

Chemoselective Iodination of Alcohols with $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}/\text{NaI}$ over SiO_2 under Microwave Irradiation

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A simple and effective procedure for conversion of primary, secondary, allylic and benzylic alcohols into the corresponding iodides is described using $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}/\text{NaI}$ over SiO_2 under microwave irradiation. Benzylic alcohols are selectively converted in the presence of saturated alcohols into their corresponding benzylic iodides under these conditions.

Key Words : Iodination, $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$, Microwave, SiO_2 , Solvent-free conditions

Introduction

Heterogenous organic reactions have proven useful in the laboratory as well as industry. These reactions are effected by reagents immobilized on porous solid supports and have advantages over the conventional solution phase reactions because of good dispersion of active reagent sites and easier work-up. The recyclability of some of these solid supports renders these processes into truly ecofriendly green protocols.^{1,2} In recent years, there has been increasing interest in various chemical transformations involving environmentally friendly reagents such as solid supported catalysts and those are assisted by microwave under solvent-free conditions,³ *viz.* 1,3-dipolar cycloadditions,^{4a} Friedel-Craft alkylations,^{4b} Diels-Alder reactions,^{4c} *etc.* The combination of supported reagents and microwave irradiation can be used to carry out a wide range of reactions in short times and with high conversion and selectivity without the need of solvents. This approach can prove beneficial since the recovery of solvents from conventional reaction systems always results in some losses. Recovery of both products and supported reagent or catalyst is generally possible by simple filtration and evaporation, leading to an efficient and low-waste route to arrange of products.⁵

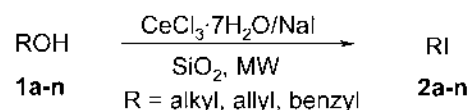
Halogen-containing compounds are very useful intermediates in organic synthesis.⁶ They react with nucleophiles such as amines or alkoxides to give the corresponding substituted products and can be lithiated to introduce electrophiles via a halogen-lithium exchange reaction.⁷ Alkyl iodides or bromides 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.⁸ 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 halogens, and in some cases iodides are the only reactive halides.⁹

A number of synthetic methods for transformation of alcohols into iodides have been developed during the past two decades.¹⁰ Some methods involve mild conditions and the use of iodo,^{11a} bromotrimethylsilanes,^{11b} chlorotrimethylsilane-sodium iodide,^{11c,d} hexamethyldisilazane-iodine,^{11e} P_2I_4 in CS_2 ,^{11f} *N,N*-diethylaniline-borane- I_2 ,^{11g} $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}/\text{NaI}$ system,^{11h} sodium iodide over KSF-clay under microwave irradiation,¹¹ⁱ and $\text{KI}/\text{H}_2\text{SO}_4$ supported on natural kaolinitic clay under microwave irradiation^{11j} 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.¹² However, some of these suffer from drawbacks, which include the use of toxic and/or hazardous materials, expensive reagents, long reaction time, low yields and tedious work up procedure. 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.

Cerium (III) chloride has emerged as a lewis acid imparting high region-and chemoselectivity in various reactions,¹³ since this compound is a very cheap, nontoxic, and water-tolerant reagent.¹⁴

We now report that $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}/\text{NaI}$ over SiO_2 can bring about the conversion of alcohols into iodides when irradiated in a domestic microwave oven (Scheme 1).



Scheme 1

Results and Discussion

The results of the iodination reactions are summarized in Table 1. The data indicate that iodination of a variety of

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Table 1. Conversion of alcohols into alkyl iodides using $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}/\text{NaI}$ over SiO_2 under microwave irradiation^a

Entry	Substrate	Reagent	Product ^b	Time/ min	Yield %
1		$\text{CeCl}_3 \cdot 7\text{H}_2\text{O}/\text{NaI}$, SiO_2		3	93
2	"	$\text{CeCl}_3 \cdot 7\text{H}_2\text{O}/\text{NaI}$, Al_2O_3 (acidic)	"	3	40
3	"	$\text{CeCl}_3 \cdot 7\text{H}_2\text{O}/\text{NaI}$, Montmorillonite K10	"	3	80
4		$\text{CeCl}_3 \cdot 7\text{H}_2\text{O}/\text{NaI}$, SiO_2		2	94
5		"		3	87
6		"		4	90
7		"		3	85
8		"		3	90
9		"		1	98
10		"		7	60
11		"		1.5	90
12		"		1.5	90
13		"		1.5	90
14 ^d		"		10	60
15 ^d		"		10	60
16 ^d		"		10	60

^aAll reactions were carried out in microwave oven with alcohol/NaI/ $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ (1 : 1 : 1) molar ratio. ^bAll 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. ^cYields refer to pure isolated products. ^dIn closed Teflon container.

allylic or benzylic and saturated primary or secondary alcohols occurs using $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}/\text{NaI}$ in a domestic microwave oven. The iodination of benzyl alcohol was selected for optimization of the reaction conditions. No transformation took place when NaI without $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ and SiO_2 were heated under reflux for 12 h in acetonitrile. It was also observed that when benzyl alcohol, in the presence of NaI and $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ without SiO_2 , or in the presence of NaI and SiO_2 without $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ were subjected to microwave irradiation, gave a low yield of benzyl iodide. These results implying that $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$, SiO_2 and microwave play an important role in this reaction. This was further confirmed when other solid supports such as Al_2O_3 and montmorillonite K10 were employed. Treatment of benzyl alcohol with $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}/\text{NaI}$ over Al_2O_3 under microwave irradiation gave the corresponding iodide in low yield (Table 1, entry 2). Under the same conditions, $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}/\text{NaI}$ over montmorillonite K10 under microwave irradiation gave benzyl iodide in 80% yield (Table 1, entry 3).

Benzyl alcohol with $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}/\text{NaI}$ over SiO_2 under microwave irradiation provided benzyl iodide in excellent yield (Table 1, entry 1). We have tested various benzylic alcohols with both electron-donating and electron-withdrawing groups on the aryl ring (Table 1, entries 4-10). In the case of primary and secondary alcohols the conversion into the corresponding iodides needs closed Teflon container and proceeds in longer reaction times (Table 1, entries 14-16). Furthermore, under the same reaction conditions, allylic alcohols formed allylic iodides, nonavailable commercially due to its rapid decomposition during storage. It has been observed that the attack of the iodide ion does not involve allylic rearrangement (Table 1, entries 11-12). Displacement of allylic alcohols containing a terminal double bond gave iodides accompanied by allylic rearrangement (Table 1, entry 13) as observed by E. Marcantoni.^{11b}

Chemoselective iodination of benzylic alcohols was carried out in the presence of saturated alcohols as well as phenols. When a mixture of equimolar amounts of benzyl alcohol and 1-heptanol were treated with one equimolar $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}/\text{NaI}$ over SiO_2 under microwave irradiation, only benzyl alcohol was selectively converted to benzyl iodide and 1-heptanol remained unchanged. The results are

Table 2. Selective synthesis of benzyl iodides

Entry	Substrate	Product	Time/ min	Yield %
1	Benzyl alcohol	Benzyl iodide		93
2	Heptanol	1-Iodoheptane	2	00
3	4-methoxybenzyl alcohol	4-Methoxybenzyl iodide		98
4	5-Nonanol	5-Iodononan	2	00
5	4-Nitrobenzyl alcohol	4-Nitrobenzyl iodide		60
6	Cyclohexanol	Cyclohexyl iodide	7	00
7	2-Hydroxybenzyl alcohol	2-Hydroxybenzyl iodide		94
8	Phenol	No reaction	5	00

^aYields of pure isolated product: products are characterized spectroscopically (IR, ^1H NMR, GC) and by comparison with authentic samples.

Table 3. Comparison of $CeCl_3 \cdot 7H_2O/NaI$ over SiO_2 under microwave irradiation for the conversion of alcohols into iodides with other reagents

Entry	Substrate	Reagent	Reaction conditions	Time	Yield (%)	Ref
1	Benzyl alcohol	$CeCl_3 \cdot 7H_2O/NaI$, SiO_2	MW ^a	3 min	93	
2	"	NaI, montmorillonite KSF	MW	5 min	55	11i
3	"	KI/ H_2SO_4 , natural kaolinitic clay	MW	5 min	92	11j
4	"	$CeCl_3 \cdot 7H_2O/NaI$, SiO_2	refluxing acetonitrile	12 h	90	17
5	"	$CeCl_3 \cdot 7H_2O/NaI$	refluxing acetonitrile	20 h	90	11h
6	"	I_2	refluxing petroleum ether	1.5 h	56	10k
7	"	P_2I_4 , CS_2	RT	0.5 h	89	11f
8	"	<i>N,N</i> -diethylaniline: BF_3 and I_2	RT	12 h	86	11g
9	"	$NaI/BF_3 \cdot O(C_2H_5)_2$	refluxing chloroform	4 h	68	12b
10	"	"	refluxing acetonitrile	4 h	70	12b
11	"	$NaI/BF_3 \cdot O(C_2H_5)_2$	RT	25 min	94	12c
12	"	$Me_3SiCl-NaI$	RT	20 min	98	11c, d
13	Cyclohexanol	$CeCl_3 \cdot 7H_2O/NaI$, SiO_2	MW	10 min	60	
14	"	NaI, montmorillonite KSF	MW	5.8 min	00	11i
15	"	$CeCl_3 \cdot 7H_2O/NaI$	refluxing acetonitrile	96 h	79	11h
16	"	P_2I_4 , CS_2	RT	96 h	88	11f
17	"	I_2	refluxing petroleum ether	2 h	37	10k
18	2-Methylcyclohexanol	KI/ H_2SO_4 , natural kaolinitic clay	MW	6 min	00	11j

^aMicrowave irradiation.

shown in Table 2.

In order to show the advantage of using microwave irradiation, some of our results compared with those reported in the literature (Table 3). As shown in Table 3, the iodination of alcohols with $CeCl_3 \cdot 7H_2O/NaI$ over SiO_2 under microwave irradiation is a simple and efficient method. Higher yields and shorter reaction times are important features of this method.

In conclusion, the present study for the conversion of alcohols into iodides, shows that our method may represent a valuable alternative to those reported in the literature. The superiority of this method over the existing methods coupled with the ease of operation, the simplicity of work-up, and the environmental advantage makes the process very useful.

Experimental Section

SiO_2 (mesh, 27-30) was purchased from Fluka. All the reactions were carried out in a domestic microwave oven National: NN-C988 W model (2450 MHz) in beaker and in some cases in closed Teflon container. Infrared (IR) spectra was recorded on Bruker VECTOR 22 spectrometer. 1H NMR spectra were measured on Bruker DRX500 AVANCE and JEOL JNM-EX90A spectrometers, using $CDCl_3$ as solvent. All the products were characterized by IR, 1H NMR, and GC data and also by comparison with authentic samples.^{15,16}

General procedure for the conversion of Alcohols to Iodides: Sodium iodide (0.150 g, 1 mmol), $CeCl_3 \cdot 7H_2O$ (0.372 g, 1 mmol), SiO_2 (1 g) and alcohol (1 mmol) were thoroughly mixed in a mortar and exposed to microwave

irradiation for 30 s using high level (900 W). The reaction mixture was cooled to room temperature (1 min) and irradiated again for 30 s. After completion of the reaction (TLC or GC), ether (10 mL) was added and washed with aqueous saturated sodium hydrogen carbonate solution, followed by deiodination with sodium hydrogen sulfite. The resultant organic layer was extracted with ether (3×10 mL) and the combined extract dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure to afford corresponding iodide in almost pure form. If necessary, products were purified by column chromatography (eluent, hexane-ethyl acetate, 95 : 5). The products were identified by IR, 1H NMR, and GC. Spectral data for some compounds are as follows:

2a: 1H NMR (90 MHz, $CDCl_3$): δ = 4.5 (s, 2H, $ArCH_2$), 7.4 (m, 5H, Ar-H); **2c:** 1H NMR (90 MHz, $CDCl_3$): δ = 4.2 (s, 2H, $ArCH_2$), 7.29 (m, 4H, Ar-H); **2e:** 1H NMR (90 MHz, $CDCl_3$): δ = 3.8 (s, 3H, OCH_3), 4.4 (s, 2H, $ArCH_2$), 7.1 (m, 4H); **2f:** 1H NMR (500 MHz, $CDCl_3$): δ = 4.4 (s, 2H, $ArCH_2$), 7.29 (m, 4H); **2g:** 1H NMR (500 MHz, $CDCl_3$): δ = 3.8 (s, 3H, OCH_3), 3.9 (s, 2H, $ArCH_2$), 6.82 (d, 2H), 7.07 (d, 2H); **2h:** 1H NMR (90 MHz, $CDCl_3$): δ = 4.4 (s, 2H, $ArCH_2$), 7.50 (d, 2H), 8.12 (d, 2H); **2j:** 1H NMR (500 MHz, $CDCl_3$): δ = 3.4 (d, 2H, CH_2I), 6.6 (m, 1H, =CH), 6.8 (d, 1H, PhCH), 7.20 (d, 5H); **2l:** 1H NMR (90 MHz, $CDCl_3$): δ = 0.9 (br t, 3H), 1.1-1.9 (m, 10H), 3.10 (t, 2H, CH_2I); **2n:** 1H NMR (90 MHz, $CDCl_3$): δ = 1.45 (m, 6H), 2.15 (m, 4H), 4.4 (m, 1H, CHI).

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- Sodium iodide (0.150 g, 1 mmol), CeCl₃·7H₂O (0.372 g, 1 mmol), SiO₂ (1 g) and alcohol (1 mmol) were refluxed in acetonitrile (10 mL) for 12-14 h. After completion of reaction the mixture was filtered and washed with ether. The filtrate was washed with saturated sodium hydrogen carbonate solution, followed by deiodinization with sodium hydrogen sulfite and dried over anhydrous Na₂SO₄. The extracts were then concentrated and the residue chromatographed on a silica gel column to give the corresponding iodides. Benzyl iodide: 12 h, 90%_o; 2-chlorobenzyl iodide: 14 h, 80%_o; 4-chlorobenzyl iodide: 14 h, 90%_o.