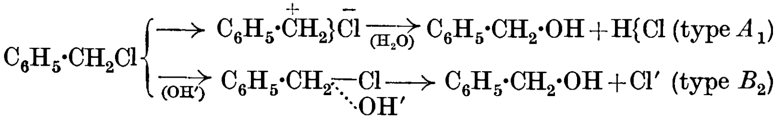
CLVI.—*The Nature of the Alternating Effect in Carbon Chains. Part XXV. The Mechanism of Aromatic Side-chain Substitution.*

By Christopher Kelk Ingold and Eugene Rothstein.

The general problem of the influence of nuclear substituents on reactions in side chains attached to an aromatic nucleus is greatly simplified by the assumption that side-chain reactions fall into two main categories, in one of which (type *A*) facilitation occurs by the *influx* of electrons towards, and in the other (type *B*) by a *recession* of electrons from, the side chain concerned. Theoretically, each of these types requires further subdivision. For instance, the circumstances of the general mechanism *A* would obtain if in the first stage * of reaction a potential anion became ionised or dissociated (type A_1); equally, they would obtain if, in the first stage, a potential (or actual) cation became attracted or co-ordinated (type A_2). Again, the conditions required for mechanism *B* would be present, either if a potential cation were initially ionised or dissociated (type B_1), or if a potential (or actual) anion were initially attracted or co-ordinated (type B_2). As an example, two mechanisms are possible for the hydrolysis (or alcoholysis) of benzyl chloride :



$$C_6H_5{\cdot}CH_2Cl\begin{cases}\longrightarrow C_6H_5{\cdot}\overset{+}{C}H_2\}\overset{-}{Cl} \xrightarrow[(H_2O)]{} C_6H_5{\cdot}CH_2{\cdot}OH+H\{Cl\ (\text{type } A_1)\\ \xrightarrow[(OH')]{} C_6H_5{\cdot}CH_2\underset{\cdot\cdot OH'}{\cdots}Cl \longrightarrow C_6H_5{\cdot}CH_2{\cdot}OH+Cl'\ (\text{type } B_2)\end{cases}$$

and the probable assumption that the first predominates in neutral or acid solution, whilst the second supervenes in strongly alkaline solution, removes the apparent inconsistency between the results of Franzen and Rosenberg on the alkaline decomposition (*J. pr. Chem.*, 1920, **101**, 333) and those of Olivier and Berger (*Rec. trav. chim.*, 1923, **42**, 775; 1927, **46**, 605) on the acid hydrolysis of benzyl chloride and its nuclear substitution products. Other applications of the above classification of side-chain reactions have been given elsewhere (*Ann. Reports*, 1927, p. 155).

The substitution of halogen, nitroxyl, etc., for a side-chain hydrogen atom might *a priori* belong to either of the two main categories, for substitutions analogous to both types are known in Organic Chemistry. For instance, nuclear aromatic substitution is a process analogous to *A*, since it requires available electrons at the point of reaction : the initial process is to *attract* a potential cation (*e.g.*, entrant Hal or NO_2) and thus the order of facilitation by substituents is $NH_2 > OMe > Me > H$, etc. On the other hand, the α-halogenation of carbonyl compounds is analogous to *B*, since it requires the recession of electrons from the point of substitution : the initial process is to *split off* a cation (*viz.*, H^+) (compare Orton, Hughes, and Watson, J., 1927, 2461), so that the order of facilitation is $COMe > COCl > CO_2H > H$, etc. (compare Ingold, Shoppee, and Thorpe, J., 1926, 1477).

If mechanism *B* (prior ionisation of hydrogen) were to operate in the side-chain halogenation of toluene and similar substances, there are few substituents which would facilitate its action more strongly than an *o*- or a *p*-nitro-group, for *o*- and *p*-nitrotoluenes are

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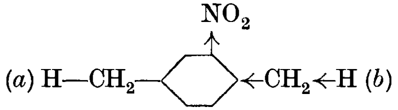
* In the absence of evidence that intermediate products are present in appreciable concentration during the progress of a reaction the first hypothetical stage may be regarded as the rate-determining stage.

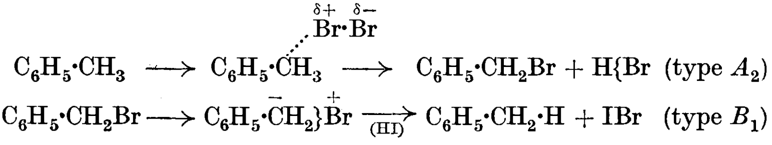
known to undergo reactions indicating that their side-chain hydrogen is prone to ionisation; indeed, these compounds even exhibit certain similarities to nitromethane and other pseudo-acids. A *m*-nitro-group would also be expected to exert a facilitating action, but it would be much weaker (Ingold and Shaw, J., 1927, 2918) and, accordingly, the nitro-group in nitro-*p*-xylene (formula below) should orient side-chain substitution in the direction of the group marked (*b*). On the other hand, if the mechanism were of type *A* (prior attraction of potential cation by electrons), it should be inhibited very strongly by an *o*- or a *p*-nitro-group, and only to a much smaller extent by a *m*-nitro-group (*ibid.*), and thus in nitro-*p*-xylene predominating substitution should occur in the side-chain marked (*a*):



Furthermore, if mechanisms *A* and *B* operated simultaneously in side-chain substitution of toluene and *p*-xylene, substitution in the nitro-xylene would occur mainly in the group marked (*b*), for the effect of the nitroxyl group is generally to suppress process *A* and facilitate *B*.

We have therefore examined the side-chain bromination of nitro-*p*-xylene and find that side-chain substitution occurs to the extent of at least 76% in the side chain (*a*). We conclude that the side-chain halogenation (and probably also nitration) of alkylbenzenes and their nuclear substitution products proceeds by mechanism *A*; a similar mechanism probably applies to the substitutions of methane and other aliphatic hydrocarbons.

On comparing this conclusion with that which might be derived from the work of Lapworth and Shoesmith on the reverse process, namely, the reduction of substituted benzyl halides (J., 1922, **121**, 1392, and later), mechanisms (all in good agreement with the available data) may be formulated to complete the exemplification of the general classification of side-chain substitutions, already partly illustrated (above) by the hydrolysis of benzyl chloride:



$$C_6H_5{\cdot}CH_3 \longrightarrow C_6H_5{\cdot}\overset{\overset{\delta+\ \ \delta-}{Br{\cdot}Br}}{CH_3} \longrightarrow C_6H_5{\cdot}CH_2Br + H\{Br \quad (\text{type } A_2)$$

$$C_6H_5{\cdot}CH_2Br \longrightarrow C_6H_5{\cdot}\overset{-}{C}H_2\}\overset{+}{Br} \xrightarrow[(HI)]{} C_6H_5{\cdot}CH_2{\cdot}H + IBr \quad (\text{type } B_1)$$

EXPERIMENTAL.

Side-chain Bromination of Nitro-p-*xylene*.—Dry bromine (30 g.) was very gradually added to a solution of nitro-*p*-xylene (25·0 g.)

in glacial acetic acid (30 c.c.) under reflux in a glycerol bath at 120°, the crystalline deposit which collected in the condenser being returned from time to time to the reaction mixture. The deep red product was poured into water, neutralised with sodium carbonate, and extracted with ether, a process which removed a small amount of a tarry substance insoluble both in ether and in water. The residue (28·2 g.) from the ethereal extract, which preliminary experiments had shown to contain unbrominated nitro-*p*-xylene as well as its bromination products, was heated with an excess of 33% alcoholic trimethylamine for 12 hours at 100°, and the quaternary bromides derived from side-chain-brominated products were precipitated by the addition of much dry ether and collected. From the ethereal solution nitro-*p*-xylene (16·3 g.) was recovered by distillation. The bromide precipitate was taken up in boiling alcohol (which removed a very small amount of an insoluble salt which has not yet been investigated), and the quaternary bromide (yield 62%, taking count of the nitro-*p*-xylene recovered), obtained by evaporation of the alcohol, was converted into the corresponding picrate, m. p. 138°, the identification of which is described below. The yield (*vide infra*) corresponds to the formation of not less than 77% of 3-nitro-*p*-xylyl bromide.

3-*Nitro*-p-*xylyl Bromide* [ω(1)-*Bromo*-3-*nitro*-p-*xylene*].—The bromination product obtained from the ethereal extract (above) is largely solid and a proportion of it (37%, based on the nitro-*p*-xylene used, *less* that recovered) was isolated in the pure condition. 3-*Nitro*-p-*xylyl bromide* crystallises from methyl alcohol in needles, m. p. 76° (Found: C, 42·4; H, 3·6. $C_8H_8O_2NBr$ requires C, 41·8; H, 3·5%). On treatment with alcoholic trimethylamine under the conditions mentioned in the preceding paragraph it is converted into the same quaternary bromide in 81% yield. The mother-liquors from the crystalline bromonitro-hydrocarbon contained a further quantity of this substance, together with unchanged nitro-*p*-xylene, and the mixture was therefore treated with trimethylamine; a yield of the quaternary salt stoicheiometrically equivalent to a further 31% of 3-nitro-*p*-xylyl bromide was then obtained. The total quantity of this compound produced cannot therefore be less than 68%, and, since the quaternary salt is produced in 81% yield from the pure bromide, is probably not less than 76%, which agrees with the previous figure. Since part of the remainder represents unidentified material, this figure is a minimum for the proportion of substitution in the *m*-methyl group.

3-*Nitro*-p-*xylyl*-ω-*trimethylammonium Picrate*.—3-Nitro-*p*-xylyl chloride was prepared by the action of dichlorodimethyl ether on *o*-nitrotoluene (Stephen, Short, and Gladding, J., 1920, **117**, 524), and had m. p. 48° (not 45° as recorded, *loc. cit.*). Treatment with alcoholic trimethylamine yielded a quaternary ammonium *chloride*, which was precipitated by addition of dry ether. The corresponding *picrate* separated from dilute alcohol in needles, m. p. 138° (Found : C, 47·2; H, 4·6. $C_{17}H_{19}O_9N_5$ requires C, 46·7; H, 4·3%), and was identical with the same salt obtained, as described above, from the bromination product of nitro-*p*-xylene. This identification orients the nitro-*p*-xylyl bromide, m. p. 76°.

We wish to thank the Chemical Society for a grant which has defrayed much of the cost of this work.

THE UNIVERSITY, LEEDS. [*Received, March* 22*nd*, 1928.]