SUPPORTING INFORMATION

Synthetic deoxynojirimycin derivatives bearing a thiolated, fluorinated or unsaturated *N*-alkyl chain: identification of potent α-glucosidase and trehalase inhibitors as well as F508del-CFTR correctors

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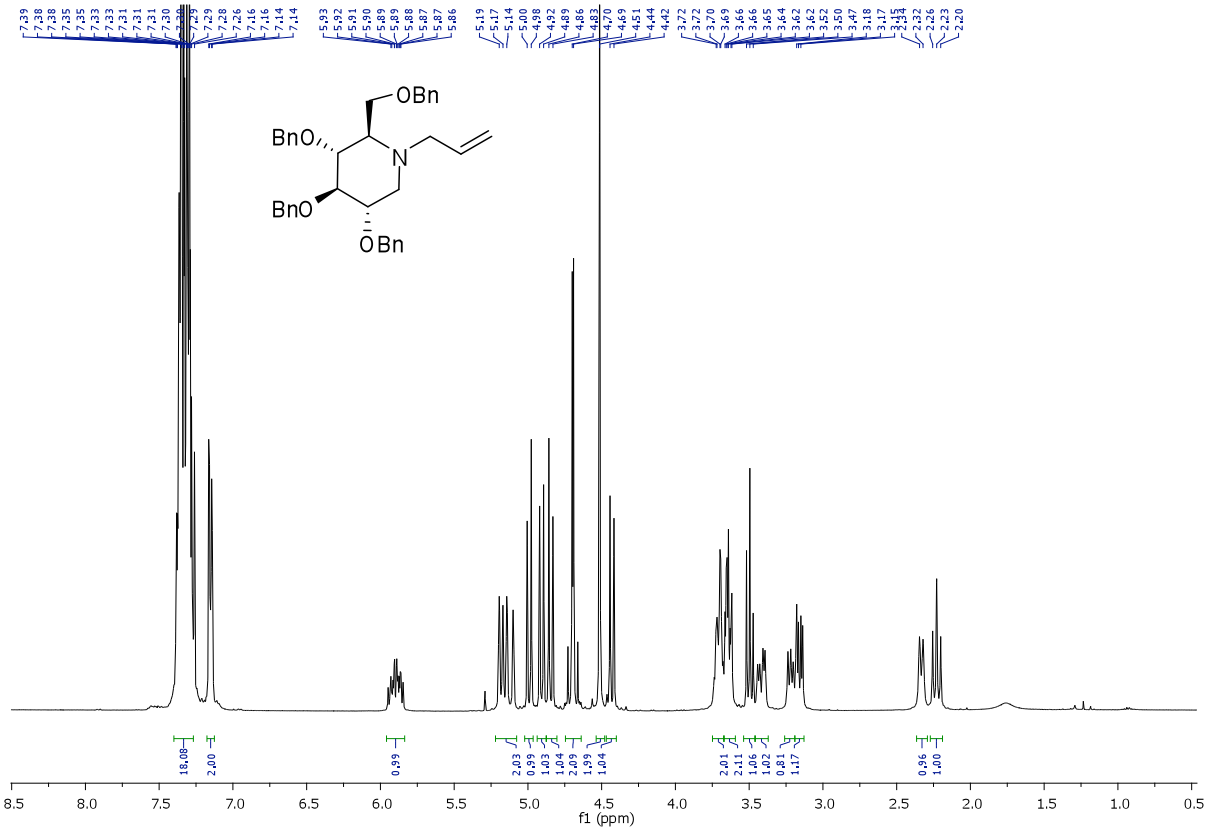
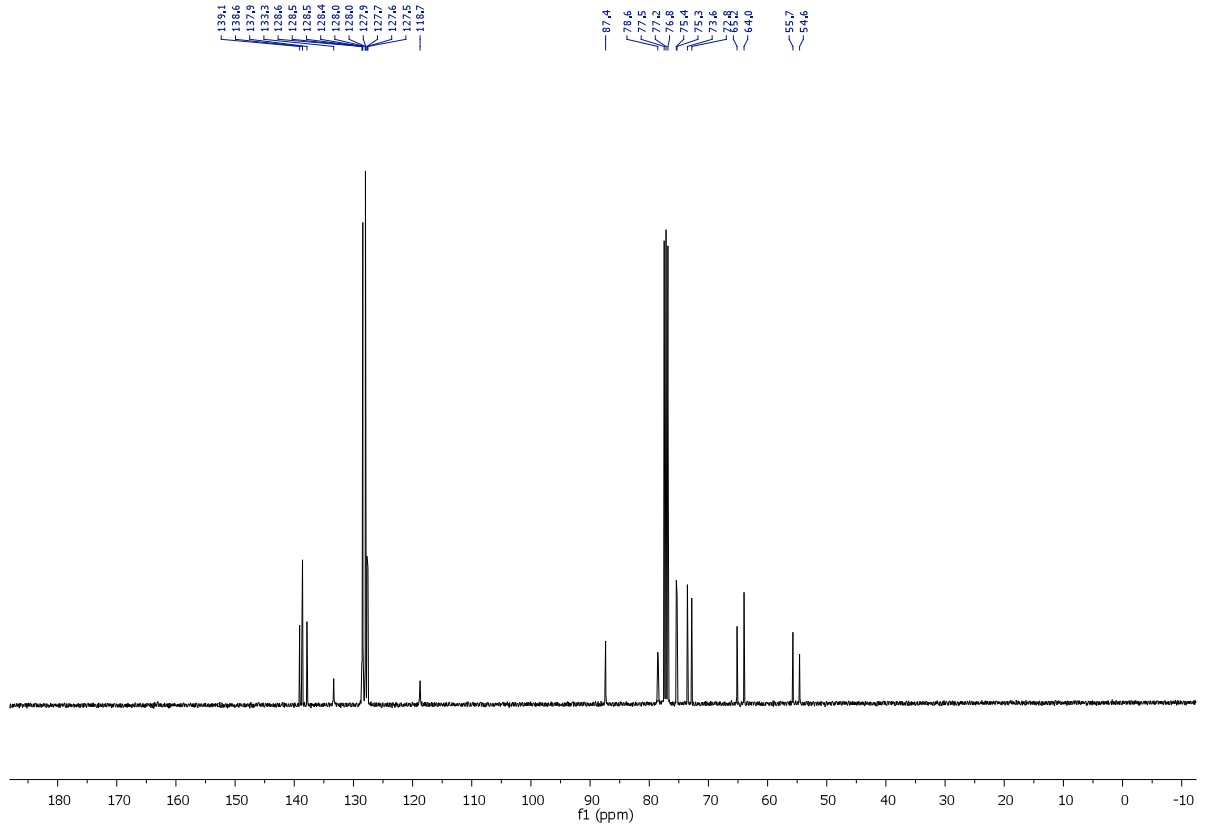
Copies of ^{1}H, ^{19}F and ^{13}C spectra and Tables of glycosidase inhibition

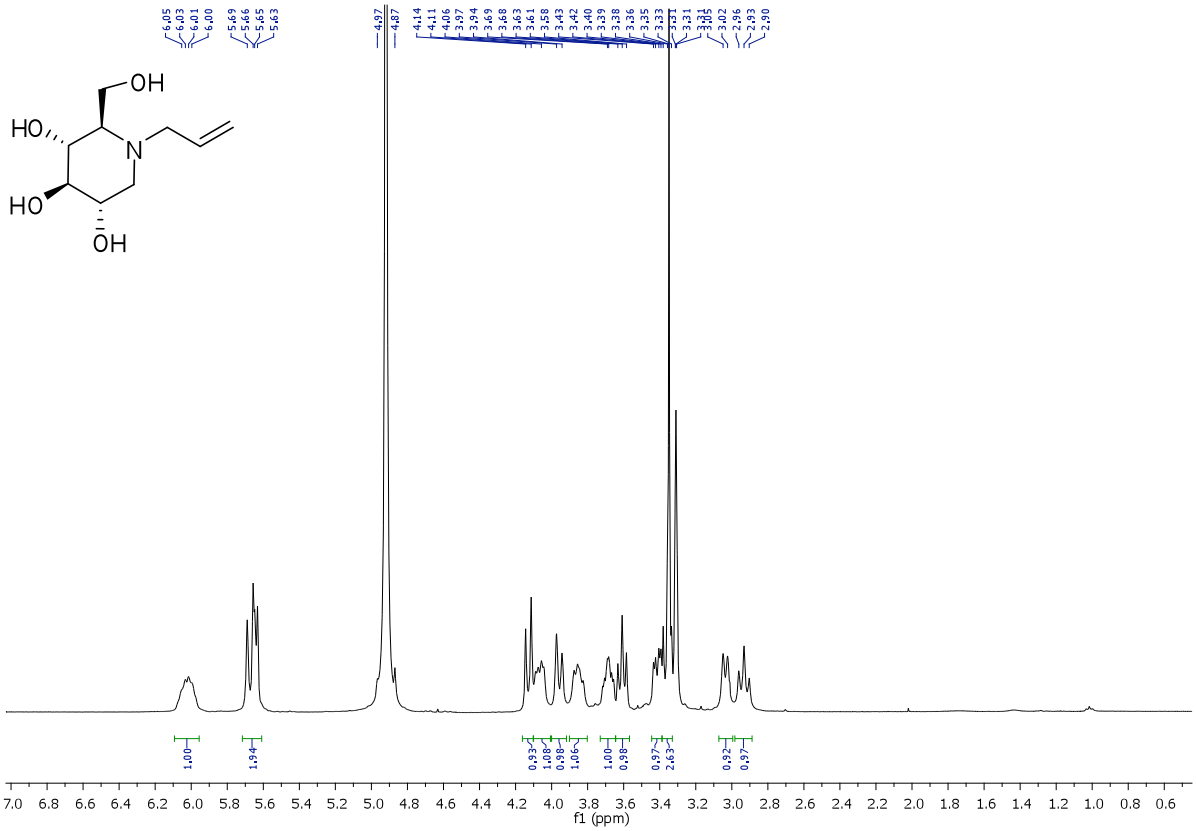
^{1}H NMR spectrum of compound **2a** (400 MHz, $CDCl_3$)



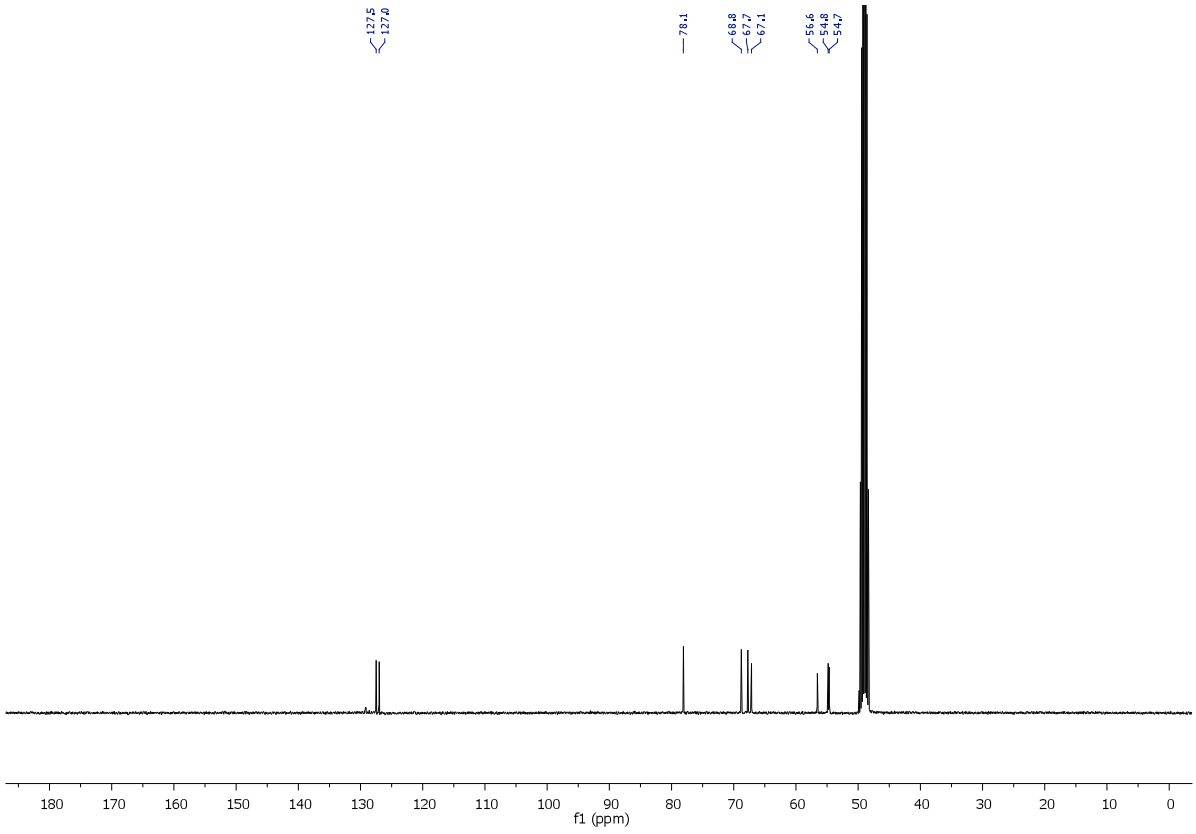
^{13}C NMR spectrum of compound **2a** (100 MHz, $CDCl_3$)



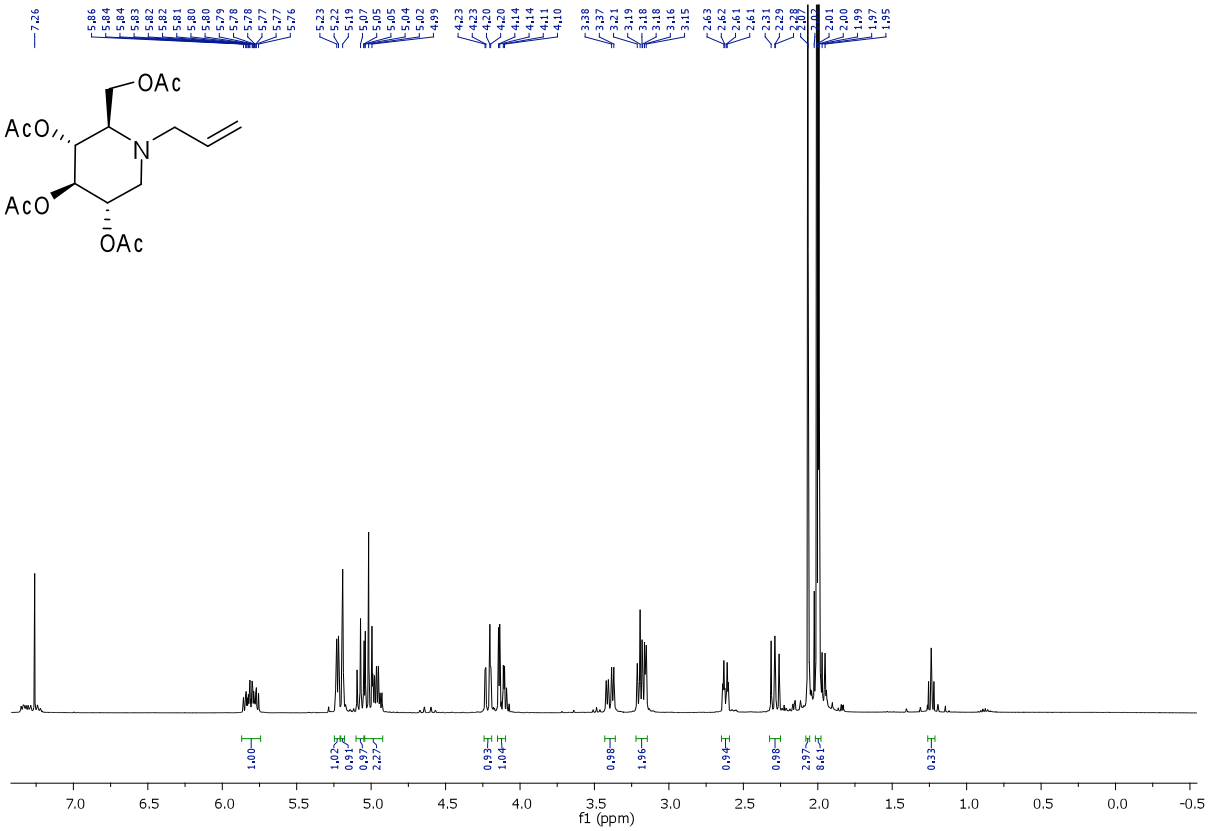
^{1}H NMR spectrum of compound **3a** (400 MHz, CD_3OD)



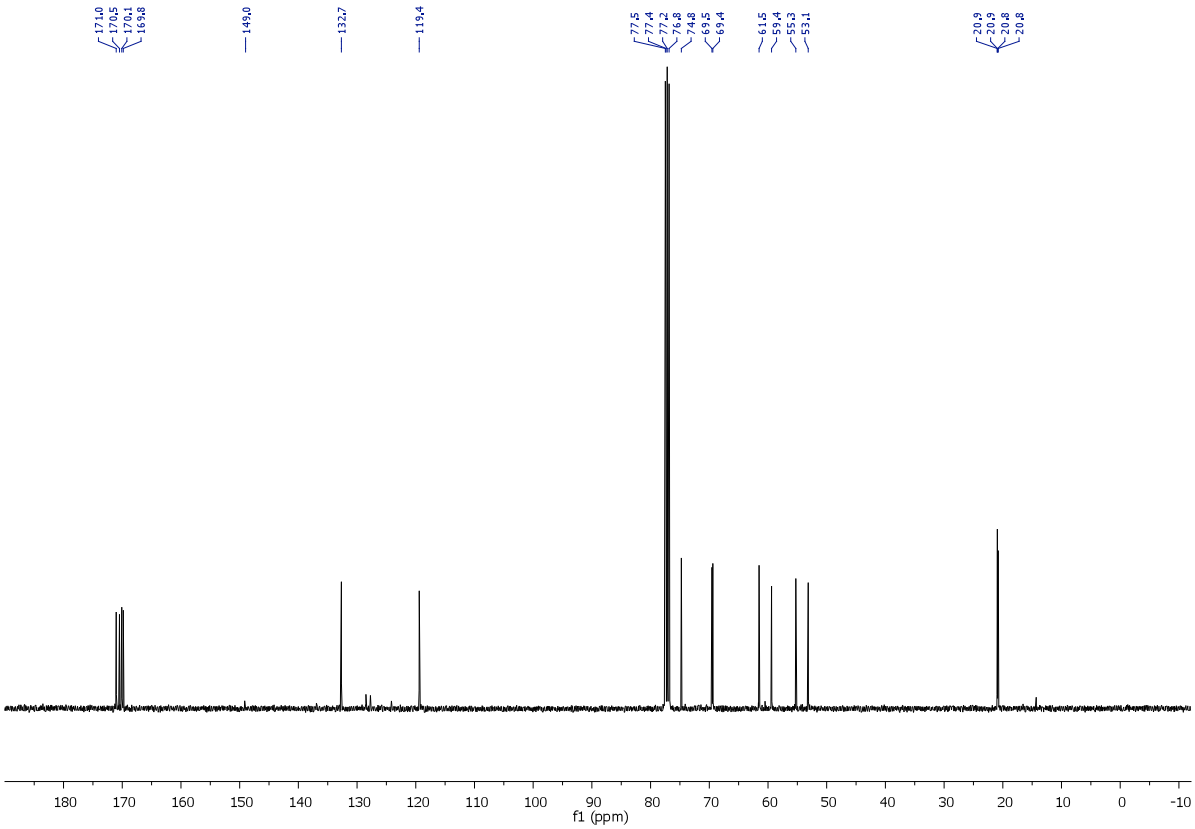
^{13}C NMR spectrum of compound **3a** (100 MHz, CD_3OD)



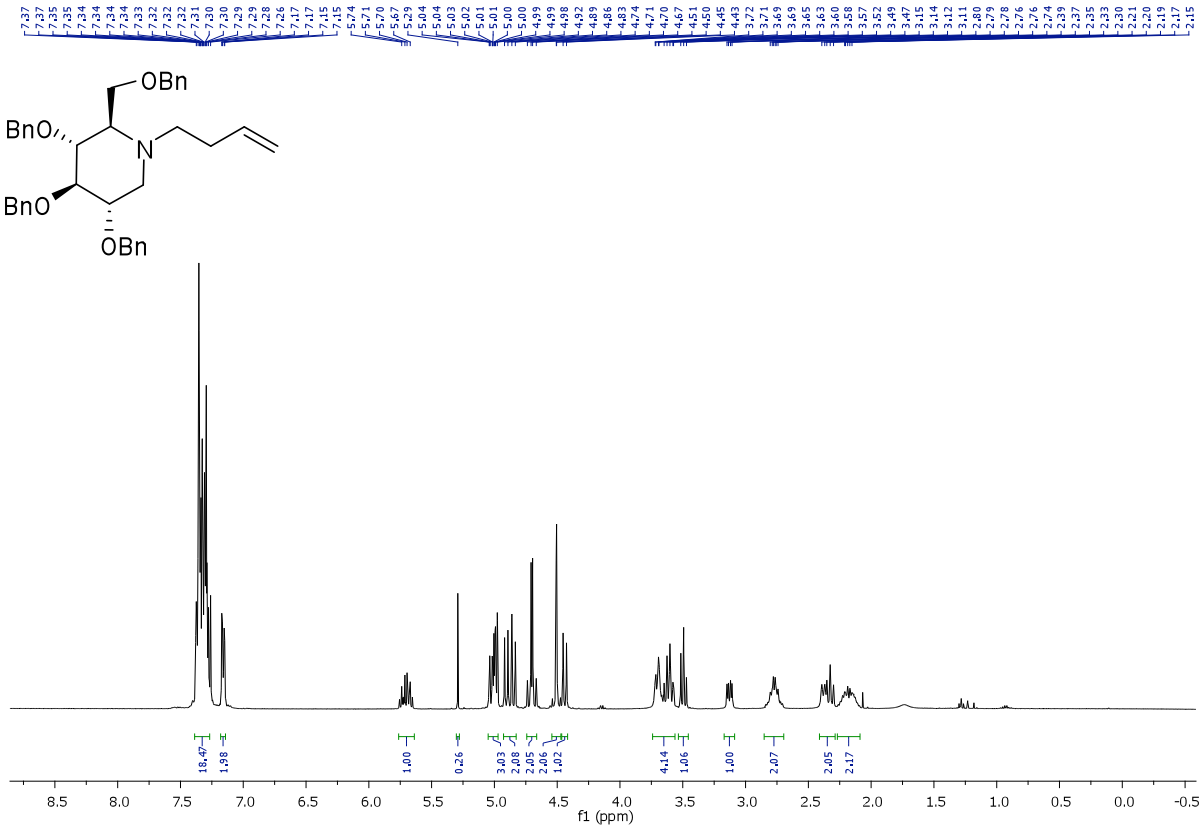
^{1}H NMR spectrum of compound **4a** (400 MHz, $CDCl_3$)



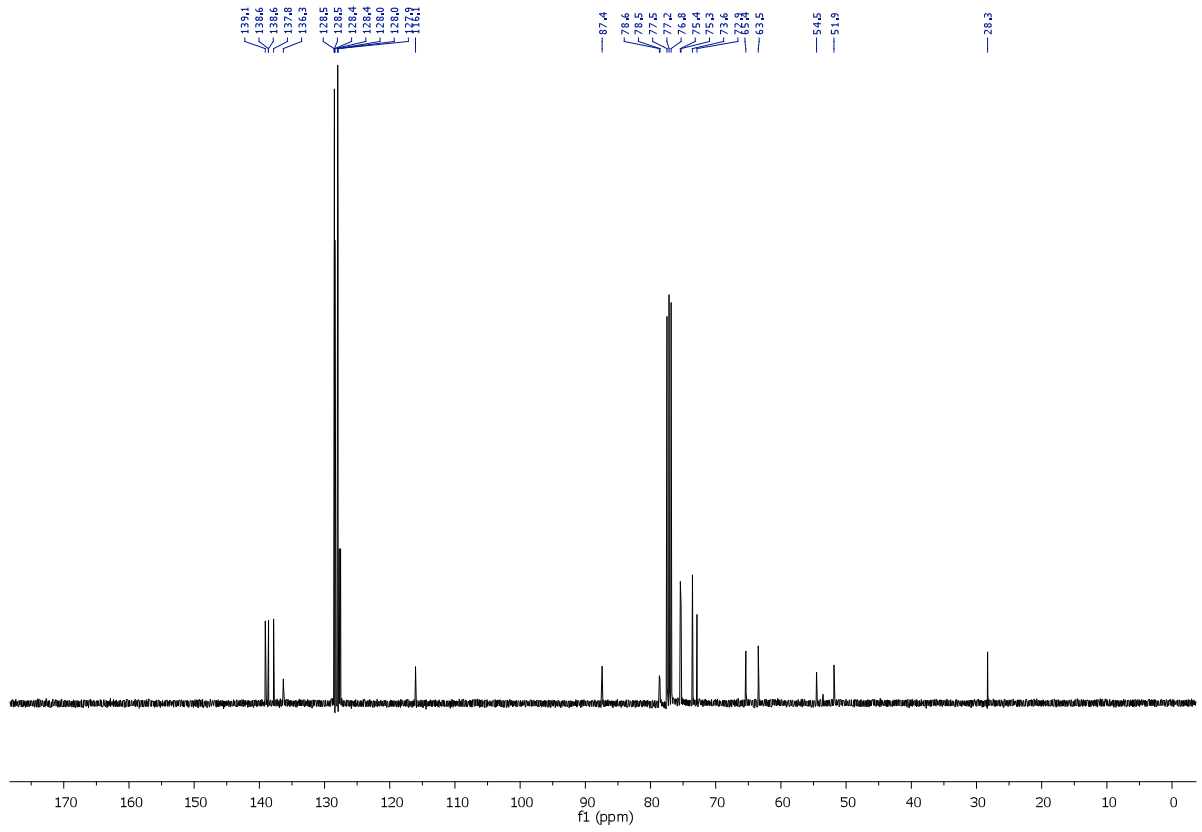
^{13}C NMR spectrum of compound **4a** (100 MHz, $CDCl_3$)



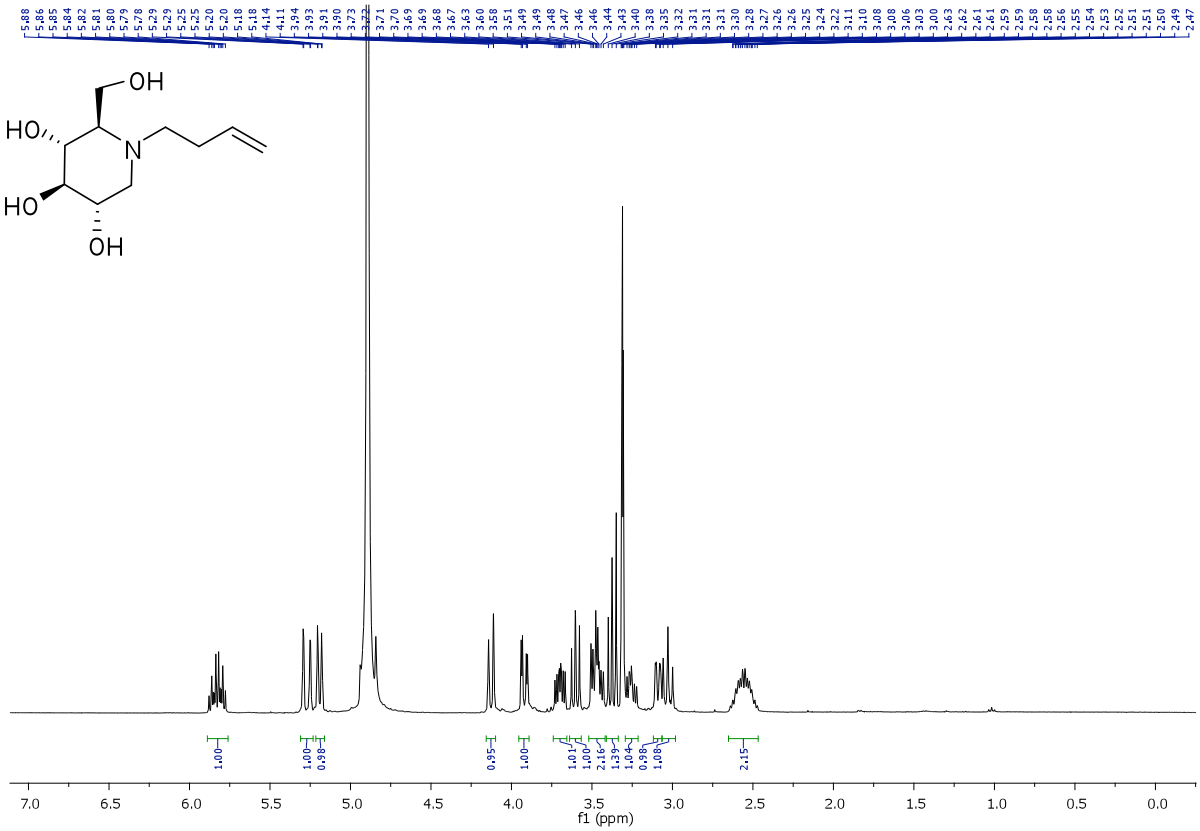
^{1}H NMR spectrum of compound **2b** (400 MHz, $CDCl_3$)



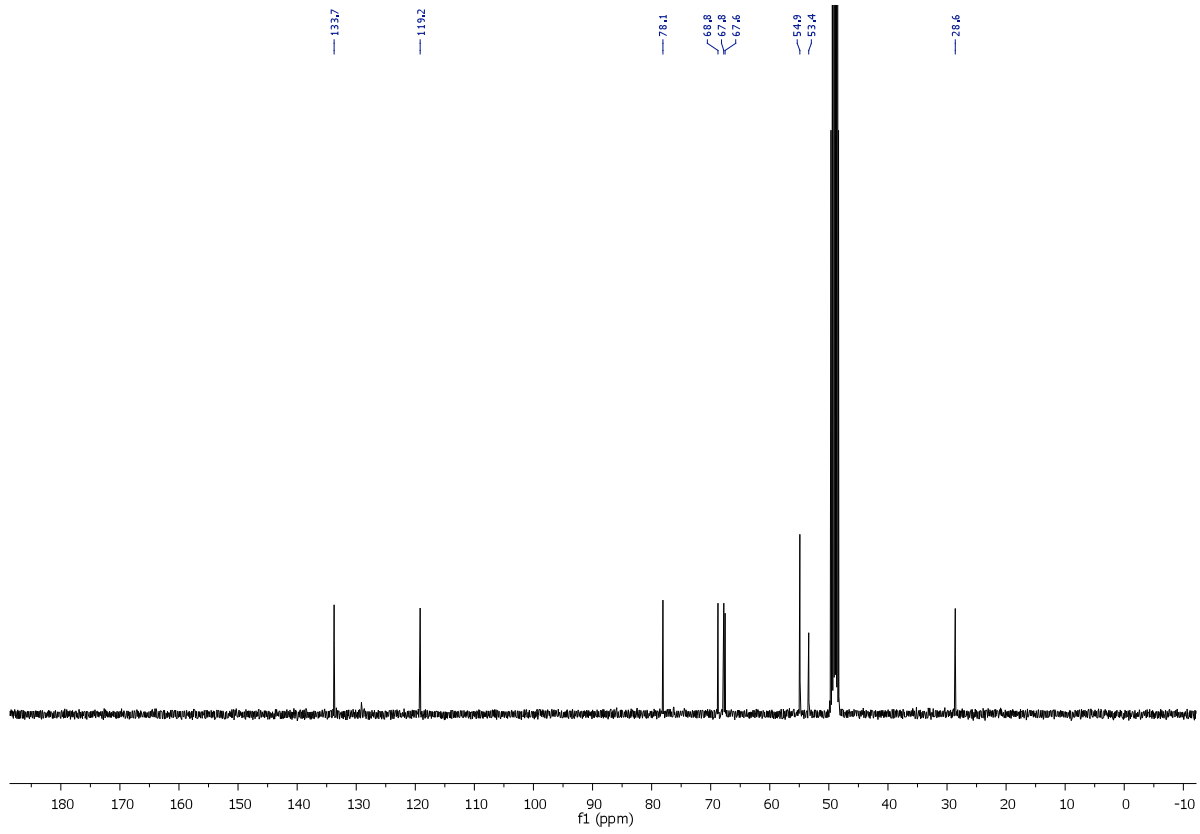
^{13}C NMR spectrum of compound **2b** (100 MHz, $CDCl_3$)



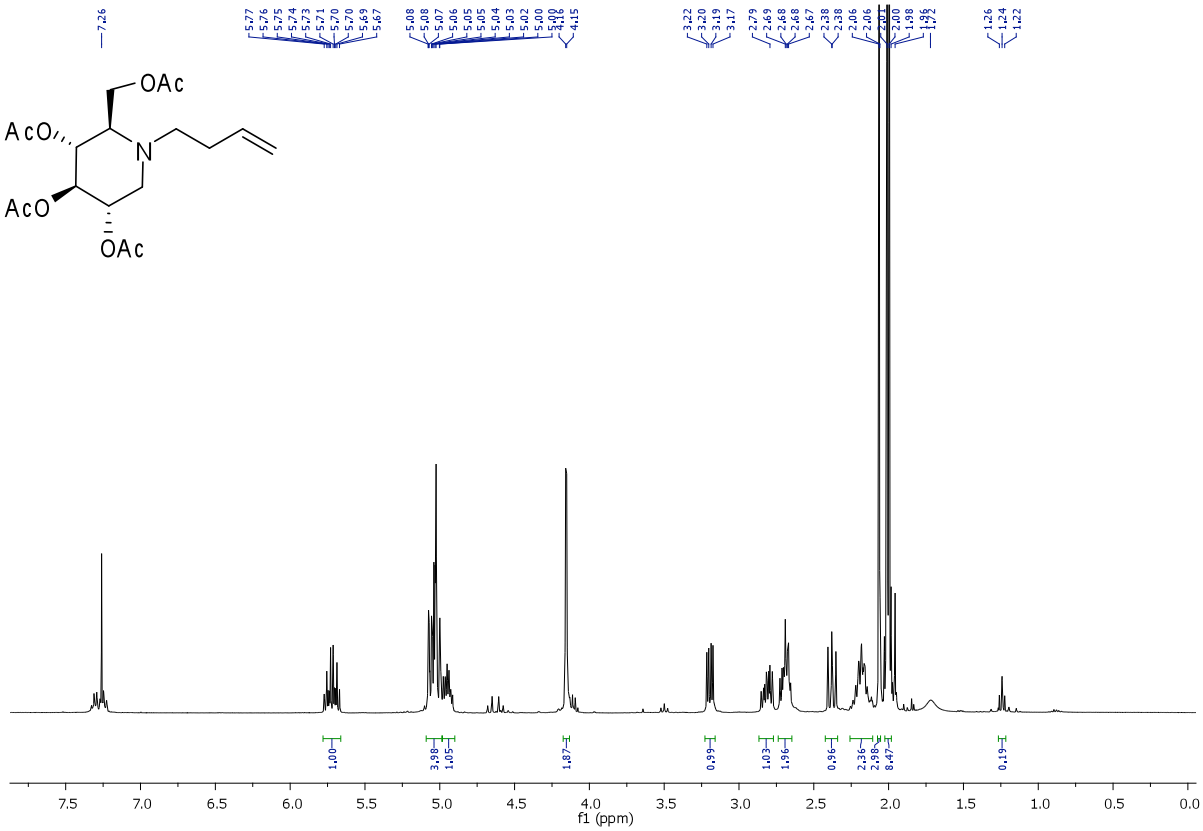
^{1}H NMR spectrum of compound **3b** (400 MHz, CD_3OD)



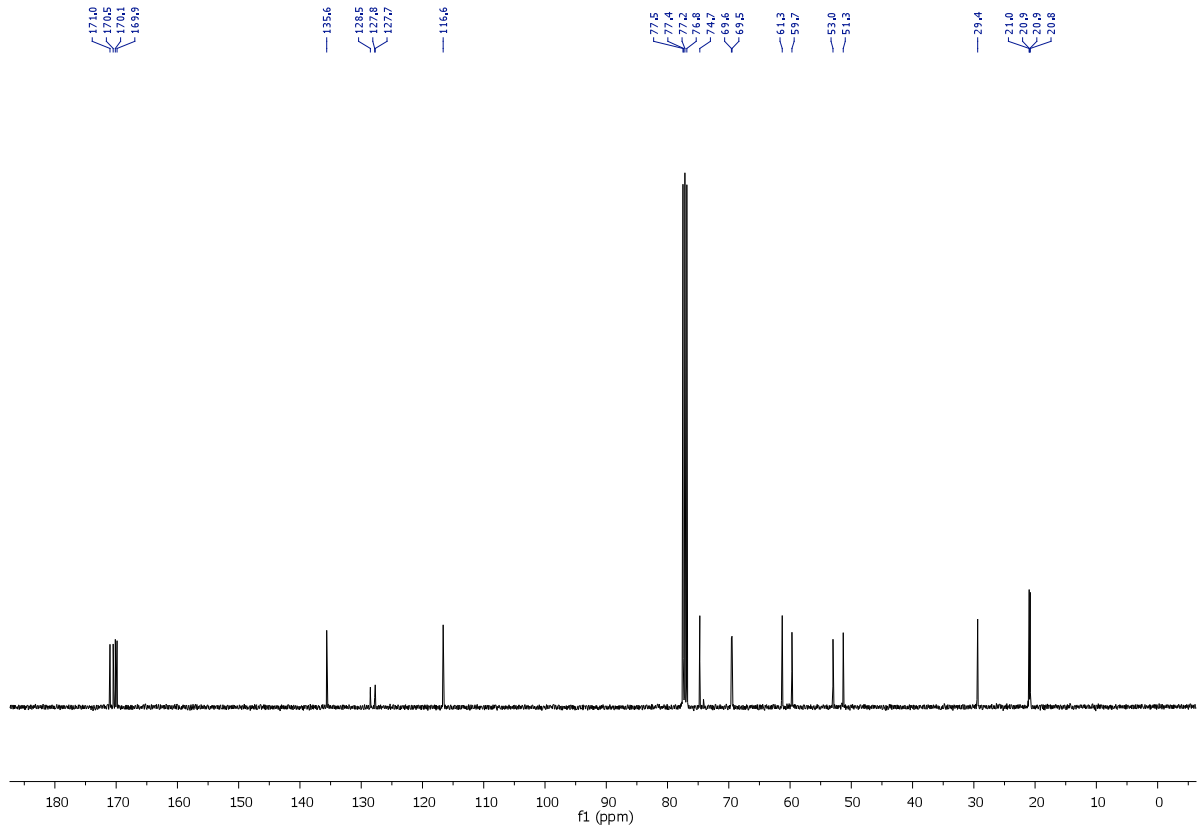
^{13}C NMR spectrum of compound **3b** (100 MHz, CD_3OD)



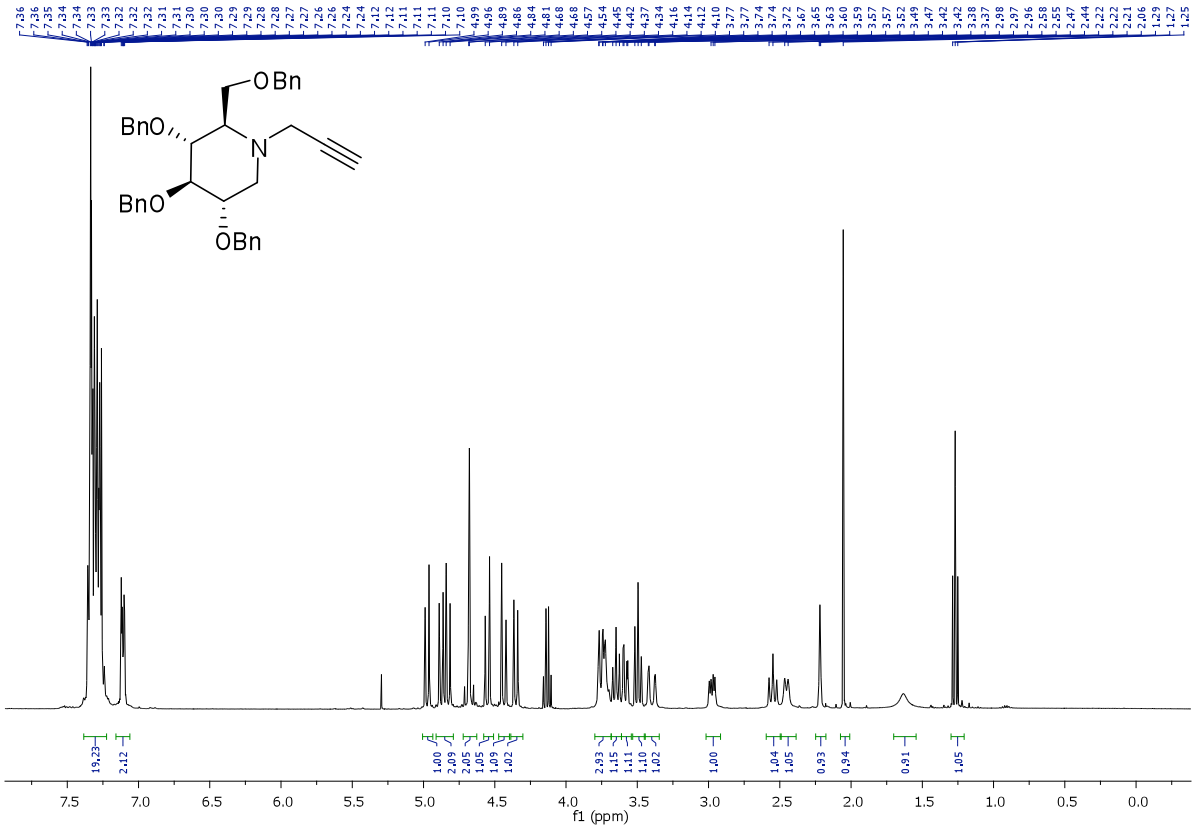
^{1}H NMR spectrum of compound **4b** (400 MHz, $CDCl_3$)



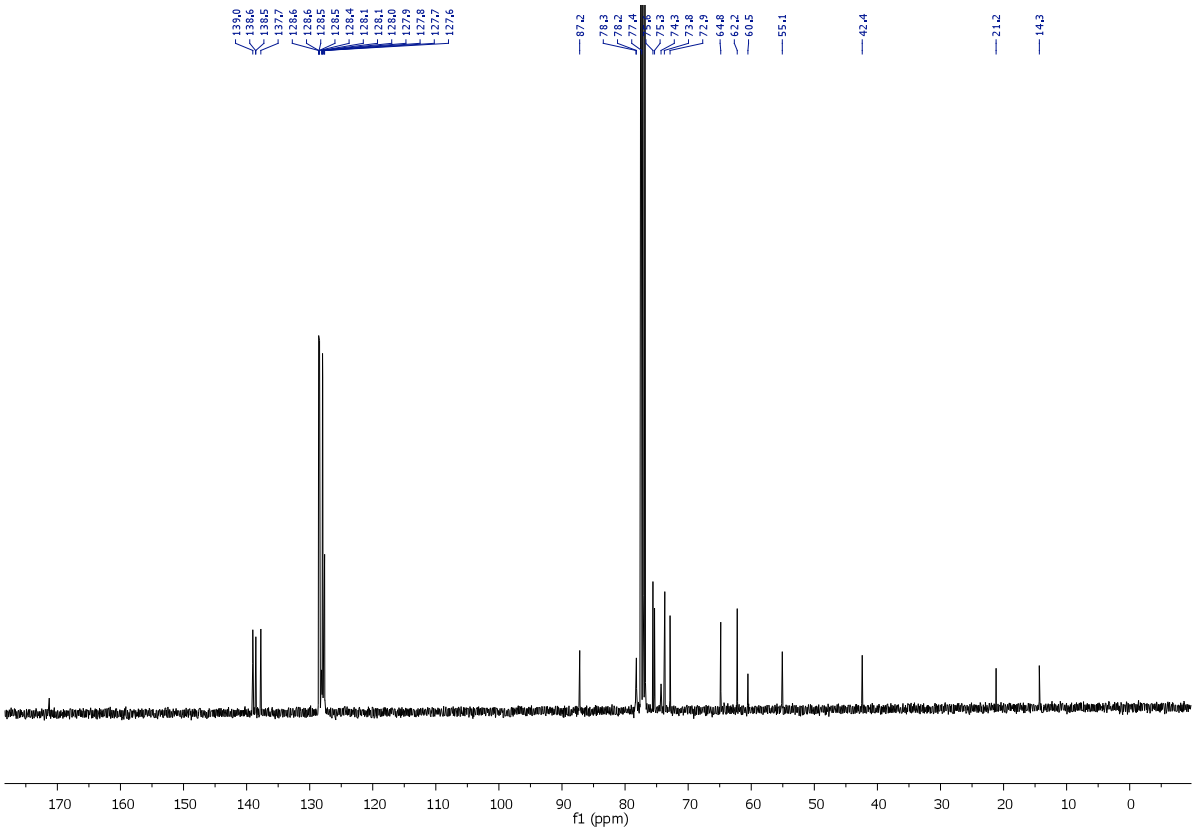
^{13}C NMR spectrum of compound **4b** (100 MHz, $CDCl_3$)



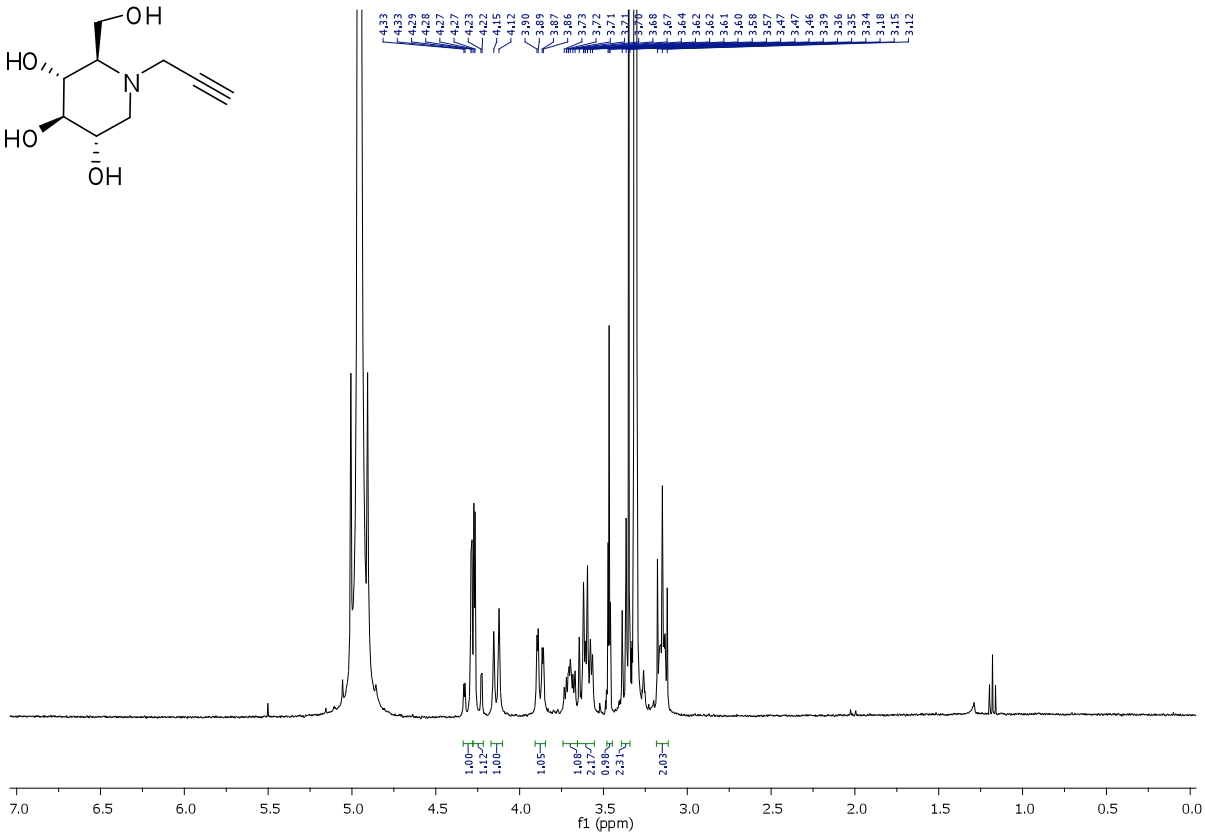
^{1}H NMR spectrum of compound **2c** (400 MHz, $CDCl_3$)



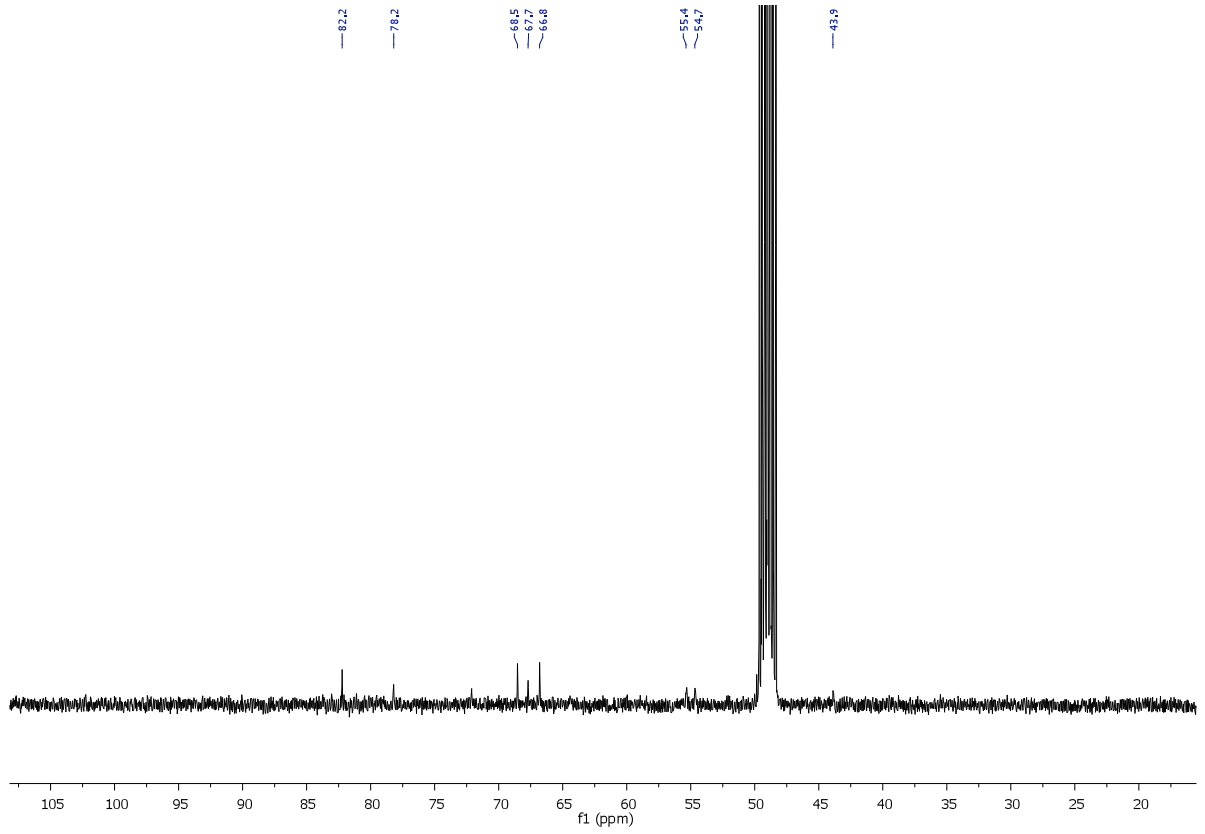
^{13}C NMR spectrum of compound **2c** (100 MHz, $CDCl_3$)



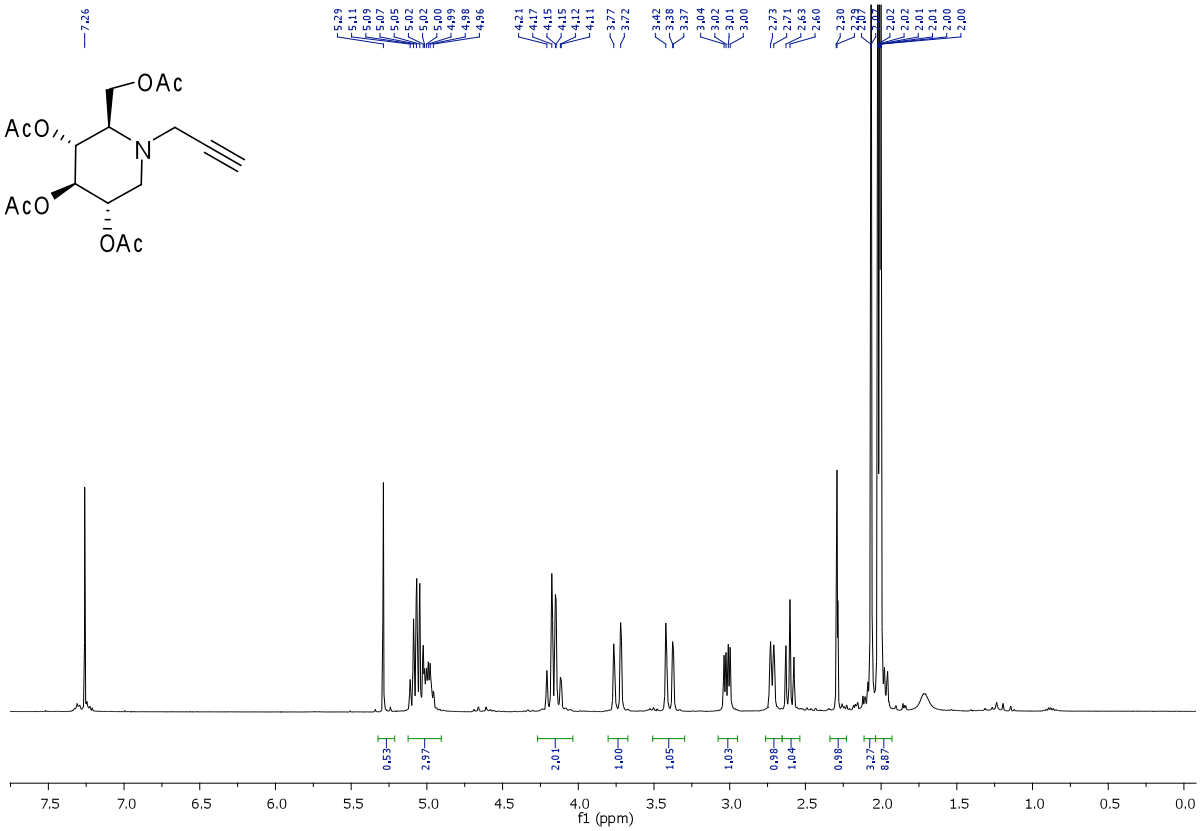
^{1}H NMR spectrum of compound **3c** (400 MHz, CD_3OD)



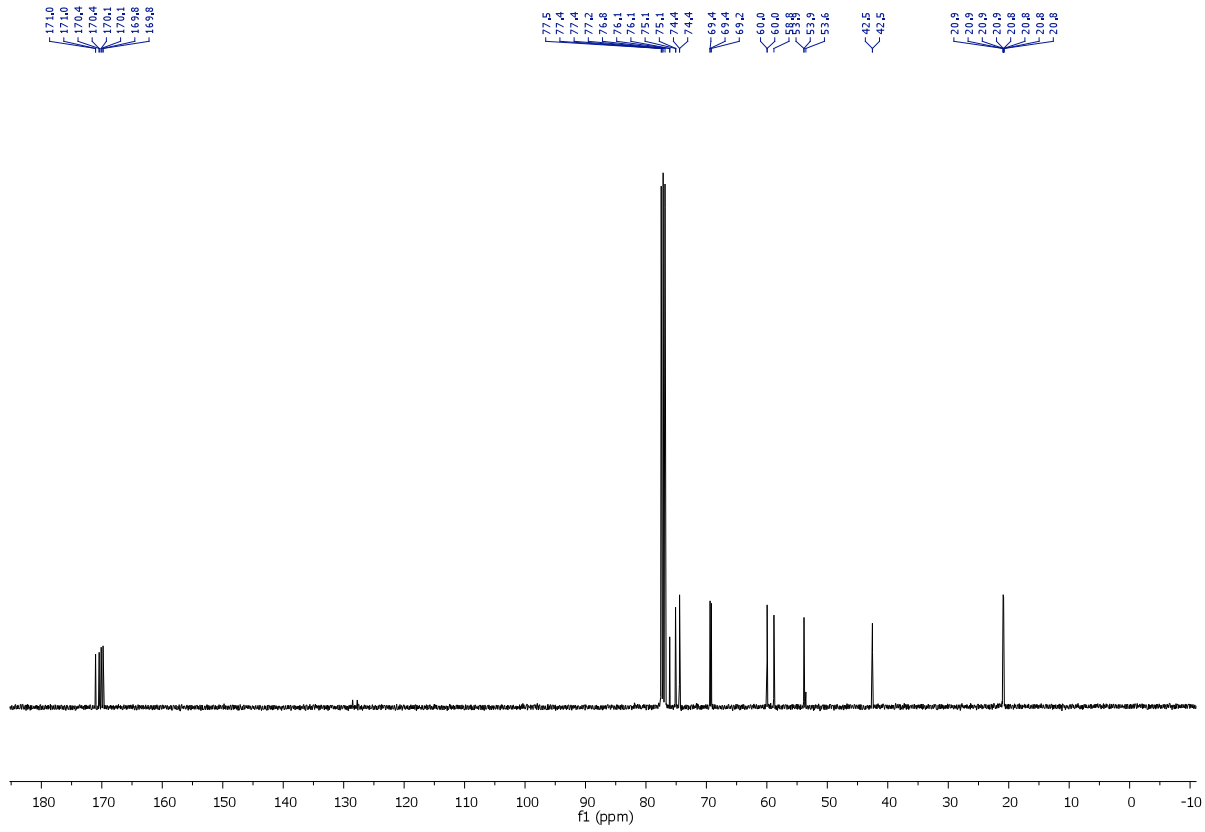
^{13}C NMR spectrum of compound **3c** (100 MHz, CD_3OD)



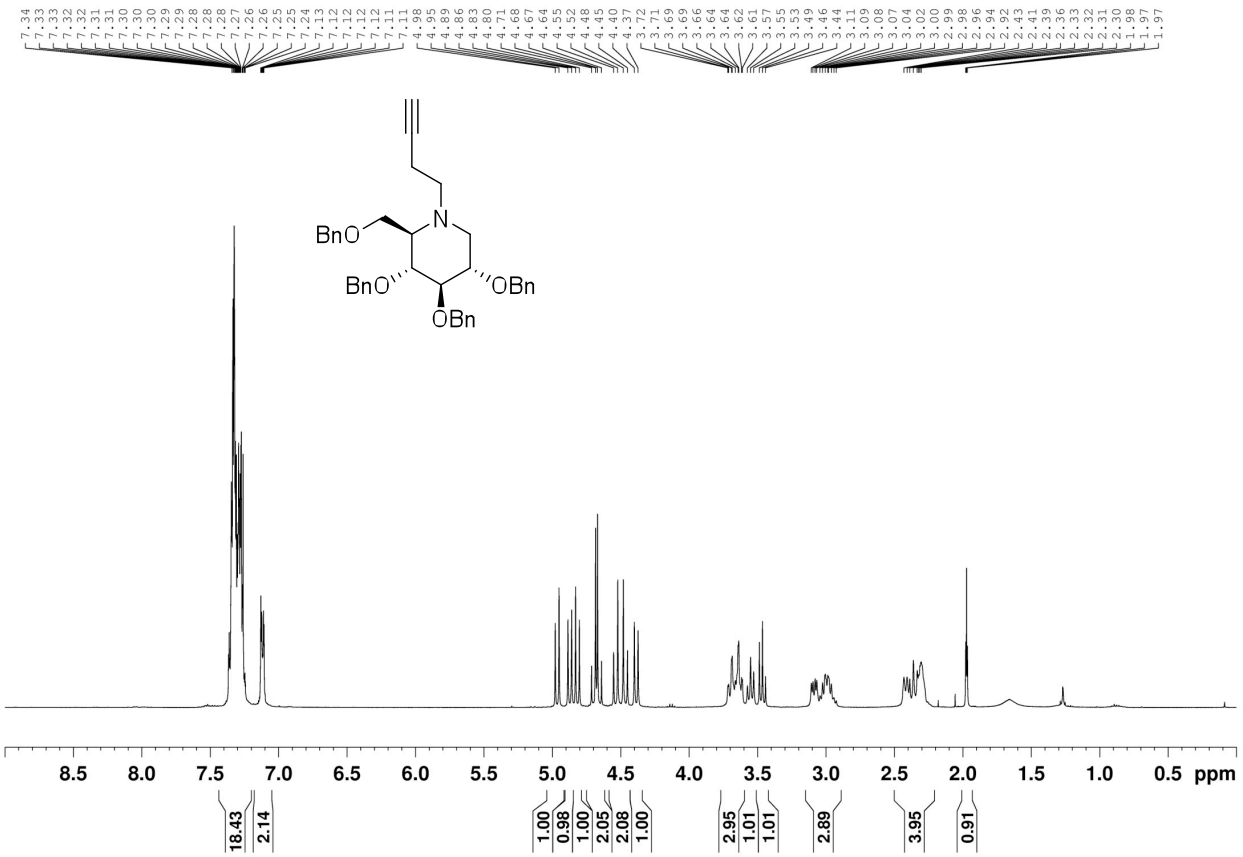
^{1}H NMR spectrum of compound **4c** (400 MHz, $CDCl_3$)



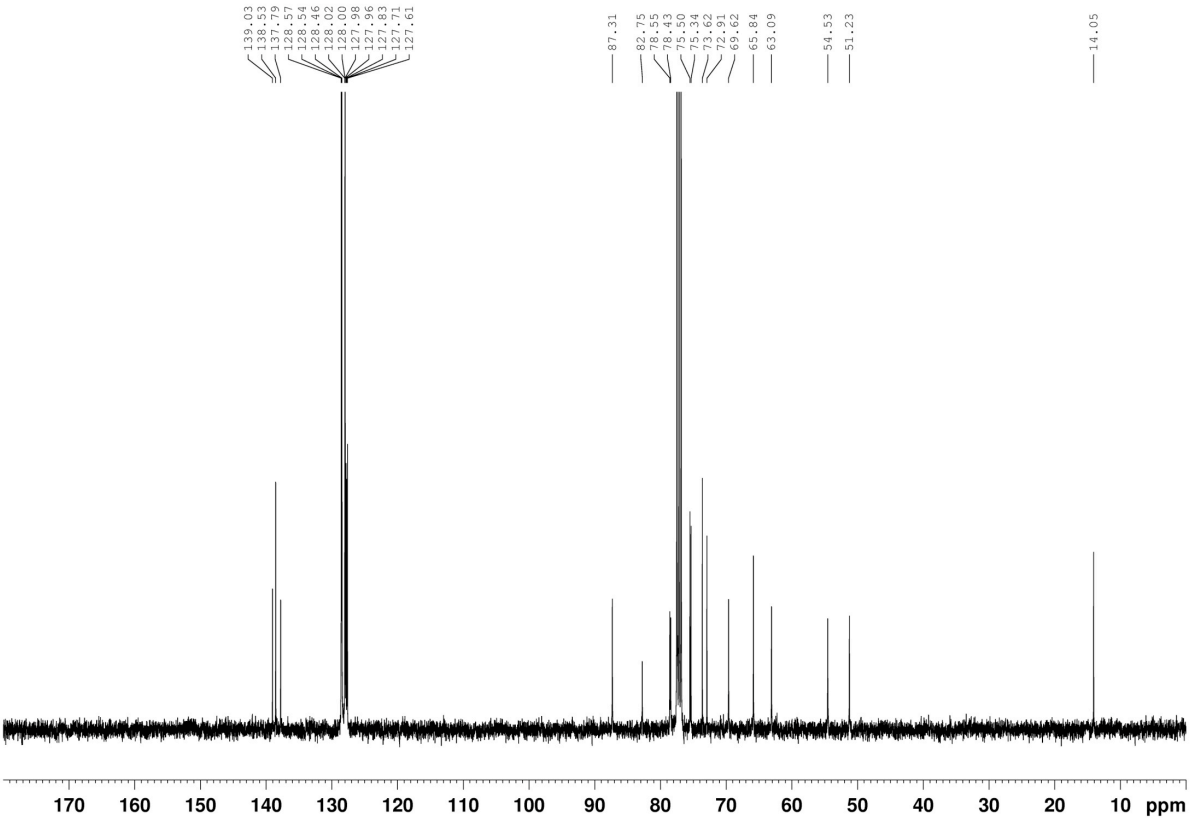
^{13}C NMR spectrum of compound **4c** (100 MHz, $CDCl_3$)



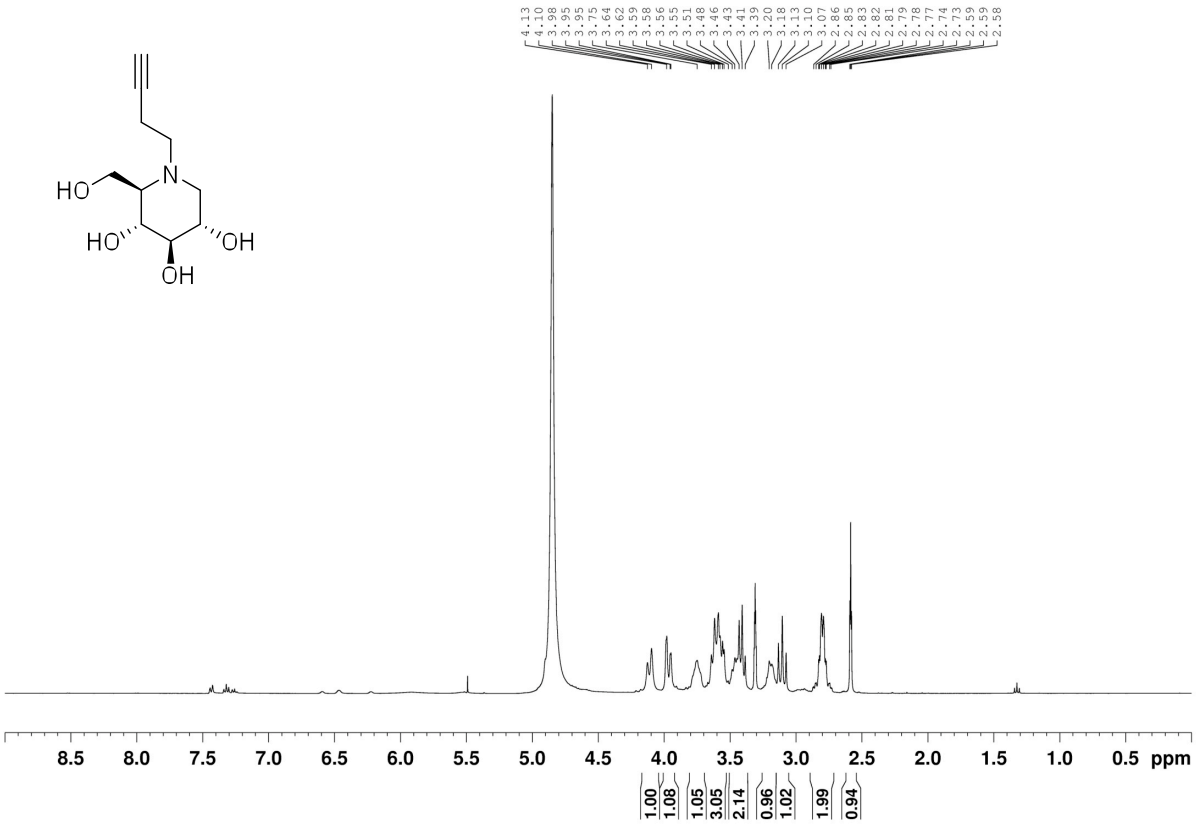
^{1}H NMR spectrum of compound **2d** (400 MHz, $CDCl_3$)



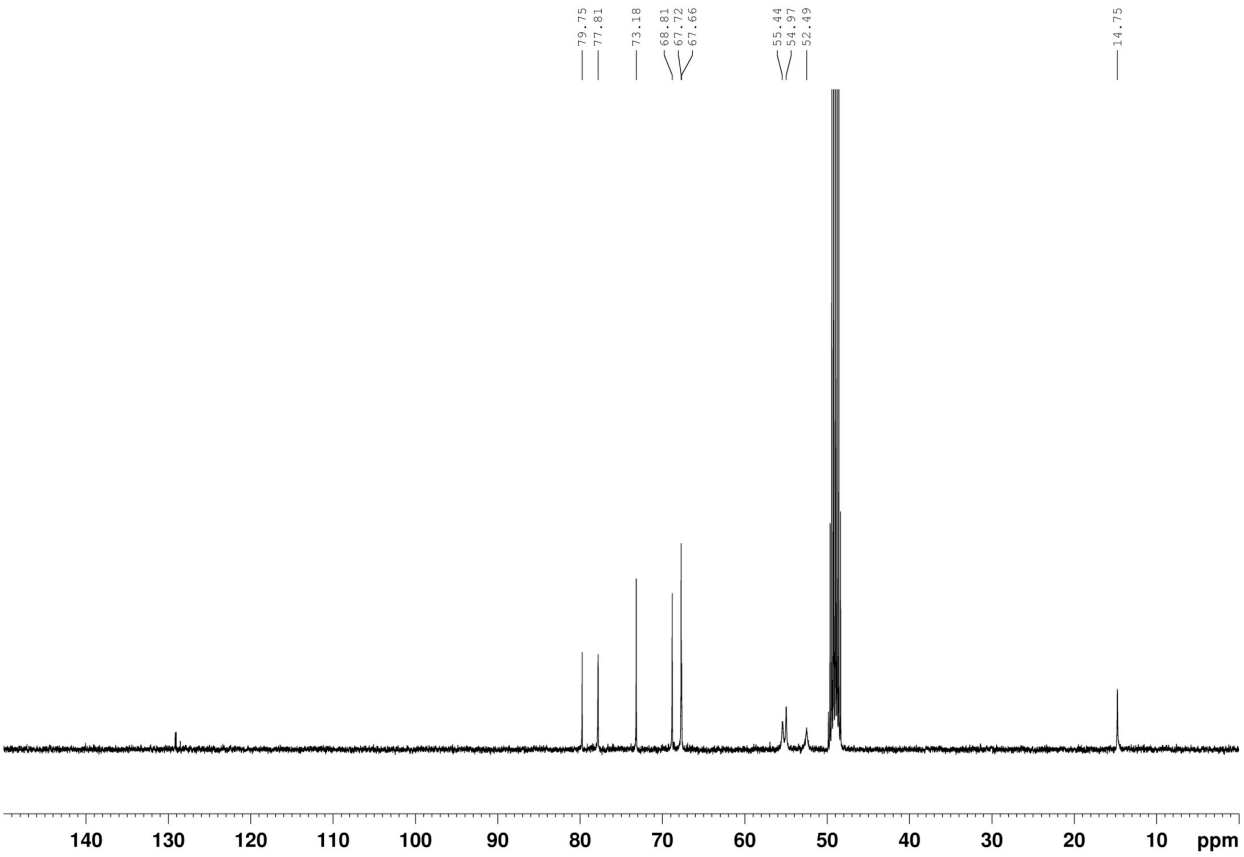
^{13}C NMR spectrum of compound **2d** (100 MHz, $CDCl_3$)



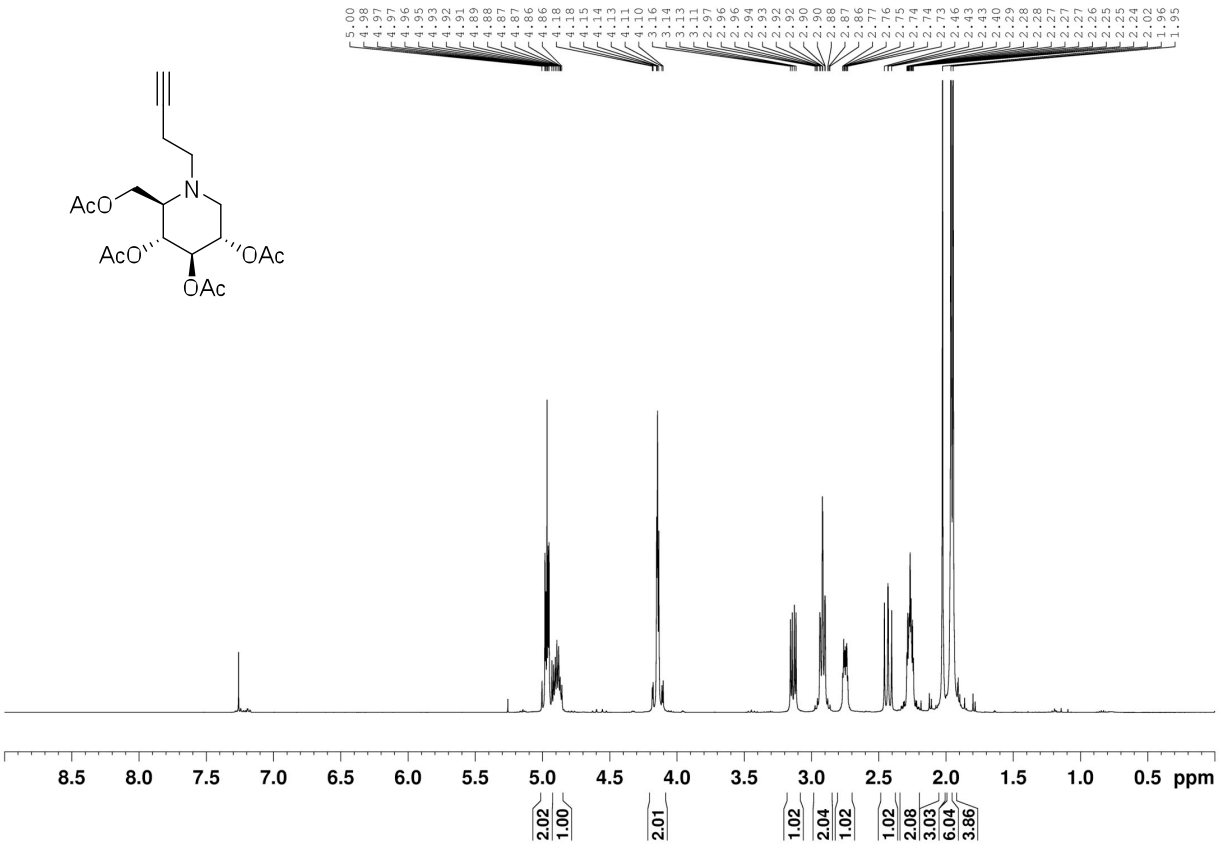
^{1}H NMR spectrum of compound **3d** (400 MHz, CD_3OD)



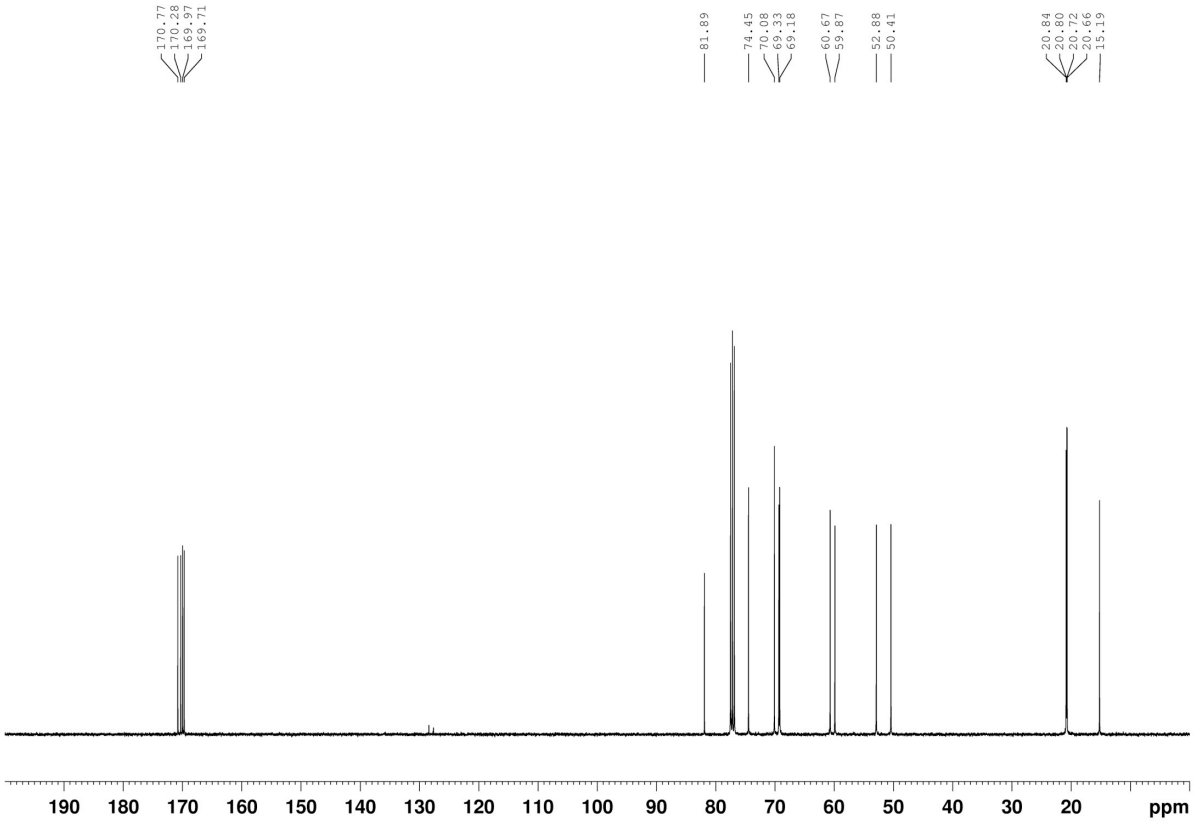
^{13}C NMR spectrum of compound **3d** (100 MHz, CD_3OD)



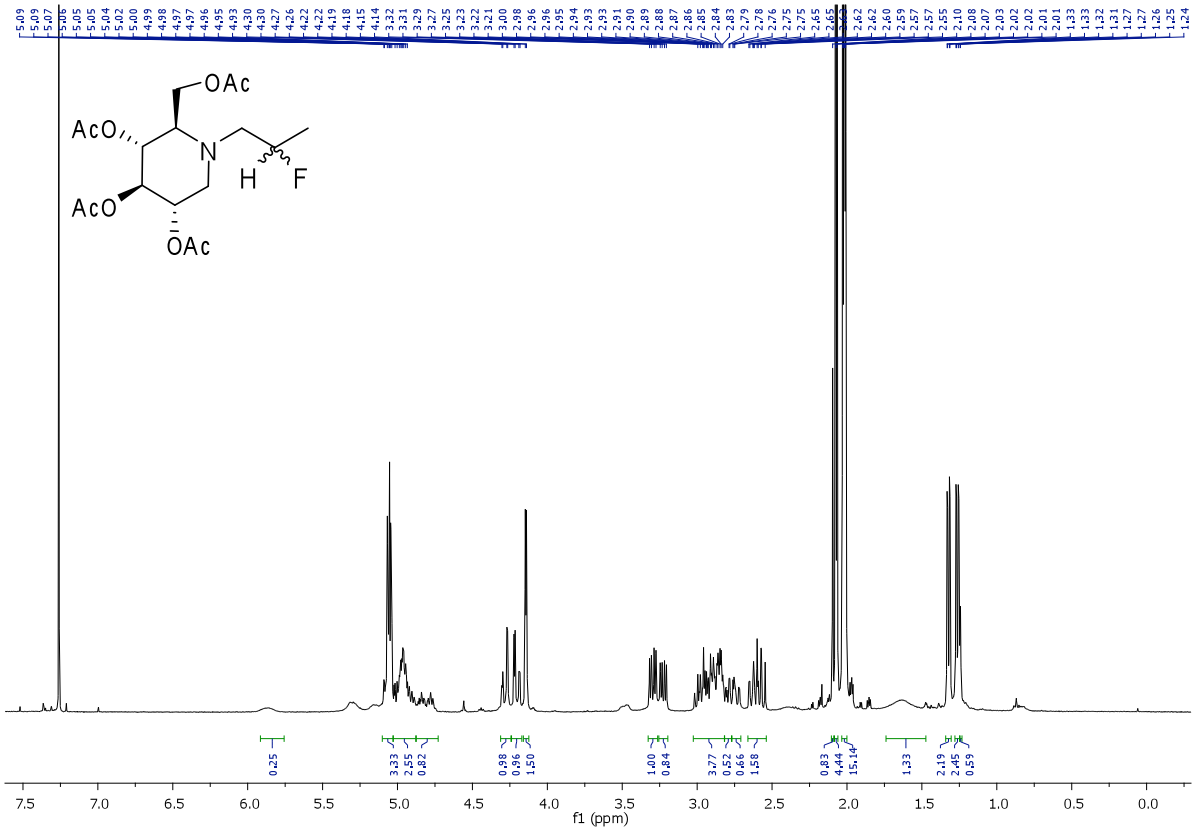
^{1}H NMR spectrum of compound **4d** (400 MHz, $CDCl_3$)



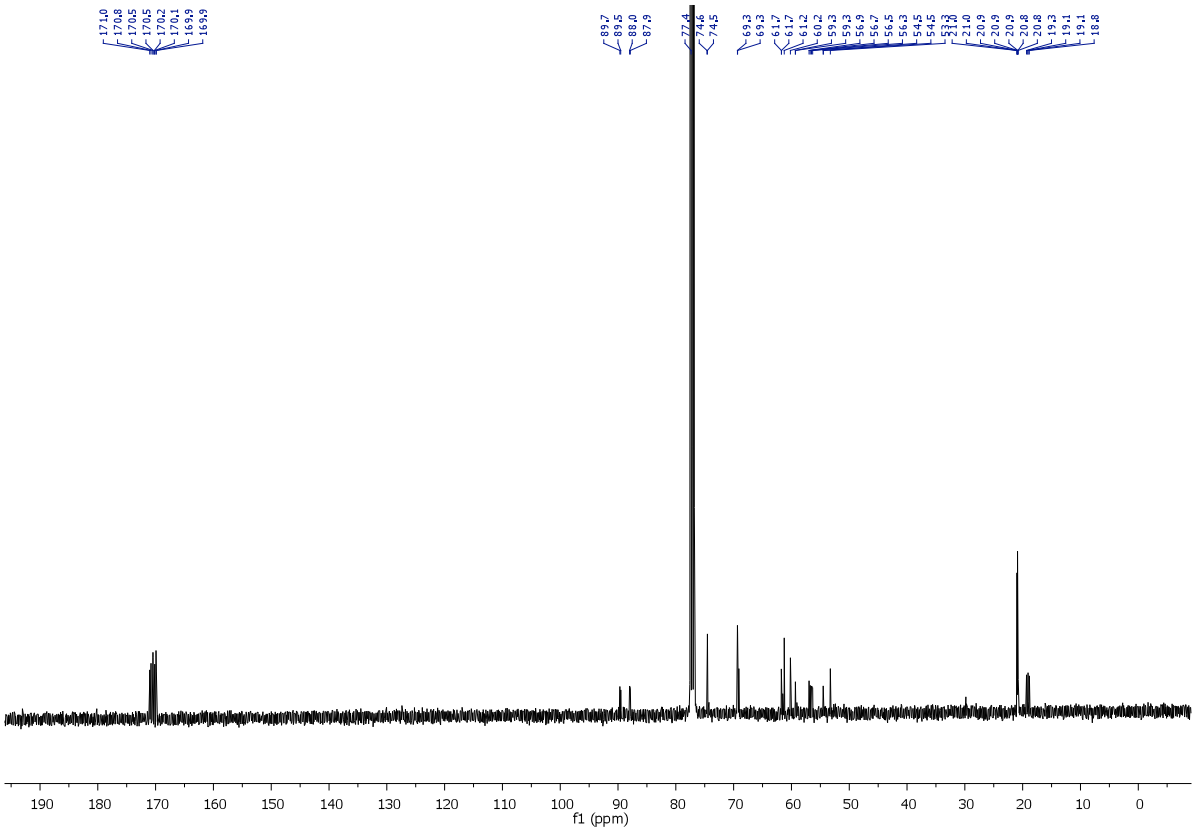
^{13}C NMR spectrum of compound **4d** (100 MHz, $CDCl_3$)



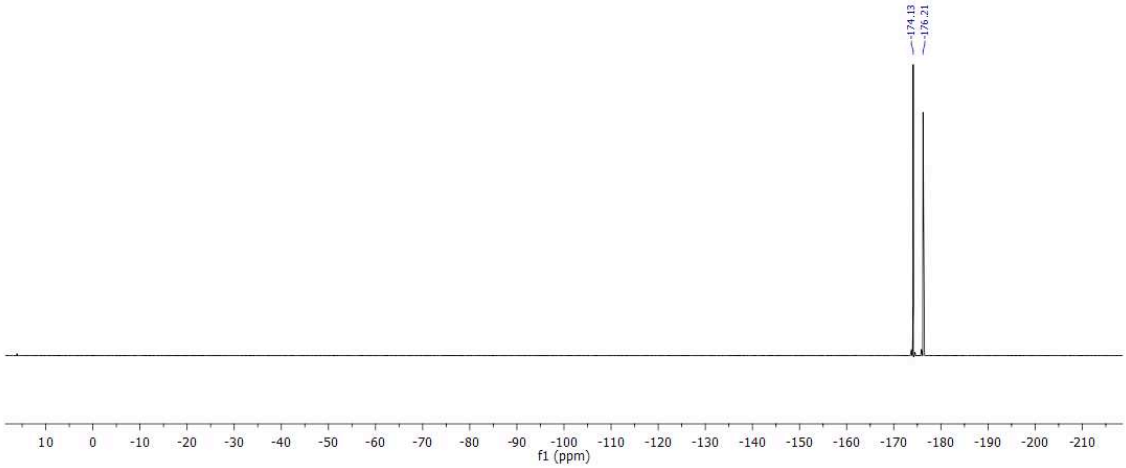
^{1}H NMR spectrum of compound **5a** (400 MHz, $CDCl_3$)



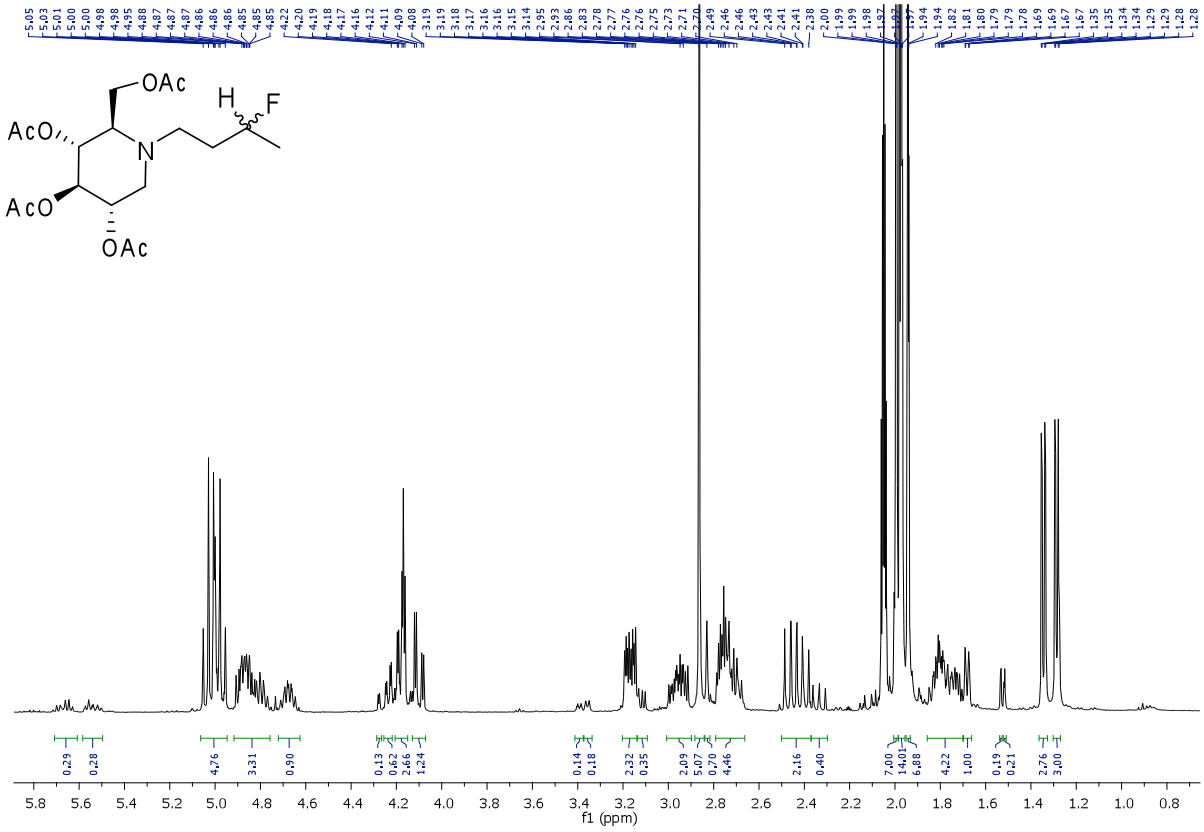
^{13}C NMR spectrum of compound **5a** (100 MHz, $CDCl_3$)



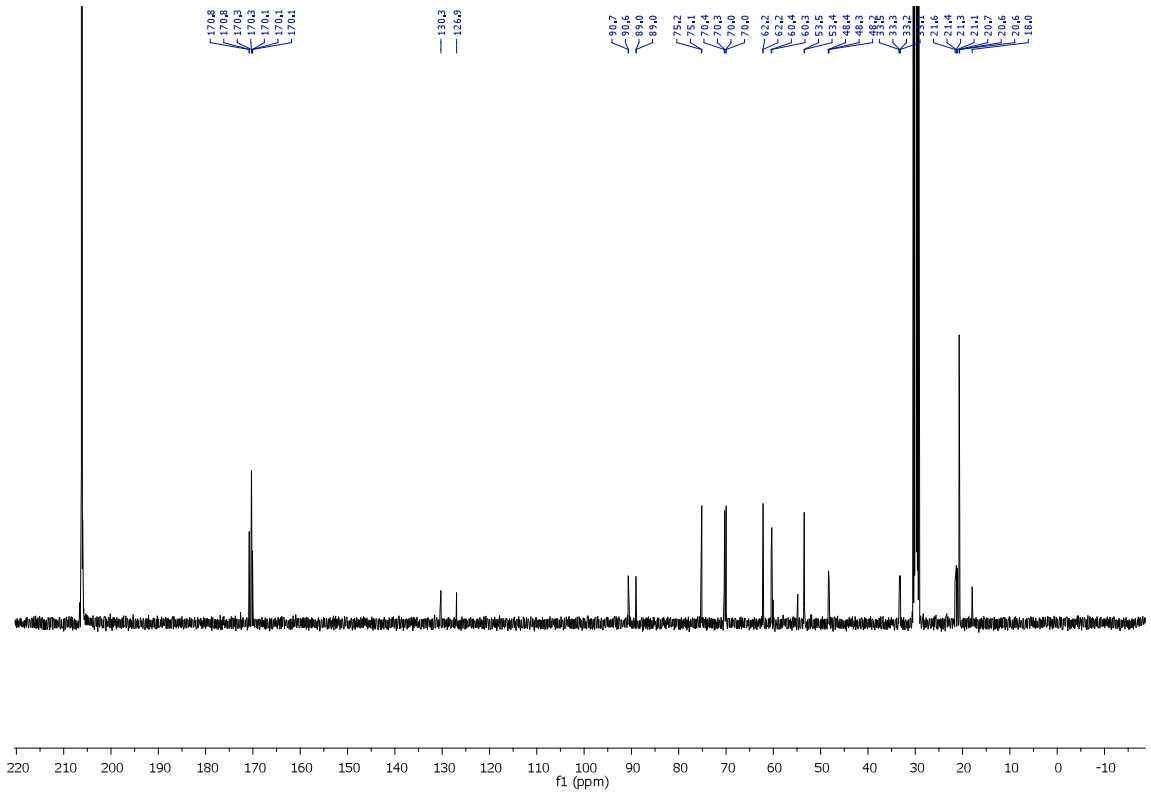
^{19}F NMR spectrum of compound **5a** (376 MHz, $CDCl_3$)



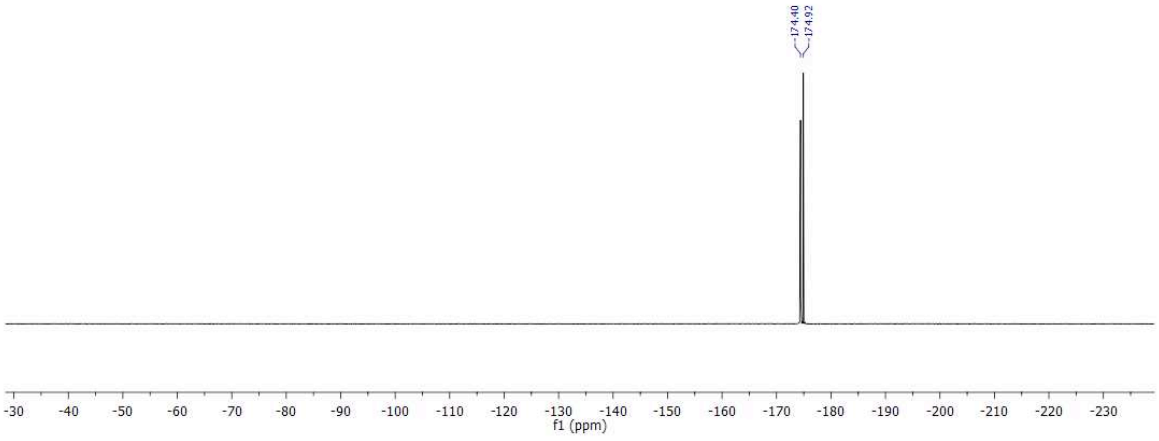
^{1}H NMR spectrum of compound **5b** (400 MHz, Acetone-d6)



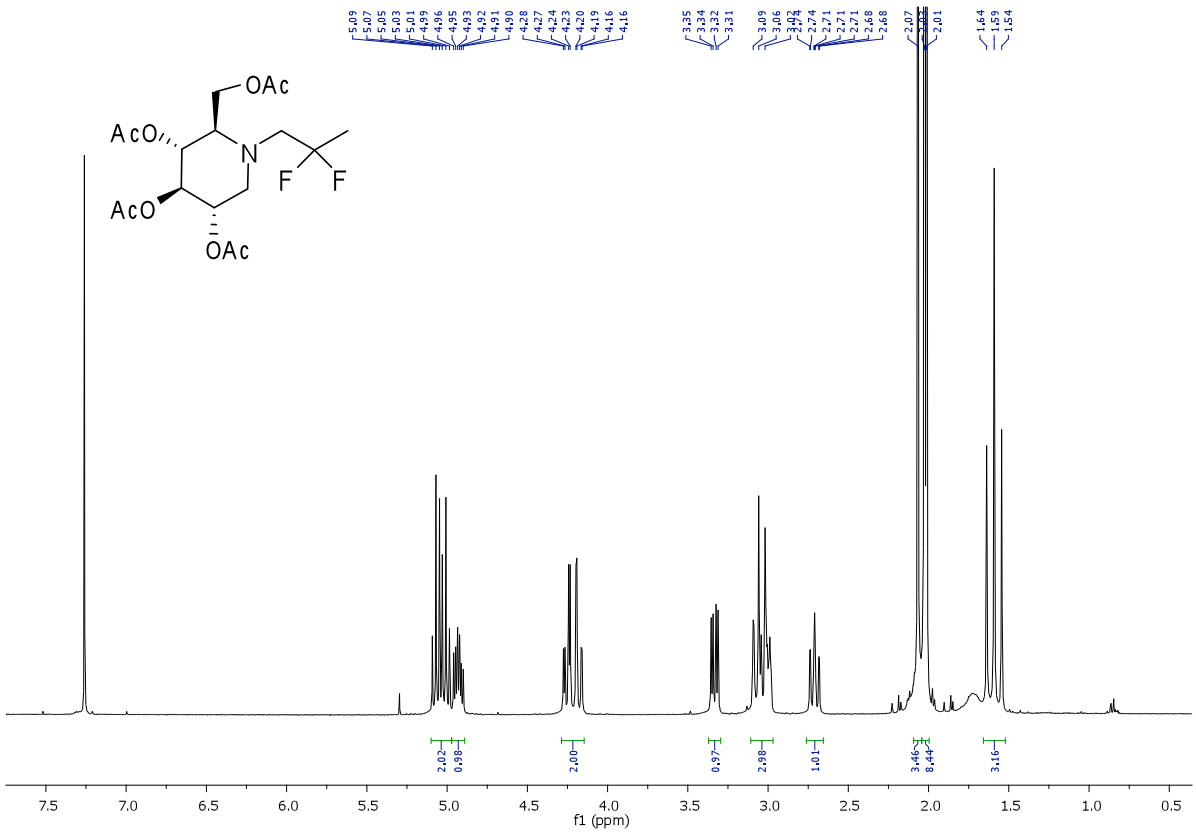
^{13}C NMR spectrum of compound **5b** (100 MHz, Acetone-d6)



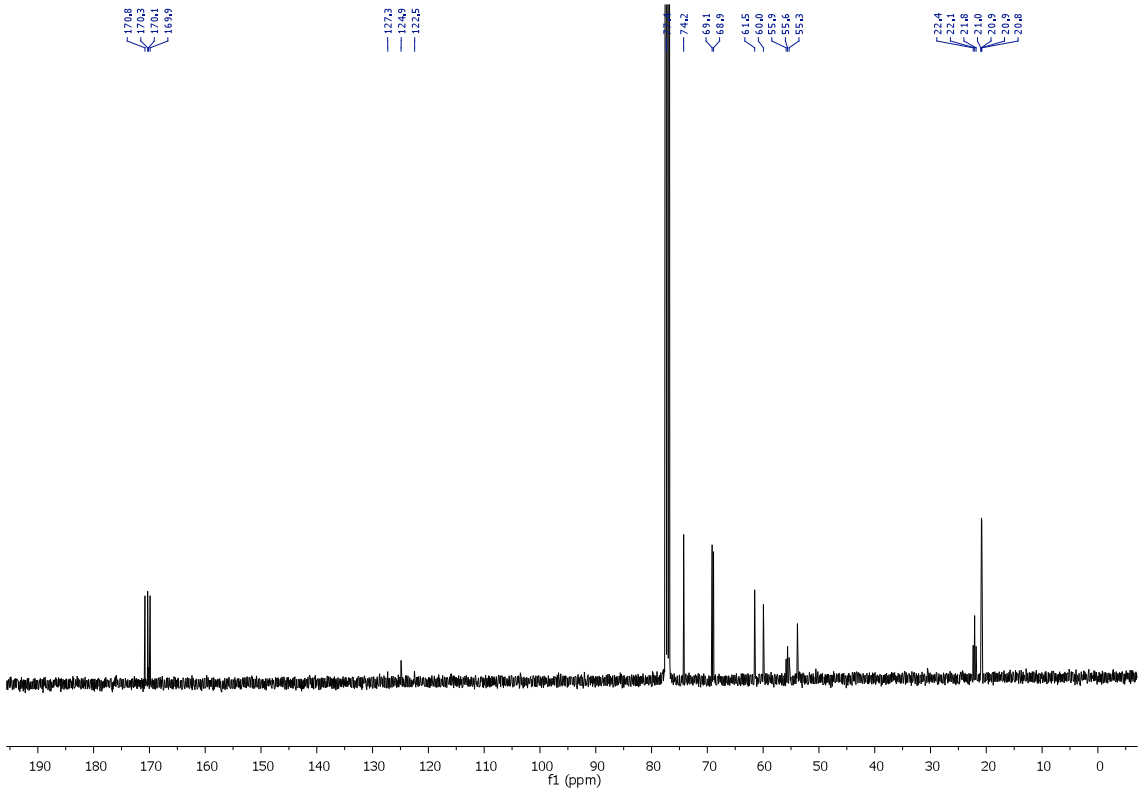
^{19}F NMR spectrum of compound **5b** (376 MHz, Acetone-d6)



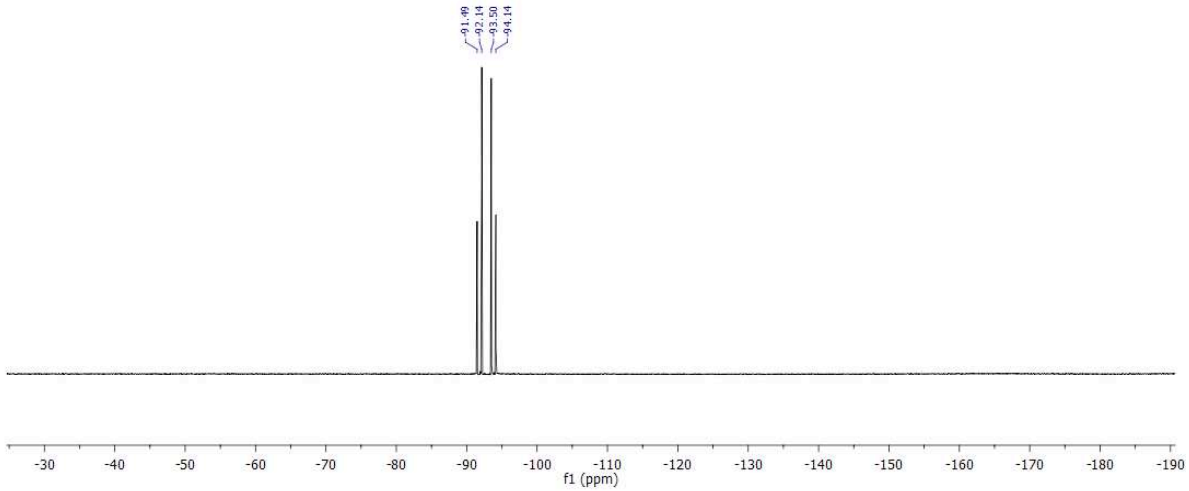
^{1}H NMR spectrum of compound **5c** (400 MHz, $CDCl_3$)



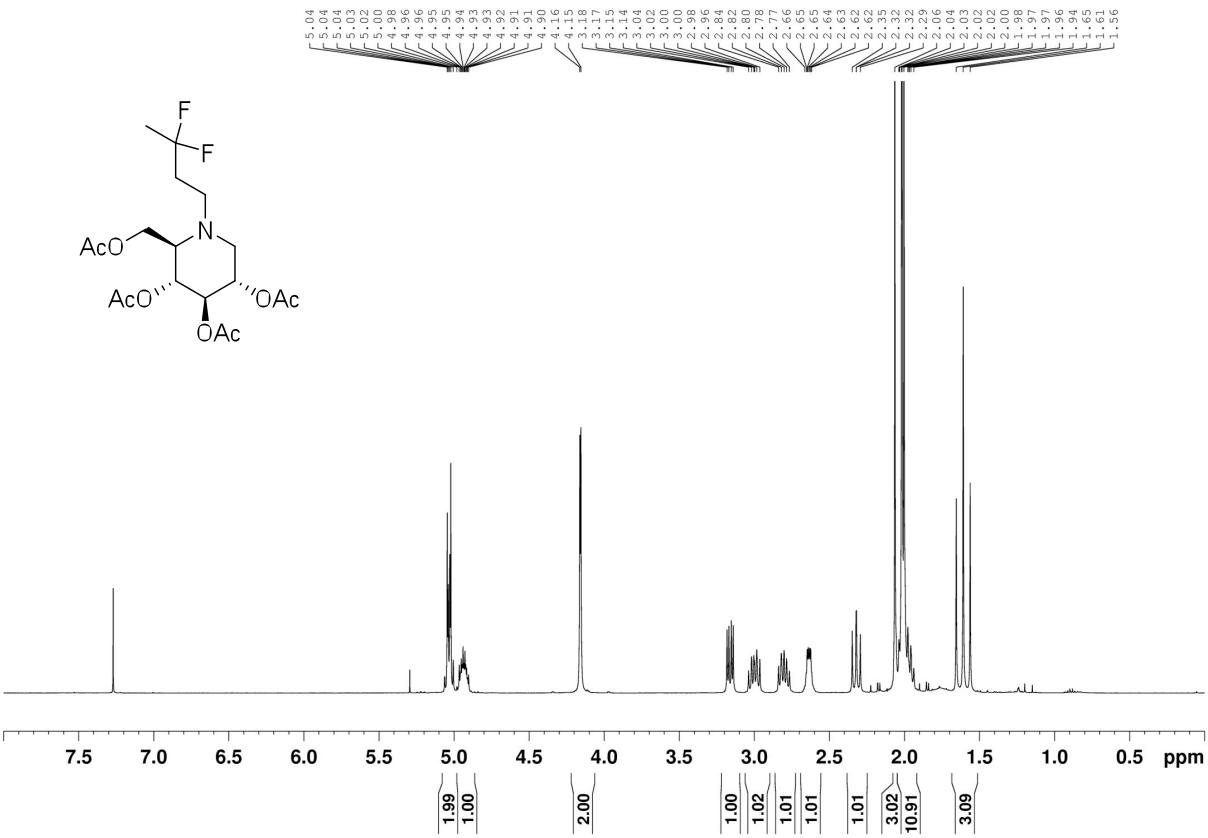
^{13}C NMR spectrum of compound **5c**(100 MHz, $CDCl_3$)



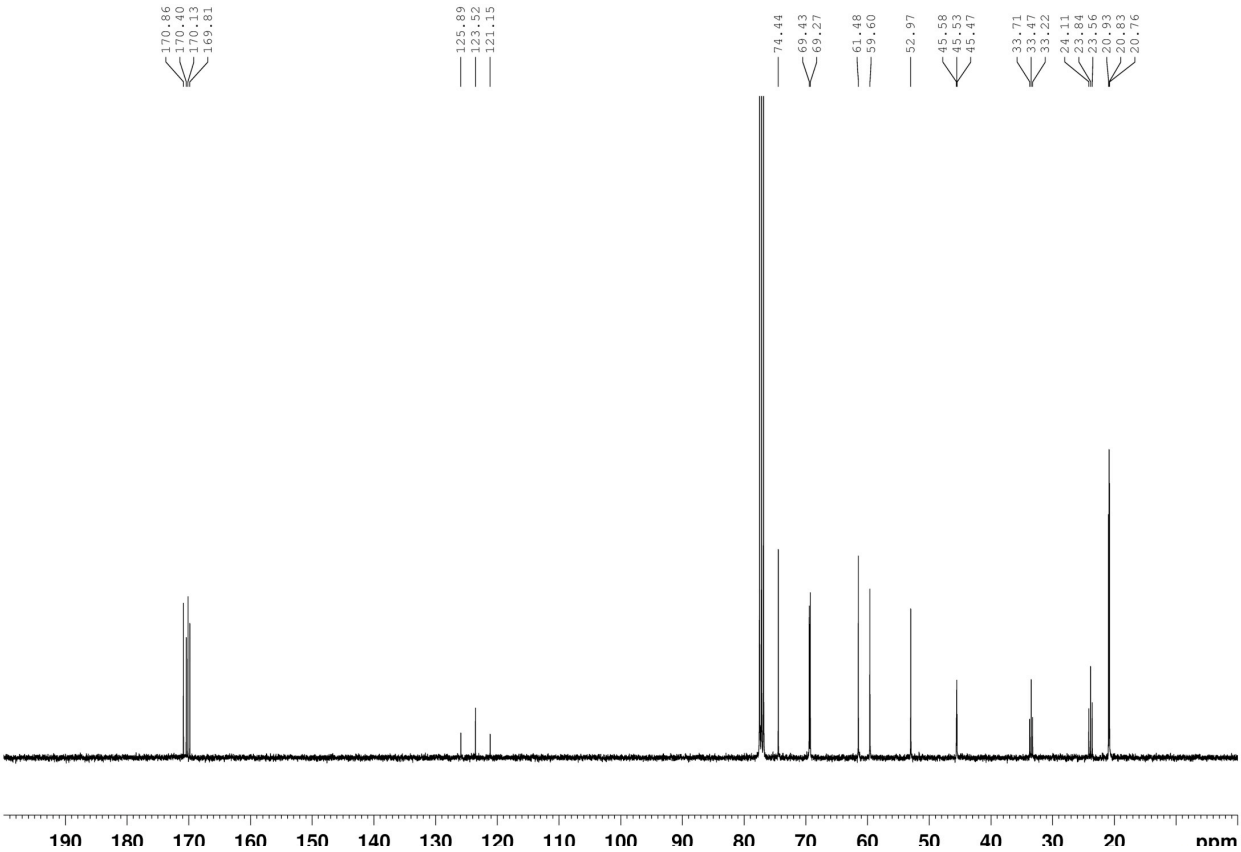
^{19}F NMR spectrum of compound **5c** (376 MHz, $CDCl_3$)



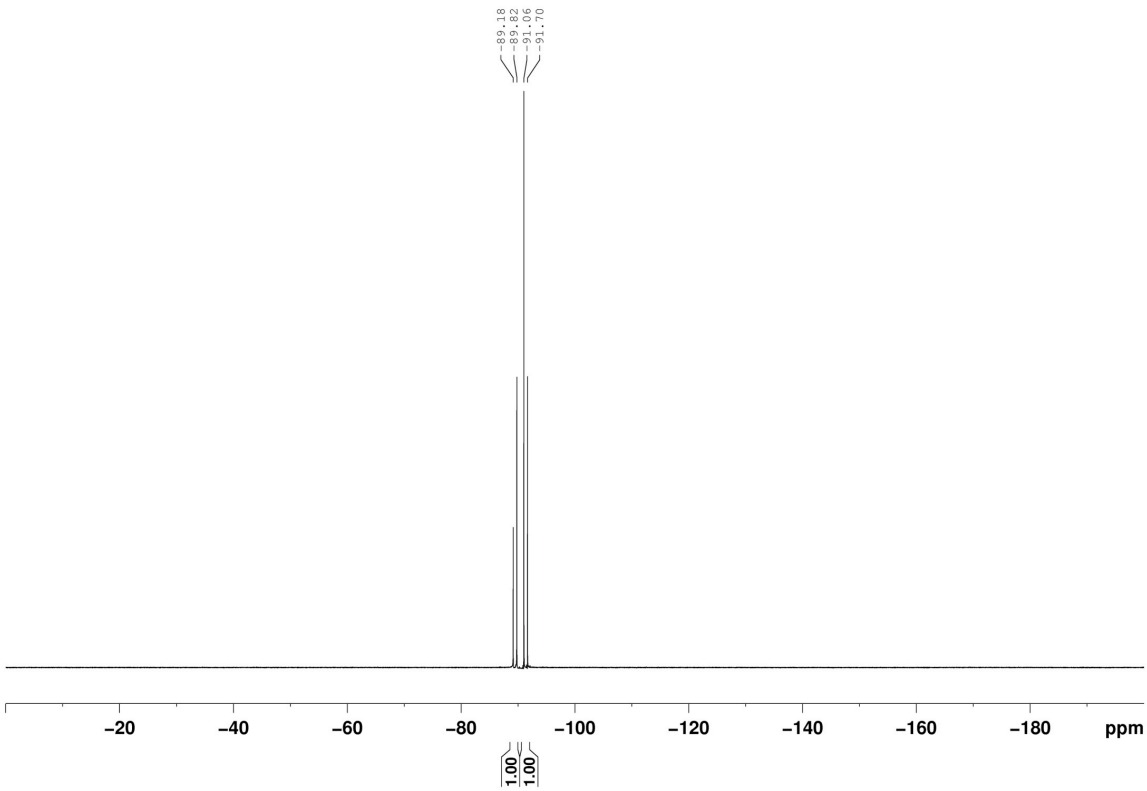
^{1}H NMR spectrum of compound **5d** (400 MHz, $CDCl_3$)



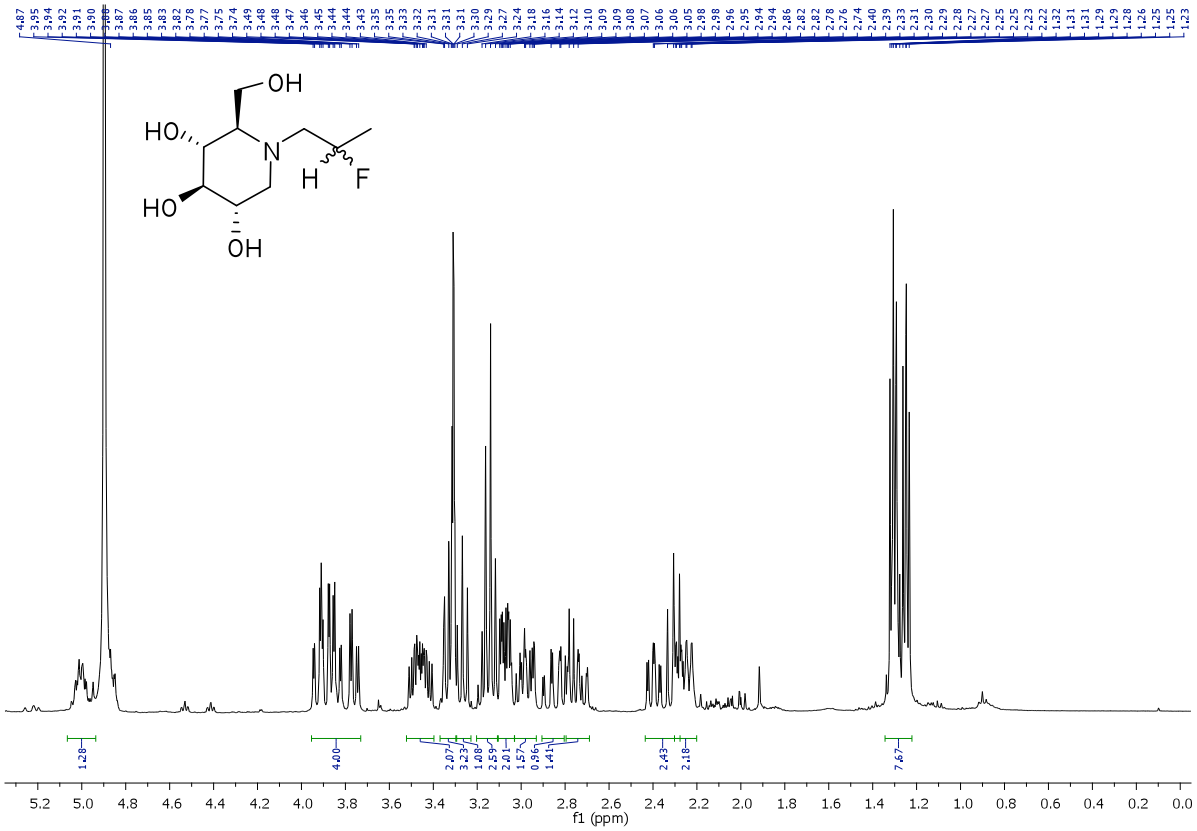
^{13}C NMR spectrum of compound **5d** (100 MHz, $CDCl_3$)



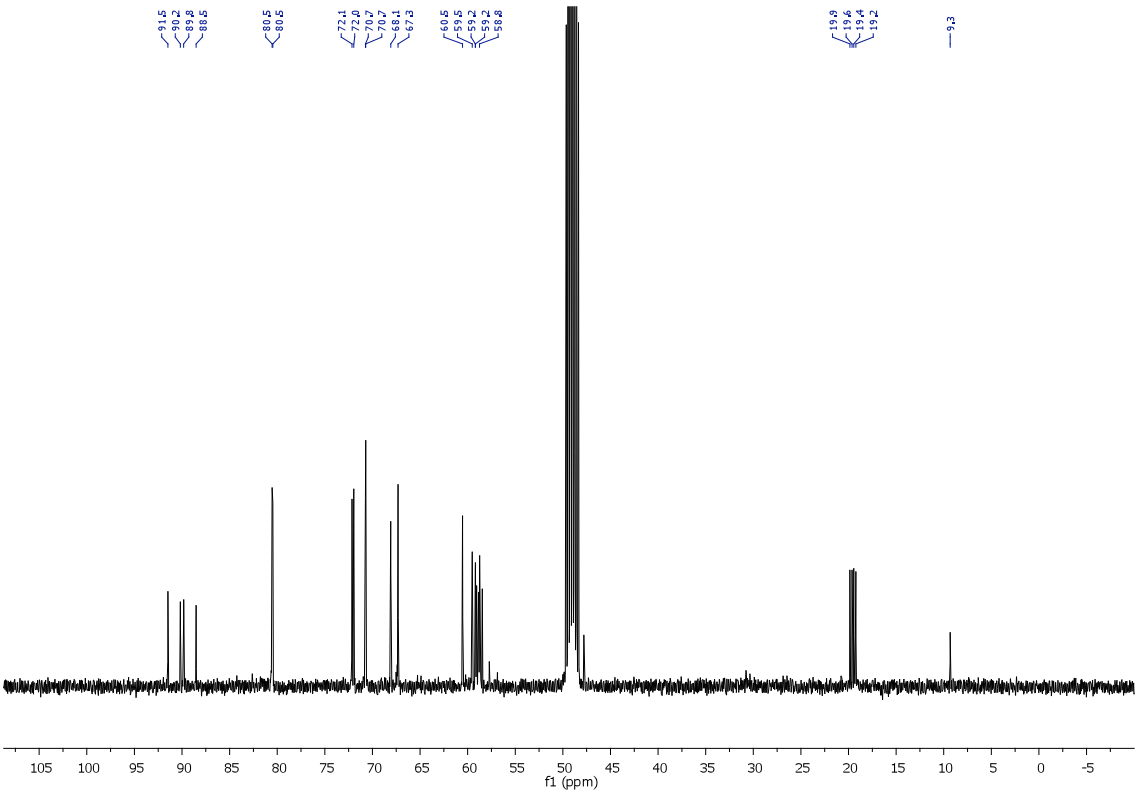
^{19}F NMR spectrum of compound **5d** (376 MHz, $CDCl_3$)



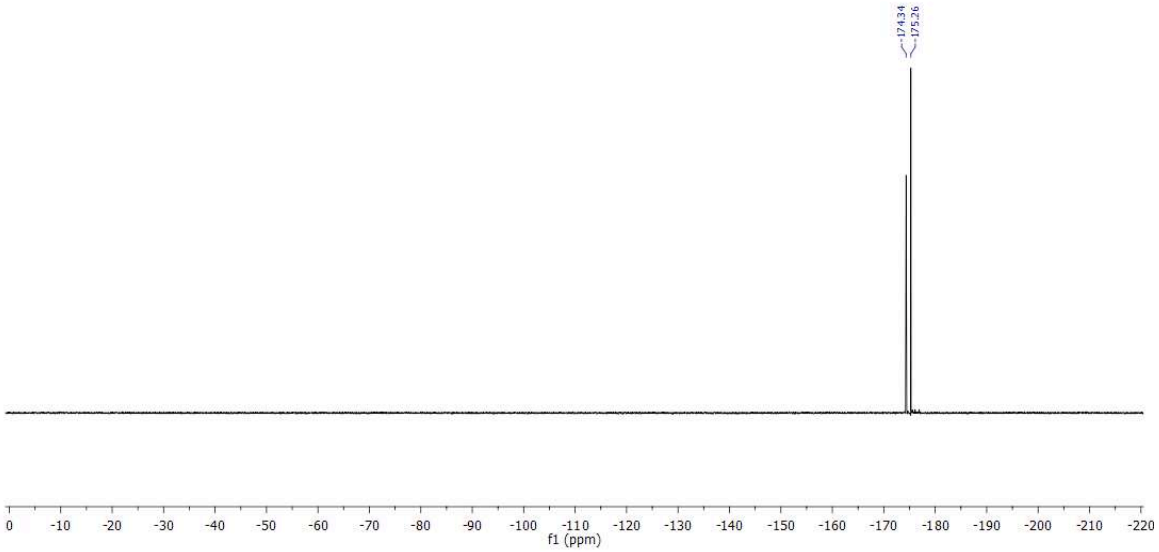
^{1}H NMR spectrum of compound **6a** (400 MHz, CD_3OD)



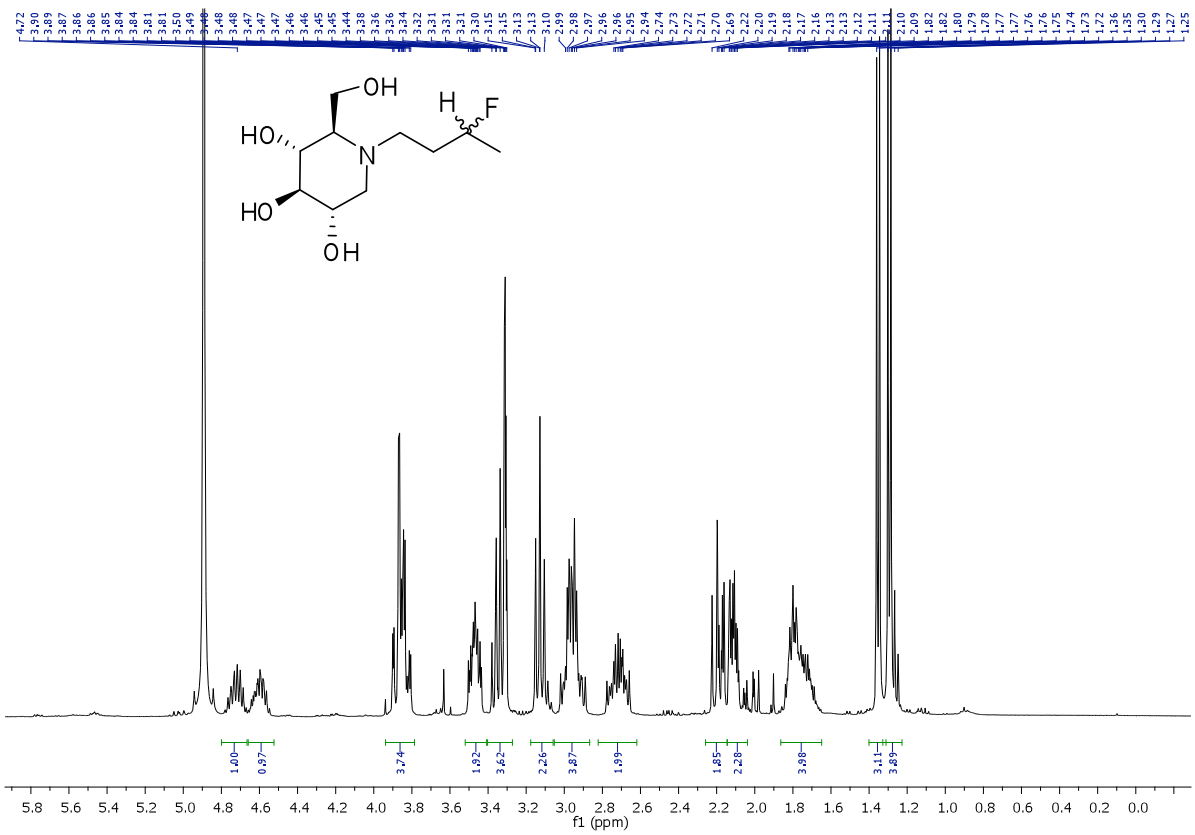
^{13}C NMR spectrum of compound **6a** (100 MHz, CD_3OD)



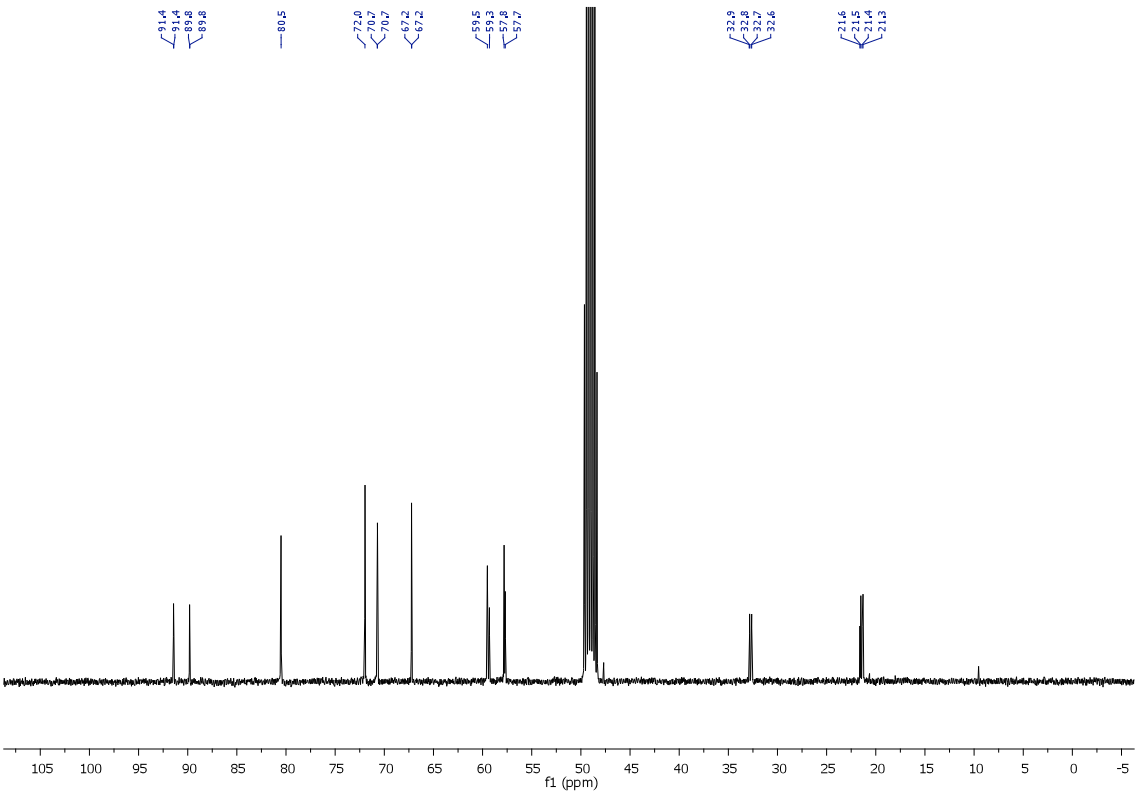
^{19}F NMR spectrum of compound **6a** (376 MHz, CD_3OD)



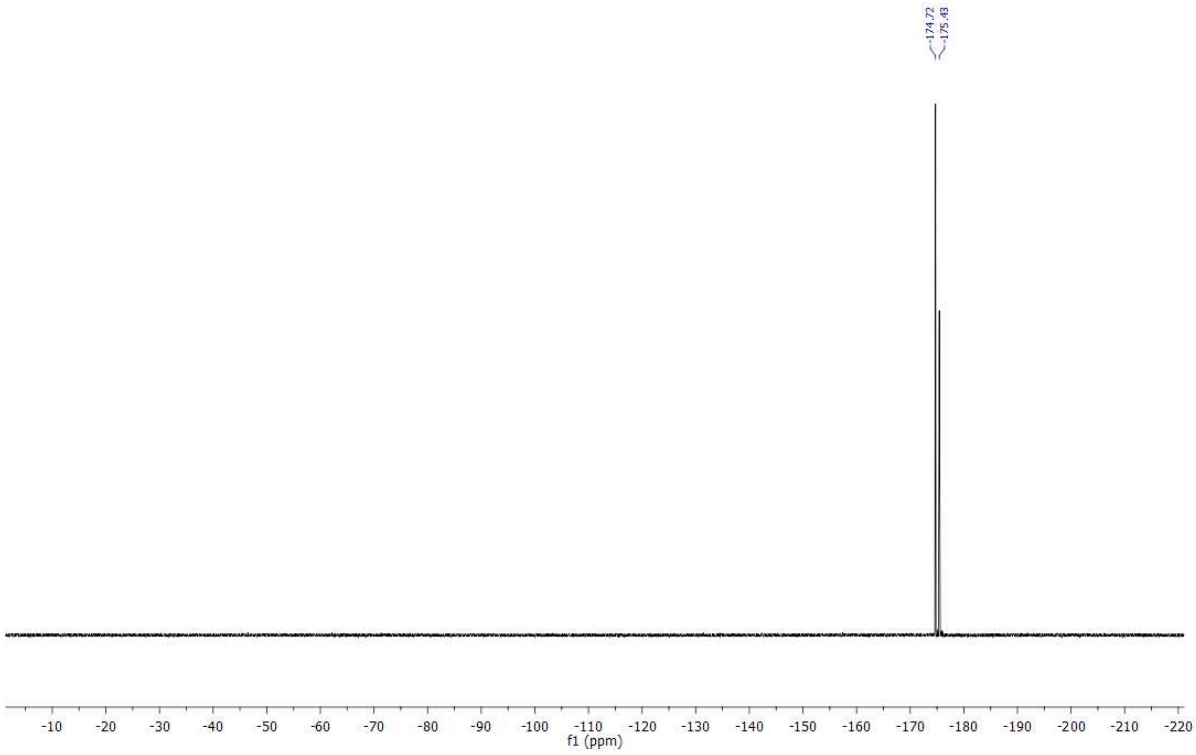
^{1}H NMR spectrum of compound **6b** (400 MHz, CD_3OD)



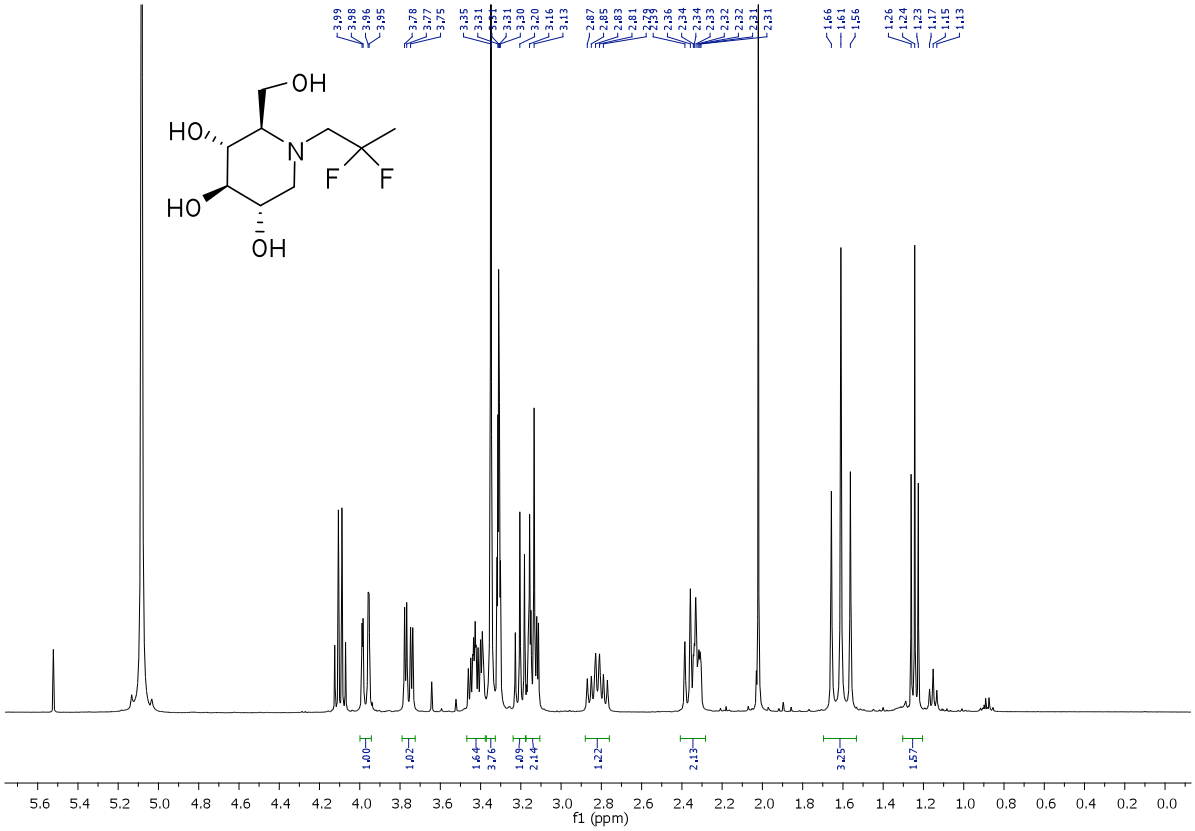
^{13}C NMR spectrum of compound **6b** (100 MHz, CD_3OD)



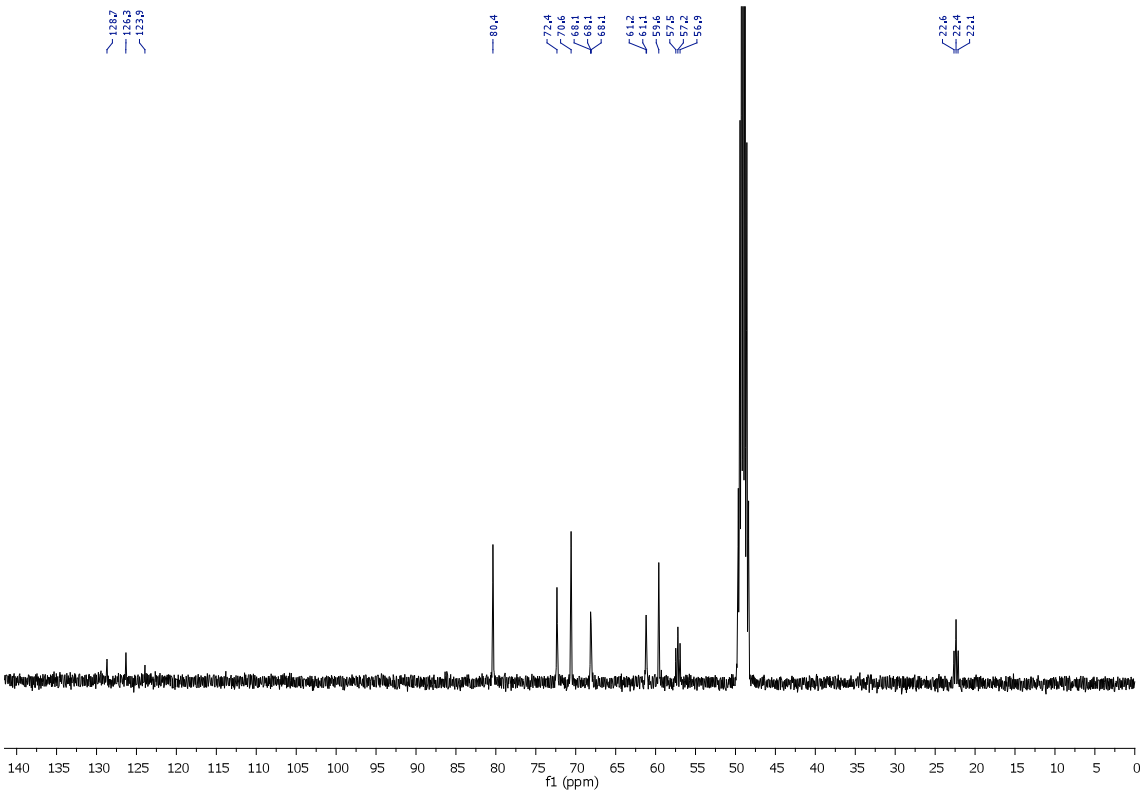
^{19}F NMR spectrum of compound **6b** (376 MHz, CD_3OD)



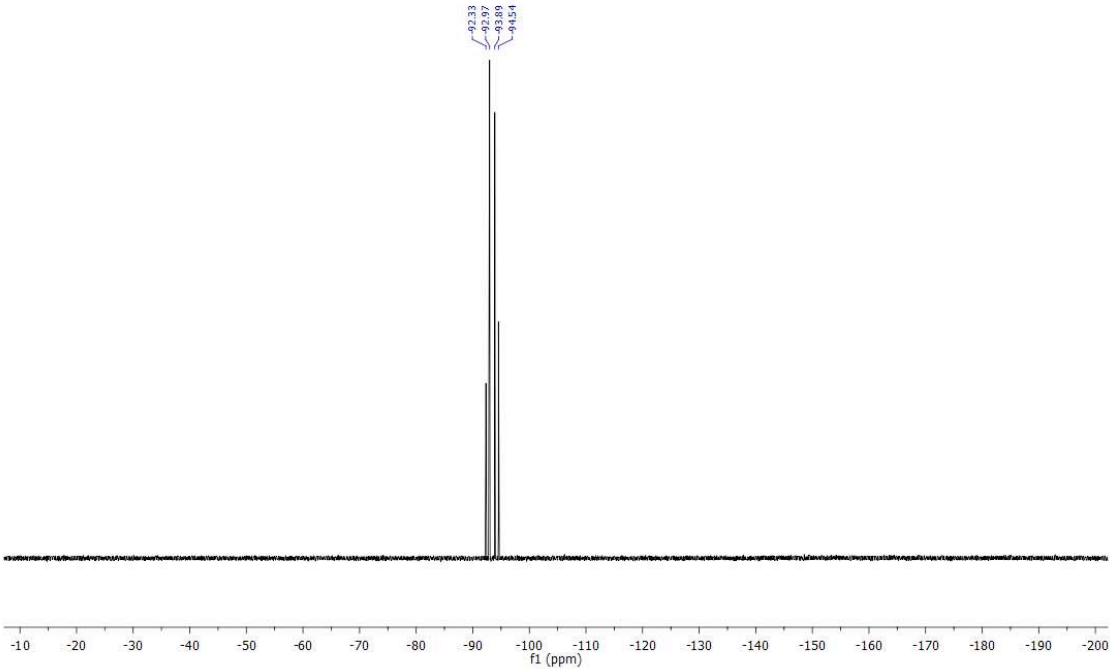
^{1}H NMR spectrum of compound **6c** (400 MHz, CD_3OD)



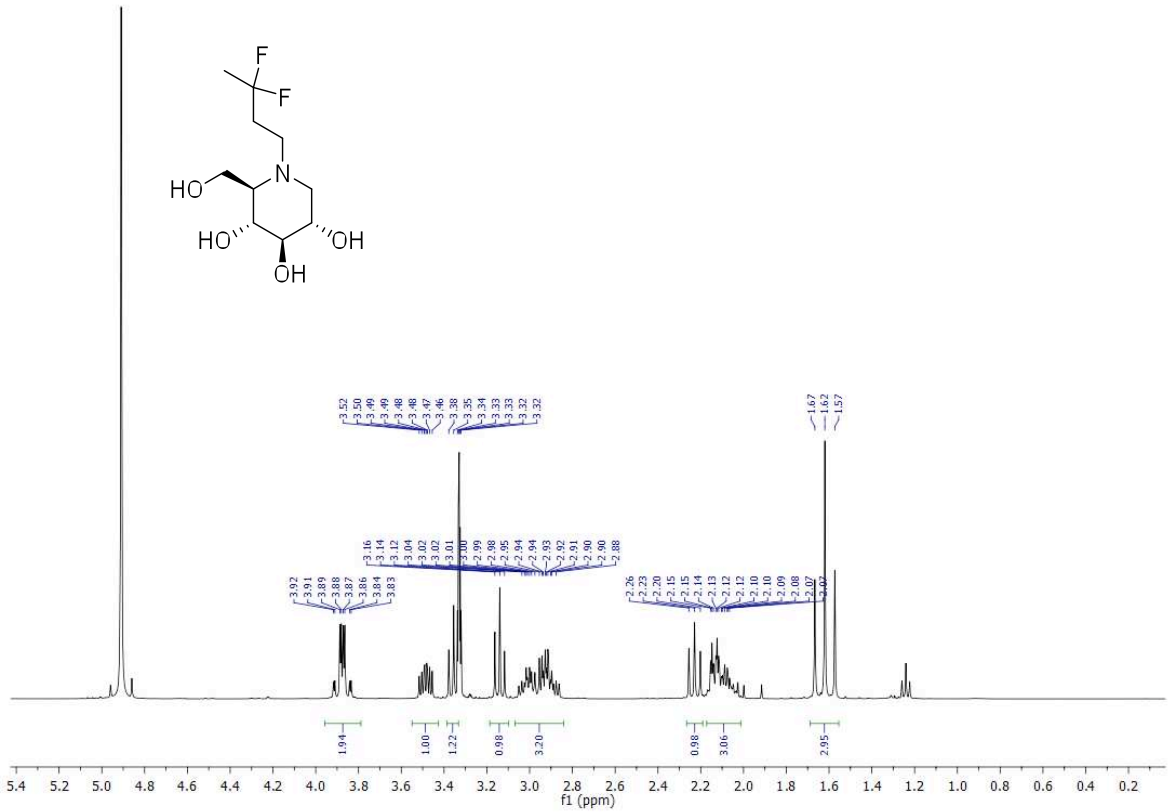
^{13}C NMR spectrum of compound **6c** (100 MHz, CD_3OD)



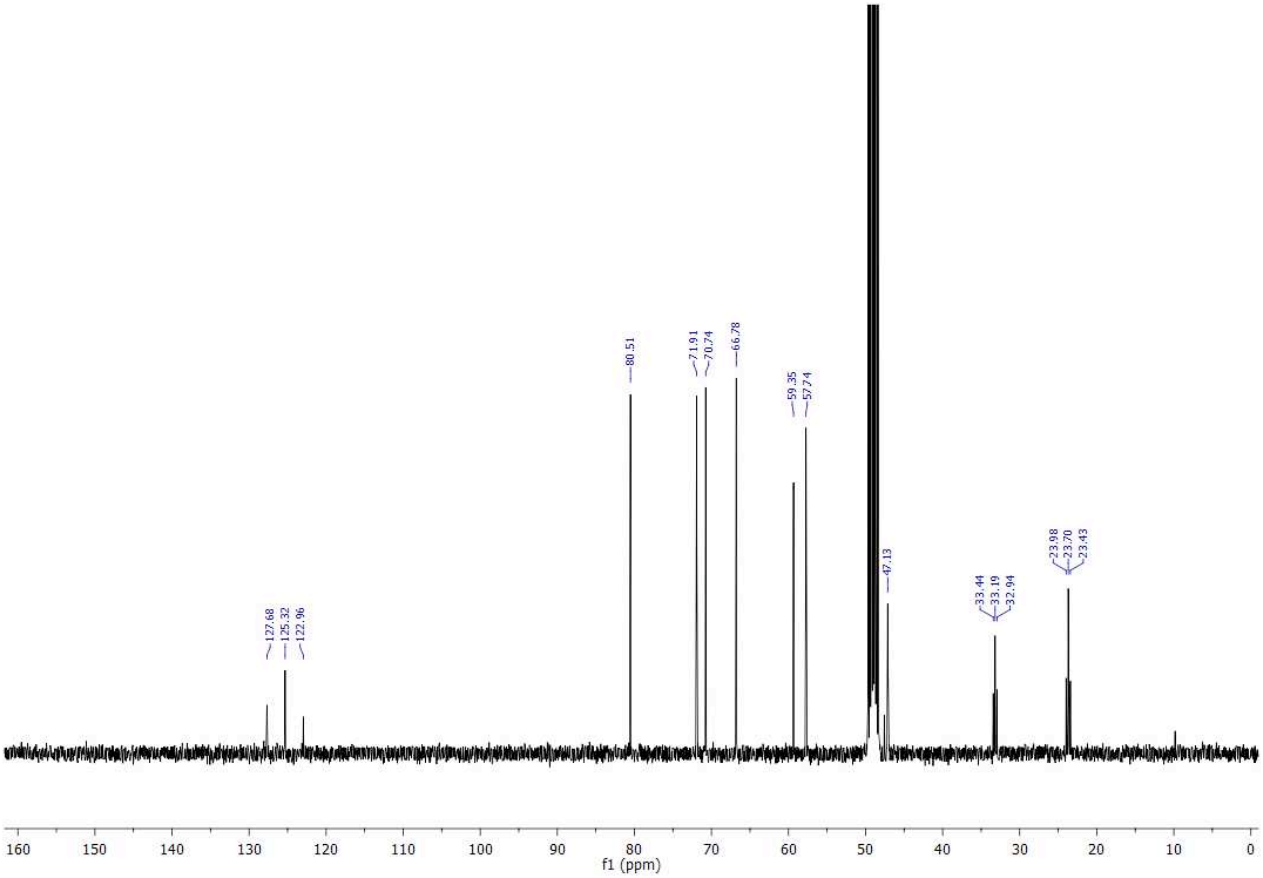
^{19}F NMR spectrum of compound **6c** (376 MHz, CD_3OD)



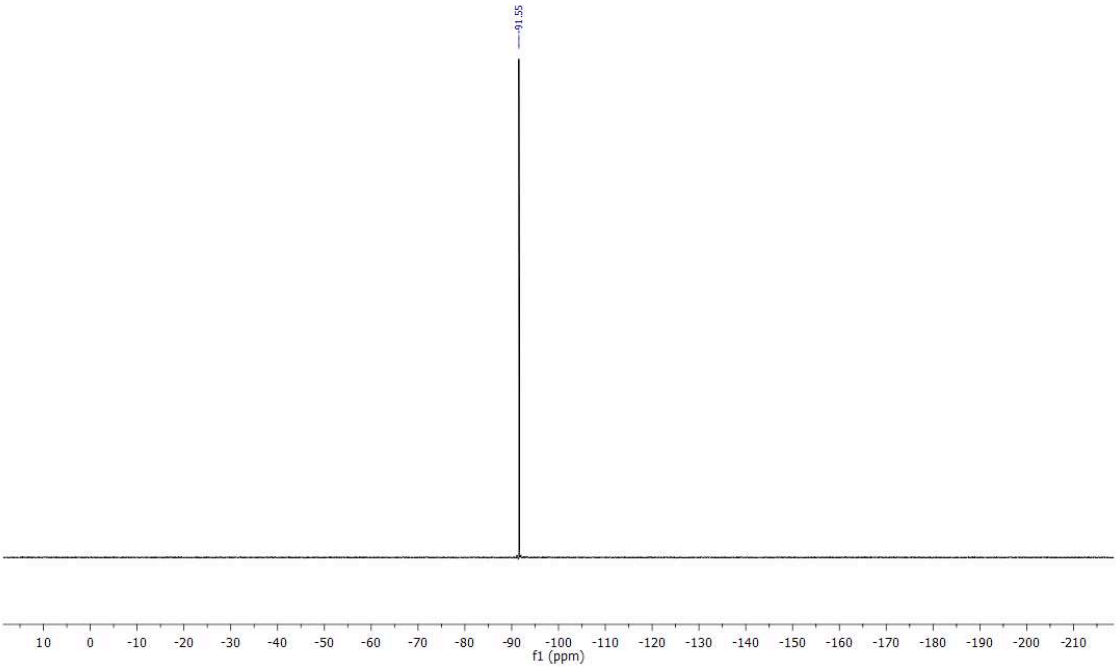
^{1}H NMR spectrum of compound **6d** (400 MHz, CD_3OD)



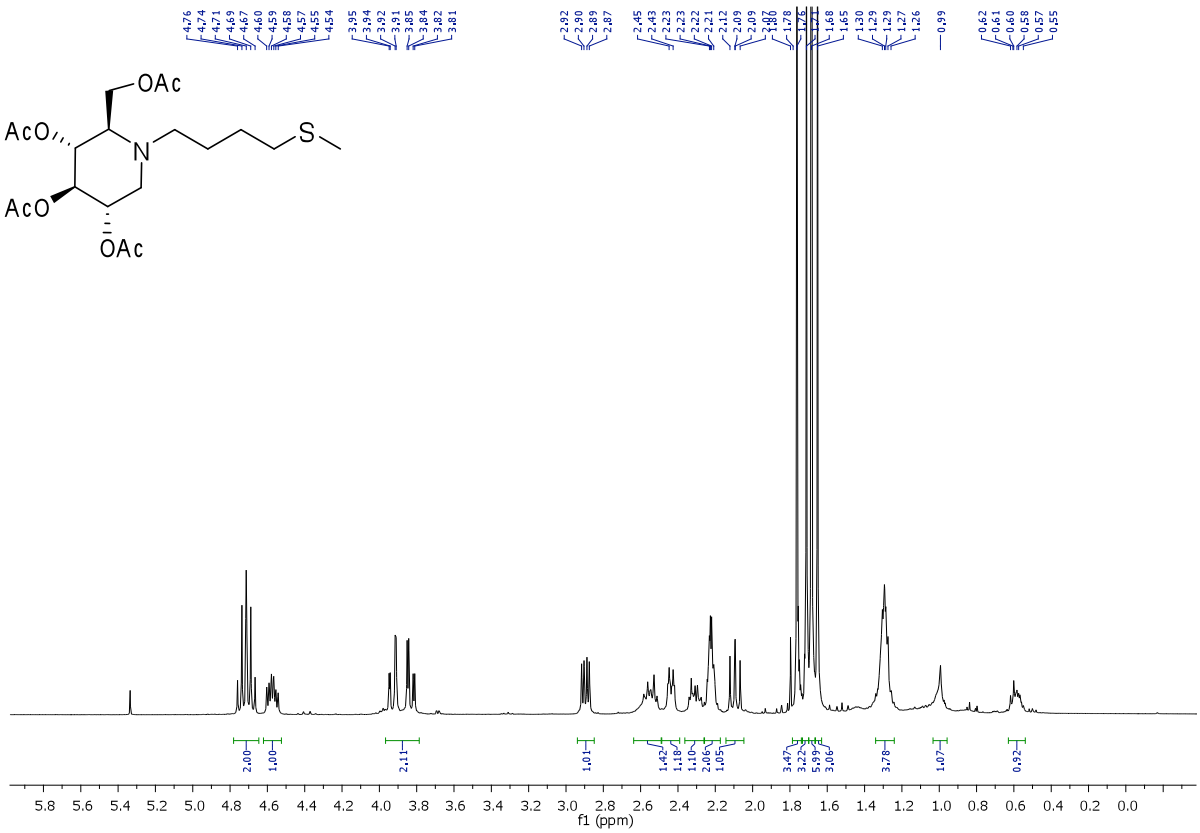
^{13}C NMR spectrum of compound **6d** (100 MHz, CD_3OD)



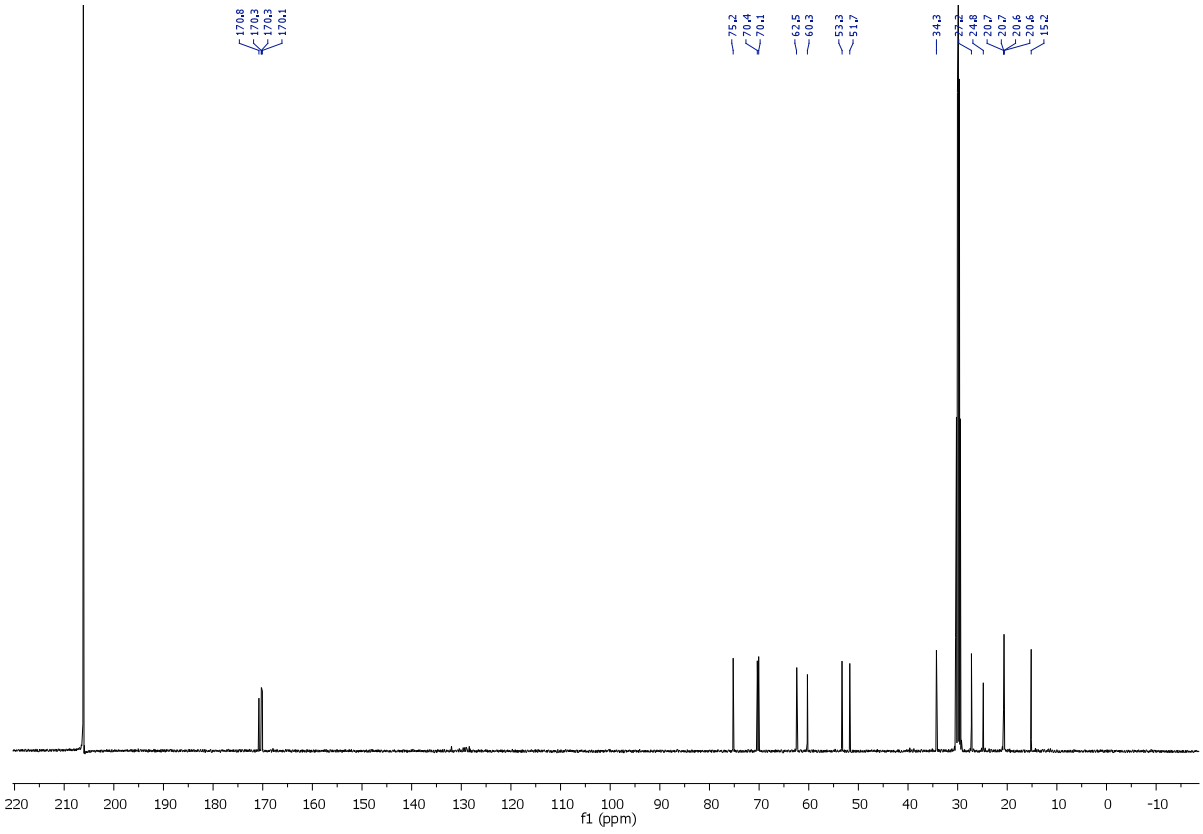
^{19}F NMR spectrum of compound **6d** (376 MHz, CD_3OD)



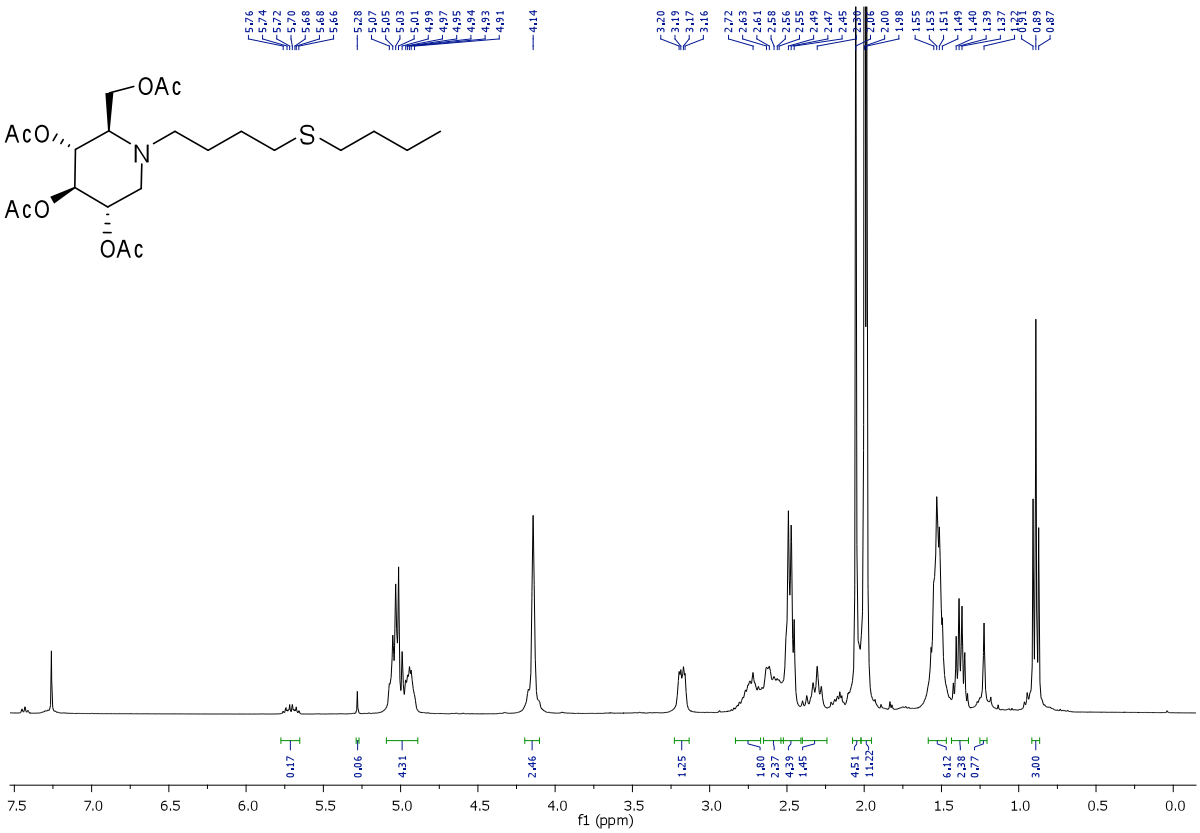
^{1}H NMR spectrum of compound **7a** (400 MHz, Acetone-d_6)



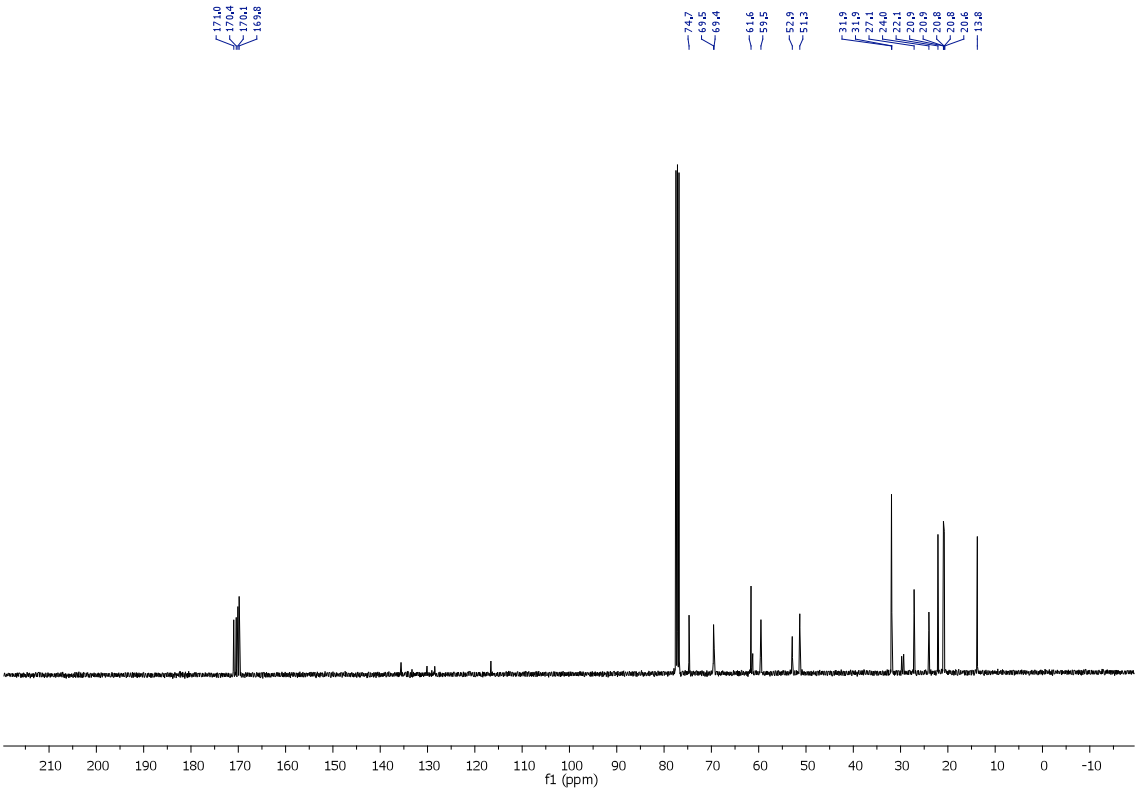
^{13}C NMR spectrum of compound **7a** (100 MHz, Acetone-d_6)



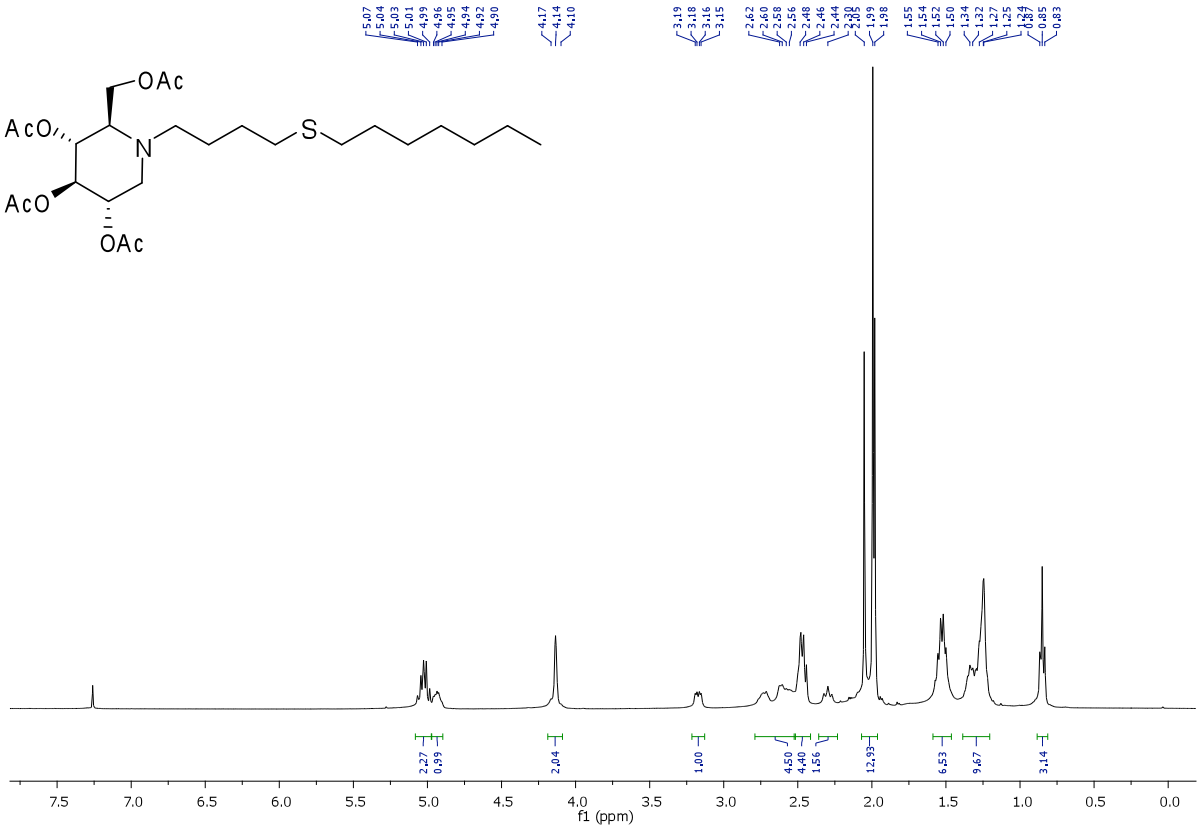
^{1}H NMR spectrum of compound **7b** (400 MHz, $CDCl_3$)



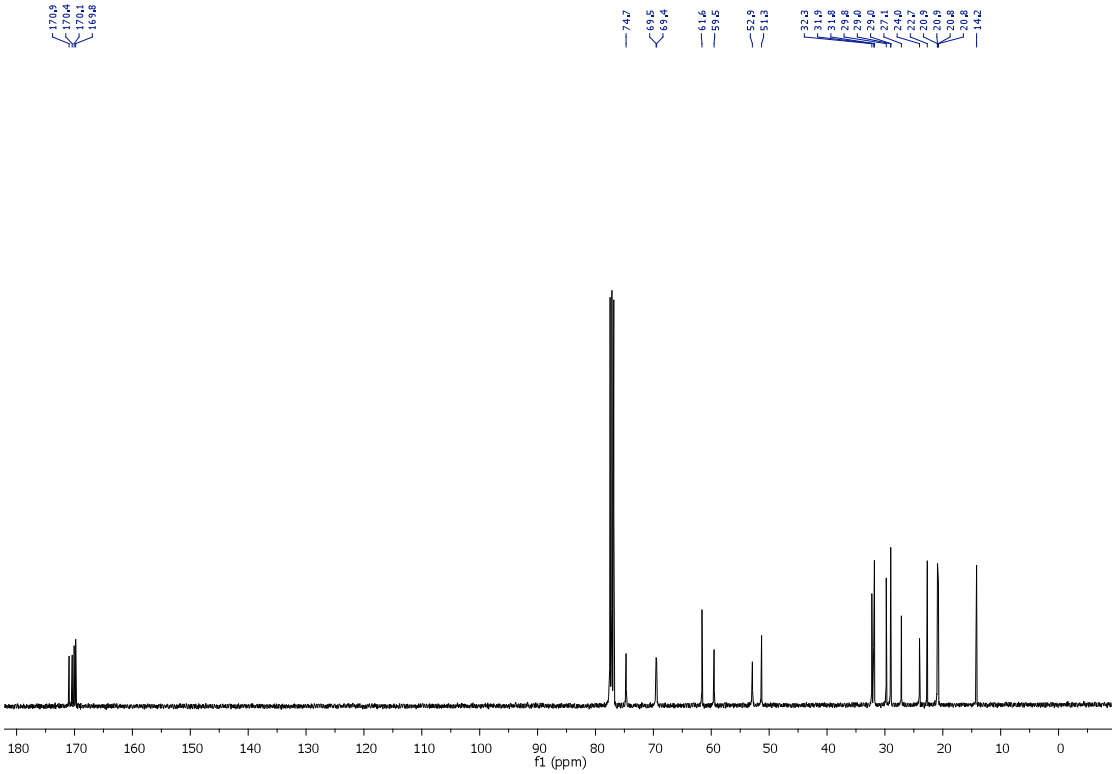
^{13}C NMR spectrum of compound **7b** (100 MHz, $CDCl_3$)



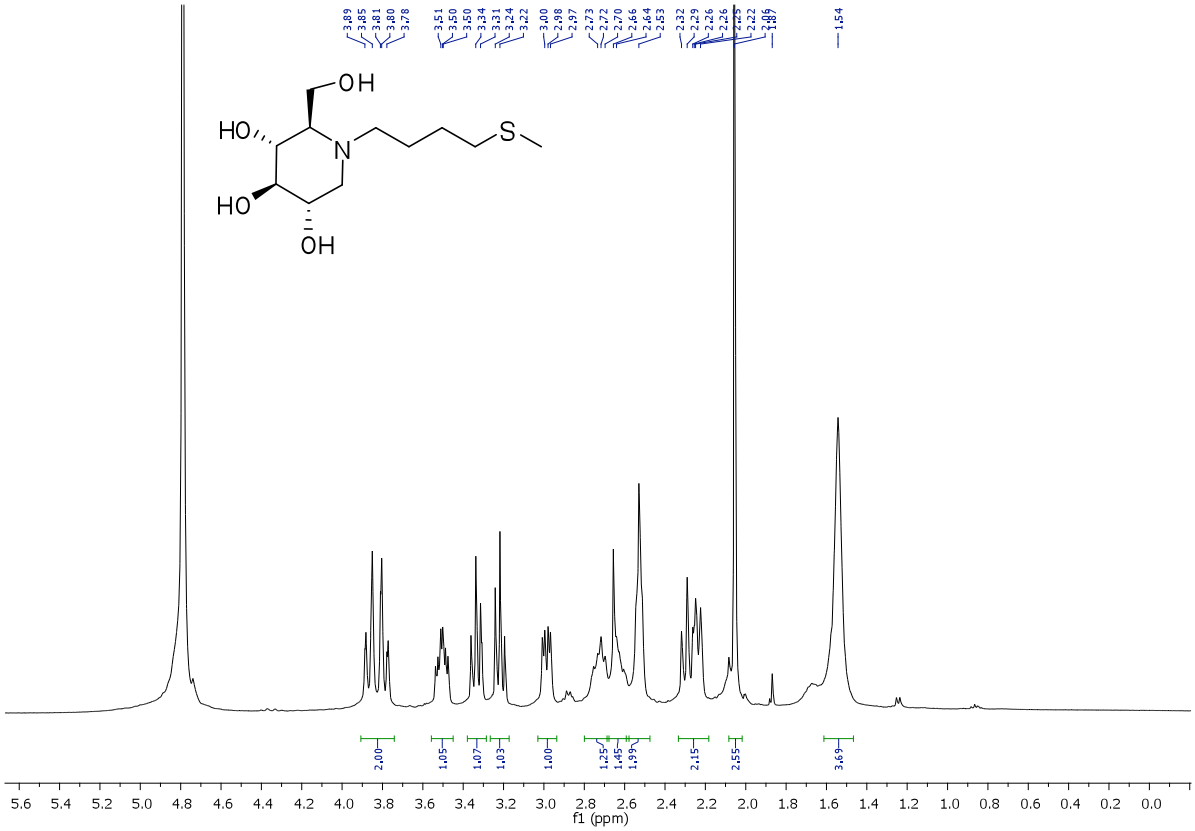
^{1}H NMR spectrum of compound **7c** (400 MHz, $CDCl_3$)



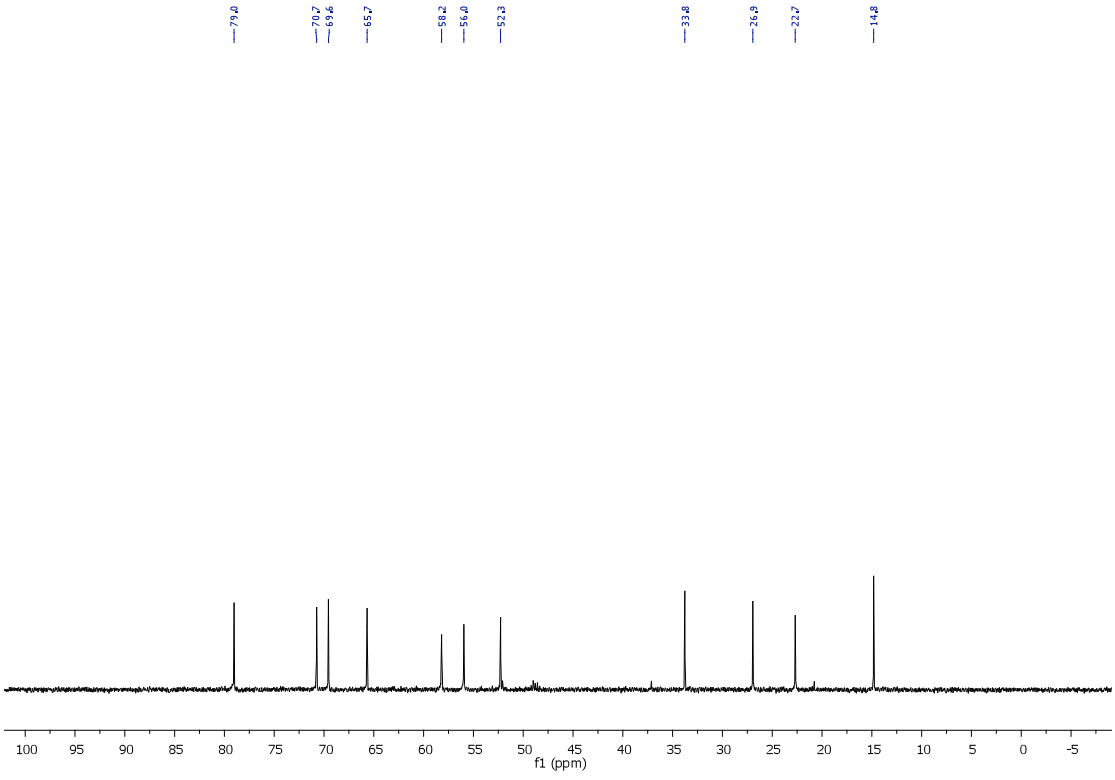
^{13}C NMR spectrum of compound **7c** (100 MHz, $CDCl_3$)



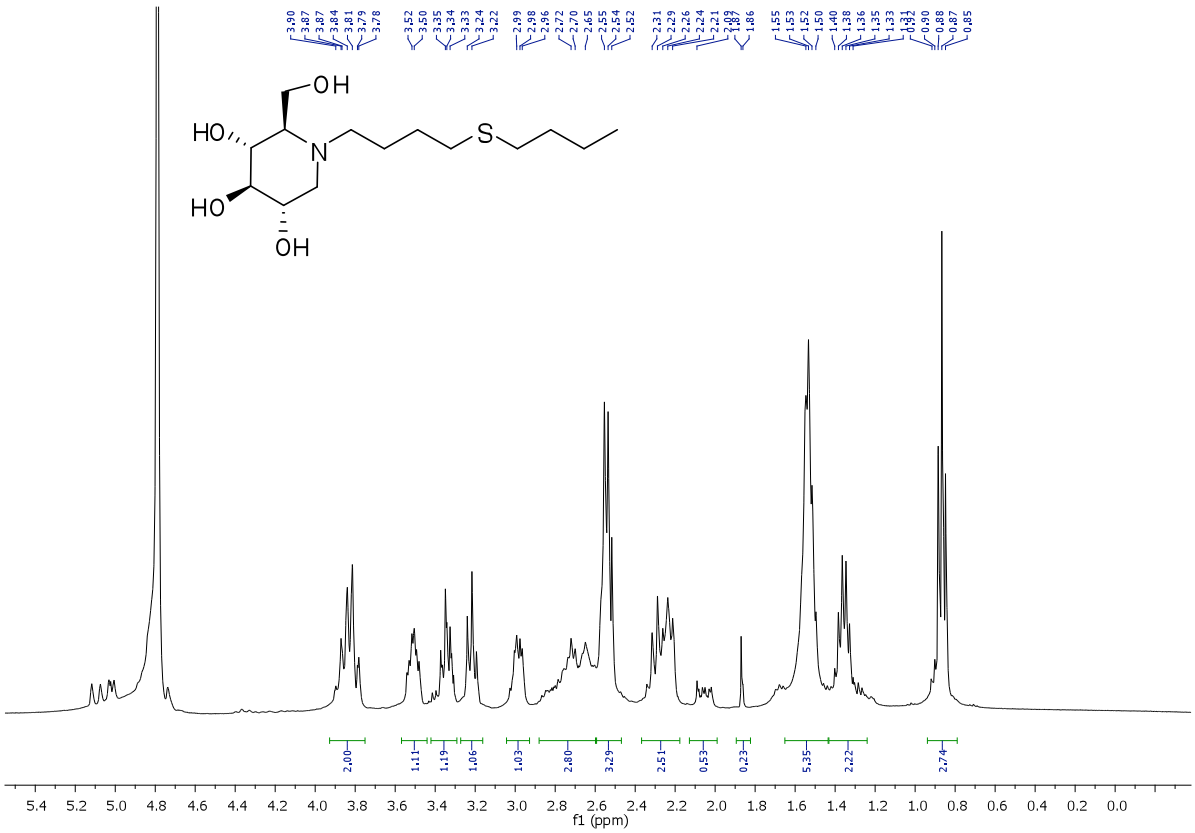
^{1}H NMR spectrum of compound **8a** (400 MHz, D_2O)



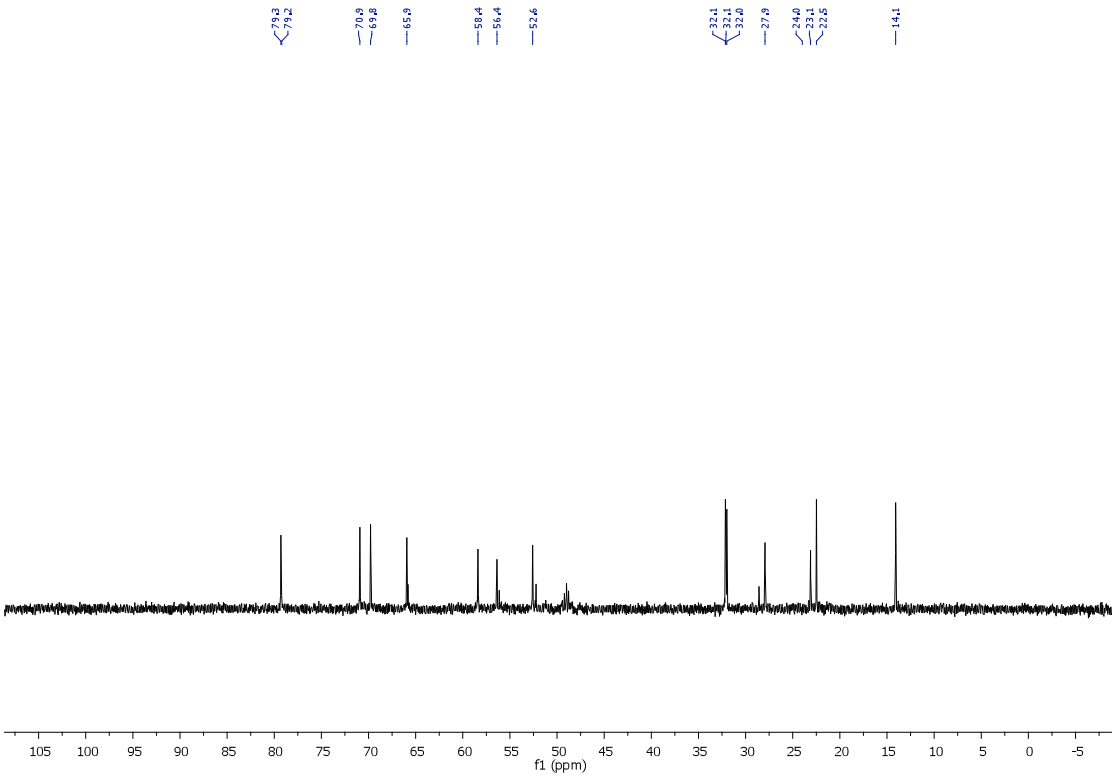
^{13}C NMR spectrum of compound **8a** (100 MHz, D_2O)



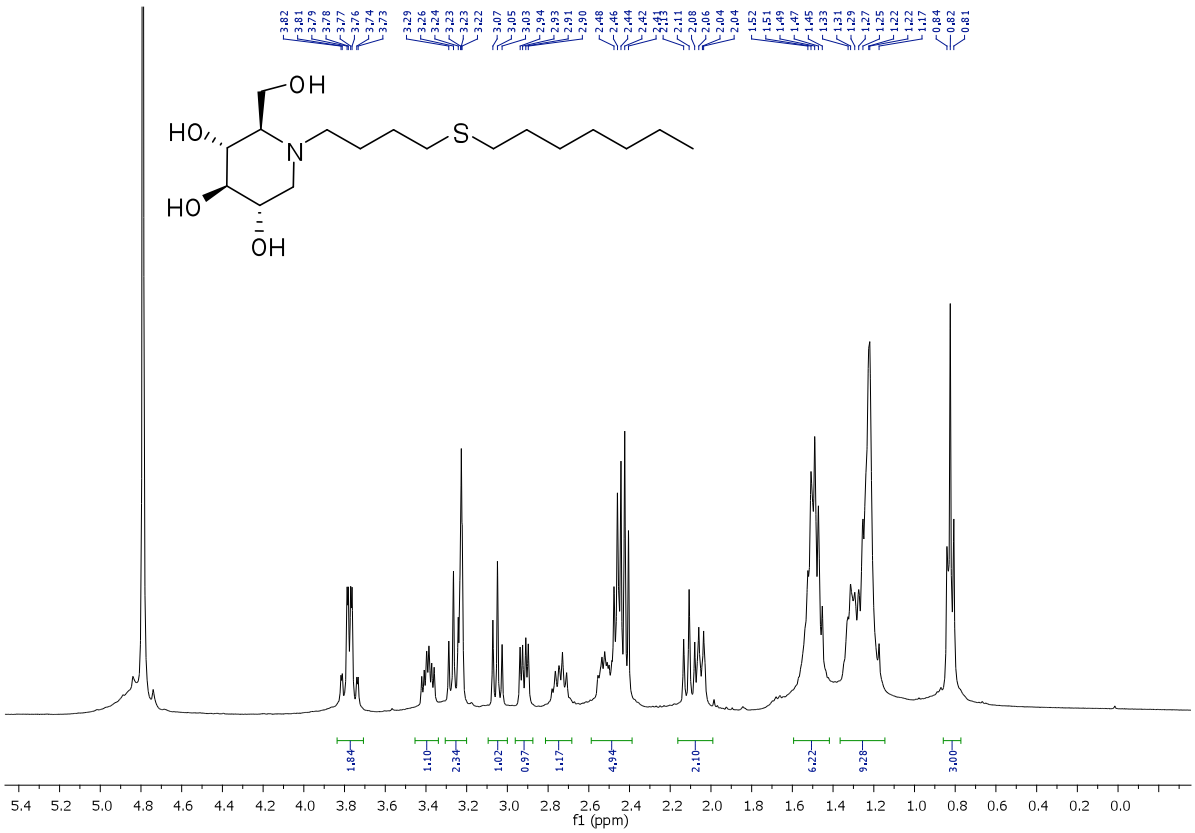
^{1}H NMR spectrum of compound **8b** (400 MHz, D_2O)



^{13}C NMR spectrum of compound **8b** (100 MHz, D_2O)



^{1}H NMR spectrum of compound **8c** (400 MHz, CD_3OD)



^{13}C NMR spectrum of compound **8c** (100 MHz, CD_3OD)

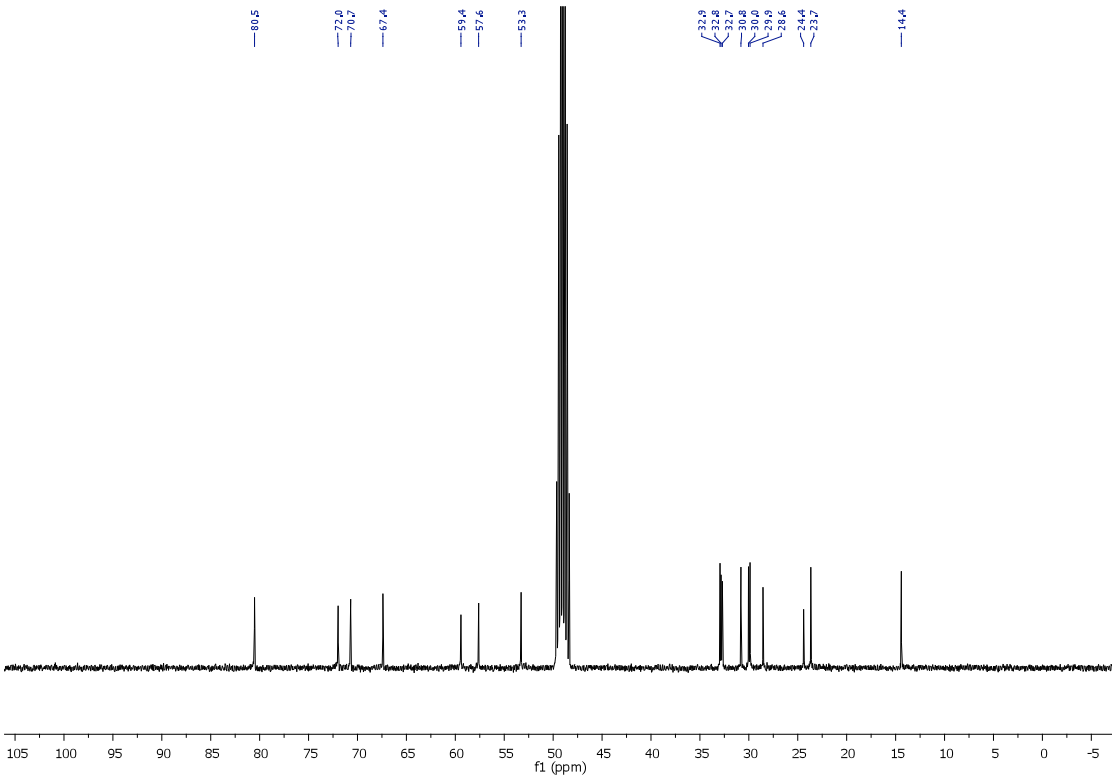
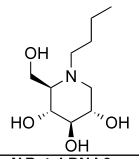
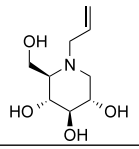
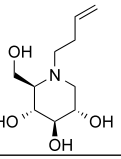
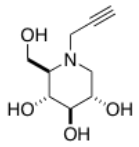
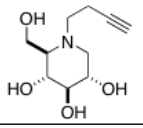
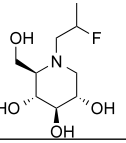
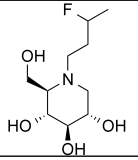
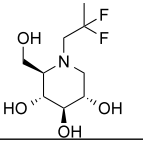
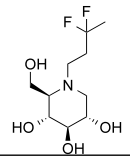


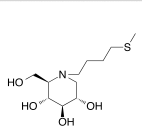
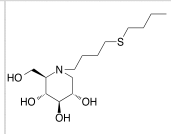
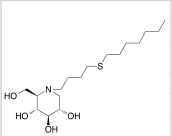
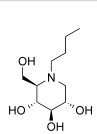
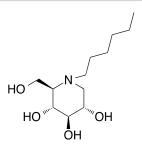
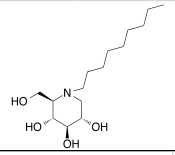
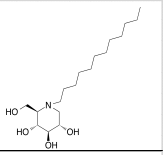
Table 1. Concentration of iminosugars giving 50 % inhibition of various glycosidases

		IC$_{50}$ (μM)								
										
enzyme		***N*-Butyl-DNJ 9a**	**3a**	**3b**	**3c**	**3d**	**6a**	**6b**	**6c**	**6d**
α-glucosidase										
	Yeast	NI (1.7%)	NI (9.3%)	NI (5.9%)	NI (5.1%)	NI (6.3%)	[a]NI [b](1.5%)	NI (1.7%)	NI (1.1%)	NI (0%)
	Aspergillus niger	91	81	34	NI (37.6%)	32	224	170	NI (26.7%)	411
	Rice	0,44	0,28	0,48	0,91	0,44	0,84	0,63	19	0,96
	Rat intestinal maltase	1,1	2,2	2,5	12	6,9	18	7,4	94	14
β-glucosidase										
	Almond	475	NI (39.8%)	679	NI (8.6%)	639	259	628	NI (21.0%)	332
	Bovine liver	[a]NI [b](0%)	NI (3.6%)	NI (9.2%)	NI (24.2%)	NI (8.0%)	NI (43.0%)	NI (41.3%)	NI (28.7%)	NI (17.3%)
α-galactosidase										
	Coffee beans	302	NI (16.2%)	NI (12.7%)	467	NI (30.0%)	NI (43.4%)	NI (49.5%)	471	NI (36.5%)
β-galactosidase										
	Bovine liver	NI (7.6%)	NI (6.8%)	NI (8.7%)	NI (5.6%)	NI (12.8%)	644	566	NI (47.7%)	NI (13.0%)
α-mannosidase										
	Jack bean	NI (12.8%)	NI (9.2%)	NI (7.5%)	NI (0.4%)	NI (6.5%)	NI (10.1%)	NI (8.8%)	NI (0.8%)	NI (25.5%)
β-mannosidase										
	Snail	NI (15.5%)	NI (15.9%)	NI (16.4%)	NI (2.0%)	NI (3.7%)	NI (17.6%)	NI (10.9%)	NI (7.1%)	NI (16.7%)
α-L-fucosidase										
	Bovine kidney	NI (4.8%)	NI (7.5%)	NI (0%)	NI (4.0%)	NI (8.6%)	NI (7.9%)	NI (8.8%)	NI (4.2%)	NI (0.4%)
β-glucuronidase										
	E.coli	NI (16.5%)	NI (8.7%)	NI (36.5%)	NI (12.3%)	NI (26.8%)	NI (6.2%)	NI (3.8%)	NI (13.9%)	NI (24.2%)
α,α-trehalase										
	Porcine kidney	79	522	188	NI (9.6%)	NI (40.0%)	NI (21.7%)	133	NI (21.7%)	259
amyloglucosidase										
	Aspergillus niger	964	909	483	NI (3.2%)	398	NI (28.3%)	NI (40.9%)	NI (2.2%)	NI (23.3%)
	Rhizopus sp	ND	459	386	NI (11.6%)	223	NI (26.0%)	NI (26.0%)	NI (3.1%)	NI (12.1%)
α-L-rhamnosidase										
	Penicillium decumbens	429	651	333	NI (20.6%)	281	164	453	NI (37.4%)	NI (47.8%)
glucosyltransferase										
	HL60	8,8	61	5,6	NI (0%)	276	NI (49.8%)	10	736	43

[a] NI : No inhibition (less than 50% inhibition at 1000 μM).

[b] ( ) : inhibition % at 1000 μM

Table 2 . Concentration of iminosugars giving 50 % inhibition of various glycosidases

		IC_{50} (μM)						
								
enzyme		**8a**	**8b**	**8c**	**9a**	**9b**	**9c**	**9d**
α-glucosidase								
	Yeast	[a] NI [b] (8.8%)	NI (24.7%)	NI (32.9%)	NI (12.7%)	NI (43.0%)	NI (30.5%)	[c] NI [d] (0%)
	Aspergillus niger	67	75	40	91	137	69	75
	Rice	0,67	0,3	0,22	0,44	0,37	0,21	0,16
	Rat intestinal maltase	1,6	1,2	0,78	1,1	1,2	0,79	0,48
β-glucosidase								
	Almond	39	85	55	475	79	157	82
	Bovine liver	NI (30.2%)	NI (48.8%)	114	[a]NI [b](0%)	NI (37.3%)	742	23
α-galactosidase								
	Coffee beans	417	156	57	302	NI (47.8%)	521	c NI d (19.2%)
β-galactosidase								
	Bovine liver	NI (45.6%)	416	62	NI (7.6%)	NI (47.7%)	374	12,7
α-mannosidase								
	Jack beans	NI (13.1%)	NI (20.0%)	NI (21.8%)	NI (12.8%)	NI (15.8%)	NI (10.9%)	c NI d (0.1%)
β-mannosidase								
	Helix pomatia	NI (0%)	NI (0%)	NI (0%)	NI (15.5%)	NI (0%)	NI (0%)	c NI d (0%)
α-L-fucosidase								
	Bovine kidney	NI (0%)	NI (0%)	NI (0%)	NI (4.8%)	NI (34.0%)	NI (0.1%)	c NI d (0%)
β-glucronidase								
	E.coli	NI (11.2%)	NI (22.9%)	985	NI (16.5%)	473	660	28,5
α,α-trehalase								
	Porcine kidney	21	14	17	79	13	3,3	24
amyloglucosidase								
	Aspergillus niger	566	405	288	964	NI (47.4%)	565	c NI d (23.0%)
	Rhizopus sp	NI (49.2%)	519	607	NI (42.7%)	NI (33.6%)	712	c NI d (9.1%)
α-L-rhamnosidase								
	Penicillium decumbens	215	103	29	429	393	72	34
glucosyltransferase								
	HL60	31	90	28	8,8	1,8	1,6	5,6

[a] NI : No inhibition (less than 50% inhibition at 1000 μM).

[b] ( ) : inhibition % at 1000 μM

[c] NI : No inhibition (less than 50% inhibition at 100 μM).

[d] ( ) : inhibition % at 100 μM