Supplementary Material

Auxiliary-controlled diastereoselective synthesis of a *syn* C-6-epimer of the ADAM 10 inhibitor GI254023X

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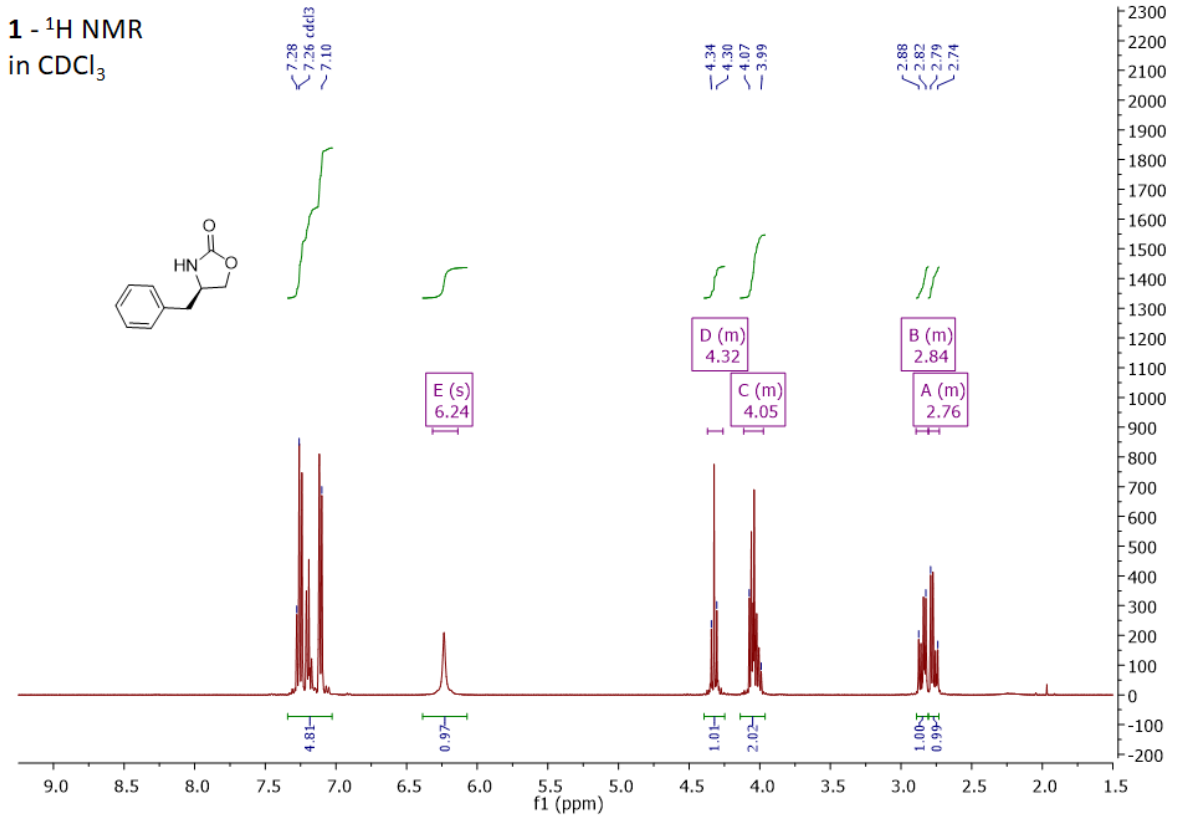
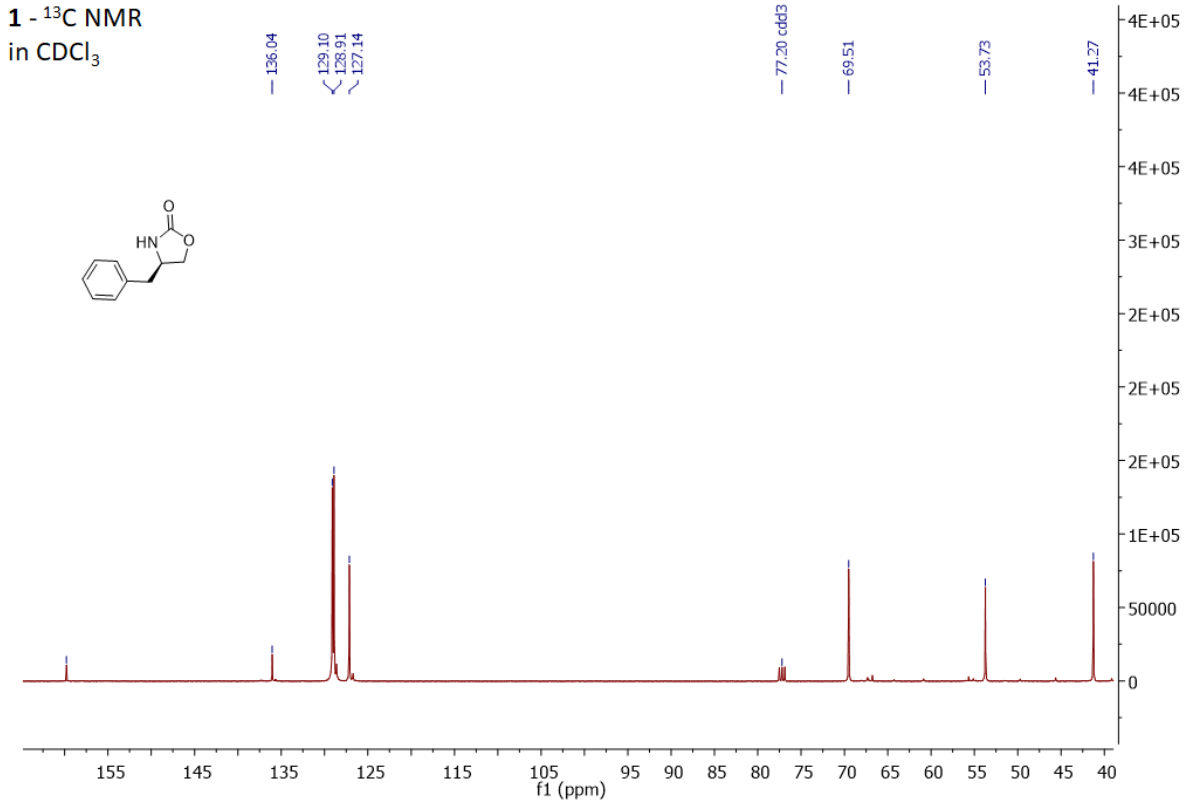
(*R*)-4-Benzyloxazolidin-2-one (1)

1 - ^{1}H NMR
in $CDCl_3$

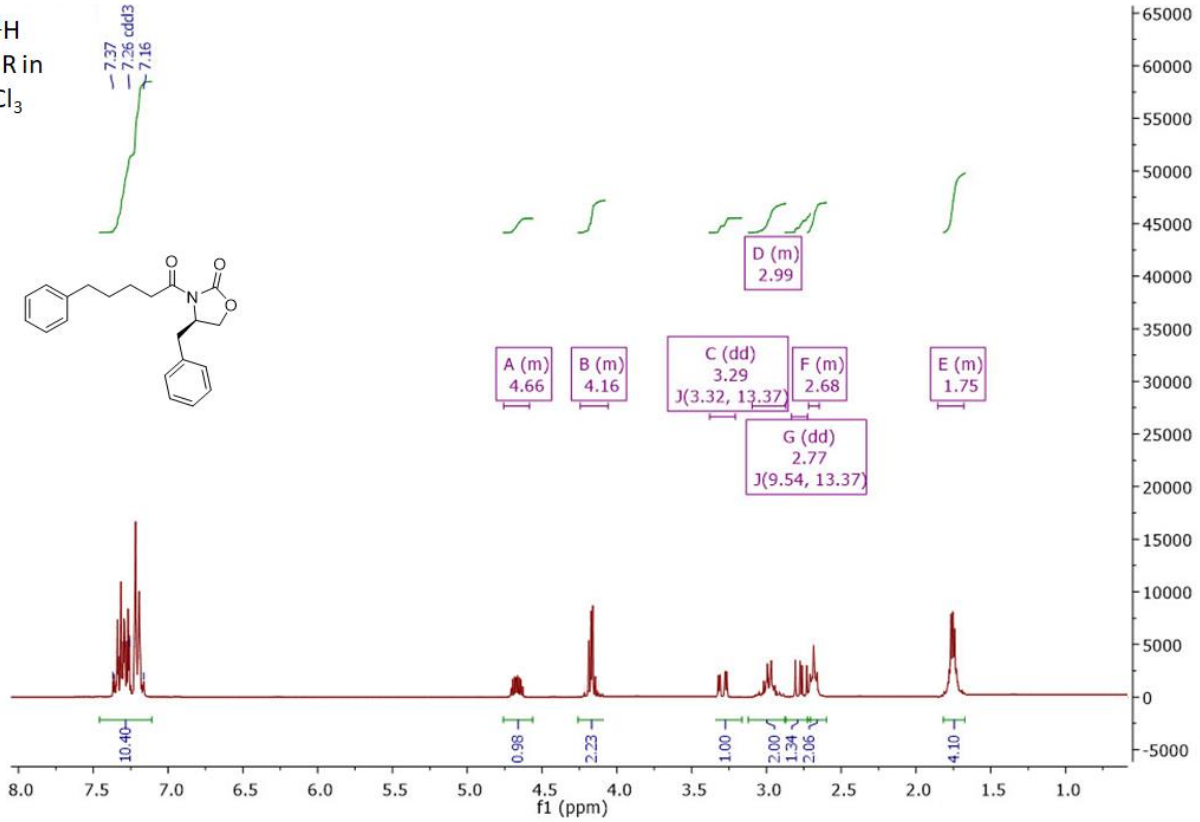


1 - ^{13}C NMR
in $CDCl_3$

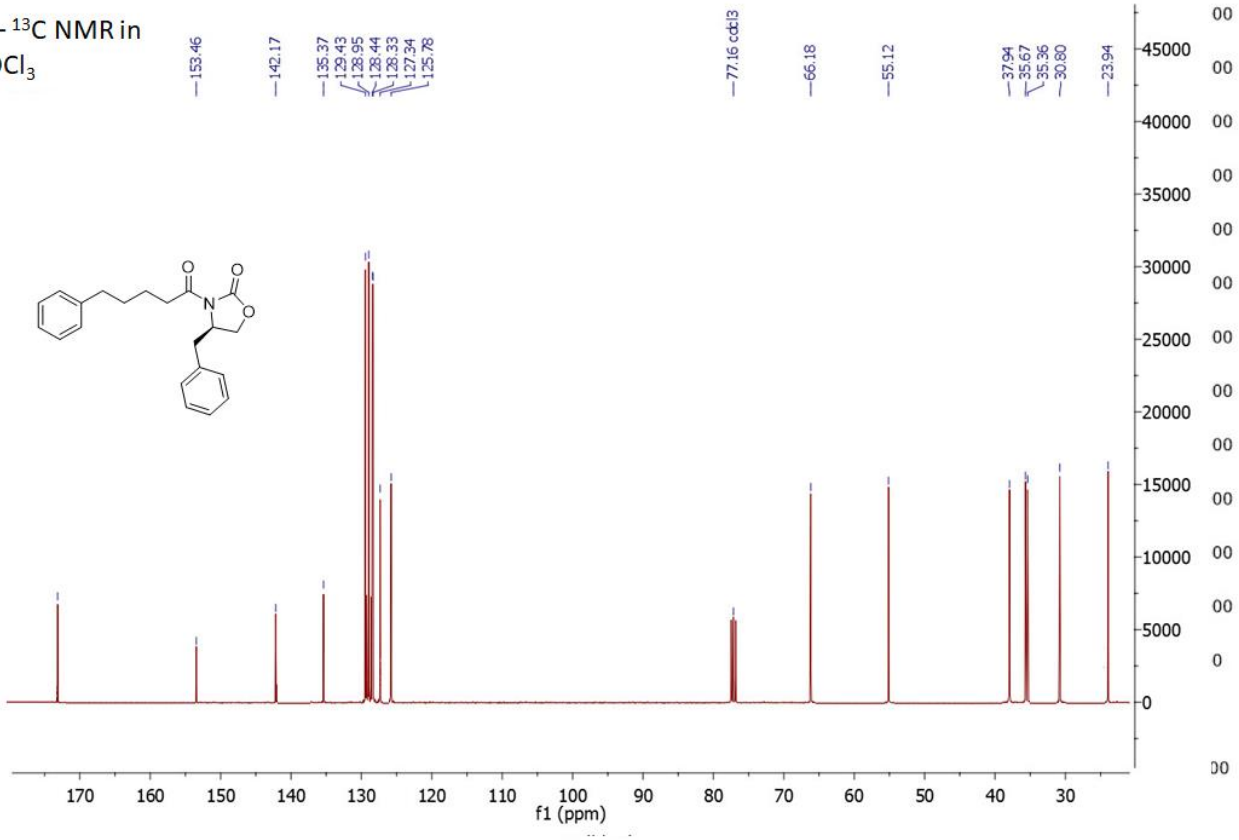


(*R*)-4-Benzyl-3-(5-phenylpentanoyl)oxazolidin-2-one (3)

3 - ^{1}H NMR in $CDCl_3$

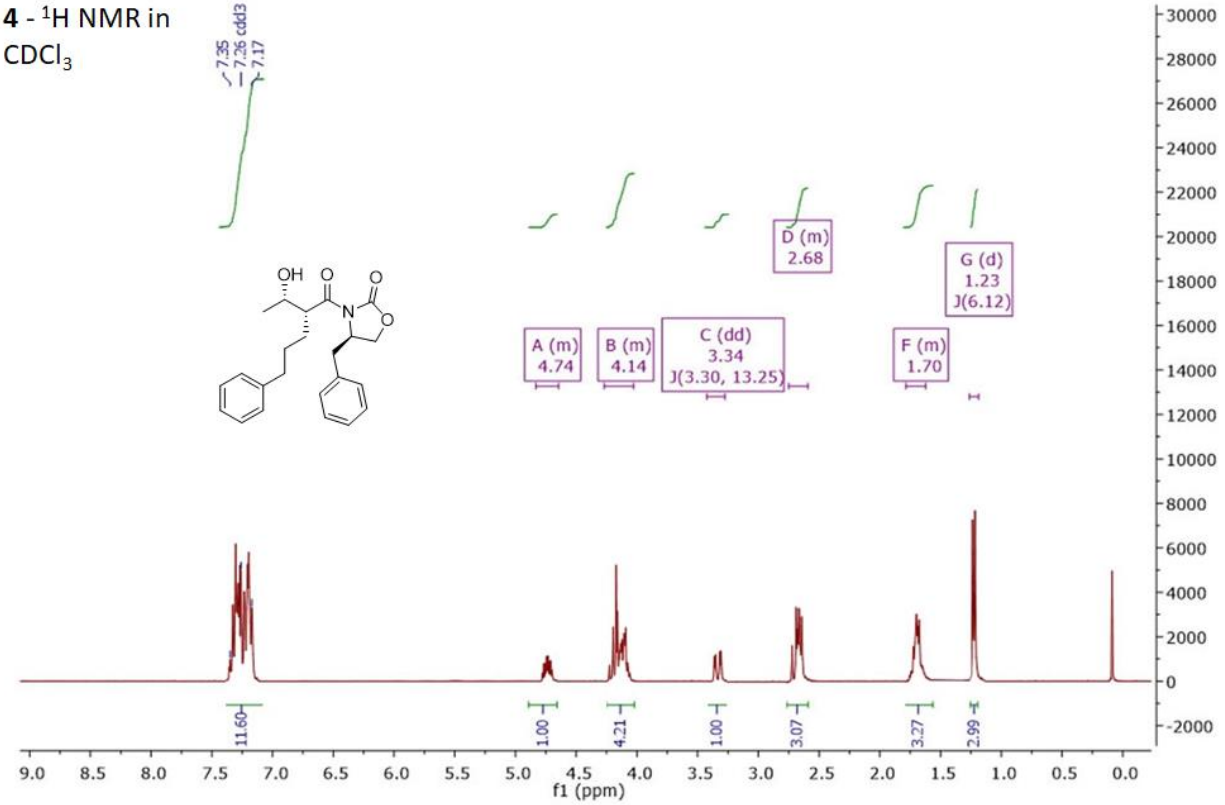


3 – ^{13}C NMR in $CDCl_3$

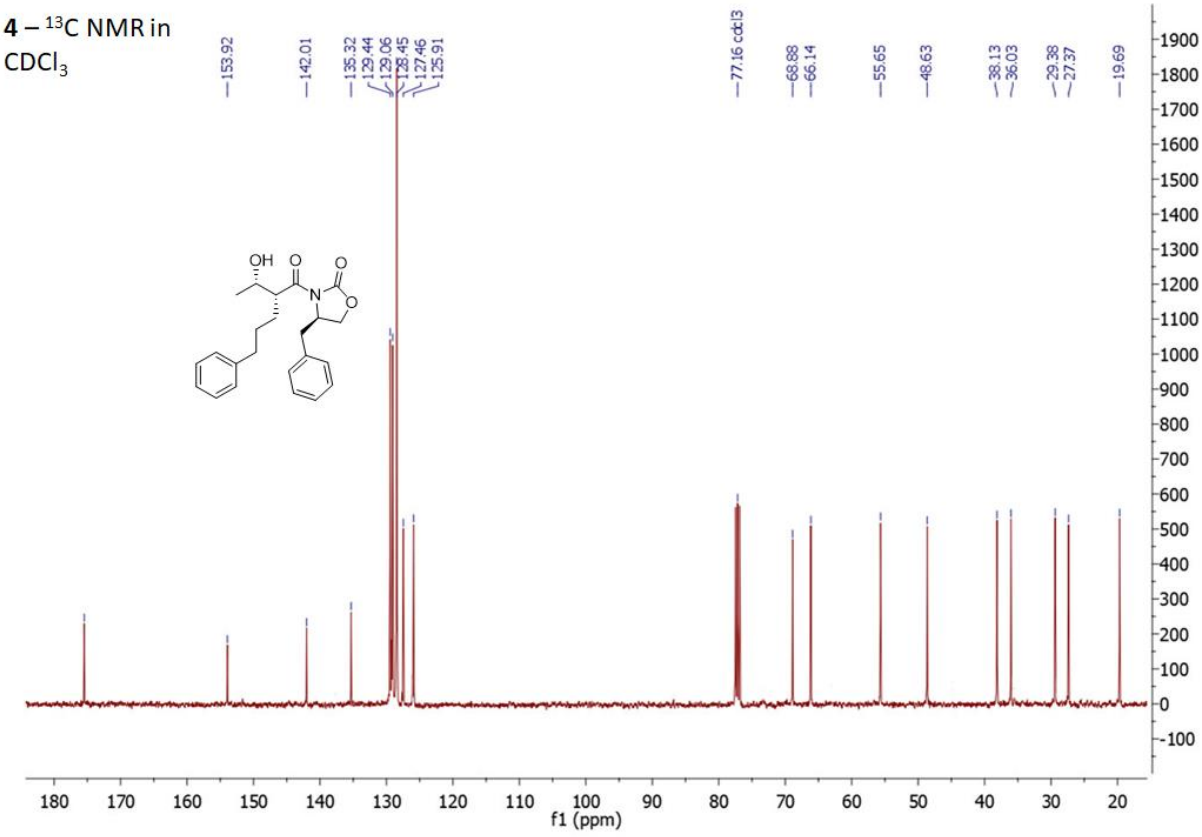


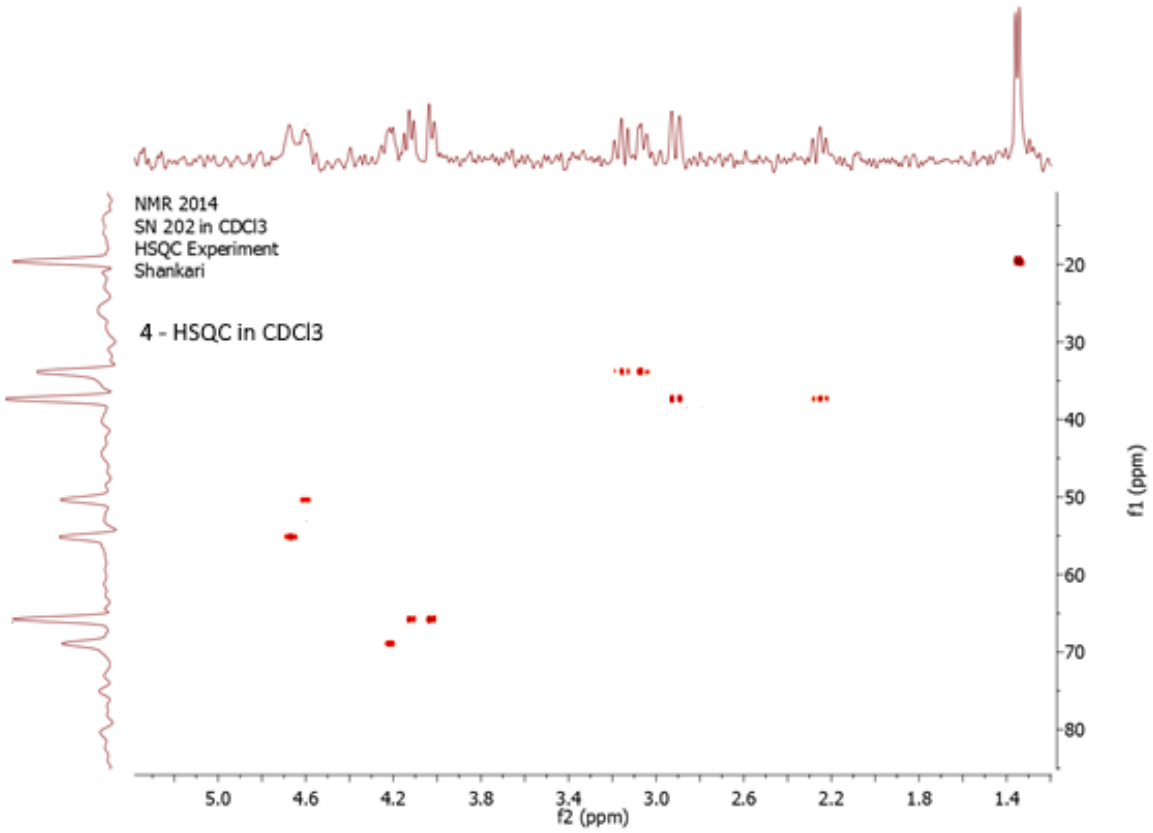
(*R*)-4-Benzyl-3-((*R*)-2-((*S*)-1-hydroxyethyl)-5-phenylpentanoyl)oxazolidin-2-one (4)

4 - ^{1}H NMR in $CDCl_3$



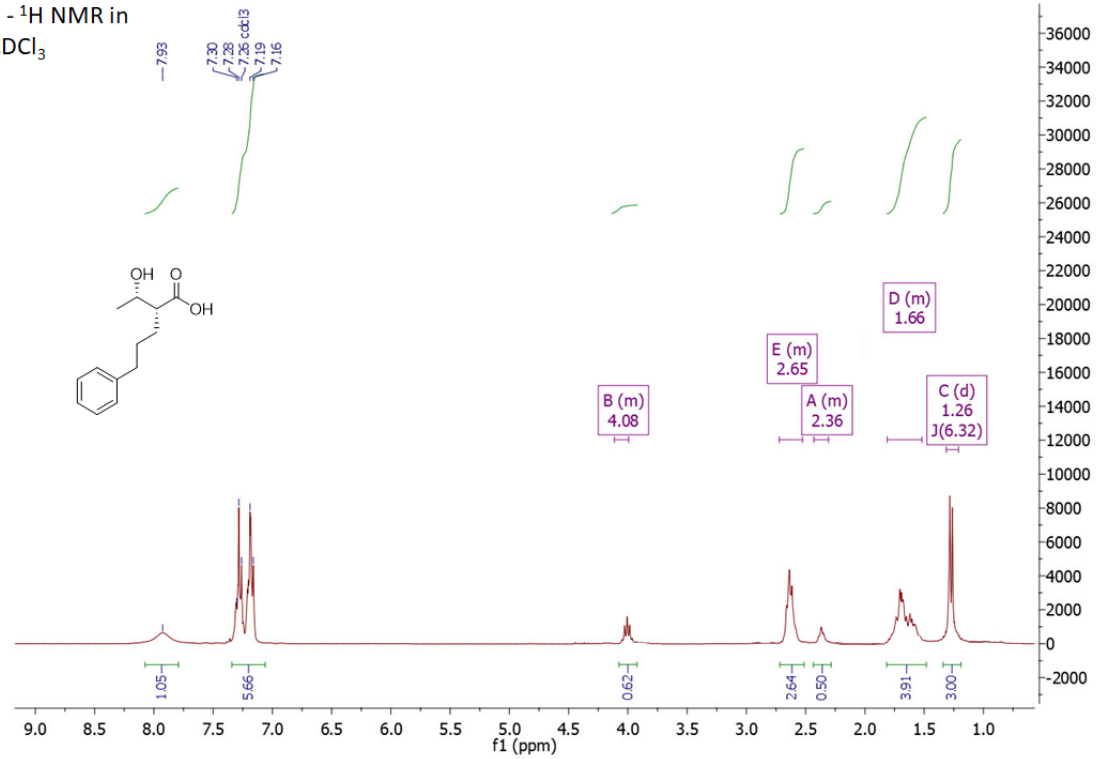
4 – ^{13}C NMR in $CDCl_3$



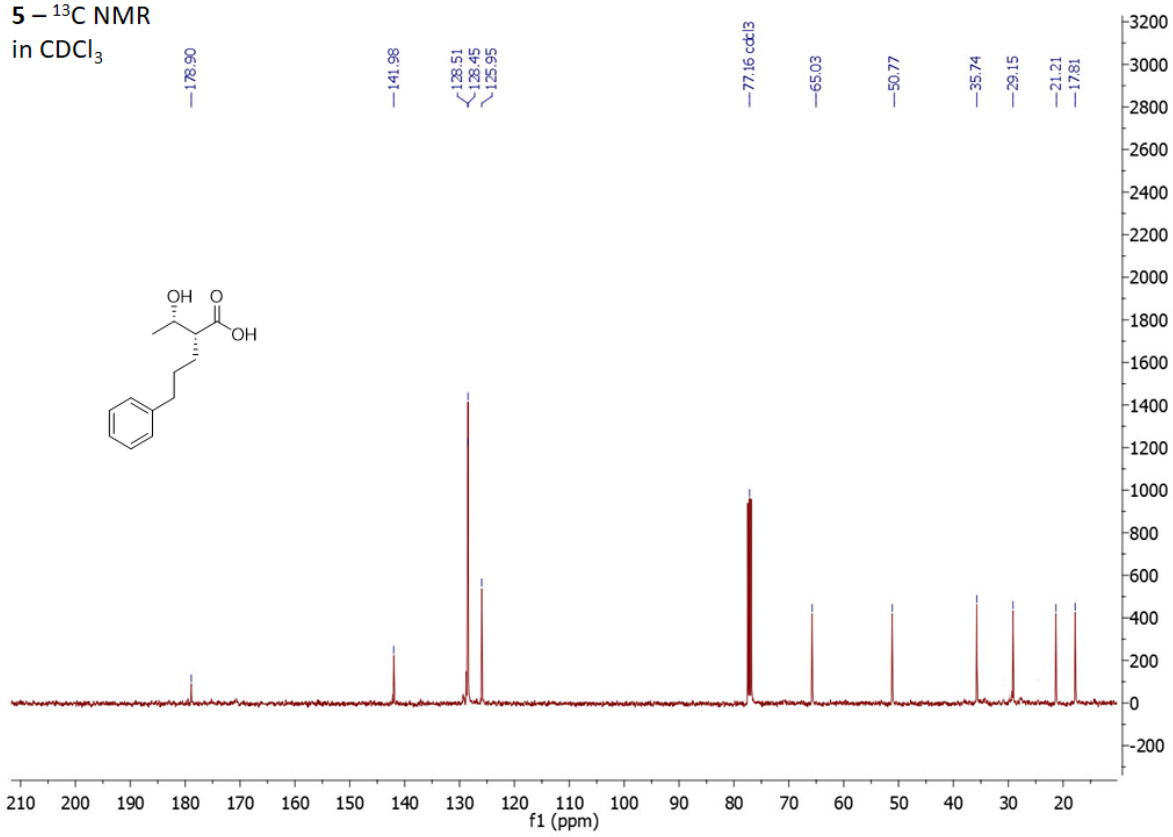

NMR 2014
SN 202 in CDCl3
HSQC Experiment
Shankari
4 - HSQC in CDCl3
f1 (ppm)
f2 (ppm)

(*R*)-2-((*S*)-1-Hydroxyethyl)-5-phenylpentanoic acid (5)

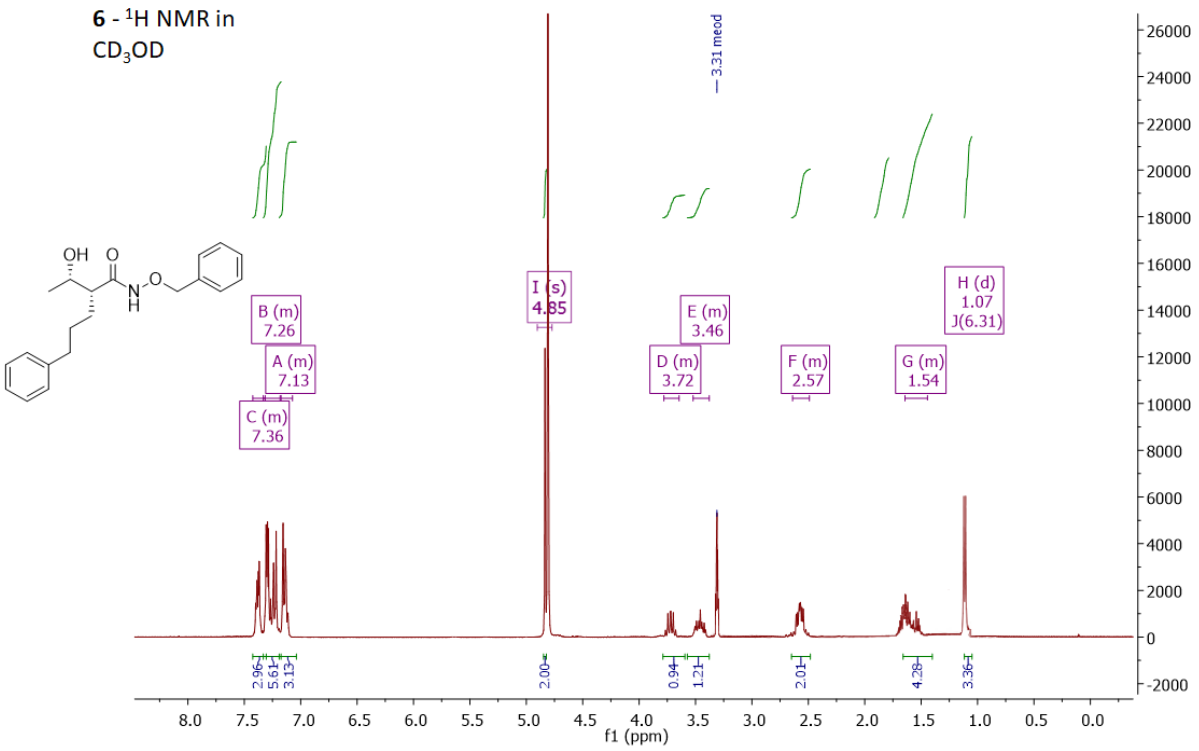
5 - ^{1}H NMR in $CDCl_3$

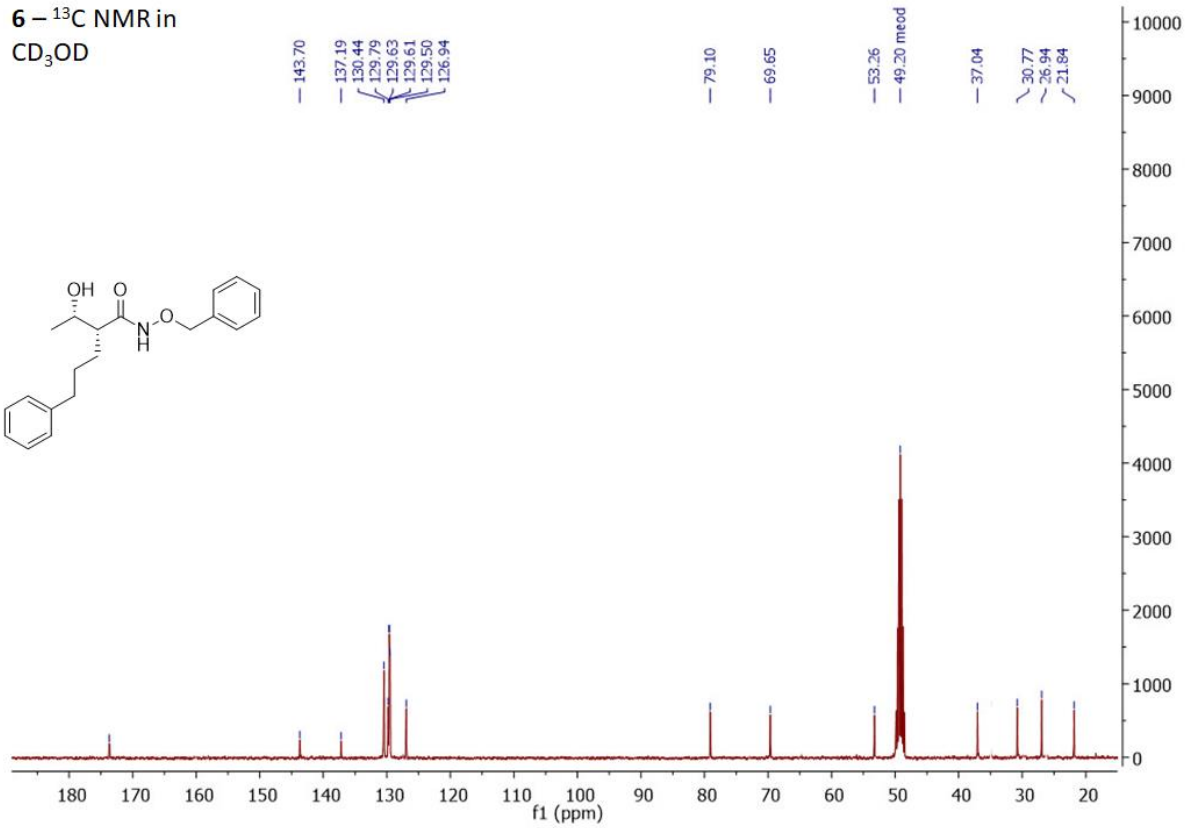


5 – ^{13}C NMR in $CDCl_3$

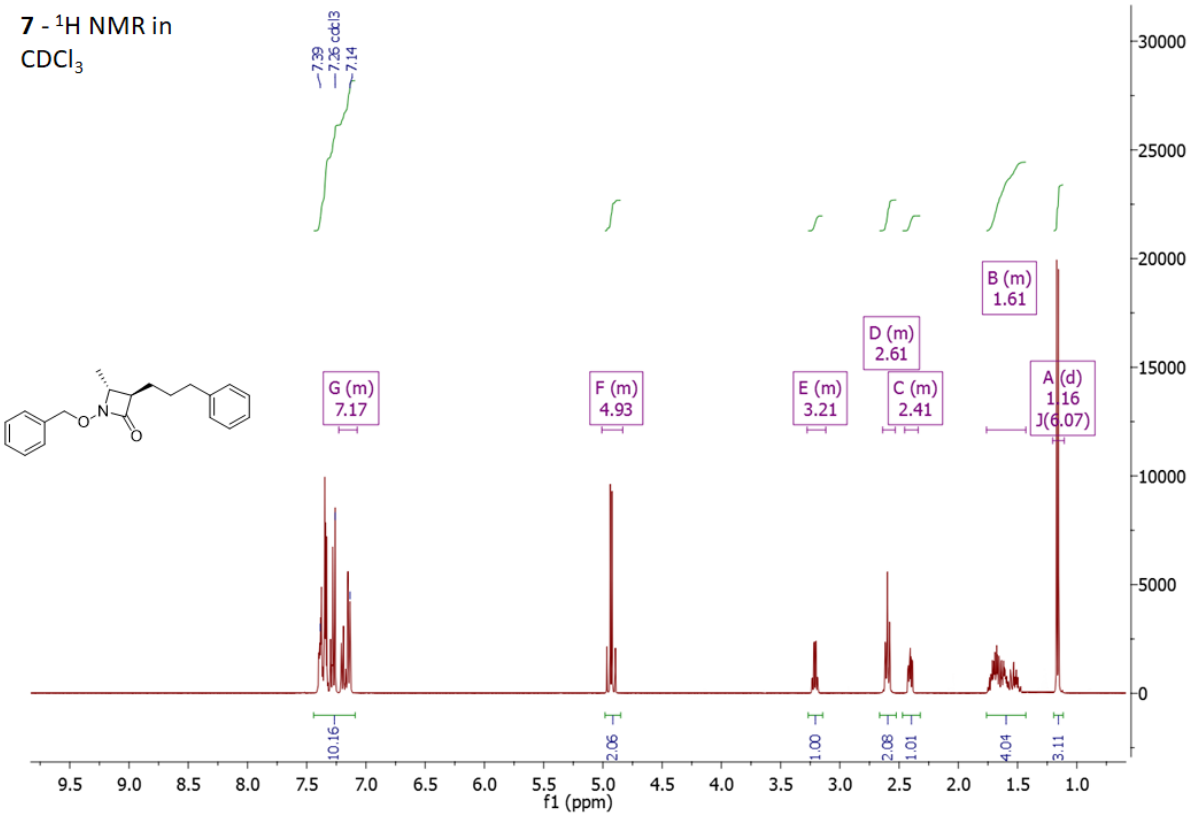


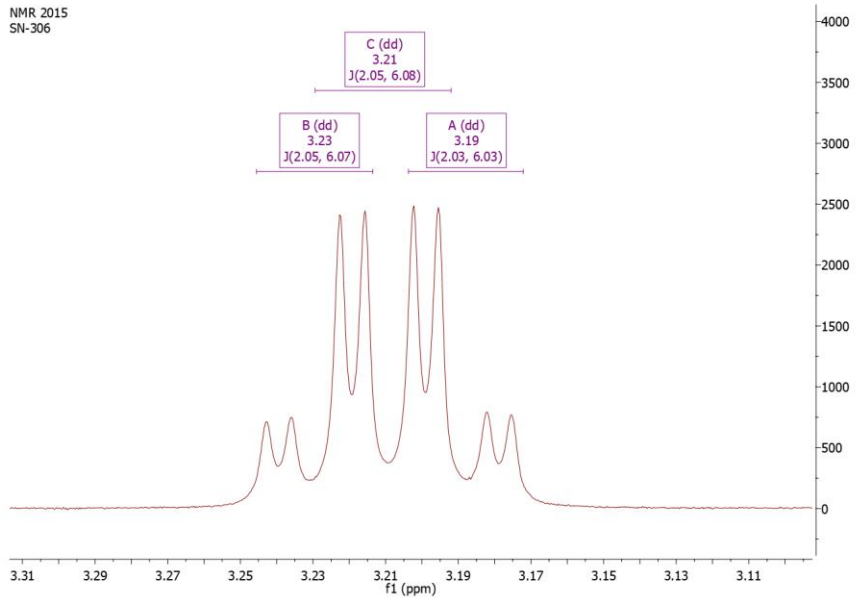
(*R*)-*N*-(Benzyloxy)-2-((*S*)-1-hydroxyethyl)-5-phenylpentanamide (6)





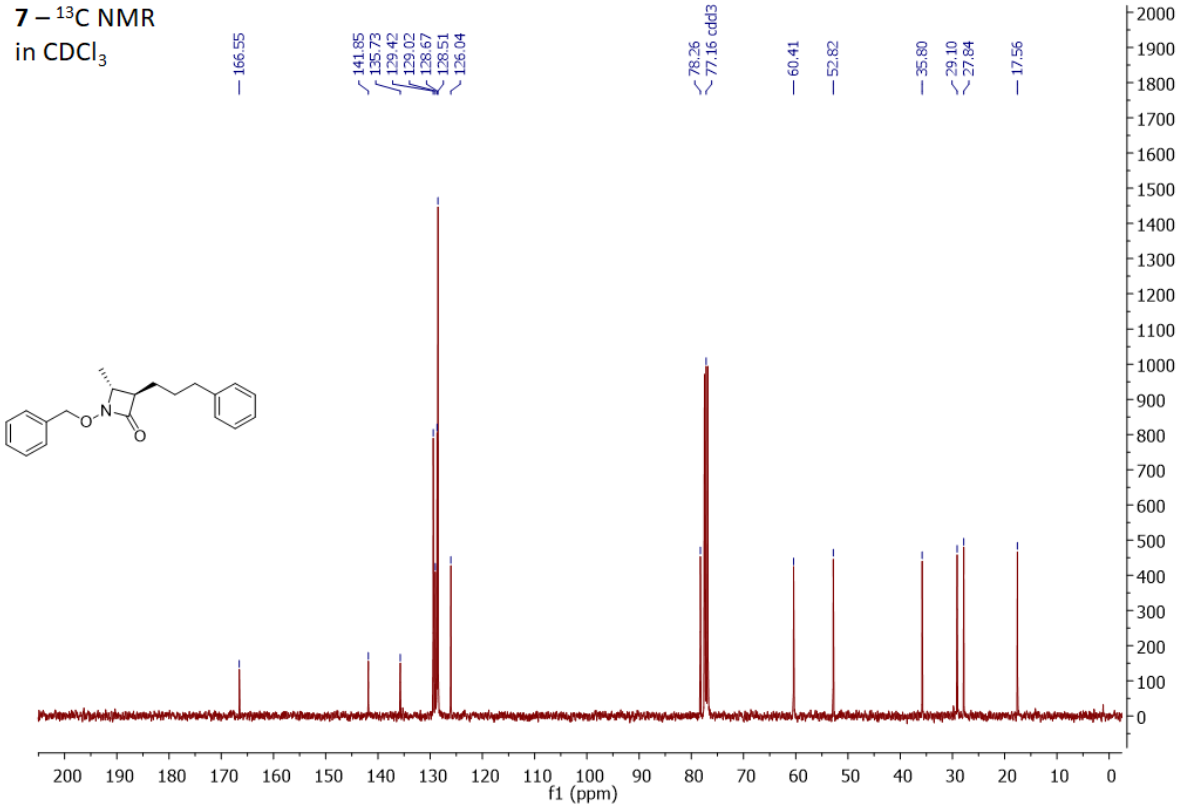
(3*R*,4*R*)-1-(Benzyloxy)-4-methyl-3-(3-phenylpropyl)azetidin-2-one (7)





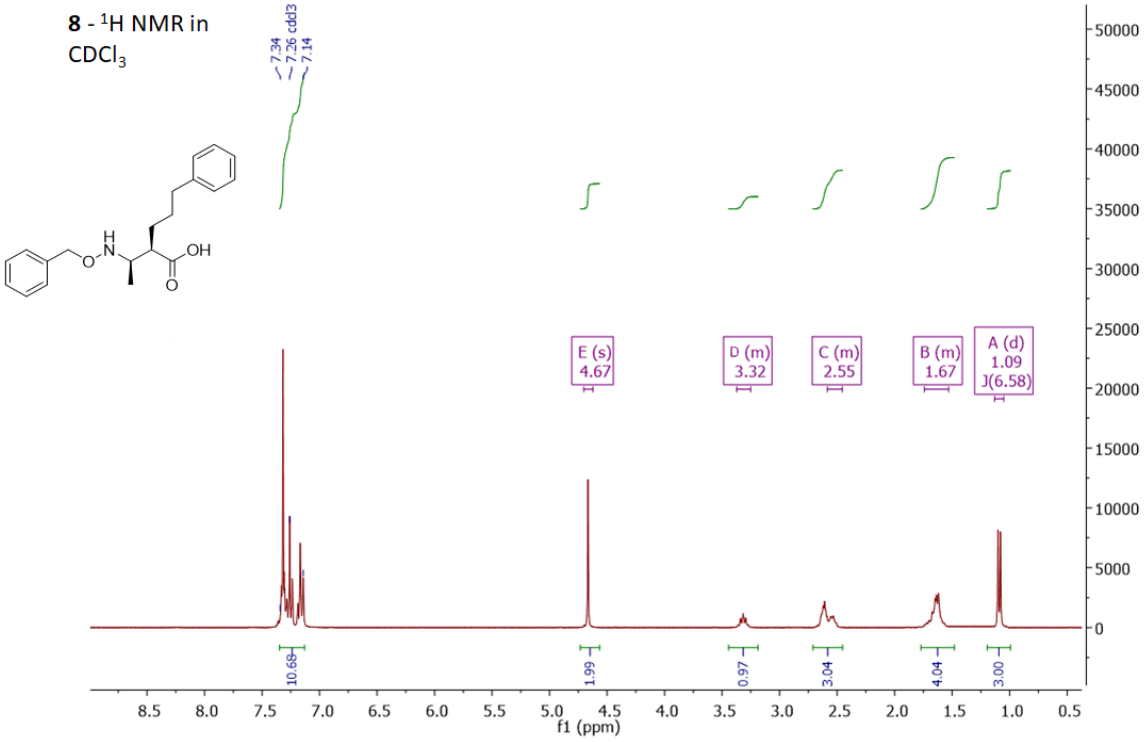
Expansion of the 3.17-3.25 ppm signal for H-4 of **7** is shown above, revealing a dq with *J* = 2.0, 6.1 Hz vicinal couplings. This confirms the *trans*-relative stereochemistry between H-3 and H-4 based on a near 90 ° dihedral angle and, hence, a low vicinal *J* value (2.0 Hz). In the Hoettecke paper (reference 7 in the text) for the *cis*-isomer (**14** in the text of their paper), their *J* value was recorded as close to 6 Hz. The *cis*-stereochemistry of **14** was confirmed by X-ray. The absolute stereochemistry in our case was taken to be in accordance with the Evans' model.

7 – ^{13}C NMR
in $CDCl_3$

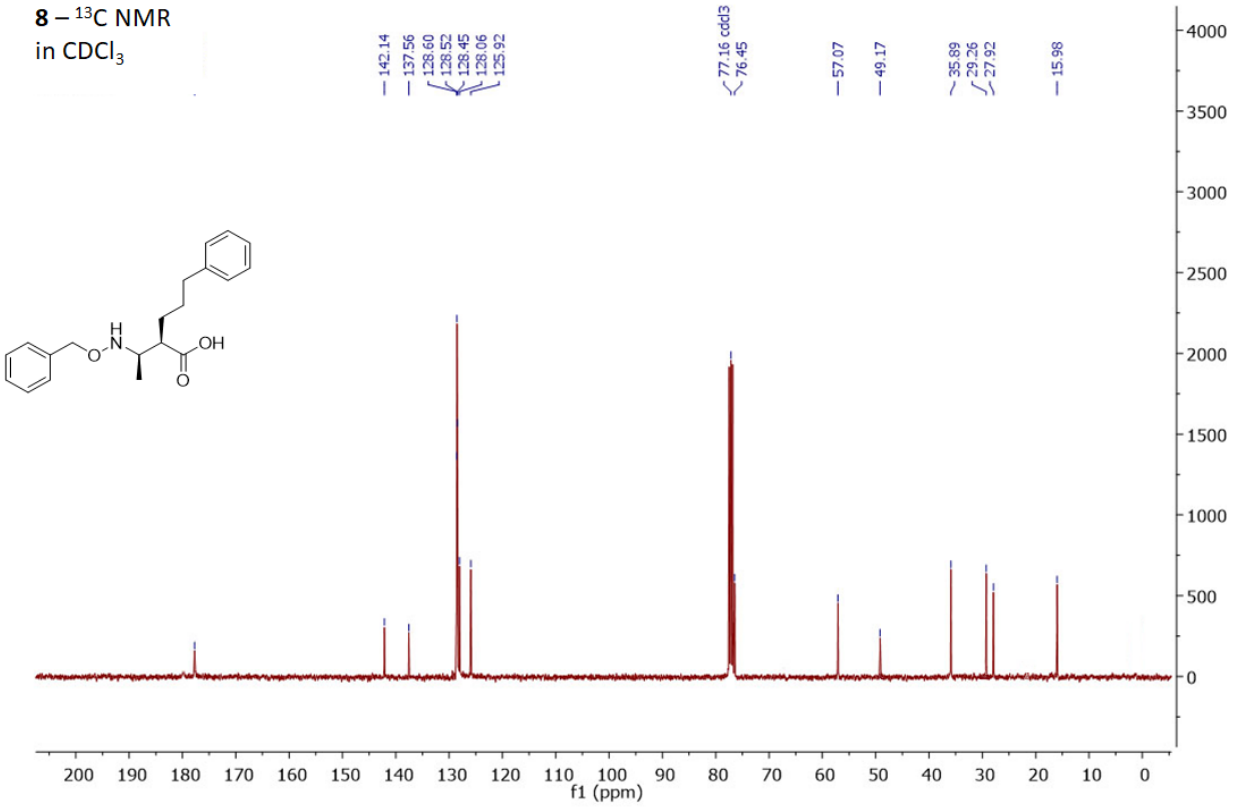


(*R*)-2-((*R*)-1-((Benzyloxy)amino)ethyl)-5-phenylpentanoic acid (8)

8 - ^{1}H NMR in $CDCl_3$

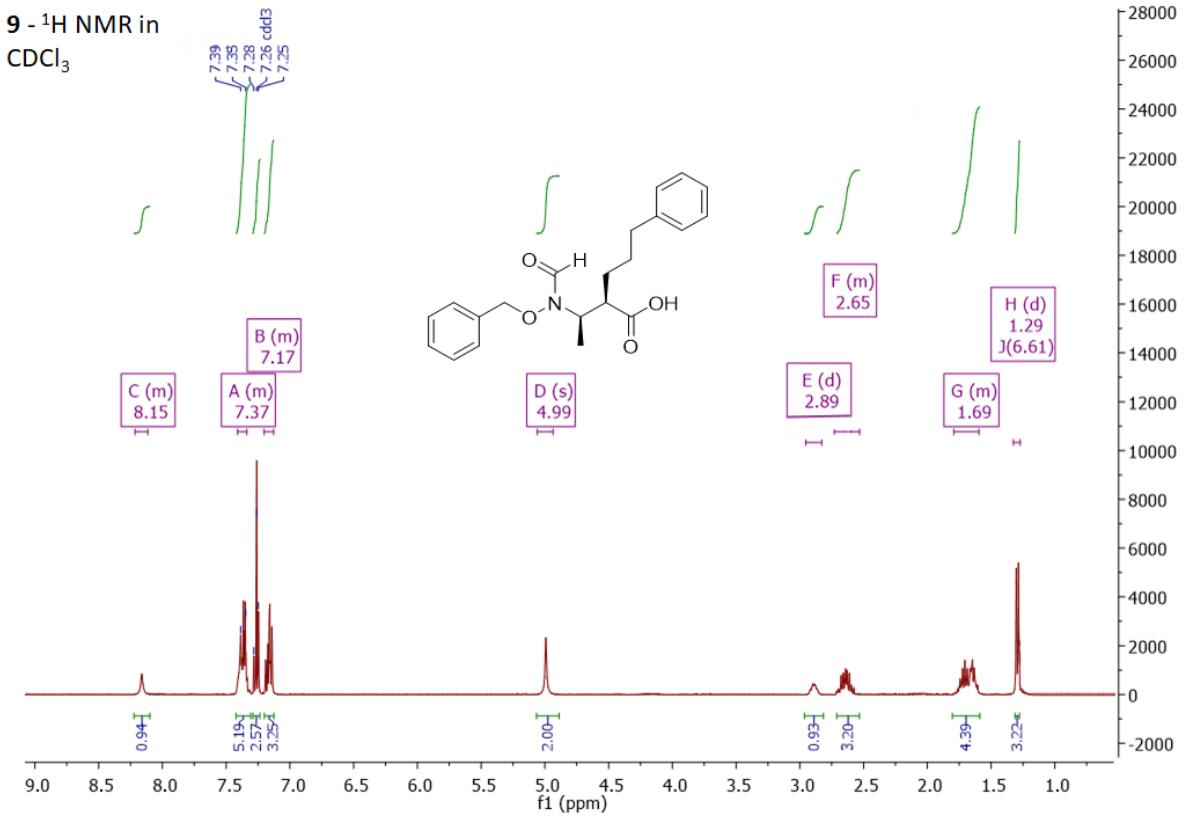


8 – ^{13}C NMR in $CDCl_3$

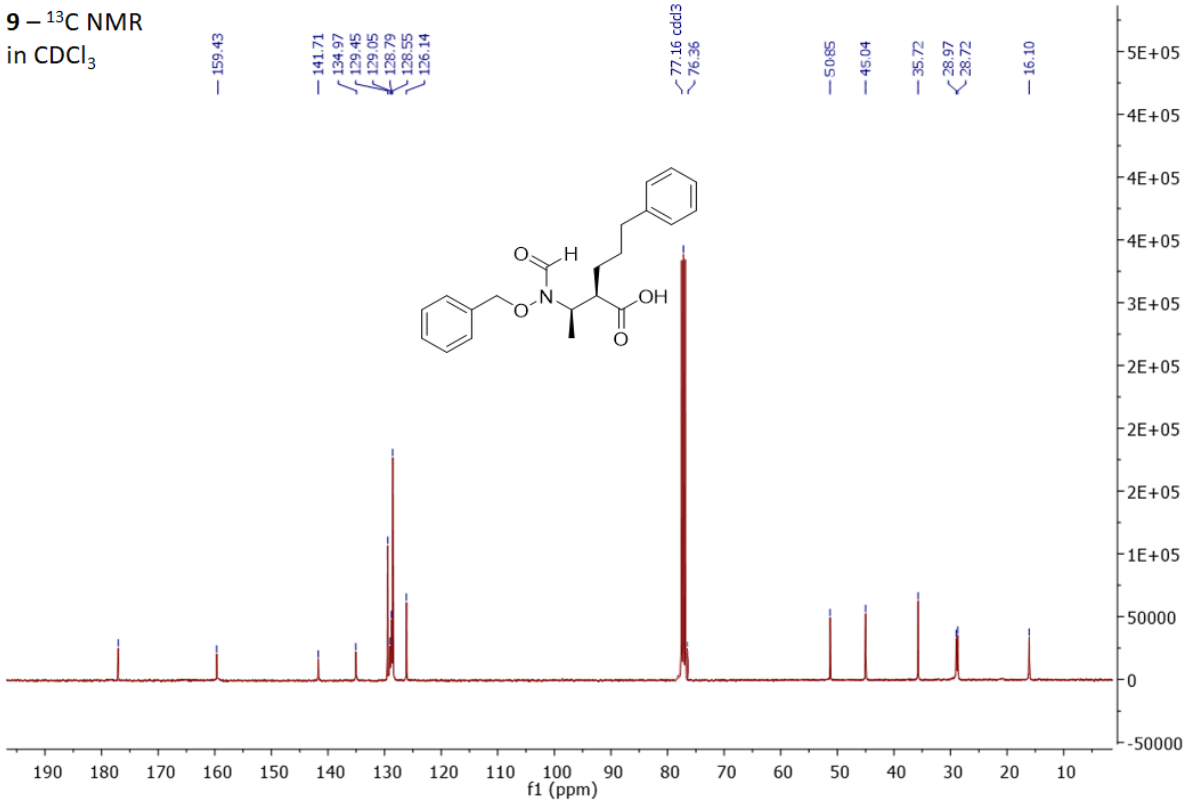


(*R*)-2-((*R*)-1-(*N*-(Benzyloxy)formamido)ethyl)-5-phenylpentanoic acid (9)

9 - ^{1}H NMR in $CDCl_3$

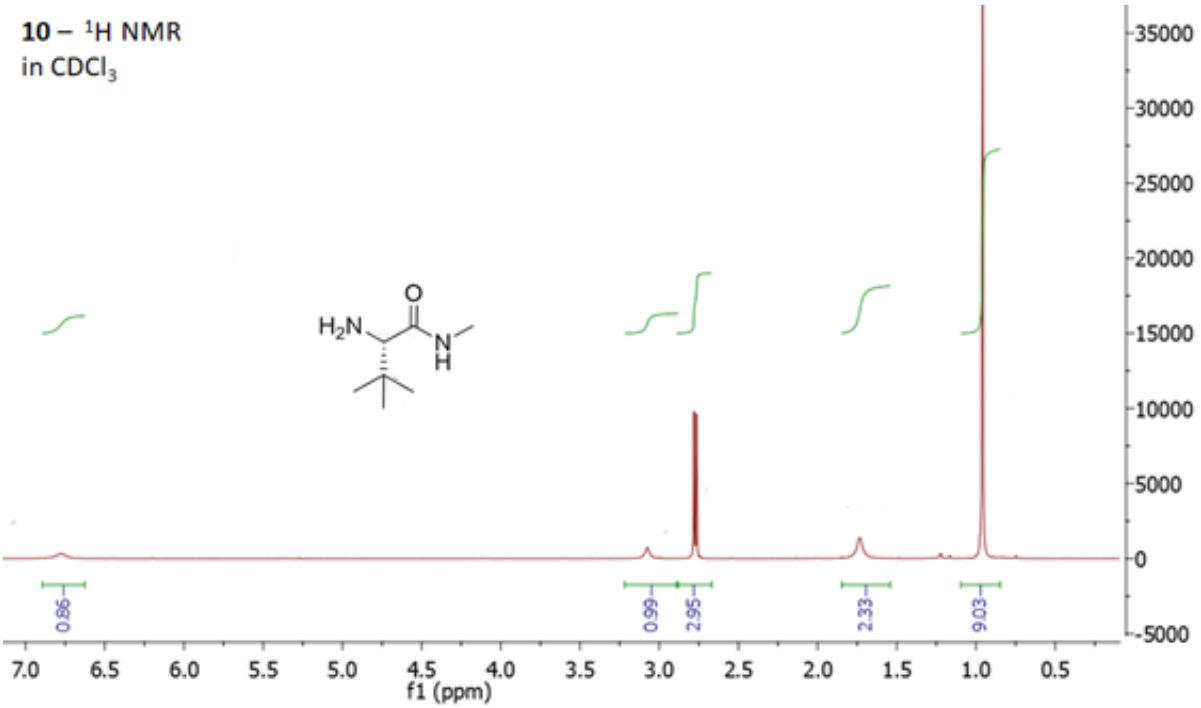


9 – ^{13}C NMR in $CDCl_3$

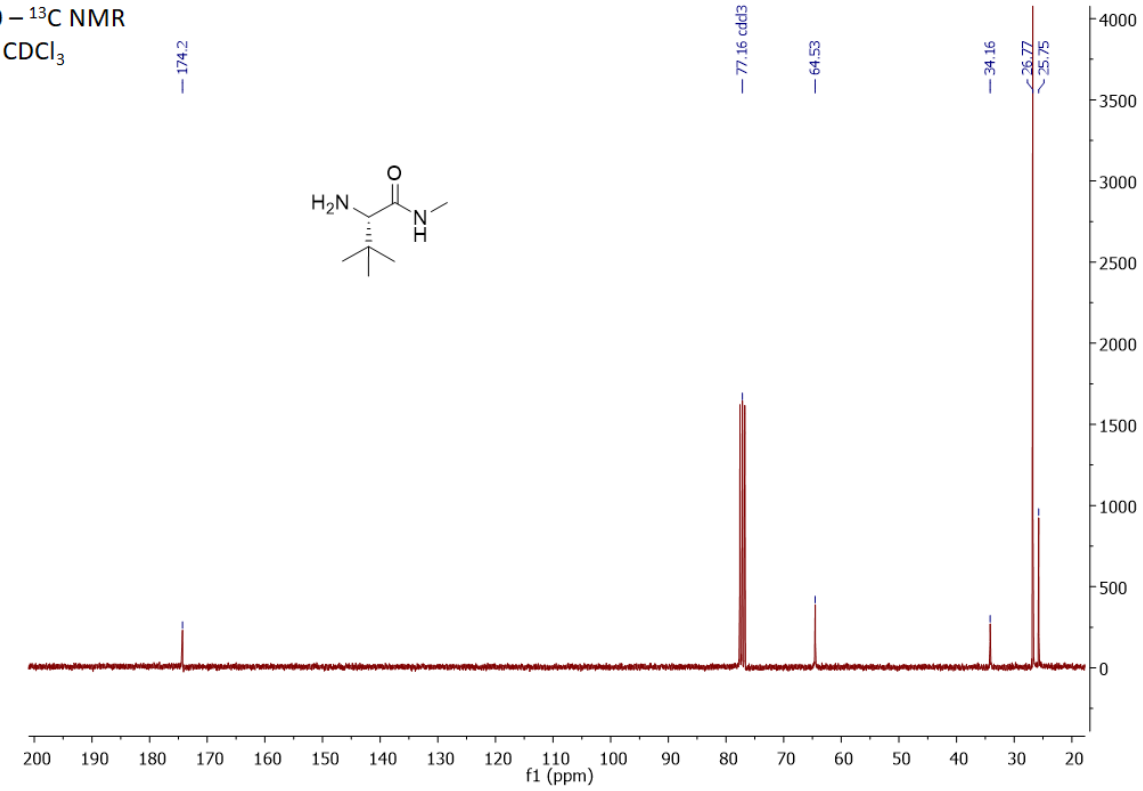


(*S*)-2-Amino-*N*,3,3-trimethylbutanamide (10)

10 – ^{1}H NMR
in $CDCl_3$

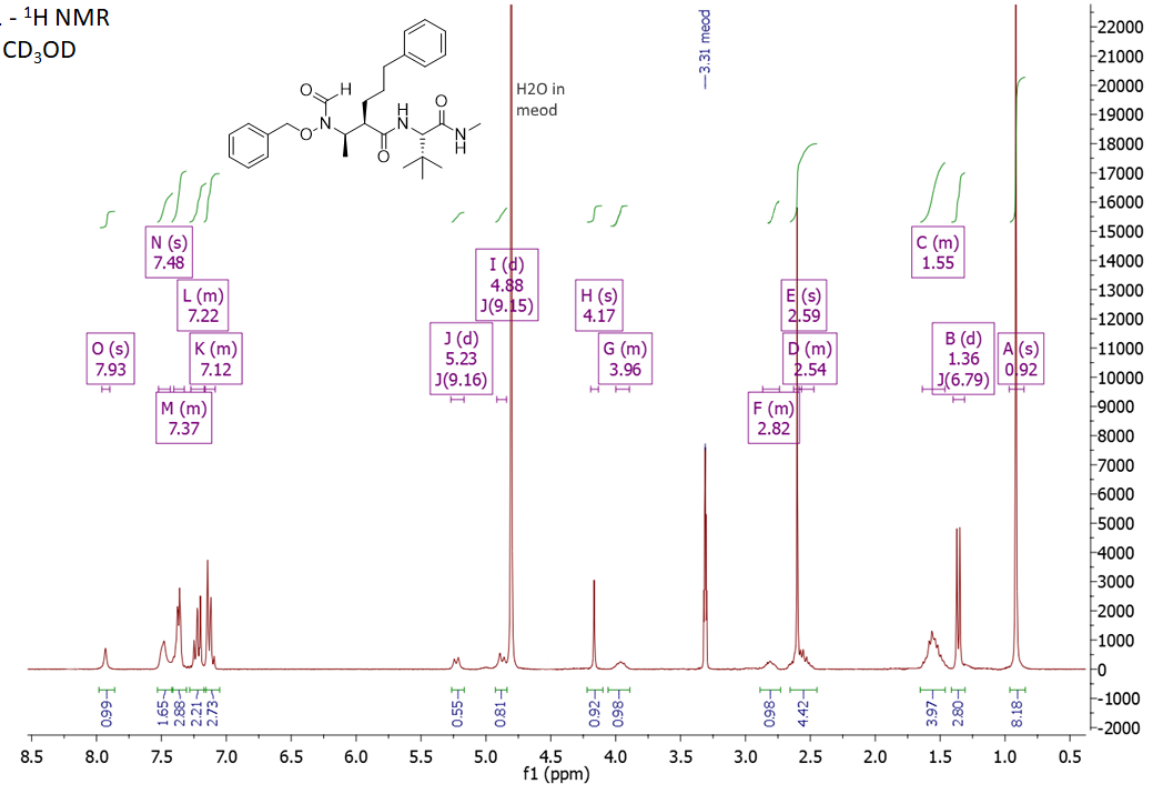


10 – ^{13}C NMR
in $CDCl_3$

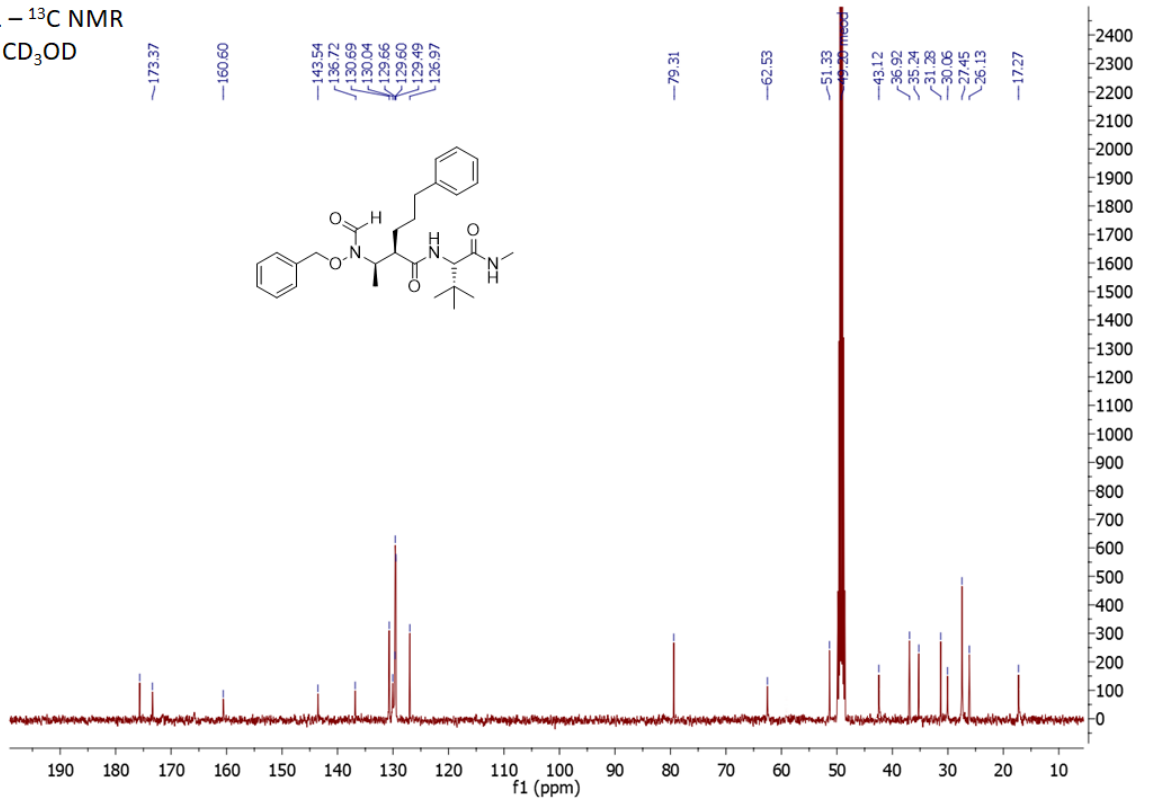


(*R*)-2-((*R*)-1-(*N*-(Benzyloxy)formamido)ethyl)-*N*-((*R*)-3,3-dimethyl-1-(methylamino)-1-oxobutan-2-yl)-5-phenylpentanamide (11)

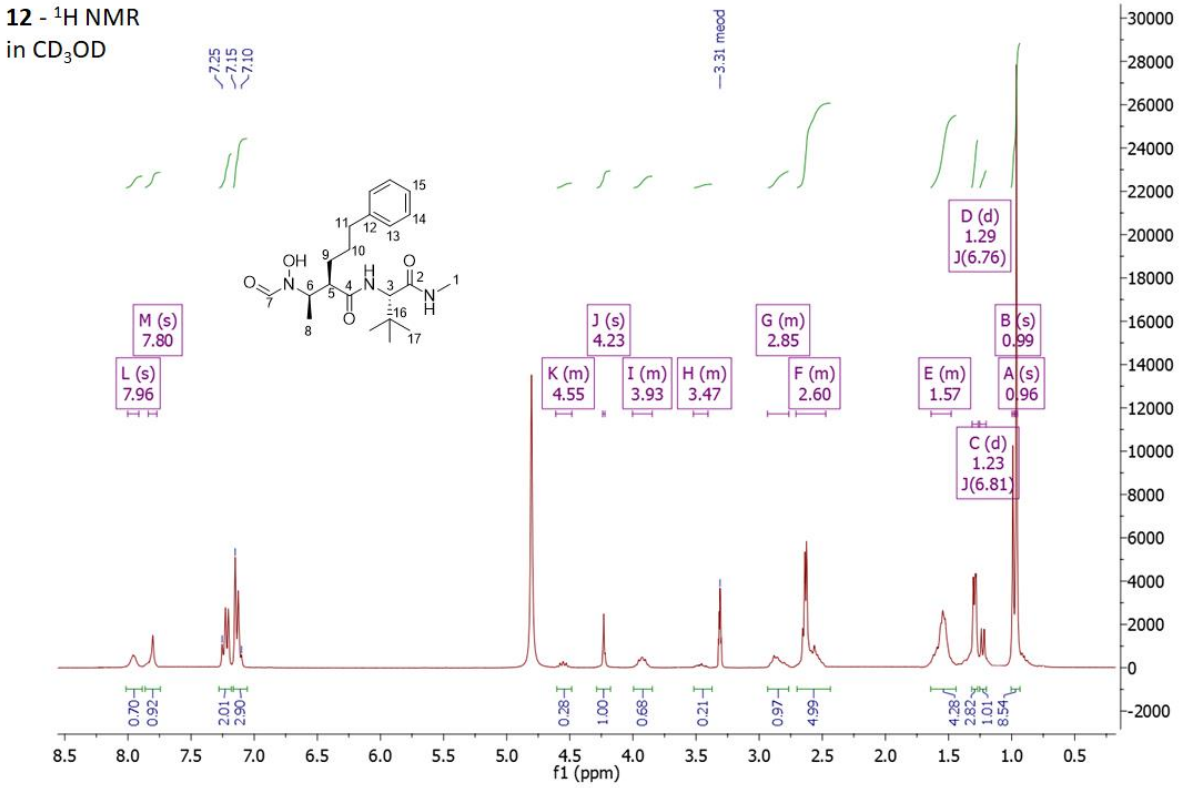
11 - ^{1}H NMR
in CD_3OD

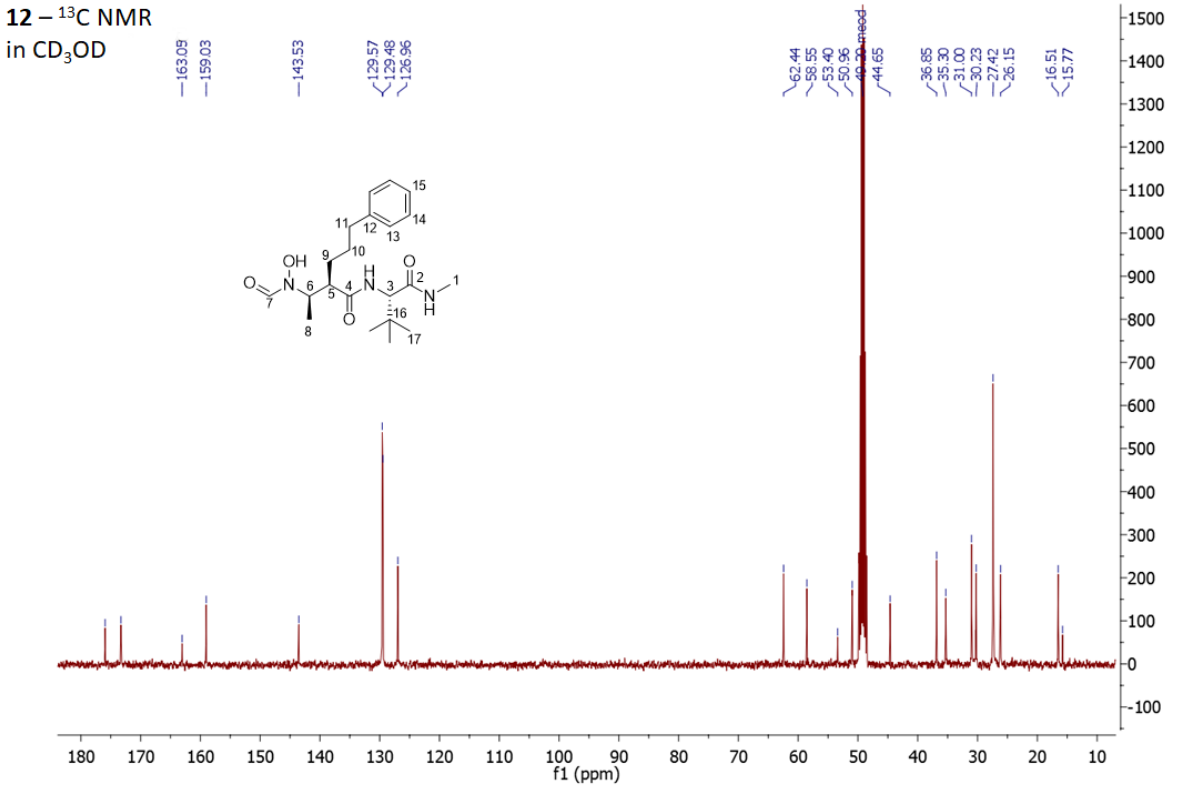


11 – ^{13}C NMR
in CD_3OD



(*R*)-*N*-((*R*)-3,3-Dimethyl-1-(methylamino)-1-oxobutan-2-yl)-2-((*R*)-1-(*N*-hydroxyformamido)ethyl)-5-phenylpentanamide (12)





Chiral HPLC analysis of **12** on a Chiracel OD column with the eluent composed of Hex (60%): *i*-PrOH (40%), for 20 min with a flow rate of 1 mL/min at λ = 254 nm