

Electronic Supplementary Information

A Quantum Chemical Study on the Anti-SARS-CoV-2 Activity of TMPRSS2 Inhibitors

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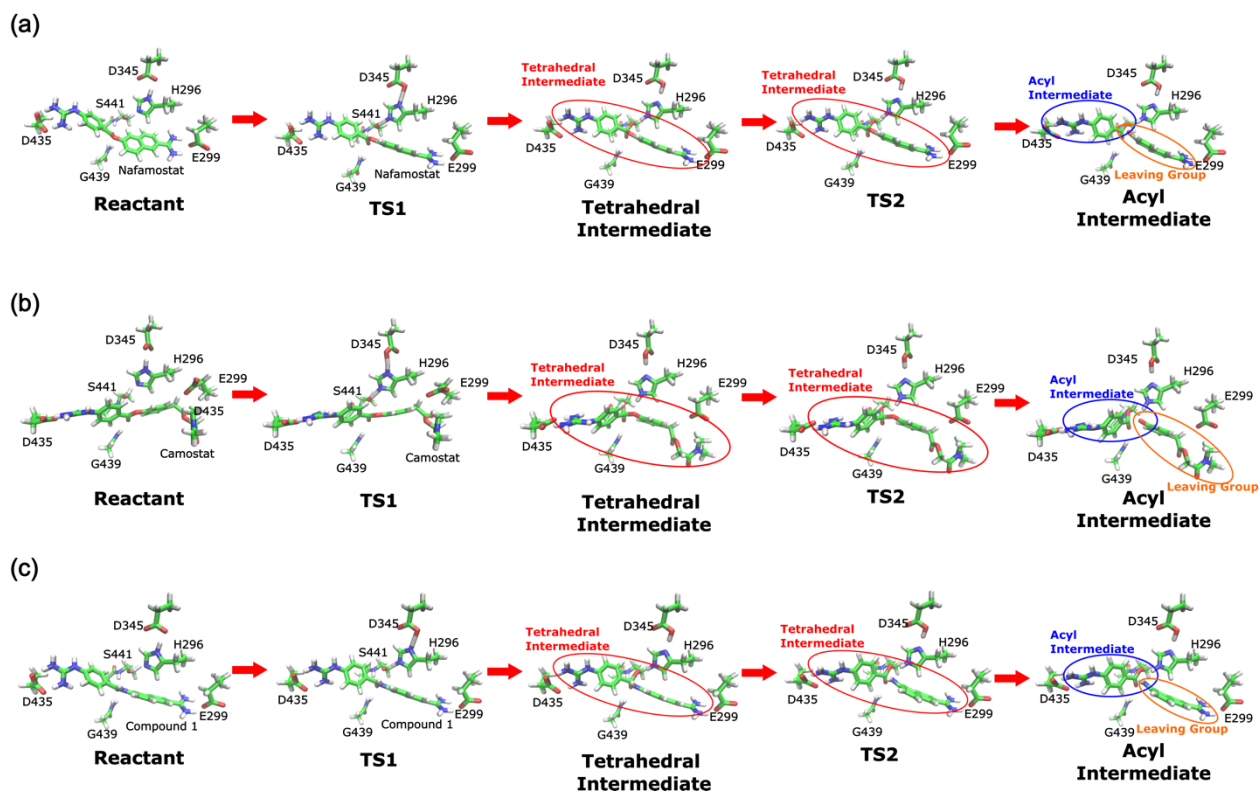


Fig. S1 Optimized structures of (a) nafamostat, (b) camostat, and (c) compound **1** by the cluster + PCM model. The five states in the acylation reaction (reactants, TS1, tetrahedral intermediates, TS2, and acyl intermediates) are shown.

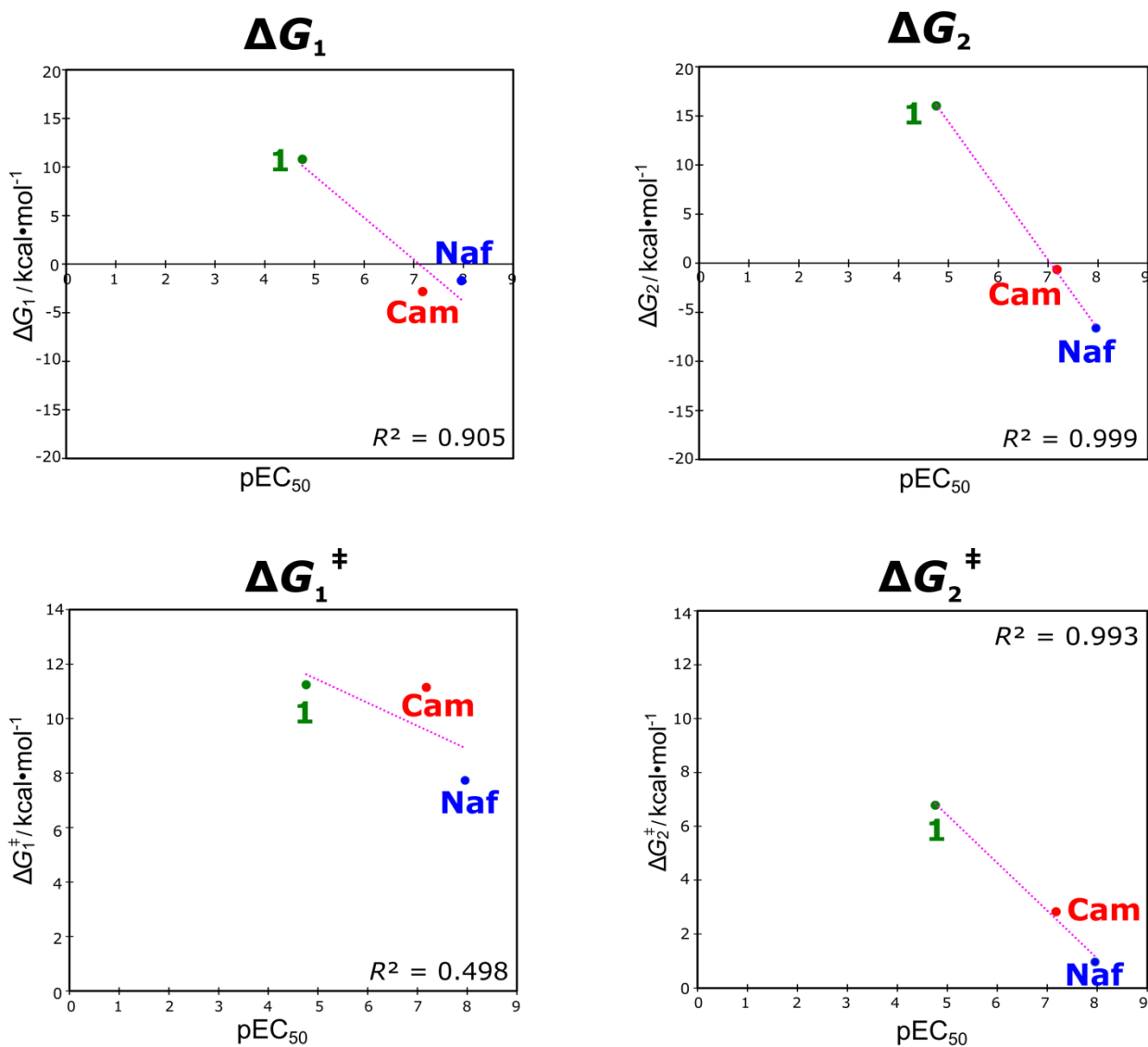


Fig. S2 Scatter plots between the experimental pEC₅₀ and the free energy difference (ΔG_1 , ΔG_2 , ΔG_1^\ddagger , and ΔG_2^\ddagger). In the figure, nafamostat, camostat, and compound **1** are abbreviated as Naf, Cam, and **1**, respectively.

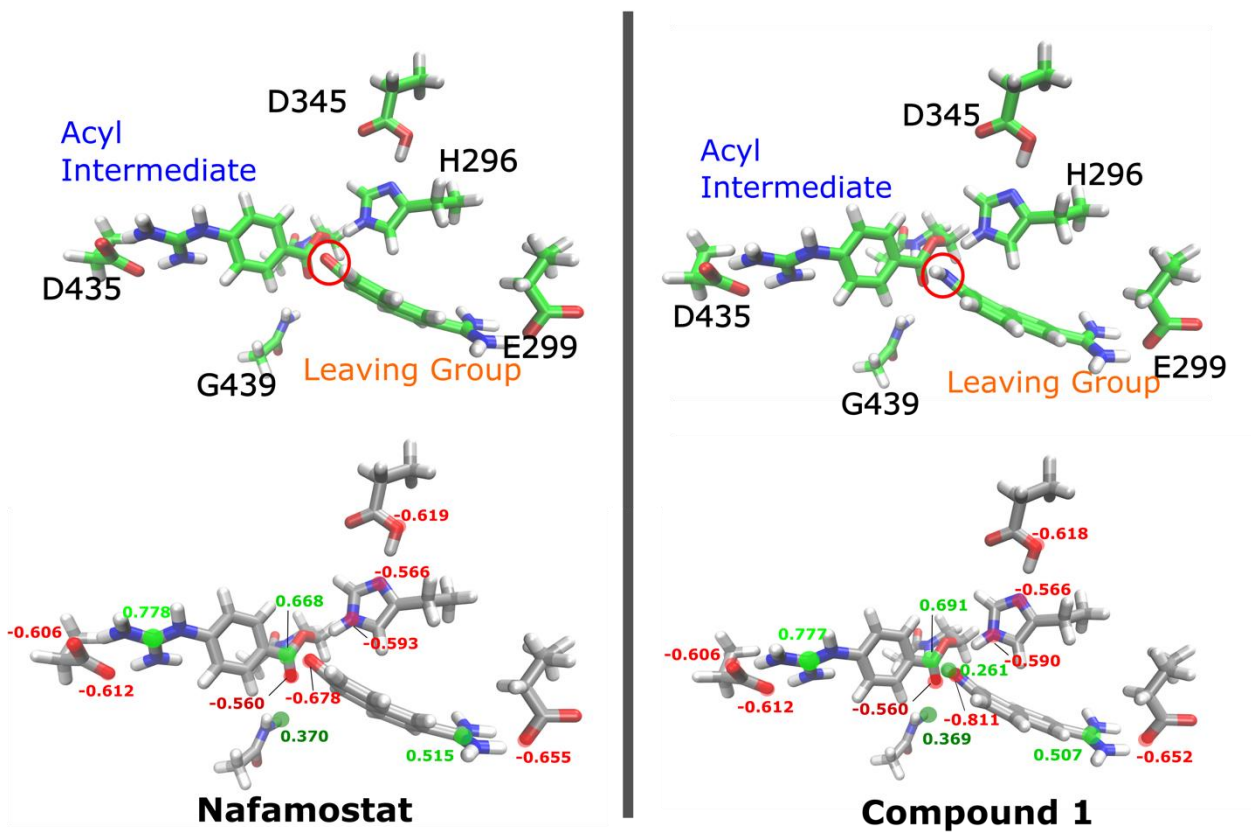


Fig. S3 Mulliken charge distribution calculated for nafamostat and compound **1** (in a.u.). Acyl intermediates, leaving groups, and surrounding amino acids (Asp345, His296, Ser441, Asp435, Glu299, and Gly439) are shown.

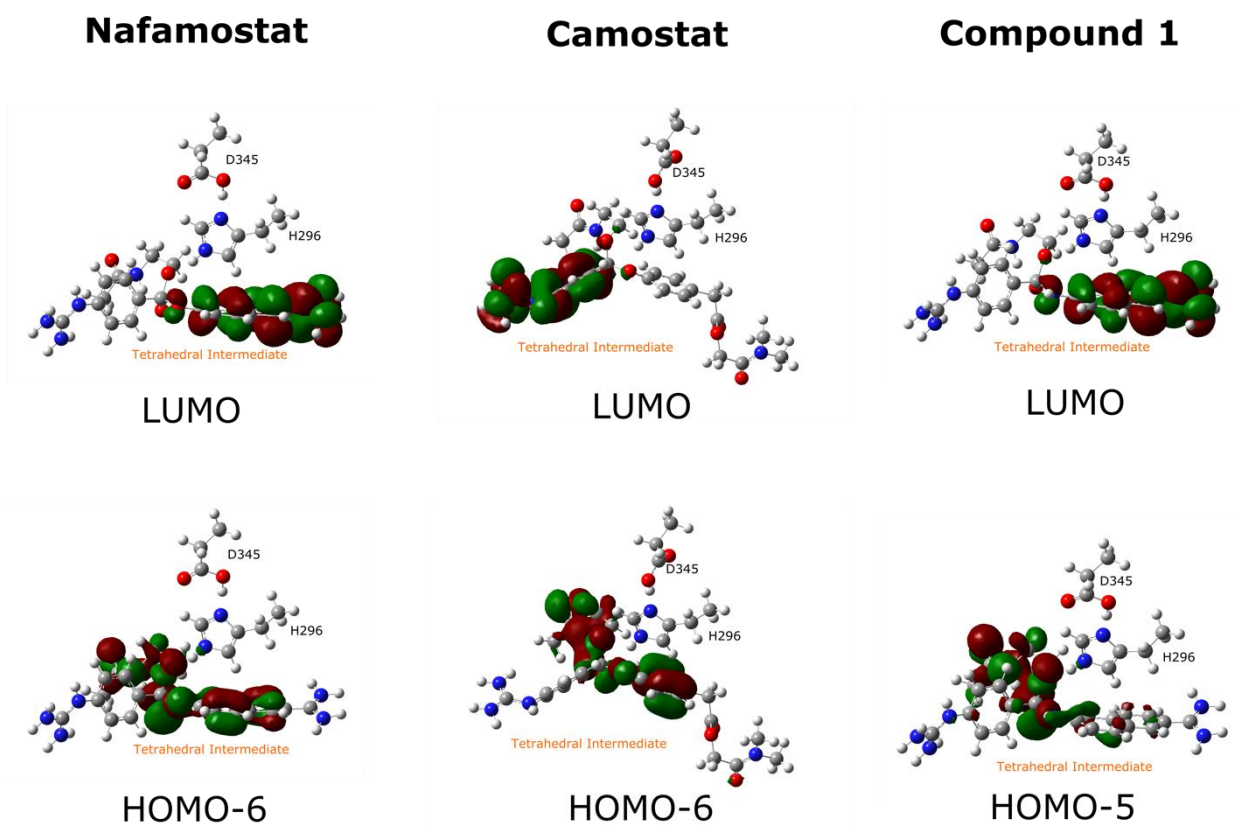


Fig. S4 Shape of molecular orbitals of tetrahedral intermediates involved in the acylation. The LUMO and HOMO-6 for nafamostat and camostat, and LUMO and HOMO-5 for compound **1** are illustrated.

Detailed energy data

Table S1 Comparison of activation energies (ΔG_1^\ddagger) calculated by the cluster + PCM model (kcal/mol)^a.

	B3LYP-GD3BJ	M062X	APFD
Nafamostat	7.74	7.79	6.48
Camostat	11.15	12.38	9.15
Compound 1	11.24	13.27	9.26

^a The 6-31G(d) basis set was used.

Table S2 Free energies of TMPRSS2 inhibitors calculated by the cluster + PCM model (a.u.)^a.

	Reactant	TS1	Tetrahedral Intermediate	TS2	Acyl Intermediate
Nafamostat	-2879.26175	-2879.24942	-2879.26449	-2879.26296	-2879.27232
Camostat	-3090.74045	-3090.72269	-3090.74501	-3090.74050	-3090.74150
Compound 1	-2859.39580	-2859.37788	-2859.37865	-2859.36786	-2859.37030

^a B3LYP-GD3BJ/6-31G(d) was used.

Table S3 Electronic energies of TMPRSS2 inhibitors calculated by the ONIOM method (a.u.)^a.

	Reactant	Tetrahedral Intermediate	Acyl Intermediate
Nafamostat	-2879.82236	-2879.84543	-2879.85897
Camostat	-3091.29498	-3091.31997	-3091.30899
Compound 1	-2859.99456	-2859.97476	-2859.96946

^a B3LYP-GD3BJ/6-31G(d) was used.

Atomic coordinates of optimized structures

Nafamostat (reactant)

C	5.179	-9.257	76.286
H	4.695	-9.184	77.269
H	5.276	-10.327	76.065
N	3.568	-7.489	75.546
H	3.579	-6.965	76.486
C	4.260	-8.647	75.272
C	2.766	-7.228	74.497
H	2.093	-6.384	74.493
N	2.898	-8.144	73.536
C	3.836	-9.041	74.019
H	4.130	-9.911	73.449
C	10.495	-11.763	76.737
H	9.899	-11.216	77.480
H	10.856	-12.677	77.221
C	9.596	-12.168	75.564
H	9.206	-11.268	75.074
H	8.732	-12.729	75.945
C	10.331	-13.083	74.559
O	10.379	-12.672	73.327
O	10.824	-14.134	74.979
C	2.240	-4.826	79.195
H	1.566	-3.995	78.959
H	1.680	-5.507	79.854
C	2.546	-5.570	77.881
O	1.792	-5.377	76.903
O	3.570	-6.337	77.910
C	-10.071	-8.605	67.047
H	-9.652	-9.081	66.156
H	-11.152	-8.790	67.059
C	-9.423	-9.221	68.291
O	-8.521	-10.090	68.111
O	-9.792	-8.747	69.409
O	0.666	-11.251	64.082
N	0.555	-10.300	66.163
H	0.262	-10.328	67.130
O	0.765	-4.297	67.612
N	0.991	-6.188	68.822
H	0.818	-7.191	68.796
C	2.478	-6.969	70.600
H	3.215	-6.593	71.322
H	3.028	-7.607	69.880
O	1.476	-7.706	71.263
H	1.895	-7.976	72.142
C	-2.017	-8.313	70.176
C	-3.297	-7.941	70.569

C	-4.185	-8.907	71.056
C	-3.779	-10.240	71.189
C	-2.494	-10.609	70.807
C	-1.616	-9.652	70.283
C	-0.265	-10.016	69.806
O	0.354	-9.400	68.958
O	0.187	-11.152	70.404
C	1.542	-11.479	70.423
C	2.514	-10.514	70.493
C	3.859	-10.901	70.677
C	4.188	-12.286	70.825
C	3.147	-13.248	70.716
C	1.844	-12.856	70.508
C	5.523	-12.639	71.144
C	6.497	-11.665	71.287
C	6.176	-10.297	71.062
C	4.890	-9.928	70.771
C	7.838	-12.004	71.793
N	8.520	-11.120	72.503
N	8.386	-13.197	71.582
N	-5.505	-8.531	71.426
C	-6.631	-9.000	70.794
N	-7.818	-8.532	71.158
N	-6.546	-9.936	69.856
H	-1.319	-7.574	69.801
H	-3.617	-6.907	70.481
H	-4.466	-10.972	71.598
H	-2.169	-11.637	70.916
H	2.238	-9.469	70.504
H	3.388	-14.302	70.819
H	1.039	-13.580	70.444
H	5.751	-13.681	71.346
H	6.955	-9.546	71.121
H	4.640	-8.883	70.633
H	8.038	-10.307	72.860
H	7.981	-13.844	70.924
H	9.273	-13.399	72.079
H	-7.880	-7.849	71.899
H	-8.666	-8.700	70.525
H	-5.636	-10.118	69.456
H	-7.399	-10.118	69.237
H	-5.602	-7.627	71.870
H	9.416	-11.514	72.960
C	-9.796	-7.087	67.059
H	-8.753	-6.936	67.244
H	-10.065	-6.622	66.134
H	-10.365	-6.653	67.855
C	3.500	-4.321	79.917
H	3.211	-3.639	80.690

H	4.044	-5.136	80.345
H	4.119	-3.811	79.207
C	11.695	-10.905	76.303
H	12.275	-10.665	77.170
H	12.297	-11.465	75.617
H	11.364	-10.004	75.834
C	6.600	-8.655	76.397
H	6.588	-7.615	76.651
H	7.103	-9.203	77.167
H	7.118	-8.790	75.470
C	1.932	-5.784	69.825
H	1.229	-5.227	70.408
H	2.781	-5.170	69.607
C	0.549	-5.492	67.754
C	-0.280	-6.028	66.572
H	-1.098	-5.365	66.380
H	0.340	-6.091	65.702
H	-0.657	-7.000	66.812
C	0.239	-11.206	65.233
C	-0.751	-12.368	65.438
H	-1.582	-12.249	64.774
H	-0.260	-13.296	65.232
H	-1.100	-12.365	66.450
H	1.250	-9.608	65.918

Nafamostat (TS1)

C	5.170	-9.235	76.234
H	4.661	-9.201	77.205
H	5.259	-10.295	75.966
N	3.519	-7.464	75.582
H	3.530	-6.964	76.571
C	4.260	-8.574	75.231
C	2.715	-7.144	74.564
H	2.014	-6.325	74.607
N	2.897	-7.993	73.545
C	3.867	-8.898	73.949
H	4.190	-9.702	73.307
C	10.503	-11.802	76.681
H	9.729	-11.218	77.199
H	10.842	-12.583	77.368
C	9.913	-12.490	75.448
H	9.608	-11.745	74.703
H	9.001	-13.043	75.719
C	10.891	-13.513	74.811
O	10.791	-13.686	73.526
O	11.672	-14.122	75.547
C	2.234	-4.820	79.199
H	1.564	-3.984	78.968

H	1.674	-5.498	79.861
C	2.518	-5.564	77.885
O	1.773	-5.354	76.904
O	3.520	-6.366	77.910
C	-10.016	-8.620	67.063
H	-9.718	-9.064	66.109
H	-11.069	-8.860	67.250
C	-9.121	-9.174	68.176
O	-8.076	-9.794	67.817
O	-9.434	-8.864	69.364
O	0.666	-11.251	64.082
N	0.555	-10.300	66.163
H	0.285	-10.354	67.136
O	0.765	-4.297	67.612
N	0.991	-6.188	68.822
H	0.872	-7.198	68.759
C	2.491	-6.999	70.590
H	3.334	-6.619	71.198
H	2.955	-7.647	69.815
O	1.598	-7.699	71.390
H	2.263	-7.932	72.525
C	-1.339	-7.690	70.822
C	-2.694	-7.412	70.992
C	-3.648	-8.431	70.881
C	-3.237	-9.740	70.601
C	-1.886	-10.006	70.410
C	-0.930	-8.989	70.516
C	0.493	-9.385	70.244
O	1.039	-9.272	69.155
O	0.851	-10.306	71.200
C	2.100	-10.847	71.340
C	3.223	-10.488	70.628
C	4.464	-11.089	70.949
C	4.535	-12.069	71.993
C	3.347	-12.420	72.688
C	2.157	-11.822	72.370
C	5.785	-12.628	72.329
C	6.938	-12.241	71.670
C	6.870	-11.276	70.627
C	5.663	-10.724	70.276
C	8.231	-12.777	72.116
N	9.330	-12.032	72.086
N	8.330	-14.011	72.591
N	-5.014	-8.132	71.125
C	-6.095	-8.608	70.436
N	-7.314	-8.358	70.904
N	-5.946	-9.314	69.321
H	-0.585	-6.927	70.956
H	-3.012	-6.399	71.223

H	-3.964	-10.543	70.558
H	-1.571	-11.024	70.204
H	3.165	-9.748	69.845
H	3.397	-13.155	73.485
H	1.242	-12.055	72.903
H	5.835	-13.329	73.157
H	7.774	-10.998	70.094
H	5.609	-9.991	69.478
H	9.239	-11.034	71.958
H	7.561	-14.658	72.502
H	9.245	-14.263	73.025
H	-7.422	-8.008	71.845
H	-8.176	-8.627	70.338
H	-5.052	-9.283	68.851
H	-6.812	-9.604	68.765
H	-5.199	-7.364	71.756
H	10.151	-12.457	72.602
C	-9.796	-7.087	67.059
H	-8.753	-6.936	67.244
H	-10.065	-6.622	66.134
H	-10.365	-6.653	67.855
C	3.500	-4.321	79.917
H	3.211	-3.639	80.690
H	4.044	-5.136	80.345
H	4.119	-3.811	79.207
C	11.695	-10.905	76.303
H	12.275	-10.665	77.170
H	12.297	-11.465	75.617
H	11.364	-10.004	75.834
C	6.600	-8.655	76.397
H	6.588	-7.615	76.651
H	7.103	-9.203	77.167
H	7.118	-8.790	75.470
C	1.932	-5.784	69.825
H	1.229	-5.227	70.408
H	2.781	-5.170	69.607
C	0.549	-5.492	67.754
C	-0.280	-6.028	66.572
H	-1.098	-5.365	66.380
H	0.340	-6.091	65.702
H	-0.657	-7.000	66.812
C	0.239	-11.206	65.233
C	-0.751	-12.368	65.438
H	-1.582	-12.249	64.774
H	-0.260	-13.296	65.232
H	-1.100	-12.365	66.450
H	1.261	-9.615	65.927

Nafamostat (tetrahedral intermediate)

C	5.191	-9.277	76.276
H	4.702	-9.242	77.258
H	5.310	-10.340	76.030
N	3.572	-7.499	75.581
H	3.545	-6.741	76.973
C	4.253	-8.663	75.281
C	2.746	-7.262	74.575
H	2.049	-6.439	74.528
N	2.870	-8.216	73.621
C	3.827	-9.115	74.054
H	4.098	-9.980	73.474
C	10.504	-11.802	76.686
H	9.720	-11.212	77.180
H	10.841	-12.562	77.398
C	9.930	-12.528	75.467
H	9.649	-11.808	74.687
H	9.002	-13.055	75.735
C	10.898	-13.586	74.872
O	10.681	-13.926	73.638
O	11.782	-14.060	75.593
C	2.207	-4.797	79.230
H	1.529	-3.959	79.047
H	1.673	-5.499	79.886
C	2.426	-5.485	77.897
O	1.696	-5.305	76.930
O	3.477	-6.293	77.903
C	-10.007	-8.624	67.037
H	-9.769	-9.032	66.051
H	-11.042	-8.880	67.288
C	-9.029	-9.202	68.065
O	-7.934	-9.648	67.612
O	-9.338	-9.074	69.287
O	0.666	-11.251	64.082
N	0.555	-10.300	66.163
H	0.308	-10.350	67.145
O	0.765	-4.297	67.612
N	0.991	-6.188	68.822
H	0.914	-7.208	68.729
C	2.449	-7.035	70.536
H	3.139	-6.736	71.331
H	3.000	-7.643	69.811
O	1.444	-7.824	71.172
H	2.304	-8.270	72.766
C	-1.331	-7.533	71.170
C	-2.714	-7.423	71.316
C	-3.554	-8.449	70.874
C	-3.000	-9.574	70.246
C	-1.623	-9.650	70.072
C	-0.770	-8.649	70.551

C	0.735	-8.858	70.357
O	1.145	-9.008	69.160
O	0.902	-10.111	71.266
C	2.067	-10.746	71.393
C	3.224	-10.503	70.659
C	4.419	-11.184	70.974
C	4.439	-12.154	72.032
C	3.226	-12.428	72.723
C	2.081	-11.747	72.416
C	5.656	-12.763	72.390
C	6.837	-12.450	71.732
C	6.813	-11.520	70.655
C	5.638	-10.915	70.286
C	8.103	-13.006	72.212
N	9.243	-12.332	72.078
N	8.158	-14.185	72.821
N	-4.945	-8.356	71.151
C	-5.986	-8.758	70.366
N	-7.215	-8.747	70.879
N	-5.798	-9.156	69.114
H	-0.681	-6.754	71.548
H	-3.143	-6.545	71.793
H	-3.636	-10.394	69.932
H	-1.190	-10.526	69.602
H	3.196	-9.797	69.842
H	3.229	-13.168	73.520
H	1.155	-11.923	72.954
H	5.665	-13.440	73.240
H	7.727	-11.310	70.108
H	5.624	-10.208	69.463
H	9.203	-11.347	71.859
H	7.365	-14.807	72.808
H	9.072	-14.431	73.261
H	-7.334	-8.656	71.877
H	-8.064	-8.951	70.266
H	-4.919	-8.938	68.665
H	-6.640	-9.437	68.525
H	-5.197	-7.807	71.962
H	10.056	-12.747	72.602
C	-9.796	-7.087	67.059
H	-8.753	-6.936	67.244
H	-10.065	-6.622	66.134
H	-10.365	-6.653	67.855
C	3.500	-4.321	79.917
H	3.211	-3.639	80.690
H	4.044	-5.136	80.345
H	4.119	-3.811	79.207
C	11.695	-10.905	76.303
H	12.275	-10.665	77.170

H	12.297	-11.465	75.617
H	11.364	-10.004	75.834
C	6.600	-8.655	76.397
H	6.588	-7.615	76.651
H	7.103	-9.203	77.167
H	7.118	-8.790	75.470
C	1.932	-5.784	69.825
H	1.229	-5.227	70.408
H	2.781	-5.170	69.607
C	0.549	-5.492	67.754
C	-0.280	-6.028	66.572
H	-1.098	-5.365	66.380
H	0.340	-6.091	65.702
H	-0.657	-7.000	66.812
C	0.239	-11.206	65.233
C	-0.751	-12.368	65.438
H	-1.582	-12.249	64.774
H	-0.260	-13.296	65.232
H	-1.100	-12.365	66.450
H	1.264	-9.620	65.922

Nafamostat (TS2)

C	5.190	-9.278	76.287
H	4.709	-9.235	77.273
H	5.308	-10.342	76.049
N	3.574	-7.500	75.571
H	3.558	-6.720	76.956
C	4.244	-8.677	75.293
C	2.731	-7.289	74.574
H	2.034	-6.466	74.517
N	2.835	-8.271	73.647
C	3.794	-9.163	74.088
H	4.051	-10.047	73.531
C	10.504	-11.803	76.686
H	9.713	-11.209	77.166
H	10.838	-12.552	77.410
C	9.944	-12.547	75.472
H	9.676	-11.839	74.676
H	9.010	-13.066	75.735
C	10.915	-13.618	74.905
O	10.684	-14.011	73.691
O	11.817	-14.050	75.631
C	2.209	-4.799	79.228
H	1.528	-3.962	79.047
H	1.675	-5.504	79.880
C	2.427	-5.482	77.892
O	1.682	-5.318	76.934
O	3.494	-6.269	77.885

C	-10.002	-8.625	67.035
H	-9.772	-9.026	66.043
H	-11.033	-8.888	67.295
C	-9.011	-9.210	68.046
O	-7.896	-9.591	67.578
O	-9.330	-9.158	69.270
O	0.666	-11.251	64.082
N	0.554	-10.300	66.164
H	0.312	-10.369	67.144
O	0.765	-4.297	67.612
N	0.991	-6.188	68.822
H	0.915	-7.202	68.719
C	2.423	-7.032	70.559
H	3.090	-6.737	71.374
H	2.978	-7.671	69.866
O	1.366	-7.780	71.174
H	2.247	-8.359	72.814
C	-1.404	-7.717	71.406
C	-2.788	-7.703	71.584
C	-3.582	-8.698	71.008
C	-2.983	-9.696	70.226
C	-1.608	-9.676	70.027
C	-0.802	-8.702	70.625
C	0.693	-8.783	70.388
O	1.120	-9.033	69.238
O	0.893	-10.164	71.494
C	2.020	-10.826	71.589
C	3.176	-10.599	70.829
C	4.370	-11.290	71.109
C	4.411	-12.265	72.165
C	3.209	-12.537	72.880
C	2.062	-11.851	72.602
C	5.631	-12.877	72.496
C	6.803	-12.569	71.818
C	6.758	-11.637	70.741
C	5.578	-11.028	70.397
C	8.075	-13.121	72.276
N	9.219	-12.461	72.089
N	8.143	-14.283	72.916
N	-4.974	-8.710	71.295
C	-6.000	-8.999	70.441
N	-7.233	-9.097	70.934
N	-5.793	-9.183	69.144
H	-0.788	-6.959	71.875
H	-3.251	-6.923	72.183
H	-3.584	-10.496	69.807
H	-1.135	-10.454	69.437
H	3.146	-9.883	70.020
H	3.226	-13.284	73.670

H	1.147	-12.030	73.158
H	5.652	-13.554	73.346
H	7.660	-11.430	70.174
H	5.551	-10.321	69.573
H	9.179	-11.479	71.859
H	7.346	-14.899	72.949
H	9.064	-14.516	73.348
H	-7.364	-9.160	71.933
H	-8.074	-9.193	70.284
H	-4.911	-8.893	68.746
H	-6.622	-9.413	68.512
H	-5.246	-8.289	72.173
H	10.039	-12.863	72.609
C	-9.796	-7.087	67.059
H	-8.753	-6.936	67.244
H	-10.065	-6.622	66.134
H	-10.365	-6.653	67.855
C	3.500	-4.321	79.917
H	3.211	-3.639	80.690
H	4.044	-5.136	80.345
H	4.119	-3.811	79.207
C	11.695	-10.905	76.304
H	12.275	-10.665	77.170
H	12.297	-11.465	75.617
H	11.364	-10.004	75.834
C	6.600	-8.655	76.397
H	6.588	-7.615	76.652
H	7.103	-9.203	77.167
H	7.118	-8.790	75.470
C	1.932	-5.784	69.824
H	1.229	-5.227	70.408
H	2.781	-5.170	69.607
C	0.549	-5.492	67.754
C	-0.280	-6.028	66.572
H	-1.098	-5.365	66.380
H	0.340	-6.091	65.702
H	-0.657	-7.000	66.812
C	0.240	-11.206	65.233
C	-0.751	-12.368	65.438
H	-1.582	-12.249	64.774
H	-0.260	-13.296	65.232
H	-1.100	-12.365	66.450
H	1.273	-9.628	65.930

Nafamostat (acyl intermediate)

C	5.190	-9.281	76.356
H	4.747	-9.179	77.356
H	5.306	-10.359	76.186

N	3.512	-7.580	75.533
H	3.544	-6.674	76.882
C	4.189	-8.776	75.365
C	2.588	-7.530	74.585
H	1.858	-6.741	74.473
N	2.650	-8.628	73.790
C	3.660	-9.432	74.280
H	3.896	-10.385	73.840
C	10.498	-11.796	76.690
H	9.695	-11.186	77.128
H	10.816	-12.516	77.449
C	9.967	-12.591	75.495
H	9.762	-11.925	74.646
H	9.002	-13.061	75.740
C	10.921	-13.726	75.034
O	10.656	-14.253	73.881
O	11.840	-14.077	75.783
C	2.215	-4.806	79.221
H	1.527	-3.974	79.047
H	1.681	-5.514	79.871
C	2.405	-5.490	77.877
O	1.584	-5.397	76.974
O	3.524	-6.199	77.798
C	-9.986	-8.627	67.041
H	-9.772	-9.019	66.042
H	-11.005	-8.908	67.322
C	-8.965	-9.225	68.019
O	-7.799	-9.399	67.549
O	-9.321	-9.408	69.219
O	0.666	-11.251	64.082
N	0.555	-10.300	66.163
H	0.328	-10.400	67.144
O	0.765	-4.297	67.612
N	0.991	-6.188	68.822
H	0.963	-7.192	68.667
C	2.310	-7.026	70.634
H	2.887	-6.756	71.519
H	2.869	-7.754	70.041
O	1.099	-7.644	71.137
H	1.960	-8.936	73.092
C	-1.575	-8.078	71.723
C	-2.937	-8.260	71.946
C	-3.647	-9.226	71.224
C	-2.975	-10.030	70.292
C	-1.621	-9.825	70.061
C	-0.910	-8.847	70.764
C	0.506	-8.604	70.387
O	1.013	-9.068	69.369
O	0.947	-10.326	72.168

C	1.920	-11.156	72.131
C	3.025	-11.037	71.246
C	4.196	-11.778	71.426
C	4.281	-12.748	72.493
C	3.114	-12.981	73.283
C	1.983	-12.241	73.100
C	5.507	-13.363	72.774
C	6.658	-13.076	72.040
C	6.557	-12.178	70.934
C	5.370	-11.567	70.634
C	7.950	-13.574	72.476
N	9.081	-12.931	72.160
N	8.078	-14.668	73.226
N	-5.032	-9.403	71.481
C	-6.028	-9.481	70.540
N	-7.278	-9.684	70.950
N	-5.772	-9.364	69.246
H	-1.032	-7.321	72.275
H	-3.457	-7.639	72.671
H	-3.509	-10.814	69.766
H	-1.092	-10.439	69.341
H	2.980	-10.282	70.468
H	3.160	-13.738	74.065
H	1.109	-12.380	73.731
H	5.561	-14.017	73.641
H	7.429	-11.998	70.311
H	5.308	-10.882	69.793
H	9.013	-11.969	71.865
H	7.294	-15.283	73.376
H	9.015	-14.834	73.644
H	-7.449	-9.966	71.903
H	-8.090	-9.632	70.260
H	-4.872	-9.006	68.956
H	-6.582	-9.428	68.546
H	-5.341	-9.155	72.411
H	9.924	-13.259	72.692
C	-9.796	-7.087	67.059
H	-8.753	-6.936	67.244
H	-10.065	-6.622	66.134
H	-10.365	-6.653	67.855
C	3.500	-4.321	79.917
H	3.211	-3.639	80.690
H	4.044	-5.136	80.345
H	4.119	-3.811	79.207
C	11.695	-10.905	76.303
H	12.275	-10.665	77.170
H	12.297	-11.465	75.617
H	11.364	-10.004	75.834
C	6.600	-8.655	76.397

H	6.588	-7.615	76.651
H	7.103	-9.203	77.167
H	7.118	-8.790	75.470
C	1.932	-5.784	69.825
H	1.229	-5.227	70.408
H	2.781	-5.170	69.607
C	0.549	-5.492	67.754
C	-0.280	-6.028	66.572
H	-1.098	-5.365	66.380
H	0.340	-6.091	65.702
H	-0.657	-7.000	66.812
C	0.239	-11.206	65.233
C	-0.751	-12.368	65.438
H	-1.582	-12.249	64.774
H	-0.260	-13.296	65.232
H	-1.100	-12.365	66.450
H	1.293	-9.646	65.936

Camostat (reactant)

C	4.852	-9.159	77.104
H	4.426	-9.020	78.104
H	4.953	-10.238	76.952
N	2.726	-7.927	76.536
H	2.524	-7.553	77.518
C	3.867	-8.585	76.116
C	2.002	-7.612	75.442
H	1.064	-7.076	75.495
N	2.588	-8.027	74.320
C	3.767	-8.624	74.738
H	4.461	-9.043	74.029
C	9.986	-12.041	76.869
H	10.228	-13.003	77.343
H	9.445	-12.274	75.948
C	8.999	-11.251	77.741
H	9.076	-10.185	77.482
H	9.219	-11.343	78.810
C	7.527	-11.674	77.461
O	7.187	-11.616	76.231
O	6.814	-12.025	78.423
C	2.520	-4.956	80.278
H	1.587	-4.430	80.027
H	2.264	-5.620	81.114
C	2.892	-5.844	79.068
O	2.103	-6.835	78.883
O	3.882	-5.526	78.380
C	-9.483	-8.870	68.157
H	-9.463	-9.574	67.313
H	-10.420	-9.044	68.694

C	-8.301	-9.258	69.066
O	-8.537	-9.989	70.069
O	-7.163	-8.830	68.706
O	0.192	-11.333	64.942
N	1.183	-10.627	66.834
H	1.404	-10.703	67.825
O	1.421	-4.610	67.985
N	1.798	-6.557	68.975
H	1.560	-7.545	69.016
C	2.542	-6.963	71.296
H	2.960	-6.391	72.134
H	3.377	-7.540	70.860
O	1.521	-7.821	71.763
H	1.797	-8.013	72.708
C	5.408	-16.637	74.898
N	6.381	-15.565	74.769
C	6.293	-14.523	75.789
C	7.320	-15.648	73.790
O	7.402	-16.601	73.008
C	8.346	-14.520	73.680
O	7.667	-13.280	73.429
C	8.466	-12.198	73.304
O	9.678	-12.277	73.244
C	7.697	-10.897	73.347
C	6.263	-10.933	72.880
C	5.875	-10.369	71.661
C	4.536	-10.334	71.255
C	3.581	-10.895	72.098
C	3.947	-11.492	73.307
C	5.278	-11.497	73.704
O	2.198	-10.843	71.906
C	1.533	-10.459	70.807
O	2.031	-10.266	69.705
C	0.073	-10.420	71.089
C	-0.420	-10.434	72.401
C	-1.788	-10.464	72.633
C	-2.689	-10.505	71.560
C	-2.203	-10.473	70.245
C	-0.831	-10.410	70.023
N	-4.063	-10.650	71.861
C	-5.146	-10.229	71.136
N	-6.344	-10.723	71.448
N	-5.028	-9.342	70.163
H	5.535	-17.331	74.068
H	5.548	-17.171	75.847
H	4.393	-16.221	74.886
H	6.519	-14.940	76.779
H	6.944	-13.673	75.604
H	5.269	-14.134	75.815

H	8.944	-14.424	74.592
H	9.009	-14.763	72.849
H	7.710	-10.663	74.425
H	8.287	-10.150	72.811
H	6.627	-9.921	71.015
H	4.246	-9.873	70.322
H	3.168	-11.878	73.956
H	5.568	-11.860	74.686
H	0.273	-10.400	73.233
H	-2.164	-10.458	73.652
H	-2.883	-10.531	69.404
H	-0.458	-10.370	69.007
H	-6.388	-11.590	71.966
H	-7.211	-10.412	70.910
H	-4.179	-8.799	70.092
H	-5.887	-9.106	69.567
H	-4.275	-11.025	72.776
C	-9.348	-7.428	67.632
H	-8.298	-7.281	67.499
H	-9.851	-7.276	66.699
H	-9.718	-6.731	68.354
C	6.269	-8.546	77.080
H	6.831	-8.930	77.908
H	6.760	-8.817	76.166
H	6.208	-7.482	77.150
C	3.600	-3.950	80.697
H	3.251	-3.416	81.557
H	4.499	-4.476	80.948
H	3.798	-3.262	79.905
C	11.276	-11.308	76.443
H	12.077	-11.351	77.154
H	11.587	-11.777	75.532
H	11.025	-10.287	76.253
C	0.330	-11.411	66.159
C	1.259	-5.835	67.981
C	2.075	-5.961	70.249
H	1.213	-5.396	70.535
H	2.909	-5.302	70.125
C	-0.600	-12.485	66.752
H	-1.619	-12.227	66.548
H	-0.377	-13.434	66.310
H	-0.452	-12.541	67.810
C	0.458	-6.347	66.770
H	-0.588	-6.204	66.947
H	0.748	-5.805	65.895
H	0.656	-7.389	66.626
H	1.756	-10.012	66.272

Camostat (TS1)

C	4.843	-9.126	77.087
H	4.389	-8.958	78.069
H	4.923	-10.209	76.941
N	2.803	-7.786	76.415
H	2.569	-7.359	77.412
C	3.907	-8.543	76.057
C	2.112	-7.487	75.311
H	1.207	-6.899	75.291
N	2.713	-8.010	74.236
C	3.848	-8.662	74.686
H	4.518	-9.158	74.008
C	9.996	-12.070	76.860
H	10.251	-13.000	77.387
H	9.507	-12.375	75.928
C	8.945	-11.295	77.672
H	8.868	-10.273	77.279
H	9.227	-11.240	78.731
C	7.580	-12.016	77.501
O	6.919	-11.692	76.458
O	7.289	-12.907	78.331
C	2.551	-4.972	80.242
H	1.614	-4.477	79.950
H	2.278	-5.644	81.068
C	3.007	-5.856	79.060
O	2.103	-6.663	78.629
O	4.168	-5.741	78.628
C	-9.488	-8.868	68.155
H	-9.459	-9.574	67.313
H	-10.430	-9.044	68.684
C	-8.312	-9.244	69.074
O	-8.544	-9.987	70.068
O	-7.181	-8.788	68.727
O	0.192	-11.333	64.942
N	1.183	-10.627	66.834
H	1.352	-10.638	67.836
O	1.421	-4.610	67.985
N	1.798	-6.557	68.975
H	1.628	-7.562	69.004
C	2.609	-6.983	71.276
H	3.112	-6.374	72.055
H	3.431	-7.499	70.742
O	1.729	-7.877	71.866
H	2.269	-7.999	73.179
C	5.397	-16.793	74.976
N	6.339	-15.699	74.804
C	6.475	-14.790	75.943
C	7.152	-15.707	73.715
O	7.123	-16.588	72.849
C	8.172	-14.576	73.584

O	7.476	-13.323	73.492
C	8.260	-12.224	73.420
O	9.470	-12.286	73.311
C	7.470	-10.949	73.593
C	6.088	-10.925	72.988
C	5.798	-10.159	71.855
C	4.496	-10.038	71.356
C	3.469	-10.706	72.017
C	3.745	-11.526	73.117
C	5.041	-11.625	73.605
O	2.120	-10.586	71.745
C	1.531	-9.816	70.776
O	2.032	-9.587	69.673
C	0.060	-9.838	71.044
C	-0.428	-9.982	72.350
C	-1.784	-10.160	72.579
C	-2.677	-10.232	71.501
C	-2.202	-10.069	70.194
C	-0.841	-9.853	69.979
N	-4.028	-10.558	71.784
C	-5.147	-10.117	71.138
N	-6.311	-10.715	71.406
N	-5.101	-9.107	70.288
H	5.363	-17.375	74.056
H	5.703	-17.444	75.806
H	4.403	-16.392	75.203
H	7.094	-15.227	76.735
H	6.877	-13.820	75.664
H	5.484	-14.596	76.366
H	8.860	-14.546	74.435
H	8.746	-14.756	72.674
H	7.375	-10.866	74.695
H	8.090	-10.130	73.220
H	6.599	-9.612	71.362
H	4.279	-9.424	70.494
H	2.918	-12.017	73.620
H	5.254	-12.181	74.512
H	0.267	-9.958	73.179
H	-2.157	-10.265	73.594
H	-2.876	-10.156	69.349
H	-0.469	-9.742	68.966
H	-6.289	-11.648	71.793
H	-7.192	-10.410	70.895
H	-4.258	-8.555	70.222
H	-5.946	-8.926	69.655
H	-4.190	-11.066	72.643
C	-9.348	-7.428	67.632
H	-8.298	-7.281	67.499
H	-9.851	-7.276	66.699

H	-9.718	-6.731	68.354
C	6.269	-8.546	77.080
H	6.831	-8.930	77.908
H	6.760	-8.817	76.166
H	6.208	-7.482	77.150
C	3.600	-3.950	80.697
H	3.251	-3.416	81.557
H	4.499	-4.476	80.948
H	3.798	-3.262	79.905
C	11.276	-11.308	76.443
H	12.077	-11.351	77.154
H	11.587	-11.777	75.532
H	11.025	-10.287	76.253
C	0.330	-11.411	66.159
C	1.259	-5.835	67.981
C	2.075	-5.961	70.249
H	1.213	-5.396	70.535
H	2.909	-5.302	70.125
C	-0.600	-12.485	66.752
H	-1.619	-12.227	66.548
H	-0.377	-13.434	66.310
H	-0.452	-12.541	67.810
C	0.458	-6.347	66.770
H	-0.588	-6.204	66.947
H	0.748	-5.805	65.895
H	0.656	-7.389	66.626
H	1.733	-9.984	66.281

Camostat (tetrahedral intermediate)

C	4.859	-9.170	77.172
H	4.393	-8.857	78.114
H	4.968	-10.261	77.224
N	2.915	-7.886	76.175
H	2.564	-7.021	77.615
C	3.917	-8.837	76.054
C	2.260	-7.887	75.021
H	1.410	-7.269	74.771
N	2.792	-8.787	74.160
C	3.845	-9.402	74.802
H	4.432	-10.167	74.320
C	10.028	-12.016	77.000
H	9.728	-11.523	77.937
H	10.261	-13.059	77.247
C	8.856	-12.026	76.007
H	8.658	-11.011	75.637
H	7.954	-12.377	76.526
C	9.131	-12.990	74.817
O	9.254	-12.463	73.672

O	9.232	-14.207	75.123
C	2.574	-4.968	80.181
H	1.603	-4.495	79.981
H	2.373	-5.761	80.912
C	3.039	-5.619	78.880
O	2.250	-6.625	78.503
O	4.018	-5.241	78.259
C	-9.492	-8.866	68.154
H	-9.431	-9.580	67.320
H	-10.460	-9.052	68.635
C	-8.371	-9.268	69.135
O	-8.575	-10.291	69.850
O	-7.317	-8.568	69.114
O	0.192	-11.333	64.942
N	1.183	-10.627	66.834
H	1.269	-10.531	67.848
O	1.421	-4.610	67.985
N	1.797	-6.556	68.975
H	1.639	-7.575	69.000
C	2.382	-7.075	71.249
H	2.606	-6.636	72.228
H	3.262	-7.639	70.926
O	1.258	-7.944	71.428
H	2.437	-9.041	73.231
C	10.860	-16.392	70.731
N	9.490	-16.045	71.067
C	9.299	-15.479	72.409
C	8.519	-16.279	70.150
O	8.703	-16.910	69.104
C	7.101	-15.772	70.443
O	7.009	-14.480	71.059
C	7.528	-13.451	70.341
O	8.009	-13.604	69.238
C	7.419	-12.146	71.096
C	5.989	-11.646	71.180
C	5.533	-10.638	70.325
C	4.244	-10.110	70.417
C	3.362	-10.609	71.386
C	3.788	-11.669	72.205
C	5.085	-12.167	72.114
O	2.138	-10.091	71.701
C	1.273	-9.235	70.735
O	1.669	-9.255	69.516
C	-0.142	-9.775	70.993
C	-0.643	-10.031	72.273
C	-1.949	-10.482	72.449
C	-2.767	-10.703	71.336
C	-2.270	-10.469	70.050
C	-0.971	-9.990	69.891

N	-4.096	-11.194	71.514
C	-5.222	-10.598	71.024
N	-6.405	-11.197	71.211
N	-5.163	-9.438	70.394
H	10.903	-16.684	69.683
H	11.512	-15.529	70.908
H	11.215	-17.225	71.354
H	9.959	-16.004	73.103
H	9.525	-14.409	72.470
H	8.278	-15.615	72.758
H	6.580	-15.770	69.485
H	6.591	-16.445	71.138
H	7.857	-12.287	72.096
H	8.037	-11.424	70.557
H	6.212	-10.230	69.580
H	3.915	-9.330	69.746
H	3.091	-12.061	72.940
H	5.404	-12.964	72.780
H	-0.007	-9.873	73.137
H	-2.340	-10.660	73.447
H	-2.894	-10.666	69.184
H	-0.577	-9.785	68.903
H	-6.400	-12.187	71.412
H	-7.262	-10.809	70.719
H	-4.283	-8.944	70.359
H	-6.029	-9.057	69.903
H	-4.239	-11.878	72.245
C	-9.347	-7.428	67.632
H	-8.298	-7.281	67.499
H	-9.852	-7.276	66.699
H	-9.719	-6.731	68.354
C	6.269	-8.545	77.079
H	6.831	-8.930	77.908
H	6.760	-8.817	76.167
H	6.208	-7.482	77.150
C	3.600	-3.950	80.697
H	3.251	-3.416	81.557
H	4.499	-4.476	80.948
H	3.798	-3.262	79.905
C	11.276	-11.308	76.443
H	12.077	-11.352	77.154
H	11.588	-11.777	75.533
H	11.025	-10.287	76.254
C	0.330	-11.411	66.159
C	1.259	-5.835	67.981
C	2.076	-5.961	70.249
H	1.213	-5.396	70.535
H	2.909	-5.302	70.125
C	-0.600	-12.485	66.752

H	-1.619	-12.227	66.548
H	-0.377	-13.434	66.310
H	-0.452	-12.541	67.810
C	0.458	-6.347	66.770
H	-0.588	-6.204	66.947
H	0.748	-5.805	65.895
H	0.656	-7.389	66.626
H	1.686	-9.951	66.275

Camostat (TS2)

C	4.864	-9.174	77.199
H	4.413	-8.850	78.144
H	4.980	-10.263	77.267
N	2.921	-7.898	76.186
H	2.578	-7.018	77.603
C	3.907	-8.869	76.091
C	2.250	-7.941	75.039
H	1.404	-7.321	74.778
N	2.755	-8.885	74.212
C	3.806	-9.486	74.867
H	4.373	-10.283	74.413
C	10.027	-12.023	76.993
H	9.673	-11.486	77.886
H	10.280	-13.042	77.308
C	8.902	-12.139	75.955
H	8.680	-11.163	75.505
H	7.988	-12.486	76.457
C	9.247	-13.175	74.843
O	9.209	-12.764	73.647
O	9.541	-14.328	75.253
C	2.576	-4.968	80.177
H	1.604	-4.497	79.978
H	2.377	-5.765	80.903
C	3.045	-5.612	78.873
O	2.262	-6.621	78.493
O	4.022	-5.224	78.254
C	-9.500	-8.866	68.154
H	-9.430	-9.579	67.320
H	-10.473	-9.048	68.624
C	-8.390	-9.269	69.146
O	-8.610	-10.275	69.879
O	-7.325	-8.584	69.116
O	0.192	-11.333	64.942
N	1.183	-10.627	66.834
H	1.277	-10.561	67.846
O	1.421	-4.610	67.985
N	1.797	-6.556	68.975
H	1.660	-7.572	68.984

C	2.360	-7.085	71.244
H	2.588	-6.674	72.231
H	3.209	-7.692	70.919
O	1.197	-7.920	71.419
H	2.391	-9.208	73.294
C	10.558	-16.868	70.867
N	9.236	-16.489	71.334
C	9.199	-15.844	72.652
C	8.163	-16.796	70.562
O	8.222	-17.521	69.564
C	6.794	-16.238	70.974
O	6.793	-14.889	71.458
C	7.206	-13.944	70.572
O	7.523	-14.216	69.432
C	7.201	-12.568	71.197
C	5.801	-11.993	71.307
C	5.388	-10.948	70.475
C	4.140	-10.340	70.609
C	3.236	-10.783	71.597
C	3.624	-11.892	72.383
C	4.884	-12.467	72.256
O	2.079	-10.177	71.904
C	1.116	-9.129	70.710
O	1.595	-9.241	69.557
C	-0.241	-9.730	71.007
C	-0.740	-9.892	72.304
C	-2.032	-10.369	72.508
C	-2.836	-10.703	71.412
C	-2.335	-10.573	70.114
C	-1.049	-10.072	69.921
N	-4.163	-11.189	71.615
C	-5.281	-10.598	71.097
N	-6.473	-11.172	71.304
N	-5.203	-9.468	70.418
H	10.485	-17.214	69.837
H	11.229	-16.002	70.927
H	10.979	-17.671	71.488
H	9.942	-16.326	73.293
H	9.420	-14.772	72.627
H	8.226	-15.966	73.124
H	6.156	-16.327	70.093
H	6.370	-16.826	71.793
H	7.694	-12.627	72.179
H	7.811	-11.932	70.550
H	6.076	-10.574	69.719
H	3.856	-9.527	69.954
H	2.922	-12.250	73.132
H	5.172	-13.290	72.904
H	-0.111	-9.643	73.149

H	-2.426	-10.472	73.516
H	-2.950	-10.858	69.266
H	-0.660	-9.939	68.918
H	-6.485	-12.153	71.546
H	-7.319	-10.792	70.788
H	-4.316	-8.987	70.370
H	-6.063	-9.086	69.913
H	-4.313	-11.825	72.386
C	-9.347	-7.428	67.632
H	-8.298	-7.281	67.499
H	-9.852	-7.276	66.699
H	-9.719	-6.731	68.354
C	6.269	-8.545	77.079
H	6.831	-8.930	77.908
H	6.760	-8.817	76.167
H	6.208	-7.482	77.150
C	3.600	-3.950	80.697
H	3.251	-3.416	81.557
H	4.499	-4.476	80.948
H	3.798	-3.262	79.905
C	11.276	-11.308	76.443
H	12.077	-11.352	77.154
H	11.588	-11.777	75.533
H	11.025	-10.287	76.254
C	0.330	-11.411	66.159
C	1.259	-5.835	67.981
C	2.076	-5.961	70.249
H	1.213	-5.396	70.535
H	2.909	-5.302	70.125
C	-0.600	-12.485	66.752
H	-1.619	-12.227	66.548
H	-0.377	-13.434	66.310
H	-0.452	-12.541	67.810
C	0.458	-6.347	66.770
H	-0.588	-6.204	66.947
H	0.748	-5.805	65.895
H	0.656	-7.389	66.626
H	1.701	-9.959	66.280

Camostat (acyl intermediate)

C	4.867	-9.176	77.208
H	4.421	-8.850	78.155
H	4.985	-10.265	77.277
N	2.937	-7.887	76.185
H	2.590	-7.010	77.592
C	3.905	-8.876	76.104
C	2.261	-7.941	75.040
H	1.425	-7.310	74.772

N	2.748	-8.907	74.227
C	3.790	-9.513	74.891
H	4.338	-10.330	74.449
C	10.025	-12.009	77.004
H	9.686	-11.463	77.898
H	10.267	-13.030	77.319
C	8.891	-12.119	75.976
H	8.715	-11.158	75.476
H	7.961	-12.394	76.496
C	9.177	-13.228	74.919
O	9.106	-12.891	73.702
O	9.456	-14.361	75.390
C	2.578	-4.968	80.174
H	1.605	-4.498	79.975
H	2.380	-5.768	80.898
C	3.050	-5.608	78.869
O	2.268	-6.614	78.483
O	4.030	-5.217	78.255
C	-9.507	-8.868	68.151
H	-9.447	-9.574	67.310
H	-10.475	-9.042	68.632
C	-8.384	-9.276	69.124
O	-8.657	-10.132	70.012
O	-7.251	-8.745	68.920
O	0.192	-11.333	64.942
N	1.183	-10.627	66.834
H	1.281	-10.576	67.846
O	1.421	-4.610	67.985
N	1.797	-6.556	68.975
H	1.662	-7.570	68.978
C	2.350	-7.090	71.241
H	2.596	-6.692	72.228
H	3.176	-7.722	70.906
O	1.166	-7.897	71.430
H	2.369	-9.264	73.319
C	10.315	-17.204	71.145
N	9.000	-16.747	71.561
C	8.957	-16.063	72.859
C	7.935	-17.039	70.774
O	7.989	-17.805	69.806
C	6.578	-16.409	71.115
O	6.613	-15.051	71.572
C	7.074	-14.137	70.676
O	7.419	-14.446	69.554
C	7.086	-12.748	71.269
C	5.696	-12.148	71.393
C	5.291	-11.104	70.555
C	4.059	-10.469	70.703
C	3.156	-10.873	71.712

C	3.539	-11.983	72.506
C	4.784	-12.586	72.365
O	2.026	-10.233	72.004
C	1.012	-9.064	70.708
O	1.515	-9.233	69.584
C	-0.314	-9.678	71.057
C	-0.828	-9.687	72.359
C	-2.113	-10.162	72.604
C	-2.890	-10.651	71.547
C	-2.366	-10.687	70.252
C	-1.089	-10.185	70.012
N	-4.224	-11.102	71.781
C	-5.322	-10.533	71.195
N	-6.534	-11.032	71.464
N	-5.203	-9.493	70.390
H	10.262	-17.549	70.113
H	11.029	-16.377	71.229
H	10.667	-18.028	71.782
H	9.625	-16.586	73.549
H	9.272	-15.015	72.811
H	7.954	-16.086	73.281
H	5.978	-16.489	70.208
H	6.092	-16.961	71.925
H	7.593	-12.793	72.245
H	7.695	-12.132	70.603
H	5.975	-10.753	69.783
H	3.784	-9.655	70.043
H	2.845	-12.316	73.274
H	5.064	-13.406	73.022
H	-0.220	-9.312	73.172
H	-2.523	-10.139	73.609
H	-2.962	-11.093	69.441
H	-0.688	-10.170	69.006
H	-6.587	-11.974	71.826
H	-7.370	-10.664	70.926
H	-4.295	-9.065	70.277
H	-6.041	-9.166	69.809
H	-4.395	-11.618	72.634
C	-9.347	-7.428	67.632
H	-8.298	-7.281	67.499
H	-9.852	-7.276	66.699
H	-9.719	-6.731	68.354
C	6.269	-8.545	77.079
H	6.831	-8.930	77.908
H	6.760	-8.817	76.167
H	6.208	-7.482	77.150
C	3.600	-3.950	80.697
H	3.251	-3.416	81.557
H	4.499	-4.476	80.948

H	3.798	-3.262	79.905
C	11.276	-11.308	76.443
H	12.077	-11.352	77.154
H	11.588	-11.777	75.533
H	11.025	-10.287	76.254
C	0.330	-11.411	66.159
C	1.259	-5.835	67.981
C	2.076	-5.961	70.249
H	1.213	-5.396	70.535
H	2.909	-5.302	70.125
C	-0.600	-12.485	66.752
H	-1.619	-12.227	66.548
H	-0.377	-13.434	66.310
H	-0.452	-12.541	67.810
C	0.458	-6.347	66.770
H	-0.588	-6.204	66.947
H	0.748	-5.805	65.895
H	0.656	-7.389	66.626
H	1.705	-9.960	66.283

Compound **1** (reactant)

C	5.183	-9.265	76.290
H	4.702	-9.198	77.274
H	5.292	-10.335	76.069
N	3.485	-7.566	75.585
H	3.493	-7.044	76.522
C	4.250	-8.669	75.281
C	2.679	-7.318	74.535
H	1.963	-6.511	74.545
N	2.875	-8.193	73.548
C	3.863	-9.044	74.009
H	4.221	-9.870	73.411
C	10.487	-11.788	76.653
H	9.762	-11.229	77.260
H	10.820	-12.648	77.243
C	9.812	-12.316	75.383
H	9.496	-11.482	74.743
H	8.895	-12.867	75.638
C	10.712	-13.285	74.576
O	10.489	-13.343	73.296
O	11.550	-13.964	75.177
C	2.230	-4.821	79.211
H	1.578	-3.981	78.946
H	1.650	-5.456	79.898
C	2.492	-5.631	77.929
O	1.670	-5.525	76.992
O	3.539	-6.365	77.940
C	-10.094	-8.600	67.040

H	-9.665	-9.085	66.159
H	-11.179	-8.763	67.029
C	-9.483	-9.213	68.301
O	-8.574	-10.081	68.147
O	-9.871	-8.729	69.407
O	0.666	-11.251	64.082
N	0.555	-10.300	66.163
H	0.226	-10.291	67.121
O	0.765	-4.297	67.612
N	0.991	-6.188	68.822
H	0.848	-7.197	68.773
C	2.461	-6.976	70.611
H	3.210	-6.601	71.322
H	2.998	-7.640	69.906
O	1.441	-7.667	71.292
H	1.881	-8.004	72.129
C	-1.926	-7.843	70.086
C	-3.229	-7.437	70.354
C	-4.180	-8.368	70.792
C	-3.820	-9.708	70.968
C	-2.521	-10.111	70.685
C	-1.564	-9.185	70.249
C	-0.160	-9.624	69.979
O	0.465	-9.297	68.965
C	1.601	-10.972	71.149
C	2.705	-10.607	70.402
C	3.980	-11.113	70.749
C	4.109	-12.033	71.840
C	2.948	-12.409	72.563
C	1.729	-11.888	72.230
C	5.388	-12.501	72.205
C	6.519	-12.062	71.541
C	6.398	-11.145	70.462
C	5.159	-10.698	70.071
C	7.839	-12.511	72.012
N	8.880	-11.690	72.025
N	8.008	-13.748	72.459
N	-5.503	-7.948	71.077
C	-6.632	-8.541	70.572
N	-7.821	-8.097	70.960
N	-6.543	-9.562	69.727
H	-1.181	-7.121	69.770
H	-3.512	-6.397	70.224
H	-4.551	-10.424	71.326
H	-2.256	-11.157	70.801
H	2.597	-9.907	69.587
H	3.042	-13.098	73.398
H	0.843	-12.161	72.798
H	5.477	-13.165	73.060

H	7.289	-10.821	69.932
H	5.066	-10.004	69.241
H	8.728	-10.699	71.906
H	7.293	-14.444	72.315
H	8.947	-13.966	72.861
H	-7.887	-7.405	71.692
H	-8.694	-8.413	70.438
H	-5.655	-9.711	69.267
H	-7.417	-9.892	69.206
H	-5.615	-7.005	71.426
H	9.737	-12.083	72.508
C	-9.796	-7.087	67.059
H	-8.753	-6.936	67.244
H	-10.065	-6.622	66.134
H	-10.365	-6.653	67.855
C	3.500	-4.321	79.917
H	3.211	-3.639	80.690
H	4.044	-5.136	80.345
H	4.119	-3.811	79.207
C	11.695	-10.905	76.303
H	12.275	-10.665	77.170
H	12.297	-11.465	75.617
H	11.364	-10.004	75.834
C	6.600	-8.655	76.397
H	6.588	-7.615	76.651
H	7.103	-9.203	77.167
H	7.118	-8.790	75.470
C	1.932	-5.784	69.825
H	1.229	-5.227	70.408
H	2.781	-5.170	69.607
C	0.549	-5.492	67.754
C	-0.280	-6.028	66.572
H	-1.098	-5.365	66.380
H	0.340	-6.091	65.702
H	-0.657	-7.000	66.812
C	0.239	-11.206	65.233
C	-0.751	-12.368	65.438
H	-1.582	-12.249	64.774
H	-0.260	-13.296	65.232
H	-1.100	-12.365	66.450
H	1.225	-9.587	65.907
N	0.312	-10.463	70.948
H	-0.296	-10.560	71.750

Compound **1** (TS1)

C	5.175	-9.244	76.252
H	4.682	-9.227	77.231
H	5.268	-10.300	75.969

N	3.495	-7.482	75.655
H	3.499	-6.958	76.704
C	4.250	-8.575	75.274
C	2.687	-7.153	74.650
H	1.974	-6.345	74.700
N	2.887	-7.984	73.615
C	3.871	-8.885	73.987
H	4.204	-9.664	73.322
C	10.506	-11.806	76.685
H	9.708	-11.214	77.155
H	10.839	-12.548	77.418
C	9.960	-12.563	75.472
H	9.688	-11.861	74.672
H	9.032	-13.092	75.734
C	10.949	-13.622	74.915
O	10.729	-14.023	73.699
O	11.851	-14.042	75.645
C	2.223	-4.814	79.213
H	1.556	-3.976	78.989
H	1.669	-5.487	79.883
C	2.473	-5.561	77.900
O	1.724	-5.354	76.928
O	3.471	-6.383	77.914
C	-10.029	-8.618	67.047
H	-9.754	-9.051	66.082
H	-11.080	-8.851	67.253
C	-9.115	-9.194	68.132
O	-8.071	-9.795	67.738
O	-9.408	-8.913	69.332
O	0.666	-11.251	64.082
N	0.555	-10.300	66.163
H	0.306	-10.358	67.143
O	0.765	-4.297	67.612
N	0.991	-6.188	68.822
H	0.886	-7.202	68.756
C	2.458	-7.013	70.589
H	3.295	-6.656	71.220
H	2.917	-7.675	69.827
O	1.528	-7.691	71.362
H	2.319	-7.951	72.688
C	-1.298	-7.636	70.986
C	-2.665	-7.397	71.124
C	-3.599	-8.372	70.754
C	-3.156	-9.586	70.213
C	-1.792	-9.798	70.045
C	-0.850	-8.841	70.443
C	0.603	-9.252	70.281
O	1.157	-9.221	69.166
C	2.114	-10.855	71.484

C	3.237	-10.701	70.681
C	4.450	-11.330	71.033
C	4.520	-12.148	72.211
C	3.348	-12.308	72.998
C	2.185	-11.681	72.647
C	5.745	-12.738	72.575
C	6.887	-12.539	71.816
C	6.822	-11.737	70.642
C	5.636	-11.160	70.263
C	8.160	-13.099	72.280
N	9.310	-12.465	72.063
N	8.203	-14.240	72.953
N	-4.972	-8.131	71.017
C	-6.054	-8.587	70.316
N	-7.262	-8.475	70.862
N	-5.919	-9.130	69.114
H	-0.556	-6.921	71.317
H	-3.009	-6.455	71.543
H	-3.862	-10.367	69.960
H	-1.452	-10.746	69.638
H	3.174	-10.084	69.795
H	3.391	-12.921	73.894
H	1.296	-11.796	73.261
H	5.792	-13.310	73.497
H	7.711	-11.609	70.032
H	5.587	-10.555	69.362
H	9.288	-11.495	71.783
H	7.387	-14.827	73.017
H	9.129	-14.480	73.383
H	-7.345	-8.283	71.850
H	-8.132	-8.720	70.296
H	-5.056	-8.981	68.610
H	-6.781	-9.484	68.592
H	-5.174	-7.466	71.751
H	10.129	-12.868	72.583
C	-9.796	-7.087	67.059
H	-8.753	-6.936	67.244
H	-10.065	-6.622	66.134
H	-10.365	-6.653	67.855
C	3.500	-4.321	79.917
H	3.211	-3.639	80.690
H	4.044	-5.136	80.345
H	4.119	-3.811	79.207
C	11.695	-10.905	76.303
H	12.275	-10.665	77.170
H	12.297	-11.465	75.617
H	11.364	-10.004	75.834
C	6.600	-8.655	76.397
H	6.588	-7.615	76.651

H	7.103	-9.203	77.167
H	7.118	-8.790	75.470
C	1.932	-5.784	69.825
H	1.229	-5.227	70.408
H	2.781	-5.170	69.607
C	0.549	-5.492	67.754
C	-0.280	-6.028	66.572
H	-1.098	-5.365	66.380
H	0.340	-6.091	65.702
H	-0.657	-7.000	66.812
C	0.239	-11.206	65.233
C	-0.751	-12.368	65.438
H	-1.582	-12.249	64.774
H	-0.260	-13.296	65.232
H	-1.100	-12.365	66.450
H	1.265	-9.620	65.926
N	0.895	-10.253	71.235
H	0.281	-10.217	72.039

Compound **1** (tetrahedral intermediate)

C	5.192	-9.280	76.265
H	4.700	-9.258	77.246
H	5.318	-10.339	76.007
N	3.528	-7.531	75.615
H	3.496	-6.797	77.010
C	4.255	-8.655	75.275
C	2.720	-7.268	74.601
H	2.004	-6.461	74.577
N	2.896	-8.169	73.605
C	3.873	-9.057	74.015
H	4.190	-9.879	73.396
C	10.502	-11.801	76.685
H	9.712	-11.206	77.164
H	10.834	-12.551	77.410
C	9.941	-12.544	75.470
H	9.680	-11.836	74.672
H	9.003	-13.057	75.731
C	10.908	-13.621	74.908
O	10.662	-14.029	73.700
O	11.818	-14.044	75.627
C	2.201	-4.793	79.240
H	1.532	-3.950	79.046
H	1.661	-5.478	79.910
C	2.404	-5.506	77.919
O	1.679	-5.323	76.949
O	3.434	-6.340	77.939
C	-10.017	-8.621	67.046
H	-9.752	-9.046	66.074

H	-11.061	-8.865	67.269
C	-9.076	-9.188	68.113
O	-8.008	-9.730	67.699
O	-9.376	-8.955	69.322
O	0.666	-11.251	64.082
N	0.555	-10.300	66.163
H	0.321	-10.351	67.148
O	0.765	-4.297	67.612
N	0.991	-6.188	68.822
H	0.915	-7.214	68.739
C	2.445	-7.034	70.542
H	3.166	-6.727	71.309
H	2.968	-7.659	69.810
O	1.450	-7.798	71.208
H	2.350	-8.192	72.728
C	-1.316	-7.451	71.122
C	-2.696	-7.286	71.243
C	-3.571	-8.278	70.790
C	-3.052	-9.423	70.168
C	-1.675	-9.551	70.016
C	-0.787	-8.589	70.512
C	0.717	-8.906	70.375
O	1.156	-9.008	69.164
C	2.056	-10.794	71.448
C	3.202	-10.641	70.665
C	4.391	-11.315	70.998
C	4.428	-12.198	72.132
C	3.232	-12.385	72.879
C	2.091	-11.709	72.552
C	5.640	-12.805	72.501
C	6.808	-12.571	71.789
C	6.770	-11.723	70.645
C	5.597	-11.126	70.260
C	8.072	-13.124	72.273
N	9.225	-12.490	72.064
N	8.117	-14.261	72.958
N	-4.958	-8.128	71.056
C	-6.016	-8.581	70.321
N	-7.231	-8.552	70.866
N	-5.857	-9.041	69.087
H	-0.640	-6.702	71.516
H	-3.097	-6.392	71.716
H	-3.711	-10.219	69.842
H	-1.271	-10.441	69.543
H	3.156	-9.988	69.803
H	3.245	-13.056	73.735
H	1.190	-11.842	73.145
H	5.660	-13.415	73.401
H	7.673	-11.574	70.060

H	5.573	-10.485	69.384
H	9.204	-11.520	71.785
H	7.309	-14.862	73.005
H	9.037	-14.498	73.391
H	-7.323	-8.427	71.863
H	-8.093	-8.787	70.284
H	-4.997	-8.835	68.598
H	-6.704	-9.399	68.548
H	-5.194	-7.534	71.838
H	10.041	-12.889	72.592
C	-9.796	-7.087	67.059
H	-8.753	-6.936	67.244
H	-10.065	-6.622	66.134
H	-10.365	-6.653	67.855
C	3.500	-4.321	79.917
H	3.211	-3.639	80.690
H	4.044	-5.136	80.345
H	4.119	-3.811	79.207
C	11.695	-10.905	76.303
H	12.275	-10.665	77.170
H	12.297	-11.465	75.617
H	11.364	-10.004	75.834
C	6.600	-8.655	76.397
H	6.588	-7.615	76.651
H	7.103	-9.203	77.167
H	7.118	-8.790	75.470
C	1.932	-5.784	69.825
H	1.229	-5.227	70.408
H	2.781	-5.170	69.607
C	0.549	-5.492	67.754
C	-0.280	-6.028	66.572
H	-1.098	-5.365	66.380
H	0.340	-6.091	65.702
H	-0.657	-7.000	66.812
C	0.239	-11.206	65.233
C	-0.751	-12.368	65.438
H	-1.582	-12.249	64.774
H	-0.260	-13.296	65.232
H	-1.100	-12.365	66.450
H	1.264	-9.621	65.920
N	0.885	-10.125	71.223
H	0.227	-10.170	71.991

Compound 1 (TS2)

C	5.188	-9.278	76.333
H	4.730	-9.187	77.328
H	5.300	-10.353	76.147
N	3.581	-7.522	75.506

H	3.586	-6.650	76.877
C	4.215	-8.739	75.331
C	2.697	-7.408	74.526
H	2.008	-6.586	74.405
N	2.741	-8.490	73.709
C	3.699	-9.349	74.213
H	3.914	-10.297	73.750
C	10.503	-11.805	76.683
H	9.698	-11.208	77.134
H	10.829	-12.536	77.429
C	9.976	-12.584	75.476
H	9.733	-11.900	74.652
H	9.034	-13.094	75.726
C	10.964	-13.672	74.971
O	10.765	-14.107	73.767
O	11.848	-14.073	75.736
C	2.219	-4.809	79.216
H	1.526	-3.980	79.043
H	1.688	-5.526	79.858
C	2.426	-5.479	77.867
O	1.621	-5.375	76.951
O	3.545	-6.191	77.800
C	-9.998	-8.625	67.033
H	-9.777	-9.019	66.037
H	-11.023	-8.896	67.303
C	-8.992	-9.222	68.025
O	-7.851	-9.505	67.549
O	-9.332	-9.286	69.242
O	0.666	-11.251	64.082
N	0.553	-10.300	66.164
H	0.323	-10.387	67.146
O	0.765	-4.297	67.612
N	0.991	-6.188	68.822
H	0.906	-7.201	68.727
C	2.348	-7.021	70.616
H	2.979	-6.733	71.461
H	2.897	-7.725	69.984
O	1.193	-7.661	71.174
H	2.095	-8.711	72.943
C	-1.508	-7.986	71.648
C	-2.884	-8.089	71.842
C	-3.626	-9.047	71.143
C	-2.976	-9.901	70.240
C	-1.607	-9.768	70.033
C	-0.857	-8.818	70.734
C	0.630	-8.746	70.470
O	1.085	-9.073	69.355
C	2.087	-11.011	71.785
C	3.241	-10.755	71.008

C	4.420 -11.480	71.195
C	4.467 -12.551	72.161
C	3.259 -12.893	72.838
C	2.114 -12.176	72.642
C	5.687 -13.170	72.455
C	6.870 -12.791	71.822
C	6.813 -11.785	70.810
C	5.632 -11.166	70.502
C	8.146 -13.319	72.276
N	9.282 -12.638	72.088
N	8.247 -14.480	72.920
N	-5.016 -9.169	71.414
C	-6.024 -9.313	70.498
N	-7.266 -9.489	70.940
N	-5.787 -9.286	69.195
H	-0.936 -7.244	72.192
H	-3.387 -7.421	72.537
H	-3.535 -10.673	69.723
H	-1.095 -10.426	69.341
H	3.218 -9.938	70.297
H	3.269 -13.728	73.536
H	1.209 -12.429	73.189
H	5.705 -13.910	73.251
H	7.715 -11.527	70.262
H	5.603 -10.399	69.733
H	9.218 -11.651	71.884
H	7.465 -15.113	72.967
H	9.161 -14.675	73.377
H	-7.422 -9.704	71.914
H	-8.093 -9.471	70.264
H	-4.896 -8.942	68.866
H	-6.603 -9.423	68.516
H	-5.311 -8.868	72.333
H	10.099 -13.010	72.631
C	-9.796 -7.087	67.059
H	-8.753 -6.936	67.244
H	-10.065 -6.622	66.134
H	-10.365 -6.653	67.855
C	3.500 -4.321	79.917
H	3.211 -3.639	80.690
H	4.044 -5.136	80.345
H	4.119 -3.811	79.207
C	11.695 -10.905	76.304
H	12.275 -10.665	77.170
H	12.297 -11.465	75.617
H	11.364 -10.004	75.834
C	6.600 -8.655	76.397
H	6.588 -7.615	76.652
H	7.103 -9.203	77.167

H	7.118	-8.790	75.470
C	1.933	-5.784	69.824
H	1.229	-5.227	70.408
H	2.781	-5.170	69.607
C	0.549	-5.492	67.754
C	-0.280	-6.028	66.572
H	-1.098	-5.365	66.380
H	0.340	-6.091	65.702
H	-0.657	-7.000	66.812
C	0.241	-11.206	65.232
C	-0.751	-12.368	65.438
H	-1.582	-12.249	64.774
H	-0.260	-13.296	65.232
H	-1.100	-12.365	66.450
H	1.280	-9.635	65.935
N	1.057	-10.152	71.818
H	0.255	-10.497	72.341

Compound **1** (acyl intermediate)

C	5.189	-9.279	76.367
H	4.750	-9.164	77.367
H	5.301	-10.358	76.208
N	3.531	-7.572	75.513
H	3.554	-6.657	76.863
C	4.190	-8.781	75.371
C	2.616	-7.526	74.554
H	1.898	-6.730	74.421
N	2.666	-8.639	73.780
C	3.658	-9.450	74.296
H	3.883	-10.414	73.873
C	10.500	-11.800	76.686
H	9.690	-11.194	77.117
H	10.817	-12.516	77.451
C	9.984	-12.604	75.491
H	9.772	-11.941	74.641
H	9.026	-13.089	75.733
C	10.959	-13.725	75.034
O	10.727	-14.236	73.868
O	11.864	-14.078	75.801
C	2.217	-4.809	79.218
H	1.526	-3.978	79.047
H	1.686	-5.522	79.864
C	2.409	-5.485	77.869
O	1.583	-5.396	76.970
O	3.533	-6.186	77.780
C	-9.990	-8.627	67.039
H	-9.772	-9.018	66.041
H	-11.013	-8.903	67.313

C	-8.978	-9.227	68.023
O	-7.814	-9.424	67.556
O	-9.337	-9.389	69.225
O	0.666	-11.251	64.082
N	0.555	-10.300	66.163
H	0.329	-10.401	67.144
O	0.765	-4.297	67.612
N	0.991	-6.188	68.822
H	0.958	-7.193	68.671
C	2.301	-7.026	70.638
H	2.880	-6.758	71.522
H	2.852	-7.762	70.049
O	1.081	-7.627	71.140
H	1.974	-8.968	73.080
C	-1.600	-8.038	71.714
C	-2.963	-8.215	71.937
C	-3.672	-9.194	71.232
C	-2.997	-10.016	70.317
C	-1.642	-9.818	70.085
C	-0.930	-8.829	70.775
C	0.491	-8.599	70.403
O	0.998	-9.072	69.390
C	1.941	-11.262	72.168
C	3.064	-11.056	71.313
C	4.243	-11.775	71.459
C	4.339	-12.820	72.458
C	3.159	-13.137	73.201
C	2.010	-12.420	73.045
C	5.569	-13.426	72.715
C	6.729	-13.066	72.021
C	6.619	-12.098	70.974
C	5.425	-11.493	70.697
C	8.021	-13.563	72.438
N	9.151	-12.902	72.139
N	8.166	-14.680	73.153
N	-5.057	-9.367	71.491
C	-6.051	-9.460	70.549
N	-7.302	-9.654	70.960
N	-5.791	-9.369	69.254
H	-1.057	-7.270	72.251
H	-3.484	-7.577	72.645
H	-3.531	-10.808	69.804
H	-1.110	-10.446	69.380
H	3.010	-10.251	70.587
H	3.203	-13.954	73.920
H	1.133	-12.655	73.645
H	5.622	-14.139	73.534
H	7.493	-11.861	70.374
H	5.360	-10.756	69.899

H	9.072	-11.925	71.898
H	7.390	-15.307	73.292
H	9.100	-14.838	73.581
H	-7.476	-9.913	71.920
H	-8.114	-9.608	70.268
H	-4.892	-9.015	68.960
H	-6.600	-9.443	68.553
H	-5.368	-9.096	72.414
H	9.989	-13.230	72.674
C	-9.796	-7.087	67.059
H	-8.753	-6.936	67.244
H	-10.065	-6.622	66.134
H	-10.365	-6.653	67.855
C	3.500	-4.321	79.917
H	3.211	-3.639	80.690
H	4.044	-5.136	80.345
H	4.119	-3.811	79.207
C	11.695	-10.905	76.303
H	12.275	-10.665	77.170
H	12.297	-11.465	75.617
H	11.364	-10.004	75.834
C	6.600	-8.655	76.397
H	6.588	-7.615	76.651
H	7.103	-9.203	77.167
H	7.118	-8.790	75.470
C	1.932	-5.784	69.825
H	1.229	-5.227	70.408
H	2.781	-5.170	69.607
C	0.549	-5.492	67.754
C	-0.280	-6.028	66.572
H	-1.098	-5.365	66.380
H	0.340	-6.091	65.702
H	-0.657	-7.000	66.812
C	0.239	-11.206	65.233
C	-0.751	-12.368	65.438
H	-1.582	-12.249	64.774
H	-0.260	-13.296	65.232
H	-1.100	-12.365	66.450
H	1.295	-9.648	65.936
N	0.953	-10.371	72.207
H	0.222	-10.678	72.854