

Anticancer Cytotoxic Activity of Bispidine Derivatives Associated with the Increasing Catabolism of Polyamines

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Supplementary Material

Spectral NMR data sectionFigures S2–S8

Spectral IR data section.....Figures S9–S21

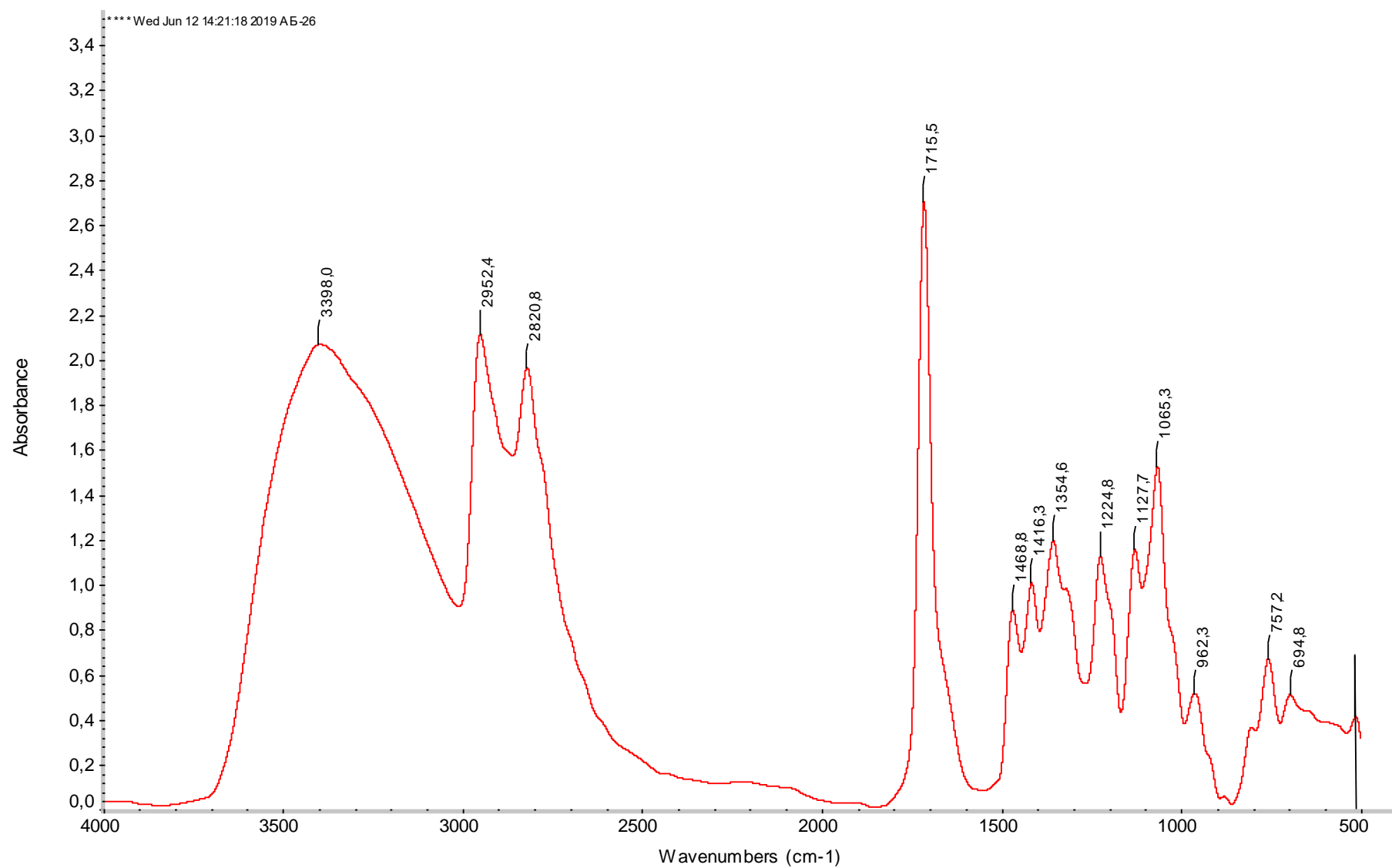


Figure S1. IR spectrum of 1-(3-hydroxypropyl)piperidin-4-one (1 b)

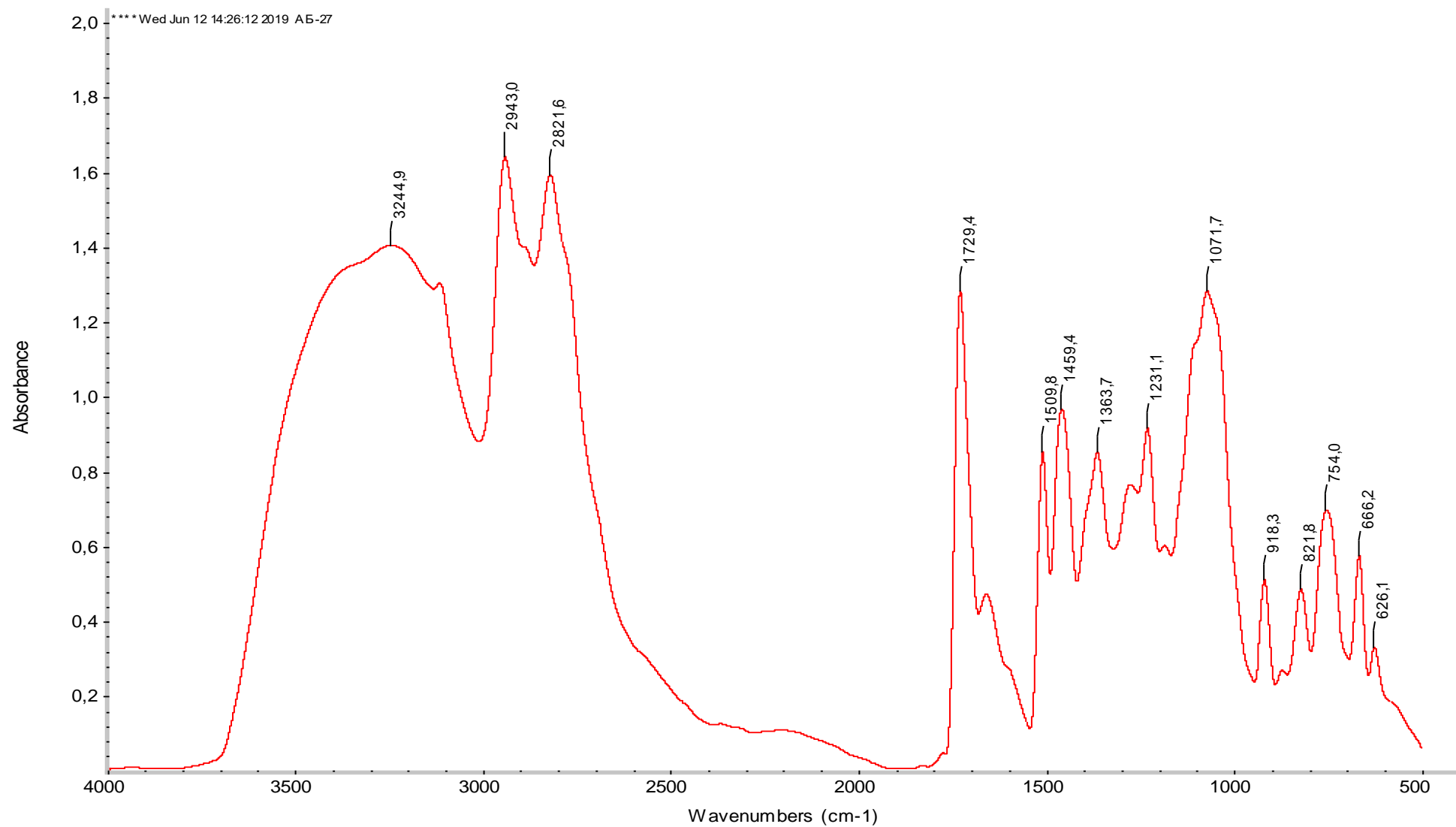


Figure S2. IR spectrum of 3-(3-hydroxypropyl)-7-[3-(1*H*-imidazol-1-yl)propyl]-3,7-diazabicyclo[3.3.1]nonan-9-one (2b)

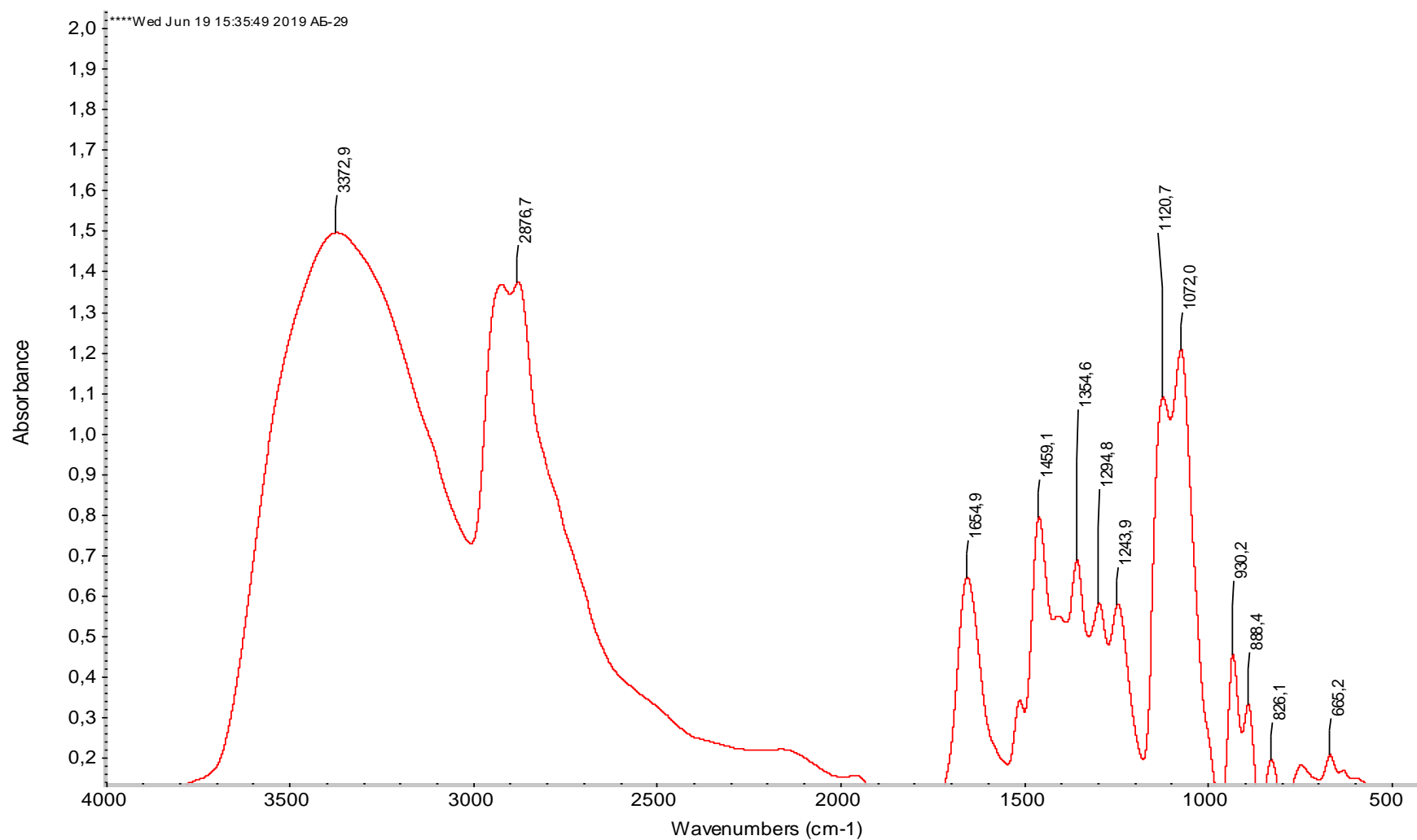


Figure S3. IR spectrum of 3-(3-hydroxypropyl)-7-[3-(1*H*-imidazol-1-yl)propyl]-3,7-diazabicyclo[3.3.1]nonane (3b)

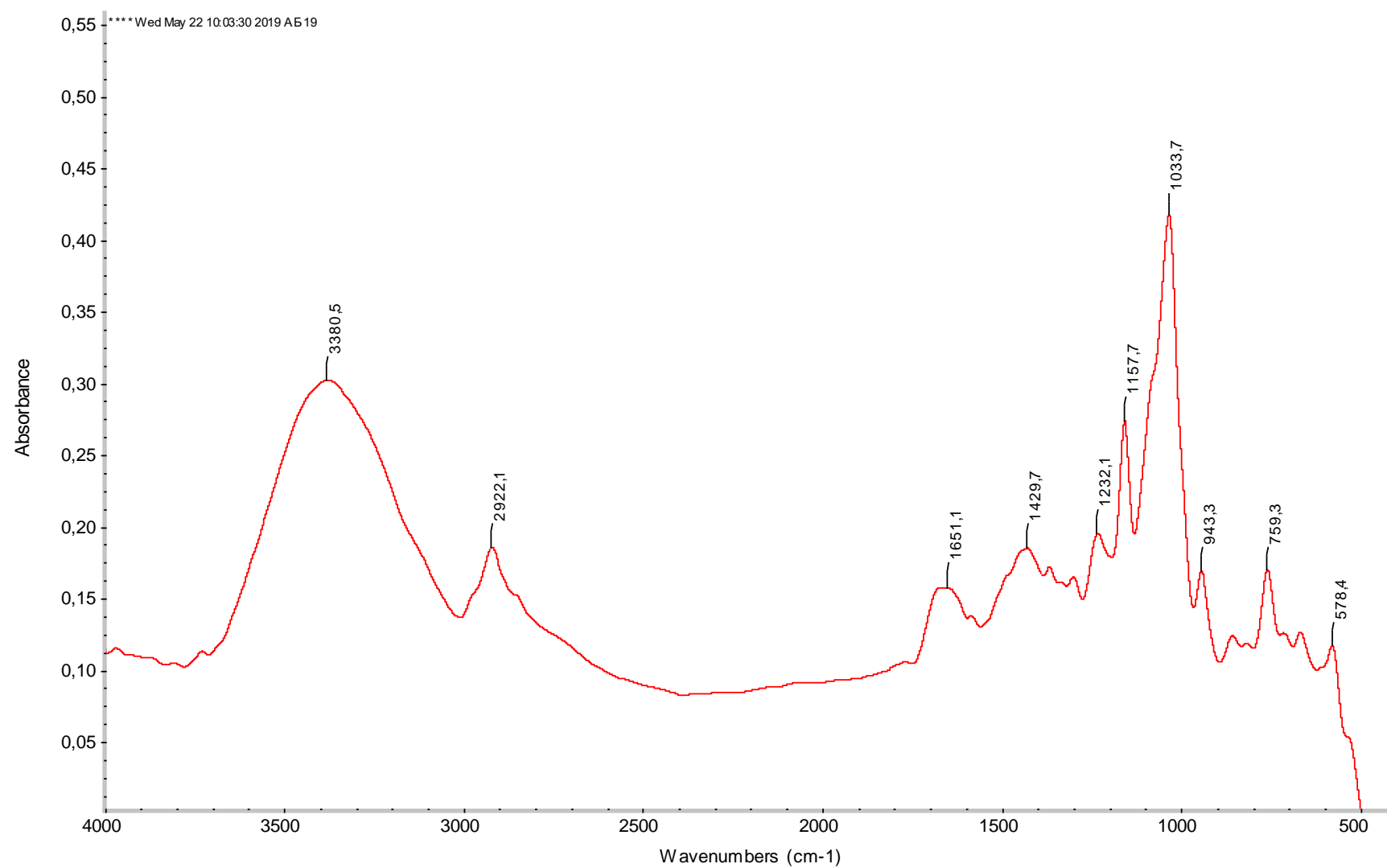


Figure S4. IR spectrum of oxime 3-Boc-7-[3-(1*H*-imidazol-1-yl)propyl]-3,7-diazabicyclo[3.3.1]nonan-9-one (5a)

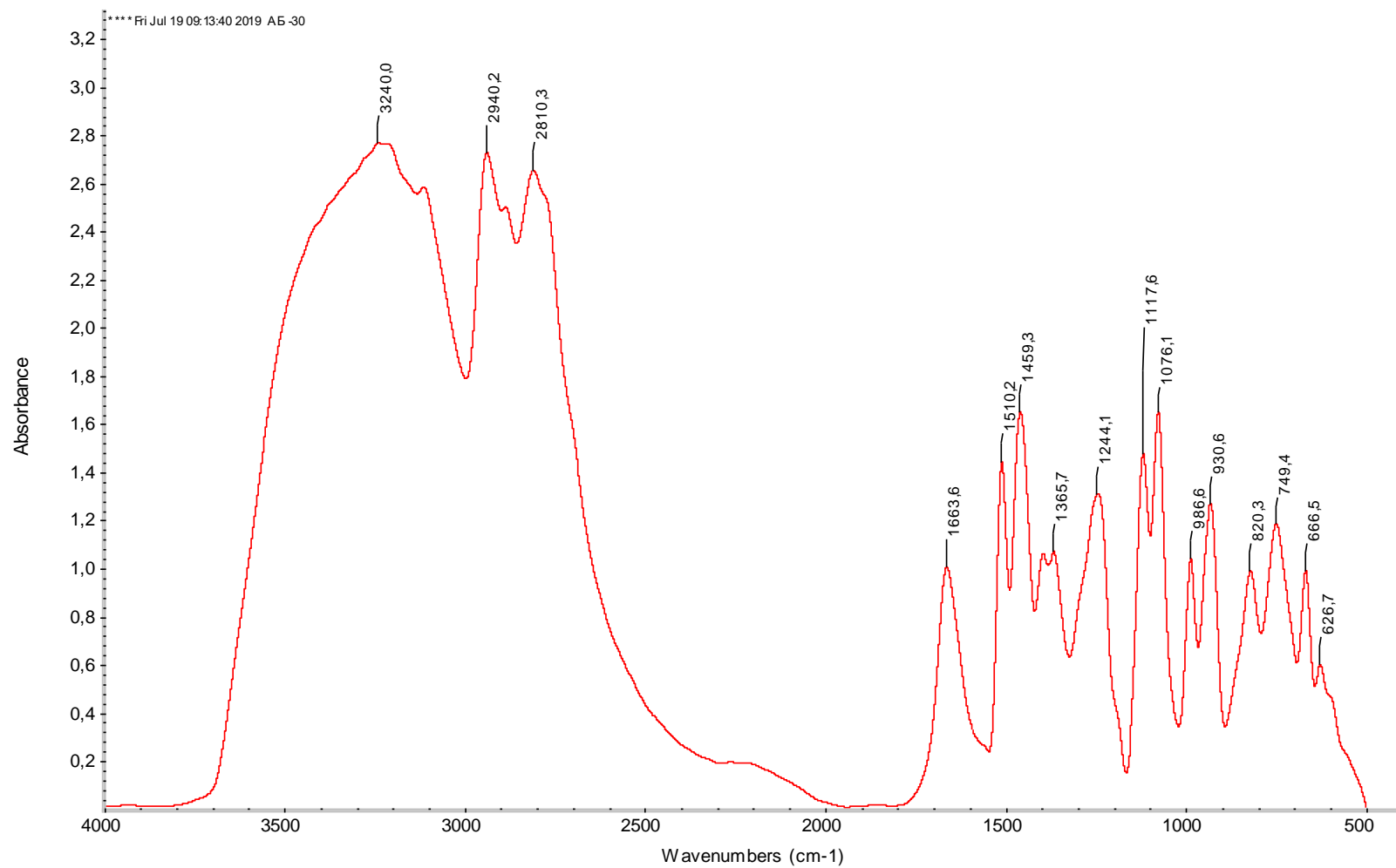


Figure S5. IR spectrum of oxime of 3-(3-hydroxypropyl)-7-[3-(1*H*-imidazol-1-yl)propyl]-3,7-diazabicyclo[3.3.1]nonan-9-one (5b)

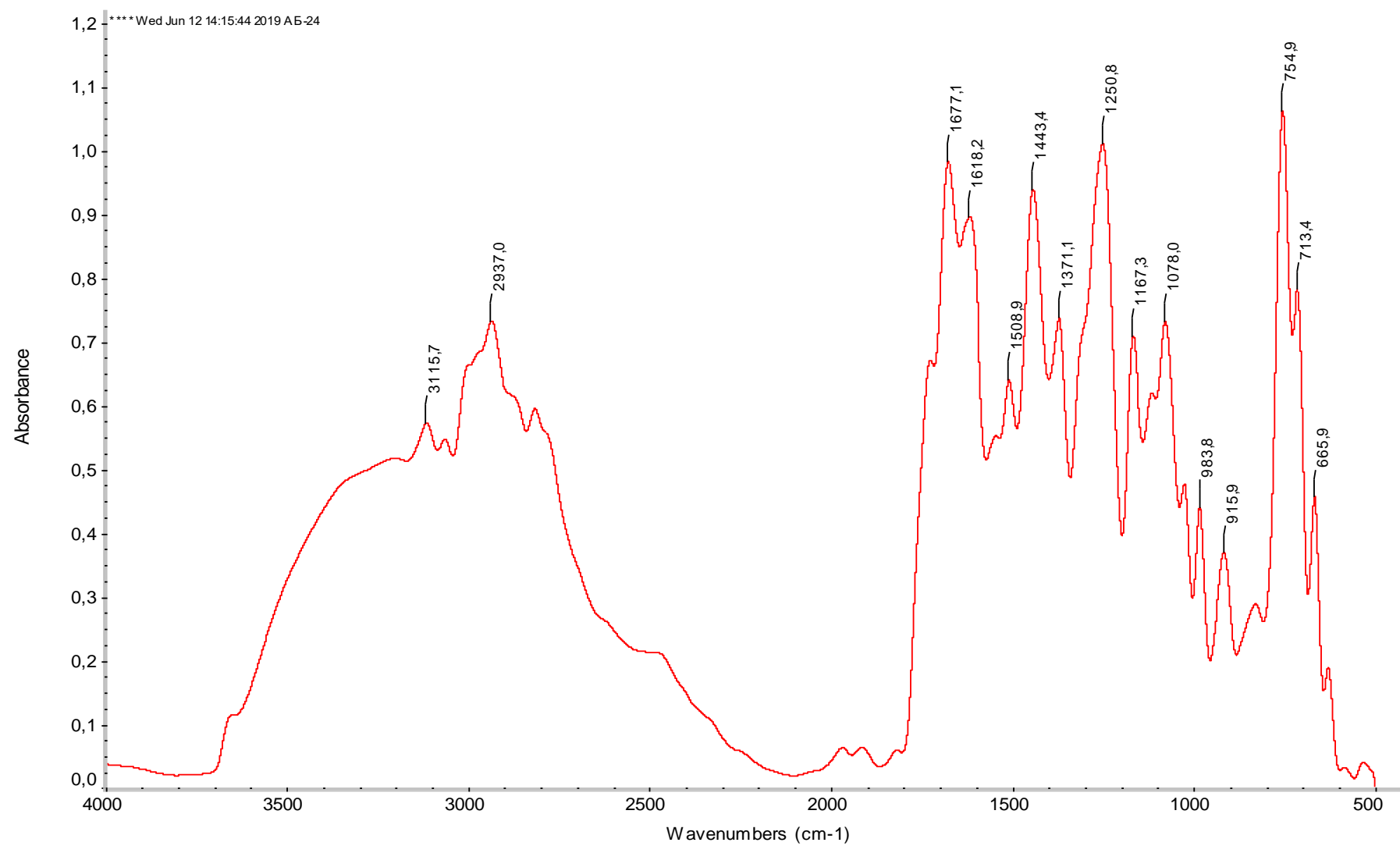


Figure S6. IR spectrum of O-benzoyloxime 3-(3-Boc)-7-[3-(1*H*-imidazol-1-yl)propyl]-3,7-diazabicyclo[3.3.1]nonan-9-one (6a)

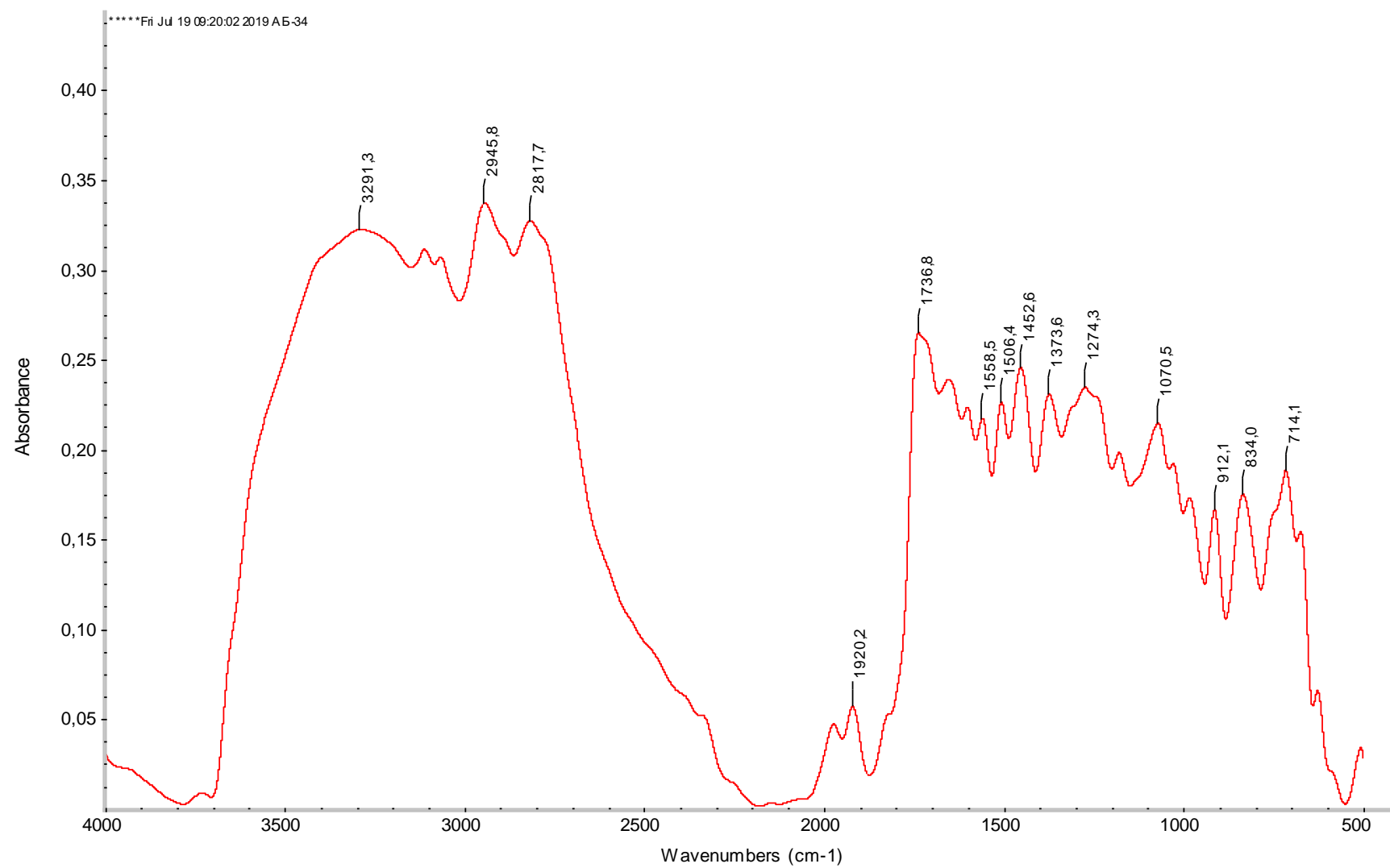


Figure S7. IR spectrum of O-benzoyl oxime of 3-(3-hydroxypropyl)-7-[3-(1*H*-imidazol-1-yl)propyl]-3,7-diazabicyclo[3.3.1]nonan-9-one (6b)

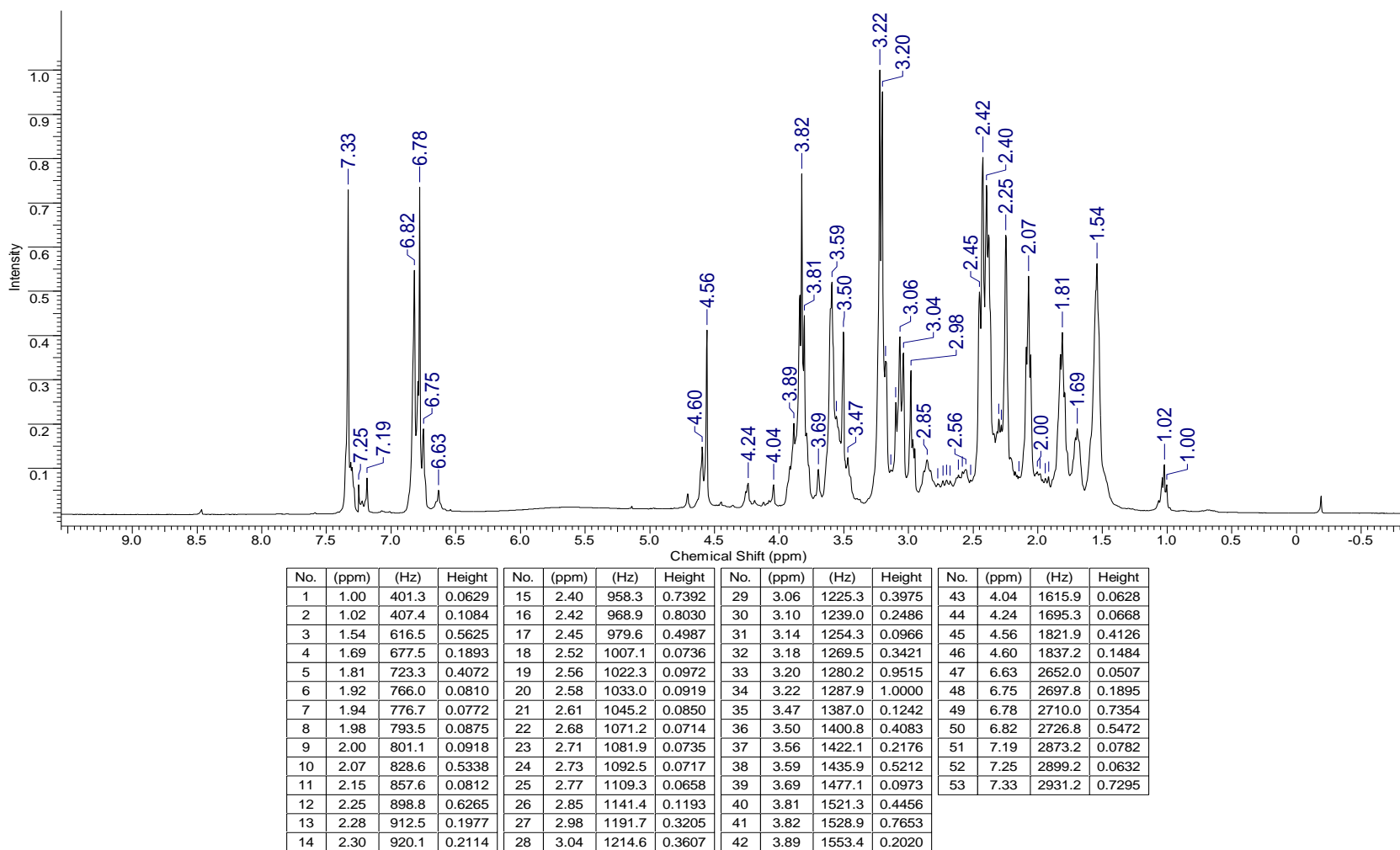
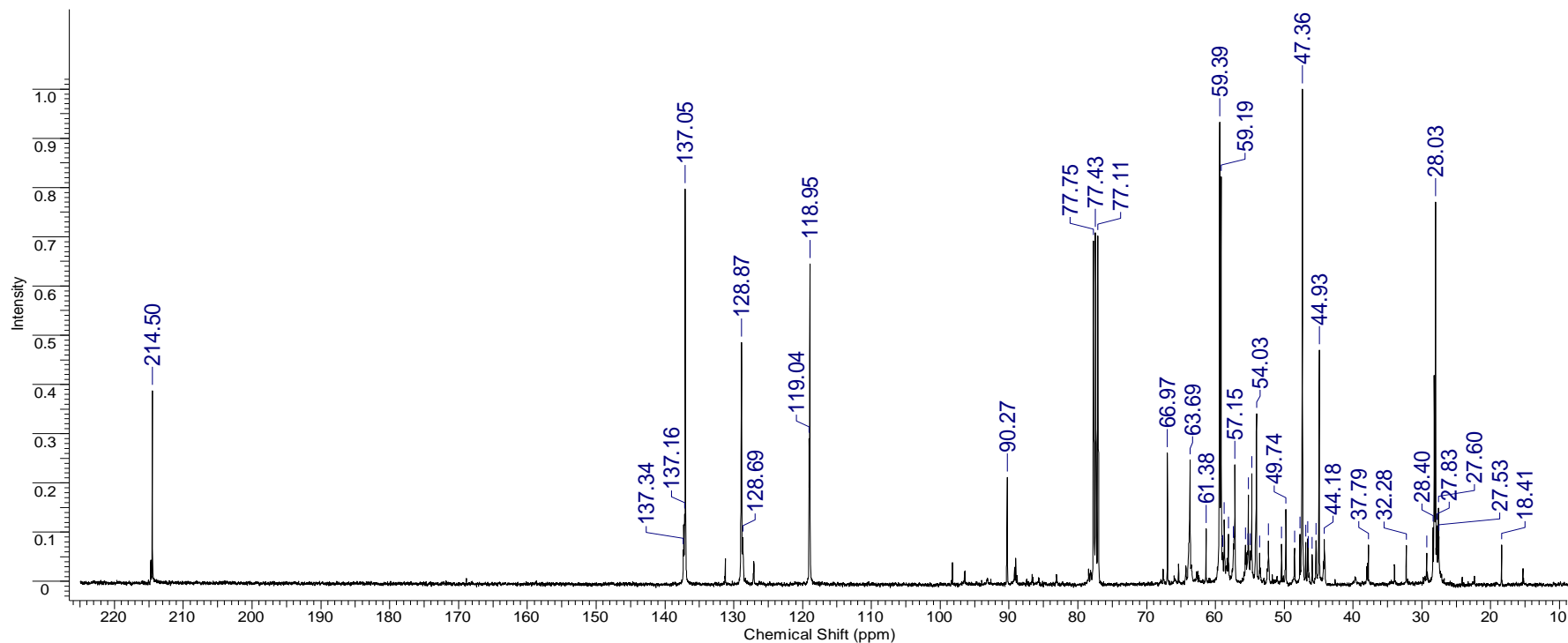
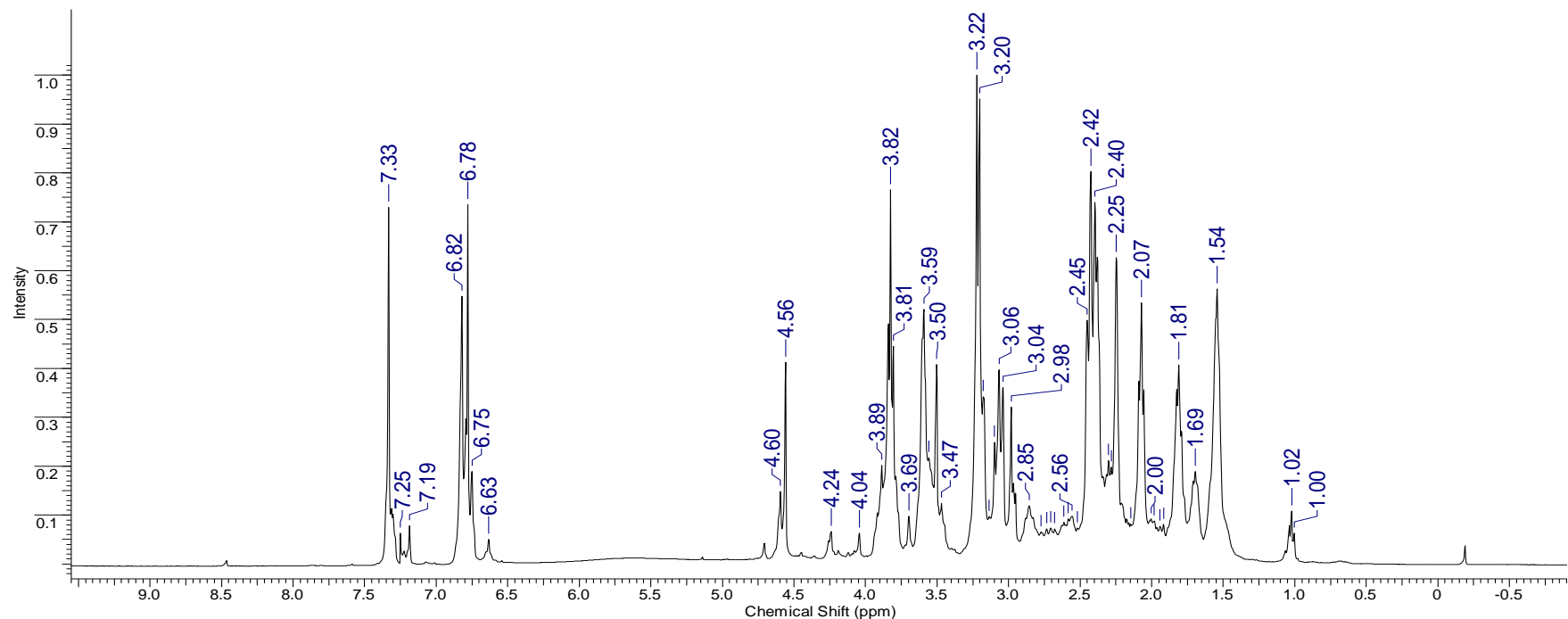


Figure S8. ^1H NMR spectrum of 1-(3-hydroxypropyl)piperidin-4-one (**1b**) in CHCl_3



No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height
1	18.41	1850.9	0.0738	16	45.94	4618.0	0.0548	31	55.30	5559.2	0.0621	46	77.63	7804.0	0.3023
2	27.53	2767.2	0.0915	17	46.50	4674.6	0.0559	32	55.54	5583.2	0.0588	47	77.75	7815.5	0.6918
3	27.60	2774.9	0.1485	18	46.58	4682.2	0.0867	33	55.65	5593.7	0.0739	48	90.27	9073.9	0.2111
4	27.70	2784.5	0.0537	19	46.87	4712.0	0.0789	34	57.15	5745.2	0.2371	49	118.95	11957.0	0.6447
5	27.83	2797.9	0.1132	20	47.36	4760.8	1.0000	35	57.40	5770.1	0.0766	50	119.04	11966.6	0.2898
6	27.93	2807.5	0.0674	21	47.74	4799.2	0.0955	36	58.13	5843.9	0.0958	51	128.69	12936.6	0.0891
7	28.03	2818.0	0.7700	22	48.50	4875.9	0.0669	37	58.71	5901.4	0.1253	52	128.87	12954.8	0.4853
8	28.22	2837.2	0.4182	23	49.74	5000.5	0.1465	38	58.94	5925.4	0.0579	53	137.05	13777.1	0.7972
9	28.40	2854.4	0.1099	24	50.37	5063.7	0.0756	39	59.19	5950.3	0.8214	54	137.16	13787.7	0.1362
10	29.31	2946.5	0.0573	25	52.32	5259.2	0.0819	40	59.39	5970.4	0.9327	55	137.26	13798.2	0.1148
11	32.28	3244.5	0.0732	26	53.59	5386.7	0.0569	41	61.38	6169.8	0.1068	56	137.34	13805.9	0.0634
12	37.79	3798.5	0.0739	27	54.03	5431.8	0.3406	42	63.69	6402.7	0.2461	57	214.50	21562.8	0.3870
13	44.18	4440.7	0.0848	28	54.71	5499.8	0.2190	43	66.97	6732.4	0.2609				
14	44.93	4516.4	0.4697	29	54.94	5522.8	0.0615	44	77.11	7751.3	0.7021				
15	45.39	4562.4	0.0829	30	55.23	5551.6	0.1754	45	77.43	7783.8	0.7081				

Figure S9. ^{13}C NMR spectrum of 1-(3-hydroxypropyl)piperidin-4-one (**1b**) in CHCl_3



No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height
1	1.00	401.3	0.0629	15	2.40	958.3	0.7392	29	3.06	1225.3	0.3975	43	4.04	1615.9	0.0628
2	1.02	407.4	0.1084	16	2.42	968.9	0.8030	30	3.10	1239.0	0.2486	44	4.24	1695.3	0.0668
3	1.54	616.5	0.5625	17	2.45	979.6	0.4987	31	3.14	1254.3	0.0966	45	4.56	1821.9	0.4126
4	1.69	677.5	0.1893	18	2.52	1007.1	0.0736	32	3.18	1269.5	0.3421	46	4.60	1837.2	0.1484
5	1.81	723.3	0.4072	19	2.56	1022.3	0.0972	33	3.20	1280.2	0.9515	47	6.63	2652.0	0.0507
6	1.92	766.0	0.0810	20	2.58	1033.0	0.0919	34	3.22	1287.9	1.0000	48	6.75	2697.8	0.1895
7	1.94	776.7	0.0772	21	2.61	1045.2	0.0850	35	3.47	1387.0	0.1242	49	6.78	2710.0	0.7354
8	1.98	793.5	0.0875	22	2.68	1071.2	0.0714	36	3.50	1400.8	0.4083	50	6.82	2726.8	0.5472
9	2.00	801.1	0.0918	23	2.71	1081.9	0.0735	37	3.56	1422.1	0.2176	51	7.19	2873.2	0.0782
10	2.07	828.6	0.5338	24	2.73	1092.5	0.0717	38	3.59	1435.9	0.5212	52	7.25	2899.2	0.0632
11	2.15	857.6	0.0812	25	2.77	1109.3	0.0658	39	3.69	1477.1	0.0973	53	7.33	2931.2	0.7295
12	2.25	898.8	0.6265	26	2.85	1141.4	0.1193	40	3.81	1521.3	0.4456				
13	2.28	912.5	0.1977	27	2.98	1191.7	0.3205	41	3.82	1528.9	0.7653				
14	2.30	920.1	0.2114	28	3.04	1214.6	0.3607	42	3.89	1553.4	0.2020				

Figure S10. ^1H NMR spectrum of 3-(3-hydroxypropyl)-7-[3-(1*H*-imidazol-1-yl)propyl]-3,7-diazabicyclo[3.3.1]nonan-9-one (**2b**)_{in} CHCl_3

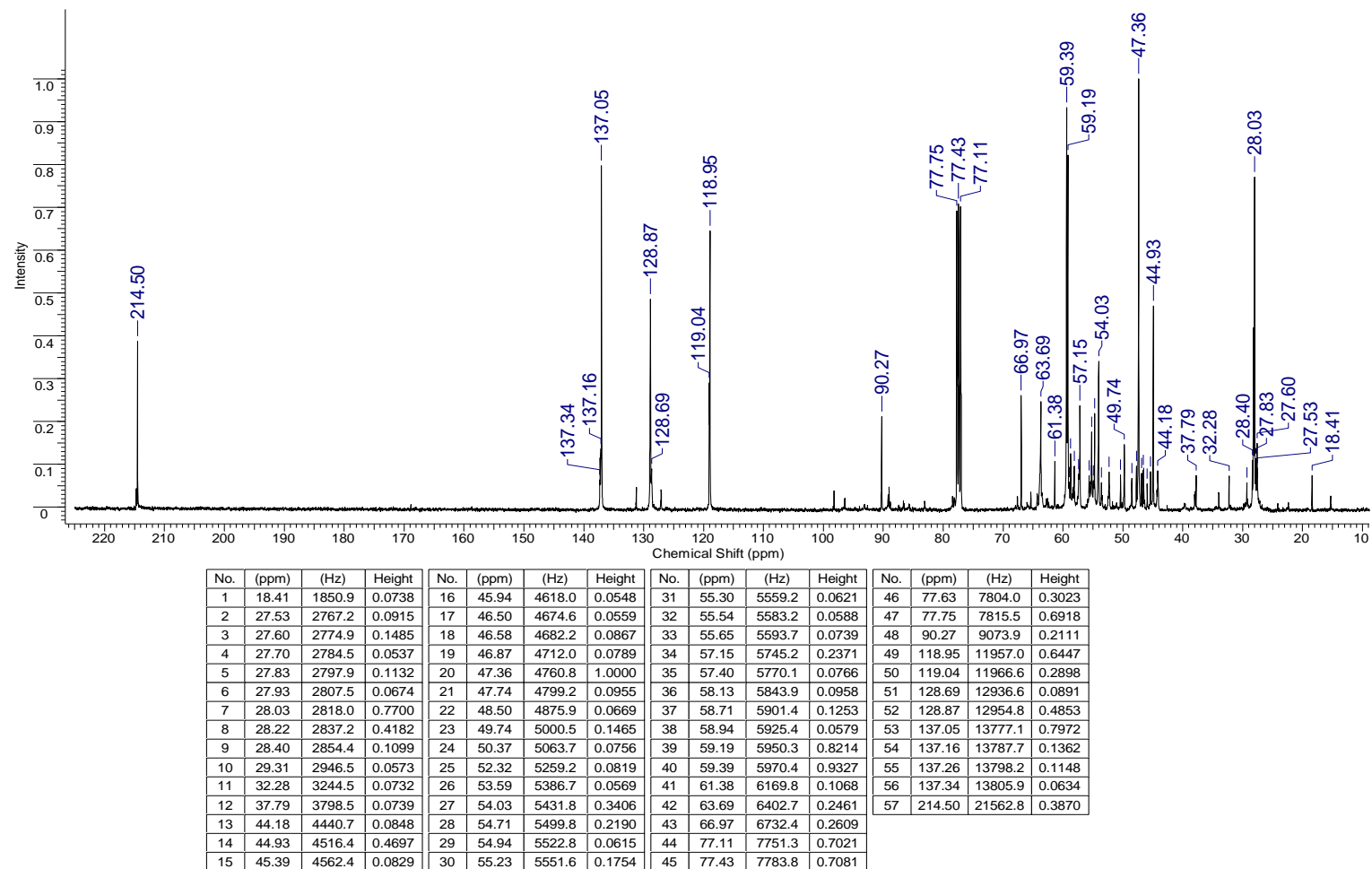
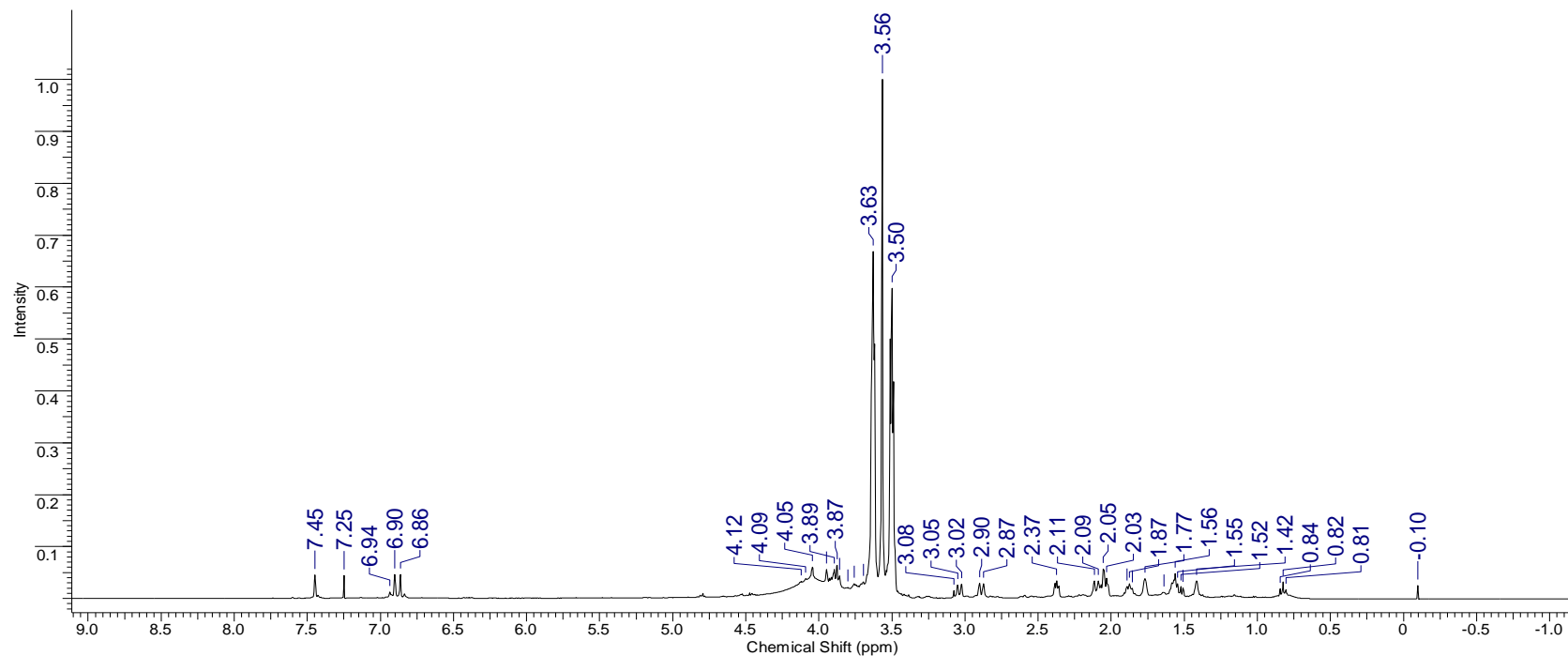
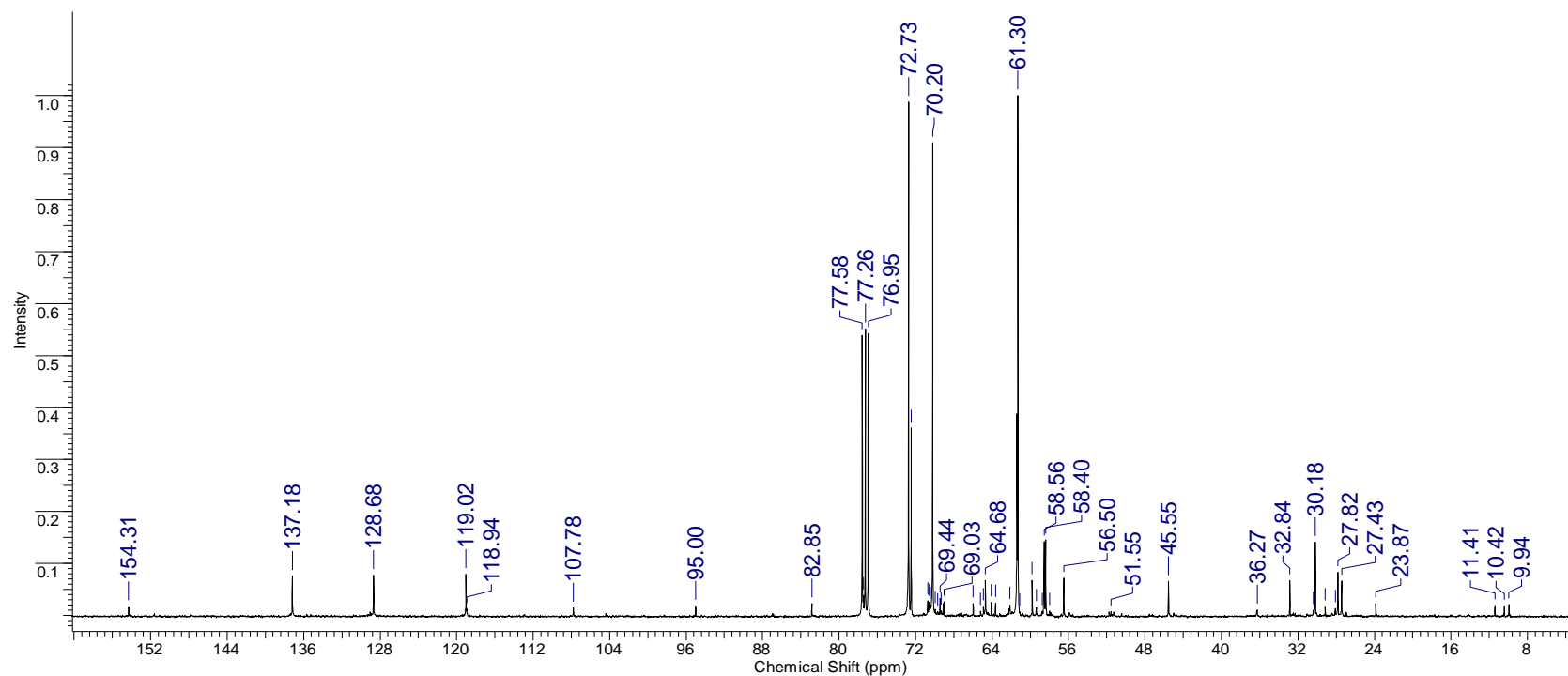


Figure S11. ^{13}C NMR spectrum of 3-(3-hydroxypropyl)-7-[3-(1*H*-imidazol-1-yl)propyl]-3,7-diazabicyclo[3.3.1]nonan-9-one (**2b**)_{in} CHCl_3



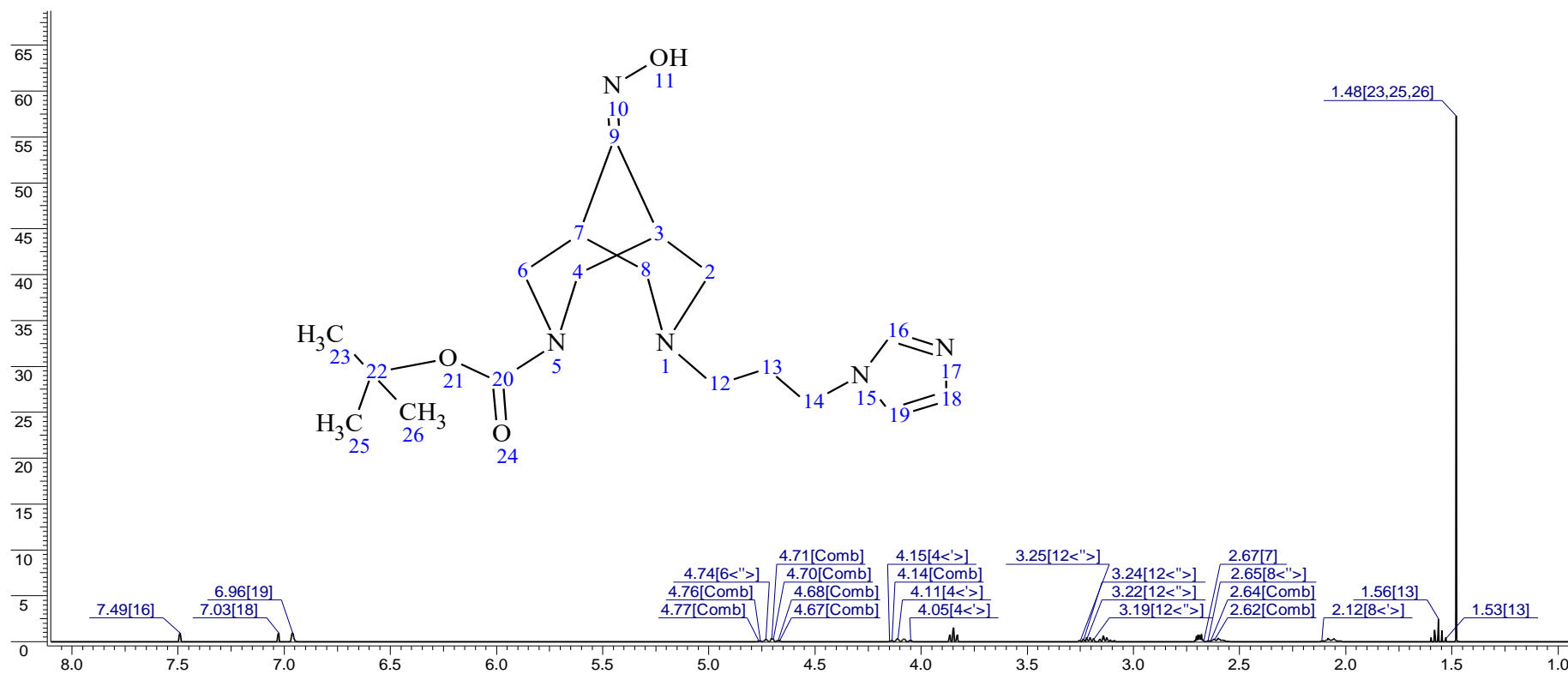
No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height
1	-0.10	-39.7	0.0254	12	1.85	741.6	0.0200	23	3.05	1219.2	0.0260	34	3.95	1577.8	0.0556
2	0.81	322.0	0.0169	13	1.87	749.2	0.0289	24	3.08	1229.9	0.0155	35	4.05	1617.4	0.0602
3	0.82	329.6	0.0317	14	1.89	756.8	0.0232	25	3.50	1399.2	0.5973	36	4.09	1635.8	0.0385
4	0.84	337.2	0.0189	15	2.03	811.8	0.0389	26	3.56	1425.2	1.0000	37	4.12	1648.0	0.0326
5	1.42	566.1	0.0334	16	2.05	820.9	0.0566	27	3.63	1451.1	0.6684	38	6.86	2743.5	0.0458
6	1.51	602.7	0.0208	17	2.09	834.7	0.0333	28	3.69	1477.1	0.0324	39	6.90	2758.8	0.0462
7	1.52	608.8	0.0234	18	2.11	845.3	0.0335	29	3.76	1503.0	0.0281	40	6.94	2772.5	0.0128
8	1.55	618.0	0.0284	19	2.37	949.1	0.0339	30	3.80	1519.8	0.0213	41	7.25	2897.7	0.0442
9	1.56	624.1	0.0478	20	2.87	1149.0	0.0287	31	3.86	1542.7	0.0438	42	7.45	2977.0	0.0452
10	1.64	654.6	0.0117	21	2.90	1159.7	0.0297	32	3.87	1548.8	0.0637				
11	1.77	706.5	0.0378	22	3.02	1208.5	0.0277	33	3.89	1556.4	0.0561				

Figure S12. ^1H NMR spectrum of 3-(3-hydroxypropyl)-7-[3-(1*H*-imidazol-1-yl)propyl]-3,7-diazabicyclo[3.3.1]nonane (**3b**) in CHCl_3



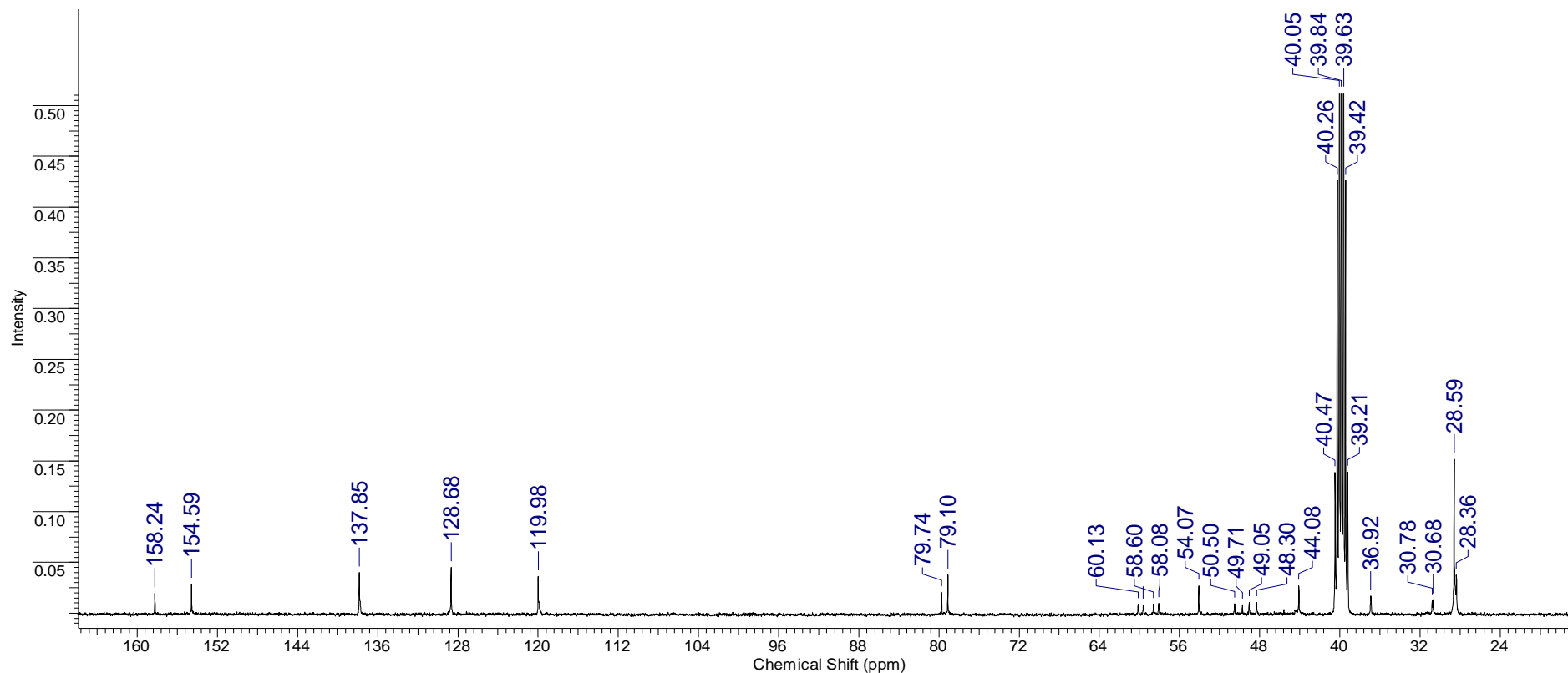
No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height
1	9.94	998.9	0.0216	16	56.50	5680.0	0.0718	31	64.89	6523.5	0.0179	46	76.95	7735.0	0.5423
2	10.42	1047.7	0.0183	17	57.98	5828.6	0.0089	32	65.20	6554.1	0.0086	47	77.26	7766.6	0.5518
3	11.41	1147.4	0.0198	18	58.40	5870.7	0.1460	33	65.97	6631.8	0.0235	48	77.46	7786.7	0.0385
4	23.87	2399.2	0.0231	19	58.56	5887.0	0.1426	34	69.03	6939.4	0.0264	49	77.58	7799.2	0.5388
5	27.43	2757.6	0.0668	20	58.73	5904.3	0.0086	35	69.08	6944.2	0.0230	50	82.85	8328.2	0.0231
6	27.82	2796.9	0.0834	21	59.37	5968.5	0.0160	36	69.31	6967.2	0.0091	51	95.00	9550.3	0.0184
7	28.11	2825.7	0.0138	22	59.80	6011.6	0.0681	37	69.44	6980.6	0.0328	52	107.78	10834.6	0.0148
8	29.16	2931.1	0.0179	23	61.09	6141.0	0.0073	38	69.70	7006.5	0.0079	53	118.94	11956.0	0.0118
9	30.18	3033.7	0.1410	24	61.30	6162.1	1.0000	39	69.95	7031.4	0.0124	54	119.02	11964.7	0.0791
10	30.40	3055.7	0.0104	25	61.40	6172.7	0.3879	40	70.20	7057.3	0.9083	55	128.68	12935.6	0.0773
11	32.84	3301.1	0.0678	26	62.14	6246.5	0.0206	41	70.45	7082.2	0.0201	56	137.18	13790.6	0.0760
12	36.27	3646.1	0.0116	27	62.20	6252.2	0.0132	42	70.61	7098.5	0.0257	57	154.31	15512.0	0.0180
13	36.33	3651.9	0.0098	28	63.63	6396.0	0.0236	43	70.73	7110.0	0.0288				
14	45.55	4578.7	0.0660	29	64.07	6441.0	0.0246	44	72.45	7283.5	0.3608				
15	51.55	5182.6	0.0080	30	64.68	6502.4	0.0674	45	72.73	7311.3	0.9870				

Figure S13. ^{13}C NMR spectrum of 3-(3-hydroxypropyl)-7-[3-(1*H*-imidazol-1-yl)propyl]-3,7-diazabicyclo[3.3.1]nonane (**3b**)_in_ CHCl_3



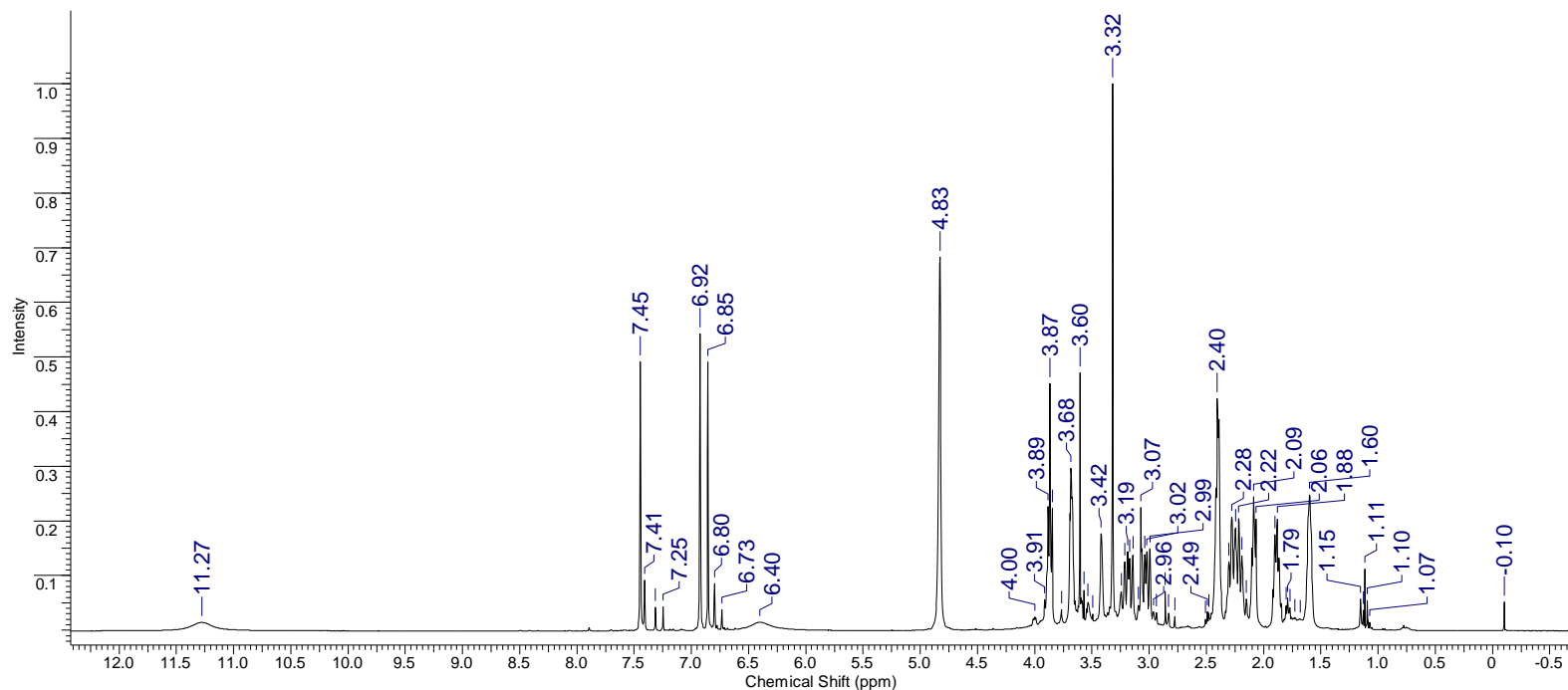
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6<'>	1	4.72	0.63	16	1	7.49	0.11
6<'>	1	4.10	0.40	18	1	7.03	0.09
7	1	2.69	0.68	19	1	6.96	0.15
8<'>	1	2.60	0.34	23,25,26	9	1.48	0.05
8<'>	1	2.07	0.33				

Figure S14. ^1H NMR spectrum of oxime of 3-(3-Boc)-7-[3-(1*H*-imidazol-1-yl)propyl]-3,7-diazabicyclo[3.3.1]nonan-9-one (**5a**)_{in_DMSO}



No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height
1	28.36	2850.6	0.0375	11	40.26	4046.8	0.4265	21	59.60	5991.5	0.0082
2	28.59	2873.6	0.1518	12	40.47	4067.9	0.1388	22	60.13	6044.2	0.0088
3	30.68	3084.5	0.0135	13	44.08	4431.1	0.0269	23	79.10	7951.6	0.0378
4	30.78	3094.1	0.0124	14	48.30	4855.7	0.0106	24	79.74	8015.8	0.0204
5	36.92	3711.3	0.0169	15	49.05	4930.5	0.0108	25	119.98	12061.5	0.0362
6	39.21	3941.3	0.1391	16	49.71	4997.6	0.0084	26	128.68	12935.6	0.0453
7	39.42	3962.4	0.4265	17	50.50	5076.2	0.0090	27	137.85	13857.6	0.0401
8	39.63	3983.5	0.8513	18	54.07	5435.6	0.0267	28	154.59	15539.8	0.0288
9	39.84	4004.6	1.0000	19	58.08	5838.2	0.0097	29	158.24	15906.8	0.0196
10	40.05	4025.7	0.8513	20	58.60	5890.9	0.0086				

Figure S15. ^{13}C NMR spectrum of oxime of 3-(3-Boc)-7-[3-(1*H*-imidazol-1-yl)propyl]-3,7-diazabicyclo[3.3.1]nonan-9-one (**5a**)_in_DMSO



No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height
1	-0.10	-41.2	0.0513	18	2.19	875.9	0.1362	35	3.07	1228.3	0.2248	52	3.89	1553.4	0.2263
2	1.07	428.8	0.0146	19	2.22	886.5	0.2042	36	3.10	1237.5	0.0456	53	3.91	1564.0	0.0559
3	1.10	437.9	0.0547	20	2.24	897.2	0.1873	37	3.14	1255.8	0.1377	54	4.00	1599.1	0.0239
4	1.11	445.6	0.1123	21	2.28	911.0	0.2066	38	3.17	1268.0	0.1311	55	4.83	1930.2	0.6824
5	1.13	451.7	0.0362	22	2.31	921.6	0.1253	39	3.19	1274.1	0.1438	56	6.40	2558.9	0.0146
6	1.15	460.8	0.0565	23	2.40	961.3	0.4237	40	3.21	1284.8	0.1253	57	6.73	2691.7	0.0377
7	1.60	639.4	0.2477	24	2.48	990.3	0.0311	41	3.24	1297.0	0.0703	58	6.80	2717.6	0.0857
8	1.68	671.4	0.0209	25	2.49	996.4	0.0336	42	3.32	1327.5	1.0000	59	6.85	2740.5	0.4908
9	1.73	691.2	0.0228	26	2.51	1002.5	0.0200	43	3.42	1367.2	0.1763	60	6.92	2768.0	0.5424
10	1.77	708.0	0.0406	27	2.77	1109.3	0.0253	44	3.49	1396.2	0.0298	61	7.25	2897.7	0.0426
11	1.79	715.6	0.0588	28	2.83	1132.2	0.0311	45	3.53	1413.0	0.0504	62	7.31	2923.6	0.0420
12	1.81	721.8	0.0444	29	2.86	1142.9	0.0714	46	3.57	1426.7	0.0730	63	7.41	2961.7	0.0917
13	1.88	752.3	0.2029	30	2.94	1173.4	0.0321	47	3.60	1440.4	0.4707	64	7.45	2977.0	0.4913
14	1.90	759.9	0.1748	31	2.96	1184.1	0.0335	48	3.68	1472.5	0.2965	65	11.27	4507.5	0.0142
15	2.06	825.5	0.2029	32	2.99	1196.3	0.1489	49	3.77	1506.1	0.0370				
16	2.09	834.7	0.2438	33	3.02	1208.5	0.1435	50	3.85	1538.1	0.2225				
17	2.15	860.6	0.0573	34	3.04	1214.6	0.1384	51	3.87	1545.7	0.4513				

Figure S16. ^1H NMR spectrum of oxime of 3-(3-hydroxypropyl)-7-[3-(1*H*-imidazol-1-yl)propyl]-3,7-diazabicyclo[3.3.1]nonan-9-one (5b)_in_ CHCl_3

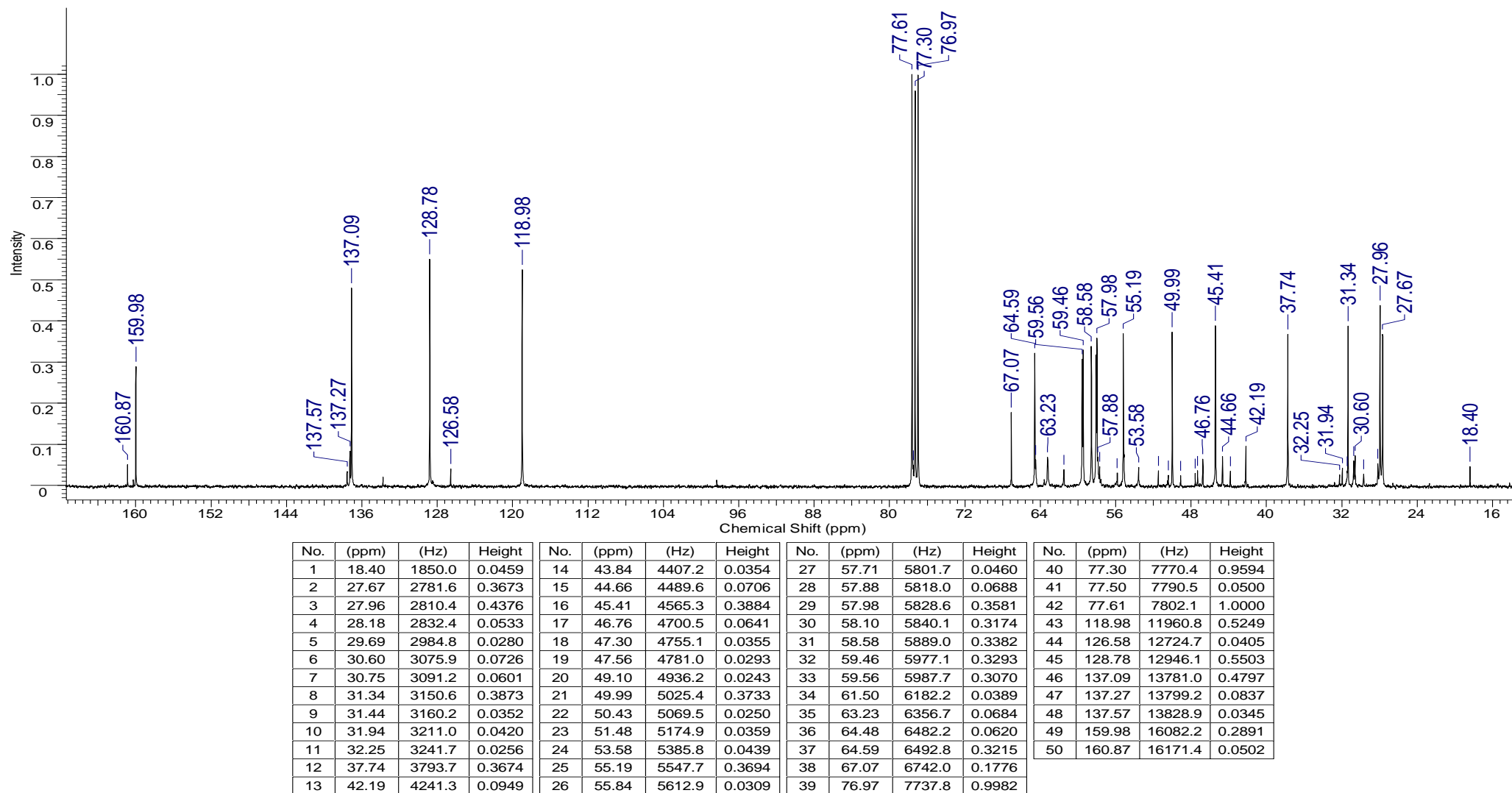


Figure S17. ^{13}C NMR spectrum of oxime of 3-(3-hydroxypropyl)-7-[3-(1*H*-imidazol-1-yl)propyl]-3,7-diazabicyclo[3.3.1]nonan-9-one (5b)_{in} CHCl_3

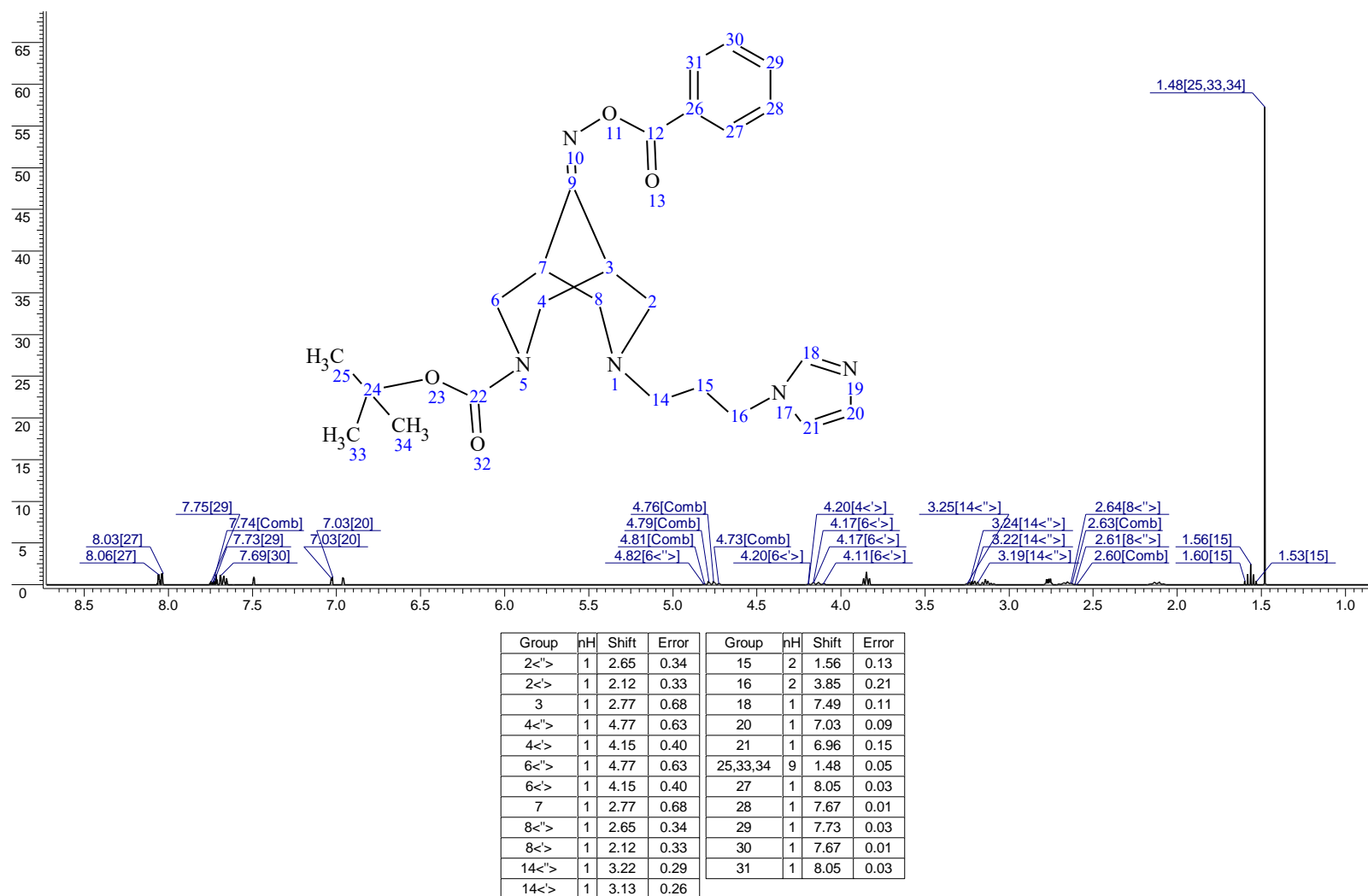
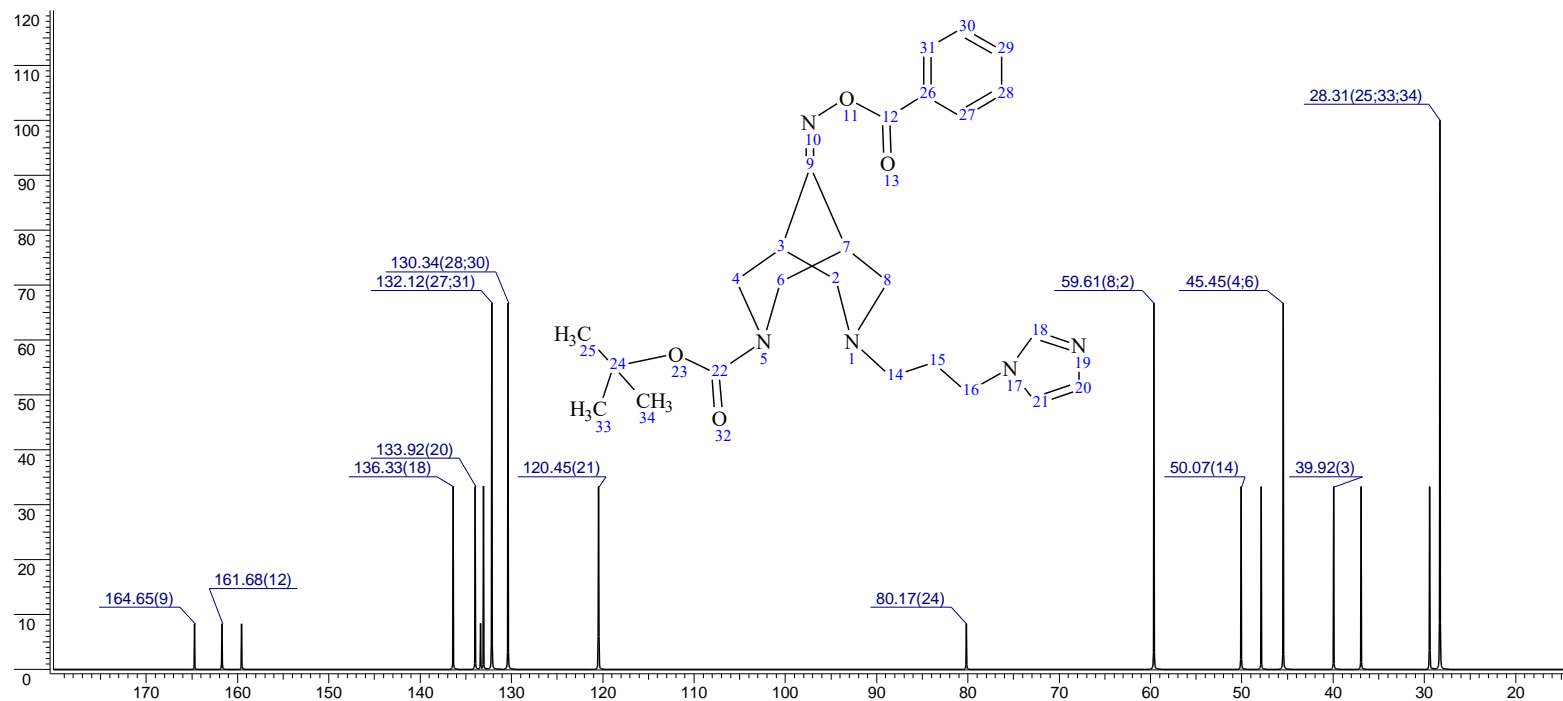


Figure S18. ^1H NMR spectrum of O-benzoyloxime of 3-(3-Boc)-7-[3-(1H-imidazol-1-yl)propyl]-3,7-diazabicyclo[3.3.1]nonan-9-one (6a) in DMSO



Carbon No.	CHn	Chem. Shifts	Conf. Limits	Carbon No.	CHn	Chem. Shifts	Conf. Limits
2	CH ₂	59.61	2.4	21	CH	120.45	2
3	CH	39.92	8.7	22	C	159.52	2.7
4	CH ₂	45.45	5.3	24	C	80.17	1
6	CH ₂	45.45	5.3	25	CH ₃	28.31	1
7	CH	36.92	8.7	26	C	133.35	---
8	CH ₂	59.61	2.4	27	CH	132.12	1.5
9	C	164.65	1.5	28	CH	130.34	0.7
12	C	161.68	0.3	29	CH	133	1.2
14	CH ₂	50.07	4.3	30	CH	130.34	0.7
15	CH ₂	29.44	2.3	31	CH	132.12	1.5
16	CH ₂	47.85	4.7	33	CH ₃	28.31	1
18	CH	136.33	2	34	CH ₃	28.31	1
20	CH	133.92	1.5				

Figure S19. ^{13}C NMR spectrum O-benzoyloxime of 3-(3-Boc)-7-[3-(1*H*-imidazol-1-yl)propyl]-3,7-diazabicyclo[3.3.1]nonan-9-one (6a)_in_DMSO

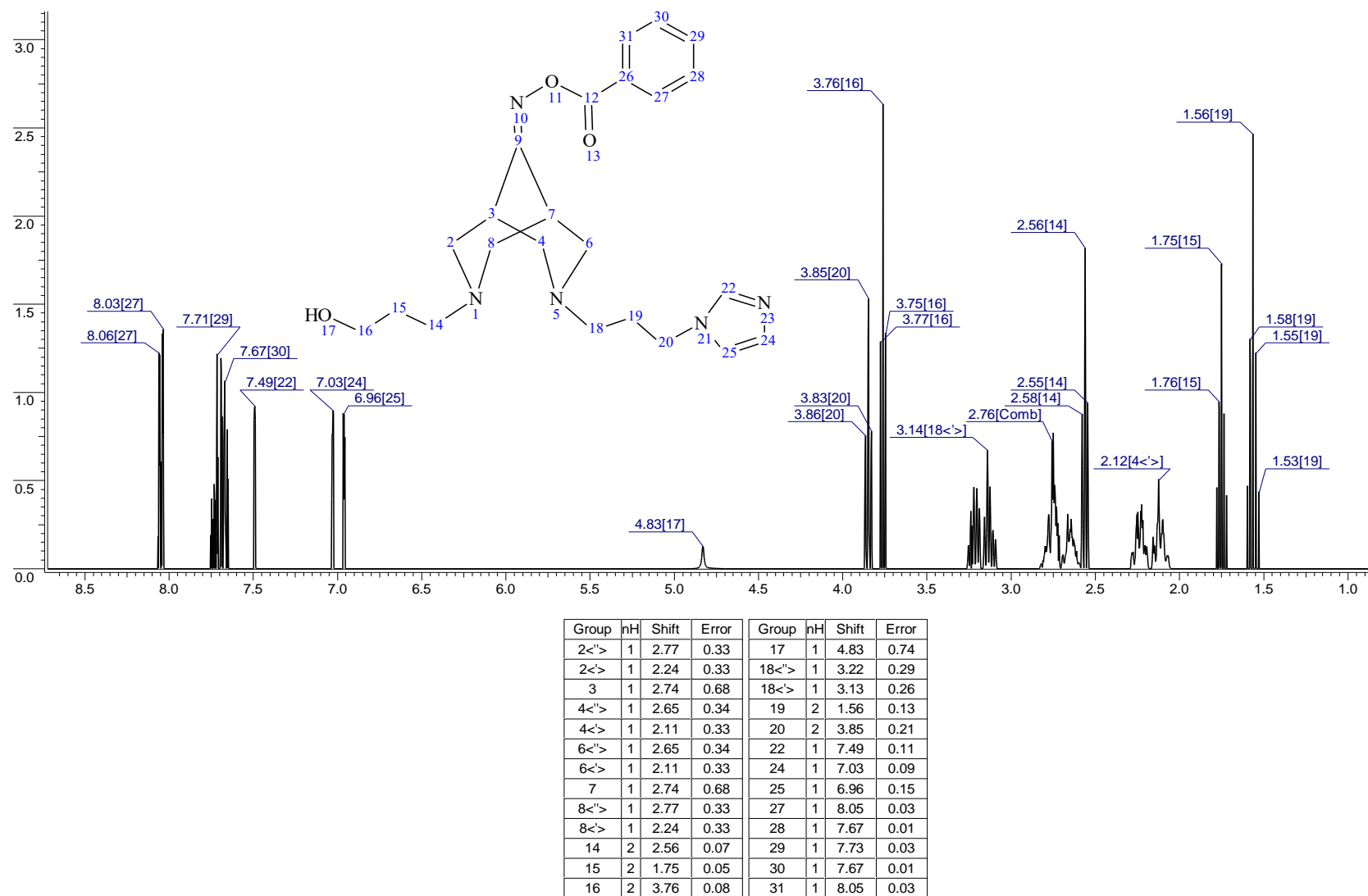


Figure S20. ¹H NMR spectrum of O-benzoyloxime of 3-(3-hydroxypropyl)-7-[3-(1H-imidazol-1-yl)propyl]-3,7-diazabicyclo[3.3.1]nonan-9-one (6b)_in_CHCl₃

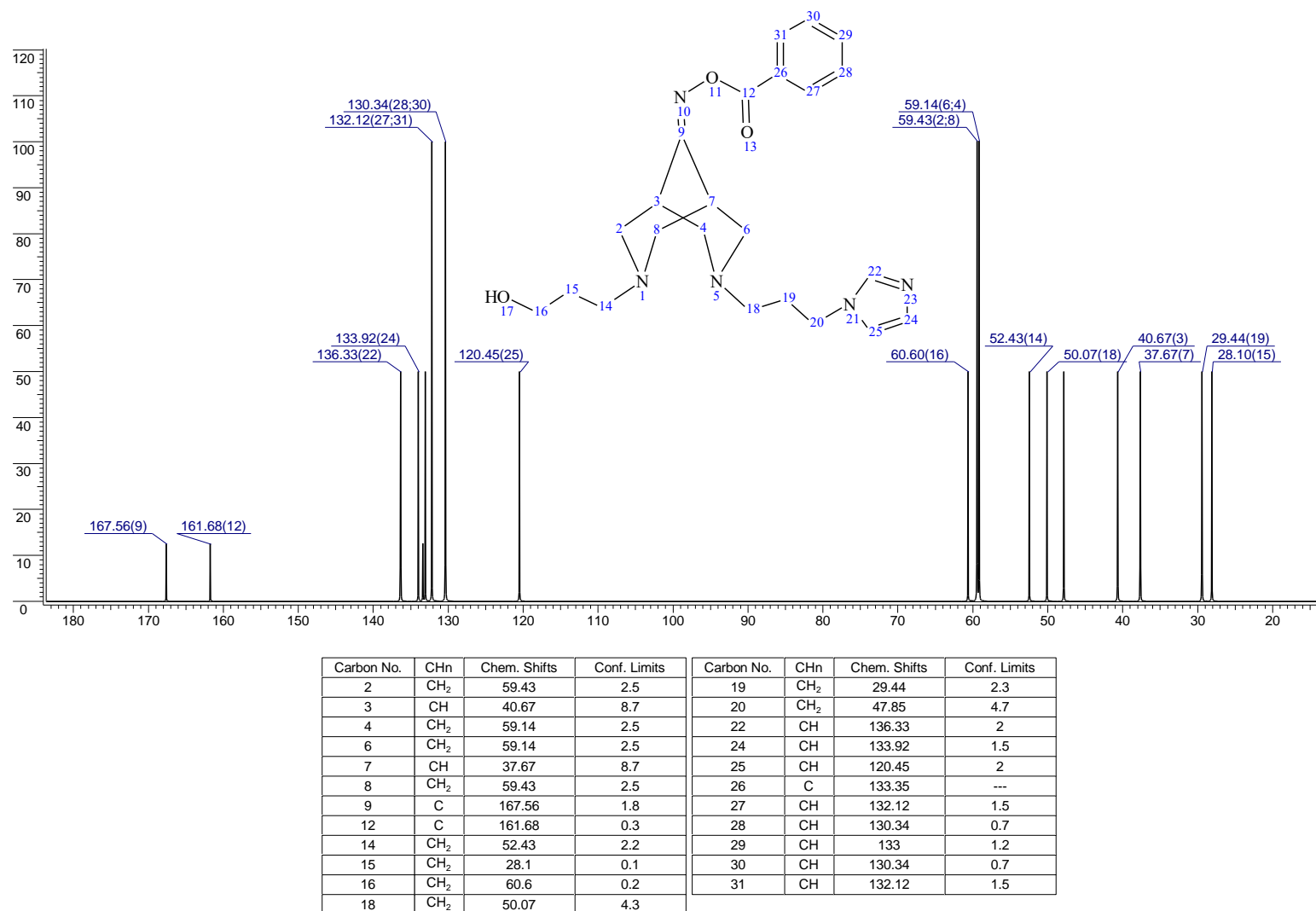


Figure S21. ¹³C NMR spectrum of O-benzoyloxime of 3-(3-hydroxypropyl)-7-[3-(1H-imidazol-1-yl)propyl]-3,7-diazabicyclo[3.3.1]nonan-9-one (6b)_in_CHCl₃