

Selective Iodination of Alcohols with NaI/Amberlyst 15 in Acetonitrile

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Abstract: A simple and effective procedure for conversion of primary, secondary, allylic and benzylic alcohols into the corresponding iodides is described using NaI/Amberlyst 15 in acetonitrile at room temperature. Selective conversion of benzylic alcohols in the presence of saturated alcohols into the corresponding benzylic iodides is achieved under these conditions.

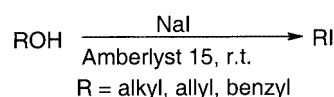
Key words: iodination, Amberlyst 15, benzylic alcohol, saturated alcohol, iodides

Halogen-containing compounds are very useful intermediates in organic synthesis.¹ They react with nucleophiles such as amines or alkoxides to give the corresponding substituted products and can be lithiated to introduce electrophiles via a halogen–lithium exchange reaction.² Alkyl iodides or bromides are widely used for ionic and radical carbon-carbon coupling reactions, and also act as intermediates in substitution, elimination and rearrangement reactions. The most common precursors to alkyl halides are alcohols. Therefore, the conversion of alcohols into alkyl iodides is a frequently used functional group transformation.³ Although alkyl iodides are less stable than the corresponding chloride or bromide, and iodine is the most expensive of the common halogens, they are far more reactive than the other halides, and in some cases iodides are the only reactive halides.⁴

A number of synthetic methods for transformation of alcohols into iodides has been developed during the past two decades.^{5–8} Some methods involve mild conditions and the use of iodotrimethylsilane,⁹ bromotrimethylsilane,¹⁰ chlorotrimethylsilane-sodium iodide,¹¹ hexamethyldisilazane-iodine,¹² P₂I₄ in CS₂,¹³ *N,N*-diethylaniline-borane-I₂,¹⁴ CeCl₃·7H₂O/NaI system,¹⁵ sodium iodide over KSF-clay under microwave irradiation,¹⁶ and KI/H₂SO₄ supported on natural kaolinitic clay under microwave irradiation¹⁷ as reagents. More recently, some useful reports have been published regarding the selective conversion of allylic, benzylic and other (primary, secondary and tertiary) alcohols into halides.^{18–22} However, some of these suffer from drawbacks, which include the use of toxic and/or hazardous materials, reagents that are not commercially available, long reaction times, low yields and tedious work-up procedures. As such mild and efficient methods that can be used to promote the transformation of

hydroxyl groups into iodides are of increasing importance to overcome such difficulties.

We report herein an exceedingly mild preparation of iodides from alcohols by the use of a NaI/Amberlyst 15 system in acetonitrile at room temperature (Scheme 1).



Scheme 1

The results of the iodination reactions are summarized in Table 1. The data indicate that iodination of a variety of allylic or benzylic and saturated primary or secondary alcohols occurs using a NaI/Amberlyst 15 system in acetonitrile at room temperature. The iodination of benzyl alcohol was selected for optimization of the reaction conditions. It was observed that when benzyl alcohol was treated with NaI without Amberlyst 15, no change took place, implying that Amberlyst 15 plays an important role in this reaction. This was further confirmed when other solid supports such as SiO₂, Al₂O₃, Zeolite HY, Montmorillonite K10 and Montmorillonite KSF were employed. Treatment of benzyl alcohol with NaI/SiO₂, NaI/Al₂O₃ and NaI/Montmorillonite K10 gave the corresponding iodide in low yield (Table 1, entries 2–4). Under the same conditions, NaI/Zeolite HY and NaI/Montmorillonite KSF gave benzyl iodide in 40% and 60% yield respectively (Table 1, entries 5 and 6). We have also examined the effect of solvent in this reaction. When benzyl alcohol reacted with NaI/Amberlyst 15 in various solvents such as acetonitrile, ethyl acetate, chloroform, dioxane, dichloromethane and THF, we found that the reaction proceeded most rapidly and give optimal yields in acetonitrile.

Benzyl alcohol with NaI/Amberlyst 15 provided benzyl iodide in excellent yield (Table 1, entry 1).²⁴ We have tested various benzylic alcohols with both electron-donating and electron-withdrawing groups on the aryl ring (Table 1, entries 8–14) and have observed that, as expected, the reaction is slightly accelerated by an electron-donating group (Table 1, entry 13). Certainly, the substitution of the electron-withdrawing group onto the aromatic ring retards the transformation (Table 1, entry 14), while, no significant difference in reactivity was observed when performing the reaction with substituents such as Cl, OH, and OMe groups at the *ortho* and *meta* positions (Table 1, entries 8–11). In the case of primary alcohols the conversion into the corresponding iodides

requires longer reaction times (Table 1, entry 18). Likewise, secondary alcohols such as cyclohexanol and 5-nonanol were also converted into the corresponding alkyl iodides (Table 1, entries 19 and 20). Furthermore, under the same reaction conditions, allylic alcohols formed allylic iodides, usually not available commercially due to their rapid decomposition during storage. It has been ob-

served that the attack of the iodide ion on primary allylic alcohols does not involve allylic rearrangement (Table 1, entries 15 and 16); whereas displacement of allylic alcohols containing a terminal double bond gave iodides accompanied by allylic rearrangement (Table 1, entry 17).

Table 1 Conversion of Alcohols into Alkyl Iodides Using NaI/Amberlyst15^a

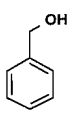
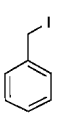
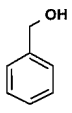
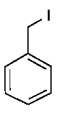
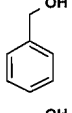
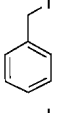
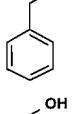
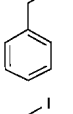
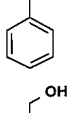
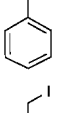
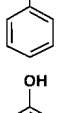
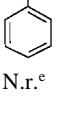
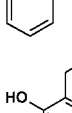
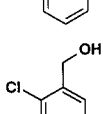
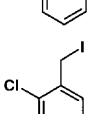
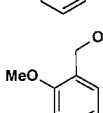
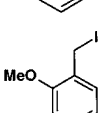
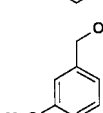
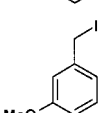
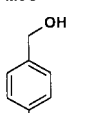
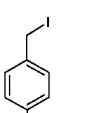


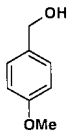
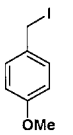
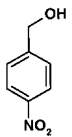
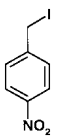
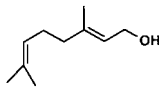
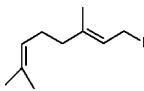
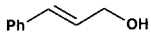
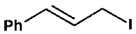
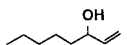
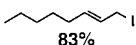
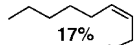
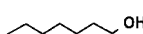
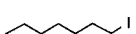
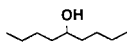
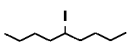


Entry	Substrate	Reagent	Product ^b	Time	Yield (%) ^c
1		NaI, Amberlyst 15, r.t. ^d		1 h	95 ^f
2		NaI, SiO ₂ , r.t.		4 h	20
3		NaI, Al ₂ O ₃ , r.t.		5 h	10
4		NaI, Montmorillonite K10, r.t.		4 h	10
5		NaI, ZeolitheHY, r.t.		3 h	40
6		Montmorillonite KSF, r.t.		3 h	60
7		NaI, Amberlyst 15, r.t.	N.r. ^e	5 h	–
8		NaI, Amberlyst 15, r.t.		50 min	95
9		NaI, Amberlyst 15, r.t.		1 h	88 ^f
10		NaI, Amberlyst 15, r.t.		75 min	90
11		NaI, Amberlyst 15, r.t.		1 h	87 ^f
12		NaI, Amberlyst 15, r.t.		1 h	90 ^f

Table 1 Conversion of Alcohols into Alkyl Iodides Using NaI/Amberlyst15^a (continued)

Entry	Substrate	Reagent	Product ^b	Time	Yield (%) ^c
13		NaI, Amberlyst 15, r.t.		45 min	98
14		NaI, Amberlyst 15, r.t.		3.5 h	60 ^f
15		NaI, Amberlyst 15, r.t.		50 min	90
16		NaI, Amberlyst 15, r.t.		50 min	90
17		NaI, Amberlyst 15, r.t.	 83%  17%	45 min	90
18		NaI, Amberlyst 15, r.t.		10 h	80 ^f
19		NaI, Amberlyst 15, r.t.		10 h	80 ^f
20		NaI, Amberlyst 15, r.t.		10 h	80 ^f

^a All reactions were carried out at r.t. with alcohol/NaI (1:1) molar ratio.

^b All Products were characterized spectroscopically (IR, ¹H NMR, GC) and showed physical and spectral data in accordance with their expected structure and by comparison with authentic samples.

^c Yields refer to pure isolated products. All starting materials were commercially available.

^d Room temperature.

^e No reaction.

^f Purified by column chromatography.

Chemoselective iodination of benzylic alcohols was carried out in the presence of saturated alcohols as well as phenols. The results are shown in Table 2.

In conclusion, the present study for the conversion of alcohols into iodides, shows that our method represents a valuable alternative to those reported in the literature.

Table 2 Selective Synthesis of Benzyl Iodides

Entry	Substrate	Product	Time (h)	Yield (%) ^a
1	Benzyl alcohol	Benzyl iodide	2	95
	Heptanol	1-Iodoheptane		
2	4-Methoxybenzyl alcohol	4-Methoxybenzyl-iodide	2	98
	5-Nonanol	5-Iodononan		
3	4-Nitrobenzyl alcohol	4-Nitrobenzyl iodide	4	60
	Cyclohexanol	Cyclohexyl iodide		
4	2-Hydroxybenzyl alcohol	2-Hydroxybenzyl iodide	5	95
	Phenol	n.r. ^b		

^a Yields of pure isolated product; products are characterized spectroscopically (IR, ¹H NMR, GC) and by comparison with authentic samples.^{23,25.}

^b No reaction.

Acknowledgment

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- (24) **General Procedure for the Conversion of Alcohols to Iodides (Table 1).** To a stirred suspension of alcohol (1 mmol) and NaI (0.150 g, 1 mmol) in MeCN (10 mL) was added amberlyst 15 (H⁺-form, 1 g), and the resulting mixture was stirred at r.t. After completion of the reaction (TLC or GC), Et₂O (10 mL) was added and washed with aq sat. NaHCO₃ solution, followed by NaHSO₄. The resultant organic layer was extracted with Et₂O (3 × 10 mL) and the combined extract dried over anhyd Na₂SO₄. The solvent was removed under reduced pressure to afford iodides in almost pure form. If necessary, products were purified by column chromatography (eluent: hexane–EtOAc). The products were identified by IR, ¹H NMR, and GC.
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