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OXIDATION OF SECONDARY ALCOHOLS TO KETONES BY MEANS OF IODOBENZENE DICHLORIDE AND PYRIDINE

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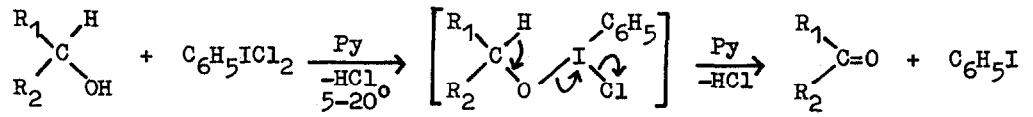
The need for new methods of preparation of carbonyl compounds from alcohols has recently stimulated the search for mild and selective oxidising agents. Some of the new methods, involving the formation of intermediate complex sulfonium[1,2] and ammonium[3] ions are particularly interesting. The mechanisms of these reactions suggest that in appropriate conditions iodobenzene dichloride (IBD) could react with secondary and primary alcohols to give mixed iodo disalts 1 which in turn should readily decompose to the corresponding carbonyl compounds. The results of investigations carried out in the author's laboratory proved that this conclusion is correct, although other authors[4] reported that IBD is not a suitable reagent for oxidation of diols. In the presence of weak bases in inert solvents IBD smoothly oxidises secondary alcohols to the corresponding ketones.The reaction can be carried out in mild and experimentally convenient conditions. It proceeds according to Scheme A which probably involves the formation of mixed iodo disalt 1:

Scheme A:



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The following procedure has been found to be suitable for small scale preparations:

A solution of secondary alcohol (1 eq.) in chloroform was added in one portion, with stirring, to a suspension of IBD (1.5 - 3 eq.) in dry chloroform containing an excess of pyridine. During the addition the suspension was cooled to 0 - 5° and care was taken to exclude atmospheric moisture. The reaction mixture was allowed to stand at room temperature for 30 min. and then it was treated with an aqueous sodium thiosulphate solution. The clear yellow reaction mixture became colourless. The chloroform layer was separated and washed subsequently with dilute hydrochloric acid and with water and after drying the solvent was evapourated. For steroid and other non volantative compounds the resulting ketone was freed from iodobenzene by repeated addition of small amounts of water and evapouration in a rotatory evaporator.

In the experiments carried out in the author's laboratory the following yields of ketones were obtained:

5α-cholestan-3β-ol	5α-cholestan-3-one	81%	5)
5α-cholestan-3α-ol		72%	5)
androsterone	5α-androstan-3,17-dione	67%	5)
cyclohexanol	cyclohexanone	82%	6)
4-t-butylcyclohexanol	4-t-butylcyclohexanone	86%	6)
benzhydrol	benzophenone	49%	6)

All the products were identified by direct comparison with pure authentic specimens (IR, m.pt., tlc and/or glc).

The oxidation of primary alcohols carried out in identical conditions was found to be a much more complex process.

The usefulness of IBD as oxidising agent is limited to the oxidation of saturated alcohols, mainly as a result of its tendency to chlorinate substrates containing C = C bonds, which is also drawback of Corey and Kim dimethyl sulfoxide-chlorine reagent[1c]. As it could be expected[7], the addition of chlorine to double bonds in reactions of unsaturated compounds with IBD carried out in chloroform or similar solvents at room temperature in the dark was rather slow, but in the presence of pyridine the chlorination was fast. Thus a mixture of cholest-5-ene 2 (1 eq.) and IBD (1.3 eq.) in carbon tetrachloride left to stand in the dark at room temperature contained the unsaturated substrate even after 12 hrs; in analogous conditions, but in the presence of pyridine, the substrate reacted completely during about 15 mins. It is of interest that in the presence of pyridine 5,6β-dichloro-5α-cholestane 3 (trans-dichloride) was formed as the only reaction product, whereas in the heat or light induced chlorination (200 W incandescence lamp) IBD gave a mixture of trans-dichloride 3 and hitherto unknown 5,6α-dichloro-5α-cholestane[8] 4 (cis-dichloride) in the ratio of about 7:3.

In the course of the above described work it was found that iodosobenzene in inert solvents reacts vigorously with aliphatic acyl chlorides to give IBD and acid anhydrides. This reaction, which has not been reported until the present time, takes place according to the Scheme B:

Scheme B:

$$C_6H_5IO + 2RCOCl \longrightarrow C_6H_5ICl_2 + (RCO)_2O$$

$$C_6H_5IO + R\text{-}C(=O)Cl \longrightarrow [C_6H_5\text{-}I^+\text{-}O\text{-}CO\text{-}R]\,Cl^- \rightleftarrows [C_6H_5\text{-}I^+\text{-}Cl]\,RCOO^- \xrightarrow{RCOCl}$$

$$\longrightarrow C_6H_5ICl_2 + (RCO)_2O$$

In the reaction of iodosobenzene with oxalyl chloride in chloroform the formation of IBD precipitate is accompanied by the evolution of carbon dioxide and carbon monoxide. Benzoyl chloride reacts with iodosobenzene on prolonged standing or at elevated temperatures.

Further work on application of IBD and related complexes to oxidation of organic compounds is now in progress.

References and Footnotes

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5. Yields of isolated and recrystallised products

6. Isolated as 2,4-dinitrophenylhydrazone

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8. The structure was consistent with nmr, mol wt and combustion analysis data; m.p. 113-114°, $[\alpha]_D^{27}$ -14,4° /c.1,1 $CHCl_3$/.