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Copper-catalyzed imination of pyridines using PhI=NTs as nitrene precursor

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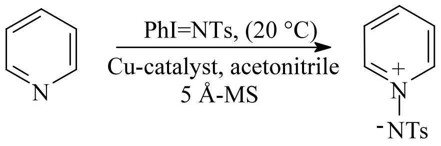
Abstract—The reaction of PhI=NTs with pyridines in the presence of a catalytic amount of Cu(II) triflate afforded the corresponding *p*-tolylsulfonyliminopyridinium ylides in excellent yields. © 2003 Elsevier Science Ltd. All rights reserved.

1-Aminopyridinium ylides are important synthetic intermediates as they undergo 1,3 dipolar cycloaddition reactions with a variety of dipolarophiles to yield indolizine derivatives, which have been used in the synthesis of alkaloids,[1] and undergo photoisomerization to yield 1(1*H*),2-diazepine derivatives.[2] The chemistry of 1-aminopyridinium ylides is underdeveloped due to the lack of availability of methods for their synthesis. Although these compounds can be prepared either by acylation of 1-aminopyridinium salts followed by deprotonation[3] or by thermal decomposition of azides in the presence of pyridines,[4] both the methods suffer from drawbacks such as very low yields of 1-aminopyridinium ylides, formation of side products due to competing hydrogen abstraction and insertion reactions, and the hazardous nature of azides such as sulfonyl azides which are extremely shock sensitive reagents.[5] It is therefore important to develop a new methodology for the preparation of 1-aminopyridinium ylides.

Recently Evans et al. reported that [*N*-(*p*-tolylsulfonyl)imino]phenyliodinane (PhI=NTs)[6] is an efficient nitrene precursor for aziridination of alkenes in the presence of copper-based catalysts.[7] Hence, we thought it would be worthwhile to use this reagent as a nitrene precursor and accordingly we now report a first catalytic method for the preparation of *p*-tolylsulfonyliminopyridinium ylides by the reactions of pyridines with the nitrene from PhI=NTs generated in situ in the presence of Cu(II) triflate as catalyst (Scheme 1).

To evaluate the catalytic efficiency of various copper catalysts, the reaction of pyridine with PhI=NTs was studied using different copper-based catalysts with acetonitrile as the solvent (substrate/PhI=NTs molar ratio = 2:1) in the presence of 5 Å molecular sieves. The results are summarized in Table 1 and show that Cu(II) triflate is the most active catalyst for this reaction. To examine the versatility of Cu(II) triflate as a catalyst, a variety of pyridines and fused pyridine derivatives were reacted with the nitrene generated from PhI=NTs.[7] These results are presented in Table 2 and clearly indicate that pyridines containing electron-donating



Scheme 1.

Table 1. Imination of pyridine with different copper catalysts[a]

Entry	Catalyst	Additive	Yield[b] (%)
1	$Cu(OTf)_2$	–	60
2	$Cu(OTf)_2$	MS-5 Å	75
3	$Cu(acac)_2$	MS-5 Å	70
4	CuCl	MS-5 Å	60
5	$CuCl_2$	MS-5 Å	50

[a] Reaction conditions: Substrate/PhI=NTs (2:1), catalyst (5 mol%), acetonitrile (5 ml), 8 h, under a nitrogen atmosphere in the presence of 5 Å molecular sieves.

[b] Isolated yields.

Keywords: pyridines; pyridinium ylides; copper; PhI=NTs.

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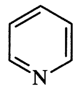
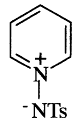
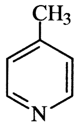
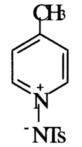
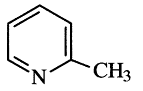
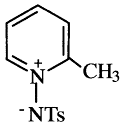
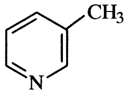
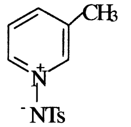
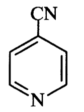
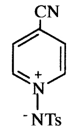
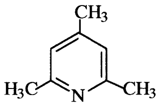
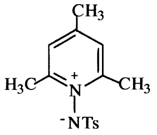
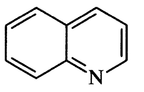
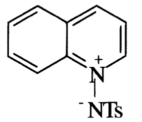
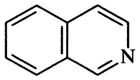
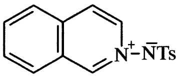
Table 2. Imination of pyridines with PhI=NTs using Cu(II) triflate as catalyst[a]

Entry	Substrate	Product	Reaction time (h)	Yield[b] (%)	M.P. Found (Reported)
1			8	75	215(210)[2]
2			5	85	165(-)
3			6	80	160(-)
4			8	75	165(-)
5			12	55	162(-)
6			10	60	150(-)
7			12	40	225(228)[8]
8			12	45	223-224(227-228)[9]

a Reaction conditions: As described in the text

b Isolated yields

groups (Table 2, entries 2–4) are more reactive and give better yields of the products. Similarly pyridines (Table 2, entries 1–6) were found to be more reactive as compared to their fused ring derivatives (Table 2, entries 7 and 8). Although, in all the reactions described in Tables 1 and 2, we used PhI=NTs as the nitrene precursor, to evaluate the efficiency of other nitrene precursors, the reaction of pyridine was also studied with Chloramine-T, and Bromamine-T in the presence of Cu(II) triflate as catalyst. The use of PhI=NTs as the nitrene precursor gave the highest yield of the *p*-tolylsulfonylpyridinium ylide with Cu(II) triflate as catalyst. All these reactions were associated with the formation of *p*-toluenesulfonamide as the by-product along with desired products. Reactions conducted without the use of 5 Å molecular sieves showed a significant increase in *p*-toluenesulfonamide formation. To investigate the effect of solvents the imination of pyridine was also performed in different solvents such as acetonitrile, nitromethane, dichloroethane and toluene under similar reaction conditions with PhI=NTs using Cu(II) triflate as catalyst. Among the solvents studied, acetonitrile and nitromethane were found to be the best solvents for this reaction.

In summary, the present method represents the first example of a catalytic method for the imination of pyridines and fused pyridine derivatives to form the corresponding *p*-tolylsulfonyliminopyridinium ylides using PhI=NTs, Chloramine-T and Bromamine-T as nitrene precursors. The better yields of the products, mild reaction conditions and easy preparation/availability of these nitrene precursors make this method an attractive one.

Typical experimental procedure: To a stirred suspension of pyridine (1.4 mmol), PhI=NTs (0.67 mmol) and 5 Å molecular sieves (100 mg) in dry acetonitrile (5 ml) was added Cu(II) triflate (0.03 mmol, 5 mol%) under a nitrogen at room temperature (20°C). Stirring was continued for 8 h (completion of the reaction as indicated by complete dissolution of PhI=NTs) and then the molecular sieves were removed by filtration. The filtrate obtained was evaporated under vacuum to give an oil, which was purified by passing through a silica gel column using dichloromethane as eluent. Evaporation of the solvent yielded *N*-(*p*-tolylsulfonyl)iminopyridinium ylide, mp 215°C (lit. 210°C) in a yield of 92%. Other pyridinium ylides were prepared similarly.

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