Electronic Supplementary Information

Polyhydroxylated pyrrolidine and 2-oxapyrrolizidine as glycosidase inhibitors

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Structural determination of the pivotal compound 12 (CCDC 918733)

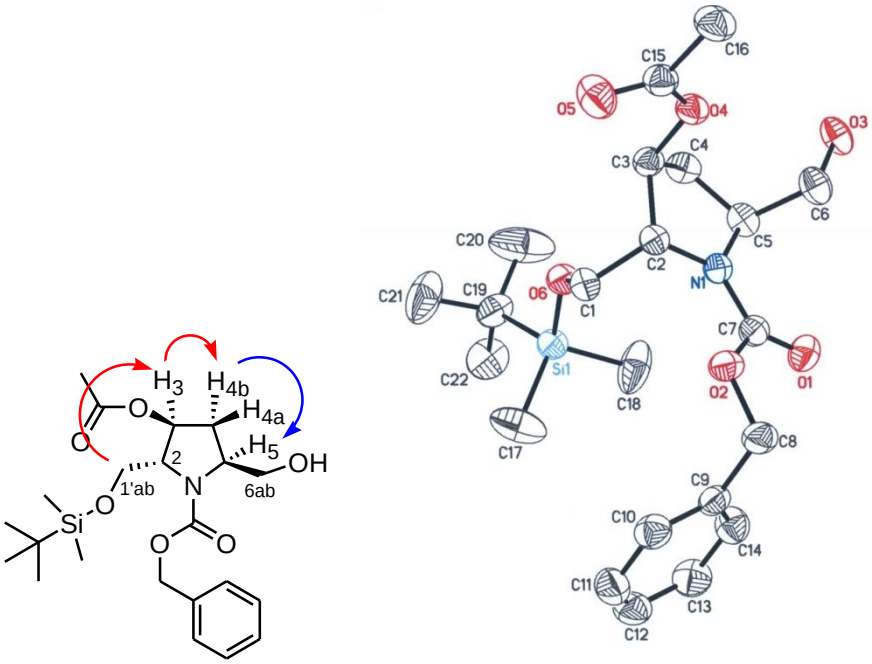


Figure S1. ORTEP drawing of compound **12** in X-ray diffraction analysis.

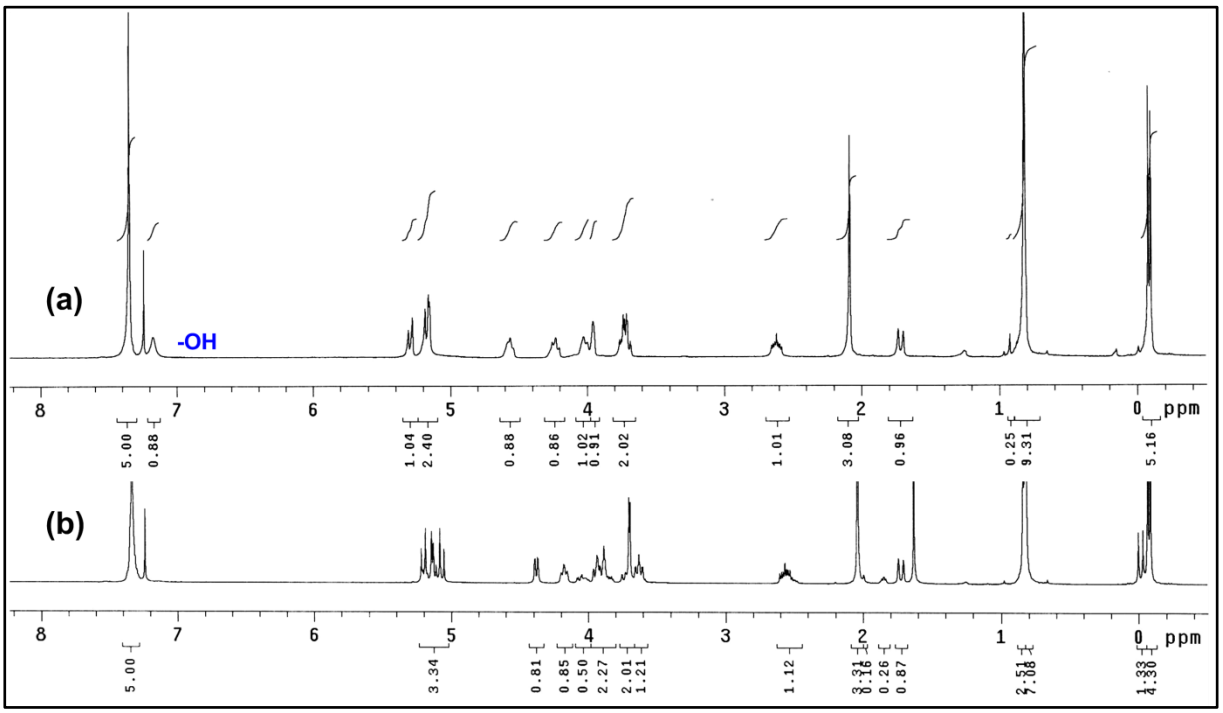


Figure S2. ^{1}H NMR spectra of compound **12** ($CDCl_3$, 400 MHz): (a) Coalescence in the presence of $ZnCl_2$, and (b) mixture of rotamers in the absence of $ZnCl_2$.

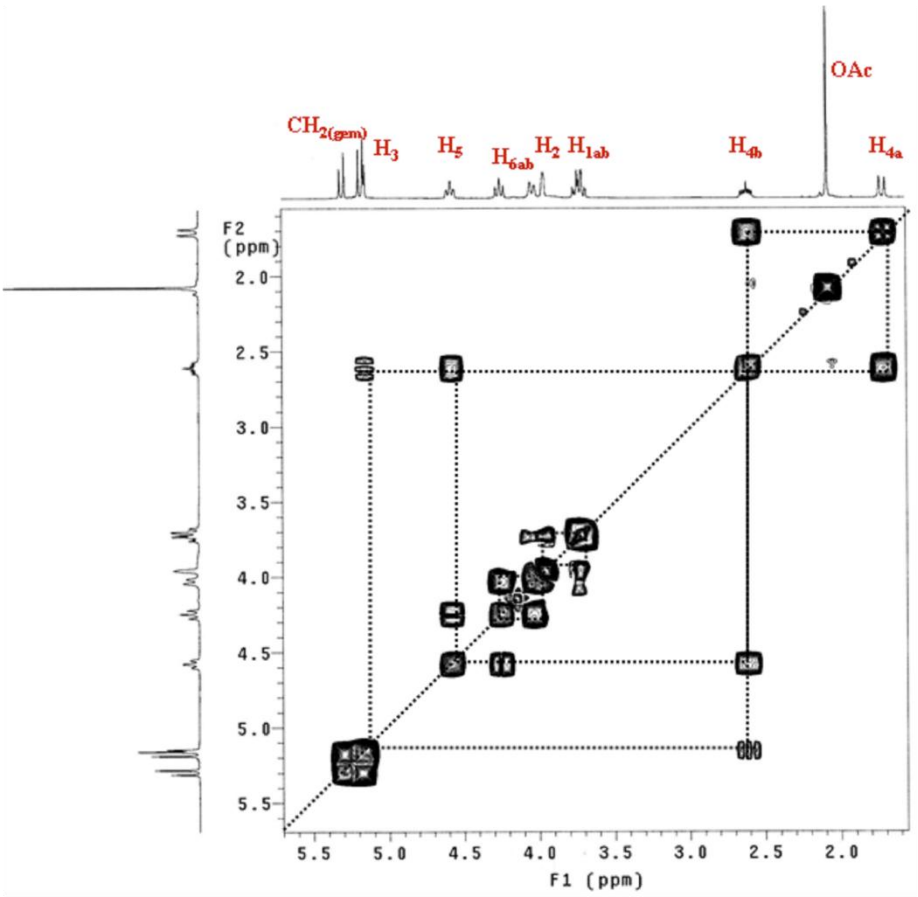


Figure S3. ^{1}H–^{1}H COSY of compound **12** in the presence of $ZnCl_2$ ($CDCl_3$, 400 MHz): δ 3.76–3.68 (H_{1ab}), 3.96 (H_2), 5.15 (H_3), 2.61/1.72 (H_{4ab}), 4.56 (H_5), and 4.23/3.02 ($H6_{ab}$).

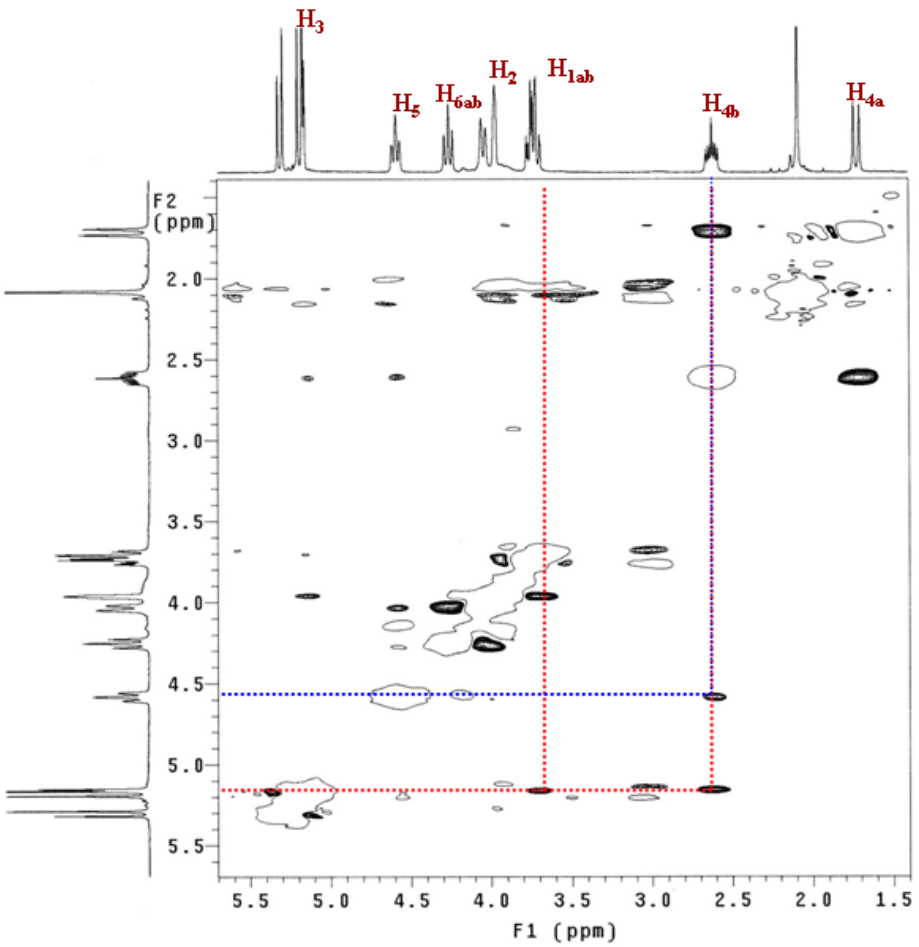
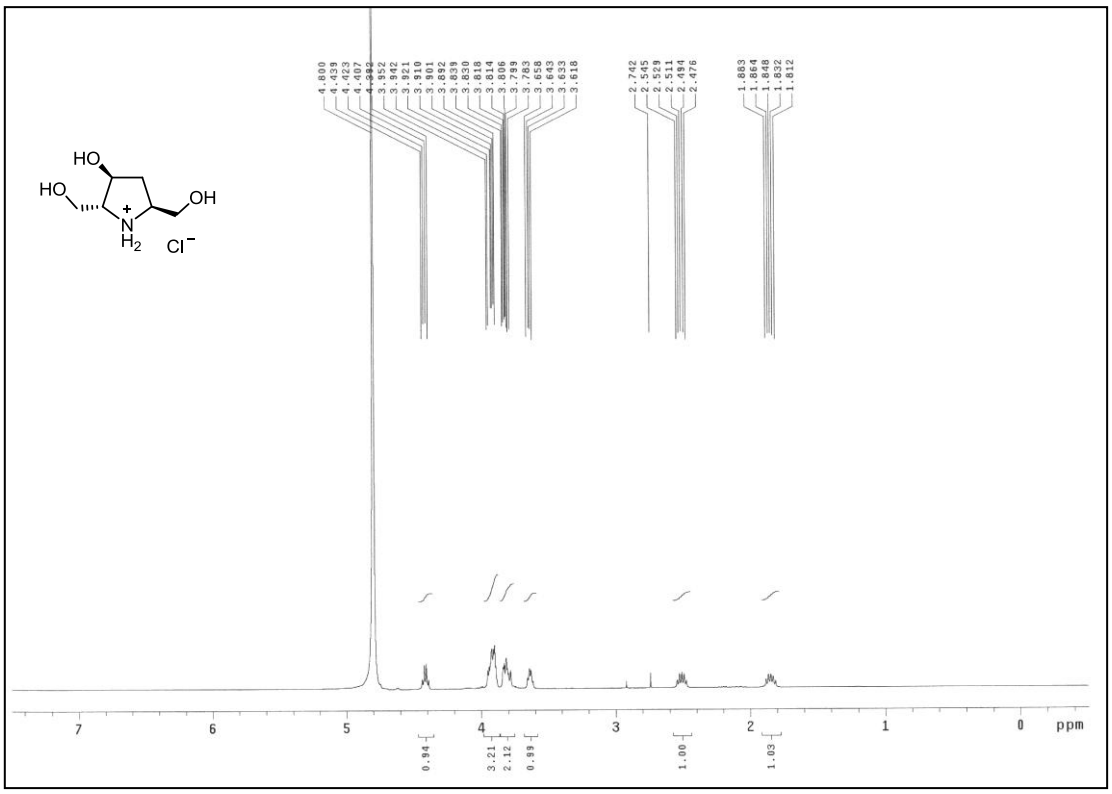
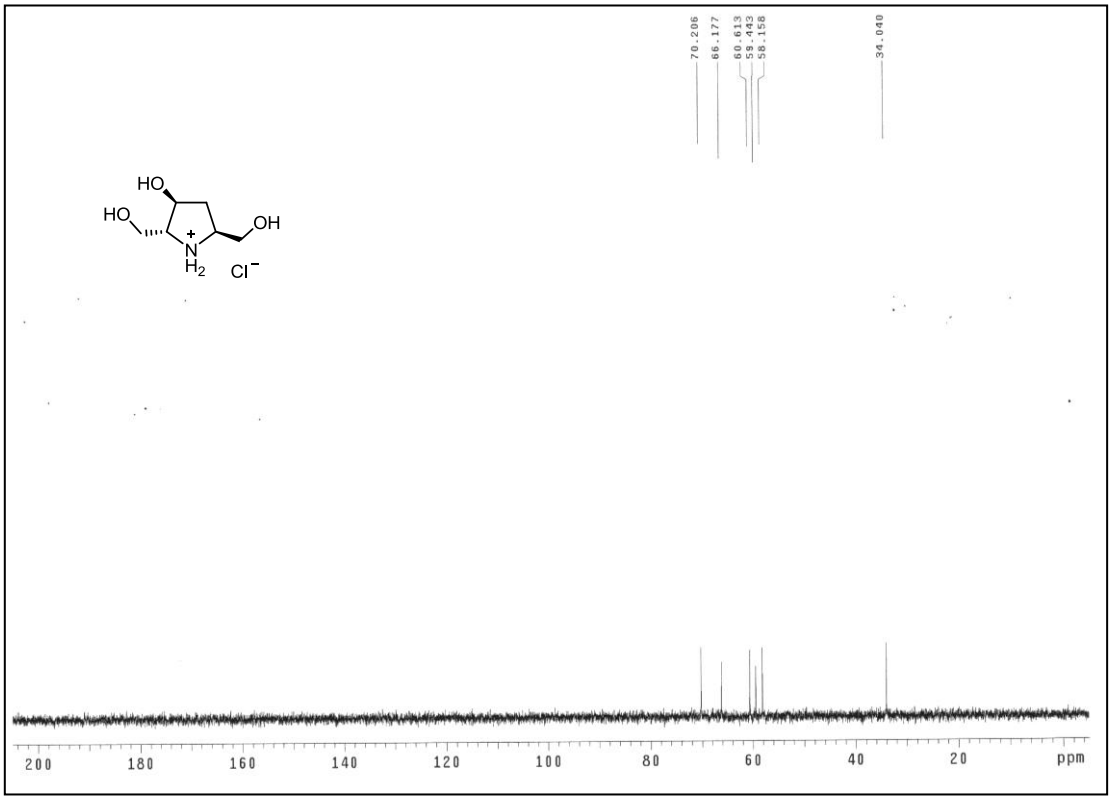


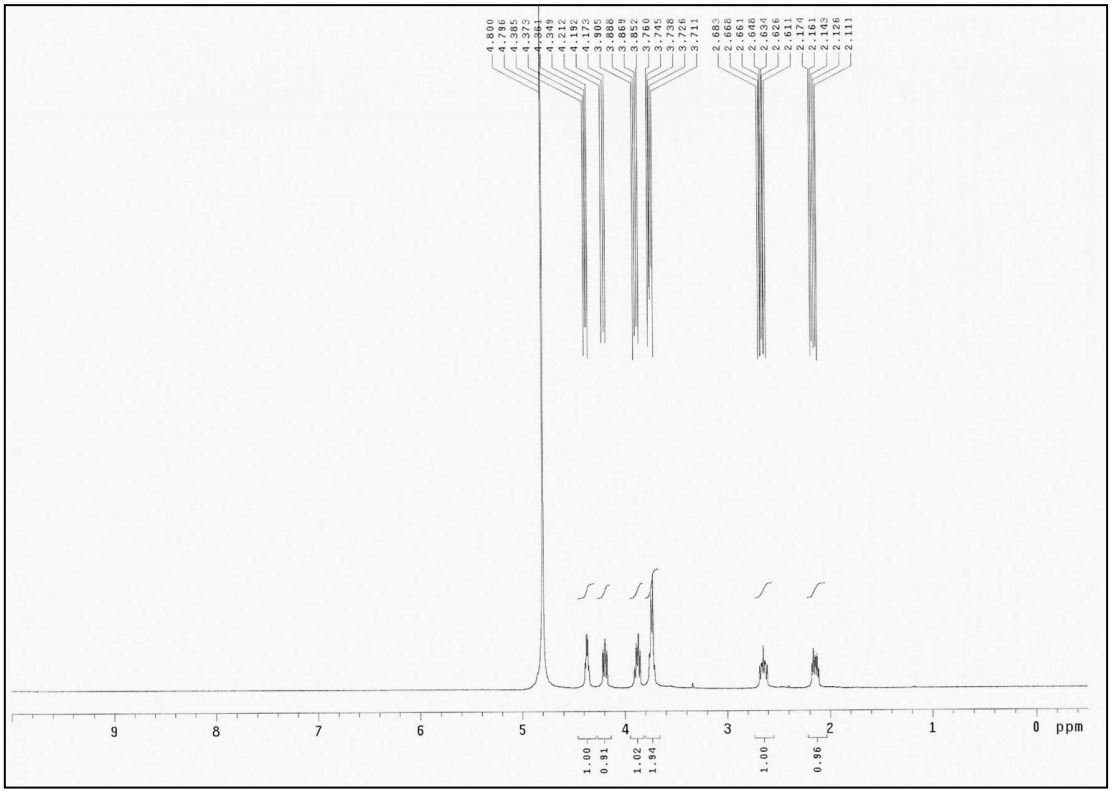
Figure S4. ^{1}H–^{1}H NOESY of compound **12** in the presence of $ZnCl_2$ ($CDCl_3$, 400 MHz): The NOE correlations of H_3 with H_{4b} and $H_{1'ab}$ as well as H_{4b} with H_5 are observed.



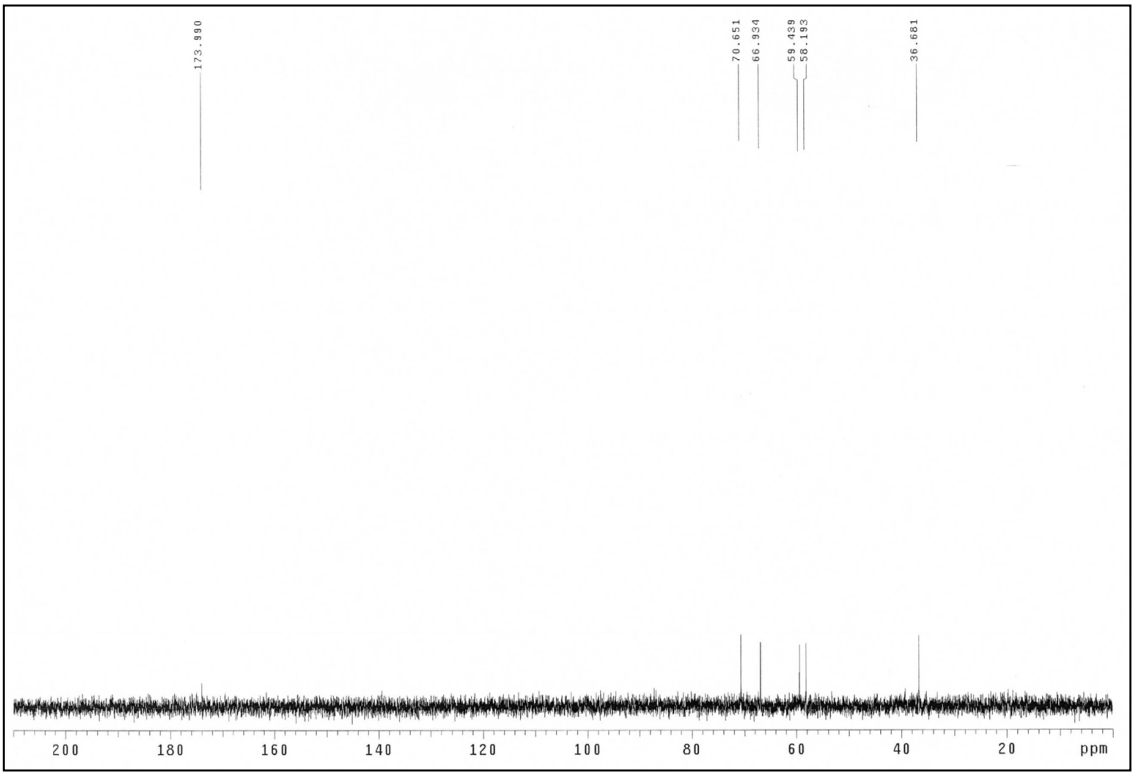
^{1}H NMR spectrum of compound **1** (as the HCl salt, 400 MHz, D_2O)



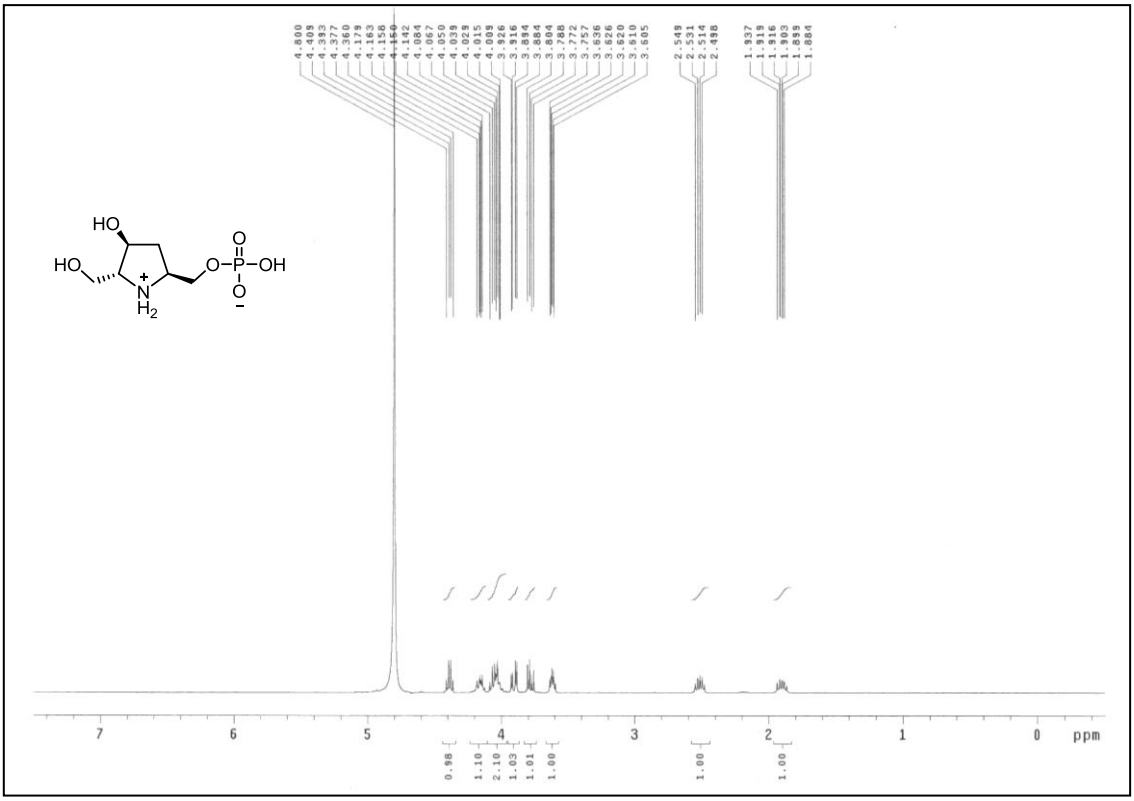
^{13}C NMR spectrum of compound **1** (as the HCl salt, 100 MHz, D_2O)



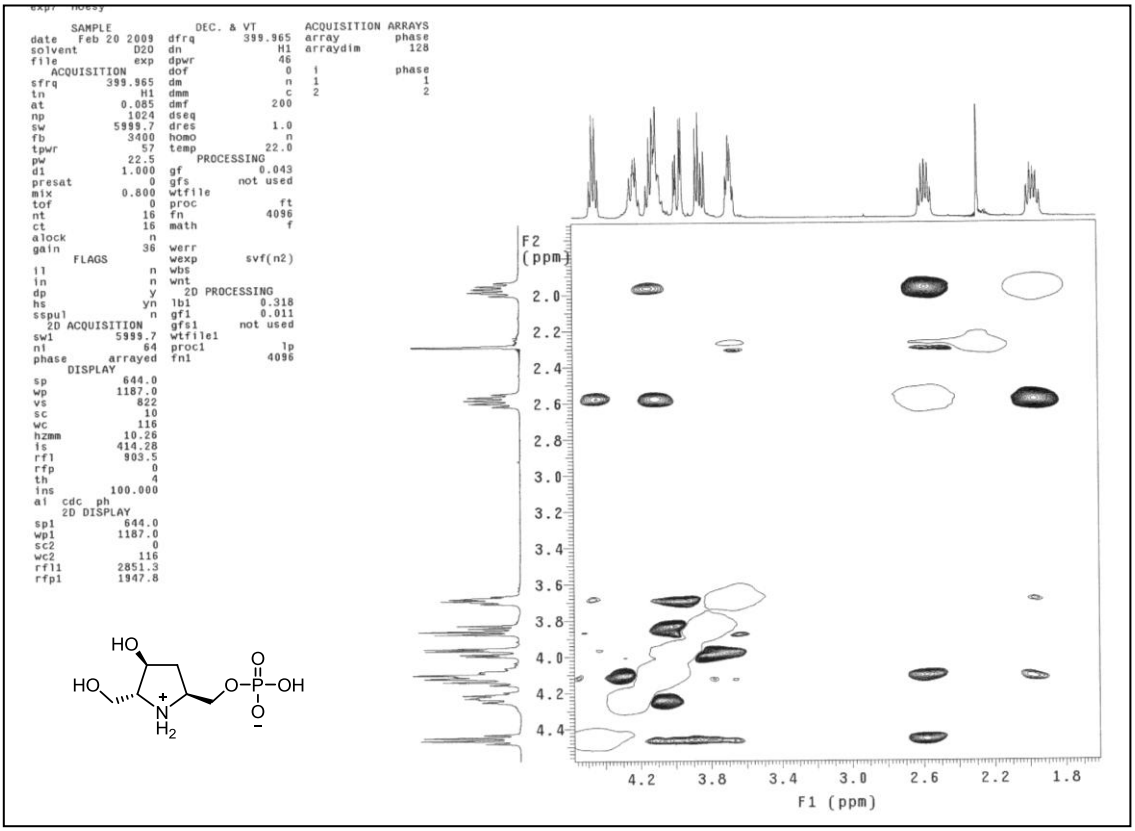
^{1}H NMR spectrum of compound **2** (400 MHz, D_2O)



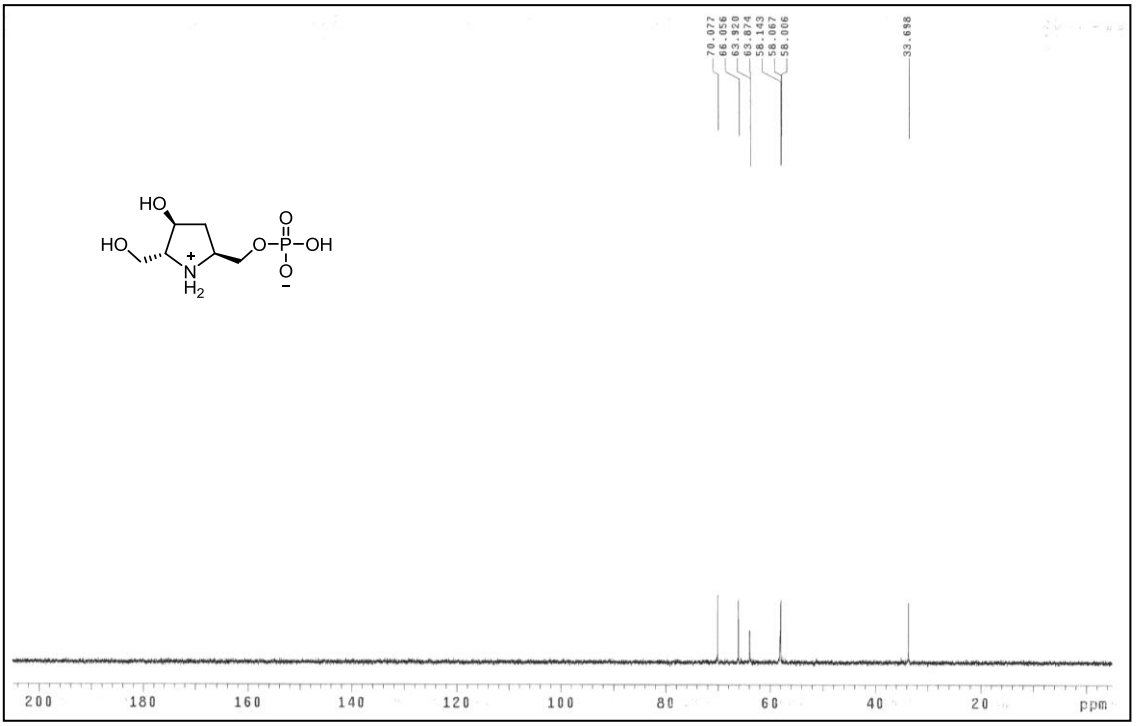
^{13}C NMR spectrum of compound **2** (100 MHz, D_2O)



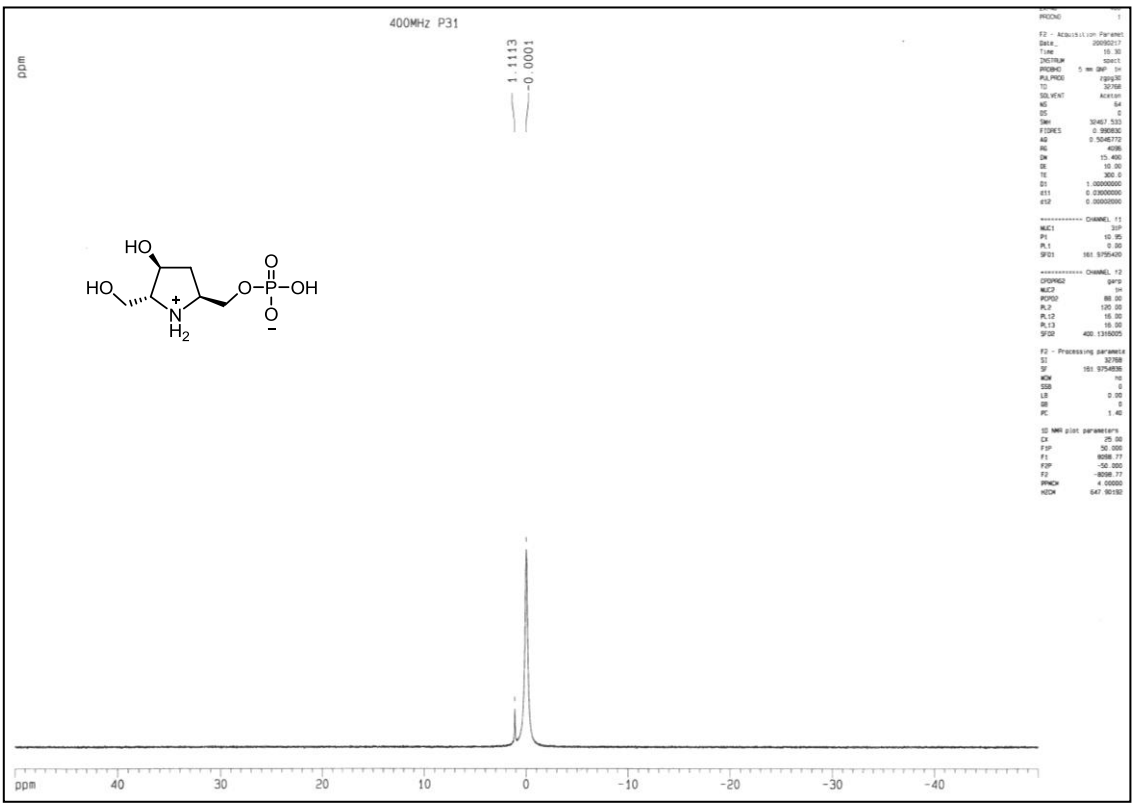
^{1}H NMR spectrum of compound **3** (400 MHz, D_2O)



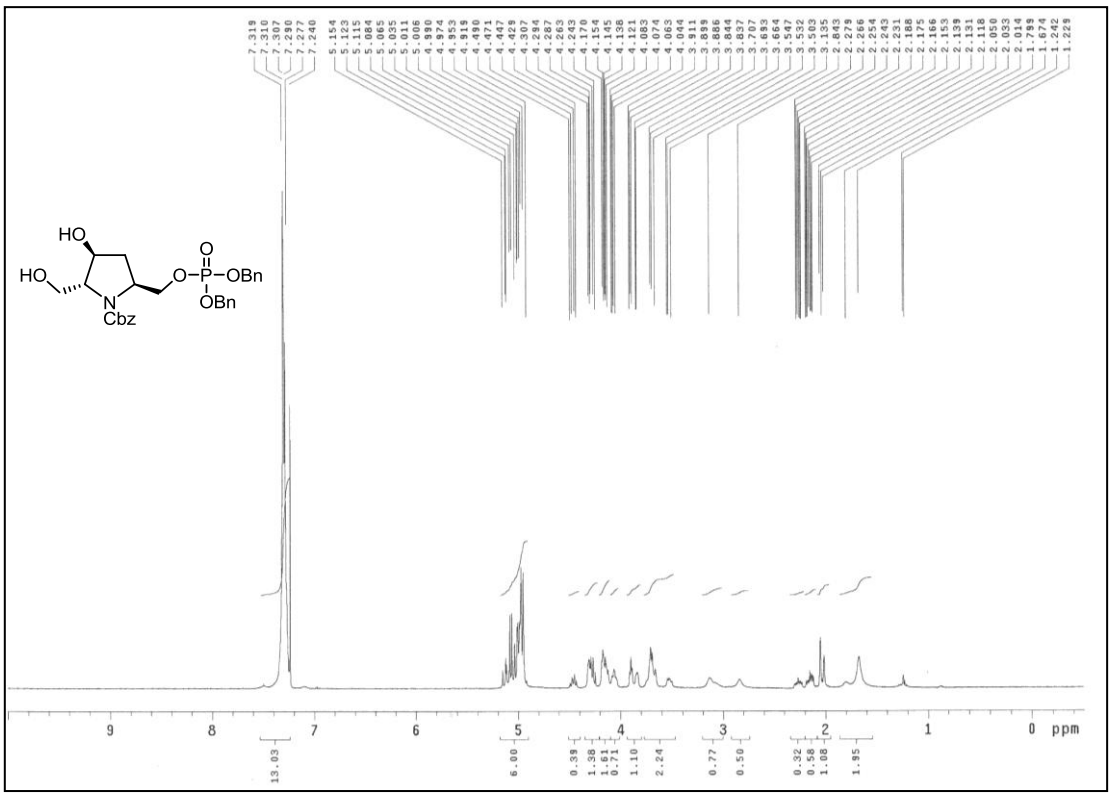
^{1}H–^{1}H NOESY NMR spectrum of compound **3** (400 MHz, D_2O)



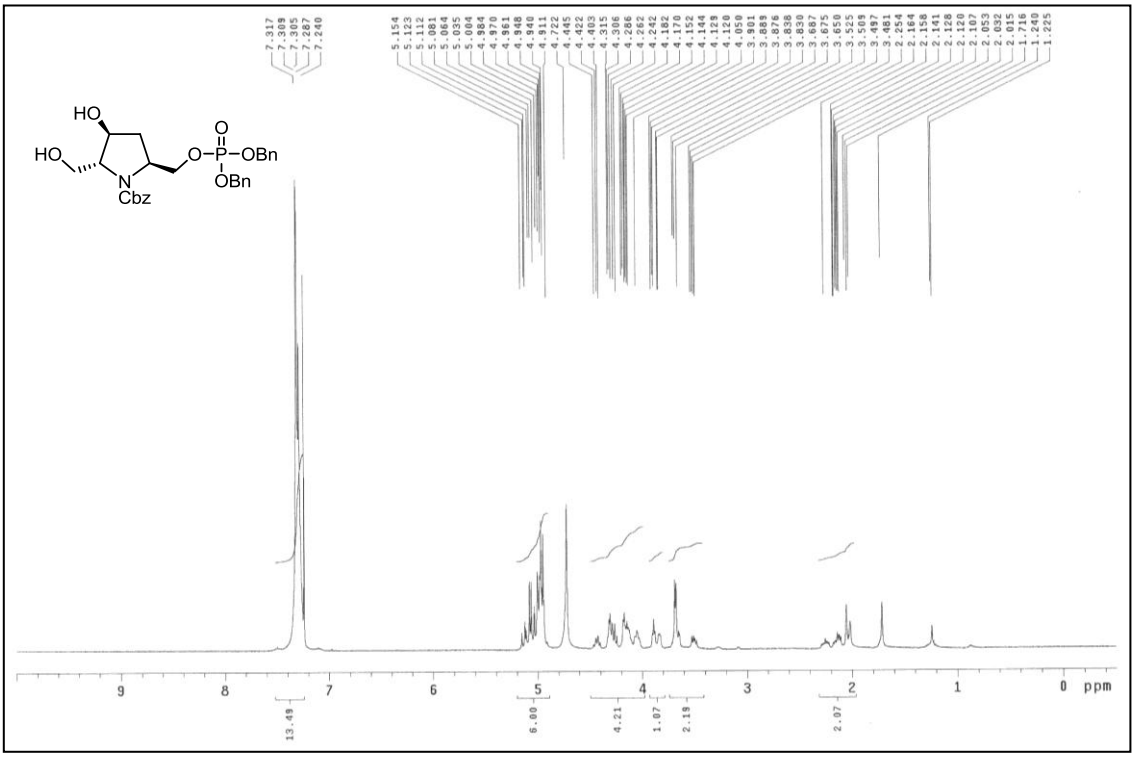
^{13}C NMR spectrum of compound **3** (100 MHz, D_2O)



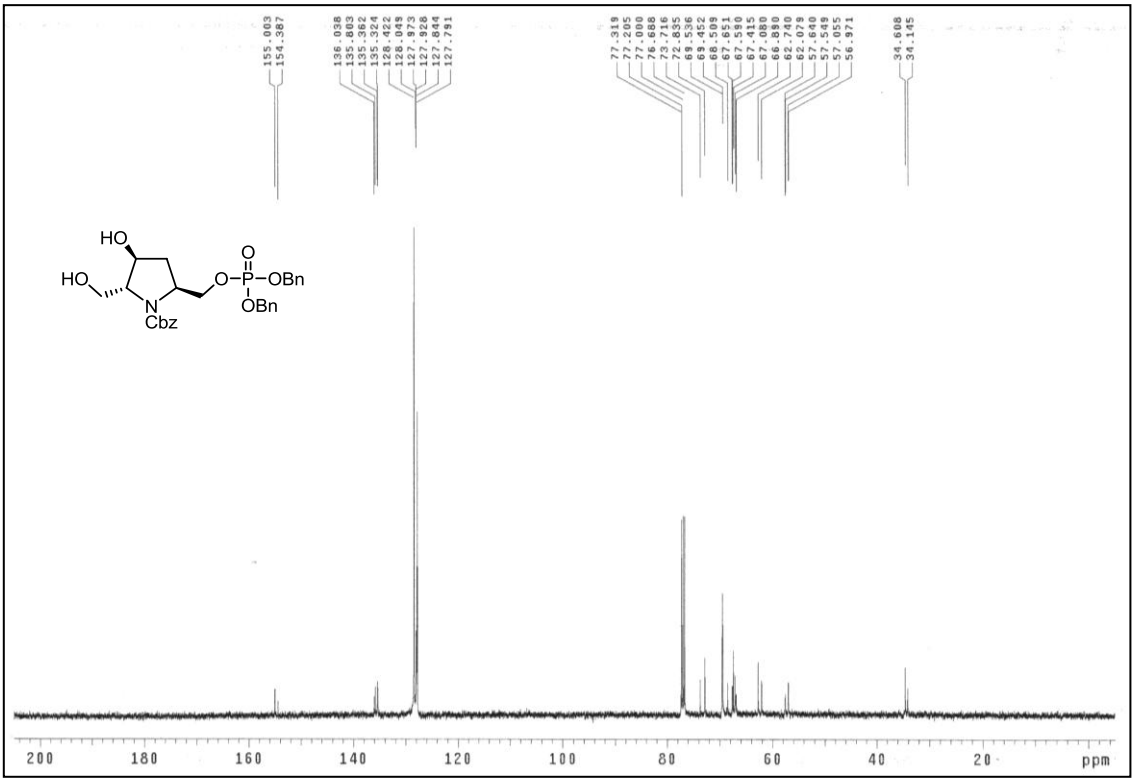
^{31}P NMR spectrum of compound **3** (162 MHz, standard 85% $H_3PO_{4(aq)}$ in D_2O)



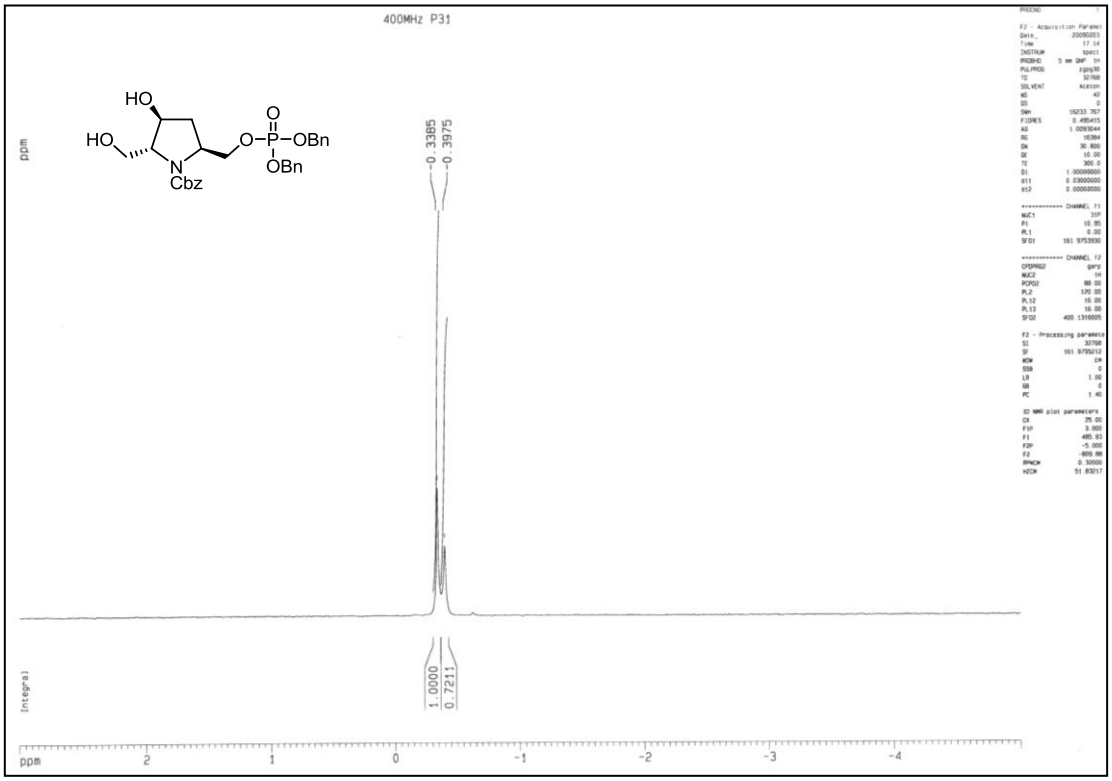
^{1}H NMR spectrum of compound **3**-Cbz dibenzyl ester (400 MHz, $CDCl_3$, rotameric mixture)



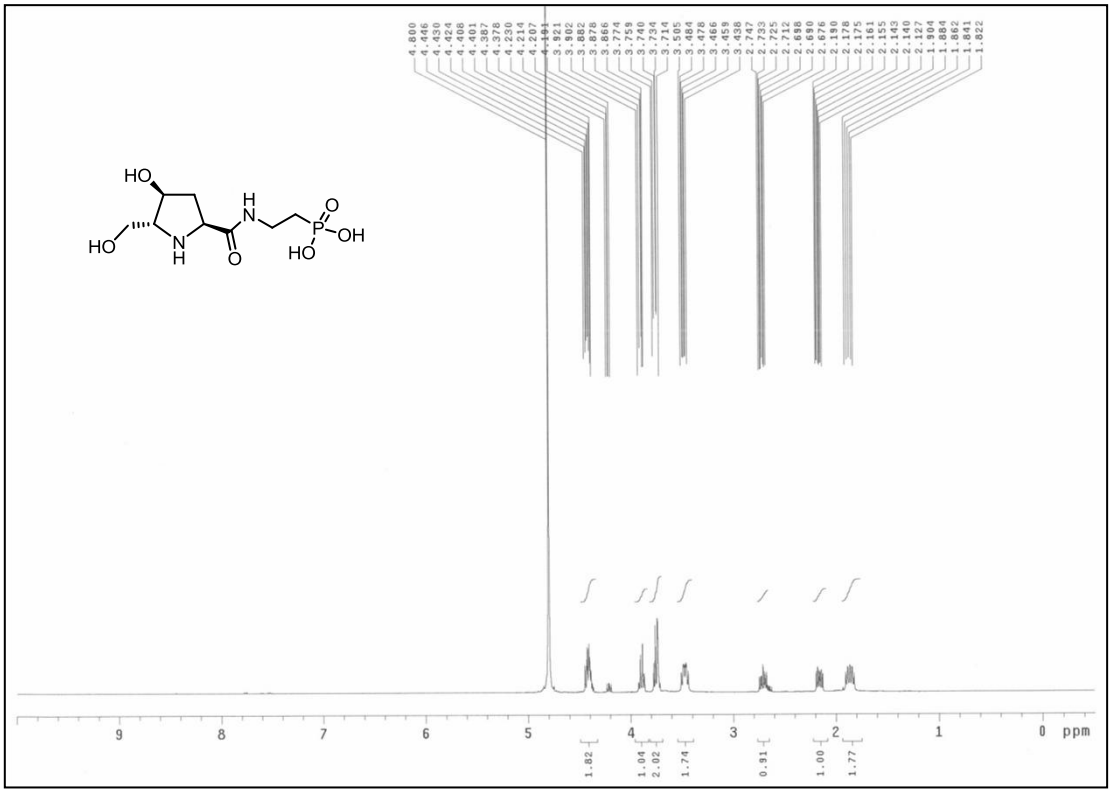
^{1}H NMR spectrum of compound **3**-Cbz dibenzyl ester (400 MHz, $CDCl_3$, rotameric mixture, D_2O exchange)



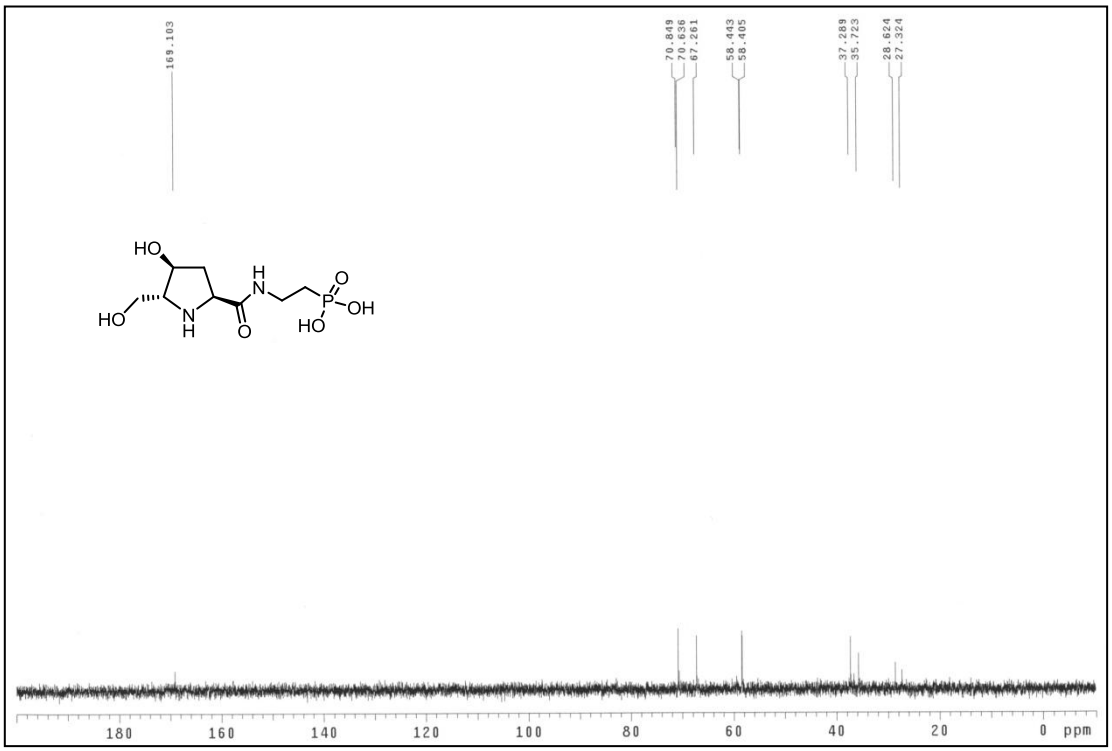
^{13}C NMR spectrum of compound **3**-Cbz dibenzyl ester (100 MHz, $CDCl_3$, rotameric mixture)



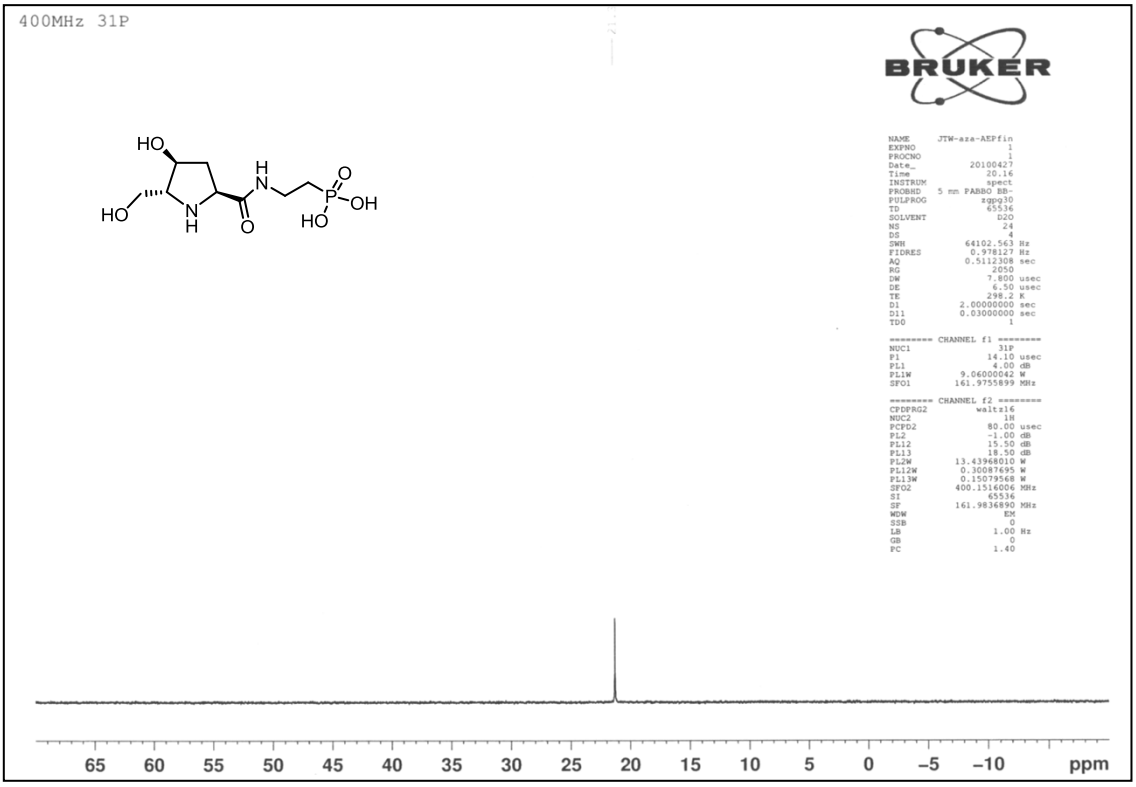
^{31}P NMR spectrum of compound **3**-Cbz dibenzyl ester (162 MHz, $CDCl_3$, rotameric mixture)



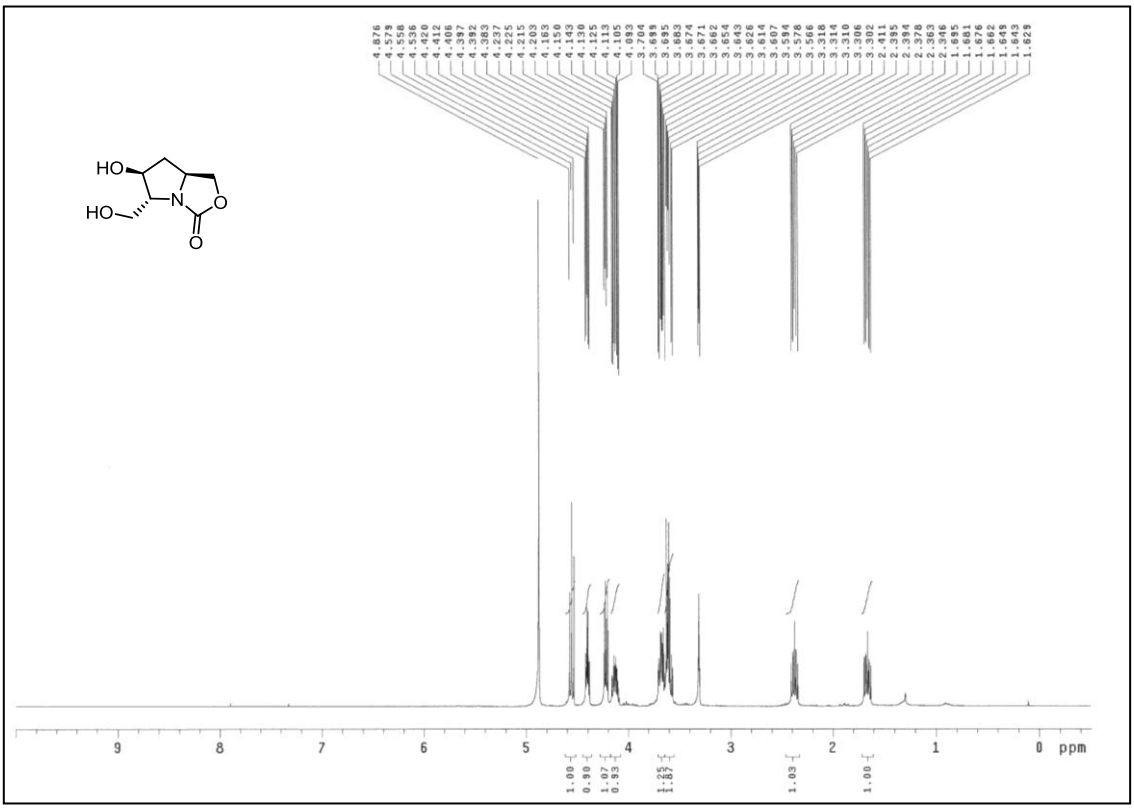
^{1}H NMR spectrum of compound **4** (400 MHz, D_2O)



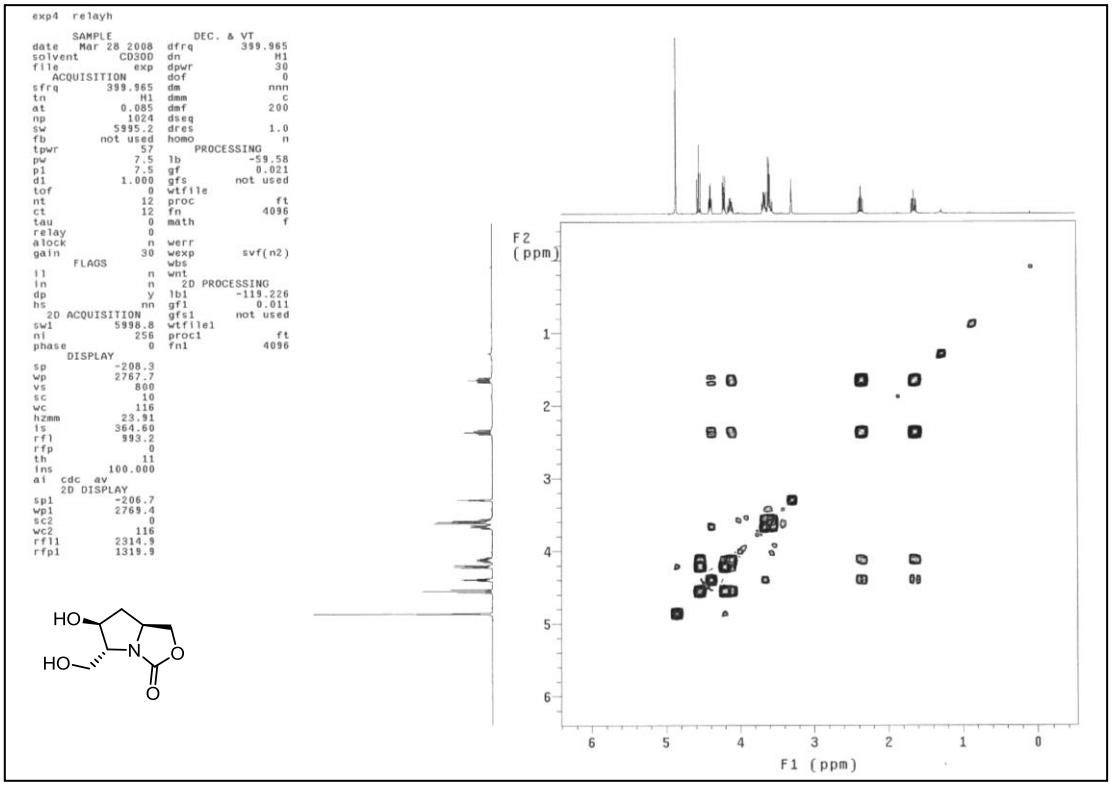
^{13}C NMR spectrum of compound **4** (100 MHz, D_2O)



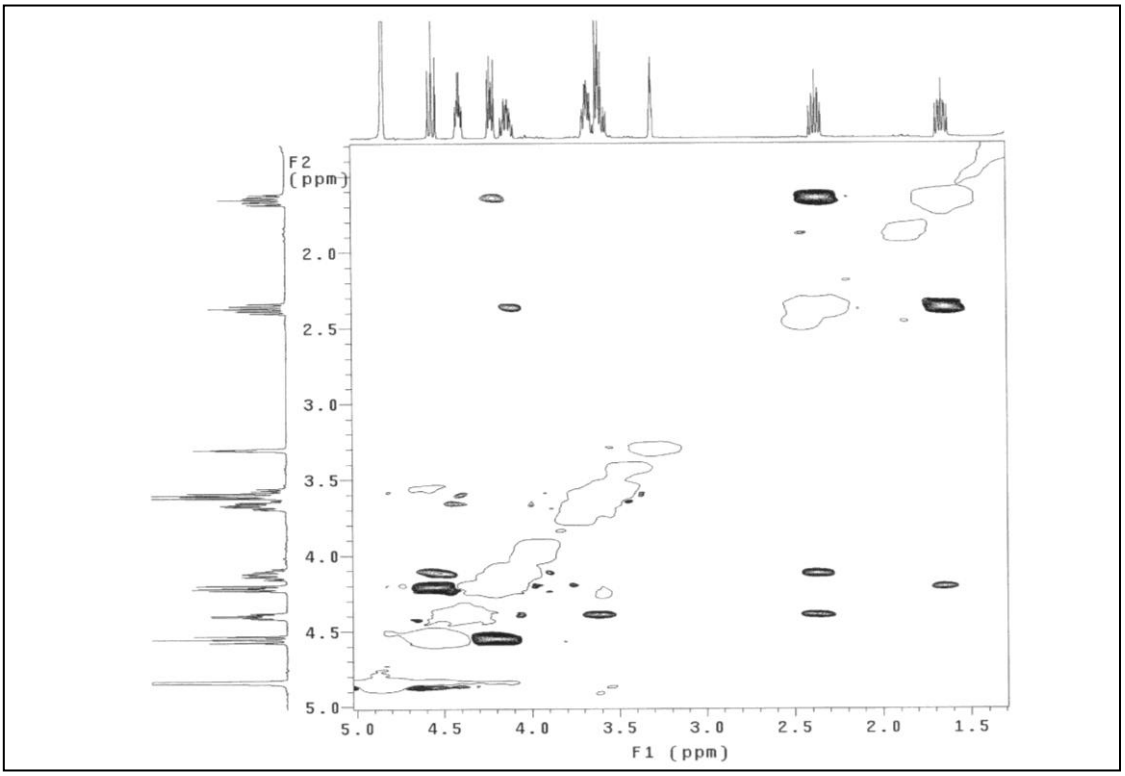
^{31}P NMR spectrum of compound **4** (162 MHz, D_2O)



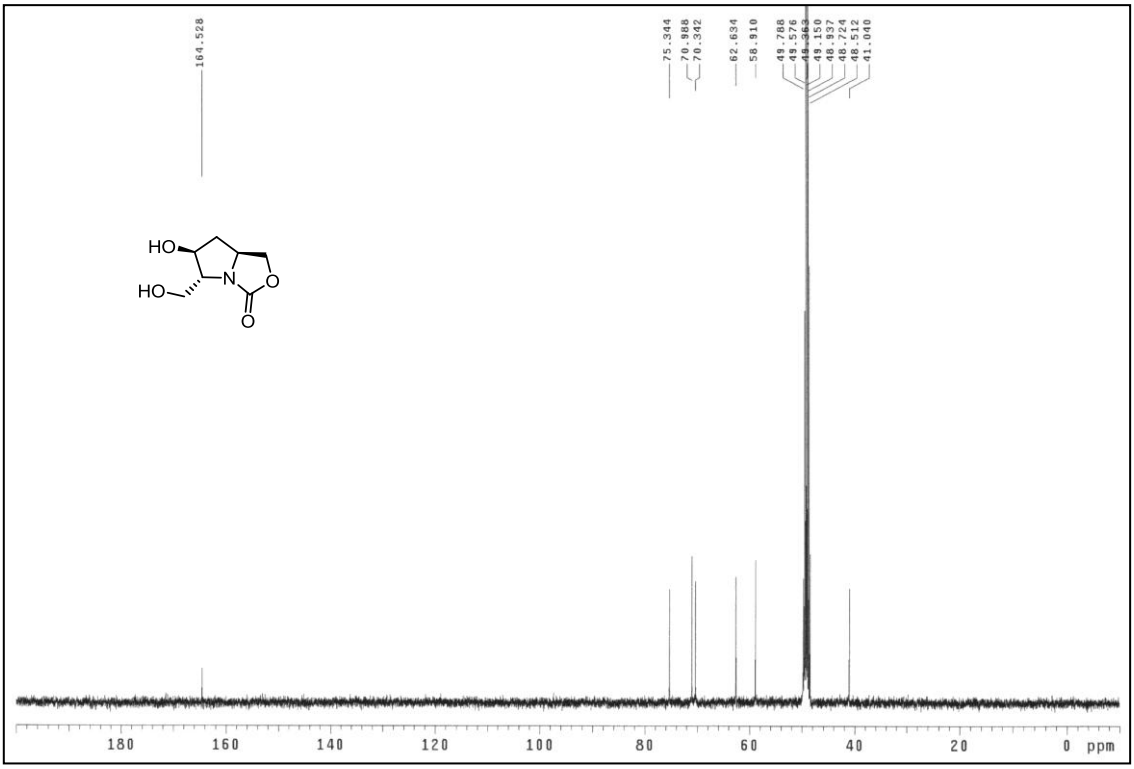
^{1}H NMR spectrum of compound **5** (400 MHz, CD_3OD)



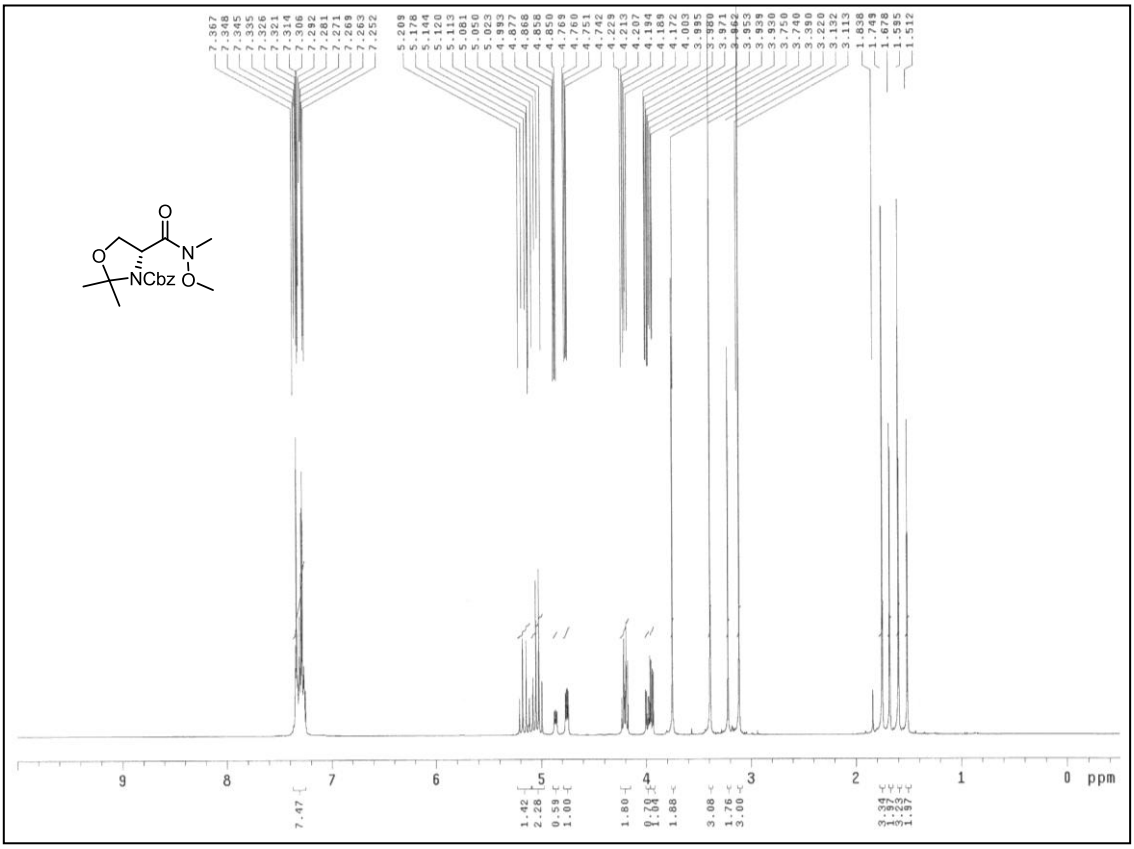
^{1}H–^{1}H COSY NMR spectrum of compound **5** (400 MHz, CD_3OD)



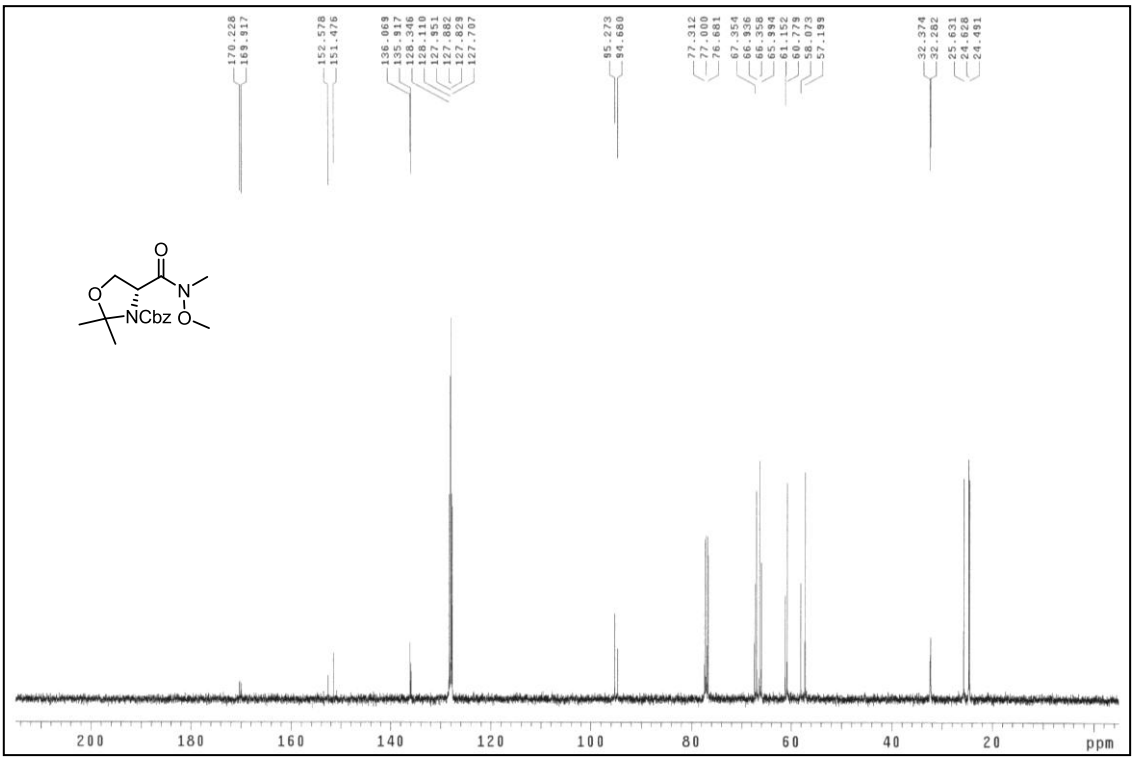
^{1}H–^{1}H NOESY NMR spectrum of compound **5** (400 MHz, CD_3OD)



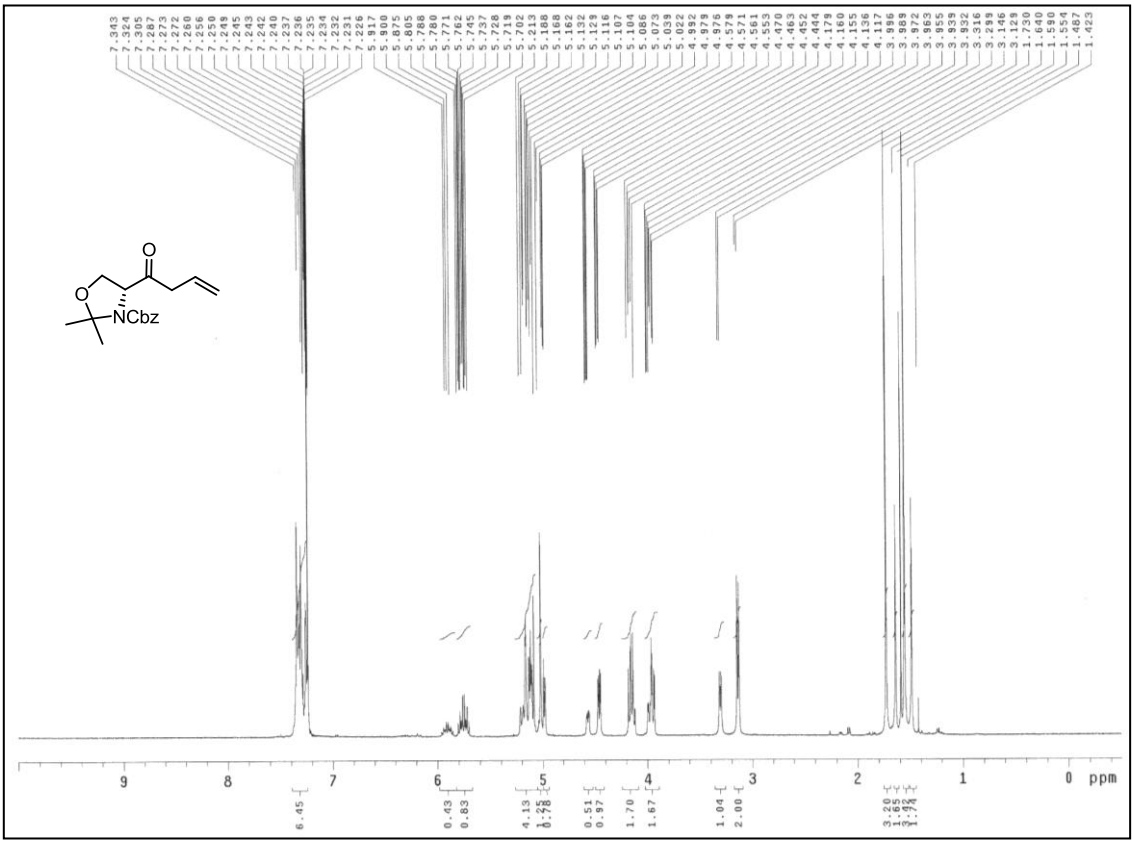
^{13}C NMR spectrum of compound **5** (100 MHz, CD_3OD)



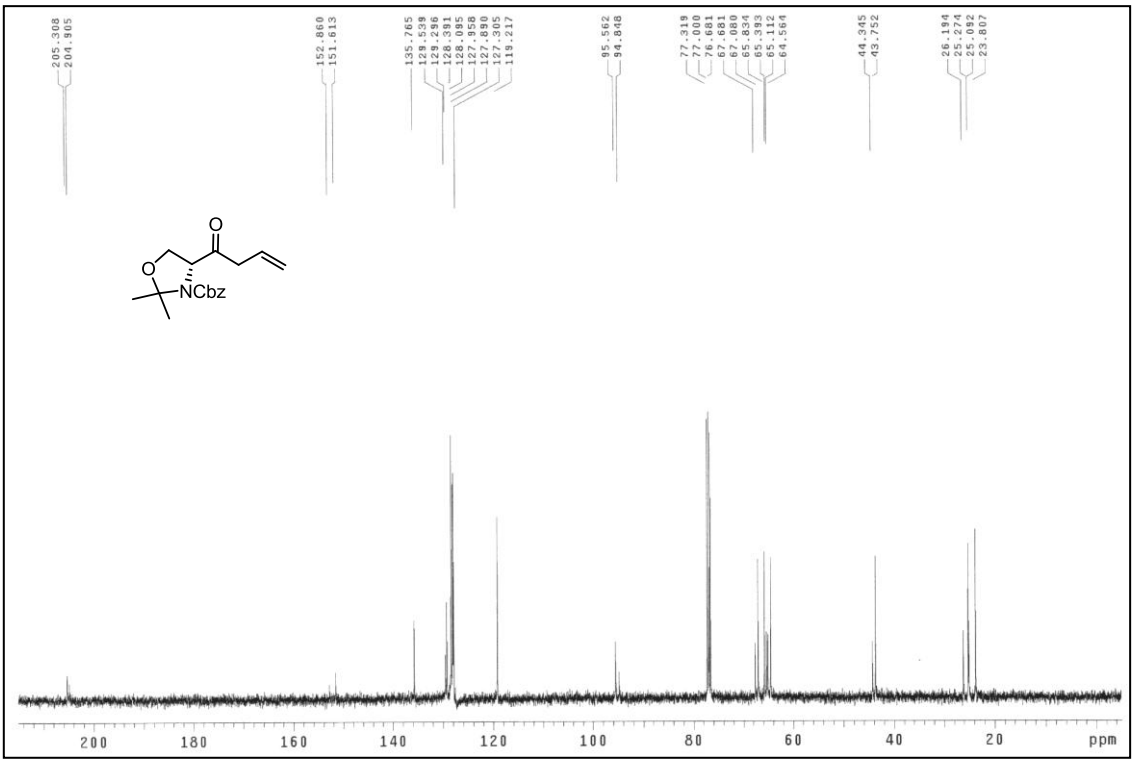
^{1}H NMR spectrum of compound **6** (400 MHz, $CDCl_3$, rotameric mixture)



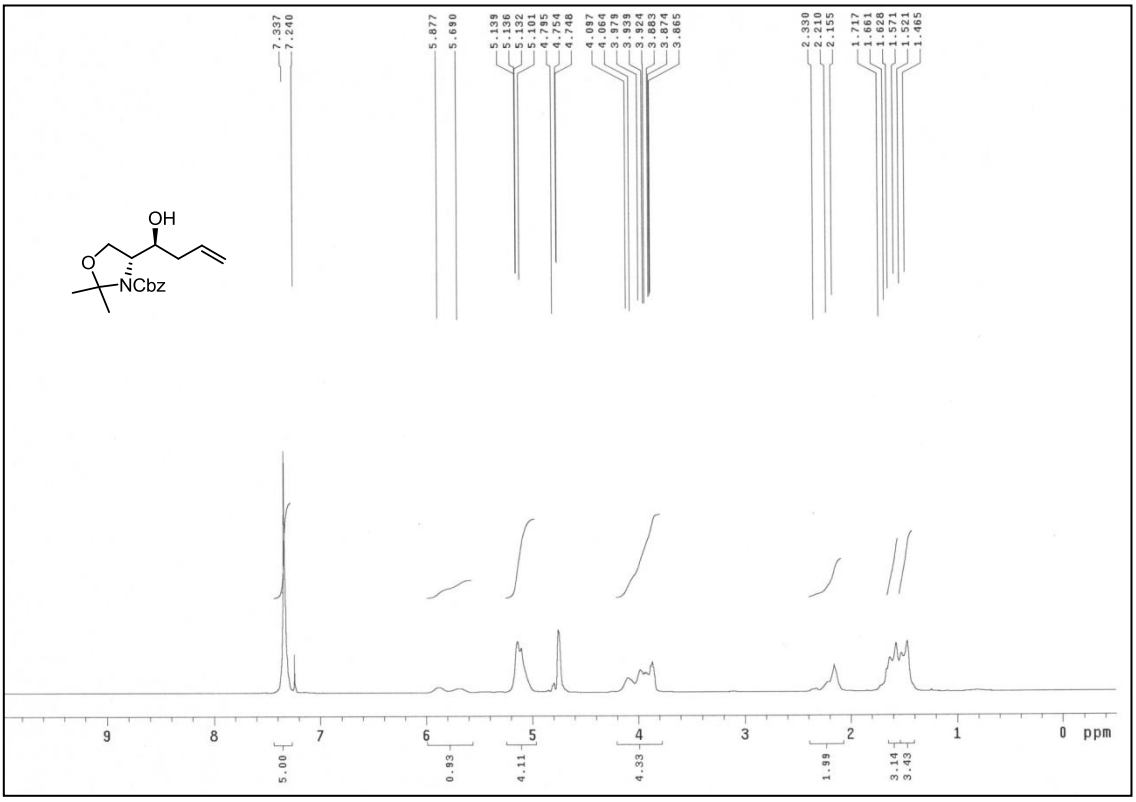
^{13}C NMR spectrum of compound **6** (100 MHz, $CDCl_3$, rotameric mixture)



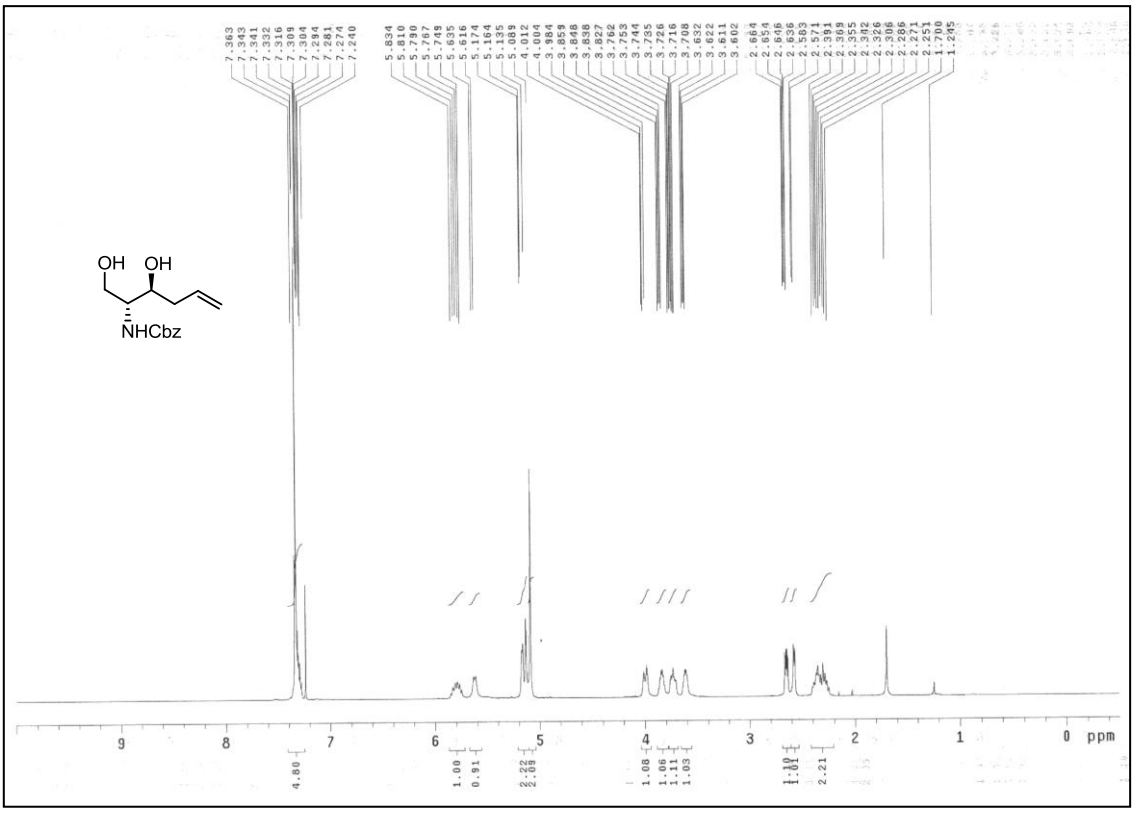
^{1}H NMR spectrum of compound **7** (400 MHz, $CDCl_3$, rotameric mixture)



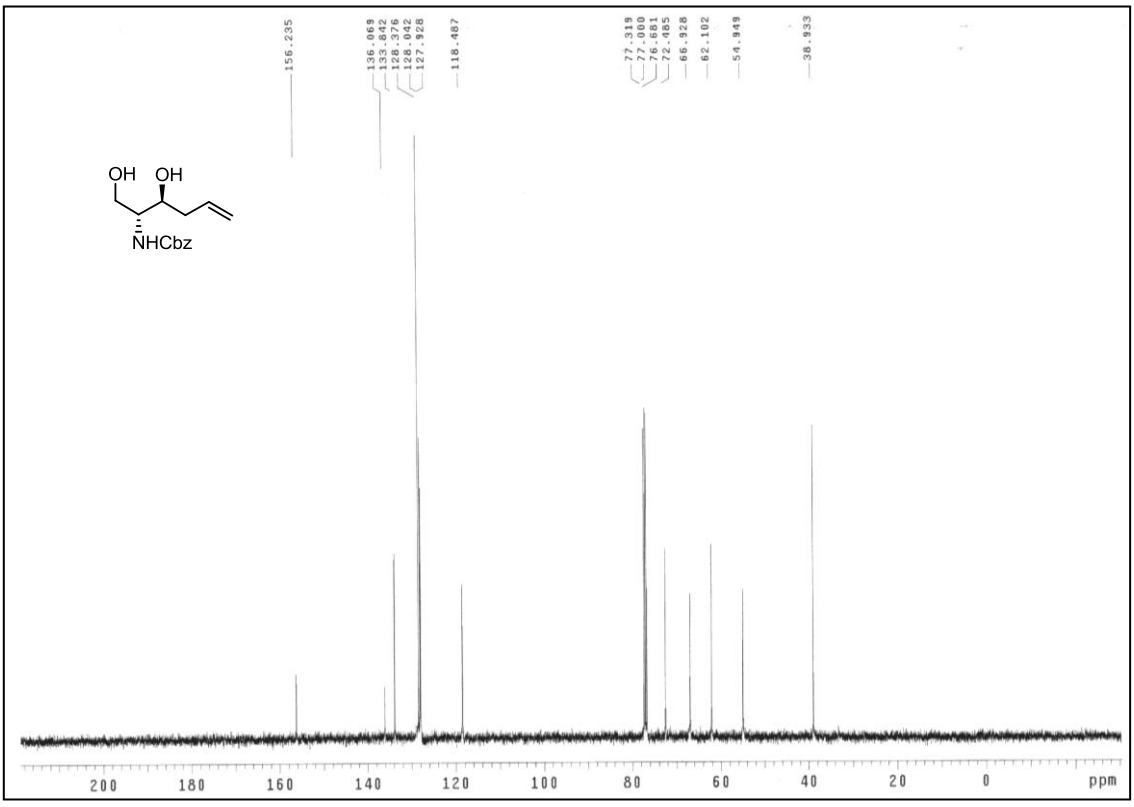
^{13}C NMR spectrum of compound **7** (100 MHz, $CDCl_3$, rotameric mixture)



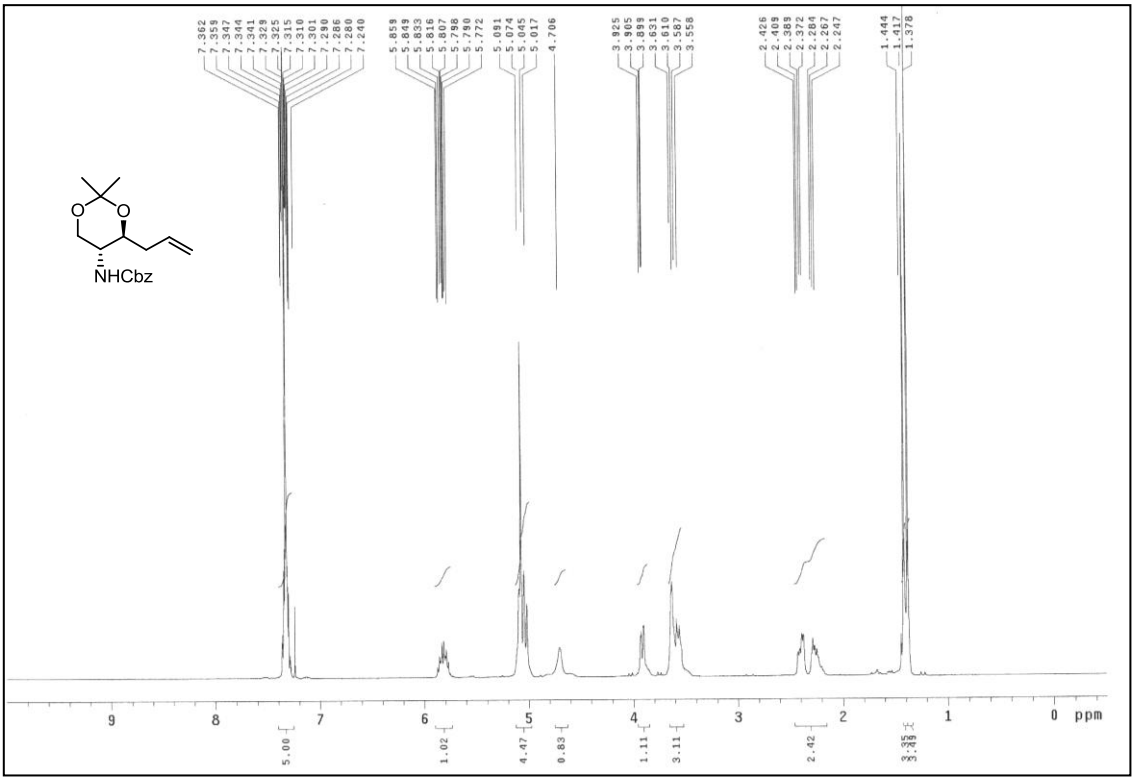
^{1}H NMR spectrum of compound **7** *N,O*-acetal (400 MHz, $CDCl_3$, rotameric mixture)



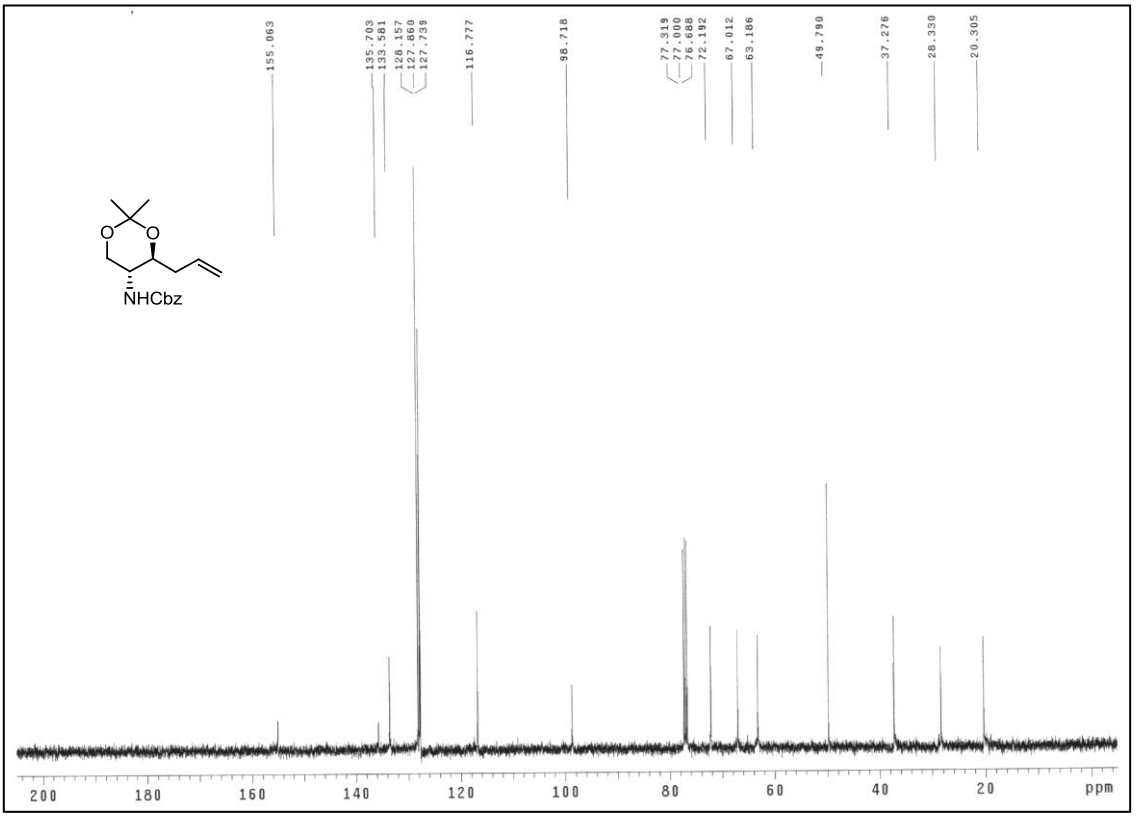
^{1}H NMR spectrum of compound **8** (400 MHz, $CDCl_3$)



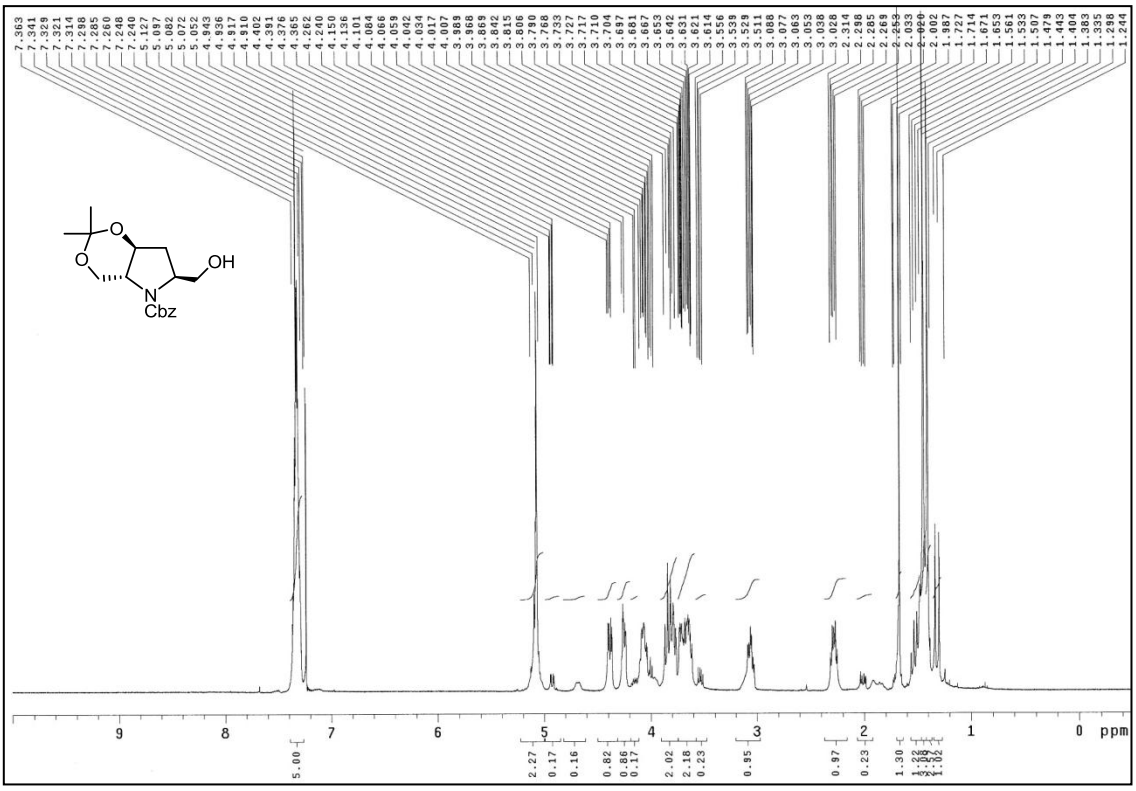
^{13}C NMR spectrum of compound **8** (100 MHz, $CDCl_3$)



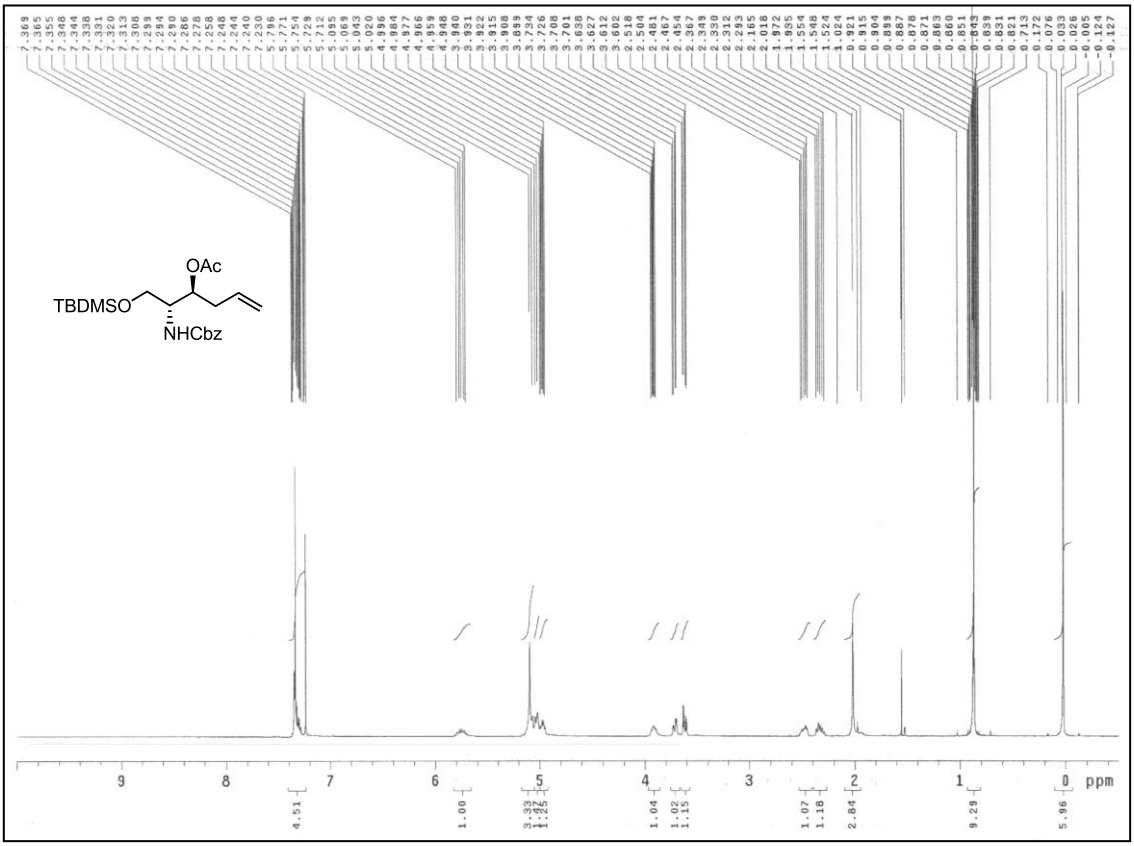
^{1}H NMR spectrum of compound **9** (400 MHz, $CDCl_3$)



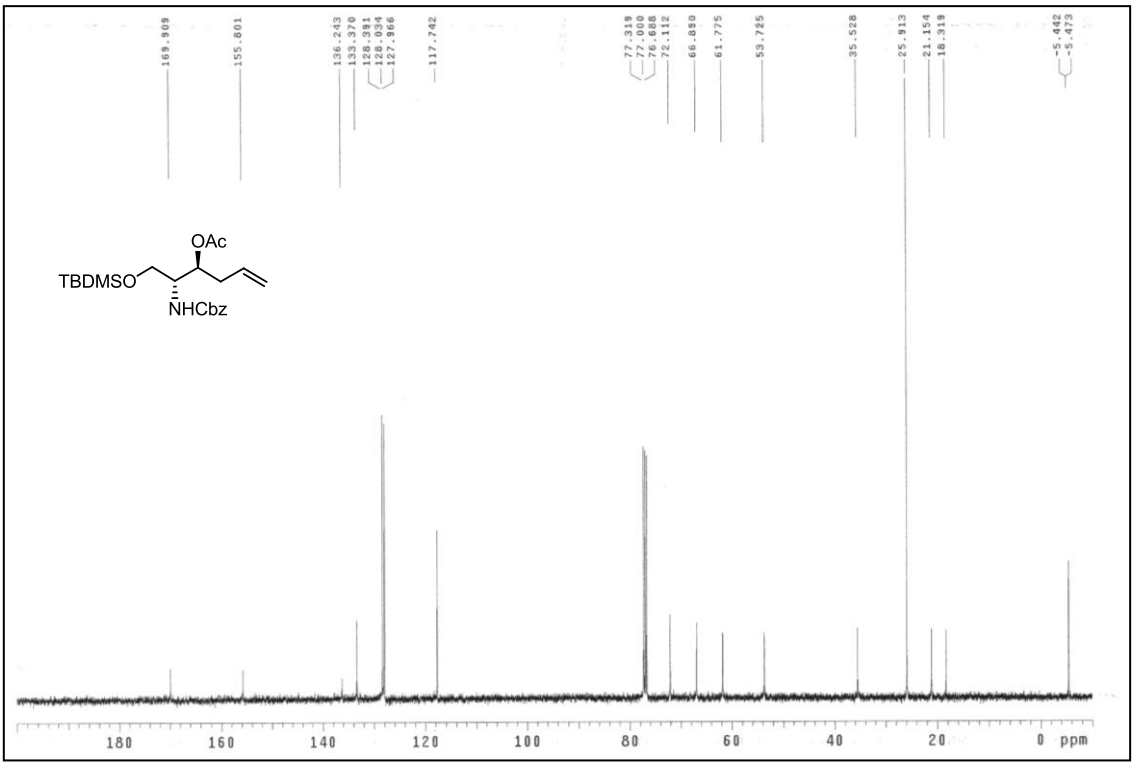
^{13}C NMR spectrum of compound **9** (100 MHz, $CDCl_3$)



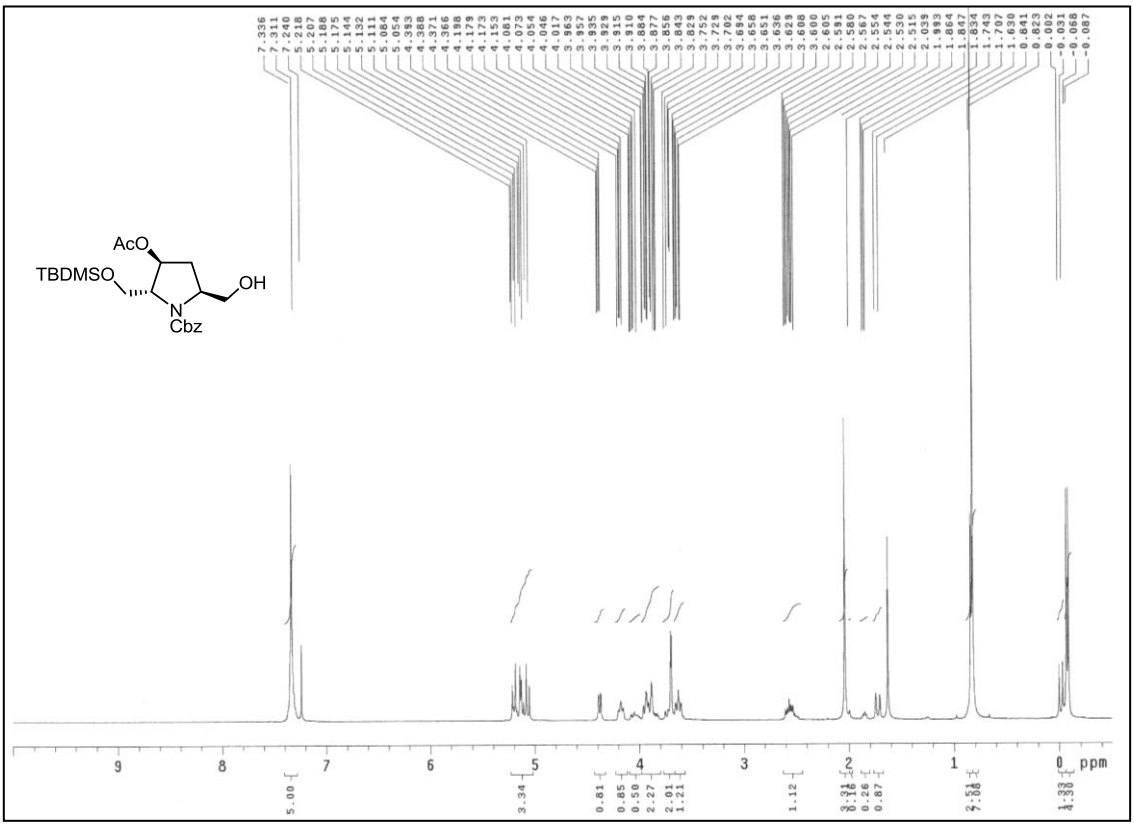
^{1}H NMR spectrum of compound **10** (400 MHz, $CDCl_3$, rotameric mixture)



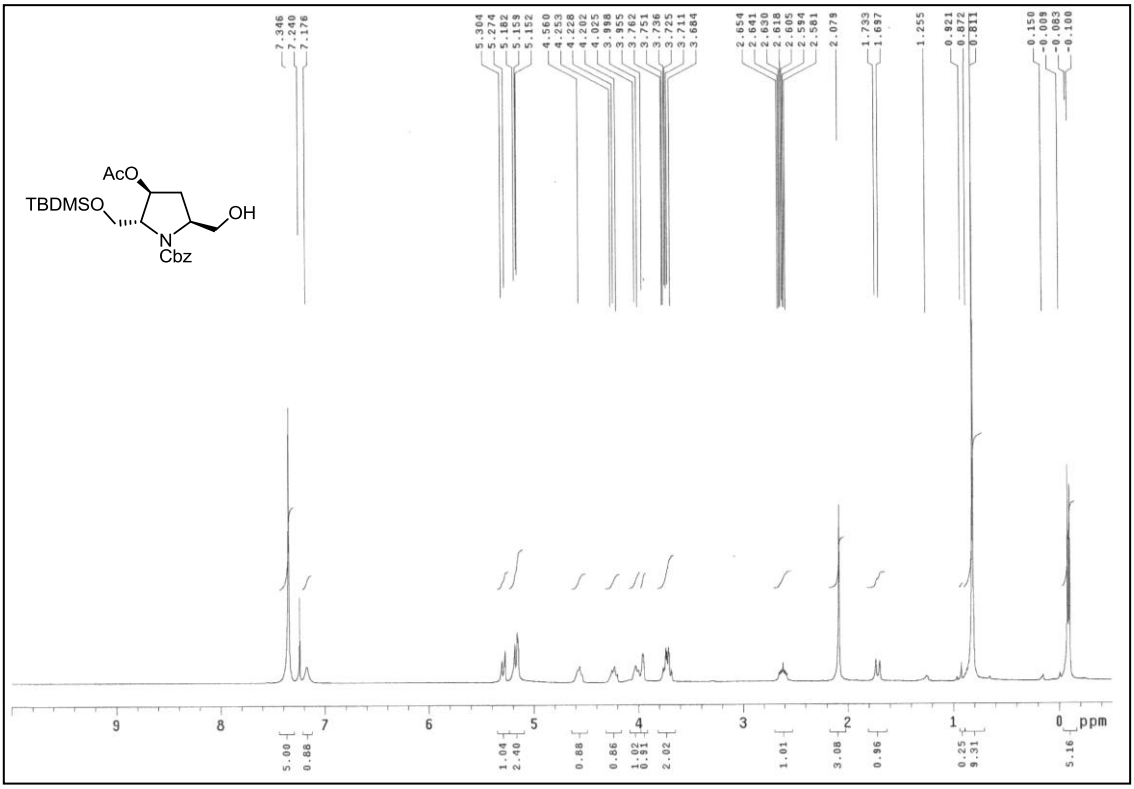
^{1}H NMR spectrum of compound **11** (400 MHz, $CDCl_3$)



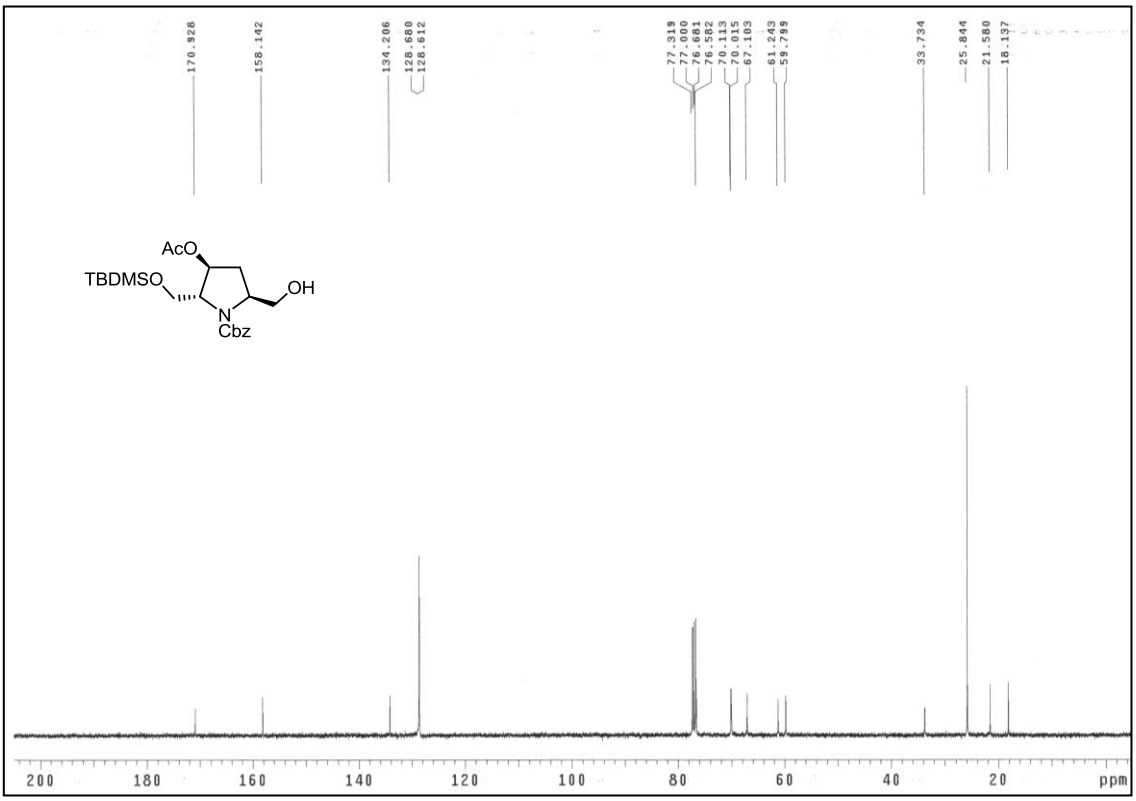
^{13}C NMR spectrum of compound **11** (100 MHz, $CDCl_3$)



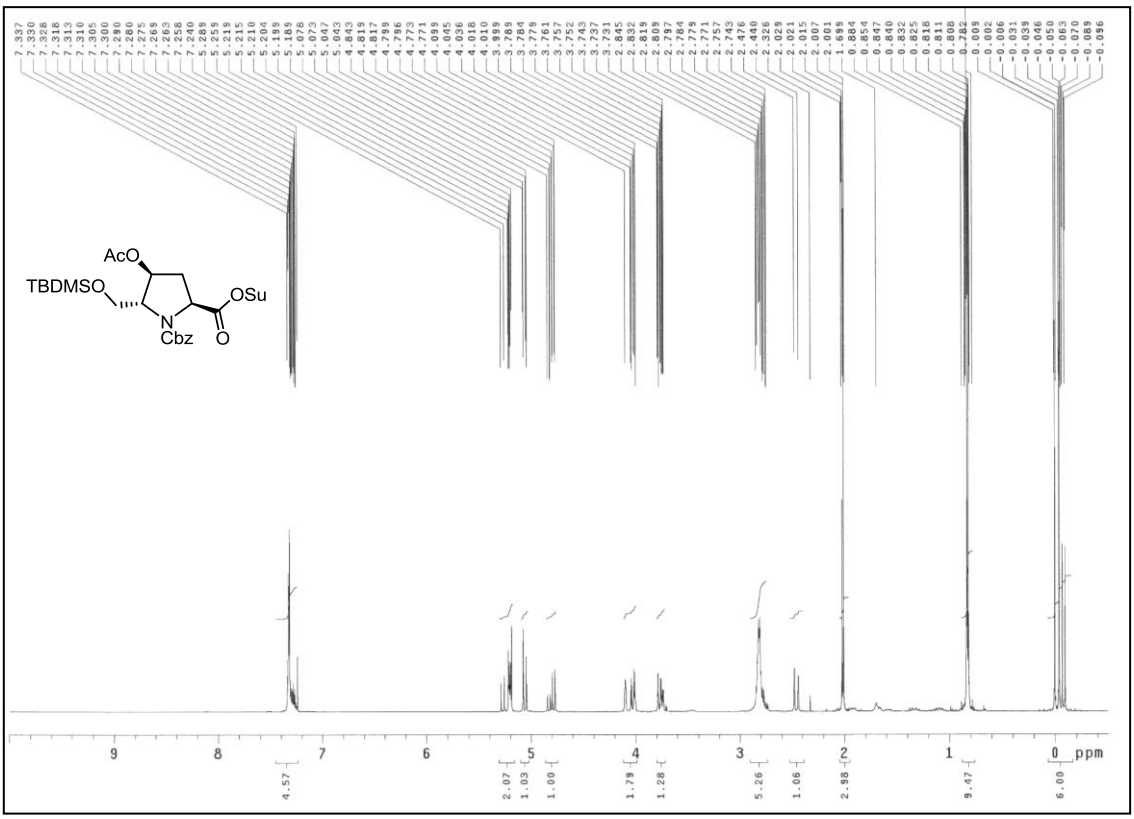
^{1}H NMR spectrum of compound **12** (400 MHz, $CDCl_3$, rotameric mixture)



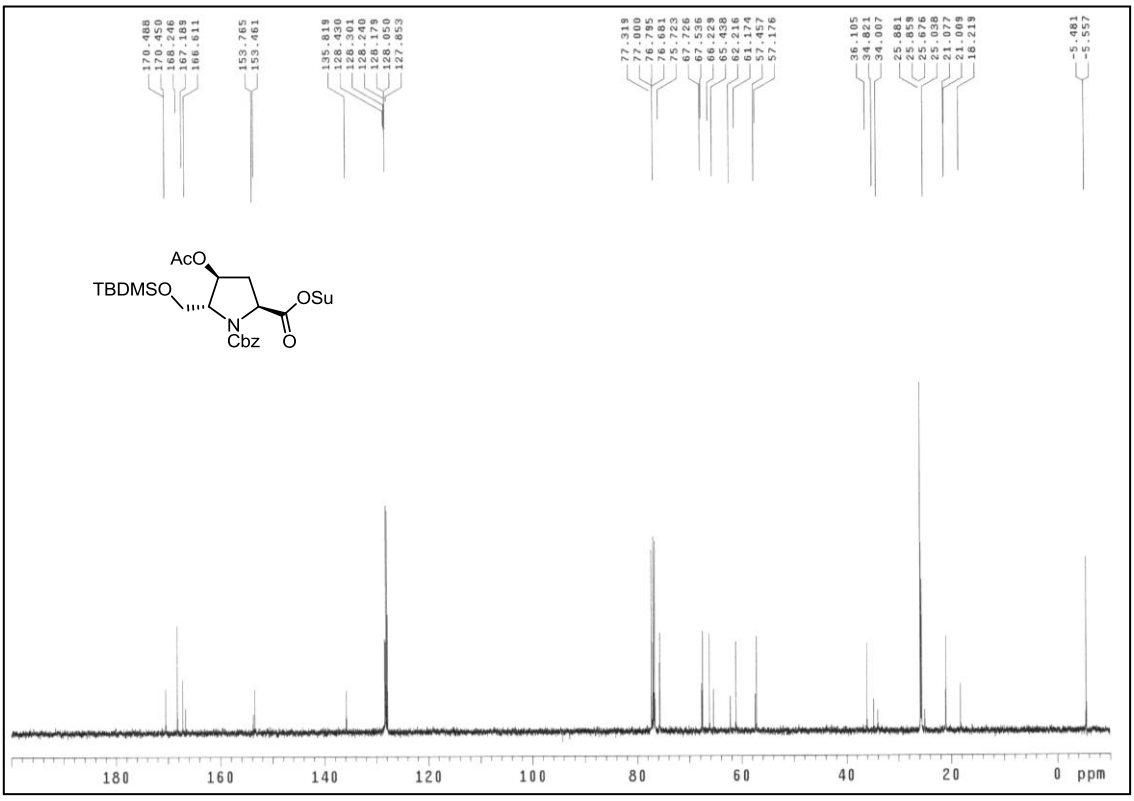
^{1}H NMR spectrum of compound **12** (400 MHz, $ZnCl_2$ in $CDCl_3$)



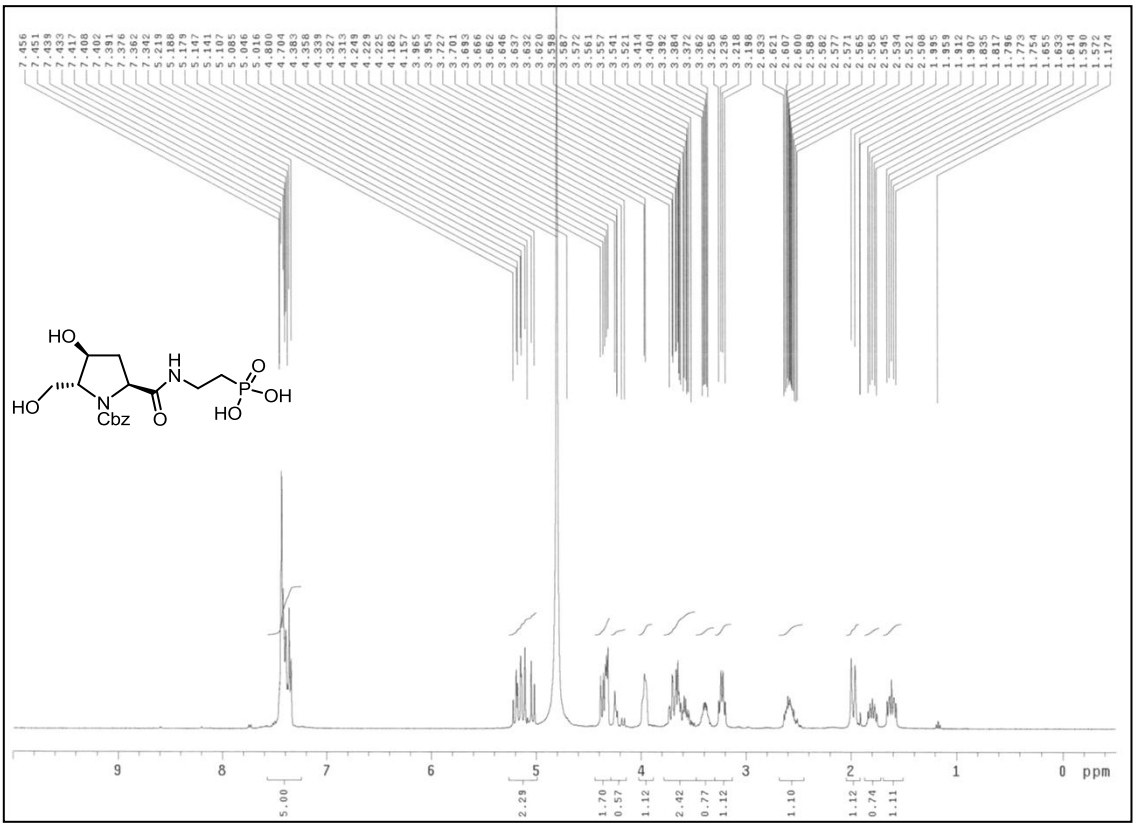
^{13}C NMR spectrum of compound **12** (100 MHz, $ZnCl_2$ in $CDCl_3$)



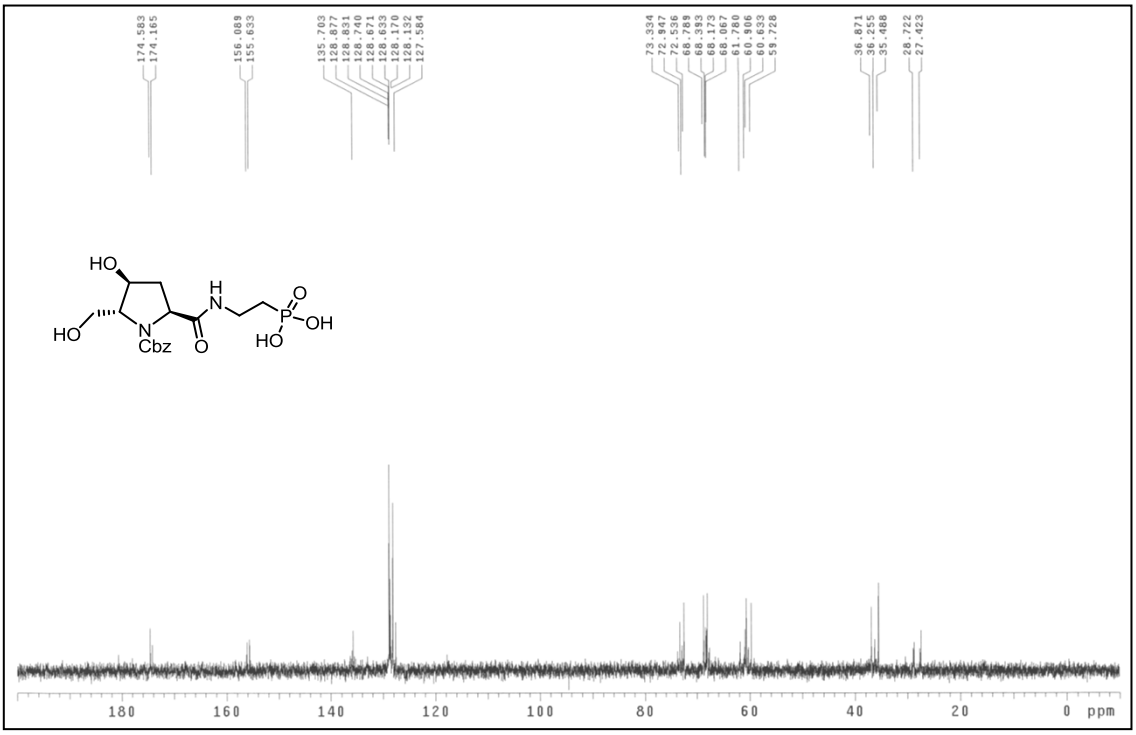
^{1}H NMR spectrum of compound **13**-OSu (400 MHz, $CDCl_3$, rotameric mixture)



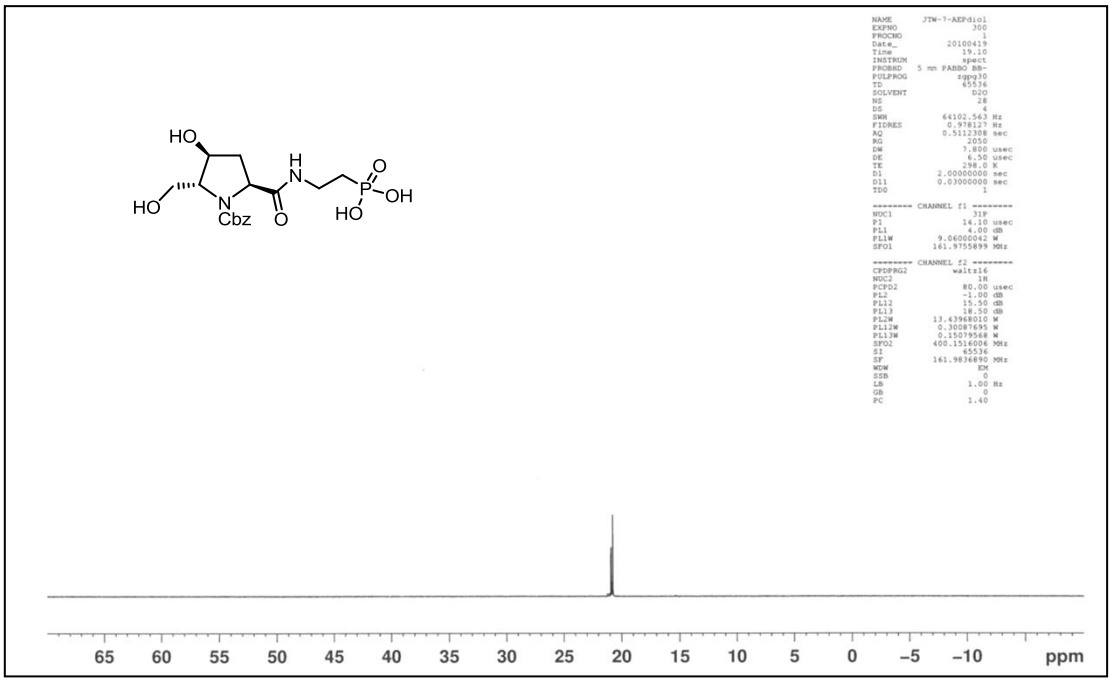
^{13}C NMR spectrum of compound **13**-OSu (100 MHz, $CDCl_3$)



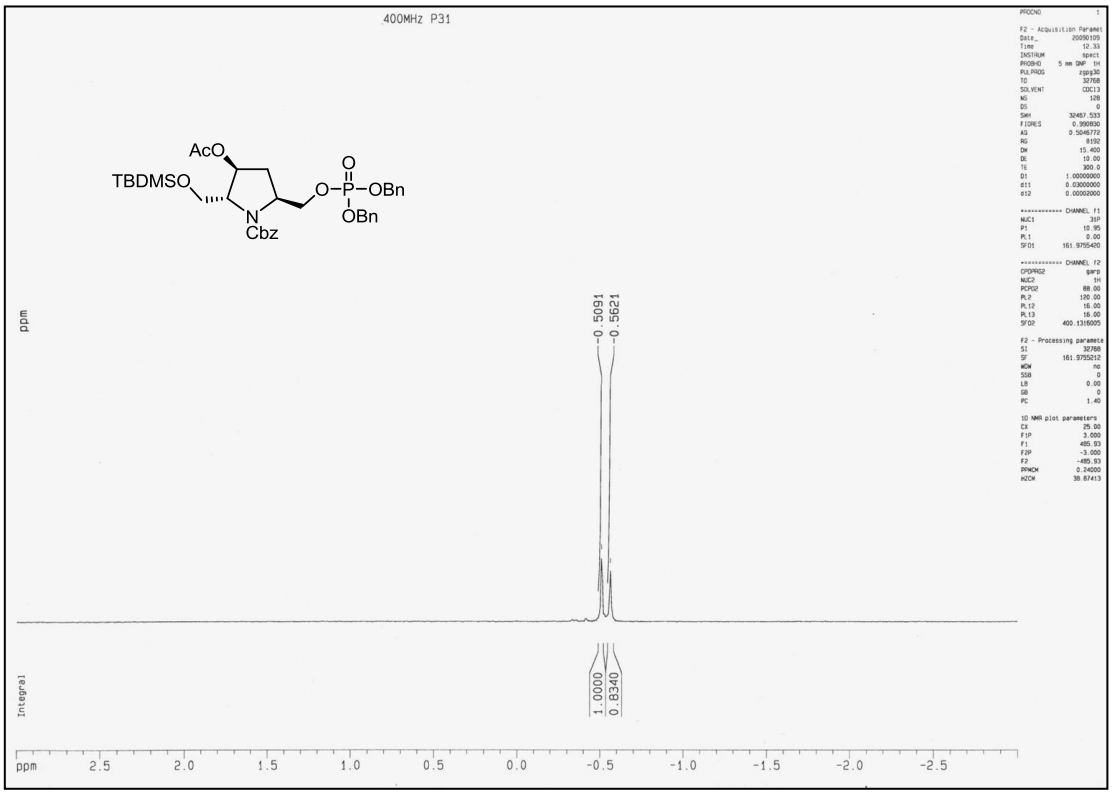
^{1}H NMR spectrum of compound **14** (400 MHz, D_2O, rotameric mixture)



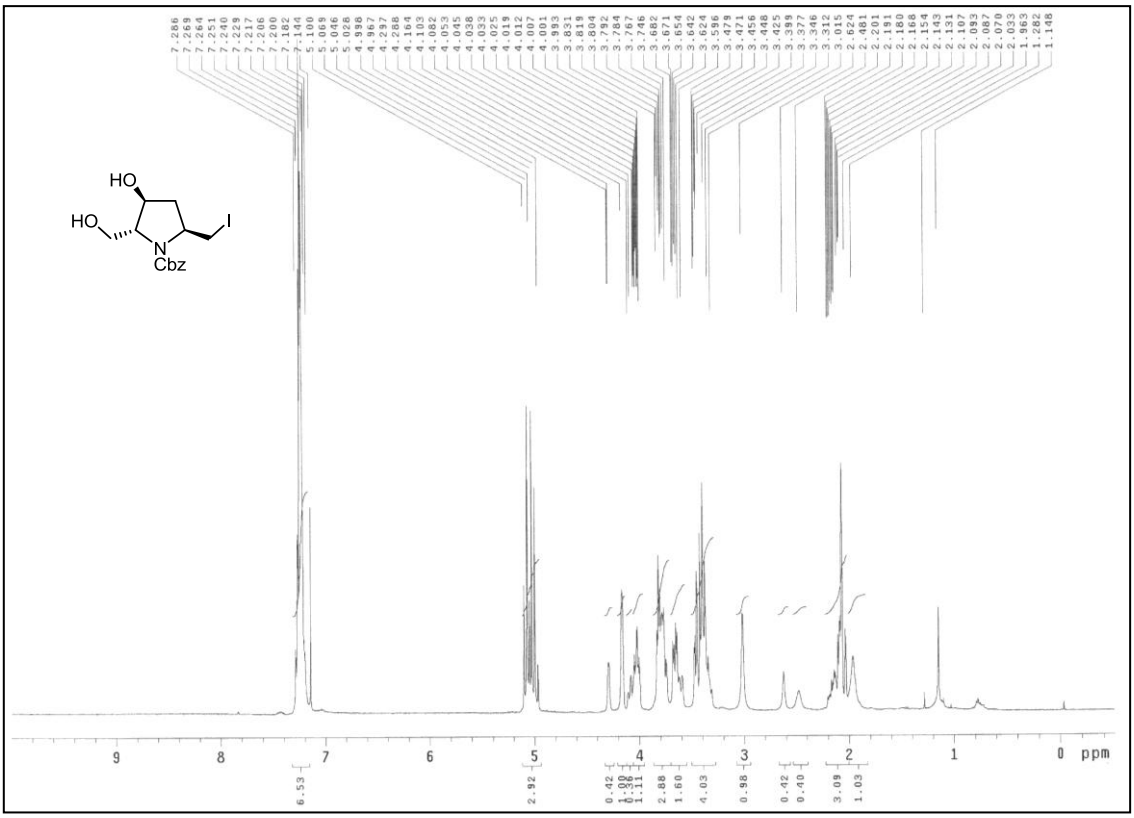
^{13}C NMR spectrum of compound **14** (100 MHz, D_2O rotameric mixture)



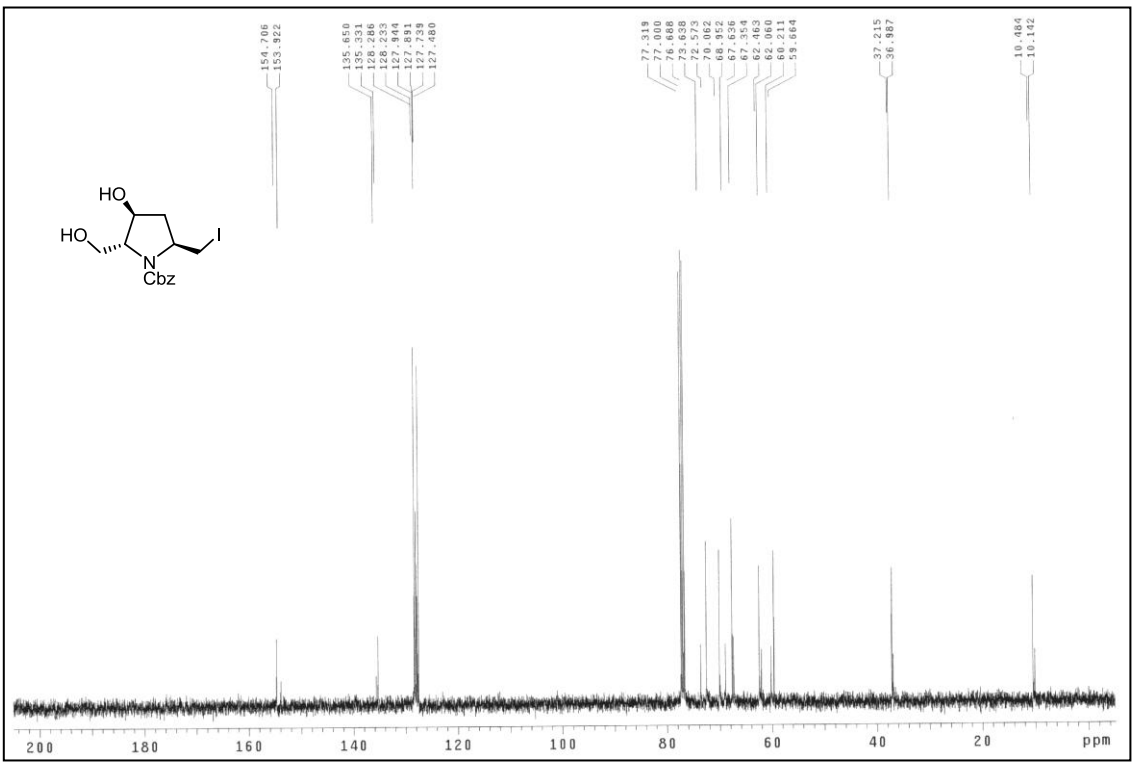
^{31}P NMR spectrum of compound **14** (162 MHz, D_2O rotameric mixture)



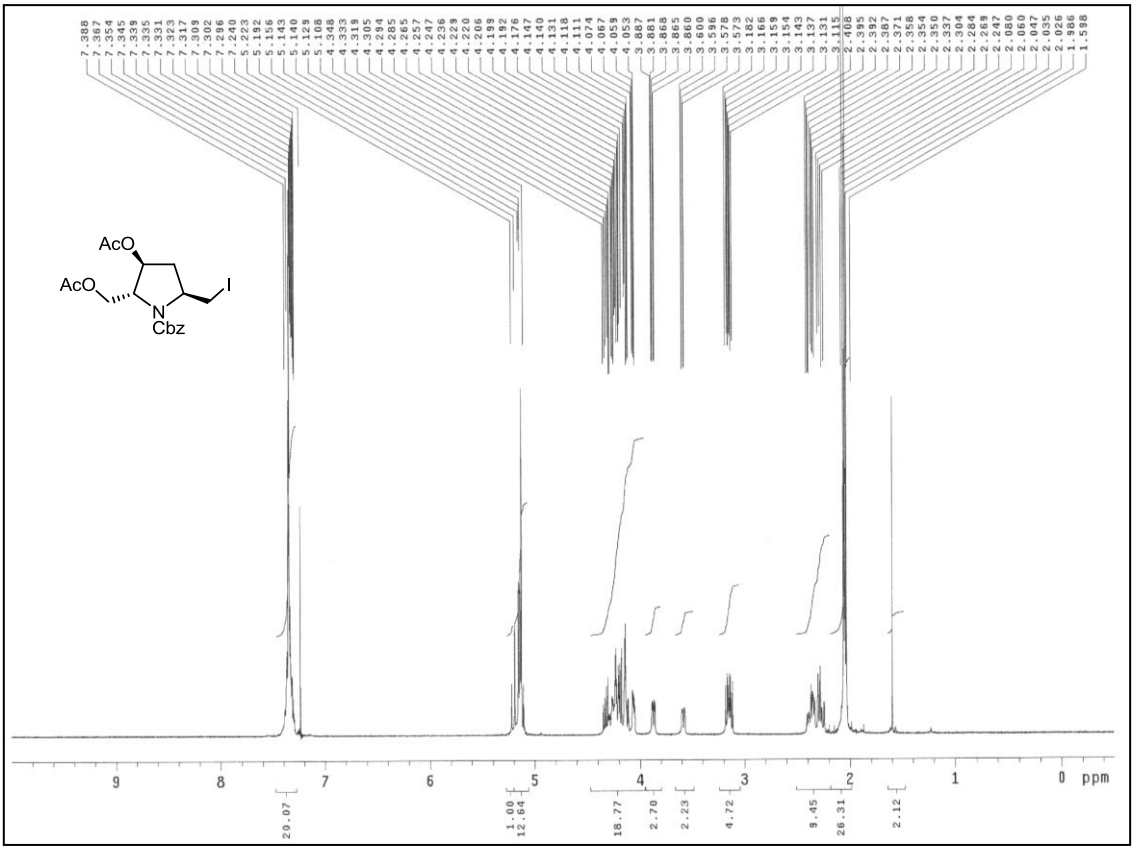
^{31}P NMR spectrum of compound **15** (162 MHz, $CDCl_3$, rotameric mixture)



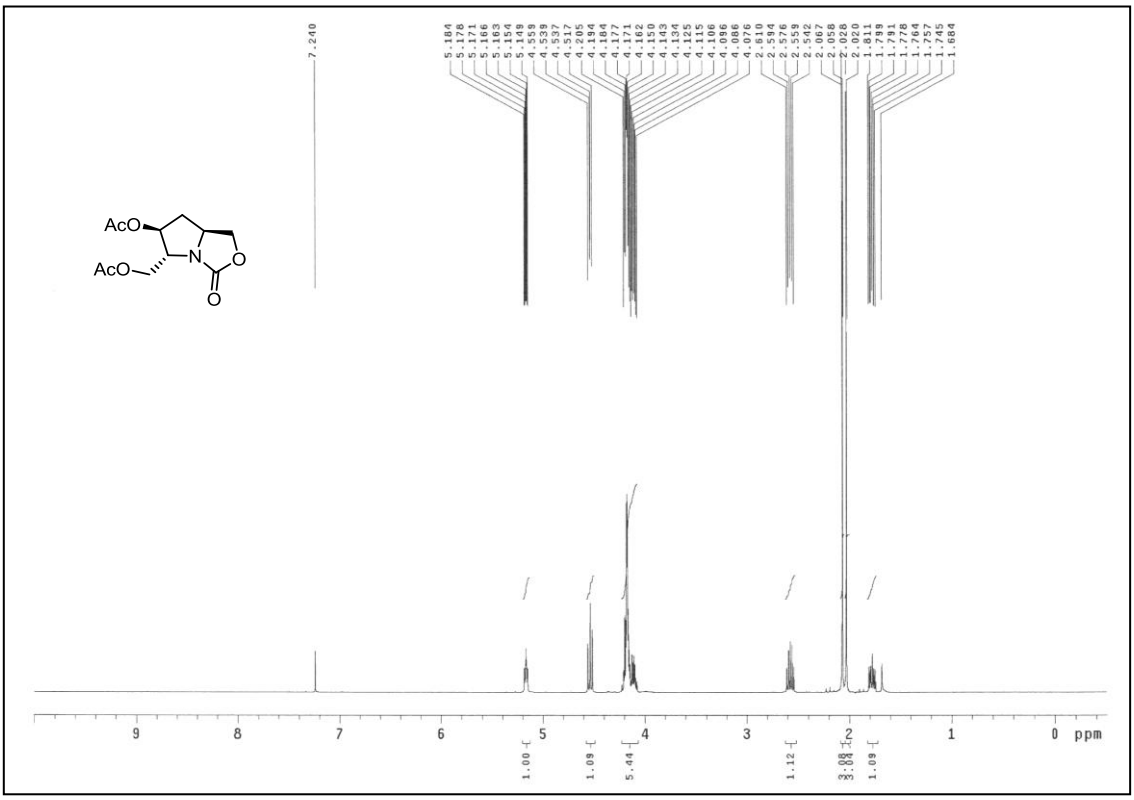
^{1}H NMR spectrum of compound **16** (400 MHz, $CDCl_3$, rotameric mixture)



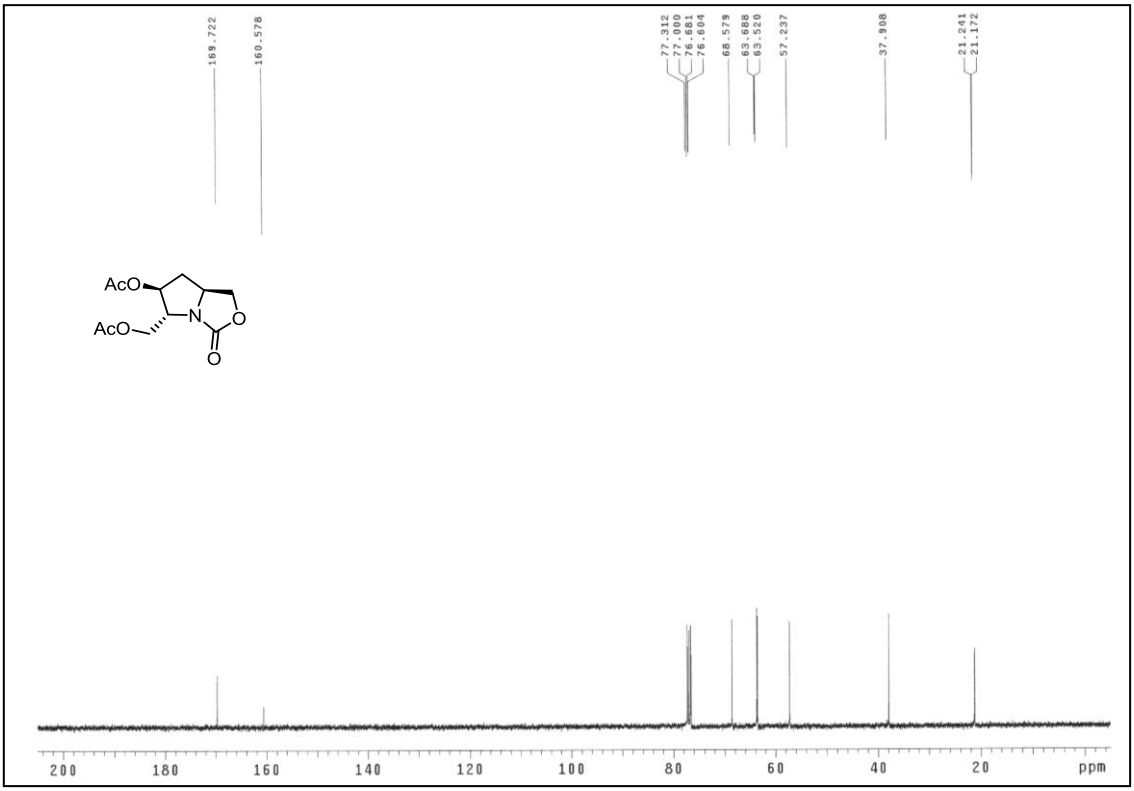
^{13}C NMR spectrum of compound **16** (100 MHz, $CDCl_3$, rotameric mixture)



^{1}H NMR spectrum of compound **16**-Ac_2 (400 MHz, $CDCl_3$, rotameric mixture)



^{1}H NMR spectrum of compound **17** (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of compound **17** (100 MHz, $CDCl_3$)

X-ray crystallographic data for compound **12** (ic13737)

Table 1. Crystal data and structure refinement for ic13737.

Identification code	ic13737	
Empirical formula	C22 H34 N O6 Si	
Formula weight	436.59	
Temperature	295(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	C2	
Unit cell dimensions	a = 23.812(7) Å	α= 90°.
	b = 6.6660(7) Å	β= 123.79(3)°.
	c = 18.297(4) Å	γ = 90°.
Volume	2413.8(9) $Å^3$	
Z	4	
Density (calculated)	1.201 Mg/m^3	
Absorption coefficient	1.155 mm^{-1}	
F(000)	940	
Crystal size	0.25 x 0.20 x 0.15 mm^3	
Theta range for data collection	3.74 to 68.00°.	
Index ranges	-27<=h<=28, -6<=k<=8, -21<=l<=20	
Reflections collected	6282	
Independent reflections	3105 [R(int) = 0.0298]	
Completeness to theta = 68.00°	98.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.59567	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3105 / 1 / 280	
Goodness-of-fit on F^2	1.034	
Final R indices [I>2sigma(I)]	R1 = 0.0575, wR2 = 0.1555	
R indices (all data)	R1 = 0.0612, wR2 = 0.1659	
Absolute structure parameter	0.06(5)	
Largest diff. peak and hole	0.430 and -0.277 e.$Å^{-3}$	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for ic13737. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Si(1)	6590(1)	4936(2)	5948(1)	59(1)
O(1)	7782(2)	3599(5)	9171(2)	74(1)
O(2)	7831(1)	6837(4)	8837(2)	62(1)
O(3)	9331(3)	-47(8)	9254(3)	67(1)
C(6)	9038(2)	1779(6)	9247(3)	70(1)
O(3')	8859(7)	1111(19)	9783(7)	157(5)
C(6')	9038(2)	1779(6)	9247(3)	70(1)
O(4)	9523(1)	4951(4)	8440(2)	59(1)
O(5)	9596(2)	7926(5)	7947(2)	89(1)
O(6)	7395(1)	5541(4)	6431(2)	60(1)
N(1)	8201(1)	4445(4)	8354(2)	50(1)
C(1)	7759(2)	6942(5)	7128(2)	55(1)
C(2)	8370(1)	5977(5)	7926(2)	49(1)
C(3)	8816(2)	4795(6)	7713(2)	55(1)
C(4)	8605(2)	2632(6)	7661(3)	63(1)
C(5)	8433(2)	2410(5)	8336(2)	58(1)
C(7)	7926(2)	4853(6)	8819(2)	55(1)
C(8)	7533(2)	7522(8)	9295(3)	69(1)
C(9)	6777(2)	7825(6)	8655(2)	56(1)
C(10)	6540(2)	9640(7)	8236(3)	70(1)
C(11)	5857(2)	9948(9)	7644(3)	83(1)
C(12)	5401(2)	8447(9)	7462(3)	82(1)
C(13)	5633(2)	6619(9)	7887(3)	84(1)
C(14)	6319(2)	6306(7)	8478(3)	74(1)
C(15)	9851(2)	6603(6)	8477(2)	60(1)
C(16)	10564(2)	6609(8)	9263(3)	78(1)
C(17)	6072(3)	7122(11)	5873(5)	123(3)
C(18)	6504(3)	3032(13)	6610(4)	129(3)
C(19)	6329(2)	3927(10)	4854(3)	84(1)
C(20)	6824(3)	2285(17)	4969(6)	179(5)
C(21)	6351(4)	5613(17)	4304(4)	149(4)
C(22)	5608(3)	3115(13)	4351(4)	115(2)

Table 3. Bond lengths [Å] and angles [°] for ic13737.

Si(1)-O(6)	1.653(2)	C(19)-Si(1)-C(17)	113.1(3)
Si(1)-C(18)	1.844(6)	C(7)-O(2)-C(8)	118.0(3)
Si(1)-C(19)	1.861(4)	O(3)-C(6)-C(5)	114.2(4)
Si(1)-C(17)	1.864(6)	C(15)-O(4)-C(3)	117.0(3)
O(1)-C(7)	1.216(5)	C(1)-O(6)-Si(1)	126.0(2)
O(2)-C(7)	1.345(5)	C(7)-N(1)-C(5)	121.1(3)
O(2)-C(8)	1.443(4)	C(7)-N(1)-C(2)	124.3(3)
O(3)-C(6)	1.399(7)	C(5)-N(1)-C(2)	114.2(3)
C(6)-C(5)	1.537(5)	O(6)-C(1)-C(2)	111.4(3)
O(4)-C(15)	1.329(5)	N(1)-C(2)-C(1)	114.0(3)
O(4)-C(3)	1.457(4)	N(1)-C(2)-C(3)	102.2(3)
O(5)-C(15)	1.197(5)	C(1)-C(2)-C(3)	113.6(3)
O(6)-C(1)	1.421(4)	O(4)-C(3)-C(4)	107.5(3)
N(1)-C(7)	1.357(4)	O(4)-C(3)-C(2)	110.0(3)
N(1)-C(5)	1.472(4)	C(4)-C(3)-C(2)	104.5(3)
N(1)-C(2)	1.473(4)	C(5)-C(4)-C(3)	105.9(3)
C(1)-C(2)	1.516(5)	N(1)-C(5)-C(4)	101.8(3)
C(2)-C(3)	1.539(5)	N(1)-C(5)-C(6)	111.4(3)
C(3)-C(4)	1.513(6)	C(4)-C(5)-C(6)	113.3(3)
C(4)-C(5)	1.510(6)	O(1)-C(7)-O(2)	124.2(3)
C(8)-C(9)	1.519(5)	O(1)-C(7)-N(1)	124.8(4)
C(9)-C(10)	1.374(6)	O(2)-C(7)-N(1)	111.0(3)
C(9)-C(14)	1.387(6)	O(2)-C(8)-C(9)	110.4(3)
C(10)-C(11)	1.379(6)	C(10)-C(9)-C(14)	119.2(3)
C(11)-C(12)	1.374(7)	C(10)-C(9)-C(8)	119.4(4)
C(12)-C(13)	1.385(8)	C(14)-C(9)-C(8)	121.5(4)
C(13)-C(14)	1.385(6)	C(9)-C(10)-C(11)	120.6(4)
C(15)-C(16)	1.496(5)	C(12)-C(11)-C(10)	120.7(5)
C(19)-C(22)	1.526(6)	C(11)-C(12)-C(13)	119.3(4)
C(19)-C(21)	1.528(9)	C(14)-C(13)-C(12)	120.0(4)
C(19)-C(20)	1.534(10)	C(13)-C(14)-C(9)	120.3(4)
O(6)-Si(1)-C(18)	109.7(2)	O(5)-C(15)-O(4)	123.4(3)
O(6)-Si(1)-C(19)	104.96(16)	O(5)-C(15)-C(16)	124.7(4)
C(18)-Si(1)-C(19)	111.4(3)	O(4)-C(15)-C(16)	111.9(3)
O(6)-Si(1)-C(17)	111.8(2)	C(22)-C(19)-C(21)	107.6(5)
C(18)-Si(1)-C(17)	106.0(4)	C(22)-C(19)-C(20)	110.5(6)

C(21)-C(19)-C(20)	108.1(7)	C(21)-C(19)-Si(1)	109.2(5)
C(22)-C(19)-Si(1)	111.6(3)	C(20)-C(19)-Si(1)	109.8(4)

Symmetry transformations used to generate equivalent atoms.

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for ic13737. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Si(1)	49(1)	67(1)	54(1)	-5(1)	24(1)	-6(1)
O(1)	84(2)	76(2)	71(2)	10(1)	49(2)	-5(2)
O(2)	58(1)	69(2)	64(1)	-5(1)	37(1)	1(1)
O(3)	72(3)	35(2)	67(3)	2(2)	22(2)	10(2)
C(6)	73(2)	51(2)	67(2)	2(2)	28(2)	2(2)
O(3')	235(13)	114(8)	115(7)	37(6)	94(8)	21(9)
C(6')	73(2)	51(2)	67(2)	2(2)	28(2)	2(2)
O(4)	47(1)	64(1)	61(1)	3(1)	27(1)	-2(1)
O(5)	72(2)	73(2)	98(2)	19(2)	33(2)	-7(2)
O(6)	48(1)	75(2)	51(1)	-8(1)	22(1)	-6(1)
N(1)	51(1)	50(2)	48(1)	-1(1)	26(1)	-2(1)
C(1)	54(2)	50(2)	52(2)	1(1)	25(1)	-4(1)
C(2)	45(1)	49(2)	46(2)	-5(1)	21(1)	-5(1)
C(3)	51(1)	65(2)	50(2)	-5(2)	28(1)	-1(2)
C(4)	61(2)	57(2)	66(2)	-16(2)	33(2)	-3(2)
C(5)	58(2)	44(2)	59(2)	-8(2)	24(2)	-6(2)
C(7)	47(1)	63(2)	49(2)	-4(2)	24(1)	-6(2)
C(8)	58(2)	92(3)	55(2)	-10(2)	30(2)	7(2)
C(9)	56(2)	69(2)	52(2)	-6(2)	35(2)	-3(2)
C(10)	71(2)	67(3)	83(2)	1(2)	49(2)	-6(2)
C(11)	78(2)	82(3)	92(3)	24(3)	50(2)	14(2)
C(12)	54(2)	107(4)	78(3)	-2(3)	33(2)	4(2)
C(13)	66(2)	92(3)	93(3)	-5(3)	43(2)	-19(2)
C(14)	78(2)	64(3)	80(2)	8(2)	43(2)	-4(2)
C(15)	54(2)	61(2)	67(2)	1(2)	34(2)	-1(2)
C(16)	51(2)	88(3)	81(3)	-2(2)	29(2)	-7(2)
C(17)	65(3)	112(5)	158(6)	-37(5)	43(3)	5(3)
C(18)	116(4)	179(7)	72(3)	7(4)	40(3)	-76(5)
C(19)	60(2)	131(4)	55(2)	-23(2)	28(2)	-22(2)
C(20)	92(4)	251(12)	164(7)	-126(8)	52(4)	-3(6)
C(21)	120(4)	237(12)	67(3)	19(5)	38(3)	-50(6)
C(22)	76(3)	160(6)	79(3)	-36(4)	25(2)	-45(4)