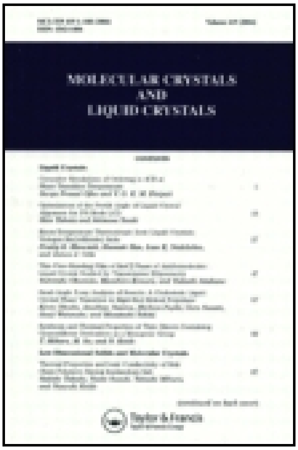

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Synthesis and Mesomorphic Properties of 4- Substituted Phenyl and Phenylthio-4′-[(S)-β- Ethoxypropoxy]-Benzoatest

M. E. Neubert [a] & S. Sabol-keast [a]

[a] Liquid Crystal Institute, Kent State University, Kent, OH, 44242

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Synthesis and Mesomorphic Properties of 4-Substituted Phenyl and Phenylthio-4′-[(S)-β-Ethoxypropoxy]-Benzoates†

M. E. NEUBERT AND S. SABOL-KEAST
Liquid Crystal Institute, Kent State University, Kent, OH 44242

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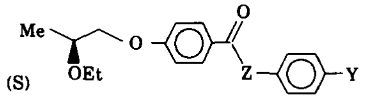
A variety of esters and thioesters of the type



$Z = O \quad Y = C_7H_{15}, OC_7H_{15}$ and COC_9H_{19}
$Z = S \quad Y = C_7H_{15}$, and $OC_{12}H_{25}$

were prepared by esterification of the acid with the phenols and thiols using the carbodiimide method. These compounds were of interest as possible ferroelectric liquid crystals. The required acid was prepared by basic hydrolysis of the ester obtained by alkylating methyl-4-hydroxybenzoate with the tosylate of (S)-2-(tetrahydro-2-pyranoxy)-1-propanol synthesized in two steps from (S)-ethyl lactate. Transition temperatures for these esters/thioesters were determined by hot-stage polarizing microscopy but no mesophases were observed in the esters and only a cholesteric phase in the $Y = OC_{12}$ thioester.

Keywords: liquid crystals, ferroelectrics, phenylthiobenzoates, optically active, NMR

INTRODUCTION

The report of ferroelectric S_C properties with large P_S values in the 2-ethoxy-1-propoxy esters *1*[1]

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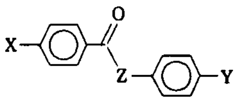
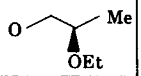
†Presented at the Second International Symposium of Ferroelectric Liquid Crystals, Abstract No. P73, Goteborg, Sweden, June, 1989.

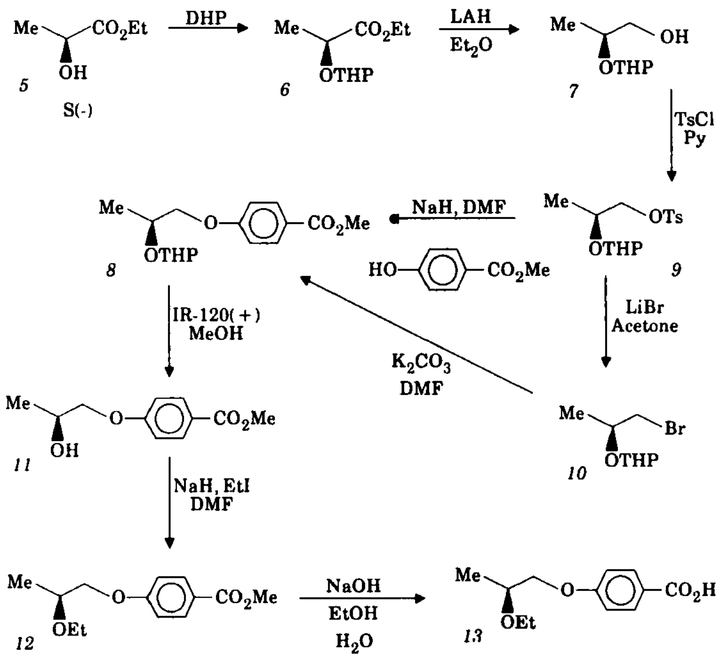


	Z	X	Y
1	O	RO	
2a *2b*	O S		R', OR'
3a *3b*	O S	R', OR'	

prompted us to investigate the mesomorphic properties of the esters/thioesters with this group on the acid end *2* as possible new ferroelectric liquid crystals or as components in mixtures with the chiral esters *3a* and *3b* known to have S_A and S_C* phases but low P_S values.[2,3]

SYNTHESIS

Our approach to the synthesis of the required branched chain acid was patterned after that used to prepare the phenols[1] (Scheme 1). Ghirardelli's method[4] was used



SCHEME 1

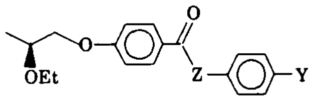
to prepare the THP protected tosylate *9* from S(-) ethyl lactate *5*. Accomplishing this synthesis in the laboratory was more difficult than anticipated due to the difficulty in purifying these compounds, especially in separating the THP ether *6* from the starting alcohol *5*. The tosylate *9* was not purified due to its poor stability which required that it either be used immediately or stored at 5° under N_2. A variety of conditions had to be tried before this tosylate was successfully converted to the ether *8*. An attempt to convert this first to the bromide *10* did not help. The best results were obtained using a more concentrated soln of NaH in DMF than reported for the phenol, and applying some heat to give a crude yield of 71.1%. Although the alcohol *11* could not be purified by chromatography, the ether *12* could be, but trace amounts of impurities were still evident in a NMR spectrum. Hydrolysis of this ester *12* to the acid *13* gave a solid which was purified by recrystallization. Reverse phase HPLC suggested it was 98 + % pure and elemental analysis and NMR confirmed both the purity and structure. The esters/thioesters *2* were prepared by esterifying this acid with the appropriate phenols and thiols using the carbodiimide method as previously described.[5] Their structures were confirmed by NMR (Table II). Details for these synthetic procedures are provided in the experimental section.

MESOMORPHIC PROPERTIES

Transition temperatures for the esters *2a* and thioesters *2b* were determined by hot-stage polarizing microscopy (Table I). No mesophases were observed in the esters *2a*, although a short range cholesteric phase was observed in the alkoxy thioester *2b* (Y = OC_{12}). Melting temperatures were lowered considerably from those for the analogous straight chain esters. Our recent study of mesomorphic properties of straight-chain alkyl/alkoxy phenylbenzoates using a computer data base provides a possible explanation.[6] Among these esters a chain length of at least

TABLE I

Transition Temperatures (°C) and Optical Rotations for



Z	Y	K[a]	Ch	I[a]	$[\alpha]_{22}^{D}$
O	C_7	Liquid to	> -20		(-)13.78 (CH_2Cl_2)
O	OC_7	5.9	----	21.5-23.0	(-)10.19 (CH_2Cl_2)
O	COC_9	60.5	----	73.7-75.3	(-)10.28 ($CHCl_3$)
S	C_7	Liquid to	> -20		(b)
S	OC_{12}	24.3	(30.1-30.5)	38.4-39.6	(-)9.43 (CH_2Cl_2)

a. K = crystallization temperature, Ch = cholesteric and I = isotropic liquid. See experimental section for procedural details.

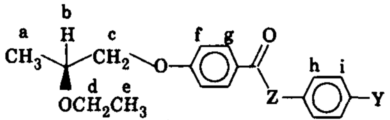
b. Not enough material was available to determine the rotation.

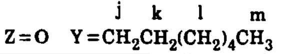
six carbon atoms on the acid side is needed to observe any smectic phases although nematic phases can occur. Thus, the ethoxy branched chain with only a three carbon backbone might not be long enough to observe mesophases when this chain is on the acid end. No mesophases were observed in the acid *13*.

EXPERIMENTAL

Anhydrous Na_2SO_4 was used to dry all organic extracts. S(-)-Ethyl lactate with $[\alpha]_{22}^{D} = (-)9.96$ (CH_2Cl_2) was obtained from Aldrich Chemical Co. DMF was dried over Linde molecular sieves #4A, distilled and stored over molecular sieves.

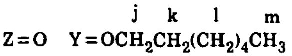
Table II - NMR Data for





$Z = O \quad Y = \overset{j}{CH_2}\overset{k}{CH_2}(\overset{l}{CH_2})_4\overset{m}{CH_3}$

δ	multiplicity	J(Hz)	Number of Protons	Identification
8.13	d	9.00	2	g
7.20	d	8.45	2	i
7.09	d	7.48	2	h
7.04-6.95	m	---	2	f
4.10-3.77	m	---	2	c
3.72-3.50	m	---	3	b,d
2.61	t	7.60	2	j
1.70-1.56	m	---	2	k
1.42-1.17	m	---	14	l,a,e
0.88	t	6.00	3	m



$Z = O \quad Y = \overset{j}{OCH_2}\overset{k}{CH_2}(\overset{l}{CH_2})_4\overset{m}{CH_3}$

δ	multiplicity	J(Hz)	Number of Protons	Identification
8.12	d	6.51	2	g
7.09	d	7.60	2	h
6.99, 6.97	2d	5.86	2	f
6.90	d	9.42	2	i
4.07-3.73	m	---	4	c,j
3.66-3.50	m	---	3	b,d
1.84-1.69	m	---	2	k
1.49-1.11	m	---	14	l,a,e
0.90	t	6.00	3	m

$Z=O \quad Y=CO\overset{j}{CH_2}\overset{k}{CH_2}(\overset{l}{CH_2})_6\overset{m}{CH_3}$

δ	multiplicity	J(Hz)	Number of Protons	Identification
8.13	d	9.66	2	g
8.03	d	8.44	2	i
7.30	d	9.60	2	h
7.00	d	7.28	2	f
4.14-3.52	m	---	5	b,c,d
2.95	t	7.71	2	j
1.83-1.68	m	---	2	k
1.45-1.18	m	---	18	l,a,e
0.88	t	5.79	3	m

$Z=S \quad Y=\overset{j}{CH_2}\overset{k}{C_6H_{13}}$

δ	multiplicity	J(Hz)	Number of Protons	Identification
7.91	d	7.0	2	g
7.32	d	7.0	2	h
7.15	d	7.0	2	i
6.86	d	8.0	2	f
3.99-3.94	m	---	1	b
3.79-3.69	m	---	2	c or d
3.60-3.40	m	---	2	c or d
2.60	t	7.0	2	j
1.75-0.78	m	---	19	a,e,k

$Z=S \quad Y=O\overset{j}{CH_2}\overset{k}{CH_2}(\overset{l}{CH_2})_9\overset{m}{CH_3}$

δ	multiplicity	J(Hz)	Number of Protons	Identification
7.98	d	9.87	2	g
7.38	d	8.55	2	h
6.95	d	7.22	4	f,i
4.08-3.91	m	---	4	c,j
3.90-3.75	m	---	1	b
3.70-3.50	m	---	2	d
1.87-1.73	m	---	2	k
1.51-1.15	m	---	24	l,a,e
0.88	t	6.19	3	m

Sodium hydride (80% in oil) was thoroughly washed once with hexane immediately before use. Repeated washings seemed to give less reactive material. The synthesis of the 4-substituted phenols and thiols have been previously described.[7-11]

TLC data were obtained using Anal-Tech silica gel GHLF Uniplates with UV and I_2 as the detectors. All compounds were purified until they showed only one spot by TLC unless otherwise noted. Flash chromatography was performed on Aldrich grade 60 (mesh 230–400) silica gel. The elemental analysis was obtained from Oneida Research Services, Inc., Whitesboro, NY.

Gas chromatographs were run on a Varian 3700 instrument using a 3% SP-200 on 80/100 Supelco port 6′ × $\frac{1}{8}$″ SS column and HPLC on a Waters 300 Prep instrument. Optical rotations were determined using a Polyscience SR6 instrument and IR spectra on a Pye-Unicam 3-200 spectrophotometer. NMR spectra were run in $CDCl_3$ with TMS as an internal standard using a General Electric GN300 instrument, except for the tosylate *9* which was run in CCl_4 on a Varian EM360 instrument.

Transition temperatures (°C) were determined using a Leitz Laborlux 12 Pol polarizing microscope fitted with a modified and calibrated Mettler FP-2 heating stage at a rate of 2°/min as previously described.[12] Samples were cooled at 2°/min until they crystallized to obtain the crystallization temperature so that no monotropic phases occurring below this temperature were missed.

Ethyl-S(-)-2-(tetrahydro-2-pyranoxy) propanoate, *6*

Ghirardelli's procedure was used except that the reaction was run at RT and maintained by using a water bath kept at RT. The crude product was carefully distilled using a Vigreaux column by increasing the temperature very slowly. The following fractions were collected at 0.4 mm Hg: DHP at <35°, a mixture of the unreacted alcohol *5* and the ether *6* at 66° and the pure product at 66° (80.6% yield). Analytical data for the ether *6*: TLC (EtOAc, I_2) R_f = 0.71 (starting alcohol R_f = 0.49); IR (film) 1740 (str, CO_2Et) and no OH at 3400 cm^{-1}; GLC t_R = 0.90 sec at 170°, ~98–99% pure and NMR (CCl_4) δ4.67 (m, 1, $\overset{*}{C}HCO_2$), 4.44–3.04 (m, 5, $OCHOCH_2$ of THP + CO_2CH_2) and 2.3–0.74 (m, 12, $3CH_2$ + $2CH_3$).

(S)-2-(Tetrahydro-2-pyranoxy)-1-propanol, *7*

Use of Ghirardelli's method gave a 77.7% yield of this alcohol: TLC (EtOAc) R_f = 0.55 (starting ester *6* R_f = 0.71) ($CHCl_3$) R_f = 0.10 (R_f for *6* = 0.15); IR (film) 3400 cm^{-1} (br, str, OH) and no ester absorption, and NMR δ4.57 and 4.51 (2d, J = 2.16 Hz, 1, OCHO), 4.03–3.74 (m, 2, CH_2OH), 3.66–3.39 (m, 3, $O\overset{*}{C}H$, OCH_2 of THP), 2.65 (t, 1, OH), 1.94–1.46 (m, 6, $3CH_2$) and 1.20, 1.12 (2d, J = 6.38 and 6.32 Hz, 3, CH_3).

(S)-1-(p-Toluenesulfonoxy)-2-(tetrahydro-2-pyranoxy)-propane, *9*

Using Ghirardelli's procedure, a 95.7% of the crude clear light gold tosylate *9* was isolated: TLC ($CHCl_3$) R_f = 0.19 (R_f for *7* = 0.10, R_f for tosyl chloride = 0.70), (EtOAc) R_f = 0.68 (R_f for *7* = 0.55); IR (film) 1600 (med Ar) and no OH at 3400 cm^{-1} and NMR δ7.77 (d, J = 8.0 Hz, 2, ArH ortho to S), 7.33 (d, J = 6.0

Hz, 2, ArH ortho to Me), 4.61 (br, s, 1, OCH of THP), 4.13–3.19 (m, 5, $\overset{*}{C}HCH_2$ + OCH_2 of THP), 2.44 (s, 3, Ar Me) and 1.87–1.02 (m, 9,Me + $3CH_2$). This material was either used immediately or stored at 5° under N_2.

Methyl 4-[(S)-2-(tetrahydro-2-pyranoxy) propoxy]-benzoate, *8*

Sodium hydride (18.3g, 0.64 mole) was dried for 15 min under a stream of N_2 to be sure it was dry. Then a soln of the methyl 4-hydroxybenzoate (72.3g, 0.48 mol) in 1.5*l* of DMF was added dropwise, the mixture stirred for 15 min, a soln of the tosylate *9* (100g, 0.32 mol) in 500 ml DMF added dropwise and the rxn mixture stirred for 17 hr at RT. This was then heated at ~70–80° for 7–8 hr, stirred at RT for 2.75 hr and then rotovaped. The residue was dissolved in H_2O and extracted with Et_2O (2×). The Et_2O extract was washed with 5% aq KOH and H_2O, dried and filtered. The filtrate was rotovaped to give 66.5g (71.1%) of the crude product *8* as an orange liquid: TLC (40% EtOAc in hexane) R_f = 0.56 (major) and 0.49 (very faint), (R_f for starting phenol = 0.35 and tosylate *9* = 0.64) and ($CHCl_3$) R_f = 0.15 (major), 0.36 (faint) and 0.07 (faint); IR (film) 1720 (str, CO_2R), 1600, 1500 (str with sh, Ar) and no OH at 3400 cm^{-1} and NMR δ7.97 (d, J = 8.56 Hz, 2, ArH ortho to CO_2Me); 7.80 and 7.33 (2d, tosylate impurity); 6.94 (d, J = 8.14 Hz) and 6.91 (d, J = 7.59 Hz, 2, ArH ortho to OR); 4.84–4.66 (m, 1, THP CH), 4.25–3.89 (m, 2, CH_2OAr), 3.87 (s, 3, CO_2Me), 3.58–3.33 (m, 3, $\overset{*}{C}H$ and THP OCH_2); 2.43 (s, impurity) and 1.83–1.1 (m, 9, Me and 3THP CH_2).

Methyl 4-[(S)-2-hydroxypropoxy] benzoate, *11*

To a stirred suspension of 1.07 g of Amberlite ion exchange resin IR-120 (plus) in 500 ml MeOH was added dropwise, a soln of the ether *8* (96g, 33 mmole) in 210 ml MeOH. This mixture was heated in a 45° oil bath for 3.5–4 hr, cooled to RT, filtered and the filtrate rotovaped to give 6.6g (95.0%) of the crude alcohol, *11*: TLC (50% EtOAc in hexane) R_f = 0.34 (major), 0.54 (minor) and 0.00 (minor) (R_f for *8* = 0.50) and ($CHCl_3$) R_f = 0.11 (major), 0.21 (minor) and 0.00 (minor); IR (film) 3400 (str OH), 1720 (str, CO_2R) and 1620 cm^{-1} (str, Ar) and NMR δ7.96–7.93 (m, 2, ArH ortho to CO_2), 7.76 and 7.3 (2d, tosylate impurity) 6.92–6.88 (m, 2, ArH ortho to OR), 4.24–3.52 (m, 6, CO_2CH_3 + $\overset{*}{C}HCH_2$), 2.40 (s, impurity), 2.02 (s, 1, OH) and 1.3–1.12 (m, 3, Me).

Methyl 4-[(S)-2-Ethoxypropoxy] benzoate, *12*

A soln of the above alcohol *11* (43.5g, 0.21 mole) in 400 ml DMF was added dropwise to a stirred suspension of NaH (11.9g, 0.50 mole) in 1.25*l* of DMF under N_2 at RT. This mixture was stirred for 15 min and then EtI (50.1g, 0.32 mole) added dropwise. Stirring was continued for 4 hr, additional EtI added (~20g), stirring continued for 17 hr and then the mixture rotovaped. The residue was dissolved in H_2O and extracted with Et_2O (2×). The Et_2O extract was washed with H_2O, dried, filtered and the filtrate rotovaped to give 34.2g (69.3%) of the crude product *12* as a yellow liquid. This material was purified by flash chromatography using 6% EtOAc in hexane to give 22.4g (45.5%) of the purified liquid ether *12*: TLC ($CHCl_3$) R_f = 0.26 (R_f for *11* = 0.11); IR (film) 1715 (str, CO_2R), 1620, 1600 (str with sh, Ar) and no OH at 3400 cm^{-1} and NMR δ7.99, 7.97 (2d, J = 5.15, 2, ArH ortho to CO_2Me), 6.94, 6.91 (2d, J = 4.39, 2, ArH ortho to OR), 4.4–4.3 (m, 1, $\overset{*}{C}H$), 4.1–3.5 (m, 7, $2OCH_2$ + OMe) and 1.4–1.16 (m, 6, 2Me).

4-[(S)-2-Ethoxypropoxy] benzoic Acid, *13*

To a stirred soln of NaOH (14.0g, 0.35 mole) in 72 ml H_2O and 108 ml abs EtOH was added the ester *12* (21.0g, 0.088 mole). This mixture was refluxed for 4.5 hr, allowed to cool to RT and then rotovaped. The residue was dissolved in H_2O, washed with Et_2O, acidified with concd HCl and extracted with Et_2O (2×). The Et_2O extract was washed with H_2O, dried, filtered and the filtrate rotovaped to give 18.4g (100%) of the crude acid *13*. This material was recrystallized from hexane using a dry ice bath to give 15.2g (77.0%) of the purified acid *13*: transition temperatures (°C) 54.8–59.4 (K-I) and 29.9 (I-K), TLC ($CHCl_3$) R_f = 0.00 (R_f for *12* = 0.26); HPLC (C_{18} reverse phase column, MeOH) t_R = 3.23 min, estd purity = 98 + %; IR (Nujol) 3000 (br, acid OH), 1665 (br str, CO_2H) and 1595, 1570 cm^{-1} (str with sh, Ar) and NMR δ12.32 (br s, 1, CO_2H), 8.04 (d, J = 7.09 Hz) and 8.03 (d, J = 3.48 Hz, 2, ArH ortho to CO_2H); 6.97 (d, J = 4.32 Hz) and 6.94 (d, J = 8.97 Hz, 2, ArH ortho to OR), 4.08–3.49 (m, 5, $\overset{*}{C}HCH_2$ + CH_2) and 1.35–1.15 (m, 6, 2Me).

Acknowledgment

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