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Efficient oxidation of benzylic alcohols with [hydroxy(tosyloxy)iodo]benzene under microwave irradiation

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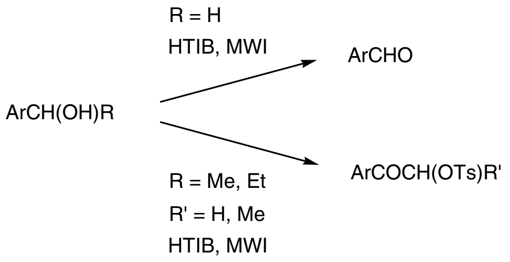
Abstract—An efficient method for the oxidation of benzylic alcohols with [hydroxy(tosyloxy)iodo]benzene under solvent-free microwave irradiation conditions is described.

The oxidation of benzylic alcohols to carbonyl compounds is a fundamental transformation in organic synthesis and numerous methods utilizing various reagents have been reported.[1,2] However, the majority of known methods commonly suffer from one or more disadvantages such as difficulty in manipulation, long reaction times, and utilization of toxic reagents. Therefore, it is still desirable to develop a new efficient oxidant with properties of high stability, low toxicity, and ready availability for the benzylic oxidations. Hypervalent iodine reagents have received a great deal of attention due to their versatility in oxidation processes.[3,4] In general, pentavalent iodine reagents such as Dess–Martin periodinane[5] and *o*-iodoxybenzoic acid[6] have been widely used for efficient oxidation of alcohols to the carbonyl compounds. However, reported methods for the oxidation of alcohols mediated by trivalent iodine reagents have been quite limited. Examples of these methods include oxidation of alcohols with iodosobenzene[7] and iodobenzene diacetate.[8] Furthermore, to the best of our knowledge, there has been no example of utilization of the [hydroxy(tosyloxy)iodo]benzene (HTIB, Koser's reagent) for the oxidation of primary benzylic alcohols into the corresponding aldehydes. Among other hypervalent iodine reagents, HTIB represents as one of the most versatile reagents and its use in a variety of organic transformations are well documented.[9,10] Recently, microwave induced synthetic technique has received considerable attention as a useful tool to accelerate a wide variety of organic transformations.[11] In particular, the microwave promoted reactions under solvent-free reaction conditions provided many advantages such as eco-friendlier conditions and very rapid reaction, experimental simplicity, and high yields.[12]

In connection with our interest in application of hypervalent iodine(III) sulfonates to microwave promoted organic transformations,[13] we considered of interest to study the effect of HTIB in oxidation of primary benzylic alcohols. We now wish to report our finding, which enables facile and efficient oxidation of primary benzylic alcohols to the corresponding aldehydes. Treatment of neat primary benzylic alcohol (1.0 mmol) with HTIB (1.2 mmol) under microwave irradiation using a household microwave oven for 40–160 s provided the corresponding aldehydes in high yields (Scheme 1).[14] A range of primary benzylic alcohols were investigated using present conditions and results are summarized in Table 1.



Scheme 1.

Keywords: Alcohols; Aldehydes; Hypervalent elements; Microwave irradiation; Oxidations.

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Table 1. Microwave-assisted oxidation of benzylic alcohols with HTIB

Entry	Substrate	Product	Yield (%)[a]
1	$PhCH_2OH$	$PhCHO$	98
2	$4\text{-}MeC_6H_4CH_2OH$	$4\text{-}MeC_6H_4CHO$	90
3	$4\text{-}ClC_6H_4CH_2OH$	$4\text{-}ClC_6H_4CHO$	93
4	$4\text{-}NO_2C_6H_4CH_2OH$	$4\text{-}NO_2C_6H_4CHO$	94
5	$2\text{-}NO_2C_6H_4CH_2OH$	$2\text{-}NO_2C_6H_4CHO$	82
6	$3,5\text{-}(NO_2)_2C_6H_3CH_2OH$	$3,5\text{-}(NO_2)_2C_6H_3CHO$	78
7	Ph_2CHOH	Ph_2CO	86
8	$PhCH(OH)CH_2Ph$	$PhCOCH_2Ph$	90
9	$C_6H_5CH(OH)COOMe$	$C_6H_5COCOOMe$	85
10	$C_6H_5CH(OH)COOEt$	$C_6H_5COCOOEt$	88
11	$2\text{-}Cl\text{-}C_6H_4CH(OH)COOMe$	$2\text{-}Cl\text{-}C_6H_4COCOOMe$	90
12	$PhCH(CH_3)OH$	$PhCOCH_2OTs$	75[b]
13	$4\text{-}BrC_6H_4CH(CH_3)OH$	$4\text{-}BrC_6H_4COCH_2OTs$	72[b]
14	$4\text{-}ClC_6H_4CH(CH_3)OH$	$4\text{-}ClC_6H_4COCH_2OTs$	78[b]
15	$PhCH(Et)OH$	$PhCOCH(Me)OTs$	67[b]

[a] Isolated yields.

[b] Obtained by use of 2.5 equiv of HTIB.

All of the reactions completed very cleanly without any noticeable side products. The present method could equally work with electron rich and very electron deficient benzylic alcohols (entries 2 and 6).

α-Keto esters received much attention due to their useful biological properties and many efforts have been made for the oxidation of α-hydroxy esters to the corresponding α-keto esters.[15,16] Attempts to oxidise a series of α-hydroxy under the present reaction conditions were successful in obtaining high yields of α-keto esters (entries 9–11). Application of present method for the oxidation of primary aliphatic alcohols gave very low conversion and product mixtures are obtained in cases of oxidation of allylic alcohols.

After established optimal conditions for oxidations of primary benzylic alcohols, we next examined the oxidation reactions of several secondary benzylic alcohols as substrates. Whereas the oxidation reactions of secondary benzylic alcohols under present conditions gave product mixtures, use of excess amounts of HTIB (2.5 equiv) with microwave irradiation for extended reaction times (4–5 min) smoothly furnished α-tosyloxy ketones in high yields (entries 12–15). The yields of these reactions are comparable to those obtained from oxidation of α-methylbenzyl alcohols by α-tosyloxylation in organic solvents with poly[4-hydroxy-(tosyloxy)iodo]styrenes or iodosobenzene/PTSA.[17–19] α-Tosyloxyketones are very useful intermediates in organic synthesis.[10] Conventionally, α-tosyloxy ketones have been obtained from α-tosyloxylation reaction of ketones with HTIB.[20] Thus, this new solvent-free protocol can be served as a useful alternative to the existing method for the direct preparation of α-tosyloxy ketones from secondary benzyl alcohols. Typical experimental procedure for α-tosyloxylation is as follows: a neat mixture of *sec*-phenethyl alcohol (0.122 g, 1.0 mmol) and HTIB (0.981 g, 2.5 mmol) were mixed and placed in a 50 mL glass tube. The reaction mixture was inserted in an alumina bath inside a household microwave oven and irradiated (700 W) six times for a period of 40 s with 10 s intervals. The reaction mixture was extracted with dichloromethane (2 × 25 mL) and washed with water (40 mL). The dichloromethane layer was separated and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by flash column chromatography (SiO_2, ethyl acetate–hexane = 1:4) to afford pure α-tosyloxyacetophenone.

In summary, microwave promoted reactions of benzylic alcohols with HTIB provides a rapid and convenient way to prepare corresponding carbonyl compounds in solvent-free conditions. The advantages of the present method in conjunction with eco-friendly conditions and fast reaction rates should make this protocol a valuable alternative to the other reported methods.

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