Stable D-xylose ditriflate in divergent syntheses of dihydroxy prolines, pyrrolidines, tetrahydrofuran-2-carboxylic acids, and cyclic β-amino acids.

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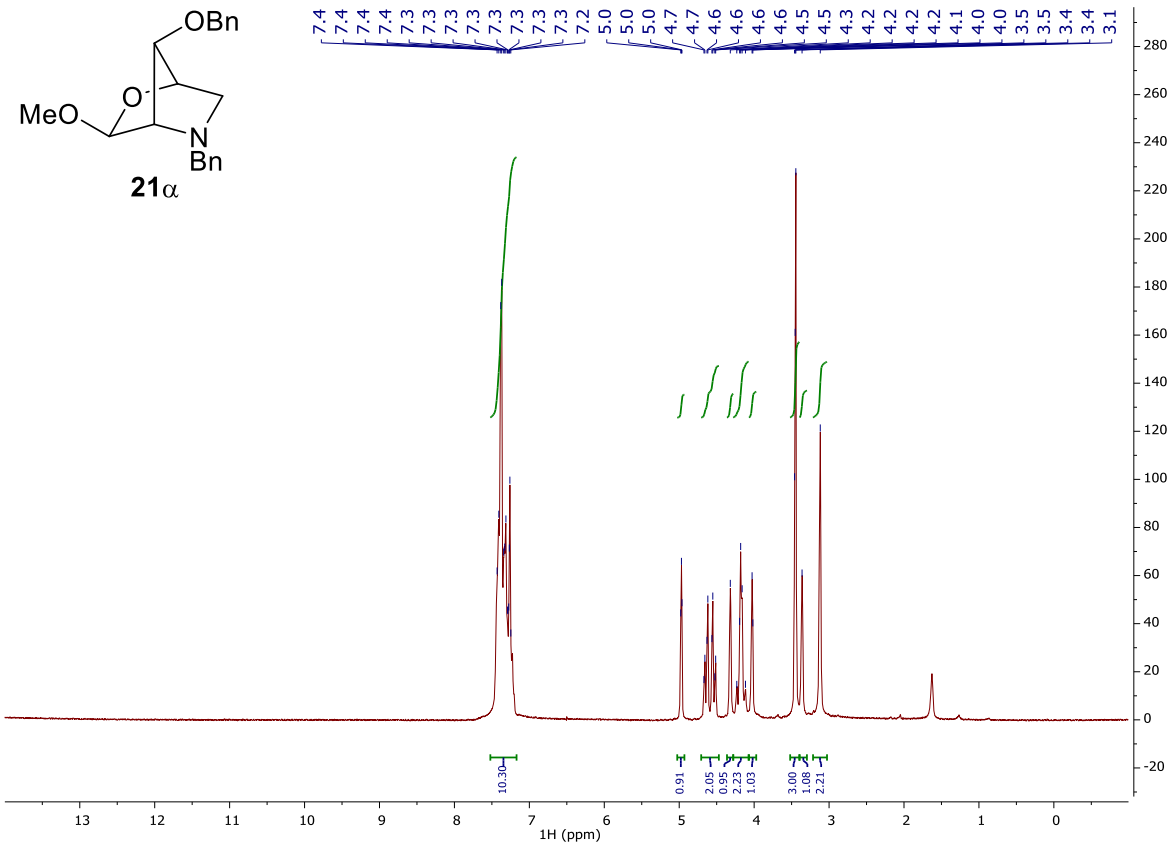
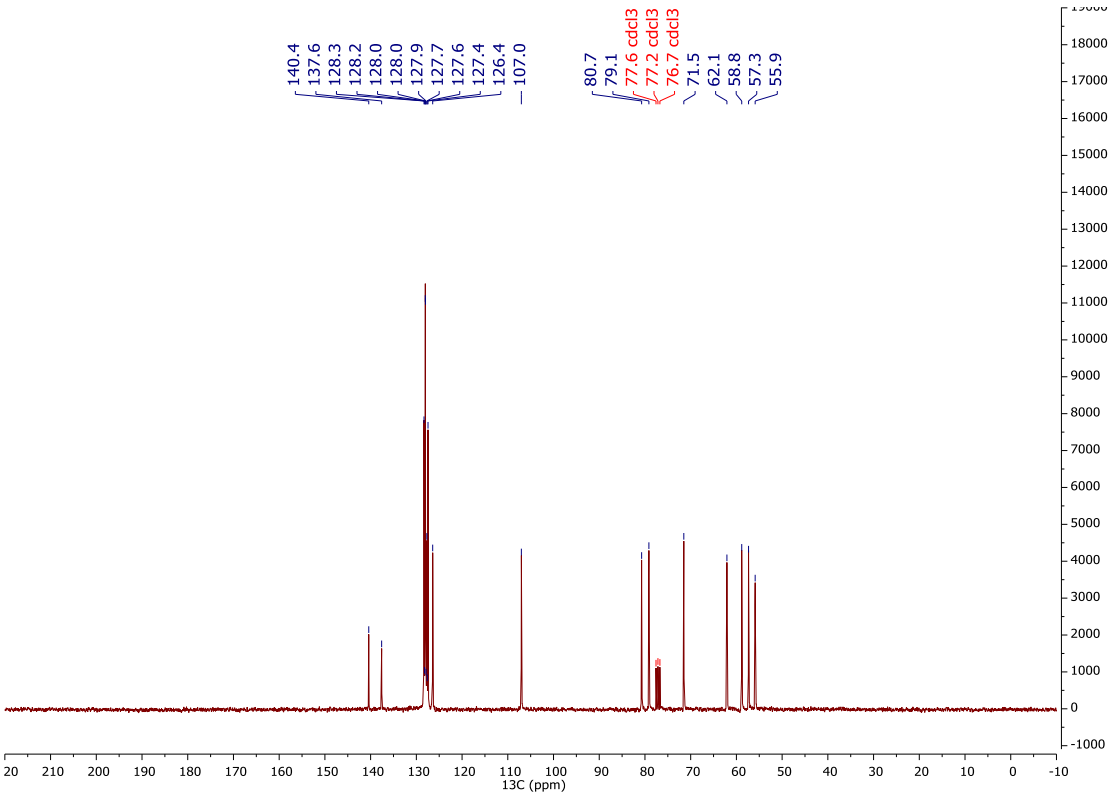
SUPPORTING INFORMATION

(*1R,3S,4S,7R*)-5-Benzyl-7-(benzyloxy)-3-methoxy-2-oxa-5-azabicyclo[2.2.1]heptane (21α)

^{1}H-NMR

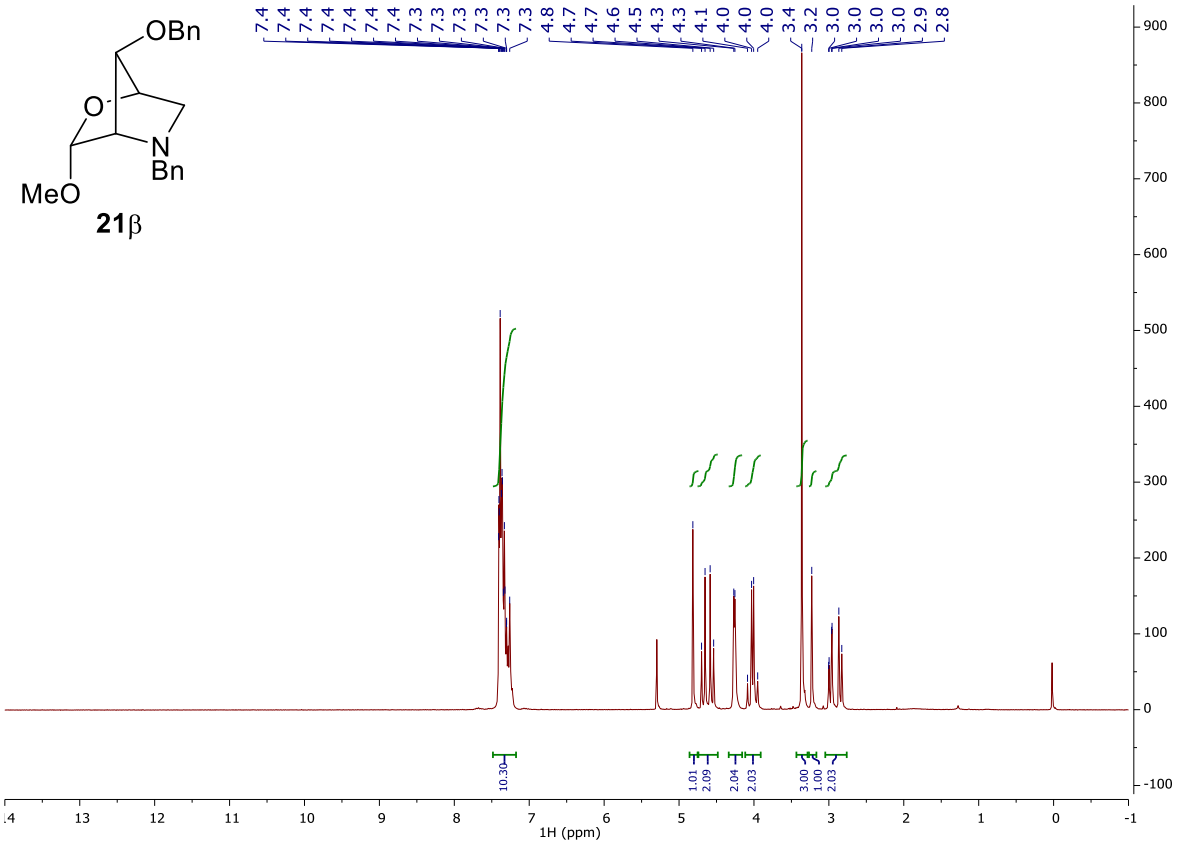


^{13}C-NMR

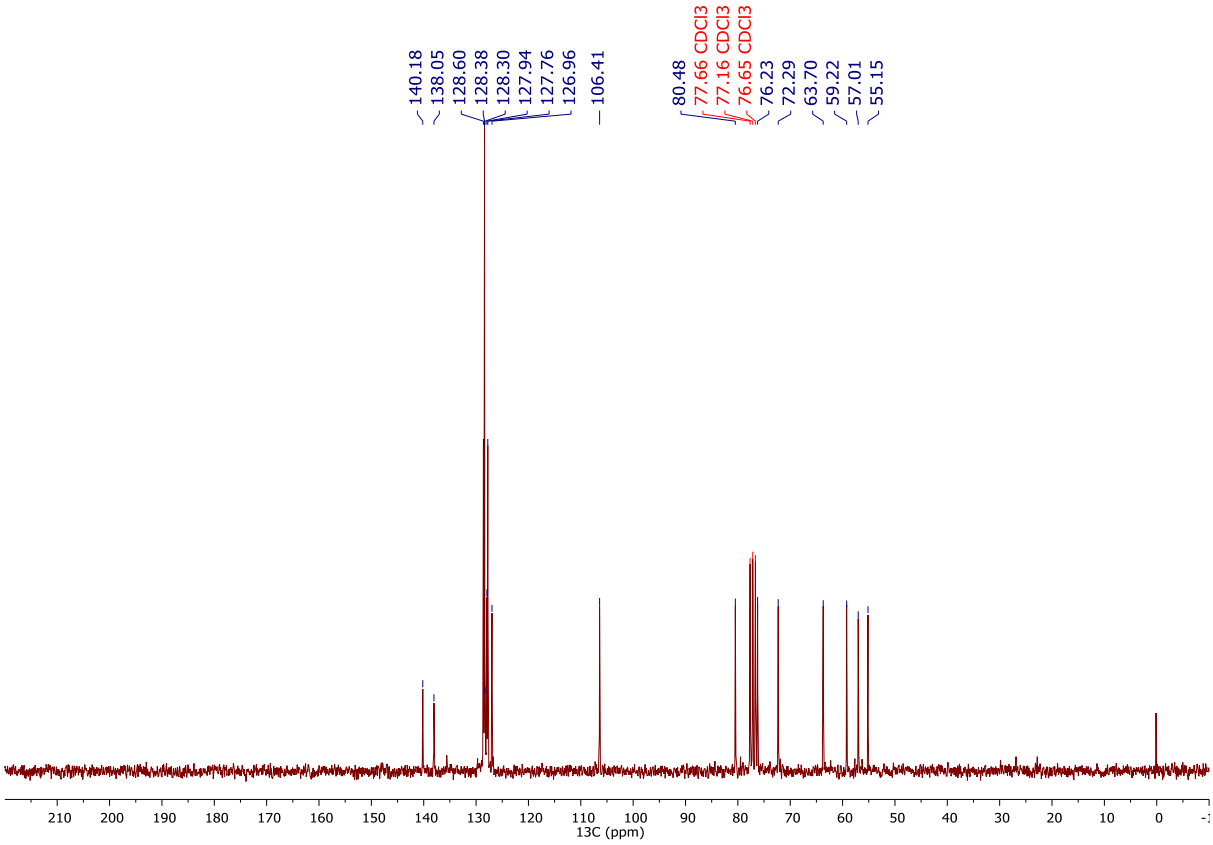


(*1R,3R,4S,7R*)-5-benzyl-7-(benzyloxy)-3-methoxy-2-oxa-5-azabicyclo[2.2.1]heptane (21β)

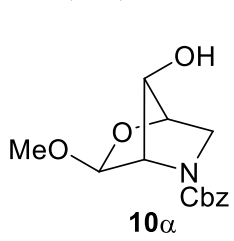
^{1}H-NMR



^{13}C-NMR 6β



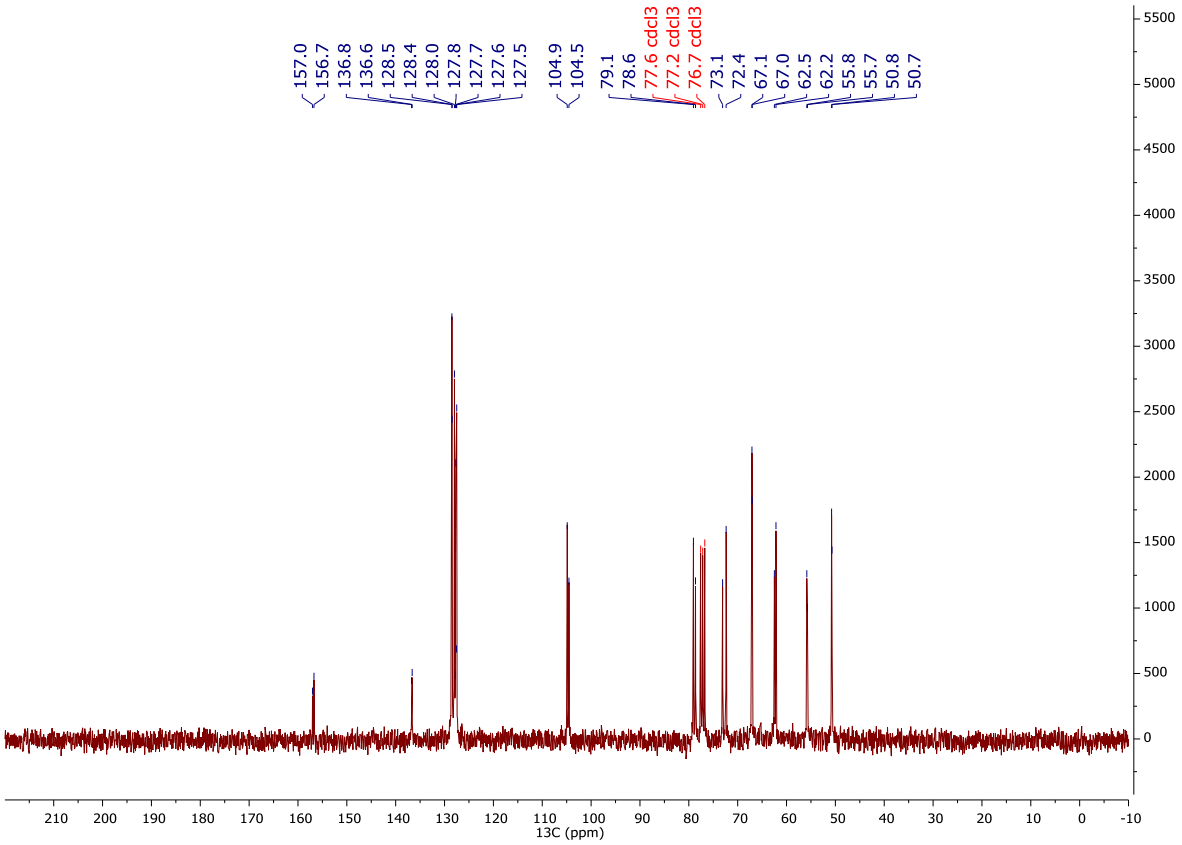
Benzyl (*1R,3S,4S,7R*)-7-hydroxy-3-methoxy-2-oxa-5-azabicyclo[2.2.1]heptane-5-carboxylate (10α)



10α

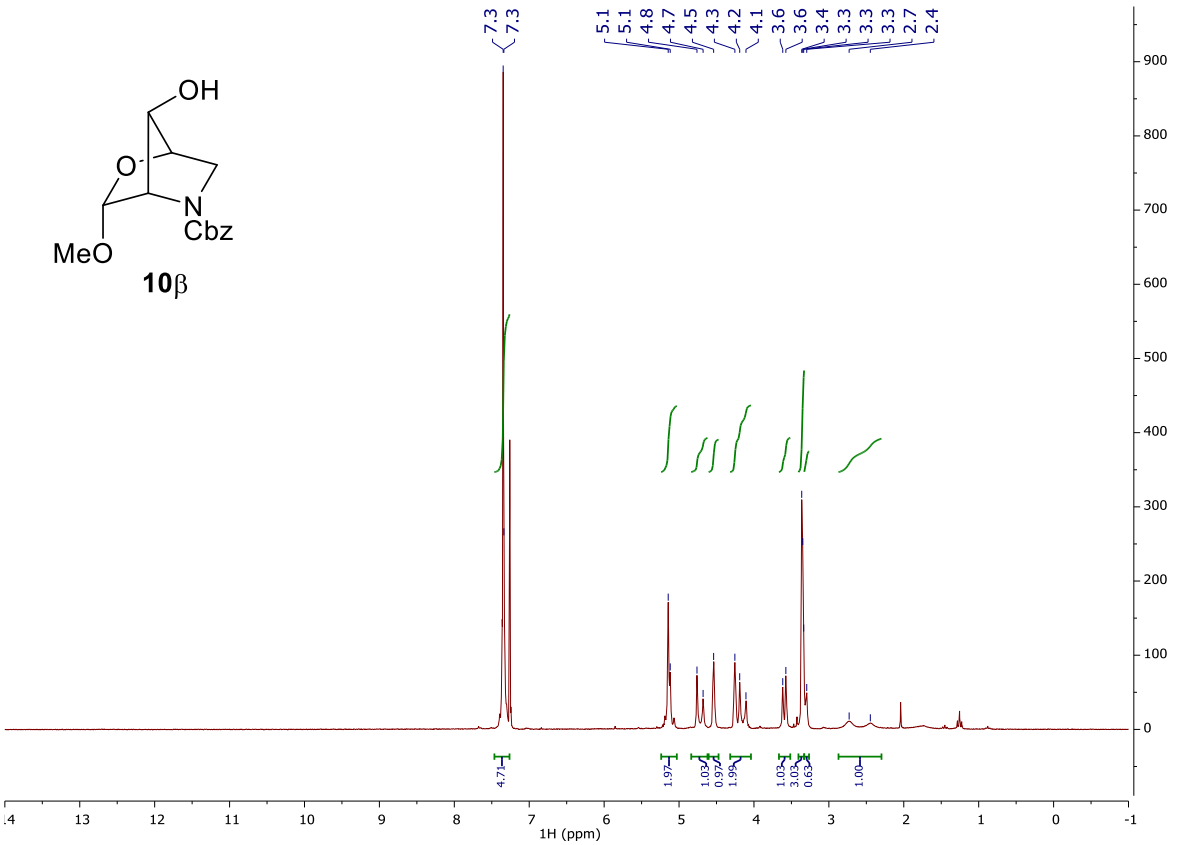
^{1}H-NMR

^{13}C-NMR

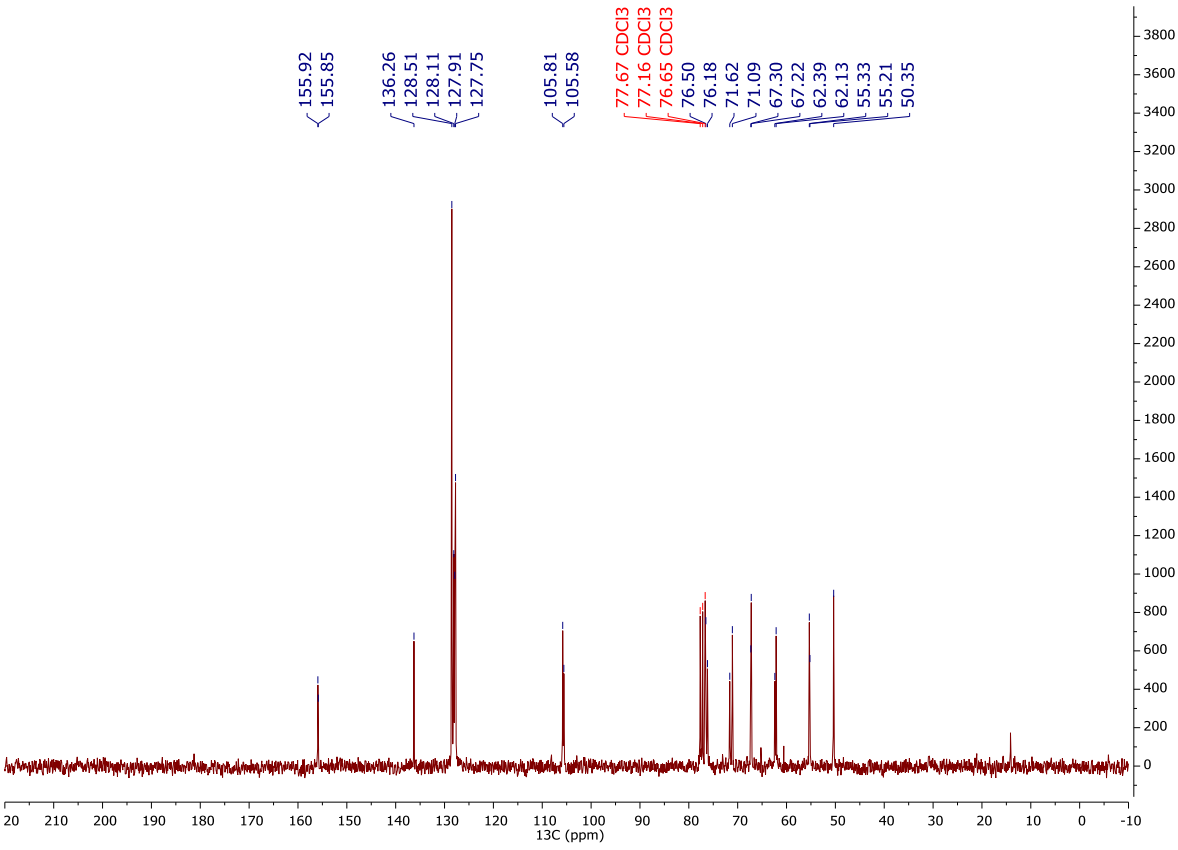


Benzyl (*1R,3R,4S,7R*)-7-hydroxy-3-methoxy-2-oxa-5-azabicyclo[2.2.1]heptane-5-carboxylate (10β)

^{1}**H-NMR**

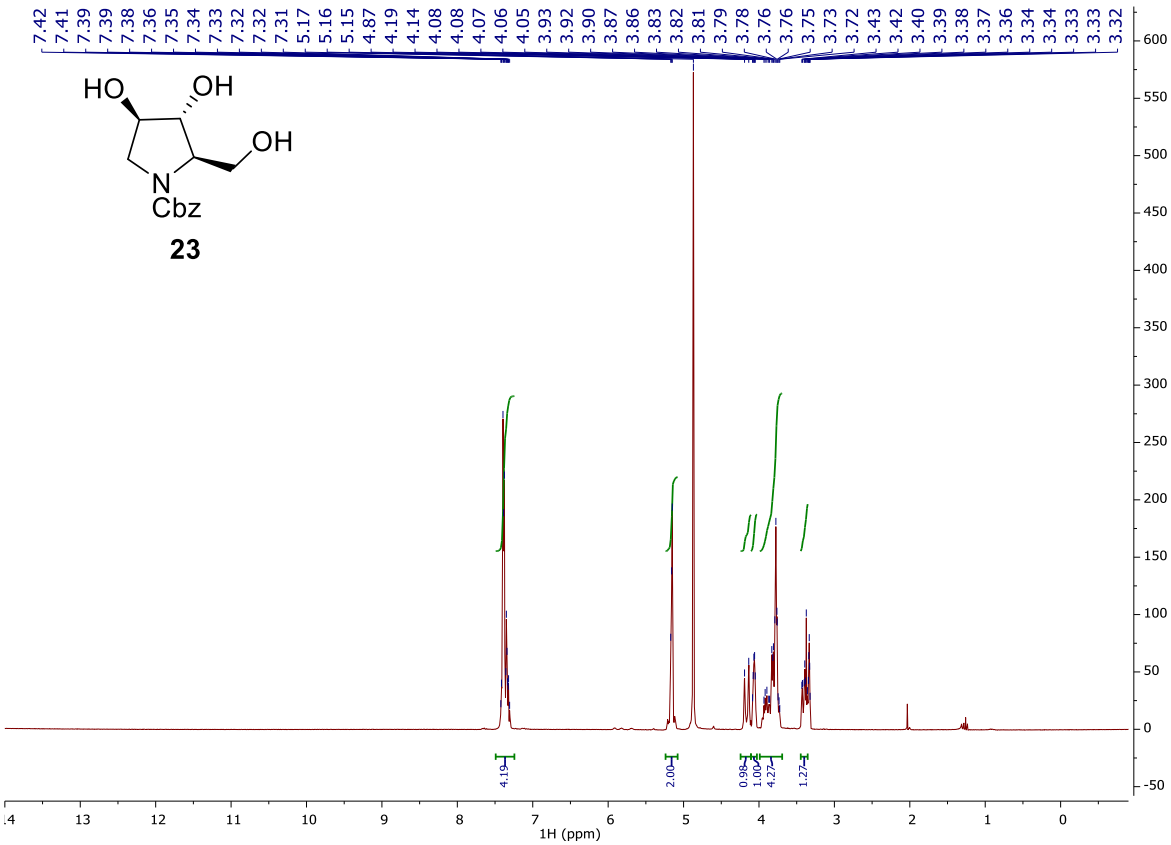


^{13}**C-NMR**

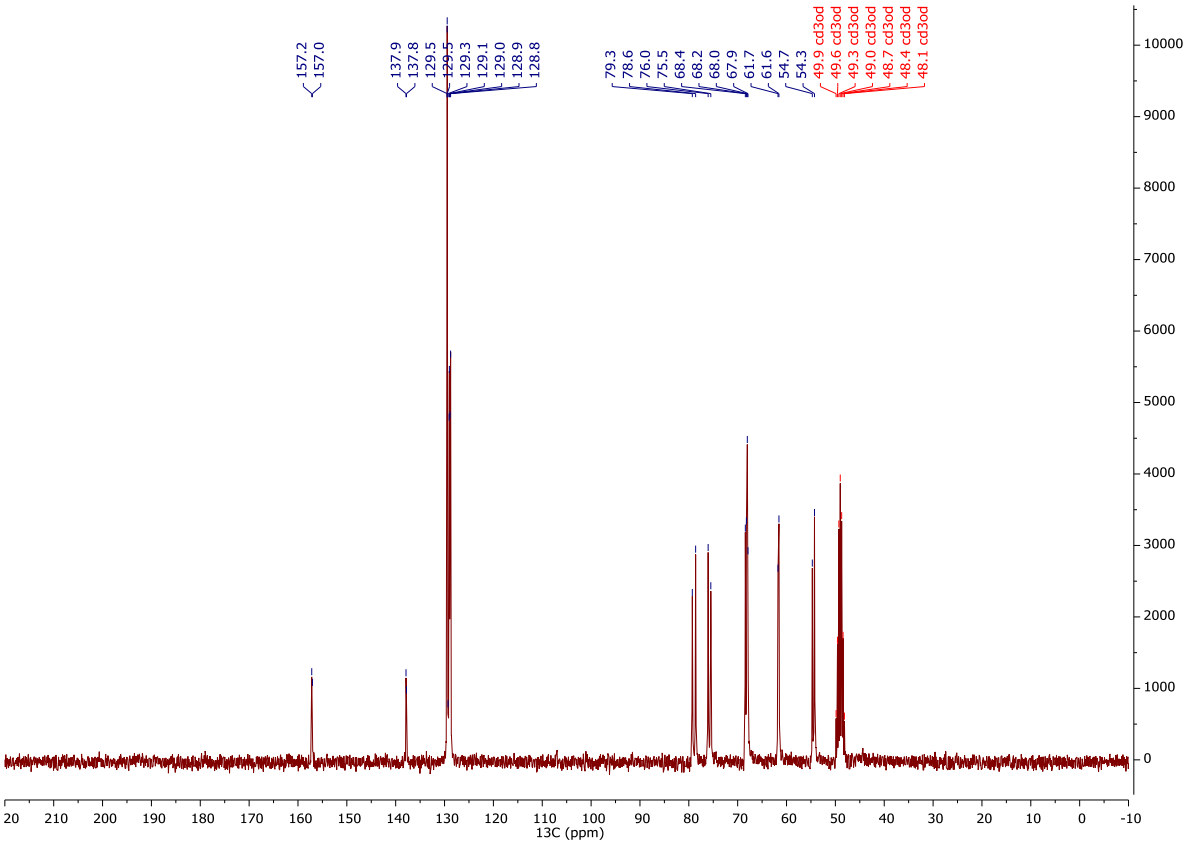


Benzyl (*2R,3R,4R*)-3,4-dihydroxy-2-(hydroxymethyl)pyrrolidine-1-carboxylate (23)

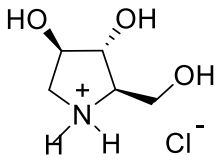
^{1}H-NMR



^{13}C-NMR



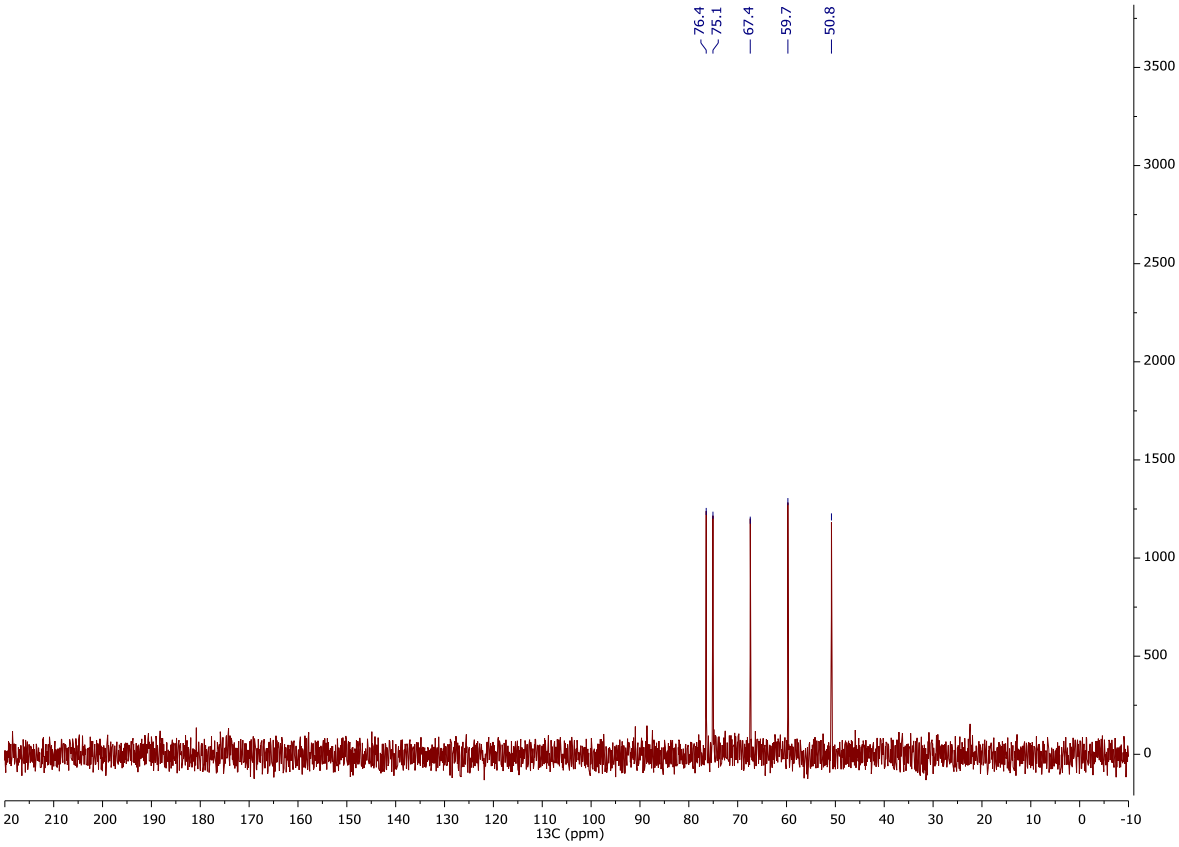
(*2R,3R,4R*)-2-(Hydroxymethyl)pyrrolidine-3,4-diol (DAB) (14.HCl)



14.HCl

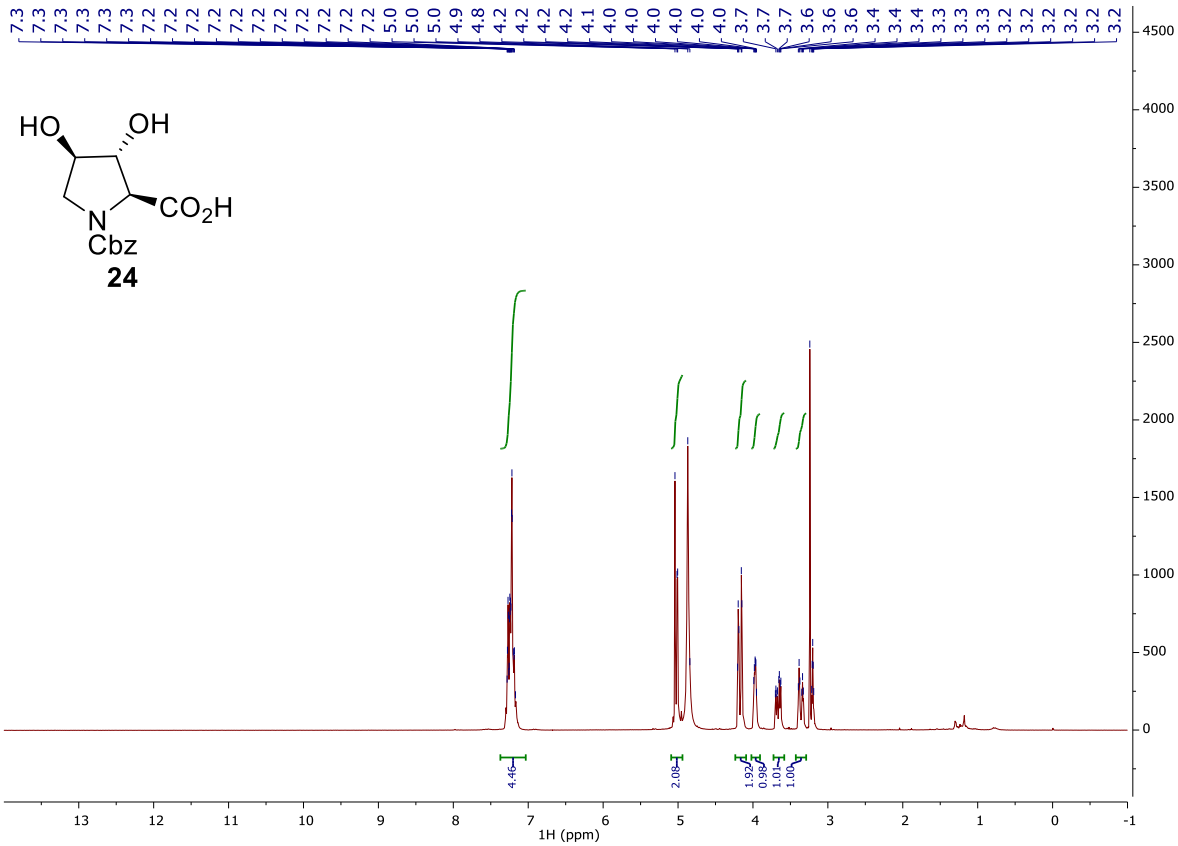
^{1}H-NMR

^{13}C-NMR

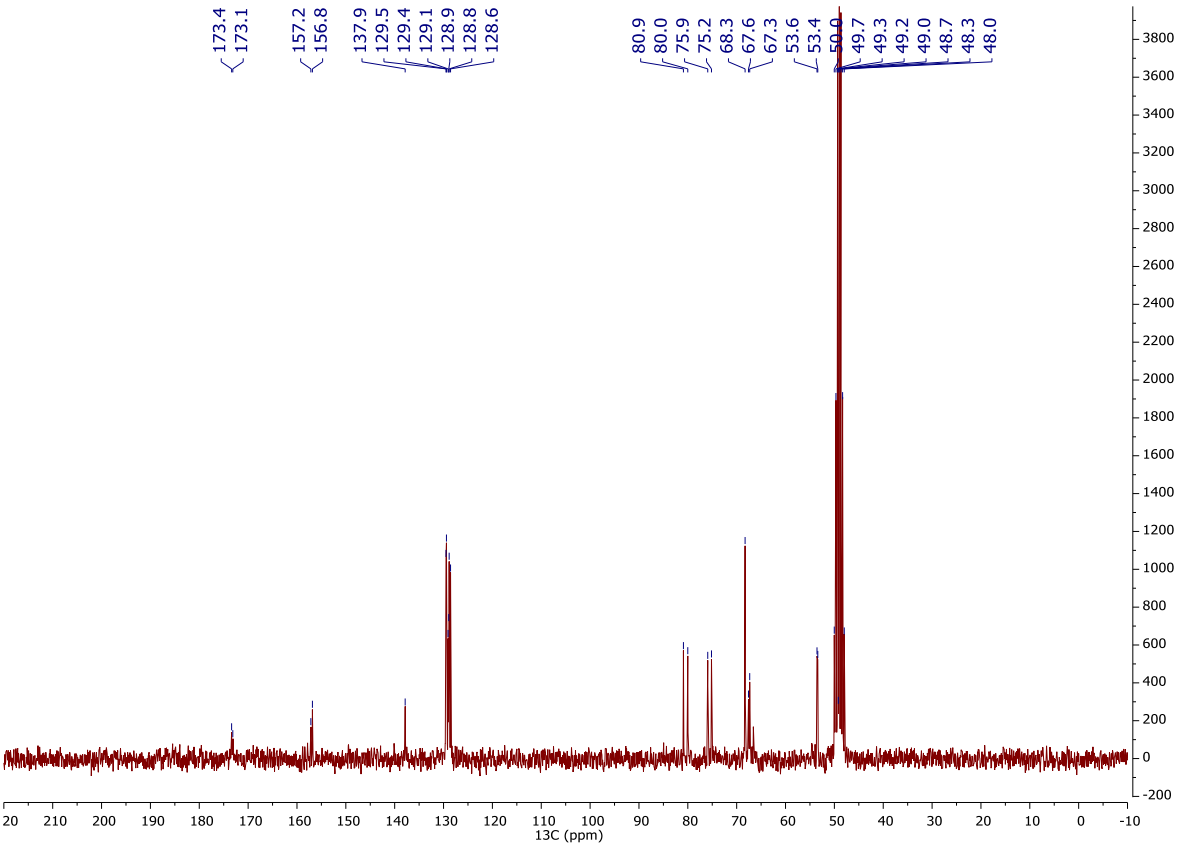


(3*R*,4*R*)-*N*-((Benzyloxy)carbonyl)-3,4-dihydroxy-*L*-proline (24)

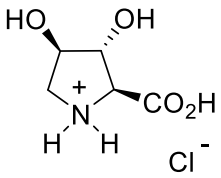
^{1}**H-NMR**



^{13}**C-NMR**



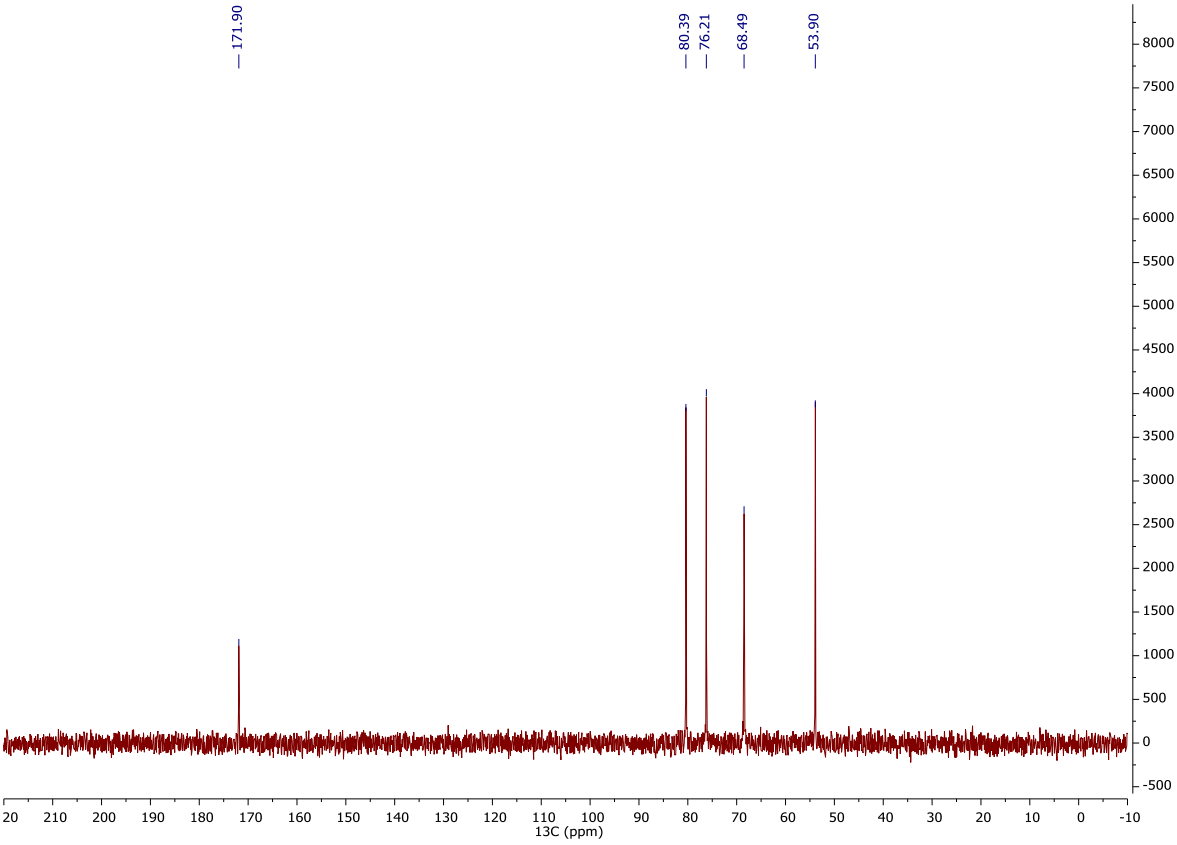
(3*R*,4*R*))-3,4-Dihydroxy-*L*-proline (15.HCl)



15.HCl

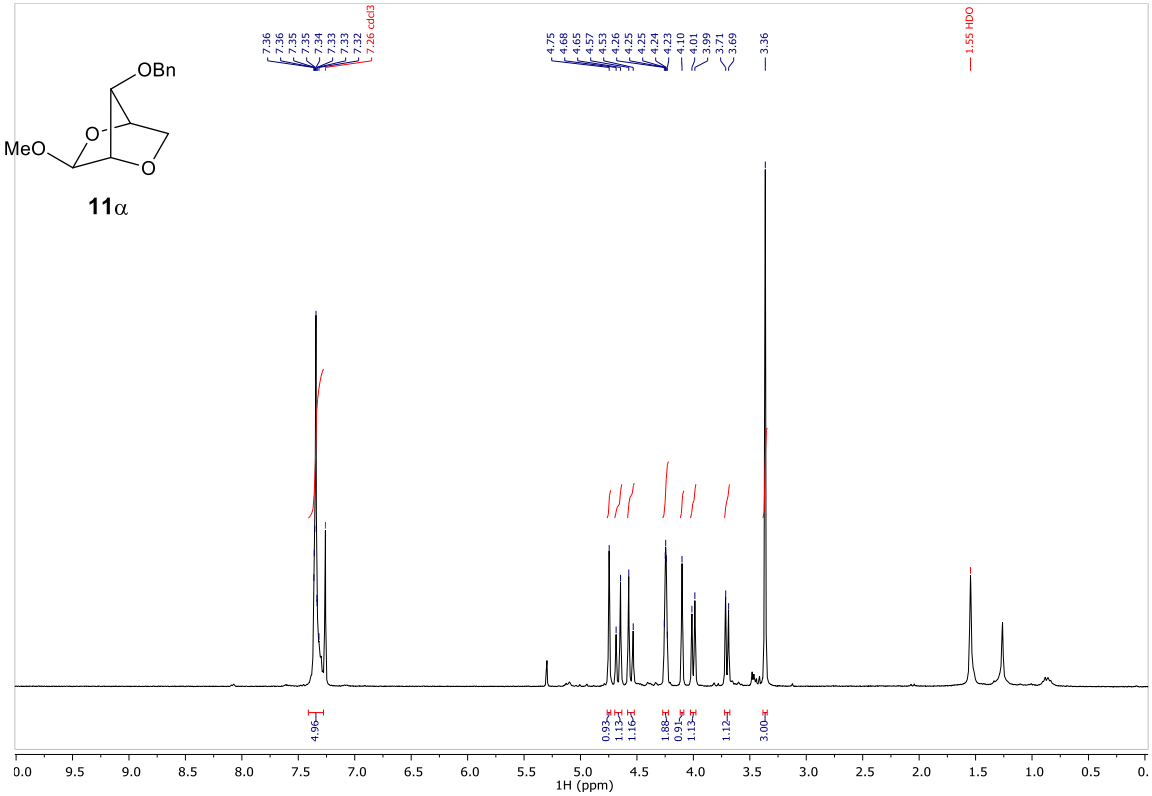
^{1}H-NMR

^{13}C-NMR

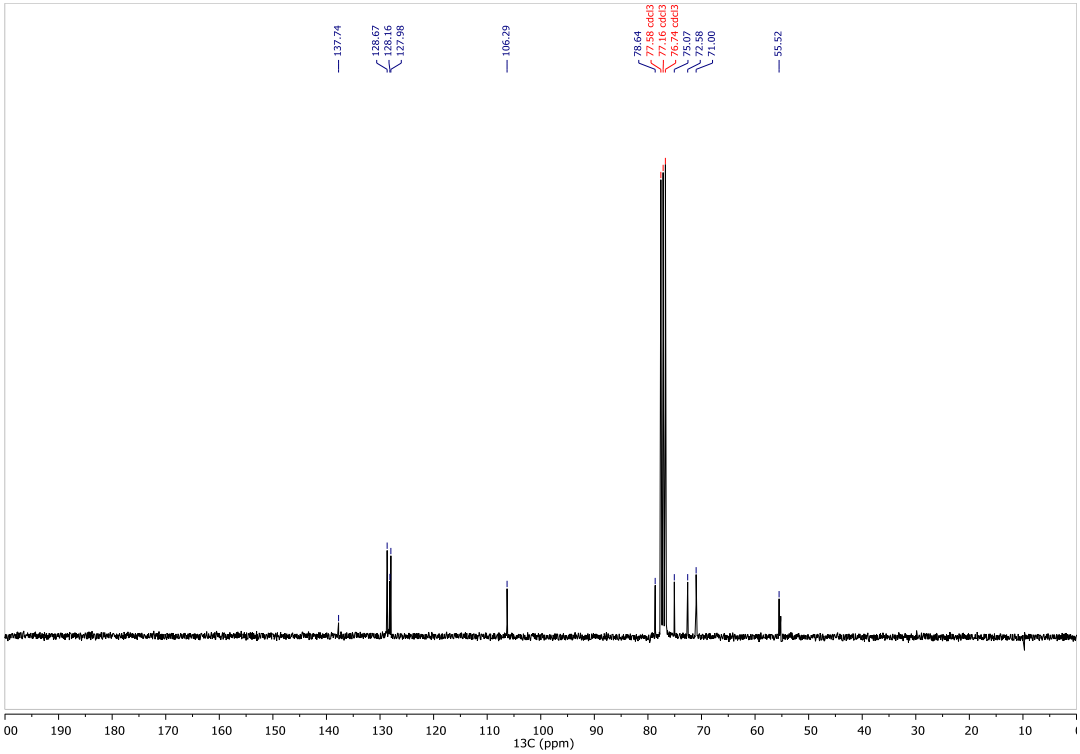


(1*R*,3S,4S,7S)-7-(Benzyloxy)-3-methoxy-2,5-dioxabicyclo[2.2.1]heptane (11α)

^{1}H-NMR

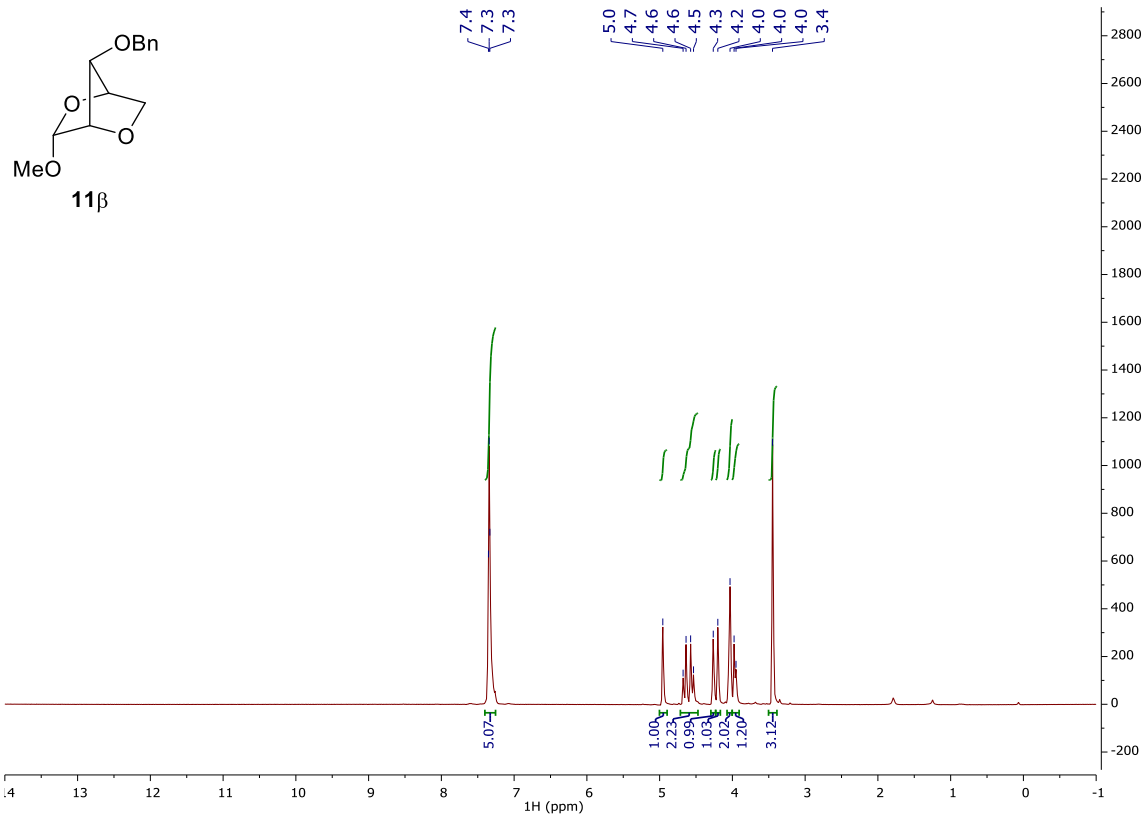


^{13}C-NMR

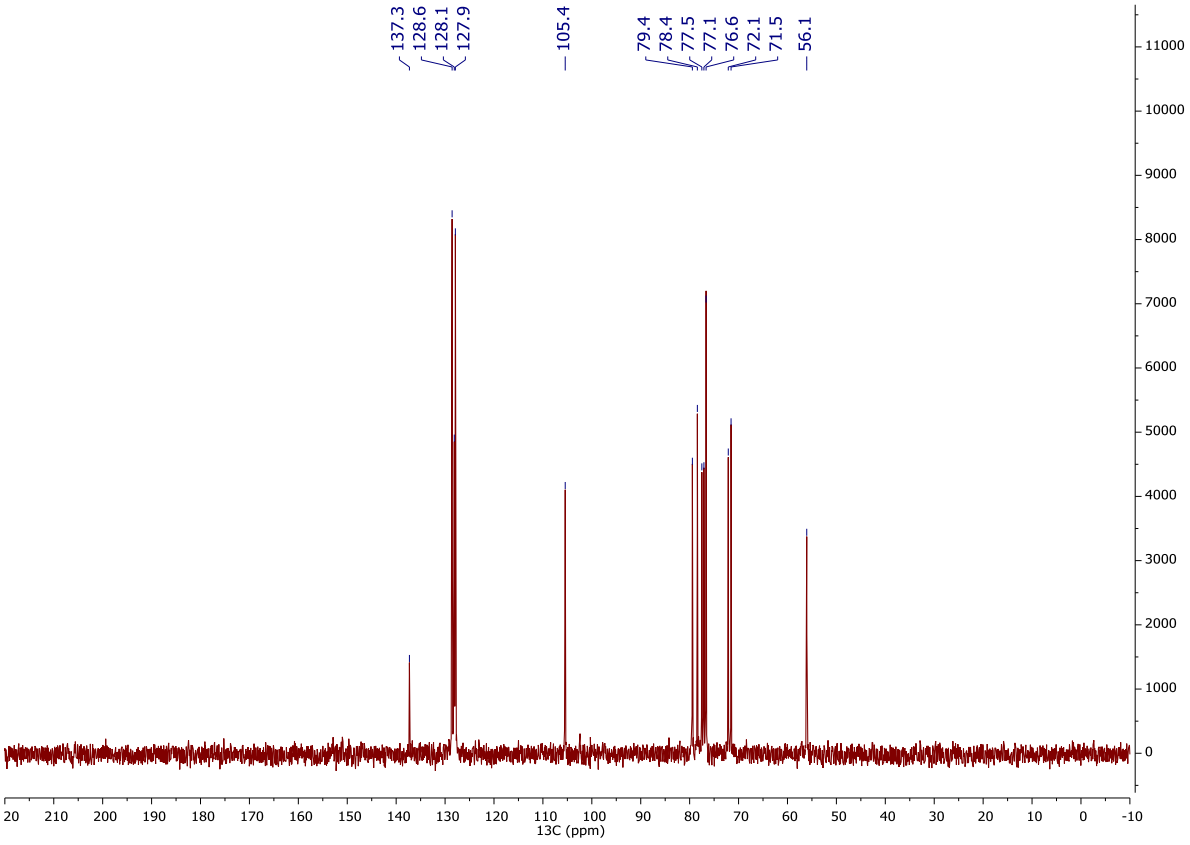


(1*R*,3S,4S,7S)-7-(benzyloxy)-3-methoxy-2,5-dioxabicyclo[2.2.1]heptane (11β)

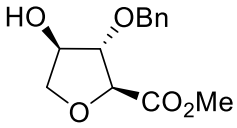
^{1}H-NMR



^{13}C-NMR



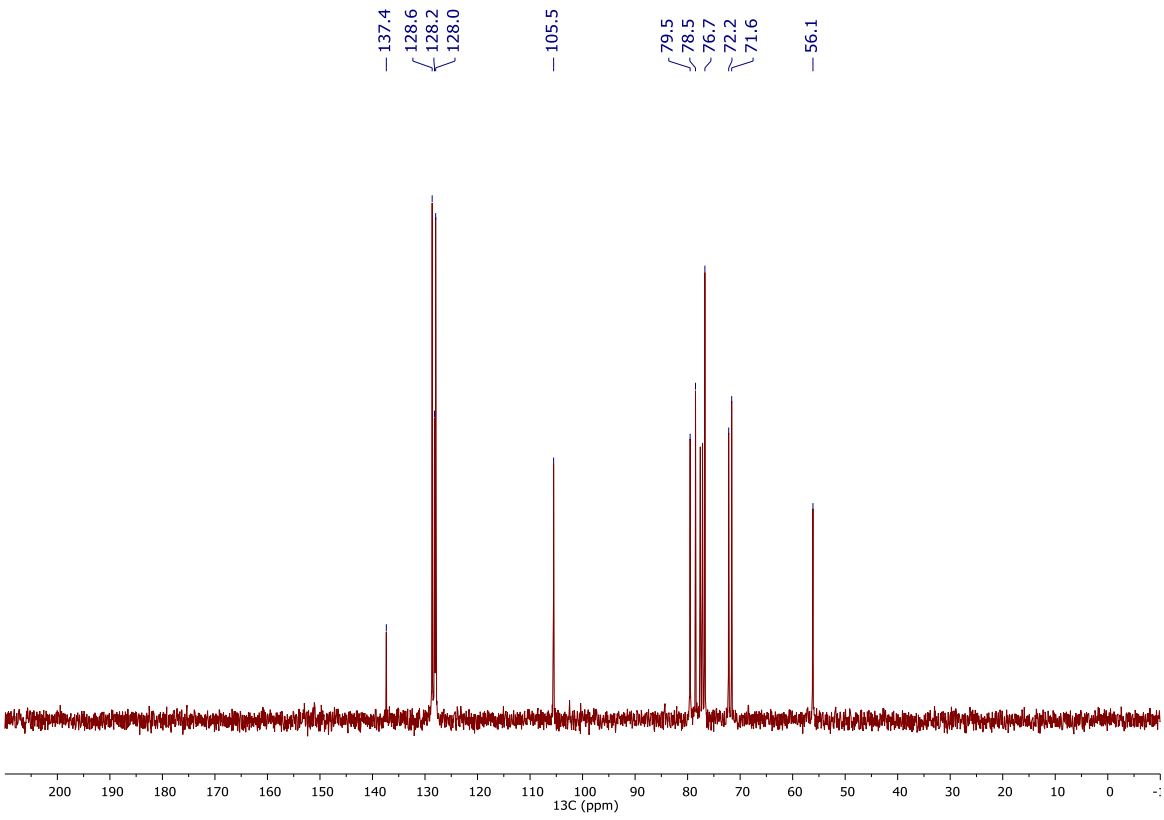
Methyl (2*S*,3*S*,4*R*)-3-(benzyloxy)-4-hydroxytetrahydrofuran-2-carboxylate (27)



27

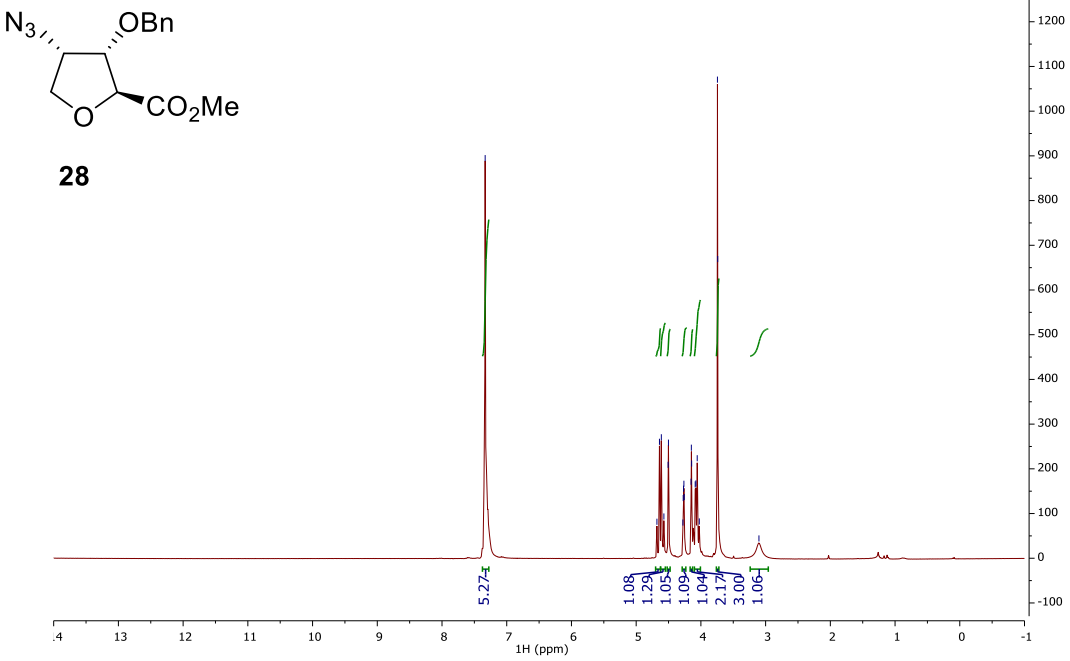
^{1}H-NMR

^{13}C-NMR

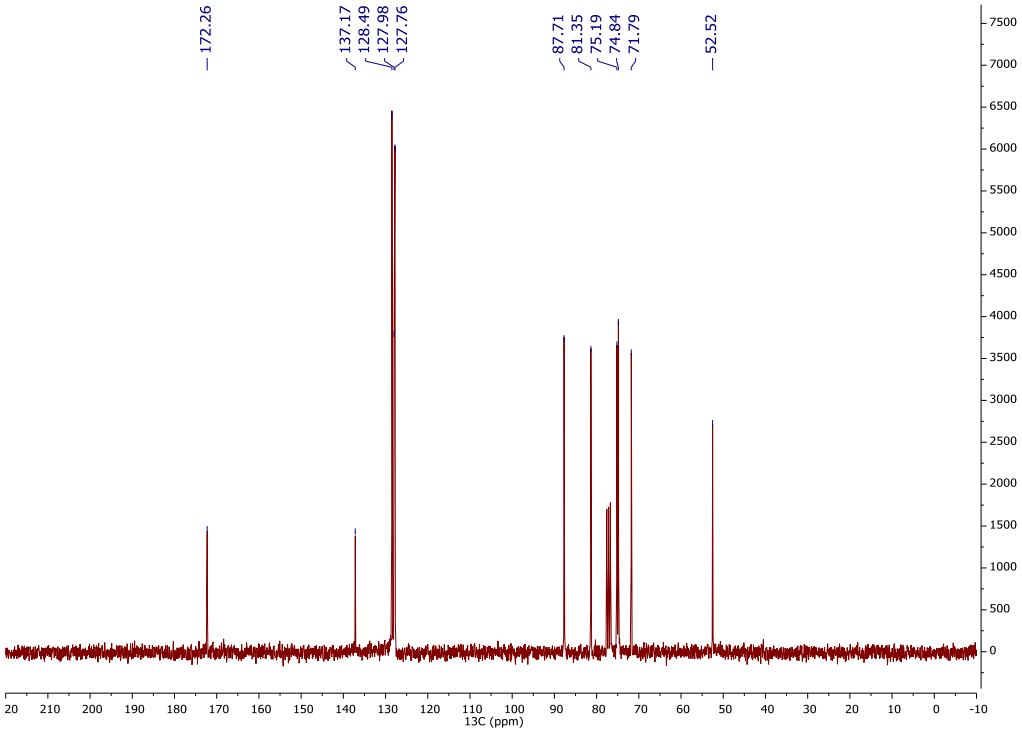


Methyl (2*S*,3*S*,4*S*)-4-azido-3-(benzyloxy)tetrahydrofuran-2-carboxylate (28)

^{1}H-NMR

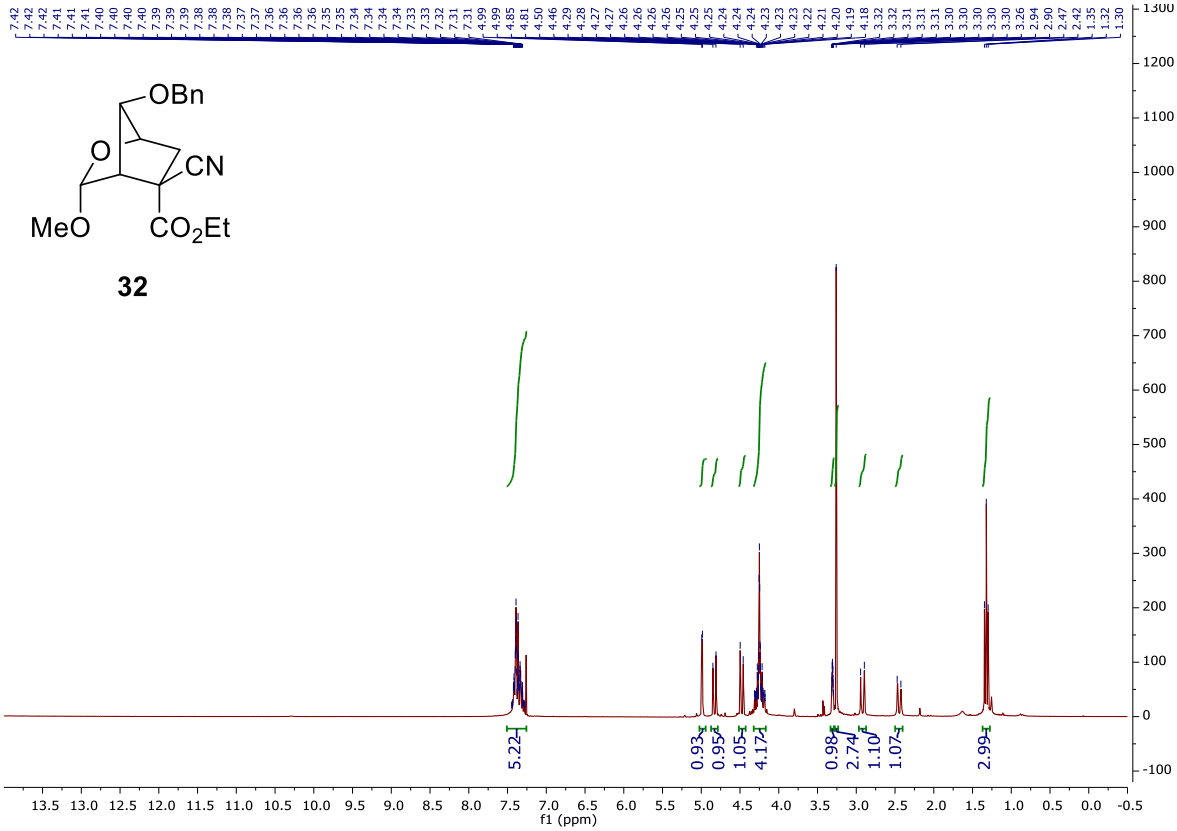


^{13}C-NMR

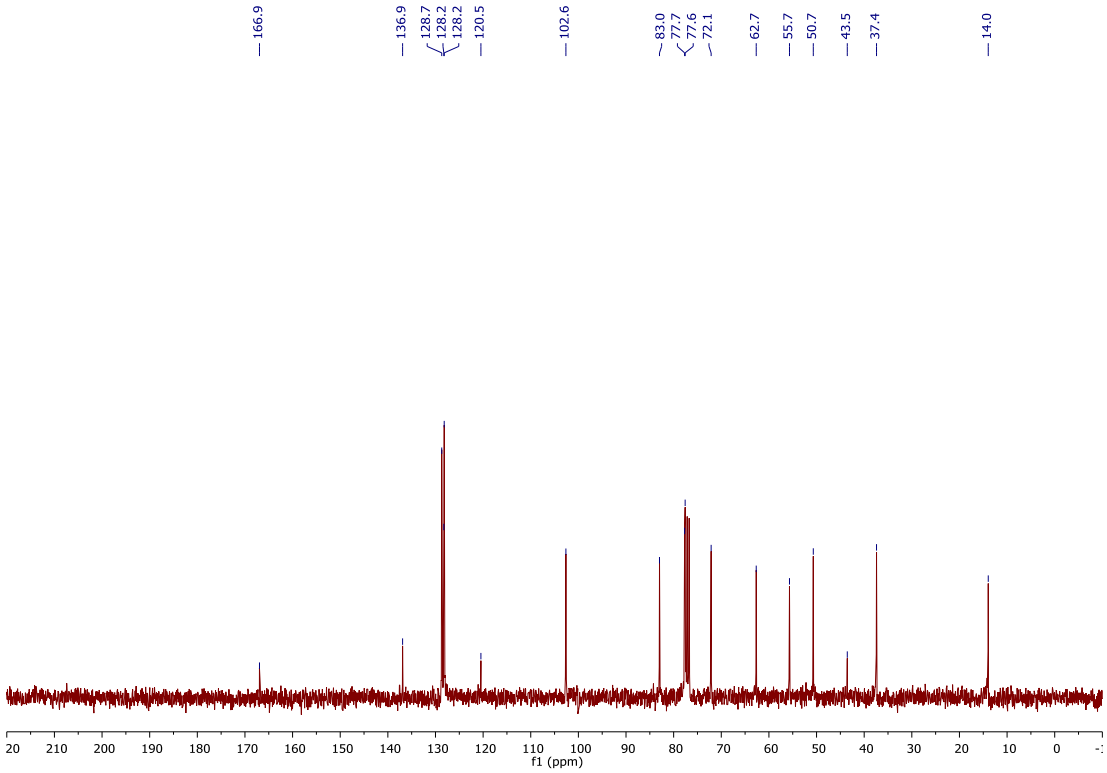


(Ethyl (1*R*,3*R*,4*S*,5*S*,7*R*)-7-(benzyloxy)-5-cyano-3-methoxy-2-oxabicyclo[2.2.1]heptane-5-carboxylate (32)

^{1}H-NMR

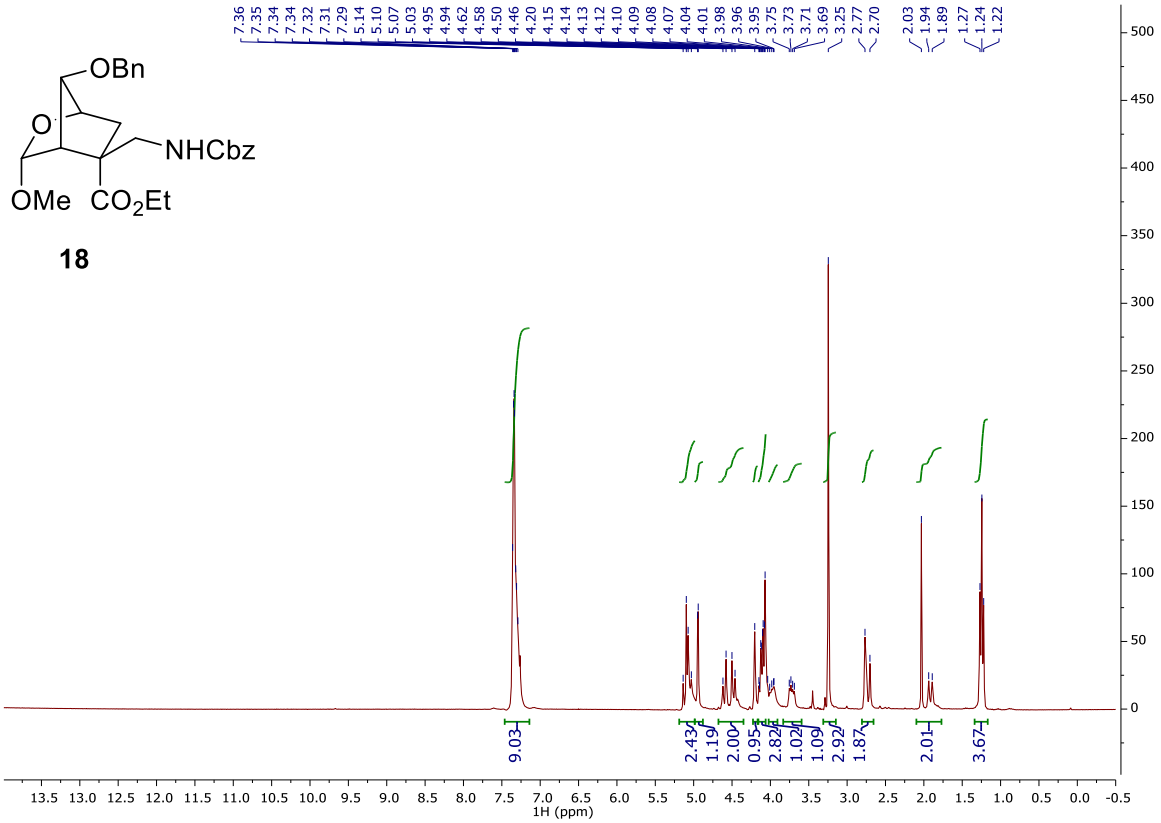


^{13}C-NMR

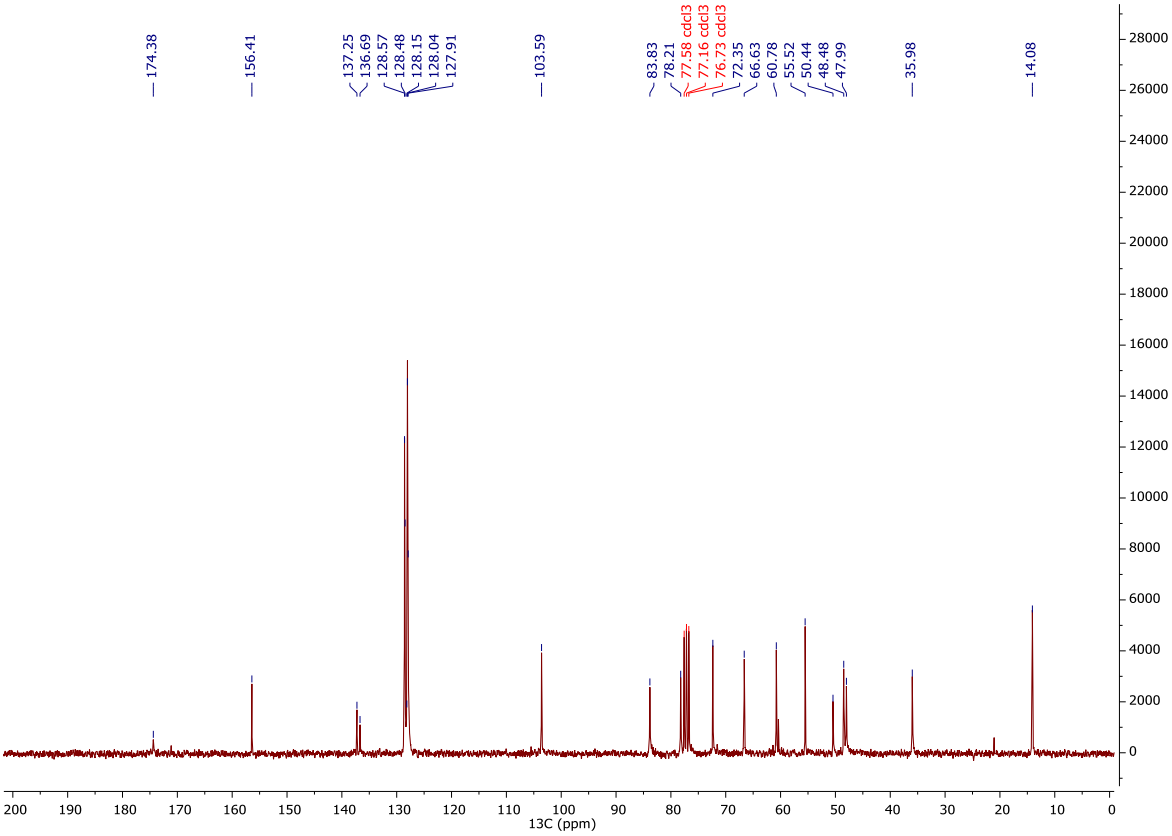


Ethyl (1*R*,3*R*,4*S*,5*S*,7*R*)-7-(benzyloxy)-5-((((benzyloxy)carbonyl)amino)methyl)-3-methoxy-2-oxabicyclo[2.2.1]heptane-5-carboxylate (18)

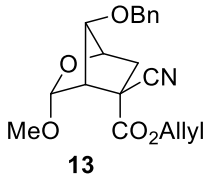
^{1}**H-NMR**



^{13}**C-NMR**



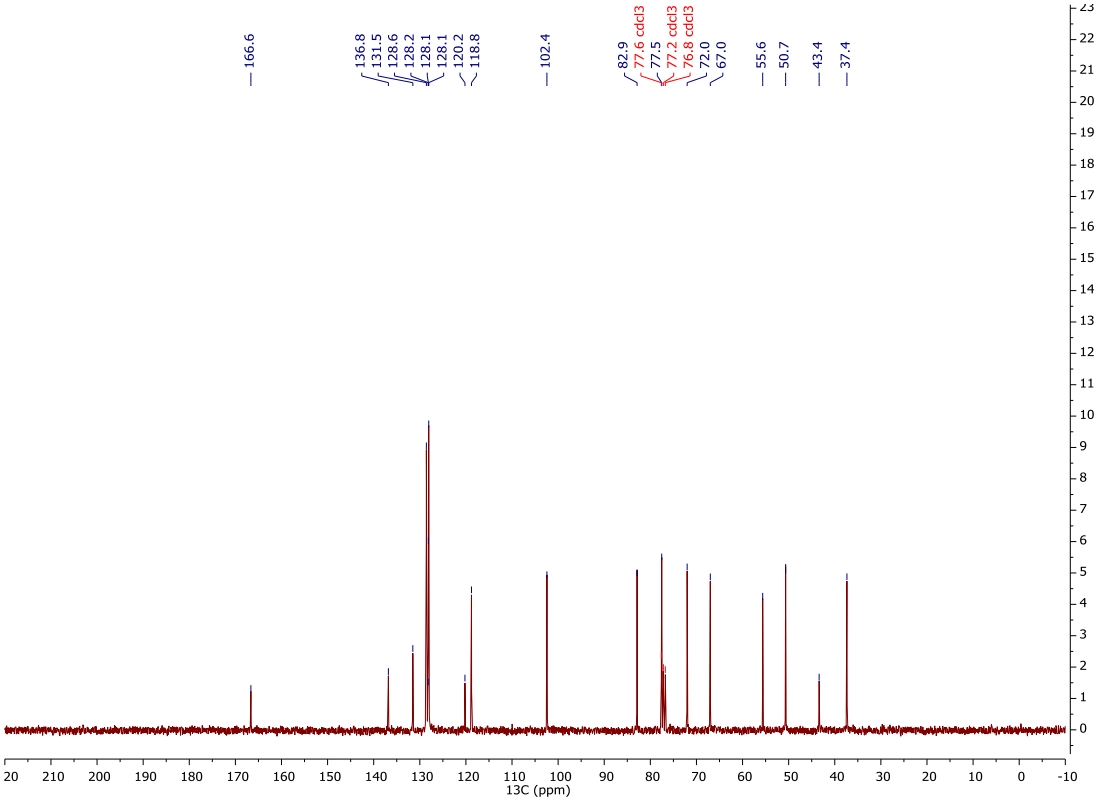
Allyl (1*R*,3*R*,4*S*,5*S*,7*R*)-7-(benzyloxy)-5-cyano-3-methoxy-2-oxabicyclo[2.2.1]heptane-5-carboxylate (13)



13

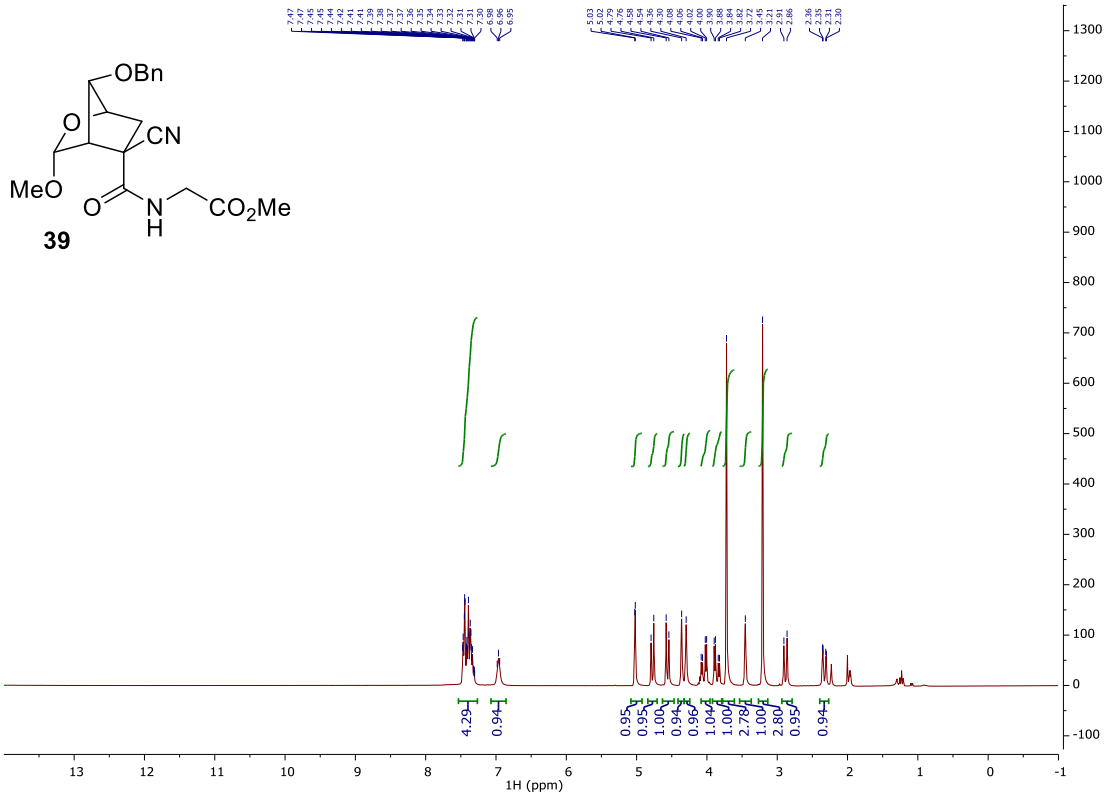
^{1}H-NMR

^{13}C-NMR

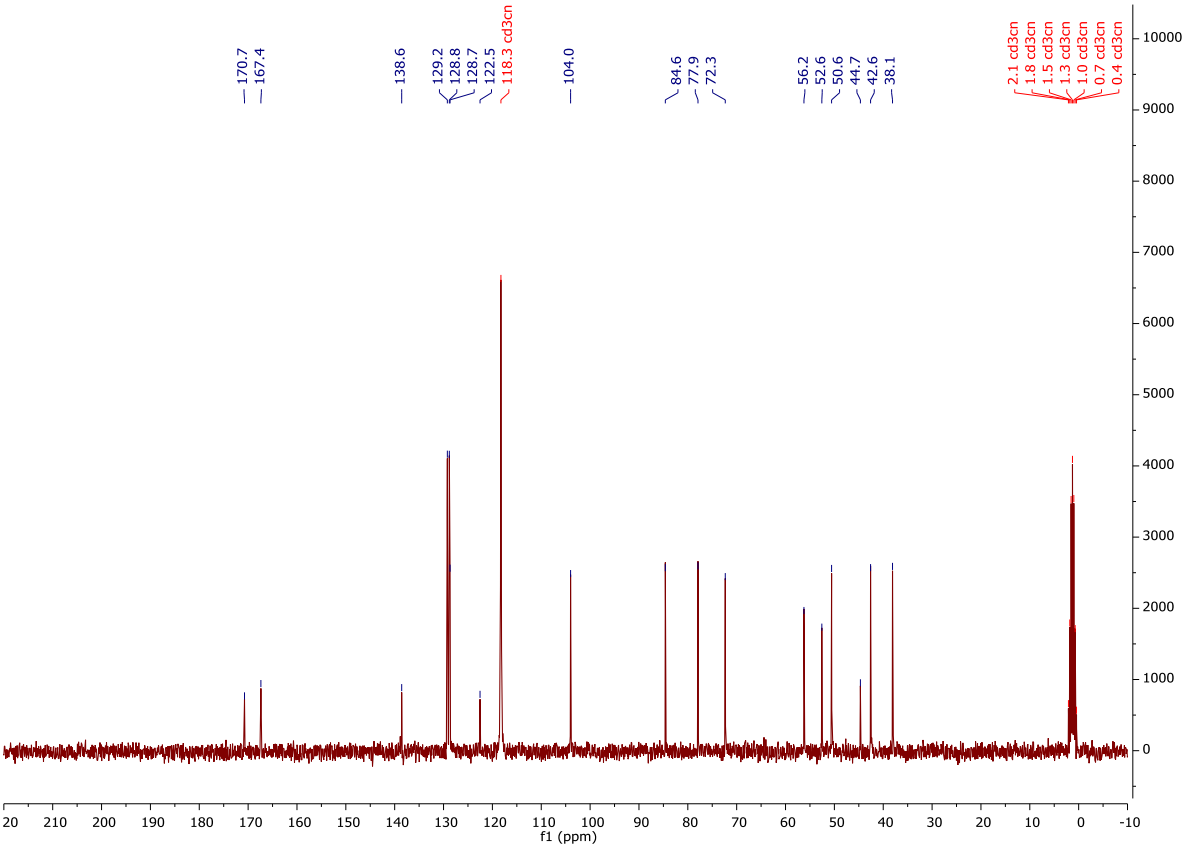


Methyl ((1*R*,3*R*,4*S*,5*S*,7*R*)-7-(benzyloxy)-5-cyano-3-methoxy-2-oxabicyclo[2.2.1]heptane-5-carbonyl)glycinate (39)

^{1}H-NMR

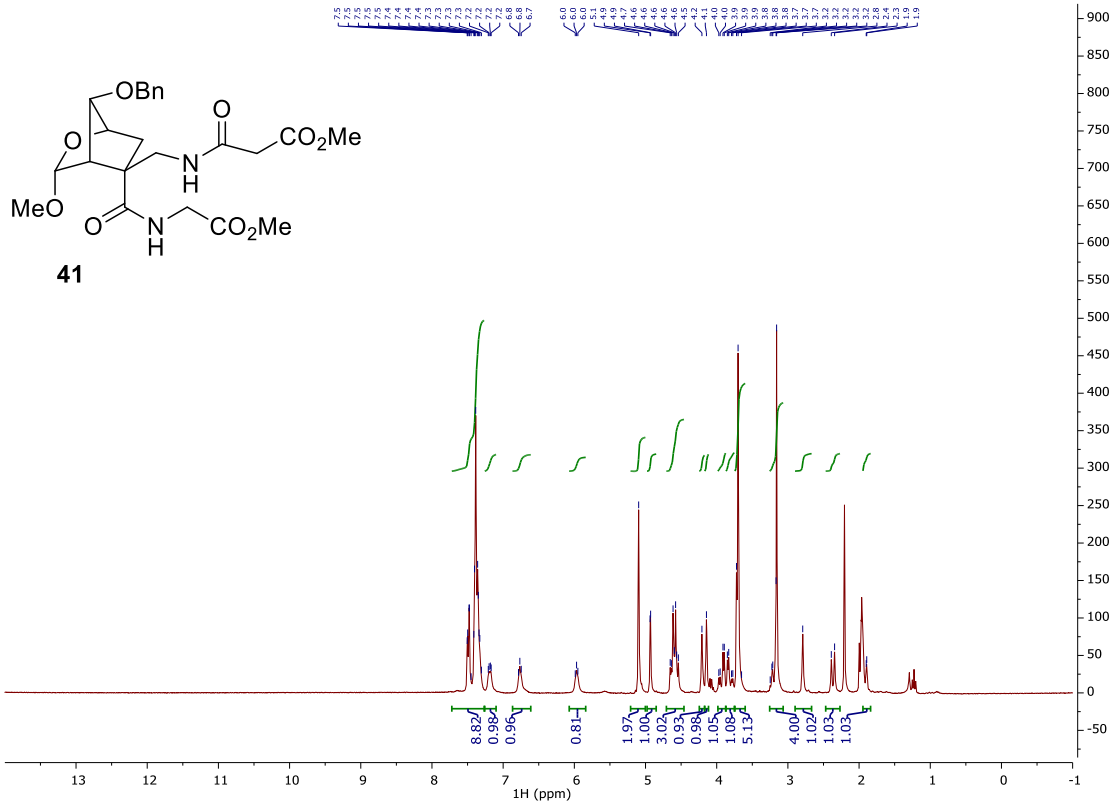


^{13}C-NMR

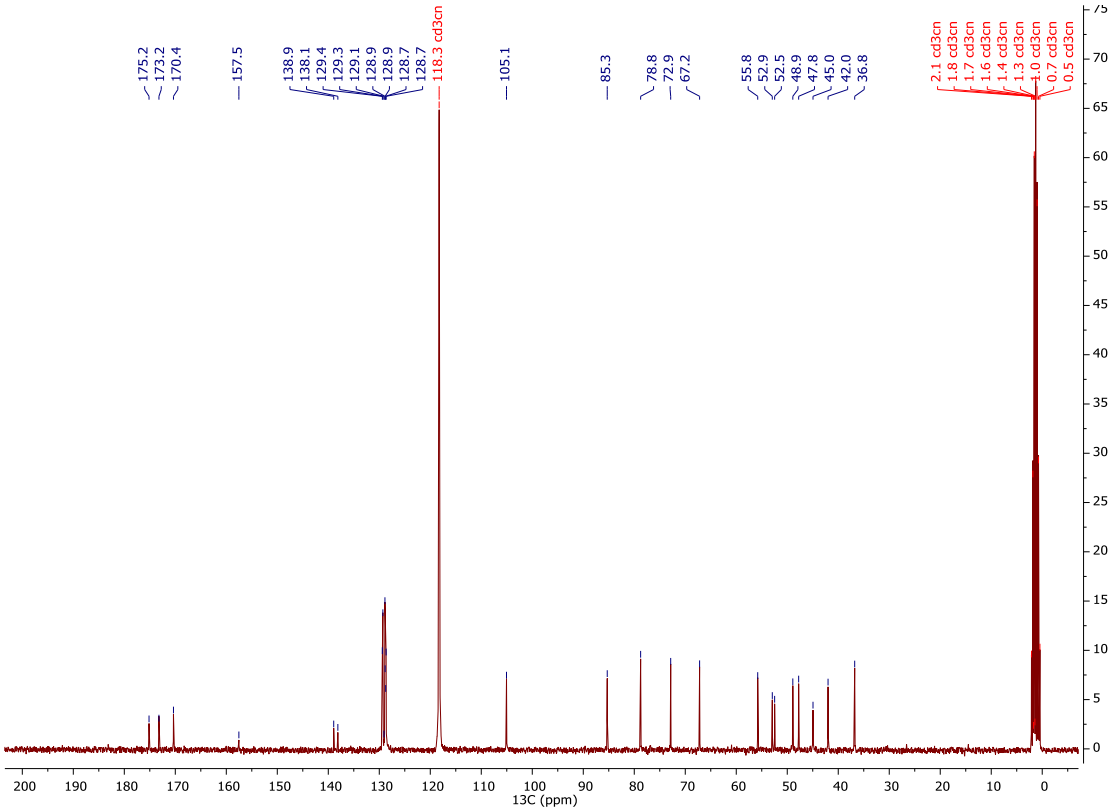


Methyl ((1*R*,3*R*,4*S*,5*S*,7*R*)-7-(benzyloxy)-5-((2-(((benzyloxy)carbonyl)amino)acetamido)methyl)-3-methoxy-2-oxabicyclo[2.2.1]heptane-5-carbonyl)glycinate (41)

^{1}H-NMR

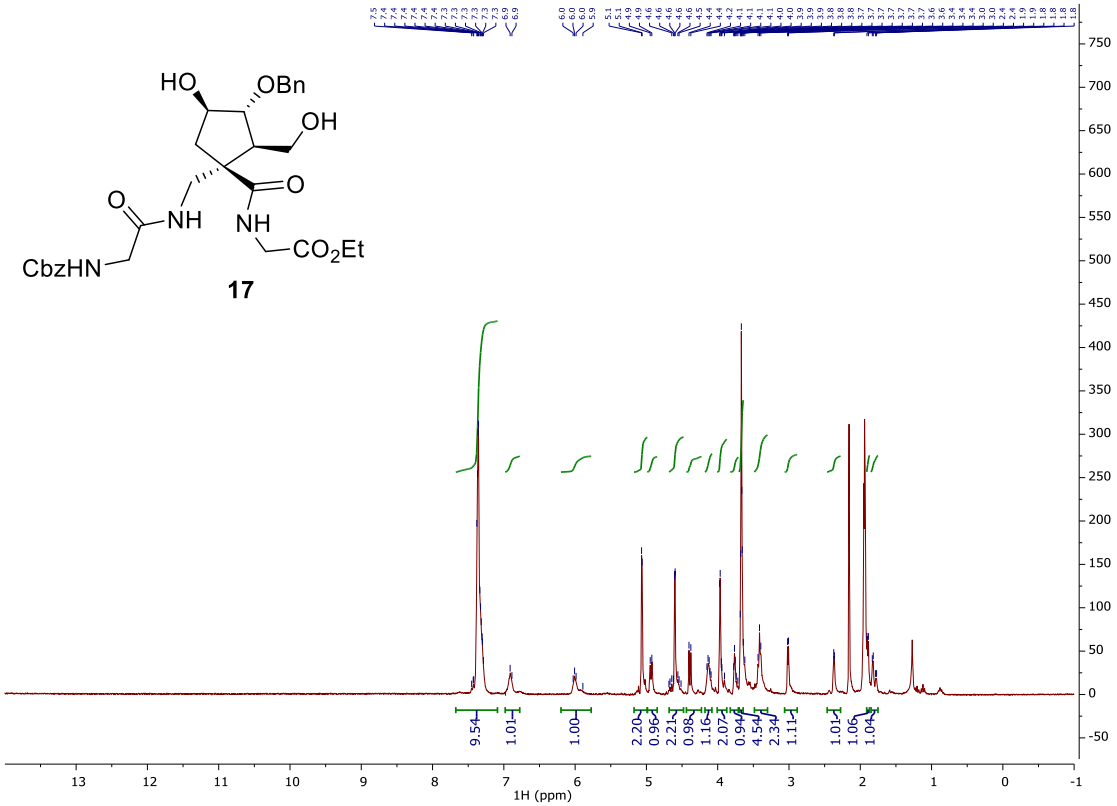


^{13}C-NMR

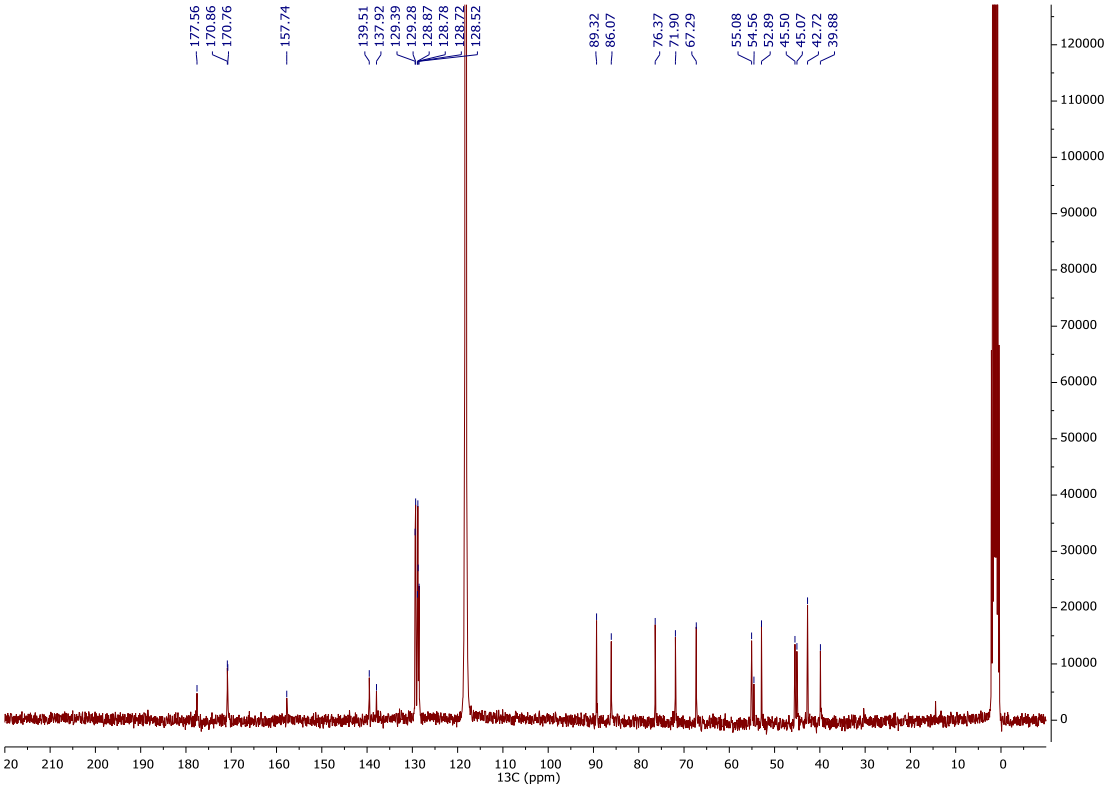


Methyl ((1*S*,2*R*,3*R*,4*R*)-3-(benzyloxy)-1-((2-(((benzyloxy)carbonyl)amino)acetamido)methyl)-4-hydroxy-2-(hydroxymethyl)cyclopentane-1-carbonyl)glycinate (17)

^{1}H-NMR

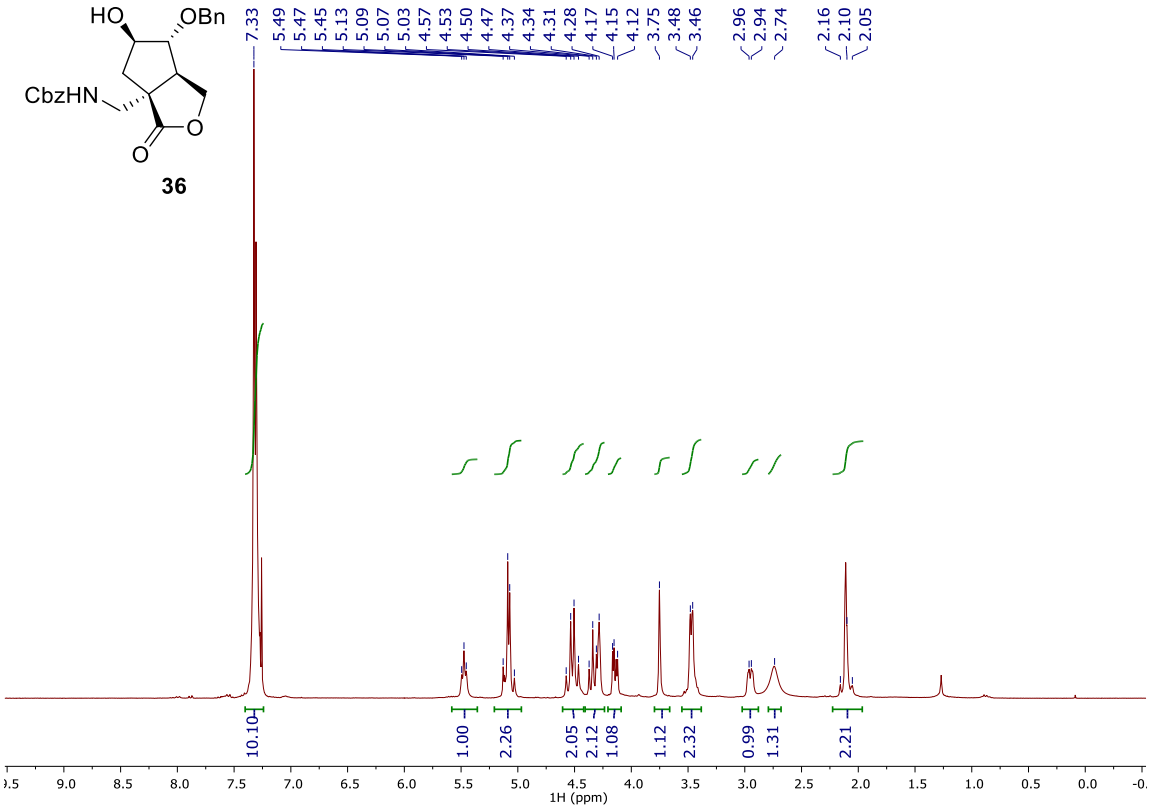


^{13}C-NMR

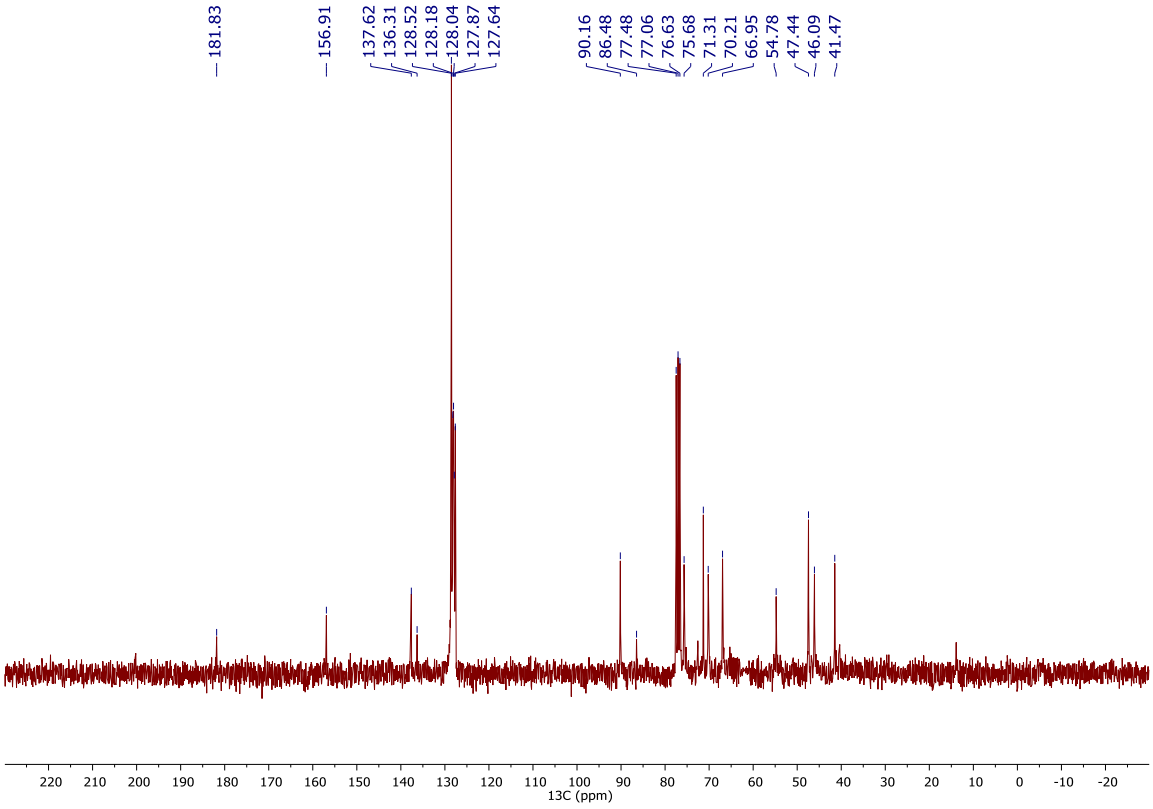


Benzyl ((3a*R*,5*R*,6*R*,6a*R*)-6-(benzyloxy)-5-hydroxy-3-oxotetrahydro-1*H*-cyclopenta[*c*]furan-3a(3*H*)-yl)carbamate (36)

^{1}H-NMR

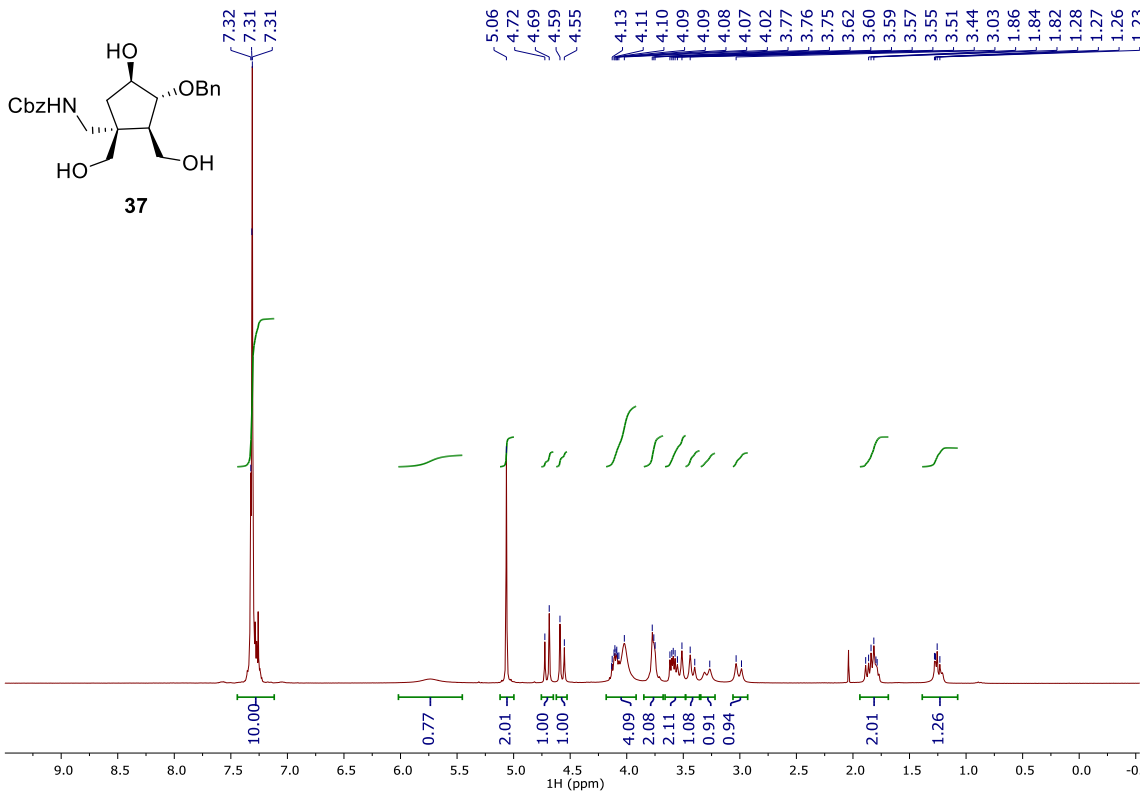


^{13}C-NMR

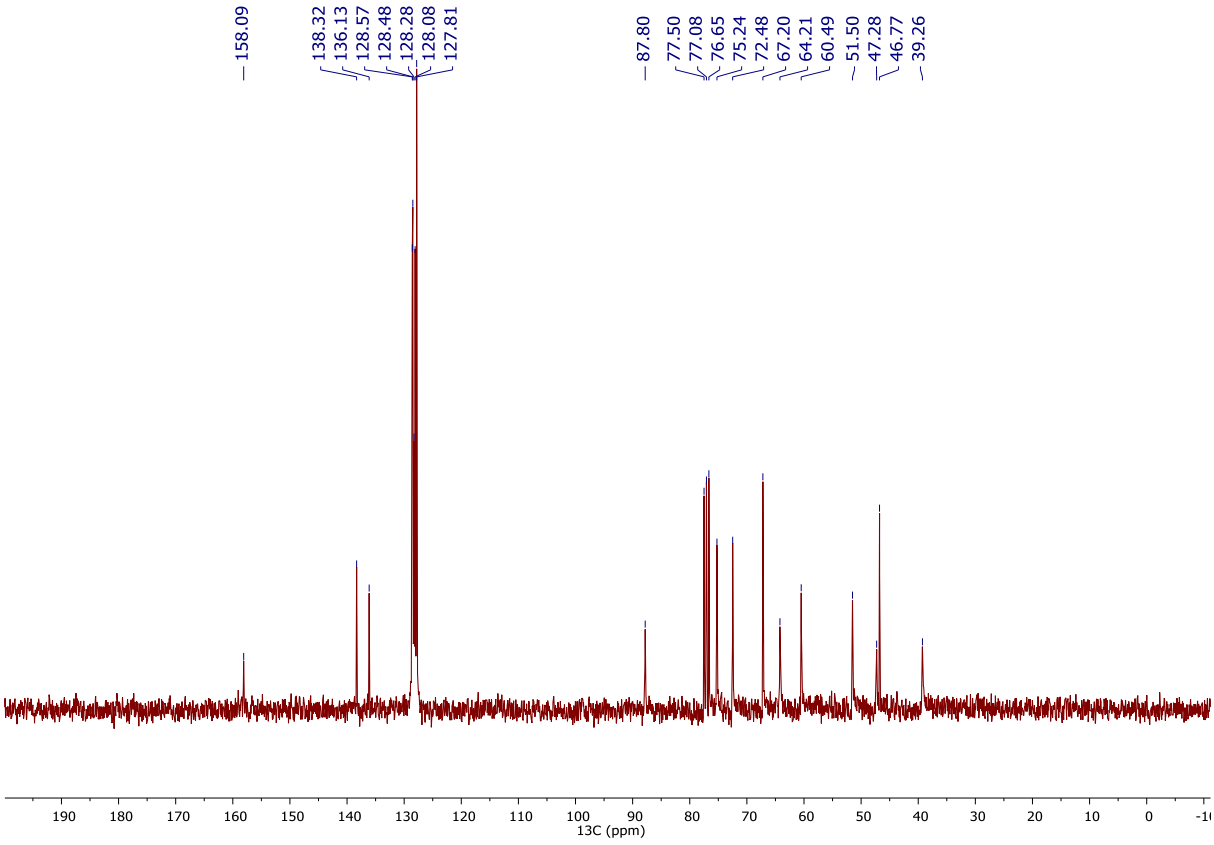


Benzyl (((1*S*,2*R*,3*R*,4*R*)-3-(benzyloxy)-4-hydroxy-1,2-bis(hydroxymethyl)cyclopentyl)methyl)carbamate (37)

^{1}H-NMR

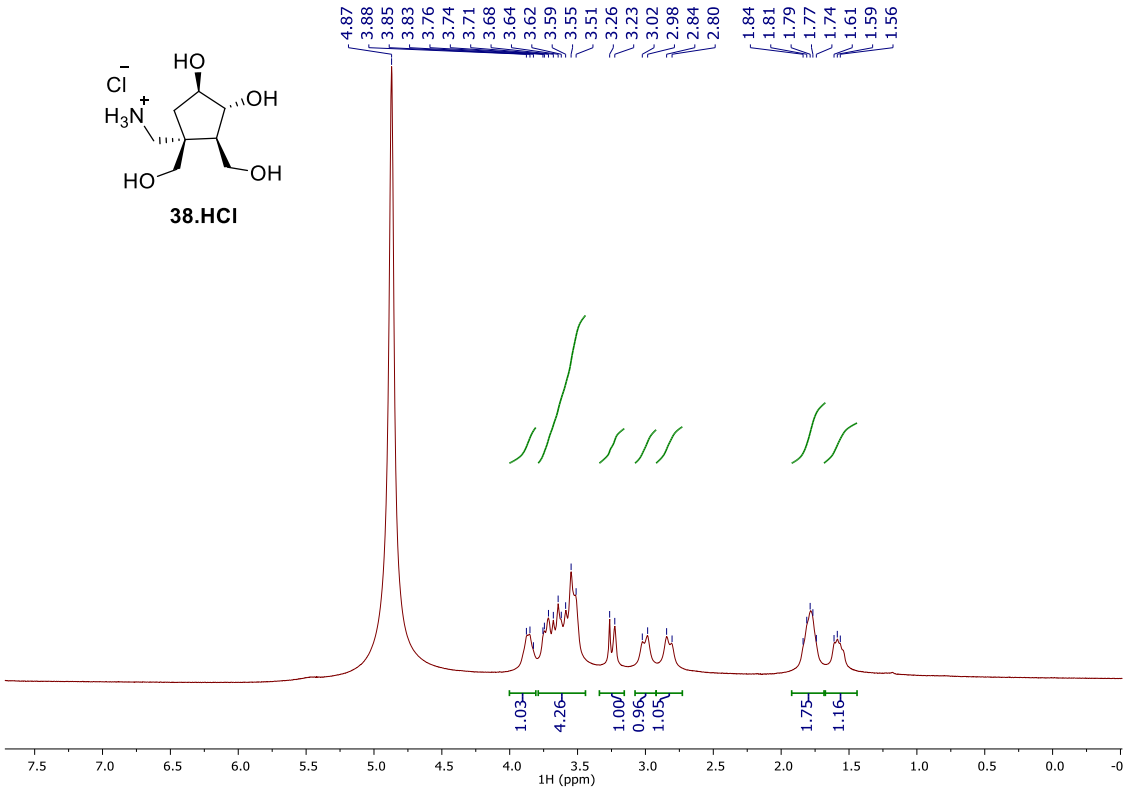


^{13}C-NMR

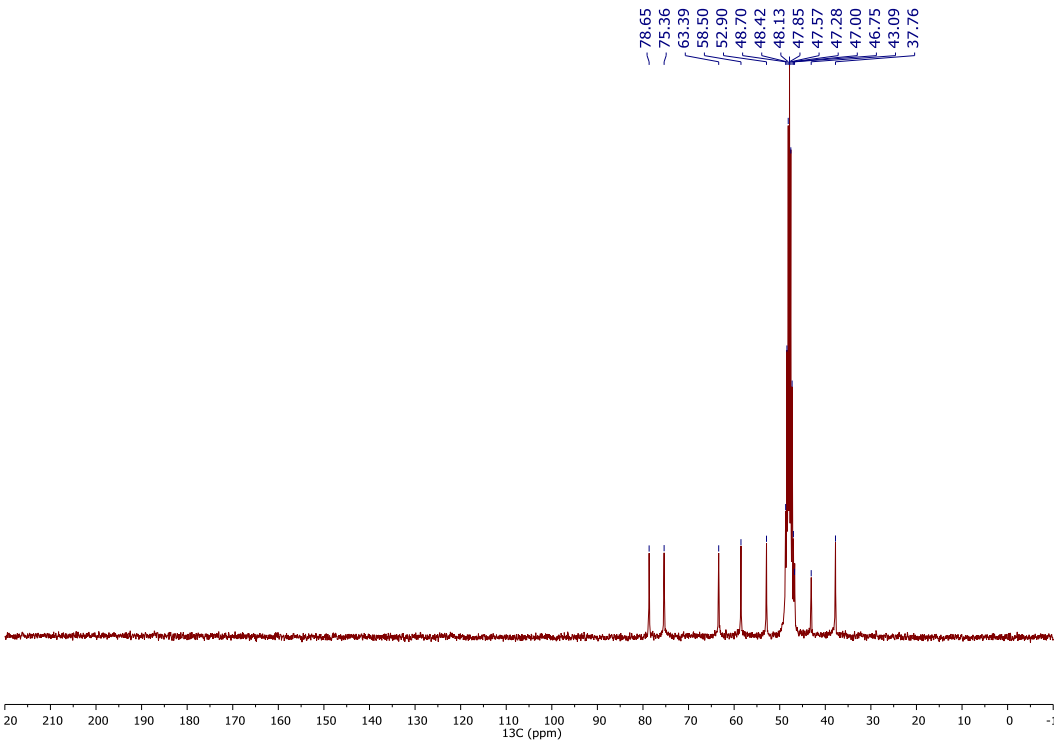


((1*S*,2*R*,3*R*,4*R*)-3,4-dihydroxy-1,2-bis(hydroxymethyl)cyclopentyl)methanaminium chloride (38.HCl)

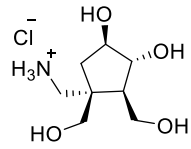
^{1}H-NMR



^{13}C-NMR



((1*S*,2*R*,3*R*,4*R*)-3,4-dihydroxy-1,2-bis(hydroxymethyl)cyclopentyl)methanaminium chloride (38.HCl)



38.HCl

Concentration of iminosugars giving 50 % inhibition of various glycosidases

enzyme	reLB0816e30
α-glucosidase	
rice	NI (0%)
rat intestinal maltase	NI (0%)
yeast	NI (0%)
human lysosome	NI (0%)
β-glucosidase	
almond	NI (0%)
bovine liver	NI (18.2%)
α-galactosidase	
coffee beans	NI (0%)
β-galactosidase	
bovine liver	NI (11.2%)
α-mannosidase	
Jack bean	NI (0%)
β-mannnosidase	
snail	NI (0%)
α-L-fucosidase	
bovine kidney	NI (0%)
α-L-rhamnosidase	
Penicillium decumbens	NI (1.93%)
Amyloglucosidase	
A.niger	NI (0.617%)
Trehalase	
Porcine kidney	NI (7.71%)
β-glucuronidase	
E.coli	NI (4.35%)
bovine liver	NI (0%)

Methods for the Glycosidase Inhibition Studies

The enzymes -glucosidase (from yeast, rice), -glucosidase (from almonds, bovine liver), -galactosidase (from coffee beans), -galactosidase (from bovine liver), -mannosidase (from jackbeans), -mannosidase (from snails), -L-fucosidase (from bovine kidney), -L-rhamnosidase (fromPenicillium decumbens), -glucuronidases (from Escherichia coli), , -trehalase (from porcine kidney), amyloglucosidase (from Aspergillus niger), p-nitrophenyl glycosides, and various disaccharides werepurchased from Sigma-Aldrich Co. Brush border membranes were prepared from the rat small

intestine according to the method of Kessler et al. [35], and were assayed at pH 6.8 for rat intestinal maltase using maltose. For rat intestinal glucosidases and porcine kidney trehalase activities, the reaction mixture (0.2 mL) contained 25 mM substrate and the appropriate amount of enzyme, and the incubations were performed for 10 min at 37 C. The reaction was stopped by heating at 100 C for 3 min. After centrifugation (600 g; 10 min), 0.035 mL of the resulting reaction mixture were added to 2.1 mL of the Glucose CII-testWako (Wako Pure Chemical Ind., Osaka, Japan). The absorbance at 505 nm was measured to determine the amount of the released D-glucose. Other glycosidase activities were determined using an appropriate p-nitrophenyl glycoside as substrate at the optimum pH of each enzyme. The reaction mixture (0.2 mL) contained 2 mM of the substrate and the appropriate amount of enzyme. The reaction was stopped by adding 0.4 mL of 400 mM Na2CO3. The released p-nitrophenol was measured spectrometrically at 400 nm.

Figure S1. Single Crystal XRD- for compound **32**,
with thermal ellipsoids drawn at the 50% probability
level and CCDC: 2180680

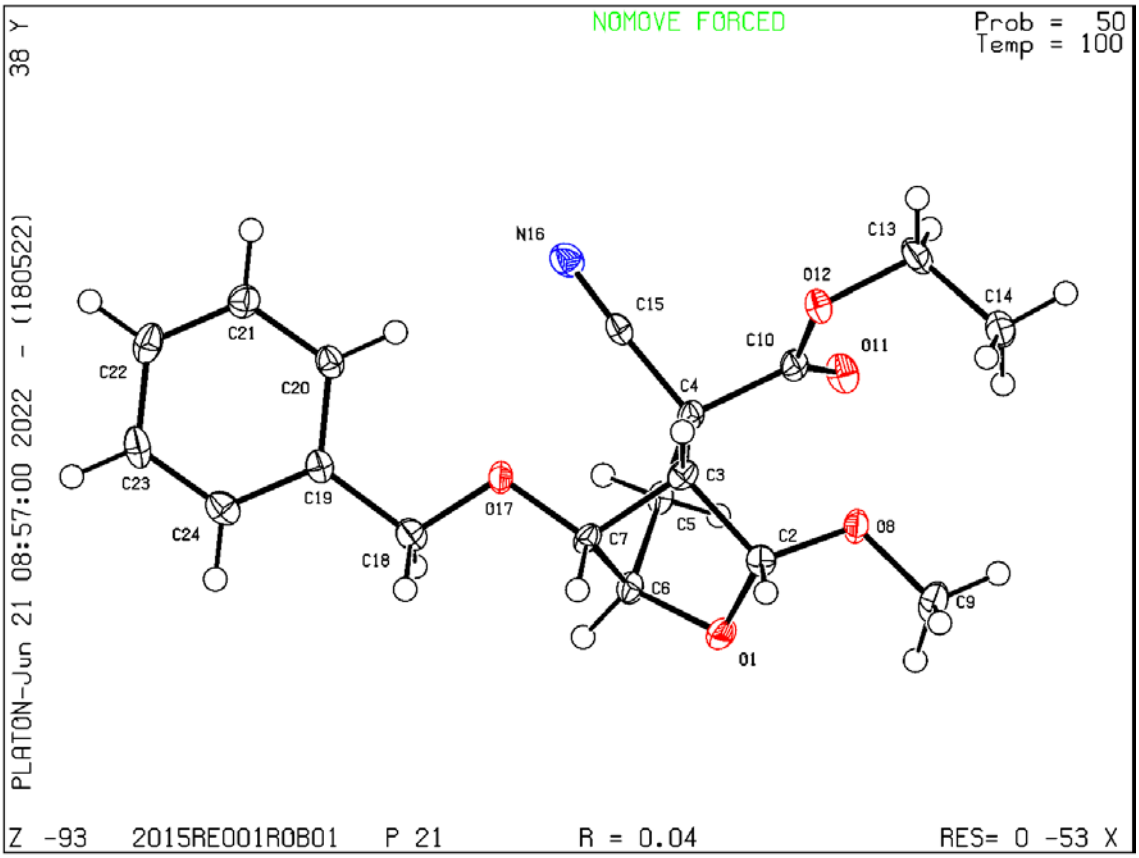


Table S2. Crystal data and structure refinement for compound **32**, and CCDC: 2180680

Bond precision:	C-C = 0.0041 A		Wavelength=0.71073
Cell:	a=5.8300(5)	b=16.7011(12)	c=8.4430(6)
	alpha=90	beta=90.811(5)	gamma=90
Temperature:	100 K		

	Calculated	Reported
Volume	821.99(11)	821.99(11)
Space group	P 21	P 21
Hall group	P 2yb	P 2yb
Moiety formula	C18 H21 N O5	C18 H21 N O5
Sum formula	C18 H21 N O5	C18 H21 N O5
Mr	331.36	331.36
Dx,g cm-3	1.339	1.339
Z	2	2
Mu (mm-1)	0.098	0.098
F000	352.0	352.0
F000'	352.19	
h,k,lmax	7,21,10	7,21,10
Nref	3658[1893]	3577
Tmin,Tmax	0.979,0.996	0.828,0.959
Tmin'	0.960	

Correction method= # Reported T Limits: Tmin=0.828 Tmax=0.959
AbsCorr = MULTI-SCAN

Data completeness= 1.89/0.98 Theta(max)= 27.191

R(reflections)= 0.0433(2628) wR2(reflections)= 0.0801(3577)

S = 0.951 Npar= 219