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THE MECHANISM OF THE BROMINATION OF HEXAMETHYLBENZENE IN ACETIC ACID[1]

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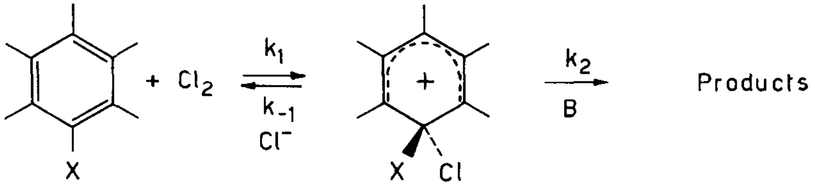
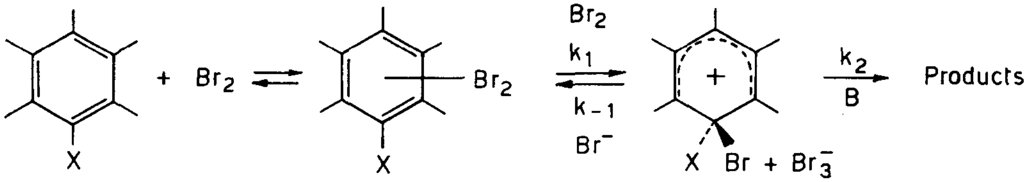
According to the two-stage mechanism of electrophilic aromatic substitution, the halogenation by molecular chlorine and bromine can be formulated by equations (1) and (2), respectively[2].



(1)



(2)

X = H, CH_3

Such formulations include conventional ($X = H$) as well as nonconventional ($X = CH_3$) reactions[3], i.e., either replacement of nuclear hydrogen (and other good leaving groups) or rearrangement to nonconventional products such as the side-chain halogenation of polymethylbenzene derivatives. It has been shown that chlorination is first-order in each reactant and that the reaction rate is determined by the formation of the intermediate benzenonium ion in both hydrogen replacement and side-chain substitution[4]. When the steady-state treatment is applied to equation (1), the results are consistent with the condition $\underline{k}_2[B] \gg \underline{k}_{-1}[Cl^-]$, which leads to the observed rate law, rate = $\underline{k}_1[\text{substrate}][Cl_2]$, and to the observed lack of hydrogen isotope effect for the nuclear hydrogen replacement[5].

On going over to the bromination reaction, the formation of the intermediate benzenonium ion is still rate-determining for the conventional substitution, although preliminary π-complex formation is responsible for the predominance of a kinetic term which is second-order in halogen. Accordingly, on application of the steady-state treatment to equation (2), the observed rate law, rate = $\underline{k}_1K_1[\text{substrate}][Br_2]^2$, follows the condition $\underline{k}_2[B] \gg \underline{k}_{-1}K_2[Br_2][Br^-]$, K_1 and K_2 being the equilibrium constants for π-complex formation and tribromide ion, Br_3^-, formation, respectively.

Unlike chlorination, bromination is subject to a clean-cut change in rate law when the timing of the process changes. Thus, under the reverse condition $\underline{k}_{-1}K_2[Br_2][Br^-] \gg \underline{k}_2[B]$, the kinetic order in bromine drops to one and a rate law, equation (3), is predicted. When such a case occurs, the decomposition

$$\text{rate} = \frac{\underline{k}_1\underline{k}_2K_1}{\underline{k}_{-1}K_2}\,\frac{[\text{substrate}][Br_2][B]}{[Br^-]} \tag{3}$$

of the benzenonium ion becomes rate-limiting.

We have now gathered convincing evidence that equation (3) applies to the side-chain bromination of hexamethylbenzene, equation (4), in acetic acid solution.

$$C_6(CH_3)_6 + Br_2 \longrightarrow C_6(CH_3)_5CH_2Br + HBr \tag{4}$$

The main facts supporting this view are the following.

(a) In the dark, reaction (4) is second-order, first-order in each reactant. Equation (3) reduces to this form when Br^- is the only base present

([B] = [Br]).

(b) The rate constant, $\underline{k}_{obs} = 2.08 \times 10^{-3}\ M^{-1}sec^{-1}$ at 30°C, is much too low. This is quite clearly indicated by the fact that whereas both nuclear chlorination and bromination proceed at normal reaction rates (i.e., in agreement with substituent effects, reagent effects, etc.) and the rate ratio hexamethylbenzene/pentamethylbenzene is 40 for chlorination (in agreement with the polar influence of an additional methyl group), such rate ratio is as small as ~ 1/50 for bromination[6]. Thus, the side-chain bromination of hexamethylbenzene is at least 2,000 times less reactive than expected. A large portion of such a discrepancy is not steric in origin, since the overall retarding factor that is involved when a methyl group is located at the position of attack[7] is less than 4.

(c) The reaction is base-catalyzed, the $\underline{k}_{obs}$ value, as calculated from the initial rate[8], being $1.6 \times 10^{-1}\ M^{-1}sec^{-1}$ at 0.1 M CH_3CO_2Na.

The changes that are observed on going from chlorination to bromination can be rationalized in terms of the combination of two effects, an increase in the rate constant for the back reaction, $\underline{k}_{-1}$, and a decrease in the rate constant for the decomposition to the side-chain product, $\underline{k}_2$. That the former effect plays a role is indicated by the appearance of small isotope effects already in the nuclear bromination of polymethylbenzenes[5]. Furthermore, the back reaction is expected to be better assisted by the nucleophilic attack of Br^- on Br, rather than by attack of Cl^- on Cl[9]. As to the latter effect, C-H bond-breaking at the methyl group undergoing replacement is apparently less assisted in bromination in agreement with the basicity order $Cl^- > Br^-$[10].

It should be emphasized that the present results provide a new evidence for the occurrence of two-stage-mechanisms in the reaction of aromatics with electrophiles. An interesting application of the present views is reported in the following communication.

REFERENCES

1. Part VII in the Series, "Nonconventional Paths in Electrophilic Aromatic Reactions". Part VI in ref. 7.
2. P.B.D.de la Mare and J.H.Ridd, Aromatic Substitution, Butterworths, London, 1959. R.O.C.Norman and R.Taylor, Electrophilic Substitution in

Benzenoid Compounds, Elsevier, Amsterdam, 1965.

3. E.Baciocchi and G.Illuminati, Progr.Phys.Org.Chem., 5, 1 (1967).
4. E.Baciocchi, A.Ciana, G.Illuminati, and C.Pasini, J.Am.Chem.Soc., 87, 3953 (1965).
5. E.Baciocchi, G.Illuminati, and G.Sleiter, Tetrahedron Letters, 30 (1963); E.Baciocchi, G.Illuminati, G.Sleiter, and F.Stegel, J.Am.Chem.Soc., 89, 125 (1967).
6. Here the rate ratio was obtained from values of time at 10% reaction, the concentrations being 0.02 M in each reactant.
7. E.Baciocchi and G.Illuminati, J.Am.Chem.Soc., 89, 4017 (1967).
8. In the presence of a base different from Br^- the reaction is slowed down as the concentration of Br^- increases in agreement to equation (3).
9. Observations supporting this view have been obtained in a systematic investigation of dehalogenation reactions promoted by halide ions (E.Baciocchi and P.L.Bocca, Ric.sci., 37, 1182 (1967) and unpublished results).
10. T.L.Smith and J.H.Elliot, J.Am.Chem.Soc., 75, 3566 (1953).