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Synthesis of optically active 4,4,4-trifluoro-3-{4-(4-methoxyphenyl) phenyl}butanoic acid and its application to chiral dopant for nematic liquid crystals

Kenta Tojo, Yoshio Aoki *, Mikio Yasutake, Takuji Hirose

Department of Applied Chemistry, Faculty of Engineering, Saitama University, 255 Shimo-ohkubo, Sakura-ku, Saitama 338-8570, Japan

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Abstract

We synthesized an optically active 4,4,4-trifluoro-3-{4-(4-methoxyphenyl)phenyl}butanoic acid (**5***). New chiral dopants for nematic liquid crystals were derived from (*R*)-(−)-**5***, and their helical twisting power (HTP) values were measured. Their HTP values were largely influenced by the linkage between the asymmetric frame and the core moiety. The chiral dopant, (*R*)-(+)-4,4,4-trifluoro-1-(4-hexyloxyphenyl)-3-{4-(4-methoxyphenyl)phenyl}-1-butanone ((*R*)-(+)-**7***) showed the largest HTP value (−21.7 μm^{-1}).

Keywords: Trifluoromethyl asymmetric frame; Chiral dopant; Helical twisting power; Nematic liquid crystals

1. Introduction

Chirality is one of the most interesting subjects in the field of liquid crystals. Chiral nematic liquid crystals having macro helical structure are currently used in liquid crystal display (LCD) devices. Generally the chiral nematic materials consist of achiral host mixtures of nematic liquid crystals, and a chiral dopant with a large helical twisting power (HTP) [1]. The helical structure of the chiral nematic liquid crystals is induced by the interaction between the host liquid crystalline molecules and the chiral dopants. Therefore, many optically active compounds for application in nematic mixtures have been synthesized. We have reported the HTP values of optically active 3-phenylpropanoic acid derivatives [2]. On the other hand, a noble compound derived from optically active tartaric acid was reported as a chiral dopant, and its HTP value did not have a temperature dependence [3]. Ferrarini et al. reported a correlation between the molecular structure and helicity of chiral atropisomers [4], and some optically active biphenyl or binaphthyl derivatives were reported as atropisomeric chiral dopants [5a,b]. Recently, Hamakubo et al. reported a chiral dopant with a helical chirality [6].

A tilted smectic phase such as smectic C phase, made up of optically active compounds shows ferroelectric properties, and the liquid crystals are called ferroelectric liquid crystals (FLCs) [7]. The microsecond response speeds of FLCs are very fast compared with that of nematic liquid crystals. On the other hand, noble liquid crystals showing antiferroelectric chiral smectic phases have been reported [8]. Antiferroelectric liquid crystal (AFLC) materials are expected to be applicable to high speed display devices.

Fluorinated liquid crystal materials are very effective for improving the physical properties of liquid crystals. Nematic liquid crystalline materials with a fluoro or trifluoromethyloxy group at the aromatic ring show low rotational viscosity and appropriate dielectric anisotropy. In FLC materials, *ortho* difluorophenyl structure is useful for generating the smectic C phase [9]. In addition, the liquid crystalline materials with a fluorine atom at the chiral center are useful for increasing the spontaneous polarization of liquid crystals [10]. A trifluoromethyl asymmetric frame is effective for showing AFLC phase [8,11]. We have reported the physical properties of optically active 4,4,4-trifluoro-3-(4-methoxyphenyl)butanoic acid derivatives, which showed interesting mesophases such as AFLC phases and the twist grain boundary (TGB) phase [12a–c].

* Corresponding author. Tel.: +81 48 858 9548; fax: +81 48 858 9548.
E-mail address: aoki@apc.saitama-u.ac.jp (Y. Aoki).

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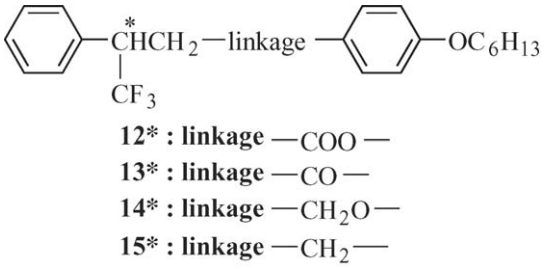


Fig. 1. Structure of TFPBA derivatives (**12***–**15***).

On the other hand, we have been investigating the relationship between the existence of a polar group at the chiral center and their HTP values for nematic liquid crystals. We have reported the HTP values of optically active 4,4,4-trifluoro-3-phenylbutanoic acid (TFPBA) derivatives (**12***, **13***, **14***, **15***, Fig. 1) [13]. As a consequence, a trifluoromethyl asymmetric frame was found to effectively increase the HTP value of the chiral dopant. A trifluoromethyl group is a strong polar group, so the electronic effect of a trifluoromethyl group is probably effective for generating a large HTP value.

In the present paper, we report the synthesis and the HTP evaluation of the new chiral dopants for nematic liquid crystals, having a trifluoromethyl asymmetric frame and a biphenyl structure at the chiral center, 4,4,4-trifluoro-3-{4-(4-methoxyphenyl)phenyl}butanoic acid (**5***) derivatives (**6***, **7***, **10***, **11***, Fig. 2).

2. Results and discussion

An optically active key intermediate 4,4,4-trifluoro-3-{4-(4-methoxyphenyl)phenyl}butanoic acid (**5***) was synthesized in the usual manner (Scheme 1) [5]. An absolute configuration of **5*** was decided through X-ray analysis of the diastereomeric salt of (−)-**5*** and (1*S*, 2*R*)-(−)-2-(benzylaminocyclohexane) methanol, and it was clarified that (−)-**5*** has (*R*)-configuration [14]. All new chiral dopants (**6***, **7***, **10***, **11***) were derived from

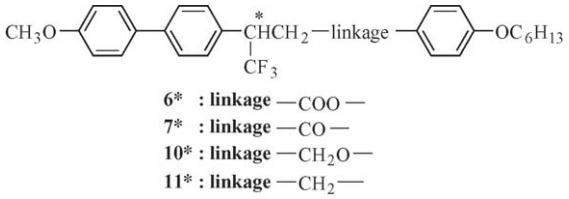


Fig. 2. Structure of new chiral dopants.

(*R*)-(−)-**5*** (Scheme 2), and did not show any mesophases. Therefore, only their HTP values for nematic liquid crystals were determined.

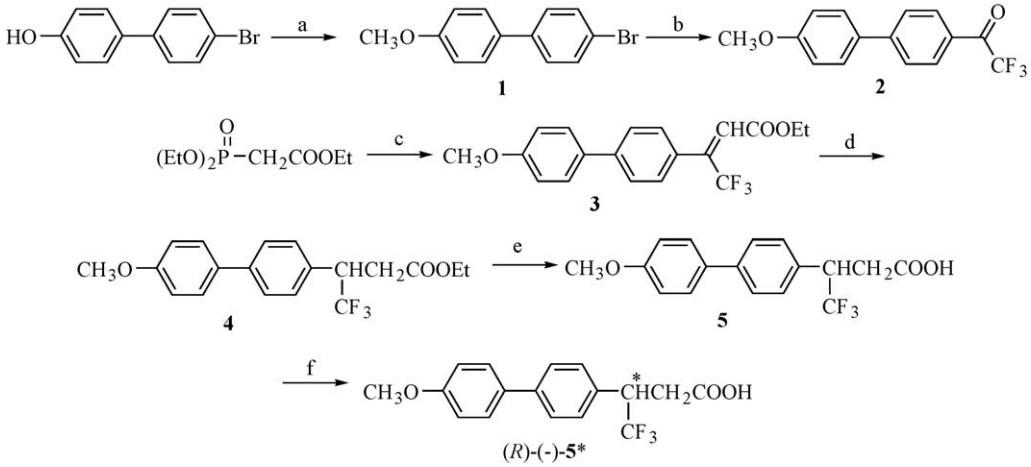
The chiral nematic liquid crystalline mixtures were prepared by adding chiral dopant (1 wt.%) to the host nematic liquid crystal (ZLI-1132, Merck) [15]. The helical pitches in the chiral nematic phases were measured using Cano wedge cells [16]. The HTP can be calculated by Eq. (1), where p is the pitch of the chiral nematic phase in μm and c is the mass fraction of the chiral dopant. In order to describe the HTP per molecule, we have suggested the molar helical twisting power (MHTP), as defined in Eq. (2), where Md is the molecular weight of the chiral dopant [2]. In the present paper, we discuss the MHTP values of the chiral dopants

$$\mathrm{HTP}\,(\mu\mathrm{m}^{-1}) = (pc)^{-1} \tag{1}$$

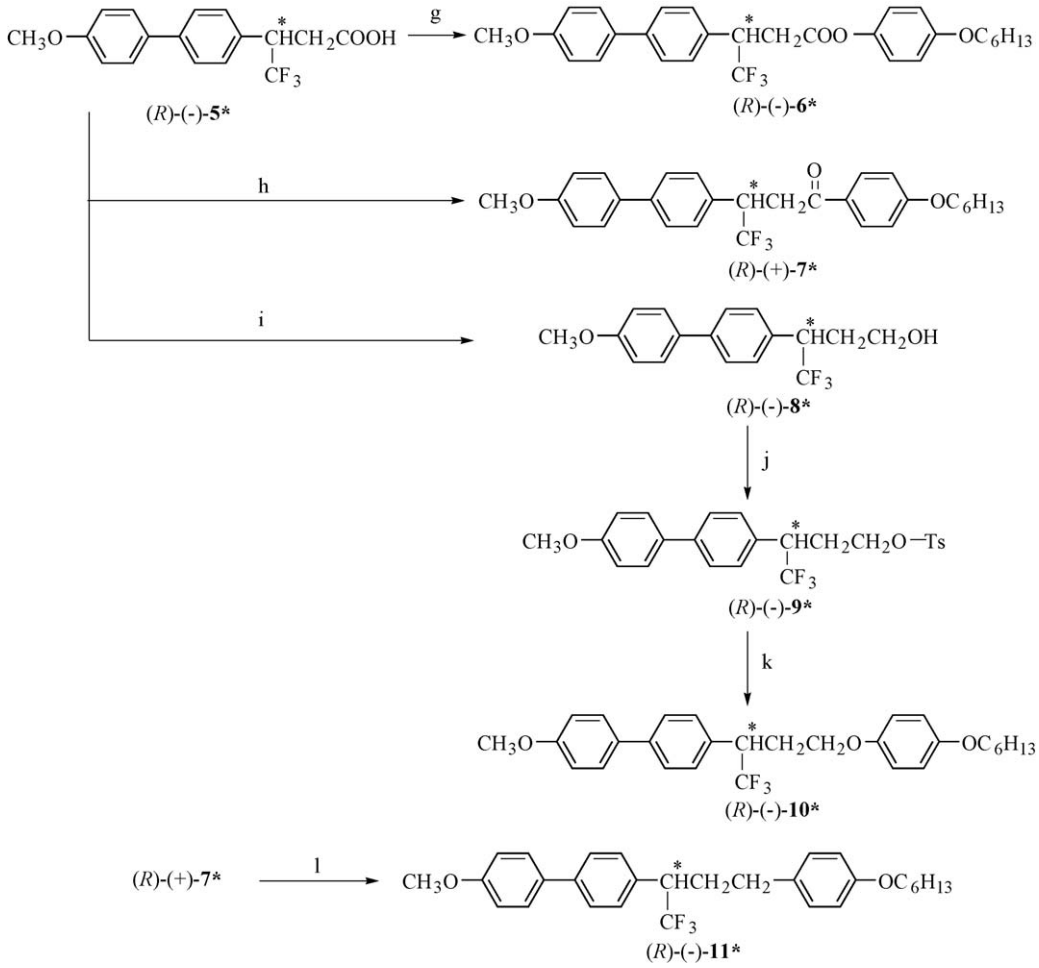
$$\mathrm{MHTP}\,(\mu\mathrm{m}^{-1}\,\mathrm{mol}^{-1}\,\mathrm{kg}) = \mathrm{HTP}\,\mathrm{Md} \times 10^{-3} \tag{2}$$

The helical senses of the chiral nematic phases were determined by the contact method using the reference mixture prepared from the host liquid crystal and cholesteryl nonanoate, which has a helix with a minus sense (left-handed). The HTP, MHTP values and helical senses of the new chiral dopants are summarized in Table 1.

The order of absolute MHTP values in these chiral dopants was **7*** > **10*** > **6*** > **11***. In the case of the chiral dopants



Scheme 1. Synthesis of optically active 4,4,4-trifluoro-3-{4-(4-methoxyphenyl)phenyl}butanoic acid (**5***): (a) CH_3I, K_2CO_3, THF, CH_3CN, 60 °C. (b) 1: Mg, dry THF. 2: CF_3COONa, 0 °C. (c) 1: NaH, dry THF. 2: **2**, 60 °C. (d) H_2, cat. Pt, EtOH, THF. (e) 1: KOHaq, 2: 1 M HClaq. (f) Optical resolution, (1*R*, 2*S*)-(−)-(2-benzylaminocyclohexane) methanol.



Scheme 2. Synthesis of new chiral dopants, **6***, **7***, **10***, **11***: (g) 4-hexyloxyphenol, DCC, DMAP, dry $CHCl_3$. (h) 1: $SOCl_2$, reflux. 2: hexyloxybenzene, $AlCl_3$, dry CS_2, −20 °C. (i) $LiAlH_4$, dry THF, reflux. (j) TsCl, DABCO, dry CH_3CN. (k) 4-hexyloxyphenol, K_2CO_3, CH_3CN, THF, 60 °C. (l) Et_3SiH, CF_3COOH.

derived from an optically active TFPBA, the order of the MHTP values was the same as that of the **5*** derivatives. On the other hand, the PM3 calculations of (*R*)-**6*** and (*R*)-**12*** showed that the conformation of (*R*)-**6*** was similar to that of (*R*)-**12*** (Fig. 3). Therefore these results suggest that the conformations of **5*** derivatives and TFPBA derivatives are similar to each other, and the order of MHTP values of **5*** derivatives was the same as that of the TFPBA derivatives.

Table 1
HTP and MHTP values of new chiral dopants, **6***, **7***, **10***, **11***

	Linkage	HTP[a] (μm^{-1})	MHTP[b] (μm^{-1} mol^{-1} kg)
6*	–COO–	+8.3	+4.2
7*	–CO–	−21.7	−10.5
10*	$–CH_2O–$	+14.3	+6.9
11*	$–CH_2–$	+3.2	+1.5

[a] HTP (μm^{-1}) = $(pc)^{-1}$; *p*: helical pitch (μm), *c*: weight ratio of the chiral dopant (*c*: 0.01).
[b] MHTP (μm^{-1} mol^{-1} kg) = HTP Mw × 10^{-3}; Mw: molecular weight of the chiral dopant, host L.C.: ZLI-1132 (Merck).

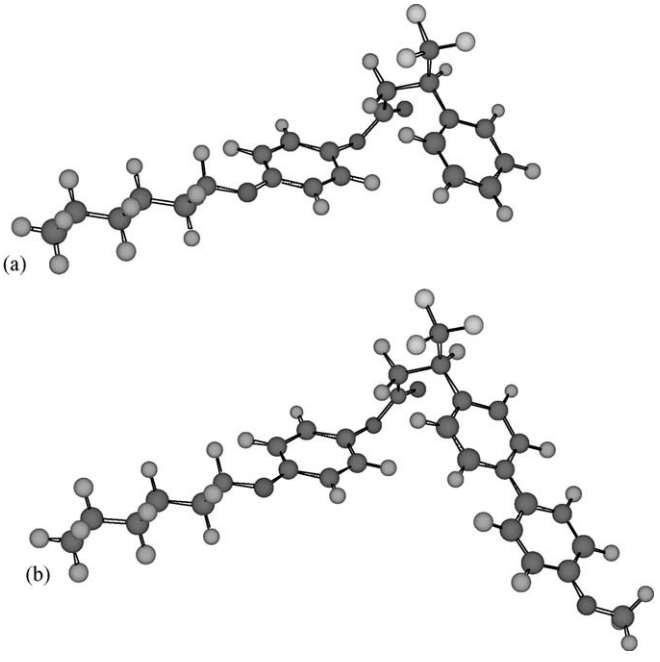


Fig. 3. PM3 models of (a) (*R*)-**12*** and (b) (*R*)-**6***.

All of the new chiral dopants were derived from (*R*)-(−)-**5***, and **6***, **10***, **11*** induced a right-handed helical sense of the chiral nematic phase. However, **7*** induced the opposite helical sense. Interestingly, only **7*** showed plus optical rotation, while other chiral dopants showed minus optical rotations.

The corresponding MHTP values of the new chiral dopants (**6***: +4.2 μm^{-1} mol^{-1} kg, **7***: −10.5 μm^{-1} mol^{-1} kg, **10***: +6.9 μm^{-1} mol^{-1} kg) were 20–45% larger than those of the TFPBA derivatives (**12***: 2.9 μm^{-1} mol^{-1} kg, **13***: 7.9 μm^{-1} mol^{-1} kg, **14***: 5.8 μm^{-1} mol^{-1} kg). On the other hand, the MHTP value of **11*** (+1.5 μm^{-1} mol^{-1} kg) was 29% smaller than that of **15*** (2.1 μm^{-1} mol^{-1} kg). In most cases, a biphenyl structure at the chiral center was found to increase the MHTP value.

We synthesized new chiral dopants having a trifluoromethyl group and a biphenyl group at the chiral center. New chiral dopants showed relatively large HTP values. It is suggested that a trifluoromethyl and a biphenyl asymmetric frame is useful for increasing HTP value for nematic liquid crystals.

3. Experimental

3.1. General

All compounds were characterized by ^{1}H NMR (Bruker AC-300P or AC-200), IR (JASCO FT/IR-460), and MS (JEOL DX-303). Their specific rotations, i.e. $[\alpha]_D$ values were determined using a JASCO DIP-370. The purities of the products were measured by gas chromatography or high performance liquid chromatography (HPLC). Optical purities were also determined by an HPLC system equipped with a chiral column (Dicel AD-H). The X-ray crystal structure analysis was performed using a Bruker SMART APEX diffractmeter.

3.1.1. 4-(4-Methoxyphenyl)bromobenzene (*1*)

Potassium carbonate (41.4 g, 150 mmol) was added to a solution of 4-(4-hydroxyphenyl)bromobenzene (25 g, 100 mmol), THF (80 ml) and acetonitrile (20 ml), and the reaction mixture was stirred for 20 min at room temperature. Then iodomethane (21.3 g, 150 mmol) was added to the reaction mixture, and the mixture was stirred for 3 days at 60 °C. After evaporating the THF and acetonitrile, chloroform was added, and potassium carbonate was filtrated off. Hydrochloric acid (6 M) was added to the solution, and the phases were separated. The aqueous phase was shaken with chloroform, and the combined organic phases were washed with saturated aqueous sodium hydrogen carbonate and brine. The organic phases were dried over sodium sulphate. Removal of the solvent and purification by recrystallization from toluene (100 ml) and hexane (100 ml) yielded 22.0 g (83.7 mmol, 83.7%) of **1** as a colorless needles: mp 143.5–143.8 °C; IR (KBr): 1604, 1523, 1482, 1289, 1255, 1199, 1179, 1079, 1037, 1010, 811; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.54 (d, J = 8.8 Hz, 2H, aromatic), 7.49 (d, J = 8.8 Hz, 2H, aromatic), 7.40 (d, J = 8.3 Hz, 2H, aromatic), 6.98 (d, J = 8.8 Hz, 2H, aromatic), 3.85 (s, 3H, OCH_3); MS (EI): m/z = 262 [M^+].

3.1.2. 1,1,1-Trifluoro-4-(4-methoxyphenyl)acetophenone (*2*)

Under nitrogen, a dry THF solution of 4-(methoxyphenyl)-bromobenzene (22.0 g, 83.7 mmol) was slowly added to a mixture of magnesium powder (2.13 g, 87.5 mmol) and dry THF, and the reaction mixture was stirred for 4 h at 60 °C. Under nitrogen, the mixture was slowly added to the dry THF solution of 60% NaH (3.68 g, 92.1 mmol) and trifluoroacetic acid at 0 °C. The mixture was then stirred for 36 h. Thereafter, 6 M hydrochloric acid was added. After evaporating the THF, chloroform was added, and the phases were separated. The aqueous phase was shaken with chloroform, and the combined organic phases were washed with saturated aqueous sodium hydrogen carbonate and brine. The organic phases were dried over sodium sulphate. Removal of the solvent and purification by reduced-pressure distillation yielded 7.41 g (26.5 mmol, 31.6%) of **2** as a light yellow solid; mp 107.2–108.0 °C; IR (KBr): 2345, 1710, 1654, 1598, 1561, 1542, 1526, 1498, 1178, 1089, 1063; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.12 (d, J = 8.8 Hz, 2H, aromatic), 7.72 (d, J = 8.8 Hz, 2H, aromatic), 7.60 (d, J = 8,8 Hz, 2H, aromatic), 7.20 (d, J = 8.8 Hz, 2H, aromatic), 3.87 (s, 3H, OCH_3); MS (EI): m/z = 278 [M^+].

3.1.3. Ethyl 4,4,4-trifluoro-3-{4-(4-methoxyphenyl)phenyl}but-2-enoate (*3*)

Under nitrogen, a dry THF solution of ethyl diethylphosphonoacetate (13.0 g, 58.0 mmol) was slowly added to a dry THF solution of 60% NaH (2.32 g, 58.0 mmol) at 0 °C, and the mixture was stirred for 3 h at room temperature. A dry THF solution of 1,1,1-trifluoro-4-(4-methoxyphenyl)acetophenone (14.8 g, 52.7 mmol) was added, and the mixture was stirred for 15 h at 60 °C. The mother liquor was decanted from the precipitate. The precipitate was washed well by mixing it at 60 °C with several 25 ml portions of THF and decanting at room temperature. After evaporating the solvent, 6 M hydrochloric acid and toluene were added and stirred for few minutes. The phases were separated, and the aqueous phase was shaken with toluene. The combined organic phases were washed with saturated aqueous sodium hydrogen carbonate and brine. The organic phase was dried over sodium sulphate. Removal of the solvent and purification by reduced-pressure distillation yielded 18.0 g (51.4 mmol, 97.5%) of **3** as a light yellow liquid; IR (neat): 2986, 2838, 1730, 1659, 1608, 1580, 1525, 1499, 1465, 1374, 1285, 1255, 1180, 1133, 1025, 824, 757, 664; ^{1}H NMR (200 MHz, $CDCl_3$): 7.58 (d, J = 6.3 Hz, 2H, aromatic), 7.55 (d, J = 6.3 Hz, 2H, aromatic), 7.34 (d, J = 8.3 Hz, 2H, aromatic), 6.98 (d, J = 8.3 Hz, aromatic), 6.62 (d, J = 1.5 Hz, C=CH), 4.08 (q, J = 7.3 Hz, 2H, OCH_2), 3.86 (s, 3H, OCH_3), 1.09 (t, J = 7.3 Hz, 3H, CH_3); MS (EI): m/z = 350 [M^+].

3.1.4. Ethyl 4,4,4-trifluoro-3-{4-(4-methoxyphenyl)phenyl}butanoate (*4*)

Under hydrogen, ethyl 4,4,4-trifluoro-3-{4-(4-methoxyphenyl)phenyl}but-2-enoate (19.5 g, 55.6 mmol), platinum black (1.45 g), 16 ml of 95% ethanol, and 25 ml of THF were stirred for 18 h at room temperature. The platinum black was filtered off, followed by removal of the solvent, which yielded 19.1 g

(54.3 mmol, 97.7%) of **4** as a white solid; mp 103.1–103.6 °C; IR (KBr): 2694, 1730, 1606, 1501, 1383, 1333, 1272, 1205, 1159, 1112, 1037, 829, 807; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54 (d, J = 5.9 Hz, 2H, aromatic), 7.51 (d, J = 6.6 Hz, 2H, aromatic), 7.37 (d, J = 8.1 Hz, 2H, aromatic), 6.97 (d, J = 8.8 Hz, 2H, aromatic), 4.14–4.01 (m, 2H, OCH_2), 3.99–3.89 (m, 1H, C*H), 3.85 (s, 3H, OCH_3), 3.08–3.01 (m, 1H, C*CH_2), 2.95–2.87 (m, 1H, C*CH_2), 1.15 (t, J = 7.2 Hz, 3H, CH_3); MS (EI): m/z = 352 [M^+].

3.1.5. 4,4,4-Trifluoro-3-{4-(4-methoxyphenyl)phenyl}butanoic acid (5)

An aqueous solution of 85% potassium hydroxide (10.8 g, 162 mmol) was poured into a mixture of ethyl 4,4,4-trifluoro-3-{4-(4-methoxyphenyl)phenyl}butanoate (19.0 g, 54.3 mmol), 20 ml of 95% ethanol, and 100 ml of THF. This mixture was stirred for 2 h at room temperature. After evaporating the ethanol, ether and 6 M hydrochloric acid were added, and the phases were separated. The aqueous phase was shaken with ether, and the combined organic phases were dried over sodium sulphate. Removal of the solvent yielded 17.3 g (53.3 mmol, 98.3%) of **5** as a white solid; mp 178.2–179.1 °C; IR (KBr): 2960, 2367, 1716, 1500, 1429, 1254, 1170, 1112; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.63 (d, J = 1.8 Hz, 2H, aromatic), 7.60 (d, J = 2.2 Hz, 2H, aromatic), 7.49 (d, J = 8.1 Hz, 2H, aromatic), 7.03 (d, J = 8.8 Hz, 2H, aromatic), 4.13–3.97 (m, 1H, C*H), 3.79 (s, 3H, OCH_3), 3.39 (br, 1H, OH), 3.07–2.96 (m, 2H, CH_2); MS (EI): m/z = 324 [M^+]; anal. calcd for $C_{17}H_{15}F_3O_3$: C, 63.96; H, 4.66. Found: C, 62.89; H, 4.52.

3.1.6. Optically active 4,4,4-trifluoro-3-{4-(4-methoxyphenyl)phenyl}butanoic acid (5*)

Racemic 4,4,4-trifluoro-3-{4-(4-methoxyphenyl)phenyl}-butanoic acid (3.00 g, 9.26 mmol) and (1*R*, 2*S*)-(+)-2-benzylaminocyclohexane methanol (2.03 g, 9.26 mmol) were dissolved in 95% ethanol (100 ml) with heating. After cooling to room temperature, the resulting, insoluble diastereomeric salt was filtered off and recrystallized three times. Optically active (+)-**5*** was liberated by adding 1 M hydrochloric acid. After (+)-**5*** was extracted into ether, and the aqueous phase was shaken with ether, and the combined organic phases were dried over sodium sulphate. Removal of the solvent yielded 574 mg (1.77 mmol) of (+)-**5*** as a white solid; mp 182.1–182.2 °C; $[\alpha]_D$ + 48.2° (*C* 1.01, 95% EtOH). The (−)-**5*** was obtained in a similar manner by using (1*S*, 2*R*)-(−)-2-benzylaminocyclohexane methanol; mp 182.2–183.0 °C, $[\alpha]_D$ − 48.7° (95% EtOH, *C* 1.00).

3.1.7. Ethyl 4,4,4-trifluoro-3-{4-(4-methoxyphenyl)phenyl}butanoate (4*)

In order to determine the optical purity of (+)-**5***, their ethyl esters (**4***) were prepared from (+)-**5***.

Under nitrogen, (+)-**5*** (24 mg, 0.074 mmol) and phosphoryl chloride (34 mg, 0.22 mmol) were dissolved in 99% ethanol (2 ml), and the mixture was boiled for 2 h. After cooling to room temperature, water and toluene were added, and the phases were separated. The aqueous phase was washed with toluene, and the combined organic phases were washed with sodium hydrogen carbonate and brine, and dried over sodium sulphate. Removal of the solvent and purification by preparative thin-layer chromatography (TLC) yielded (+)-**4*** quantitatively.

The optical purity of (+)-**4*** was determined using HPLC with a chiral column, 'CHIRALCEL AD-H' (4.6 mm × 250 mm, carrier solvent hexane: 2-propanol = 15:85); the optical purity of (+)-**4*** was 99% ee.

3.1.8. (R)-(−)-4-Hexyloxyphenyl 4,4,4-trifluoro-3-4-{4-(4-methoxyphenyl)phenyl}butanoate (6*)

Under nitrogen, 4-*N*,*N*-dimethylaminopyridine (34 mg, 0.28 mmol) was added to the mixture of (*R*)-(−)-4,4,4-trifluoro-3-{4-(4-methoxyphenyl)phenyl}butanoic acid (36 mg, 0.19 mmol) and 4-hexyloxyphenol (60 mg, 0.19 mmol) and dry chloroform (3 ml), and the mixture was stirred for 10 min at room temperature. A dry chloroform solution (1 ml) of *N*,*N*′-dicyclohexylcarbodiimide (38 mg, 0.19 mmol) was added, and the reaction mixture was stirred for 10 h at room temperature. After toluene was added the resulting mixture was filtered. Hydrochloric acid (1 M) was then added to the filtrate, and the phases were separated. The organic phase was washed with saturated sodium hydrogen carbonate and brine and dried over sodium sulphate. Removal of the solvent and purification by preparative TLC yielded 75 mg (0.15 mmol, 81.1%) of (*R*)-(−)-**6*** as a white solid; mp 89.1–89.4 °C; IR (KBr): 2938, 1748, 1610, 1507, 1379, 1275, 1249, 1189, 1152, 1112, 1034, 1028, 965, 822; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.56 (d, J = 8.5 Hz, 2H, aromatic), 7.52 (d, J = 8.5 Hz, 2H, aromatic), 7.41 (d, J = 8.1 Hz, 2H, aromatic), 6.97 (d, J = 8.5 Hz, 2H, aromatic), 6.79 (d, J = 9.6 Hz, 2H, aromatic), 6.74 (d, J = 9.2 Hz, 2H, aromatic), 3.99–4.0 (m, 1H, C*H), 3.86 (t, J = 6.6 Hz, 2H, OCH_2), 3.81 (s, 3H, OCH_3), 3.30–3.08 (m, 2H, C*CH_2), 1.72 (quin, J = 6.6 Hz, 2H, $OCCH_2$), 1.38–1.41 (m, 2H, CH_2), 1.32–1.27 (m, 4H, CH_2), 0.88 (t, J = 6.6 Hz, 3H, CH_3); MS (EI): m/z = 500 [M^+]; $[\alpha]_D$ − 104° (*C* 0.924, $CHCl_3$); anal. calcd for $C_{29}H_{31}F_3O_4$: C, 69.59; H, 6.24. Found: C, 69.29; H, 6.21.

3.1.9. (R)-(+)-4,4,4-Trifluoro-1-(4-hexyloxyphenyl)-3-{4-(4-methoxyphenyl)phenyl}-1-butanone (7*)

Under nitrogen, thionyl chloride (4 ml) was added to (*R*)-(−)-4,4,4-trifluoro-3-{4-(4-methoxyphenyl)phenyl} butanoic acid (134 mg, 0.413 mmol), and heated under reflux for 3 h. After the removal of thionyl chloride, dry carbon disulfide (1 ml) was poured into the residue, and the dry carbon disulfide (1 ml) solution of hexyloxybenzene (219 mg, 1.24 mmol) was added to the mixture. Aluminum chloride (220 mg, 1.64 mmol) was then added to the mixture at −20 °C, and stirred for 4 h at room temperature. Then, 6 M hydrochloric acid and ether were added to the reaction mixture, and the phases were separated. The organic phase was washed with brine and dried over sodium sulphate. Removal of the solvent and purification by preparative TLC yielded 69 mg (0.14 mmol, 34.5%) of (*R*)-(+)-**7*** as a white solid; mp 84.8–85.5 °C; IR (KBr): 2935, 1677, 1602, 1501, 1307, 1249, 1164, 1104, 838, 814; ^{1}H NMR (300 MHz, $CDCl_3$):

δ = 7.90 (d, J = 9.2 Hz, 2H, aromatic), 7.51–7.41 (m, 6H, aromatic), 6.94 (d, J = 8.8 Hz, 2H, aromatic), 6.90 (d, J = 9.2 Hz, 2H, aromatic), 4.31–4.23 (m, 1H, C*H), 3.99 (t, J = 6.6 Hz, 2H, OCH_2), 3.81 (s, 3H, OCH_3), 3.74–3.50 (m, 2H, C*CH_2), 1.78 (quin, J = 6.6 Hz, 2H, $OCCH_2$), 1.48–1.32 (m, 6H, CH_2), 0.90 (t, J = 7.0 Hz, 3H, CH_3); MS (EI): m/z = 484 [M^+]; $[\alpha]_D$ + 82° (C 0.55, $CHCl_3$); anal. calcd for $C_{29}H_{31}F_3O_3$: C, 71.88; H, 6.45. Found: C, 71.1; H, 6.34.

*3.1.10. (R)-(−)-4,4,4-Trifluoro-3-{4-(4-methoxyphenyl)phenyl}butanol (**8***)*

Under nitrogen, (*R*)-(−)-4,4,4-trifluoro-3-{4-(4-methoxyphenyl)phenyl}butanoic acid (130 mg, 0.40 mmol) dissolved in dry THF (1 ml) was added to the mixture of lithium aluminum hydride (30 mg, 0.80 mmol) and dry THF (2 ml), and was heated under reflux for 12 h. After cooling to room temperature, 1 M hydrochloric acid and ether were added, and the phases were separated. The aqueous phase was shaken with ether, and combined organic phases were washed with saturated sodium hydrogen carbonate and brine and dried over sodium sulphate. Removal of the solvent and purification by preparative TLC yielded 100 mg (0.32 mmol, 80.6%) of (*R*)-(−)-**8*** as a white solid; mp 119.0–119.5 °C; IR (KBr): 3400, 2956, 1606, 1500, 1321, 1275, 1255, 1117, 1037, 812; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54 (d, J = 6.2 Hz, 2H, aromatic), 7.52 (d, J = 7.0 Hz, 2H, aromatic), 7.34 (d, J = 8.1 Hz, 2H, aromatic), 6.98 (d, J = 8.8 Hz, 2H, aromatic), 3.85 (s, 3H, OCH_3), 3.77–3.55 (m, 2H, CH_2O), 3.42–3.51 (m, 1H, C*H), 2.03–2.37 (m, 2H, C*CH_2), 1.30 (br, 1H, OH); MS (EI): m/z = 310 [M^+]; $[\alpha]_D$ − 52.7° (C 1.02, $CHCl_3$).

*3.1.11. (R)-(−)-4,4,4-Trifluoro-3-{4-(4-methoxyphenyl)phenyl}buthyl tosylate (**9***)*

Under nitrogen, 1,4-diazabicyclo[2.2.2]octane (106 mg, 0.948 mmol) dissolved in dry acetonitrile (2 ml) was poured into a mixture of (*R*)-(−)-4,4,4-trifluoro-3-{4-(4-methoxyphenyl)phenyl}butanol (98 mg, 0.32 mmol) and dry acetonitrile (1 ml) at room temperature, and a dry acetonitrile solution (2 ml) of tosyl chloride (89 mg, 0.47 mmol) was then added to the reaction mixture, followed by stirring for 12 h. Ether and 1 M hydrochloric acid were added, and the phases were separated. The aqueous phase was shaken with ether, and the combined organic phases were washed with saturated sodium hydrogen carbonate and brine and dried over sodium sulphate. Removal of the solvent and purification by preparative TLC yielded 113 mg (0.244 mmol, 77.2%) of (*R*)-(−)-**9*** as a white solid; mp 134.4–135.1 °C; IR (KBr): 2962, 2366, 2345, 1604, 1500, 1361, 1253, 1175, 1110, 976, 815, 557; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.67 (d, J = 8.1 Hz, 2H, aromatic), 7.48 (d, J = 8.8 Hz, 2H, aromatic), 7.45 (d, J = 8.1 Hz, 2H, aromatic), 7.25 (d, J = 8.5 Hz, 2H, aromatic), 7.18 (d, J = 8.1 Hz, 2H aromatic), 6.97 (d, J = 8.5 Hz, 2H, aromatic), 4.08 (dt, J_1 = 9.5 Hz, J_2 = 4.8 Hz, 1H, C*H), 3.82 (s, 3H, OCH_3), 3.78–3.69 (m, 1H, CH_2O), 3.99–3.50 (m, 1H, CH_2O), 2.48–2.37 (m, 1H, C*CH_2), 2.34 (s, 3H, Ar–CH_3), 2.17–2.05 (m, 1H, C*CH_2); MS (EI): m/z = 464 [M^+]; $[\alpha]_D$ − 49.4° (C 1.00, $CHCl_3$).

*3.1.12. (R)-(−)-[4-{3-(4-Hexyloxyphenyloxy)-1-trifluoromthylpropyl}phenyl]-4-methoxybenzene (**10***)*

Under nitrogen, potassium carbonate (330 mg, 2.39 mmol) was added to a mixture of 4-hexyloxyphenol, acetonitrile (2 ml) and THF (2 ml) and was then stirred for 5 min at room temperature. The THF (2 ml) solution of (*R*)-(−)-4,4,4-trifluoro-3-{4-(4-methoxyphenyl)phenyl}buthyl tosylate (113 mg, 0.244 mmol) was poured into the reaction mixture and was stirred for 2 days at 60 °C. After cooling to room temperature, toluene and 1 M hydrochloric acid were added, and the phases were separated. The aqueous phase was shaken with ether, and the combined organic phases were washed with saturated sodium hydrogen carbonate and brine and dried over sodium sulphate. Removal of the solvent and purification by preparative TLC yielded 93 mg (0.191 mmol, 78.2%) of (*R*)-(−)-**10*** as a light yellow solid; mp 58.3–59.1 °C; IR (KBr): 2925, 2855, 1603, 1509, 1477, 1232, 1159, 1114, 1066, 1039, 821; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53 (d, J = 3.3 Hz, 2H, aromatic), 7.50 (d, J = 3.7 Hz, 2H, aromatic), 7.34 (d, J = 8.07, 2H, aromatic), 6.97 (d, J = 8.8 Hz, 2H, aromatic), 6.77 (d, J = 7.0 Hz, 4H, aromatic), 3.92–3.87 (m, 2H, OCH_2), 3.84 (s, 3H, OCH_3), 3.76–3.64 (m, 3H, C*H, OCH_2), 2.60–2.50 (m, 1H, C*CH_2), 2.28–2.16 (m, 1H, C*CH_2), 1.74 (quin, J = 7.0 Hz, 2H, $OCCH_2$), 1.46–1.31 (m, 6H, CH_2), 0.89 (t, J = 5.3 Hz, CH_3); MS (EI): m/z = 486 [M^+]; $[\alpha]_D$ − 127° (C 1.00, $CHCl_3$); anal. calcd for $C_{29}H_{33}F_3O_3$: C, 71.59; H, 6.84. Found: C, 71.28; H, 6.97.

*3.1.13. (R)-(−)-1,1,1,-Trifluoro-2-{4-(4-methoxyphenyl)phenyl}-4-(4-hexyloxyphenyl)butane (**11***)*

Under nitrogen, a trifluoroacetic acid (1 ml) solution of triethylsilane (22 mg, 0.19 mmol) was poured into a mixture of (*R*)-(+)-4,4,4-trifluoro-1-(4-hexyloxyphenyl)-3-{4-(4-methoxyphenyl)phenyl}-1-butanone (30 mg, 0.062 mol) and trifluoroacetic acid (1 ml) and was stirred for 5 h at room temperature. After adjusting the pH to approximately 11 through the addition of 1 M sodium hydroxide, ether was added to the mixture, and the phases were separated. The aqueous phase was shaken with ether, and the combined organic phases were washed with brine and dried over sodium sulphate. Removal of the solvent and purification by preparative TLC yielded 28 mg (0.060 mmol, 96.1%) of (*R*)-(−)-**11*** as a colorless liquid; IR (KBr): 2933, 1611, 1512, 1463, 1248, 1177, 1154, 1111, 820; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57–7.52 (m, 4H, aromatic), 7.32 (d, J = 8.1 Hz, 2H, aromatic), 7.01–6.96 (m, 4H, aromatic), 6.81 (d, J = 8.5 Hz, 2H, aromatic), 3.92 (t, J = 6.6 Hz, 2H, OCH_2), 3.85 (s, 3H, OCH_3), 3.30–3.15 (m, 1H, C*H), 2.61–2.17 (m, 4H, C*CH_2, C*CCH_2), 1.77 (quin, J = 7.0 Hz, 2H, $OCCH_2$), 1.45–1.30 (m, 6H, CH_2), 0.90 (t, J = 5.1 Hz, 3H, CH_3); MS (EI): m/z = 470 [M^+]; $[\alpha]_D$ − 50° (C 0.29, $CHCl_3$); anal. calcd for $C_{29}H_{33}F_3O_2$: C, 74.02; H, 7.07. Found: C, 73.97; H, 7.15.

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[14] CCDC 290218 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

[15] The host liquid crystalline mixture (ZLI-1132, Merck) consists of 4-(4-propylcyclohexyl)cyanobenzene (24 wt.%), 4-(4-penthylcyclohexyl)cyanobenzene (36 wt.%), 4-(4-heptylcyclohexyl)cyanobenzene (25 wt.%), and 4-{4-(4-pentylcyclohexyl)phenyl}cyanobenzene (15 wt.%). The host liquid crystalline mixture shows nematic liquid crystal phase at the range from −6 to 70 °C. The dielectric anisotropy ($\Delta\varepsilon$) of the host nematic liquid crystalline mixture is +10.7, and the optical anisotropy (Δn) of the host liquid crystalline mixture is 0.14.

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