JOC Notes

Novel Oxidative α-Tosyloxylation of Alcohols with Iodosylbenzene and *p*-Toluenesulfonic Acid and Its Synthetic Use for Direct Preparation of Heteroaromatics

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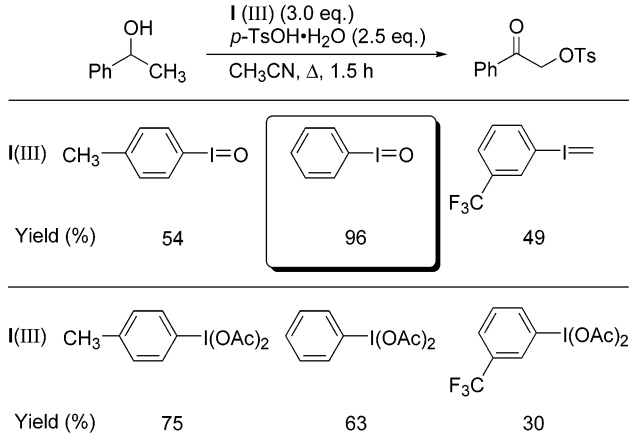
Abstract: α-Tosyloxyketones and α-tosyloxyaldehydes were directly prepared from alcohols by treatment with iodosylbenzene and *p*-toluenesulfonic acid monohydrate in good yields. This method can be used for the direct preparation of thiazoles, imidazoles, and imidazo[1,2-*a*]pyridines from alcohols in good to moderate yields by the successive treatment with iodosylbenzene and *p*-toluenesulfonic acid monohydrate, followed by thioamides, benzamidine, and 2-aminopyridine, respectively.

Today, extensive studies on hypervalent iodine compounds have been carried out, and the synthetic use of these compounds has been well studied.[1] Among them, [hydroxy(tosyloxy)iodo]benzene (Koser's reagent, HTIB) is a useful reagent for α-tosyloxylation of ketones.[2] α-Tosyloxyketones are very important precursors for the construction of various heterocyclic compounds such as thiazoles, selenazoles, oxazoles, imidazoles, etc.[3] In this paper, we would like to report a novel direct oxidative α-tosyloxylation of alcohols. This method was successfully applied to the direct preparation of thiazoles, imidazoles, and imidazo[1,2-*a*]pyridines by the treatment of alcohols with iodosylbenzene and *p*-toluenesulfonic acid and subsequent treatment with thioamides, benzamidine, and 2-aminopyridine, respectively. The key step in this reaction is the formation of aldehydes and ketones. To our knowledge, the direct preparation of α-tosyloxyketones from alcohols with iodosylbenzene and *p*-toluenesulfonic acid monohydrate has not hitherto been reported. At first, the reactivity of hypervalent iodine reagents, i.e., iodosylbenzene, 4-methyl-1-iodosylbenzene, 3-(trifluoromethyl)-1-iodosylbenzene, (diacetoxyiodo)benzene, 4-methyl-1-(diacetoxyiodo)benzene, and 3-(trifluoromethyl)-1-(diacetoxyiodo)benzene, in the oxidative α-tosyloxylation of 1-phenylethanol in the presence of *p*-toluenesulfonic acid monohydrate in acetonitrile was studied as shown in Table 1. Here, iodosylarenes showed better reactivity than (diacetoxyiodo)arenes. In the substituent effect of iodosylarenes, the parent iodosylbenzene showed the most effective reactivity. Thus, on the basis of these results, the oxidative α-tosyloxylation of alcohols with iodosylbenzene and *p*-toluenesulfonic acid monohydrate in acetonitrile was carried out as shown in Table 2. Generally, secondary alcohols give α-tosyloxyketones in high yields, whereas primary alcohols give α-tosyloxyaldehydes in moderate yields. The reactive species for the oxidative α-tosyloxylation of alcohols should be [hydroxy(tosyloxy)iodo]benzene (HTIB). Practically, the same treatment of alcohols with HTIB generates the corresponding α-tosyl-

TABLE 1. Oxidative α-Tosyloxylation of 1-Phenylethanol Using Various Hypervalent Iodine Reagents



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[‡] Department of Chemistry.

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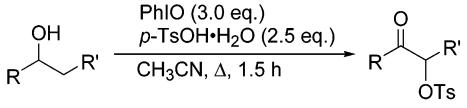
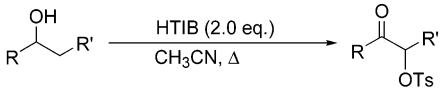
TABLE 2. Oxidative α-Tosyloxylation of Alcohols



R	R′	yield (%)
C_6H_5	H	96
p-$CH_3C_6H_4$	H	84[a]
p-ClC_6H_4	H	96
p-$O_2NC_6H_4$	H	99
C_6H_5	CH_3	94[a]
C_6H_5	n-C_7H_{15}	87[a]
n-C_5H_{11}	n-C_4H_9	80[a,b]
H	n-$C_{11}H_{23}$	53[a]
H	$(CH_2)_3C_6H_5$	49
$-(CH_2)_4-$		52[a,b]

[a] Reaction time was 2.5 h. [b] Reaction temperature was 60 °C.

SCHEME 1. Oxidative α-Tosyloxylation of Alcohols with HTIB



R = C_6H_5, R' = H	1.5 h	99 %
R = C_6H_5, R' = CH_3	1.5 h	70%
R = p-$CH_3C_6H_4$, R' = H	2.5 h	7%
R = H, R' = n-$C_{11}H_{23}$	2.5 h	0%

oxyketones in good yields as shown in Scheme 1. However, the yields of the products strongly depend on the alcohols used. Especially, treatment of alcohols bearing an electron-rich aromatic group, such as a tolyl group or an anisyl group, with HTIB gives the corresponding α-tosyloxyketones in poor yields, and α-tosyloxyaldehydes from primary alcohols with HTIB were not formed at all. Thus, the present method for the direct α-tosyloxylation of alcohols with iodosylbenzene and *p*-toluenesulfonic acid monohydrate is highly effective and useful for the preparation of α-tosyloxyketones and α-tosyloxyaldehydes.

The effect of sulfonic acids with methanesulfonic acid, *p*-toluenesulfonic acid, and *p*-nitrobenzenesulfonic acid was studied, and consequently *p*-toluenesulfonic acid showed the most effective reactivity. Moreover, as a part of our study on environmentally benign organic synthesis[4] we have studied the preparation of α-tosyloxyacetophenone from 1-phenylethanol in a room-temperature ionic liquid (1-butyl-3-methylimidazolium hexafluorophosphate) media and a solvent-free reaction. However, the yields were decreased to 30% and 53%, respectively. Thus, effective acceleration for the reactions of the ionic liquid media and solvent-free conditions was not observed.

Under the same conditions, treatment of 1-phenylethanol and 1-phenylpropanol with iodosylbenzene and diphenylphosphoric acid generates α-(diphenylphosphoryloxy)acetophenone and α-(diphenylphosphoryloxy)-propiophenone in 79% and 62% yields, respectively, as shown in Scheme 2.

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SCHEME 2. Oxidative α-Phosphoryloxylation of Alcohols

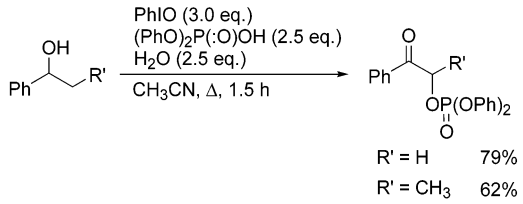
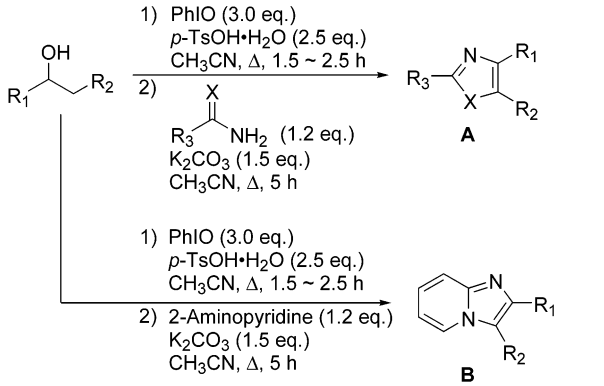


TABLE 3. Direct Preparation of Heterocyclic Compounds

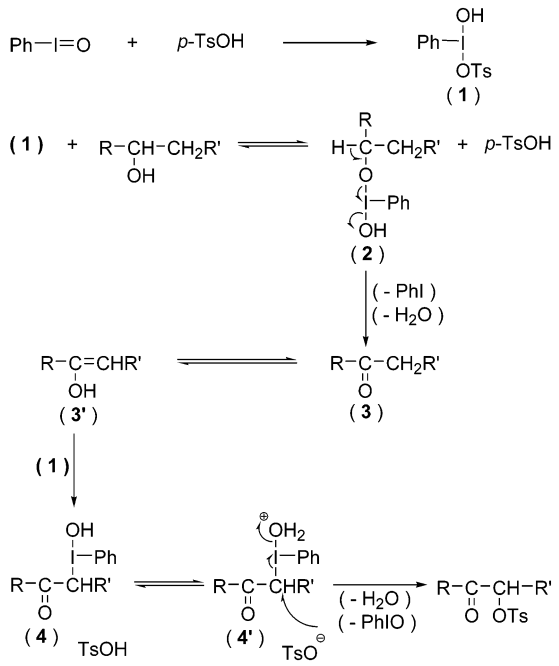


	R_1	R_2	R_3	X	yield (%)
A	C_6H_5	H	CH_3	S	59
A	p-ClC_6H_4	H	CH_3	S	53
A	p-$NO_2C_6H_4$	H	CH_3	S	64
A	C_6H_5	H	C_6H_5	S	48
A	C_6H_5	H	C_6H_5	NH	48
A	p-ClC_6H_4	H	C_6H_5	NH	64
B	C_6H_5	H			83
B	p-ClC_6H_4	H			48

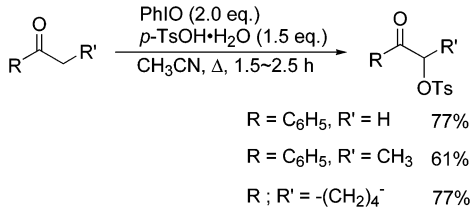
On the basis of these results, direct preparation of thiaozles, as typical heteroaromatics, was carried out by the treatment of alcohols with iodosylbenzene and *p*-toluenesulfonic acid monohydrate and subsequent treatment with thioamide in the presence of potassium carbonate. As shown in Table 3, thiazoles were obtained in good yields from the starting alcohols. Imidazoles and imidazo[1,2-*a*]pyridines were also obtained in good to moderate yields by the same treatment of alcohols with iodosylbenzene and *p*-toluenesulfonic acid monohydrate, followed by the reaction with benzamidine and 2-aminopyridine in the presence of potassium carbonate, respectively.

On the basis of these results, a reasonable reaction mechanism is shown in Scheme 3. Here, [hydroxy(tosyloxy)iodo]benzene **1** is smoothly formed in situ by the reaction of iodosylbenzene and *p*-toluenesulfonic acid monohydrate.[2] Alcohols reacts with compound **1** to form the corresponding carbonyl compounds **3** via the intermediates **2**. In the presence of *p*-toluenesulfonic acid, carbonyl compounds **3** tautomerize to the corresponding enol forms **3′**, which then react with compound **1** to provide α-tosyloxyketones or α-tosyloxyaldehydes via the intermediates **4** and **4′**. Practically, under the same conditions, treatment of alcohols with compound **1** generates the corresponding α-tosyloxycarbonyl compounds as mentioned in Scheme 1, and the same treatment of carbonyl compounds with iodosylbenzene and *p*-toluene-

SCHEME 3. Reaction Mechanism for Oxidative α-Tosyloxylation of Alcohols



SCHEME 4. Oxidative α-Tosyloxylation of Ketones



sulfonic acid monohydrate produces the corresponding α-tosyloxycarbonyl compounds as shown in Scheme 4.

In conclusion, the present reaction is a simple and facile method for the direct preparation of α-tosyloxyaldehydes and α-tosyloxyketones from alcohols with iodosylbenzene and *p*-toluenesulfonic acid monohydrate and can be used for the direct preparation of heteroaromatics such as thiazoles, imidazoles, and imidazo[1,2-*a*]pyridine, respectively, from secondary and primary alcohols, by the successive treatment with iodosylbenzene and *p*-toluenesulfonic acid monohydrate, followed by the treatment with thioamide, amidine, and 2-aminopyridine in the presence of potassium carbonate.

Experimental Section

General. All reactions were carried out under an argon atmosphere. ^{1}H NMR spectra were recorded on a 400 MHz spectrometer. Chemical shifts are reported as ppm downfield from tetramethylsilane (TMS) in δ units, and J values are given in Hz. IR spectra were recorded on a FT/IR-200 spectrometer. Microanalyses were performed with 240B and 240 elemental analyzers at Chemical Analysis Center of Chiba University. Melting points were determined on a melting point apparatus in open capillary tubes and are uncorrected. Silica gel 60 was used for column chromatography, Kieselgel 60 F254 was used for TLC, and Wakogel B-5F was used for preparative TLC.

General Procedure for Oxidative α-Tosyloxylation of Alcohols. To a solution of alcohol (1.0 mmol) in acetonitrile (10 mL) were added *p*-toluenesulfonic acid monohydrate (2.5 mmol) and iodosylbenzene (3.0 mmol). The mixture was refluxed for 1.5 h under an argon atmosphere, and then the reaction mixture was poured into water and extracted with chloroform three times. The combined organic layer was dried over Na_2SO_4. After filtration, the solvent was evaporated under reduced pressure, and the residue was purified by preparative TLC on silica gel (eluent, hexane/ethyl acetate = 3/1) to give the corresponding α-tosyloxyketone.

General Procedure for Direct Preparation of Thiazoles from Alcohols. To a solution of alcohols (1.0 mmol) in acetonitrile (10 mL) were added *p*-toluenesulfonic acid monohydrate (2.5 mmol) and iodosylbenzene (3.0 mmol). The mixture was refluxed for 1.5 h under an argon atmosphere, and then the reaction mixture was poured into water and extracted with chloroform three times. The combined organic layer was dried over Na_2SO_4. After filtration, the solvent was removed under reduced pressure. Acetonitrile (6 mL), potassium carbonate (1.5 mmol), and thioamide (1.2 mmol) were added to the residue. The mixture was refluxed for 5 h under an argon atmosphere, and then the reaction mixture was poured into water and extracted with chloroform three times. The combined organic layer was dried over Na_2SO_4. After filtration, the solvent was evaporated under reduced pressure and the residue was purified by preparative TLC on silica gel (eluent, hexane/ethyl acetate = 3/1) to give the corresponding thiazole.

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Supporting Information Available: Characterization data for all α-tosyloxyketones, α-tosyloxyaldehydes, thiazoles, imidazoles, and imidazo[1,2-*a*]pyridines and copies of their ^{1}H NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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