Torquoselective Ring-Opening of Fused Cyclobutenamides: Evidence for a *Cis,Trans*-Cyclooctadienone Intermediate

Xiao-Na Wang,[†] Elizabeth H. Krenske,*[,‡] Ryne C. Johnston,[‡,§]
K. N. Houk,*[,¶] and Richard P. Hsung*[,†]

[†]Division of Pharmaceutical Sciences and Department of Chemistry, University of Wisconsin, Madison, WI 53705

[‡]School of Chemistry and Molecular Biosciences, The University of Queensland, Brisbane, QLD 4072, Australia

[¶]Department of Chemistry and Biochemistry, University of California, Los Angeles, CA 90095

Supporting Information Part 3

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Theoretical Investigations of the Roles of Protonation and Hydrogen Bonding in the Rearrangements of 4,6- and 4,5-Fused Cyclobutenamides

4,6-Fused Cyclobutenamides

The computed barrier for the Nazarov cyclization of *cis,trans*-cyclooctadienone **2**-*E,E* is prohibitively high (**TS7**, $\Delta G^{\ddagger} = 47.5$ kcal/mol, see Figure 2 of the paper). We propose that the cyclization is accelerated by protonation of the carbonyl oxygen, and that the source of the proton is an adventitious water molecule. Experimental evidence supporting the notion of H$^+$ catalysis is found in the observations that the thermal rearrangement of cyclobutenamide **1** to 5,5-bicyclic product **3** is inhibited by either base or 4 Å molecular sieves (Table 1, entries 4 and 5).

We explored the possibility that the barrier for the Nazarov cyclization step could be lowered by hydrogen bonding between the carbonyl oxygen of **2**-*E,E* and a water molecule. The energy profile for such a process is shown in Figure S1. Hydrogen bonding to the carbonyl oxygen in the TS for Nazarov cyclization ([H$_2$O]**TS7**) is predicted not to be sufficiently stabilizing to allow the Nazarov cyclization to proceed at an experimentally significant rate. The barrier is lowered by only 5.8 kcal/mol compared to the thermal reaction. Additionally, complexation to a single water molecule is disfavored by over 7 kcal/mol (Figure S2).
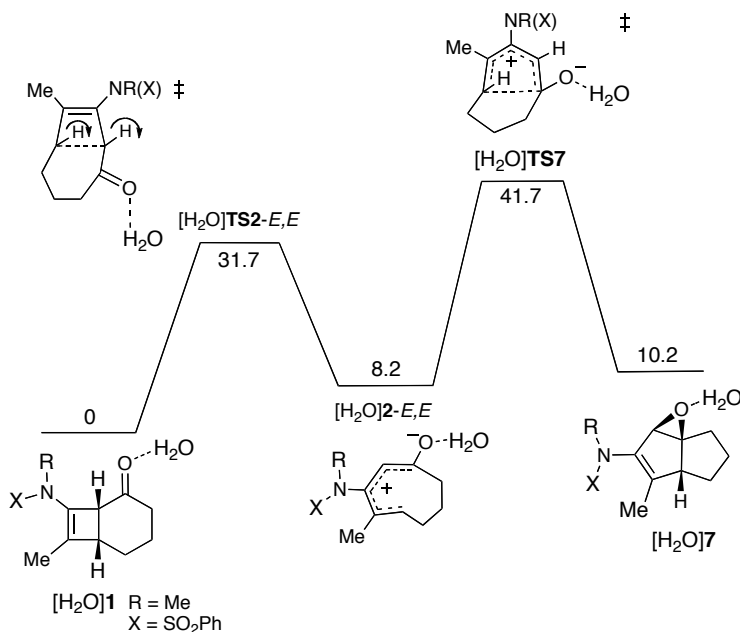

Figure S1. Free energy profile for rearrangement of 4,6-fused cyclobutenamide **1** as a hydrogen-bonded complex with a water molecule. ΔG in kcal/mol.
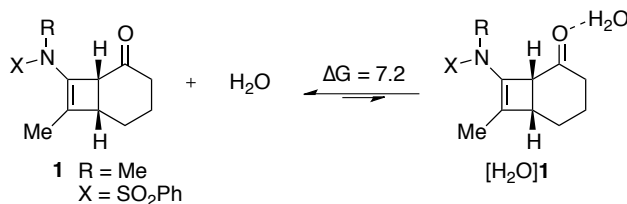

Figure S2. Equilibrium for water complexation to **1**.

In light of these results, protonation appears to be the only feasible possibility for accelerating the Nazarov cyclization. Figure S3 shows the free energy profile for rearrangement of protonated cyclobutenamide [H$^+$]**1**, displaying not only the Nazarov cyclization step (reproduced from Figure 2 of the paper) but also the preceding ring-opening of cyclobutenamide **1** and the subsequent reactions of the 5,5-bicyclic species [H$^+$]**7**. The barrier for ring-opening of cyclobutenamide **1** is decreased by 11 kcal/mol upon protonation of the carbonyl oxygen ($\Delta G^{\ddagger}$ = 21.3 kcal/mol, cf. 32.3 kcal/mol for the uncatalyzed reaction). Therefore, H$^+$ catalysis of the ring-opening of **1** cannot be ruled out. However, catalysis of this step is not an absolute requirement, as the uncatalyzed barrier is low enough to be compatible with the reaction temperature (100–120 °C).
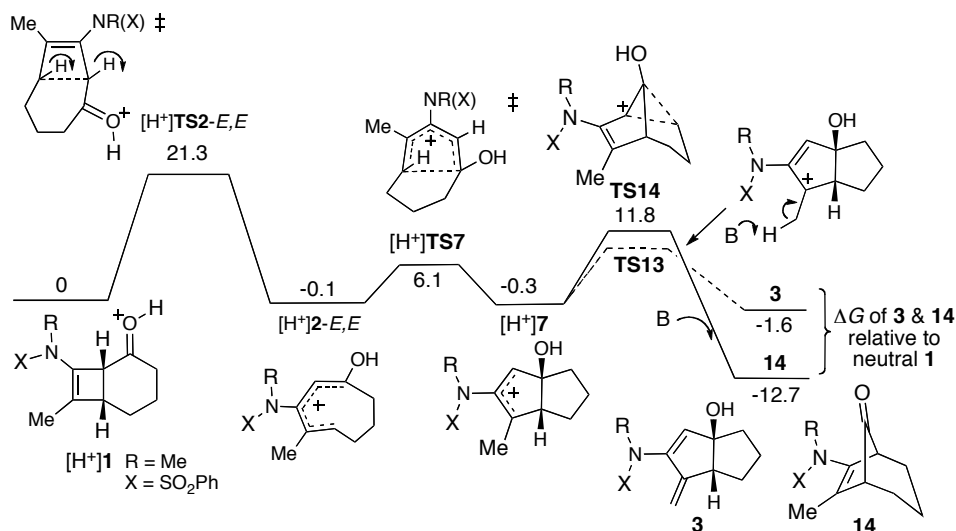
Figure S3. Free energy profile for H$^+$-catalyzed rearrangements of cyclobutenamide **1**.

Protonation of the carbonyl oxygen need not occur solely at the level of the intermediate cyclooctadienone. The starting cyclobutenamide may also be protonated. However, calculations (Figure S4) indicate that the carbonyl oxygen is not the most basic site of cyclobutenamide **1**; the enamide β-carbon is significantly more basic than oxygen. Moreover, *C*-protonation, if it occurred, would be expected to allow entry into the alternative rearrangement pathway that furnishes Ficini-type amido-dienes (see below). Experimentally, Ficini-type amido-dienes are not obtained during the thermal rearrangements of 4,6-fused cyclobutenamides **1**.

Figure S4. Relative energies of isomeric protonated cyclobutenamides.

The 5,5-bicyclic intermediate [H$^+$]**7** resulting from the Nazarov cyclization of [H$^+$]**2**-*E,E* (Figure S3) has two possible fates: (i)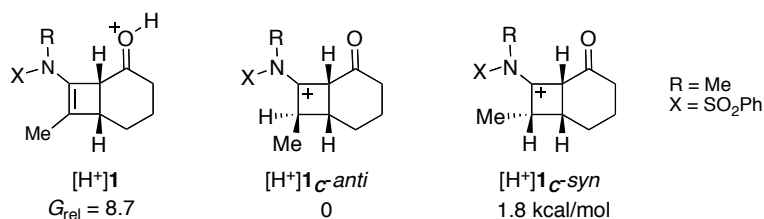 it may undergo deprotonation (**TS13**) to give the observed 5,5-bicyclic product **3**, or (ii) it may undergo a 1,2-alkyl shift (**TS14**) to afford a bicyclic ketone (**14**). The 1,2-alkyl shift is computed to be relatively facile ($\Delta G^{\ddagger}$ = 11.8 kcal/mol) and thermodynamically much more favorable (ΔG = −12.7 kcal/mol relative to **1**) than deprotonation leading to **3** (ΔG = −1.6 kcal/mol). However, we find no experimental evidence for the formation of **14**. Therefore, deprotonation of [H$^+$]**7** must be rapid, with $\Delta G^{\ddagger}$ << 11.8 kcal/mol, to explain the observed formation of **3**.

Rapid deprotonation of [H$^+$]**7** is likely to require a strong base to be present in the immediate vicinity of the cation after it has formed. We propose that this base is OH$^-$, which is derived from a water molecule that is the source of the proton that activates **2**-*E,E*. Thus, the mechanism of the Nazarov cyclization is proposed to consist of the following steps: (i) an adventitious water molecule donates a proton to the carbonyl oxygen of **2**-*E,E* (or to cyclobutenone **1** which undergoes ring-opening); (ii) Nazarov cyclization furnishes the ion pair of [H$^+$]**7** and OH$^-$; and (iii) OH$^-$ then rapidly deprotonates [H$^+$]**7** to give **3** (either directly, or by initial *O*-deprotonation followed by tautomerization) and regenerate the catalyst.

C-Protonation of cyclobutenamides **1** is a plausible first step in a Ficini-type rearrangement leading to amido-dienes **16** (Figure S5). The calculated barrier for ring-opening of the isomerized cyclobutenamide **15**-*anti* (28.8 kcal/mol), leading to amido-diene **16**-*cis*, is 4 kcal/mol lower than the barrier for ring-opening of cyclobutenamide **1** to *cis,trans*-cyclooctadienone **2**-*E,E* (**TS7**, 32.3 kcal/mol, Figure 2). Experimentally, amidodienes **16** are obtained when 0.4 CSA is present in the reaction mixture, but not under thermal conditions. The isomerization of **1** to **15** is likely to be rate-limiting under thermal conditions (similar to the case proposed for the 4,5-fused system), explaining why Ficini's amido-dienes are not observed under thermal conditions.
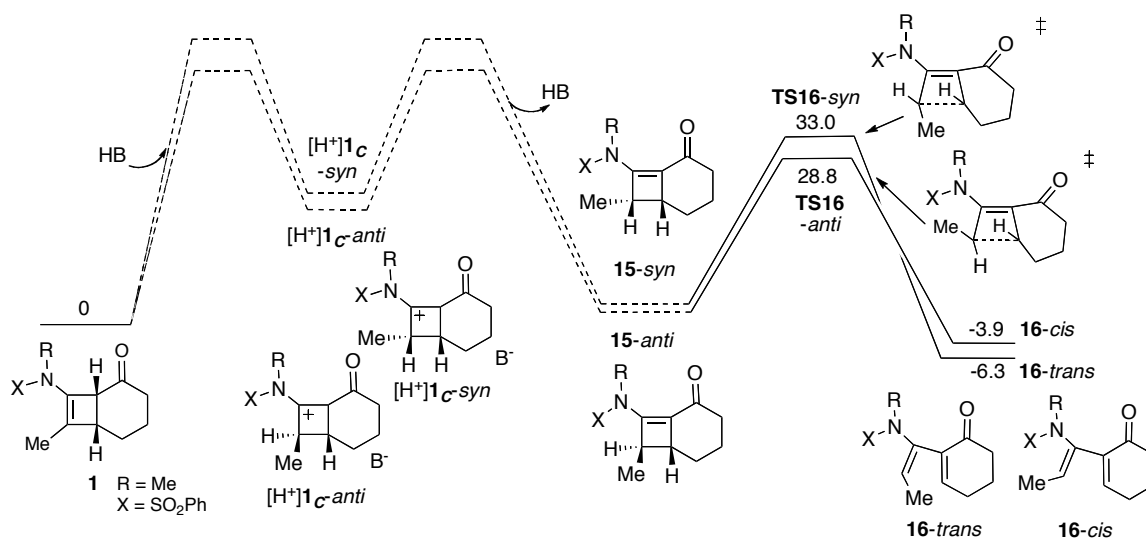
Figure S5. Rearrangement of 4,6-fused cyclobutenamide **1** to Ficini-type amido-dienes **16**-*cis* and **16**-*trans*.

4,5-Fused Cyclobutenamides

We propose that the rearrangements of 4,5-fused cyclobutenamides **8** to amidodienes **12** are acid-catalyzed and that the mechanism of acid catalysis is analogous to that proposed for the 4,6-fused systems in Figure S5. That is, the acid protonates the enamide β-carbon of **8** and the conjugate base then effects deprotonation α to the carbonyl group to give **11**. Under the conditions used to effect thermal rearrangement (195 °C, xylenes), the conversion of **8** to **11** is rate-limiting because the concentration of acid catalyst is minute. Deliberate addition of an acid catalyst (0.4 equiv CSA) accelerates the rearrangement to furnish an 85–92% yield of amido-dienes **12a–c** in only 6 hours (see ref. 19 of the paper).

Theoretical Calculations

Geometries were optimized at the B3LYP/6-31G(d) level of theory[1] in the gas phase. Vibrational frequency calculations were used to determine the nature of each stationary point (local minimum or first-order saddle point) and to compute unscaled zero-point energy and thermochemical corrections. Single-point energies were computed at the M06-2X/6-311+G(d,p) level of theory[2] in the gas phase on the B3LYP geometries. Solvation energies were computed from single-point calculations in implicit toluene using the SMD method.[3] The M06-2X potential energies were used in conjunction with the B3LYP thermochemical corrections and solvation energies to obtain free energies in solution. A standard state of 298.15 K and 1 mol/L was used.

Underneath the Cartesian coordinates for the optimized geometries are listed the following energies:

B3LYP/6-31G(d) electronic energy (E)
B3LYP/6-31G(d) enthalpy at 298.15 K (H)
B3LYP/6-31G(d) Gibbs free energy at 298.15 K and 1 mol/L (G)
M06-2X/6-311+G(d,p) potential energy (E_{M06-2X})
Sum of B3LYP/6-31G(d) potential energy and free energy of solvation in toluene at 298.15 K and 1 mol/L (E_{solv})

All energies are given in Hartree.

[1] (a) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B*, **1988**, *37*, 785–789. (b) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 1372–1377. (c) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648–5652. (d) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623–11627.
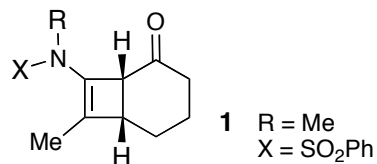[2] (a) Y. Zhao, D. G. Truhlar, *Theor. Chem. Acc.* **2008**, *120*, 215–241. (b) Y. Zhao, D. G. Truhlar, *Acc. Chem. Res.* **2008**, *41*, 157–167.
[3] Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B* **2009**, *113*, 6378–6396.

Computed Geometries and Energies

In each species below, the group NRX is modeled as NMe(SO₂Ph).

Cyclobutenamide 1

1 R = Me
        X = SO₂Ph

```
C    -2.248864     1.106298    -0.388227
C    -2.541819     1.997627    -1.543934
H    -2.516971     1.444295    -2.492712
H    -3.549924     2.423623    -1.449251
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C    -1.259688     0.975558     0.520682
C    -1.926709    -0.176565     1.286796
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H    -4.003193     0.381881     0.697975
C    -1.118771    -1.467363     1.298386
O    -0.203620    -1.607300     2.093408
C    -1.477432    -2.565039     0.305654
H    -0.564894    -3.129447     0.088789
H    -2.149870    -3.253344     0.843293
C    -2.182432    -2.068737    -0.965179
H    -2.464688    -2.927426    -1.585752
H    -1.486777    -1.464874    -1.561035
C    -3.424744    -1.240999    -0.614115
H    -4.131361    -1.874585    -0.058951
H    -3.945454    -0.924506    -1.527372
N    -0.059695     1.650870     0.809358
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C     1.549546    -0.782213    -1.483689
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C     3.015831    -2.476124    -0.569622
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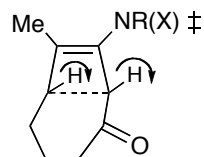

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H   -4.533783     0.720633     1.759301
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C   -2.632022     1.341817     1.052224
O   -2.758556     2.475154     1.507654
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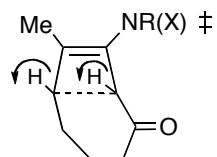

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C    -2.215020    -0.314955     1.064729
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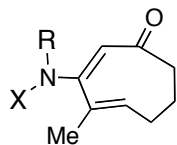

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C     2.431935     2.370892    -1.329452
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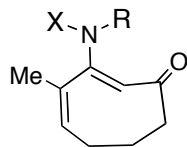0 imaginary frequencies
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H	3.950661	−0.337277	−1.721729
C	0.941627	1.779975	1.502129
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H	0.839531	1.796872	−1.178792
H	1.761477	3.246046	−1.504309
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H	2.428164	3.285387	0.995919
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0 imaginary frequencies
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H = −1299.268904
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E_{solv} = −1299.636447

TS7
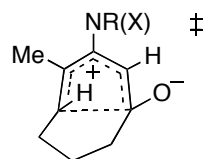
C	2.623816	−0.001854	−0.790933
C	1.784514	1.076986	−0.299566
C	0.792510	0.571894	0.567117
C	1.176743	−0.655924	1.105246
H	0.584244	−1.237309	1.803887
C	2.359544	−1.267318	0.458597
O	1.838075	−2.374053	0.005042
C	3.789780	−1.269507	1.038235
H	3.921579	−0.443260	1.750664
H	3.963773	−2.215764	1.560989
C	4.714460	−1.076975	−0.176563
H	4.655156	−1.972190	−0.807810
H	5.764889	−0.932462	0.098947
C	4.134702	0.138972	−0.945152
H	4.462153	0.154270	−1.990573
H	4.489717	1.065977	−0.476973
C	1.993080	2.529600	−0.567708
H	1.573350	2.777576	−1.551255
H	1.491753	3.158658	0.172461
H	3.061088	2.769346	−0.601412
N	−0.367017	1.308870	0.920757
C	−0.896835	1.163416	2.284622
H	−1.659753	1.926323	2.443481
H	−1.330604	0.171914	2.474566
H	−0.073846	1.333337	2.983290
S	−1.565220	1.421495	−0.314535
O	−2.508389	2.447751	0.132480
O	−0.826795	1.549075	−1.572178
C	−2.422277	−0.160055	−0.309649
C	−3.764085	−0.186329	0.078285
C	−4.444859	−1.404273	0.079905
C	−3.783154	−2.576562	−0.290346
C	−2.438350	−2.537469	−0.667609
C	−1.746415	−1.326841	−0.687820
H	−0.700258	−1.313310	−0.974313
H	−1.919397	−3.448982	−0.948315
H	−4.315334	−3.523810	−0.283736
H	−5.491024	−1.434612	0.370786
H	−4.258123	0.737013	0.360043
H	2.131111	−0.567469	−1.580194

1 imaginary frequency
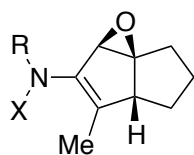E = −1299.578783
H = −1299.234526
G = −1299.299739
E_{M06-2X} = −1299.437142
E_{solv} = −1299.600443

7


```
C    -3.14348    1.29461    0.01040
C    -2.81503   -0.02379    0.33649
C    -3.77882   -1.03234    0.35988
C    -5.09856   -0.71334    0.03373
C    -5.43828    0.59707   -0.30614
C    -4.46355    1.59955   -0.31538
S    -1.12138   -0.41492    0.78998
O    -1.10134   -1.79455    1.30328
N    -0.32260   -0.32962   -0.74018
C    -0.69715   -1.41953   -1.66043
C     1.08813   -0.11668   -0.62740
C     1.69603    1.08588   -0.69510
C     3.20168    0.92976   -0.56498
C     3.40400   -0.58923   -0.42377
C     2.08116   -1.22115   -0.42893
H     1.83436   -2.12747    0.11901
C     4.55785   -0.86227    0.51032
C     4.39444    0.29022    1.52515
C     3.90479    1.51586    0.69944
C     1.04391    2.40882   -0.93248
H     1.10422    3.04048   -0.03646
H    -0.01142    2.28500   -1.18915
H     1.54555    2.95274   -1.74365
O     3.03000   -1.40222   -1.53180
O    -0.58322    0.68406    1.59492
H     3.68314    1.30916   -1.47633
H     3.24055    2.15506    1.28941
H     4.75691    2.13307    0.39463
H     5.31625    0.50493    2.07497
H     3.63193    0.01296    2.26214
H     5.50855   -0.77878   -0.03417
H     4.51933   -1.85547    0.96768
H    -1.78354   -1.43879   -1.77902
H    -0.24496   -1.19762   -2.62980
H    -0.35642   -2.40449   -1.31899
H    -2.37891    2.06394    0.02650
H    -4.73371    2.62019   -0.57074
H    -6.46634    0.84126   -0.55910
H    -5.85931   -1.48849    0.04950
H    -3.49211   -2.04056    0.63909
0 Imaginary Frequencies
E =    -1299.627424
H =    -1299.279931
G =    -1299.347356
```
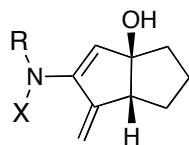$E_{M06-2X} = -1299.495628$
$E_{solv} = -1299.648271$

3

C	2.265178	−1.290516	−1.033362
C	2.274810	−0.219750	−0.138817
C	2.769463	−0.354693	1.160271
C	3.246788	−1.597299	1.573607
C	3.232722	−2.682823	0.692901
C	2.746477	−2.530165	−0.607111
S	1.701968	1.389521	−0.691856
O	1.374995	1.286221	−2.121672
N	0.310494	1.593398	0.282166
C	−0.102283	2.999105	0.478736
C	−0.737804	0.635507	0.164872
C	−1.465335	0.182858	1.368528
C	−2.535815	−0.792973	0.902088
C	−2.248070	−1.014966	−0.631484
C	−1.176193	0.001206	−0.941285
C	−3.581969	−0.739290	−1.350384
C	−4.310238	0.256676	−0.437839
C	−3.996370	−0.264391	0.978351
C	−1.199363	0.536377	2.632106
O	−1.827647	−2.338596	−0.975858
O	2.633439	2.426111	−0.237579
H	−0.801573	0.158863	−1.945880
H	−1.769094	0.133410	3.464917
H	−0.395701	1.225811	2.872829
H	−2.439591	−1.741824	1.439582
H	−4.126145	0.493541	1.757532
H	−4.668214	−1.097935	1.217045
H	−5.384770	0.315979	−0.640727
H	−3.897046	1.264453	−0.572845
H	−4.132046	−1.687276	−1.401766
H	−3.438696	−0.381608	−2.375438
H	−0.854052	3.012040	1.270075
H	0.763240	3.585354	0.787572
H	−0.535152	3.429974	−0.433136
H	1.894931	−1.142892	−2.041922
H	2.746732	−3.372246	−1.293327
H	3.607434	−3.648738	1.020143
H	3.633115	−1.717728	2.581537
H	2.781838	0.499400	1.828966
H	−0.928451	−2.453774	−0.626824

0 imaginary frequencies
E = −1299.641321
H = −1299.293681
G = −1299.360053
E_{M06-2X} = −1299.519476
E_{solv} = −1299.661173

[H⁺]1
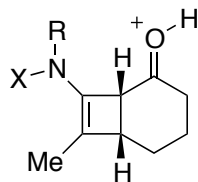
C	1.11746	−1.17804	1.42378
C	0.17748	−2.21323	1.92806
H	0.11672	−3.05896	1.23089
H	0.52948	−2.61739	2.88548
H	−0.82764	−1.80657	2.06490
C	0.99337	0.12634	1.11452
C	2.55511	0.29480	0.81020
H	3.05931	0.99284	1.48507
C	2.61650	−1.23406	1.15073
H	3.20241	−1.40611	2.06155
C	2.69869	0.67077	−0.58240
O	2.70875	1.94987	−0.80891
C	2.85925	−0.29841	−1.69860
H	2.30629	0.05499	−2.57702
H	3.93319	−0.24111	−1.95464
C	2.49495	−1.74527	−1.33366
H	2.85643	−2.40498	−2.12741
H	1.40415	−1.83623	−1.31050
C	3.09755	−2.15053	0.01842
H	4.19372	−2.11555	−0.03365
H	2.83218	−3.18770	0.25166
N	−0.02549	1.06103	1.08661
C	0.10903	2.25061	1.95582
S	−0.83715	1.27514	−0.44379
H	0.19467	1.90318	2.98808
H	0.98466	2.85546	1.69357
H	−0.78206	2.86881	1.85612
O	0.10234	0.79328	−1.47689
O	−1.32144	2.65186	−0.44871
C	−2.21760	0.14732	−0.37984
C	−3.31710	0.48132	0.41821
C	−4.40401	−0.38906	0.45468
C	−4.38835	−1.56475	−0.30253
C	−3.28861	−1.87574	−1.10471
C	−2.18914	−1.01754	−1.14975
H	−1.33755	−1.22863	−1.78638
H	−3.33060	1.40844	0.98157
H	−5.26772	−0.14407	1.06489
H	−5.24239	−2.23480	−0.27446
H	−3.28912	−2.78049	−1.70488
H	2.63197	2.16218	−1.76204

0 Imaginary Frequencies
E =   −1300.005529
H =   −1299.645730
G =   −1299.714696
E_{M06-2X} = −1299.865507
E_{solv} = −1300.063997

[H⁺]1_C-anti
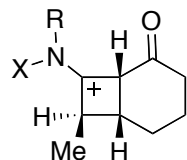
C	3.792149	0.296226	0.647047
C	2.728134	0.109096	−0.243960
C	2.729957	−0.891041	−1.225059
C	3.832052	−1.739330	−1.295386
C	4.902647	−1.575022	−0.409860
C	4.886695	−0.560961	0.552252
S	1.363680	1.234223	−0.179061
O	0.749142	1.373644	−1.490509
N	0.072126	0.241094	0.779511
C	0.590284	−0.630112	1.854681
C	−1.181735	0.390139	0.509682
C	−2.385864	−0.322911	1.049049
C	−3.280875	0.756336	0.354343
C	−4.474304	0.261922	−0.466550
C	−4.221231	−1.077720	−1.171211
C	−3.766800	−2.159147	−0.166232
C	−2.457552	−1.779072	0.476560
C	−2.007962	1.306107	−0.383296
C	−1.792000	2.822662	−0.331331
O	−1.484569	−2.494044	0.559066
O	1.647942	2.352451	0.705624
H	−0.901796	3.130880	−0.880253
H	−2.660239	3.306027	−0.791503
H	−1.715366	3.180702	0.700392
H	−2.459237	−0.411620	2.140302
H	−3.610971	1.498472	1.087816
H	−3.642530	−3.140631	−0.631650
H	−4.523684	−2.255573	0.627165
H	−5.136394	−1.415219	−1.667424
H	−3.467230	−0.971685	−1.962777
H	−5.336125	0.150057	0.203937
H	−4.753243	1.032139	−1.196158
H	1.079586	−1.501529	1.420156
H	1.298546	−0.050314	2.450978
H	−0.236271	−0.962540	2.479700
H	3.769354	1.101588	1.373346
H	1.903700	−0.988282	−1.921031
H	3.860628	−2.520472	−2.048210
H	5.760236	−2.237560	−0.477014
H	5.728980	−0.431139	1.224197
H	−1.943418	0.952038	−1.421400

0 imaginary frequencies
E = −1300.031192
H = −1299.670790
G = −1299.738215
E$_{M06-2X}$ = −1299.880936
E$_{solv}$ = −1300.090162

[H⁺]1$_c$-syn
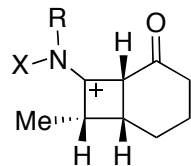
C	3.760991	0.152249	−0.708020
C	2.717161	−0.062417	0.201329
C	2.564583	0.700673	1.365933
C	3.481502	1.719308	1.610838
C	4.525502	1.956473	0.710510
C	4.668274	1.175737	−0.439740
S	1.590929	−1.393977	−0.107340
O	1.050316	−1.927590	1.132139
N	0.123124	−0.516446	−0.895743
C	0.424484	0.071874	−2.220698
C	−1.071003	−0.586744	−0.406836
C	−2.383237	−0.170240	−1.008480
C	−3.093995	−1.069882	0.062545
C	−4.353511	−0.507888	0.734424
C	−4.393665	1.022638	0.873445
C	−4.053644	1.723553	−0.460152
C	−2.664927	1.360653	−0.919853
C	−1.716531	−1.206511	0.821481
C	−1.524950	−0.424203	2.133182
O	−1.795871	2.152082	−1.213492
O	2.053697	−2.220117	−1.209409
H	−2.276406	−0.751585	2.857576
H	−0.539046	−0.635604	2.551044
H	−1.626904	0.656621	2.000008
H	−2.518330	−0.449025	−2.061966
H	−3.330737	−2.041883	−0.379596
H	−4.114507	2.812404	−0.384736
H	−4.765568	1.396303	−1.233306
H	−5.394775	1.332403	1.189785
H	−3.706836	1.371717	1.652406
H	−5.213860	−0.819063	0.128378
H	−4.490536	−0.983860	1.712711
H	1.350677	0.643457	−2.141458
H	0.550876	−0.733321	−2.947750
H	−0.375882	0.755361	−2.494907
H	3.870078	−0.479572	−1.582902
H	1.765389	0.491580	2.068426
H	3.387568	2.321391	2.508878
H	5.238022	2.750369	0.912758
H	5.490474	1.355856	−1.124788
H	−1.403769	−2.241457	0.983731

0 imaginary frequencies
E = −1300.028986
H = −1299.668242
G = −1299.735852
E_{M06-2X} = −1299.878270
E_{solv} = −1300.087907

[H⁺]TS2
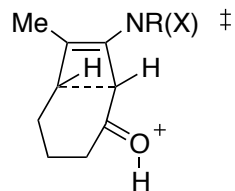
C	1.06445	0.64504	−0.54942
C	2.13736	1.48772	−0.55806
C	2.31586	2.91261	−0.10959
H	1.68370	3.15577	0.74697
H	3.35300	3.10563	0.17915
H	2.08303	3.61746	−0.91790
C	3.21448	0.63959	−1.10708
H	3.21453	0.43132	−2.17597
C	4.53926	0.52510	−0.39091
H	4.69304	1.45447	0.16875
H	5.35932	0.43045	−1.10938
C	4.59649	−0.66034	0.62052
H	5.03162	−1.54069	0.13758
H	5.24327	−0.40896	1.46550
C	3.17787	−1.01665	1.13484
H	3.23340	−1.83502	1.85788
H	2.70048	−0.15680	1.60884
C	2.39025	−1.47392	−0.04726
O	2.63806	−2.73110	−0.35853
C	1.59285	−0.68436	−0.89150
H	1.13013	−1.21433	−1.72924
N	−0.30174	0.84881	−0.37600
C	−0.82827	2.22589	−0.37329
H	−1.90021	2.18927	−0.57610
H	−0.34817	2.77381	−1.18568
H	−0.66222	2.74047	0.57778
S	−1.11554	−0.23793	0.74925
O	−0.51298	−1.55291	0.49432
O	−1.05615	0.36384	2.08181
C	−2.79759	−0.21870	0.16210
C	−3.10939	−0.86368	−1.03932
C	−4.43591	−0.87652	−1.46312
C	−5.42581	−0.26294	−0.68840
C	−5.09834	0.36596	0.51455
C	−3.77385	0.39347	0.95252
H	−3.49822	0.86609	1.88889
H	−5.87224	0.83172	1.11656
H	−6.45874	−0.28180	−1.02288
H	−4.69974	−1.37222	−2.39217
H	−2.33509	−1.35188	−1.62130
H	2.10028	−3.03767	−1.11355

1 Imaginary Frequency
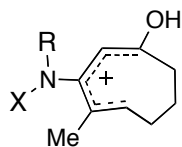E = −1299.975498
H = −1299.616606
G = −1299.685591
E_{M06-2X} = −1299.830204
E_{solv} = −1300.034433

[H⁺]2-*E,E*


```
C   -1.786793    1.086885    0.837609
C   -3.111017    0.902298    1.091302
C   -4.238351    1.676207    0.515330
C   -4.669476    0.774194   -0.697216
C   -3.453424    0.172790   -1.462278
C   -2.808745   -1.048623   -0.829844
C   -1.663875   -1.193043   -0.044408
C   -1.008133   -0.146068    0.653822
C   -1.142768    2.417462    0.501877
H   -0.377137    2.316250   -0.273928
H   -1.887899    3.136698    0.154831
H   -0.662995    2.863818    1.380212
H   -3.408437   -0.058881    1.505858
H   -5.086210    1.791303    1.197794
H   -3.944400    2.667025    0.161177
H   -5.268064    1.369033   -1.394390
H   -5.310582   -0.039412   -0.341419
H   -3.804041   -0.166486   -2.443037
H   -2.694709    0.942164   -1.628474
O   -3.458122   -2.144850   -1.219633
H   -1.248619   -2.192890    0.018795
N    0.269508   -0.226793    1.090893
C    0.756098    0.594462    2.217274
H   -0.101314    0.960417    2.782267
H    1.360827    1.435508    1.867678
H    1.355696   -0.043221    2.869368
S    1.526624   -1.337699    0.416896
O    0.875147   -2.066189   -0.665246
O    2.089461   -1.996789    1.587041
C    2.704391   -0.186762   -0.260186
C    2.487684    0.324565   -1.545049
H    1.621351    0.017511   -2.121488
C    3.428347    1.204161   -2.076016
H    3.285734    1.605408   -3.074555
C    4.560593    1.554280   -1.333021
H    5.291943    2.235999   -1.756632
C    4.766599    1.022839   -0.057738
H    5.656500    1.283904    0.506282
C    3.835880    0.141725    0.492789
H    3.991817   -0.301348    1.470384
H   -3.075938   -2.953677   -0.830081
0 imaginary frequencies
E = -1300.012090
H = -1299.651077
G = -1299.719354
E_{M06-2X} = -1299.864964
E_{solv} = -1300.070073
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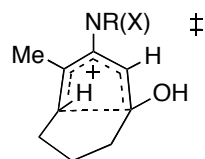
[H⁺]TS7

C	2.569022	1.084567	−1.105878
C	2.763178	−0.025776	−0.276839
C	3.948227	−0.220426	0.438907
C	4.958495	0.734781	0.326174
C	4.777220	1.855328	−0.487690
C	3.588779	2.028734	−1.204070
S	1.472607	−1.250473	−0.155019
O	0.708385	−1.276578	−1.405928
N	0.335533	−0.582594	1.009656
C	0.884078	−0.175901	2.311178
C	−0.859042	−0.080281	0.551542
C	−1.722028	−0.783644	−0.379929
C	−2.630559	0.090059	−1.028062
C	−2.847609	1.259218	0.551312
C	−1.495082	1.047541	1.033743
C	−4.105723	0.487552	0.955721
C	−4.968950	0.273675	−0.306282
C	−4.037271	−0.320143	−1.410292
C	−1.822379	−2.276857	−0.397952
O	−3.055289	2.568826	0.262073
O	2.006608	−2.454737	0.467492
H	−1.013981	1.812510	1.636188
H	−3.813140	−0.470804	1.393922
H	−4.636862	1.055696	1.731160
H	−5.385165	1.229582	−0.648385
H	−5.824333	−0.373477	−0.094284
H	−4.311295	0.058186	−2.397995
H	−4.140226	−1.407288	−1.443485
H	−1.615474	−2.663090	−1.401613
H	−1.123053	−2.736881	0.301156
H	−2.839091	−2.589755	−0.131082
H	1.624177	−0.916229	2.619515
H	1.351309	0.815053	2.278139
H	0.074698	−0.177413	3.045505
H	1.654999	1.189601	−1.680663
H	3.461748	2.892535	−1.849222
H	5.569740	2.592658	−0.573592
H	5.889438	0.596860	0.867143
H	4.080507	−1.108914	1.046796
H	−2.190121	0.930979	−1.558387
H	−4.004091	2.785277	0.253297

1 imaginary frequency
E = −1299.995960
H = −1299.637531
G = −1299.703595
E_{M06-2X} = −1299.853052
E_{solv} = −1300.055607

[H⁺]7

R
|
N
/ \
X
Me   OH   H
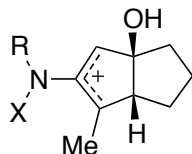
C   −3.18775   1.26190   −0.19594
C   −2.80599   0.00507   0.28494
C   −3.72973   −1.02246   0.49830
C   −5.07197   −0.78148   0.20420
C   −5.46913   0.46359   −0.28789
C   −4.53198   1.48307   −0.48491
S   −1.10114   −0.28446   0.70187
O   −0.97805   −1.55065   1.42865
N   −0.32934   −0.49028   −0.87677
C   −0.73604   −1.73278   −1.56862
C   1.06682   −0.29758   −0.73681
C   1.70023   0.97241   −0.85023
C   3.16627   0.86100   −0.62772
C   3.40713   −0.64890   −0.32628
C   2.03581   −1.24081   −0.47094
H   1.85057   −2.30751   −0.37454
C   3.90357   −0.69494   1.15025
C   3.46617   0.64076   1.77571
C   3.65932   1.64934   0.63043
C   1.00716   2.23337   −1.14075
H   0.59459   2.61088   −0.19076
H   0.14097   2.05415   −1.78734
H   1.67420   2.99052   −1.55895
O   4.29542   −1.21138   −1.27482
O   −0.47781   0.93795   1.22569
H   3.69632   1.17170   −1.53692
H   3.13367   2.59601   0.78087
H   4.72038   1.87786   0.48856
H   4.05159   0.89426   2.66340
H   2.41290   0.60280   2.07937
H   4.99908   −0.74220   1.09446
H   3.55414   −1.57504   1.69990
H   −1.81681   −1.70371   −1.71948
H   −0.25569   −1.74726   −2.54981
H   −0.48091   −2.64110   −1.01042
H   −2.45491   2.05148   −0.32068
H   −4.85052   2.45275   −0.85450
H   −6.51602   0.64541   −0.51162
H   −5.80577   −1.56441   0.36775
H   −3.40322   −1.97534   0.90026
H   4.68309   −2.02467   −0.91066
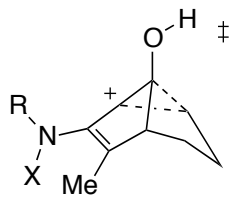0 Imaginary Frequencies
E =   −1300.004998
H =   −1299.646279
G =   −1299.714300
E_{M06-2X} = −1299.864628
E_{solv} = −1300.064629

[H⁺]TS14


```
C    3.55986   -1.17341   -0.29633
C    2.72367   -0.05416   -0.25875
C    3.21576    1.23883   -0.05048
C    4.58534    1.40444    0.14193
C    5.43708    0.29547    0.11565
C    4.92900   -0.98662   -0.10571
S    0.98286   -0.27183   -0.55261
O    0.71983   -1.65584   -0.98813
N    0.26019   -0.06138    1.03042
C    0.74308   -1.01671    2.04980
C   -1.15319    0.00560    0.89137
C   -1.89768    1.15137    0.83412
C   -3.34670    0.81201    0.52590
C   -3.34288   -0.70305    0.52728
C   -2.02135   -1.14649    0.67737
H   -1.70989   -2.18298    0.75978
C   -2.75988   -1.01731   -1.30258
H   -3.63797   -1.64042   -1.47920
H   -1.84294   -1.56149   -1.54022
C   -2.81474    0.40185   -1.83495
C   -3.72562    1.24073   -0.92009
C   -1.39203    2.54567    0.92483
H   -0.38200    2.55974    1.33931
H   -2.05416    3.16631    1.53900
H   -1.34570    3.00378   -0.07224
O   -4.50245   -1.33792    0.75761
H   -4.36961   -2.28383    0.94540
O    0.45620    0.84681   -1.34327
H   -4.04992    1.20175    1.26916
H   -3.59993    2.31613   -1.07110
H   -4.78163    1.00110   -1.08488
H   -3.19558    0.36073   -2.86355
H   -1.80598    0.81871   -1.88754
H    0.51320   -2.06334    1.81004
H    1.82449   -0.90968    2.15099
H    0.28280   -0.74666    3.00306
H    3.14501   -2.15740   -0.48563
H    5.59718   -1.84151   -0.13724
H    6.50426    0.43400    0.26108
H    4.98951    2.39904    0.30260
H    2.54505    2.09120   -0.05573
```
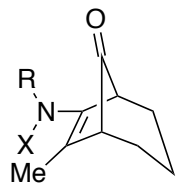1 Imaginary Frequency
E =   -1299.983787
H =   -1299.625858
G =   -1299.691702
E_{M06-2X} = -1299.847927
E_{solv} = -1300.042359

14


```
C    3.30762    0.07190    0.74134
C    2.29332   -0.03099   -0.21414
C    1.98010    1.03549   -1.06235
C    2.68981    2.22946   -0.93683
C    3.70181    2.34760    0.01958
C    4.01316    1.27069    0.85255
S    1.34572   -1.55530   -0.32863
O    2.12873   -2.61326    0.31538
N   -0.04380   -1.34631    0.65923
C    0.20380   -1.37683    2.10765
C   -1.05170   -0.45606    0.19319
C   -1.99273   -0.76273   -0.72851
C   -2.85183    0.46829   -0.98977
C   -1.86013    1.56264   -0.58898
C   -1.20383    0.98995    0.67166
H   -0.26961    1.49737    0.92702
C   -2.27221    1.16363    1.79767
H   -2.47798    2.23749    1.90147
H   -1.87013    0.82676    2.76083
C   -3.57214    0.39771    1.47225
C   -4.04102    0.58724    0.01334
C   -2.22323   -2.06296   -1.42606
H   -3.28477   -2.34144   -1.38633
H   -1.62439   -2.86244   -0.98503
H   -1.94552   -1.98926   -2.48501
O   -1.64569    2.62126   -1.13088
O    0.86379   -1.67549   -1.70361
H   -3.19809    0.56582   -2.02414
H   -4.81374   -0.15198   -0.23093
H   -4.49698    1.57745   -0.11820
H   -4.36706    0.70695    2.16099
H   -3.40798   -0.67061    1.65212
H    0.88241   -2.20034    2.33041
H    0.62943   -0.43818    2.49099
H   -0.75001   -1.56473    2.60782
H    3.54935   -0.78263    1.36411
H    4.80967    1.35996    1.58588
H    4.25350    3.27915    0.11061
H    2.45315    3.06438   -1.58963
H    1.20428    0.92513   -1.81208
0 Imaginary Frequencies
E =    -1299.665775
H =    -1299.317346
G =    -1299.383245
E_{M06-2X} = -1299.537327
E_{solv} = -1299.686708
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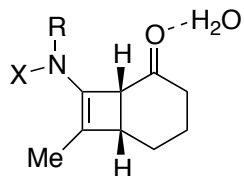
[H₂O]1

C	-0.41325	1.83234	0.97501
C	0.80207	2.68274	0.83952
H	0.93775	3.02775	-0.19446
H	0.71086	3.58117	1.46408
H	1.70704	2.14414	1.13369
C	-0.66719	0.53457	1.22885
C	-2.19617	0.68237	1.20725
H	-2.68021	0.50512	2.17495
C	-1.89338	2.19536	0.88652
H	-2.21005	2.86445	1.69855
C	-2.88081	-0.18149	0.16239
O	-3.15528	-1.34193	0.44285
C	-3.19219	0.40836	-1.19996
H	-3.09217	-0.39877	-1.93415
H	-4.26040	0.67986	-1.17238
C	-2.35986	1.64589	-1.56040
H	-2.72543	2.06399	-2.50547
H	-1.31973	1.34378	-1.73216
C	-2.42907	2.71066	-0.45738
H	-3.47437	3.02457	-0.32551
H	-1.87230	3.61010	-0.75257
N	0.13555	-0.60402	1.46879
C	-0.36436	-1.50673	2.53102
S	0.78066	-1.38774	0.07893
H	-0.37395	-0.93511	3.46337
H	-1.37232	-1.87403	2.31063
H	0.31879	-2.34875	2.63303
O	-0.12377	-1.23037	-1.07432
O	1.19335	-2.72216	0.51949
C	2.25199	-0.42402	-0.28096
C	3.29087	-0.39527	0.65380
C	4.45417	0.30729	0.34730
C	4.57525	0.96212	-0.88297
C	3.53503	0.91334	-1.81155
C	2.36209	0.21507	-1.51532
H	1.54451	0.15624	-2.22518
H	3.18823	-0.91525	1.60056
H	5.26881	0.33926	1.06498
H	5.48589	1.50611	-1.11770
H	3.63423	1.41440	-2.77013
H	-2.99880	-2.52684	-1.25244
O	-2.59462	-2.68862	-2.12387
H	-1.66442	-2.46121	-1.95803

0 Imaginary Frequencies

E = -1376.071071

H = -1375.695419

G = -1375.768619

E_{M06-2X} = -1375.948130

E_{solv} = -1376.093684

[H₂O]TS2

[H$_2$O]TS2

Me — NR(X) ‡

H   H

O

H$_2$O
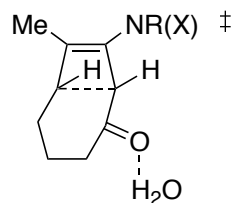
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C   -1.07794   -0.69700   -0.54478
C   -2.26245   -1.35234   -0.77540
C   -2.62853   -2.78742   -0.50874
H   -2.53597   -3.40612   -1.41203
H   -1.98870   -3.22427    0.26400
H   -3.66642   -2.87818   -0.17231
C   -3.13953   -0.29973   -1.24591
H   -2.91249    0.18444   -2.18999
C   -4.53066   -0.12599   -0.68968
H   -4.88865   -1.09921   -0.33238
H   -5.23317    0.21695   -1.45801
C   -4.54089    0.86278    0.51253
H   -4.68405    1.88733    0.15052
H   -5.39118    0.63656    1.16609
C   -3.21773    0.81370    1.30797
H   -3.31266    1.40698    2.22135
H   -2.96386   -0.21431    1.58434
C   -2.12673    1.46436    0.46847
O   -1.98614    2.69183    0.54630
C   -1.33439    0.71706   -0.52160
H   -0.61998    1.37831   -1.01966
N    0.22430   -1.22620   -0.47124
C    0.59479   -2.41261   -1.25253
H    1.66784   -2.38641   -1.46458
H    0.05792   -2.36521   -2.20247
H    0.36228   -3.35211   -0.74156
S    1.18552   -0.93518    0.92607
O    0.44923    0.02425    1.74852
O    1.58027   -2.24593    1.45557
C    2.65802   -0.14730    0.26977
C    2.60062    1.19117   -0.12930
C    3.76030    1.78727   -0.62303
C    4.94935    1.05819   -0.71160
C    4.98985   -0.27611   -0.30225
C    3.83909   -0.88936    0.19555
H    3.85033   -1.91816    0.53849
H    5.91658   -0.83977   -0.36251
H    5.84843    1.53293   -1.09548
H    3.72525    2.82774   -0.93179
H    1.68737    1.77480   -0.06394
H   -0.41736    3.39885   -0.14914
O    0.41367    3.59680   -0.63639
H    0.10468    4.00954   -1.45617
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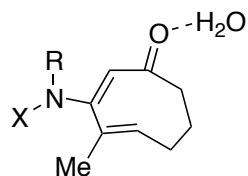1 Imaginary Frequency
E =   -1376.024800
H =   -1375.651240
G =   -1375.725422
E$_{M06-2X}$ = -1375.894778
E$_{solv}$ = -1376.047223

[H₂O]2-*E,E*

C	0.94929	−0.00131	−1.64805
C	2.24822	−0.18203	−1.98326
C	3.23833	0.90334	−2.23600
C	3.92274	1.09438	−0.83949
C	2.93014	0.98677	0.35081
C	2.56537	−0.45500	0.76017
C	1.26359	−1.11604	0.48797
C	0.44683	−0.89183	−0.58450
C	0.10327	1.17973	−2.07038
H	−0.13809	1.83432	−1.22341
H	0.60394	1.77692	−2.83649
H	−0.85367	0.84816	−2.48934
H	2.69591	−1.13881	−1.71716
H	3.99532	0.64601	−2.98564
H	2.75808	1.83702	−2.54594
H	4.42563	2.06741	−0.80659
H	4.70451	0.33877	−0.70392
H	3.44058	1.40039	1.22685
H	2.03215	1.58244	0.15547
O	3.38730	−1.09204	1.42847
H	0.99490	−1.86510	1.22374
N	−0.84864	−1.44991	−0.69020
C	−1.39344	−1.80851	−2.00976
H	−0.56007	−1.83269	−2.71353
H	−2.13939	−1.08764	−2.36604
H	−1.85340	−2.79598	−1.96129
S	−1.98160	−1.41697	0.59499
O	−1.26242	−1.61230	1.85116
O	−3.05923	−2.31060	0.16925
C	−2.61966	0.26167	0.59254
C	−1.96420	1.24105	1.34452
H	−1.10911	0.97156	1.95465
C	−2.44657	2.54940	1.31325
H	−1.95209	3.31876	1.89932
C	−3.56964	2.86624	0.54400
H	−3.94331	3.88623	0.52765
C	−4.22264	1.87462	−0.19131
H	−5.10580	2.11965	−0.77429
C	−3.75080	0.56147	−0.17077
H	−4.26133	−0.22761	−0.71240
H	4.93295	−0.13504	1.94951
O	5.58049	0.56049	2.18813
H	5.60421	0.52805	3.15583

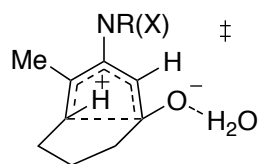0 Imaginary Frequencies
E =   −1376.053156
H =   −1375.677679
G =   −1375.754799
E$_{M06-2X}$ = −1375.930310
E$_{solv}$ = −1376.076381

[H₂O]TS7


```
C    1.73069    1.46672   -0.65847
C    2.61197    0.43480   -0.31255
C    3.92073    0.69826    0.09894
C    4.35755    2.02212    0.15797
C    3.48900    3.06179   -0.17947
C    2.17994    2.78464   -0.58194
S    2.06533   -1.27636   -0.38226
O    1.33191   -1.48271   -1.63257
N    0.89142   -1.44189    0.87214
C    1.40802   -1.26053    2.23707
C   -0.38987   -0.92383    0.56078
C   -1.28671   -1.57178   -0.31902
C   -2.33554   -0.65153   -0.73999
H   -1.97658    0.01029   -1.52840
C   -2.29582    0.55307    0.53726
C   -0.99658    0.18245    1.14609
C   -3.66248    0.21804    1.17846
C   -4.58924   -0.09588   -0.00854
C   -3.79203   -1.09455   -0.88704
C   -1.21261   -3.01910   -0.66239
O    3.18974   -2.12850    0.00449
H   -0.52224    0.84835    1.85969
H   -3.57103   -0.65628    1.83804
H   -4.00778    1.07085    1.77079
H   -4.77410    0.83903   -0.54852
H   -5.55848   -0.50048    0.30224
H   -4.13363   -1.09273   -1.92757
H   -3.93096   -2.11221   -0.50050
H   -2.21317   -3.46046   -0.70909
H   -0.76390   -3.12482   -1.65895
H   -0.58690   -3.57537    0.04028
H    0.64198   -1.60827    2.93460
H    2.29881   -1.87869    2.35441
H    1.65796   -0.21615    2.46891
H    0.71082    1.26357   -0.96680
H    1.50165    3.59271   -0.83847
H    3.83168    4.09150   -0.12837
H    5.37602    2.23854    0.46727
H    4.57888   -0.12531    0.35303
H   -3.48006    2.84817   -0.00867
O   -4.33825    3.29025   -0.21719
H   -4.22329    3.56720   -1.13818
O   -2.05378    1.77937    0.11681
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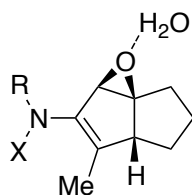1 Imaginary Frequency
E =   -1376.006894
H =   -1375.634939
G =   -1375.708136
E$_{M06-2X}$ = -1375.876400
E$_{solv}$ = -1376.031114

[H₂O]7


```
C    -3.16485    0.89981   -1.06479
C    -2.96390    0.34138    0.20034
C    -3.99401   -0.30188    0.88656
C    -5.24972   -0.39988    0.28327
C    -5.46159    0.14412   -0.98430
C    -4.42209    0.79523   -1.65597
S    -1.35112    0.49830    0.97439
O    -1.48595    0.06734    2.37529
N    -0.42186   -0.63590    0.08319
C    -0.67910   -2.04692    0.44265
C     0.96317   -0.29284   -0.02604
C     1.58638    0.00053   -1.18552
C     3.07845    0.17591   -0.96251
C     3.25361   -0.07052    0.54513
C     1.92955   -0.33042    1.11500
H     1.63894   -0.09222    2.13445
C     4.34392    0.82186    1.08364
C     4.12415    2.09111    0.23042
C     3.70898    1.58526   -1.18176
C     0.97938    0.01570   -2.54895
H     1.22335    0.94279   -3.08357
H    -0.10715   -0.08804   -2.49681
H     1.37876   -0.81811   -3.14138
O     2.96092   -1.39118    1.02345
O    -0.79725    1.81718    0.65465
H     3.61180   -0.58316   -1.54913
H     3.01851    2.28094   -1.66873
H     4.58844    1.49945   -1.82896
H     5.00838    2.73515    0.19601
H     3.30858    2.67840    0.66774
H     5.32724    0.37523    0.88265
H     4.26805    1.00036    2.16024
H    -1.73304   -2.27881    0.26243
H    -0.05528   -2.66352   -0.20908
H    -0.43968   -2.26193    1.49145
H    -2.35177    1.41602   -1.56428
H    -4.59340    1.22582   -2.63844
H    -6.44032    0.06682   -1.44985
H    -6.06112   -0.89711    0.80705
H    -3.80930   -0.70268    1.87742
H     2.52822   -2.63407   -0.36031
O     2.25180   -3.15124   -1.14429
H     2.63156   -4.03026   -0.99724
```

0 Imaginary Frequencies
E =   -1376.052133
H =   -1375.676901
G =   -1375.751665
E_{M06-2X} = -1375.931181
E_{solv} = -1376.073458

Cyclobutenamide 8

8 R = Me
X = SO$_2$Ph
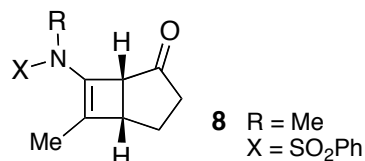
```
C    1.492145    0.600116   -0.057487
C    2.742552    1.033596    0.223536
C    3.380512    2.101783    1.048278
H    3.981094    2.767780    0.413706
H    4.067730    1.676152    1.793297
H    2.650676    2.719570    1.578300
C    3.396115   -0.045137   -0.638592
C    1.950177   -0.576974   -0.917898
H    1.570121   -0.628620   -1.939015
H    3.933461    0.340477   -1.512787
C    4.164939   -1.176881    0.083018
C    3.085332   -2.073759    0.718919
C    1.840739   -1.894791   -0.160192
O    0.909609   -2.673982   -0.218483
H    3.356402   -3.131321    0.783525
H    2.827837   -1.750235    1.736259
H    4.887076   -0.794949    0.813312
H    4.734024   -1.753026   -0.656916
N    0.202656    0.908603    0.400516
C    0.042256    1.662628    1.649225
S   -1.046384    1.161836   -0.754568
H    0.240335    2.733041    1.527362
H   -0.979689    1.536741    2.016744
H    0.728285    1.238746    2.386260
O   -1.520531    2.544576   -0.625580
O   -0.543405    0.654503   -2.031084
C   -2.349240    0.082316   -0.154712
C   -3.558752    0.651269    0.246667
C   -4.400720   -1.571247    0.692786
C   -3.183006   -2.123865    0.283899
C   -2.144245   -1.300820   -0.147921
H   -1.195221   -1.728321   -0.459486
H   -3.038602   -3.200231    0.299843
H   -5.204721   -2.221956    1.026031
H   -5.536614    0.239513    0.988447
H   -3.682390    1.728262    0.215544
C   -4.589079   -0.188565    0.673843
0 imaginary frequencies
E = -1260.328932
H = -1260.011556
G = -1260.075980
E_{M06-2X} = -1260.200982
E_{solv} = -1260.349318
```
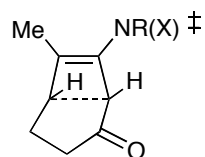
TS9

C	2.031635	0.745909	−1.381755
C	2.314493	0.013612	−0.225104
C	3.296487	0.427593	0.678300
C	4.000775	1.604149	0.419009
C	3.721264	2.350306	−0.727744
C	2.742122	1.920266	−1.627287
S	1.368499	−1.473986	0.124296
O	0.922336	−2.027113	−1.152978
N	−0.029730	−0.936296	0.958278
C	0.181190	−0.568538	2.368680
C	−1.053487	−0.283387	0.223261
C	−1.558991	1.014020	0.567754
C	−2.971915	1.375519	0.881043
O	−3.201678	2.382410	1.538887
C	−1.788719	−0.796302	−0.826070
C	−2.436534	0.368622	−1.364260
C	−3.930392	0.513959	−1.270169
C	−4.134950	0.566869	0.271818
C	−2.114820	−2.223899	−1.158388
O	2.124330	−2.270935	1.091913
H	−1.558033	−2.562328	−2.038819
H	−1.848145	−2.888455	−0.331746
H	−3.183326	−2.343498	−1.376520
H	−1.847952	1.163992	−1.808078
H	−4.481441	−0.322940	−1.715378
H	−4.275772	1.437156	−1.745287
H	−4.125899	−0.454326	0.672806
H	−5.073055	1.043221	0.566229
H	−0.880611	1.772461	0.969868
H	0.769515	0.350552	2.489211
H	0.686796	−1.390376	2.875601
H	−0.801094	−0.414304	2.819833
H	1.285323	0.384621	−2.080911
H	2.537129	2.495469	−2.525668
H	4.273154	3.264905	−0.925874
H	4.771828	1.932844	1.109889
H	3.514870	−0.178244	1.551069

1 imaginary frequency
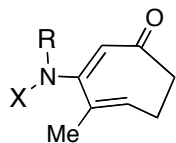E = −1260.274152
H = −1259.959032
G = −1260.023539
E_{M06-2X} = −1260.145252
E_{solv} = −1260.295250

9-*E,E*


```
C     1.768364     1.060684    -1.226215
C     2.229500     0.130430    -0.290451
C     3.301250     0.414340     0.559160
C     3.917542     1.663165     0.471490
C     3.462404     2.606163    -0.452403
C     2.393450     2.304761    -1.300451
S     1.407718    -1.460194    -0.162464
O     0.857253    -1.789643    -1.474670
N     0.072476    -1.192721     0.905212
C     0.418545    -1.181375     2.333972
C    -1.008184    -0.406331     0.452355
C    -1.624322     0.520756     1.256381
C    -2.936206     1.218018     1.040660
O    -3.181232     2.180574     1.758485
C    -1.724151    -0.682333    -0.803145
C    -2.233749     0.450901    -1.345726
C    -3.709251     0.687638    -1.469053
C    -4.062875     0.741861     0.059975
C    -2.232635    -2.077681    -1.077508
O     2.294467    -2.379517     0.551017
H    -1.407759    -2.714659    -1.410579
H    -2.665626    -2.542614    -0.182461
H    -2.989024    -2.068121    -1.868017
H    -1.687980     1.371092    -1.140703
H    -3.942357     1.632120    -1.969764
H    -4.273099    -0.110365    -1.960757
H    -4.913927     1.398242     0.264390
H    -4.333253    -0.275076     0.374903
H    -1.175595     0.824722     2.198333
H     0.874974    -0.233902     2.651126
H     1.106161    -2.001811     2.532308
H    -0.502929    -1.336894     2.899530
H     0.949635     0.803393    -1.889999
H     2.049723     3.036403    -2.025840
H     3.946319     3.576650    -0.517223
H     4.757027     1.895144     1.120463
H     3.654896    -0.339468     1.254326
```
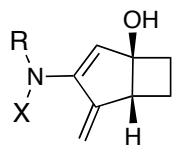0 imaginary frequencies
E = -1260.293844
H = -1259.976672
G = -1260.041250
E_{M06-2X} = -1260.167396
E_{solv} = -1260.314168

10


```
C     4.121249     0.038406     0.293038
C     2.814866     0.692041     0.862435
C     2.435606     1.070515    -0.612966
C     3.870398     0.730162    -1.074152
C     1.373541     0.055296    -0.947599
C     0.965699    -0.625463     0.145968
C     1.726439    -0.226033     1.356247
N    -0.076350    -1.589400     0.250481
C     0.337745    -2.996726     0.433039
C     1.462105    -0.587756     2.617798
O     2.062152     2.397524    -0.939687
S    -1.476710    -1.378004    -0.709717
O    -2.398273    -2.427024    -0.264121
C    -2.055994     0.219079    -0.128399
C    -2.077446     1.298110    -1.012632
C    -2.565890     2.527470    -0.565317
C    -3.027559     2.662058     0.745572
C    -3.010459     1.568362     1.616054
C    -2.526493     0.335656     1.181390
O    -1.160604    -1.251414    -2.139998
H     0.977599    -0.071108    -1.948476
H     2.058269    -0.219774     3.447858
H     0.636110    -1.250404     2.859003
H     3.011445     1.546084     1.515052
H     4.054187    -1.052238     0.247430
H     5.046012     0.309146     0.809311
H     4.448824     1.652231    -1.187412
H     3.976183     0.127053    -1.981121
H     1.096647    -3.015831     1.217266
H    -0.525028    -3.585217     0.744965
H     0.761870    -3.420385    -0.486168
H    -1.725377     1.164394    -2.029594
H    -2.590717     3.375741    -1.243427
H    -3.407537     3.620104     1.089430
H    -3.377694     1.674672     2.632664
H    -2.514775    -0.524542     1.842215
H     1.146760     2.524188    -0.639312
0 imaginary frequencies
E = -1260.299365
H = -1259.982633
G = -1260.046929
E_{M06-2X} = -1260.185003
E_{solv} = -1260.318658
```
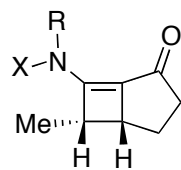
11-*syn*


```
C    1.619327    1.154402   -1.073297
C    1.085609    0.170003   -0.016217
C    2.075147   -0.747922   -0.249109
C    2.702166    0.040825   -1.370138
H    2.581462   -0.401225   -2.369002
H    0.938913    1.344949   -1.911275
C    2.137360    2.487885   -0.531807
H    2.776891    2.346940    0.346068
H    2.725786    2.997511   -1.303715
H    1.303158    3.132250   -0.246873
C    4.193566    0.082509   -0.968685
H    4.385075    0.886481   -0.249330
H    4.876044    0.224776   -1.813412
C    4.388800   -1.293014   -0.267178
H    5.217529   -1.329233    0.445782
H    4.562602   -2.085189   -1.010592
C    3.047093   -1.592222    0.448574
O    2.908283   -2.310320    1.428787
N    0.118060    0.260120    0.959403
C    0.017201   -0.799939    1.983826
S   -1.306865    1.197034    0.729295
H   -0.135575   -0.338912    2.960445
H   -0.816576   -1.477183    1.764301
H    0.945079   -1.375265    1.984306
O   -0.969729    2.275615   -0.197141
O   -1.819572    1.455074    2.072659
C   -2.452047    0.088470   -0.097439
C   -3.389292   -0.614734    0.663042
C   -4.263868   -1.488586    0.015411
C   -4.195689   -1.649842   -1.369596
C   -3.258355   -0.932728   -2.118624
C   -2.378864   -0.056321   -1.485685
H   -1.660930    0.522801   -2.056673
H   -3.216535   -1.050855   -3.197459
H   -4.879114   -2.330773   -1.869016
H   -5.001018   -2.037661    0.593934
H   -3.440157   -0.458456    1.735049
0 imaginary frequencies
E = -1260.316718
H = -1259.998895
G = -1260.063114
E_{M06-2X} = -1260.187291
E_{solv} = -1260.336814
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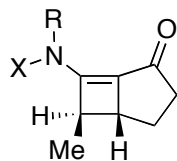
11-anti

C	−1.805436	1.152909	−1.071438
C	−2.130171	2.634793	−1.247729
H	−1.197105	0.791465	−1.908840
H	−1.218976	3.235338	−1.282983
H	−2.684032	2.785621	−2.182135
H	−2.755975	2.996368	−0.423398
C	−1.261919	0.666786	0.280381
C	−2.334074	−0.142811	0.530966
C	−3.020569	0.190037	−0.769079
H	−3.970857	0.734306	−0.683289
C	−3.218089	−1.208950	−1.391531
H	−2.290322	−1.537166	−1.878259
H	−4.021199	−1.262420	−2.134544
C	−3.490221	−2.100462	−0.145780
H	−3.245048	−3.158569	−0.277329
H	−4.549609	−2.046348	0.144969
C	−2.646260	−1.492045	1.009044
O	−2.301145	−2.076526	2.023014
N	−0.113458	0.906150	1.006804
C	0.034684	0.259037	2.324862
S	1.335703	1.469584	0.275997
H	0.505753	−0.725910	2.239577
H	0.626888	0.906822	2.971277
H	−0.963282	0.118459	2.741263
O	0.950440	2.197865	−0.930630
O	2.097853	2.096052	1.353563
C	2.204722	−0.019172	−0.224800
C	3.116979	−0.606431	0.655438
C	3.770364	−1.776579	0.267423
C	3.512604	−2.342434	−0.982837
C	2.605918	−1.737866	−1.857540
C	1.944855	−0.569110	−1.483104
H	1.256899	−0.074301	−2.160064
H	2.418526	−2.172089	−2.835286
H	4.025339	−3.252735	−1.280416
H	4.485271	−2.241047	0.940231
H	3.323179	−0.139525	1.612410

0 imaginary frequencies
E = −1260.317664
H = −1260.000174
G = −1260.065686
E_{M06-2X} = −1260.188873
E_{solv} = −1260.338089

TS12-*trans*
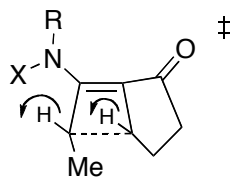
C	−2.374297	1.494509	−0.815174
C	−2.196217	0.070840	−0.528445
C	−3.367627	−0.510504	0.027448
H	−3.775103	−1.442715	−0.348114
C	−4.287735	0.591858	0.520318
H	−4.168796	0.747245	1.601938
H	−5.347832	0.379806	0.345285
C	−3.781671	1.841159	−0.265903
H	−3.732063	2.759089	0.327621
H	−4.439025	2.045836	−1.120141
O	−1.600534	2.287687	−1.329943
C	−1.174094	−0.827991	−0.214575
C	−1.702964	−1.609199	0.878412
H	−1.517619	−2.688509	0.858653
C	−1.798375	−1.070570	2.290649
H	−2.620195	−1.539233	2.844542
H	−1.937026	0.015060	2.309618
H	−0.870022	−1.306146	2.830000
N	−0.042307	−1.112055	−0.969651
C	0.071872	−0.493901	−2.304553
S	1.437220	−1.521418	−0.182193
H	0.960764	−0.884451	−2.799048
H	0.101977	0.599162	−2.243059
H	−0.809405	−0.790170	−2.879829
O	2.257792	−2.182825	−1.196279
O	1.065988	−2.185375	1.067181
C	2.209540	0.045742	0.225019
C	1.822480	0.715985	1.388737
C	2.407155	1.946425	1.683471
C	3.748237	1.807887	−0.329632
C	3.170573	0.576225	−0.638466
C	3.364910	2.492663	0.825162
H	3.816849	3.452134	1.060410
H	4.500622	2.229154	−0.990026
H	3.469533	0.020896	−1.520785
H	1.092929	0.270985	2.056564
H	2.118353	2.476264	2.586542

1 imaginary frequency
E = −1260.275643
H = −1259.960817
G = −1260.024943
E$_{M06-2X}$ = −1260.143031
E$_{solv}$ = −1260.295858

TS12-*cis*
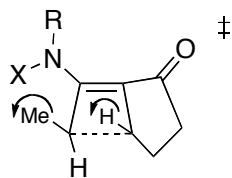
C	3.359195	−0.037812	−0.127109
C	4.044285	1.188905	−0.713449
C	3.361235	2.363937	0.052552
C	2.048888	1.807169	0.658702
C	2.115498	0.360604	0.442699
H	3.847421	1.275450	−1.790440
H	5.132210	1.177422	−0.590090
H	3.142856	3.239944	−0.565751
H	3.999521	2.703410	0.878022
O	1.163927	2.478272	1.167475
C	1.257968	−0.705036	0.178376
C	1.940008	−1.442767	−0.857802
H	2.040632	−0.918043	−1.804460
C	2.028717	−2.943689	−0.947979
H	3.009117	−3.233541	−1.346110
H	1.263973	−3.347471	−1.620597
H	1.898833	−3.415665	0.030944
N	0.142197	−1.110462	0.914197
C	−0.051653	−0.494693	2.242325
S	−1.306157	−1.544849	0.080742
H	−0.889167	−0.985762	2.737559
H	−0.214899	0.586260	2.169988
H	0.856331	−0.677258	2.822453
O	−0.891541	−2.136732	−1.190658
O	−2.117809	−2.280773	1.050190
C	−2.135655	0.006388	−0.277642
C	−3.117204	0.475621	0.597731
C	−3.735504	1.696239	0.326039
C	−3.370537	2.430656	−0.803886
C	−2.391389	1.945497	−1.674618
C	−1.766425	0.726597	−1.417114
H	−1.019358	0.325816	−2.093334
H	−2.117270	2.514503	−2.558239
H	−3.853584	3.381652	−1.009997
H	−4.504250	2.070335	0.995955
H	−3.400065	−0.118185	1.460101
H	3.949652	−0.839871	0.303736

1 imaginary frequency
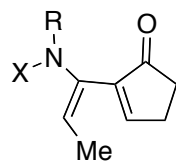E = −1260.281788
H = −1259.966984
G = −1260.031705
E_{M06-2X} = −1260.148871
E_{solv} = −1260.302379

12-*trans*

The starting point for optimization of this molecule was the conformation observed in the X-ray crystal structure of **12c**-*trans*.

C	3.055389	-1.007922	0.134196
C	2.132812	-0.036867	0.270152
C	2.449058	1.072129	-0.674076
C	3.743899	0.702695	-1.406472
C	4.119858	-0.697744	-0.884702
C	0.930662	-0.054657	1.133656
C	0.644315	0.914322	2.022850
C	1.502594	2.099245	2.353401
O	1.797141	2.086342	-0.853904
N	0.104811	-1.229148	1.005508
C	-0.665405	-1.672370	2.176476
H	0.009636	-1.663304	3.035349
S	-0.738143	-1.409814	-0.487058
C	-2.003283	-0.133401	-0.490290
C	-3.318500	-0.486032	-0.177080
C	-4.301234	0.504503	-0.170379
C	-3.963582	1.826349	-0.468384
C	-2.643411	2.164486	-0.776930
C	-1.648650	1.186380	-0.791894
H	-4.731970	2.594782	-0.464475
O	-1.405690	-2.711634	-0.409816
O	0.211000	-1.103577	-1.556651
H	-3.560950	-1.522325	0.032178
H	-5.329684	0.241150	0.060219
H	-2.383747	3.192596	-1.012430
H	-0.622528	1.445829	-1.032065
H	-1.012543	-2.689857	1.997333
H	-1.532005	-1.033936	2.401754
H	4.508329	1.458932	-1.195362
H	3.562760	0.725397	-2.485705
H	4.112282	-1.453722	-1.681214
H	5.122439	-0.734893	-0.438162
H	3.034522	-1.949081	0.676564
H	-0.285065	0.837847	2.582581
H	1.061836	3.021597	1.954333
H	2.510766	2.011936	1.942375
H	1.585795	2.222366	3.440905

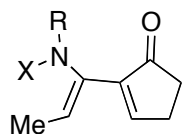0 imaginary frequencies
E = -1260.344986
H = -1260.028199
G = -1260.094237
E_{M06-2X} = -1260.217847
E_{solv} = -1260.365016

12-*cis*

The starting point for optimization of this molecule was the conformation observed in the X-ray crystal structure of **12c**-*cis*.

C	1.444267	1.742189	0.470668
C	2.094339	0.594200	0.172252
C	3.522511	0.930609	-0.134850
C	3.688241	2.448748	0.004317
C	2.302033	2.977658	0.411848
C	1.517682	-0.758656	0.165555
C	2.209868	-1.848096	-0.220632
C	1.720819	-3.260069	-0.261425
O	4.419211	0.166348	-0.444599
N	0.159006	-0.830844	0.653471
C	-0.038926	-1.044950	2.091699
H	0.106929	-2.091533	2.384222
S	-1.099455	-1.310487	-0.369478
C	-2.275575	0.047154	-0.248634
C	-2.064066	1.198139	-1.013493
C	-2.974392	2.249429	-0.919738
C	-4.082943	2.146293	-0.073673
C	-4.290068	0.986534	0.674352
C	-3.386335	-0.074863	0.587597
H	-4.790582	2.968038	-0.006741
O	-0.563519	-1.323570	-1.731292
O	-1.758230	-2.488654	0.211268
H	-1.210556	1.253753	-1.681247
H	-2.824744	3.146024	-1.514701
H	-5.159401	0.900979	1.320121
H	-3.544337	-0.995261	1.139368
H	-1.045860	-0.733454	2.384230
H	0.679932	-0.417619	2.625465
H	4.042744	2.857349	-0.948202
H	4.467173	2.658545	0.745304
H	2.315948	3.493595	1.381812
H	1.898339	3.703243	-0.307524
H	0.389787	1.787580	0.724333
H	3.228243	-1.672066	-0.555286
H	2.459552	-3.929766	0.197079
H	1.602835	-3.584616	-1.303987
H	0.757801	-3.400000	0.235038

0 imaginary frequencies

E = -1260.346014

H = -1260.029128

G = -1260.096424

E_{M06-2X} = -1260.215589

E_{solv} = -1260.367233

TS16-*syn*
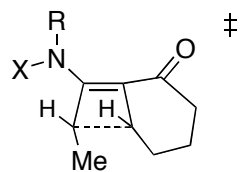
C	−1.486529	−1.830528	0.718794
C	−1.771267	−1.443611	2.152651
H	−2.633422	−1.989164	2.556197
H	−0.904132	−1.707223	2.773975
H	−1.213217	−2.885994	0.617525
C	−0.955262	−0.928313	−0.262237
C	−1.992049	−0.028740	−0.555216
C	−3.164995	−0.760304	−0.194911
H	−3.367828	−1.698333	−0.701439
N	0.218444	−1.151448	−0.979926
C	0.371520	−0.567560	−2.324635
H	−0.515270	−0.842173	−2.902092
H	0.442086	0.523397	−2.283439
H	1.248321	−1.008315	−2.798695
S	1.677684	−1.504753	−0.134063
O	1.287550	−2.161982	1.113770
O	2.557544	−2.155544	−1.105364
C	2.388153	0.090445	0.277364
C	3.353236	0.645275	−0.565627
C	3.882141	1.897793	−0.252985
C	3.447048	2.578554	0.885526
C	2.485972	2.007718	1.723919
C	1.949549	0.756680	1.424845
H	1.217464	0.292457	2.076616
H	2.156844	2.534932	2.614700
H	3.861192	3.554258	1.123826
H	4.636935	2.338557	−0.897795
H	3.692619	0.093318	−1.435291
C	−2.013937	1.397803	−0.885706
O	−1.043140	2.035639	−1.285048
C	−4.358998	−0.051732	0.397224
H	−4.640625	−0.516970	1.354037
H	−5.226543	−0.195254	−0.265881
C	−3.373292	2.058118	−0.638734
H	−3.998096	1.919405	−1.534396
H	−3.207418	3.133833	−0.525868
H	−1.956610	−0.370608	2.259098
C	−4.080476	1.450825	0.587962
H	−5.018679	1.981764	0.785056
H	−3.446186	1.598848	1.472105

1 imaginary frequency
E = −1299.601526
H = −1299.256305
G = −1299.322777
E_{M06-2X} = −1299.460995
E_{solv} = −1299.622224

TS16-*anti*
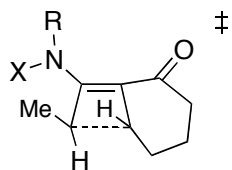
C	1.840487	-0.888882	-1.399101
C	2.292993	-0.130833	-0.315977
C	3.269664	-0.613632	0.556799
C	3.796860	-1.887181	0.341137
C	3.348059	-2.659140	-0.731902
C	2.375283	-2.159670	-1.601699
S	1.583317	1.493778	-0.032124
O	2.481349	2.229749	0.859019
N	0.142593	1.216892	0.870820
C	0.336841	0.713795	2.244025
C	-1.034684	0.886845	0.190550
C	-1.692874	1.715708	-0.778976
C	-1.605845	3.216811	-0.845439
C	-1.961122	-0.121520	0.484348
C	-3.205999	0.464754	0.087551
C	-4.295009	-0.396545	-0.516238
C	-3.798620	-1.833503	-0.752306
C	-3.051665	-2.378147	0.479975
O	1.167514	2.033240	-1.327007
H	-4.669675	0.045225	-1.450166
H	-5.157223	-0.408394	0.169542
H	-3.121829	-1.851960	-1.617397
H	-4.643330	-2.485725	-1.001408
H	-1.951995	1.226697	-1.713958
H	-2.571327	3.631890	-1.161161
H	-0.852753	3.537638	-1.573783
H	-1.341578	3.650012	0.124339
H	1.204984	1.211562	2.676387
H	0.448669	-0.374628	2.262288
H	-0.549290	0.990993	2.820874
H	1.099202	-0.478386	-2.075833
H	2.035731	-2.758602	-2.441838
H	3.760764	-3.650851	-0.894827
H	4.560708	-2.273152	1.009998
H	3.619214	0.008349	1.373602
H	-3.543959	1.354228	0.610490
C	-1.807644	-1.544052	0.798899
H	-3.718913	-2.359912	1.355527
H	-2.731239	-3.415456	0.342578
O	-0.779828	-2.053873	1.237127

1 imaginary frequency
E = -1299.607332
H = -1299.262190
G = -1299.329407
E_{M06-2X} = -1299.466469
E_{solv} = -1299.628295

16-*cis*
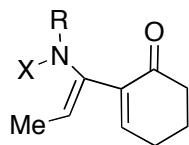
C	3.474660	-0.248720	0.650389
C	2.409314	-0.181083	-0.249322
C	2.111347	-1.246690	-1.103702
C	2.884421	-2.404913	-1.037060
C	3.942850	-2.491964	-0.127834
C	4.239174	-1.415697	0.710102
S	1.409442	1.314455	-0.334742
O	2.199278	2.377518	0.301922
N	0.078432	0.969870	0.648483
C	0.265672	1.117371	2.096281
C	-1.271343	1.062429	0.134326
C	-1.793812	2.251164	-0.225324
C	-1.109701	3.581398	-0.195362
C	-2.001095	-0.237037	0.093807
C	-1.349329	-1.398795	0.354499
C	-1.957137	-2.770973	0.394297
C	-3.478820	-2.732149	0.547912
C	-4.061341	-1.703162	-0.421691
O	0.912025	1.440505	-1.705489
H	0.229324	2.164983	2.417204
H	4.543655	-3.396086	-0.081671
H	1.300830	-1.153385	-1.819050
H	2.667287	-3.236197	-1.701988
H	5.072296	-1.477799	1.404516
H	3.709179	0.609960	1.270206
H	1.223720	0.686731	2.401492
H	-0.531994	0.559678	2.594228
H	-3.915043	-3.722213	0.372277
H	-3.733585	-2.448374	1.577724
H	-1.492309	-3.350078	1.203301
H	-1.686986	-3.301964	-0.534589
H	-0.281170	-1.343940	0.546280
H	-2.815991	2.243572	-0.583678
H	-1.769206	4.333088	0.256883
H	-0.901848	3.917632	-1.220047
H	-0.159183	3.574366	0.343007
C	-3.468036	-0.309857	-0.227996
H	-3.845884	-2.009283	-1.457702
H	-5.147332	-1.607541	-0.334106
O	-4.184653	0.670547	-0.371150

0 imaginary frequencies
E = -1299.656096
H = -1299.308617
G = -1299.377703
$E_{M06-2X} = -1299.518353$
$E_{solv} = -1299.677819$

16-*trans*
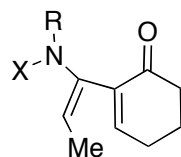
C	−1.918976	1.203990	−0.713282
C	−2.225183	−0.147209	−0.516177
C	−3.538186	−0.580173	−0.314000
C	−4.568547	0.360661	−0.314605
C	−4.280016	1.713110	−0.508606
C	−2.961445	2.131307	−0.705870
S	−0.902093	−1.364627	−0.502474
O	0.072153	−0.990782	−1.528303
N	−0.124372	−1.191694	1.023923
C	−0.943205	−1.649285	2.155340
C	0.709856	−0.030831	1.203476
C	0.425612	0.900796	2.130062
C	1.299713	2.058326	2.512647
C	1.945478	−0.011904	0.363505
C	2.826773	−1.032655	0.410528
C	4.084721	−1.116437	−0.404314
C	4.512427	0.249696	−0.951707
C	3.311607	0.974344	−1.568790
O	−1.514907	−2.695436	−0.488728
H	−0.301885	−1.666447	3.039542
H	−5.084996	2.443179	−0.509459
H	−3.739155	−1.637571	−0.180284
H	−5.594897	0.035458	−0.169242
H	−2.739857	3.183566	−0.859665
H	−0.893625	1.525377	−0.866051
H	−1.295167	−2.658670	1.942032
H	−1.809364	−1.003659	2.360061
H	4.921551	0.854733	−0.131333
H	5.313147	0.134509	−1.691098
H	3.905124	−1.818397	−1.235764
H	4.885098	−1.568599	0.195744
H	2.603736	−1.877842	1.060323
H	−0.513708	0.820097	2.672401
H	0.900795	2.997200	2.108124
H	2.320222	1.946650	2.137589
H	1.345731	2.164739	3.603950
H	3.566686	1.972332	−1.937674
C	2.148667	1.112804	−0.597011
H	2.930144	0.398440	−2.425967
O	1.393845	2.075163	−0.649004

0 imaginary frequencies

E = −1299.659406

H = −1299.312227

G = −1299.380068

E_{M06-2X} = −1299.524597

E_{solv} = −1299.679712

Complete Citation for Reference 11

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, and D. J. Fox, Gaussian 09, Revision D.01, Gaussian, Inc., Wallingford CT, 2013.