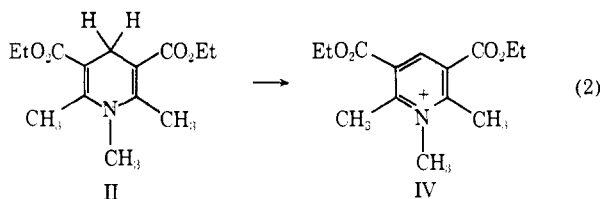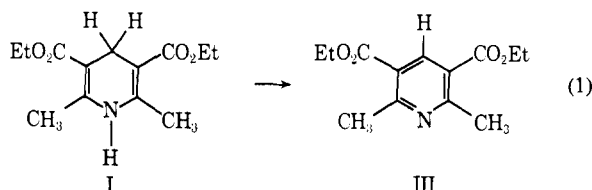# Peroxide Oxidations of Dihydropyridine Derivatives[1]

E. S. Huyser,* J. A. K. Harmony, and F. L. McMillian

*Contribution from the Department of Chemistry, University of Kansas,
Lawrence, Kansas 66044. Received July 19, 1971*

Abstract: The reactions of 1,4-dihydro-3,5-dicarboethoxy-2,6-lutidine (I) and its *N*-methyl derivative II with *tert*-butyl peroxide, acetyl peroxide, and benzoyl peroxide have been investigated. With the exception of *tert*-butyl peroxide, which reacts with II to yield an oxidative dimerization product, I and II are oxidized by these peroxidic agents to the corresponding pyridine or pyridinium cation, respectively. Kinetic analysis and product isolation studies indicate that the latter reactions proceed by free-radical chain mechanisms. In the case of the acyl peroxides, the chain reactions are initiated by bimolecular interactions involving the peroxide and the dihydropyridines.

The dihydropyridine derivatives 1,4-dihydro-3,5-dicarboethoxy-2,6-lutidine (I) and *N*-methyl-1,4-dihydro-3,5-dicarboethoxy-2,6-lutidine (II) have been reported to reduce a variety of functionalities. I and II are oxidized to the corresponding pyridines III and IV in the process. Many of the reported re-

ductions appear to proceed by hydride ion transfer from the dihydropyridine to the functionality that is reduced. Among these are reductions by I of chloranil to tetrachlorohydroquinone,[2] maleic anhydride to succinic anhydride,[2] benzoylformic and pyruvic acids to mandelic and lactic acids, respectively,[3] and 1-phenyl-4,4,4-trifluoro-2-butenone to the corresponding butyrophenone.[4] Other reactions of these dihydropyridines, for example, the reduction of the carbonyl group of 2-mercaptobenzophenone[5] and reduction of polyhalomethanes[6] and *tert*-butyl peroxide,[7] display characteristics of free-radical chain reactions. The work described in this article indicates that free-radical chain reactions are operative in the oxidations of these dihydropyridines with acyl peroxides.

***tert*-Butyl Peroxide.** Previous work showed that I reacted with *tert*-butyl peroxide in a free-radical chain reaction.[7] The chain propagating steps in the se-

quence are abstraction of a 4 hydrogen by a *tert*-butoxy radical (reaction 4) yielding the monohydropyridyl radical (HPy·) which reduces the peroxide (reaction 5) yielding the pyridine, *tert*-butyl alcohol, and a chain-carrying *tert*-butoxy radical. The chain reaction is initiated by the unimolecular decomposition of the peroxide (reaction 3). Support for a chain reaction involving the peroxide comes from the observation that the overall decomposition rate of the peroxide is markedly enhanced by the presence of I. The reduction of *tert*-butyl peroxide by HPy· (reaction 5) pro-

tert-Butyl Peroxide Oxidation of I

$$ROOR \xrightarrow{k_3} 2RO\cdot \tag{3}$$

$$HPy\cdot + ROOR \xrightarrow{k_5} III + ROH + RO\cdot \tag{5}$$

$$\frac{-d[ROOR]}{dt} = k_3[ROOR] + k_5[HPy\cdot][ROOR] \tag{6}$$

ceeds by a hydrogen transfer mechanism as evidenced by a primary isotope effect ($k_H/k_D = 2.39$ at 125°) in the reaction of the *N*-deuterio derivative of I.[8]

Oxidation of the *N*-methyl derivative II with *tert*-butyl peroxide follows a markedly different course. No induced decomposition is observed when the peroxide is heated at 125° with II in *sym*-collidine. The reaction products are *tert*-butyl alcohol and V, the oxidative dimer of II. Dimerization of the pyridyl radi-

cals (MePy·) formed by abstraction of a 4 hydrogen from II accounts for the formation of V. Since MePy· has no nitrogen-bonded hydrogen, the radical cannot react with the peroxide by hydrogen atom transfer and apparently is not able to do so by electron transfer.

(1) This work was supported by a grant (AM-09517) from the National Institutes of Health.

(2) R. Linstead, J. Hannah, and E. A. Baude, *J. Chem. Soc.*, 3257 (1960).

(3) F. H. Westheimer and R. H. Abeles, *J. Amer. Chem. Soc.*, **80**, 5459 (1960); K. Wallenfel and D. Hofman, *Tetrahedron Lett.*, 10 (1959).
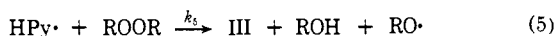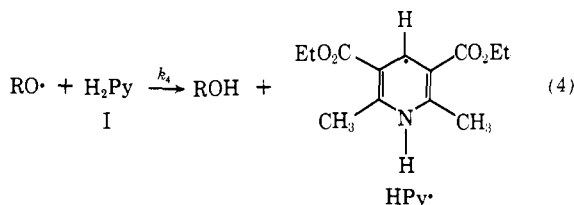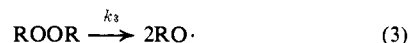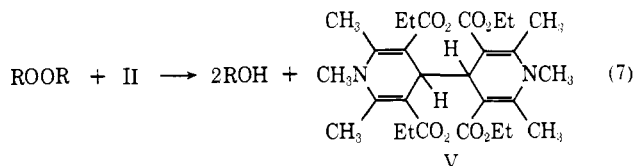
(4) F. H. Westheimer, B. E. Norcross, and P. E. Klinedinst, Jr., *J. Amer. Chem. Soc.*, **84**, 797 (1962).

(5) F. H. Westheimer and K. A. Schellenberg, *J. Org. Chem.*, **30**, 1859 (1965).

(6) F. H. Westheimer, J. L. Kurz, and R. Hutton, *J. Amer. Chem. Soc.*, **83**, 584 (1961).

(7) E. S. Huyser, C. J. Bredeweg, and R. M. VanScoy, *ibid.*, **86**, 4148 (1964).

(8) E. S. Huyser and A. A. Kahl, *J. Org. Chem.*, **35**, 3742 (1970).

$$RO\cdot + II \longrightarrow ROH +$$

(MePy·)

(8)

$$2MePy\cdot \longrightarrow V \qquad (9)$$
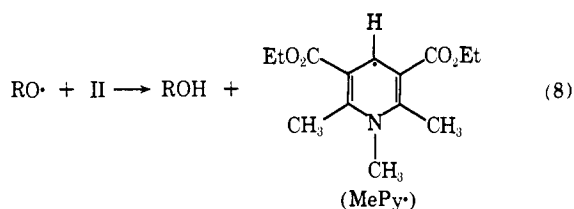
Acyl Peroxides. Acetyl peroxide (Ac_2O_2) and benzoyl peroxide (Bz_2O_2) oxidize I spontaneously at temperatures below those required for the unimolecular decomposition of the peroxides ($>50°$). This behavior contrasts markedly with the *tert*-butyl peroxide reaction with I which requires thermal decomposition of the peroxide to initiate the chain sequence 4 and 5. Product and kinetic analyses, however, indicate that the oxidations of I by these acyl peroxides are also free-radical chain reactions.

Acetyl peroxide is reduced by I to acetic acid, methane, and carbon dioxide and the dihydropyridine is oxidized to III in the process. The product distribu-

$$Ac_2O_2 + I \longrightarrow CH_4 + CO_2 + CH_3CO_2H + III \qquad (10)$$
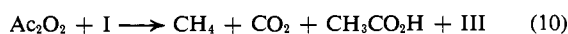
tion data in Table I support the stoichiometry given in

Table I. Reaction of Ac_2O_2 with I in Acetonitrile at 40°

Reactants consumed, mmol		Products formed, mmol			
I	Ac_2O_2	III	AcOH	CH_4	CO_2
1.99	1.80	2.29	1.75	2.15	1.91
2.01	2.25	2.27	1.91	2.15	1.99
2.14	2.14	2.39	2.02	2.36	2.03
1.76	1.91		1.86	1.72	1.86

$$CH_3\cdot + I \xrightarrow{k_{12}} CH_4 + HPy\cdot \qquad (12)$$

$$HPy\cdot + Ac_2O_2 \xrightarrow{k_{13}} III + CH_3CO_2H + (CH_3CO_2\cdot) \qquad (13)$$

$$\hphantom{HPy\cdot + Ac_2O_2 \xrightarrow{k_{13}} III} \longrightarrow CH_3\cdot + CO_2$$

$$CH_3\cdot + HPy\cdot \xrightarrow{k_{14}} CH_4 + III \qquad (14)$$

occurred (reaction 15).

$$H_2Py + AcOOAc \longrightarrow HPy^+ + AcO^- + HOAc \qquad (15)$$

Initiation of the chain sequence by a bimolecular reaction between the two reactants yielding a pair of chain-carrying radicals would not be limited by the temperature requirements of a unimolecular homolytic cleavage of a covalent bond. The mode of initiation of the chain sequence finds support in the kinetic analysis of the reaction of I and Ac_2O_2. At temperatures ranging from 10 to 40° and concentration ratios of Ac_2O_2:I ranging from about 200 to 500 the reaction was first order in each of the reactants. The derived steady-state rate law for the sequence 11–14, which includes the cross termination reaction 14, is given by eq 16. Some representative rate data for the reaction

$$\text{rate} = \left(\frac{k_{11}k_{12}k_{13}}{k_{14}}\right)^{1/2}[I][Ac_2O_2] \qquad (16)$$

of I with Ac_2O_2 in various solvents are given in Table II. The activation parameters for the reaction indicate that it apparently is influenced to some extent by the medium. It is not possible to designate at this point with any confidence the nature of these solvent interactions to any particular step in the reaction sequence since the parameters are determined from a combination of rate constants. It is worth noting, however, that changes in the enthalpy of activation are
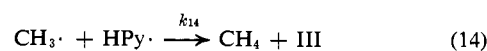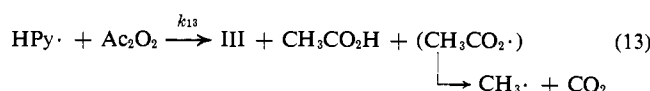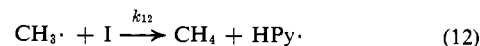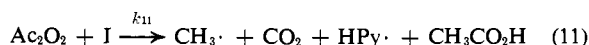
Table II. Kinetic Data for Reaction of I with Ac_2O_2 in Various Solvents[a]

Solvent	$-10^3k'$ (l. mol^{-1} sec^{-1})			Activation parameters	
	10°	30°	40°	$\Delta H^{\pm}$, kcal mol^{-1}	$\Delta S^{\pm}$, eu[b]
tert-Butyl alcohol		2.96 (0.07)[c]	7.61 (0.23)[c]	20.29 (0.24)[d]	−3.24 (0.74)[d]
Methyl ethyl ketone	1.00 (0.01)[c]	11.4 (0.01)	31.7 (1.2)	19.76 (0.22)	−2.35 (0.78)
Ethyl acetate	1.72 (0.01)	13.8 (0.06)	33.6 (0.25)	16.93 (0.43)	−11.26 (1.51)
tert-Amyl alcohol	0.64 (0.08)	3.82 (0.22)	10.2 (0.01)	15.44 (0.09)	−18.52 (0.30)
Acetic acid	9.42 (0.01)[e]	19.9 (0.06)	39.1 (0.02)	12.39 (0.46)	−25.51 (1.57)
Acetonitrile	2.33 (0.03)	8.44 (0.17)	18.8 (0.13)	11.47 (0.41)	−30.03 (0.57)
Benzene	4.42 (0.12)	15.2 (0.01)	30.9 (0.04)	10.69 (0.18)	−31.49 (0.57)
Acetone	6.55 (0.04)	7.22 (0.29)	19.9 (0.03)	19.53 (0.10)	−4.00 (0.35)

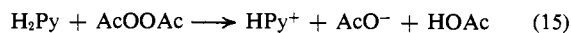[a] Initial concentrations: [I] $= 1.43 \times 10^{-4}$; [Ac_2O_2] $= 2.42 \times 10^{-2}$. [b] Calculated at 25°. [c] Average deviations for a minimum of three kinetic runs. Standard deviations for each individual run were less than 1%. [d] A probable error, calculated from the standard deviations of the activation parameters based on the rate constants and the average deviations of the rate constants. See L. L. Schaleger and F. A. Long, *Advan. Phys. Org. Chem.*, **1**, 1 (1963). [e] Rate constant at 20°.

eq 10 for the reaction. The formation of methane and carbon dioxide as reaction products can be accounted for in terms of the free-radical chain sequence 12 and 13. The unstable acetoxy radical ($CH_3CO_2\cdot$) formed in the reaction of HPy· with the peroxide decomposes to carbon dioxide and a chain-carrying methyl radical which reacts with I to yield methane. Only acetic acid would be expected as a reduction product of the peroxide if direct hydride transfer from I to Ac_2O_2

Ac_2O_2 Oxidation of I

$$Ac_2O_2 + I \xrightarrow{k_{11}} CH_3\cdot + CO_2 + HPy\cdot + CH_3CO_2H \qquad (11)$$

generally compensated for by entropy of activation changes. Such compensation has been noted previously in both radical-forming[9] and chain-propagating[10] reactions.

The reduction of benzoyl peroxide (Bz_2O_2) by I also occurs spontaneously at room temperature yielding the pyridine III and benzoic acid although trace amounts of

(9) M. G. Alden and J. E. Leffler, *J. Amer. Chem. Soc.*, **76**, 1425 (1959); M. D. Cohen, J. E. Leffler, and L. M. Barbato, *ibid.*, **76**, 4169 (1954); J. E. Leffler and R. A. Hubbard, *J. Org. Chem.*, **19**, 1089 (1954); E. S. Huyser and R. M. VanScoy, *ibid.*, **33**, 3524 (1968).

(10) C. Walling and P. Wagner, *J. Amer. Chem. Soc.*, **85**, 2333 (1963); **86**, 3368 (1964).

carbon dioxide were observed. These products could be explained in terms of a hydride transfer from I to Bz_2O_2 but kinetic analysis of the reaction supports a free-radical chain mechanism.

The rate laws for the reaction of benzoyl peroxide with I at 30° in acetonitrile were determined from the observed rates of oxidation of about 5% of I at various initial concentration ratios of the reactants (method of initial rates). At concentration ratios of $[Bz_2O_2]$:[I] in the range of 175–340 (items 1–3 in Table III),

Table III. Kinetic Data for Reaction of Benzoyl Peroxide with I in Acetonitrile at 30°

Item	$[Bz_2O_2]$ $\times 10^2$	$[I]$ $\times 10^4$	$[Bz_2O_2]$:[I]	10^6 rate, mol l.$^{-1}$ min^{-1}
1	0.254	1.43	17.5	0.742
2	2.54	1.43	175	8.45
3	2.54	0.743	340	4.42
4	11.3	1.43	790	85.2
5	11.3	0.74	1520	30.0
6	7.26	0.35	2090	5.90
7	11.3	0.35	3260	7.56

the reaction is first order in each component and the rate law (17) is similar to that observed in the acetyl peroxide reactions. However, as the concentration ratio is increased to a range of 1500–3200, the observed rate is essentially three-halves order in I and half order

$$\text{rate} = k'[Bz_2O_2]^{1.06}[I]^{0.99} \qquad (17)$$

in Bz_2O_2 as shown in the calculated rate law 18.

$$\text{rate} = k'[Bz_2O_2]^{0.56}[I]^{1.54} \qquad (18)$$

A change in the rate law as the concentration ratio of the reactants is increased is not consistent with the hydride transfer mechanism which should 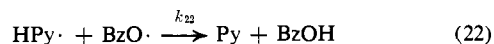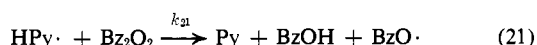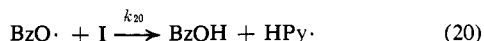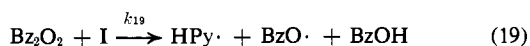be first order in each reagent at all concentration ratios. The observed change is consistent, however, with a free-radical chain mechanism initiated in the bimolecular process 19 and terminated either by the cross termination process 22 at lower $[Bz_2O_2]$:[I] ratios or by a bimolecular

Bz_2O_2 Oxidation of I

$$Bz_2O_2 + I \xrightarrow{k_{19}} HPy\cdot + BzO\cdot + BzOH \qquad (19)$$

$$BzO\cdot + I \xrightarrow{k_{20}} BzOH + HPy\cdot \qquad (20)$$

$$HPy\cdot + Bz_2O_2 \xrightarrow{k_{21}} Py + BzOH + BzO\cdot \qquad (21)$$

$$HPy\cdot + BzO\cdot \xrightarrow{k_{22}} Py + BzOH \qquad (22)$$

$$2BzO\cdot \xrightarrow{k_{23}} Bz_2O_2 \qquad (23)$$
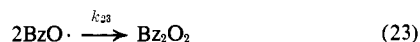
reaction of benzoyloxy radicals ($BzO\cdot$) at the higher ratios (eq 23). The derived steady-state rate laws for the reaction when terminated by eq 22 and 23 are shown in eq 24 and 25, respectively. Termination by reaction

$$\text{rate} = \left(\frac{k_{19}k_{20}k_{21}}{k_{22}}\right)^{1/2} [Bz_2O_2][I] \qquad (24)$$

$$\text{rate} = \left(\frac{k_{19}}{2k_{23}}\right)^{1/2} k_{21}[Bz_2O_2]^{1/2}[I]^{3/2} \qquad (25)$$

23, with the consequence of rate law 25 being operative, could be expected for a reaction in which the ratio of

peroxide to I is high since the steady-state concentrations of the benzoyloxy radicals would be larger than that of the monohydropyridyl radicals. At lower ratios of peroxide to I, the steady-state concentrations of $BzO\cdot$ and $HPy\cdot$ apparently are comparable and cross termination occurs.

No change in the rate law could be observed in the reaction of acetyl peroxide with I in the concentration ratio of peroxide to I ranging from 10 to 5700 indicating that only the cross termination reaction 14 is operative. At higher concentration ratios of acetyl peroxide to I, the reaction rates were too rapid to be accurately measured with our equipment.[11]

Product isolation and kinetic analysis of the reactions of acetyl and benzoyl peroxides with II, N-methyl-1,4-dihydro-3,5-dicarboethoxy-2,6-lutidine, were complicated by interactions of the pyridinium cation IV formed as the oxidation product with the carboxylate anion produced by reduction of the peroxide. The formation of the complexes became evident from the spectral analysis of the reaction mixtures which, in contrast to those of I with the acyl peroxide, became highly colored when only small amounts of the reactants had been consumed. In addition to the absorptions expected from II and the pyridinium cation IV (see the Experimental Section), the reaction mixtures showed absorption in the regions of 400–450 and 300–315 nm. The former can be ascribed to a charge transfer complex VI formed from IV and a carboxylate anion.[12] The

VI
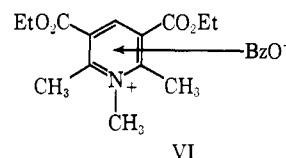
absorption in the 300–315-nm region has been tentatively assigned to an addition product resulting from bonding of carboxylate ion to the 4 position of the pyridinium cation VII. Similar addition products

VII
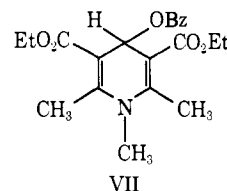
have been reported for a variety of anions when allowed to react with pyridinium cations.[13] Mixing acetonitrile solutions of the perchlorate salt of the pyridinium cation IV both with sodium benzoate and with sodium acetate produced a reaction solution having the same anomalous absorptions as those of the reaction mixtures of the acyl peroxides with II.

Perchlorate ion apparently does not form either charge transfer or covalent products with the pyridi-

(11) The kinetic order of I in its reaction with a 300-fold excess of BrCCl$_3$ has been reported to be greater than unity and appears to approach three-halves order (ref 6). The observed kinetics for this reaction, which also occurs spontaneously in the dark, can be explained in terms of a bimolecular process initiating a free-radical chain process that is terminated by coupling of two trichloromethyl radicals.

(12) (a) R. S. Mulliken, J. Amer. Chem. Soc., **78**, 15 (1956); (b) J. Phys. Chem., **56**, 801 (1952); (c) E. M. Kosower and P. E. Klinedinst, Jr., ibid., **78**, 3493 (1956); (d) E. M. Kosower, "Molecular Biochemistry," McGraw-Hill, New York, N. Y., 1962, p 180.

(13) Reference 12d, p 175.

nium cation analogous to VI and VII, respectively.[14] Furthermore, the binding constant of perchlorate with the pyridinium cation is high enough that if the former is present in sufficient concentration (5–20 times that of the carboxylate ion), no evidence of either the charge transfer complex or the addition product resulting from interaction of IV with the carboxylate ions was found in the spectrum of the reaction mixtures of the acyl peroxides with II. Thus, by performing the reactions of the acyl peroxides with II in acetonitrile–water mixtures containing sufficient sodium perchlorate to prevent formation of the anomalous products, both product isolation and kinetic analysis of the reaction were possible. The reduction products of acetyl and benzoyl peroxides obtained from their reaction with II (Tables IV and V) are the same as those obtained

Table IV. Reactions of Ac_2O_2 with II at $40°$[a]

Reactants consumed, mmol		Products formed, mmol			
II	Ac_2O_2	IV	AcOH	CH_4	CO_2
1.88	2.43	1.61[b]	c	1.94	2.04
1.89	2.27	1.54[b]	c	2.02	1.80

[a] CH_3CN–H_2O solution containing $NaClO_4$. [b] Isolated as perchlorate salt. [c] Detected qualitatively but not determined quantitatively.

Table V. Reaction of Bz_2O_2 with II at $40°$ [a]

Reactants consumed, mmol		Products formed, mmol	
II	Bz_2O_2	IV	BzOH
1.94	2.17	1.61[b]	4.12
1.89	2.12	1.44[b]	4.09

[a] CH_3CN–H_2O solution containing $NaClO_4$. [b] Amount determined isolated as perchlorate salt.

from the reactions of these peroxides with I.

Reactions of acetyl and benzoyl peroxide with II were spontaneous at temperatures below those required for unimolecular decomposition of the peroxides. Both reactions were first order in each of the reactants, and the rates did not appear to be affected by the presence of perchlorate ion in concentrations sufficient to prevent formation of charge transfer or addition products between the pyridinium cation and the carboxylate ions formed. There was no evidence of change in the rate law even at high ratios of the peroxide to II where the rates became too rapid to allow for reliable measurements with the available equipment. Some representative rate data are given in Table VI.

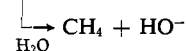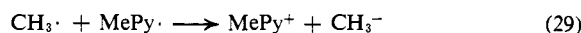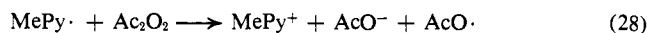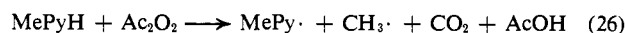**Table VI.** Kinetic Data for Reactions of Acyl Peroxides with II[a]

Peroxide	$10^3k'$, mol l.$^{-1}$ sec^{-1}			Activation parameters	
	$12°$	$30°$	$40°$	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, eu[b]
Ac_2O_2[c]	2.84	8.85	17.5	10.8 (0.2)[d]	−32.2 (0.6)[d]
Bz_2O_2[e]	5.48	26.7	85.0	16.5 (0.3)	−11.2 (1.0)

[a] 6.7% H_2O in CH_3CN. [b] Calculated at $25°$. [c] [II] = 1.6 × 10^{-4} M, [Ac_2O_2] = 2.42 × 10^{-2} M, [ClO_4]$^-$ = 6.1 × 10^{-4} M. [d] Probable errors in parentheses. [e] [II] = 1.6 × 10^{-4} M; [Bz_2O_2] = 7.30 × 10^{-3} M; [ClO_4^-] = 2.8 × 10^{-2} M.
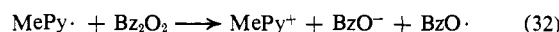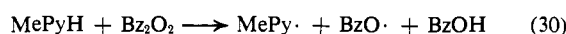
(14) E. M. Kosower, *J. Amer. Chem. Soc.*, **78**, 3497 (1956).

In view of the similarity of the products and the kinetic analysis of the reactions, it seems quite likely that the oxidations of II by acyl peroxides proceed by mechanisms analogous to those suggested for acyl peroxidations of I but differ markedly from the oxidations of II by *tert*-butyl peroxide. Although hydrogen

Ac_2O_2 Oxidation of II

$$MePyH + Ac_2O_2 \longrightarrow MePy\cdot + CH_3\cdot + CO_2 + AcOH \quad (26)$$

$$CH_3\cdot + MePyH \longrightarrow CH_4 + MePy\cdot \quad (27)$$

$$MePy\cdot + Ac_2O_2 \longrightarrow MePy^+ + AcO^- + AcO\cdot \quad (28)$$
$$IV \qquad \qquad \longrightarrow CH_3\cdot + CO_2$$

$$CH_3\cdot + MePy\cdot \longrightarrow MePy^+ + CH_3^- \quad (29)$$
$$\longrightarrow CH_4 + HO^-$$
$$H_2O$$

Bz_2O_2 Oxidation of II

$$MePyH + Bz_2O_2 \longrightarrow MePy\cdot + BzO\cdot + BzOH \quad (30)$$

$$BzO\cdot + MePyH \longrightarrow BzOH + MePy\cdot \quad (31)$$

$$MePy\cdot + Bz_2O_2 \longrightarrow MePy^+ + BzO^- + BzO\cdot \quad (32)$$

$$BzO\cdot + MePy\cdot \longrightarrow MePy^+ + BzO^- \quad (33)$$

atom transfer from the methyl pyridyl radical to the peroxide is not an available route for its interaction with the peroxide, electron transfer to acyl peroxides yielding the pyridinium cation IV may occur. The inability of the methyl pyridyl radical to react in a similar manner with *tert*-butyl peroxide is indicative of a considerably higher potential for reduction of the dialkyl peroxide by electron transfer although the peroxide can be reduced by the hydrogen atom transfer mechanism if the appropriate radical is present.

Experimental Section

Materials. Reagent grade solvents (*sym*-collidine, acetic acid, *tert*-butyl alcohol, acetone, *tert*-amyl alcohol, methyl ethyl ketone, and ethyl acetate) were distilled twice before using. Acetonitrile was dried 24 hr over calcium hydride, filtered, and distilled from 1 g of phthalic anhydride and several pellets of sodium hydroxide. Benzene was washed twice with concentrated sulfuric acid, twice with water, and twice with sodium hydroxide solution, dried over magnesium sulfate, and distilled from sodium. Reagent grade *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. Benzoyl peroxide (Wallace and Tiernan, Inc.) was purified by precipitation from chloroform with methanol.

1,4-Dihydro-3,5-dicarboethoxy-2,6-lutidine (I) was prepared from ethyl acetoacetate, formalin, and ammonium hydroxide by the method of Singer and McElvain[15] (mp 186–187.5°).

3,5-Dicarboethoxy-2,6-lutidine (III) was obtained by oxidation of I with nitric acid–sulfuric acid[15] (mp 72–73°).

N-Methyl-3,5-dicarboethoxy-2,6-lutidinium perchlorate (IV) was prepared by methylation of III with freshly distilled dimethyl sulfate followed by precipitation with 1 N sodium perchlorate as described by Mumm[16] (mp 105–107°).

N-Methyl-1,4-dihydro-3,5-dicarboethoxy-2,6-lutidine (II) was produced by reduction of IV with sodium dithionite in sodium bicarbonate following the procedure of Mumm and Diederichsen[17] (mp 85.5–87°). This material was refrigerated under nitrogen.

Kinetic Measurements. The rates of decomposition of *tert*-butyl peroxide in the presence and absence of N-methyl-1,4-dihydro-3,5-dicarboethoxy-2,6-lutidine were determined by the gas chromatographic method described previously by Huyser, Bredeweg, and VanScoy.[7] The rates of oxidation of dihydropyridines by acyl peroxides were determined spectrophotometrically in the

(15) A. Singer and S. M. McElvain, "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1943, p 214.
(16) O. Mumm, *Justus Liebigs Ann. Chem.*, **605**, 1 (1957).
(17) O. Mumm and J. Diederichsen, *ibid.*, **538**, 195 (1938).

following manner. A 2.25×10^{-4} M standard solution of each dihydropyridine in each of the solvents listed in Tables II and VI was prepared. The standard solution (2 ml) was pipetted into a Pyrex or quartz cuvette and allowed to attain the desired temperature in a thermostated Beckman DU-2 cell compartment. Reaction was initiated by the addition of 1.0 ml of peroxide thermally equilibrated at the same temperature. The concentration of peroxide was at least ten times that of the dihydropyridine. Rates of reaction were obtained by following the disappearance of I (λ_{363}, ϵ 6333) or II (λ_{350}, ϵ 5760) through at least 2 half-lives. When only initial rates were required, they were determined from the first 5% of reaction.

Rate constants for the reaction of dihydropyridines with acyl peroxides were obtained by a least-squares treatment of the data, and the activation parameters were calculated from a least-squares treatment of the reaction rate constants at the various temperatures.

Reaction of *N*-Methyl-1,4-dihydro-3,5-dicarboethoxy-2,6-lutidine (II) with *tert*-Butyl Peroxide. A mixture consisting of II (5.34 g, 2 mmol), *tert*-butyl peroxide (5.50 g, 3.9 mmol), and 7 ml of *sym*-collidine contained in a sealed Pyrex tube was heated in an oil bath at 125° for 18 hr. The volatile components were removed by distillation under reduced pressure. The residue was dissolved in ethanol and analyzed by thin-layer chromatography. Analysis showed the presence of two components, one of which was unreacted II. The other component, a dimer, was isolated by fractional recrystallization from 95% ethanol (yield 0.9 g), mol wt (determined in camphor) 515 ± 21, mp 190–191° (lit.[18] 193°). Spectral evidence confirmed the structure of the dimer to be V.

Reaction of Dihydropyridines I and II with Acetyl Peroxide. Approximately 2 mmol of I or II was weighed into a 200-ml round-bottomed three-necked flask and a suitable amount of solvent was added. Acetonitrile served as solvent for I, and a 16.7% H_2O–CH_3CN mixture containing 1 M $NaClO_4 \cdot H_2O$ served as solvent for II. The reaction vessel was connected to a reflux condenser, placed in a water bath maintained at 40 ± 1°, and allowed to equilibrate 1 hr. The condenser was joined to a preweighed trap containing a layer of indicating calcium sulfate and a layer of ascarite, which in turn was joined to a gas buret and reservoir bulb filled with mercury. A dropping funnel containing a known amount of acetyl peroxide in dimethyl phthalate was connected to the flask and the entire system was flushed with nitrogen for 30 min, and then closed to the atmosphere. Reaction was initiated by slow addition of the peroxide to the dihydropyridine solution. Slightly reduced pressure was maintained in the system throughout

the duration of the reaction (about 24 hr). The amount of unreacted peroxide at the end of reaction was determined by iodometric titration.[19] The amount of CO_2 produced was found from the change in weight of the ascarite trap. Methane was determined quantitatively from its volume in the gas buret and it identity confirmed by comparison of its ir spectrum with that of an authentic sample (Sadtler IR Spectrum 4063). The amount of acetic acid produced was determined gas chromatographically. The amounts of dihydropyridine at the beginning and end of the reaction were determined spectrophotometrically. The amounts of the pyridines formed were determined in the following manner. Reaction mixtures containing 3,5-dicarboethoxy-2,6-lutidine (III) were made 1.2 N in HCl and continuously extracted with ether for 24 hr. The acidic solutions were subsequently diluted and the concentration of III determined spectrophotometrically (λ_{276}, ϵ 8480). *N*-Methyl-3,5-dicarboethoxy-2,6-lutidinium cation IV was isolated as its perchlorate salt from the reaction mixture and weighed and identified by ir, nmr, and melting point. The isolation was accomplished by removal of the dimethyl phthalate from the reaction mixture with ether and addition of $NaClO_4$, followed by extraction of the salt in chloroform. The chloroform was removed under a stream of nitrogen; the solid salt was dried overnight and weighed.

Reaction of Dihydropyridines I and II with Benzoyl Peroxide. Approximately 2 mmol of dihydropyridine and 5 mmol of benzoyl peroxide were added to 75 ml of solvent (described previously) in a 200-ml round-bottomed flask equipped with a reflux condenser. After the mixture was flushed with nitrogen for 30 min, the flask was placed in a 40 ± 1° water bath, and the reaction was allowed to proceed for 24 hr. Peroxide, dihydropyridines, and pyridines were analyzed by the methods described for reaction of I and II with acetyl peroxide. The reaction solutions were extracted three times with a total volume of 100 ml of 1 N Na_2CO_3. The amount of benzoic acid in the Na_2CO_3 layers was measured by the absorbance at 270 nm (ϵ 547).

Charge Transfer Complexes of the *N*-Methyl-3,5-dicarboethoxy-2,6-lutidinium Cation. *N*-Methyl-3,5-dicarboethoxy-2,6-lutidinium perchlorate (0.0788 g (0.216 mmol)) was dissolved in 10 ml of acetonitrile. This solution was shaken vigorously in a separatory funnel for 5 min with 10 ml of a 1 N solution of sodium benzoate or sodium acetate. The organic layer was removed and diluted, and its spectrum obtained using the Cary-14 recording spectrophotometer (λ_{max} (nm) IV–NaOAc 285, 310, 405; IV–NaOBz 280, 315, 410). Similar absorptions were observed in reaction mixtures of II with acetyl and benzoyl peroxides in acetonitrile with no sodium perchlorate added.

(18) O. Mumm and H. Ludwig, *Ber. Deut. Chem. Ges. B*, **59**, 1605 (1926).

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