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CHEMISTRY OF TRIVALENT IODINE:PART II MECHANISM OF ACTION OF PHENYLIODOSO ACETATE ON p-SUBSTITUTED ACETANILIDES AND N-ALKYLANILINES+

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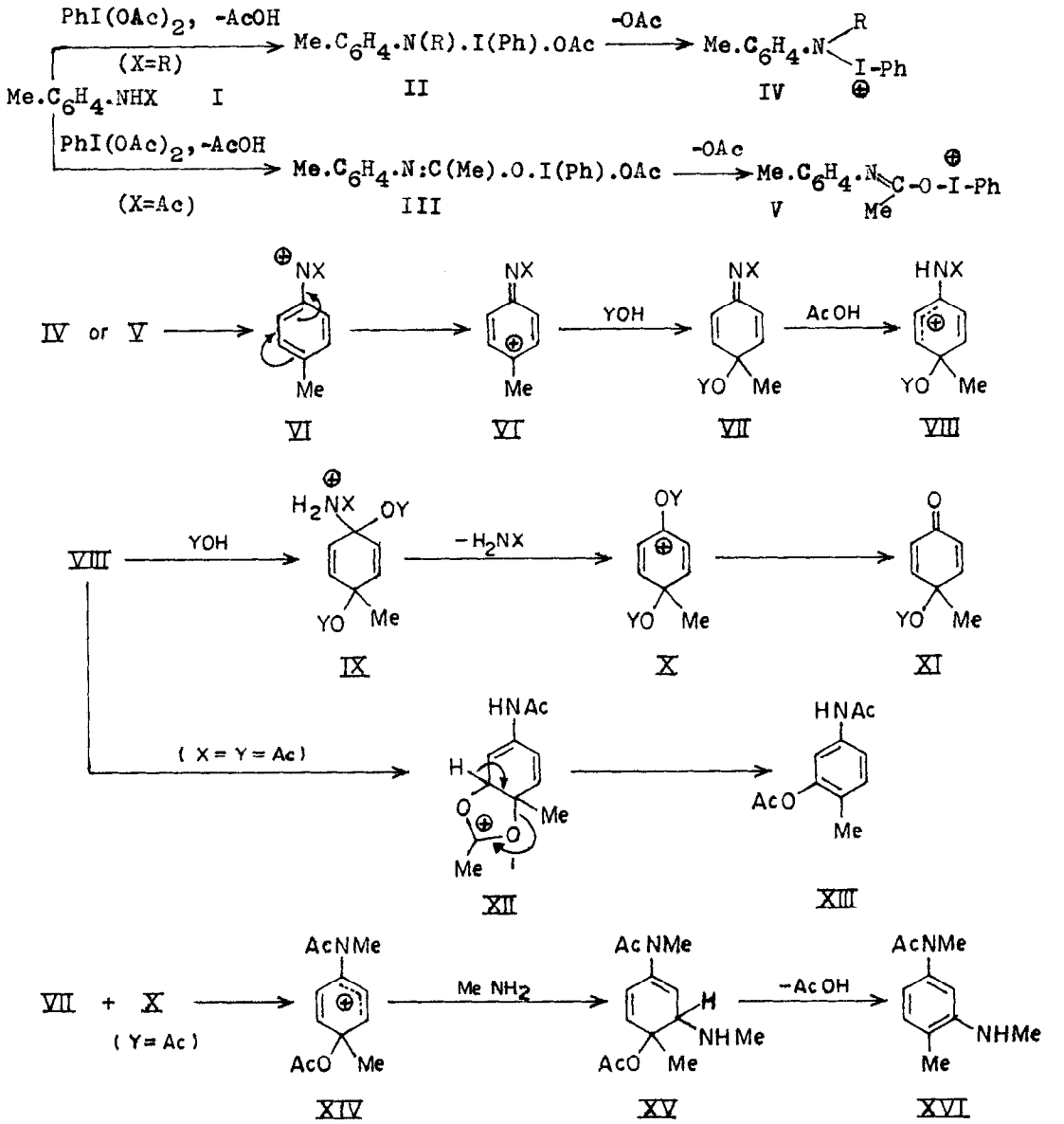
The reaction of phenyliodoso acetate with acetanilides having electron donating substituents like Me or OMe in the para position have been known to give good yields of meta-acetoxylated products in acetic acid solution[1]. Mineral acids catalyze the reaction without causing any appreciable change in product composition. Since evidence for the presence of radicals in the reaction mixture could not be obtained[2], a radical mechanism for the reaction suggested in one of the earlier studies[3] appears unlikely. It has been suggested that the reaction is an electrophilic displacement involving direct transfer of acetoxyl cation from phenylacetoxyiodonium ion to the substrate[2]. The meta orientation that is obtained has been attributed to steric effect of the acetamido group which is assumed to block ortho attack.

It appeared to us that this mechanistic picture is unsatisfactory at least on two counts. In the first place, it is difficult to accept that steric effect is the factor that determines the meta orientation of the acetoxyl group. The steric hindrance encountered by the phenylacetoxyiodonium ion as it approaches the two positions ortho to the acetamido group will not be of the same magnitude. At the less hindered of these positions, the steric effect will be roughly of the same order as that encountered at positions ortho to the methyl group. The well known behaviour of aceto-p-toluidide (I, X=Ac) in nitration indicates that the siteof electrophilic attack on the ring is determined by electronic activation rather than by steric factors. Secondly, the N-methyl derivative of this substrate does not react with phenyliodoso acetate. In an effort to throw more light on the nature of the reaction, we have studied it in methanolic medium and also examined the action of the reagent on N-methyl and N-t-butyl-p-toluidines (I, X=Me, t-Bu). The results indicate that these reactions proceed through dienone imine intermediates of type VII, and that, in the meta-acetoxylation reaction, the acetoxyl group actually enters the aromatic ring as a nucleophile.

Equimolecular quantities (0.02 moles each) of aceto-p-toluidide (I, X=Ac) and phenyliodoso acetate were reacted together in methanol (70 ml) under the same conditions (room temp., 24 hrs) as employed earlier[2] for the reaction in acetic acid and the solvent removed under suction at 40-45°. From the residue, in addition to iodobenzene, 4-methyl-4-methoxy-cyclohexa-2,5-dien-1-one (XI, Y=Me, ~ 0.90 g) and unreacted substrate (~ 1.10 g) could be isolated by chromatography over silica gel employing benzene, benzene-chloroform mixtures and pure chloroform as eluting solvents in the order mentioned. The dienone was readily identified by its melting point (63°)[4], elemental analysis, mass spectral mol. wt. and NMR spectrum [Me: 1.4 δ , s; OMe: 3.17 δ s; four vinyl protons: 6.46 δ weakly perturbed quartet]. The conversion was about 33% and the yield about 52%. A similar experiment employing N-t-butyl-p-toluidine (I, X=t-Bu) gave about the same yield of dienone; but, in addition, substantial amounts of t-butylammonium acetate (~ 1.02 g, 45%) could also be isolated as a reaction product. Most of it was obtained as a precipitate on acetone treatment of the residue left after removal of solvent from reaction mixture and some from the chromatographic column on final elution with methanol. When the reaction medium was changed to acetic acid, t-butyl ammonium acetate could again be isolated in fair yield (~38%); but, instead of the methoxydienone, the corresponding acetoxy derivative [b.p. 173-5°/6 mm; mol. wt. 166; PMR absorptions:- Me: 1.57 δ, OAc: 2.02 δ, perturbed four proton quartet centred at 6.50 δ] was obtained in about 57% yield at about the same conversion. With N-methyl-p-toluidine the reaction gave a more complex mixture of products, and dienone yields were smaller. In acetic acid solution, in addition to XI (Y=Ac), small amounts (~11%) of another compound (m.p. 99°) of the molecular formula $C_{11}H_{16}ON_2$ could be isolated. This was characterized as XVI on the basis of NMR, mass and IR spectral data. Also, we have confirmed the acetoxylation reaction reported for the acetyl derivatives of p-toluidine and p-anisidine in acetic acid solution. Actually, the yields in our hands appeared to be somewhat better.

These results suggest that all these reactions proceed through a common ionic mechanism which involves initial attack by phenylacetoxy iodonium ion on the amino or acetamido group of the substrate to give acetic acid and an iodoso intermediate II or III. The probable courses of the reactions involved are indicated in Chart-1. In the case of the anilide, structure III is suggested on the consideration that the reagent would prefer the most basic site for attack. Conductance measurements[5] show that phenyliodoso acetate is weakly dissociated in the hydroxylic solvents employed here and, presumably, the intermediates II and III also behave likewise. Cleavage of the cationic part (IV or V) of either intermediate gives iodobenzene and a substrate fragment

CHART-1



which is a resonance stabilized nitrenium ion (VI). Reaction of the nitrenium ion with the solvent (YOH) leads to a cyclohexa-2,5-diene-1-one imine derivative (VII). It is of interest here to note that VII_a (X=t.Bu, Y=Me) has been isolated in an analogous reaction of N-chloro-N-t-butyl-p-toluidine with silver ions[6,7]. However, in the presence of the acetic acid, which is available as a reaction product even in methanolic solution and under the

work-up conditions employed, the dienone imines are unstable, and in methanol VII_a, VII_b (X=Me, Y=Me) and VII_c (X=Ac, Y=Me) are solvolyzed to XI (Y=Me). When acetic acid is the medium employed for the reaction, VII_f (X=Y=Ac) is rearranged to the meta-acetoxylated derivative (XIII) as indicated while VII_d (X=t-Bu, Y=Ac) and VII_e (X=Me, Y=Ac) are apparently mostly solvolyzed to XI (Y=Ac). The acetoxyl rearrangement can, in principle, take place by an addition-elimination mechanism or by intramolecular migration of the acetoxyl group as indicated in the Chart. The absence of any significant meta-methoxylation suggests that the latter is the preferred path as in the rearrangement of p-quinol acetates studied earlier under mineral acid catalysis[8]. The formation of XVI is in consonance with the suggested mechanistic scheme and may be readily rationalized as shown in the Chart.

The simultaneous occurrence of both ionic and radical pathways in the decomposition of phenyliodoso acetate has been recorded earlier[9]. In view of this, the possibility of side reactions taking place through radical pathways in the cases under consideration here cannot be precluded.

The oxidation of phenols to quinol acetates and quinones studied earlier by Siegel and Antony[10] presumably follows a similar path. Further work on all these reactions is in progress.

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