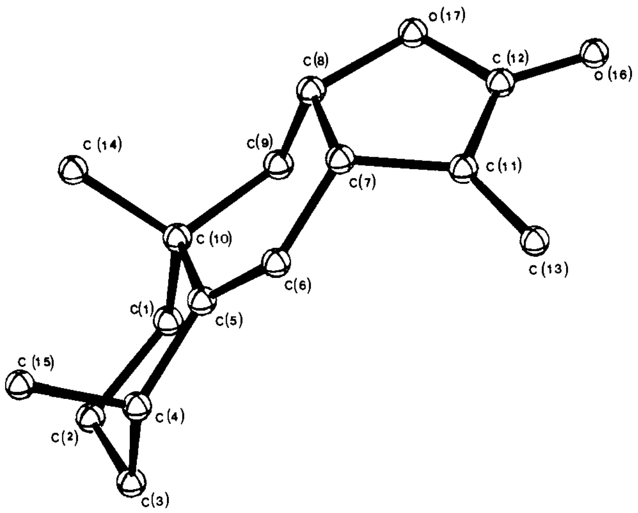

Figure 1. A computer-generated perspective drawing of 7,8-epialantolactone (**9**). Hydrogens are omitted for clarity.

11.365 (2) Å; $\beta = 122.77$ (5)°. The systematic extinctions conformed to the common monoclinic space group $P2_1/c$ and a density measurement indicated one molecule of composition $C_{15}H_{20}O_2$ per asymmetric unit. All unique diffraction maxima with $2\theta \leq 114°$ were collected on a fully automated four-circle diffractometer using graphite monochromated Cu K_α (1.54178 Å) X-rays and a variable speed ω-scan technique. A total of 1861 diffraction maxima were surveyed and, after correction for Lorentz, polarization and background effects, 1738 (9390) were judged observed ($F_o \geq 3\epsilon(F_o)$).[11] The structure was solved using a multisolution weighted sign determining procedure. All of the nonhydrogen atoms were visible on the subsequent E synthesis and hydrogens were located on a difference synthesis. The structure was refined by the full-matrix least-squares technique using anisotropic nonhydrogens and fixed isotropic hydrogens to the current residual of 0.095.

Figure 1 is a computer generated perspective drawing of the final X-ray model less hydrogens. All bond distances and angles generally agree well with generally accepted values.

There is abundant experimental evidence suggesting that the preferred mode of addition of organocuprates to α,β-unsaturated ketones is that favoring antiparallel approach of the reagent to the π system of the enone.[12] In cyclohexenone ring systems, the stereochemical result is generally axial substitution.[13] To our knowledge, stereochemistry of organocuprate addition to activated vinylcyclopropanes has not been tested. We note that the addition of lithium dimethylcuprate to **7** results in axial substitution at C(4). Thus, the advantageous tandem S_N2' dehydrobromination-organocuprate addition (**6b** → **7** → **8a**) serves to substitute an alkyl group for a halogen atom with complete stereochemical control.[14] The overall yield of *dl*-epialantolactone **9** from diene lactone **3a** is ~48%.

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Supplementary Material Available: Tables of fractional coordinates, bond distances, and bond angles for **9** (2 pages). Ordering information is given on any current masthead page.

References and Notes

(1) A. G. Schultz and J. D. Godfrey, *J. Org. Chem.*, **41**, 3494 (1976).
(2) D. J. Brecknell and R. M. Carman, *Tetrahedron Lett.*, 73 (1978).
(3) J. A. Marshall and N. Cohen, *J. Org. Chem.*, **29**, 3727 (1964); W. Cocker and T. B. H. McMurry, *Tetrahedron*, **8**, 181 (1960); J. A. Marshall, N. Cohen, and A. R. Hochstetler, *J. Am. Chem. Soc.*, **88**, 3408 (1966).
(4) W. Haefliger and T. Petrzilka, *Helv. Chim. Acta*, **49**, 1937 (1966).
(5) Compounds **3a**, **6a**, **6b**, **7**, **8a**, and **9** gave satisfactory elemental analyses.
(6) R. O. Hutchins, D. Rotstein, N. Natale, J. Fanelli, and D. Dimmel, *J. Org. Chem.*, **41**, 3328 (1976), and references cited therein.
(7) Herz and co-workers report that the vicinal coupling constant for bridgehead protons in ring-fused γ-lactones is generally ≤8–9 Hz for a cis fusion and >10 Hz for a trans fusion: H. Herz, K. Aota, M. Holub, and Z. Samek, *J. Org. Chem.*, **35**, 2611 (1970).
(8) This approach to activated fused ring vinylcyclopropanes should be generally useful; for a recent report concerning cyclopropane ring construction by an intramolecular enolate alkylation, see M. Isobe, H. Iio, T. Kawai, and T. Goto, *Tetrahedron Lett.*, 703 (1977). For examples of activated cyclopropane synthesis by the well-explored intramolecular diazo ester addition to proximate olefins, see E. J. Corey and P. L. Fuchs, *J. Am. Chem. Soc.*, **94**, 4014 (1975); F. E. Ziegler, A. F. Marino, O. A. C. Petroff, and W. L. Studt, *Tetrahedron Lett.*, 2035 (1974); R. D. Clark and C. H. Heathcock, *ibid.*, 529 (1975); B. M. Trost, D. F. Taber, and J. B. Alper, *ibid.*, 3857 (1976). See ref 9 for additional examples.
(9) P. A. Grieco and R. Finkelhor, *J. Org. Chem.*, **38**, 2100 (1973), and references cited therein for related additions of lithium dialkylcuprates; J. M. Stewart and G. K. Pagenkopf, *ibid.*, **34**, 7 (1969); S. Danishefsky and R. K. Singh, *ibid.*, **40**, 3807 (1975); D. F. Taber, *J. Am. Chem. Soc.*, **99**, 3513 (1977); K. Kondo, T. Umemoto, Y. Takahatake, and D. Tunemoto, *Tetrahedron Lett.*, 113 (1977); G. Daviaud and Ph. Miginiac, *ibid.*, 997 (1972); S. Danishefsky, G. Rovnyak, and R. Cavanaugh, *Chem. Commun.*, 636 (1969); S. Danishefsky and G. Rovnyak, *J. Chem. Soc., Chem. Commun.*, 820, 821 (1972).
(10) J. P. Martin, P. Watts, and F. Johnson, *Chem. Commun.*, 27 (1970).
(11) All crystallographic calculations were done on a Prime 400 computer operated by the Materials Science Center and the Department of Chemistry, Cornell University. The principal programs used were REDUCE and UNIQUE, data reduction programs, M. E. Leonowicz, Cornell University, 1978; BLS, block-diagonal least-squares refinement, K. Hirotsu, Cornell University, 1978; ORFLS (modified), full-matrix least squares, W. R. Busing, K. O. Martin, and H. S. Levy, Oak Ridge, ORNL-TM-305; ORTEP, crystallographic illustration program, C. Johnson, Oak Ridge, ORNL-3794; BOND, structural parameters and errors, K. Hirotsu, Cornell University, 1978; MULTAN-76, direct methods and fast fourier transform, G. Germain, P. Main, and M. Woolfson, University of York.
(12) G. A. Posner, *Org. React.*, **19**, 1–114 (1972).
(13) See, however, R. K. Boeckman and S. M. Silver, *Tetrahedron Lett.*, 3497 (1973), for a study of the stereochemical factors influencing the addition of organometallic reagents to cyclohexenones.
(14) Substitution reactions of lithium dimethylcuprate with bromocyclohexanes proceed nonstereospecifically in only moderate yield. Competing elimination and reduction also occur: E. J. Corey and G. H. Posner, *J. Am. Chem. Soc.*, **89**, 3911 (1967). Reaction of **6b** with lithium dimethylcuprate (5 equiv) gives a complex mixture of products which contains little if any **8a**.
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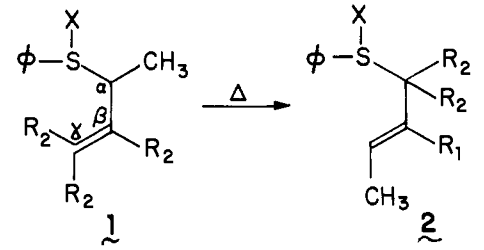
Kinetic Isotope Effects in the Mechanisms of Thermal Allylic Rearrangements

Sir:

The reversible, thermal interconversion of allylic sulfoxides and sulfenates has been shown to occur via a pericyclic process.[1] The corresponding 1,3 migration of a phenylsulfinyl group across an allylic framework (referred to in subsequent discussion here as the sulfoxyallylic rearrangement) appears to be a much slower and, presently, a mechanistically unresolved accompanyment which initially escaped detection in the course of discovery of the more mobile 2,3-sigmatropic change. Recently, however, both the analogous thiaallylic[2-7] and the sulfoxyallylic rearrangements[8] have been widely applied in synthetic schemes and have earned the designations of synthons.[7,8] In the thermal thiaallylic rearrangement the 1,3 migration of sulfur has been shown[3-6] to involve a hypervalent sulfur intermediate, probably possessing a trigonal-bipyramid-like structure and capable of permutational isomerism. The evidence for this reaction course rests on solvent and substituent rate effects,[5,6] sulfur (heavy atom) isotope effects,[3] and secondary (side chain) deuterium isotope effects,[4] all of which are consonant only with an associative transition state (TS). Because of the apparent structural similarities it was assumed[4,8] that the sulfoxyallylic rearrangement takes place

Table I. Experimental Isotope Effects



isotopes	X[a]	R_1	R_2	k_L/k_H[a]
$^{32}S/^{34}S$	oxygen	H	H	1.0191 ± 0.0021[b,c]
$^{32}S/^{34}S$	e pair	H	H	1.0040 ± 0.0016[d]
H/D	oxygen	H	D	1.0285 ± 0.0021 (per D)[b,e]
H/D	e pair	H	D	0.936 ± 0.004 (per D)[f]
H/D	oxygen	D	H	1.0027 ± 0.0017[b,d]
H/D	e pair	D	H	0.918 ± 0.015[f]

[a] Rate ratio of the light (L) and heavy (H) isotopes, for the cases of sulfoxides (where X = oxygen) and sulfides (where X = electron pair). [b] For the purpose of mass spectrometric analysis the unreacted sulfoxide, **1** (X = oxygen), was quantitatively converted into the corresponding sulfide, **1** (X = electron pair), using Si_2Cl_6 in benzene at 0 °C. Reduction under these circumstances did not induce any rearrangement. [c] An average of four individual values, each based on 20 000 mass spectrometric determinations, were calculated from isotope ratio measurements on unreacted **1** after partial reaction forming **2**. Measurements were taken over a range of 38 to 68% conversion. A similar computation based on this method has been previously described.[12] [d] Reference 3. [e] An average of five individual values were calculated over a range of 38 to 78% conversion. [f] Reference 4.

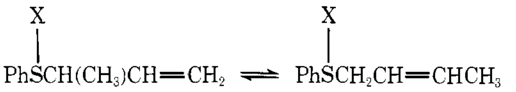
by an analogous mechanism, since a sulfoxy center normally exhibits a higher tendency to accept hypervalency and octet expansion.[9,10] We can now report, however, that this expectation is not fulfilled and that an entirely different course of migration prevails in the sulfoxyallylic process based on evidence gleaned from kinetic and isotope effect studies.

Using as the starting material the natural abundance sulfur isotope composition of the allylic sulfoxide substrate **1** (X = O) the heavy-atom isotope effect attending the thermal rearrangement of **1** → **2** (X = O) was carried out by applying the high precision, mass spectrometric method developed earlier[3] for these purposes. The data obtained from such measurements in runs covering the range of ~38–68% completion are listed in Table I. The extrapolated value of k_{32}/k_{34} computed from these data is to be compared with those deduced theoretically for alternative transition states of sulfoxyallylic rearrangement (see Table II) and, in turn, with the analogous TS of thiallylic rearrangement which has been previously characterized by means of the heavy-atom isotope effect criterion. Plainly, the experimental value of k_{32}/k_{34} for the sulfoxyallylic rearrangement is in close agreement only with that estimated for a dissociative TS, in sharp contrast to the results previously found[3] supporting an associative TS of the thiaallylic rearrangement.

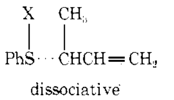
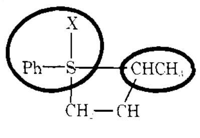
The thiaallylic mechanism has also been verified by secondary deuterium isotope effect studies[4] which corroborate extensive bonding in the TS between the sulfur seat of reaction and both the γ (terminal) carbon and the β carbon of the allylic side chain, suggesting a sort of pyramidal arrangement of the allylic carbons stemming from the hypervalent sulfur vertex.[4] The experimental measurements of the k_H/k_D values in secondary deuterium isotope effect studies of the sulfoxyallylic rearrangement have also been carried out; the data are also summarized in Table I. Comparison of these results with those determined earlier[4] for the corresponding thiaallylic rearrangement again reveals the sharp differences in mechanistic patterns of the two thermal rearrangements. The inverse isotope effects at both the β and γ allylic centers in the thiaallylic, which are indicative of increased bonding in the (associative) TS, are replaced in the sulfoxyallylic by normal isotope effects, confirming the decreased bonding at these centers in a dissociative TS.

In the simplest rationalization of these results it can be said that the replacement of the unshared pair on sulfur in the thiaallylic substrate by a highly electronegative oxygen has created a great deal of polar character on the allylic moiety, accompanied presumably by bond lengthening and bond mobility in the TS. Assuming this activated complex is modeled on an actual intermediate it cannot as yet be said, however, whether a dipolar **3a** or tetrapolar **3b** ion pair is developing in the TS, depending on the extent to which the oxygen has exerted its influence on the charge distribution. A decision be-

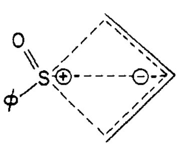
Table II. Sulfur Isotope Effects in Comparable Thermal Allylic Rearrangements Estimated from Transition-State Models



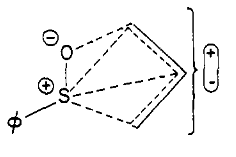
$$\underset{\mathbf{1}}{\overset{X}{\overset{|}{Ph\text{S}}}CH(CH_3)CH{=}CH_2} \rightleftharpoons \underset{\mathbf{2}}{\overset{X}{\overset{|}{Ph\text{S}}}CH_2CH{=}CHCH_3}$$

	TS Model			
	 $\overset{X}{\overset{\vert}{PhS}}\cdots\overset{CH_3}{\overset{\vert}{C}}HCH{=}CH_2$ dissociative		 associative[a]	
	X = :	X = 0	X = :	X = 0
effective mass model	(77 + S)···(55)	(93 + S)···(55)	(77 + S)—(28)	(93 + S)—(28)
estimated[b,c] k_{32}/k_{34}	1.0120	1.0130[d] 1.0194[e]	1.0048	1.0066
experimental agreement	1.0191 ± 0.0021	1.0040 ± 0.0016		

[a] For purposes of calculation[13] the TS structure was defined as diatomic in which the circles represent the equivalent of two atoms joined by the critical bond with group masses as shown. [b] Isotope effects were estimated by evaluating the Bigeleisen equation.[14] The μ and $\mu^{\ddagger}$ terms of this formulation were obtained from (i) laser Raman spectra of **1**, (ii) Hooke's Law calculations, and (iii) literature values reported for the Raman spectra of substituted thietanes.[15] [c] Not corrected[16,17] for naturally abundant ^{13}C or ^2H. [d] Calculated by considering only the stretching frequency of the S–C critical bond (Slater's simplification).[13d] [e] Calculated by including the stretching frequencies of the S–C bond as well as the S–O bond in the Bigeleisen equation. This follows from the cut-off method which states that all bonds which are affected by isotopic substitution should be included in model calculations.



3a

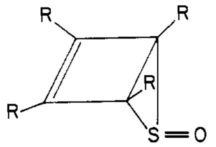


3b

tween these alternatives awaits the outcome of kinetic studies presently in progress.

The extraordinarily facile automerization of the sulfoxide of perfluorotetramethyl(Dewar thiophene) (**4**), characterized by Ross, Seiders, and Lemal[11] and tentatively favored by these authors to proceed by an unusual pseudopericyclic 1,3-sigmatropic route, merits some comment. On the other hand, cyclobutadiene complexed to phenylthio moieties have been proposed to occur during the isomerization of 2-phenyl- to 3-phenylthiophene in glow discharges[18] and to explain ^{13}C labeling patterns found in electron impact studies.[19] Similar square pyramidal structures have been suggested[4] as possible thiaallylic rearrangement intermediates. Finally, π-face bonding of rectangular, singlet cyclobutadiene with carbon monoxide, hydrogen cyanide, and benzene has been considered in recent theorietical investigations.[20]

However, in view of the dissociative pathway identified for the conversion of **1** → **2** (X = O), the possibility now exists that the automerization of **4** passes through an intermediate with



4 (R = CF_3)

the structure of an ion pair of dipolar or multipolar character, whose geometry is a reflection of charge interactions of considerable complexity.

References and Notes

(1) P. Bickart, F. W. Carson, J. Jacobus, E. G. Miller, and K. Mislow, *J. Am. Chem. Soc.*, **90**, 4869 (1968).
(2) H. Kwart and N. Johnson, *J. Am. Chem. Soc.*, **92**, 6064 (1970).
(3) H. Kwart and J. Stanulonis, *J. Am. Chem. Soc.*, **98**, 4009 (1976).
(4) H. Kwart and T. J. George, *J. Am. Chem. Soc.*, **99**, 5214 (1977).
(5) H. Kwart and N. A. Johnson, *J. Am. Chem. Soc.*, **99**, 3441 (1977).
(6) H. Kwart and N. A. Johnson, *J. Org. Chem.*, **42**, 2855 (1977).
(7) P. Brownbridge and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 2125 (1976), and earlier references cited therein.
(8) D. A. Evans and G. C. Andrews, *Acc. Chem. Res.*, **7**, 147 (1974); see also note 22 in ref 4.
(9) J. I. Musher, *Angew. Chem., Int. Ed. Engl.*, **8**, 54 (1969).
(10) H. Kwart and K. G. King, "d-Orbitals in the Chemistry of Silicon, Phosphorus and Sulfur", Springer-Verlag, Berlin, Heidelberg, New York, 1977.
(11) J. A. Ross, R. P. Seiders, and D. M. Lemal, *J. Am. Chem. Soc.*, **98**, 4325 (1976).
(12) H. Kwart, D. A. Benko, J. Streith, and J. L. Schuppiser, *J. Am. Chem. Soc.*, **100**, 6052 (1978).
(13) (a) The calculation procedures employed here were essentially identical with those discussed by H. Kwart and W. E. Barnette, *J. Am. Chem. Soc.*, **99**, 614 (1977), and are consistent with the simplified methods discussed elsewhere: (b) M. J. Stern and M. Wolfsberg, *J. Chem. Phys.*, **45**, 4105 (1966); (c) W. H. Saunders, Jr., *Chem. Ind.* (*London*), 1661 (1963); (d) N. B. Slater, *Proc. R. Soc.* (*London*), *Ser. A*, 194, 112 (1948).
(14) J. Bigeliesen and M. G. Mayer, *J. Chem. Phys.*, **15**, 261 (1947); J. Bigeleisen, *ibid.*, **17**, 675 (1949); see also J. Bigeleisen, *Adv. Chem. Phys.*, **1** (1958).
(15) Y. Etienne, R. Soulas, and H. Lumbroso in "The Chemistry of Heterocyclic Compounds", Vol. 19, Part 2, A. Weissberger, Ed., Interscience, New York 1964, p 671.
(16) The dissociative model calculations here lead to a minimum value for k_{32}/k_{34}. Correction for ^{13}C and ^{2}H in natural abundance effects would lead to a slightly higher value.
(17) The associative model calculations here yield a maximum value of k_{32}/k_{34}. Correction for natural abundance ^{13}C and ^{2}H would result in a slightly lower value.
(18) J. Skramstadt and B. Smedsrud, *Acta Chem. Scand., Ser. B*, **31**, 625 (1977).
(19) W. D. Weringa, H. J. M. Sinnige, and M. J. Janssen, *Org. Mass Spectrom.*, **5**, 1399 (1971).
(20) K. B. Lipkowitz, *J. Am. Chem. Soc.*, **100**, 7535 (1978).

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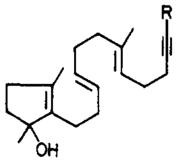
Biomimetic Polyene Cyclizations.[1] Participation of the Phenylacetylenic Group as a Terminator and the Formation of C/D Cis Steroidal Products

Sir:

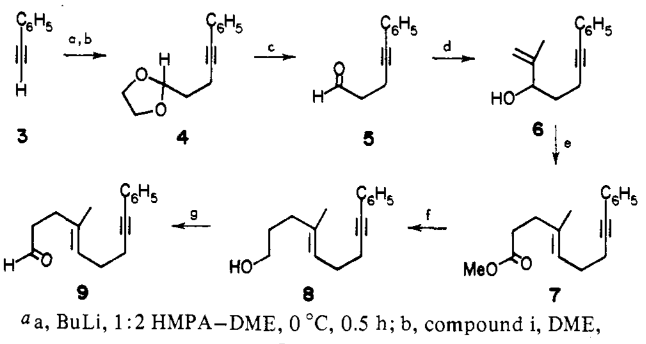
The participation of the methylacetylenic group as a terminator of biomimetic polyene cyclizations, so as to form directly the five-membered D ring of steroid precursors, has been well documented;[2] e.g., the conversion **1** into **13** (Me in place of C_6H_5) occurs in yields approaching 70%.[3] The remaining material consists principally of olefinic byproducts, apparently derived from deprotonation of a tricyclic cation.[4] It was hoped that use of a more nucleophilic terminator, i.e., the phenylacetylenic in place of the methylacetylenic group, would lead to increased yields of tetracyclic material. Therefore an examination of the cyclization of the trienynol **2** was undertaken, and the present communication represents a preliminary report of this study which has yielded some unexpected results.



1 (R = Me)
2 (R = C_6H_5)

The trienynol **2** was synthesized in a convergent manner, the key step being a Wittig reaction between the aldehyde **9** and the phosphorane formed from the known phosphonium salt **10**.[3] The aldehyde **9** was prepared as outlined in Scheme I. Treatment of the lithium salt of **3** with the ethylene glycol acetal[5] of 3-bromopropanal produced the acetal **4**[6,7] in 82% yield. Hydrolysis of the acetal function gave the aldehyde **5**[6,7] in 78% yield, which was treated with isopropenylmagnesium bromide to produce the allylic alcohol **6**[6,7] in 93% yield. This alcohol was converted to the enyne ester **7**[6,7] in 91% yield by means of the orthoacetate Claisen reaction.[8] Reduction of the

Scheme I[a]



[a] a, BuLi, 1:2 HMPA–DME, 0 °C, 0.5 h; b, compound i, DME,

i

0 °C, 2 h; c, 1:1 5% HCl–$(CH_3)_2CO$, 23 °C, 48 h; d, $i\text{-}C_3H_5MgBr$, THF, 0 °C, 1 h; e, $CH_3C(OCH_3)_3$, 0.5% $C_2H_5CO_2H$, 95 °C, 48 h; f, $LiAlH_4$, THF, 0 °C, 1 h; g, $CrO_3\cdot 2C_5H_5N$, CH_2Cl_2, 23 °C, 0.5 h.

0002-7863/79/1501-1279$01.00/0