

Short Communication

[Hydroxy(tosyloxy)iodo]benzene Mediated α -Azidation of Ketones

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Abstract: Reaction of various ketones with [hydroxy(tosyloxy)iodo]benzene (HTIB) followed by treatment of the α -tosyloxy ketones thus generated *in situ* with NaN_3 offers a one-pot procedure for the synthesis of α -azido ketones. The HTIB used in this conversion may also be generated *in situ* by using iodobenzene in combination with *p*-toluene-sulphonic acid.

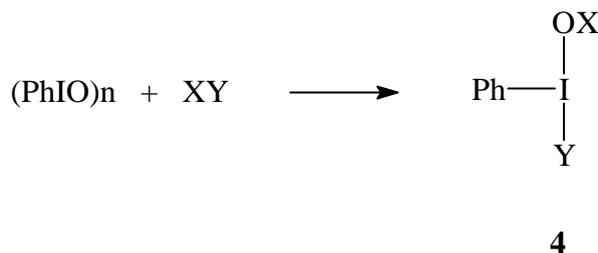
Keywords: Hypervalent iodine, α -azido ketones, [hydroxy(tosyloxy)iodo]benzene, iodobenzene.

Introduction

The application of organohypervalent iodine reagents is a fertile and attractive field in organic synthesis [1]. Of the various hypervalent iodine reagents, iodobenzene diacetate (IBD) [2] and [hydroxy(tosyloxy)iodo]benzene (HTIB) (Koser's reagent) [3] have been found to be more versatile than other reagents such as iodobenzene (IOB), etc. The relatively lesser utility of IOB is due to its polymeric nature [4], which makes it insoluble in common solvents. To overcome such difficulties, combination reagents were developed. For example, the utility of IOB is greatly enhanced when it is combined with acids [5], bases [6] or salts [7]. These reactions are thought to proceed via generation *in situ* of the I(III) species **4** (Scheme 1). Continuing our investigations on the use of I(III) reagents, we

now report a one pot α -azidation of ketones using HTIB or the combination reagent [(PhIO)_n + *p*-TsOH] [8] and NaN₃.

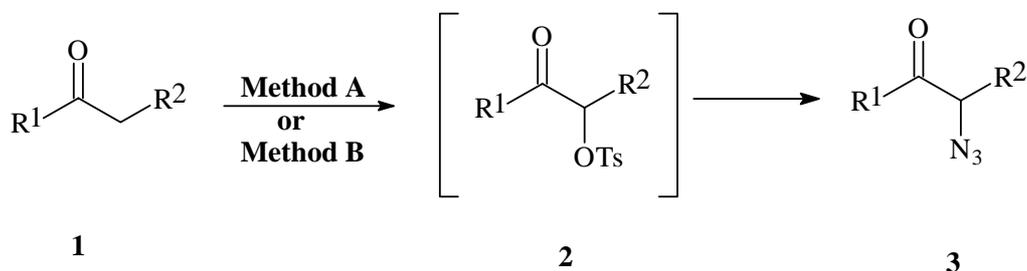
Scheme 1



Results and Discussion

Based on previous reports on the use of [hydroxy(tosyloxy)iodo]benzene (HTIB) [9] in one-pot syntheses of α -functionalized ketones, we first attempted the azidation of **1a** using HTIB. Accordingly, acetophenone (**1a**) was oxidized with one equivalent of HTIB in acetonitrile and subsequently the α -tosyloxy ketone **2a** generated *in situ* was treated with sodium azide. The reaction resulted in the formation of the corresponding α -azido acetophenone **3a** in 80% yield (Method A, Scheme 2). In order to study the scope of this approach, various ketones **1b-1g** were subjected to α -azidation using one equivalent of HTIB and NaN₃ to afford the corresponding α -azido ketones **3b-3g** in yields ranging from 69% to 81% (Table 1).

Scheme 2



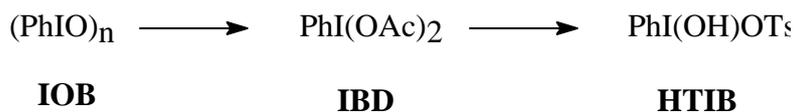
Method A: (i) HTIB/ CH₃CN, reflux 2 h; (ii) NaN₃, rt, 2-3 h

Method B: (i) (PhIO)_n + *p*-TsOH/CH₃CN, reflux 2 h; (ii) NaN₃, rt, 2-3 h

In another important development, we established that it is possible to use a combination of iodosobenzene and *p*-toluenesulphonic acid [(PhIO)_n + *p*-TsOH] in place of HTIB. This combination reagent generates HTIB *in situ*, which then reacts with ketones **1** to give the intermediary α -tosyloxy ketones **2** (Method B).

It is evident from the results summarized in Table 1 that Method A and Method B work equally well, although Method B is more convenient than Method A as the former avoids the preparation of HTIB. It is to be mentioned that the reported preparation of HTIB consists of two steps starting from iodosobenzene [10,11] (Scheme 3).

Scheme 3

Table 1. α -Azido ketones **2** prepared according to Scheme 2

Compound	R ¹	R ²	Yield (%) ^a	
			Method A	Method B
2a	H	H	80	76
2b	4-CH ₃ C ₆ H ₄	H	69	74
2c	4-CH ₃ OC ₆ H ₄	H	72	70
2d	4-BrC ₆ H ₄	H	78	71
2e	4-ClC ₆ H ₄	H	70	69
2f	H	CH ₃	81	71
2g		-(CH ₂) ₄ -	81	83

^aYields of isolated pure product based on the amount of ketones **1** used.

Conclusions

In summary, the present study offers a better alternative to the existing methods for the synthesis of α -azido ketones, which are valuable intermediates for various transformations [12] and are generally prepared by the reaction of α -halo ketones [12] or α -nosyloxy ketones [13] with sodium azide.

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Experimental

General

All reagents were purchased from commercial sources and were used without further purification. Iodosobenzene and HTIB were prepared according to literature procedures [9, 10] starting from iodobenzene. Melting points were taken in open capillaries and are uncorrected. ¹H-NMR spectra were recorded on a Bruker 300 MHz instrument using TMS as an internal standard. IR spectra were recorded on a Buck Scientific IR M-500 spectrophotometer.

Representative one-pot procedure for the preparation of α -azido ketones: α -azidoacetophenone (2-azido-1-phenylethanone)(**3a**):

Method A. Using HTIB/NaN₃:

To a solution of acetophenone (**1a**, 1.20 g, 10 mmol) in acetonitrile (20 mL) was added HTIB (4.13 g, 11 mmol) and the resulting solution was refluxed for 2 h. After cooling to room temperature sodium azide (1.30 g, 2.0 mmol) was added and reaction mixture was stirred for 2 h. Most of the solvent was distilled off and the residual mixture was dissolved in CH₂Cl₂, washed with cold water and dried over Na₂SO₄. α -Azidoacetophenone (**3a**) separated out from organic layer after trituration with pet. ether as a pale yellow oil (1.28 g). IR (Nujol): 2196, 2100, 1697, 1286 cm⁻¹; ¹H-NMR (CDCl₃): δ 7.36-7.87 (m, 5H, aromatic protons), 4.41 (s, 2H, CH₂) [12a].

Similarly, other α -azido ketones **3b-3g** were prepared from the corresponding ketones **1b-1g** in good yields (Table 1). The identities of the products were confirmed by comparison of their melting points and spectral data with those reported in literature.

2-Azido-1-(4-methylphenyl)ethanone (**3b**): Mp 56-57°C (Lit. [12b] mp 58-60°C).

2-Azido-1-(4-methoxyphenyl)ethanone (**3c**): Mp 67-68°C (Lit. [12b] mp 68-71°C).

2-Azido-1-(4-bromophenyl)ethanone (**3d**): Mp 85-86°C (Lit. [12b] mp 86-87°C).

2-Azido-1-(4-chlorophenyl)ethanone (**3e**): Mp 65-67°C; IR (KBr): 2918, 2105, 1692, 1591 cm⁻¹; ¹H-NMR (CDCl₃): δ 7.80 (d, $J = 7.2$ Hz, 2H, aromatic protons), 7.6 (d, $J = 7.2$ Hz, 2H, aromatic protons), 4.51 (s, 2H, CH₂).

2-Azido-1-phenyl-1-propanone (**3f**) [12a]: Pale yellow oil; IR (Nujol): 2897, 2115, 2009, 1696 cm⁻¹; ¹H-NMR (CDCl₃): δ 7.2-7.8 (m, 5H, aromatic protons), 4.6 (q, $J = 5.7$ Hz, 1H, CH), 1.5 (d, $J = 6.2$ Hz, 3H, CH₃).

2-Azidocyclohexanone (**3g**) [12d]: Pale yellow oil; IR (Nujol): 2932, 2863, 2105, 1721, 1451 cm⁻¹; ¹H-NMR (CDCl₃): δ 3.7 (dd, $J = 9.7$ Hz, 2.8 Hz, 1H, -CH-), 1.5-2.4 (m, 8H, -(CH₂)₄-).

Method B. Using (PhIO)_n + *p*-TsOH/NaN₃:

To iodosobenzene (2.20 g, 10 mmol) in acetonitrile (20 mL) was added *p*-toluenesulphonic acid (1.72 g, 10 mmol), the mixture was stirred at room temperature for 5 min. To the resulting suspension, acetophenone (**1a**, 1.20 g, 10 mmol) was added and the mixture was refluxed for 2 h. After cooling to room temperature sodium azide (1.30 g, 2.0 mmol) was added and stirred for 2 h. Usual work up (as given in Method A) gave 1.24 g of **3a**. Compounds **3b-3g** were similarly prepared in good yields from the corresponding ketones **1b-1g** (Table 1).

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Sample availability: Contact the authors.