Favorskii Rearrangement of some α-Bromo-ketones

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THE base-induced rearrangement of α-halogenoketones to give carboxylic acid derivatives (Favorskii rearrangements[1]) occurs by at least two mechanisms. The stereochemistry[2,3] and structure[4] of many Favorskii products can be explained in terms of a cyclopropanone intermediate. However, a "benzylic-like" rearrangement appears to operate when the substrate ketone bears no α′-hydrogen,[5] when the α′-hydrogen is relatively non-acidic,[6] or when steric or strain factors inhibit cyclopropanone formation.[7] In addition, the formation of a dipolar intermediate which may precede (or follow) cyclopropanone formation is supported by theoretical considerations,[8] loss of stereospecificity upon rearrangement in polar solvents,[8] the formation of α-substitution products[9] as a side reaction, and the trapping of a possible Favorskii intermediate.[10]

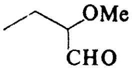
The intermediacy of a dipolar ion was first suggested to explain the fact that isomeric acyclic α-halogenoketones (*e.g.* $PhCl{\cdot}CH{\cdot}CO{\cdot}CH^3$ and $PhCH_2{\cdot}CO{\cdot}CH_2Cl$) appear to "dehydrohalogenate" to form a common intermediate leading to the same product.[1,11]

We report here (Table) our results with the isomeric pairs of α-bromobutan-2-ones and α-bromo-3-methylbutan-2-ones which provide strong evidence against (*a*) a "benzylic-like" rearrangement, (*b*) a bromine atom exchange from the α- and α′-position, and (*c*) the occurrence of a dipolar ion prior to rearrangement. Comparison of these results with the cleavage of cyclopropanones (or the corresponding hemiacetals) provides strong evidence (*a*) for the intervention of cyclopropanones [*e.g.* (I)] in the Favorskii rearrangement of the acyclic α-halogenoketones studied and (*b*) for the occurrence of side products from base attack on the α-halogenoketone carbonyl group, not from attack on a dipolar species such as (III).

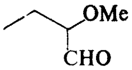
Reactions with sodium methoxide

	Solvent	$Me_2CH{\cdot}CO_2Me$ %	$MeCO{\cdot}CH(OH)Me$ %	$EtCO{\cdot}CH_2OR$ %
(I and (IA)	CH_2Cl_2	100		
	MeOH	100		
(IV)	CH_2Cl_2[a]	16		24
	Et_2O	*ca.* 42		
	MeOH[b]	9		13
(XII)	CH_2Cl_2[c]	8	29	
	Et_2O	36	25	
	MeOH[d]		9	
		$Me_3C{\cdot}CO_2Me$ %	$MeCO{\cdot}CMe_2{\cdot}OR$ %	$Me_2CH{\cdot}CO{\cdot}CH_2OR$ %
(II) and (IIA)	CH_2Cl_2	100		
	MeOH	100		
(VIII)	CH_2Cl_2[e]	2		51
	Et_2O	2		
	$MeOH_4$	9		54
(XVI)	CH_2Cl_2	41	28	
	Et_2O	100		
	MeOH	6	7	

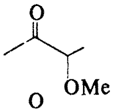
The data reported here require at least two, or possibly more, reaction paths to explain the formation of the major products. Possibilities are: (*a*) cyclopropanone formation to account for the formation of rearranged ester and (*b*) attack on the α-halogenoketone carbonyl to form epoxy-ethers which subsequently decompose directly, or upon work up to, yield α-methoxy-ketones and/or α-hydroxy-ketones

a


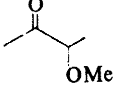
(37%) formed by v.p.c. rearrangement of (VI)

b


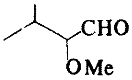
(45%)

c


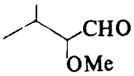
(9%) formed by v.p.c. rearrangement of (XIV)

d


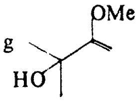
(89%)

e


(9%) formed by v.p.c. rearrangement of (X)

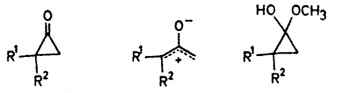
f


(35%)

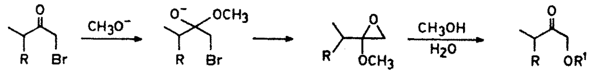
g


(56%) formed by v.p.c. rearrangement of (XVIII)

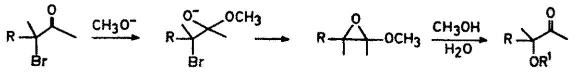
However, two additional pathways to the α-methoxy-ketones are available through (*c*) either S_N2 displacement of halide by base or (*d*) formation of an allene oxide. Displacement by base on an epoxy-ether would simply explain the formation of α-methoxy-ketones. Since the methoxy-epoxides, (VI) and (X) have been detected as the major product before aqueous work up and (VII) and (XI) are not formed until after work-up, route (*b*) is confirmed as the major route for formation of the α-substitution products. It should be noted that rearrangement of these epoxides often accompanies their work-up.



(I) $R^1 = H, R^2 = CH_3$ (II) $R^1 = R^2 = CH_3$ (III) (IA) $R^1 = H, R^2 = CH_3$ (IIA) $R^1 = R^2 = CH_3$



(IV) R=H (VIII) $R = CH_3$ (V) (IX) (VI) (X) (VII) $R^1 = H$ or CH_3 (XI) $R^1 = H$ or CH_3



(XII) R=H (XVI) $R = CH_3$ (XIII) (XVII) (XIV) (XVIII) (XV) $R^1 = H$ or CH_3 (XIX) $R^1 = H$ or CH_3

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