the alkyl amide derivatives **1c** and **2c** with those of aryl alkylamine derivatives **1a,b** and **2a,b** offer little evidence to support such a hypothesis.

The sign of the Cotton effect for the *cis*-vinyl amide derivatives is opposite to that of the dimedone derivatives of the same optically active amines. This was intimated in the work of Potapov[7] with optically active amine Schiff base derivatives of 1-arylpropane-1,3-dione. In that case, both *cis* and *trans* forms were isolated and found to exhibit specific rotations of differing sign between 400 and 500 $m\mu$. In solution, mutarotation was observed resulting in an equilibrium of *cis* and *trans* forms. Earlier studies by Dudek and Volpp[8] have pointed out the importance of the terminal methyl group in this system in stabilizing the *cis*-vinyl amide form. With compounds **1** and **2** (**a**–**d**) no evidence was obtained for the presence of the *trans*-vinyl amide isomer in solution.

[7] V. M. Potapov, *Tetrahedron*, 23, 4357 (1967).

[8] G. O. Dudek and G. P. Volpp, *J. Am. Chem. Soc.*, 85, 2697 (1963).

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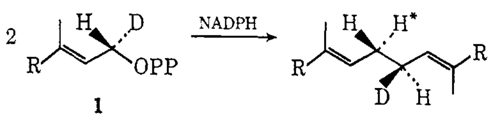
An *in Vitro* Model for the Enzymatic Coupling of Farnesol

Sir:

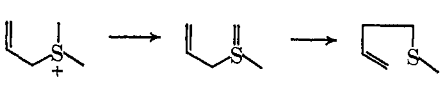
The enzymatic coupling of farnesol pyrophosphate to yield the hydrocarbon squalene has received considerable study,[1] resulting in a detailed description of the stereochemical relationships of the starting material and product, as expressed by the conversion **1** to **2** (R = geranyl-CH_2–).



1 **2**

Thus a hydrogen atom is lost from the terminus of one unit, being replaced stereospecifically by hydrogen from the dihydronicotinamide coenzyme, while the other unit undergoes an inversion of configuration at C-1 during the coupling process. Three mechanisms have been considered for this process,[1,2] but the published experimental work does not yet allow an unequivocal decision to be made concerning the mechanism, one group favoring a pathway involving a sulfur ylide[3] and another investigator providing evidence for a cyclopropane-containing intermediate.[4] More recently it has been suggested that the formation of phytoene, the precursor of the carotenoids, proceeds by a coupling mechanism similar to that operative in the squalene case.[5]

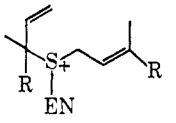
We[6] and others[7,8] have independently observed a very facile rearrangement of sulfonium ylides, which may be expressed by structures **3**–**5**. This reaction involves



3 **4** **5**

a concerted rearrangement of six electrons and is apparently driven by the formal valence change of sulfur from four to two. Such processes have been described in many places in the earlier literature[6] and proceed in a wide variety of molecular environments, even allowing substitution of heteroatoms into the cyclic array of ylide **4**. The recognition and facility of this process induced us to test whether it would be a chemically feasible method of coupling two farnesol-like molecules, and we report here the successful conclusion of these experiments.

On the assumption that the enzymatic coupling process involved a thiol we deduced that the linking of two farnesyl pyrophosphates to such a function might occur in the unsymmetrical sense, exemplified by salt **6** (R = geranyl-CH_2–). Therefore we prepared sulfide **7**[9]



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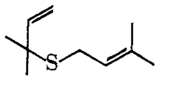

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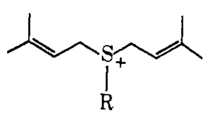
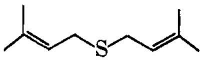


8

and carried out alkylations of this species. Our usual procedure[6] (triethyloxonium fluoroborate in dichloromethane), however, led exclusively to the rearranged salt **8** (R = C_2H_5),[6] and so we investigated this reaction by nmr. From −30° to room temperature sulfide **7** is readily isomerized to its symmetrical isomer **9**[6] by both Lewis acids (boron trifluoride ether) and protonic acids (trifluoroacetic acid), and this isomerization is faster than the alkylation, hence the production of **8**.

However, by using the less hindered reagent, trimethyloxonium fluoroborate in nitromethane,[10] alkylation was rapid at −20° and led to the required salt **10** (nmr (deuteriochloroform, −20°),[11] δ 1.73–1.86 (12 H, 4-CH_3), 2.69 (3 H, -SCH_3), 3.68–4.15 (2 H, multiplet, S-CH_2–), 5.38 (1 H, triplet, olefinic, J = 8 cps), 5.83 (2 H, vinyl, multiplet), 6.15 (1 H, quartet, vinyl, J_1 = 10, J_2 = 15 cps)) recovered by precipitation with precooled ether. This compound was reasonably stable up to 5° but at +15° was gradually isomerized into **8** (R = CH_3), however at a rate much slower than the



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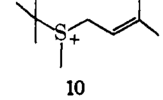

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[1] J. W. Cornforth, R. H. Cornforth, C. Donninger, and G. Popjak, *Proc. Roy. Soc.* (London), **B163**, 492, 1966; J. W. Cornforth and G. Ryback, *Ann. Rept. Progr. Chem.*, **62**, 428 (1965); R. B. Clayton, *Quart. Rev.* (London), **19**, 168 (1965); I. D. Frantz and G. J. Schroepfer, *Ann. Rev. Biochem.*, **36**, 691 (1967).

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[4] H. C. Rilling, *J. Biol. Chem.*, **241**, 3233 (1966).

[5] R. J. H. Williams, G. Britton, J. M. Charlton, and T. W. Goodwin, *Biochem. J.*, **104**, 767 (1967).

[6] J. E. Baldwin, R. E. Hackler, and D. P. Kelly, *Chem. Commun.*, 537, 538 (1968).

[7] R. B. Bates and D. Feld, *Tetrahedron Letters*, 417 (1968).

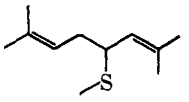
[8] G. M. Blackburn, W. D. Ollis, J. D. Plackett, C. Smith, and I. O. Sutherland, *Chem. Commun.*, 186 (1968).

[9] C. G. Moore and B. R. Trego, *Tetrahedron*, 18, 205 (1962).

[10] This homogeneous system was first brought to our notice by Dr. R. A. Olofson.

[11] All chemical shift data are expressed relative to tetramethylsilane, and spectra were obtained at room temperature and 60 Mc, unless otherwise stated.

original sulfide isomerization. Treatment of salt **10** with *n*-butyllithium at -30°[7] gave the expected rearrangement product **11**[12] (bp 94° (12 mm); $n^{24.5}$D 1.4918; nmr (carbon tetrachloride), δ 1.61–1.77 (12 H, four CH_3), 1.91 (3 H, SCH_3), 2.16 (2 H, multiplet, $-CH_2-$), 330 (1 H, multiplet, $>CHS-$, $J_1 = 10$, $J_2 = 8$, $J_3 = 6.5$ cps), 5.08 (2 H, multiplet, olefinic)), reduced by sodium in liquid ammonia[13] to the squalene-like hydrocarbon **12** (bp 169° (740 mm); n^{24}D 1.4490; nmr (carbon tetrachloride), δ 1.58 (6 H, two CH_3), 1.67 (6 H, two CH_3), 1.98 (4 H, multiplet, $-CH_2-$), 5.08 (2 H, multiplet, olefinic)), along with some 19% of the double bond isomer **13** (nmr (carbon tetrachloride), δ 0.94 (6 H, two CH_3, $J = 6.5$ cps), 1.58 (3 H, one CH_3), 1.68 (3 H, one CH_3), 2.63 (2 H, multiplet, $-CH_2-$), 4.90–5.30 (3 H, multiplet, vinylic)). The homogeneous hydrocarbon **12**, purified by gas–liquid partition chromatography,[14] was identical in all spectroscopic and gas–liquid partition chromatographic properties with those of an authentic sample.[15]



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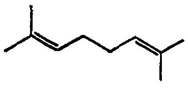

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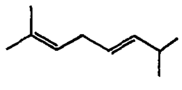

13

These results confirm the chemical validity of the postulated mechanism[16] and lead in general to a simple procedure for coupling allyl units in the tail-to-tail manner,[17] since the unsymmetrical sulfides are readily available from the corresponding disulfides.[9]

Acknowledgments. We are indebted to Eli Lilly and Company, Indianapolis, Ind., for their generous financial support. One of us (R. E. H.) wishes to thank the Sun Oil Company for a fellowship.

[12] Most runs gave material contaminated (15%) by the isomer resulting from rearrangement of the salt (8, R = CH_3). These two sulfides were separated by preparative gas–liquid partition chromatography.

[13] R. C. Krug and S. Tocker, *J. Org. Chem.*, **20**, 1 (1955). In our hands this is the preferred desulfurization procedure, since the more usual Raney nickel gave complex mixtures on reaction with allylic sulfides.

[14] All gas–liquid partition chromatographic separations were conducted on a 20 ft × 3/8 in. column of SE-30 on Chromosorb W (40–60).

[15] Repetition of the literature procedures for olefin **12** [*e.g.*, P. G. Stevens and S. C. Spalding, *J. Am. Chem. Soc.*, **71**, 1687 (1949)] involving dehydration of 2,7-dimethyloctane-2,7-diol gave mixtures of 1,6- and 2,6-dienes (nmr) which we were unable to separate. However, the Grignard coupling procedure [H. Staudinger, W. Kreis, and W. Schilt, *Helv. Chim. Acta*, 5, 743 (1922)] yielded a separable mixture of dienes.

[16] Nothing is yet known of the stereochemistry of the various centers created in such reactions.

[17] Coupling of allyl units in a tail-to-tail manner has also been described by K. B. Sharpless, R. P. Hanzlik, and E. E. van Tamelen, *J. Am. Chem. Soc.*, **90**, 209 (1968).

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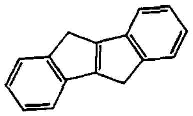
Tests of the Singlet Mechanism for *cis–trans* Photoisomerization of the Stilbenes

Sir:

The mechanism proposed for the direct photoisomerization of the perhydro- and perdeuteriostilbenes involves rotation about the central bond in the S^1 state and decay from a common twisted singlet state.[1] Intersystem crossing to the triplet states is considered inefficient,[2] and the only process competing with twisting about the central bond from *trans* S^1 states is fluorescence. The requirement, that inhibition of rotation about the central bond results in a corresponding increase in the fluorescence quantum yield, is a consequence of this mechanism. The following concerns tests of this requirement.

An electronic model of *trans*-stilbene which is restricted to a planar configuration is indeno[2,1-*a*]indene (**1**). **1** was prepared from ethyl phenylacetate using a modification of the available synthesis.[3–5] The ultraviolet absorption spectrum of **1** provides strong evidence that this molecule is a good electronic model for *trans*-stilbene. The fluorescence quantum yield, Φ_F, of **1** was determined using *p*-terphenyl and sodium salicylate as standards.[6] Using Berlman's value of 0.87 for the fluorescence quantum yield of *p*-terphenyl at room temperature in the presence of air,[8] the Φ_F of **1** at 295°K is found to be 0.94. Using Weber and Teale's value of 0.28 for Φ_F of sodium salicylate,[9] the Φ_F of **1** at 295°K is found to be 1.04.[10] In agreement with these observations, the fluorescence quantum yield of **1** is *temperature independent* in the range 301–77°K.[11] These findings, which contrast the observations with *trans*-stilbene,[12–14] are in agreement with the singlet mechanism for stilbene photoisomerization.



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Also in accord with the singlet mechanism are the recent findings showing $S^1 \rightarrow T$ intersystem crossing to be inefficient for 1,2,3-triphenylcyclopropene (**2**)[15] and 1,2-diphenylcyclobutene (**3**).[16] In the latter case, Φ_F was shown to approach 1.0 at room temperature.[16]

The significance of the above observations lies in that a requirement of the singlet mechanism is fully realized.

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[1] J. Saltiel, *J. Am. Chem. Soc.*, 89, 1037 (1967).

[2] J. Saltiel, E. D. Megarity, and K. G. Kneipp, *ibid.*, 88, 2336 (1966).

[3] K. Brand and K. O. Müller, *Ber.*, **55**, 601 (1922).

[4] S. Wawzonek, *J. Am. Chem. Soc.*, **62**, 745 (1940).

[5] C. T. Blood and R. P. Linstead, *J. Chem. Soc.*, 2263 (1952).

[6] The apparatus used for the fluorescence studies has been described.[7] Degassed solutions of **1** in methylcyclohexane–3-methylpentane (6:1) were employed. *p*-Terphenyl solutions were not degassed, and ethanol was used as solvent for sodium salicylate. *trans*-Stilbene and **1** used in this work were zone refined.

[7] (a) J. Eisinger, M. Gueron, and R. G. Shulman, "Advances in Biological and Medical Physics," Academic Press, New York, N. Y., 1967; (b) J. Eisinger, to be published.

[8] I. B. Berlman, "Handbook of Fluorescence Spectra of Aromatic Molecules," Academic Press, New York, N. Y., 1965, p 138.

[9] G. Weber and R. W. J. Teale, *Trans. Faraday Soc.*, **54**, 640, (1958).

[10] Our independent comparison of sodium salicylate and *p*-terphenyl fluorescence quantum yields gives 0.26 for the quantum yield of sodium salicylate if we assume Berlman's value for *p*-terphenyl.

[11] The estimated uncertainty in the relative fluorescence of **1** as a function of temperature is less than ±3%. No phosphorescence could be detected from **1** within this temperature range.

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[13] S. Malkin and E. Fischer, *J. Phys. Chem.*, 68, 1153 (1964).

[14] D. Gegiou, K. A. Muszkat, and E. Fischer, *J. Am. Chem. Soc.*, **90**, 12 (1968).

[15] C. D. DeBoer and R. Breslow, *Tetrahedron Letters*, 1033 (1967).

[16] C. D. DeBoer and R. H. Schlessinger, *J. Am. Chem. Soc.*, **90**, 803 (1968).