Synthesis of New Chiral Dopants Derived from 2-Phenylpropanoic Acid Derivatives for Nematic Liquid Crystals

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New chiral dopants for nematic liquid crystals were synthesized using optically active 2-phenylpropanoic acid derivatives. The magnitude of the helical twisting power (HTP) was largely influenced by the terminal group of the asymmetric frame and the core structures. (*S*)-1-[4-(*trans*-4-Butylcyclohexyl)phenyl]-2-phenylpropane-1-one showed a large HTP value (20.4 μm^{-1}). The relationship between the HTP and the molecular structures of the chiral dopants is discussed.

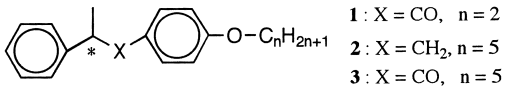
Chiral nematic liquid crystals, which are applicable to super twisted nematic (STN) devices, are attractive materials. Recently, liquid crystals are being widely applied to the STN mode of flat panel display devices of portable computers and TV sets, because a liquid-crystal display (LCD) is of greater advantage than, or over, a cathode-ray tube (CRT) concerning size, thickness, weight, and power consumption.[1] Generally, the chiral nematic materials used for a LDC consist of achiral host liquid crytal mixtures, which have low viscosities and a wide temperature range of the nematic phase, and a chiral dopant having a large helical twisting power (HTP). This chiral dopant induces chirality of the whole material of the liquid crystal mixture. Chirality is one of the most interesting subjects concerning liquid crystals.[2,3]

The HTP can be calculated by (Eq. 1),[4] where p is the pitch of the chiral nematic phase in μm and c is the mass fraction of the dopant. On the other hand, in order to discuss a HTP by a molecule, we have proposed molar helical twisting power (MHTP),[5] which is defined as follows (Eq. 2). Here, m is the moles of the dopant per 1 kg of the mixture. Mw is the molecular weight of the chiral dopant. In both expressions, chiral dopants are required to have the ability to shorten the helical pitch of the chiral nematic phase. To satisfy this requirement, many optically active compounds have been synthesized.[1] We have also synthesized a variety of chiral compounds for the same purpose.[5,6] However, the relationship between the HTP values and the molecular structures of chiral dopants is not clarified.

$$\mathrm{HTP} = (\mathrm{pc})^{-1} \quad (1)$$

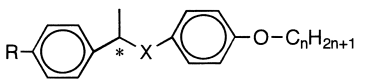
$$\mathrm{MHTP} = (\mathrm{pm})^{-1} = \mathrm{HTP}\cdot\mathrm{Mw}/1000\ (\mu m^{-1}\ mol^{-1}\ kg) \quad (2)$$

We recently reported new chiral dopants, **1***–**3***, prepared from optically active 2-phenylpropanoic acid (Fig. 1), and showed that their HTPs were largely influenced by the linkage structures between the asymmetric frame and the core moieties.[5] In this paper, we report on the synthesis of some analogues of the new chiral dopants, **4***–**7***, derived from optically active 2-phenylpropanoic acid derivatives, and discuss the relationship between the HTP and the molecular structures of the dopants (Fig. 2).

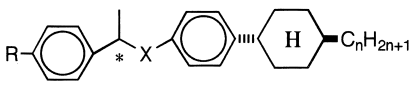


1 : X = CO, n = 2
2 : X = CH_2, n = 5
3 : X = CO, n = 5

Fig. 1. The structural formula of the chiral dopant.



4 : R = *n*-C_4H_9, X = CO, n = 5
5 : R = *n*-C_4H_9, X = CH_2, n = 5



6 : R = H, X = CO, n = 4
7 : R = H, X = CH_2, n = 4

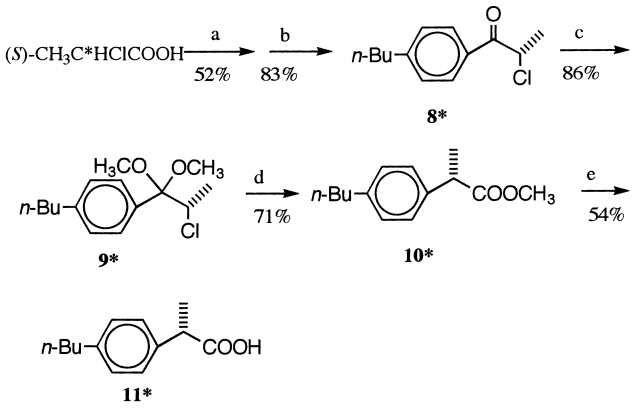
Fig. 2. The structural formula of new chiral dopants.

Results and Discussion

Synthesis of Optically Active 2-(4-Butylphenyl)propanoic Acid. (*S*)-2-(4-Butylphenyl)propanoic acid (**11***) was prepared from (*S*)-2-chloropropanoic acid and butylbenzene using an analogous method, which was employed in the synthesis of ibuprofen (Scheme 1).[7]

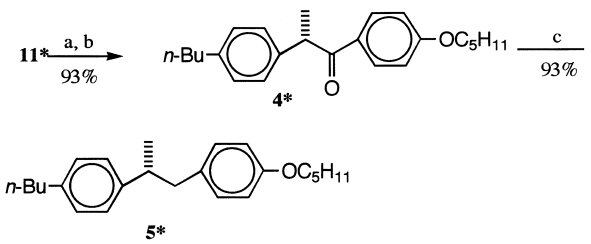
Synthesis of Chiral Dopants. A new chiral dopant **4*** was synthesized by the Friedel-Crafts reaction of (*S*)-2-(4-butylphenyl)propanoic acid (**11***) with pentyloxybenzene. The reduction of **4*** with lithium aluminium hydride (lithium tetrahydridoaluminate) gave **5*** (Scheme 2).

In order to study the effect of a core structure, a chiral dopant having a cyclohexylbenzen structure was synthesized. Optically active 2-phenylpropanoic acid was converted to the corresponding acid chloride, which was treated with *trans*-1-butyl-4-phenylcyclohexane in the presence of anhydrous aluminium chloride to give **6***. The reduction of **6*** with triethyl-



a) PhCOCl, 150 °C. b) *n*-BuPh, $AlCl_3$, CH_2Cl_2, 0 °C. c) $HC(OCH_3)_3$, H_2SO_4, MeOH, 70 °C.
d) $ZnCl_2$, toluene, 130 °C. e) HCl, acetone, 60 °C.

Scheme 1. Synthetic route of (*S*)-2-(4-Butylphenyl)propanoic acid (**11***).



a) $SOCl_2$, 70 °C. b) $PhOC_5H_{11}$, $AlCl_3$, CS_2, r.t.
c) $LiAlH_4$, $AlCl_3$, ether, 40 °C.

Scheme 2. Syntheis of(*R*)-2-(4-butylphenyl)-1-(4-pentyloxyphenyl)propane (**5***).

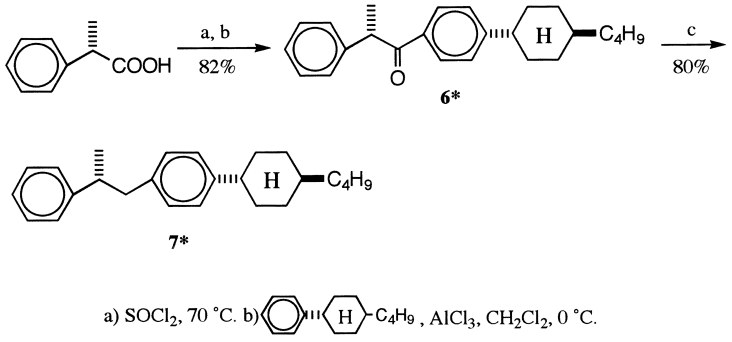
silane gave **7*** (Scheme 3).

Relationship between Structure and Helical Twisting Power of 2-Phenylpropanoic Acid Derivatives. The HTP of each chiral dopant was measured as a one weight percent mixture with the host liquid crystal (ZLI-1132); the results are summarized in Table 1. The introduction of a butyl group at the benzene ring of the 2-phenylpropanoyl group, i.e. the chiral center, significantly reduced the HTP value. The introduction of an alkyl group on both sides make a chiral dopant more symmetrical, and seems to be the reason for the reduction of HTP. Thus, dopants **4*** and **5*** exhibited smaller HTP values than **2*** and **3***, respectively.

The chiral dopant **5***, having a methylene linkage at the chiral center, showed a larger HTP value than **4*** having the ketone carbonyl one. This tendency agrees well with the previously reported results.[5] A carbonyl group is more rigid than a methylene group and has a relatively large polarization. The steric effect of a dopant molecule seems to be more important than its rigidity or polarity to induce the helical microstructure of the whole matrix. However, the details of the steric effect are not still clear, as demonstrated for **6*** and **7*** in the next paragraph.

The HTP value of the dopant **6***, which has a cyclohexylbenzen core and a carbonyl linkage, was larger than of **7***, which has the same core, but a methylene linkage. This is completely opposite to the precious results. The chiral dopant **6*** exhibited the largest HTP value (20.4 μm^{-1}), probably due to the flexible and nonpolar cyclohexane structure. In particular, the MHTP value of **6*** (7.09 μm^{-1} mol^{-1} kg) increased more than twice that of **2*** (3.05 μm^{-1} mol^{-1} kg). On the other hand, MHTP of **7***, which had the same core, but a methylene linkage, showed almost the same MHTP of **3*** and two thirds of **6***. The structural change from **3*** to **7***, the introduction of a flexible cyclohexyl group into the flexible asymmetric core, did not work for higher HTP.

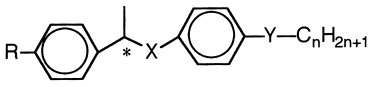
In conclusion, it was shown that optically active 2-phenyl-

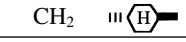


a) $SOCl_2$, 70 °C. b) , $AlCl_3$, CH_2Cl_2, 0 °C.
c) Et_3SiH, CF_3COOH, r.t.

Scheme 3. Syntheis of (*R*)-1-[4-(*trans*-4-butylcyclohexyl)phenyl]-2-phenylpropane (**7***).

Table 1. HTP[a] and MHTP[a] of Chiral Dopants



Compound	R	X	Y	n	HTP/μm^{-1}	MHTP/$\mu m^{-1}\ mol^{-1}\ kg$
1*[b]	H	CH_2	O	2	19.1	4.58
2*[b]	H	CO	O	5	10.3	3.05
3*[b]	H	CH_2	O	5	17.0	4.79
4*	n-C_4H_9	CO	O	5	2.5	0.91
5*	n-C_4H_9	CH_2	O	5	9.2	3.23
6*	H	CO		4	20.4	7.09
7*	H	CH_2		4	12.9	4.30

a) Host liquid crystal (ZLI-1132):dopant = 99:1 (by weight). b) Reported in the Ref. 6.

propanoic acid derivatives can be a good chiral center for dopants, and that the cyclohexylbenzen core is effective to induce a helical structure for a nematic liquid crystal. As a result, a good chiral dopant **6*** having a cyclohexylbenzen group at the chiral center was developed for chiral nematic liquid crystal applications.

Experimental

The structures of all intermediates and products were confirmed by ^{1}H NMR spectroscopy (Bruker ARX-400, 400 MHz) and infrared spectroscopy (Perkin-Elmer FT-1640). The optical purity was determined by high-performance liquid chromatography using a set of JASCO LC 900 series (detector: JASCO CD-1595, chiral column, "CHIRALCEL OJ" (Daicel Chem. Ind., Ltd., 4.6 mm × 250 mm)). Specific rotations were measured with a JASCO DIP-370 polarimeter. The helical pitch of a chiral nematic phase was measured using wedge-shaped samples (Cano-wedge cell, tan θ = 0.0083, 0.0140, 0.0194, 0.0288, E. H. C. Ind., Ltd.,) by means of the resulting Cano lines.[8] The liquid crystal (LC) sample was prepared by adding one weight percent of a chiral dopant into the achiral host LC mixture, ZLI-1132 (Merck).

Synthesis of (*S*)-1-(4-Butylphenyl)-2-chloropropane-1-one (8*): (*S*)-2-Chloropropanoic acid (3.186 g, 29.3 mmol) was distilled with benzoyl chloride (8.120 g, 57.7 mmol) to give an acid chloride as a colorless liquid (1.938 g, 52%). To a mixture of anhydrous aluminium chloride (0.589 g, 4.41 mmol) in dry dichloromethane (5 mL) were added the acid chloride (0.460 g, 3.62 mmol) and butylbenzene at ice-water temperature (0.484 g, 3.61 mmol). The mixture was stirred for 5 h at that temperature, and hydrolyzed with 4 M (= mol/dm^{-3}) hydrochloric acid, and extracted with dichloromethane. The organic layer was washed with a 5% sodium hydrogencarbonate solution, and dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to give a light-yellow liquid (0.678 g, 83%). ^{1}H NMR ($CDCl_3$) δ 0.93 (3H, t, J = 7.2 Hz), 1.33–1.39 (2H, m), 1.58–1.66 (2H, m), 1.74 (3H, d, J = 6.8 Hz), 2.67 (2H, t, J = 7.8 Hz), 5.24 (1H, q, J = 6.6 Hz), 7.29 (2H, d, J = 8.2 Hz), 7.93 (2H, d, J = 8.2 Hz). IR (neat) 3030, 2957, 2931, 2860, 1689, 1606, 1181, 955 cm^{-1}. $[\alpha]_D^{25}$ +28.0° (*c* 0.9, $CHCl_3$).

Synthesis of (*S*)-1-(4-Butylphenyl)-2-chloro-1,1-dimethoxypropane (9*): To a methanol solution (5 mL) of **8*** (0.610 g, 2.27 mmol) and trimethyl orthoformate (0.758 g, 7.14 mmol) was added 5 drops of conc. sulfuric acid. The mixture was refluxed under nitrogen for 24 h, and then neutralized with sodium methoxide, cooled to room temperature, and diluted with dichloromethane (40 mL) and water (40 mL). The organic layer was dried with anhydrous sodiun sulfate, and concentrated under a vacuum to give a light-yellow liquid (0.638 g, 86%). ^{1}H NMR ($CDCl_3$) δ 0.92 (3H, t, J = 7.2 Hz), 1.31 (3H, d, J = 6.7 Hz), 1.33–1.38 (2H, m), 1.59–1.63 (2H, m), 2.63 (2H, t, J = 7.8 Hz), 3.21 (3H, s), 3.36 (3H, s), 4.38 (1H, q, J = 6.7 Hz), 7.17 (2H, d, J = 8.1 Hz), 7.39 (2H, d, J = 8.1 Hz). IR (neat) 3030, 2957, 2933, 2858, 2832, 1693,1607, 1336, 1180, 1090, 1055 cm^{-1}. $[\alpha]_D^{24}$ +9.6° (*c* 0.9, $CHCl_3$).

Synthesis of (*S*)-Methyl 2-(4-butylphenyl)propanoate (10*): The mixture of **9*** (0.638 g, 2.36 mmol) and anhydrous zinc chloride (0.063 g, 0.46 mmol) in toluene (5 mL) was refluxed for 23 h, then cooled to room temperature, diluted with toluene (10 mL), and filtered. After the solvent was evaporated under reduced pressure, the remaining mixture was purified by column chromatography (silica gel: 27 g, 10% ethyl acetate in hexane) to give a light-yellow liquid (0.369 g, 71%). ^{1}H NMR ($CDCl_3$) δ 0.91 (3H, t, J = 7.3 Hz), 1.34–1.37 (2H, m), 1.48 (3H, d, J = 7.2 Hz), 1.58–1.60 (2H, m), 2.58 (2H, t, J = 7.8 Hz), 3.65 (3H, s), 3.69 (1H, q, J = 7.2 Hz), 7.13 (2H, d, J = 8.0 Hz), 7.19 (2H, d, J = 8.0 Hz). IR (neat) 2955, 2931, 2858, 1738, 1693 cm^{-1}. $[\alpha]_D^{23}$ +38.2° (*c* 1.0, $CHCl_3$).

Synthesis of (*S*)-2-(4-Butylphenyl)propanoic Acid (11*): **10*** (0.369 g, 1.67 mmol) was hydrolyzed by refluxing for 3 h in the presence of conc. hydrochloric acid (5 mL) and acetone (5 mL). The resulting solution was evaporated under reduced pressure and the remaining mixture was basified by dilute sodium hydroxide solution, and washed with diethyl ether. The aqueous layer was acidified by conc. hydrochloric acid (1 mL) and the aqueous layer was extracted with diethyl ether, and dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to give a light-yellow liquid (0.187 g, 54%). ^{1}H NMR ($CDCl_3$) δ 0.91 (3H, t, J = 7.2 Hz), 1.31–1.37 (2H, m), 1.49 (3H, d, J = 7.1 Hz), 1.54–1.61 (2H, m), 2.58 (2H, t, J = 7.8 Hz), 3.70 (1H, q, J = 7.2 Hz), 7.13 (2H, d, J = 8.0 Hz), 7.22 (2H, d, J = 8.0 Hz). IR (neat) 3095, 2932, 2855, 2725, 2637, 1707, 1514 cm^{-1}. $[\alpha]_D^{22}$ +43.0° (*c* 1.0, $CHCl_3$).

Synthesis of (*S*)-2-(4-Butylphenyl)-1-(4-pentyloxyphenyl) propane-1-one (4*): After (*S*)-2-(4-butylphenyl)propanoic acid **11*** (0.187 g, 0.85 mmol) was stirred in thionyl chloride (2 mL) for 1 h at 70 °C, the mixture was concentrated. To the remaining mixture were added a solution of pentyloxybenzene (0.406 g, 2.47

mmol) in carbon disulfide (4 mL) and anhydrous aluminium chloride (0.190 g, 1.42 mmol). The mixture was stirred for 3 h at room temperature, hydrolyzed by ice-water (20 mL) and conc. hydrochloric acid (0.5 mL), and extracted with diethyl ether. The organic layer was dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the remaining mixture was purified by column chromatography (silica gel: 31 g, 10% ethyl acetate in hexane) to give a light-yellow liquid (0.291 g, 93%). ^{1}H NMR ($CDCl_3$) δ 0.89 (3H, t, J =7.3 Hz), 0.91 (3H, t, J = 6.8 Hz), 1.31–1.39 (6H, m), 1.49 (3H, d, J = 6.8 Hz), 1.53–1.56 (2H, m), 1,75–1.77 (2H, m), 2.53 (2H, t, J = 7.8 Hz), 3.95 (2H, t, J = 6.5 Hz), 4.61 (1H, q, J = 6.8 Hz), 6.83 (2H, d, J = 8.8 Hz), 7.08 (2H, d, J = 8.0 Hz), 7.18 (2H, d, J = 8.0 Hz), 7.93 (2H, d, J = 8.8 Hz). IR (neat) 3051, 2956, 2870, 1674, 1601, 1509 cm^{-1}. $[\alpha]_D^{23}$ +33.0° (*c* 1.1, $CHCl_3$).

Synthesis of (*R*)-2-(4-Butylphenyl)-1-(4-pentyloxyphenyl) propane (5*): To a mixture of lithium aluminium hydride (0.037 g, 0.98 mmol) and anhydrous aluminium chloride (0.156 g, 1.17 mmol) in dry diethyl ether (4 mL) was added a solution of **4*** (0.291 g, 0.79 mmol) in dry diethyl ether (2 mL). The reaction mixture was refluxed for 0.5 h, hydrolyzed by 4 M hydrochloric acid (20 mL), and extracted with diethyl ether. The organic layer was dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the remaining mixture was purified by column chromatography (silica gel: 12 g, 10% ethyl acetate in hexane) to give a colorless liquid (0.239 g, 85%). ^{1}H NMR ($CDCl_3$) δ 0.92 (6H, t, J = 7.2 Hz), 1.91 (3H, d, J = 6.7 Hz), 1.34–1.43 (6H, m), 1.55–1.58 (2H, m), 1.73–1.80 (2H, m), 2.57 (3H, t, J = 7.8 Hz), 2.62–2.68 (1H, m), 2.85–2.95 (2H, m), 6.76 (2H, d, J = 8.4 Hz), 6.97 (2H, d, J = 8.4 Hz). IR (neat) 3008, 2956, 2870, 1613, 1511 cm^{-1}. $[\alpha]_D^{23}$ −46.3° (*c* 0.9, $CHCl_3$).

Synthesis of (*S*)-1-[4-(*trans*-4-Butylcyclohexyl)phenyl]-2-phenylpropane-1-one (6*): After (*S*)-2-phenylpropionic acid (0.235 g, 1.56 mmol) was stirred in thionyl chloride (2 mL) for 1 h at 70 °C, the mixture was concentrated. To the remaining mixture were added a solution of *trans*-1-butyl-4-phenylcyclohexane (0.512 g, 2.37 mmol) in dry dichloromethane (8 mL) and anhydrous aluminium chloride (0.319 g, 2.39 mmol). The mixture was stirred for 5 h at room temperature, hydrolyzed by ice and 4 M hydrochloric acid (10 mL), and extracted with dichloromethane. The organic layer was dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the remaining mixture was purified by column chromatography (silica gel: 30 g, 10% ethyl acetate in hexane) to give a white solid (0.448 g, 82%). The optical purity of **6*** (94%ee) was determined by HPLC analysis; carrier solvent, 5% 2-propanol/hexane; flow rate, 0.5 mL/min; detection wavelength, 254 nm; retention time, (+)-form, 11 min, CD: positive, (−)-form, 14 min, CD: negative. ^{1}H NMR ($CDCl_3$) δ 0.90 (3H, t, J = 3 Hz), 1.00–1.15 (2H, m), 1.23–1.48 (9H, m), 1.51 (3H, d, J = 6.7 Hz), 1.80–1.90 (4H, m), 2.42–2.56 (1H, m), 4.67 (1H, q, J = 6.7 Hz), 7.18–7.33 (7H, m), 7.88 (2H, d, J = 8.3 Hz). IR (KBr) 3084, 3027, 2920, 2850, 1677, 1604, 1457 cm^{-1}. $[\alpha]_D^{24}$ +63.4° (*c* 0.6, $CHCl_3$). Found: C, 85.15; H, 9.36%. Calcd for $C_{25}H_{32}O$: C, 86.15; H, 9.25%.

Synthesis of (*R*)-1-[4-(*trans*-4-Butylcyclohexyl)phenyl]-2-phenylpropane (7*): To a solution of **6*** (0.106 g, 0.30 mmol) in trifluoroacetic acid (2 mL) was added the triethylsilane (0.105 g, 0.90 mmol). The mixture was stirred for 4 h at room temperature, hydrolyzed by 3 M sodium hydroxide solution (10 mL), and extracted with diethyl ether. The organic layer was dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the remaining mixture was purified by thin-layer chromatography (silica gel, hexane) to give a white solid (0.080 g, 80%). ^{1}H NMR ($CDCl_3$) δ 0.89 (3H, t, J = 6.9 Hz), 0.95–1.08 (2H, m), 1.21 (3H, d, J = 6.6 Hz), 1.25–1.45 (9H, m), 1.80–1.93 (4H, m), 2.40–2.49 (1H, m), 2.65–2.75 (1H, m), 2.90–3.08 (2H, m), 7.01 (2H, d, J = 8.0 Hz), 7.08 (2H, d, J = 8.0 Hz), 7.15–7.33 (5H, m). IR (KBr) 3084, 3028, 2923, 2844, 1602, 1452 cm^{-1}. $[\alpha]_D^{22}$ −37.6° (*c* 0.7, $CHCl_3$).

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