



A simple, mild and selective iodination of alcohols

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Abstract: A simple and highly regio-selective procedure for the conversion of allylic, benzylic and aliphatic alcohols to their corresponding iodides using $PPh_3/I_2/4$ -DMAP in dichloromethane at room temperature is presented.

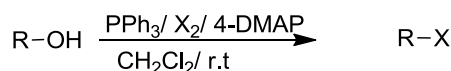
Keywords: Iodination; Benzylic Alcohol; Aliphatic alcohols; Chemoselective, Iodides.

I. Introduction

Organic halides are valuable intermediates in organic synthesis.¹ Alkyl bromides and iodides serve as intermediates in a wide variety of reactions and rearrangements which makes the conversion of alcohols into the corresponding halides a very important transformation in organic synthesis.^{2,3} The most common precursors to alkyl halides are alcohols, and their conversion into alkyl halides is the frequently encountered functional group-transformation reactions. Among the halides, iodides are the most reactive, and in some cases, it shows unique reactivity.⁴ A number of methods for the transformation of alcohols into alkyl iodides were reported which includes BF_3-Et_2O/NaI ,⁵ P_2I_4 ,⁶ P_4/I_2 ,⁷ $Cl_2SO-DMF/KI$,⁸ MgI_2 ,⁹ HI ,¹⁰ $ClSiMe_3/NaI$,¹¹ $R_3PI_2-Et_2O$, or $C_6H_6/HMPA$,¹² $CeCl_3.7H_2O/NaI$,¹³ $PPh_3/DDQ/R_4N^+X^-$,¹⁴ $KI/BF_3.Et_2O$,¹⁵ $ZrCl_4/NaI$,¹⁶ I_2 /petroleum ether,¹⁷ and KI/SSA .¹⁸ The existing reported methods suffer from drawbacks such as high temperature,¹⁹ long reaction times,²⁰ low yields, drastic conditions, non-commercially available materials and tedious work-up procedures.²¹ Thus introducing new methods with mild, higher efficiency and selectivity, less toxicity, shorter reaction time, easy handling and also using inexpensive and commercially available materials are still a challenge for the synthetic organic chemists.

II. Results and discussion

Due to the afore mentioned limitations of the existing protocols and in continuation of our ongoing research interest in this area and developing new methods in organic synthesis,²² herein a simple and efficient procedure for the iodination of alcohols using a combination of triphenylphosphine and iodine under room temperature has been investigated (Scheme 1).



R = allylic, benzylic or other 1° group
X = I, Br

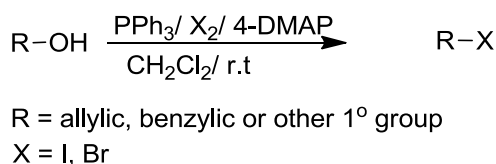
Scheme 1

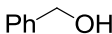
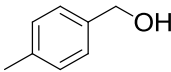
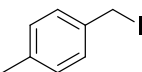
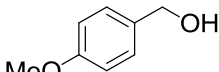
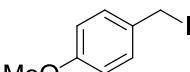
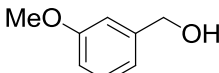
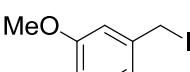
The iodination of benzyl alcohol was selected for optimization of the reaction conditions. Initially, the conversion of benzyl alcohol to benzyl iodide with triphenylphosphine, iodine and 4-DMAP in the presence of

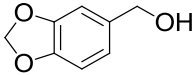
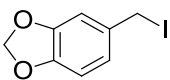
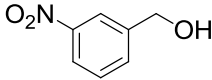
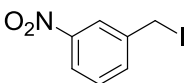
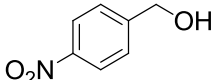
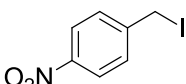
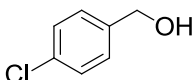
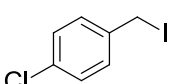
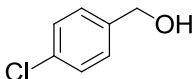
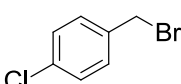
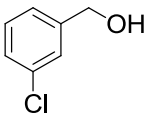
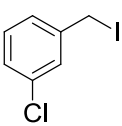
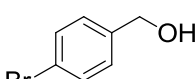
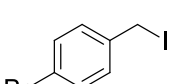
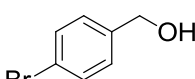
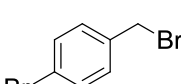
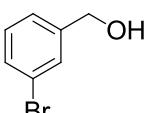
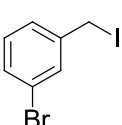
various solvents such as diethyl ether, ethyl acetate, *n*-hexane, acetone, dimethyl foramide and dichloromethane at room temperature was studied. Among the various solvent tested for the reactions, dichloromethane was found to be the best solvent for these transformations. Henceforth, the iodination of various benzylic, allylic and aliphatic alcohols in the presence $\text{Ph}_3\text{P}/\text{I}_2/4\text{-DMAP}$ in anhydrous dichloromethane was further studied. A variety of alcohols were smoothly converted to the corresponding iodides using $\text{I}_2/\text{Ph}_3\text{P}/4\text{-DMAP}$ system at room temperature. The generality of the method was examined using aryl, allyl, alkyl alcohols and the results of the iodination reactions are summarized in Table 1.

It was observed that benzylic alcohols are also highly reactive under our reaction condition and yields were relatively less dependent on the substitution pattern on the phenyl rings. Under the optimized conditions, we tried chemoselective conversion of butan-1,3-diol (Table 1, entry 18) with our protocol. To our pleasure, the reaction gave exclusively 4-Iodobutan-2-ol leaving the secondary alcohol intact. Furthermore, reaction on 2-methylpent- 2,4-diol (Table 1, entry 19) was carried out to study chemoselectivity between secondary and tertiary alcohol which showed selectivity towards secondary alcohol. The structure of the product was confirmed by DEPT-135 study. Next, to test the scope and limitation of this methodology, we employ this reagent system in bromination by replacing the iodine with bromine. We are pleased to get the desired bromide in excellent yield (Table 1, entry 9, 12).

Table 1. Conversion of alcohols to halides^a



Entry	R	Product	Time(min)	Yield (%) ^b
1			10	91
2			15	93
3			15	83
4			15	76

5			10	88
6			8	79
7			8	96
8			10	92
9			15	91
10			10	95
11			10	85
12			10	92
13			10	85

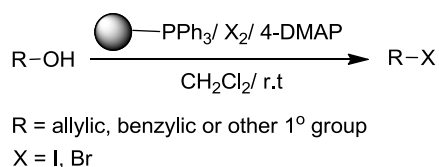
14			10	87
15			15	81
16			15	83
17			15	79
18			15	81
19			30	83

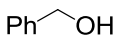
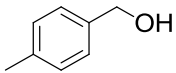
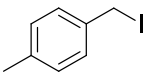
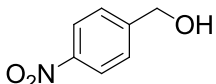
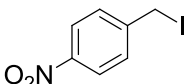
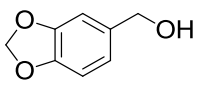
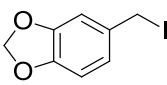
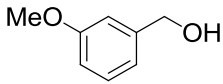
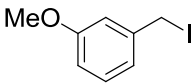
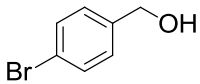
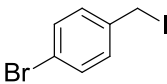
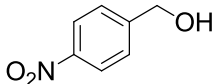
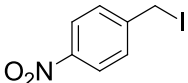
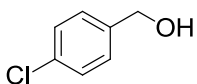
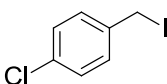
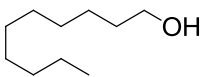
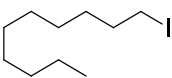
^a Molar ratio of alcohol/ PPh₃/X₂/4-DMAP = 1: 1.2: 1.2 : 2.

^bYields refer to pure isolated products and were characterized by comparison of their physical and spectral data (IR, ¹H NMR, ¹³C NMR, MS) with authentic samples.

This iodination method was also tried with resin-bound triphenyl phosphine reagent instead of triphenylphosphine results of which are shown in Table 2. Use of polymer-supported reagent has the advantage of easy purification of the desired products from the byproduct resin-bound triphenylphosphine oxide. It is well documented in the literature²³ that the resin-bound phosphines oxide formed in the reaction can be reduced to the original phosphine by using trichlorosilane.

Table 2. Conversion of alcohols to halides^a



Entry	R	Product	Time/h	Yield (%) ^b
1			15	86
2			30	88
3			15	91
4			20	80
5			20	88
6			15	91
7			15	90
8			15	82
9			30	79

^a Molar ratio of alcohol/ Polymer-bound PPh₃/X₂/4-DMAP = 1:1.2:1.2:2.

^bYields refer to pure isolated products and were characterized by comparison of their physical and spectral data (IR, ¹H NMR, ¹³C NMR, MS) with authentic samples.

In conclusion, a simple and high chemoselective process for the iodination of benzylic, allylic and aliphatic alcohols using $\text{Ph}_3\text{P/I}_2/4\text{-DMAP}$ at room temperature has been demonstrated. The mild reaction conditions, short reaction times, good to excellent yields and operational simplicity of the protocol are the advantages of this method.

III. Experimental

Iodination of alcohol (General procedure)

To a solution of triphenylphosphine (1.2 mmol) in anhydrous dichloromethane (10 mL) at room temperature was added 4-DMAP (2 mmol), iodine (1.2 mmol) and stirred for approximately 2 min. The alcohol (1 mmol) was then added to the reaction mixture and stirred at the same temperature. After complete conversion of the alcohol (as indicated by TLC), the reaction was quenched with an aqueous solution of sodium thiosulfate (20 ml). The organic solvents were removed and the aqueous solution extracted with diethyl ether (3 20ml). The combined organic layers were washed with saturated aqueous NaCl (2X20 mL, dried (Na_2SO_4), filtered and concentrated. The residue was purified by column chromatography (2% EtOAc in hexane) to get the desired iodide product. Since the reaction was found to be mildly exothermic, during scale-up, the reaction was initially cooled using a water bath to avoid any possible temperature rise.

Iodination of alcohol (General procedure)

To a suspension of resin-bound triphenylphosphine (1.2 mmol) in anhydrous dichloromethane (15 mL) at room temperature was added 4-DMAP (2 mmol), iodine (1.2 mmol) and stirred for approximately 2 min. The alcohol (1 mmol) was then added to the reaction mixture and stirred at the same temperature. After complete conversion of the alcohol (as indicated by TLC), the reaction was quenched with an aqueous solution of sodium thiosulfate (20 ml). The organic solvents were removed and the aqueous solution extracted with diethyl ether (3 20ml). The combined organic layers were washed with saturated aqueous NaCl (2X20 mL, dried (Na_2SO_4), filtered and concentrated. The residue was purified by column chromatography (2% EtOAc in hexane) to get the desired iodide product. Since the reaction was found to be mildly exothermic, during scale-up, the reaction was initially cooled using a water bath to avoid any possible temperature rise.

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