Electronic Supplementary Information

Cucurbit[7]uril host-guest complexes of the histamine H_2-receptor antagonist ranitidine

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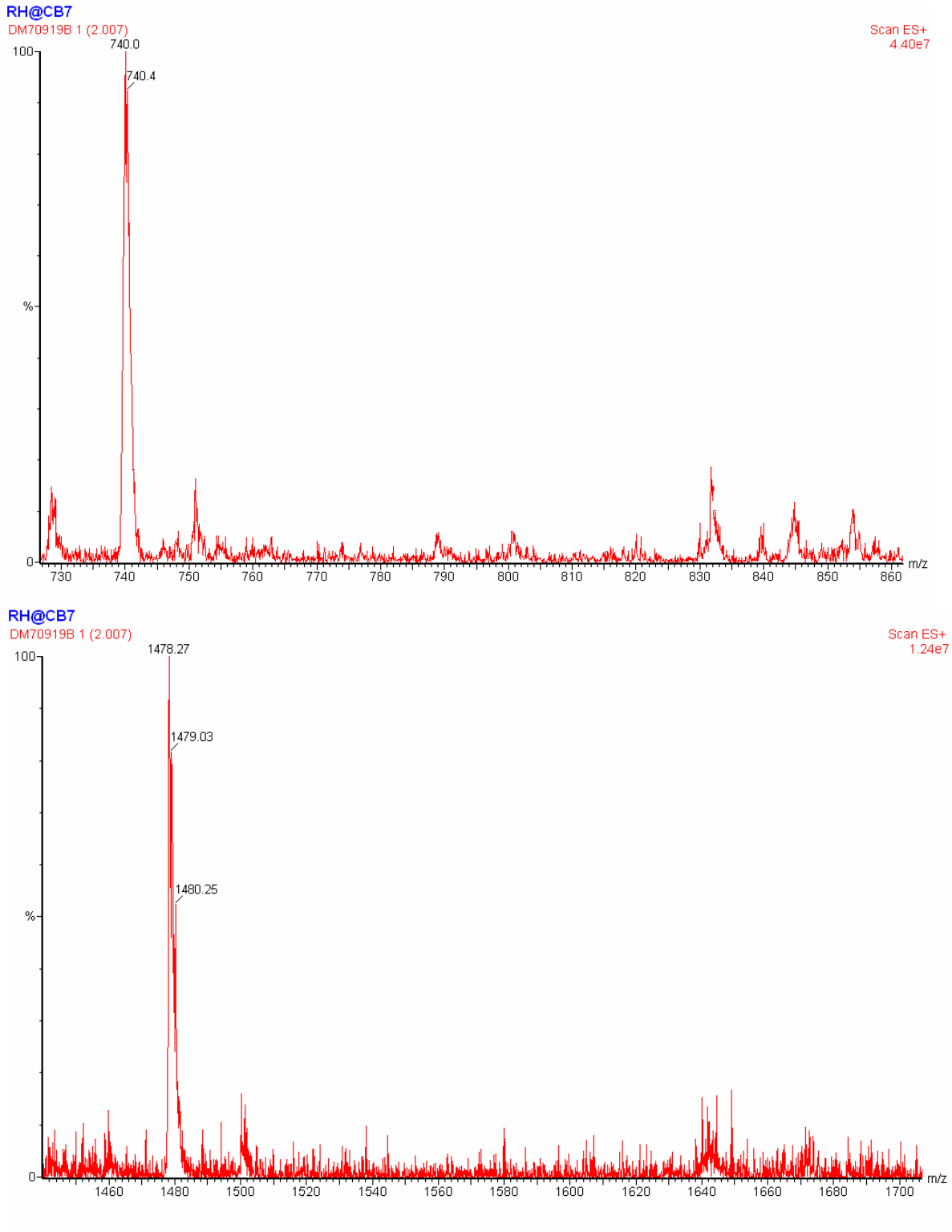


Figure S1 Electrospray mass spectra of $\{RH_2 \bullet CB[7]\}^{2+}$ (top) and $\{RH \bullet CB[7]\}^{+}$ (bottom) in aqueous solution.

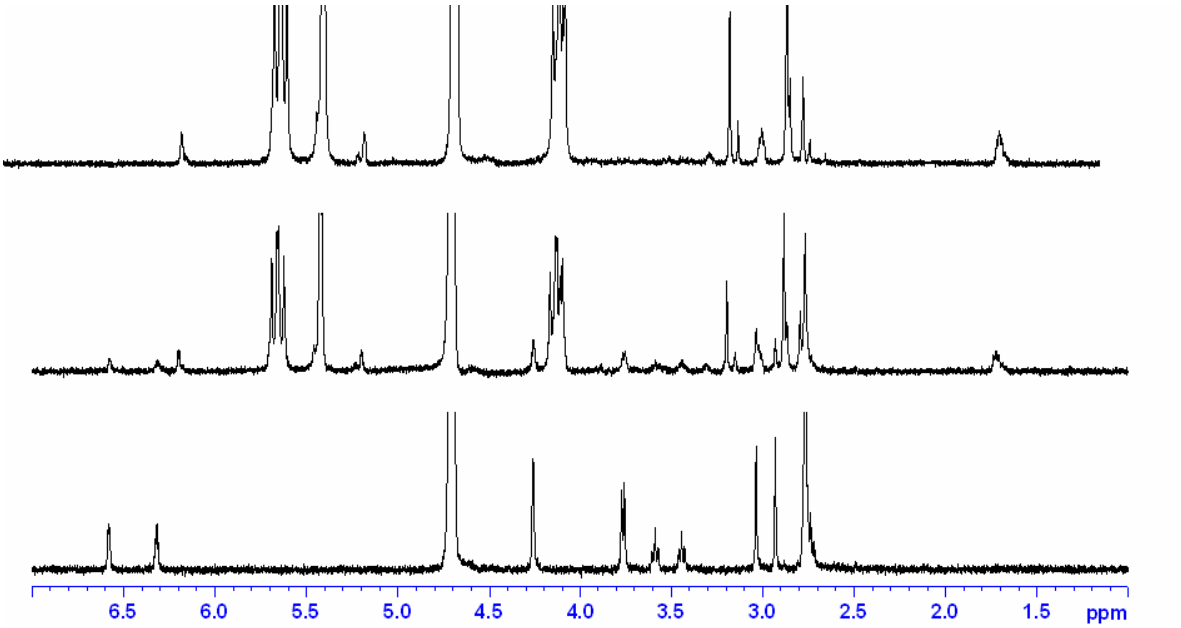


Figure S2 ^{1}H NMR spectra of (a) ranitidine at pD 1.5, (b) ranitidine at pD 1.5 with 0.7 equivalents of CB[7], and (c) ranitidine at pD 1.5 with 1.4 equivalents of CB[7], in D_2O.

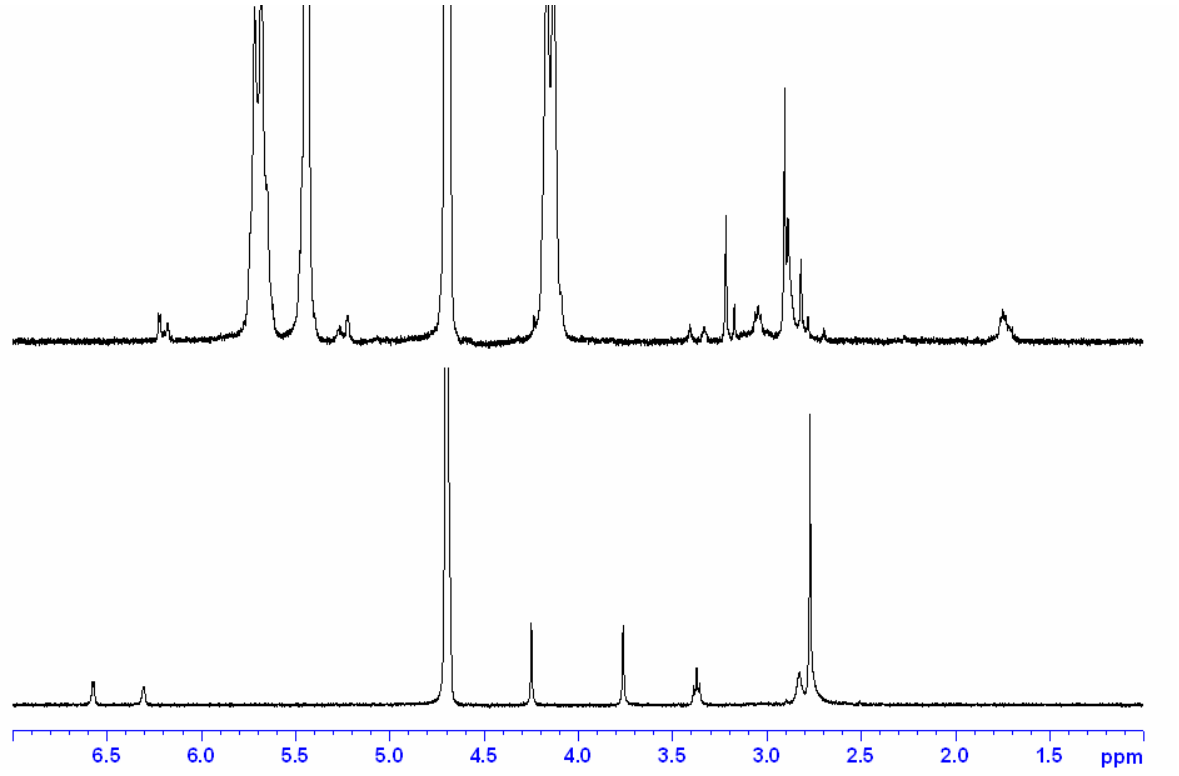


Figure S3 ^{1}H NMR spectra of (a) ranitidine at pD 4.8 and (b) raniditine at pD 4.8 in the presence of 1.4 equivalents of CB[7] in D_2O.

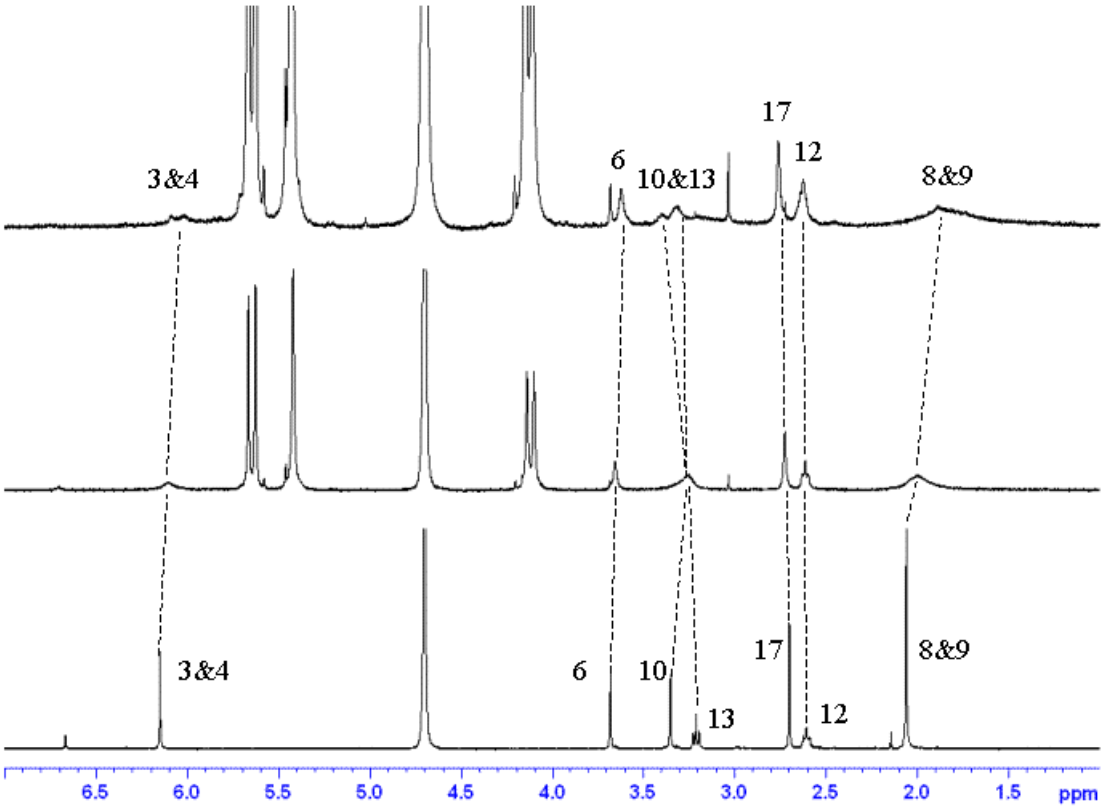


Figure S4 ^{1}H NMR spectra of (a) ranitidine at pD 12, (b) ranitidine at pD 12 with 0.5 equivalents of CB[7], and (c) ranitidine at pD 12 with 1.2 equivalents of CB[7], in D_2O.

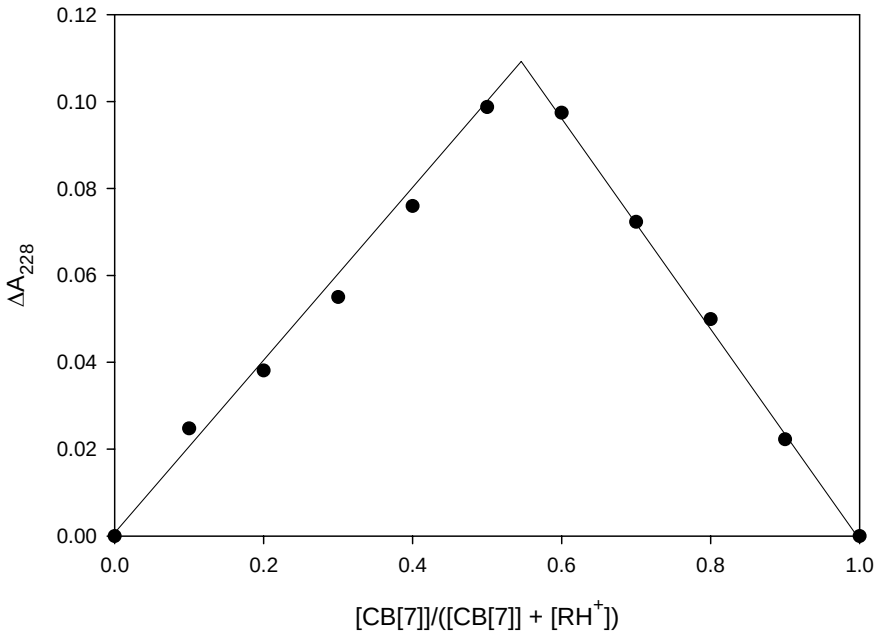


Figure S5 UV-visible Job's plot of ΔA against [RH]/([RH]+[CB[7]]) for rantitidine and cucurbit[7]uril (total concentration is 5.0 x 10^{-5} M), monitored at 228 nm.

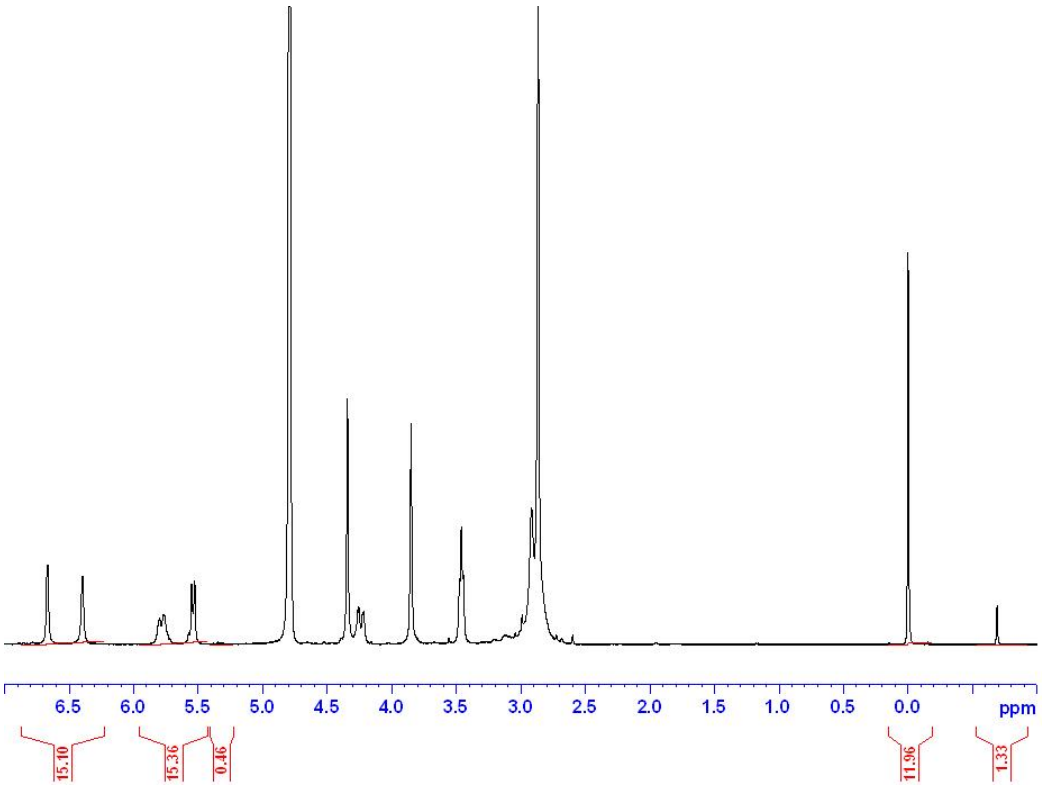


Figure S6 ^{1}H NMR competition binding study of diprotonated ranitidine with cucurbit[7]uril in the presence of the competing TSP guest

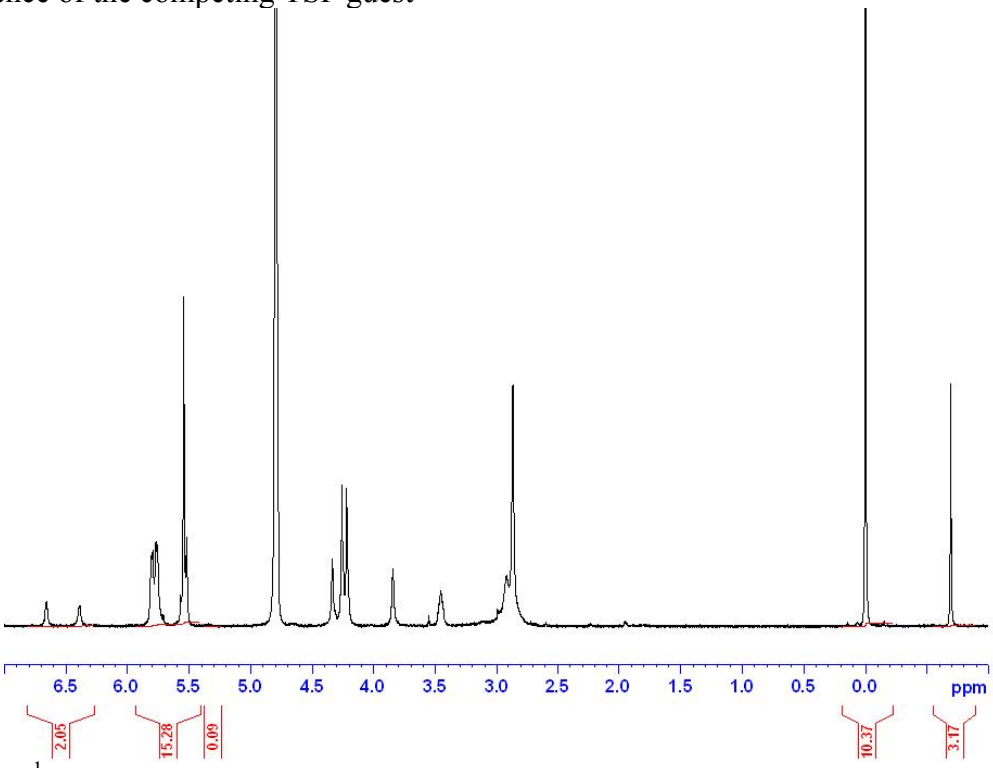


Figure S7 ^{1}H NMR competition binding study of monoprotonated ranitidine with cucurbit[7]uril in the presence of the competing TSP guest

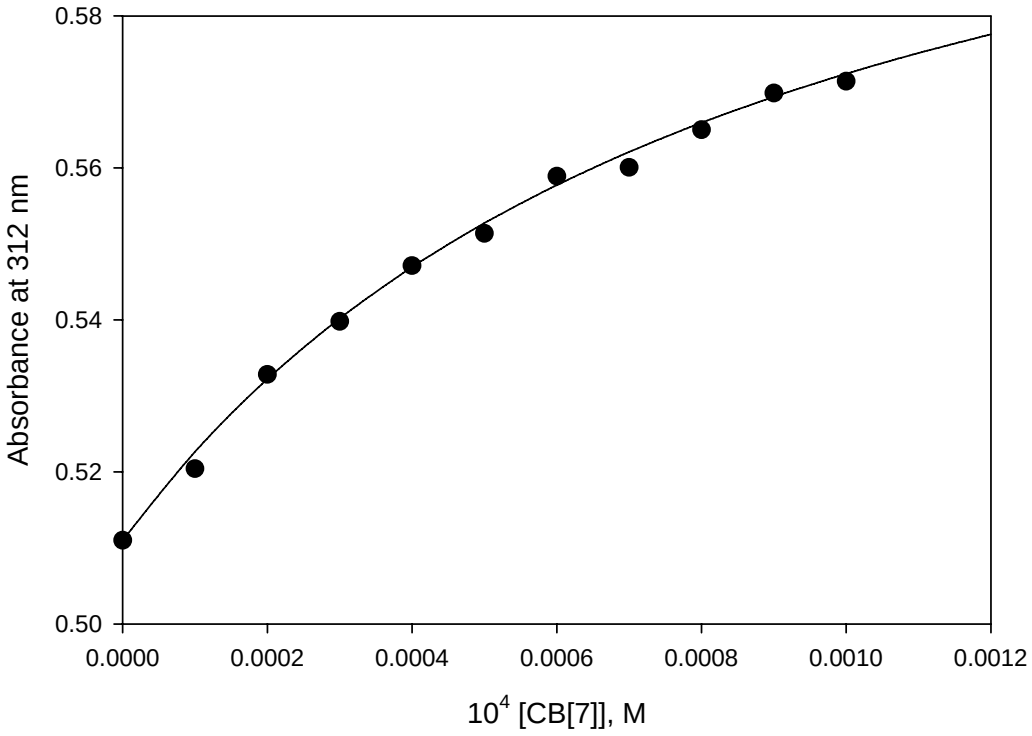
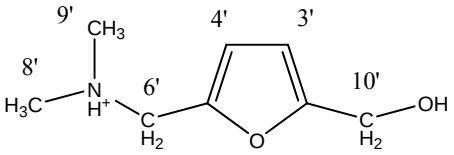
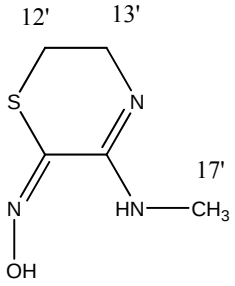


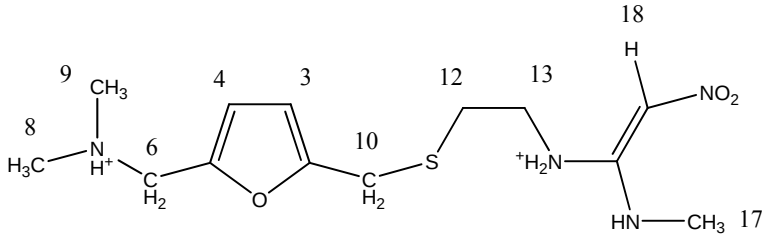
Figure S8 UV titration (monitored at 312 nm) of ranitidine (5 x 10^{-5} M) with CB[7] in aqueous solution (pH = 13.0) at 25 °C. The solid curve corresponds to a non-linear least squares fit with a stability constant of $K_{CB[7]}{}^{3}$ = 1.2 x 10^{3} M^{-1}.



5-N,N-dimethylaminomethyl-2-furylmethanol



3-methylamino-5,6-dihydro-2*H*-1,4-thiazin-2-one



diprotonated ranitidine

Figure S9. Structures of the diprotonated ranitidine (bottom) and the main thermal decomposition products (top).

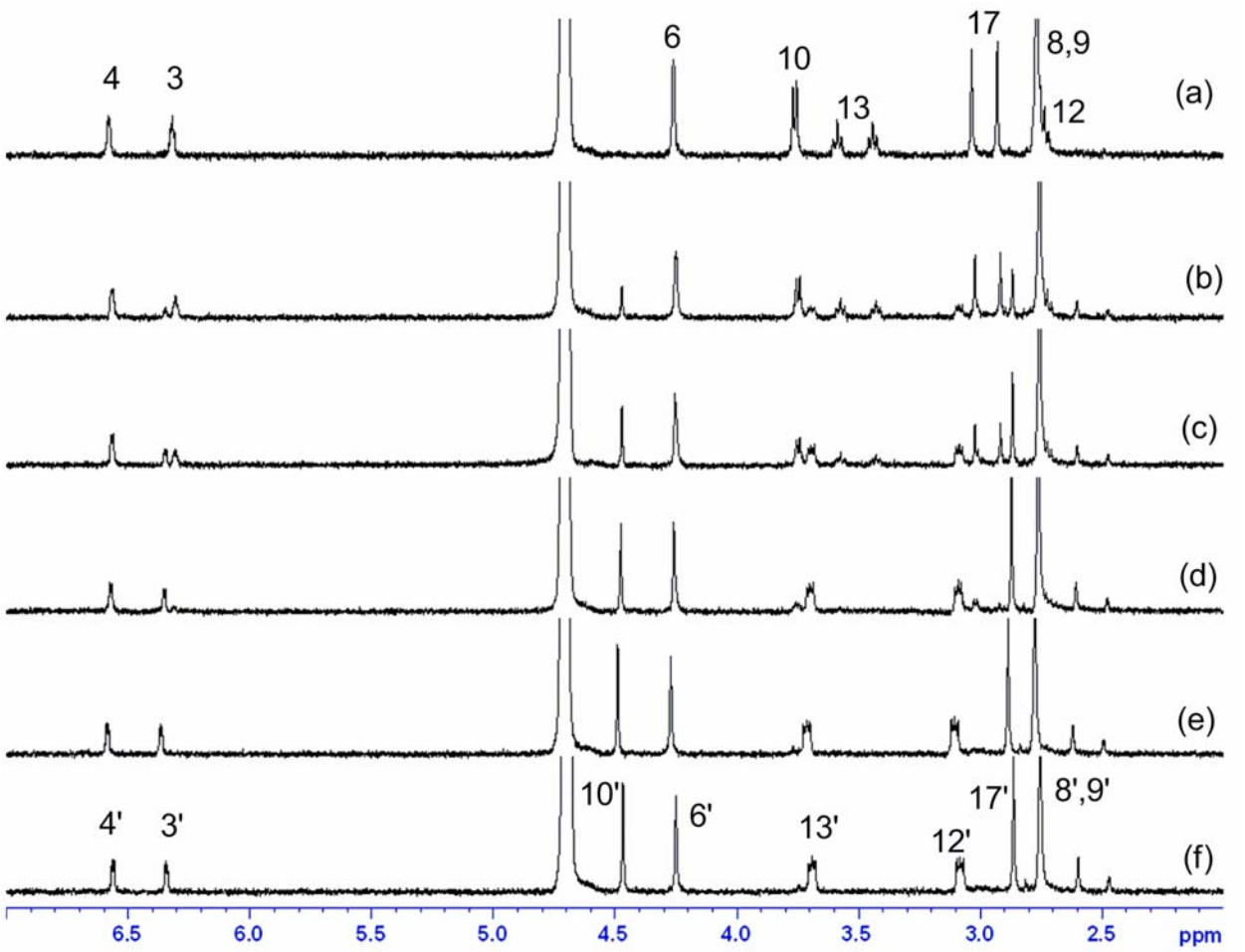


Figure S10 ^{1}H NMR spectra of ranitidine (pD 1.5) at 50 °C after (a) 0 days, (b) 2 days, (c) 4 days, (d) 6 days, (e) 10 days, and (f) 13 days.

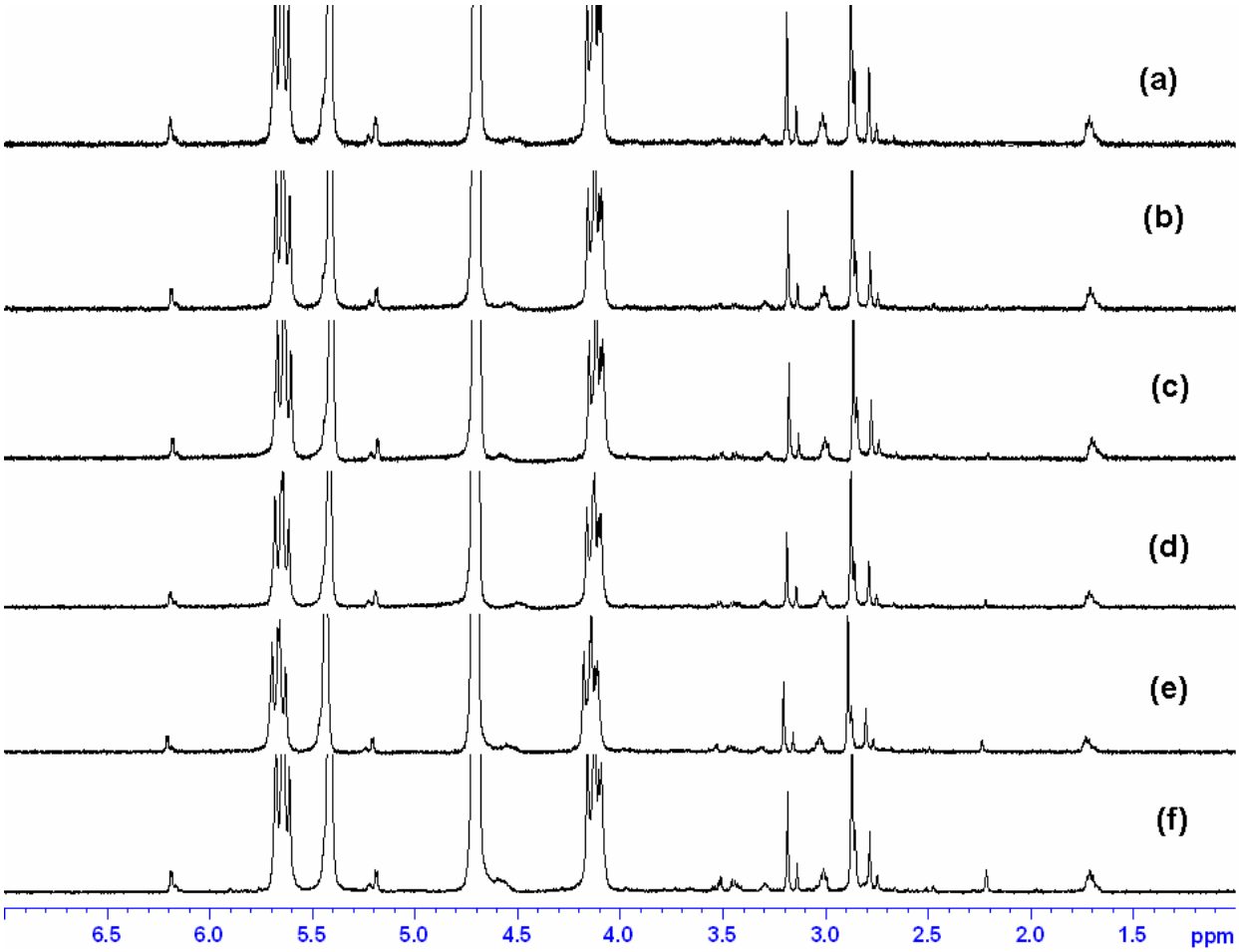


Figure S11 ^{1}H NMR spectra of the CB[7]-ranitidine host-guest complex at 50 °C in D_2O (pD 1.5) after (a) 0 days, (b) 2 days, (c) 4 days, (d) 6 days, (e) 10 days, and (f) 13 days.

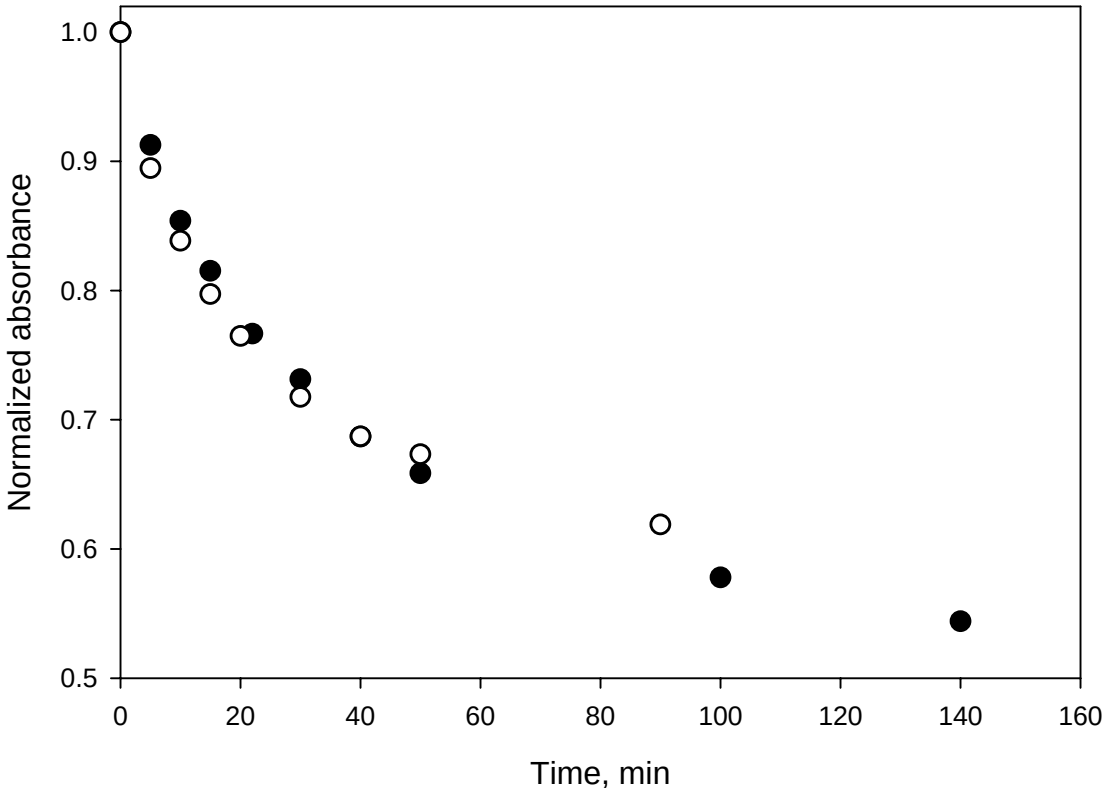


Figure S12. Dependence of absorbance at 226 nm (normalized) on irradiation (254 nm) time for ranitidine (●) and $\{RH_2 \bullet CB[7]\}^{2+}$ at pH 1.5.

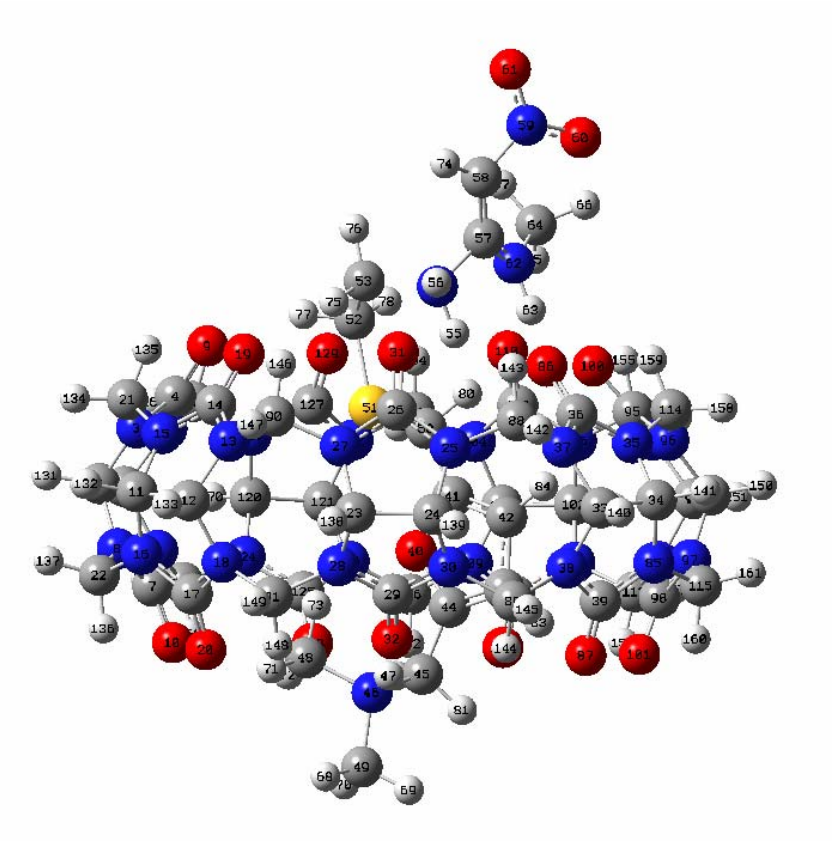


Figure S13 Energy-minimized structure of {(*E*)-RH_2•CB[7]}$^{2+}$ with atomic labeling

Table S1. Cartesian coordinates of {(*E*)-RH_2•CB[7]}$^{2+}$

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	C	-5.713290	2.108645	1.123739
2	6	C	-6.202299	0.610023	0.976031
3	7	N	-5.298312	-0.099252	1.856625
4	6	C	-4.433698	0.726716	2.531644
5	7	N	-4.699267	2.014637	2.145803
6	7	N	-5.241972	2.418189	-0.212479
7	6	C	-5.448411	1.399079	-1.105176
8	7	N	-6.037317	0.355702	-0.436131
9	8	O	-3.648539	0.383028	3.390499
10	8	O	-5.222657	1.440883	-2.297262
11	6	C	-5.484487	-2.901376	0.043641
12	6	C	-4.472367	-3.992024	-0.493806
13	7	N	-3.502588	-4.079796	0.569758
14	6	C	-3.662384	-3.101867	1.520423
15	7	N	-4.811831	-2.419484	1.234852
16	7	N	-5.572737	-1.970587	-1.057961
17	6	C	-4.692536	-2.252864	-2.065406
18	7	N	-4.000756	-3.387624	-1.725441

19	8	O	-2.953852	-2.943988	2.495644
20	8	O	-4.587004	-1.659485	-3.121032
21	6	C	-5.395211	-1.499990	2.198413
22	6	C	-6.477741	-0.834095	-1.138900
23	6	C	-1.222304	-5.198743	-1.466449
24	6	C	0.328986	-5.163390	-1.730141
25	7	N	0.867636	-4.976128	-0.401371
26	6	C	-0.092574	-4.814871	0.559147
27	7	N	-1.308230	-4.993576	-0.034070
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32	8	O	-0.856114	-2.422364	-3.607740
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41	6	C	0.775572	0.811943	-0.310179
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52	6	C	-0.651272	-0.710499	3.279093
53	6	C	-0.347203	-2.132009	3.760140
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58	6	C	2.285534	-2.848869	5.361103
59	7	N	3.339767	-2.743113	6.298561
60	8	O	4.375489	-2.095987	6.001920
61	8	O	3.177158	-3.382065	7.354671
62	7	N	2.678973	-0.932521	3.886179
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64	6	C	3.229371	0.112174	4.789427
65	1	H	3.096799	1.049964	4.276638
66	1	H	4.262417	-0.069999	5.021142
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69	1	H	-0.966133	0.653178	-6.136195
70	1	H	-2.233986	1.779056	-5.621104
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72	1	H	-3.027224	1.718733	-3.247618
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103	6	C	1.722094	5.450232	0.230742
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105	6	C	2.333650	3.910816	1.904488
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111	8	O	1.319532	3.940876	-2.925487
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117	6	C	0.267056	5.170150	2.322896
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119	6	C	-4.092178	3.140648	2.825361
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122	7	N	-1.041035	4.750770	1.866351
123	7	N	-3.041574	3.825106	2.098786
124	7	N	-3.525379	4.188285	-0.266875
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129	8	O	-1.289067	3.017769	3.366533
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131	1	H	-7.227209	0.456676	1.275034
132	1	H	-6.457883	-3.295168	0.288641

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136	1	H	-6.553181	-0.572354	-2.180575
137	1	H	-7.441893	-1.132211	-0.754421
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149	1	H	-3.462021	-4.995025	-2.920841
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151	1	H	6.409789	2.842359	-0.799518
152	1	H	3.929385	5.645617	-0.120811
153	1	H	1.691799	6.523695	0.339345
154	1	H	5.454983	4.010964	1.191387
155	1	H	4.581485	2.981417	2.331804
156	1	H	3.726367	3.774976	-3.226673
157	1	H	4.886310	4.574348	-2.153056
158	1	H	6.387498	-1.672926	0.200366
159	1	H	5.129897	-1.472860	1.422064
160	1	H	5.167173	-0.530383	-4.172388
161	1	H	6.458132	-1.121830	-3.112071
162	1	H	-0.519573	5.295528	-2.308167
163	1	H	-0.347568	6.613518	-1.142936
164	1	H	0.434564	4.694903	3.275016
165	1	H	0.260353	6.246521	2.435546
166	1	H	-4.836826	3.683714	-1.758639
167	1	H	-5.566926	4.459587	-0.346946
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169	1	H	-4.868363	3.854678	3.066411
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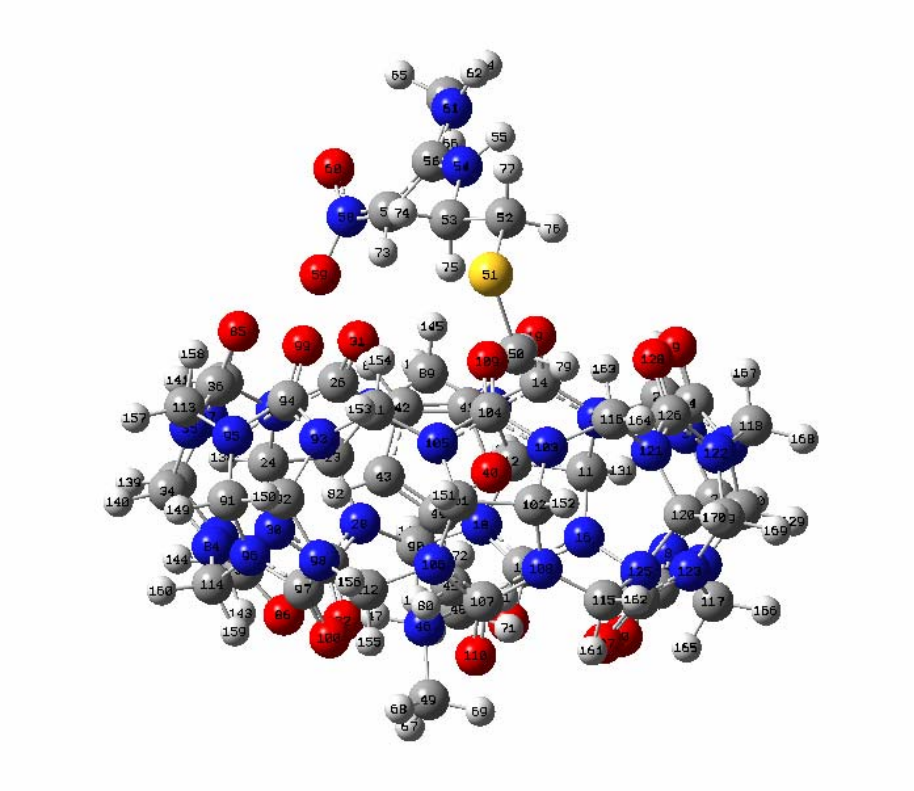

Figure S14. Energy-minimized structure of {(*E*)-RH•CB[7]}$^{+}$ with atomic labeling

Table S2. Cartesian coordinates for {*E*-RH•CB[7]}$^{+}$

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	C	0.366105	5.909080	-0.736054
2	6	C	-1.138280	5.648959	-1.150051
3	7	N	-1.682066	5.019539	0.030155
4	6	C	-0.780622	4.918877	1.065310
5	7	N	0.399795	5.486525	0.641344
6	7	N	1.093449	5.079320	-1.673035
7	6	C	0.283127	4.420278	-2.562332
8	7	N	-1.009692	4.803945	-2.314348
9	8	O	-1.015113	4.498261	2.175214
10	8	O	0.657267	3.704478	-3.470254
11	6	C	-4.019697	3.533588	-1.853792
12	6	C	-4.747865	2.134680	-1.977807
13	7	N	-4.475822	1.531420	-0.693523
14	6	C	-3.773561	2.341220	0.156124

15	7	N	-3.582395	3.546539	-0.478761
16	7	N	-2.969650	3.421344	-2.843314
17	6	C	-3.002309	2.241624	-3.546521
18	7	N	-4.086089	1.523339	-3.108591
19	8	O	-3.452083	2.084531	1.300172
20	8	O	-2.253573	1.932645	-4.449441
21	6	C	-3.080825	4.701776	0.235299
22	6	C	-2.078701	4.490258	-3.240848
23	6	C	-4.810599	-1.503253	-2.038761
24	6	C	-4.176101	-2.943875	-1.961684
25	7	N	-3.683369	-3.006493	-0.613077
26	6	C	-3.725352	-1.789421	0.025475
27	7	N	-4.388929	-0.907973	-0.792374
28	7	N	-4.188687	-0.936175	-3.216510
29	6	C	-3.148593	-1.693422	-3.684930
30	7	N	-3.146963	-2.872579	-2.983150
31	8	O	-3.280862	-1.561795	1.129073
32	8	O	-2.403630	-1.414821	-4.604619
33	6	C	-1.510815	-5.306678	-1.326700
34	6	C	-0.041587	-5.741458	-0.931337
35	7	N	0.016822	-5.447227	0.474631
36	6	C	-1.104241	-4.785787	0.936486
37	7	N	-1.997873	-4.715882	-0.105609
38	7	N	-1.287152	-4.379126	-2.419365
39	6	C	0.026165	-4.049144	-2.567697
40	8	O	0.955738	0.611563	0.120794
41	6	C	0.362096	0.101307	1.270441
42	6	C	0.438919	-1.239712	1.247408
43	6	C	1.137197	-1.599025	0.032968
44	6	C	1.434734	-0.462269	-0.615647
45	6	C	2.177411	-0.192959	-1.877790
46	7	N	1.325714	-0.490846	-3.118657
47	1	H	1.001540	-1.448854	-3.068963
48	6	C	0.112324	0.420344	-3.226544
49	6	C	2.197014	-0.402655	-4.356454
50	6	C	-0.188952	1.096749	2.246800
51	16	S	-0.229156	0.397203	3.940653
52	6	C	-1.882082	0.895681	4.505497
53	6	C	-2.993816	-0.015683	3.957856
54	7	N	-4.278618	0.367597	4.597125
55	1	H	-4.233750	1.070626	5.290347
56	6	C	-5.506071	-0.012297	4.179355
57	6	C	-5.558798	-0.782812	3.027797
58	7	N	-6.617975	-1.409276	2.449593
59	8	O	-6.402280	-1.870823	1.258265
60	8	O	-7.737125	-1.560115	3.019498
61	7	N	-6.521044	0.468368	4.923309
62	1	H	-6.268672	0.815823	5.813529
63	6	C	-7.949380	0.613836	4.573697
64	1	H	-8.323306	1.449940	5.146844
65	1	H	-8.510588	-0.274829	4.792572
66	1	H	-8.056203	0.832006	3.526170
67	1	H	1.580483	-0.607778	-5.216028
68	1	H	2.981425	-1.135330	-4.258045
69	1	H	2.606867	0.593036	-4.406573
70	1	H	-0.548256	0.031334	-3.981366
71	1	H	0.442866	1.415807	-3.469514

72	1	H	-0.376056	0.421167	-2.265550
73	1	H	-4.659725	-0.981986	2.509358
74	1	H	-2.769779	-1.049049	4.169403
75	1	H	-3.061500	0.116597	2.894580
76	1	H	-2.070654	1.923127	4.232399
77	1	H	-1.839986	0.824921	5.584067
78	1	H	-1.184768	1.401054	1.961277
79	1	H	0.442685	1.966577	2.272900
80	1	H	3.040197	-0.829827	-1.966511
81	1	H	2.480432	0.837032	-1.949163
82	1	H	1.385135	-2.585965	-0.276699
83	1	H	0.089271	-1.910868	1.994308
84	7	N	0.769708	-4.882051	-1.776542
85	8	O	-1.290891	-4.415833	2.071052
86	8	O	0.478965	-3.212630	-3.337696
87	6	C	-3.347191	-4.217029	0.102810
88	6	C	-2.297634	-3.965590	-3.382126
89	6	C	-5.029883	0.269255	-0.242551
90	6	C	-4.534705	0.335405	-3.815234
91	6	C	3.334796	-5.165454	0.294600
92	6	C	4.499081	-4.260395	0.859310
93	7	N	3.829788	-3.532930	1.918136
94	6	C	2.568801	-4.015510	2.191881
95	7	N	2.300001	-5.016494	1.279730
96	7	N	3.071262	-4.539984	-0.992033
97	6	C	3.973080	-3.554179	-1.309066
98	7	N	4.885305	-3.482177	-0.293765
99	8	O	1.859874	-3.688831	3.112761
100	8	O	3.986450	-2.915670	-2.345432
101	6	C	6.014644	-1.013224	1.567171
102	6	C	6.043819	0.569503	1.552704
103	7	N	4.888580	0.921467	2.339200
104	6	C	4.153965	-0.173026	2.751535
105	7	N	4.813522	-1.305013	2.313416
106	7	N	5.982160	-1.340168	0.160836
107	6	C	5.881792	-0.240689	-0.655325
108	7	N	5.963401	0.872007	0.140640
109	8	O	3.178112	-0.146801	3.460571
110	8	O	5.817756	-0.254586	-1.865726
111	6	C	4.468845	-2.610803	2.842459
112	6	C	6.080291	-2.667211	-0.397328
113	6	C	1.092758	-5.815504	1.375440
114	6	C	2.188556	-5.069763	-2.007972
115	6	C	6.099696	2.186651	-0.445295
116	6	C	4.635943	2.236198	2.896201
117	6	C	2.526573	5.113712	-1.870745
118	6	C	1.498055	5.710751	1.561394
119	6	C	3.671119	4.933639	0.421678
120	6	C	4.749324	3.888196	0.920059
121	7	N	4.053492	3.218237	1.998160
122	7	N	2.639667	4.829994	1.420213
123	7	N	3.327617	4.415140	-0.887561
124	6	C	4.054866	3.306520	-1.241709
125	7	N	4.982550	3.086826	-0.255317
126	6	C	2.827305	3.770885	2.277480
127	8	O	3.951518	2.687140	-2.282170
128	8	O	2.081885	3.444400	3.174038

129	1	H	0.669543	6.940970	-0.828273
130	1	H	-1.683486	6.548101	-1.393917
131	1	H	-4.657107	4.379088	-2.061843
132	1	H	-5.809902	2.207762	-2.152267
133	1	H	-3.680579	5.558468	-0.044229
134	1	H	-3.188322	4.495238	1.286887
135	1	H	-1.616391	4.172199	-4.160342
136	1	H	-2.659476	5.389329	-3.402253
137	1	H	-5.885021	-1.504359	-2.124671
138	1	H	-4.871922	-3.742879	-2.162992
139	1	H	-2.137887	-6.122478	-1.650287
140	1	H	0.177042	-6.779540	-1.127419
141	1	H	-4.055844	-4.984034	-0.179513
142	1	H	-3.427783	-4.006174	1.155611
143	1	H	-1.784650	-3.639117	-4.271067
144	1	H	-2.906520	-4.833316	-3.600178
145	1	H	-4.923735	0.246208	0.822541
146	1	H	-6.080865	0.231921	-0.488768
147	1	H	-4.064464	0.356602	-4.783865
148	1	H	-5.609637	0.386337	-3.915516
149	1	H	3.609184	-6.201278	0.167191
150	1	H	5.340741	-4.819161	1.238154
151	1	H	6.877209	-1.457247	2.040758
152	1	H	6.941616	0.988763	1.981622
153	1	H	5.370948	-3.071048	3.228399
154	1	H	3.760395	-2.450819	3.639128
155	1	H	6.289762	-2.539600	-1.445864
156	1	H	6.888000	-3.198417	0.086233
157	1	H	1.351891	-6.851445	1.205388
158	1	H	0.710223	-5.679270	2.373320
159	1	H	2.433516	-4.557206	-2.922746
160	1	H	2.372678	-6.131755	-2.114185
161	1	H	6.210331	2.030583	-1.505289
162	1	H	6.983027	2.663580	-0.041232
163	1	H	3.926631	2.107224	3.697641
164	1	H	5.570811	2.627420	3.279504
165	1	H	2.716803	4.639241	-2.818914
166	1	H	2.844638	6.149074	-1.897708
167	1	H	1.103873	5.547151	2.550473
168	1	H	1.838014	6.731788	1.452160
169	1	H	4.042170	5.944316	0.349496
170	1	H	5.667305	4.337671	1.265940

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