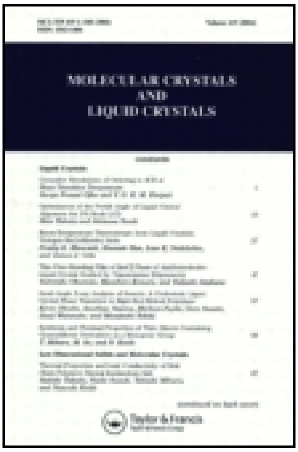

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Synthesis and Properties of Optically Active Phenoxypropionates. Effect of Halogeno Substituent in the Core on Physical Properties

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Synthesis and Properties of Optically Active Phenoxypropionates. Effect of Halogeno Substituent in the Core on Physical Properties

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Chiral phenoxypropionates having halogenated 2,5-diphenylpyrimidine cores were synthesized and the effect of a halogeno-substituent on the physical properties such as mesomorphic behavior, spontaneous polarization (Ps) and response time (τ) were investigated. The introduction of a halogen atom to the phenyl ring of 2,5-diphenylpyrimidine core led to a decrease in the thermal stability of mesophases. The Ps values in the achiral host liquid crystal mixture were increased by introducing the halogen atom. However, response times were not improved.

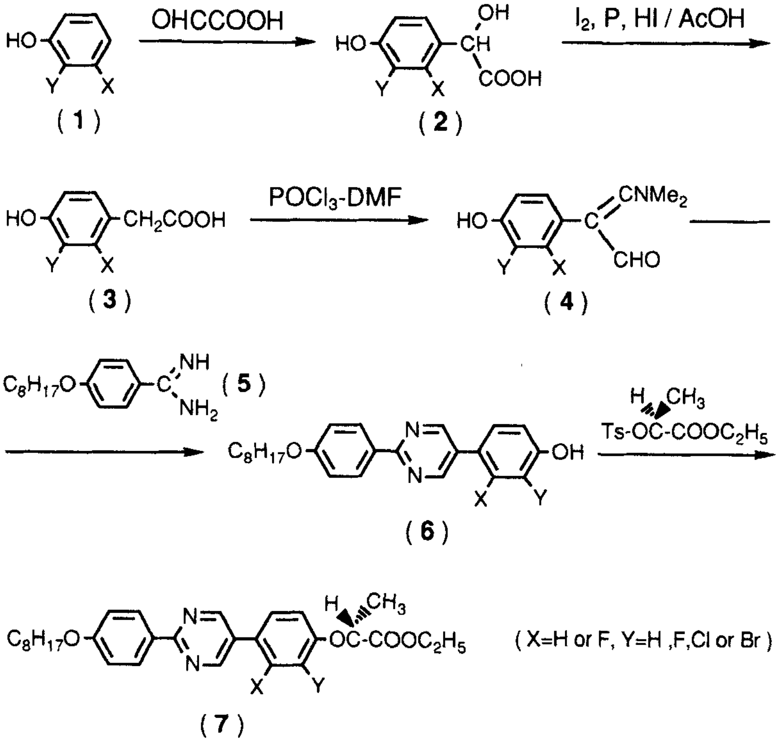
Keywords: ferroelectric liquid crystal, phenoxypropionate, halogeno-substituent

1. INTRODUCTION

Since the discovery of ferroelectricity in the chiral smectic C(Sc*) phase by R. Meyer in 1975[1] and the proposal of electro-optical devices using ferroelectric liquid crystals by Clark and Lagerwall in 1980,[2] extensive studies have been done on ferroelectric liquid crystal materials and their applications.[3] One of the most important features for ferroelectric liquid crystal (FLC) devices is fast switching. In order to realize fast switching, ferroelectric liquid crystal (FLC) mixtures are made by adding a chiral compound (chiral dopant) having large spontaneous polarization (Ps) to achiral host liquid crystal mixtures with low viscosity and a wide temperature range around room temperature.[4] In the previous work,[5] we synthesized some optically active phenoxypropionates and found that they have large spontaneous polarizations (Ps's), and are excellent chiral dopants because the doping of those compounds induced large Ps values and a suitable tilt angle (ca. 20 degrees) for an application in the birefringent mode, and those FLC mixtures showed a short response times. Especially, a compound with 2,5-diphenylpyrimidine core showed the largest Ps value of 240 nC/cm^2. We thought that by introducing a halogen atom to the phenyl ring of the 2,5-diphenylpyrimidine core, we could make chiral compounds with a larger Ps values. Therefore we synthesized chiral phenoxypropionates having halogenated 2,5-diphenylpyrimidine cores and evaluated their Ps values and also investigated their abilities as chiral dopants.

2. SYNTHESIS

The synthetic route of halogeno compounds (**7b**–**7e**) is shown in Scheme I. The synthesis of unsubstituted compound (**7a**) was described in a previous paper.[5] The reaction of ortho or meta halogenophenol (**1**) with glyoxylic acid afforded halogenated 4-hydroxy mandelic acid (**2**), which was reduced with phosphorous (red), iodine and hydriodic acid to give halogenated 4-hydroxy phenylacetic acid (**3**). The Vilsmeier reaction of **3** and subsequent alkaline hydrolysis afforded 2-[2- or 3-(halogeno)-4-(hydroxy)phenyl]-3-dimethylaminoacrolein (**4**). Condensation of **4** with 4-*n*-octyloxybenzamidine (**5**) gave 5-[2- or 3-(halogeno)-4-(hydroxy)phenyl]-2-[4-(octyloxy)phenyl]-pyrimidine (**6**), which reacted with ethyl (*S*)-2-*p*-toluenesulfonyloxypropionate to afford **7**. This reaction involves the Walden inversion at the asymmetric C-atom and thus leads to (*R*) absolute configuration. The final products were purified by column chromatography on silica-gel using hexane and ether as the eluent followed by recrystallization from ethanol. The optical purity of the



SCHEME I Synthesis route of optically active phenoxypropionates having halogenated 2,5-diphenylpyrimidine as a core.

compound is very important. So, we measured the enantiomeric excess of **7a** as a representative by HPLC with a chiral column and obtained e.e. of 94.7%. Other compounds (**7b**–**7e**) are considered to have similar enantiomeric excesses because all reactions of **6** with ethyl (*S*)-2-*p*-toluenesulfonyloxypropionate were carried out in the same manner.

3. MEASUREMENTS OF PHYSICAL PROPERTIES

The phase transition temperature was measured with a polarizing microscope equipped with a heating stage and a differential scanning calorimeter (DSC). Identity of the mesophases was confirmed by examining the texture of a thin sample sandwiched between glass slides.[6] Measurements of Ps value, response time and tilt angle were carried out on 2 μm thick cells consisting of two ITO glass slides coated with polyimide rubbed in the same direction. The spontaneous polarization (Ps) was measured by the triangular wave method (± 10 V, 200 Hz).[7] The sense of Ps was determined by the field reversal method by optical observation of the director motion.[8] The response time (τ) was defined as the time difference between voltage reversal and a 90% change in optical transmission by applying a rectangular wave (± 10 V, 200 Hz). The tilt angle (θ) was measured from the scale on the microscope turntable between the two extreme optical states, corresponding to the two polarities of a DC field applied across the sample cell.

4. RESULTS AND DISCUSSION

4.1. Physical Properties of Compounds 7a–7e

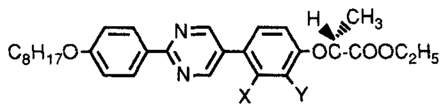
The phase transition temperatures and Ps values of compounds **7a**–**7e** are listed in Table I. The parent compound (**7a**) and fluoro derivatives (**7b** and **7e**) show mesomorphic behavior, while the chloro substituent in **7c** and bromo substituent in **7d** prevent the formation of mesophases. The thermal stabilities of the mesophases are decreased by increasing the Van der Waals volume of the lateral halogeno substituents (Van der Waals volume; F = 0.58 nm, Cl = 1.20 nm and Br = 1.44 nm),[9] due to the increase in the intermolecular distance. A compound with an ortho fluoro substituent in the phenyl ring relative to the chiral terminal chain (**7b**) shows the monotropic Sc* phase and the Ps value is essentially the same as that of the parent compound **7a**.

4.2. Properties in Achiral Host Liquid Crystal Mixture

To compare the magnitudes of spontaneous polarizations of these compounds and evaluate the abilities as chiral dopants, we made FLC mixtures by adding 5 wt% of these compounds to achiral Sc host liquid crystal mixtures composed of 2-[4-(*n*-hexyloxy)phenyl]-5-*n*-nonylpyrimidine (33.3 wt%), 2-[4-(*n*-octyloxy)phenyl]-5-*n*-octylpyrimidine (33.3 wt%) and 2-[4-(*n*-decyloxy)phenyl]-5-*n*-octylpyrimidine (33.3 wt%). The physical properties of the resulting FLC mixtures are shown in Table

TABLE I

Phase transition temperatures and Ps values of compounds **7a–7e**



Compound	X	Y	Cr	Sx	Sc^*	N^*	I	Ps (nC/cm^2) $T_{\text{Ac-10℃}}$ [b]	Ps (nC/cm^2) max.[c]
7a	H	H	· 51.0	(· 46.0)	· 69.0	· 91.5	·	+220	+240
7b	H	F	· 74.7	—	(· 67.2)	(· 74.7)	·	+225	+260
7c	H	Cl	· 62.5	—	—	—	·	—	—
7d	H	Br	· 53.0	—	—	—	·	—	—
7e	F	H	· 59.5	—	—	· 63.0	·	—	—

Phase Transition Temperature (℃)[a]

a) Cr: crystalline solid, Sx: unidentified smectic phase, Sc^*: chiral smectic C phase, N^*: chiral nematic phase, I: isotropic liquid phase. ( ) indicates a monotropic transition. b) The value at a temperature 10℃ below the upper limit of the Sc^* phase. c) maximum value.

TABLE II

Properties of compounds **7a–7e** in achiral liquid crystal mixture[a]

Compound	Ps(nC/cm^2)	τ (μs)	θ (deg)	Phase Transition Temp.(℃)[b] Sc^*	S_A	N^*	I
7a	+2.5	110	19.0	· 55.3	· 62.0	· 68.0	·
7b	+3.8	108	20.5	· 57.1	· 63.1	· 67.7	·
7c	+3.4	115	19.5	· 52.7	· 60.0	· 65.1	·
7d	+3.5	120	20.5	· 57.3	· 60.7	· 66.1	·
7e	+2.2	130	23.0	· 54.5	· 58 4	· 66.3	·
Host[c]	—	—	—	· 53.0	· 60.0	· 65.0	·

a) Chiral compound was added 5 wt% to the host liquid crystal mixture. Measurements of Ps, τ and θ were carried out at 25℃. b) Sc^*: chiral smectic C phase, S_A: smectic A phase, N^*: chiral nematic phase, I: isotropic liquid phase. c) Consisted of 2-phenylpyrimidines.

II. The influence of halogeno substituents in the phenyl ring of the ortho or meta position relative to the chiral terminal group on the physical properties of these compounds is summarized as follows: (1) Ps values of ortho-halogeno derivatives (**7b–7d**) are larger than that of an unsubstituted compound (**7a**), that is, the dipole moment of the ortho-halogen atom contributes to the enhancement of the Ps values.

This must imply that both dipole moments of the ortho halogen atom and terminal chiral group align in the same direction. It is strange that the Ps value of the ortho-fluoro derivative (**7b**) in a non-chiral host liquid crystal mixture is 1.5 times larger than that of the parent compound (**7a**), though the maximum Ps values of these compounds are nearly equal. This is probably due to the fact that although compound **7b** has a larger Ps value than that of **7a** potentially, it is not observed because of a narrow Sc* range of compound **7b**. (2) Response times are not improved, though the Ps values are increased by introducing the halogen atoms. As the response time (τ) can be represented by $\tau = \eta/(\text{Ps} \times E)$, where η is the rotational viscosity, Ps is the spontaneous polarization and E is the applied electric field,[10] the above result suggests that the rotational viscosities are also increased by introducing the halogen atoms. (3) The replacement of the meta hydrogen by a fluorine atom does not lead to a noticeable change in the physical properties.

Conclusion

The introduction of a lateral halogeno-substituent to the phenyl ring of 2,5-diphenylpyrimidine core led to a decrease in the thermal stability of mesophases in the order of Br, Cl > F > H. The Ps values in achiral host liquid crystal mixtures were increased by introducing the halogen atom. However, response times were not improved.

5. EXPERIMENTAL

IR, ^{1}H NMR and mass spectra were recorded on a Shimadzu IR-408, Varian EM-360 and Hitachi M-80, respectively, under standard conditions. Elemental analyses were carried out with a Perkin-Elmer 2400 CHN Elemental Analyzer. The optical purity of compound **7a** was measured by HPLC with a chiral column "CHIRALCEL OD," produced by Daicel Chemical Industries, Ltd. The phase transition temperatures were determined using a Rigaku Denki DSC-8230 apparatus and texture observations were made using a Nikon XTP-II polarizing microscope in conjunction with a Mettler FP-82 hot stage and FP-80 control unit. A typical procedure for the synthesis is described for **7b**. Other compounds were prepared according to a similar method as **7b**.

3-Fluoro-4-Hydroxymandelic Acid (2: X = H, Y = F)

To a solution of glyoxylic acid (40% solution in water, 85.0 g, 0.46 mol) and NaOH (16.3 g, 0.41 mol) in water (250 ml) was added 2-fluorophenol (11.2 g, 0.10 mol) and the PH of this solution was adjusted to 10.0 with 4N-NaOH. After stirring for 20 h at 30°C, the reaction mixture was acidified with aqueous HCl and extracted several times with ethyl acetate. The combined organic extracts were washed with water and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to yield 3-fluoro-4-hydroxymandelic acid as pale yellow crystal (18.4 g, 98.9%). IR (Nujol) 3485, 3420, 1710, 1620, 1605, 1516, 1286, 1236, 1188, 1145, 1115 cm^{-1}; NMR (D_2O) $\delta = 5.24$ (1H, s), 6.99–7.27 (3H, m); Mass: m/z 186 (m^+).

3-Fluoro-4-hydroxyphenylacetic Acid (3: X = H, Y = F)

To a solution of 3-fluoro-4-hydroxymandelic acid (4.5 g, 24.2 mmol) in acetic acid (25 ml) was added phosphorous (1.2 g, 38.7 mmol), iodine (0.5 g, 2.0 mmol), hydriodic acid (57%, 0.5 ml, 2.2 mmol) and water (0.5 ml), and the mixture was heated under reflux for 3 h. The reaction mixture was filtrated and the filtrate was evaporated. The resulting residue was dissolved in water and extracted several times with ether. The combined ethereal extracts were washed with water, and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was purified by column chromatography on silica-gel with dichloromethane-methanol as eluent to yield 3-fluoro-4-hydroxyphenylacetic acid (1.96 g, 47.7%). IR (Nujol) 3395, 1685, 1629, 1511, 1421, 1350, 1279, 1254, 1154, 1102 cm^{-1}; NMR (acetone-d_6) δ = 3.57 (2H, s), 6.54–6.76 (2H, m), 7.16 (1H, t, J = 9 Hz), 9.43 (1H, bs); Mass: m/z 170 (m^+).

3-Dimethylamino-2-[3-(fluoro)-4-(hydroxy)phenyl]acrolein (4: X = H, Y = F)

Phosphorous oxychloride (11.1 g, 72.4 mmol) was added slowly to dry DMF (6.8 g, 93.0 mmol) at 0°C and the mixture was stirred for half an hour. A solution of 3-fluoro-4-hydroxyphenylacetic acid (5.0 g, 29.4 mmol) in dry DMF (15 ml) was slowly added to the above solution and then the mixture was heated at 50°C for half an hour, and subsequently at 70°C for 3 h. The reaction mixture was poured into water and neutralized with potassium carbonate (23.0 g). A solution of NaOH (20.0 g) in water (30 ml) was added to this solution and the mixture was heated at 50°C for half an hour. After cooling to room temperature, the reaction mixture was acidified with concentrated HCl and the resulting precipitates were collected by filtration and recrystallized from ethanol to yield 3-dimethylamino-2-[3-(fluoro)-4-(hydroxy)phenyl]acrolein (2.0 g, 32.6%). IR (Nujol) 1620, 1549, 1517, 1482, 1286, 1202, 1185, 1138, 1122 cm^{-1}; NMR ($CDCl_3$) δ = 2.85 (6H, s), 6.72–6.94 (4H, m), 9.03 (1H, s); Mass: m/z 209 (m^+).

5-[3-(Fluoro)-4-(hydroxy)phenyl]-2-[4-(*n*-octyloxy)phenyl]pyrimidine (6: X = H, Y = F)

A solution of 3-dimethylamino-2-[3-(fluoro)-4-(hydroxy)phenyl]acrolein (0.80 g, 3.8 mmol) and 4-octyloxybenzamidine (**5**, 1.0 g, 4.0 mmol) in pyridine (8.0 ml) was stirred at 70°C for 24 h. After cooling to room temperature, the reaction mixture was poured into cold water and the resulting precipitates were collected by filtration and recrystallized from ethanol to yield 5-[3-(fluoro)-4-(hydroxy)phenyl]-2-[4-(*n*-octyloxy)phenyl]pyrimidine (1.0 g, 53.0%). IR (Nujol) 1602, 1580, 1520, 1255, 1170, 1120 cm^{-1}; NMR ($CDCl_3$) δ = 0.83–0.96 (3H, m), 1.17–1.95 (12H, m), 4.10 (2H, t, J = 7 Hz), 7.06 (2H, d, J = 9 Hz), 7.17 (1H, t, J = 8 Hz), 7.49 (1H, dd, J = 8 Hz and 2 Hz), 7.62 (1H, dd, J = 8 Hz and 2 Hz), 8.46 (2H, d, J = 8 Hz), 9.04 (2H, s); Mass; m/z 394 (m^+).

(*R*)-5-[4-{1-(Ethoxycarbonyl)ethoxy}-3-(fluoro)phenyl]-2-[4-(*n*-octyloxy)phenyl]-pyrimidine (7b: X = H, Y = F)

To a suspension of sodium hydride (60% assay in mineral oil, 176 mg, 0.93 mmol) in dry DMF (1 ml) was added dropwise a solution of 5-[3-(fluoro)-4-(hydroxy)phenyl]-2-[4-(*n*-octyloxy)phenyl]pyrimidine (0.35 g, 0.89 mmol) in dry DMF (5 ml) at 0°C and the resulting mixture was stirred for 1 h. Ethyl (*S*)-2-*p*-toluenesulfonyloxypropionate (0.29 g, 1.12 mmol) was added dropwise and the mixture was stirred at room temperature for 2 h. The reaction mixture was poured into 5% HCl and extracted twice with ether. The extracts were washed with water and dried over anhydrous $MgSO_4$. The solvent was evaporated and the resulting solid was purified by column chromatography on silica-gel with hexane-ether as eluent, followed by recrystallization from ethanol to yield **7b** (0.20 g, 45.6%). IR (Nujol): 1730, 1605, 1580, 1520, 1300, 1250, 1170, 1140 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.84–0.95 (3H, m), 1.15–1.90 (18H, m), 4.04 (2H, t, *J* = 7 Hz), 4.25 (2H, q, *J* = 7 Hz), 4.84 (1H, q, *J* = 7 Hz), 6.95–7.11 (3H, m), 7.25–7.44 (2H, m), 8.40 (2H, d, *J* = 9 Hz), 8.89 (2H, s); Mass: m/z 494 (m^+); Found: C, 70.23; H, 7.07; N, 5.65; F, 3.82%. Calcd for $C_{29}H_{35}FN_2O_4$: C, 70.42; H, 7.13; N, 5.66; F, 3.84%.

(*R*)-5-[3-(Chloro)-4-{1-(Ethoxycarbonyl)ethoxy}phenyl]-2-[4-(*n*-octyloxy)phenyl]-pyrimidine (7c: X = H, Y = Cl)

IR (Nujol): 1730, 1602, 1578, 1275, 1165 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.85–0.96 (3H, m), 1.20–1.86 (18 H, m), 4.04 (2H, t, *J* = 7 Hz), 4.25 (2H, q, *J* = 7 Hz), 4.82 (1H, q, *J* = 7 Hz), 6.94–7.03 (3H, m), 7.41 (1H, dd, *J* = 9 Hz and 2 Hz), 7.64 (1H, d, *J* = 2 Hz), 8.40 (2H, d, *J* = 9 Hz), 8.89 (2H, s); Mass: m/z 510 (m^+); Found: C, 68.10; H, 6.84; N, 5.54; Cl, 6.84%. Calcd for $C_{29}H_{35}ClN_2O_4$: C, 68.15; H, 6.90; N, 5.48; Cl, 6.39%.

(*R*)-5-[3-(Bromo)-4-{1-(Ethoxycarbonyl)ethoxy}phenyl]-2-[4-(*n*-octyloxy)phenyl]-pyrimidine (7d: X = H, Y = Br)

IR (Nujol): 1730, 1602, 1578, 1508, 1285, 1256, 1165 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.86–0.93 (3H, m), 1.17–1.86 (18H, m), 4.04 (2H, t, *J* = 7 Hz), 4.25 (2H, q, *J* = 7 Hz), 4.82 (1H, q, *J* = 7 Hz), 6.92 (1H, d, *J* = 9 Hz), 7.00 (2H, d, *J* = 9 Hz), 7.46 (1H, dd, *J* = 9 Hz and 2 Hz), 7.81 (1H, d, *J* = 2 Hz), 8.40 (2H, d, *J* = 9 Hz), 8.89 (2H, s); Mass: m/z 554 (m^+); Found: C, 62.68; H, 6.51; N, 4.97; Br, 14.60%. Calcd for $C_{29}H_{35}BrN_2O_4$: C, 62.70; H, 6.35; N, 5.04; Br, 14.38%.

(*R*)-5-[4-{1-(Ethoxycarbonyl)ethoxy}-2-(fluoro)phenyl]-2-[4-(*n*-octyloxy)phenyl]-pyrimidine (7e: X = F, Y = H)

IR (Nujol): 1378, 1620, 1602, 1580, 1505, 1257, 1169 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.86–0.95 (3H, m), 1.12–1.86 (18H, m), 4.04 (2H, t, *J* = 7 Hz), 4.25 (2H, q, *J* = 7 Hz), 4.78 (1H, q, *J* = 7 Hz), 6.72–6.84 (2H, m), 7.00 (2H, d, *J* = 9 Hz), 7.38 (1H, t, *J* = 9 Hz), 8.41 (2H, d, *J* = 9 Hz), 8.89 (2H, s); Mass: m/z 494 (m^+); Found: C, 70.05; H, 7.33; N, 5.64; F, 4.02%. Calcd for $C_{29}H_{35}FN_2O_4$: C, 70.42; H, 7.13; N, 5.66; F, 3.84%.

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