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A CONVENIENT METHOD FOR THE TRANSFORMATION OF ALCOHOLS TO ALKYL IODIDES USING 2-FLUOROPYRIDINIUM SALT

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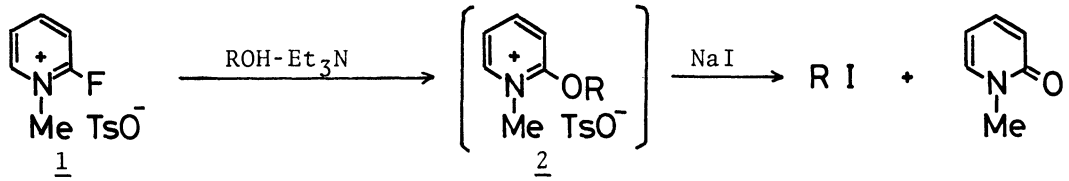
1-Methyl-2-alkoxypyridinium salts, easily formed in situ from 1-methyl-2-fluoropyridinium salt and alcohols, react with sodium iodide to give the corresponding alkyl iodides in good yields.

During the course of our synthetic investigation utilizing 2-halopyridinium salts, a convenient method has been recently reported for the preparation of 2-pyridyl or phenyl sulfides.[1] We wish to report here a transformation of alcohols to alkyl iodides using 1-methyl-2-fluoropyridinium p-toluenesulfonate 1 and sodium iodide. This transformation includes two reaction steps: i) The formation of a key intermediate 2-alkoxypyridinium salt 2, and ii) the reaction of 2 with sodium iodide.



1 2

The transformation of alcohols to alkyl iodides has been effected by several methods.[2] Recently Scheffold and Saladin described the carbodiimidinium iodide method[3] along the similar concept to our method.

At first the effect of the solvents was examined for the preparation of 3-phenylpropyl iodide as a model. The formation of 2-alkoxypyridinium salt 2 is very fast in dichloromethane, chloroform or acetonitrile (within 10 min at room temperature), and slower in benzene or acetone (1 hr). The reaction of 2 with sodium iodide was carried out in various solvent systems, and benzene-acetone (1:1) was found to be the best (Table 1).

Table 1 The solvent effect for the reaction of 2 with sodium iodide.

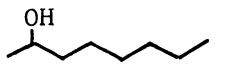
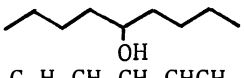
solvent	temp.	yield[a] (%)
CH_3CN	refl.	89
$CHCl_3$-$(CH_3)_2CO$ (1:1)	refl.	87
$(CH_3)_2CO$	refl.	78
C_6H_6-$(CH_3)_2CO$ (1:1)	refl.	94

a) Yields are based on 3-phenyl-1-propanol which was treated with 2 molar amounts of sodium iodide for 1 hr.[4]

A typical procedure is described for the preparation of 3-phenylpropyl iodide. To a suspension of 1 (1.2 mmol) in benzene (1 ml) was added a mixture of 3-phenyl-1-propanol (1 mmol) and triethylamine (1.2 mmol) in benzene (1 ml) under an argon atmosphere and the mixture was stirred for 1 hr at room temperature to give a clear yellow solution. Then an acetone solution (2 ml) of sodium iodide (2 mmol) was added and the resulting mixture was heated to reflux for 1 hr. After evaporation of the solvent, 10 ml of water was added. An organic layer was extracted with hexane, and the extracts were condensed under reduced pressure to give the almost pure (nmr spectrum) sample of 3-phenylpropyl iodide, which was purified by thin layer chromatography. During the work-up, 1-methyl-2-pyridone and unchanged 2-alkoxypyridinium salt were easily removed by simple washing with water.

In a similar manner, various primary and secondary alcohols were converted to the corresponding iodides in good yields in refluxing benzene-acetone (1:1) with 2 molar amounts of sodium iodide (Table 2).

Table 2 The preparation of alkyl iodides.

ROH	time (hr)	yield (%)
$C_6H_5CH_2CH_2CH_2OH$	1	94
$C_6H_5CH_2CH_2OH$	1	93
$C_6H_5CH_2OH$	1	90
$CH_3(CH_2)_6CH_2OH$	1	80
	1	60
	2	91
	2	80
$C_6H_5CH_2CH_2\underset{\displaystyle OH}{\underset{\vert}{C}}HCH_3$	2	79

It should be noted that the present method is of quite general utility; alkyl iodides are obtained starting from alcohols, in good yields, by a simple procedure using readily available pyridinium salt.

References and Notes

1) T. Mukaiyama, S. Ikeda, and S. Kobayashi, Chem. Lett., 1159 (1975).

2) I. T. Harrison and S. Harrison, "Compendium of Organic Synthetic Methods", Wiley-Interscience, New York, N. Y., 1971, p. 331.
Idem, "Compendium of Organic Synthetic Methods", Vol. II, Wiley-Interscience, New York, N. Y., 1974, p. 137.

3) R. Scheffold and E. Saladin, Angew. Chem., 84, 158 (1972); Angew. Chem. internat. Edit., 11, 229 (1972).

4) When an equimolar amount of sodium iodide was used, 3-phenylpropyl iodide was obtained in only 74% yield. Further it was found that tetra-n-butylammonium iodide can act as an iodinating reagent, for example, 3-phenylpropyl iodide was obtained in 85% yield in refluxing benzene-acetone (1:1).

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