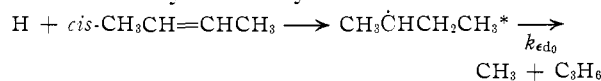
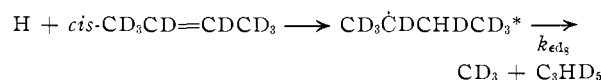


systems, at room temperature. However, the theory shows that under suitable circumstances the total magnitude of the present effect may easily equal (or even greatly exceed) the customary magnitudes of primary isotope effects. In this communication we describe some results of a study using the chemical activation technique in which this expectation is realized.

The *sec*-butyl radical system



has been well studied.<sup>3</sup> The *sec*-butyl radicals produced at 25° have excess average internal energy,  $\epsilon^+$ , with respect to the critical energy  $\epsilon_0$  for C–C rupture of ~10 kcal./mole, while according to the theory the largest isotope effects should occur when  $\epsilon \rightarrow \epsilon_0$ , *i.e.*, as  $\epsilon^+ \rightarrow 0$ . Nonetheless, the butyl radical decomposition still affords the possibility of a very large effect upon replacement of eight hydrogens by deuterium. We have studied the reaction



at 25° over a range of pressures,  $p$ . It has been shown previously<sup>3</sup> that as  $p \rightarrow 0$  the apparent experimental average rate constant  $k_a$  for decomposition has the form  $k_{a0} = \langle 1/k_e \rangle^{-1}$ , while at limitingly high pressures  $k_{a\infty} = \langle k_e \rangle$ . We find that the ratio  $k_{ad_0}/k_{ad_3}$  increases from the value  $(k_{ad_0}/k_{ad_3})_\infty = 4.0$  to an appreciably larger ratio ( $\geq 6.0$ ) for  $(k_{ad_0}/k_{ad_3})_0$ , whose limiting magnitude is unfortunately obscured in this system by experimental error. This variation with pressure may be understood readily, since the average energy of the decomposing radicals, as well as the rate constant  $k_a$ , is lower at  $p \rightarrow 0$  than it is at  $p \rightarrow \infty$ ; *i.e.*, the average value of  $\epsilon^+$  is lower at  $p \rightarrow 0$  than at  $p \rightarrow \infty$ .

Values of the preceding limiting ratios also were calculated according to the accurate quantum statistical treatments previously developed<sup>6</sup> for these chemical activation systems. The numerators and denominators of the above rate constant ratios each have the form of Eq. (1) of reference 6, with the specific collision rate  $\omega$  set at the limits  $\infty$  and 0, respectively. The radical and activated complex models were quite similar to those previously used, in which all internal rotational and vibrational degrees of freedom were taken as active.<sup>6</sup> Frequencies for the C<sub>4</sub>HD<sub>8</sub> system were estimated from the infrared data on C<sub>3</sub>D<sub>6</sub><sup>7</sup> and C<sub>3</sub>D<sub>8</sub>,<sup>8</sup> and were checked with the aid of the Teller–Redlich Product Rule. The ratios calculated for one (non-optimal) set of assumptions are:  $p =$

(5) (a) B. S. Rabinovitch, D. H. Dills, W. H. McLain and J. H. Current, *J. Chem. Phys.*, **32**, 1245 (1960); (b) J. H. Current and B. S. Rabinovitch, to be submitted. These authors describe the magnitude of non-equilibrium primary kinetic isotope effects in related systems of ethyl radicals.

(6) R. E. Harrington, B. S. Rabinovitch and R. W. Diesen, *J. Chem. Phys.*, **32**, 1245 (1960); B. S. Rabinovitch and J. H. Current, *ibid.*, **35**, 2250 (1961).

(7) (a) R. Lord and P. Venkateswarlu, *J. Opt. Soc. Am.*, **43**, 1079 (1953); (b) L. M. Sverdlov, *Prod. Acad. Sci. U.S.S.R.* (Chem. Sect.), **106**, 21 (1956) (Engl. transl.).

(8) H. L. McMurry and V. Thornton, *J. Chem. Phys.*, **19**, 1014 (1951).

$\infty$ , 4.2; and  $p = 0$ , 5.4. The agreement is quite satisfactory. The present experiments do not give a “pure” secondary effect since the average energy of the C<sub>4</sub>HD<sub>8</sub> radicals produced is actually larger than that of the C<sub>4</sub>H<sub>8</sub> radicals, *i.e.*,  $f(\epsilon)_{d_8} \neq f(\epsilon)_{d_6}$ ; this factor tends to reduce the observed effect, so that the intrinsic isotopic rate ratio at the same radical energies is even larger than the values found here.

The present low pressure secondary isotopic ratio is indeed in the conventional range of magnitudes of primary H–D isotope effects at 25°, and the ratios exceed by a factor of ~2 the largest magnitudes previously observed for C–H, C–D secondary intermolecular kinetic isotope effects.<sup>4,9</sup> At –78° the ratios will be even larger.

This study is being extended to other systems and a full account will be given. Part of this work was supported by the Office of Naval Research.

(9) K. T. Leflek, J. A. Llewellyn and R. E. Robertson, *Can. J. Chem.*, **38**, 2171 (1960); V. J. Shiner, *J. Am. Chem. Soc.*, **75**, 2925 (1953).

(10) General Electric Foundation pre-doctoral fellow.

(11) Visiting Scientist; John Simon Guggenheim Memorial Fellow, 1961–62, and Petroleum Research Fund International Award Fellow, 1961–62. N.R.C. Contribution No. 6833.

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RECEIVED MARCH 9, 1962

## RADICAL AND THERMAL REARRANGEMENT OF ISOPHORONE OXIDE<sup>1</sup>

Sir:

The paucity of intramolecular rearrangements to carbon radicals, as contrasted with the rich and varied lore of carbonium ion rearrangements, has been noted by several authors.<sup>2,3</sup> We now report instances of radical and thermal rearrangements of an  $\alpha,\beta$ -epoxy ketone, which not only supplement the well documented acid and base catalyzed rearrangements of this class of substrates, but represent examples of intramolecular, free radical, acyl group rearrangements.<sup>4,5</sup>

These transformations were first observed with 4-methyl-3,4-epoxy-2-pentanone; however, the tendency of this material to form tars resulted in the use of the less reactive isophorone oxide (I) for detailed investigation. When heated with radical initiators, I was transformed into a mixture of

(1) This investigation was supported in part by a research grant A-4936 from the National Institutes of Health, Arthritis and Metabolic Diseases Division.

(2) D. J. Cram, “Steric Effects in Organic Chemistry,” Edited by M. S. Newman, John Wiley and Sons, Inc., New York, N. Y., Chapter 5, p. 283.

(3) J. A. Berson, C. J. Olsen and J. S. Walia, *J. Am. Chem. Soc.*, **82**, 5000 (1960). References (2) and (7) of this communication constitute a useful record of prior investigations.

(4) D. H. R. Barton, *et al.*, *J. Am. Chem. Soc.*, **83**, 4481 (1961), have reported the photolytic conversion of steroid 11-hydroxy-17-keto nitrite esters to 18-nor-D-homo- $\Delta^{13(17\alpha)}$ -11 $\beta$ -hydroxy-17-keto steroids.

(5) Previous reports of thermal rearrangements of  $\alpha,\beta$ -epoxy ketones have not excluded acid catalyzed rearrangement induced by acidic decomposition products, and present no evidence suggesting a radical mechanism: J. Reese, *Ber.*, **75**, 384 (1942); G. V. Pigulevsky and I. K. Mironova, *J. Gen. Chem., U.S.S.R.*, (English translation), **27**, 1184 (1957); H. O. House and R. L. Wasson, *J. Am. Chem. Soc.*, **78**, 4394 (1956).

1,5,5-trimethyl-2-hydroxycyclohexene-3-one (II) and 2,4,4-trimethylcyclopentanone (III). The major product was always the diosphenol II, but the ratio of II/III varied from 4 to 1.9 as the temperature of the reaction was increased from 215 to 255°. Acid catalyzed rearrangement of I by the diosphenol II does not occur, and although carboxylic acids (*e.g.*, acetic and benzoic acid) catalyze rearrangement at 235°, the amount of acid (0.5% acetic acid) conceivably formed from the oxygen of the peroxide initiator was found to induce only 7% rearrangement in 6 hr. Furthermore, the ratio of II/III in the products (5.5) differs significantly from that observed for the radical process at the same temperature (3.3).

TABLE I  
REACTIONS<sup>a</sup> OF ISOPHORONE OXIDE<sup>b</sup>

Additives <sup>c</sup>	Temp., °C.	Time, hr.	Extent of reaction, %
...	200	16	None
<i>tert</i> -C <sub>4</sub> H <sub>9</sub> O <sub>2</sub> H	200	16	5
<i>tert</i> -C <sub>4</sub> H <sub>9</sub> (O <sub>2</sub> ) <sub>2</sub> (20%)	150	8.0	1
...	235	6.0	None
<i>tert</i> -C <sub>4</sub> H <sub>9</sub> O <sub>2</sub> H	235	6.0	28
<i>tert</i> -C <sub>4</sub> H <sub>9</sub> O <sub>2</sub> H, surface area doubled	235	6.0	26
C <sub>6</sub> H <sub>5</sub> OCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> <sup>e</sup>	235	6.0	8
<i>p</i> -C <sub>6</sub> H <sub>5</sub> -C <sub>6</sub> H <sub>5</sub> OCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	235	6.0	18
C <sub>2</sub> Cl <sub>6</sub> <sup>f</sup>	235	6.0	100 <sup>g</sup>
IV	235	6.0	90
II (3%)	235	6.0	None
CH <sub>3</sub> CO <sub>2</sub> H (0.5%)	235	6.0	7
...	235	7.5	5
...	235	12	100
C <sub>6</sub> H <sub>5</sub> NHCH <sub>3</sub>	235	12	None
(CH <sub>2</sub> ) <sub>4</sub> S	235	12	None
<i>m</i> -C <sub>6</sub> H <sub>4</sub> (NO <sub>2</sub> ) <sub>2</sub>	235	12	14
10 <sup>2</sup> increase in surface area	235	6.0	80 <sup>h</sup>

<sup>a</sup> Carefully degassed mixtures were heated in sealed tubes under a nitrogen atmosphere. <sup>b</sup> Neat, peroxide free samples of epoxide were used. <sup>c</sup> Additives were present in about 1% amounts unless stated otherwise. <sup>d</sup> The reaction products were II, III, and CO, and were resolved by vapor phase chromatography on a 2-m., 30% silicone column. The error is roughly 10% of the reported value. <sup>e</sup> Benzyl phenyl ether gives benzyl radicals at temperatures near 250°. W. A. Waters, "The Chemistry of Free Radicals," Oxford University Press, New York, N. Y., 1946, p. 171. <sup>f</sup> Hexachloroethane has been used to initiate the polymerization of isobutyric acid and ethene at 238–250°: J. R. Roland and J. Harmon, U. S. Patent 2,433,015 (1947). <sup>g</sup> Tarry materials are formed. The extent of reaction is determined only by analysis of the volatile portion.

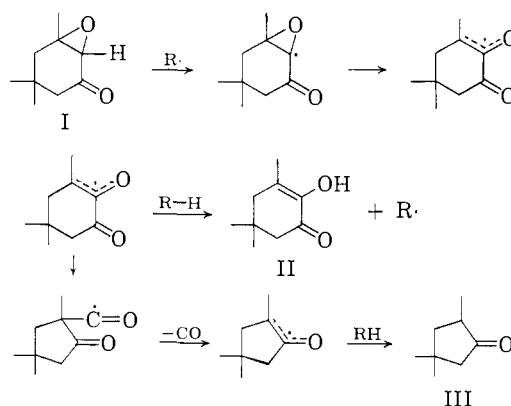
The evidence presented in the table supports a radical chain mechanism<sup>6</sup> such as the one suggested in Chart I.<sup>7</sup> The first two steps of this

(6) The failure of a variety of peroxide and azo initiators to promote reaction at temperatures below 200° is unusual, but does not necessarily contradict a radical mechanism. The high temperatures required for reaction may instead reflect a high activation energy for the removal of a hydrogen atom from an oxirane ring. It is interesting to note that base catalyzed exchange of the oxirane hydrogen in piperitone oxide occurs only with extreme difficulty: H. O. House and W. F. Gilmore, *J. Am. Chem. Soc.*, **83**, 3972 (1961).

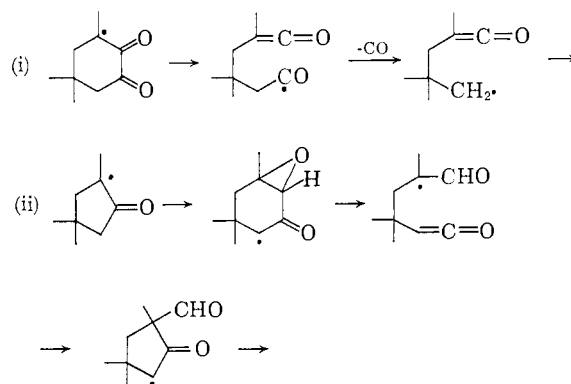
(7) This mechanism is not unique and a referee has offered sequence (i) as an alternative to the acyl group rearrangement. Since a different carbon atom is lost as CO in these two proposals, we plan to eliminate one of them by investigating the course of the reaction using isophorone prepared from acetone-2-C<sup>14</sup>. Another rationale for the formation of

mechanism are completely analogous to the rationale recently offered by Gritter and Wallace<sup>8</sup> to account for the products obtained from radical initiated reactions of propylene oxide. The last steps involve a partitioning of the resulting radical intermediate between hydrogen abstraction and acyl group migration; the former produces II, while the latter leads *via* decarbonylation and hydrogen abstraction to III.<sup>9</sup>

CHART I  
RADICAL CHAIN MECHANISM



In view of the above discussion, we were surprised to find that a neat sample of I was quantitatively converted to a 3:1 mixture of II and III, when heated in an inert atmosphere for 12 hr. at 235°. This transformation was completely inhibited by traces of *N*-methylaniline or tetrahydrothiophene and partially inhibited by nitrobenzene, suggesting that a very slow thermal process was producing species capable of initiating the radical chain. In order to demonstrate that an independent thermal reaction of I could actually occur,<sup>10</sup> dilute decalin solutions of I containing an excess of methylaniline were shown to undergo apparent first order de-III is presented in equation (ii). We have attempted to trap ketene intermediates by effecting the radical reaction in the presence of water.



Not only have no carboxylic acids been formed, but the ratio of II/III has remained 3.2 (after correcting for the amount of reaction induced by water itself).

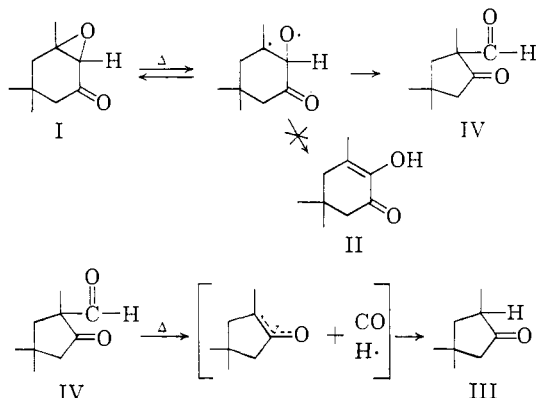
(8) R. J. Gritter and T. J. Wallace, *J. Org. Chem.*, **26**, 282 (1961).

(9) The cyclopentanone III is not a secondary rearrangement product derived from II, since prolonged (12 hr.) heating of the latter with peroxide initiators produced no change.

(10) The possibility that traces of oxygen baked from the walls of the vial was responsible for the initiation of the radical reaction could not be overlooked.

composition at 270° yielding the cyclopentanone III as the sole product.<sup>11</sup> A rationale for this thermal reaction is offered in Chart II. The absence of II in the products contrasts strikingly

CHART II  
THERMAL MECHANISM



with its predominance in the radical process, and implies that the intermediate diradical produced by the reversible cleavage of the oxirane ring does not rearrange by a simple intramolecular hydrogen shift (Chart II). Instead, acyl group rearrangement again occurs, this time leading to the keto aldehyde IV. The subsequent thermal decarbonylation of IV easily was confirmed experimentally.<sup>12</sup> Furthermore radical initiating species are apparently produced in this process, since IV has proven to be a very efficient initiator for the radical chain reaction.

The compounds encountered in this work have all been positively identified by physical and chemical comparisons with known substances.

It is of interest to note that the photochemical transformation of I does not lead to any of the products described in this report.<sup>13</sup>

(11) This thermal transformation is apparently a complex surface reaction, since a doubling of the surface area resulted in a 115% increase in the apparent first order rate constant. The last entry in the table describes another manifestation of this surface dependency.

(12) 2-Formyl-2,4,4-trimethylcyclopentanone (IV) was prepared by the method of H. O. House and R. L. Wasson, *J. Am. Chem. Soc.*, **79**, 1488 (1957), and exhibited a straightforward first order decomposition to III at 235°.

(13) Unpublished work of C. K. Johnson and W. Reusch.

(14) Portions of this work were reported at the 140th meeting of the American Chemical Society, Chicago, Illinois, September 7, 1961.

KEDZIE CHEMICAL LABORATORY WILLIAM REUSCH<sup>14</sup>  
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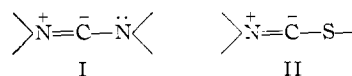
RECEIVED OCTOBER 4, 1961

#### STEPWISE ELECTRON ABSTRACTION FROM A TETRAAMINOETHYLENE

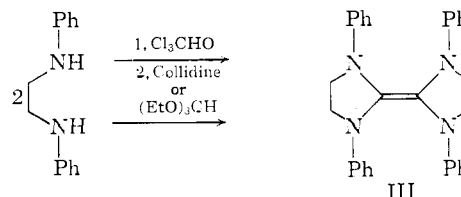
Sir:

Breslow's beautiful studies on the mechanism of thiamine action have demonstrated the remarkable facility with which zwitterions of the types I and II can be formed.<sup>1</sup> The presence of these species was revealed by their ability to undergo nucleophilic addition reactions as well as by deuterium exchange

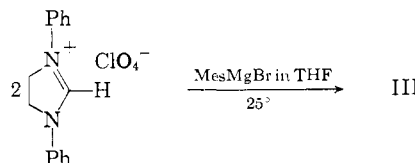
(1) R. Breslow, *J. Am. Chem. Soc.*, **79**, 1762 (1957), and subsequent papers.



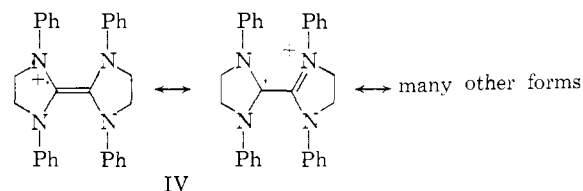
experiments. Recently Wanzlick<sup>2</sup> has succeeded in preparing the dimer (III) of a type I zwitterion by the two routes shown below.



We wish to report a new synthesis for this substance and our findings on the nature of its ready oxidation. Whereas Wanzlick's routes to III required elevated temperatures, we have learned that 1,3-diphenylimidazolium perchlorate is transformed into this compound by the action of the hindered base mesitylmagnesium bromide in tetrahydrofuran at room temperature.



The dimer III displays the intriguing property of forming violet solutions in a variety of solvents, a phenomenon attributed by Wanzlick to  $\pi$ -complex formation with the solvent. Our observation that this color developed even in such solvents as dichloromethane cast considerable doubt on this hypothesis. When shaken with degassed acetonitrile, the dimer gave a colorless solution which rapidly became violet upon exposure to air, a fact which argued for oxidation of the ethylene to the radical cation IV reminiscent of a Wurster cation. Indeed, chloroform solutions of III in the air gave e.s.r. signals which varied in strength according to the intensity of the violet color.



Solutions of IV prepared by air oxidation invariably faded a few minutes after air was excluded even when excess III was present. The further transformation of IV in air is not yet understood in detail, but it is known from Wanzlick's work<sup>2</sup> that the ultimate product of air oxidation of III is 1,3-diphenylimidazolid-2-one.

In contrast to the complex air oxidation, the action of iodine upon III proved to be clear-cut. Addition of an acetonitrile solution of iodine to a suspension of III in the same solvent led to the development of the intense violet color characteristic of IV, a color which did not disappear during two

(2) H. W. Wanzlick, *et al.*, *Angew. Chem.*, **72**, 494 (1960); *ibid.*, **73**, 493 (1961); *Ber.*, **94**, 2389 (1961).