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ALKOXIDE OXIDATION BY HYDRIDE TRANSFER TO DICHLOROCARBENE; GROUP MIGRATIONS IN CARBENE REACTIONS

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The sparse and somewhat controversial information that has appeared on the reactions of alkoxides with chloroform in alcohol solution (1,2,3,4) has led us to investigate several systems that might clarify the mechanistic paths.

When chloroform (0.0058 mole) is slowly added to a benzyl alcohol solution of sodium benzyloxide (0.14 mole; argon atm.), a vigorous exothermic reaction ensues. Treatment of the reaction mixture with hot aqueous sodium hydroxide, to effect hydrolysis of ester products, followed by extraction of the acidic and nonacidic materials, results in the isolation of dibenzyl ether (24.8-44.3% yield[†]), benzyl orthoformate (15.2-44.3% yield), benzoic acid, phenylacetic acid, mandelic acid,[‡] and one as yet unidentified acid.[*] Methylene chloride was identified as a volatile constituent given off during the exothermic initial portion of the reaction.

$$C_6H_5CH_2ONa + CHCl_3 \xrightarrow[\text{alcohol}]{\text{benzyl}} \xrightarrow[\text{2) } H_3O^+]{\text{1) } OH^-} CO + CH_2Cl_2 + (C_6H_5CH_2)_2O +$$

$$(C_6H_5CH_2O)_3CH + C_6H_5COOH + \underset{\text{I}}{C_6H_5CH_2COOH} + \underset{\text{II}}{C_6H_5CHOHCOOH}$$

[†] All yields are based on chloroform.

[‡] The mole ratio of benzoic to phenylacetic to mandelic acid was approximately 12:1:7 (average of two runs). The absolute yield of all acids collectively was $\leq 5\%$.

[*] The n.m.r. spectrum of the acid mixture (in acetone) showed an unidentified AB quartet at τ 5.38 (area 2; J = 12 c.p.s.) and a singlet at τ 4.94 (area 1) in addition to absorption in the phenyl region.

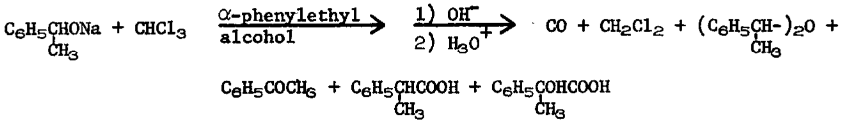
We feel that the products are best explained by considering two distinct initial reaction paths, one involving hydride abstraction from alkoxide by dichlorocarbene and the other involving displacement of chloride from dichlorocarbene by alkoxide to form an intermediate chlorobenzyloxycarbene (III).

$$C_6H_5CH_2O^- + CCl_2 \longrightarrow C_6H_5CHO + HCCl_2^-$$

$$C_6H_5CH_2O^- + CCl_2 \longrightarrow \underset{\text{III}}{C_6H_5CH_2O\ddot{C}Cl} + Cl^-$$

Previously, acetone (4) and methyl ethyl ketone (2) have been observed as minor products in the reactions of secondary alkoxides with chloroform. Under the conditions of our reaction, the direct product of such a hydride transfer, benzaldehyde, undergoes a Tischenko reaction to form benzyl benzoate (isolated as benzoic acid). No previous hydride transfers from primary alkoxides to dichlorocarbene have been reported (5). Similar oxidation of sodium α-phenylethoxide occurred to the extent of 29.0% based on acetophenone isolated as the 2,4-dinitrophenylhydrazone.

Of particular interest are the products, phenylacetic acid(I) (from sodium benzyloxide) and hydratropic acid(IV) (from α-phenylethoxide), which appear to arise from the formal insertion of a one-carbon fragment into a carbon-oxygen bond.

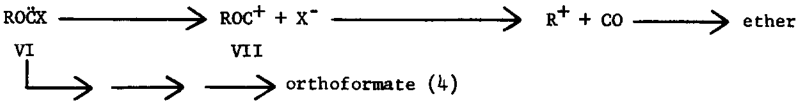


$$C_6H_5\underset{CH_3}{C}HONa + CHCl_3 \xrightarrow[\text{alcohol}]{\alpha\text{-phenylethyl}} \xrightarrow[2)\ H_3O^+]{1)\ OH^-} CO + CH_2Cl_2 + (C_6H_5\underset{CH_3}{C}H-)_2O +$$

$$C_6H_5COCH_6 + C_6H_5\underset{CH_3}{C}HCOOH + C_6H_5\underset{CH_3}{C}OHCOOH$$

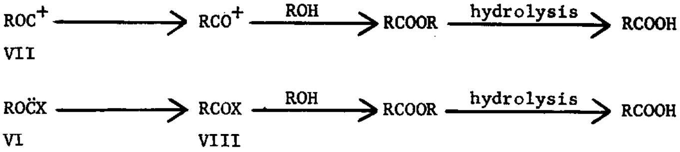
IV V

A previous report by Skell (2) that the alkene product distribution resulting from the treatment of aliphatic alcohols with chloroform and base was similar to that arising from the diazotization of the corresponding amines with nitrous acid and an observation by Hine (4) that ether products are formed with equal ease from the treatment of primary and secondary alcohols with chloroform and base, have led to the postulate (5) that the intermediate haloalkoxycarbene, VI, breaks down, probably via a short lived isocarboxonium ion,[†] VII, to the simple carbonium ion which reacts to form the observed products.[‡] In spite of the fact that the isocarboxonium ion intermediate has been postulated because it is isoelectronic with the diazonium ion (2) and therefore is a reasonable intermediate, no previous direct evidence has been presented for its existence. One could equally well describe the formation of the carbonium ion by a concerted breakdown of carbene VI. The formation of acids I and IV can be explained either by migration of a benzyl or α-phenylethyl group from oxygen to the electron deficient carbon atom in ion VII or by a rearrangement of carbene VI to acid chloride VIII.[*] While the former mechanism has a multitude of analogies



$$\underset{\mathrm{VI}}{\mathrm{RO\ddot{C}X}} \longrightarrow \underset{\mathrm{VII}}{\mathrm{ROC^+}} + \mathrm{X^-} \longrightarrow \mathrm{R^+ + CO} \longrightarrow \text{ether}$$

$$\hookrightarrow \; \longrightarrow \; \longrightarrow \text{orthoformate (4)}$$



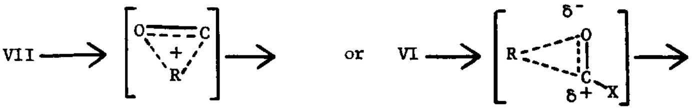
$$\underset{\mathrm{VII}}{\mathrm{ROC^+}} \longrightarrow \mathrm{RCO^+} \xrightarrow{\mathrm{ROH}} \mathrm{RCOOR} \xrightarrow{\text{hydrolysis}} \mathrm{RCOOH}$$

$$\underset{\mathrm{VI}}{\mathrm{RO\ddot{C}X}} \longrightarrow \underset{\mathrm{VIII}}{\mathrm{RCOX}} \xrightarrow{\mathrm{ROH}} \mathrm{RCOOR} \xrightarrow{\text{hydrolysis}} \mathrm{RCOOH}$$

[†] We suggest the term isocarboxonium ion to describe carboxonium ions (sometimes termed oxocarbonium ions) (6) in which the oxygen atom is bound to carbon.

[‡] In view of our present results and the previous observations of Skell (2), the concerted formation of a small amount (3%) of optically active 2-methyl-2-butanol-3-d from the treatment of optically active α-d-neopentyl alcohol with potassium hydroxide and bromoform by Mosher and Sanderson (3), probably represents a very minor pathway for the breakdown of haloalkoxycarbenes in general and might even be a path unique to the neopentyl system.

[*] Although less plausible routes to acid I exist, including hydrolysis of 1,1,1-trichloro-2-phenylethane formed from attack of the benzyl carbonium ion on trichloromethyl anion, we feel that the driving force probably comes from transition state delocalization of the electron deficiency present in ion VII, or from delocalization during the rearrangement of VI.



in 1,2-migrations to electron deficient centers, the latter mechanism may also have precedent in the proposed carbenoid pathway of the Wolff rearrangement as well as other closely related reactions (7,8).

Because no product corresponding to I or IV, had been reported by Hine (4) for the reaction of sodium isopropoxide in isopropyl alcohol with chloroform, we carefully repeated this reaction. The product mixture was hydrolyzed with base, acidified, and continuously extracted with ether. As expected, a small amount of isobutyric acid (identified as the methyl ester by vapor phase chromatographic comparison with an available sample) was found. This observation helps to establish the generality of the path leading to a product which is formally the oxidized homolog of the original alkoxide.

Mandelic acid[†] (II) and atrolactic acid[†] (V) also represent products of a type that has not been previously reported for haloform, alkoxide reactions. One can envision an attack of the newly formed methylene chloride anion (from hydride abstraction) on the aldehyde carbonyl group to form anion IX.

$$C_6H_5CHO + {}^{-}CHCl_2 \longrightarrow C_6H_5\overset{O^-}{C}HCHCl_2$$

IX

Although the exact path by which IX is converted to mandelic acid is not completely clear, hydrolysis to the aldehyde followed by a Cannizzaro reaction during the treatment with hot aqueous alkali would appear to be the most direct route. It is unlikely that the α-hydroxy acid arises via hydrolysis

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[†] Both acids were identified by direct comparison of the n.m.r. spectrum with that of an authentic sample. In addition, a small sample of mandelic acid isolated from the reaction mixture and recrystallized from chloroform gave a m.p. 117-118° (not depressed when mixed with authentic material) and had a neutrality equivalent of 156 (theory 152).

of an intermediate epoxide formed by intramolecular displacement of chloride by IX since haloepoxides are readily opened by alkoxides (9) and this would predict the formation of an α-alkoxy acid as the final product. Work is being actively carried out to clarify and extend these results.

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