We consider two attractive possibilities for the chromophore excited at 356 nm, III and IV in Figure 1. If structure III is correct, the 1658-cm^{-1} band would be assigned to the quininoid C=N stretch, shifting to 1633 cm^{-1} on replacement of the NH proton in D_2O. A similar assignment (1624 cm^{-1}) has been made for a DABA–Zn^{II} complex,[12] also though to exist in a quininoid form. The remaining bands of the 356-nm ternary complex RR spectrum would also be expected to arise from vibrational modes in the quininoid fragment. Structure III would be favored by the same kind of protein interactions which are suggested to account for the altered PABA-Glu vibrational spectrum. These interactions would be central to the enzyme mechanism because they would favor breaking of the N-10 methylene–PABA bond over the N-5 methylene–tetrahydropterin bond in the cofactor (I, Figure 1) and disfavor reformation of this bond, which is believed to be the process by which the ternary complex undergoes dissociation. The coexistence of structures II and III would imply conformational heterogeneity in the protein, since without different protein interactions II and III are simply resonance forms. Different dispositions of the proposed charges or H-bonds in alternative protein conformations could, however, favor different electronic structures and different positions of the nuclei. Another possibility is that in a fraction of the molecules proton transfer occurs to or from protein acceptor or donor groups so that a tautomer of III is produced, with the proton on the CO rather than the N end of the quininoid fragment.

Alternatively, structure IV (or its N-10 analogue) has been suggested by Santi et al.[13] and others[14,15] to be an intermediate in the TSase catalytic mechanism. It has a $^+N{=}CH_2$ bond attached to the tetrahydropterin ring, which would be capable of exchange with D_2O.[16] This bond too could account for the observed 1658-cm^{-1} band, which shifts to 1633 cm^{-1} in D_2O. The remaining bands in the 356-nm spectrum could be attributed to vibrational modes of the tetrahdropterin moiety, with which the $^+N{=}CH_2$ bond is in conjugation. Accumulation of IV would also be in keeping with the proposed PABA-Glu perturbing protein interactions, since these would destabilize the methylene–PABA bond, and stabilize IV, which is otherwise a high-energy intermediate.[17]

At this point III and IV are both viable candidates for the species giving rise to the 356-nm spectrum. We hope to resolve the ambiguity via RR and NMR isotope labeling experiments. In either case it is important to recognize that the 322- and 375-nm absorption bands are absent unless the cofactor and FdUMP are both bound to the enzyme. It is only in the ternary complex that the protein interactions which are responsible for the perturbed PABA-Glu absorption and vibrational spectra, and also for the stabilization of either structure III or IV, are developed. During enzyme turnover these same activating interactions can be induced by binding of the natural substrate, 2′-deoxyuridylate, with the cofactor. They may well be involved in other enzymatic reactions utilizing N-10 linked tetrahydrofolates.

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(13) Santi, D. V.; McHenry, C. S.; Sommer, H. *Biochemistry* **1974**, *13*, 471.

(14) Sharma, R. K.; Kisliuk, R. L.; Verma, S. P.; Wallach, P. F. H. *Biochim. Biophys. Acta* **1975**, *391*, 19.

(15) Benkovic, S. J.; Benkovic, P. A.; Comfort, D. R. *J. Am. Chem. Soc.* **1969**, *91*, 5270.

(16) Poe, M.; Benkovic, P. A.; Comfort, D. R. *J. Am. Chem. Soc.* **1969**, *91*, 5270.

(17) A referee has brought to our attention that only one ^{19}F NMR peak is seen for the ternary complexes,[7] not two as might be expected for coexisting structures of the kind proposed here. It is quite possible, however, that the structures interconvert (via protein fluctuations) rapidly on the NMR time scale. It is also possible that one of the two structures is a minority species, difficult to detect by NMR, since we have no information at this point about resonance enhancement factors.

(18) Fodor, S.; Rava, R. P.; Copeland, R. A.; Spiro, T. G. *J. Raman Spectrosc.*, in press.

Design and Synthesis of New Ferroelectric Liquid Crystals. 2. Liquid Crystals Containing a Nonracemic 2,3-Epoxy Alcohol Unit

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Tilted smectic liquid crystal (LC) phases, when composed of nonracemic molecules, possess a spontaneous ferroelectric polarization, or macroscopic dipole moment, deriving from anisotropic orientation of molecular dipoles in the LC phase.[2] We have suggested that this polarization (*P*, in units of nC/cm^2, or D/molecule) may be considered in terms of a novel type of molecular recognition occurring in the LC phase and have developed a model in principle allowing prediction of the sign (handedness) and magnitude of the polarization for specific compounds.[3] In this paper we describe a prototypical example of a new class of liquid crystal materials possessing the *trans*-2,3-epoxy alcohol chiral unit. This compound represents an ideal test of our model for the polarization, and indeed exhibits for the first time *predictable sign of the ferroelectric polarization* in a material with high polarization density.

The model states that individual molecules of the phase are ordered with respect to *conformation* and *rotational orientation* by a time-average surface of constant molecular mean field, or binding site, resulting from interactions with neighboring molecules. When applied to the well-known *p*-alkoxyphenyl *p*-alkoxybenzoates, the binding site takes the shape of a bent cylinder,[3] and the preferred conformation has the alkoxy tail units staggered with the carbons of the tails aligned in a plane, as shown in Figure 1. This plane is congruent with the smectic C tilt plane, and the preferred rotational orientation of the molecules is such that the tails are less tilted than the phenyl benzoate core.

Ferroelectric polarization results when the material is made nonracemic by incorporation of a stereogenic center in one of the tails. Typical ferroelectric LC molecules reported to date possess a 2-methylbutyl or 2-alkoxypropyl chiral tail.[3] Unfortunately, lack of data on the conformations present in the C* phase and the average rotational orientation of the molecules with respect to the tilt plane precludes interpretation of the observed polarization on a molecular level in these cases.

For display device applications, it is desirable to obtain ferroelectric LCs with high polarization density.[4] Thus, compounds with a large dipole moment oriented *normal* to the tilt plane in Figure 1 are desired. Given this goal, incorporation of the *trans*-2,3-epoxy alcohol unit into the tail of alkoxyphenyl alkoxybenzoate LCs, as shown in Figure 2 for an *S,S* enantiomer, seems particularly attractive. Our model suggests that the molecular dipole due to the epoxide unit in such a material should be oriented normal to the tilt plane, exactly as required, and the rigidity inherent in the epoxide ring should reduce conformational averaging of this dipole. This suggests that the polarization should be significantly enhanced relative to the 2-methylbutyl- or 2-

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(2) Meyer, R. B.; Liêbert, Strzelecki, L.; Keller, P. *J. Phys.* **1975**, *36*, L-69.

(3) Paper no. 1 in the series: Walba, D. M.; Slater, S. C.; Thurmes, W. N.; Clark, N. A.; Handschy, M. A.; Supon, F. *J. Am. Chem. Soc.* **1986**, *108*, 5210–5221.

(4) (a) Clark, N. A.; Lagerwall, S. T. *Appl. Phys. Lett.* **1980**, *36*, 899. (b) Handschy, M. A.; Clark, N. A. *Appl. Phys. Lett.* **1982**, *41*, 39. (c) Clark, N. A.; Handschy, M. A.; Lagerwall, S. T. *Mol. Cryst. Liq. Cryst.* **1983**, *94*, 213–234.

0002-7863/86/1508-7424$01.50/0

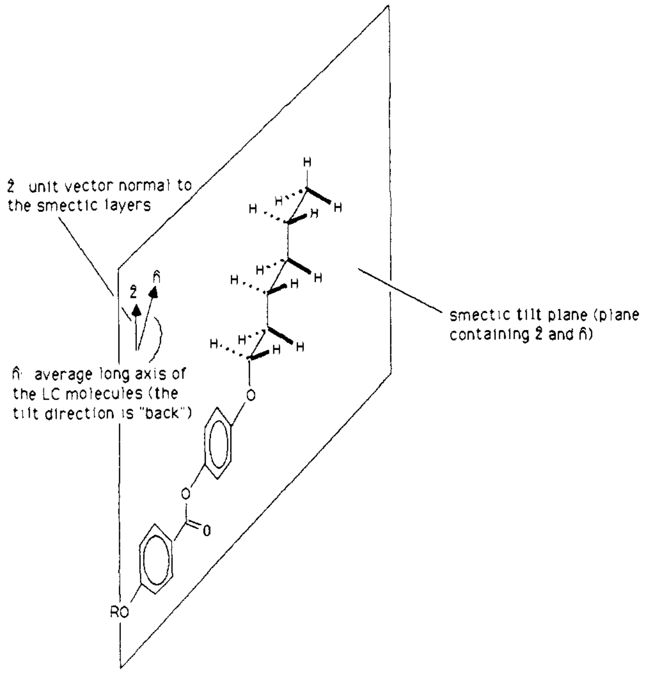
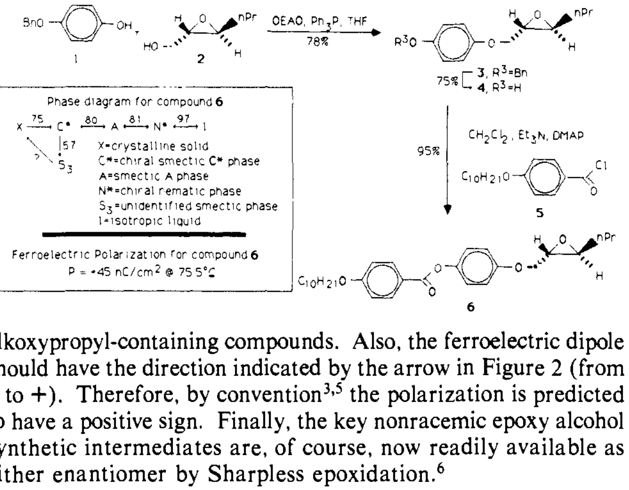


Figure 1. Possible preferred orientation of a simple *p*-(alkoxyphenyl) benzoate in the C phase, showing the smectic tilt plane.

Scheme I. Synthesis and Some LC Properties of Compound **6**



alkoxypropyl-containing compounds. Also, the ferroelectric dipole should have the direction indicated by the arrow in Figure 2 (from − to +). Therefore, by convention[3,5] the polarization is predicted to have a positive sign. Finally, the key nonracemic epoxy alcohol synthetic intermediates are, of course, now readily available as either enantiomer by Sharpless epoxidation.[6]

A synthesis of epoxide-containing LCs of the type shown in Figure 2 was therefore developed, as shown in Scheme I. Nonracemic (2*S*,3*S*) epoxy alcohol **2** was prepared according to Sharpless[6] and was shown to be 86% enantiometrically enriched by GC analysis of the derived α-methoxy-α-(trifluoromethyl)phenylacetic acid (MTPA) esters.[7] The crucial coupling of alcohol **2** with *p*-(benzyloxy)phenol[8] (**1**) could not be accomplished in our hands by any of the standard Williamson etherification techniques via the tosylate. However, direct Mitsunobu coupling[9] of the epoxy alcohol with the phenol proceeded efficiently, affording the benzyl ether **3** in good yield. Hydrogenolysis of the benzyl ehter gave phenol **4**, which was then coupled in a straightforward manner with *p*-(decyloxy)benzoyl chloride (**5**)[10] to give the target liquid crystal material **6** in 95% yield.[11]

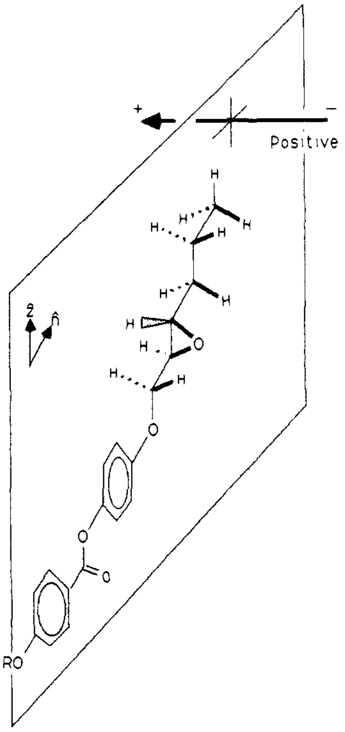


Figure 2. Proposed preferred orientation of compounds of type **6** in the C* phase. The direction of the experimentally observed polarization is indicated in the Figure.

The phase sequence and observed polarization of compound **6** are also given in the scheme. As indicated, compound **6** possesses a stable C* phase between 75 and 80 °C and a monotropic C* phase down to about 60 °C. Also, the sign of *P* is positive as predicted, and the magnitude of *P* is found to be 45 nC/cm^2.[12] This value is enhanced relative to the 2-methylbutyl and 2-alkoxypropyl analogues by a factor of 25 and 3.5, respectively. Assuming a density of 0.8 gm/cm^3 for compound **6**, the effective dipole per molecule contributing to *P* is about 0.1 D/molecule. While it is not certain that the epoxide moiety is in fact the major molecular dipole contributing to *P*, we feel that the data are best rationalized by utilizing the simple model described herein.

If compound **6** were perfectly ordered as shown in Figure 2, as in a crystalline solid, a ferroelectric polarization density of about (2 D/molecule) × (1/ϵ) would be expected, where ϵ is a dielectric constant close in magnitude to the mean dielectric constant of the medium,[3] which for these materials should be about ϵ = 3. A polarization density of about $^2/_3$ D/molecule would therefore be expected for a perfectly ordered material according to the model. The observed polarization is thus attenuated by about a factor of 7 relative to the expected maximum value. In the ferroelectric liquid crystal phase there are several mechanisms for this attenuation, including conformational averaging and rotational motions. At this stage the origins of the observed attenuation for compound **6** are not known.

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(5) Clark, N. A.; Lagerwall, S. T. *Ferroelectrics* **1984**, *59*, 25–67.

(6) (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5976. (b) Hill, J. G.; Sharpless, K. B. *Org. Synth.* **1984**, *63*, 66–78.

(7) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543–2549.

(8) *p*-(Benzyloxy)phenol was purchased from Kodak and recrystallized once from ethanol.

(9) Mitsunobu, O. *Synthesis* **1981**, 1.

(10) *p*-(Decyloxy)benzoic acid was obtained from Frinton Laboratories and was purified by recrystallization from ethanol prior to use. The corresponding acid chloride was prepared by treatment of the acid with Aldrich Gold Label oxalyl chloride in benzene.

(11) The material used in the liquid crystal characterizations must be very pure. The product, clean by NMR, obtained from the coupling reaction was purified by a multiple flash chromatography and by several recrystalizations. The sample utilized to obtain the data shown in the scheme had an isotropic–smectic A coexistence range of less than 2 °C.

(12) The magnitude of *P* was measured by integration of the dynamic current response on reversing the applied electric field: (a) Martinot-Lagarde, Ph. *J. Phys.* **1976**, *37*, C-3, 129. (b) Martinot-Lagarde, Ph. *J. Phys. Lett.* **1977**, *38*, L-17.