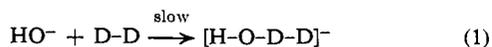
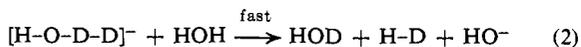


sition state. This is in accord with formation of an intermediate through addition of hydroxide ion to D_2 (eq 1)¹² and that this intermediate subsequently reacts



with water leading to isotopic exchange (eq 2).



The observed increasing slope of the $\log k-H_-$ plot with changing medium could be caused by varying solvation effects between reactants, transition state(s), and intermediate(s). It is also possible that the change of slope signifies a gradually changing mechanism, as would be the case if hydroxyl ion became gradually displaced by the dimsyl anion as the reactive basic species.^{14,15} However, it is probable that the dimsyl anion could become important only when the DMSO content is very high.

Further information concerning the mechanism of the $D_2\text{-OH}^-$ interaction will be obtained from studies now under way of kinetic isotope effects in the DMSO-water system. Also, measurements in other dipolar aprotic media such as hexamethylphosphoric triamide, which, in contrast to DMSO, does not contain exchangeable protons,¹⁶ will aid in determining the role of the aprotic component in the D_2 exchange reaction.

(12) It has been proposed¹³ that, for a process involving rate-determining addition of base to substrate, a more appropriate correlation is between $\log k$ and J_- where $J_- = H_- + \log a_{\text{H}_2\text{O}}$. In the present case this plot is also curved with an initial slope of 0.25 increasing to 0.53. Both types of plot have the underlying weakness that the indicators used to set up the acidity functions are generally quite different structurally from the reactants in the kinetic studies.

(13) K. Bowden and R. S. Cook, *J. Chem. Soc. B*, 1765 (1971).

(14) J. I. Brauman and N. J. Nelson, *J. Amer. Chem. Soc.*, **88**, 2332 (1966).

(15) E. Buncel, E. A. Symons, and A. W. Zabel, *Chem. Commun.*, 173 (1965).

(16) J. E. Hofmann, A. Schriesheim, and D. D. Rosenfeld, *J. Amer. Chem. Soc.*, **87**, 2523 (1965).

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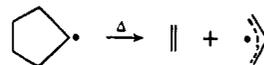
Received February 12, 1972

Stereochemistry of the Cleavage of the Cyclopentyl Radical

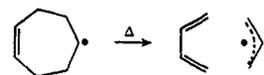
Sir:

The predictions of concertedness and of stereochemistry for cycloadditions involving neutral, cationic, or anionic π systems, as derived from orbital symmetry considerations, have thus far been borne out in each experimental test.¹ However, similar predictions for cycloadditions involving radical π systems are much more ambiguous in nature. Longuet-Higgins and Abrahamson in 1965 pointed out very succinctly that for electrocyclic reactions, and thus analogously for cycloadditions such as that shown below for the cyclopentyl radical, the ground state of the reactant corre-

(1) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Verlag Chemie, Academic Press, Weinheim/Bergstr., Germany, 1970.



lates only with an *excited* state of the products.² Boche and Szeimies, on the other hand, have only recently claimed that, in the case of the cyclopropyl \rightarrow allyl radical conversion, the need for crossing *can* be obviated and correlation may be made without the need for excited states.³ The frontier orbital approach⁴ does not really distinguish, as far as orbital symmetry is concerned, between this reaction and that involving the anion. This approach would predict *nonconcertedness* for the similar cleavage of the 4-cycloheptenyl radical,



while the Longuet-Higgins approach in comparing these two systems would be to predict that neither should be smoothly concerted, but that the cyclopentyl radical cleavage would have an energetically *more accessible* concerted pathway than would the cycloheptenyl radical cleavage.

Obviously the question remains as to *how important* these factors are which would superficially predict that *no* cycloadditions involving radical π systems are allowed.

Heretofore, no experimental measure of the concertedness of such reactions has been presented. We wish to report the results of a stereochemical study of the retrocycloaddition of a cyclopentyl radical system.

Bis(3,4-dimethylcyclopentyl)formyl peroxide (*cis-1*)⁵ and its trans isomer, *trans-1*, were utilized as the precursors for generation of low concentrations of the *cis*- or *trans*-3,4-dimethylcyclopentyl radicals, *cis-2* or *trans-2*, in the gas phase.⁶

Scheme I outlines the general sequence of product formation in the pyrolysis of *cis-1*, while Table I presents the conditions and the results of all of the pyrolyses. Note that the relative yields of the products are greatly dependent upon the pyrolysis temperature and on the concentration of peroxide on the absorbant. The cleavage process is clearly enhanced relative to disproportionation processes by increasing temperature.

The necessity for such high temperatures to observe this reaction is most likely just a result of the very short contact times under our conditions, since the activation energy for this cleavage for the parent cyclopentyl radical has been determined to be about 37 kcal/mol.⁷ *cis*- and *trans*-2-butene are found to be themselves

(2) H. C. Longuet-Higgins and E. W. Abrahamson, *J. Amer. Chem. Soc.*, **87**, 2045 (1965).

(3) G. Boche and G. Szeimies, *Angew. Chem., Int. Ed. Engl.*, **10**, 911, 912 (1971).

(4) K. Fukui and H. Fujimoto in "Mechanisms of Molecular Migrations," Vol. 2, B. S. Thyagarajan, Ed., Interscience, New York, N. Y., 1969, p 117.

(5) The isomer used was probably the all-syn species since the synthesis proceeded *via* a catalytic reduction of the ethyl ester of 3,4-dimethylcyclopent-3-ene carboxylic acid.

(6) In a typical run, 0.005 mol of **1** on Chromosorb P (10 g) was dropped in very small portions into a vertical Vycor tube, partially filled with small pieces of Vycor tubing, evacuated to ~ 0.5 mm pressure, and heated to 505°. The products were condensed in a series of traps, one at room temperature, and two successive traps cooled to -195° . Vacuum line techniques combined with glpc analyses produced estimates of product yields.

(7) R. Walsh, *Int. J. Chem. Kinet.*, **2**, 71 (1970), and references therein.

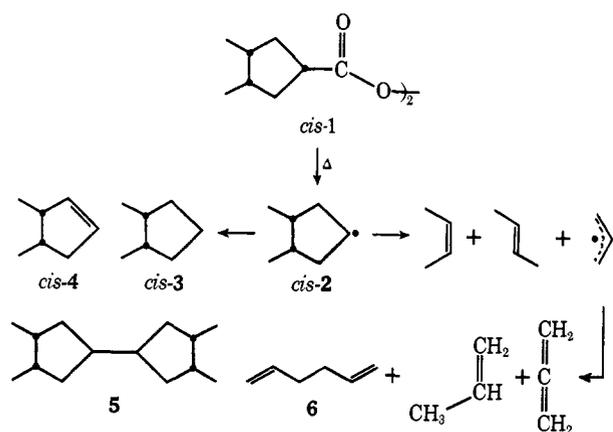
Table I. Pyrolyses of *cis*- and *trans*-Bis(3,4-dimethylcyclopentyl)formyl Peroxides (*cis*- and *trans*-1)^{a,b}

Per-oxide	Pyrol temp, °C	Chromosorb P, g	CO ₂ ^c		$\text{CH}_2=\text{C}=\text{CH}_2$				<i>trans</i> -3	<i>trans</i> -4	<i>cis</i> -3	<i>cis</i> -4			5 ^d
<i>trans</i> -1 ^e (0.005)	505	10	73.6	3.8	3.6	12.1	5.4	5.2	11.0	16.3	0.4	0.5		5.5	21.4
<i>cis</i> -1 ^f (0.005)	505	10	70.5	3.7	3.6	10.7	4.7	2.8	0.6	0.9	6.6	10.3	5.3		21.8
<i>cis</i> -1 ^f (0.010)	505	5	86.1	3.1	1.8	4.3	2.3	1.0	0.2	0.3	3.7	5.6	6.9		59.3
<i>cis</i> -1 ^f (0.005)	602	10	95.3	12.9	11.7	7.1	4.2	0.7	0.7	1.2	12.4	13.6	1.1		5.6

^a Less than 5% of volatile products are unaccounted for by glpc analysis for 505° reactions, and less than 14% for the 602°. ^b All starting materials and products were completely characterized spectroscopically and through elemental analyses, and most products were compared with authentic samples. ^c Analyzed using Ascarite as an absorbant. ^d The stereochemistry of 5 is still ambiguous. ^e 98% pure *trans* (2% *cis*). ^f 94.5% pure *cis* isomer (5.5% *trans*).

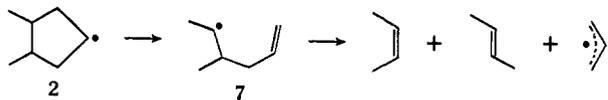
stable under the reaction conditions at 505°, but isomerize substantially at 602°.⁸

Scheme I



The conclusion that one seems compelled to reach from the data in Table I is that a partially cleaved intermediate, such as 7, must intercede in this reaction at least to a significant extent, as depicted in Scheme II.¹⁰ Under conditions (505°) where *no* isomerization

Scheme II



of the 2-butenes is found to occur, one obtains near identical ratios of *cis*- and *trans*-2-butenes from cleavage of the *cis*- or *trans*-3,4-dimethylcyclopentyl radicals. The fact that disproportionation products 3 and 4 in each case show only minimal loss of stereochemistry refutes the possibility of substantial reversibility of the initial single-bond cleavage. Thus the possibility of concurrent, but independent, geometrical isomerization and concerted cleavage seems unambiguously ruled out.

It thus appears that Longuet-Higgins' conclusion that radical electrocyclic processes should not be concerted has been borne out by experiment. It remains

(8) This is rather curious since the geometrical isomerizations of the 2-butenes have an activation energy of >60 kcal/mol.⁹

(9) (a) B. S. Rabinovitch and K. W. Michel, *J. Amer. Chem. Soc.*, **81**, 5065 (1959); (b) R. B. Kundall and T. F. Palmer, *Trans. Faraday Soc.*, **57**, 1936 (1961).

(10) No disproportionation products from 7 have yet been distinguished, although they might be present as minor constituents.

to be demonstrated whether differences in stereospecificity can be detected for more, or less, "allowed" radical processes. A point of interest in this regard is our very preliminary observation that the 4-cycloheptenyl radical, generated analogously, cleaves to butadiene in 13% yield at temperatures >650°. Indications are that this reaction is not nearly so clean as that of 1. Additional results relating to these studies and related ones will be reported in the future.

(11) Fellow of the Alfred P. Sloan Foundation, 1970–1972.

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Total Synthesis of Prostaglandins.

II. Prostaglandin E₁

Sir:

Several elegant total synthetic routes leading to prostaglandin E₁ (PGE₁) have already appeared.¹ We herein report a short novel total synthesis of PGE₁ in its naturally occurring form. The topologically obvious dissection of the prostanic acid skeleton into C₇ and C₈ side chains and a cyclopentane ring is the structural basis for our approach to the synthesis of prostaglandins. Recently we described our procedure for uniting the side chains and ring in a five-step synthesis of *dl*-15-deoxyprostaglandin E₁ from cyclopentadiene.² As an extension of this study, we have now completed the synthesis of PGE₁ (V).

The following series of reactions was used for the preparation of 3(*S*)-(α-ethoxy)ethoxy-1-lithio-1-*trans*-octene (I). The hydroalumination method of Zweifel and Whitney³ was used to convert 3(*S*)-1-octynol,⁴

(1) (a) E. J. Corey, N. H. Andersen, R. M. Carlson, J. Paust, E. Vedejs, I. Vlattas, and R. E. K. Winter, *J. Amer. Chem. Soc.*, **90**, 3245 (1968); (b) E. J. Corey, I. Vlattas, N. H. Andersen, and K. Harding, *ibid.*, **90**, 3247 (1968); (c) W. P. Schneider, U. Axen, F. H. Lincoln, J. E. Pike, and J. L. Thompson, *ibid.*, **91**, 19 (1969); (d) E. J. Corey, R. Noyori, and T. K. Schaaf, *ibid.*, **92**, 2586 (1970); and (e) D. Taub, R. D. Hoffsommer, C. H. Kuo, H. L. Slaters, Z. S. Zelawski, and N. L. Wendler, *Chem. Commun.*, 1258 (1970).

(2) Paper I in this series: C. J. Sih, R. G. Salomon, P. Price, G. Peruzzotti, and R. Sood, *J. Chem. Soc., Chem. Commun.*, 240 (1972).

(3) G. Zweifel and C. C. Whitney, *J. Amer. Chem. Soc.*, **89**, 2753 (1967).

(4) J. Fried, C. Lin, M. Mehra, W. Kao, and P. Dalven, *Ann. N. Y. Acad. Sci.*, **180**, 38 (1971).