

Supporting information

Short α/β -peptides as catalysts for intra- and intermolecular aldol reactions

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Table of contents

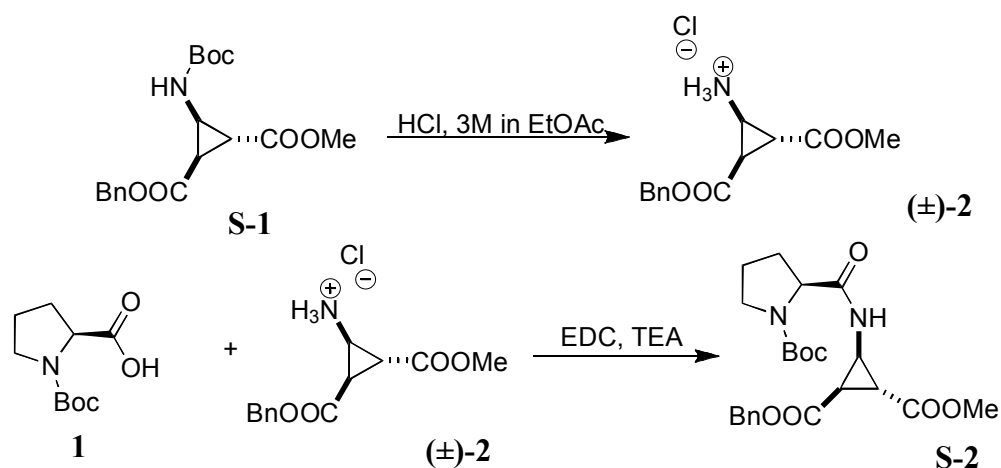
General information	S-2
Representative procedure for catalysts preparation	S-2
General procedure for catalytic asymmetric aldol reaction	S-5
Experimental data	S-7
Copies of ^1H and ^{13}C	S-12
Copies of GC and HPLC chromatograms	S-42 - S-63

General Information

Reactions were carried out in closed 10 mL vials following the procedure subsequently reported; distilled, water free solvents have been employed in all reactions that did not involve water presence. Dry DCM for peptide coupling has been obtained from a molecular sieves solvent purification system. Analysis grade acetone has been employed in the catalysis involving water containing mixtures. Aldehyde substrates have been distilled before use. Silica gel 60 (0.063-0.200 mm) was used for the column chromatography, TLC analysis was done on silica gel 60 F₂₅₄ coated on aluminium sheets; ninhydrine coloration was employed to check the reaction progress during peptide synthesis, vanilline was employed to follow the formation of the products of catalysis. ¹H (300 MHz) and ¹³C (75.5 MHz) NMR spectra were recorded on a 300 MHz Spectrometer in CDCl₃ (7.27 ppm for ¹H, 77 ppm for ¹³C) or CD₃OD (3.31 ppm for ¹H, 49.1 ppm for ¹³C). IR spectra were recorded using a *golden gate*, single reflection, ATR system. The *ee* was determined by chiral HPLC on a Chiralpak-AS column or by chiral GC on a CP Chirasil-Dex CB column (injector temperature, 250°C, detector temperature, 250°C) after trimethylsilylation (only for intermolecular aldol reaction) of the product. The trimethylsilylation was carried out directly on the GC sample, dissolved in DCM by addition of one drop of pure trimethylsilylimidazole. The absolute configuration was assigned by comparison of the optical rotation for the isolated compound, with the values reported in literature.

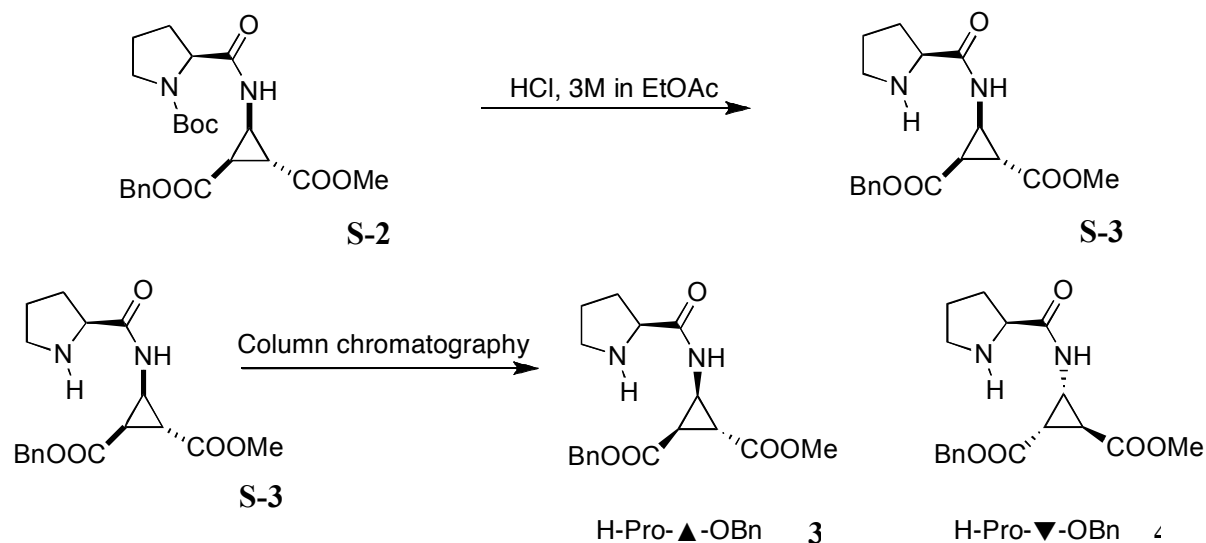
Representative procedure for catalysts preparation

Dipeptide preparation and separation of diastereomers:



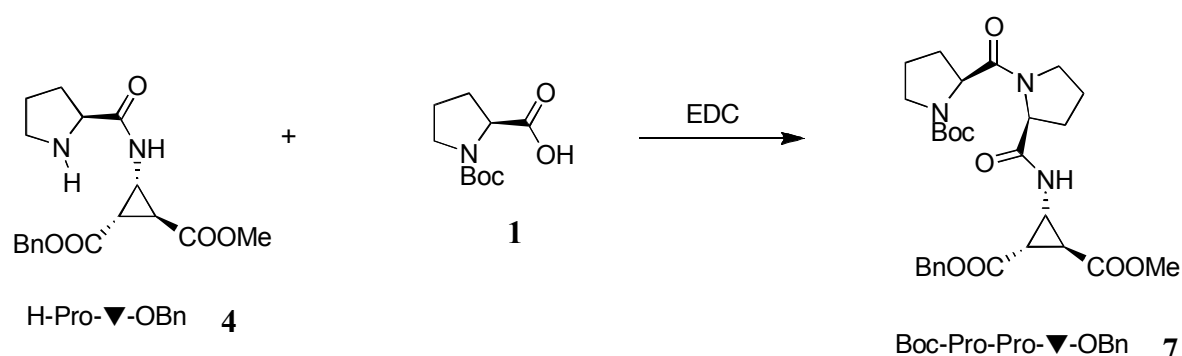
Racemic building block **S-1** (2.0 g, 5.7 mmol, 1.0 equiv.) was dissolved in a saturated solution of HCl in EtOAc (*c*≈3 mol/L), 20 mL, at 0°C. After stirring for 2 hours the acid was removed under reduced pressure, leaving a white/pinkish solid as a residue. To this deprotected building block **(±)-2** a solution of *N*-Boc-L-proline (**1**) (1.5 g, 7.1 mmol, 1.25 equiv.) and EDC·HCl (1.4 g, 7.1 mmol, 1.25 equiv.) in DCM (25 mL), which was stirred beforehand for 30 min, was added. Using a dropping funnel TEA (0.87 mL, 6.8 mmol, 1.2 equiv.) in DCM (20 mL) was added over a period of 1.5 h. The mixture was stirred overnight. Then the reaction was quenched with water (20 mL) and the solution acidified to pH 3 using KHSO₄ solution (1 M), then extracted with DCM. The organic phase was extracted successively with NaHCO₃ solution and brine, dried over Na₂SO₄, filtered and evaporated

under reduced pressure. Purification by chromatography on silica gel (1:1 hexanes/EtOAc) yielded 1.78 g (70%) of the mixture of diastereomers **S-2**.

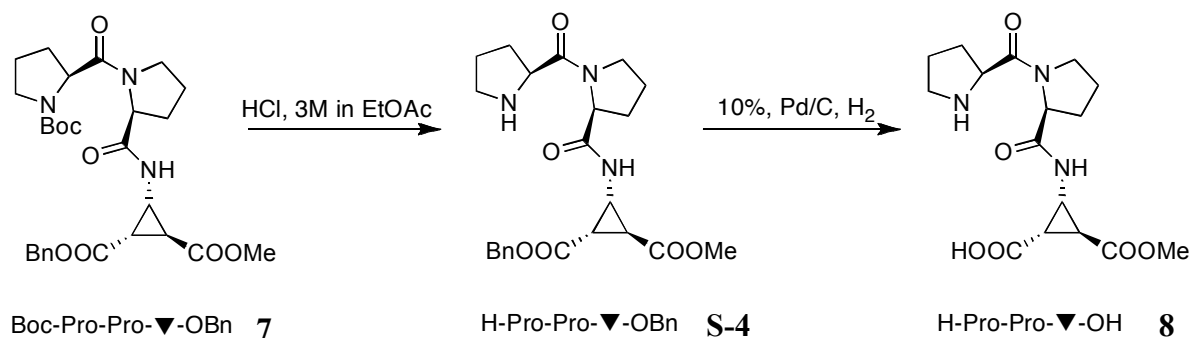


To the mixture of diastereomers **S-2** (2.0 g, 4.5 mmol) was added at 0°C a saturated solution of HCl in EtOAc (15 mL, $c \approx 3$ mol/L). After stirring for 1.5 hours the acid was removed under reduced pressure leaving a white wax as a residue. It was dissolved in water (20 mL) and extracted with Et₂O, the aqueous phase was then adjusted to basic pH using NaHCO₃ saturated solution and then extracted with DCM (3x20 mL). The organic phase was dried over Na₂SO₄, filtrated and evaporated under reduced pressure to yield **S-3** (1.52 g, 4.4 mmol, 98%). The two diastereomers **3** and **4** were separated using column chromatography (DCM/MeOH 15:1) to give pure **4** (570 mg, 38% $R_f=0.25$) and pure **3** (570 mg, 38%, $R_f=0.20$) along with the recovered mixture **S-3** (380 mg).

Synthesis of the tripeptide Pro-Pro-▼:

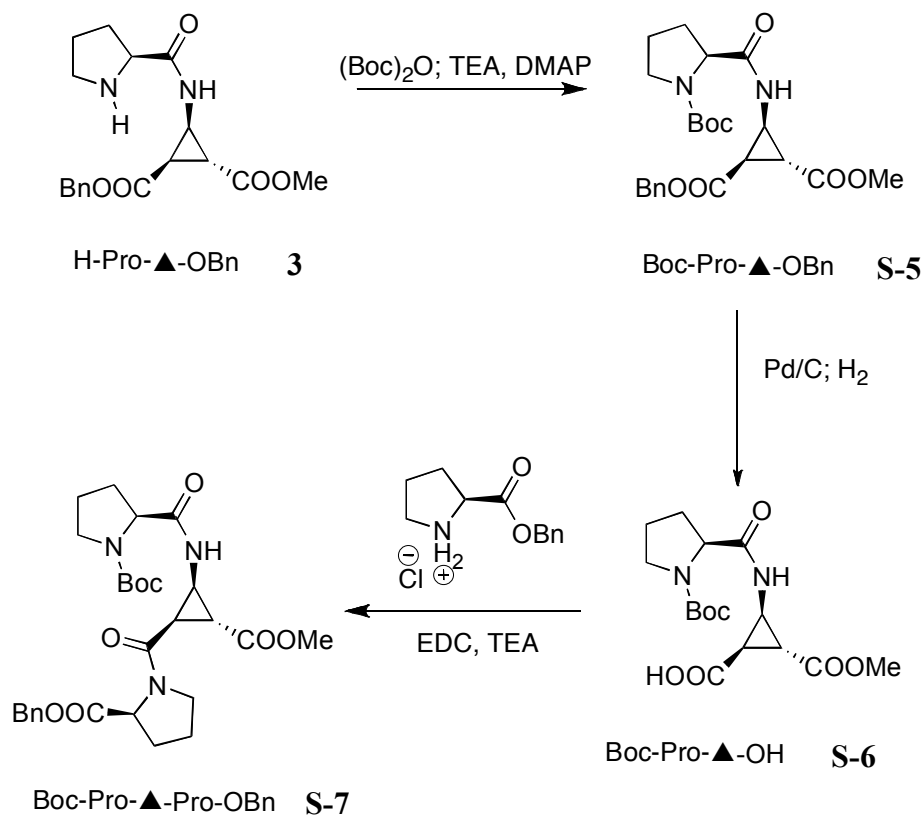


N-Boc-L-proline (300 mg, 1.4 mmol) was dissolved in DCM (10 mL) and EDC·HCl (295mg, 1.54 mmol, 1.1 equiv.) was added. After 30 min **4** (580 mg, 1.68 mmol, 1.2 equiv.) was added and the reaction was stirred overnight. Then DCM (10 mL) and water (10 mL) were added and the pH was adjusted to 4 by addition of small amounts of KHSO₄ solution (1M). The organic phase was extracted and then extracted successively with NaHCO₃ solution (sat.) (10 mL) and brine (10 mL). The organic phase was dried over Na₂SO₄, filtered and evaporated under reduced pressure to give **7** (495 mg, 0.91 mmol, 65%).



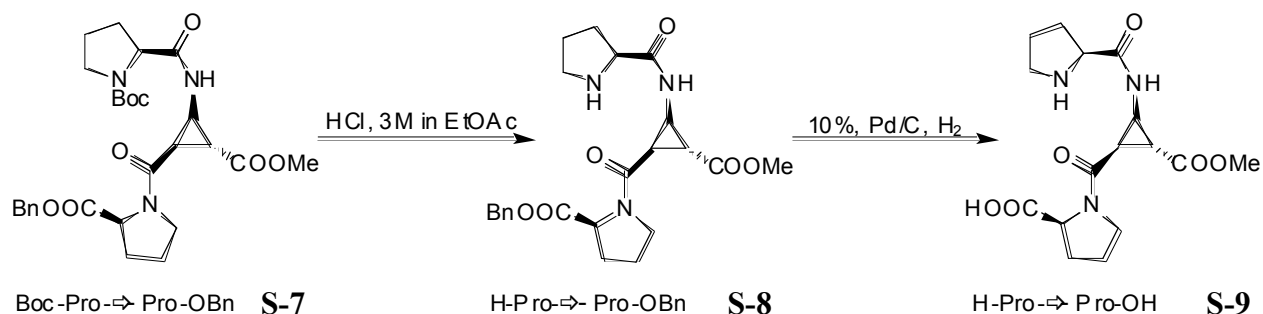
The preparation of **8** was completed by deprotection of the amino and carboxylic acid functionalities. Boc-group deprotection of **7** (495 mg, 0.91 mmol) to furnish product **S-4** (360 mg, 90%) was performed as reported for **S-3**. Debenzylation was carried out by dissolving **S-4** (200 mg, 0.45 mmol) in MeOH and adding Pd/C (10 m%, 20 mg). Stirring under H₂ atmosphere was continued for 1.5 hours. After this period the Pd/C residue was filtered through celite and the collected solvent was evaporated to provide **8** (160 mg, quantitative).

Synthesis of tripeptide Pro-▲-Pro:



3 (500 mg, 1.44 mmol) was dissolved in DCM (10 mL) and then Boc₂O (330 mg, 1.5 mmol, 1.5 equiv.) was added. A mixture of TEA (0.15 mL, 1.1 mmol, 1.1 equiv.) and DMAP (18 mg, 0.15 mmol, 0.15 equiv.) in DCM (10 mL) was then added dropwise into the mixture over a

period of 1 h, and stirring continued for 10 h. The reaction was quenched with water and KHSO₄ solution (1 M) was used to acidify the solution, which was then extracted with DCM. The combined organic phases were extracted with brine, dried over Na₂SO₄, evaporated under reduced pressure to give **S-5** (580 mg, 90%). The following debenzoylation was performed according to the procedure described above for the synthesis of **8** and proceeded in quantitative yield, affording 460 mg **S-6**. Dipeptide **S-6** (360 mg, 1.0 mmol) was then dissolved in DCM (15 mL) and EDC·HCl (200 mg, 1.05 mmol, 1.05 equiv.) and added to the solution. After stirring for 30 min NH(HCl)-Pro-OBn (290 mg, 1.2 mmol, 1.2 equiv.) followed by TEA (0.17 mL, 1.2 mmol, 1.2 equiv.) were added and the mixture was stirred for 24 h. DCM (10 mL) and water (10 mL) were added and the aqueous phase was adjusted to pH 4 using a KHSO₄ solution (1M). The organic phase was extracted and extracted with NaHCO₃ solution (sat.) (10 mL) and brine (10 mL). The organic phase was dried over Na₂SO₄, filtered and evaporated under reduced pressure to give compound **S-7** (380 mg, 70%).



Deprotection of **S-7** to furnish the final peptide catalyst has been carried out as described above for **7** and **S-4**, leading to **H-Pro- Δ -Pro-OH**, **S-9** (240 mg, quantitative).

General procedure for catalytic asymmetric aldol reaction

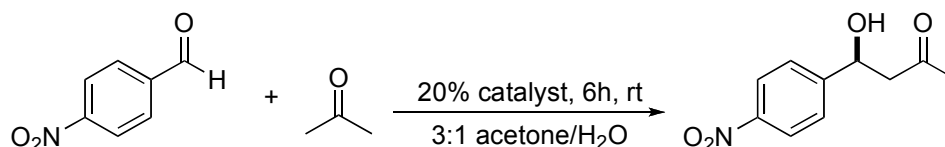
Intermolecular aldol reaction:

a) **Water free conditions:** 0.01 to 0.04 mmol (5 to 20% catalyst) of the selected catalyst were added to 0.2 mmol of aldehyde and dissolved under N₂ atmosphere in 2 mL of dry acetone or CHCl₃/acetone mixture in a 10 mL vial. The reaction was stirred for the time indicated, subsequently, the solvent was evaporated and 5 mL of EtOAc and 2 mL of water were added to the crude material. The organic phases were extracted again with 1 mL of water, dried (Na₂SO₄), concentrated and purified on silica (3:1 hexanes/EtOAc) to yield the desired aldol product.

Catalyst recovery: the combined water layers were extracted with Et₂O (2 mL) and frozen at –20°C. Lyophilization of the sample allowed the recovery of the catalyst (90-95%), which could be reused without any loss in performance.

b) **Homogeneous acetone/water mixture:** p-nitrobenzaldehyde (38 mg, 0.25 mmol) and catalyst (H-Pro- Δ -Pro-OH) (17.7 mg, 0.05 mmol) were dissolved in 0.75 mL of a 3:1 acetone/water (molar ratio 1:30:42 aldehyde/acetone/water), and the reaction mixture was stirred for 6 hours at room temperature. Acetone was evaporated under reduced pressure and EtOAc (5 mL) and water (2 mL) were added to the resulting suspension. The organic layers were separated, extracted with water (1 mL), dried (Na₂SO₄) and evaporated. The residue was purified on silica (3:1 hexanes/EtOAc) to yield **11a** (50 mg, 95% yield, 71% ee).

Catalyst recovery: the combined aqueous layers were extracted with Et₂O (2 mL) and frozen at –20°C. Lyophilization allowed recovery of the catalyst (90-95%), which could be reused without any loss in performance.



cycle	time	Yield	ee	catalyst recovery
1	6h	95%	71%	90%
2	6h	92%	71%	95%
3	6h	96%	71%	93%

Table S-1: catalytic cycles with fresh (1) and recovered (2,3) catalyst.

Reaction between aromatic aldehydes and cyclohexanone (homogeneous): in a 5 mL vial, 0.03 mmol of H-Pro-▲-Pro-OH were added to 0.15 mmol of aldehyde, followed by 20 µL of water and 0.4 mL of ketone; the reaction was left stirring for 24 h. After this period 3 mL of EtOAc and 1 mL of water were added to the crude material. The organic phases were extracted with 1 mL of water and dried (Na₂SO₄), evaporated and purified on silica (4:1 hexanes/EtOAc) to furnish the desired aldol product.

Catalyst recovery: the combined water layers were extracted with 2 mL Et₂O and frozen at –20°C. Lyophilization of the sample allowed the recovery of 90-95% of the catalyst.

Reaction between aromatic aldehydes and cyclohexanone (heterogeneous): in a 5 mL vial, 0.03 mmol of H-Pro-▲-Pro-OH were added to 0.15 mmol of aldehyde, followed by 40 µL of water and 0.4 mL of ketone; the reaction mixture was stirred for 48 h. After this period 3 mL of EtOAc and 1 mL of water were added to the crude material. The organic phases were extracted with 1 mL of water and dried (Na₂SO₄), evaporated and purified on silica (4:1 hexanes/EtOAc) to furnish the desired aldol product.

Catalyst recovery: the combined water layers were extracted with 2 mL Et₂O and frozen at –20°C. Lyophilization of the sample allowed the recovery of 90-95% of the catalyst.

Intramolecular aldol reaction:

0.03 mmol of the selected catalyst were added to 0.3 mmol of **13** in 1ml of CHCl₃. The reaction mixture was stirred at room temperature, the progress of the reaction was followed by GC. After 24 hours the solvent was evaporated under reduced pressure and the crude material was dissolved in 5 mL of EtOAc and extracted with 2 mL of water. The organic phases were dried (Na₂SO₄), evaporated and purified on silica (3:1 hexanes/EtOAc).

Experimental data

H-Pro-▲-OBn (3), $^1\text{H-NMR}$ (300 MHz; CDCl_3) δ : 8.42 (brs, 1H); 7.35 (m, 5H); 5.15 (q, 2H); 4.10 (m, 1H); 3.72 (m, 1H); 3.68 (s, 3H); 3.66 (m, 1H); 2.96 (m, 1H); 2.85 (m, 1H); 2.58 (m, 1H); 2.37 (m, 1H); 1.93 (m, 1H); 1.67 (m, 2H). ^{13}C (75.5 MHz, CDCl_3) δ : 26.3, 26.6, 28.6, 30.8, 36.2, 47.3, 52.5, 60.6, 67.4, 128.5, 128.6, 128.8, 135.4, 169.7, 170.2, 176.4; (ES-MS) for 346.15, $\text{C}_{18}\text{H}_{22}\text{N}_2\text{O}_5$, (MH^+) was found: 347.1; High resolution mass (EI-MS) for 346.1529, $\text{C}_{18}\text{H}_{22}\text{N}_2\text{O}_5$, 346.1528 was found ($\delta = 0.3$ ppm). FT-IR (film) ν_{max} : 3325.0, 2968.3, 2957.4, 1723.8, 1667.6, 1510.5, 1407.3, 1300.0, 1179.6; mp: 114°C.

H-Pro-▼-OBn (4), $^1\text{H-NMR}$ (300 MHz; CDCl_3) δ : 8.45 (d, 1H); 7.35 (m, 5H); 5.15 (q, 2H); 4.04 (m, 1H); 3.70 (m, 1H); 3.69 (m, 3H); 2.94 (m, 1H); 2.76 (m, 1H); 2.57 (m, 1H); 2.37 (m, 1H); 2.04 (m, 1H); 1.80 (m, 1H); 1.59 (m, 1H). ^{13}C (75.5 MHz, CDCl_3) δ : 176.3, 170.1, 169.4, 135.3, 128.6, 128.5, 128.3, 67.2, 60.5, 52.4, 47.2, 36.1, 30.7, 28.5, 26.7, 26.1. (ES-MS) for 346.15, $\text{C}_{18}\text{H}_{22}\text{N}_2\text{O}_5$, (MH^+) was found: 347.1; High resolution mass (EI-MS) for 346.1529, $\text{C}_{18}\text{H}_{22}\text{N}_2\text{O}_5$, 346.1529 was found. FT-IR (film) ν_{max} : 3322.0, 2975.3, 2955.5, 1723.4, 1673.5, 1508.4, 1451.4, 1309.9, 1177.1; oil

H-Pro-▲-OH, $^1\text{H-NMR}$ (300 MHz; CDCl_3) δ : 4.27 (m, 1H); 3.72 (s, 3H); 3.57 (dd, $J = 4.6$; 7.9 Hz, 1H); 3.35 (m, 2H); 2.42 (m, 1H); 2.35-2.00 (m, 5H). ^{13}C (75.5 MHz, CDCl_3) δ : 172.3, 172.2, 170.9, 61.2, 53.0, 47.4, 36.3, 31.0, 29.6, 28.1, 24.9. High resolution mass (EI-MS) for 256.1059, $\text{C}_{11}\text{H}_{16}\text{N}_2\text{O}_5$, 256.1054 was found ($\delta = 0.2$ ppm). FT-IR (solid) ν_{max} : 3439, 3207, 2955, 1678, 1639, 1543, 1146; mp: 130-132°C.

H-Pro-▼-OH, $^1\text{H-NMR}$ (300 MHz; CDCl_3) δ : 4.27 (m, 1H); 3.72 (s, 3H); 3.62 (dd, $J = 5.1$; 7.4 Hz, 1H); 3.35 (m, 2H); 2.38 (m, 1H); 2.27 (m, 2H); 2.05 (m, 3H). ^{13}C (75.5 MHz, CDCl_3) δ : 174.2, 172.0, 170.0, 61.0, 52.8, 47.2, 36.3, 30.8, 30.6, 28.5, 25.1. High resolution mass (EI-MS) for 256.1059, $\text{C}_{11}\text{H}_{16}\text{N}_2\text{O}_5$, 256.1053 was found ($\delta = 0.2$ ppm). FT-IR (solid) ν_{max} : 3379, 3241, 3059, 1732, 1686, 1447, 1167; mp: 132-134°C.

H-Pro-▲-Pro-OH (S-9), $^1\text{H-NMR}$ (300 MHz; CD_3OH) δ : 8.79-8.27 (bs, signal doubling because of rotamers, 1H); 4.24 (m, 2H); 3.93 (m, 1H); 3.78 (m, 1H); 3.73 (s, 3H); 3.48-3.65 (m, 2H); 3.38 (m, 1H); 2.50-2.69 (m, 2H); 2.28 (m, 1H); 2.20 (m, 1H); 1.97 (m, 3H); 1.90 (m, 3H). ^{13}C (75.5 MHz, CD_3OD) δ : (major conformer) 177.0, 172.3, 171.3, 166.6, 60.9, 53.0, 50.0, 48.8, 47.6, 36.3, 31.3, 30.9, 30.4, 26.7, 25.7, 25.0. (ES-MS) for 353.1, $\text{C}_{16}\text{H}_{23}\text{N}_3\text{O}_6$, (MH^+) was found: 354.1; High resolution mass (EI-MS) for 353.1587, $\text{C}_{16}\text{H}_{23}\text{N}_3\text{O}_6$, 353.1593 was found ($\delta = 1.7$ ppm). FT-IR (solid) ν_{max} : 2963.4, 1725.1, 1616.7, 1438.9, 1299.1, 1195.8, 1176.3; mp: 184-186°C.

H-Pro-▼-Pro-OH, $^1\text{H-NMR}$ (300 MHz; CD_3OD) δ : 4.58-4.32 (m, 1H); 4.18 (m, 1H); 3.90 (m, 1H); 3.71 (s, 3H); 3.55 (m, 1H); 3.34 (m, 3H); 2.71 (m, 1H); 2.51 (m, 1H); 2.38 (m, 1H); 2.18 (m, 1H); 2.02 (m, 6H). ^{13}C (75.5 MHz, CD_3Cl) δ : (major conformer) 172.5, 171.7, 170.6, 166.2, 61.1, 54.9, 52.9, 47.2, 36.0, 31.0, 30.8, 30.5, 26.5, 25.3, 25.1. (ES-MS) for 353.1, $\text{C}_{16}\text{H}_{23}\text{N}_3\text{O}_6$, (M-H^+) was found: 352.1; High resolution mass (EI-MS) for 353.1587, $\text{C}_{16}\text{H}_{23}\text{N}_3\text{O}_6$, 353.1581 was found ($\delta = 1.7$ ppm). FT-IR (solid) ν_{max} : 2977.5, 1723.1, 1668.7, 1615.6, 1438.1, 1409.2, 1293.5, 1196.4, 1169.4; mp: 169-171°C.

H-Pro-Pro-▲-OH, $^1\text{H-NMR}$ (300 MHz; CD_3OD) δ : 4.59 (m, 1H); 4.47 (m, 1H); 3.76 (s, 3H + m, 1H); 3.68 (m, 3H); 3.44 (m, 1H); 2.55 (m, 1H); 2.38 (m, 2H); 2.26 (m, 2H); 2.05 (m, 5H). ^{13}C (75.5 MHz, CD_3OD) δ : (major conformer) 175.1, 174.6, 172.8, 169.0, 79.6, 62.3, 52.9, 47.6, 46.3, 36.4, 30.7, 29.67, 28.6, 26.0, 25.3, 24.2; (ES-MS) for 353.1, $\text{C}_{16}\text{H}_{23}\text{N}_3\text{O}_6$,

(MH⁺) was found: 354.1; High resolution mass (EI-MS) for 353.1587, C₁₆H₂₃N₃O₆, 353.1583 was found (δ = 1.1 ppm). FT-IR (solid) ν_{max} : 2956.5, 1723.1, 1617.5, 1514.6, 1437.9, 1410.2, 1299.5, 1194.8, 1171.2; wax.

H-Pro-Pro- ∇ -OH (8), ¹H-NMR (300 MHz; CD₃OD) δ : 4.59-4.14 (m, signal doubling because of rotamers, 2H); 3.69 (s, 3H + m, 1H); 3.64 (m, 1H); 3.48 (m, 1H); 3.78 (m, 2H); 2.49 (m, 1H); 2.34 (m, 1H); 2.24 (m, 2H); 2.08 (m, 6H). ¹³C (75.5 MHz, CD₃OD) δ : (major conformer) 175.2, 174.3, 172.98, 169.2, 62.5, 60.6, 52.8, 47.5, 46.2, 36.2, 33.0, 30.4, 29.6, 29.0, 26.0, 25.3. (ES-MS) for 353.1, C₁₆H₂₃N₃O₆, (MH⁺) was found: 354.1; High resolution mass (EI-MS) for 353.1587, C₁₆H₂₃N₃O₆, 353.1584 was found (δ = 0.9 ppm). FT-IR (solid) ν_{max} : 2961.5, 1725.1, 1615.5, 1517.6, 1437.8, 1409.2, 1296.5, 1195.8, 1171.2, 1045.8; mp: 169-171°C.

H-Pro- \blacktriangle -Pro- ∇ -OH, ¹H-NMR (300 MHz; CD₃OD) δ : 4.20 (m, 2H); 3.77 (m, 1H); 3.73 (s, 3H); 3.71 (s, 3H); 3.48 (m, 2H); 3.32 (m, 2H); 2.73-2.55 (m, signal doubling because of rotamers, 2H); 2.47 (m, 1H); 2.37 (m, 1H); 2.25 (m, 1H); 2.04 (m, 3H); 1.92 (m, 4H). ¹³C (75.5 MHz, CD₃OD) δ : 175.7, 172.3, 172.1, 171.4, 171.0, 167.7, 62.2, 60.8, 53.1, 53.0, 48.9, 47.6, 36.6, 36.1, 31.2, 31.0, 30.8, 28.1, 26.7, 26.6, 25.4, 25.0. (ES-MS) for 494.2, C₂₂H₃₀N₄O₉, (MH⁺) was found: 495.2; High resolution mass (EI-MS) for 494.2013, C₂₂H₃₀N₄O₉, 494.2003 was found (δ = 2.0 ppm). FT-IR (solid) ν_{max} : 2988.5, 2976.5, 1734.1, 1687.1, 1669.4, 1616.4, 1612.5, 1423.6, 1412.5, 1294.6, 1200.5, 1198.2, 1167.5; mp: 230-232°C.

H-Pro- ∇ -Pro-Pro-OH, ¹H-NMR (300 MHz; CD₃OD) δ : 4.46-3.94 (m, signal doubling because of rotamers, 3H); 3.72 (s, 3H); 3.66 (m, 2H); 3.58 (m, 2H), 3.49 (m, 2H); 3.37 (m, 1H); 2.67 (m, 2H); 2.27 (m, 3H); 2.04 (m, 9H). ¹³C (75.5 MHz, CD₃OD) δ : 172.4, 172.1, 171.4, 168.7, 166.1, 71.4, 61.8, 53.0, 50.5, 47.4, 46.3, 36.0, 31.6, 31.3, 30.7, 30.3, 29.2, 28.8, 26.2, 25.2, 24.2. (ES-MS) for 450.2, C₂₂H₃₀N₄O₉, (MH⁺) was found: 451.2; High resolution mass (EI-MS) for 450.2114, C₂₁H₃₀N₄O₇, 450.2108 was found (δ = 1.3 ppm). FT-IR (film) ν_{max} : 2983.5, 2960.4, 1720.1, 1687.1, 1618.4, 1422.6, 1411.0, 1294.6, 1200.5, 1198.2, 1167.5; oil.

H-Pro- β -Ala-Pro-OH, ¹H-NMR (300 MHz; CD₃OD) δ : 4.35 (m, 1H); 4.20 (m, 1H); 3.62 (m, 1H); 3.53 (m, 3H); 3.34 (m, 2H); 2.66 (m, 1H); 2.49 (m, 1H); 2.38 (m, 1H); 2.24 (m, 1H); 2.02 (m, 5H); 1.88 (m, 1H). ¹³C (75.5 MHz, CD₃OD) δ : 177.4, 171.8, 169.8, 62.8, 61.2, 47.4, 36.7, 34.0, 32.8, 31.0, 30.7, 25.7, 25.2. (ES-MS) for 283.1, C₁₃H₂₁N₃O₄, (MH⁺) was found: 284.1; High resolution mass (EI-MS) for 283.1532, C₁₃H₂₁N₃O₄, 283.1531 was found (δ = 0.3 ppm). FT-IR (solid) ν_{max} : 2958.3, 2744.4, 1622.7, 1556.6, 1445.7, 1303.5, 1195.3, 1169.4; wax.

H-Pro- \blacktriangle -Asp-OH, ¹H-NMR (300 MHz; CD₃OD) δ : 4.58 (m, 1H); 4.20 (m, 1H); 3.73 (s, 3H); 3.48 (m, 1H); 3.35 (m, 2H); 2.84 (m, 1H); 2.67 (m, 2H); 2.45 (m, 1H); 2.36 (m, 1H); 2.02 (m, 3H). ¹³C (75.5 MHz, CD₃OD) δ : 176.2, 175.6, 171.2, 170.6, 170.1, 61.0, 52.7, 52.0, 47.4, 38.5, 35.9, 31.1, 29.5, 28.3, 24.9. (ES-MS) for 371.2, C₁₅H₂₁N₃O₈, (MH⁺) was found: 372.3; High resolution mass (PI-LSIMS) for 372.1408, C₁₅H₂₁N₃O₈, 372.1413 was found (δ = 1.3 ppm). FT-IR (solid) ν_{max} : 2965.3, 2856.3, 1643.4, 1622.0, 1444.5, 1195.3. mp: decomposition at 240-245°C.

H-Pro- ∇ -Asp-OH, ¹H-NMR (300 MHz; CD₃OD) δ : 4.62 (m, 1H); 3.85 (m, 1H); 3.77 (s, 3H); 3.67-3.42 (m, 2H); 3.04 (m, 1H); 2.82 (m, 1H); 2.70 (m, 1H); 2.63-2.38 (m, 3H); 2.08 (m, 3H). ¹³C (75.5 MHz, D₂O) δ : 174.6, 174.4, 173.3, 170.6, 59.8, 52.8, 51.2, 46.4, 34.7, 34.5, 30.7, 29.5, 29.0, 27.1, 23.7. (ES-MS) for 371.2, C₁₅H₂₁N₃O₈, (MH⁺) was found: 372.3; High

resolution mass (PI-LSIMS) for 372.1408, $C_{15}H_{21}N_3O_8$, 372.1412 was found ($\delta = 1.1$ ppm). FT-IR (solid) ν_{\max} : 2967.3, 2864.3, 1648.3, 1580.4, 1442.5, 1190.8. mp: decomposition at 240-245°C.

H-Pro- Δ -Glu-OH, 1H -NMR (300 MHz; CD_3OD) δ : 4.41 (m, 1H); 4.20 (m, 1H); 3.71 (s, 3H); 3.52-3.71 (m, 3H); 2.52 (m, 2H); 2.40 (m, 2H); 2.15 (m, 1H); 2.02 (m, 5H). ^{13}C (75.5 MHz, D_2O) δ : 178.3, 174.1, 173.0, 170.6, 59.8, 54.2, 52.3, 46.4, 34.8, 31.1, 30.1, 29.5, 27.1, 26.0, 23.7. (ES-MS) for 385.2, $C_{16}H_{23}N_3O_8$, (MH^+) was found: 386.0; High resolution mass (PI-LSIMS) for 386.1563, $C_{16}H_{23}N_3O_8$, 386.1567 was found ($\delta = 1.0$ ppm). FT-IR (solid) ν_{\max} : 2965.3, 2856.3, 1643.4, 1622.0, 1444.5, 1195.3. decomposition at 245-250°C.

4-Hydroxy-4-(4'-nitrophenyl)-butan-2-one (11a), $[\alpha]_D^{20} = -51.4$ ($c = 0.5$, $CHCl_3$) for (*S*)-enantiomer, 88% *ee*. 1H -NMR (300 MHz; $CDCl_3$) δ : 8.15 (d, $J = 6.8$ Hz, 2H); 7.46 (d, $J = 6.8$ Hz, 2H); 5.18 (m, 1H); 3.65 (d, $J = 3.2$ Hz, 1H); 2.89 (m, 2H); 2.18 (s, 3H). ^{13}C (75.5 MHz, $CDCl_3$) δ : 208.6, 150.2, 147.4, 129.1, 126.7, 124.5, 123.9, 69.2, 51.9, 31.2. Enantiomeric excess determined by chiral GC as reported in the general information, at 165°C, t_R is 13.65 min for (*S*)-enantiomer, 14.04 min for (*R*)-enantiomer.

4-Hydroxy-4-phenyl-butan-2-one (11b), $[\alpha]_D^{20} = -51.3$ ($c = 1.0$, $CHCl_3$) for (*S*)-enantiomer, 79% *ee*. 1H -NMR (300 MHz; $CDCl_3$) δ : 7.27-7.38 (m, 5H); 5.15 (m, 1H); 3.32 (d, $J = 3.0$ Hz, 1H); 2.87 (m, 2H); 2.21 (s, 3H). ^{13}C (75.5 MHz, $CDCl_3$) δ : 209.2, 142.7, 128.6, 127.7, 125.7, 69.9, 52.0, 30.8. Enantiomeric excess determined by chiral GC as reported in the general information, at 120°C, t_R is 9.77 min for (*S*)-enantiomer, 10.12 min for (*R*)-enantiomer.

4-Hydroxy-4-(2'-chlorophenyl)-butan-2-one (11c), $[\alpha]_D^{20} = -101.3$ ($c = 1.2$, $CHCl_3$) for (*S*)-enantiomer, 80% *ee*. 1H -NMR (300 MHz; $CDCl_3$) δ : 7.61 (m, 1H); 7.44-7.18 (m, 3H); 5.50 (m, 1H); 3.61 (brs, 1H); 3.01-2.63 (m, 2H); 2.22 (s, 3H). ^{13}C (75.5 MHz, $CDCl_3$) δ : 209.3, 140.1, 131.1, 129.3, 128.6, 127.3, 127.1, 66.6, 50.0, 30.6. Enantiomeric excess determined by chiral GC as reported in the general information, at 120°C, t_R is 17.86 min for (*S*)-enantiomer, 18.38 min for (*R*)-enantiomer.

4-Hydroxy-4-(4'-chlorophenyl)-butan-2-one (11d), $[\alpha]_D^{22} = -67.8$ ($c = 1.0$, $CHCl_3$), for (*S*)-enantiomer, 84% *ee*. 1H -NMR (300 MHz; $CDCl_3$) δ : 7.27-7.21 (m, 4H); 5.08 (m, 1H); 3.31 (brd, 1H); 2.78 (m, 2H); 2.15 (s, 3H). ^{13}C (75.5 MHz, $CDCl_3$) δ : 219.0, 141.2, 133.4, 128.7, 127.0, 69.2, 51.8, 30.8. Enantiomeric excess determined by chiral GC as reported in the general information, at 140°C, t_R is 10.80 min for (*S*)-enantiomer, 11.15 min for (*R*)-enantiomer.

4-Hydroxy-4-(2'-bromophenyl)-butan-2-one (11e), $[\alpha]_D^{22} = -77.8$ ($c = 1.5$, $CHCl_3$), for (*S*)-enantiomer, 82% *ee*. 1H -NMR (300 MHz; $CDCl_3$) δ : 7.61-7.41 (m, 4H); 5.44 (m, 1H); 3.56 (brs, 1H); 2.99 (m, 1H); 2.65 (m, 1H); 2.22 (s, 3H). ^{13}C (75.5 MHz, $CDCl_3$) δ : 204.2, 141.6, 137.6, 129.0, 127.9, 127.3, 121.2, 68.8, 50.1, 30.6. Enantiomeric excess determined by chiral GC as reported in the general information, at 130°C, t_R is 16.64 min for (*S*)-enantiomer, 17.12 min for (*R*)-enantiomer.

4-Hydroxy-4-(2'-nitrophenyl)-butan-2-one (11f), $[\alpha]_D^{20} = +91.2$ ($c = 1.0$, $CHCl_3$) for (*R*)-enantiomer, 91% *ee*. 1H -NMR (300 MHz; $CDCl_3$) δ : 7.93 (m, 2H); 7.67 (m, 1H); 7.44 (m, 1H); 5.68 (dd, $J = 1.8$; $J = 9.7$, 1H); 3.73 (brs, 1H); 3.18 (d, $J = 1.8$, 1H); 2.72 (m, 1H); 2.24 (s, 3H). ^{13}C (75.5 MHz, $CDCl_3$) δ : 208.9, 147.1, 138.4, 133.9, 128.3, 128.2, 124.5, 65.6, 51.1, 30.5. Enantiomeric excess determined by chiral GC as reported in the general information, at 160°C, t_R is 8.15 min for (*S*)-enantiomer, 10.55 min for (*R*)-enantiomer.

4-Hydroxy-4-(cyclohexyl)-butan-2-one (11g), $[\alpha]^{22}_{\text{D}} = -35.3$ ($c = 2.0$, CHCl_3), for (*S*)-enantiomer 82% *ee*. $^1\text{H-NMR}$ (300 MHz; CDCl_3) δ : 3.82 (m, 1H); 2.89 (brs, 1H); 2.53 (m, 2H); 2.18 (s, 3H); 1.75-1.60 (m, 5H); 1.25-0.95 (m, 6H). ^{13}C (75.5 MHz, CDCl_3) δ : 210.7, 71.9, 47.5, 42.8, 30.7, 29.0, 28.1, 26.4, 26.2, 25.9. Enantiomeric excess determined by chiral GC as reported in the general information, at 100°C, t_{R} is 32.31 min for (*S*)-enantiomer, 33.11 min for (*R*)-enantiomer.

2-(Hydroxy(4-nitrophenyl)methyl)cyclohexanone (13a), $[\alpha]^{22}_{\text{D}} = +11.8$ ($c = 1.0$, CHCl_3), for *anti/syn* = 6:1 and 95% *ee* (*anti*). $^1\text{H-NMR}$ (300 MHz; CDCl_3) δ (*anti*): 8.12 (d, $J = 8.7$ Hz, 2H); 7.34 (d, $J = 8.7$ Hz, 2H); 4.82 (d, 1H); 4.05 (brs, 1H); 2.53 (m, 1H); 2.38 (m, 2H); 2.01 (m, 1H); 1.68-1.23 (m, 5H). ^{13}C (75.5 MHz, CDCl_3) δ : 214.7, 148.5, 147.5, 127.9, 123.5, 73.9, 57.2, 42.7, 30.7, 27.6, 24.7. Diastereomeric ratio and enantiomeric excess determined by chiral GC as reported in the general information, at 170°C, t_{R} is 39.84 and 40.61 min (major) for the *anti* diastereomer, 44.59 and 46.10 for the *syn* diastereomer.

2-(Hydroxy(4-chlorophenyl)methyl)cyclohexanone (13b), $[\alpha]^{22}_{\text{D}} = +20.4$ ($c = 1.0$, CHCl_3), for *anti/syn* = 9:1 and 91% *ee* (*anti*). $^1\text{H-NMR}$ (300 MHz; CDCl_3) δ (*anti*): 7.30 (d, $J = 8.4$ Hz, 2H); 7.27 (d, $J = 8.4$ Hz, 2H); 4.76 (d, 1H); 3.97 (brs, 1H); 2.60-2.44 (m, 2H); 2.35 (m, 1H); 2.10 (m, 1H); 1.82-1.45 (m, 4H); 1.29 (m, 1H). ^{13}C (75.5 MHz, CDCl_3) δ : 215.3, 139.5, 133.6, 128.6, 128.4, 74.2, 57.4, 42.7, 30.7, 27.7, 24.7. Diastereomeric ratio and enantiomeric excess determined by chiral GC as reported in the general information, at 145°C, t_{R} is 36.71 and 37.47 min (major) for the *anti* diastereomer, 39.78 and 41.89 for the *syn* diastereomer.

2-(Hydroxy(2-bromophenyl)methyl)cyclohexanone (13c), $[\alpha]^{22}_{\text{D}} = +14.0$ ($c = 2.5$, CHCl_3), for *anti/syn* = 90:1 and 95% *ee* (*anti*). $^1\text{H-NMR}$ (300 MHz; CDCl_3) δ (*anti*): 7.50 (m, 2H); 7.34 (m, 1H); 7.13 (m, 1H); 5.30 (m, $J = 7.7$, 1H); 3.85 (brs, 1H); 2.76 (m, 1H); 2.44 (m, 2H); 2.08 (m, 1H); 1.88-1.46 (m, 5H). ^{13}C (75.5 MHz, CDCl_3) δ : 215.3, 140.8, 132.5, 129.1, 128.8, 127.9, 123.4, 72.9, 57.7, 42.8, 30.6, 27.8, 25.0. Diastereomeric ratio and enantiomeric excess determined by chiral GC as reported in the general information, at 160°C, t_{R} is 18.36 and 20.24 min (major) for the *anti* diastereomer, 23.89 and 25.69 for the *syn* diastereomer.

2-(Hydroxy(2-chlorophenyl)methyl)cyclohexanone (13d), $[\alpha]^{22}_{\text{D}} = +19.4$ ($c = 2.7$, CHCl_3), for *anti/syn* = 70:1 and 98% *ee* (*anti*). $^1\text{H-NMR}$ (300 MHz; CDCl_3) δ (*anti*): 7.53 (m, 1H); 7.29 (m, 2H); 7.19 (m, 1H); 5.33 (dd, $J = 3.7$; $J = 8.2$, 1H); 4.05 (d, $J = 3.7$, 1H); 2.66 (m, 1H); 2.44 (m, 1H); 2.32 (m, 1H); 2.07 (m, 1H); 1.84-1.50 (m, 5H). ^{13}C (75.5 MHz, CDCl_3) δ : 215.2, 139.1, 132.9, 129.2, 128.8, 128.3, 127.3, 70.4, 57.6, 42.7, 30.4, 27.8, 24.9. Diastereomeric ratio and enantiomeric excess determined by chiral GC as reported in the general information, at 160°C, t_{R} is 13.57 and 14.98 min (major) for the *anti* diastereomer, 17.29 and 18.77 for the *syn* diastereomer.

2-(Hydroxy(4-nitrophenyl)methyl)cyclopentanone (13e), $^1\text{H-NMR}$ (300 MHz; CDCl_3) δ : 8.18 (d, $J = 8.7$ Hz, 2H); 7.51 (d, $J = 8.7$ Hz, 2H); 5.41 (d, 0.67H, *syn*); 4.83 (d, 0.34H, *anti*); 4.78 (brs, 0.34H, *anti*); 2.74 (brs, 0.67H, *syn*); 2.50-1.67 (m, 7H). ^{13}C (75.5 MHz, CDCl_3) δ (*syn*): 219.6, 150.2, 127.3, 126.4, 123.7, 70.5, 56.2, 39.0, 22.4, 20.4. Diastereomeric ratio and enantiomeric excess determined by chiral GC as reported in the general information, at 165°C, t_{R} is 31.42 and 32.33 min (major) for the *syn* diastereomer, 36.33 and 39.16 min (major) for the *anti* diastereomer.

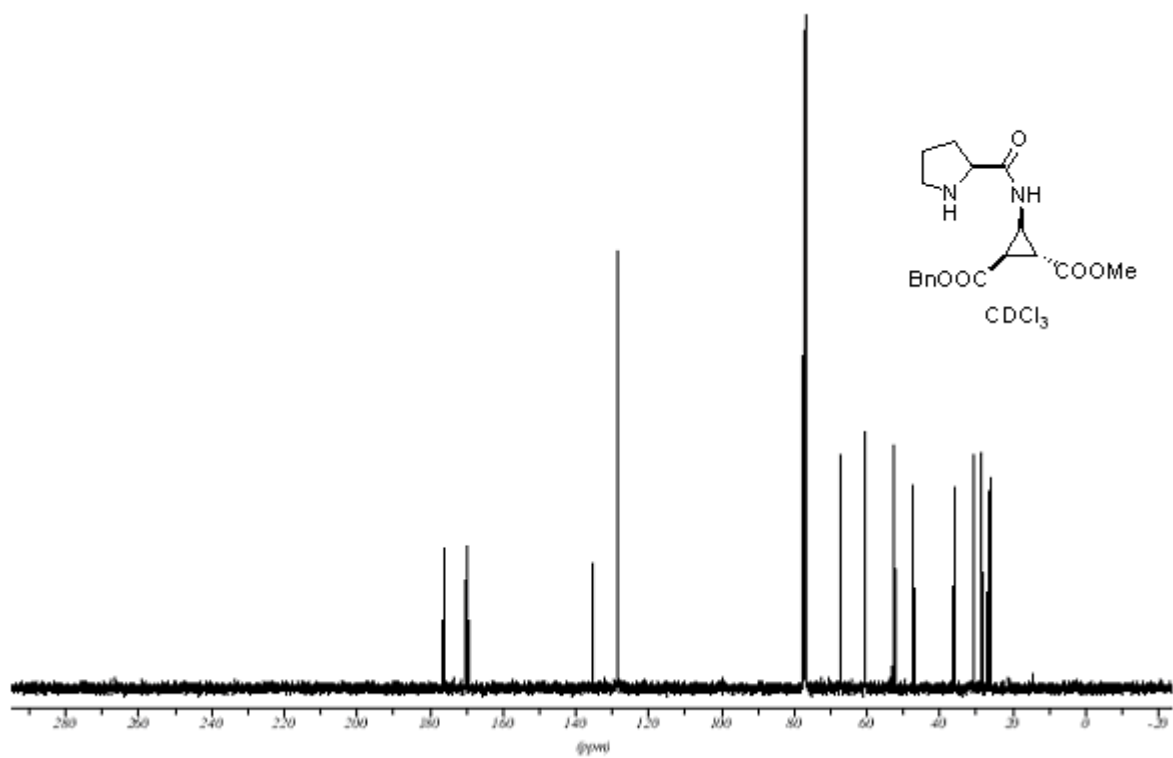
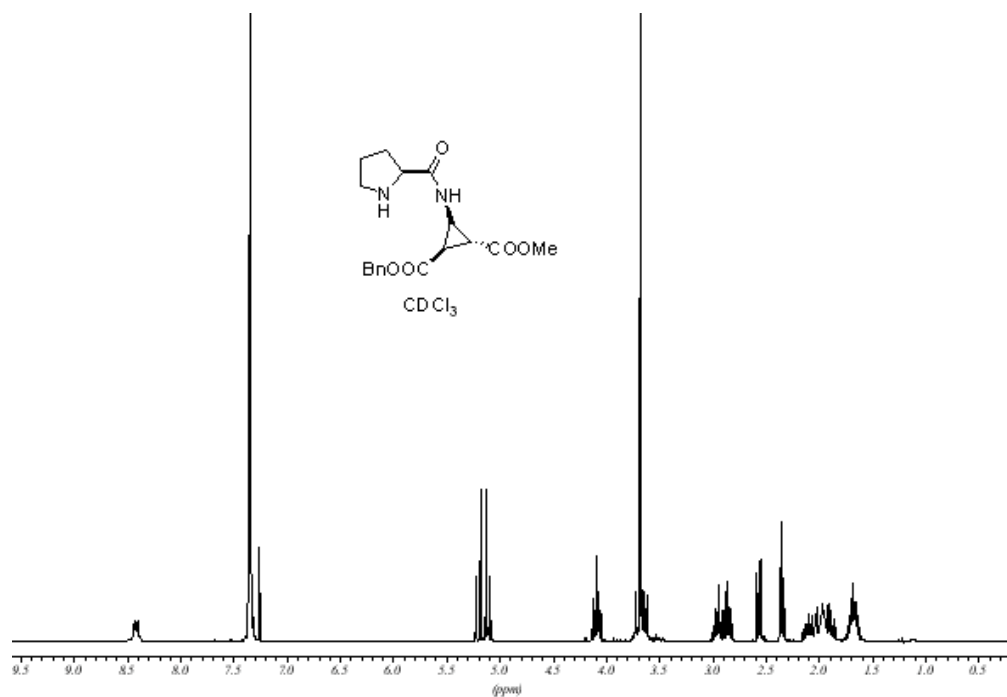
3-(Hydroxy(4-nitrophenyl)methyl)-tetrahydropyran-4-one (13f), $[\alpha]^{22}_{\text{D}} = +39.0$ ($c = 2.2$, CHCl_3), for *anti/syn* = 1:2 and 87% *ee* (*syn*). $^1\text{H-NMR}$ (300 MHz; CDCl_3) δ : 8.22 (d, $J = 8.9$,

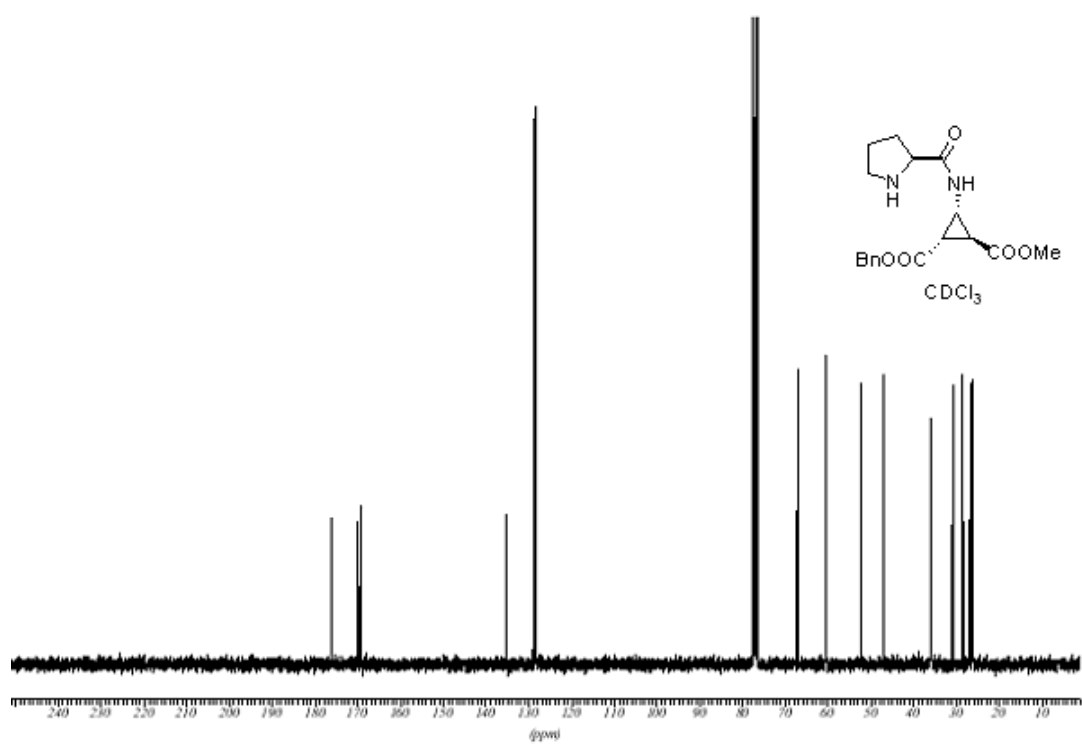
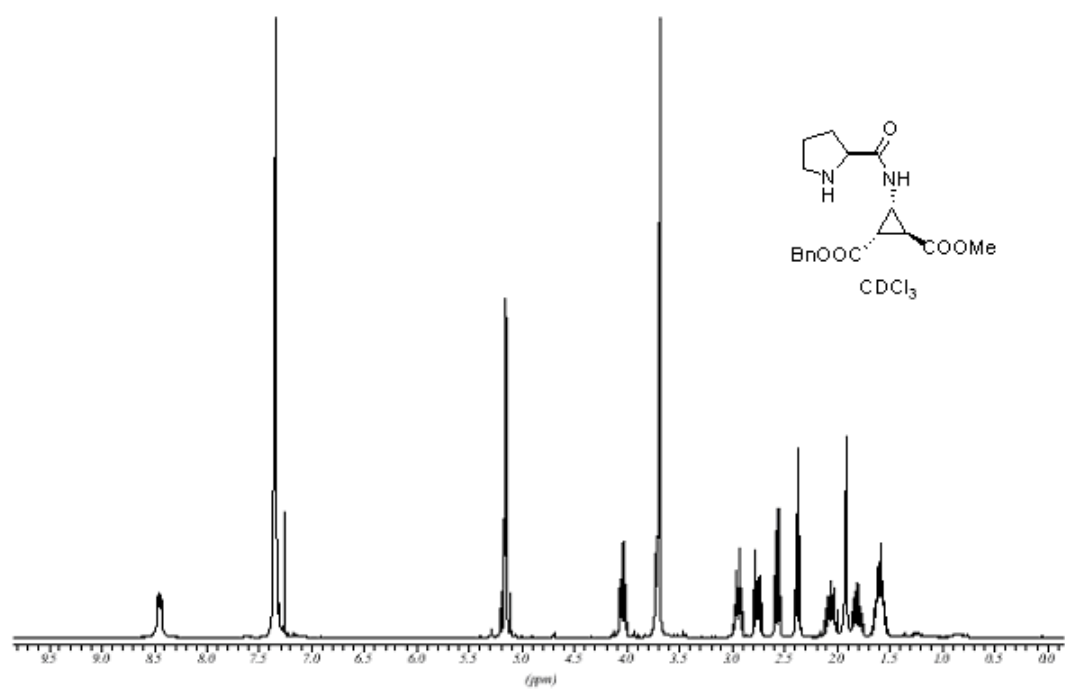
2H); 7.51 (d, $J = 8.9$, 2H); 5.54 (s, 0.61H, *syn*); 4.98 (d, 0.39H, *anti*); 4.23 (m, 1H); 3.77 (m, 3H); 3.46 (m, 0.39H, *anti*); 2.97-2.85 (m, 1H + m, 0.61H, *syn*); 2.71 (m, 1H); 2.50 (m, 1H). ^{13}C (75.5 MHz, CDCl_3) δ (*syn*): 207.3, 147.0, 126.4, 125.3, 122.7, 67.9, 67.3, 66.5, 56.2, 42.1. ^{13}C (75.5 MHz, CDCl_3) δ (*anti*): 208.3, 146.3, 126.4, 125.3, 122.9, 70.3, 68.8, 67.3, 56.6, 41.9. Diastereomeric ratio and enantiomeric excess determined by chiral GC as reported in the general information, at 180°C, t_R is 26.18 and 26.57 min (major) for the *anti* diastereomer, 29.53 and 30.94 min (major) for the *syn* diastereomer.

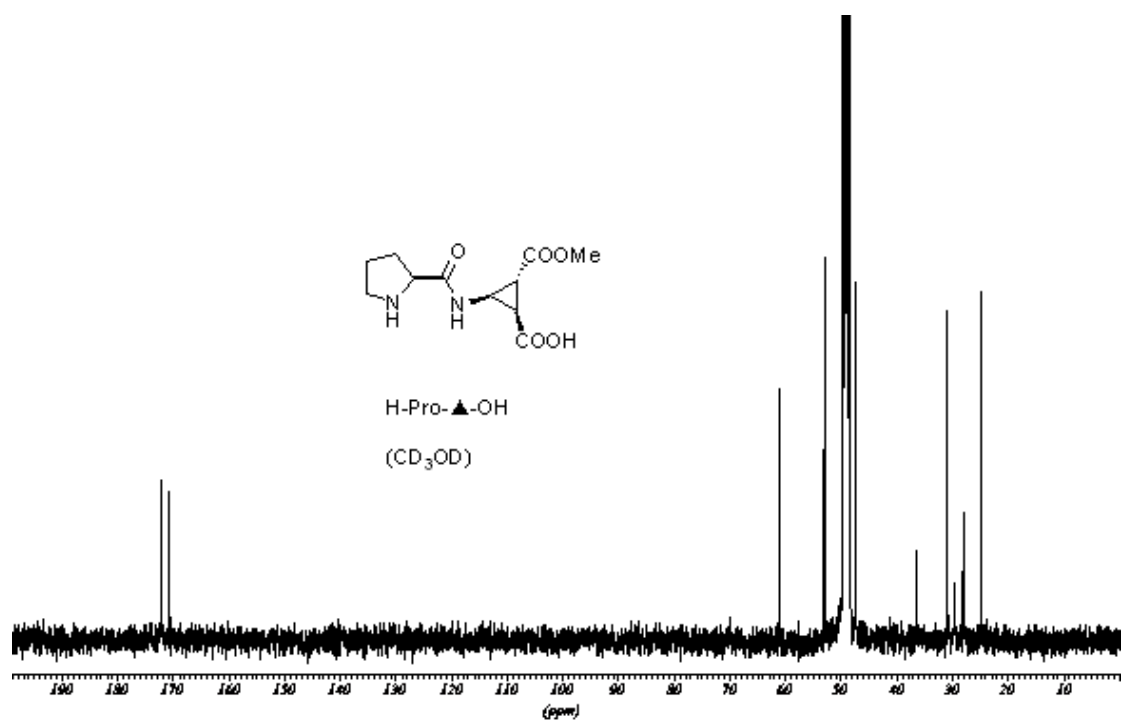
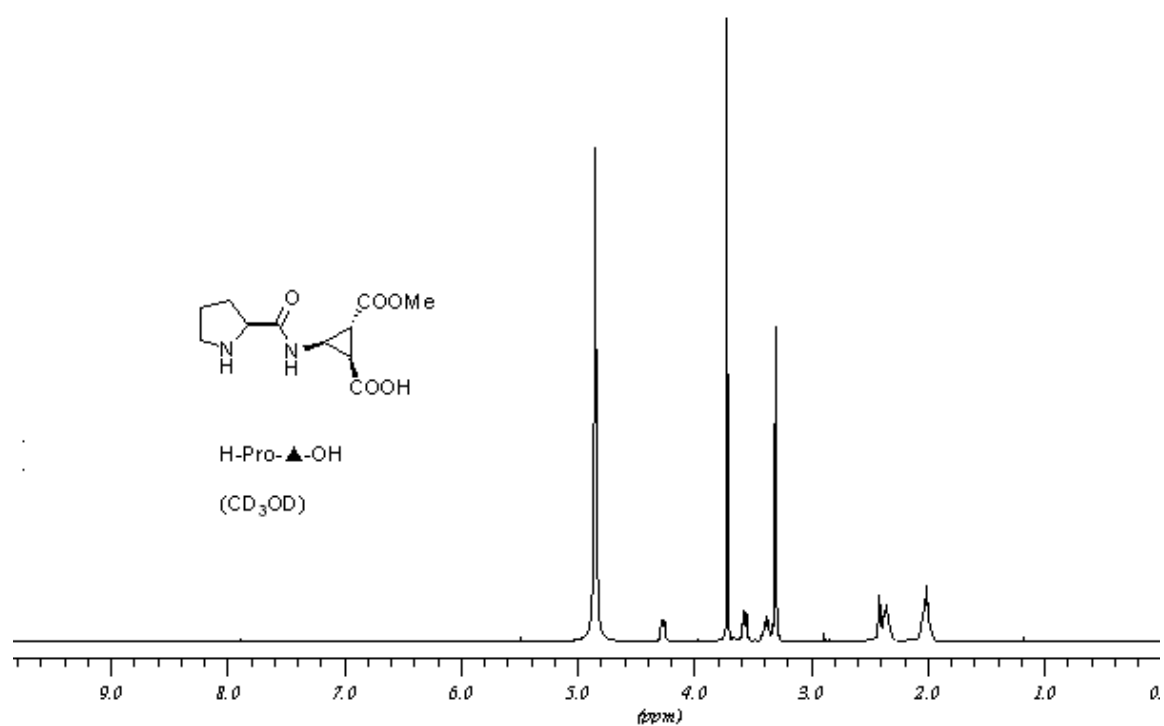
1H-Indene-1,5-(6H)-dione-2,3,7,7a-tetrahydro-7a-methyl (15a), $[\alpha]_D^{22} = +244$ ($c = 0.5$, CHCl_3), for (*S*)-enantiomer (83%) *ee*. $^1\text{H-NMR}$ (300 MHz; CDCl_3) δ : 5.96 (s, 1H); 2.95 (m, 1H); 2.77 (m, 2H); 2.58-2.36 (m, 3H); 2.09 (m, 1H); 1.83 (m, 1H); 1.31 (s, 3H). ^{13}C (75.5 MHz, CDCl_3) δ : 216.5, 198.2, 169.7, 123.9, 48.7, 35.9, 32.9, 29.2, 26.8, 20.6. Enantiomeric excess determined by chiral GC, at 155°C, t_R is 5.8 min for (*R*)-enantiomer, 6.2 min for (*S*)-enantiomer and 3.8 min for the starting material.

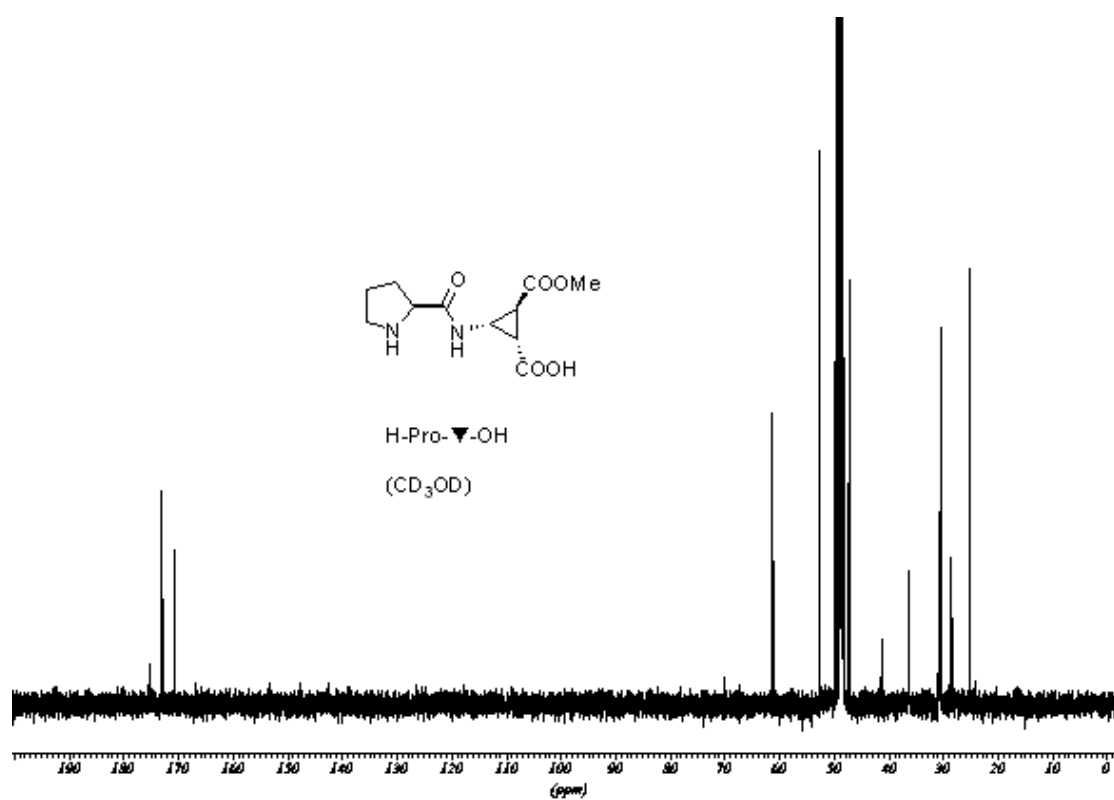
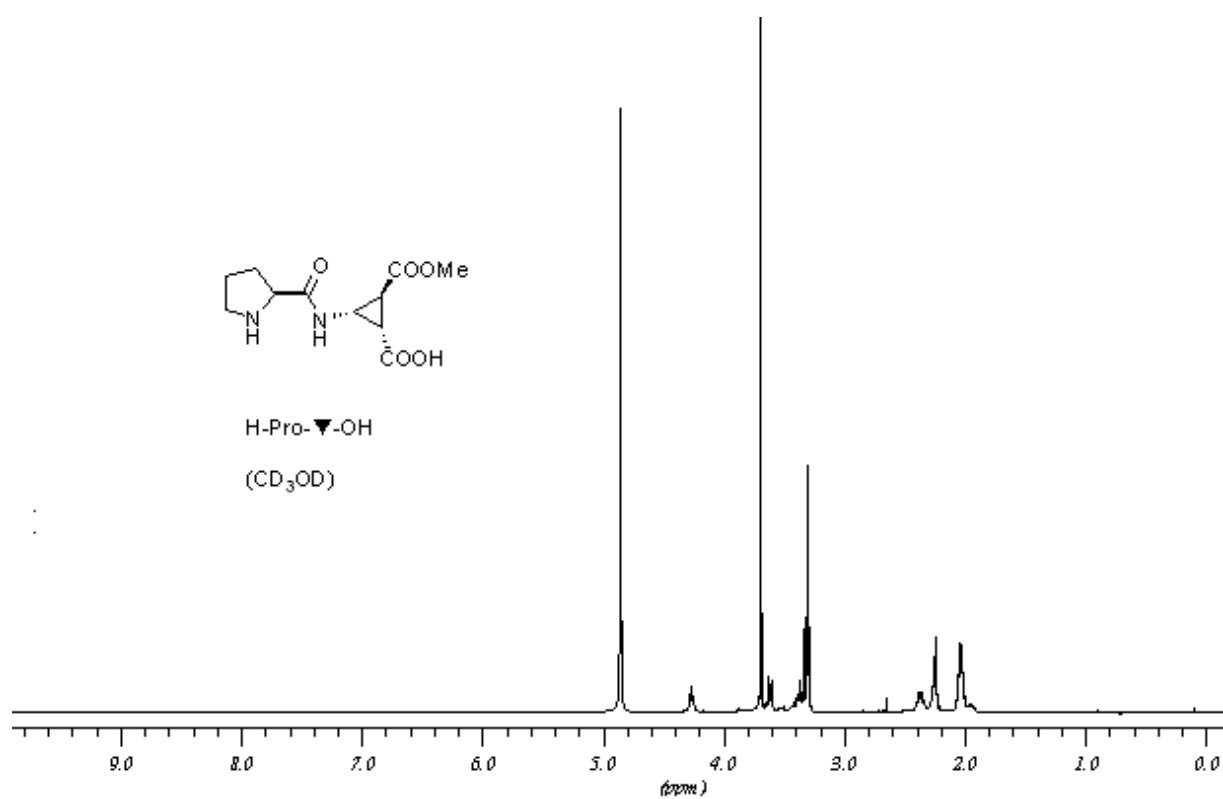
1,6-(2H,7H)-Naphthalenedione-3,4,8,8a-tetrahydro-8a-methyl (15b), $[\alpha]_D^{22} = +107.5$ ($c = 2.0$, CHCl_3), for (*S*)-enantiomer (92%) *ee*. $^1\text{H-NMR}$ (300 MHz; CDCl_3) δ : 5.85 (s, 1H); 2.75-2.63 (m, 2H); 2.51-2.38 (m, 4H); 2.18-2.08 (m, 3H); 1.75-1.64 (m, 1H); 1.44 (s, 3H). ^{13}C (75.5 MHz, CDCl_3) δ : 210.2, 198.0, 165.7, 125.8, 50.5, 37.4, 33.7, 31.8, 29.7, 23.4, 21.0. Enantiomeric excess determined by chiral GC, at 140°C, t_R is 21.5 min for (*R*)-enantiomer, 22.5 min for (*S*)-enantiomer and 11.2 min for the starting material.

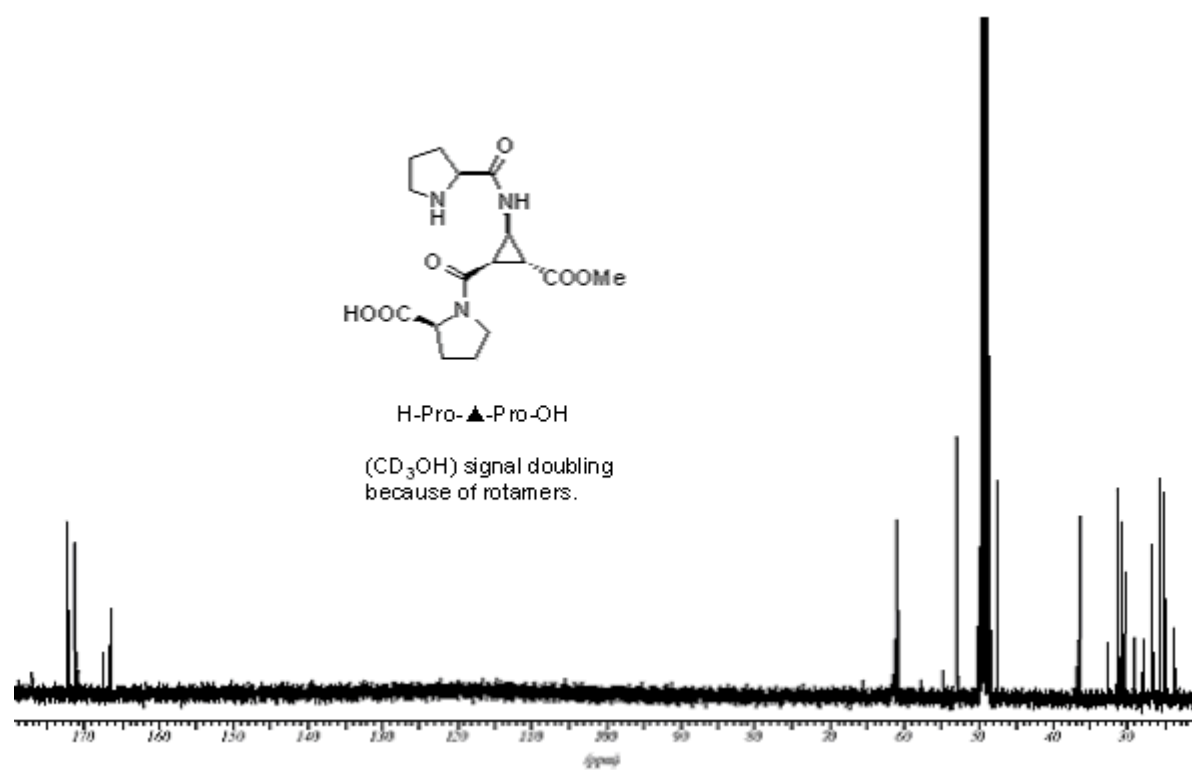
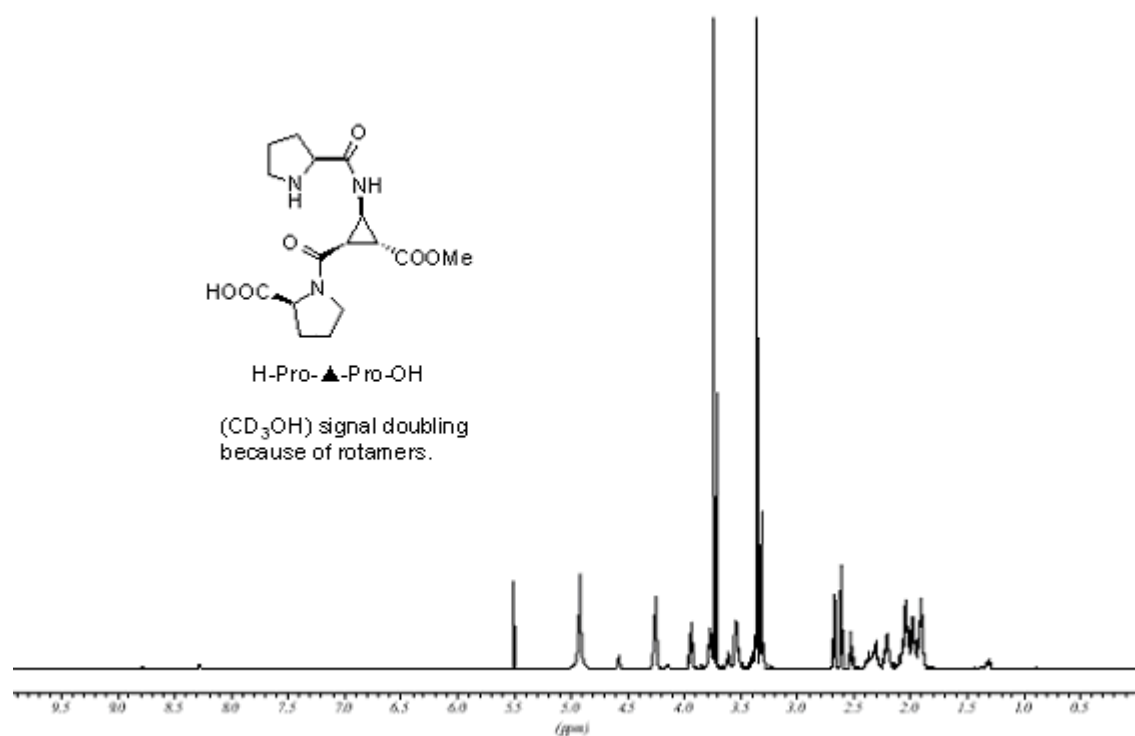
Copies of ^1H and ^{13}C spectra

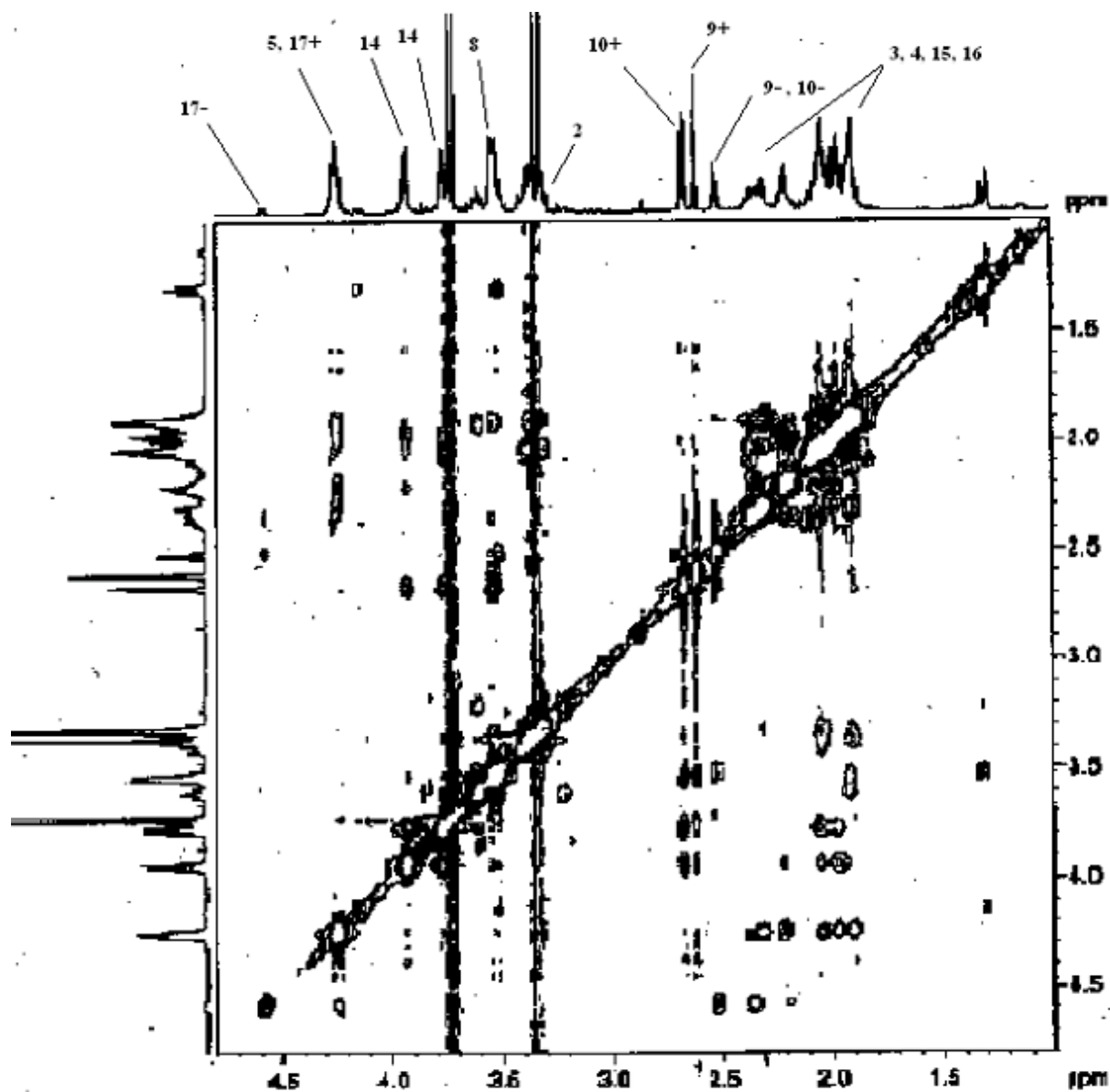
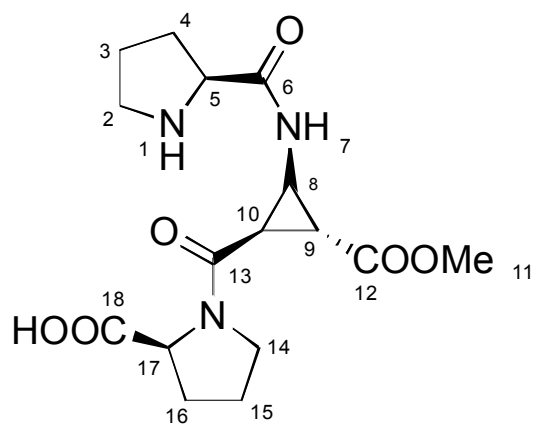




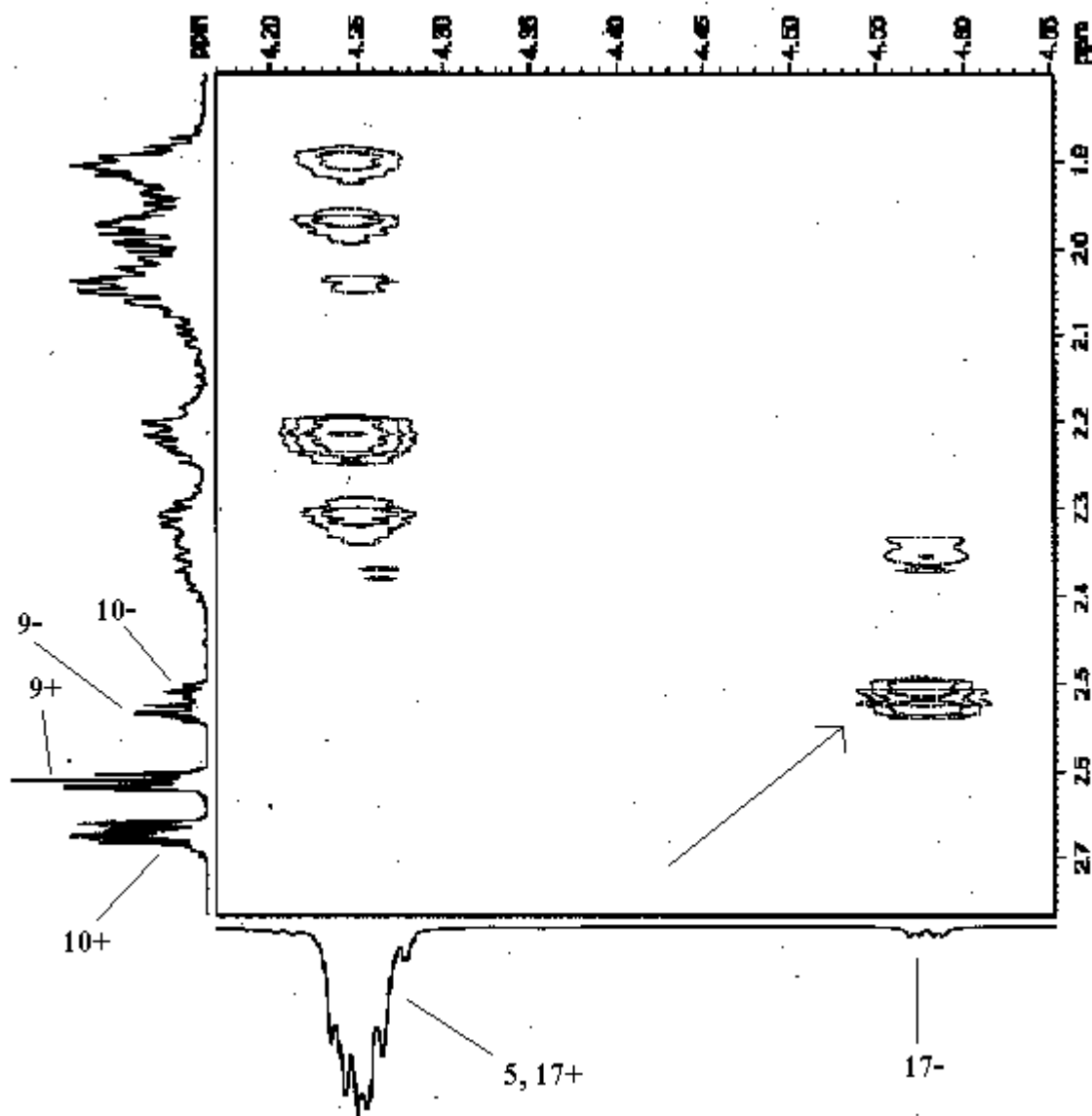




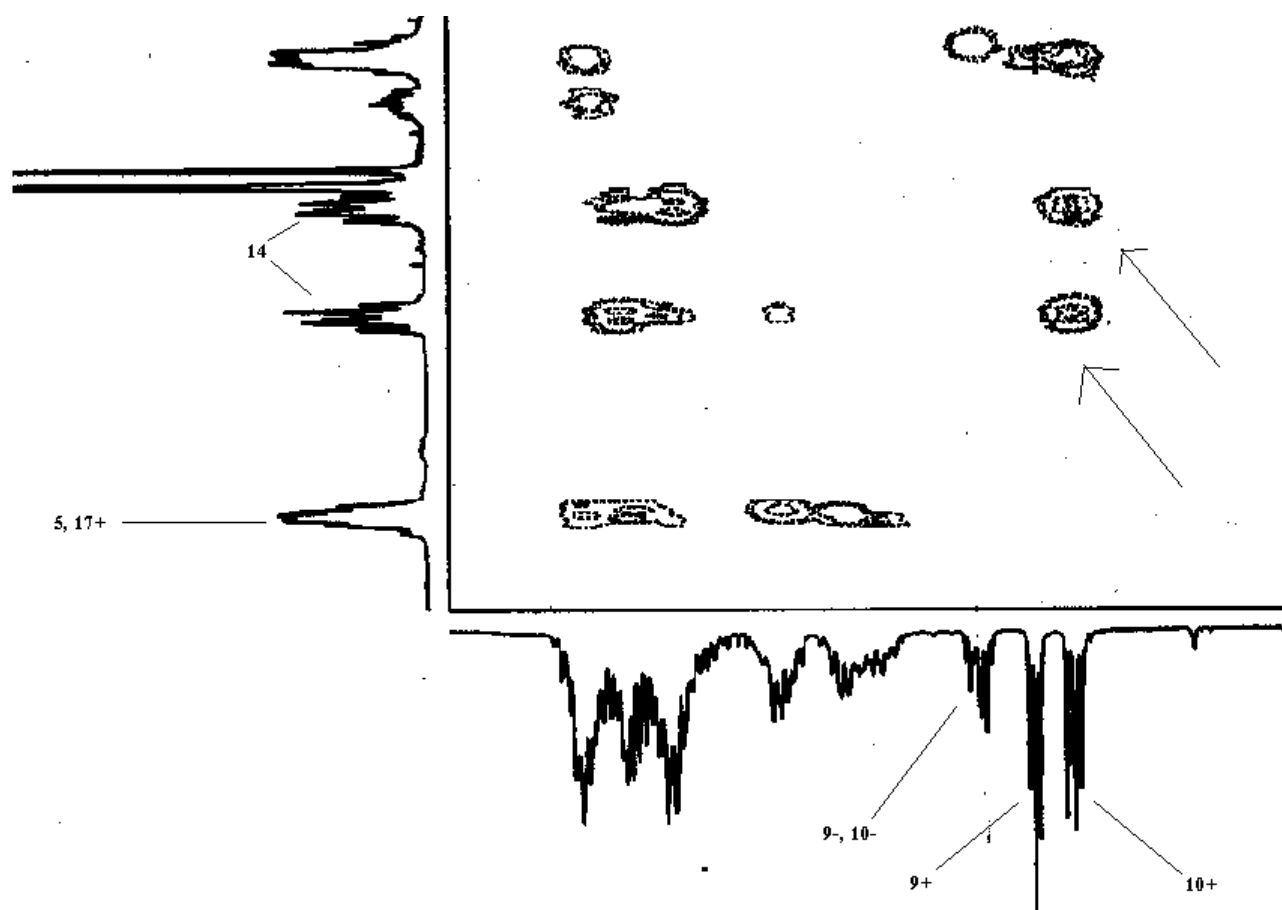




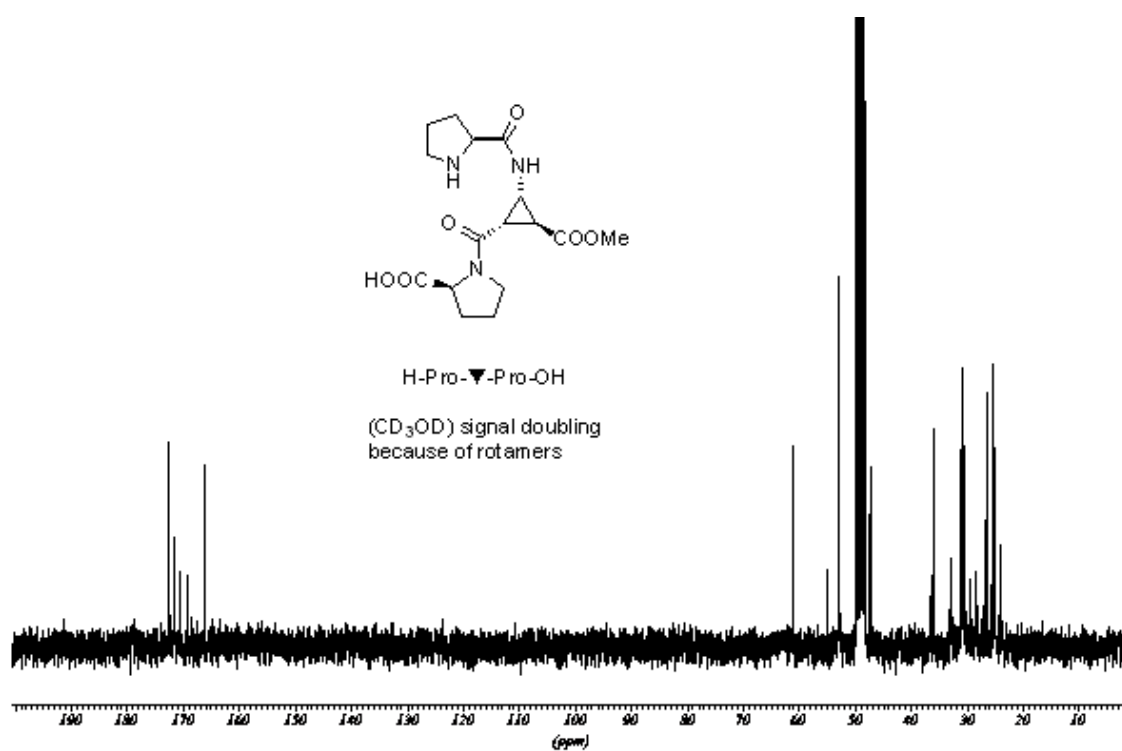
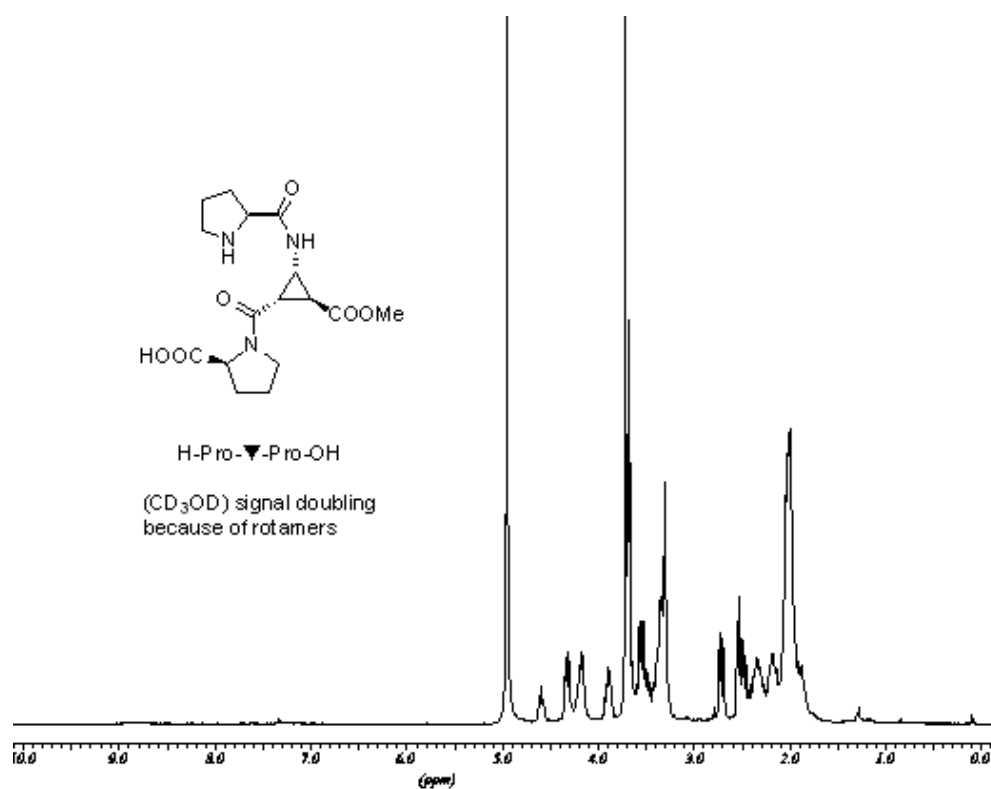
The ^1H -NMR signals have been unequivocally assigned by means of bidimensional NMR studies (HSQC, HMBC, NOEs). It is evident how some signals (9, 10, 17) double because of the presence of two different populations of conformers: trans and cis, in a ratio of about 3:1. The NOESY spectrum shows how proton 10 couples in the major conformation with the two protons 14, but not with 17, as expected for trans conformer (see text), while for the minor conformation the opposite is true, as expected for the cis conformer.

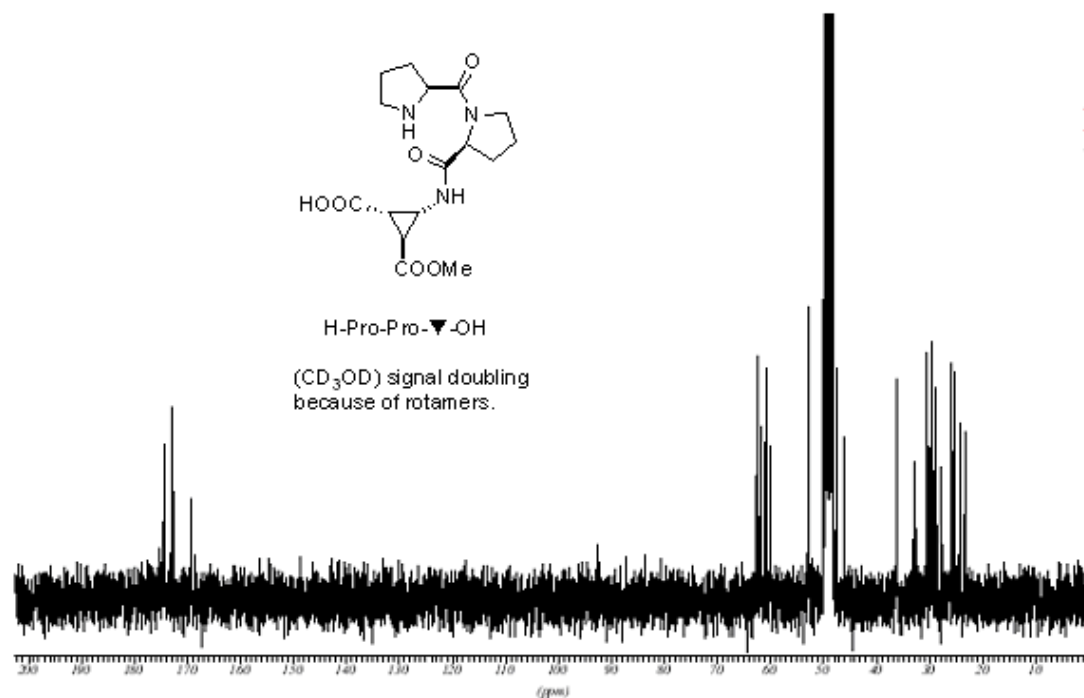
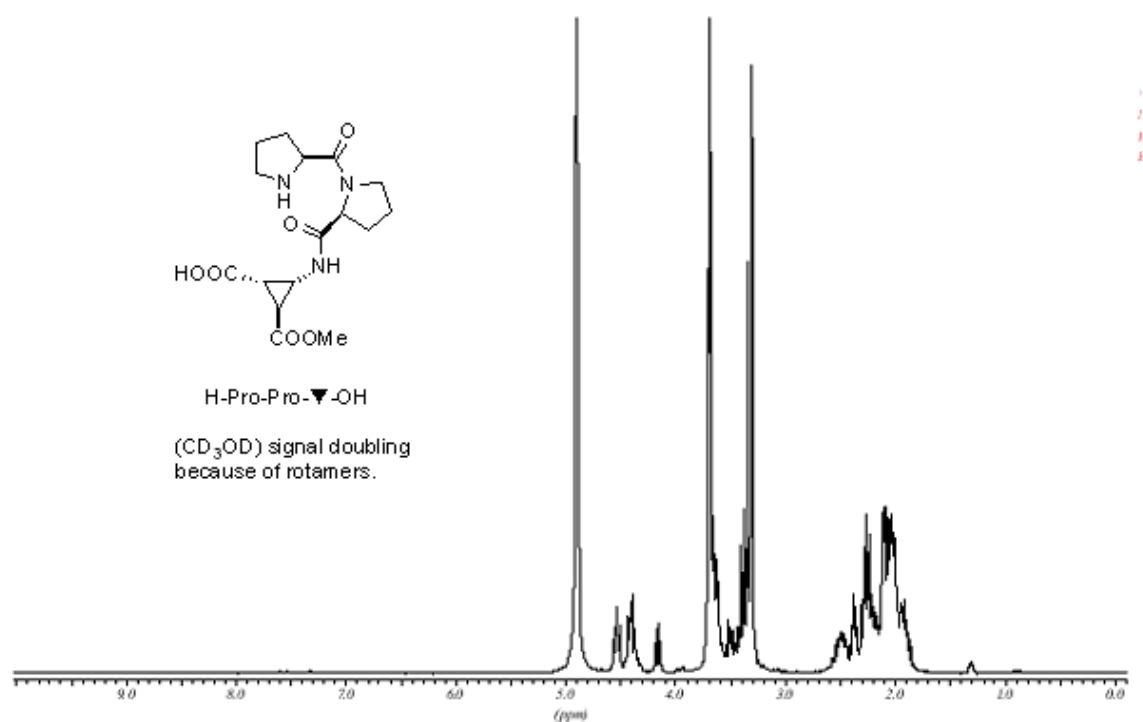


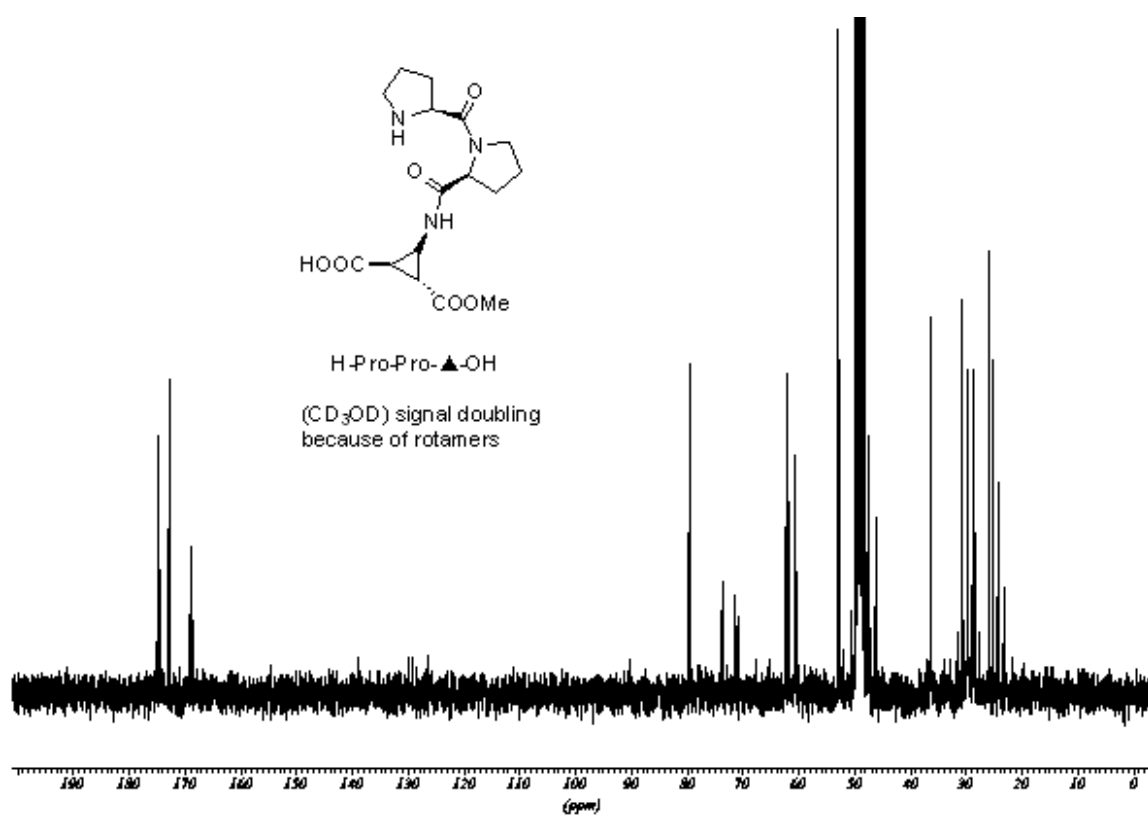
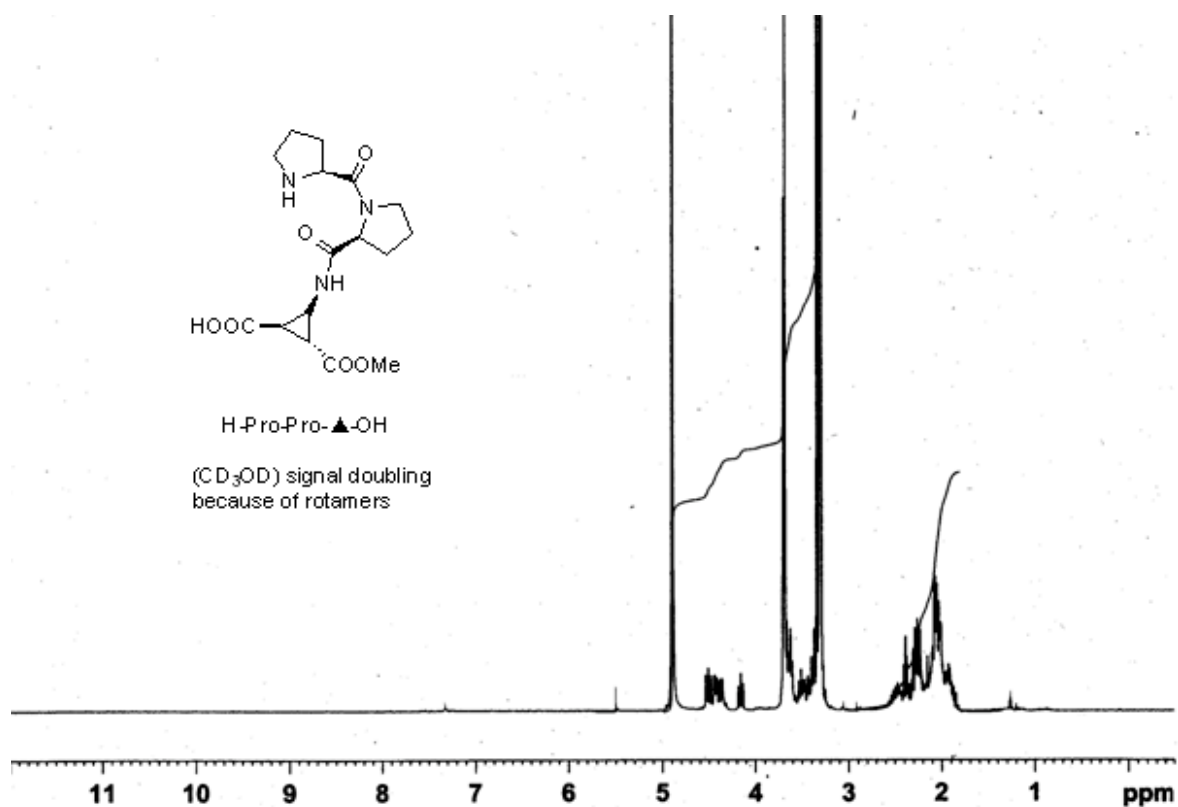
(NOESY spectrum magnified, to show the coupling between 10- and 17-, which proves the existence of a stable cis population.)

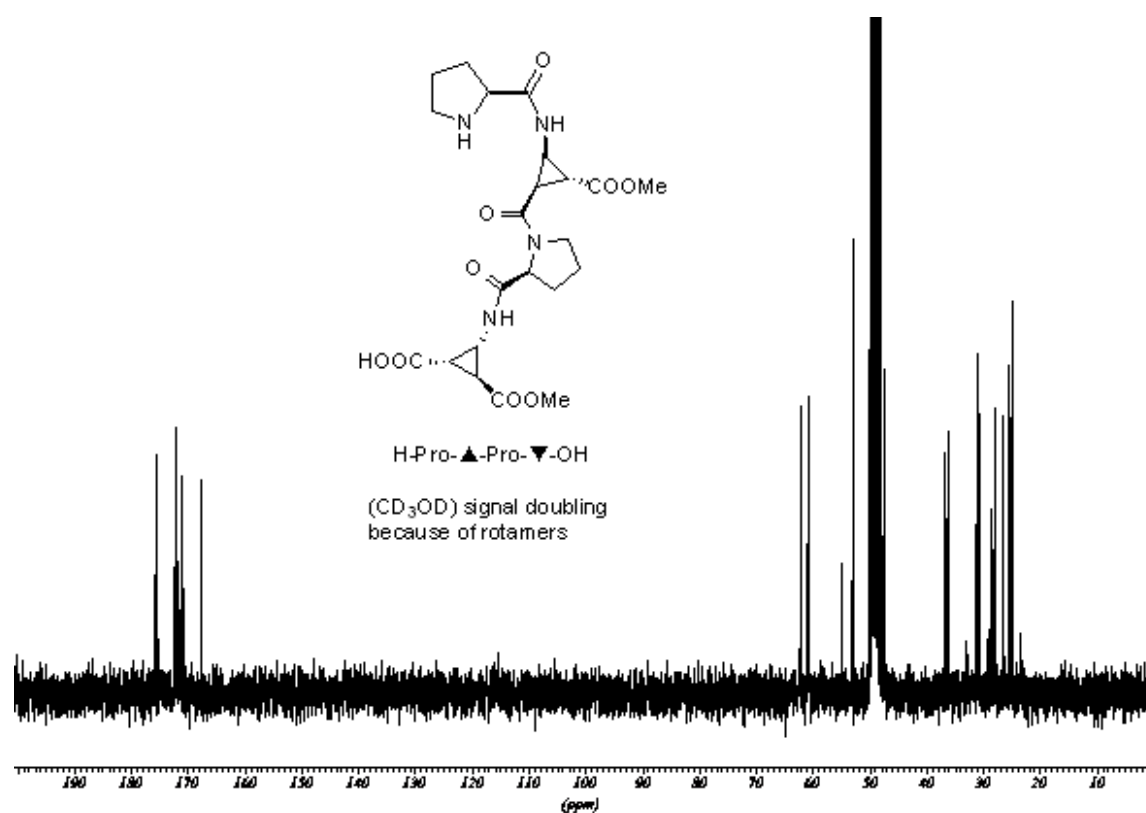
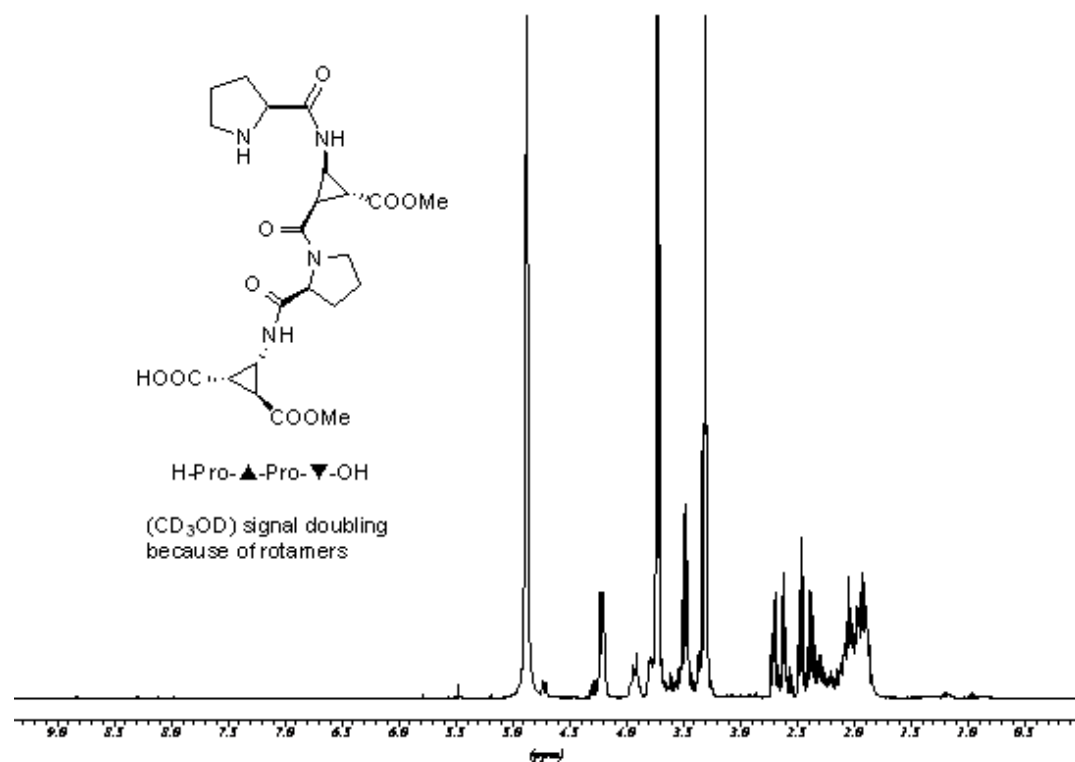


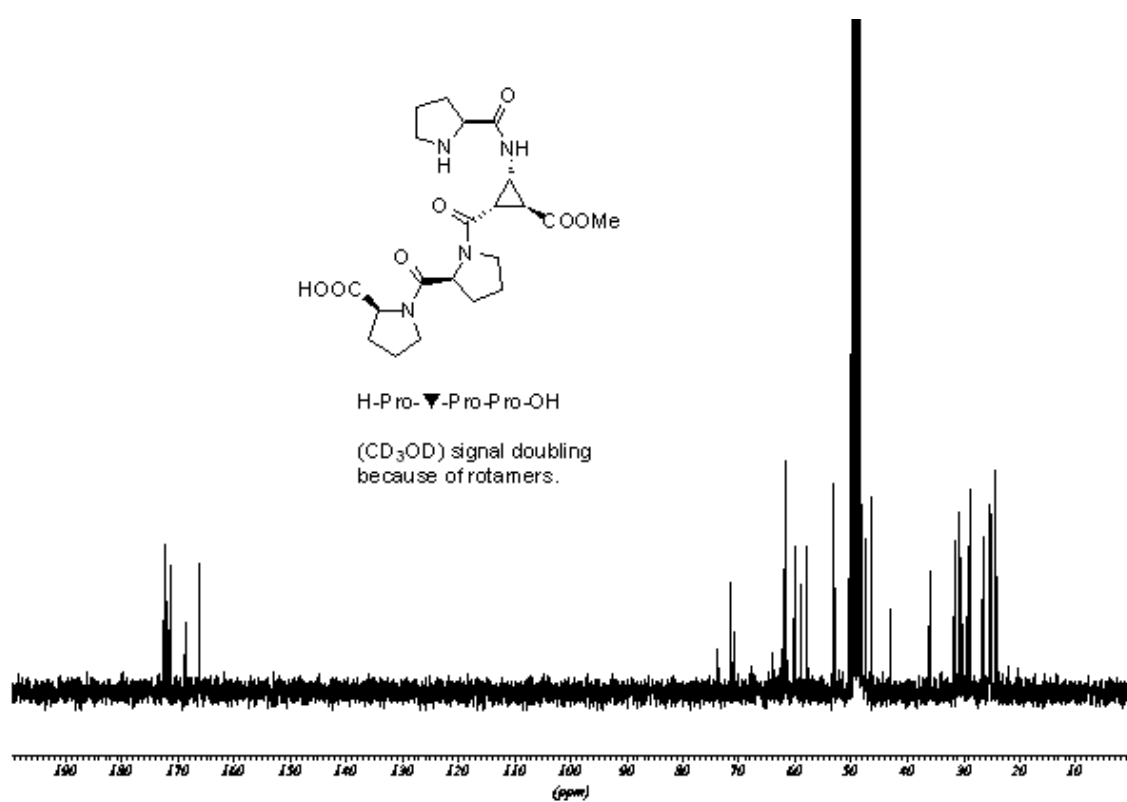
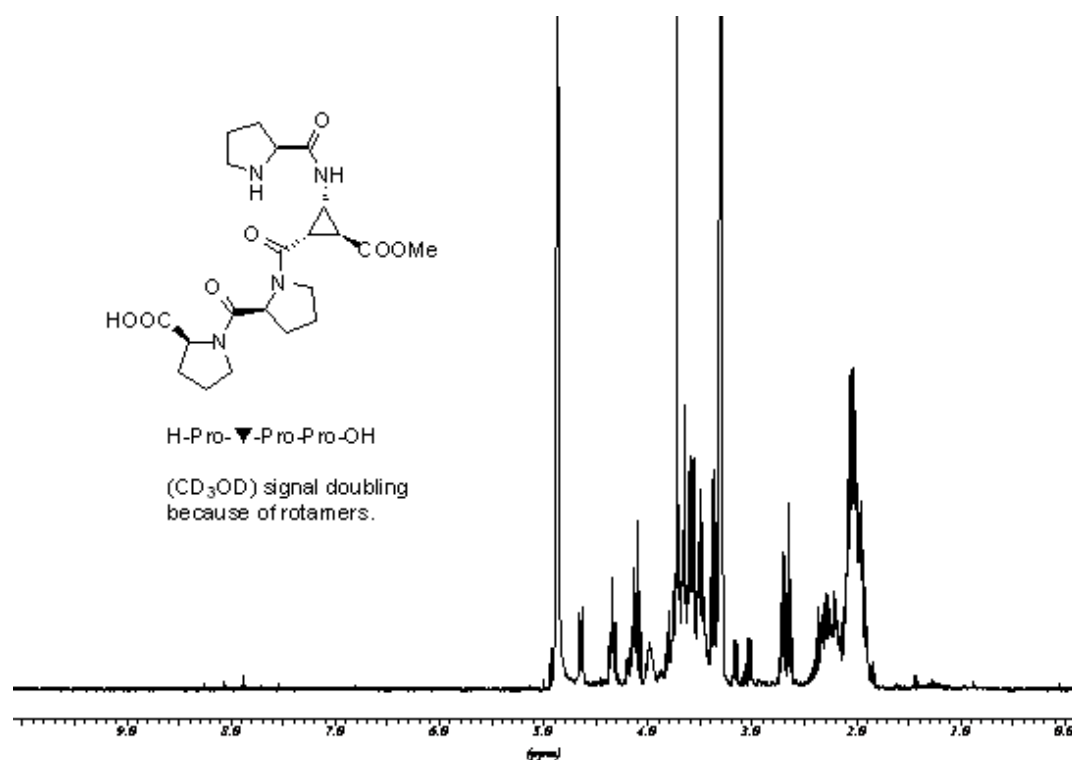
(NOESY spectrum magnified, to show the coupling between 10+ and 14 and the absence of coupling between 10+ and 17+, or 10- and 14)

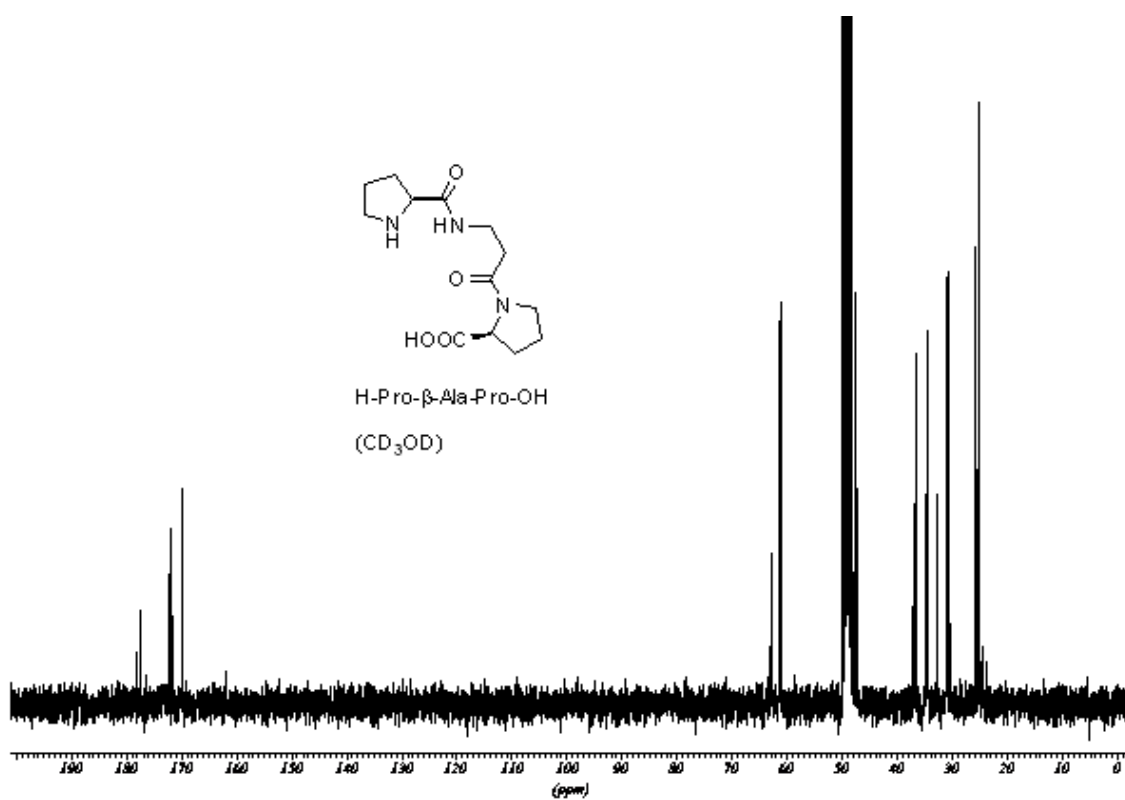
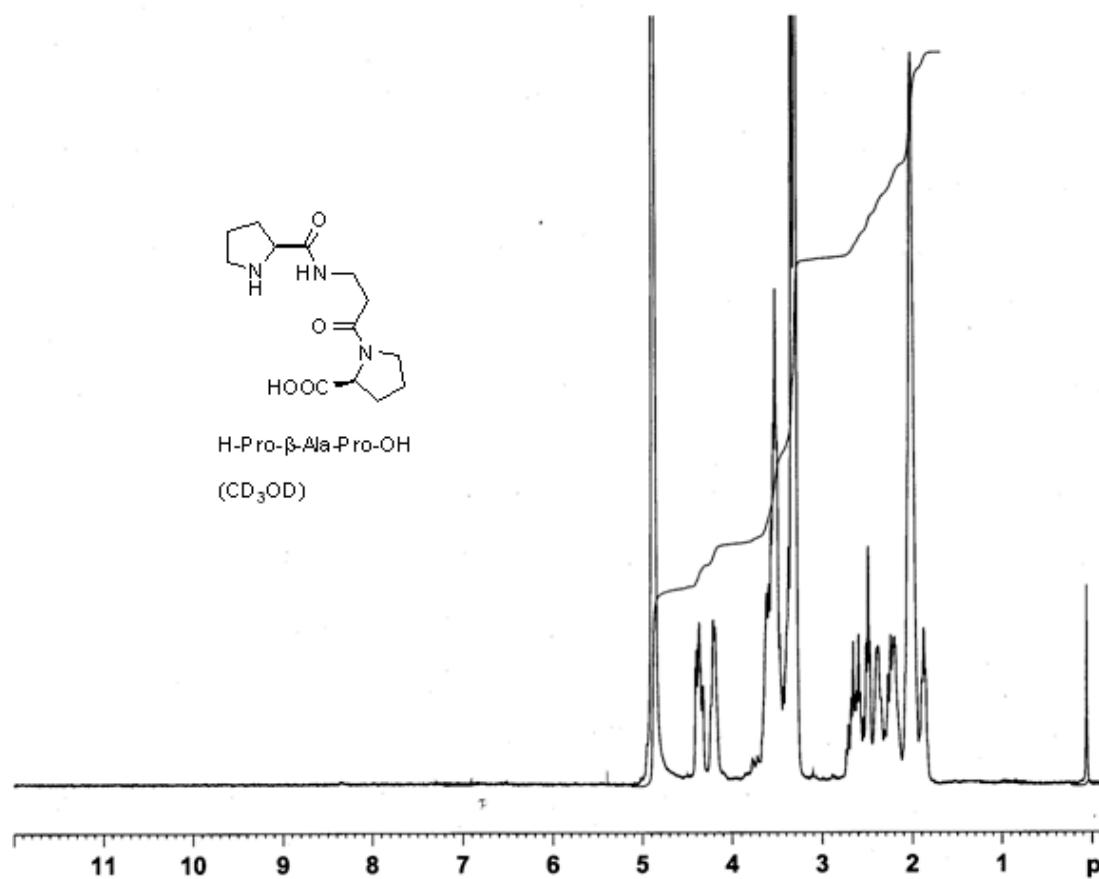


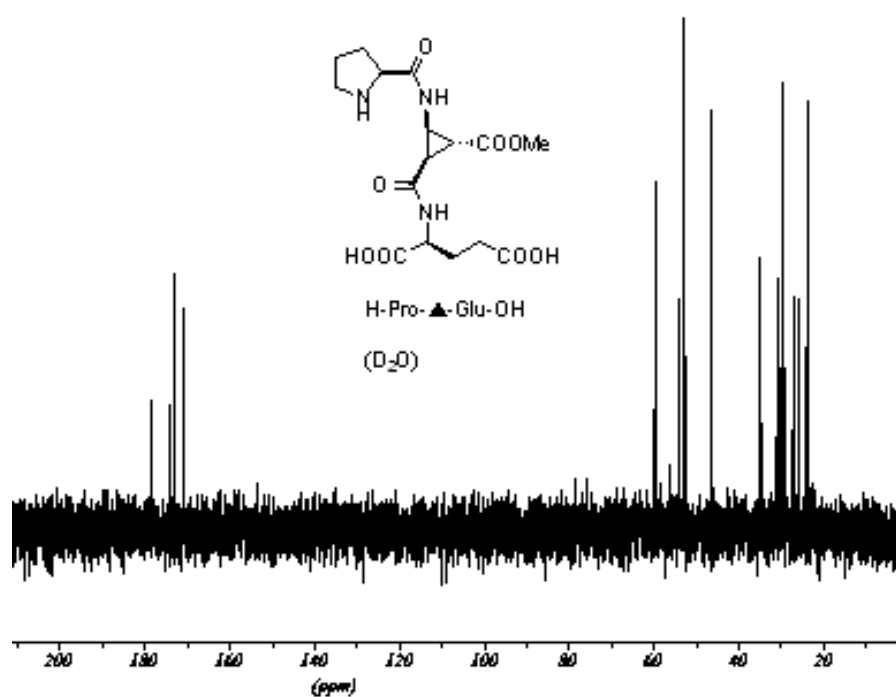
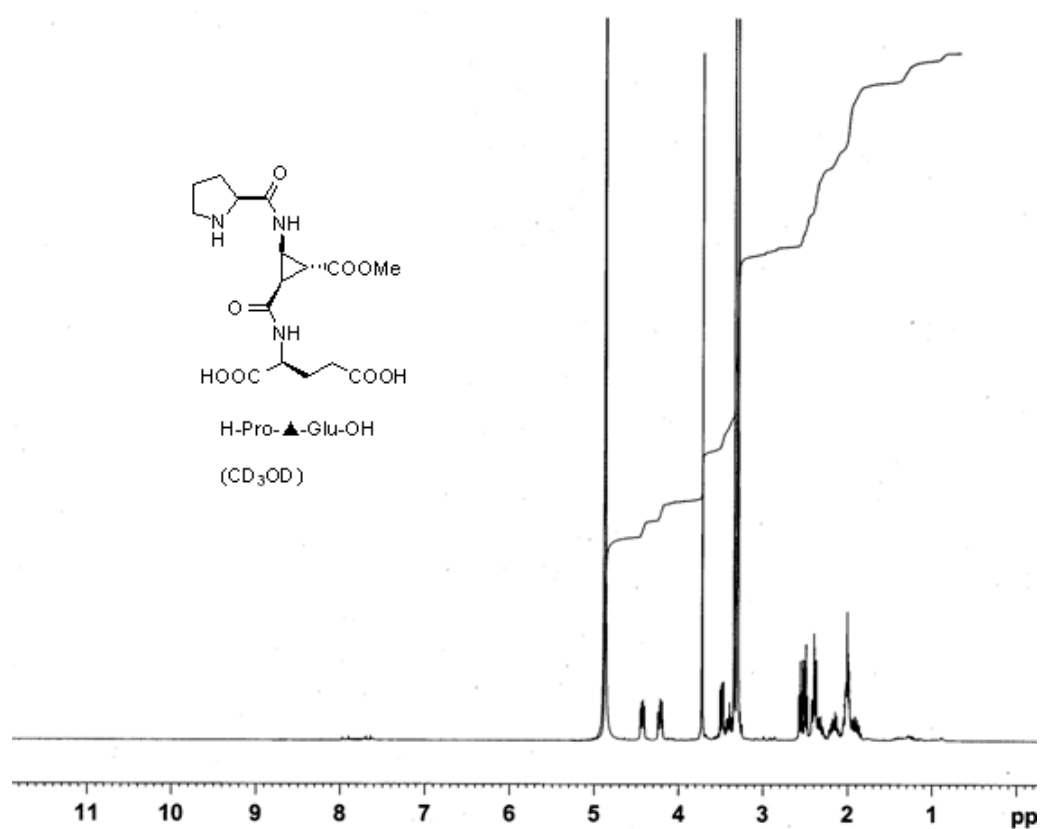


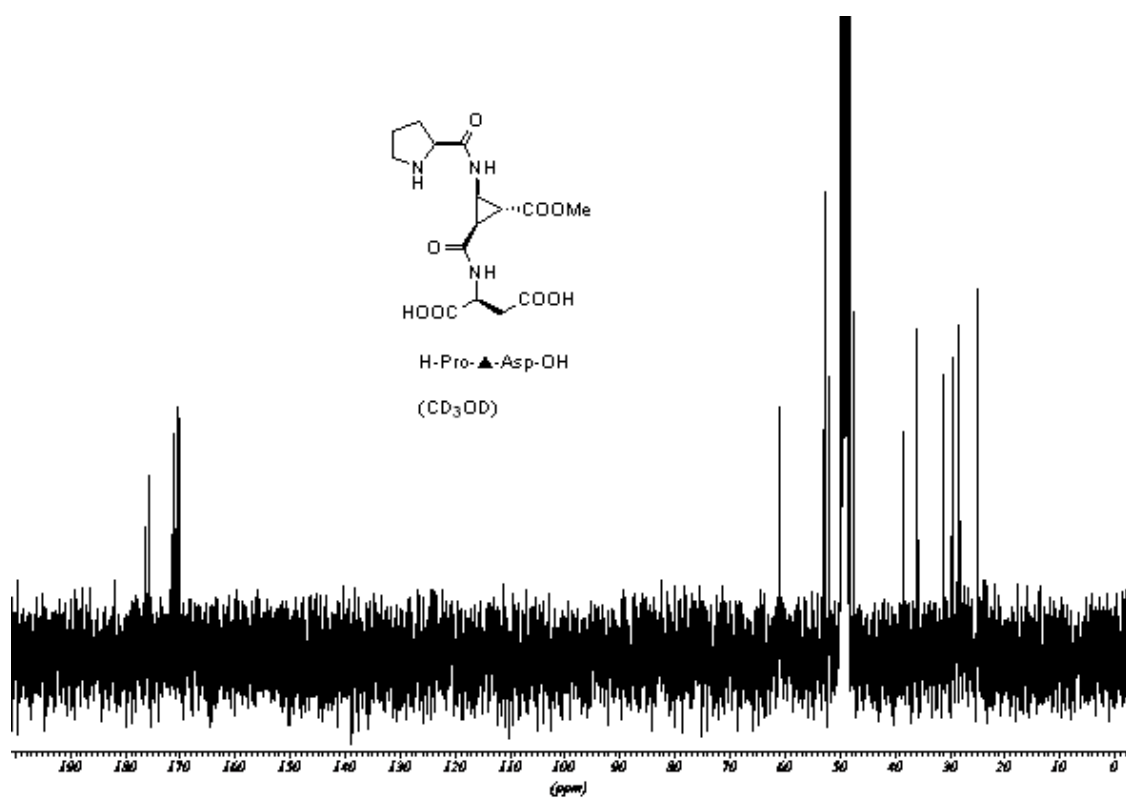
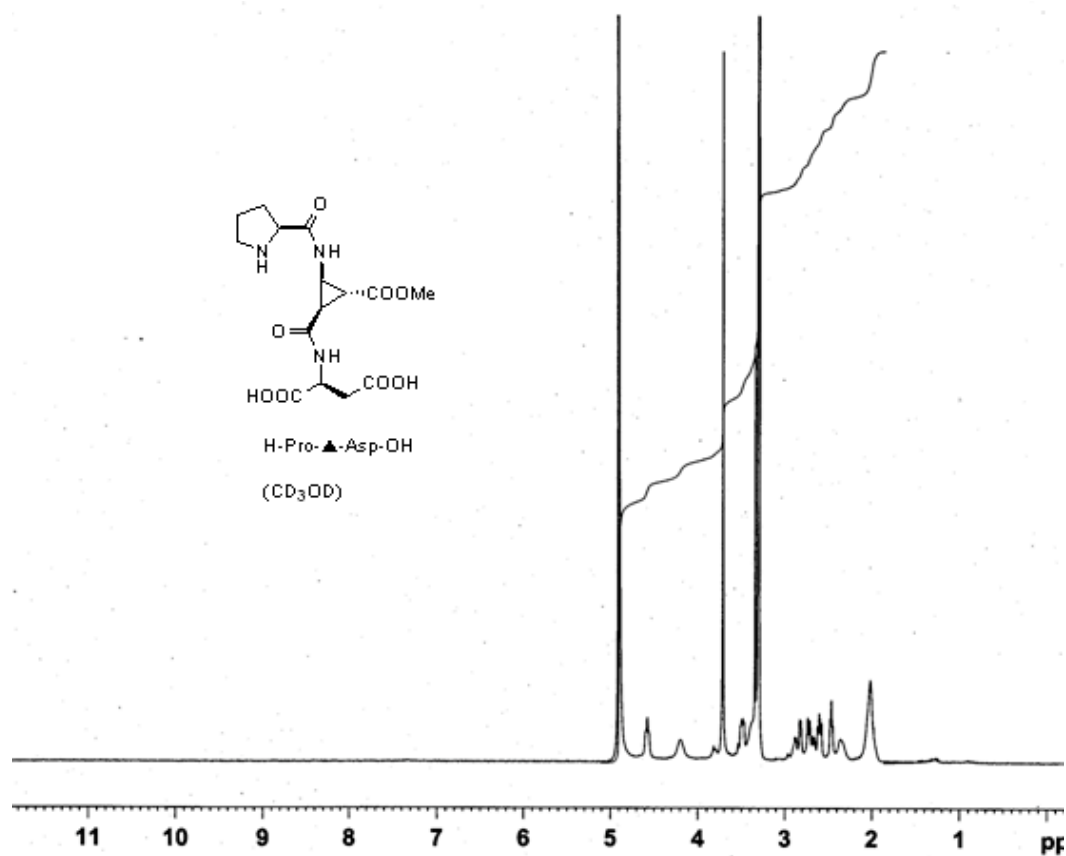


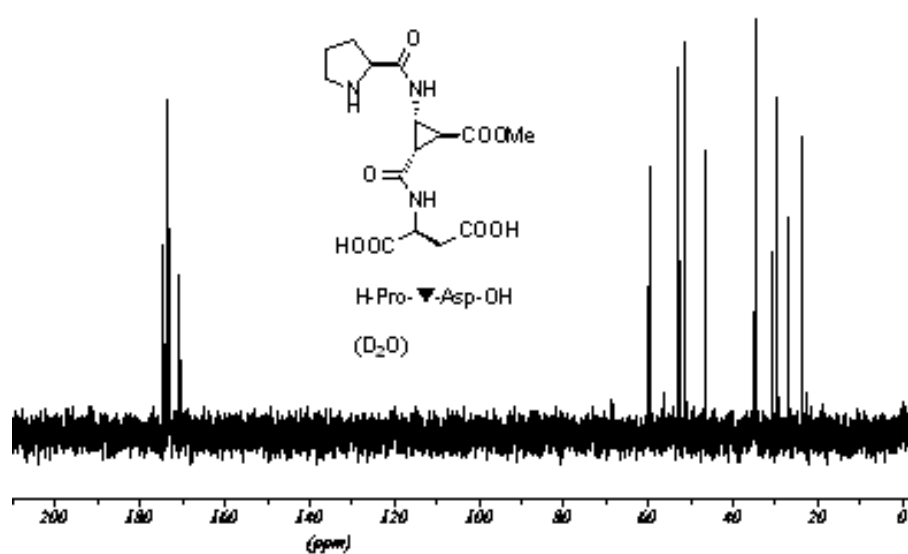
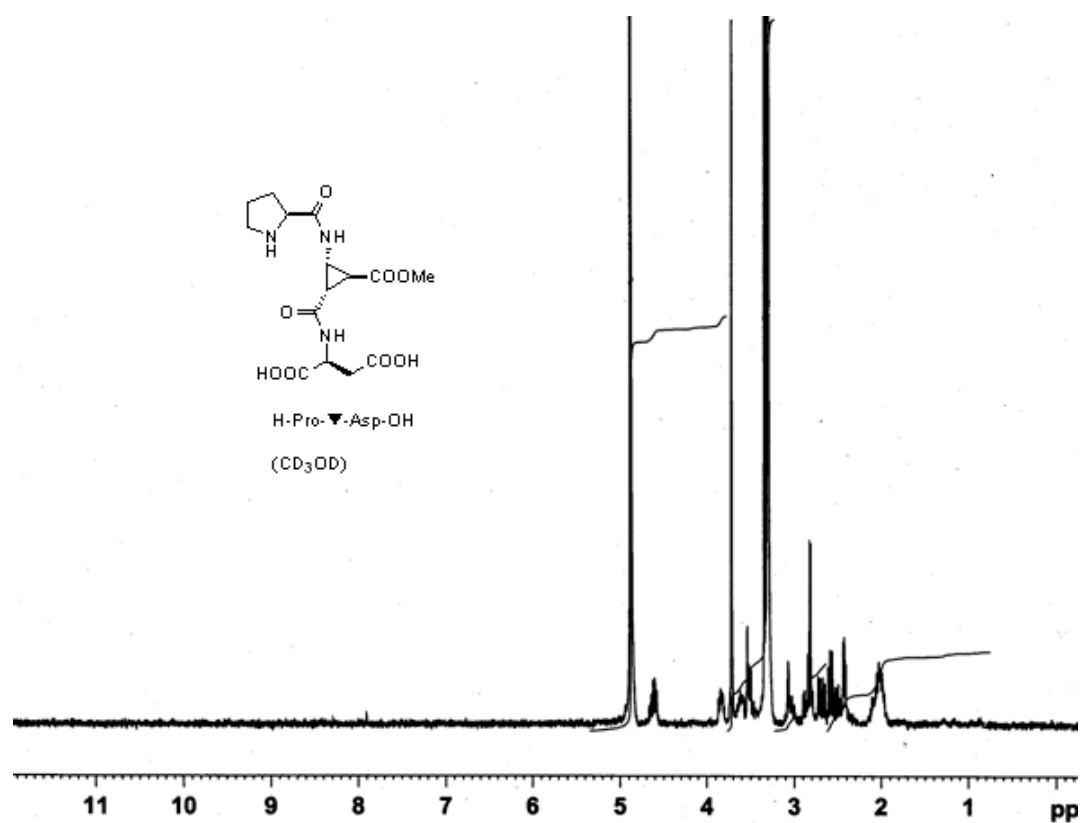


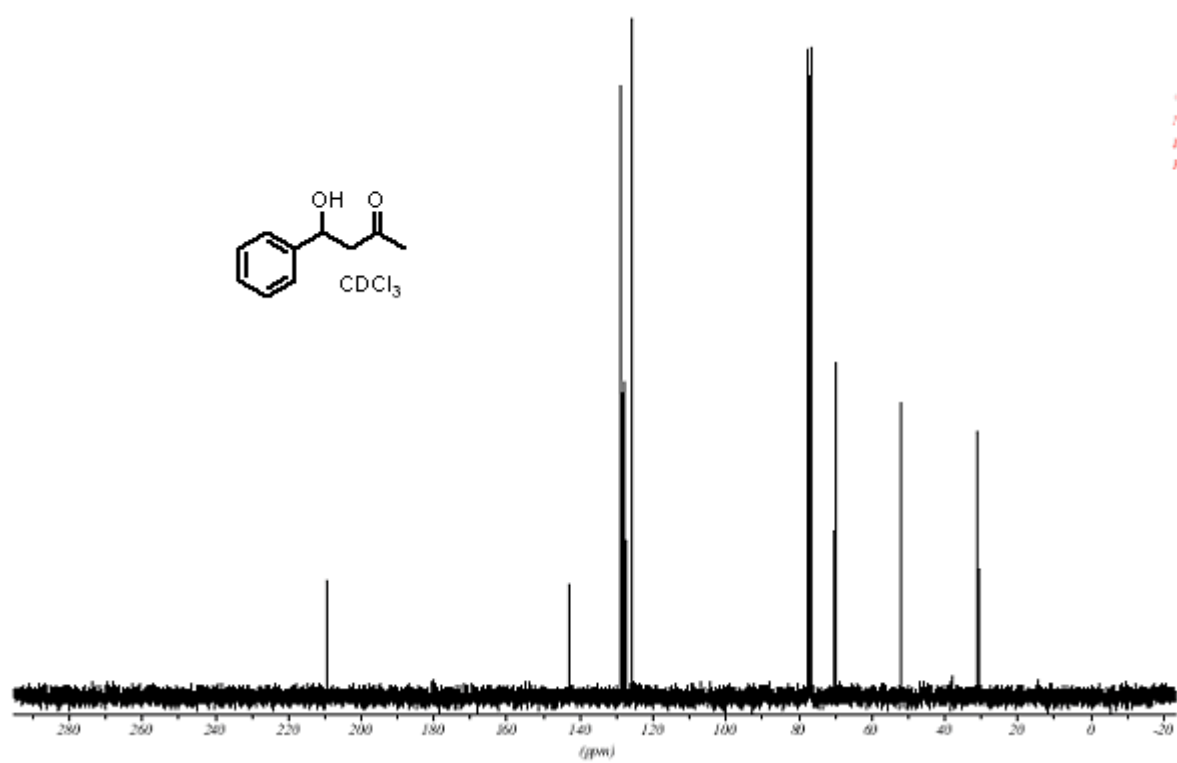
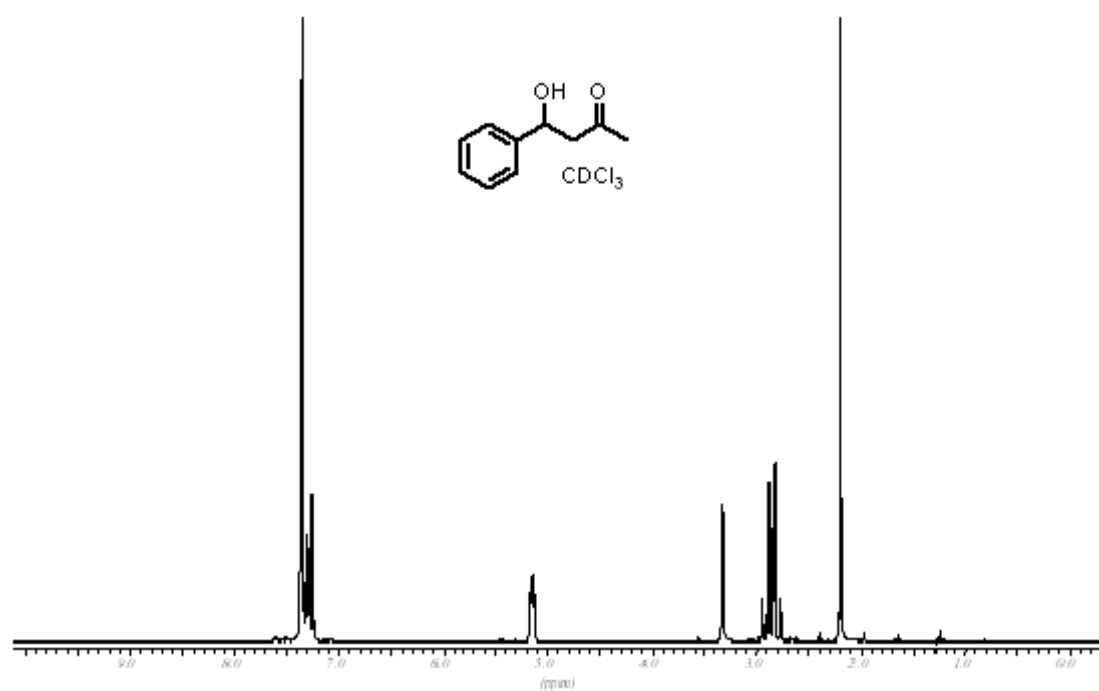


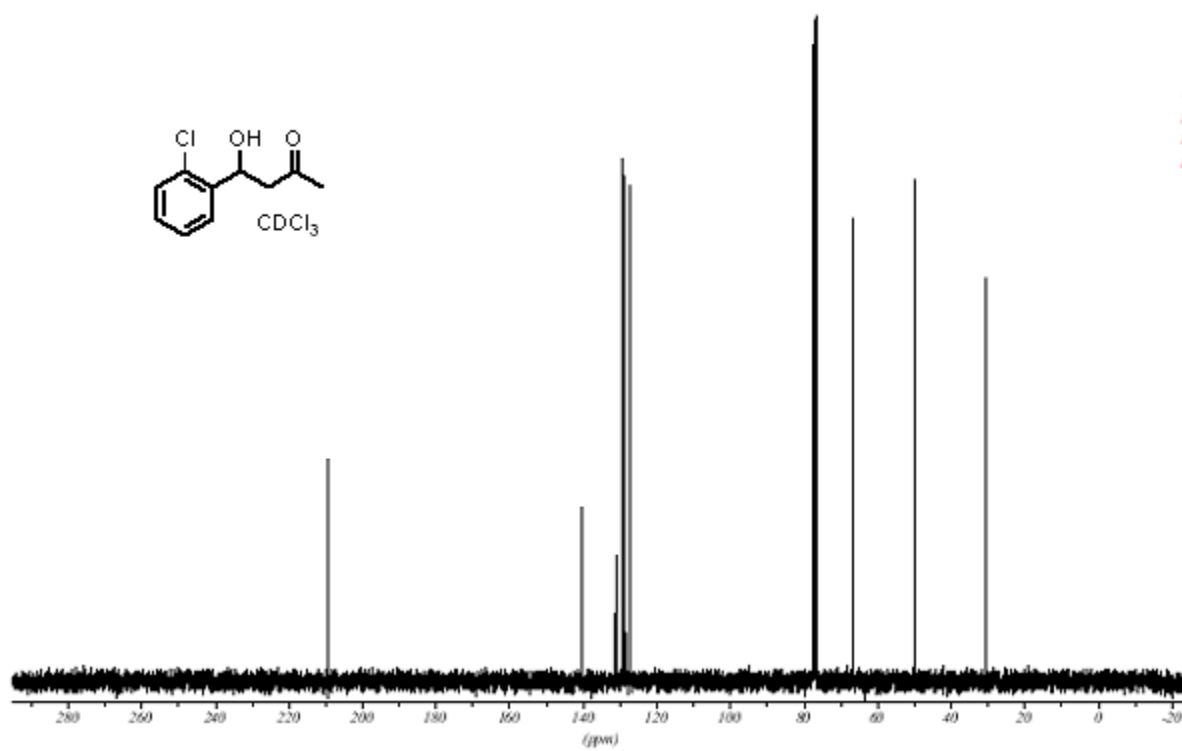
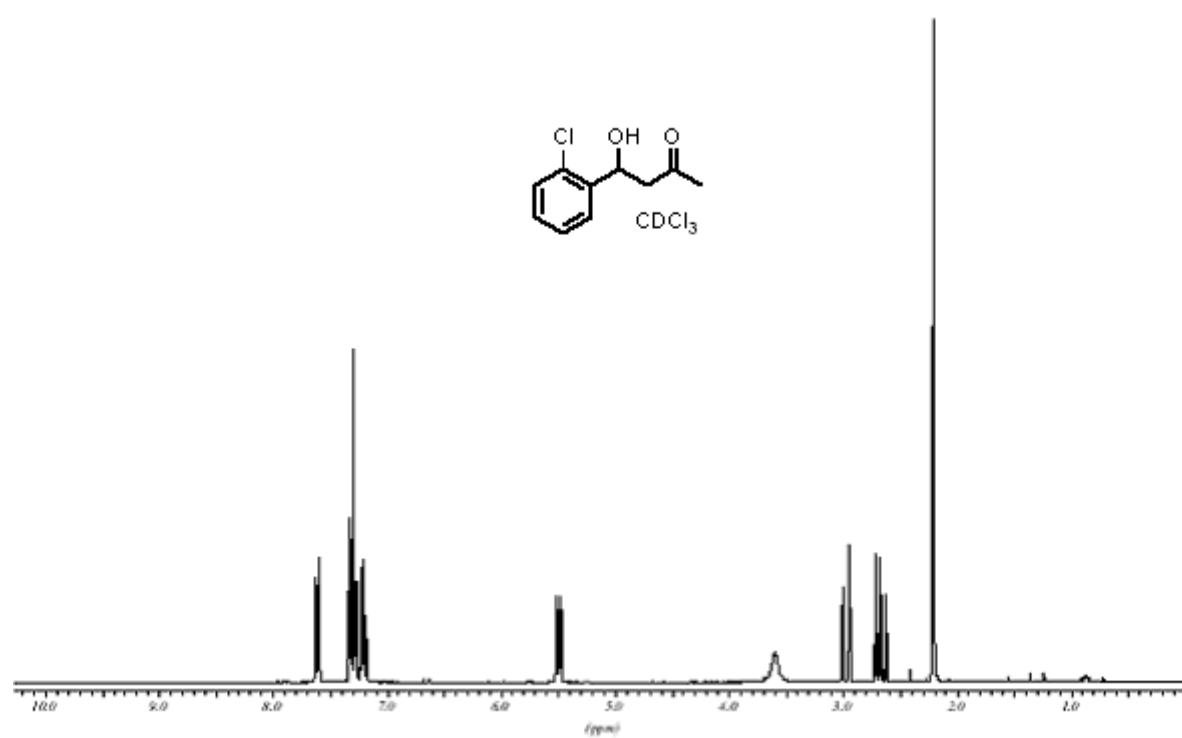


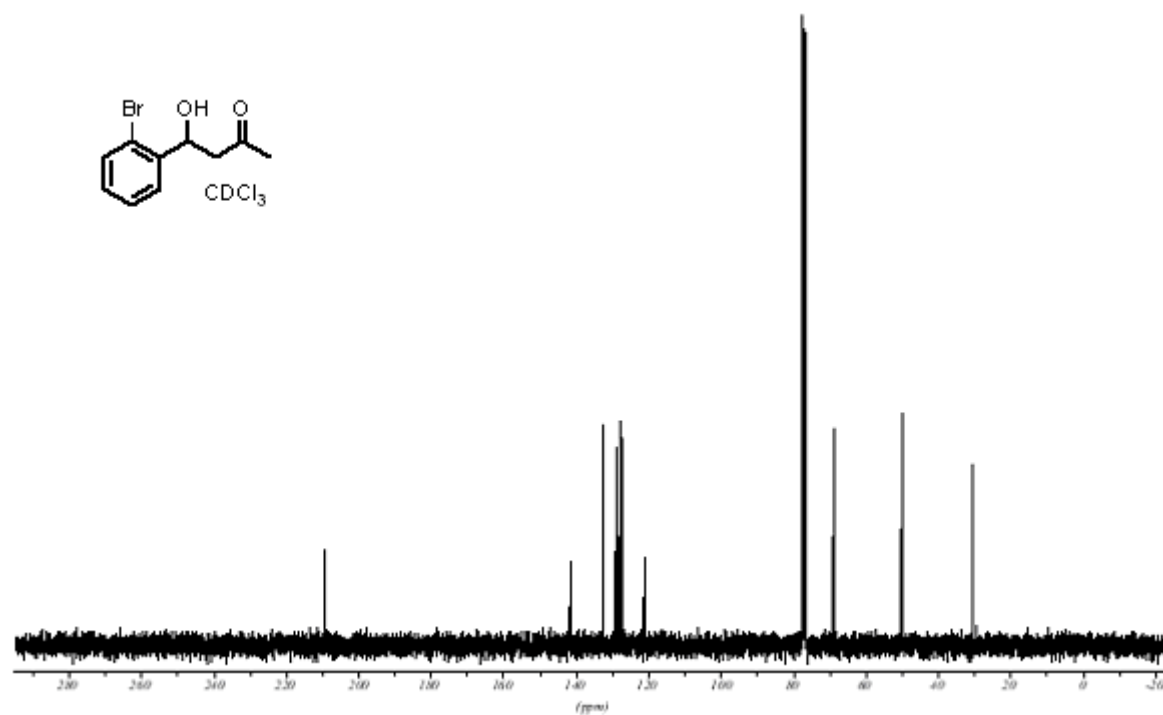
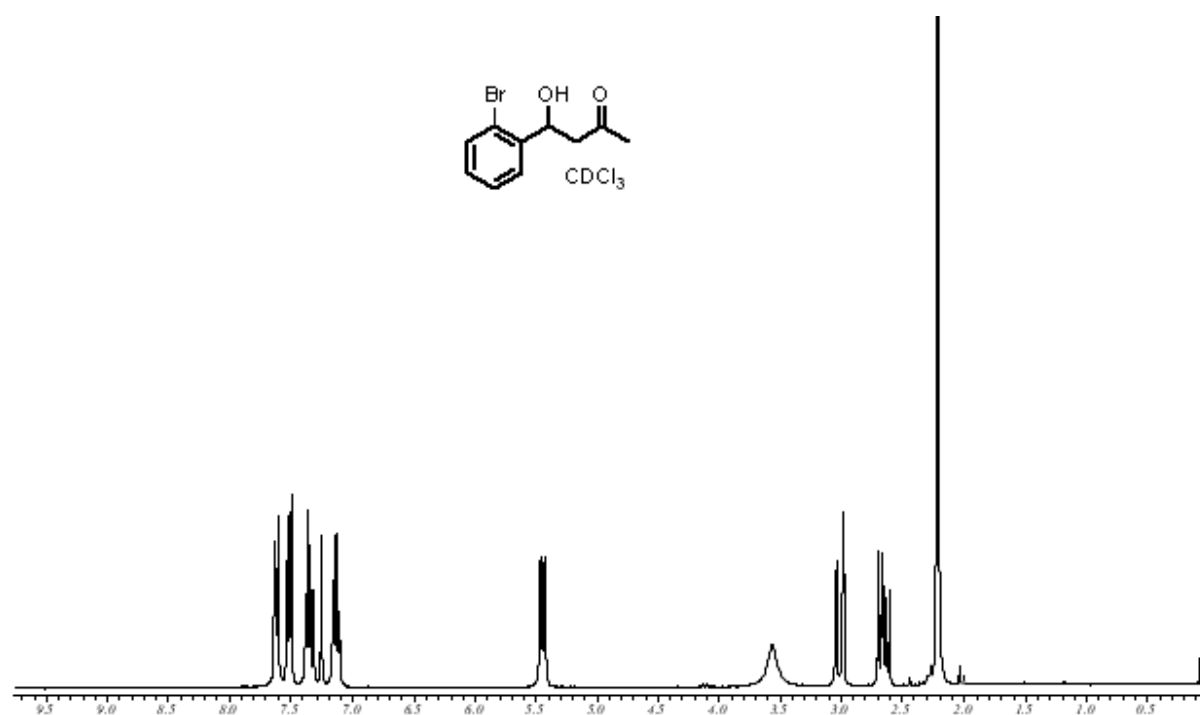


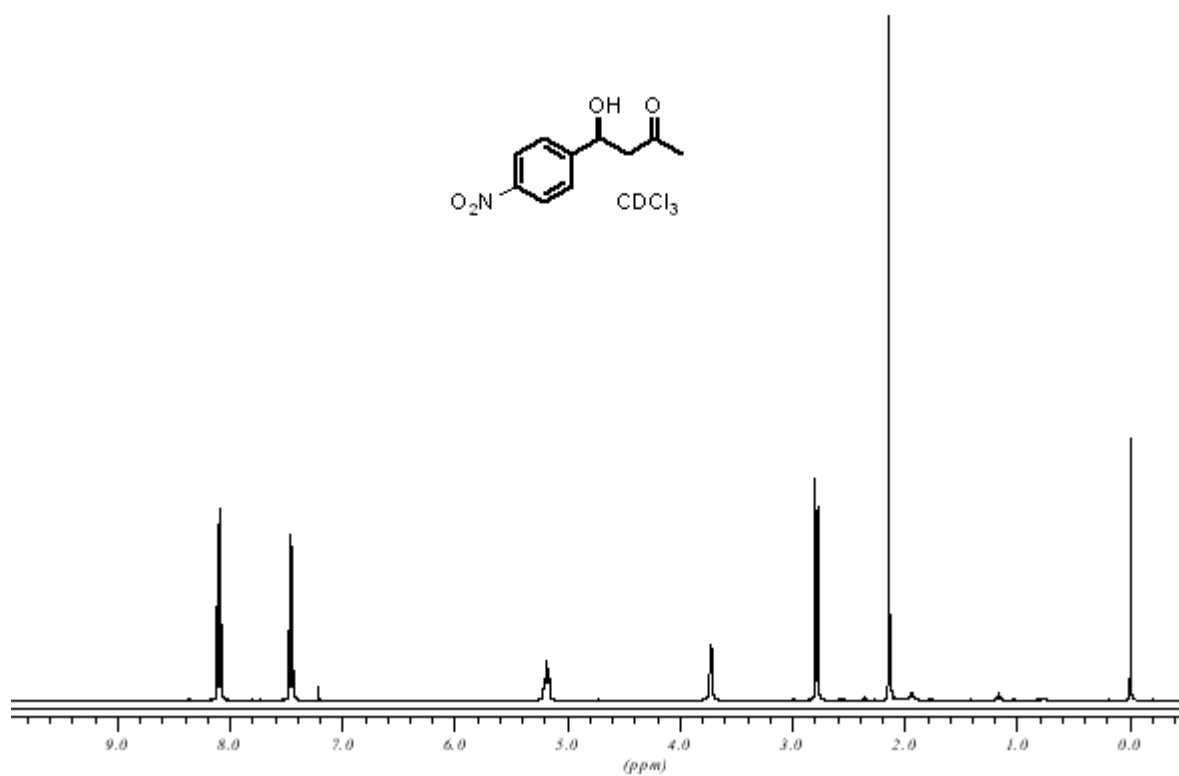
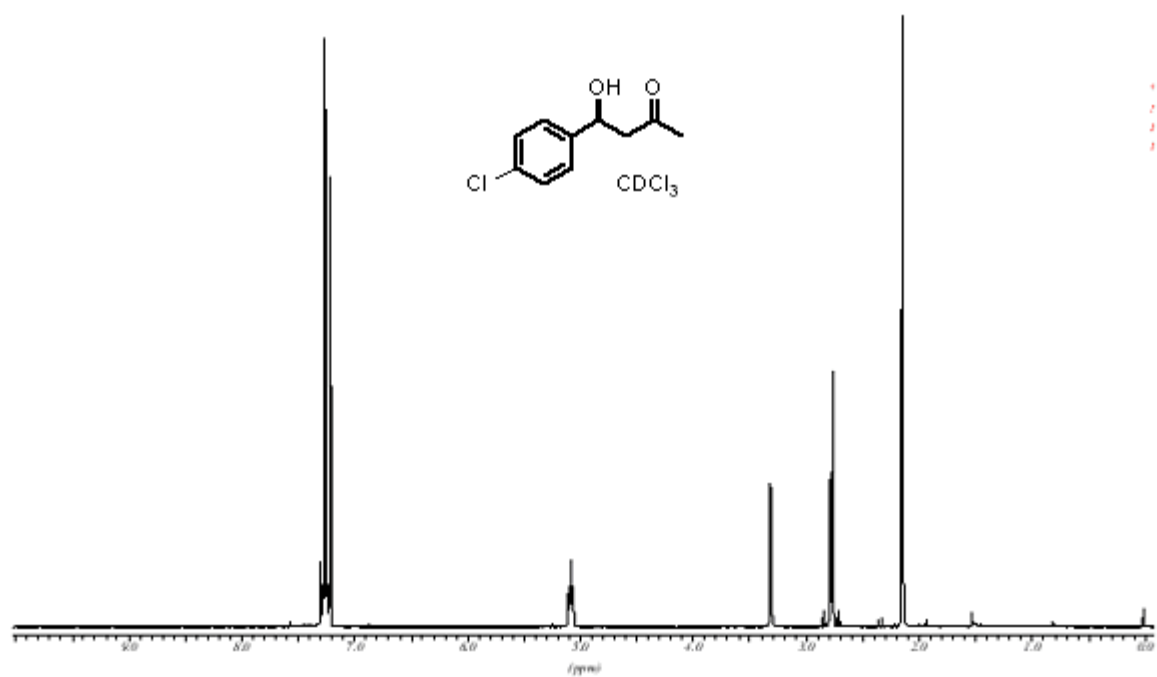




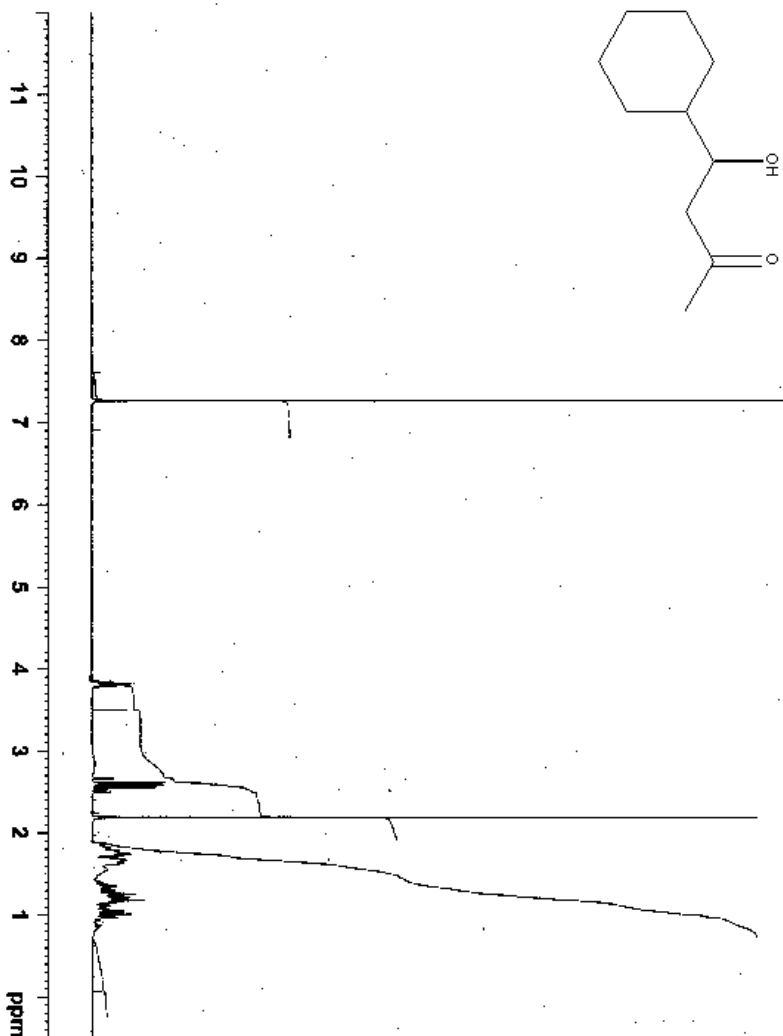
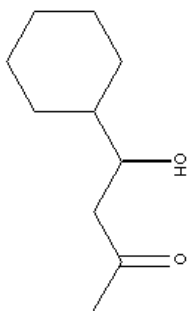








D`Elia, aldol reaction w. cyclohexylaldehyd
 rau_PROTONLP_16 CDCl3 (c:\Bruker\Xwin-nmr) AK Reiser 30



Universitat Regensburg
 RMF IV, Chemie/Pharmazie
 Zentrale Analytik NMR
 Gerat: Avance 300

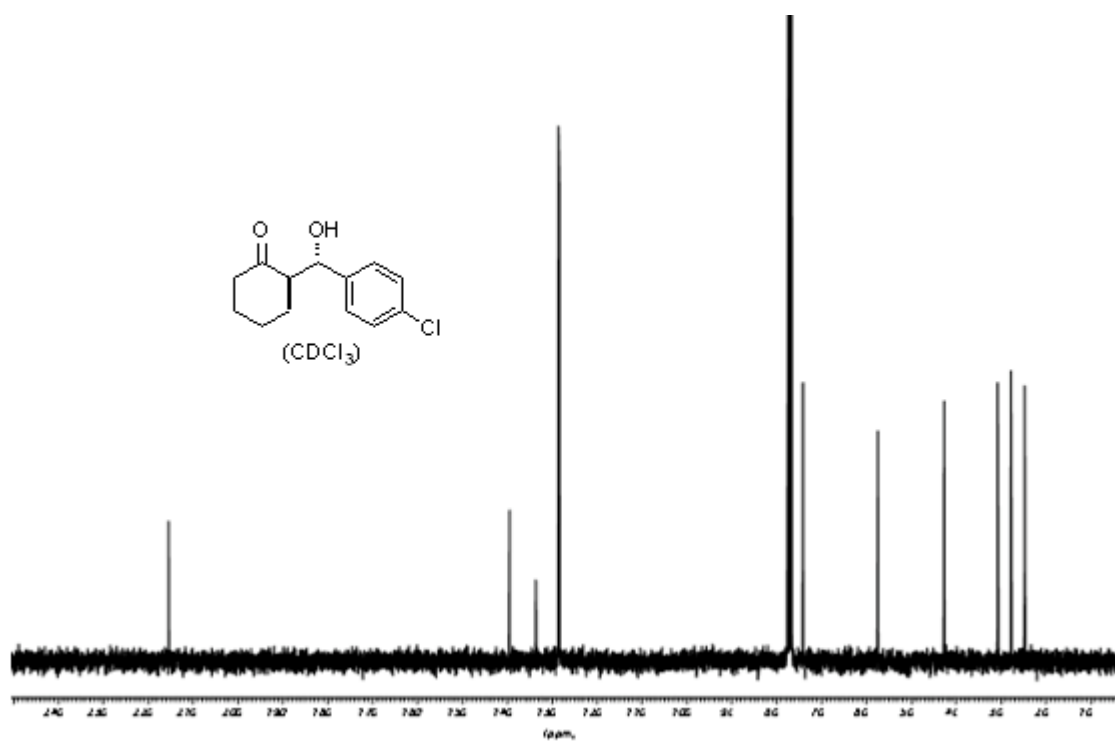
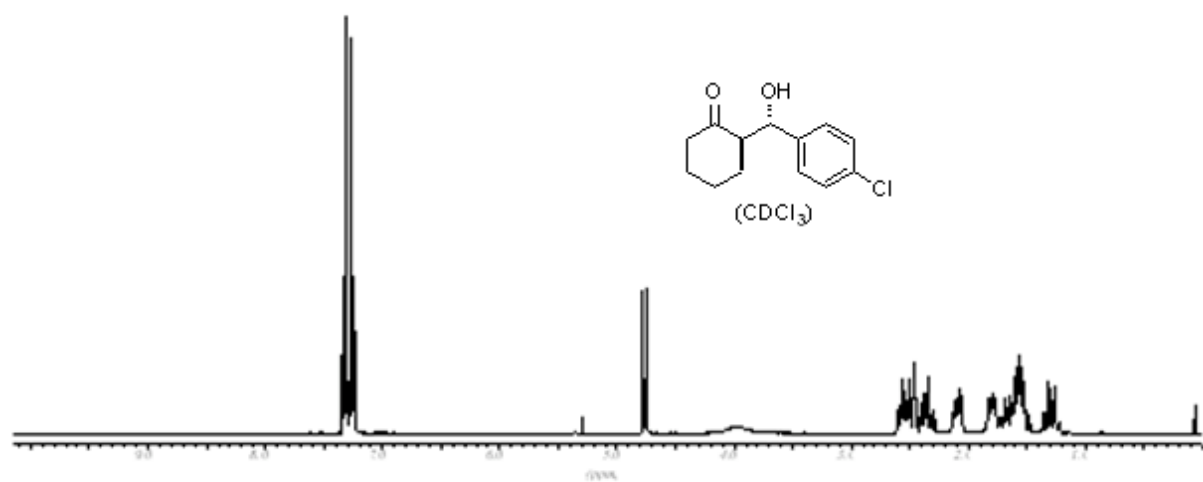
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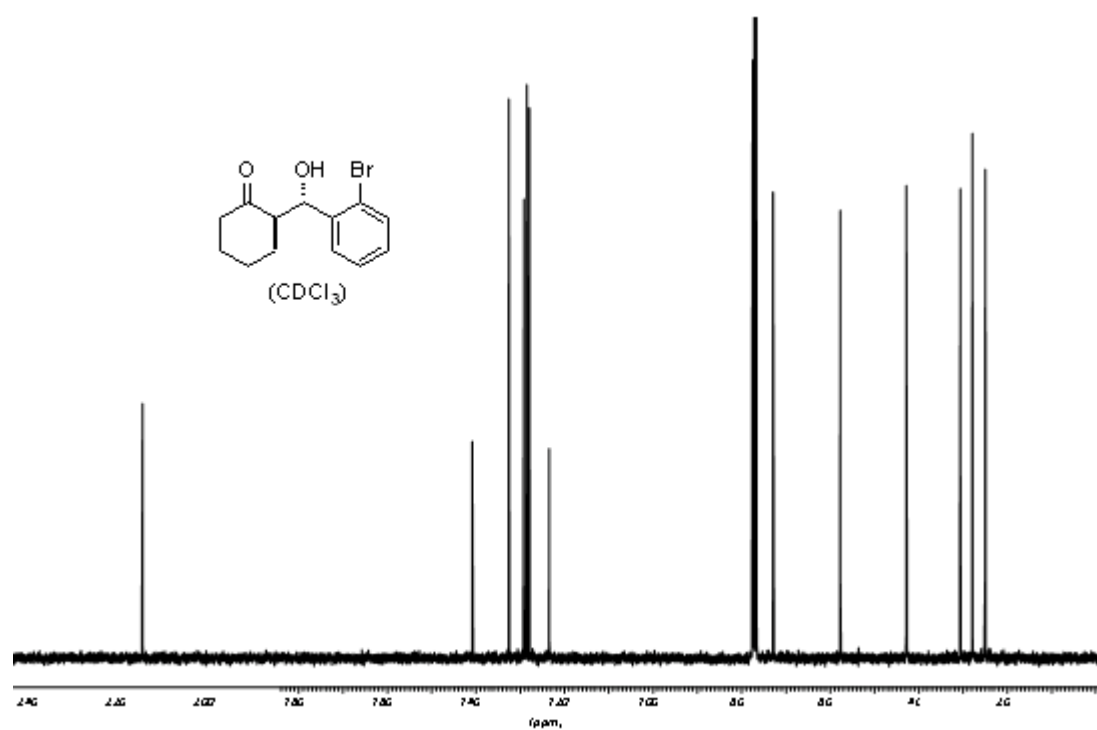
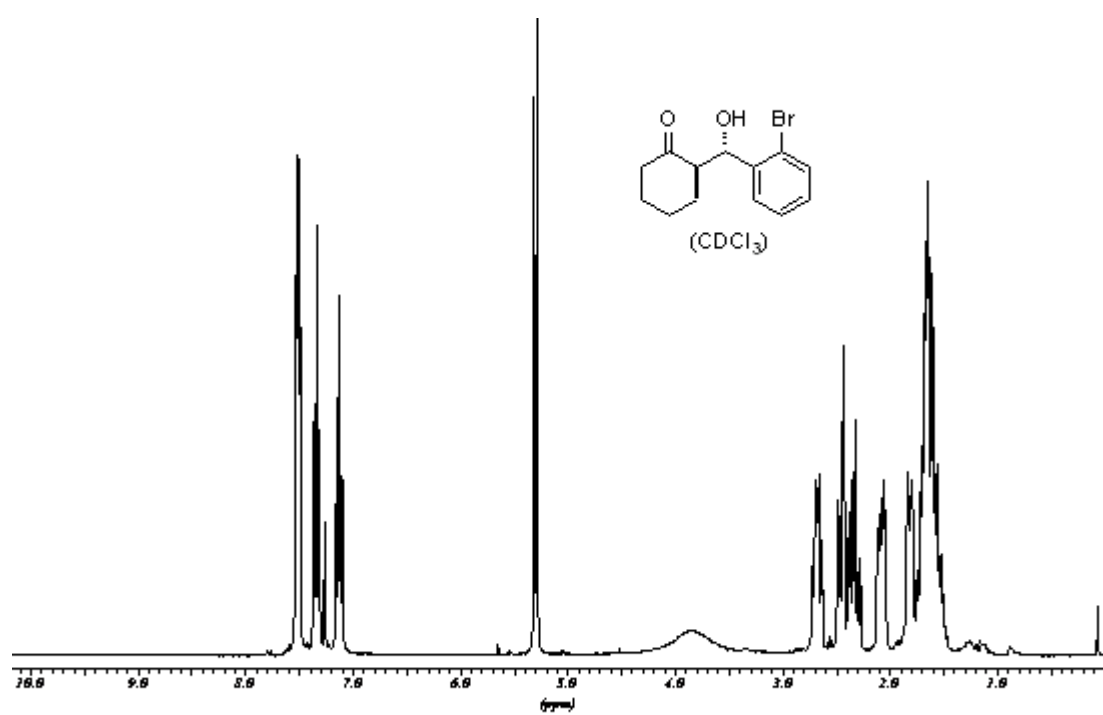
Current Data Parameters
NAME      May04-2006
EXPNO     60
PROCNO    1

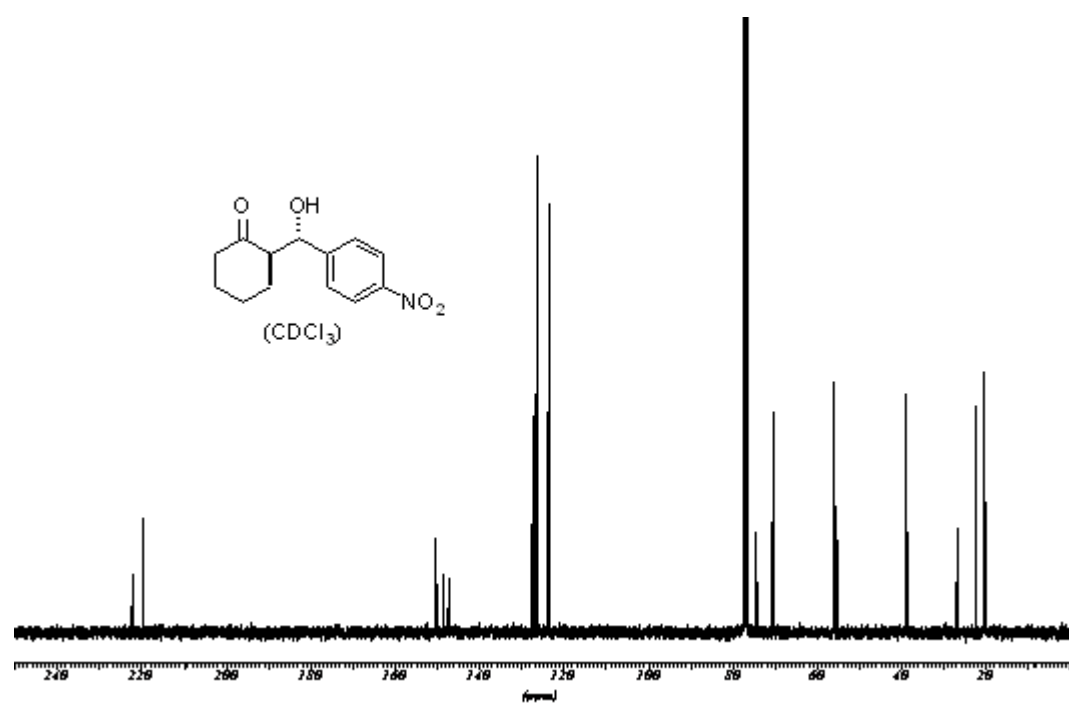
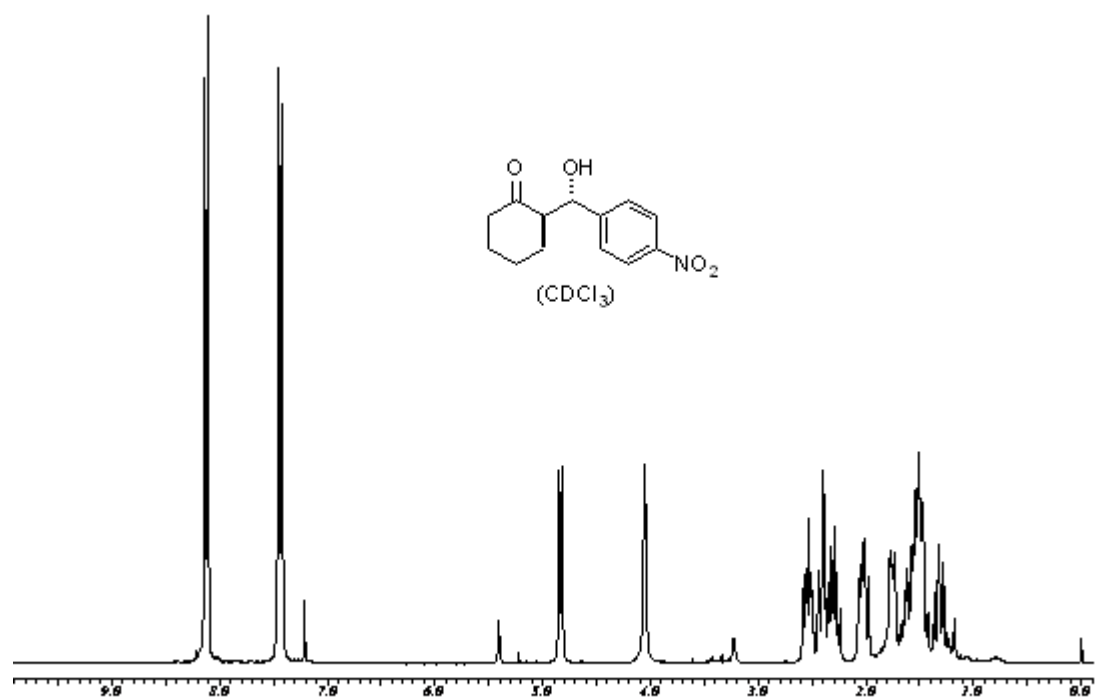
F2 - Acquisition Parameters
Date_     20060504
Time      13.07
INSTRUM   spect
PROBHD    5 mm QNP 1H/13
PULPROG   zg30
TD         65536
SOLVENT   CDCl3
NS         16
DS         2
SWH        8992.806 Hz
FIDRES     0.137219 Hz
AQ         3.6438515 sec
RG         2580.3
DW         55.600 usec
DE         6.00 usec
TE         296.0 K
D1         2.00000000 sec
D2         0.00000000 sec
MCREST    0.00000000 sec
MCNMRX    0.01500000 sec

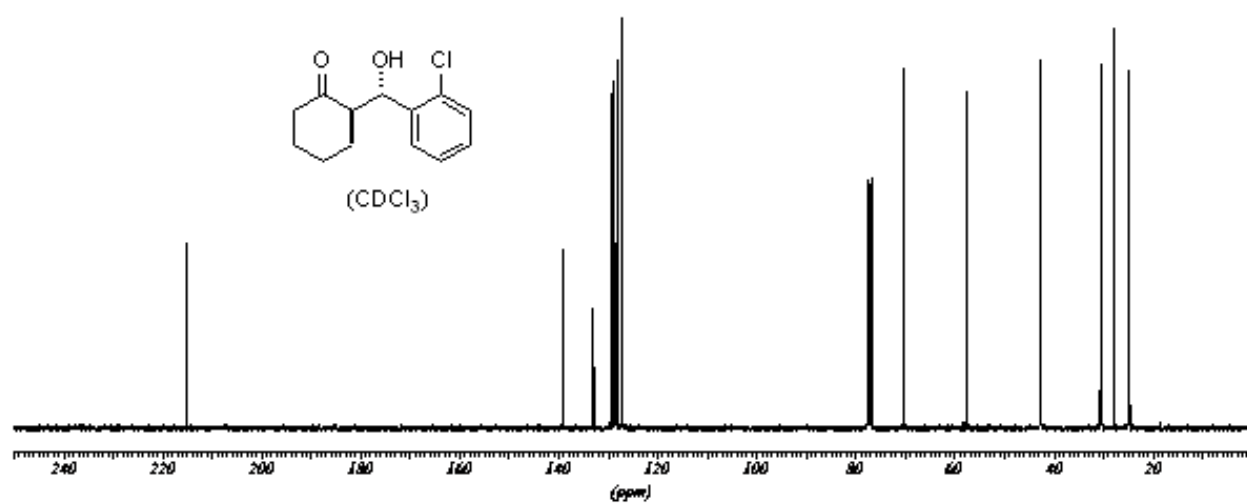
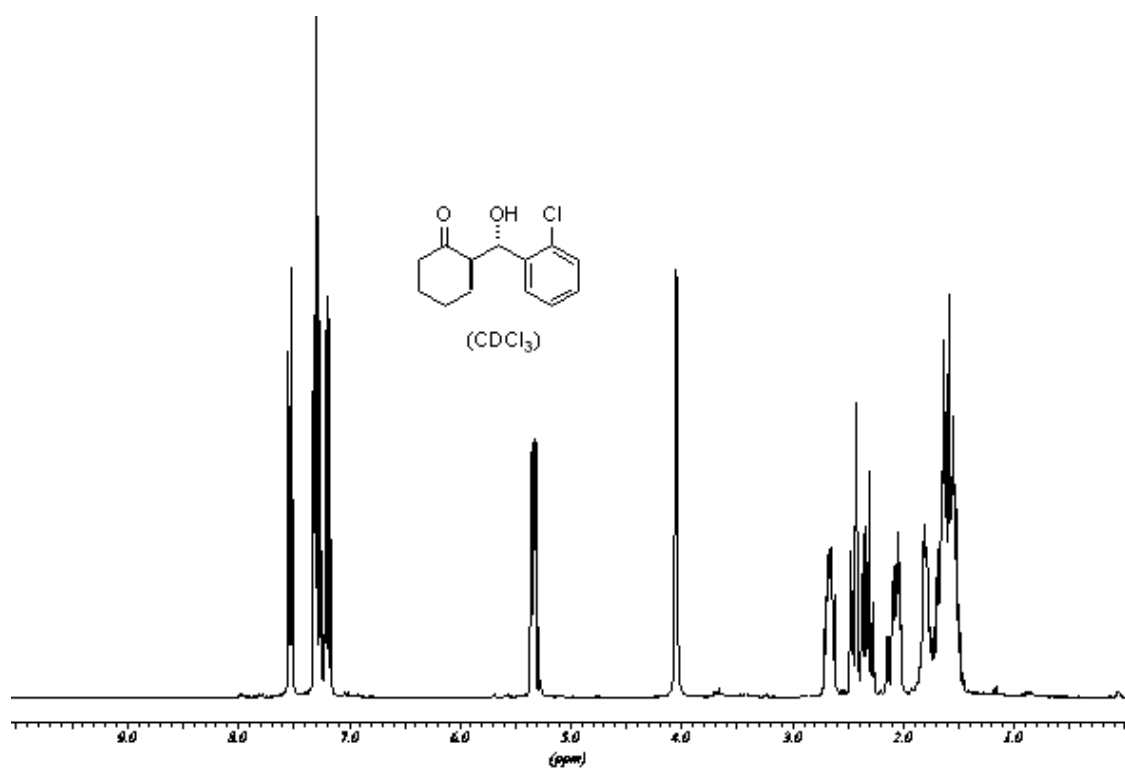
===== CHANNEL f1 =====
NUC1       131
P1         7.80 usec
PL         1.00 dB
SFO1       300.1315007 MHz

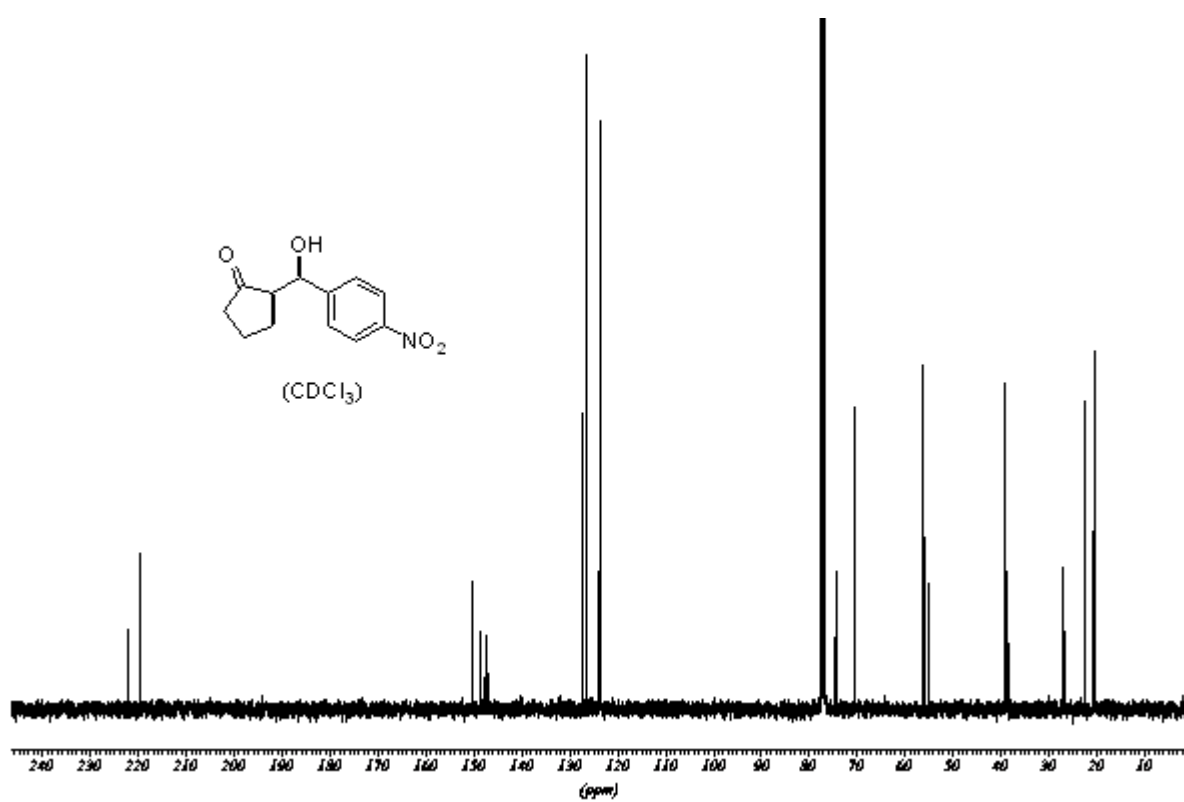
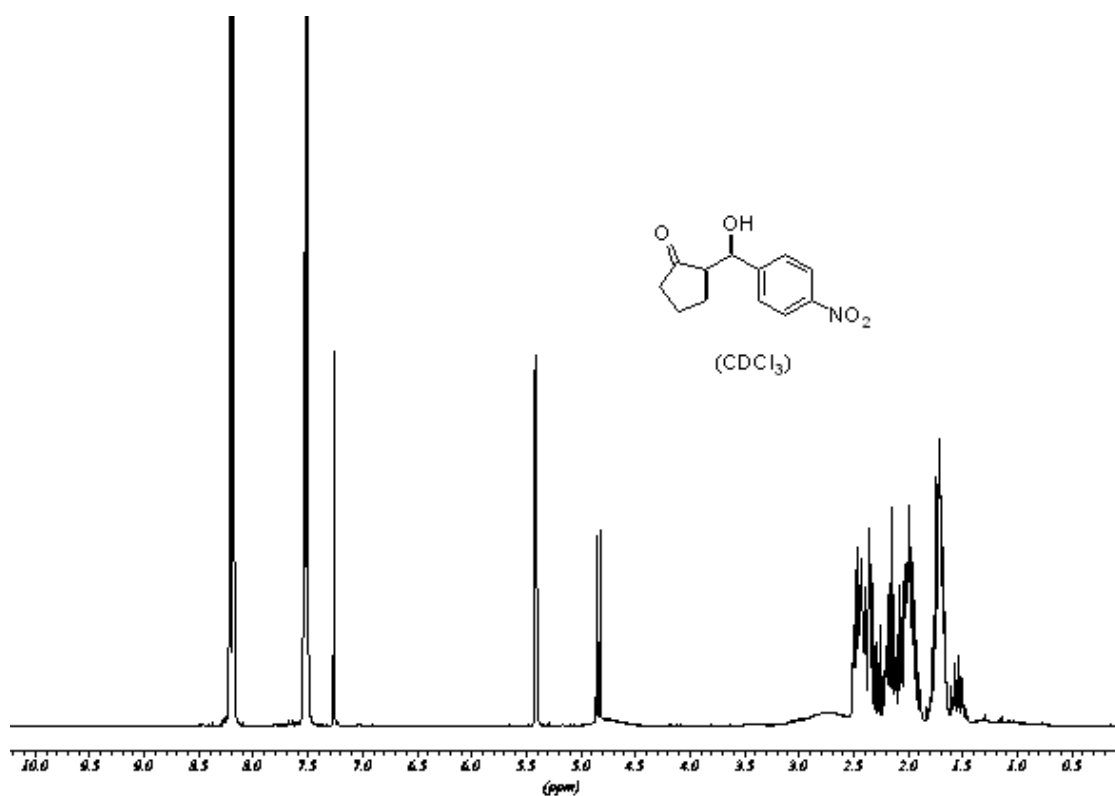
F2 - Processing parameters
SI         32768
SF         300.1300121 MHz
WDW        EM
SSB        0
GB         0
PC         1.00
  
```

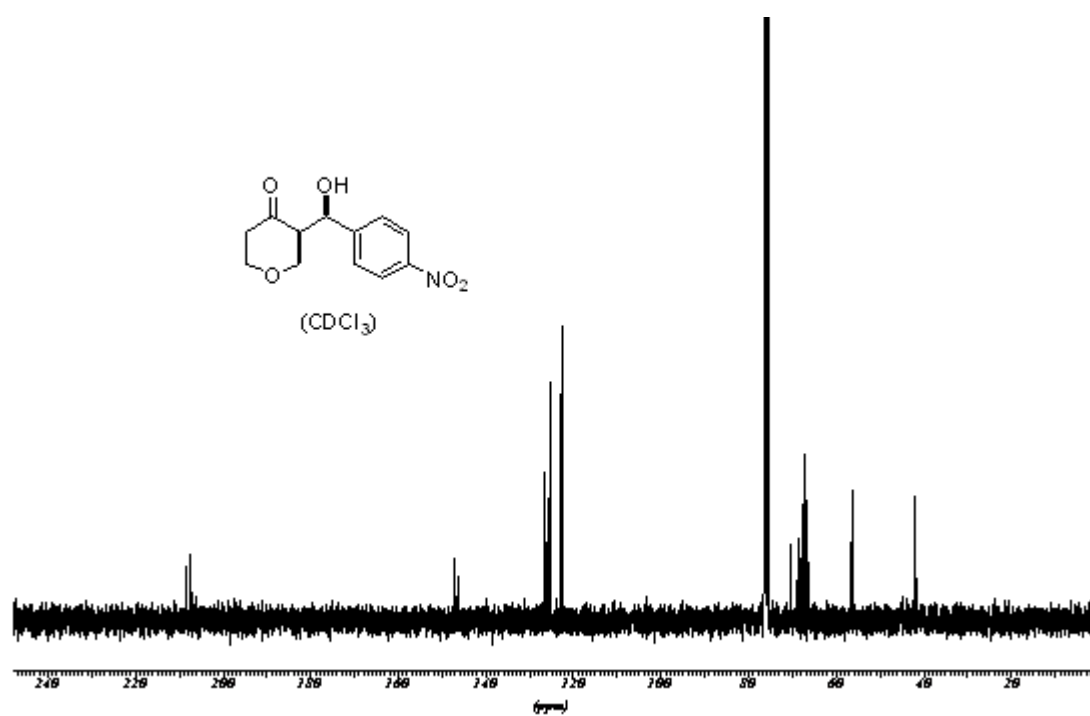
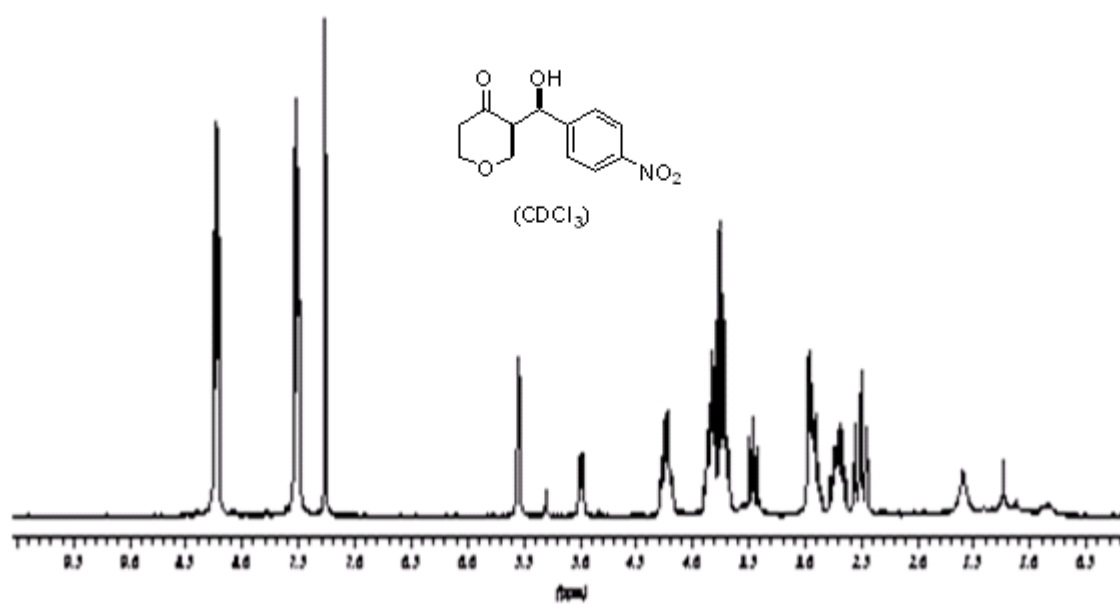


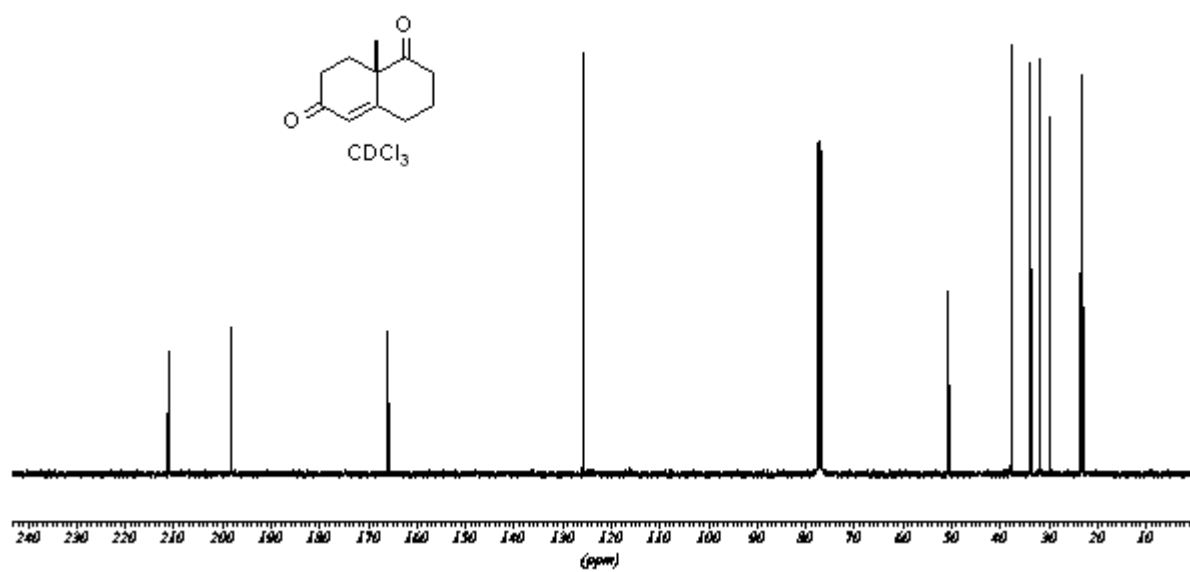
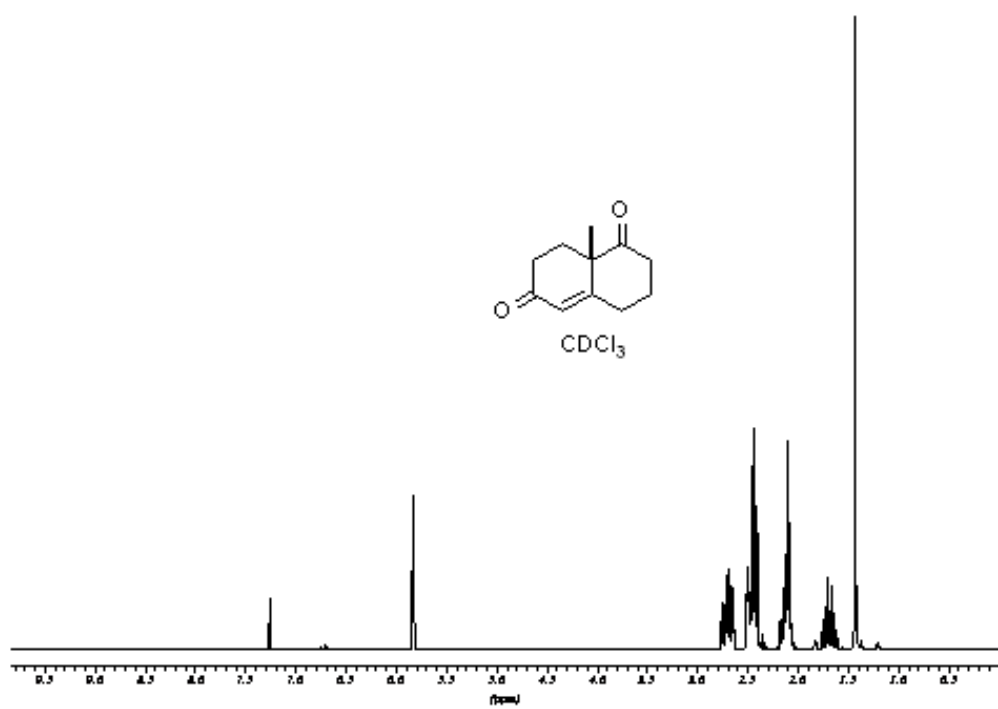


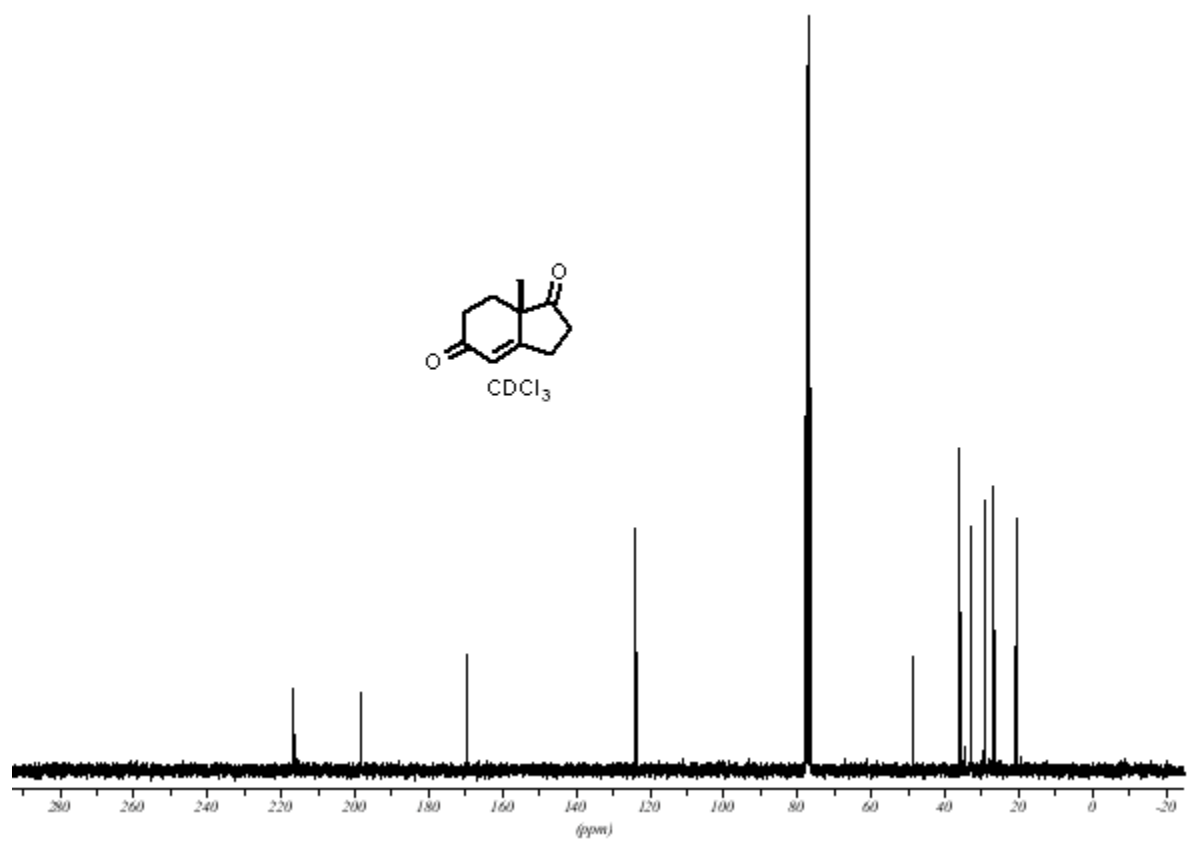
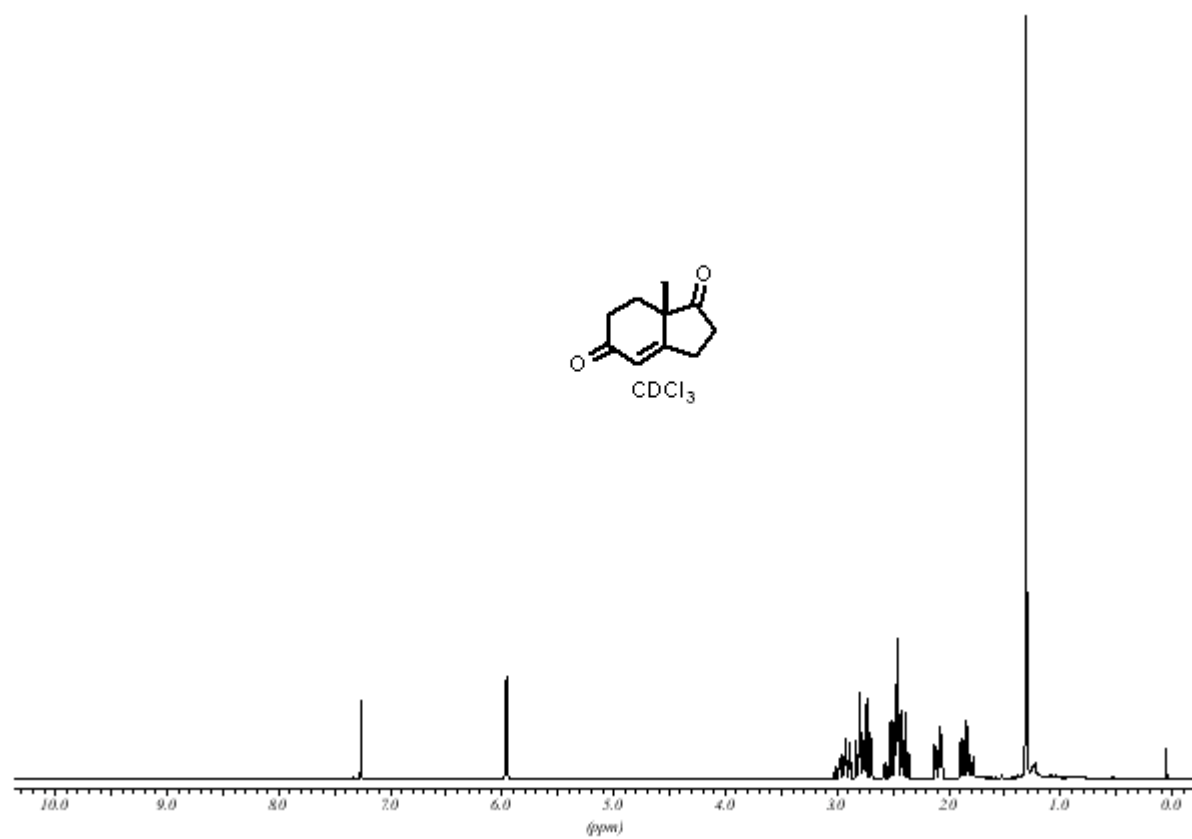




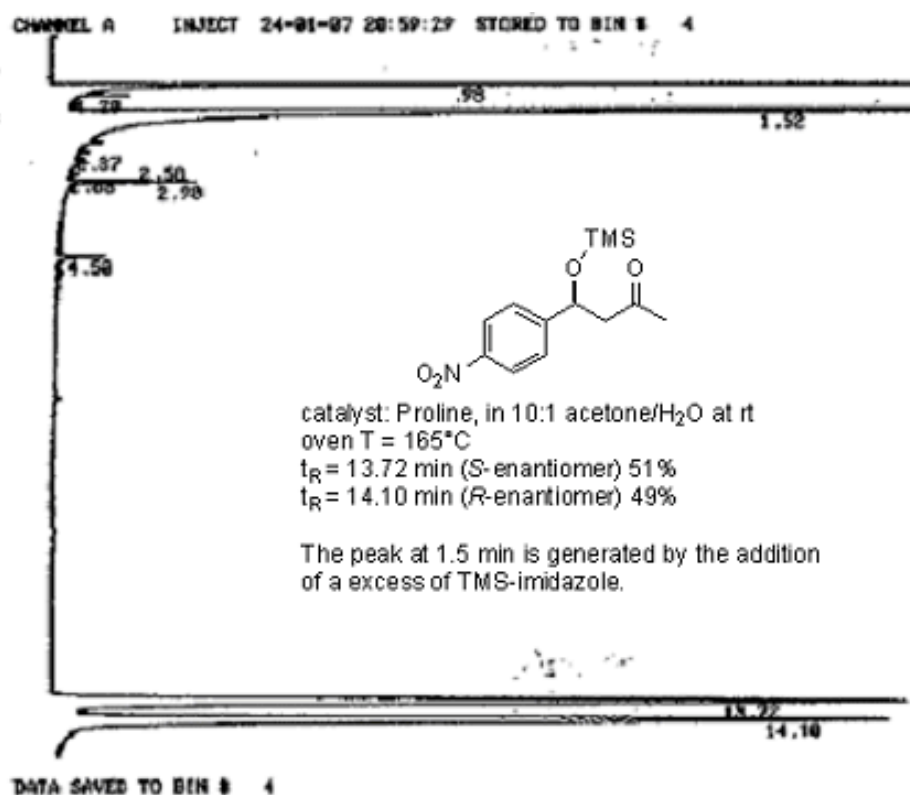








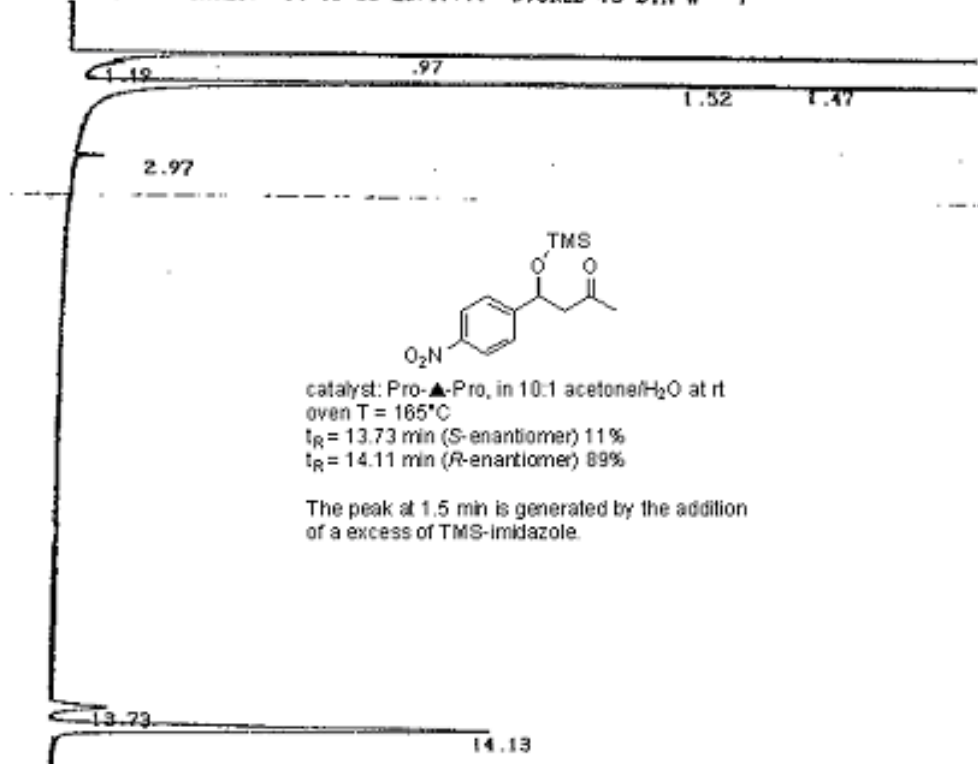
Copies of GC and HPLC chromatograms



24-01-97 20:59:29 CH= "A" PS= 1.

FILE 1.	METHOD 0.	RUN 4	INDEX 4	BIN 4
PEAK#	AREA	RT	AREA	BC
1	07.451	0.96	589207	02
2	0.037	1.2	246	03
3	0.1	1.52	54579	01
4	0.005	2.37	33	01
5	0.01	2.50	66	01
6	0.000	2.63	56	01
7	0.185	2.98	710	01
8	0.04	4.5	267	01
9	0.006	7.4	40	01
10	2.179	13.72	14603	02
11	2.06	14.1	13879	03
TOTAL	100.		670048	

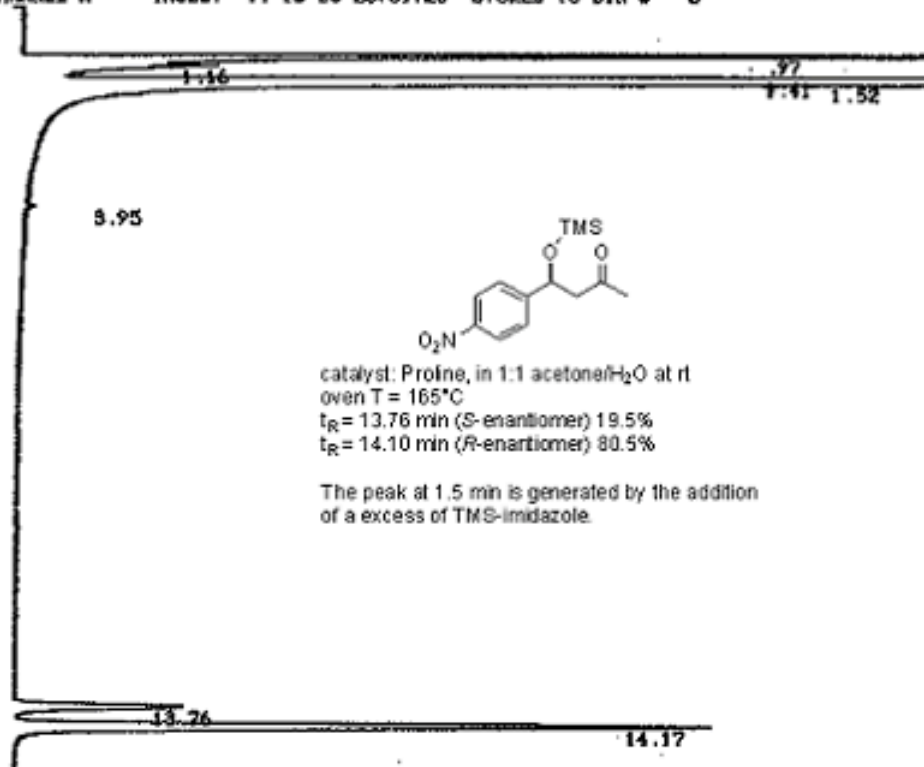
CHANNEL A INJECT 14-10-06 20:17:11 STORED TO BIN # 1



DATA SAVED TO BIN # 1

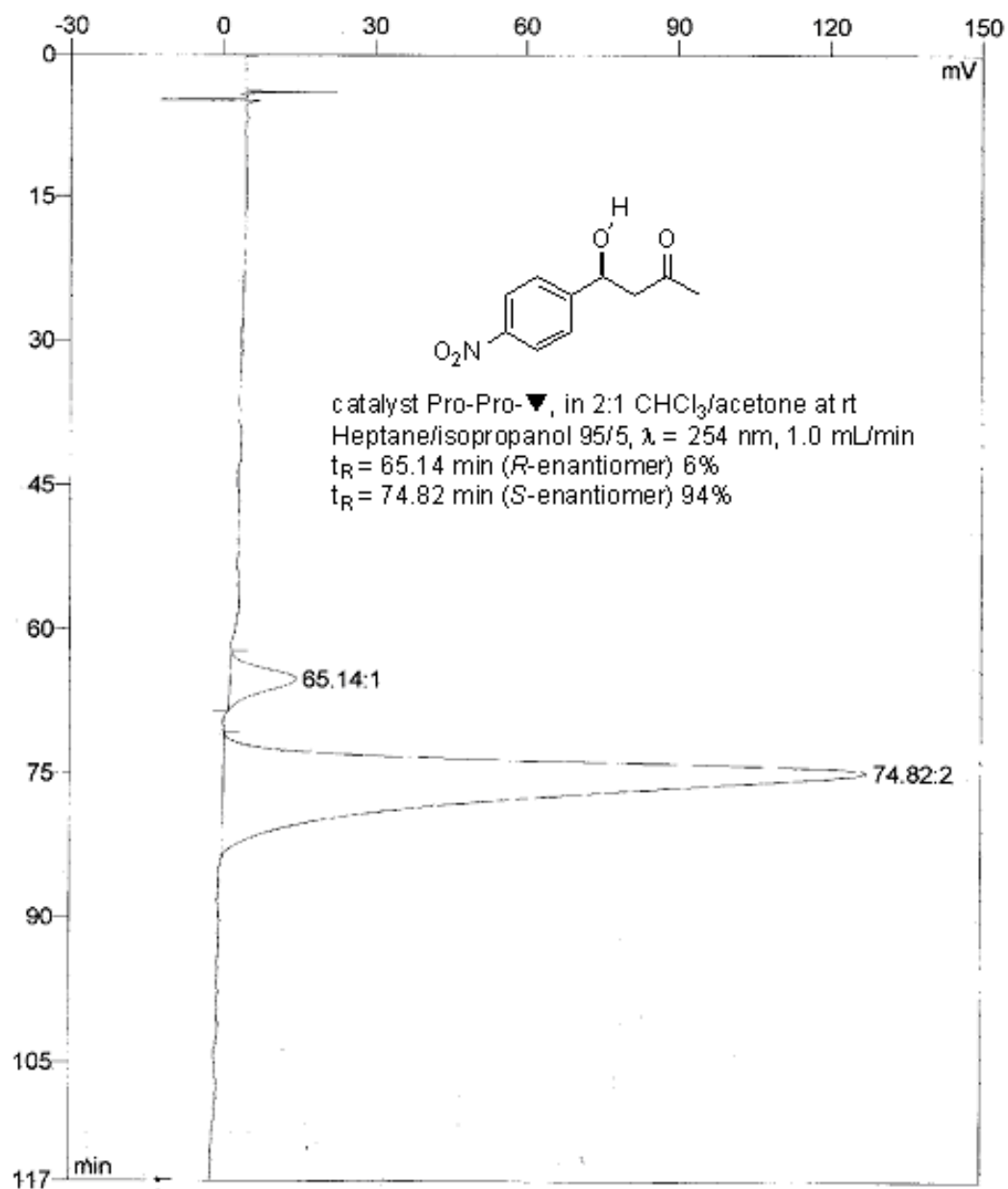
14-10-06 20:17:11				CH= "A"	PS= 1.
FILE 1.	METHOD 0.	RUN 1	INDEX 1	BIN 1	
PEAK#	AREA%	RT	AREA BC		
1	90.697	0.97	276971 02		
2	0.286	1.19	874 02		
3	0.021	1.47	63 02		
4	6.52	1.52	19910 08		
5	0.042	2.97	128 01		
6	0.262	13.73	801 01		
7	2.172	14.13	6632 01		
TOTAL	100.		305379		

CHANNEL A INJECT 14-10-06 20:51:26 STORED TO BIN # 3

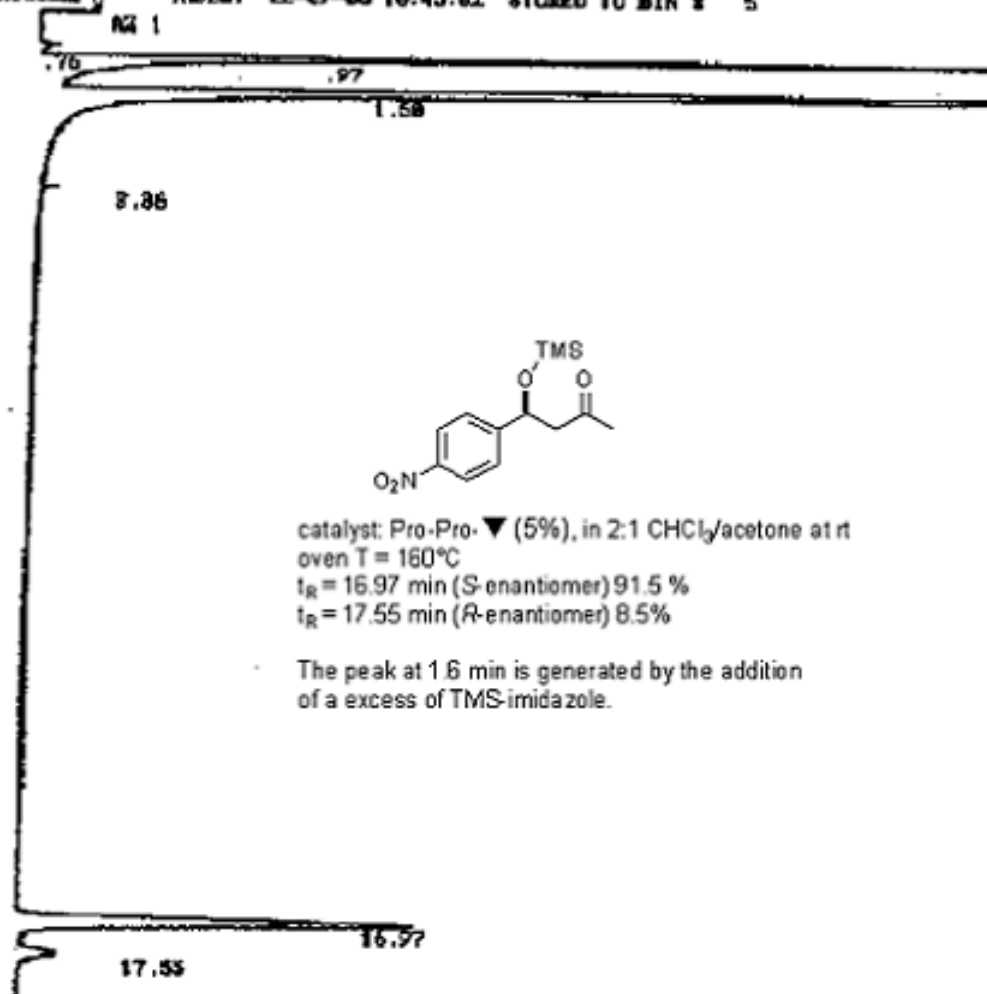


DATA SAVED TO BIN # 3

14-10-06 20:51:26				CH= "A"	PS= 1
FILE 1.	METHOD 0.	RUN 3	INDEX 3	BIN 3	
PEAK#	AREAX	RT	AREA BC		
1	98.284	0.97	1205135 02		
2	0.185	1.16	2468 02		
3	3.543	1.41	47287 02		
4	4.999	1.52	66732 03		
5	0.003	3.95	35 01		
6	0.191	13.76	2555 02		
7	0.795	14.17	10610 03		
TOTAL	100		1334822		



CHANNEL 8 INJECT 22-29-86 10:45:02 STORED TO BIN 5

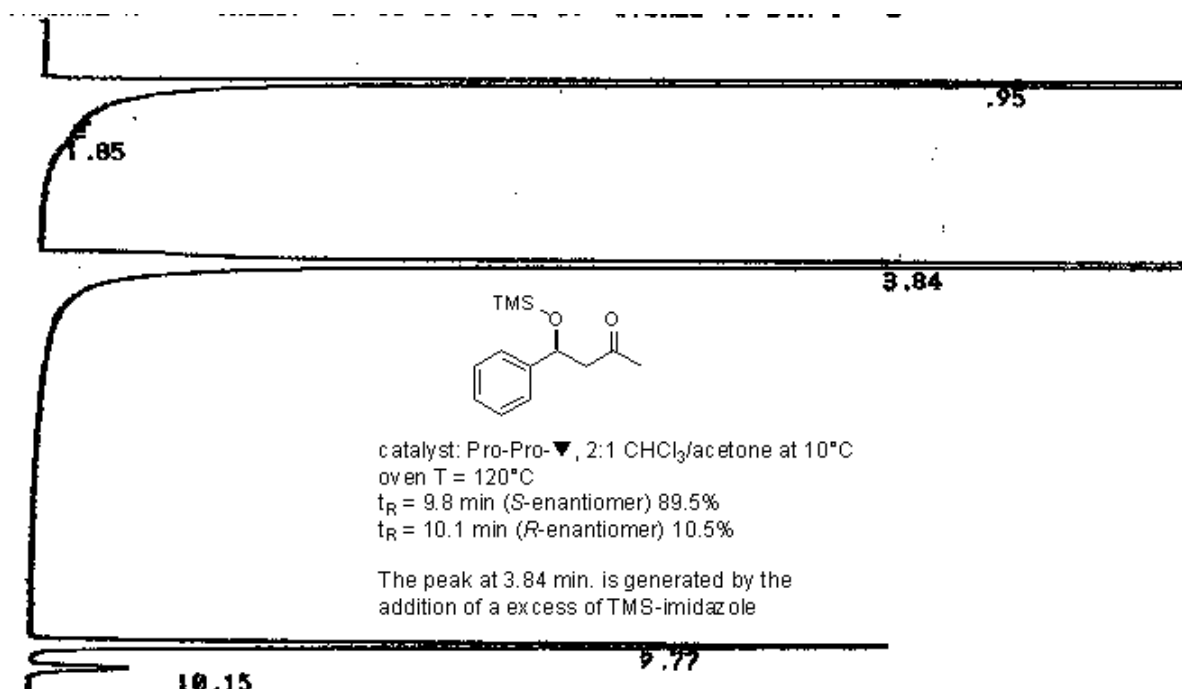


catalyst: Pro-Pro- ∇ (5%), in 2:1 CHCl_3 /acetone at rt
oven $T = 160^\circ\text{C}$
 $t_R = 16.97$ min (S-enantiomer) 91.5 %
 $t_R = 17.55$ min (R-enantiomer) 8.5%

The peak at 1.6 min is generated by the addition of a excess of TMS-imidazole.

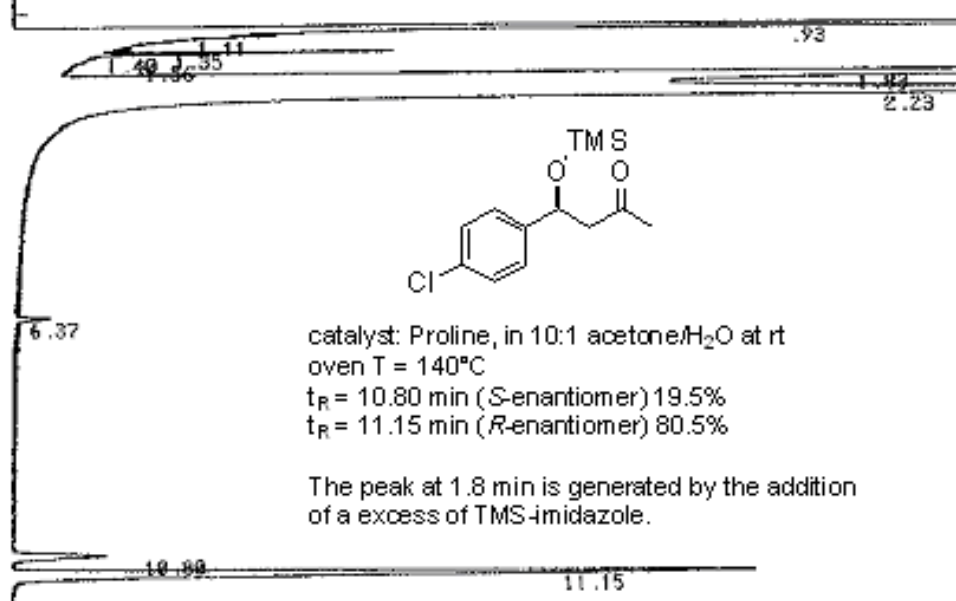
DATA SAVED TO BIN 5

22-29-86 10:45:02					
FILE 1. METHOD 8. RUN 5 INDEX 5					
PEAK#	AREA	RT	AREA DC	BIN	5
1	0.013	0.76	118 02		
2	94.990	0.97	630450 02		
3	4.122	1.58	36478 03		
4	0.000	3.36	75 01		
5	0.775	16.97	6030 01		
6	0.073	17.55	645 01		
TOTAL	100.		882595		



27-10-06 10:25:31				CH= "A" PS= 1.	
FILE 1.	METHOD 0.	RUN 8	INDEX 3	BIN	P
PEAKS	AREAX	RT	AREA.BC		
1	96.176	0.95	900328	01	
2	0.804	1.05	41	01	
3	2.098	3.84	27133	01	
4	0.824	9.77	7712	01	
5	0.098	10.15	916	01	
TOTAL	100.		936130		

CHANNEL A INJECT 21-11-06 18:19:28 STORED TO BIN # 3



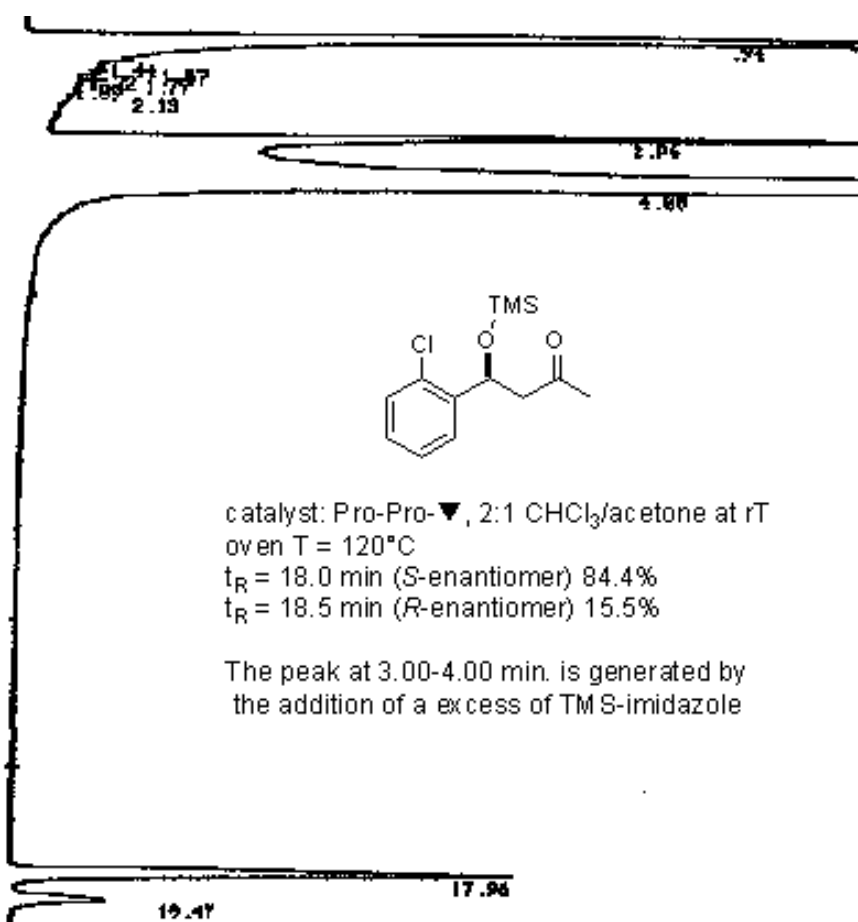
DATA SAVED TO BIN # 3

21-11-06 18:19:28

FILE 1. METHOD 0. RUN 3 INDEX

PEAK#	AREA%	RT	AREA BC
1	89.592	0.93	1433966 02
2	0.264	1.11	4221 02
3	0.027	1.35	429 02
4	0.221	1.4	3536 00
5	0.001	1.56	9 05
6	3.108	1.83	49743 02
7	6.159	2.23	98580 03
8	0.014	6.37	228 01
9	0.061	10.8	978 01
10	0.554	11.15	8870 01

TOTAL 100. 1600560

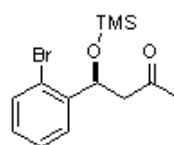
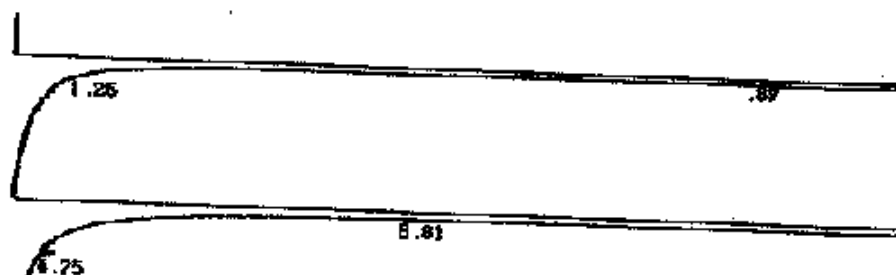


catalyst: Pro-Pro- \blacktriangledown , 2:1 CHCl_3 /acetone at rT
 oven T = 120°C
 t_R = 18.0 min (S-enantiomer) 84.4%
 t_R = 18.5 min (R-enantiomer) 15.5%

The peak at 3.00-4.00 min. is generated by
 the addition of a excess of TMS-imidazole

07-11-06 18:07:12 CH- "A" PS- 1.

FILE 1.	METHOD 0.	NAME 0	INDEX 0	RTN 0
PEAK#	AREA#	RT	AREA BC	
1	90.87	0.94	155825 02	
2	9.879	1.44	1062 02	
3	0.049	1.57	1271 02	
4	0.783	1.72	569 02	
5	0.030	1.77	715 02	
6	0.008	1.89	1476 02	
7	0.14	2.12	2505 02	
8	0.321	2.96	16953 02	
9	7.882	4.	145113 03	
10	0.364	17.96	10405 01	
11	0.305	19.47	1927 01	
TOTAL	182.		1841824	



catalyst: Pro-Pro- ∇ , 2:1 CHCl_3 /acetone at 0°C
 oven $T = 130^\circ\text{C}$
 $t_R = 24.0$ min (*S*-enantiomer) 91%
 $t_R = 24.6$ min (*R*-enantiomer) 9%

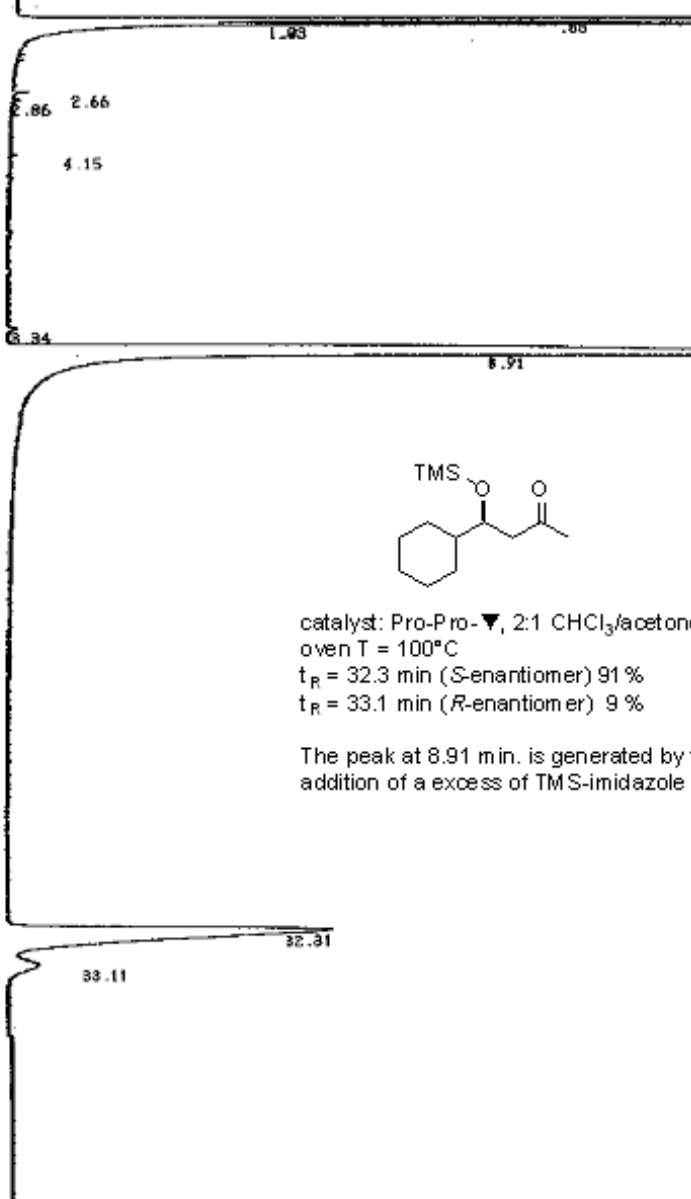
The peak at 3.81 min. is generated by
 the addition of a excess of TMS-imidazole

PEAK#	AREA%	RT	AREA	BC
1	93.506	0.09	792009	02
2	0.424	1.25	3595	03
3	5.559	3.81	47005	02
4	0.065	4.75	551	03
5	0.369	23.96	3129	01
6	0.037	24.56	314	01

DATA SAVED TO BIN 4 1

TOTAL 100.

INEL A INJECT 16-06-86 20:02:39 STORED TO BIN # 3



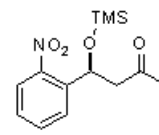
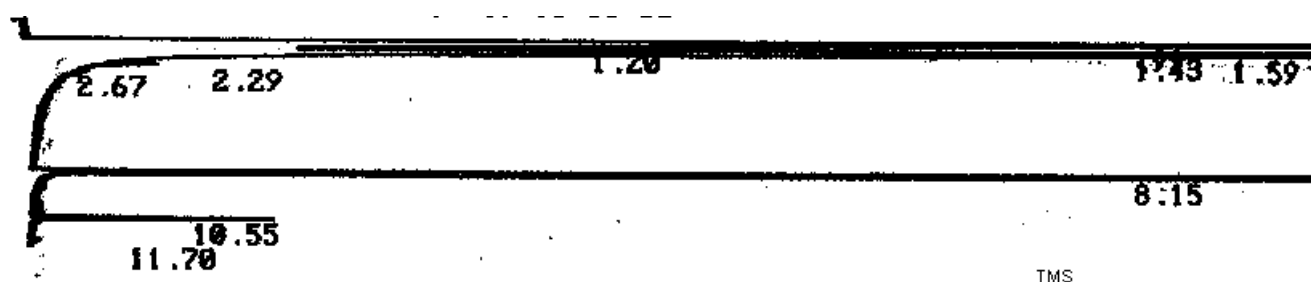
catalyst: Pro-Pro- ∇ , 2:1 CHCl_3 /acetone at rT
 oven T = 100°C
 t_R = 32.3 min (S-enantiomer) 91 %
 t_R = 33.1 min (R-enantiomer) 9 %

The peak at 8.91 min. is generated by the
 addition of a excess of TMS-imidazole

DATA SAVED TO BIN # 3

16-06-86 20:02:39

FILE	1.	METHOD	0.	RUN	3	INDEX	3
PEAK#	AREA	RT	AREA	BC			
1	94.441	0.88	1086699	02			
2	0.08	1.03	10129	03			
3	0.009	2.66	98	01			
4	0.004	2.86	45	01			
5	0.003	4.15	36	01			
6	0.007	8.34	79	01			
7	2.908	8.91	34383	01			
8	1.518	32.31	17466	02			
9	0.15	33.11	1724	03			
TOTAL	100.		1150659				



INPUT OVERRANGE AT RT= 0.99

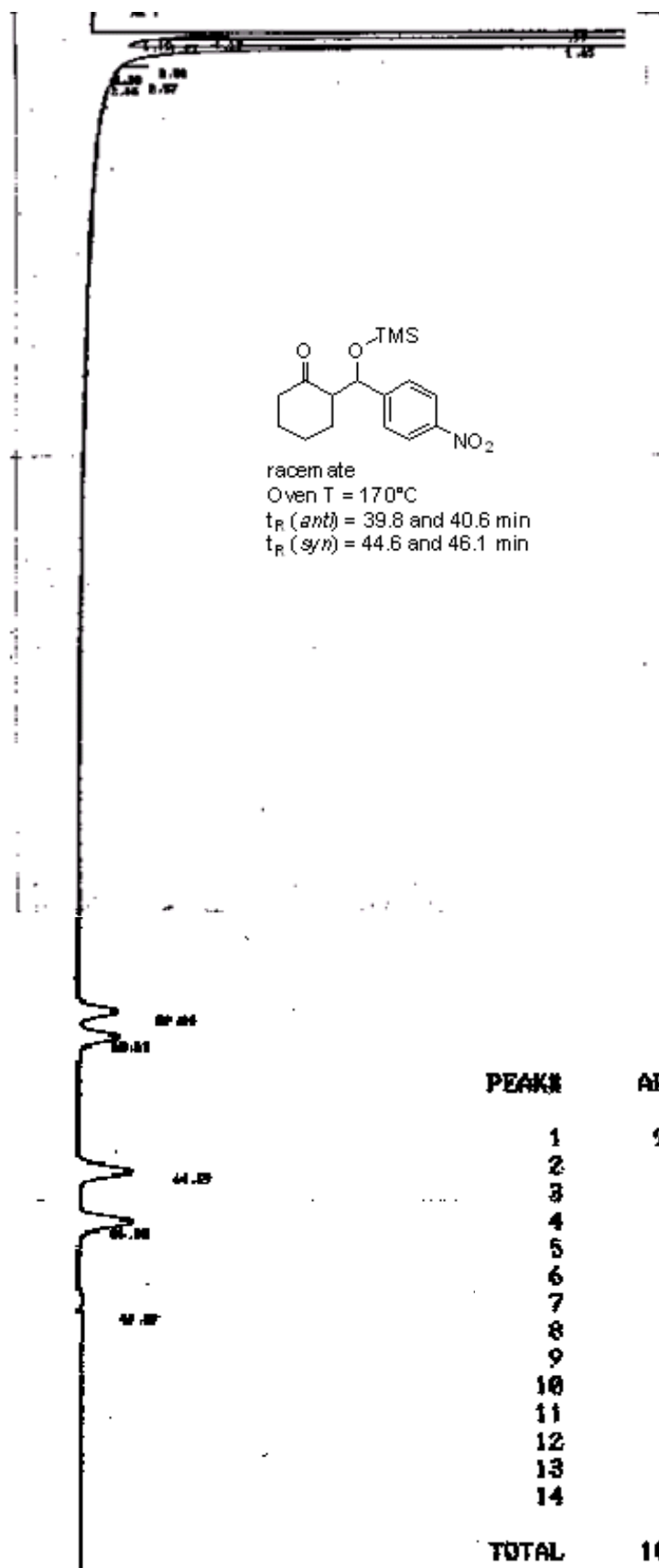
catalyst: Pro- Δ -Pro, 10:1 acetone/H₂O at rT
oven T = 160°C
t_R = 8.15 min (S-enantiomer) 95.5%
t_R = 10.5 min (R-enantiomer) 4.5%

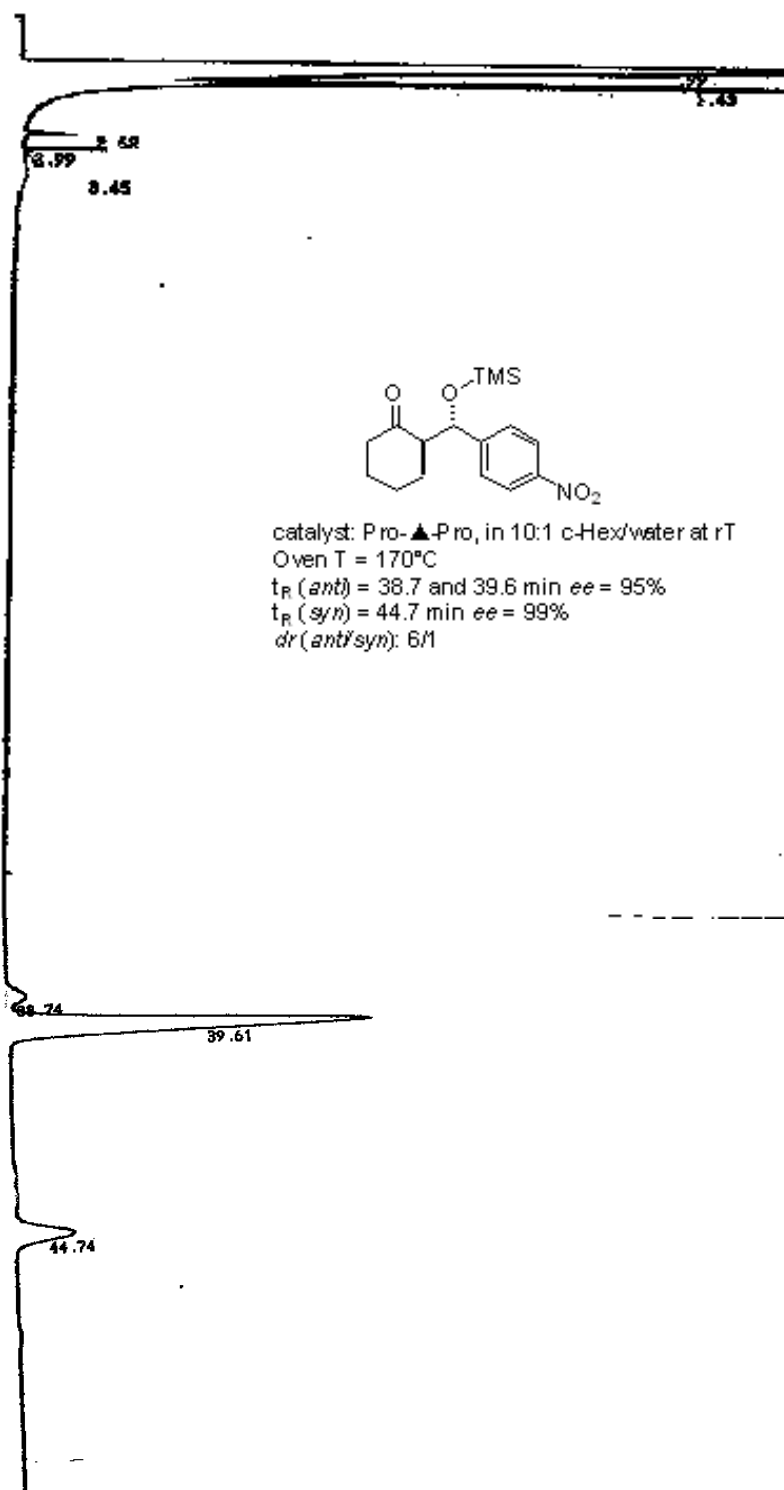
14-12-07 15:53:53

The peak at 1.59 min. is generated by
the addition of a excess of TMS-imidazole

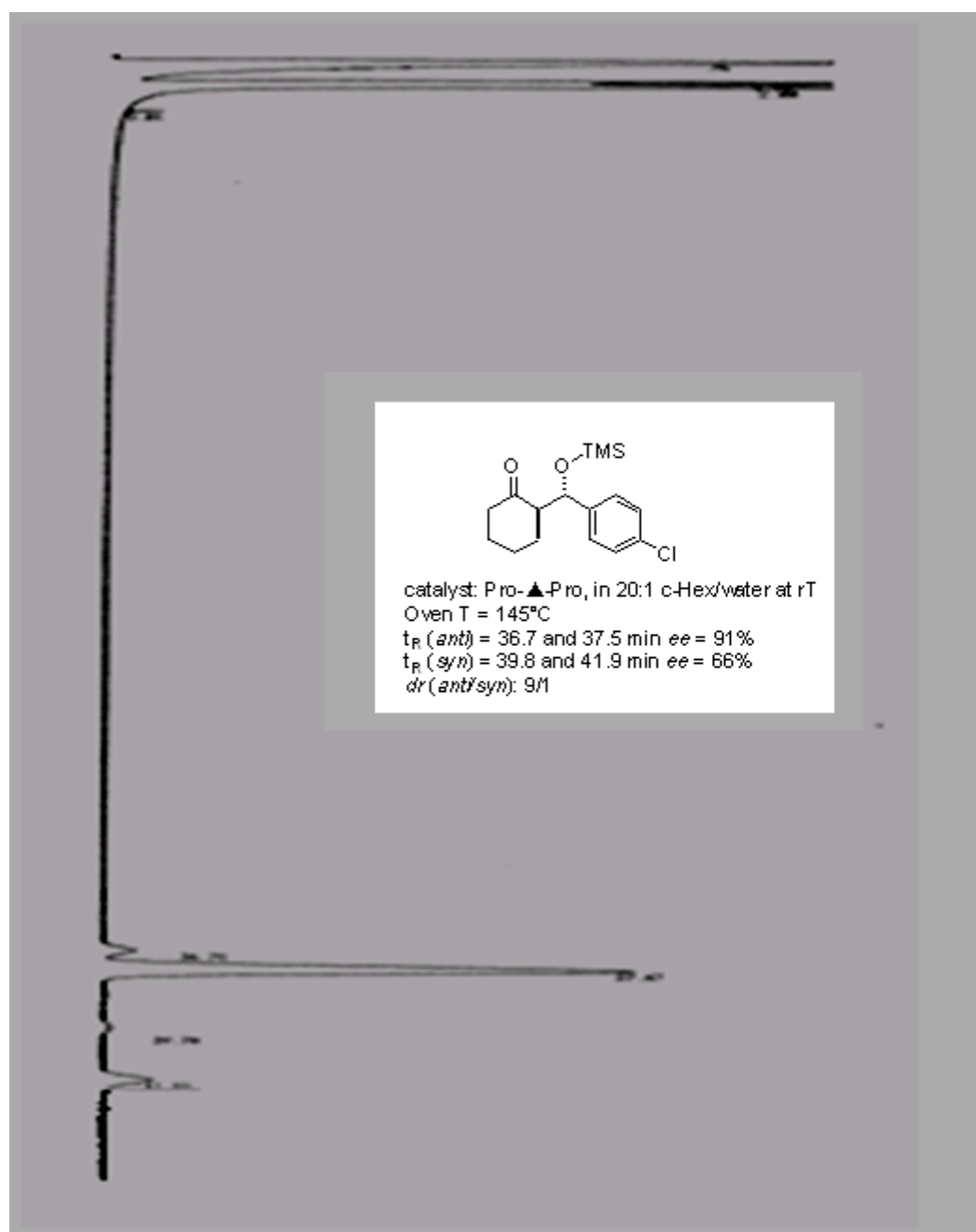
FILE 1. METHOD 0. RUN 6 INDEX 6

PEAK#	AREA%	RT	AREA	BC
1	85.166	0.99	1618820	02
2	0.398	1.2	7557	02
3	7.155	1.43	136005	02
4	4.959	1.59	94252	02
5	0.04	2.29	767	03
6	0.001	2.67	24	01
7	2.176	8.15	41368	01
8	0.1	10.55	1902	01
9	0.004	11.7	78	01

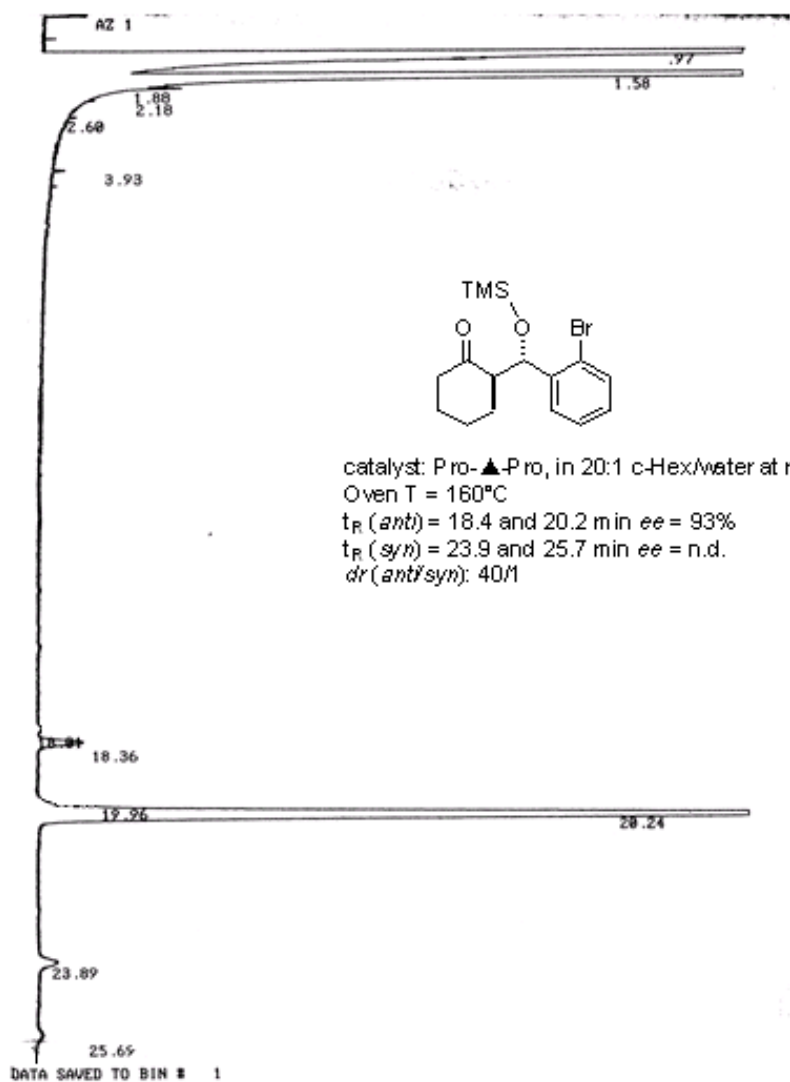




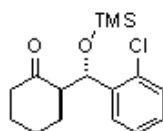
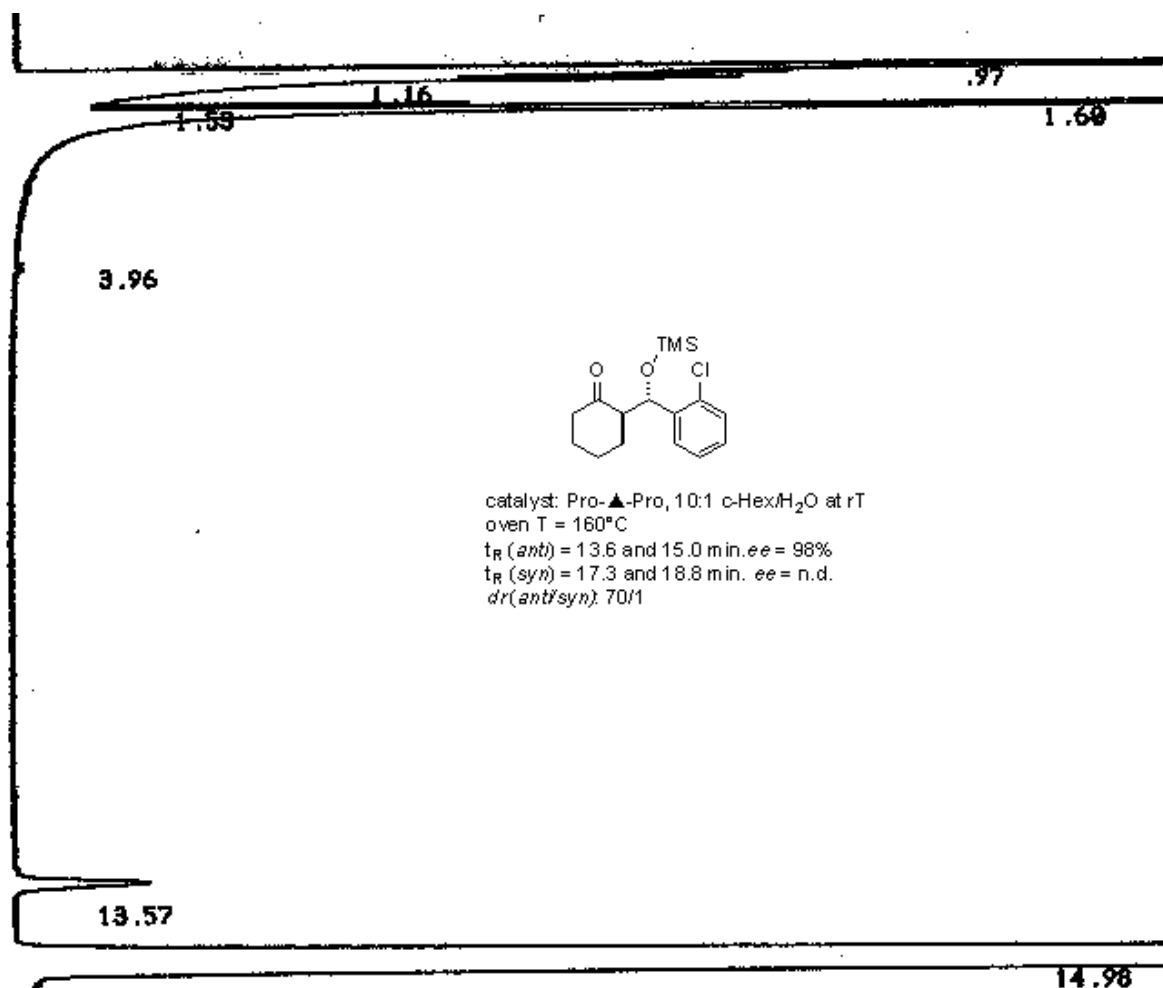
PEAKS	AREA X	RT	AREA BC
1	92.016	0.99	640185 02
2	3.955	1.43	27515 03
3	0.082	2.62	568 01
4	0.078	2.99	543 01
5	0.149	3.45	1040 01
6	0.155	38.74	1077 02
7	3.031	39.61	21007 03
8	0.535	44.74	3720 01



PEAK#	AREA%	RT	AREA	BC
1	95.085	0.96	1940578	02
2	0.751	1.79	15323	02
3	2.552	2.	52076	03
4	0.007	3.01	144	01
5	0.064	36.71	1310	02
6	1.383	37.47	28233	03
7	0.021	39.78	421	01
8	0.137	41.89	2803	01
TOTAL	100.		2040888	

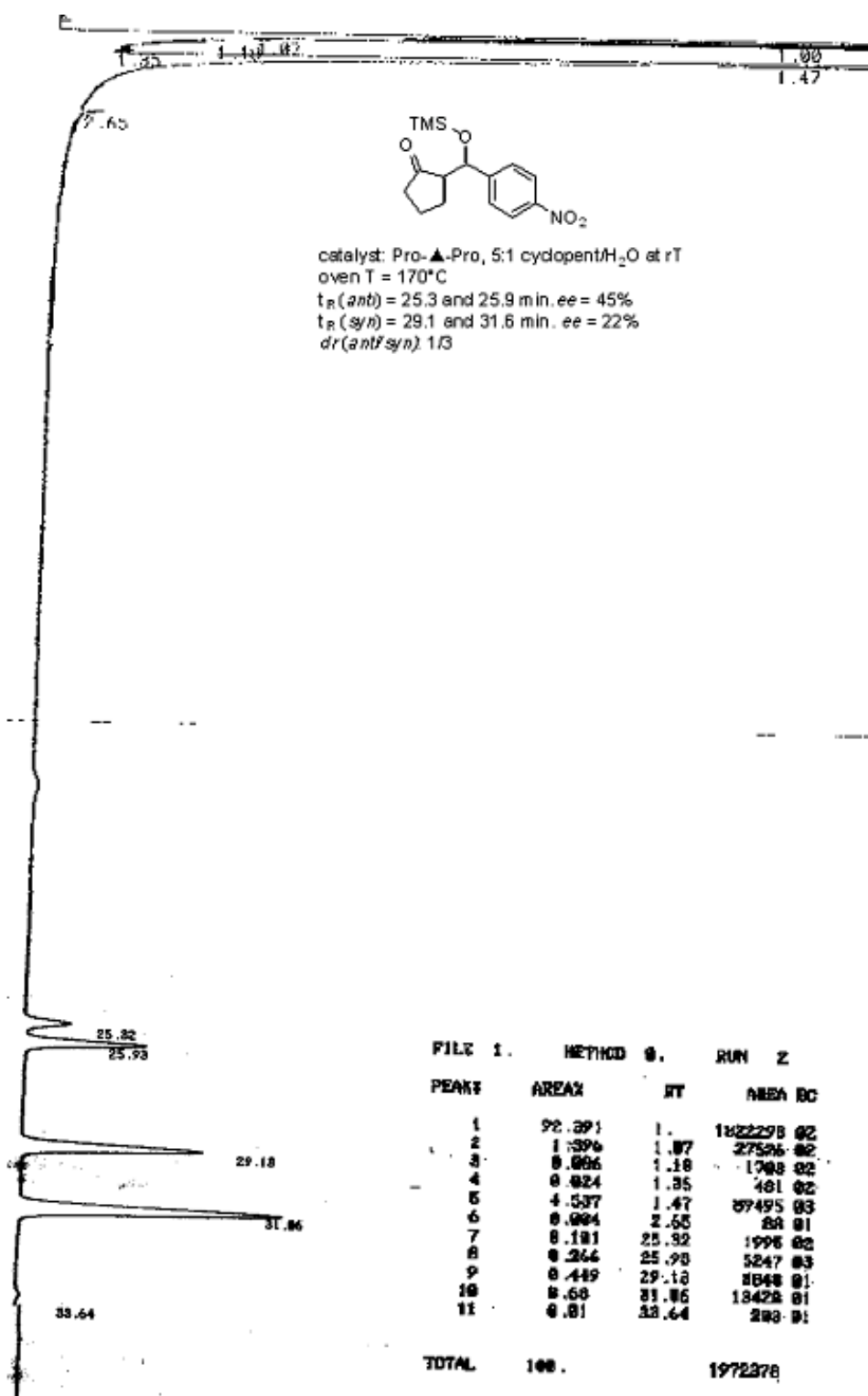


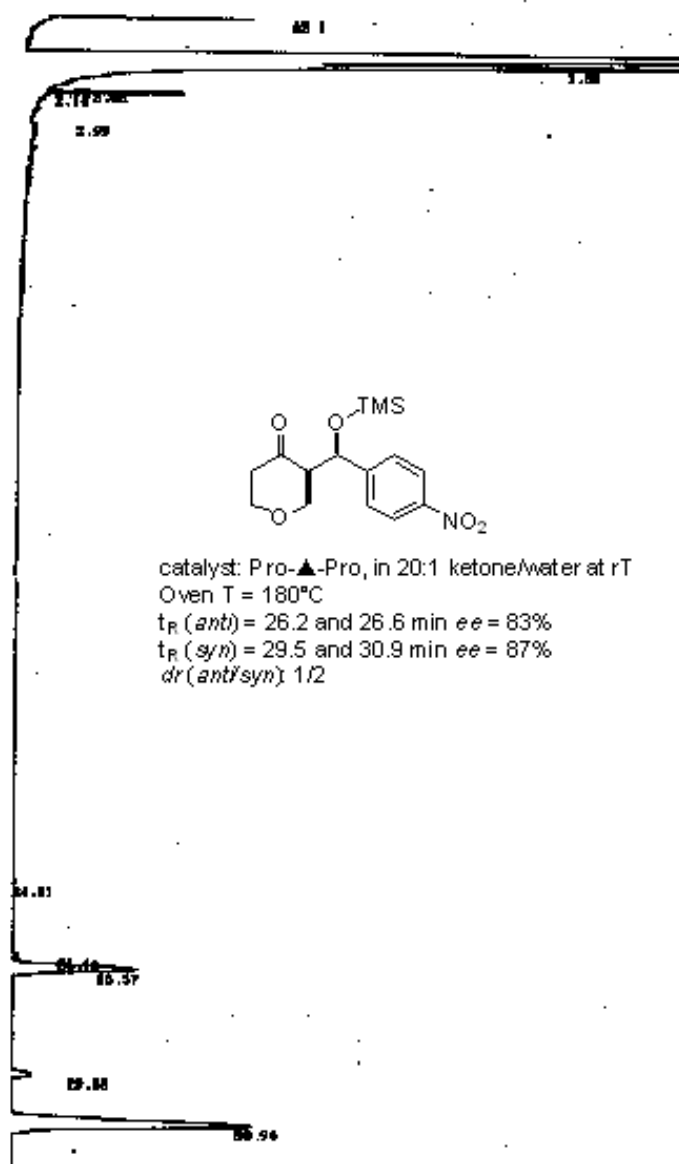
PEAK#	AREA%	RT	AREA BC
1	91.452	0.97	1740630 02
2	6.55	1.58	124678 02
3	0.154	1.88	2926 02
4	0.055	2.18	1039 02
5	0.007	2.6	126 03
6	0.004	3.93	75 01
7	0.007	18.01	127 02
8	0.062	18.36	1186 03
9	0.06	19.96	1141 02
10	1.609	20.24	30628 03
11	0.031	23.89	585 01
12	0.01	25.69	195 01
TOTAL	100.		1903336



catalyst: Pro- Δ -Pro, 10:1 c-Hex:H₂O at rT
oven T = 160°C
 t_R (anti) = 13.6 and 15.0 min. ee = 98%
 t_R (syn) = 17.3 and 18.8 min. ee = n.d.
dr(anti/syn): 70/1

PEAK#	AREAX	RT	AREA BC
1	85.14	0.97	1418437 02
2	0.518	1.16	8553 02
3	0.07	1.53	1169 02
4	3.186	1.6	53873 03
5	0.001	3.96	13 01
6	0.11	13.57	1836 01
7	10.814	14.98	180167 01
8	0.15	17.29	2494 01
9	0.007	18.77	120 01
TOTAL	100.		1666889



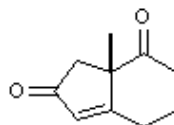


PEAK#	AREA%	RT	AREA	BC
1	93.498	0.99	1632826	02
2	5.284	1.31	92278	02
3	0.024	1.92	420	02
4	0.006	2.02	110	02
5	0.055	2.14	965	03
6	0.001	2.99	14	01
7	0.023	24.11	403	01
8	0.025	26.18	438	02
9	0.315	26.57	5507	03
10	0.066	29.53	1145	01
11	0.703	30.94	12269	01
TOTAL	100.		1746375	

CHANNEL A INJECT 07-05-07 20:09:29 STORED TO BIN # 5

1.23
1.71
2.17

0.97



catalyst: Pro- Δ -Pro, in CHCl_3 at rT
oven T = 155°C
 t_R = 6.22 min (*R*-enantiomer) 8.5%
 t_R = 6.56 min (*S*-enantiomer) 91.5%

5.57

6.22

6.56

07-05-07 20:09:29

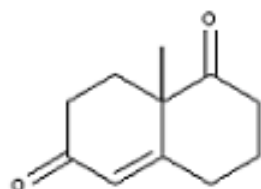
CH= "A" IS= 1.

FILE 1.	METHOD 0.	RUN 5	INDEX 5	BIN #
PEAKS	AREAX	RT	AREA BC	
1	96.265	0.97	498812 02	
2	0.183	1.23	949 03	
3	0.004	1.71	19 01	
4	0.039	2.17	201 01	
5	0.009	5.57	47 01	
6	0.276	6.22	1430 01	
7	2.805	6.56	14933 01	

CHANNEL A INJECT 21-12-86 14:39:54 STORED TO BIN 8. - 1

1.57 1.30 .96

2.22



Cat: Proline in CHCl_3 at r.t. after 24h

Oven T=140°C, Injector T=250°C, Detector T=250°C

rt = 11.19 min. starting material

rt = 21.53 min. (R-enantiomer) 21.5%

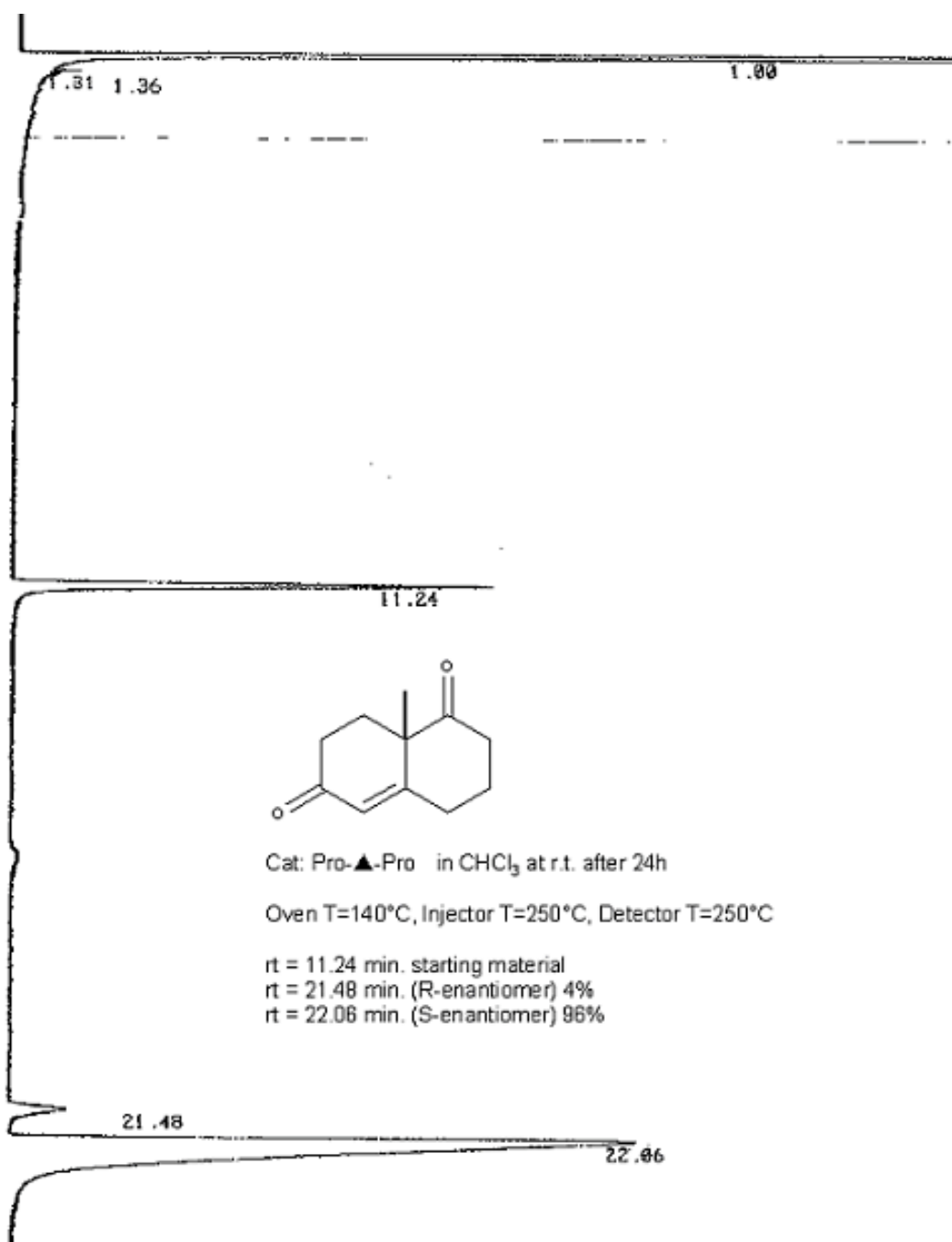
rt = 22.45 min. (S-enantiomer) 78.5%

11.19

21.53

22.45

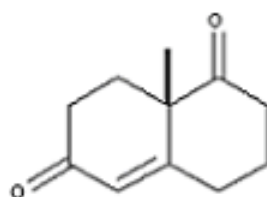
ET 0



CHANNEL A INJECT 09-01-07 19:19:43 STORED TO BIN # 6

1.31
1.31
1.86

.97



Cat: Pro- Δ -Pro in CHCl_3 at r.t. isolated after 3 days

Oven T=140°C, Injector T=250°C, Detector T=250°C

rt = 21.65 min. (R-enantiomer) 4%

rt = 22.49 min. (S-enantiomer) 96%

21.65

22.49