A Theoretical Study of the Nornicotine-Catalyzed Mannich Reaction in Wet Solvents and Water

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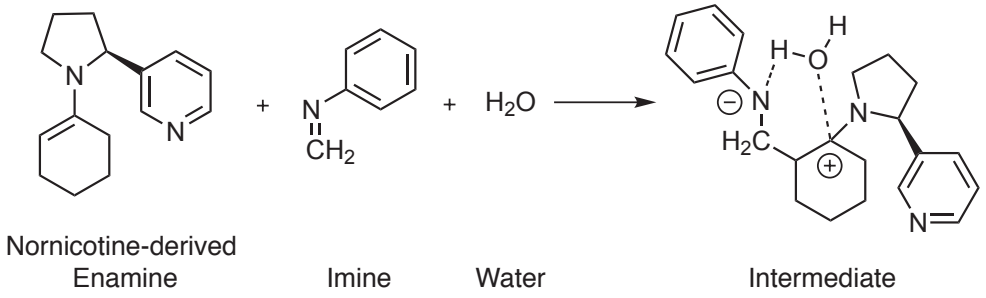
Supplementary Material

S.1 Gauging DFT functionals

S.1.1 Complete Model



Scheme S.1: Reaction scheme of the complete model.

$$\Delta E = E_{\text{Intermediate}} - E_{\text{Nornicotine-derived Enamine}} - E_{\text{Imine}} - E_{\text{Water}} \tag{S.1}$$

Method	ΔE (kcal/mol)
MP2/Def2-TZVPP	−4.45
M06-2X/Def2-TZVPP	−0.99
B3LYP/Def2-TZVPP	17.61
BMK/Def2-TZVPP	7.32

Table S.1: ΔE calculated by single point at several computational levels with the basis set Def2-TZVPP and geometry optimized at the M06-2X/Def-SVP level

Method	ΔE (kcal/mol)
MP2/Def2-TZVPP	−2.90
M06-2X/Def2-TZVPP	0.59
B3LYP/Def2-TZVPP	13.15
BMK/Def2-TZVPP	6.28

Table S.2: ΔE calculated from single point calculations with selected methods all using the Def2-TZVPP basis set. Geometries from B3LYP/Def-SVP optimisations.

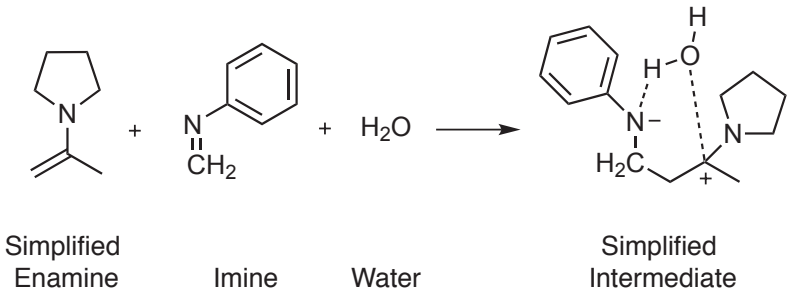
Method	ΔE (kcal/mol)
MP2/Def2-TZVPP	−4.45
M06-2X/Def2-TZVPP	−0.99
B3LYP/Def2-TZVPP	17.61
BMK/Def2-TZVPP	7.32

Table S.3: ΔE calculated from single point calculations with selected methods using geometries from M06-2X/Def-SVP optimisations.

Method	ΔE (kcal/mol)
MP2/6-31++G(d,p)	−5.34
MP2/6-311++G(d,p)	−5.83
MP2/6-311++G(2d,2p)	−5.70
M06-2X/6-31++G(d,p)	−4.66

Table S.4: ΔE calculated from single point calculations with selected methods using geometries from M06-2X/Def-SVP optimisations.

S.1.2 Simplified Model



Scheme S.2: Reaction scheme for the simplified model.

$$\Delta E_{\mathrm{s}} = E_{\text{Simplified Intermediate}} - E_{\text{Simplified Enamine}} - E_{\text{Imine}} - E_{\text{Water}} \tag{S.2}$$

Method	ΔE_{s} (kcal/mol)
MP2/Def2-TZVPP	−13.36
M06-2X/Def2-TZVPP	−9.45
B3LYP/Def2-TZVPP	9.38
BMK/Def2-TZVPP	−1.00

Table S.5: ΔE_{s} from single point calculations using geometries optimised at the MP2/Def-SVP level.

Method	ΔE_s (kcal/mol)
MP2/6-311++G(2d,2p)	−13.95
M06-2X/6-311++G(2d,2p)	−9.95
B3LYP/6-311++G(2d,2p)	9.09
BMK/6-311++G(2d,2p)	−1.40

Table S.6: ΔE_s from single point calculations using geometries optimised at the MP2/Def-SVP level.

Method	ΔE_s (kcal/mol)
MP2/Def2-TZVPP	−13.36
M06-2X/Def2-TZVPP	−9.45
B3LYP/Def2-TZVPP	9.38
BMK/Def2-TZVPP	−1.00

Table S.7: ΔE calculated from single point calculations with selected methods using geometries from MP2/Def-SVP optimisations.

Method	ΔE_s (kcal/mol)
MP2/6-31++G(d,p)	−14.42
MP2/6-311++G(d,p)	−14.89
MP2/6-311++G(2d,2p)	−13.95
M06-2X/6-31++G(d,p)	−13.19

Table S.8: ΔE calculated from single point calculations with selected methods using geometries from MP2/Def-SVP optimisations.

S.2 Barriers in the transition from the E to the Z rotamer

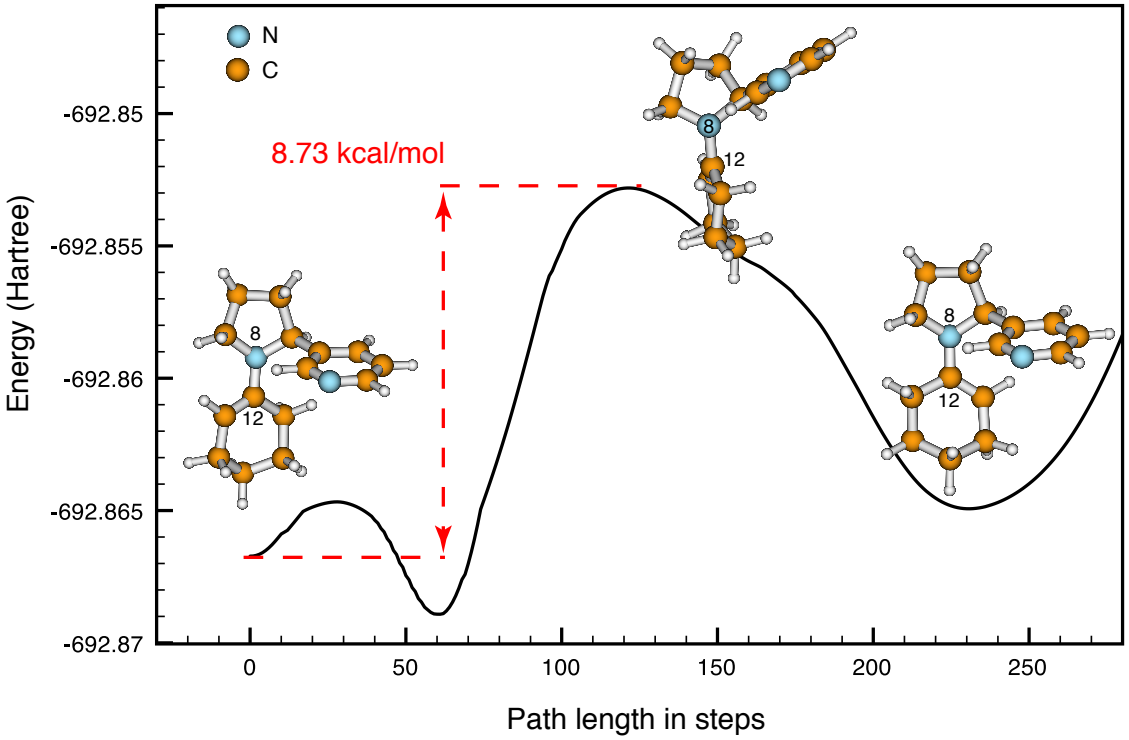


Figure S.1: Reaction path for the rotation of the cyclohexene ring in the nornicotine-derived enamine at the M06-2X/6-31++G(d,p) level. The E-rotamer is on the left and the Z-rotamer on the right side of the plot.

S.3 Complete Gaussian 09 reference

M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Gaussian 09, Revision B.01, Gaussian Inc., Wallingford CT, 2010

S.4 Selected computational data

S.4.1 NE1 in DMSO

	X [Angs]	Y [Angs]	Z [Angs]	q_Mul [e]
C	4.016432	-1.762098	-0.894042	-0.398942
C	3.730590	-0.623748	-1.875825	-0.493323
C	2.495964	0.183859	-1.436012	0.282056
C	2.668967	0.667237	-0.016644	-0.459963
C	3.017209	-0.397106	0.992450	0.017766
C	4.229014	-1.221549	0.521282	-0.386117
H	2.308938	1.038902	-2.091311	0.166156
H	4.603124	0.040053	-1.927871	0.164742
H	3.564215	-1.013309	-2.884535	0.193168
H	3.169695	-2.462112	-0.894219	0.149174
H	4.899063	-2.324098	-1.215920	0.174690
H	3.191111	0.070302	1.964953	0.171761
H	2.134985	-1.047900	1.068480	0.224644
H	5.124879	-0.587858	0.536186	0.166800
H	4.404272	-2.038258	1.227796	0.192361
H	1.613045	-0.466985	-1.450365	0.240516
O	2.598336	1.852347	0.287321	-0.404792
C	-1.137119	0.139998	2.591044	-0.380993
C	-1.072441	-1.216173	1.882526	-0.287552
C	-1.016414	-0.809784	0.396445	-0.789908
C	-0.197848	1.012877	1.744362	-0.043826
H	-2.160173	0.530389	2.554816	0.186902
H	-0.834119	0.088914	3.639279	0.183590
H	-1.916419	-1.873213	2.106395	0.183490
H	-0.146042	-1.739621	2.144163	0.165239
H	-0.558010	-1.611087	-0.200098	0.144921
H	0.809646	1.045112	2.181544	0.162679
H	-0.550795	2.047494	1.664704	0.150243
N	-0.139266	0.357932	0.422262	-0.453367
C	-2.409448	-0.564465	-0.161452	0.460930
C	-2.991636	0.705041	-0.198613	-0.780510
C	-4.464223	-1.391565	-1.108093	-0.098032
H	-2.431338	1.572502	0.147313	0.241977
H	-5.084564	-2.197313	-1.485410	0.185183
C	-3.179024	-1.629513	-0.636466	0.143954
H	-2.768279	-2.637095	-0.637256	0.183845
C	-4.945657	-0.082536	-1.091664	-0.113299
H	-5.946444	0.141055	-1.452723	0.180547
N	-4.228417	0.953565	-0.648343	-0.105148

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H  -0.300108   1.012292  -0.338352   0.406231
O   0.316424   3.014160  -0.912290  -0.799715
H   1.199099   2.760156  -0.586405   0.460113
H   0.463723   3.476299  -1.744645   0.411809

E(RM062X) = -845.694698366
frequencies    5.0988  22.8801  26.8667  44.4993  49.3560  61.1627
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S.4.2 NE-ts12 in DMSO

```
   X  [Angs]  Y  [Angs]  Z  [Angs]  q_Mul [e]
C  -3.230627  -2.118741  -0.611129  -0.373559
C  -2.271085  -2.233011   0.574026  -0.566332
C  -1.081788  -1.287515   0.388555   0.806907
C  -1.581691   0.161249   0.251870  -1.684787
C  -2.532997   0.299628  -0.936439   0.467656
C  -3.707703  -0.675888  -0.781453  -0.514578
H  -0.392136  -1.342407   1.239610   0.169148
H  -2.797916  -1.973843   1.499841   0.174526
H  -1.906944  -3.259955   0.680059   0.180119
H  -2.715327  -2.444079  -1.526266   0.153908
H  -4.088965  -2.784946  -0.473276   0.156274
H  -2.916517   1.322409  -0.981950   0.160528
H  -2.008050   0.089666  -1.877607   0.148652
H  -4.291072  -0.382378   0.099124   0.172512
H  -4.366026  -0.587873  -1.651743   0.173372
H  -0.532885  -1.594548  -0.509825   0.117158
O  -2.155953   0.620159   1.403483  -0.479166
C   0.750001   3.074219  -0.566449  -0.370857
C   1.180482   2.035936  -1.605616  -0.357872
C   0.684763   0.680702  -1.034746  -0.208417
C  -0.587285   2.520741  -0.103653   0.250884
H   1.454303   3.115216   0.271723   0.162335
H   0.657648   4.078222  -0.983587   0.220463
H   2.256322   2.019959  -1.786715   0.209535
H   0.677228   2.232277  -2.556459   0.200362
H   0.138454   0.127969  -1.802215   0.198199
H  -1.350019   2.657608  -0.872444   0.178409
H  -0.952226   2.903290   0.848456   0.214539
N  -0.302701   1.057447   0.044901  -0.827141
C   1.800039  -0.196072  -0.513565  -0.048213
C   2.535656   0.133717   0.629360  -0.177467
C   3.239144  -2.107281  -0.746305   0.032469
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H   2.282516   1.015596   1.215876   0.273693
H   3.551877  -3.008339  -1.261859   0.194978
C   2.172701  -1.345019  -1.209762   0.072521
H   1.629166  -1.641977  -2.103370   0.209559
C   3.899555  -1.689633   0.406813  -0.221671
H   4.736246  -2.260724   0.800721   0.182065
N   3.560606  -0.589721   1.088247  -0.064265
H   0.126952   0.972584   1.014847   0.385562
O  -0.131408   0.827893   2.670771  -0.925147
H  -1.268089   0.725467   2.165780   0.560223
H  -0.045975   1.644106   3.176191   0.392913

E(RM062X) = -845.686737004
frequencies -759.8736  33.3740  42.7441  56.4218  88.0569  93.5166
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S.4.3 NE2 in DMSO

```
   X  [Angs]  Y  [Angs]  Z  [Angs]  q_Mul [e]
C  -3.251532  -2.107021  -0.655451  -0.379891
C  -2.353625  -2.193376   0.579241  -0.611670
C  -1.137054  -1.278667   0.424937   0.785467
C  -1.550581   0.180973   0.180095  -2.007992
C  -2.485884   0.276470  -1.033676   0.600479
C  -3.690130  -0.662869  -0.901230  -0.523751
H  -0.492179  -1.317200   1.312106   0.153194
H  -2.924876  -1.897128   1.467394   0.165786
H  -2.016155  -3.222611   0.740472   0.174896
H  -2.697016  -2.473836  -1.531316   0.156466
H  -4.127396  -2.754173  -0.536841   0.153486
H  -2.831600   1.308129  -1.144958   0.160995
H  -1.925181   0.017176  -1.940051   0.138862
H  -4.314261  -0.328367  -0.063993   0.172677
H  -4.302374  -0.597380  -1.807023   0.165947
H  -0.537986  -1.632379  -0.422853   0.118573
O  -2.298655   0.669512   1.279472  -0.306862
C   0.726900   3.034354  -0.543280  -0.371251
C   1.074989   2.004416  -1.619308  -0.174229
C   0.625823   0.653189  -1.009531  -0.746273
C  -0.580112   2.477580   0.003171   0.367185
H   1.489858   3.059986   0.242164   0.149748
H   0.616110   4.044806  -0.942488   0.200297
H   2.129684   1.997210  -1.903213   0.194442
H   0.482986   2.205332  -2.518432   0.187832
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H	0.122347	0.062576	-1.784276	0.114295
H	-1.403526	2.722816	-0.681340	0.138707
H	-0.839095	2.860029	0.993650	0.174131
N	-0.327700	1.021650	0.070545	-0.564633
C	1.790246	-0.180780	-0.510154	0.298208
C	2.591383	0.229843	0.560614	-0.376548
C	3.242212	-2.093571	-0.690913	-0.020340
H	2.365293	1.155731	1.086172	0.227314
H	3.535306	-3.026635	-1.159676	0.187281
C	2.141464	-1.371506	-1.143513	0.113676
H	1.552337	-1.733964	-1.983268	0.206653
C	3.965095	-1.591074	0.387390	-0.174998
H	4.830821	-2.125931	0.769690	0.179213
N	3.653322	-0.446491	1.007493	-0.068102
H	0.232149	0.863585	1.838218	0.470644
O	0.121923	0.731271	2.812369	-0.708467
H	-1.734892	0.623338	2.071655	0.455489
H	0.403774	1.550983	3.235149	0.423068

E(RM062X) = -845.710105395

frequencies	22.2896	43.3763	74.8481	80.9868	90.8690	115.3604

S.4.4 NE-ts23 in DMSO

	X [Angs]	Y [Angs]	Z [Angs]	q_Mul [e]
C	-2.964043	-2.634168	-0.126396	-0.376569
C	-2.147999	-2.255235	1.111290	-0.541332
C	-0.966249	-1.358703	0.735243	0.369143
C	-1.424339	-0.091774	-0.004374	-1.242812
C	-2.282632	-0.463366	-1.223789	0.694091
C	-3.452139	-1.380566	-0.854331	-0.472043
H	-0.402826	-1.050247	1.625052	0.168885
H	-2.793294	-1.724897	1.822215	0.162159
H	-1.778179	-3.152868	1.618182	0.167754
H	-2.334885	-3.226850	-0.806122	0.156470
H	-3.813502	-3.265616	0.155794	0.151508
H	-2.654782	0.451883	-1.694454	0.169098
H	-1.640946	-0.970866	-1.955987	0.144426
H	-4.145577	-0.832032	-0.205250	0.172490
H	-4.004958	-1.653404	-1.759793	0.162357
H	-0.274819	-1.925643	0.098796	0.148500
O	-2.268897	0.673972	0.843616	-0.490020
C	0.762080	2.495392	-1.506629	-0.461307

C	1.165871	1.186640	-2.182704	-0.136543
C	0.811767	0.125792	-1.115709	-1.139053
C	-0.543733	2.097364	-0.826688	0.171993
H	1.506487	2.785700	-0.756165	0.175125
H	0.637554	3.323654	-2.207673	0.189860
H	2.214592	1.141152	-2.486520	0.170072
H	0.542828	1.023559	-3.069538	0.183078
H	0.467923	-0.788084	-1.618315	0.104265
H	-1.364426	2.109436	-1.560602	0.115438
H	-0.816807	2.762728	-0.003626	0.143027
N	-0.262535	0.742707	-0.321993	-0.155891
C	2.019213	-0.250753	-0.273535	0.414135
C	2.280246	0.336105	0.966259	-0.616640
C	4.067430	-1.482490	0.016047	-0.079221
H	1.568327	1.049714	1.373091	0.248428
H	4.801405	-2.206356	-0.321325	0.188245
C	2.943782	-1.184107	-0.746299	0.303741
H	2.780671	-1.674388	-1.704070	0.202019
C	4.232892	-0.829254	1.236959	-0.143401
H	5.100390	-1.036645	1.858785	0.177283
N	3.359864	0.064631	1.712101	-0.081568
H	-2.756938	2.843753	1.536009	0.404092
O	-2.127414	3.067756	2.234177	-0.781186
H	-1.737873	0.987548	1.592877	0.435735
H	-2.624058	3.578332	2.883483	0.424171

E(RM062X) = -845.701398996

frequencies -44.4676 36.8206 45.9715 54.4280 62.6474 96.7496 114.5256

S.4.5 NE3 in DMSO

	X [Angs]	Y [Angs]	Z [Angs]	q_Mul [e]
C	2.596399	-2.721758	0.669114	-0.380824
C	1.661076	-2.689607	-0.541379	-0.522530
C	0.607382	-1.590629	-0.390272	0.108237
C	1.250314	-0.211897	-0.183294	-1.712104
C	2.219839	-0.245585	1.008735	0.900649
C	3.262407	-1.360039	0.874801	-0.395673
H	-0.042338	-1.539237	-1.272860	0.167103
H	2.247709	-2.506936	-1.449832	0.161586
H	1.162676	-3.656256	-0.667789	0.171132
H	2.016377	-2.979702	1.566568	0.156719
H	3.355626	-3.501025	0.543354	0.157110

H	2.715084	0.725645	1.104729	0.142547
H	1.629018	-0.403321	1.920686	0.145489
H	3.913481	-1.140816	0.019198	0.176867
H	3.897984	-1.373975	1.766577	0.166329
H	-0.035558	-1.824639	0.467294	0.140910
O	2.055161	0.100539	-1.324648	-0.445587
C	-0.560885	2.971630	0.383340	-0.471777
C	-1.083915	2.045990	1.481569	-0.143144
C	-0.847668	0.631427	0.897145	-1.171603
C	0.677894	2.216528	-0.082050	0.359076
H	-1.285428	3.049603	-0.435119	0.179598
H	-0.333469	3.977949	0.741544	0.186860
H	-2.129354	2.214431	1.750171	0.176258
H	-0.473444	2.167430	2.382981	0.186995
H	-0.530890	-0.040417	1.707269	0.106383
H	1.504869	2.382791	0.625991	0.154082
H	1.020069	2.520809	-1.074904	0.161037
N	0.218790	0.818790	-0.100940	-0.110037
C	-2.114012	0.050067	0.293206	0.535265
C	-2.454632	0.244652	-1.047436	-0.528205
C	-4.189950	-1.146941	0.517747	-0.079864
H	-1.766441	0.779827	-1.697158	0.227459
H	-4.905807	-1.714465	1.102493	0.190561
C	-3.013087	-0.667369	1.083301	0.240047
H	-2.788422	-0.854024	2.131532	0.196813
C	-4.431981	-0.887823	-0.830396	-0.176252
H	-5.341693	-1.246902	-1.305433	0.175153
N	-3.584633	-0.204990	-1.607200	-0.080387
H	3.342628	1.409598	-1.131235	0.471499
O	4.018911	2.099770	-1.001830	-0.764265
H	1.462518	0.192939	-2.085330	0.454608
H	4.858048	1.629745	-0.946703	0.385883

E(RM062X) = -845.706706692
frequencies 25.2711 39.2584 40.9774 45.5895 68.9107 97.0065

S.4.6 NE-ts34 in DMSO

	X [Angs]	Y [Angs]	Z [Angs]	q_Mul [e]
C	-3.944879	-1.493715	-0.147682	-0.504082
C	-2.698632	-1.924297	-0.954384	-0.265427
C	-1.401307	-1.558318	-0.207659	0.351409
C	-1.350237	-0.059804	-0.129233	-1.714742

```
C  -2.627954   0.626006   0.277555   0.343042
C  -3.620917  -0.374792   0.859534  -0.406219
H  -1.438806  -1.941405   0.813379   0.240662
H  -2.708271  -3.001319  -1.139349   0.200828
H  -2.690108  -1.439067  -1.937622   0.193039
H  -4.724306  -1.156154  -0.838720   0.163215
H  -4.353309  -2.352840   0.393642   0.161536
H  -2.396604   1.430141   0.980956   0.171180
H  -3.045974   1.090011  -0.629196   0.209789
H  -3.175191  -0.793438   1.766470   0.228728
H  -4.535908   0.145941   1.154612   0.172194
H  -0.520086  -1.979239  -0.691707   0.179125
O  -0.156535   2.371994   2.231311  -0.927412
C   0.855072   2.472977  -1.502538  -0.371063
C   1.196128   1.244056  -2.346820  -0.324032
C   0.731087   0.064122  -1.474982  -0.834729
C  -0.494175   2.109667  -0.888162   0.121455
H   1.602014   2.623007  -0.717107   0.165252
H   0.797298   3.387799  -2.094023   0.208686
H   2.255070   1.162091  -2.597895   0.200437
H   0.615801   1.251518  -3.274636   0.191484
H   0.405505  -0.767526  -2.104195   0.152898
H  -1.322745   2.381568  -1.551508   0.173951
H  -0.649893   2.539559   0.103326   0.253683
N  -0.449822   0.630401  -0.776645   0.327873
C   1.794651  -0.426956  -0.517420   0.695177
C   2.067201   0.221936   0.691306  -0.838637
C   3.586668  -1.937644   0.010768   0.033506
H   1.462111   1.068500   1.013534   0.268914
H   4.210178  -2.795047  -0.216747   0.189178
C   2.575134  -1.532241  -0.853416  -0.119849
H   2.390170  -2.070955  -1.779913   0.202821
C   3.779288  -1.217768   1.187568  -0.163681
H   4.560127  -1.505939   1.886956   0.182414
N   3.037180  -0.158574   1.530492  -0.009936
H  -0.386158   1.325279   2.216890   0.515692
O  -0.731124  -0.028095   2.091671  -0.828310
H  -0.102832   2.636064   3.155571   0.405727
H   0.058908  -0.571920   2.199899   0.404220

E(RM062X) = -845.662835846
frequencies -210.4355  39.0336  47.6777  57.4457  71.5854  77.9028
```

S.4.7 NE4 in DMSO

	X [Angs]	Y [Angs]	Z [Angs]	q_Mul [e]
C	-3.860318	-0.814259	-1.156255	-0.359729
C	-2.593689	-1.218121	-1.942503	-0.547972
C	-1.286983	-0.988618	-1.149776	0.132551
C	-1.341988	0.247780	-0.321227	-0.156389
C	-2.535164	0.426152	0.563696	-0.193540
C	-3.571166	-0.673544	0.339625	-0.452238
H	-1.168431	-1.775825	-0.390588	0.297228
H	-2.626556	-2.279703	-2.200582	0.182354
H	-2.541782	-0.665294	-2.884383	0.177409
H	-4.233030	0.148984	-1.525059	0.164823
H	-4.655343	-1.544780	-1.327952	0.178675
H	-2.159850	0.449842	1.598541	0.281255
H	-2.969919	1.413974	0.353652	0.199756
H	-3.192540	-1.615131	0.752753	0.203991
H	-4.482958	-0.419923	0.886867	0.179797
H	-0.416681	-1.025608	-1.804381	0.165881
O	-0.479684	0.360400	2.940914	-1.181521
C	0.986162	2.921656	0.389460	-0.321891
C	1.369319	2.517447	-1.035030	-0.346070
C	0.828427	1.083625	-1.155370	-1.060648
C	-0.413979	2.337156	0.559518	0.018594
H	1.670831	2.472382	1.115865	0.181374
H	0.992917	4.002140	0.537879	0.209717
H	2.442535	2.553835	-1.229317	0.204173
H	0.859799	3.157077	-1.762314	0.191577
H	0.543622	0.853351	-2.184412	0.186704
H	-1.188840	3.017400	0.190575	0.198872
H	-0.630894	2.004539	1.579782	0.263928
N	-0.402775	1.137173	-0.319670	0.101323
C	1.791547	0.033157	-0.644200	0.932069
C	1.815209	-0.358605	0.697503	-1.114047
C	3.602705	-1.494872	-1.024357	-0.018375
H	1.107201	0.057492	1.418746	0.323710
H	4.326711	-1.975824	-1.672549	0.188934
C	2.707927	-0.552225	-1.517781	-0.118861
H	2.715762	-0.279276	-2.570499	0.202348
C	3.542243	-1.821405	0.329785	-0.102706
H	4.223024	-2.559129	0.746802	0.185107
N	2.669936	-1.271064	1.179948	0.031304
H	-0.631779	-0.923499	2.388910	0.485192

```
O  -0.766766  -1.868434   1.898943  -0.879803
H  -0.244523   0.285661   3.872549   0.393587
H   0.120698  -2.223132   1.769785   0.391556

E(RM062X) = -845.666502324
frequencies   35.7705  47.9051  60.4945  73.2016  88.5811  96.1957
```

S.4.8 NE-ts45 in DMSO

```
   X  [Angs]  Y  [Angs]  Z  [Angs]  q_Mul [e]
C  -3.787035  -0.204912  -1.416206  -0.332688
C  -2.514801  -0.525717  -2.220906  -0.603168
C  -1.231444  -0.503112  -1.353478   0.245698
C  -1.342181   0.460006  -0.213746  -0.385112
C  -2.474864   0.287582   0.667924  -0.199092
C  -3.593939  -0.557852   0.061613  -0.430717
H  -1.099985  -1.479090  -0.860121   0.265953
H  -2.590450  -1.521648  -2.666275   0.180577
H  -2.400960   0.183911  -3.044925   0.169768
H  -4.009355   0.867159  -1.483526   0.166633
H  -4.641815  -0.737181  -1.844368   0.175411
H  -1.902821  -0.318622   1.586067   0.415625
H  -2.819459   1.227788   1.107394   0.186081
H  -3.355195  -1.626490   0.154851   0.164301
H  -4.516479  -0.393983   0.624858   0.177897
H  -0.346253  -0.337977  -1.967599   0.167160
O  -1.029633  -1.020178   2.499660  -1.045377
C   1.004803   2.737820   1.340329  -0.421919
C   1.425134   2.797243  -0.128951  -0.340506
C   0.864909   1.485024  -0.703129  -1.103955
C  -0.411771   2.170137   1.272317   0.078918
H   1.656317   2.056110   1.896568   0.192917
H   1.030076   3.711855   1.830504   0.204390
H   2.504030   2.872454  -0.275037   0.194918
H   0.943877   3.643106  -0.629390   0.189444
H   0.627595   1.592033  -1.764997   0.196175
H  -1.163754   2.955391   1.137453   0.203911
H  -0.681275   1.551094   2.131999   0.188010
N  -0.389477   1.317053   0.063068   0.059403
C   1.800797   0.308002  -0.513379   0.858682
C   1.631186  -0.630296   0.505898  -1.004694
C   3.729574  -0.944654  -1.207198  -0.016104
H   0.800952  -0.552146   1.210088   0.337890
```

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H   4.574505  -1.110790  -1.866088   0.191155
C   2.879164   0.138992  -1.383913  -0.025302
H   3.043608   0.844472  -2.195118   0.204624
C   3.462897  -1.834954  -0.166575  -0.076315
H   4.097712  -2.702884  -0.007605   0.186808
N   2.437085  -1.688259   0.675441  -0.035490
H  -0.647804  -2.290510   1.662516   0.467630
O  -0.370046  -3.068045   1.068954  -0.844288
H  -1.482102  -1.246650   3.321072   0.400738
H   0.588639  -2.983032   0.979595   0.394009

E(RM062X) = -845.659446369
frequencies -748.8251  28.6130  39.6523  55.2047  60.4485  74.8603
```

S.4.9 NE5 in DMSO

```
   X  [Angs]  Y  [Angs]  Z  [Angs]  q_Mul [e]
C   3.979691   0.348529  -1.508815  -0.326142
C   2.667104   0.035850  -2.267182  -0.629051
C   1.408270   0.256838  -1.406724   0.334801
C   1.572913  -0.372824  -0.042082  -0.508022
C   2.719218  -0.069075   0.623720   0.153448
C   3.718730   0.826364  -0.067618  -0.461497
H   1.250416   1.335646  -1.264328   0.237200
H   2.583997   0.651856  -3.167583   0.176779
H   2.670242  -1.006932  -2.600747   0.163611
H   4.597527  -0.553987  -1.461777   0.164901
H   4.561721   1.104135  -2.046723   0.161046
H   1.405511   1.381995   1.554615   0.458603
H   2.950266  -0.495109   1.595201   0.196138
H   3.353100   1.865131  -0.104939   0.166802
H   4.657441   0.854343   0.492436   0.161813
H   0.526406  -0.114784  -1.931457   0.162541
O   0.828419   2.033240   1.996263  -0.772570
C  -0.686690  -2.408952   2.004979  -0.435538
C  -1.016593  -2.877251   0.586382  -0.379735
C  -0.558105  -1.692086  -0.288853  -1.555559
C   0.658143  -1.708604   1.816362   0.094269
H  -1.436675  -1.689754   2.352035   0.180452
H  -0.635997  -3.227233   2.725439   0.193115
H  -2.070993  -3.118353   0.434559   0.177084
H  -0.418463  -3.758600   0.333699   0.181026
H  -0.225511  -2.058149  -1.267916   0.169743
```

```
H   1.499504  -2.416161   1.887259   0.168821
H   0.829351  -0.909387   2.548958   0.153431
N   0.564738  -1.151262   0.473136  -0.125803
C  -1.670172  -0.679502  -0.512245   0.751344
C  -1.695286   0.546886   0.149211  -0.674815
C  -3.725627  -0.015736  -1.574895  -0.024093
H  -0.895579   0.809876   0.840436   0.313422
H  -4.549517  -0.198523  -2.255707   0.192711
C  -2.716605  -0.954544  -1.396033   0.133494
H  -2.736439  -1.894496  -1.943598   0.203708
C  -3.653711   1.183039  -0.866066  -0.079428
H  -4.417850   1.945899  -0.986305   0.184853
N  -2.659104   1.462935  -0.020145  -0.093240
H  -0.517388   3.228669   1.372470   0.418418
O  -1.288447   3.746022   1.087420  -0.840074
H   1.261141   2.247605   2.831050   0.440459
H  -1.909100   3.086916   0.721682   0.411534

E(RM062X) = -845.691673513
frequencies   24.5268  36.1077  41.6855  53.4125  58.1993  78.9413
```

S.4.10 AN1 in DMSO - EFS path

```
   X  [Angs]  Y  [Angs]  Z  [Angs]  q_Mul [e]
C   0.741658  -0.221755   3.239127  -0.253737
C  -0.043954   1.034200   2.860758  -0.451226
C  -1.235643   0.512440   2.017577  -0.725582
C   0.590150  -1.076048   1.986123  -0.229761
H   1.786172  -0.006667   3.477916   0.212143
H   0.281176  -0.727175   4.094262   0.176925
H   0.583192   1.674108   2.229017   0.210082
H  -0.382021   1.626980   3.713636   0.181202
H  -2.132722   0.423349   2.646284   0.158021
H   0.729667  -2.147342   2.168373   0.167915
H   1.311672  -0.768284   1.211480  -0.185740
N  -0.787187  -0.819286   1.588010  -0.010996
C  -1.549638   1.478683   0.893733  -0.354843
C  -0.812391   1.479318  -0.294068  -0.523999
C  -2.762481   3.358981   0.006490  -0.054168
H  -0.033363   0.733457  -0.452225   0.662322
H  -3.531135   4.119824   0.084250   0.197546
C  -2.548695   2.441235   1.030951  -0.054237
H  -3.156337   2.467999   1.932481   0.198475
```

```
C  -1.965020   3.280889  -1.131480  -0.123800
H  -2.095743   3.981006  -1.952159   0.161568
N  -1.007854   2.357380  -1.283584   0.190625
H   0.398517  -2.472789  -0.081359   0.087414
C  -0.678065  -2.398032  -0.218436   0.082941
C  -1.304404  -3.307187  -1.248416  -0.464425
C  -1.378050  -1.535784   0.553106   0.060951
C  -2.822872  -3.393779  -1.089682  -0.473364
H  -0.860646  -4.307839  -1.178026   0.157480
H  -1.070434  -2.946705  -2.262579   0.143289
C  -2.879320  -1.389673   0.419548  -0.058255
C  -3.403943  -1.997673  -0.880713  -0.343369
H  -3.066187  -4.015232  -0.217246   0.158829
H  -3.268862  -3.875825  -1.965753   0.168406
H  -3.169602  -0.336355   0.476968   0.131853
H  -3.346424  -1.883184   1.283972   0.209173
H  -4.497950  -2.025854  -0.857367   0.159163
H  -3.113841  -1.356498  -1.724568   0.179347
H   0.789065  -0.948885  -3.673458   0.185212
C   1.327652  -1.025332  -2.730038   0.091186
N   1.960651  -0.007189  -2.303844  -0.249795
H   1.287751  -1.977465  -2.192574   0.149216
C   2.682566  -0.088263  -1.084223  -0.267664
C   3.352657  -1.244703  -0.667971  -0.046300
C   2.738319   1.068423  -0.297657  -0.045261
C   4.039258  -1.248471   0.544973   0.021290
H   3.358157  -2.128499  -1.298937   0.190843
C   3.414999   1.053779   0.919483  -0.249729
H   2.235608   1.966838  -0.647213   0.190058
C   4.065606  -0.105423   1.345369  -0.327103
H   4.561970  -2.145845   0.861051   0.192422
H   3.438247   1.949461   1.532675   0.196840
H   4.600406  -0.114752   2.289798   0.188985
O   1.004503   2.530115  -3.340412  -0.815483
H   0.264712   2.515530  -2.699204   0.396685
H   1.493308   1.714436  -3.127594   0.450429

E(RM062X) = -1094.85784648
frequencies    18.4701  23.5777  26.6300  37.3991  44.9982  50.1859
```

S.4.11 AN-ts12 in DMSO - EFS path

	X [Angs]	Y [Angs]	Z [Angs]	q_Mul [e]
C	-0.158604	-0.334125	3.342071	-0.410789
C	1.010936	-1.138997	2.787564	-0.201120
C	1.622640	-0.205560	1.727114	-0.844321
C	-0.735334	0.308189	2.084299	0.238037
H	-0.893942	-0.950294	3.862611	0.217963
H	0.199386	0.439656	4.028913	0.179366
H	0.642581	-2.047046	2.296812	0.185955
H	1.753801	-1.427814	3.533681	0.195704
H	2.341728	0.472355	2.205819	0.144935
H	-1.266487	1.239056	2.291131	0.171357
H	-1.411109	-0.372902	1.554835	0.085871
N	0.459015	0.587448	1.260113	0.115285
C	2.332362	-0.989158	0.647089	-0.038832
C	1.627688	-1.530630	-0.428269	-0.970222
C	4.299051	-2.031331	-0.252812	-0.035811
H	0.563930	-1.313370	-0.540603	0.664073
H	5.360224	-2.252007	-0.224678	0.194419
C	3.698851	-1.247664	0.729442	0.287506
H	4.287325	-0.835578	1.546001	0.199376
C	3.509101	-2.521684	-1.289334	-0.123535
H	3.944257	-3.129390	-2.078015	0.176391
N	2.196916	-2.275750	-1.381910	0.115352
H	-1.520338	2.087286	0.501743	0.142641
C	-0.601951	2.294353	-0.039935	-0.843761
C	-0.499768	3.700314	-0.613335	-0.338947
C	0.546021	1.632914	0.425789	0.197353
C	0.914005	4.273652	-0.521480	-0.440930
H	-1.209032	4.351323	-0.092138	0.174314
H	-0.806761	3.699073	-1.671159	0.146323
C	1.913723	2.009785	-0.089818	0.046011
C	1.905921	3.228142	-1.017028	-0.546615
H	1.147488	4.534574	0.519147	0.167258
H	0.986292	5.191216	-1.113068	0.178041
H	2.359207	1.151070	-0.603341	0.218971
H	2.553554	2.207381	0.781274	0.204301
H	2.920489	3.632028	-1.075670	0.174300
H	1.626458	2.923464	-2.033332	0.164594
H	-0.167254	1.338531	-2.215527	0.188320
C	-1.059293	1.134470	-1.619549	-0.034949
N	-1.284327	-0.150630	-1.352010	-0.470891

```
H  -1.887162   1.816984  -1.844527   0.196843
C  -2.486028  -0.522768  -0.763903  -0.144933
C  -3.506109   0.358709  -0.342969  -0.052008
C  -2.681441  -1.901014  -0.522261   0.043931
C  -4.658820  -0.125410   0.276309  -0.139827
H  -3.409248   1.429076  -0.495116   0.120321
C  -3.832016  -2.375002   0.094617  -0.279420
H  -1.897476  -2.587376  -0.833566   0.175795
C  -4.835910  -1.489803   0.501974  -0.327532
H  -5.425003   0.578599   0.590221   0.173028
H  -3.948110  -3.442235   0.262672   0.168543
H  -5.734203  -1.857575   0.987246   0.162854
O  -0.108330  -1.951006  -3.158330  -0.808390
H   0.725558  -2.230161  -2.742845   0.429788
H  -0.520902  -1.329645  -2.508684   0.407709

E(RM062X) = -1094.84000817
frequencies  -389.4486  15.3121  39.5817  42.6264  46.0555  56.1370
```

S.4.12 AN2 in DMSO - EFS path

```
   X  [Angs]  Y  [Angs]  Z  [Angs]  q_Mul [e]
C  -0.142780  -0.266540   3.404122  -0.364399
C   1.064080  -1.032635   2.875410  -0.357322
C   1.608369  -0.137396   1.747922  -0.677812
C  -0.777288   0.263055   2.126107   0.165499
H  -0.835475  -0.895646   3.964587   0.229268
H   0.170923   0.565925   4.041385   0.188231
H   0.746349  -1.991992   2.453705   0.187066
H   1.835837  -1.222347   3.622933   0.207798
H   2.310651   0.595572   2.160044   0.195472
H  -1.407162   1.135799   2.284578   0.197167
H  -1.348641  -0.508116   1.597175   0.098221
N   0.399730   0.624730   1.288474   0.226426
C   2.274488  -0.935891   0.654798   0.024896
C   1.526685  -1.523665  -0.366697  -0.701086
C   4.215242  -1.964154  -0.308097   0.028017
H   0.455749  -1.326474  -0.445521   0.677854
H   5.280656  -2.163498  -0.325654   0.196387
C   3.648942  -1.161256   0.677573  -0.083454
H   4.268130  -0.712091   1.450336   0.202086
C   3.384208  -2.500163  -1.288897  -0.170183
H   3.793430  -3.122730  -2.079889   0.177024
```

```
N   2.064558  -2.282759  -1.326568   0.118928
H  -1.669154   1.941063   0.552205   0.087113
C  -0.848483   2.169383  -0.124508  -0.674353
C  -0.701864   3.703389  -0.284134  -0.411346
C   0.404691   1.518108   0.346774   0.202325
C   0.748342   4.186754  -0.201384  -0.387399
H  -1.309717   4.206106   0.472581   0.185251
H  -1.115019   3.981174  -1.261980   0.167049
C   1.677308   1.856930  -0.376326   0.270088
C   1.647950   3.258233  -1.011399  -0.654059
H   1.085543   4.195944   0.843992   0.174277
H   0.818230   5.213904  -0.569629   0.190093
H   1.822327   1.082263  -1.142685   0.292051
H   2.521598   1.768036   0.313908   0.174781
H   2.671687   3.636867  -1.059683   0.196882
H   1.280309   3.204093  -2.041613   0.152375
H  -0.458198   1.796033  -2.235222   0.163949
C  -1.213380   1.478320  -1.503747  -0.499837
N  -1.253915   0.053699  -1.466694  -0.591803
H  -2.160559   1.962446  -1.804876   0.176429
C  -2.301670  -0.540511  -0.847143  -0.017461
C  -3.427386   0.118772  -0.265484  -0.007554
C  -2.298755  -1.966802  -0.732433  -0.011564
C  -4.435407  -0.594363   0.382669  -0.112792
H  -3.516593   1.199418  -0.323598   0.127910
C  -3.307927  -2.657846  -0.081649  -0.310598
H  -1.466866  -2.507823  -1.179970   0.153462
C  -4.395908  -1.984507   0.495310  -0.344810
H  -5.270111  -0.043778   0.812014   0.156740
H  -3.250216  -3.742469  -0.020502   0.155587
H  -5.182853  -2.527465   1.008127   0.154193
O   0.122366  -1.215358  -3.366726  -0.798643
H   0.785572  -1.744595  -2.899012   0.413512
H  -0.404718  -0.745722  -2.633148   0.462065

E(RM062X) = -1094.85011024
frequencies    14.6368  40.1152  47.3087  54.7893  61.4911  78.5661
```

S.4.13 AN3 in DMSO - EFS path

	X [Angs]	Y [Angs]	Z [Angs]	q_Mul [e]
C	0.155429	0.082944	3.562146	-0.405773
C	1.040999	-1.018580	2.988634	-0.295953
C	1.597983	-0.421277	1.682812	-0.994727
C	-0.508802	0.656706	2.318255	0.133592
H	-0.580692	-0.290709	4.274869	0.224411
H	0.757562	0.855078	4.050337	0.187934
H	0.438948	-1.903096	2.758635	0.170088
H	1.853737	-1.321956	3.650023	0.214381
H	2.540277	0.100257	1.879498	0.171334
H	-0.871860	1.672710	2.454221	0.188270
H	-1.325970	0.022602	1.954154	0.141276
N	0.587728	0.627678	1.313069	0.390257
C	1.797063	-1.461304	0.606523	0.808518
C	0.699216	-2.080396	0.004807	-1.015181
C	3.192850	-2.918078	-0.689303	0.165383
H	-0.314457	-1.756523	0.243586	0.308670
H	4.165912	-3.280169	-1.001410	0.205723
C	3.070108	-1.891325	0.242743	-0.184840
H	3.953254	-1.431463	0.679768	0.193949
C	2.032100	-3.477270	-1.218329	-0.204006
H	2.091872	-4.285086	-1.943084	0.172932
N	0.801180	-3.069138	-0.884982	0.138535
H	-1.153692	2.400310	0.672709	0.117240
C	-0.353639	2.413467	-0.065084	-0.255072
C	0.222708	3.847162	-0.199029	-0.420487
C	0.711405	1.427962	0.300472	-0.192874
C	1.747610	3.868446	-0.363907	-0.388315
H	-0.067355	4.440869	0.671353	0.182973
H	-0.248526	4.311351	-1.073937	0.175460
C	1.902011	1.361376	-0.599891	0.159999
C	2.215120	2.720701	-1.257928	-0.525626
H	2.227575	3.766339	0.618768	0.173124
H	2.060879	4.833323	-0.771775	0.187914
H	1.659203	0.594757	-1.365218	0.367127
H	2.771792	1.008413	-0.040959	0.137523
H	3.292869	2.778379	-1.428755	0.202039
H	1.739568	2.794431	-2.241530	0.144849
H	-0.253588	2.173254	-2.222280	0.156552
C	-0.961250	1.927632	-1.426250	-0.743899
N	-1.220467	0.523639	-1.511715	-0.356787

```
H  -1.858591   2.541839  -1.594604   0.197243
C  -2.286517  -0.061047  -0.896191  -0.165795
C  -3.232407   0.643129  -0.111895   0.131073
C  -2.480591  -1.461250  -1.037168  -0.138318
C  -4.296138  -0.022615   0.497385  -0.074428
H  -3.140266   1.716169   0.024049   0.131608
C  -3.542628  -2.106579  -0.421180  -0.158820
H  -1.770483  -2.023139  -1.640677   0.175083
C  -4.466740  -1.399012   0.358923  -0.344597
H  -5.000063   0.553166   1.093070   0.168350
H  -3.654522  -3.180049  -0.552070   0.170712
H  -5.293985  -1.908915   0.841076   0.158442
O   0.616619  -0.509343  -2.910914  -0.970058
H   0.789822  -1.419631  -2.643666   0.385521
H  -0.456603  -0.047778  -2.132719   0.497470

E(RM062X) = -1094.84327687
frequencies    18.1569  30.1087  39.7554  56.2751  64.4291  70.2714
```

S.4.14 AN-ts34 in DMSO - EFS path

```
   X  [Angs]  Y  [Angs]  Z  [Angs]  q_Mul [e]
C  -0.313857  -0.856064   2.897973  -0.301561
C   1.047432  -1.472180   2.578941  -0.307003
C   1.662747  -0.526416   1.523755  -0.098464
C  -0.749595  -0.347340   1.532463   0.133103
H  -1.020745  -1.578945   3.308069   0.221052
H  -0.216850  -0.019786   3.597185   0.182799
H   0.912679  -2.469193   2.149088   0.171134
H   1.705263  -1.562681   3.444518   0.210390
H   2.341706   0.177699   2.011381   0.131935
H  -1.565943   0.370320   1.551318   0.158838
H  -1.045819  -1.178287   0.883571   0.075905
N   0.494768   0.256880   1.009305   0.454418
C   2.413567  -1.262741   0.437954  -0.488554
C   1.741924  -2.109486  -0.450231  -0.710942
C   4.445852  -1.907301  -0.666085  -0.056429
H   0.657967  -2.202116  -0.399315   0.364840
H   5.521667  -1.855801  -0.790319   0.202770
C   3.796527  -1.165864   0.319017   0.628754
H   4.360156  -0.515729   0.984190   0.222121
C   3.679722  -2.717639  -1.498173  -0.083158
H   4.152017  -3.308462  -2.278498   0.180960
```

```
N   2.346961  -2.822772  -1.399525   0.035031
H  -1.250125   2.104509   0.917489   0.170558
C  -0.617322   2.202159   0.029133  -0.433285
C  -0.362781   3.717028  -0.189086  -0.438500
C   0.618353   1.365012   0.319892  -1.035198
C   1.021742   4.218327   0.205192  -0.388029
H  -1.144869   4.271069   0.338244   0.185509
H  -0.493191   3.934171  -1.256616   0.151385
C   2.007430   1.943184   0.199431   0.638638
C   2.064728   3.319066  -0.447463  -0.598465
H   1.151652   4.203644   1.295686   0.160880
H   1.134524   5.257160  -0.119125   0.180525
H   2.652540   1.228834  -0.312524   0.141870
H   2.384296   2.044802   1.228713   0.206172
H   3.075160   3.718472  -0.321525   0.179953
H   1.868865   3.238890  -1.522545   0.175686
H  -0.859099   1.987785  -2.082186   0.202484
C  -1.439293   1.712584  -1.201336  -0.683625
N  -1.703313   0.308029  -1.297119  -0.375841
H  -2.371721   2.287067  -1.210321   0.175296
C  -2.813867  -0.340365  -0.830880  -0.220141
C  -3.848019   0.316353  -0.131602  -0.035183
C  -2.935147  -1.734561  -1.030580   0.113481
C  -4.956289  -0.395815   0.325333  -0.117055
H  -3.784002   1.381554   0.066982   0.126347
C  -4.042320  -2.429465  -0.562262  -0.161768
H  -2.145900  -2.257484  -1.565552   0.165942
C  -5.071179  -1.769725   0.118449  -0.410133
H  -5.737748   0.138367   0.858901   0.177046
H  -4.104410  -3.500551  -0.734193   0.176069
H  -5.936180  -2.315465   0.479832   0.152189
O   0.861879   0.487795  -2.002287  -0.800481
H   1.665177  -0.041307  -1.932954   0.394653
H  -0.873133  -0.188353  -1.638821   0.495082

E(RM062X) = -1094.82978601
frequencies  -134.4059  19.3854  37.6695  41.8606  54.9115  66.9387
```

S.4.15 AN-ts24 in DMSO - ZFR path

M06-2X/6-31G(d) optimized geometry

	X [Angs]	Y [Angs]	Z [Angs]	q_Mul [e]
C	-2.013355	3.149711	0.991121	-0.351349
C	-1.805135	3.133801	-0.523906	-0.321247
C	-1.137359	1.767160	-0.761039	-0.089239
C	-2.500886	1.730882	1.277846	-0.171393
H	-1.065243	3.338845	1.503526	0.188351
H	-2.736086	3.899748	1.314627	0.203247
H	-1.183809	3.951839	-0.892627	0.199291
H	-2.769218	3.162506	-1.041391	0.194694
H	-1.348692	1.392949	-1.766353	0.217384
H	-3.587880	1.656007	1.181420	0.210461
H	-2.175619	1.306908	2.232357	0.220640
N	-1.858304	0.916023	0.220934	-0.434981
C	0.356327	1.827451	-0.532651	0.081324
C	0.949798	1.401342	0.654593	-0.005375
C	2.534258	2.516463	-1.260016	-0.190268
H	0.351113	0.878119	1.400574	0.167625
H	3.207246	2.938651	-1.998126	0.194537
C	1.176199	2.391023	-1.512512	-0.168462
H	0.753111	2.725629	-2.457100	0.198503
C	3.018562	2.095122	-0.021072	0.025690
H	4.074988	2.198191	0.216849	0.178153
N	2.251535	1.553284	0.923457	-0.454402
H	-0.402828	-0.547044	-1.299282	0.179142
C	-1.184722	-1.164022	-0.847684	-0.221150
C	-2.261148	-1.511463	-1.911372	-0.314463
C	-1.903556	-0.382919	0.218956	0.476629
C	-3.474092	-2.224360	-1.302433	-0.314920
H	-1.792443	-2.128941	-2.685060	0.186193
H	-2.596480	-0.586862	-2.398814	0.173752
C	-2.999040	-1.108587	0.933650	-0.345505
C	-4.067781	-1.425409	-0.139246	-0.324043
H	-3.188586	-3.222630	-0.951669	0.172442
H	-4.232315	-2.371016	-2.078023	0.179375
H	-3.409952	-0.521041	1.751616	0.199816
H	-2.598724	-2.024785	1.368350	0.205586
H	-4.886358	-1.976902	0.332110	0.187941
H	-4.487755	-0.483469	-0.516376	0.167561
C	2.218859	-1.653253	-0.994553	-0.226294
C	1.779589	-1.833001	0.332211	0.304336

```
C   2.726358  -1.631791   1.360865  -0.210625
C   4.034532  -1.275602   1.078333  -0.177829
C   4.461339  -1.106359  -0.241465  -0.200875
C   3.539073  -1.297423  -1.266143  -0.190037
H   1.528976  -1.783013  -1.823060   0.151356
H   2.401212  -1.768150   2.389652   0.148811
H   4.733768  -1.129213   1.897784   0.159426
H   5.487371  -0.829952  -0.462540   0.154643
H   3.843869  -1.163974  -2.301237   0.160002
N   0.506640  -2.228320   0.696150  -0.716184
C  -0.507052  -2.444223  -0.301902  -0.174842
H  -0.097813  -2.984367  -1.164547   0.171847
H  -1.268264  -3.101285   0.130575   0.169861
O  -0.804375  -0.786448   2.426496  -0.941472
H   0.072879  -1.686644   1.538625   0.374578
H  -0.135185  -0.262677   2.892895   0.341756

E(RM062X) = -1094.76140562
frequencies  -78.5759  23.6230  41.5079  61.3054  64.0677  76.6106


M06-2X/6-31G++(d,p) single point energy calculation

E(RM062X) = -1094.84248860
frequencies  -16.6249  35.0818  44.2772  46.6685  58.9007  76.0659
```

S.4.16 AN4 in DMSO - EFS path

```
   X  [Angs]  Y  [Angs]  Z  [Angs]  q_Mul [e]
C   0.635972  -0.253065   3.112339  -0.498274
C   1.925479  -0.810010   2.515704  -0.203081
C   2.047779  -0.029936   1.194714  -0.973207
C  -0.254587  -0.170111   1.872378   0.414869
H   0.211819  -0.882081   3.898649   0.196602
H   0.809474   0.748716   3.523174   0.174488
H   1.809474  -1.879837   2.303635   0.163589
H   2.810271  -0.680356   3.143587   0.196356
H   2.536603   0.931900   1.420442  -0.007242
H  -1.062797   0.557862   1.977673   0.159195
H  -0.728079  -1.144555   1.686700   0.110073
N   0.652827   0.167481   0.751151   0.126518
C   2.901757  -0.748253   0.173822   0.774288
C   2.432209  -1.896439  -0.471153  -0.798417
```

C	4.950356	-1.059708	-1.046890	0.167216
H	1.427017	-2.255370	-0.256863	0.319758
H	5.959467	-0.760357	-1.308517	0.192430
C	4.195915	-0.332781	-0.127874	0.182728
H	4.608537	0.555748	0.345468	0.191773
C	4.379342	-2.185395	-1.632756	-0.171626
H	4.937785	-2.774868	-2.355374	0.174754
N	3.138750	-2.607089	-1.352529	-0.005015
H	-1.743811	1.241852	0.060790	0.095870
C	-0.950682	1.393469	-0.684394	0.171077
C	-1.229832	2.721482	-1.398903	-0.014285
C	0.397420	1.454672	0.068118	-2.558111
C	-1.201802	3.909761	-0.437904	-0.377387
H	-2.207834	2.656865	-1.891184	0.153167
H	-0.480865	2.865723	-2.188357	0.181099
C	0.427673	2.666738	1.020592	0.421038
C	0.135467	3.984099	0.297641	-0.523753
H	-2.011131	3.796447	0.297245	0.165871
H	-1.390964	4.841721	-0.981124	0.163401
H	1.403144	2.714816	1.521166	0.170746
H	-0.322406	2.516688	1.806411	0.162058
H	0.130945	4.805115	1.022277	0.161644
H	0.935679	4.197997	-0.421856	0.144617
H	0.004766	0.095231	-2.123134	0.173769
C	-0.985539	0.217108	-1.676062	0.118817
N	-1.366099	-1.066969	-1.108248	-0.328739
H	-1.671781	0.449812	-2.498208	0.174052
C	-2.648811	-1.279568	-0.618897	-0.147245
C	-3.731970	-0.443123	-0.943228	-0.283118
C	-2.898743	-2.402769	0.195422	0.253927
C	-5.015251	-0.737953	-0.481245	-0.178710
H	-3.579680	0.441631	-1.552486	0.116605
C	-4.179608	-2.681357	0.653810	-0.292972
H	-2.071891	-3.060730	0.453441	0.161737
C	-5.255479	-1.853240	0.317594	-0.323113
H	-5.834040	-0.076112	-0.749119	0.176206
H	-4.340683	-3.555634	1.278237	0.167993
H	-6.255649	-2.073311	0.675448	0.152932
O	1.391429	1.614360	-0.933530	-0.347887
H	2.179620	2.020905	-0.551520	0.469719
H	-0.635163	-1.446385	-0.517933	0.531201

```
E(RM062X) = -1094.89193079
frequencies    15.5880  35.7980  39.7191  47.0590  52.3791  68.1000
```

S.5 Alcohols as solvent

S.5.1 ZBS - Aminol formation

```
DMSO data
Cartesian coordinates (standard orientation)
C      1.045701     1.221709     3.327484
C     -0.216925     1.654985     2.591392
C     -0.123112     0.931053     1.235686
C      2.092367     1.222101     2.220730
H      1.314597     1.891148     4.146225
H      0.935165     0.206277     3.719487
H     -0.206022     2.737747     2.426465
H     -1.144913     1.395575     3.104999
H     -0.576976    -0.062520     1.310816
H      2.910457     0.535213     2.421413
H      2.480551     2.227557     2.020799
N      1.341726     0.746678     1.036850
C     -0.806271     1.714084     0.140696
C     -0.161966     2.735658    -0.560826
C     -2.775184     2.227363    -1.128441
H      0.885774     2.958274    -0.360173
H     -3.813555     2.055496    -1.391086
C     -2.144932     1.461340    -0.153388
H     -2.677013     0.663952     0.362244
C     -2.038631     3.216962    -1.776776
H     -2.498060     3.828737    -2.548808
N     -0.753429     3.473713    -1.504497
H      0.112293    -0.020388    -1.079451
C      1.098145    -0.489686    -1.079709
C      1.850333    -0.036757    -2.345294
C      1.893476     0.010528     0.109910
C      3.225424    -0.711991    -2.480246
H      1.966619     1.053541    -2.314639
H      1.225646    -0.257899    -3.216644
C      3.392767     0.035057    -0.042560
C      3.900491    -0.930579    -1.110070
H      3.860859    -0.091192    -3.118651
H      3.119305    -1.675347    -2.989307
H      3.863697    -0.184770     0.914125
H      3.656779     1.070649    -0.309665
```

```
H      4.983947    -0.814782    -1.196963
H      3.727272    -1.949635    -0.751473
H      1.777376    -2.564662    -1.011246
C      0.838964    -2.016016    -1.097309
N     -0.017353    -2.458124    -0.021754
H      0.410264    -2.261031    -2.075210
C     -1.363377    -2.152035    -0.002138
C     -2.103955    -1.827512    -1.157953
C     -2.056969    -2.195158     1.228624
C     -3.475201    -1.586586    -1.079533
H     -1.613949    -1.762963    -2.123989
C     -3.421713    -1.942601     1.293874
H     -1.500938    -2.436778     2.131812
C     -4.150769    -1.639251     0.138689
H     -4.016761    -1.340762    -1.989042
H     -3.922049    -1.983582     2.257477
H     -5.216561    -1.443992     0.191101
O      1.975326    -1.831592     1.614588
H      2.629074    -2.530210     1.480060
H      0.535928    -2.342776     0.861368

SCF energy       : -1094.84298427
Gibbs free energy: -1094.414184

Frequencies
-154.4011    34.9212    42.9970    51.5635    62.9796    67.5284    75.6114
  84.1267   103.0055   119.8406   135.7593   154.0087   180.0439   184.6341


water data

SCF energy       : -1094.84338404
Gibbs free energy: -1094.414528

Frequencies
-153.2751    34.7580    43.7776    51.5834    63.2069    67.5436    75.9962
  84.4239   102.9200   121.3193   135.9675   154.2870   180.1724   184.7017


methanol data

SCF energy       : -1094.84256122
Gibbs free energy: -1094.413816
```

```
Frequencies
-155.6031    35.0188    42.2206    51.5274    62.7011    67.5204    75.2413
  83.9104   103.0059   118.5080   135.5385   153.7472   179.9351   184.5752


ethanol data

SCF energy       : -1094.84213623
Gibbs free energy: -1094.413442

Frequencies
-156.8527    35.0712    41.4498    51.5016    62.3571    67.5141    74.8903
  83.7367   103.1425   117.3988   135.3375   153.5222   179.8143   184.5000


n-propanol data

SCF energy       : -1094.84176796
Gibbs free energy: -1094.413115

Frequencies
-157.8986    35.0387    40.8646    51.4592    62.0647    67.5079    74.6237
  83.6264   103.2083   116.5964   135.1739   153.3517   179.7201   184.4441
```

S.5.2 EBR - Aminol formation

```
Cartesian coordinates (standard orientation)
C     -0.379571    -2.615150     0.364715
C      1.134539    -2.722290     0.533328
C      1.593748    -1.257426     0.667788
C     -0.517329    -1.396734    -0.538423
H     -0.826436    -3.506233    -0.079980
H     -0.866388    -2.413019     1.324235
H      1.581092    -3.166978    -0.362767
H      1.446577    -3.309584     1.398720
H      1.551455    -0.943271     1.716978
H     -1.499541    -0.936310    -0.484562
H     -0.285461    -1.645592    -1.581078
N      0.528484    -0.484129    -0.024150
C      2.972911    -1.029366     0.097146
C      3.173188    -0.859333    -1.275107
```

C	5.355566	-0.883502	0.346755
H	2.317291	-0.835212	-1.948959
H	6.253402	-0.883490	0.954622
C	4.096969	-1.038917	0.920168
H	3.986665	-1.159802	1.995184
C	5.441960	-0.716380	-1.033519
H	6.408762	-0.586982	-1.512564
N	4.373234	-0.701082	-1.839305
H	-1.082651	0.885700	-1.400271
C	-0.682196	1.557476	-0.634396
C	0.010947	2.736034	-1.346444
C	0.393107	0.807119	0.136733
C	0.606456	3.754656	-0.358520
H	-0.717245	3.219843	-2.005229
H	0.799004	2.338277	-1.996324
C	1.555809	1.621223	0.641807
C	1.166225	3.072604	0.907083
H	-0.152516	4.489250	-0.071292
H	1.400087	4.310070	-0.867226
H	2.331913	1.586816	-0.137737
H	1.972933	1.154224	1.534965
H	0.427755	3.085713	1.714197
H	2.042646	3.612759	1.274154
C	-3.940239	0.347563	-1.020322
C	-3.438512	0.159168	0.282789
C	-3.818238	-1.015889	0.970328
C	-4.655771	-1.952924	0.381440
C	-5.153675	-1.756483	-0.911631
C	-4.787435	-0.599920	-1.597490
H	-3.665784	1.228132	-1.592180
H	-3.431970	-1.176651	1.974084
H	-4.923072	-2.847884	0.936581
H	-5.809112	-2.489360	-1.370096
H	-5.158550	-0.427382	-2.604160
N	-2.605370	1.053218	0.924018
C	-1.877432	2.072985	0.207591
H	-2.533949	2.629153	-0.471079
H	-1.514065	2.787049	0.949357
O	-0.425535	0.537633	2.283778
H	-1.941565	0.667039	1.645333
H	-0.287605	1.249528	2.922016

```
SCF energy       : -1094.84126088
Gibbs free energy: -1094.413621

Frequencies
-215.4836    24.3924    32.2234    38.9939    45.2953    61.7845    70.4057
  78.9617   114.1904   123.5633   158.5068   172.3708   182.6530   191.7503


water data

SCF energy       : -1094.84163873
Gibbs free energy: -1094.413971

Frequencies
-214.5633    25.4576    32.2782    39.0153    45.2659    61.7566    70.7953
  79.1939   113.4630   123.3925   158.3644   172.3756   182.6391   191.7035


methanol data

SCF energy       : -1094.84086032
Gibbs free energy: -1094.413246

Frequencies
-216.2707    23.3748    32.1925    38.9772    45.3389    61.8165    70.0124
  78.7680   114.9479   123.7586   158.6545   172.3804   182.6709   191.8041


ethanol data

SCF energy       : -1094.84045721
Gibbs free energy: -1094.412861

Frequencies
-217.1154    22.4884    32.1779    38.9818    45.3979    61.8583    69.7546
  78.6156   115.6290   123.9610   158.7936   172.4064   182.6578   191.8520


n-propanol data

SCF energy       : -1094.84010733
Gibbs free energy: -1094.412564
```

```
Frequencies
-220.7393    21.8308    32.0951    38.9969    45.9204    61.8782    67.2331
  78.3625   115.9116   124.1616   159.1979   172.3108   182.4507   192.3447
```

S.6 MD data for the transition NE2 to NE3

Ab initio molecular dynamics

- RHF/3-21G, PCM model for DMSO
- Berendsen thermostat, 375 °C, 300 fs coupling constant
- Step size 1 fs; 14.5 ps simulation; 2.5 ps initial equilibration
- The N atoms hardly attract the H_2O molecule.
- The H_2O molecule can escape from aminol.
- The H_2O molecule partially detaches and moves to the over side.
- water_flip_very_short.mov shows the movement of the H_2O molecule.