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Regio- and Stereoselective Synthesis of β-Halohydrins from 1,2-Epoxides with Ammonium Halides in the Presence of Metal Salts

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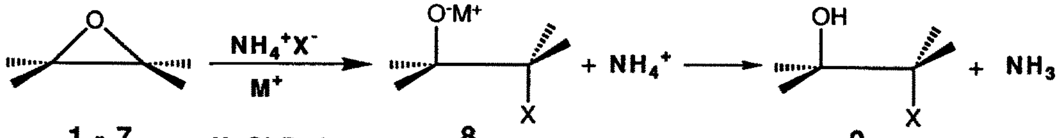
Abstract: *A simple efficient, stereoselective, and regioselective method for the synthesis of β-chlorohydrins, β-bromohydrins, and β-iodohydrins by the direct opening of 1,2-epoxides with the corresponding ammonium halide in acetonitrile, in the presence of metal salts, is described. This new method appears to be of general use and competitive with the other methods previously reported.*

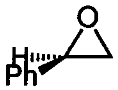
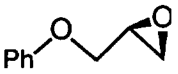
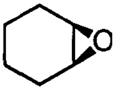
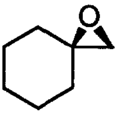
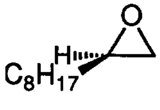
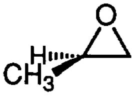
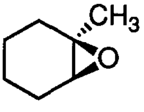
The most common method for the synthesis of 1,2-halohydrins from 1,2-epoxides is their ring opening either with hydrogen halides or with hydrohalogenic acids.[1] However, these procedures suffer from certain limitations when protic acid-sensitive substrates are used. A great effort has been made in the last few years to find new mild procedures for converting epoxides into halohydrins.[1] For example, silyl halides can be added to epoxides to give halohydrins:[2] in these cases, however, the primary reaction products are the *O*-silyl protected derivatives.[2] Other methods require the use of a halogen and triphenylphosphine,[3] or disubstituted boron halides [dialkyl boron halogenides,[4] B-bromobis(dimethylamino)borane[5] and monochloroborane-dimethylsulfide[6]]; other protocols involve the use of complex halide metal salts such as $Pd(PhCN)_2Cl_2$,[7] Li_2NiBr_4,[8] Li_2CuCl_4,[9] and Li_2CuBr_4[10] as sources of halide to trasform epoxides into halohydrins. Recently, it has been found that 1,2-epoxides can be cleanly converted into vicinal halohydrins by means of lithium halides in the presence of an acid with pKa<13 (*e.g.* acetic acid, phenol, nitromethane).[11] However, not all the above-mentioned methodologies[2-11] are suitable to give chloro-, bromo-, and iodohydrins.

We found that common metal salts efficiently catalyze the addition of amines,[12a] azide[12b] and cyanide ions[12c] to 1,2-epoxides in non-protic solvents. In an attempt to explore the capacity of this simple catalysis, we looked for an equivalent methodology for the conversion of 1,2-epoxides into β-halohydrins. Now, we have found that ammonium halides (NH_4Cl, NH_4Br, and NH_4I) react with 1,2-epoxides in acetonitrile in the presence of a metal



1 - 7   X=Cl,Br,I   **8**   **9**

Table. Reaction of epoxides 1-7 with NH_4X in acetonitrile in the presence of metal salts, and under representative acidic conditions ($HX/CHCl_3$) (X=Cl,Br,I).

entry	epoxide[a]	reagents and reaction conditions[b]		reaction time (h) and temperature	α attack[c]	β attack[d]	yield[e]
1		$HCl/CHCl_3$	A	0.25 (r.t.)	>99[f]	<1	99
2		$NH_4Cl/LiClO_4$	B	4 (80°C)	55[f]	45[g]	92
3		$NH_4Cl/Mg(ClO_4)_2$	B	4 (80°C)	75[f]	25[g]	50
4		$NH_4Cl/NaClO_4$	B	4 (80°C)	60[f]	40[g]	50
5		$HBr/ CHCl_3$	A	0.25 (r.t)	>99[h]	<1	97
6		$NH_4Br/LiClO_4$	B	4 (80°C)	45[h]	55[i]	96
7		$HI / CHCl_3$	A	0.25 (r.t)	>99[j]	<1	94
8		$NH_4I/LiClO_4$	B	3 (r.t)	67[j]	33[k]	96
9		NH_4Cl	C	24 (80°C)	no	reaction	
10	**1**	NH_4Br	C	4 (80°C)	no	reaction	
11		NH_4I	C	6 (r.t)	57[j]	43[k]	50
12		$HCl/CHCl_3$	A	0.25 (r.t)	<1	>99[l]	96
13		$NH_4Cl/LiClO_4$	B	24 (65°C)	<1	>99[l]	95
14		$HBr/CHCl_3$	A	0.25 (r.t.)	<1	>99[m]	96
15		$NH_4Br/LiClO_4$	B	16 (65°C)	<1	>99[m]	96
16		$NH_4I/LiClO_4$	B	2 (r.t.)	<1	>99[n]	94
17	**2**	NH_4Br	C	16 (65°C)	<1	>99[m]	21
18		NH_4I	C	2 (r.t.)	<1	>99[n]	95
19		$NH(CH_3)_2{\cdot}HCl$	D	24 (65°C)	<1	>99[l]	45[o]
20		$HCl/CHCl_3$	A	0.25 (r.t.)		[p]	99
21		$NH_4Cl/LiClO_4$	B	24 (65°C)		[p]	75
22		$HBr /CHCl_3$	A	0.25 (r.t.)		[q]	98
23	**3**	$NH_4Br/LiClO_4$	B	24 (65°C)		[q]	80
24		$NH_4I/LiClO_4$	B	16 (65°C)		[r]	82
25		NH_4I	C	16 (65°C)	no reaction		
26		$HCl /CHCl_3$	A	0.25 (r.t.)	64[s]	36[t]	99
27		$NH_4Cl/LiClO_4$	B	65 (65°C)	<1	>99[t]	54
28		$HBr/CHCl_3$	A	0.25 (r.t.)	59[u]	41[v]	99
29		$NH_4Br/LiClO_4$	B	46 (65°C)	<1	>99[v]	40
30		$NH_4Br/Mg(ClO_4)_2$	B	28 (65°C)	<1	>99[v]	93
31		$HI/CHCl_3$	A	0.25 (r.t.)	29[w]	71[x]	94
32		$NH_4I/LiClO_4$	B	24 (65°C)	<1	>99[x]	90
33		NH_4Cl	C	65 (65°C)	no	reaction	
34		NH_4Br	C	46 (65°C)	<1	>99[v]	36
35	**4**	NH_4I	C	24 (65°C)	<1	>99[x]	75
36		HCl gas/Et_2O	E	1 (0°C)	23[y]	77[z]	99
37		$HCl /CHCl_3$	A	0.25 (r.t.)	33[y]	67[z]	99
38		$NH_4Cl/ LiClO_4$	B	24 (65°C)	4[y]	96[z]	99
39		$HBr/CHCl_3$	A	15 (r.t.)	33[a']	67[b']	97
40		$NH_4Br/ LiClO_4$	B	24 (65°C)	34[a']	66[b']	90
41		$HI/CHCl_3$	A	0.25 (r.t.)	23[c']	77[d']	98
42	**5**	$NH_4I/LiClO_4$	B	24 (65°C)	12[c']	88[d']	92
43		$NH_4I/LiClO_4$	B	2 (r.t.)	<1	>99[e']	99
44	**6**	NH_4I	C	2 (r.t.)	no	reaction	
45		$HCl /CHCl_3$	A	0.25 (r.t.)	55[f']	45[g']	99
46		$NH_4Cl/LiClO_4$	B	24 (65°C)	8[f']	84[g']	95[h']
47		$HBr /CHCl_3$	A	0.25 (r.t.)	53[i']	35[j']	98[h']
48		$NH_4Br/LiClO_4$	B	24 (65°C)	2[i']	86[j']	94[h']
49	**7**	$NH_4I/LiClO_4$	B	16 (r.t.)	<1	>99[k']	90

[a] All the reactions were carried out on racemic material. [b] Reaction conditions A-E, see Experimental. [c] Attack of the nucleophile on the more substituted oxirane carbon.[d] Attack of the nucleophile on the less substituted oxirane carbon. [e] Yields based on weight, GC analysis and ^{1}H NMR examination of the isolated crude reaction product. [f] Compound **10**, X=Cl, ref. 2b, 6, 9. [g] Compound **11**,X=Cl, ref.2b,6,9. [h] Compound **10**,X=Br, ref. 10. [i] Compound **11**,X=Br, ref. 10. [j] Compound **10**,X=I, ref.11.[k] Compound **11**, X=I, ref.11. [l] Compound **12**, X=Cl, ref.11. [m] Compound **12**,X=Br, ref.11.[n] Compound **12**, X=I, ref.11.[o] The corresponding β-amino alcohol **21** was also present (50%) (see Experimental). [p] Compound **13**, X=Cl, ref.9. [q] Compound **13**, X=Br, ref.10,11.[r] Compound **13**, X=I, ref.11.[s] Compound **14**, X=Cl. [t] Compound **15**, X=Cl.[u] Compound **14**, X=Br.[v] Compound **15**, X=Br. [w] Compound **14**, X=I.[x] Compound **15**, X=I.[y] Compound **16**, X=Cl, ref.9,14. [z] Compound **17**, X=Cl, ref. 9,14. [a'] Compound **16**, X=Br. [b'] Compound **17**, X=Br.[c'] Compound **16**, X=I.[d'] Compound **17**, X=I. [e'] Compound **18**, X=I, ref. 15[f'] Compound **19**, X=Cl, ref.3. [g'] Compound **20**, X=Cl, ref.3. [h'] *2-methylcyclohexanone* is also present: 8% (entry 46), 12 % (entries 47 and 48). [i'] Compound **19**, X=Br, ref.3. [j'] Compound **20**, X=Br, ref.3. [k'] Compound **20**, X=I, ref.3.

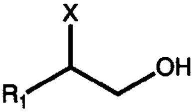
salt to give the corresponding β-halohydrins; in the course of the reaction, free ammonia is also developed. The results obtained with some representative epoxides (**1-7**) are summarized in the Table and compared with the corresponding ones obtained in the reaction of the same epoxides in $CHCl_3$ with hydrohalogenic acid. The yields obtained with this new methodology are quite fair. Reaction times range from 2h at room temperature for the most reactive epoxides (**2** and **6**) to 65 h at 65°C for the least reactive one (**4**). The reactivity order of the three halides is $I^- > Br^- > Cl^-$. $LiClO_4$ turned out to be the most effective catalyst, other metal salts, such as $Mg(ClO_4)_2$ (with the exception of entry 30,Table), and $NaClO_4$ being less effective than $LiClO_4$ (compare entries 2-4, Table) or not effective at all [$Zn(OSO_2CF_3)_2$, not shown in the Table]. When the reactions are carried out under the same experimental conditions without any metal salt being added, the starting epoxides are recovered completely unreacted (entries 9, 10, 25, 33, 44, Table), except in the case of the reaction of the epoxides **1**, **2** and **4** with NH_4I and NH_4Br, where some amounts of the addition products are observed (entries 11, 17, 18, 34, 35, Table), even if the yields are considerably lower than in the corresponding metal salt-catalyzed ones. Attempts to effect the $LiClO_4$-catalyzed addition reactions with quaternary ammonium halides, rather than with the unsubstituted ammonium salts, were unsuccessful. However, when other non-quaternary ammonium halides are used, such as $(CH_3)_2NH{\cdot}HCl$, the reactions can occur (entry 19, Table). The reactions are completely *anti*-stereoselective as shown from the reactions of the epoxides **3** and **7**, in which only the *trans* isomers were detected. A *contra*-Markovnikov-type[13] regioselectivity is generally observed with the only exception of reactions of epoxide **1** where almost equivalent amounts of the two regioisomers are obtained. Interestingly, in many cases, this type of regioselectivity appears to be different and alternative to the one observed in the ring-opening of the same epoxides with hydrohalogenic acids, under classic acidic conditions (see Table).

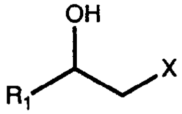
In accordance with a previous hypothesis about the role of the catalyst in the above-mentioned metal salt-catalyzed addition to 1,2-epoxides,[12] the metal ion coordinates initially to the oxirane oxygen, thus favouring the addition of the nucleophile (halide ion) to yield the haloalkoxide **8**. The strong base alkoxide (**8**) reacts with the acidic ammonium ion, thus affording the stable halohydrin **9** and free ammonia. It may be pointed out that when a quaternary ammonium halide is used, the transformation **8**→**9** is not possible and therefore the overall reaction does not occur appreciably.

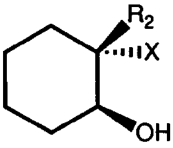
In conclusion, this new procedure for the preparation of 1,2-halohydrins from 1,2-epoxides appears to be of general use for the formation of chlorohydrins, bromohydrins or iodohydrins. The use both of a non protic-solvent and of a mild Lewis acid catalyst makes this methodology suitable to be applied to protic solvent- and acid-sensitive substrates. The reactions are completely *anti*-stereoselective. As for the regioselectivity, the attack of the nucleophile preferentially occurs at the less substituted oxirane carbon.

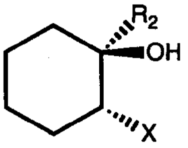
Identification of the β-Halohydrins

The β-halohydrins obtained throughout this study were identified by comparison (^{1}H NMR and GC), when possible, with authentic samples prepared in accordance with literature procedures,[2-11,14,15] and confirmed or established by their ^{1}H NMR spectra (200 MHz, see Experimental). The re-examination of some methods reported in the literature, has allowed us, in two cases,[2b,14] to find some mistakes in the regiochemical assignement of the opening products. In the first case,[2b] the opening reaction of epoxide **1** with Me_3SiCl in the presence of $P(Ph)_3$ at -50°C, repeated in accordance with ref.2b, afforded a 96.5: 3.5 mixture of regioisomers **10** and **11** (X=Cl), contrary to the literature data, where practically only regioisomer **11** (X=Cl) was detected.[2b] In this case the exact regiochemistry of chlorohydrin **11** (X=Cl) has been unequivocally established by its exclusive formation in the $BH_3 \cdot Me_2S$ reduction of the commercially available 2-chloroacetophenone (see Experimental). In the second case,[14] a control reaction carried out on epoxide **5** in Et_2O with gaseous HCl at 0°C, in accordance with ref.14, yielded a 23:77 mixture of chlorohydrins **16** and **17** (X=Cl) (^{1}H NMR),









10 R_1=Ph **11**

R_1=$PhOCH_2$ **12**

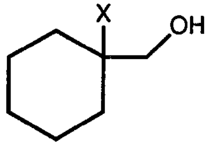
16 R_1=C_8H_{17} **17**

R_1=CH_3 **18**

13 R_2=H

19 R_2=CH_3 **20**

X=Cl, Br, I



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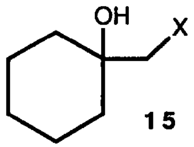

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indicating that the ratio between the regioisomers originally given for this reaction[14] should be reversed (see Experimental).

Experimental

Melting points were detected on a Kofler apparatus and are uncorrected. IR spectra were performed on a Perkin-Elmer 1310 spectrophotometer. ^{1}H NMR spectra were determined with a Bruker AC-200 spectrometer on $CDCl_3$ solutions. GC analyses were performed on a Perkin-Elmer 8420 apparatus (FI detector) with a 30 m x 0.25 mm (i.d.) x 0.25 μm (film thickness) DB-WAX fused silica capillary column (nitrogen flow 2 ml/min).

Reaction Conditions A (Table). A solution of the epoxide (1.0 mmol) in $CHCl_3$ (10 ml) was treated with 36% aqueous HCl (3 ml), or 48% aqueous HBr (3 ml), or with 65% aqueous HI (0.2 ml), then stirred at room temperature for 15 min. Evaporation of the washed (saturated aqueous $NaHCO_3$ and water) organic solution afforded a crude oily residue which was analyzed by GC and ^{1}H NMR.

In the case of epoxide **4**, where the corresponding β-halohydrins **14** and **15** (X=Cl, Br, I) were not previously described, the crude reaction mixture was subjected to preparative TLC with 8:2 petroleum ether/ether as the eluant. Extraction of the two most intense bands (the faster moving band contained **15**, X=Cl, Br, I) afforded the corresponding pure β-halohydrins which, if solids, were recrystallized from pentane. β-Halohydrins **15** (X=Cl,Br,I) may also be obtained practically pure in the reaction of epoxide **4** with NH_4X (X=Cl,Br,I) (see Table), following the procedure described in Reaction Conditions B.

In the case of epoxide **5**, where the corresponding β-bromohydrins and β-iodohydrins **16** and **17** (X=Br,I) were not previously described (for the β-chlorohydrins **16** and **17**, X=Cl, see Reaction Conditions E), the crude reaction mixture was subjected to preparative TLC with 8:1.5:0.5 hexane/AcOEt/diisopropyl ether as the eluant. Extraction of the two most intense bands (the faster moving band contained **17**, X=Br,I) afforded pure β-halohydrins **16** and **17** (X=Br,I) as liquids.

1-Chloro-1-hydroxymethylcyclohexane (14,X=Cl), liquid; IR ν_{max} (neat) 3390, 1440, 1255, 1108, 1040, 875, 780 cm^{-1} ; ^{1}H NMR δ 3.67 (s, 2H, C*H*$_2$OH). Anal. Calcd for $C_7H_{13}ClO$: C, 56.41; H 8.71. Found: C, 56.24; H, 8.90.

1-Chloromethyl-1-cyclohexanol (15, X=Cl), solid, mp 67-68°C; IR ν_{max} (Nujol) 3273, 1267, 1251, 1234, 1147, 1130, 970, 958, 852, 835, 761 cm^{-1} ; ^{1}H NMR δ 3.60 (s, 2H, CH_2Cl). Anal. Calcd for $C_7H_{13}ClO$: C, 56.41; H 8.71. Found: C, 56.24; H, 8.90.

1-Bromo-1-hydroxymethylcyclohexane (14, X=Br), liquid; IR ν_{max} (neat) 3360, 1440, 1245,1115, 1040, 845, 760 cm^{-1} ; ^{1}H NMR δ 3.77 (s, 2H, C*H*$_2$OH). Anal. Calcd for $C_7H_{13}BrO$: C, 43.48; H 6.67. Found: C, 43.75; H, 6.34.

1-Bromomethyl-1-cyclohexanol (15, X=Br), solid, mp 80-81°C; IR ν_{max} (Nujol) 3225, 1430, 1220, 1130, 940, 840, 820 cm^{-1} ; ^{1}H NMR δ 3.53 (s, 2H, CH_2Br). Anal. Calcd for $C_7H_{13}BrO$: C, 43.48; H 6.67. Found: C, 43.54; H, 6.75.

1-Iodo-1-hydroxymethylcyclohexane (**14**, X=I), slightly unstable semisolid; IR ν_{max} (neat) 3375, 1440, 1240, 1110, 1020, 860, 840, 760 cm^{-1} ; ^{1}H NMR δ 3.43 (s, 2H, CH_2I). Anal. Calcd for $C_7H_{13}IO$: C, 34.91; H 5.38. Found: C, 34.51; H, 5.25.

1-Iodomethyl-1-cyclohexanol (**15**, X=I), solid, mp 68-69°C; IR ν_{max} (Nujol) 3296, 1319, 1224, 1136, 1039, 945, 912, 848, 833 cm^{-1} ; ^{1}H NMR δ 3.73 (s, 2H, C*H*$_2$OH). Anal. Calcd for $C_7H_{13}IO$: C, 34.91; H 5.38. Found: C, 34.71; H, 5.09.

2-Bromo-1-decanol (**16**, X=Br), liquid; IR ν_{max} (neat) 3325, 1430, 1060, 1000 cm^{-1} ; ^{1}H NMR δ 4.15 (m, 1H, CHBr), 3.75 (m, 2H, C*H*$_2$OH). Anal. Calcd for $C_{10}H_{21}BrO$: C, 50.60; H 8.79. Found: C, 50.45; H, 8.95.

1-Bromo-2-decanol (**17**, X=Br), liquid; IR ν_{max} (neat) 3345, 1450, 1410, 1210, 1010, 710 cm^{-1} ; ^{1}H NMR δ 3.76 (m, 1H, C*H*OH), 3.53 and 3.39 (2dd, 2H, J= 3.4, 7.1 and 10.5 Hz, CH_2Br). Anal. Calcd for $C_{10}H_{21}BrO$: C, 50.60; H 8.79. Found: C, 50.25; H, 8.54.

2-Iodo-1-decanol (**16**, X=I), liquid; IR ν_{max} (neat) 3350, 1450, 1370, 1010 cm^{-1} ; ^{1}H NMR δ 4.20 (m, 1H, CHI), 3.76 and 3.68 (2dd, 2H, J=4.1, 6.2 and 11.4 Hz, C*H*$_2$OH). Anal. Calcd for $C_{10}H_{21}IO$: C, 42.10; H 7.50. Found: C, 42.40; H, 7.75.

1-Iodo-2-decanol (**17**, X=I), liquid; IR ν_{max} (neat) 3373, 1450, 1400, 1175, 1010 cm^{-1} ; ^{1}H NMR δ 3.50 (m, 1H, C*H*OH), 3.38 and 3.23 (2dd, J= 3.5, 6.8 and 10.1 Hz, CH_2I). Anal. Calcd for $C_{10}H_{21}IO$: C, 42.10; H 7.50. Found: C, 42.34; H, 7.83.

Reaction Conditions B (Table). A solution of the epoxide (5.0 mmol) in acetonitrile (5 ml) was treated with the metal salt (7.5 mmol) and NH_4X (X= Cl,Br,I, 7.5 mmol). The resulting reaction mixture was stirred for the time and at the temperature shown in the Table, then, if necessary, cooled down to r.t, diluted with water and extracted with ether. Evaporation of the washed (water) ether extracts afforded a crude reaction mixture which was analyzed by GC and ^{1}H NMR.

Reaction Conditions C (Table). As in Reaction Conditions B, no metal salt being added.

Reaction Conditions D (Table). A solution of the epoxide **2** (0.75 g, 5 mmol) in acetonitrile (5 ml) was treated with $LiClO_4$ (0.80 g, 7.5 mmol) and $NH(CH_3)_2{\cdot}HCl$ (0.61 g, 7.5 mmol) and the resulting reaction mixture was stirred at 65 °C for 24 h. Usual workup as in Reaction Conditions B, afforded a crude reaction product consisting of a 1:1 mixture (^{1}H NMR and GC) of chlorohydrin **12**[11] and *1-(N,N-dimethylamino)-3-phenoxy-2-propanol* (**21**); acid-base extraction of the crude reaction mixture afforded pure **21** as a liquid: IR ν_{max} (neat) 3350, 1595, 1490, 1450, 1245, 1170, 1040, 760 cm^{-1}; ^{1}H NMR δ 7.31-7.23, and 6.98-6.90 (2m,2H and 3H,respectively, aromatic protons), 4.12-4.01 (m,1H,C*H*OH), 3.96 (d,2H,J=5.2 Hz, OCH_2), 2.54 and 2.37 (2dd,2H,J=3.7, 9.4 and 12.1 Hz,CH_2N), 2.31 [s,6H,$N(CH_3)_2$]. Anal. Calcd for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.77; N, 7.17. Found: C,67.85; H, 8.97; N, 7.15. Oxalate, m.p.110-112°C. Anal.Calcd for $C_{13}H_{18}NO_6$: C, 54.92; H, 6.38; N, 4.92. Found: C, 54.81; H, 6.50; N, 4.77.

Reaction Conditions E (Table). Proceeding as previously described,[14] a solution of the epoxide **5** (0.31 g, 2 mmol) in anhydrous Et_2O (5 ml) was treated at 0 °C with gaseous HCl. After 1h at the same temperature, the usual workup[14] gave a 23:77 mixture of chlorohydrins **16** and **17** (X=Cl) (GC and ^{1}H NMR) which was subjected to preparative TLC with 7:3 petroleum ether/ether as the eluant. Extraction of the two most intense bands (the faster moving band contained **17**, X=Cl) afforded pure chlorohydrins **16** and **17** (X=Cl).

2-Chloro-1-decanol (16, X=Cl), liquid; IR ν_{max} (neat) 3406, 1363, 1222, 1087 cm^{-1} ; ^{1}H NMR δ 4.02 (m, 1H, CHCl), 3.79 and 3.66 (2dd, J=3.8, 7.0 and 12.0 Hz, C*H*$_2$OH). Anal. Calcd for $C_{10}H_{21}ClO$: C, 62.26; H 10.75. Found: C, 62,54; H, 10.65.

1-Chloro-2-decanol (17, X=Cl), liquid; IR ν_{max} (neat) 3385, 1263, 1058, 740 cm^{-1} ; ^{1}H NMR δ 3.79 (m, 1H, C*H*OH), 3.63 and 3.47 (2dd, 2H, J=3.3, 7.1 and 11.0 Hz, CH$_2$Cl) [Ref.14, ^{1}H NMR (CCl$_4$,90 MHz) δ 3.73, 3.55 and 3.41, J=7.2, 3.5, and 11.0 Hz)]. Anal. Calcd for $C_{10}H_{21}ClO$: C, 62.26; H 10.75. Found: C, 62.35; H, 10.54.

The regiochemical result obtained in this reaction indicates that the ratio between **16** and **17** (X=Cl) originally reported for this reaction,[14] should be reversed.

Reaction of Epoxide 1 with Me$_3$SiCl. Proceeding as previously described,[2b] a solution of the epoxide **1** (0.60 g, 5 mmol) in ethanol-free CHCl$_3$ (4 ml) was treated with P(Ph)$_3$ (5.0 mg, 0.02 mmol) and Me$_3$SiCl (0.54 g, 5.0 mmol) at -50°C for 15 min. Evaporation of the washed (water) organic solution yielded a crude reaction product consisting of a 96.5:3.5 mixture of chlorohydrins **10** and **11** (X=Cl)[2b,6,9] (^{1}H NMR and GC) which was subjected to preparative TLC with 7:3 petroleum ether/ether as the eluant. Extraction of the most intense band afforded pure chlorohydrin **10** (X=Cl), as a liquid, whose ^{1}H NMR spectrum was perfectly consistent with the previously reported one.[6]

BH$_3$·Me$_2$S Reduction of 2-Chloroacetophenone. A solution of 2-chloroacetophenone (0.30 g, 2.0 mmol) in anhydrous Et$_2$O (50 ml) was treated under stirring at room temperature with 10 M BH$_3$·Me$_2$S (0.6 ml). After 2 h stirring at the same temperature, the reaction mixture was cooled down to 0°C and treated with MeOH (5 ml). Evaporation of the organic solution afforded pure *2-chloro-1-phenyl-1-ethanol* (**11**) (X=Cl),[2b,6,9] as a liquid; IR ν_{max} (neat) 3350, 1450, 1200, 1060, 760, 720, 695 cm^{-1}; ^{1}H NMR δ 7.39-7.32 (m,5H, aromatic protons), 4.89 (dd, 1H, J=3.54, 8.65 Hz, C*H*OH), 3.73 and 3.63 (2dd, 2H, J=3.9, 8.6 and 11.0 Hz, CH$_2$Cl). Anal.Calcd for C_8H_9ClO: C, 61.31; H, 5.80. Found: C, 61.54; H, 5.90.

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