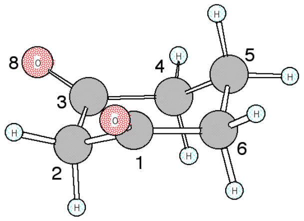
Supplementary Information

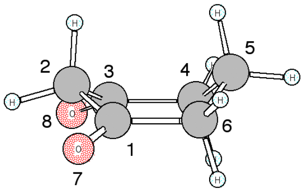
Mechanism of the Cysteine Sulfenic Acid *O*—Sulfenylation of 1,3-Cyclohexanedione

Fillmore Freeman[a]



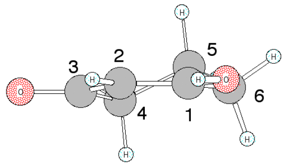
1

τ = C1-C2-C3-C4 = 44.1^{0}
τ = C2-C3-C4-C5 = -50.7^{0}
τ = C3-C2-C1-C6 = -44.1^{0}
τ = C3-C4-C5-C6 = 56.6^{0}



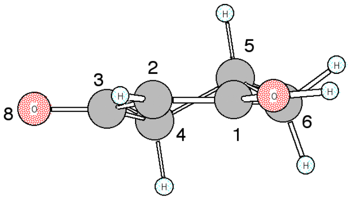
1a

τ = C2-C1-C6-C5 = 7.6^{0}
τ = C2-C3-C4-C5 = -7.6^{0}
τ = C3-C2-C1-C6 = 38.6^{0}
τ = C3-C4-C5-C6 = 54.0^{0}



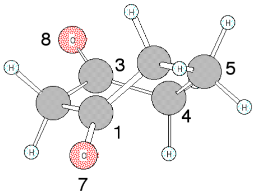
1b

τ = C1-C2-C3-C4 = 2.4^{0}
τ = C2-C3-C4-C5 = -31.8^{0}
τ = C3-C2-C1-C6 = 3.2^{0}
τ = C3-C4-C5-C6 = 55.2^{0}



1c

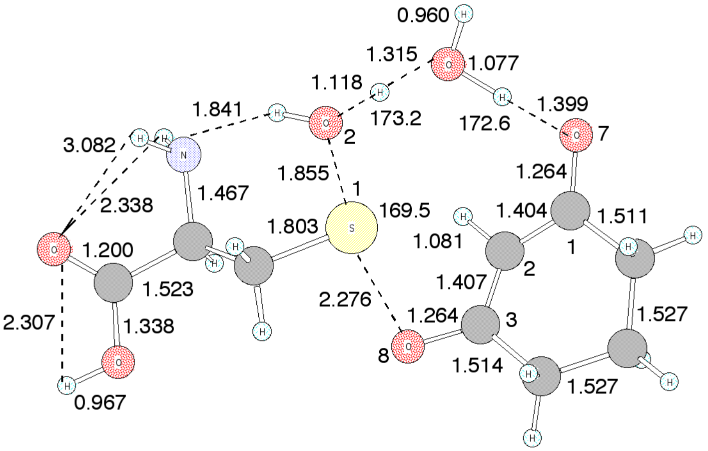
τ = C1-C2-C3-C4 = 2.6^{0}
τ = C2-C3-C4-C5 = -32.1^{0}
τ = C3-C2-C1-C6 = 3.2^{0}
τ = C3-C4-C5-C6 = 55.3^{0}



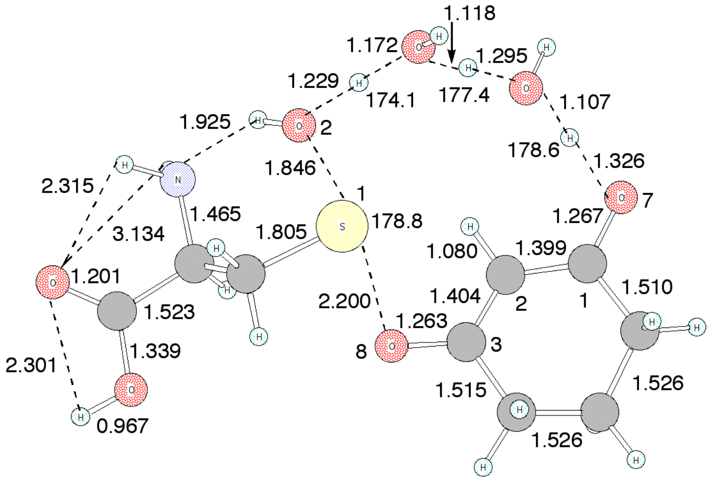
1d

τ = C1-C2-C3-C4 = 30.6^{0}
τ = C2-C3-C4-C5 = -61.8^{0}
τ = C3-C2-C1-C6 = 30.6^{0}
τ = C3-C4-C5-C6 = 29.1^{0}

Figure SI-1. Atom numbering and dihedral angles (τ) in the M062x/6-311+G(d,p) geometry optimized chair diketo (**1**), boat diketo (**1a**), half-chair *s-cis*-ketoenol (**1b**), half-chair *s-trans*-ketoenol (**1c**), and twist diketo (**1d**) tautomers of 1,3-cyclohexanedione (CHD).



TSH_2O



TS$2H_2O$

Figure SI-2. M062X/6-311+G(d,p) optimized one water-assisted (**TS**H_2O), and two waters-assisted (**TS**$2H_2O$), transition state structures for the *O*-sulfenylation reactions of cysteine sulfenic acid (Cys-SOH, **5**) with the *s-cis*-ketoenol tautomer (**1b**) of 1,3-cyclohexanedione (**1**).

Table SI-1. Relative Energies of Low Energy Tautomers of 1,3-Cyclohexanedione (**1**)

level of theory	E_{rel}[a]			
	boat diketo (**1a**)	*s-cis*-ketoenol (**1b**)	*s-trans*-ketoenol (**1c**)	twist diketo (**1d**)
B3LYP[b]	0.9	2.5	4.5	3.7
B3PW91[b]	0.8	2.3	4.4	3.7
M062X[b]	0.9	2.2	4.4	3.7
CAM-B3LYP[b]	0.6	2.9	5.1	3.6
BD(T)[bc]	1.5	2.3	4.3	3.9
CCSD(T)[bc]	1.5	2.4	4.4	3.9
QCISD(T)[bc]	1.5	2.5	4.6	3.9

[a] $E_{rel} = E_{tautomer} - E_{\text{chair diketo tautomer}}$ (**1**). [b] 6-311+G(d,p) basis set. [c] cc-pVTZ basis set. [d] B3LYP/6-311+G(d,p) optimized structure.

Table SI-2. Energy Barriers to the Cysteine Sulfenic Acid (Cys-SOH, **5**) *O*-Sulfenylation of 1,3-Cyclohexanedione (**1**) Through Water-Assisted Transition States

level of theory[b]	ΔE[a]		
	TSH_2O	**TS**$2H_2O$	**TS**$3H_2O$
B3LYP	23.7	8.8	7.4
B3PW91	16.1	7.2	5.3
M062X	16.2	8.9	6.6
CAM-B3LYP	24.7	9.2	7.1

[a] $\Delta E = E_{\text{transition state}} - E_{\text{reactants}}$. [b] 6-311+G(d,p) basis set.

COMPUTATIONAL QUANTUM CHEMISTRY METHODS

Calculations were carried out with the Gaussian[9] and Spartan[10] computational programs. No constraints were imposed on the structures in the equilibrium geometry calculations or in the transition structure optimizations. In order to obtain accurate information concerning the optimum levels of theory for consistently predicting electronic structures, noncovalent interactions, and relative energies, we utilized the density functionals B3LYP, B3PW91, M062X, and CAM-B3LYP with the 6-311+G(d,p) triple-ζ basis set. Equilibrium geometry and frequency calculations were carried out using the density functionals B3LYP, B3PW91, M062X, and CAM-B3LYP with the triple-ζ 6-311+G(d,p) basis set. B3LYP is the most widely used density functional. The meta-hybrid generalized gradient approximation M062X functional is known for taking in account of weak noncovalent interactions and for predicting accurate activation barriers. CAM-B3LYP is the long range corrected version of B3LYP using the Coulomb attenuating method. BD(T), CCSD(T), and QCISD(T) with the cc-pVTZ basis set were used for high level single point energy calculations. CCSD(T) is known to give excellent energy results and in this study BD(T) and QCISD(T) predict very similar or the same relative energy values as CCSD(T).

The relative energies (E_{rel}) and energy barriers include the electronic energies plus the zero point vibrational energies (ZPVE). Vibrational frequency analyses were carried out in order to assess the nature of the stationary points and to obtain zero point vibrational energies. The characteristics of local minima and transition states were verified by establishing that the former did not have an imaginary frequency and that the latter had one imaginary frequency. Intrinsic reaction coordinate (IRC) calculations were used to unambiguously connect transition state structures to their respective reactants and products. Bond angles and dihedral or torsion angles (τ) are given in degrees, bond lengths and nonbonded distances in angstroms (Å), and relative energies in kcal/mol. The value of the bond angle is placed near the second atom in the angle.

Complete citation for reference 4

Gaussian 09, Revision **D.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, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.

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