Causation in a Cascade: The Origins of Selectivities in Intramolecular Nitrone Cycloadditions

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SUPPORTING INFORMATION

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Calculated Geometries and Energies

The B3LYP/6-31+G(d) geometry of the lowest-energy conformer of each species is reported below, along with the following energies:
B3LYP/6-31+G(d) electronic energy (E)
B3LYP/6-31+G(d) zero-point energy (ZPE)
B3LYP/6-31+G(d) free energy at 298.15 K and 1 atm (G)
M06-2X/6-311+G(d,p) single-point electronic energy ($E_{M06-2X,LBS}$)
M06-2X/6-31+G(d) single-point electronic energy (E_{M06-2X})
M06-2X/6-31+G(d) single-point energy in methanol ($E_{M06-2X,MeOH}$)
M06-2X/6-31+G(d) single-point energy in chlorobenzene ($E_{M06-2X,PhCl}$)

All energies are in Hartree.

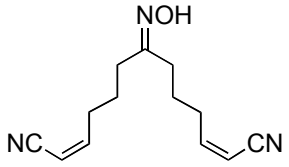
To explore the effect of basis set size, B3LYP and M06-2X energies were computed with both the 6-31+G(d) and 6-311+G(d,p) basis sets for the cycloadducts **4**–**6** and the transition states leading to them (**TS-4**–**TS-6**). Results are given in Table S1. With B3LYP, the larger basis set give poorer estimates of thermodynamics and kinetics than the smaller basis set does. With M06-2X, the smaller basis set gives values of Δ*G* within 1.1 kcal/mol of the larger basis set values, while the $\Delta G^{\ddagger}$ values agree to within 0.3 kcal/mol.

Table S1. Effect of functional and basis set size on the computed thermodynamics and kinetics for intramolecular 1,3-dipolar cycloadditions of **3** to give **4**, **5**, or **6**. [a]

	Δ*G*			$\Delta G^{\ddagger}$		
	4	**5**	**6**	**TS-4**	**TS-5**	**TS-6**
B3LYP/6-31+G(d)	7.9	4.0	–2.1	26.3	31.0	31.6
B3LYP/6-311+G(d,p)	9.6	5.8	–0.2	26.7	31.3	31.9
M06-2X/6-31+G(d)	–7.9	–11.3	–19.0	20.7	24.5	23.3
M06-2X/6-311+G(d,p)	–7.0	–10.2	–18.1	21.0	24.5	23.2

[a] Δ*G* and $\Delta G^{\ddagger}$ in kcal/mol, computed from the electronic energy at the stated level of theory in conjunction with the B3LYP/6-31+G(d) thermochemical corrections. The B3LYP/6-31+G(d) optimized geometries are used throughout.

Oxime 2



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H	2.194914	0.205968	-1.061627
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C	3.567670	0.180896	0.615665
H	3.760678	0.793033	1.509661
H	3.292145	-0.821119	0.965295

C	4.822937	0.118701	-0.200567
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H	-3.509265	-2.186703	1.495387
C	-5.321407	-1.518749	0.722098
H	-5.897208	-2.007232	1.504385
C	-6.084413	-0.797592	-0.250326
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H	0.498766	4.437163	0.163564

0 imaginary frequencies

E = -745.011704

ZPE = 0.281297

G = -744.782926

$E_{M06\text{-}2X,LBS}$ = -744.866714

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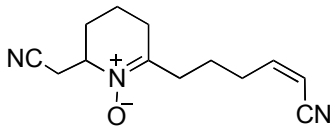
$E_{M06\text{-}2X,PhCl}$ = -744.720249

Nitrone 3



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H	1.286626	1.007556	1.573510
C	-0.783827	2.042939	0.276150
H	-0.935672	2.532491	1.252299
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H	5.832324	-1.316078	-1.672473
C	5.821184	0.323751	-0.297111
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N	-6.123313	-0.897967	-0.651738

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G = -744.791436
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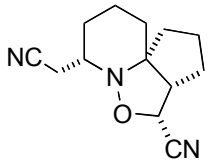
Cycloadduct 4



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H	3.424003	0.748708	-0.928415
H	2.259491	0.769991	-2.251083
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H	1.989401	2.223983	0.437875
H	2.183571	2.944256	-1.145920
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H	-0.213624	3.039203	-0.347094
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H	0.370850	1.520599	1.814127

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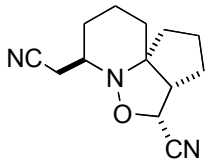
Cycloadduct 5



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H	0.163525	-1.942364	1.737728
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H	2.381498	-2.714754	0.959334
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N	3.394855	2.900245	0.108546
C	-3.811119	1.334841	0.430066
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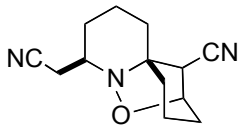
Cycloadduct 6

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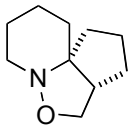
Model of cycloadduct 4 after replacement of CN and CH_2CN groups by H



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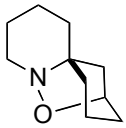
Model of cycloadduct 6 after replacement of CN and CH_2CN groups by H



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H	3.152301	-2.047509	-1.713955
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H	0.715556	0.666225	1.670015
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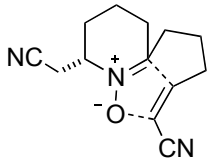
TS-4



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C	1.748179	-0.981379	1.369639
H	1.877216	0.008353	1.815076
H	1.533635	-1.694081	2.178781
C	3.001569	-1.387307	0.587771
H	2.942478	-2.442761	0.293325
H	3.901491	-1.286810	1.204223
C	3.067889	-0.470872	-0.657301
H	3.561160	-0.979199	-1.493982
H	3.676954	0.408378	-0.423592
C	1.668306	-0.014585	-1.072379
H	1.216129	-0.535593	-1.915506
C	1.298141	1.344162	-0.952307
H	0.491638	1.738721	-1.563032
C	2.169094	2.339625	-0.416407
N	2.884185	3.159008	0.002707

C	0.081149	-2.312422	-0.053254
C	-2.235391	-1.410295	-0.250598
H	-0.113476	-2.926669	0.839889
H	0.902266	-2.808335	-0.581773
H	-3.153670	-1.362874	-0.846055
H	-2.505665	-1.842739	0.723457
C	-1.173265	-2.274072	-0.927608
H	-1.545800	-3.291777	-1.090833
H	-0.936979	-1.861222	-1.918154

1 imaginary frequency

E = -744.991595

ZPE = 0.285052

G = -744.749465

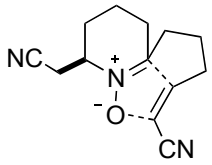
$E_{M06\text{-}2X,LBS}$ = -744.856490

$E_{M06\text{-}2X}$ = -744.671049

$E_{M06\text{-}2X,MeOH}$ = -744.720498

$E_{M06\text{-}2X,PhCl}$ = -744.711355

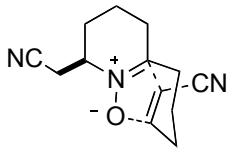
TS-5



N	-0.312361	-0.049455	0.932415
O	0.233774	1.091212	1.231923
C	-1.787733	-0.008918	0.741168
C	-2.168000	1.067645	-0.313906
H	-2.175230	0.341864	1.702815
C	0.533178	-0.971175	0.358634
C	1.870600	-1.200431	1.060643
H	2.149453	-0.291859	1.600277
H	1.761119	-2.010404	1.795277
C	2.913615	-1.542405	-0.006501
H	2.752418	-2.559332	-0.385332
H	3.926438	-1.521839	0.409245
C	2.747893	-0.497565	-1.140378
H	2.919393	-0.951485	-2.122719
H	3.502103	0.286977	-1.025088
C	1.349077	0.134348	-1.097183
H	0.678313	-0.142405	-1.910696
C	1.194452	1.473355	-0.650735
H	0.367331	2.074383	-1.010523
C	2.274044	2.227364	-0.107079
N	3.161011	2.847244	0.327125
C	-0.092867	-2.240711	-0.213092
C	-2.347057	-1.401883	0.435232
H	-0.043139	-3.023808	0.559068
H	0.535801	-2.594211	-1.037471
H	-3.407380	-1.311060	0.175816
H	-2.296567	-2.011772	1.346796
C	-1.542948	-2.081833	-0.673377
H	-1.967215	-3.064658	-0.907845
H	-1.591625	-1.495676	-1.601102
C	-3.616531	1.265697	-0.381623
H	-1.695152	2.013177	-0.030547

```
H   -1.808363    0.795317   -1.312869
N   -4.769254    1.401664   -0.426870
1 imaginary frequency
E = -744.985133
ZPE = 0.285520
G = -744.742043
```
$E_{M06\text{-}2X,LBS}$ = -744.851822
$E_{M06\text{-}2X}$ = -744.666002
$E_{M06\text{-}2X,MeOH}$ = -744.716433
$E_{M06\text{-}2X,PhCl}$ = -744.707118

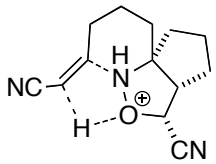
TS-6




```
O    0.518148   -1.225385    0.427785
N    0.575643    0.103332    0.542839
C   -0.608424    0.726817    0.635138
C   -0.678466    2.229694    0.493572
C   -1.235972   -0.385461   -1.366519
C   -1.727214    0.124720    1.474996
C    0.459003    2.839262   -0.329636
H   -1.655685    2.476239    0.060991
H   -0.681751    2.663066    1.506954
C    1.793552    2.208914    0.072223
H    0.280093    2.665103   -1.398660
H    0.483068    3.925054   -0.184389
C    1.743345    0.695686   -0.150136
H    2.617388    2.621115   -0.522307
H    2.017217    2.422706    1.127484
H    1.615388    0.489364   -1.221992
C    3.035292   -0.001069    0.341513
C   -2.550079    0.144918   -1.417226
H   -0.593310   -0.040835   -2.175389
C   -0.899927   -1.610824   -0.730513
H   -2.664236    0.544004    1.092135
C   -1.850987   -1.405587    1.610497
H   -1.606606    0.550201    2.485086
H   -2.777549   -1.610783    2.161845
C   -1.883747   -2.181943    0.271163
H   -1.026590   -1.781534    2.220153
H   -0.259884   -2.301030   -1.271649
H   -1.661063   -3.236103    0.465351
H   -2.891985   -2.140729   -0.161255
N   -3.617736    0.620169   -1.465776
H    2.978620   -0.166740    1.423284
C    3.339616   -1.270115   -0.327414
H    3.882302    0.672143    0.159982
N    3.639727   -2.243246   -0.885041
1 imaginary frequency
E = -744.984297
ZPE = 0.285420
G = -744.741110
```
$E_{M06\text{-}2X,LBS}$ = -744.854049

$E_{M06\text{-}2X} = -744.668052$
$E_{M06\text{-}2X,MeOH} = -744.718916$
$E_{M06\text{-}2X,PhCl} = -744.709692$

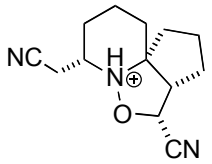
Lowest-energy TS located for formation of 8 (corresponding to a Cope elimination reaction of protonated 4)



C	-1.884116	1.704750	-0.607109
C	-2.361778	0.404209	-0.759546
C	-2.695801	-0.622352	0.295371
C	-2.158726	-2.071739	0.048378
C	-0.622581	-2.389720	0.228513
C	0.234836	-1.144189	-0.065139
N	-0.411588	-0.612793	-1.278038
O	0.333961	0.525911	-1.661481
C	0.299049	-0.232819	1.202706
C	1.741751	-1.138404	-0.480241
H	-0.365350	-3.226154	-0.434347
H	-0.416937	-2.726418	1.248023
H	-2.711044	-2.738981	0.717026
H	-2.460025	-2.362976	-0.965848
H	-2.460345	-0.250485	1.293893
H	-3.794261	-0.699932	0.263455
H	-2.699829	0.149455	-1.762624
H	-2.061858	2.407774	-1.422757
C	-1.697670	2.302978	0.685974
H	-0.340372	1.304716	-1.171372
H	-0.342533	-1.261647	-2.066290
N	-1.527095	2.781221	1.732710
H	0.384877	0.827205	0.956722
H	-0.573783	-0.331846	1.843424
H	1.996127	-1.938408	-1.182684
C	1.828279	0.220408	-1.267626
H	2.293534	0.118233	-2.249674
C	2.355777	1.391682	-0.590741
N	2.806677	2.328649	-0.074597
C	1.581621	-0.699944	1.928540
H	1.998320	0.110336	2.531598
H	1.354707	-1.520968	2.616243
C	2.561562	-1.184406	0.822831
H	2.888836	-2.213165	0.998243
H	3.469074	-0.576299	0.766825

1 imaginary frequency
E = -745.266209
ZPE = 0.295115
G = -745.012184
$E_{M06\text{-}2X,LBS} = -745.146619$

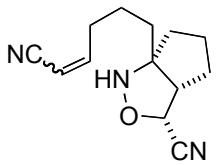
Protonated 4



C	2.061569	-1.282910	0.326727
C	1.802631	-0.046564	-0.556175
C	2.208581	1.305940	0.073380
C	1.398892	2.484872	-0.495230
C	-0.125144	2.376958	-0.195911
C	-0.600777	0.908883	-0.074587
N	0.328656	0.090801	-0.962406
O	-0.293315	-1.160991	-1.213331
C	-0.720567	0.391385	1.376469
C	-1.972984	0.538768	-0.686078
H	-0.691932	2.901185	-0.974088
H	-0.358139	2.878663	0.747713
H	1.781481	3.420333	-0.078046
H	1.569334	2.559024	-1.578960
H	2.088709	1.254105	1.161081
H	3.276237	1.450748	-0.114480
H	2.317229	-0.192050	-1.511093
H	1.692273	-2.192510	-0.157263
C	3.506663	-1.406883	0.542780
H	1.567846	-1.195576	1.299274
H	0.349926	0.571430	-1.871105
N	4.654352	-1.472823	0.698090
H	-0.613912	-0.697326	1.407509
H	0.027722	0.823764	2.045204
H	-2.203447	1.138498	-1.572322
C	-1.757010	-0.939570	-1.158710
H	-2.136662	-1.094005	-2.173042
C	-2.301440	-1.979106	-0.281661
N	-2.745012	-2.798499	0.409490
C	-2.165950	0.778576	1.771369
H	-2.560883	0.085573	2.518037
H	-2.187876	1.776548	2.220315
C	-2.994862	0.762549	0.452358
H	-3.507024	1.715987	0.296560
H	-3.767952	-0.010201	0.456745

0 imaginary frequencies
E = -745.365996
ZPE = 0.303343
G = -745.105365
$E_{M06-2X,LBS}$ = -745.246330

Bicyclic intermediate 8



C	-0.898559	0.018058	0.223377
C	-2.120910	0.394783	-0.710763
C	-2.657805	1.754365	-0.207080

C	-1.475927	2.371701	0.559687
C	-0.862164	1.159304	1.272146
H	0.145080	1.343809	1.658908
H	-1.490150	0.864689	2.121019
H	-0.753712	2.818303	-0.137876
H	-1.786956	3.161160	1.252383
H	-3.027663	2.382008	-1.024168
H	-3.494420	1.598015	0.484626
H	-1.812924	0.456873	-1.759938
N	-1.265818	-1.274794	0.853978
H	-0.959269	-2.041227	0.242131
O	-2.697180	-1.331872	0.802530
C	-3.042825	-0.826465	-0.506880
H	-2.821826	-1.603753	-1.256717
C	-4.484289	-0.562597	-0.549783
N	-5.624766	-0.358880	-0.620736
C	0.417624	-0.138091	-0.561369
C	1.615761	-0.662794	0.248163
H	0.241595	-0.808011	-1.418012
H	0.674485	0.839271	-0.991614
H	1.825604	0.008879	1.088777
H	1.379421	-1.640224	0.689412
C	2.882709	-0.785535	-0.625524
H	2.673801	-1.474740	-1.458683
H	3.126414	0.186118	-1.071277
C	4.057212	-1.312851	0.142739
H	3.936216	-2.293605	0.602982
C	5.236910	-0.691803	0.329626
H	6.026666	-1.160657	0.911361
C	5.542385	0.599319	-0.206929
N	5.809775	1.649916	-0.632959

0 imaginary frequencies

E = -745.010868

ZPE = 0.285926

G = -744.771054

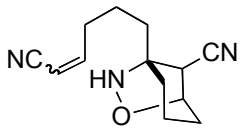
$E_{M06\text{-}2X,LBS}$ = -744.880232

$E_{M06\text{-}2X}$ = -744.693248

$E_{M06\text{-}2X,MeOH}$ = -744.746096

$E_{M06\text{-}2X,PhCl}$ = -744.736184

Bicyclic intermediate 9



C	-2.229905	0.515772	-0.934816
C	-1.074169	-0.195052	-0.150453
N	-1.396684	-1.618131	-0.403010
H	-1.069166	-1.855296	-1.344230
O	-2.855501	-1.691465	-0.570890
H	-2.081352	0.356950	-2.011415
C	-3.402425	-0.362731	-0.447591
H	-4.269406	-0.321105	-1.113355
C	-3.765019	-0.067230	1.011747
H	-4.632343	-0.674106	1.295952
H	-4.065087	0.985388	1.100336

C	-2.369840	1.949707	-0.712526
N	-2.464947	3.096847	-0.550740
C	-2.569190	-0.393786	1.926038
H	-2.729065	0.028390	2.924850
H	-2.509560	-1.481076	2.042884
C	-1.226873	0.109168	1.357704
H	-1.125763	1.192948	1.500332
H	-0.407302	-0.365206	1.906633
C	0.316843	0.148142	-0.709167
C	1.484829	-0.683234	-0.151489
H	0.288997	0.034974	-1.804400
H	0.504378	1.212983	-0.518298
H	1.586980	-0.517622	0.927021
H	1.282473	-1.754193	-0.282870
C	2.818460	-0.319030	-0.838679
H	2.715225	-0.483762	-1.922661
H	3.035751	0.746473	-0.698916
C	3.960177	-1.153411	-0.340407
H	3.859894	-2.232426	-0.459272
C	5.086532	-0.706800	0.246052
H	5.854181	-1.402359	0.576205
C	5.363708	0.678171	0.476378
N	5.611119	1.798806	0.675404

0 imaginary frequencies

E = -745.017746

ZPE = 0.286559

G = -744.776971

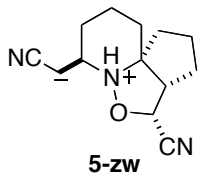
$E_{M06\text{-}2X,LBS}$ = -744.889860

$E_{M06\text{-}2X}$ = -744.702685

$E_{M06\text{-}2X,MeOH}$ = -744.753481

$E_{M06\text{-}2X,PhCl}$ = -744.744223

Zwitterion 5-zw (Optimized in methanol)



5-zw

O	0.208098	1.348368	0.303266
N	-0.488377	0.172289	-0.089760
C	0.575182	-0.888520	-0.233008
C	1.744303	-0.096238	-0.905657
C	1.298759	1.386938	-0.671972
C	3.048855	-0.566164	-0.208254
C	2.621640	-1.706217	0.740316
C	1.175846	-1.349477	1.115895
C	-1.752623	-0.179938	0.811629
C	-2.351628	-1.368581	0.030205
C	-1.365293	-2.505450	-0.304681
C	-0.089634	-2.020463	-1.026259
C	-2.642426	0.975847	1.021359
C	-3.549026	1.404290	0.073264
N	-4.353624	1.773723	-0.723783
C	2.303215	2.309971	-0.141605
N	3.099742	3.064041	0.238699
H	-1.280596	-0.519223	1.812156

H	-3.177820	-1.763339	0.637885
H	-2.799174	-0.982979	-0.900849
H	-1.088851	-3.030004	0.618951
H	-1.874936	-3.242691	-0.938475
H	0.624215	-2.847748	-1.148275
H	-0.337611	-1.652394	-2.034897
H	1.774048	-0.277125	-2.053307
H	1.172976	-0.514029	1.831491
H	0.630026	-2.184621	1.569312
H	3.271349	-1.788809	1.619123
H	2.650220	-2.672348	0.219587
H	3.500198	0.246452	0.373424
H	3.797651	-0.886639	-0.940189
H	0.895988	1.830870	-1.623478
H	-2.429306	1.652753	1.848144
H	-0.900356	0.398580	-1.100219

0 imaginary frequencies

E = -744.932752

ZPE = 0.284474

G = -744.689927

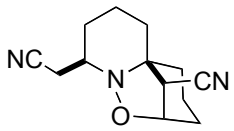
$E_{M06\text{-}2X,LBS}$ = -744.810299

$E_{M06\text{-}2X}$ = -744.624894

$E_{M06\text{-}2X,MeOH}$ = -744.729650

$E_{M06\text{-}2X,PhCl}$ = -744.709866

Cycloadduct 10



C	2.569507	-1.664792	-0.171300
C	1.230148	-1.454453	0.538892
C	1.041893	0.012221	0.991916
C	0.716263	0.635288	-0.409706
C	2.005948	0.580908	-1.273862
C	2.586360	-0.833162	-1.466857
O	0.153181	-1.641175	-0.410979
N	-0.259452	-0.341926	-0.946682
C	0.178375	2.080401	-0.393711
C	-1.306554	2.212372	-0.044362
C	-2.121718	1.264187	-0.929420
C	-1.712497	-0.197162	-0.694712
C	2.169354	0.603263	1.703120
N	3.046575	1.098976	2.282777
H	-2.190726	-0.828407	-1.452279
H	0.804702	2.671642	0.285321
H	0.330629	2.500502	-1.395962
H	-1.482937	2.001784	1.018888
H	-1.624933	3.249362	-0.202701
H	-3.197310	1.363997	-0.746618
H	-1.953769	1.515528	-1.984653
C	-2.221125	-0.734039	0.683047
H	0.171421	0.092398	1.650777
H	2.746767	1.239915	-0.801666
H	1.774590	1.011461	-2.254267
H	3.606710	-0.761624	-1.860943

H	1.987244	-1.355235	-2.219729
H	1.062534	-2.171476	1.348626
H	2.691751	-2.728873	-0.403487
H	3.388030	-1.386302	0.504996
C	-3.679655	-0.861275	0.690839
H	-1.782706	-1.719831	0.863892
H	-1.938038	-0.083063	1.517433
N	-4.838151	-0.949182	0.674893

0 imaginary frequencies

E = -745.032108

ZPE = 0.289143

G = -744.783947

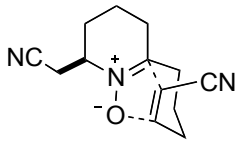
$E_{M06\text{-}2X,LBS}$ = -744.915261

$E_{M06\text{-}2X}$ = -744.730603

$E_{M06\text{-}2X,MeOH}$ = -744.774491

$E_{M06\text{-}2X,PhCl}$ = -744.766563

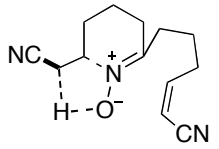
TS-10



C	-1.772008	-0.090746	-0.695107
N	-0.307542	-0.206833	-0.888734
C	0.591118	0.746228	-0.603941
C	0.123393	2.154443	-0.312985
C	-1.337416	2.255896	0.133231
C	-2.208978	1.377501	-0.768483
O	0.155373	-1.462868	-0.853612
C	1.995802	0.665807	-1.191537
C	2.633671	-0.711498	-1.454060
C	2.640816	-1.671127	-0.239294
C	1.346501	-1.578262	0.544931
C	1.149690	-0.418977	1.351452
C	2.204058	0.424363	1.782754
N	3.044756	1.153350	2.143248
H	-2.204729	-0.646515	-1.533378
H	0.803137	2.579516	0.435755
H	0.274201	2.752170	-1.226077
H	-1.435187	1.949371	1.182438
H	-1.667742	3.299324	0.085420
H	-3.269327	1.444596	-0.501251
H	-2.123263	1.721075	-1.807803
C	-2.219927	-0.814154	0.604402
H	0.288056	-0.403667	2.016005
H	2.645926	1.268040	-0.547907
H	1.945872	1.207667	-2.150268
H	3.667854	-0.539254	-1.777610
H	2.115658	-1.194159	-2.285959
H	0.889207	-2.507346	0.875501
H	2.799781	-2.694736	-0.593653
H	3.477084	-1.428662	0.428865
C	-3.672852	-0.989080	0.640186
H	-1.742283	-1.798705	0.639700
H	-1.915007	-0.259522	1.497774
N	-4.827992	-1.110604	0.651494

1 imaginary frequency
E = -744.983267
ZPE = 0.285886
G = -744.739110
$E_{M06-2X,LBS}$ = -744.854647
E_{M06-2X} = -744.668267
$E_{M06-2X,MeOH}$ = -744.716841
$E_{M06-2X,PhCl}$ = -744.708108

TS-2Z

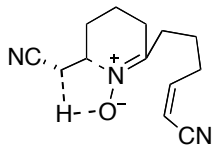


C	-2.871875	0.509443	-1.494978
H	-1.325744	1.723271	-0.733905
C	-2.058885	0.980894	-0.411532
C	-2.531775	1.229439	1.004662
H	-3.194241	0.419187	1.334003
H	-3.138266	2.144377	0.996106
C	-1.339131	1.408327	1.960905
H	-0.679830	2.192209	1.564326
H	-1.690863	1.763854	2.936205
C	-0.525367	0.121076	2.179779
H	-1.048850	-0.537358	2.891321
H	0.437064	0.356717	2.653985
C	-0.278266	-0.712444	0.944728
N	-0.899614	-0.382720	-0.127162
O	-0.854067	-1.118695	-1.242266
H	-1.716937	-0.676888	-1.727755
C	0.609195	-1.930104	1.023475
H	0.294328	-2.654008	0.265225
H	0.466184	-2.390768	2.009406
C	2.112557	-1.606793	0.851563
H	2.428499	-0.885991	1.616917
H	2.678189	-2.528467	1.040775
C	2.469143	-1.053887	-0.546077
H	2.174838	-1.790289	-1.306049
H	1.892909	-0.144792	-0.747029
C	3.935907	-0.769209	-0.676244
H	4.604724	-1.628977	-0.711644
C	4.502958	0.451101	-0.730043
H	5.580712	0.565566	-0.813949
C	3.746878	1.665081	-0.670993
N	3.141436	2.658401	-0.609638
H	-2.793046	1.028533	-2.446851
C	-4.112306	-0.135465	-1.226710
N	-5.112011	-0.697305	-0.996650

1 imaginary frequency
E = -744.975908
ZPE = 0.280268
G = -744.743258
$E_{M06-2X,LBS}$ = -744.837299
E_{M06-2X} = -744.646320

$E_{M06\text{-}2X,MeOH}$ = -744.705333
$E_{M06\text{-}2X,PhCl}$ = -744.694555

TS-2E



C	0.929036	-1.498554	-1.684861
C	2.313236	-0.905094	-1.329234
C	2.284183	0.619815	-1.077462
C	3.644821	1.152841	-0.731290
C	4.107149	1.362354	0.516268
C	3.324078	1.092122	1.683498
N	2.693463	0.850668	2.632819
C	-0.097806	-1.310747	-0.594760
N	-1.003507	-0.404791	-0.655037
O	-1.152089	0.397058	-1.713801
C	-0.131803	-2.257719	0.581584
C	-1.153257	-1.920965	1.682939
C	-2.503143	-1.405522	1.150743
C	-2.347005	-0.041902	0.511963
C	-3.335032	0.601371	-0.300763
H	-4.129734	-0.008853	-0.729291
H	-2.144800	0.748783	-1.476535
C	-3.657284	1.966465	-0.062495
H	-1.799712	0.649132	1.156750
H	-2.952761	-2.112775	0.440222
H	-3.209085	-1.303517	1.985000
H	-0.727547	-1.161557	2.351677
H	-1.308134	-2.817320	2.294413
H	-0.345529	-3.253677	0.161208
H	0.874166	-2.333906	1.015232
H	0.556365	-1.049337	-2.610269
H	1.051382	-2.575794	-1.858482
H	2.999963	-1.134055	-2.154157
H	2.716679	-1.406526	-0.440518
H	1.906906	1.128306	-1.973349
H	1.582991	0.842558	-0.265739
H	4.324987	1.362348	-1.556008
H	5.113169	1.735438	0.689649
N	-3.912190	3.095193	0.108478

1 imaginary frequency
E = -744.973706
ZPE = 0.280337
G = -744.741112
$E_{M06\text{-}2X,LBS}$ = -744.835077
$E_{M06\text{-}2X}$ = -744.644068
$E_{M06\text{-}2X,MeOH}$ = -744.704372
$E_{M06\text{-}2X,PhCl}$ = -744.693443

Comparison of B3LYP and M06-2X Geometries for Selected Species

The geometries of cycloadducts **4**–**6** and transition states **TS-4**–**TS-6** were optimized with M06-2X/6-31+G(d), for comparison with the B3LYP/6-31+G(d) geometries. Results are shown in Figures S1 and S2.

For cycloadducts **4**–**6**, the M06-2X geometries differ only slightly from the B3LYP geometries. The newly-formed C–O and C–C bond lengths change by ≤0.02 Å. M06-2X single-point energies (values in square brackets) give values of ΔG that are 0.3–0.7 kcal/mol more negative when the M06-2X geometries are used than when the B3LYP geometries are used. These margins are small when compared to the differences between the B3LYP and M06-2X//B3LYP reaction energies, which amount to 15–17 kcal/mol.

For transition states **TS-4**–**TS-6**, most of the forming bond lengths change by 0.05–0.07 Å when the geometry is re-optimized with M06-2X. Additionally, for **TS-4**, the sense of asynchronicity reverses. The values of $\Delta G^{\ddagger}$ predicted from the M06-2X-optimized geometries are 0.5–1.4 kcal/mol lower than those obtained from M06-2X single-point calculations on the B3LYP geometries. In comparison, on going from B3LYP to M06-2X//B3LYP there is a 5.6–8.3 kcal/mol reduction in the barriers. The predicted kinetic product is the same in all cases.

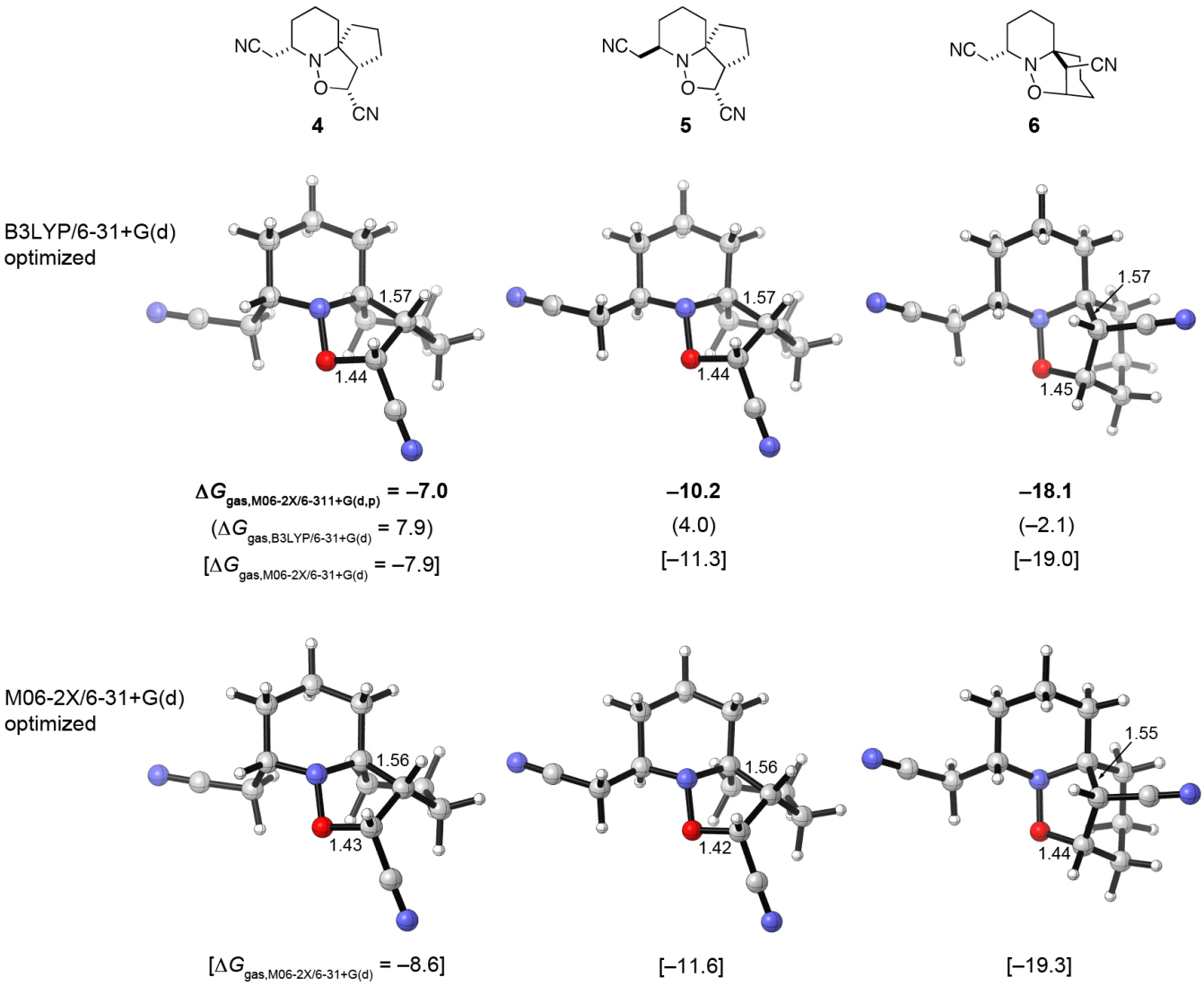


Figure S1. Calculated structures of the tricyclic products **4**, **5**, and **6**, optimized at the B3LYP/6-31+G(d) and M06-2X/6-31+G(d) levels. Gibbs free energies relative to the nitrone **3** are shown (kcal/mol). Bond lengths are in Å.

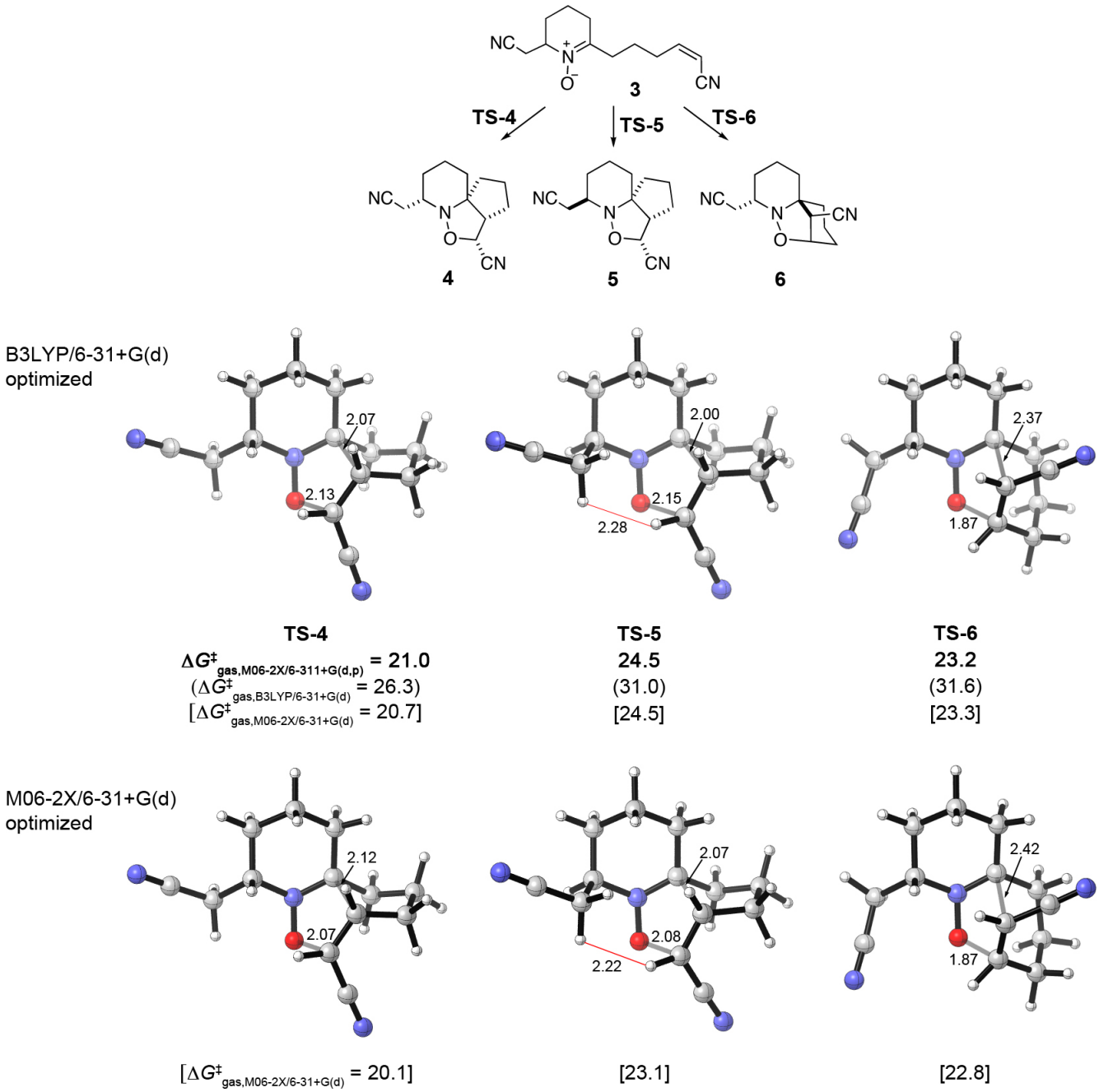


Figure S2. Calculated transition structures for intramolecular 1,3-dipolar cycloadditions of the nitrone **3** leading to the tricyclic species **4**, **5**, and **6**, optimized at the B3LYP/6-31+G(d) and M06-2X/6-31+G(d) levels. Gibbs free energies relative to the nitrone **3** are shown (kcal/mol). Bond lengths are in Å.

Complete Citation for Ref. 7

M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, 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, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople, Gaussian 03, Revision E.01, Gaussian, Inc., Wallingford CT, 2004.

Complete Citation for Ref. 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, 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 A.02, Gaussian, Inc., Wallingford CT, 2009.