Zirconium tetrachloride mediated regioselective transformation of *N*-tosylaziridines into β-chlorosulfonamides[1]

Biswanath Das*, Maddeboina Krishnaiah and Keetha Laxminarayana

Organic Chemistry Division-I, Indian Institute of Chemical Technology, Hyderabad-500 007, India

Regioselective ring opening of *N*-tosylaziridines has efficiently been carried out with $ZrCl_4$ at room temperature to afford the corresponding β-chlorosulfonamides in high yields within a short reaction time.

Keywords: *N*-tosylaziridine, $ZrCl_4$, β-chlorosulfonamide

Aziridines are important intermediates in organic synthesis.[2] They behave as carbon electrophiles capable of reacting with different nucleophiles.[3] On treatment with suitable metal halides they can be converted into β-chloroamines which are useful precursors for the synthesis of various bioactive compounds.[4] However, the methods involving the ring opening of aziridines with metal halides are limited.[5] Moreover, the metal chlorides, such as $CeCl_3.7H_2O$ and $ZnCl_2$ work under reflux conditions[5a,c] and $InCl_3$ requires longer reaction times.[5b] Thus, an efficient, mild and useful method for the conversion of aziridines into β-chloroamines is required.

Recently, $ZrCl_4$ has been used in various chemical transformations as it possesses an interesting reactivity, is less costly and is less toxic than other reagents.[6] In continuation of our work[7] on the applications of $ZrCl_4$ in synthesis we have recently observed that it can be used for the cleavage of *N*-tosylaziridines to form the corresponding β-chlorosulfonamides. Several *N*-tosylaziridines were treated with $ZrCl_4$ at room temperature to form a series of β-chlorosulfonamides in high yields (Scheme 1, Table 1). The conversion was complete within 30–70 min. *N*-Tosyl aziridines possessing aromatic or aliphatic substituents underwent the conversion smoothly. The presence of an electron-donating or electron withdrawing group on the aromatic ring did not effect the reaction.

The ring opening of *N*-tosylaziridines with $ZrCl_4$ was found to be highly regioselective. *N*-Tosyl-2-aryl aziridines furnished the products by nucleophile attack of the chloride ion at the benzylic position and *N*-tosyl-2-alkyl aziridines formed the products by the attack at the terminal position. The cleavage of bicyclic *N*-tosyl aziridines afforded the corresponding *N*-tosyl-β-chloroamines which possessed a *trans*-configuration. The structures and stereochemistry of the products were established from their analytical and spectroscopic (^1H, ^{13}C NMR and MS) data. In the ^1H NMR spectra of the β-chlorosulfonamides **2a–2h** the proton of the –NH– group appeared as a triplet while in the spectra of **2i–2m** it appeared as a doublet. Thus the regiochemistry of the products was clearly settled. In the cyclic β-chlorosulfonamides **2n–2p** the coupling constants of the ring proton attached to –Cl suggested the *trans*- stereochemistry of the molecules.

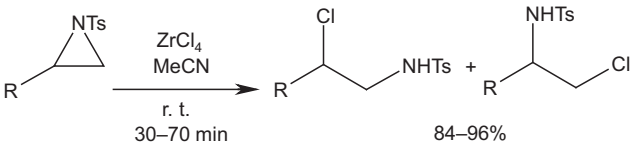
In conclusion, we have developed a simple, mild and suitable method for the preparation of β-chlorosulfonamides by $ZrCl_4$ mediated ring opening of *N*-tosylaziridines at room temperature. The application of a less costly reagent, short reaction times, high yields and good regioselectivity are the notable advantages of the method.

Experimental

General experimental procedure for conversion of N-tosylaziridines into β-chlorosulfonamides

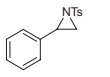
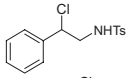
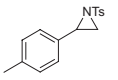
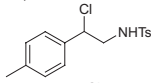
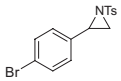
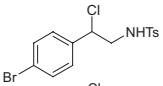
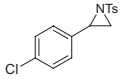
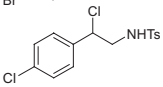
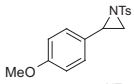
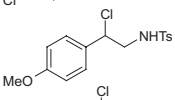
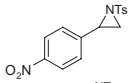
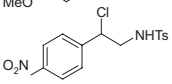
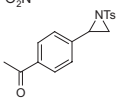
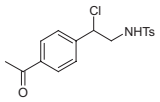
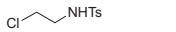
To a solution of an *N*-tosylaziridine (1 mmol) in MeCN (5 ml), $ZrCl_4$ (0.5 mmol) was added. The mixture was stirred at room temperature

* Correspondent. E-mail: biswanathdas@yahoo.com



Scheme 1

Table 1 $ZrCl_4$ mediated ring-opening of *N*-tosylaziridines[a]

Entry	Aziridine **1**	Product **2**	Time/ min	Isolated yield/%[b]
a			30	88
b			40	85
c			40	84
d			40	89
e			40	85
f			40	86
g			50	86
h			35	92
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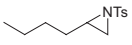
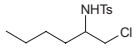
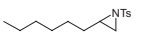
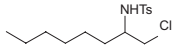
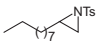
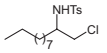
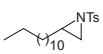
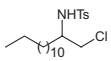
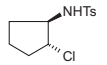
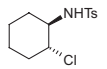
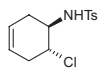
j			70	85(7)
k			70	83(8)
l			60	82(7)
m			60	83(6)
n			50	95
o			50	96
p			60	94

[a]All the products were characterised by spectroscopic (^1H, ^{13}C NMR and MS) and analytical data.
[b]Yield reported in parentheses is for other regioisomer.

and the reaction was monitored by TLC. After completion, the mixture was diluted with EtOAc (10 ml) and subsequently washed with brine (20 ml) and water (2 × 10 ml). The organic layer was separated, dried over Na_2SO_4 and concentrated. The crude product was purified by column chromatography (silica gel, hexane–EtOAc) to afford pure β-chlorosulfonamide.

The spectroscopic and analytical data of the products are given below.

2a: Colourless solid; m.p. 95–96°C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.73 (d, *J* = 8.4 Hz, 2H), 7.43–7.11 (m, 7H), 4.88 (t, *J* = 6.5 Hz, 1H), 4.87 (dd, *J* = 5.9, 7.1 Hz, 1H), 3.36–3.53 (m, 2H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): 143.3, 137.6, 136.4, 129.4, 128.5, 128.4, 126.9, 126.6, 61.4, 50.0, 21.3; FABMS: *m/z* 310, 312 $[M + H]^{+\cdot}$, Anal. Calcd. for $C_{15}H_{16}ClNO_2S$: C, 58.15; H, 5.12; N, 4.52%. Found: C, 58.16; H, 4.98; N, 4.43%.

2b: Colourless solid; m.p. 119–120°C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.72 (d, *J* = 8.0 Hz, 2 H), 7.30 (d, *J* = 8.0 Hz, 2 H), 7.16 (d, *J* = 8.0 Hz 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 4.85 (t, *J* = 7.1 Hz, 1H), 4.81 (t, *J* = 7.1 Hz, 1H), 3.38 (t, *J* = 7.1 Hz, 2H), 2.42 (s, 3H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): 143.8, 137.7, 137.1, 135.4, 129.1, 128.8, 127.2, 126.6, 61.2, 52.5, 21.5, 21.4; FABMS: *m/z* 324, 326 [[M + H]$^{+\cdot}$, Anal. Calcd. for $C_{16}H_{18}ClNO_2S$: C, 59.35; H, 5.56; N, 4.33%. Found: C, 59.36; H, 5.49; N, 4.32%.

2c: Colourless solid; m.p. 98–100°C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.70 (d, *J* = 8.2 Hz, 2H), 7.32–7.16 (m, 6H), 4.86 (dd, *J* = 6.2, 7.8 Hz, 1H), 4.80 (t, *J* = 6.8 Hz,1H), 3.50–3.28 (m, 2H), 2.43 (s, 3H); FABMS: *m/z* 388, 390, 392 [[M + H]$^{+\cdot}$, Anal. Calcd. for $C_{15}H_{15}ClBrNO_2S$: C, 46.33; H, 3.86, N, 3.60%. Found: C, 46.41; H, 3.91, N, 3.63%.

2d: Colourlss solid; m.p. 100–102°C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.71 (d, *J* = 8.4 Hz, 2H), 7.35–7.20 (m, 6H), 4.87 (dd, *J* = 6.2, 7.8 Hz, 1H), 4.81 (t, *J* = 6.8 Hz,1H), 3.50–3.33 (m, 2H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): 143.5, 137.3, 136.2, 134.4, 129.6, 128.7, 128.5, 126.7, 60.5, 50.0, 21.5; FABMS: *m/z* 344, 346, 348 $[M + H]^{+\cdot}$, Anal. Calcd. for $C_{15}H_{15}Cl_2NO_2S$: C, 52.33; H, 4.36; N, 4.07%. Found: C, 52.31, H, 4.32; N, 4.05%.

2e: Colourless solid; m.p. 118–120°C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.62 (d, *J* = 8.1 Hz, 2H), 7.21 (d, *J* = 8.1 Hz, 2H), 7.03 (d, *J* = 8.6 Hz, 2H), 6.76 (d, *J* = 8.6 Hz, 2H), 4.89 (dd, *J* = 5.9, 7.2 Hz, 1H), 4.82 (t, *J* = 6.6 Hz,1H), 3.80 (s, 3H), 3.61–3.36 (m. 2H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): 159.1, 143.2, 136.7, 129.3, 129.1, 127.9, 126.9, 113.7, 60.9, 55.0, 55.2, 21.5; FABMS: *m/z* 340, 342 $[M + H]^{+\cdot}$, Anal. Calcd. for $C_{16}H_{18}ClNO_3S$: C, 56.55; H, 5.30; N, 4.12%. Found: C, 56.52, H, 5.36, N, 4.10%.

2f: Yellow solid; m.p. 112–113°C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.15 (d, *J* = 8.6 Hz 2H), 7.68 (d, *J* = 8.1 Hz, 2H), 7.49 (d, *J* = 8.6 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 5.20 (t, *J* = 6.5 Hz, 1H), 5.00 (t, *J* = 6.7 Hz, 1H), 3.54–3.38 (m, 2H), 2.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): 147.5, 144.6, 143.8, 136.2, 129.6, 128.3, 126.6, 123.7, 59.6, 49.8, 21.4; FABMS: *m/z* 355, 357 $[M + H]^{+\cdot}$, Anal. Calcd. for $C_{15}H_{15}ClN_2O_4S$: C, 50.78; H, 4.23; N, 7.90%. Found: C, 50.75, H, 4.28, N, 7.76%.

2g: Colourless solid; m.p. 120–121°C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.90 (d, *J* = 8.2 Hz, 2H), 7.79 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.0 Hz 2H), 5.01 (t, *J* = 6.5 Hz, 1H), 4.92 (dd, *J* = 6.2, 7.4 Hz, 1H), 3.55–3.30 (m, 2H), 2.41 (s, 3H) 2.32 (s, 3H); FABMS: *m/z* 352, 354 $[M + H]^{+\cdot}$, Anal. Calcd. for $C_{17}H_{18}ClNO_3S$: C, 58.04, H, 5.12, N, 3.98%. Found: C, 58.01, H, 5.15, N, 4.01%.

2h: White solid; m.p. 97–98°C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 4.95 (t, *J* = 6.8 Hz, 1H), 3.55 (t, *J* = 5.8, 5.7 Hz, 2H), 3.31–3.28 (m, 2H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): 144.3, 136.5, 127.4, 128.5, 45.7, 45.3, 21.4; FABMS: *m/z* 234, 236 $[M + H]^{+\cdot}$, Anal. Calcd. for $C_9H_{12}ClNO_2S$: C, 46.25; H, 5.14; N, 6.00%. Found: C, 46.32; H, 5.19; N, 5.89%.

2i: White solid; m.p. 101–102°C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 5.30 (d, *J* = 6.2 Hz, 1H), 3.45–3.30 (m, 2H), 3.15 (m, 1H), 2.40 (s, 3H), 1.49–1.35 (m, 2H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): 143.2, 136.8, 128.4, 127.4, 54.5, 46.7, 30.5, 21.3, 14.2; FABMS: *m/z* 262, 264 $[M + H]^{+\cdot}$, Anal. Calcd. for $C_{11}H_{16}ClNO_2S$: C, 50.48; H, 6.12; N, 5.35%. Found: C, 50.51; H, 6.15; N, 5.32%.

2j: White solid; m.p. 103–104°C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.75 (d, *J* = 8.0 Hz, 2 H), 7.24 (d, *J* = 8.0 Hz, 2 H), 5.32 (d, *J* = 6.0 Hz, 1H), 3.46–3.32 (m, 2 H), 3.17 (m, 1H), 2.40 (s, 3H), 1.52–1.33 (m, 2H), 1.29–1.02 (m, 4 H), 0.82 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz): 144.2, 137.0, 129.8, 126.7, 51.2, 44.3, 31.7, 27.8, 21.9, 21.4, 13.4; FABMS: *m/z* 290, 292 $[M + H]^{+\cdot}$, Anal. Calc. for $C_{13}H_{20}ClNO_2S$: C, 53.89; H, 6.91; N, 4.84%. Found: C, 53.78; H, 6.96; N, 4.95%.

2k: White solid; m.p. 98–99°C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.30 (d, *J* = 8.2 Hz, 2H), 7.81 (d, *J* = 8.2 Hz, 2H), 4.61 (d, *J* = 6.0 Hz, 1H), 3.46–3.30 (m, 2H), 3.12 (m, 1H), 2.41 (s, 3H), 1.39–1.12 (m, 10H), 0.81 (t, *J* = 7.2 Hz, 3H); FABMS: *m/z* 318, 320 $[M + H]^{+\cdot}$, Anal. Calc. for $C_{15}H_{24}ClNO_2S$: C, 56.69; H, 7.56; N, 4.41%. Found: C, 56.68; H, 7.52; N, 4.46%.

2l: Colourless liquid; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.30 (d, *J* = 8.2 Hz, 2H), 7.80 (d, *J* = 8.2 Hz, 2H), 4.65 (d, *J* = 6.0 Hz, 1H), 3.45–3.28 (m, 2H), 3.10 (m, 1H), 2.40 (s, 3H), 1.38–1.10 (m, 16H), 0.83 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): 143.2, 136.8, 128.3, 127.4, 56.4, 47.2, 33.1, 31.2, 30.2, 30.0, 28.2, 27.9. 28.1, 23.2, 21.3, 13.6; FABMS: *m/z* 360, 362 $[M + H]^{+\cdot}$, Anal. Calc. for $C_{18}H_{30}ClNO_2S$: C, 60.08; H, 8.34; N, 3.89%. Found: C, 60.10; H, 8.29; N, 3.85%.

2m: Colourless liquid; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.29 (d, *J* = 8.0 Hz, 2H), 7.80 (d, *J* = 8.0 Hz, 2H), 4.71 (d, *J* = 7.0 Hz, 1H), 3.48–3.30 (m, 2H), 3.15 (m, 1H), 2.40 (s, 3H), 1.35–1.10 (m, 22H), 0.82 (t, *J* = 7.2 Hz, 3H); FABMS: *m/z* 402, 404 $[M + H]^{+\cdot}$, Anal. Calc. For $C_{21}H_{36}ClNO_2S$: C, 62.76; H, 8.97; N, 3.49%. Found: C, 62.79; H, 8.91; N, 3.52%.

2n: White solid; m.p. 86–87°C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.81 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.3 Hz, 2H), 5.92 (d, *J* = 6.0 Hz, 1H), 4.08 (ddd, *J* = 9.8, 9.1, 3.7 Hz, 1H), 3.54 (m, 1H) 2.45 (s, 3H), 2.21–2.02 (m, 2H), 1.88–1.69 (m, 3H), 1.43 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): 144.1, 137.5, 130.0, 127.2, 63.5, 54.4, 34.7, 30.8, 21.9, 21.3; FABMS: *m/z* 274, 276 $[M + H]^{+\cdot}$, Anal. Calc. for $C_{12}H_{16}ClNO_2S$: C, 52.65; H, 5.85; N, 5.12%. Found: C, 52.78; H, 5.81; N, 5.23%.

2o: White solid; m.p. 100–102°C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.80 (d, *J* = 8.04 Hz, 2H), 7.30 (d, *J* = 8.04 Hz, 2H), 4.85 (d, *J* = 6.5 Hz, 1H), 3.71 (ddd, *J* = 9.5, 9.1, 3.8 Hz, 1H), 3.20 (m, 1H), 2.40 (s, 3H), 2.10–2.30 (m, 2H), 1.75–1.55 (m, 3H), 1.40–1.20 (m, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): 143.3, 137.0, 129.4, 127.1, 62.1, 58.6, 34.9, 32.4, 24.3, 23.4, 21.6: FABMS: *m/z* 288, 290 $[M + H]^{+\cdot}$, Anal. Calc. for $C_{13}H_{18}ClNO_2S$: C, 54.26; H, 6.26; N, 4.87%. Found: C, 54.29; H, 6.28; N, 4.71%.

2p: Whilte solid; m.p. 92–93°C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.79 (d, *J* = 8.0 Hz 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 5.75 (d, *J* = 7. 0 Hz, 1H), 5.61–5.38 (m, 2H), 4.10 (ddd, *J* = 9.5, 9.1, 3.9 Hz, 1H), 3.39 (m, 1H), 2.42 (s, 3H), 2.30–1.95 (m, 4H); FABMS: *m/z* 286, 288 $[M + H]^{+\cdot}$, Anal. Calc. For $C_{13}H_{16}ClNO_2S$: C, 54.64; H, 5.60; N, 4.90%. Found: C, 54.68; H, 5.62; N, 4.87%.

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