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Synthesis and characterization of fluorous (*S*)- and (*R*)-1-phenylethylamines that effect heat facilitated resolution of (±)-2-(8-carboxy-1-naphthylsulfinyl)benzoic acid via diastereomeric salt formation and study of their circular dichroism

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Dedicated to Professor Boris Žemva for his creative work in noble gas chemistry.

Abstract

Perfluoroalkyl- or nonafluoro-*tert*-butoxy-alkyl-substituted enantiopure amines having the structure $PhCHCH_3(NR^1R^2)$ [R^1 = H, CH_3; R^2 = $(CH_2)_3C_8F_{17}$, $(CH_2)_2OC(CF_3)_3$; R^1 = R^2 = $(CH_2)_3C_8F_{17}$, $(CH_2)_2OC(CF_3)_3$] are obtained in high yields, when (*S*)-(−)-1-phenylethylamine is reacted with readily accessible alkylating reagents or fluorous 2° amines (R^1 = H; R^2 = $(CH_2)_3C_8F_{17}$, $(CH_2)_2OC(CF_3)_3$) are methylated in a Leuckart–Wallach reaction. The solubility patterns of these novel chiral amines and their hydrochlorides are qualitatively described for a broad spectrum of solvents and the fluorous partition coefficients of the free bases are determined by GC. A novel method for the resolution of enantiomers is disclosed here, which involves the use a half-equivalent of the selected resolving agent in solvent water that displays low solubility for the crystalline diastereomeric salt(s) formed even at temperatures near to its boiling point. Compound (*S*)-(−)-$PhCHCH_3[NH(CH_2)_3C_8F_{17}]$ is found to satisfy all the latter conditions and successfully used for the heat facilitated resolution of the title racemic acid. The circular dichroism (CD) spectra of six novel fluorous (*S*)-(−)-1-phenylethylamine derivatives are measured in ethanol, trifluoroethanol and hexafluoropropan-2-ol and discussed in detail.

Keywords: Alkylation; Chiral amines; Circular dichroism; Fluorine; Fluorophilicity; Optical resolution; Specific rotation; Synthesis

1. Introduction

Fluorous amines have been receiving increasing attention because they are suitable precursors for the synthesis of fluorous scavangers, reagents and recoverable catalyst precursor ligands [1]. With the use of chiral fluorous nitrogen ligand–metal systems [2], asymmetric catalyses were established for the cyclopropanation of styrenes [3], epoxidation of olefins [4], hydrogen-transfer reduction of ketones [4] and hydrolytic kinetic resolution of terminal epoxides [5]. Complexes of fluorous chiral amines with relatively stable σ-bonded metal centers, in particular those are bonded through a M–C σ-bond, are the subjects of a recent study for the development of systems, that could provide an increased stability with respect to metal leaching [6]. Although fluorous cinchona derivatives have been prepared and used in asymmetric organocatalysis to afford up to 40% enantiomeric excesses in the Diels–Alder reaction of anthrone and *N*-methylmaleimide [7], the potential of such chiral amines for optical resolution has not been explored yet. The relative frequencies (%) of the use of a selection of basic resolving agents indicate that brucine (21%), quinine (16%) and (*S*)- and (*R*)-1-phenylethylamine (12%) are the first three candidates if

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the resolution of a racemic acid via diastereomeric salt formation is considered [8]. For development of novel resolving agents that allow effective fluorous recovery [8], we choose (*S*)- and (*R*)-1-phenylethylamine, since both enantiomeric forms are commercially available. The syntheses of fluorous amines are well documented and rely on the access to appropriate fluorinated building blocks [9,10].

2. Results and discussion

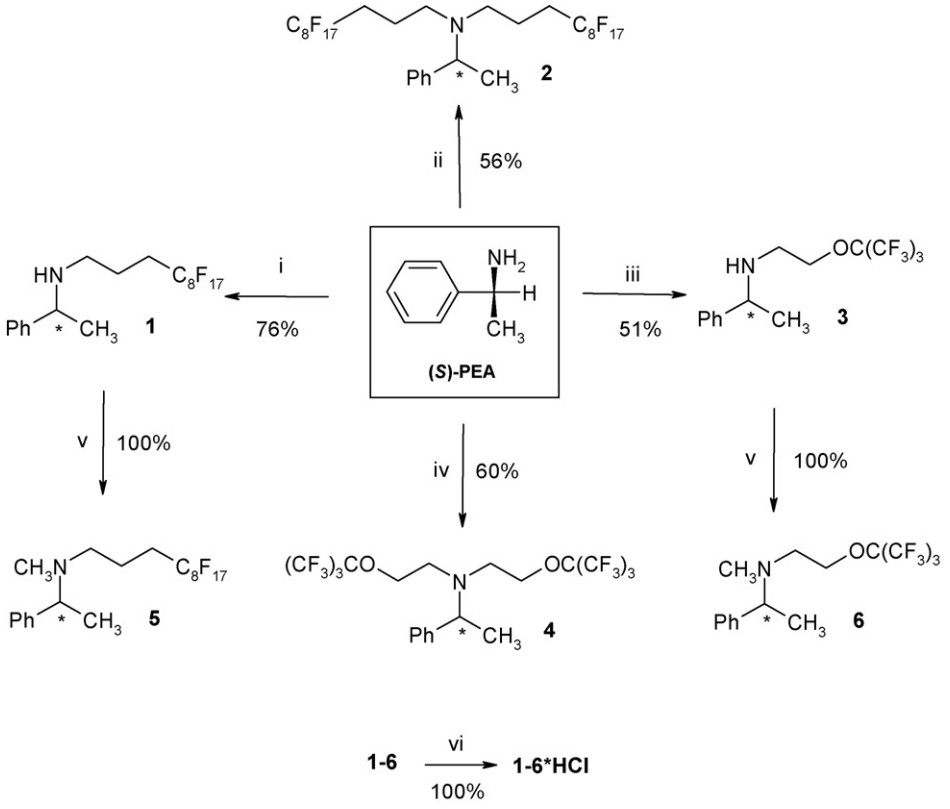
2.1. Synthesis of a series of N-fluoroalkylated (S)-(−)-PEA derivatives

The reaction of (*S*)-(−)-1-phenylethylamine ((*S*)-**PEA**) with: (i) 3-(perfluorooctyl)propyl iodide (**7**), (ii) 3-(perfluorooctyl)propanal (**8**)/$NaBH(OAc)_3$/THF, (iii) 2-(perfluoro-*tert*-butyloxy)ethyl tosylate (**9**) and (iv) 2-(perfluoro-*tert*-butyloxy)ethyl triflate (**10**), respectively, afforded fluorous amines **1**–**4** in good isolated yields (Scheme 1). The secondary *N*-[3-(perfluorooctyl)propyl]-(*S*)-PEA **1** was prepared as reported by Pozzi and co-workers [3], but isolated by vacuum distillation. For the synthesis of *N*,*N*-bis[3-(perfluorooctyl)-propyl]-(*S*)-PEA **2** we applied a two-step *N*-alkylation method developed by Gladysz and co-workers [9a]. The bulky *N*-[2-(perfluoro-*tert*-butyloxy)ethyl]-(*S*)-PEA **3** and *N*,*N*-bis[2-(perfluoro-*tert*-butyloxy)ethyl]-(*S*)-PEA **4** were prepared by using 2-(perfluoro-*tert*-butyloxy)ethyl tosylate (**9**) and -triflate (**10**), respectively, as alkylating reagents. The Leuckart–Wallach methylation [11] of **1** and **3** with formaldehyde and formic acid afforded 3° amines **5** and **6**, respectively, in quantitative yields.

The chiral bases **1**–**6** synthesized here are colorless and volatile liquids, which can easily be converted to their storageable hydrochlorides **1**–**6***HCl, appearing as white crystals, in quantitative yields (Scheme 1).

All new compounds were characterized by ^{1}H NMR, ^{13}C NMR and ^{19}F NMR, IR and MS spectroscopy, as described in Section 4. The NMR properties showed numerous patterns, but usually of a routine nature. For example, the N*C*$H_2$$CH_2$ ^{13}C signals were grouped in ranges (2° amines **1**,**3** and **1**,**3***HCl δ = 43.5–46.6; 3° amines **2**,**4**,**5**,**6** and (**2**,**5**,**6**)*HCl δ = 48.4–53.7) such as for the *C*H_2OC$(CF_3)_3$ ^{13}C signals (**3**,**4**,**6** and (**3**,**4**,**6**)*HCl, δ = 60.7–69.6), always downfield of the *C*$H_2C_8F_{17}$ signals (**1**,**2**,**5** and (**1**,**2**,**5**)*HCl δ = 28.2–28.8).

Some of these amine hydrochlorides in $CDCl_3$ solution displayed proton multiplets doubled according to a temporary diastereomeric form which can be attributed to the hindered nitrogen inversion on the protonated nitrogen or the appearance of small intensity carbon signals of a higher energy diastereomeric form (Section 4).



Scheme 1. Synthesis of selected 2° and 3° fluorous (*S*)-(−)-1-phenylethylamine derivatives. (i) $C_8F_{17}(CH_2)_3I$ (**7**)/K_2CO_3/CH_3CN, 80 °C; (ii) 1: $C_8F_{17}(CH_2)_2CHO$ (**8**)/THF, 2: $NaBH(OAc)_3$, r.t.; (iii) $(CF_3)_3CO(CH_2)_2OTs$ (**9**)/K_2CO_3/CH_3CN, 90 °C; (iv) $(CF_3)_3CO(CH_2)_2OSO_2CF_3$ (**10**)/K_2CO_3/CH_3CN, 90 °C; (v) CH_2O/H_2O/HCO_2H, 90 °C; (vi) HCl/THF.

Table 1
Solubility behavior of enantiomeric and racemic 1-phenyethylamine derivatives and their hydrochlorides at ambient temperature

Entry	Compound	BTF	$CF_3C_6F_{11}$	*n*-Hexane	THF	Acetone	MeOH	CH_2Cl_2	$CHCl_3$	Ether	CH_3CN
1	(±)-**1**	++	++	++	++	++	++	++	++	++	++
2	(−)-**1**	++	++	++	++	++	++	++	++	++	++
3	(±)-**1***HCl	−	−	+	+	+	++	+	++	−	−
4	(−)-**1***HCl	−	−	+	++	++	++	++	++	−	−
5	(±)-**2**	++	++	++	++	++	++	++	++	++	++
6	(−)-**2**	++	++	++	++	++	++	++	++	++	++
7	(−)-**2***HCl	++	−	−	+	++	++	++	++	−	−
8	(−)-**3**	++	++	++	++	++	++	++	++	++	++
9	(±)-**3***HCl	−	−	−	+	+	++	+	++	−	−
10	(−)-**3***HCl	−	−	−	+	+	++	+	++	−	−
11	(−)-**4**	++	++	++	++	++	++	++	++	++	++
12	(−)-**4***HCl	++	−	−	++	++	++	++	++	−	+
13	(±)-**5**	++	++	++	++	++	++	++	++	++	++
14	(−)-**5**	++	++	++	++	++	++	++	++	++	++
15	(±)-**5***HCl	−	−	−	−	+	++	++	++	−	−
16	(−)-**5***HCl	−	−	−	−	+	++	++	++	−	+
17	(−)-**6**	++	++	++	++	++	++	++	++	++	++
18	(−)-**6***HCl	−	−	−	−	+	++	++	++	−	+

(++), 1 volume or weight of sample dissolves in 3 volumes or weights of solvent; (+), 1 volume or weight of sample dissolves in 6–9 volumes or weights of solvent; (−), 1 volume or weight of sample does not dissolve in 12 volumes or weights of solvent.

2.2. Phase properties of N-fluoroalkylated (S)-(−)-PEA derivatives

The liquid free amines **1–6** and their solid HCl salts displayed good miscibility and/or solubilities in broad spectrum organic solvents at ambient temperature, but all hydrochlorides were found sparingly soluble or insoluble in ether and *c*-$CF_3C_6F_{11}$ (Table 1). Only the bis(perfluoroalkylalkyl)- and bis(perfluoroalkoxyalkyl)-derivatives among the HCl salts tested were found to be soluble in benzotrifluoride (Table 1, entries 7 and 12). Methanol and chloroform displayed good solvation power in all cases (Table 1, entries 1–18).

No differences were observed in the solubility characteristics of the free bases either racemic or pure enantiomeric forms were tested (Table 1, entries 1 and 2, 5 and 6, 13 and 14). The (±)-**1***HCl and the enantiopure (−)-**1***HCl samples appeared to have different solubilities in THF, acetone and CH_2Cl_2. This property could be used for enantiomeric enrichment of a partially resolved sample, since the salt of the pure enantiomer has higher solubility than the corresponding racemate (Table 1, entries 3 and 4). On the other hand the (±)-**3***HCl and (−)-**3***HCl, as well as the (±)-**5***HCl and (−)-**5***HCl pairs showed similar solubility patterns (Table 1, entries 9 and 10, 13 and 14). These qualitative data disclosed the rather complex nature of structure–solubility correlation.

We thought that GC determination of fluorous partition coefficients, P_{exp}, for (−)-PEA derivatives could be a probe of their phase behavior (cf. Section 4). Indeed, the experimentally determined partition coefficients were in good agreement with expected trends. These values are increased either by the number of fluorous ponytails (Table 2, entries 1 and 2, 3 and 4) or the removal of the polar and hydrogen-bond forming >NH groups with an *N*-methylation reaction (Table 2, entries 1–5 and 3–6). To show that specific fluorophilicity, f_{spec}, correlates with cohesion parameter, $\delta_{de\ Wolf}$, the fluorous isotherm of the free amines was calculated with a group contribution method [12,13]. Good linear fitting was found as expected: the lower $\delta_{de\ Wolf}$, the larger the f_{spec} is (Fig. 1).

2.3. Resolution via diastereomeric salt formation under optimal conditions

Optical resolution of racemates via diastereomeric salt formation is regarded to one of the most powerful tools for the production of the pure enantiomers [8]. The separation of the formed p- and n-salts is generally carried out by fractional crystallization. Effective processes can be elaborated in two stage optimization starting with the selection of the resolving agent, followed by the setting of the process paramaters

Table 2
Calculated specific fluorophilicity values and cohesion parameters of fluorous (−)-PEA derivatives

Compound	Structure	V_m ($cm^3\ mol^{-1}$)	$\delta_{de\ Wolf}$ ($MPa^{1/2}$)	P_{exp}	f_{spec}
1	$PhCHMe(NH(CH_2)_3C_8F_{17})$	373	14.88	0.290	−0.651
2	$PhCHMe(N((CH_2)_3C_8F_{17})_2)$	625	13.73	4.860	0.496
3	$PhCHMe(NH(CH_2)_2OC(CF_3)_3)$	290	15.67	0.154	−1.268
4	$PhCHMe(N((CH_2)_2OC(CF_3)_3)_2)$	393	14.78	1.010	0.0035
5	$PhCHMe(NMe(CH_2)_3C_8F_{17})$	457	14.39	0.401	−0.392
6	$PhCHMe(NMe(CH_2)_2OC(CF_3)_3)$	310	15.13	0.165	−1.141

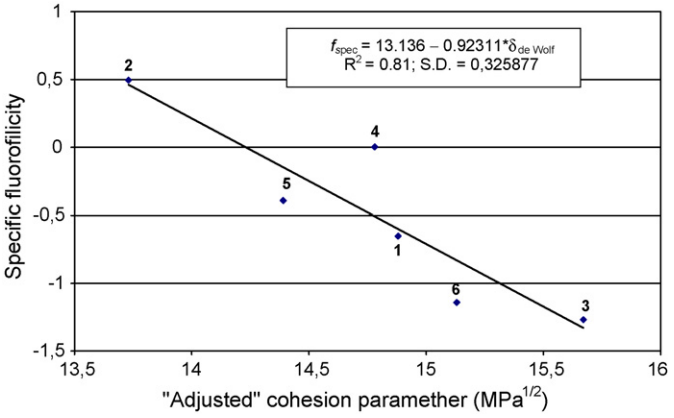


Fig. 1. Fluorous isotherm of (−)-PEA derivatives calculated from de Wolf increments.

including stoichiometry of the resolving agent, selection and volume of the solvent, and the temperature regime.

Based on simplified models (cf. ‘‘resolution equations (a), (b) and (c)’’ in ref. [14]) and literature data [8], we thought to devise an ideal process. Water is the solvent of choice and half-equivalent of the resolving agent is used here at a temperature, which effects the crystallization of the higher melting diastereomeric salt.

Our approach involves the mixing of two equivalents of racemic acid (±)-HA with one equivalent of the enantiopure chiral base (−)-B and one equivalent of NaOH. This treatment leads to the formation of two diastereomeric salts, (−,−)-BHA (p-salt) and (−,+)-BHA (n-salt), besides the sodium salts of the enantiomeric acids, (−)-NaA and (+)-NaA. If the resolving agent, (−)-B, was selected to afford either the p- or the n-salt with higher melting point then the set temperature of solvent water, then the first phase separated melt of the mixed diastereomeric salts could change its composition on prolonged heating and stirring due to exchange of enantiomeric anions between the organic melt and the bulk water phases until a composition finally crystallized.

Indeed, the reaction of the racemic sulfoxide dicarboxylic acid (±)-**SO** with one of the seven chiral bases tested (Table 3), resulted in the formation of a crystalline precipitate ((+)-{**1*****SO*****1**}) and partial resolution of (±)-**SO** (Scheme 2). The pure (*S*)-(+)- and (*R*)-(−)-**SO** enantiomers were obtained with selective precipitation of the racemic portion with dioxane as reported [14,15]. It should be added, that no crystalline diastereomers were formed with this (±)-**SO**, when its resolution has been attempted with cinchona and other alkaloids [14].

Selective reactions of nonracemic enantiomer mixtures provide valuable tools for obtaining pure enantiomers from partially resolved samples [16]. Unlike to this heat facilitated optical resolution procedure the general practice applies cooling instead of heating to effect diastereomeric salt crystallizations [8,17].

Our procedure combines the advantages of the methods of Pope and Peachey [18], and that of Kantor and Hauser who first reported that prolonged heating of the initially precipitated diastereomeric salts with insufficient amount of solvent could improve separation efficacy [19]. The scope and limitations of this novel non-conventional resolution method are being investigated and further results will be published later [17].

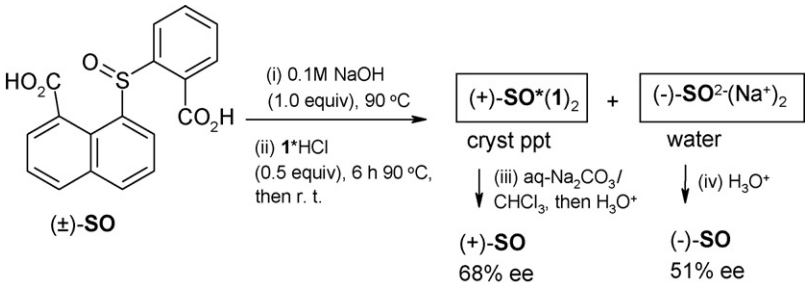
2.4. Circular dichroism spectra of the fluorous (S)-(−)-PEA derivatives

The circular dichroism (CD) spectra of 1-phenylethylamine (PEA) and its derivatives have been discussed in detail [20,21]. We measured the far-UV (195–250 nm, ^1B_b and ^1L_a transitions) and near-UV (240–330 nm, ^1L_b transition) CD spectrum of fluorous derivatives of (*S*)-PEA in different solvents. In ethanol in the spectrum of (*S*)-PEA-perchlorate two minima were observed at 209 and at 213 nm. The intensity of these two peaks

Table 3
Preliminary experiments for the selection of the appropriate resolving agent (cf. Section 4.10)

Conditions	**PEA***HCl	**1***HCl	**2***HCl	**3***HCl	**4***HCl	**5***HCl	**6***HCl
SO + 1/2**B**; 90 → 20 °C	Clear solution	Crystalline precipitate	Sticky precipitate	Sticky precipitate	Sticky precipitate	Sticky precipitate	Sticky precipitate
$\mathbf{SO}_{\text{from } H_2O}$: $[\alpha]_{578\ (DMF)}$	0	−260[a]	0	−2.5	+2.1	−3.0	0

[a] Corresponds to 51% enantiomeric excess (cf. ref. [15]).



Scheme 2. Heat facilitated resolution of (±)-2-(8-carboxy-1-naphthylsulfinyl)benzoic acid ((±)-**SO**).

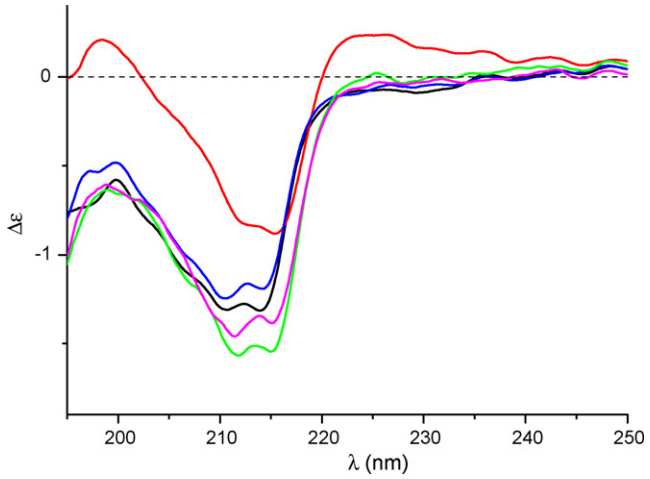


Fig. 2. Far-UV CD spectra of compounds **1***HCl (—), **2***HCl (—), **3***HCl (—), **5***HCl (—) and **6***HCl (—) in ethanol.

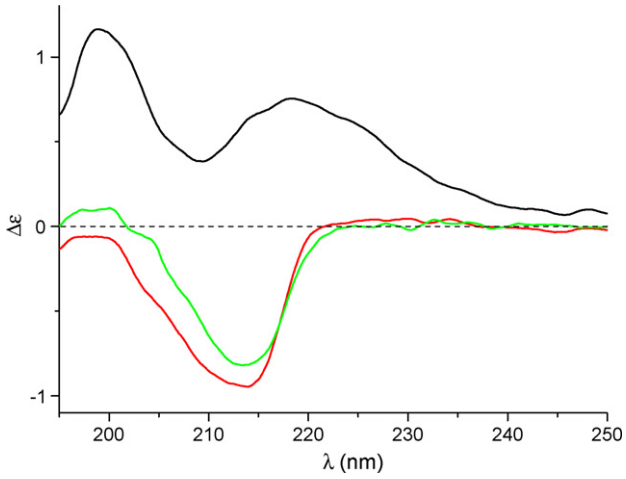


Fig. 3. Far-UV CD spectra of compound 4*HCl in ethanol (—), in TFE (—) and in HFP (—).

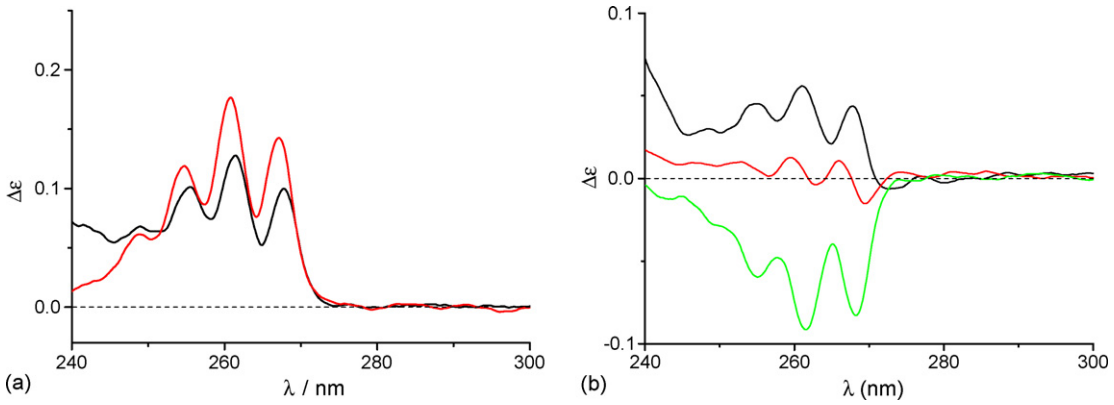


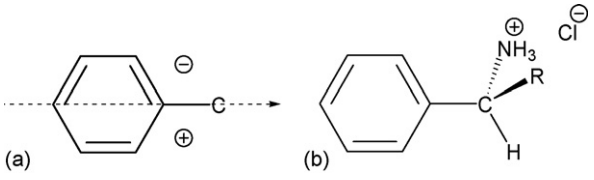
Fig. 4. Near-UV CD spectra of compound 2*HCl (a) and compound 4*HCl (b) in ethanol (—), in TFE (—) and in HFP (—).

increased and red shifted with fluorinated alkyl substitution of the amino group (Fig. 2). However, in the case of the tertiary amine with two identical perfluoroalkyl substituents **2***HCl, two positive bands also appeared in the far-UV region. In the CD spectrum of **4***HCl only positive peaks can be seen in ethanol (Fig. 2).

The replacement of ethanol by trifluoroethanol (TFE) or 1,1,1,3,3,3-hexafluoropropan-2-ol (HFP) increased the intensity of the negative bands in the far-UV spectra of **1***HCl, **2***HCl, **3***HCl, **5***HCl and **6***HCl. The effect of TFE is more expressed in the case of molecules which have one linear fluorinated alkyl groups. However, in the fluorinated solvents TFE and HFP the spectra of **4***HCl are dominated by a negative band at 214 and 213 nm, respectively (Fig. 3). We suppose that these unexpected spectral differences are caused by the bulky fluorinated alkyl groups which considerably influence the conformation.

In the near-UV CD spectrum the Cotton effects associated with the ^1L_b transition of the benzene ring were observed between 240 and 275 nm for all molecules and in different solvents. We observed four or five vibrational bands out of the six theoretical bands. The same effects were found as in the far-UV spectrum: the intensity of the vibrational peaks in TFE was increased and appeared with some red shift (see e.g. Fig. 4a). In the case of **4***HCl the solvent effect is most significant: in HFIP the vibrational peaks became negative (Fig. 4b).

The quadrant sector rule as applied to α-substituted phenylethane may be depicted as shown in Scheme 3a [22]. In Scheme 3a, the signs refer to the rotatory contributions of groups lying above the phenyl ring plane. The sign of the rotational perturbation of a group lying in a particular sector was deduced empirically [22]. It was concluded that an alkyl group is not capable of a rotationally significant interaction with the phenyl chromophore. Thus, it is the protonated amino group the position of which determines the sign of the ^1L_b band. In Scheme 3b, the prevailing conformer of compounds (**1**–**6**)*HCl of (*S*)-configuration can be seen. The NH_3^+ group is located in a positive quadrant. In agreement with this, the sign of the ^1L_b band is positive. The only exception is the CD spectrum of **4***HCl in HFP that suggest a drastic conformational change.



Scheme 3. The quadrant sector rule of the substituted benzene ring [22].

The optical activity of the HCl salts of *N*-polyfluoroundecyl-PEA derivatives is determined by the aromatic chromophore perturbed by the $-CH_3$ and $-NH^{(+)}<$ groups. Comparison of the far-UV region of the CD spectra in ethanol and TFE of compounds **1***HCl, **3***HCl, **5***HCl and **6***HCl led to the conclusion that the relative amount of conformers is similar. The CH_3 group attached to N in **5***HCl stabilizes the dominant conformer. The presence of two polyfluoroundecyl groups in **2***HCl does not affect the sign of the ^1L_a band at 215 nm in ethanol or TFE, but gives rise to a positive long-wavelength band at 225 nm and a positive band in the ^1B_b region (at 199 nm). It is **4***HCl the spectrum of which in ethanol features only positive bands between 195 and 240 nm. The attached two (perfluoro-*tert*-butyloxy)ethyl groups appears to influence the conformational equilibrium but an interaction between the phenyl ring and the (perfluoro-*tert*-butyloxy)ethyl group(s) cannot be excluded either.

The sign of the Cotton effects in the region 240–275 nm can be predicted based on a quadrant sector rule [22] (Scheme 3). The ^1L_b band region of **4***HCl with the typical vibrational fine structure shows an expressed solvent sensitivity. While all the splitted bands of **1***HCl, **2***HCl, **3***HCl, **5***HCl and **6***HCl in ethanol and TFE are positive similarly to the spectrum of PEA, the near-UV region shows a negative band pattern in HFP and an averaged, almost zero spectrum in TFE (Fig. 4b). It is compound **4***HCl which differs in both CD spectral and conformational behavior from all the other members of the family of **1***HCl, **2***HCl, **3***HCl, **5***HCl and **6***HCl.

3. Conclusions

In conclusion, a series of light fluorous (*S*)-(−)-1-phenylethylamine derivatives was synthesized by the alkylation of (*S*)-(−)-PEA, that may be used for the production of high value enantiomerically pure acids in this novel half-equivalent resolution method involving hot water as the solvent of choice for diastereomeric salt crystallizations. Amines **1**–**6** could supplement the inventory of fluorine containing chiral α-phenylethylamines, which became accessible on laboratory through to industrial scales via asymmetric syntheses developed at Central Glass [23].

4. Experimental

4.1. General description of methods and materials

FC-72 and *c*-$CF_3C_6F_{11}$ were purchased from Fluorochem, while fluorous reagents **7** [9j], **8** [9a] and **9** [10] were prepared as reported. The other reagents and solvents were Aldrich, Fluka or Uvasol products. Fourier-transformed infrared spectra were recorded neat, as a film on a Bruker Equinox FTIR spectrophotometer, ν_{max} in cm^{-1}. The intensity of the bands is characterized as broad (br), strong (s), medium (m) or weak (w). ^1H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on Varian INOVA 500 (500 MHz for ^1H) spectrometer at 25 °C. Data were expressed as chemical shifts in part per million (ppm) relative to TMS (^1H, $\delta = 0$), $CDCl_3$ (^{13}C, $\delta = 77.0$) or for ^{19}F ($CFCl_3$, $\delta = 0$) on the δ scale. Coupling constants *J* were given in Hz. Mass spectrometric experiments were performed on a Bruker Esquire 3000plus ion trap mass spectrometer, equipped with electrospray ionization source. Spectra were acquired in positive ionization mode, in the 15–2000 *m/z* range. Samples were dissolved in methanol. Identification of molecular weights was performed by electrospray ionization mass spectrometry (ESI-MS). All compounds displayed intensive protonated molecular ion ($[M + H]^+$) in the mass spectra. CD spectra were recorded on a Jasco J-810 dichrograph (calibrated with ammonium *d*-10-camphor-sulfonate) at room temperature using 0.1 cm cell for measurements between 195 and 250 nm and 1 cm between 240 and 330 nm. Ethanol (Uvasol), 2,2,2-trifluoroethanol (Aldrich, 99%+) and 1,1,1,3,3,3-hexafluoropropan-2-ol (Uvasol) were used as solvents and the concentration was 1 mM dm^{-3}. Optical rotations were determined on a Carl Zeiss Polamat A polarimeter with a 1 dm cell and DMF or MeOH sample solutions at 25 °C. Melting points were determined on a Boetius micro-melting point apparatus and are uncorrected. All reactions were monitored by GC (Hewlett-Packard 5890 Series II, PONA [cross-linked methylsilicone gum] 50 m × 0.2 mm × 0.5 μm column, H_2 carrier gas, FID detection). Fluorous partition coefficients (P_{exp}) were determined by GC as follows: in a 2 ml volumetric flask the given compounds (10 mg) were extracted in a 1.00 ml to 1.00 ml mixture of pre-equilibrated *c*-$CF_3C_6F_{11}$ and toluene. The closed vessel was first immersed in a water bath (50 °C) for 30 min with frequent shaking, and then allowed to cool to 25 °C. After standing overnight at this temperature 300 ± 3 μl aliquots of the separated upper and lower phases were withdrawn and diluted with 300 ± 3 μl $C_6H_5CF_3$, which served as an internal standard for GC analysis. An average of 7–11 injections for each entry resulted in listed values (Table 1).

4.2. General procedure for the syntheses of amine hydrochlorides (*1–6*HCl*)

Amines **1**–**6** (0.20 g) were dissolved in THF (5 ml) and cooled to 0 °C, and then two to three drops of 12 M HCl was added. The mixtures were evaporated under vacuum and dried to afford the title salts in quantitative yields.

4.3. N-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11-heptadecafluoroundecyl)-(1S)-1-phenylethylamine (*1*) and hydrochloride (*1*HCl*)

Slightly modified procedure to that reported in ref. [3]. A mixture of (*S*)-(−)-**PEA** (1.23 g, 10 mmol), **7** (5.87 g, 10 mmol), K_2CO_3 (3.45 g, 25 mmol) and acetonitrile (30 ml) was sealed in a 100 ml glass ampoule and stirred at 80 °C for 96 h. Then, the ampoule was opened at r.t. and the mixture partitioned between water (25 ml) and ether (3 × 20 ml). The ether layer was separated, dried (Na_2SO_4) and compound **1** was isolated by fractional distillation. Yield: 4.43 g (76%) colorless liquid, bp = 150–155 °C/0.5 mmHg; $[\alpha]_{546} = -18.3$ (*c* = 1, MeOH); with agreeable (^1H, ^{13}C, ^{19}F)

NMR spectra to that reported [3]. ^{1}H NMR ($CDCl_3$): δ 1.35 (3H, d, J = 6.6 Hz, CH_3), 3.75 (1H, q, J = 6.6 Hz, CH), 2.60; 2.47 (2H, m, NCH_2), 2.12 (2H, m, CH_2CF_2), 1.72 (2H, m, $CH_2C\underline{H}_2CH_2$), 7.35–7.22 (5H, m, H(Ar.). ^{13}C NMR ($CDCl_3$): δ 21.0 (CH_3), 24.4 ($CH_2\underline{C}H_2CH_2$), 28.8 (t, $^2J_{CF}$ = 22.5 Hz, $\underline{C}H_2CF_2$), 46.6 (NCH_2), 58.3 (CH), 126.5 ($\underline{C}$(Ar.), *o*-CH), 127.0 ($\underline{C}$(Ar.), *p*-CH), 128.5 ($\underline{C}$(Ar.), *m*-CH), 145.6 ($\underline{C}$(Ar.), *g*-CH). ^{19}F NMR ($CDCl_3$): δ −81.3 (3F, t, J = 9.9 Hz, F-8, CF_3), −114.4 (2F, m, F-1, CF_2), −122.4 (6F, m, F-2, 3, 6, CF_2), −123.2 (2F, m, F-5, CF_2), −124.0 (2F, m, F-4, CF_2), −126.6 (2F, m, F-7, CF_2).

1*HCl: mp 185 °C, $[\alpha]_{546}$ = −11.2 (c = 1, MeOH). ^{1}H NMR ($CDCl_3$): δ 1.92 (3H, d, J = 6.7 Hz, CH_3), 4.26 (1H, m, CH), 2.82; 2.73 (2H, m, NCH_2), 2.31 (2H, m, CH_2CF_2), 2.10 (2H, m, $CH_2C\underline{H}_2CH_2$), 7.64–7.38 (5H, m, H(Ar.)), 10.4; 10.1 (2H, N^+H_2). ^{13}C NMR ($CDCl_3$): δ 17.4 (CH_3), 20.5 ($CH_2\underline{C}H_2CH_2$), 28.3 (t, $^2J_{CF}$ = 22.5 Hz, $\underline{C}H_2CF_2$), 45.0 (NCH_2), 59.5 (CH), 127.8 ($\underline{C}$(Ar.), *o*-CH), 129.5 ($\underline{C}$(Ar.), *p*-CH), 129.6 ($\underline{C}$(Ar.), *m*-CH), 135.6 ($\underline{C}$(Ar.), *g*-CH). ^{19}F NMR ($CDCl_3$): δ −81.4 (3F, t, J = 9.9 Hz, F-8, CF_3), −114.9 (2F, m, F-1, CF_2), −122.5 (6F, m, F-2, 3, 6, CF_2), −123.4 (2F, m, F-5, CF_2), −124.0 (2F, m, F-4, CF_2), −126.8 (2F, m, F-7, CF_2). IR (KBr) ν, cm^{-1}: 3437 (br), 2770 (m), 1242 (vs), 1206 (vs), 1150 (vs). ESI-MS: m/z = 582.1 $[M + H]^+$; calcd. for $[C_{19}H_{17}F_{17}N]^+$ 582.1.

*4.4. N,N-bis(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11-heptadecafluoroundecyl)-(1S)-1-phenylethylamine (**2**) and hydrochloride (**2***HCl)*

To a solution of aldehyde **8** (2.14 g, 4.5 mmol) in dry THF (30 ml) was added (*S*)-**PEA** (0.23 g, 1.86 mmol) and stirred at r.t. for 10 min. After the addition of $NaBH(OAc)_3$ (1.19 g, 5.62 mmol) the mixture was stirred for 20 h. Then, 1N NaOH (20 ml) was added and the mixture extracted with ether (3 × 50 ml). The organic layers were separated and dried (Na_2SO_4) and the solvent removed under vacuum. The crude product was purified by column chromatography (silica gel, hexane/ether, 9:1) to afford the title compound **2**. Yield: 1.93 g (56%) colorless liquid, $[\alpha]_{546}$ = −2.82 (c = 1, MeOH). ^{1}H NMR ($CDCl_3$): δ 1.34 (3H, d, J = 6.8 Hz, CH_3), 3.90 (1H, q, J = 6.8 Hz, CH), 2.57; 2.40 (4H, m, NCH_2), 2.08; 1.91 (4H, m, CH_2CF_2), 1.68 (4H, m, $CH_2C\underline{H}_2CH_2$), 7.33–7.22 (5H, m, H(Ar.)). ^{13}C NMR ($CDCl_3$): δ, 18.6 (CH_3), 13.8 ($CH_2\underline{C}H_2CH_2$), 28.5 (t, $^2J_{CF}$ = 22.0 Hz, $\underline{C}H_2CF_2$), 48.4 (NCH_2), 57.7 (CH), 127.0 ($\underline{C}$(Ar.), *p*-CH), 127.8 ($\underline{C}$(Ar.), *o*-CH), 128.1 ($\underline{C}$(Ar.), *m*-CH), 142.9 ($\underline{C}$(Ar.), *g*-CH). ^{19}F NMR ($CDCl_3$): δ −81.4 (3F, t, J = 9.9 Hz, F-8, CF_3), −114.9 (2F, m, F-1, CF_2), −122.5 (6F, m, F-2, 3, 6, CF_2), −123.3 (2F, m, F-5, CF_2), −124.4 (2F, m, F-4, CF_2), −126.7 (2F, m, F-7, CF_2). Prochirality of carbons in the chains are averaged out due to fast nitrogen inversion. IR (neat) ν, cm^{-1}: 2977 (w), 1242 (vs), 1208 (vs), 1152 (s).

2*HCl: mp 102–104 °C, $[\alpha]_{546}$ = −2.8 (c = 1, MeOH). ^{1}H NMR ($CDCl_3$): δ 1.93 (3H, d, J = 6.4 Hz, CH_3), 4.41 (1H, m, CH), 3.4–2.8 (4H, m, NCH_2), 2.5–1.95, (8H, m, CH_2CF_2, $CH_2C\underline{H}_2CH_2$), 7.7–7.5 (5H, m, H(Ar.)), 12.7 (1H, N^+H). ^{13}C NMR ($CDCl_3$): δ 17.7 (CH_3), 15.1; 15.5 ($CH_2\underline{C}H_2CH_2$), 28.2 (t, $^2J_{CF}$ = 22.0 Hz, $\underline{C}H_2CF_2$), 48.8; 49.6 (NCH_2), 64.3 (CH), 130.2 ($\underline{C}$(Ar.), *p*-CH), 128.8 ($\underline{C}$(Ar.), *o*-CH), 129.6 ($\underline{C}$(Ar.), *m*-CH), 134.1 ($\underline{C}$(Ar.), *g*-CH). ^{19}F NMR ($CDCl_3$): δ −81.4 (3F, t, J = 9.9 Hz, F-8, CF_3), −114.0 (2F, m, F-1, CF_2), −122.5 (6F, m, F-2, 3, 6, CF_2), −123.3 (2F, m, F-5, CF_2), −123.8 (2F, m, F-4, CF_2), −126.7 (2F, m, F-7, CF_2). Prochirality of carbons in the chains can be seen on some signals due to hindered nitrogen inversion. IR (KBr) ν, cm^{-1}: 3431 (br), 2948 (w), 1241 (vs), 1205 (vs), 1149 (s). ESI-MS: m/z = 1042.2 $[M + H]^+$; calcd. for $[C_{30}H_{22}F_{34}N]^+$ 1042.2.

*4.5. N-{2-[1,1-bis(trifluoromethyl)-2,2,2-trifluoroethoxy]ethyl)}-(1S)-1-phenylethylamine (**3**) and hydrochloride (**3***HCl)*

A stirred mixture of (*S*)-**PEA** (2.42 g, 20 mmol), tosylate **9** (6.68 g, 20 mmol) and K_2CO_3 (6.9 g, 50 mmol) in dry acetonitrile was heated at 90 °C under an argon atmosphere for 60 h. The insoluble salts were filtered off and the solvent was removed under vacuum, then the crude product distilled to afford the title amine **5**. Yield: 3.9 g (51%) colorless liquid, bp 108–110 °C/15 mmHg, $[\alpha]_{546}$ = −24.2 (c = 1, MeOH). ^{1}H NMR ($CDCl_3$): δ 1.35 (3H, d, J = 6.6 Hz, CH_3), 3.79 (1H, q, J = 6.6 Hz, CH), 4.07 (2H, m, OCH_2), 2.80; 2.67 (2H, m, NCH_2), 7.34–7.22 (5H, m, H(Ar.)). ^{13}C NMR ($CDCl_3$): δ 24.5 (CH_3), 46.6 (NCH_2), 58.0 (CH), 69.6 (OCH_2), 120.3 (q, J = 292.5, CF_3), 126.5 ($\underline{C}$(Ar.), *o*-CH), 127.0 ($\underline{C}$(Ar.), *p*-CH), 128.5 ($\underline{C}$(Ar.), *m*-CH), 145.2 ($\underline{C}$(Ar.), *g*-CH). ^{19}F NMR ($CDCl_3$): δ −70.9 (CF_3). IR (neat) ν, cm^{-1}: 2970 (w), 1269 (vs), 1253 (vs), 1161 (s) and 972 (s).

3*HCl: mp 205–209 °C, $[\alpha]_{546}$ = −11.2 (c = 1, MeOH). ^{1}H NMR ($CDCl_3$): δ 1.85 (3H, d, J = 7.0 Hz, CH_3), 4.33 (1H, q, J = 7.0 Hz, CH), 4.69; 4.39 (2H, m, OCH_2), 3.05 (2H, m, NCH_2), 7.34–7.22 (5H, m, H(Ar.)), 10.6; 10.2 (2H, N^+H_2). ^{13}C NMR ($CDCl_3$): δ 20.4; [18.4] (CH_3), 43.5 (NCH_2), 59.3; [58.2] (CH), 65.1 (OCH_2), 120.0 (q, J = 292.0, CF_3), 127.7 ($\underline{C}$(Ar.), *o*-CH), 129.6 ($\underline{C}$(Ar.), *p*-CH), 129.6 ($\underline{C}$(Ar.), *m*-CH), 135.4 ($\underline{C}$(Ar.), *g*-CH). ^{19}F NMR ($CDCl_3$): δ −70.7 (CF_3). Small intensity carbon signals (for carbons CH and CH_3 in square brackets) of a higher energy temporary diastereomeric form appear. Note the nontypical nonequivalency of N^+H_2 hydrogens in the proton spectrum as well. IR (KBr) ν, cm^{-1}: 3436 (br), 2745 (m), 1267 (vs), 1168 (m), 973 (m). ESI-MS: m/z = 384.1 $[M + H]^+$; calcd. for $[C_{14}H_{15}F_9NO]^+$ 384.1.

*4.6. N,N-bis{2-[1,1-bis(trifluoromethyl)-2,2,2-trifluoroethoxy]ethyl)}-(1S)-1-phenylethylamine (**4**) and hydrochloride (**4***HCl)*

A stirred mixture of (*S*)-**PEA** (0.48 g, 4.0 mmol), triflate **10** (3.5 g, 8.6 mmol) and K_2CO_3 (2.36 g, 17.1 mmol) in dry acetonitrile (13 ml) was heated at 90 °C under argon atmosphere for 72 h. Water (20 ml) and ether (20 ml) was added to the mixture, then the aqueous phase was separated and extracted with ether (2 × 10 ml). The ether layers were combined and dried (Na_2SO_4), and then the solvent was removed. The crude product was purified by vacuum

distillation to afford the title amine **4**. Yield: 1.53 g (60%) colorless liquid, bp 114–118 °C/0.5 mmHg, $[\alpha]_{546} = -5.8$ ($c = 1$, MeOH). ^{1}H NMR ($CDCl_3$): δ 1.37 (3H, d, $J = 6.8$ Hz, CH_3), 3.90 (1H, q, $J = 6.8$ Hz, CH), 3.94 (4H, m, OCH_2), 2.92–2.76 (4H, m, NCH_2), 7.34-7.22 (5H, m, H(Ar.)). ^{13}C NMR ($CDCl_3$): δ 16.19 (CH_3), 50.9 (NCH_2), 69.3 (CH), 60.7 (OCH_2), 120.4 (q, $J = 293.0$, CF_3), 127.5 (C(Ar.), *o*-CH), 127.1 (C(Ar.), *p*-CH), 128.3 (C(Ar.), *m*-CH), 143.3 (C(Ar.), *g*-CH). ^{19}F NMR ($CDCl_3$): δ −71.0 (CF_3). IR (neat) ν, cm^{-1}: 2977 (w), 1307 (vs), 1248 (vs), 1154 (vs) and 972 (vs).

4*HCl: mp 141–144 °C, $[\alpha]_{546} = -8.0$ ($c = 1$, MeOH). ^{19}F NMR ($CDCl_3$): δ −70.6 (CF_3). Because of conformational motions at room temperature the proton and carbon NMR spectra contain many diffuse non-characteristic signals, only the fluorine data is given. IR (KBr) ν, cm^{-1}: 3438 (br), 1267 (vs), 1257 (vs), 1154 (s) and 973 (s). ESI-MS: $m/z = 646.1$ $[M + H]^+$; calcd. for $[C_{20}H_{18}F_{18}NO_2]^+$ 646.1.

*4.7. Methyl N-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11-heptadecafluoroundecyl)-(1S)-1-phenylethylamine (**5**) and hydrochloride (**5***HCl)*

A stirred solution of 2° amine **1** (1.74 g, 3 mmol), formic acid (1 ml) and formaldehyde (1 ml, 37% in H_2O) was heated at 90 °C for 2 h. Then, the mixture was cooled, treated with 1 M NaOH (10 ml) and extracted with ether (3 × 5 ml). Then, the organic phase was separated, dried (Na_2SO_4) and evaporated. The residue was distilled to afford the title amine **7**. Yield: 1.02 g (57%) colorless liquid, bp 164–169 °C/15 mmHg), $[\alpha]_{546} = -11.0$ ($c = 1$, MeOH). ^{1}H NMR ($CDCl_3$): δ 1.34 (3H, d, $J = 6.8$ Hz, CH_3), 3.55 (1H, q, $J = 6.8$ Hz, CH), 2.44; 2.33 (2H, m, NCH_2), 2.18 (3H, CH_3), 2.05 (2H, m, CH_2CF_2), 1.71 (2H, m, $CH_2C\underline{H}_2CH_2$), 7.33–7.21 (5H, m, H(Ar.)). ^{13}C NMR ($CDCl_3$): δ 18.1 ($CHC\underline{H}_3$), 18.0 ($CH_2\underline{C}H_2CH_2$), 28.6 (t, $^2J_{CF} = 22.5$ Hz, $\underline{C}H_2CF_2$), 38.0 (NCH_3), 52.8 (NCH_2), 63.5 (CH), 127.6 (C(Ar.), *o*-CH), 126.9 (C(Ar.), *p*-CH), 128.1 (C(Ar.), *m*-CH), 143.9(C(Ar.), *g*-CH). ^{19}F NMR ($CDCl_3$): δ −81.3 (3F, t, $J = 9.9$, F-8, CF_3), −114.7 (2F, m, F-1, CF_2), −122.3 (6F, m, F-2, 3, 6, CF_2), −123.2 (2F, m, F-5, CF_2), −124.0 (2F, m, F-4, CF_2), −126.6 (2F, m, F-7, CF_2). IR (neat) ν, cm^{-1}: 2978 (w), 1242 (vs), 1209 (vs) and 1152 (vs).

5*HCl: mp 133–155 °C, $[\alpha]_{546} = -10.4$ ($c = 1$, MeOH). ^{1}H NMR ($CDCl_3$): δ 1.91; 1.92 (3H, CH_3), 4.32; 4.47 (1H, CH), 2.86; 2.65 (3H, CH_3), 3.4–1.8 (6H, m, $NC\underline{H}_2C\underline{H}_2C\underline{H}_2CF_2$), 7.66–7.42 (5H, m, H(Ar.)), 12.6; 10.2 (1H, N^+H). ^{13}C NMR ($CDCl_3$): δ 17.0; 17.4 ($CHC\underline{H}_3$), 15.4; 15.6 ($CH_2\underline{C}H_2CH_2$), 28.3; 28.5 ($\underline{C}H_2CF_2$), 35.3; 38.6 (NCH_3), 51.3; 53.6 (NCH_2), 64.9; 66.4 (CH), 128.7; 129.2 (C(Ar.), *o*-CH), 130.0; 130.2 (C(Ar.), *p*-CH), 129.4; 129.5 (C(Ar.), *m*-CH), 132.9; 133.9 (C(Ar.), *g*-CH). ^{19}F NMR ($CDCl_3$): δ −81.3 (3F, t, $J = 9.2$, F-8, CF_3), −114.2 (2F, m, F-1, CF_2), −122.4 (6F, m, F-2, 3, 6, CF_2), −123.2 (2F, m, F-5, CF_2), −123.8 (2F, m, F-4, CF_2) and −126.6 (2F, m, F-7, CF_2). Each carbon signals and most of the proton multiplets doubled according to a temporary diastereomeric form due to hindered nitrogen inversion on the protonated nitrogen. IR (KBr) ν, cm^{-1}: 3435 (br), 2925 (w), 1244 (vs) and 1217 (vs), 1146 (vs). ESI-MS: $m/z = 596.1$ $[M + H]^+$; calcd. for $[C_{20}H_{19}F_{17}N]^+$ 596.1.

*4.8. N-methyl-N-{2-[1,1-bis(trifluoromethyl)-2,2,2-trifluoroethoxy]ethyl)}-(1S)-1-phenylethylamine (**6**) and hydrochloride (**6***HCl)*

A stirred solution of amine **3** (1.49 g, 3.9 mmol), formic acid (1.3 ml) and formaldehyde (1.3 ml 37% in H_2O) was heated at 90 °C for 2 h. Then, the mixture was cooled, treated with 1 M NaOH (15 ml) and extracted with ether (3 × 10 ml). Then, the organic phase was separated, dried (Na_2SO_4) and evaporated. The residue was distilled to afford the title amine **6**. Yield: 1.11 g (72%) colorless liquid, bp 114 °C/15 mmHg, $[\alpha]_{546} = -14.5$ ($c = 1$, MeOH). ^{1}H NMR ($CDCl_3$): δ 1.35 (3H, d, $J = 6.8$ Hz, $CHC\underline{H}_3$), 3.61 (1H, q, $J = 6.8$ Hz, CH), 2.27 (3H, NCH_3), 4.02 (2H, m, OCH_2), 2.75; 2.60 (2H, m, NCH_2), 7.33–7.21 (5H, m, H(Ar.)). ^{13}C NMR ($CDCl_3$): δ 18.4 ($CH\underline{C}H_3$), 39.6 (NCH_3), 53.2 (NCH_2), 63.7 (CH), 68.5 (OCH_2), 120.4 (q, $J = 293.9$, CF_3), 127.5 (C(Ar.), *o*-CH), 126.9 (C(Ar.), *p*-CH), 128.2 (C(Ar.), *m*-CH), 143.9 (C(Ar.), *g*-CH). ^{19}F NMR ($CDCl_3$): δ −70.9 (CF_3). IR (neat) ν, cm^{-1}: 2978 (w), 1268 (vs), 1252 (vs), 1156 (s) and 971 (s).

6*HCl: mp 160–165 °C, $[\alpha]_{546} = -11.3$ ($c = 1$, MeOH). ^{1}H NMR ($CDCl_3$): δ 1.89; 1.90 (3H, d, $J = 6.8$ Hz, $CHC\underline{H}_3$), 4.80; 4.93 (1H, CH), 2.66; 2.90 (3H, NCH_3), 4.41; 4.55 (2H, m, OCH_2), 3.85–3.0 (2H, m, NCH_2), 7.72–7.40 (5H, m, H(Ar.)), 12.9; 13.0 (1H, N^+H). ^{13}C NMR ($CDCl_3$): δ 17.0; 17.2 ($CH\underline{C}H_3$), 36.5; 38.9 (NCH_3), 51.9; 53.7 (NCH_2), 64.6; 64.7 (CH), 66.0; 66.6 (OCH_2), 119.9 (q, $J = 292.5$, CF_3), 128.7; 129.0 (C(Ar.), *o*-CH), 130.0; 130.2 (C(Ar.), *p*-CH), 129.4; 129.5 (C(Ar.), *m*-CH), 133.9; 133.2 (C(Ar.), *g*-CH). ^{19}F NMR ($CDCl_3$): δ −70.6 (CF_3). Each carbon signals and most of the proton multiplets doubled according to a temporary diastereomeric form due to hindered nitrogen inversion on the protonated nitrogen. Note the doubling of N^+H signal in the proton spectrum, as well. IR (KBr) δ, cm^{-1}: 3431 (br), 2921 (w), 1268 (vs), 1155 (s) and 972 (s). ESI-MS calculated: 397.1 *m/z*, measured: 397.1 *m/z*. ESI-MS: $m/z = 398.1$ $[M + H]^+$; calcd. for $[C_{15}H_{17}F_9NO]^+$ 398.1.

*4.9. 2-[1,1-Bis(trifluoromethyl)-2,2,2-trifluoroethoxy]ethyl trifluoromethanesulfonate (**10**)*

The solution of trifluoromethanesulfonic anhydride (10.0 g, 35.4 mmol) in dichloromethane (60 ml) was cooled to −20 °C and a solution of 2-(nonafluoro-*tert*-butoxy)ethyl alcohol **9** (10 g, 35.4 mmol) and dry pyridine (2.8 g, 35.4 mmol) in dioxane (20 ml) was added. The mixture was then stirred at 0 °C for 1 h. Salts were filtered off and the solvents were removed by evaporation. The residue was purified by distillation to afford triflate **10**. Yield: 6.0 g (47%) colorless liquid, bp 107–115 °C/15 mmHg. ^{1}H NMR ($CDCl_3$): δ 4.68 (2H, t, $J = 4.4$ Hz), 4.35 (2H, t, $J = 4.4$ Hz). ^{13}C NMR ($CDCl_3$): δ 120.1 (3C, q, $J = 292$ Hz), 118.6 (1C, q, $J = 292$ Hz), 79.9 (1C, m), 73.3 (1C, s), 66.5 (1C, s). ^{19}F NMR ($CDCl_3$): δ −71.2

(9F, s), −75.6 (3F, s). IR (neat) ν, cm^{-1}: 1271 (vs), 1253 (vs), 1168 (s), 1146 (s) and 974 (s).

4.10. General procedure of the selection of the resolving agent

The racemic acid (±)-**SO***H_2O (35.9 mg, 0.10 mmol) was first dissolved in 0.10 M aq-NaOH (2.00 ml) at 100 °C, then the clear solution obtained treated with a half-equivalent of the chiral base selected from the (−)-**EPA***HCl and (−)-**1**–**6***HCl family. The mixtures were heated at 90 °C for 6 h and then cooled to r.t. One of the seven bases, **1***HCl, effected crystallization (Table 3). This salt was filtered out, then the clear aqueous phase acidified with 1 M H_2SO_4 to pH 2 at 0 °C. The precipitated **SO***H_2O was filtered and washed with water, then dried (i.v. P_2O_5).

4.11. Optical resolution of (±)-2-(8-carboxy-1-naphthylsulfinyl)benzoic acid

The racemic acid (±)-**SO***H_2O (0.359 g, 1.00 mmol) was dissolved in 0.1 M NaOH (20 ml) and heated to 100 °C. Then, **1***HCl (0.62 g, 1.00 mmol) was added and the mixture was stirred at 90 °C for 6 h. After cooling to r.t. the crystals were filtered off, washed with water and dried to give the diastereomeric salt with (+)-rotation {(+)-**SO***((−)-**1**$)_2$} (0.61 g, mp 90.5–91.5 °C, $[\alpha]_{578} = +77$, $c = 0.5$, DMF). To liberate the (+)-acid the latter salt was dissolved in $CHCl_3$ (10 ml) and treated with 1 M Na_2CO_3 (3 × 3 ml). The alkaline phase was acidified with 1 M H_2SO_4 to pH 2. The precipitate was filtered, washed with water and dried to yield (+)-**SO***H_2O (0.117 g, $[\alpha]_{578} = +343$, ee = 68%, $c = 0.5$, DMF). The resolving agent amine (*S*)-(−)-**1** (0.46 g, 79%) was recovered by the evaporation of the $CHCl_3$ phase. The clear aqueous filtrate of the (+)-diastereomeric salt {(+)-**SO***((−)-**1**$)_2$} was acidified with 1 M H_2SO_4 to pH 2 and the precipitated (−)-acid was filtered off, washed with water and dried to give the partially resolved acid (−)-**SO***H_2O (0.18 g, $[\alpha]_{578} = -259.5$, ee = 51%, $c = 0.5$, DMF). These partially resolved (+)- and (−)-acid samples showed identical properties and spectral data to that reported in ref. [15].

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