Synthesis and Characterization of Alkali-stable Bridged Phthalein Dyes and an Investigation of the Regiochemical Effects on their Near-IR Absorbance

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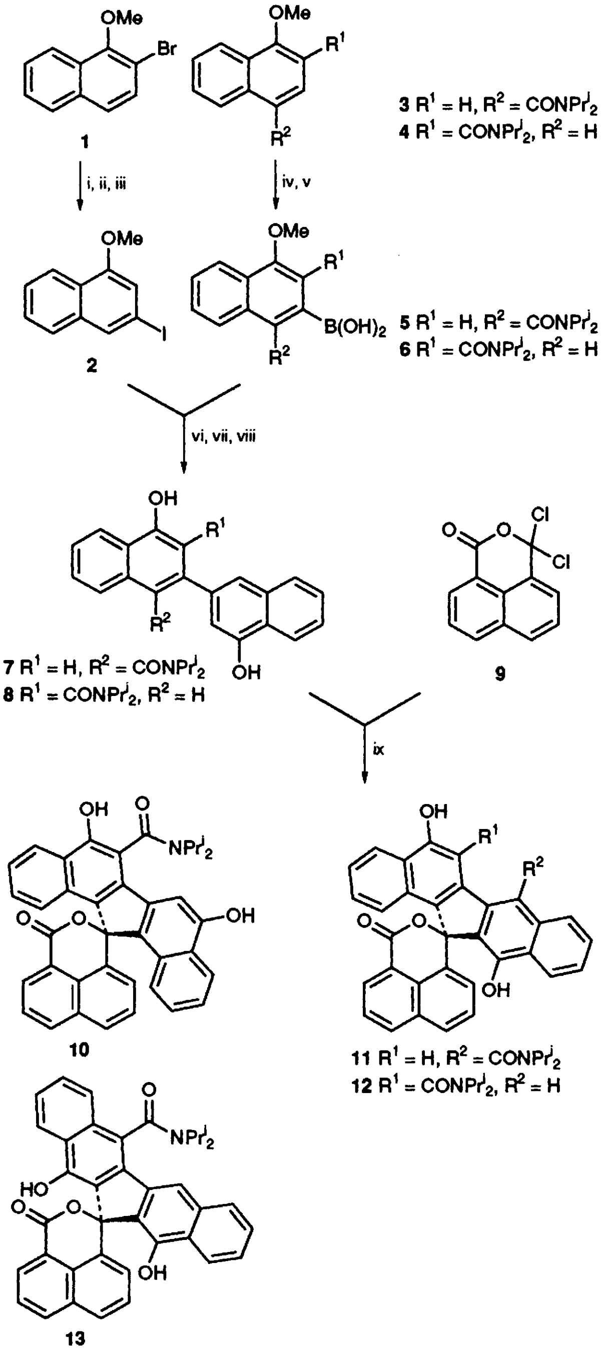
Novel bridged phthalein dyes substituted with a diisopropylamide *ortho* to the bridge are stable at high pH; with a chromogenically active auxochrome *ortho* to the *meso* carbon, a hypsochromic shift, band narrowing, and an increased molar absorptivity of the near-infrared absorbance are observed relative to the regioisomer in which the chromogenically active auxochrome is *para*.

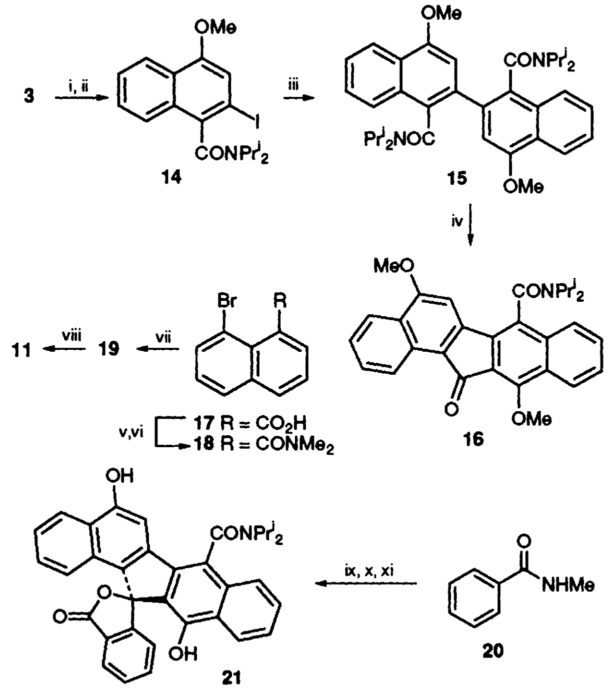
Bi- and tri-arylmethane dyes bridged *meta* to the *meso* carbon exhibit large bathochromic shifts relative to their unbridged counterparts.[1] We have discovered equally remarkable regiochemical effects on the near-IR absorbance properties of bridged phthalein dyes. These materials have utility for light filtration in photographic processes[2] and may have utility for analytical pH measurements that can be monitored by near-IR detection.[3] Additionally, the regiochemical results may prove to be applicable to other classes of arylmethane dyes.[4]



Scheme 1 *Reagents and conditions*: i, $NaNH_2$, NH_3, −35 °C, 51%; ii, $NaNO_2$, H_2SO_4, $MeCO_2H$, −10 °C; iii, NaI, I_2, 0 °C, 18%; iv, BuLi, TMEDA, THF, $B(OMe)_3$, −78 °C; v, HCl, water; vi, 1 : 1.4 equiv. **2** : **5** or **6** 5–10 mol% $Pd(PPh_3)_4$, PhMe, 2 mol l^{-1}, K_2CO_3, 80 °C, 4–8 h, 60–85%, vii, BCl_3, CH_2Cl_2, viii, BBr_3, CH_2Cl_2; ix, $AlCl_3$, *o*-dichlorobenzene, 0–25 °C, 72 h, 10–20%

A general synthetic route to prepare these materials (Scheme 1) relied upon directed metallation technology,[5] to prepare the boronic acids **5** and **6**, followed by their subsequent palladium-catalysed coupling[6] with 3-iodo-1-methoxynaphthalene to prepare the biaryls **7** and **8**. The subsequent aluminium chloride catalysed condensation of **7** and **8** with the dichloride **9**[7] proceeded in modest yields to afford mixtures of the regioisomeric naphthalein dyes, **10**, **12** (11 : 1 isolated), and **11**, **13** (6 : 1 isolated), which were separated and purified by column chromatography and recrystallized from tetrahydrofuran (THF)–MeCN.

Particularly diagnostic for the structural assignment of the individual regioisomers were the ^{13}C resonances for the carbon which correlates with the only singlet in the proton spectra (*ortho* to the bridge) by heteronuclear correlation spectroscopy (HETCOR). These resonances are well isolated and were observed at either δ 103 (**10**, **11**) or δ 113 (**12**, **13**)



Scheme 2 *Reagents and conditions*: i, BuLi, TMEDA, THF, Me_3SiCl, −78 °C; ii, ICl, CH_2Cl_2, 0 °C, 81%; iii, **6** (1.4 equiv.), 5 mol% $Pd(PPh_3)_4$, PhMe, 2 mol l^{-1} K_2CO_3, 80 °C, 8 h, 61%; iv, BuLi (3 equiv.), TMEDA, THF, 80%; v, $SOCl_2$; vi, $HNMe_2$, CH_2Cl_2, 0 °C; vii, 2 equiv. Bu^tLi, 5 : 1 ether–THF, −100 °C, add to **16**, 21%; viii, $BBr_3{\cdot}Me_2S$, tetrachloroethane, 70 °C, 24 h, 11%; ix, 2.2 equiv. BuLi, 25 °C, add to **16** (0.75 equiv.), −78 °C; x, $MeCO_2H$, 80 °C, 77%, 2 steps; xi, $BBr_3{\cdot}Me_2S$, xylene, 140 °C, 11 h, 65%

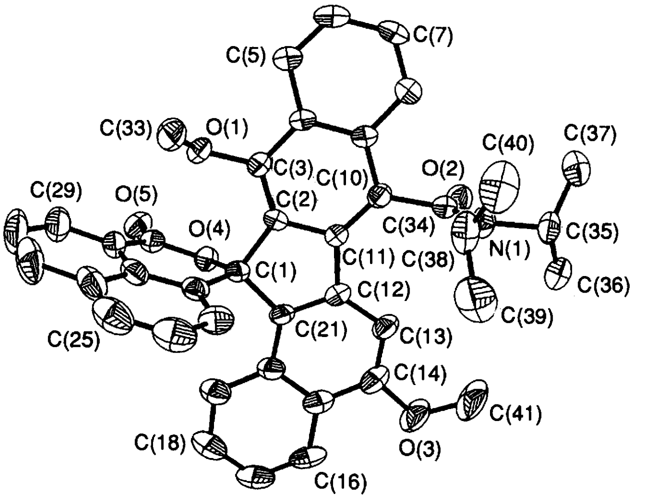


Fig. 1 Structure of **19**. Atoms represented as 50% probability ellipsoids. Hydrogen atoms omitted for clarity. Selected distances (Å) and torsional angles (°): C(1)–C(2) 1.534(26); C(1)–C(21) 1.511(26); C(2)–C(11) 1.436(26); C(11)–C(12) 1.481(26); C(12)–C(21) 1.376(27); C(10)–C(34) 1.527(20); O(1)–C(3) 1.380(23); O(3)–C(14) 1.361(28); C(13)–C(12)–C(11)–C(10) −2.2; C(12)–C(11)–C(10)–C(34) 5.3; N(1)–C(34)–C(10)–C(11) −97.9; O(2)–C(34)–C(10)–C(11) 84.5; C(10)–C(34)–N(1)–C(35) −174.4; C(10)–C(34)–N(1)–C(38) 3.9; C(34)–N(1)–C(38)–C(39) 115.4; C(34)–N(1)–C(38)–C(40) −118.7

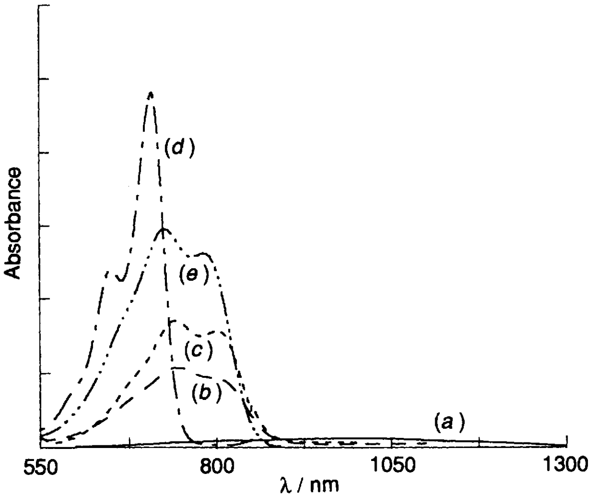
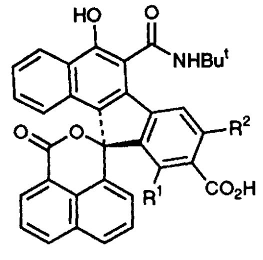


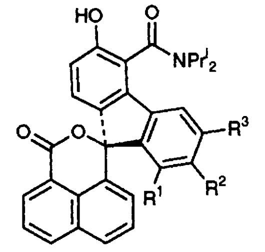
Fig. 2 Near-IR absorption spectra at 24 °C in mol l^{-1} NaOH–MeOH (4 : 1), λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}) of (*a*) **10** 1010 (666, 80 °C), (*b*) **11** 748 (5720) (7730, 80 °C not shown), (*c*) **12** 744 (9060), (*d*) **13** 708 (25 600), (e) **21** 721 (15 700).

which agrees with estimated chemical shifts of δ 112 and δ 117, respectively. Further confirmation for this relative assignment was obtained by the independent synthesis of **11** by a completely regioselective pathway (Scheme 2).

Upon reaction with excess of BuLi–tetramethylethylenediamine (TMEDA) at low temperatures, the symmetrical binaphthalene **15**, cleanly underwent regiospecific ring-closure to form the unsymmetrical fluorenone **16**. The unstable *peri*-metallated intermediate derived from **18** was immediately condensed with **16** to give the protected intermediate **19**. The final demethylation to liberate **11** was unusually difficult but could be accomplished with the boron tribromide–dimethyl sulfide complex ($BBr_3{\cdot}Me_2S$) with careful control of the reaction temperature. Cleavage of the methyl ethers from the



22 R^1 = H, R^2 = OH
23 R^1 = OH, R^2 = H



24 R^1 - R^2 = [CH]$_4$, R^3 = OH
25 R^1 = OH, R^2 - R^3 = [CH]$_4$

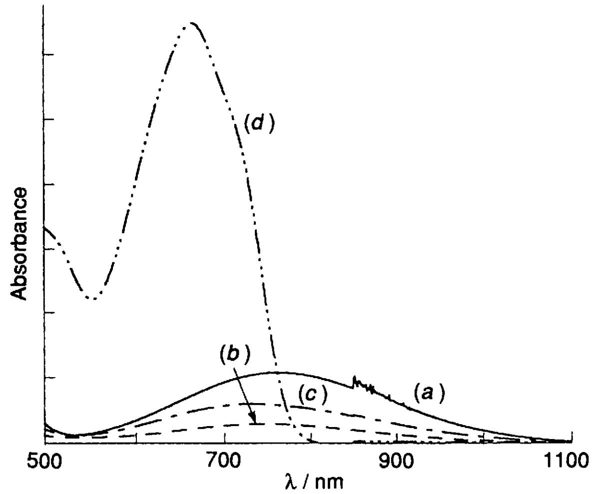


Fig. 3 Near-IR absorption spectra at 24 °C in 2 mol l^{-1} NaOH–MeOH (4 : 1), λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}) of (*a*) **22** 759 (1670), (*b*) **23** 747 (450), (*c*) **24** 731 (930), (*d*) **25** 664 (10 100)

analogous phthalide was more facile and good yields of **21** could be obtained while minimizing competing decomposition.

Unambiguous structural assignment was obtained by X-ray structure analysis of **19**† (Fig. 1) in which the disposition of the methoxy groups is clearly seen. An additional noteworthy structural feature is the orientation of the diisopropylamide. The plane formed by the amide carbonyl and nitrogen is perpendicular to the plane formed by the chromophore ring system. Additionally, the four methyls of the isopropyl groups appear as distinct doublets in the ^1H NMR spectra which is indicative of restricted rotation. This geometry results in enhanced alkali stability for these compounds in their coloured form at high pH (2 mol l^{-1} NaOH) by sterically blocking the *meso* carbon to nucleophilic attack by hydroxide. Especially noteworthy is the base stability of **21**. Analogues in which the diisopropylamide is replaced by a proton completely decolorize in seconds at high pH; hence the bridged compounds are inherently more prone to hydroxide attack than their unbridged counterparts.[8]

As seen in the absorption spectra for these materials (Fig. 2), progressively permuting the structure from one in which both hydroxy groups are *para* to the *meso* carbon, **10**, to those in which one hydroxy is *ortho* and one is *para*, **11** and **12**, and finally to a structure in which both are *ortho*, **13**, results in a narrowing of the principal absorption bandwidth, a hypsochromic shift in the absorption maximum, and an increased molar absorptivity. Two of the compounds (**10**, **12**) exhibited positive thermochromic behaviour. In contrast, the phthalide analogue of **12**, compound **21**, is not thermochromic.

These absorption effects are not seen in all cases (Fig. 3).

For example, for compound **23**, although the phenolic hydroxy group is *ortho* to the *meso* carbon, the long-wavelength absorbance is not significantly affected relative to **22** in which both hydroxy groups are *para*. In this case, based on resonance energy arguments, the phenolic hydroxy group is not chromogenically active.[9] In contrast, for the indicator dye **25**, the absorbance changes are observed relative to **24**, since the chromogenically active naphtholic hydroxy is *ortho* to the *meso* carbon.

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Footnotes

† Single crystals for X-ray analysis were obtained by slow evaporation of a solution of **19** in chloroform.

Crystal data for **19**: $C_{41}H_{35}NO_5 \cdot 1.97CHCl_3$, $M = 856.6$, monoclinic, $a = 17.920(1)$, $b = 15.810(1)$, $c = 14.649(1)$ Å, $\beta = 96.33(1)°$, $U = 4125(4)$ Å^3, space group $P2_1/c$ (no. 14), $Z = 4$, $D_c = 1.38$ g cm^{-3}, $F(000) = 1767$, colourless plates 0.18 × 0.40 × 0.50 mm, μ(Cu-Kα) = 4.124 mm^{-1}. Data were collected on a Enraf-Nonius CAD-4 diffractometer in the range $3.0° < \theta < 136.3°$, ω scan mode with scan width = $0.50 + 0.142\tan\theta$, scan speed 1.65–8.24° min^{-1}, graphite monochromated Cu-Kα radiation ($\lambda = 1.54184$ Å); 8151 measured, 7454 unique reflections, giving 4234 data with $F_o > 4\sigma(F_o)$. Lorentz–polarization, linear decay corrections and absorption correction *via* empirical psi scan method were applied. The structure was determined by direct methods and refined by full-matrix least-squares analysis. All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were introduced in idealized positions and added to the structure factor calculations. One solvent molecule was disordered and was refined as three chloroform molecules with their site occupancy factors refined. The final R values were: $R = 0.089$, $R_w = 0.097$. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

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