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Zirconyl nitrate mediated regioselective ring opening of epoxides and aziridines: an easy synthesis of β-nitrato-alcohols and -sulfonamides☆

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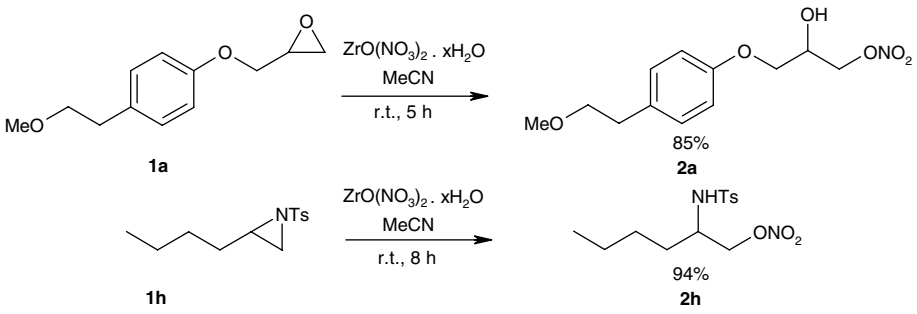
Abstract—Epoxides and aziridines are cleaved efficiently and regioselectively in the presence of zirconyl nitrate at room temperature to afford the corresponding β-nitrato-alcohols and -sulfonamides, respectively, in high yields.

Ring-opening reactions of epoxides and aziridines have extensively been studied with a large number of nucleophiles.[1] However, there are few applications of the nitrate ion as the nucleophile for these reactions.[2] Alkyl nitrates are versatile synthetic intermediates.[3] β-Nitrato-alcohols and -sulfonamides are examples of functionalized alkyl nitrates and could be utilized in organic synthesis. β-Nitrato-alcohols have been previously prepared from epoxides by treatment with concentrated HNO_3,[2a] CAN,[2b] or NO in air.[2c] However, the first method suffered from low yields and strongly acidic conditions, which might effect other functional groups. The reaction of CAN with epoxides was generally carried out at high temperatures (80 °C) and with styrene oxide, the reaction afforded benzaldehyde as the major product. Moreover, the regioselectivity of the opening of some epoxides was poor.[2b] The reaction of NO with epoxides[2c] and aziridines[3] was found to require long reaction times (12–32 h). Thus an improved method for ring opening of both epoxides and aziridines with nitrate ions is still required.

In continuation of our work,[4] on the development of useful synthetic methodologies, we have found that zirconyl nitrate can be utilized efficiently for the ring opening of epoxides and aziridines to form the corresponding β-nitrato-alcohols and -sulfonamides, respectively (Scheme 1).



Scheme 1.

Keywords: Epoxide; Aziridine; Zirconyl nitrate; Ring opening; β-Nitrato-alcohols and -sulfonamides.
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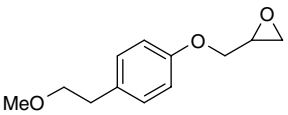
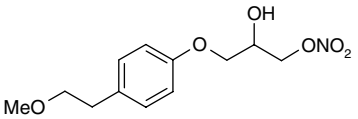
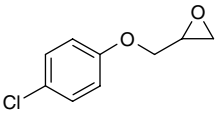
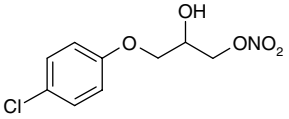
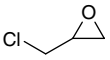
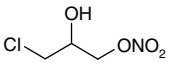
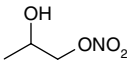
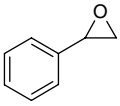
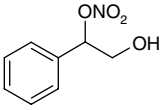
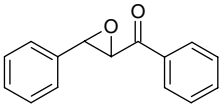
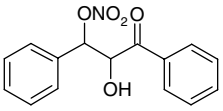
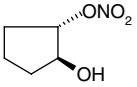
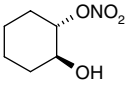
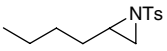
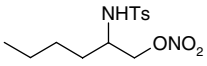
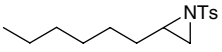
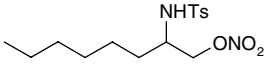
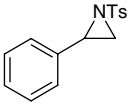
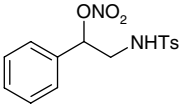
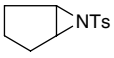
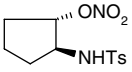
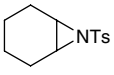
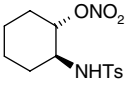
Table 1. Zirconyl nitrate mediated ring opening of epoxides and aziridines[a]

Entry	Epoxide/aziridine **1**	Product **2**	Time (h)	Isolated yield (%)
a			5	85
b			4.5	87
c			1	90
d			1	83
e			0.5	94
f			1	80
g			0.5	90
h			0.5	92
i			8	94
j			8	91
k			1	70[b]
l			4.5	84
m			4.5	83

[a] The structures of the products were established from their spectral (IR, ^{1}H, ^{13}C NMR and MS) and analytical data and by comparison of the values with those reported earlier for the known compounds.[2,3]

[b] The corresponding β-*N*-tosyl amino alcohol (18%) was also produced.

Several epoxides and *N*-tosylaziridines underwent ring cleavage smoothly with zirconyl nitrate in MeCN at room temperature (Table 1).[5] Zirconyl nitrate is inexpensive and nontoxic. The reaction conditions are mild and the experimental procedure is simple. No additional catalyst was required for the reaction. The β-nitrato-alcohols and -sulfonamides were produced in high yields. The ring opening of both epoxides and aziridines occurred with excellent regioselectivity. 2-Alkylepoxides and *N*-tosyl-2-alkylaziridines yielded the products formed by cleavage at the 3-position while 2-arylepoxides and *N*-tosyl-2-arylaziridines afforded the products formed by opening at the benzylic position. Bicyclic epoxides (Table 1, entries g and h) and aziridines (entries l and m) were also cleaved efficiently with zirconyl nitrate. In those cases, the nitrate ion approached from

the axial direction. The ring opening was completely *anti*-stereoselective forming only the *trans*-isomers.[5]

The structures of the products were established from their spectral (IR, ^{1}H and ^{13}C NMR and MS) data[5] and by comparison of the values with those reported for the known compounds.[2,3] In the ^{1}H NMR spectra, the –C*H*$_2$ONO$_2$, >C*H*ONO$_2$ and Ar–C*H*(ONO$_2$)– protons of similar systems related to the products are known to resonate around δ 4.5, 4.8 and 5.8, respectively.[2,3] The structures of the β-nitrato-alcohols and -sulfonamides formed in the present conversion were clearly derived with the help of these reported spectral values.[5] The ^{13}C NMR spectra also supported the proposed structures.[2,3,5] In the ^{1}H NMR spectra of the nitrato-compounds derived from bicyclic epoxides and aziridines, the coupling constants of the ring protons adjacent to the –ONO$_2$ and –OH (or –NHTs) groups clearly suggested their *trans*-configuration.[5] For example, the *J* values of these two protons for **2g** are 10.0, 9.2 and 4.3 Hz and 9.8, 9.2 and 4.3 Hz. The molecular weight of each product was deduced from its FAB mass spectrum. The EI mass spectra for products **2e** and **2i** were also studied. These spectra showed *m*/*z* signals corresponding to [M$^{+\cdot}$–ONO$_2$].[5]

In conclusion, we have developed a simple and efficient method for the preparation of β-nitrato-alcohols and -sulfonamides by the ring opening of epoxides and aziridines using zirconyl nitrate at room temperature. High yields and excellent regio- and stereoselectivity are the advantages of this protocol.

Acknowledgments

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5. General experimental procedure for the synthesis of β-nitrato-alcohols and -sulfonamides: To a solution of epoxide or *N*-tosylaziridine (1 mmol) in MeCN (5 mL) was added zirconyl nitrate (1.2 mmol). The mixture was stirred at room temperature and the reaction was monitored by TLC. After completion, the reaction was quenched with water (10 mL) and the mixture was extracted with EtOAc (3 × 5 mL). The combined organic extracts were dried and concentrated to afford a crude product, which was subjected to column chromatography (silica gel, hexane–EtOAc, 9:1) to obtain pure β-nitrato-alcohols or -sulfonamides.

The spectral (IR, ^{1}H, ^{13}C NMR and MS) and analytical data of some representative products are given below.

Product **2a**: R_f: 0.47 (silica gel, hexane–EtOAc, 7:3); IR (KBr): ν_{max} 3389, 1636, 1512, 1458 cm^{-1}; ^{1}H NMR (CDCl$_3$, 200 MHz): δ 7.12 (2H, d, J = 8.0 Hz), 6.80 (2H, d, J = 8.0 Hz), 4.69–4.51 (2H, m), 4.23 (1H, m), 4.01 (2H, d, J = 5.2 Hz), 3.52 (2H, t, J = 7.0 Hz), 3.31 (3H, s), 2.78 (2H, t, J = 7.0 Hz), 2.02 (1H, br s); ^{13}C NMR (CDCl$_3$, 75 MHz); δ 157.2, 132.5, 130.0, 114.8, 73.8, 73.2, 68.7, 67.2, 58.8, 35.3; FABMS: *m*/*z* 272 [M+H]$^+$·; Anal. Calcd for C$_{12}$H$_{17}$NO$_6$: C, 53.14; H, 6.27; N, 5.17%. Found: C, 53.27; H, 6.32; N, 5.12%.

Product **2e**: R_f: 0.51 (silica gel, hexane–EtOAc, 7:3); IR (KBr): ν_{max} 3410, 1637, 1530, 1453 cm^{-1}; ^{1}H NMR (CDCl$_3$, 200 MHz): δ 7.41–7.28 (5H, m), 5.86 (1H, dd, J = 8.3, 3.8 Hz), 3.91 (1H, dd, J = 12.8, 8.3 Hz), 3.79 (1H, dd, J = 12.8, 3.8 Hz), 2.18 (1H, br s); ^{13}C NMR (CDCl$_3$, 75 MHz); δ 133.6, 129.2, 127.3, 127.0, 85.4, 67.3; FABMS: *m*/*z* 184 [M+H]$^+$·; EIMS: *m*/*z* (%) 121 (M$^{+\cdot}$–ONO$_2$)(12), 104(48); Anal. Calcd for C$_8$H$_9$NO$_4$: C, 52.46; H, 4.92; N, 7.65%. Found: C, 52.63; H, 4.83; N, 7.72%.

Product **2g**: R_f: 0.58 (silica gel, hexane–EtOAc, 7:3); IR (KBr): ν_{max} 3364, 1633, 1439 cm^{-1}; ^{1}H NMR (CDCl$_3$, 200 MHz): δ 4.76 (1H, ddd, J = 10.0, 9.2, 4.3 Hz), 3.61 (1H, ddd, J = 9.8, 9.2, 4.3 Hz), 2.92 (1H, br s), 2.22–2.02 (2H, m), 1.88–1.63 (2H, m), 1.42–1.21 (2H, m); ^{13}C NMR (CDCl$_3$,75 MHz); δ 79.4, 75.2, 31.0, 28.6, 20.8; FABMS: *m*/*z* 148 [M+H]$^+$·; Anal. Calcd for C$_5$H$_9$NO$_4$: C, 40.82; H, 6.12; N, 9.52%. Found: C, 40.85; H, 6.21; N, 9.63%.

Product **2i**: R_f: 0.53 (silica gel, hexane–EtOAc, 7:3); IR (KBr): ν_{max} 3392, 1612, 1483 cm^{-1}; ^{1}H NMR (CDCl$_3$, 200 MHz): δ 7.72 (2H, d, J = 8.0 Hz), 7.31 (2H, d, J = 8.0 Hz), 5.41 (1H, d, J = 8.3 Hz), 4.32 (2H, d, J = 5.3 Hz), 3.46 (1H, m), 2.44 (3H, s), 1.65 (1H, m), 1.44 (1H, m), 1.28 (1H, m), 1.21–1.02 (3H, m), 0.77 (3H, t, J = 7.0 Hz); ^{13}C NMR (CDCl$_3$, 75 MHz); δ 144.1, 137.5, 129.4, 127.0, 76.2, 56.1, 31.8, 26.2, 22.4, 13.8; FABMS: *m*/*z* 317 [M+H]$^+$·; EIMS: *m*/*z* (%) 254 (M$^{+\cdot}$–ONO$_2$)(8), 170(6), 146(4); Anal. Calcd for C$_{13}$H$_{20}$N$_2$O$_5$S: C, 49.37; H, 6.33; N, 8.86%. Found: C, 49.13; H, 6.42; N, 8.71%.

Product **2k**: R_f: 0.52 (silica gel, hexane–EtOAc, 7:3); IR (KBr): ν_{max} 3412, 1638, 1465, 1405 cm^{-1}; ^{1}H NMR (CDCl$_3$, 200 MHz): δ 7.67 (2H, d, J = 8.0 Hz), 7.31–7.18 (7H, m), 5.73 (1H, dd, J = 8.3, 5.3 Hz), 5.21(1H, t, J = 6.8 Hz), 3.32–3.18 (2H, m), 2.38 (3H, s); ^{13}C NMR (CDCl$_3$, 75 MHz); δ 144.2, 136.6, 134.5, 129.4, 129.1, 128.7, 127.1, 126.2, 83.7, 45.4, 21.3; FABMS: *m*/*z* 337 [M+H]$^+$·; Anal. Calcd for C$_{15}$H$_{16}$N$_2$O$_5$S: C, 53.57; H, 4.76; N, 8.33%. Found: C, 53.32; H, 4.83; N, 8.14%.

Product **2m**: R_f: 0.48 (silica gel, hexane–EtOAc, 7:3); IR (KBr): ν_{max} 3378, 1629, 1452, 1401 cm^{-1}; ^{1}H NMR (CDCl$_3$, 200 MHz): δ 7.79 (2H, d, J = 8.0 Hz), 7.31 (2H, d, J = 8.0 Hz), 5.86 (1H, d, J = 6.8 Hz), 5.05 (1H, ddd, J = 9.8, 9.1, 4.5 Hz), 3.56 (1H, m), 2.42 (3H, s), 2.12 (1H, m), 1.88 (1H, m), 1.81–1.62 (2H, m), 1.58–1.47 (2H, m), 1.29–1.21 (2H, m); ^{13}C NMR (CDCl$_3$, 75 MHz); δ 144.0, 137.2, 129.5, 127.1, 83.0, 53.6, 32.5, 28.7, 23.6, 23.2, 21.2; FABMS: *m*/*z* 315 [M+H]$^+$·; Anal. Calcd for C$_{13}$H$_{18}$N$_2$O$_5$S: C, 49.68; H, 5.73; N, 8.92%. Found: C, 49.91; H, 5.88; N, 8.70%.