Supporting Information

for

Preparation of neuroprotective condensed 1,4-benzoxazepines by regio- and diastereoselective domino Knoevenagel–[1,5]-hydride shift cyclization reaction

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Spectroscopic data and details of calculations

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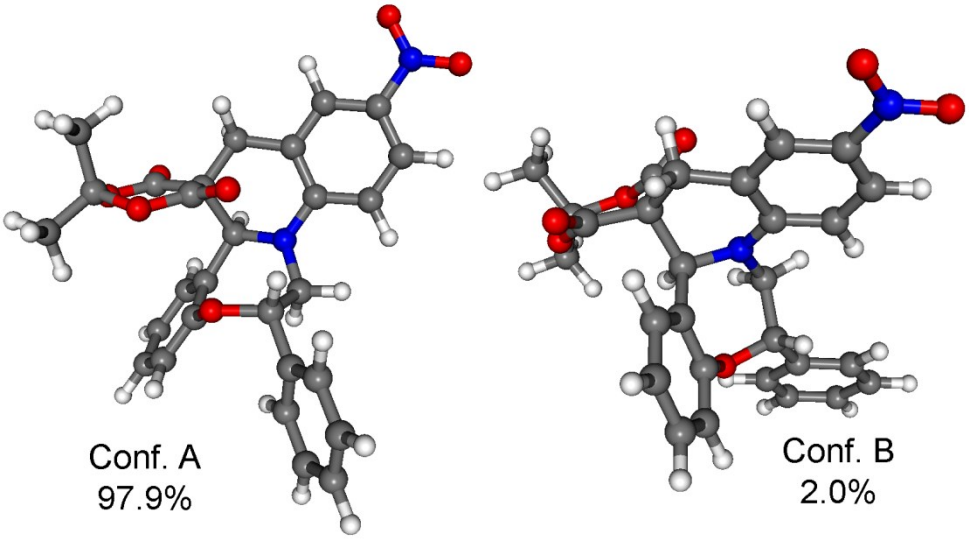


Figure S1. Low-energy conformers (> 1%) of *trans*-(2*S*,15a*S*)-**7b** optimized at B3LYP/6-31G(d) *in vacuo*. Boltzmann-weights for the same conformers in the B3LYP/TZVP PCM/$CHCl_3$ calculations are 95.8% and 3.6%, respectively.

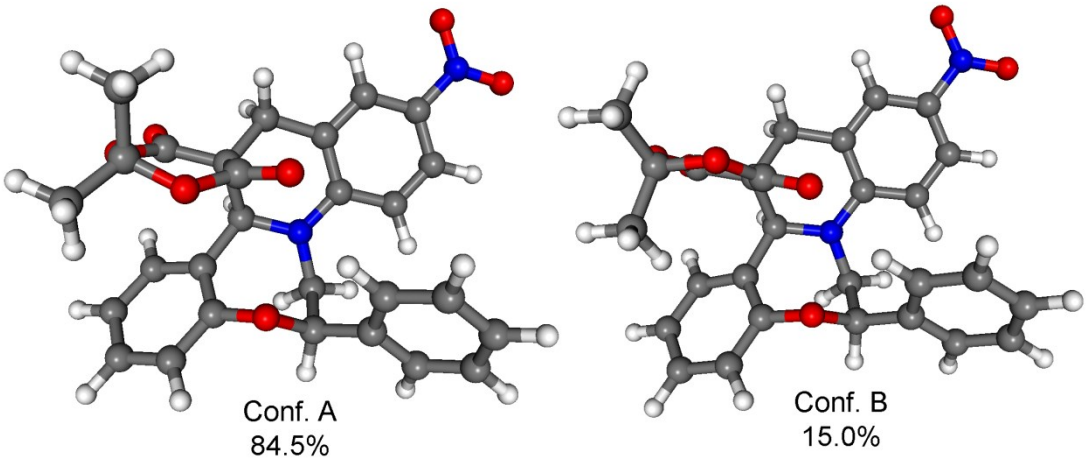


Figure S2. Low-energy conformers (> 1%) of *cis*-(2*R*,15a*S*)-**7b** optimized at B3LYP/6-31G(d) *in vacuo*. Boltzmann-weights for the same conformers in the B3LYP/TZVP PCM/$CHCl_3$ calculations are 82.5% and 14.1%, respectively.

Tables

Table S1. Cartesian coordinates of the low-energy DFT-optimized MMFF conformers of *trans*-(2*S*,15a*S*)-**7d**, model compound of **7a**, calculated at B3LYP/6-31G(d) level of theory *in vacuo*.

Conformer A		Standard Orientation (Ångstroms)		
I	Atom	X	Y	Z
1	C	1.877613	-1.936478	-2.305506
2	C	3.235946	-2.181183	-2.508297
3	C	4.177468	-1.600925	-1.657664
4	C	3.759724	-0.764479	-0.623027
5	H	1.143020	-2.405060	-2.954347
6	H	3.553140	-2.825092	-3.323043
7	H	5.237380	-1.791301	-1.801270
8	H	4.469357	-0.293244	0.049089
9	C	0.480525	1.478316	-0.872731
10	C	1.327253	1.512783	0.409322
11	O	2.025182	0.256440	0.643615
12	C	2.398599	-0.518403	-0.427019
13	C	1.433017	-1.119212	-1.257204
14	H	1.124309	1.405059	-1.755443
15	H	-0.022859	2.440012	-0.941635
16	C	-0.057932	-0.972252	-1.016289
17	N	-0.509407	0.407565	-0.890426
18	N	0.768155	-3.880898	0.702833
19	C	-0.173601	-3.309465	-0.132108
20	C	-0.617175	-1.880054	0.186767
21	C	-0.177653	-1.369035	1.553308
22	N	0.779257	-2.119065	2.226588
23	C	1.306858	-3.351488	1.873538
24	O	-0.591066	-3.912411	-1.105896
25	O	-0.642488	-0.365368	2.061528
26	O	2.143386	-3.933207	2.531312
27	C	-2.694114	-0.418384	-0.219461
28	C	-1.864011	0.639208	-0.676231
29	C	-2.454841	1.902893	-0.916865
30	C	-3.805418	2.121260	-0.711439
31	C	-4.601938	1.069722	-0.258516
32	C	-4.049376	-0.184009	-0.013695
33	H	-1.860667	2.723597	-1.299312
34	H	-4.253481	3.087472	-0.907277
35	H	-4.693249	-0.975443	0.353601
36	C	4.013443	4.902816	0.480949
37	C	4.141167	3.938756	-0.521639
38	C	3.282838	2.839883	-0.552646
39	C	2.286805	2.685723	0.423944
40	C	2.170983	3.656616	1.426211
41	C	3.025241	4.759783	1.455442
42	H	4.681854	5.759240	0.502314
43	H	4.909888	4.043293	-1.282680
44	H	3.400203	2.095161	-1.334881
45	H	1.406765	3.544937	2.191941
46	H	2.921075	5.502968	2.241289
47	H	1.125089	-1.728068	3.095999
48	H	1.107413	-4.801060	0.444215
49	H	-0.561443	-1.419700	-1.882054
50	H	0.648432	1.584035	1.262028
51	C	-2.158123	-1.803690	0.063265
52	H	-2.435673	-2.487314	-0.746521
53	H	-2.621269	-2.191827	0.977657
54	N	-6.025064	1.284735	-0.035933
55	O	-6.476350	2.414775	-0.243315
56	O	-6.702371	0.326492	0.347060

B3LYP Energy = -1673.11036861 a.u.; E+ZPVE = -1672.678981 a.u.

Table S2. Cartesian coordinates of the low-energy DFT-optimized MMFF conformers of *trans*-(2*S*,15a*S*)-**7b** calculated at B3LYP/6-31G(d) level of theory *in vacuo*.

Conformer A		Standard Orientation (Ångstroms)		
I	Atom	X	Y	Z
1	C	1.862775	-1.540671	-2.568441
2	C	3.219378	-1.768063	-2.799962
3	C	4.165682	-1.277079	-1.900194
4	C	3.754151	-0.545010	-0.786498
5	H	1.125110	-1.944372	-3.255784
6	H	3.530925	-2.331419	-3.674284
7	H	5.224698	-1.454088	-2.066988
8	H	4.467397	-0.139263	-0.076333
9	C	0.478179	1.721045	-0.803473
10	C	1.335412	1.628281	0.469349
11	O	2.028958	0.355685	0.577292
12	C	2.394138	-0.315300	-0.561691
13	C	1.424298	-0.829877	-1.442968
14	H	1.116020	1.732887	-1.693451
15	H	-0.023265	2.685722	-0.774382
16	C	-0.065831	-0.702777	-1.184444
17	N	-0.514425	0.658864	-0.921206
18	O	0.752749	-3.760632	0.209153
19	C	-0.167480	-3.108433	-0.536256
20	C	-0.630136	-1.725943	-0.076365
21	C	-0.193217	-1.340478	1.329520
22	O	0.776636	-2.095538	1.914958
23	C	0.917228	-3.485905	1.612233
24	O	-0.530690	-3.584557	-1.586141
25	O	-0.641466	-0.385853	1.915251
26	C	-0.127151	-4.281266	2.392822
27	C	-2.703371	-0.228966	-0.351787
28	C	-1.868173	0.869635	-0.689238
29	C	-2.456712	2.153209	-0.795551
30	C	-3.808508	2.350464	-0.578431
31	C	-4.610208	1.257941	-0.247887
32	C	-4.059785	-0.015471	-0.133344
33	H	-1.859149	3.009799	-1.081682
34	H	-4.253732	3.333110	-0.672528
35	H	-4.707225	-0.840349	0.142909
36	C	4.034258	4.991408	0.824432
37	C	3.048694	4.767843	1.786449
38	C	2.190519	3.673904	1.665365
39	C	2.299598	2.792802	0.582636
40	C	3.293086	3.027556	-0.380356
41	C	4.155489	4.116762	-0.257742
42	H	4.705668	5.840747	0.917299
43	H	2.949786	5.440503	2.634130
44	H	1.429200	3.497613	2.421754
45	H	3.405404	2.352798	-1.224326
46	H	4.922293	4.283959	-1.009551
47	H	-0.572403	-1.059938	-2.088792
48	H	0.666325	1.622755	1.332511
49	C	2.350591	-3.855588	1.949989
50	H	-0.003558	-4.106276	3.464952
51	H	-1.139990	-3.975699	2.107635
52	H	-0.017505	-5.349248	2.185733
53	H	2.540484	-3.669016	3.010200
54	H	2.523766	-4.912718	1.732069
55	H	3.033968	-3.247932	1.351623
56	C	-2.170077	-1.637351	-0.206621
57	H	-2.442870	-2.234610	-1.083437
58	H	-2.644581	-2.113833	0.659482
59	N	-6.034488	1.449919	-0.016742
60	O	-6.715789	0.457709	0.258524
61	O	-6.484317	2.595855	-0.109336

B3LYP Energy = -1717.41808982 a.u.; E+ZPVE = -1716.938660 a.u.

Conformer B		Standard Orientation (Ångstroms)		
I	Atom	X	Y	Z
1	C	0.757476	0.793089	2.760935
2	C	0.425583	0.503770	4.087268
3	C	-0.851806	0.052817	4.410191
4	C	-1.797304	-0.119031	3.399154
5	H	1.746886	1.175265	2.551161
6	H	1.172009	0.640591	4.864118
7	H	-1.114280	-0.168369	5.440918
8	H	-2.803176	-0.467368	3.611985
9	C	-1.401047	-0.684533	-0.965442
10	C	-2.305412	-1.105728	0.212170
11	O	-2.443810	0.011287	1.116996
12	C	-1.458360	0.161173	2.077599
13	C	-0.175800	0.636207	1.730268
14	H	-1.870449	0.178127	-1.454064
15	H	-1.347786	-1.477944	-1.713867
16	C	0.042862	0.923994	0.240297
17	N	-0.056985	-0.301507	-0.563403
18	O	0.219604	2.973619	-1.943994
19	C	1.133246	1.985128	-1.699330
20	C	1.357443	1.667674	-0.209439
21	C	1.505270	2.990960	0.550428
22	O	0.585062	3.941346	0.219248
23	C	0.196027	4.171929	-1.148160
24	O	1.624260	1.372513	-2.607651
25	O	2.298186	3.197942	1.431937
26	C	1.177823	5.169329	-1.758821
27	C	2.308420	-0.710478	-0.256833
28	C	1.002536	-1.199039	-0.525384
29	C	0.828689	-2.579917	-0.772764
30	C	1.902187	-3.455043	-0.749358
31	C	3.174126	-2.959804	-0.467340
32	C	3.373546	-1.601184	-0.226828
33	H	-0.158307	-2.980606	-0.968691
34	H	1.767931	-4.514179	-0.930899
35	H	4.380076	-1.247944	-0.031385
36	C	-6.179652	-2.291693	-1.279362
37	C	-5.935884	-0.955266	-0.956526
38	C	-4.692207	-0.567260	-0.457544
39	C	-3.679201	-1.515713	-0.269498
40	C	-3.932549	-2.855026	-0.589485
41	C	-5.174344	-3.242150	-1.094213
42	H	-7.149392	-2.591754	-1.666917
43	H	-6.717310	-0.211993	-1.090854
44	H	-4.508615	0.468367	-0.190010
45	H	-3.157553	-3.603151	-0.434048
46	H	-5.358177	-4.286050	-1.333346
47	H	-0.798632	1.546116	-0.074599
48	H	-1.835297	-1.937794	0.751706
49	C	-1.240657	4.661582	-1.121482
50	H	1.173482	6.098424	-1.182654
51	H	2.193476	4.759878	-1.750871
52	H	0.897844	5.382037	-2.794036
53	H	-1.306645	5.583822	-0.538419
54	H	-1.584012	4.855919	-2.140978
55	H	-1.887456	3.907558	-0.664991
56	C	2.589346	0.763748	-0.041711
57	H	3.353967	1.085422	-0.756788
58	H	3.015822	0.925553	0.950943
59	N	4.309780	-3.870845	-0.425512
60	O	5.419553	-3.400530	-0.159366
61	O	4.100130	-5.065009	-0.657637

B3LYP Energy = -1717.41427030 a.u.; E+ZPVE = -1716.934998 a.u.

Table S3. Cartesian coordinates of the low-energy DFT-optimized MMFF conformers of *cis*-(2*R*,15a*S*)-**7d**, model compound of **7a**, calculated at B3LYP/6-31G(d) level of theory *in vacuo*.

Conformer A		Standard Orientation (Ångstroms)		
I	Atom	X	Y	Z
1	C	3.432189	-0.394337	-1.833627
2	C	4.661339	0.264956	-1.850140
3	C	4.807022	1.479960	-1.180527
4	C	3.714154	2.040514	-0.520622
5	H	3.325285	-1.341882	-2.354280
6	H	5.498532	-0.170025	-2.387906
7	H	5.761177	1.999042	-1.184324
8	H	3.787144	2.995291	-0.009181
9	C	-0.029739	1.445198	-1.740367
10	C	0.438735	2.529093	-0.730447
11	O	1.430934	1.971681	0.153553
12	C	2.487493	1.375508	-0.503802
13	C	2.330419	0.129866	-1.141009
14	H	0.702930	1.372879	-2.550493
15	H	-0.961173	1.759573	-2.208635
16	C	1.042491	-0.685694	-1.081320
17	N	-0.175006	0.128939	-1.132634
18	N	3.261636	-2.442646	0.910401
19	C	2.237828	-2.602761	-0.003966
20	C	1.007671	-1.699032	0.151337
21	C	0.950112	-0.959918	1.486619
22	N	2.146851	-0.843808	2.186603
23	C	3.317621	-1.562482	1.989084
24	O	2.336428	-3.407936	-0.913200
25	O	-0.069864	-0.474744	1.934236
26	O	4.292849	-1.459481	2.701292
27	C	-1.493714	-1.767195	-0.367216
28	C	-1.414222	-0.444502	-0.878893
29	C	-2.623597	0.262455	-1.087565
30	C	-3.854393	-0.328792	-0.863436
31	C	-3.908531	-1.643146	-0.401937
32	C	-2.735205	-2.345164	-0.137641
33	H	-2.612422	1.299497	-1.394226
34	H	-4.773723	0.218240	-1.031556
35	H	-2.805909	-3.352526	0.257262
36	C	-2.804765	4.284800	1.515385
37	C	-2.116870	3.189053	2.038637
38	C	-1.056706	2.613545	1.335596
39	C	-0.672455	3.137868	0.096422
40	C	-1.359643	4.245109	-0.419951
41	C	-2.423709	4.813100	0.280525
42	H	-3.629878	4.727120	2.067089
43	H	-2.408040	2.772285	2.999022
44	H	-0.534722	1.757572	1.745818
45	H	-1.055928	4.672877	-1.373894
46	H	-2.945016	5.672728	-0.132111
47	H	2.119084	-0.282533	3.031336
48	H	4.095891	-2.999576	0.759745
49	H	1.058759	-1.368187	-1.943981
50	H	0.909640	3.328796	-1.322968
51	C	-0.255318	-2.568014	-0.045262
52	H	-0.024241	-3.272719	-0.851246
53	H	-0.432078	-3.166952	0.855324
54	N	-5.195788	-2.277205	-0.166964
55	O	-5.201677	-3.440338	0.248579
56	O	-6.214723	-1.618983	-0.397947

B3LYP Energy = -1673.10783505 a.u.; E+ZPVE = -1672.676362 a.u.

Table S4. Cartesian coordinates of the low-energy DFT-optimized MMFF conformers of *cis*-(2*R*,15a*S*)-**7b** calculated at B3LYP/6-31G(d) level of theory *in vacuo*.

Conformer A		Standard Orientation (Ångstroms)		
I	Atom	X	Y	Z
1	C	3.285862	0.226919	-2.018875
2	C	4.445873	1.000718	-1.981320
3	C	4.483387	2.157981	-1.203328
4	C	3.350284	2.546246	-0.489105
5	H	3.266522	-0.676217	-2.621474
6	H	5.312725	0.698285	-2.561204
7	H	5.381704	2.767990	-1.166660
8	H	3.336498	3.453474	0.106981
9	C	-0.350026	1.692372	-1.711284
10	C	0.030357	2.722566	-0.612707
11	O	1.100147	2.198945	0.193643
12	C	2.193293	1.766647	-0.526212
13	C	2.148137	0.574383	-1.274941
14	H	0.368209	1.767408	-2.533863
15	H	-1.319930	1.946187	-2.137750
16	C	0.948167	-0.369824	-1.284931
17	N	-0.344653	0.320089	-1.222743
18	O	3.389284	-2.159082	0.374937
19	C	2.348874	-2.270291	-0.475866
20	C	1.051079	-1.510338	-0.172383
21	C	0.999429	-0.907983	1.225607
22	O	2.200913	-0.696158	1.838202
23	C	3.252342	-1.656610	1.719842
24	O	2.483090	-2.908810	-1.493629
25	O	-0.016714	-0.549176	1.761561
26	C	4.544319	-0.924379	2.034748
27	C	-1.456812	-1.748825	-0.585682
28	C	-1.514050	-0.380414	-0.962391
29	C	-2.786699	0.238256	-1.031564
30	C	-3.950065	-0.474796	-0.802453
31	C	-3.871183	-1.827803	-0.474865
32	C	-2.631225	-2.449577	-0.347773
33	H	-2.875248	1.298704	-1.224305
34	H	-4.918343	0.006539	-0.861377
35	H	-2.597452	-3.492772	-0.054019
36	C	-3.313094	3.859951	1.870793
37	C	-2.437961	2.863474	2.304900
38	C	-1.342578	2.489410	1.523813
39	C	-1.113959	3.118150	0.295051
40	C	-1.988478	4.127287	-0.131568
41	C	-3.085935	4.493545	0.647330
42	H	-4.164582	4.145073	2.482846
43	H	-2.607945	2.367104	3.256471
44	H	-0.671847	1.710067	1.865010
45	H	-1.806868	4.636550	-1.076709
46	H	-3.754395	5.278874	0.304499
47	H	1.005452	-0.947444	-2.218871
48	H	0.391688	3.622652	-1.134808
49	C	2.965769	-2.838247	2.643078
50	H	5.390976	-1.610585	1.949325
51	H	4.504229	-0.526299	3.052115
52	H	4.677363	-0.098894	1.331149
53	H	2.882796	-2.491741	3.676715
54	H	2.025016	-3.326096	2.365031
55	H	3.771449	-3.573941	2.571620
56	C	-0.139195	-2.464528	-0.419935
57	H	0.106076	-3.044677	-1.315820
58	H	-0.215132	-3.180691	0.406658
59	N	-5.085883	-2.588258	-0.233483
60	O	-4.973410	-3.780851	0.069026
61	O	-6.167145	-2.002129	-0.345722

B3LYP Energy = -1717.41661743 a.u.; E+ZPVE = -1716.937000 a.u.

Conformer B		Standard Orientation (Ångstroms)		
I	Atom	X	Y	Z
1	C	3.336209	0.721719	-1.817511
2	C	4.404360	1.605039	-1.663468
3	C	4.274075	2.713407	-0.826282
4	C	3.063813	2.943242	-0.175033
5	H	3.446173	-0.137249	-2.471755
6	H	5.330655	1.426728	-2.201573
7	H	5.099802	3.407490	-0.697111
8	H	2.915338	3.811009	0.460221
9	C	-0.467335	1.768702	-1.671394
10	C	-0.246593	2.793681	-0.522075
11	O	0.823939	2.353221	0.327694
12	C	1.994825	2.056054	-0.330151
13	C	2.122593	0.904586	-1.132907
14	H	0.273896	1.952278	-2.455918
15	H	-1.440253	1.934782	-2.135125
16	C	1.032759	-0.159872	-1.293846
17	N	-0.333756	0.385156	-1.239540
18	O	3.434305	-2.369221	0.288765
19	C	2.545609	-2.081232	-0.682406
20	C	1.228627	-1.383992	-0.316596
21	C	1.090359	-1.025809	1.160786
22	O	2.028190	-1.520058	2.017980
23	C	3.366017	-1.831617	1.624687
24	O	2.772626	-2.447784	-1.812353
25	O	0.134251	-0.456126	1.617464
26	C	4.228377	-0.576691	1.699120
27	C	-1.264507	-1.795044	-0.692515
28	C	-1.434240	-0.416190	-0.990612
29	C	-2.753778	0.100829	-0.999186
30	C	-3.848765	-0.710091	-0.759247
31	C	-3.656198	-2.063125	-0.480862
32	C	-2.368741	-2.593434	-0.431107
33	H	-2.932041	1.156568	-1.149524
34	H	-4.852664	-0.304026	-0.767635
35	H	-2.242970	-3.643359	-0.191499
36	C	-3.781399	3.536224	1.842830
37	C	-2.831872	2.615135	2.288004
38	C	-1.677430	2.367948	1.542796
39	C	-1.463645	3.050966	0.340252
40	C	-2.413171	3.984244	-0.097156
41	C	-3.570066	4.222191	0.645083
42	H	-4.678921	3.722050	2.426648
43	H	-2.990503	2.078382	3.219447
44	H	-0.947991	1.643274	1.884104
45	H	-2.244632	4.535714	-1.020783
46	H	-4.297477	4.949630	0.294610
47	H	1.191817	-0.610146	-2.283337
48	H	0.048609	3.741264	-1.000526
49	C	3.833300	-2.945223	2.548189
50	H	5.256357	-0.816373	1.413235
51	H	4.221722	-0.189959	2.722041
52	H	3.850399	0.199084	1.029032
53	H	3.804662	-2.601256	3.585386
54	H	3.178016	-3.813655	2.442438
55	H	4.855657	-3.235847	2.292748
56	C	0.107285	-2.410629	-0.675247
57	H	0.370585	-2.811815	-1.660463
58	H	0.135779	-3.252794	0.025912
59	N	-4.798690	-2.921076	-0.219828
60	O	-4.584290	-4.110433	0.037958
61	O	-5.924983	-2.416651	-0.271244

B3LYP Energy = -1717.41520537 a.u.; E+ZPVE = -1716.935371 a.u.

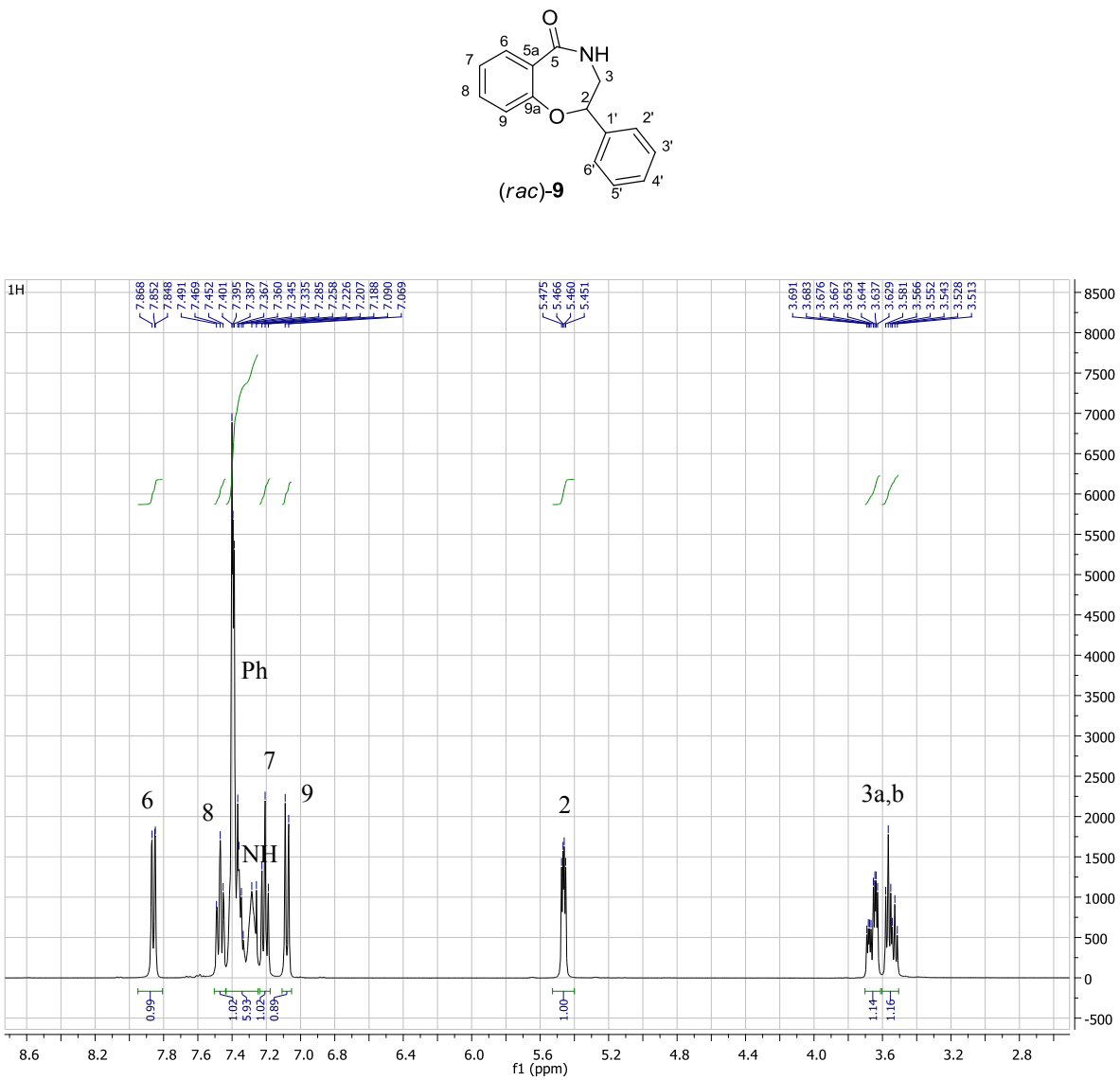


Figure S3. ^{1}H-NMR spectra of (*rac*)-**9** measured in $CDCl_3$ (400 MHz).

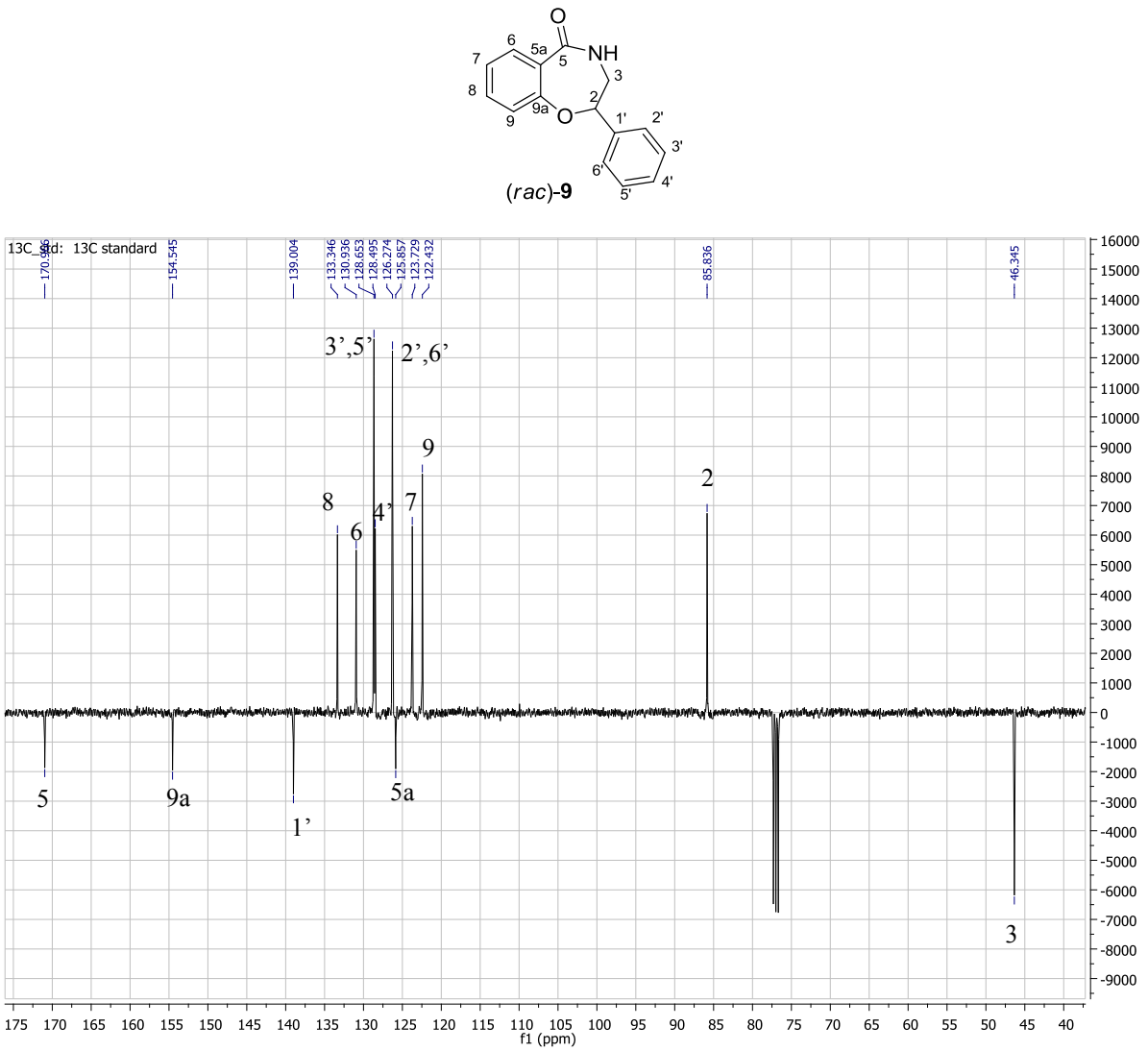


Figure S4. ^{13}C-NMR spectra of (*rac*)-**9** measured in $CDCl_3$ (100 MHz).

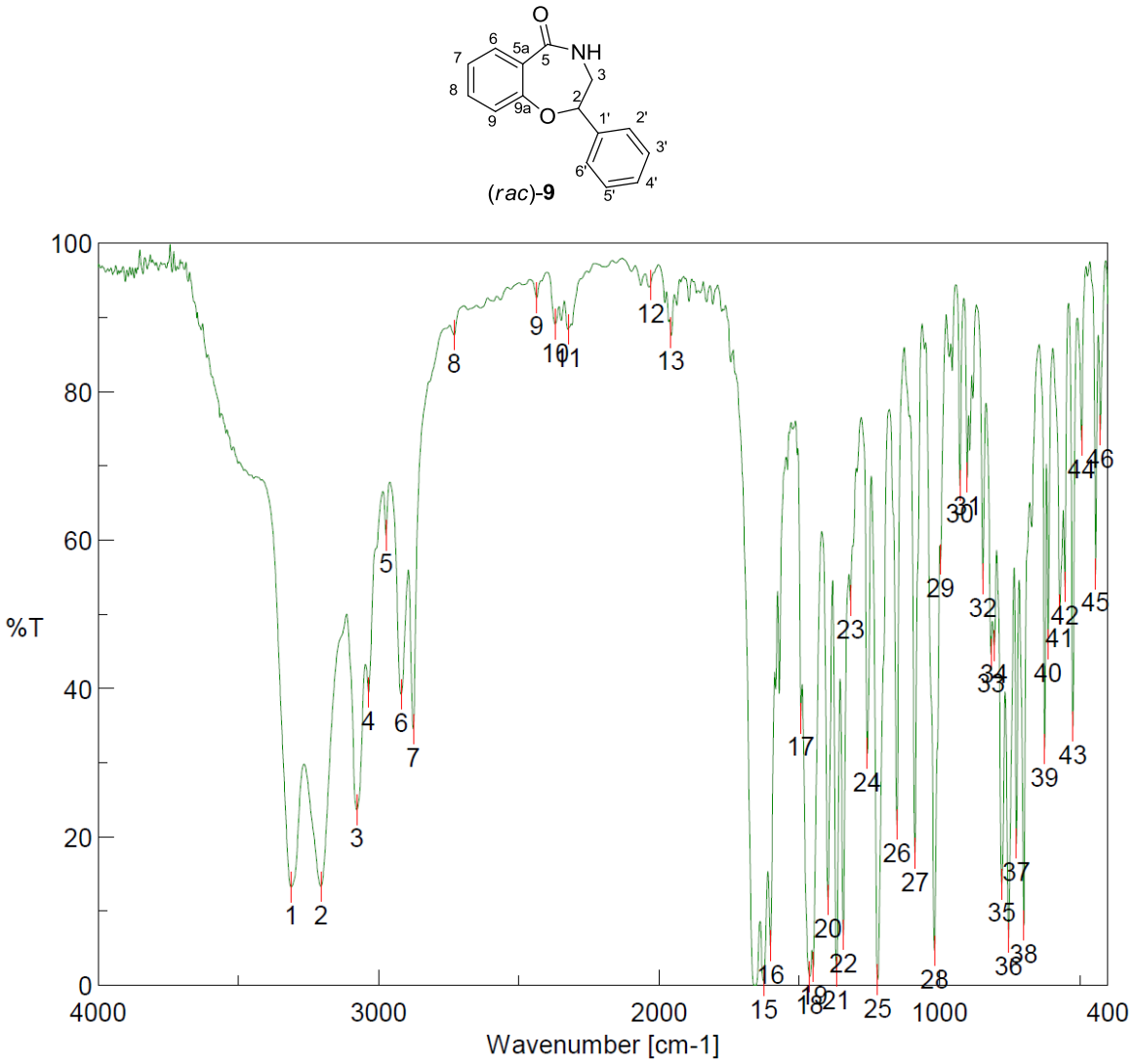


Figure S5. IR spectra of (*rac*)-**9** recorded as KBr disc.

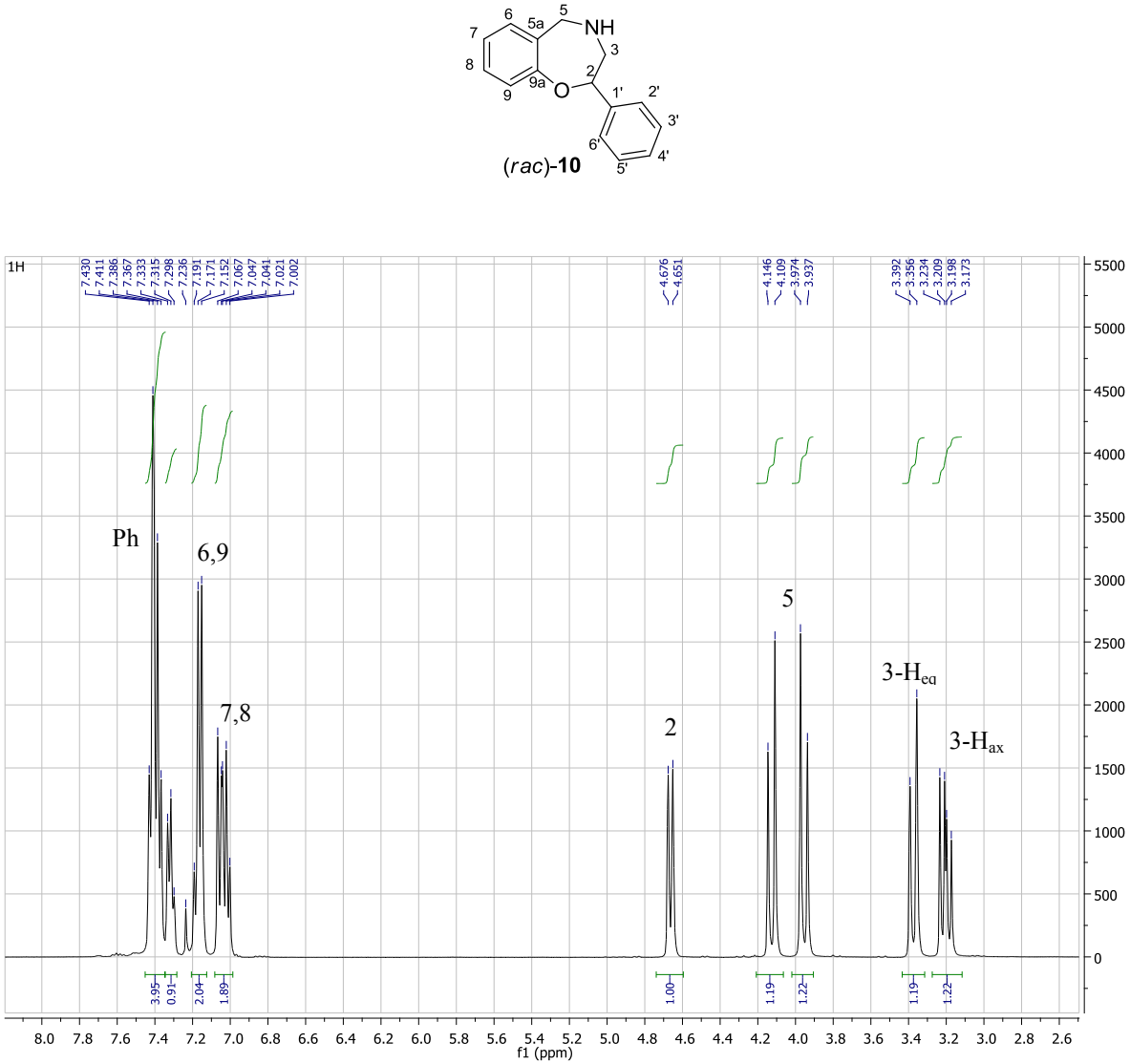


Figure S6. ^{1}H-NMR spectra of (*rac*)-**10** measured in $CDCl_3$ (400 MHz).

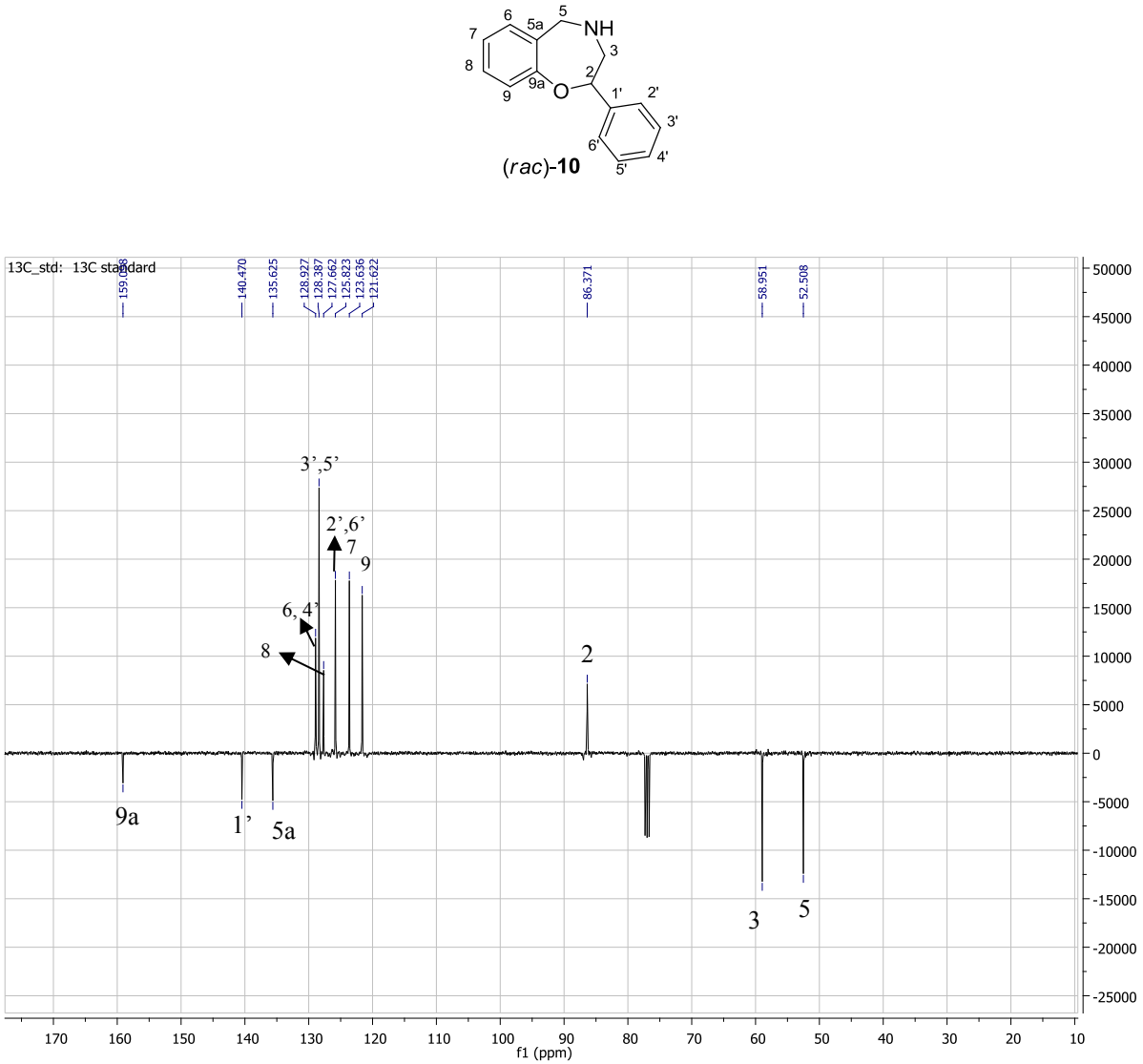


Figure S7. ^{13}C-NMR spectra of (*rac*)-**10** measured in $CDCl_3$ (100 MHz).

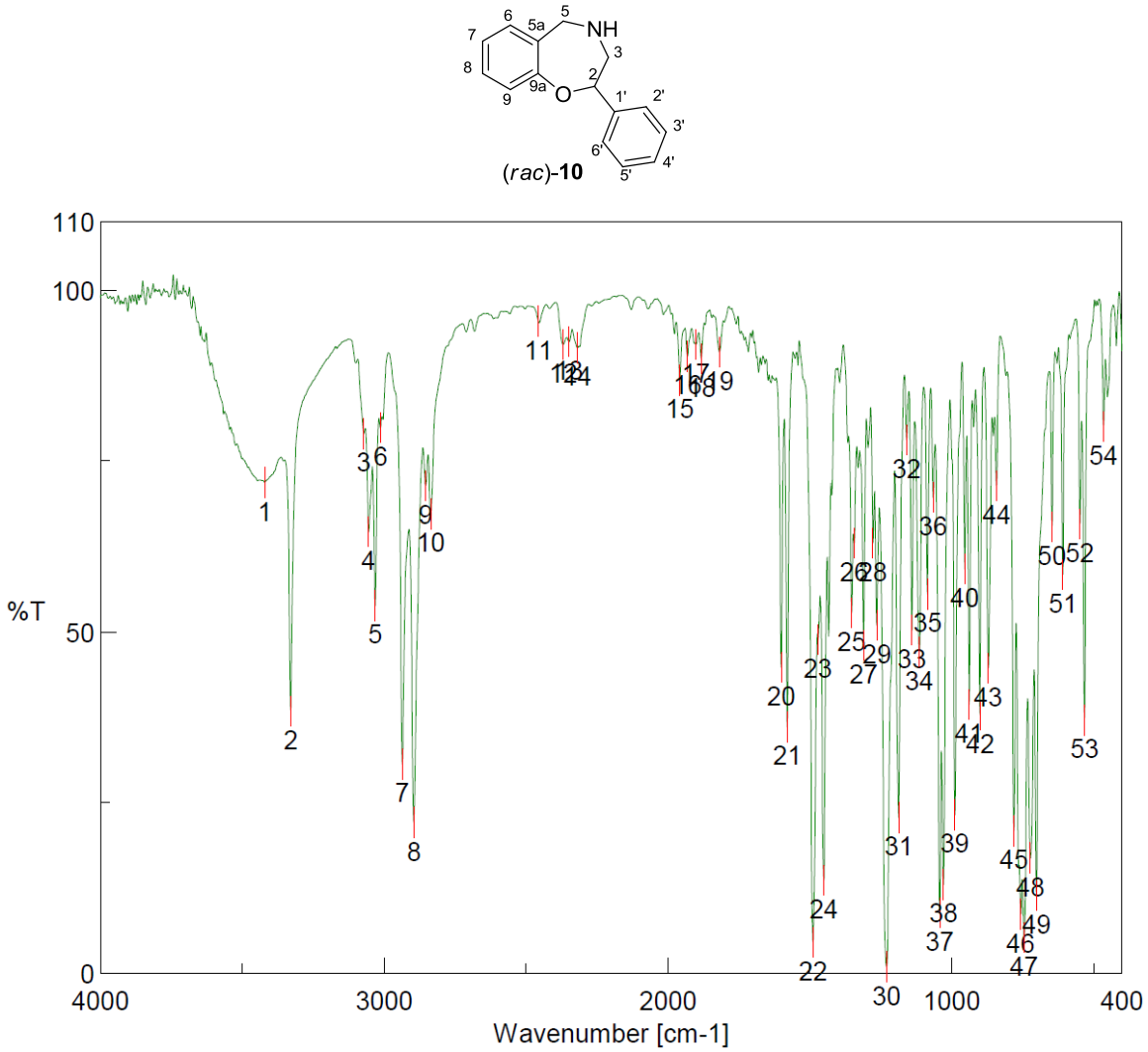
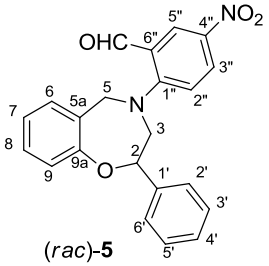


Figure S8. IR spectra of (*rac*)-**10** recorded as KBr disc.



(*rac*)-**5**

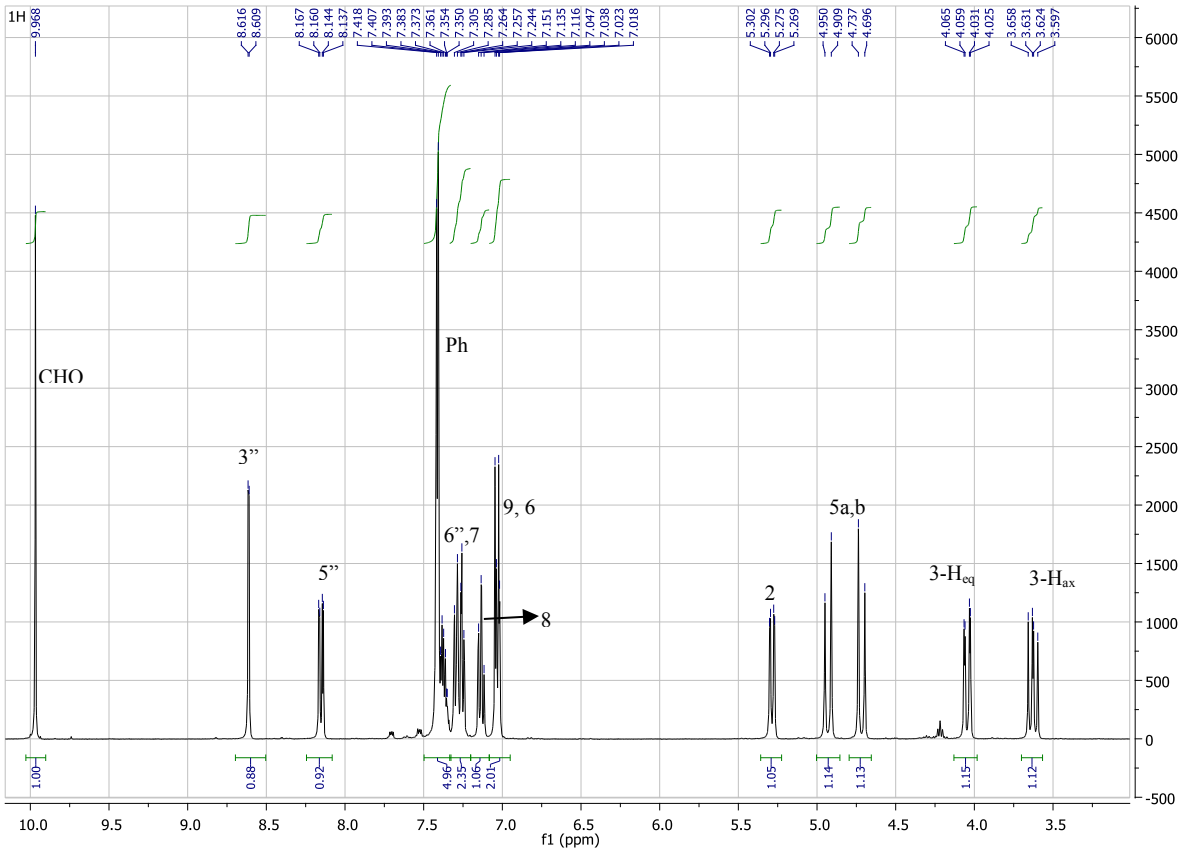


Figure S9. ^{1}H-NMR spectra of (*rac*)-**5** measured in $CDCl_3$ (400 MHz).

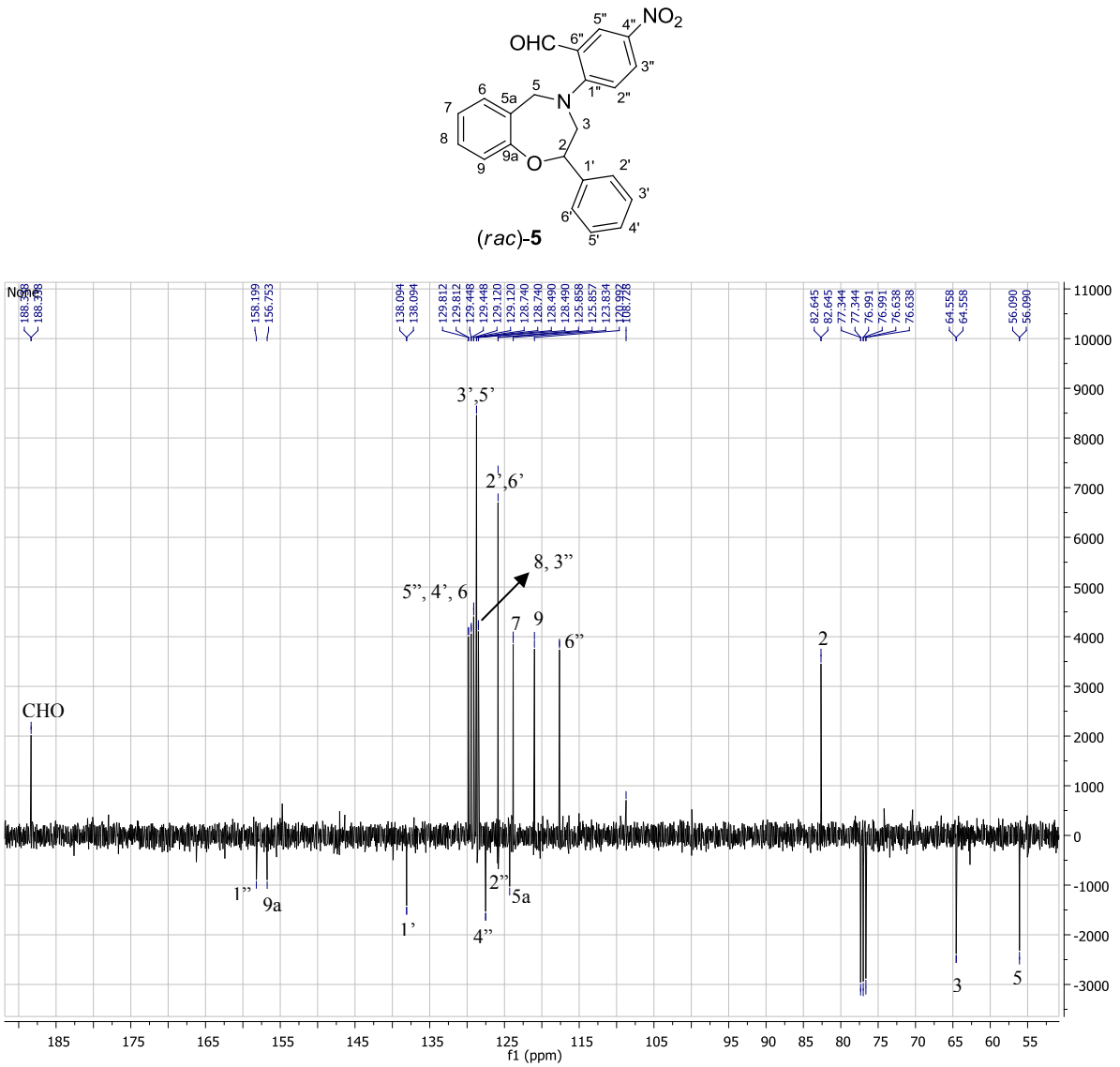


Figure S10. ^{13}C-NMR spectra of (*rac*)-**5** measured in $CDCl_3$ (100 MHz).

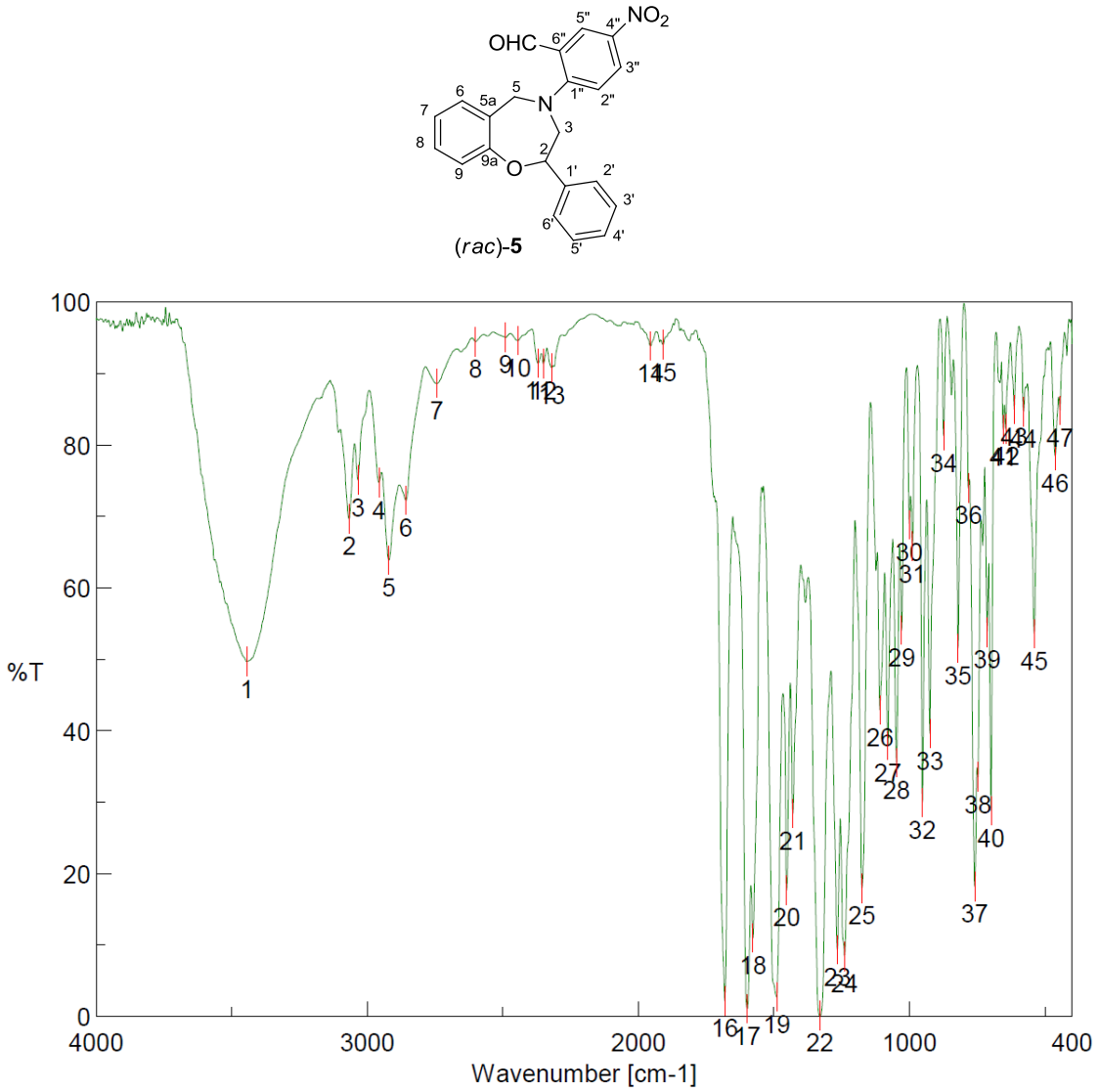


Figure S11. IR spectra of (*rac*)-**5** recorded as KBr disc.

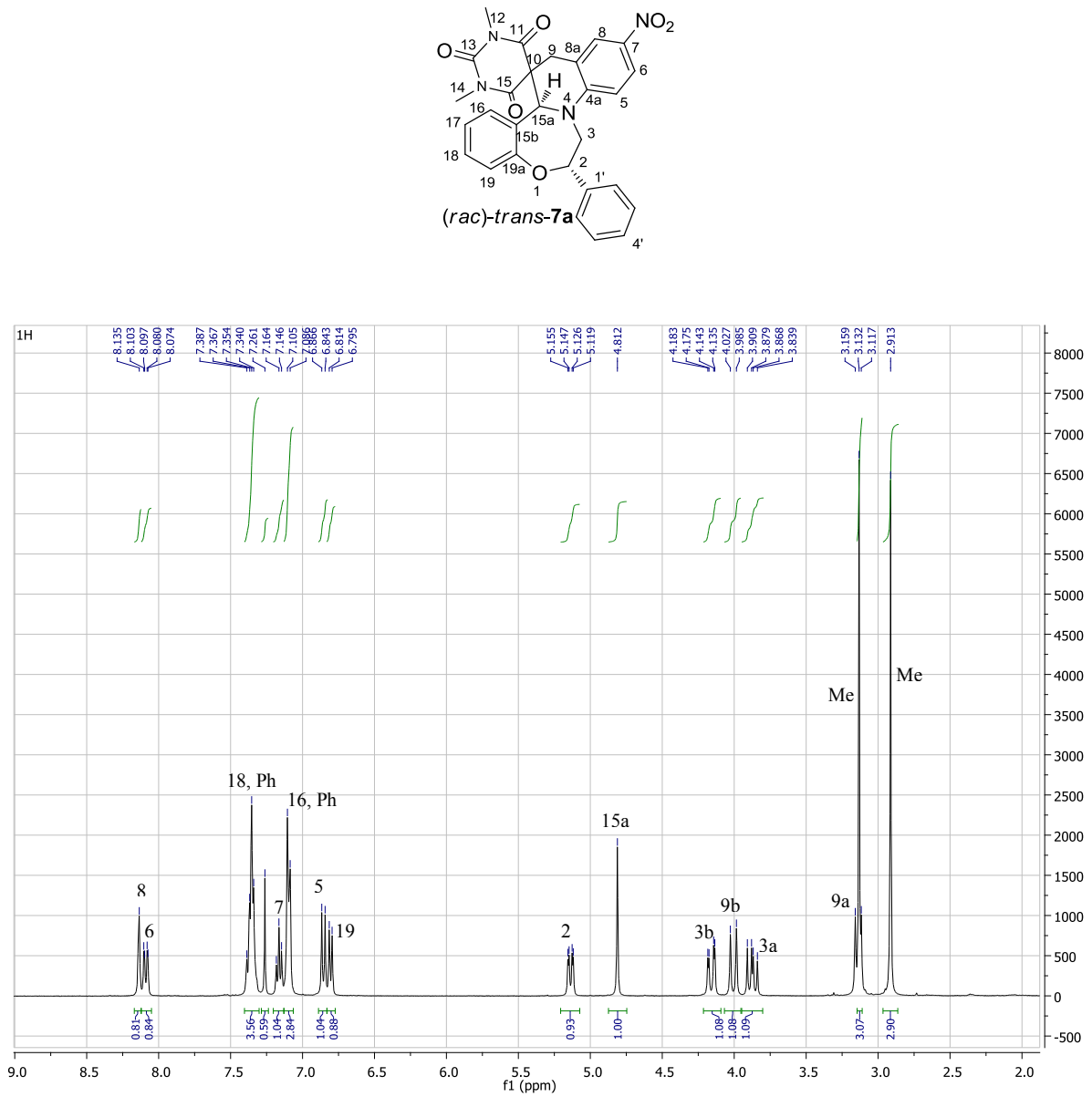


Figure S12. ^{1}H-NMR spectra of (*rac*)-**7a** measured in $CDCl_3$ (400 MHz).

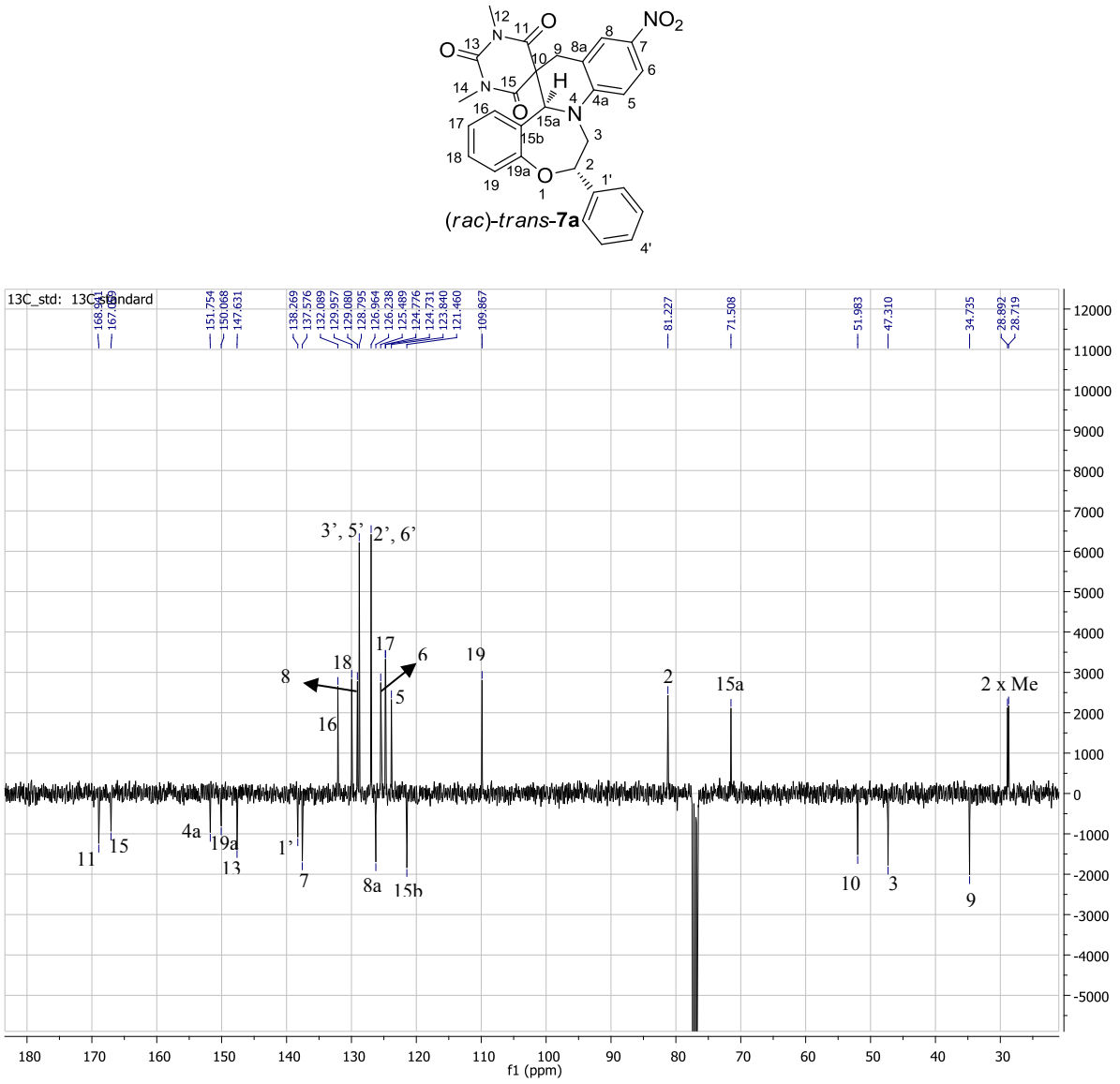


Figure S13. ^{13}C-NMR spectra of (*rac*)-**7a** measured in $CDCl_3$ (100 MHz).

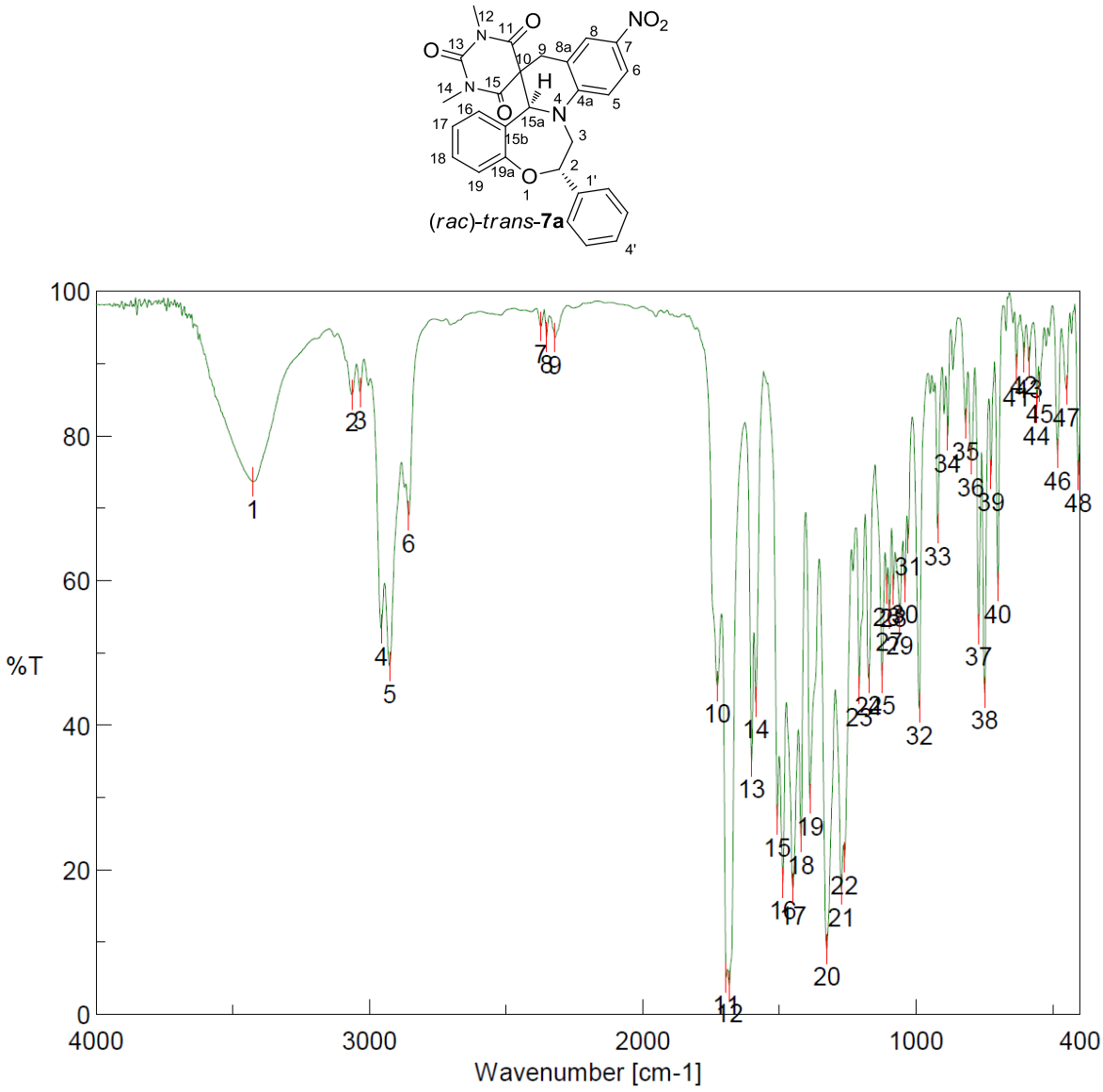
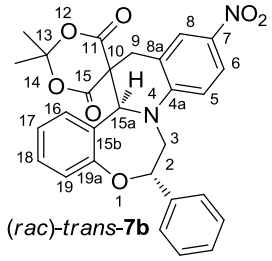


Figure S14. IR spectra of (*rac*)-**7a** recorded as KBr disc.



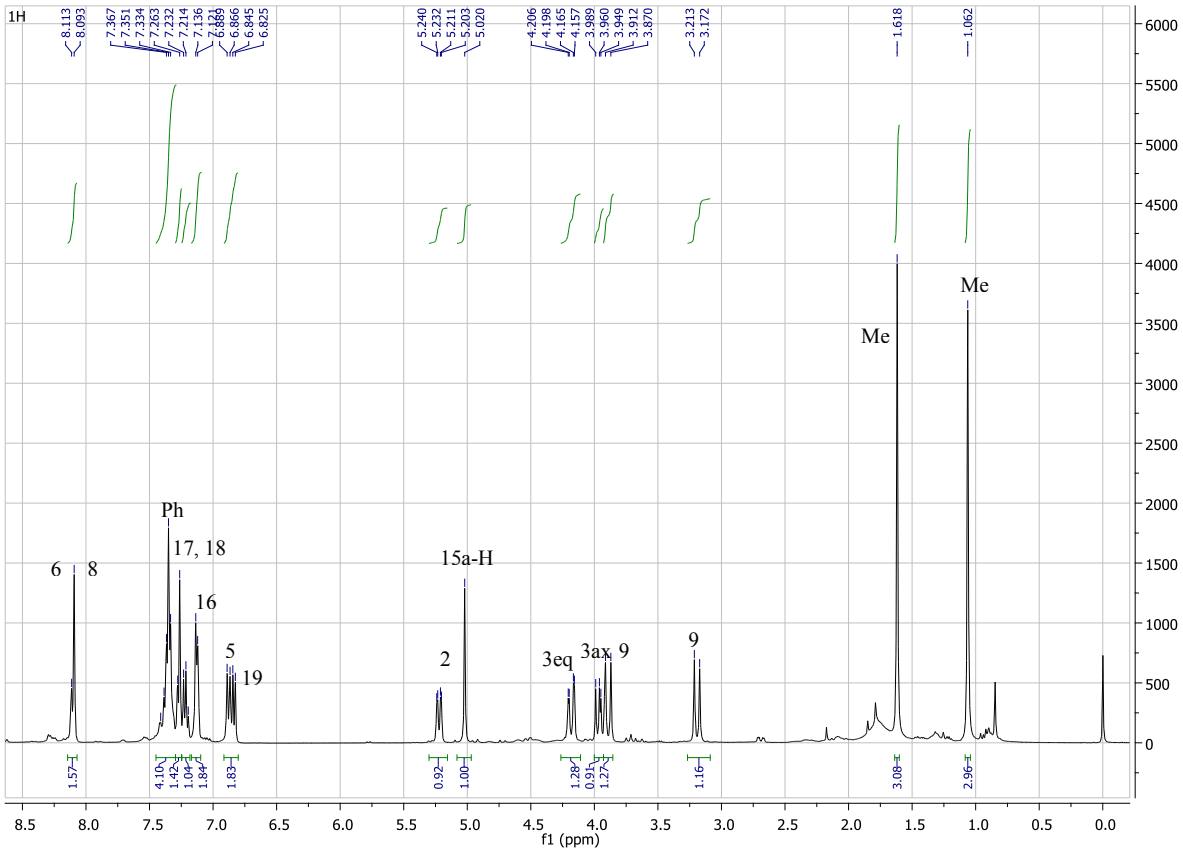
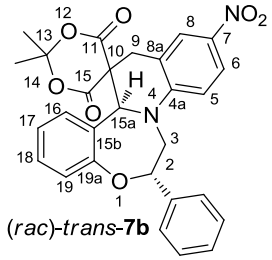


Figure S15. ^{1}H-NMR spectra of (*rac*)-**7b** measured in $CDCl_3$ (400 MHz).



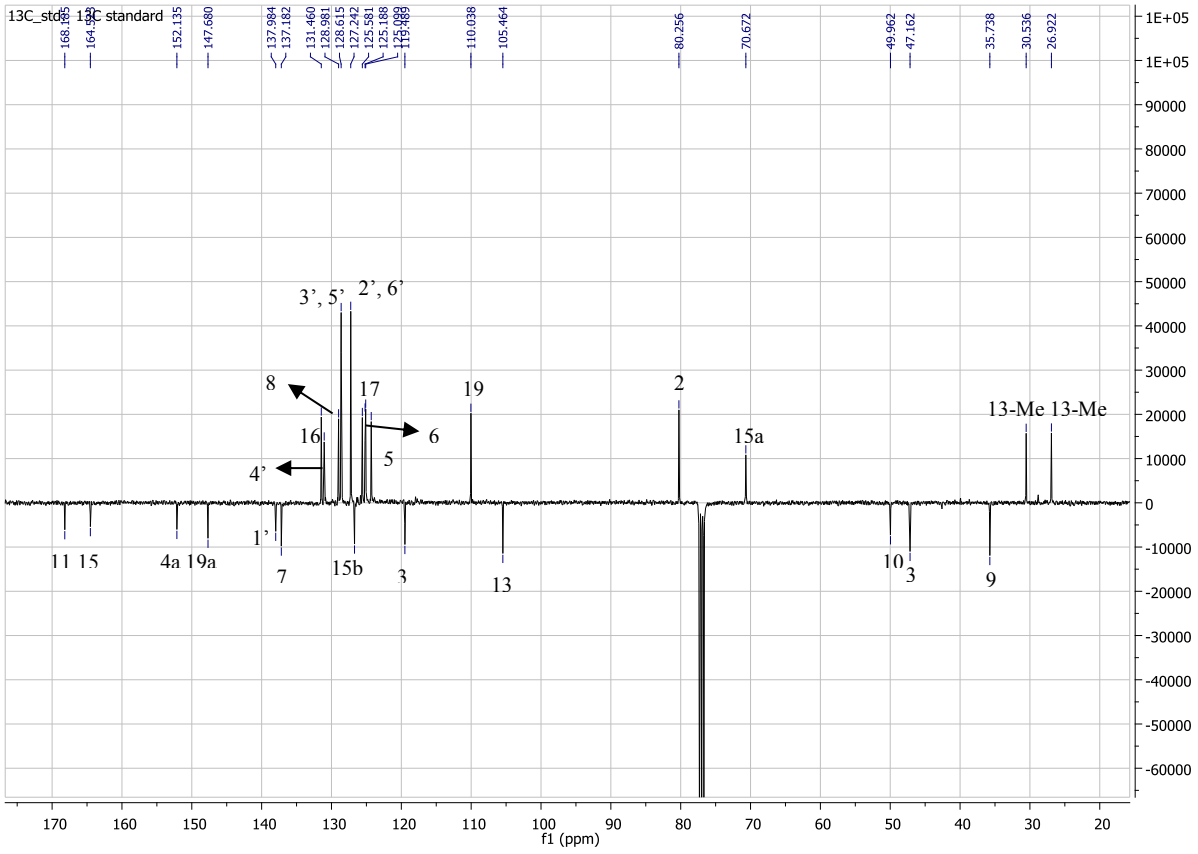


Figure S16. ^{13}C-NMR spectra of (*rac*)-**7b** measured in $CDCl_3$ (100 MHz).

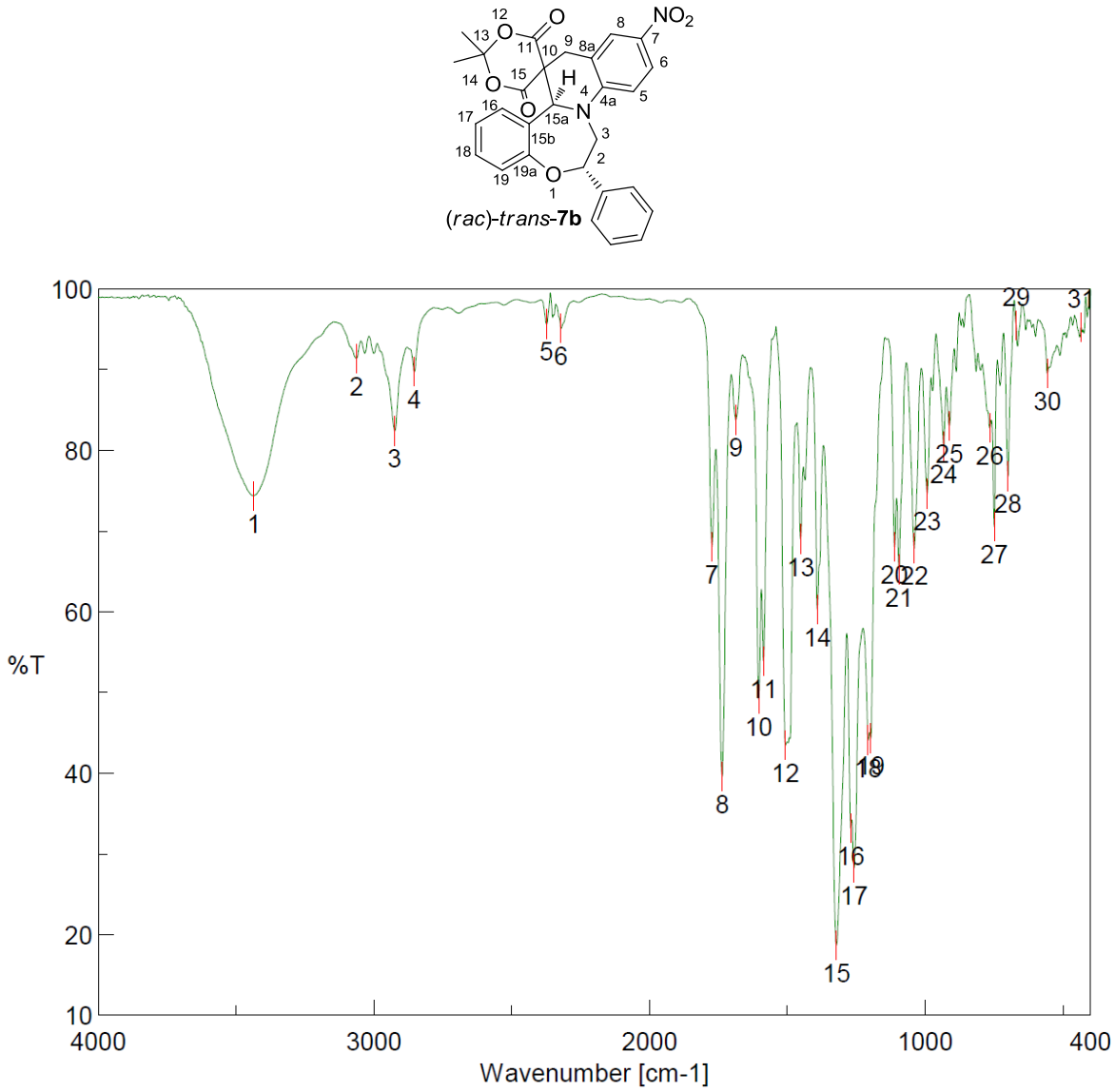


Figure S17. IR spectra of (*rac*)-**7b** recorded as KBr disc.

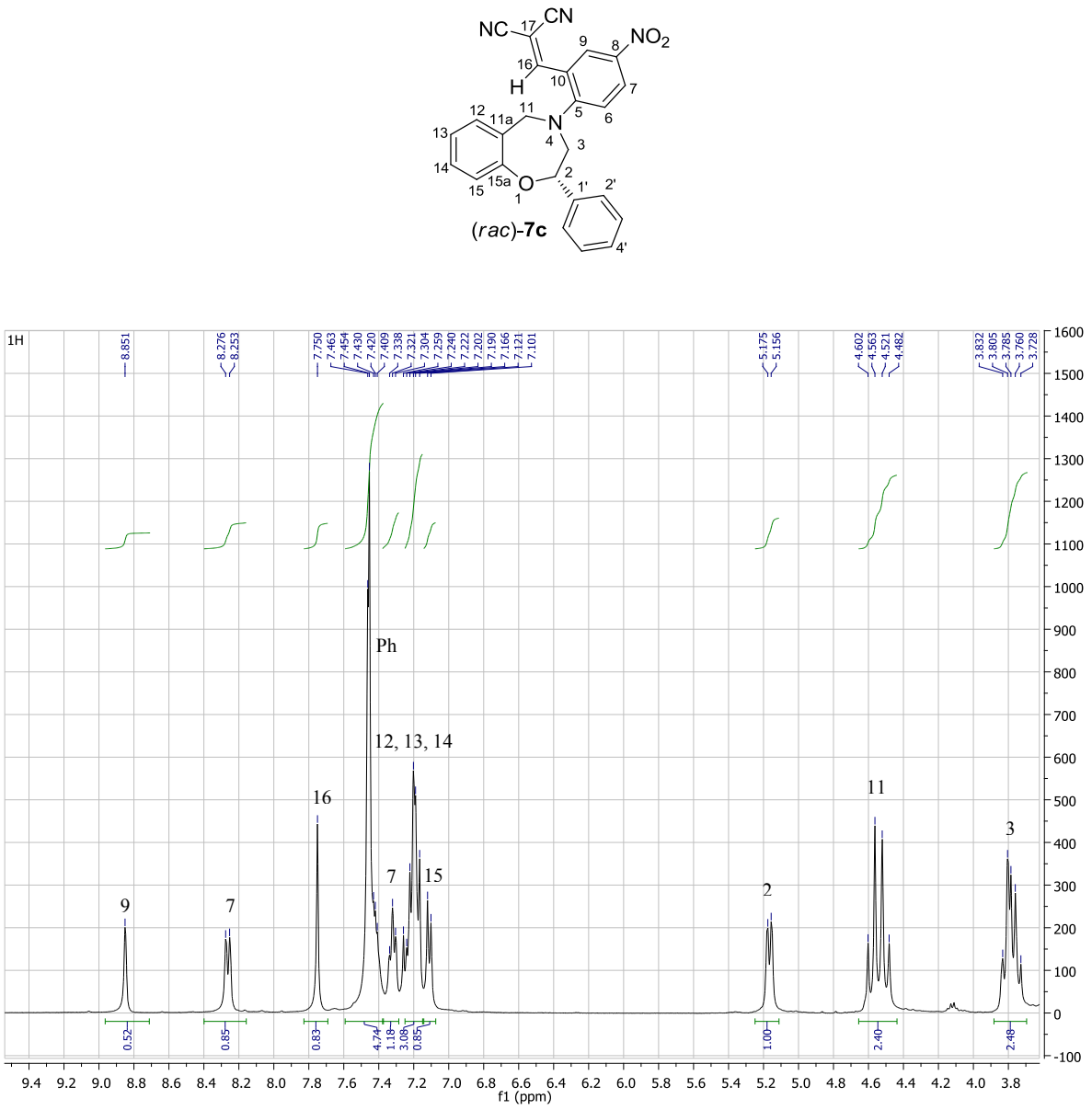


Figure S18. ^{1}H-NMR spectra of (*rac*)-**7c** measured in $CDCl_3$ 400 MHz.

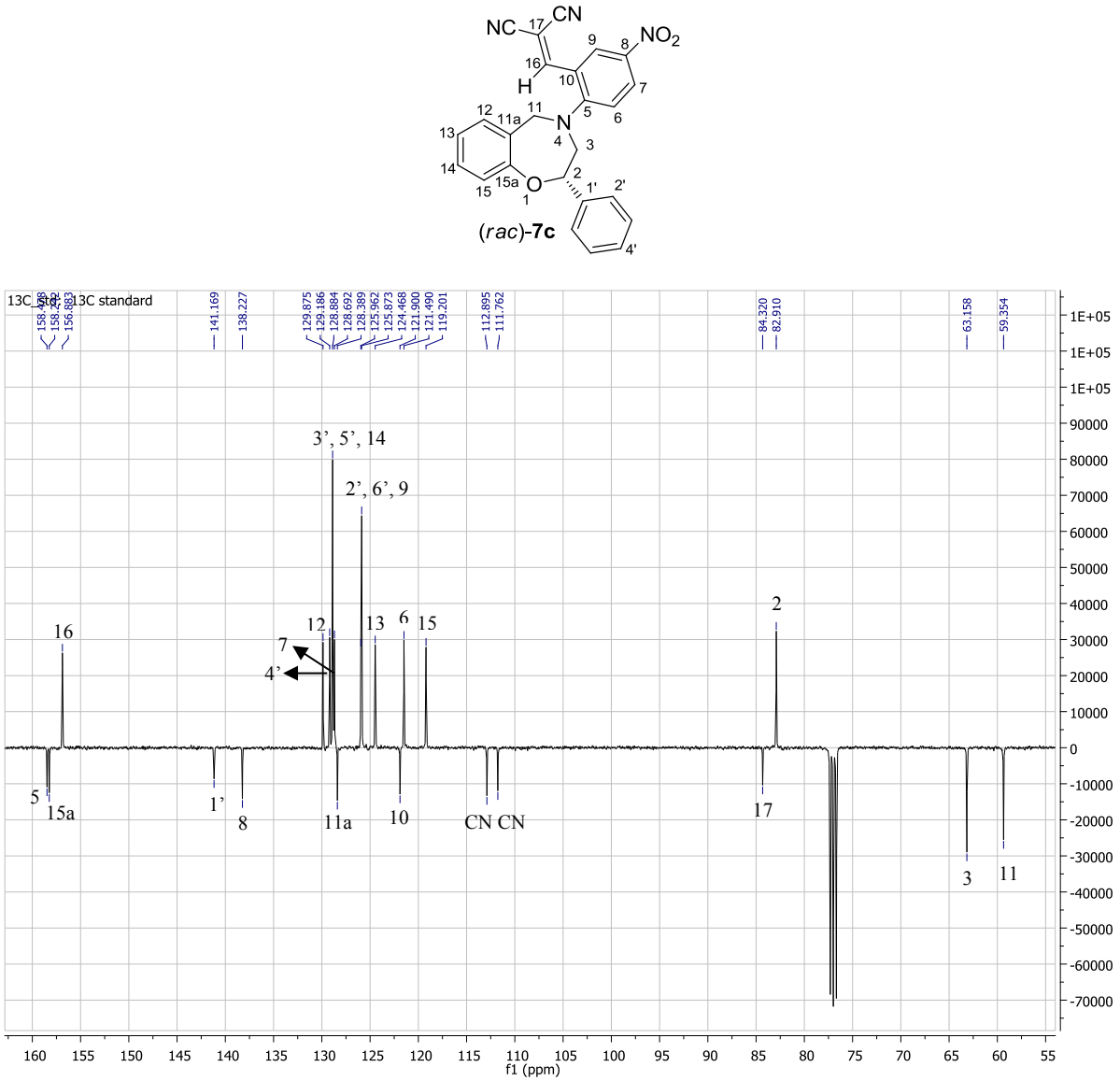


Figure S19. ^{13}C-NMR spectra of (*rac*)-**7c** measured in $CDCl_3$ 100 MHz.

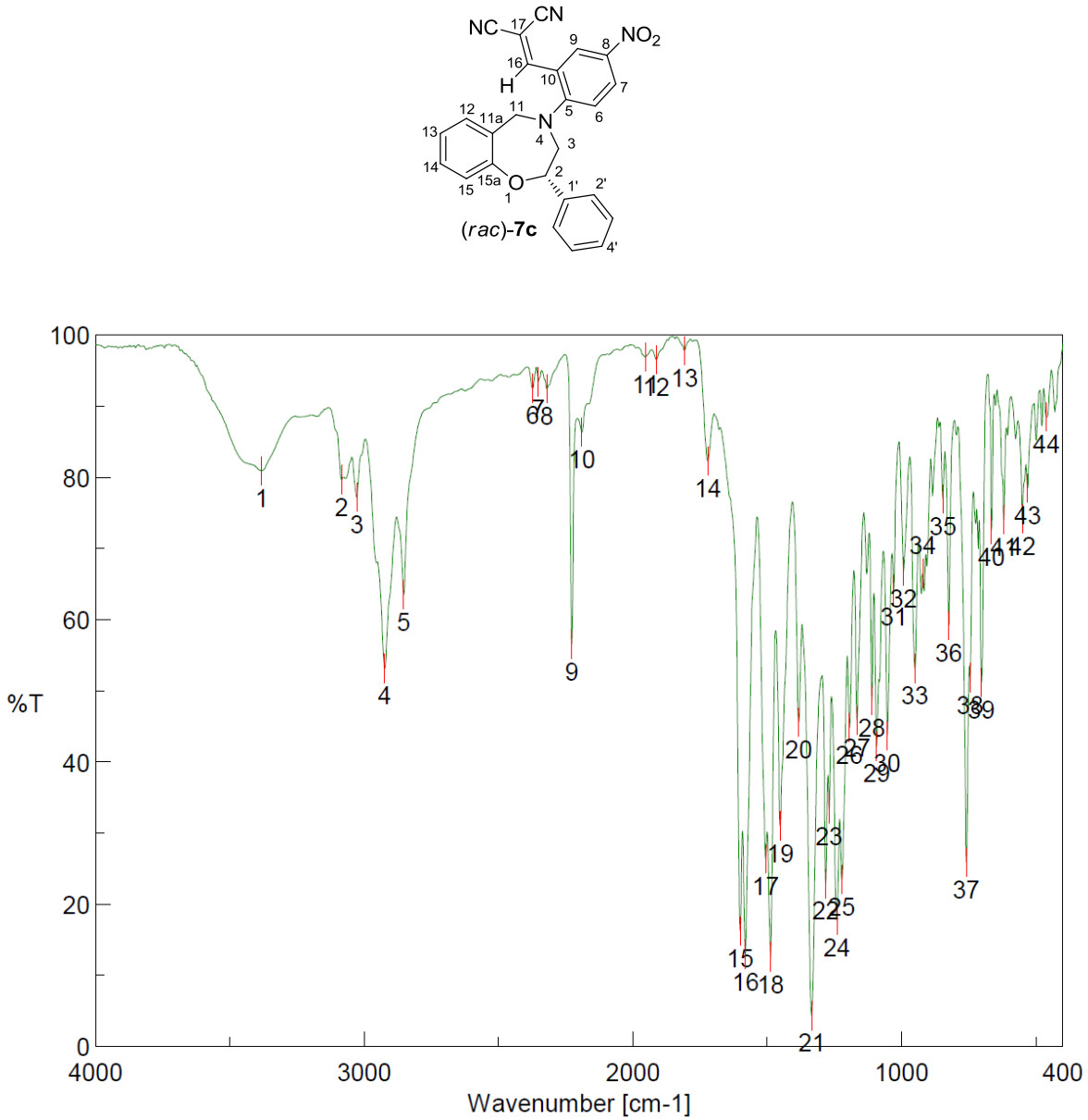


Figure S20. IR spectra of (*rac*)-**7c** recorded as KBr disc.