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Phase Diagram and Preparation of CE2 Enantiomers

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The synthesis of (L)-(−)-4″-(2-methylbutylphenyl) 4′-(2-methylbutyl)-4-biphenylcarboxylate (CE2) and related chiral liquid crystals has been discussed by Gray and McDonnell. We present here the first synthesis of the *enantiomer* of CE2 and we use it to measure the temperature-chirality phase diagram of the blue phases of CE2. This diagram is compared with that obtained using the CE2 "racemate" containing nonenantiomeric optical isomers of CE2. The synthesis of (R)-(+)-2-methylbutan-1-ol which has been developed will be broadly useful for the preparation of other chiral liquid crystals having optically active (R)-2-methylbutyl sidechains.

I. INTRODUCTION

The use of chiral liquid crystals for both technological and purely scientific ends is well established.[1] In either application it is often desirable to choose a particular chiral material on the basis of its nonchiral, i.e. chemical, properties—for example one might seek a mixing compatibility with a certain nematic material, or perhaps a particular transition temperature. Nevertheless, once these non-chiral properties have been specified and the desired chiral material has

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been chosen, it is still possible *experimentally to adjust* its actual chirality. This can be accomplished either by mixing the chiral material with its enantiomer or, equivalently, by mixing it with its racemate. Either method will reduce the chirality of the final chiral mixture with a minimal effect on the chemical properties. In the language of the Landau theory of phase transitions[2] we may say that the coefficient of the chiral term in the Landau free energy is altered while the remaining coefficients remain essentially unchanged.

This ability experimentally to adjust chirality alone has been exploited in recent investigations of the so-called *blue phases*—BPI, BPII, and BPIII—which appear near the clearing temperature of tightly twisted chiral liquid crystals.[3] Theoretical studies[4,5] show that blue phases are brought about by chirality alone; experimentally, phase diagrams in which temperature is plotted against chirality, where chirality is adjusted using chiral-racemic mixtures, generally bear out this assertion.[6–8]

One of the most tightly twisted commercially available[9] chiral liquid crystals is 4″-(2-methylbutylphenyl) 4′-(2-methylbutyl)-4-biphenyl-carboxylate (CE2), whose molecules consist essentially of a rigid backbone with two (S)-2-methylbutyl endchains. Because of its high chirality, CE2 has pronounced blue phases and has already been studied[8,11] or recommended for study[12] in several papers. Unfortunately, the presence of *two* asymmetric carbons makes the synthesis of racemic CE2 difficult, and the only "racemic" CE2 available to date has contained equal amounts of the four isomers (R, R), (S, S), (R, S) and (S, R). Whether this material gives the same results as the true CE2 racemate is therefore open to question.

In the first part of this paper we discuss the synthesis of CE2R, the (R, R) form of CE2. [Our notation will henceforth be: CE2R is the (R, R) enantiomer synthesized in our laboratory; CE2S is the (S, S) enantiomer obtained from BDH; and CE2* is the "racemate" containing nonenantiomeric isomers.] The second part of the paper addresses the question of whether the CE2R/CE2S racemate behaves similar to CE2*. We accomplish this by measuring the CE2R/CE2S temperature-concentration phase diagram and we compare it to the CE2S/CE2* phase diagram. Although there are some quantitative differences, the two diagrams are qualitatively the same. We believe the new techniques developed for this synthesis will be useful for preparation of other liquid crystals having optically active 2-methylbutyl endchains, and for preparing liquid crystals where there are two chiral endchains rather than only one.

II. SYNTHESIS

In Gray and McDonnell's original synthesis of CE2S,[10] both of the 2-methylbutyl sidechains were derived from commercially available (S)-(−)-2-methylbutan-1-ol. The first obstacle to the synthesis of CE2R was therefore the unavailability of (R)-(+)-2-methylbutan-1-ol from a commercial source.[13] Commercially available (S)-(+)-methyl 3-hydroxy-2-methylpropionate (2) was converted to the (R)-(+) alcohol in five steps, as shown in Scheme 1.

Scheme 1.   Synthesis of (R)-(+)-2-Methylbutan-1-ol
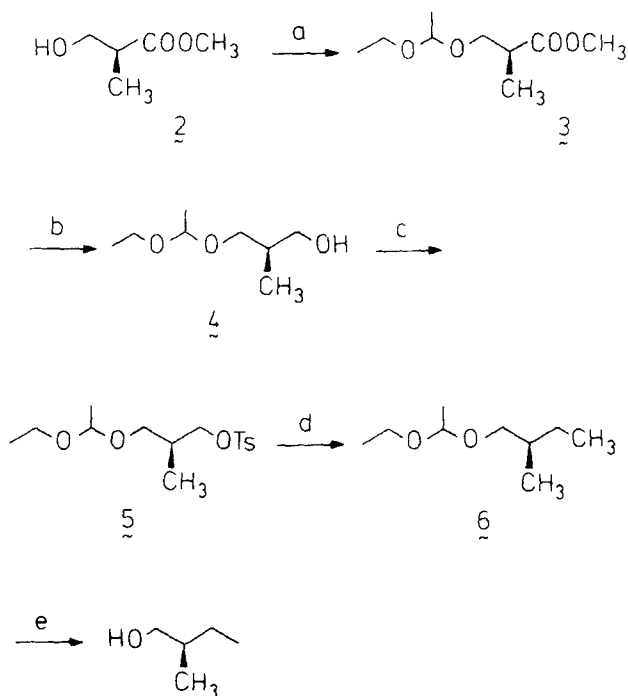
SCHEME 1

(a) ethyl vinyl ether, pyridinium tosylate, dichloromethane
(b) lithium aluminum hydride, ether, − 78°C
(c) tosyl chloride, triethylamine, dichloromethane
(d) lithium dimethylcuprate, ether, 0°C
(e) aq. tetrahydrofuran, pyridinium tosylate, reflux

The synthesis of (R)-(+)-2-methylbutan-1-ol was accomplished in 68% overall yield from commercially available hydroxyester. This process is efficient and is amenable to making large quantities. For the next step, which involves coupling the chiral alkyl fragment to each of the aromatic moieties, Gray and McDonnell used a ferric chloride-catalyzed method. Unfortunately, the yields of this method are rather modest, which was probably acceptable in the original CE2S synthesis since the alcohol starting material was relatively cheap and commercially available. In our case, this method would result in unacceptable losses of the valuable (R)-(+) isomer, therefore the following alternative and more efficient coupling procedure was developed.

The major side reaction to be avoided during the transition metal-catalyzed coupling of alkyl organometallic reagents bearing a beta hydrogen atom with alkyl or aryl halides is the reductive elimination of a metal hydride. The carboxylic acid fragment of CE2R was there-
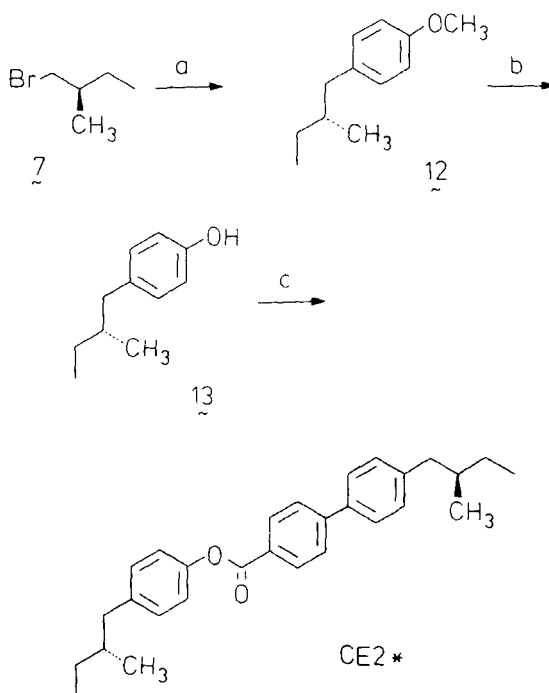
Scheme 2.   Synthesis of the Carboxylic Acid Fragment of CE2R
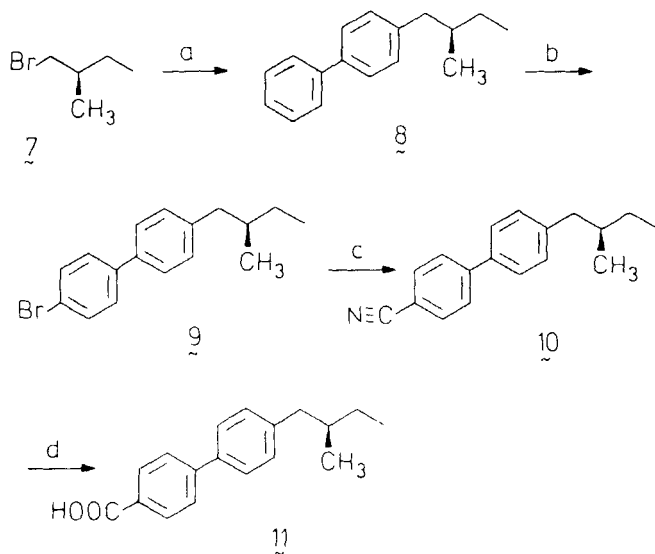
SCHEME 2

(a) magnesium, ether; 4-bromobiphenyl, PdCl$_2$(dppf)
(b) bromine, chloroform
(c) cuprous cyanide, N,N-dimethylformamide
(d) potassium hydroxide, 70% aq. ethanol

Scheme 3. Synthesis of the Phenol Fragment and Esterification to CE2R

SCHEME 3

(a) magnesium, ether; 4-bromoanisole, PdCl$_2$(dppf)
(b) aluminum, iodine, ether
(c) 11, pyridine, dicyclohexyl carbodiimide, tosic acid

fore constructed (Scheme 2) by coupling the Grignard reagent derived from 7 with 4-bromobiphenyl using PdCl$_2$(dppf),[14] a catalyst which is known to retard the reductive elimination of metal hydride. The yield for this coupling reaction was 74–75%. It is worth pointing out that this improved procedure can be used for the coupling of either enantiomer and should be considered the method of choice for the synthesis of both CE2R and CE2S.

The synthesis of the phenol fragment of CE2R is summarized in Scheme 3. 4-Bromoanisole was coupled with the Grignard reagent derived from 7 with catalytic PdCl$_2$(dppf) in 78% yield. The esterification of carboxylic acid 11 with phenol 13 was accomplished with dicyclohexyl carbodiimide in pyridine in the presence of p-toluene-

sulfonic acid catalyst in 69% yield. This concludes the enantiospecific total synthesis of CE2R from (R)-(+)-2-methylbutan-1-ol.

The optical purity of the (R)-(+)-2-methylbutan-1-ol which was used for the preparation of CE2R was >95% as determined by Mosher analysis. Expansion of the high-field region of the NMR spectrum of CE2R revealed no shoulders on any of the peaks, from which we conclude that the purity was >95%. We should note here that the NMR spectrum of the commercially obtained CE2S *did* exhibit shoulders on certain high-field peaks, which we speculate is due to the presence of (R, S) and/or (S, R) isomers.

A detailed description of this synthesis will be published elsewhere.[15]

III. PHASE DIAGRAM

In order to measure the temperature-chirality phase diagram, CE2S was obtained from BDH[9] and used as received. The cholesteric-BPI transition temperatures were 113.8°C for CE2S and 116.0°C for CE2R, while the nematic-isotropic transition temperature was 119.04°C for the CE2S/CE2R racemate. The slight quantitative difference in the separate transition temperatures of CE2S and CE2R is consistent with the differing purities of the two materials mentioned previously and does not qualitatively affect our subsequent results.

Figure 1(a) shows the temperature-concentration phase diagram for CE2, where the concentration X represents the enantiomeric excess of CE2S in a mixture of CE2S and CE2R. [In terms of the masses M_S and M_R of CE2S and CE2R, $X = (M_S - M_R)/(M_S + M_R)$.] Phase boundaries were determined by observation of textures, using a Zeiss Universal microscope and either transmitted or reflected light. Specific methods for identifying the phase boundaries have been discussed elsewhere.[8] Since the reflected colors move from visible to ultraviolet as chirality is increased, we only report concentrations below X = 0.5. Also the R and L sides of the diagram are essentially mirror images of each other and so we have mainly developed the R side. Previous studies on chiral-racemic mixtures[8] have shown that the chirality $q = X/P_0$, where P_0 is the pitch of the pure chiral material. Thus the abscissa of Figure 1(a) is also proportional to the chirality.

In order to facilitate comparison of Figure 1(a) with the diagram derived from the CE2* "racemate," the data of Figure 1(a) are replotted in Figure 1(b) where the ordinate has been changed to T– T_{iso}. Figure 1(b) now looks similar to Figure 2, the temperature-concentration phase diagram using the CE2* "racemate." In Figure
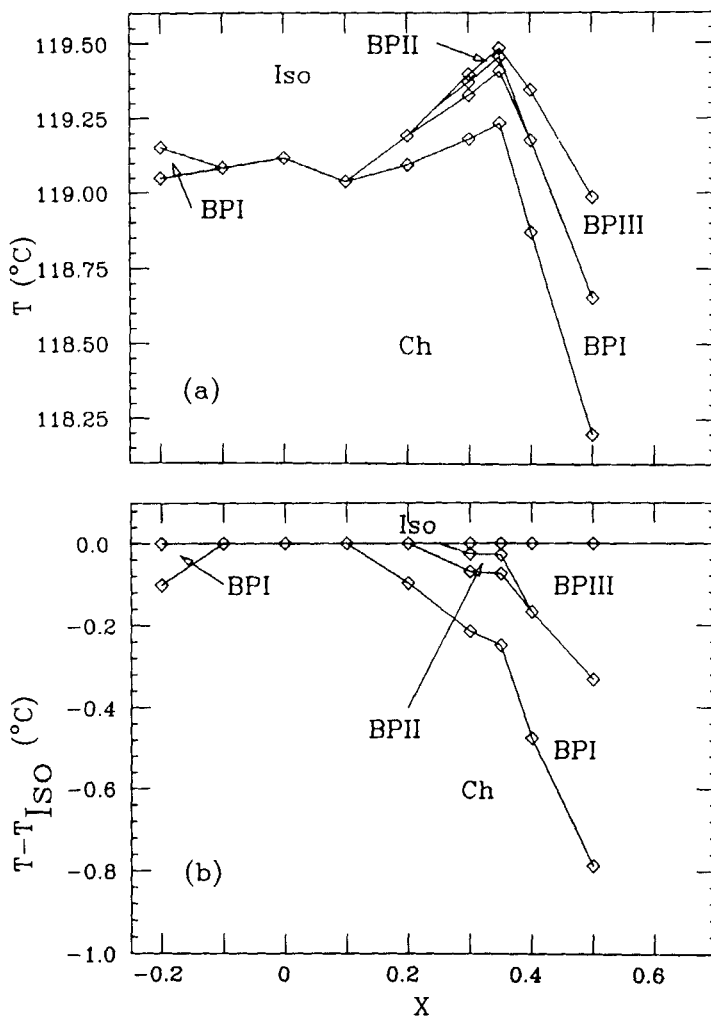
FIGURE 1   Phase diagrams showing blue phase transition temperatures versus X, the enantiomeric excess of CE2S in CE2R. BPI, BPII, BPIII are blue phases, Ch is cholesteric, and Iso is isotropic phase. (a) Absolute temperature; (b) Temperature relative to T_{Iso}, the isotropic transition temperature.

2, X is the mole fraction of CE2S in CE2*; it plays essentially the same role as X in Figure 1. Qualitatively the two sets of data are very similar in that the blue phases appear at about the same concentrations and only BPI and BPIII survive at high temperature. In Figure 1(a), however, the isotropic transition temperature increases by about
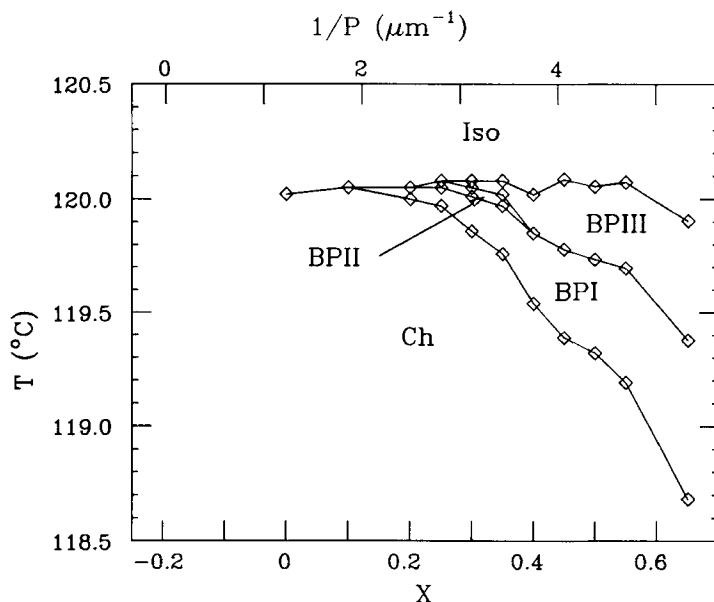
FIGURE 2   Phase diagram showing blue phase transition temperatures. Here X is the mole fraction of CE2S in "racemic" CE2*.

0.4° C before decreasing to the lower temperature of the pure CE2S material. In Figure 2, as a result of the presence of non-enantiomeric isomers, the isotropic transition temperature is essentially constant.

IV. CONCLUSIONS

We have outlined a procedure for synthesizing CE2R which is generally applicable to constructing any liquid crystal possessing a rigid backbone and either one or two chiral 2-methylbutyl endchains. Mixing this material with its enantiomer, CE2S, allows the chirality of the resulting mixture to be adjusted and we have presented the temperature-chirality phase diagram in the blue phase temperature region. In order to see if the features of the blue phases are excessively dependent on the details of the particular chemical system, we have compared this diagram with a similar one in which CE2S is mixed with the "racemate" containing *all four* possible stereoisomers of CE2. Although some quantitative differences are evident, the qualitative features of the two diagrams are the same. This result is con-

sistent with previous measurements[8] in which phase diagrams of different blue phase materials were revealed to have the same topology.

Acknowledgments

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