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BASE CATALYSED CLEAVAGE OF PHENACYLTRIALKYLAMMONIUM SALTS[+]

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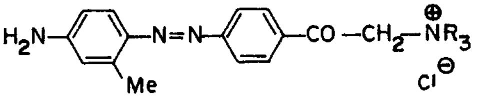
Among the various transformations that phenacyltrialkylammonium salts can undergo under the influence of bases,[1,2] formation of acetophenones does not appear to have been observed so far. We wish to report here some instances of this reaction and consider evidence which suggests that it is a redox cleavage involving oxidation of one of the alkyls of the quaternary ammonium moiety.

When 4-(2'-methyl-4'-aminophenylazo)-phenacyltrimethylammonium chloride (I_a, R=Me; 1 g) was treated with sodium hydroxide (0.8 - 1.0 g) in 80% ethanol (20-30 ml) for 2 to 3 hrs at reflux and the reaction products submitted to chromatography (silica gel, benzene), a pale orange compound (m.p. 152°) was isolated which was recognized to be (II) on the basis of elemental analysis and spectral data. The product mixture for chromatography was obtained as a brown powder by concentration of the reaction mixture to half its original volume followed by precipitation with excess of water. Compound (II) had a mass spectral molecular weight of 253, and IR absorptions at 1660, 3050 and 3150 cm^{-1} showed that the carbonyl and amino functions of the starting material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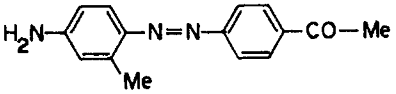
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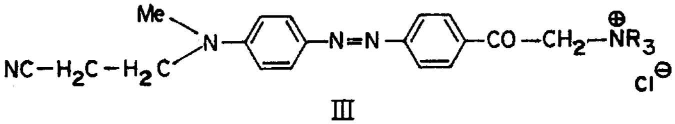
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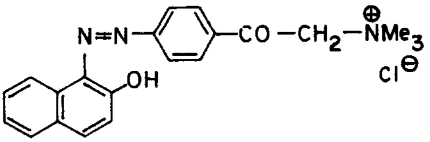
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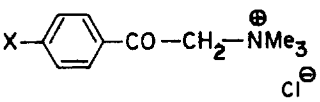
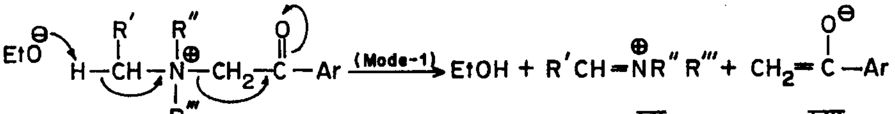

V

were intact in it. The NMR spectrum showed the absence of the trimethylammonium and methylene groups of the starting material. The presence of a new singlet three proton signal at 7.33 τ, was assignable to a methyl ketone. The yield of this product was about 27%. Similar results were obtained with compounds III and IV and the corresponding yields of aryl methyl ketones (m.p's 130 and 181°) were 25 and 22% respectively.

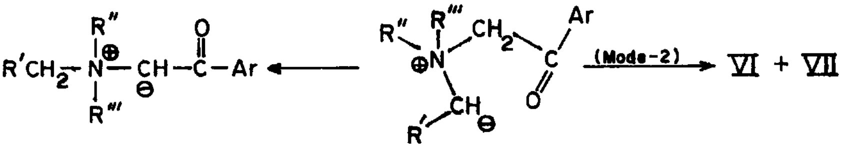
The reduction of the C-N linkage involved in the reaction suggested that it can take place in one of two ways, one involving oxidation of solvent alcohol and the other involving oxidation of one of the methyls of the trimethylammonium moiety. For the first of these two possibilities, acetaldehyde and trimethylamine would be the reaction products. Although the former of these products would be expected to undergo condensation reactions under the reaction conditions, the reaction mixture could still be expected to indicate the presence of aldehydes. On the other hand, if the reduction of the phenacyl moiety had involved the oxidation of one of the methyls of the trimethylammonium moiety, formaldehyde and dimethylamine would be the anticipated products. The reaction mixture gave only a weak test with Tollens reagent, but, dimethylamine could be definitely identified as a reaction product by distilling the reaction mixture and passing the issuing vapours into a solution of picryl chloride in acetone. Evaporation of this solution and chromatography of the residue gave small amounts of the known 1:1 adduct[3] of N,N-dimethylpicramide with picryl chloride. There was no indication of the presence of any trimethylpicrylammonium chloride in the mixture. The dimethyl picramide - picrylchloride adduct was identified by comparison of its m.p., elemental analysis and NMR spectrum with those of an authentic sample. The cleavage reaction had apparently taken the second course. Most of the formaldehyde that was formed in the reaction was presumably destroyed in a Cannizaro reaction under the reaction conditions. The above conclusion regarding the nature of the reaction was verified by submitting the triethyl analogue (I_b, R=Et) of (I_a) to the reaction. In this case, the reaction mixture gave a positve Tollens test with the reaction mixture. The test was stronger with the brown powder than with the liquor from which it was separated, showing that the acetaldehyde formed in the reaction had undergone complex condensation reactions.

In an attempt to get some idea of the electronic requirements for the reaction, it was tried with unsubstituted phenacyltrimethylammonium chloride (V, X=H) as well as its p-acetamido and p-nitro derivatives (V, X=NHAc and NO_2). The first two of these did not give any reduction products, but, with the nitro derivative, p-nitropropiophenone (m.p. 112°) was obtained in very small yields (~ 6%). An electron acceptor group in the para position of the phenacyl moiety is apparently necessary for the reaction. Its absence or the presence of an electron donor group in the same position has a deleterious effect on the same. Moreover, the reaction did not seem to take place in a purely aqueous or purely alcoholic medium. This appears to suggest two things: first, the effective reagent in the aqueous ethanolic solution is the ethoxide ion rather than the hydroxide ion which is apparently not a strong enough base and, second, the presence of water helps the reaction by making the medium more strongly solvating.

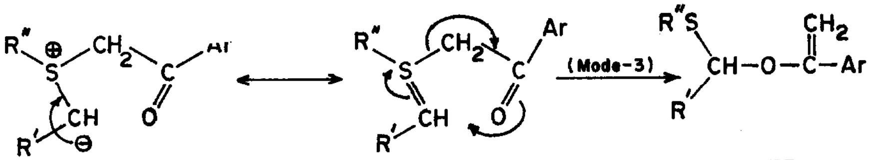
We suggest that the probable mechanism of the reaction, consistent with the present observations, is a bimolecular elimination as indicated in mode-1, involving ethoxide attack on the α-proton of one of the alkyls of the trialkylammonium moiety. The electron acceptor group in the p-position in the phenacyl moiety apparently assists the formation of the enolate ion (VII).



VI VII



IX VIII



X X XI

Hydrolysis of the iminium ion (VI) gives the aldehyde and secondary amine obtained in the reaction. A unimolecular mechanism (E_1cB, mode-2) involving the ammonium ylide (VIII), may also, in principle, be considered. However, it is less likely since this ylide is unstable and it will rearrange to the more stable ylide (IX). The mechanism of formation of p-nitropropiophenone from p-nitrophenacyltrimethylammonium chloride is not quite clear. An obvious possibility is that a Stevens rearrangement precedes the reductive cleavage and the tertiary amine formed is getting quaternized by alkyl transfer from the unreacted starting material. However, no Stevens product has been isolated in any one of these cases.

It is of considerable interest to compare the behaviour obtained here with that reported earlier for the base catalyzed transformation of phenacyldialkylsulphonium salts into α-thioalkyl enol ethers (XI)[4]. The latter reaction has been considered to be an instance of a Stevens [3,2] shift[1,4], i.e. an intramolecular rearrangement of an intermediate ylide of the type (X) as indicated in mode-3. A similar mechanism cannot be written for the nitrogen ylide (VIII) since nitrogen, being a first row element, cannot expand its octet. On the other hand, in the light of the present results, there can be genuine doubt as to the reality of the intramolecular rearrangement suggested for the sulphonium case. Mechanisms involving ion-pair formation through decomposition of a preformed ylide and directly through a concerted reaction of the type suggested here are both worthy alternatives for consideration.

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