

Electronic Supplementary Information(ESI)

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EXPERIMENTAL SECTION

1. General Information

Solvents were purified and dried by standard procedures before use; petroleum ether of boiling range 60–80 °C was used. Melting points are uncorrected. Optical rotations were measured using sodium D line on a polarimeter. ¹H NMR and ¹³C NMR were recorded on 200, 400, 500 MHz NMR spectrometers. HRMS data for new compounds were recorded using Orbitrap mass analyzer associated with Accela 1250 pump. HPLC was performed with variable wavelength detector. Column chromatography was carried out by using silica gel of the selected particle size of 100-200 mesh or 230-400 mesh. D-proline, L-proline and diazadicarboxylates were purchased from Sigma-Aldrich. Racemic proline was prepared by mixing of both the enantiomers before use.

2. General Experimental Procedure:

(a) **Preparation of sulfur ylide:** NaH (5 mmol, previously washed with petroleum ether to remove oil) was added to an oven-dried three-necked flask, followed by the addition of dry DMSO (15 mL) through a septum to it, and the whole slurry was stirred at 25 °C under N₂ atmosphere. Then trimethyloxosulfonium iodide (5 mmol) was added to the slurry over a period of 5 min *via* a solid addition funnel and stirred until it became a homogenous solution.

(b) **Sequential α -Amination/Wittig Olefination/Corey–Chaykovsky Reaction:** To a cold solution of azadicarboxylate (2.5 mmol) and L-proline (10 mol %) in dry CH₃CN (25 mL) at 0 °C was added aldehydes (**2a-k**, 3 mmol) and the mixture was stirred for 3 h at 0 °C. Then ethyl 2-(triphenyl- λ^5 -

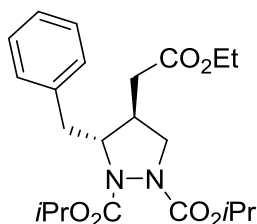
phosphanylidene) acetate (3.75 mmol) was added and stirred further for 45 min. This was followed by the addition of a solution of dimethyloxosulfonium methylide (5 mmol) in dry DMSO at 25 °C and allowed to stir for 2 h at the same temperature. The progress of the reaction can be monitored by TLC. It was then quenched by the addition of an aq. NH₄Cl solution. The mixture was concentrated in vacuum to remove acetonitrile, and concentrate was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine, dried over anhyd Na₂SO₄, and concentrated under reduced pressure to give the crude products, which were then purified by flash column chromatography (230-400 mesh) using petroleum ether and ethyl acetate as eluents to afford the pure products **4a-k**.

(c) **Sequential α -Amination/Wittig Olefination/N-alkylation/Michael Reaction:** To a cold solution of azadicarboxylate (2.5 mmol) and L-proline (10 mol %) in dry CH₃CN (25 mL) at 0 °C was added aldehydes (**2**, 2.5 mmol) and the mixture was stirred for 3 h at 0 °C. Then ethyl 2-(triphenyl- λ^5 -phosphanylidene) acetate (3.75 mmol) was added and stirred further for 45 min. This was followed by the addition of ethyl bromoacetate (3.75 mmol) and Cs₂CO₃ (6.25 mmol) and allowed to stir for 6 h at 50 °C. The progress of the reaction can be monitored by TLC. It was then quenched by the addition of an aq. NH₄Cl solution. The mixture was concentrated in vacuum to remove acetonitrile, and concentrate was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine, dried over anhyd Na₂SO₄, and the concentrated under reduced pressure to give the crude products, which were then purified by flash column chromatography (230-400 mesh) using petroleum ether and ethyl acetate as eluents to afford the pure products **5a-h**.

(d) **Synthesis of 1,3-diamino acid 7 by N-N reduction of pyrazolidines 4:** NH₃ was bubbled into a solution of pyrazolidine **4** (0.2 mmol) in THF (10 mL) at -78 °C, until approximately 10 mL were condensed. Excess Na was added and the solution turned dark blue. The resulting mixture was stirred at -40 °C for 1 h. Then the reaction was quenched by careful addition of solid NH₄Cl, and NH₃ was allowed to evaporate slowly. The residue was diluted with EtOAc (15 mL) and filtered, and the solvents were

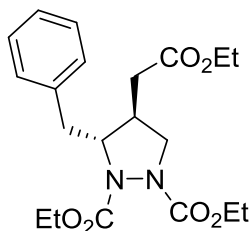
evaporated in a rotary evaporator. The resulting residue was purified by flash chromatography over SiO₂, with hexane/ethyl acetate/NEt₃ 20/1/1 as eluent, to give 1,3-diamino acid **7** as spectroscopically pure, colorless syrup.

Diisopropyl (3*R*,4*S*)-3-benzyl-4-(2-ethoxy-2-oxoethyl) pyrazolidine-1,2-dicarboxylate (R' = *i*Pr, **4a**)



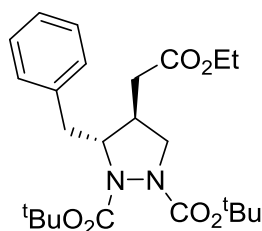
Yield: 841 mg, 80%; gum; $[\alpha]_D^{25} +17.156$ (c 1.2, CHCl₃); 86% ee (Chiracel OD-H 250 x 4.6 mm), *n*-hexane/*i*-PrOH, 95:5, 0.5 mL/min, 220 nm), *t_r* = 18.190 min (major), *t_r* = 20.973 min (minor); IR (CHCl₃, cm⁻¹) *v*_{max} 701, 741, 921, 1029, 1197, 1187, 1238, 1316, 1340, 1375, 1467, 1701, 1733, 2981, 2358; **¹H NMR** (200 MHz, CDCl₃): δ 1.12-1.31 (m, 15H), 2.18 (d, *J* = 7.5 Hz, 2H), 2.54-2.60 (dd, *J* = 4.1, 7.2 Hz, 1H), 2.61-2.70 (dd, *J* = 4.6, 11.2 Hz, 1H), 2.90-3.00 (m, 2H), 4.03-4.28 (m, 4H), 4.82-5.05 (m, 2H), 7.24-7.28 (m, 5H); **¹³C NMR** (50 MHz, CDCl₃): δ 14.0, 21.6, 21.7, 21.9, 37.2, 40.2, 41.3, 51.7, 60.4, 65.4, 69.6, 69.8, 126.4, 128.2, 129.2, 137.3, 156.0, 156.2, 170.7; HRMS (ESI) Calcd for C₂₂H₃₃O₆N₂ [M + H]⁺ 421.2333; Found 421.233.

Diethyl (3*R*,4*S*)-3-benzyl-4-(2-ethoxy-2-oxoethyl) pyrazolidine-1,2-dicarboxylate (R' = Et, **4a**)



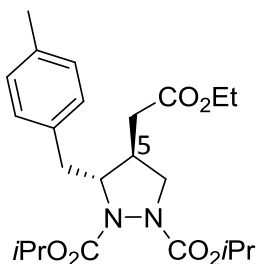
Yield: 775 mg, 79%; gum; $[\alpha]_D^{25} +5.76$ (c 0.5, CHCl_3); 81% ee (Chiracel AD-H, 250 x 4.6 mm), n -hexane/ i -PrOH, 90:10, 0.5 mL/min, 220 nm), $t_r = 23.547$ min (major), $t_r = 27.613$ min (minor); IR (CHCl_3 , cm^{-1}) ν_{max} 702, 744, 925, 1030, 1198, 1188, 1237, 1313, 1347, 1378, 1466, 1708, 1739, 2988, 2355; $^1\text{H NMR}$ (200 MHz, CDCl_3): δ 1.16- 1.35 (m, 9H), 2.16 (d, $J = 6.3$ Hz, 2H), 2.54-2.61 (m, 1H), 2.63- 2.73 (dd, $J = 7.1, 13.4$ Hz, 1H), 2.90-3.03 (m, 2H), 4.02-4.29 (m, 8H), 7.24-7.27 (m, 5H); $^{13}\text{C NMR}$ (50 MHz, CDCl_3): δ 14.13, 14.35, 37.12, 40.33, 41.35, 51.98, 60.60, 62.22, 65.61, 77.32, 126.60, 128.36, 129.35, 137.29, 156.64, 156.78, 170.87; HRMS (ESI) Calcd for $\text{C}_{20}\text{H}_{29}\text{O}_6\text{N}_2$ $[\text{M} + \text{H}]^+$ 393.2020; Found 393.2019.

Di-tert-butyl (3*R*,4*S*)-3-benzyl-4-(2-ethoxy-2-oxoethyl) pyrazolidine-1,2-dicarboxylate ($\text{R}' = \text{tBu}$, **4a**)



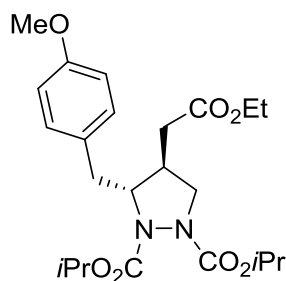
Yield: 785 mg, 70%; gum; $[\alpha]_D^{25} +6.606$ (c 1.18, CHCl_3); 80% ee (Chiracel AD-H 250 x 4.6 mm), n -hexane/ i -PrOH, 90:10, 0.5 mL/min, 254 nm), $t_r = 7.2$ min (minor), $t_r = 30.6$ min (major); IR (CHCl_3 , cm^{-1}) ν_{max} 705, 745, 926, 1023, 1191, 1189, 1232, 1317, 1349, 1374, 1466, 1707, 1739, 2982, 2350; $^1\text{H NMR}$ (200 MHz, CDCl_3): δ 1.23 (t, $J = 7.07$ Hz, 3H), 1.37-1.50 (m, 18H), 2.19 (d, $J = 7.5$ Hz, 2H), 2.53-2.71 (m, 2H), 2.83-2.99 (m, 2H), 3.99-4.22 (m, 4H), 7.19-7.26 (m, 5H); $^{13}\text{C NMR}$ (50 MHz, CDCl_3): δ 14.11, 27.97, 28.14, 37.39, 40.19, 41.32, 51.40, 60.51, 65.35, 80.86, 126.39, 128.21, 129.37, 137.67, 155.26, 155.63, 171.00; HRMS (ESI) Calcd for $\text{C}_{24}\text{H}_{36}\text{O}_6\text{N}_2$ $[\text{M} + \text{Na}]^+$ 471.2466; Found 471.2465.

Diisopropyl (3*R*,4*S*)-4-(2-ethoxy-2-oxoethyl)-3-(4-methylbenzyl) pyrazolidine-1,2-dicarboxylate (**4b**)



Yield: 771 mg, 71%; gum; $[\alpha]_D^{25} +4.812$ (c 1.08, CHCl₃); 84% ee (Chiracel AD-H 250 x 4.6 mm), *n*-hexane/*i*-PrOH, 90:10, 0.5 mL/min, 220 nm), $t_r = 16.253$ min (minor), $t_r = 17.317$ min (major); IR (CHCl₃, cm⁻¹) ν_{\max} 760, 920, 1105, 1181, 1240, 1369, 1508, 1730, 2355; **¹H NMR** (400 MHz, CDCl₃): δ 1.15-1.30 (m, 15H), 2.16 (d, $J = 7.5$ Hz, 2H), 2.31 (s, 3H), 2.57-2.66 (m, 2H), 2.92-2.96 (m, 2H), 4.05-4.11 (m, 3H), 4.21-4.24 (dd, $J = 7.9, 10.9$ Hz, 1H), 4.88-4.95 (quint. $J = 6.4$ Hz, 1H), 4.97-5.01 (quint. $J = 6.4$ Hz, 1H), 7.07 (d, $J = 7.8$ Hz, 2H), 7.12-7.14 (d, $J = 8.2$ Hz, 2H); **¹³C NMR** (50 MHz, CDCl₃): δ 14.18, 21.08, 21.84, 22.06, 37.39, 39.94, 41.33, 51.88, 60.60, 65.60, 69.83, 69.96, 129.09, 129.24, 134.34, 135.91, 156.29, 156.46, 170.96; HRMS (ESI) Calcd for C₂₃H₃₅O₆N₂ [M + H]⁺ 435.2490; Found 435.2490.

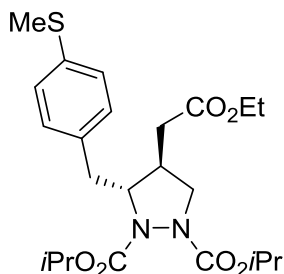
Diisopropyl (3*R*,4*S*)-4-(2-ethoxy-2-oxoethyl)-3-(4-methoxybenzyl) pyrazolidine-1,2-dicarboxylate (**4c**)



Yield: 754 mg, 67%; gum; $[\alpha]_D^{25} +6.031$ (c 1.16, CHCl₃); 87% ee (Chiracel AD-H 250 x 4.6 mm), *n*-hexane/*i*-PrOH, 90:10, 0.5 mL/min, 220 nm), $t_r = 26.780$ min (minor), $t_r = 29.630$ min (major); IR (CHCl₃, cm⁻¹) ν_{\max} 760, 921, 1108, 1180, 1247, 1380, 1375, 1513, 1734, 2361; **¹H NMR** (200 MHz, CDCl₃): δ 1.20-1.31 (m, 15H), 2.16-2.20 (d, $J = 6.2$ Hz, 2H), 2.54-2.64 (m, 2H), 2.84-2.99 (m, 2H), 3.78 (s, 3H), 4.01-4.17 (m, 4H), 4.86-5.01 (m, 2H), 6.78-6.82 (d, $J = 8.7$ Hz, 2H), 7.15-7.19 (d, $J = 8.7$ Hz, 2H); **¹³C NMR** (100 MHz, CDCl₃): δ 14.20, 21.88, 37.35, 39.45, 41.31, 51.86, 55.07, 60.64, 65.73, 69.67,

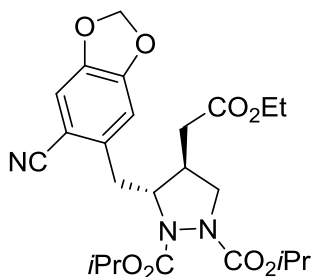
69.85, 69.97, 113.80, 114.06, 129.55, 130.32, 156.43, 158.37, 171.03; HRMS (ESI) Calcd for C₂₃H₃₄O₇N₂ [M + Na]⁺473.2258; Found 473.2254.

Diisopropyl (3*R*,4*S*)-4-(2-ethoxy-2-oxoethyl)-3-(4-(methylthio)benzyl) pyrazolidine-1,2-dicarboxylate
(4d)



Yield: 875 mg, 75%; gum; [α]_D²⁵ +5.280 (c 1.06, CHCl₃); 77% ee (Chiracel AS-H 250 x 4.6 mm), *n*-hexane/*i*-PrOH, 90:10, 0.5 mL/min, 220 nm), *t*_r = 16.2 min (minor), *t*_r = 18.6 min (major); IR (CHCl₃, cm⁻¹) *v*_{max} 760, 922, 1040, 1147, 1192, 1258, 1319, 1341, 1359, 1477, 1711, 1738, 2980, 2359; ¹H NMR (200 MHz, CDCl₃): δ 1.12- 1.31 (m, 15H), 2.22 (d, *J* = 7.4 Hz, 2H), 2.46 (s, 3H), 2.55-2.69 (m, 2H), 2.81-3.00 (m, 2H), 4.04-4.15 (q, *J* = 6.9 Hz, 2H), 4.17-4.27 (m, 2H), 4.85-5.07 (m, 2H), 7.18 (s, 4H); ¹³C NMR (100 MHz, CDCl₃): δ 14.16, 15.99, 21.77, 37.33, 39.73, 41.38, 51.76, 60.65, 65.53, 69.98, 126.82, 129.85, 134.47, 136.37, 156.31, 170.95; HRMS (ESI) Calcd for C₂₃H₃₄O₆N₂S [M + Na]⁺489.2030; Found 489.2027.

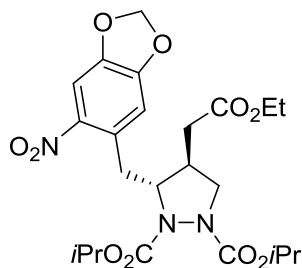
Diisopropyl (3*R*,4*S*)-3-((6-cyanobenzo[d][1,3]dioxol-5-yl)methyl)-4-(2-ethoxy-2-oxoethyl) pyrazolidine-1,2-dicarboxylate (4e)



Yield: 795 mg, 65%; brownish gum; [α]_D²⁵ +42.775 (c 1.0, CHCl₃); 81% ee (Chiracel AD-H 250 x 4.6 mm), *n*-hexane/*i*-PrOH, 80:20, 0.5 mL/min, 254 nm), *t*_r = 27.337 min (minor), *t*_r = 30.393 min (major); IR

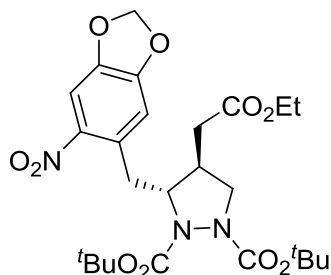
(CHCl₃, cm⁻¹) ν_{\max} 760, 928, 1035, 1107, 1181, 1237, 1271, 13401, 1468, 1487, 1506, 1732, 2222, 2983; ¹H NMR (200 MHz, CDCl₃): δ 1.06-1.34 (m, 15H), 2.29-3.17 (m, 6H), 4.08-4.30 (m, 4H), 4.75-5.09 (m, 2H), 6.03 (s, 2H), 6.98 (s, 1H), 7.05 (s, 1H); ¹³C NMR (50 MHz, CDCl₃): δ 14.16, 21.67, 21.80, 22.06, 36.91, 38.61, 42.13, 51.85, 60.85, 64.97, 69.99, 70.28, 102.12, 104.76, 110.93, 111.64, 117.93, 138.43, 146.58, 151.39, 156.06, 170.77; HRMS (ESI) Calcd for C₂₄H₃₁O₈N₃ [M + Na]⁺ 512.2003; Found 512.2004.

Diisopropyl (3*R*,4*S*)-4-(2-ethoxy-2-oxoethyl)-3-((6-nitrobenzo[d][1,3]dioxol-5-yl)methyl)pyrazolidine-1,2-dicarboxylate (**4f**)



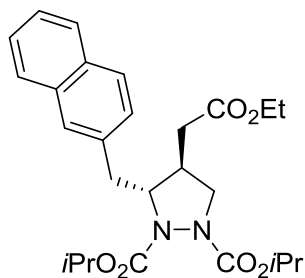
Yield: 879 mg, 69%; yellow gum; $[\alpha]_{\text{D}}^{25}$ -4.640 (c 1.12, CHCl₃); 92% ee (Chiracel AD-H 250 x 4.6 mm), *n*-hexane/*i*-PrOH, 80:20, 0.5 mL/min, 254 nm), t_r = 25.400 min (minor), t_r = 28.067 min (major); IR (CHCl₃, cm⁻¹) ν_{\max} 760, 817, 871, 926, 1034, 1106, 1179, 1259, 1327, 1382, 1485, 1521, 1704, 1731, 2981; ¹H NMR (200 MHz, CDCl₃): δ 1.07-1.38 (m, 15H), 2.39-2.76 (m, 5H), 2.90-2.99 (dd, J = 7.8, 11.6 Hz, 1H), 3.42-3.50 (dd, J = 2.4, 13.1 Hz, 1H), 4.17 (q, J = 7.2 Hz, 3H), 4.29-4.38 (dd, J = 7.5, 11.6 Hz, 1H), 4.73 (sep, J = 6.0 Hz, 1H), 5.00 (sep, J = 6.3 Hz, 1H), 6.08 (s, 2H), 7.04 (s, 1H), 7.65 (s, 1H); ¹³C NMR (50 MHz, CDCl₃): δ 14.14, 21.53, 21.67, 21.93, 22.04, 30.76, 36.65, 39.18, 43.05, 52.05, 60.78, 64.82, 69.70, 70.27, 102.71, 105.35, 112.57, 131.19, 142.68, 146.79, 151.53, 156.18, 170.93; HRMS (ESI) Calcd for C₂₃H₃₁O₁₀N₃ [M + Na]⁺ 532.2333; Found 532.2331.

Di-tert-butyl (3*R*,4*S*)-4-(2-ethoxy-2-oxoethyl)-3-((6-nitrobenzo[d][1,3]dioxol-5-yl)methyl) pyrazolidine-1,2-dicarboxylate (**4g**)



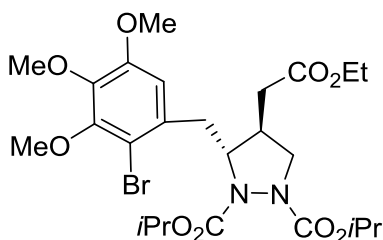
Yield: 887 mg, 66%; yellow solid; mp: 130 – 132 °C; $[\alpha]_D^{25}$ -3.796 (c 1.0, CHCl₃); 90% ee (Chiracel AD-H 250 x 4.6 mm), *n*-hexane/*i*-PrOH, 90:10, 0.5 mL/min, 254 nm), t_r = 29.292 min (minor), t_r = 34.651 min (major); IR (CHCl₃, cm⁻¹) ν_{\max} ; 769, 876, 936, 1054, 1140, 1194, 1269, 1337, 1386, 1490, 1531, 1714, 1741, 2990; **¹H NMR** (200 MHz, CDCl₃): δ 1.25-1.32 (m, 12H), 2.38-.70 (m, 4H), 2.90-2.99 (m, 1H), 3.35-3.43 (dd, J = 2.5, 13.1 Hz, 1H), 4.13-4.31 (m, 4H), 6.08 (s, 2H), 7.10 (s, 1H), 7.54 (s, 1H); **¹³C NMR** (50 MHz, CDCl₃): δ 14.28, 27.95, 28.38, 37.05, 39.06, 43.04, 60.87, 80.98, 81.55, 102.69, 105.48, 112.86, 131.41, 142.84, 146.74, 151.45, 155.52, 171.10; HRMS (ESI) Calcd for C₂₅H₃₅O₁₀N₃ [M + Na]⁺ 560.2215; Found 560.2214.

Diisopropyl (3*R*,4*S*)-4-(2-ethoxy-2-oxoethyl)-3-(naphthalen-2-ylmethyl) pyrazolidine-1,2-dicarboxylate (**4h**)



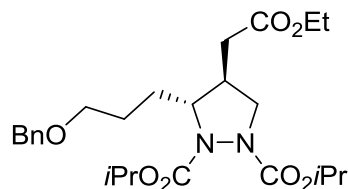
Yield: 800 mg, 68%; gum; $[\alpha]_D^{25}$ -5.247 (c 0.8, CHCl₃); 83% ee (Chiracel OD-H 250 x 4.6 mm), *n*-hexane/*i*-PrOH, 90:10, 0.5 mL/min, 254 nm), t_r = 16.741 min (minor), t_r = 18.284 min (major); IR (CHCl₃, cm⁻¹) ν_{\max} 760, 923, 1110, 1240, 1375, 1510, 1733, 2359; ¹H NMR (200 MHz, CDCl₃): δ 1.13 (t, J = 7.1 Hz, 3H), 1.22-1.35 (m, 12H), 2.62-2.68 (m, 1H), 2.88-3.06 (m, 2H), 3.61 (br s, 1H), 3.91-4.01 (q, J = 7.2 Hz, 2H), 4.24-4.39 (m, 2H), 4.85-5.10 (m, 2H), 7.36- 8.24 (m, 8H); ¹³C NMR (50 MHz, CDCl₃): δ 13.85, 21.49, 21.61, 21.85, 36.72, 38.34, 41.83, 52.05, 60.27, 63.82, 69.50, 69.91, 123.55, 125.39, 125.94, 127.39, 127.50, 128.59, 131.79, 133.29, 133.67, 155.61, 156.49, 170.60; HRMS (ESI) Calcd for C₂₆H₃₄O₆N₂ [M + Na]⁺493.2309; Found 493.2305.

Diisopropyl (3*R*,4*S*)-3-(2-bromo-3,4,5-trimethoxybenzyl)-4-(2-ethoxy-2-oxoethyl) pyrazolidine-1,2-dicarboxylate (**4i**)



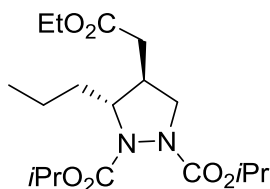
Yield: 1.061 g, 72%; gum; $[\alpha]_D^{25}$ +26.867 (c 1.54, CHCl₃); 94% ee (Chiracel AD-H 250 x 4.6 mm), *n*-hexane/*i*-PrOH, 95:5, 0.5 mL/min, 220 nm), t_r = 40.837 min (major), t_r = 66.290 min (minor); IR (CHCl₃, cm⁻¹) ν_{\max} 760, 922, 1109, 1182, 1249, 1377, 1389, 1515, 1737, 2365; ¹H NMR (200 MHz, CDCl₃): δ 1.02-1.31 (m, 15H), 2.22-2.46 (m, 2H), 2.58-2.81 (m, 2H), 2.94-3.04 (m, 2H), 3.86 (s, 6H), 3.88 (s, 3H), 4.07-4.32 (m, 4H), 4.81 (quint, J = 6.2 Hz, 1H), 5.00 (quint, J = 6 Hz, 1H), 6.85 (s, 1H); ¹³C NMR (50 MHz, CDCl₃): δ 14.06, 21.53, 21.72, 21.91, 21.97, 37.00, 40.37, 41.89, 52.05, 56.17, 60.63, 60.70, 60.81, 63.61, 69.61, 69.88, 110.50, 110.95, 132.57, 141.75, 150.46, 152.35, 155.89, 159.21, 170.82; LC-MS (ESI) m/z : 591.2 [M + 1]⁺

Diisopropyl (3*R*,4*S*)-3-(3-(benzyloxy)propyl)-4-(2-ethoxy-2-oxoethyl) pyrazolidine-1,2-dicarboxylate (**4j**)



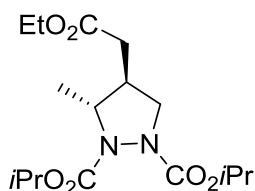
Yield: 837 mg, 70%; gum; $[\alpha]_D^{25} +4.597$ (c 1.0, CHCl₃); 92% ee (Chiracel AD-H 250 x 4.6 mm), *n*-hexane/*i*-PrOH, 90:10, 0.5 mL/min, 220 nm), $t_r = 25.810$ min (major), $t_r = 30.130$ min (minor); IR (CHCl₃, cm⁻¹) ν_{\max} 760, 920, 1113, 1179, 1246, 1374, 1386, 1512, 1738, 2363; ¹H NMR (200 MHz, CDCl₃): δ 1.20-1.29 (m, 15H), 1.62-1.77 (m, 4H), 2.27-2.52 (m, 3H), 2.90-2.98 (dd, $J = 5.4, 11.5$ Hz, 1H), 3.93-3.99 (m, 1H), 4.07-4.48 (m, 3H), 4.48 (s, 2H), 4.87- 5.02 (m, 2H), 7.30 (s, 5H); ¹³C NMR (50 MHz, CDCl₃): δ 14.01, 21.80, 26.27, 30.34, 37.54, 41.48, 51.36, 60.46, 63.90, 69.55, 69.65, 72.61, 77.20, 127.25, 128.08, 138.37, 156.45, 156.65, 170.91; HRMS (ESI) Calcd for C₂₅H₃₈O₇N₂ [M + Na]⁺ 501.257; Found 501.2568.

Diisopropyl (3*R*,4*S*)-4-(2-ethoxy-2-oxoethyl)-3-propylpyrazolidine-1,2-dicarboxylate (**4k**)



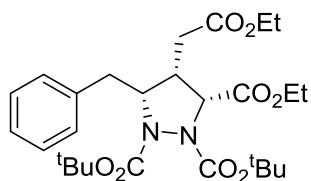
Yield: 735 mg, 79%; gum; $[\alpha]_D^{25} -1.143$ (c 1.0, CHCl₃); IR (CHCl₃, cm⁻¹) ν_{\max} 1238, 1512, 1611, 1735; ¹H NMR (200 MHz, CDCl₃): δ 0.945 (t, $J = 5.6$ Hz, 3H), 1.22-1.30 (m, 15H), 1.35-1.46 (m, 4H), 2.28-2.55 (m, 3H), 2.89-2.98 (dd, $J = 5.3, 11.5$ Hz, 1H), 3.94 (br s, 1H), 4.09-4.22 (m, 3H), 4.90-5.02 (m, 2H); ¹³C NMR (50 MHz, CDCl₃): δ 13.65, 14.18, 19.31, 21.95, 35.96, 37.82, 41.58, 51.52, 60.59, 63.98, 69.58, 77.35, 156.69, 171.12; HRMS (ESI) Calcd for C₁₈H₃₃O₆N₂ [M + H]⁺ 373.2333; Found 373.2333.

Diisopropyl (3*R*,4*S*)-4-(2-ethoxy-2-oxoethyl)-3-methylpyrazolidine-1,2-dicarboxylate (**4i**)



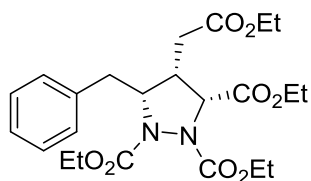
Yield: 688 mg, 80%; gum; $[\alpha]_D^{25}$ -1.817 (c 1.1, CHCl₃); ν_{\max} 1236, 1518, 1617, 1736; **¹H NMR** (200 MHz, CDCl₃): δ 1.24-1.31 (m, 18H), 2.29-2.47 (m, 3H), 2.86-2.93 (m, 1H), 3.88- 3.96 (m, 1H), 4.14 (q, J = 7.2 Hz, 2H), 4.96 (sep, J = 6.2 Hz, 2H); **¹³C NMR** (50 MHz, CDCl₃): δ 14.05, 19.64, 21.82, 21.90, 36.67, 43.25, 51.81, 59.94, 60.53, 69.52, 69.71, 77.20, 155.97, 156.82, 170.94; HRMS (ESI) Calcd for C₁₉H₂₉O₆N₂ [M + H]⁺ 345.2020; Found 345.2019.

1,2-di-*tert*-butyl 3-ethyl (3*S*,4*R*,5*R*)-5-benzyl-4-(2-ethoxy-2-oxoethyl)pyrazolidine-1,2,3-tricarboxylate (**5a**, R' = *t*-Bu)



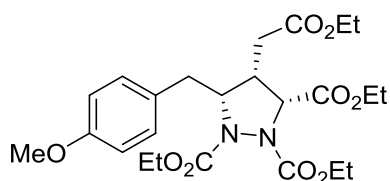
Yield: 650 mg, 50%; gum; $[\alpha]_D^{25}$ +36.7 (c 1.2, CHCl₃); 86% ee (Chiracel OD-H (250 × 4.6 mm), *n*-Hexane:*i*-PrOH, 90:10, 0.5 mL/min, 254 nm), t_r = 29.1 min (minor), t_r = 39.7 min (major); IR (CHCl₃, cm⁻¹): ν_{\max} 741, 1061, 1621, 1738; **¹H NMR** (500 MHz, CDCl₃) δ : 1.19-1.37 (m, 15H), 1.46 - 1.51 (m, 9H), 2.46 (dd, J = 17.1, 8.9 Hz, 1H), 2.52 - 2.57 (m, 1H), 3.11 - 3.17 (m, 2H), 4.07 - 4.28 (m, 5H), 4.42 (br s, 1H), 4.52 (d, J = 10.1 Hz, 1H), 7.19 (d, J = 6.7 Hz, 1H), 7.22 - 7.27 (m, 3 H), 7.27 - 7.30 (m, 1H); **¹³C NMR** of (126 MHz, CDCl₃) δ : 14.1, 14.2, 27.8, 28.3, 30.9, 33.7, 41.7, 60.9, 61.4, 62.6, 63.1, 80.9, 81.2, 126.0, 127.8, 128.1, 129.8, 138.8, 153.1, 155.3, 168.7, 170.4; HRMS (ESI) Calcd for C₂₇H₄₀N₂O₈ [M+Na]⁺ 543.2677; Found 543.2670.

Triethyl (3*S*,4*R*,5*R*)-5-benzyl-4-(2-ethoxy-2-oxoethyl)pyrazolidine-1,2,3-tricarboxylate (**5a**, R' = Et)



Yield: 836 mg, 72%; gum; $[\alpha]_{25}^D +26.7$ (c 1.34, CHCl₃); 96% ee (Chiracel OD-H (250 × 4.6 mm), *n*-Hexane:*i*-PrOH, 90:10, 0.5 mL/min, 254 nm), $t_r = 10.2$ min (minor), $t_r = 11.1$ min (major); IR (CHCl₃, cm⁻¹): ν_{\max} 740, 1065, 1620, 1735; ¹H NMR (500 MHz, CDCl₃) δ : 1.09 (br s, 3H), 1.29 (t, $J = 7.0$ Hz, 6H), 1.33 (t, $J = 7.0$ Hz, 3H), 2.42-2.51 (m, 2H), 2.58 -2.64 (1H), 3.16 (br s, 2H), 4.02 (d, $J = 6.4$ Hz, 2H), 4.16-4.29 (m, 6H), 4.56 (br s, 2H), 7.17 (d, $J = 4.5$ Hz, 1H), 7.25 (br s, 4H); ¹³C NMR of (126 MHz, CDCl₃) δ : 14.0, 14.1, 14.3, 14.5, 30.9, 33.5, 41.8, 60.8, 60.9, 61.5, 62.0, 62.5, 63.4, 126.1, 128.0, 129.5, 138.2, 154.1, 157.3, 168.5, 170.2; HRMS (ESI) Calcd for C₂₃H₃₂N₂O₈ [M+Na]⁺ 487.2051; Found 487.2045.

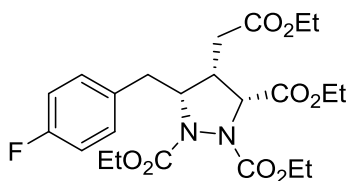
triethyl (3*S*,4*R*,5*R*)-4-(2-ethoxy-2-oxoethyl)-5-(4-methoxybenzyl)pyrazolidine-1,2,3-tricarboxylate (**5b**)



Yield: 952 mg, 77%; gum; $[\alpha]_{25}^D +22.8$ (c 1.2, CHCl₃); 96% ee (Chiracel OD-H (250 × 4.6 mm), *n*-Hexane:*i*-PrOH, 90:10, 0.5 mL/min, 254 nm), $t_r = 15.1$ min (minor), $t_r = 12.5$ min (major); IR (CHCl₃, cm⁻¹): ν_{\max} 739, 1068, 1622, 1738; ¹H NMR (500 MHz, CDCl₃) δ : 1.12 (br s, 3H), 1.29 (t, $J = 7.0$ Hz, 6H), 1.33 (t, $J = 7.0$ Hz, 3H), 2.41-2.62 (m, 3H), 3.07-3.15 (m, 2H), 3.77 (s, 3H), 4.04 (br s, 2H), 4.14-4.28 (m, 6H), 4.48 (s, 1H), 4.53 (d, $J = 8.5$ Hz, 1H), 6.78 (d, $J = 7.9$ Hz, 2H), 7.15 (d, $J = 6.1$ Hz, 2H); ¹³C

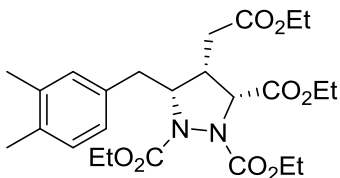
NMR of (126 MHz, CDCl₃) δ : 14.1, 14.1, 14.6, 30.9, 32.6, 41.8, 55.0, 60.8, 61.0, 61.5, 62.1, 62.6, 63.6, 77.0, 96.1, 113.5, 130.4, 154.0, 157.5, 158.1, 168.5, 170.3; HRMS (ESI) Calcd for C₂₄H₃₄N₂O₉ [M+Na]⁺ 517.2157; Found 517.2151.

triethyl (3*S*,4*R*,5*R*)-4-(2-ethoxy-2-oxoethyl)-5-(4-fluorobenzyl)pyrazolidine-1,2,3-tricarboxylate (**5c**)



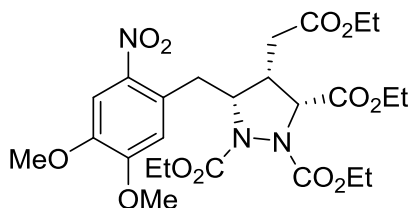
Yield: 772 mg, 64%; gum; $[\alpha]_{25}^D$ +31.9 (c 0.5, CHCl₃); 95% ee (Chiracel OD-H (250 × 4.6 mm), *n*-Hexane:*i*-PrOH, 90:10, 0.5 mL/min, 254 nm), t_r = 93.6 min (minor), t_r = 86.0 min (major); IR (CHCl₃, cm⁻¹): ν_{\max} 740, 1066, 1621, 1740; ¹H NMR (400 MHz, CDCl₃) δ : 1.12 (br s, 3H), 1.29 (t, J = 7.0 Hz, 6H), 1.33 (t, J = 7.0 Hz, 3H), 2.41-2.62 (m, 3H), 3.07-3.15 (m, 2H), 3.77 (s, 3H), 4.04 (br s, 2H), 4.14-4.28 (m, 6H), 4.48 (s, 1H), 4.53 (d, J = 8.5 Hz, 1H), 6.78 (d, J = 7.9 Hz, 2H), 7.15 (d, J = 6.1 Hz, 2H); ¹³C NMR of (101 MHz, CDCl₃) δ : 14.0, 14.2, 14.5, 33.6, 39.3, 44.2, 60.9, 61.3, 62.0, 62.3, 62.8, 64.4, 115.2, 115.4 (d, J = 20.8 Hz), 131.0 (d, J = 7.7 Hz), 132.5, 156.0, 160.7 (d, J = 245.0 Hz), 168.4, 170.5; HRMS (ESI) Calcd for C₂₃H₃₁FN₂O₈ [M+Na]⁺ 505.1957; Found 505.1955.

triethyl (3*S*,4*R*,5*R*)-5-(3,4-dimethylbenzyl)-4-(2-ethoxy-2-oxoethyl)pyrazolidine-1,2,3-tricarboxylate (**5d**)



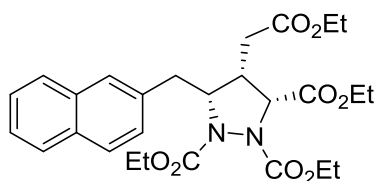
Yield: 924 mg, 75%; gum; $[\alpha]_{25}^D +12.3$ (c 1.2, CHCl_3); 94% ee (Chiracel OD-H (250 × 4.6 mm), *n*-Hexane:*i*-PrOH, 90:10, 0.5 mL/min, 254 nm), $t_r = 19.8$ min (minor), $t_r = 14.3$ min (major); IR (CHCl_3 , cm^{-1}): ν_{max} 741, 1061, 1624, 1739; ^1H NMR (500 MHz, CDCl_3) δ : 1.21 -1.28 (m, 9H), 1.31 (t, $J = 7.0$ Hz, 3H), 1.85-1.95 (m, 1H), 2.09 (br s, 1H), 2.22 (s, 1H), 2.68 (dd, $J = 12.8, 8.2$ Hz, 1H), 2.77 -2.82 (m, 1H), 3.10 (s, 1H), 4.02 (d, $J = 4.5$ Hz, 1H), 4.07-4.27 (m, 8H), 4.96 (d, $J = 7.6$ Hz, 1H), 6.94 (d, $J = 7.3$ Hz, 1H), 7.00 (s, 1H), 7.02 (s, 1H); ^{13}C NMR of (126 MHz, CDCl_3) δ : 13.9, 14.0, 14.4, 19.3, 19.6, 33.6, 39.9, 44.4, 60.6, 61.1, 62.0, 62.1, 62.7, 64.2, 126.7, 129.7, 134.0, 134.7, 136.4, 156.1, 168.4, 170.45 ; HRMS (ESI) Calcd for $\text{C}_{25}\text{H}_{36}\text{N}_2\text{O}_8$ $[\text{M}+\text{Na}]^+$ 515.2364; Found 515.2360.

triethyl (3*S*,4*R*,5*R*)-5-(4,5-dimethoxy-2-nitrobenzyl)-4-(2-ethoxy-2-oxoethyl)pyrazolidine-1,2,3-tricarboxylate (**5e**)



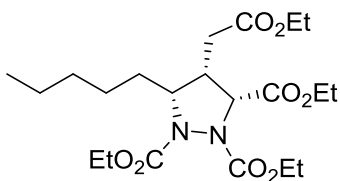
Yield: 911 mg, 64%; yellow gum; $[\alpha]_{25}^D -1.19$ (c 0.1, CHCl_3); 88% ee (Chiracel OD-H (250 × 4.6 mm), *n*-Hexane:*i*-PrOH, 90:10, 0.5 mL/min, 254 nm), $t_r = 34.0$ min (minor), $t_r = 30.4$ min (major); IR (CHCl_3 , cm^{-1}): ν_{max} 740, 1064, 1197, 1273, 466, 1522, 1618, 1736, 2345; ^1H NMR (500 MHz, CDCl_3) δ : 0.99 (br s, 2 H), 1.09 (t, $J = 6.7$ Hz, 1H), 1.25 (d, $J = 7.0$ Hz, 3H), 1.31 - 1.36 (m, 6H), 2.43 - 2.52 (m, 1H), 2.71 (dd, $J = 17.2, 6.3$ Hz, 1H), 3.0 (t, $J = 12.5$ Hz, 1H), 3.26 (d, $J = 13.1$ Hz, 1H), 3.33 - 3.40 (m, 1H), 3.93 (s, 3H), 3.93-4.03 (m, 2H), 4.03 (m, 3H), 4.14 - 4.32 (m, 6H), 4.60 - 4.64 (m, 1H), 4.67 (d, $J = 10.0$ Hz, 1H), 7.12 (s, 1H), 7.60 (s, 1H); ^{13}C NMR of (126 MHz, CDCl_3) δ : 14.1, 14.2, 14.4, 31.2, 31.7, 42.4, 56.2, 56.8, 61.2, 61.3, 61.7, 61.8, 62.0, 62.6, 107.5, 116.8, 129.1, 140.5, 147.5, 153.1, 153.5, 156.1, 170.0, 170.1; HRMS (ESI) Calcd for $\text{C}_{25}\text{H}_{35}\text{N}_3\text{O}_{12}$ $[\text{M}+\text{Na}]^+$ 592.2113; Found 592.2106.

triethyl (3*S*,4*R*,5*R*)-4-(2-ethoxy-2-oxoethyl)-5-(naphthalen-2-ylmethyl)pyrazolidine-1,2,3-tricarboxylate (**5f**)



Yield: 1016 mg, 79%; gum; $[\alpha]_{25}^D +60.3$ (c 1.6, CHCl₃); 94% ee (Chiracel OD-H (250 × 4.6 mm), *n*-Hexane:*i*-PrOH, 90:10, 0.5 mL/min, 254 nm), $t_r = 29.1$ min (minor), $t_r = 24.0$ min (major); IR (CHCl₃, cm⁻¹): ν_{\max} 738, 1061, 1622, 1740; ¹H NMR (500 MHz, CDCl₃) δ : 1.15 (t, $J = 7.0$ Hz, 3H), 1.19 (t, $J = 7.0$ Hz, 3H), 1.28- 1.34 (m, 6H), 1.77 (br s, 1H), 2.87-2.93 (m, 2H), 3.99 (d, $J = 5.6$ Hz, 3H), 4.05-4.12 (m, 3H), 4.23-4.36 (m, 6H), 5.05 (d, $J = 7.9$ Hz, 1H), 7.35 (d, $J = 6.7$ Hz, 2H), 7.48 (t, $J = 7.0$ Hz, 1H), 7.57 (s, 1H), 7.74 (dd, $J = 7.0, 2.1$ Hz, 1H), 7.82 (d, $J = 7.9$ Hz, 1H), 8.33 (s, 1H); ¹³C NMR of (126 MHz, CDCl₃) δ : 13.9, 14.0, 14.4, 33.4, 39.0, 45.3, 60.5, 61.1, 62.2, 62.9, 64.2, 124.1, 125.3, 125.8, 126.4, 127.3, 127.8, 128.6, 131.9, 133.1, 133.7, 156.3, 157.6, 168.2, 170.2; HRMS (ESI) Calcd for C₂₇H₃₄N₂O₈ [M+Na]⁺ 537.2207; Found 537.2205.

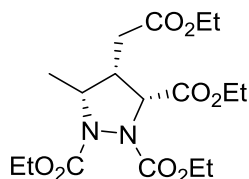
triethyl (3*S*,4*R*,5*R*)-4-(2-ethoxy-2-oxoethyl)-5-pentylpyrazolidine-1,2,3-tricarboxylate (**5g**)



Yield: 800 mg, 72%; $[\alpha]_{25}^D +1.5$ (c 2.0, CHCl₃); IR (CHCl₃, cm⁻¹): ν_{\max} 1620, 1624, 1732, 1736; ¹H NMR (400 MHz, CDCl₃) δ : 0.88 (t, $J = 6.7$ Hz, 3H); 1.25-1.31 (m, 17H), 1.39-1.45 (m, 2H), 1.58-1.65 (m, 1H), 2.33 (dd, $J = 8.7, 17.0$ Hz, 1H), 2.42 (dd, $J = 6.7, 16.8$ Hz, 1H), 2.78 (q, $J = 6.7, 14.8$ Hz, 1H), 3.94 (q, $J = 5.7$ Hz, 1H), 4.13-4.27 (m, 8 Hz), 4.94 (d, $J = 8.0$ Hz, 1H); ¹³C NMR of (101 MHz, CDCl₃) δ : 14.1,

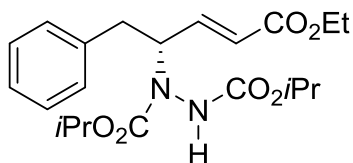
14.2, 14.5, 14.5, 22.5, 25.2, 31.6, 33.7, 33.9, 44.4, 60.9, 61.2, 62.2, 62.2, 62.7, 63.7, 156.4, 158.0, 168.6, 170.8; HRMS (ESI) Calcd for C₂₁H₃₆N₂O₈ [M+Na]⁺ 467.2364; Found 467.2367.

triethyl (3*S*,4*R*,5*R*)-4-(2-ethoxy-2-oxoethyl)-5-methylpyrazolidine-1,2,3-tricarboxylate (**5h**)



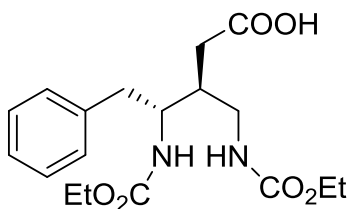
Yield: 602 mg, 62%; gum; [α]₂₅^D -11.6 (c 1.7, CHCl₃); IR (CHCl₃, cm⁻¹): ν_{\max} 1197, 1618, 1736, 1738; ¹H NMR (200 MHz, CDCl₃) δ : 1.24 - 1.33 (m, 15 H), 2.34 - 2.52 (m, 2 H), 2.99 - 3.15 (m, 1 H), 4.04 - 4.61 (m, 10 H); ¹³C NMR of (50 MHz, CDCl₃) δ : 13.7, 13.9, 14.0, 14.33, 14.39, 30.9, 41.4, 43.9, 46.4, 56.4, 60.8, 61.3, 61.9, 62.7, 64.0, 96.0, 153.7, 156.8, 170.2, 170.5; HRMS (ESI) Calcd for C₁₇H₂₈N₂O₈ [M+Na]⁺ 411.1738; Found 411.1732.

Diisopropyl (*R,E*)-1-(5-ethoxy-5-oxo-1-phenylpent-3-en-2-yl)hydrazine-1,2-dicarboxylate (**6**)

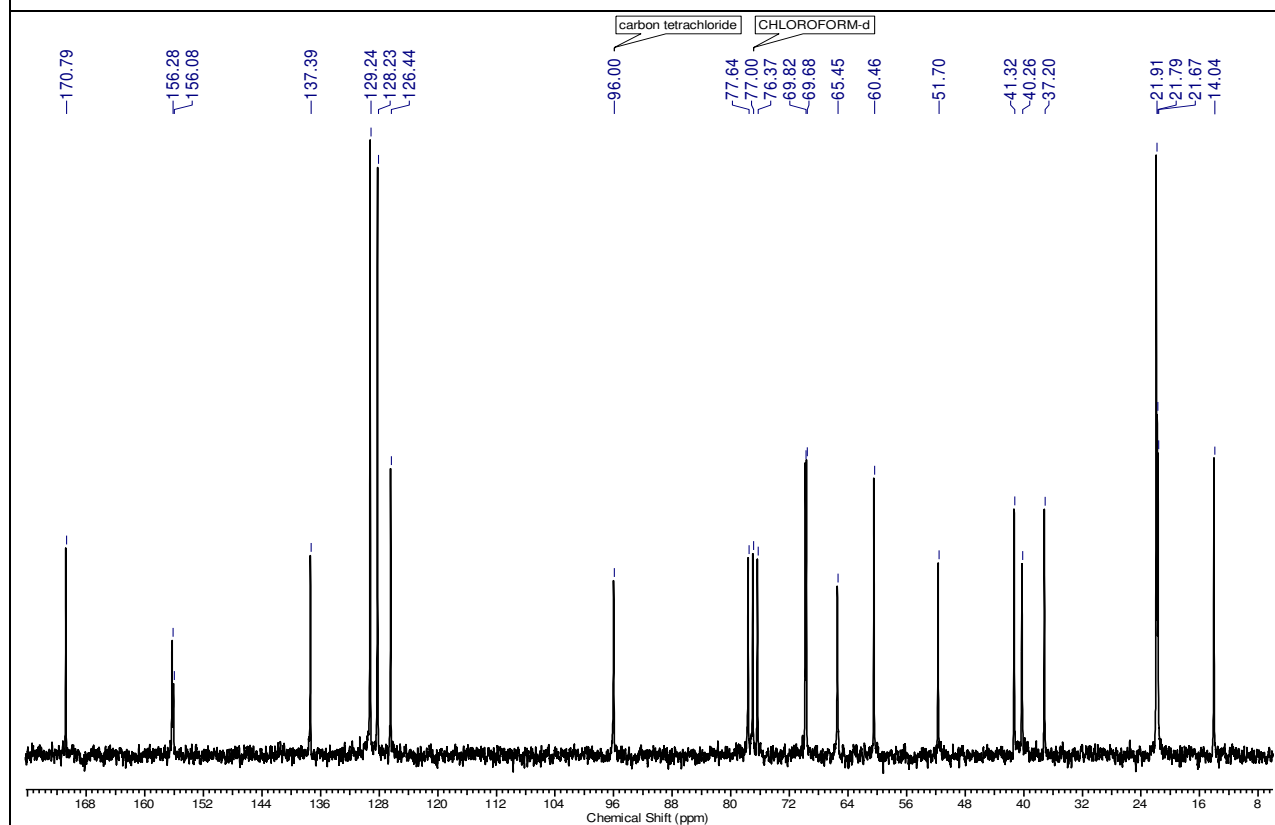
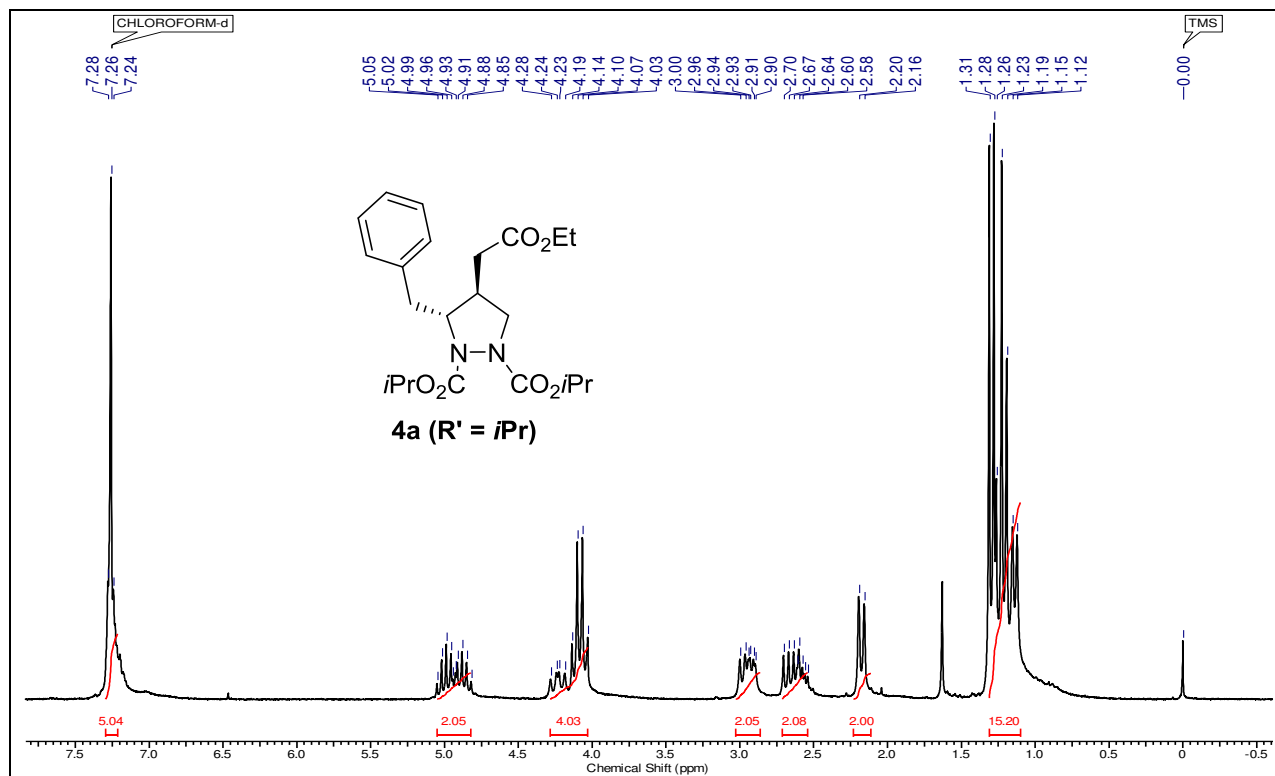


Yield: 912.6 mg, 90%; gum; ¹H NMR (200 MHz, CDCl₃) δ : 1.16-1.31 (m, 15H), 2.92-3.10 (m, 2H), 4.17 (q, *J* = 7.07 Hz, 2H), 4.81-5.02 (m, 2H), 5.88 (d, *J* = 16.29 Hz, 1H), 6.12 (br s, 1H), 6.89-7.00 (dd, *J* = 2.7, 18.3 Hz, 1H), 7.17-7.32 (m, 5H); ¹³C NMR (126 MHz, CDCl₃) δ : 14.2, 21.88, 21.94, 37.73, 60.31, 69.88, 70.32, 122.84, 126.71, 128.60, 128.97, 137.06, 144.55, 154.90, 165.86.

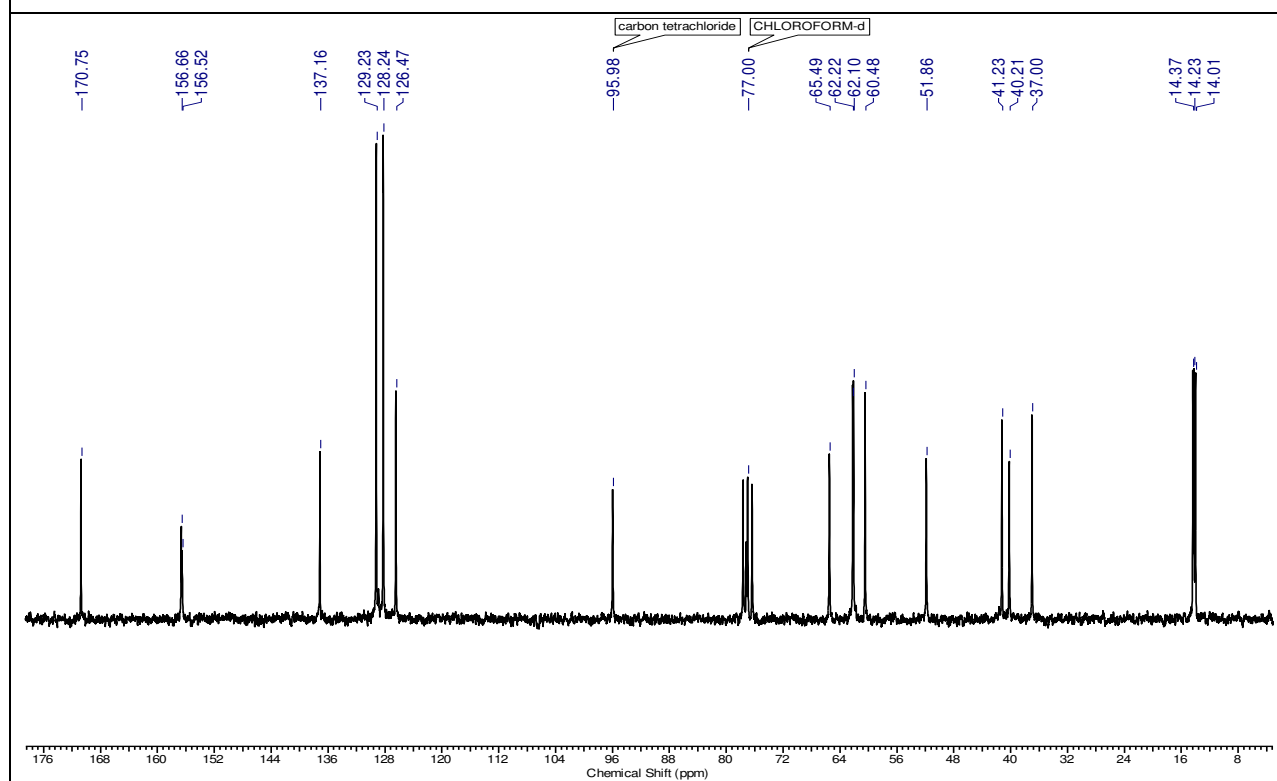
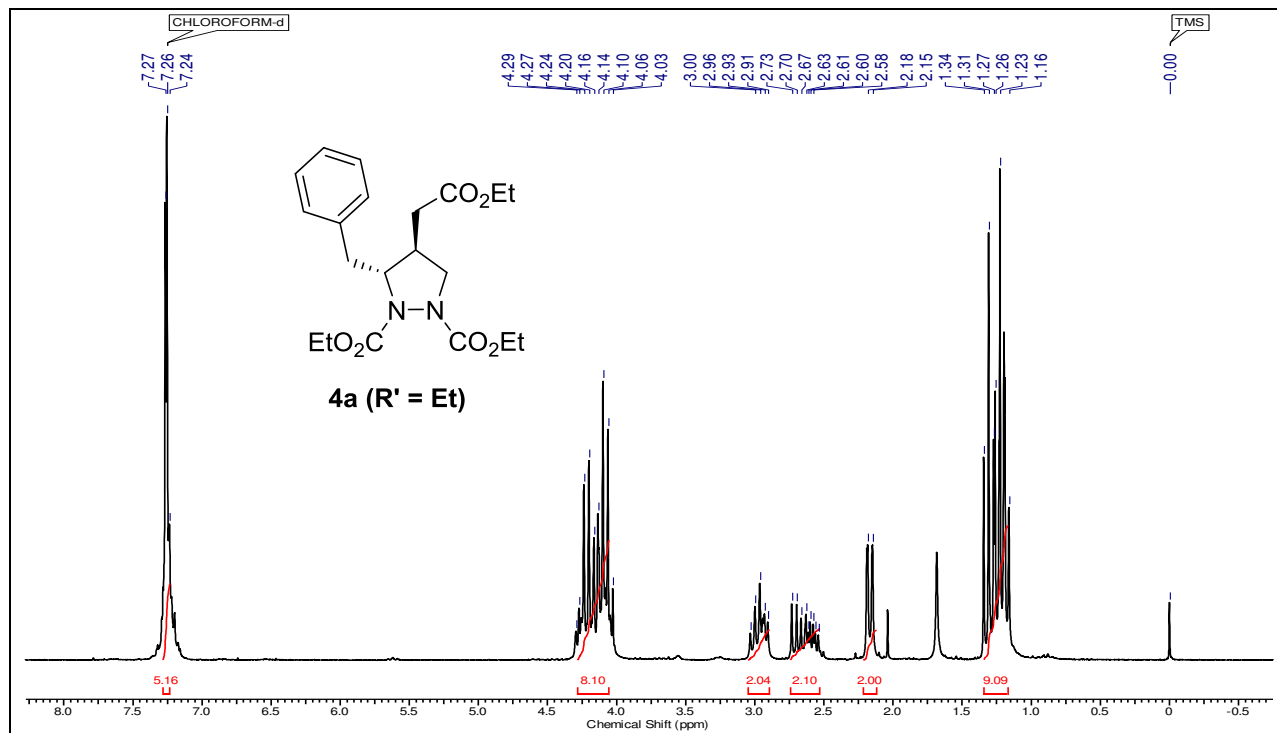
(3*S*,4*R*)-4-((ethoxycarbonyl)amino)-3-(((ethoxycarbonyl)amino)methyl)-5-phenylpentanoic acid (**7**)



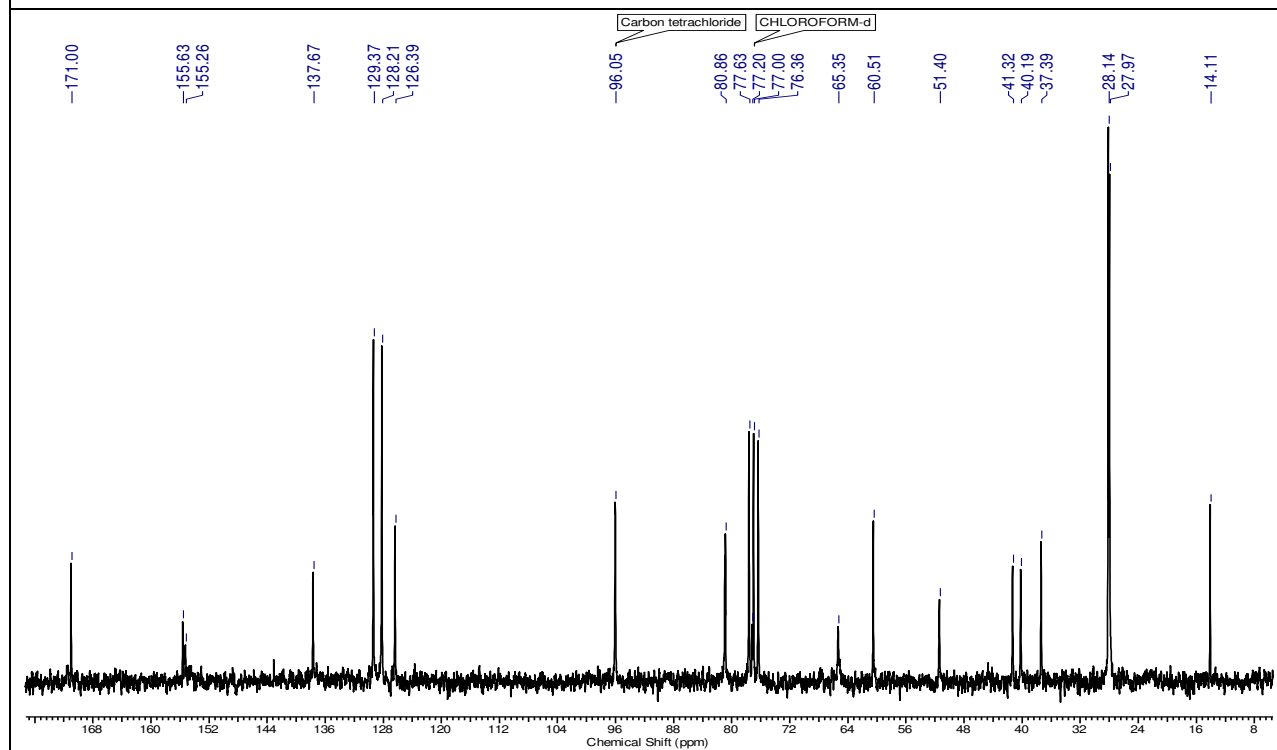
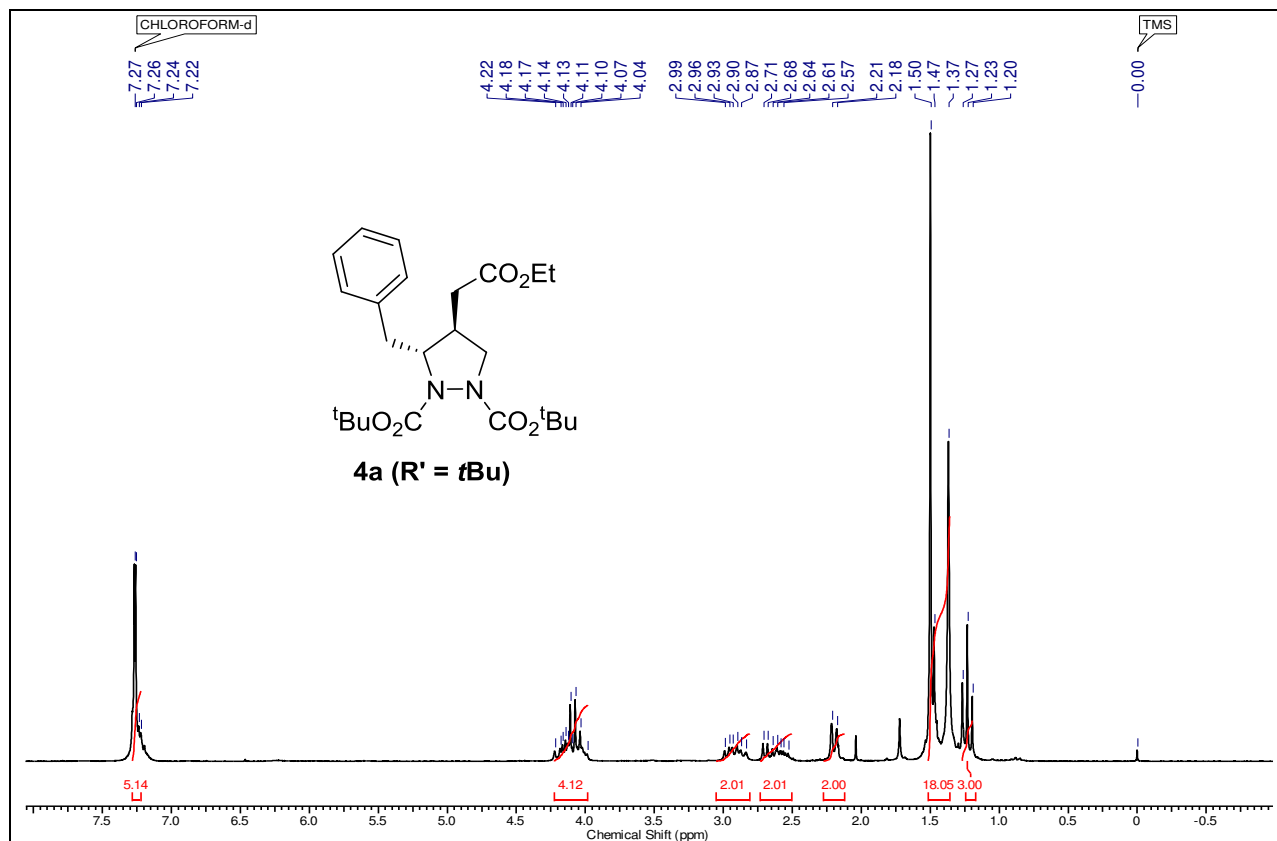
Yield: 56 mg, 60%; gum; $[\alpha]_D^{25}$ -1.490 (c 1.12, CHCl₃); **¹H NMR** (400 MHz, DMSO-D₆): δ 1.07 (t, *J* = 7.3 Hz, 3H), 1.20 (t, *J* = 7.3 Hz, 3H), 2.14-2.30 (m, 2H), 2.42-2.47 (m, 1H), 2.75 (t, *J* = 5.5 Hz, 2H), 2.89-2.94 (dd, *J* = 7.3, 10.9 Hz, 2H), 3.96-4.12 (m, 7H), 7.18-7.30 (m, 5H), 8.31 (s, 1H), 12.31 (s, 1H); **¹³C NMR** (50 MHz, DMSO-D₆): δ 14.19, 14.40, 36.04, 41.02, 51.44, 61.59, 61.75, 65.32, 126.30, 128.10, 129.38, 137.83, 156.37, 172.83; LC-MS (ESI) *m/z*: 365.2 [M - 1]⁺



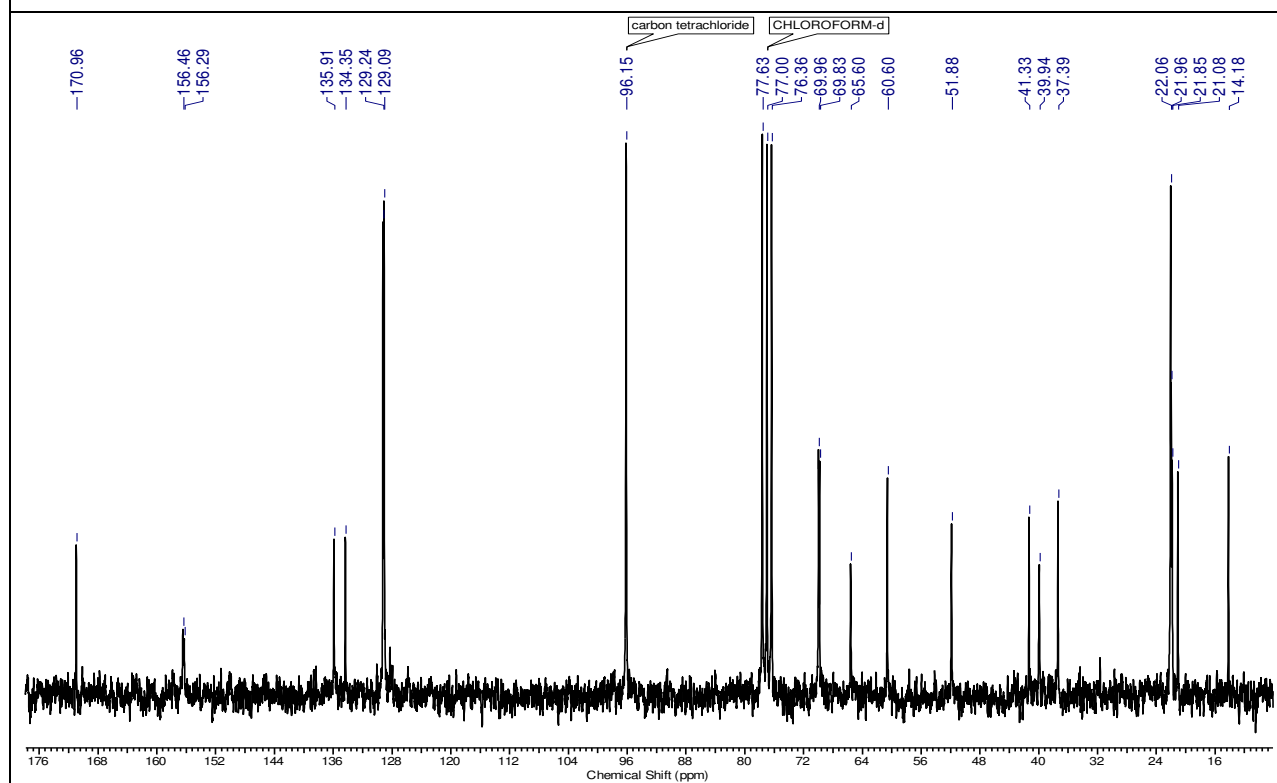
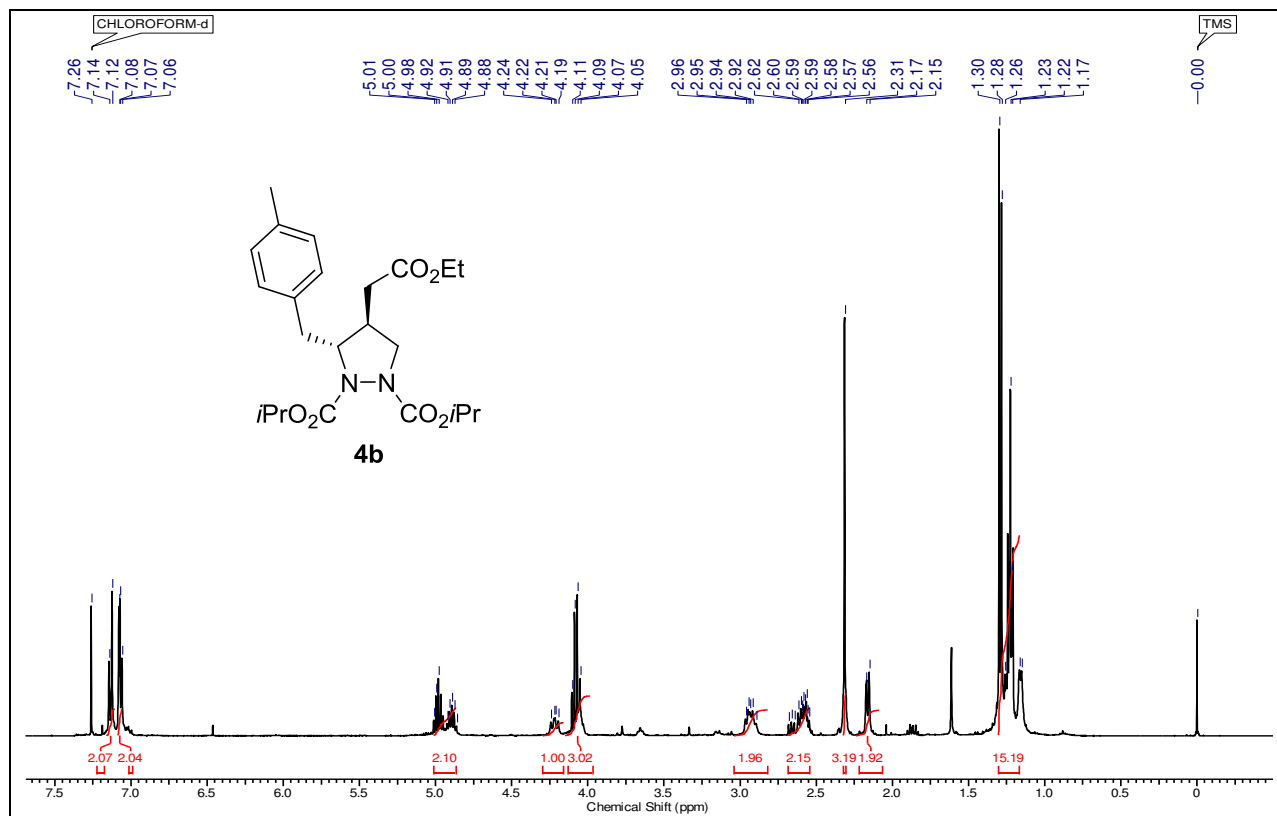
^1H & ^{13}C spectra of **4a (R' = iPr)**



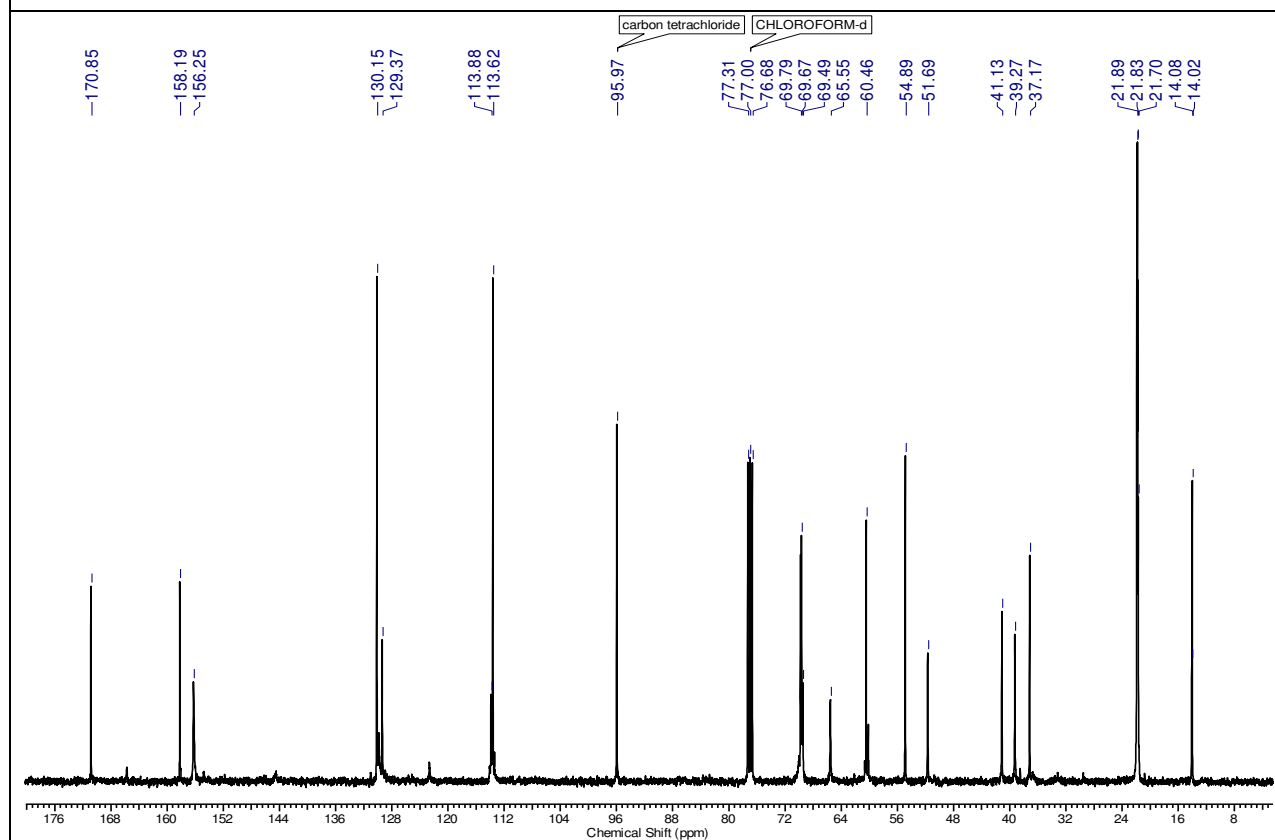
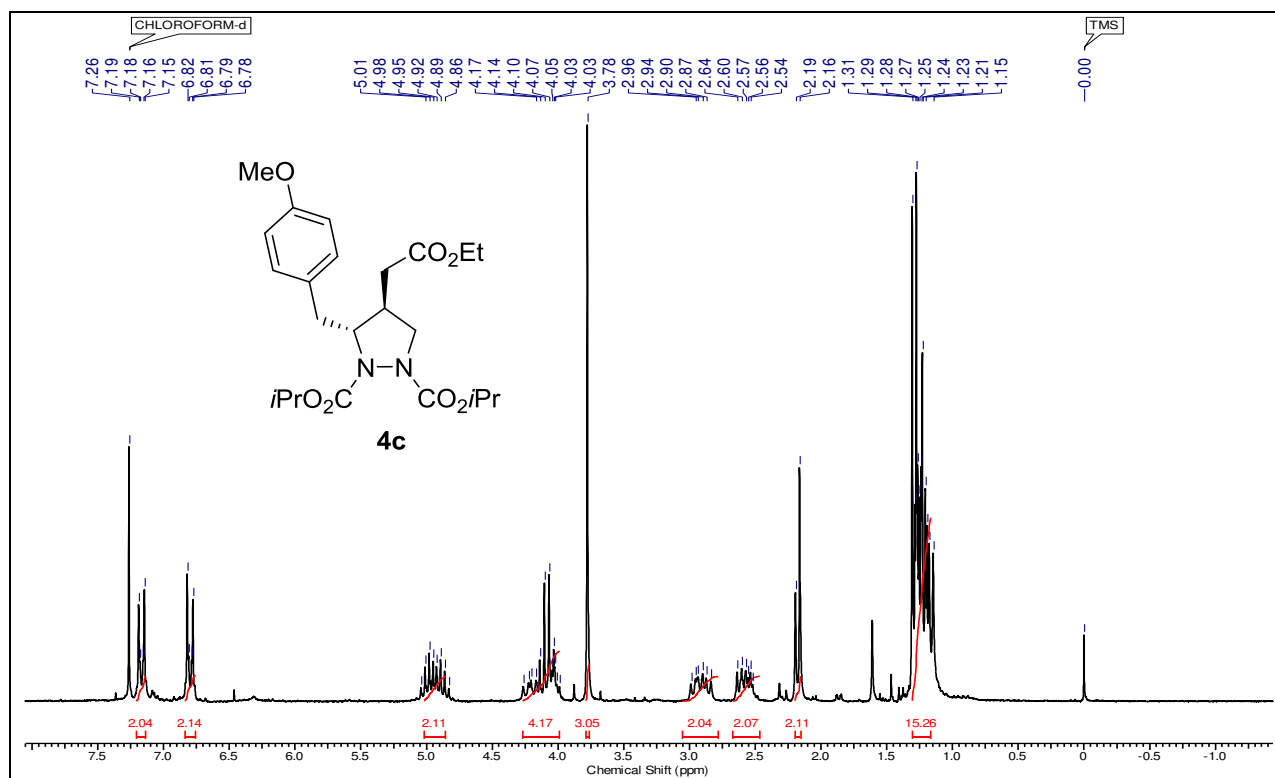
¹H & ¹³C spectra of 4a (R' = Et)



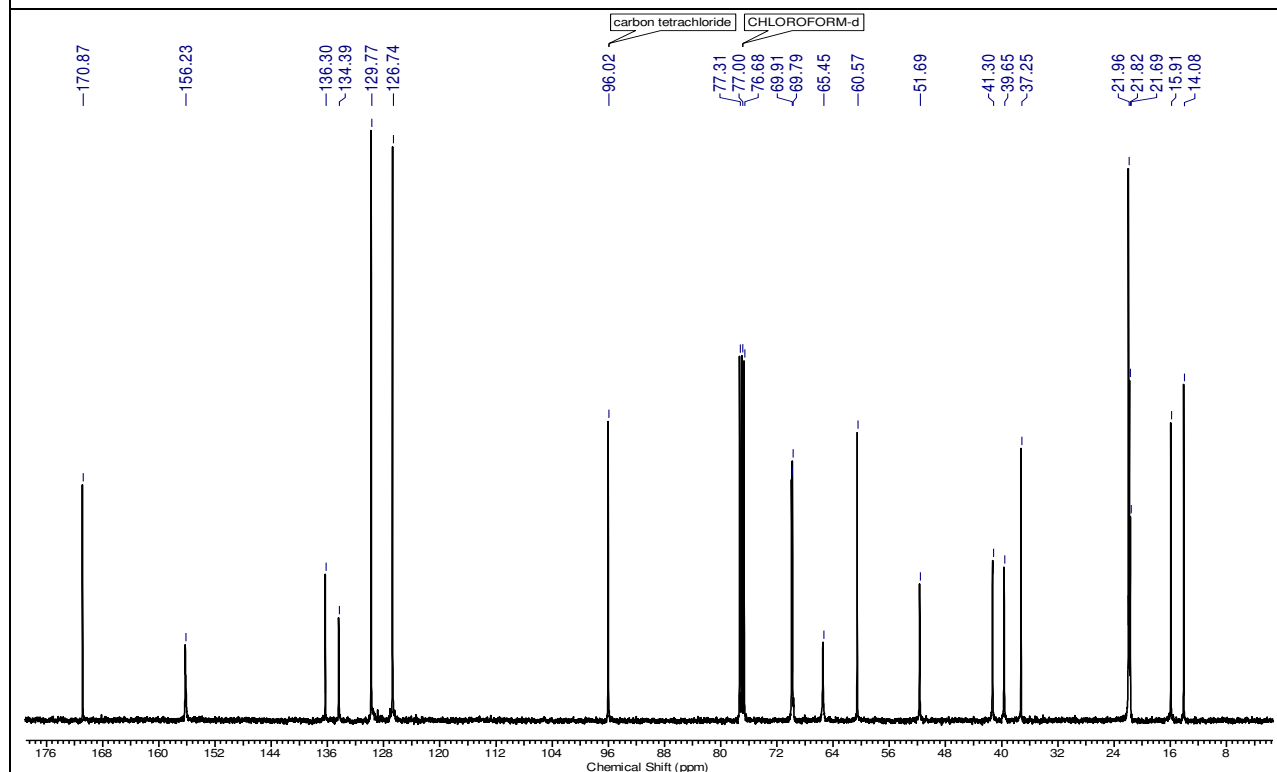
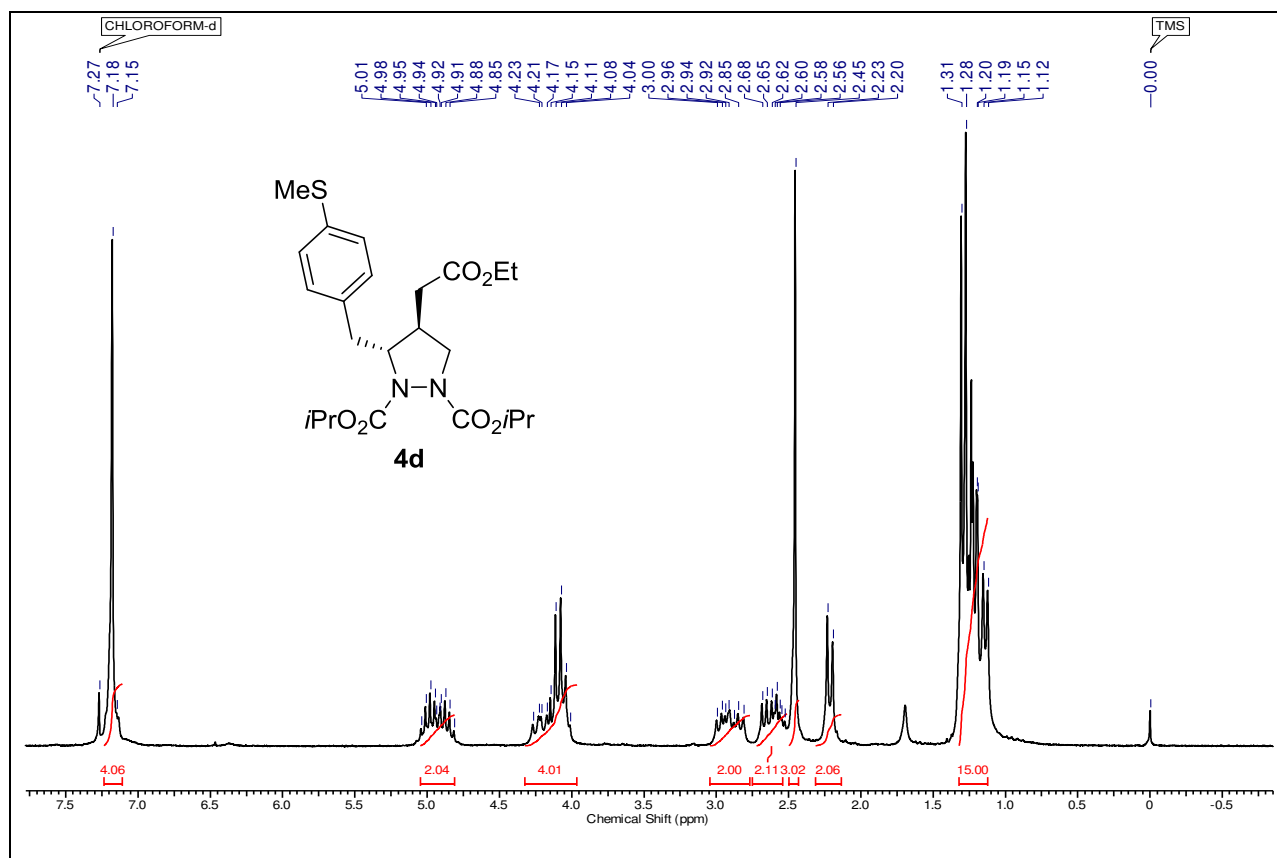
¹H & ¹³C spectra of **4a** (R' = t-Bu)



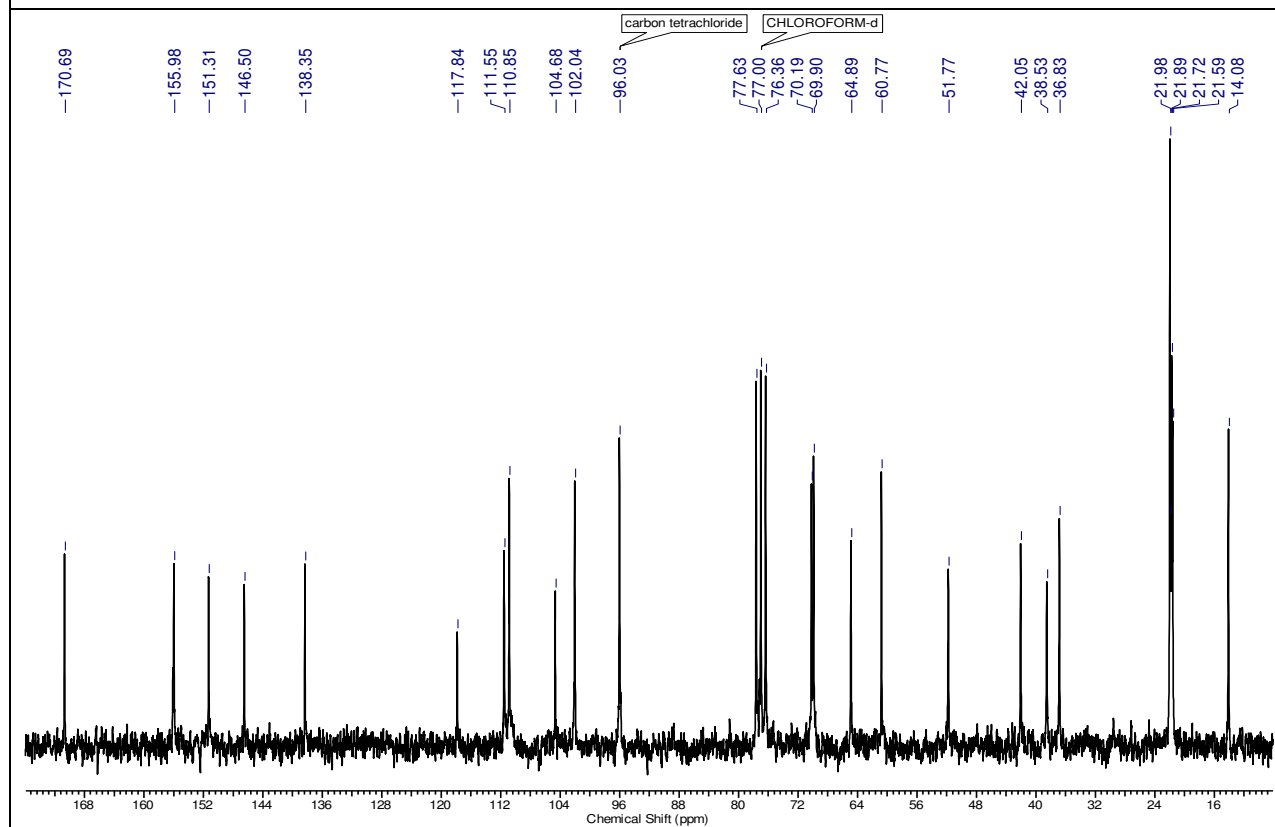
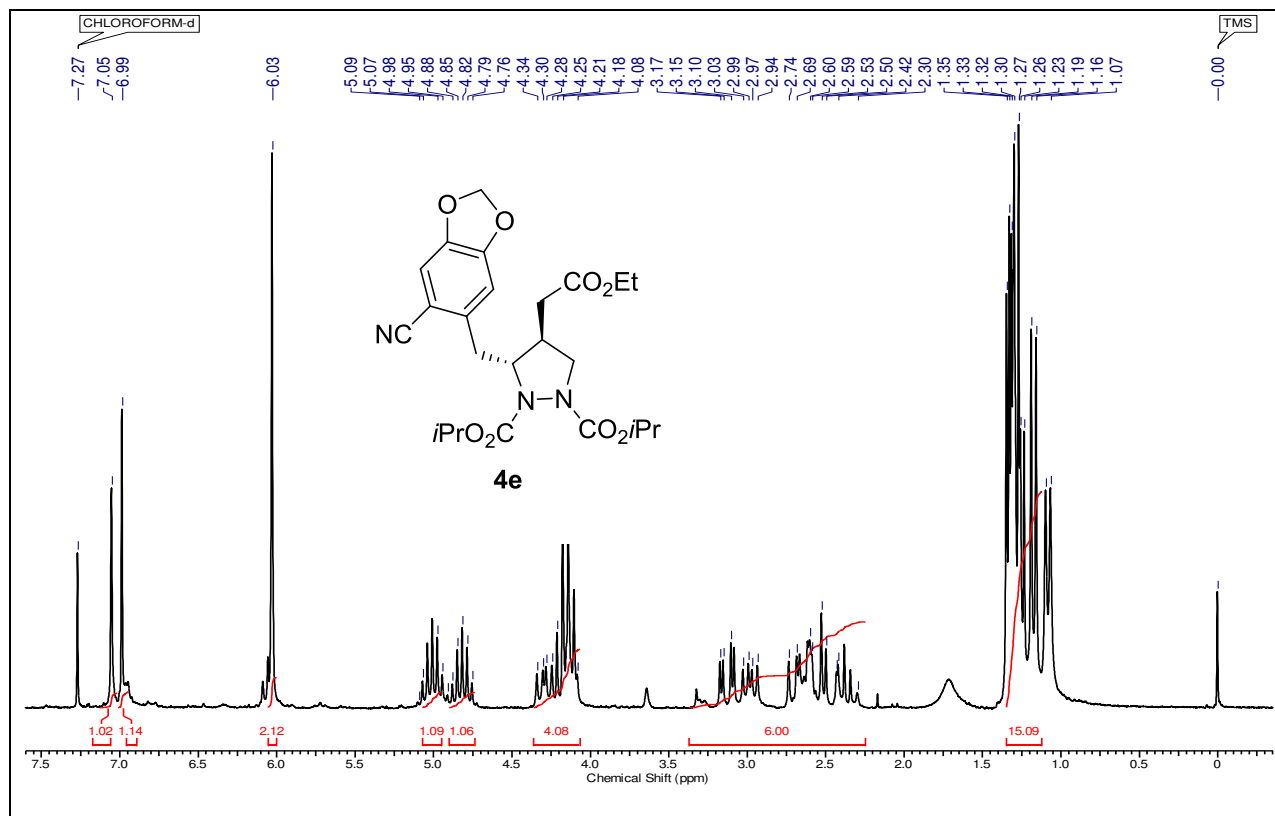
^1H & ^{13}C spectra of **4b**



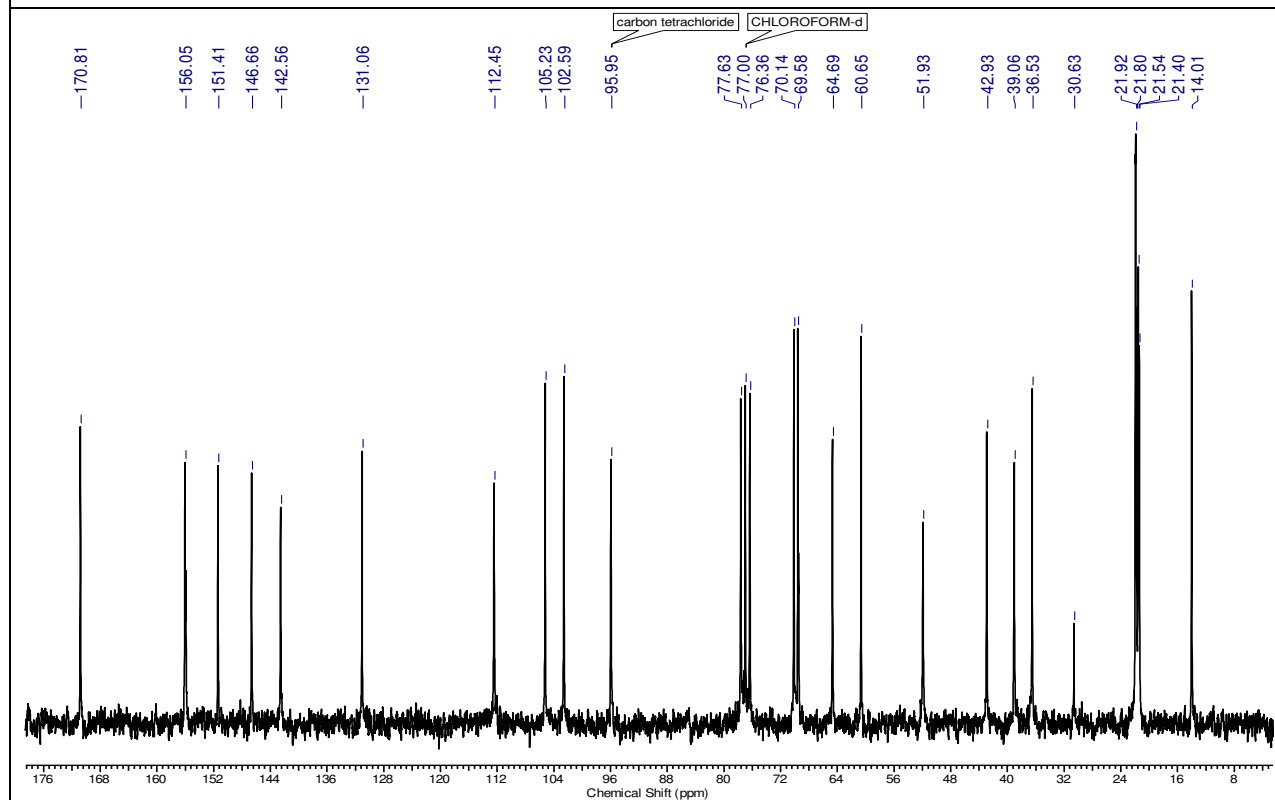
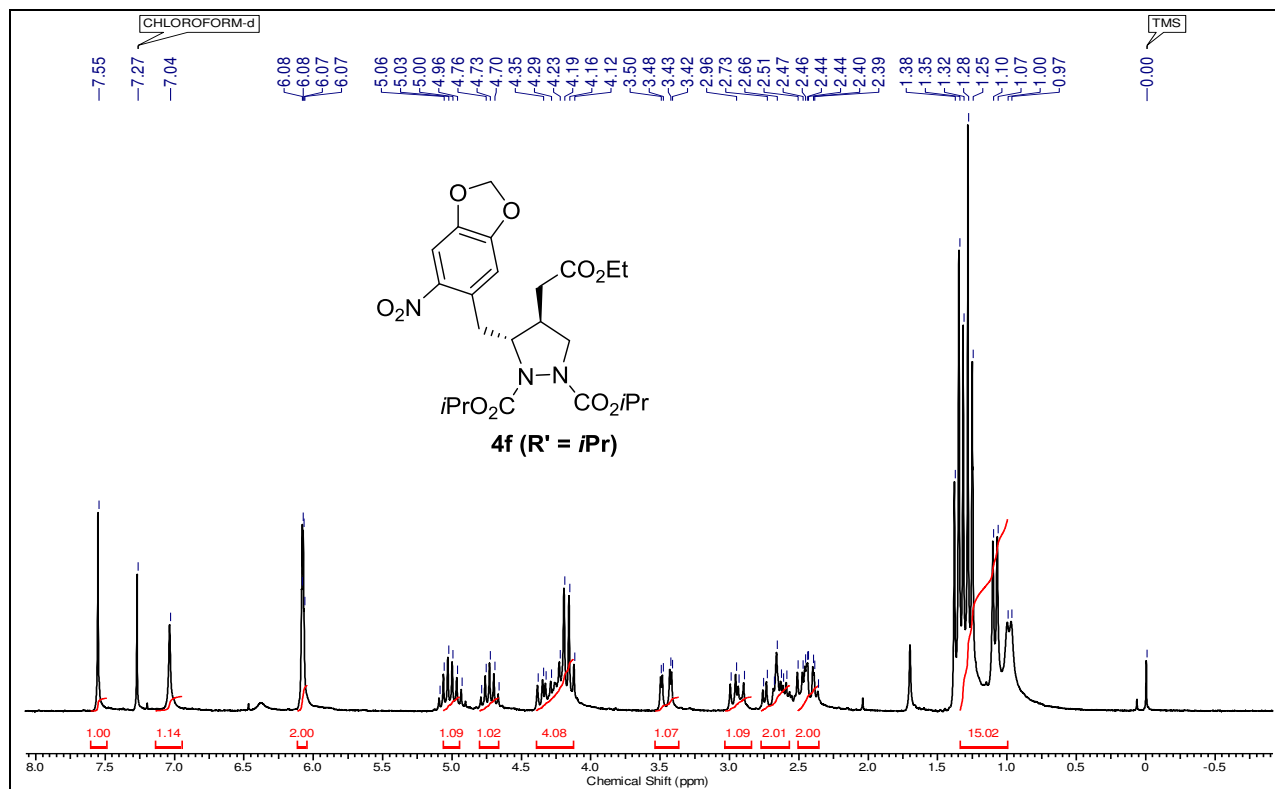
¹H & ¹³C spectra of 4c



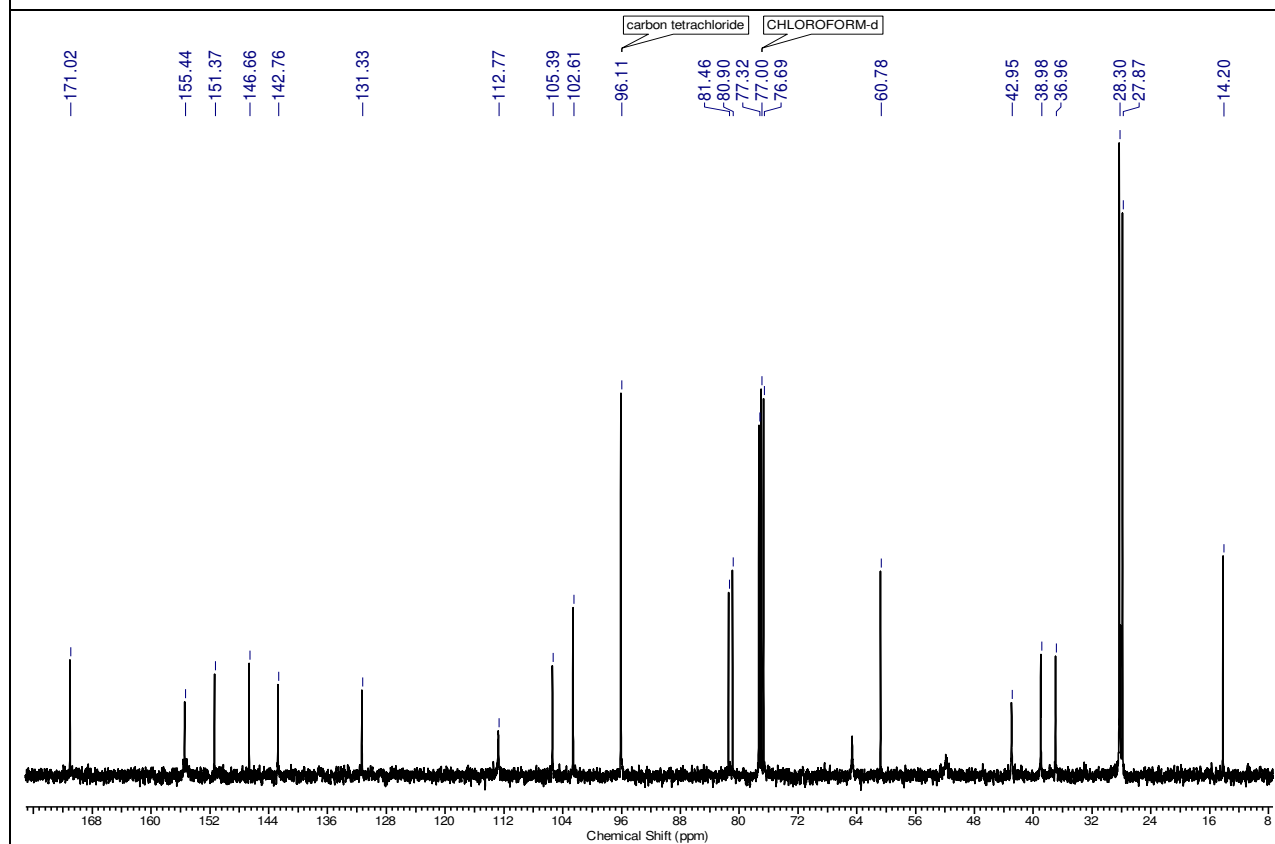
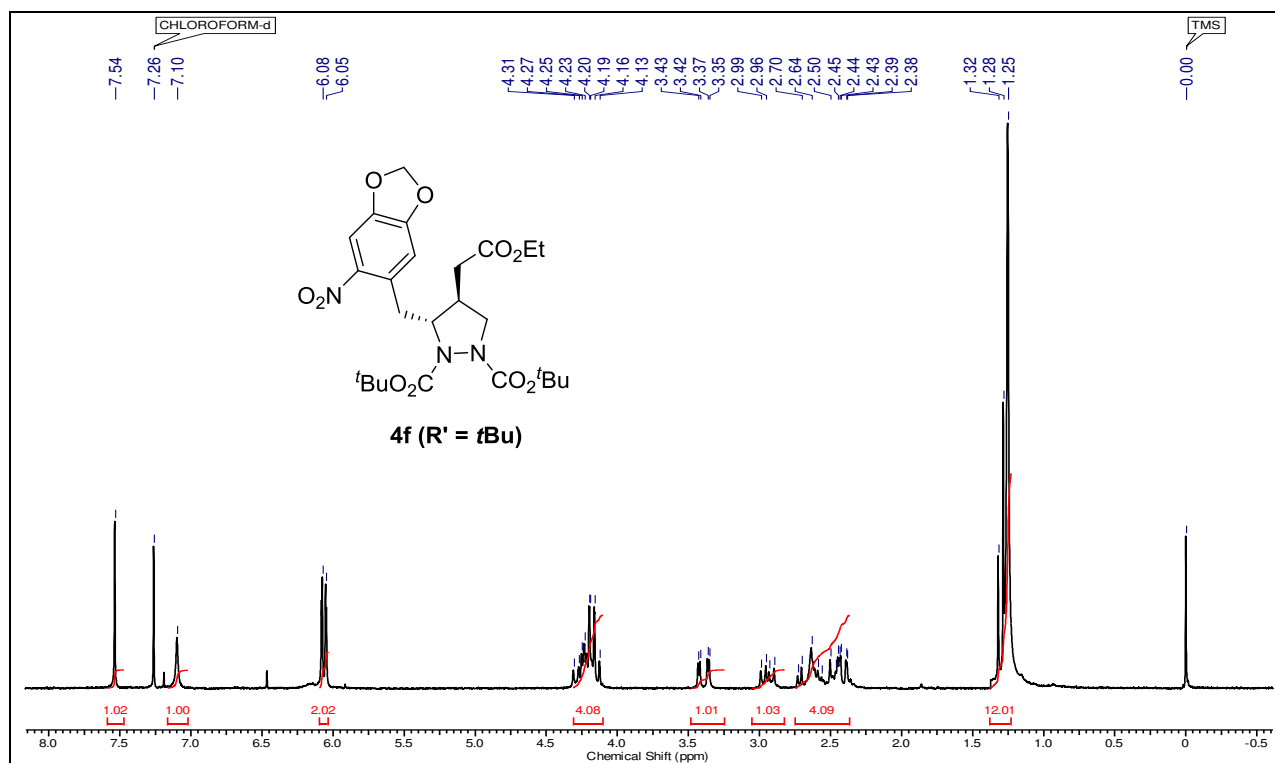
¹H & ¹³C spectra of **4d**



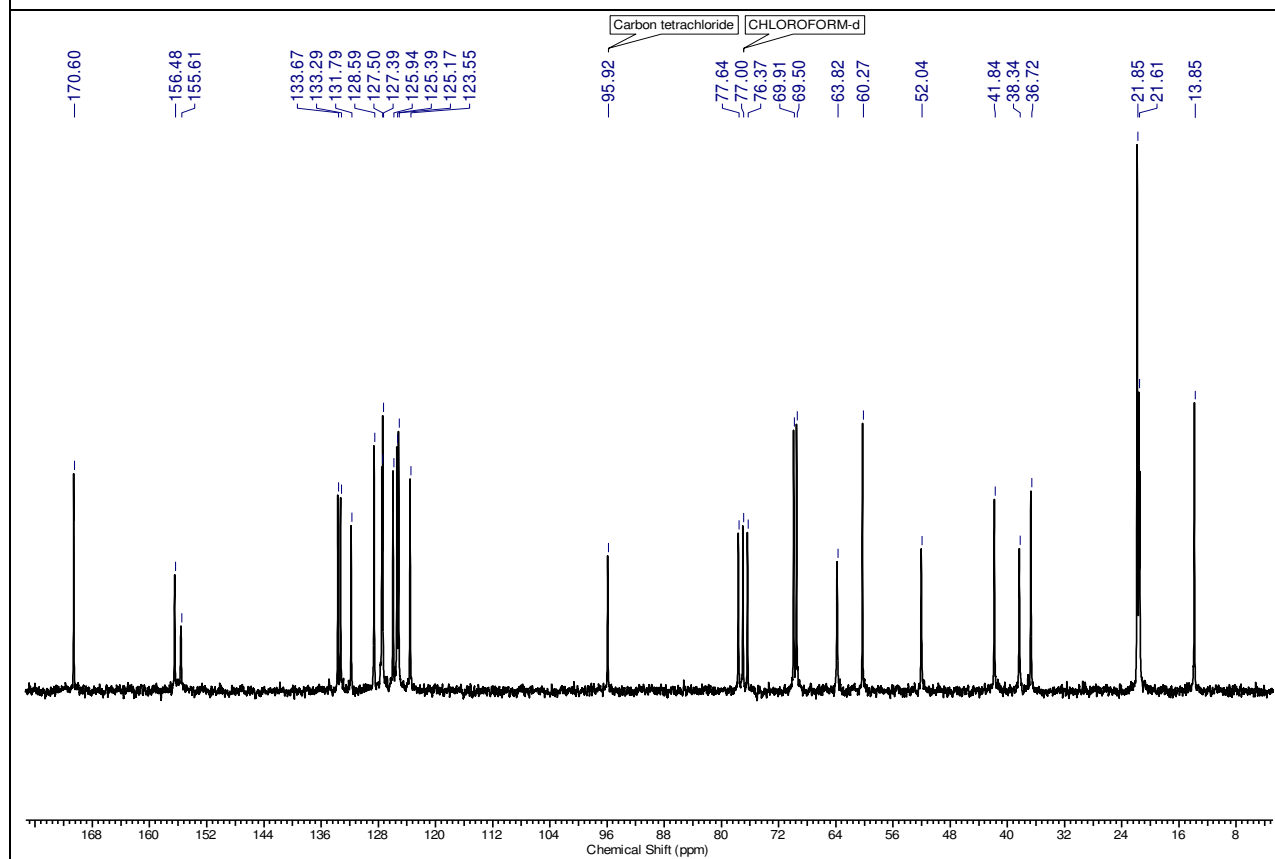
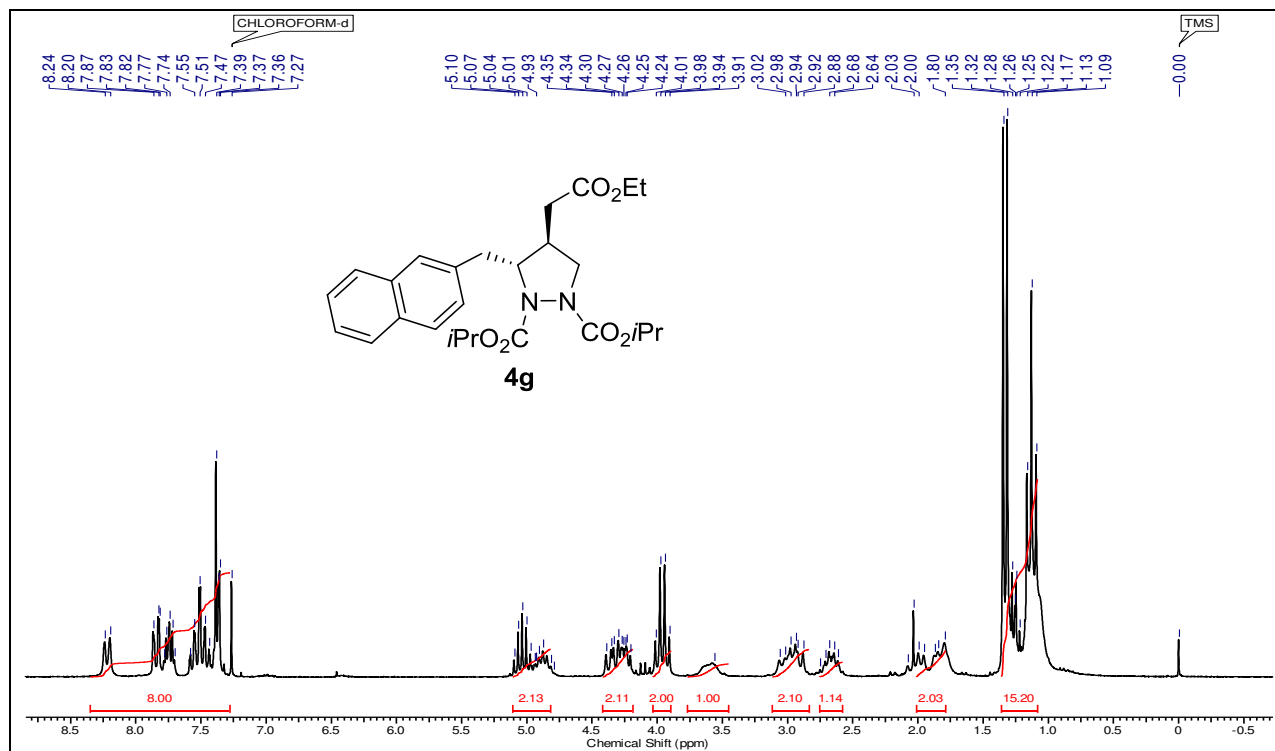
¹H & ¹³C spectra of **4e**



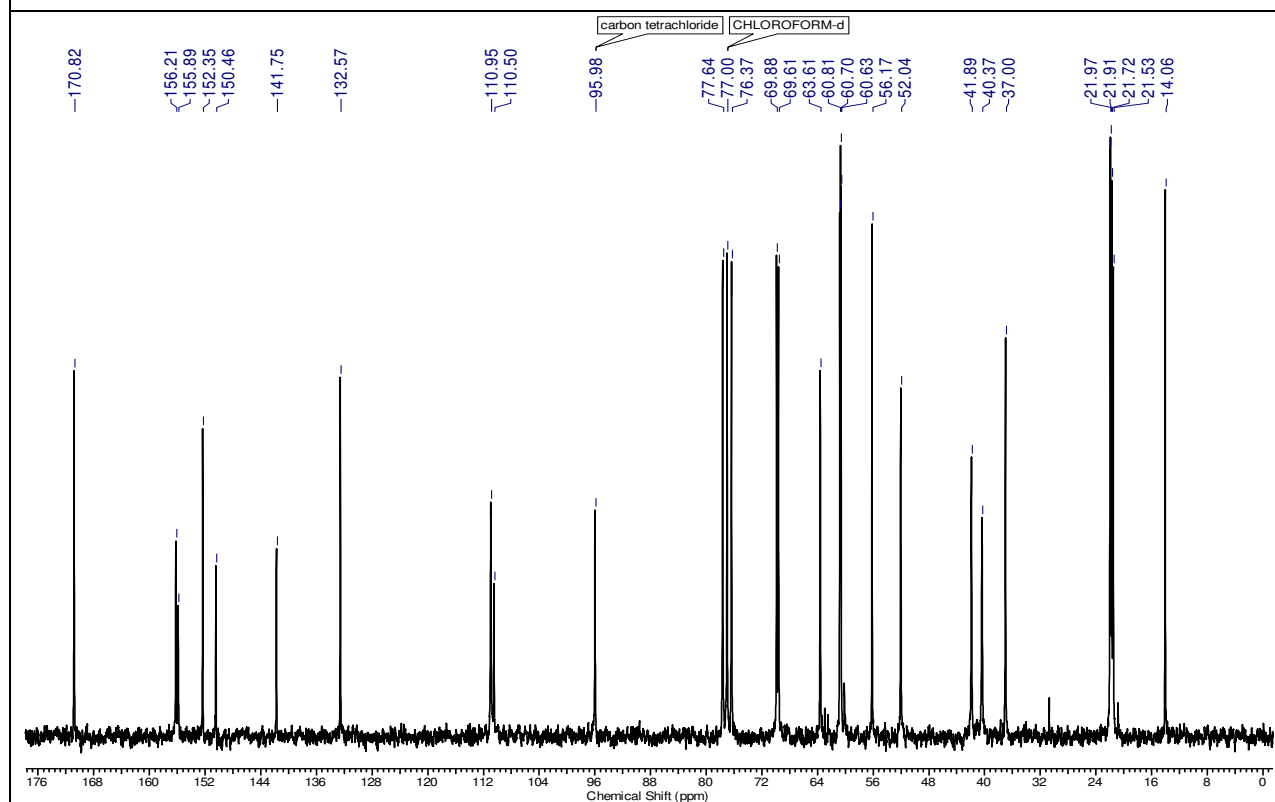
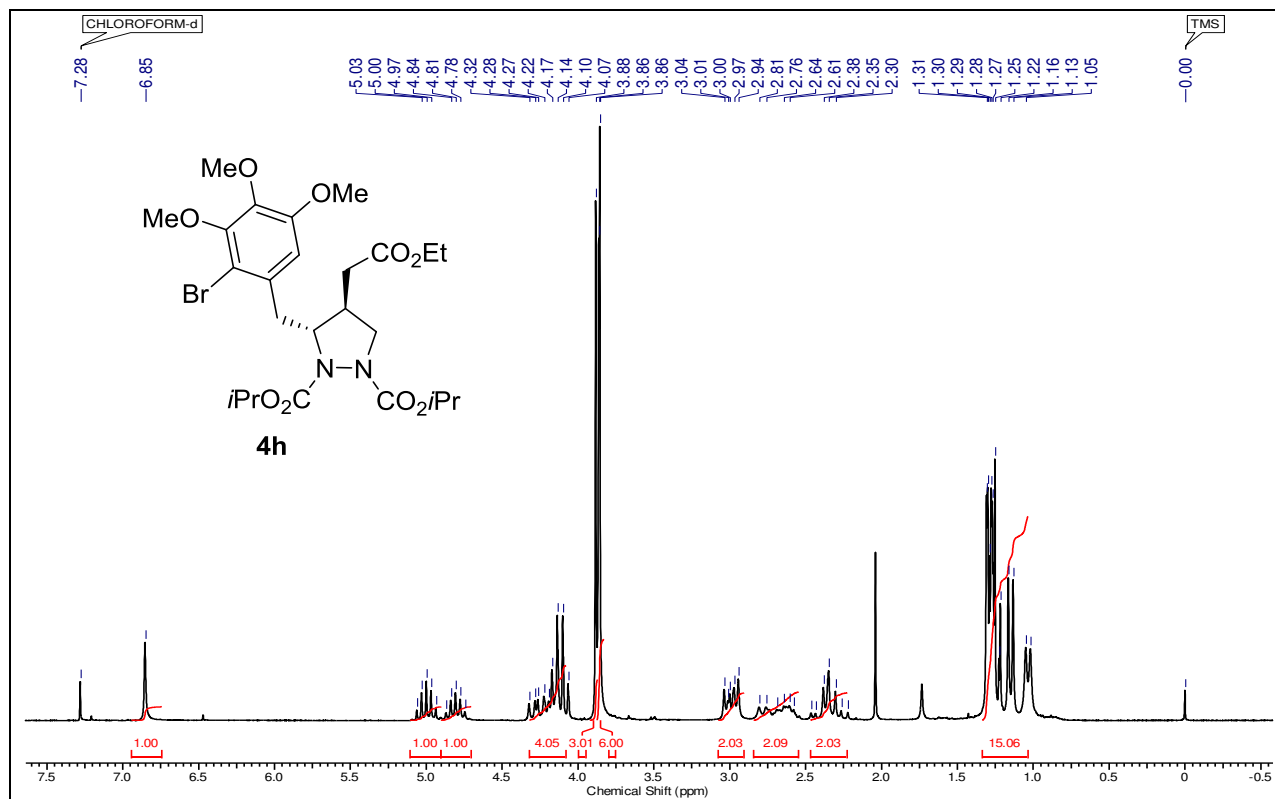
^1H & ^{13}C spectra of **4f**



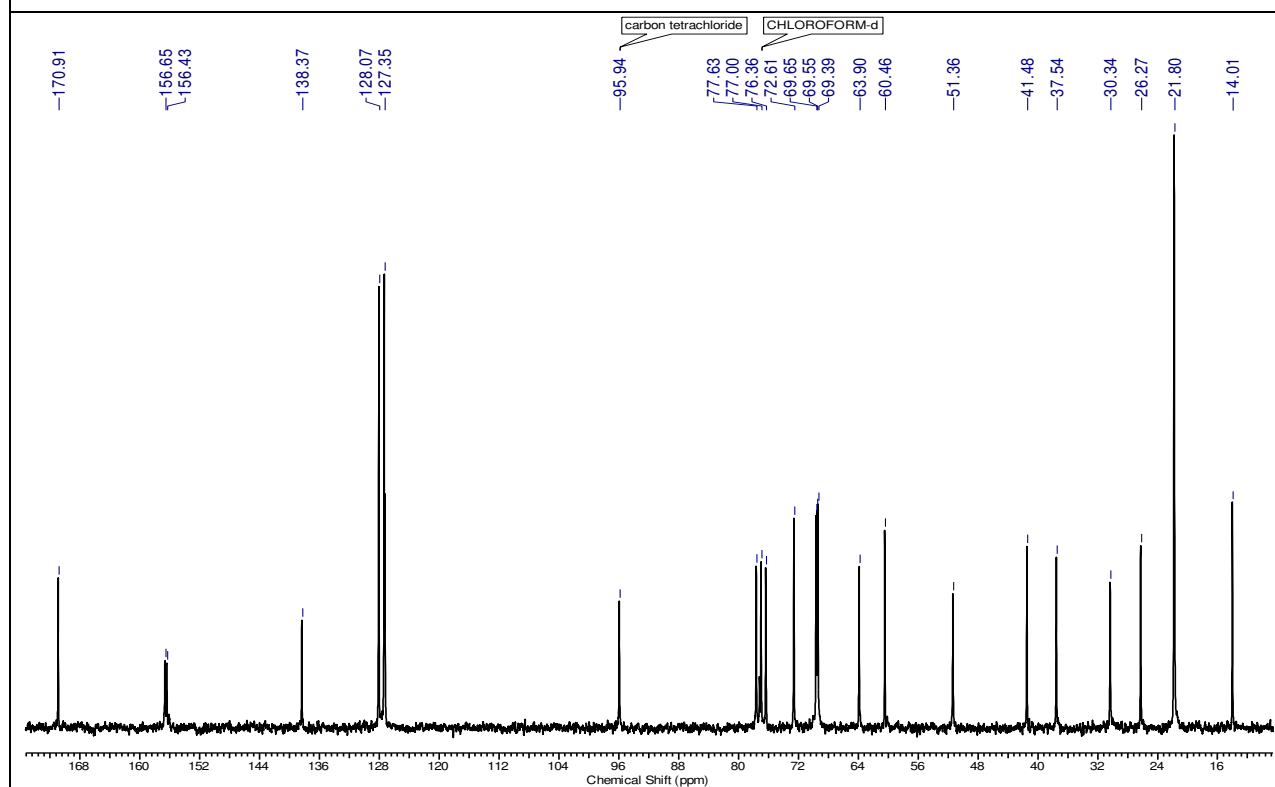
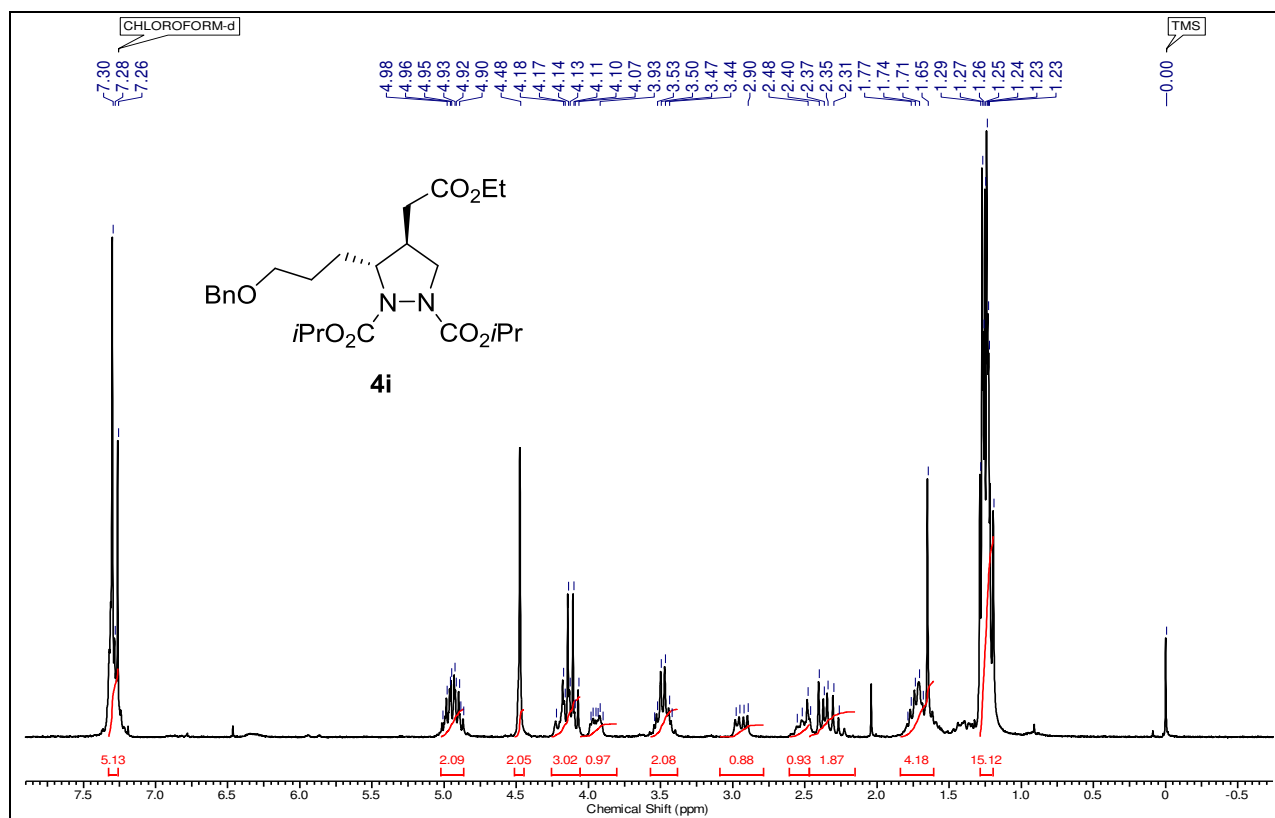
^1H & ^{13}C spectra of **4f**



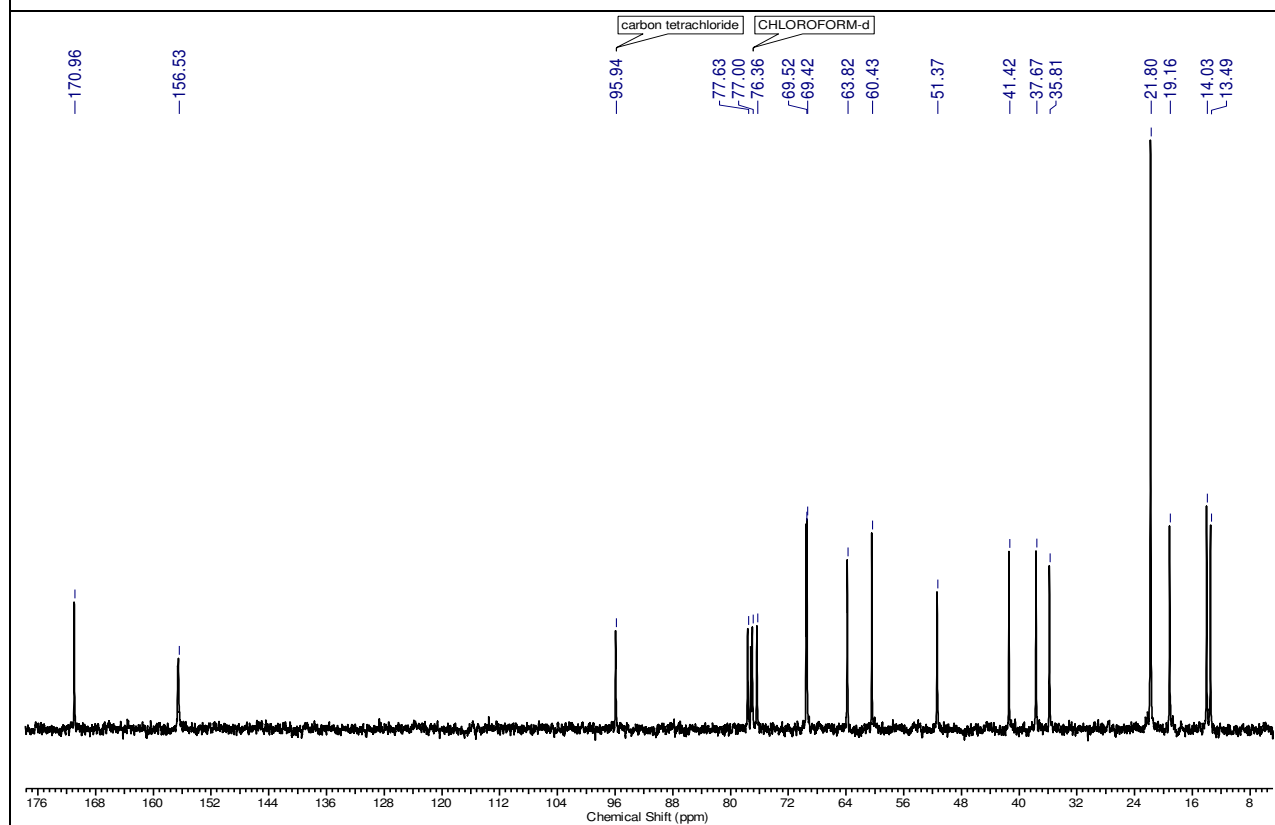
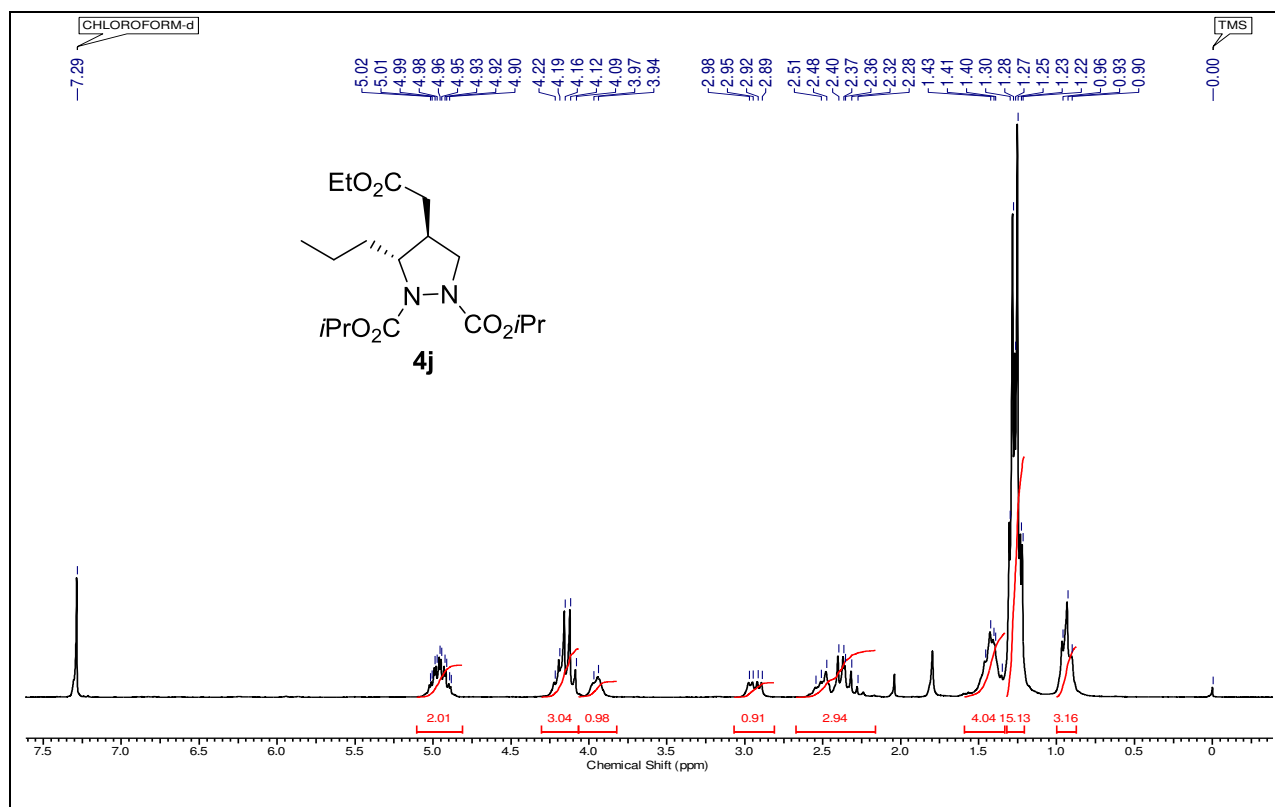
^1H & ^{13}C spectra of **4g**



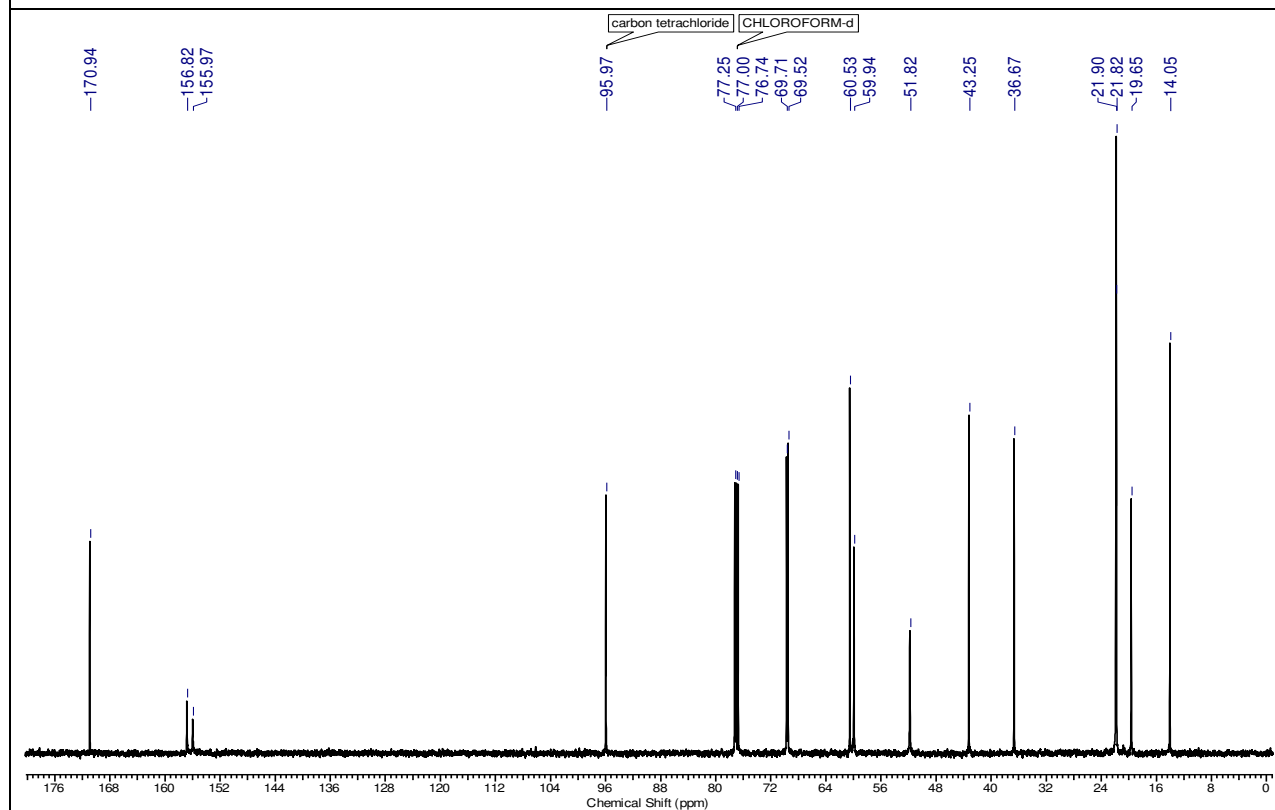
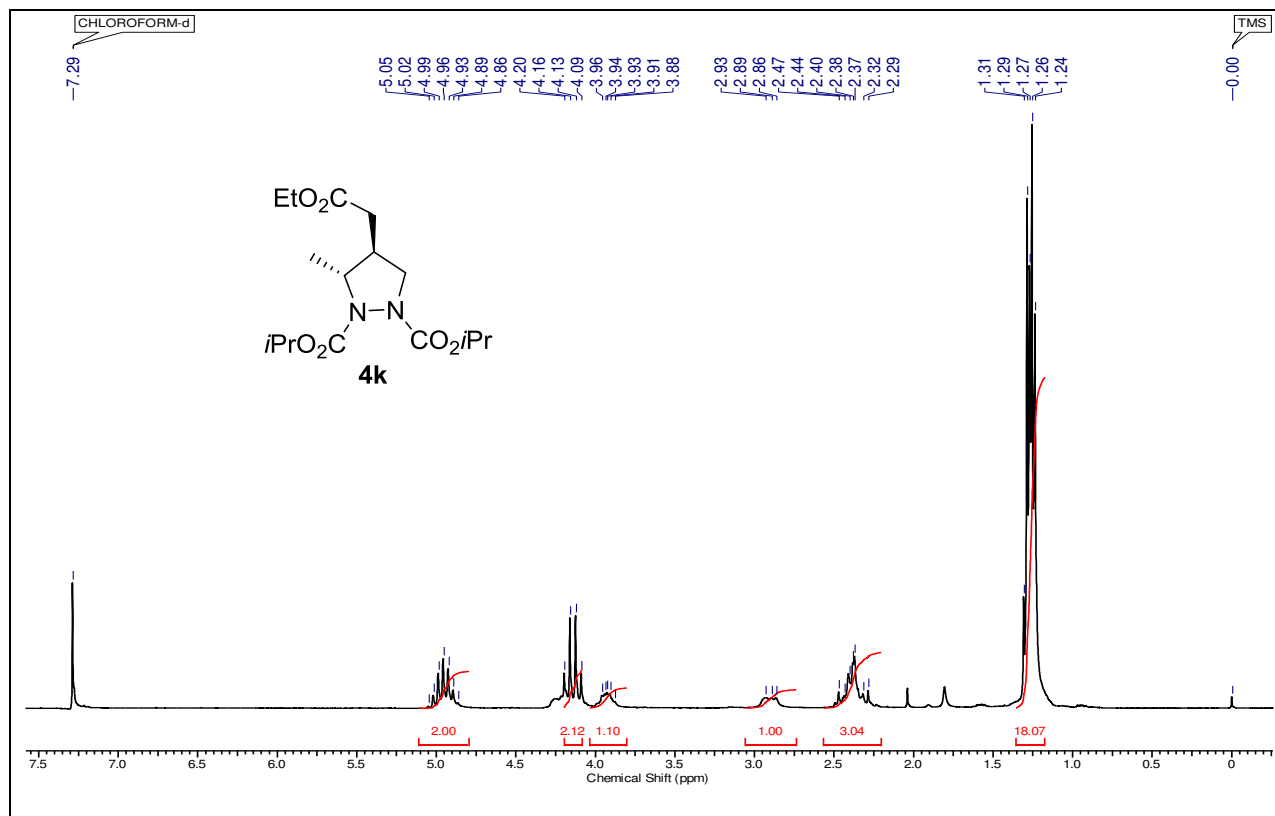
¹H & ¹³C spectra of **4h**



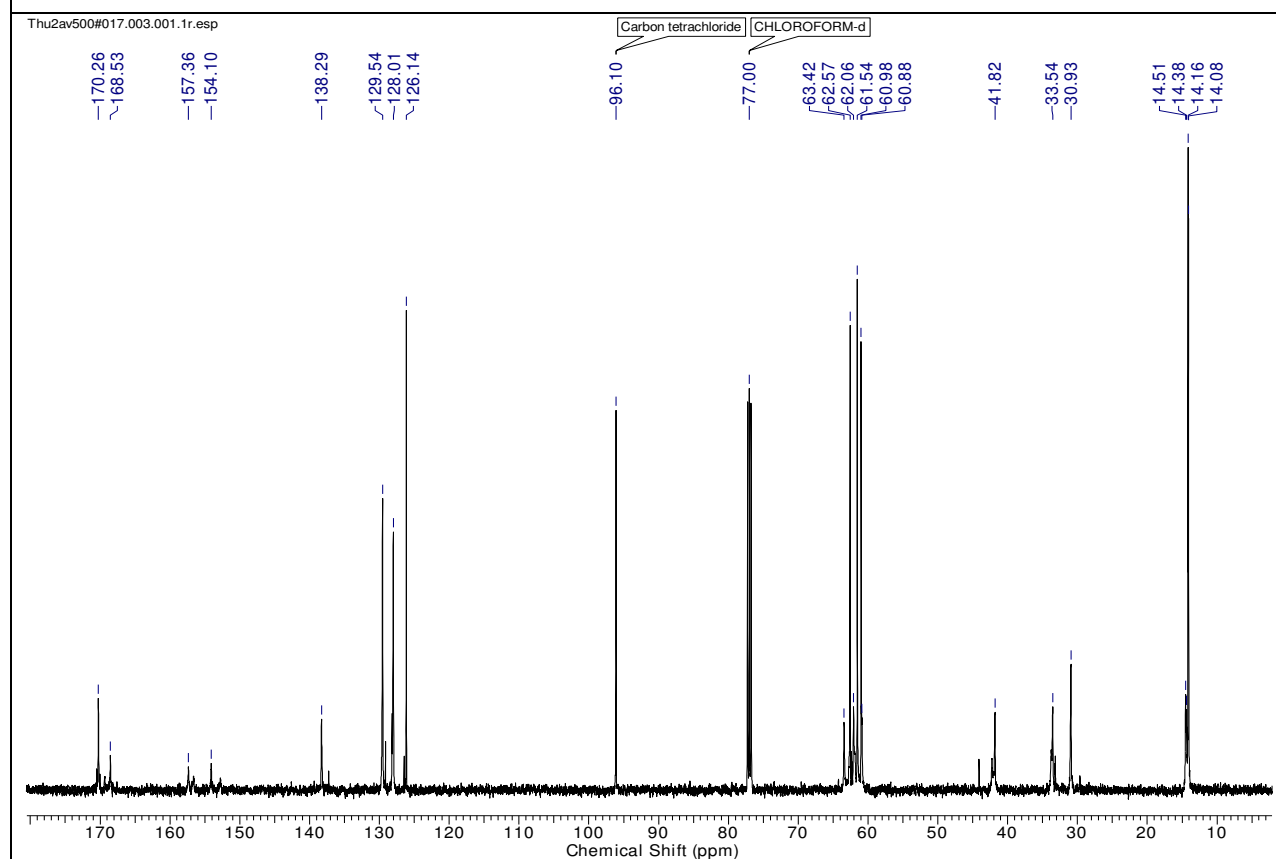
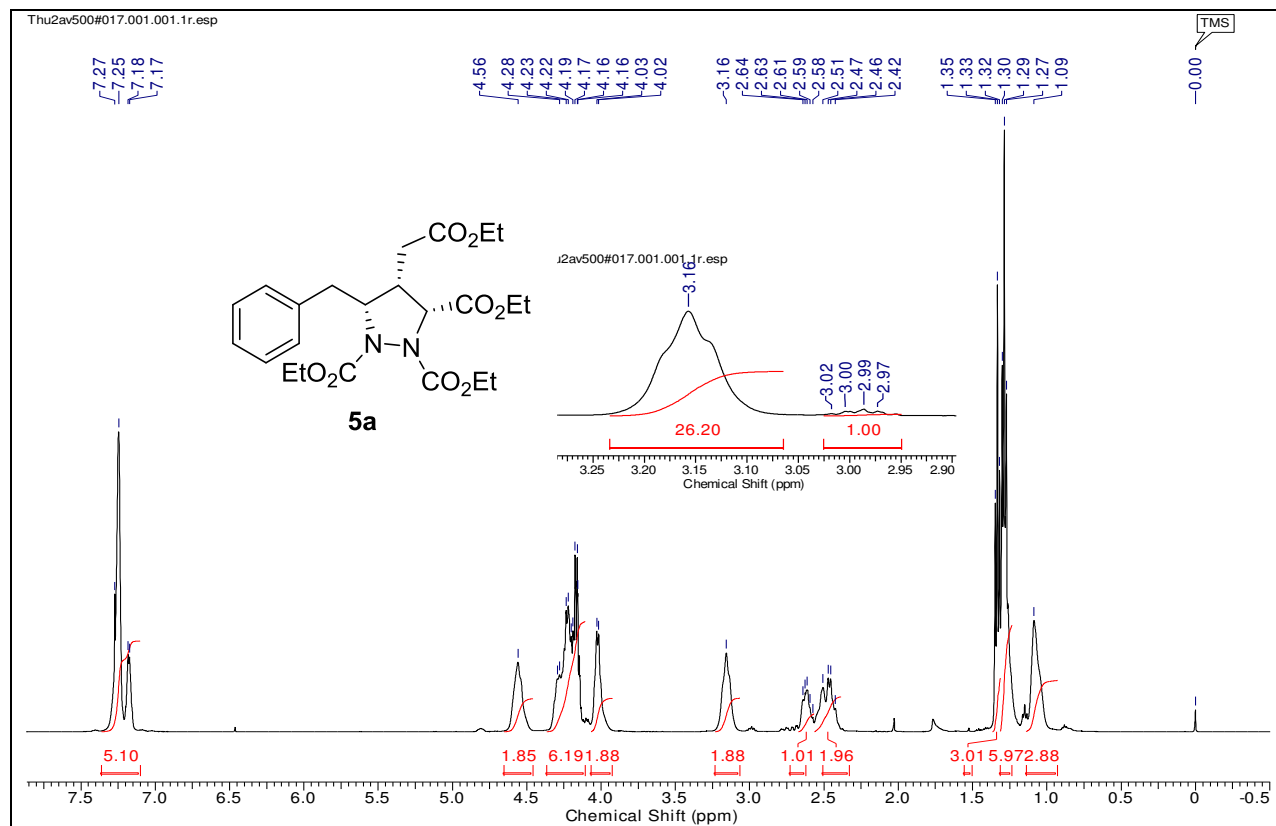
¹H & ¹³C spectra of **4i**



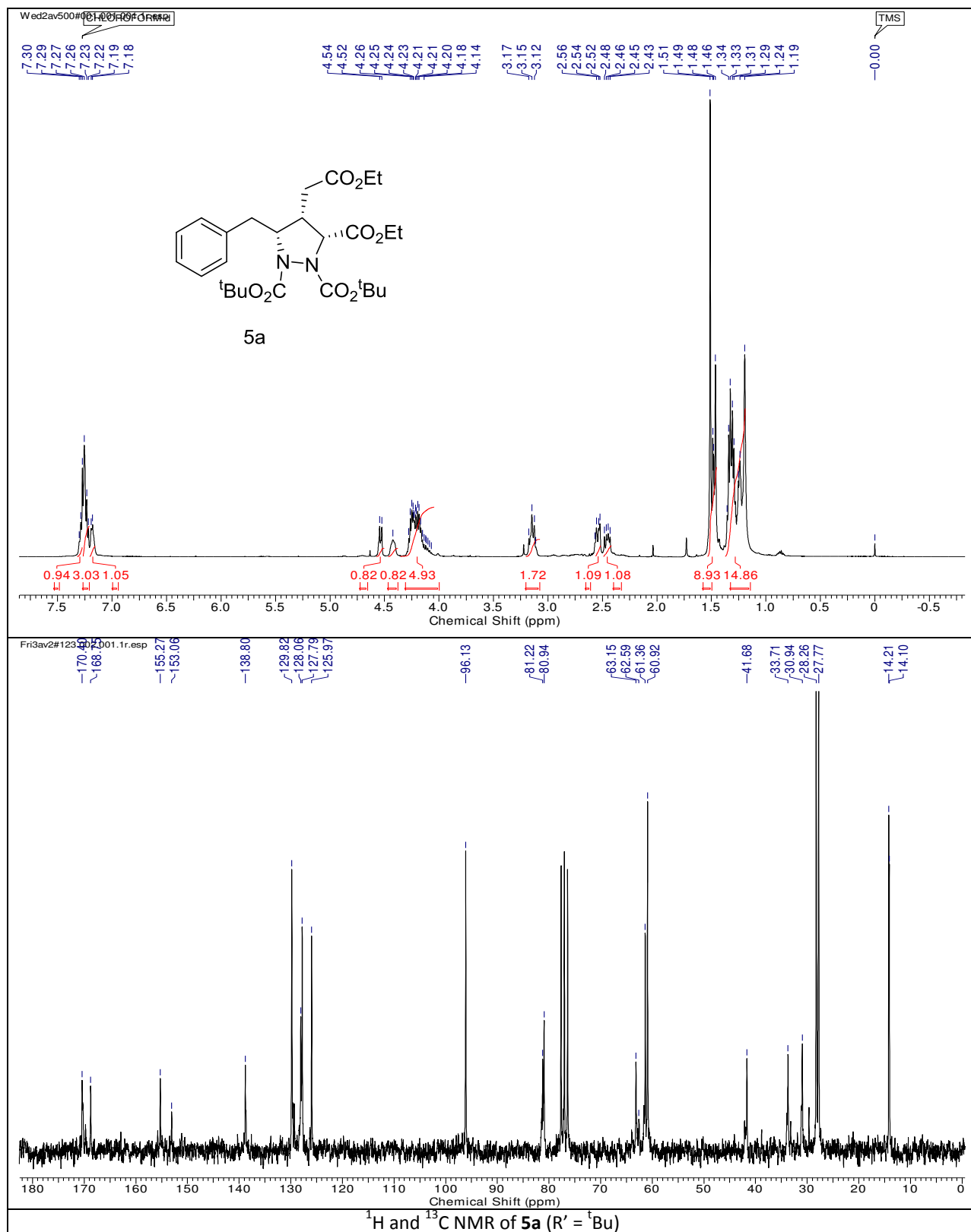
^1H & ^{13}C spectra of **4j**

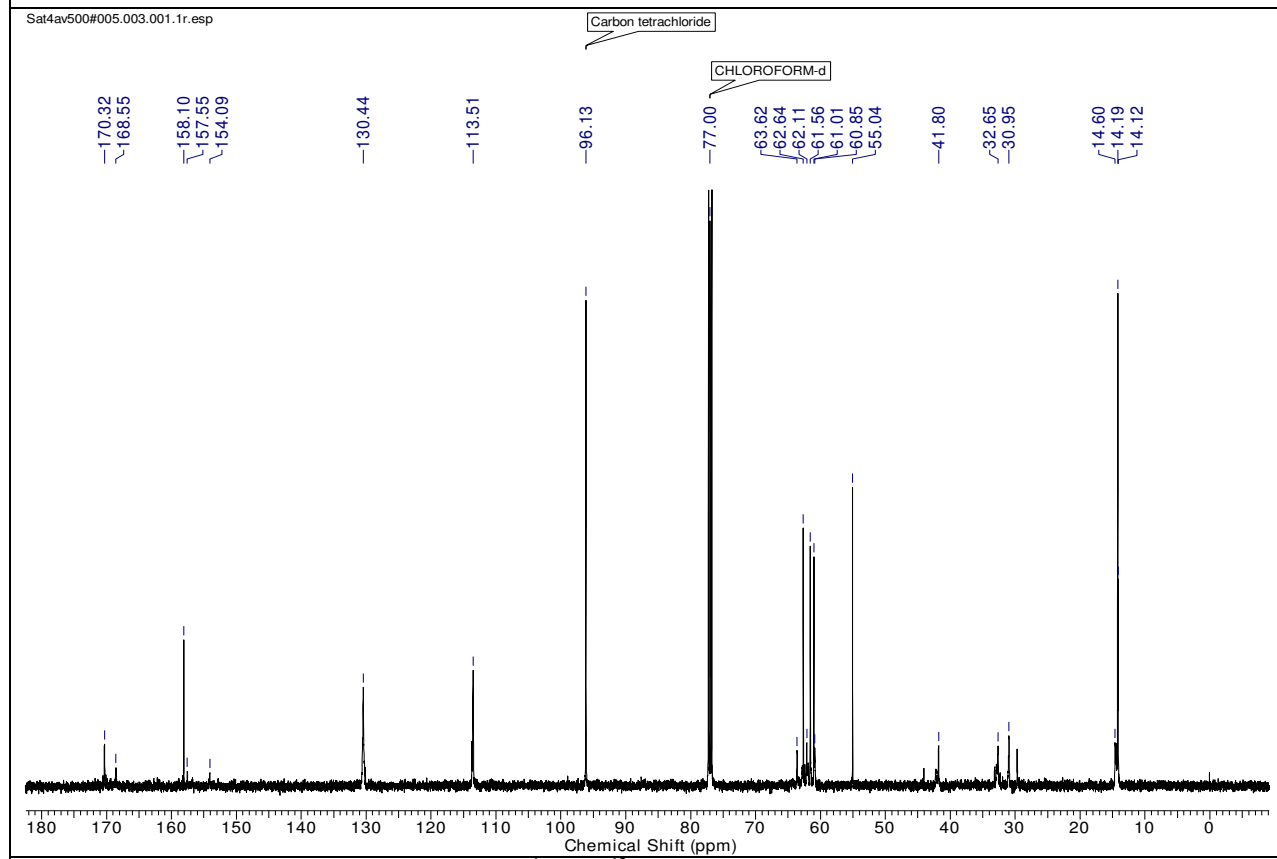
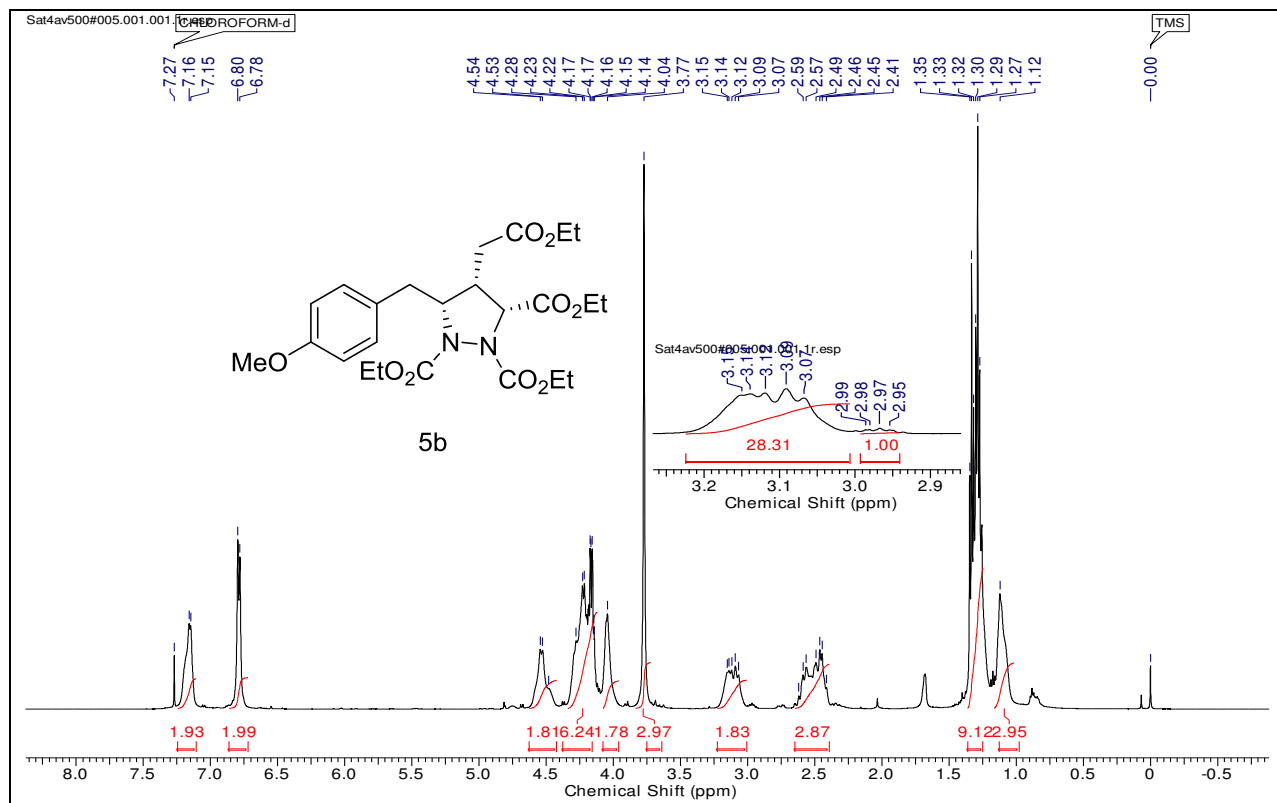


¹H & ¹³C spectra of **4k**

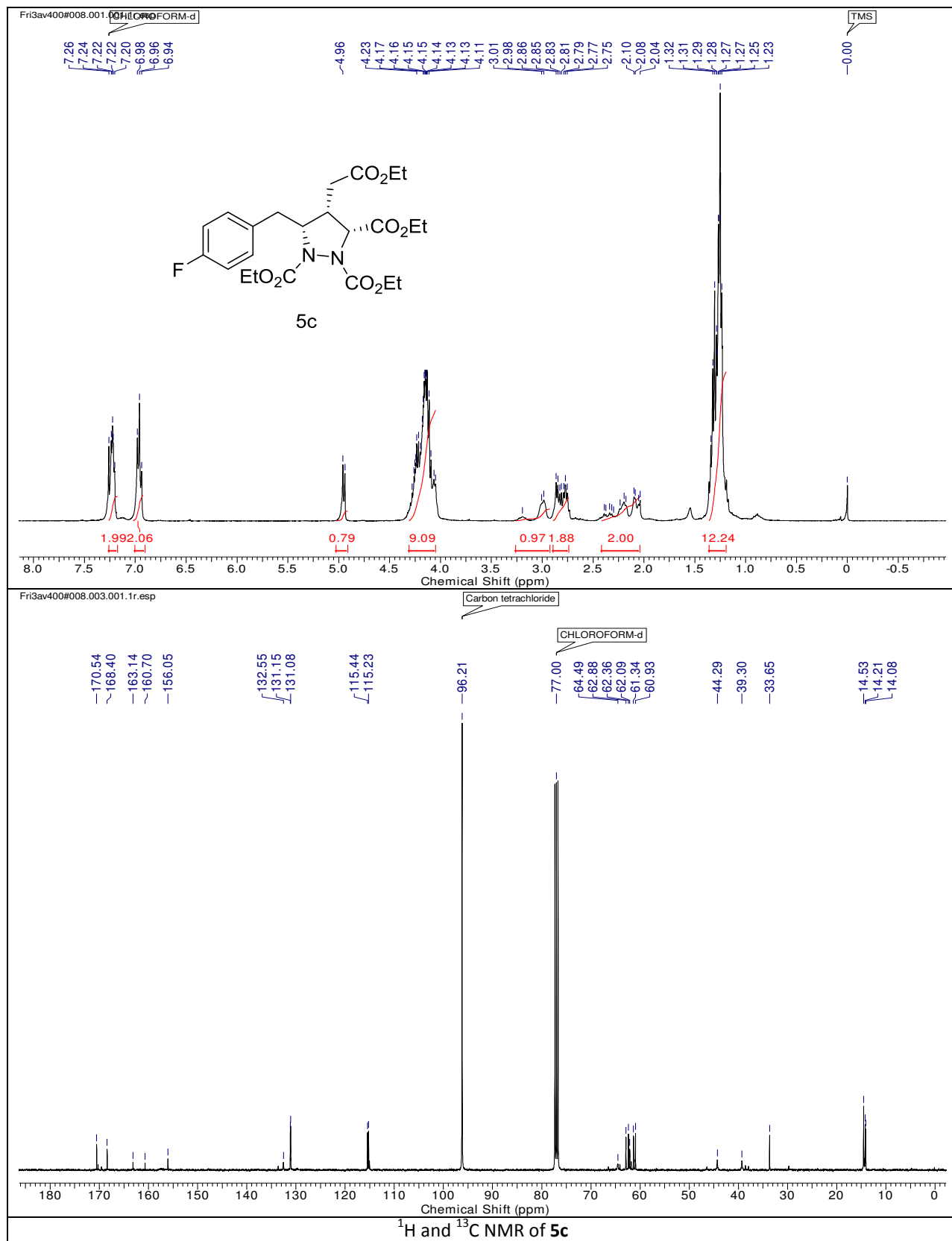


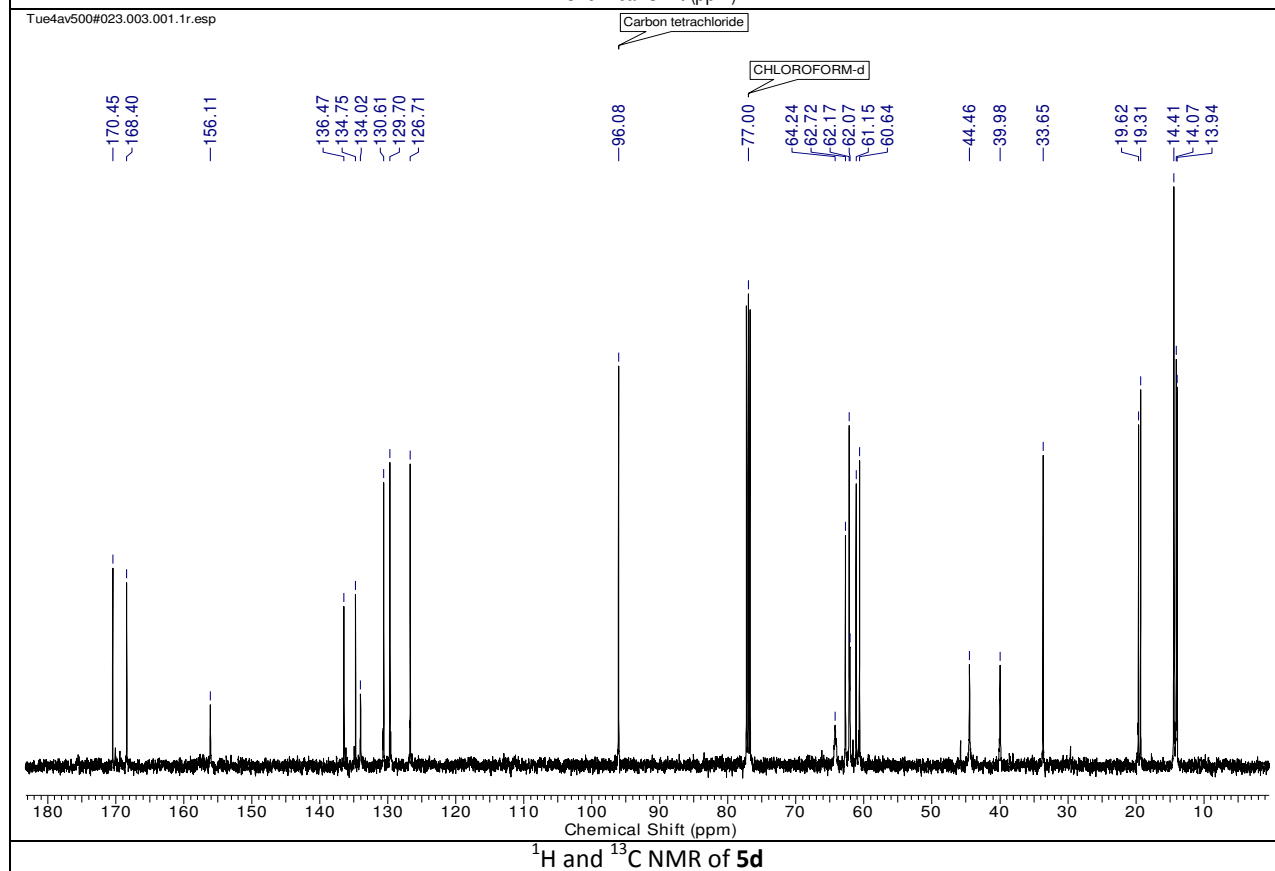
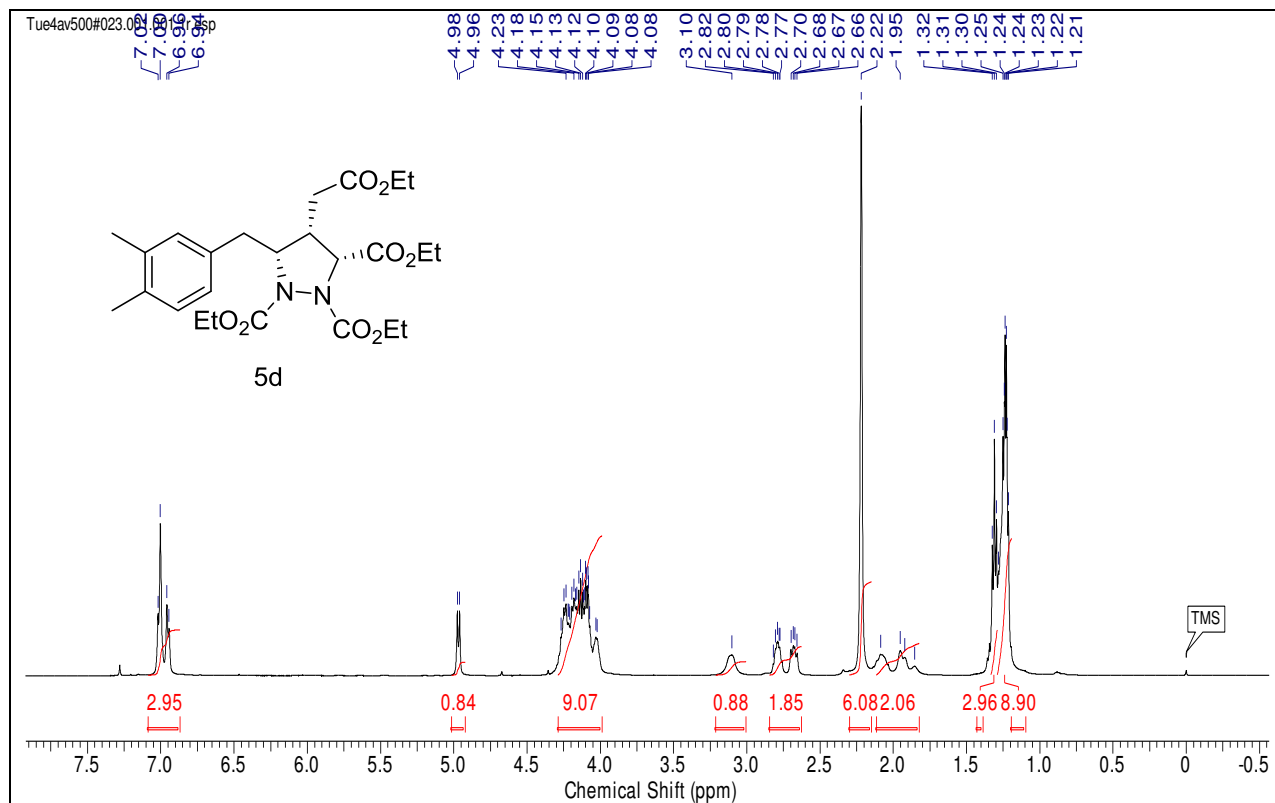
¹H and ¹³C NMR of **5a** (R' = Et)

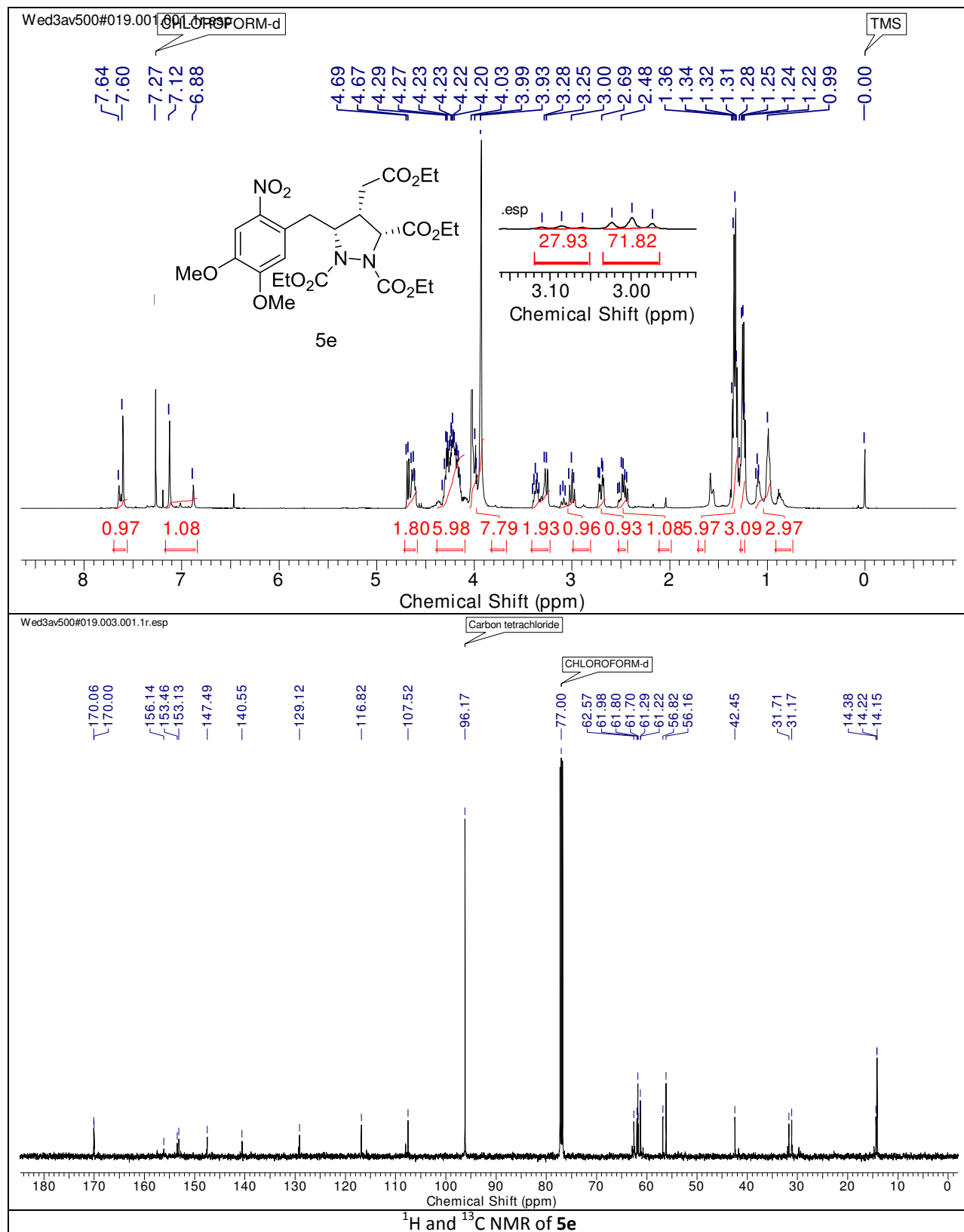


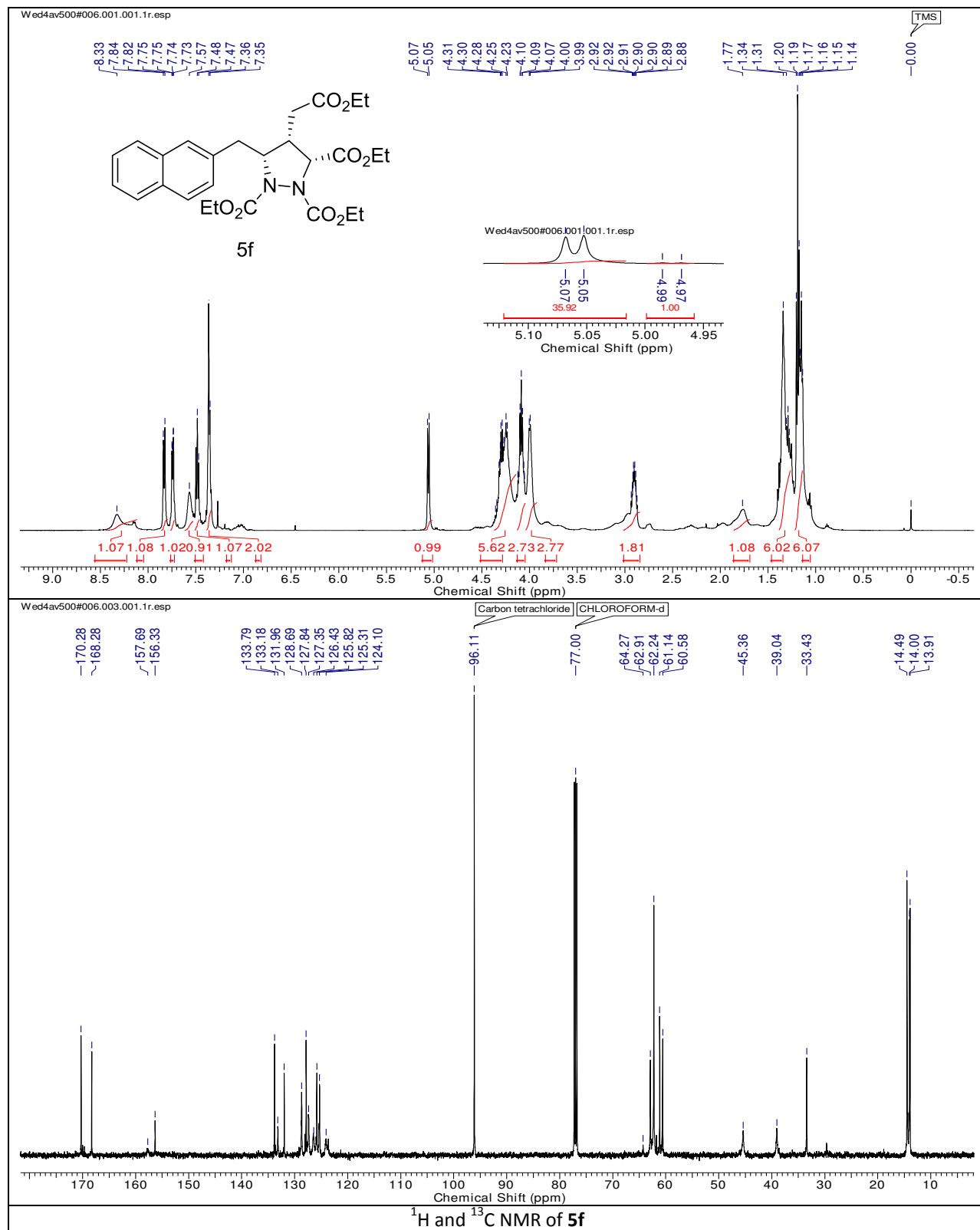


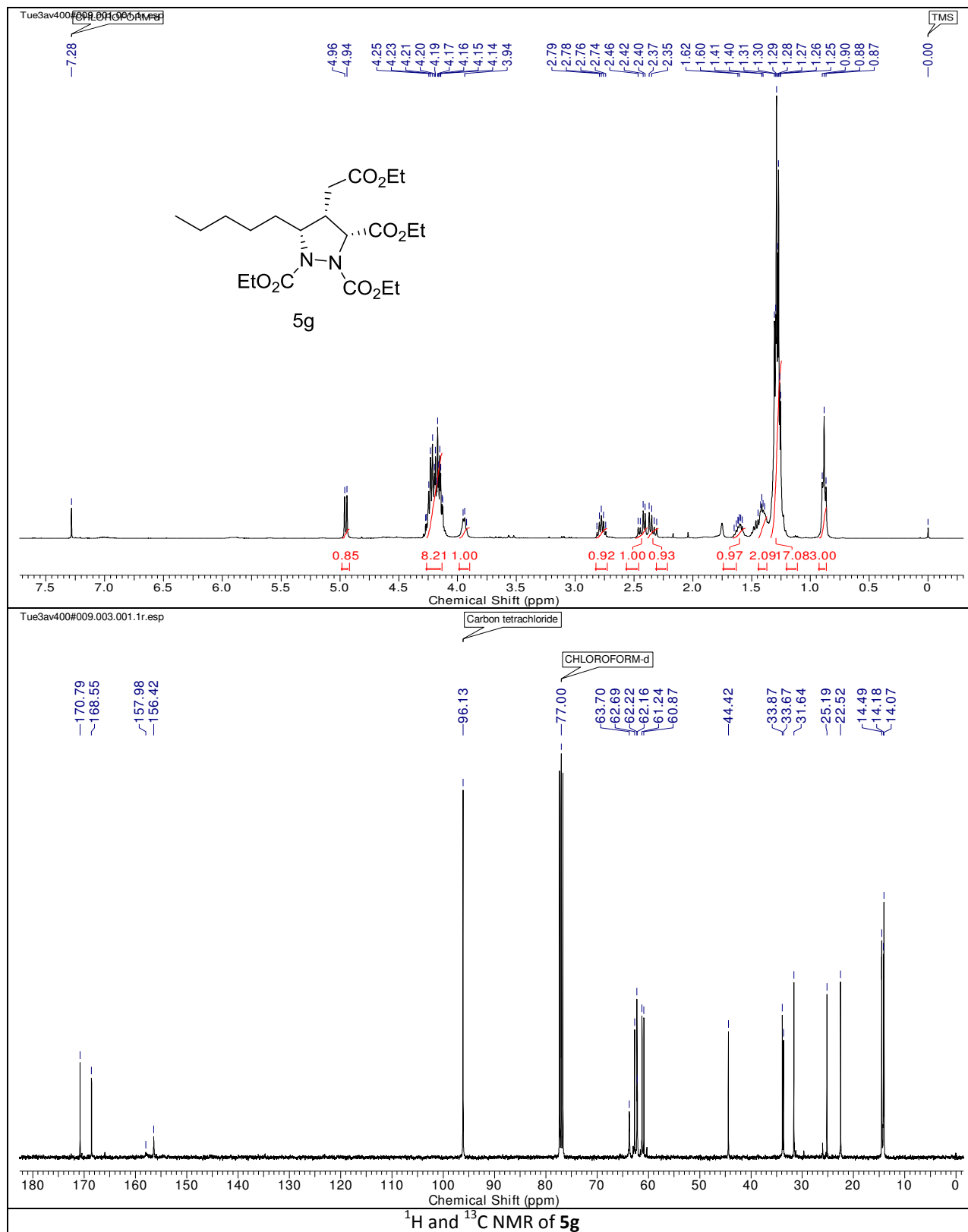
¹H and ¹³C NMR of 5b

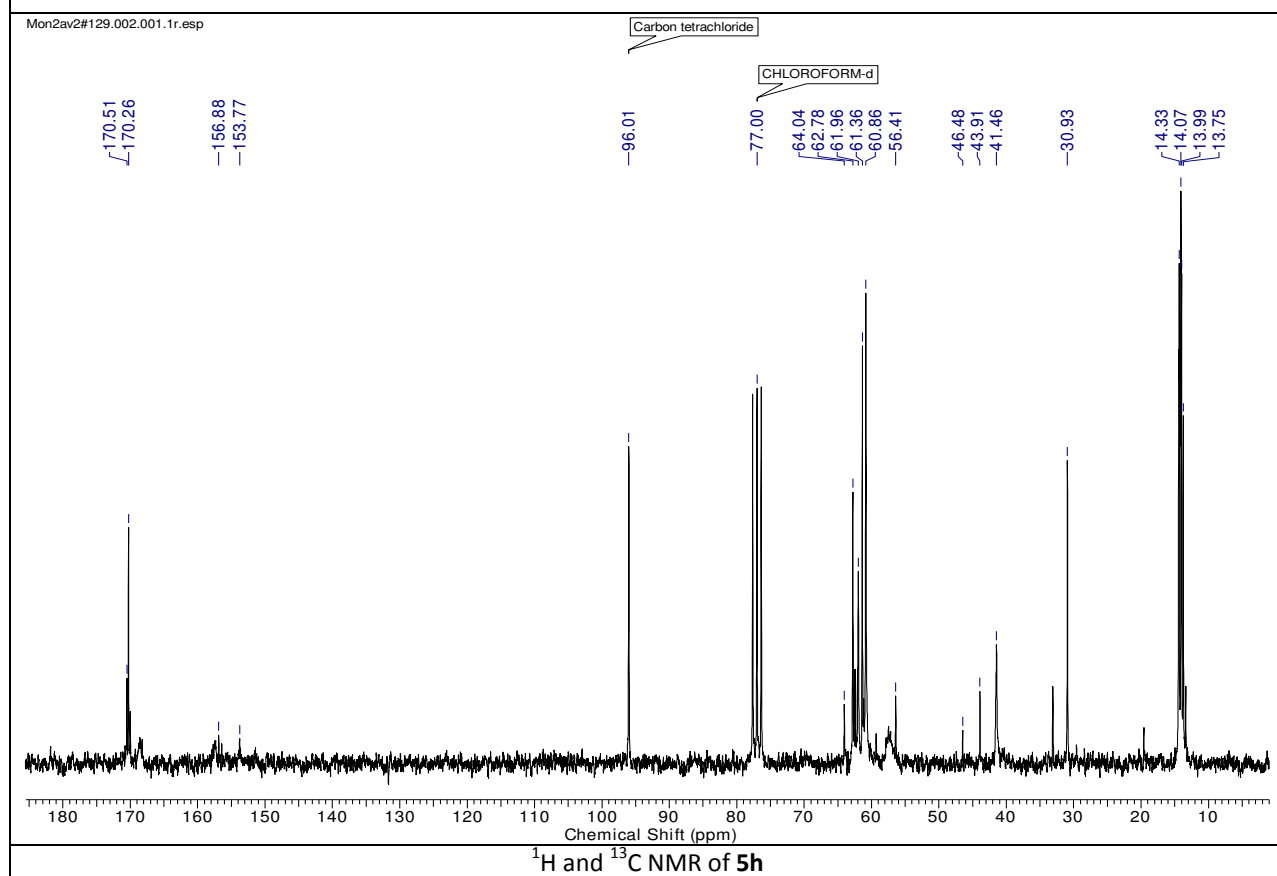
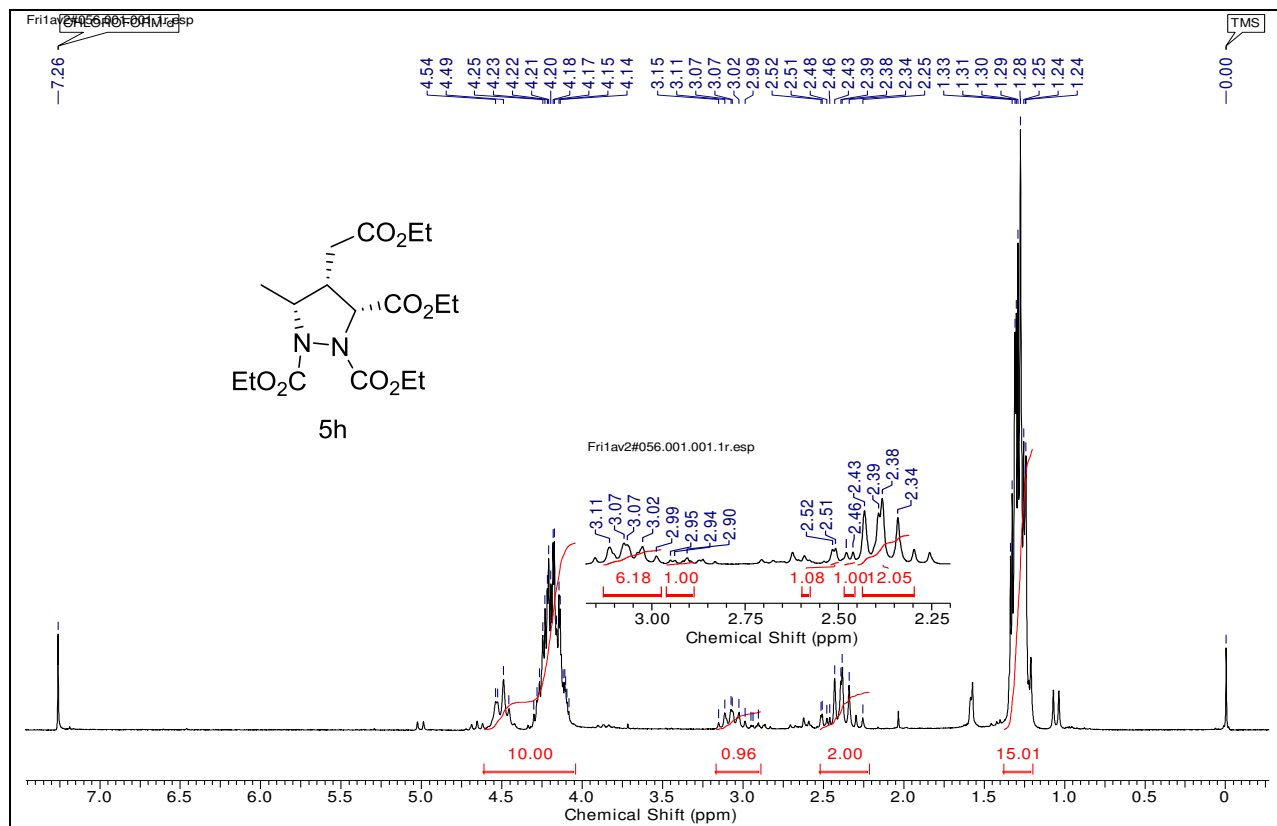


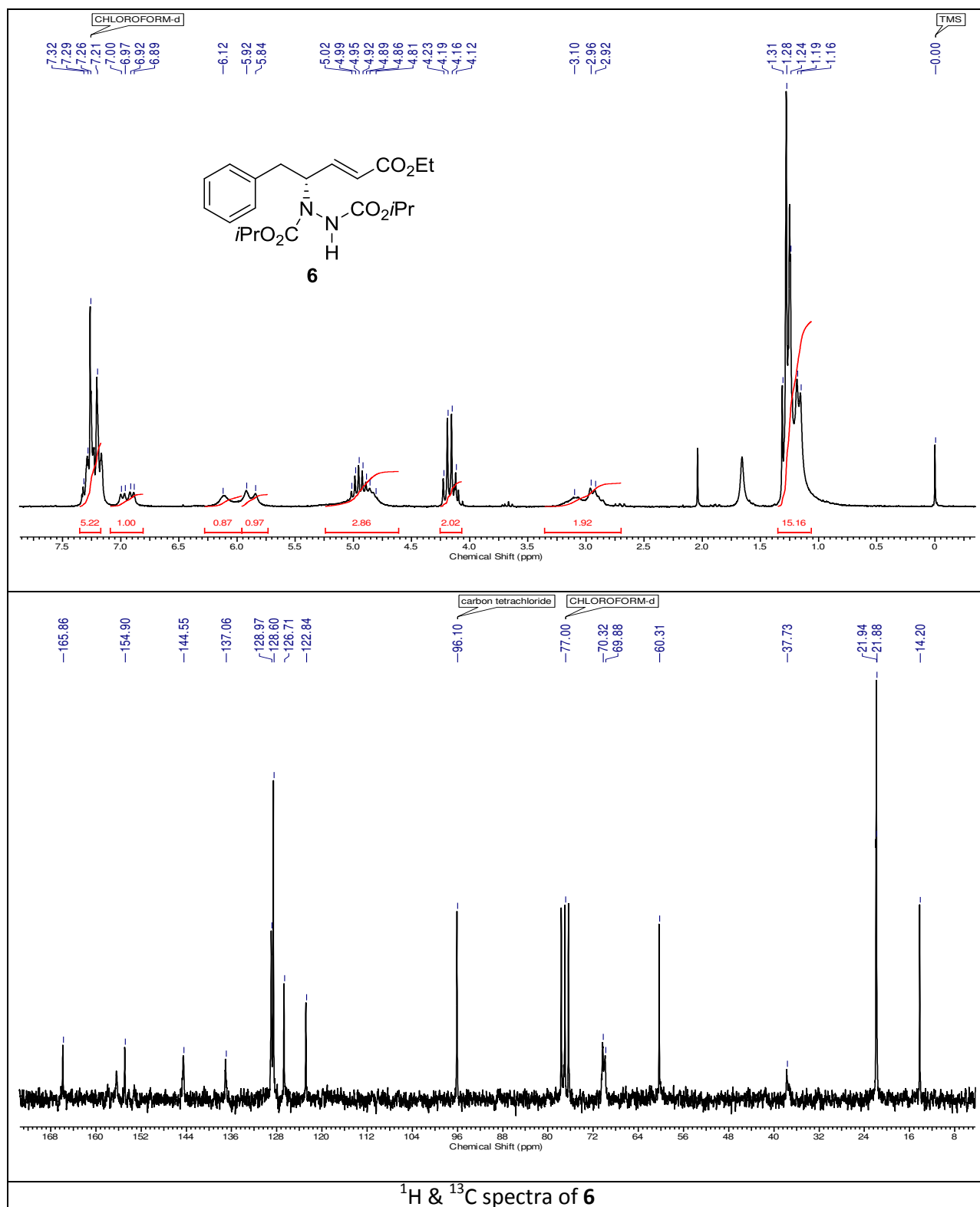


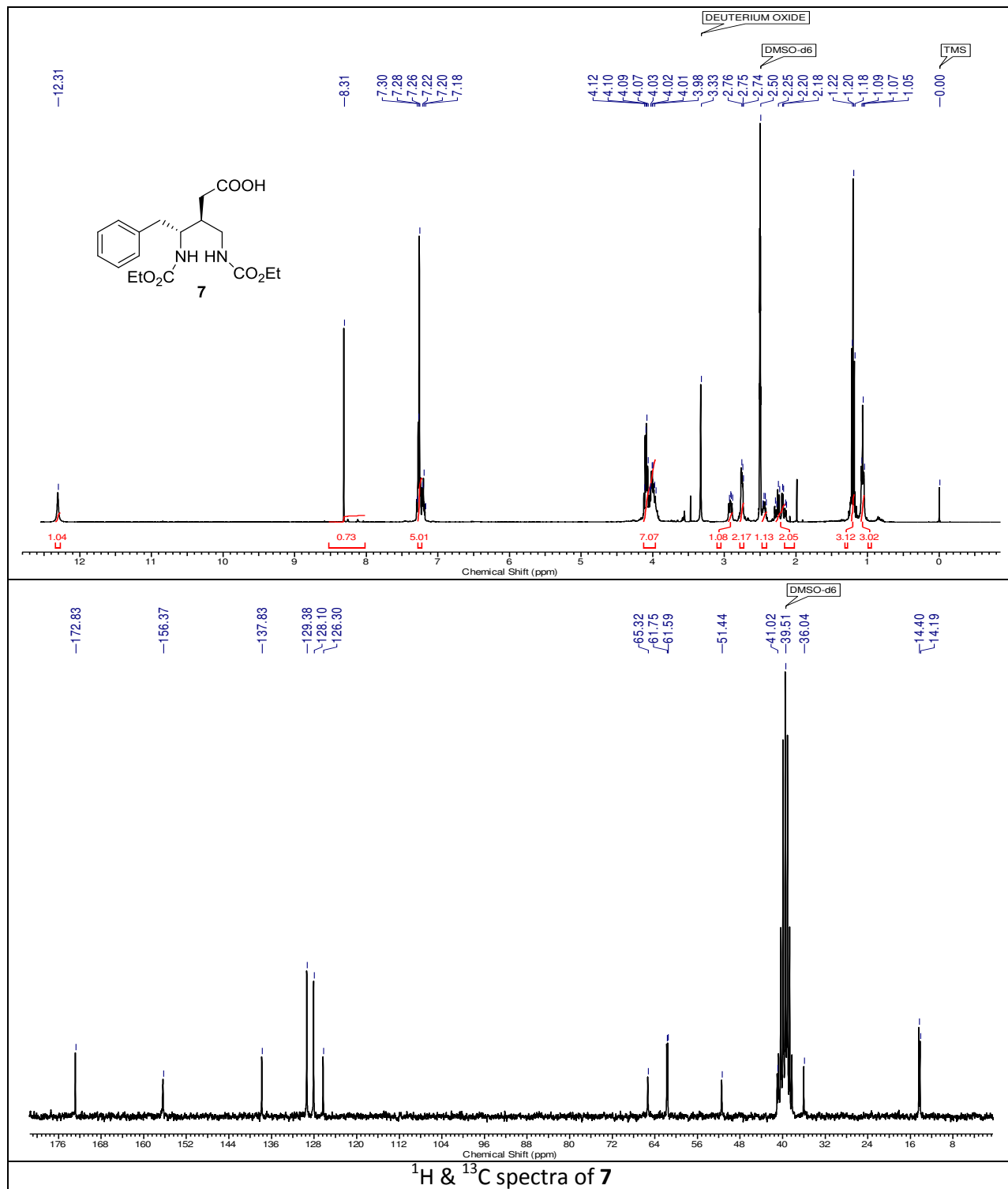


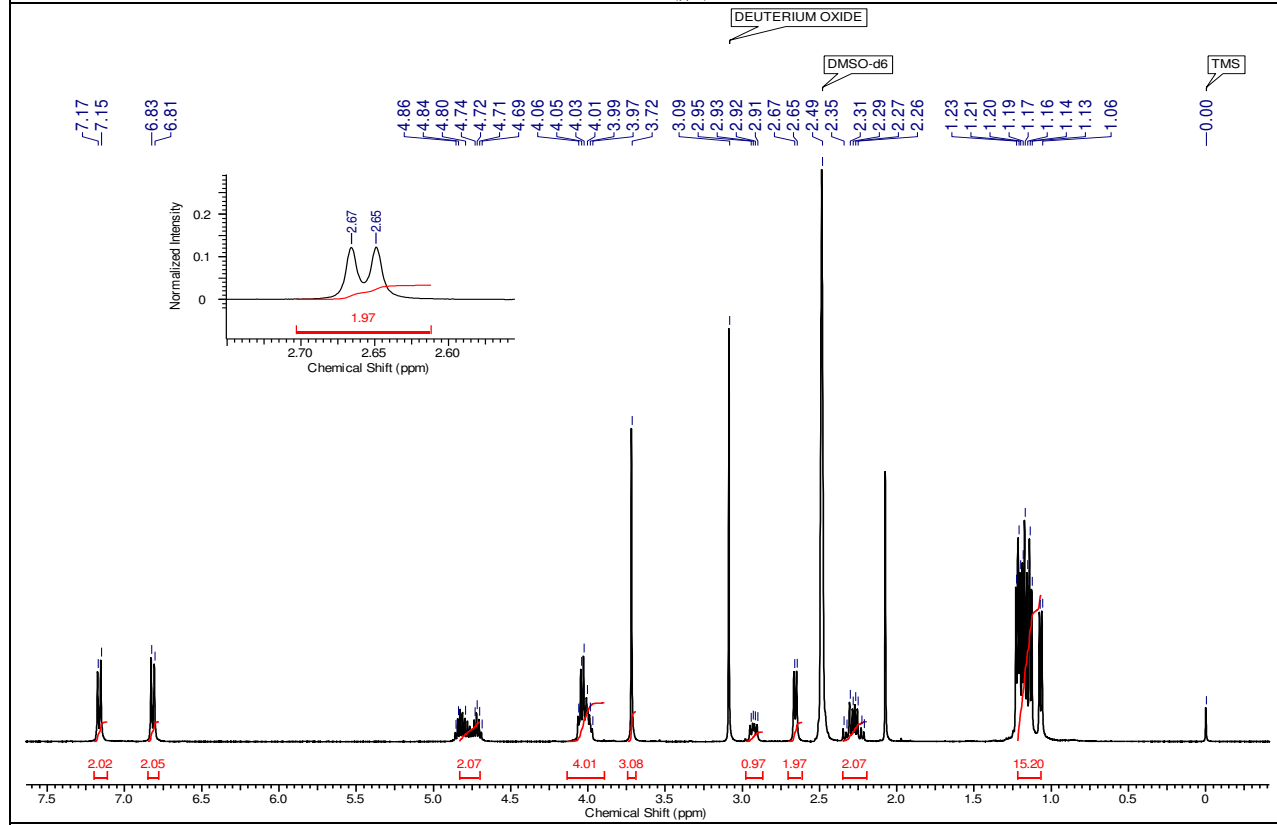
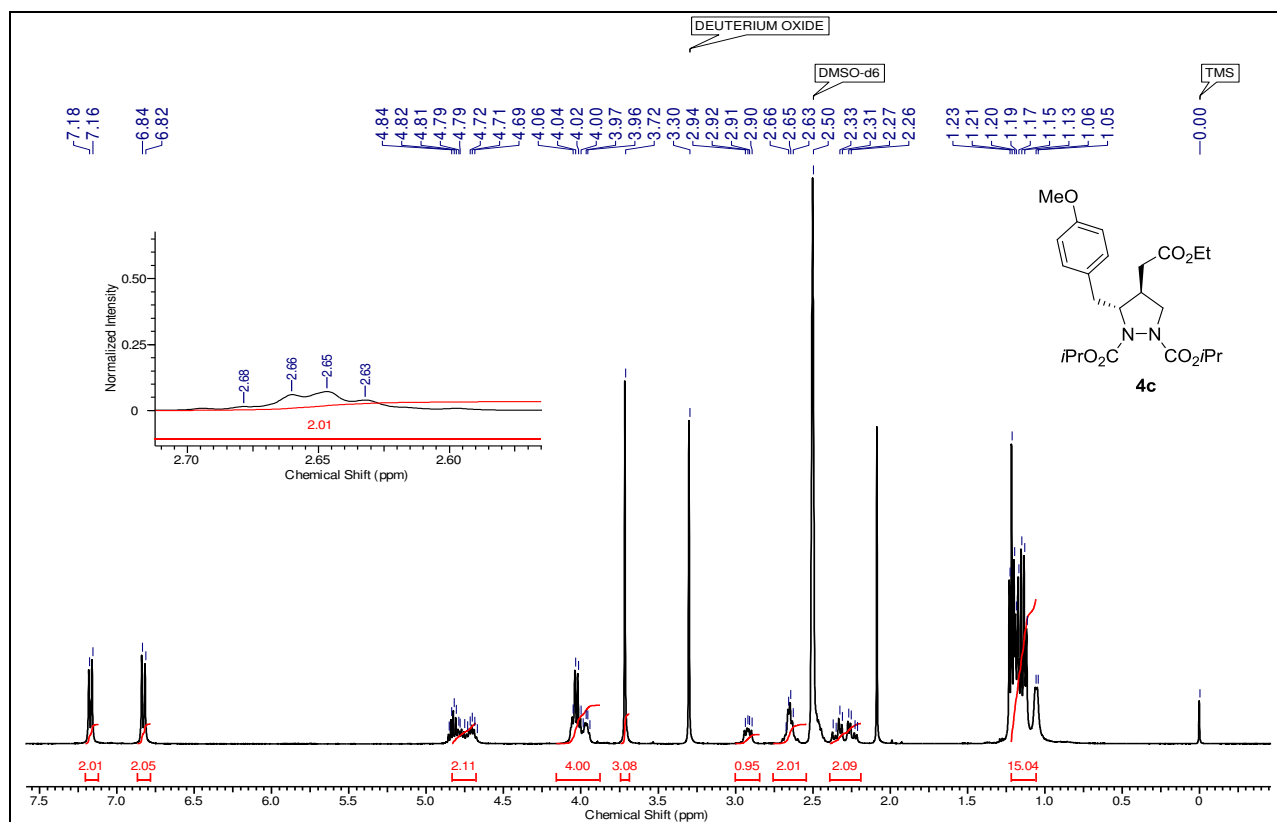




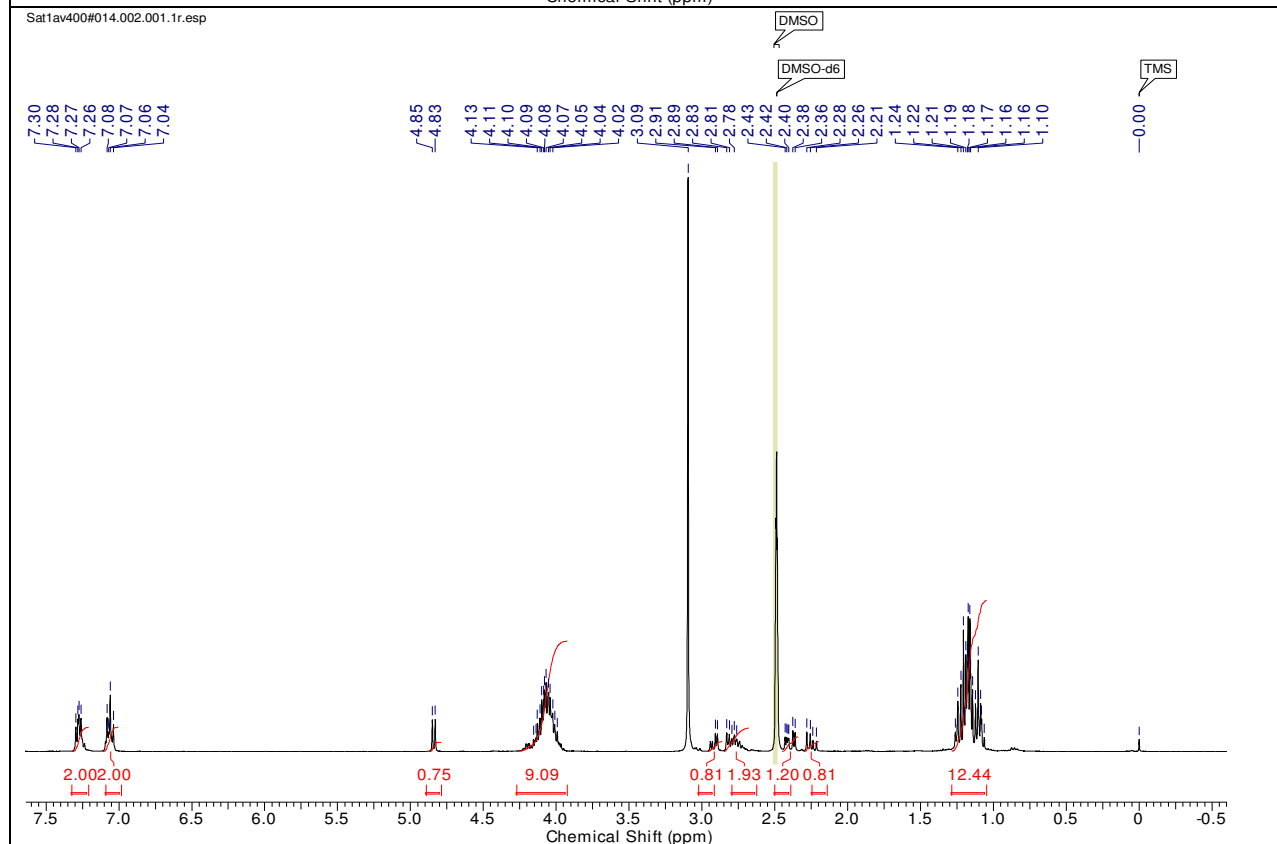
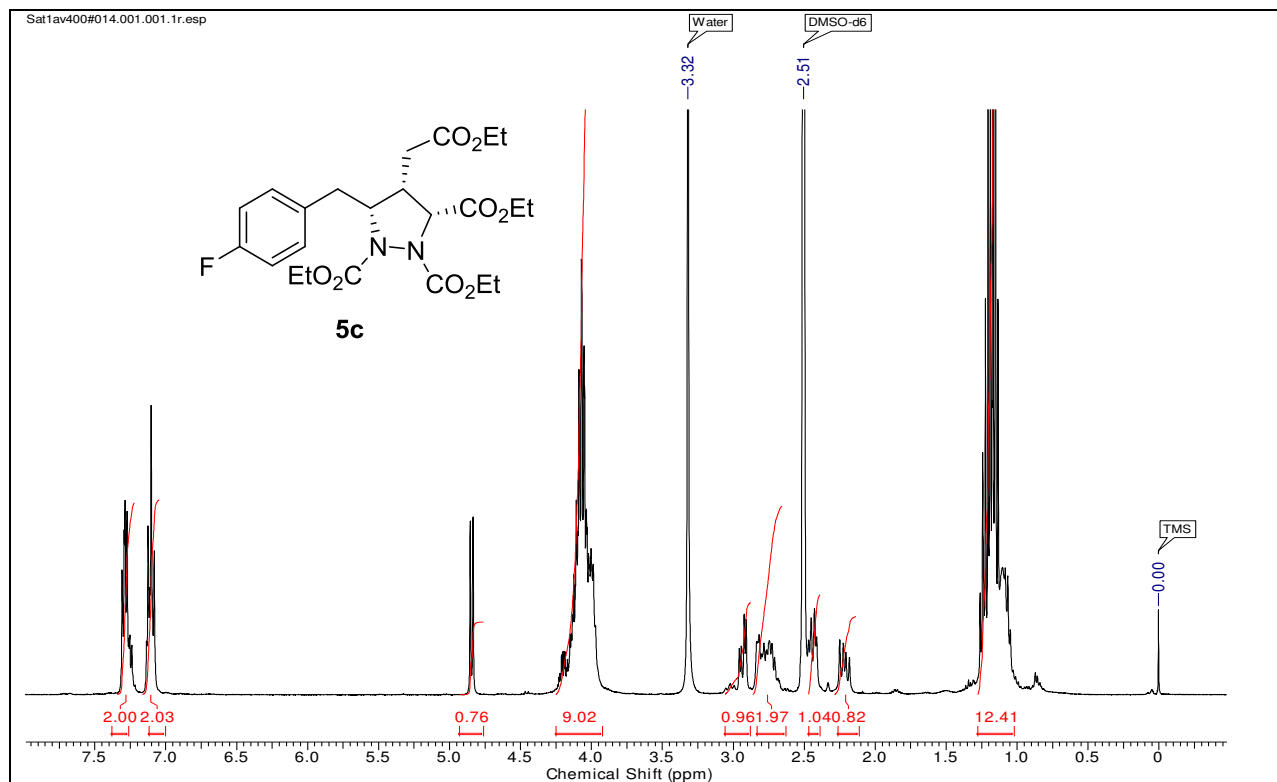




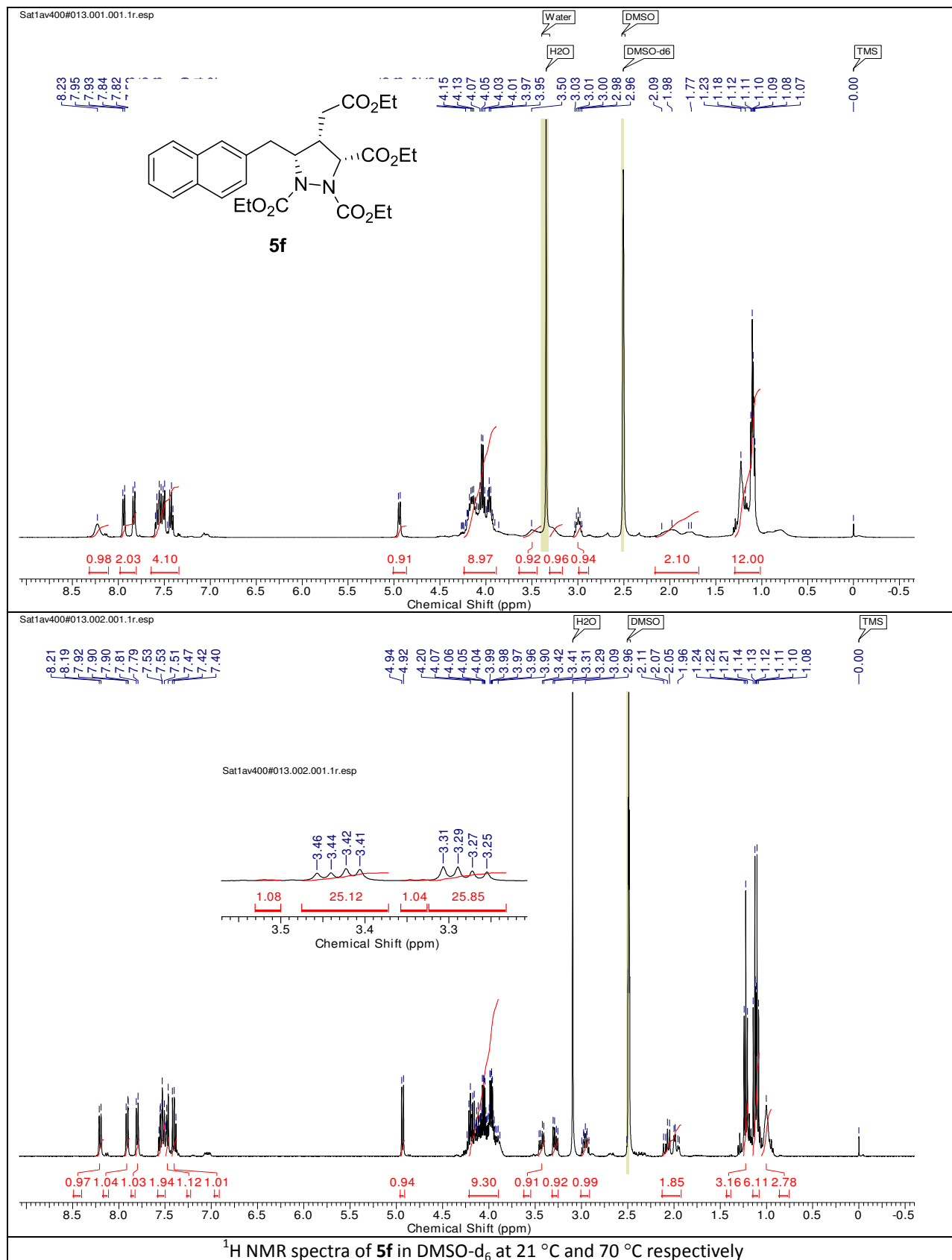


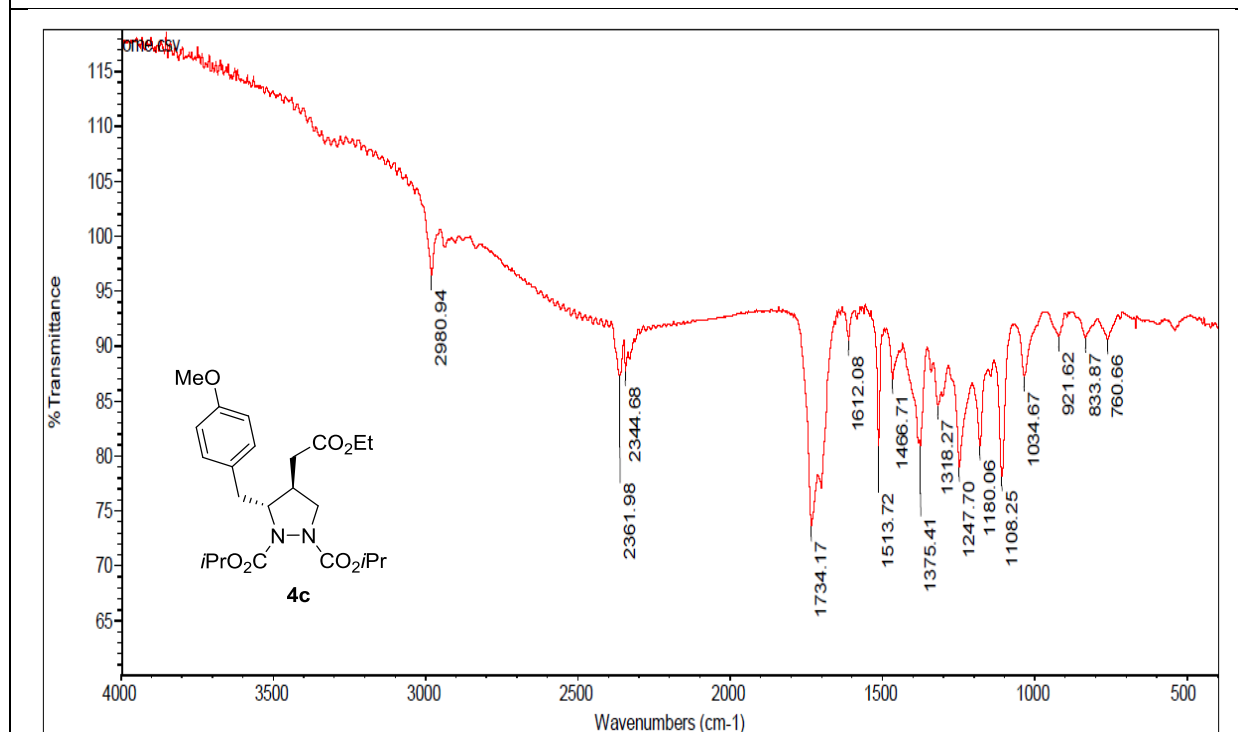
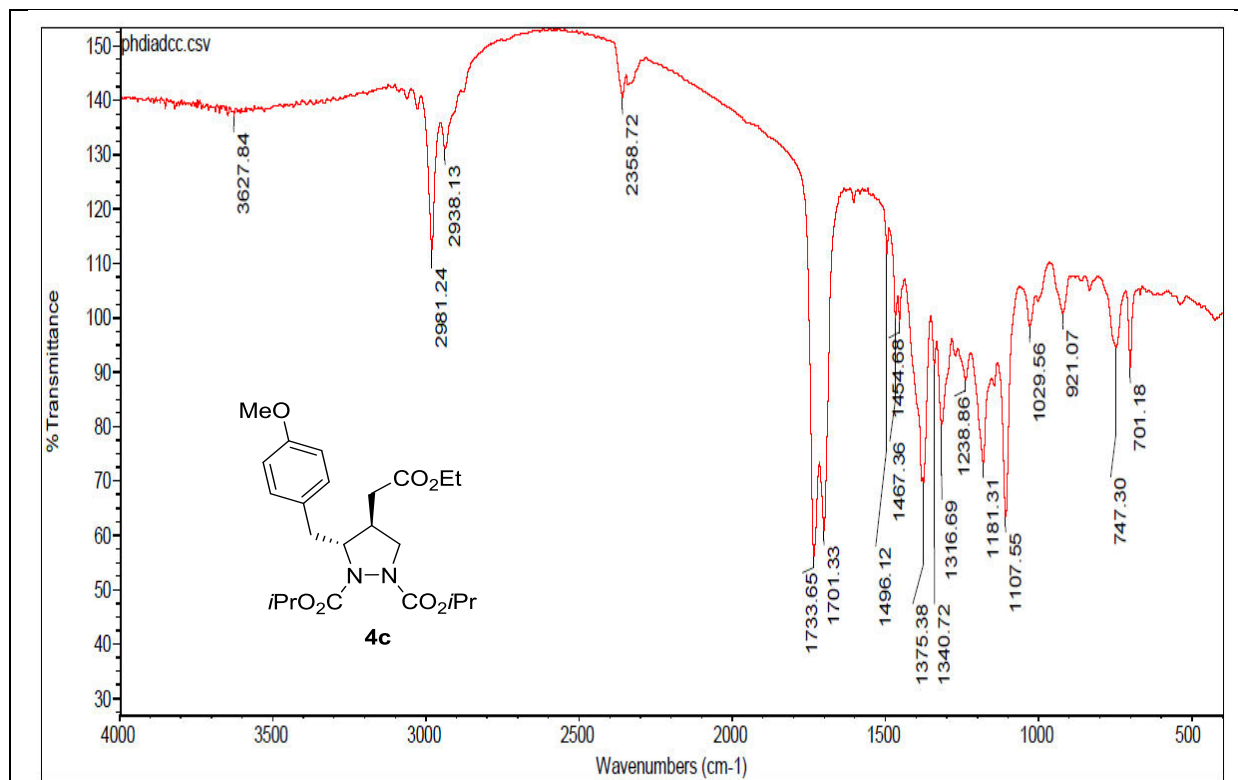


¹H NMR spectra of **4c** in DMSO-d₆ at 27 °C and 70 °C

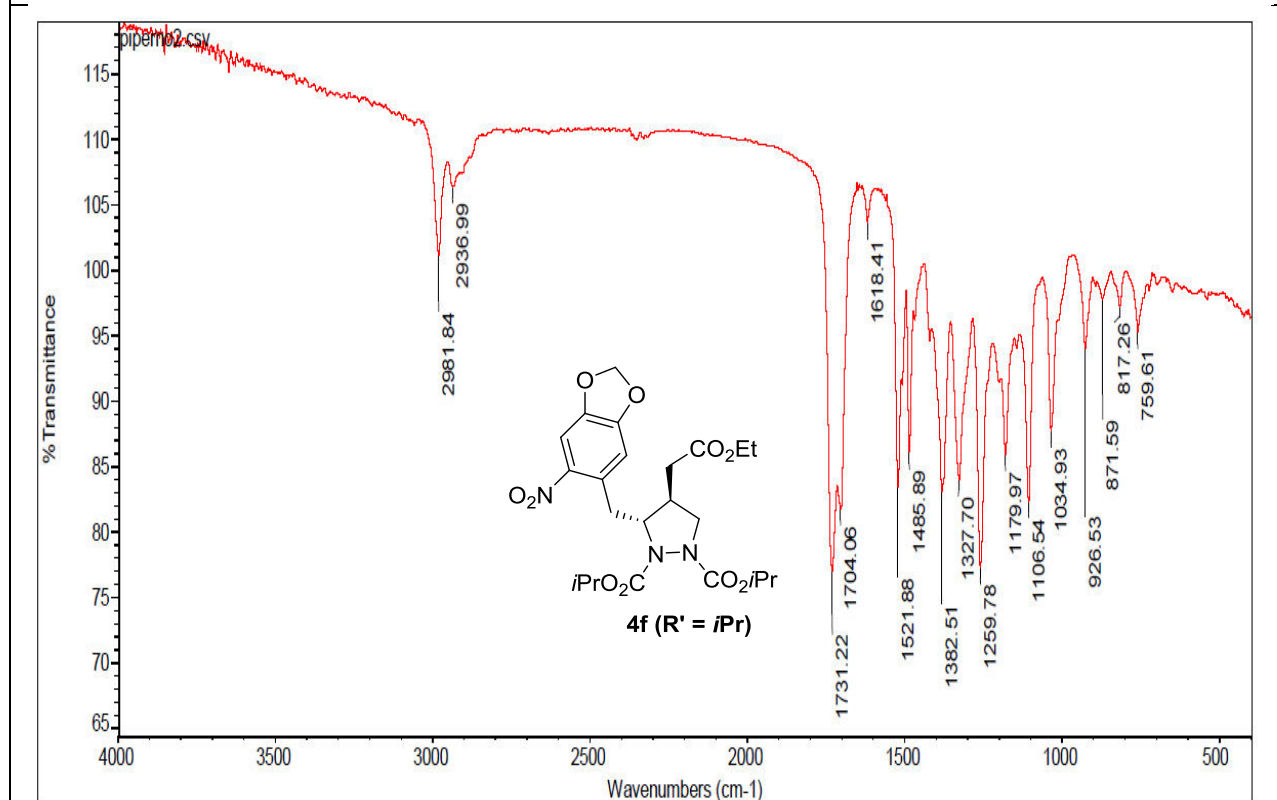
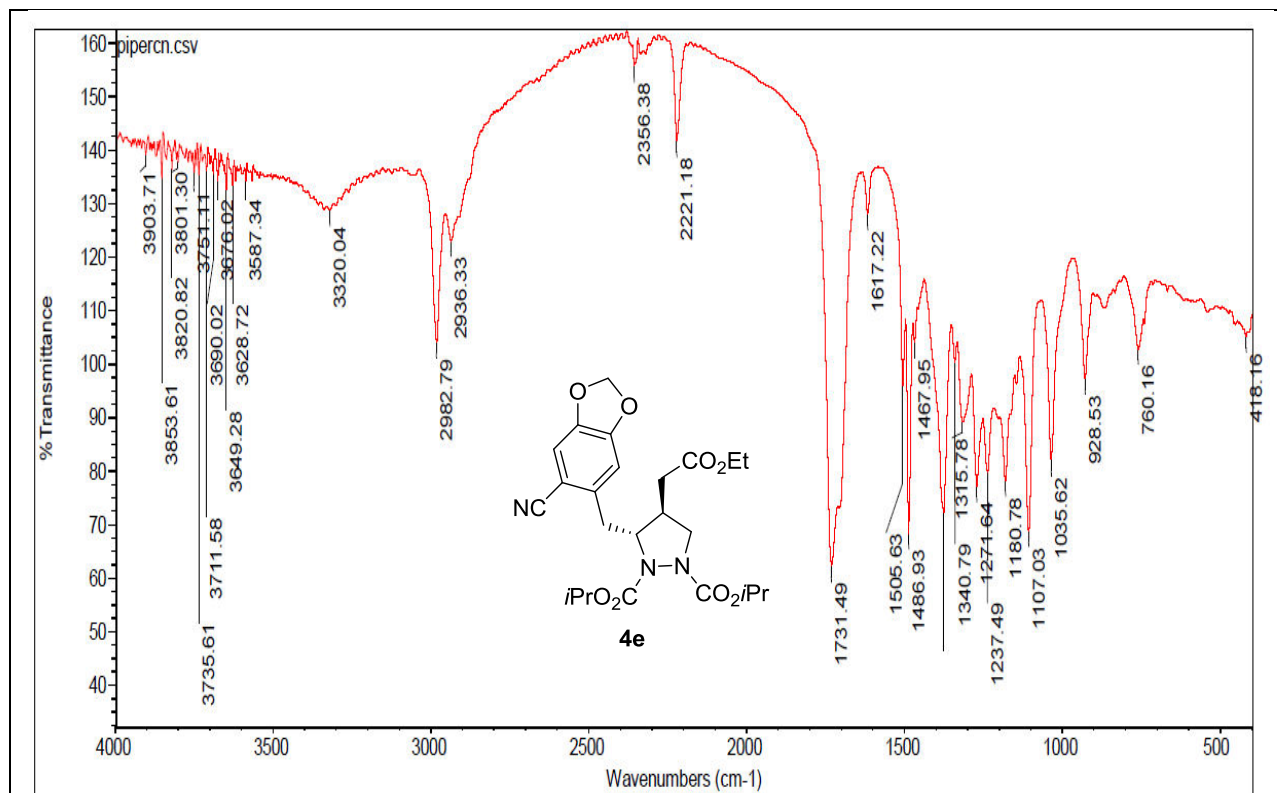


¹H NMR spectra of **5c** in DMSO-d₆ at 27 °C and 70 °C respectively

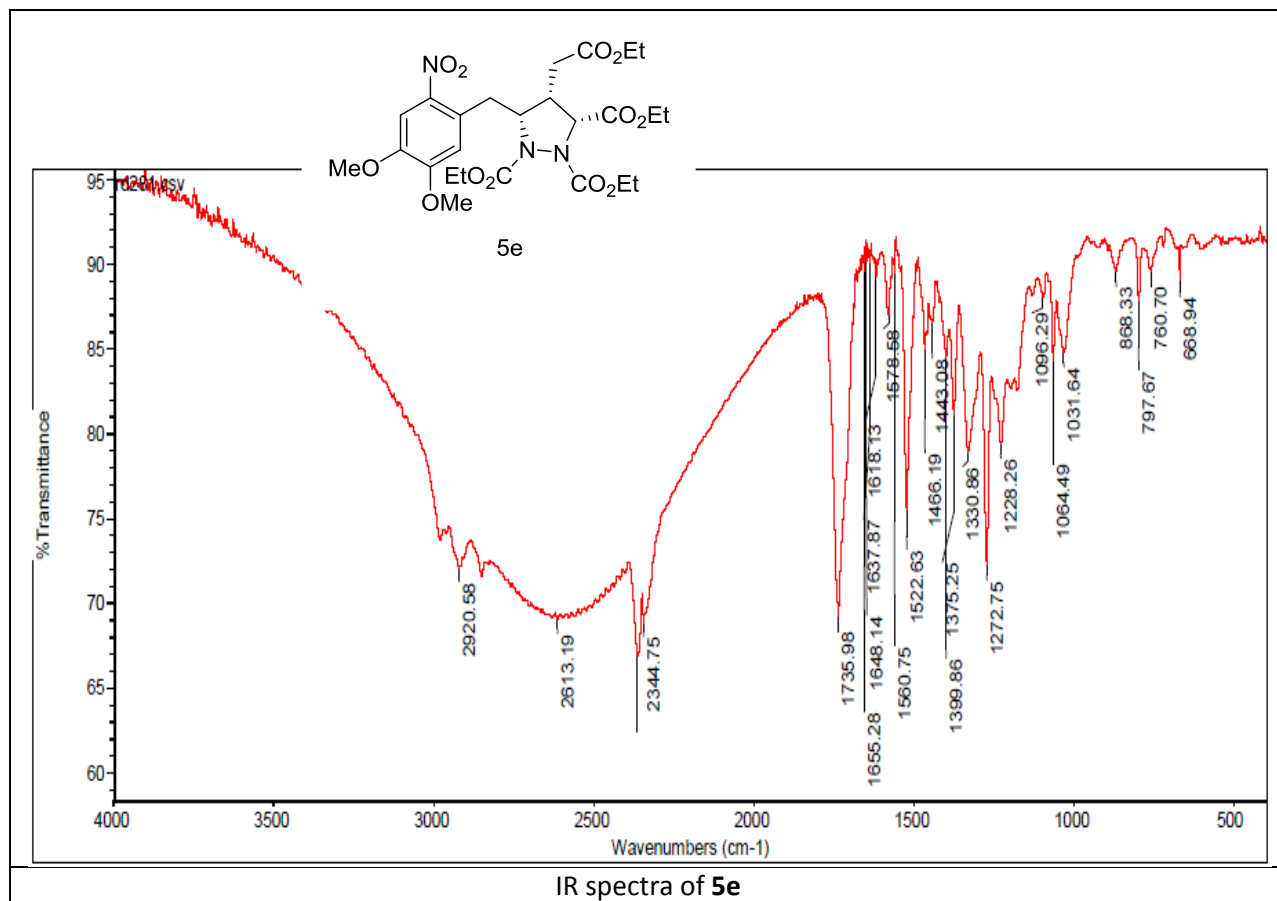


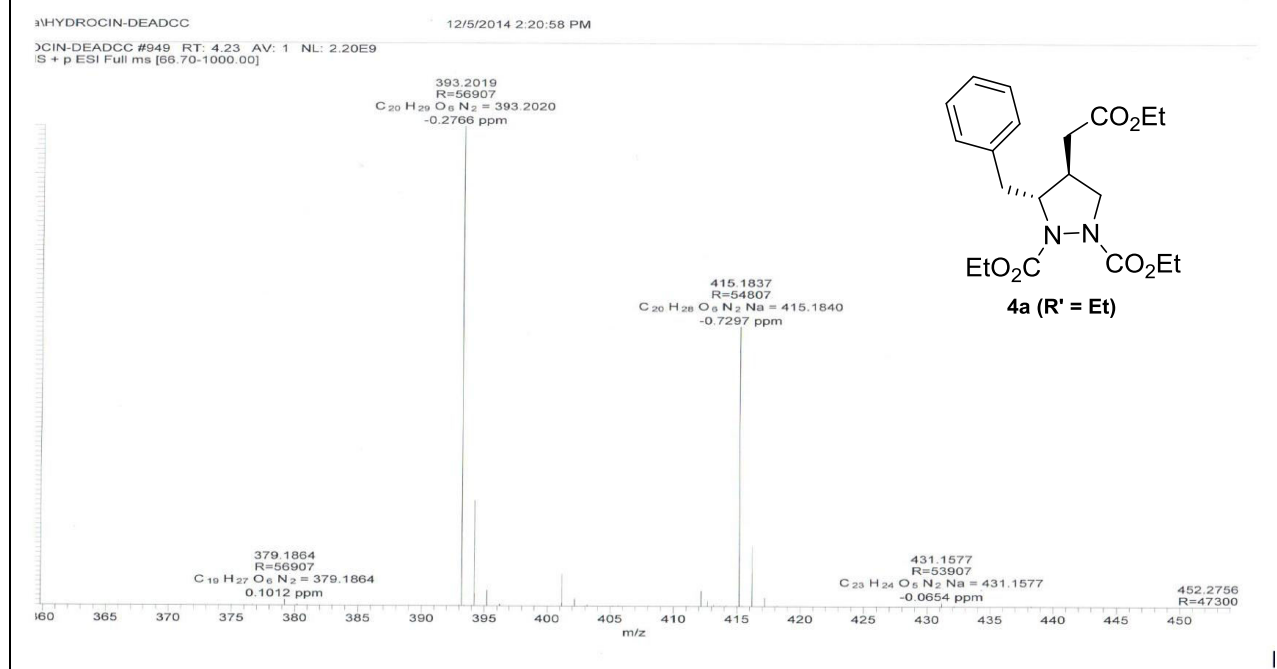
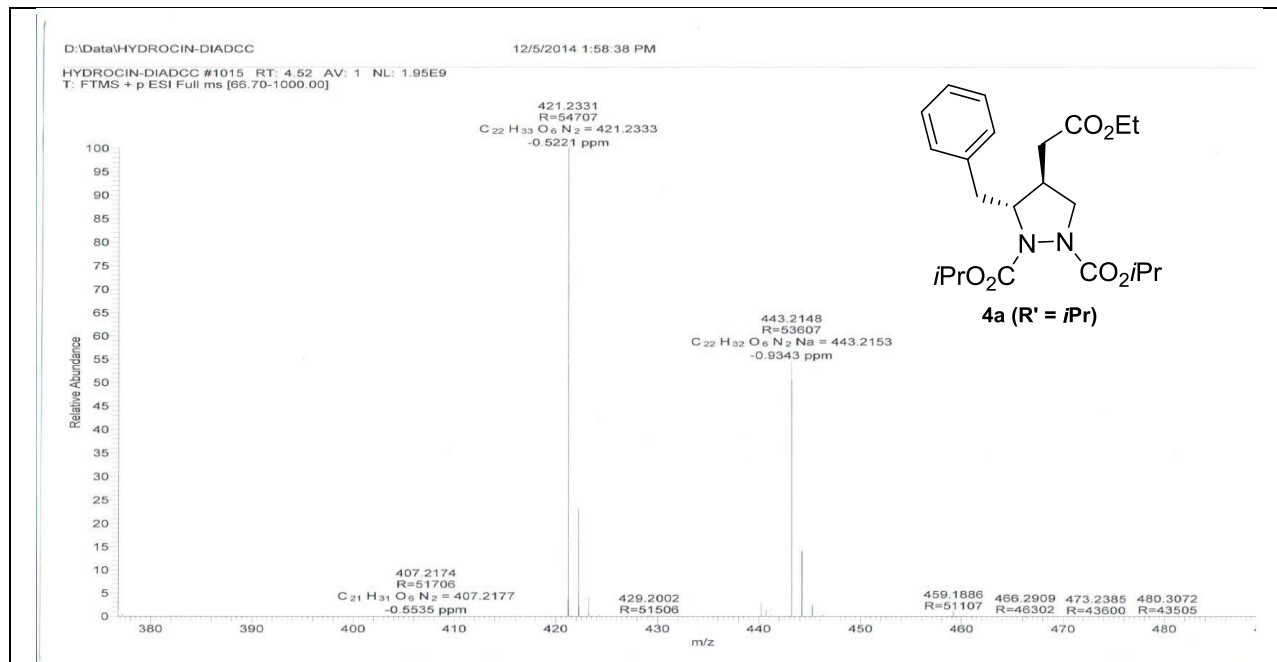


IR spectrum of **4a** ($R' = iPr$) and **4c**

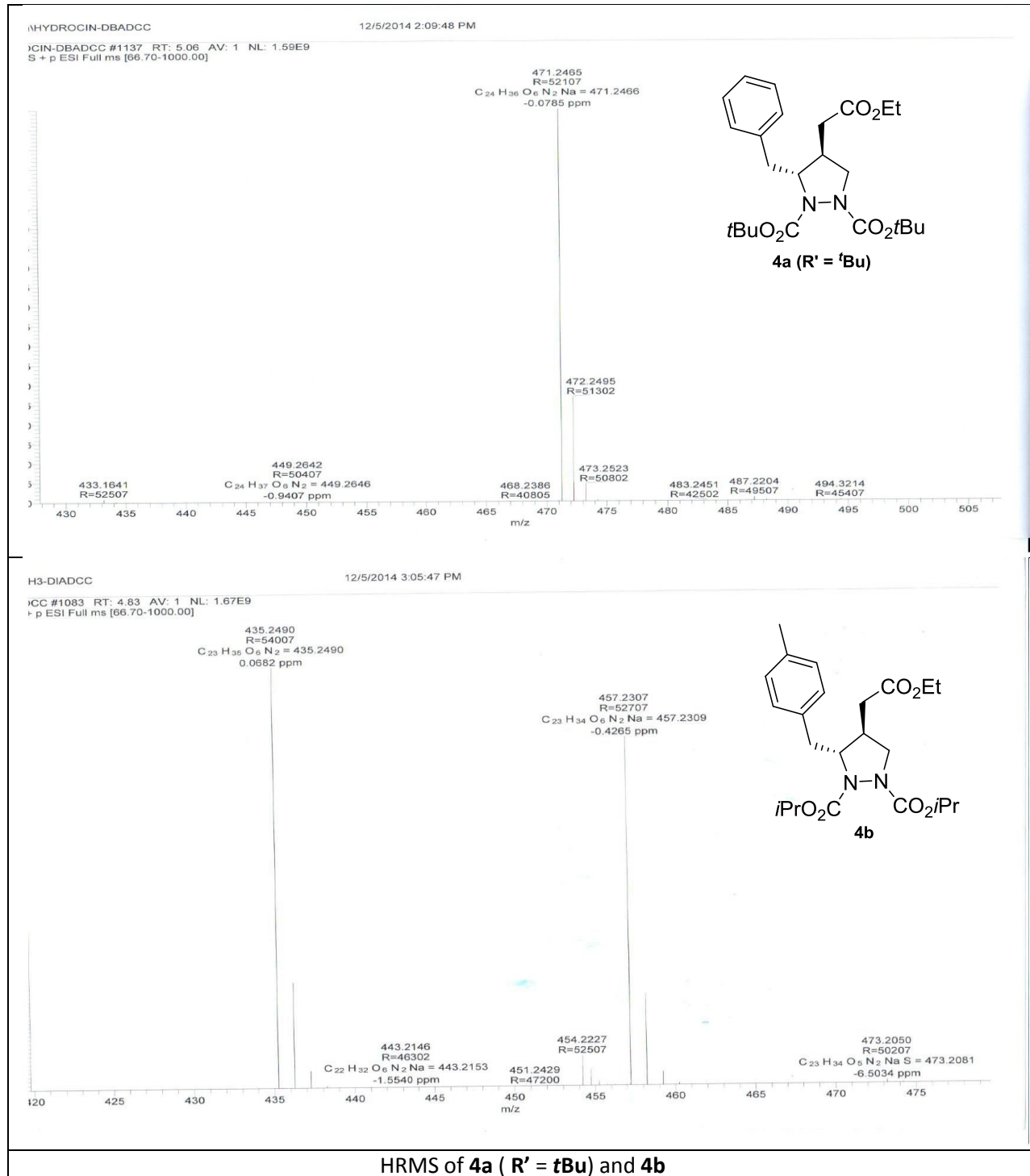


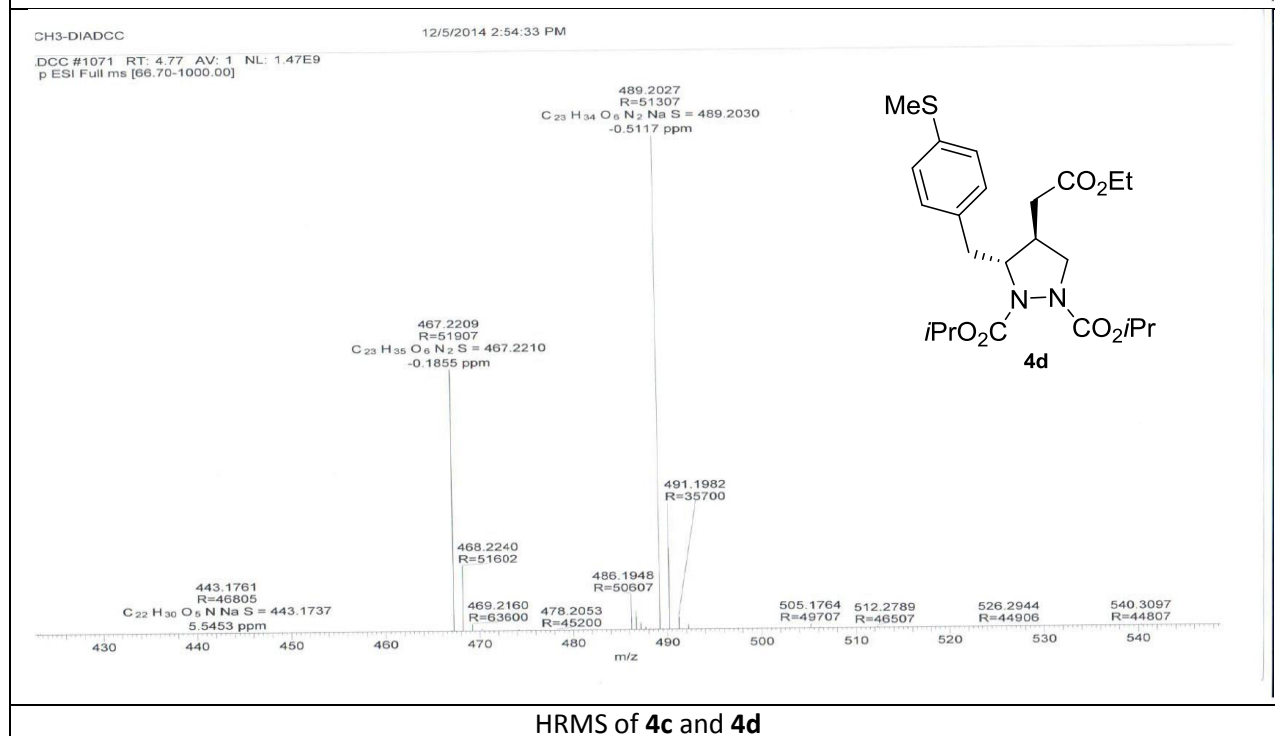
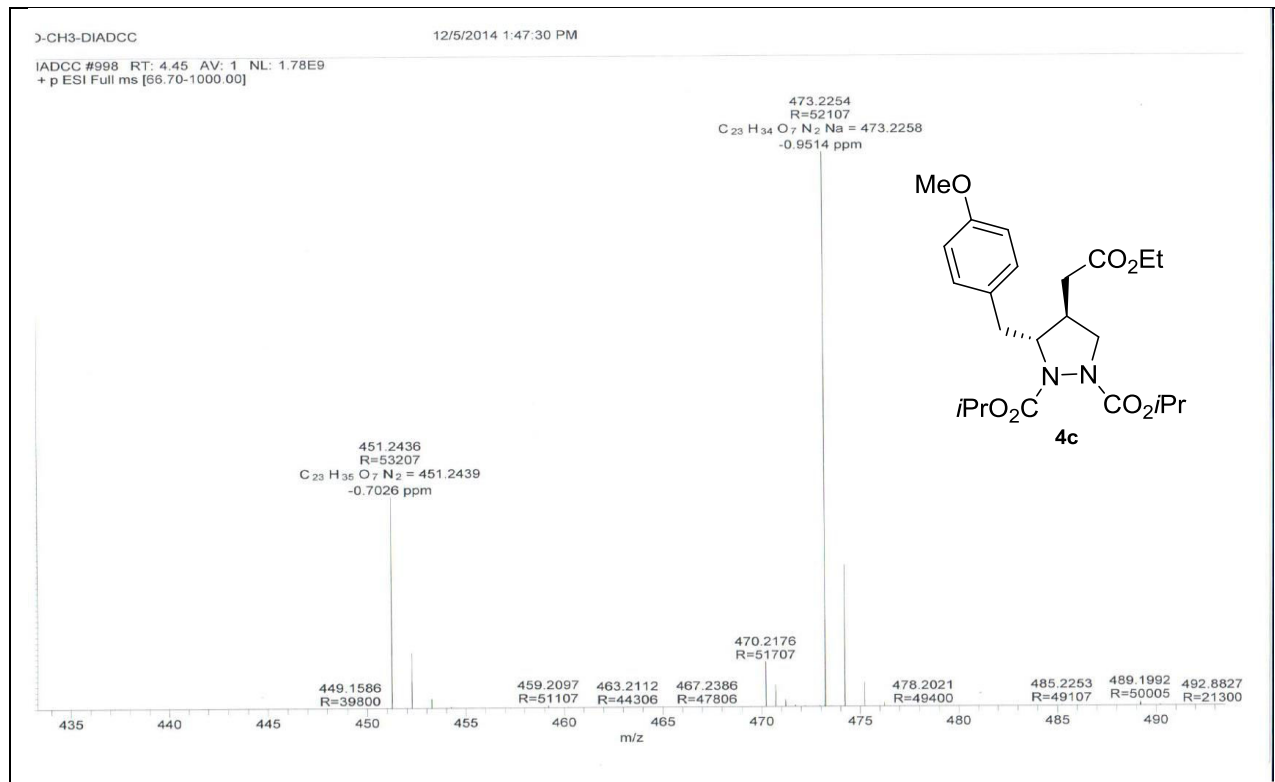
IR spectrum of **4e** and **4f** (R' = *i*Pr)

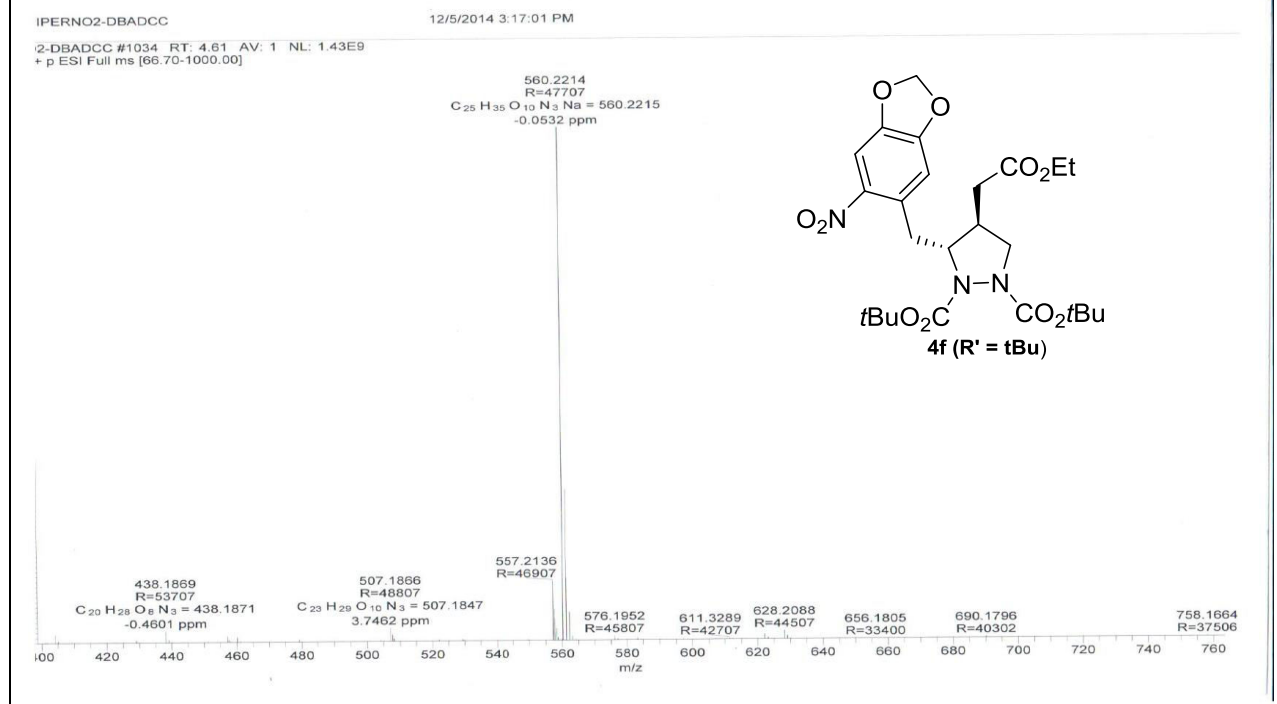
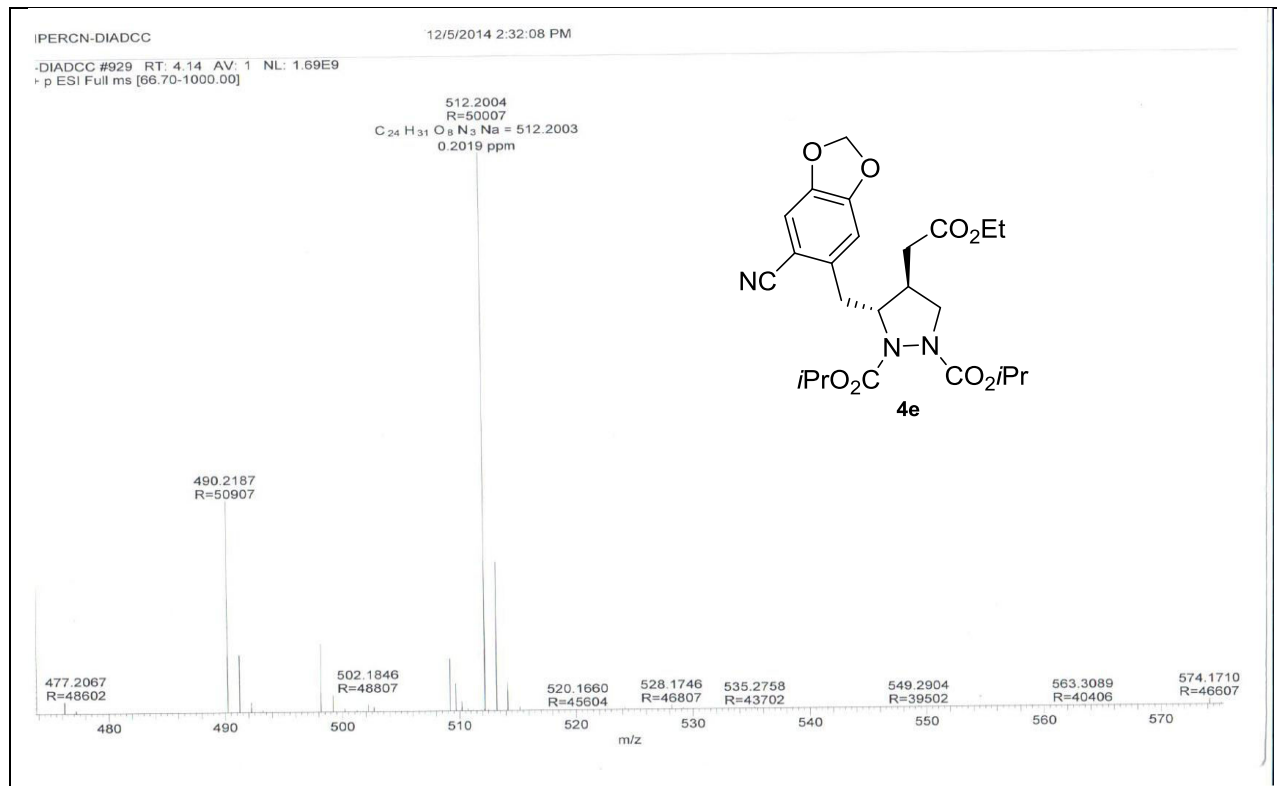




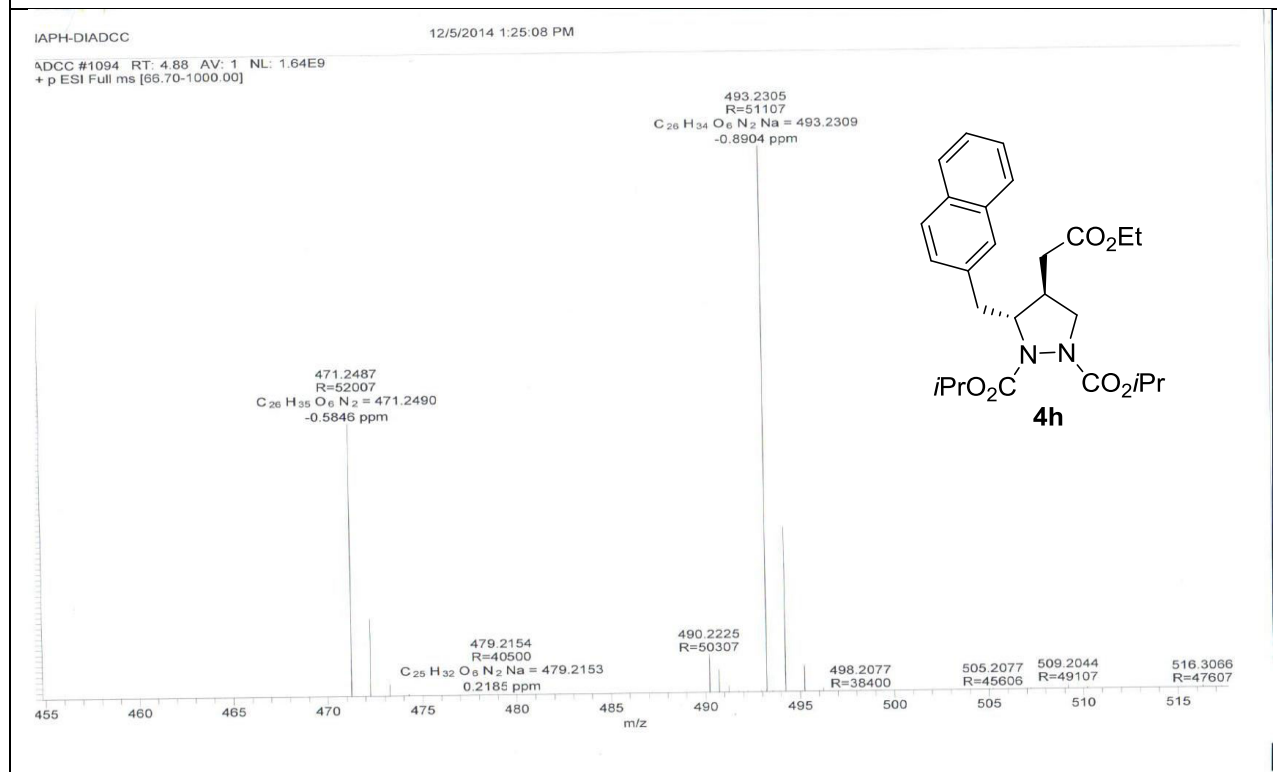
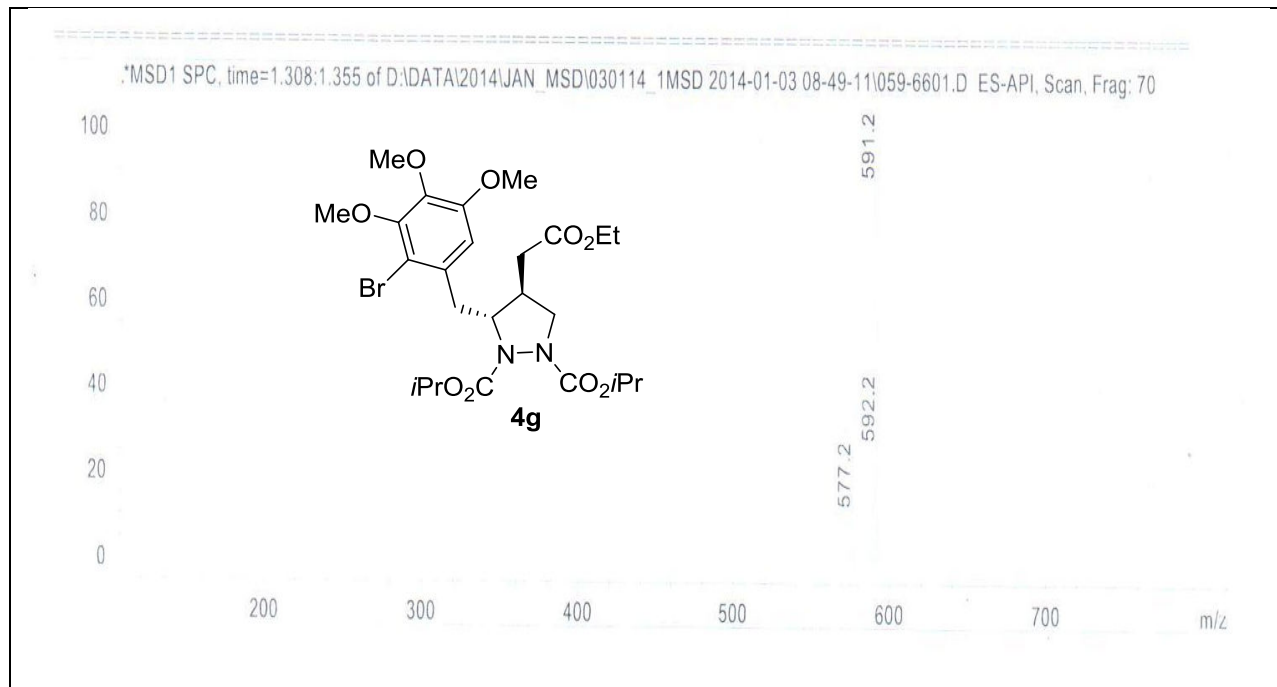
HRMS of **4a** (R' = iPr, Et)



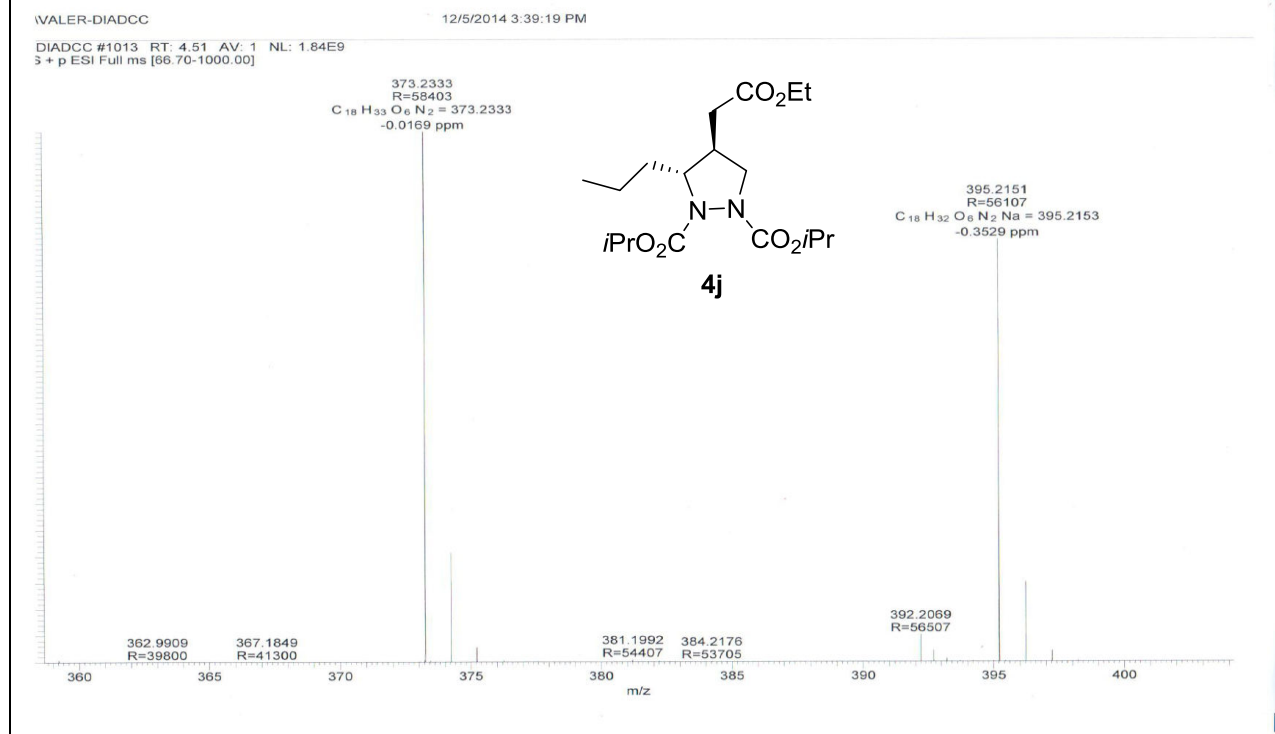
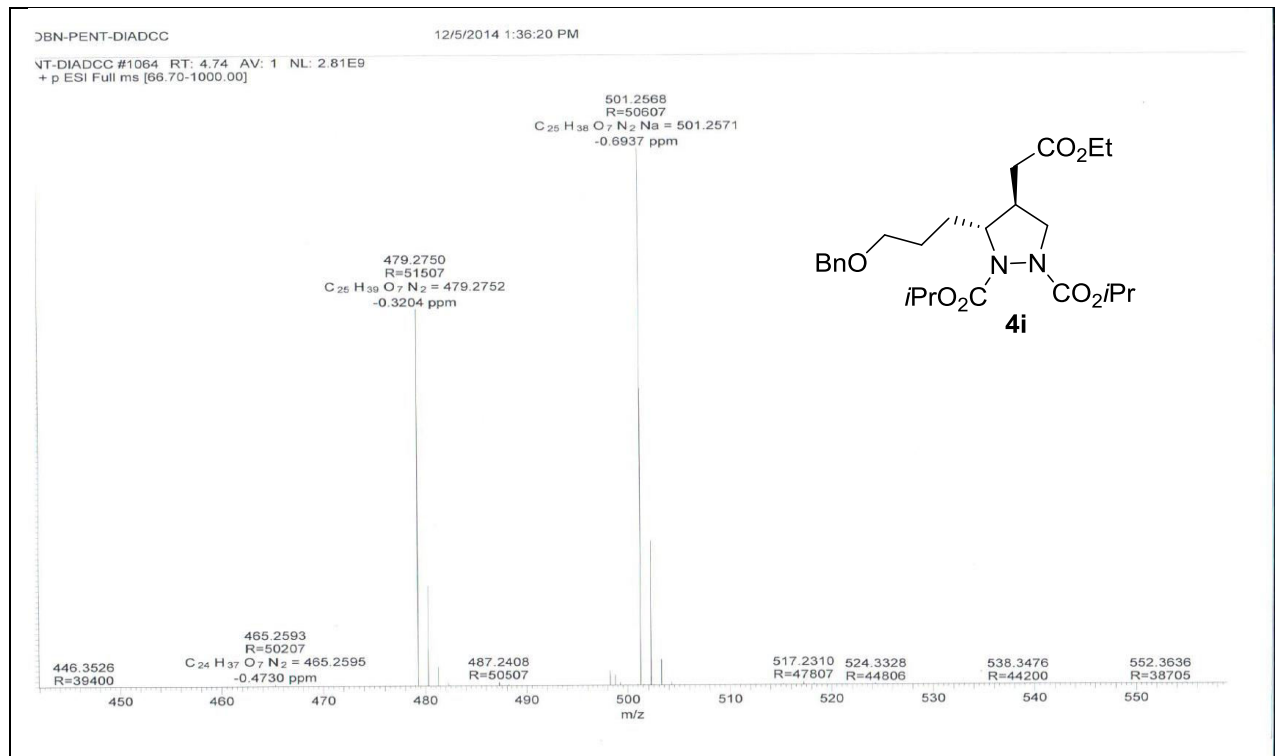




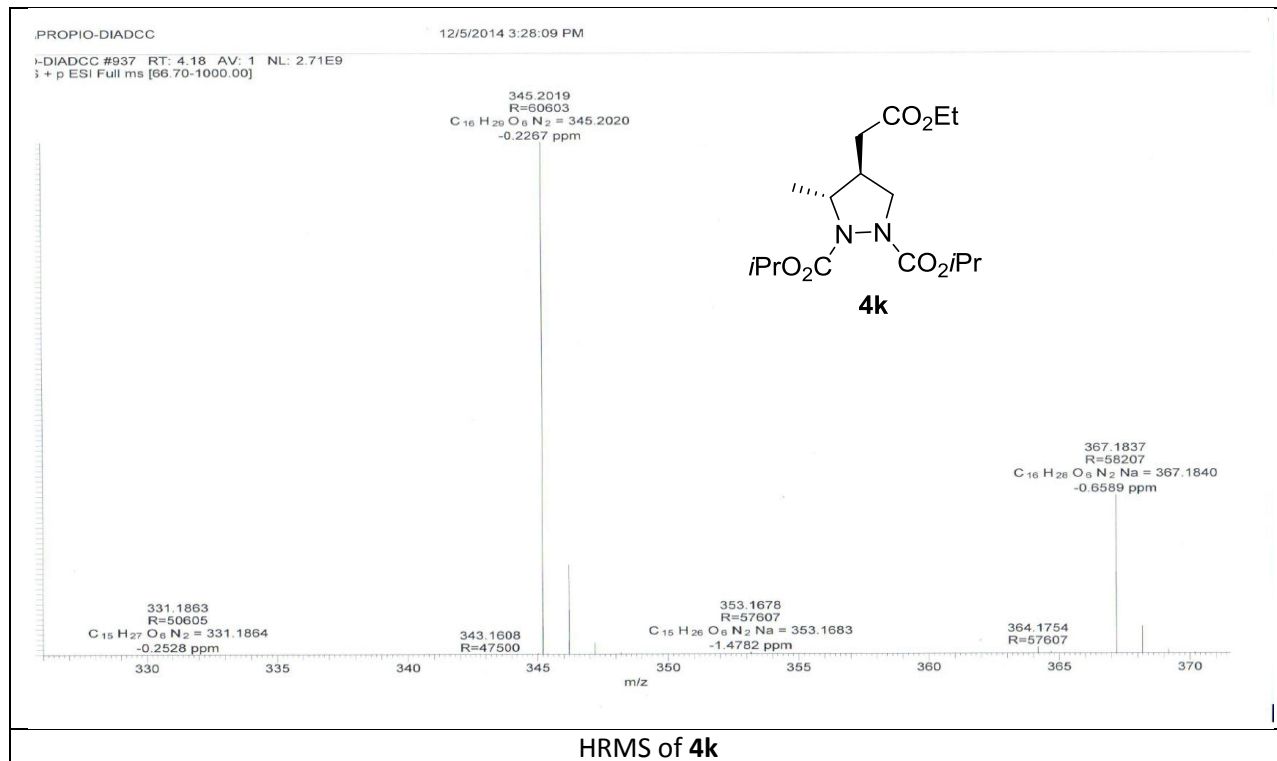
HRMS of **4e** and **4f (R' = tBu)**

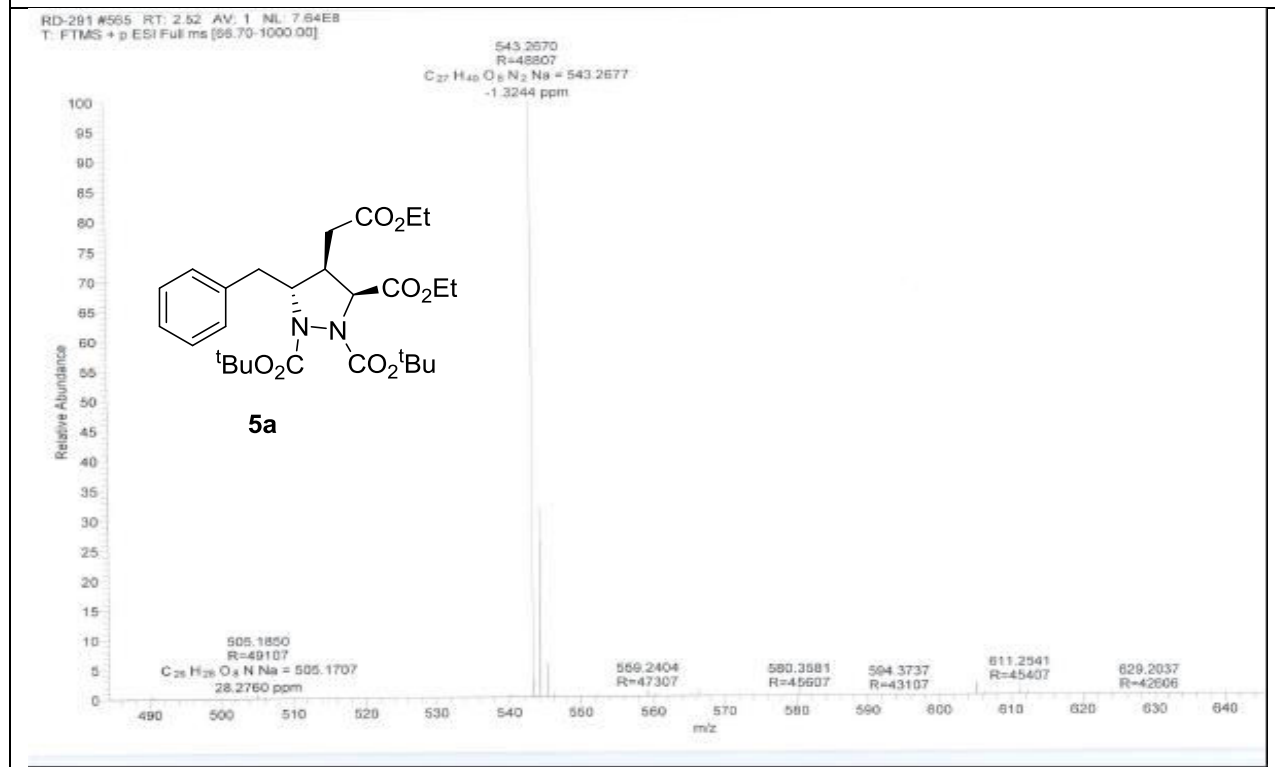
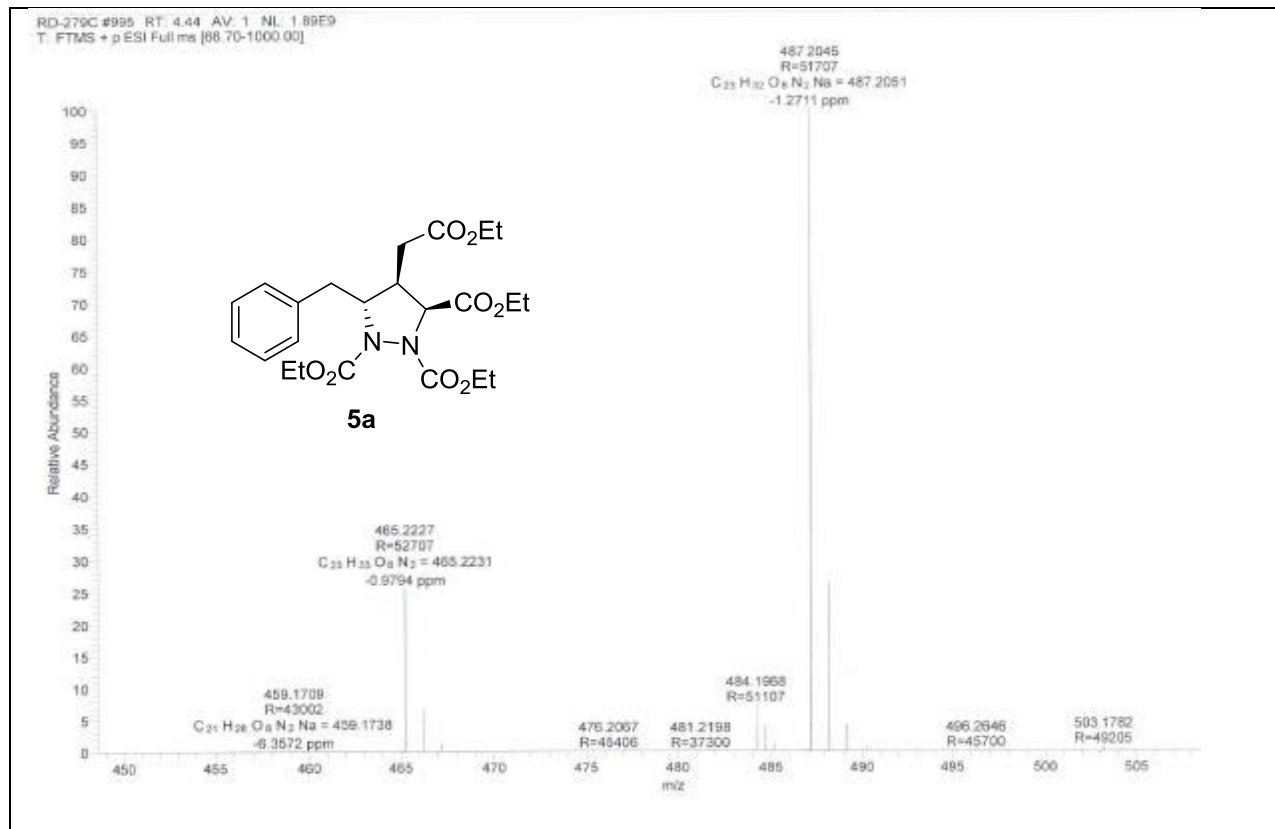


LC-MS and HRMS of **4g** and **4h**



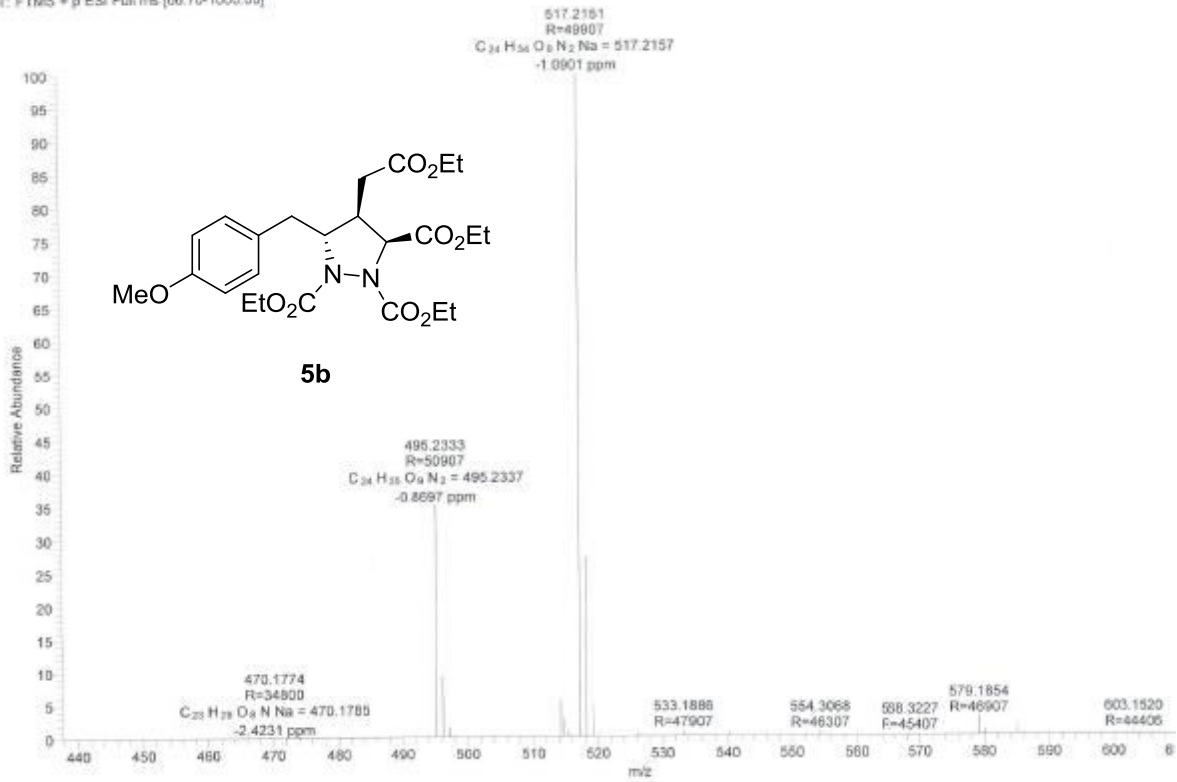
HRMS of **4i** and **4j**



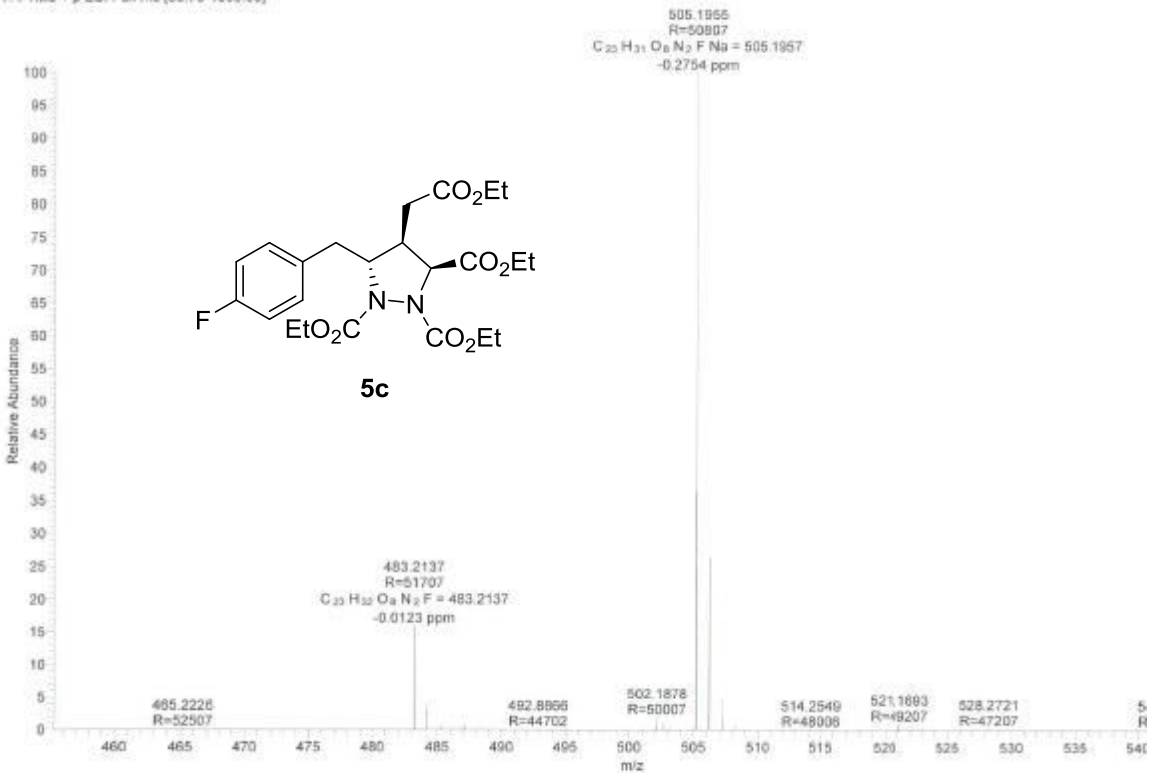


HRMS of **5a** (R' = Et or ^tBu)

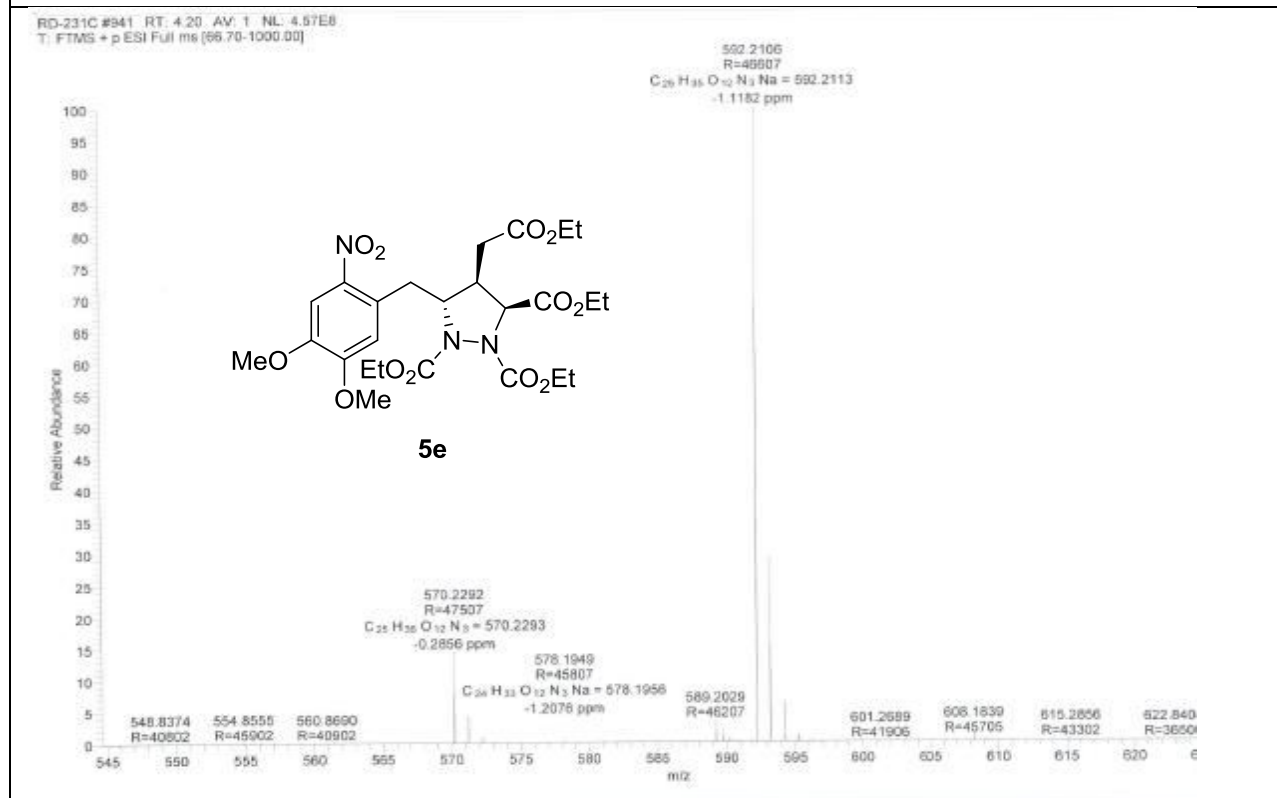
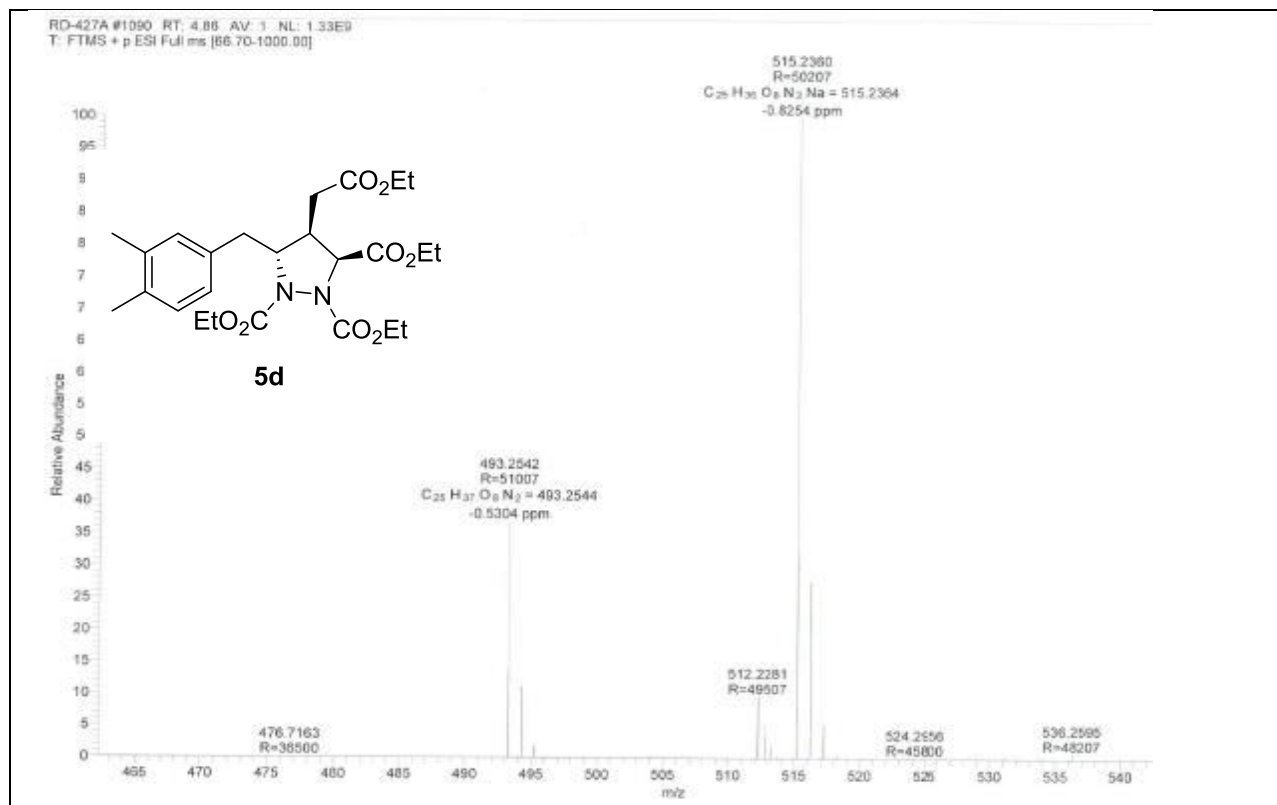
RD-325 #444 RT: 1.88 AV: 1 NL: 7.31E8
T: FTMS + p ESI Full ms [88.70-1000.00]



RD-330B #984 RT: 4.39 AV: 1 NL: 6.62E8
T: FTMS + p ESI Full ms [88.70-1000.00]

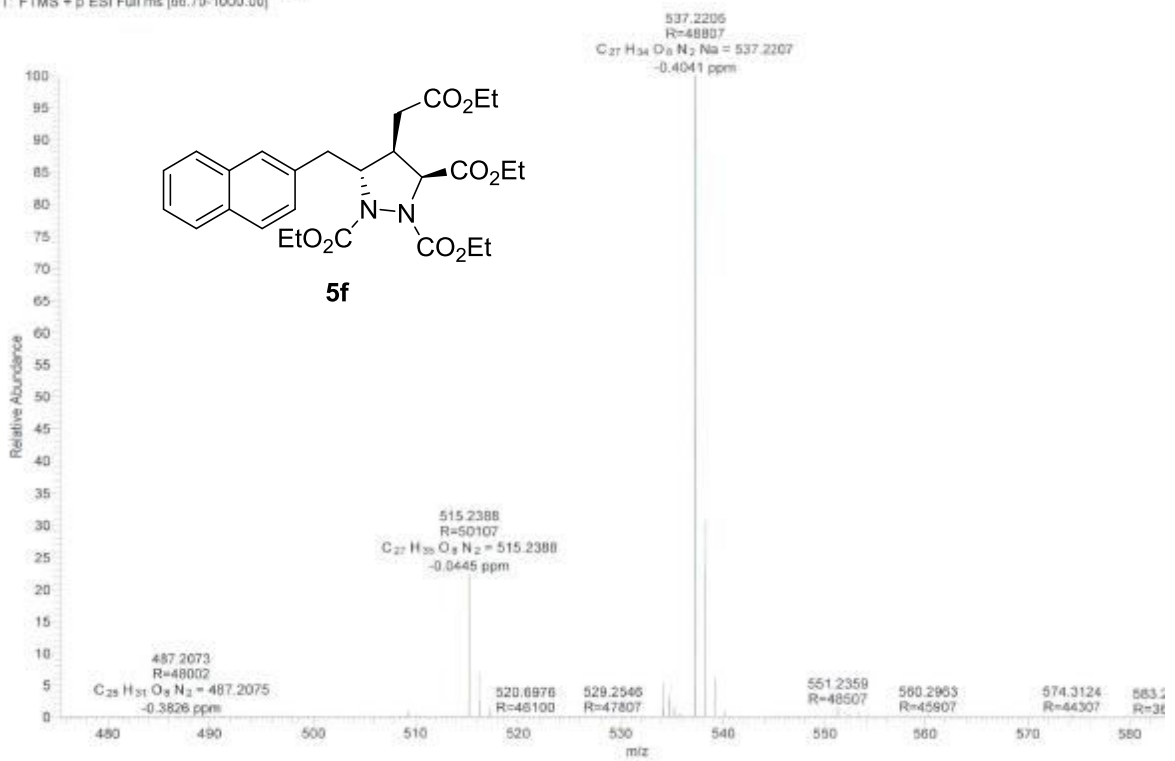


HRMS of 5b and 5c

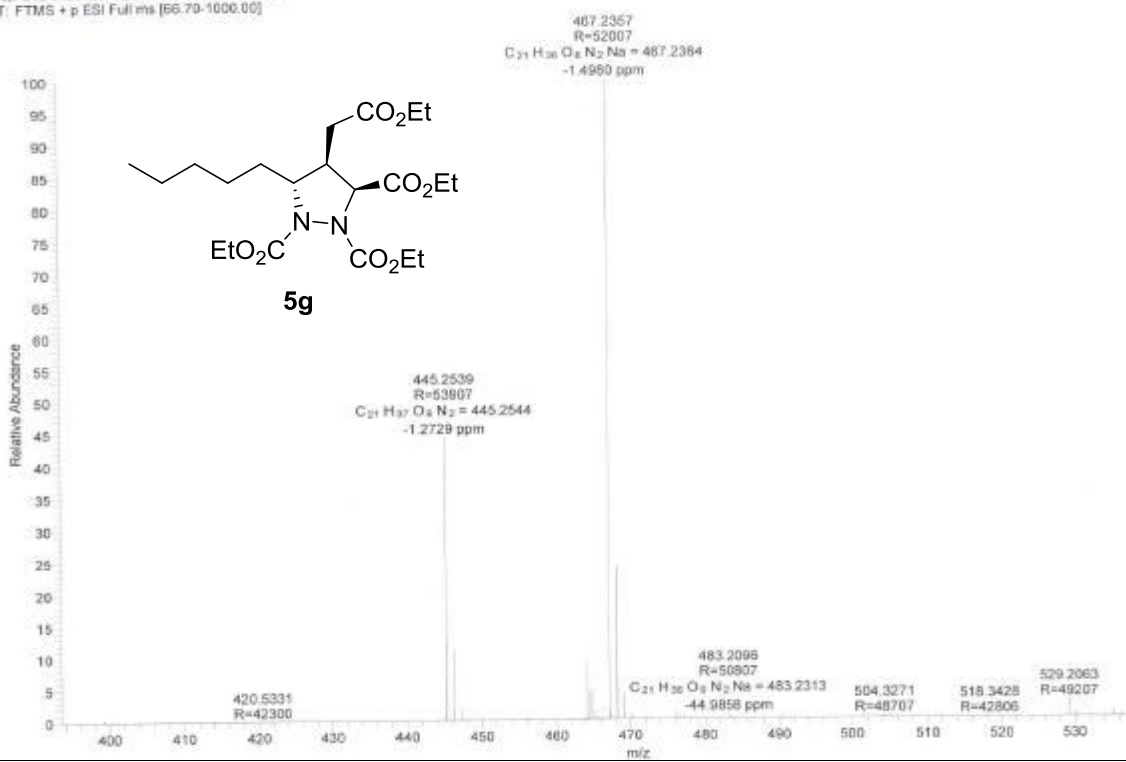


HRMS of **5d** and **5e**

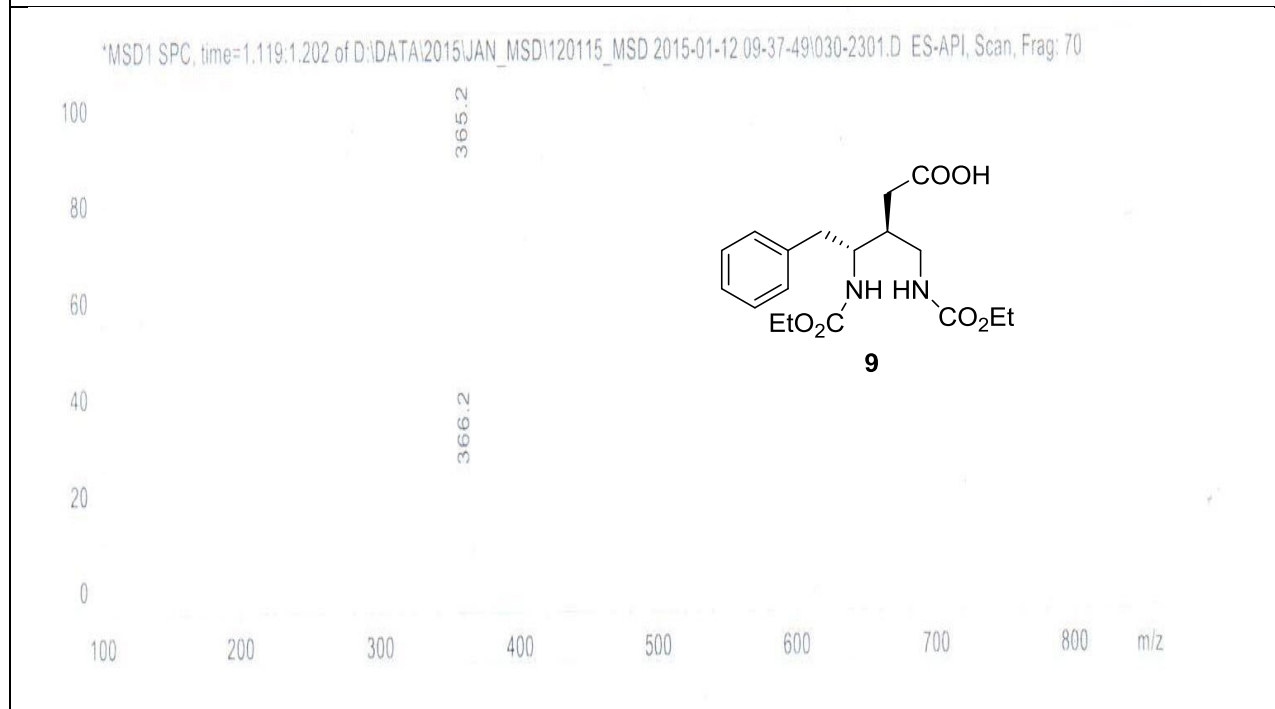
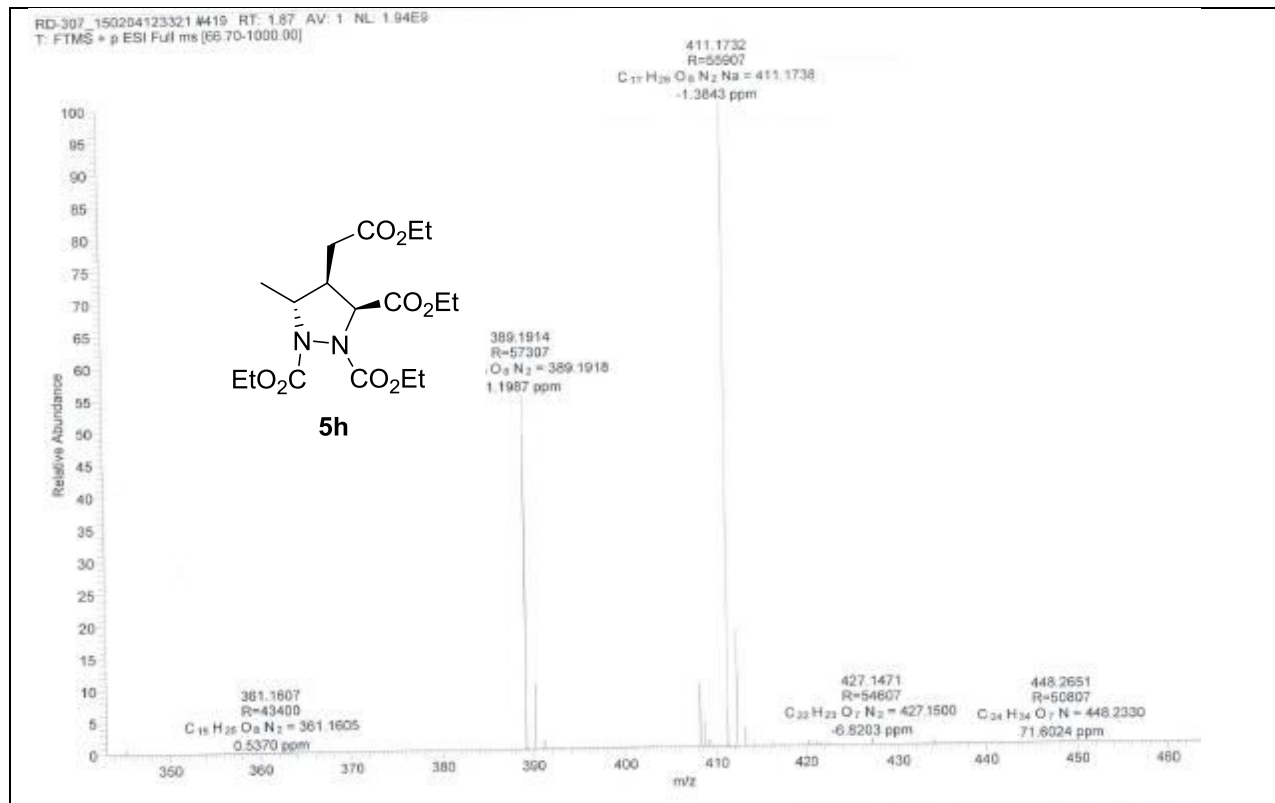
RD-439B #1088 RT: 4.85 AV: 1 NL: 8.97E8
T: FTMS + p ESI Full ms [66.70-1000.00]



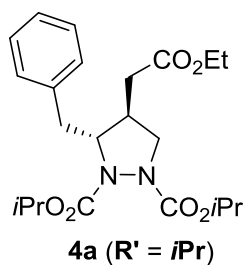
RD-312 #496 RT: 2.21 AV: 1 NL: 1.32E9
T: FTMS + p ESI Full ms [66.70-1000.00]



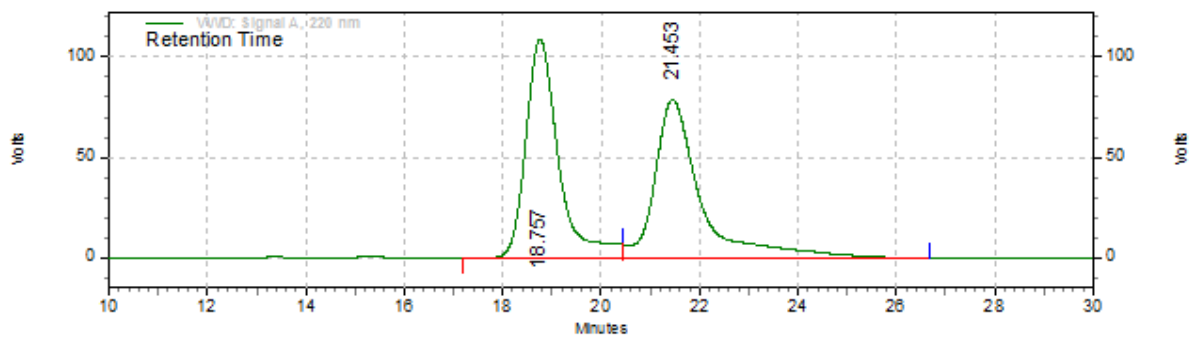
HRMS of **5f** and **5g**



HRMS of **7h** and **9**

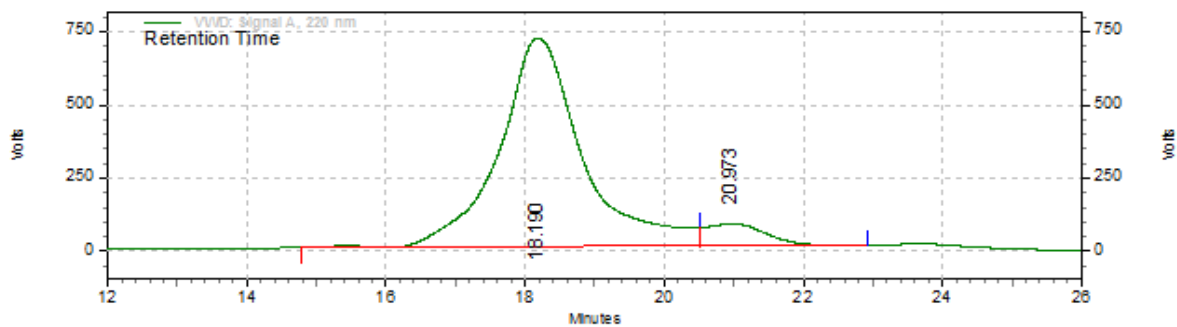


Racemic Sample:

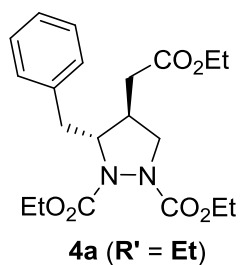


Retention Time	Area	Area %	Height
18.757	84618996	49.69	1825321
21.453	85657844	50.31	1321061

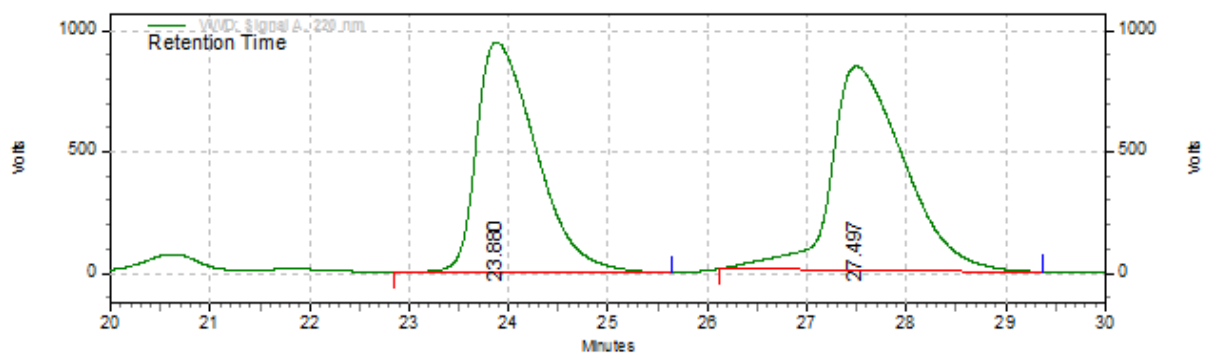
Enantio-enriched sample: **86% ee**



Retention Time	Area	Area %	Height
18.190	1002409191	93.76	11991940
20.973	78236881	6.24	1297069

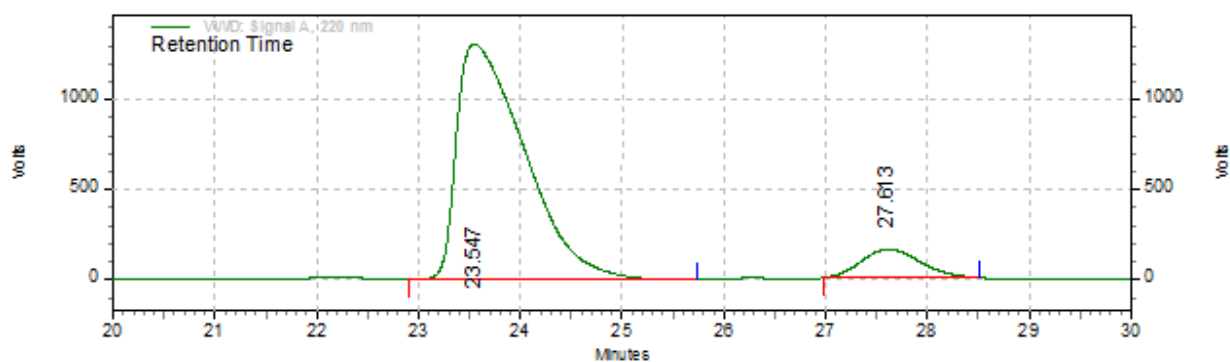


Racemic sample:

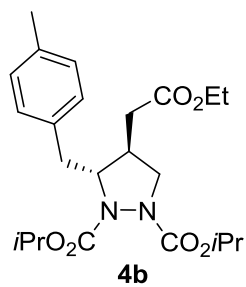


Retention Time	Area	Area %	Height
23.880	659119152	47.80	15911939
27.497	719688844	52.20	14078455

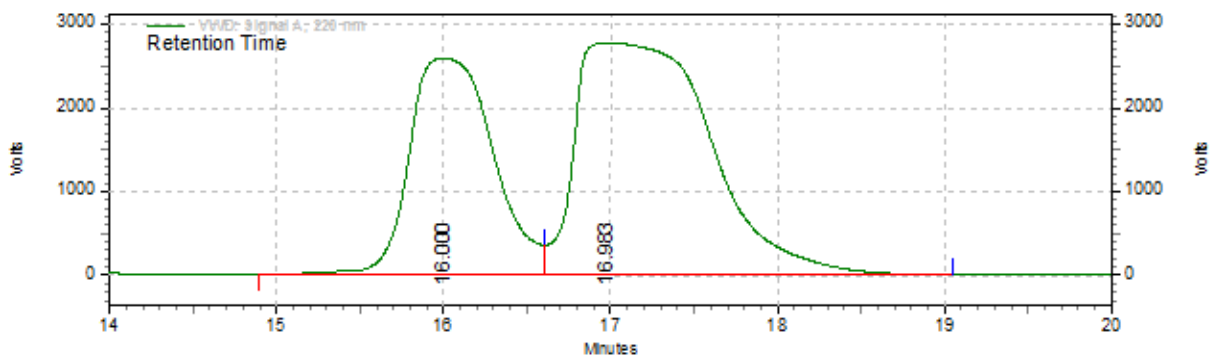
Enantio-enriched sample: **81% ee**



Retention Time	Area	Area %	Height
23.547	1017434138	90.44	21970544
27.613	107570511	9.56	2654812

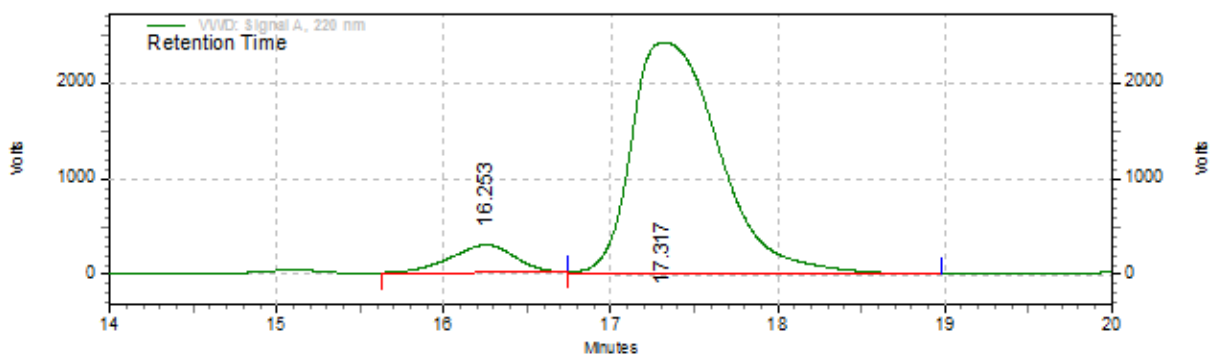


Racemic sample:

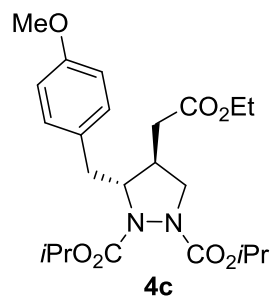


Retention Time	Area	Area %	Height
16.000	1495482427	36.60	43252175
16.983	2590137720	63.40	46412467

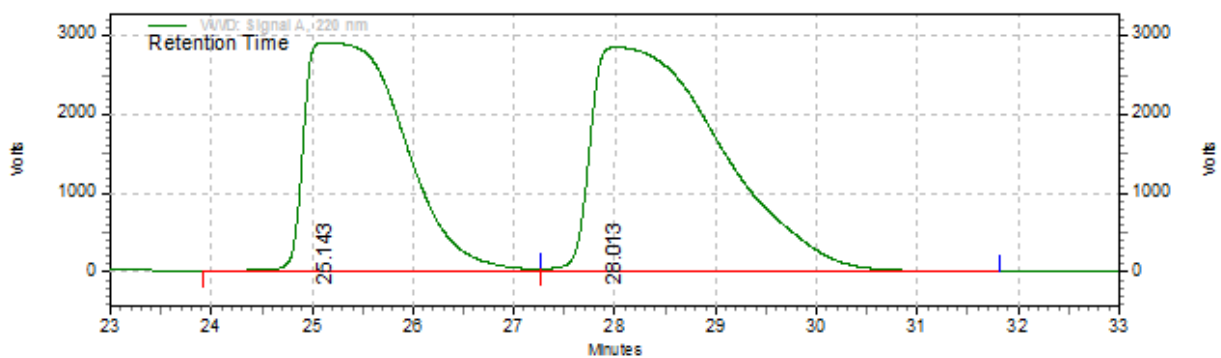
Enantio-enriched sample: **84% ee**



Retention Time	Area	Area %	Height
16.253	127949994	7.96	4800475
17.317	1479570056	92.04	40616457

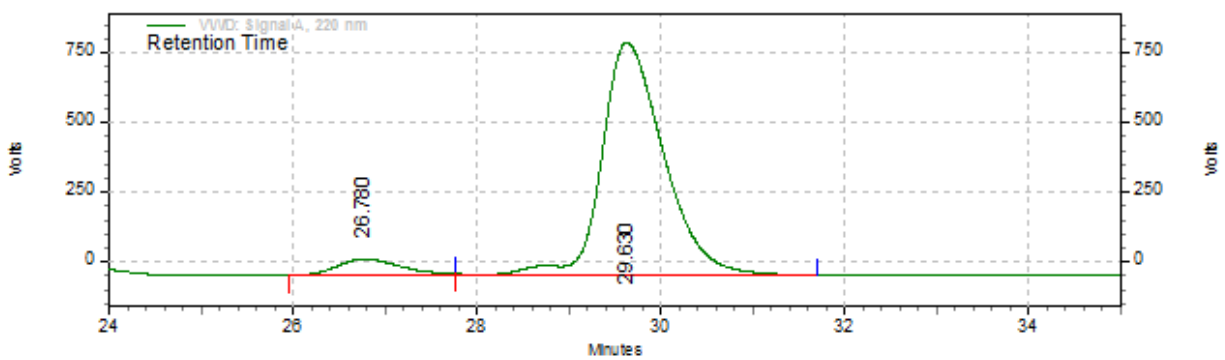


Racemic sample:

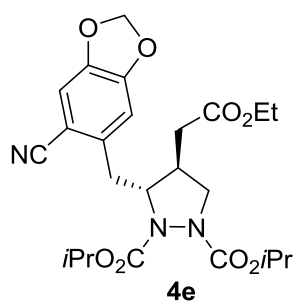


Retention Time	Area	Area %	Height
25.143	3281681142	43.84	48695184
28.013	4204639512	56.16	47665050

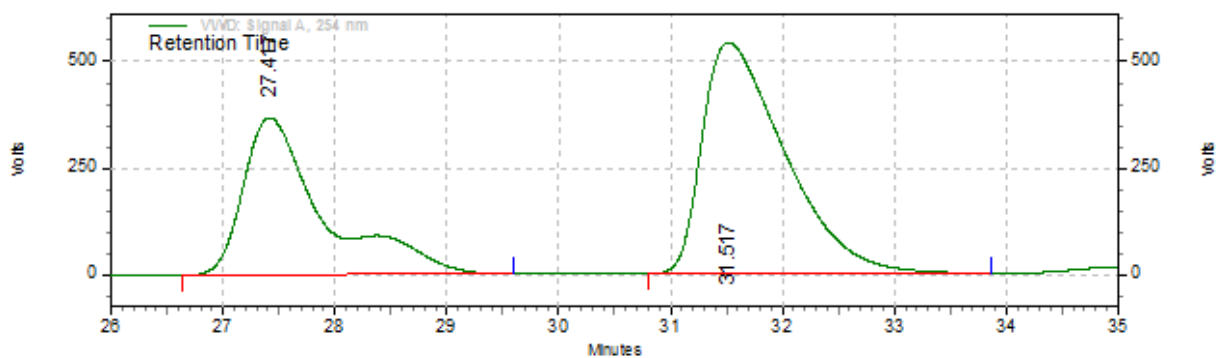
Enantio-enriched sample: **87% ee**



Retention Time	Area	Area %	Height
26.780	48849942	6.52	993265
29.630	660992825	93.48	14060767

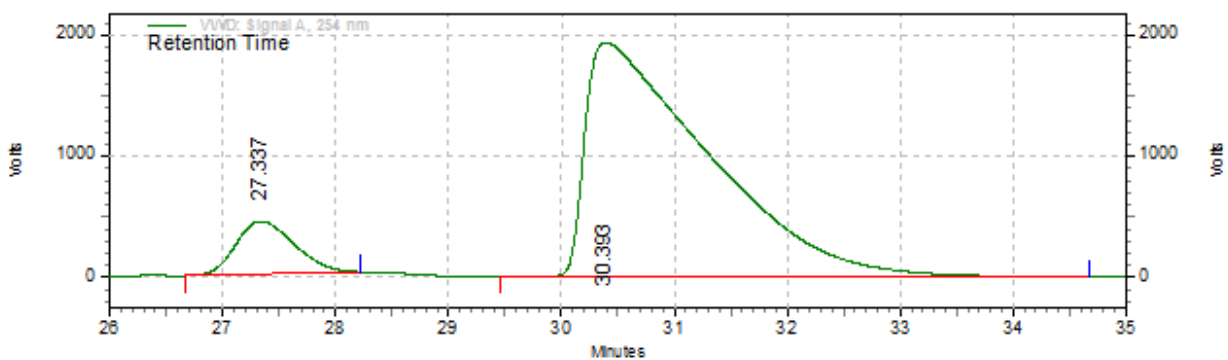


Racemic sample:

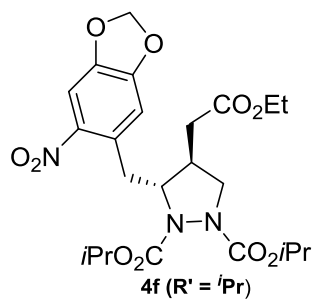


Retention Time	Area	Area %	Height
27.417	306923430	39.80	6158411
31.517	464169000	60.20	9048503

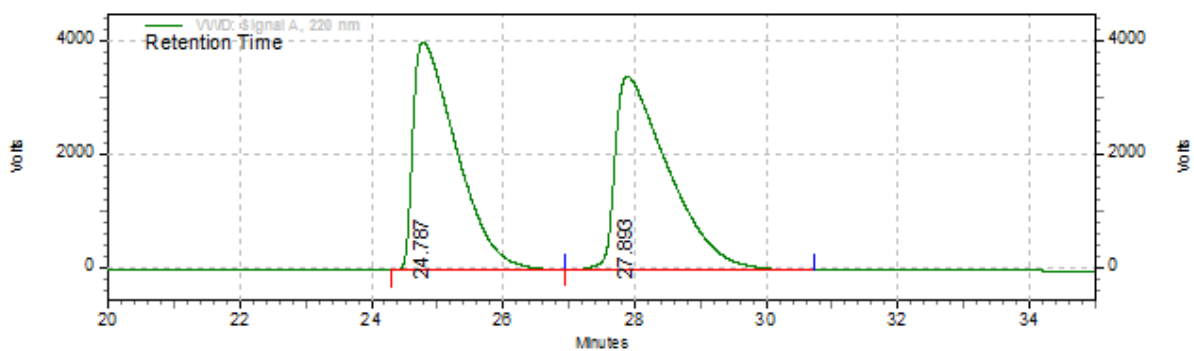
Enantio-enriched sample: **81% ee**



Retention Time	Area	Area %	Height
27.337	262934762	9.66	7342472
30.393	2460238647	90.34	32571042

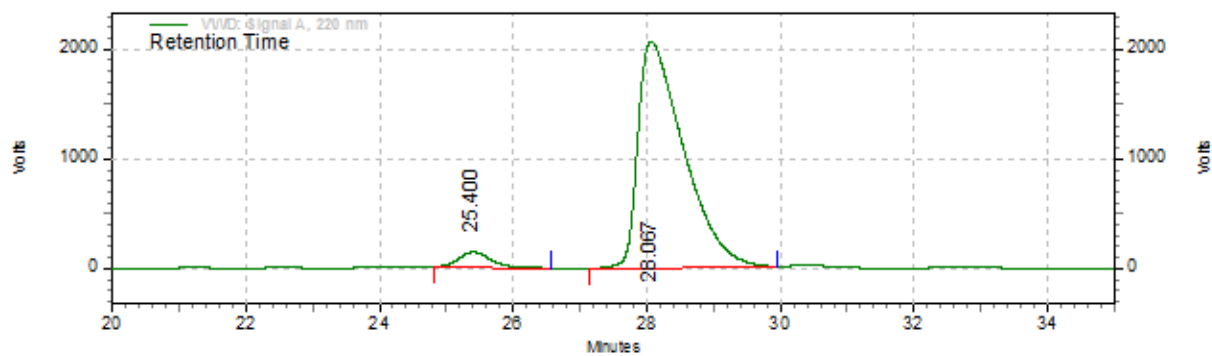


Racemic sample:

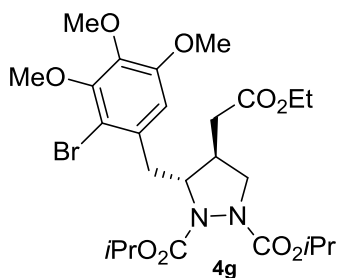


Retention Time	Area	Area %	Height
24.787	3107985469	48.94	67448379
27.893	3242276467	51.06	57271731

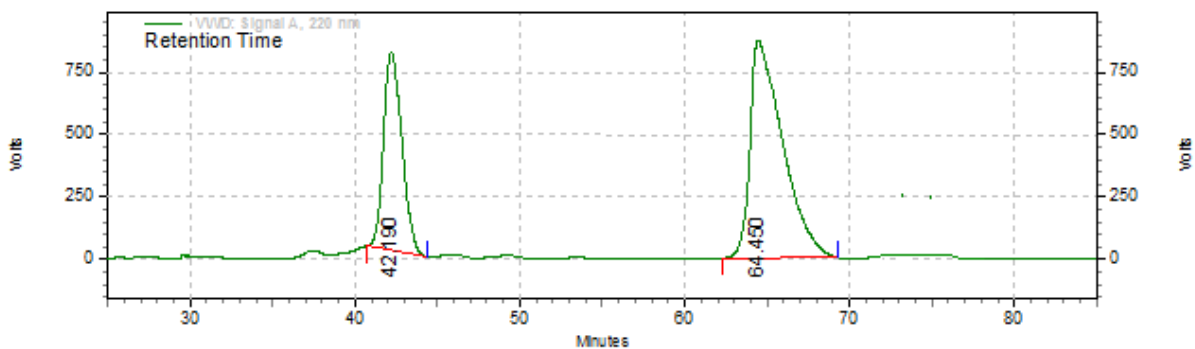
Enantio-enriched sample: **92% ee**



Retention Time	Area	Area %	Height
25.400	71363378	4.17	2237840
28.067	1640468138	95.83	34610990

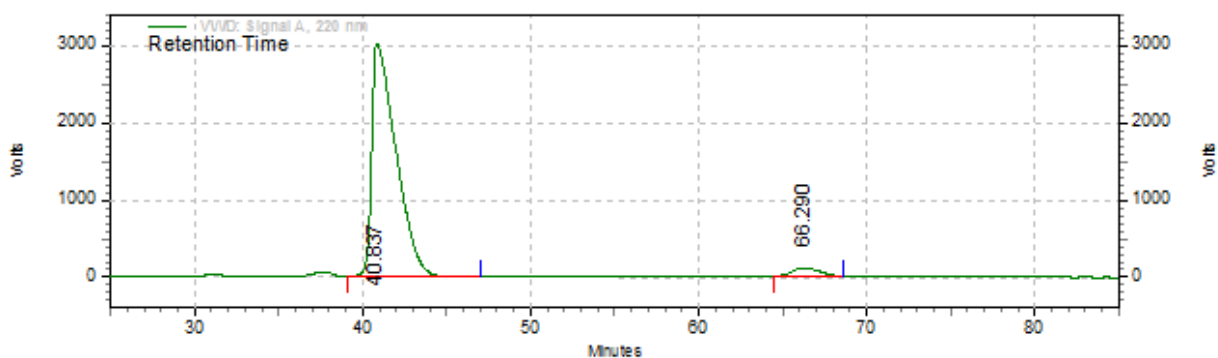


Racemic sample:

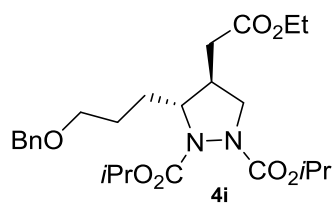


Retention Time	Area	Area %	Height
42.190	1035684039	34.02	13350151
64.450	2008736351	65.98	14628097

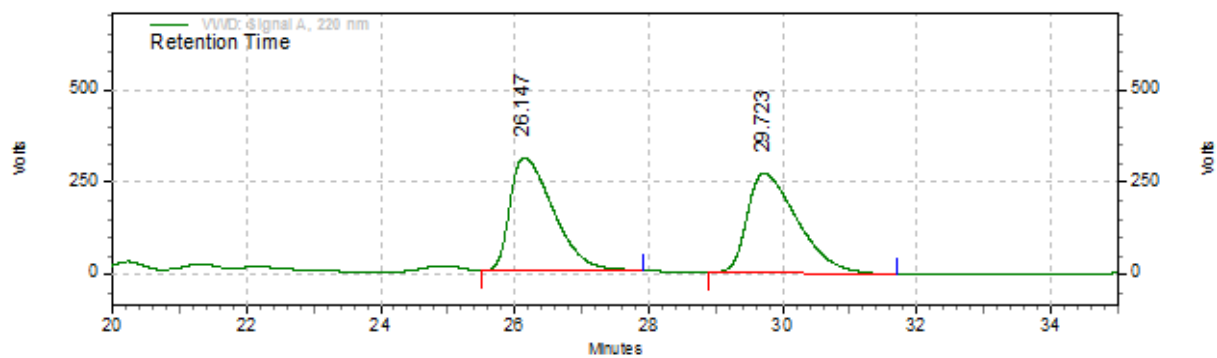
Enantio-enriched sample: **94% ee**



Retention Time	Area	Area %	Height
40.837	5055800703	97.17	50698385
66.290	211276274	2.83	1857010

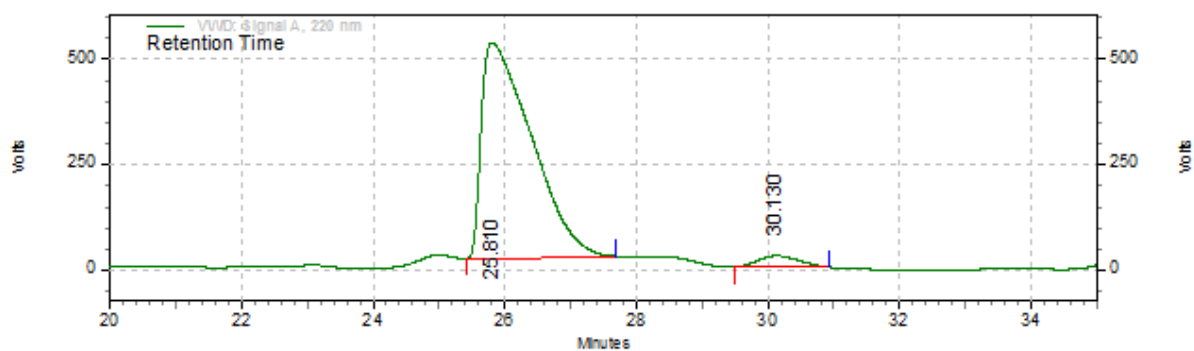


Racemic sample:

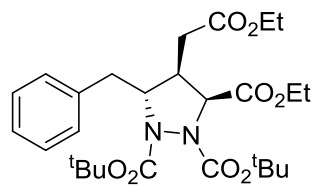


Retention Time	Area	Area %	Height
26.147	230752367	49.27	5136672
29.723	237610219	50.73	4523819

Enantio-enriched sample: **92% ee**

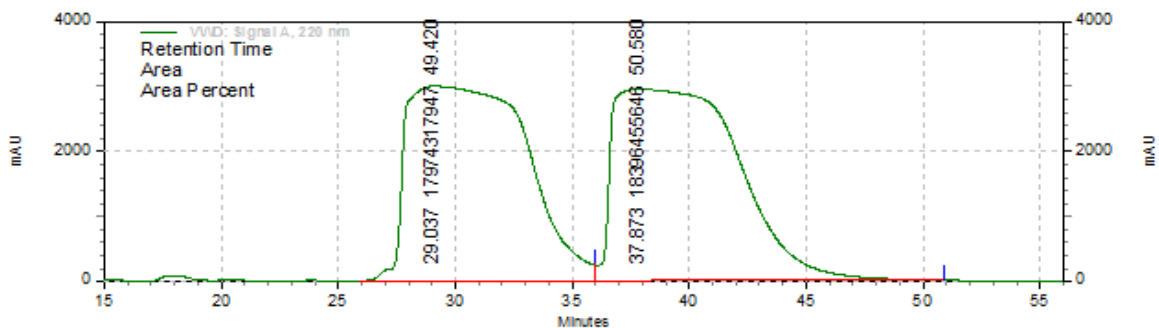


Retention Time	Area	Area %	Height
25.810	452815957	95.95	8587946
30.130	19116198	4.05	449632



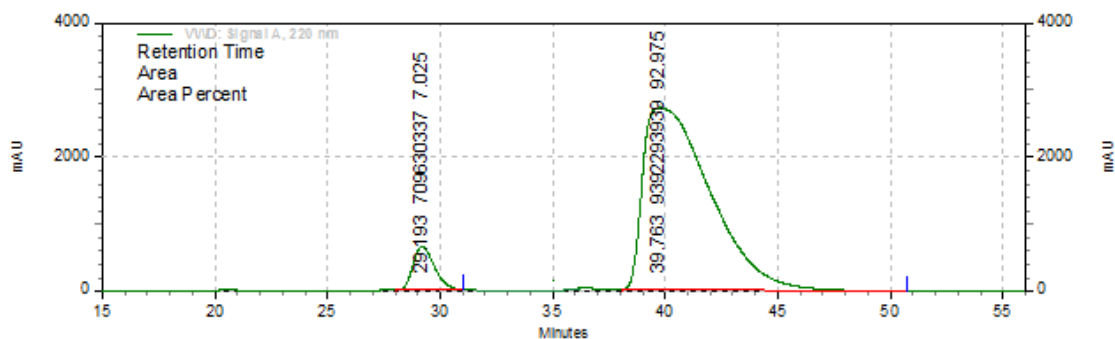
5a

Racemic Sample:

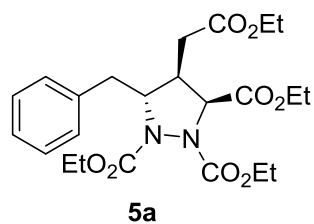


Retention Time	Area	Area %	Height
29.037	17974317947	49.42	50173222
37.873	18396455646	50.58	49320278

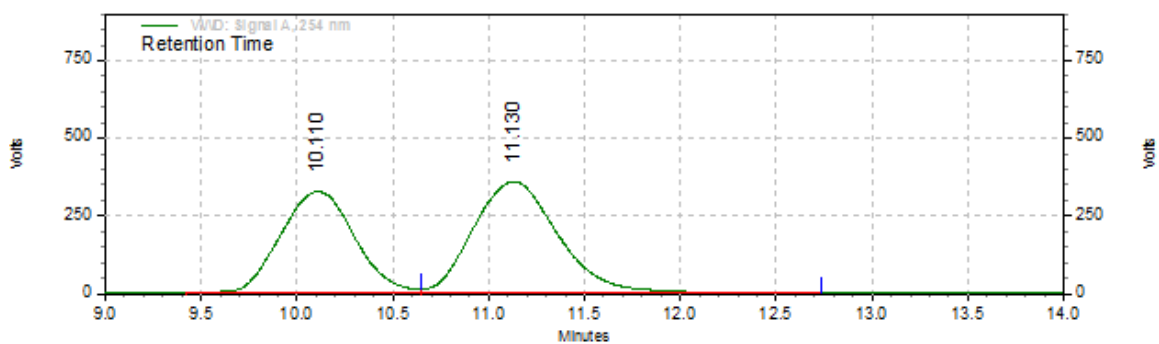
Enantio-enriched sample: **86% ee**



Retention Time	Area	Area %	Height
29.193	709630337	7.02	10738881
39.763	9392293939	92.98	45406319

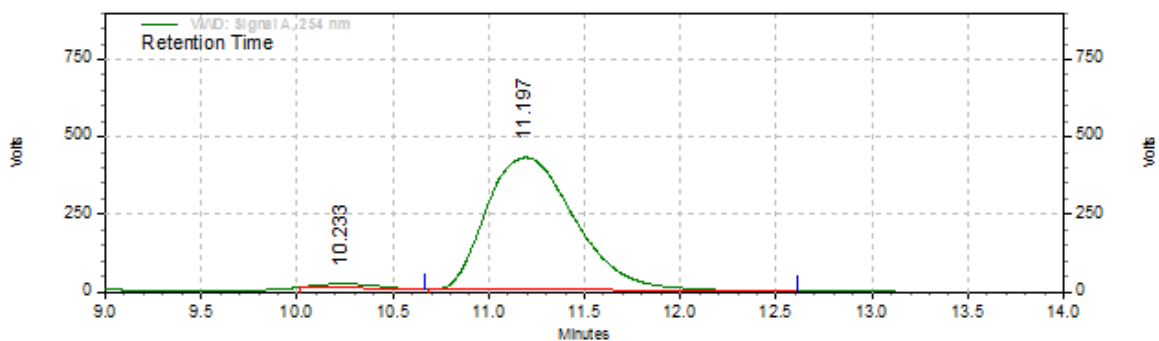


Racemic Sample:

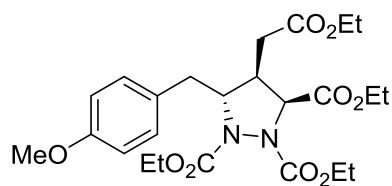


Retention Time	Area	Conc.	Height
10.110	144551914	44.12	5436080
11.130	183100775	55.88	6000627

Enantio-enriched sample: **96% ee**

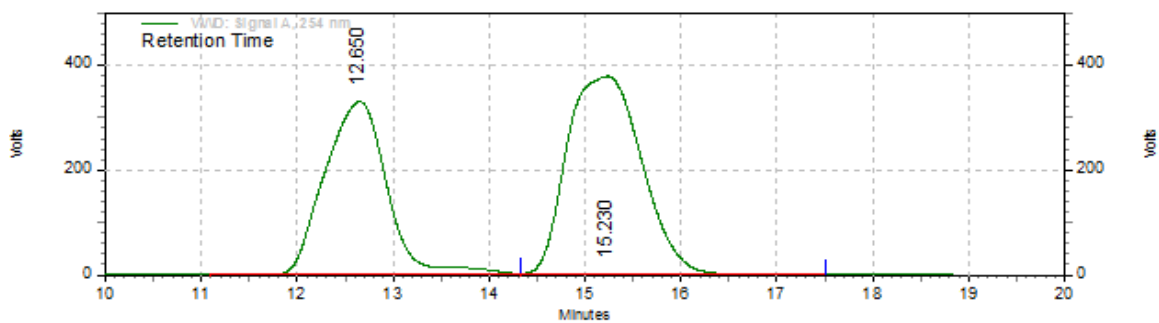


Retention Time	Area	Conc.	Height
10.233	4980694	2.10	229461
11.197	231657212	97.90	7181886



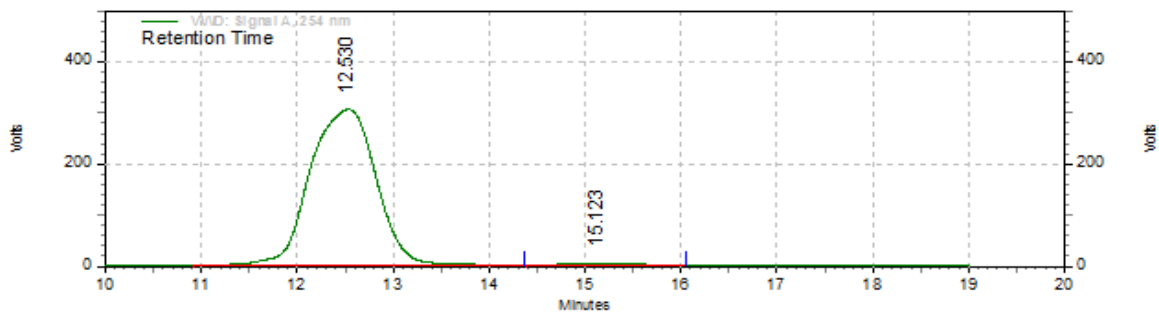
5b

Racemic sample:

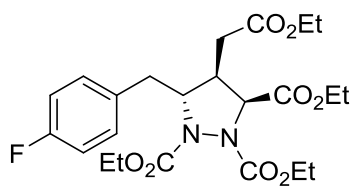


Retention Time	Area	Conc.	Height
12.650	249172903	42.05	5529972
15.230	343374744	57.95	6341927

Enantio-enriched sample: **96% ee**

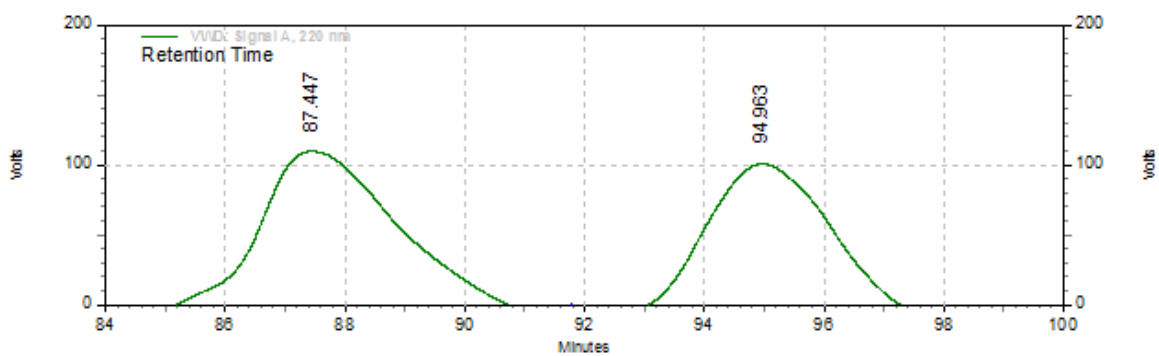


Retention Time	Area	Conc.	Height
12.530	244951558	98.33	5128098
15.123	4168475	1.67	83636



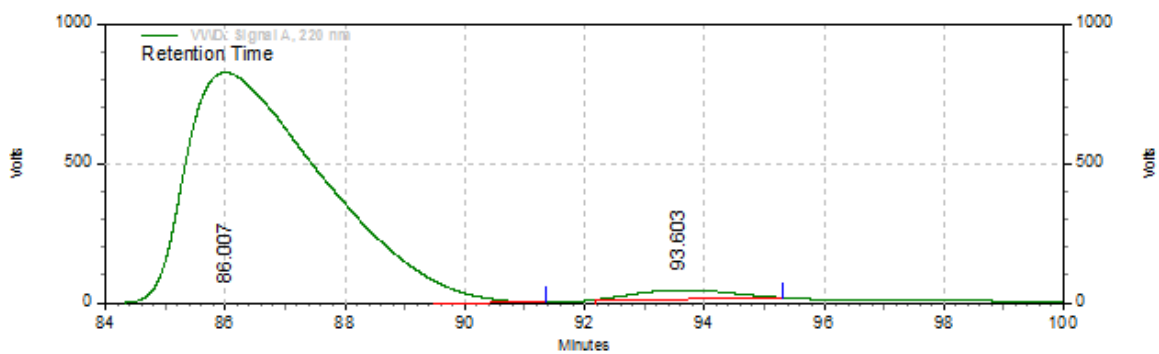
5c

Racemic sample:

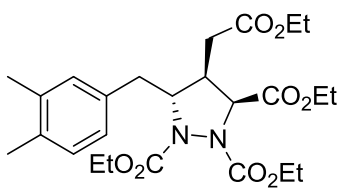


Retention Time	Area	Conc.	Height
87.447	381012622	54.30	2095550
94.963	320714209	45.70	1982892

Enantio-enriched sample: **95% ee**

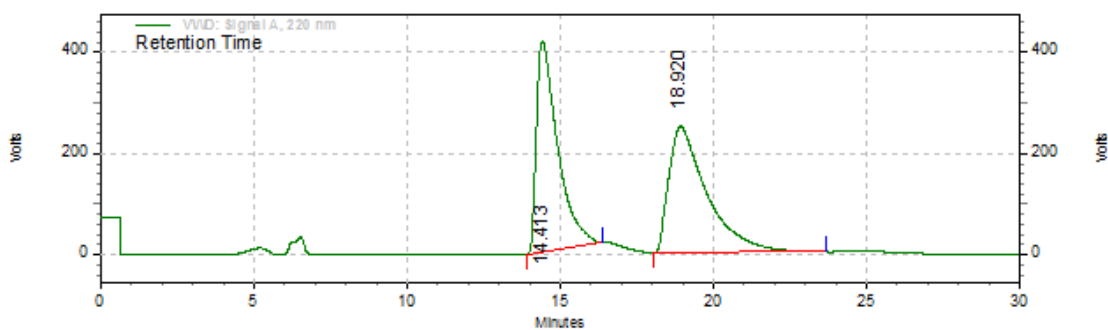


Retention Time	Area	Conc.	Height
86.007	2207902336	97.49	13887984
93.603	56955538	2.51	527171



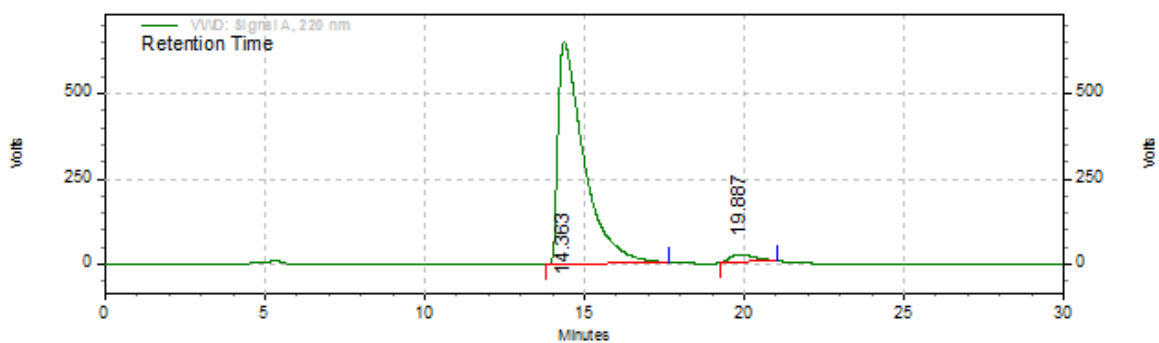
5d

Racemic sample:



Retention Time	Area	Conc.	Height
14.413	337981933	48.29	6997053
18.920	361975051	51.71	4187736

Enantio-enriched sample: **94% ee**



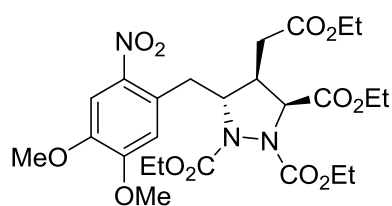
Retention Time	Area	Conc.	Height
14.363	612546105	96.72	10911976
19.887			

19.887

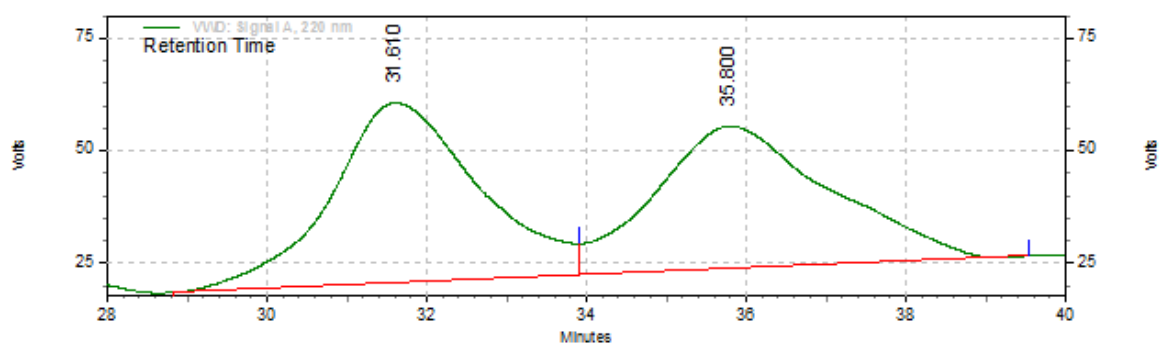
20741660

3.28

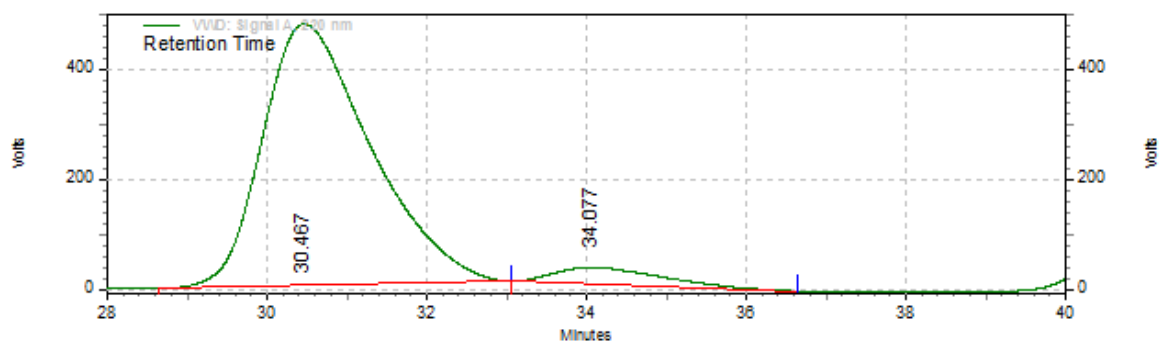
374813

**5e**

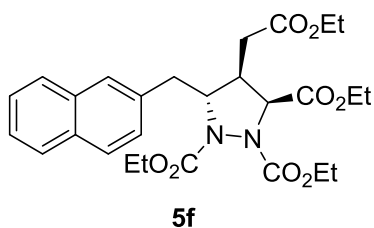
Racemic sample:



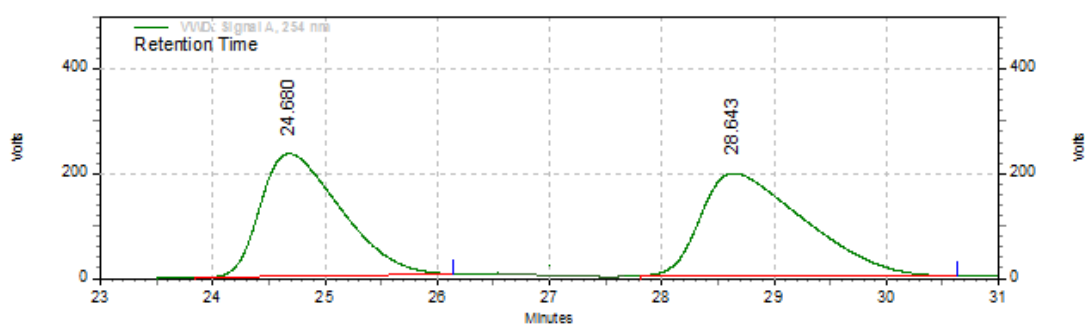
Retention Time	Area	Conc.	Height
31.610	86274582	51.54	671354
35.800	81118792	48.46	532527

Enantio-enriched sample: **88% ee**

Retention Time	Area	Conc.	Height
30.467	747787806	94.00	7954334
34.077	47766301	6.00	511065

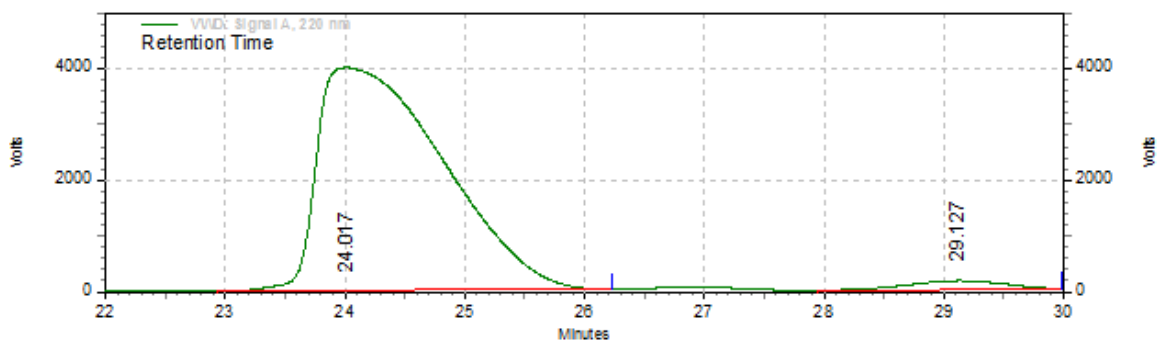


Racemic sample:



Retention Time	Area	Conc.	Height
24.680	195736780	48.25	3938803
28.643	209044985	51.75	3282065

Enantio-enriched sample: **94% ee**



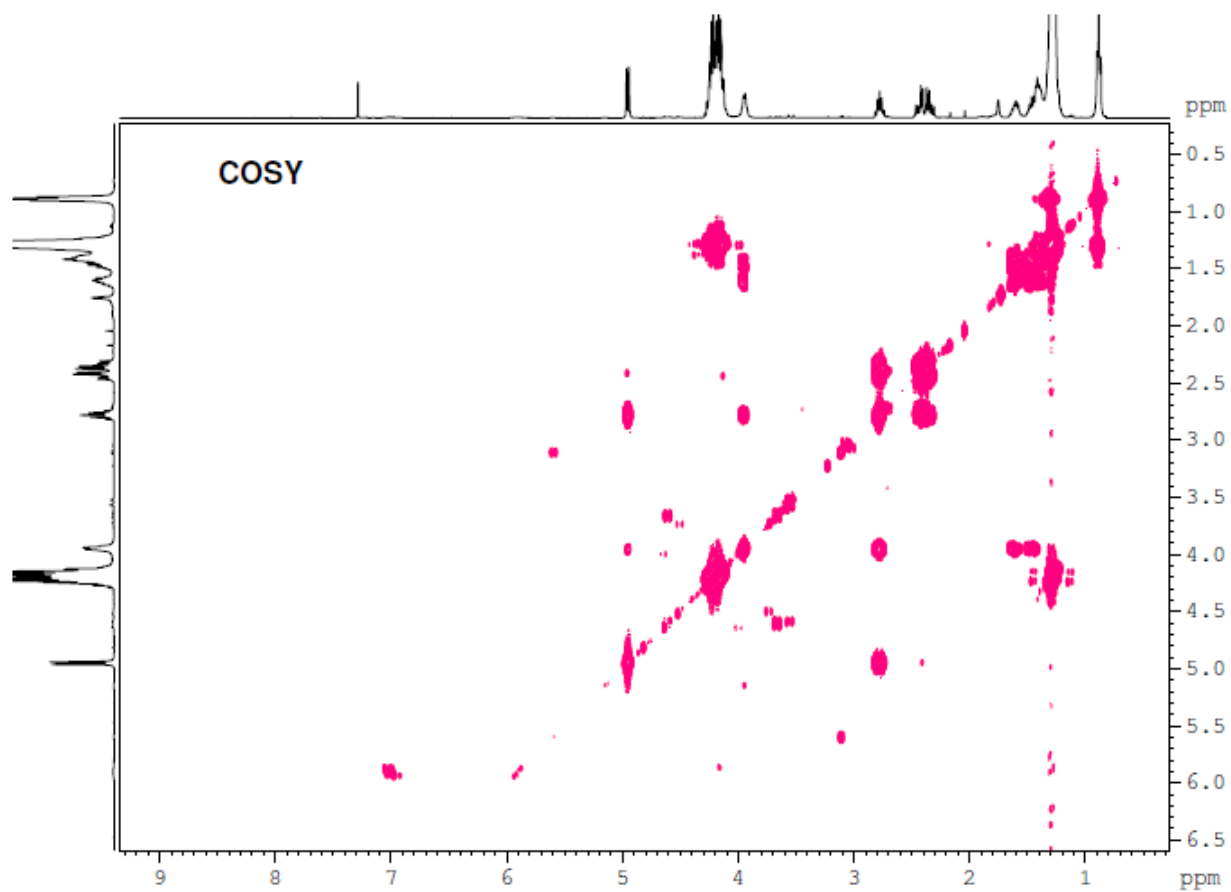
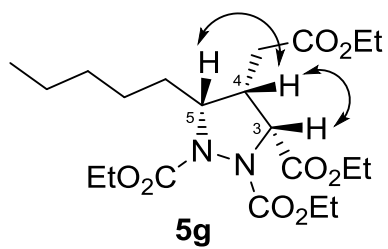
Retention Time	Area	Conc.	Height
24.017	4883290118	97.22	67088890
29.127			

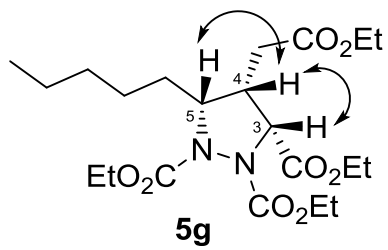
29.127

139847311

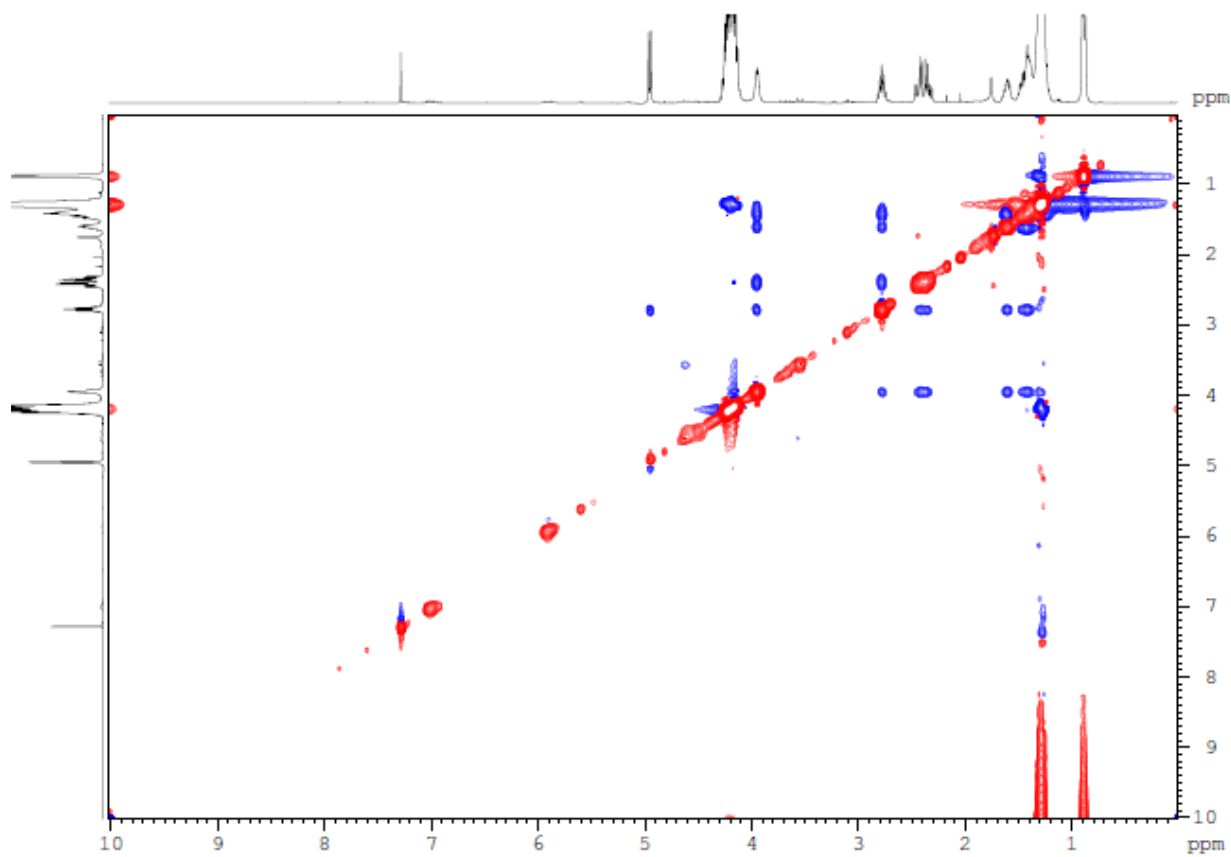
2.78

2575790

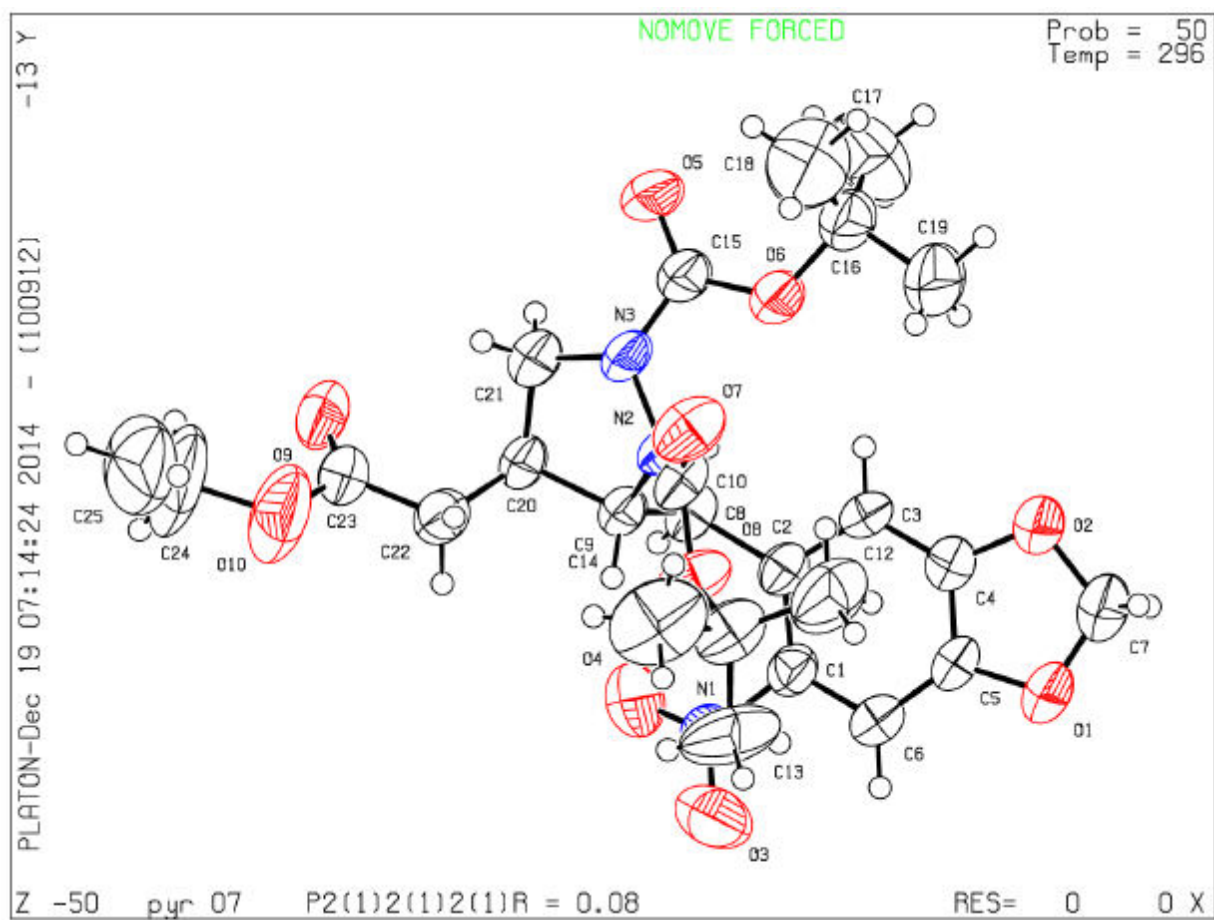
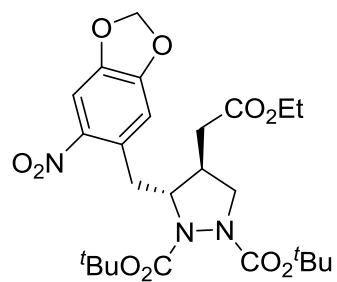




NOESY



Crystal data of **4f**:



	4f
Mol. Formula	C ₂₅ H ₃₄ N ₃ O ₁₀
<i>Mr</i>	536.55
<i>Temp.</i> (K)	296(2)
Crystal System	Orthorhombic
Space group	<i>P2(1)2(1)2(1)</i>
<i>a</i> /Å	10.9122(16)
<i>b</i> /Å	11.4715(18)
<i>c</i> /Å	23.486(3)
<i>α</i> /°	90
<i>β</i> /°	90
<i>γ</i> /°	90
<i>V</i> /Å ³	2939.9(8)
<i>Z</i> , <i>D</i> _{calc} /g cm ⁻³	4, 1.212
<i>μ</i> /mm ⁻¹	0.094
F (000)	1140
<i>θ</i> max/°	25.00
Absor.correction	multi-scan
Refln. collected	11426
Unique Refln.	5061
Observed Refln.	3619
<i>R</i> _{int}	0.0749
No. of Parameter	350
<i>R</i> _{1_obs} , <i>R</i> _{1_all}	0.0774, 0.1004
<i>wR</i> _{2_obs} , <i>wR</i> _{2_all}	0.1916, 0.2113
GoF	1.043
<i>Δρ</i> _{max} , <i>Δρ</i> _{min} /eÅ ⁻³	0.343, -0.287

Crystal data table: