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First examples of *C*-arylation of aziridines catalyzed by indium triflate

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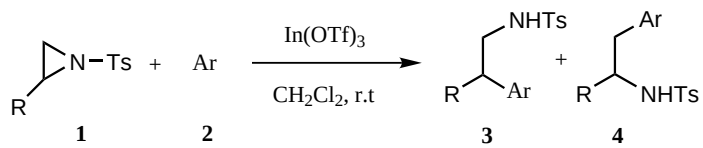
Abstract—Aziridines react smoothly with arenes in the presence of a catalytic amount of indium triflate at ambient temperature to afford the corresponding β-aryl amine derivatives in excellent yields with high regioselectivity.

Aziridines are versatile building blocks for the synthesis of many nitrogen-containing biologically interesting molecules.[1] They are well known carbon electrophiles capable of reacting with various nucleophiles and their ability to undergo regioselective ring-opening reactions contributes largely to their synthetic value.[2] As a result, several procedures have been reported for the regioselective ring opening of aziridines with various nucleophiles such as organometallic reagents,[3] silyl nucleophiles,[4] Wittig reagents,[5] amines,[6] halides,[7] hydroxyl compounds[8] and alkenes[9] to generate ring-opened products. However, there is no report on the regioselective ring opening of aziridines with arenes. Metal triflates are unique Lewis acids that are currently of great research interest.[10] Particularly, indium salts are attractive[11] because they are quite stable to water and are reusable, and, in addition, they are highly effective for the activation of nitrogen-containing compounds. Therefore, indium salts are efficient catalysts compared to traditional Lewis acids in several carbon–carbon bond forming reactions and have found wide applications in organic synthesis.

In this report, we wish to highlight our new findings that activated aziridines can be regioselectively opened with arenes using a catalytic amount of indium triflate. Treatment of styrene *N*-tosyl aziridine with 1,2-dimethoxybenzene in the presence of 5% $In(OTf)_3$ at ambient temperature gave the corresponding ring-opened products **3**[12] and **4** in 92% yield (Scheme 1).

Likewise, several arenes reacted well to give the respective β-aryl amine derivatives in high yields. The reaction of simple and less hindered arenes with styrene *N*-tosyl aziridine gave predominantly the ring-opened product **3** with a trace amount of **4**, whereas more hindered arenes afforded the product **3** with a considerable amount of **4**. The ratio of products was determined from the ^1H NMR spectrum of the crude product. Styrene *N*-tosyl aziridine underwent cleavage by arenes that attacked at benzylic as well as the terminal positions resulting in the formation of aryl amines as a mixture of **3** and **4**. The regioisomers could not be separated by column chromatography on silica gel. In all cases, the reactions proceeded efficiently in high



1 **2** **3** **4**

R=C_6H_5,4-MeC_6H_4,4-ClC_6H_4
Ar=aryl,naphthyl,anthracenyl

Scheme 1.

Keywords: inidium reagents; aziridines; *C*-arylation; β-aryl amines.

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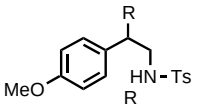
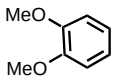
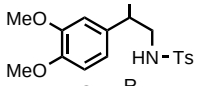
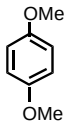
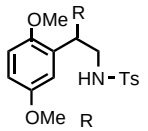
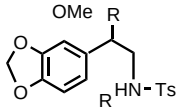
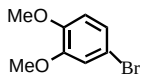
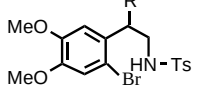
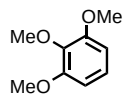
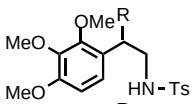
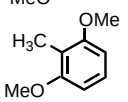
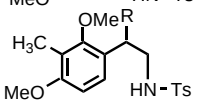
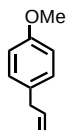
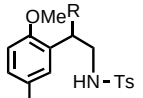
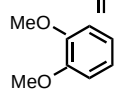
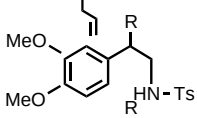
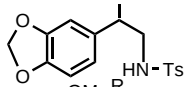
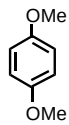
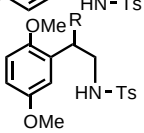
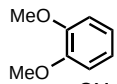
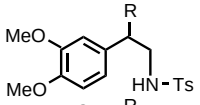
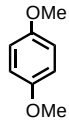
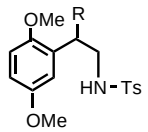
yields at ambient temperature. The method is clean and highly regioselective. The extent of electron density and the nature of the substituent on the aromatic ring shows some effect on this conversion. The activated arenes gave the ring-opened products in excellent yields in a short reaction time (Table 1). However, arenes carrying electron-withdrawing substituents such as nitro or halide groups on the aromatic ring require comparatively longer reaction times to attain yields comparable with those of their electron-rich counterparts. Furthermore, unactivated arenes such as benzene, fluorobenzene, xylene, naphthalene and anthracene also reacted well with aziridines in the presence of 10% $In(OTf)_3$ to give the products in good yields (Table 2). In contrast, metal halides such as $InCl_3$, $ZrCl_4$, $BiCl_3$, $YbCl_3$, and $FeCl_3$ gave the products as a mixture of β-aryl amine and β-chloro amines in a 1:1 ratio. The best results were obtained when

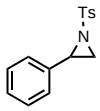
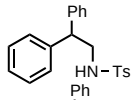
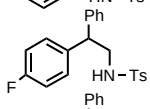
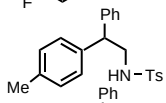
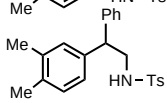
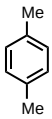
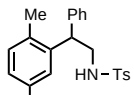
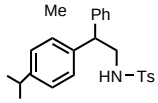
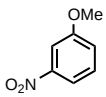
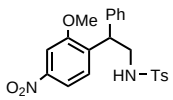
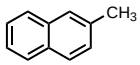
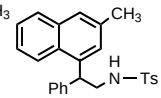
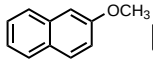
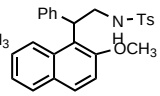
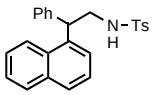
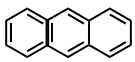
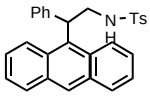
Table 1. $In(OTf)_3$-catalyzed *C*-arylation of aziridines with activated arenes

entry	aziridine	arene	product[a]	time (h)	yield[b] (%)	ratio (3:4)
a	 (R=C_6H_5)			1.0	87	95:5
b	"			1.5	92	100:0
c	"			1.0	90	93:7
d	"			1.5	88	100:0
e	"			2.5	85	94:6
f	"			1.0	90	100:0
g	"			2.0	89	97:3
h	"			1.5	80	94:6
i	 (R=4-ClC_6H_4)			2.5	85	100:0
j	"			1.5	87	100:0
k	"			2.0	84	97:3
l	 (R=4-MeC_6H_4)			1.5	88	100:0
m	"			1.0	90	95:5

a. All products were characterized by ^1H NMR, ^{13}C NMR, IR and mass spectroscopy.

b. Isolated and unoptimized yields.

Table 2. $In(OTf)_3$-catalyzed *C*-arylation of aziridines with unactivated arenes

entry	aziridine	arene	product[a]	time (h)	yield[b] (%)	ratio[c] (3:4)
a.				4.5	75	100:0
b.	"			6.0	70	100:0
c.	"			4.0	78	100:0
d.	"			3.5	84	97:3
e.	"			4.0	87	95:5
f.	"			5.0	85	96:4
g.	"			6.0	75	95:5
h.	"			5.5	78	70:30
i.	"			5.0	80	80:20
j.	"			6.0	70	90:10
k	"			6.5	68	70:30

a. All products were characterized by ^1H NMR, ^{13}C NMR, IR and mass spectroscopy; b. Isolated and unoptimized yields; c. Ratio of products resulting from internal attack vs terminal attack.

metal triflates were used as catalysts. Similar yields and selectivity were also obtained with 5% $Sc(OTf)_3$ or 10%$Yb(OTf)_3$ under the same reaction conditions. However, in the absence of catalyst, the reaction did not yield any product, even at reflux temperature. The lowering of the reaction temperature was detrimental to the efficiency of this procedure. The scope of indium triflate-catalyzed *C*-arylation of aziridines was initially investigated with respect to the activated aromatics illustrated in Table 1. Indium triflate was found to be the best catalyst for the regioselective ring opening of aziridines with activated arenes, and surprisingly, the only catalyst effective for the *C*-arylation of unactivated aromatics (Table 2), albeit requiring a higher catalyst loading (10 mol%) and longer reaction times (8–10 h). Finally, the catalyst was recovered from the aqueous layer and reused in subsequent reactions without decrease in activity.

In summary, we have found that $In(OTf)_3$ is a new and highly efficient Lewis acid for the regioselective ring opening of aziridines with arenes. In addition to its efficiency, simplicity, and milder reaction conditions, this method provides excellent yields of products with high regioselectivity.

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12. *Experimental procedure*: A mixture of *N*-tosyl aziridine (5 mmol), arene (5 mmol) and $In(OTf)_3$ or $Sc(OTf)_3$ (5 mol%) in dichloromethane (15 mL) was stirred at ambient temperature for an appropriate time (Table 1). After complete conversion, as indicated by TLC, the reaction mixture was diluted with water (10 mL) and extracted with dichloromethane (2×15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated in vacuo and the resulting product was purified by column chromatography on silica gel (Merck, 100–200 mesh, ethyl acetate–hexane, 1:9) to afford pure β-aryl amine.

Spectral data for product **3e** (Table 1): ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.40 (s, 3H), 3.50 (dd, 2H, $J=6.7$, 7.5 Hz), 3.78 (s, 3H), 3.85 (s, 3H), 4.38 (t, 1H, $J=6.7$ Hz), 4. 50 (t, 1H, $J=7.5$ Hz), 6.63 (d, 1H, $J=0.8$ Hz), 6.98 (d, 1H, $J=0.8$ Hz), 7.15–7.28 (m, 7H), 7.68 (d, 2H, $J=8.0$ Hz); FAB MS: 491, 489 $M,^+$ 468, 439, 411, 391, 339, 307, 274, 221, 184, 154, 136, 121, 109, 91, 81, 69; IR (KBr): 3340, 2928, 2850, 1580, 1150, 1080, 833 cm^{-1}.

Product **3f** (Table 1): ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.42 (s, 3H), 3.45 (dd, 2H, $J=6.8$, 7.5 Hz), 3.58 (s, 3H), 3. 80 (s, 6H), 4.38 (t, 1H, $J=7.5$ Hz), 4. 45 (t, 1H, $J=6.8$ Hz), 6.50 (d, 1H, $J=8.0$ Hz), 6.65 (d, 1H, $J=8.0$ Hz), 7.10 (d, 2H, $J=8.0$ Hz), 7.18–7.30 (m, 5H), 7.65 (d, 2H, $J=8.0$ Hz); FAB MS: 441 M^+, 274, 257, 154, 136, 121, 109, 91, 81, 69, 55; IR (KBr): 3345, 2920, 2853, 1587, 1150, 1090, 835 cm^{-1}.

Product **3i** (Table 1): ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.40 (s, 3H), 3.40 (dd, 2H, $J=6.8$, 7.5 Hz), 3.75 (s, 3H), 3. 80 (s, 3H), 3.98 (t, 1H, $J=7.5$ Hz), 4. 58 (t, 1H, $J=6.8$ Hz), 6.58 (d, 1H, $J=0.9$ Hz), 6.60 (dd, 1H, $J=0.9$, 8.0 Hz), 6.70 (d, 1H, $J=8.0$ Hz), 7.05 (d, 2H, $J=8.0$ Hz), 7.25 (d, 2H, $J=7.8$ Hz), 7.30 (d, 2H, $J=7.8$ Hz), 7.65 (d, 2H, $J=8.0$ Hz); FAB MS: 445 M^+, 274, 261, 203, 184, 154, 145, 133, 105, 91, 81, 69; IR (KBr): 3350, 2925, 2847, 1595, 1145, 1090, 840 cm^{-1}.