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SUPPORTING INFORMATION

Structural isomers of saligenin-based β2-agonists: synthesis and insight into the reaction mechanism

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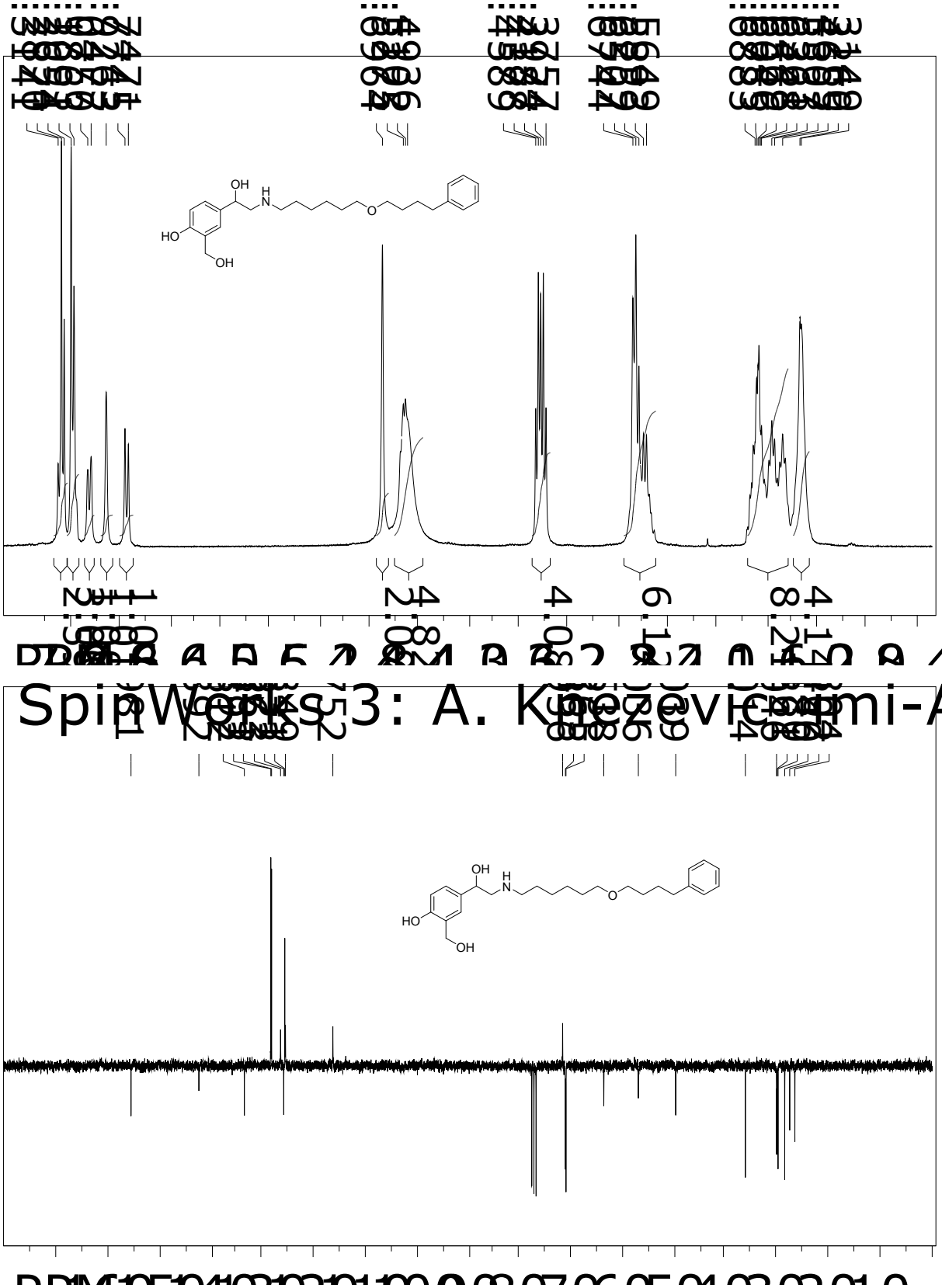
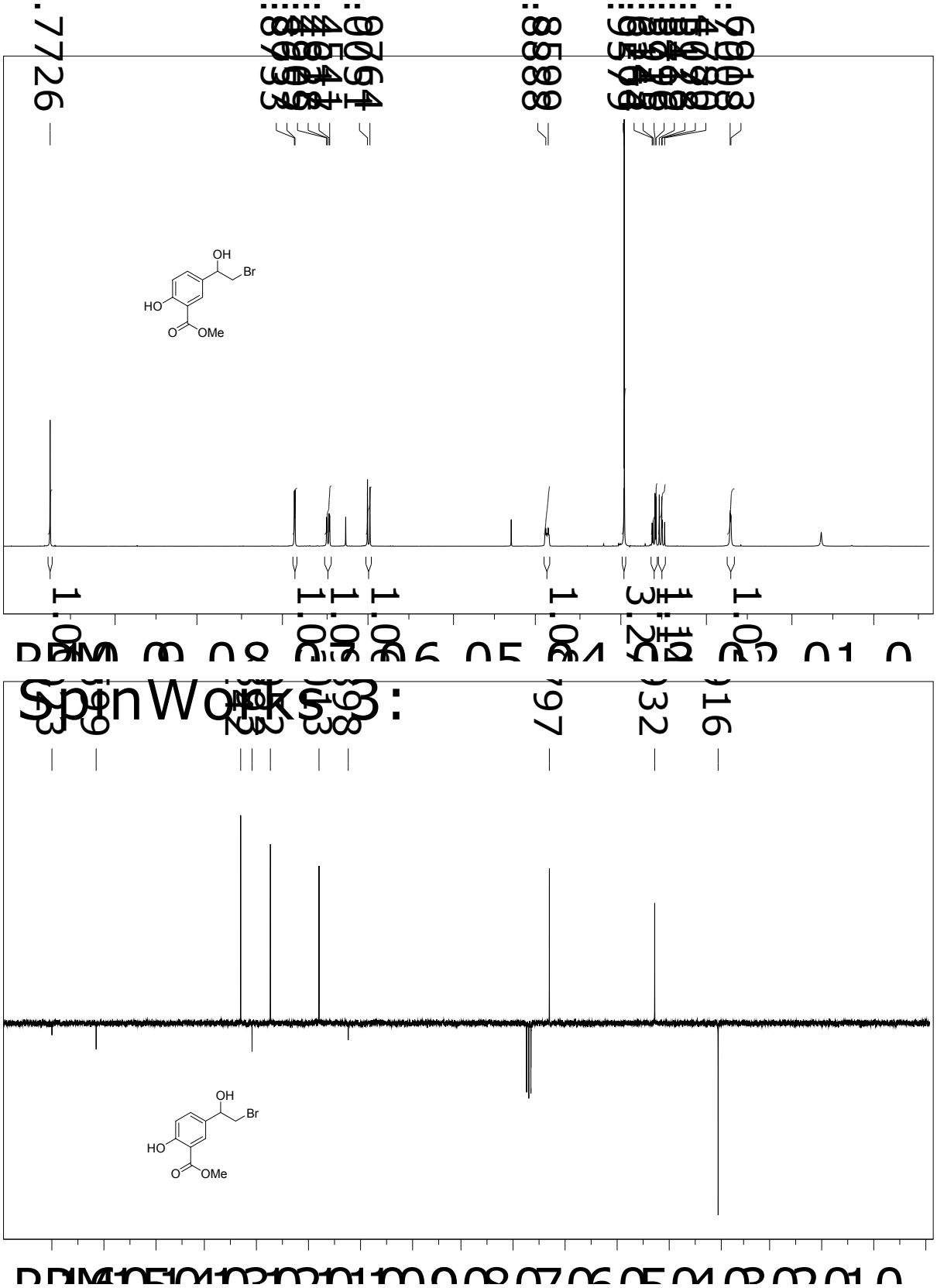
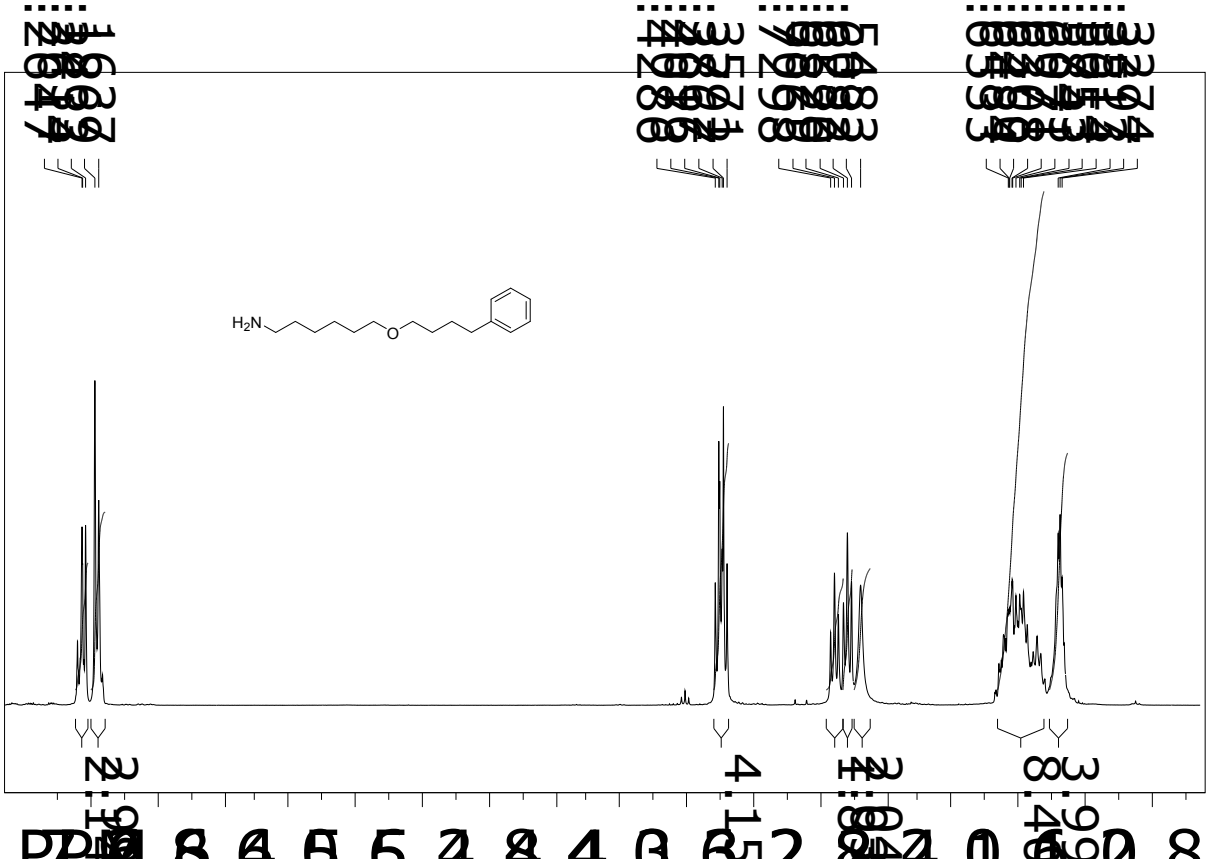


NMR spectra of methyl 5-(2-bromo-1-hydroxy-ethyl)-salicylate (**3**)



NMR spectra of 6-(4-phenyl-butoxy)-hexylamine (**4**)



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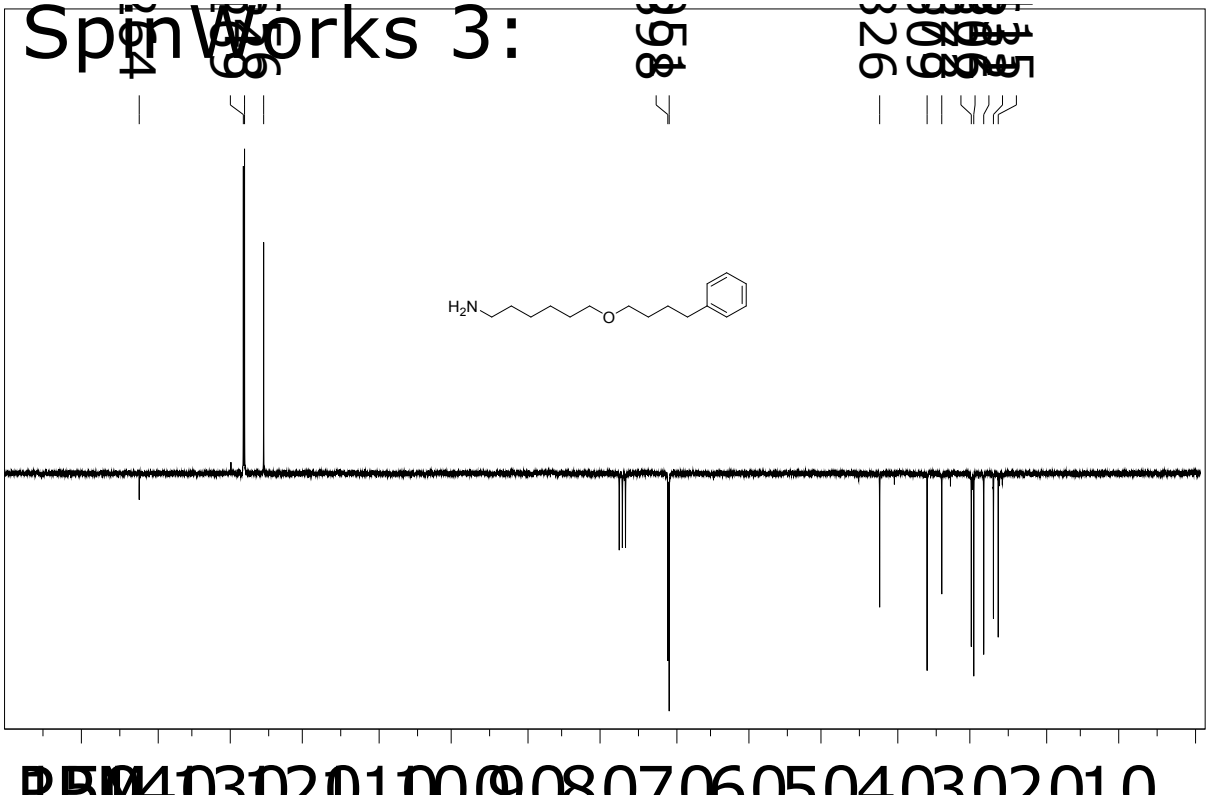
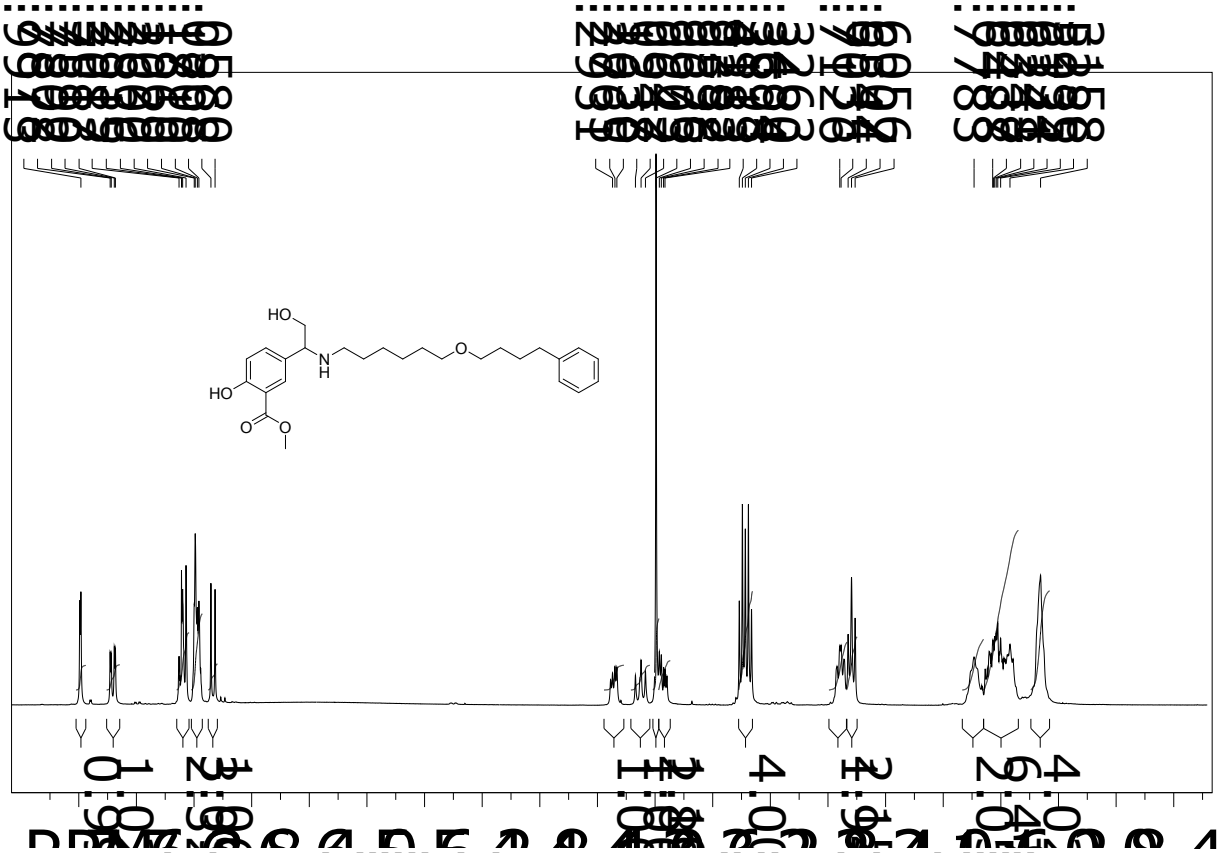
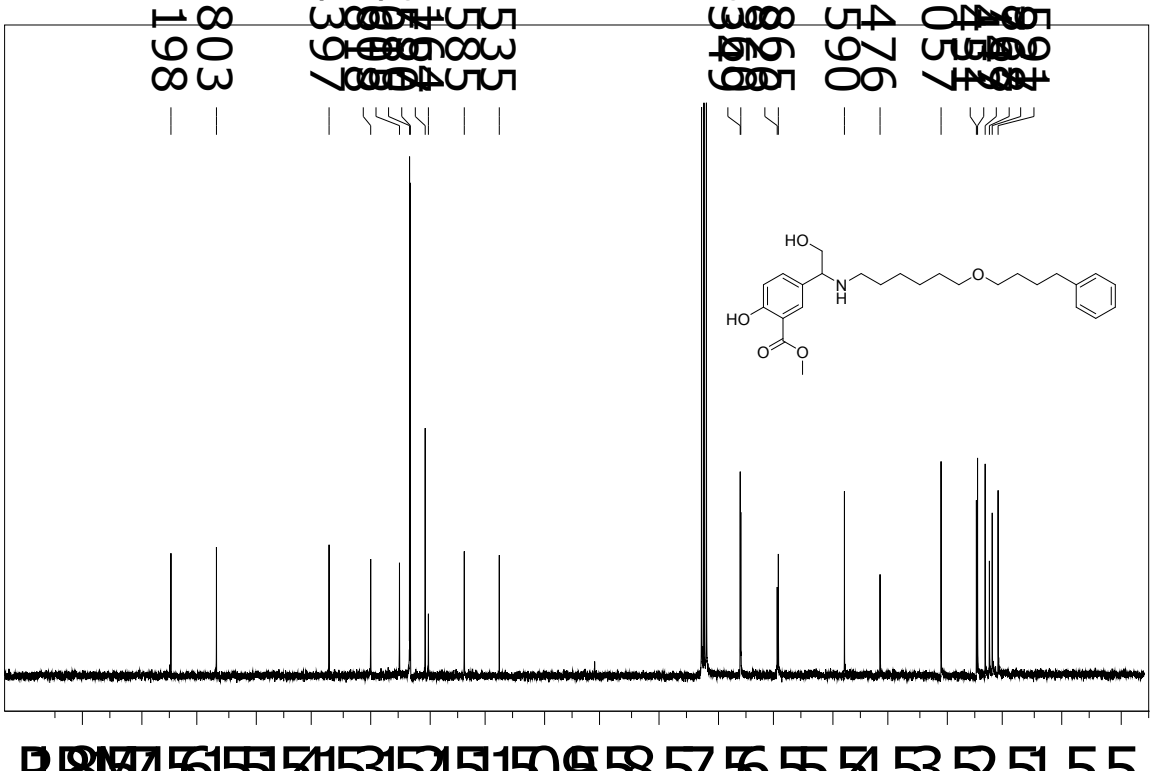
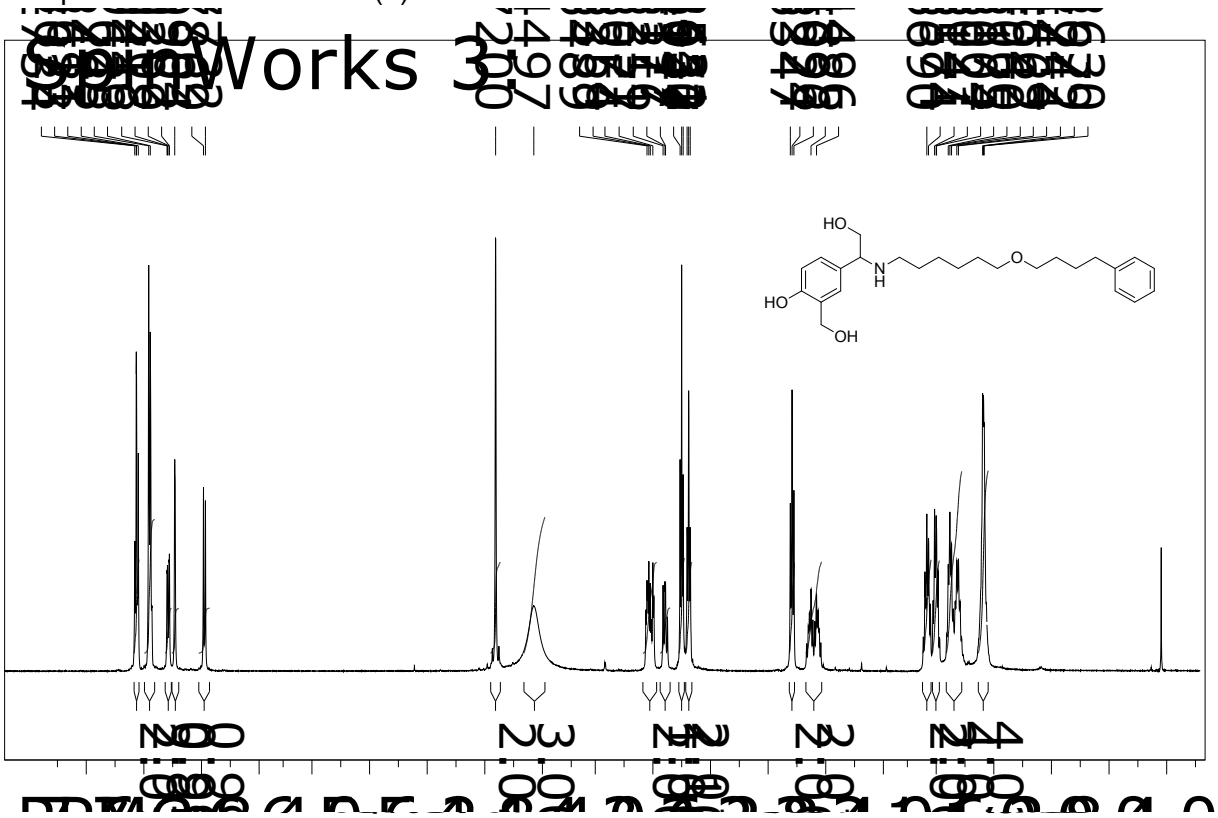


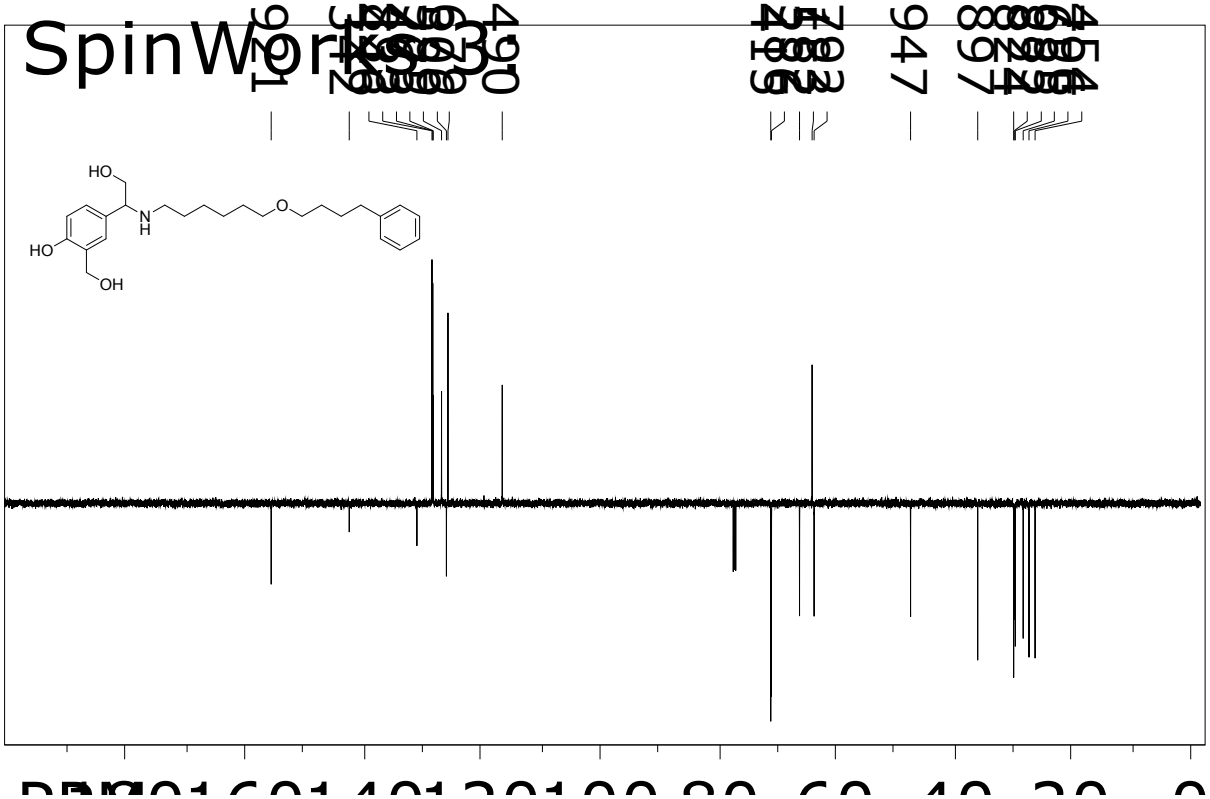
NMR spectra of methyl 5-{2-hydroxy-1-[6-(4-phenyl-butoxy)-hexylamino]-ethyl}-salicylate (**6**)



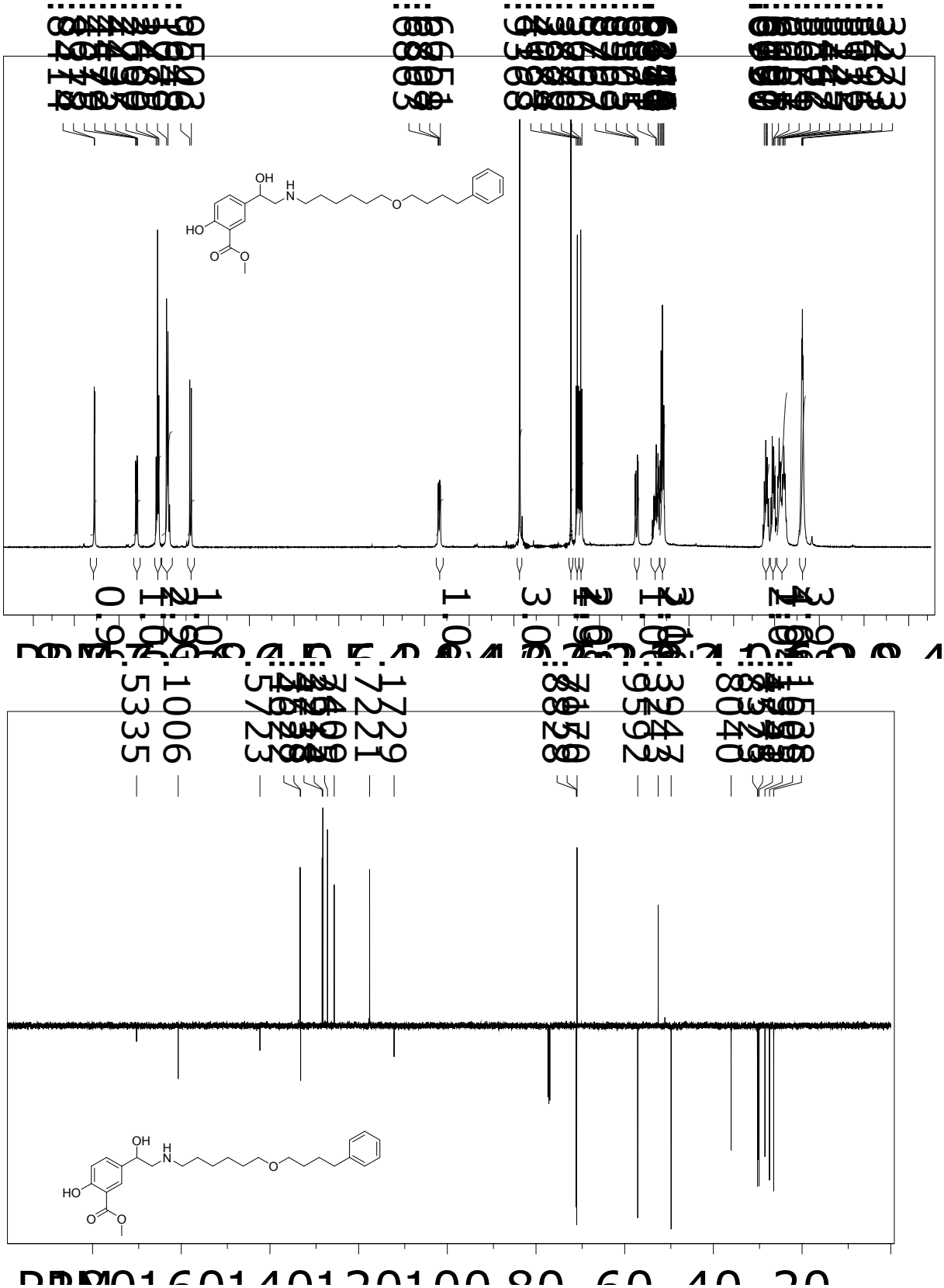


NMR spectra of iso-salmeterol (**7**)





NMR spectra of methyl 5-{2-[6-(4-phenyl-butoxy)-hexylamino]-1-hydroxy-ethyl}-salicylate (**10**)

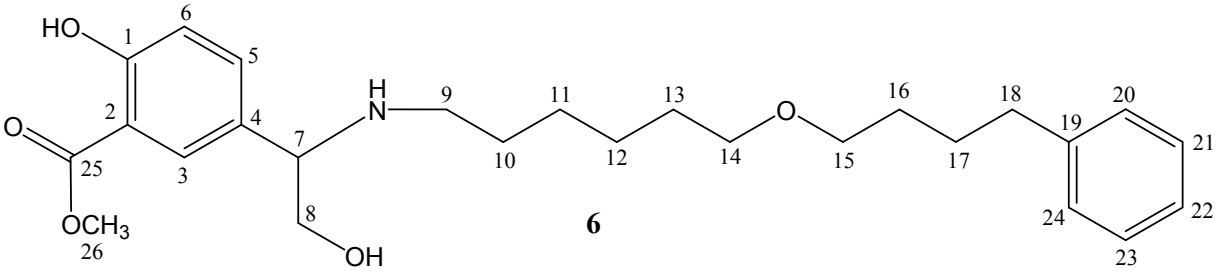


^{1}H and ^{13}C NMR chemical shifts (δ/ppm)[a] and H-H coupling ($^{3}J_{HH}$/Hz)[b] of **6** and **10**

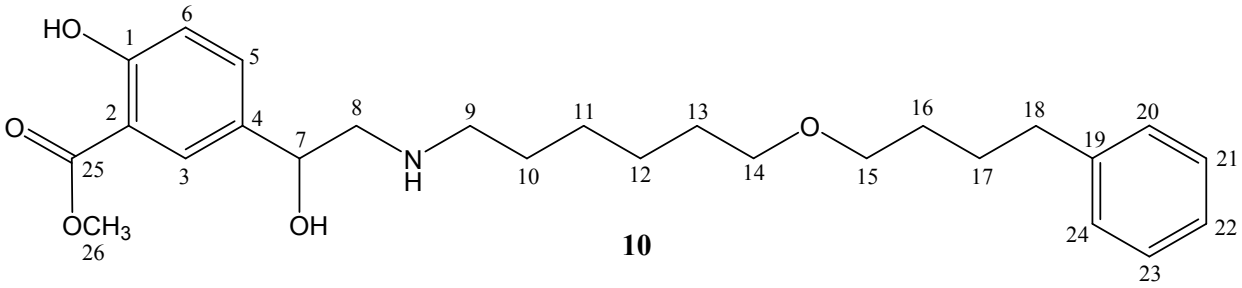
Compound / Atom	6		10	
	^{1}H δ/ppm, ^{3}J/Hz	**^{13}C δ/**ppm	**^{1}H δ/**ppm, ^{3}J/Hz	**^{13}C δ/**ppm
1		113.5		112.1
2		160.0		156.9
3	7.91 (1H), (s)	130.3	7.77 (1H), (s)	127.0
4		132.7		135.5
5	7.60 (1H), 8.61 Hz (d)	135.5	7.47 (1H), 8.51 Hz (d)	133.4
6	7.02 (1H), 8.58 Hz (d)	117.9	6.93 (1H), 8.52 Hz (d)	116.8
7	4.17 (1H), (bs)	61.9	4.57 (1H), 6.21 Hz (t)	70.4
8	3.65-3.75 (2H), (m)	62.4	2.54-2.61 (2H), (m)	57.3
9	2.55 (2H), 7.56 Hz (t)	34.9	2.45-2.53 (2H), (m)	48.8
10	1.45-1.51 (2H), (m)	28.8	1.43-1.52 (2H), (m)	29.1
11	1.18-1.25 (2H), (m)	29.9	1.23-1.29 (2H), (m)	25.5 or 26.5
12	1.18-1.25 (2H), (m)	25.9	1.23-1.29 (2H), (m)	25.5 or 26.5
13	1.38-1.44 (2H), (m)	29.1	1.34-1.40 (2H), (m)	29.4
14	3.27 or 3.31 (2H), 6.45 Hz, (t)	69.8	3.30 or 3.34 (2H), 6.46 Hz (t)	65.6 or 69.8
15	3.27 or 3.31 (2H), 6.45 Hz, (t)	69.8	3.30 or 3.34 (2H), 6.46 Hz (t)	65.6 or 69.8
16	1.45-1.51 (2H), (m)	28.8	1.43-1.52 (2H), (m)	29.1
17	1.53-1.61 (2H), (m)	27.7	1.55-1.62 (2H), (m)	27.6
18	2.48-2.52 (2H), (m)	45.5	2.54-2.61 (2H), (m)	34.8
19		142.2		142.0
20	7.23-7.28 (1H), (m)	128.3	7.23-7.28 (1H), (m)	128.0 or 128.1
21	7.13-7.18 (1H), (m)	125.7 or 128.3	7.16-7.20 (1H), (m)	128.0 or 128.1
22	7.13-7.18 (1H), (m)	125.7 or 128.3	7.13-7.15 (1H), (m)	125.5
23	7.13-7.18 (1H), (m)	125.7 or 128.3	7.16-7.20 (1H), (m)	128.0 or 128.1
24	7.23-7.28 (1H), (m)	128.3	7.23-7.28 (1H), (m)	128.0 or 128.1
25		168.8		169.2
26	3.90 (3H), (s)	52.6	3.90 (3H), (s)	52.2
1-OH	5.35 (1H), (bs)		5.30 (1H), (bs)	
8-OH	3.27 or 3.31 (2H), 6.45 Hz, (t)		3.30 or 3.34 (2H), 6.46 Hz (t)	
-NH-	3.27 or 3.31 (2H), 6.45 Hz, (t)		3.30 or 3.34 (2H), 6.46 Hz (t)	

[a] Recorded in DMSO-d_6 solution. Referred to TMS. Number of protons and multiplicity in brackets.
[b] (bs) broad singlet, (s) singlet, (d) doublet, (t) triplet, (m) multiplet,

Numeration of compounds **6** and **10** used for presentation of NMR results



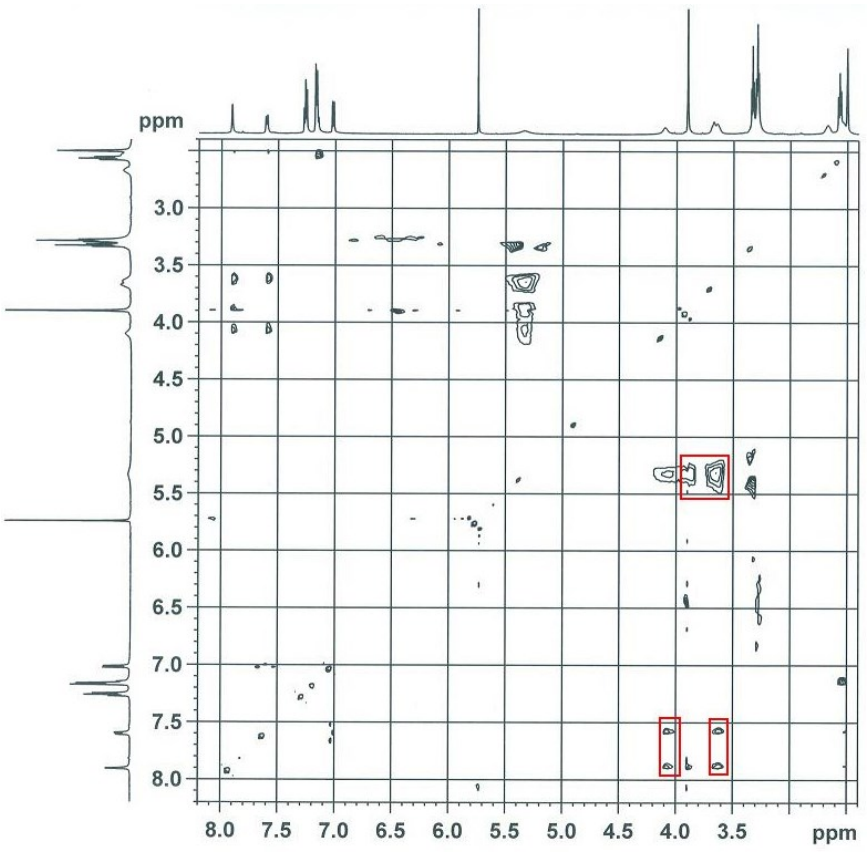
6



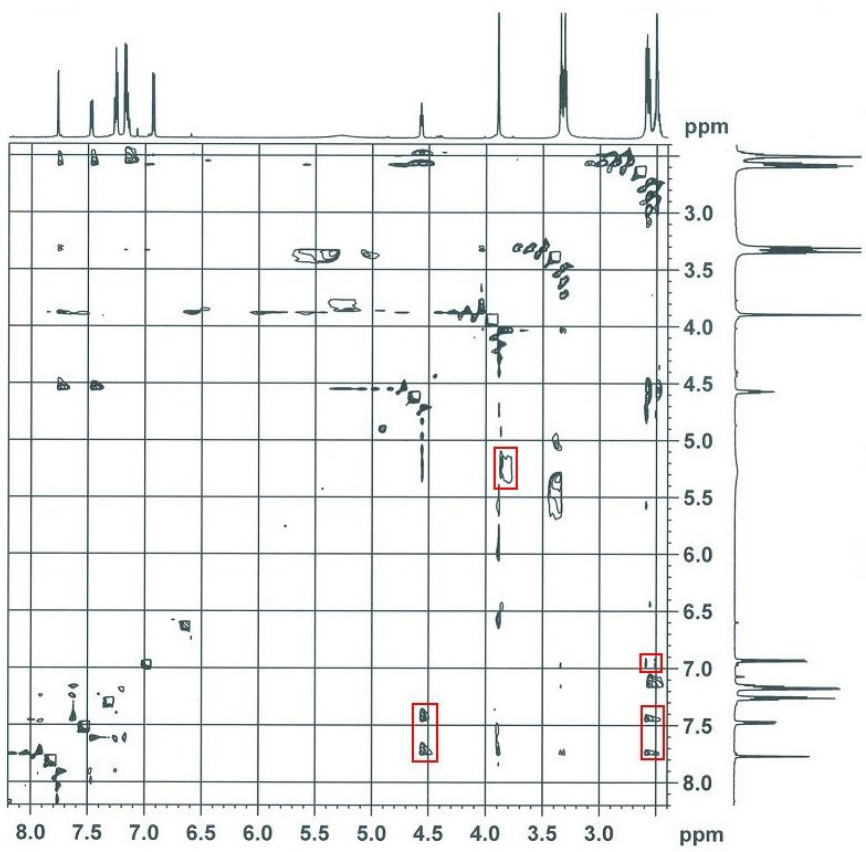
10

NOESY spectra of compounds **6** and **10**

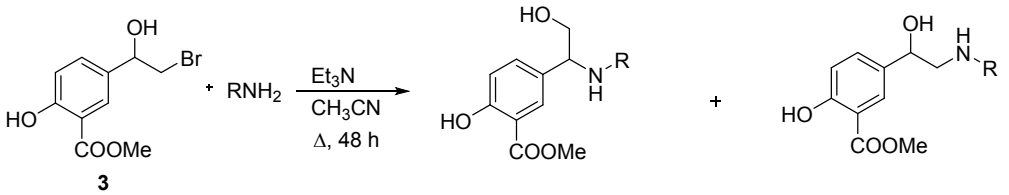
Compound **6**



Compound **10**



NMR shifts of H and C atoms between hydroxyl and amino group in the products of reaction between **3** and primary amines

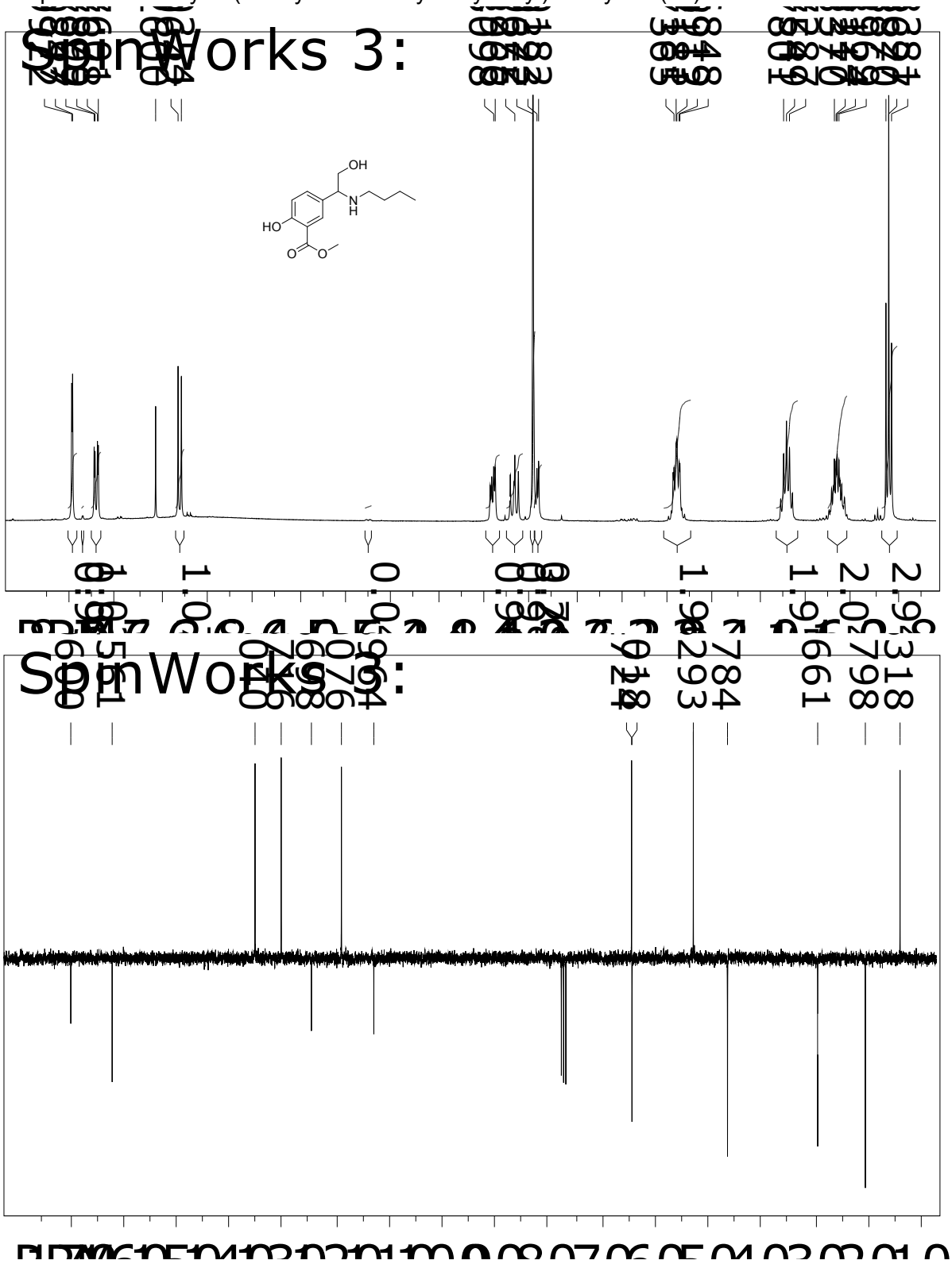


R = $(CH_2)_6O(CH_2)_4Ph$	80 %	**6**	R = $(CH_2)_6O(CH_2)_4Ph$	-	**10**
$BuNH_2$	80 %	**11**	$BuNH_2$	3 %	**13**
t-$BuNH_2$	78 %	**12**	t-$BuNH_2$	-	**14**

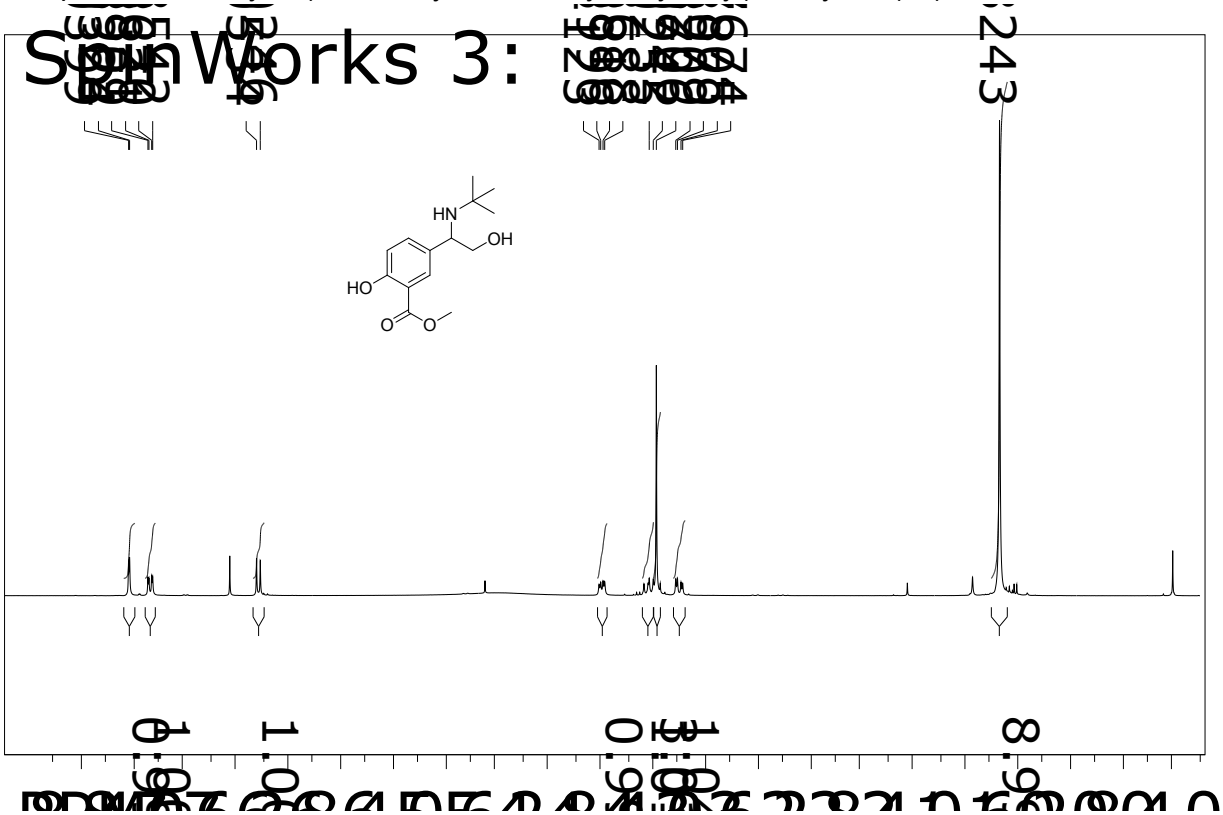
2-aryl β-amino alcohol isomers			1-aryl β-amino alcohol isomers		
	δH / ppm	δC / ppm		δH / ppm	δC / ppm
6	4.23, 4.04, 3.88	64.28, 64.09	**10**	4.60, 2.79, 2.63	70.14, 56.38
11	4.33, 4.14, 3.93	64.19, 64.12	**13**	5.41, 3.20, 3.09	68.33, 54.84
12	4.39, 4.03, 3.79	64.70, 61.06	**14**	4.52, 2.88, 2.54	71.54, 50.20

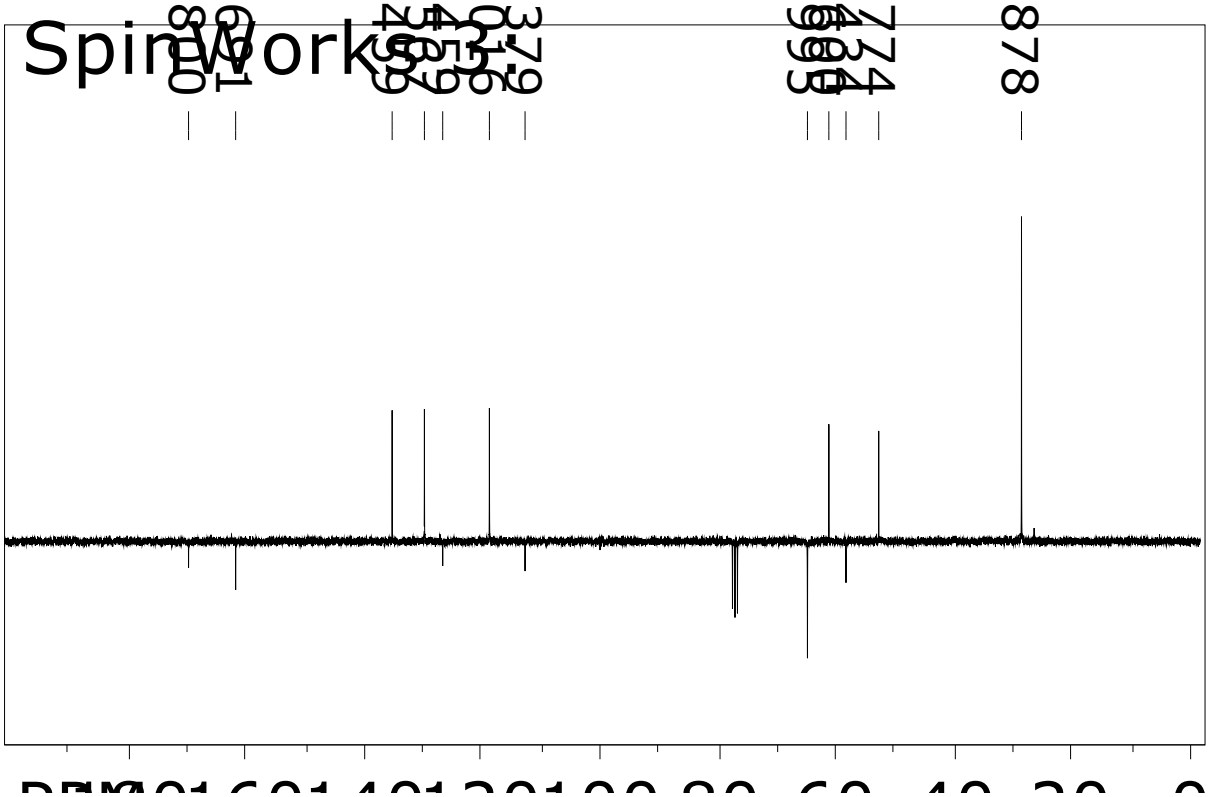
^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) were recorded in $CDCl_3$

NMR spectra of methyl 5-(1-butylamino-2-hydroxy-ethyl)-salicylate (**11**)

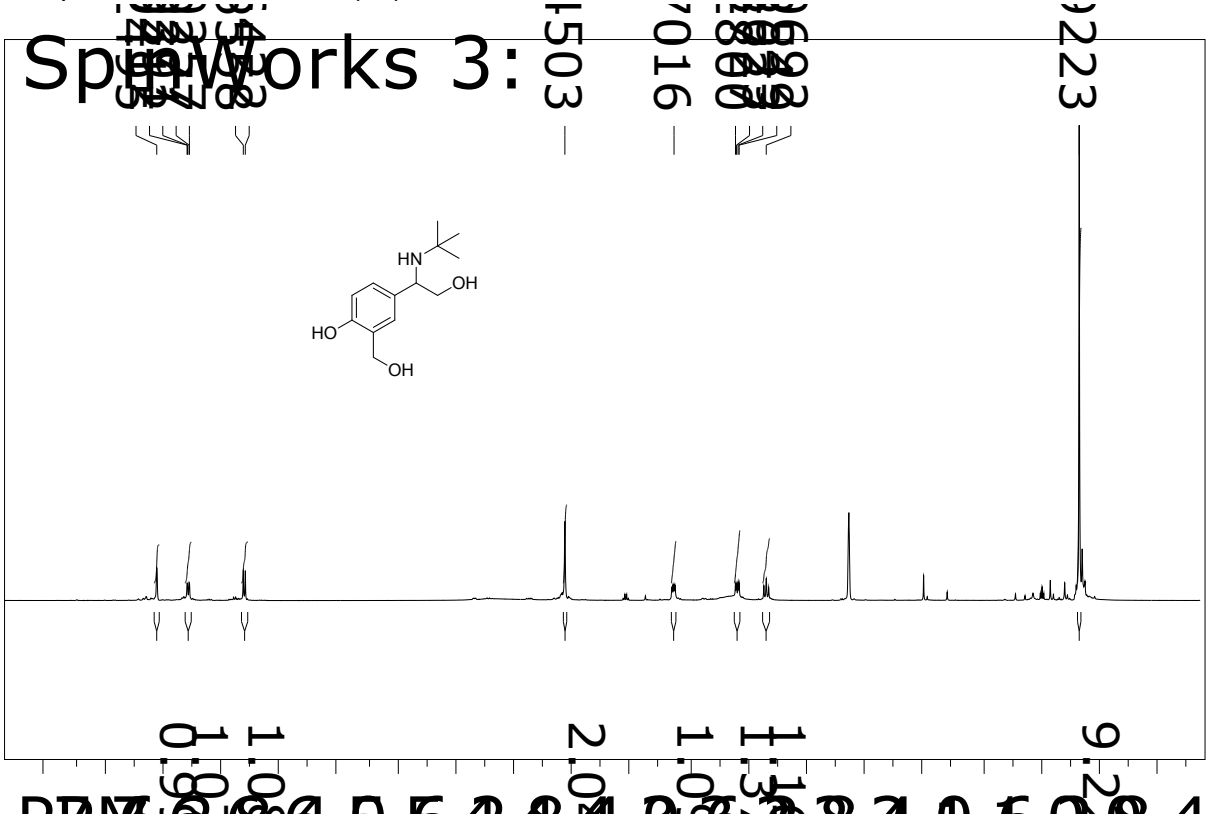


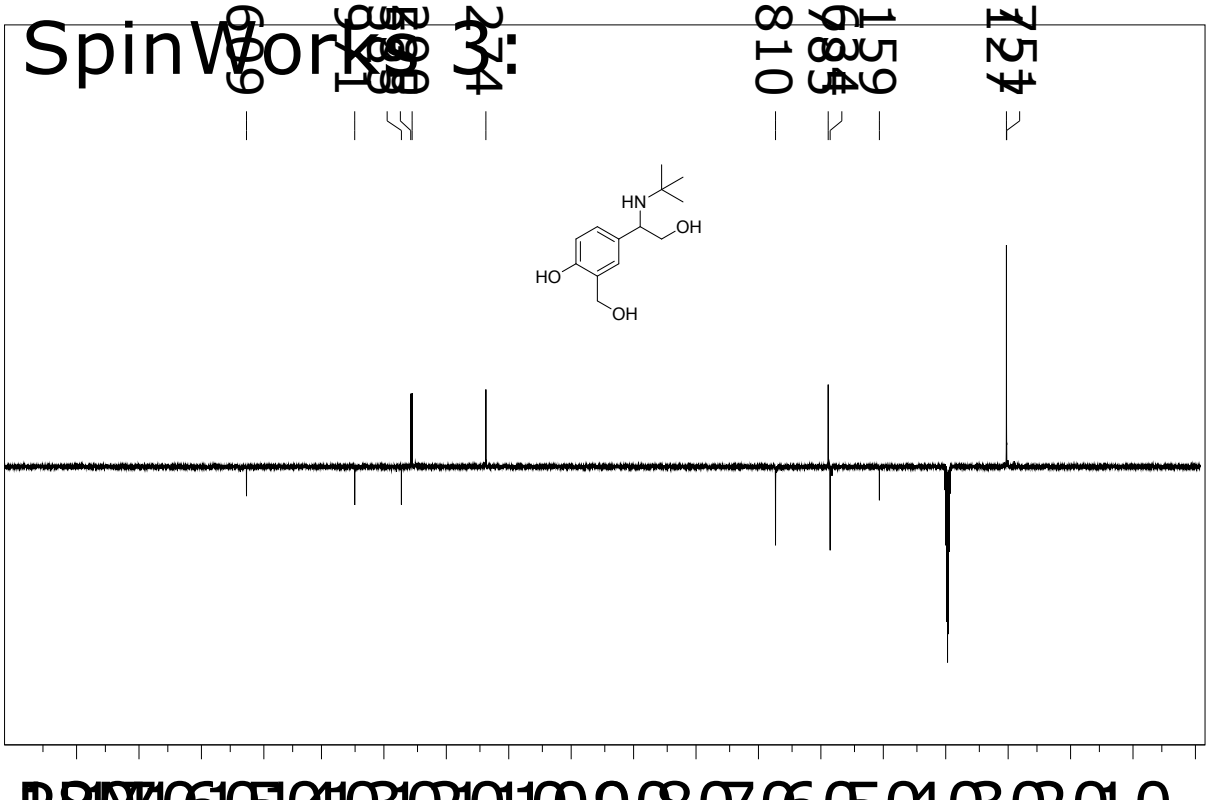
NMR spectra of methyl 5-(1-*tert*-butylamino-2-hydroxy-ethyl)-salicylate (**12**)



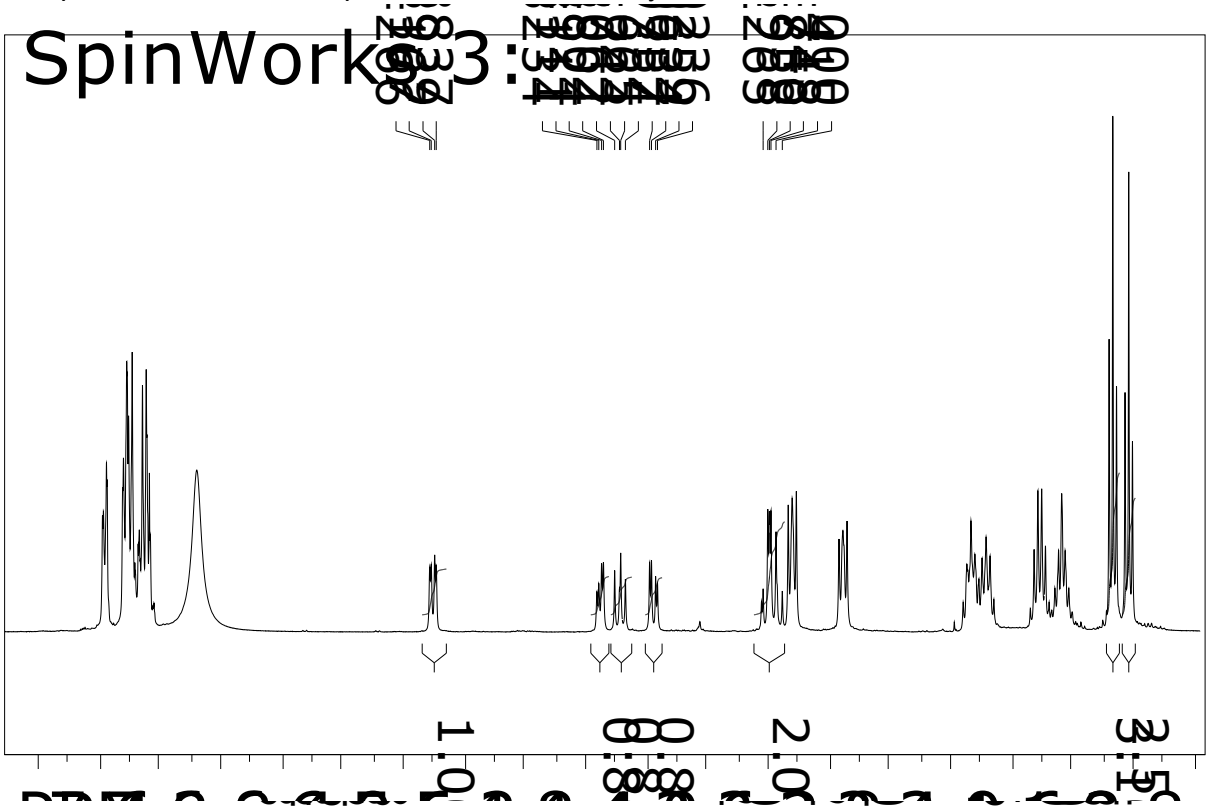


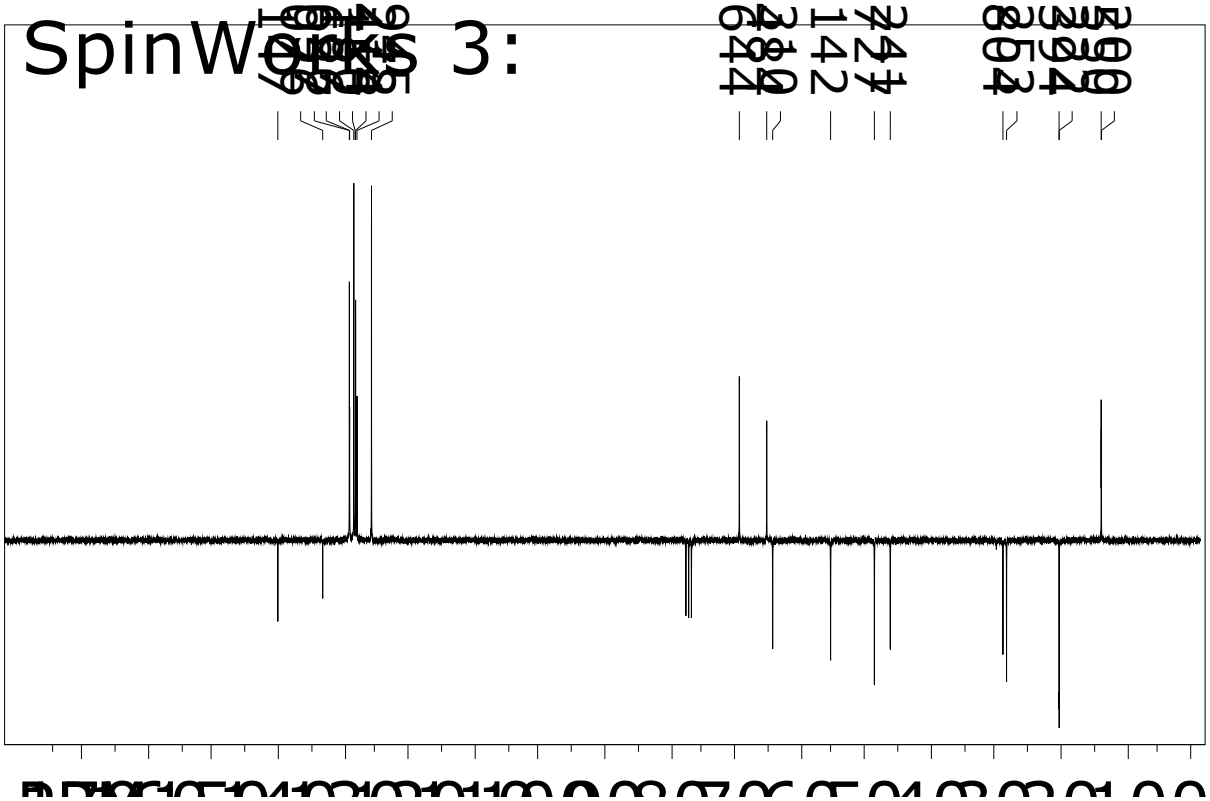
NMR spectra of iso-albuterol (**17**)



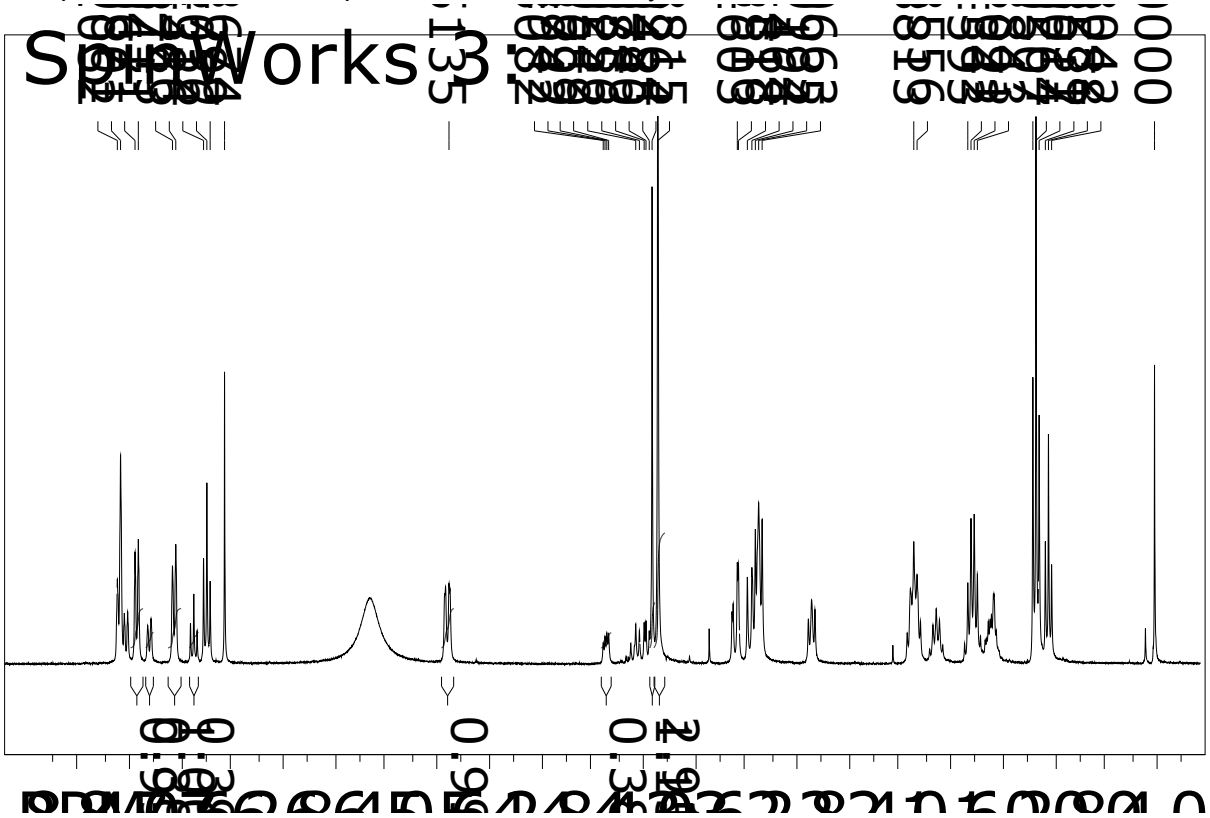


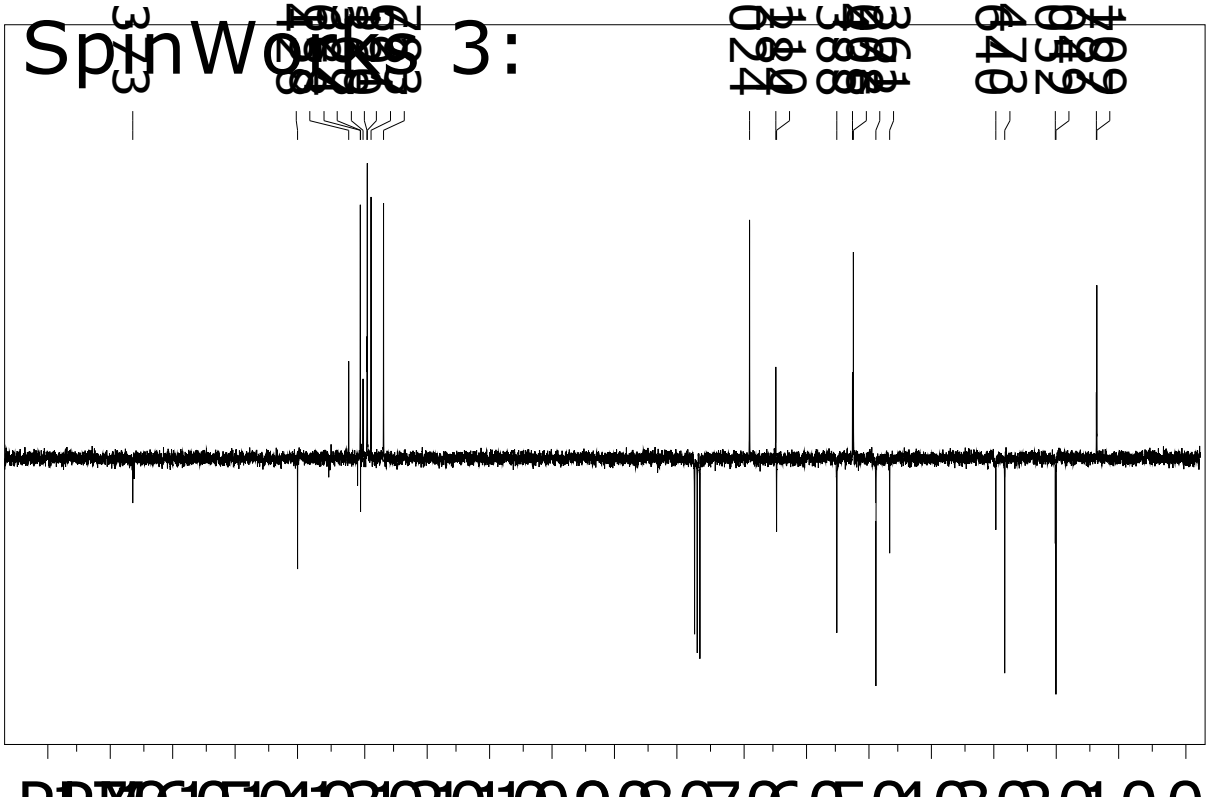
NMR spectra of the reaction product of **15** and *n*-butylamine





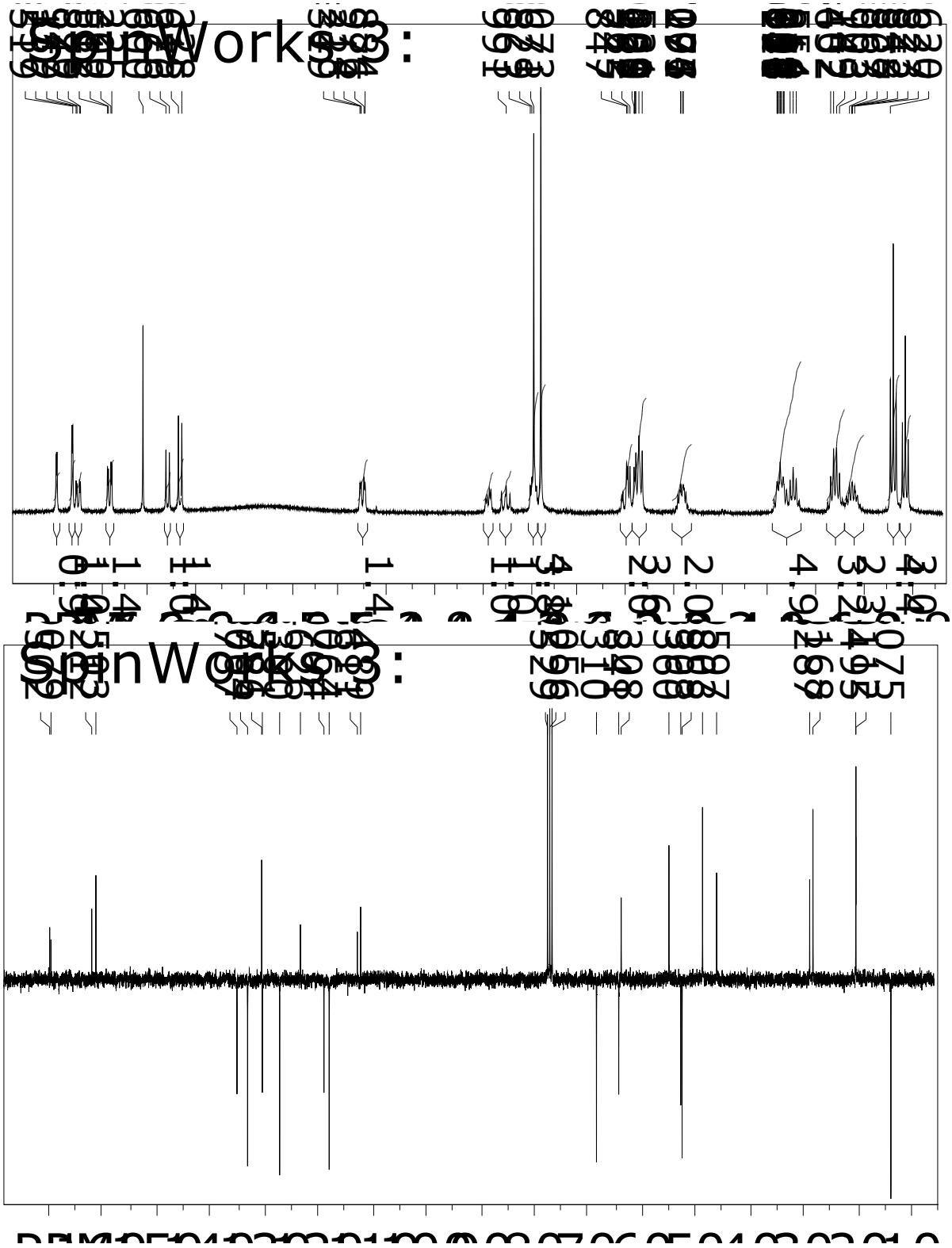
NMR spectra of the reaction product of **16** and *n*-butylamine



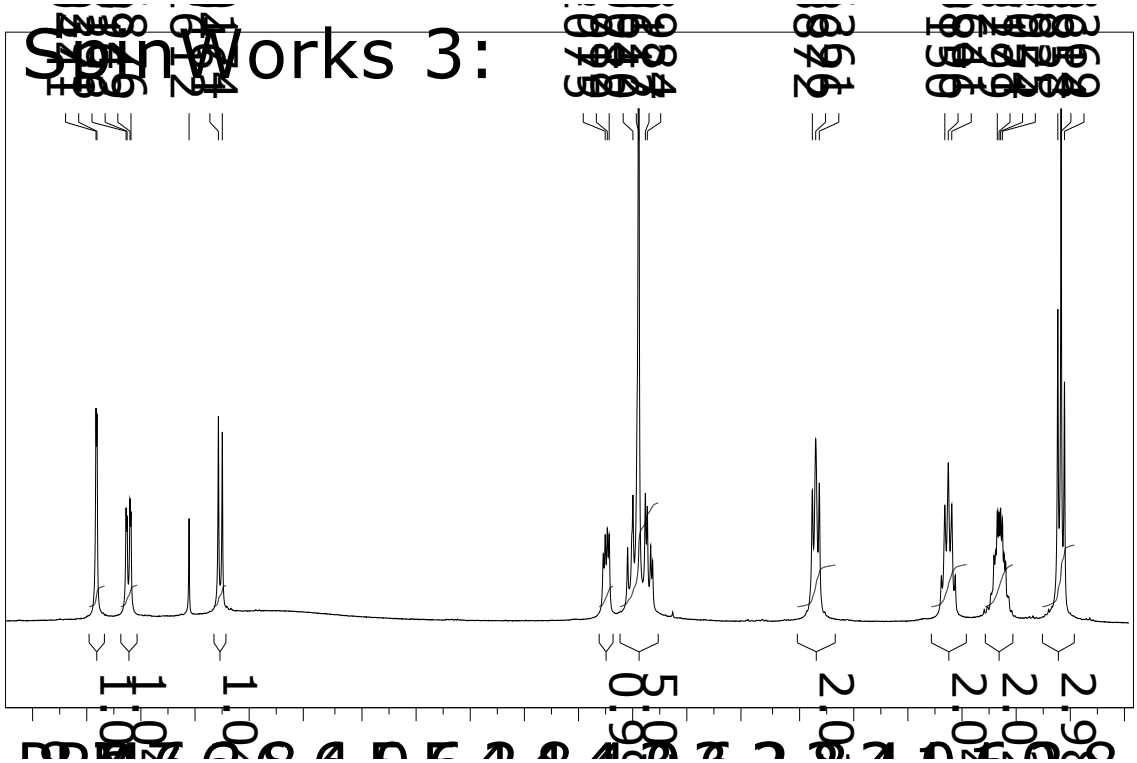


NMR spectra of reaction products of **3** with $BuNH_2$

*Reaction of **3** with $BuNH_2$ in THF, Et_3N base (Table 2, entry 2)*

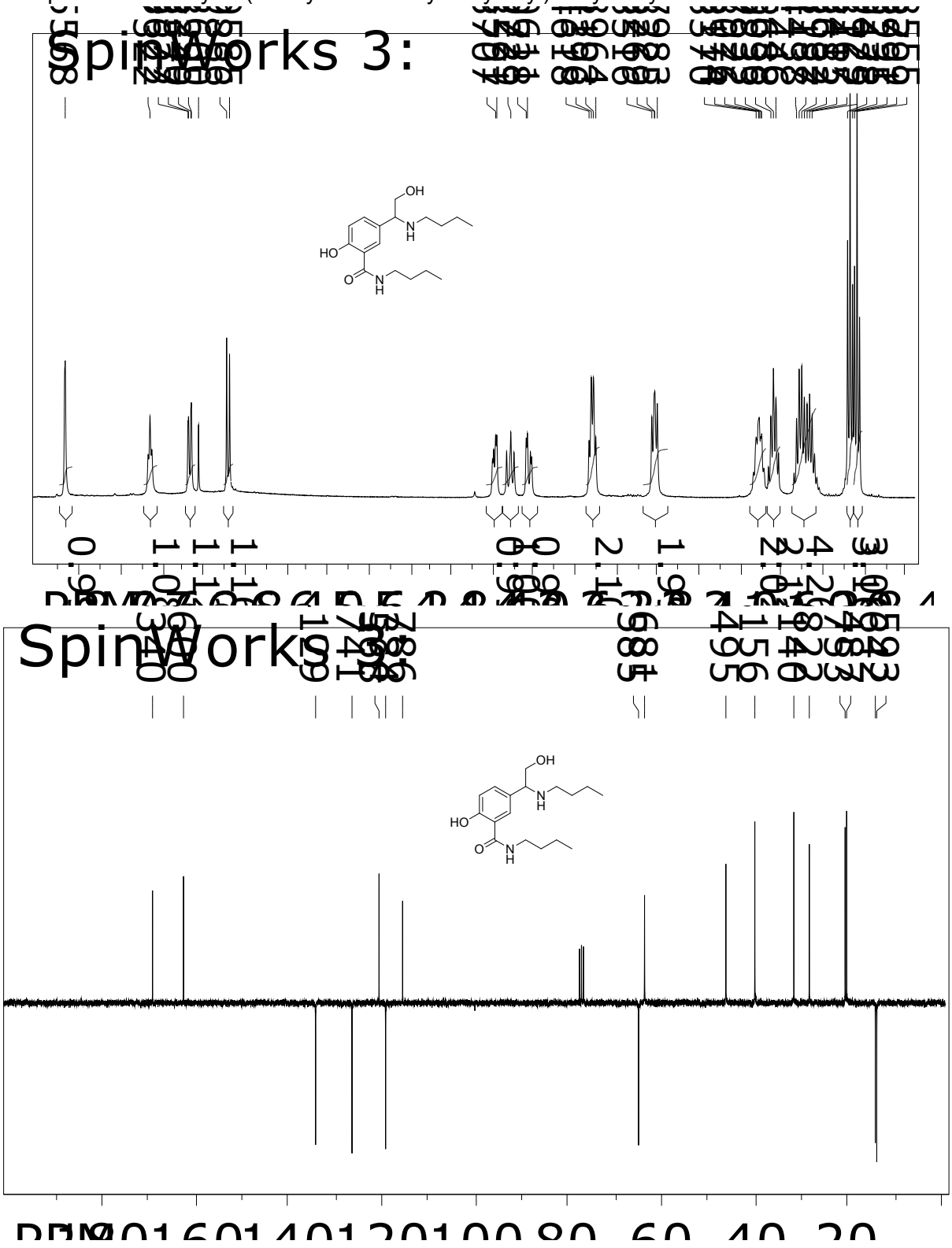


*Reaction of **3** with $BuNH_2$ in i-PrOH, Et_3N base (Table 2, entry 6)*

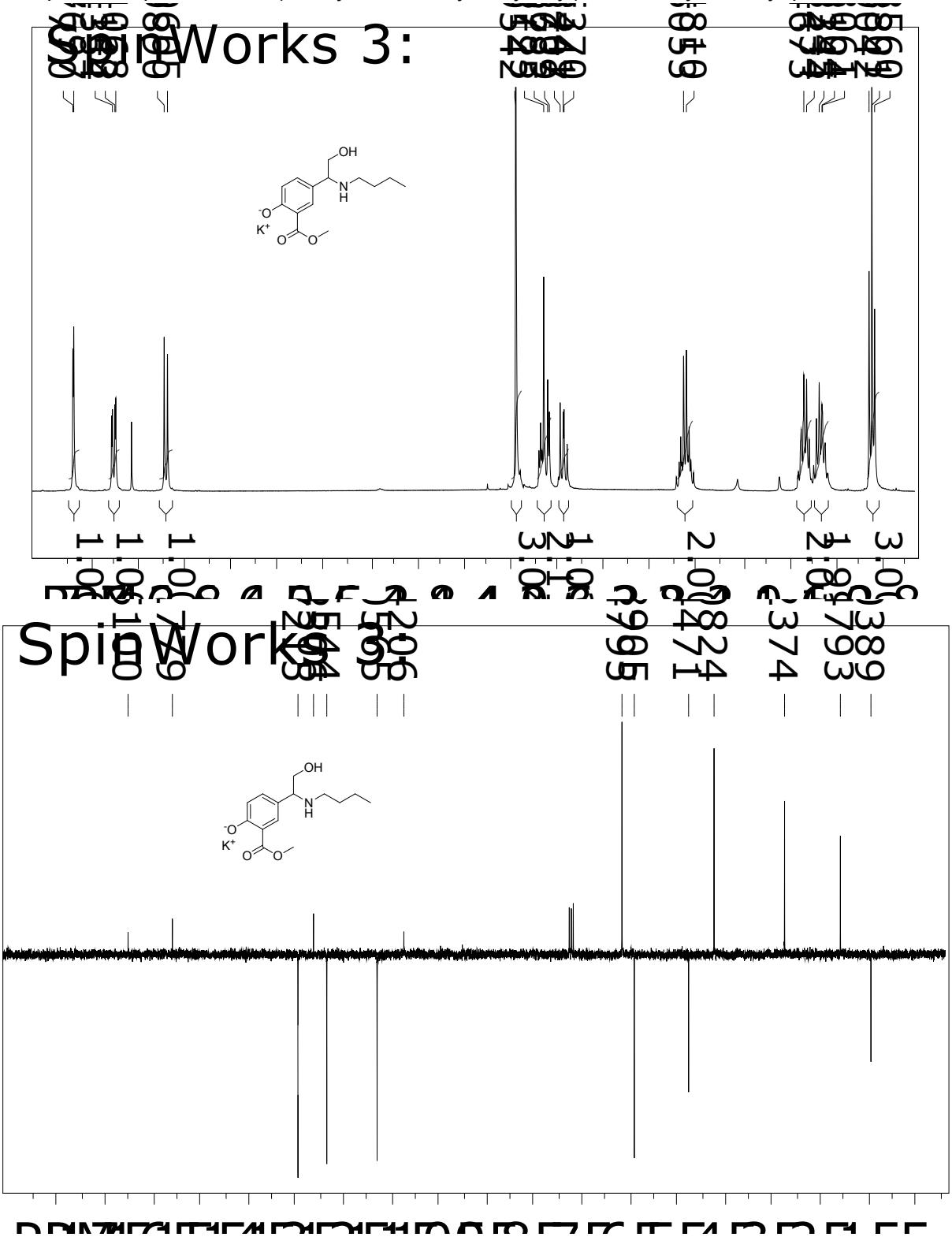


*Reaction of **3** with $BuNH_2$ in CH_3CN, diethylaniline base (Table 2, entry 10)*

NMR spectra of *N*-butyl-5-(1-butylamino-2-hydroxyethyl)-2-hydroxy-benzamide

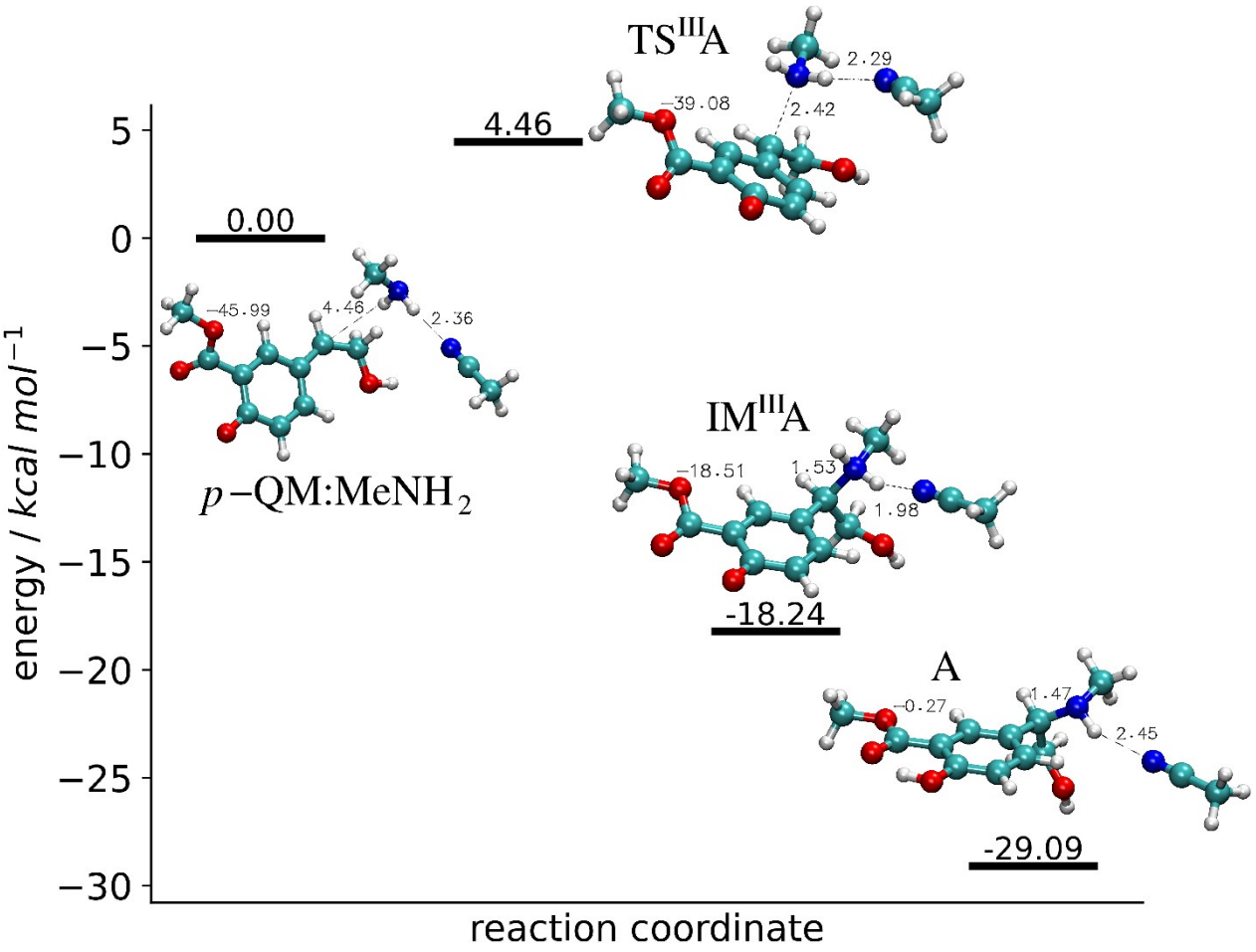


NMR spectra of potassium 4-(1-butylamino-2-hydroxyethyl)-2-methoxycarbonyl-phenolate



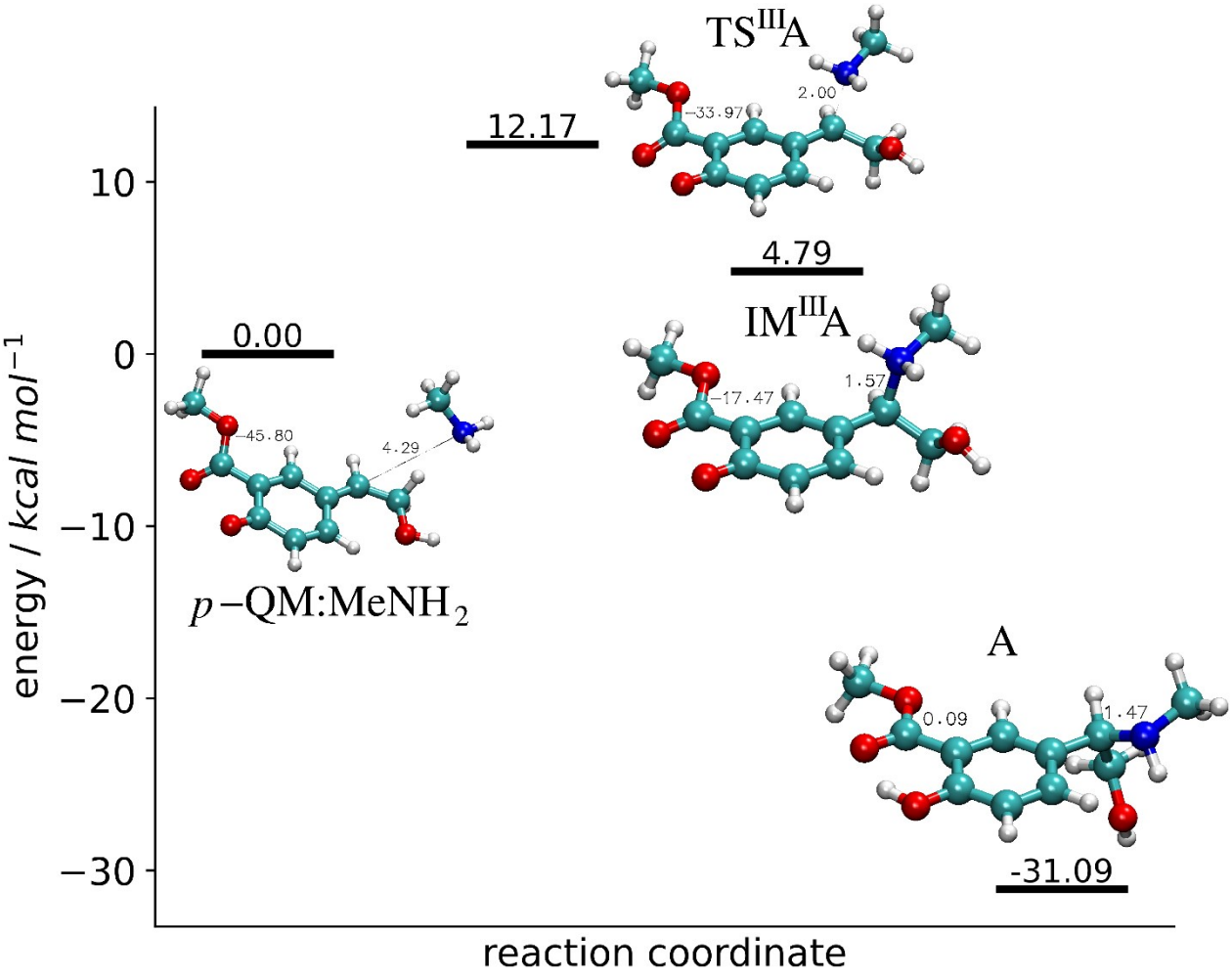
The energy profile for half reaction from *para*-quinone methide – methylamine reaction complex with explicit solvent (acetonitrile) molecule

The energy profile for half reaction from *para*-quinone methide – methylamine reaction complex to β-aryl-β-amino alcohol isomer with explicit solvent (acetonitrile) molecule. The distance between nitrogen and C^{β} carbon atom is in Angstrom, and the dihedral angle C3-C2-C-O is in degrees. B3LYP/aug-cc-pVDZ with SMD solvation model (acetonitrile) was used for geometry optimization, followed by B2-PLYP/aug-cc-pVDZ with SMD solvation model (acetonitrile) single point calculations.



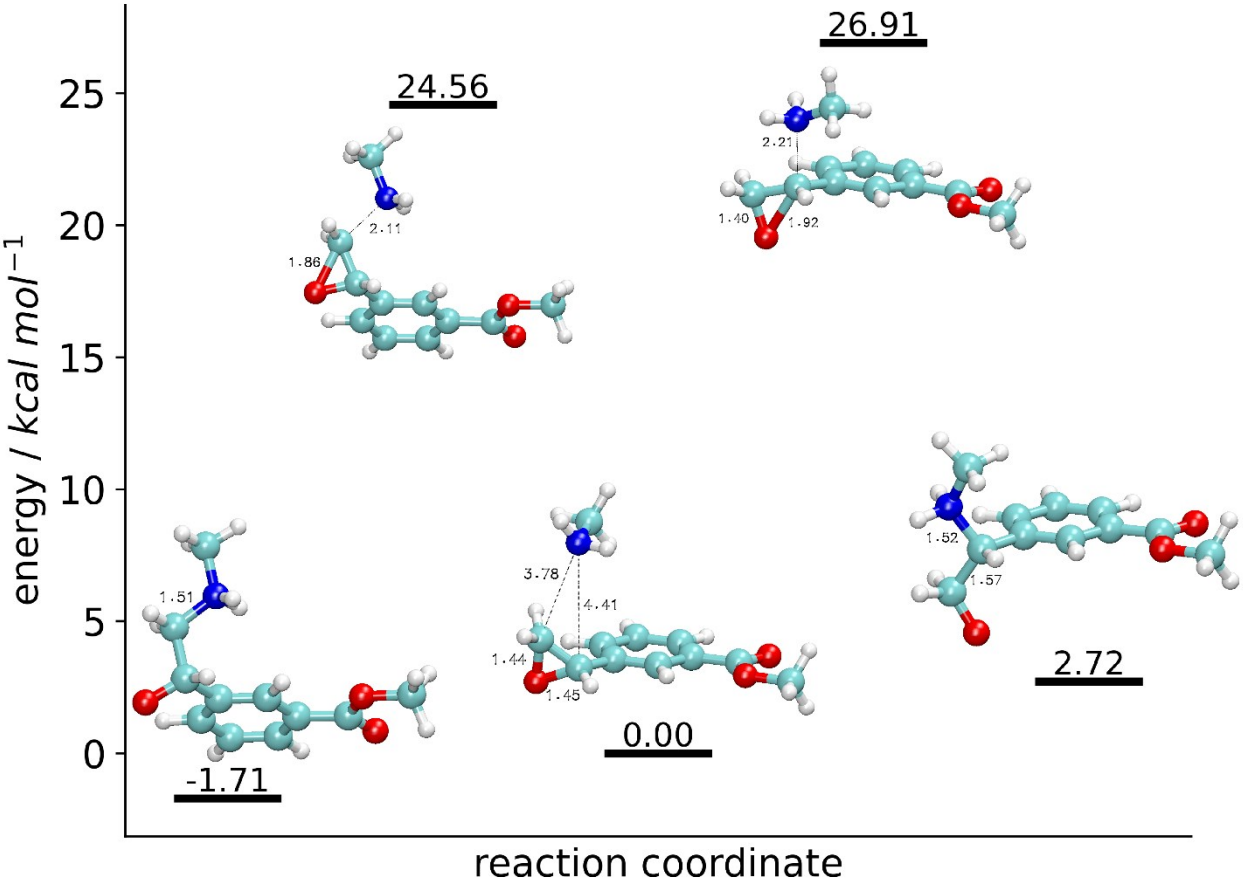
The energy profile for half reaction from *para*-quinone methide – methylamine reaction complex in hexane

The energy profile for half reaction from *para*-quinone methide – methylamine reaction complex to β-aryl-β-amino alcohol isomer. The distance between nitrogen and C^{β} carbon atom is in Angstrom, and the dihedral angle C3-C2-C-O is in degrees. B3LYP/aug-cc-pVDZ with SMD solvation model (*n*-hexane, ε_r = 1.8819) was used for geometry optimization, followed by B2-PLYP/aug-cc-pVTZ with SMD solvation model (*n*-hexane) single point calculations.



The energy profile for half reaction from epoxy-**16** – methylamine reaction complex

The relevant distances between selected atoms are in Angstrom. B3LYP/aug-cc-pVDZ with SMD solvation model was used for geometry optimization, followed by B2-PLYP/aug-cc-pVTZ with SMD solvation model single point calculations for accurate energy calculations.



Reaction between **3** and $MeNH_2$ via *para*-quinone methide intermediate (Cartesian coordinates and computed total energies of the ***p*-QM:MeNH$_2$** complex; **TS^{III}A**, **IM^{III}A** and **A**)

Table 1: The Cartesian coordinates of the ***p*-QM:MeNH$_2$** complex, optimized on the B3LYP/aug-cc-pVDZ, using SDM solvation model (ε = 35.688). Energy = -783.939268 hartree.

C	-0.692546	-2.358586	1.007722
C	-1.844859	-1.455362	0.901812
C	-1.671370	-0.288461	0.004502
C	-0.474342	-0.059673	-0.603610
C	0.664505	-0.953049	-0.466165
C	0.483977	-2.129123	0.374585
C	-2.831671	0.611979	-0.268395
O	-2.475899	1.912923	-0.242698
O	-3.960458	0.231808	-0.518763
C	-3.509724	2.862908	-0.593430
C	1.811554	-0.622778	-1.135747
H	-0.824714	-3.232313	1.647464
H	-0.351215	0.814451	-1.243642
H	1.315030	-2.818859	0.488969
H	-4.346590	2.794565	0.111440
H	-3.033395	3.845071	-0.525925
H	-3.865366	2.679666	-1.614558
O	-2.878162	-1.651007	1.558053
C	3.138148	-1.279001	-1.226954
H	1.783840	0.297033	-1.726548
H	3.340588	-1.450779	-2.301579
H	3.889236	-0.535984	-0.895718
N	4.670347	2.186802	0.825311
H	4.804993	1.786142	1.752507
H	4.152631	1.486541	0.296066
C	3.878579	3.421556	0.927617
H	4.437548	4.164426	1.512994
H	3.724058	3.838694	-0.077040
H	2.888824	3.289690	1.399532
O	3.255362	-2.486728	-0.486046
H	4.151841	-2.824389	-0.617128

Table 2: The Cartesian coordinates of the transition state complex (**TS^{III}A**), optimized on the B3LYP/aug-cc-pVDZ, using SDM solvation model (ε = 35.688). Energy = -783.933389 hartree. One mode with imaginary frequency, v = -139.3794i cm^{-1}.

C	0.021992	0.014922	-0.021921
C	0.026590	-0.029079	1.439516
C	1.361294	0.010945	2.068481
C	2.495516	0.014679	1.291977
C	2.463475	0.044461	-0.142839
C	1.162073	0.039986	-0.768963
C	1.486652	0.093915	3.549680
O	2.534372	-0.631477	4.010905
O	0.770339	0.750808	4.284819
C	2.803960	-0.527996	5.426268
C	3.677268	0.069122	-0.825075
H	-0.958519	0.010027	-0.501191
H	3.472064	0.023615	1.777163
H	1.103324	0.057435	-1.854599
H	1.952200	-0.899305	6.008671
H	3.683950	-1.154343	5.599998
H	3.016490	0.512154	5.702298
O	-1.035525	-0.130140	2.087290
C	3.937797	0.362485	-2.265266
H	4.570670	0.185755	-0.211757
H	3.958119	1.466779	-2.353922
H	4.942691	0.002707	-2.526594
N	4.337332	-2.229574	-0.994309
H	3.571883	-2.644798	-1.520413
H	4.234603	-2.517892	-0.023942
C	5.638920	-2.622697	-1.537403
H	5.705554	-2.307397	-2.586748
H	6.436168	-2.119118	-0.974519
H	5.821075	-3.709863	-1.494711
O	2.956541	-0.194834	-3.139706
H	3.192322	0.058107	-4.042649

Table 3: The Cartesian coordinates of the intermediary product (**IM^{III}A**), optimized on the B3LYP/aug-cc-pVDZ, using SDM solvation model (ε = 35.688). Energy = -783.961298656 hartree.

C	0.196856	-1.538349	1.785827
C	-1.194543	-1.162870	1.604887
C	-1.395211	0.001117	0.742414
C	-0.287562	0.694308	0.212839
C	1.034096	0.298998	0.419306
C	1.253297	-0.850191	1.225748
C	-2.751683	0.460359	0.388966
O	-2.783261	1.793970	0.073847
O	-3.768825	-0.217103	0.341603
C	-4.050411	2.303854	-0.377679
C	2.149161	1.105503	-0.198131
H	0.385980	-2.415308	2.409326
H	-0.478925	1.566621	-0.412490
H	2.270481	-1.198529	1.406332
H	-4.813303	2.207089	0.405259
H	-3.876934	3.361098	-0.602973
H	-4.386088	1.777065	-1.280343
O	-2.120332	-1.801078	2.189622
C	3.236980	0.335402	-0.949471
H	1.713628	1.831682	-0.893289
H	2.742061	-0.386844	-1.614183
H	3.829869	1.022599	-1.569952
N	2.823814	1.956373	0.885313
H	3.374289	1.330851	1.484506
H	2.081180	2.336980	1.479442
C	3.690052	3.076191	0.412687
H	4.557883	2.668895	-0.110365
H	3.099133	3.710928	-0.253438
H	4.016576	3.643824	1.289095
O	4.078930	-0.324663	0.005138
H	4.831467	-0.709314	-0.463561

Table 4: The Cartesian coordinates of the final product (**A**), optimized on the B3LYP/aug-cc-pVDZ, using SDM solvation model (ε = 35.688). Energy = -783.980878377 hartree.

C	-0.151043	-2.165957	0.950533
C	-1.402222	-1.622589	0.625855
C	-1.473897	-0.293752	0.136253
C	-0.282727	0.446477	-0.014056
C	0.963575	-0.087388	0.303942
C	1.005741	-1.408176	0.791850
C	-2.792330	0.272925	-0.194384
O	-2.760143	1.531874	-0.640659
O	-3.851283	-0.356169	-0.074098
C	-4.033300	2.133805	-0.981129
C	2.220877	0.748770	0.088982
H	-0.104422	-3.186624	1.329629
H	-0.350137	1.466946	-0.388366
H	1.959147	-1.860460	1.060726
H	-4.684516	2.168001	-0.100092
H	-3.788818	3.145212	-1.316327
H	-4.516986	1.568694	-1.786229
C	2.675845	0.700976	-1.381536
H	1.954098	1.798128	0.284010
H	1.839481	1.000317	-2.032324
H	3.503160	1.409858	-1.538604
N	3.274566	0.390095	1.049646
H	3.681256	-0.502410	0.776986
C	4.347763	1.380009	1.161163
H	4.883549	1.586952	0.216745
H	3.932373	2.328672	1.530055
H	5.084512	1.024962	1.894012
O	3.102646	-0.635330	-1.686094
H	3.426921	-0.649874	-2.595785
O	-2.501383	-2.392344	0.798657
H	-3.274560	-1.842966	0.521455

Reaction between **3** and $MeNH_2$ via S_N2 mechanism (Cartesian coordinates and computed total energies of the initial complexes and transition states)

Table 5: The Cartesian coordinates of the initial complex of **3** and $MeNH_2$, for S_N2 reaction and methylamine attack to α-carbon, optimized on the B3LYP/aug-cc-pVDZ, using SDM solvation model (ε = 35.688). Energy = -3358.75669863 hartree.

C	-1.523384	-1.056900	-1.937578
C	-2.623646	-0.578795	-1.206905
C	-2.440383	-0.175816	0.138819
C	-1.154732	-0.258413	0.716023
C	-0.062606	-0.720165	-0.007620
C	-0.270630	-1.125383	-1.342879
O	-3.825057	-0.528500	-1.822288
C	-3.603262	0.316699	0.897602
O	-3.334189	0.675094	2.155304
O	-4.740968	0.397036	0.417477
C	-4.445393	1.170753	2.942640
C	1.335370	-0.818333	0.592175
C	2.368429	0.076243	-0.090139
Br	2.006855	2.019881	0.214025
O	1.358446	-0.662323	2.007033
H	-1.674742	-1.375141	-2.968675
H	-1.036257	0.041270	1.754151
H	0.567601	-1.508993	-1.926765
H	-4.466378	-0.175411	-1.157527
H	-5.217866	0.398760	3.036059
H	-4.017672	1.405635	3.920806
H	-4.864862	2.071597	2.480122
H	1.708804	-1.839774	0.413848
H	3.365050	-0.095223	0.323981
H	2.374828	-0.055189	-1.174204
H	1.217836	0.273482	2.218653
C	5.064903	-2.842113	-2.503072
H	4.509013	-2.809437	-3.450308
H	5.558300	-1.869031	-2.372576
H	5.850097	-3.612967	-2.594803
N	4.124353	-3.063224	-1.394490
H	3.674638	-3.971280	-1.500610
H	4.635061	-3.111317	-0.514132

Table 6: The Cartesian coordinates of the transition state complex of **3** and $MeNH_2$, for S_N2 reaction and methylamine attack to α-carbon, optimized on the B3LYP/aug-cc-pVDZ, using SDM solvation model (ε = 35.688). Energy = -3358.73578743 hartree. One mode with imaginary frequency, v = -413.1919i cm^{-1}.

C	-1.569692	-0.844028	-3.564711
C	-2.644650	-0.299679	-2.844524
C	-2.429302	0.161830	-1.522318
C	-1.138602	0.068566	-0.959434
C	-0.070730	-0.460109	-1.673262
C	-0.309821	-0.922548	-2.983545
O	-3.853559	-0.241834	-3.446411
C	-3.565734	0.725189	-0.772804
O	-3.269084	1.131238	0.464210
O	-4.707290	0.818805	-1.241639
C	-4.354940	1.692549	1.242426
C	1.318268	-0.600144	-1.050702
C	2.433762	-0.026521	-1.915554
Br	2.071056	2.365194	-1.536366
O	1.393008	-0.110617	0.281837
H	-1.743576	-1.202629	-4.578854
H	-0.985144	0.419090	0.057306
H	0.503365	-1.356522	-3.565809
H	-4.473487	0.163132	-2.791284
H	-5.150391	0.949982	1.373933
H	-3.909067	1.951791	2.206232
H	-4.751215	2.587758	0.749471
H	1.524282	-1.675040	-0.952325
H	3.420169	0.076660	-1.485276
H	2.302872	0.141570	-2.974302
H	1.469515	0.859297	0.209030
C	4.339601	-1.721548	-3.649142
H	3.894940	-1.199351	-4.506052
H	5.114503	-1.076978	-3.214499
H	4.817538	-2.644181	-4.013216
N	3.301841	-1.974714	-2.645373
H	2.554884	-2.554664	-3.023415
H	3.682605	-2.457462	-1.833330

Table 7: The Cartesian coordinates of the initial complex of **3** and $MeNH_2$, for S_N2 reaction and methylamine attack to β-carbon, optimized on the B3LYP/aug-cc-pVDZ, using SDM solvation model (ε = 35.688). Energy = -3358.75681100 hartree.

C	-1.680892	-0.220587	-2.938214
C	-2.824209	0.240760	-2.265161
C	-2.708410	0.684606	-0.924834
C	-1.445144	0.659079	-0.295248
C	-0.310827	0.213844	-0.962109
C	-0.451631	-0.233018	-2.292956
O	-4.000682	0.236152	-2.928901
C	-3.916005	1.158340	-0.226298
O	-3.709706	1.554169	1.032050
O	-5.034854	1.191742	-0.753983
C	-4.866042	2.034315	1.761889
C	1.063719	0.176343	-0.303987
C	2.098544	1.078990	-0.973027
Br	1.670106	3.020052	-0.750021
O	1.023402	0.376905	1.104780
H	-1.780465	-0.569925	-3.965527
H	-1.377755	0.990412	0.737871
H	0.421670	-0.603570	-2.832226
H	-4.678927	0.586547	-2.300379
H	-5.620597	1.243129	1.839718
H	-4.486275	2.300781	2.751724
H	-5.289918	2.913744	1.263508
H	1.472773	-0.838926	-0.432402
H	3.081565	0.950962	-0.512853
H	2.154187	0.911401	-2.050635
H	0.846102	1.313837	1.280245
C	2.990354	-3.254702	-1.895169
H	3.405526	-3.033105	-0.902529
H	1.899149	-3.329321	-1.793052
H	3.370505	-4.242261	-2.210190
N	3.320253	-2.157799	-2.817652
H	4.330820	-2.095940	-2.930796
H	2.952626	-2.365964	-3.744898

Table 8: The Cartesian coordinates of the transition state complex of **3** and $MeNH_2$, for S_N2 reaction and methylamine attack to β-carbon, optimized on the B3LYP/aug-cc-pVDZ, using SDM solvation model (ε = 35.688). Energy = -3358.65875411 hartree. One mode with imaginary frequency, v = -390.2313i cm^{-1}.

C	-1.160374	0.220901	-3.555760
C	-2.301472	0.225562	-2.737905
C	-2.159486	0.020554	-1.341232
C	-0.873111	-0.185635	-0.805739
C	0.258999	-0.181014	-1.612869
C	0.096414	0.027346	-2.996658
O	-3.502515	0.427020	-3.319077
C	-3.364481	0.033303	-0.493204
O	-3.130227	-0.161861	0.805989
O	-4.504361	0.210799	-0.940535
C	-4.282359	-0.148241	1.685348
C	1.623609	-0.407724	-0.998756
C	2.681048	0.626487	-1.296287
Br	2.338319	2.945970	-2.221990
O	1.770838	1.597651	0.552378
H	-1.280219	0.381307	-4.626676
H	-0.768380	-0.342599	0.264967
H	0.966374	0.041335	-3.653563
H	-4.174550	0.399699	-2.593615
H	-4.974659	-0.953925	1.415220
H	-3.876347	-0.311226	2.687083
H	-4.789617	0.821657	1.629275
H	1.534466	-0.549393	0.076440
H	3.482344	0.702897	-0.571295
H	3.023422	0.584522	-2.328553
H	1.816389	2.483049	0.171728
C	1.446938	-2.967592	-1.126200
H	1.397872	-2.993186	-0.034201
H	0.444272	-2.927391	-1.557035
H	1.987912	-3.840003	-1.503952
N	2.201570	-1.745573	-1.533308
H	3.164219	-1.830476	-1.189799
H	2.274787	-1.708360	-2.555842

Reaction between epoxy-**3** and $MeNH_2$ (Cartesian coordinates and computed total energies of the initial complexes and transition states)

Table 9: The Cartesian coordinates of the initial complex of epoxy-**3** and $MeNH_2$ optimized on the B3LYP/aug-cc-pVDZ, using SDM solvation model (ε = 35.688). Energy = -783.945806 hartree.

C	-0.336196	2.231991	-0.177462
C	1.000238	1.816720	-0.307829
C	1.283670	0.454936	-0.581428
C	0.214504	-0.454023	-0.716313
C	-1.109300	-0.047086	-0.574951
C	-1.369247	1.314158	-0.307470
C	2.688923	0.034567	-0.721346
O	2.855452	-1.263957	-0.981240
O	3.643186	0.814018	-0.607819
C	4.220695	-1.730071	-1.123341
C	-2.206243	-1.047363	-0.711786
O	-3.444440	-0.598384	-1.331431
H	-0.540786	3.282742	0.026295
H	0.435395	-1.497514	-0.935307
H	-2.398249	1.659802	-0.208754
H	4.777872	-1.557188	-0.195430
H	4.135078	-2.800843	-1.325741
H	4.710446	-1.218536	-1.959964
O	1.971536	2.744061	-0.169520
C	-3.459012	-0.986966	0.059994
H	2.831433	2.271532	-0.294922
H	-1.880733	-2.031555	-1.057426
H	-4.002614	-1.909902	0.274353
H	-3.616323	-0.165566	0.762440
N	-3.495098	-1.951728	3.515679
H	-4.226764	-2.444163	3.006113
H	-3.715792	-0.961717	3.424322
C	-3.524056	-2.341232	4.932446
H	-2.743923	-1.791380	5.476918
H	-4.488577	-2.154324	5.437479
H	-3.297415	-3.412874	5.019619

Table 10: The Cartesian coordinates of the transition state complex (**TS^{II}A**), optimized on the B3LYP/aug-cc-pVDZ, using SDM solvation model (ε = 35.688). Energy = -783.913933 hartree.

C	-0.080530	0.289990	-0.146352
C	-0.008725	0.086826	1.243469
C	1.258189	-0.072166	1.862252
C	2.417318	-0.023326	1.066637
C	2.353095	0.178961	-0.314127
C	1.078019	0.333500	-0.906392
C	1.317400	-0.278765	3.320509
O	2.550651	-0.413389	3.811212
O	0.310389	-0.324620	4.037825
C	2.664167	-0.613963	5.242588
C	3.591587	0.190353	-1.103824
O	3.803812	2.054866	-1.752665
H	-1.060191	0.413364	-0.606932
H	3.388546	-0.140799	1.543256
H	0.994735	0.494548	-1.980215
H	2.150601	-1.536276	5.537267
H	3.737390	-0.694717	5.433632
H	2.241313	0.243058	5.779155
O	-1.160779	0.052527	1.941443
C	3.708039	0.838522	-2.419623
H	-0.913219	-0.094870	2.888438
H	4.518703	0.113255	-0.543352
H	4.610951	0.529353	-2.982784
H	2.829962	0.723972	-3.084397
N	3.745749	-1.948784	-1.550048
H	4.466692	-1.988934	-2.267776
H	2.865602	-2.216408	-1.986287
C	4.071813	-2.827633	-0.422685
H	3.283737	-2.753437	0.336766
H	4.167553	-3.883230	-0.721449
H	5.020452	-2.505078	0.024595

Table 11: The Cartesian coordinates of the final product **A** via epoxide mechanism, optimized on the B3LYP/aug-cc-pVDZ, using SDM solvation model (ε = 35.688). Energy = -783.943408 hartree.

C	0.024163	-2.360860	0.084515
C	-1.224946	-1.718432	0.076216
C	-1.279172	-0.304029	-0.000126
C	-0.074435	0.426369	-0.059680
C	1.166171	-0.204606	-0.054625
C	1.192897	-1.614049	0.014041
C	-2.595396	0.358356	-0.008077
O	-2.545531	1.690434	-0.077640
O	-3.665156	-0.260911	0.046783
C	-3.815017	2.389777	-0.086366
C	2.438536	0.601428	-0.158368
O	2.729372	0.518113	-2.577559
H	0.054427	-3.448648	0.139870
H	-0.123392	1.512282	-0.113127
H	2.148242	-2.140739	0.009204
H	-4.368085	2.181927	0.836830
H	-3.554673	3.449675	-0.147132
H	-4.407334	2.088658	-0.957987
O	-2.335694	-2.483033	0.142492
C	3.333771	0.264648	-1.400393
H	-3.105810	-1.862777	0.123233
H	2.195890	1.669717	-0.188311
H	4.277026	0.863388	-1.223698
H	3.659464	-0.806236	-1.256807
N	3.281994	0.422914	1.098649
H	4.214064	0.802309	0.895167
H	3.427384	-0.576892	1.272190
C	2.760622	1.066723	2.338729
H	1.790260	0.628826	2.585511
H	3.474515	0.885600	3.148084
H	2.661380	2.139606	2.152065

Table 12: The Cartesian coordinates of the transition state complex (**TS^{II}B**), optimized on the B3LYP/aug-cc-pVDZ, using SDM solvation model (ε = 35.688). Energy = -783.915797 hartree.

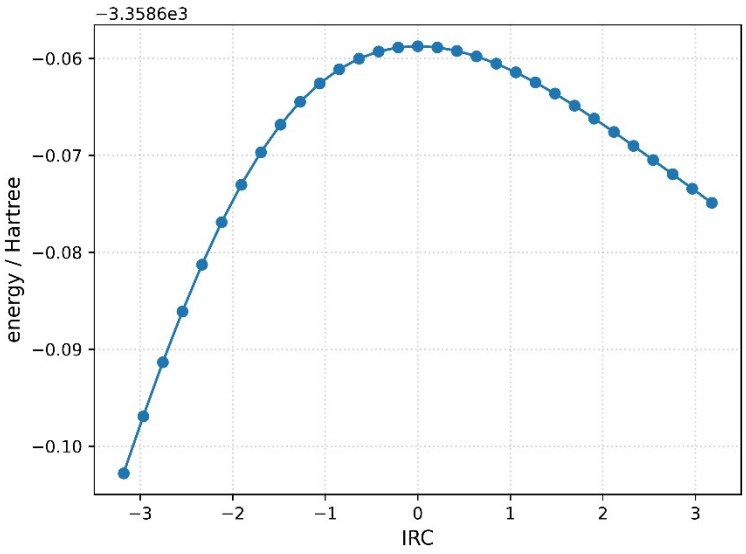
C	0.008998	-0.174161	0.008168
C	0.018913	-0.155523	1.412723
C	1.258584	-0.165440	2.100754
C	2.456323	-0.197893	1.354021
C	2.450981	-0.225695	-0.036905
C	1.205638	-0.206613	-0.697879
C	1.255057	-0.132672	3.572793
O	2.468964	-0.138194	4.131000
O	0.219001	-0.103377	4.249466
C	2.519438	-0.101703	5.578585
C	3.746562	-0.272012	-0.821079
O	3.761402	0.382755	-2.056382
H	-0.950456	-0.157208	-0.508774
H	3.406023	-0.195745	1.887712
H	1.185243	-0.206252	-1.787702
H	2.020093	-0.982749	5.998052
H	3.584193	-0.110686	5.826188
H	2.046155	0.813932	5.951580
O	-1.168154	-0.121074	2.059413
C	3.999691	-1.433421	-1.686523
H	-0.960833	-0.106963	3.025857
H	4.589217	-0.021232	-0.151275
H	5.005260	-1.577746	-2.065806
H	3.166015	-1.846999	-2.243611
N	4.163963	-3.220750	-0.581922
H	4.902121	-3.082625	0.105663
H	3.292002	-3.339033	-0.069737
C	4.442466	-4.384155	-1.432558
H	3.632392	-4.498411	-2.164107
H	5.381046	-4.217478	-1.976427
H	4.531594	-5.320061	-0.860036

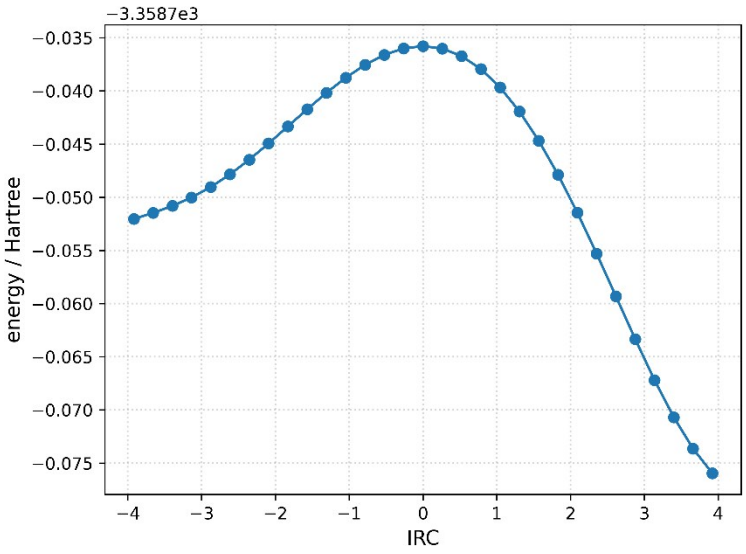
Table 13: The Cartesian coordinates of the final product **B** via epoxide mechanism, optimized on the B3LYP/aug-cc-pVDZ, using SDM solvation model (ε = 35.688). Energy = -783.950202 hartree.

C	-0.246485	-2.260353	0.681522
C	-1.423728	-1.492198	0.670494
C	-1.414964	-0.216770	0.054790
C	-0.214760	0.254309	-0.529618
C	0.953352	-0.500809	-0.528458
C	0.910568	-1.770817	0.088155
C	-2.655539	0.573308	0.042883
O	-2.554296	1.758832	-0.567754
O	-3.715343	0.186997	0.554338
C	-3.750528	2.574269	-0.606458
C	2.246771	-0.015394	-1.215914
O	2.738341	-0.897276	-2.124177
H	-0.266628	-3.241275	1.157083
H	-0.217385	1.235514	-1.003763
H	1.808736	-2.389391	0.088721
H	-4.078259	2.817298	0.411012
H	-3.458838	3.481917	-1.141555
H	-4.549526	2.051730	-1.145023
O	-2.530476	-2.010832	1.252236
C	3.335577	0.290515	-0.148941
H	-3.244683	-1.336250	1.143515
H	1.982586	0.989322	-1.651371
H	4.232389	0.670623	-0.648968
H	3.586565	-0.605343	0.429865
N	2.917393	1.347835	0.843537
H	2.630483	2.184841	0.325271
H	2.076840	1.027266	1.335509
C	3.957741	1.720908	1.843804
H	4.222700	0.827570	2.416592
H	4.830867	2.104685	1.308651
H	3.548250	2.490152	2.505947

Intrinsic reaction coordinate (IRC) curves for the transition states

Forward and backward IRC path from transition states $TS^{I}A$ (left) and $TS^{I}B$ (right) on B3LYP/aug-cc-pVDZ with SMD solvation model.





Forward and backward IRC path from transition states $TS^{II}A$ (left) and $TS^{II}B$ (right) on B3LYP/aug-cc-pVDZ with SMD solvation model.