**1-(Phenylamino)pseudo-mauveine: a new water soluble phenazine dye**

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**Graphical abstract**



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***N*-phenyl-*p*-phenylenediamine, 4-nitrosodiphenylamine**

**Abstract**

1-(Phenylamino)pseudomauveine was prepared by the oxidation of 1,3,5-tri(phenylamino)benzene and *p*-phenylenediamine with potassium dichromate. The absorption maximum of 535 nm is shifted hypsochromically by about 20 nm compared to that for pseudo-mauveine. Condensation of 1,3,5-tri(phenylamino)benzene with 4-nitrosodiphenylamine under strongly acidic conditions gave 1,3,7-tri(phenylamino)-5-phenyl-phenazinium sulfate and 10-phenyl-6,8-(phenylamino)-2,10-dihydrophenazin-2-one.

**1. Introduction**

Mauveine was characterised as an important phenazine dye in the 19th century by independent syntheses of pseudo-mauveine **3** from the aromatic building blocks **1-2** and **4-5** by oxidation under mildly acidic conditions (Scheme 1).1 *p*-Phenylenediamine **1** was oxidatively condensed with 1,3-di(phenylamino)benzene **2** and *N*-phenyl-*m*-phenylenediamine **4** was condensed with *N*-phenyl-*p*-phenylenediamine **5**. The trimer **7** was used to make pseudo-mauveine **3** and other derivatives more recently.2 The yields for these reactions are improved over those for conventional mauveine syntheses because the building blocks **2**, **4** and **5** are pre-assembled as dimers. Pseudo-mauveine **3** was also converted to phenosafranine **8** by oxidation with lead dioxide (Scheme 2).3 The conversion of an asymmetric dye to a symmetric one helps to verify the correct structure. Mauveine was used to dye silk from hot water as the dye is poorly soluble in cold water which also restricts its use as a biological stain. In this paper we report a novel synthesis of a phenazinium sulfate salt which fortuously has good water solubility.



**Scheme 1** 1+3 and 2+2 assembly routes to pseudo-mauveine



**Scheme 2** Perkin’s oxidation of pseudo-mauveine **3** to phenosafranine **8**

**2. Discussion**

**(i) Synthesis of 1,3-di(phenylamino)-5-phenyl-7-aminophenazinium sulfate (1-(phenylamino)pseudo-mauveine)**

A 10 g sample of 1,3,5-tri(phenylamino)benzene **9**4 was available from a previous project in the authors group on the synthesis of polyaromatic amines as charge transport materials. The oxidation of compound **9** and *p*-phenylenediamine **1** with K2Cr2O7 in H2O/H+ was unsuccessful owing to the poor water solubility of compound **9**. However, we showed previously that acetone/water mixtures can be used in these syntheses for poorly water soluble building blocks.5-7 The oxidation of compound **9** and *p*-phenylenediamine **1** with K2Cr2O7 in water/acetone (1.5:1.0) was successful as the building block is easily dissolved in a water/acetone mixture (Scheme 3). The acetone must be evaporated before filtration of the reaction mixture as it solubilises the mauveine-like product **10**. Isolation of the product **10** is aided by the absorption of the chromophore onto insoluble by-products. However, because the yield of 35% is much higher than the typical yields of 1-5% obtained for the assembly of four aromatic amine building blocks,5-7 more material remains in solution. The product was purified by usual chromatographic methods. On a column, MeOH successfully eluted front running impurities first, then cNH3/MeOH (20:80) eluted the pure product.



Purple dye λmax 535 nm

**Scheme 3** Synthesis of1,3-di(phenylamino)-5-phenyl-7-aminophenazinium sulfate **10** (the ring positions are numbered).

The structure of compound **10** was established by spectroscopic methods including accurate mass spectrometry. The 1H NMR spectrum showed upfield singlets for the protons at positions 2, 4 and 6 and a downfield doublet for the proton at position 9 (see experimental). The 13C NMR spectrum showed the required 24 signals. The UV spectrum was unusual because the λmax  of 535 nm was shifted hypsochromically by 15 nm compared to mauveine chromophores which have λmax around 550-555 nm. The phenazine core has four sites (positions 1, 3, 7 and 9) where substituents can conjugate to the positive charge. The new phenylamino group is therefore conjugated to the chromophore and we had expected a bathochromic shift in the absorption maximum. The conjugation of the two phenylamino groups is therefore not additive. A second surprise came from the water solubility of this compound. It freely dissolves in water with stirring despite having an extra phenyl ring. Presumably a larger dipole enhances the water solubility as the extra phenylamino nitrogen lone pair conjugates to the chromophore, and molecular rotation may affect packing in the solid state.

**(ii) Synthesis of 1,3,7-tri(phenylamino)-5-phenylphenazinium sulfate**

Owing to the success of this synthesis to make compound **10** an attempt was made to prepare further derivatives of pseudo-mauveine **3** substituted with more phenylamino groups. A mixture of 1,3,5-tri(phenylamino)benzene **9** and *N*-phenyl-*p*-phenylenediamine **5** were oxidised the same way using K2Cr2O7 in water/acetone (1.5:1.0) with some acid (Scheme 4).



Blue dye λmax 562 nm

**Scheme 4** Synthesis of 1,3,7-tri(phenylamino)-5-phenyl-phenazinium sulfate **11**

One product was formed which was isolated and characterised as 1,3,7-tri(phenylamino)-5-phenyl-phenazinium sulfate **11** by spectroscopic methods including accurate mass spectrometry. Much of the 1H NMR data for compound **11** is similar to that for compound **10** owing to the similarity in structure and an extra set of phenyl protons are present. This compound is less soluble and acquistion of 13 C NMR data was not possible. This compound is now blue rather than purple, the characteristic colour of pseudo-mauveine **3**. The absorption maximum occurred at 562 nm which is shifted 10 nm bathochromically compared to pseudo-mauveine **3**. However, the absorption is very broad extending out into the red end of the spectrum which will account for its change in colour from purple to blue. Since the absorption maxmiumof pseudo-mauveine **3** is bathochromically shifted compared to that of phenosafranine **8**, the bathochromic shift in the absorption maximum observed here was anticipated.

Fischer and Hepp previously reported the synthesis of 3,7-di(phenylamino)-5-phenylphenazinium sulfate **13** by the condensation of 4-nitrosodiphenylamine **12** with 1,3-di(phenylamino)benzene **2** in cHCl/EtOH with air as oxidant (Scheme 5).8-10 They also reported other condensations using 4-nitrosoaniline.11-14



**Scheme 5** Fischer and Hepp’s synthesis of compound **13**

We therefore attempted the condensation of 4-nitrosodiphenylamine **12** with 1,3,5-tri(phenylamino)benzene **9** under similar conditions (Scheme 6). Two products were isolated. One was the expected product, compound **11** (11 %) and the other was a hydrolysis product tentatively assigned as structure **14** (18%). The UV spectrum of compound **14** showed an absorption maximum at 519 nm. The IR spectrum showed no conventional carbonyl group around 1700 cm-1 but a low stretch at 1585 cm-1. It showed a carbonyl group in the 13C NMR at 172 ppm and the expected 24 peaks in total. An expected molecular ion and accurate mass spectrum for M+ + H was obtained. Treatment of compound **11** under the same acidic conditions did not give compound **14** which showed that compound **11** is not a precursor to it. Treatment of 1,3,5-tri(phenylamino)benzene **9** with 4-nitrosophenol **15** under the same



**Scheme 6** Synthesis with 4-nitrosodiphenylamine **12** and attempted synthesis with 4-nitrosophenol **15**.

acidic conditions failed to form compound **14** (Scheme 6) which ruled out an initial hydrolysis of 4-nitrosodiphenylamine **12** to 4-nitrosophenol **15** (Scheme 7). Scheme 8 describes a proposed route to the formation of compounds **11** and **14**.



**Scheme 7** A possible *in situ* hydrolysis of4-nitrosodiphenylamine **12** to 4-nitrosophenol **15** which was not observed.

This involves an initial acid catalysed condensation of 1,3,5-tri(phenylamino)benzene **9** onto the nitroso group of 4-nitrosodiphenylamine **12** and the elimination of water to give intermediate **19**. In principle there are three different phenylamino groups, one of which might hydrolyse off from the molecule. Only one hydrolysis product is formed. The facile hydrolysis of the phenylamino group, drawn on intermediate **19** as an imminium salt, to give intermediate **20** is the most likely because molecular twisting will favour this canonical form and the 1,3,5-tri(phenylamino)benzene ring is more stable. This molecular twisting is likely owing to steric congestion in the planar form. Cyclisation and aerial oxidation to compound **14** can then occur.



**Scheme 8** Proposed route to both compounds **11** and **14**.

Since two chromophores were isolated in the condensation reaction of 4-nitrosodiphenylamine **12** with 1,3,5-tri(phenylamino)benzene **9** caution should be taken in interpreting Fischer and Hepps studies with nitrosated building blocks as similar hydrolysed products might also occur under the strongly acidic conditions used.8-14

The TLC characteristics of compound **14** are quite unusual (Scheme 9). At first we were puzzled as compound **14** eluted from a column ahead of compound **11** using MeOH as eluent but then ran more slowly up a TLC plate behind compound **11** using secBuOH/EtOAc/H2O/HOAc as eluent (Scheme 9). The TLC spot is also purple using cNH3/MeOH as eluent and blue using secBuOH/EtOAc/H2O/HOAc as eluent. These observations are rationalised by assuming that protonation occurs in mild acid and deprotonation occurs in mild base or water. This behaviour is different from pseudo-mauveine **3** and other mauveine chromophores which do not deprotonate with cNH3/MeOH. The rapid elution of compound **14** with MeOH, and its purple rather than blue colour, when purifying it after its synthesis from compounds **9** and **12**, suggests that it is deprotonated during precipitation or filtration and washing with water. It is only weakly basic. A strong dipole would suggest canonical form **22**,resembling a meso-ionic, and might explain the lack of an IR carbonyl stretch.



**Scheme 9** Protonation and deprotonation of compound **14** in different TLC solvents

**3. Summary**

Two new derivatives of pseudo-mauveine **3** have been prepared which are substituted with phenylamino groups. Both have an additional phenylamino group in the 1 position. This substitution causes good rt water solubility in compound **10**. The syntheses of these compounds requires the use of an acetone/water mixture to solubilise the starting material 1,3,5-tri(phenylamino)benzene **9**.

**4. Experimental**

IR spectra were recorded on a Perkin-Elmer Spectrum Two diamond anvil IR spectrometer. UV spectra were recorded using a Perkin-Elmer Lambda 25 UV-VIS spectrometer with EtOH as the solvent. 1H and 13C NMR spectra were recorded at 400 MHz and 100.5 MHz respectively using a Varian 400 spectrometer. Chemical shift values, δ, are given in ppm relative to the residual solvent, and coupling constants, *J* are given in Hz. Low resolution and high resolution mass spectra were obtained at the University of Wales, Swansea using electron impact ionisation and chemical ionisation. Melting points were determined on a Kofler hot-stage microscope. 4-Nitrosodiphenylamine and 4-nitrosophenol were purchased from TCI Europe.

*1,3,5-tri(Phenylamino)benzene* **9**4

METHOD A: The literature procedure was followed but with the following modifications. Anhydrous phloroglucinol (5.00 g, 40 mmol), aniline (16.6 g, 178 mmol) and iodine (0.2 g, 2 %) were heated at 190 °C for 8 h with the removal of residual H2O. The mixture was allowed to cool then diluted with MeOH which precipitated the crude product as a brown solid. Repeated trituration with MeOH was followed by recrystallisation from dichloromethane/light petroleum to yield the *title compound* (10.5 g, 75 %) as long colourless needles, mp 200-201 °C (lit. 200-201 °)4  (Found : C, 82.3; H, 5.8; N, 11.9. C24H21N3 requires C, 82.1; H, 6.0; N, 12.0 %); λmax (CH2Cl2)/nm 298 (log ε 4.38); νmax (KBr)/cm-1 : 3384s, 3374s, 3033m, 1615w, 1601w, 1578s, 1491s, 1462s, 1433m, 1407s, 1299s, 1248s, 1192w, 1170s, 1073w, 992m, 958w, 895m, 826w, 753s, 722m, 699w, 637w and 612w; δH (250 MHz; CDCl3) 5.61 (3H, s, NH), 6.33 (3H, s, Ar), 6.89-6.95 (3H, t, *J =* 7.2), 7.04-7.10 (6H, d, *J* = 8.1) and 7.19-7.26 (6H, dd, *J* = 7.3 and 8.1); δC (62.9 MHz; CDCl3) 99.5, 118.7, 121.2, 129.1, 142.9 and 145.5; *m/z* 351 (M+, 100 %).

METHOD B : Anhydrous phloroglucinol (5.0 g, 40 mmol) was mixed with aniline (16.6 g, 178 mmol) and cHCl (2 ml). The reaction mixture was stirred at room temperature for 1 h and then heated to reflux at 190 °C for 1 h. After cooling the reaction mixture was treated with 5M dil HCl (10 ml) which resulted in solidification of the mixture. The solid was slurried or triturated several times with MeOH to remove excess aniline. Recrystallisation from dichloromethane/light petroleum yielded the *title compound* (12.5 g, 90 %) as long colourless needles, mp 200-201 °C, which were identical to the spectroscopic properties for the material prepared by Method A.

*1-(Phenylamino)pseudo-mauveine* **10** [*1,3-di(phenylamino)-5-phenyl-7-amino-phenazinium sulfate]*: A mixture of 1,3,5-tri(phenylamino)benzene **9**4 (382 mg, 1.10 mmol) and *p*-phenylenediamine (118 mg, 1.10 mmol) in water and acetone (150 ml/100 ml) with cH2SO4 (6 drops, 0.3 ml) were treated with K2Cr2O7 (320 mg, 1.10 mmol) and heated at 40-50 0C for 1h with stirring in a beaker covered with a petri dish. The petri dish was then removed and heating and stirring continued for a further 2-3 h to evaporate the acetone. The acetone must be evaporated before the mixture is filtered. After allowing to cool the mixture was filtered through a fine pore sinter and washed with H2O. The precipitate was extracted with MeOH (6 x 50 ml) in the sinter each time agitating the precipitate. The combined MeOH extracts were evaporated to dryness then purified by chromatography on silica gel. After elution with MeOH elution with cNH3/MeOH (20/80) gave the *title compound* (194 mg, 35%) as a dark glistening solid, mp > 230 0C. λmax (ethanol)/nm 535 (log ε 4.9) and 276 (5.3); νmax (diamond anvil) 1607w, 1585s, 1470s, 1388w, 1354w, 1302s, 1225s, 1163s, 1021s, 875w, 824s, 749s, 689s and 591s; δH(400 MHz; CD3OD) 5.57 (1H, s), 5.85 (1H, s), 6.73 (1H, s), 7.01 (2H, d, *J* = 7.6 Hz), 7.06-7.09 (2H, m), 7.10 (1H, t, *J* = 6.8 Hz), 7.21 (2H, d, *J* = 7.6 Hz), 7.30-7.38 (4H, m), 7.41 (2H, d, *J* = 7.6 Hz), 7.68-7.76 (3H, m) and 7.82 (1H, d, *J* = 8.8 Hz); δC (100.1 MHz; CDCl3) 87.3, 93.0, 93.8, 119.4, 122.3, 122.4, 124.4, 125.0, 127.5, 128.9, 129.2, 129.9, 130.5, 131.2, 132.8, 133.4, 136.6, 137.3, 137.5, 138.6, 139.3, 145.1, 154.9 and 157.5; *m/z* (Orbitrap ASAP) 454.2021 (M+, 100%) C30H24N5 requires 454.2026.

*1,3,7-tri(Phenylamino)-5-phenyl-phenazinium sulfate* **11** *:* A mixture of 1,3,5-tri(phenylamino)benzene **9** (382 mg, 1.10 mmol) and *N*-phenyl-*p*-phenylenediamine (200 mg, 1.10 mmol) in water and acetone (150 ml/100 ml) with cH2SO4 (6 drops, 0.3 ml) were treated with K2Cr2O7 (320 mg, 1.10 mmol) and heated at 40-50 0C for 1h with stirring in a beaker covered with a petri dish. The petri dish was then removed and heating and stirring continued for a further 2-3 h to evaporate the acetone. The acetone must be evaporated before the mixture is filtered. After allowing to cool the mixture was filtered through a fine pore sinter and washed with H2O. The precipitate was extracted with MeOH (6 x 50 ml) in the sinter each time agitating the precipitate. The combined MeOH extracts were evaporated to dryness then purified by chromatography on silica gel. After elution with MeOH elution with cNH3/MeOH (20/80) gave the *title compound* (198 mg, 34%) as a dark solid, mp > 230 0C. λmax (ethanol)/nm 562 (log ε 4.9) and 287 (4.9); νmax (diamond anvil) 2977w, 2903w, 1584s, 1463s, 1355s, 1302s, 1229s, 1191s, 1066vs, 876s, 823s, 747vs, 596vs, 757vs and 458; δH(400 MHz; CD3OD) 5.68 (1H, d, *J* = 2.0 Hz), 6.31 (1H, d, *J* = 2.0 Hz), 6.80 (1H, d, *J* = 2.0 Hz), 7.09 (3H, d, *J* = 8.0 Hz), 7.13 (2H, d, *J* = 12.0 Hz), 7.28 (5H, t, *J* = 8.0 Hz), 7.40-7.45 (4H, m), 7.48 (2H, d, *J* = 6.0 Hz), 7.68 (2H, t, *J* = 4.0 Hz), 7.75 (3H, t, *J* = 7.20 Hz) and 8.08 (1H, d, *J* = 9.20 Hz); δC (100.1 MHz; CDCl3) *m/z* (Orbitrap ASAP) 530.2323 (M+, 100%) C36H28N5 requires 530.2339. The compound was not soluble enough to record a carbon 13 spectrum.

*Synthesis of 10-phenyl-6,8-(phenylamino)-2,10-dihydrophenazin-2-one* **14**:

1,3,5-tri(Phenylamino)benzene **9** (100 mg, 0.285 mmol) and 4-nitrosodiphenylamine **12** (56 mg, 0.285 mmol) in EtOH (10 ml) and cHCl (5 ml) were heated to dryness in a beaker over 3 h in a fume hood. After the addition of water the product was filtered off and purified by chromatography on silica gel. MeOH eluted the *title compound* (23 mg, 18%) as a dark green solid, mp > 220 0C. λmax (ethanol)/nm 519 (log ε 4.39) and 295 (4.45); νmax (diamond anvil) 1585vs, 1557s, 1489s, 1436s, 1304s, 1239s, 1218vs, 1175s, 1124s, 874w, 815w, 751s and 695vs; δH(400 MHz; CD3OD) 5.32 (1H, s), 6.20 (1H, d, *J* = 2.0), 6.26 (1H, d, *J* = 1.6), 7.04 (2H, d, *J* = 8.0), 7.09-7.12 (4H, m), 7.20 (2H, d, *J* = 7.6), 7.23 (3H, dd, *J* = 8 and 7.6), 7.38 (2H, d, *J* = 7.6), 7.62 (1H, t, *J* = 7.2 and 7.2), 7.71 (2H, t, *J* = 7.6 and 7.6) and 7.93 (1H, d, *J* = 8.8); δC (100.1 MHz; CDCl3) 86.4, 94.9, 97.8, 115.7, 120.9, 122.7, 123.7, 124.7, 127.7, 128.8, 128.9, 129.9, 131.0, 133.1, 136.0, 137.2, 137.6, 138.9, 139.7, 140.5, 150.5, 157.7, 157.8 and 172.6; *m/z* (Orbitrap ASAP) 455.1863 (M+ + H, 100%) C30H23N4O requires 455.1866. cNH3/MeOH (20:80) eluted 1,3,7-tri(phenylamino)-5-phenyl-phenazinium sulfate **11** (18 mg, 11%) as a blue solid with identical spectroscopic properties to the material reported previously.

*Attempted synthesis of*  *10-phenyl-6,8-(phenylamino)-2,10-dihydrophenazin-2-one* **14** Method 1: 1,3,7-tri(Phenylamino)-5-phenyl-phenazinium sulfate **11** (10 mg, 0.017 mmol) was heated to dryness in EtOH (2 ml) and cHCl (1 ml). The dry product (10 mg, 100%) had the same spectroscopic properties as the starting material and was pure by TLC (secBuOH:EtOAc:H2O:HOAc) (60:30:9.5:0.5)

*Attempted synthesis of 10-phenyl-6,8-(phenylamino)-2,10-dihydrophenazin-2-one* **14** Method 2: 1,3,5-tri(Phenylamino)benzene **9** (100 mg, 0.285 mmol) and 4-nitrosophenol **15** (35 mg, 0.285 mmol) in EtOH (10 ml) and cHCl (5 ml) were heated to dryness in a beaker over 3 h in a fume hood. After the addition of water the reaction was filtered and the precipitated material was purified by chromatography on silica gel. None of the *title compound* had formed.

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