

FREE RADICAL PATHWAY FOR THE BAEYER-VILLIGER REACTION

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(Received 12 April 1967; in revised form 17 May 1967)

There is a great deal of interest in the stereochemistry of the Baeyer-Villiger reaction and the nature of the factors which influence the preferential migration of one group over another (2,3). This communication presents evidence for a free radical pathway for this reaction in addition to the accepted cationic mechanism (4,5,6).

We have determined the migratory aptitudes of substituted phenyl in the Baeyer-Villiger reaction for a series of p,p'-unsymmetrically substituted benzophenones. Both peroxyacetic acid and trifluoroperoxyacetic acid in refluxing methylene chloride were investigated as the oxidizing agents in the reaction. Trifluoroacetic acid was used as the acid catalyst (5) in all the reactions studied to facilitate the nucleophilic attack of the peroxyacid on the carbonyl carbon. The ester products from each reaction were hydrolyzed, and the relative yields of the two benzoic acids determined spectrophotometrically. These data were used to obtain the migratory aptitudes shown in Tables I and II.

When trifluoroperoxyacetic acid was used as the oxidizing agent the results shown in Table I were obtained. The typical order for activation (toward electrophiles) of the ring is found, that is, activating groups favor migration and electron-withdrawing groups retard migration. A Hammett plot of the data gives a good line with a ρ value of -0.77 (the migration step). This value is in agreement with the results of Hawthorne and Emmons (5), who obtained a ρ value of -1.10 for the total reaction in ethylene chloride.* Part of the discrepancy between the two values is due to the different values of σ used to obtain ρ . The value of -0.77 was obtained from a σ^+ plot and the value of -1.10 was obtained from a σ plot. The fact that both values are small and negative adds support to the accepted mechanism. The migratory aptitudes are in agreement with what would be expected from a cationic transition state.

* Hawthorne and Emmons obtained their value by measuring the overall rate of the reaction and suggest that for the rearrangement step is a major contributor to the reported ρ value.

TABLE I
Relative Migratory Aptitude of p-Substituted Phenyl Groups
Using Trifluoroperoxyacetic Acid

p-Substituent	Migratory Aptitude	p-Substituent	Migratory Aptitude
NO ₂	1.00	Br	13.94
t-Butyl	7.93	CH ₃	26.05
Cl	12.15	CH ₃ O	251.00

When peroxyacetic acid was used as the oxidizing agent, the results shown in Table II were obtained. These data do not support an ionic mechanism. A Hammett plot of the data, in contrast to the earlier results with trifluoroperoxyacetic acid, shows no correlation. Examination of Table II reveals that groups which are deactivating relative to hydrogen in aromatic electrophilic substitution actually enhance migration of the phenyl ring to which they are attached. This order of migration is observed in known free radical migrations. Bartlett and Cotman (7) studied the thermal decomposition of p-nitrotriphenylmethyl hydroperoxide and found the ratio of phenyl migration to p-nitrophenyl migration was from 1:3 to 1:4 and suggested that enhanced p-nitrophenyl migration is a good test for a free radical mechanism.

TABLE II
Relative Migratory Aptitude of p-Substituted Phenyl Groups
Using Peroxyacetic Acid

p-Substituent	Migratory Aptitude	p-Substituent	Migratory Aptitude
H	1.00	CH ₃	8.88
Cl	1.22	OH	26.80
Br	2.14	CH ₃	152.50
NO ₂	3.20		

Augood, Hey and Williams (8) determined the rates at which phenyl radicals, generated by the decomposition of benzoyl peroxide, attack benzene, chlorobenzene and nitrobenzene. The observed rate ratios are 1 (benzene):1.7 (chlorobenzene):4.0 (nitrobenzene) which are in good agreement with the relative rates of migration which we have observed for these

three groups in the Baeyer-Villiger Reaction; 1 (benzene):1.2 (chlorobenzene):3.2 (nitrobenzene).

The change in mechanism with the change in oxidizing agent can be explained by the following rationale: The Criegee intermediate, formed by the attack of the peracid on the carbonyl carbon of the ketone-acid complex, may decompose by either heterolytic or homolytic cleavage of the oxygen-oxygen bond. The accepted cationic mechanism calls for heterolytic cleavage of this bond, a process which is enhanced by the strong inductive effect of the trifluoroacetyl group, however, when peroxyacetic acid is used as the oxidant the much smaller inductive effect of the acetyl group favors homolytic cleavage and leads to a free radical rearrangement. It is possible that the more active aryl groups still migrate by a cationic mechanism or perhaps both mechanisms are open to these groups. We feel that in as much as all substituents will stabilize a free radical relative to hydrogen that the enhanced migration of both +R and -R groups relative to hydrogen is not "a priori" evidence of a change in mechanism with a change in the nature of the substituent group. Other factors that undoubtedly affect the mechanism are the ionizing power of the solvent, the nature of the acid catalyst and the temperature of the reaction.

It might be expected that a change in mechanism would lead to a change in products. Aryl migration to oxygen radicals is well documented (7,9) so the ester product resulting from such a migration in the Baeyer-Villiger reaction should be no surprise. One would expect to observe the evolution of carbon dioxide from acetoxy radicals produced in the homolytic cleavage. We have not observed a gross evolution of gas from the system and are currently running experiments to determine the yield of carbon dioxide. A low yield of carbon dioxide would not be unexpected. It is easy to visualize the free acetoxy radical abstracting a hydrogen from the protonated oxygen of the incipient ester while within the solvent cage.* It is in an excellent position to do so, the carbonyl oxygen of the acetoxy group is very likely hydrogen bonded to this proton in the Criegee intermediate, and this conformation is likely to continue even during the homolytic cleavage.

The free radical mechanism explains the anomalous migrations of p-chlorophenyl and

* Martin, Taylor and Drew (10) have observed the reaction of acetoxy radicals with cyclohexene within the solvent cage to form the ester and report that this reaction is competitive with decarboxylation.

p-bromophenyl during the Baeyer-Villiger oxidation (using peroxyacetic acid) of the p-halobenzophenones in the absence of sulfuric acid as observed by Doering and Speers (11).

A free radical mechanism is consistent with the data for our system under the conditions employed; substituted benzophenones oxidized with peroxyacetic acid in methylene chloride solvent using trifluoroacetic acid as the acid catalyst.

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