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Short communication

An improved protocol for regioselective ring opening of aziridines with tetrabutylammonium halides using ammonium-12-molybdophosphate as a catalyst☆

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Abstract

Regioselective ring opening of aziridines with tetrabutylammonium halides to form the corresponding β-haloamines has efficiently been carried out at room temperature using ammonium-12-molybdophosphate as a catalyst. The products are formed in excellent yields within a short period of time.

Keywords: Aziridine; Tetrabutylammonium halide; Ring opening; Ammonium-12-molybdophosphate; Regioselectivity

Aziridines are versatile intermediates in various important organic syntheses [1]. They can easily be prepared and cleaved with different nucleophiles. On treatment with metal halides they can be converted into β-haloamines which are useful precursors for the synthesis of bioactive molecules [2]. However, the conversions of many of aziridines with metal halides suffer from certain drawbacks such as long reaction times, poor regioselectivity and high temperature. Metal halides can be replaced with tetrabutylammonium halides as nucleophilic halide sources. Tetrabutylammonium halides are nontoxic, inexpensive and widely applied in phase transfer catalysis. Earlier they were used once in the presence of β-cyclodextrin but the times required for the conversions were 3.5–6 h and proper adjustment of pH for the reaction was also required [3]. We felt that the protocol of the application of these reagents for ring opening of aziridines could be improved by using a suitable catalyst in the conversion.

In continuation of our work [4] on the development of useful synthetic methodologies we have recently observed that *N*-tosylaziridines can efficiently be cleaved with tetrabutylammonium halides (TBAX) using ammonium-12-molybdophosphate [AMP], $(NH_4)_3$ $[PMo_{12}O_{40}]$ [5] as a catalyst at room temperature to form the corresponding *N*-tosyl-β-haloamines (Scheme 1).

Several *N*-tosylaziridines (**1**) were treated with tetrabutylammonium bromide (or iodide) in the presence of AMP (Table 1). The products, *N*-tosyl-β-bromo (or iodo) amines (**2**) were formed in excellent yields within 45 min. *N*-Tosylaziridines containing both aromatic and aliphatic moiety underwent the conversions well. The aromatic moiety may also contain electron-donating as well as electron-withdrawing groups.

The ring opening of aziridines took place with high regioselectivity. *N*-Tosyl-2-aryl aziridines yielded the products by cleavage at the benzylic position while *N*-tosyl-2-alkylaziridines afforded the products formed by opening at the terminal position. The cleavage of symmetrical bicyclic *N*-tosylaziridines gave the *N*-tosyl-β-haloamines whose stereochemistry was found to the *trans*. The structures and stereochemistry of the prepared β-haloamines were settled from their spectral (^{1}H NMR and MS) data.

In recent years heteropoly acids and their salts have attracted much attention because of their interesting catalytic activity and capability of conducting the reaction in cleaner manner compared to conventional liquid acid catalysts [6]. However, the synthetic utility of these catalysts has not been fully explored. The present catalyst, AMP (the ammonium salt of a heteropoly acid) is highly effective for the cleavage of aziridine ring with

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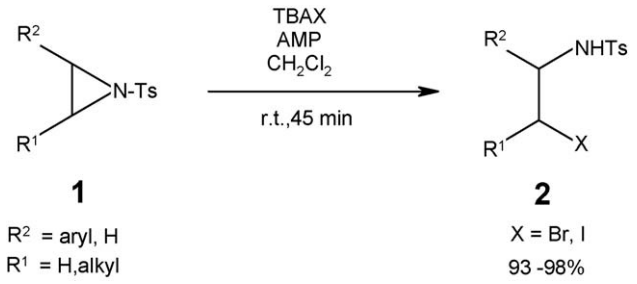
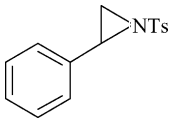
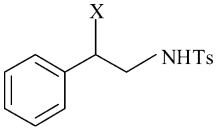
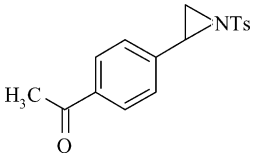
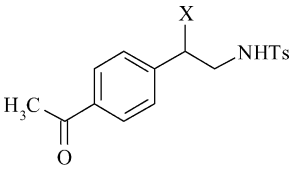
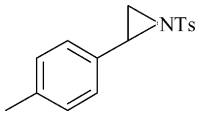
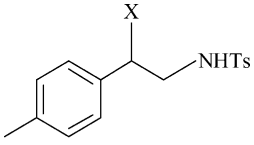
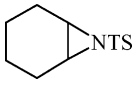
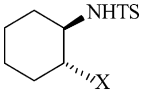
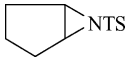
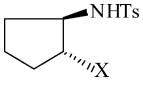
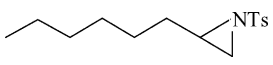
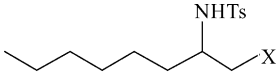
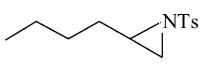
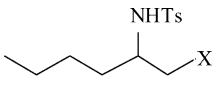


Scheme 1.

tetrabutylammonium halides at room temperature. The catalyst works under heterogeneous, conditions. It can easily be handled and removed from the reaction mixture by simple filtration. In absence of this catalyst the conversion afforded only a trace amount of products even after 2 h.

In conclusion, we have demonstrated a mild, efficient, rapid and high-yielding protocol for the preparation of β-haloamines by ring opening of aziridines with tetrabutylammonium bromide and iodide using ammonium salt of a heteropoly acid. Metal halides have been avoided here for preparation of these compounds. The method is highly regio- and stereoselective. Thus a novel useful application of the catalyst (AMP) is disclosed.

Table 1
Ring opening of aziridines with tetrabutylammonium halides using AMP[a]

Entry	Substrate (**1**)	Reagent	Product (**2**)	Isolated yield (%)
				
a		TBABr	X = Br	98
b		TBAl	X = I	96
				
c		TBABr	X = Br	97
d		TBAl	X = I	96
				
e		TBABr	X = Br	95
f		TBAl	X = I	93
				
g		TBABr	X = Br	97
h		TBAl	X = I	94
				
i		TBABr	X = Br	93
j		TBAl	X = I	94
				
k		TBABr	X = Br	95
l		TBAl	X = I	94
				
m		TBABr	X = Br	97
n		TBAl	X = I	96

[a] The structures of the prepared β-haloamines were settled from their spectral (^{1}H NMR and MS) data.

1. Experimental

1.1. General procedure for ring opening of aziridine

To a solution of *N*-tosylaziridine (1 mmol) in CH_2Cl_2 (5 ml) tetrabutylammonium halide (1.5 mmol) and AMP (10 mol%) were added. The mixture was stirred at room temperature for 45 min and filtered. The filtrate was concentrated and water (10 ml) was added. The organic material was extracted with EtOAc (3× 10 ml) and the solvent was subsequently removed from the extract. The residue was purified by column chromatography over silica gel using hexane–EtOAc, 9:1 as eluent to obtain pure *N*-tosyl-β-haloamines.

The Spectral (^{1}H NMR and MS) data of some representative compounds are given below.

2c: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.70 (2H, d, J = 8.0 Hz), 7.32–7.24 (4H, m), 6.98 (2H, d, J = 8.0 Hz), 5.27 (1H, brs), 4.78 (1H, dd, J = 6.0, 4.0 Hz), 3.15 (1H, m) 2.92 (1H, m), 2.41 (3H, s), 2.29 (3H, s); EIMS: *m*/*z* 397, 395 ($M^{+\bullet}$).

2h: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.82 (2H, d, J = 8.0 Hz), 7.28 (2H, d, J = 8.0 Hz), 5.20 (1H, d, J = 6.0 Hz), 3.99 (1H, td, J = 9.0, 4.0 Hz), 3.22 (1H, m) 2.45 (3H s), 2.32 (1H, m), 2.23 (1H, m), 1.95 (1H, m), 1.72 (1H, m), 1.54 (1H, m), 1.37–1.32 (3H, m); EIMS: *m*/*z* 379 ($M^{+\bullet}$).

2n: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.78 (2H, d, J = 8.0 Hz), 7.30 (2H, d, J = 8.0 Hz), 4.65 (1H, d, J = 6.0 Hz), 3.23–3.11 (2H, m) 2.92 (1H m), 2.45 (3H, s), 1.51–1.40 (2H, m), 1.30–1.07 (4H, m), 0.82 (3H, t, J = 7.0 Hz); EIMS: *m*/*z* 381 ($M^{+\bullet}$).

Acknowledgements

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