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A facile C-arylation of *N*-tosyl aziridines via Ag(I) catalysis

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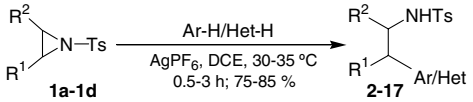
Abstract—*N*-Tosyl aziridines react with a variety of arenes and heteroarenes in the presence of 1–2% of silver hexafluorophosphate at room temperature to afford the corresponding β-aryl amine derivatives in excellent yields and with high regioselectivity.

Aziridines are versatile building blocks, widely used for the synthesis of many nitrogen-containing natural products and biologically interesting molecules.[1] A diverse range of organic architecture can be generated by the regioselective ring opening reaction of aziridines with various nucleophiles.[2] The latter include organo-Li/Mg/Cu reagents,[3] silyl nucleophiles,[4] Wittig reagents,[5] amines,[6] metal halides,[7] hydroxyl compounds,[8] boronic acids,[9] carbonyl compounds,[10a] nitriles[10b] and alkenes.[11] In contrast to the above, there are only a few reports on the regioselective ring opening of aziridines by an arene nucleophile, which usually employs Lewis acid mediation. The Lewis acids used include stoichiometric $AlCl_3$ (1 equiv),[12] $BF_3{\cdot}Et_2O$ (3 equiv)[13] and catalytic $In(OTf)_3$ (5–10 mol %).[14]

Our recent interest in late transition metal catalyzed aromatic alkylation reactions[15] prompted us to investigate the reactivity of *N*-tosyl aziridines with arenes. This endeavour led to the novel finding that under ambient conditions, only 1–2% of $AgPF_6$ promoted a highly regioselective ring opening of *N*-tosyl aziridines with a variety of arenes and heteroarenes leading to the corresponding β-aryl amine derivatives in excellent yields (Scheme 1). We believe that such reactivity might originate from the well-known binding ability of Ag(I) towards arenes and aziridines.[16,17]

Reaction of *N*-tosyl-2-phenyl aziridine **1a** with anisole as the arene as well as the solvent, and $AgPF_6$ (1 mol %) as catalyst at room temperature did not proceed to completion even after 3 h (vide TLC), and work-up afforded a



1a: R^1= C_6H_5, R^2= H; **1b**: R^1= 4-ClC_6H_4, R^2= H;
1c: R^1= 4-MeC_6H_4, R^2= H; **1d**: R^1= R^2= C_6H_5

Scheme 1. C-Arylation of *N*-tosyl aziridines.

50% yield of *N*-tosyl-2-phenyl-2-(4-methoxyphenyl)-ethylamine **2**. The reaction rate remained unaltered even at higher temperature. The product yield also failed to improve when the reaction was conducted with 2 equiv of anisole and dichloromethane as solvent. However, in dichloroethane (DCE) as solvent, the yield of **2** increased to 65% after 3 h. Gratifyingly, by employing 2 mol % of the catalyst, the reaction proceeded to completion within 1 h and amine **2** was isolated in 80% yield. Screening of other solvents demonstrated the superiority of DCE (Table 1). Notably the catalytic activity of $AgPF_6$ was completely inhibited in water, ethanol and tetrahydrofuran as solvents. Amongst the other silver

Table 1. C-Arylation of *N*-tosyl aziridine **1a**: solvent screening[a]

Entry	Solvent	Yield of **2** (%)
1	DCE	80
2	DCM	65
3	$MeNO_2$	60
4	MeCN	15
5	EtOH	Nil
6	H_2O	Nil
7	THF	Nil

[a] Reagents and conditions: aziridine **1a** (1 mmol), anisole (2 mmol), $AgPF_6$ (2 mol %), time (1 h).

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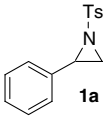
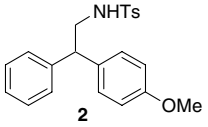
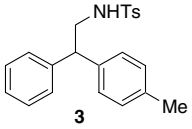
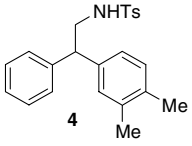
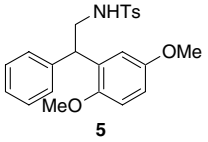
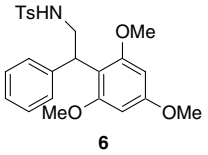
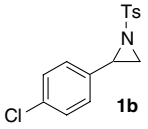
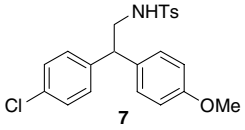
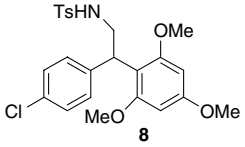
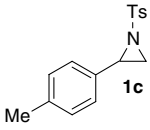
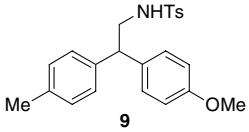
Table 2. C-Arylation of *N*-tosyl aziridine **1a**: catalyst screening[a]

Entry	Silver salt	Yield of **2** (%)
1	$AgPF_6$	80
2	$AgBF_4$	75
3	AgOAc	Trace
4	$AgNO_3$	Nil
5	Ag_2SO_4	Nil
6	Ag_3PO_4	Nil

[a] Reagents and conditions: aziridine **1a** (1 mmol), anisole (2 mmol), catalyst (2 mol %), DCE (3 ml), time (1 h).

Table 3. $AgPF_6$ catalyzed regioselective ring opening of *N*-tosyl aziridines with arenes as nucleophiles[a]

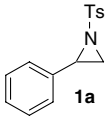
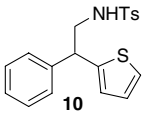
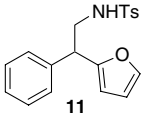
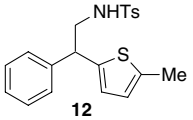
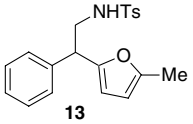
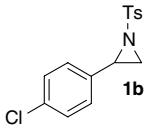
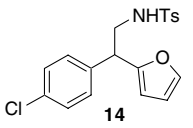
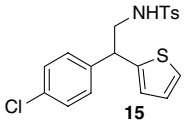
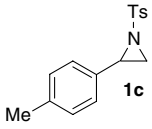
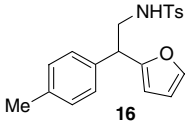
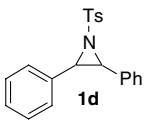
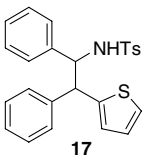
Entry	Aziridine	Product	Time (h)	Yield (%)
1	 **1a**	 **2**	1	80
2	**1a**	 **3**	3	75
3	**1a**	 **4**	1.5	78
4	**1a**	 **5**	1	82
5	**1a**	 **6**	0.5	85
6	 **1b**	 **7**	1.5	80
7	**1b**	 **8**	1	82
8	 **1c**	 **9**	1	85

[a] Reagents and conditions: aziridine (1 mmol), arene (2 mmol), $AgPF_6$ (2 mol %), DCE (3 ml).

salts screened for their catalytic activity (Table 2), only $AgBF_4$ was promising.

The generality of the reaction was successfully tested under the optimized conditions with *N*-tosyl aziridines **1a**–**1d** and various arenes and heteroarenes as nucleophiles, giving rise to the corresponding β-substituted ethylamines **2**–**17** (Tables 3 and 4).[18] The products were fully characterized by ^1H, ^{13}C, IR, HRMS and by X-ray crystallography (in the case of **6**). The important observations are highlighted below.

Table 4. $AgPF_6$ catalyzed regioselective ring opening of *N*-tosyl aziridines with heteroarenes as nucleophiles[a]

Entry	Aziridine	Product	Time (h)	Yield (%)
1	 **1a**	 **10**	0.5	80
2	**1a**	 **11**	0.5	80
3	**1a**	 **12**	0.5	85
4	**1a**	 **13**	0.5	85
5	 **1b**	 **14**	1	85
6	**1b**	 **15**	1	85
7	 **1c**	 **16**	0.5	85
8	 **1d**	 **17**	3	75

[a] Reagents and conditions: aziridine (1 mmol), heteroarene (2 mmol), $AgPF_6$ (2 mol %), DCE (3 ml).

1. The ring opening of *N*-tosyl aziridines proved to be highly regioselective with exclusive attack of the arene/heteroarene at the benzylic position.
2. The trends in the reactivity of arenes show that for ring-activated arenes, reactions were complete within shorter reaction times, and the product yields were very good. In contrast, benzene and ring-deactivated arenes reacted more slowly giving rise to the desired product in poor yields along with unreacted aziridine.
3. The reactions proceeded with greater facility in the case of furan, and thiophene derivatives as indicated by shorter reaction times, and consistently good yields (Table 4). In all cases, the substitution took place exclusively at the 2-position of the heteroarene.
4. It was further observed that the nature of the substituent on the aromatic ring of the *N*-tosyl aziridine had some effect on the conversion, and the reactivity followed the trend **1c** > **1a** > **1b** > **1d**. In contrast reaction of an aziridine bearing an alkyl substituent, for example, *N*-tosyl-2-hexyl aziridine failed.

In summary, we have presented an efficient method for the preparation of β-aryl ethylamine derivatives from *N*-tosyl aziridines and arenes/heteroarenes using catalytic $AgPF_6$. The very mild conditions, clean TLC profiles, high regioselectivity and operational simplicity are expected to make this reaction attractive to chemists. Efforts are underway to broaden the scope of the arylation to an asymmetric version.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.07.200.

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18. *General procedure*: The procedure given below was followed in all cases. All products showed satisfactory ^1H, ^{13}C NMR, DEPT, IR and HRMS data, which are given in Supplementary data. *Synthesis of N-[2-(4-Methoxyphenyl)-2-phenyl-ethyl]-4-methyl-benzenesulfonamide* (**2**): A mixture *N*-tosyl aziridine **1a** (1 mmol, 273 mg), anisole (2 mmol, 100μl) and $AgPF_6$ (0.02 mmol, 5 mg) in 3 ml of dry dichloroethane were stirred at room temperature. Following completion (vide TLC), the reaction mixture was diluted with water (5 ml) and extracted with dichloroethane (4 × 5 ml). The combined organic layers were dried over anhydrous sodium sulfate, concentrated in vacuo and the resulting product was purified by column chromatography on silica gel (100–200 mesh, ethyl acetate–petroleum ether, 1:10) to afford pure β-aryl ethylamine derivative **2** (305 mg, 80% with respect to **1a**). ^1H NMR (400 MHz, $CDCl_3$): δ 2.46 (s, 3H), 3.46–3.57 (m, 2H), 3.78 (s, 3H), 4.02 (t, 1H, $J = 8$ Hz), 4.29 (t, 1H, $J = 6$ Hz), 6.82 (d, 2H, $J = 8.8$ Hz), 7.01 (d, 2H, $J = 8.4$ Hz), 7.09 (d, 2H, $J = 6.8$ Hz), 7.20–7.33 (m, 5H), 7.74 (d, 2H, $J = 8.4$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$): 21.61, 47.40, 49.70, 55.30, 114.27, 127.09, 127.19, 127.84, 128.88, 128.96, 129.79, 132.63, 136.72, 141.04, 143.58, 158.62; HRMS (ESI) calcd for $C_{22}H_{23}NO_3S$ $[M+Na]^+ = 404.1296$, found 404.1293. IR (KBr): 3283, 2932, 1512, 1324, 1153, 1092, 820 cm^{-1}.