Primary Isotope Effects in Hydrogen Atom Transfer Reactions from α-Hydroxyalkyl and Monohydropyridyl Radicals¹

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The rates of oxidation of O-d-2-butanol and N-d-3,5-dicarbethoxy-1,4-dihydro-2,6-lutidine by *tert*-butyl peroxide are slower than those of nondeuterated samples of these compounds. This isotope effect is ascribed to hydrogen atom transfer reactions of radicals derived from these species to the oxygen-oxygen linkage of the peroxide. No isotope effect was observed in the reactions of either acetyl peroxide or *tert*-butyl peracetate with the secondary alcohol or oxidation of the dihydropyridine with acetyl peroxide. A route other than hydrogen atom transfer, possibly a direct displacement or an electron transfer process, likely is operative in the reduction of the peroxide by the radicals derived from these compounds.

The enhanced decomposition rates of *tert*-butyl peroxide (I),³ acetyl peroxide (II),⁴ and *tert*-butyl peracetate (III),⁵ in primary and secondary alcohols has been attributed to participation of the peroxides in a chain

reaction with the α -hydroxyalkyl radical (IV) derived from the alcohol. Three modes of interaction of the alcohol-derived radical with the peroxide linkage that appear feasible are a hydrogen atom transfer reaction (eq 1), an electron transfer (eq 2), and a direct displacement (eq 3). In this study we have sought support for the hydrogen atom transfer reaction (eq 1) by deter-

$$R_{2}\dot{C}OH + R'OR' \qquad R_{2}\dot{C}OH + R'OH + (R'O) (1)$$

$$R_{2}\dot{C}OH + R'O^{-} + (R'O) (2)$$

$$R_{2}\dot{C}OH + (R'O) (2)$$

$$R_{2}COH + (R'O) (3)$$

$$R_{2}COH + (R'O) (3)$$

$$R_{2}COH + R'OH (3)$$

mining the deuterium isotope effect (if any) in the interaction of the radical derived from O-d-2-butanol (V) with these peroxides. The rates of reaction of *tert*-butyl peroxide and acetyl peroxide in the presence of 3,5-dicarbethoxy-1,4-dihydro-2,6-lutidine (VI) and its N-deuterated derivative (VII) were also measured to determine if the hydrogen atom transfer is operative in the interaction of the monohydropyridyl radical (VIII) with these peroxide linkages.⁶



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Discussion and Results

The oxidation of a secondary alcohol with *tert*-butyl peroxide (I) proceeds by the mechanism shown in eq 4-7. The decomposition rate of the peroxide is the

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$$I \longrightarrow 2(CH_3)_3 CO$$
 (4)

$$(CH_3)_3CO \cdot + R_2CHOH \xrightarrow{\kappa_3} (CH_3)_3COH + IV$$
 (5)

$$IV + I \xrightarrow{\kappa_{5}} R_{2}C = O + (CH_{3})_{3}COH + (CH_{3})_{8}CO \cdot (6)$$

$$k_{7}$$

$$(CH_{\mathfrak{d}})_{\mathfrak{d}}CO \cdot + IV \xrightarrow{\sim} (CH_{\mathfrak{d}})_{\mathfrak{d}}COH + R_{\mathfrak{d}}C=0$$
 (7)

sum of the rates of reaction 4 and 6 shown in eq 8. The

$$\frac{-\mathbf{d}[\mathbf{I}]}{\mathbf{d}t} = k_4[\mathbf{I}] + k_6[\mathbf{IV}][\mathbf{I}] \tag{8}$$

derived steady state rate law for the decomposition of the peroxide as given in eq 9 is applicable if the crosstermination process 7 is operative. The reaction is indeed first order in peroxide at a concentration ratio of alcohol-peroxide in the range of 5-1 for the first half-life of the peroxide.

$$\frac{-\mathrm{d}[\mathrm{I}]}{\mathrm{d}t} = \left[\frac{3}{4}k_4 \pm \frac{k_4}{2} \left(\frac{1}{4} + 2\frac{k_5k_6}{k_4k_7} \left[\mathrm{R_2CHOH}\right]\right)^{1/2}\right] [\mathrm{I}] \quad (9)$$

The decomposition rate of *tert*-butyl peroxide in 2-butanol containing varying amounts of the oxygendeuterated alcohol (V) (Table I) is slower in the deu-

TABLE I

RATE DATA FOR DECOMPOSITION OF *tert*-BUTYL PEROXIDE IN 2-BUTANOL AND O-d-2-BUTANOL

Initial molar			
ratio of	%	k'	Standard
alcohol-peroxide	O-d-2-Butanol	\times 10 ⁴ sec ⁻¹	deviation
4.84	0	0.454	0.009
5.07	0	0.453	0.005
5.13	0	0.458	0.014
5.26	80	0.322	0.004
4.96	80	0.313	0.002
5.01	80	0.343	0.009
5.00	90	0.297	0.006
4.87	90	0.287	0.002
5.06	90	0.288	0.002
5.01	99	0.276	0.004
5.10	99	0.277	0.007
5.07	90	0.285	0.008

terated alcohol. The reaction rates were followed through about one half-life of the peroxide minimizing

 ⁽²⁾ NASA Fellow, 1966-1969. Taken in part from the thesis submitted by A. A. K. in partial fulfillment of the requirements for the M.S. degree from the University of Kansas, 1969.

⁽³⁾ E. S. Huyser and C. J. Bredeweg, J. Amer. Chem. Soc., 86, 2401 (1964).

⁽⁴⁾ M. S. Kharasch, H. N. Friedlander, and W. H. Urry, J. Org. Chem., 14, 91 (1949).

⁽⁵⁾ C. Walling and J. C. Azar, ibid., 33, 3888 (1968).

⁽⁶⁾ E. S. Huyser, C. J. Bredeweg, and R. M. Van Scoy, J. Amer. Chem. Soc., **86**, 4148, (1964).

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the amount of exchange between the deuterated alcohol and tert-butyl alcohol produced in the reaction. The pseudo-first-order rate constants in Table I include all of the terms in the brackets of the rate law 9. Retardation of reactions 4, 5, or 6 or enhancement of reaction 7 by the deuterated alcohol would be required to account for the observed effect. The magnitude of the isotope effect $(k'_{\rm H}/k'_{\rm D})$ in the 99% deuterated alcohol is 1.63 and indicative of a primary isotope effect. Oxygenhydrogen bond rupture occurs only in eq 6 and 7. A sizable inverse isotope effect would be required to explain the observed results in terms of the termination reaction. Retardation of the reaction of the α -hydroxyalkyl radical with a peroxide linkage (reaction 6) is a more likely explanation for the observed effect. Since the reaction rate constant k_6 is a square root term in k', a closer approximation of the minimum isotope effect, assuming all other terms in the bracket are the same for both alcohols, is 1.63² or 2.66. Although the reduction of the peroxide linkage by the α -hydroxyalkyl radical is significantly exothermic (approximately 35-40 kcal/ mol), the isotope effect is indicative of extensive bond breaking of the oxygen-hydrogen bond in the transition state as would be the case if the hydrogen atom transfer (reaction 1) were operative.

$$\begin{bmatrix} \delta^+ & \delta^- \\ R_2 C - O \cdots H \cdots O \cdots O \\ & & | & | \\ & & R & R \end{bmatrix}$$

The lack of an isotope effect in the reaction of O-d-2butanol with both acetyl peroxide and *tert*-butyl peracetate (Table II) indicates that the interactions of the

 TABLE II

 RATE DATA FOR DECOMPOSITION OF ACETYL PEROXIDE (II) AND

 tert-Butyl Peracetate (III) in 2-Butanol

AND $O-d-2$ -BUTANOL (V)						
	Mole		Standard			
Alcohol	ratio	$k' imes 10^4$, sec ⁻¹	deviation			
Acetyl Peroxide (70°)						
2-Butanol	4.91	0.578	0.002			
	4.84	0.580	0.005			
	4.99	0.568	0.006			
O-d-2-Butanol	4.91	0.584	0.004			
	4.89	0.562	0.006			
	5.00	0.578	0.007			
tert-Butyl Peracetate (90°)						
2-Butanol	5.03	0,980	0.002			
	5.02	0.959	0.002			
	5.00	0.944	0.002			
O-d-2-Butanol	4.96	0.953	0.001			
	4.99	0.959	0.002			
	5.00	0.950	0.002			

 α -hydroxyalkyl radical with these peroxide linkages are not hydrogen atom transfer reactions. The direct displacement by the alcohol-derived radical on the peroxide was originally proposed to account for the reactions of alcohols with acetyl peroxide.⁴ This suggestion finds support in the reaction of ether-derived α -alkoxyalkyl radicals with acyl peroxides which yield isolable acylals as reaction products.⁷

 α -Aminoalkyl radicals having at least one nitrogenbonded hydrogen react with *tert*-butyl peroxide as evidenced by the induced decomposition of the peroxide in

(7) W. E. Cass, J. Amer. Chem. Soc., 69, 500 (1947).

primary and secondary amines.⁶ A particularly marked enhancement of the decomposition rate of *tert*-butyl peroxide was observed in the reactions with 3,5-dicarbethoxy-1,4-dihydro-2,6-lutidine (VI) which is oxidized to the corresponding pyridine derivative IX in the chain process shown in eq 10 and 11. An isotope effect is ob-

VIII + I
$$\rightarrow$$

EtO₂C \rightarrow CO₂Et + (CH₃)₃COH + (CH₃)₃CO (10)
IX (CH₃)₃CO + VI \rightarrow (CH₃)₃COH + VIII (11)

served (Table III) when the rate of reaction of the per-

TABLE III

Decomposition Rates of *tert*-Butyl Peroxide in Tetrahydrofuran Solution of Dihydropyridines VI and VII at 125° (Mole Ratio of THF-Dihydropyridine*tert*-Butyl Peroxide 36:2:1)

Compd	$k' \times 10^4$ sec ⁻¹	Standard deviation
3,5-Dicarbethoxy-1,4-dihydro-	0.636	0.028
2,6-lutidine (VI)	0.666	0.015
	0.620	0.019
1-Deuterio-3,5-dicarbethoxy-1,4-	0.407	0.006
dihydro-2,6-lutidine (VII)	0.409	0.006
	0.402	0.006

oxide with VI is compared with that of 1-deuterio-3,5dicarbethoxy-1,4-dihydro-2,6-lutidine (VII). Although both steps in the chain sequence are rapid, a considerable amount of reaction of the peroxide still occurs by the unimolecular decomposition (eq 4). Reaction with both VI and VII are first order in peroxide through the first half-life of the peroxide indicating cross termination of the chain sequence (eq 12). The derived rate law is

VIII + (CH₃)₃CO·
$$\xrightarrow{k_{12}}$$
 IX + (CH₃)₃COH (12)

$$\frac{-\mathrm{d}[\mathrm{I}]}{\mathrm{d}t} = \left[\frac{3}{4}k_4 \pm \frac{k_4}{2} \left(\frac{1}{4} + 2\frac{k_{10}k_{11}}{k_4k_{12}} \left[\mathrm{VI}\right]\right)^{1/2}\right] [\mathrm{I}] \qquad (13)$$

essentially the same as that given in eq 9, namely eq 13. The isotope effect on the observed rates of reaction of VI and VII with I is 1.58 and $k_{\rm H}/k_{\rm D}$ for reaction 10 is approximately 2.5 indicating appreciable breaking of the nitrogen-hydrogen bond in the transition state of the reaction.



The pseudo-first-order rate constants found for the acetyl peroxide oxidations of VI and VII are given in Table IV. No isotope effect was observed in this reaction which is spontaneous at room temperature but likely proceeds by a free-radical chain mechanism involving interaction of the monohydropyridyl radical VIII with peroxide.⁸ The reduction of the peroxide by

⁽⁸⁾ A more complete description of this reaction will be reported in a later publication.

Rate Data for Oxidation of VI and VII with Acetyl Peroxide in Acetonitrile at 30°

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	-initial conce	entrations		
	[Peroxide]	[Amine]		Standard
Amine	\times 10 ⁻²	$\times 10^{-4}$	$k' imes 10^4$ sec $^{-1}$	deviation
VI	2.48	1.57	0.220	0.008
	2.48	1.57	0.217	0.012
	2.48	1.57	0.218	0.012
VII	2.48	1.52	0.208	0.014
	2.48	1.52	0.214	0.017
	2.48	1.52	0.209	0.016

VIII probably does not involve breaking of the nitrogen-hydrogen bond in the transition state of the reaction and may likely be an electron-transfer process.

Experimental Section

Materials.—*tert*-Butyl peroxide (Wallace and Tiernan, Inc.) and a 25% solution of acetyl peroxide in dimethyl phthalate (Wallace and Tiernan, Inc.) were used without further purification. *tert*-Butyl peracetate (Wallace and Tiernan, Inc.) (75% perester in benzene) was purified by vacuum distillation. The following commercial reagents were distilled twice before using: 2-butanol (from sodium), tetrahydrofuran (from sodium), and acetonitrile (from phosphorous pentoxide).

3,5-Dicarbethoxy-1,4-dihydro-2,6-lutidine (VI) was prepared from acetoacetic ester, formaldehyde, and ammonia by the method of Singer and McElvain⁹ (mp 183-185°).

1-Deuterio-3,5-dicarbethoxy-1,4-dihydro-2,6-lutidine (VII) was prepared by allowing a mixture of 5 g of VI to reflux for 2 hr with 10 ml of deuterium oxide in 100 ml of dimethoxyethane. The compound was isolated and recrystallized from ethanol and the process repeated twice with fresh deuterium oxide. After the final exchange, no nitrogen-hydrogen bond could be observed in either the infrared or the nmr spectra of the material.

O-d-2-Butanol (V) was prepared by reaction of the sodium alkoxide with deuterium oxide in the following manner. Freshly distilled 2-butanol (500 ml) and sodium (20 g) cut in small pieces

(9) A. Singer and S. M. McElvain, "Organic Syntheses," Coll. Vol. II, Wiley, New York, N. Y., 1943, p 214. were placed in a 1-l. round-bottomed flask equipped with a reflux condenser. After the initial rapid reaction the mixture was heated at reflux for an additional 16 hr during which period all of the sodium reacted. Excess 2-butanol was removed under a vacuum leaving a white solid which was heated under vacuum for an additional 24 hr. Deuterium oxide (20 ml) was added to the dry solid producing a reddish brown mixture. The organic layer was distilled twice yielding *O*-d-2-butanol that by nmr analysis was 99% deuterated (30.2 g, 47% theory).

Peroxide Decomposition Rates.—The rates of reaction of *tert*butyl peroxide in 2-butanol and O-D-2-butanol were determined by the gas chromatographic method described previously.³ The decomposition rate of *tert*-butyl peroxide in the tetrahydrofuran solutions of VI and VII were also made by the gas chromatographic analysis of the unreacted peroxide as previously described.⁴

The decomposition rates of acetyl peroxide and *tert*-butyl peracetate in the presence of 2-butanol and O-d-2-butanol were determined by the method described by Silbert and Swern;¹⁰ 1-ml samples of the reaction mixture were pipeted into a flask through which nitrogen had been passed for 20 sec. A saturated sodium iodide solution (about 2 ml) and 15 ml of freshly distilled glacial acetic acid containing 0.002% ferric chloride were added to the contents in the flask. The flask was stoppered and permitted to stand in the dark for 10–15 min. About 50 ml of distilled water was added to the solution which was titrated to a starch-iodine end point with 0.2 N thiosulfate to determine the amount of molecular iodine produced. A blank determination was run on all of the reagents.

Spectrophotometric Determination of Oxidation of Dihydrolutidines with Acetyl Peroxide.—Stock solutions of VI and VII in acetonitrile and of the acetyl peroxide-dimethyl phthalate solution in the same solvent were prepared. Samples of these solutions were thermostated at 30° before mixing. Immediately after mixing, the solutions were placed in a thermostatically controlled cell compartment of a Beckman DU spectrophotometer. The rates of reaction of the dihydropyridine derivatives were followed by measuring their absorption at 363 m μ as a function of time.

Registry No.—I, 110-05-4; II, 110-22-5; III, 107-71-1; 2-butanol, 78-92-2; V, 4712-39-4; VI, 1149-23-1; VII, 25894-44-4.

(10) L. S. Silbert and D. Swern, Anal. Chem., 30, 385 (1958).

Substituent Effects in Alkali Metal-Ketyl Ion Pairs. An Infrared Scrutiny

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The carbonyl stretching frequency (ir) of alkali metal-4,4'-disubstituted ketyl ion pairs shows a startling deviation from the expected influence of five para substituents. Measurements indicate that the ketyl C-O bond is strengthened, rather than loosened, by electron-donating substituents. Plots of $\sigma_R^+ vs$. ketyl frequency are given. A possible explanation lies in the consideration of ion pairing by the counterion M⁺ with increased electron density at the ketyl site. Such ion pairing might be able to reduce the antibonding influence of the added electron, thus allowing bonding π electrons to exert a stronger bonding force between the carbon and the oxygen atoms.

The utility of the carbon-oxygen stretching frequency of ketones as a sensitive indicator of electron density changes has long been recognized. Shifts in the carbonyl frequency are subject to both inductive and mesomeric effects which change the electron density at the carbon-oxygen bond.² Correlation of Hammett σ values with the carbonyl stretching frequencies in five 4,4'-disubstituted benzophenones has been shown to be nearly linear.³ In essence, the studies all show that the greater the electron density at the C=O site, the lower the frequency (in cm⁻¹).

A one-electron reduction of a ketone results in a ketyl with the commonly given valence bond structure of $> C - \overline{O}$. Such a structure does not reflect the fact that only one of the π electrons of the C=O bond has been essentially "cancelled" by the introduction of the new electron into the lowest antibonding orbital of the

(3) N. Fuson, M.-L. Jósien, and E. M. Shelton, J. Amer. Chem. Soc., 76, 2526 (1954).

⁽¹⁾ Laboratório Químico, Universidade de Coimbra, Coimbra, Portugal, to whom correspondence should be addressed.

^{(2) (}a) R. E. Kagarise, J. Amer. Chem. Soc., 77, 1377 (1955); (b) N. B. Colthup, L. H. Daly, and S. E. Wiberley, "Introduction to Infrared and Raman Spectroscopy," Academic Press, New York, N. Y., 1964, p 241 ff.