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NUCLEOPHILIC AROMATIC SUBSTITUTION. IV - Steric effects in thioalcoxy-dehalogenation of some halogeno-aromatic compounds (*)

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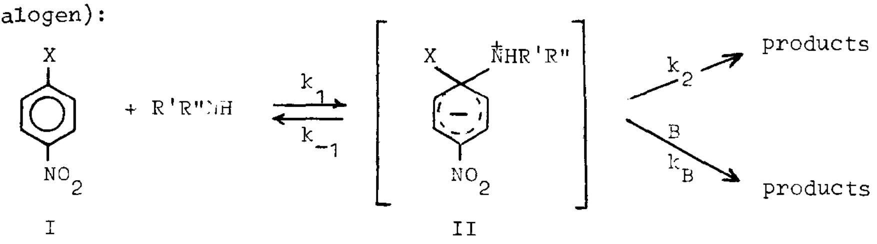
In nucleophilic substitution reactions on aromatic substrates the steric effects are less important than in the same reactions on aliphatic substrates and have not been fully investigated (1).

Studies on the steric hindrance of the entering nucleophile and leaving group have been reported mainly for reactions of various amines with halogeno-nitrobenzenes either in protic (2) or in aprotic solvents (3). The relative data have been interpreted differently (2,3).

We feel that the choice of amines to investigate the steric effects of the nucleophile as well as of the leaving group upon the rates might cause some inconvenience.

It has been recently shown that the reaction rates of aromatic Sn_{Ar} reactions depend upon the relative importance of steps 1 and 2 in the commonly accepted (4) scheme below (X = Halogen):



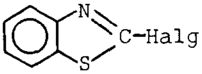
This in turn will depend upon the nature of the leaving halogen, especially in a low polarity medium.

In order to avoid such complications, we decided to investigate the steric effects of different negatively charged nucleophiles on reaction rates in a typical protic solvent (MeOH). Under these conditions, the formation of intermediate (II) is generally thought to be the rate determining step (4).

Therefore mercaptide anions (RS^-; where R=CH_3, C_2H_5, iC_3H_7, C_3H_7, C_4H_9, iC_4H_9, sec.C_4H_9, ter.C_4H_9) were chosen as nucleophiles. This choice, however, prevented the use of halogeno-nitrobenzenes as aromatic substrates; in fact a relevant reduction reaction of the "activating" nitro groups in the aromatic substrate has been found in the presence of mercaptide anions; similar reactions are observed with branched alkoxide-ions (5).

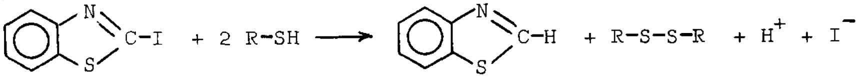
Therefore, in this study, some halogeno-benzo-thiazoles (III) have been employed as aromatic substrates.

III



(Halg = F, Cl, Br)

Our previous studies (6) pointed out that this class of compounds behaves like typical "activated" substrates in aromatic Sn_{Ar} reactions ; no appreciable side reactions of reduction occur with RS^-, except in the case of 2-iodo-benzo-thiazole (in III, Halg = I), which, in the presence of free mercaptan, is reduced according to the following scheme:



This reaction, which is similar to that observed for the same substrate reacting with thiophenol (7), is under investigation and will be referred to elsewhere.

In methanol, together with the thioalkoxy substitution, we have observed some methoxy substitution caused by the methoxide ion present in the solution because of the equilibrium:

$$R\text{-}S^- + CH_3OH \rightleftharpoons R\text{-}SH + CH_3O^-$$

Operating in the presence of a large excess of free mercaptan, it is possible, however, to reduce the methoxy substitution to a negligible percentage (about 1-2%); and the second order kinetic constants measured do not vary with initial concentrations either of the substrate or of the anionic nucleophile. The obtained data are reported in the table (rate constants in $mol^{-1}sec^{-1}l$).

TABLE

Experimental rate constants (10^3 k) for reactions of 2-halogeno-benzothiazoles with alkyl-mercaptide ions in methanol at 30°

	halogen in 2-halogeno-benzothiazoles		
Alkyl-group in the mercaptide ion	F	Cl	Br
CH_3	1600	15.	23
C_2H_5	990	7.2	11
C_3H_7	1010	7.8	12
iC_3H_7	450	2.5	4.2
C_4H_9	1150	8.8	14.0
iC_4H_9	1150	8.9	14.0
sec.C_4H_9	460	2.8	4.5
ter.C_4H_9	73	0.19	0.28

We note the following points:

i) The reaction is sensitive to steric effects as indicated by the fact that the methyl-mercaptide is the most reactive nucleophile in all the series studied.

ii) the α-branching does reduce the reactivity ($CH_3 \rightarrow CH_3{-}CH_2 \rightarrow (CH_3)_2{=}CH \rightarrow (CH_3)_3{\equiv}C{-}$), whereas the β- and the ω-branching do not cause any steric effect and they only slightly influence the rates because of their usual electronic effect.

iii) the steric effect depends on the leaving halogen, sequence F<Cl<Br, being observed, as indicated from the respective values of the ratio $k_{CH_3S^-}/k_{(CH_3)_3CS^-}$ (F = 22; Cl = 79; Br = 82).

Our results indicate that steric effects seem to be present in these reactions although they are not markedly large in respect to the steric effects observed in the reactions of p-nitro-halogeno-benzenes with amines. (2,3).

It should be considered that in the reaction with mercaptide ions the bond forming step is rate determining. Under these circumstances it is logical to assume that as the percentage of bond forming in the transition state gets smaller [i.e. the forming C to nucleophile bond gets longer (8)] the steric effects become less important.

In our reaction a relatively small percentage of bond forming in the t.s. is evidenced by the electronic effects of the substituents in the nucleophile on the reaction rates (β- and ω-branching), which are practically absent. This is also in agreement with the previously reported (9) kinetic data for the similar reactions of some aryl substituted thiophenates on the same substrates (III), in which the substituent effects in the thiolate are modest ($\rho \simeq 0{,}5$) (9).

The considerations above seem to justify the relatively small steric effects observed. These, however, regularly increase as the size of the leaving halogen increases; this supports our conclusion that, in Sn_{Ar} reactions with anionic nucleophiles, the changes in reaction rates can be principally ascribed to changes in interactions between entering and leaving groups (10).

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