Assignment of the stereochemistry at C-6 for the allyl rearrangement product 7 was based on nmr data[10] (Table II). Examination of 6-β-ammoniumpenicillanates showed that the resonance for the β-methyl group at C-2 was shifted significantly downfield from the α-methyl resonance. This deshielding phenomenon is probably a result of the proximity of the positively charged transannular ammonium function. Epimerization of the natural 6-β isomer to the 6-α-ammonium derivative results in a pronounced upfield shift of the C-2 β-methyl resonance. Nuclear Overhauser effects (NOE) of the C-2 methyl groups with the protons at C-3 and C-5 were determined on the ammonium compounds to show that they had the normal penicillin conformation (a) and that the downfield resonance was indeed due to the β-methyl.[11] The methiodide 7 clearly fits the pattern of the compounds with the natural β-ammonium stereochemistry.

Formation of 5 probably involves a [2,3]-sigmatropic rearrangement of the derived nitrogen ylide **11**.[12] Similar allylic migration of nitrogen ylides under mild temperature conditions are well documented[13] but to our knowledge it has not been previously established that the carbanionic center retains its configuration.[14] The present results may be rationalized in the following way. In the aprotic benzene–DMF system the ylide **11** is converted by a [2,3]-sigmatropic rearrangement to **5**, the stereochemistry at C-6 being determined by more ready alignment of the allylic terminus from the α face of the β-lactam. The driving force for rearrangement is provided by the relief of the charge separation inherent in the betaine **11**. However, in the aqueous case epimerization could be achieved *via* an enol, a species with the same geometry as the betaine but lacking the driving force of charge separation. Thus although our system does proceed with retention of configuration at C-6, the result may not be a general stereochemical phenomenon, but is rather a consequence of the adjacent geometry in this molecule.

Acknowledgments. We wish to acknowledge our many helpful discussions with Drs. R. D. G. Cooper and M. Gorman of the Lilly Research Laboratories.

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[10] We wish to thank Dr. P. V. Demarco and T. Elzey of the Lilly Research Laboratories for determination and interpretation of the nmr data.

[11] R. D. G. Cooper, P. V. Demarco, J. C. Cheng, and N. D. Jones, *J. Amer. Chem. Soc.*, **91**, 1408 (1969).

[12] This is an example of a widely occurring general process in allylically substituted ylides, *cf.* J. E. Baldwin, J. E. Brown, and R. W. Cordell, *Chem. Commun.*, 31 (1970).

[13] R. W. Jemison and W. D. Ollis, *ibid.*, 294 (1969); B. J. Millard and T. S. Stevens, *J. Chem. Soc.*, 3397 (1963).

[14] There are, however, several examples of stereochemical induction at the terminus of Stevens 1,2 rearrangements: R. K. Hill and T. H. Chan, *J. Amer. Chem. Soc.*, **88**, 866 (1966); H. Joshua, R. Gans, and K. Mislow, *ibid.*, **90**, 4884 (1968).

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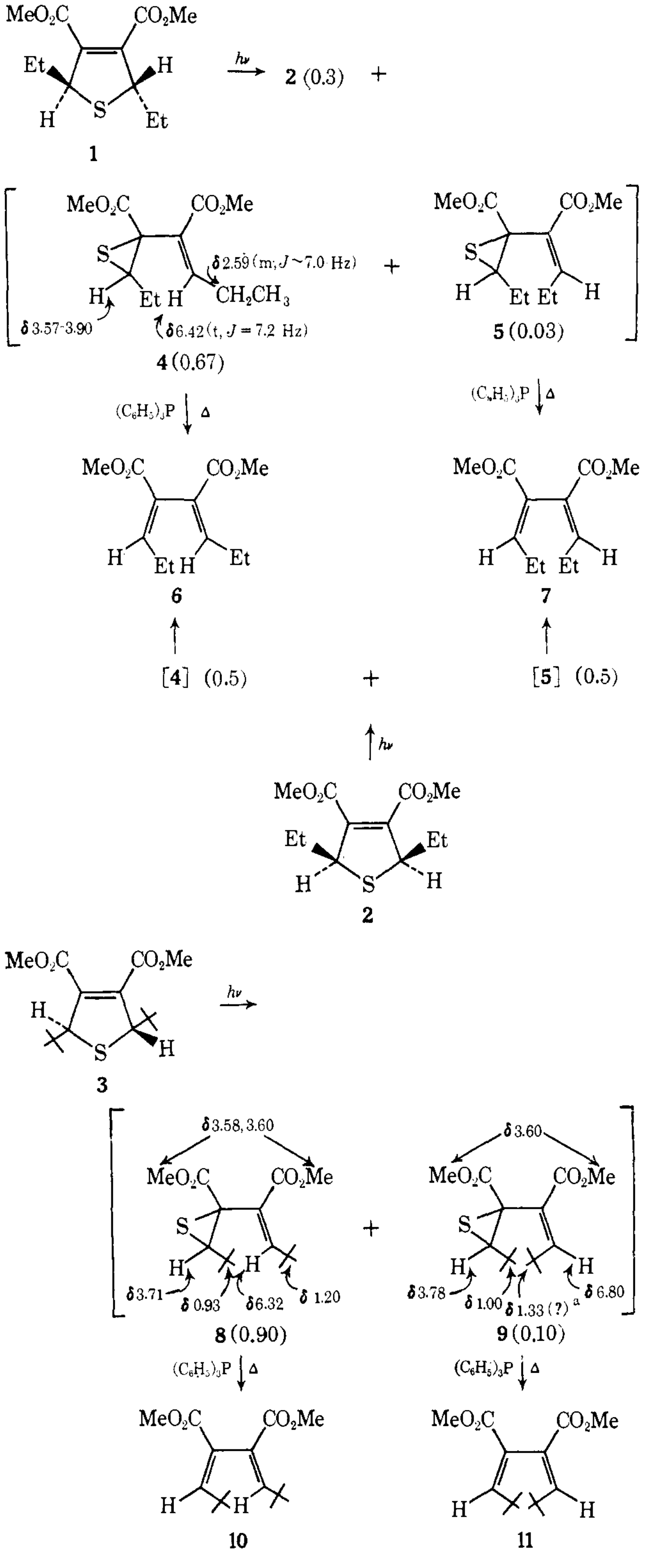
Photochemistry of 2,5-Dihydrothiophenes. A Facile, Stereoselective Ring Contraction

Sir:

The 2,5-dihydrothiophenes **1–3** recently became available through the stereospecific thermal addition of thiocarbonyl ylides[1] to dimethyl acetylenedicarboxylate.

Chart I



[a] Overlap with adsorptions from **11** makes assignment difficult in the CAT spectrum.

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[1] R. M. Kellogg, S. Wassenaar, and J. Buter, *Tetrahedron Lett.*, 4689 (1970).

Table I. Nmr Spectral Data for Dienes **6**, **7**, **10**, **11**, and **12**

Diene	Nmr (CCl_4)[a]
4,5-Dicarbomethoxy-(3*Z*,5*E*)-3,5-octadiene (**6**)	δ 1.04, 1.07 (overlapping t, 6, *J* = 7.0, 1,8-CH_3), 2.15 (m,[b] 2,7-CH_2), 2.62 (m,[b] 2,2-CH_2), 3.66, 3.67 (overlapping s, 6, OCH_3), 5.82 (t, 1, *J* = 7.5, 3-*H*), 6.75 (t, 1, *J* = 7.5, 6-*H*)
4,5-Dicarbomethoxy-(3*E*,5*E*)-3,5-octadiene (**7**)	δ 0.94 (t, 6, *J* = 7.0, 1,8-CH_3), 1.95 (m,[b] 4,2,7-CH_2), 3.60 (s, 6, OCH_3), 6.80 (t, 2, *J* = 7.4, 3,6-*H*)
4,5-Dicarbomethoxy-2,2,7,7-tetramethyl-(3*Z*,5*E*)-3,5-octadiene (**10**)	δ 1.12 (s, 9, (*E*)-*tert*-Bu), 1.22 (s, 9, (*Z*)-*tert*-Bu), 3.64 (s, 6,4,5-OCH_3), 5.72 (s, 1,3-H), 6.67 (s, 1,6-*H*)
4,5-Dicarbomethoxy-2,2,7,7-tetramethyl-(3*E*,5*E*)-octadiene (**11**)	δ 1.09 (s, 18, (*E*)-*tert*-Bu), 3.67 (s, 6,3,5-OCH_3), 6.72 (s, 2,3,6-*H*)
4,5-Dicarbomethoxy-(3*Z*,5*Z*)-3,5-octadiene (**12**)	δ 0.90 (t, 6, *J* = 7.0, 1,8-CH_3), 2.55 (m,[b] 4,2,7-CH_2), 3.63 (s, 6, OCH_3), 6.00 (t, 2, *J* = 7.0, 3,6-*H*)

[a] Taken at 60 MHz. [b] For **6** assignments of methylene and vinyl protons further shown by decoupling experiments. Multiplets consist of poorly resolved eight-line patterns. *J* values in hertz.

I have found that **1–3** on irradiation isomerize stereoselectively to unstable vinyl episulfides that may be desulfurized to afford stable dienes. The reactions are shown in Chart I. The ultimate diene products account quantitatively for consumed **1** and **3**;[2] product ratios (in parentheses) were obtained by extrapolation to zero time of vinyl episulfide *vs.* time plots (lowest experimental conversions *ca.* 0.5%).

Uv spectra of **1–3** (96% EtOH) show n–π^* maxima at 2740 Å, $\epsilon \simeq 650$. Irradiation (2540 Å, 10^{-2} *M* in *n*-hexane or ether) of degassed solutions leads to rapid formation (Φ_{dis} for **1** = 0.32) of thermally and photochemically unstable photoproducts, the appearance of which may be monitored by either nmr or glpc (see below). On brief (10 min) treatment with triphenylphosphine in hot benzene these intermediates are desulfurized quantitatively yielding the dienes shown in Chart I; these were isolated by preparative glpc. The photoproducts themselves lose sulfur on standing, extended irradiation, or attempted isolation by chromatographic means (glpc, tlc, column). They may, however, be detected quantitatively by direct injection[2] onto glass glpc columns; the retention times are in all cases 0.5–0.9 times those of the dihydrothiophene precursors. The area ratios for these intermediates correspond with those for the dienes formed after their treatment with triphenylphosphine thereby indicating the desulfurizations to be stereospecific.

Stereochemical assignments for the dienes **6**, **7**, **10**, and **11** obtained by desulfurization of the intermediates with triphenylphosphine are made on the basis of the nmr data given in Table I. Nonequivalence of the vinylic protons and alkyl substituents of **6** and **10** requires the *Z*,*E* assignments. The carbomethoxy group deshields substituents cis to it more effectively than vinyl;[4a–c] on this basis **7** and **11** clearly have *E*,*E* configurations. The "missing" 3*Z*,5*Z* isomer **12** possible from **1** or **2** was obtained as one of the steady-state components from irradiation of **6**; its absence in reaction mixtures from **1** and **2** was established by glpc.

All attempts to isolate pure **4** or **5** were fruitless;[5] the partial nmr spectrum of **4** shown in Chart I was obtained from mixtures with **1**. Fortunately, **8** and **9** proved more stable and were separated and secured (2–3 mg each) by careful preparative glpc[2] as *ca.* 80:20 mixtures with their desulfurization products **10** and **11**, respectively. Mass spectra showed the parent peak at *m*/*e* 314 ($C_{16}H_{26}O_4S^+$, isomeric with **3**) with unique fragmentations at *m*/*e* 299, 283, 257, 225, and 201.[6] Carbonyl absorptions appear in the infrared spectra at 1738 and 1720 cm^{-1} (sh). The nmr spectra of both **8** and **9** clearly show nonequivalent *tert*-butyl groups, a single vinylic proton, a single proton absorbing at higher field, and in the case of **8** nonequivalent carbomethoxy groups. These combined data, coupled with the observed facile stereospecific desulfurizations by triphenylphosphine,[7] *require* assignment of vinyl episulfide structures to the photoproducts.[8]

Since **9** should retain configuration during desulfurization to **11**, no ambiguity exists in its stereochemical assignment. For **8** the episulfide linkage could be, in principle, at potentially *E* or potentially *Z* double bonds. The former alternative is preferred (the other structure is not shown) in view of the similarities in chemical shifts of the tertiary protons in **8** and **9** consistent with similar arrangements about the episulfide rings. In addition, the vinylic proton in **8** is more deshielded than that of **9**, indicating the difference in configuration of these two compounds to lie in the vinyl moiety. Structure **4** is likewise preferred

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(2) Quantitative conversion has not been verified rigorously for **2** obtained only in milligram amounts from tedious glpc separation of mixtures with **1**.[1] Moreover, isolation is severely hampered by its tendency to undergo thermally induced dehydrogenation to 3,4-dicarbomethoxy-2,5-diethylthiophene (prepared for comparison by treatment of the sulfoxide of **1** with acetic anhydride).[3] This problem was overcome only by injection *directly* onto a ¼-in. glass Carbowax column at 200°; the effluent was fed into a *stainless steel* splitter (10:1) at the same temperature. Essentially the same technique was used for the isolation of **8** and **9**.

In nondegassed solutions both **1** and **3** undergo 3–4% photooxidation to the thiophenes. Rigid degassing virtually eliminates this problem.

Correct elemental analyses were obtained for the diene products; uv and ir spectra accord with expectation.

(3) M. P. Cava and N. M. Pollack, *J. Amer. Chem. Soc.*, **88**, 4112 (1966).

(4) (a) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 2nd ed, Pergamon Press, London, 1969, pp 184–192; (b) J. N. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, London, 1966, pp 710–742, and references contained therein; (c) for related arguments in structure determination, see B. M. Trost, *Accounts Chem. Res.*, **3**, 120 (1970).

(5) Although separation by analytical glpc on glass columns is possible, complete pyrolysis occurs in the detector under all practicable preparative conditions.

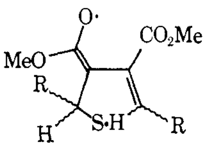
(6) The remote possibility that **8** and **9** have dimeric compositions was eliminated by an osmometric determination in ethyl acetate of the apparent molecular weight of a freshly irradiated solution of **3** containing 23% of a 9:1 ratio of **8**:**9**. The apparent molecular weight was 315 ± 2 and for pure **3** under the same conditions a value of 308 ± 0 (real mol wt = 314) was found; if the photoproducts were dimers an apparent molecular weight of 350 would have been found.

(7) Desulfurization of episulfides is known to be stereospecific: N. P. Neureiter and F. G. Bordwell, *J. Amer. Chem. Soc.*, **81**, 578 (1959); B. M Trost and S. Ziman, *Chem. Commun.*, 181 (1969).

(8) Nmr data on episulfides are scarce. The absorptions for the tertiary proton seem reasonable when compared to the spectra of various steroidal episulfides: K. Tori, T. Komeno, and T. Nakagawa, *J. Org. Chem.*, **29**, 1136 (1964).

over that with the episulfide linkage at the alternate double bond; this follows from the similarities of the chemical shifts of the tertiary and vinylic protons to those for **8** and from the high degree of deshielding of the methylene group indicating it to be cis to carbomethoxy. Structure **5** is that expected for the precursor of **7** but is assigned only on that basis.

The stereoselectivity of the transformations of **1–3** is not accommodated readily by extant theory. Application of some of the Zimmerman postulates[9] to the $n-\pi^*$ excited states of **1–3** does allow rationalization of the gross details of these unique ring contractions.[10] Biradical **13** would be a key intermediate and its formation finds precedent in the photoreactions of some structurally related isothiochromanones.[11] The chief products from the reactions of **1** and **3** may be accounted for by assuming a high preference for outward rotation of the alkyl group at the potentially vinylic carbon concomitant with nascent thiyl radical elimination;[12] readdition of the thiyl radical must then occur so as to arrange the alkyl and carbomethoxy groups trans on the episulfide ring. The pronounced tendency of cis isomer **2** to yield ultimate product **7** is more difficult to explain; also the irreversible isomerization of **1** to **2** (note Chart I) is puzzling. The alternative Woodward–Hoffmann theory[13] (assuming concerted reaction) encounters even more serious difficulties.[14] The transformations of **1** and **3** to **4** and **8**, respectively, are nominally $_{\sigma}2_s + _{\pi}2_s$ reactions with only one of two allowed products (episulfide linkage at alternate double bond) being formed.[15,16] Problems arise again with **2**, however. Ultimate product **7** could come from an allowed *supra–supra* reaction but the total absence of equally allowed ultimate product **12** seems inconsistent with prediction.[17]



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Consideration of molecular models suggests that conformational factors might complement the above arguments to a significant degree. Further work is in progress.

Acknowledgment. The expert assistance of Mrs. K. S. Rozema with CAT and decoupling experiments is acknowledged gratefully. Mr. J. Buter prepared a supply of **3**.

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[9] H. E. Zimmerman, *Advan. Photochem.*, **1**, 183 (1963).

[10] (a) Structurally related 2,3,5,5-tetraphenyl-2,5-dihydrofuran undergoes photochemical ring opening concomitant with group migration: D. W. Boykin, Jr., and R. E. Lutz, *J. Amer. Chem. Soc.*, **86**, 5046 (1964); (b) butadiene sulfones lose SO_2 photochemically yielding primarily conrotatory diene products: J. Saltiel and L. Metts, *ibid.*, **89**, 2232 (1967). The thermal reaction is exclusively disrotatory: W. L. Mock, *ibid.*, **88**, 2857 (1966); S. D. McGregor and D. M. Lemal, *ibid.*, **88**, 2858 (1966). Pyrolysis of the sulfones of **1** and **3** at 290° produces exclusively dienes **6** and **10** (disrotatory products).

[11] W. C. Lumma Jr., and G. A. Berchtold, *J. Org. Chem.*, **34**, 1566 (1969).

[12] Review of thiyl radicals: R. M. Kellogg, "Methods in Free-Radical Chemistry," E. S. Huyser, Ed., Marcel Dekker, New York, N. Y., 1969, pp 1–120.

[13] R. B. Woodward and R. Hoffmann, *Angew. Chem.*, **81**, 797 (1969).

[14] For trenchant criticism of the applicability of the Woodward–Hoffmann rules in photochemical reactions see: W. Th. A. M. van der Lugt and L. J. Oosterhoff, *J. Amer. Chem. Soc.*, **91**, 6042 (1969).

[15] But high preference for one of two "allowed" pathways in a photochemical rearrangement has been observed in other systems; see, for example: L. A. Paquette and O. Cox, *ibid.*, **89**, 5633 (1967); W. R. Roth and B. Peltzer, *Justus Liebigs Ann. Chem.*, **685**, 56 (1965).

[16] This transformation remains $2_s + 2_s$ even if, against probability, the position of the episulfide linkage is incorrectly assigned in **4** and **8**.

[17] The Woodward–Hoffmann theory does explain nicely the total absence of any *a priori* energetically favorable cycloreversion of **1–3** to thiocarbonyl ylide and acetylenic ester; the allowed *supra–antara* geometry for photochemical cycloreversion is unattainable preventing this reaction. A search of the literature on Δ^3-unsaturated sulfur containing five-membered heterocycles indicates that similar considerations may obtain in some strikingly dichotomous thermal and photochemical reactions. For example: (a) R. M. Kellogg and S. Wassenaar, *Tetrahedron Lett.*, 1987 (1970) [subsequently also reported by D. H. R. Barton and B. J. Willis, *Chem. Commun.*, 1225 (1970)] observed that Δ^3-1,3,4-thiadiazolines decompose thermally to N_2 and thiocarbonyl ylides and photochemically to azines and singlet sulfur (W. L. Prins and R. M. Kellogg, work in progress); (b) R. W. Hoffmann and H. J. Luthardt (*Chem. Ber.*, **101**, 3861 (1968)) observed that Δ^3-1,3,4-oxadiazolines thermally give N_2 and carbonyl ylides but photochemically give (likely) a carbene and diazo compound; (c) H. H. Inhoffen, R. Jonas, H. Kröshe, and U. Eder (*Justus Liebigs Ann. Chem.*, **694**, 19 (1966)) found that Δ^3-1,3,4-thiadiazoline 1,1-dioxides lose N_2 and SO_2 pyrolytically but give a ketazine and SO_2 photochemically.

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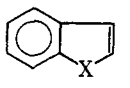
The Isolation of Isobenzofuran, a Stable but Highly Reactive Molecule

Sir:

The series of π excessive heterocyclic compounds containing a single heteroatom and isoelectronic with naphthalene falls distinctly into two classes.[1] The parent compounds in the so-called "normal" series[2] (**1**: X = O; benzofuran; X = S, benzothiophene; and X = NH, indole) are well known and quite stable, whereas the isoconjugate isomers (**2**: X = O, isobenzofuran; X = S, isothianaphthalene; and X = NH, isoindole), with the exception of isothianaphthalene,[3] have resisted isolation although they are known as transient reaction intermediates.[4,5] Dewar and his coworkers[2] have recently reported the results of a series of calculations, employing the semiempirical SCF–MO π approximation method, which indicate that isobenzofuran is practically devoid of aromatic character (E_R = 2.4 kcal/mol)[6] and predict, on the basis



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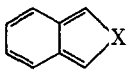

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[1] For a definition of π excessive, as well as work on the related 10π-azulene system, see A. G. Anderson, Jr., and D. M. Forkey, *J. Amer. Chem. Soc.*, **91**, 924 (1969).

[2] M. J. S. Dewar, A. J. Harget, N. Trinajstic, and S. D. Worley, *Tetrahedron*, **26**, 4505 (1970).

[3] (a) R. Mayer, H. Kleinert, S. Richter, and K. Gewald, *J. Prakt. Chem.*, 20, 244 (1963); (b) M. P. Cava and N. M. Pollack, *J. Amer. Chem. Soc.*, **88**, 4112 (1966).

[4] Isobenzofuran: (a) L. F. Fieser and M. J. Haddadin, *Can. J. Chem.*, **43**, 1599 (1965); (b) R. McCulloch, A. R. Rye, and D. Wege, *Tetrahedron Lett.*, 5231 (1969); (c) W. S. Wilson and R. N. Warrener, *ibid.*, 5203 (1970).

[5] Isoindole: R. Kreher and J. Seubert, *Z. Naturforsch. B*, **20**, 75 (1965).

[6] These calculations predict that isoindole should be more stable (E_R = 11.6 kcal/mol); this may account for the increased stability of N-substituted isoindoles.[7] The parent compound, however, has only been isolated as its Diels–Alder adduct with maleic anhydride or *N*-phenylmaleimide.[5]