Dichroic Dyestuffs. A Synthesis of Dialkyl-8-amino-1,4,5-trihydroxy- and 1,4,5,8-Tetrahydroxy-anthraquinones.

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A general synthesis of 2,6- and 3,6-dialkyl-8-amino-1,4,5-trihydroxy- and the related tetrahydroxy-quinones was developed from 2- and 3-alkyl-1,4,5-trihydroxyanthraquinones *via* nitration, reduction, aldol condensation, and hydrolysis. The utility of these as dichroic dyestuffs was estimated by measurement of the order parameter, *S*.

There have been a variety of approaches adopted for the production of coloured liquid crystal displays. One uses dichroic dye molecules which, when dissolved in certain liquid crystals tend to orientate in the same direction as the molecules of the liquid crystal. In one device[1] the molecules are aligned with their long axes parallel to the director of a helical cholesteric phase. This director is, in turn, parallel to the plane surfaces of a cell which appears coloured. When a voltage is applied across the cell the molecules reorientate parallel to the field and the cell appears to be colourless. An indication of the usefulness of dyes for such applications is given by the *order parameter*,

$$S = \frac{A_1 - A_2}{A_1 + 2A_2}$$

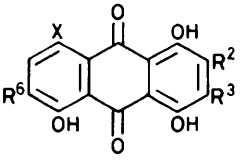
where A is the absorbance of the dye in a nematic liquid crystal, parallel (A_1) and perpendicular (A_2) to the director of aligned films. A variety of structurally diverse dyestuffs have been used,[2] including anthraquinones. In the last case the order parameter is improved by lengthening the molecules along the major axis. In order to further examine how S varies with structure we have developed a general synthesis of the title quinones and synthesised specific compounds within these classes.

Initially we attempted to apply the aldol condensations, which had been successfully used by Marschalk[3] and by Lewis,[4] for the alkylation of leuco-1,4,5,8-tetrahydroxyanthraquinone (**36**). Limited success was achieved using the latter as condensation of (**36**) with propanal and piperidinium acetate in Pr^{i}OH gave a 1:1 mixture of compounds (**1**) and (**2**). Reduction of this mixture and repetition of the alkylation procedure gave a mixture of the quinones (**2**), (**3**), and (**4**). The dialkylated quinones (**3**) and (**4**) could not be separated but ^{1}H n.m.r. spectroscopy supported their formulation as the 2,6- and 2,7-dipropyl compounds. Owing to the difficulty in purifying compounds (**1**) and (**36**) and their low solubility in organic solvents this approach was not investigated further.

2-Alkyl-1,4,5-trihydroxyanthraquinones can be prepared by Marschalk condensation[5] or by nitronate addition[5] to the parent quinone. The 3-alkyl compounds are the predominant products in the Lewis condensation with leuco-5-hydroxy-quinizarin.[5] † Conversion of these compounds into the required dyestuffs necessitated alkylation at C-6 or C-7 and introduction of an OH or NH_2 group at C-8. An obvious solution to the latter problem is *via* nitration. Classical methods of nitration were unsatisfactory when applied to the propyl quinone (**11**). However, reaction with $Cu(NO_2)_2$–CF_3CO_2H at 4 °C gave an 85% yield of the nitroquinone (**20**); use of an excess of $Cu(NO_2)_2$ gave the 3,8-dinitro derivative. When the nitro-compound (**20**) was submitted to the reaction conditions for the nitronate alkylation the only new product formed was the amino compound (**35**) (10%), identical to material obtained by catalytic hydrogenation of compound (**20**). When the nitro

† Quinizarin = 1,4-dihydroxyanthraquinone.

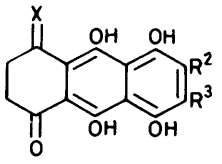
Table 1.



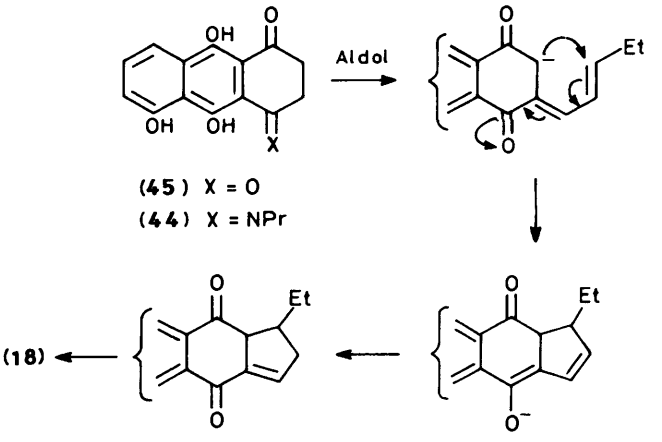
	R^2	R^3	R^6	X	Order parameter[a]
(1)	H	H	H	OH	
(2)	Pr	H	H	OH	
(3)	Pr	H	Pr	OH	0.62
(4)	H	Pr	Pr	OH	
(5)	Pr	H	Pentyl	OH	0.62
(6)	Hexyl	H	Hexyl	OH	0.64
(7)	H	Hex	Hexyl	OH	
(8)	$-CHEt(CH_2)_2-$		H	OH	0.57
(10)	H	H	H	H	
(11)	Pr	H	H	H	
(12)	H	Pr	H	H	
(13)	Hexyl	H	H	H	
(14)	H	Hexyl	H	H	
(15)	Bz	H	H	H	
	H	Bz	H	H	
(16)	$(CH_2)_5OH$	OH	H	H	
(17)	$-(CH_2)_2CHEt-$		H	H	
(18)	$-CHEt(CH_2)_2-$		H	H	
(19)	$-(CH_2)_5-$		H	H	0.57
(20)	Pr	H	H	NO_2	
(21)	H	Pr	H	NO_2	
(22)	Hexyl	H	H	NO_2	
(23)	H	Hexyl	H	NO_2	
(24)	$(CH_2)_5OH$	H	H	NO_2	
(25)	$-CHEt(CH_2)_2-$		H	NO_2	
(26)	Pr	H	Pr	NH_2	0.72
(27)	Pr	H	Pentyl	NH_2	0.70
(28)	Pr	H	Nonyl	NH_2	0.75
(29)	H	Pr	Pr	NH_2	0.71
(30)	Hexyl	H	Hexyl	NH_2	0.73
(31)	H	Hex	Hexyl	NH_2	
(32)	$(CH_2)_5OH$	H	Pr	NH_2	
(33)	$-CHEt(CH_2)_2-$		Pr	NH_2	0.65
(34)	Pr	H	Bz	NH_2	0.48
(35)	Pr	H	H	NH_2	0.67

[a] Measured in liquid crystal E43

Table 2.



Compd.	R_2	R_3	X
(**36**)	H	H	O
(**37**)	H	H	O
(**38**)	Pr	H	NH
(**39**)	H	Pr	NH
(**40**)	Hexyl	H	NH
(**41**)	H	Hexyl	NH
(**42**)	$-CHEt(CH_2)_2-$		NH
(**43**)	$(CH_2)_5OH$	H	NH



Scheme.

quinone (**20**) was reduced with Zn–AcOH a brown, polar product was isolated. Its ^1H n.m.r. spectrum [δ_H 16.5, 13.9, 11.3, 10.6 (all 1 H, s, exchangeable with ^2H_2O), 6.96 (1 H, s), 2.84 (4 H, m), 2.66 (2 H, t, *J* 7.5 Hz), 1.65 (2 H, m), and 0.98 (3 H, t, *J* 7.5 Hz)] suggested that the imino tautomer (**38**) was the major species present in solution. Condensation of this leuco-compound (**38**) with propanal in EtOH containing piperidinium acetate gave the dipropyl amino quinone (**26**) (55%). The 2,6-dipropyl structure was originally assigned from the δ_H of the two aromatic protons at 7.15 and 6.92, the latter being in accord with the H being *ortho* to an amino group. Support for this assignment came from the proof[6] that the *N*-propyl imine (**44**) condensed with propanal exclusively at the methylene α- to the carbonyl group.

The conversion of the amino group to hydroxyl followed the method developed by Marshall,[7] *i.e.* $Na_2S_2O_4$ reduction to the leuco-derivative and alkaline hydrolysis followed by aerial oxidation. We have found that use of Claisen's alkali rather than NaOH–water improves yields significantly.

With the development of this route a number of 2-and/or 3-alkyl-1,4,5-trihydroxyanthraquinones were prepared by Marschalk or Lewis condensations using leuco-5-hydroxyquinizarin (**45**). As described previously[5] condensation of compound (**45**) and 2-hydroxytetrahydropyran gave the 3-hydroxy-2-(5-hydroxypentyl)quinone (**16**) but, to our surprise, use of the standard conditions with hexanal and with benzaldehyde gave 1:1 mixtures of 2-and 3-substituted compounds (**13**) and (**14**) and (**15**) respectively; it may be that selective condensations are more sensitive to base and aldehyde concentrations than hitherto expected. The tetracycle (**19**) was prepared from the alcohol (**16**) by oxidation to the aldehyde (PCC), reduction to the leuco-intermediate and cyclisation ($Na_2S_2O_4$–NaOH). Condensation of pent-2-enal with (**45**) gave the tetracycle (**17**) under Lewis conditions; its structure followed from spectroscopic data and the demonstration that the analogous compound prepared from but-2-enal was the regioisomer indicated. The tetracycle is formed by an aldol condensation followed by Michael addition rather than the reverse (see Scheme). Lewis condensation with tetrahydropyran-2-ol was unsuccessful.

Application of the nitration–reduction–condensation route to these various 1,4,5-trihydroxyanthraquinones led to the compounds listed in the Table 1 with their order parameters. Unsurprisingly, nitration of the benzoylquinones (**15**) did not lead to clean 8-nitration.

Perusal of the order parameters in Table 1 allows some tentative conclusions to be drawn on the relationship of order parameters to structure in this class of dyes: (*a*) the 8-amino substituent is superior to an 8-hydroxy- group; (*b*) alkyl groups in both rings A and C are beneficial but there is no significant difference between 2,6- and 2,7-substitution; (*c*) between C-3, and C-9 the lengths of the alkane chains have no significant effects; (*d*) both benzyl substitution and ethyl cyclopentane annulation are inferior to alkane substituents.

Experimental

^1H N.m.r. spectra were measured at 300 MHz in CD_2Cl_2. U.v. and i.r. spectra were measured in $CHCl_3$.

Nitration of 1,4,5-*Trihydroxy*-2-*propylanthraquinone* (**11**).—The quinone (**2**) (1.329 g) was suspended in CF_3CO_2H (30 ml) and the mixture cooled to 0 °C. $Cu(NO_2)_2 \cdot 3H_2O$ (591 mg) was added to the stirred mixture and the temperature maintained below 5 °C. 5M-HCl was added to precipitate the red product which was filtered off, washed with water, and dried to give the red *nitroquinone* (**20**) (1.129 g), m.p. 148 °C (CH_2Cl_2) (Found: M^+, 343.0692. $C_{17}H_{13}NO_7$ requires *M*, 343.0692); δ_H 12.99, 12.71, 12.52 (all 1 H, s, exchanged with ^2H_2O) 7.71 (1 H, d, *J* 9 Hz), 7.40 (1 H, d, *J* 9 Hz), and 7.33 (1 H, s).

Reaction of the quinone (**2**) with 1.1 mol of $Cu(NO_2)_2 \cdot 3H_2O$ as above gave the purple 3,8-*dinitroquinone* (40%), m.p. 136 °C (Found: M^+, 388.0545. $C_{17}H_{12}N_2O_9$ requires *M*, 388.0545); δ_H 12.59 (2 H, s), 12.48 (1 H, s), 7.76 (1 H, d, *J* 9.6 Hz), and 7.52 (1 H, d, *J* 9.6 Hz).

The following mononitro compounds were prepared as above.

Compd.	Yield (%)	M.p. (°C)	M^+	*M*
(**21**)	70	163—165	343.0695	343.0692
(**22**) + (**23**)	90	115	385.1159	385.1161
(**25**)	78	181—182	369.0847	369.0848
(**24**)	65	139—141	381.1574	381.1576

Reduction of 1,4,5-*Trihydroxy*-8-*nitro*-2-*propylanthraquinone* (**20**).—The nitroquinone (**20**) (108 mg) was dissolved in CH_2Cl_2 (35 ml) and AcOH (3 ml) and Zn dust (*ca.* 2 g) were added. The mixture was stirred for 3 h when it was filtered, and the filtrate washed with water (3 × 50 ml), dried, and concentrated to give the brown *imino ketone* (**38**) (99 mg), m.p. 325 °C (decomp.) (Found: C, 64.0; H, 5.2; N, 4.3%; M^+, 315.1111. $C_{17}H_{17}NO_5$ requires C, 64.7; H, 5.4; N, 4.2%; *M*, 315.1107); δ_H 16.55, 13.88, 11.25, 10.59 (all 1 H, s, exchanged with ^2H_2O), 6.98 (1 H, s), 2.86 (4 H, br s), 2.67 (2 H, t, *J* 7.5 Hz), 1.66 (2 H, m), and 0.98 (3 H, t, *J* 7.5 Hz).

The following compounds were prepared in a similar way.

Compd.	Yield (%)	M.p. (°C)	M^+	M
(**39**)	95	310 (decomp.)	315.1111	315.1107
(**40**) + (**41**)	72	113—115	357.1577	357.1576
(**42**)	97	98—99	341.1250	341.1263
(**43**)	85	185—187	359.1371	359.1369

Alkylation of the Imino Ketone (**38**).—The imino compound (**38**) (125 mg) was suspended in EtOH (10 ml) under a N_2 atmosphere. After warming to 60 °C, propanal (360 mg) was added followed by piperidinium acetate (65 mg) in EtOH (1 ml). The reaction boiled under reflux for 3 h when it was cooled and acidified with 5M-HCl, and the precipitate filtered off, washed with water, and dried. Dry column chromatography [Silica HF_{254}; EtOAc–light petroleum (b.p. 40—60 °C) gradient elution] gave the purple *amine* (**26**) (77 mg), m.p. 190 °C (Found: C, 67.4; H, 5.6; N, 3.8%; M,$^+$ 355.1400. $C_{20}H_{21}O_5N$ requires C, 67.6; H, 5.9; N, 3.9%; M, 355.1420); δ_H 13.50, 13.44, 12.83 (all 1 H, s, exchanged with ^2H_2O), 7.13 (1 H, s), 6.92 (1 H, s), 2.70 (2 H, t, J 7.5 Hz), 2.67 (2 H, t, J 7.5 Hz), 1.70 (4 H, m), 1.01 (6 H, t, J 7.5 Hz); $\lambda_{max.}$ 525 (6 500), 559 (11 000), and 598 nm (11 000).

The following compounds were prepared by similar methods.

Compd.	Yield (%)	M.p. (°C)	M^+	M
(**27**)	57	158	383.1740	383.1733
(**28**)	51	155	439.2358	439.2358
(**29**)	58	148—151	355.1423	355.1420
(**30**) + (**31**)	38	145	439.2359	439.2359
(**32**)	11	169—171	399.1684	399.1682
(**33**)	65	139—141	381.1575	381.1576
(**34**)	33	187—189	403.1427	403.1420

1,4,5,8-*Tetrahydroxy*-2-*pentyl*-6-*propylanthraquinone* (**5**).—The amine (**27**) (30 mg) was dissolved in a solution of KOH (3.5 g), water (19 ml), and MeOH (15 ml), and $Na_2S_2O_4$ (1 g) was added. The solution, under a N_2 atmosphere, was boiled under reflux for 2 h while the colour changed from orange to blue. The cooled solution was aerated, acidified (3M-HCl), and extracted with CH_2Cl_2 (3 × 20 ml). Concentration of the dried extract gave the lilac *tetrahydroxyquinone* (**5**) (29 mg) after recrystallisation from CH_2Cl_2, m.p. 130—132 °C (Found: M^+ 384.1571. $C_{22}H_{24}O_6$ requires M, 384.1573); δ_H 12.40, 12.83 (each 2 H, s, exchanged with ^2H_2O) and 7.14 (2 H, s); $\lambda_{max.}$ 491, 512, 524, 553, and 565 nm).

The following compounds were also prepared by this method.

Compd.	Yield (%)	M.p. (°C)	M^+	M
(**6**) + (**7**)	93	98—100	440.2206	440.2199
(**8**)	78	145—148	340.0950	340.0497

Preparation of the Tetracycle (**18**).—Pent-2-enal was treated with leuco-5-hydroxyquinizarin (**45**) and piperidinium acetate in EtOH as described previously for the leuco-compound (**38**). Work-up as before gave the *tetracyclic quinone* (**18**) (62%), m.p. 202—205 °C [Found: M^+, 324.0997. $C_{19}H_{16}O_5$ requires M, 324.0998); δ_H 13.34, 12.66, 12.38 (all 1 H, s), 7.92 (1 H, dd, J 8 and 1.2 Hz), 7.74 (1 H, t, J 8 Hz), 7.34 (1 H, dd, J 8 and 1.2 Hz), 3.48 (1 H, m), 3.05 (2 H, m), 2.34 (1 H, m), 2.00 (2 H, m), 1.59 (1 H, m), 1.01 (3 H, t, J 7.5 Hz).

Acknowledgements

We wish to thank the S.E.R.C. and I.C.I. Organics Division for financial support, and Ms. F. Saunders, R.S.R.E., Great Malvern for the measurement of Order Parameters.

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Received 27*th March* 1986; *Paper* 6/604