[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

Peresters. VI.[1] Ethyl, Benzyl, *p*-Nitrobenzyl and *p*-Methoxybenzyl *t*-Butylperoxyoxalates

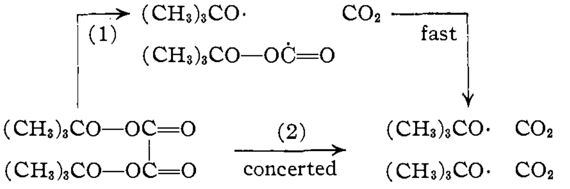
BY PAUL D. BARTLETT AND RICHARD E. PINCOCK

RECEIVED SEPTEMBER 24, 1959

In an exploration of decomposition mechanisms of peresters, a series of compounds have been prepared in which one carboxyl group of oxalic acid is esterified with *t*-butyl hydroperoxide and the other with an alcohol. The products of thermal decomposition of these mixed peresters are those to be expected of concerted O–O and C–C fission, with the carbalkoxy group remaining intact and leading to *t*-butyl alkyl carbonate, alkyl formate and the ester ROOCR′ derived from the solvent R′H. No corresponding products are formed from di-*t*-butyl peroxyoxalate (Part V). The relative first-order rate constants for decomposition of the peresters $ROOCCOO{-}OC(CH_3)_3$ are: R = p-$O_2NC_6H_4CH_2$, 1; $C_6H_5CH_2$, 2.8; C_2H_5, 3.5; p-$CH_3OC_6H_4CH_2$, 5.3; $(CH_3)_3CO$, 20. The rates afford no clear answer to the question whether both O–O bonds of di-*t*-butyl peroxyoxalate (Part V) undergo simultaneous fission in the rate-determining step of its decomposition, or whether one short-lived $(CH_3)_3COOOC\cdot$ radical is involved. In the attack of alkali upon ethyl *t*-butylperoxyoxalate, any initial attack on the carbethoxy group leads to ionic fission of the O–O bond and loss of peroxide titer. The peroxide titer of the hydrolysis product shows that the perester group is attacked about 2.3 times as fast as the ester group.

Introduction

The high rate, low activation energy and simple products of decomposition of di-*t*-butylperoxyoxalate (I) show unequivocally that at least one molecule of carbon dioxide is formed in the rate-determining step,[1] the activation energy being lowered by the incipient formation of this stable compound. It is not so easy to distinguish between the mechanisms 1 and 2, involving participation of two and three bond fissions, respectively, in the rate-determining step. An uncommonly easy bond fission may result either from the formation of a specially stabilized direct product (such as carbon dioxide or benzyl radical) or from a destabilization in the ground state of the decomposing molecule, as in the Swain–Stockmayer–Clarke mechanism for substituent effects in benzoyl peroxides.[2,3] It seemed that ethyl *t*-butylperoxyoxalate (III) might show facilitated decomposition on the second basis but not on the first, and a study of the product and rate of its thermal decomposition should be useful in distinguishing between mechanisms 1 and 2.



Results

Preparation and Properties of Oxalate Peresters.—The general method used to prepare oxalate monoperesters was reaction in the presence of pyridine of mono-*t*-butylperoxyoxalyl chloride (II) with an alcohol. The solvent used was pentane or ether and the temperature was kept between −8 and 0°. The precipitation of white pyridinium chloride occurred immediately, and the reaction mixture was worked up soon after the addition was complete. The mixture was washed with cold solutions of 10% sulfuric acid, 10% sodium carbonate and with water. The pentane phase was dried with magnesium sulfate and either cooled to obtain the crystalline peresters or, in the case of non-crystalline peresters, evaporated under vacuum at less than room temperature to leave the perester as an oily residue. The temperature was usually kept below 10° throughout the preparation. Only in transferring and weighing pure samples of the peresters was the temperature near room temperature for short periods of time.

The low thermal stability of oxalate peresters prevented the use of distillation as a method of purification. Chromatography on Florisil resulted in some decomposition of ethyl *t*-butylperoxyoxalate and this method was considered not to be useful. This limited the purification of the liquid perester to use of thorough washing to remove pyridine, *t*-butyl hydroperoxide and other starting material. The use of pure starting materials and in some cases the use of excess of the more water-soluble reactant made the purifications quite easy. In the case of crystalline peresters recrystallization from pentane between room temperature and −25° was used.

The purity of the samples was determined roughly by iodometric titration in acetic acid.[4] The peroxalates were found to react with iodide ion in acetic acid faster than simple monoperesters under the same conditions, but unless optimum conditions were determined for each perester the results were variable and usually low even on highly purified samples of crystalline di-*t*-butyl peroxyoxalate. The titers given are only rough measures of peroxide content since they are often the result of only one or two titrations under arbitrary conditions unless otherwise noted.

The carbon–hydrogen analyses and the infrared spectra also were used as criteria of purity. The infrared spectrum of each sample of perester was shown to be free of extraneous bands and the only reasonable impurities possible in small amounts would have been hydrocarbons. These would not affect the kinetic studies nor the product studies in the small amounts which may have been present. Usually the complete kinetic and product studies were done using samples from which the analytical sample had been taken.

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(1) Part V, P. D. Bartlett, E. P. Benzing and R. E. Pincock, THIS JOURNAL, **82**, 1762 (1960).

(2) C. G. Swain, W. H. Stockmayer and J. T. Clarke, *ibid.*, **72**, 5426 (1950).

(3) P. D. Bartlett and C. Rüchardt, *ibid.*, **82**, 1756 (1960).

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

The pure peresters were stored at −25° and showed no decomposition over a long period of time at this temperature. A sample of di-*t*-butyl peroxyoxalate over a year old showed no change in crystal form nor peroxide activity. At room temperature most of the peresters slowly decomposed with noticeable change within a week.

All of the oxalate peresters exploded when quickly put into a flame, the compounds containing an aromatic system less violently. With the exception of di-*t*-butyl peroxyoxalate they could be handled easily at room temperature with no special precautions. Di-*t*-butyl peroxyoxalate was especially sensitive to stress and a small crystal of it would explode with surprising force when rubbed on a solid surface with a spatula. All of the peroxalates exploded when placed on a steel block and struck with a hammer.

The infrared spectra of these peresters were distinctive. They all possessed two carbonyl bands usually at 5.56 and 5.70 μ. The bands of the *t*-butyl group always occurred at 3.35, 7.21 and 7.34 μ.

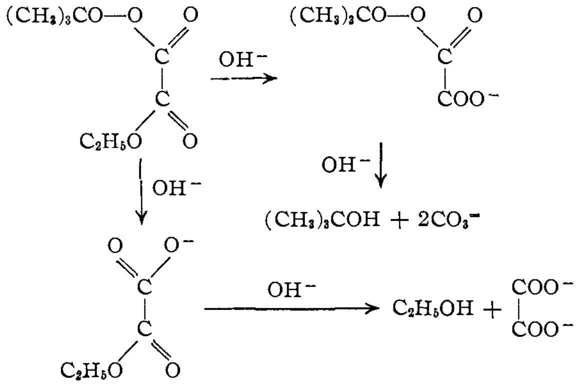
The hydrolytic reactions of several oxalic acid derivatives afford examples of ionic fragmentation reactions.[5] It was noted by Staudinger[6] that oxalyl chloride on hydrolysis yields only hydrogen chloride, carbon dioxide and carbon monoxide. We have found that any reaction which gives rise to the ion $(CH_3)_3CO{-}OOC{-}COO^-$ results in fragmentation to carbon dioxide and *t*-butoxide ion with loss of peroxide titer. This occurs on hydrolysis of *t*-butylperoxyoxalyl chloride

$$\underset{\text{II}}{(CH_3)_3CO{-}OOC{-}COCl} \xrightarrow{H_2O} (CH_3)_3CO{-}OOC{-}COOH + HCl$$

$$\downarrow$$

$$(CH_3)_3COH + 2CO_2 + HCl$$

Since alkyl oxalates hydrolyze normally, the behavior of a monoalkyl monoalkylperoxyoxalate on hydrolysis depends upon whether the initial attack of the hydrolytic agent is upon the carboxyl group bearing the peroxy or the normal alkyl group.



Three weighed samples of ethyl *t*-butylperoxyoxalate were added to 10% barium chloride solutions and hydrolyzed in the presence of excess sodium hydroxide. Immediate precipitation occurred with disappearance of the non-aqueous phase. After about five minutes titration showed the consumption of 2.21, 2.22 and 2.25 equivalents of base per mole of ester. These three solutions were acidified with 1:8 sulfuric acid. A little manganous sulfate was added and the solutions were heated to 90° and titrated with 0.1 *N* potassium permanganate solution. Despite fading endpoints, fair agreement was obtained: 1.03, 1.11 and 1.03 moles of oxalic acid produced per mole of original ester. In three other samples instead of titration of the oxalic acid with permanganate, the *t*-butyl hydroperoxide was titrated with potassium iodide in acetic acid. The results indicated 0.664, 0.714 and 0.645 mole of peroxide per mole of perester.

Of these inconsistent results the least reliable are the oxalate titrations. From the results of the others, we conclude that the first attack of hydroxyl ion on ethyl *t*-butylperoxyoxalate occurs on the perester group to an extent not less than 64% nor more than 89%. It is not unexpected that the inductive effect of the second oxygen atom should make the perester group additionally susceptible to basic hydrolysis.

Decomposition Products.—Studies of the products of thermal decomposition were carried out in benzene and cumene. The purpose of the latter solvent was to provide an environment in which intermediate free radicals would have a maximum chance of capturing a hydrogen atom. Table I shows the results obtained in benzene and cumene.

TABLE I

PRODUCTS OF DECOMPOSITION OF ETHYL *t*-BUTYLPEROXYOXALATE AT 45°

Product	Moles per mole of perester In benzene after 42 hr.	 In cumene after 37 hr.
Carbon dioxide	1.31	1.12
t-Butyl alcohol	0.54	0.75
Acetone	.18	..
Methane	.03	..
Ethane	.11[a]	.20[b]
Ethylene	.04	
Ethyl *t*-butyl carbonate	.23	.28
Ethyl benzoate	.07	..
Ethyl phenyldimethylacetate	..	.23
Ethyl formate	..	.15
Biphenyl	.02	..
Bicumyl	..	.32
t-Butyl group accounted for	.95	1.00
Carbonyl group accounted for	1.62	1.78

[a] Includes some butane. [b] Ethane + ethylene.

Table II shows the product study from benzyl *t*-butylperoxyoxalate in benzene.

As in the case of di-*t*-butyl peroxyoxalate,[1] the effect of cumene as a solvent is seen in shortening the life of the *t*-butoxy radical and converting it to *t*-butyl alcohol rather than allowing its decomposition to acetone and methyl radical as in the case of the benzene solvent. Unlike the case of di-*t*-butyl peroxyoxalate, products of the intact carbethoxy group are found in the form of ethyl benzoate, ethyl *t*-butyl carbonate, ethyl phenyl-

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(5) C. A. Grob, p. 114 in "Theoretical Organic Chemistry" (Kekulé Symposium), Buttersworth Publications, Ltd., London, 1959.

(6) H. Staudinger, *Ber.*, **41**, 3558 (1908).

TABLE II

PRODUCTS OF DECOMPOSITION OF BENZYL *t*-BUTYLPEROXYOXALATE IN BENZENE AT 45° AFTER 108 HOURS

Product	Moles per mole of perester
Carbon dioxide	1.52
t-Butyl alcohol	0.45
Acetone	.22
Methane	.04
Benzyl *t*-butyl carbonate	.24
Bibenzyl	.21
t-Butyl group accounted for	.91
Benzyl group accounted for	.66

dimethylacetate and ethyl formate. The occurrence of these products is evidence that the decomposition of ethyl *t*-butylperoxyoxalate involves fission at only two bonds and that the formation of ethyl radical, when it occurs, is the result of secondary decomposition of the carbethoxy radical. This decomposition is not instantaneous but resembles that of the *t*-butoxy radical in that it can be forestalled by reaction with other radicals or with a good source of hydrogen atoms. The product study thus shows a sharp difference between di-*t*-butyl peroxyoxalate and ethyl *t*-butylperoxyoxalate, but it is not clear from these results alone whether this difference is due to a three-bond decomposition in the former case or to a high degree of instability of the carbo-*t*-butylperoxy radical.

The similarity of products between the benzyl and the ethyl ester indicates that despite the relative stability of the benzyl radical the benzyl-to-oxygen cleavage is not an essential part of this decomposition mechanism either.

Rates of Decomposition.—As with di-*t*-butylperoxyoxalate, the monoethyl and monobenzyl monoperesters decompose thermally with first-order kinetics, the rate being increased by about 20% on increasing the concentration of the perester from 0.04 to 0.4 molar. If this small increase is due to a 3/2 order induced decomposition superposed upon the spontaneous decomposition, then the amount of the induced decomposition[7] in the lower concentration must be very small. Table III summarizes the rate measurements carried out in benzene at three temperatures.

Table IV summarizes the comparative rate constants at 45° for these monoperesters and di-*t*-butyl peroxyoxalate and also summarizes the activation parameters.

It is doubtful whether the small changes in ΔS^* in the series are of any significance. There is a steady decline in rate constant and increase in ΔH^* from di-*t*-butyl peroxyoxalate to *p*-nitrobenzyl *t*-butyl peroxyoxalate. An attempt to plot the results for the three benzyl esters according to the Hammett equation yields a bent line, concave upward if σ is plotted, and convex if σ^+ is used as the basis of comparison.

TABLE III

FIRST-ORDER RATE CONSTANTS FOR DECOMPOSITION OF MONOPERESTERS ROOCCOOOC$(CH_3)_3$ IN BENZENE

R	Concn., *M*	First-order rate constant, sec.$^{-1}$ × 10^5 45°	55°	65°
C_2H_5	0.0456	4.48		
	.278	4.79		
	.0450		16.3	
	.265		18.3	
	.0480			59.3
	.260			65.3
$C_6H_5CH_2$	.0441	3.64		
	.0445	3.67		
	.480	4.37		
	.0492		13.3	
	.493		15.8	
	.0489			46.9
	.497			53.0
p-$CH_3OC_6H_4CH_2$	.0440	6.69		
	.483	7.74		
	.0485		24.8	
	.489		28.0	
	.0530			82.7
	.494			102.0
p-$O_2NC_6H_4CH_2$	.0452	1.30		
	.474	1.53		
	.0502		4.89	
	.489		6.18	
	.0536			18.9
	.460			21.6

TABLE IV

RELATIVE RATE CONSTANTS AND ACTIVATION PARAMETERS FOR DECOMPOSITION OF ROOCCOOOC$(CH_3)_3$ IN BENZENE

R	Relative rate at 45°	ΔH^*, kcal.	ΔS^*, cal./deg.
$(CH_3)_3CO$	20.0	25.5	5.1
$CH_3OC_6H_4CH_2$	5.2	26.2	4.6
C_2H_5	3.5	26.9	6.0
$C_6H_5CH_2$	2.8	26.6	4.5
$O_2NC_6H_4CH_2$	1.0	27.9	6.8

Decomposition of Ethyl *t*-Butylperoxyoxalate in Isopropyl Ether.—Ethyl *t*-butylperoxyoxalate is much less susceptible to induced decomposition in isopropyl ether than is di-*t*-butyl peroxyoxalate. It was possible to study the rate and products of this decomposition at 45° instead of 0° as was necessary in the case of the diperester. The exothermic reaction raised the temperature of the reacting solution about 1°. Table V summarizes the products from two decompositions of this sort.

TABLE V

DECOMPOSITION OF ETHYL *t*-BUTYLPEROXYOXALATE IN ISOPROPYL ETHER AT 45°

	Mole/mole of original perester I (1.018 g. EBPO in 10 ml. *i*-Pr_2O, 36 hr.)	II (2.533 g. EBPO in 25 ml. *i*-Pr_2O, 42 hr.)
Condensable gases	0.217	0.219
Carbon dioxide (by vol.)	.174	.164
(by wt.)	.170	.165
Isobutylene	.043	.04
Other hydrocarbon		.01
Residue	(.80 g.)	(1.48 g.)
Oxalic acid	.066	0.074

Products identified by infrared spectra: isopropyl alcohol, *t*-butyl alcohol, acetone, ethyl oxalate, isopropenyl isopropyl ether.

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[7] K. Nozaki and P. D. Bartlett, THIS JOURNAL, **68**, 1686 (1946); P. D. Bartlett and K. Nozaki, *ibid.*, **69**, 2299 (1947).

A 0.0476 *M* solution of ethyl *t*-butylperoxyoxalate in isopropyl ether decomposed about 3.5 times as fast as in benzene, and the kinetics was more nearly of the 3/2 order than of any other. However, there was inhibition by the reaction products and it was not possible to make a detailed analysis of the kinetics. These observations, together with the low yield of carbon dioxide, show that the decomposition of isopropyl ether is chiefly induced by attack of ether radicals. A mechanism analogous to that proposed for di-*t*-butyl peroxyoxalate[1] will account for the facts, in view of the fact that in the monoperester attack at the perester group will not cause destruction of the oxalic acid unit. Under the experimental conditions monoethyl oxalate, readily formed in the decomposition, would undergo disproportionation into the diethyl oxalate and oxalic acid which were found among the products.[8] In the presence of oxalic acid, isobutylene is formed from *t*-butyl alcohol even at 45°, and the water formed effects some hydrolysis of the isopropyl isopropenyl ether. The occurrence of these processes was verified in a test decomposition of di-*t*-butyl peroxyoxalate in benzene at 45° in the presence of added oxalic acid.

Discussion

The product studies show a distinction between di-*t*-butyl peroxyoxalate and all the monoperesters indicating that the latter, at least, do not undergo concerted fission at three bonds, whereas this is a possibility for the diperester. The rate studies, on the other hand, show no discontinuity between the monoperesters and the diperester. In rate and activation energy the *p*-methoxy and *p*-nitro substituted monoperesters are farther apart than are the *p*-methoxy compound and the diperester. The ethyl *t*-butylperoxyoxalate ester falls in rate between the benzyl and the *p*-methoxybenzyl. Although these results offer no dramatic evidence for the mechanism of the di-*t*-butylperoxyoxalate decomposition, they are consistent with a simple unifying hypothesis.

We can see from the product studies that the benzyl–oxygen bond is not involved in the rate-determining step of the decomposition of the monoperesters. The effect of substitution in the benzyl group must therefore be exerted through its effect on the remote C–C bond of the oxalate group. Electron withdrawal or accession at this carbon atom must affect the concerted two-bond fission in the same way as discussed for the substituted phenylperacetates in Part IV[3] of this series. The electrostatic nature of this effect accounts for the ethyl ester being as high in the series as it is: despite the cationic stability of the benzyl group (which cannot come into play in these decompositions) the phenyl–C bond of that group has a dipole unfavorable to the development of positive charge on its side of the cleaving oxalate bond. Ethyl, which lacks the aromatic group, has a somewhat more favorable effect.

Now, if di-*t*-butyl peroxyoxalate were to undergo decomposition with the concerted cleavage of only two bonds, the data for the monoperesters would lead us to expect that the inductive effect of that *t*-butylperoxy group not involved in the cleavage would be unfavorable. Oxygen is a strongly electronegative element, and whether we compare the *t*-butylperoxy group, with its considerable anionic stability, to the ethoxy group, or the *t*-butoxy group to the ethyl group, it would be expected that the mono- and diperesters would fall in the opposite order of decomposition rate. The most obvious factor tending toward the observed order is the possible participation of the O–O bond of the second *t*-butylperoxy group in the rate-determining concerted cleavage. The evidence for the three-bond cleavage mechanism is then, not the simplicity of the decomposition products and not the high rate of decomposition of di-*t*-butyl peroxyoxalate, but the extent to which this rate exceeds expectations from the effects of substitution in compounds for which the two-bond mechanism is established.

Experimental

Sources and purification of starting materials were as described in Part V.[1]

_t_-Butylperoxyoxalyl Chloride.—To a stirred solution of 12.6 g. of oxalyl chloride in 40 ml. of anhydrous pentane at 0° was added dropwise over one hour a solution of 4.5 g. of *t*-butyl hydroperoxide in 40 ml. of pentane. The solution was allowed to stand at 0° for 2.5 hours and then the pentane and excess oxalyl chloride was evaporated under reduced pressure while keeping the flask cooled in an ice-bath. The separation was completed by allowing the oily residue to warm to room temperature under vacuum for a few minutes. The colorless oily residue amounted to 8.3 g. (92%) of crude *t*-butylperoxyoxalyl chloride suitable for use in further preparations. That *t*-butyl hydroperoxide, di-*t*-butyl peroxyoxalate or oxalyl chloride were not present in very high concentrations was shown by absence of their characteristic infrared bands. This compound reacts violently with water with liberation of much heat and gas.

The analytical sample was prepared by molecular disillation between room temperature and −70° and had $n^{22}\text{D}$ 1.4232.

Anal. Calcd. for $C_6H_9O_4Cl$: C, 39.90; H, 5.02. Found: C, 40.12; H, 5.12.

Titration of this compound in the absence of water by use of an acetic acid–isopropyl alcohol solution with added solid potassium iodide gave 0.84 to 1.06 equivalents per mole of peroxy acid chloride. These low results were probably caused by the presence of some water in the solvents. At any rate the peroxide content was almost completely destroyed by adding water before the addition of solid potassium iodide. Only 0.1 equivalent of iodine per mole of perester was liberated if it was first hydrolyzed before adding any iodide ion.

Ethyl _t_-Butylperoxyoxalate. Method I.—Monoethyloxalic acid was prepared by equilibration of diethyl oxalate with anhydrous oxalic acid at 130°. The fraction boiling at 62–67° (0.5 mm.) had $n^{18}\text{D}$ 1.4262, reported[9] $n^{20}\text{D}$ 1.4236. Ethoxalyl chloride was prepared from monoethyloxalic acid by refluxing it with thionyl chloride for 11 hours. The fraction boiling at 130–140°, reported[8] 134°, was used for preparation of ethyl *t*-butylperoxyoxalate.

Ethoxalyl chloride, 8.2 g., in 30 ml. of pentane was added over 45 minutes to 4.7 g. of pyridine and 5.4 g. of *t*-butyl hydroperoxide in 40 ml. of pentane at 0°. After washing with 10% sulfuric acid, 10% sodium carbonate and with water, the pentane layer was dried and the pentane evaporated under vacuum at less than room temperature to leave 6.8 g. (59%) of oily ethyl *t*-butylperoxyoxalate. This colorless product had $n^{23}\text{D}$ 1.4172 and was 89% pure by peroxide titration. It slowly decomposes and turns yellow if allowed to stand at room temperature.

Method II.—A solution of 1.4 g. of pyridine and 0.78 g. of absolute ethanol in 20 ml. of pentane was added over 30 minutes to a solution of 3.2 g. of freshly prepared *t*-butyl

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(8) C. Contzen-Crowet, *Bull. soc. chim. Belg.*, **35**, 170 (1926).

(9) E. Fourneau and S. Sabetay, *Bull. soc. chim.*, **41**, 537 (1927); **43**, 859 (1928).

peroxyoxalyl chloride in 20 ml. of pentane at 0°. After working up as in method I, 1.8 g. (54%) of ethyl *t*-butylperoxyoxalate was obtained which was identical by infrared analyses to that prepared by method I.

Anal. Calcd. for $C_8H_{14}O_5$: C, 50.52; H, 7.42. Found: C, 50.86; H, 7.54.

Benzyl *t*-Butylperoxyoxalate.—To 8.3 g. of *t*-butyl peroxyoxalyl chloride in 40 ml. of anhydrous ether at 0° was added dropwise over one hour a solution of 4.0 g. of benzyl alcohol and 3.0 g. of pyridine in 40 ml. of ether. After stirring at 0° for 15 minutes longer the mixture was washed with 10% sulfuric acid solution, 10% sodium carbonate solution and with water. Drying and evaporation of the ether left 5.8 g. (62%) of oily residue which crystallized on shaking. After slow recrystallization with seeding from pentane between room temperature and −25° the fine white crystals melted at 33.0–34.2° at a heating rate of 2 degrees per minute. This perester was 88.8% pure by peroxide titration. The use of an excess of the acid chloride in this preparation makes the purification of the product easier since the excess is converted to water-soluble compounds on hydrolysis.

Anal. Calcd. for $C_{13}H_{16}O_5$: C, 61.89; H, 6.39. Found: C, 61.89; H, 6.22.

***p*-Methoxybenzyl *t*-Butylperoxyoxalate.**—*t*-Butylperoxyoxalyl chloride, 8.2 g., reacted with 3 g. of pyridine and 5.2 g. of anisyl alcohol in anhydrous ether at 0°. After working up by washing as usual, 7.7 g. (72%) of a thick oil was obtained. The compound failed to crystallize but titrated 87.4% pure. It was insoluble in pentane at room temperature, soluble in benzene and carbon tetrachloride and separated from cyclohexane as an oil when the solution was cooled.

Anal. Calcd. for $C_{14}H_{18}O_6$: C, 59.56; H, 6.43. Found: C, 59.43; H, 6.78.

***p*-Nitrobenzyl *t*-Butylperoxyoxalate.**—*t*-Butylperoxyoxalyl chloride, 8.6 g., in 40 ml. of ether was cooled to 0° and a solution of 6.1 g. of *p*-nitrobenzyl alcohol and 3.2 g. of pyridine in about 100 ml. of ether was added over 45 minutes. After stirring at 0° for an hour and working up as usual the ether was evaporated under vacuum to leave a white solid residue. This was recrystallized from 50% pentane–ether to yield 4.5 g. (38%) of white fluffy needles with melting point 62.5–64° at a heating rate of 1 degree per minute. More perester can be recovered from the mother liquors. Peroxide titration indicated 91.4% purity. This compound was stable when rubbed with a spatula and a sample of it appeared to be stable at room temperature for over two weeks.

Anal. Calcd. for $C_{13}H_{15}O_7N$; C, 52.52; H, 5.09. Found: C, 52.38; H, 5.12.

Kinetic and Product Study Procedures.—The general procedure for kinetic and product studies was as described in Part V.

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[CONTRIBUTION NO. 46 FROM THE GRADUATE DEPARTMENT OF BIOCHEMISTRY, BRANDEIS UNIVERSITY]

The Effect of Structure on Reactivity in Semicarbazone Formation[1]

BY BRUCE M. ANDERSON AND WILLIAM P. JENCKS

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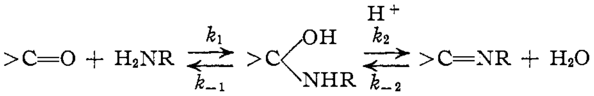
The rate and equilibrium constants for the individual steps of semicarbazone formation from a series of substituted benzaldehydes exhibit linear ρ–σ correlations: the rate and equilibrium constants of the addition step are favored by electron withdrawal and the acid-catalyzed dehydration step is favored by electron-donating substituents. The observed rate constants for semicarbazone formation at neutral *p*H are the resultant of these opposing effects and show only a slight variation with σ. At acid *p*H the rate constants increase with electron-withdrawing substituents, as expected for a shift to a rate-limiting addition step, and at an intermediate *p*H there is a break in the ρ–σ curve. Semicarbazone formation from carbonyl compounds with electron-withdrawing substituents is also subject to base catalysis, which may prove to be a useful preparative method.

In a recent study of oxime and semicarbazone formation,[2] evidence was presented in support of the reaction path



$$>C=O + H_2NR \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} >C\begin{matrix}OH\\NHR\end{matrix} \underset{k_{-2}}{\overset{H^+\;k_2}{\rightleftarrows}} >C=NR + H_2O$$

In the case of semicarbazone formation at neutral *p*H, the first step in the reaction is the rapid attack of the nitrogen base upon the carbonyl compound to form an intermediate addition compound. The second step is the rate-limiting, acid-catalyzed dehydration of the intermediate addition compound to form semicarbazone. Methods were described for the determination of the separate rate and equilibrium constants for these reactions. It was of interest to examine the electronic effects upon the individual steps by studying the reactions of a series of substituted benzaldehydes. The present report describes ρ–σ relationships for the individual steps in the formation of semicarbazones and a base catalysis of semicarbazone formation from benzaldehydes substituted with electron-withdrawing groups.

Experimental

Materials.—The carbonyl compounds were either redistilled under nitrogen at reduced pressure or twice recrystallized and were stored at −15°. Solutions of the carbonyl compounds in 25% ethanol containing 10^{-4} *M* ethylenediaminetetraacetic acid were made up just before use. Solutions of twice-recrystallized semicarbazide hydrochloride were neutralized with NaOH just before use. Glass-distilled water was used throughout. Solutions of semicarbazide in D_2O were prepared by dissolving semicarbazide hydrochloride in 99.8% D_2O, evaporating to dryness, and redissolving in D_2O at the desired concentration. The D_2O solutions of semicarbazide hydrochloride were neutralized with NaOD prepared by a similar procedure.

Ultraviolet measurements were made on a Beckman model DU spectrophotometer or a Zeiss model PMQ II spectrophotometer. Infrared spectra were obtained with a Perkin–Elmer model 21 spectrophotometer using KBr pellets.

Kinetic measurements were carried out spectrophotometrically as previously described.[2] All kinetic determinations were made with the concentration of semicarbazide greatly in excess of that of the carbonyl compound so that pseudo first-order kinetics were obtained. The reactions were studied in 25% ethanol (25 vol. ethanol–75 vol. water) and NaCl was used to maintain a constant ionic strength of

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(1) Presented at the 135th National Meeting of the American Chemical Society in Boston, Mass., April, 1959.

(2) W. P. Jencks, THIS JOURNAL, **81**, 475 (1959).