

A NEW METHOD FOR THE EFFICIENT CONVERSION OF ALCOHOLS INTO IODIDES
VIA TREATMENT WITH TRIMETHYLSILYL IODIDE

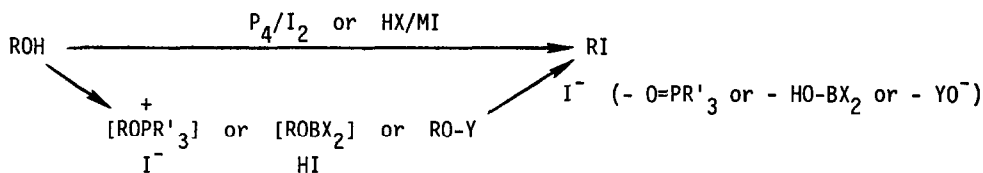
Michael E. Jung* and Paul L. Ornstein¹

Contribution No. 3809 from the Department of Chemistry,
University of California, Los Angeles, California 90024

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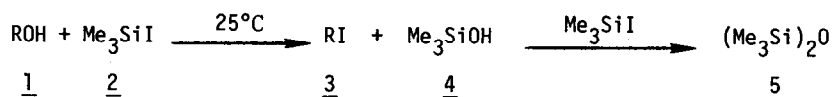
The conversion of alcohols into alkyl iodides is very often a useful and necessary organic transformation. We wish now to report a simple and efficient one-step method for the conversion of alcohols into iodides under mild conditions via treatment of the alcohols or their trimethylsilyl ethers with the interesting electrophilic reagent, trimethylsilyl iodide.²

The two classical methods for this reaction are a) the use of red phosphorus and molecular iodine,³ and b) the reaction of alcohols with hydrogen iodide, usually generated *in situ* from alkali iodide and acid.⁴ Several newer methods have appeared recently which utilize a variety of phosphorus and boron derivatives and in which formation of a molecule containing a very stable phosphorus-oxygen double bond (phosphonate⁵ and phosphate⁶ derivatives) or a boron-oxygen single bond⁷ provides a large part of the driving force for the reaction. Finally, conversion of the alcohol into a good leaving group followed by nucleophilic attack by iodide ion forms the basis of several other recent techniques for this transformation.⁸



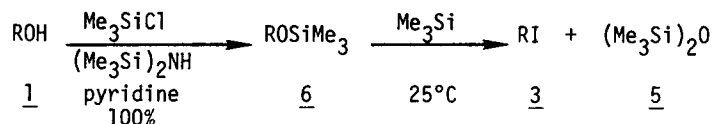
We have recently reported the use of trimethylsilyl iodide for the efficient conversion of alkyl carboxylates into trimethylsilyl carboxylates (and hence carboxylic acids)⁹ and for the transformation of dialkyl and aryl alkyl ethers into the corresponding alkyl and aryl trimethylsilyl ethers

(and hence alcohols and phenols)¹⁰. When trimethylsilyl iodide 2 is added to a solution of the alcohol 1 in a chlorinated hydrocarbon solvent (CCl_4 , CHCl_3 , CH_2Cl_2) at 25° under a nitrogen atmosphere, a facile reaction occurs which is best monitored by NMR spectroscopy. The protons α to the oxygen disappear over a period of time and are replaced by the protons α to iodide in the corresponding alkyl iodide, 3. The silicon-containing byproducts in this reaction are a mixture of trimethylsilanol 4 and hexamethyldisiloxane 5, the exact composition of which depends on the

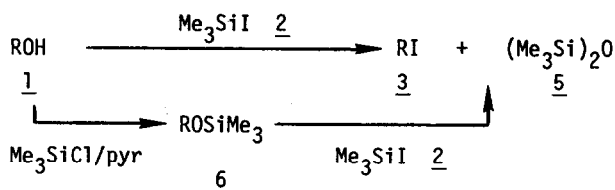


amount of trimethylsilyl iodide present. In this procedure hydrogen iodide is always produced.

With molecules containing acid-sensitive functional groups, an alternate technique has been devised which avoids the production of hydrogen iodide. The trimethylsilyl ether 6 of the alcohol 1 is prepared by normal, mild base-catalyzed procedures and then reacted with trimethylsilyl iodide 2 to afford the desired alkyl iodide 3 and hexamethyldisiloxane 5.



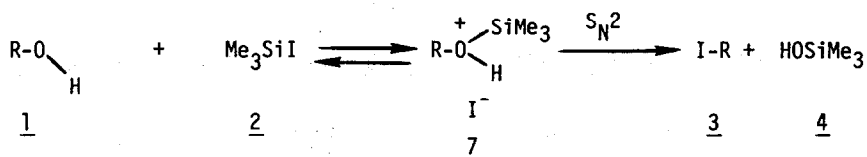
The results of the conversion of a series of alcohols into the corresponding iodides by both of these new techniques, that is, reaction of trimethylsilyl iodide with the alcohol itself or with the preformed trimethylsilyl ether are shown in the Table. From this data several interesting observations can be made. First, it is obvious that primary, secondary, and tertiary alcohols all can be converted into the corresponding iodides in good yields. Secondly, no general statement can be made concerning the preference of one of the two methods over the other; either method may give a higher yield depending on the particular alcohol. Finally, the reaction proceeds predominantly with inversion of configuration. For example, when optically pure (+)-2-octanol 1q was treated with trimethylsilyl iodide, the 2-octyl iodide obtained was 87% optically pure and of inverted configuration. The same general result was also observed for the conversion via the optically active trimethylsilyl ether 6q, i.e., (-)-2-octyl iodide was obtained in 88.6% purity. These results imply inversions of 93.5% and 94.3% respectively. Thus the stereochemical course of the reaction of secondary alcohols with trimethylsilyl iodide appears to follow an $\text{S}_{\text{N}}2$ -type of reaction mechanism, probably via the silylated intermediate, 7.

TABLE^aCONVERSION OF ALCOHOLS INTO IODIDES WITH TRIMETHYLSILYL IODIDE

| <u>STARTING ALCOHOL</u> | | <u>PRODUCTS AND YIELDS</u> | | |
|-------------------------|---|----------------------------|--------------------|------------------------|
| <u>Compound</u> | <u>R</u> | <u>Time(hr)</u> | <u>via Alcohol</u> | <u>via Silyl Ether</u> |
| <u>a</u> | CH ₃ | 0.5 | (100) ^c | --- |
| <u>b</u> | CH ₃ CH ₂ | 5 | (99) ^c | --- |
| <u>c</u> | (CH ₃) ₂ CH | 24 | (96) ^c | --- |
| <u>d</u> | (CH ₃) ₃ C | 0.2 | (100) ^c | --- |
| <u>e</u> | cyclopentyl | 0.4 | (100) ^c | --- |
| <u>f</u> | CH ₃ (CH ₂) ₃ CHCH ₂ CH ₃ | 2 | (100) ^c | --- |
| <u>g</u> | n-C ₁₅ H ₃₁ CH ₂ | 24 | 88 | 79 |
| <u>h</u> | n-C ₁₁ H ₂₃ CH ₂ | 24 | 76 | 81 |
| <u>i</u> | n-C ₉ H ₁₉ CH ₂ | 24 | 73 | 88 |
| <u>j</u> | PhCH ₂ | 24 | 85 | 67 |
| <u>k</u> | PhCH ₂ CH ₂ | 24 | 87 | 84 |
| <u>l</u> | cyclohexyl | 24 | 81 | 75 |
| <u>m</u> | CH ₃ (CH ₂) ₃ CHCH ₂ CH ₃ CH ₃ | 24 | 63 | 76 |
| <u>n</u> | ClCH ₂ CH ₂ CH ₂ CH ₂ | 24 | 80 | 76 |
| <u>o</u> | 4-Me-cyclohexyl | 24 | 84 | 80 |
| <u>p</u> | d1-2-octyl | 24 | 79 | 82 |
| <u>q</u> | d-S-2-octyl | 24 | 95 ^d | 75 ^e |
| <u>r</u> | CH ₃ CH(OH)CH ₂ CH ₂ CH ₂ OH | 24 | 75 ^f | --- |

Footnotes for Table

- a) All reactions were conducted in CHCl₃ or CDCl₃ solvent at 25°C under N₂.
- b) Yields are for isolated purified products after aqueous workup (with bisulfite wash). The iodides were identified by comparison (bp, NMR) with authentic samples.
- c) These yields were determined by NMR measurements alone without isolation of products.
- d) Starting with (+)-2-octanol, $[\alpha]_D^{25} = +10.38^\circ$, (-)-2-octyl iodide, $[\alpha]_D^{25} = -47.7^\circ$, was obtained. This iodide is 87% optically pure,¹¹ implying 93.5% inversion.
- e) Starting with the silyl ether, $[\alpha]_D^{25} = +12.7^\circ$, made from (+)-2-octanol, (-)-2-octyl iodide, $[\alpha]_D^{25} = -49.5^\circ$, was obtained (88.6% pure)¹¹ implying 94.3% inversion.
- f) The product is 1,4-diiodopentane.



Further studies into the utility of trimethylsilyl iodide for synthetic transformations are currently underway.

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