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NON-CONVENTIONAL PATHS IN ELECTROPHILIC AROMATIC REACTIONS - XI. THE ORIENTATION IN THE CHLORINATION OF ISODURENE IN ACETIC ACID[1]

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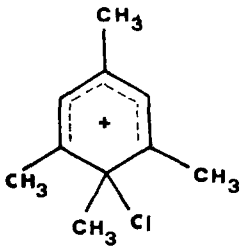
The electrophilic side-chain substitutions of alkylaromatics are raising considerable interest in several research groups. The scope of these reactions has been considerably widened and now includes halogenation (Cl_2, Br_2, ICl),[2-6] nitration,[7-9] thiocyanation,[10] and isotope exchange.[11] It is rewarding that the essential features of the mechanism originally proposed by two of us for the halogenation of alkylbenzenes[2,3,5] have been found substantially valid for all the other reactions investigated so far.

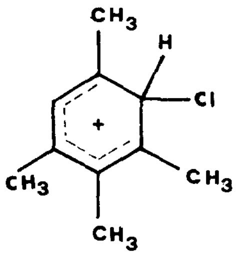
The σ-adduct intermediate is assumed to result from σ-bond formation of the electrophile with a reactive ring-position occupied by an alkyl group. The course of the subsequent rearrangement of the incoming reagent from nucleus to side-chain depends on the position at which proton loss occurs relative to the site of electrophilic attack and gives rise to a heretofore unsettled problem of orientation. So far, an ortho-orientation has been preferred[3,4,5,7] in the hypothesis of an intramolecular allylic-type rearrangement, but no definite evidence has yet been obtained.

In order to tackle the orientation problem, we have now carried out a product analysis of the dark chlorination of isodurene in acetic acid. The crude reaction product (which on separate analysis was found to contain 14% of mobile halogen) has been treated with Ag_2O in H_2O-dioxane in order to convert any side-chain chlorinated material into the corresponding alcohols. The recovered material was chromatographed on deactivated silica gel to give about 85% of ring chlorinated isodurene, 12% of 3,4,5-trimethylbenzylalcohol (I) (m.p. 70-71°C), and 3% of 3,4,5-trimethylbenzylacetate (II) *. The structure of (I) has been proved by comparison with an authentic specimen obtained by reduction of 3,4,5-trimethylbenzoic acid, whereas the structure of (II) has been verified by hydrolysis to (I). Moreover, VPC analysis showed, by comparison with authentic specimens, that out of the two other isomeric alcohols, 2,3,5-trimethylbenzylalcohol, if any, was present in amounts no higher than 0.2%, whereas 2,4,6-trimethylbenzylalcohol could not be detected at all. Thus, these results clearly show that side-chain chlorination of isodurene occurs exclusively, or nearly so, at the methyl group located at position 5.

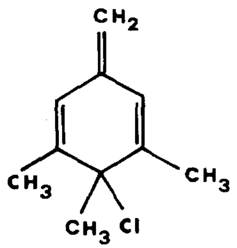
In isodurene positions 2 and 4 are the most activated ones for an electrophilic attack. However, the products of side-chain chlorination should come only from σ-complex (III) (attack at position 2) and not from σ-complex (IV) (attack at position 4), since the percentage of side-chain chlorinated materials was found by us to be the same as for isodurene and ring-deuterated isodurene ** . Thus, the formation of 5-substituted side-chain products strongly indicates that out of the two possible intermediates (V) and (VI) coming from



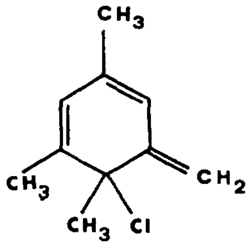
III



IV



V



VI

(*) Mole percent by yields of isolated products. The recovery of materials was 92%.

(**) The absence of a partitioning isotope effect could be consistent with an initial attack of chlorine at position 4 only by assuming a one-step cis-addition (see P.C. Myhre, G.S. Owen, and L.L. James, J.Amer.Chem.Soc., **90**, 2115 (1968)). However, in this case it seems difficult to explain why of the two possible addition products only that producing 3,4,5-trimethylbenzylchloride is actually formed.

(III), the former, possessing the more stable[12] para-quinonoid structure, is likely to play a major role in the reaction mechanism.

More generally, this result would imply that among the several possible reaction paths devised to rationalize the conversion of the firstly formed σ-complex into the side-chain chlorinated products[2,3,5,13] those involving an ortho-quinonoid structure, such as (VI), or an intramolecular migration of chlorine to the adjacent methyl group are relatively unimportant in systems where para-quinonoid structures can also be formed.[14] Similarly, we can definitively rule out the incursion of a quino-benzylic rearrangement or of any other mechanism requiring substitution to take place at the methyl group bonded to the tetrahedral carbon atom in the σ-complex.[15]

The formation of the side-chain chlorinated products from (V) probably results from an electrophilic attack of chlorine on the methylene group. In such a case, the formation of the accompanying acetate would require an S_N2' reaction of the solvent with (V). An alternative (or parallel) reaction path is the rearrangement of (V) to the side-chain product _via_ ion pair formation. The latter path would easily account for the formation of the acetate by exchange of the ion pair with the solvent.

Work is in progress to obtain further information on the relative importance of these possibilities.

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