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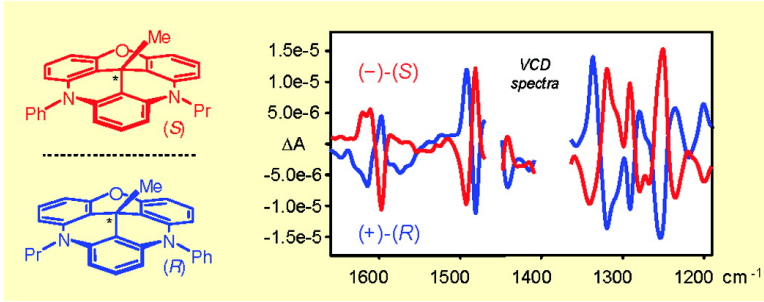

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Synthesis, Resolution, and VCD Analysis of an Enantiopure Diazaoxatricornan Derivative

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Abstract: Using simple organic synthetic transformations, a novel diazaoxatricornan derivative, the 12*c*-methyl-12-phenyl-8-propyl-12,12*c*-dihydro-8*H*-4-oxa-8,12-diazadibenzo[*cd*,*mn*]pyrene (**6a**), was prepared. This novel chiral cup-shaped molecule was isolated in racemic form and in excellent yield after the addition of methyl lithium to the BF_4 salt of a novel unsymmetrical diazaoxatriangulenium cation. Compound **6a** was found to be stable under classical laboratory conditions—something not obvious considering the extreme stability of the carbenium ion precursor, the electron-rich nature of the core, and the strain induced by the pyramidalization of the central carbon. The enantiomers were readily separated by chiral stationary phase chromatography, and the absolute configuration of (−)-(*S*)-**6a** was determined by a comparison of the experimental and theoretical vibrational circular dichroism (VCD) spectra. This isolation of (−)-(*S*)-**6a** and (+)-(*R*)-**6a** constitutes thus the first report of a nonracemic closed-capped chiral bowl molecule for which the chirality is due to the intrinsic dissymmetry of the central core of the structure only.

Introduction

Construction of fully ring-closed polycyclic structures distorted from planarity have long been regarded as remarkable synthetic targets.[1] These bowl-shaped molecules can exhibit unusual molecular properties and/or abnormal chemical behaviors.[1,2] Some of the edifices are potential intermediates for the generation of fullerenes, carbon nanotubes, and other artificial bent structures and receptors.[1,3] To our knowledge, most of the reported structures are achiral. The few chiral fully fused polycyclic derivatives have been characterized in racemic form only owing to their configurational lability or to a lack of resolution.[4–6] In this context, the isolation of an enantiopure closed-capped bowl-shaped molecule would be an important novelty, with the synthesis, resolution, and absolute configuration assignment of the nonracemic structure being possibly a challenging task.

Previously, Siegel et al. have reported the synthesis of trioxatricornan derivatives that constitute an interesting class

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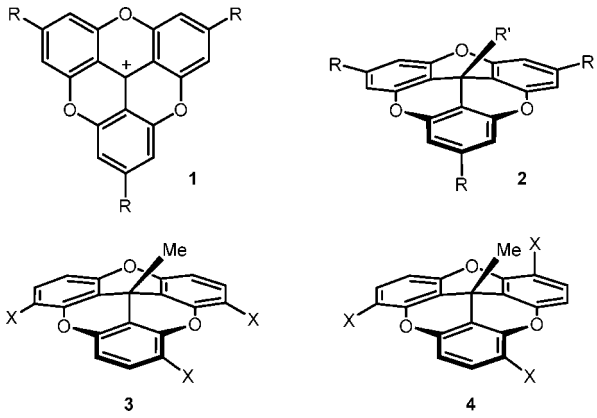

Figure 1. Trioxatriangulenium cation **1** and trioxatricornan derivatives **2**, **3**, and **4**. R = H, *t*Bu; R′ = Me, vinyl, allyl, CH_2COCH_3; X = NO_2, Br, $SiMe_3$.

of polyaromatic molecular cavities useful for the construction of macrocyclic cages. The synthesis of these organic building blocks is straightforward, versatile, and can be achieved on a large scale through the simple addition of a hydride or an organometallic reagent to salts of trioxatriangulenium cations of type **1**. Typical examples are compounds **2** detailed in Figure 1 (R = H, *t*-Bu; R′ = H, alkyl, allyl, vinyl, etc.).[6,7]

Such trioxatricornans are achiral by virtue of the symmetrical distribution of the substituents at the periphery of the core structure. However, any unsymmetrical pattern for functional groups or side chains at the exterior of the molecule creates a dissymmetry and the occurrence of molecular chirality. Regioisomeric derivatives **3** and **4** (Figure 1), prepared by electrophilic substitution reactions onto compounds of type **2** (R = H, R′ = Me), are two typical examples of chiral analogues with C_1- and C_3-symmetry, respectively. To the best of our knowledge, compounds of type **3** and **4** have only been reported in racemic form.

Recently, Laursen and Krebs have shown that nitrogen analogues of the trioxatriangulenium cation **1** can also be readily prepared and, for the interest of this study, diazaoxatriangulenium cations **5** in particular (Figure 2, $R^1 = R^2 =$ *n*-Pr, *n*-Hex, *n*-Oct).[8,9] This novel family of carbenium ions, featuring both aza and oxa bridge(s), have been studied for their photochemical and photophysical properties. Their global chemical reactivity is, however, undocumented. In terms of chirality, it occurred to us that these planar achiral derivatives could actually constitute an interesting platform for the formation of novel closed-capped chiral bowl molecules. In fact, any addition of a nucleophile to the central sp^2 carbon of an unsymmetrical diazaoxatriangulenium cation (**5**, $R^1 \neq R^2$) would generate a curved diazaoxatricornan derivative that would be chiral due to the symmetry-breaking presence of the different nitrogen substituents.

However, close examination of the known properties of these carbenium ions **5** was raising several issues about the feasibility of the project. First of all, it was debatable whether these highly stable carbenium ions (pK_{R+} 19.4 for **5** vs 9.1 for **1**) would be electrophilic enough to react with hydride or organometallic reagents and afford products of type **6**, diazaoxatricornan derivatives. Then, if possible, it was unclear whether these compounds **6** would actually be stable under air (oxidative) and moisture conditions, with the very electron-rich nature of the core favoring possible electron transfer and/or ionic decomposition pathways.[10] Finally, it was uncertain whether two different nitrogen substituents could be introduced at the periphery of **6** (e.g., Figure 2, $R^1 \neq R^2$),[11] with this condition being an absolute must for the creation of a central stereogenic sp^3 center upon the addition of the nucleophilic reagent. Herein, we report that chiral compounds of type **6** can indeed be made as we detail the synthesis, resolution, and vibrational circular dichroism (VCD) analysis of a quasi-enantiopure diazaoxatricornan derivative (**6a**, Figure 2, R′ = Me, R^1 = Ph, R^2 = *n*-Pr), with compound **6** being furthermore the first nonracemic closed-capped chiral bowl molecule for which the chirality is due to the intrinsic dissymmetry of the central core only.

Results and Discussion

Choice of a Target. Having decided that the target of the study would be a chiral compound of type **6**, the next task was the choice of the substituents R′, R^1, and R^2 taking in consideration the need for (1) two different substituents on the N atoms, (2) apical and lateral side chains with minimal degrees of freedom (to help the VCD characterization of the product), and (3) efficient conditions to separate the enantiomers of the target after its synthesis in racemic form. As just mentioned, diazaoxatricornan derivative **6a** was chosen, and the selection process of the three groups R′, R^1, and R^2 is detailed below.

First, it was decided to introduce a methyl as the apical group R′. This alkyl group is devoid of any conformational issue and possibly easily introduced as the last step of the synthesis by nucleophilic addition of methyl Grignard or methyl lithium to the central carbon of an appropriate diazaoxatriangulenium precursor of type **5** (Figure 2 and Scheme 1). Next, a phenyl group was selected as substituent R^1, as the planar rigid nature of this group was also fitting the second selection rule. In terms of synthesis, its incorporation into the global framework was considered to be trivial, as literature precedents indicated that anilines react at elevated temperature with salts of the tris(2,6-dimethoxyphenyl)carbenium ion **7** to afford in good yields aryl-substituted acridinium derivatives of type **8** (vide infra, Scheme 1).[12]

The choice of a *n*-propyl group as the final substituent R^2 was straightforward. In terms of synthesis, it was quite clear that only an aliphatic amine would react with an acridinium moiety of type **8**;[8,12] the formation of the second nitrogen bridge requires forcing conditions and nucleophilic amines (25 equiv, 110 °C, NMP). The *n*-propyl group was then selected for its good literature precedents as nucleophile in this type of ring

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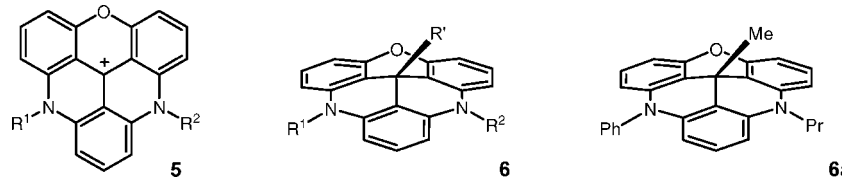
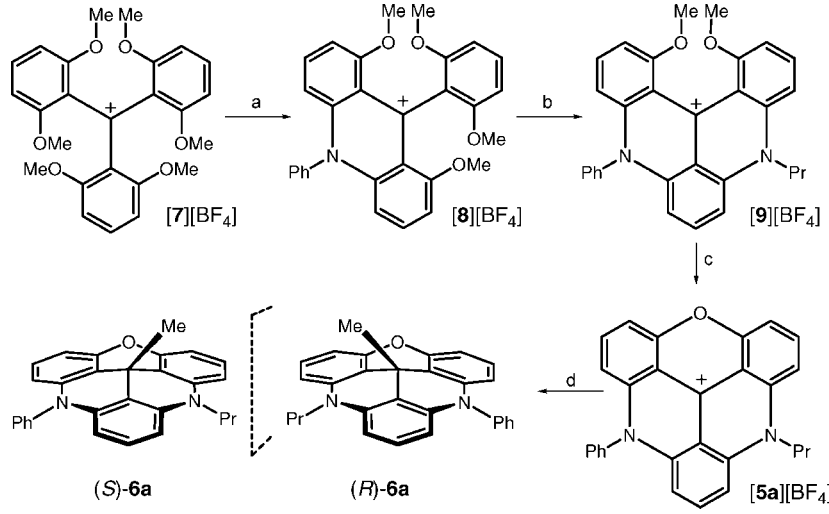


Figure 2. Diazaoxatriangulenium cations **5** ($R^1 = R^2 =$ *n*-Pr, *n*-Hex, *n*-Oct) and chiral diazaoxatricornan derivatives **6** (R′, $R^1 \neq R^2$).

Scheme 1[a]



[a] Conditions: (a) $PhNH_2$ (22 equiv), NMP, 120 °C, 1.5 h, 95%; (b) *n*-$PrNH_2$ (25 equiv), NMP, 110 °C, 2.5 h, 45%; (c) LiI (100 equiv), NMP, 180 °C, 1.5 h, 65%; (d) MeLi (1.3 equiv), THF, 20 °C, 16 h, 97%.

closure and despite a high probability of an occurrence of several conformers in the final product, with the second aza ring closure being deemed easier to perform with higher boiling *n*-$PrNH_2$ than gaseous $MeNH_2$.

Synthesis and Basic Optical Properties. With the selection of substituents made, the synthesis was started. First, purple tris(2,6-dimethoxyphenyl)carbenium tetrafluoroborate salt [**7**][BF_4] was synthesized using a procedure similar to that reported by Wada et al.[13] Then treatment of [**7**][BF_4] with aniline (22 equiv, NMP, 120 °C) gave the red acridinium salt [**8**][BF_4] in an excellent yield (95%).[12] After that, following classical conditions,[8] [**8**][BF_4] was reacted with *n*-propylamine (25 equiv, NMP, 110 °C) to afford the green quinacridinium salt [**9**][BF_4], albeit in modest yield (45%).[14] Finally, conversion of [**9**][BF_4] into the hexacyclic diazaoxatriangulenium salt [**5a**][BF_4] was achieved by reaction with LiI (NMP, 180 °C, 65% yield). Subsequent addition of MeLi resulted in the formation of desired diazaoxatricornan **6a** in racemic form and excellent yield (97%). All the steps and compounds are detailed in Scheme 1.

Not surprisingly, novel salts [**8**][BF_4], [**9**][BF_4], and [**5a**][BF_4] are also colorful dyes, and their electronic absorption spectra are reported in the Supporting Information and as a brief preview in Figure 3 (CH_2Cl_2, 10^{-4} mol·L^{-1}).

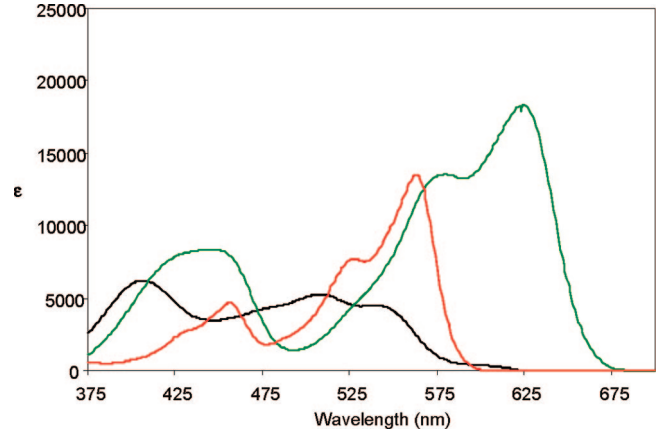


Figure 3. Absorption spectra of compounds [**8**][BF_4] (black), [**9**][BF_4] (green), and [**5a**][BF_4] (red) (CH_2Cl_2, 10^{-4} mol·L^{-1}).

Enantiomeric Chromatographic Separation on Chiral Stationary Phases. With targeted compound *rac*-**6a** in hand, we turned our attention to its enantiomeric resolution. Preparative chromatographic resolution on chiral stationary phases is now recognized as a very powerful and general method to separate and isolate enantiomers of racemic compounds in good yield and high optical purity.[15,16] This approach was applied to *rac*-**6a** to gain the single pure enantiomers. In order to perform the preparative resolution of *rac*-**6a**, we first developed an appropriate separation method by screening a number of chiral stationary phases with different mobile phase mixtures. Most of these chiral

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(14) The relative low yield might be due to an aerobic photooxidative decomposition of *n*-$PrNH_2$ catalyzed by acridinium salt [**8**][BF_4]. For examples, see: (a) Shinkai, S.; Hamada, H.; Kuroda, H.; Manabe, O. *J. Org. Chem.* **1981**, *46*, 2333–2338. (b) Nicolas, C.; Herse, C.; Lacour, J. *Tetrahedron Lett.* **2005**, *46*, 4605–4608. (c) Ohkubo, K.; Nanjo, T.; Fukuzumi, S. *Bull. Chem. Soc. Jpn.* **2006,** *79*, 1489−1500, and references therein.

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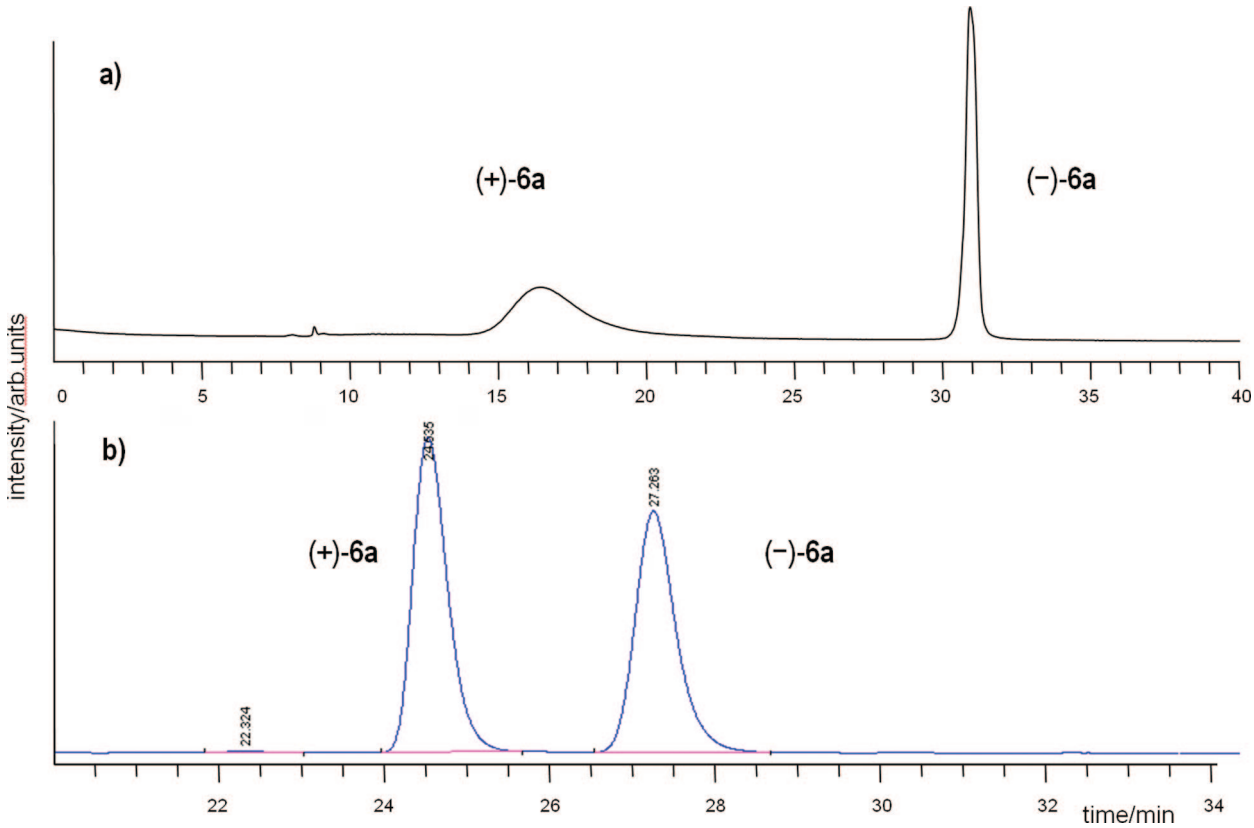

Figure 4. Analytical chromatographic resolution of *rac*-**6a** on (a) Chiralcel OJ-H, *n*-hexane/methanol 995:5, 0.5 mL·min^{-1}, 23 °C, $\lambda = 254$ nm and (b) Chiralpak AD-H, *n*-hexane/2-propanol 995:5, 1 mL·min^{-1}, 23 °C, $\lambda = 254$ nm.

stationary phases were based on polysaccharide derivatives and are commercially available. A good separation could be achieved on the cellulose-based phase Chiralcel OJ using a mixture of hexane/methanol 995:5 (volume) and on the amylose-based phase Chiralpak AD using a mixture of hexane/2-propanol 995:5 (volume) (Figure 4).[17]

However, because the separation factor was much higher on Chiralcel OJ (2.49 compared to 1.23 on Chiralpak AD), the preparative separation was performed on the cellulose-based phase. For that purpose, a larger (25 mm × 250 mm) in-house packed column containing Chiralcel OJ was employed and the same mobile phase mixture was applied. As the solubility of the racemate **6a** was very poor in the mobile phase (about 0.02%), the separation of 70 mg had to be carried out by repetitive injections which were all fractionated in three major fractions. After pooling of the corresponding fractions from the multiple injections, they were evaporated to dryness. Fractions 1 and 3, which contained highly enriched amounts of the first and last eluting enantiomers, respectively, were redissolved in the applied mobile phase and reinjected on the same column (Chiralcel OJ) to afford, after fractionation and evaporation, the desired enantiomers in high enantiomeric excesses. Interestingly, the optically enriched materials obtained after the first chromatographic run are very soluble in the applied mobile phase.

In summary, the two enantiomers could be separated analytically by chromatography on chiral stationary phases (Figure 4).

(17) The unusual peak shape and elution profile on Chiralcel OJ (Figure 4, top trace) of the enantiomers of **6a** is a known phenomenon in enantioselective chromatography and has been observed in some instances in our laboratories and other research groups. Although we have no clear explanation for this feature, it indicates that both enantiomers exhibit quite different adsorption kinetics, suggesting that they interact with different sites within the chiral polymer matrix.

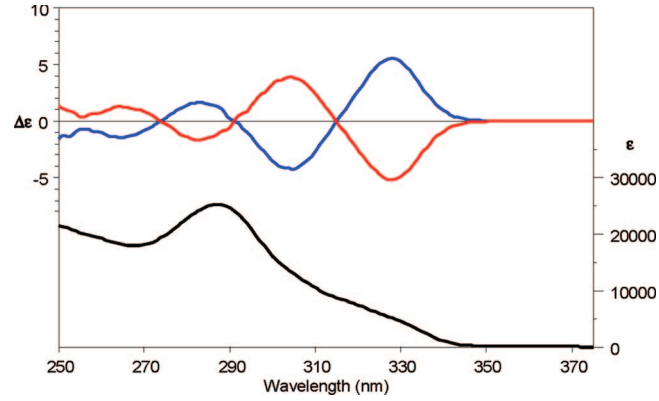

Figure 5. Electronic absorption spectrum of **6a** (black, bottom) and ECD spectra (top) of the most (blue) and least (red) eluted fractions (CH_2Cl_2, 10^{-4} mol·L^{-1}), (+)-**6a** and (−)-**6a**, respectively.

The two enantiomers were obtained on preparative scale in very high enantiomeric purity. From a batch of 70 mg of racemic **6a**, two separated fractions were afforded in good yields, 26 mg (99.2% ee) and 19 mg (98.1% ee) for the first and second eluted fractions, respectively. These fractions correspond to (+)-**6a** and (−)-**6a** as indicated by the specific optical rotation values, $[\alpha]^{20}_D = +16.1$ and -13.2 (CH_2Cl_2, $c = 0.1$ g/100 mL), respectively.

Electronic circular dichroism (ECD) spectra of these most and least eluted compounds displayed totally symmetrical curves in the 250−350 nm region. The spectra are reported in Figure 5. At the lowest energy, positive and negative Cotton effects ($\Delta\epsilon_{328} = +5.5$ and -5.2) are observed for (+)-**6a** and (−)-**6a**, respectively. If one follows the spectrum of one of the separated

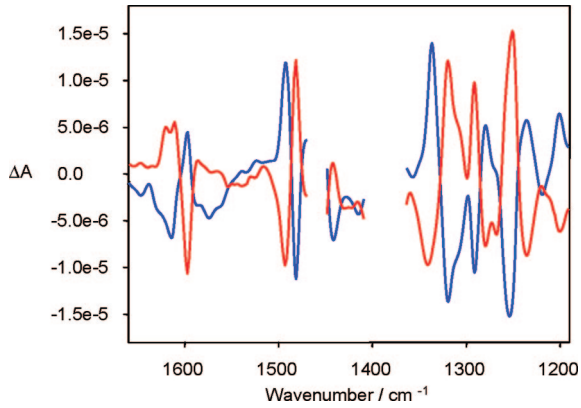

Figure 6. VCD spectra of the most (first, blue) and least (second, red) eluted fractions of **6a**. The spectra were measured in CD_2Cl_2 at a concentration of 11.3 mg/mL. Some parts of the spectra are missing due to strong solvent absorption in these regions.

enantiomers, then a series of sequentially opposite Cotton effects can be observed from 250 to 350 nm. Whereas the $\epsilon/\Delta\epsilon$ ratio is rather large at the highest energy and near the maximum of the electronic absorption ($\epsilon/\Delta\epsilon_{287} \sim 20\,000$), a more classical ratio is obtained around 328 nm ($\epsilon/\Delta\epsilon \sim 1000$).

Absolute Configuration Determination. Vibrational circular dichroism (VCD) measures the tiny differences in absorption of left and right circularly polarized infrared radiation by chiral enantioenriched samples.[18] The method is a sensitive probe of chirality and was used in the past to determine the absolute configuration of enantiomers and also the conformation of molecules.[19] VCD has become a valuable alternative tool for absolute configuration determination especially in cases where suitable single crystals cannot be grown for analysis by X-ray crystallography. The structural information (absolute configuration, conformation) contained in a VCD spectrum can be extracted by comparison with spectra obtained from electronic structure calculations. It has been demonstrated in the past that VCD spectra calculated by density functional theory (DFT) methods have predictive quality.[20] This allows assignment of the absolute configuration since enantiomers have mirror image VCD spectra. A rather large variety of structurally different chemical substances have been analyzed by VCD in the past. To our knowledge, experimental and theoretical studies on compounds similar to chiral tricornan derivative **6a** have not been reported to date.

Figure 6 shows the VCD spectra of the enantiomers of **6a** separated by CSP HPLC. The measured signals are small, which intuitively agrees with the fact that chirality is due to the intrinsic dissymmetry of the central core of the structure only. The VCD spectra of the two enantiomers are almost mirror images, and deviations thereof are attributed mainly to noise.

In order to determine the absolute configuration of the enantiomers in the two eluted fractions, DFT calculations at the B3PW91,6-31G(d,p) level of theory were performed on the (*S*)-**6a** enantiomer.[21] Prior to the calculation of VCD spectra, we searched for the conformations of the molecule (vide infra, Figure 7).

The tricornan skeleton is rigid and does not bring conformational degrees of freedom. Also, concerning the phenyl residue of the nitrogen-bridging atom in position 4, there is only one possible conformation. Due to steric repulsion between the diazaoxatricornan protons H_3 and H_5 and *o*,*o*′-protons of aniline, the phenyl residue is perpendicular to the tricornan system. Finally, concerning the linear propyl chain, there are two important degrees of freedom corresponding to two dihedral angles centered around the N−C and a C−C bond. This entails overall $3 \times 3 = 9$ plausible conformers. Two are unstable and seven have energies according to the calculations, ranging from 0.0 to 2.91 kcal·mol^{-1}.

The most stable conformer (**3**, 0.0 kcal·mol^{-1}) is the one where the propyl chain is in an antiperiplanar conformation and points away from the tricornan skeleton. Then, IR and VCD of all nine conformers were calculated.[22] Figure 8 compares calculated IR and VCD spectra of conformer **3** and of a Boltzmann distribution of all stable conformers.

It revealed that only minor differences between VCD and IR spectra of the Boltzmann average and conformer **3** were observable due to the presence of the latter at 85% compared to other conformers.

At last, comparison between simulated and experimental IR and VCD spectra undoubtedly showed that the second eluted (levoratory) fraction corresponds to (*S*)-**6a** enantiomer (vide supra, Figures 9 and 10).[23]

Perspectives

Herein, using simple organic synthetic transformations, we have reported the synthesis of a novel racemic diazaoxatricornan derivative. The enantiomers of which were readily separated by chiral stationary phase chromatography. The absolute configuration of (−)-(*S*)-**6a** was determined by a comparison of the experimental and theoretical VCD spectra. Many of the chiroptical properties of compound **6a** have been examined, and apart from VCD, this compound has displayed rather strong manifestations of molecular chirality. A posteriori, the initial selection of Me, Ph, and *n*-Pr as substituents R′, R^1, and R^2 seems to have been ideal for the purposed study as it has allowed us to establish the feasibility of the synthetic protocol, the efficiency of CSP-HPLC as a resolution method, and the global chemical stability of the chiral cup-like molecule **6a**—things that were not completely obvious at the start of the study. This isolation of (−)-(*S*)-**6a** and (+)-(*R*)-**6a** constitutes thus the first

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(21) The CIP (Cahn−Ingold−Prelog) System has been used for the absolute configuration assignment of the enantiomers of **6a**. The prioritization of the substituents around the central (and only) stereogenic quaternary sp^3 center has been performed according to the sequence rules detailed in the following articles: (a) Cahn, R. S.; Ingold, C.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 385–415. (b) Prelog, V.; Helmchen, G. *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 567−583. In **6a**, the three sp^2 carbons adjacent to the central sp^3 center are hierarchically ranked in the following order (from the highest to the next lower rank) (i) the sp^2 carbon closer to the O atom and the NPh moiety, respectively, then (ii) the carbon between the O atom and the NPr group, and finally (iii) the carbon flanked by the NPh and NPr moities, with the apical methyl group being the substituent with the lowest priority of all.

(22) IR and VCD spectra for all nine conformers of (*S*)-**6a** are reported in the Supporting Information.

(23) Even if the agreement between calculated and experimental IR and VCD spectra is not perfect, absolute configuration can be still determined. Indeed, some characteristic bands such as modes 16,17, 21, 3, and 6 can be assigned without ambiguity.

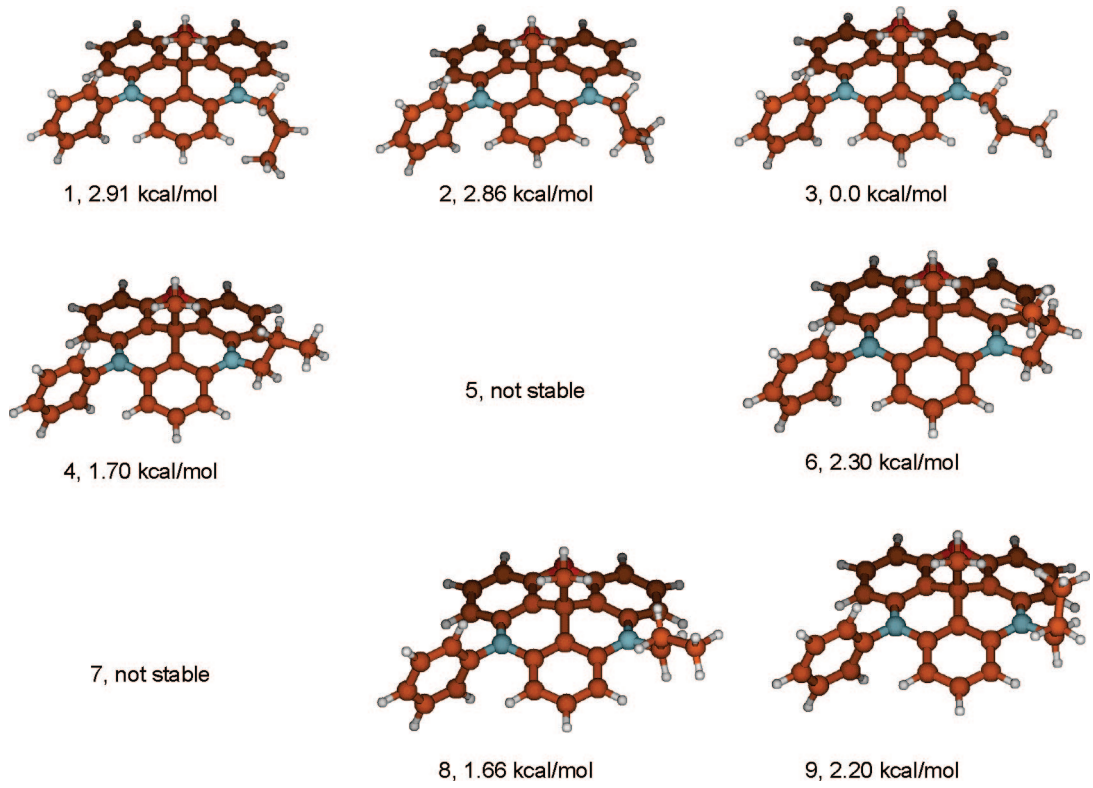

Figure 7. Structures and relative energies of possible conformers of enantiomer (*S*)-**6a**. All calculations were made at the B3PW91,6-31G(d,p) level of theory by relaxing all degrees of freedom without constraint.

report of a nonracemic closed-capped chiral bowl molecule for which the chirality is due only to the intrinsic dissymmetry of the central core of the structure.

Materials and Methods

9-(2,6-Dimethoxyphenyl)-1,8-dimethoxy-10-phenylacridinium tetrafluoroborate salt or [8][BF_4]. Compound [**7**][BF_4] (0.72 g, 1.4 mmol) was dissolved in 1-methyl-2-pyrrolidone (NMP) (10 mL), and aniline (3 mL, 31 mmol) was added. The initially purple reaction mixture was heated to 120 °C under dinitrogen atmosphere for 1.5 h. After cooling to 25 °C, the crude mixture was poured into ether (15 mL) and the resulting dark red precipitate was collected by filtration over a Büchner funnel. The title compound was further purified by dissolution in acetone and selective precipitation by addition of Et_2O, affording the desired tetrafluoroborate salt [**8**][BF_4] (0.73 g, 95%): mp 223 °C; ^{1}H NMR (CD_3CN, 400 MHz) $\delta = 7.97$ (d, $J = 7.8$ Hz, 1H), 7.96 (d, $J = 8.1$ Hz, 1H), 7.89 (t, $J = 3.3$ Hz, 3H), 7.61 (m, 2H), 7.49 (t, $J = 8.6$ Hz, 1H), 7.08 (d, $J = 8.1$ Hz, 2H), 6.92 (d, $J = 9.1$ Hz, 2H), 6.83 (d, $J = 8.5$ Hz, 2H), 3.62 (s, 6H), 3.58 (s, 6H); ^{13}C NMR (CD_3CN, 100 MHz) $\delta = 160.2$ (C), 155.8 (C), 143.0 (C), 139.5 (CH), 138.8 (C), 131.4 (CH), 131.4 (CH), 119.6 (C), 119.3 (C), 111.0 (C), 106.5 (C), 103.7 (C), 56.8 (CH_3), 55.6 (CH); ^{19}F NMR (282 MHz, CD_2Cl_2) $\delta = -151.5$ (20%), -151.6 (80%); UV/vis (CH_3CN, 10^{-4} M, λ_{max} (log ϵ)) 541 (3.65), 509 (3.7), 359 (3.56); IR (neat) $\nu =$ 2941, 2839, 1596, 1575, 1495, 1468, 1432, 1374, 1360, 1346, 1277, 1263, 1250, 1105, 1082, 1046, 980, 817, 783, 764, 730, 701, 681, 653 cm^{-1}; MS *m/z* (ES) 406.1, 452.3; HRMS (ESI, *m/z*) calcd for $C_{29}H_{26}NO_4^+$ [M^+], 452.1856; found, 452.1865.

Racemic-5-phenyl-9-propyl-1,13-dimethoxyquinacridinium tetrafluoroborate salt or [9][BF_4]. At 25 °C, *n*-propylamine (2.5 mL, 58.0 mmol) was added to a solution of 9-(2,6-dimethoxyphenyl)-1,8-dimethoxy-10-phenyl-9,10-dihydroacridinium tetrafluoroborate salt [**8**][BF_4] (0.72 g, 1.33 mmol) in NMP (10 mL). The reaction mixture was heated at 120 °C under a dinitrogen atmosphere for 2.5 h and then allowed to cool to 25 °C. Addition of water (~25 mL) afforded a green precipitate, which was filtered over a Büchner funnel, washed with water, several times with Et_2O, and collected. The title compound was further purified by (i) dissolution of crude product in CH_2Cl_2 and (ii) selective precipitation by addition of Et_2O, affording the dimethoxyquinacridinium tetrafluoroborate salts [**9**][BF_4] (0.32 g, 44%): mp 332 °C; ^{1}H NMR (CD_3CN, 400 MHz) $\delta = 7.96$ (m, 2H), 7.82 (m, 3H), 7.67 (t, $J = 8.1$ Hz, 1H), 7.60−7.52 (br s, 1H), 7.54 (m, 2H), 7.48−7.40 (br s, 1H), 6.97 (d, $J = 8.1$ Hz, 1H), 6.91 (d, $J = 7.8$ Hz, 1H), 6.66 (d, $J = 8.3$ Hz, 1H), 6.55 (d, $J = 8.8$ Hz, 1H), 4.72−4.64 (m, 1H), 4.82−4.40 (m, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 2.13−2.03 (m, 2H), 1.20 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (CD_3CN, 100 MHz) $\delta = 160.8$ (C), 160.4 (C), 144.6 (C), 144.5 (C), 143.4 (C), 141.4 (C), 139.7 (C), 139.2 (C), 138.3 (CH), 137.5 (CH), 137.0 (CH), 131.5 (CH), 119.8 (C), 114.2 (C), 113.3 (C), 109.7 (CH), 108.6 (CH), 107.2 (CH), 106.0 (CH), 104.1 (CH), 104.0 (CH), 56.6 (CH_3), 56.5 (CH_3), 52.2 (CH_2), 20.4 (CH_2), 11.1 (CH_3); ^{19}F NMR (376 MHz, CD_3CN) $\delta = -151.7$ (20%), -151.8 (80%); UV/vis (CH_2Cl_2, 10^{-4} M, λ_{max} (log ϵ)) 624 (4.25), 580 (4.13), 446 (3.91); IR (neat) $\nu = 2973$, 2945, 2884, 2836, 1603, 1579, 1553, 1494, 1345, 1253, 1247, 1172, 1046, 1033, 814, 760 cm^{-1}; MS *m/z* (ES) 401.3, 447.1; HRMS (ESI, *m/z*) calcd for $C_{30}H_{27}N_2O_2^+$ [M^+], 447.2067; found, 447.2072.

8-Phenyl-12-propyl-12,12*c*-dihydro-8*H*-4-oxa-8,12-diazadibenzo[*cd*,*mn*]pyrenium tetrafluoroborate salt or [5a][BF_4]. At 25 °C, LiI (58.0 mmol) was added to a solution of racemic-5-phenyl-9-propyl-1,13-dimethoxyquinacridinium tetrafluoroborate salt [**9**][BF_4] (0.3 g, 0.56 mmol) in NMP (10 mL). The reaction mixture was heated at 180 °C for 1.5 h and then allowed to cool to room temperature. Addition of water (~25 mL) afforded a precipitate, which was filtered over a Büchner funnel, washed with water, several times with Et_2O, and collected. Purification by column chromatography over silica gel (CH_2Cl_2/MeOH 99:1, 24 × 2.5 cm) gave a red material corresponding to salt [**5a**][BF_4] (0.46 g, 65%): mp 298 °C; ^{1}H NMR (CD_3CN, 400 MHz) $\delta = 8.14$ (t, $J = 8.8$ Hz, 1H), 8.05 (t, $J = 8.6$ Hz, 1H), 7.95−7.81 (m, 4H), 7.69 (d, $J = 8.8$ Hz, 1H), 7.55−7.50 (m, 3H), 7.39 (d, $J = 8.1$ Hz, 1H), 7.31

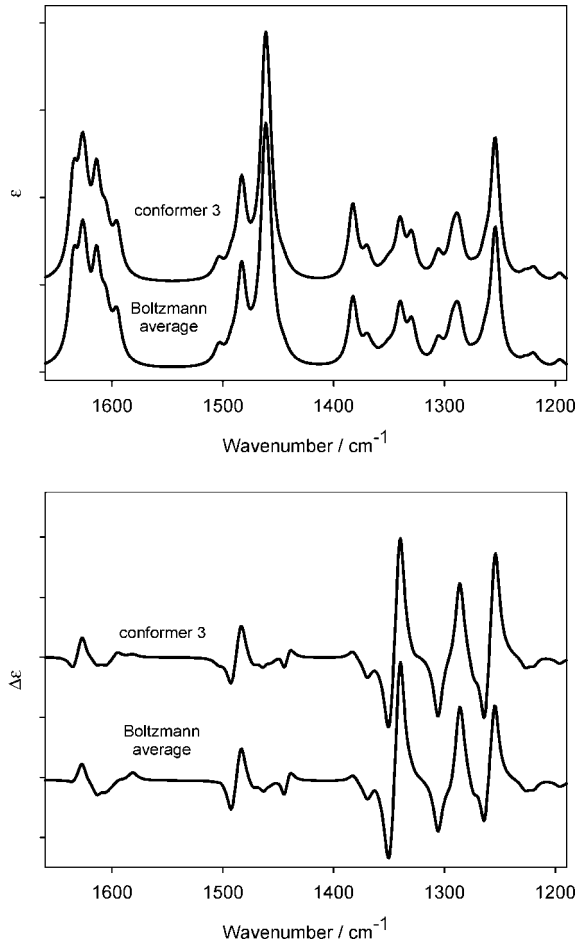

Figure 8. Calculated IR (top) and VCD (bottom) spectra: Comparison between conformer **3** and Boltzmann average of all seven conformers for $T = 298$ K.

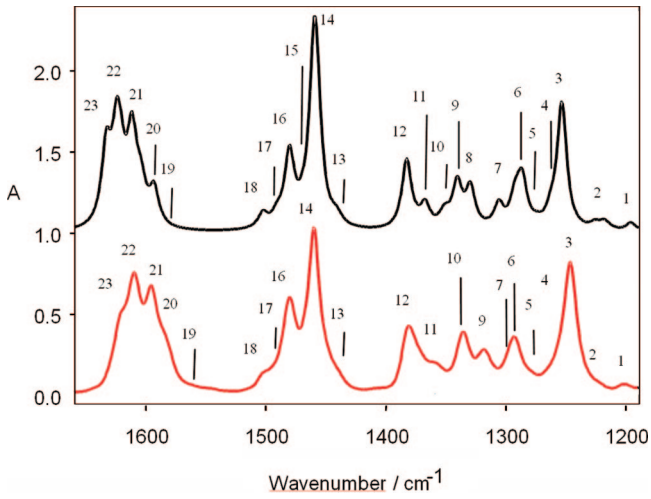

Figure 9. Experimental (red) and calculated (black) IR spectra of the least (second) eluted (levoratory) fraction and (*S*)-**6a**, respectively; $T = 298$ K. The calculations were performed at the B3PW91,6-31G(d,p) level.

(d, $J = 8.4$ Hz, 1H), 6.62 (d, $J = 8.6$ Hz, 1H), 6.58 (d, $J = 8.6$ Hz, 1H), 4.51 (t, $J = 8.3$ Hz, 2H), 2.05−1.95 (m, 2H), 1.21 (t, $J = 7.28$ Hz, 1H); ^{13}C NMR (CD_3CN, 100 MHz) $\delta = 153.9$ (C), 153.4 (C), 143.7 (C), 142.3 (C), 141.7 (C),141.6 (C), 141.1 (C), 140.2 (CH), 139.8 (CH), 139.1 (CH), 138.5 (C), 133.0 (CH), 131.8 (CH), 129.3 (CH), 112.4 (C), 111.2 (CH), 110.5 (CH), 109.5 (CH), 109.5 (CH), 109.0 (C), 108.4 (C), 107.9 (CH), 107.1 (CH), 50.3 (CH_2),

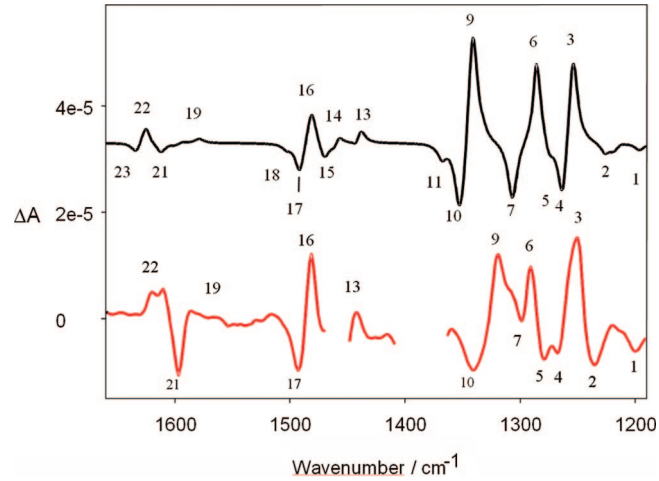

Figure 10. Experimental (red) and calculated (black) VCD spectra of the least (second) eluted (levoratory) fraction and (*S*)-**6a**, respectively; $T = 298$ K. The calculations were performed at the B3PW91,6-31G(d,p) level.

19.9 (CH_2), 11.1 (CH_3); ^{19}F NMR (376 MHz, CD_3CN) $\delta = -151.7$ (20%), −151.8 (80%); UV/vis (CH_2Cl_2, 10^{-4} M, λ_{max} (log ϵ)) 563 (4.13), 527 (3.88), 456 (3.66); IR (neat) $\nu = 2963$, 1607, 1583, 1523, 1488, 1453, 1338, 1303, 1247, 1189, 1167, 1147, 1098, 1071, 1054, 815, 765, 732, 703 cm^{-1}; MS *m*/*z* (ES) 358.1, 401.3; HRMS (ESI, *m*/*z*) calcd for $C_{28}H_{21}N_2O^+$ [M^+], 401.1648; found, 401.165.

Racemic 12*c*-Methyl-12-phenyl-8-propyl-12,12*c*-dihydro-8*H*-4-oxa-8,12-diazadibenzo[*cd*,*mn*]pyrene 6a. The reaction was conducted under dinitrogen atmosphere. To a suspension of 8-phenyl-12-propyl-12,12*c*-dihydro-8*H*-4-oxa-8,12-diazadibenzo[*cd*,*mn*]pyrenium tetrafluoroborate salt [**5a**][BF_4] (60 mg, 0.12 mmol) in THF (4 mL) at 0 °C was added an excess of MeLi in ether (100 μL, 0.16 mmol). The red suspension progressively disappeared to give an orange solution which was stirred overnight (16 h). The reaction was quenched by addition of two drops of ethanol and ether (10 mL). The organic layer was washed with water, dried over Na_2SO_4, and concentrated in vacuo to give **6a** as a white glassy solid (50 mg, 97%): mp 201 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) $\delta = 7.61$ (t, $J = 7.3$ Hz, 2H), 7.51 (m, 1H), 7.35 (m, 2H), 7.19 (t, $J = 8.1$ Hz, 1H), 6.95 (dt, $J = 8.3$, 3.3 Hz, 2H), 6.74 (d, $J = 8.4$ Hz, 1H), 6.70 (dd, $J = 8.1$, 1 Hz, 1H), 6.66 (d, $J = 8.4$ Hz, 1H), 6.53 (d, $J = 8.4$ Hz, 1H), 5.96 (d, $J = 8.1$ Hz, 1H), 5.88 (d, $J = 8.1$ Hz, 1H), 3.87 (m, 2H), 1.85 (m, 2H), 1.44 (s, 3H), 1.07 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) $\delta = 151.9$ (C), 151.7 (C), 141.7 (C), 141.5 (C), 140.8 (C), 140.3 (C), 140.0 (C), 131.0 (CH), 130.7 (CH), 128.4 (CH), 127.7 (CH), 127.2 (CH), 127.2 (CH), 108.4 (CH), 108.3 (CH), 108.1 (CH), 106.9 (CH), 106.7 (CH), 105.3 (CH), 47.8 (CH_2), 29.8 (CH_3), 27.1 (C), 18.7 (CH_2), 11.3 (CH_3); UV/vis (CH_2Cl_2, 10^{-4} M, λ_{max} (log ϵ)) 287 (4.49); IR (film) $\nu = 2953$, 2924, 2868, 1621, 1607, 1593, 1480, 1455, 1353, 1335, 1320, 1293, 1242, 1151, 1042, 783, 762, 745, 730, 700, 652 cm^{-1}; MS *m*/*z* (ES) 417.2, 401.3, 358.3; HRMS (ESI-TOF-MS) calcd (%) for $C_{29}H_{25}N_2O$ [$M + H^+$], 417.1966; found, 417.1953.

Preparative Enantiomeric Separation of *rac*-6a. Preparative enantioselective chromatographic separation was performed using a prep HPLC column (25 mm × 250 mm) packed with Chiralcel OJ (20 μm particle size) and a mixture of *n*-hexane/methanol 995/5 (volume) as the mobile phase. The chromatography was carried out at a flow rate of 20 mL/min under isocratic conditions and at room temperature. Detection was carried out by UV at 254 nm. Seventy milligrams of *rac*-**6a** was dissolved in 300 mL of hexane/methanol 995/5. Portions of 50 mL of this solution were injected repetitively (six times), and three fractions were isolated for each run. Fractions 1 and 3 of each run were pooled and evaporated to give highly enriched amounts of the first and last eluting enantiomers, respectively. Both enantiomerically enriched materials were redissolved in the applied mobile phase and reinjected on the same

column (Chiralcel OJ) to afford, after fractionation and evaporation, the desired enantiomers in high enantiomeric excesses.

(+)-(*R*)-**6a** (26 mg): ee > 99.2% as determined by HPLC (Chiralpak AD-H, *n*-hexane/2-propanol 99:1, 0.2 mL min^{-1}, 23 °C, $\lambda = 254$ nm, $t_R = 23.74$ min); CD (CH_2Cl_2, 1×10^{-4} M, 20 °C) λ ($\Delta\epsilon$) 328 (5.5), 304 (−4.2), 282 (1.6); $[\alpha]_D = +16.1 \pm 1.4$ ($c = 0.1$g/100 mL, CH_2Cl_2).

(−)-(*S*)-**6a** (19 mg): ee > 98.1% as determined by HPLC (Chiralpak AD-H, *n*-hexane/2-propanol 99:1, 0.2 mL min^{-1}, 23 °C, $\lambda = 254$ nm, $t_R = 26.95$ min); CD (CH_2Cl_2, 1×10^{-4} M, 20 °C) λ ($\Delta\epsilon$) 328 (−5.20), 304 (3.9), 282 (−1.7); $[\alpha]_D = -13.2 \pm 1.6$ ($c = 0.1$g/100 mL, CH_2Cl_2).

Vibrational Circular Dichroism. A Bruker PMA 50 accessory coupled to a Tensor 27 Fourier transform infrared spectrometer was used to measure IR and VCD spectra. Modulation of the handedness of the circular polarized light was achieved by a photoelastic modulator (Hinds PEM 90) set at 1/4 retardation, and a lock-in amplifier (SR830 DSP) was used for demodulation. To enhance the signal/noise ratio, an optical low-pass filter (<1800 cm^{-1}) was put before the photoelastic modulator. Solutions of **6a** were prepared in CD_2Cl_2 at a concentration of 11.3 mg/mL. All spectra were measured at a resolution of 6 cm^{-1} in a cell equipped with CaF_2 windows and a 0.5 mm Teflon spacer. The VCD spectrum of a racemic mixture of **6a** served as the reference. This spectrum was subtracted from the VCD spectra of the enantiomers. Both samples and reference were measured 4 h in time slices of 20 min, corresponding to about 24 000 scans for each sample and reference, respectively.

Calculation of the IR and VCD spectra was performed using Gaussian03.[24] The B3PW91 hybrid functional[25] was used with a 6-31G(d,p) basis set.[26] Prior to the calculation of the IR and VCD spectra, complete structural relaxation was performed on all conformers. Normal mode analysis revealed that all stationary points found were true minima. For the simulation of the spectra, calculated IR and VCD intensities were convoluted with Lorentzian line shapes with a full width at half-maximum of 6 cm^{-1}.

Acknowledgment. We are grateful for financial support of this work by the Swiss National Science Foundation, the State Secretariat for Education and Research, the Schmidheiny Foundation, and the Société Académique de Genève.

Supporting Information Available: ^{1}H NMR, ^{13}C NMR, ^{19}F NMR, UV, LRMS, and HRMS spectra of salts [**8**][BF_4], [**9**][BF_4], [**5a**][BF_4], and chiral bowl **6a**. Calculated IR and VCD spectra for the different conformers of (*S*)-**6a**, and complete ref 24. This material is available free of charge via the Internet at http://pubs.acs.org.

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