Communication

Iodobenzene-Catalyzed Synthesis of Imidazo[1,2-*a*]pyridines from Aryl Ketones with *m*CPBA in Ionic Liquid

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Iodobenzene-catalyzed synthesis of imidazo[1,2-*a*]pyridines from aryl ketones with *m*CPBA as a cooxidant in ionic liquid is described. The method is simple, rapid and practical, generating Imidazo[1,2-*a*]pyridines from the aryl ketone without isolation of α-tosyloxyketones in good to excellent yields.

Keywords: Iodobenzene; *m*CPBA; Ionic liquid.

INTRODUCTION

Imidazo[1,2-*a*]pyridines are of interest due to their antiinflammatory,[1] potential antirhinoviral,[2] long-acting local anesthetic[3] and antiulcer agents,[4] for whitening fine fabrics,[5] as anthelmintic or bacteriostatic agents,[6] and as fluorescent materials.[7] They are also versatile intermediates for synthetic transformations.[8]

Imidazo[1,2-*a*]pyridines have generally been prepared by the condensation of α-halocarbonyl compound with 2-aminopyridine (Chichibabin reaction).[9] Other methods based on 2-aminopyridine[10] and an alternative strategy of building imidazo[1,2-*a*]pyridines from a variety of substituted imidazoles are also reported.[11]

Ionic liquids have become very popular as organic reaction media due to the promotion of ionic reaction and recyclable reaction media.[12] Thus, these solvents possess interesting and useful advantages for organic reactions such as negligible vapor pressure, low flammability, high thermal stability, and easyreusability. Therefore, these solvents have been successfully used in Freidel-Crafts reaction,[13] hydrogenation,[14] Diel-Alder reactios,[15] Heck, Suzuki, Sonogashira, and olefin-metathesis reactions,[16] Michael additions,[17] oxidation,[18] condensation reaction,[19] formation of imines,[20] 1,2-rearrangement,[21] esterification of carboxylic acids and carboxylates,[22] Williamson ether synthesis,[23] and Grignard reaction.[24]

Hypervalent iodine(III) reagents have been used extensively in organic synthesis due to their low toxicity, ready availability and easy handling.[25] Recently, iodobenzene-catalyzed efficient α-tosyloxylation of ketones with *m*-chloroperbenzioc acid (*m*CPBA) and *p*-toluenesulfonic acid (PTSA) was reported to give the corresponding α-tosyloxy ketones.[26] Here, as a part of our efforts to develop greener organic reaction procedure,[27] we would like to report PhI-catalyzed α-tosyloxylation of aryl ketones to prepare imidazo[1,2-*a*]pyridines (**3**) in ethylmethylimidazolium([emim]OTs) without isolation of α-tosyloxyketones (**2**) in good to excellent yields (Scheme I). Recently, study on the synthetic use of organic catalysts has become important, due to their less toxicity than that of organometallic catalysts.

RESULTS AND DISCUSSION

As shown in Scheme I, our experiments involving a one-pot procedure for the preparation of imidazo[1,2-*a*]pyridines (**3**) by nucleophilic substitution reactions of α-tosyoxy ketone intermediates (**2**) with the 2-aminopyridines in [emim]OTs at room temperature was successful. The results are summarized in the Table 1. When the reaction was conducted in the classical molecular solvent, such as acetonitrile, the preparation of 2-phenylimidazo[1,2-*a*]pyridine (**3a**) needs refluxing for 6 h; however, in [emim]OTs, the reaction took place at room temperature for 0.5 h and gave a higher yield.

A plausible reaction pathway for the present reaction is shown in Scheme II. Thus, PhI is oxidized by *m*CPBA in

Scheme I

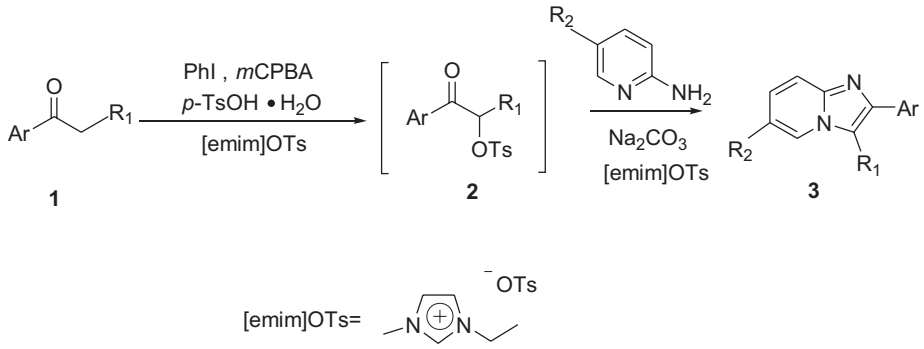


Table 1. Preparation of imidazo[1,2-*a*]pyridines **3a-k**

Entry	Ar	R_1	R_2	Yield (%)
3a	Ph	H	H	82
3b	4-MeC_6H_4	H	H	75
3c	4-MeOC_6H_4	H	H	83
3d	4-FC_6H_4	H	H	85
3e	4-ClC_6H_4	H	H	80
3f	4-BrC_6H_4	H	H	77
3g	2-Furyl	H	H	81
3h	2-Thienyl	H	H	82
3i	Ph	Me	H	76
3j	Ph	H	Cl	78
3k	4-MeOC_6H_4	H	Cl	84

the presence of PTSA to generate [hydroxyl(tosyloxy)-iodo]benzene (HTIB) in situ, which then reacts whith the enol form of ketone to provide α-tosyloxyketone intermediate (**2a**). Nucleophilic substitution reaction of **2a** with 2-aminopyridine to give imidazo[1,2-*a*]pyridine (**3a**).

In conclusion, we have described a novel and efficient method for the synthesis of imidazo[1,2-*a*]pyridines using [emim]OTs as reaction medium. The important features of this procedure are enhanced reaction rate, mild reaction condition, high yield and green aspects such as avoiding hazardous organic solvents, toxic catalysts and waste.

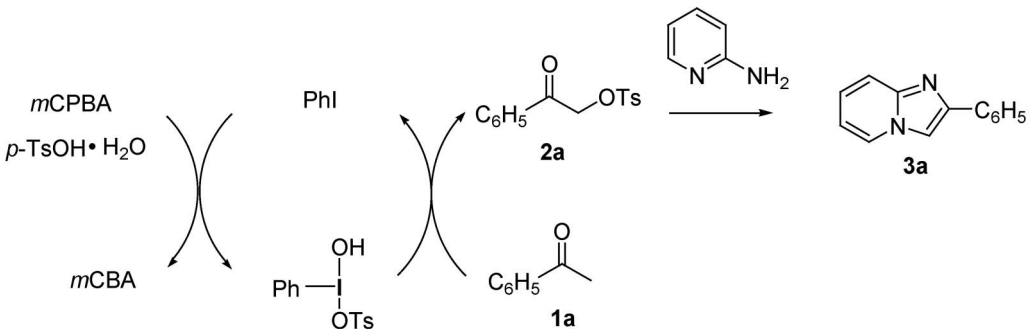
EXPERIMENTAL SECTION

All melting points are uncorrected. The IR spectra were recorded on a Shimadzu IR-27 G spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Unity Plus 400 MHz. Chemical shifts (δ) were measured in ppm with respect to TMS. MS were obtained on a JEOL JMS D-300 instrument.

General one-pot procedure for the synthesis of imidazo[1,2-*a*]pyridines (3)

To a mixture of aryl ketone (**1**) (1.0 mmol), PhI (1.0 mmol), and PSTA·H_2O (1.1 mmol) in [emim]OTs (2 mL) was added *m*CPBA (1.1 mmol) and stirred for 1 h at 80 °C. Then 2-aminopyridine (1.0 mmol) and sodium carbonate (0.6 mmol) were added to the reaction mixture and was stirred at room temperature for 0.5 h to complete the reaction. Subsequently, the reaction mixture was extracted with EtOAc (3 × 5 mL). The extract was washed with aq sat. $NaHCO_3$ solution once and dried and the solvent was removed under reduced pressure. The residue was chromato-

Scheme II



graphed on silica gel using a mixture of AcOEt-cyclohexane (1:2) as eluent to give **3**.

2-Phenylimidazo[1,2-*a*]pyridine (3a)

Mp 131-133 °C (lit.[28] mp 130-132 °C) yield 82%. IR (KBr) ν: 1630 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 6.78 (dt, J = 1.2, 6.8 Hz, 1H), 7.15-7.19 (m, 1H), 7.33 (t, J = 7.2 Hz, 1H), 7.42-7.46 (m, 2H), 7.64 (dd, J = 0.8, 8.8 Hz, 1H), 7.87 (s, 1H), 7.94-7.97 (m, 2H), 8.12 (td, J = 1.2, 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 108.1, 112.5, 117.5, 124.8, 125.6, 126.1, 128.0, 128.4, 128.7, 129.9, 133.4, 133.5, 145.6; EI-MS *m/z* (relative intensity) 194 (M^+), 116, 89, 78, 63, 51, 50.

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