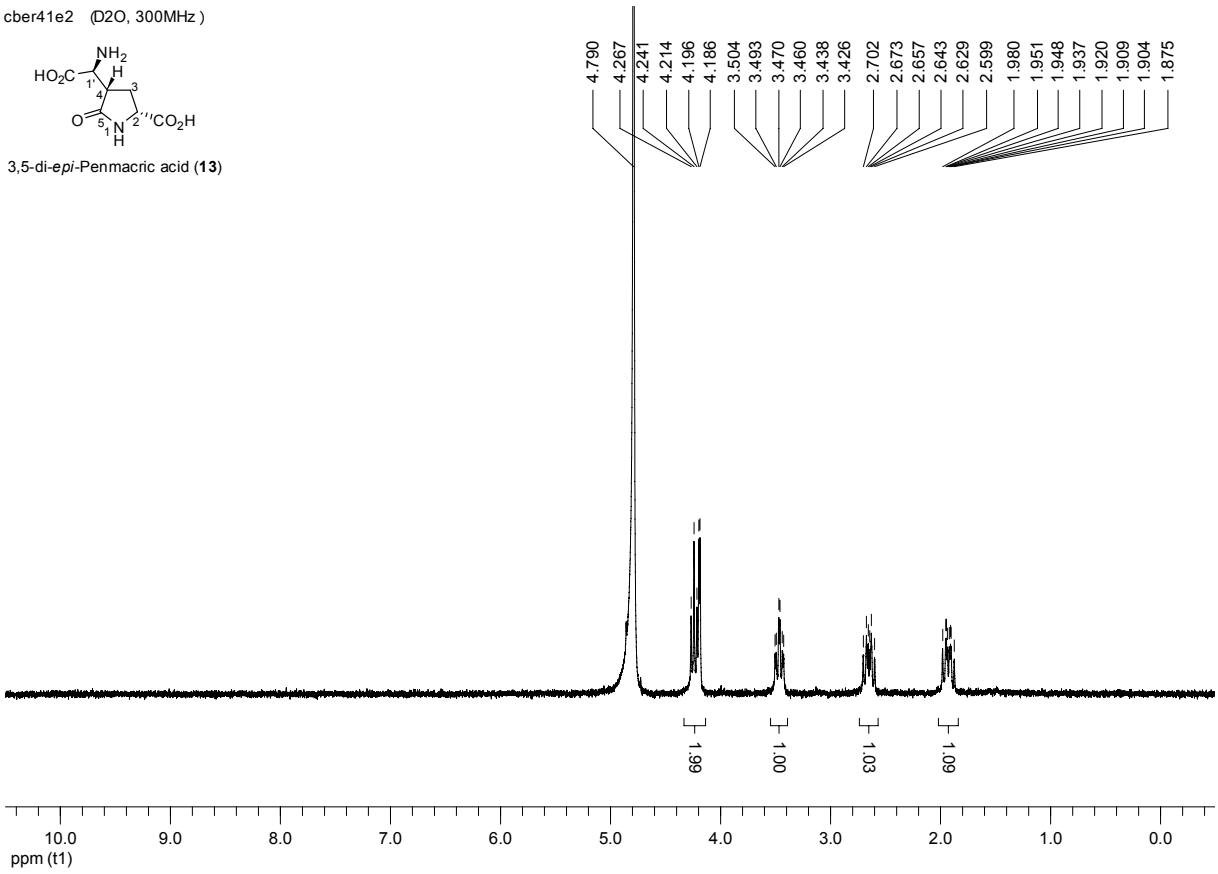

cber35e2 (CDCl3, 100MHz)
171.773
171.051
170.333
156.140
148.744
84.033
80.255
77.319
77.000
76.682
57.070
52.776
52.423
52.370
45.747
28.059
27.687
24.331
NHBoc
MeO2C
H
CO2Me
Boc
11
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)

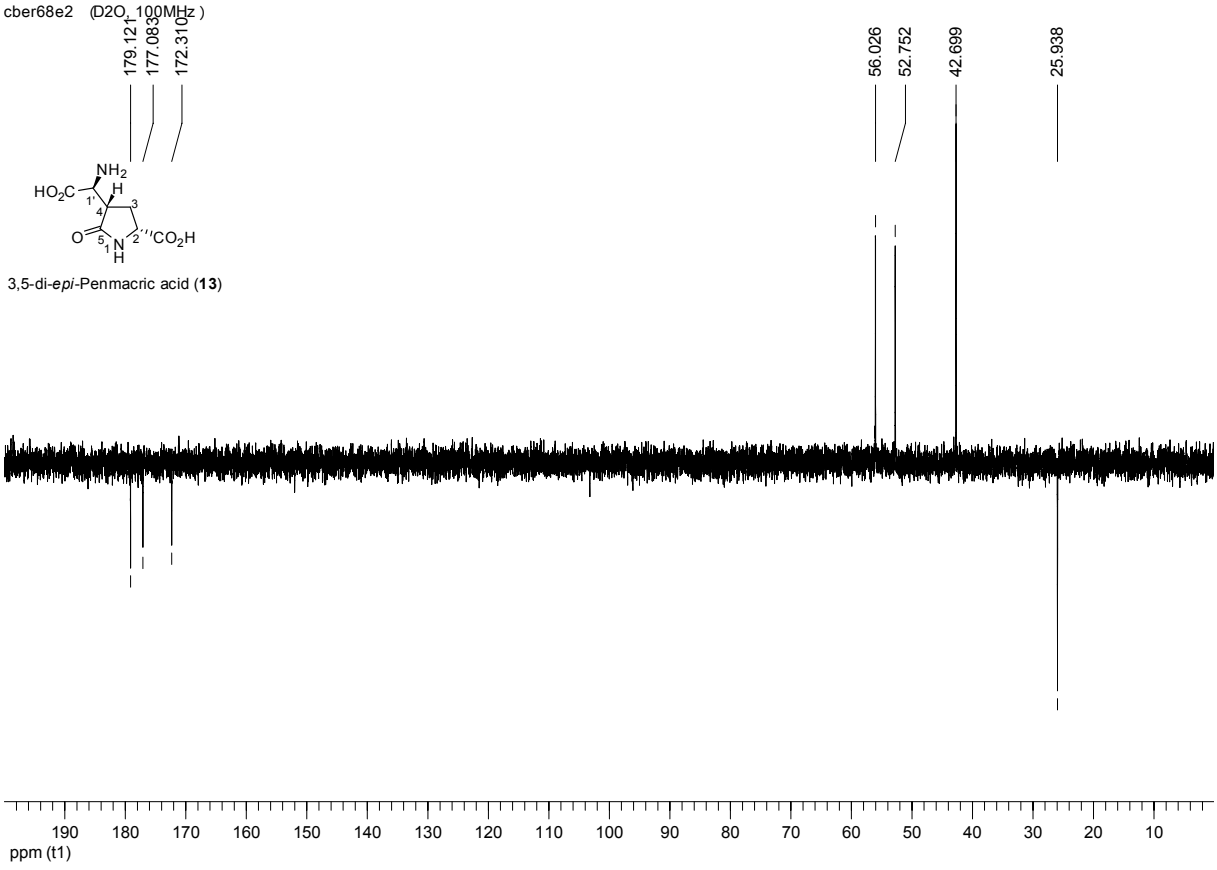

cber35e4 (CDCl3, 300MHz)
NHBoc
MeO2C
H
CO2Me
Boc
12
7.259
5.643
4.598
4.584
4.569
4.556
4.542
4.517
4.513
4.488
3.795
3.758
3.106
3.093
3.073
3.059
3.040
3.027
2.601
2.569
2.557
2.523
2.491
2.159
2.129
2.103
2.086
2.061
1.490
1.438
0.91
1.92
2.94
1.00
1.12
0.97
8.58
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


cber35e4 (CDCl3, 100MHz)
172.132
171.321
170.515
155.184
148.872
83.986
80.257
77.318
77.000
76.681
57.030
52.945
52.612
52.541
45.403
28.134
27.753
24.042
NHBoc
MeO2C
H
CO2Me
Boc
12
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)


cber4e2 (D2O, 300MHz)
Penmacric acid (1)
4.790
4.237
4.210
4.182
3.953
3.929
3.139
3.110
3.080
3.061
3.051
2.797
2.769
2.754
2.743
2.728
2.701
2.009
1.975
1.937
1.902
1.536
1.476
1.00
1.00
1.00
1.00
1.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


cber40e2 (D2O, 100MHz)
178.863
177.655
172.036
56.121
54.996
41.727
29.302
Penmacric acid (1)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)


cber41e2 (D2O, 300MHz)
3,5-di-epi-Penmacric acid (13)
4.790
4.267
4.241
4.214
4.196
4.186
3.504
3.493
3.470
3.460
3.438
3.426
2.702
2.673
2.657
2.643
2.629
2.599
1.980
1.951
1.948
1.937
1.920
1.909
1.904
1.875
1.99
1.00
1.03
1.09
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


cber68e2 (D2O, 100MHz)
179.121
177.083
172.310
56.026
52.752
42.699
25.938
3,5-di-epi-Penmacric acid (13)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)