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Journal of Molecular Catalysis A: Chemical 256 (2006) 16–20
JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL
www.elsevier.com/locate/molcata

N-methylpyrrolidine-2-one hydrotribromide: An efficient and new catalyst for the aziridination of alkenes using Chloramine-T under solvent free conditions

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Received 18 February 2006; received in revised form 3 April 2006; accepted 5 April 2006
Available online 24 May 2006

Abstract

N-methylpyrrolidin-2-one hydrotribromide (MPHT) was found to be an efficient catalyst for the aziridination of a variety of both electron deficient as well as electron rich olefins using Chloramine-T as nitrogen source under solvent free conditions to yield corresponding aziridines in very good yields.

Keywords: Aziridination; MPHT; Olefins; Chloramine-T

1. Introduction

Aziridination of alkenes is an important synthetic transformation as aziridines are synthetically important building blocks, extensively used as electrophiles [1,2] and are present as substructures in various pharmaceuticals and natural products in which they exhibit potent and diverse biological activities [3–5]. Among the various methods reported in the literature, the transition metal catalyzed reaction of nitrene generated in situ, with olefins is an efficient and direct approach for the preparation of aziridines. Although several transition metal-based synthetic methods have been reported in the literature using PhI=NTs, Chloramine-T and Bromamine-T as nitrene precursors [6–14]. However these methods suffer from drawbacks such as use of expensive/toxic transition metals as catalysts, commercial unavailability/inconvenience of the use of PhI=NTs along with the generation of PhI as byproduct and lower yields of the products due to the competing C–H abstractions and insertion processes [12,15]. Therefore in the recent years the main emphasis is being placed towards the development of transition metal free synthetic methodologies as such methods avoids the use of toxic and expensive transition metals as catalysts.

Crystalline organic ammonium tribromides (OATB) [16,17] such as pyridine hydrobromide perbromide ($PyHBr_3$) [18], tetramethylammonium perbromide (TMATB) [19,20], phenyltrimethylammonium tribromide (PTATB) [21] and cetyltrimethylammonium tribromide (CTATB) [22] owing to their ease of handling and ability to maintain desired stoichiometry are more convenient and safer than molecular bromine that is a hazardous and toxic chemical. So the use of such crystalline organic ammonium tribromides in organic synthesis has gained considerable attention in the recent past. In this context phenyltrimethylammonium tribromide [23] pyridinium bromide perbromide [24], *N*-bromamides [12] have been reported in the literature for the aziridination of alkenes using Chloramine-T as nitrene donor. However these methods associated with the drawbacks such as (i) formation of allylic amination products from reactive substrates such as cyclohexene, (ii) use of toxic and volatile organic solvents. In continuation to our studies on the development of synthetic methods using non-metal catalytic systems herein we report a first example of the solvent free aziridination of alkenes using *N*-methylpyrrolidin-2-one hydrotribromide (MPHT) as a new and efficient catalyst and Chloramine-T as nitrene donor under mild reaction conditions (Scheme 1).

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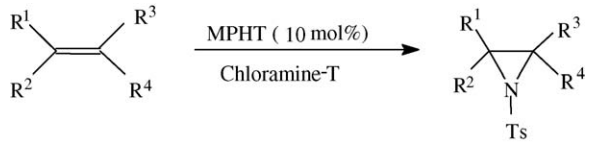
doi:10.1016/j.molcata.2006.04.029



Scheme 1.

2. Results and discussion

A variety of alkenes under reaction conditions [3 equiv. of olefin, 1 equiv. of Chloramine-T in presence of catalytic amount of MPHT at room temperature] were selectively converted to the corresponding aziridines in very good yields under solvent free conditions. These results are presented in Table 1. Among the various alkenes studied α-methyl styrene (Table 1, entry 10) and those substituted with electron donating groups on benzene ring (Table 1, entries 3 and 9) were found to be more reactive while *trans*-methylcinnamate (Table 1, entry 12) was found to be least reactive under these reaction conditions. To evaluate the efficiency of this method we carried out the aziridination of 4-methylstyrene, styrene and cyclohexene in acetonitrile solvent using 1 equiv. of substrate and 1 equiv. of Chloramine-T in presence of catalytic amount of MPHT at room temperature under nitrogen atmosphere. These results are summarized in Table 1 (entries 2, 4 and 8). While, olefins were selectively converted to corresponding aziridines, but the reaction rates were found to be slow and required longer reaction times. In efforts to avoid the use of toxic organic solvents we also performed the aziridination of 4-methylstyrene (1 equiv.) with Chloramine-T (1 equiv.) in presence of catalytic amount of MPHT using water as solvent at room temperature. The reaction was found to be very slow

Table 1
MPHT catalyzed aziridination of olefins with Chloramine-T

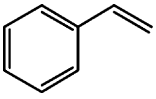
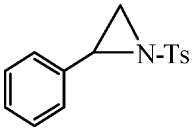
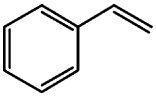
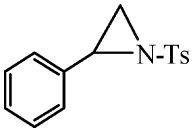
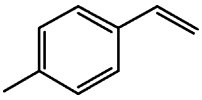
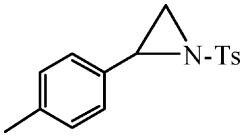
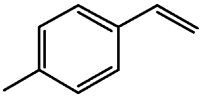
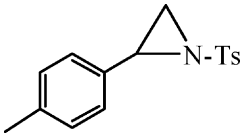
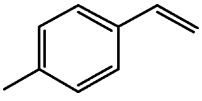
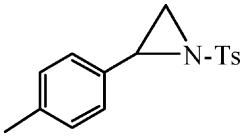
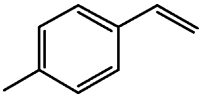
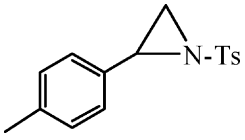
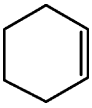
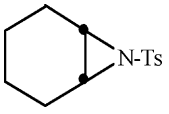
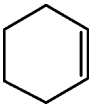
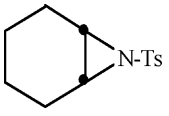
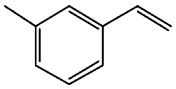
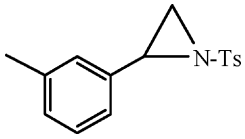
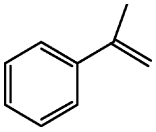
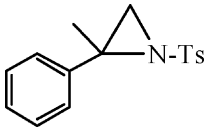
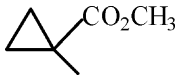
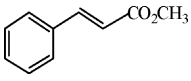
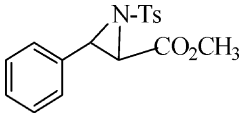
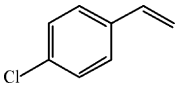
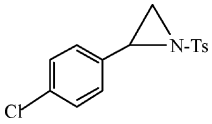
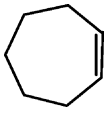
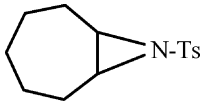
Entry	Olefin	Aziridine	Reaction time (h)	Yield (%)[a]
1			2.5	85[b]
2			4.5	75[c]
3			2.0	90[b]
4			3.5	85[c]
5			1.0	92[d]
6			3.5	20[e]
7			3.5	75[b]
8			5.0	65[c]

Table 1 (*Continued*)

Entry	Olefin	Aziridine	Reaction time (h)	Yield (%)[a]
9			2.5	85[b]
10			1.5	92[b]
11	$CH_2{=}C(CH_3)CO_2CH_3$		5.5	80[b]
12			7.0	65[c]
13			4.5	78[b]
14			4.0	65[b]

[a] Isolated yields.
[b] Reaction conditions: substrate, 3 mmol; Chloramine-T, 1 mmol; MPHT, 10 mol%, at room temperature under solvent free conditions.
[c] Experiments carried out using acetonitrile as solvent.
[d] Experiment carried out using [bmim]BF_4 as solvent.
[e] Experiment carried out using water as solvent.

and yielded intricate mixture of the products along with a small amount of aziridine.

The ionic liquids due to their unique properties such as non-volatility, good thermal stability to air and water, tunable miscibility for various organic and inorganic compounds, ease of recovery and recyclability have been distinguished as very good alternatives of the volatile and toxic organic solvents in synthetic organic chemistry [25–27,29]. To explore the potential of these green, solvents, the aziridination of 4-methylstyrene was carried out in ionic liquid [bmim]BF_4 under similar reaction conditions. The reaction was found to be faster and gave maximum yield of the corresponding aziridine [*N*-(*p*-tolylsulfonyl)2-(phenyl)aziridine] with in 1 h (Table 1, entry 5), probably due to the increased polarity of ionic liquids.

Although the mechanism of the reaction is not clear at this stage and the reaction probably initiated via the generation of bromonium ion (Br^+) from MPHT regent, as depicted in the Scheme 2. This generated bromonium ion initially reacts with olefin to afford intermediate **2**, which undergoes ring opening by $Ts(Cl)N^-$ to give β-bromo-*N*-chloro-*p*-toluene sulfonamide **3**. Attack of Br^- on *N*-chloro group of presumed intermediate **3** generates the anion **4**, which on subsequent cyclization yielded corresponding aziridine and the regenerated Br^- species again react with Chloramine-T to initiate another catalytic cycle.

3. Experimental

3.1. General

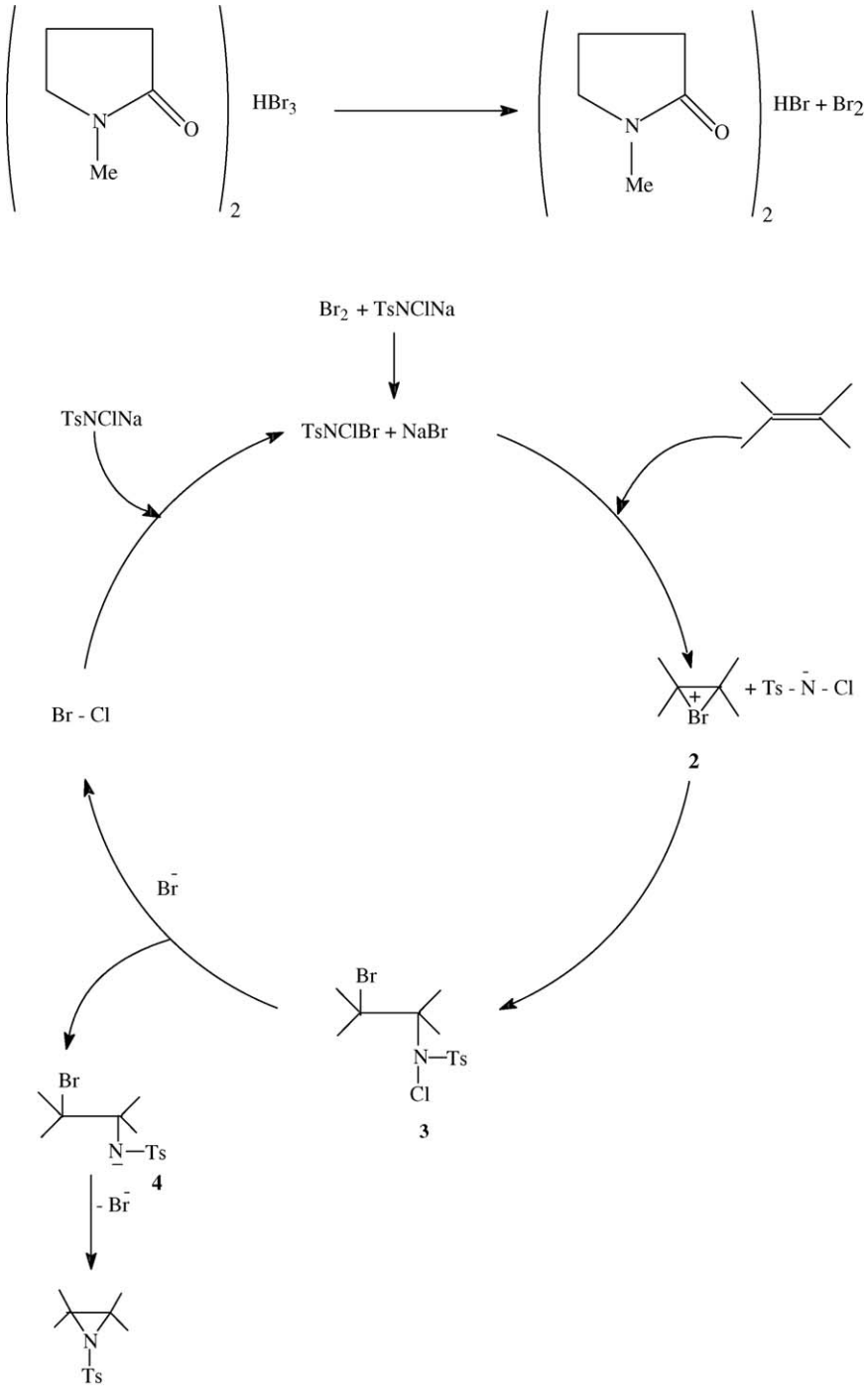
The melting points were determined in open-capillaries on a Buchi apparatus and are uncorrected. The ^1H NMR spectra were recorded on Bruker 300 MHz spectrometer and the chemical shifts are expressed in δ parts per million relative to tetramethylsilane (TMS) as the internal standard. The IR spectra were recorded on a Perkin-Elmer FTIR X 1760 instrument

3.2. Materials

All the olefins and ionic liquid [bmim]BF_4 were purchased from Aldrich and used without further purification. Hydrated Chloramine-T was purchased from Aldrich and dried under vacuum at 100 °C. *N*-methylpyrrolidine-2-one hydrotribromide (MPHT) was prepared following the literature procedure [28]. Acetonitrile was distilled and dried over CaH_2 before use.

3.3. Typical experimental procedure

To a stirred mixture of styrene (0.312 g, 3 mmol), anhydrous Chloramine-T (0.228 g, 1 mmol) was added MPHT



Scheme 2.

(0.13 g, 10 mol%) and continued the reaction at ambient temperature (25 °C) under solvent free conditions. Progress of the reaction was monitored by TLC (SiO_2). After completion, the reaction mixture was taken in dichloromethane and organic layer was washed with water (three times). The combined organic layer was dried over anhydrous $MgSO_4$ and the solvent was evaporated under vacuum to afford crude product, which was purified by column chromatography on silica gel using ethyl acetate/hexane (4:6) as eluent to yield pure (*N*-(*p*-tolylsulfonyl)2-(phenyl)aziridine) (yield 0.223 g, 85%).

3.4. Product identification

3.4.1. N-(p-tolylsulfonyl)-2-phenylaziridine (Table 1, entry 1)

m.p.: 85–86 °C (lit 87–88 °C) [30]. IR (KBr) cm^{-1}: 3017, 1600, 1520, 1327, 1162. ^1H NMR (300 MHz; $CDCl_3$): δ 2.38

(d, J = 4.5 Hz, 1H), 2.43 (s, 3H), 2.98 (d, J = 7.2 Hz, 1H), 3.77 (dd, J = 7.2, 4.5 Hz, 1H), 7.27–7.33 (m, 7H), 7.86 (d, 2H).

3.4.2. N-(p-tolylsulfonyl)-2-(p-methylphenyl)aziridine (Table 1, entry 3)

m.p.: 135–137 °C (lit 136–137 °C) [30]. IR (KBr) cm^{-1}: 3034, 1600, 1516, 1360, 1158. ^1H NMR (300 MHz; $CDCl_3$): δ 2.30 (s, 3H), 2.36 (d, J = 4.2 Hz, 1H), 2.42 (s, 3H), 2.96 (d, 7.2 Hz, 1H)), 3.73 (dd, 7.2, 4.2 Hz, 1H), 7.33–7.09 (m, 6H), 7.87 (d, 2H).

3.4.3. N-(p-tolylsulfonyl)-7-azabicyclo[4.1.0]heptene (Table 1, entry 7)

m.p.: 52–53 °C (lit 54–55 °C) [30]. IR (KBr) cm^{-1}: 3010, 1594, 1312, 1155. ^1H NMR (300 MHz; $CDCl_3$): δ 1.20–1.84 (m, 8H), 2.48 (s, 3H), 2.88 (m, 2H), 7.33 (d, 2H), 7.72 (d, 2H).

3.4.4. N-(p-tolylsulfonyl)-2-(m-methylphenyl)aziridine (Table 1, entry 9)

m.p.: 130–131 °C (lit 131–132 °C) [30]. IR (KBr) cm^{-1}: 3032, 1600, 1525, 1355, 1160. ^1H NMR (300 MHz; $CDCl_3$): δ 2.31 (s, 3H), 2.34 (d, J = 4.5 Hz, 1H), 2.43 (s, 3H), 2.97 (d, J = 7.4 Hz, 1H), 3.72 (dd, J = 7.4, 4.5 Hz, 1H), 7.10–7.31 (m, 6H), 7.85 (d, 2H).

3.4.5. N-(p-tolylsulfonyl)-2-methyl-2-phenylaziridine (Table 1, entry 10)

m.p.: 81 °C (lit 82–83 °C) [30]. IR (KBr) cm^{-1}: 3060, 2990, 1600, 1549, 1330, 1160. ^1H NMR (300 MHz; $CDCl_3$): δ 2.01 (s, 3H), 2.30 (s, 1H), 2.43 (s, 3H), 2.79 (s, 1H), 7.27–7.34 (m, 7H), 7.85 (d, 2H).

3.4.6. N-(p-tolylsulfonyl)-2-methyl-2-carbmethoxyaziridine (Table 1, entry 11)

Colorless oil. IR (KBr) cm^{-1}: 3015, 2980, 2950, 1752, 1600, 1324, 1156. ^1H NMR (300 MHz; $CDCl_3$): δ 1.89 (s, 3H), 2.42 (s, 3H), 2.54 (s, 1H), 2.77 (s, 1H), 3.71 (s, 3H), 7.33 (d, 2H), 7.86 (d, 2H).

3.4.7. trans-N-(p-tolylsulfonyl)-2-(carbomethoxy)-3-phenylaziridine (Table 1, entry 12)

m.p.: 42–43 °C (lit 44–45 °C) [30]. IR (KBr) cm^{-1}: 3060, 1744, 1604, 1336, 1156. ^1H NMR (300 MHz; $CDCl_3$): δ 2.50 (s, 3H), 3.45 (d, 1H), 3.90 (s, 3H), 4.30 (d, 1H), 7.20–7.40 (m, 7H), 7.85 (d, 2H).

3.4.8. N-(p-tolylsulfonyl)-2-(p-chlorophenyl)aziridine (Table 1, entry 13)

m.p.: 112–113 °C (lit 113–114 °C) [30]. IR (KBr) cm^{-1}: 3052, 1596, 1370, 1182. ^1H NMR (300 MHz; $CDCl_3$): δ 2.34 (d, J = 4.2 Hz, 1H), 2.45 (s, 3H), 2.85 (d, J = 7.0 Hz, 1H), 3.77 (dd, J = 7.0, 4.2 Hz, 1H), 7.15–7.37 (m, 6H), 7.83 (d, 2H).

3.4.9. N-(p-tolylsulfonyl)-8-azabicyclo[5.1.0]octane (Table 1, entry 14)

m.p.: 87–88 °C (lit 88–89 °C) [30]. IR (KBr) cm^{-1}: 3010, 2954, 2770, 1602, 1315, 1165. ^1H NMR (300 MHz; $CDCl_3$): δ 1.19–1.82 (m, 10H), 2.43 (s, 3H), 3.10 (m, 2H), 7.31 (d, 2H), 7.84 (d, 2H).

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