Investigation of Cyclopropane Stereomutation by Quasiclassical Trajectories on an Analytical Potential Energy Surface

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The mechanism of stereomutation of cyclopropane has been a topic of considerable interest and debate for many years.[1,2] It has generated extensive theoretical effort[1] and fostered some of the most elegant experiments in the history of physical organic chemistry.[2] However there is, to date, no consensus on the mechanism. In this paper, we report quasiclassical molecular dynamics on an analytical potential energy surface for the reaction, obtained by fitting the results of CASPT2N/6-31G*//GVB-PP(1)/6-31G* calculations.

It is by now generally agreed that cyclopropane stereomutation occurs by C−C bond homolysis to give a trimethylene biradical.[3] It is the kinetics and stereochemistry of formation and closure of this biradical that have been the subject of controversy. The principal debate has concerned the relative magnitude of the mechanistic rate constants for single and double internal rotations of the terminal methylenes of the biradical. Two experiments[2ac,4] appear to have shown a strong preference for double rotation; whereas, a third seems to have shown near equality of the rate constants for the two processes.[2d,5] All three experiments involved measurement of phenomenological rate constants for loss of optical activity (k_a) and for approach to equilibrium of geometrical isomers (k_i) of isotopically labeled cyclopropanes. The first two experiments employed optically active cyclopropane-*1,2-d₂* and required that some estimate be made of the secondary isotope effect which discriminates between homolysis of doubly labeled and singly labeled C−C

bonds. The third experiment employed optically active cyclopropane-*1-¹³C-1,2,3-d₃* and required no such estimate, provided that ¹³C isotope effects could be neglected. Calculations of the H/D isotope effect showed that no plausible value could bring the results from cyclopropane-*1,2-d₂* and cyclopropane-*1-¹³C-1,2,3-d₃* into concordance.[1e,f]

In the present work, stationary points on the trimethylene potential energy (PE) surface were located at the GVB(1)/6-31G* level[6] and were characterized by computation of harmonic vibrational frequencies. The energies of these stationary points were then recomputed at the CASPT2N/6-31G* level.[7] Additionally, 39 other structures at values of the C−C−C angle varying from 100° to 120° and with a variety of dihedral angles for internal rotation about the two C−C bonds were computed at the GVB level. All other geometrical parameters were optimized at these points. The energies of the 39 points were then recomputed at the CASPT2N level.

An analytical function, which used the C−C−C angle and the two dihedral angles as independent variables, was fit to all of the CASPT2N energies. The remaining 18 geometrical degrees of freedom were described by molecular-mechanics functions with force constants and geometrical constants adjusted to fit energies of all 39 points, as well as the geometries and vibrational frequencies of the key stationary points. Details of the equations, as well as the quality of the fit to the ab initio data can be found in the Supporting Information.

Consistent with other high-level ab initio calculations on trimethylene,[1e−g] this surface exhibits only a small preference for conrotatory over disrotatory closure.[8] The PE barrier on the analytical surface is 1.6 kcal/mol higher for disrotation than for conrotation. The conrotatory transition state connects a C_2 minimum, 0.49 kcal/mol lower in energy, to cyclopropane. As on the GVB potential surface,[1e] the two mirror-image C_2 minima are connected by a pathway that involves passage around a mountain top at the (0,0) geometry of trimethylene. However, the transition states that connect the C_2 minima, via a higher energy C_s minimum, lie only 0.043 kcal/mol above the conrotatory transition state; the (0,0) mountain top too is only slightly higher in potential energy (0.17 kcal/mol) than the conrotatory transition state. Thus, the potential surface is rather flat in this region. In fact, with inclusion of zero-point energies, the shallow C_2 and C_s minima vanish.

The GVB calculations located a true transition structure for monorotatory closure of trimethylene. This was very close in both energy and geometry to a second-order stationary point corresponding to the rigorously C_s (0,90) trimethylene. The analytical surface could not be made to reproduce the existence of the transition structure without introducing spurious "ripples" elsewhere in the surface. Consequently the second-order (0,90) structure was used as the stationary point for direct monorota-

(1) (a) Smith, F. T. *J. Chem. Phys.* **1958,** *29,* 235. (b) Hoffmann, R. *J. Am. Chem. Soc.* **1968,** *90,* 1475. (c) Benson, S. W.; O'Neal, H. *J. Chem. Phys.* **1968,** *72,* 1866. (d) Chapuisat, X.; Jean, Y. *J. Am. Chem. Soc.* **1975,** *97,* 6325. (e) Getty, S. J.; Davidson, E. R.; Borden, W. T. *J. Am. Chem. Soc.* **1992,** *114,* 2085. (f) Baldwin, J. E.; Yamaguchi, Y.; Schaefer, H. F., III *J. Phys. Chem.* **1994,** *98,* 7513. (g) Doubleday, C., Jr. *J. Phys. Chem.* **1996,** *100,* 3520.

(2) (a) Pedersen, L. D.; Berson, J. A. *J. Am. Chem. Soc.* **1975,** *97,* 238. (b) Berson, J. A.; Pedersen, L. D.; Carpenter, B. K. *J. Am. Chem. Soc.* **1976,** *98,* 122. (c) Cianciosi, S. J.; Ragunathan, N.; Freedman, T. R.; Nafie, L. A.; Baldwin, J. E. *J. Am. Chem. Soc.* **1990,** *112,* 8204. (d) Cianciosi, S. J.; Ragunathan, N.; Freedman, T. R.; Nafie, L. A.; Lewis, D. K.; Glenar, D. A.; Baldwin, J. E. *J. Am. Chem. Soc.* **1991,** *113,* 1864.

(3) (a) Chambers, T. S.; Kistiakowsky, G. B. *J. Am. Chem. Soc.* **1934,** *56,* 399. (b) Berson, J. A. *Science* **1994,** *266,* 1338. (c) Pedersen, S.; Herek, J. L.; Zewail, A. H. *Science* **1994,** *266,* 1359.

(4) A subsequent statistical analysis of the data in ref 2c has led Baldwin to conclude that the uncertainty in the data is too large to warrant any definitive conclusion to be drawn about the ratio of single- to double-rotation rate constants from that experiment. Baldwin, J. E. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed.; Wiley: New York, 1995; Vol. 2, Chapter 9.

(5) In the first experiment, a single-rotation event was defined as exchange of the two hydrogen sites at one methylene of cyclopropane, regardless of the mechanism by which the exchange occurred.[2a,b] In the second and third experiments, a single-rotation event was defined as exchange of the two hydrogen sites at one terminal methylene of the biradical.[2c,d] The first definition leads to a mechanistic rate constant for single rotation that is approximately a factor of 2 larger than the second. (See Supporting Information for a complete discussion.) In this paper the second definition of single rotation is used. With this definition, a stereorandom trimethylene would have equal rate constants for single and double rotation.

(6) GVB calculations were carried out using the Gaussian 94 suite of programs: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. *Gaussian 94, Revision B.3*; Gaussian, Inc.: Pittsburgh, PA, 1995.

(7) CASPT2N calculations were carried out using the MOLCAS suite of programs: Andersson, K.; Blomberg, M. R. A.; Fülscher, M. P.; Karlström, G.; Kellö, V.; Lindh, R.; Malmqvist, P.-Å.; Noga, Olsen, J.; Roos, B. O.; Sadlej, A. J.; Siegbahn, P. E. M.; Urban, M.; Widmark, P.-O. *MOLCAS-3*; University of Lund, Sweden.

(8) The CISD+Q/DZP calculations cited in ref 1f found the order of potential energies of the transition structures for ring opening to be conrotation < monorotation < disrotation. The calculations in refs 1e and 1g found the order to be conrotation < disrotation < monorotation, as the present work does. All of the calculations agree that the energy differences between these three transition structures are very small (about 1−2 kcal/mol).

Table 1. Ratio of Double to Single Methylene Rotations in the Reactive Trajectories from Each of the Specified Starting Regions[a]

stationary point	total no. of trajectories	net double/single rotations	
		1,2 bond	1,3 bond
conrotation	3000	5.84	6.00
disrotation	6000	2.84	3.26
monorotation	3000	0.40	0.36

[a] The numbering of the label positions refers to the cyclopropane-1,2-d_2 reactant. The differences in results for the 1,2- and 1,3-deuterium-labeled biradicals are of marginal significance because the sampling error is estimated to give uncertainties of ±0.20, ±0.14 and ±0.05 in the ratios from the conrotation, disrotation and monorotation starting points, respectively.

tion. This was found to be 2.2 kcal/mol higher in PE than the conrotatory transition state.

The small difference in energy between the disrotatory and conrotatory transition structures might lead one to expect a small ratio of rate constants for double- and single-methylene rotations. Transition-state theory (TST) predicts that most of the cyclopropanes forming trimethylene by disrotation should reclose to cyclopropane by the lower energy conrotation pathway, and the combination of disrotatory opening and conrotatory closure corresponds to a net single rotation.[1e,f] Inclusion of direct monorotation pathways leads to the expectation of nearly equal rate constants for double and single rotation. A TST analysis for cyclopropane-*1,2-d₂* on the present surface, involving simultaneous application of the steady-state approximation to 19 stereo- and label-isomers of trimethylene-1,2-d_2 and -1,3-d_2, yields a ratio of double- to single-rotation rate constants of only 1.18 at 400 °C. This figure appears to be in good agreement with the results of the third experiment,[2d] but not with the results of the first two.[2a,c,4]

The molecular dynamics analysis for trimethylene-1,2-d_2 and -1,3-d_2 began by generation of quasiclassical canonical ensembles ($T = 400$ °C) in the vicinities of conrotation, disrotation, and monorotation stationary points. Molecular rotations were included, but the rotational energy was not quantized. Trajectories were each followed forward to product and backward to reactant,[9] with the equations of motion being integrated in a laboratory-fixed Cartesian frame, using a modified Bulirsch–Stoer algorithm.[10] A total of 12 000 trajectories was examined.[11] The stereochemical results are summarized in Table 1.

For reactions conducted at the high-pressure limit, an overall stereochemistry can be computed by weighting the results from the three classes of stationary points, according to their free energies at 400 °C and to the fraction of reactive trajectories from each starting region. These weighting factors, including statistical contributions that favor monorotation, are 68.3% conrotation, 19.7% disrotation, and 12.0% monorotation for cleavage of the doubly-labeled bond and 68.5%, 19.5%, and 12.0%, respectively, for cleavage of the singly-labeled bonds. Using harmonic vibrational frequencies, the secondary deuterium isotope effect is computed to be $z_{12} = 1.09$ at 400 °C for cleavage of singly-labeled over doubly-labeled bonds. In total, the ratio of double to single rotations for stereomutation of cyclopropane-*1,2-d₂* at 400 °C is calculated to be 4.73 ± 0.11.

This ratio is clearly very different from that deduced by TST analysis. The principal source of the difference is readily apparent from Table 1. According to the dynamic model, trimethylenes formed by disrotation *do not* preferentially reclose by conrotation as TST assumes. Most of them follow direct

trajectories[12] across the surface and exit by disrotation, *despite the fact that this means crossing a higher barrier.* Dynamic matching[13] of entrance and exit channels can apparently outweigh barrier-height effects. In the present example, a simple analysis based on conservation of angular momentum of the rotating methylenes would do quite well in predicting the qualitative outcome.[1d,14]

With $z_{12} = 1.09$, the isotope effect calculated from the harmonic vibration frequencies, the ratio of double to single rotations computed here leads one to expect that k_i/k_a should be 1.210 ± 0.007 for cyclopropane-*1,2-d₂*. However, it is quite possible that the use of harmonic vibrational partition functions, especially for the torsional motions of the terminal methylenes, is a bad approximation[1g] and leads to too large a value of z_{12}.

In order to check for unanticipated isotope effects on the dynamics, 2000 trajectories have been run for trimethylene-*1-* and -*2-¹³C-1,2,3-d₃*. The results were within the sampling error of those for the d_2 isotopomer (double to single rotation favored by a factor of 4.4 ± 0.3). Thus, the apparent agreement between experiment and theory for stereomutation of cyclopropane-*1-¹³C-1,2,3-d₃* that is found when a TST kinetic model is used, disappears when the reaction is analyzed by quasiclassical dynamics. While the simulation results can be expected to depend to some degree on the details of the underlying PE surface, the fact that a direct dynamic analysis on a rather different surface has come up with a quite similar final result[15] suggests that the dependence on details of the surface may not be strong.

Finally, it is worth noting that the mode of the lifetime distribution for trimethylene-d_2, found in these calculations, is around 140 fs (varying somewhat with isotope distribution[16]): similar to the lifetime from variational unimolecular rate theory[1g] and from direct dynamics on a semiempirical surface.[17] During this brief period, the biradical is quite clearly able to execute internal rotations of the terminal methylenes, indicating that the methylene rotational time constant of 1.8 ps, recently estimated for another biradical[18] is probably much too long. It does appear, therefore, that even very short-lived biradicals can undergo stereochemical isomerization.

Supporting Information Available: Calculational details (17 pages) and QuickTime animations. See any current masthead page for ordering and Internet access instructions.

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(9) We thank Drs. William Hase and Charles Doubleday, Jr., for pointing out the necessity of the backward tracking of the trajectories.

(10) Stoer, J.; Bulirsch, R. *Introduction to Numerical Analysis*; Springer-Verlag: New York, 1980.

(11) For color versions of the potential surfaces and QuickTime animations of some of the trajectories, see Supporting Information. This material is also available at http://www.chem.cornell.edu/~bkc1/dynamics.htm1.

(12) Carpenter, B. K. *J. Am. Chem. Soc.* **1996**, *118*, 10329.

(13) Carpenter, B. K. *J. Am. Chem. Soc.* **1995**, *117*, 6536.

(14) Angular momentum for internal rotation of the methylenes would be a strictly conserved quantity only if there were no barrier to rotation and no coupling to other motions.

(15) Doubleday, C., Jr.; Bolton, K.; Hase, W. L. *J. Am. Chem. Soc.* **1997**, *119*, 5251.

(16) This is consistent with the existence of a secondary H/D isotope effect on the lifetime of trimethylene: Baldwin, J. E.; Freedman, T. B.; Yamaguchi, Y.; Schaefer, H. F., III. *J. Am. Chem. Soc.* **1996**, *118*, 10934.

(17) Doubleday, C., Jr.; Bolton, K.; Peslherbe, G. H.; Hase, W. L. *J. Am. Chem. Soc.* **1996**, *118*, 9923.

(18) Horn, B. A.; Herek, J. L.; Zewail, A. H. *J. Am. Chem. Soc.* **1996**, *118*, 8755. Direct dynamics calculations on the same biradical studied by Horn *et al.* also indicate a much faster internal rotation rate than that assumed by these authors.[12,13]