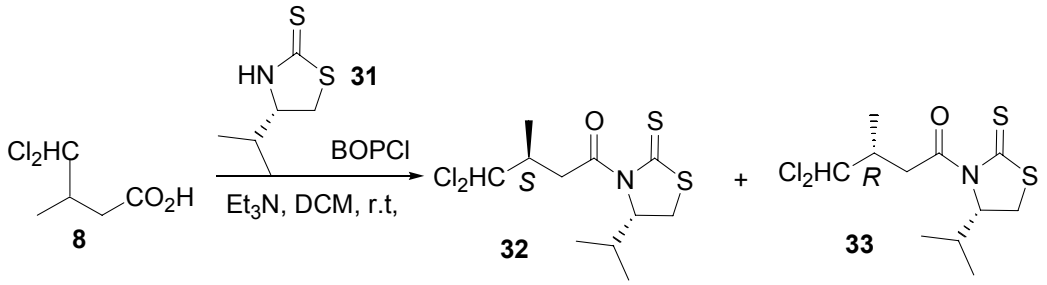
**Synthesis of Dysideaproline using Organocatalysis**

Ernest Owusu-Ansah, Amanda C. Durow, John R. Harding, Angela C. Jordan,
Susan J. O'Connell and Christine L. Willis*

**Supporting Information**

**Determination of the enantiopurity of the product from reduction of aldehyde 18.**



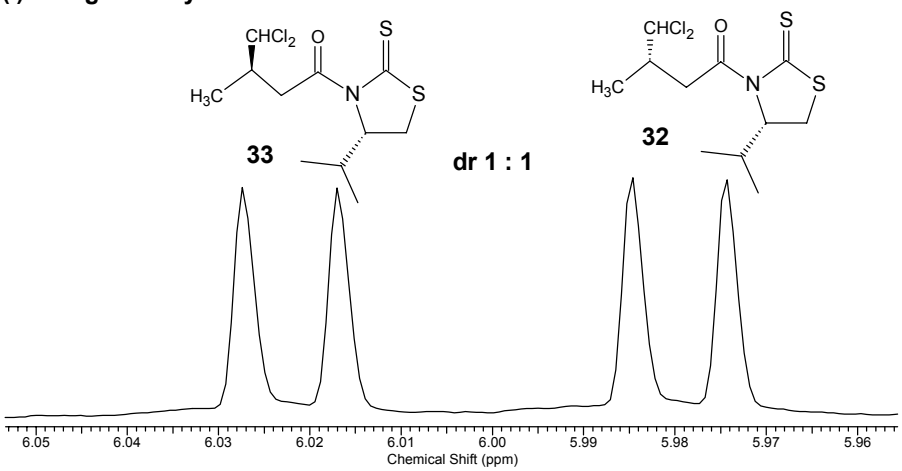

**Using acid 8 derived from the imidazolidinone catalysed reaction** Thiazolidinethione **31** (0.092 g, 0.44 mmol, 1.5 eq), prepared as described previously,[1] and bis(2-oxo-3-oxazolidinyl)phosphinic chloride (0.074 g, 0.29 mmol) were suspended in dry DCM (10 ml) under nitrogen. 4,4-Dichloro-3-methylbutanoic acid **8** (0.050 g, 0.29 mmol) and triethylamine (0.1 ml, 0.58 mmol, 2.5 eq) were added to the resulting mixture stirred for 24 h at room temperature. The solvent was removed *in vacuo* and the residue purified by column chromatography eluting with 5 % EtOAc in petrol. Diastereomer **32** (0.075 g, 83 %, dr *ca* 18:1) was isolated as a bright yellow oil; $[\alpha]_D^{23}$ + 24.7 (*c* 1, $CHCl_3$); $\nu_{max}/cm^{-1}$ 2986, 1762, 1155; $\delta_H$ (400 MHz, $CDCl_3$), 1.00 (3H, d, *J* 6.7, CHC*H*$_3$), 1.04 (3H, d, *J* 6.7, CHC*H*$_3$), 1.24 (3H, d, *J* 6.6, $CH_3$) 2.24 (1H, m, C*H*$(CH_3)_2$), 2.85 (1H, m, 3'-H), 3.14 (1H, br d, *J* 11.0, 9.2, 5-*H*H), 3.52 (1H, dd, *J* 18.0, 9.2, 2'-H*H*), 3.53 (2H, m, 2'-*H*H and 5-H*H*), 5.14 (1H, dd, J 7.6 and 6.8, 4-H), 5.98 (1H, d, *J* 3.1, $CHCl_2$); $\delta_C$ (100 MHz, $CDCl_3$), 15.1 ($CH_3$) 18.4 ($CH_3$), 18.9 ($CH_3$), 30.5 (C-2'), 41.5 (*C*H$(CH_3)_2$), 41.6 (C-5) 71.6 (C-4), 76.6 (C-4'), 178.1 (C-1') and 201.3 (C-2); *m/z* (CI) 318 (6 %), 316 (28 ), 314 (35, $MH^+$), 162 (100), $C_{11}H_{18}O^{35}Cl_2S_2$ requires 314.0206, found 314.0207.

1. D. Delaunay, L. Toupet, M. Le Corre *J. Org. Chem*., **1995**, *60*, 6604.

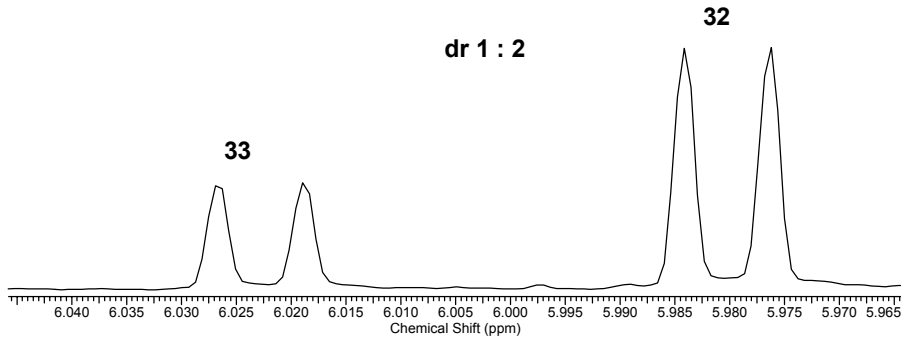
**Using acid 8 derived from the proline catalysed reaction** Thiazolidinethione **31** (0.205 g, 0.98 mmol, 1.5 eq) and bis(2-oxo-3-oxazolidinyl)phosphinic chloride (0.166 g, 0.65 mmol) were suspended in dry DCM (10 ml) under nitrogen. 4,4-Dichloro-3-methylbutanoic acid **8** (0.112 g, 0.65 mmol) and triethylamine (0.2 ml, 1.6 mmol, 2.5 eq) were added to the resulting mixture stirred for 24 h at room temperature. The solvent was removed *in vacuo* and the residue purified by column chromatography eluting with 5 % EtOAc in petrol. A mixture of **32** and **33** (0.199 g, 79 %, dr 2:1) was isolated as a bright yellow oil. The $^{1}$H-NMR spectrum showed signals at δ 5.98 (d, *J* 3.1) and δ 6 6.(d *J* 3.1) integrating *ca*. 2:1 (see figure).

**Using acid 8 derived from the dibenzylamine catalysed reaction** Thiazolidinethione **31** (0.22 g, 1.07 mmol, 1.5 eq) and bis (2-oxo-3-oxazolidinyl) phosphinic chloride (0.18 g, 0.7 mmol) were suspended in dry DCM (10 ml) under nitrogen. 4,4-Dichloro-3-methylbutanoic acid **8 (**from dibenzylamine catalyst) (0.122 g, 0.7 mmol) and triethylamine (0.3 ml, 1.75 mmol, 2.5 eq) were added to the resulting mixture stirred for 24 h at room temperature. The solvent was removed *in vacuo* and the residue purified by column chromatography eluting with 5 % EtOAc in petrol. A mixture of **32** and **33** (0.154 g, 70 %, dr 1:1) was isolated as a bright yellow oil. The $^{1}$H-NMR spectrum showed signals at δ 5.98 (d, *J* 3.1) and δ 6 6.(d *J* 3.1) integrating 1:1 (see figure).

**(i) Using dibenzylamine**




**(ii) Using proline**




**(iii) Using imidazolidinone 21**

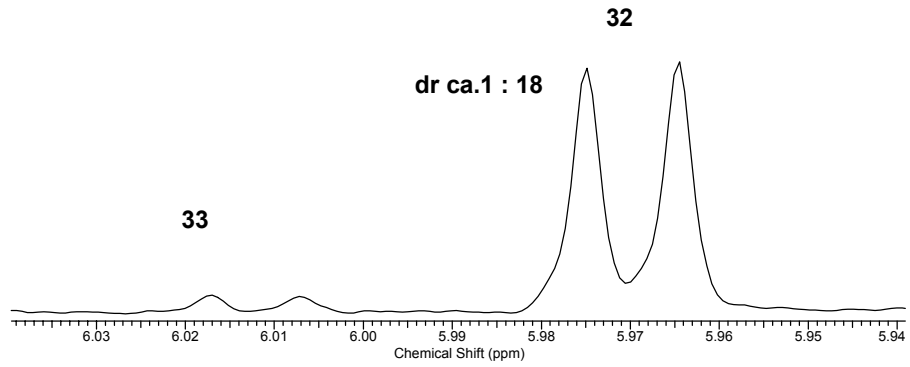
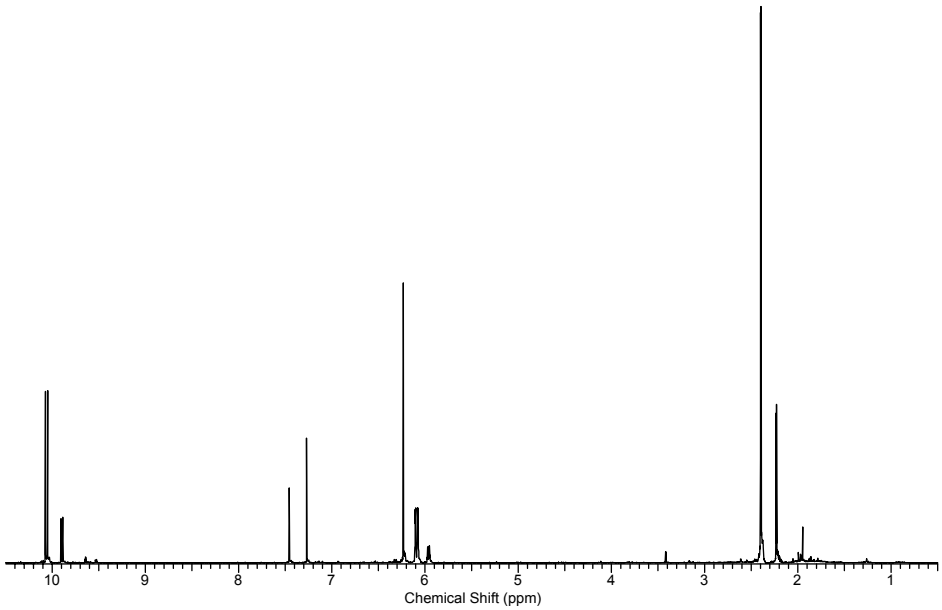
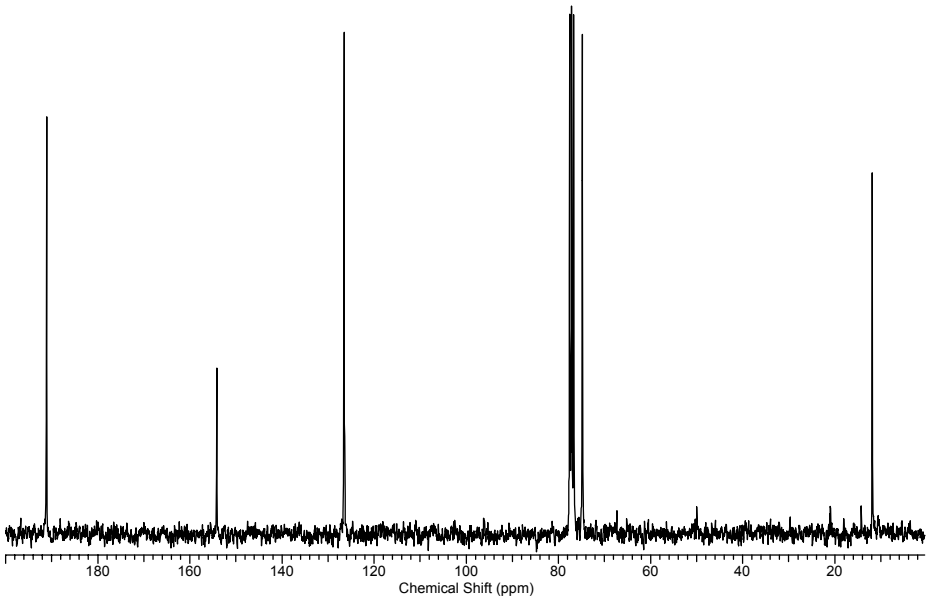
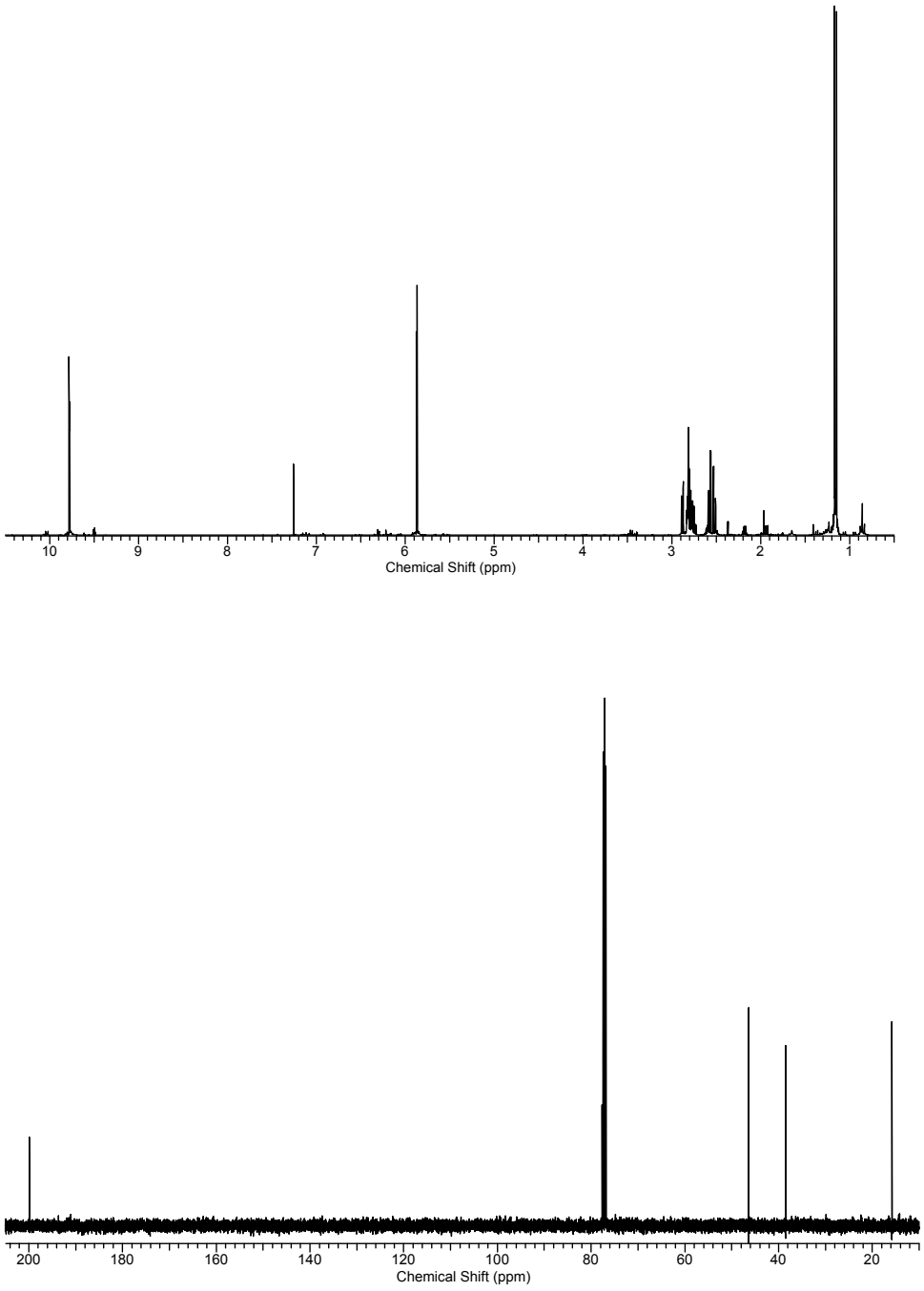



**Figure showing $^{1}$H NMR signals assigned to $CHCl_2$**

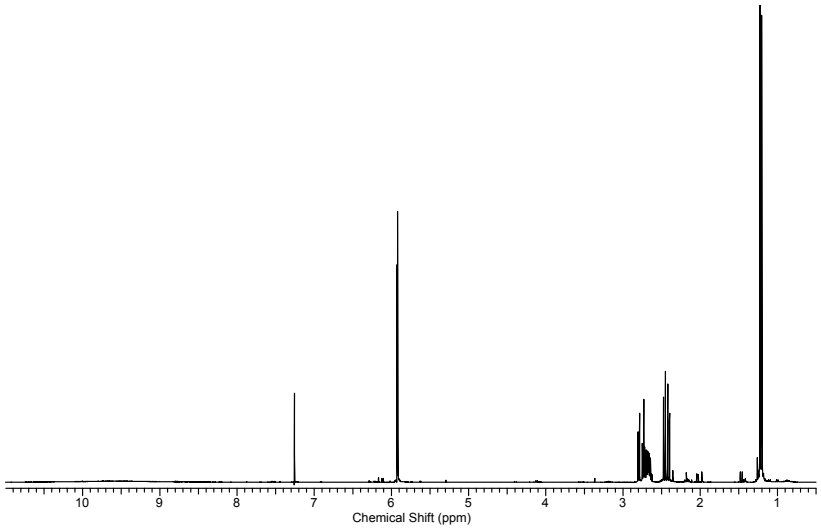


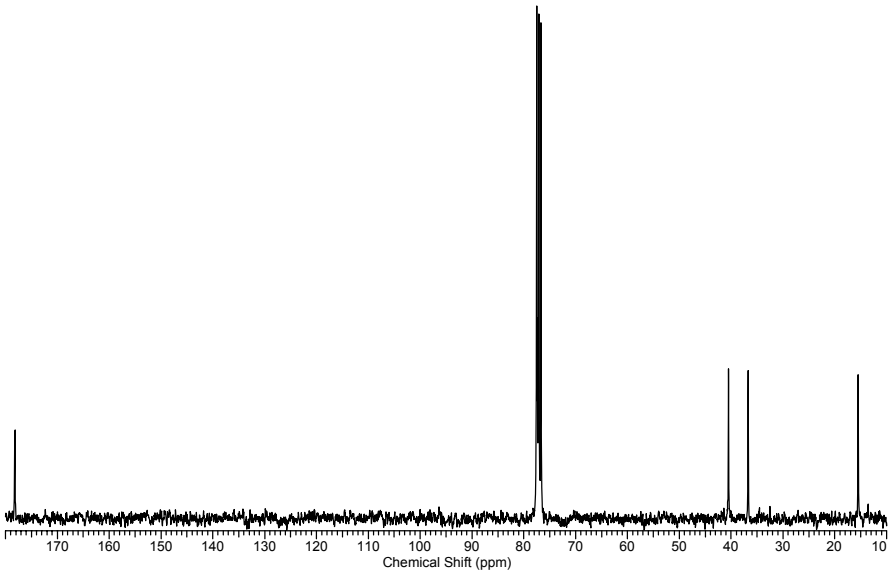

$^{1}$H- and $^{13}$C NMR spectra of unsaturated aldehyde **18**



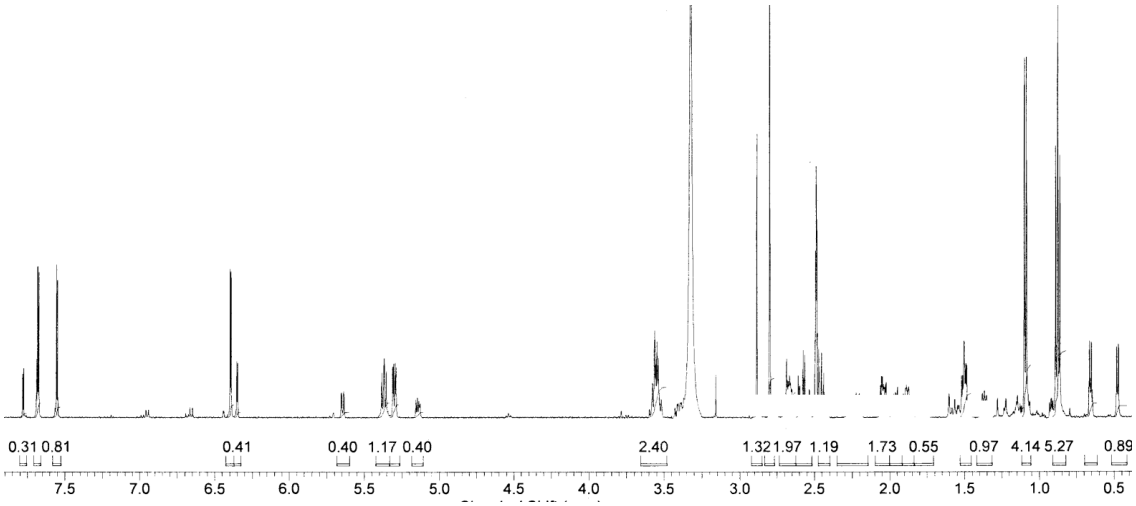

$^{1}$H- and $^{13}$C NMR spectra of aldehyde **20**.



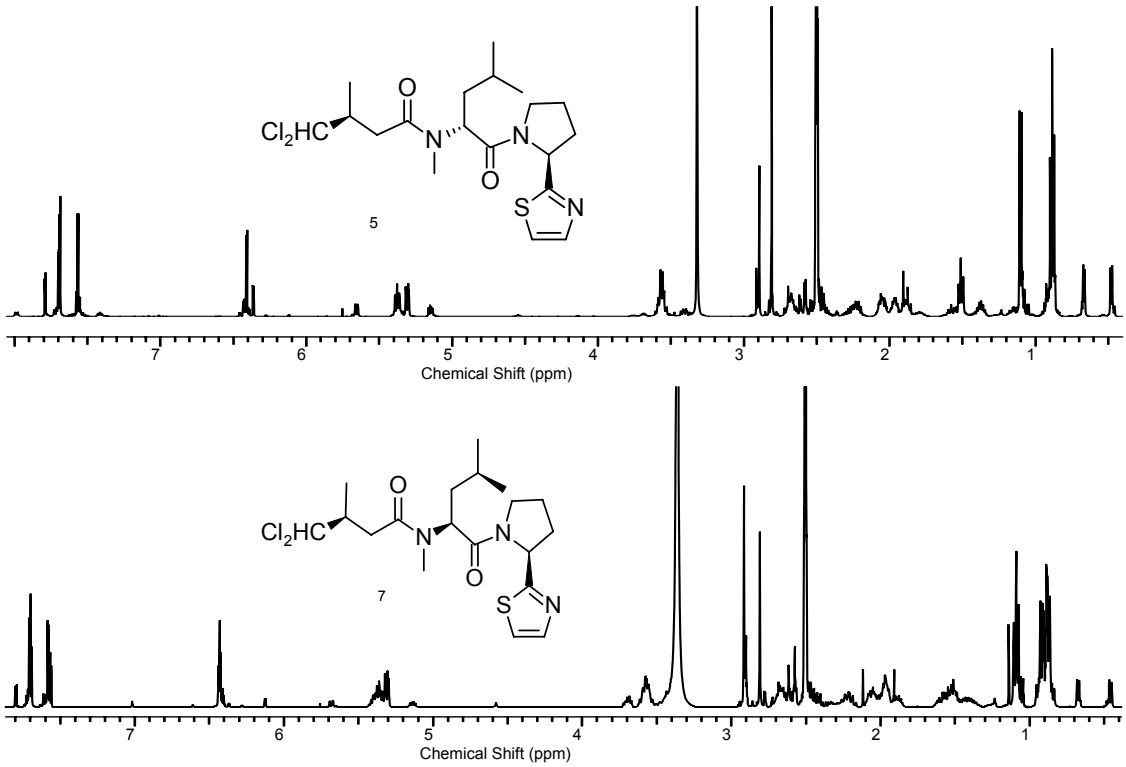

$^{1}$H NMR of dichloro acid **8**




$^{13}$C NMR of dichloro acid **8**




Natural product




$^{1}$H NMR of dysideaproline E (isolated from *Dysidea*)[3] , synthetic dysideaproline **5** and diastereomer **7**