Copper(I) Catalysed Replacement of Bromine by Chloride Ion in Bromobenzoic Acids

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In previous investigations of dichlorocuprate(I) ion catalysed bromine-chlorine exchange reactions of bromonitrobenzenes in aqueous hydrochloric acid-acetic acid medium, a large accelerating effect of a nitro group, *ortho* to the reaction site, together with steric and polar effects of a substituent in the other *ortho* position, was observed.[1] In the determination of the exchange reaction of 2-bromo-3-X-nitrobenzenes an increase of the rate of reaction correlated well with an increasing van der Waals volume of the halogen in the 3-position. The deactivating power of an alkyl group in the 3-position, as compared to a halogen atom of comparable size, was also noticed. These results, together with a large negative entropy of activation for the exchange reactions, led to the suggestion of a tetrahedral intermediate, in which the *ortho* nitro group and the bromine undergoing replacement interact with the dichlorocuprate(I) ion.[1-2]

Both the steric and the polar effects of a substituent in the 3-position have been rather extensively investigated, but a closer study of the significance of the group in the 1-position seems justified, since this group is thought to be included in the intermediate complex.

In the present work the exchange reactions of 2,3-dibromobenzoic acid and 2-bromobenzoic
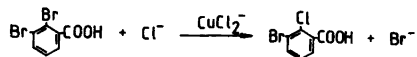
acid have been kinetically studied at 80–100 °C. The COOH group has the same steric requirement as the NO_2 group and also has unshared electrons. The reaction mixtures were analysed by GLC, ^1H NMR and mass spectra. The dichlorocuprate(I) ion catalysed exchange reaction of 2,3-dibromobenzoic acid gave, in addition to 3-bromo-2-chlorobenzoic acid, 1 % of a by-product, indicating debromination and suggesting the formation of 3-bromobenzoic acid. This
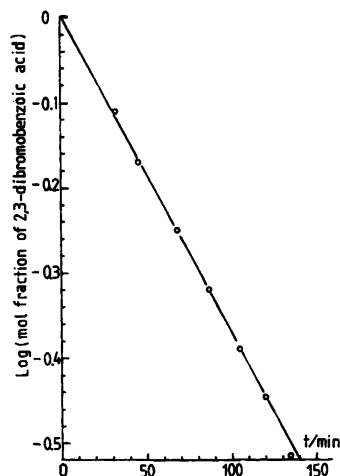
Fig. 1. Representative bromine-chlorine exchange of 2,3-dibromobenzoic acid forming 3-bromo-2-chlorobenzoic acid at 90 °C.

reductive dehalogenation has been previously observed in connection with copper(I) catalysed reactions of 2,3-dihalogenonitrobenzenes.[3] The exchange product of 2-bromobenzoic acid was 2-chlorobenzoic acid. The by-products constitute <1 % of the yield and were not identified.

The pseudo first-order kinetics are illustrated for 2,3-dibromobenzoic acid in Figs. 1–2. The rate constant k_{obs}, was calculated from the slope of the line, and the second-order rate constant, k_2, was estimated from the $CuCl_2^-$-concentration as described in Ref. 2, see Table 1.
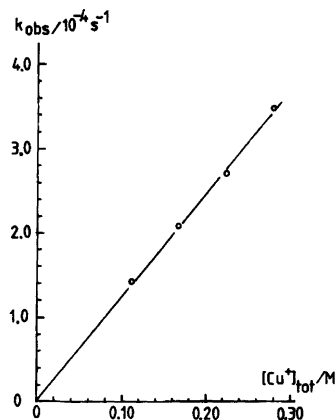
Fig. 2. k_{obs} for 2,3-dibromobenzoic acid *versus* $[Cu^+]_{tot}$. $[Cl^-]$=5.25 M and [substrate]=0.056 M.

Table 1. Dichlorocuprate(I) ion catalysed bromine-chlorine exchange reactions. $[Cu^+]_{tot}=0.112$ M, $[Cl^-]=5.25$ M and [substrate]=0.056 M.

| Temp. /°C	$CuCl_2^-$[a] /M	k_{obs}[b] /10^{-4} s^{-1}	k_2[c] /10^{-4} 1 mol^{-1} s^{-1}
2,3-Dibromobenzoic acid			
79.95	0.056	0.706(18)[e]	12.6
89.98	0.063	1.43(2)	22.8
98.05	0.076	2.17(9)	28.5
2-Bromobenzoic acid			
89.98	0.063	0.27(1)	4.3
2,3-Dibromonitrobenzene[d]			
89.98	0.063	1.83	29.2
2-Bromonitrobenzene[d]			
89.98	0.063	0.28	4.4

[a] Estimated from the data in Ref. 2. [b] Pseudo first-order rate constant. [c] Second-order rate constant, calculated on substrate and $CuCl_2^-$. [d] Values from Ref. 1. [e] The errors are 2 S.E. from the least-squares method calculations. 2–4 different runs in every calculation.

Table 2. Activation enthalpies and entropies. The temperature interval was 79.95–98.05 °C.

Compound	$\Delta H^{\neq}$/kJ mol^{-1}	$\Delta S^{\neq}$/J K^{-1} mol^{-1}
2,3-Dibromo-benzoic acid	47(12)[a]	−168(33)[a]
2,3-Dibromo-nitrobenzene[b]	51(4)	−155(11)

[a] The errors are 3 S.E. from the least-squares method calculations. [b] Values from Ref. 1.

The rate of exchange in 2,3-dibromobenzoic acid is somewhat slower than the exchange rate of 2,3-dibromonitrobenzene. The activation parameters are of the same magnitude (see Table 2). The COOH group, as well as the NO_2 group, is able to form a tetrahedral intermediate complex involving the dichlorocuprate(I) anion and the bromine undergoing replacement, see Fig. 3. The present work supports the earlier suggestions. An experiment with 1,2,3-tribromobenzene and the dichlorocuprate(I) ion gave no exchange products. The van der Waals
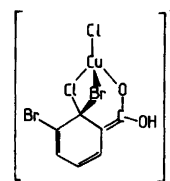
Fig. 3. The proposed intermediate complex of 2,3-dibromobenzoic acid and the dichlorocuprate(I) anion.

volume of a bromine, a nitro group or a carboxyl group is of the same magnitude, about 16 cm^3 mol^{-1}. All these groups have positive σ-values. It may be an unfavourable configuration of the plausible intermediate complex for the 1,2,3-tribromobenzene, which makes the exchange reaction impossible.

Experimental. Melting points were determined with a Kofler Hot-Stage Microscope. ^{1}H NMR spectra were obtained with a Bruker WH 270 instrument with TMS as internal standard. The mass spectra were recorded on a Finnigan 1020 instrument. The GLC investigations were carried out on a Perkin Elmer 3920 B chromatograph with a hot wire detector and equipped with a Hewlett Packard 3380 A integrator. Carrier gas was He and a 3 mm×2 m SE-30 column was used. The 2-chloro compounds were synthesized for calibration purposes.

2,3-Dibromobenzoic acid was prepared from 2,3-dibromomethylbenzene by permanganate oxidation.[4] An amount of 5.0 g (0.020 mol) gave a yield of 2.7 g of the 2,3-dibromobenzoic acid (48 %). M.p. 151–152 °C, lit[5a] 149–150 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.83 (H-4 or H-6, q), 7.81 (H-6 or H-4,q), 7.28 (H-5, q) and 10.0 (OH, s). $J_{4-5,5-6}$=7.75 Hz and J_{4-6}=1.55 Hz. MS: A 1:2:1 triplet at *m/e* 278, 280 and 282.

3-Bromo-2-chlorobenzoic acid was synthesized from 3-bromo-2-chloromethylbenzene as described above for the 2,3-dibromobenzoic acid and gave a yield of 21 %. M.p. 170.5–171.5 °C, lit[5b] 165 °C. ^{1}H NMR (270 MHz, $CDCl_3$, $[(CD_3)_2CO]$: δ 7.92 [7.93] (H-6 or H-4, q), 7.87 [7.83] (H-4 or H-6, q), 7.25 [7.41] (H-5, q) and 6.25 [5.63] (OH, s). $J_{4-5\ or\ 5-6}$=7.75 Hz, $J_{5-6\ or\ 4-5}$=8.05 Hz and J_{4-6}=1.55 Hz. MS: A 3:4:1 triplet at *m/e 234, 236 and 238.*

2-Bromobenzoic acid was prepared from 2-aminobenzoic acid (6.85 g, 0.05 mol) according to Gunstone and Tucker.[6] The yield was 68 % (6.9 g). M.p. 149.5–150.5 °C, lit[5c] 150 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 8.03 (1 H, multiplet), 7.73 (1 H, multiplet) and 7.42 (2 H, multiplet). MS for the methyl ester: A 1:1

doublet at *m/e 214 and 216.*

Copper(I) catalysed bromine-chlorine exchange. The reactions were performed in an argon atmosphere with the apparatus and method described in Ref. 2. The aqueous hydrochloric acid-acetic acid medium had 45 volume % of acetic acid, the hydrochloric acid concentration was 5.25 M. At different times, aliquots were taken from the reaction mixture, they were cooled and then extracted with ether. Diazomethane was added in excess, and the methyl esters of the benzoic acids were analysed by GLC.

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