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A CONVENIENT SYNTHESIS OF 6,6'-DIALKOXYTHIOINDIGO DYES SUITABLE FOR DOPING INTO A LIQUID CRYSTAL HOST

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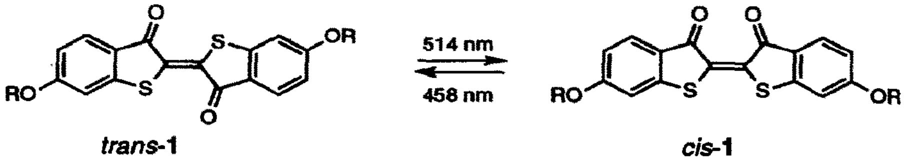
Abstract: A convenient synthesis of symmetrical 6,6'-di-*n*-alkoxythioindigo dyes suitable for doping into a liquid crystal host is reported, along with measurements of solubility limits for the dyes in nematic and smectic liquid crystals with broad temperature range.

Thioindigo dyes undergo reversible *cis-trans* isomerization upon irradiation at two different wavelengths in the visible region of the spectrum.[1] The photochromic properties of compounds such as 6,6'-diethoxythioindigo (**1a**) are particularly well suited to photoresponsive media applications since the absorption maxima for the *cis*- and *trans*-isomers of **1a** coincide almost exactly with two of the wavelengths available from an ionized argon laser (458 and 514.5 nm).[2] However, the low solubility of 6,6'-diethoxythioindigo in organic media has precluded further investigation of such compound as photochromic dopant in a liquid crystal host, which may form the basis for a liquid crystal display (LCD) that can be addressed photochemically.[3] Ross has reported that lengthening and/or branching of the alkoxy side-chain of **1** results in a significant increase in solubility in organic solvents;[4] Whitten subsequently demonstrated that 6,6'-di-*n*-hexyloxythioindigo (**1b**) can form organized monolayers either as a pure compound or mixed with another surfactant.[5] In order to determine systematically the effect of chain lengthening on the solubility of 6,6'-dialkoxythioindigo dyes in nematic and smectic liquid crystal hosts, we have developed a general synthetic route to **1** in six steps, starting from *bis*-(3-hydroxyphenyl)disulfide (**3**). The synthesis of 6,6'-di-*n*-hexyloxy-, 6,6'-di-*n*-octyloxy-, 6,6'-di-*n*-decyloxy- and 6,6'-di-*n*-dodecyloxythioindigo (**1b-e**) via this route, and measurements of the dye solubilities in three broad-range liquid crystal hosts are reported herein.

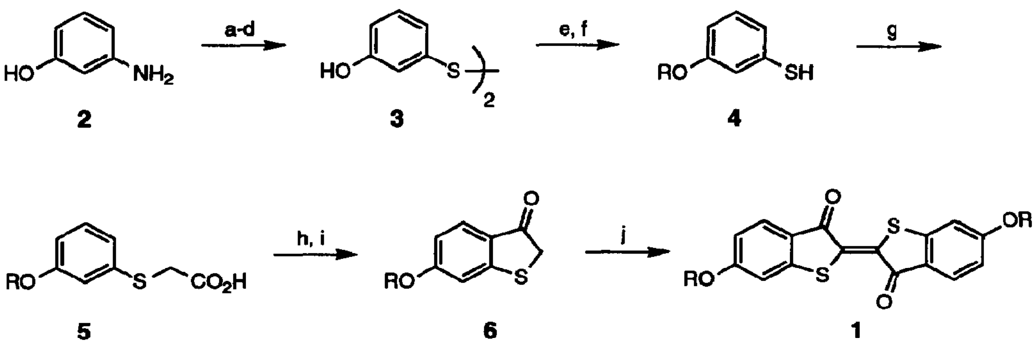


trans-**1** *cis*-**1**

a, R = C_2H_5; **b**, R = n-C_6H_{13}; **c**, R = n-C_8H_{17}; **d**, R = n-$C_{10}H_{21}$; **e**, R = n-$C_{12}H_{25}$

The reaction conditions described in the original synthesis of 6,6'-dimethoxythioindigo by Friedlaender proved unsuitable to the preparation of analogues with longer alkyl chains.[6] Our synthetic approach to compounds such as **1b-e** , which is summarized in Scheme I, is based in part on an adaptation of a more recent synthesis of branched 5,5'-dialkylthioindigo dyes by Meier and Lüttke.[7] The synthesis begins by dialkylation of *bis*-(3-hydroxyphenyl)disulfide (**3**), a protected form of 3-hydroxythiophenol that can be obtained in gram quantities from 3-aminophenol (**2**) according to a known procedure.[8] The alkylated disulfides, obtained in 70-90% yield from **3**, are reduced with LiAlH$_4$ to give the corresponding 3-alkoxythiophenols **4b-e** (90-95% yield), which are then converted to the (*m*-alkoxyphenyl)thioacetic acids **5b-e** in 40-65% yield. The corresponding 6-alkoxy-2,3-dihydrobenzothiophen-3-ones **6b-e** are obtained in 46-62% yield via a Friedel-Crafts cyclization of the acid chlorides derived *in situ* from **5b-e**; formation of the other possible regioisomer could not detected by ^{1}H NMR. The regiochemical assignments were made based on the ^{1}H NMR spectra of the aromatic region of **6b-e**, and further confirmed by corresponding ^{1}H NMR data for **1b-e**.[9] Oxidation of **6b-e** with a large excess of potassium ferricyanide in refluxing EtOH typically gives the 6,6'-dialkoxythioindigo **1b-e** in 20-30% yield after purification by flash chromatography on silica gel using benzene as eluant. The compounds were further purified by recrystallization from benzene to give bright red crystalline solids that are readily soluble in benzene, chloroform, and even hexanes. This approach proved to be unsuitable for the synthesis of **1** with secondary alkoxy substituents as the Friedel-Crafts cyclization to **6** led to cleavage of the ether linkages. Further attempts at the cyclization of **5** using polyphosphoric acid also led to cleavage of secondary alkoxy substituents.[10]

Scheme I [a]



[a] Reagents: (a) NaNO$_2$, conc HCl, 5 °C; (b) KSC(S)OEt, 80 °C; (c) NaOH, 95% EtOH, reflux; (d) FeCl$_3$·9H$_2$O, EtOH, 25 °C; (e) C$_n$H$_{2n+1}$Br, K$_2$CO$_3$, acetone, reflux; (f) LiAlH$_4$, Et$_2$O, reflux; (g) i, ClCH$_2$CO$_2$Na, aq NaOH, N$_2$; ii, aq HCl; (h) SOCl$_2$; (i) AlCl$_3$, CS$_2$, 25 °C; (j) K$_3$Fe(CN)$_6$, EtOH.

As previously observed by Ross,[4] our work shows that increasing the length of the R group results in a significant lowering of the melting point of **1**, from 342 °C for **1a** to 180 °C for **1e**, as well as an increase in the solubility of the dye in organic solvents. Solubility limits were measured for compounds **1b-e** in three liquid crystal phases with broad temperature range using a Nikon Labophot-2 polarizing microscope fitted with an Instec HS1-i hot stage.[11] Two of the liquid crystalline solvents each exhibit a broad nematic phase (**M15**, 48 to 68 °C; **CCH2/4**, 25 to 58 °C); the third exhibits a broad smectic C phase ((±)-**MDB**, 35 to 70 °C), and is useful as a host in forming ferroelectric S_C* liquid crystal phases via doping with an optically active compound.[12] As shown in Table I, our results suggest that rod-like 6,6'-dialkoxythioindigo dopants are most compatible with a smectic liquid crystal host, which may be due in part to the planarity and rigidity of the thioindigo core.[13] The solubility of **1** in (±)-**MDB** was found to be a function of the alkoxy chain length, leveling off at R = $C_{10}H_{21}$ with a solubility limit of nearly 3 mol%. The thioindigo dyes were found to be significantly less soluble in the nematic hosts **M15** and **CCH2/4**, and virtually insoluble in 5-*n*-alkyl-2-(4-*n*-alkyloxyphenyl)pyrimidine nematic hosts.[14] These results strongly suggest that suitably substituted 6,6'-dialkoxythioindigo dyes can be used as photochromic dopants in a S_C liquid crystal host; dopant concentrations for such systems typically range from 1 to 10 mol%.[3] It is envisioned that 6,6'-dialkoxythioindigo dopants in which the side-chain R contains an asymmetric center may form the basis for a ferroelectric S_C* liquid crystal display that can be addressed photochemically.[15]

Table I. Solubility Limits for Compounds **1b-e** in Liquid Crystal Solvents

	Solubility limit (mol%)[b]			
Solvent[a]	**1b**	**1c**	**1d**	**1e**
(±)-**MDB**	1.4	2.0	2.8	2.5
M15	1.5	1.3	1.2	1.4
CCH2/4	1.1	1.0	1.0	1.2

[a] (±)-**MDB**: 4-[(±)-(4-methylhexyl)oxy]phenyl 4-(*n*-decyloxy)benzoate;[16] **M15**: 4'-(*n*-pentyloxy)-4-biphenylcarbonitrile;[17] **CCH2/4**: a 65/35 (by wt) mixture of *trans,trans*-4'-ethyl- and 4'-*n*-butyl-4-bicyclohexylcarbonitrile.[18]
[b] Error estimated at ± 0.4 mol%.

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   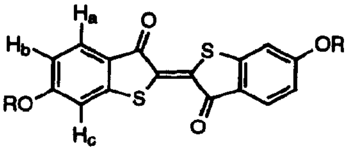

   Compound **1b**: mp 208-210 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.92 (t, 6H), 1.30-1.55 (m, 12H), 1.76-1.90 (m, 4H), 4.07 (t, 4H), 6.82 (dd, J = 2.1, 8.6 Hz, $2H_b$), 6.96 (d, J = 2.1 Hz, $2H_c$), 7.84 (d, J = 8.6 Hz, $2H_a$); MS (70 eV, EI) m/e 496 (M^+, 100), 412 (M-C_6H_{12}, 9), 328 (M-$C_{12}H_{24}$, 34).
   Anal. Calcd for $C_{28}H_{32}O_4S_2$: C, 67.71; H, 6.49; S, 12.91. Found: C, 67.48; H, 6.57; S, 12.79.
   Compound **1c**: mp 198-200 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.89 (t, 6H), 1.22-1.51 (m, 20H), 1.76-1.90 (m, 4H), 4.07 (t, 4H), 6.81 (dd, J = 2.1, 8.5 Hz, $2H_b$), 6.95 (d, J = 2.1 Hz, $2H_c$), 7.84 (d, J = 8.6 Hz, $2H_a$); MS (70 eV, EI) m/e 552 (M^+, 100), 440 (M–C_8H_{16}, 7), 328 (M–$C_{16}H_{32}$, 28).
   Anal. Calcd for $C_{32}H_{40}O_4S_2$: C, 69.53; H, 7.29; S, 11.60. Found: C, 69.78; H, 7.32; S, 11.63.
   Compound **1d**: mp 197-198 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.88 (t, 6H), 1.20-1.50 (m, 28H), 1.74-1.88 (m, 4H), 4.08 (t, 4H), 6.81 (dd, J = 2.1, 8.5 Hz, $2H_b$), 6.96 (d, J = 2.1 Hz, $2H_c$), 7.84 (d, J = 8.6 Hz, $2H_a$); MS (70 eV, EI) m/e 609 (M^+, 100), 468 (M–$C_{10}H_{20}$, 6), 328 (M–$C_{20}H_{40}$, 30).
   Anal. Calcd for $C_{36}H_{48}O_4S_2$: C, 71.01; H, 7.94; S, 10.53. Found: C, 70.92; H, 8.38; S, 10.35.
   Compound **1e**: mp 180-183 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.88 (t, 6H), 1.25-1.45 (m, 36H), 1.75-1.90 (m, 4H), 4.08 (t, 4H), 6.82 (dd, J = 2.1, 8.6 Hz, $2H_b$), 6.96 (d, J = 2.1 Hz, $2H_c$), 7.84 (d, J = 8.6 Hz, $2H_a$); MS (70 eV, EI) m/e 665 (M^+, 100), 497 (M–$C_{12}H_{24}$, 4), 328 (M–$C_{24}H_{48}$, 26).
   Anal. Calcd for $C_{40}H_{56}O_4S_2$: C, 72.24; H, 8.49; S, 9.64. Found: C, 72.47; H, 8.33; S, 9.39.
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