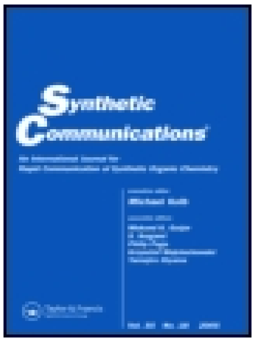

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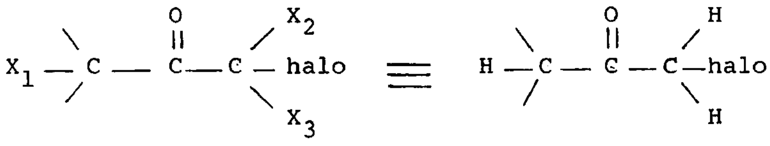
AN EXPEDITIOUS STUDY OF THE NATURE OF HALOGEN(S) AT α-POSITIONS IN CARBONYL COMPOUNDS

V.K. Ahluwalia*, Bhupinder Mehta+ and Manju Rawat

Department of Chemistry, University of Delhi, Delhi 110007, India.

Abstract: The detailed study, of the behaviour of di/tri halo carbonyls to act as the synthetic equivalents of corresponding mono α-halo carbonyls, is carried out.

The synthetic utility of α-halo carbonyl compounds is well known for more than a century. The strange phenomenon of α,α/α,α'-dihalo and α,α,α-trihalo-carbonyl compounds to behave as synthetic equivalents of their corresponding mono-α-halocarbonyl compounds, during the heterocyclization, is established and attested by various articles reported in literature[1,2].



$$X_1-C-\overset{\overset{O}{\|}}{C}-\underset{X_3}{\overset{X_2}{C}}-\text{halo} \equiv H-C-\overset{\overset{O}{\|}}{C}-\underset{H}{\overset{H}{C}}-\text{halo}$$

X_1, X_2, X_3 = H or/and halo   halo = Br or Cl

It has been shown that halocarbonyl compounds, of the

+Present Address: Department of Chemistry, Swami shraddhanand College (University of Delhi), Alipur, Delhi 110036, India.

type mentioned, on reaction with thioamides yield the same thiazole. The dehalogenation process was attributed to strong nucleophilicity of sulphur and is reported to occur after the heterocyclization[3] via the formation of enolate ion, later on, parallel observations were encountered during the synthesis of 3,4-diaryl-2(5H)-furanones from phenylacetic acid and α,α-dibromoacetophenones[4]. The mechanism for dehalogenation in furanones as well as thiazoles is established to occur prior to heterocyclization[4], contrary to earlier reported mechanism[3].

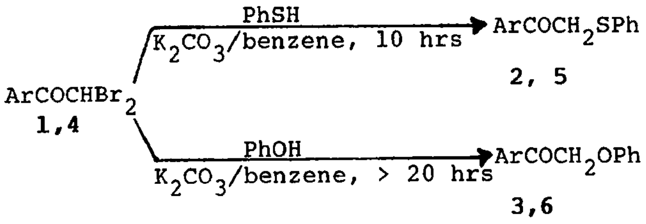
An extensive study of the above observations compelled us to think as to, why there's a change in nature of the other halo atom(s), after the formation of a linkage of halocarbonyls with sulphur and oxygen of the reacting species? Besides, is it the 5-membered ring system which is responsible for the process of dehalogenation?

In present communication, besides the experiments performed, the theoretical profile in context with the preceding queries has been discussed.

Thus, in view of above, (dibromoacetyl)-4-methoxybenzene 1 (0.0015 mol) was refluxed with thiophenol (0.003 mol) in K_2CO_3/benzene. The reaction as monitored by tlc was found to be complete in 6 hrs. giving the product in quantitative yields, characterized as 1-(mercaptophenylacetyl)-4-methoxybenzene 2 (mp 85-86°, Lit.mp[5] 85°). further it was confirmed by its comparison (mp[5], mmp coIR) with an authentic sample prepared by refluxing equimolar amounts of 1-(bromoacetyl)-4-methoxybenzene and thiophenol in K_2CO_3/benzene for an hour.

In a similar manner the reaction of 1 (0.0015 mol) was carried out with phenol (0.003 mol). The reaction was monitored on tlc for upto 20 hrs., but it showed the formation of a single product in traces of amount along with the unreacted **1**. Further, the HPLC analysis of the reaction mixture showed the formation of 1.2% product. The product was analysed[6] to be 1-(oxophenylacetyl)-4-methoxybenzene **3**, as revealed from HPLC of the authentic sample prepared from an equimolar amounts of 1-(bromoacetyl)-4-methoxybenzene and phenol. The reaction took nearly 3 hrs. for completion.

Further similar results were obtained with the reaction of phenacyl dibromide **4** with thiophenol and phenol to give the corresponding 1-(mercaptophenylacetyl)benzene[5] **5** and 1-(oxophenylacetyl)benzene[6] **6**.



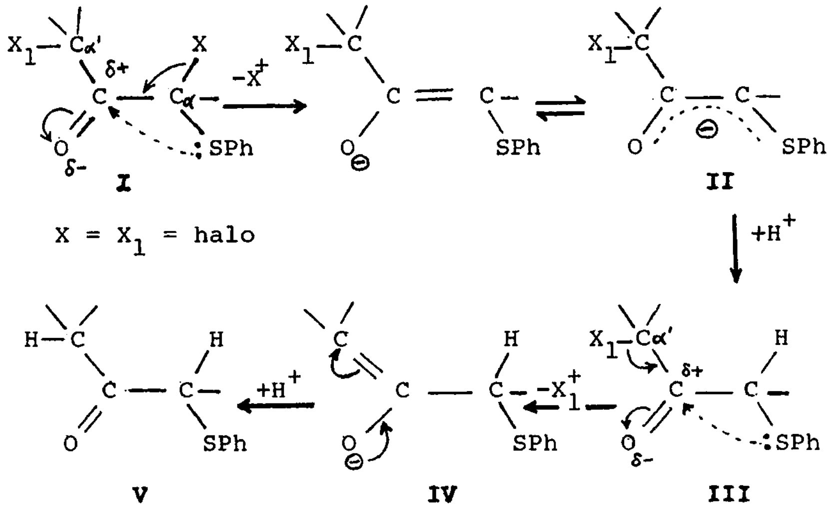
1,2,3. Ar = (4-OCH_3) C_6H_4-

4,5,6 Ar = C_6H_5-

Earlier it has been reported[2] that dehalogenation takes place from both the positions adjacent to carbonyl group. Keeping in view the above, bromination of acetone was carried out. The mixture of mono and different di/tri-bromoacetone derivatives[7,8] **7**, thus obtained, was refluxed with thiophenol (in excess) in K_2CO_3/benzene for 10 hrs. Workup of the reaction mixture yielded α-mercaptophenyl acetone **8** as an oil[5].

$$\underset{\mathbf{7}}{X_1CH_2COCH(X)Br} \xrightarrow[K_2CO_3/\text{benzene}]{PhSH} \underset{\mathbf{8}}{CH_3COCH_2SPh}$$

X, x_1 = H or/and Br



$X = X_1 =$ halo

SCHEME - A

Discussion: The above experiments clearly indicate that dehalogenation process is not by virtue of 5-membered ring system. The thiophenol and phenol are also performing the dual role, of nucleophilic attack, as well as, carrying out the subsequent dehalogenation. However, the effect is more pronounced in case of thiophenol compared to phenol due to strong nucleophilicity of sulphur towards halogen. An obvious change in the nature of the other halo atom(s) is attributed to increased carbanion character, or, in other words, to the stable enolate ion. The driving force for the formation of enolate ion is, probably, the nucleophilic sulphur, which assists in enhancing the polarization of carbonyl group (Str. **I**, SCHEME A). The impact of polarization is to such an extent, that electrons are pulled away from α (and α') positions, thereby causing the removal of halo atom(s) as halonium ion(s) (SCHEME A). The same situation can be depicted in case of phenol. In the reactions involving dibromo derivatives, the longer reaction duration is attributed to steric hinderance. However, this effect is overcome by the nucleophilicity of sulphur, in reactions with thiophenol.

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References and Notes

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6. Characterization data of compounds **3**, and **6**.
   3. Oil; PMR ($CDCl_3$) δ : 3.83 (s, 3H, $-OCH_3$), 5.1(s, 2H, $-CH_2-$); 6.9(d, J=9 Hz, 2H, ArH), 7.0-7.5(m, 5H, Ar-H), 7.8(d, J = 9 Hz, 2H, ArH).
   6.mp.78°; PMR ($CDCl_3$) δ : 5.2(s, 2H, CH_2), 7.1-7.6(m, 8H, ArH), 7.7-8.0(m, 2H, ArH).
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