Antimony trichloride: A mild and efficient reagent for chemoselective ring opening of oxiranes

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Received 6 January 2011; accepted (revised) 29 September 2011

Antimony trichloride mediates regioselective, stereoselective and chemoselective ring opening of oxiranes under mild laboratory conditions with semiquantitative yields. A new route to α-acetoxychalcones is also explored.

Keywords: Ring opening, oxiranes, stereoselective, chemoselective, α-acetoxychalcones, antimony trichloride

Epoxides are valuable intermediates in organic synthesis as they serve as illogical electrophile and their nucleophilic cleavage leads to 1,2 difunctionalized systems and also because it usually leads to trans-stereochemistry. Conversion of epoxides to halo-hydrins had been studied extensively with a variety of reagents like magnesium halides, SnCl$_2$·2H$_2$O, TMSCl, alkylammonium halides, thionyl chloride, zirconyl chloride, etc. Chlorohydrins and other halo-hydrins gain importance from the fact that they are intermediates in the synthesis of a vast range of biologically active natural and synthetic products, unnatural amino acids and chiral auxiliaries for asymmetric synthesis. They also find application in the synthesis of homochiral β-blockers. Because of these synthetic utilities, a newer, cheap and accessible method for transformation of epoxides to halo-hydrins is still in demand and a field of active research interest. In continuation of the work on exploring the scope of antimony trichloride (SbCl$_3$) as catalyst and reagent in organic transformation, herein is investigated the ring opening of epoxides with SbCl$_3$ (Scheme I).

Results and Discussions

The reaction of oxiranes with antimony trichloride gave high yield of ring opening products and was found to be regioselective, stereoselective and chemoselective. Reaction of SbCl$_3$ with epoxides derived from chalcones and monoarylloxiranes did proceed smoothly to furnish halo-hydrins as exclusive product. Various solvents such as DCM, DMF, ethylene glycol, ethanol, nitromethane and acetonitrile were investigated for the reaction. Out of these, acetonitrile proved to be the best in terms of both reaction time and yield.

Monoaryl oxiranes on similar treatment furnished products which were formed in accordance with Markownikoffs’ rule, the chlorine being attached to the carbon which could form the most stable carbocation (Table I, entries 6-10).

For aliphatic epoxides, steric effect was dominant and the product of steric control was formed. The chlorine atom attached itself to the least substituted carbon atom. (Table I, entries 10-13) (Ref 2a). In compound 2m both chlorine atoms are attached to the terminal carbons as supported by the $^1$H and $^{13}$C NMR data. A 4H doublet in $^1$H NMR and only two peaks at δ 46.2 and 71.3 confirmed the proposed structure. Had the chlorine not been on the terminal carbon, there would be no peak at about δ 46 in the $^{13}$C NMR spectrum for all the compounds (2k - 2m). Exclusively threo-isomers were obtained from chalcone epoxides$^{b,5}$.

To confirm the regioselectivity and stereoselectivity of the reaction, X-ray crystallographic analysis of 3-chloro-2-hydroxy-1-phenyl-3-p-tolyl-propan-1-one was performed (2b, Table I, entry 2, Figure 1) (Ref 6). The structure revealed that in case of epoxy derivative of chalcones, the chloride ion from SbCl$_3$ attacked the β-carbon from the carbonyl group and the OH group was attached to the α-carbon and was cis to the chlorine atom. As mentioned earlier, epoxides usually undergo ring opening leading to the trans product. Formation of the cis chlorohydrin could be explained by initial complexation of
Scheme I

Table I — Reaction of epoxides with antimony trichloride

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Product</th>
<th>Yield (%)</th>
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<tr>
<td>1</td>
<td>Ph</td>
<td>1a</td>
<td>88</td>
</tr>
<tr>
<td>2</td>
<td>Ph</td>
<td>1b</td>
<td>92</td>
</tr>
<tr>
<td>3</td>
<td>Ph</td>
<td>1c</td>
<td>89</td>
</tr>
<tr>
<td>4</td>
<td>Ph</td>
<td>1d</td>
<td>90</td>
</tr>
<tr>
<td>5</td>
<td>Ph</td>
<td>1e</td>
<td>92</td>
</tr>
<tr>
<td>6</td>
<td>MeO</td>
<td>1f</td>
<td>90</td>
</tr>
<tr>
<td>7</td>
<td>Cl</td>
<td>1g</td>
<td>92</td>
</tr>
<tr>
<td>8</td>
<td>MeO</td>
<td>1h</td>
<td>90</td>
</tr>
</tbody>
</table>

—Contd
SbCl₃ with oxo group and oxygen atom of the epoxide ring. Then nucleophilic attack of chloride in an intramolecular fashion from the same side of the oxygen atom led to only a small dihedral angle between OH and Cl in the resulting chlorohydrin (Scheme I).

¹H NMR spectra of 2b (Table I, entry 2) showed a one proton broad singlet at δ 4.11, a one proton doublet with coupling constant 2.1 Hz at δ 5.24 and a one proton multiplet at δ 5.38-5.42. In D₂O solvent, the peak at δ 4.11 disappeared and the peaks at δ 5.24 and 5.39 appeared as sharp one proton doublets with coupling constant 2.1 Hz which revealed that the peak at δ 4.11 was due to OH proton, the peak at δ 5.24 due to H-C-Cl and the peak at δ 5.39 due to H-C-OH. For all the compounds of the series 2a-f, the H-C-Cl had
coupling constant value of about 2.1 Hz indicating that the compounds had syn orientation of OH and Cl. However, 1,2-diaryloxiranes when subjected to the same reaction condition or even catalytic amount of catalyst, underwent a rearrangement (Scheme II) to produce diaryl acetaldehydes as the sole product. This was formed via 1,2-shift of an aryl group on the electron deficient carbon atom (Table II).

Prior to the determination of X-ray structure, a reaction was performed to confirm the β-attachment of chlorine atom. This provided a route to α-acetoxy chalcones (Table III), an as yet unexplored class of compounds (Scheme III). The aforesaid compounds were formed via acetylation followed by elimination in one pot.

In conclusion antimony trichloride mediates regioselective, stereoselective and chemoselective ring opening of oxiranes under mild laboratory reaction conditions with semiquantitative yields.

**Experimental Section**

**General experimental procedure**

To a solution of an epoxide (1.0 mmol) in 3 mL acetonitrile, SbCl$_3$ (0.5 mmol for Table I, entries 1-5, 1.2 mmol for Table I, entries 6-13, 0.2 mmol for Table II, entries 1-4) was added and stirred at RT for 20 min. The progress of the reaction was monitored by TLC. On completion of reaction, the reaction mixture was quenched with water, extracted with DCM, dried over anhydrous Na$_2$SO$_4$ and the DCM layer concentrated and purified by short column chromatography over silica gel by eluting with 8-25% ethyl acetate-petroleum ether.

**Spectral data**

$^1$H NMR spectra were recorded with a Bruker 300 (300 MHz) spectrometer as solutions in CDCl$_3$. Chemical shifts are expressed in δ (ppm) and are referenced to TMS as an internal standard. All coupling constants are absolute values and are expressed in Hz. The description of the signals include: s = singlet, d = doublet, t = triplet, m = multiplet and dd = doublet of doublet. $^{13}$C NMR spectra were recorded with a Bruker 300 (75 MHz) spectrometer as solutions in CDCl$_3$ with complete proton decoupling.

2a: Off-white solid, m.p. 77°C. $^1$H NMR (300 MHz, CDCl$_3$): δ 4.12 (d, $J = 7.5$ Hz, 1H), 5.25 (d, $J = 2.1$ Hz, 1H), 5.41 (dd, $J = 2.1$, 7.5 Hz, 1H), 7.32-7.45 (m, 3H), 7.51-7.63 (m, 4H), 7.68-7.78 (m, 1H) 7.94 (d, $J = 7.2$ Hz, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 62.8, 75.0, 126.4, 126.9, 127.4, 127.6, 128.1, 129.2, 132.7, 133.5, 198.2.

2b: White solid, m.p. 83°C. $^1$H NMR (300 MHz, CDCl$_3$): δ 2.36 (s, 3H), 4.11 (d, $J = 6.0$ Hz, 1H), 5.24 (d, $J = 2.1$ Hz, 1H), 5.38-5.42 (m, 1H), 7.19 (d, $J = 8.1$ Hz, 2H), 7.44 (d, $J = 8.1$ Hz, 2H), 7.52-7.59 (m, 2H), 7.64-7.71 (m, 1H), 7.91-7.96 (m, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 21.1, 63.8, 76.2, 127.8, 128.6, 129.1, 129.2, 132.7, 133.4, 133.5, 198.7.

2c: Off-white solid, m.p. 91°C. $^1$H NMR (300 MHz, CDCl$_3$): δ 4.14 (d, $J = 6.9$ Hz, 1H), 5.21 (d, $J =...
2.1 Hz, 1H), 5.32-5.42 (m, 1H), 7.36 (d, J = 8.7 Hz, 2H), 7.50 (d, J = 8.7 Hz, 2H), 7.75 (t, J = 7.8 Hz, 2H), 7.65-7.73 (m, 1H), 7.92 (d, J = 7.8 Hz, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 62.9, 75.8, 114.4, 126.2, 128.0, 128.6, 129.1, 130.0, 132.4, 134.4, 134.7, 137.2, 140.6, 144.1, 144.6, 168.5, 190.7.

2d: Off-white solid, m.p. 88°C. $^1$H NMR (300 MHz, CDCl$_3$): δ 3.91 (s, 3H), 4.22 (brs, 1H), 5.26 (d, J = 2.1 Hz, 1H), 5.32-5.40 (m, 1H), 7.02 (dd, J = 2.1, 7.2 Hz, 2H), 7.30-7.41 (m, 3H), 7.54-7.60 (m, 2H), 7.94 (dd, J = 2.1, 6.9 Hz, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 55.7, 64.3, 75.6, 114.4, 126.2, 128.0, 128.8, 131.0, 138.4, 164.5, 197.4.

2k: Pale yellow liquid. $^1$H NMR (300 MHz, CDCl$_3$): δ 2.66 (d, J = 5.1 Hz, 1H), 3.70-3.83 (m, 2H), 4.00-4.10 (m, 2H), 4.18-4.25 (m, 1H), 6.85-7.01 (m, 3H), 7.28-7.39 (m, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 46.4, 69.0, 70.5, 115.1, 122.0, 130.2, 158.2 (Ref 2a).

2l: Pale yellow liquid. $^1$H NMR (300 MHz, CDCl$_3$): δ 2.32 (s, 3H), 2.97 (brs, 1H), 3.78 (dd, J = 5.5, 11.3 Hz, 1H), 4.04-4.10 (m, 2H), 4.21 (dd, J = 5.3, 11.3 Hz, 1H), 4.21 (quintet, J = 5.3 Hz, 1H), 6.84 (d, J = 8.1 Hz, 2H), 7.11 (d, J = 8.1 Hz, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 20.5, 46.0, 68.8, 69.9, 114.5, 130.0, 130.7, 156.1.

2m: Colourless liquid. $^1$H NMR (300 MHz, CDCl$_3$): δ 2.67 (brs, 1H), 3.68 (d, J = 5.1 Hz, 4H), 4.00-4.14 (m, 1H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 71.3, 46.2 (Ref 2a).

4a: Colourless viscous liquid. $^1$H NMR (300 MHz, CDCl$_3$): δ 2.36 (s, 3H), 6.89 (s, 1H), 7.35-7.56 (m, 5H), 7.57-7.68 (m, 3H), 7.86-7.93 (m, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 20.7, 128.4, 128.8, 129.4, 129.5, 130.0, 132.2, 132.5, 136.9, 144.6, 168.5, 190.6.

4b: Colourless viscous liquid. $^1$H NMR (300 MHz, CDCl$_3$): δ 2.34 (s, 3H), 3.89 (s, 3H), 6.81 (s, 1H), 6.97 (d, J = 9.0 Hz, 2H), 7.31-7.42 (m, 3H), 7.55-7.65 (m, 2H), 7.90 (d, J = 9.0 Hz, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 20.7, 55.4, 113.7, 128.0, 128.7, 129.3, 129.6, 130.1, 131.8, 132.3, 144.6, 163.3, 168.4, 189.3.

4c: Colourless viscous liquid. $^1$H NMR (300 MHz, CDCl$_3$): δ 2.36 (s, 3H), 2.40 (s, 3H), 6.89 (s, 1H), 7.23 (d, J = 8.1 Hz, 2H), 7.45-7.56 (m, 5H), 7.84-7.90 (m, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 20.8, 21.6, 128.4, 129.5, 129.7, 130.0, 130.4, 132.4, 137.2, 140.6, 144.1, 168.5, 190.7.

Acknowledgements

The authors gratefully acknowledge the financial and infrastructural support from UGC-CAS and PURSE-DST programme of the Department of Chemistry, Jadavpur University. RK thanks CSIR, New Delhi for award of fellowship.

References

CCDC-787786 (for 3-chloro-2-hydroxy-1-phenyl-3-p-tolylpropan-1-one, Table I, entry 2 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/datarequest/cif.