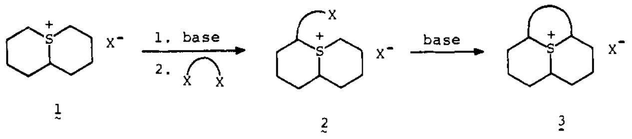
Communications to the Editor

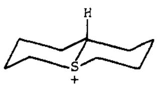
On the Stereostructure of Eastman's Sulfonium Salt. Pyramidal Inversion Barrier of an Unstabilized Sulfonium Ylide

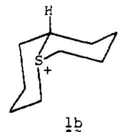
Sir:

In 1959, Eastman and Kritchevsky reported the synthesis of bicyclic sulfonium salt **1**.[1] This salt is of interest to us as a substrate for further annelation with the ultimate goal of producing macrocycles (**1** → **3**). Although several crystalline,



sharp-melting salts were prepared ($X^- = Br^-$, picrate, I^-),[1] no information regarding the stereostructure (**1a** or **1b**) was adduced. We have examined this question and find that Eastman's sulfonium salt is a 1:1 mixture (molecular compound) of stereoisomers **1a** and **1b**. We have also determined


1a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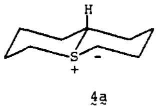
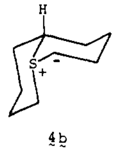
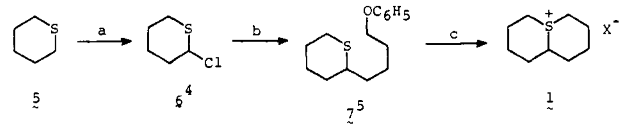
the activation parameters for pyramidal inversion of the sulfonium salt (**1b** → **1a**) and the derived sulfonium ylide (**4a** → **4b**).


4a


4b

Because Eastman's reported synthesis of **1** is somewhat tedious (six steps from 1-chloro-4-phenoxybutane, 23% overall yield), we have developed the alternative synthesis outlined in Chart I, which produces **1** ($X^- = Br^-$, mp 266-267 °C) in 30-43% overall yield. The corresponding fluoborate salt (**1**, $X^- = BF_4^-$, mp 174-175 °C)[2] is obtained by treatment of the bromide with dimethoxycarbonium fluoborate.[3]

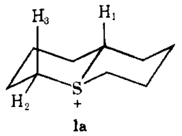
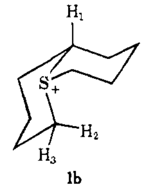
Chart I



[a] N-Chlorosuccinimide, benzene. [b] $C_6H_5OCH_2CH_2CH_2CH_2MgCl$.[1] [c] HBr, $(CH_3CO)_2O$.

Thermal equilibration of the 1:1 mixture of sulfonium fluoborates **1a** and **1b** in chloroform or methylene chloride at 110 °C for 24 h affords an equilibrium mixture (70% **1a**, 30% **1b**) from which pure **1a** ($X^- = BF_4^-$) may be obtained by repeated crystallization. Treatment of the 1:1 mixture of **1a** and **1b** ($X^- = BF_4^-$) with *n*-butyllithium in THF at −23 °C yields a mixture of ylides **4a** and **4b**, which is allowed to equilibrate for 2 h, then is quenched with fluoboric acid to afford sulfonium salt **1b** ($X^- = BF_4^-$, mp 173-173.5 °C), uncontaminated by stereoisomer **1a**. From this result, it is concluded that equilibrium **4a** ⇌ **4b** is biased heavily in favor of **4b**.

Table I. ^1H NMR Resonances of Salts 1a and 1b[a]

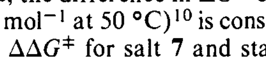
	 1a	 1b
H-1	3.286 (tt, J = 11.9, 2.3 Hz)	3.694 (tt, J = 7.8, 3.9 Hz)
H-2	3.558 (broad d, J = 11.8, 2-3)	3.228 (m)[b]
H-3	3.156 (ddd, J = 13.3, 11.8, 2.5)	3.481 (m)[b]

[a] Spectra were determined on 1% solution in D_2O. Data are presented as δ (ppm downfield from internal $Me_3SiCD_2CD_2CO_2^-Na^+$), (multiplicity, coupling constants in Hz). [b] These assignments are uncertain and may be reversed.

Stereostructures of **1a** and **1b** were assigned on the basis of the 360-MHz ^1H NMR spectra of pure **1b** and a sample highly enriched in isomer **1a**. Pertinent ^1H NMR resonance are summarized in Table I. The most conclusive indication is the resonance due to the bridgehead proton in the more stable sulfonium salt **1a** (δ 3.286 ppm), which appears as a triplet of triplets with coupling constants typical of axial-axial and axial-equatorial arrangements. Having made stereostructural assignments based on high-resolution ^1H NMR spectra, it is convenient to use ^{13}C NMR to analyze mixtures of the two stereoisomeric salts; assignments are tabulated in Table II.[6]

Activation parameters for pyramidal inversion of salt **1** ($X^- = BF_4^-$) were determined by thermal equilibration of the 1:1 mixture of stereoisomers in CD_2Cl_2 at three temperatures over the range 90.07-105.80 °C. Analysis was accomplished by ^{13}C NMR. A plot of ln k/T vs. $1/T$ gives $\Delta H^{\ddagger} = 28.0 \pm 0.9$ kcal mol^{-1} and $\Delta S^{\ddagger} = -3.1 \pm 2.5$ eu. Activation parameters for pyramidal inversion of ylide **4** were determined at −23 and −32 °C, starting with a 7:3 mixture of salts **1a** and **1b** ($X^- = BF_4^-$). The ylide mixture was prepared by deprotonation with *n*-BuLi at −72 °C. The samples were warmed to the appropriate temperature and kept for a period of time, then quenched by the addition of fluoboric acid. A plot of ln k/T vs. $1/T$ gives $\Delta H^{\ddagger} = 20.5$ kcal mol^{-1} and $\Delta S^{\ddagger} = 6$ eu.[7]

The observed activation parameters for pyramidal inversion of salt **1** are similar to those reported for other sulfonium salts.[8] Although activation parameters for pyramidal inversion of an unstabilized sulfonium ylide have not previously been reported, Darwish has studied sulfonium salt **7**[8c] and the corresponding stabilized ylide **8**.[9] Salt **7** undergoes inversion with $\Delta H^{\ddagger} = 29.2$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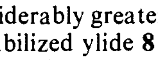
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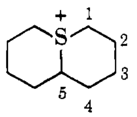
kcal mol^{-1} and $\Delta S^{\ddagger} = +2$ eu, corresponding to $\Delta G^{\ddagger}_{50°} = 28.6$ kcal mol^{-1}. Ylide **8** inverts with $\Delta H^{\ddagger} = 23.3$ kcal mol^{-1} and $\Delta S^{\ddagger} = -2.5$ eu, corresponding to $\Delta G^{\ddagger}_{50°} = 24.1$ kcal mol^{-1}. The *difference* in $\Delta H^{\ddagger}$ between salt **1** (**1a** → **1b**) and ylide **4** (**4b** → **4a**) of 7.5 kcal mol^{-1} is similar to the difference in $\Delta H^{\ddagger}$ (5.9 kcal mol^{-1}) between sulfonium salt **7** and ylide **8**. On the other hand, the difference in $\Delta G^{\ddagger}$ between salt **1** and ylide **4** (10.4 kcal mol^{-1} at 50 °C)[10] is considerably greater than the analogous $\Delta\Delta G^{\ddagger}$ for salt **7** and stabilized ylide **8** (4.5 kcal mol^{-1} at 50 °C).[11] This difference originates largely in the

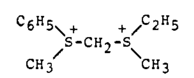
Table II. ^{13}C NMR Chemical Shifts of Salts 1a and 1b[a]



Carbon	1a	1b
1	38.3	30.7
2	23.9	20.0
3	23.5	19.9
4	30.7	26.1
5	53.3	42.6

[a] Spectra were determined on *ca.* 25% solutions in $CDCl_3$. Data are presented in ppm downfield from internal Me_4Si.

entropy terms. While $\Delta S^{\ddagger}$ for ylide **8** is more negative than $\Delta S^{\ddagger}$ for salt **7** by 4.5 eu, $\Delta S^{\ddagger}$ for ylide **4** is *more positive* than $\Delta S^{\ddagger}$ for salt **1** by 9.1 eu. Finally, it has recently been shown that conversion of 1,3-bissulfonium salt **9** to the corresponding ylide decreases $\Delta G^{\ddagger}$ for pyramidal inversion at sulfur by at least 5 kcal mol^{-1}.[12,13]



$$\overset{C_6H_5}{\underset{CH_3}{}}\overset{+}{S}-CH_2-\overset{+}{S}\overset{C_2H_5}{\underset{CH_3}{}}$$

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We are now engaged in studying the stereochemistry of the reaction of ylides **4a** and **4b** with various electrophiles.

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References and Notes

(1) R. H. Eastman and G. Kritchevsky, *J. Org. Chem.*, **24**, 1428 (1959).
(2) Anal. Found: C, 44.19; H, 6.98; S, 12.89.
(3) R. F. Borch, *J. Org. Chem.*, **34**, 627 (1969).
(4) D. L. Tuleen and R. H. Bennett, *J. Heterocycl. Chem.*, **6**, 115 (1969).
(5) Anal. Found: C, 71.70; H, 8.79.
(6) Note that each carbon in the more stable sulfonium salt **1a** resonates downfield from the corresponding carbon in isomer **1b**, a situation parallel to that found in *trans*- and *cis*-decalin; J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, N.Y., 1972, p 66.
(7) The precision of these parameters is obviously not high because of the difficulty of maintaining precise temperature control in this range and also because equilibration rates were determined at only two temperatures. However, treatment of the rates at −23 and −32 °C by the Eyring equation yields $\Delta G^{\ddagger}_{-23°}$ = 18.92 kcal mol^{-1} and $\Delta G^{\ddagger}_{-32°}$ = 18.97 kcal mol^{-1}, suggesting that the activation parameters are reasonably good.
(8) (a) D. Darwish and G. Tourigny, *J. Am. Chem. Soc.*, **88**, 4303 (1966); (b) R. Scartazzini and K. Mislow, *Tetrahedron Lett.*, 2719 (1967); (c) D. Darwish, *Mech. React. Sulfur Compd.*, **3**, 33 (1968); (d) A. Garbesi, N. Corsi, and A. Fava, *Helv. Chim. Acta*, **53**, 1499 (1970).
(9) D. Darwish and R. L. Tomilson, *J. Am. Chem. Soc.*, **90**, 5938 (1968).
(10) Extrapolated values.
(11) The free energy of activation of ylide **8** was calculated from the published rate constant, using the Eyring equation.
(12) S. Wolfe, P. Chamberlain, and T. F. Garrard, *Can. J. Chem.*, **54**, 2847 (1976).
(13) The $\Delta G^{\ddagger} \geq$ 25 kcal mol^{-1} reported for salt **9** is highly approximate, having been determined from a single analysis at −10 °C. The $\Delta G^{\ddagger}$ = 19.7 kcal mol^{-1} for the derived ylide was determined at 2.4° by monitoring the equilibration at several points, although complete experimental data are not available.[12]

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MINDO/3 Study of the Addition of Singlet Oxygen ($^1\Delta_gO_2$) to 1,3-Butadiene

Sir:

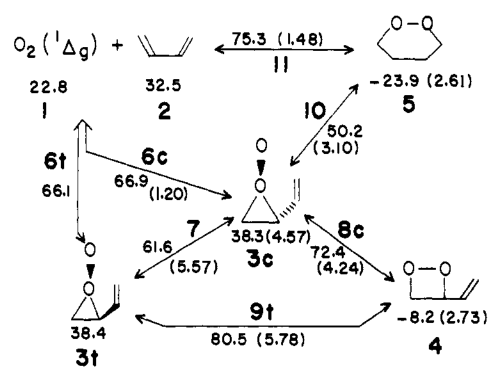

Figure 1. Heats of formation (kcal/mol) and dipole moments (D, in parentheses) of species involved in the reaction of $^1\Delta_g$ O_2 with 1,3-butadiene and of transition states involved in their interconversions.

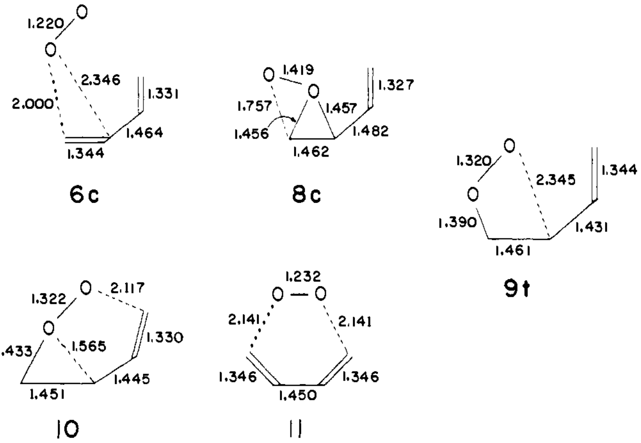

Figure 2. Geometries of transition states (bond lengths in Å).

The well-known[1] π-cycloaddition of singlet molecular oxygen ($^1\Delta_gO_2$, **1**) to conjugated dienes to form six-membered cyclic peroxides bears an obvious resemblance to the Diels–Alder reaction, and both processes were until recently thought to involve synchronous[2] pericyclic mechanisms. However McIver[3] has shown that π-cycloadditions are unlikely to involve symmetrical transition states and MINDO/3[4] studies[5] here have indeed shown that the transition states for several typical Diels–Alder reactions are very unsymmetrical,[6] one of the new bonds being almost completely formed, the other hardly at all. Our MINDO/3 calculations[9] for several reactions of **1** with olefins have moreover indicated that these are two-step[2] processes, involving peroxiranes or zwitterions as stable intermediates. We therefore felt it of interest to extend our MINDO/3 studies to the reaction of **1** with 1,3-butadiene (**2**).

Figure 1 shows the reactions we studied, using the techniques previously described.[9] The calculated heats of formation and dipole moments of the various stable species and transition states are also indicated in Figure 1 while Figure 2 shows the structures calculated for the transition states. These results imply that the first step in the reaction of **1** with **2** is the formation of a peroxirane which can exist as a cis (**3c**) or trans (**3t**) isomer. The activation energy for addition is 10.8 kcal/mol and the transition states (**6c**, **6t**) are reactant-like in their geometric and electronic structures. The intermediate *cis*-peroxirane (**3c**) can rearrange easily ($\Delta E^{\ddagger}$, 11.9 kcal/mol) to the cyclic peroxide **5**.

The overall activation energy for formation of **5** by this two-step route is less by 9.2 kcal/mol than by concerted 1,4-π-cycloaddition of **1** to **2**. This latter reaction could indeed be studied only by enforcing C_s symmetry. The corresponding "transition state" (**11**), while a stationary point on the potential surface, is *not* a true transition state because the force constant matrix has two negative eigenvalues (cf. ref 9 and 10).

The intermediates, **3c** and **3t**, can also rearrange to vinyl-