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Regio and Diastereoselective Oxygen assisted Opening by Monochloroborane-Dimethylsulfide of Epoxides to *anti* Chlorohydrins.

Paolo Bovicelli*, Paolo Lupattelli, Maria Teresa Bersani

Centro C.N.R. di studio per la chimica delle Sostanze Organiche Naturali, Dipartimento di Chimica, Università "La Sapienza", P.le A.Moro, 5- 00174 Roma, Italy.

Enrico Mincione

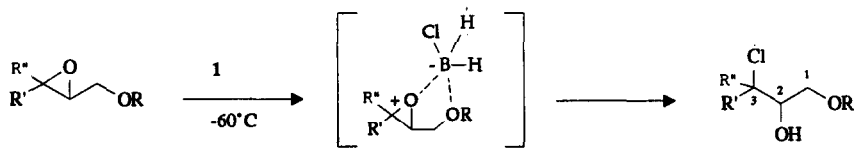
D.A.B.A.C., Università della Tuscia, V.S.Camillo De Lellis, 01100 Viterbo, Italy.

***Abstract.**: The opening reaction of epoxides by monochloroborane-dimethylsulfide* **1** *proceeds by oxygen anchimeric assistance in a regio and diastereoselective manner to give the corresponding anti chlorohydrins.*

In the previous work, we reported that monochloroborane-dimethylsulfide **1** is a useful reagent for the chemoselective conversion of epoxides into chlorohydrins[1].

Here we report that the opening reaction by **1** of α-oxysubstituted epoxides is anchimerically assisted to give the corresponding regio and stereodefined *anti* chlorohydrins.

Scheme 1



2	R=H, R'=Ph, R"=H	
4	R=Bn, R'=Ph, R"=H	
6	R=Ac, R'=Ph, R"=H	
8	R=$SiMe_2$t-Bu, R'=Ph, R"=H	
10	R=Bn, R'=C_3H_7, R"=H	
12	R=Bn, R'=R"=CH_3	

ratio 1,2/1,3 diol

3	> 98:2
5	"
7	"
9	"
11	86:14
13	90:10

As reported in scheme 1, highly regio selective conversions were obtained by the opening of phenyl substituted epoxides **2, 4, 6, 8**[2].

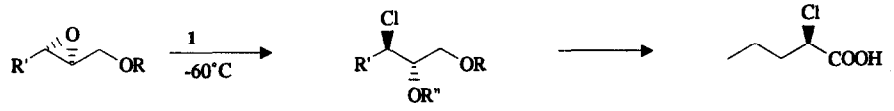
These results agree with the preliminary formation of the intermediate **A**, the effect of the pronounced electrophilicity of chloroborane. The following nucleophilic attack of chlorine on the epoxidic carbons therefore proceeded regioselectively with carbon exo regarding the five membered ring intermediate **A** (scheme 1), to give the regiodefined chlorohydrins.

The stereochemical course of this opening was then investigated.

The previous results[1] agree with an S_N2 'borderline' mechanism with a partial positive charge which develops on the electrophilic epoxide carbon[3]. The chiral α-benzyloxyepoxide **10** (scheme 2) obtained by Sharpless method[4,5] in >96% ee[6], was submitted to ring opening by **1**, to ascertain if racemization occurs in the opening of epoxides to chlorohydrins.

By NMR analysis on the acetate **11a** we observed that the chiral chlorohydrin **11** appeared to be only one diastereoisomer[7]. The oxidation of the corresponding diol **11b** to (2R)-2-chloropentanoic acid **14** confirmed the *anti* configuration of **11**.

Scheme 2



2 R=H, R'=Ph
4 R=Bn, R'=Ph
10 R=Bn, R'=C_3H_7

3 R=R"=H, R'=Ph
3a R=R"=Ac, R'=Ph
5 R=Bn, R'=Ph, R"=H
5a R=Bn, R'=Ph, R"=Ac

11 R=Bn, R'=C_3H_7, R"=H
11a R=Bn, R'=C_3H_7, R"=Ac
11b R=R"=H, R'=C_3H_7

14

When ^{1}H-NMR analysis was performed with chiral shift salts we finally concluded that **11** was formed in ee>96% as the starting epoxide **10.** Consequently, no racemization occurred in the epoxide opening.

Despite the partial positive charge on the benzylic carbon we observed that the benzylic chiral epoxides **2** and **4** were converted to the *anti*-chlorohydrins **3** and **5** respectively, with the same high diastereoselectivity.

Stereo and regiodefined chlorohydrins are useful synthetic intermediates. Polyfunctionalized stereodefined compounds such as **5** appear to be versatile starting material for the construction of biological compounds (heterocycles, polyols etc., work in progress). Moreover, our finding demonstrated that this method also produces α-chloroacids in high ee.

References and Notes

1. Bovicelli,P.; Mincione,E.; Ortaggi,G. *Tetr.Lett.* **1991**, *32*, 3719.
2. The 1,2/1,3 diol ratio in the opening of the following aliphatic epoxides: R'=C_3H_7, R=Ac, MEM, $SiMe_2tBu$, H, was respectively 80:20, 75:25, 70:30, 60:40.
3. Parker,R.E.; Isaac,N.S. *Chem.Rev.* **1959**, *59*, 737.
4. Gao,Y.; Hanson,R.M.; Klunder,J.M.; Ko,S.Y.; Masamuna,H.; Sharpless,K.B. *J.Am.Chem.Soc.* **1987**, *109*, 5765.
5. Bonini, C.; Righi, G.; Sotgiu, G.; *J. Org. Chem.* **1991**, *56*, 6206.
6. Ee >96% indicates that the other isomer was not detectable by NMR analysis.
7. **11a**; ^{1}H-NMR δ[8]:5.15 (1H, ddd, J_1=4Hz, J_2=5.5Hz,J_3=10Hz, C_2-H), 4.54 (2H, s, OCH_2Ph);4.1-4.2 (1H, m, C_3-H), 3.76 (1H, dd, J_1=5.5Hz, J_2=10.8Hz, C_1-Ha), 3.67 (1H, dd, J_1=4Hz, J_2=10.8Hz, C_1-Hb), 2.10 (3H, s, CH_3COO), 1.4-1.8 (4H, m, C_4-H, C_5-H), 0.90 (3H, t, J=7.7Hz, C_6-H). ^{13}C-NMR δ: 170.4, 137.9, 128.5, 127.9, 127.7, 74.6, 73.2, 68.4, 60.3, 35.4, 19.3, 13.2. Enantiomeric purity of **11a** was determined by ^{1}H-NMR analysis using Eu(hfc)$_3$ as chiral shift reagent (ee >96% was found).
   14; ^{1}H-NMR δ: 4.3 (1H, dd, J_1=6Hz, J_2=7.8Hz, C_2-H), 1.95 (2H, m, C_3-H), 1.5 (2H, m, C_4-H), 0.9 (3H, J=7.3Hz, C_5-H). ^{13}C-NMR δ: 175.8, 56.5, 19.0, 13.1. $[\alpha]_D$ +13.7 (MeOH, c=1); reported $[\alpha]_D$ -13.3 for the *S* isomer[9]. **5**; ^{1}H-NMR δ: 7.5-7.3 (10H, m, Ar-H); 4.97 (1H, d, J=7.5Hz, CHCl), 4.68 (2H, s, OCH_2Ph); 4.2 (1H, m, CHOH), 3.74 (1H, dd, J_1=5.5Hz, J_2=10Hz, CHaOBn); 3.66 (1H, dd, J_1=3.8Hz, J_2=10Hz, CH_3OBn), 2.5 (1H, d, J=5Hz, OH). ^{13}C-NMR δ: 138.1, 137.8, 128.8, 128.6, 128.3, 127.9, 73.9, 73.5, 70.5, 62.3. **3a**; ^{1}H-NMR δ: 7.25-7.35 (5H, m, Ar-H), 5.43 (1H, ddd, J_1=3.2Hz, J_2=5.6Hz, J_3=7.7Hz, CHOAc), 5.05 (1H, d, J=7.7Hz, CHCl), 4.4 (1H, dd, J_1=3.2Hz, J_2=12.2Hz, CHaOAc), 4.25 (1H, dd, J_1=5.6Hz, J_2=12.2Hz, CHbOAc). ^{13}C-NMR δ: 170.6, 169.8, 137.0, 129.0, 128.7, 128.0, 73.5, 62.5, 59.8, 29.5, 20.5, 20.3. Enantiomeric purity >96%[10] was determined by ^{1}H-NMR analysis on the acetates **3a** and **5a**, using Eu(hfc)$_3$ as chiral shift reagent.
8. The NMR signals of the chlorohydrins **11a, 5, 3a,** were in accordance with only one diastereoisomer.
9. Gaffield, W.; Galetto, W.G.; *Tetrah.* 1971, *27*, 915.
10. A further confirmation of the anti configuration was obtained when the chlorohydrins **3** and **5** were completely reconverted to the starting epoxides by standing in a $CHCl_3$ or a KOH/MeOH solution.

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