(Salen)chromium Complex Mediated Asymmetric Ring Opening of *meso*- and Racemic Epoxides with Different Fluoride Sources

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Abstract: The asymmetric ring opening of five *meso*- and three racemic epoxides with different fluorinating reagents in the presence of stoichiometric or slightly sub-stoichiometric amounts of Jacobsen's enantiopure (salen)chromium chloride complex **A** gave the corresponding optically active vicinal fluorohydrins. Silver fluoride was used as one of the fluoride sources either in the presence of $Bu_4N^+H_2F_3^-$ in diethyl ether or in acetonitrile. The latter reactions starting from cyclohexene oxide (**1**) showed maximum 72% ee in the formed fluorohydrin **2** isolated in 90% yield. From other *meso*-epoxides such as cyclopentene oxide and cycloheptene oxide the corresponding fluorohydrins were isolated in 80% and 82% yield with 65% and 62% ee, respectively. In case of ring opening under similar conditions of the racemic styrene oxide or phenyl glycidyl ether 83% and 75% of the fluorohydrins with fluorine in the primary position were isolated with 74% ee and 65% ee, respectively. Tetrahydronaphthalene oxide yielded a 2:1 mixture of *trans*- (23% ee) and *cis*-2-fluoro-3,4-benzocyclohexenol (2% ee) suggesting competing S_N2 and S_N1 type ring openings. Other epoxides such as cyclooctene oxide, *cis*-stilbene oxide and α-methylstyrene oxide did not react or gave the fluorohydrins with very small enantiomeric excess.

Keywords: catalysis; enantioselectivity; epoxide ring opening; fluorohydrins; transition metals.

Introduction

During the past years both the academic and the economic interest in fluorinated compounds has steadily grown because of their unique properties.[1] Most importantly, a single fluorine substituent does not change the steric demand of a molecule but, on the other hand, it can modify the electronic properties such as acidity of neighboring groups or the dipole moment fairly dramatically. This is particularly important for tuning of the biological activity of pharmaceuticals or agrochemicals.[2]

In this respect enantioselective syntheses are of particular interest. Recently, asymmetric syntheses of fluorinated compounds have been reviewed.[3] There are many different methods to construct optically active fluorinated molecules from fluorinated building blocks by asymmetric carbon-carbon bond formations, deracemizations of fluorinated compounds or substitution of halogens, oxygen or nitrogen functions with fluoride in compounds which are already optically active. Moreover, there are two methods for the electrophilic asymmetric introduction of fluorine into a molecule. The electrophilic fluorination of the α-position in carbonyl compounds using (i) Differding's *N*-fluorocamphorsultam and analogues,[4] or *N*-fluoro compounds derived from *Cinchona* alkaloids,[5] and (ii) a catalytic enantioselective electrophilic fluorination of β-ketoesters containing a tertiary carbon center using Seebach-type enantiopure titanium TADDOLate complexes and selectfluor® as the source of positive fluorine.[6]

In contrast, there was only one example of an enantioselective nucleophilic fluorination, namely a kinetic resolution (maximum 16% ee) during fluorodehydroxylation of silyl ethers using an (*S*)-proline-based analogue of DAST,[7] when we recently described the enantioselective introduction of fluoride into symmetric or racemic epoxides with potassium hydrogen difluoride in the presence of equimolar amount of Jacobsen's enantiopure (salen)chromium chloride complex **A.** This complex has successfully been applied as a pre-catalyst in asymmetric epoxide ring opening with azide previously.[8] For the synthesis of optically active fluorohydrins, however, stoichiometric or slightly sub-stoichiometric amounts of the enantiopure Lewis acid **A** have been necessary to effect moderate enantioselectivity. In all cases the formation of the corresponding chlorohydrins was observed as a side reaction. For example, an 89:11 mixture of (*R*,*R*)-(−)-2-fluorocyclohexanol (**2**) (55% ee) and (*R*,*R*)-(−)-2-chlorocyclohexanol (**3**) (20% ee) was formed from cyclohexene oxide (**1**) and KHF_2 using 100 mol % of (*S*,*S*)-(+)-(salen)chromium chloride. With 10 mol % of this Lewis acid only 11% ee was found in the fluorohydrin **2**.[9]

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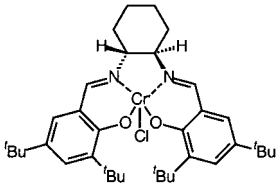
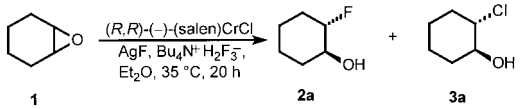
Now we present further attempts to improve the selectivity and the chemical yield of epoxide ring opening with fluorinating reagents mediated by the enantiopure Lewis acid **A**. Furthermore, we tried to lower the necessary quantity of **A** well below stoichiometric amount.

Results and Discussion

Ring opening of epoxides with different fluoride sources proceeds diastereoselectively in an *anti*-fashion. The regiochemistry of ring opening can be directed by the used fluorinating reagent. With the comparably acidic HF itself or Olah's reagent (Py × 9 HF), fluorohydrins with the fluorine substituent in the position which is better stabilized in the carbocationic intermediate are formed following an S_N1 like pathway, while with more nucleophilic reagents such as trialkylamine hydrogen fluorides or potassium hydrogen difluoride the regioisomers bearing the fluorine substituent in the less hindered position are formed preferably according to an S_N2 like mechanism.[9,10] Until recently, besides our mentioned method,[9] syntheses of optically active fluorohydrins have been restricted to the ring opening of enantiopure epoxides with different achiral fluorinating reagents,[11] or deracemization using classical or enzymatic processes,[12] or asymmetric reductions of fluorinated carbonyl compounds.[13]



A



1 **2a** **3a**

88% cv 59% yield (65% ee)

Scheme 1.

Now we have combined the enantiopure Lewis acid **A** with different sources of fluoride equivalents for the asymmetric ring opening of cyclohexene oxide (**1**) (Tables 1 and 2) and other *meso*- and racemic epoxides (Table 3) in order to overcome the drawbacks[9] of KHF_2 as the source of fluoride ion.

Ring opening of **1** with Olah's reagent (Table 1, entry 1) or triethylamine tris(hydrogen fluoride) ($Et_3N \times 3$ HF)[14] (entry 2) in diethyl ether in the presence of 20 mol % of (*R*,*R*)-(−)-(salen)chromium chloride **A**, however, gave mixtures of (*S*,*S*)-(+)-2-fluorocyclohexanol (**2**) and (*S*,*S*)-2-chlorocyclohexanol (**3**) with no or very low enantiomeric excesses. Also tetrabutylammonium dihydrogen trifluoride ($Bu_4N^+H_2F_3^-$) in dichloroethane, which already has been used for ring opening of epoxides without catalysts earlier,[15] gave **2** with low ee in a mixture with **3** (entry 3). The enantioselectivity was higher (60% ee) with 20 mol % of **A** in diethyl ether as the solvent at low conversion (entry 4). However, this reaction is quite slow and the Lewis acid **A** is not stable under these reaction conditions giving rise for the formation of significant quantity of **3**. At extended reaction time, more **2** is formed, but, at least partially, non-catalytically. Consequently the ee dropped to 41% after 50 hours of reaction time (entry 5). Obviously, chloride is split off from **A** and opens epoxide **1** giving **3** first under catalytic effect of remaining **A**, but later in a non-catalytic way. This could explain the low enantioselectivity observed in **3** (9% ee). Using 100 mol % of **A** (entry 6) only 10% of **2** (57% ee), but 65% of **3** were formed. In a similar stoichiometric reaction of **1** with **A** in

Table 1. Ring opening of cyclohexene oxide (**1**) with different fluorinating reagents in the presence of (*R*,*R*)-(−)-(salen)chromium chloride (**A**).

Entry	A [mol %]	Solvent	Temperature [°C]	Time [h]	Fluoride Source	Ratio (GC)[a]		ee **2**/**3**[b] [%]
						2 [%]	**3** [%]	
1	20	Et_2O	−78 → +20	75	Py × 9 HF	40	30[c]	0/7
2	20	Et_2O	0 → +20	85	$Et_3N \times 3$ HF	5	20[c]	10/20
3	20	$C_2H_4Cl_2$	0 → +20	90	$Bu_4N^+H_2F_3^-$	26	5	6/n.d.
4	20	Et_2O	−20 → +20	20	$Bu_4N^+H_2F_3^-$	4	21	60/9
5	20	Et_2O	0 → +20	50	$Bu_4N^+H_2F_3^-$	16	11	41/n.d.
6	100	Et_2O	35	35	$Bu_4N^+H_2F_3^-$	10	65	57/n.d.
7	100	Et_2O	35	20	AgF	0	100	–/0
8	20	Et_2O	20	115	AgF (20 mol %) $Et_3N \times 3$ HF[d]	19	23[c]	43/3

[a] Portion of the product mixture (GC) besides starting material **1**.
[b] Determined by GC using a chiral β-cyclodextrin phase.
[c] Formation of higher molecular weight products (cf. Ref.[9]) was observed.
[d] 130 mol %.

Table 2. Ring opening of cyclohexene oxide (**1**) with $Bu_4N^+H_2F_3^-$ in the presence of (*R*,*R*)-(−)-(salen)chromium chloride (**A**) and AgF.

Entry	A [mol %]	AgF [mol %]	$Bu_4N^+H_2F_3^-$ [mol %]	Solvent	Temp. [°C]	Time [h]	Ratio (GC)[a]		ee [%][b] of **2**
							2 [%]	**3** [%]	
1	10	10	100	Et_2O	20	40	18	0	68
2	10	10	100	Et_2O	20	140	18	0	68
3	20	20	100	Et_2O	20	140	42	2	67
4	20	20	100	Et_2O	35	20	36	0	66
5	100	100	100	Et_2O	35	20	88[c]	2	65
6	100	50	100	Et_2O	35	20	52	35	65
7	100	100	100	DMF	90	20	55	19	18
8	100	100	100	TBME	70	20	18	70	58
9	20	20	100	CH_2Cl_2	80[d]	20	100	0	4
10	10	100	about 2	Et_2O	35	35	20	0	60
11	100	100	about 2	Et_2O	35	40	88[e]	4	65

[a] The difference to 100% is the remaining epoxide **1**.
[b] Determined by GC using a chiral β-cyclodextrin phase.
[c] 59% isolated yield (based on converted **1**).
[d] Sealed tube.
[e] 61 % isolated yield.

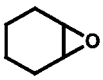
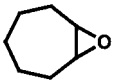
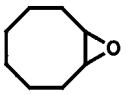
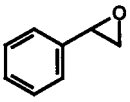
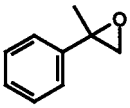
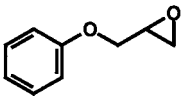
the presence of $TMSN_3$, Jacobsen et al. observed exclusive formation of the chlorohydrin **3** with $<50\%$ ee. Also with other halide sources and different metal salen complexes low enantioselectivity was observed.[8d]

It might be that, in the presence of the used amine HF reagents, chloride is split off from the complex **A** and transferred to the epoxide with low enantioselectivity. A comparative mechanism[17] described for the catalytic asymmetric ring opening of epoxides with azide seems not to operate in this case. Also, a halogen exchange at the metal center seems not to occur. Accordingly, we tried to use AgF for the first time both as the fluoride source in epoxide ring opening and to trap chloride. However, the reaction of **1** in diethyl ether in the presence of 100 mol % of **A** and 100 mol % of AgF gave no fluorohydrin **2** at all. The chlorohydrin **3** was formed exclusively as a racemate (entry 7).

As a consequence of these results, we used next $Et_3N \times 3$ HF as the hydrofluorinating reagent, 20 mol % of **A** as the mediator and added 20 mol % of AgF in order to remove liberated chloride from the reaction mixture by formation of AgCl. However, after 115 hours at 20 °C, a mixture of 55% of **1**, 19% of **2** (43% ee) and 23% of **3** (3% ee) was found (entry 8). Thus, no free chloride seems to be generated under these conditions. For the formation of **2**, the chromium complex **A** probably acts exclusively as a conventional Lewis acid activating the epoxide for ring opening by the respective fluoride equivalent. However, in non of the reactions (except Table 1, entries 1 and 3, but these results are falsified by non-catalytic formation of **2** and succeeding higher molecular weight products), the formed amount of **2** exceeds the amount of used **A**. Obviously, the mediator is not regenerated from an intermediate compound under the reaction conditions and **2** is liberated only during the work-up process. The chloride forming **3** is perhaps cleaved from the mentioned intermediate compound and subsequently opens the epoxide. When catalyst **A** was refluxed in diethyl ether with an equimolar amount of AgF, no AgCl was isolated but some amount of a solid was formed, which could not be isolated. This solid dissolved when equimolar amounts of both **1** and $Bu_4N^+H_2F_3^-$ were added to the mixture and the fluorohydrin **2** was isolated after usual work-up. In a next set of experiments we examined this reaction in more detail (Table 2).

Ring opening of epoxides with $Bu_4N^+H_2F_3^-$ without Lewis acids needed heating to 100 °C or even more for several hours.[15] In the presence of **A**, ring opening occurred at room temperature. However, the amount of formed **2** depends on the quantity of the applied complex **A**. In entries 1 – 4 a two-fold amount of **2** with respect to the used **A** and AgF was formed in the presence of 100 mol % of $Bu_4N^+H_2F_3^-$. Elongation of the reaction time did not increase the yield of **2** and the enantiomeric excess was almost independent from the amount of the Lewis acidic complex **A** and AgF, when used in an 1:1 ratio (entries 1 – 5, Scheme 1). In contrast, when 100 mol % of **A** and only 50 mol % of AgF were used, 35% of the chlorohydrin **3** was formed again (entry 6). Also when other solvents than diethyl ether such as DMF or TBME were used, a significant amount of **3** was found, even in the presence of 100 mol % of AgF related to **A** (entries 7 and 8). Thus, a direct transfer of chloride from **A** to the epoxide seems to occur. In CH_2Cl_2 in a sealed tube at 80 °C in the presence of 20 mol % of both **A** and AgF the fluorohydrin **2** was formed exclusively, but with as low as 4% ee. Thus, the non-catalytic ring opening leading to the racemic product seems to be the major reaction.

Table 3. Results of ring opening of *meso*- and racemic epoxides with silver fluoride (1.5 equivalents) in acetonitrile mediated by (*R,R*)-(−)-(salen)chromium chloride (**A**).

Epoxide	Lewis acid [mol %]	Temperature [°C]	Reaction Time [h]	Fluorohydrin [%, GC]	Yield[a] [%]	Enantiomeric excess [%][b]
	100	50	72	80[c]	80	62
	50	70	50	85[c]	75	44
	100[d]	50	50	100[c]	90	72
	80	70	20	100[c]	85	66
	50	70	20	100[c]	–	n.d.
	10	50	50	traces	–	n.d.
	50	60	20	50[e]	82	65
	100	70	190	no reaction	–	–
	100	90[f]	240	11	n.d.	n.d.
	50	50	5	43[g]	83	74
	50	70	30	28[h]	n.d.	< 1
	50	40	10	50[i]	75	65

[a] Isolated yield, calculated on the basis of consumed epoxide.
[b] Determined by GC using a β-cyclodextrin phase.
[c] ^{1}H and ^{19}F NMR data agree with those published for the racemic compound.[18,19]
[d] (*S,S*)-(+)-**A** was used.
[e] ^{1}H, ^{13}C and ^{19}F NMR data agree with those published for the racemic compound.[20]
[f] Pressure vessel.
[g] (*S*)-(+)-2-Fluoro-1-phenylethanol.[15b]
[h] 2-Fluoro-2-phenylpropanol.
[i] 1-Fluoro-3-phenoxypropan-2-ol (absolute configuration not determined), ^{1}H and ^{19}F NMR spectra agree with those published for the racemic compound.[10e,21]

The results presented in Tables 1 and 2 suggest that neither AgF itself nor $Bu_4N^+H_2F_3^-$ seems to be directly the fluoride sources. In order to investigate whether $Bu_4N^+H_2F_3^-$ only increases the solubility of AgF in diethyl ether because of its phase transfer properties, we employed about 2 mol % of $Bu_4N^+H_2F_3^-$ (entries 10 and 11). Again, double the molar amount of **2** related to **A** was formed in case of application of 10 mol % of **A**, 100 mol % of AgF and 2 – 5 mol % of $Bu_4N^+H_2F_3^-$. This means that also under these conditions the regeneration of the mediator from a probably covalently bound intermediate seems not to occur. Thus, an intermediate formed from one molecule of the complex **A** and two molecules of a compound derived from the epoxide **1** is not excluded. However, even with 100 mol % of each **A** and AgF the reaction was not complete after 40 hours at 35 °C and also a small quantity of **3** was formed under these conditions.

Accordingly, we decided to apply acetonitrile as a more polar solvent in order to (i) increase the solubility of AgF and (ii) to supply the possibility for coordination of a solvent molecule to the complex in order to perhaps facilitate the disjunction of the metal complex from the intermediate.

The reaction of cyclohexene oxide (**1**) and other *meso*- and racemic epoxides with AgF in acetonitrile in the presence of stoichiometric or slightly sub-stoichiometric amount of the (*R,R*)-(−)-(salen)chromium complex **A** provided **2** and other vicinal fluorohydrins with good enantiomeric excess avoiding the formation of chlorohydrins as side products, which were found under the previous conditions or applying KHF_2.[9] The results are summarized in Table 3.

In the most selective experiment, treatment of cyclohexene oxide (**1**) with silver fluoride in acetonitrile with 100 mol % of (*S,S*)-(+)-(salen)chromium chloride at

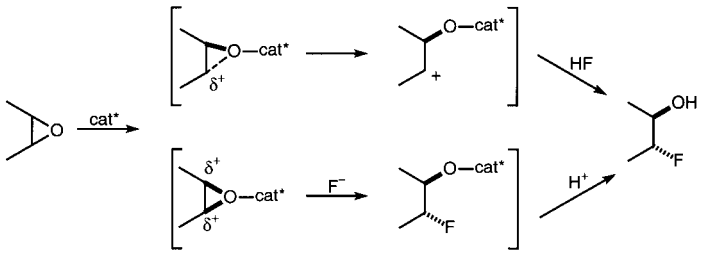
35 °C for 40 hours gave (*R*,*R*)-(−)-2-fluorocyclohexanol in 90% isolated yield with 72% ee. The ring opening of cyclopentene oxide in the presence of 100 mol % of **A** yielded 80% of the corresponding fluorohydrin with 62% ee. The enantiomeric excess dropped to 44% when only 50 mol % of **A** was used. Under these conditions from cycloheptene oxide 82% of the fluorohydrin was isolated showing 65% ee. Cyclooctene oxide did not react, even after 190 hours at 70 °C and from *cis*-stilbene oxide only 11% (GC) of a fluorohydrin was formed after 240 hours at 90 °C in a sealed tube.

A surprising result was found for the reaction of the racemic tetrahydronaphthalene oxide with AgF in the presence of 50 mol % of the (*S*,*S*)-(+)-(salen)complex. Two *cis/trans* isomeric fluorohydrins with benzylic fluorine were isolated in a 2:1 ratio. While the *trans*-compound showed 23% ee, the corresponding *cis*-isomer was formed with only 2% ee (Scheme 2, relative stereochemistry is shown, absolute configuration has not been determined).

This result can be explained in terms of the probable mechanism of the ring opening (Scheme 3). In general, asymmetric ring opening of epoxides mediated by enantiopure Lewis acids is most enantioselective in such cases when the nucleophile is delivered directly from the metal center with opening of the epoxide (S_N2) or by activation of the epoxide by a Lewis acid and concerted attack of an external nucleophile (S_N2-like),[8,16] likewise by a comparative mechanism with participation of a second molecule of the metal complex.[8d,17]

In contrast, in an S_N1-like ring opening due to the long distance of the cationic center from of the chiral metal complex covalently bound to the former epoxide oxygen atom, the steering effect will be less efficient leading to poor enantioselectivity. Thus, the *cis*-isomer should be formed in an S_N1-like process while the *trans*-isomer seems to be formed both by an S_N2-type mechanism and the competing S_N1 reaction. Consequently, the enantiomeric excess is relatively low compared to the related reactions of styrene oxide and phenyl glycidyl ether (see Table 3). In the latter epoxides the terminal position is better accessible to the nucleophile in an S_N2-type process. The corresponding fluorohydrins were isolated in 83% and 75% yield with 74% and 65% ee, respectively (Table 3).

We are continuing our investigations with alternative reaction conditions and other enantiopure Lewis acids, particularly fluorinated ones (cf. Ref.[22]), in order to avoid competition with other nucleophiles and to find conditions for a catalytic ring opening with fluoride equivalents.



Scheme 3.

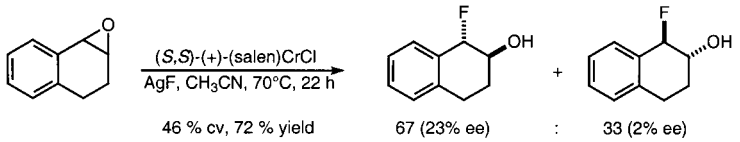
Experimental Section

General Remarks

^{1}H NMR (300.13 MHz), ^{13}C NMR (75.5 MHz), and ^{19}F NMR (282.4 MHz) spectra were recorded in $CDCl_3$ on a Bruker WM 300 apparatus with TMS for ^{1}H NMR, $CDCl_3$ for ^{13}C NMR, and $CFCl_3$ for ^{19}F NMR as internal standards. Mass spectra (70 eV) were obtained by GC/MS using a Varian GC 3400 (quartz capillary column HP1 (0.33 μm) dimensions: 25 m, Ø 0.2 mm). GC was performed on a Hewlett-Packard 5890 II gas chromatograph with HP1 (0.52 μm, 25 m, Ø 0.33 mm, 40–280 °C, heating rate 10 °C/min, N_2 as carrier gas). The enantiomeric excesses were determined by chiral GC (β-cyclodextrin column, Supelco, Beta-Dex® 120 (0.25 μm, 30 m, ∅ 0.25 mm, isothermic, temperature between 80 °C and 110 °C depending on the products, N_2 as carrier gas). (Salen)chromium chloride has been prepared according to Ref.[23] All starting materials and reagents were obtained from Acros (Janssen) or Fluka. The used solvents were purified by distillation.

Ring Opening of Cyclohexene Oxide (1) with Different Hydrofluorinating Reagents in the Presence of the (Salen)chromium Complex A; General Procedure

Under an argon atmosphere the appropriate amount of the chromium complex **A** (cf. Table 1) and cyclohexene oxide (**1**) (147 mg, 1.5 mmol) were dissolved in diethyl ether (5 mL) and stirred for 15 min at room temperature or below this temperature (cf. Table 1). Using a syringe, the respective hydrofluorinating reagent (2 mmol), dissolved in diethyl ether (5 mL) or, in case of $Bu_4N^+H_2F_3^-$, as a commercially available solution (50–55%) in 1,2-dichloroethane, was added. The mixture was stirred at the given temperature for the time given in Table 1. In order to monitor the progress of the reaction samples of the reaction mixture were taken, diluted with



Scheme 2.

diethyl ether (1 mL), neutralized with aqueous ammonia, washed with water, dried with magnesium sulfate, filtered (short column with 2 cm of silica gel, 2 mL of diethyl ether), and analyzed by gas chromatography. After the reaction time given in Table 1, the mixture was poured into a 2 M aqueous ammonia solution (10 mL), the phases were separated and the aqueous phase was extracted with diethyl ether (5 × 10 mL). The combined organic layer was washed with water (2 × 10 mL) and dried with magnesium sulfate. The solvent was evaporated and the crude product was filtered (column with 3 cm of silica gel, diethyl ether) in order to remove traces of the metal complex, and oligomeric material. After removing the solvent the residue was analyzed by GC and chiral GC. The product mixtures were separated by column chromatography (silica gel 70–260 mesh, cyclohexane/ethyl acetate, 5:1). The reaction conditions and enantiomeric excesses are given in Table 1.

Ring Opening of Cyclohexene Oxide (1) with AgF and Tetrabutylammonium Dihydrogen Trifluoride in the Presence of the (Salen)chromium Complex A

According to the general procedure, cyclohexene oxide (**1**; 0.5 or 1 mmol) was treated with AgF and $Bu_4N^+H_2F_3^-$ in the presence of the (salen)chromium complex **A** under the conditions listed in Table 2.

(*S*,*S*)-(+)-2-Fluorocyclohexanol (2): In a typical experiment, the complex (*R*,*R*)-(−)-**A** (632 mg, 1.0 mmol) and AgF (128 mg, 1.0 mmol) was stirred in dry diethyl ether (10 mL) at 35 °C for 3 hours. Then cyclohexene oxide (**1**; 98 mg, 1.0 mmol) was added, and after further 15 min of stirring at this temperature, $Bu_4N^+H_2F_3^-$ (0.7 mL of a 50–55% solution in 1,2-dichloroethane, 1.0 mmol) was added. After 20 hours of refluxing, the reaction was stopped at 88% conversion of **1** and worked up as described above to give (*S*,*S*)-(+)-**2.** Yield: 61 mg (59%, based on 88% conversion); mp 21–22 °C (solidified in the refrigerator, Ref.[18]: mp 22 °C); $[\alpha]_D^{20}$: +12.0 (*c* 1.0, $CHCl_3$, 65% ee, GC) (Lit.[24]: $[\alpha]_D^{20}$: +16.4 (*c* 1.0, $CHCl_3$, >95% ee, GC).

Additionally 2% of the chlorohydrin **3** was detected by GC. The spectroscopic data of **2** agree with those published for the racemic compound.[9a,18,19]

Ring Opening of Epoxides with AgF in the Presence of the (Salen)chromium Complex A in Acetonitrile; General Procedure

Under an argon atmosphere a mixture of the epoxide (1.0 mmol) and the chromium complex (632 mg, 1.0 mmol, or 316 mg, 0.5 mmol) in dry acetonitrile (5 mL) was stirred for 15 min at room temperature, treated with AgF (191 mg, 1.5 mmol, or 96 mg, 0.75 mmol) and heated with stirring at the temperature and for the time given in Table 3. In order to monitor the progress of the reaction a sample of the reaction mixture was taken and worked up. After the reaction time given in Table 3, the mixture was cooled to room temperature, poured into water (25 mL), and extracted with dichloromethane (5 × 10 mL). The combined organic layer was washed with water (2 × 10 mL) and dried with magnesium sulfate. The solvent was evaporated and the crude product was filtered (column with 3 cm of silica gel, cyclohexane/ethyl acetate, 5:1) in order to remove traces of the metal complex, silver salts, and oligomeric material. After removing the solvent the residue was analyzed by GC and chiral GC. Pure fluorohydrins were isolated by column chromatography (silica gel 70–260 mesh, cyclohexane/ethyl acetate, 5:1). Yields and enantiomeric excesses are given in Table 3. Spectroscopic data of the optically active fluorohydrins agree with those published for the racemic compounds (see Table 3).

Ring Opening of Tetrahydronaphthalene Oxide with AgF in the Presence of A in Acetonitrile

According to the protocol given above, tetrahydronaphthalene oxide (146 mg, 1.0 mmol) was reacted with AgF (89 mg, 0.7 mmol) in the presence of (*S*,*S*)-(+)-**A** (316 mg, 0.5 mmol) in acetonitrile (5 mL). After work-up, the epoxide was separated by column chromatography to release a 2:1 mixture of the *cis/trans*-isomeric fluorohydrins. Yield: 54 mg (72%, based on 46% conversion). The isomers were partially separated by column chromatography under the conditions mentioned above.

***trans*-2-Fluoro-3,4-benzocyclohexenol:** ^{1}H NMR: δ = 1.88 (m, 1H, H_{5a}), 2.15 (m, 1H, H_{6a}), 2.50 (br s, 1H, OH), 2.90 (m, 2H, H_{5e} and H_{6e}), 4.13 (m, 1H, H_1), 5.40 (dd, 1H, $^2J_{HF}$ = 53.2 Hz, $^3J_{HH}$ = 7.1 Hz, H_2), 7.12 (m, 1H, arom), 7.26 (m, 2H, arom), 7.46 (m, 1H, arom); ^{13}C NMR: δ = 26.9 (s, C5), 27.7 (d, $^3J_{CF}$ = 7.1 Hz, C6), 70.6 (d, $^2J_{CF}$ = 19.1 Hz, C1), 94.4 (d, $^1J_{CF}$ = 173.1 Hz, C2), 126.3 (s, C7'), 127.8 (d, $^3J_{CF}$ = 7.5 Hz, C8'), 128.3 (s, C6'), 128.5 (d, $^4J_{CF}$ = 3.1 Hz, C5'), 133.0 (d, $^2J_{CF}$ = 18.4 Hz, C3), 136.1 (d, $^3J_{CF}$ = 4.8 Hz, C4); ^{19}F NMR: δ = −178.6 (dd, $^2J_{FH}$ = 53.2 Hz, $^3J_{FH}$ = 13.3 Hz). ^{1}H and ^{19}F NMR data agree with published results.[18]

***cis*-2-Fluoro-3,4-benzocyclohexenol:** ^{1}H NMR: δ = 2.03 (m, 2H, H_{5a} and H_{6a}), 2.85 (m, 1H, H_{5e}), 3.05 (m, 1H, H_{6e}), 4.05 (m, 1H, H_1), 5.45 (dd, 1H, $^2J_{HF}$ = 53.2 Hz, $^3J_{HH}$ = 2.9 Hz), 7.15 (m, 1H, arom), 7.30 (m, 2H, arom), 7.41 (m, 1H, arom); ^{13}C NMR: δ = 26.2 (d, $^3J_{CF}$ = 2.4 Hz, C6), 27.3 (s, C5), 68.9 (d, $^2J_{CF}$ = 18.7 Hz, C1), 90.5 (d, $^1J_{CF}$ = 171.8 Hz, C2), 126.3 (s, C6′), 128.6 (d, $^4J_{CF}$ = 2.9 Hz, C5′), 129.5 (d, $^4J_{CF}$ = 2.2 Hz, C7'), 130.6 (d, $^3J_{CF}$ = 4.5 Hz, C8'), 132.0 (d, $^2J_{CF}$ = 17.8 Hz, C3), 137.1 (d, $^3J_{CF}$ = 4.3 Hz, C4); ^{19}F NMR: δ = −176.5 (dd, $^2J_{FH}$ = 53.0 Hz, $^3J_{FH}$ = 19.1 Hz).

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