Synthetic Methods and Reactions; 37[1]. Selective Organic Oxidations with Iodine Pentafluoride in 1,1,2-Trichlorotrifluoroethane Solution

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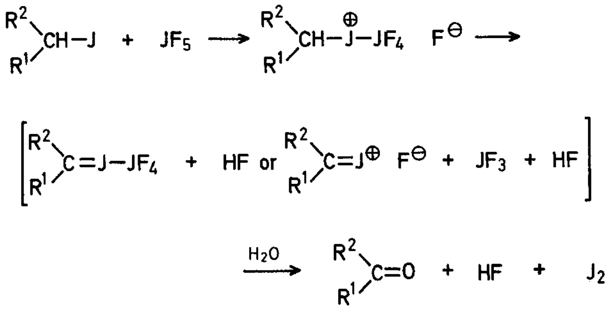
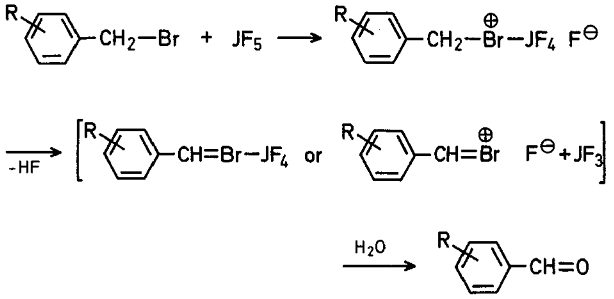
The use of hypervalent iodine compounds as oxidizing agents in organic chemistry is well established, as illustrated in a recent review of the reactions of polyvalent organic iodine compounds[2]. Particularly, the iodine(V) and iodine(VII) salts of the corresponding oxoacids are smooth, yet powerful oxidizing agents[3]. The work of Stevens[4] has shown iodine pentafluoride to promote the oxidative dehydrogenation of some amines and brings about the oxidative condensation of amides. As no more detailed study of the use of iodine pentafluoride as an oxidizing agent in organic synthesis has been reported, we now wish to report our observation of the facile and selective oxidation of organic compounds with iodine pentafluoride in 1,1,2-trichlorotrifluoroethane solution.

Alkyl iodides and benzylic bromides are oxidized with iodine pentafluoride to the corresponding carbonyl compounds in satisfactory to good yield (see Table 1). The reactions can be envisioned as proceeding through an intermediate iodine(III) or bromine(III) species, respectively.

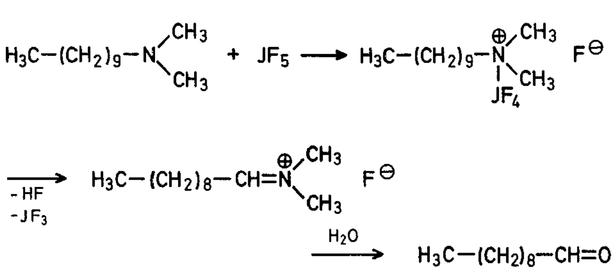


The reactions of benzylic bromides are assisted by the adjacent phenyl ring in stabilizing the developing charge deficiency[5].

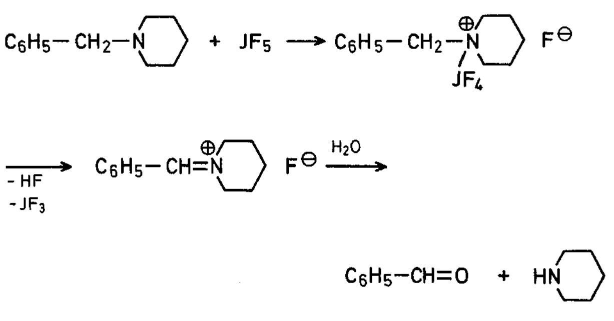


The reaction of alkyl iodides is selective; alkyl bromides react only slightly, and alkyl chlorides not at all. Likewise benzyl chlorides are unreactive under the reaction conditions. Existing methods for the oxidation of alkyl halides require activation[6], rigorous conditions[7], or transformation to a more readily oxidized intermediate[8], and consequently are generally less selective.

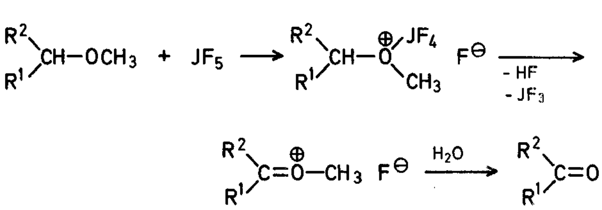
Although the dehydrogenation of amines to nitriles was studied[4], the use of iodine pentafluoride to oxidize tertiary amines to carbonyl compounds was unreported. The oxidation of tertiary amines must necessarily proceed through an iminium intermediate as suggested by Stevens[9].



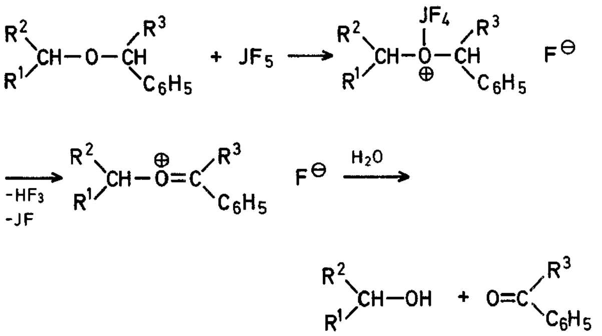
The reaction proceeds regiospecifically for the oxidation of dimethylamines and diethylamines, as well as for *N*-alkylpiperidines (see Table 1).



Ethers are also oxidatively cleaved to alcohols and carbonyl compounds. The reactions of methyl ethers are regiospecific.



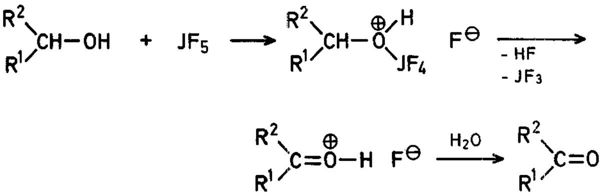
The reactions of iodine pentafluoride with benzyl and benzhydryl ethers to readily give the parent alcohol, as well as benzaldehyde or benzophenone, respectively, can serve to further enhance the utility of these ethers as protecting groups for alcohols (see Table 2).



R^1 = alkyl
R^2 = H, cycloalkyl
R^3 = H, C_6H_5

Alcohols themselves can be further oxidized with excess iodine pentafluoride to carbonyl compounds (see Table 1).

The high reactivity of the postulated oxonium ion intermediate may account for the lower yields of carbonyl products. In the reaction of primary alcohols both aldehydes and carboxylic acids were produced.



It has been previously stated that the reactions of iodine pentafluoride were difficult to control[10]. However, we have found iodine pentafluoride in 1,1,2-trichlorotrifluoroethane solution to be a convenient and readily handled general oxidizing agent which does not require any special precautions under the reaction conditions described.

Table 1. Oxidation of Alkyl Halides, Amines and Alcohols to Carbonyl Compounds

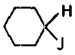
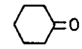
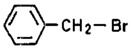
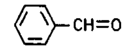
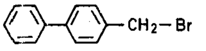
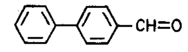
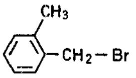
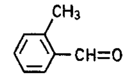
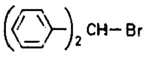
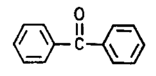
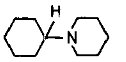
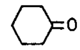
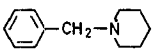
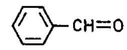
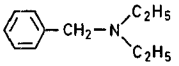
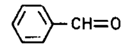
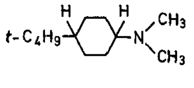
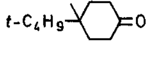
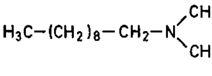
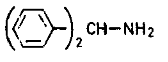
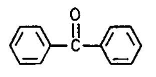
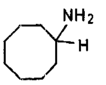
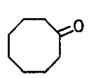
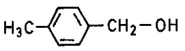
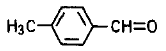
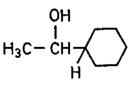
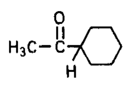
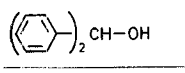
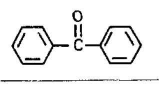
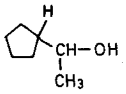
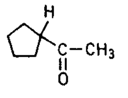
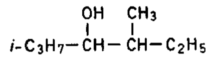
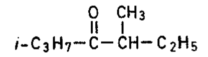
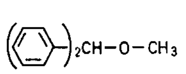
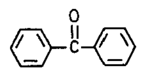
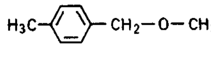
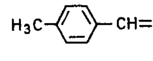
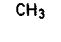
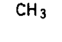
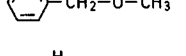
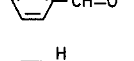
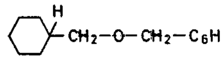
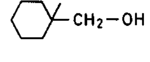
Substrate	Product	Yield[a] [%]	C=O Stretch [cm^{-1}]
$H_3C-(CH_2)_5-\overset{J}{\overset{\vert}{C}}H-CH_3$	$H_3C-(CH_2)_5-\overset{O}{\overset{\Vert}{C}}-CH_3$	56	1715
$H_3C-(CH_2)_6-\overset{J}{\overset{\vert}{C}}H-CH_3$	$H_3C-(CH_2)_6-\overset{O}{\overset{\Vert}{C}}-CH_3$	40	1714
$H_3C-(CH_2)_{10}-\overset{J}{\overset{\vert}{C}}H-CH_3$	$H_3C-(CH_2)_{10}-\overset{O}{\overset{\Vert}{C}}-CH_3$	32	1715
$H_3C-(CH_2)_8-CH_2-J$	$H_3C-(CH_2)_8-CH=O$	24	1720
$H_3C-(CH_2)_5-CH_2-J$	$H_3C-(CH_2)_5-CH=O$	46	1714
		63	1720
		65	1701
		27	1690
		43	1703
		86	1663
		17	1720
		43	1700
		30	1705
		17	1718
	$H_3C-(CH_2)_8-CH=O$	54	1720
		53	1664
		20	1703
		39	1702
$n\text{-}C_4H_9-\overset{OH}{\overset{\vert}{C}}H-C_3H_7\text{-}n$	$n\text{-}C_4H_9-\overset{O}{\overset{\Vert}{C}}-C_3H_7\text{-}n$	56	1715
$H_3C-\overset{OH}{\overset{\vert}{C}}H-C_5H_{11}\text{-}n$	$H_3C-\overset{O}{\overset{\Vert}{C}}-C_5H_{11}\text{-}n$	28	1718
		23	1715
		42	1668

Table 1. (Continued)

Substrate	Product	Yield[a] [%]	C=O stretch [cm^{-1}]
		18	1715
 $i\text{-}C_3H_7-CH(OH)-CH(CH_3)-C_2H_5$	 $i\text{-}C_3H_7-C(=O)-CH(CH_3)-C_2H_5$	76	1712

[a] Yields reported are those of isolated products purified by chromatography and characterized by comparison of their spectral and physical properties with those of the authentic materials.

Table 2. Oxidative Cleavage of Ethers to Alcohols and Carbonyl Compounds

Ether	Product	Yield [%]	C=O stretch [cm^{-1}]
		43	1665
		96	1698
 $n\text{-}C_4H_9-CH(CH_3)-O-CH_3$	 $n\text{-}C_4H_9-CH(CH_3)-OH$	49	1712
		43	1705
		31	—
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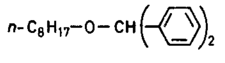
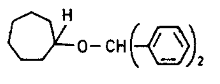
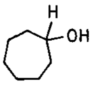
	$n\text{-}C_8H_{17}-OH$	71	—
		24	—

[a] Yields reported are those of isolated products purified by chromatography and characterized by comparison of their physical and spectral properties with those of the authentic materials.

Oxidation of Diphenylmethyl Bromide to Benzophenone:

Diphenylmethyl bromide (2.47 g, 0.01 mol) dissolved in 1,1,2-trichlorotrifluoroethane (100 ml) is treated with freshly distilled iodine pentafluoride (3.6 g, 0.03 mol) with stirring at room temperature. After 2 h, the reaction mixture is quenched with water (50 ml), the aqueous phase is separated, the organic layer is washed with saturated sodium hydrogen sulfite solution, and dried ($MgSO_4$). The solvent is removed on a rotary evaporator and the product is purified by chromatography on absorbent alumina, eluting first with petroleum ether (b.p. 36–55°) (350 ml), followed by benzene (350 ml) to give benzophenone; yield: 1.33 g (73%); m.p. of 2,4-dinitrophenylhydrazone: 221°.

Oxidation of a Tertiary Amine to an Aldehyde; Typical Procedure:

To iodine pentafluoride (4.8 g, 0.022 mol) dissolved in 1,1,2-trichlorotrifluoroethane (100 ml) is added *N*-benzylpiperidine (1.75 g, 0.01 mol) dissolved in the same solvent (10 ml). After stirring for 2 h at room temperature, the reaction is quenched with water (75 ml) and the organic phase separated. The organic phase is washed with aqueous saturated sodium hydrogen sulfite until colorless, washed with water, and dried over anhydrous magnesium sulfate. Evaporation of the solvent gives benzaldehyde; yield: 0.47 g (43%).

Oxidative Cleavage of Methyl Ethers to Carbonyl Compounds; Typical Procedure:

To iodine pentafluoride (2.4 g, 0.011 mol) dissolved in 1,1,2-trichlorotrifluoroethane (100 ml) is added 4-methylbenzyl methyl ether (0.70 g, 0.005 mol) in the same solvent (10 ml). After stirring at room temperature for 1 h, the reaction is quenched with water (75 ml). The organic phase is separated, washed with saturated aqueous sodium hydrogen sulfite and water, and dried over anhydrous magnesium sulfate. Evaporation of the solvent gives 4-methylbenzaldehyde; yield: 0.57 g (96%).

Oxidative Cleavage of Benzyl Ethers to Alcohols; Typical Procedure:

To iodine pentafluoride (2.4 g, 0.011 mol) dissolved in 1,1,2-trichlorotrifluoroethane (100 ml) is added dropwise cyclohexyl benzyl ether (1.02 g, 0.005 mol) in the same solvent (10 ml). After stirring at room temperature for 1 h, the reaction is quenched with water (75 ml). The organic phase is separated, washed with saturated sodium hydrogen sulfite and water, and dried over anhydrous magnesium sulfate. Evaporation of the solvent gives a mixture of benzaldehyde and cyclohexanol which is separated by chromatography on 30 g of adsorbent alumina eluting with 300 ml of benzene followed by 250 ml of chloroform; cyclohexanol is isolated from the chloroform solution; yield: 0.18 g (31%).

Oxidation of an Alcohol to a Ketone; Typical Procedure:

To iodine pentafluoride (4.0 g, 0.018 mol) dissolved in 1,1,2-trichlorotrifluoroethane (100 ml) is added 2,4-dimethyl-3-hexanol (1.30 g, 0.01 mol) dissolved in the same solvent (10 ml). After stirring at room temperature for 1 h, the reaction is quenched with water (75 ml). The organic phase is separated, washed with saturated sodium hydrogen sulfite and water, and dried over anhydrous magnesium sulfate. Evaporation of the solvent gives a crude product which is purified by chromatography on aluminum oxide (Merck) with benzene to give 2,4-dimethyl-3-hexanone; yield: 0.98 g (76%).

Support of our work by the National Science Foundation is gratefully acknowledged.

Received: December 15, 1976

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