Cyclopropyl Building Blocks for Organic Synthesis, 60[‡]

Synthesis and Properties of Optically Active Dispiro[2.0.2.1]heptane Derivatives as Novel Ferroelectric Liquid Crystalline Compounds

Kazutoshi Miyazawa,[a,b] Dmitrii S. Yufit,[c] Judith A. K. Howard,[c] and Armin de Meijere*[a]

Dedicated to Professor Günter Helmchen on the occasion of his 60th birthday

Keywords: Chirality / Dispiro[2.0.2.1]heptane / Liquid crystals / Lipases / Spiro compounds

Enantioselective enzymatic acylation, using Lipase PS® (*Pseudomonas* sp., immobilized on Celite, Amano Pharmaceutical Co., Ltd.), of *endo*-dihalosubstituted and nonsubstituted dispiro[2.0.2.1]heptylmethanol and *endo*-4-methylenespiropentylmethanol provided the corresponding optically active compounds in high enantiomeric excesses (> 95% *ee*). Difluorocarbene addition onto the optically active *endo*-4-methylenespiropentylmethanol yielded the first enantiomerically pure difluorodispiro[2.0.2.1]heptylmethanols. The obtained optically active dispiro[2.0.2.1]heptane derivatives were used in syntheses of phenylpyrimidine derivatives, providing novel ferroelectric liquid crystalline compounds with unique physical properties.

Introduction

Ferroelectric liquid crystalline compounds with improved working characteristics are sought after for industrial development of the surface-stabilized liquid crystal (SSFLC) display mode.[1] To achieve the properties desired, an impressive number of optically active liquid crystalline compounds has been synthesized, and their physical properties have been investigated.[2] Since physical properties of ferroelectric liquid crystalline compounds totally depend on the chemical structures of their chiral moieties, different kinds of chiral entities have been proposed and examined with respect to their potentials. Almost all the compounds reported, however, have alkyl-branched alkyl side chains as their chiral moieties.[3] Therefore, the creation and exploration of quite unusual, chemically novel, chiral moieties is potentially important.

Optically active derivatives of higher analogs of spiropentane (so-called [*n*]triangulanes[4,5]), which have not yet been reported in the field of liquid crystal chemistry, should be very interesting and worthwhile subjects for examination as to their potential as novel chiral moieties for ferroelectric liquid crystalline compounds. Side chains consisting of spirofused cyclopropane rings are much more rigid than the alkyl- and halogen-substituted alkyl groups normally used, and they would thus be expected to have restricted rotational mobility; this normally decreases the effective dipole moments of liquid crystalline compounds. This decreased rotational mobility would in turn help to induce greater spontaneous polarization. We therefore designed the new structures − possessing ordinary mesogenic units but with unprecedented optically active dispiro[2.0.2.1]heptyl moieties in one of their side chains − shown in Figure 1, and developed easily executable syntheses for them.

Results and Discussion

The starting materials *rac*-**8** and *rac*-**9** were synthesized by dihalocarbene addition onto THP-protected bicyclopropylidenemethanol **5**,[4a] followed by deprotection under acidic conditions (Scheme 1). $CHCl_3$ and NaOH[6] were used for *rac*-**8**, and CF_2Br_2, PPh_3, KF, and 18-crown-6[7] for *rac*-**9**. It should be noted that the dihalocarbene additions occurred only from the side opposite to the tetrahydropyranyloxymethyl moiety, yielding the *endo* adducts as single diastereomers. The starting material *rac*-**10** was prepared by reduction of readily available ethyl *endo*-dispiro[2.0.2.1]heptanecarboxylate[8] with $LiAlH_4$.[9]

The key step in the syntheses of optically active liquid crystalline dispiro[2.0.2.1]heptyl derivatives **1**, **2**, and **3** was in each case the enantioselective cleavage of the racemates

[‡] Part 59: I. Emme, C. Bruneau, A. de Meijere, P. Dixneuf, *Synlett* **2000**, 1315−1317. − Part 58: M. Korder, H. Winsel, A. de Meijere, *Eur. J. Org. Chem.* **2000**, 3235−3245.

[a] Institut für Organische Chemie, Georg-August-Universität Göttingen,
Tammannstrasse 2, 37077 Göttingen, Germany
Fax: (internat) + 49-(0)551/399475
E-Mail: Armin.deMeijere@chemie.uni-goettingen.de
[b] Chisso Petrochemical Corporation, Specialty Chemicals Research Center,
5-1 Goikaigan, Ichihara, Chiba 290-8551, Japan
[c] Department of Chemistry, University of Durham,
South Rd., Durham DH1 3LE, UK

  1434−193X/00/1224−4109 $ 17.50+.50/0

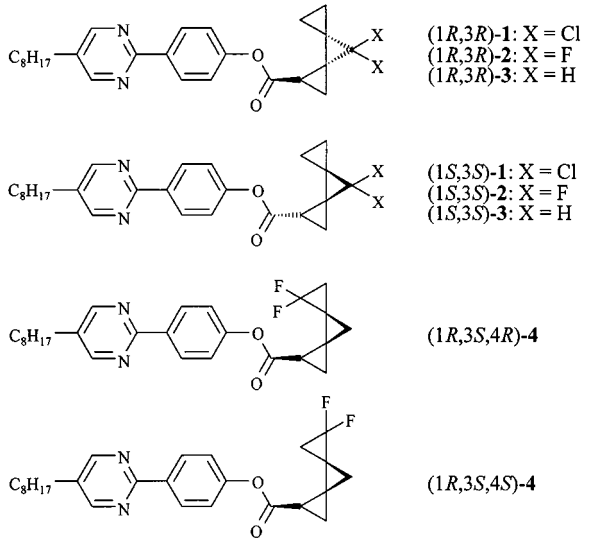
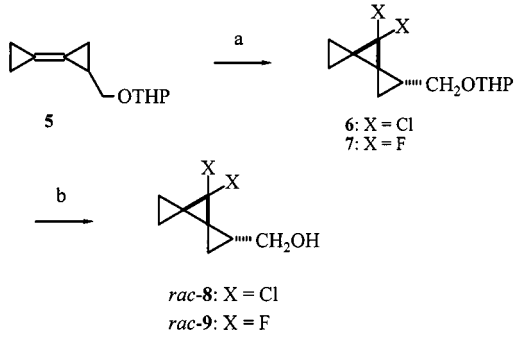


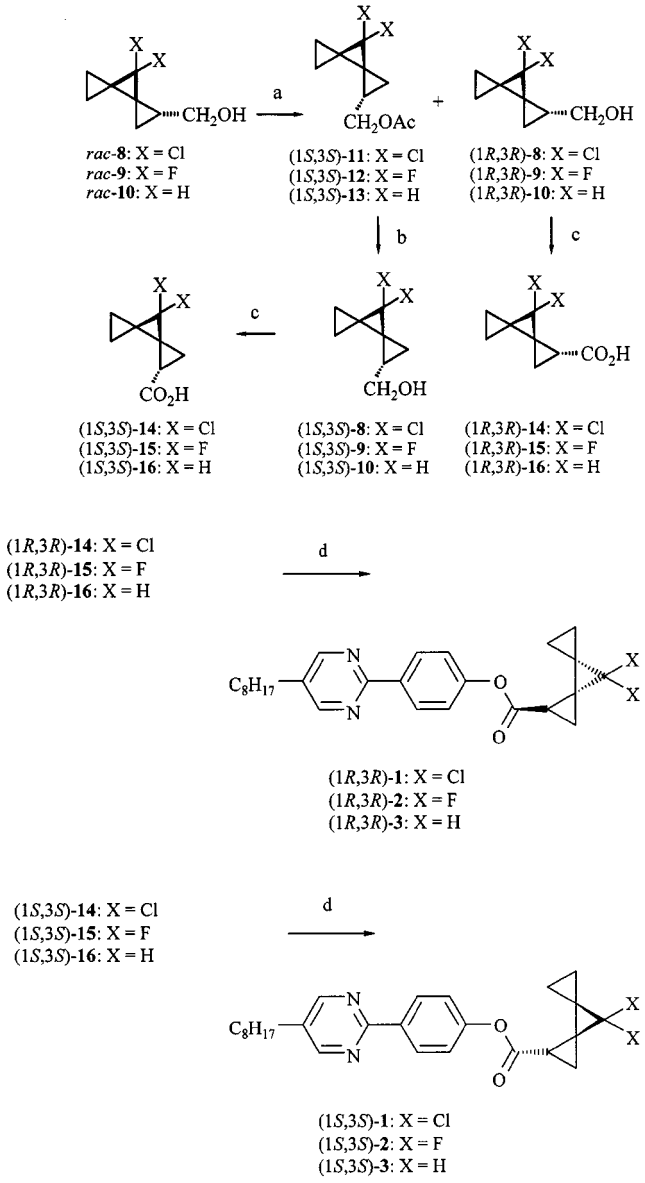
Figure 1. Chemical structures of the optically active novel ferroelectric liquid crystals



Scheme 1. (a) $CHCl_3$, NaOH, room temp. for **6**; CBr_2F_2, PPh_3, KF, 18-crown-6, DME, room temp. for **7**; (b) PPTS, MeOH, ΔT

rac-**8**, *rac*-**9**, and *rac*-**10**. It was performed by means of an enantioselective enzymatic acylation, catalyzed by Lipase PS® (*Pseudomonas* sp., Amano Pharmaceutical Co., Ltd.). The enzymatic reactions were carried out at room temperature and usually completed within 12 h. With all three substrates *rac*-**8**, *rac*-**9**, and *rac*-**10**, the enzymatic transformations operated exclusively, and thus enantioselectively, on the (1*S*,3*S*)-configured alcohols, resulting in mixtures of the corresponding acetates (1*S*,3*S*)-**11**, (1*S*,3*S*)-**12**, and (1*S*,3*S*)-**13**, and the unchanged alcohols (1*R*,3*R*)-**8**, (1*R*,3*R*)-**9**, and (1*R*,3*R*)-**10**. The acetates were easily separated from the alcohols by simple column chromatography, to give the enantiomerically pure (1*S*,3*S*)-**11**, (1*S*,3*S*)-**12**, and (1*S*,3*S*)-**13** (39−44%), as well as (1*R*,3*R*)-**8**, (1*R*,3*R*)-**9**, and (1*R*,3*R*)-**10** (33−37%) (Scheme 2). Conversion of the acetates (1*S*,3*S*)-**11**, (1*S*,3*S*)-**12**, and (1*S*,3*S*)-**13** into the alcohols (1*S*,3*S*)-**8**, (1*S*,3*S*)-**9**, and (1*S*,3*S*)-**10** was achieved by heating in a large excess of methanol with a catalytic amount of concentrated sulfuric acid (72−98%). The enantiomeric purities of (1*R*,3*R*)- and (1*S*,3*S*)-**8**, -**9**, and -**10** were determined in all cases to be > 95% *ee*, by conversion of the alcohols into Mosher esters and analysis of their ^1H NMR spectra.

Jones oxidation of the optically active alcohols gave the corresponding enantiomerically pure carboxylic acids



Scheme 2. (a) Vinyl acetate, Lipase PS, Et_2O, room temp.; (b) H_2SO_4, MeOH, ΔT; (c) CrO_3, H_2SO_4, H_2O, acetone, room temp.; (d) 4-(5-octylpyrimid-2-yl)phenol, DCC, DMAP, CH_2Cl_2, room temp.

(1*R*,3*R*)- and (1*S*,3*S*)-**14**, -**15**, and -**16**, respectively, in 39−83% yield. The absolute configuration of the compound (1*R*,3*R*)-**14** was confirmed as (1*R*,3*R*) by an X-ray crystal structure analysis of the corresponding (*R*)-(+)-α-phenylethylamide (Figure 2).[10] Esterification of the optically active acids (1*R*,3*R*)- and (1*S*,3*S*)-**14**, -**15**, and -**16** with 4-(5-octylpyrimid-2-yl)phenol was carried out using DCC activation, to give the desired liquid-crystalline compounds **1**, **2**, and **3** in 63−99% yields.

In order to synthesize the enantiomerically pure difluorodispiro[2.0.2.1]heptane derivatives (1*R*,3*S*,4*R*)-**4** and (1*R*,3*S*,4*S*)-**4**, optical resolution was performed at the stage of 4-methylenespiropentylmethanol[4b] (*rac*-**17**) by enzymatic enantioselective acylation with vinyl acetate to give the acetate (1*S*,3*R*)-**18** and the unchanged alcohol (1*R*,3*S*)-**17** (Scheme 3). The alcohol (1*R*,3*S*)-**17** by cyclopropanation

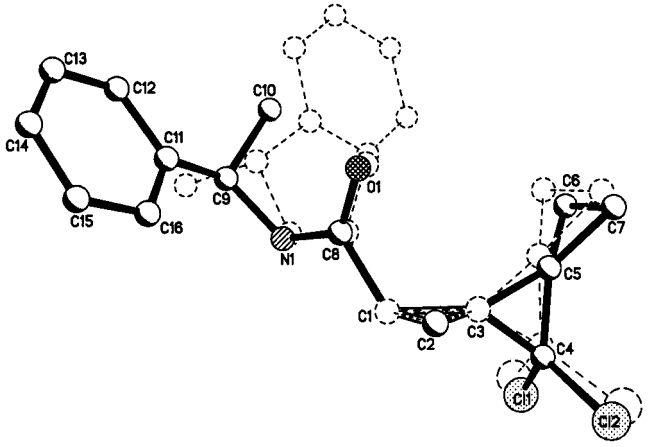
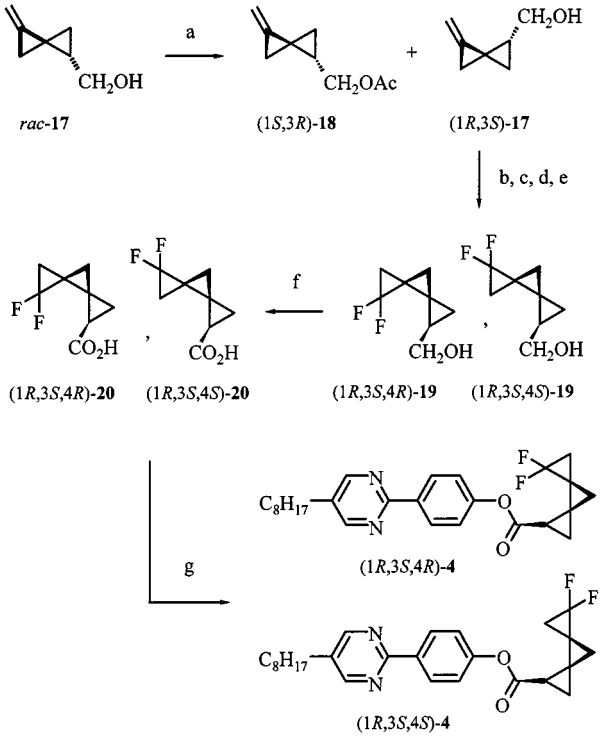


Figure 2. Molecular geometry of (1*R*,3*R*)-*N*-[(1*R*)-1-phenylethyl]-7,7-dichlorodispiro[2.0.2.1]heptane-1-carboxamide (superimposition of two independent molecules with distinctively different conformations is shown)[10]

with CH_2N_2 in the presence of $Pd(OAc)_2$ was converted into (1*R*,3*S*)-dispiro[2.0.2.1]hept-1-ylmethanol.[11] Its specific rotation was compared to that of an authentic sample,[5] confirming the absolute configuration of the unchanged alcohol **17** as (1*R*,3*S*). The high enantiomeric excess (> 95% *ee*) of the unchanged alcohol (1*R*,3*S*)-**17** was confirmed by Mosher's method.[12] After protection with dihydropyran, it was treated with difluorocarbene, generated from CBr_2F_2, PPh_3, KF, and 18-crown-6,[7] to give compounds (1*R*,3*S*,4*R*)-**19** as the less polar fraction and (1*R*,3*S*,4*S*)-**19** as the more polar fraction; these were separated by column chromatography. Jones oxidation of (1*R*,3*S*,4*R*)-**19** and (1*R*,3*S*,4*S*)-**19** gave the two acids (1*R*,3*S*,4*R*)-**20** and (1*R*,3*S*,4*S*)-**20**. X-ray crystal structure analyses showed that (1*R*,3*S*,4*R*)-**20** had two fluorine atoms on the same side as the CO_2H group, while (1*R*,3*S*,4*S*)-**20** had them on the opposite side (Figure 3). Crystals of (1*R*,3*S*,4*R*)-**20** contain two crystallographically independent molecules with identical geometries. The molecular geometries of both compounds correspond well to those expected.[10] To be precise, the presence of fluorine substituents results in an elongation of the distal bond C(5)−C(7) and a shortening of the two proximal bonds C(6)−C(5) and C(6)−C(7) in that cyclopropane ring. For the cyclopropane ring possessing the π-acceptor carboxyl group, the effect is opposite, and the proximal bonds C(1)−C(2) and C(1)−C(3) are longer than the distal C(2)−C(3) one. The difference in bond lengths between the two isomers is negligible and the orientations of COOH groups in both molecules are similar. In both compounds, the molecules form centrosymmetric hydrogen-bonded dimers typical of carb-



Scheme 3. (a) Vinyl acetate, Lipase PS, Et_2O, room temp.; (b) DHP, PPTS, CH_2Cl_2, room temp.; (c) CBr_2F_2, PPh_3, KF, 18-crown-6, DME, room temp.; (d) PPTS, MeOH, Δ*T*; (e) separation by column chromatography; (f) CrO_3, H_2SO_4, H_2O, acetone, room temp.; (g) 4-(octylpyrimid-2-yl)phenol, DCC, DMAP, CH_2Cl_2, room temp.

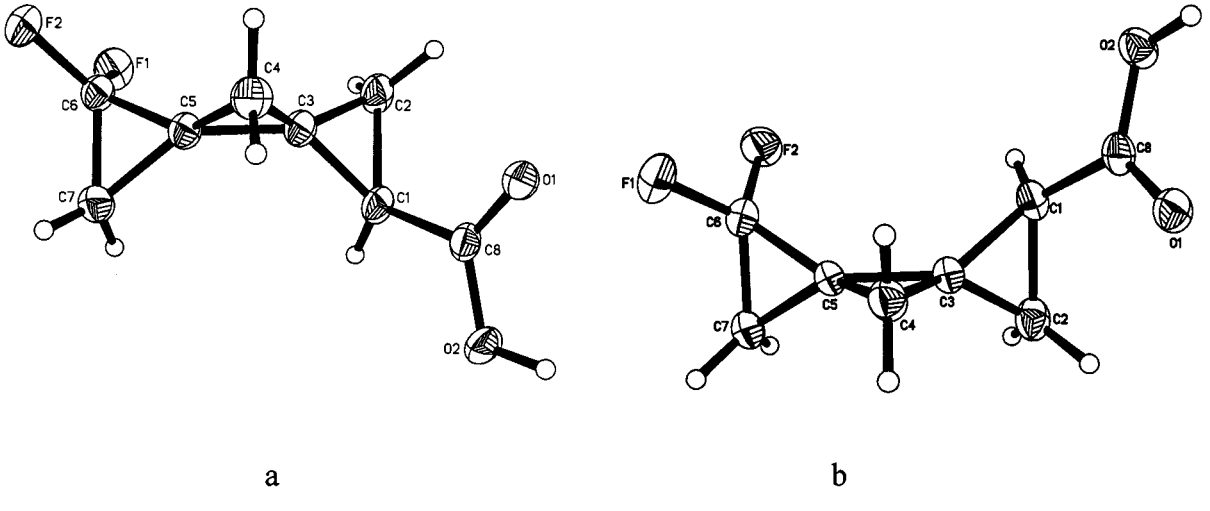


Figure 3. Structures of the acids (1*R*,3*S*,4*S*)-**20** (a) and one of the independent molecules of (1*R*,3*S*,4*R*)-**20** (b) in the crystal[10]

oxylic acids. Dimers are connected by a number of weak CH−F contacts; the shortest in both structures are with the hydrogens on the C(1) atom.

Subsequent esterification of the two acids (1*R*,3*S*,4*S*)-**20** and (1*R*,3*S*,4*R*)-**20** with 4-(5-octylpyrimid-2-yl)phenol gave the two liquid-crystalline compounds (1*R*,3*S*,4*R*)-**4** and (1*R*,3*S*,4*S*)-**4** in enantiomerically pure form.

Phase-Transition Temperatures, Properties of SmC* Mixtures and Helical Twisting Power of the Novel Compounds

An evaluation of the synthesized novel liquid-crystalline compounds as chiral dopants was performed for mixtures containing 10 wt-% of the novel compounds in an achiral SmC mixture comprising 2-(4-hexyloxyphenyl)-5-octylpyrimidine (30 wt-%), 2-(4-octyloxyphenyl)-5-octylpyrimidine (20 wt-%), 2-(4-nonyloxyphenyl)-5-octylpyrimidine (10 wt-%), 2-(4-decyloxyphenyl)-5-heptylpyrimidine (10 wt-%), 2-(4′-pentyl-1,1′-biphenyl-4-yl)-5-octylpyrimidine (20 wt-%), and 2-(4′-heptyl-1,1′-biphenyl-4-yl)-5-octylpyrimidine (10 wt-%) (hereinafter called base mixture A: phase sequence Cr 4 SmC 65 SmA 79 N 90 I). The transition temperatures were measured with a polarizing microscope (Nikon XTP-11) in conjunction with a Mettler FP 82 hot stage and an FP 80 control unit. The magnitude of Ps was measured using the triangular wave method,[13] and the sign of Ps was determined according to the convention of Lagerwall et al., using the field reversal method by optical observation of the director motion.[14] The tilt angle was determined, using crossed Nicol prisms, as one half of the rotation angle between the two maximum extinction positions associated with the oppositely directed polarizations.[15] The helical pitch in the N* phase was determined on N* mixtures containing 1 wt-% of the novel compounds in ZLI-1132 ® (Merck GmbH) nematic mixture, by the Cano wedge method.[16] The helical twist sense was determined by observation of textures of a contact preparation, using a specimen of known twist sense as a component of the binary system. The response time was measured from the transmission characteristics, as determined with a photodiode, through crossed polarizers applying a square wave voltage. The value τ is defined as the time from field reversal to 90% response.

Table 1. Transition temperatures of the novel compounds

Compound	C–I (°C)	I–C (°C)
(1*R*,3*R*)-**1**	70	55
(1*S*,3*S*)-**1**	70	51
(1*R*,3*R*)-**2**	79	65
(1*S*,3*S*)-**2**	78	66
(1*R*,3*R*)-**3**	44	10
(1*S*,3*S*)-**3**	44	6
(1*R*,3*S*,4*R*)-**4**	102	72
(1*R*,3*S*,4*S*)-**4**	80	60

Transition temperatures of the novel compounds with dispiro[2.0.2.1]heptyl moieties in their side chains are listed in Table 1. None of the compounds prepared showed any mesophase. Introduction of halogen atoms, especially fluorine atoms, onto the dispiro[2.0.2.1]heptyl moiety increased the melting point. The large dipole moments of these molecules might stabilize their crystallinities.

The transition temperatures, response times (τ), Ps values, tilt angles (θ) and helical twisting senses of the N* phase, of SmC* mixtures containing 10 wt-% of the novel compounds in the base mixture A are shown in Table 2. All the SmC* mixtures show moderate values of Ps and short response times (< 100 μs). Dihalogen substitution in the 7-position induces the largest Ps value and the quickest response. In particular, twofold fluorine substitution in the 7-position results in the shortest response time (41 μs).

Table 2. Properties of the novel compounds in the base mixture A[a]

Compound	Transition temperatures (°C) SmC*	SmA	N*	I	τ (μsec)	Ps (nC/cm²)	θ (°)	Helical sense of Nm*[b]
(1*R*,3*R*)-**1**	• 37.0	• 74.4	• 82.4	•	56	−3.8	11.7	R
(1*S*,3*S*)-**1**	• 39.5	• 74.4	• 83.1	•	56	+3.5	12.8	L
(1*R*,3*R*)-**2**	• 37.0	• 74.9	• 81.6	•	41	−2.9	11.7	R
(1*S*,3*S*)-**2**	• 36.4	• 75.1	• 81.4	•	41	+3.0	8.6	L
(1*R*,3*R*)-**3**	• 40.1	• 68.8	• 77.7	•	92	+2.3	12.2	R
(1*S*,3*S*)-**3**	• 41.3	• 67.2	• 77.2	•	88	−1.9	13.0	L
(1*R*,3*S*,4*R*)-**4**	• 49.2	• 73.0	• 81.2	•	81	−4.7	14.0	R
(1*R*,3*S*,4*S*)-**4**	• 46.7	• 76.0	• 84.3	•	149	+3.3	16.1	R

[a] Measured at 25 °C. − [b] L and R indicate left- and right-handed, respectively.

It may be noted that fluorine and chlorine substitution in the 7-position at the central cyclopropane ring reverses the sign of the Ps. For instance, the nonhalogenated compound (1*R*,3*R*)-**3** displays a right-handed helical twisting sense in the N* phase, which has the same direction as those of the halogenated compounds (1*R*,3*R*)-**1** and (1*R*,3*R*)-**2**, but exhibits a positive spontaneous polarization (+Ps) while the compounds (1*R*,3*R*)-**1** and (1*R*,3*R*)-**2** show a negative Ps.

An extremely interesting phenomenon is the unusual relationship between the properties of the compounds (1*R*,3*S*,4*R*)-**4** and (1*R*,3*S*,4*S*)-**4**. In their Ps values they show opposite signs, with almost the same magnitude, although both compounds exhibit right-handed helical twisting senses in the N* phase. The only structural difference between the two diastereomeric compounds concerns the positions of the two fluorine substituents. This could be a useful feature, by means of which an SmC* mixture with an infinite length of N* helical twisting pitch, providing a homogeneous alignment in an LC cell, might easily be achieved. More importantly, this result strongly suggests

that the directions of Ps and helical twisting sense must be derived from different origins.

A mixture containing 5 wt-% of (1*R*,3*S*,4*R*)-**4** and 5 wt-% of (1*R*,3*S*,4*S*)-**4** in the base mixture A was prepared. The resulting mixture displayed a phase sequence SmC* 47.2 SmA 75.0 N* 84.6 I with almost 0 nC cm^{-2} for the Ps value, and virtually the same right-handed helical sense in the N* phase as the mixtures containing 10% of (1*R*,3*S*,4*R*)-**4** or (1*R*,3*S*,4*S*)-**4**. This result indicates that the mixture of (1*R*,3*S*,4*R*)-**4** and (1*R*,3*S*,4*S*)-**4** can be used as a chiral dopant without separating the two diastereoisomers. Furthermore, by mixing (1*R*,3*S*,4*R*)-**4** and (1*S*,3*R*,4*R*)-**4**, or (1*S*,3*R*,4*S*)-**4** and (1*R*,3*S*,4*S*)-**4**, SmC* mixtures with large Ps values and infinite helical twisting pitches can probably be prepared.

The temperature dependencies of helical pitches of N* mixtures containing 1 wt-% of the novel compounds in the nematic base mixture ZLI-1132 are listed in Table 3. The helical twisting power (HTP) and its temperature dependence were found to be strongly influenced by the chemical structures; in general, dihalogen substitution makes the helical twisting power greater. Among the novel compounds, (1*R*,3*R*)-**2** and (1*S*,3*S*)-**2** showed the largest HTP and, remarkably, the smallest temperature dependence.

Table 3. Helical twisting power of the novel compounds

Compound	N* Helical pitch (μm)					
	60 °C	50 °C	40 °C	30 °C	25 °C	20 °C
(1*R*,3*R*)-**1**	15.8	16.1	16.4	16.7	16.9	16.7
(1*S*,3*S*)-**1**	15.8	15.9	16.2	16.4	16.5	16.6
(1*R*,3*R*)-**2**	13.4	13.4	13.4	13.4	13.5	13.5
(1*S*,3*S*)-**2**	14.0	14.1	14.1	14.0	14.1	14.1
(1*R*,3*R*)-**3**	–	–	–	–	–	–[a]
(1*S*,3*S*)-**3**	–	–	–	–	–	–[a]
(1*R*,3*S*,4*R*)-**4**	19.7	20.7	22.4	24.2	26.1	26.8
(1*R*,3*S*,4*S*)-**4**	34.7	34.7	34.6	34.2	33.7	33.5

[a] No helical structure was formed in the Cano wedge cell.

Conclusion

Synthetic approaches have been developed to optically active dispiro[2.0.2.1]heptane derivatives; they include enzymatic optical resolutions of *endo*-dispiro[2.0.2.1]heptylmethanol and *endo*-4-methylenespiropentylmethanol. Starting from the optically active key intermediates, novel ferroelectric liquid-crystalline compounds were synthesized. These compounds incorporating dispiro[2.0.2.1]heptyl moieties have some interesting properties. SmC* mixtures containing 10 wt-% of the fluorinated compounds (1*R*,3*R*)-**2** and (1*S*,3*S*)-**2** in the base mixture showed the shortest response times. The two diastereomeric compounds (1*R*,3*S*,4*R*)-**4** and (1*R*,3*S*,4*S*)-**4**, with difluorine substitution on the terminal cyclopropane ring, exhibited the extremely strange phenomenon of noncorrelating Ps signs and N* phase senses, which strongly suggests that the sign of the Ps and the sense of helical twisting must have different origins. As well as this, a reversal of the sign of Ps was observed on going from 7,7-dihalodispiro[2.0.2.1]heptane to the nonsubstituted dispiro[2.0.2.1]heptane derivatives. This novel chemical class of dispiro[2.0.2.1]heptanes thus deserves more thorough investigation in order to understand the origin of this as yet unique phenomenon.

Experimental Section

General Remarks: All reactions with moisture- and air-sensitive substrates or reagents were carried out under dry nitrogen. Diethyl ether and dimethoxyethane were distilled from sodium benzophenone ketyl, and dichloromethane was distilled from P_2O_5 prior to use. All other commercial reagents were used as received unless otherwise mentioned. Melting points are uncorrected. All new compounds were purified by column chromatography on silica gel (silica gel 60, 0.063−0.200 mm) or recrystallization. Their chemical structures were fully confirmed by spectroscopic techniques − IR [Bruker IFS 66 (FT−IR)], ^{1}H NMR (250 MHz), ^{13}C NMR (62.9 MHz, additional DEPT), mass spectrometry (Varian MAT CH 7, MAT 731) − and their molecular formulas were established by elemental analysis, carried out at the Mikroanalytisches Laboratorium des Instituts für Organische Chemie der Universität Göttingen.

7,7-Dichlorodispiro[2.0.2.1]heptylmethyl Tetrahydropyranyl Ether (6): Chloroform (7.26 g, 61 mmol) was added slowly to a mixture of **5**[4a] (2.99 g, 15.4 mmol), 50% aqueous NaOH (4.88 g, 61 mmol), and tetrabutylammonium bromide (49 mg, 0.15 mmol) at room temperature, and the resulting suspension was stirred for 12 h. Workup as usual, followed by silica gel column chromatography (R_f = 0.52, pentane/diethyl ether, 5:1) gave 4.24 g (99%) of **6** as a colorless oil. − IR (film): $\tilde{\nu}$ = 2942, 1032 cm^{-1}. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.87−1.22 (m, 3.5 H), 1.26−1.34 (m, 1.5 H), 1.43−2.01 (m, 8 H), 3.22 (dd, *J* = 10.5, 6.5 Hz, 0.5 H, *CH*$_2$*O*), 3.37−3.50 (m, 2 H, *CH*$_2$*O*), 3.71−3.85 (m, 1.5 H, *CH*$_2$*O*), 4.54−4.60 (m, 1 H, *OCHO*). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*): δ = 8.45, 8.49, 8.5, 8.8, 12.7, 12.8 (*each*, −, *cPr*−*C*), 19.2, 19.4 (*each*, −, *CH*$_2$), 21.3, 21.5 (*each*, +, *cPr*−*C*), 25.3 (−, *CH*$_2$), 28.9, 29.3 (*each*, C_{quat}, *cPr*−*C*), 30.5 (−, *CH*$_2$), 32.1, 32.5 (*each*, C_{quat}, *cPr*−*C*), 62.0, 62.1, 66.4, 67.2 (*each*, −, *CH*$_2$*O*), 67.7, 67.8 (*each*, C_{quat}, *CCl*$_2$), 97.8, 98.3 (*each*, +, *OCHO*). − MS (70 eV, CI); *m*/*z* (%): 294/296/298 (28/16/2) [M + NH_4^+], 102 (100). − $C_{13}H_{18}Cl_2O_2$ (277.19): calcd. C 56.33, H 6.55; found C 56.65, H, 6.74.

7,7-Dichlorodispiro[2.0.2.1]heptylmethanol (*rac*-8): A mixture of **6** (4.24 g, 15.3 mmol), methanol (90 mL) and PPTS (500 mg, 2.1 mmol) was stirred at 50 °C for 12 h. Workup and purification by column chromatography (R_f = 0.25, pentane/diethyl ether, 1:1) gave 2.04 g (69%) of *rac*-**8** as colorless crystals, m.p. 44.5−46.5 °C. − IR (KBr): $\tilde{\nu}$ = 3325, 1034 cm^{-1}. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.85−1.09 (m, 3 H, *cPr*−*H*), 1.23−1.30 (m, 2 H, *cPr*−*H*), 1.46 (dd, *J* = 8.3, 5.3 Hz, 1 H, *cPr*−*H*), 1.78 (br s, 1 H, *OH*), 1.92−2.15 (m, 1 H, *cPr*−*H*), 3.37−3.53 (m, 2 H, *CH*$_2$*O*). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*): δ = 8.7, 8.8, 12.7 (*each*, −, *cPr*−*C*), 23.8 (+, *cPr*−*C*), 28.8, 33.0 (*each*, C_{quat}, *cPr*−*C*), 63.6 (−, *CH*$_2$*O*), 67.6 (C_{quat}, *CCl*$_2$). − MS (70 eV, EI); *m*/*z* (%): 191/193/

195 (15/9/1) [$M^+ - H$], 77 (100). − $C_8H_{10}Cl_2O$ (193.07): calcd. C 49.77, H 5.22; found C 49.92, H, 5.12.

7,7-Difluorodispiro[2.0.2.1]heptylmethyl Tetrahydropyranyl Ether (7): To a mixture of **5**[4a] (10 g, 51.5 mmol), KF (15 g, 258 mmol), and 18-crown-6 (1.36 g, 5.15 mmol) in DME (100 mL) at room temperature, was added in 3 portions a suspension prepared from PPh_3 (40 g, 153 mmol) and CBr_2F_2 (32 g, 153 mmol) in DME (50 mL). The resulting colorless suspension was stirred overnight and the solvent removed under reduced pressure. The residue was purified by column chromatography on silica gel (R_f = 0.48, pentane/diethyl ether, 5:1), to give 7.35 g (58%) of **7** as a colorless oil. − IR (film): $\tilde{\nu}$ = 3077, 1685, 1261 cm^{-1}. − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.86−1.20 (m, 4 H, *cPr*−*H*), 1.23−1.38 (m, 1 H, *cPr*−*H*), 1.53−1.91 (m, 8 H, *cPr*−*H*, CH_2), 3.20 (dd, *J* = 10.5, 6.3 Hz, 0.5 H, CH_2O), 3.39−3.48 (m, 2 H, CH_2O), 3.76−3.82 (m, 1.5 H, CH_2O), 4.56−4.59 (m, 1 H, *OCHO*). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*): δ = 5.8, 5.9, 6.0, 6.2, 10.4, 10.5 (*each*, −), 17.7 (C_{quat}, t, J_{CF} = 11.3 Hz, *cPr*−*C*), 17.8 (C_{quat}, t, J_{CF} = 11.3 Hz, *cPr*−*C*), 18.9, 19.1 (*each*, +, *cPr*−*C*), 19.4, 19.5 (*each*, −), 21.4 (C_{quat}, t, J_{CF} = 11.4 Hz, *cPr*−*C*), 21.8 (C_{quat}, t, J_{CF} = 11.4 Hz, *cPr*−*C*), 25.3, 30.6 (*each*, −), 62.2, 62.3, 66.8, 67.8 (*each*, −, CH_2O), 98.2, 98.7 (*each*, +, *OCHO*), 115.3 (C_{quat}, t, J_{CF} = 296 Hz, CF_2), 115.4 (C_{quat}, t, J_{CF} = 296 Hz, CF_2). − MS (70 eV, CI); *m*/*z* (%): 262 (100) [M + NH_4^+]. − $C_{13}H_{18}F_2O_2$ (244.28): C 63.92, H 7.43; found C 63.82, H 7.38.

7,7-Difluorodispiro[2.0.2.1]heptylmethanol (*rac*-9): A mixture of **7** (7.35 g, 30.1 mmol), methanol (160 mL), and PPTS (800 mg, 3.3 mmol) was stirred at 50 °C for 12 h. Workup as usual and purification by column chromatography on silica gel (R_f = 0.26, pentane/diethyl ether 1:1) gave 3.09 g (64%) of *rac*-**9** as colorless crystals, m.p. 38−40 °C. − IR (KBr): $\tilde{\nu}$ = 3333, 1250, 1139 cm^{-1}. − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.80−1.14 (m, 3 H, *cPr*−*H*), 1.17−1.29 (m, 2 H, *cPr*−*H*), 1.38 (dd, *J* = 7.6, 5.9 Hz, 1 H, *cPr*−*H*), 1.70 (br s, 1 H, *OH*), 1.89 (q, *J* = 5.9 Hz, 1 H, *cPr*−*H*), 3.49 (d, *J* = 6.9 Hz, 2 H, CH_2O). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*): δ = 6.0, 6.1, 10.3 (*each*, −, *cPr*−*C*), 17.6 (C_{quat}, t, J_{CF} = 11.2 Hz, *cPr*−*C*), 21.4 (+, *cPr*−*C*), 22.1 (C_{quat}, t, J_{CF} = 11.2 Hz, *cPr*−*C*), 63.7 (−, d, J_{CF} = 3.6 Hz, CH_2O), 115.1 (C_{quat}, t, J_{CF} = 290 Hz, CF_2). − MS (70 eV, CI); *m*/*z* (%): 178 (100) [M + NH_4^+]. − $C_8H_{10}F_2O$ (160.16): C 59.99, H 6.29; found C 60.31, H, 6.55.

Optical Resolution of *endo*-7,7-Dichlorodispiro[2.0.2.1]heptylmethanol (*rac*-8): A mixture of *rac*-**8** (2.04 g, 10.6 mmol), vinyl acetate (455 mg, 5.29 mmol), Lipase PS (400 mg), and diethyl ether (16 mL) was stirred at room temperature for 12 h. The Lipase PS was removed by filtration, and the filtrate was concentrated in vacuo. The resulting residue was subjected to column chromatography on silica gel to give 1.07 g (43%) of the acetate (1*S*,3*S*)-**11** and 756 mg (37%) of (1*R*,3*R*)-**8** as the unchanged alcohol. The acetate (1*S*,3*S*)-**11** (1.00 g, 4.27 mmol) was refluxed in methanol (60 mL) with a catalytic amount of conc. H_2SO_4 for 0.5 h. Workup as usual and purification by column chromatography gave 800 mg (97%) of (1*S*,3*S*)-**8**.

(Compound 1*S*,3*S*)-11: Colorless oil. R_f = 0.36 (pentane/diethyl ether, 5:1). − IR (film): $\tilde{\nu}$ = 1743, 1236 cm^{-1}. − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.93−1.05 (m, 4 H, *cPr*−*H*), 1.25−1.30 (m, 2 H, *cPr*−*H*), 1.50 (dd, *J* = 8.5, 5.4 Hz, 1 H, *cPr*−*H*), 2.02 (s, 3 H, CH_3), 3.87 (dd, *J* = 11.5, 6.7 Hz, 1 H, CH_2O), 3.95 (dd, *J* = 11.5, 6.9 Hz, 1 H, CH_2O). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*): δ = 8.7, 8.8, 13.2 (*each*, −, *cPr*−*C*), 20.3 (+, CH_3), 20.8 (+, *cPr*−*C*), 28.8, 32.9 (*each*, C_{quat}, *cPr*−*C*), 64.8 (−, CH_2O), 67.2 (C_{quat}, CCl_2), 170.8 (C_{quat}, CO_2). − MS (70 eV, EI); *m*/*z* (%): 234/236/238 (100/66/11) [M^+]. − $C_{10}H_{12}Cl_2O_2$ (235.11): C 51.09, H 5.14; found C 51.11, H 5.19. − $[\alpha]_D^{25}$ = +52.0 (*c* = 0.98; $CHCl_3$).

Compound (1*R*,3*R*)-8: Colorless crystals, m.p. 51−53 °C, R_f = 0.18 (pentane/diethyl ether, 1:1). − $C_8H_{10}Cl_2O$ (193.07): calcd. C 49.77, H 5.22, found C 50.06, H 5.52. − $[\alpha]_D^{25}$ = −54.9 (*c* = 1.07; $CHCl_3$). IR, ^1H NMR, ^{13}C NMR, and MS spectra were identical to those of *rac*-**8**.

Compound (1*S*,3*S*)-8: Colorless crystals, m.p. 56−57 °C, R_f = 0.18 (pentane/diethyl ether, 1:1). − $[\alpha]_D^{25}$ = +53.0 (*c* = 1.05, $CHCl_3$). IR, ^1H NMR, ^{13}C NMR, and MS spectra were identical to those of *rac*-**8**.

Following the same procedure as for the optical resolution of *rac*-**8**, the compounds *rac*-**9** and *rac*-**10** were optically resolved to yield (1*R*,3*R*)-**9** and -**10**, (1*S*,3*S*)-**12** and -**13**, and (1*S*,3*S*)-**9** and -**10**.

Compound (1*S*,3*S*)-12: Colorless oil (1.70 g, 44%), R_f = 0.45 (pentane/diethyl ether, 5:1). − IR (film): $\tilde{\nu}$ = 1748, 1257 cm^{-1}. − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.87−0.99 (m, 3 H, *cPr*−*H*), 1.20−1.41 (m, 2 H, *cPr*−*H*), 1.63 (dd, *J* = 7.8, 5.8 Hz, 1 H, *cPr*−*H*), 1.95 (m, 1 H, *cPr*−*H*), 2.04 (s, 3 H, CH_3), 3.92 (d, *J* = 6.7 Hz, 2 H, CH_2O). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*): δ = 5.81 (−, 2 C, *cPr*−*C*), 10.5 (−, *cPr*−*C*), 17.5 (C_{quat}, t, J_{CF} = 11.4 Hz, *cPr*−*C*), 17.7 (+, CH_3), 20.6 (+, *cPr*−*C*), 22.0 (C_{quat}, t, J_{CF} = 11.4 Hz, *cPr*−*C*), 64.7 (−, CH_2O), 114.7 (C_{quat}, t, J_{CF} = 290 Hz, CF_2), 170.6 (C_{quat}, CO_2). − MS (70 eV, EI); *m*/*z* (%): 202 (< 0.1) [M^+], 43 (100). − $C_{10}H_{12}F_2O_2$ (202.20): calcd. C 59.40, H 5.98; found C 59.71, H, 5.84. − $[\alpha]_D^{25}$ = +16.4 (*c* = 1.03; $CHCl_3$).

Compound (1*R*,3*R*)-9: Yellow syrup (995 mg, 33%), R_f = 0.21 (pentane/diethyl ether, 1:1). − $C_8H_{10}F_2O$ (160.16): calcd. C 59.99, H 6.29; found C 59.88, H 6.34. − $[\alpha]_D^{25}$ = −15.2 (*c* =1.56; $CHCl_3$). IR, ^1H NMR, ^{13}C NMR, and MS spectra were identical to those of *rac*-**9**.

Compound (1*S*,3*S*)-9: Yellow syrup (1.24 g, 98%), R_f = 0.26 (pentane/diethyl ether, 1:1). − $C_8H_{10}F_2O$ (160.16): calcd. C 59.99, H 6.29; found C 59.74, H 6.44. − $[\alpha]_D^{25}$ = +13.2 (*c* = 1.22, $CHCl_3$). IR, ^1H NMR, ^{13}C NMR, and MS spectra were identical to those of *rac*-**9**.

Compound (1*S*,3*S*)-13: Colorless oil (480 mg, 39%), R_f = 0.68 (pentane/diethyl ether, 5:1). − IR (film): $\tilde{\nu}$ = 1741, 1233 cm^{-1}. − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.46−0.87 (m, 5 H, *cPr*−*H*), 1.05−1.21 (m, 3 H, *cPr*−*H*), 1.58−1.67 (m, 1 H, *cPr*−*H*), 2.02 (s, 3 H, CH_3), 3.72 (dd, *J* = 11.4, 7.8 Hz, 1 H, CH_2O), 3.94 (dd, *J* = 11.4, 6.5 Hz, 1 H, CH_2O). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*): δ = 5.1, 5.2, 10.5, 12.9 (*each*, −, *cPr*−*C*), 13.0 (C_{quat}, *cPr*−*C*), 17.4 (+, *cPr*−*C*), 18.2 (C_{quat}, *cPr*−*C*), 21.0 (+, CH_3), 67.2 (−, CH_2O), 171.1 (C_{quat}, CO_2). − MS (70 eV, CI); *m*/*z* (%): 184 (100) [M + NH_4^+]. − $C_{10}H_{14}O_2$ (166.22): calcd. C 72.26, H 8.49; found C 72.31, H 8.70. − $[\alpha]_D^{25}$ = +18.1 (*c* = 0.73; $CHCl_3$).

Compound (1*R*,3*R*)-10: Colorless oil (321 mg, 35%), R_f = 0.16 (pentane/diethyl ether, 5:1). − IR (film): $\tilde{\nu}$ = 3338 cm^{-1}. − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.49−0.95 (m, 4 H, *cPr*−*H*), 1.01−1.33 (m, 5 H, *cPr*−*H*, *OH*), 1.58−1.72 (m, 1 H, *cPr*−*H*), 3.44 (dd, *J* = 15.0, 4.2 Hz, 2 H, CH_2O). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*) δ 5.2, 5.3, 10.1 (*each*, −, *cPr*−*C*), 12.9 (C_{quat}, *cPr*−*C*), 13.0 (−, *cPr*−*C*), 18.4 (C_{quat}, *cPr*−*C*), 21.3 (+, *cPr*−*C*), 65.8 (−, CH_2O). − MS (70 eV, CI); *m*/*z* (%): 142 (48) [M + NH_4^+], 107 (100). − $C_8H_{12}O$ (124.18): calcd. C 77.38, H 9.74; found C 77.17, H 9.71. − $[\alpha]_D^{25}$ = +6.1 (*c* = 1.25; $CHCl_3$).

Compound (1*S*,3*S*)-10: Colorless oil (224 mg, 72%), R_f = 0.40 (pentane/diethyl ether, 1:1). − $[\alpha]_D^{25}$ = −7.4 (*c* = 1.17, $CHCl_3$). IR, ^{1}H NMR, ^{13}C NMR, and MS spectra were identical to those of (1*R*,3*R*)-**10**.

(1*R*,3*R*)-7,7-Dichlorodispiro[2.0.2.1]heptanecarboxylic Acid [(1*R*,3*R*)-14]: To a solution of (1*R*,3*R*)-**8** (500 mg, 2.59 mmol) in acetone (15 mL) was added dropwise a mixture of CrO_3 (2.76 g, 27.6 mmol), H_2SO_4 (2.3 mL), and H_2O (10 mL), until the reddish color remained permanent. After 0.5 h of stirring at this temperature, the resulting mixture was diluted with water (15 mL). Workup as usual, followed by column chromatography on silica gel (R_f = 0.5, pentane/diethyl ether, 1:1) and recrystallization (hexane), gave 430 mg (80%) of (1*R*,3*R*)-**14** as colorless crystals, m.p. 78.5−80.0 °C. − IR (KBr): $\tilde{\nu}$ = 3339, 1703, 1444, 1309 cm^{-1}. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.05−1.41 (m, 4 H, *cPr*−*H*), 1.61 (t, *J* = 5.0 Hz, 1 H, *cPr*−*H*), 1.83 (dd, *J* = 8.4, 4.8 Hz, 1 H, *cPr*−*H*), 2.37 (dd, *J* = 8.4, 5.3 Hz, 1 H, *cPr*−*H*), 11.20 (br s, 1 H, *OH*). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*): δ = 8.0, 9.4, 16.7 (*each*, −, *cPr*−*C*), 22.9 (+, *cPr*−*C*), 29.9, 36.7 (*each*, C_{quat}, *cPr*−*C*), 65.7 (C_{quat}, CCl_2), 178.2 (C_{quat}, CO_2). − MS (70 eV, EI); *m*/*z* (%): 205/207/209 (2/1/0.6) [M^+ − H], 125/127 (100/44). − $C_8H_8Cl_2O_2$ (207.06): calcd. C 46.41, H 3.89; found C 46.55, H 4.00. − $[\alpha]_D^{25}$ = −150.0 (*c* = 1.29; $CHCl_3$).

In the same manner, starting from (1*R*,3*R*)-**9** and -**10**, and from (1*S*,3*S*)-**8**, -**9**, and -**10**, the corresponding carboxylic acids (1*R*,3*R*)-**15** and -**16**, and (1*S*,3*S*)-**14**, -**15**, and -**16**, respectively, were prepared.

Compound (1*S*,3*S*)-14: Colorless crystals (448 mg, 83%), m.p. 85−87 °C, R_f = 0.5 (pentane/diethyl ether, 1:1). − $C_8H_8Cl_2O_2$ (207.06): calcd. C 46.41, H 3.89, found C 46.61, H 4.04. − $[\alpha]_D^{25}$ = +148.8 (*c* = 1.32; $CHCl_3$). IR, ^{1}H NMR, ^{13}C NMR, and MS spectra were identical to those of (1*R*,3*R*)-**14**.

Compound (1*R*,3*R*)-15: Colorless crystals (599 mg, 79%), m.p. 81.5−83.0 °C, R_f = 0.4 (pentane/diethyl ether, 1:1). − IR (KBr): $\tilde{\nu}$ = 3340, 1685, 1591, 1430, 1310, 965 cm^{-1}. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.92−1.26 (m, 4 H, *cPr*−*H*), 1.55−1.60 (m, 1 H, *cPr*−*H*), 1.62−1.73 (m, 1 H, *cPr*−*H*), 2.33 (dd, *J* = 8.0, 4.9 Hz, 1 H, *cPr*−*H*), 10.80 (br s, 1 H, *OH*). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*): δ = 2.4, 5.0, 14.2 (*each*, −, *cPr*−*C*), 18.7 (C_{quat}, t, J_{CF} = 11.4 Hz, *cPr*−*C*), 20.4 (+, *cPr*−*C*), 26.2 (C_{quat}, t, J_{CF} = 11.7 Hz, *cPr*−*C*), 113.6 (C_{quat}, t, J_{CF} = 291 Hz, CF_2), 178.4 (C_{quat}, CO_2). − MS (70 eV, EI); *m*/*z* (%): 173 (7) [M^+ − H], 129 (100). − $C_8H_8F_2O_2$ (174.15): calcd. C 55.18, H 4.63; found C 55.51, H 4.86. − $[\alpha]_D^{25}$ = −91.7 (*c* = 1.35; $CHCl_3$).

Compound (1*S*,3*S*)-15: Colorless crystals (540 mg, 71%), m.p. 80.5−83.0 °C, R_f = 0.5 (pentane/diethyl ether, 1:1). − $C_8H_8F_2O_2$ (174.15): calcd. C 55.18, H 4.63; found C 55.38, H 4.77. − $[\alpha]_D^{25}$ = +89.8 (*c* = 1.26; $CHCl_3$). IR, ^{1}H NMR, ^{13}C NMR, and MS spectra were identical to those of (1*R*,3*R*)-**15**.

Compound (1*R*,3*R*)-16: Colorless crystals (121 mg, 39%), m.p. 46−49 °C, R_f = 0.19 (pentane/diethyl ether, 5:1). − IR (KBr): $\tilde{\nu}$ = 3334, 2993, 1694 cm^{-1}. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.72−1.08 (m, 4 H, *cPr*−*H*), 1.14−1.43 (m, 2 H, *cPr*−*H*), 1.44−1.47 (m, 2 H, *cPr*−*H*), 2.03 (dd, *J* = 6.9, 4.9 Hz, 1 H, *cPr*−*H*), 11.40 (br s, 1 H, *OH*). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*): δ = 3.8, 5.3, 12.1 (*each*, −, *cPr*−*C*), 13.9 (C_{quat}, *cPr*−*C*), 14.9 (−, *cPr*−*C*), 20.8 (+, *cPr*−*C*), 23.6 (C_{quat}, *cPr*−*C*), 180.8 (C_{quat}, CO_2). − MS (70 eV, EI); *m*/*z* (%): 138 (2) [M^+], 93 (100). − $C_8H_{10}O_2$ (138.17): calcd. C 69.55, H 7.30; found C 69.85, H, 7.04. − $[\alpha]_D^{25}$ = −89.7 (*c* = 1.03; $CHCl_3$).

Compound (1*S*,3*S*)-16: Colorless crystals (169 mg, 80%), m.p. 44−46 °C, R_f = 0.16 (pentane/diethyl ether, 5:1). − $C_8H_{10}O_2$ (138.17): calcd. C 69.55, H 7.30; found C 69.70, H 7.11. − $[\alpha]_D^{25}$ = +86.2 (*c* = 1.34; $CHCl_3$). IR, ^{1}H NMR, ^{13}C NMR, and MS spectra were identical to those of (1*R*,3*R*)-**16**.

4-(5-Octylpyrimid-2-yl)phenyl (1*R*,3*R*)-7,7-Dichlorodispiro[2.0.2.1]-heptanecarboxylate [(1*R*,3*R*)-1]: A mixture of the acid (1*R*,3*R*)-**14** (260 mg, 1.23 mmol), 4-(5-octylpyrimid-2-yl)phenol (535 mg, 1.88 mmol), DCC (312 mg, 1.51 mmol), DMAP (15 mg, 0.123 mmol), and dichloromethane (10 mL) was stirred at room temperature for 16 h. Workup as usual, followed by purification with silica gel column chromatography (pentane/diethyl ether, 5:1, R_f = 0.41), gave 410 mg (69%) of (1*R*,3*R*)-**1** as colorless crystals, m.p. 70 °C. − IR (KBr): $\tilde{\nu}$ = 2954, 1738, 1197, 1163, 1138 cm^{-1}. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 5.5 Hz, 3 H, *Oct*−CH_3), 1.15−1.41 (m, 14 H, *Oct*−CH_2, *cPr*−*H*), 1.56−1.65 (m, 2 H, *Oct*−CH_2), 1.78 (t, *J* = 5.0 Hz, 1 H, *cPr*−*H*), 1.91 (dd, *J* = 8.2, 5.9 Hz, 1 H, *cPr*−*H*), 2.58 (t, *J* = 7.4 Hz, 2 H, *Oct*−CH_2), 2.68 (dd, *J* = 8.2, 5.0 Hz, 1 H, *cPr*−*H*), 7.17 (d, *J* = 8.6 Hz, 2 H, *Ar*−*H*), 8.43 (d, *J* = 8.6 Hz, 2 H, *Ar*−*H*), 8.58 (s, 2 H, *Ar*−*H*). − ^{13}C NMR (62.9 Hz, $CDCl_3$, *additional DEPT*): δ = 8.1, 9.4 (*each*, −, *cPr*−*C*), 14.0 (+, *Oct*−CH_3), 16.6 (−, *cPr*−*C*), 22.6 (−, *Oct*−CH_2), 23.1 (+, *cPr*−*C*), 29.0, 29.1, 29.2 (*each*, −, *Oct*−CH_2), 29.9 (C_{quat}, *cPr*−*C*), 30.1, 30.7, 31.7 (*each*, −, *Oct*−CH_2), 36.7 (C_{quat}, *cPr*−*C*), 65.9 (C_{quat}, CCl_2), 121.3, 129.1 (*each*, +, *Ar*−*C*), 133.0, 135.4 (*each*, C_{quat}, *Ar*−*C*), 152.1 (C_{quat}, *Ar*−*C*), 156.9 (+, *Ar*−*C*), 161.6 (C_{quat}, *Ar*−*C*), 169.6 (C_{quat}, CO_2). − MS (70 eV, EI); *m*/*z* (%): 472/474 (12/8) [M^+], 284 (100). − $C_{26}H_{30}Cl_2N_2O_2$ (473.44): C 65.96, H 6.39, N 5.92; found C 66.23, H 6.18, N 5.86. − $[\alpha]_D^{25}$ = −110.9 (*c* = 1.25, $CHCl_3$).

Following the same procedure as for (1*R*,3*R*)-**1**, compounds (1*R*,3*R*)-**2** and -**3**, and (1*S*,3*S*)-**1**, -**2**, and -**3** were prepared from (1*R*,3*R*)-**15** and -**16**, and (1*S*,3*S*)-**14**, -**15**, and -**16**, respectively.

Compound (1*S*,3*S*)-1: Colorless needles (426 mg, 76%), m.p. 70 °C, R_f = 0.79 (pentane/diethyl ether, 1:1). − $C_{26}H_{30}Cl_2N_2O_2$ (473.44): calcd. C 65.96, H 6.39, N 5.92; found C 65.97, H 6.29, N 6.02. − $[\alpha]_D^{25}$ = +110.5 (*c* = 1.00; $CHCl_3$). IR, ^{1}H NMR, ^{13}C NMR, and MS spectra were identical to those of (1*R*,3*R*)-**1**.

Compound (1*R*,3*R*)-2: Colorless crystals (548 mg, 99%), m.p. 79 °C, R_f = 0.67 (pentane/diethyl ether, 1:1). − IR (KBr): $\tilde{\nu}$ = 2957, 1744, 1202, 1167, 1152 cm^{-1}. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 5.8 Hz, 3 H, *Oct*−CH_3), 1.12−1.29 (m, 14 H, *Oct*−CH_2), 1.58−1.73 (m, 5 H, *cPr*−*H*), 2.61 (t, *J* = 7.8 Hz, 2 H, *Oct*−CH_2), 7.18 (d, *J* = 8.8 Hz, 2 H, *Ar*−*H*), 8.43 (d, *J* = 8.8 Hz, 2 H, *Ar*−*H*), 8.60 (s, 2 H, *Ar*−*H*). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*): δ = 4.8, 6.5 (*each*, −, *cPr*−*C*), 13.8 (+, *Oct*−CH_3), 13.9 (−, *cPr*−*C*), 18.5 (C_{quat}, t, J_{CF} = 11.3 Hz, *cPr*−*C*), 20.4 (+, *cPr*−*C*), 22.4 (−, *Oct*−CH_2), 26.0 (C_{quat}, t, J_{CF} = 12.0 Hz, *cPr*−*C*), 28.8, 28.9, 29.0, 29.8, 30.4, 31.6 (*each*, −, *Oct*−CH_2), 113.6 (C_{quat}, t, J_{CF} = 292 Hz, *cPr*−*C*), 121.0, 128.9 (*each*, +, *Ar*−*C*), 132.7, 135.2 (*each*, C_{quat}, *Ar*−*C*), 152.1 (C_{quat}, *Ar*−*C*), 156.7 (+, *Ar*−*C*), 161.3 (C_{quat}, *Ar*−*C*), 169.6 (C_{quat}, d, J_{CF} = 3.9 Hz, CO_2). − MS (70 eV, CI); *m*/*z* (%): 441 (100) [M^+ + H]. − $C_{26}H_{30}F_2N_2O_2$ (440.53): C 70.89, H 6.86, N 6.36; found C 70.76, H 7.06, N 6.28. − $[\alpha]_D^{25}$ = −45.4 (*c* = 1.44; $CHCl_3$).

Compound (1*S*,3*S*)-2: Colorless needles (632 mg, 84%), m.p. 78 °C, R_f = 0.23 (pentane/diethyl ether, 5:1). − $C_{26}H_{30}F_2N_2O_2$ (440.53): calcd. C 70.89, H 6.86, N 6.36; found C 70.75, H 6.94, N 6.32. − $[\alpha]_D^{25}$ = +44.0 (*c* = 1.42; $CHCl_3$). IR, ^{1}H NMR, ^{13}C NMR, and MS spectra were identical to those of (1*R*,3*R*)-**2**.

Compound (1*R*,3*R*)-3: Colorless crystals (167 mg, 63%), m.p. 44 °C, R_f = 0.58 (pentane/diethyl ether, 5:1). − IR (KBr): $\tilde{\nu}$ = 2924, 1747 cm^{-1}. − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.82−1.01 (m, 5 H, *Oct*−CH_3, *cPr*−*H*), 1.26−1.40 (m, 13 H, *Oct*−CH_2, *cPr*−*H*), 1.54−1.67 (m, 5 H, *cPr*−*H*), 2.31 (dd, *J* = 6.7, 4.9 Hz, 1 H, *cPr*−*H*), 2.61 (t, *J* = 7.4 Hz, 2 H, *Oct*−CH_2), 7.17 (d, *J* = 8.8 Hz, 2 H, *Ar*−*H*), 8.41 (d, *J* = 8.8 Hz, 2 H, *Ar*−*H*), 8.60 (s, 2 H, *Ar*−*H*). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*): δ = 4.1, 5.4, 12.3 (*each*, −, *cPr*−*C*), 13.9 (C_{quat}, *cPr*−*C*), 14.0 (+, *Oct*−CH_3), 14.8 (−, *cPr*−*C*), 21.0 (+, *cPr*−*C*), 22.5 (−, *Oct*−CH_2), 23.6 (C_{quat}, *cPr*−*C*), 28.9, 29.1, 29.2, 30.0, 30.6, 31.7 (*each*, −, *Oct*−CH_2), 121.4, 129.0 (*each*, +, *Ar*−*C*), 132.8, 135.0 (*each*, C_{quat}, *Ar*−*C*), 152.6 (C_{quat}, *Ar*−*C*), 157.0 (+, *Ar*−*C*), 161.7 (C_{quat}, *Ar*−*C*), 171.7 (C_{quat}, CO_2). − MS (70 eV, EI); *m*/*z* (%): 404 (100) [M^+]. − $C_{26}H_{32}N_2O_2$ (404.55): C 77.19, H 7.97, N 6.92; found C 77.09, H 8.08, N 7.00. − $[\alpha]_D^{25}$ = −39.7 (*c* = 1.10; $CHCl_3$).

Compound (1*S*,3*S*)-3: Colorless crystals (234 mg, 73%), m.p. 44 °C, R_f = 0.33 (pentane/diethyl ether, 5:1). − $C_{26}H_{32}N_2O_2$ (404.55): C 77.19, H 7.97, N 6.92; found C 77.24, H 7.94, N 7.04. − $[\alpha]_D^{25}$ = +34.6 (*c* = 1.14; $CHCl_3$). IR, ^1H NMR, ^{13}C NMR, and MS spectra were identical to those of (1*R*,3*R*)-**3**.

Optical Resolution of *endo*-4-Methylenespiropentylmethanol (*rac*-17): Optical resolution was carried out by enzymatic enantioselective acylation using Lipase PS, as according to the procedure for the optical resolution of *rac*-**8**, to yield an acetate (1*S*,3*R*)-**18** (621 mg, 50%, R_f = 0.51, pentane/diethyl ether, 5:1) as a colorless oil and an alcohol (1*R*,3*S*)-**17** (387 mg, 43%, R_f = 0.10, pentane/diethyl ether, 5:1) as a colorless oil.

Compound (1*S*,3*R*)-18: IR (film): $\tilde{\nu}$ = 1741, 1232 cm^{-1}. − ^1H NMR (250 MHz, $CDCl_3$): δ = 1.07 (t, *J* = 4.6 Hz, 1 H, *cPr*−*H*), 1.25−1.41 (m, 3 H, *cPr*−*H*), 1.60−1.69 (m, 1 H, *cPr*−*H*), 2.03 (s, 3 H, CH_3), 4.01 (dd, *J* = 11.4, 7.0 Hz, 1 H, CH_2O), 4.14 (dd, *J* = 11.4, 7.0 Hz, 1 H, CH_2O), 5.15 (t, *J* = 2.3 Hz, 1 H, $C{=}CH_2$), 5.28 (s, 1 H, $C{=}CH_2$). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*): δ = 7.8, 14.6 (*each*, −, *cPr*−*C*), 15.4 (C_{quat}, *cPr*−*C*), 19.4 (+, CH_3), 20.9 (+, *cPr*−*C*), 67.4 (−, CH_2O), 99.2 (−, $C{=}CH_2$), 134.7 (C_{quat}, $C{=}CH_2$), 171.1 (C_{quat}, CO_2). − MS (70 eV, CI); *m*/*z* (%): 187 (100), 170 (34) [M + NH_4^+]. − $C_9H_{12}O_2$ (152.19): C 71.03, H 7.95; found C 71.28, H 8.18. − $[\alpha]_D^{25}$ = +140.3 (*c* = 1.38; $CHCl_3$).

Compound (1*R*,3*S*)-17: IR (film): $\tilde{\nu}$ = 3344, 1039 cm^{-1}. − ^1H NMR (250 MHz, $CDCl_3$): δ = 1.05 (t, *J* = 4.6 Hz, 1 H, *cPr*−*H*), 1.25 (dd, *J* = 8.0, 4.3 Hz, 1 H, *cPr*−*H*), 1.33−1.44 (m, 2 H, *cPr*−*H*), 1.47 (br s, 1 H, *OH*), 1.59−1.61 (m, 1 H, *cPr*−*H*), 3.66 (dd, *J* = 11.1, 6.7 Hz, 1 H, CH_2O), 3.70 (dd, *J* = 11.1, 6.6 Hz, 1 H, CH_2O), 5.16 (t, *J* = 2.2 Hz, 1 H, $C{=}CH_2$), 5.29 (s, 1 H, $C{=}CH_2$). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*): δ = 7.8, 14.4 (*each*, −, *cPr*−*C*), 15.2 (C_{quat}, *cPr*−*C*), 23.1 (+, *cPr*−*C*), 65.7 (−, CH_2O), 99.0 (−, $C{=}CH_2$), 135.1 (C_{quat}, $C{=}CH_2$). − MS (70 eV, EI); *m*/*z* (%): 110 (0.4) [M^+], 67 (100). − $[\alpha]_D^{25}$ = −194.5 (*c* = 1.29; $CHCl_3$). The spectral data were identical to those of the racemate.[4b]

Synthesis of Difluorodispiro[2.0.2.1]heptylmethanols (1*R*,3*S*,4*R*)-19 and (1*R*,3*S*,4*S*)-19: To a mixture of THP-protected (1*R*,3*S*)-**17** (1.02 g, 5.25 mmol), KF (2.44 g, 42 mmol), 18-crown-6 (139 mg, 0.526 mmol), and DME (30 mL) at room temperature was added portionwise, over 6 h, $[CF_2BrPPh_3]^+Br^-$, generated from CBr_2F_2 (7.71 g, 36.7 mmol) and PPh_3 (6.89 g, 26.3 mmol) in DME (25 mL). Workup as usual gave a mixture of two fluorinated compounds, which were deprotected and then separated by column chromatography on silica gel (pentane/diethyl ether, 1:1), to give (1*R*,3*S*,4*R*)-**19** (269 mg, 32%, R_f = 0.26) as a yellow oil and (1*R*,3*S*,4*S*)-**19** (317 mg, 38%, R_f = 0.18) as a yellow, viscous oil.

Compound (1*R*,3*S*,4*R*)-19: IR (film): $\tilde{\nu}$ = 3334, 1209, 1037 cm^{-1}. − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.82 (t, *J* = 4.8 Hz, 1 H, *cPr*−*H*), 1.04 (t, *J* = 4.8 Hz, 1 H, *cPr*−*H*), 1.36−1.69 (m, 6 H, *OH*, *cPr*−*H*), 3.55 (dd, *J* = 11.2, 7.3 Hz, 1 H, CH_2O), 3.72 (dd, *J* = 11.2, 6.4 Hz, 1 H, CH_2O). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*): δ = 9.1 (−, d, J_{CF} = 3.2 Hz, *cPr*−*C*), 10.6 (−, d, J_{CF} = 2.3 Hz, *cPr*−*C*), 15.9 (−, t, J_{CF} = 10.9 Hz, *cPr*−*C*), 18.4 (+, *cPr*−*C*), 19.2 (C_{quat}, t, J_{CF} = 10.7 Hz, *cPr*−*C*), 20.0 (C_{quat}, d, J_{CF} = 2.9 Hz, *cPr*−*C*), 65.2 (−, CH_2O), 114.0 (C_{quat}, t, J_{CF} = 289 Hz, CF_2). − MS (70 eV, CI); *m*/*z* (%): 195 (100), 178 (98) [M + NH_4^+]. − $C_8H_{10}F_2O$ (160.16): calcd. C 59.99, H 6.29; found C 59.81, H 6.36. − $[\alpha]_D^{25}$ = −50.6 (*c* = 1.03; $CHCl_3$).

Compound (1*R*,3*S*,4*S*)-19: IR (film): $\tilde{\nu}$ = 3338, 1207, 1024 cm^{-1}. − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.84 (t, *J* = 4.8 Hz, 1 H, *cPr*−*H*), 1.17 (dd, *J* = 8.5, 5.3 Hz, 1 H, *cPr*−*H*), 1.25−1.52 (m, 5 H, *OH*, *cPr*−*H*), 1.67 (t, *J* = 8.5 Hz, 1 H, *cPr*−*H*), 3.66 (d, *J* = 6.8 Hz, 2 H, CH_2O). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*): δ = 9.5 (−, *cPr*−*C*), 10.4 (−, d, J_{CF} = 1.9 Hz, *cPr*−*C*), 15.9 (−, t, J_{CF} = 10.9 Hz, *cPr*−*C*), 18.1 (+, d, J_{CF} = 2.9 Hz, *cPr*−*C*), 19.1 (C_{quat}, t, J_{CF} = 10.7 Hz, *cPr*−*C*), 20.0 (C_{quat}, d, J_{CF} = 3.1 Hz, *cPr*−*C*), 65.2 (−, CH_2O), 113.9 (C_{quat}, t, J_{CF} = 290 Hz, CF_2). − MS (70 eV, CI); *m*/*z* (%): 177 (6) [M + NH_4^+ − H], 176 (100). − $C_8H_{10}F_2O$ (160.16): C 59.99, H 6.29; found C 59.92, H 6.13. − $[\alpha]_D^{25}$ = −106.9 (*c* = 1.37; $CHCl_3$).

Synthesis of (1*R*,3*S*,4*R*)-5,5-Difluorodispiro[2.0.2.1]heptane-1-carboxylic Acid [(1*R*,3*S*,4*R*)-20]: To a solution of (1*R*,3*S*,4*R*)-**19** (231 mg, 1.44 mmol) in acetone (10 mL) at 0 °C was added dropwise a mixture of CrO_3 (2.76 g, 27.6 mmol), H_2SO_4 (2.3 mL), and H_2O (10 mL), until the reddish color remained permanent. After 0.5 h of stirring at this temperature, workup as usual and purification by column chromatography on silica gel (pentane/diethyl ether, 1:1, R_f = 0.45) provided 204 mg (81%) of (1*R*,3*S*,4*R*)-**20** as colorless crystals, m.p. 111−114 °C. − IR (KBr): $\tilde{\nu}$ = 3085, 1694, 1237 cm^{-1}. − ^1H NMR (250 MHz, $CDCl_3$): δ = 1.44 (dd, *J* = 8.0, 4.5 Hz, 1 H, *cPr*−*H*), 1.53−1.75 (m, 5 H, *cPr*−*H*), 2.12 (dd, *J* = 8.0, 4.5 Hz, 1 H, *cPr*−*H*), 11.02 (br s, 1 H, *OH*). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*): δ = 12.1 (−, d, J_{CF} = 1.9 Hz, *cPr*−*C*), 13.8 (−, d, J_{CF} = 3.1 Hz, *cPr*−*C*), 16.0 (−, t, J_{CF} = 11.0 Hz, *cPr*−*C*), 18.7 (+, *cPr*−*C*), 20.0 (C_{quat}, t, J_{CF} = 11.0 Hz, *cPr*−*C*), 24.5 (C_{quat}, d, J_{CF} = 3.1 Hz, *cPr*−*C*), 113.1 (C_{quat}, t, J_{CF} = 289 Hz, CF_2), 179.4 (C_{quat}, CO_2). − MS (70 eV, CI); *m*/*z* (%): 192 (100) [M + NH_4^+]. − $C_8H_8F_2O_2$ (174.15): C 55.18, H 4.63; found C 55.09, H 4.71. − $[\alpha]_D^{25}$ = −241.7 (*c* = 1.10; $CHCl_3$).

In the same manner, (1*R*,3*S*,4*S*)-**20** was synthesized from (1*R*,3*S*,4*S*)-**19**. Colorless crystals (243 mg, 78%), m.p. 107−110.5 °C, R_f = 0.41 (pentane/diethyl ether, 1:1). − IR (KBr): $\tilde{\nu}$ = 3065, 1701, 1324, 1228, 1208 cm^{-1}. − ^1H NMR (250 MHz, $CDCl_3$): δ = 1.52−1.60 (m, 3 H, *cPr*−*H*), 1.70−1.79 (m, 3 H, *cPr*−*H*), 1.99 (dd, *J* = 8.0, 4.7 Hz, 1 H, *cPr*−*H*), 11.65 (br s, 1 H, *OH*). − ^{13}C NMR (250 MHz, $CDCl_3$, *additional DEPT*): δ = 12.1, 14.5 (*each*, −, *cPr*−*C*), 16.2 (−, t, J_{CF} = 11.0 Hz, *cPr*−*C*), 19.1 (+, d, J_{CF} = 3.0 Hz, *cPr*−*C*), 20.1 (C_{quat}, t, J_{CF} = 11.0 Hz, *cPr*−*C*), 25.0 (C_{quat}, *cPr*−*C*), 113.0 (C_{quat}, t, J_{CF} = 290 Hz, CF_2), 179.5 (C_{quat}, CO_2). − MS (70 eV, EI); *m*/*z* (%): 173 (7) [M^+ − H], 109 (100). − $C_8H_8F_2O_2$ (174.15): C 55.18, H 4.63; found C 55.21, H 4.79. − $[\alpha]_D^{25}$ = −322.9 (*c* = 0.97; $CHCl_3$).

Synthesis of 4-(5-Octylpyrimid-2-yl)phenyl 5,5-Difluorodispiro[2.0.2.1]heptane-1-carboxylate [(1*R*,3*S*,4*R*)-4]: A mixture of

(1*R*,3*S*,4*R*)-**20** (131 mg, 0.75 mmol), 4-(5-octylpyrimid-2-yl)phenol (277 mg, 0.97 mmol), DCC (200 mg, 0.97 mmol), DMAP (9 mg, 0.074 mmol), and dichloromethane (10 mL) was stirred at room temperature for 21 h. Workup as usual, followed by silica gel column chromatography (pentane/diethyl ether, 5:1, R_f = 0.11), gave 224 mg (68%) of (1*R*,3*S*,4*R*)-**4** as colorless crystals, m.p. 102 °C. − IR (KBr): $\tilde{\nu}$ = 3026, 1748, 1207 cm^{-1}. − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 6.4 Hz, 3 H, *Oct*−CH_3), 1.27−1.32 (m, 12 H, *Oct*−CH_2), 1.51−1.81 (m, 6 H, *cPr*−*H*), 2.36 (dd, *J* = 8.0, 4.7 Hz, 1 H, *cPr*−*H*), 2.61 (t, *J* = 7.4 Hz, 2 H, *Oct*−CH_2), 7.23 (d, *J* = 8.8 Hz, 2 H, *Ar*−*H*), 8.44 (d, *J* = 8.8 Hz, 2 H, *Ar*−*H*), 8.61 (s, 2 H, *Ar*−*H*). − ^{13}C NMR (250 MHz, $CDCl_3$, *additional DEPT*): δ = 12.2, 13.8 (*each*, −, *cPr*−*C*), 14.0 (+, *Oct*−CH_3), 16.0 (−, t, J_{CF} = 10.7 Hz, *cPr*−*C*), 18.9 (+, *cPr*−*C*), 20.0 (C_{quat}, t, J_{CF} = 11.3 Hz, *cPr*−*C*), 22.5 (−, *Oct*−CH_2), 24.5 (C_{quat}, d, J_{CF} = 3.1 Hz, *cPr*−*C*), 28.9, 29.1, 29.2, 30.1, 30.9, 31.7 (*each*, −, *Oct*−CH_2), 113.1 (C_{quat}, t, J_{CF} = 284 Hz, CF_2), 121.5, 129.0 (*each*, +, *Ar*−*C*), 132.9, 135.2, 152.4 (*each*, C_{quat}, *Ar*−*C*), 156.9 (+, *Ar*−*C*), 161.6 (C_{quat}, *Ar*−*C*), 170.7 (C_{quat}, CO_2). − MS (70 eV, EI); *m*/*z* (%): 440 (77) [M^+], 284 (100). − $C_{26}H_{30}F_2N_2O_2$ (440.53): calcd. C 70.89, H 6.86, N 6.36; found C 71.06, H 6.94, N 6.40. − $[\alpha]_D^{25}$ = −158.1 (*c* = 1.06; $CHCl_3$).

Following the same procedure, (1*R*,3*S*,4*S*)-**4** was synthesized from (1*R*,3*S*,4*S*)-**20**: Colorless crystals (193 mg, 59%), m.p. 80 °C, R_f = 0.15 (pentane/diethyl ether, 5:1). − IR (KBr): $\tilde{\nu}$ = 3077, 1751, 1329, 1200 cm^{-1}. − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 6.3 Hz, 3 H, *Oct*−CH_3), 1.27−1.32 (m, 12 H, *Oct*−CH_2), 1.59−1.71 (m, 4 H, *cPr*−*H*), 1.82−1.84 (m, 2 H, *cPr*−*H*), 2.22 (dd, *J* = 8.1, 4.8 Hz, 1 H, *cPr*−*H*), 2.62 (t, *J* = 7.3 Hz, 2 H, *Oct*−CH_2), 7.21 (d, *J* = 8.8 Hz, 2 H, *Ar*−*H*), 8.44 (d, *J* = 8.8 Hz, 2 H, *Ar*−*H*), 8.61 (s, 2 H, *Ar*−*H*). − ^{13}C NMR (62.9 MHz, $CDCl_3$, *additional DEPT*): δ = 12.0 (−, d, J_{CF} = 1.9 Hz, *cPr*−*C*), 14.0 (+, *Oct*−CH_3), 14.3 (−, *cPr*−*C*), 16.2 (−, t, J_{CF} = 10.9 Hz, *cPr*−*C*), 19.1 (+, d, J_{CF} = 3.1 Hz, *cPr*−*C*), 20.0 (C_{quat}, t, J_{CF} = 10.9 Hz, *cPr*−*C*), 22.5 (−, *Oct*−CH_2), 24.8 (C_{quat}, d, J_{CF} = 2.3 Hz, *cPr*−*C*), 28.9, 29.1, 29.2, 30.0, 30.6, 31.7 (*each*, −, *Oct*−CH_2), 113.1 (C_{quat}, t, J_{CF} = 285 Hz, CF_2), 121.4, 129.0 (*each*, +, *Ar*−*C*), 132.9, 135.2, 152.4 (*each*, C_{quat}, *Ar*−*C*), 156.9 (+, *Ar*−*C*), 161.6 (C_{quat}, *Ar*−*C*), 170.7 (C_{quat}, CO_2). − MS (70 eV, EI); *m*/*z* (%): 440 (67) [M^+], 284 (100). − $C_{26}H_{30}F_2N_2O_2$ (440.53): C 70.89, H 6.86, N 6.36; found C 70.95, H 6.99, N 6.37. − $[\alpha]_D^{25}$ = −195.6 (*c* = 1.26; $CHCl_3$).

Acknowledgments

This work was supported by the Fonds der Chemischen Industrie. K. M. is grateful to Chisso Corporation for their financial support. We are grateful to Dr. S. I. Kozhushkov for the donation of compound *rac*-**10**, as well as for his help in preparing the final manuscript, and to Dr. B. Knieriem for his careful proofreading of the manuscript.

[1] N. A. Clark, S. T. Lagerwall, *Appl. Phys. Lett.* **1980**, *36*, 899−901.
[2] *LiqCryst 3.2*, Database of Liquid Crystalline Compounds, © **1999** Volker Vill and LCI Publisher, Hamburg.
[3] Cf.: [3a] R. B. Meyer, L. Liebert, L. Strzelecki, P. Keller, *J. Phys. Lett.* **1975**, *36*, 69−71. − [3b] T. Inukai, S. Saito, H. Inoue, K. Miyazawa, K. Furukawa, *Mol. Cryst. Liq. Cryst.* **1986**, *141*, 251−266.
[4] Compounds consisting exclusively of *n* spiro-fused cyclopropane rings have been termed [*n*]triangulanes, cf. for racemic compounds of this kind: [4a] K. A. Lukin, S. I. Kozhushkov, A. A. Andrievsky, B. I. Ugrak, N. S. Zefirov, *J. Org. Chem.* **1991**, *56*, 6176−6179. − [4b] K. A. Lukin, A. Yu. Masunova, B. I. Ugrak, N. S. Zefirov, *Tetrahedron* **1991**, *47*, 5769−5780. − [4c] N. S. Zefirov, S. I. Kozhushkov, B. I. Ugrak, K. A. Lukin, O. V. Kokoreva, D. S. Yufit, Y. T. Struchkov, S. Zoellner, R. Boese, A. de Meijere, *J. Org. Chem.* **1992**, *57*, 701−708. − [4d] A. de Meijere, S. I. Kozhushkov, T. Spaeth, N. S. Zefirov, *J. Org. Chem.* **1993**, *58*, 502−505. − [4e] Review: A. de Meijere, S. I. Kozhushkov, *Chem. Rev.* **2000**, *100*, 93−142.
[5] For the first report on an optically active [*n*]triangulane, see: A. de Meijere, A. F. Khlebnikov, R. R. Kostikov, S. I. Kozhushkov, P. R. Schreiner, A. Wittkopp, D. S. Yufit, *Angew. Chem.* **1999**, *111*, 3682−3685; *Angew. Chem. Int. Ed. Engl.* **1999**, *38*, 3472−3474.
[6] E. V. Dehmlow, *Angew. Chem.* **1974**, *86*, 187−196; *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 170−203.
[7] [7a] D. J. Burton, D. G. Naae, *J. Am. Chem. Soc.* **1973**, *95*, 8467−8468. − [7b] Y. Bessard, U. Müller, M. Schlosser, *Tetrahedron* **1990**, *46*, 5213−5221.
[8] P. E. Eaton, K. A. Lukin, *J. Am. Chem. Soc.* **1993**, *115*, 11370−11375.
[9] The compound *rac*-**10** was donated by Dr. S. I. Kozhushkov, Institut für Organische Chemie, Georg-August-Universität Göttingen.
[10] F. H. Allen, *Acta Crystallogr.* **1980**, *B36*, 81−96. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-145924 {*N*-[(*R*)-1-phenylethyl]-(1*R*,3*R*)-7,7-dichlorodispiro[2.0.2.1]heptane-1-carboxamide}, -144318 [(1*R*,3*S*,4*S*)-**20**], and -144319 [(1*R*,3*S*,4*R*)-**20**]. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) (+) 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].
[11] [11a] R. Paulissen, A. J. Hubert, P. Teyssie, *Tetrahedron Lett.* **1972**, 1465−1466. − [11b] U. Mende, B. Radüchel, W. Skuballa, H. Vorbrüggen, *Tetrahedron Lett.* **1975**, 629−632.
[12] J. A. Dale, D. L. Dull, H. S. Mosher, *J. Org. Chem.* **1969**, *34*, 2543−2549.
[13] K. Miyasato, S. Abe, H. Takezoe, A. Fukuda, E. Kuze, *Jpn. J. Appl. Phys.* **1983**, *22*, 661−663.
[14] S. T. Lagerwall, I. Dahl, *Mol. Cryst. Liq. Cryst.* **1984**, *114*, 151−187.
[15] Ph. Martinot−Lagarde, R. Duke, G. Durand, *Mol. Cryst. Liq. Cryst.* **1981**, *75*, 249−286.
[16] R. R. Cano, *Bull. Soc. Fr. Mineral Cristallogr.* **1967**, *90*, 333−351.

Received June 23, 2000
[O00314]