The synthesis of mauveine A and mauveine B from *N-tert*-butyl-*p*-toluidine

M. John Plater*

Department of Chemistry, University of Aberdeen, Meston Walk, Aberdeen AB24 3UE, UK

The oxidation of a mixture of *N-tert*-butyl-*p*-toluidine/aniline/*o*-toluidine (1 : 1.5 : 1.5) with $K_2Cr_2O_7$ in H^+/H_2O followed by de-*tert*-butylation with acid gives mauveine **A** and mauveine **B**. These compounds dye silk the same shade of red mauve as that of silk dyed by authentic mauveine.

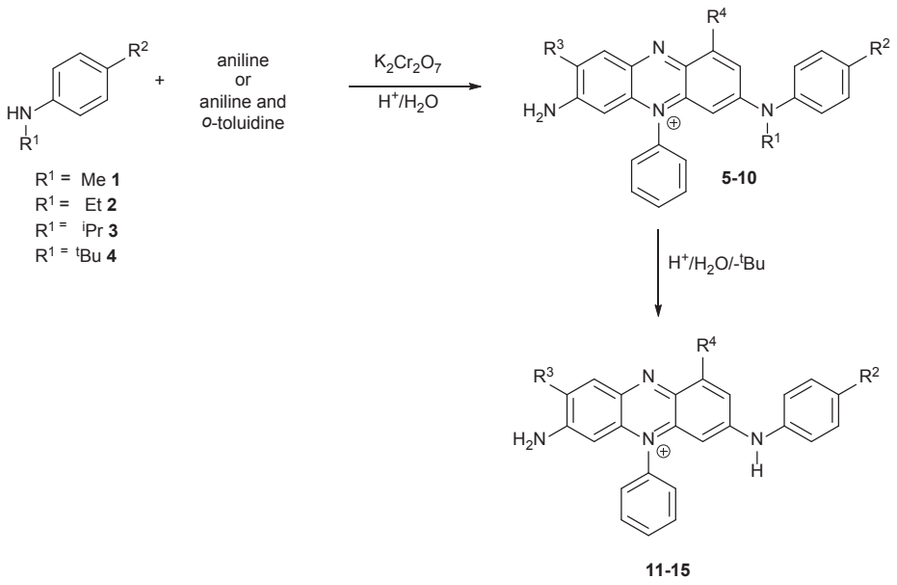
Keywords: mauveine, mauve, *tert*-butyl, *o*-toluidine, *p*-toluidine, dyeing

In 1856, Perkin obtained a purple ethanolic solution of mauveine by extracting a black precipitate, which had precipitated from the oxidation of aniline sulfate by potassium dichromate in water.[1] The synthesis of mauveine was commercialised since it gave silk an attractive purple colour. A factory for its manufacture and for other dyestuffs was built in 1857 at Greenford Green which was the beginning of the coal-tar dye industry.[2] Perkin began research on the molecular structure of mauveine[3–6] and later others showed that the core is a phenazine moiety.[7–10] Over a century later, two key components of mauveine were characterised as mauveine A and mauveine B by NMR spectroscopy and mass spectrometry.[11,12] Further analysis has also shown the mixture to be more complex with 12 homologues present.[13,14] Despite the commercialisation of mauveine, its synthesis is still seen as a challenge particularly to get silk the same colour as that dyed using Perkin's authentic mauveine.[15] Attempts to do this back in 1956 by W.H. Cliffe and others for the centenary celebrations failed. Silk dyed with mauveine made and purified by Perkin's method (the oxidation of aniline/*o*-toluidine/*p*-toluidine mixtures with $K_2Cr_2O_7/H^+/H_2O$) was a blue shade of mauve rather than the red shade of mauve which was obtained with authentic mauveine. I have, therefore, examined some different methods of making mauveine using either *N*-phenyl-*p*-phenylenediamine[16,17] or *N*-alkyl-*p*-toluidines[18] and compared the colours of silk dyed with these and that dyed with authentic mauveine. Perkin filed one later patent in 1863 on the alkylation of the leuco-base of mauveine and commented on its red shade of mauve on silk but the method does not appear to have been exploited.[19]

Results and discussion

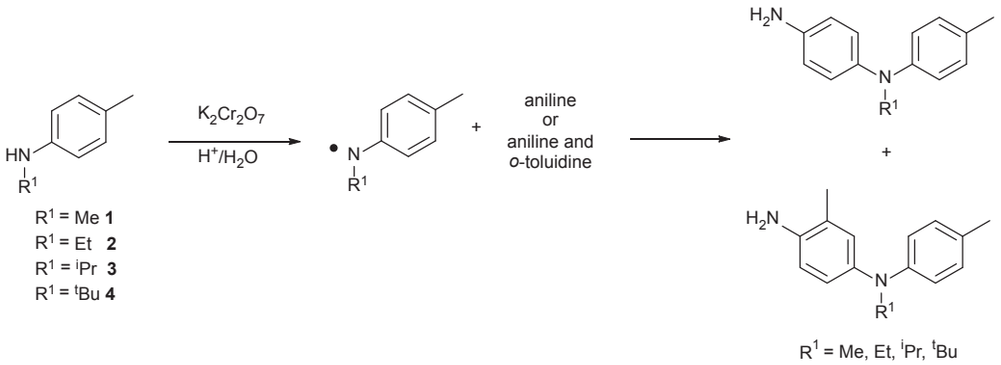
Synthesis

Scheme 1 shows how mauveine and some derivatives were prepared by the oxidation of *N*-alkyl-*p*-toluidines using $K_2Cr_2O_7$. Table 1 summarises the chromophores that have been prepared. The yields for these reactions are improved compared to those obtained for the oxidation of aniline/*o*-toluidine/*p*-toluidine mixtures.[16] Key intermediate dimers in the mechanism are shown in Scheme 2. The *N*-alkyl substituent probably serves to stabilise an aminyl radical, which reacts with aniline or *o*-toluidine by homolytic aromatic substitution.[16] The radical would be stabilised by hyperconjugation from the alkyl group. The dimers formed are key electron-rich building blocks which can undergo further oxidation and coupling leading to tetramers (mauveine).[16] Initially I considered that the *N*-methyl group at position 3 in compounds **5**–**7** might be oxidatively removed by abstraction of hydrogen forming a carbocation stabilised by a nitrogen lone pair of electrons. This would



Scheme 1 The synthesis of mauveine (C_{25b} **11**, A **14**, B **15**) and mauveine derivatives by *N*-alkyl-*p*-toluidines. See Table 1 for the R group substituents. Compounds **12** and **13** were isolated but not separated (see Scheme 5).

* Correspondent. E-mail: m.j.plater@abdn.ac.uk



Scheme 2 Proposed formation of *N*-alkyl-*N*-tolyl-*p*-phenylene dimers as key intermediates in mauveine synthesis (see also ref. 17).

Table 1 Summary of the compounds prepared by the oxidation of *N*-alkyl-*p*-toluidines **1**–**4** with either aniline or aniline and *o*-toluidine using $K_2Cr_2O_7$

Compound	R^1	R^2	R^3	R^4	Yield/%
5[a]	Me	Me	H	H	6.3
6[a]	Me	Me	Me	H	6.0
7[a]	Me	Me	Me	Me	7.0
8	Et	Me	H	H	3.5
9	^{i}Pr	Me	H	H	6.0
10	^{t}Bu	Me	H	H	1
11	H	Me	H	H	1.1
14[b]	H	Me	Me	H	1.3
15[b]	H	Me	Me	Me	3.5

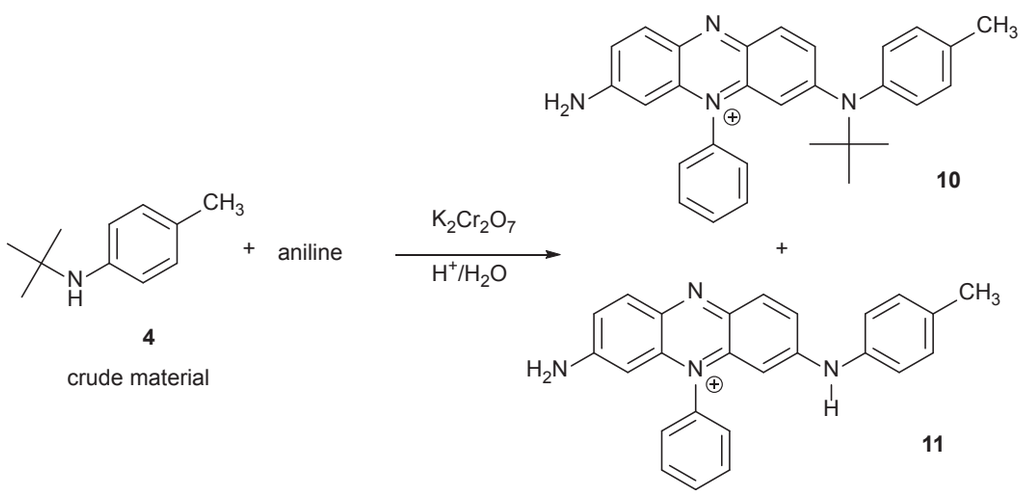
The yield for compounds **11**, **14**–**15** includes the formation of *N*-*tert*-butyl-*p*-toluidine and a de-*tert*-butylation step. Compounds **12** and **13** were isolated as a mixture in 8% yield (see Scheme 5).

[a]The syntheses of compounds **5**–**7** have been reported previously and are included for clarity.[18]

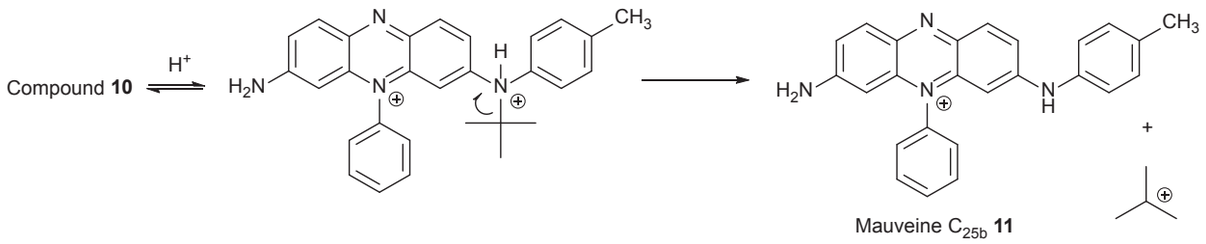
[b]Starting from purified *N*-*tert*-butyl-*p*-toluidine the combined yield of mauveine A **14** and mauveine B **15** was 5%.

react with water deprotecting the chromophore. This lone pair is, however, involved in conjugation to the chromophore and may not be readily available. Indeed, I was unable to carry out the oxidation of either the *N*-methyl group of compound **5**[18] or the *N*-isopropyl group of compound **9** in dilute sulfuric acid. These conditions are more vigorous than those of the parent synthesis because the acid is stronger without aromatic amines present. The *N*-isopropyl group of compound **9** has two extra methyl groups that would stabilise a carbocation so its stability was unexpected. Interestingly compound **9** with this *N*-alkyl substituent gave a better yield of product (Table 1).

Having prepared *N*-methyl,[18] *N*-ethyl and *N*-isopropyl derivatives my attention turned to making an *N*-*tert*-butyl derivative of mauveine. The simplest synthesis of *N*-*tert*-butyl-*p*-toluidine **4** involves heating the hydrochloride salt of *p*-toluidine in ^{t}BuOH at about 150 °C. [20,21] A bulky alcohol is advantageous because it only alkylates the amine once. It also allows a reactive carbocation intermediate to form easily which can alkylate the amine. Aromatic amines were also methylated and ethylated this way and are discussed by Perkin in the Hofmann Memorial Lecture.[2] The literature preparation was repeated to make *N*-*tert*-butyl-*p*-toluidine **4** by heating the hydrochloride salt of *p*-toluidine in ^{t}BuOH at about 150 °C for 24 h. Analysis by TLC (Et_2O : light petroleum, 25 : 75) showed an acceptably clean reaction with a new less polar product and a small amount of *p*-toluidine left. Heating for shorter periods can leave more starting material. This crude reaction product was used directly in the next stage without further purification. The product in ^{t}BuOH was diluted in H_2O/H^+ and oxidised with $K_2Cr_2O_7$ (Scheme 3). Since ^{t}BuOH is a tertiary alcohol, it will not be oxidised by $K_2Cr_2O_7$. The reaction turned purple after 4–5 h. This is an interesting building block to use in mauveine synthesis because its steric bulk might stabilise an aminyl free radical, it cannot easily be oxidised like an isopropyl group, and, owing to the stability of the *tert*-butyl carbocation, it might be deprotected more readily. Steric compression in the product might also facilitate deprotection.



Scheme 3 The oxidation of *N*-*tert*-butyl-*p*-toluidine and aniline with $K_2Cr_2O_7$.

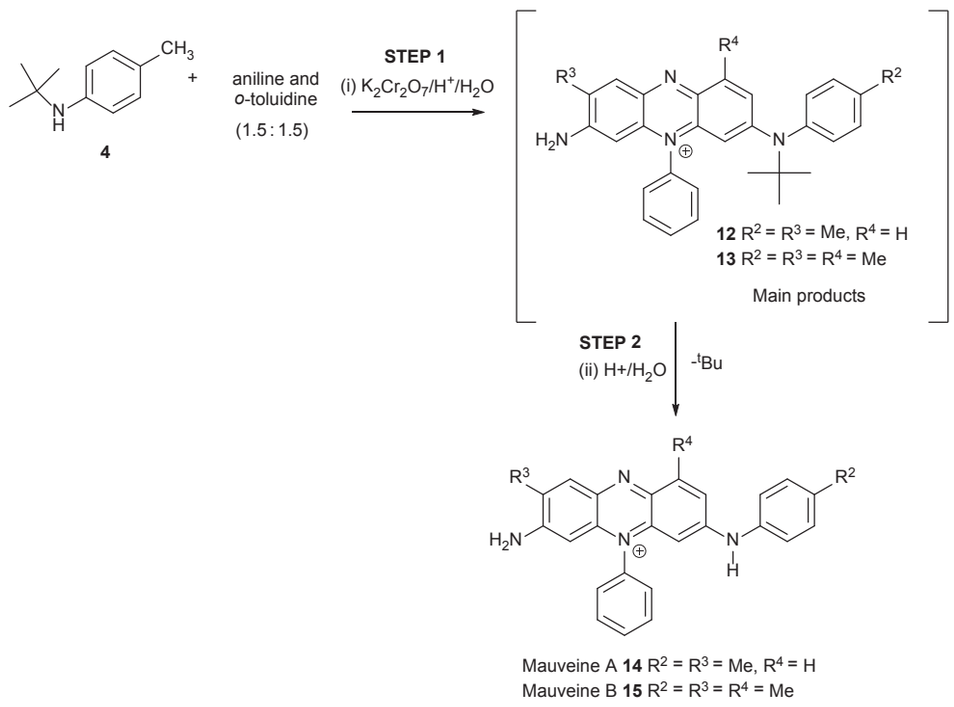


Scheme 4 Proposed mechanism for the de-*tert*-butylation of chromophore **10** catalysed by acid.

Standard work-up and chromatography gave initially a small amount of mauveine chromophore C_{25b} **11** followed by the major product **10**, which had retained the *tert*-butyl group. The separation works well as *N*-alkylated chromophores are more polar.[18] Compound **10** was fully characterised and showed typical ^{1}H NMR and ^{13}C NMR data. A *tert*-butyl group of 9H occurred at 1.36 ppm and a single methyl group at 2.4 ppm. Singlets of 1H for positions 4 and 5 were present at 5.95 and 6.02 ppm. The tolyl ring shows two doublets at 6.94 and 7.26 ppm. The doublet for position 2 is partially masked by the doublet at 7.26 ppm. The two *ortho*-phenyl protons occur as a doublet at 7.47 ppm. Downfield resonances for positions 1 and 8 occurred at 7.80 ppm (masked by the 3-phenyl proton multiplet) and 7.90 ppm. Despite the bulk of the nitrogen atom at position 3, the spectrum remains well resolved and the compound is stable. The ^{13}C NMR spectrum showed resonances at 19.8 (Me), 28.8 ($C\underline{Me}_3$) and 58.8 ppm (N–$\underline{C}Me_3$). The UV-VIS spectrum showed λ_{max} at 550 nm and 280 nm showing that the bulk of the *tert*-butyl group had not prevented conjugation of the nitrogen atom to the chromophore. The compound showed a strong molecular ion at *m/z* 433 and a fragmentation of ^{t}Bu at *m/z* 377 (50%). The product **10** was then treated with cHCl (5 mL) in MeOH (10 mL). The mixture was heated to 40–50 °C and evaporated to dryness. The *tert*-butyl group was removed under these conditions to give product **11** which was fully characterised spectroscopically. Only one alkyl group was present at 2.29 ppm (3H) in the ^{1}H NMR spectrum and only one alkyl carbon was present at 19.5 ppm in the ^{13}C NMR spectrum. Product **11** might arise in the reaction from the oxidative coupling of residual *p*-toluidine with aniline, or from *in situ* loss of the *tert*-butyl group. Scheme 4 shows a possible mechanism for the acid-catalysed loss of the *tert*-butyl group.

Initial protonation of the tertiary nitrogen atom is followed by loss of a *tert*-butyl cation. This will be facilitated by formation of the stable mauveine chromophore. Compound **11** stains silk a so-called blue shade of mauve and is different from the red shade of mauve on silk stained from 1862 authentic mauveine. It does, however, resemble the blue shade of mauve photographed previously, which came from a mauveine rich in mauveine C_{25b}.[13] A sample of compound **9** was treated under identical acidic conditions but was not deprotected and gave only recovered starting material. The *N*-isopropyl group is stable under these conditions.

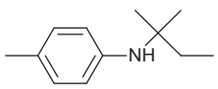
The reactions shown in Schemes 3 and 4 were then repeated by oxidising a mixture of *N*-*tert*-butyl-*p*-toluidine/aniline/*o*-toluidine with $K_2Cr_2O_7$ followed by deprotection with acid. This reaction turned purple after 1 h so was faster and more efficient. Although two fractions were collected from step 1 (*tert*-butylated material in 8% yield and a small amount of non-*tert*-butylated material) only the final products mauveine A **14** and mauveine B **15** were separated and characterised after acid treatment of the *tert*-butylated material (Step 2) (Scheme 5).



Scheme 5 A two-step synthesis of mauveine A **14** and mauveine B **15**.

The intermediate *tert*-butyl-substituted chromophores **12** and **13** were not separated from each other or characterised. Mauveine A **14** and mauveine B **15** showed spectroscopic data including ^{1}H NMR spectra identical to those previously reported from authentic mauveine.[11,14] The combined yields are slightly higher than that for the formation of mauveine C_{25b} **11**. This is typical of reactions that use a mixture of aniline/*o*-toluidine rather just aniline. The yields are lower than expected but two extra steps are included. These are the formation of the *N*-*tert*-butyl-*p*-toluidine **4** (isolated yield of 62%)[21] and later the de-*tert*-butylation step to give the product. However, a similar combined yield of 5% was obtained for a mixture of mauveine A **14** and B **15** starting from **4** as a pure isolated starting material. This is preferred because only a trace of the de-*tert*-butylated products **14** and **15** is formed in the first step. These were combined with the main product. This shows that they must predominantly form from unreacted *p*-toluidine in the unpurified starting material **4**.

An attempt to synthesise *N*-*tert*-amyl-*p*-toluidine **16**, from *tert*-amyl-alcohol and *p*-toluidine hydrochloride, by the same method used for the formation of *N*-*tert*-butyl-*p*-toluidine **4**, was unsuccessful and gave only recovered *p*-toluidine (Scheme 6). The different reactivity of the two tertiary alcohols, or the stability of the products, is striking.



16

Scheme 6 Structure of *N*-*tert*-amyl-*p*-toluidine.

Silk dyeing

Silk dyeing and TLC analysis (*sec*BuOH : EtOAc : H_2O : HOAc 60 : 30 : 9.5 : 0.5) was done using a mauveine A/B mixture prepared from the oxidation of pure *N*-*tert*-butyl-*p*-toluidine/aniline/o-toluidine followed by de-*tert*-butylation of all the product or from the de-*tert*-butylation of a pure mixture of compounds **12** and **13**. By TLC analysis the R_f values of the two compounds **14** and **15** are the same as those of 1862 authentic mauveine and the slightly different shade of the two spots on a TLC plate is very characteristic. The colour of silk dyed with them is identical to that of silk dyed with authentic mauveine. They were purified by chromatography eluting with *sec*BuOH/EtOAc/H_2O/HOAc (60 : 30 : 9.5 : 0.5). Each product or with both combined gives a brighter shade on silk than the product obtained by elution from a column with cNH_3/MeOH (20 : 80). This is the first time that I have accurately reproduced the shade of authentic mauveine on silk with a mauveine chromophore (where R^1 = H and an *N*-tolyl group at position 3). In our hands, the oxidation of a mixture of aromatic amines by Perkin's method is lower yielding and more complex. Methods for making mauveine by Perkin's method (generally referred to as the aqueous potassium dichromate/H_2SO_4 oxidation of a mixture of aniline/*o*-toluidine/*p*-toluidine) have been studied previously.[16] Even after purification twice by column chromatography, cNH_3/MeOH (20 : 80) and then *sec*BuOH/EtOAc/H_2O/HOAc (60 : 30 : 9.5 : 0.5), or by changing the counterion to different anions such as chloride, bromide and acetate and trituration with H_2O, the material still stains silk a blue shade of mauve that does not closely match the red shade of 1862 authentic mauveine. Analysis by TLC of the material prepared here showed it to contain less mauveine A **14** and more mauveine B **15** compared to authentic mauveine probably because the ratio of *o*-toluidine/aniline oxidised was greater in our starting materials. By oxidising a mixture of *N*-*tert*-butyl-*p*-toluidine/*o*-toluidine/aniline with a greater ratio of aniline present (1.0 : 1.5 : 2.0 or 1.0 : 1.5 : 2.5) TLC analysis of the purified material showed the ratio of mauveine A **14** to mauveine **B 15** to have increased. Using approximately 1.8 equiv. of aniline gave mauveine that by eye matched the A/B ratio of authentic mauveine. Our TLC studies on the isolated products from the oxidation of *N*-methyl-*p*-toluidine/*o*-toluidine/aniline showed that as the ratio of *o*-toluidine/aniline was varied the ratio of *N*-methyl mauveine A **6** to *N*-methyl mauveine B **7** also varied.[18] More *o*-toluidine favours *N*-methyl mauveine B. Purified mauveine made by Perkin's method does not separate into two resolved spots on a TLC plate. It separates into four spots (Fig. 1) indicative of a more complex mixture of products. This observation is similar to the results from the HPLC traces published previously.[14] The additional two spots presumably contribute to a blue mauve shade of stained silk. In mauveine made by Perkin's method, note that mauveine B is quite a weak TLC spot and, yet in authentic mauveine, mauveine B is a stronger spot than mauveine A (see Fig. 1). This is one reason why I am sceptical that Perkin made mauveine this way. The two profiles are different and I have not been able to wash out the extra chromophores. Heating and cooling a sample in water and filtering, twice, still leaves a mixture of chromophores. Much material is also lost. Other HPLC studies suggest that these compounds are correctly assigned as mauveine A, B_2, B and C.[14] Since mauveine B_2 and C have been characterised[14] and contain a 4-methylphenyl group at position 5, the synthesis of authentic mauveine appears to lack any *p*-toluidine. If *p*-toluidine is present it may compete with aniline to give 4-methylphenyl rather than phenyl at the 5-position (Scheme 7), whereas *N*-*tert*-butyl-*p*-toluidine does not.

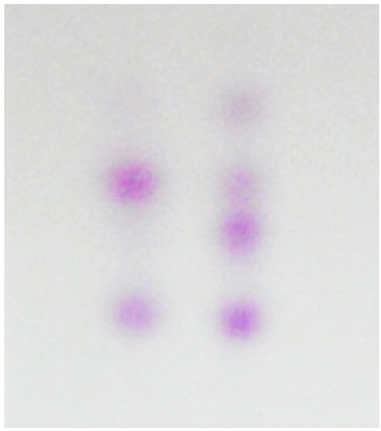
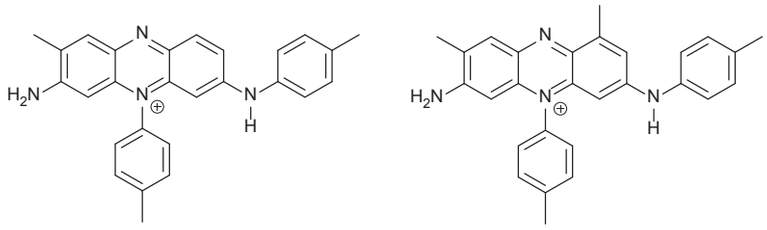


Fig. 1 Left: Top spot (mauveine B) and lower spot (mauveine A) of authentic mauveine. Right: Mauveine made by Perkin's method (oxidation of aniline/*o*-toluidine/*p*-toluidine 25 : 50 : 25 or 37.5 : 37.5 : 25 or 33 : 33 : 33). A larger scale synthesis from aromatic amine (4 g) (37.5 : 37.5 : 25) also gave a dominant top spot (mauveine C). A number of TLC plates were run as a check for reproducibility. The eluent was *sec*BuOH : EtOAc : H_2O : HOAc (60 : 30 : 9.5 : 0.5).

It was also noted previously that oxidation of *N*-phenyl-*p*-phenylenediamine and either pure aniline or pure *o*-toluidine gave single characterisable chromophores, but when a mixture of aniline/*o*-toluidine (1.5 : 1.5) was used instead with *N*-phenyl-*p*-phenylenediamine the reaction was a complex mixture of mauveine chromophores from which no pure data were obtained.[16] This reaction should have given mauveine C_{25a} (substituted at position 8 only with a methyl group). Hence an *N*-alkyl group at position 3 helps to control the reaction pathway.[18]



Scheme 7 The structures of mauveine B_2 and mauveine C.[14]

Conclusion

Mauveine A **14** and mauveine B **15** have been prepared by the oxidation of a mixture of pure *N*-*tert*-butyl-*p*-toluidine/aniline/*o*-toluidine followed by the acid-catalysed removal of the *tert*-butyl group. They stain silk a red mauve shade, which matches that of silk stained with Perkins 1862 authentic mauveine. The chromophores can be separated or left combined. The mauveine chromophore C_{25b} **11** stains silk a blue shade of mauve showing how the shade is finely adjusted by the methyl group substituents. This chromophore was not present in our mixture of mauveine A **14** and mauveine B **15** which will enhance the red shade of mauve on silk. The yield is lower for the oxidation of *N*-*tert*-butyl-*p*-toluidine/aniline/*o*-toluidine compared to the yield for the oxidation of *N*-isopropyl-*p*-toluidine/aniline/*o*-toluidine. The steric hindrance of the *tert*-butyl group appears to hinder the reaction but the yield is still higher and the product purer than that obtained for the oxidation of mixtures of aniline/*o*-toluidine/*p*-toluidine. An *N*-alkyl group at position 3 favours a selective reaction pathway to mauveine A and mauveine B derivatives. Our studies suggest that Perkin's synthesis of mauveine lacked any *p*-toluidine but used an *N*-alkylated *p*-toluidine instead that was subsequently deprotected in the product. The *tert*-butyl group is one such example of a traceless substituent that is stable in the the mauveine synthesis but can be removed.

Experimental

IR spectra were recorded on an ATI Mattson FTIR spectrometer using potassium bromide discs. UV spectra were recorded using a PerkinElmer Lambda 25 UV-VIS spectrometer with EtOH as the solvent. ^{1}H and ^{13}C 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 by reference 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.

N-Methyl,[18] *N*-ethyl and *N*-isopropyl-*p*-toluidines were commercially available. The solvent mixture *sec*BuOH : EtOAc : H_2O : HOAc (60 : 30 : 9.5 : 0.5) was used for column chromatography to get high grade mauveine for comparison with authentic mauveine dyed on silk. The solvent mixture cNH_3/MeOH (20 : 80) was used to purify crude reaction mixtures. Silk strips were cut from a gentleman's handkerchief and silk dyeing was done from hot water with stirring. The preparation of *N*-*tert*-butyl-*p*-toluidine by heating *p*-toluidine HCl in ^{t}BuOH for less than 24 h leaves some unreacted *p*-toluidine detectable by TLC. An increased quantity of non-tertiary butylated chromophores form in the product upon oxidation when mixed with aromatic amines.

3-[4-Methylphenyl(ethylamino)]-5-phenyl-7-aminophenazinium sulfate (**8**): *N*-Ethyl-*p*-toluidine (250 mg, 1.85 mmol) and aniline (517 mg, 5.55 mmol, 3.0 equiv.) were dissolved in distilled H_2O (200 mL) in a beaker and acidified with cH_2SO_4 (six drops, 0.3 mL) followed by the addition of $K_2Cr_2O_7$ (909 mg, 3.1 mmol, 1.67 equiv.). The mixture was stirred and heated at 70–80 °C for 4 h then cooled and filtered through a fine pore (4–8 μm porosity) sinter. The precipitate was washed with H_2O and then extracted with portions of MeOH (40 mL × 6) each time with agitation in the sinter. The combined extracts were evaporated to dryness by heating in a beaker on a hotplate. The product was purified by column chromatography on silica gel. Elution with cNH_3/MeOH (20 : 80) gave the title compound (29.6 mg; 3.5%) as a dark solid, m.p. > 220 °C. λ_{max} (ethanol)/nm 552 (log ε 4.64) and 278 (4.61); ν_{max} (diamond anvil) 3290(br), 1550(vs), 1402(vs), 1341(s), 1187(w), 1124(w), 1017(w) and 924(w); δ_H(400 MHz; CD_3OD) 1.15 (3H, t, *J* = 7.1 Hz), 2.38 (3H, s), 3.76 (2H, q, *J* = 7.1 Hz), 5.70 (1H, s), 5.99 (1H, s), 7.04 (2H, d, *J* = 8.0 Hz), 7.26 (2H, d, *J* = 8.3 Hz), 7.32–7.28 (2H, m), 7.42 (2H, d, *J* = 7.6 Hz), 7.70–7.78 (3H, m) and 7.92 (2H, t, *J* = 8.1 Hz); δ_C (100.1 MHz; $CDCl_3$) 13.4, 22.0, 96.2, 97.2, 120.1, 125.0, 129.3, 129.8, 132.8, 132.9, 133.5, 134.9, 136.0, 137.1, 138.3, 138.7, 139.7, 140.4, 143.2, 156.4 and 161.5 (two peaks are missing); *m/z* (Orbitrap ASAP) 405.2071 (M^+, 100%) $C_{27}H_{25}N_4$ requires 405.2074.

3-[4-Methylphenyl(isopropylamino)]-5-phenyl-7-aminophenazinium sulfate (**9**): *N*-Isopropyl-*p*-toluidine hydrochloride (200 mg, 1.08 mmol) and aniline (300 mg, 3.23 mmol, 3.0 equiv.) were dissolved in distilled H_2O (200 mL) in a beaker acidified with cH_2SO_4 (six drops, 0.3 mL) followed by the addition of $K_2Cr_2O_7$ (526 mg, 1.79 mmol, 1.67 equiv.). The mixture was stirred and heated at 70–80 °C for 4 h and then cooled and filtered through a fine pore (4–8 μm porosity) sinter. The precipitate was washed with H_2O and then extracted with portions of MeOH (40 mL × 6), each time with agitation in the sinter. The combined extracts were evaporated to dryness by heating in a beaker on a hotplate. The product was purified by column chromatography on silica gel. Elution with cNH_3/MeOH (20 : 80) gave the title compound (30.3 mg; 6.0%) as a dark solid, m.p. > 220 °C. λ_{max} (ethanol)/nm 550 (log ε 4.64) and 275 (4.61); ν_{max} (diamond anvil) 2969(br), 1590(vs), 1550(s), 1505(s), 1471(vs), 1371(s), 1315(s), 1286(s), 1190(s), 1173(s), 1105(vs), 875(w), 829(s), 810(s), 793(s), 695(w), 619(w) and 600(w); δ_H(400 MHz; CD_3OD) 1.12 (6H, d, *J* = 6.6 Hz), 2.39 (3H, s), 4.35 (1H, m), 5.50 (1H, s), 5.91 (1H, s), 6.91 (2H, d, *J* = 8.1 Hz), 7.17 (2H, d, *J* = 9.3 Hz), 7.25 (2H, d, *J* = 7.8 Hz), 7.37 (2H, d, *J* = 6.8 Hz), 7.71 (3H, m) and 7.81 (2H, d, *J* = 9.5 Hz); δ_C (100.1 MHz; $CDCl_3$) 21.2, 21.3, 51.4, 95.0, 96.7, 119.3, 123.5, 128.7, 130.9, 131.8, 132.5, 134.0, 135.1, 136.4, 137.2, 137.6, 137.8, 138.7, 138.9, 140.2, 156.4 and 160.0 (one peak is missing); *m/z* (Orbitrap ASAP) 419.2226 (M^+, 100%) $C_{28}H_{27}N_4$ requires 419.2230.

Attempted oxidation of 3-[4-methylphenyl(isopropylamino)]-5-phenyl-7-aminophenazinium sulfate (**9**): Compound **9** (8 mg, 0.0171 mmol) in H_2O (100 mL) acidified with cH_2SO_4 (0.5 mL, 10 drops) was heated to 50–60 °C and treated with $K_2Cr_2O_7$ (15 mg, 0.051 mmol) for 15 min. A precipitate quickly formed which was filtered off after cooling. The filtrate was treated with base to precipitate any remaining chromophore but very little was present. The first precipitate was shown by ^{1}H NMR to be identical with the starting material and also had the same R_f value.

3-[4-Methylphenyl(amino)]-5-phenyl-7-aminophenazinium sulfate (**11**) *and 3-[4-methylphenyl(tert-butylamino)]-5-phenyl-7-aminophenazinium sulfate* (**10**) *Method 1*: Standard procedure: *p*-Toluidine hydrochloride (266 mg, 1.87 mmol) and *tert*-butanol (3 mL) were sealed in a 23 mL PTFE lined Parr digestion bomb and heated at 150 °C for 24 h. After cooling the mixture was added to distilled H_2O (200 mL) containing cH_2SO_4 (six drops, 0.3 mL) and aniline (520 mg, 5.6 mmol) followed by the addition of $K_2Cr_2O_7$

(916 mg, 3.1 mmol, 1.67 equiv.). The mixture was stirred and heated at 70–80 °C for 5 h then cooled and filtered through a fine pore (4–8 μm porosity) sinter. The precipitate was washed with H_2O and then extracted with portions of MeOH (40 mL × 6), each time with agitation in the sinter. The combined extracts were evaporated to dryness by heating in a beaker on a hotplate. The product was purified by chromatography on silica gel. Elution with cNH_3/MeOH (20 : 80) gave the first title compound (3 mg, 0.4%) as a dark solid, m.p. > 220 °C. λ_{max} (ethanol)/nm 554 (log ε 4.7) and 282 (4.6); ν_{max} (KBr) 3427(br), 1596(s), 1530(w), 1504(s), 1476(s), 1384(s), 1318(s), 1173(s) and 1134(s); δ_H(400 MHz; CD_3OD) 2.29 (3H, s), 6.00(1H, s), 6.28 (1H, s), 7.02 (2H, d, *J* = 8.2 Hz), 7.10 (2H, d, *J* = 8.2 Hz), 7.85 (1H, d, *J* = 9.0), 7.41 (1H, d, *J* = 9.0 Hz), 7.50 (2H, d, *J* = 7.3 Hz), 7.75 (1H, d, *J* = 7 Hz), 7.81 (2H, t, *J* = 7.8 Hz), 7.93 (1H, d, *J* = 8.8 Hz) and 7.9 (1H, d, *J* = 9.6 Hz); δ_C(100.1 MHz; $CDCl_3$) 19.5, 93.5, 93.6, 121.7, 122.0, 127.4, 129.2, 129.6, 130.7, 131.2, 133.2, 133.9, 135.5, 135.8, 136.3, 136.3, 136.8, 137.4, 137.4, 153.0 and 158.1; *m/z* (Orbitrap ASAP) 377.1760 (M^+, 100%) $C_{25}H_{21}N_4$ requires 377.1761. This was followed by the second title compound (9 mg, 1%) as a dark solid, m.p. > 220 °C. λ_{max} 550 (log ε 4.6) and 280 (4.5); ν_{max} (KBr) 3144(br), 1597(vs), 1533(s), 1487(vs), 1400(vs), 1345(s), 1313(vs), 1110(vs), 874(w), 815(w) and 618(w); δ_H(400 MHz; CD_3OD) 1.36 (9H, s), 2.41 (3H, s), 5.95 (1H, s), 6.02 (1H, s), 6.94 (2H, d, *J* = 7.0 Hz), 7.10 (1H, d, *J* = 9.0 Hz), 7.26 (2H, d, *J* = 7.0 Hz), 7.30 (1H, d, *J* = 9.0 Hz), 7.47 (2H, d, *J* = 5.0 Hz), 7.80 (4H, m), 7.90 (1H, d, *J* = 9.0 Hz); δ_C(100.1 MHz; $CDCl_3$) 19.8, 28.8, 58.8, 93.4, 98.6, 121.6, 121.9, 127.5, 129.3, 130.4, 130.7, 131.2, 131.3, 133.8, 134.8, 135.0, 136.4, 137.4, 137.7, 138.5, 140.3, 154.9 and 158.2; *m/z* (Orbitrap ASAP) 433.2383 (M^+, 100%) and 377.1759 (52) $C_{29}H_{29}N_4$ requires 433.2387 and fragment $C_{25}H_{21}N_4$ requires 377.1761.

3-[4-Methylphenyl(amino)]-5-phenyl-7-aminophenazinium sulfate (**11**): Compound **10** (9 mg, 0.019 mmol) was added to a mixture of MeOH (10 mL) and treated with cHCl (5 mL). After heating for 1 h the mixture was evaporated to dryness in a beaker. MeOH (30 mL) was added and it was purified by chromatography on silica gel. cNH_3/MeOH (20 : 80) eluted the title compound **11** (6 mg, 74%) with the same spectroscopic data as compound **11** above. Total combined yield of compound **11** (9 mg, 1.1%).

1-Methyl-3-[4-methylphenyl(amino)]-5-phenyl-7-amino-8-methylphenazinium sulfate (**15**) (*mauveine B*) *and 3-[4-methylphenyl (amino)]-5-phenyl-7-amino-8-methylphenazinium sulfate* (**14**) (*mauveine A*): These were made by method 1 following the standard procedure except that aniline was replaced by a mixture of aniline (261 mg, 0.0028 mmol, 1.5 equiv.) and *o*-toluidine (300 mg, 0.0028 mmol, 1.5 equiv.). The combined methanol extracts were heated to dryness and purified by chromatography on silica gel. Elution with cNH_3/MeOH (20 : 80) gave a mixture of the *tert*-butyl-substituted derivatives of the title compounds (73 mg, 8.0%). Some deprotected material, with a different shade, elutes first and was separated at this stage. The title compounds were deprotected by warming with a mixture of cHCl (5 mL) and MeOH (10 mL) for 1 h and evaporating to dryness. The crude product was then re-purified by chromatography on silica gel. Elution with cNH_3/MeOH (20 : 80) gave a mixture which was then purified again by chromatography on silica gel. Elution with *sec*BuOH : EtOAc : H_2O : HOAc (60 : 30 : 9.5 : 0.5) gave the title compound mauveine B (31 mg, 3.5%) as a dark solid, m.p. > 220 °C followed by the title compound mauveine A (11 mg, 1.3%) as a dark solid, m.p. > 220 °C which were both identified by comparison of their spectroscopic data (^{1}H NMR, accurate mass spectrum, R_f value and colour of dyed silk) with authentic material.[11,14] The intermediate mixture of *tert*-butyl-substituted chromophores **12** and **13** were isolated but not separated. Data for mauveine B **15**: δ_H(400 MHz; CD_3OD) 2.29 (3H, s), 2.32 (3H, s), 2.78 (3H, s), 6.08 (1H, s), 6.17 (1H, s), 7.00 (2H, d, *J* = 8.0 Hz), 7.10 (2H, d, *J* = 8.0 Hz), 7.27 (1H, s), 7.48 (2H, d, *J* = 8.0 Hz), 7.76–7.80 (3H, m) and 7.89 (1H, s); *m/z* (Orbitrap ASAP) 405.2073 (M^+, 100%) $C_{27}H_{25}N_4$ requires 405.2074; 419.2227 (10) $C_{28}H_{27}N_4$ requires 419.222; data for mauveine A **14**: δ_H(400 MHz; CD_3OD) 2.30 (3H, s), 2.38 (3H, s), 6.12 (1H, s), 6.33 (1H, s), 7.03 (2H, d, *J* = 7.0), 7.11 (2H, d, *J* = 7.0 Hz), 7.42 (1H, d, *J* = 9.6 Hz), 7.51 (2H, d, *J* = 7.0 Hz), 7.74–7.84 (3H, m), 7.87 (1H, s) and 8.01 (1H, d, *J* = 9.6 Hz); *m/z* (Orbitrap ASAP) 391.1918 (M^+, 100%) $C_{26}H_{23}N_4$ requires 391.1917. A TLC plate run with the same eluent is similar to that of authentic mauveine. Increasing the ratio of aniline from 1.5 to 2.0 to 2.5 equiv. increases the quantity of mauveine A formed.

Mauveine A (**14**) *and mauveine B* (**15**) *Method 2*: A sample of *N-tert*-butyl-*p*-toluidine **4**[21] was made by method 1. The crude reaction mixture was diluted with 2M KOH, extracted with DCM (30 mL) and then the DCM layer was washed with H_2O. This layer was concentrated under reduced pressure and purified by chromatography on silica gel, rather than by distillation. Elution with Et_2O/light petroleum 40–60 (25 : 75) gave *N-tert*-butyl-*p*-toluidine **4** (100 mg, 0.61 mmol) with identical spectroscopic properties to literature material. Oxidation by method 1 followed by chromatography on silica gel gave a mixture of the *tert*-butyl-substituted derivatives of mauveine A **12** and B **13** (20 mg, 7%) and de-*tert*-butylation gave a mixture of the above *title compounds* (14 mg, 5%) with the same spectroscopic properties to the material from the previous synthesis. A trace of de-*tert*-butylated material that formed in the reaction, which elutes first and has a different shade, was combined with the *tert*-butylated material so that all of the chromophore was treated with acid. After de-*tert*-butylation with acid method 1 was followed to purify the products. After oxidation and filtration the *tert*-butyl-substituted products were extracted more easily from the precipitate to give clear washings with MeOH (40 mL × 4).

Attempted synthesis of N-tert-amyl-p-toluidine (**16**): *p*-Toluidine hydrochloride (266 mg, 1.87 mmol) and *tert*-amyl-alcohol (3 mL) were sealed in a 23 mL PTFE lined Parr digestion bomb and heated at 150 °C for 24 h. After cooling the reaction mixture was diluted with 2M KOH and extracted with DCM (30 mL). This layer was dried over $MgSO_4$ then concentrated under reduced pressure and purified by chromatography on silica gel. Elution with Et_2O/light petroleum 40–60 (25 : 75) gave the starting material *p*-toluidine (148 mg, 74%) identified by comparison of its R_f value to authentic material and by ^{1}H NMR spectroscopy.

This work, in part, was completed by the author at the Department of Chemistry, University of Malaya, Faculty of Science, Kuala Lumpur, 50603, Malaysia.

I am grateful to the EPSRC national mass spectrometry service centre for mass spectra and to the Manchester Museum of Science and Industry (MoSI) and the trustees for providing a sample of authentic mauveine (or archived mauveine).

Received 4 December 2013; accepted 11 January 2014
Paper 1302325 doi: 10.3184/174751914X13912601347455
Published online: 7 March 2014

References

1 W.H. Perkin, GB1984, AD **1856**, 1–4.
2 W.H. Perkin, *The British coal tar industry, its origin, development, and decline*, ed. W.M. Gardner. J.B. Lippincott Company and Kessinger Publishing LLC, Philadelphia, 1915, pp. 141–187.
3 W.H. Perkin, *J. Chem. Soc.*, 1896, **69**, 596.
4 W.H. Perkin, *Proc. R. Soc.*, 1863, **12**, 713.
5 W.H. Perkin, *J. Chem. Soc.*, 1879, **35**, 717.
6 W.H. Perkin, *J. Chem. Soc.*, 1862, **14**, 230.
7 O. Fischer and E. Hepp, *Ber.*, 1888, **21**, 2617.
8 O. Fischer and E. Hepp, *Ber.*, 1893, **26**, 1194.
9 O. Fischer and E. Hepp, *Liebigs Ann. Chem.*, 1892, **272**, 306.
10 R. Nietzki, *Ber.*, 1896, **29**, 1442.
11 O. Meth-Cohn and M. Smith, *J. Chem. Soc., Perkin Trans.*, I 1994, 5.
12 O. Meth-Cohn and A.S. Travis, *Chem. Brit.*, 1995, **31**, 547.
13 M.M. Sousa, M.J. Melo, A.J. Parola, P.J.T. Morris, H.S. Rzepa and J. Sergio Seixas de Melo, *Chem. Eur. J.*, 2008, **14**, 8507.
14 J. Seixas de Melo, S. Takato, M. Sousa, M.J. Melo and A.J. Parola, *Chem. Commun.*, 2007, 2624.
15 W.H. Cliffe, *J. Soc. Dyers Colourists*, 1956, **72**, 563.
16 M.J. Plater, *J. Chem. Res.*, 2011, **35**, 304.
17 C. Heichert and H. Hartmann, *Z. Naturforsch*, 2009, **6**, 747.
18 M.J. Plater, *J. Chem. Res.*, 2013, **37**, 427.
19 W.H. Perkin, GB 2762 AD 1863, 1–5.
20 A. Beil and M.B. Knowles, 1954 US 2692287.
21 P.G. Gassman, G.A. Campbell and R.C. Frederick, *J. Am. Chem. Soc.*, 1972, **94**, 3884.