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The Amination of Bromanil with 2,5-Diaminobenzenesulphonic Acid

G. Hallas, A. B. Wareing

Department of Colour Chemistry & Dyeing, University of Leeds, Leeds, UK, LS2 9JT

A. H. M. Renfrew & J. A. Taylor

Research Centre, Zeneca Specialties, PO Box No. 42, Hexagon House, Blackley, Manchester, UK, M9 3DA

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ABSTRACT

The amination of bromanil with 2,5-diaminobenzenesulphonic acid at 60°C, unlike that of chloranil, leads to the total loss of halogen. Reaction at 0°C, however, results in the formation of 2,5-bis-(4-amino-3-sulphoanilino)-3,6-dibromo-1,4-benzoquinone. This dianilide, unlike the corresponding dichloro derivative, is readily reduced by warming it in aqueous solution with an excess of 2,5-diaminobenzenesulphonic acid.

1 INTRODUCTION

The reaction of amines with tetrahalo-1,4-benzoquinone results in the substitution of labile halo substituents[1,2] by nitrogen and directly affords, unlike benzoquinone itself, aminated products in the quinone oxidation state. While a number of nitrogen heterocycles, e.g. pyrazole, imidazole and 1,2,4-triazole[1] can give rise to sequential substitution, aromatic and aliphatic amines furnish 1 : 2 adducts in which 2 mol of amine react with 1 mol of quinone with a marked preference for 1,4-orientation of the quinone ring.

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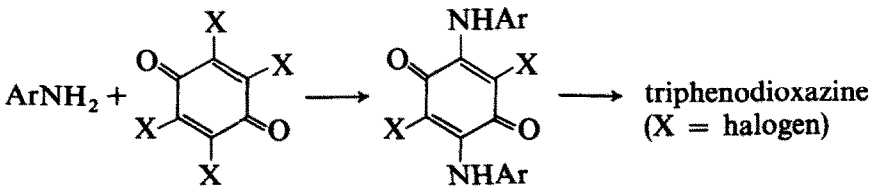
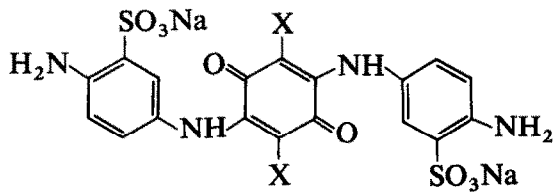


Scheme 1

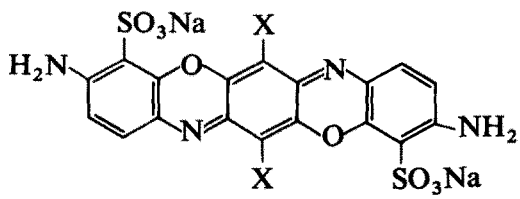
Bisarylaminobenzoquinones are key intermediates in the synthesis of triphenodioxazine dyes[3] (Scheme 1).

Many examples of the reaction of aromatic amines with both chloranil and bromanil have been recorded[1-8] and, without exception, a 2,5-bis-(arylamino)-3,6-dihalo-1,4-benzoquinone is obtained. The reaction of chloranil and 2,5-diaminobenzenesulphonic acid falls within this classification and gives 2,5-bis-(4-amino-3-sulphoanilino)-3,6-dichloro-1,4-benzoquinone (**I**; X=Cl) in good yield.[9]



I

During an attempted synthesis of a triphenodioxazine derivative (**II**; X=Br) it has been found that when bromanil is reacted with 2,5-diaminobenzenesulphonic acid, under the same experimental conditions as for chloranil, the expected dibromobenzoquinone (**I**; X=Br) is not formed.



II

In this paper the product of this reaction and the probable reaction pathway are investigated.

2 EXPERIMENTAL

2.1 General

Electronic absorption spectra were measured in water with a Perkin-Elmer SP800 double-beam spectrophotometer, ^{1}H NMR spectra were measured with a Bruker WM250 spectrometer and FAB mass spectra by using a JEOL SX 102 high resolution mass spectrometer. HPLC analyses were performed with a Varian 500 liquid chromatograph with a 15 cm ODS Hypersil column and water containing 0·25% dicyclohexylammonium dihydrogen phosphate—acetonitrile as eluent.

2.2 2,5-Bis-(4-amino-3-sulphoanilino)benzoquinone

Method 1—from bromanil

2,5-Diaminobenzenesulphonic acid (3·80, 0·02 mol) was slurried in water (25 ml) and sufficient sodium hydroxide solution (2 M) was added to give a solution of pH 7. Bromanil (MTM Research Chemicals Ltd.) (99%, 4·23 g, 0·01 mol) was then added and the resulting suspension was heated, with stirring, for 6 h at 55 to 60°C while maintaining a pH of 6 to 7, then cooled. (The reaction mixture was found to contain 30% of the desired product as determined by HPLC†) Sodium thiocyanate (20 g) was added and the reaction mixture was stirred for 1 h at room temperature to give a solid which was isolated by filtration, washed thoroughly with acetone and oven-dried at 50°C overnight to give a brown product (0·5 g, 10·1%). Purification of this material was achieved by Soxhlet extraction of impurities and of residual thiocyanate with acetone to give a dark brown powder, $\lambda_{max} = 430$ nm.

M.p. > 300°C. Found: C 37·1, H 3·1, N 9·5, S 11·0;
$C_{18}H_{14}N_4O_8S_2Na_2.3H_2O$ requires C 37·4, H 3·5, N 9·7, S 11·1.
$(M-H)^-$ at *m/z* = 479.

δ_H(250 MHz; D_2O) 5·67(2H, s, ArH *ortho* to C=O), 6·75(2H, d, ArH *meta* to SO_3Na), 6·96(2H, dd, ArH *para* to SO_3Na) and 7·49(2H, d, ArH *ortho* to SO_3Na).

Method 2—from 1,4-benzoquinone

2,5-Diaminobenzenesulphonic acid (3·80 g, 0·02 mol) was slurried in water (25 ml) and sufficient sodium hydroxide solution (2 M) was added to give a solution of pH 7. 1,4-Benzoquinone (98%, 1·10 g, 0·01 mol) was

† HPLC yields determined by comparison with an internal standard of 2,5-bis-(3-sulphoanilino)benzoquinone.

added and the resulting suspension was heated, with stirring, for 6 h at 55 to 60°C while maintaining a pH of 6 to 7 and then cooled. A brown solid (2·25 g, 42·7%) was isolated by the method described above and found to be identical to the previous material by HPLC analysis, absorbance and NMR spectroscopy.

M.p. > 300°C. Found: C 37·4, H 3·2, N 9·5, S 10·5; $C_{18}H_{14}N_4O_8S_2Na_2.3H_2O$ requires C 37·4, H 3·5, N 9·7, S 11·1.

2.3 2,5-Bis-(4-amino-3-sulphoanilino)-3,6-dibromo-1,4-benzoquinone

2,5-Diaminobenzenesulphonic acid (3.80 g, 0·02 mol) was slurried in water (25 ml) and sufficient sodium hydroxide solution (2 M) was added to give a solution of pH 7. Bromanil (99%, 4·23 g, 0·01 mol) was added and the resulting suspension was stirred for 6 h at 0 to 5°C while maintaining a pH of 6 to 7. (The mixture contained 62% of the desired product as determined by HPLC.) Sodium thiocyanate (20 g) was added and the reaction mixture was stirred for 1 h at room temperature to give a solid which was isolated by filtration, washed thoroughly with acetone and oven-dried at 50°C overnight to yield a brown solid (2·82 g, 41·3%).

Purification of this solid was achieved by removal of impurities and residual thiocyanate by Soxhlet extraction with acetone to give a brown powder, λ_{max} = 452 nm.

M.p. > 300°C. Found: C 30·3, H 2·2, N 7·8, Br 20·7, S 9·0; $C_{18}H_{12}Br_2N_4O_8S_2Na_2.2H_2O$ requires C 30·1, H 2·2, N 7·8, Br 22·3, S 8·9.

$(M-H)^-$ at *m/z* = 635.

δ_H(250 MHz; DMSO–D6) 5·69(4H, s, NH_2), 6·53(2H, d, ArH *meta* to SO_3Na), 6·84(2H, dd, ArH *para* to SO_3Na), 7·23(2H, d, ArH *ortho* to SO_3Na) and 9·59(2H, s, NH).

2.4 3,10-Diamino-6,13-dibromo-4,11-disulphotriphenodioxazine

2,5-Bis-(4-amino-3-sulpho)anilino-3,6-dibromobenzoquinone (3·0 g, 4·40 mmol) was carefully added to 20% oleum (30 ml) and ammonium persulphate (1·8 g, 13·6 mmol) was then added over 5 min and the mixture was stirred at 45°C for 90 min. After being left to cool to room temperature, the mixture was poured on to ice to give a dark blue solid which was isolated by filtration and washed with saturated brine. The solid so obtained was slurried in water (20 ml) and reisolated by filtration after adjusting the pH to 7. The resulting solid was washed in turn with water and with acetone, and dried to give a blue product (2·0 g, 67%). Further purification by dialysis in water afforded a dark blue product, λ_{max} = 596 nm.

M.p. >300°C. Found: C 30·3, H 2·2, N 7·8, Br 21·2, S 9·0; $C_{18}H_8Br_2N_4O_8S_2Na_2.2H_20$ requires C 30·3, H 1·7, N 7·8, Br 22·4, S 9·0.

2.5 5-Bis-[4-(β-aminoethyl)amino-3-sulphoanilino]-3,6-dibromo-1,4-benzoquinone

2-(β-Aminoethyl)amino-5-aminobenzenesulphonic acid (6·3 g, 0·02 mol) was slurried in water (25 ml), and the pH was adjusted to 7. Bromanil (99%, 4·23 g, 0·01 mol) was added and the mixture was stirred at 60°C for 6 h maintaining a pH of 7. The resulting suspension was cooled, the product isolated by filtration, thoroughly washed with acetone and oven-dried at 40°C overnight to give a brown solid (6·9 g, 95%). Purification of the material was achieved by Soxhlet extraction of impurities with acetone.

M.p. >300°C. Found: C 34·7, H 3·9, Br 20·5, N 11·0, S 8·8; $C_{22}H_{24}Br_2N_6O_8S_2.2H_2O$ requires C 34·7, H 3·7, Br 21·0, N 11·1, S 8·4.

2.6 Reduction of 2,5-bis-(4-amino-3-sulphoanilino)-3,6-dibromobenzoquinone to 2,5-bis-(4-amino-3-sulphoanilino)benzoquinone in the presence of 2,5-diaminobenzenesulphonic acid.

2,5-Bis-(4-amino-3-sulpho)anilino-3,6-dibromobenzoquinone (2·10 g, 0·003 mol) was added to a solution of 2,5-diaminobenzenesulphonic acid (2·30 g, 0·012 mol) in water (50 ml) at pH 7. The solution was heated at 60°C for 6 h while maintaining a pH of 6 to 7. (The mixture contained 40% of the desired product as determined by HPLC). The product was identical by HPLC analysis to that derived from Method 2. The reaction solution was diluted to 100 ml and analysed for ionic bromide.

Found: Br 0·6%; required for 0·006 mol Br 0·5%.

3 RESULTS AND DISCUSSION

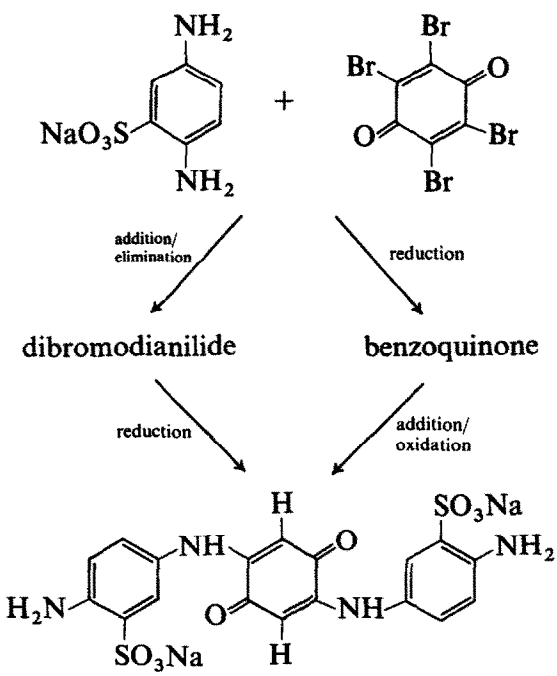
Acid formation during the reaction of bromanil with 2,5-diaminobenzenesulphonic acid, under the conditions used for chloranil, was monitored by alkali addition. Unlike the chloranil reaction, which required two equivalents of sodium hydroxide solution, that with bromanil required additional base. The chloranil reaction gave a product readily isolated by salting with sodium chloride and which was shown to be essentially one compound by HPLC. On the other hand, the bromanil reaction was much more complex (7 peaks) and it was not possible to isolate a single product by the same salting procedure, despite many attempts.

The dianilide intermediate derived from chloranil was readily cyclised to the triphenodioxazine derivative, whereas cyclised material could not be obtained from the bromanil reaction mixture under a variety of conditions. Ordinarily, the expected dibromodianilide should be capable of cyclisation.

Salting with common salt, under a variety of conditions, failed to yield a pure product. By contrast, substitution of sodium thiocyanate (Lewis, D. M., 1992, pers. comm.) for sodium chloride resulted in the isolation of an essentially pure product; HPLC analysis showed a dominant peak, λ_{max} = 430 nm (cf. 452 nm for the chloranil analogue).

Elemental analysis revealed the absence of bromine; NMR and mass spectra (parent ion *m/z* = 479) were consistent with the formation of 2,5-bis-(4-amino-3-sulphoanilino)-1,4-benzoquinone (I; X=H). This structure was confirmed by the unambiguous synthesis of 2,5-bis-(4-amino-3-sulphoanilino)-1,4-benzoquinone (I; X=H) from the reaction of 1,4-benzoquinone and 2,5-diaminobenzenesulphonic acid; the two products were found to be identical. Accordingly, all four bromine atoms were lost from the bromanil during the reaction (Scheme 2).

Two possible pathways for the loss of halogen are shown in Scheme 2. One route involves reduction of the bromanil in the presence of 2,5-



Scheme 2

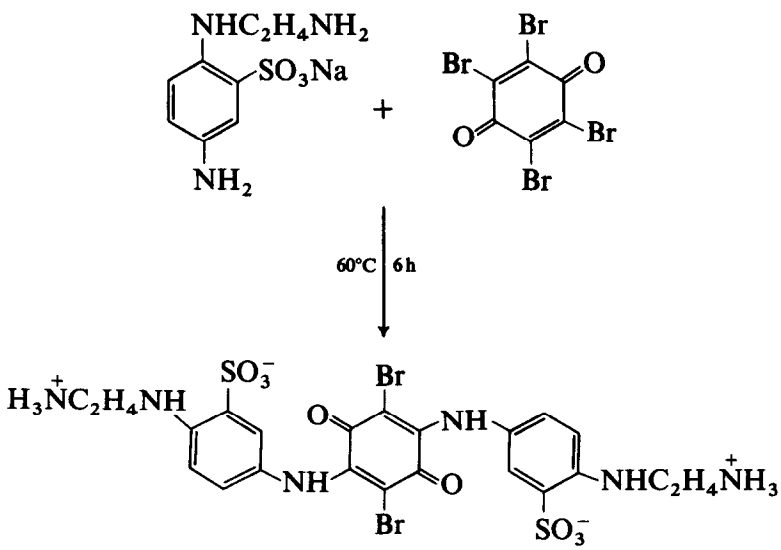
diaminobenzenesulphonic acid to the 1,4-benzoquinone, followed by an addition/oxidation step with the amine to give the product. Alternatively, an addition/elimination step with the amine to give the dibromobenzoquinone product (I, X=Br) is followed by reduction and loss of the bromine.

To investigate these possibilities, the closely-related 2-(β-aminoethyl)amino-5-aminobenzenesulphonic acid was heated with bromanil at 60°C for 6 h at pH 7 to form 2,5-bis-[4-(β-aminoethyl)amino-3-sulphoanilino]-3,6-dibromo-1,4-benzoquinone (Scheme 3) in excellent yields (95%). In this case, the zwitterionic dianilide precipitates on formation and is, therefore, unable to undergo further reaction.

This finding is consistent with the reaction of bromanil and 2,5-diaminobenzenesulphonic acid proceeding via a dibromobenzoquinone derivative which is subsequently reduced (Scheme 2).

Several attempts were made to stabilise the soluble dibromodianilide product by carrying out the reaction at different temperatures. Accordingly, the reaction of bromanil with 2,5-diaminobenzenesulphonic acid was repeated at 0 to 5°C for 6 h and the desired 2,5-bis-(4-amino-3-sulphoanilino)-1,4-dibromobenzoquinone (I; X=Br) was isolated.

The dibromobenzoquinone was reduced to the dihydro analogue by heating an aqueous solution with an excess of 2,5-diaminobenzenesulphonic acid at 60°C (confirming the lability of the bromine atoms under the original reaction conditions). The stepwise reduction via an intermediate compound, tentatively assigned as the monobromodianilide, was



Scheme 3

observed by HPLC. Titration of the reaction solution showed that all the bromine had been removed as ionic bromide.

The unsubstituted 2,5-bis-(4-amino-3-sulphoanilino)-1,4- benzoquinone (**I**; X=H) could not be cyclised to a triphenodioxazine under a variety of reaction conditions. However, the dibromo analogue (**I**; X=Br) cyclised under standard conditions to give the corresponding dibromo-triphenodioxazine (**II**; X=Br).

These results support the reaction of bromanil with 2,5-diaminobenzenesulphonic acid proceeding by an addition/elimination step to form 2,5-bis-(4-amino-3-sulphoanilino)-1,4-dibromobenzoquinone (**I**; X=Br), followed by reduction to the dihydro analogue (**I**; X=H).

The facile reduction of the dibromobenzoquinone (**I**; X=Br) compared with the dichloro analogue (**I**; X=Cl) parallels the known carbon–halogen bond strengths.[10]

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