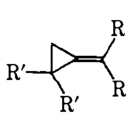
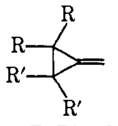
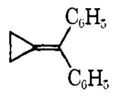
equilibrium mixture of **1a** and **2** in which a ratio of the integrated areas for the vinyl and cyclopropyl absorptions of 1.04:1.00 is established. A quantitative evaluation of the dependence upon temperature of the rate of the equilibration results in the expression log $(k_1 + k_{-1}) = 10.77 - (22{,}800/2.303RT)$.



1a, R = D; R' = C_6H_5
b, R = H; R' = C_6H_5



2, R = D; R' = C_6H_5



3

The remarkably facile exchange[9] of the vinylic and allylic methylene groups of **1a** occurs to the exclusion of formation of **3**,[11] which is anticipated to be thermodynamically the more stable isomer.[12] Attempts to set **1b** and **3** into equilibrium fail even under conditions considerably more drastic than those required for the degenerate isomerization. Thus, heating of **1b** for 9.5 hr at 140°, the temperature at which an irreversible rearrangement to 2-methyl-3-phenylindene (**4**) assumes kinetic significance,[13] produces no **3** (as little as 5% could have been detected). Approach of the equilibrium from the other side is equally unsuccessful; isomer **3** is stable up to 190°, at which temperature it rearranges to 1-phenyl-3,4-dihydronaphthalene (**5**),[14] with neither **1b** nor **4** being detectable.

The observation that no more than 5% of **3** is formed under the conditions stated, coupled with the reasonable assumption that the preexponential factor for the hypothetical first-order isomerization of **1b** to **3** would be at least as great as that for the degenerate isomerization, allows the conclusion that the energy of activation for the former process is at least 6.5 kcal/mol greater than that of the latter reaction. This difference represents a conservative estimate of the selectivity accorded to the methylenecyclopropane rearrangement by the phenyl groups.

The fundamental importance of the phenyl substituents in the isomerization also is evident in the magnitude of the activation parameters for the interconversion of **1a** and **2** ($\Delta H^{\ddagger}_{52^\circ} = 22.1$ kcal/mol, $\Delta S^{\ddagger}_{52^\circ} = -11.5$ eu) as compared to those calculated from Chesick's data[3] on the equilibration of 2-methylmethylenecyclopropane and ethylidenecyclopropane ($\Delta H^{\ddagger}_{52^\circ} = 39.8$ kcal/mol, $\Delta S^{\ddagger}_{52^\circ} = 3.2$ eu). The negative entropy of activation for the isomerization can be associated, at least in part, with the requirement of a specific orientation of the phenyl rings in order to induce cleavage of the ring. The low enthalpy of activation tempts interpretation as requiring a concerted reaction mechanism, but the value can, in fact, be shown to be consistent with a stepwise process as well. This is accomplished by first noting that a decrease of *ca.* 18 kcal/mol in the dissociation energy of a carbon–carbon bond, cleavage of which generates a benzhydryl radical, is anticipated.[15] If the energy of the transition state for bond cleavage reflects a major portion of this decrease, as well as most of the stabilization available from release of ring strain and from allylic delocalization, factors evaluated previously,[3] a minimum enthalpy of activation of 19–22 kcal/mol can be derived.[17]

Whether the methylenecyclopropane rearrangement is characterized as a stepwise or a concerted process, the proposal that electron delocalization involving substituents is important in defining the energy of the transition state for rearrangement accounts most economically for the positional selectivity noted here.

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(9) It is of interest to note that a similar exchange through a methylenecyclopropane rearrangement is not detectable when the *exo*-carbon atom of **1** is substituted with either one or two methyl groups.[10] It is likely that methyl–phenyl interactions in the rearrangement products (**2**, R' = C_6H_5, R = R = CH_3 or R = CH_3, R = H) markedly destabilize these isomers so that their concentrations at equilibrium are negligible.

(10) M. Jones, Jr., and M. E. Hendrick, unpublished results.

(11) Prepared according to the procedure of K. Sisido and K. Utimoto, *Tetrahedron Lett.*, 3267 (1966).

(12) The expectation that **3** would be favored thermodynamically is supported by the observation that fluorenylidenecyclopropane is formed irreversibly upon thermolysis of 2-methylenespiro[cyclopropane-1,9'-fluorene], the product of addition of fluorenylidene to allene.[10]

(13) M. Jones, Jr., M. E. Hendrick, J. C. Gilbert, and J. R. Butler, unpublished results.

(14) Identified by comparison of its ir and nmr spectra with those of an authentic specimen synthesized according to the method of H. Christol, C. Martin, and M. Mousseron, *Bull. Soc. Chim. Fr.*, 1696 (1960).

(15) The decrease in the carbon–carbon bond dissociation energy afforded by the benzhydryl group can be estimated in the following way. The difference in the dissociation energies of the benzylic bonds of phenylacetic acid (55 kcal/mol) and diphenylacetic acid (52 kcal/mol) approximately reflects the energy difference expected upon formation of a primary benzylic *vs.* a secondary benzylic radical.[16] Thus, the stabilization available from delocalization at the transition state for bond cleavage is about the same whether one or two phenyl groups is present. The magnitude of benzylic stabilization is estimated at *ca.* 18 kcal/mol on the basis of the dissociation energies for the carbon–carbon bonds of butane (87 kcal/mol, C_2–C_3 bond) and *n*-propylbenzene (69 kcal/mol, benzylic bond).[16]

(16) J. A. Kerr, *Chem. Rev.*, **66**, 465 (1966).

(17) A slight decrease in this predicted value might result if buttressing effects present in **1** are relieved by ring opening.

(18) NDEA Title IV Fellow, 1967–1970.

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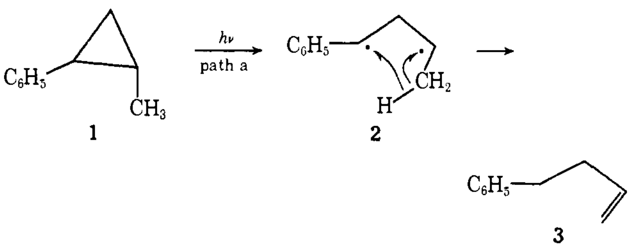
The Photoisomerizations of 2-Methylphenylcyclopropanes. Deuterium Labeling

Sir:

The photoisomerizations of various 2-methylphenylcyclopropanes to 4-phenyl-1-butenes have been described[1,2] and the reaction appears to be a common one for phenylcyclopropanes substituted in this manner. Mechanistic speculation has centered on the intermediacy of diradical **2** which would afford the observed product *via* migration of a methyl hydrogen to the benzylic position. An alternate mechanism, involving initial hydrogen migration to the *ortho* position of the benzene ring, followed by rearomatization of the intermediate tetraene **4**, has also been suggested. The latter



1 **2** **3**

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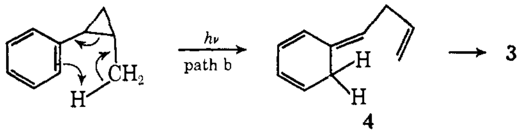
(1) H. Kristinsson and G. W. Griffin, *J. Amer. Chem. Soc.*, **88**, 378 (1966).

(2) H. Kristinsson and G. W. Griffin, *Tetrahedron Lett.*, 3259 (1966).

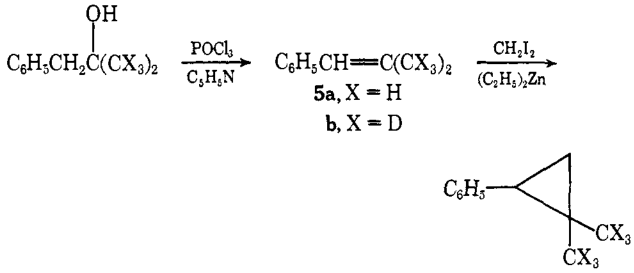
case is of interest since the initial step would represent a novel photochemical 1,5-homocyclic hydrogen migra-



4

tion[3] whereas the former, if concerted, would be an example of a $\sigma^2 + \sigma^2$ photochemical cycloaddition.[4]

We wish to report the results of a tracer experiment which clearly excludes one of these mechanistic possibilities. Our study is based on the fact that the methylenecyclohexadiene moiety in the hypothetical intermediate **4** has a symmetry plane such that the hydrogen which has migrated from the methyl group and the original aromatic hydrogen become indistinguishable. Subsequent migration of one of the methylene hydrogens to afford **3** should take place regardlesss of the origin of the migrating hydrogen. Since path a must result in the transfer of a methyl hydrogen to the benzylic position, a suitably labeled starting material can provide mechanistic information. The compound chosen for this study was 2,2-dimethylphenylcyclopropane (**6a**) and the synthesis of the required labeled material **6b** is outlined below.



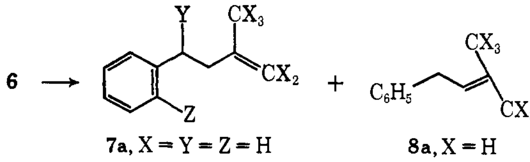
$$\mathrm{C_6H_5CH_2\overset{OH}{\overset{|}{C}}(CX_3)_2 \xrightarrow[C_5H_5N]{POCl_3} C_6H_5CH{=}C(CX_3)_2 \xrightarrow[(C_2H_5)_2Zn]{CH_2I_2}}$$

5a, X = H
b, X = D

6a, X = H
b, X = D

Phosphorus oxychloride–pyridine dehydration of the alcohol obtained from benzylmagnesium chloride and acetone-d_6 afforded a 50% yield of β,β-dimethyl-d_6-styrene (**5b**) which could be easily separated from the accompanying nonconjugated olefin by preparative glpc. Although normal Simmons–Smith conditions are ineffective in this case, treatment of **5b** with diiodomethane in the presence of diethylzinc[5] gave **6b** in 75% yield. The infrared spectrum of **6b** showed pertinent maxima at 2070 and 2205 cm^{-1}. The nmr spectrum consisted solely of a signal ascribed to aromatic protons at τ 2.85 and two multiplets at τ 8.17 and 9.29 due to benzylic and nonbenzylic cyclopropyl protons in the ratio 5:1:2. The methyl resonances at τ 8.80 and 9.22 present in the nmr spectrum of **6a** were absent. The mass spectrum of **6b** showed its parent peak at *m/e* 152.[6]

Irradiation of a cyclohexane solution of **6a** proceeded to give the expected 2-methyl-4-phenyl-1-butene (**7a**)[2] in addition to 2-methyl-4-phenyl-2-butene (**8a**), a previously unreported product.[7,8] In a similar manner irradiation of **6b** afforded the major product **7** whose infrared spectrum showed pertinent maxima at 2300, 2225, 2190, and 2050 cm^{-1}. The mass spectrum had its parent peak at *m/e* 152.[6] The nmr spectrum was most informative



7a, X = Y = Z = H
b, X = Y = D, Z = H
c, X = Z = D, Y = H

8a, X = H
b, X = D

and showed resonances at τ 2.89 (aromatic protons), 7.33 (benzylic proton), and 7.73 (allylic protons) in the ratio 5:1:2. These data are consistent only with compound **7b**. Confirmatory evidence was obtained by alkaline permanganate oxidation of photoproduct **7b**. Mass spectral analysis of the methyl benzoate obtained on diazomethane work-up of the acid indicated that this material was >95% d_0. Since path b would lead to a ratio of **7c**/**7b** of >1 (assuming a primary kinetic isotope effect) whereas path a would result only in the formation of **7b** these experiments clearly establish the course of this reaction as one defined by following path a.[9] A more detailed description of the mechanism of these reactions must await the results of further experiments.

Acknowledgment. We are grateful to the Frederick Gardner Cottrell Fund of the Research Corporation for the partial support of this work.

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[3] The thermal analog of this reaction is well known in 2-methylvinylcyclopropanes: H. M. Frey and R. Walsh, *Chem. Rev.*, **69**, 103 (1969).

[4] For examples see: R. Hoffmann, Abstracts of the 21st Organic Chemistry Symposium of the American Chemical Society, Salt Lake City, Utah, June 1969, p 111.

[5] J. Furukawa, N. Kawabata, and J. Nishimura, *Tetrahedron*, **24**, 53 (1968). An adaptation of this method, using diethylzinc generated *in situ*, was employed.

[6] A low-voltage mass spectrum of this material indicated that it was >95% d_6.

[7] The structures of **8a** and **8b** were established by comparison of their nmr and infrared spectra with those of an authentic sample.

[8] The formation of **8b** on irradiation of **6b** indicates that **8** is a primary photoproduct resulting from 1,2-hydrogen migration and that **8** does not result from isomerization of **7**. Since the formation of **8a** and **8b** both take place without the migration of deuterium they may be used as internal standards to calculate a primary kinetic isotope effect for the formation of **7** (*i.e.*, in the initial stages of the reaction k_H/k_D = **7a**/**8a**/**7b**/**8b**). This result has been confirmed by the simultaneous irradiation of 4.9 × 10^{-3} *M* solutions of **6a** and **6b** in a "merry-go-round" apparatus. Analysis by glpc for **7a** and **7b** at low conversion gives a value of $k_H/k_D = 2.6 \pm 0.3$ for the reaction **6** → **7**.

[9] G. W. Griffin and E. Waldau have come to the same conclusion on the basis of experiments which indicate that *trans,trans*-2,3-dimethylphenylcyclopropane photoisomerizes to terminal olefin faster than *cis,-cis*-2,3-dimethylphenylcyclopropane does (G. W. Griffin and E. Waldau, personal communication).

[10] National Science Foundation Undergraduate Research Participant.

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Isolation and Characterization of an Active-Site Peptide from Triose Phosphate Isomerase[1]

Sir:

I have shown that 1-hydroxy-3-iodo-2-propanone phosphate (iodoacetol phosphate, IAP), a reagent structurally similar to the substrate dihydroxyacetone phosphate (DHAP), reacts specifically with a single, essential residue of each catalytic subunit of rabbit-muscle triose phosphate isomerase (TPI); this reaction

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[1] This research was sponsored by the U. S. Atomic Energy Commission under contract with the Union Carbide Corporation.