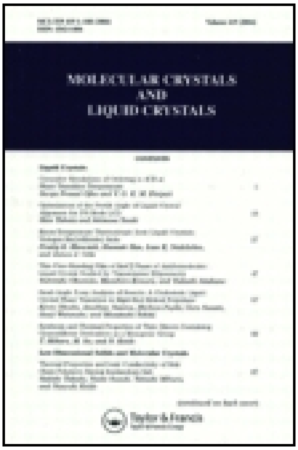


Molecular Crystals and Liquid Crystals
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gmcl16

Preparation of Liquid Crystal Intermediates: 4-Substituted Alkoxybenzenes

Mary E. Neubert [a] , S. J. Laskos Jr. [a b] , L. J. Maurer [a c] , L. T. Carlino [a d] & J. P. Ferrato [a]

[a] Liquid Crystal Institute, Kent State University, Kent, Ohio, 44242
[b] Liquid Crystal Displays, Beechwood, Ohio
[c] Teledyne Monarch Rubber, Hartville, Ohio
[d] Hewlett Packard, Palo Alto, California

To cite this article: Mary E. Neubert , S. J. Laskos Jr. , L. J. Maurer , L. T. Carlino & J. P. Ferrato (1978): Preparation of Liquid Crystal Intermediates: 4-Substituted Alkoxybenzenes, Molecular Crystals and Liquid Crystals, 44:3-4, 197-210

To link to this article: http://dx.doi.org/10.1080/00268947808084980

Mol. Cryst. Liq. Cryst., 1978, Vol. 44, pp. 197–210

Printed in Holland

Preparation of Liquid Crystal Intermediates: 4-Substituted Alkoxybenzenes†

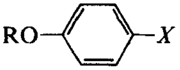
MARY E. NEUBERT, S. J. LASKOS, JR.,‡ L. J. MAURER,‡
L. T. CARLINO,§ and J. P. FERRATO
Liquid Crystal Institute, Kent State University, Kent, Ohio 44242

(*Received June 7, 1977*)

Improvements in the O-alkylation of 4-substituted phenols with alkyl bromides in the presence of base by using anhydrous conditions has led to better methods for the preparation of 4-substituted alkoxybenzenes in which the substituent is either an aldehyde or a protected functional group. The protected groups can be benzyloxy, acetamido and carboxylic acid methyl ester which are easily converted to hydroxy, amino and acid chloride groups. A mixture of *N*,*N*-dimethylformamide and benzene containing molecular sieves and sodium hydroxide as the base along with an azeotropic distillation provides the necessary anhydrous conditions to avoid hydrolysis of the protecting groups. A variety of mesomorphic compounds such as 4,4′-disubstituted phenylbenzoates, phenylthiobenzoates, benzylideneamino (Schiff's bases) compounds and azoxybenzenes in which at least one of the terminal substituents is an alkoxy group can be prepared from these 4-substituted alkoxybenzenes.

INTRODUCTION

4-Substituted Alkoxybenzenes of the type **1** are on interest as starting materials in the preparation of a



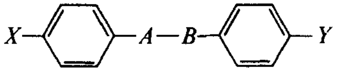
R = alkyl chain

X			
OH	**1a**	COCl	**1c**
CHO	**1b**	NH_2	**1d**

1

[†] Presented in part at the Sixth International Liquid Crystal Conference, Kent, Ohio, 1976.
[‡] Present address: Liquid Crystal Displays, Beechwood, Ohio.
[‡] Present address: Teledyne Monarch Rubber, Hartville, Ohio.
[§] Present address: Hewlett Packard, Palo Alto, California.

variety of mesomorphic compounds such as those of type **2**



2

in which A–B is a functional group such as ester, thiolester, anil (Schiffs base) or azoxy and *X* and/or *Y* is an alkoxy group. Since a homologous series is often needed in the study of mesomorphic properties, methods for preparing 4-substituted alkoxybenzenes **1** which involve as few reactions with as high of yields as possible and with the capability of being performed easily on a 0.5–1.0 molar scale are highly desirable. This need for good synthetic procedures became even more apparent when we decided to prepare several of the above mesogenic compounds containing terminal perdeuterated alkoxy chains.[1]

We have developed a general method for synthesizing these intermediates through the use of an anhydrous alkylation of 4-substituted phenols with alkyl bromides in the presence of sodium hydroxide. The anhydrous conditions make it possible to alkylate phenols containing water sensitive protected functional groups as the 4-substituent which then can be easily converted to a functional group useful in the preparation of mesomorphic compounds.

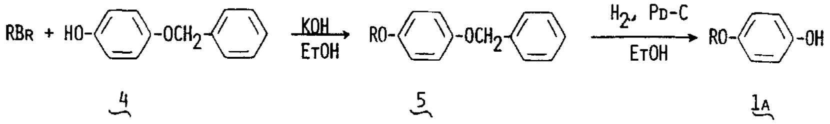
SYNTHESIS

X = OH (1a)

A variety of methods for preparing 4-alkoxyphenols are available in the literature but the most commonly used one involves a Williamson type alkylation of hydroquinone (scheme 1).[2,3] In our earliest use of this method

SCHEME 1

for the synthesis of the phenols, we isolated a mixture of the desired phenol **1a**, the diether **3** and hydroquinone.[4] Complete separation of these compounds to obtain pure phenol could be achieved only by column chromatography; an effective but time-consuming method on a large scale. Initially, however, we preferred this method over one suggested to us by Klanderman[5] in which the commercially available 4-benzyloxyphenol **4** could be alkylated and the resulting diether **5** cleaved by hydrogenolysis to



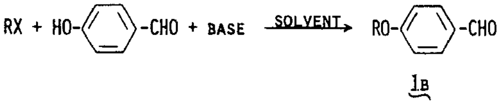
SCHEME 2

the phenol **1a** (scheme 2). The low solubility of the diether **5** in ethanol (particularly with the larger *R* groups) made it difficult to hydrogenate large enough quantities at any one time in a typical 500 ml Parr apparatus bottle. An attempt to use tetrahydrofuran as the solvent gave no hydrogenolysis and we were unable to obtain good results with an acidic cleavage of the benzyl ether.

This problem has now been resolved by maintaining the temperature of the hydrogenolysis at *ca.* 73° which permits *ca.* 25 g of most of the diethers tried to remain dissolved in 200 ml of ethanol. Somewhat more dilute solutions had to be used with chain lengths longer than C_{10}. However, as long as a solution was maintained, reduction was usually fairly rapid so that it was relatively easy to do a number of reductions and combine the crude products before recrystallization in order to obtain a large quantity of material. This, we found to be less time-consuming and much simpler than the earlier method but the alkylation of hydroquinone can still be a useful procedure if hydrogenation equipment is not available. A typical example of the new procedure is given in the experimental section. Unlike the other O-alkylations reported in this paper, alkylation of 4-benzyloxyphenol **4** with alkyl bromides can be done successfully in ethanol in high yields. Data for the phenols, benzyl ethers and some of the diethers we isolated earlier are given in Table I.

X = CHO (1b)

4-Alkoxybenzaldehydes **1b** have been prepared primarily by the alkylation of 4-hydroxybenzaldehyde under basic conditions and using a variety of halides and solvents (scheme 3). The range of yields obtained using these methods makes it difficult to choose a general procedure; the yields often depend on the chain length of R as well as the reagents used. The problem is to use a solvent which will dissolve both the phenolic salt and the alkyl



SCHEME 3

TABLE I

Data for 4-alkoxyphenols

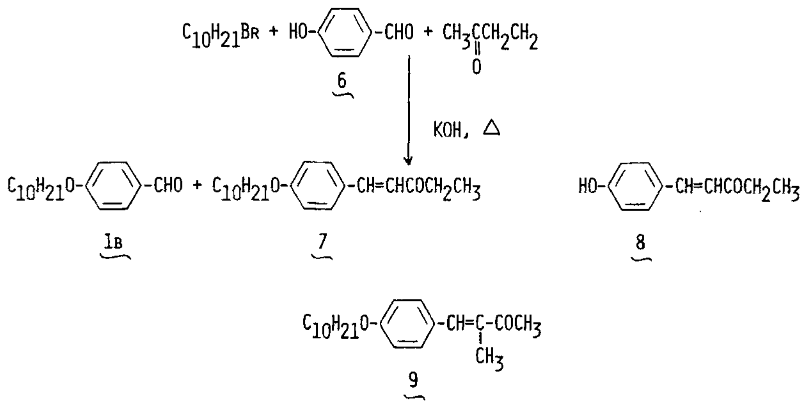
	5		**1a**		**3**	
R	m.p. (°C)	purified % yield	m.p. (°C)[a]	purified % yield	m.p. (°C)[b]	% yield
C_2	—	—	65–67	25.0	73–75	27.8
C_3	—	—	55–57	—	52–54	18.0
C_4	—	—	64–65	—	—	—
C_5	—	—	51.5–53	50.3	38–43 (impure)	19.8
C_6	—	—	48	32.8	59	30.9
	64–66	75–77	46–47.5	91.3	—	—
C_7	—	—	60–61	30.5	55–60	48.6
	73–74	76.7	64–65	73.5	—	—
C_8	—	—	63–64	27.0	50.52	36.4
	72–73	69.8	62–63	70.2	—	—
C_{10}	78–80	71.2	70–73	95.4	—	—
C_{12}	80–83	69.2	80–82	88.0	—	—
C_{14}	84–86	78.2	85–86	96.7	—	—
C_{16}	87–89	77.7	90–92	93.6	—	—
C_{18}	88–92	83.9	89–92	75.3	—	—

[a] The C_2 and C_4 homologs were commercially available at the time this work was done and the C_6 and C_7 compounds have become available more recently. However, some of these materials seem to be contaminated with hydroquinone (Ref. 6). The C_2 through C_8 homologs are reported in the literature. Our melting points compare favorably with those found in Ref. 2.

[b] Melting points for the C_2 and C_5 homologs are given in Ref. 2.

halide. Ethanol being a good protic as well as a polar solvent, works reasonably well only with the reactive alkyl iodides. Cyclohexanone has been used more successfully with the alkyl bromides.[7]

Although methyl ethyl ketone would not usually be chosen as a solvent in such a reaction because of the possibility that an Aldol type condensation might occur in the presence of strong base, Hsu obtained the aldehydes **1b** in yields as high as *ca.* 80% which suggested that this was not actually a serious problem.[8] However, we have found that an Aldol condensation often does occur between either the starting hydroxyaldehyde **6** or the resulting alkoxyaldehyde **1b** ($R = C_{10}$) (or perhaps both) with methyl ethyl ketone to give the olefin **7** after dehydration (scheme 4). This, of course, gives lower yields of the desired aldehyde **1b**. The presence of a quartet at 2.55δ for the ethyl methylene protons and the absence of olefinic and acetyl methyl protons in the nmr spectrum confirms that this material is the expected olefin **7** and not its isomer **9**. An ir spectrum of the phenolic material isolated from the basic extract suggested that both phenols **6** and **8** were present which tends to support the concept that at least some condensation occurs

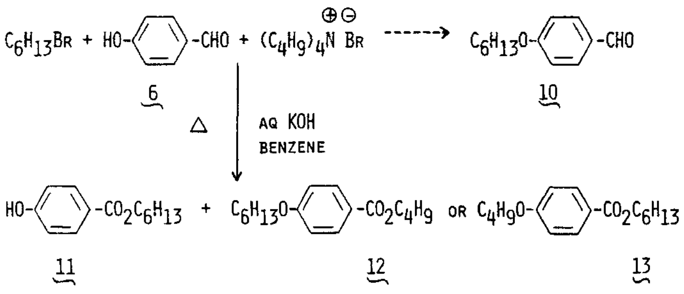


SCHEME 4

on the starting aldehyde. However, this was not investigated further since it was obvious that this method for preparing the aldehydes **1b** is not as good as was originally thought.

Deitrich and Steiger were able to obtain the aldehydes **1b** in good yields by alkylating 4-hydroxybenzaldehyde with alkyl bromides in the polar but aprotic solvent, dimethylformamide[9] (scheme 3). We were able to confirm their work obtaining the aldehydes in yields of *ca.* 76% when the solvent was properly purified and the reaction kept anhydrous.

The main disadvantage to this method is that the time consumed to remove the higher boiling solvent is greater, especially on a large-scale reaction. Since phase-transfer catalysis has recently been used in the alkylation of alcohols[10, 11] and of thiophenols[12], it seemed that the use of a two phase system would dissolve all the reactants but yet allow for the isolation of the product from a low boiling solvent. Consequently, several attempts were made to alkylate 4-hydroxybenzaldehyde with *n*-hexyl bromide using phase-transfer catalysis conditions (scheme 5). Unfortunately, this was a poor



SCHEME 5

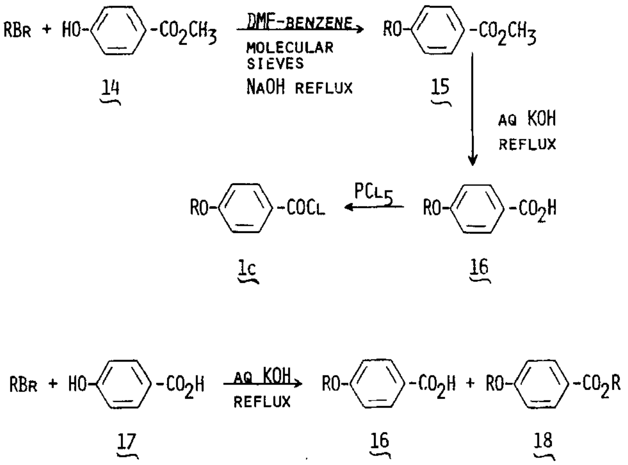
choice since aromatic aldehydes can undergo oxidation in the presence of aqueous base to acids. A typical example is the Cannizzaro reaction. Our results indicate that the aldehyde was oxidized to the acid and then esterified by either the hexyl bromide or the tetrabutylammonium bromide. Quaternary ammonium salts have been used to esterify acids as well as to alkylate phenols.[13] Instead of the desired aldehyde **10**, a mixture of the esters **11** and **12** and/or **13** was isolated. The ester **11** was separated from the latter by column chromatography and their structures determined by nmr and mass spectral data. However, this did not differentiate between the two isomeric esters **12** and **13** and no further attempt was made to do so.

Although the removal of dimethylformamide from the reaction mixture is an inconvenience in the use of the alkylation method of Dietrich and Steiger, it remains our method of choice for preparing the 4-alkoxybenzaldehydes, **1a**. As shown below, it also has proved to be a useful procedure, in a modified form, for the alkylation of 4-substituted phenols which contain substituents that are readily hydrolyzed under aqueous basic conditions.

X = COCl (**1c**)

In the alkylation method of Dietrich and Steiger, anhydrous conditions are maintained by using benzene as a co-solvent to azeotrope any water present into a Dean–Stark trap. Although we found this procedure adequate for the preparation of 4-alkoxybenzaldehydes **1a**, it did not prevent the hydrolysis of the water sensitive groups such as the ester and amide groups. This was achieved, however, by adding molecular sieves to the rection mixture. In this manner, 4-hydroxybenzoic acid methyl ester, **14**, was alkylated to form the ether **15** in yields of *ca.* 88% (scheme 6). The crude ester was pure enough to be hydrolyzed to the acid **16** and converted to the desired acid chloride **1c** without purification.

Although this method involves an additional step compared to the commonly used alkylation of 4-hydroxybenzoic acid **17**,[14,15] we feel that it offers a better approach, particularly in the preparation of perdeuterated alkoxybenzoyl chlorides. Alkylation of the acid **17** using one equivalent of the alkyl bromide gives a mixture of the two acids **16** and **17** along with the ester **18**. The composition of this mixture is dependent on the chain length of R and the reaction conditions but it is usually difficult to separate cleanly the desired acid **16** from the other components and to isolate it in a good yield. Often this problem is avoided by using an excess of the bromide so that a mixture of only the alkoxybenzoic acid **16** and the ester **17** is formed. This mixture is then hydrolyzed to yield only the acid **16**. Although at times useful, this approach is wasteful of the alkyl bromide which becomes a critical factor when using an expensive bromide.

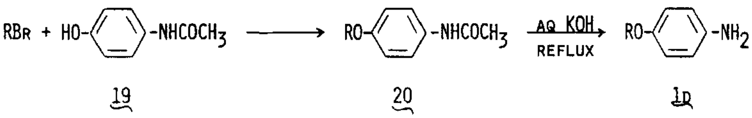


SCHEME 6

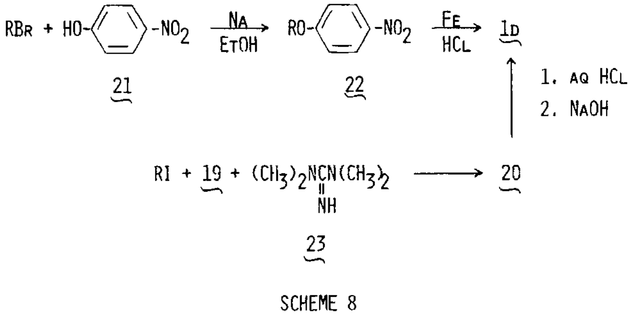
This method also avoids the use of metallic sodium usually used in the alkylation of 4-hydroxybenzoates.[16] The use of sodium hydroxide rather than potassium hydroxide is preferred since the commercial sodium salt does not contain the water of hydration found in the potassium salt. We prefer to use phosphorous pentachloride instead of thionyl chloride to form the acid chloride because it gave a cleaner reaction and avoided the decomposition and/or polymerization of the acid chloride which sometimes occurred during distillation when thionyl chloride was used.

$X = NH_2$ (1d)

The same procedure used to alkylate the ester **14** was used to alkylate 4-hydroxyacetanilide, **19** to give the ether **20** which on hydrolysis formed the aniline **1d** in good yields (scheme 7). This is an improvement over the previously used methods in which 4-nitrophenol **21** is alkylated and reduced to the aniline **1d** (scheme 8)[17] or the use of tetramethylguanidine **23** as the base in the alkylation of 4-hydroxyacetanilide **19** with an alkyl iodide followed by acid hydrolysis.[18]



SCHEME 7



SCHEME 8

CONCLUSIONS

We have developed improved methods for the synthesis of 4-substituted alkoxybenzenes in which the substituent is a hydroxy, aldehyde, acid chloride or amino group. The primary method used involves the o-alkylation of phenols substituted in the 4-position containing either these functional groups or a protected version of them with alkyl bromides under basic and anhydrous conditions with the use of dimethylformamide as the solvent. These 4-substituted alkoxybenzenes are useful intermediates for the preparation of a variety of mesomorphic compounds.

EXPERIMENTAL SECTION

Materials

All starting materials which were commercially available were used without purification. Dimethylformamide (DMF) and benzene were dried over Linde #4A molecular sieves, $\frac{1}{16}''$ pellets or 8 × 12 beads overnight, distilled at atmospheric pressure (bp of the DMF fraction used was 151–152°) and stored over molecular sieves before use. All other solvents were used without purification except 2-butanone which was purified by distillation. Organic extracts were dried over anhyd. Na_2SO_4 followed by molecular sieves.

Experimental techniques

Melting points were determined in capillary tubes using a Hoover–Thomas instrument and are corrected. Tlc data were obtained using Analtech silica gel GF 2.5 × 10 cm Uniplates® (250 μ) with uv light and iodine as detectors. Davidson 60–200 mesh silica gel served as the adsorbent for column chromatography. A Perkin-Elmer model 700 (ir), Varian A-60 and EM-360 (nmr, armomatic protons assignments were based on comparison to literature data[19]), and Associated Electronics Industries Model MS-12 (mass spectra, 70 ev) instruments were used as analytical tools. Elemental analyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Michigan.

1-*Benzyloxy*-4-*n*-*octyloxybenzene*, **5** ($R = C_8H_{17}$) To a refluxing solution of 4-benzyloxyphenol (144.2 g, 0.720 moles) and KOH (50.5 g, 0.720 moles) in H_2O (181 ml) was added dropwise, a solution of *n*-octyl bromide (139.0 g, 0.720 moles) in abs EtOH (87 ml). Refluxing was continued for 4 hr after the addition was completed, the reaction mixture cooled in an ice bath and the resulting precipitate collected, washed with H_2O (4 × 300 ml) to remove any KBr and dissolved in $CHCl_3$ (1.2.1). This $CHCl_3$ solution was extracted with 10% aq KOH (2 × 1.4.1), washed with H_2O (3 × 1.4.1), dried, filtered and the solvent removed (Rotovap) to give 180.2 g (80.1%) of the crude product, mp 70–73°. Recrystallization from abs EtOH (700 ml) gave the purified diether **5** ($R = C_8H_{17}$): mp 72–73°; tlc ($CHCl_3$) showed one spot with $R_f = 0.70$ (starting material, $R_f = 0.11$); i.r. ($CHCl_3$) 1590 (weak Ar) and no OH at 3400 cm^{-1} (starting material OH in nujol); nmr ($CDCl_3$) $\delta 7.30$ (s, 5, benzyl Ar *H*), 6.79 (s, 4, diether Ar *H*), 4.91 (s, 2, Ar OCH_2 Ar), 3.83 (t, 2, $J = 6$Hz, Ar OCH_2 CH_2), and 2.18–0.62 (m, 15, C_7H_{15}) and mass spectrum m/e 312 (M^+).

4-*n*-*Octyloxyphenol* **1a** ($R = n\text{-}C_8H_{17}$) A solution of compound **5** ($R = C_8H_{17}$) (28.4 g, 91.0 mmoles) in abs EtOH (200 ml) at 73° was hydrogenated in a Parr apparatus (500 ml bottle fitted with a heating mantel and thermometer and containing 1–2 g 10% Pd-C (Englehard) at *ca.* 50 lb/in^2 of H_2 until no additional pressure drop occurred. An aliquot of the reduction solution was removed and tested by tlc to determine if complete hydrogenolysis had occurred. If so, the catalyst was filtered from the hot solution over Celite® on hard filter paper and the filtrate filtered again over hard paper to remove traces of carbon. The solvent was removed from the filtrate (Rotovap) to give 19.9 g (98.4%) of the crude product. This reaction was repeated four more times, the crude materials combined and recrystallized twice from ligroine (60–90°) to give 69.0 g (70.2%) of the phenol **1a** ($R = n\text{-}C_8H_{17}$): mp 62–63°; tlc ($CHCl_3$) showed one spot with $R_f = 0.14$ (starting material, $R_f = 0.69$), i.r. (Nujol) 3350 (OH) with no 1600 cm^{-1}; nmr ($CDCl_3$) $\delta 6.69$ (s, 4, Ar *H*), 5.65 (s, 1, O*H*), 3.83 (t, $J = 6$Hz, 2, Ar OCH_2) and 2.08–0.58 (m, 15, C_7H_{15}) and mass spectrum *m/e* (rel intensity) 222 (18.68 M^+) and 110 (100, M-C_8H_{16}).

Alkylation of 4-Hydroxybenzaldehyde in 2-Butanone with n-Bromodecane A mixture of 4-hydroxybenzaldehyde (122 g, 1.00 mole), *n*-bromodecane (221 g, 1.00 mole) and KOH (67.1 g, 1.00 mole) in 2-butanone (480 ml) was stirred with refluxing for 17 hr. The reaction mixture was cooled to rt, extracted with H_2O (2 × 1 l) 5% aq KOH (2 × 1 l) dried, filtered and the solvent removed (Rotovap) to give 175.5 g of crude product: tlc ($CHCl_3$) showed 3 spots with R_f = 0.13, 0.26 and 0.68 (starting material, R_f = 0.12) and i.r. (film) 2740 (weak, C*H*O), 1690, 1660 shoulder (C=O), 1600 (Ar, conjugated C=C) and 1580 (Ar) cm^{-1}. Distillation at 178° (0.95 mm) gave 91.0 g (34.7%) of a pale yellow liquid which showed two tlc spots with R_f = 0.00 and 0.36 (CH_2Cl_2). Redistillation at 235° (12.0 mm) gave 67.8 g (25.9%) of 4-*n*-decyloxybenzaldehyde, **1b** ($R = C_{10}H_{21}$): tlc (CH_2Cl_2) showed one spot with R_f = 0.36; i.r. (film) 2740 (C*H*O), 1690 (C=O) and 1600, 1580 cm^{-1} (Ar).

The pot residues from both distillations crystallized to a moist solid on cooling. These were combined and washed with petroleum ether (30–60°) to give 15.8 g (5.0%) of a pale yellow solid which was recrystalized from methanol to give 12.3 g of material. A small amount was recrystallized again to give an analytical sample of 1-[4-decyloxyphenol] 1-penten-3-one, **7**: mp 69–71.5°; tlc (benzene) showed one spot with R_f = 0.12 (aldehyde, R_f = 0.31); i.r. ($CHCl_3$) 1660 intense peak with shoulder at 1680 (C=O) 1600 much more intense than 1660 cm^{-1} (Ar + conjugated C=C?) and no OH or aldehyde CH absorptions; nmr (CCl_4) δ7.35 (d, 1, J = 8.5 Hz, Ar *H* *ortho* to olefin), 7.30 (d, 1, J = 16 Hz, *trans* CH=C*H*CHO), 6.73 (d, 2, J = 8.5 Hz, Ar *H* ortho to alkoxy group), 6.42 (d, 1, J = 16 Hz, *trans* ArC*H*=CH), 3.89 (t, 2, J = 6 Hz, ArCH_2), 2.52 (q, 2, J = 7 Hz, COCH_2-CH_3) and 2.1–0.65 (m, 22, C_9H_{19} + $COCH_2CH_3$); and mass spectrum *m*/*e* 316 (M^+).

Anal. Calcd for $C_{21}H_{32}O_2$: C, 79.69; H, 10.19. Found: C, 79.76: H, 10.12.

Removal of the solvent from the petroleum either filtrate gave 10.7 g of a yellow mixture of a solid and liquid. An i.r. spectrum (film) of this material showed a weak absorption at 2750 (C*H*O) and absorptions at 1660, 1600 and 1550 cm^{-1} but no hydroxyl absorption suggesting that this material is probably a mixture of the aldehyde **1b** ($R = C_{10}H_{21}$) and the olefin **7**.

The basic extract was acidified with concd HCl and the precipitate extracted into $CHCl_3$. The $CHCl_3$ layer was dried and the solvent removed (Rotovap) to give 6.7 g of a dark viscous liquid: tlc ($CHCl_3$) showed several polar components and i.r. (film) 3300 (intense, broad OH) 1690 (aldehyde C=O?), 1660–1640 doublet (C=O?) and 1600 cm^{-1} (Ar + conjugated (C=C). These data suggest that this material possibly contains the two phenols **11** and **14**.

4-n-Octyloxybenzyaldehyde, **1b** ($R = C_8H_{17}$) A solution of 4-hydroxybenzaldehyde (10.0 g, 80 mmoles) and KOH (4.5 g, 80 mmoles) in 120 ml of a 1 : 1 mixture of DMF-benzene was refluxed with a Dean-Stark trap until the refluxing solvent was no longer cloudy. To this refluxing solution was added dropwise *n*-octyl bromide (15.4 g, 80 mmoles) and refluxing continued for 6 hr. The insoluble solid was filtered from the cooled reaction mixture and the benzene removed from the filtrate by using a Rotovap connected to an aspirator followed by removal of the DMF with the use of vacuum pump. Distillation of the remaining liquid gave 14.9 g (75.5%) of the aldehyde **1b** ($R = C_8H_{17}$): bp 126° (0.17 mm), [lit.[8] bp 162–165 (2.3 mm)]; tlc ($CHCl_3$) showed one spot with $R_f = 0.50$ (starting material, $R_f = 0.09$); i.r. (film) 2750 (C*H*O), 1690 (intense, C=O), 1600, 1580 cm^{-1} (Ar) and no hydroxyl absorption; nmr (CCl_4) δ9.84 (s, 1, C*H*O), 7.69 (d, 2, $J = 8$ Hz, Ar *H ortho* to CHO), 6.84 (d, 2, $J = 8$ Hz, Ar *H ortho* to alkoxy), 3.91 (t, 2, $J = 6$ Hz, Ar OCH_2) and 2.02–0.70 (m, 15, C_7H_{15}) and mass spectrum *m/e* (% rel intensity) 234 (57.71, M^+), 123 (100), and 122 (89.14, HOC_6H_4-CHO).

Attempted phase transfer catalyzed alkylation of 4-Hydroxybenzaldehyde A mixture of 4-hydroxybenzaldehyde (10.0 g, 81.9 mmoles), *n*-hexyl bromide (13.5 g, 81.9 mmoles), KOH (4.59 g, 81.9 mmoles) and tetrabutylammonium bromide (26.4 g, 81.9 mmoles) in H_2O (50 ml) plus benzene (50 ml) was refluxed with stirring for 8 days. The organic layer was separated from the cooled reaction mixture, extracted with 5% aq KOH, washed with H_2O, dried, filtered and the solvent removed to give a brown liquid (30.0 g). Distillation of this liquid gave two fractions; one with a bp 75° (3.0 mm, 8.62 g)[20] and the second with a bp 174° (1.5 mm, 15.8 g). A 1.0 g sample of the second fraction was chromatographed on a column of 50 g of silica gel in ligroine (60–90°). Two major fractions were collected using $CHCl_3$ as the eluent. The analytical data for the first fraction (464.9 mg): tlc (benzene) showed one spot with $R_f = 0.55$ (4-*n*-pentyloxybenzyaldehyde, $R_f = 0.41$); i.r. (film) 1710 (C=O) and no hydroxyl absorptions: nmr ($CDCl_3$, EM-360) δ8.08 (d, 2, $J = 4.5$ Hz, Ar *H ortho* to CO_2R), 6.97 (d, 2, $J = 4.5$ Hz Ar *H ortho* to OR), 4.34–3.78 (m, 4, OCH_2) and 2.13–0.78 (m, 18, C_5H_{11} and C_3H_7) and mass spectrum *m/e* 277 suggests that this material is either 4-*n*-hexyloxy-*n*-butylbenzoate **12** or 4-*n*-butyloxy-*n*-hexylbenzoate **13** or a mixture of both. Analytical data for the second fraction (308.0 mg): tlc (benzene) showed a major spot with $R_f = 0.08$ and a minor spot with $R = 0.12$; i.r. (film) 3350 (strong, OH), 1705 (C=O, shoulder) and 1680 (broad, strong C=O); nmr ($CDCl_3$, EM-360) δ8.03 (d, 2, $J = 4.5$ Hz, Ar *H ortho* to CO_2R), 7.64 (broad s, 1, O*H*), 7.00 (δ, 2, J = 4.5 Hz, Ar *H ortho* to OH), 4.39

(t, 2, $J = 2.5$ Hz, OCH_2) and 2.3–0.32 (m, 11, C_5H_{11}); and mass spectrum m/e 222 suggests that this material is primarily 4-hydroxy-*n*-hexylbenzoate, **11**. The weight of the isolated alkoxy ester represents 46.0% of the total 15.8 g mixture and the phenolic ester 32.6% or yields of 29.5% and 30.0% respectively.

4-n-Heptyloxybenzoic acid methyl ester, **15** ($R = n\text{-}C_7H_{15}$) A mixture of 4-hydroxybenzoic acid methyl ester (152 g, 1.00 mole) and NaOH (40 g, 1.0 mole) in a 1 : 1 mixture of DMF-benzene (1.51) containing molecular sieves (200 g) was refluxed using a Dean-Stark trap. When the refluxing vapors were no longer cloudy, *n*-heptyl bromide (179 g, 1.00 mole) was added and refluxing continued for an additional 6 hr. The reaction mixture was processed in the same manner as done in the preparation of compound **1b** (C_8H_{17}) to give a solid. This was dissolved in Et_2O (500 ml), extracted with 5% aq KOH (300 ml) and washed with H_2O (2 × 500 ml). The ether layer was dried, filtered and the solvent removed to give 220 g (88%) of a colorless solid. This was recrystalized from abs EtOH to give 203 g (81.0%) of 4-*n*-heptyloxybenzoic acid methyl ester, **15** ($R = n\text{-}C_7H_{15}$): mp 41–44, i.r. ($CHCl_3$), 1700 (CO_2Me) and 1600 cm^{-1} (Ar) with no hydroxyl absorption; nmr (CCl_4) δ7.83 (d, 2, $J = 8$ Hz, Ar *H ortho* to CO_2Me), 6.75 (d, 2, $J = 8$ Hz, Ar *H ortho* to alkoxy), 3.90 (t, 2, $J = 5.5$ Hz, $ArCH_2$), 3.79 (s superimposed on 3.90t, 3, CO_2CH_3) and 2.10–0.68 (m, 13, C_6H_{13}) and mass spectrum *m/e* 250 (M^+, 27.3%) and 152 (base peak).

4-n-Heptyloxybenzoic acid, **16** ($R = n\text{-}C_7H_{15}$) A mixture of compound **15** ($R = n\text{-}C_7H_{15}$) (200 g, 0.80 mole), NaOH (128 g, 3.20 moles) in a mixture of EtOH (640 ml) and H_2O (400 ml) was refluxed for 4.5 hr. The reaction mixture was poured into H_2O (3.1), cooled and made acidic with concd HCl. The resulting precipitate was collected, washed with H_2O and dried to give 214 g (quant) of the crude product. This was dissolved in Et_2O (3.1), extracted with H_2O (2 × 1 1), dried, filtered and the Et_2O removed on a Rotovap until crystallization began. The solid was collected, washed with hexane and dried to give 154 g (81.0%) of the acid, **16** ($R = n\text{-}C_7H_{15}$): transition temperatures 93–94° ($C \rightarrow S_C$), 101–102° ($S_C \rightarrow N$) and 150–151° ($N \rightarrow I$) [lit[21] 92° ($C \rightarrow S_C$), 98° ($S_C \rightarrow N$) and 146° ($N \rightarrow I$)]: tlc ($CHCl_3$) showed one spot with $R_f = 0.07$ (starting material, $R_f = 0.59$) and i.r. ($CHCl_3$) 3200–2500 (acid OH), 1680 (acid C=O) and 1600 cm^{-1} (Ar).

4-n-Heptyloxybenzyl chloride, **1c** ($R = n\text{-}C_7H_{15}$) A mixture of the acid **16** ($R = n\text{-}C_7H_{15}$) (180 g, 0.76 mole) and PCl_5 (158 g, 0.76 mole) was stirred at rt until a pale yellow liquid was formed. After refluxing this soln for 1 hr, the $POCl_3$ was removed by distillation and the remaining liquid distilled at 135°

(0.2 mm) to give 189 g (97.0%) of the acid chloride, **1c** ($R = n\text{-}C_7H_{15}$): i.r. (film) 1740, 1760 (COCl doublet) and 1600, 1570 cm^{-1} (Ar); and nmr (CCl_4): δ7.91 (split d, 2, $J = 9$ and 2 Hz, Ar *H ortho* to COCl, 6.79 (split d, 2, $J = 9$ and 2Hz, Ar *H ortho* to alkoxy), 3.95 (t, 2, $J = 6$ Hz, Ar OCH_2) and 2.10–0.70 (m, 13, C_6H_{13}).

4-n-Heptyloxyacetanilide, **20** ($R = n\text{-}C_7H_{15}$) The same procedure used to prepare the ester **15** ($R = n\text{-}C_7H_{15}$) was employed to alkylate 4-hydroxyacetanilide (10.0 g, 66.2 mmoles) with *n*-heptyl bromide (11.8 g, 66.2 mmoles) in a 1 : 1 mixture of benzene-DMF (100 ml) with molecular sieves (13.2 g) and NaOH (2.64 g, 66.2 mmoles) to give a pink solid. This material was dissolved in $CHCl_3$, extracted with 5% aq KOH, washed with H_2O, dried, filtered and the solvent removed (Rotovap) to give 14.7 g (88.8%) of the crude product. Recrystallization from ligroine (60–90°) containing a small amount of MeOH gave 13.6 g (82.2%) of the amide, **20** ($R = n\text{-}C_7H_{15}$): mp 87–88.5° [lit[18] mp 87–88°]; tlc (1 : 1 EtOAc-$CHCl_3$) showed one spot with $R_f = 0.47$ (starting material, $R_f = 0.25$); i.r. ($CHCl_3$) 3300 (NH), 1660 (amide C=O) and 1600 cm^{-1} (Ar); nmr ($CDCl_3$) δ7.90 (broad s, 1, N*H*), 7.38 (d, 2, $J = 9$ Hz, Ar *H ortho* to amide), 6.80 (d, 2, $J = 9$ Hz, Ar *H ortho* to alkoxy), 3.90 (t, 2, $J = 6$ Hz, OCH_2), 2.1 (s, 3, $COCH_3$) and 2.05–0.60 (m, 13, C_6H_{13}) and mass spectrum *m/e* 250 (M^+).

4-n-Heptyloxyaniline, 1d ($R = n\text{-}C_7H_{15}$) The amide **20** (12 g, 48 mmoles) was hydrolyzed using van der Veen's procedure.[22] Distillation of the liquid isolated from the reaction mixture at 160° (2 mm) [lit[18] bp 181–182 (10 mm)] gave 8.20 g (82.8%) of the aniline **1d** ($R = n\text{-}C_7H_{15}$) which crystallized on cooling: mp 46–49°; tlc ($CHCl_3$) showed one spot with $R_f = 0.15$ (starting material $R_f = 0.6$) i.r. ($CHCl_3$) 3450 and 3380 (NH_2), 1610 (Ar) and no amide C=O at 1660 cm^{-1}; nmr (CCl_4) 6.73–6.25 (m, 4, Ar *H*), 3.75 (t, 2, OCH_2), 3.14 (s, 2, NH_2) and 2.0–0.7 (m, 13, C_6H_{13}) and mass spectrum *m/e* 206 (M^+).

Acknowledgements

We are indebted to R. B. Moreland and T. A. Flood for A-60 nmr data, to R. D'Sidocky for EM-360 nmr data, to T. F. Longo, Jr. for mass spectral data, to P. Bose for his help in preparing 1-benzyloxy-4-*n*-decyloxybenzene and to the National Science Foundation for financial support under grant numbers GH-36164X and DMR-74-13173.

References and Notes

1. Mary E. Neubert, S. J. Laskos, Jr., and L. J. Maurer, Abst. I-8, Sixth International Liquid Crystal Conference, Kent, Ohio, August 1976.
2. E. Klarmann, L. W. Gatyas, and V. A. Shternov, *J. Am. Chem. Soc.*, **54**, 298 (1932).

3. R. R. Read and E. Miller, *J. Am. Chem. Soc.*, **50**, 1763 (1928); **54**, 1195 (1932).
4. M. E. Neubert, L. T. Carlino, R. D'Sidocky, and D. L. Fishel in *Proceedings of the Symposium on Ordered Fluids and Liquid Crystals*, Vol. 2, J. F. Johnson and R. S. Porter, Ed., Plenum Publishing Corp., New York, N.Y., 1974, p. 293.
5. B. H. Klanderman, Eastman Kodak Co., personal communication, 1974.
6. S. J. Laskos, Jr., Liquid Crystal Displays, personal communication, 1977.
7. G. W. Gray and B. Jones, *J. Chem. Soc.*, 1467 (1954).
8. Y. Hsu, Ph.D. Thesis, Kent State University, Kent, Ohio, 1972.
9. H. J. Dietrich and E. L. Steiger, *Mol. Cryst. Liq. Cryst.*, **16**, 263 (1972).
10. A. Merz, *Angew. Chem.*, **85**, 868 (1973); *Internat. Edit.*, **12**, 846 (1973).
11. H. H. Freedman and R. A. Dubois, *Tetrahedron Lett.*, 3251 (1975).
12. A. W. Herriott and D. Picker, *J. Am. Chem. Soc.*, **97**, 2345 (1975).
13. I. Gan, J. Korth, and B. Halpern, *Synthesis*, 494 (1973).
14. B. Jones, *J. Chem. Soc.*, 1874 (1935).
15. A. J. Herbert, *Trans. Faraday Soc.*, **63**, 555 (1967).
16. J. S. Pierce, J. M. Salsbury, and J. M. Frederickson, *J. Am. Chem. Soc.*, **64**, 1691 (1942).
17. J. Billard, J. C. Dubois, and A. Zann, *J. Phys. (Paris)*, **36**, C1-355 (1975).
18. T. R. Criswell, B. H. Klanderman, and D. C. Batesky, *Mol. Cryst. Liq. Cryst.*, **22**, 211 (1973).
19. J. Beeby, S. Sternhell, T. Hoffman-Ostenhof, E. Pretsch, and W. Simon, *Anal. Chem.*, **45**, 1571 (1973).
20. This material was not investigated further at the time but could be 4-*n*-hexyloxybenzyl alcohol; the other product of a Cannizzaro reaction on the aldehyde.
21. G. W. Gray and B. Jones, *J. Chem. Soc.*, 4179 (1953).
22. J. van der Veen, W. H. de Jeu, A. H. Grobben, and J. Boven, *Mol. Cryst. Liq. Cryst.*, **17**, 291 (1972).