Organic and Biological Chemistry

The Decomposition of Acetyl Peroxide in the Presence of Acetate Salts[1]

T. Koenig and R. Wielesek[2]

Contribution from the Department of Chemistry, University of Oregon, Eugene, Oregon 97403. *Received September 30, 1968*

Abstract: Acetyl peroxide has been found to undergo a rapid reaction with acetate salts in aprotic solvents and in chlorobenzene. The reaction products include acetoxyacetic acid, carbon dioxide, methane, and methyl acetate. The reaction is inhibited by added acetic acid. When carbon-14-labeled acetate ion is used, a nonstatistical incorporation of the external salt into the acetoxyacetic acid product is observed. Some trappable radicals are produced as evidenced by the disappearance of di-*t*-butyl nitroxide. Oxygen-18-labeling experiments indicate that the acetoxy group in the product has near, but not complete equilibration of the oxygen atoms. These observations are interpreted in terms of a *formal* α-lactone intermediate formed by intramolecular oxidation of the enolate anion of acetyl peroxide. With carbon-14-labeled acetate, the carbon dioxide produced, contains some activity which is interpreted as resulting from electron exchange between acetoxy radical and acetate anion.

The mechanism of the decomposition of acetyl peroxide has been the subject of numerous investigations.[3] During the course of this work, the intervention of a well-defined acetoxy radical intermediate in the process was clearly demonstrated by the observation that oxygen atom randomization occurs at a rate comparable to that for over-all decomposition.[4] The lifetime of the species with respect to decarboxylation remains a problem. A widely quoted estimate of this lifetime is less than 10^{-9} sec.[5] The basis for this estimate was primarily the absence of any scavenging of the species by molecules whose absolute rates of reaction with other radicals (10^8 sec^{-1}) were known at that time. The implication of this short lifetime for the acetoxy radical is that very few other processes should be capable of competing, kinetically, with the formation of carbon dioxide when such a species is involved. In spite of this, reactions such as that between picoline N-oxide and acetic anhydride[6] and N-nitrosoacetanilide decompositions[7] have been interpreted in terms of radical intermediates though carbon dioxide is not a major product. The proposed rationalizations of these contradictions involve the concept of efficient cage reactions which allow the capture of the acyloxy radical species before decarboxylation.

An alternative rationalization of this dilemma, is that the *latter* reactions do not actually involve the acyloxy radical species and work reported[8,9] during the course of this research has, in fact, indicated this to be the case. Another alternative is that the lifetime of the acetoxy radical is in fact longer than Szwarc's estimate but that its susceptibility to scavenging is not simply related to the other radicals whose rate constants for reactions with scavengers were taken as the basis of the estimate of its stability. Recent studies[10] of the reaction of acyloxy radicals with olefins have indicated that this may also be a serious criticism.

The observation of Weissman's[11] group that electron exchange between tris-*p*-nitrophenylmethyl anion and the corresponding radical is a rapid, diffusion-controlled process [$k \sim 10^8$–10^9 l./(mol sec)] suggested to us that the corresponding reaction between acetate anion and acetoxy radical might serve as a more sensitive scavenger for the radical. We thus set out to test for this type of electron exchange. The kinetics for such a thermoneutral exchange were first analyzed according to Scheme I

Scheme I

$$(RCO_2)_2 \xrightarrow{k_1} nRCO_2\cdot$$

$$RCO_2\cdot \xrightarrow{k_2} CO_2$$

$$RCO_2\cdot + RCO^*{}_2^- \underset{k_e}{\overset{k_e}{\rightleftharpoons}} RCO^*{}_2\cdot + RCO_2^-$$

$$RCO^*{}_2\cdot \xrightarrow{k_2} CO_2^*$$

where n is the number of moles of carbon dioxide

(1) Presented in part at the 155th National Meeting of the American Chemical Society, San Francisco, Calif., April 2, 1968.
(2) National Defense Education Act Predoctoral Fellow, 1964–1967.
(3) A. Fry, B. M. Tolbert, and M. Calvin, *Trans. Faraday Soc.*, **49**, 1444 (1953); M. Szwarc, "Peroxide Reaction Mechanisms," J. O. Edwards, Ed., John Wiley & Sons, New York, N. Y., 1962, pp 153–174; T. Koenig and W. D. Brewer, *Tetrahedron Letters*, 2773 (1965).
(4) J. W. Taylor and J. C. Martin, *J. Am. Chem. Soc.*, **89**, 6904 (1967).
(5) L. Herk, M. Feld, and M. Szwarc, *ibid.*, **83**, 2998 (1961).
(6) S. Oae, T. Kitao, and Y. Kitashy, *ibid.*, **84**, 3359 (1962); V. J. Traynelis and A. I. Gallagher, *ibid.*, **87**, 5710 (1965).
(7) R. Huisgen and R. Horeld, *Ann.*, **562**, 137 (1949).
(8) T. Koenig, *J. Am. Chem. Soc.*, **88**, 4045 (1966); T. Cohen and J. H. Fager, *ibid.*, **87**, 5701 (1965).
(9) C. Rüchardt and E. Merz, *Tetrahedron Letters*, 2431 (1964); C. Rüchardt and B. Freudenberg, *ibid.*, 3623 (1964).
(10) J. C. Martin, J. W. Taylor, and E. H. Drew, *J. Am. Chem. Soc.*, **89**, 129 (1967); H. J. Shine, J. A. Waters, and D. M. Hoffman, *ibid.*, **85**, 3613 (1963).
(11) M. T. Jones and S. Weissman, *ibid.*, **84**, 4269 (1962).

Table I. Products[a] of Acetate-Catalyzed Decomposition of Acetyl Peroxide at Room Temperature

A_0, M	P_0, M	$CH_3CO_2CH_2CO_2H$[b]	CO_2[c]	CH_4[c]	$CH_3CO_2CH_3$[d]
0.5	0.2[e,h]	65	19	9.5	11
0.4	0.2[e]	67	15	5	
0.4	0.1[e,f]		16	6	
0.4	0.1[g]	71	12	5	
0.009	0.06[i]	79	17	3	

[a] Moles/mole of peroxide. [b] By nmr analysis. [c] By vacuum techniques on a calibrated vacuum system. [d] Glpc analysis. [e] Dimethylformamide solvent. [f] 0.9 M acetic acid added. [g] Acetonitrile solvent. [h] Residue contained solvent derived dimers. [i] Chlorobenzene solvent at 60°.

eventually formed from the peroxide. This factor (n) corrects for side reactions such as induced decomposition and cage formation of esters.

The differential equations for this reacting system can be solved using the usual steady-state assumptions and by eliminating time as a variable. The solution is

$$R + 1 = \frac{(nP_0/A_0)\alpha}{1 - e^{-\beta\alpha}} \quad (1)$$

where R is the ratio of unlabeled to labeled carbon dioxide produced, P_0 is initial peroxide concentration, A_0 is initial salt concentration (assumed to be constant), α is fraction reaction and β is given by

$$\beta = \frac{nP_0k_e}{k_eA_0 + k_2} \quad (2)$$

The physically significant rate constant ratio is

$$\frac{k_2}{k_eA_0} = \frac{nP_0}{\beta A_0} - 1 \quad (3)$$

At short reaction time [lim ($\alpha \rightarrow 0$)]

$$\frac{k_2}{k_eA_0} = R \quad (4)$$

Thus the measurement of the radioactivity in the carbon dioxide as a function of fraction reaction or at very short reaction times should yield the ratio of the rate constant for decarboxylation to that for exchange with the added acetate salts.[12]

Initial experiments with low concentrations of carbon-14-labeled acetate ion were encouraging but high concentrations of acetate ion produced a new reaction of acetyl peroxide which had to be dealt with first before the exchange results could be interpreted.

Results

Acetate-Catalyzed Decomposition of Acetyl Peroxide. When acetyl peroxide, in solvents such as dimethylformamide or acetonitrile, is added to solutions of tetraalkylammonium acetates, a rapid reaction occurs giving the products shown in Table I.

$$(CH_3CO_2)_2 \rightarrow \underset{\mathbf{1}}{CH_3CO_2CH_2CO_2H} + CO_2 + \underset{\mathbf{2}}{CH_3CO_2CH_3} + CH_4$$

(12) Initial experiments were carried out with oxygen-18-labeled peroxide and normal abundance acetate salts. These results were found to be unreliable because of the catalysis by the acetate ion of exchange of the oxygen-18 atoms of the carbon dioxide with spurious water.

Table II. Kinetics of Acetate-Catalyzed Reaction in Dimethylformamide

P_0, M	A_0, M	HOAc	$\Delta s/\Delta t$,[b] mol/min
A. Psuedo-Zero-Order Disappearance of Di-*t*-butyl Nitroxide[a]			
0.0549	0.387	0.0785	31.8
0.0549	0.387	0.14	20.9
0.0549	0.387	0.29	6.5
0.080	0.77	0.27	36.5
0.160	0.77	0.27	72.5
0.160	0.35	0.27	31.3
B. Titrimetric Rates			
			$t/2$[c], min
0.12	0.45	...	8
0.10	0.45	0.022	17.0
0.10	0.45	0.043	20.0
0.10	0.45	0.065	22.0

[a] Nitroxide concentration was 1×10^{-3} M. [b] Pseudo-zero-order slope. [c] Time for half-reaction.

The production of methane suggests that some radicals are formed during this process and further evidence for this was the observation of disappearance of the di-*t*-butyl nitroxide esr signal under these conditions. We took advantage of this fact to measure the psuedo-zero-order kinetics of the reaction. The results of these measurements are shown in Table II, along with the titrimetric rates of reaction.

The zero-order results indicate the reaction is approximately first order each in acetate ion and peroxide and shows inhibition by added (or product) acid. The order in acid is complicated by possible variations in the moles of scavengable radicals per mole of peroxide which are produced with varying acid concentration. The inverse order is approximately 1.

The titrimetric rates are consistent with zero-order rates if the efficiency of radical production is about 20%. They show again the inhibition by acid. Plots of the integrated form of (5) appear to be linear for the first one and one-half half-lives.

$$\frac{-dp}{dt} = \frac{k(\text{peroxide})(\text{acetate})}{(\text{acid})} \quad (5)$$

The inhibition by added acid does not appear to be a result of any rapid reversible proton transfers from the acetyl peroxide since addition of deuterioacetic acid does not lead to any extensive deuteration of the peroxide under the reaction conditions. This was determined by the absence of any detectable decrease in the nmr peak of the peroxide in the presence of acetate ion and a large excess of deuterioacetic acid.

Table III. Carbon-14 Distribution[a] in Acetate-Catalyzed Decomposition Products[c]

P_0, M	A_0, M	f(ester)	f(acetamide)	f(hydroxyamide)	$f(CO_2)$
0.22	0.37	0.307			0.017
0.21	0.74	0.45	0.46		
0.21	0.88	0.45	0.45	0.0029	
b	0.37	0.0004			

[a] Room temperature reaction in dimethylformamide. Results given as fraction of labeled product (f). [b] A control sample of acetoxyacetic acid (0.22 M) which was subjected to the reaction conditions and reisolated. [c] Carbon-14 content of peroxide reisolated after partial reaction was negligible. See Table V.

Table IV. Oxygen-18 Results[a] from Acetate-Catalyzed Decomposition of Acetyl Peroxide-*Carbonyl*-^{18}O (Scheme II)

P_0, M	A_0, M	Peroxide[b] ($2w$)	Ester ($x + y + 2z$)	Amide (x)	Hydroxyamide ($y + z$)
0.15	0.52	2.68	1.96	0.40	0.93
0.21	0.74[f]	2.76	1.95	0.40	0.95
0.21	0.88[c]	2.38	1.71	0.35	0.83
c			0.90, 0.90	1.79, 1.79	
d			1.23	1.14	0.01
e		1.71, 1.75			

[a] Numbers listed are atom % excess oxygen-18 per molecule. [b] From the carbon dioxide from direct decomposition in the absence of acetate ion. [c] Authentically labeled samples subjected to repeated purification procedures. [d] Authentically labeled ester from methyl glycolate and acetyl chloride-^{18}O, subjected to ammonolysis. [e] As methyl acetate from the peroxide after 0 and 40% reaction. [f] Using carbon-14-labeled acetate.

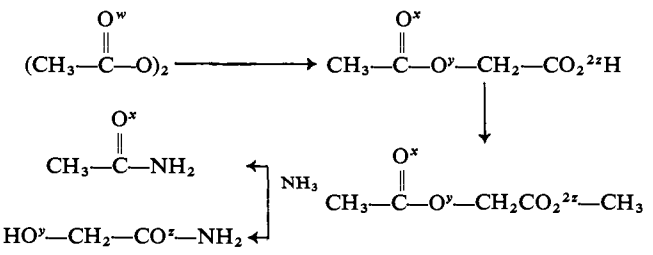
Table V. Exchange Results[a]

Solvent	Temp, °C	A_0, M	P_0, M	R[b]	α	k_d/k_eA_0	n	$k_0 \times 10^5$ [c]
C_6H_5Cl	60	...	0.04599	...	1	...	1.1	0.55
C_6H_5Cl	60	0.00976	0.0586	98.01	0.38	0.96	0.21[e]	1.33
C_6H_5Cl[d]	55	...	...	90.74	1			
C_6H_5Cl	60	0.00978	0.0586	84.03	0.52	0.82	0.17[e]	0.93
C_6H_5Cl[d]	55			76.1	1			
C_6H_5Cl	60	0.00242	0.0653	455.62	0.31	1.1	0.17[e]	0.916
C_6H_5Cl[d]	85			718.42	1			
DMF	25	0.317	0.237	58.2	1	(17.8)	0.2	
DMF	25	0.317	0.237	64.4	0.1	(18.5)	0.2	
DMF			0.116	216.4				

[a] The definitions of A_0, P_0, R, α, k_d, and k_e are those referred to in eq 1. [b] Ratio of unlabeled to carbon-14-labeled carbon dioxide produced. [c] Titrimetric rate constants. [d] Carbon dioxide obtained from the peroxide reisolated and purified after prior partial decomposition in the presence of labeled salt. [e] Acetoxyacetic acid is the main product under these conditions.

The acetate-catalyzed reaction was also carried out with carbon-14-labeled acetate ion. The product (**2**) was isolated as the methyl ester and its carbon-14 content determined. It was then cleaved in liquid ammonia (Scheme II) to acetamide and α-hydroxyacetamide. These two products were also analyzed for radioactivity. A sample of the product acid was subjected to the reaction conditions, reisolated, and its carbon-14 content determined. The results of these studies are summarized in Table III.

Scheme II



The reaction was also carried out starting with acetyl peroxide which was labeled with oxygen-18 in the carbonyl position. The product acetoxyacetic acid was isolated as the methyl ester and its oxygen-18 content determined by combustion to carbon dioxide. A sample of the product was then subjected to ammolysis conditions (Scheme II) to effect the cleavage to acetamide and hydroxyacetamide. These two products were also analyzed for oxygen-18 content. Control experiments showed that no label is lost from authentically labeled materials by the purification procedures. A sample of methyl acetoxyacetate obtained from methyl glycolate and acetyl chloride-^{18}O was subjected to the cleavage reaction. Essentially all of the label was found in the acetamide product. The oxygen-18-labeled peroxide was reisolated after 40% decomposition and treated with methoxide ion. The oxygen-18 content of the methyl acetate thus produced was essentially the same as that obtained from the identical treatment of the initial peroxide. These results are summarized in Table IV.

Electron Exchange. The rates and gaseous products of

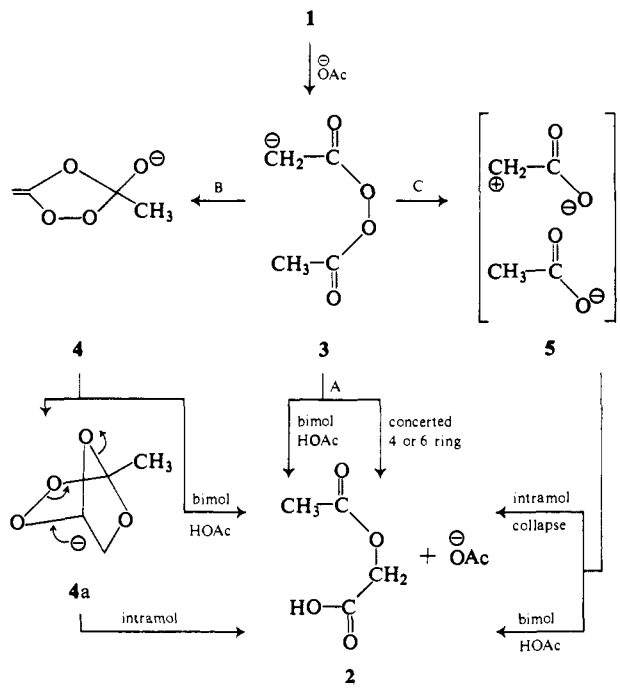
decomposition of acetyl peroxide in chlorobenzene solvent alone and with small amounts of added tetraethylammonium acetate were first compared. The carbon dioxide from decomposition of the peroxide in the presence of small amounts of carbon-14-labeled acetate was collected and its radioactivity determined. The peroxide remaining after 50% decomposition was assayed for radioactivity after washing out the salt. These results are summarized in Table V.

Discussion

While the original goal of the present research was to test for the possibility of electron exchange between acetoxy radical and acetate ion, the new reaction of the peroxide which is catalyzed by acetate ion, has to be dealt with before an interpretation of electron-exchange results can be made. From the stoichiometry of the reaction and the fact that acetate ion is a strong base in aprotic media,[13] it seems likely that the first step in this reaction is removal of a proton from the peroxide to give an enolate species. The inhibition by added acid could be interpreted as being an indication of this equilibrium. However, deuterium is not rapidly incorporated into the peroxide when deuterioacetic acid is added. Thus, the inhibition must be a result of a reduction of the basicity of the acetate, possibly by complexation with the added acid. This would then make the rate-determining step the formation of the enolate species.

Several mechanistic paths for formation of the product from the enolate species can be imagined. These are summarized in Scheme III.

Scheme III



The most direct possibility would be concerted rearrangement of the enolate *via* a four- or six-ring transition state. The fact that the product (2) incorporates some external acetate (carbon-14 data of Table III) rules against this or any other strictly intramolecular path as the sole pathway. External attack of acetic acid on **3** would be the simplest possibility to account for this observation. The incorporation of external acetate is not statistical. The controls with the product show the label is not incorporated after its formation. Thus, the mechanism for product formation cannot be solely intermolecular. Combination mechanisms with both intramolecular and intermolecular branches occurring in competition must therefore be operative.

Alternatives which are more complicated than A but which account for the above observations as well, are the formation of an ozonide structure (**4**) which could rearrange in an intramolecular fashion through **4a** to give the product or suffer attack at the methylene position by acetic acid. Enolate **3** could also decompose to the "α-lactone"–acetate pair (**5**) which would collapse in an intramolecular fashion to give the product. The α-lactone fragment could also suffer attack by external acetic acid if its lifetime were sufficiently long.[14]

The oxygen-18 experiments were carried out with the hope of distinguishing between these possibilities. The results, summarized in Table IV, indicate that the oxygen atoms of the acetoxy group are largely randomized. The methyl acetate obtained from methoxide treatment of samples of carbonyl-labeled peroxide after zero and 40% reaction contained the same amount of label so that the randomization does not precede decomposition. The ammonolysis of authentically labeled acetoxyacetic acid ester obtained from acetyl chloride-^{18}O and methyl glycolate, gave acetamide with nearly all of the label originally present in the ester. Thus, the randomization does not occur during this step.

The total oxygen-18 content of the product ester should be reduced from that in the peroxide to the extent that external acetate is incorporated. The last two runs in Table IV were carried out with carbon-14-labeled acetate ion. This allows an estimate of the fraction intermolecular reaction which gives acetoxyacetic acid without oxygen-18 in the acetoxy group. When this correction is made, esters containing 2.12 and 1.84 atom % excess oxygen-18 per molecule, respectively, are predicted. These are both higher in total oxygen-18 content than observed. The degree of incorporation of external acetate in the acetoxy group of the product can also be calculated from the oxygen-18 data as $1 - [(x + y)/w]$. The values from Table IV are 0.47 and 0.45 compared to the carbon-14 results of 0.45 and 0.45. Thus it is apparent that the loss of oxygen-18 is from the carboxy group. The carbon-14 content of the hydroxyacetamide is negligible so that oxygen atom exchange alone is what occurs. This exchange could well take place during the esterification step in the isolation procedure which requires acidification before treatment with diazomethane.

The exact extent to which the oxygen atoms of the acetoxy group in the product (**2**) are randomized is

(13) B. W. Clare, D. Cook, E. C. F. Ko, Y. C. Mac, and A. J. Parker, *J. Am. Chem. Soc.*, **88**, 1911 (1966).

(14) We have purposely avoided explicit consideration of the alternative possible forms of **3**, **4**, and **5** which are protonated on oxygen. If it is true that the inhibition by added acid is a result of complexation of the acetate ion by the added (or product) acid then the exact position of protonation during the reaction is a very complicated question which we have formally dealt with in only one of several possible ways, *i.e.*, by assuming external attack occurs by acetic acid where both the proton and a nucleophilic center are involved in the reaction.

uncertain because of the loss of label in the esterification and apparently in the ammonolysis. Ignoring these complications the data of Table IV give fraction equilibration from 85 to 92%. None of the complications appear to be serious enough to affect the qualitative conclusion that equilibration does occur to a considerable extent in the intramolecular path for the formation of **2**.

The intramolecular branches of mechanism A, with four- or six-ring rearrangement, would give product with oxygen-18 specifically in the carbonyl or alkyl position, respectively. The intramolecular branch of mechanism B (**4a**) would give carbonyl-labeled product exclusively. The best *single* rationalization of the near equilibration of oxygen-18 label appears to be mechanism C in which the enolate (**3**) undergoes heterolysis to give the "α-lactone" (or some species resembling it) acetate pair (**5**). The reactivity of such a species might approach that of a carbonium ion and several examples of collapse of cation–acylate ion pairs are known to occur with partial retention of the identity of the carbonyl oxygen atom.[15] Multiple paths are, of course, an alternative.

The intermolecular part of the reaction could arise from the partitioning of **5** between immediate collapse and exchange with external acetate. The formal kinetic model, derived above for electron exchange, is also applicable to this situation with modification of the definitions of parameters as can be seen from inspection of Scheme IV

Scheme IV

$$(RCO_2)_2 \xrightarrow{k_1'} n'\,\mathbf{5}$$

$$\mathbf{5} \xrightarrow{k_2'} \text{product}$$

$$\mathbf{5} + OA^-c^* \overset{k_e}{\rightleftharpoons} \mathbf{5}^*$$

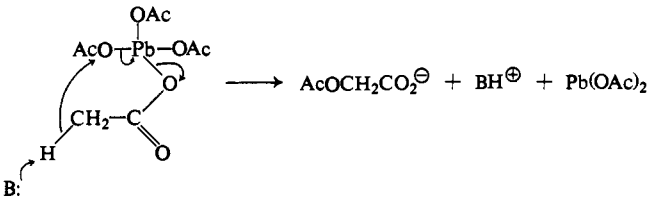
$$\mathbf{5}^* \xrightarrow{k_2'} \text{product}^*$$

where n' is the efficiency factor for formation of **5**, and the other quantities are directly analogous to eq 2 above. This scheme gives rise to eq 6 which predicts the carbon-14 content of the acetoxyacetic acid as a function of concentrations. This equation suggests that a plot of the left-

$$\frac{nP_0}{\ln(R+1) - \ln[R+1-(nP_0/A_0)]} = A_0 + (k_2'/k_e') \quad (6)$$

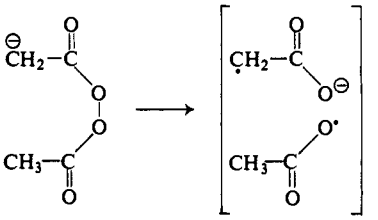
hand member against initial acetate concentration should give a line of unit slope with an intercept equal to k_2'/k_e'. Attempts to treat the data of Table III in this fashion did not produce good linear correlations. However, the function (6) is quite sensitive to the value of n and a very small variation in this quantity with acetate concentration could easily destroy the linearity. The best linear plot was obtained assuming $n = 1$, and had a slope of 1.2 and an intercept of 0.7.

There are few analogies for this type of unit process proposed here. The decomposition of lead tetraacetate in the presence of acetate ion gives similar products.[16] Norman[16b] has very recently proposed that this reaction occurs *via* concerted pathway.



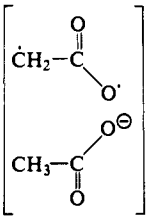
However, the present interpretation could apply equally well to these results. A formally identical sequence has been proposed to explain the oxidation of anhydrides and diphenylketene with pyridine N-oxides.[17] The reaction of phenols with peroxides could also be related.[18]

The origin of the base-catalyzed radical formation is not clearly a consequence of the above interpretation. The enolate species could undergo intramolecular net 1 electron transfer from carbon to oxygen to give radical anion–radical pair **6**. Actually, this intermediate could



6

also give the major product by simple cage collapse. However, the carbon dioxide contains quite a different amount of carbon-14 than the acetoxyacetic acid from the same run. Thus, **6** could only serve to explain the intramolecular part of the reaction. On the other hand, it is not difficult to understand the formation of both **5** and **6** from the enolate since they only differ in the identity of the peroxy oxygen atom (in **3**) which eventually captures the electron. In this sense the structure of **5** might also be written as **5a**.[19] Inter-



5a

mediates **5** and **6** could also be undergoing some interconversion. We therefore rationalize the formation radicals as competitive formation of **6** from the enolate intermediate.

The formation of the methyl acetate product could arise by decarboxylation of the acetoxy fragment of **6** followed by cage collapse on the oxygen atom although

(15) E. H. White and C. A. Aufdermarsh, *J. Am. Chem. Soc.*, **83**, 1179 (1961).

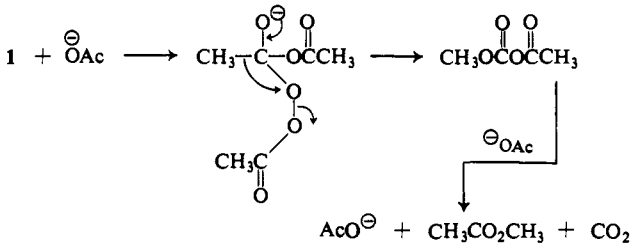
(16) (a) D. Benson, L. H. Sutcliffe, and J. Walkley, *ibid.*, **81**, 4488 (1959); (b) R. O. C. Norman and M. Poutsie, *J. Chem. Soc., B*, 781 (1968).

(17) T. Koenig, *Tetrahedron Letters*, 3127 (1965).

(18) D. B. Denney and D. Z. Denney, *J. Am. Chem. Soc.*, **82**, 1389 (1960).

(19) The detailed structure of what we have chosen to call "α-lactone" is an open question which we are pursuing presently in this as well as other contexts.

the collapse to propionate would be expected to predominate. The ester could also arise from decarboxylation of the acetoxyacetic acid. This process would have to be catalyzed by something produced during the reaction since this product alone is stable to the reaction conditions. The carbonate which would correspond to a carboxy-inversion decomposition of acetyl peroxide does rapidly give carbon dioxide and methyl acetate on exposure to acetate ion. The formation of this product could be acetate catalyzed.



Initial studies of the decomposition of acetyl peroxide in chlorobenzene indicated that low concentrations (*ca.* 10^{-3} *M*) of carbon-14-labeled acetate ion produced only minor changes in the rates and products of the decomposition process. The carbon dioxide contained activity which gave counting levels over 100 times background. The absolute level of activity in the carbon dioxide product was, however, low so that a sufficient understanding of the "side reaction" which was always potentially a contributor to the over-all decomposition process was necessary before any conclusions could be drawn as to the interpretation of the exchange which must occur.

The data of Table V are more recent and show that at 60° the base-catalyzed reaction to form acetoxyacetic acid is still the most important contributor to the destruction of the peroxide. Both rates and *n* values are indicative in this regard. However, our interpretation of this reaction still involves some acetoxy radical formation and the formalism of Scheme I can still be applied particularly at short reaction time. The values of k_2/k_eA_0 are reasonable if one assumes Weissman's[11] value of $\sim 10^9$ for the second-order electron-exchange rate constant. The major perturbation by the operation of the acetoxyacetic acid reaction is the depletion of the labeled acetate ion concentration due to incorporation of the external salt into that product.

A second major factor is the incorporation of carbon-14 into the peroxide itself. This could be a result of a direct bimolecular attack of the external acetate on the O–O bond of the peroxide.[20] Hammond[21] has shown that even when a scavenger molecule is present in moderately low concentration, there is an appreciable probability that a radical pair can be born with a scavenger in its solvation sphere. Since it now appears clear that the acetoxy radical pair is formed reversibly[4] in the decomposition of acetyl peroxide, the simplest rationalization of the data of Table V is the formation of the pair with the acetate ion as a neighbor. The electron exchange could then occur and lead to labeled carbon dioxide as well as labeled peroxide.[22] The results of Table V are preliminary at best but they do seem to justify further work designated to test these ideas. Variations in fractions of exchange with varying absolute salt concentration should prove interesting. Solvent and/or salt variations might also serve to eliminate the induced decomposition which is necessary for more exact application of our kinetic model. The results in DMF already suggest appreciable solvent effects.

(20) Edwards reports the absence of this type of exchange with benzoyl peroxide and benzoate anion: J. O. Edwards, "Peroxide Reaction Mechanisms," J. O. Edwards, Ed., John Wiley & Sons, New York, N. Y., 1962, p 97.

(21) G. S. Hammond and H. P. Waits, *J. Am. Chem. Soc.*, **86**, 1911 (1964).

Experimental Section

Nmr spectra were recorded on a Varian A-60 spectrometer, infrared spectra were recorded on a Beckman IR-5 spectrometer. Esr determinations were made on a Varian 4502 X-band instrument. Liquid scintillation counting was carried out using either a Nuclear Chicago 721 Series or Packard Model 314EX instrument. Mass spectra were determined using a modified Consolidated Electrodynamics 26-614 residual gas analyzer. Quantitative glpc was carried out on a Aerograph Hi-Fy Model 600D using a 5 ft × $^1/_8$ in. column with 5% SE-30 on Chromosorb W. The instrument response was calibrated using known samples. Other glpc analyses were done using either Aerograph Model A90P or Aerograph Autoprep Model A-700 with either 5 ft × $^1/_4$ in. 10% SE-30 on Chromosorb W, 5% SE-30 on Chromosorb W, or 5 ft × $^3/_8$ in. 5% Carbowax on Chromosorb W. Quantitative nmr analyses were done using a weighed amount of an internal standard (methyl benzoate) and weighed amounts of unknown and determining relative peak integrals.

Materials. Acetonitrile, methanol, acetone, ether, isooctane, and carbon tetrachloride were either spectral or analytical reagents from Matheson Coleman and Bell or Mallinckrodt Chemical Works and were used without further purification. Acetonitrile used in the preparation of sodium acetate-^{18}O was distilled from phosphorus pentoxide before use. Chlorobenzene (Matheson Coleman and Bell) was purified by shaking with concentrated sulfuric acid followed by water, then dried over calcium sulfate. Then it was distilled from P_2O_5 followed by distillation from KOH, bp 130°. Purification of dimethylformamide by phosphorus pentoxide reflux and vacuum distillation resulted in no change in experimental results from using spectral or analytical reagent grade (Matheson Coleman and Bell or Mallinkrodt).

Acetyl peroxide was prepared by the method of Price and Morita[23] in 25% yield. Acetyl peroxide-^{18}O was prepared in 20% yield by the method of DeTar[24] from hyperol and acetyl chloride-^{18}O. Acetyl chloride-^{18}O was prepared by hydrolysis of acetonitrile.[25] Acetoxyacetic acid was prepared from acetyl chloride and glycollic acid in 60% yield. Methyl acetoxyacetate was prepared from the acid using diazomethane and from methyl glycolate and acetyl chloride. Di-*t*-butyl nitroxide was prepared by the method of Hoffman[26] from 2-nitro-2-methylpropane in 34% yield. Tetraalkylammonium acetates were prepared by neutralization of the corresponding quaternary ammonium hydroxides with acetic acid.[27] The quaternary ammonium hydroxides were prepared by a modification[28] of Swain's procedure. Acetic acid-1-^{14}C was prepared by addition of 41 mg of sodium acetate-1-^{14}C (1 mCi, New England Nuclear Corp.) to 220 g of acetic acid.

Peroxide concentrations were determined by iodometric titration. Acetate ion concentrations and purity were determined by titration with standard acid. Carbon-14 analyses were done by scintillation counting using 2,5-diphenyloxazole (PPO) and 1,4-bis-2-(5-phenyl-

(22) Decomposition of benzoyl peroxide in the presence of labeled benzoate anion leads to extensive incorporation of label into both the peroxide and the carbon dioxide: unpublished work in these laboratories by J. Taylor.

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oxazoyl)benzene (POPOP, Packard Instrument Co.) as scintillators. Activities of carbon dioxide were determined by absorbing a measured pressure of the gas into a 1 *M* solution of Hyamine-10X (Packard Instrument Co.) in methanol on a calibrated vacuum line, followed by liquid scintillation counting.

Oxygen-18 contents of peroxides were determined by collecting the carbon dioxide formed in their decomposition. This was purified by bulb-to-bulb distillation. The position of the label was established by cleavage with methoxide in methanol to give methyl acetate. The methyl acetate was purified using glpc and analyzed for oxygen-18 by mass spectrometry using the 61/59 peak intensity ratio.[25] The solid samples were analyzed for oxygen-18 by combustion to carbon dioxide using an apparatus modeled after that described by Oliver.[29]

Kinetics. Titrimetric rates were obtained for the decomposition of the peroxide in chlorobenzene (Table V) using sealed ampoules which were immersed in a constant-temperature bath for timed intervals, removed, and quenched by cooling in ice. The ampoules were opened and their contents transferred quantitatively to an isopropyl alcohol solution containing excess potassium iodide and acetic acid. The acetate-catalyzed reactions in dimethylformamide, which occur at room temperature, were followed by removing a measured aliquot at timed intervals and quenching by addition to acetic acid isopropyl alcohol solutions.

The psuedo-zero-order disappearances of di-*t*-butyl nitroxide were followed by placing the acetate and peroxides solutions in separate chambers of a y tube. These solutions were degassed and sealed off under high vacuum. The two solutions were mixed at time zero and quickly inserted into the cavity of the esr spectrometer which had previously been tuned to a similar solution of the nitroxide. The peak intensities *vs.* times were recorded directly by the recorder.

Product Studies. The reactions were studied using two methods. In one method solutions containing peroxide and acetate were placed in separate sections of a breakseal flask, degassed by several freeze–pump–thaw cycles, and sealed under high vacuum. A simpler procedure was to place the peroxide solution in a round-bottomed flask fitted on equilibrium addition funnel which could be attached directly to the vacuum line. The two solutions were evacuated at room temperature and mixed. The reaction could be followed by pressure changes *vs.* time. Both methods gave equivalent results.

In a typical experiment, 5 ml of a DMF solution containing 2.43 mmol of acetyl peroxide was added from a pressure-equalizing addition funnel to 9 mmol of tetraethylammonium acetate in 10 ml of DMF after first degassing the two solutions. After stirring at room temperature for 4 hr, 0.55 mmol of gas had been evolved as determined by the incremental pressure in the known volume of the evacuated system. Quantitative mass spectrometry indicated this gas contained methane and carbon dioxide in a 0.47:1 mole ratio. Methyl acetate could also be detected in some samples. This product was determined quantitatively by glpc after bulb-to-bulb distillation of the first half of the solvent.

The nmr spectrum (in τ values) of the residue remaining after evaporation of the solvent showed the following peaks (besides solvent): singlet, 5.30 (water); singlet, 5.54 (methylene group of **2**); singlet, 7.80 (methyl group of **2**); singlet, 7.97 (methyl group of acetate ion); quartet, 6.71, $J = 8$ cps (methylene group of tetraethylammonium ion); triplet of triplets, 8.71, $J = 8$ cps, $J = 2$ cps (methyl group of tetraethylammonium ion). Addition of authentic acetoxyacetic acid caused peak enlargement of the singlets at τ 7.80 and 5.54. Addition of a weighed amount of methyl benzoate and integration of the nmr peaks indicated a total of 1.6 mmol of acetoxyacetic acid were present. The acid (**2**) could be isolated in poor yield (10–25%) by acidification of the residue and extraction with ether.

The neutral residue contained a complex mixture of compounds whose glpc behavior was similar to the mixture of solvent derived dimers which are formed when acetyl peroxide was decomposed without acetate in that solvent.

For the data of Table III, the procedure was identical except that carbon-14-labeled acetate ion was used. The counting was done on the methyl ester isolated by glpc. A sample of authentic acetoxyacetic acid was subjected to labeled acetate ion and the radioactivity of the methyl ester determined. The oxygen-18 experiments were carried out in an identical fashion using carbonyl-labeled peroxide.

The esterification was carried out by addition of an excess of hydrochloric acid in ether followed by dropwise addition of an ether solution of diazomethane. Evaporation of the ether and preparative glpc using a 15 ft × $\frac{1}{4}$ in. Carbowax column afforded pure methyl acetoxyacetate (20% isolated yield). The conversion of this ester to acetamide and glycolamide was effected simply by the addition of the ester to excess refluxing liquid ammonia. The two amides are obtained in quantitative yield after evaporation and were separated using a column of neutral Woelm alumina and ether eluent. A sample of methyl acetoxyacetate, obtained from methyl glycolate and acetyl chloride-^{18}O, was subjected to the same procedure.

A sample of carbonyl-labeled acetyl peroxide was treated with methoxide in methanol. The resulting methyl acetate was isolated by glpc and analyzed for oxygen-18. A portion of this same peroxide was added to a dimethylformamide solution containing acetate ion for 8 min. The mixture was then quenched by addition to a cold water–ether mixture. The ether solution was washed with dilute sodium bicarbonate, dilute hydrochloric acid and water and dried over calcium chloride. The remaining peroxide was recrystallized from the ether and redissolved in isooctane. This sample of peroxide was then treated with methoxide in methanol and the methyl acetate treated as above.

Test for Proton Exchange in Dimethylformamide. Acetyl peroxide (0.25 ml, 1.27 *M*) and 0.3 ml of tetraethylammonium acetate (1.863 *M*) were mixed in an nmr sample tube. The half-time of the reaction is about 20 min under these conditions. With addition of 0.1 ml of acetic acid (2.058 *M*), repeating the above experiment, the reaction was effectively stopped, *i.e.*, the half-time was greater than 20 min. Using 0.1 ml of acetic acid-1-*d* of (1.88 *M*) no decrease in the nmr peak of the acetyl peroxide was detected under the above conditions. Similarly, no exchange was detected with the addition of 0.1 ml of neat acetic acid-1-*d* or 0.1 ml of neat acetic acid-d_4 under the above reaction time and conditions.

Electron Exchange in Chlorobenzene. An aliquot of a solution of known concentration of acetyl peroxide and tetra-*n*-butylammonium acetate-1-^{14}C in chlorobenzene degassed through at least three freeze–pump–thaw cycles, then the peroxide solution was heated to allow the desired degree of peroxide decomposition. The yield of gas was determined on a calibrated vacuum line. The carbon dioxide was purified by bulb-to-bulb distillation and assayed for carbon-14 content as previously described. For reactions where $\alpha < 1$, an aliquot of the remaining peroxide was titrated to determine α.

Addition of 0.1 ml of chlorobenzene to a standard scintillation sample led to some quenching (27%). The normal gas purification is sufficient to remove chlorobenzene from the gas; any spurious quenching which might occur would be considerably less than 27%.

After CO_2 collection of reactions where $\alpha < 1$, the remaining solution was washed with dilute HCl, dilute $NaHCO_3$, and water (all the acetate is removed under these conditions). The chlorobenzene solution was dried with magnesium sulfate. A portion of the peroxide was degassed in a breakseal flask and complete decomposition was allowed. The activity of the carbon dioxide thus produced was determined.

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