# A Computational Study of the Origin of Stereoinduction in NHC-Catalyzed Annulation Reactions of α,β-Unsaturated Acyl Azoliums

*Eirik Lyngvi, Jeffrey W. Bode and Franziska Schoenebeck**

*Contribution from the Laboratory of Organic Chemistry, ETH Hönggerberg, CH-8093 Zürich, Switzerland. E-mail : schoenebeck@org.chem.ethz.ch*

**Full reference 8 for Gaussian09**

Gaussian 09, Revision A.01, 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, Inc., Wallingford CT, 2009.

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## Computational Details

All QM calculations were performed with the Gaussian09 suite of programs. All gas phase and solution phase B3LYP or ωB97XD optimized stationary points were verified as minima or first-order saddle points by calculation of the full Hessian in Gaussian09. Solution phase optimizations were carried out involving a CPCM dielectric continuum solvent model for toluene using UAO radii. CPCM (toluene) M06-2X/6-31++G(d,p)[1] energies were calculated on solution-phase-optimized geometries and also use ωB97XD or B3LYP enthalpy corrections at 313.15 K. PBE1PBE energies were also calculated and D3-dispersion correction was applied.[2]

We performed molecular mechanics based conformational searches [using the OPLS-AA force field as implemented in MacroModel (©Schrodinger, Inc.)]. For the protonated hemiacetals, all conformers obtained within an 8 kcal/mol energy range were then optimized with B3LYP/6-31G(d). The lowest energy conformers were subsequently optimized using an implicit solvation model (CPCM, for toluene) and the B3LYP or ωB97XD functionals with 6-31G(d) basis set and further refined through additional manual conformational search. CPCM (toluene) M06-2X/6-31++G(d,p) energies were calculated and corrected for 313.15 K. Conformational searches of TSs were done analogously, and the forming/breaking bonds of the TS geometries were frozen for that. The TS conformers were subsequently optimized at DFT level (analogously to the description above) without any constraints and verified as true TSs.

Figures were created with: CYLview, 1.0b; Legault, C. Y., Université de Sherbrooke, 2009 (http://www.cylview.org).

[1] Y. Zhao, D. G. Truhlar, *Theor. Chem. Acc.* **2008**, *120*, 215; (b) Y. Zhao, D. G. Truhlar, *Acc. Chem. Res.* **2008**, *41*, 157.
[2] (a) S. Grimme, *J. Comput. Chem.* **2006**, *27*, 1787; (b) http://toc.uni-muenster.de/DFTD3/

**XYZ coordinates and Energies:**

# Acyl Azolium 8

***Z-isomer (B3LYP/6-31G(d) gas-phase optimized)***

C -1.992720 -1.868184 -0.564017
N 0.087258 -1.818300 -0.171578
C -0.264115 -0.538526 -0.375423
N -0.989279 -2.662356 -0.294034
C 1.374526 -2.359780 0.207650
C 2.079230 -3.116111 -0.744579
C 1.827163 -2.159575 1.521331
C 3.304858 -3.652798 -0.346365
C 3.059872 -2.724861 1.859449
C 3.815287 -3.466491 0.944868
C 1.542362 -3.358961 -2.135330
C 1.027211 -1.391213 2.547500
H 3.872243 -4.240904 -1.063218
H 3.432139 -2.591313 2.871813
H 2.297014 -3.846490 -2.757125
H 0.656794 -4.003656 -2.111881
H 1.250227 -2.427530 -2.636252
H 1.052283 -0.309148 2.366938
H -0.023596 -1.702225 2.561699
H 1.434105 -1.559392 3.547593
O -0.019370 1.705866 0.158692
N -1.596516 -0.555797 -0.605999
O -3.639861 -1.376507 -2.128923
C -3.653540 0.036359 -1.911046
H -3.425688 0.449183 -2.895132
C -5.012100 0.544978 -1.367825
H -5.789318 -0.207940 -1.537707
H -5.321447 1.444501 -1.915671
C -2.582099 0.524988 -0.851983
H -2.021687 1.384922 -1.221242
C -3.396814 0.857823 0.384884
C -4.763562 0.857497 0.087993
C -5.693458 1.158582 1.084026
H -6.757667 1.161639 0.864668
C -2.932418 1.169682 1.663771
H -1.868760 1.199149 1.876734
C -3.866803 1.462328 2.657961
C -5.236998 1.454006 2.369845
H -3.528276 1.704744 3.660922
H -5.952368 1.684443 3.153932
C -3.394244 -2.179975 -0.981326
H -4.108061 -1.986598 -0.169241
H -3.476264 -3.224345 -1.285990
C 1.896111 0.646841 -0.870401

H 2.154351 -0.329070 -1.267167
C 2.882803 1.597926 -0.989654
C 0.568339 0.733120 -0.319306
C 5.153390 -4.044844 1.334436
H 5.317369 -5.022235 0.869707
H 5.971234 -3.389038 1.008862
H 5.239361 -4.162665 2.418494
H 3.767410 1.199378 -1.486185
C 3.057304 2.986747 -0.626986
C 2.108762 3.804763 0.033827
C 4.308239 3.558693 -0.975965
C 2.411195 5.129046 0.325614
H 1.147502 3.392556 0.305783
C 4.601785 4.882412 -0.682492
H 5.048322 2.945143 -1.483314
C 3.650665 5.672329 -0.028883
H 1.675512 5.746331 0.832515
H 5.564589 5.300531 -0.959292
H 3.874886 6.709518 0.203436
Zero-point correction= 0.518953
Thermal correction to Energy= 0.549135
Thermal correction to Enthalpy= 0.550079
Thermal correction to Gibbs Free Energy= 0.454143
Sum of electronic and thermal Energies= -1473.981400
Sum of electronic and thermal Enthalpies= -1473.980455
Sum of electronic and thermal Free Energies= -1474.076392

Single point energy calculated with M062X/6-31++G(d,p)
E(RM062X) = -1473.98013048

***E-isomer (B3LYP/6-31G(d) gas-phase optimized)***

C 2.243038 1.488528 -0.822829
N 0.212847 1.450724 -0.224756
C 0.593607 0.163203 -0.264462
N 1.238250 2.290711 -0.578630
C -1.057046 2.014787 0.179640
C -1.882360 2.561653 -0.817065
C -1.376500 2.042114 1.546789
C -3.092412 3.122268 -0.400547
C -2.598103 2.620943 1.899956
C -3.470920 3.159074 0.947335
C -1.487757 2.564257 -2.274992
C -0.451945 1.490417 2.606784
H -3.750258 3.554482 -1.150211
H -2.868077 2.662638 2.952051
H -2.311361 2.928148 -2.893935
H -0.622473 3.212957 -2.450512
H -1.219801 1.562674 -2.633892

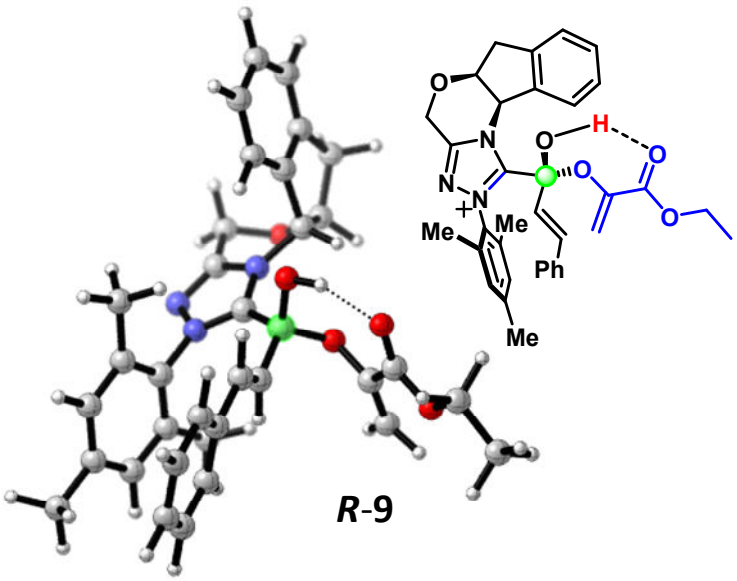
H -0.458962 0.393065 2.628349
H 0.583626 1.814794 2.455447
H -0.763510 1.832712 3.596637
O 0.485513 -2.032280 0.499600
N 1.896425 0.176705 -0.628487
O 3.756702 0.808236 -2.448462
C 3.856921 -0.550754 -2.016437
H 3.573711 -1.121238 -2.902386
C 5.278009 -0.918342 -1.519576
H 5.997895 -0.161621 -1.850260
H 5.596790 -1.869022 -1.965871
C 2.894239 -0.908481 -0.810152
H 2.330784 -1.821523 -1.004064
C 3.817378 -1.047013 0.386160
C 5.155555 -1.039234 -0.019731
C 6.171924 -1.172493 0.927327
H 7.215144 -1.168595 0.623393
C 3.467269 -1.204498 1.728275
H 2.425490 -1.246683 2.029484
C 4.487334 -1.329562 2.671920
C 5.829639 -1.310053 2.273639
H 4.238089 -1.451075 3.721847
H 6.612903 -1.409496 3.019461
C 3.585885 1.770811 -1.416305
H 4.379602 1.722778 -0.658357
H 3.595957 2.758651 -1.879355
C -3.724460 -2.495304 -0.189469
C -4.602557 -1.518759 -0.711691
C -4.241661 -3.770053 0.127520
C -5.943438 -1.814978 -0.910717
H -4.232551 -0.527373 -0.955488
C -5.585955 -4.063989 -0.074015
H -3.574566 -4.527270 0.531117
C -6.438310 -3.087324 -0.594115
H -6.611319 -1.059332 -1.313206
H -5.969573 -5.049209 0.172182
H -7.488699 -3.313214 -0.753110
C -1.603028 -1.124297 -0.227577
H -2.063483 -0.240289 -0.651326
C -2.315747 -2.256463 0.034402
H -1.754253 -3.086581 0.461239
C -0.182831 -1.099864 0.052850
C -4.792611 3.756310 1.363963
H -5.137909 4.506957 0.646925
H -5.567848 2.981697 1.427956
H -4.724647 4.228927 2.348611
Zero-point correction= 0.518600
Thermal correction to Energy= 0.548844
Thermal correction to Enthalpy= 0.549788
Thermal correction to Gibbs Free Energy= 0.454122

Sum of electronic and thermal Energies= -1473.989413
Sum of electronic and thermal Enthalpies= -1473.988469
Sum of electronic and thermal Free Energies= -1474.084135

Single point energy calculated with M062X/6-31++G(d,p)
E(RM062X) = -1473.98940943

## Structures relevant for the Keto Ester (3) - system

***Protonated R-intermediate Ester (ωB97XD/6-31G(d), 313.15 K, CPCM: toluene)***




***R*-9**

C -2.696040 -1.817432 -0.930667
N -0.608974 -1.838515 -0.660520
C -0.978262 -0.583295 -0.422204
N -1.677005 -2.624672 -0.991246
C 0.699721 -2.434317 -0.582820
C 1.427447 -2.577937 -1.762595
C 1.163548 -2.838304 0.670834
C 2.695307 -3.148545 -1.656327
C 2.434706 -3.398323 0.721133
C 3.214136 -3.556821 -0.427938
C 0.874023 -2.111846 -3.083220
C 0.334953 -2.632499 1.909947
H 3.291201 -3.271435 -2.556814
H 2.834891 -3.710265 1.682258
H 1.594818 -2.281503 -3.885702
H -0.050451 -2.641553 -3.335267
H 0.639419 -1.040409 -3.063385
H 0.203201 -1.564088 2.121000
H -0.661610 -3.074286 1.803082
H 0.816984 -3.086858 2.777875
O -0.478595 1.535364 -1.156780
C 0.428847 2.492724 -1.552948
O -0.667086 1.092507 1.116042
H -0.359089 2.024565 1.206177
N -2.309145 -0.557332 -0.576869
O -4.449974 -0.880040 -2.119626
C -4.432010 0.379648 -1.461613
H -4.252912 1.095560 -2.263664
C -5.744137 0.671160 -0.703590
H -6.551660 0.044483 -1.092984
H -6.040571 1.715245 -0.855789
C -3.309626 0.494998 -0.367082
H -2.795135 1.453188 -0.432362
C -4.045339 0.311955 0.943377
C -5.420084 0.411150 0.744517
C -6.291019 0.277945 1.820855

H -7.364507 0.353467 1.675662
C -3.508853 0.074219 2.204051
H -2.435647 0.003948 2.347126
C -4.383844 -0.066487 3.277997
C -5.763207 0.036835 3.087251
H -3.989317 -0.255568 4.271258
H -6.432553 -0.075618 3.934526
C -4.124878 -2.001609 -1.322259
H -4.770042 -2.093093 -0.439255
H -4.236467 -2.892242 -1.939833
C 0.847085 3.489292 -0.515730
O 0.445557 3.475373 0.637606
O 1.693833 4.382195 -0.984235
C 2.162081 5.391643 -0.056214
C 3.124285 6.280258 -0.810101
H 2.638965 4.884605 0.786354
H 1.294580 5.941755 0.316355
H 3.498252 7.056800 -0.136919
H 3.977255 5.706049 -1.181775
H 2.628869 6.765484 -1.655454
C 3.498252 0.176917 1.199734
C 4.284681 -0.289432 0.136792
C 4.101520 0.366460 2.448394
C 5.635205 -0.550891 0.321103
H 3.840103 -0.468227 -0.836937
C 5.455127 0.103922 2.634479
H 3.502035 0.723065 3.282058
C 6.225418 -0.355060 1.570407
H 6.231305 -0.912028 -0.511424
H 5.906733 0.256879 3.609472
H 7.281831 -0.560906 1.711561
C 0.802111 2.564028 -2.827682
H 1.439751 3.367622 -3.172439
H 0.454638 1.826984 -3.543002
C 1.341807 0.378396 -0.055513
H 1.785792 0.127101 -1.013414
C 2.062289 0.450694 1.065811
H 1.545503 0.718686 1.985326
C -0.138299 0.644586 -0.079090
C 4.600488 -4.133606 -0.320247
H 4.583899 -5.104681 0.184853
H 5.059345 -4.267035 -1.303284
H 5.241946 -3.467798 0.268081
Zero-point correction= 0.659998
Thermal correction to Energy= 0.701999
Thermal correction to Enthalpy= 0.702991
Thermal correction to Gibbs Free Energy= 0.581043
Sum of electronic and thermal Energies= -1894.309088
Sum of electronic and thermal Enthalpies= -1894.308096
Sum of electronic and thermal Free Energies= -1894.430045

Single point energy calculated with M062X/6-31++G(d,p); CPCM: toluene
E(RM062X) = -1894.90442886

***Protonated R-Intermediate Ester (B3LYP/6-31G(d) gas-phase optimized, 313.15 K)***

C -2.648876 -1.963162 -0.746554
N -0.538605 -1.960265 -0.564390
C -0.911014 -0.691129 -0.355788
N -1.623694 -2.768706 -0.820354
C 0.778573 -2.562540 -0.585298
C 1.422331 -2.693693 -1.823316
C 1.305702 -3.059974 0.616213
C 2.675078 -3.315538 -1.825125
C 2.556998 -3.674106 0.552029
C 3.259756 -3.806791 -0.652915
C 0.790241 -2.207868 -3.105888
C 0.559830 -2.939838 1.921976
H 3.199679 -3.428818 -2.770383
H 2.993407 -4.063483 1.468342
H 1.496569 -2.282831 -3.936428
H -0.092333 -2.805759 -3.362891
H 0.461598 -1.163602 -3.035321
H 0.434253 -1.891246 2.219370
H -0.438357 -3.388236 1.857702
H 1.103173 -3.447227 2.722760
O -0.340081 1.320337 -1.331139
C 0.528047 2.314255 -1.754617
O -0.680931 1.163825 0.989269
H -0.392691 2.115091 0.967234
N -2.258020 -0.680837 -0.456958
O -4.439431 -1.116905 -1.968454
C -4.393278 0.201997 -1.414057
H -4.195789 0.839350 -2.277867
C -5.707523 0.585535 -0.692579
H -6.527792 -0.049467 -1.043315
H -5.981095 1.620589 -0.937351
C -3.269174 0.392227 -0.320217
H -2.744495 1.336446 -0.462265
C -4.020647 0.333064 0.999103
C -5.398140 0.441425 0.778508
C -6.281595 0.435307 1.858076
H -7.352943 0.518685 1.696648
C -3.501333 0.224455 2.289949
H -2.430721 0.163597 2.454519
C -4.390311 0.209825 3.366277

C -5.769551 0.313770 3.151448
H -4.007805 0.121644 4.378910
H -6.448472 0.301003 3.999203
C -4.085239 -2.184326 -1.096437
H -4.718024 -2.226024 -0.200009
H -4.198644 -3.114317 -1.655643
C 0.754486 3.468985 -0.823466
O 0.298528 3.531473 0.314000
O 1.498443 4.423580 -1.364137
C 1.775610 5.597636 -0.537459
C 2.621816 6.542374 -1.364900
H 2.287056 5.258324 0.367496
H 0.818386 6.037739 -0.245261
H 2.850363 7.434875 -0.773351
H 3.566568 6.073633 -1.656491
H 2.092081 6.857408 -2.268960
C 3.486361 0.439179 1.483669
C 4.409489 -0.046050 0.537060
C 3.963573 0.809203 2.753975
C 5.759664 -0.149812 0.853956
H 4.070863 -0.351025 -0.448737
C 5.316376 0.704305 3.071664
H 3.263025 1.185062 3.495968
C 6.218779 0.225363 2.121541
H 6.460363 -0.522123 0.111804
H 5.664634 0.996595 4.057955
H 7.274320 0.143366 2.364118
C 1.014819 2.279527 -2.998410
H 1.602134 3.102263 -3.384780
H 0.807934 1.437635 -3.650190
C 1.409740 0.332962 0.058885
H 1.933055 -0.007043 -0.828040
C 2.053253 0.579618 1.212805
H 1.455545 0.926838 2.053513
C -0.069106 0.565676 -0.103068
C 4.619961 -4.460269 -0.674570
H 4.602608 -5.429832 -0.164578
H 4.973913 -4.621347 -1.696668
H 5.359461 -3.837128 -0.156237
Zero-point correction= 0.650299
Thermal correction to Energy= 0.693398
Thermal correction to Enthalpy= 0.694389
Thermal correction to Gibbs Free Energy= 0.568281
Sum of electronic and thermal Energies= -1894.853074
Sum of electronic and thermal Enthalpies= -1894.852082

Sum of electronic and thermal Free Energies= -1894.978190

***Protonated R-Intermediate Ester (B3LYP/6-31G(d) optimized, 313.15 K, CPCM: toluene)***

| | | | |
|---|---|---|---|
| C | -2.64509300 | -1.96752000 | -0.75654800 |
| N | -0.53485800 | -1.95910500 | -0.57262600 |
| C | -0.91125600 | -0.69250300 | -0.35873600 |
| N | -1.61729500 | -2.76959200 | -0.83319600 |
| C | 0.78369200 | -2.55749000 | -0.59543600 |
| C | 1.42904000 | -2.68003300 | -1.83415600 |
| C | 1.31129300 | -3.05980800 | 0.60392800 |
| C | 2.68470600 | -3.29584300 | -1.83791500 |
| C | 2.56563400 | -3.66904900 | 0.53760000 |
| C | 3.27099700 | -3.78889600 | -0.66695900 |
| C | 0.79613100 | -2.19162000 | -3.11512100 |
| C | 0.56626900 | -2.94833500 | 1.91094200 |
| H | 3.21145000 | -3.39975300 | -2.78296700 |
| H | 3.00179900 | -4.06303700 | 1.45201000 |
| H | 1.50318200 | -2.26438800 | -3.94502200 |
| H | -0.08704200 | -2.78853600 | -3.37221100 |
| H | 0.46704200 | -1.14829800 | -3.04208400 |
| H | 0.46881900 | -1.90322000 | 2.22985200 |
| H | -0.44433400 | -3.36545900 | 1.83652300 |
| H | 1.09591400 | -3.48715200 | 2.70030200 |
| O | -0.34037500 | 1.32212400 | -1.32877800 |
| C | 0.53265500 | 2.31212200 | -1.75155400 |
| O | -0.68813300 | 1.16499800 | 0.98817700 |
| H | -0.40520500 | 2.11702400 | 0.96195900 |
| N | -2.25782800 | -0.68613300 | -0.46085800 |
| O | -4.44437300 | -1.12238300 | -1.96992900 |
| C | -4.39670700 | 0.19587300 | -1.41115000 |
| H | -4.20129400 | 0.83731400 | -2.27182400 |
| C | -5.70893600 | 0.57735500 | -0.68475600 |
| H | -6.53002300 | -0.06047500 | -1.02795000 |
| H | -5.98420100 | 1.61136700 | -0.93034700 |
| C | -3.26990600 | 0.38394600 | -0.32088100 |
| H | -2.75020400 | 1.33046000 | -0.46415100 |
| C | -4.01678700 | 0.32445900 | 1.00137600 |
| C | -5.39457400 | 0.43660000 | 0.78527700 |
| C | -6.27472900 | 0.43259000 | 1.86789800 |
| H | -7.34627700 | 0.51798700 | 1.70898900 |
| C | -3.49389100 | 0.21072700 | 2.29036000 |
| H | -2.42343400 | 0.14055900 | 2.45119400 |
| C | -4.37934100 | 0.19828900 | 3.37017200 |
| C | -5.75912400 | 0.30849600 | 3.16003100 |

| | | | |
|---|---|---|---|
| H | -3.99326900 | 0.10529200 | 4.38108800 |
| H | -6.43547700 | 0.29679700 | 4.01000400 |
| C | -4.08145800 | -2.19242500 | -1.10215900 |
| H | -4.71035600 | -2.23901200 | -0.20387000 |
| H | -4.19444500 | -3.12124600 | -1.66270300 |
| C | 0.74583500 | 3.47432500 | -0.82827600 |
| O | 0.27993700 | 3.54391600 | 0.30546100 |
| O | 1.49141400 | 4.42789700 | -1.36909500 |
| C | 1.75952300 | 5.60725000 | -0.54870700 |
| C | 2.61857600 | 6.54312800 | -1.37294600 |
| H | 2.25981800 | 5.27591800 | 0.36508900 |
| H | 0.79996500 | 6.05343800 | -0.27465300 |
| H | 2.84023600 | 7.43976000 | -0.78514700 |
| H | 3.56601200 | 6.06921400 | -1.64722300 |
| H | 2.10087800 | 6.85065400 | -2.28662500 |
| C | 3.47453400 | 0.43626500 | 1.49942700 |
| C | 4.40306800 | -0.03594700 | 0.55126000 |
| C | 3.94521100 | 0.79046500 | 2.77685900 |
| C | 5.75215000 | -0.14423400 | 0.87408700 |
| H | 4.07059700 | -0.32679300 | -0.44069600 |
| C | 5.29691600 | 0.68151100 | 3.10017400 |
| H | 3.24049900 | 1.15598000 | 3.51983300 |
| C | 6.20497100 | 0.21431500 | 2.14896300 |
| H | 6.45574700 | -0.50833900 | 0.13066400 |
| H | 5.63951800 | 0.96115900 | 4.09221200 |
| H | 7.25915300 | 0.12835300 | 2.39626400 |
| C | 1.03661700 | 2.26468900 | -2.98802700 |
| H | 1.62938200 | 3.08311300 | -3.37515500 |
| H | 0.84164800 | 1.41441400 | -3.63227500 |
| C | 1.40600500 | 0.33506100 | 0.06496600 |
| H | 1.93483700 | 0.00102100 | -0.82082200 |
| C | 2.04120700 | 0.57721600 | 1.22372300 |
| H | 1.43971800 | 0.91777700 | 2.06408500 |
| C | -0.07334500 | 0.56623300 | -0.10313900 |
| C | 4.63975500 | -4.42443700 | -0.69110400 |
| H | 4.66104500 | -5.34680700 | -0.10081800 |
| H | 4.95449000 | -4.66260000 | -1.71110600 |
| H | 5.38809700 | -3.74775600 | -0.25918000 |

Zero-point correction= 0.649821
Thermal correction to Energy= 0.693008
Thermal correction to Enthalpy= 0.694000
Thermal correction to Gibbs Free Energy= 0.567677
Sum of electronic and thermal Energies= -1894.884414
Sum of electronic and thermal Enthalpies= -1894.883422
Sum of electronic and thermal Free Energies= -1895.009745

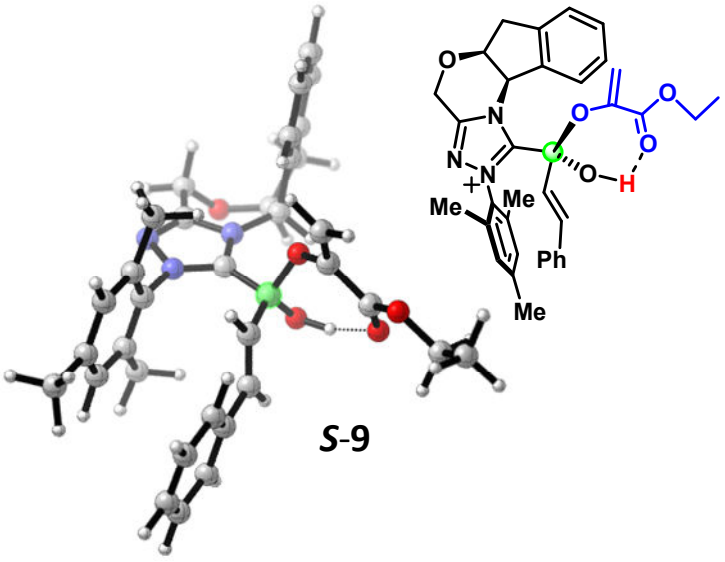
***Protonated S-Intermediate Ester (B3LYP/6-31G(d) optimized, 313.15 K, CPCM toluene)***

| | | | |
|---|---|---|---|
| C | -0.18802500 | -0.25588900 | 0.47987400 |
| C | -1.15084600 | -0.86816700 | -0.51499200 |
| C | 2.69055300 | 1.18609000 | -1.31886600 |
| N | 0.73788000 | 1.80805800 | -0.78887900 |
| C | 0.86841300 | 0.57993900 | -0.26300400 |
| N | 1.87632300 | 2.19408700 | -1.45918200 |
| C | -0.37835400 | 2.73278500 | -0.78913300 |
| C | -1.22485600 | 2.74391300 | -1.90818700 |
| C | -0.48493100 | 3.65438300 | 0.26485900 |
| C | -2.26622300 | 3.67858100 | -1.90934000 |
| C | -1.53658200 | 4.57211500 | 0.20202500 |
| C | -2.44033900 | 4.59704500 | -0.86863200 |
| C | -0.99952400 | 1.84915500 | -3.10435100 |
| C | 0.48990600 | 3.67008900 | 1.41610300 |
| H | -1.82685200 | -0.16399600 | -0.98987200 |
| H | -2.94487600 | 3.70013500 | -2.75814900 |
| H | -1.64640500 | 5.29258100 | 1.00874400 |
| H | -1.87008400 | 1.86572400 | -3.76510200 |
| H | -0.13448600 | 2.19362200 | -3.68411100 |
| H | -0.80541200 | 0.80757800 | -2.82990100 |
| H | 0.41710300 | 2.75267900 | 2.00973600 |
| H | 1.52397000 | 3.75644100 | 1.06277800 |
| H | 0.28876500 | 4.51864800 | 2.07461300 |
| O | -0.85991900 | 0.67752300 | 1.34643200 |
| C | -2.16123400 | 0.42906500 | 1.76299200 |
| C | -3.12436700 | 1.31901400 | 1.50997200 |
| H | -2.92485300 | 2.19654800 | 0.90600600 |
| H | -4.11525800 | 1.18625800 | 1.92474700 |
| O | 0.53792400 | -1.17812400 | 1.22101700 |
| H | -0.09623100 | -1.52224800 | 1.90553000 |
| N | 2.11627200 | 0.17044200 | -0.59327300 |
| O | 3.98884800 | -0.36980900 | -2.47035900 |
| C | 3.83604800 | -1.42128600 | -1.51360100 |
| H | 3.38578500 | -2.23102300 | -2.08927900 |
| C | 5.18237600 | -1.84620300 | -0.87268900 |
| H | 6.01958300 | -1.47723300 | -1.47478400 |
| H | 5.26025000 | -2.94086200 | -0.85996200 |
| C | 2.90708300 | -1.05003600 | -0.28987900 |
| H | 2.19584300 | -1.84863500 | -0.09314300 |
| C | 3.86522800 | -0.84371000 | 0.86897600 |
| C | 5.14609500 | -1.29164300 | 0.53108300 |
| C | 6.18049200 | -1.21614100 | 1.46511200 |
| H | 7.17975100 | -1.56040700 | 1.21249900 |

| | | | |
|---|---|---|---|
| C | 3.58884000 | -0.32573300 | 2.13501100 |
| H | 2.58637900 | -0.00107100 | 2.39555700 |
| C | 4.62811600 | -0.24540900 | 3.06372500 |
| C | 5.91470700 | -0.68610300 | 2.72953300 |
| H | 4.43600700 | 0.15848700 | 4.05343500 |
| H | 6.71385000 | -0.61690100 | 3.46207400 |
| C | 4.03162400 | 0.94592100 | -1.93144400 |
| H | 4.83786200 | 1.07309500 | -1.19687600 |
| H | 4.19563400 | 1.63765900 | -2.75873400 |
| C | -1.17514300 | -2.18311200 | -0.79039100 |
| H | -0.46403200 | -2.81747600 | -0.26445400 |
| C | -2.06329300 | -2.88400300 | -1.72260300 |
| C | -3.05310400 | -2.23441300 | -2.48574800 |
| C | -1.91747600 | -4.27626800 | -1.86231500 |
| C | -3.86240900 | -2.95572500 | -3.35734100 |
| H | -3.19312900 | -1.16103100 | -2.39858500 |
| C | -2.72863400 | -4.99891300 | -2.73573900 |
| H | -1.15919300 | -4.79198100 | -1.27818200 |
| C | -3.70349100 | -4.34019900 | -3.48643300 |
| H | -4.62087900 | -2.43976900 | -3.93911800 |
| H | -2.59963100 | -6.07323600 | -2.82941400 |
| H | -4.33774800 | -4.89919900 | -4.16832500 |
| C | -2.37884100 | -0.78884900 | 2.60910400 |
| O | -1.51838800 | -1.63881400 | 2.82303900 |
| O | -3.60615400 | -0.85634900 | 3.10558600 |
| C | -3.92577700 | -2.01692200 | 3.93397300 |
| C | -5.36556900 | -1.86880900 | 4.37926400 |
| H | -3.22815800 | -2.03441200 | 4.77537400 |
| H | -3.76437300 | -2.91580600 | 3.33292400 |
| H | -5.63913700 | -2.72525200 | 5.00394400 |
| H | -5.50358700 | -0.95654800 | 4.96760700 |
| H | -6.04272200 | -1.83985500 | 3.52011200 |
| C | -3.54723400 | 5.62261000 | -0.91852800 |
| H | -3.18498300 | 6.56286600 | -1.35377100 |
| H | -4.38460900 | 5.27879000 | -1.53307600 |
| H | -3.92533300 | 5.85327500 | 0.08243700 |

Zero-point correction= 0.650000
Thermal correction to Energy= 0.693126
Thermal correction to Enthalpy= 0.694118
Thermal correction to Gibbs Free Energy= 0.567296
Sum of electronic and thermal Energies= -1894.883956
Sum of electronic and thermal Enthalpies= -1894.882965
Sum of electronic and thermal Free Energies= -1895.009786

***Protonated S-intermediate Ester (ωB97XD/6-31G(d), 313.15K, CPCM: toluene)***




***S*-9**

C -0.140939 0.533879 -0.588462
C 1.332213 0.486444 -0.294230
C -2.379978 -2.341171 -0.304567
N -0.354452 -1.954321 0.114986
C -0.842484 -0.801568 -0.338336
N -1.306682 -2.933355 0.132913
C 0.969840 -2.253918 0.596813
C 1.910998 -2.749381 -0.304538
C 1.241609 -2.001861 1.942440
C 3.194380 -2.975099 0.185517
C 2.540238 -2.244926 2.380762
C 3.527451 -2.723800 1.516493
C 1.564745 -2.974309 -1.750282
C 0.180415 -1.453638 2.860498
H 1.601794 0.404517 0.753664
H 3.960311 -3.329894 -0.498556
H 2.789184 -2.047799 3.420288
H 2.423841 -3.371210 -2.294907
H 0.734697 -3.680426 -1.857211
H 1.264551 -2.036506 -2.233407
H -0.192195 -0.483898 2.507074
H -0.680138 -2.128412 2.921149
H 0.575412 -1.312867 3.868638
O -0.819977 1.418392 0.316934
C -0.164116 2.528444 0.800760
C -0.101891 2.742005 2.112348
H -0.495280 2.012475 2.811790
H 0.325192 3.656714 2.502035
O -0.457183 0.822559 -1.902792
H -0.239213 1.776535 -2.017027
N -2.137666 -1.030351 -0.597419
O -4.013902 -2.340720 -1.947894
C -4.178621 -0.930336 -2.009369
H -3.940401 -0.680964 -3.043160
C -5.601923 -0.484001 -1.613594
H -6.300543 -1.320254 -1.708351
H -5.948397 0.306087 -2.289579
C -3.231854 -0.151349 -1.025481
H -2.778447 0.710845 -1.514295
C -4.129866 0.227723 0.133145
C -5.466755 0.035742 -0.206082
C -6.467811 0.324367 0.715640
H -7.512914 0.173362 0.462306
C -3.762192 0.702298 1.387286
H -2.717482 0.848990 1.639421
C -4.765426 0.984993 2.309939
C -6.108102 0.798153 1.975173
H -4.502369 1.353576 3.296391

H -6.879233 1.020623 2.706034
C -3.723042 -2.879149 -0.673462
H -4.476695 -2.615419 0.079316
H -3.681475 -3.963259 -0.773958
C 2.256974 0.456756 -1.255325
H 1.929211 0.496146 -2.292442
C 3.693186 0.256410 -1.024733
C 4.302697 0.524458 0.207672
C 4.461607 -0.301558 -2.052272
C 5.640543 0.216225 0.412760
H 3.730650 0.982879 1.009119
C 5.800154 -0.618770 -1.844171
H 4.000068 -0.504960 -3.015081
C 6.391182 -0.364687 -0.609781
H 6.102443 0.428644 1.371886
H 6.381387 -1.060908 -2.647267
H 7.436996 -0.605462 -0.446143
C 0.342231 3.508647 -0.214065
O 0.211518 3.365113 -1.419191
O 0.942950 4.541595 0.339286
C 1.466789 5.552198 -0.557900
C 2.169453 6.585496 0.292135
H 0.629550 5.976149 -1.117758
H 2.144663 5.064719 -1.262697
H 2.568739 7.371156 -0.355381
H 1.476932 7.043382 1.003625
H 3.000398 6.137584 0.843825
C 4.926152 -2.970595 2.016692
H 5.008195 -3.970376 2.458525
H 5.654191 -2.900338 1.204307
H 5.203602 -2.245483 2.787183
Zero-point correction= 0.659544
Thermal correction to Energy= 0.701700
Thermal correction to Enthalpy= 0.702692
Thermal correction to Gibbs Free Energy= 0.579714
Sum of electronic and thermal Energies= -1894.309529
Sum of electronic and thermal Enthalpies= -1894.308538
Sum of electronic and thermal Free Energies= -1894.431515

Single point energy calculated with M062X/6-31++G(d,p); CPCM: toluene
E(RM062X) = -1894.90408486

***Protonated S-Intermediate Ester (B3LYP/6-31G(d) gas-phase optimized, 313.15 K)***

| | | | |
|---|---|---|---|
| C | -0.16330800 | -0.34028400 | 0.41593000 |
| C | -1.22785000 | -0.75825700 | -0.57446900 |
| C | 2.70869400 | 1.21343500 | -1.30721600 |
| N | 0.77181700 | 1.80639600 | -0.69589500 |
| C | 0.89512100 | 0.53535100 | -0.27937400 |

| | | | |
|---|---|---|---|
| N | 1.90437400 | 2.23778200 | -1.34696400 |
| C | -0.33064800 | 2.74199500 | -0.59071700 |
| C | -1.20232600 | 2.86064900 | -1.68491900 |
| C | -0.39237600 | 3.57833300 | 0.53482000 |
| C | -2.22655400 | 3.80722000 | -1.58290300 |
| C | -1.43068600 | 4.51345700 | 0.57425000 |
| C | -2.36033900 | 4.63977200 | -0.46592700 |
| C | -1.01560100 | 2.06719800 | -2.95741600 |
| C | 0.62036600 | 3.49632300 | 1.65000900 |
| H | -1.89299200 | 0.03792100 | -0.89352200 |
| H | -2.92210000 | 3.91274400 | -2.41180200 |
| H | -1.50489200 | 5.17173600 | 1.43631600 |
| H | -1.86612200 | 2.21308400 | -3.62815000 |
| H | -0.11435700 | 2.39767700 | -3.48766100 |
| H | -0.90924300 | 0.99151900 | -2.78109300 |
| H | 0.57689500 | 2.52747400 | 2.15855300 |
| H | 1.64000100 | 3.63046500 | 1.27006700 |
| H | 0.43769700 | 4.27754300 | 2.39209400 |
| O | -0.71674100 | 0.50456400 | 1.44600800 |
| C | -1.99381100 | 0.26177300 | 1.93584200 |
| C | -2.92369900 | 1.21871200 | 1.87901900 |
| H | -2.72439300 | 2.15739800 | 1.37479600 |
| H | -3.88378900 | 1.07552200 | 2.35796500 |
| O | 0.54766000 | -1.39268300 | 0.97288600 |
| H | -0.05851000 | -1.78806800 | 1.65744000 |
| N | 2.13325100 | 0.14208200 | -0.66582500 |
| O | 3.98547600 | -0.24708200 | -2.59659500 |
| C | 3.85721800 | -1.36665500 | -1.71950800 |
| H | 3.41949400 | -2.13939100 | -2.35363100 |
| C | 5.21451600 | -1.81439800 | -1.11700200 |
| H | 6.04033400 | -1.37390200 | -1.68644000 |
| H | 5.32164100 | -2.90350000 | -1.20249100 |
| C | 2.92495700 | -1.10348800 | -0.46831400 |
| H | 2.20949400 | -1.91208700 | -0.34040800 |
| C | 3.87974300 | -0.99369100 | 0.70528500 |
| C | 5.16800400 | -1.38752300 | 0.33050900 |
| C | 6.20038800 | -1.38038500 | 1.26967300 |
| H | 7.20543500 | -1.68429500 | 0.98967800 |
| C | 3.59357200 | -0.60124100 | 2.01372600 |
| H | 2.58446500 | -0.32370600 | 2.30256400 |
| C | 4.63066100 | -0.58865800 | 2.94733400 |
| C | 5.92483900 | -0.97341700 | 2.57632900 |
| H | 4.43130300 | -0.28333000 | 3.97029200 |
| H | 6.72213100 | -0.95859300 | 3.31379500 |
| C | 4.04056200 | 1.01943700 | -1.95616800 |

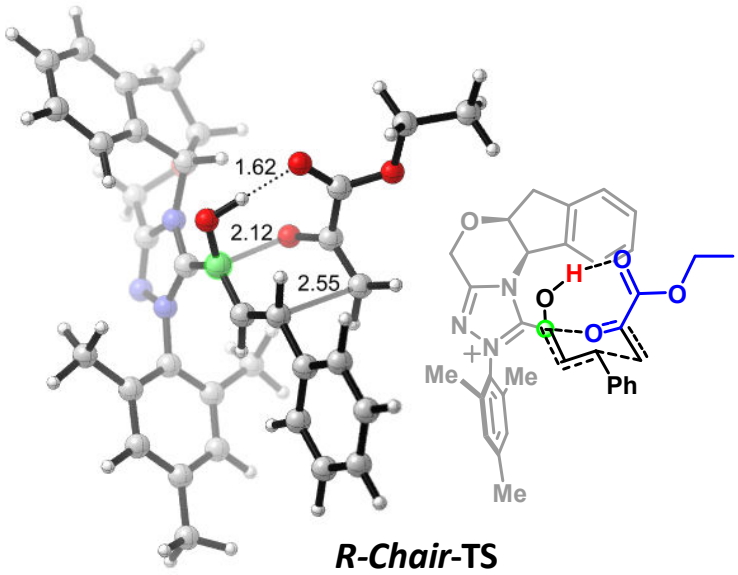
| | | | |
|---|---|---|---|
| H | 4.85722200 | 1.08477300 | -1.22389100 |
| H | 4.19566100 | 1.77529200 | -2.72769100 |
| C | -1.35363000 | -2.02115700 | -1.01814700 |
| H | -0.64184100 | -2.75328900 | -0.64054400 |
| C | -2.35054300 | -2.54849900 | -1.95256800 |
| C | -3.37745300 | -1.76449300 | -2.51330200 |
| C | -2.27971100 | -3.90864900 | -2.30412800 |
| C | -4.29417600 | -2.32460300 | -3.39589200 |
| H | -3.46437300 | -0.71300300 | -2.25465300 |
| C | -3.19797800 | -4.46987300 | -3.18909400 |
| H | -1.49504500 | -4.52793100 | -1.87589500 |
| C | -4.20765500 | -3.67869000 | -3.73791000 |
| H | -5.08139000 | -1.70749700 | -3.81938700 |
| H | -3.12595900 | -5.52195900 | -3.44852000 |
| H | -4.92619200 | -4.11208200 | -4.42745300 |
| C | -2.21558900 | -1.04638200 | 2.63500500 |
| O | -1.39825800 | -1.96230200 | 2.65236000 |
| O | -3.39578800 | -1.11475200 | 3.23458000 |
| C | -3.71401700 | -2.35912000 | 3.93357200 |
| C | -5.08282900 | -2.18822000 | 4.55836600 |
| H | -2.93250200 | -2.53800500 | 4.67679700 |
| H | -3.68416400 | -3.17226700 | 3.20294400 |
| H | -5.35468000 | -3.10613800 | 5.08961500 |
| H | -5.08801900 | -1.36275800 | 5.27655200 |
| H | -5.84387600 | -1.99551900 | 3.79610100 |
| C | -3.44858500 | 5.68438500 | -0.40818300 |
| H | -3.11684700 | 6.61564000 | -0.88497200 |
| H | -4.35044500 | 5.35448100 | -0.93331800 |
| H | -3.72058400 | 5.92612200 | 0.62377100 |

Zero-point correction= 0.650427
Thermal correction to Energy= 0.693506
Thermal correction to Enthalpy= 0.694497
Thermal correction to Gibbs Free Energy= 0.567323
Sum of electronic and thermal Energies= -1894.852553
Sum of electronic and thermal Enthalpies= -1894.851561
Sum of electronic and thermal Free Energies= -1894.978735

***Protonated R-chair TS Ester (ωB97XD/6-31G(d), 313.15K, CPCM: toluene)***

C 0.074929 0.091214 0.472353
C 1.471319 0.107068 0.458935
C -2.307296 -2.192918 -0.988236
N -0.271305 -2.251678 -0.470700
C -0.684029 -1.031187 -0.120823
N -1.275662 -2.987304 -1.024165
C 1.054393 -2.799815 -0.388563

C 1.864921 -2.690412 -1.523329
C 1.479324 -3.345854 0.821100
C 3.170304 -3.158789 -1.410991
C 2.796297 -3.799637 0.878648
C 3.651604 -3.713371 -0.220240
C 1.352274 -2.038738 -2.780758
C 0.571359 -3.395833 2.021113
H 1.974827 -0.660211 -0.109860
H 3.832201 -3.083436 -2.269913
H 3.163594 -4.226280 1.808057
H 2.135021 -1.997006 -3.540741
H 0.502907 -2.591520 -3.195190
H 1.010648 -1.013756 -2.586463
H 0.440036 -2.397746 2.456702
H -0.420047 -3.779224 1.760449
H 0.991612 -4.040893 2.795551
O -0.204169 1.233631 -1.293649
C 0.530995 2.276975 -1.175069
C 1.884893 2.319757 -1.386872
H 2.391076 1.476614 -1.842597
H 2.441885 3.241984 -1.265138
O -0.682441 0.799332 1.312967
H -0.670827 1.783426 1.120491
N -1.987385 -0.984536 -0.442248
O -3.887283 -1.155406 -2.322580
C -3.962009 0.043372 -1.564495
H -3.674305 0.820273 -2.272254
C -5.368836 0.283717 -0.973725
H -6.105643 -0.335162 -1.494297
H -5.663146 1.329030 -1.120546
C -2.998475 0.072666 -0.321077
H -2.465772 1.020627 -0.282666
C -3.904138 -0.153549 0.867880
C -5.239655 -0.035585 0.492792
C -6.245533 -0.199329 1.439711
H -7.290431 -0.108798 1.157943
C -3.541416 -0.439374 2.179593
H -2.496825 -0.523237 2.461932
C -4.549990 -0.609820 3.123679
C -5.891859 -0.488844 2.755427
H -4.292537 -0.835266 4.153661
H -6.667427 -0.624286 3.502890
C -3.668812 -2.337693 -1.580601
H -4.426622 -2.493061 -0.801583
H -3.691788 -3.176262 -2.275715
C 2.195263 1.198911 0.886433
H 1.675442 1.980870 1.435792
C 3.656523 1.273863 0.918732
C 4.254311 2.425651 1.448233
C 4.477165 0.233149 0.456945




***R-Chair*-TS**

C 5.636915 2.541563 1.511142
H 3.625535 3.235417 1.809100
C 5.858426 0.350451 0.522640
H 4.044716 -0.678829 0.055703
C 6.441699 1.503554 1.047404
H 6.086500 3.438455 1.924414
H 6.484415 -0.462017 0.167583
H 7.522358 1.590595 1.098544
C -0.092057 3.453498 -0.453494
O -0.751408 3.307022 0.572831
O 0.153580 4.619421 -0.999526
C -0.365135 5.794526 -0.321459
C 0.002611 6.995516 -1.161434
H 0.079608 5.832451 0.676227
H -1.445872 5.676458 -0.215558
H -0.373607 7.901338 -0.677790
H 1.087236 7.084591 -1.266086
H -0.443851 6.925059 -2.156863
C 5.068022 -4.219225 -0.138313
H 5.399737 -4.315752 0.898657
H 5.150568 -5.205292 -0.609145
H 5.757142 -3.549416 -0.661557
Zero-point correction= 0.656859
Thermal correction to Energy= 0.699012
Thermal correction to Enthalpy= 0.700003
Thermal correction to Gibbs Free Energy= 0.576356
Sum of electronic and thermal Energies= -1894.270137
Sum of electronic and thermal Enthalpies= -1894.269145
Sum of electronic and thermal Free Energies= -1894.392793

Single point energy calculated with M062X/6-31++G(d,p); CPCM: toluene
E(RM062X) = -1894.85943432

***Protonated R-chair TS Ester (B3LYP/6-31G(d) optimized, 313.15 K, CPCM: toluene)***

C 0.116848 0.103584 0.471788
C 1.507657 0.245171 0.403802
C -2.152322 -2.375964 -0.868606
N -0.090805 -2.292417 -0.397411
C -0.573846 -1.074947 -0.082216
N -1.071412 -3.110520 -0.900445
C 1.256835 -2.808881 -0.314958
C 2.046815 -2.755123 -1.475053
C 1.690558 -3.379112 0.890652
C 3.338214 -3.282849 -1.387577
C 2.989788 -3.893621 0.916232
C 3.825416 -3.857931 -0.206560
C 1.529382 -2.152058 -2.759808

C 0.805262 -3.435523 2.112087
H 2.054823 -0.501873 -0.153858
H 3.974534 -3.251840 -2.268363
H 3.354825 -4.339322 1.837944
H 2.321584 -2.114866 -3.511491
H 0.703763 -2.745510 -3.169634
H 1.151377 -1.132304 -2.614441
H 0.620533 -2.436287 2.525896
H -0.168907 -3.881715 1.883419
H 1.274298 -4.034323 2.896559
O -0.292987 1.292514 -1.428356
C 0.371803 2.381122 -1.305107
C 1.708715 2.551733 -1.592139
H 2.274461 1.748550 -2.050264
H 2.190173 3.516206 -1.479018
O -0.687378 0.813104 1.271576
H -0.706849 1.802236 1.055367
N -1.897114 -1.125700 -0.372683
O -3.805773 -1.509678 -2.256994
C -3.913735 -0.251733 -1.581862
H -3.626144 0.477231 -2.340610
C -5.340120 0.002774 -1.034839
H -6.059797 -0.651121 -1.538331
H -5.643387 1.035557 -1.250401
C -2.972755 -0.109886 -0.320397
H -2.480697 0.860441 -0.335924
C -3.902115 -0.291491 0.866779
C -5.237287 -0.228776 0.453710
C -6.265200 -0.348214 1.389752
H -7.305071 -0.302425 1.077506
C -3.569558 -0.465507 2.210959
H -2.532509 -0.495315 2.529107
C -4.601247 -0.591944 3.143552
C -5.939121 -0.534844 2.735003
H -4.363022 -0.733116 4.193780
H -6.731324 -0.636157 3.471372
C -3.507930 -2.635653 -1.438469
H -4.253200 -2.789659 -0.647250
H -3.485437 -3.515119 -2.082947
C 2.169441 1.370418 0.868490
H 1.587131 2.106770 1.416853
C 3.609488 1.568678 0.912196
C 4.105384 2.701262 1.591537
C 4.532874 0.672156 0.332015
C 5.473665 2.932738 1.689737

H 3.404276 3.397907 2.043830
C 5.898816 0.907660 0.430501
H 4.185285 -0.210916 -0.195089
C 6.374391 2.036876 1.107972
H 5.838176 3.808135 2.218566
H 6.599103 0.210581 -0.019874
H 7.443147 2.215005 1.181800
C -0.310460 3.505384 -0.540784
O -0.904318 3.302563 0.523104
O -0.201139 4.696274 -1.096324
C -0.799258 5.831087 -0.387597
C -0.512662 7.073475 -1.203879
H -0.358207 5.873529 0.611778
H -1.869539 5.634522 -0.285366
H -0.948700 7.943105 -0.701617
H 0.564364 7.238702 -1.304687
H -0.951605 6.997415 -2.203238
C 5.209943 -4.457075 -0.155115
H 5.642078 -4.381799 0.847524
H 5.180303 -5.522217 -0.418589
H 5.886172 -3.965673 -0.861360
Zero-point correction= 0.647298
Thermal correction to Energy= 0.690370
Thermal correction to Enthalpy= 0.691362
Thermal correction to Gibbs Free Energy= 0.565600
Sum of electronic and thermal Energies= -1894.859237
Sum of electronic and thermal Enthalpies= -1894.858245
Sum of electronic and thermal Free Energies= -1894.984007

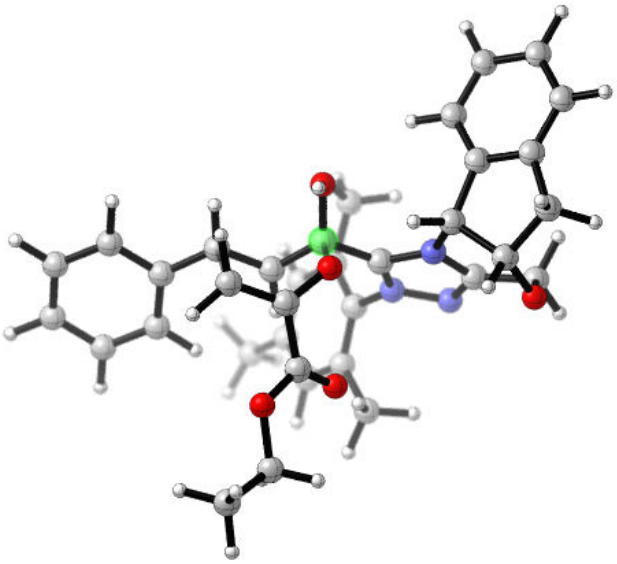
***Protonated R-chair TS Ester (B3LYP/6-31G(d) gas-phase optimized, 313.15 K)***
C 0.123250 0.103606 0.486393
C 1.511849 0.256588 0.412270
C -2.130879 -2.387157 -0.858795
N -0.070421 -2.292917 -0.386442
C -0.560442 -1.078120 -0.069170
N -1.046088 -3.115728 -0.891672
C 1.281210 -2.799668 -0.309496
C 2.064670 -2.742217 -1.473125
C 1.724030 -3.368260 0.893894
C 3.359441 -3.263943 -1.391588
C 3.025167 -3.876200 0.913344
C 3.855228 -3.838002 -0.214145
C 1.535599 -2.146881 -2.756981
C 0.842320 -3.431855 2.117728

H 2.062322 -0.489219 -0.144222
H 3.989882 -3.234081 -2.276779
H 3.396443 -4.322058 1.832669
H 2.326845 -2.089692 -3.508661
H 0.726317 -2.760364 -3.170089
H 1.131973 -1.136714 -2.611607
H 0.633241 -2.433029 2.521431
H -0.120013 -3.906665 1.895504
H 1.325345 -4.010003 2.909144
O -0.298851 1.286145 -1.416732
C 0.353961 2.379619 -1.294372
C 1.691905 2.561267 -1.575906
H 2.263593 1.766104 -2.040154
H 2.162747 3.531916 -1.470406
O -0.684446 0.805212 1.289662
H -0.718963 1.794192 1.072776
N -1.883425 -1.135687 -0.360303
O -3.777278 -1.527600 -2.256419
C -3.894524 -0.270148 -1.583904
H -3.601940 0.457807 -2.342194
C -5.326437 -0.022080 -1.048371
H -6.038695 -0.674160 -1.564858
H -5.632166 1.011049 -1.260711
C -2.965035 -0.124445 -0.313778
H -2.475419 0.847256 -0.323366
C -3.903226 -0.315364 0.864365
C -5.235338 -0.261873 0.440042
C -6.269860 -0.391864 1.366932
H -7.307659 -0.352611 1.046962
C -3.580660 -0.486846 2.211182
H -2.545961 -0.502158 2.538641
C -4.618997 -0.624052 3.134182
C -5.953412 -0.578795 2.714080
H -4.389276 -0.762649 4.186577
H -6.750873 -0.687919 3.443449
C -3.482527 -2.651367 -1.437049
H -4.232753 -2.808641 -0.650411
H -3.451736 -3.530340 -2.082544
C 2.167301 1.392345 0.863708
H 1.579775 2.124602 1.412545
C 3.606105 1.600162 0.905963
C 4.096385 2.737684 1.580564
C 4.534525 0.707844 0.327843
C 5.462835 2.978707 1.675846
H 3.391870 3.430869 2.033645

C 5.898720 0.952814 0.422741
H 4.191273 -0.180710 -0.193538
C 6.368095 2.087314 1.095084
H 5.822802 3.857558 2.202051
H 6.603459 0.259144 -0.026115
H 7.435765 2.272793 1.166299
C -0.339565 3.498067 -0.530186
O -0.924268 3.289929 0.537479
O -0.249423 4.688444 -1.089652
C -0.871265 5.815664 -0.388495
C -0.620997 7.056671 -1.218837
H -0.427120 5.877596 0.608939
H -1.935404 5.592219 -0.275429
H -1.076023 7.921007 -0.724191
H 0.450546 7.248932 -1.328711
H -1.062261 6.959174 -2.215143
C 5.240832 -4.434891 -0.168192
H 5.717575 -4.269347 0.803330
H 5.199835 -5.519849 -0.328313
H 5.886733 -4.014656 -0.944895
Zero-point correction= 0.647616
Thermal correction to Energy= 0.690651
Thermal correction to Enthalpy= 0.691642
Thermal correction to Gibbs Free Energy= 0.566079
Sum of electronic and thermal Energies= -1894.827553
Sum of electronic and thermal Enthalpies= -1894.826562
Sum of electronic and thermal Free Energies= -1894.952125

***Protonated R-boat TS Ester (B3LYP/6-31G(d) gas-phase optimized, 313.15 K)***

C -0.107202 -0.013290 0.965659
C 1.287121 -0.071825 0.913876
C -2.589421 -0.933000 -1.518536
N -0.613149 -1.501522 -1.025946
C -0.931918 -0.532678 -0.142520
N -1.640540 -1.746978 -1.899348
C 0.573164 -2.326321 -1.106081
C 1.460239 -2.109517 -2.173389
C 0.746625 -3.343842 -0.153073
C 2.586033 -2.936713 -2.236562
C 1.889976 -4.137335 -0.272021
C 2.820166 -3.951495 -1.301428
C 1.215661 -1.050279 -3.221544
C -0.249890 -3.591467 0.954894
H 1.741395 -0.311833 -0.038720



H 3.291063 -2.790147 -3.051143
H 2.050132 -4.931561 0.452755
H 2.072732 -0.981826 -3.896622
H 0.334389 -1.296417 -3.825050
H 1.044883 -0.059043 -2.787225
H -0.205176 -2.816469 1.730420
H -1.277728 -3.623689 0.575947
H -0.047274 -4.548845 1.441374
O -0.459547 2.102847 0.679251
C 0.656499 2.731398 0.526526
C 1.476204 3.100345 1.565194
H 1.125448 3.012565 2.588266
H 2.405128 3.628968 1.389020
O -0.780919 0.122165 2.148666
H -0.890407 1.093903 2.252847
N -2.206571 -0.181017 -0.439436
O -3.959395 0.804490 -2.250779
C -3.963508 1.515158 -1.010108
H -3.506028 2.474114 -1.257971
C -5.389311 1.675011 -0.426156
H -6.136164 1.531681 -1.214090
H -5.524797 2.695266 -0.043257
C -3.142661 0.808160 0.140241
H -2.534610 1.548342 0.655367
C -4.202495 0.169611 1.021203
C -5.469592 0.664065 0.693171
C -6.592246 0.231067 1.399149
H -7.580760 0.608480 1.151720
C -4.031096 -0.750925 2.056089
H -3.043274 -1.115062 2.321402
C -5.158646 -1.187220 2.754423
C -6.429393 -0.700616 2.426600
H -5.048023 -1.906721 3.560399
H -7.297572 -1.049883 2.977999
C -3.898134 -0.612547 -2.164541
H -4.738509 -1.037797 -1.598831
H -3.920429 -1.004550 -3.182501
C 2.075927 0.327304 1.982029
H 1.563372 0.536162 2.917116
C 3.522549 0.302828 2.047686
C 4.341416 -0.057380 0.953950
C 4.141212 0.634038 3.273121
C 5.723272 -0.078439 1.087642
H 3.896119 -0.330016 0.002122
C 5.524828 0.611648 3.403195

H 3.521588 0.909870 4.122659
C 6.319440 0.257140 2.309558
H 6.343366 -0.358200 0.241276
H 5.984992 0.868063 4.352458
H 7.400901 0.238988 2.407546
C 1.128276 2.865609 -0.911631
O 0.772706 2.089278 -1.778806
O 1.971263 3.885981 -1.096051
C 2.488804 4.068319 -2.444877
C 3.378070 5.295174 -2.430122
H 1.638748 4.177430 -3.124513
H 3.032779 3.162210 -2.729723
H 3.784434 5.465475 -3.432541
H 2.814121 6.184437 -2.132785
H 4.215596 5.166811 -1.737322
C 4.024846 -4.852599 -1.423548
H 3.777890 -5.753670 -1.999532
H 4.850187 -4.352841 -1.939820
H 4.381566 -5.182003 -0.442606
Zero-point correction= 0.647799
Thermal correction to Energy= 0.691150
Thermal correction to Enthalpy= 0.692141
Thermal correction to Gibbs Free Energy= 0.566020
Sum of electronic and thermal Energies= -1894.815274
Sum of electronic and thermal Enthalpies= -1894.814283
Sum of electronic and thermal Free Energies= -1894.940404

***Protonated R-boat TS Ester (B3LYP/6-31G(d) optimized, 313.15 K, CPCM: toluene)***

C -0.126655 -0.012956 0.957540
C 1.268591 -0.107056 0.928293
C -2.610010 -0.901699 -1.535248
N -0.632064 -1.476961 -1.055160
C -0.950149 -0.523566 -0.155419
N -1.660989 -1.708440 -1.931202
C 0.556800 -2.295053 -1.157274
C 1.451336 -2.033614 -2.208316
C 0.729202 -3.343989 -0.239445
C 2.581436 -2.852151 -2.295385
C 1.877369 -4.127941 -0.380230
C 2.813208 -3.899490 -1.395644
C 1.211037 -0.931233 -3.211896
C -0.268833 -3.629064 0.857622
H 1.735243 -0.357919 -0.015435
H 3.294067 -2.669482 -3.095765

H 2.038096 -4.945469 0.317833
H 2.073949 -0.829230 -3.874936
H 0.334718 -1.151498 -3.832459
H 1.032661 0.039059 -2.734790
H -0.224021 -2.877864 1.656141
H -1.296279 -3.647345 0.477588
H -0.064154 -4.600797 1.313692
O -0.434014 2.083925 0.622816
C 0.686482 2.715262 0.497594
C 1.498828 3.043144 1.554635
H 1.142020 2.917652 2.571163
H 2.437884 3.561444 1.405280
O -0.812526 0.133515 2.131341
H -0.895939 1.104752 2.252315
N -2.225203 -0.167510 -0.445320
O -3.980928 0.847850 -2.237415
C -3.983334 1.538030 -0.984060
H -3.528233 2.501838 -1.215335
C -5.407531 1.687381 -0.393613
H -6.158195 1.546985 -1.178282
H -5.543423 2.703445 -0.000942
C -3.157808 0.813602 0.151718
H -2.549586 1.546522 0.676558
C -4.213687 0.165043 1.030376
C -5.481535 0.666233 0.716289
C -6.601066 0.227420 1.424132
H -7.589940 0.609968 1.186279
C -4.038272 -0.770279 2.051216
H -3.050374 -1.143487 2.302055
C -5.162524 -1.212496 2.751784
C -6.434264 -0.717445 2.439288
H -5.048222 -1.944056 3.546385
H -7.299955 -1.071515 2.991769
C -3.920400 -0.572388 -2.172284
H -4.758800 -1.004249 -1.609944
H -3.947261 -0.950153 -3.195059
C 2.046881 0.262472 2.012182
H 1.525515 0.479967 2.940267
C 3.492015 0.208648 2.100245
C 4.321564 -0.157489 1.016559
C 4.095626 0.518171 3.338805
C 5.700640 -0.206634 1.172922
H 3.888146 -0.410312 0.054192
C 5.476774 0.468104 3.491052
H 3.466888 0.799365 4.179485

C 6.282672 0.107000 2.407689
H 6.328642 -0.490618 0.333953
H 5.925842 0.708479 4.449764
H 7.361784 0.067263 2.523245
C 1.148765 2.935947 -0.932946
O 0.699069 2.299983 -1.868155
O 2.092725 3.879194 -1.038739
C 2.612038 4.132862 -2.373901
C 3.636930 5.243461 -2.261343
H 1.774183 4.406327 -3.021599
H 3.046935 3.204538 -2.756691
H 4.048572 5.462220 -3.252107
H 3.182129 6.158161 -1.868623
H 4.461745 4.952934 -1.602943
C 4.026119 -4.786248 -1.540650
H 3.804522 -5.643396 -2.189558
H 4.865191 -4.246346 -1.990296
H 4.349383 -5.184474 -0.573930
Zero-point correction= 0.647315
Thermal correction to Energy= 0.690801
Thermal correction to Enthalpy= 0.691793
Thermal correction to Gibbs Free Energy= 0.564640
Sum of electronic and thermal Energies= -1894.847663
Sum of electronic and thermal Enthalpies= -1894.846672
Sum of electronic and thermal Free Energies= -1894.973825

***Protonated S-chair TS Ester (B3LYP/6-31G(d) gas-phase optimized, 313.15 K)***

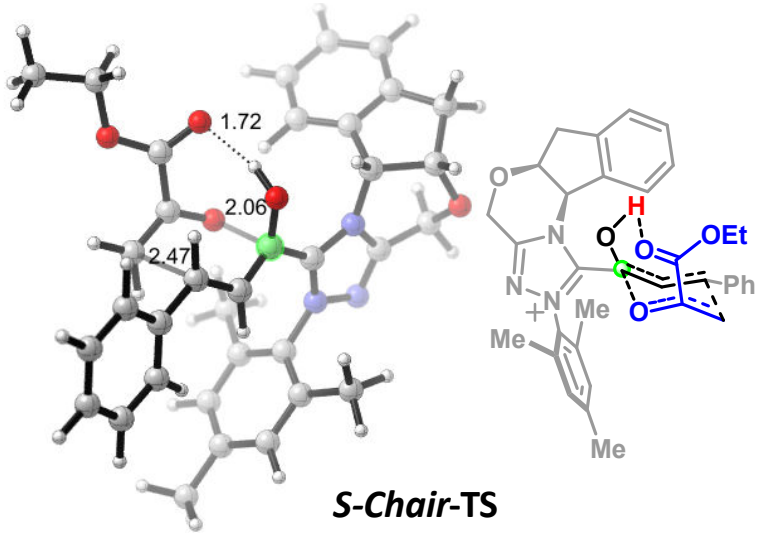
C 0.118596 0.047955 -0.868408
C 1.520369 0.074126 -0.810287
C -2.317286 -2.542575 -0.130613
N -0.242432 -2.261519 0.172148
C -0.657465 -1.141616 -0.463111
N -1.273084 -3.141036 0.374550
C 1.069890 -2.667393 0.632654
C 1.898129 -3.367273 -0.259997
C 1.412160 -2.419746 1.971773
C 3.142851 -3.783384 0.220228
C 2.670110 -2.861187 2.392888
C 3.546638 -3.542392 1.539787
C 1.474318 -3.657571 -1.679819
C 0.469752 -1.722932 2.921756
H 2.019473 -0.760334 -0.339745
H 3.805549 -4.324455 -0.450441

H 2.964325 -2.680384 3.423696
H 2.221436 -4.274377 -2.185061
H 0.519928 -4.195316 -1.710912
H 1.354155 -2.738700 -2.268064
H 0.204880 -0.721093 2.564965
H -0.459864 -2.292708 3.038270
H 0.926474 -1.627503 3.910234
O -0.175407 1.114238 1.123971
C 0.577726 2.151939 1.094845
C 1.920475 2.187434 1.397002
H 2.417627 1.302537 1.777546
H 2.479126 3.115941 1.371571
O -0.603471 0.904558 -1.596273
H -0.585927 1.860140 -1.245844
N -1.994846 -1.318751 -0.657604
O -4.023187 -2.782189 -1.699489
C -4.090928 -1.397163 -2.046611
H -3.850729 -1.383667 -3.111419
C -5.480878 -0.779338 -1.755891
H -6.236419 -1.569201 -1.688213
H -5.779417 -0.125499 -2.586153
C -3.080938 -0.487196 -1.243429
H -2.603670 0.230080 -1.905628
C -3.939761 0.183046 -0.184610
C -5.296133 0.013266 -0.483359
C -6.267431 0.575191 0.344955
H -7.323949 0.448888 0.124169
C -3.523778 0.914268 0.928413
H -2.468020 1.052137 1.147327
C -4.502699 1.466647 1.757845
C -5.861817 1.297710 1.469411
H -4.205092 2.032851 2.635790
H -6.609716 1.732335 2.126495
C -3.700696 -3.065907 -0.344804
H -4.413279 -2.619770 0.361868
H -3.711987 -4.150309 -0.223914
C 2.257717 1.179506 -1.200265
H 1.718788 2.000976 -1.666297
C 3.706092 1.272559 -1.267000
C 4.273077 2.403347 -1.891576
C 4.570713 0.276877 -0.762448
C 5.652164 2.536722 -2.012577
H 3.617926 3.175521 -2.287272
C 5.947602 0.414728 -0.882510
H 4.167096 -0.606038 -0.275749

C 6.493399 1.542794 -1.506902
H 6.071523 3.411275 -2.500530
H 6.603037 -0.357353 -0.490635
H 7.570806 1.643893 -1.598501
C -0.013527 3.385833 0.433065
O -0.620449 3.315238 -0.639656
O 0.188653 4.515532 1.081475
C -0.334610 5.744537 0.477392
C 0.023851 6.889257 1.401137
H -1.414238 5.623336 0.356182
H 0.111804 5.847229 -0.515714
H -0.355308 7.826230 0.980261
H -0.422889 6.751269 2.390191
H 1.108199 6.979026 1.516873
C 4.877693 -4.045151 2.044186
H 5.292285 -3.384643 2.812159
H 4.768926 -5.039637 2.495518
H 5.608330 -4.134074 1.234372
Zero-point correction= 0.647775
Thermal correction to Energy= 0.690564
Thermal correction to Enthalpy= 0.691555
Thermal correction to Gibbs Free Energy= 0.567185
Sum of electronic and thermal Energies= -1894.827152
Sum of electronic and thermal Enthalpies= -1894.826160
Sum of electronic and thermal Free Energies= -1894.950531

***Protonated S-chair TS Ester (ωB97XD/6-31G(d), 313.15K, CPCM: toluene)***

C 0.060521 0.021177 -0.842048
C 1.446316 -0.092776 -0.955352
C -2.470368 -2.435491 0.005519
N -0.404371 -2.199036 0.312199
C -0.770667 -1.130604 -0.409260
N -1.457107 -3.024213 0.568332
C 0.908153 -2.595631 0.752837
C 1.699707 -3.319984 -0.142673
C 1.320875 -2.243651 2.040815
C 2.994420 -3.635591 0.264569
C 2.626245 -2.579913 2.392855
C 3.478255 -3.259247 1.518831
C 1.192204 -3.697285 -1.509693
C 0.398906 -1.546260 3.002573
H 1.925839 -0.988686 -0.593926
H 3.638616 -4.186487 -0.415310
H 2.986180 -2.310005 3.382478
H 1.889479 -4.376491 -2.004201
H 0.217498 -4.191983 -1.452076




***S-Chair*-TS**

H 1.079628 -2.814562 -2.151530
H 0.102410 -0.568633 2.611924
H -0.510528 -2.134924 3.163694
H 0.888353 -1.405809 3.968865
O -0.070442 0.922590 1.007164
C 0.697670 1.950461 0.962915
C 2.065033 1.885153 1.056588
H 2.534448 0.968161 1.393274
H 2.675421 2.778886 0.996393
O -0.589559 0.961726 -1.555512
H -0.934478 1.699535 -0.984946
N -2.094880 -1.276204 -0.612941
O -4.169669 -2.702510 -1.547938
C -4.188012 -1.351240 -1.981245
H -3.977338 -1.413460 -3.048770
C -5.536166 -0.651427 -1.698261
H -6.316072 -1.397941 -1.521010
H -5.843150 -0.063172 -2.570485
C -3.116948 -0.445115 -1.270388
H -2.606543 0.180792 -1.998907
C -3.908510 0.357993 -0.262851
C -5.273047 0.240918 -0.513097
C -6.186155 0.911686 0.293364
H -7.253164 0.823802 0.111582
C -3.421209 1.126840 0.787620
H -2.355163 1.200941 0.984675
C -4.339511 1.794130 1.594189
C -5.709635 1.688577 1.347293
H -3.986214 2.399061 2.423233
H -6.412007 2.213158 1.987635
C -3.876925 -2.897342 -0.180240
H -4.562394 -2.350345 0.479845
H -3.954161 -3.963763 0.029037
C 2.220835 1.013723 -1.253393
H 1.723708 1.880570 -1.679910
C 3.682634 1.001525 -1.346088
C 4.321083 2.079034 -1.973870
C 4.463212 -0.043188 -0.826867
C 5.705079 2.108169 -2.096451
H 3.724918 2.895759 -2.372032
C 5.844965 -0.010473 -0.947704
H 3.998551 -0.882954 -0.317512
C 6.469065 1.062929 -1.583998
H 6.186554 2.946311 -2.589536
H 6.439411 -0.823037 -0.542267
H 7.550261 1.084596 -1.676927
C 0.028780 3.236686 0.524915
O -0.959793 3.233034 -0.195592
O 0.601357 4.322983 0.993655
C 0.029395 5.595930 0.598971

C 0.946657 6.679038 1.118399
H -0.973421 5.661311 1.028538
H -0.058444 5.611050 -0.490087
H 0.533027 7.657377 0.858260
H 1.041282 6.622035 2.206103
H 1.941370 6.594170 0.672339
C 4.884146 -3.599285 1.939924
H 5.379097 -2.732064 2.388054
H 4.879331 -4.396553 2.691197
H 5.485038 -3.939855 1.092754
Zero-point correction= 0.657242
Thermal correction to Energy= 0.699186
Thermal correction to Enthalpy= 0.700177
Thermal correction to Gibbs Free Energy= 0.578408
Sum of electronic and thermal Energies= -1894.270186
Sum of electronic and thermal Enthalpies= -1894.269195
Sum of electronic and thermal Free Energies= -1894.390964

Single point energy calculated with M062X/6-31++G(d,p); CPCM: toluene
E(RM062X) = -1894.85882512

***Protonated S-chair TS Ester (B3LYP/6-31G(d) optimized, 313.15 K, CPCM: toluene)***
C 0.101757 0.044144 -0.852418
C 1.505221 0.052977 -0.820734
C -2.345797 -2.534421 -0.111687
N -0.269741 -2.261281 0.192206
C -0.679524 -1.142967 -0.448059
N -1.304603 -3.135041 0.397615
C 1.040284 -2.673139 0.653696
C 1.865714 -3.378051 -0.238016
C 1.383778 -2.425726 1.992510
C 3.109035 -3.798130 0.242881
C 2.640067 -2.871081 2.414634
C 3.514412 -3.554572 1.561415
C 1.443234 -3.666538 -1.658472
C 0.445432 -1.722422 2.941480
H 2.003699 -0.788779 -0.363148
H 3.770568 -4.340311 -0.427873
H 2.936154 -2.687241 3.444258
H 2.180731 -4.301831 -2.154821
H 0.476477 -4.181127 -1.693349
H 1.346835 -2.747827 -2.250851
H 0.192960 -0.718239 2.583005
H -0.491456 -2.281079 3.053197
H 0.901672 -1.632963 3.930717
O -0.159253 1.100426 1.138747

C 0.609552 2.129625 1.112652
C 1.953012 2.144763 1.407292
H 2.442453 1.248426 1.770965
H 2.525077 3.064777 1.377303
O -0.620301 0.914486 -1.565749
H -0.603264 1.861102 -1.196616
N -2.016756 -1.315500 -0.643984
O -4.055572 -2.779466 -1.676895
C -4.112952 -1.396372 -2.036664
H -3.875898 -1.393133 -3.101672
C -5.497552 -0.764216 -1.748499
H -6.256309 -1.547378 -1.647702
H -5.801431 -0.133734 -2.594180
C -3.091132 -0.485026 -1.249789
H -2.605292 0.210193 -1.928552
C -3.940423 0.225010 -0.209760
C -5.299114 0.064541 -0.501796
C -6.261837 0.665345 0.309831
H -7.320113 0.545538 0.093904
C -3.513464 0.984786 0.879889
H -2.455691 1.112721 1.094837
C -4.483243 1.577505 1.692489
C -5.845281 1.418144 1.410515
H -4.176335 2.167704 2.551280
H -6.586371 1.883947 2.054000
C -3.732596 -3.049825 -0.318121
H -4.440470 -2.588958 0.383246
H -3.753562 -4.131895 -0.182308
C 2.245740 1.150653 -1.222286
H 1.708281 1.982484 -1.670645
C 3.693810 1.231159 -1.309576
C 4.261841 2.374268 -1.910916
C 4.555860 0.212714 -0.847439
C 5.640616 2.498031 -2.048426
H 3.608205 3.164161 -2.271812
C 5.932439 0.340582 -0.985297
H 4.151541 -0.680437 -0.381265
C 6.479794 1.481504 -1.584937
H 6.061105 3.382998 -2.516211
H 6.585295 -0.449504 -0.626609
H 7.556646 1.575010 -1.690161
C 0.025965 3.376740 0.471692
O -0.626826 3.320494 -0.574792
O 0.284100 4.501939 1.108964
C -0.215116 5.744810 0.514300

C 0.225359 6.882099 1.411256
H -1.302741 5.666911 0.440290
H 0.195804 5.822655 -0.495798
H -0.133409 7.828930 0.994777
H -0.187410 6.770969 2.418450
H 1.316387 6.928672 1.481543
C 4.847212 -4.055058 2.063529
H 5.251997 -3.402553 2.843320
H 4.745065 -5.057786 2.498108
H 5.580693 -4.123848 1.254324
Zero-point correction= 0.647350
Thermal correction to Energy= 0.690222
Thermal correction to Enthalpy= 0.691213
Thermal correction to Gibbs Free Energy= 0.566594
Sum of electronic and thermal Energies= -1894.858764
Sum of electronic and thermal Enthalpies= -1894.857773
Sum of electronic and thermal Free Energies= -1894.982392

***Protonated S-boat TS Ester (B3LYP/6-31G(d) gas-phase optimized, 313.15 K)***
C -0.263217 -0.256849 1.085125
C 1.102639 -0.031503 1.307664
C -2.971557 1.802220 -0.188561
N -0.856334 1.832660 -0.267550
C -1.160817 0.735532 0.460031
N -1.981639 2.502285 -0.669755
C 0.418766 2.400056 -0.657289
C 1.067873 3.261017 0.243718
C 0.874334 2.155750 -1.960686
C 2.265296 3.838097 -0.184574
C 2.075739 2.765431 -2.331503
C 2.785178 3.602726 -1.464260
C 0.500911 3.569803 1.609311
C 0.092914 1.306827 -2.930922
H 1.580389 0.774817 0.769359
H 2.794804 4.503902 0.492375
H 2.462753 2.581127 -3.330138
H 1.111054 4.322371 2.114651
H -0.520361 3.962271 1.539062
H 0.469779 2.684401 2.257074
H -0.173917 0.341454 -2.492063
H -0.828535 1.816795 -3.237876
H 0.685734 1.111516 -3.827244
O -0.269173 -1.603032 -0.542769
C 0.823076 -2.312502 -0.528758

C 1.074516 -3.324504 0.359277
H 0.317314 -3.651123 1.065232
H 1.996591 -3.890315 0.313688
O -0.901062 -1.189537 1.858441
H -1.151949 -1.890011 1.217836
N -2.524200 0.715503 0.517722
O -4.851848 1.965722 1.183602
C -4.717319 0.661663 1.751486
H -4.546762 0.853122 2.812893
C -5.965159 -0.223690 1.514591
H -6.836604 0.404769 1.303790
H -6.196412 -0.793817 2.424354
C -3.526870 -0.180230 1.147528
H -3.016801 -0.713002 1.947267
C -4.197115 -1.116061 0.154291
C -5.578159 -1.143968 0.380436
C -6.394132 -1.968298 -0.393609
H -7.467759 -1.996599 -0.228408
C -3.606825 -1.896041 -0.841168
H -2.535843 -1.866859 -1.024978
C -4.431812 -2.714273 -1.617232
C -5.812543 -2.751030 -1.393951
H -3.995731 -3.324882 -2.402330
H -6.439890 -3.390884 -2.007737
C -4.433485 2.108977 -0.167824
H -4.989462 1.454782 -0.852463
H -4.600985 3.148475 -0.453743
C 1.850446 -0.914299 2.065142
H 1.311005 -1.640870 2.664516
C 3.285533 -0.862345 2.245550
C 4.133420 -0.088063 1.420505
C 3.860802 -1.615958 3.292116
C 5.502162 -0.060177 1.654140
H 3.721252 0.464251 0.581588
C 5.230303 -1.577500 3.526892
H 3.217964 -2.222020 3.925447
C 6.053483 -0.798073 2.709104
H 6.147381 0.533004 1.012991
H 5.658136 -2.153808 4.341457
H 7.124477 -0.770002 2.887615
C 1.943434 -1.867981 -1.453257
O 2.118733 -0.706179 -1.765277
O 2.721441 -2.886029 -1.842058
C 3.860317 -2.547583 -2.681596
C 4.572410 -3.839837 -3.027534

H 4.501117 -1.854258 -2.127687
H 3.489154 -2.026600 -3.569022
H 5.437514 -3.623589 -3.663134
H 4.927903 -4.347629 -2.125489
H 3.909163 -4.519977 -3.570519
C 4.060992 4.273736 -1.912784
H 4.614103 3.649906 -2.621916
H 3.843118 5.224127 -2.416805
H 4.717605 4.498032 -1.066446
Zero-point correction= 0.647726
Thermal correction to Energy= 0.691043
Thermal correction to Enthalpy= 0.692035
Thermal correction to Gibbs Free Energy= 0.566261
Sum of electronic and thermal Energies= -1894.811632
Sum of electronic and thermal Enthalpies= -1894.810641
Sum of electronic and thermal Free Energies= -1894.936414

***Protonated S-boat TS Ester (B3LYP/6-31G(d) optimized, 313.15 K, CPCM: toluene)***
C -0.263583 -0.265302 1.073149
C 1.099445 -0.024449 1.303275
C -2.984601 1.804439 -0.158483
N -0.870361 1.834280 -0.258781
C -1.168548 0.729151 0.458721
N -1.999072 2.509959 -0.640951
C 0.399104 2.401789 -0.664685
C 1.065720 3.256498 0.229140
C 0.831612 2.164006 -1.977802
C 2.258542 3.831546 -0.216598
C 2.028345 2.771715 -2.366587
C 2.756525 3.599899 -1.505304
C 0.525560 3.557728 1.607024
C 0.031099 1.318927 -2.935918
H 1.569345 0.791013 0.772036
H 2.802659 4.490162 0.455586
H 2.397201 2.593114 -3.373183
H 1.126833 4.331816 2.089987
H -0.509494 3.915298 1.562385
H 0.539596 2.675601 2.259473
H -0.188181 0.336911 -2.507788
H -0.917988 1.807487 -3.187608
H 0.588610 1.163658 -3.862407
O -0.243812 -1.595198 -0.560726
C 0.851163 -2.301320 -0.542646
C 1.120094 -3.288052 0.368314

H 0.374692 -3.601015 1.091982
H 2.050322 -3.840766 0.333508
O -0.891631 -1.200245 1.848812
H -1.160485 -1.902912 1.220016
N -2.530545 0.708884 0.528443
O -4.856348 1.946874 1.228120
C -4.718937 0.631849 1.772292
H -4.548080 0.802562 2.836478
C -5.965300 -0.251413 1.519018
H -6.836150 0.377067 1.306261
H -6.200765 -0.829369 2.422208
C -3.525384 -0.196531 1.155798
H -3.011553 -0.732816 1.950221
C -4.191843 -1.128837 0.156641
C -5.572941 -1.162565 0.379923
C -6.385204 -1.983971 -0.401722
H -7.459088 -2.015377 -0.238895
C -3.597611 -1.900895 -0.842488
H -2.526244 -1.867742 -1.022662
C -4.417988 -2.716758 -1.626211
C -5.799504 -2.758469 -1.406449
H -3.978044 -3.321033 -2.414127
H -6.423837 -3.395566 -2.026334
C -4.446203 2.109057 -0.124846
H -5.005127 1.462876 -0.813945
H -4.617410 3.151114 -0.397709
C 1.852679 -0.901598 2.060544
H 1.318898 -1.642032 2.647087
C 3.285776 -0.831787 2.259885
C 4.129499 -0.002098 1.486792
C 3.862154 -1.627311 3.274152
C 5.495526 0.036028 1.735997
H 3.717637 0.595230 0.679486
C 5.229241 -1.580916 3.524093
H 3.222846 -2.275483 3.867669
C 6.048497 -0.748178 2.756173
H 6.136128 0.673594 1.134257
H 5.657877 -2.192551 4.312034
H 7.117157 -0.713362 2.946750
C 1.953085 -1.882035 -1.500146
O 2.088097 -0.741616 -1.898610
O 2.764383 -2.898801 -1.825775
C 3.889593 -2.577327 -2.689100
C 4.640538 -3.865743 -2.959098
H 4.511815 -1.834035 -2.181143

H 3.501580 -2.124625 -3.606098
H 5.497910 -3.659881 -3.608395
H 5.012138 -4.307125 -2.028896
H 3.997970 -4.596594 -3.459882
C 4.030057 4.264348 -1.970210
H 4.573770 3.633051 -2.680033
H 3.810380 5.211822 -2.479073
H 4.694180 4.491390 -1.130613
Zero-point correction= 0.647347
Thermal correction to Energy= 0.690807
Thermal correction to Enthalpy= 0.691798
Thermal correction to Gibbs Free Energy= 0.564776
Sum of electronic and thermal Energies= -1894.843851
Sum of electronic and thermal Enthalpies= -1894.842859
Sum of electronic and thermal Free Energies= -1894.969882

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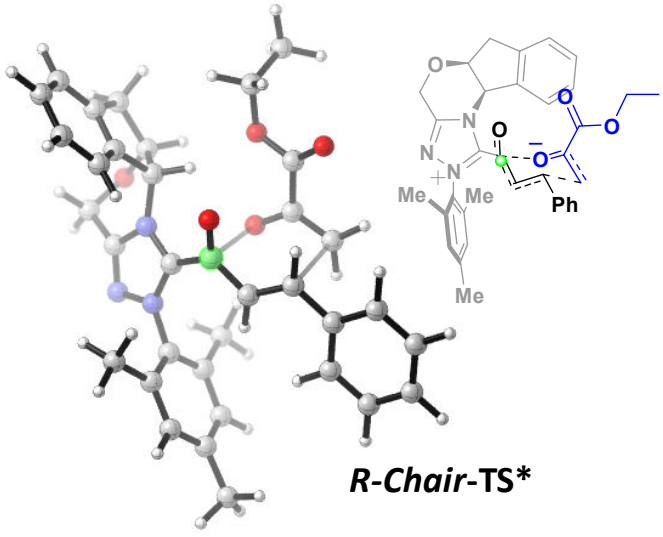
***Deprotonated R-chair TS Ester (ωB97XD/6-31G(d), CPCM: toluene)***

C 0.153992 0.141558 0.665561
C 1.555289 0.298189 0.491828
C -2.006652 -2.392074 -0.791976
N 0.001963 -2.299447 -0.187416
C -0.491046 -1.085578 0.075950
N -0.935235 -3.129090 -0.745176
C 1.357319 -2.746085 -0.047958
C 2.183300 -2.658831 -1.173111
C 1.799987 -3.174784 1.202288
C 3.517213 -3.022690 -1.006636
C 3.143507 -3.527269 1.314746
C 4.014647 -3.447596 0.227917
C 1.656685 -2.126190 -2.478951
C 0.873663 -3.204340 2.389028
H 2.130139 -0.509893 0.066910
H 4.188873 -2.959248 -1.859274
H 3.520891 -3.860879 2.278152
H 2.450606 -2.094415 -3.228866
H 0.847387 -2.756318 -2.862988
H 1.251928 -1.112104 -2.355140
H 0.643652 -2.186868 2.727238
H -0.074276 -3.695636 2.148255
H 1.333439 -3.735763 3.225484
O -0.074841 0.817046 -1.787047
C 0.254676 2.013394 -1.540951
C 1.555419 2.490086 -1.515842
H 2.333363 1.882588 -1.965001
H 1.772877 3.535950 -1.337089



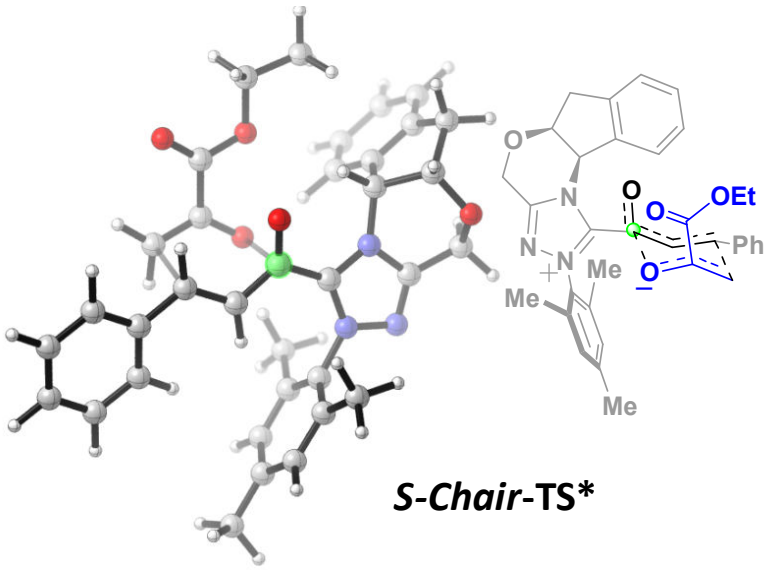

***R-Chair*-TS***

O -0.610701 0.945648 1.220695
N -1.779379 -1.144929 -0.292481
O -3.553451 -1.524001 -2.289735
C -3.658526 -0.254032 -1.650029
H -3.287964 0.457153 -2.387163
C -5.106370 0.052180 -1.205294
H -5.813600 -0.582635 -1.747421
H -5.352901 1.094172 -1.440029
C -2.811314 -0.115386 -0.342658
H -2.310812 0.850361 -0.342304
C -3.810745 -0.251148 0.778986
C -5.110488 -0.166063 0.287305
C -6.190361 -0.257862 1.159327
H -7.209074 -0.193953 0.786993
C -3.555226 -0.416602 2.134244
H -2.533181 -0.453792 2.499313
C -4.637857 -0.516805 3.005044
C -5.945027 -0.439849 2.519300
H -4.464983 -0.652407 4.068290
H -6.779106 -0.520165 3.210249
C -3.330132 -2.628448 -1.437703
H -4.120815 -2.740976 -0.683547
H -3.297096 -3.524700 -2.056904
C 2.107751 1.549339 0.620496
H 1.500449 2.319400 1.085716
C 3.553195 1.828876 0.539971
C 4.027199 3.076319 0.963460
C 4.479371 0.889048 0.065925
C 5.384027 3.378317 0.922872
H 3.317432 3.816360 1.324627
C 5.834985 1.190604 0.023311
H 4.144028 -0.085949 -0.276946
C 6.294076 2.435123 0.452571
H 5.731100 4.351018 1.258764
H 6.538309 0.450381 -0.347163
H 7.354319 2.667052 0.417741
C -0.867423 2.951193 -1.110006
O -2.045906 2.744647 -1.325928
O -0.431551 4.047284 -0.475170
C -1.440437 4.956735 -0.015082
C -0.736272 6.075525 0.722661
H -2.133584 4.413305 0.633891
H -2.005455 5.328449 -0.875362
H -1.472352 6.795663 1.092801
H -0.176615 5.682655 1.576611
H -0.041205 6.600881 0.061123
C 5.477086 -3.772526 0.391413
H 5.637275 -4.505128 1.187609
H 5.903882 -4.170238 -0.533854
H 6.040183 -2.869032 0.654225

Zero-point correction= 0.644589
Thermal correction to Energy= 0.682913
Thermal correction to Enthalpy= 0.683857
Thermal correction to Gibbs Free Energy= 0.570737
Sum of electronic and thermal Energies= -1893.864484
Sum of electronic and thermal Enthalpies= -1893.863540
Sum of electronic and thermal Free Energies= -1893.976660

Single point energy calculated with M062X/6-31++G(d,p), CPCM: toluene
E(RM062X) = -1894.44730844

***Deprotonated S-chair TS Ester (ωB97XD/6-31G(d), CPCM: toluene)***




***S-Chair*-TS***

C 0.342762 0.265447 -1.035491
C 1.711913 0.467005 -0.704748
C -1.823951 -2.572091 -0.280923
N 0.227698 -2.159150 -0.120832
C -0.312739 -1.015594 -0.564624
N -0.705743 -3.145469 0.048470
C 1.596382 -2.449842 0.203695
C 2.435856 -2.919456 -0.807705
C 2.022516 -2.200582 1.509565
C 3.770623 -3.133817 -0.477077
C 3.368621 -2.434073 1.788272
C 4.253522 -2.892129 0.811183
C 1.924294 -3.117277 -2.209337
C 1.082571 -1.633698 2.537648
H 2.246442 -0.297979 -0.166200
H 4.453992 -3.485376 -1.246013
H 3.736297 -2.239919 2.792693
H 2.666005 -3.633112 -2.823387
H 0.999940 -3.703353 -2.221734
H 1.711872 -2.150564 -2.681602
H 0.770015 -0.618625 2.253651
H 0.178457 -2.245507 2.629197
H 1.565767 -1.589995 3.516799
O -0.179719 1.127169 1.261355
C 0.188330 2.311472 0.990549
C 1.477134 2.786458 1.142685
H 2.182500 2.203341 1.723827
H 1.721266 3.818371 0.923302
O -0.359706 1.018147 -1.724366
N -1.631946 -1.271838 -0.646950
O -3.628807 -2.652489 -1.744360
C -3.787122 -1.239234 -1.852958
H -3.605916 -1.027563 -2.907268

C -5.183082 -0.783414 -1.389110
H -5.910979 -1.590259 -1.512843
H -5.521684 0.062218 -2.001532
C -2.799846 -0.439022 -0.939790
H -2.431307 0.468667 -1.418648
C -3.620717 -0.150740 0.301376
C -4.973634 -0.352210 0.039770
C -5.919045 -0.120805 1.031746
H -6.976725 -0.275054 0.837549
C -3.173403 0.286458 1.541048
H -2.116919 0.489367 1.701054
C -4.123869 0.507595 2.535970
C -5.482638 0.306202 2.285298
H -3.803291 0.850573 3.515288
H -6.208275 0.484816 3.073580
C -3.186486 -3.144183 -0.492345
H -3.866282 -2.880873 0.326722
H -3.126029 -4.229606 -0.572063
C 2.278145 1.705752 -0.864397
H 1.737647 2.439584 -1.454425
C 3.704850 1.989939 -0.622780
C 4.269745 3.149584 -1.165933
C 4.526362 1.134004 0.124808
C 5.616908 3.443023 -0.980192
H 3.642123 3.825488 -1.740972
C 5.870818 1.427488 0.312577
H 4.114212 0.235415 0.575421
C 6.423165 2.582372 -0.240390
H 6.036499 4.346198 -1.413139
H 6.490721 0.754224 0.897639
H 7.474463 2.809598 -0.091324
C -0.767499 3.275153 0.295527
O -0.444160 4.372960 -0.114936
O -2.023177 2.816720 0.212897
C -2.954776 3.730285 -0.382037
C -4.298924 3.045647 -0.502719
H -2.573207 4.041937 -1.358614
H -3.017628 4.624447 0.246952
H -5.037935 3.764732 -0.870502
H -4.253605 2.213870 -1.211531
H -4.636007 2.658030 0.462810
C 5.704190 -3.136734 1.137728
H 6.000291 -2.614940 2.051976
H 5.891592 -4.206136 1.288375
H 6.354314 -2.800775 0.324105

Zero-point correction= 0.645620
Thermal correction to Energy= 0.683305
Thermal correction to Enthalpy= 0.684250
Thermal correction to Gibbs Free Energy= 0.575551
Sum of electronic and thermal Energies= -1893.863685
Sum of electronic and thermal Enthalpies= -1893.862741
Sum of electronic and thermal Free Energies= -1893.971440

Single point energy calculated with M062X/6-31++G(d,p), CPCM: toluene
E(RM062X) = -1894.44480188

## Structures relevant in the Kojic Acid (4)* system

*OMe used instead of silyl protecting group

***Protonated R-Intermediate Kojic Acid (B3LYP/6-31G(d) optimized, 313.15 K, CPCM: toluene)***

| | | | |
|---|---|---|---|
| C | 0.18786800 | -0.23814800 | 0.20867800 |
| C | -1.05364800 | 0.59179300 | 0.41102600 |
| C | 3.38199600 | 0.87157500 | -1.21484300 |
| N | 1.45923100 | 1.72063000 | -0.95404000 |
| C | 1.37703200 | 0.49479900 | -0.42212800 |
| N | 2.71457800 | 1.96615000 | -1.46400300 |
| C | 0.45325500 | 2.75185400 | -1.10147000 |
| C | -0.27753900 | 2.79061500 | -2.29756800 |
| C | 0.32209500 | 3.71050200 | -0.08497000 |
| C | -1.21159200 | 3.82184600 | -2.43879300 |
| C | -0.62222400 | 4.71936600 | -0.28405700 |
| C | -1.40155400 | 4.78972800 | -1.44611900 |
| C | -0.05769800 | 1.78205500 | -3.39970400 |
| C | 1.15444900 | 3.65724500 | 1.17180800 |
| H | -1.55594200 | 0.92017900 | -0.49238800 |
| H | -1.79540900 | 3.87418900 | -3.35412300 |
| H | -0.74812300 | 5.47363700 | 0.48854400 |
| H | -0.79143600 | 1.91896900 | -4.19785300 |
| H | 0.94123400 | 1.88839700 | -3.83926100 |
| H | -0.14040300 | 0.75052200 | -3.03742900 |
| H | 0.91671500 | 2.76978700 | 1.77109300 |
| H | 2.22611300 | 3.62426500 | 0.94534300 |
| H | 0.96742400 | 4.53697900 | 1.79221300 |
| O | -0.06189700 | -1.26782000 | -0.81831900 |
| C | -1.23519400 | -1.99272400 | -0.77291400 |
| C | -1.92549700 | -2.11635100 | -1.93292800 |
| H | -1.65525500 | -1.61977200 | -2.85590400 |
| O | 0.69928000 | -0.80319400 | 1.35782600 |

| | | | |
|---|---|---|---|
| H | 0.05721600 | -1.54468900 | 1.60482500 |
| N | 2.60174100 | -0.05427000 | -0.57204700 |
| O | 4.56693900 | -0.85789700 | -2.22847300 |
| C | 4.12274800 | -1.88715700 | -1.33604800 |
| H | 3.59220000 | -2.58471400 | -1.98586000 |
| C | 5.29474600 | -2.56471800 | -0.58638500 |
| H | 6.23471300 | -2.39453200 | -1.12151200 |
| H | 5.13808000 | -3.65084300 | -0.55382900 |
| C | 3.16651200 | -1.36820600 | -0.19188000 |
| H | 2.32430600 | -2.04493900 | -0.05441100 |
| C | 4.05923500 | -1.29543900 | 1.03588900 |
| C | 5.26083200 | -1.97328900 | 0.80247900 |
| C | 6.22588900 | -2.05252600 | 1.80705000 |
| H | 7.16243600 | -2.57562000 | 1.63363200 |
| C | 3.79583600 | -0.69425400 | 2.26757800 |
| H | 2.85414600 | -0.18704600 | 2.44803600 |
| C | 4.76826500 | -0.76900100 | 3.26706100 |
| C | 5.97418200 | -1.44233700 | 3.03792900 |
| H | 4.58517100 | -0.30331200 | 4.23105900 |
| H | 6.72123200 | -1.49109600 | 3.82507600 |
| C | 4.73992000 | 0.43852100 | -1.66377300 |
| H | 5.46004000 | 0.44482300 | -0.83552100 |
| H | 5.10360100 | 1.09477100 | -2.45545600 |
| C | -1.54126000 | 0.85804600 | 1.63418700 |
| H | -0.98818000 | 0.47413600 | 2.48891000 |
| C | -2.75865200 | 1.60679000 | 1.96237500 |
| C | -3.54163900 | 2.27105300 | 0.99822300 |
| C | -3.16353500 | 1.66458400 | 3.30816000 |
| C | -4.69211100 | 2.95885500 | 1.37180400 |
| H | -3.24505100 | 2.26012700 | -0.04632600 |
| C | -4.31686300 | 2.35281100 | 3.68187800 |
| H | -2.56730300 | 1.15927900 | 4.06393400 |
| C | -5.08548700 | 3.00137100 | 2.71416000 |
| H | -5.28572600 | 3.46562700 | 0.61600500 |
| H | -4.61371800 | 2.38274500 | 4.72624500 |
| H | -5.98423500 | 3.53962100 | 3.00131000 |
| C | -1.68048800 | -2.71864500 | 0.42322200 |
| O | -1.11354800 | -2.63880700 | 1.54354900 |
| C | -2.84694600 | -3.54603700 | 0.20504400 |
| H | -3.23721100 | -4.12961500 | 1.02857100 |
| C | -3.45854100 | -3.61146400 | -1.00014700 |
| O | -3.01122800 | -2.90604900 | -2.06865100 |
| C | -4.67115600 | -4.42744600 | -1.35006300 |
| H | -4.41009600 | -5.09899300 | -2.18568900 |
| H | -5.45670500 | -3.74723600 | -1.72077700 |
| O | -5.07913400 | -5.13250700 | -0.20907400 |
| C | -2.42871200 | 5.88324800 | -1.61189000 |
| H | -3.29783400 | 5.70078700 | -0.96713200 |
| H | -2.01892900 | 6.85923900 | -1.33034000 |
| H | -2.78584000 | 5.94625300 | -2.64371100 |

| | | | |
|---|---|---|---|
| C | -6.23499400 | -5.95051100 | -0.39889500 |
| H | -6.68116800 | -5.80150500 | -1.38844800 |
| H | -5.95918600 | -7.00569900 | -0.29121100 |
| H | -6.97619100 | -5.69253400 | 0.36429000 |

Zero-point correction= 0.666408
Thermal correction to Energy= 0.710831
Thermal correction to Enthalpy= 0.711823
Thermal correction to Gibbs Free Energy= 0.581454
Sum of electronic and thermal Energies= -2046.268238
Sum of electronic and thermal Enthalpies= -2046.267246
Sum of electronic and thermal Free Energies= -2046.397616

***Protonated S-Intermediate Kojic Acid (B3LYP/6-31G(d) optimized, 313.15 K, CPCM: toluene)***

| | | | |
|---|---|---|---|
| C | -0.22564900 | 0.31074900 | 0.31256400 |
| C | 0.58092500 | 1.05358600 | -0.73142300 |
| C | -3.37675500 | -0.98538900 | -1.09882500 |
| N | -1.33636800 | -1.54494700 | -1.11063500 |
| C | -1.39191300 | -0.44133600 | -0.34795600 |
| N | -2.57814800 | -1.89055700 | -1.59120300 |
| C | -0.20918400 | -2.36268800 | -1.51056700 |
| C | 0.39323400 | -2.09600300 | -2.75025500 |
| C | 0.15018700 | -3.45167800 | -0.70060600 |
| C | 1.46034900 | -2.91703800 | -3.12976900 |
| C | 1.21646500 | -4.24349500 | -1.13751700 |
| C | 1.88966800 | -3.98895400 | -2.33987700 |
| C | -0.11693500 | -1.02271300 | -3.68329800 |
| C | -0.58350800 | -3.77518400 | 0.57750300 |
| H | 1.16808400 | 0.42464400 | -1.39340200 |
| H | 1.95296700 | -2.72318800 | -4.07915300 |
| H | 1.51870200 | -5.09078000 | -0.52695600 |
| H | 0.58370700 | -0.86763500 | -4.50763400 |
| H | -1.08117400 | -1.31678300 | -4.11525200 |
| H | -0.26899800 | -0.05978900 | -3.18531500 |
| H | -0.46368900 | -2.97869100 | 1.31924600 |
| H | -1.65738000 | -3.90083700 | 0.39723900 |
| H | -0.20572000 | -4.70475200 | 1.01075900 |
| O | 0.57202900 | -0.74201200 | 0.91529200 |
| C | 1.87582200 | -0.46643000 | 1.27680100 |
| C | 2.82682000 | -1.34307500 | 0.87189100 |
| H | 2.63763500 | -2.18835700 | 0.22244900 |
| O | -0.79191200 | 1.11027000 | 1.28221900 |
| H | -0.02341900 | 1.39361400 | 1.87730100 |
| N | -2.69404600 | -0.07220200 | -0.33166600 |
| O | -4.95530300 | 0.64399700 | -1.63300100 |
| C | -4.64133300 | 1.51294600 | -0.54177900 |

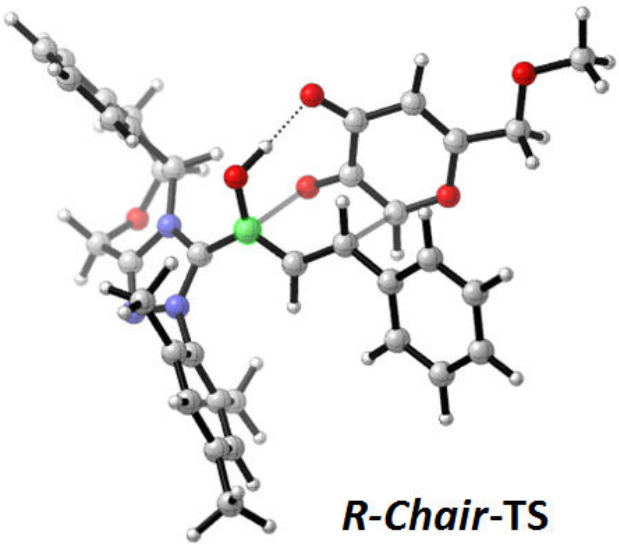
| | | | |
|---|---|---|---|
| H | -4.37472600 | 2.45177500 | -1.02883300 |
| C | -5.82681400 | 1.69020000 | 0.44220500 |
| H | -6.75615000 | 1.34102700 | -0.02071700 |
| H | -5.96785100 | 2.75463300 | 0.66859300 |
| C | -3.43888000 | 1.01514300 | 0.35626600 |
| H | -2.72886200 | 1.81978800 | 0.53068800 |
| C | -4.09028700 | 0.54167400 | 1.64237800 |
| C | -5.43528600 | 0.92162500 | 1.68122600 |
| C | -6.21824300 | 0.60422900 | 2.79235000 |
| H | -7.26472200 | 0.89429500 | 2.83202600 |
| C | -3.50024900 | -0.14587300 | 2.70402000 |
| H | -2.44909300 | -0.41513800 | 2.67558000 |
| C | -4.28882900 | -0.46776900 | 3.81003100 |
| C | -5.63863000 | -0.09661400 | 3.85206400 |
| H | -3.85075700 | -1.00595400 | 4.64551200 |
| H | -6.24024200 | -0.35415500 | 4.71913600 |
| C | -4.82799200 | -0.74545400 | -1.35902100 |
| H | -5.44579500 | -1.06383900 | -0.50860600 |
| H | -5.14549000 | -1.29016900 | -2.24915000 |
| C | 0.57674000 | 2.39373300 | -0.82776100 |
| H | -0.03939900 | 2.94235500 | -0.11800300 |
| C | 1.31871900 | 3.22453800 | -1.78067300 |
| C | 1.17182500 | 4.62136200 | -1.70085100 |
| C | 2.16812800 | 2.69636300 | -2.77242300 |
| C | 1.84624300 | 5.46558100 | -2.58141000 |
| H | 0.52184600 | 5.04408100 | -0.93872900 |
| C | 2.84066100 | 3.53893600 | -3.65151600 |
| H | 2.30530300 | 1.62240500 | -2.85789500 |
| C | 2.68224300 | 4.92647200 | -3.56032400 |
| H | 1.71914700 | 6.54134900 | -2.50286600 |
| H | 3.49164000 | 3.11564600 | -4.41119200 |
| H | 3.20921700 | 5.58061700 | -4.24892900 |
| C | 2.23355100 | 0.64529600 | 2.16388700 |
| O | 1.42123200 | 1.51153300 | 2.55492600 |
| C | 3.62601100 | 0.66054300 | 2.55196900 |
| H | 3.97609900 | 1.43775200 | 3.21887100 |
| C | 4.49811100 | -0.27259800 | 2.10507300 |
| O | 4.11448400 | -1.26953500 | 1.26989800 |
| C | 5.96128100 | -0.36511600 | 2.43386800 |
| H | 6.53997600 | -0.33281700 | 1.49433200 |
| H | 6.16018800 | -1.34817400 | 2.89506700 |
| O | 6.29903500 | 0.69119200 | 3.29180800 |
| C | 3.01741100 | -4.88249200 | -2.79730000 |
| H | 3.54762600 | -5.32544600 | -1.94865700 |
| H | 2.63305900 | -5.70856400 | -3.40934300 |

| | | | |
|---|---|---|---|
| H | 3.74060600 | -4.33371800 | -3.40839000 |
| C | 7.67017500 | 0.67660600 | 3.66589000 |
| H | 7.82308800 | 1.53048300 | 4.32830400 |
| H | 7.92859700 | -0.24894600 | 4.20013500 |
| H | 8.32492600 | 0.77555800 | 2.78815700 |

Zero-point correction= 0.667113
Thermal correction to Energy= 0.711076
Thermal correction to Enthalpy= 0.712068
Thermal correction to Gibbs Free Energy= 0.585231
Sum of electronic and thermal Energies= -2046.271846
Sum of electronic and thermal Enthalpies= -2046.270854
Sum of electronic and thermal Free Energies= -2046.397691

***Protonated R-chair TS Kojic Acid (B3LYP/6-31G(d) optimized, 313.15 K, CPCM: toluene)***

C 0.365572 0.126532 0.382136
C -0.814301 0.747475 0.039645
C 3.686820 0.745773 -0.909848
N 2.038086 1.926128 -0.299241
C 1.648291 0.651150 -0.117793
N 3.312517 1.994912 -0.807844
C 1.332441 3.147491 0.016023
C 0.852806 3.927069 -1.049058
C 1.210556 3.525971 1.363078
C 0.198342 5.117804 -0.721083
C 0.547041 4.726941 1.627177
C 0.029968 5.531846 0.605274
C 1.043580 3.520864 -2.491456
C 1.774019 2.692899 2.489882
H -0.734717 1.591216 -0.635158
H -0.182400 5.740814 -1.526386
H 0.442614 5.046389 2.660936
H 0.471371 4.177470 -3.151515
H 2.097766 3.582303 -2.784093
H 0.719923 2.490015 -2.678783
H 1.188546 1.780355 2.657295
H 2.808394 2.389530 2.293212
H 1.764030 3.261519 3.422970
O -0.245782 -1.629229 -1.390415
C -1.409664 -1.900901 -1.019911
C -2.546562 -1.160346 -1.434351
H -2.495751 -0.387460 -2.190229
O 0.567026 -0.872475 1.255975
H 0.033210 -1.713612 1.101862
N 2.705426 -0.109527 -0.483781



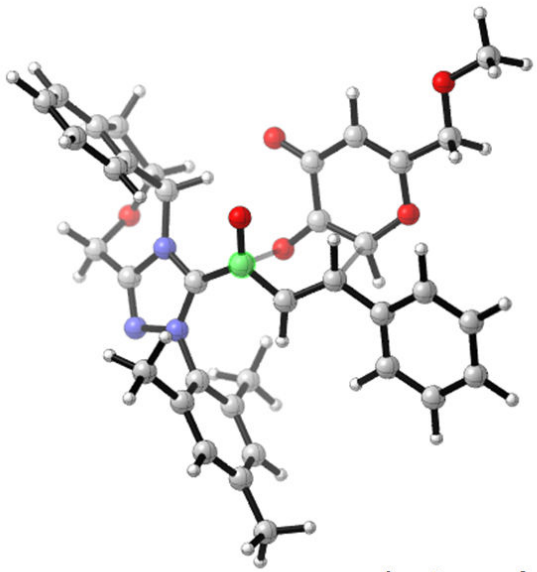
O 4.383942 -0.847318 -2.456412
C 3.694098 -1.951432 -1.857325
H 3.001798 -2.278131 -2.634347
C 4.656577 -3.081742 -1.417779
H 5.617626 -2.981821 -1.933085
H 4.241321 -4.056645 -1.704080
C 2.894644 -1.574806 -0.547871
H 1.898345 -2.018706 -0.575421
C 3.756749 -2.106431 0.584792
C 4.749410 -2.955526 0.083985
C 5.643793 -3.576163 0.956818
H 6.419024 -4.235952 0.576560
C 3.633721 -1.867279 1.954317
H 2.851355 -1.220833 2.338489
C 4.535621 -2.484693 2.823512
C 5.533644 -3.332023 2.327615
H 4.459485 -2.307864 3.892422
H 6.228948 -3.804691 3.015538
C 4.887171 0.141851 -1.563630
H 5.581881 -0.274001 -0.822455
H 5.410163 0.889146 -2.161549
C -2.103095 0.292314 0.412047
H -2.134129 -0.476033 1.180448
C -3.327298 1.083086 0.305032
C -3.448026 2.213707 -0.530053
C -4.441521 0.694675 1.076904
C -4.640674 2.925908 -0.584143
H -2.610523 2.539244 -1.139476
C -5.633915 1.412050 1.021767
H -4.359142 -0.167534 1.733522
C -5.737752 2.528632 0.189479
H -4.718886 3.795089 -1.230477
H -6.478573 1.103566 1.630510
H -6.666229 3.090039 0.143707
C -1.695319 -2.867030 0.102146
O -0.814372 -3.122849 0.945006
C -3.037422 -3.387790 0.139811
H -3.288757 -4.218994 0.786720
C -4.030292 -2.739857 -0.522632
O -3.814655 -1.627710 -1.267914
C -5.487663 -3.104880 -0.511147
H -5.799243 -3.326144 -1.547393
H -6.072973 -2.227566 -0.186260
O -5.677206 -4.206515 0.335015
C -0.703576 6.810540 0.929532

H -0.284697 7.296817 1.816145
H -0.662219 7.518490 0.096357
H -1.762378 6.609839 1.138590
C -7.025796 -4.655016 0.357335
H -7.061456 -5.506603 1.039114
H -7.702393 -3.868811 0.722144
H -7.357089 -4.974253 -0.641176
Zero-point correction= 0.664624
Thermal correction to Energy= 0.708584
Thermal correction to Enthalpy= 0.709576
Thermal correction to Gibbs Free Energy= 0.582868
Sum of electronic and thermal Energies= -2046.236727
Sum of electronic and thermal Enthalpies= -2046.235735
Sum of electronic and thermal Free Energies= -2046.362443

Single point energy calculated with M062X/6-31+G(d,p); CPCM: toluene
E(RM062X) = -2046.20967774

***Deprotonated R-chair TS Kojic Acid (ωB97XD/6-31G(d) optimized, CPCM: toluene)***

C 0.140951 0.249240 0.642443
C -1.176488 0.723546 0.454580
C 3.202038 1.519480 -0.846062
N 1.373195 2.347016 -0.230944
C 1.268964 1.043728 0.045709
N 2.578320 2.660430 -0.802374
C 0.377252 3.365696 -0.070549
C -0.418110 3.674613 -1.180154
C 0.217298 3.957366 1.179727
C -1.412824 4.629986 -0.997849
C -0.793626 4.910142 1.308785
C -1.616343 5.252766 0.237722
C -0.235154 2.950350 -2.487333
C 1.069959 3.550378 2.351987
H -1.349610 1.692915 0.012835
H -2.052302 4.890750 -1.837896
H -0.943702 5.388048 2.273419
H -0.956559 3.305699 -3.227077
H 0.771847 3.105076 -2.888823
H -0.373916 1.868586 -2.358492
H 0.763171 2.568020 2.730817
H 2.127680 3.484234 2.078916
H 0.971113 4.268579 3.169288
O -0.090765 -0.512750 -1.802957



***R-Chair*-TS***

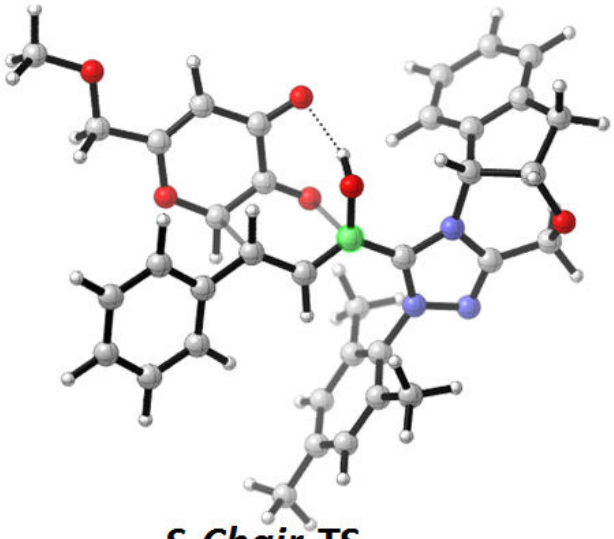
C -0.802820 -1.483555 -1.456643
C -2.199323 -1.324046 -1.267983
H -2.729824 -0.546828 -1.802467
O 0.455070 -0.821285 1.193485
N 2.441236 0.511194 -0.333489
O 4.202896 0.022838 -2.309044
C 3.778280 -1.148274 -1.617310
H 3.169121 -1.686980 -2.342114
C 4.971606 -1.990376 -1.109291
H 5.894240 -1.684185 -1.612246
H 4.807587 -3.047982 -1.344433
C 2.911602 -0.871778 -0.342045
H 2.036018 -1.521680 -0.362215
C 3.828972 -1.160805 0.819770
C 4.996964 -1.779760 0.383638
C 5.979496 -2.136535 1.301956
H 6.895820 -2.618464 0.972519
C 3.607079 -0.895282 2.165601
H 2.676110 -0.438198 2.486452
C 4.594065 -1.247518 3.082648
C 5.772469 -1.861503 2.652320
H 4.444114 -1.049313 4.139603
H 6.533869 -2.130606 3.378438
C 4.491393 1.136534 -1.490528
H 5.257140 0.911546 -0.735456
H 4.848932 1.940518 -2.133537
C -2.216224 -0.183901 0.604462
H -1.987083 -1.085685 1.168009
C -3.643276 0.203668 0.593317
C -4.096876 1.392570 0.005879
C -4.583358 -0.652716 1.176443
C -5.449173 1.712564 0.009166
H -3.391387 2.073887 -0.462127
C -5.937402 -0.333778 1.180704
H -4.242699 -1.576290 1.636876
C -6.375357 0.850835 0.595650
H -5.783588 2.637898 -0.450754
H -6.650182 -1.011875 1.640525
H -7.431809 1.101916 0.594821
C -0.212532 -2.812970 -1.073051
O 0.980089 -3.072609 -1.241861
C -1.166981 -3.774270 -0.553075
H -0.809491 -4.733668 -0.200815
C -2.494245 -3.527288 -0.553039
O -3.032828 -2.383695 -0.991979

C -3.566392 -4.468224 -0.082962
H -4.331219 -4.555861 -0.872469
H -4.066241 -4.024328 0.795158
O -3.005629 -5.709079 0.228738
C -2.721930 6.264239 0.400447
H -3.701977 5.782226 0.310609
H -2.675967 6.754532 1.376369
H -2.666000 7.036189 -0.373883
C -3.964077 -6.619174 0.712963
H -3.441030 -7.552826 0.926328
H -4.437340 -6.250769 1.635181
H -4.750020 -6.808615 -0.033017
Zero-point correction= 0.662525
Thermal correction to Energy= 0.702381
Thermal correction to Enthalpy= 0.703325
Thermal correction to Gibbs Free Energy= 0.587917
Sum of electronic and thermal Energies= -2045.194613
Sum of electronic and thermal Enthalpies= -2045.193668
Sum of electronic and thermal Free Energies= -2045.309076

Single point energy calculated with M062X/6-31++G(d,p), CPCM: toluene
E(RM062X) = -2045.80149095

***Protonated S-chair TS Kojic Acid (B3LYP/6-31G(d) optimized, 313.15 K, CPCM: toluene)***

C 0.360950 0.162670 -0.812564
C -0.849665 0.821986 -0.801808
C 3.769856 1.191966 -0.124863
N 1.834829 2.000144 0.162413
C 1.627315 0.803143 -0.435234
N 3.170809 2.249509 0.349442
C 0.903417 3.028628 0.574523
C 0.558795 4.019804 -0.359891
C 0.454770 3.035097 1.904958
C -0.312613 5.024772 0.068810
C -0.413940 4.066626 2.274580
C -0.809233 5.066263 1.377853
C 1.097748 4.008824 -1.770514
C 0.882464 1.983664 2.898687
H -0.876725 1.848776 -0.466368
H -0.598684 5.801492 -0.635753
H -0.780959 4.093567 3.297476
H 0.774381 4.902384 -2.309724
H 2.193223 3.986459 -1.780872
H 0.747210 3.136649 -2.336559



***S-Chair-TS***

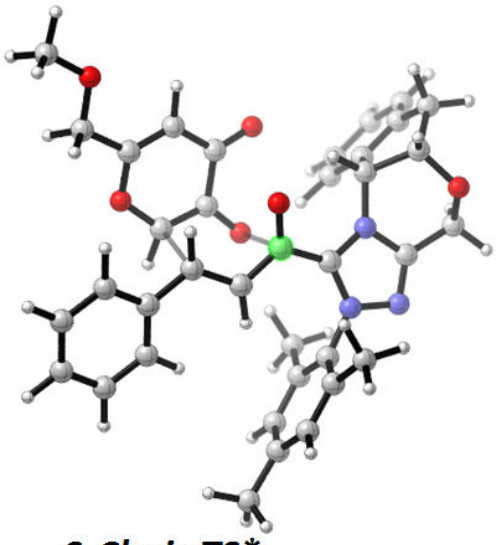
H 0.519362 0.990961 2.609780
H 1.974600 1.929385 2.973601
H 0.489755 2.217554 3.891614
O -0.137894 -0.876912 1.341467
C -1.222900 -1.440614 1.051895
C -2.466013 -0.762326 1.090648
H -2.583685 0.214256 1.541184
O 0.476650 -1.060274 -1.396204
H 0.482878 -1.811958 -0.743042
N 2.872593 0.280815 -0.619123
O 5.357528 0.493595 -1.682528
C 4.711712 -0.743655 -1.996518
H 4.494328 -0.661917 -3.062523
C 5.596127 -1.974323 -1.677189
H 6.645807 -1.673115 -1.595790
H 5.535734 -2.699384 -2.499187
C 3.378730 -0.993712 -1.187802
H 2.604694 -1.371430 -1.852254
C 3.769341 -1.998571 -0.116838
C 5.022510 -2.550341 -0.404537
C 5.567308 -3.521051 0.436206
H 6.540906 -3.953928 0.222706
C 3.037169 -2.400706 1.001335
H 2.058902 -1.983194 1.222686
C 3.591272 -3.368957 1.842246
C 4.845527 -3.923431 1.562563
H 3.040823 -3.694669 2.719979
H 5.262456 -4.674067 2.228022
C 5.226254 0.935563 -0.336216
H 5.613831 0.205116 0.385670
H 5.788755 1.864822 -0.237352
C -2.062508 0.151347 -1.085042
H -1.968875 -0.825221 -1.550084
C -3.352742 0.806353 -1.272999
C -4.373379 0.090329 -1.932125
C -3.627653 2.117200 -0.828214
C -5.622536 0.665324 -2.149889
H -4.171114 -0.916820 -2.287020
C -4.876990 2.686805 -1.045330
H -2.867711 2.693259 -0.308492
C -5.878112 1.964740 -1.705977
H -6.393677 0.103517 -2.668365
H -5.075097 3.697048 -0.699850
H -6.851484 2.416006 -1.874134
C -1.246882 -2.822647 0.445518

O -0.204495 -3.316321 -0.010466
C -2.539810 -3.463730 0.436956
H -2.631578 -4.503605 0.149371
C -3.664742 -2.746791 0.683785
O -3.651062 -1.423421 0.990722
C -5.073367 -3.268481 0.646617
H -5.661676 -2.656464 -0.058695
H -5.525351 -3.121553 1.643578
O -5.053551 -4.620850 0.278462
C -1.715937 6.188000 1.823310
H -1.129202 7.019046 2.235503
H -2.301839 6.585713 0.988958
H -2.406902 5.858801 2.605628
C -6.349560 -5.204258 0.265662
H -7.006205 -4.703360 -0.460246
H -6.220299 -6.248267 -0.025232
H -6.817704 -5.158725 1.259406
Zero-point correction= 0.665211
Thermal correction to Energy= 0.709951
Thermal correction to Enthalpy= 0.710943
Thermal correction to Gibbs Free Energy= 0.582337
Sum of electronic and thermal Energies= -2046.235891
Sum of electronic and thermal Enthalpies= -2046.234899
Sum of electronic and thermal Free Energies= -2046.363505

Single point energy calculated with M062X/6-31+G(d,p); CPCM: toluene
E(RM062X) = -2046.20845767

***Deprotonated S-chair TS Kojic Acid (ωB97XD/6-31G(d), CPCM: toluene)***

C 0.012059 -0.253700 -0.936186
C 1.273856 -0.716592 -0.496247
C -3.303904 -1.708992 -0.568082
N -1.327271 -2.381657 -0.363129
C -1.213799 -1.074542 -0.630864
N -2.631278 -2.796785 -0.334373
C -0.279916 -3.321288 -0.083031
C 0.311071 -4.000636 -1.147436
C 0.135181 -3.453488 1.244767
C 1.377957 -4.845364 -0.848659
C 1.204332 -4.311810 1.489797
C 1.843010 -5.002999 0.457257
C -0.154644 -3.781343 -2.561611
C -0.496648 -2.636909 2.339866
H 1.362591 -1.650029 0.035056
H 1.865543 -5.381649 -1.658831



***S-Chair*-TS***

H 1.556949 -4.432989 2.511136
H 0.325965 -4.488031 -3.241980
H -1.238958 -3.901145 -2.650589
H 0.096117 -2.768243 -2.897921
H -0.259491 -1.572761 2.208415
H -1.587063 -2.738140 2.336688
H -0.126733 -2.954671 3.317756
O -0.098038 0.626525 1.459732
C 0.601544 1.609218 1.110294
C 2.012150 1.524917 1.160792
H 2.490384 0.841168 1.849695
O -0.183394 0.797591 -1.569938
N -2.480559 -0.633220 -0.736795
O -4.810403 -0.681969 -2.010424
C -4.259982 0.630123 -1.887828
H -3.930649 0.879068 -2.897119
C -5.293127 1.628933 -1.334924
H -6.308055 1.307068 -1.585323
H -5.137195 2.615943 -1.787356
C -3.073251 0.701764 -0.871233
H -2.283710 1.382767 -1.189465
C -3.739777 1.153915 0.412717
C -5.005021 1.668576 0.144647
C -5.804260 2.134911 1.182954
H -6.793908 2.536719 0.984117
C -3.232258 1.103511 1.704182
H -2.217729 0.756107 1.877344
C -4.040343 1.558728 2.743051
C -5.315032 2.068242 2.486147
H -3.669374 1.527620 3.763305
H -5.930566 2.419421 3.309386
C -4.754125 -1.500303 -0.856846
H -5.274845 -1.057577 0.000414
H -5.224856 -2.451035 -1.107485
C 2.340659 0.165667 -0.554568
H 2.230752 1.013171 -1.227425
C 3.733534 -0.224519 -0.250932
C 4.780459 0.581833 -0.710894
C 4.051429 -1.367776 0.495969
C 6.106428 0.257185 -0.443222
H 4.546766 1.472810 -1.287629
C 5.375645 -1.693543 0.763384
H 3.261677 -2.009517 0.877359
C 6.409326 -0.883327 0.295102
H 6.903004 0.896700 -0.811791

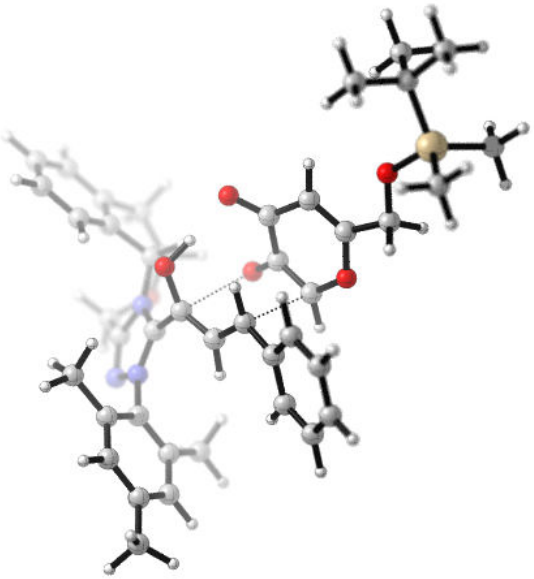
H 5.602866 -2.584162 1.342387
H 7.443337 -1.138910 0.506140
C 0.010123 2.831592 0.460895
O -1.200256 3.025191 0.395120
C 0.996571 3.788325 -0.022068
H 0.656379 4.671334 -0.548446
C 2.315142 3.634948 0.212837
O 2.833006 2.589819 0.874987
C 3.404875 4.583202 -0.198718
H 4.093537 4.056832 -0.881892
H 3.991658 4.856840 0.694354
O 2.849013 5.709930 -0.809711
C 3.039179 -5.871967 0.749303
H 3.955444 -5.269429 0.753765
H 2.953999 -6.350760 1.729136
H 3.161083 -6.652385 -0.007131
C 3.830296 6.632334 -1.217538
H 3.309342 7.472297 -1.680262
H 4.416800 6.998873 -0.362020
H 4.520848 6.188678 -1.950291
Zero-point correction= 0.661799
Thermal correction to Energy= 0.701693
Thermal correction to Enthalpy= 0.702637
Thermal correction to Gibbs Free Energy= 0.587365
Sum of electronic and thermal Energies= -2045.189949
Sum of electronic and thermal Enthalpies= -2045.189005
Sum of electronic and thermal Free Energies= -2045.304278

Single point energy calculated with M062X/6-31++G(d,p), CPCM: toluene
E(RM062X) = -2045.79702165

# Comparing boat- and chair-TS energies for TBDMS protected Kojic Acid 4

| Protonated Kojic TS, TBDMS protected | Relative Enthalpies (kcal/mol) |
|---|---|
| **R chair** | 0.00 |
| **R boat** | 4.01 |
| **S chair** | -0.10 |
| **S boat** | 6.35 |

***Protonated R-chair TS Kojic Acid, TBDMS protected***
***(B3LYP/6-31G(d) optimized, 313.15 K, CPCM: toluene)***



C 1.719210 0.104748 0.340538
C 1.059098 1.264721 0.003241
C 4.976036 -1.041360 -0.738281
N 4.127520 0.800583 -0.128974
C 3.122803 -0.092219 -0.061576
N 5.292058 0.215945 -0.564657
C 4.125713 2.201342 0.226706
C 4.194734 3.146622 -0.810219
C 4.100498 2.551144 1.586479
C 4.206972 4.494885 -0.441847
C 4.114626 3.914770 1.891258
C 4.167297 4.899113 0.897707
C 4.266451 2.741257 -2.263675
C 4.063329 1.516763 2.686372
H 1.615880 1.977590 -0.592761
H 4.255351 5.247487 -1.224685
H 4.093729 4.213782 2.936159
H 4.197245 3.620708 -2.908588
H 5.210409 2.231512 -2.486022
H 3.458840 2.054575 -2.544679
H 3.079812 1.037138 2.765523
H 4.803790 0.725454 2.525327
H 4.276393 1.982797 3.651574
O 0.446665 -0.988771 -1.596405
C -0.718593 -0.639861 -1.301595
C -1.279423 0.599972 -1.702648
H -0.779985 1.271140 -2.389273
O 1.307177 -0.892423 1.140325
H 0.437621 -1.335193 0.887221
N 3.662644 -1.277139 -0.429594
O 4.883190 -2.702822 -2.365635
C 3.668241 -3.302701 -1.897920
H 2.978351 -3.180146 -2.733890

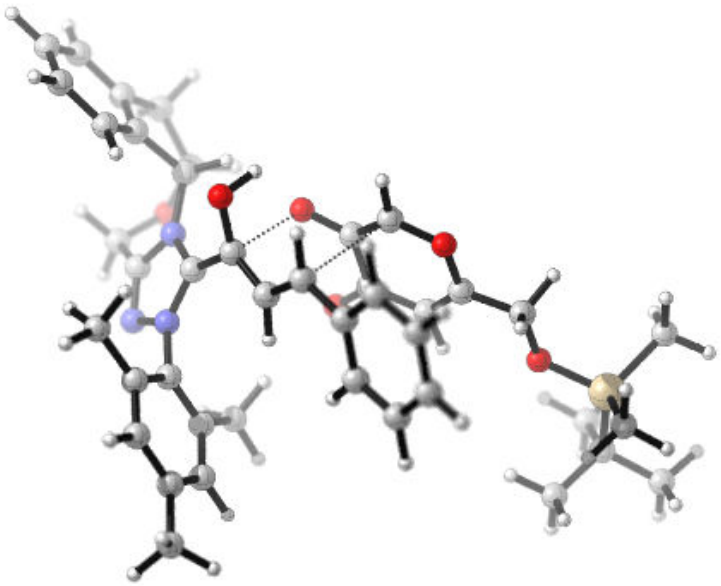
C 3.856259 -4.788919 -1.506850
H 4.767174 -5.187928 -1.965217
H 3.018239 -5.384100 -1.892085
C 3.072024 -2.621750 -0.603084
H 1.996378 -2.478797 -0.717336
C 3.433111 -3.575853 0.523014
C 3.874371 -4.797320 0.002881
C 4.233608 -5.834995 0.863684
H 4.577843 -6.786811 0.468127
C 3.337420 -3.369492 1.899989
H 2.978439 -2.425889 2.297558
C 3.706012 -4.407860 2.757900
C 4.151084 -5.631251 2.243019
H 3.643209 -4.265372 3.832804
H 4.434624 -6.429914 2.922596
C 5.742929 -2.157708 -1.369227
H 6.049972 -2.903741 -0.625012
H 6.629334 -1.772473 -1.874476
C -0.305792 1.526128 0.277274
H -0.793286 0.848415 0.973288
C -0.935580 2.841272 0.181252
C -0.375621 3.917269 -0.539128
C -2.162725 3.043271 0.846005
C -1.022420 5.146966 -0.585971
H 0.567983 3.797416 -1.062542
C -2.807328 4.276687 0.797189
H -2.600149 2.227284 1.415524
C -2.240026 5.331948 0.079557
H -0.577990 5.967044 -1.142117
H -3.747330 4.415980 1.322734
H -2.739723 6.295332 0.040093
C -1.547843 -1.377080 -0.280621
O -0.992136 -2.097769 0.570625
C -2.964143 -1.128251 -0.341100
H -3.656768 -1.739355 0.223981
C -3.430315 -0.028446 -0.987371
O -2.615986 0.846760 -1.629554
C -4.866425 0.418767 -1.059458
H -5.141733 0.484426 -2.124682
H -4.923452 1.441863 -0.655427
O -5.682946 -0.475957 -0.356592
Si -7.375466 -0.330120 -0.231028
C -7.781528 1.332827 0.565711
H -7.452892 2.171291 -0.060356
H -8.863181 1.442998 0.707924

H -7.304172 1.438578 1.546395
C -8.126705 -0.415920 -1.960253
H -7.866098 -1.350139 -2.469886
H -9.220544 -0.355622 -1.912258
H -7.786511 0.415303 -2.589739
C -7.885158 -1.806258 0.865256
C -7.481629 -3.134875 0.189540
C -7.189988 -1.709387 2.240786
C -9.416740 -1.788410 1.070419
H -7.976132 -3.269200 -0.780043
H -6.399659 -3.195908 0.025643
H -7.769928 -3.985148 0.823847
H -7.472105 -0.796872 2.780028
H -7.476861 -2.563068 2.871165
H -6.098197 -1.720179 2.145470
H -9.723339 -2.635048 1.700533
H -9.755746 -0.872487 1.569717
H -9.960983 -1.875614 0.122219
C 4.215645 6.362352 1.265200
H 3.640408 6.565787 2.173893
H 5.248740 6.680592 1.455649
H 3.823316 6.990880 0.460009

Zero-point correction= 0.823784
Thermal correction to Energy= 0.879945
Thermal correction to Enthalpy= 0.880936
Thermal correction to Gibbs Free Energy= 0.725522
Sum of electronic and thermal Energies= -2533.411166
Sum of electronic and thermal Enthalpies= -2533.410175
Sum of electronic and thermal Free Energies= -2533.565589

***Protonated R-boat TS Kojic Acid, TBDMS protected***
***(B3LYP/6-31G(d) optimized, 313.15 K, CPCM: toluene)***
C 1.994765 0.345199 0.962503
C 0.813245 1.088704 1.070510
C 4.198144 -0.229899 -1.858079
N 2.820269 1.259034 -1.257804
C 2.781207 0.328357 -0.281174
N 3.694703 0.909219 -2.254473
C 2.141040 2.532559 -1.350324
C 1.089285 2.653934 -2.274700
C 2.600128 3.598220 -0.559429
C 0.460818 3.899977 -2.356378
C 1.931423 4.818727 -0.688053

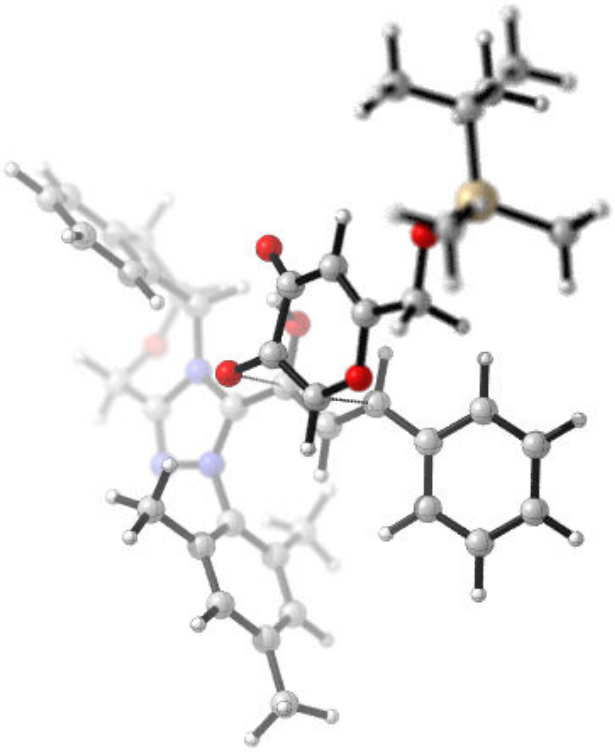
C 0.862543 4.990033 -1.574737
C 0.657670 1.506627 -3.156445
C 3.764198 3.455700 0.392351
H 0.387298 1.484668 0.157309
H -0.359967 4.021865 -3.058655
H 2.263832 5.660043 -0.085345
H -0.219489 1.790669 -3.743622
H 1.455352 1.231544 -3.855853
H 0.404378 0.606233 -2.584887
H 3.495364 2.876248 1.284403
H 4.617732 2.957700 -0.080713
H 4.097958 4.439213 0.732278
O 1.170826 -1.670321 0.879082
C -0.116039 -1.640648 0.879530
C -0.840770 -1.576749 2.062719
H -0.395576 -1.679755 3.044762
O 2.691816 -0.072052 2.062829
H 2.290253 -0.934484 2.306179
N 3.678845 -0.617916 -0.652041
O 4.445403 -2.461382 -2.479911
C 4.298382 -2.994311 -1.160200
H 3.407674 -3.620058 -1.228556
C 5.544173 -3.793364 -0.704165
H 6.146907 -4.080567 -1.572065
H 5.231275 -4.723583 -0.212423
C 4.098800 -1.897035 -0.040276
H 3.296436 -2.205220 0.626207
C 5.450768 -1.809125 0.646712
C 6.260340 -2.884859 0.266521
C 7.542383 -3.017548 0.801049
H 8.178813 -3.848904 0.510099
C 5.897458 -0.857147 1.564227
H 5.258655 -0.034191 1.868727
C 7.184155 -0.989509 2.090804
C 8.000379 -2.061669 1.710727
H 7.552714 -0.256012 2.802030
H 8.999677 -2.151027 2.127233
C 5.083782 -1.193214 -2.577818
H 6.097025 -1.198208 -2.154956
H 5.141760 -0.934664 -3.635757
C 0.105790 1.162494 2.256355
H 0.597989 0.783641 3.148747
C -1.170994 1.810229 2.470287
C -1.932270 2.388341 1.428533
C -1.682161 1.859212 3.786415



C -3.153600 2.990748 1.701419
H -1.568315 2.367713 0.406330
C -2.905185 2.463655 4.055266
H -1.105879 1.417857 4.595355
C -3.644762 3.029769 3.012877
H -3.728678 3.432769 0.893479
H -3.282446 2.495107 5.072781
H -4.600464 3.502540 3.219288
C -0.866845 -1.523188 -0.409342
O -0.268334 -1.425187 -1.484491
C -2.313447 -1.489641 -0.264918
H -2.937445 -1.437153 -1.148422
C -2.904717 -1.498567 0.950190
O -2.188593 -1.551787 2.111339
C -4.381297 -1.448350 1.241532
H -4.637961 -2.331973 1.847462
H -4.574086 -0.565219 1.871774
O -5.106908 -1.400323 0.041990
Si -6.804330 -1.489267 -0.035006
C -7.363999 -3.130718 0.709837
H -7.092854 -3.205267 1.769981
H -8.454037 -3.233064 0.650690
H -6.919479 -3.986875 0.190515
C -7.534721 -0.060495 0.960828
H -7.172640 0.911059 0.606466
H -8.629033 -0.054407 0.891424
H -7.280425 -0.144881 2.024516
C -7.197663 -1.356777 -1.897852
C -6.691771 -0.006988 -2.451444
C -6.512196 -2.506107 -2.668353
C -8.725938 -1.448576 -2.107878
H -7.173363 0.845472 -1.957092
H -5.607845 0.100820 -2.329217
H -6.913896 0.069980 -3.525350
H -6.864187 -3.490065 -2.335735
H -6.732227 -2.426915 -3.742492
H -5.422885 -2.481623 -2.550434
H -8.965651 -1.371356 -3.177807
H -9.135118 -2.402217 -1.752567
H -9.263384 -0.640506 -1.596490
C 0.183291 6.330948 -1.714608
H 0.249643 6.912196 -0.789835
H 0.655323 6.923951 -2.508592
H -0.873244 6.219005 -1.977680

Zero-point correction= 0.824129
Thermal correction to Energy= 0.880467
Thermal correction to Enthalpy= 0.881459
Thermal correction to Gibbs Free Energy= 0.726282
Sum of electronic and thermal Energies= -2533.404775
Sum of electronic and thermal Enthalpies= -2533.403783
Sum of electronic and thermal Free Energies= -2533.558960

***Protonated S-chair TS Kojic Acid, TBDMS protected***
***(B3LYP/6-31G(d) optimized, 313.15 K, CPCM: toluene)***



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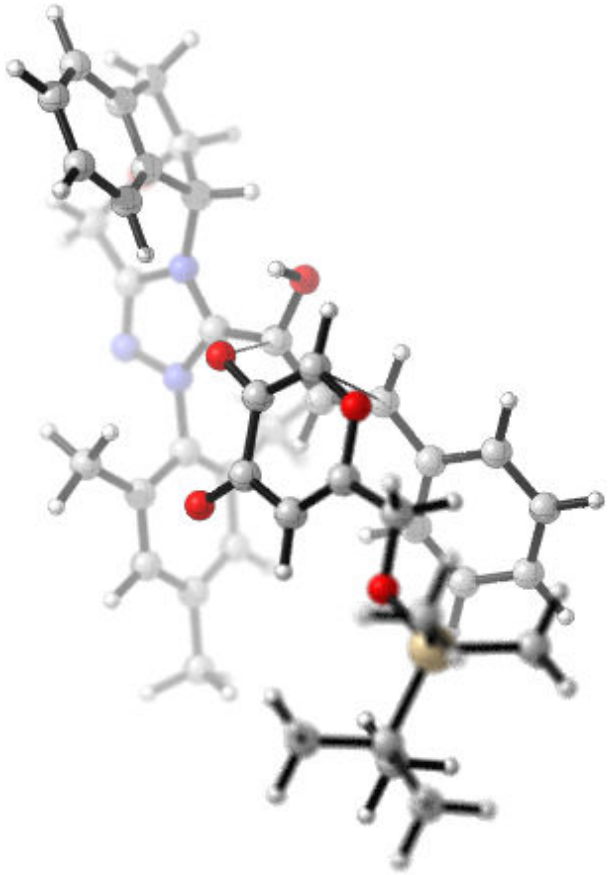
C 1.135145 1.386228 -0.817721
C 5.086833 -1.030589 -0.130401
N 3.999624 0.763440 0.151691
C 3.124867 -0.084974 -0.438376
N 5.227061 0.179305 0.337206
C 3.852223 2.143703 0.562240
C 4.152420 3.146866 -0.374437
C 3.500671 2.413963 1.894642
C 4.038709 4.472831 0.053327
C 3.405249 3.759167 2.263320
C 3.666811 4.799346 1.363364
C 4.580769 2.818521 -1.784601
C 3.238040 1.313004 2.892025
H 1.720555 2.236450 -0.497952
H 4.260032 5.269047 -0.652697
H 3.130043 3.997706 3.287640
H 4.826532 3.731715 -2.331924
H 5.465259 2.171689 -1.792832
H 3.791707 2.300034 -2.343452
H 2.356081 0.725534 2.613519
H 4.089030 0.625388 2.956735
H 3.070734 1.734022 3.886796
O 0.718994 -0.367958 1.360072
C -0.490953 -0.178470 1.077931
C -1.085946 1.106471 1.104557
H -0.592857 1.969306 1.532522
O 1.090908 -0.927589 -1.370106
H 0.644277 -1.518222 -0.703440
N 3.823370 -1.241277 -0.618992
O 5.953631 -2.539757 -1.681885
C 4.701249 -3.158846 -1.989917
H 4.570709 -2.968361 -3.056243
C 4.689657 -4.673022 -1.664703

H 5.714814 -5.050369 -1.588629
H 4.206663 -5.225046 -2.481391
C 3.479873 -2.571831 -1.179720
H 2.628129 -2.425862 -1.840441
C 3.208593 -3.608005 -0.101530
C 3.894311 -4.793706 -0.386778
C 3.765719 -5.894889 0.459696
H 4.295848 -6.819651 0.248356
C 2.383998 -3.496141 1.019054
H 1.841005 -2.580875 1.238234
C 2.264018 -4.601047 1.865565
C 2.949936 -5.789337 1.588878
H 1.630444 -4.535768 2.745234
H 2.847039 -6.638405 2.258668
C 6.111998 -2.096977 -0.338759
H 5.997835 -2.911234 0.388632
H 7.114217 -1.676647 -0.245984
C -0.240340 1.556638 -1.097998
H -0.745528 0.703692 -1.540967
C -0.897612 2.842168 -1.306290
C -2.150186 2.852825 -1.954424
C -0.341586 4.071733 -0.892892
C -2.821534 4.049462 -2.190491
H -2.584486 1.913681 -2.287137
C -1.016165 5.264136 -1.128322
H 0.617559 4.098316 -0.384259
C -2.257005 5.258202 -1.776861
H -3.780352 4.040369 -2.700071
H -0.576525 6.203661 -0.807017
H -2.778181 6.193295 -1.959577
C -1.338245 -1.282001 0.493092
O -0.796810 -2.304392 0.044762
C -2.758274 -1.027434 0.492793
H -3.454332 -1.811007 0.220701
C -3.234702 0.220765 0.728590
O -2.431278 1.279591 1.014938
C -4.679170 0.645026 0.695722
H -4.773573 1.470032 -0.027978
H -4.923649 1.065025 1.684997
O -5.495634 -0.443989 0.366395
Si -7.196055 -0.367953 0.294297
C -7.858465 0.095211 1.999873
H -7.527345 1.096289 2.301584
H -8.955029 0.105493 2.001885
H -7.530425 -0.612244 2.769512

C -7.691648 0.950512 -0.963191
H -7.263378 0.752621 -1.952172
H -8.781785 0.991330 -1.074581
H -7.363827 1.949190 -0.649359
C -7.715344 -2.124093 -0.241518
C -7.107358 -2.458644 -1.620851
C -7.223034 -3.160702 0.791775
C -9.256190 -2.196721 -0.336071
H -7.457120 -1.771668 -2.400911
H -6.012145 -2.418288 -1.603063
H -7.396975 -3.474049 -1.926991
H -7.648383 -2.982609 1.786746
H -7.522228 -4.173017 0.485146
H -6.131206 -3.152610 0.887076
H -9.568586 -3.204177 -0.644807
H -9.738528 -1.987592 0.626417
H -9.658845 -1.491925 -1.073893
C 3.590983 6.239851 1.808664
H 2.793547 6.390622 2.543272
H 4.531511 6.548599 2.282777
H 3.414576 6.912282 0.963730

Zero-point correction= 0.824638
Thermal correction to Energy= 0.880490
Thermal correction to Enthalpy= 0.881482
Thermal correction to Gibbs Free Energy= 0.728576
Sum of electronic and thermal Energies= -2533.411325
Sum of electronic and thermal Enthalpies= -2533.410333
Sum of electronic and thermal Free Energies= -2533.563239

***Protonated S-boat TS Kojic Acid, TBDMS protected***
***(B3LYP/6-31G(d) optimized, 313.15 K, CPCM: toluene)***
C -1.969854 0.062963 1.070002
C -0.857415 0.842764 1.434798
C -5.132385 0.840915 -0.535701
N -3.195608 1.694149 -0.472751
C -3.115888 0.594294 0.309038
N -4.452364 1.854488 -0.995217
C -2.203565 2.684991 -0.835481
C -2.000114 3.774719 0.027148
C -1.595090 2.569628 -2.095374
C -1.074563 4.740199 -0.379802
C -0.685379 3.569661 -2.447838
C -0.401158 4.649811 -1.604603



C -2.759403 3.925815 1.324414
C -1.931072 1.444061 -3.040225
H -0.703841 1.782972 0.923656
H -0.894082 5.594566 0.267556
H -0.190401 3.502296 -3.412992
H -2.528338 4.886952 1.790085
H -3.842284 3.883723 1.160389
H -2.508447 3.140777 2.048607
H -1.715271 0.474885 -2.582768
H -2.989052 1.474440 -3.325929
H -1.330138 1.521971 -3.949032
O -1.212253 -1.202691 -0.459072
C 0.071741 -1.354249 -0.316781
C 0.586198 -2.246499 0.610900
H -0.027348 -2.900768 1.219075
O -2.250006 -1.043916 1.824969
H -2.167667 -1.795700 1.199930
N -4.364251 0.043643 0.272173
O -7.048115 0.294176 0.681562
C -6.470704 -0.837331 1.336788
H -6.498562 -0.571565 2.394754
C -7.239213 -2.151227 1.049282
H -8.250974 -1.926201 0.696369
H -7.345766 -2.730470 1.975704
C -4.987700 -1.148774 0.896073
H -4.395598 -1.393586 1.774950
C -5.116648 -2.320257 -0.064132
C -6.390345 -2.889756 0.041835
C -6.720175 -4.007463 -0.724638
H -7.707485 -4.455453 -0.651962
C -4.156945 -2.842775 -0.932626
H -3.171832 -2.392919 -1.028935
C -4.495905 -3.958835 -1.702237
C -5.766108 -4.536915 -1.597298
H -3.767218 -4.377376 -2.390237
H -6.015097 -5.402357 -2.204716
C -6.593027 0.547871 -0.642876
H -6.783116 -0.294120 -1.321147
H -7.124692 1.426232 -1.010752
C 0.093914 0.338142 2.296303
H -0.145282 -0.588651 2.807909
C 1.349346 0.957436 2.662643
C 2.161417 0.301589 3.614794
C 1.804452 2.177790 2.112354
C 3.381516 0.842818 4.005811

H 1.820837 -0.636229 4.045604
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H 1.206038 2.702788 1.374495
C 3.814627 2.051065 3.452600
H 3.992571 0.328441 4.741224
H 3.361899 3.653140 2.078292
H 4.766245 2.477333 3.756345
C 1.049755 -0.531777 -1.096762
O 0.688250 0.348462 -1.878171
C 2.449497 -0.851557 -0.840685
H 3.217336 -0.315963 -1.384770
C 2.817779 -1.780700 0.064103
O 1.899179 -2.486641 0.789506
C 4.217970 -2.194897 0.431814
H 4.348997 -2.027545 1.512976
H 4.308853 -3.280144 0.265692
O 5.146003 -1.467559 -0.327535
Si 6.831442 -1.660995 -0.213338
C 7.374748 -1.251985 1.549241
H 6.960189 -1.963179 2.274011
H 8.466341 -1.296989 1.642845
H 7.055149 -0.246758 1.846308
C 7.277497 -3.448208 -0.625796
H 6.930439 -3.731629 -1.625693
H 8.363723 -3.594946 -0.595141
H 6.838111 -4.151133 0.092362
C 7.523576 -0.423405 -1.490924
C 7.002551 -0.773131 -2.901925
C 7.079560 1.011316 -1.131911
C 9.067238 -0.488511 -1.491583
H 7.322560 -1.772186 -3.221696
H 5.908252 -0.739670 -2.950823
H 7.390890 -0.054991 -3.638220
H 7.457436 1.323723 -0.150761
H 7.466674 1.724884 -1.873339
H 5.987848 1.106721 -1.117925
H 9.475194 0.219793 -2.226420
H 9.491810 -0.223758 -0.515395
H 9.438472 -1.484910 -1.760656
C 0.608442 5.695872 -2.011645
H 1.631898 5.334963 -1.847403
H 0.520613 5.940645 -3.075282
H 0.486054 6.617857 -1.435567

Zero-point correction= 0.824007

Thermal correction to Energy= 0.880468
Thermal correction to Enthalpy= 0.881459
Thermal correction to Gibbs Free Energy= 0.725592
Sum of electronic and thermal Energies= -2533.401050
Sum of electronic and thermal Enthalpies= -2533.400058
Sum of electronic and thermal Free Energies= -2533.555926

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*Calucation of hemiacteals and transition states for the deprotonated Pathway under $CH_4$ or $H_2O$ stabilization*

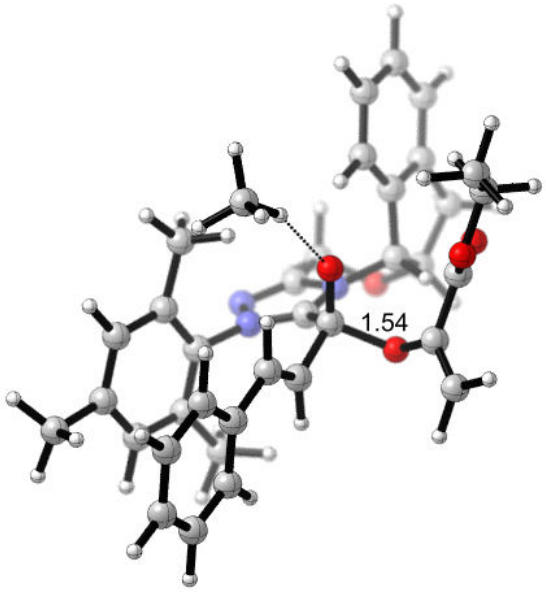


**Figure S1. Deprotonated hemiacetal 9, stabilized by $CH_4$** ;calculated at CPCM (toluene) ωB97XD/6-31G(d)

xyz coordinates and thermal data (for T=298 K)

| | | | |
|---|---|---|---|
| C | 0.06182500 | 0.34836700 | -0.59298300 |
| C | 1.54329800 | 0.34187500 | -0.93413500 |
| C | -1.83830400 | -2.78502800 | -0.11253200 |
| N | 0.15038100 | -2.14982100 | 0.08591500 |
| C | -0.48755800 | -1.09553500 | -0.42935000 |
| N | -0.68078600 | -3.22401900 | 0.27997200 |
| C | 1.52572400 | -2.21647100 | 0.49209800 |
| C | 2.45852300 | -2.73474100 | -0.40547300 |
| C | 1.86745600 | -1.68319600 | 1.73546300 |
| C | 3.80053200 | -2.66117600 | -0.04223200 |
| C | 3.22215600 | -1.63225500 | 2.05037100 |
| C | 4.19966900 | -2.08707700 | 1.16440000 |
| C | 2.02761300 | -3.30689600 | -1.72973900 |
| C | 0.81778900 | -1.11772500 | 2.65330900 |

| | | | |
|---|---|---|---|
| H | 1.82996700 | -0.22347800 | -1.81816400 |
| H | 4.55392100 | -3.03086200 | -0.73334000 |
| H | 3.52433600 | -1.19567800 | 2.99937500 |
| H | 2.88271100 | -3.72357000 | -2.26721300 |
| H | 1.28394600 | -4.09941500 | -1.59773300 |
| H | 1.57146000 | -2.53908100 | -2.36608700 |
| H | 0.36842900 | -0.22399700 | 2.20181600 |
| H | 0.01617200 | -1.84206300 | 2.83597400 |
| H | 1.25543900 | -0.84042400 | 3.61546700 |
| O | -0.57695700 | 0.72976300 | -1.94448400 |
| C | -0.62599700 | 2.08009700 | -2.06900500 |
| C | 0.13959900 | 2.75437300 | -2.92551600 |
| H | 0.86079300 | 2.23281500 | -3.54568000 |
| H | 0.04146300 | 3.82820600 | -3.03412000 |
| O | -0.33367000 | 1.06041900 | 0.40336000 |
| N | -1.76684400 | -1.49161600 | -0.54853000 |
| O | -3.65884700 | -3.08711800 | -1.53007100 |
| C | -3.98704900 | -1.70575000 | -1.64211000 |
| H | -3.94913900 | -1.51331400 | -2.71425700 |
| C | -5.37542100 | -1.38664400 | -1.04294900 |
| H | -5.96559500 | -2.30393800 | -0.95177200 |
| H | -5.92572700 | -0.71167000 | -1.70860700 |
| C | -2.99254900 | -0.76212800 | -0.88056400 |
| H | -2.71388000 | 0.10815800 | -1.47425300 |
| C | -3.74514300 | -0.35335900 | 0.36539600 |
| C | -5.08489100 | -0.71508600 | 0.27497900 |
| C | -5.95650000 | -0.42030200 | 1.31920200 |
| H | -7.00551700 | -0.69725300 | 1.26051500 |
| C | -3.23925600 | 0.31431100 | 1.47495400 |
| H | -2.19376900 | 0.61529100 | 1.48886100 |
| C | -4.11271200 | 0.59977900 | 2.52102700 |
| C | -5.45922100 | 0.23360900 | 2.44443600 |
| H | -3.74544300 | 1.11663400 | 3.40275600 |
| H | -6.12737300 | 0.46526100 | 3.26895100 |
| C | -3.14666300 | -3.48418700 | -0.27382300 |
| H | -3.82981000 | -3.23602500 | 0.54957900 |
| H | -2.99992000 | -4.56392700 | -0.30089200 |
| C | 2.42250300 | 1.02368300 | -0.20307000 |
| H | 2.02689100 | 1.56013300 | 0.65613200 |
| C | 3.87738700 | 1.09860900 | -0.40313900 |
| C | 4.64227600 | 1.85586500 | 0.49231600 |
| C | 4.54430200 | 0.42614900 | -1.43710200 |
| C | 6.02516700 | 1.94888000 | 0.35877300 |
| H | 4.14109400 | 2.37855500 | 1.30362300 |
| C | 5.92361500 | 0.51408500 | -1.57111800 |
| H | 3.97984300 | -0.18091000 | -2.13833700 |
| C | 6.67189000 | 1.27913400 | -0.67599200 |
| H | 6.59679900 | 2.54672400 | 1.06269200 |
| H | 6.41970400 | -0.01482200 | -2.37993900 |
| H | 7.74980900 | 1.35078700 | -0.78603700 |
| C | -1.68758700 | 2.75655100 | -1.25215100 |
| O | -2.81104200 | 2.31632100 | -1.12044800 |
| O | -1.28475800 | 3.92296400 | -0.74571600 |
| C | -2.24482000 | 4.61231800 | 0.07022300 |
| C | -1.53165800 | 5.78016400 | 0.71670300 |

| | | | |
|---|---|---|---|
| H | -2.63668900 | 3.91165200 | 0.81306600 |
| H | -3.07874000 | 4.93853800 | -0.55940100 |
| H | -2.22998700 | 6.33440300 | 1.35110700 |
| H | -0.70292300 | 5.42794500 | 1.33778400 |
| H | -1.13536100 | 6.46395700 | -0.03978000 |
| C | 5.65903400 | -1.89907300 | 1.48121100 |
| H | 5.86240500 | -2.05766100 | 2.54476900 |
| H | 6.28876500 | -2.58017900 | 0.90182500 |
| H | 5.95894300 | -0.87372200 | 1.23238600 |
| H | 0.60802500 | 2.30614800 | 2.24691300 |
| C | 1.29228100 | 2.61719400 | 3.04108600 |
| H | 1.76582100 | 3.56572200 | 2.77167300 |
| H | 0.74829200 | 2.73848400 | 3.98181400 |
| H | 2.06392200 | 1.85147000 | 3.16811700 |

Zero-point correction= 0.692004 (Hartree/Particle)
Thermal correction to Energy= 0.733960
Thermal correction to Enthalpy= 0.734905
Thermal correction to Gibbs Free Energy= 0.614814
Sum of electronic and zero-point Energies= -1934.367800
Sum of electronic and thermal Energies= -1934.325843
Sum of electronic and thermal Enthalpies= -1934.324899
Sum of electronic and thermal Free Energies= -1934.444989

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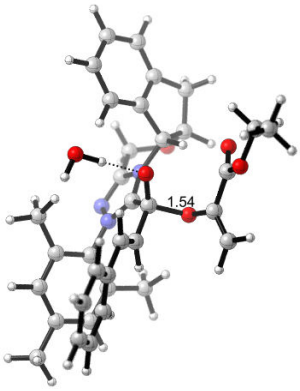


**Figure S2. Deprotonated hemiacetal 9 (R-isomer), stabilized by $H_2O$** ;calculated at CPCM (toluene) ωB97XD/6-31G(d)

xyz coordinates and thermal data (at 298K):

| | | | |
|---|---|---|---|
| C | 0.06082500 | 0.52663500 | -0.30436400 |
| C | 1.57027900 | 0.68184400 | -0.26369400 |
| C | -1.70448900 | -2.69154300 | -0.57920600 |
| N | 0.30772000 | -2.10274300 | -0.46636400 |
| C | -0.37926700 | -0.96040400 | -0.43881400 |
| N | -0.50880500 | -3.20278900 | -0.56404000 |
| C | 1.72966000 | -2.29307900 | -0.41902900 |
| C | 2.43107000 | -2.31749300 | -1.62352900 |
| C | 2.33526300 | -2.42857200 | 0.83108700 |
| C | 3.81488600 | -2.47388700 | -1.55032100 |
| C | 3.71867900 | -2.57796700 | 0.85017800 |
| C | 4.47174800 | -2.59664600 | -0.32563600 |
| C | 1.71782100 | -2.13091500 | -2.93668900 |

| | | | |
|---|---|---|---|
| C | 1.51904200 | -2.40037000 | 2.09391500 |
| H | 2.13350400 | 0.22469900 | -1.07048500 |
| H | 4.39139100 | -2.48857600 | -2.47191700 |
| H | 4.22364300 | -2.67453500 | 1.80804200 |
| H | 2.42032100 | -2.19223900 | -3.77091800 |
| H | 0.94558100 | -2.89425000 | -3.07948300 |
| H | 1.22090700 | -1.15372400 | -2.98037400 |
| H | 1.01658700 | -1.43605400 | 2.23613600 |
| H | 0.74039200 | -3.17053300 | 2.07470200 |
| H | 2.15247000 | -2.58015500 | 2.96597100 |
| O | -0.31032300 | 0.95941100 | -1.72997700 |
| C | -0.36505100 | 2.31132900 | -1.84672800 |
| C | 0.60487900 | 3.01727100 | -2.42840100 |
| H | 1.49288400 | 2.52006000 | -2.80345000 |
| H | 0.51790300 | 4.08951400 | -2.55404300 |
| O | -0.62673000 | 1.12020600 | 0.61287800 |
| N | -1.66649100 | -1.33186500 | -0.49696000 |
| O | -3.69302300 | -2.52698600 | -1.78457100 |
| C | -3.94156700 | -1.16213600 | -1.44624500 |
| H | -3.89687600 | -0.63572100 | -2.40015100 |
| C | -5.29986400 | -0.97846100 | -0.73915500 |
| H | -5.98007000 | -1.79492200 | -0.99842300 |
| H | -5.76577400 | -0.04261400 | -1.07038300 |
| C | -2.90533200 | -0.56366900 | -0.44301000 |
| H | -2.67701200 | 0.47200000 | -0.70014000 |
| C | -3.58926500 | -0.68119400 | 0.90092400 |
| C | -4.95220800 | -0.91192800 | 0.72746500 |
| C | -5.78356200 | -1.04241800 | 1.83413700 |
| H | -6.84726400 | -1.22484300 | 1.70892600 |
| C | -3.02330300 | -0.58550500 | 2.16535400 |
| H | -1.96060600 | -0.41084100 | 2.29377400 |
| C | -3.85798900 | -0.72453500 | 3.27275300 |
| C | -5.22599300 | -0.94752700 | 3.10869300 |
| H | -3.43546400 | -0.65425200 | 4.27032400 |
| H | -5.86220800 | -1.05388500 | 3.98253500 |
| C | -3.04141700 | -3.31494000 | -0.80704000 |
| H | -3.60980900 | -3.37452000 | 0.13009100 |
| H | -2.92643600 | -4.31745200 | -1.21918300 |
| C | 2.17107800 | 1.41795100 | 0.67104000 |
| H | 1.53489900 | 1.90533700 | 1.40747900 |
| C | 3.61746100 | 1.65473600 | 0.80142000 |
| C | 4.07069500 | 2.58272200 | 1.74664300 |
| C | 4.57099600 | 0.97577600 | 0.02863600 |
| C | 5.42948400 | 2.83467500 | 1.91249500 |
| H | 3.34556000 | 3.11553000 | 2.35694100 |
| C | 5.92716400 | 1.22837000 | 0.19070000 |
| H | 4.25303800 | 0.23327700 | -0.69667900 |
| C | 6.36387600 | 2.15885300 | 1.13362000 |
| H | 5.75704800 | 3.56022800 | 2.65105200 |
| H | 6.64860900 | 0.69559400 | -0.42258200 |
| H | 7.42487800 | 2.35116200 | 1.26138400 |
| C | -1.63594100 | 2.95404300 | -1.37534600 |
| O | -2.71813800 | 2.40340600 | -1.36492500 |
| O | -1.45906100 | 4.22955300 | -1.02631200 |
| C | -2.63861200 | 4.93978700 | -0.61441000 |

| | | | |
|---|---|---|---|
| C | -2.22031200 | 6.35507700 | -0.27914200 |
| H | -3.07084800 | 4.42716200 | 0.24963100 |
| H | -3.37215000 | 4.91174200 | -1.42552000 |
| H | -3.09328600 | 6.92861400 | 0.04657500 |
| H | -1.48157200 | 6.36008300 | 0.52722000 |
| H | -1.78688100 | 6.85004600 | -1.15310400 |
| C | 5.97225100 | -2.70999400 | -0.25543800 |
| H | 6.27648900 | -3.55418300 | 0.37184700 |
| H | 6.41398400 | -2.84279400 | -1.24675600 |
| H | 6.39964800 | -1.80326800 | 0.18826400 |
| H | -0.19913800 | 0.81055100 | 2.25891900 |
| O | 0.00306500 | 0.54520700 | 3.18854200 |
| H | 0.96444300 | 0.58387000 | 3.24308000 |

Zero-point correction= 0.671447 (Hartree/Particle)
Thermal correction to Energy= 0.712653
Thermal correction to Enthalpy= 0.713597
Thermal correction to Gibbs Free Energy= 0.594773
Sum of electronic and zero-point Energies= -1970.291257
Sum of electronic and thermal Energies= -1970.250051
Sum of electronic and thermal Enthalpies= -1970.249106
Sum of electronic and thermal Free Energies= -1970.367931

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**Deprotonated hemiacetal 9 (S-isomer), stabilized by $H_2O$** ;calculated at CPCM (toluene) ωB97XD/6-31G(d) at 298 K:

| | | | |
|---|---|---|---|
| C | 0.16258800 | 0.75846500 | -0.12039700 |
| C | 1.65754900 | 0.95298300 | 0.07712300 |
| C | -1.37825400 | -2.57541100 | -0.41012200 |
| N | 0.50622500 | -1.84780300 | 0.15707900 |
| C | -0.21874100 | -0.75483900 | -0.08065500 |
| N | -0.20250600 | -3.00280100 | -0.05666200 |
| C | 1.87517400 | -1.94051100 | 0.57774800 |
| C | 2.85657600 | -2.10765600 | -0.40134300 |
| C | 2.15422700 | -1.83669600 | 1.93929000 |
| C | 4.17713400 | -2.16422900 | 0.03214600 |
| C | 3.49399300 | -1.90156800 | 2.32162400 |
| C | 4.51298000 | -2.06267400 | 1.38350600 |
| C | 2.49602200 | -2.21014600 | -1.85760100 |
| C | 1.05235100 | -1.61069500 | 2.94105900 |
| H | 2.06706800 | 0.71643400 | 1.05424400 |
| H | 4.96779700 | -2.26790400 | -0.70673900 |
| H | 3.74400100 | -1.81374300 | 3.37605600 |
| H | 3.38494100 | -2.08315400 | -2.48051300 |
| H | 2.06128000 | -3.19222800 | -2.07616400 |
| H | 1.75029500 | -1.46356100 | -2.15288300 |
| H | 0.55918900 | -0.64584800 | 2.76969600 |
| H | 0.28395400 | -2.38796100 | 2.86814500 |
| H | 1.44828000 | -1.61683600 | 3.95940100 |
| O | -0.48488300 | 1.16250400 | 1.19516600 |
| C | -0.46583900 | 2.50753600 | 1.40169200 |
| C | 0.36165300 | 3.07642300 | 2.27801500 |
| H | 1.07279200 | 2.47687500 | 2.83576500 |
| H | 0.32589200 | 4.14513200 | 2.45079200 |
| O | -0.35353600 | 1.32570400 | -1.16327300 |

| | | | |
|---|---|---|---|
| N | -1.42992900 | -1.21480100 | -0.42455800 |
| O | -2.96138600 | -2.64563800 | -2.11356400 |
| C | -3.34327500 | -1.27768600 | -1.99717400 |
| H | -3.04393600 | -0.83660600 | -2.94692900 |
| C | -4.85276600 | -1.13581100 | -1.70615000 |
| H | -5.38429600 | -2.04115100 | -2.01367100 |
| H | -5.27191200 | -0.30130200 | -2.28210800 |
| C | -2.64881500 | -0.51798700 | -0.81718600 |
| H | -2.33988100 | 0.49006200 | -1.10626000 |
| C | -3.68617600 | -0.50214000 | 0.27947600 |
| C | -4.93470000 | -0.84990100 | -0.22785300 |
| C | -6.04923300 | -0.84710000 | 0.60399300 |
| H | -7.02939300 | -1.11294300 | 0.21790100 |
| C | -3.51492900 | -0.14222600 | 1.60978200 |
| H | -2.53665800 | 0.15700500 | 1.97305100 |
| C | -4.63073400 | -0.14759600 | 2.44310600 |
| C | -5.88743500 | -0.49720600 | 1.94340700 |
| H | -4.52406600 | 0.12800600 | 3.48791200 |
| H | -6.74787300 | -0.49522100 | 2.60627400 |
| C | -2.57686400 | -3.29900200 | -0.92217000 |
| H | -3.37895400 | -3.30632400 | -0.17157900 |
| H | -2.32028000 | -4.32701700 | -1.17795000 |
| C | 2.41907400 | 1.38881200 | -0.92551200 |
| H | 1.90829400 | 1.61858300 | -1.85907800 |
| C | 3.87698500 | 1.58045100 | -0.90757600 |
| C | 4.50516800 | 2.09818500 | -2.04636300 |
| C | 4.67602600 | 1.25051300 | 0.19671400 |
| C | 5.88352500 | 2.28608600 | -2.08609800 |
| H | 3.90037600 | 2.35962200 | -2.91125900 |
| C | 6.05128700 | 1.44070800 | 0.16108000 |
| H | 4.22193700 | 0.82822000 | 1.08762600 |
| C | 6.66245100 | 1.95822900 | -0.98080000 |
| H | 6.34744100 | 2.69144400 | -2.98047300 |
| H | 6.65085500 | 1.18594200 | 1.03074100 |
| H | 7.73814200 | 2.10523000 | -1.00650800 |
| C | -1.45959300 | 3.36845000 | 0.67635400 |
| O | -1.31013400 | 4.55993700 | 0.50708400 |
| O | -2.56292700 | 2.70470400 | 0.32001100 |
| C | -3.57058000 | 3.50350000 | -0.31654500 |
| C | -4.72982100 | 2.60046800 | -0.67596800 |
| H | -3.13633800 | 3.97880300 | -1.20047700 |
| H | -3.87766600 | 4.29629000 | 0.37264800 |
| H | -5.53476500 | 3.19850800 | -1.11458400 |
| H | -4.42383900 | 1.85058900 | -1.41121300 |
| H | -5.11658400 | 2.08425800 | 0.20731800 |
| C | 5.95973200 | -2.10394700 | 1.80175000 |
| H | 6.39590700 | -3.09075400 | 1.61068100 |
| H | 6.54436000 | -1.37336500 | 1.23222100 |
| H | 6.07865600 | -1.88446100 | 2.86641100 |
| H | 0.16619200 | -0.23346500 | -3.87720700 |
| H | -0.32525200 | 0.25008800 | -2.49429600 |
| O | -0.33499900 | -0.52522100 | -3.10768900 |

Zero-point correction= 0.671684 (Hartree/Particle)
Thermal correction to Energy= 0.712656
Thermal correction to Enthalpy= 0.713600

| | |
|---|---|
| Thermal correction to Gibbs Free Energy= | 0.596797 |
| Sum of electronic and zero-point Energies= | -1970.292754 |
| Sum of electronic and thermal Energies= | -1970.251782 |
| Sum of electronic and thermal Enthalpies= | -1970.250838 |
| Sum of electronic and thermal Free Energies= | -1970.367641 |

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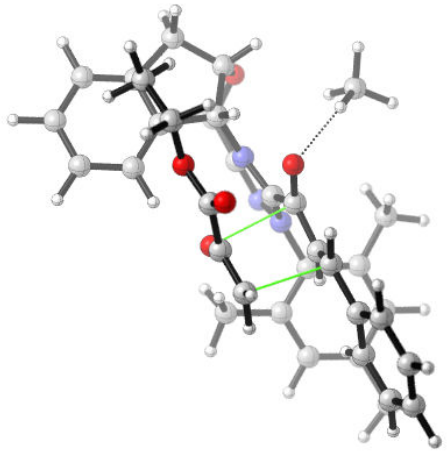

**Figure S3. Deprotonated Claisen TS, stabilized by $CH_4$** ;calculated at CPCM (toluene) ωB97XD/6-31G(d)

xyz coordinates and thermal data (at T=313.14K):

| | | | |
|---|---|---|---|
| C | -0.36911800 | 0.25025100 | 0.91764600 |
| C | -1.73997900 | 0.46652100 | 0.60547400 |
| C | 1.81346000 | -2.50601900 | -0.05319200 |
| N | -0.24511600 | -2.10931800 | -0.14094900 |
| C | 0.29402700 | -0.98683400 | 0.35395800 |
| N | 0.69338700 | -3.07370300 | -0.38696200 |
| C | -1.61883100 | -2.39333200 | -0.44794400 |
| C | -2.43348200 | -2.91318100 | 0.55960000 |
| C | -2.07569600 | -2.08155200 | -1.72911000 |
| C | -3.77383700 | -3.11867400 | 0.24899100 |
| C | -3.42701800 | -2.30893400 | -1.98910300 |
| C | -4.28753400 | -2.81525400 | -1.01459700 |
| C | -1.89096300 | -3.16309100 | 1.94071100 |
| C | -1.16166900 | -1.45450600 | -2.74608800 |
| H | -2.26331800 | -0.25534000 | 0.00088000 |
| H | -4.43858200 | -3.51022000 | 1.01506400 |
| H | -3.81816600 | -2.06951300 | -2.97461100 |
| H | -2.59987100 | -3.73943000 | 2.53956500 |
| H | -0.94172500 | -3.70698000 | 1.91179600 |
| H | -1.71088000 | -2.21195000 | 2.45631200 |
| H | -0.84280200 | -0.45712200 | -2.41111800 |
| H | -0.25950800 | -2.05738100 | -2.89610100 |
| H | -1.66849500 | -1.35337100 | -3.70884200 |
| O | 0.13110800 | 1.27299700 | -1.29785100 |
| C | -0.24179500 | 2.43554200 | -0.94680000 |
| C | -1.52955100 | 2.91763100 | -1.07360200 |
| H | -2.23311400 | 2.37329800 | -1.69337700 |

| | | | |
|---|---|---|---|
| H | -1.77952300 | 3.92889500 | -0.77765000 |
| O | 0.32702900 | 0.94922000 | 1.66989800 |
| N | 1.61719900 | -1.23020800 | 0.38824400 |
| O | 3.62748200 | -2.66061300 | 1.38868100 |
| C | 3.78547000 | -1.25513400 | 1.57405100 |
| H | 3.61868400 | -1.10340900 | 2.64059500 |
| C | 5.17437800 | -0.77241500 | 1.11642200 |
| H | 5.89923100 | -1.58992000 | 1.16675700 |
| H | 5.53112400 | 0.02302100 | 1.78313300 |
| C | 2.78040500 | -0.40718300 | 0.72278800 |
| H | 2.40760500 | 0.46272900 | 1.26455200 |
| C | 3.58563100 | -0.02855300 | -0.50437600 |
| C | 4.94284900 | -0.23795000 | -0.27332500 |
| C | 5.87532900 | 0.07448400 | -1.25545700 |
| H | 6.93621900 | -0.08417000 | -1.08368500 |
| C | 3.12170000 | 0.49486200 | -1.70407800 |
| H | 2.06200000 | 0.69970700 | -1.83695700 |
| C | 4.05896400 | 0.79650000 | -2.69015900 |
| C | 5.42202700 | 0.58914400 | -2.46920200 |
| H | 3.72454400 | 1.20817200 | -3.63778700 |
| H | 6.13738800 | 0.83289100 | -3.24931200 |
| C | 3.18212400 | -3.07792400 | 0.11056000 |
| H | 3.85496300 | -2.75512600 | -0.69275400 |
| H | 3.13241900 | -4.16659300 | 0.12134800 |
| C | -2.32088500 | 1.68063200 | 0.86392200 |
| H | -1.78529000 | 2.37602700 | 1.50302100 |
| C | -3.74951300 | 1.96987900 | 0.64200900 |
| C | -4.31117500 | 3.11176200 | 1.22508900 |
| C | -4.57680200 | 1.13709000 | -0.12532600 |
| C | -5.65904000 | 3.41178200 | 1.05673900 |
| H | -3.67928400 | 3.76987300 | 1.81590900 |
| C | -5.92221400 | 1.43711800 | -0.29543600 |
| H | -4.17053700 | 0.25000700 | -0.60296600 |
| C | -6.47045800 | 2.57481700 | 0.29557000 |
| H | -6.07513400 | 4.30175000 | 1.51932600 |
| H | -6.54616500 | 0.78186500 | -0.89651000 |
| H | -7.52249100 | 2.80692700 | 0.15990000 |
| C | 0.70495000 | 3.34423000 | -0.17037100 |
| O | 0.36958300 | 4.39254300 | 0.34594700 |
| O | 1.96766300 | 2.89857100 | -0.14125100 |
| C | 2.89083600 | 3.75988600 | 0.53879800 |
| C | 4.25477700 | 3.10416200 | 0.53931200 |
| H | 2.52813900 | 3.93673000 | 1.55558600 |
| H | 2.91328700 | 4.72576900 | 0.02397500 |
| H | 4.98757800 | 3.79508900 | 0.96833900 |
| H | 4.25339700 | 2.19230000 | 1.14299800 |
| H | 4.56930000 | 2.84407300 | -0.47550400 |
| C | -5.75363000 | -3.01360300 | -1.30164200 |
| H | -6.06460200 | -4.03805700 | -1.07177600 |
| H | -6.36132300 | -2.34167200 | -0.68516900 |
| H | -5.98623400 | -2.81365900 | -2.35090500 |
| C | 1.08978500 | -1.91148500 | 3.75656500 |
| H | 1.82536300 | -1.75389800 | 4.55002400 |
| H | 0.18193400 | -2.34053000 | 4.18768300 |
| H | 1.50604700 | -2.60119400 | 3.01678700 |

| | | | |
|---|---|---|---|
| H | 0.85549500 | -0.95271600 | 3.28538200 |

Zero-point correction= 0.693292 (Hartree/Particle)
Thermal correction to Energy= 0.738741
Thermal correction to Enthalpy= 0.739733
Thermal correction to Gibbs Free Energy= 0.612721
Sum of electronic and zero-point Energies= -1934.364740
Sum of electronic and thermal Energies= -1934.319292
Sum of electronic and thermal Enthalpies= -1934.318300
Sum of electronic and thermal Free Energies= -1934.445311

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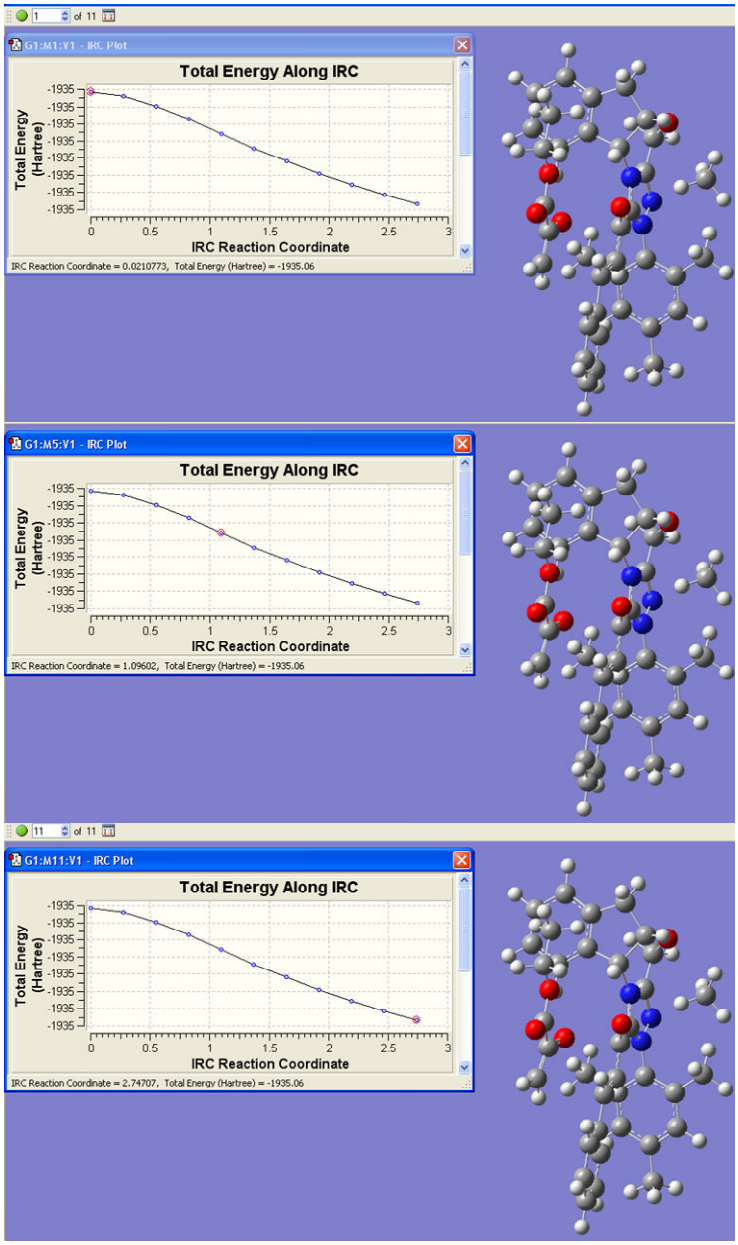


**Figure S4. IRC (forward) for S-Chair TS (Ester System 3) in the presence of $CH_4$**

## Calculation of Boltzmann weighted average

*The Boltzmann weighted average was calculated with:*

$$E_{aver} = \frac{\sum_i Ei * \exp(-Ei/kT)}{\sum_i \exp(-Ei/kT)} \quad (i=20)$$

or written differently:

$$E_{aver} = [E_1 \bullet \exp(-E_1/kT) + E_2 \bullet \exp(-E_2/kT) + ... + E_{20} \bullet \exp(-E_{20}/kT)] / Y.$$

*Whereas:*

$$Y = \exp(-E_1/kT) + \exp(-E_2/kT) + ... + \exp(-E_{20}/kT)$$

T= 313.15 K; k: Boltmann constant

As we deal with stereoselectivity, we considered only electronic energies for this approach, assuming very similar enthalpy and -TΔS corrections for the stereoisomers.

This average was calculated for each R- and S-Chair TS ensemble.

## Comparison of various methods for *R*-chair TS preference in the deprotonated pathway.

**Table S2** $\Delta\Delta H^{\ddagger}$ preference for *R*-chair TS for keto-ester **3** and kojic acid **4** at 313.15 K in the ***deprotonated*** pathway.

| **Chair-TS** of | **Method** | **ΔΔH**$^{\ddagger}$(R-S) | **ΔΔG**$^{\ddagger}$(R-S) |
|---|---|---|---|
| **3*** | M06-2X/6-31++G(d,p)[b]// ω B97XD /6-31G(d)[a] | -1.8 | -4.6 |
| **3*** | M06-2X/6-311++G(d,p)[c]// ω B97XD /6-31G(d)[a] | -2.2 | -5.0 |
| **3*** | PBE0/6-311++G(d,p)[b]// ω B97XD /6-31G(d)[a] | -4.0 | -6.8 |
| **3*** | PBE0-D3/6-311++G(d,p)[b]// ω B97XD /6-31G(d)[a] | -1.3 | -4.0 |
| **3*** | ω B97XD /6-31G(d)[a] | -0.6 | -3.3 |
| **4*** | M06-2X/6-31++G(d,p)[b]// ω B97XD /6-31G(d)[a] | -2.4 | -2.5 |
| **4*** | M06-2X/6-311++G(d,p)[c]// ω B97XD /6-31G(d)[a] | -2.6 | -2.7 |
| **4*** | PBE0/6-311++G(d,p)[b]// ω B97XD /6-31G(d)[a] | -3.2 | -3.3 |
| **4*** | PBE0-D3/6-311++G(d,p)[b]// ω B97XD /6-31G(d)[a] | -2.2 | -2.4 |
| **4*** | ω B97XD /6-31G(d)[a] | -2.9 | -3.0 |

[a] Optimization done with implicit solvation model, i.e. CPCM (toluene)
[b] Energy calculated with CPCM (toluene)
[c] Energy calculated with SMD (toluene)