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N,*N*-Dialkylsafranines with Hydroxyl Groups in the Alkyl Substituents

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ABSTRACT

*Novel safranine derivatives containing hydroxyalkyl groups, namely: 3-amino-7-[bis-(2-hydroxyethyl)amino]- (**3a**), 3-amino-7-[methyl-(2-hydroxyethyl)amino]- (**3b**), 3-amino-7-[bis-(2,3-dihydroxypropyl)amino]- (**3c**), 3-amino-7-[methyl-(2,3-dihydroxypropyl)amino]- (**3d**) and 3-amino-7-[(2-hydroxyethyl)-(2,3-dihydroxypropyl)amino]-5-phenylphenazinium chloride (**3e**), were obtained from appropriately substituted anilines by nitrosation and subsequent two-stage condensation of the nitroso compounds with aniline, i.e. the usual method to obtain* N,N-*dialkylsafranines. The products were characterized by typical electron absorption and by the molecular weights of the respective picrates, which were determined photometrically. The new products were prepared with a view to end-use in bright copper plating.*

1 INTRODUCTION

3,7-Diamino-5-arylphenazinium salts (safranines), most often alkylated in one amino group, and their derivatives (azosafranines and related polymeric dyes) are of interest as components of additives to acid electrolytic baths for bright copper plating.[1–5] A disadvantage of the products of this type has been their relatively low solubility in water, further decreasing in the presence of organic disulphides containing sulphonic groups, another

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component of copper brighteners. As a result of such incompatibility, precipitation in the brightener compositions has been sometimes observed.

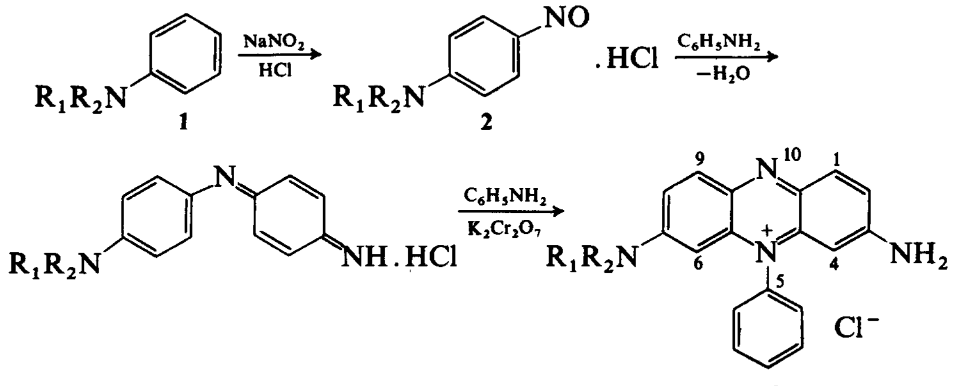
In an attempt to improve copper brightener compositions, new *N*,*N*-dialkylsafranines (**3a–e** in Scheme 1) containing hydroxyl groups in one or both of the alkyl substituents have been synthesized. Reference 6 provides data about their solubilities in water. These are four to more than 30 times greater than that of *N*,*N*-diethylsafranine (**3f**), which is used in copper brightener production.[4,5] The high solubility of **3a–e**, respectively of their polymers, prevents precipitation and conveys stability and constant quality to the brightener compositions.[7]

The case of *N*-polyethylenoxysafranines[8] seems to be closest to the subject of this work described in literature.

2 RESULTS AND DISCUSSION

The synthesis of *N*-hydroxyalkylsafranines **3a–e**, as represented in Scheme 1 and described in Section 3, has been performed according to the procedure of Cobenzl[9] for *N*,*N*-dialkylsafranines, with some modifications. The essential point is that *N*-hydroxyalkylanilines (**1a–e**), instead of dialkylanilines, have been successfully used as precursor intermediates.

The said initial substances were obtained following principly the method of Adkins and Simington for **1a**,[10] combining aniline with a



3

a, $R_1 = R_2 = HOCH_2CH_2$

b, $R_1 = HOCH_2CH_2$ $R_2 = CH_3$

c, $R_1 = R_2 = HOCH_2CH(OH)CH_2$

d, $R_1 = HOCH_2CH(OH)CH_2$ $R_2 = CH_3$

e, $R_1 = HOCH_2CH(OH)CH_2$ $R_2 = HOCH_2CH_2$

f, $R_1 = R_2 = CH_3CH_2$[9]

Scheme 1

chlorohydrin (2-chloroethanol or 3-chloro-1,2-propyleneglycol) to give **1a,c** ($R_1 = R_2$) or an *N*-monosubstituted aniline (*N*-methylaniline *N*-(2-hydroxyethyl)aniline) with the respective chlorohydrin to give **1b,d,e** ($R_1 \neq R_2$).

The chemical nature of **3a–e**, which follows from the synthetic route shown, is consistent with their physical properties (dark coloured powders, eventual green reflections and intensely violet coloured aqueous solutions) and absorption maxima at 275 nm and about 550 nm, which are typical of safranines. It is supported also by their chemical behaviour, as analogues of **3f** in diazotization and subsequent polycondensation.[11] However, further evidence for their chemical identity was required.

The presence of many inorganic salts and by-products in the reaction mixtures, and the high solubility of **3a–e**, made the isolation and purification of these products very difficult. Chromatographically pure samples were obtained by preparative thin-layer chromatography (TLC) of **3a–e** on silica gel, transformation of the chlorides into picrates and recrystallization of the latter. However, elemental analysis of the purified picrates failed to confirm the expected formulae, due probably to low combustibility of the samples, as noticed for nitrogen-containing heterocycles.[12]

The mass-spectrometric analysis of the picrates was also ineffective in identifying of **3a–e**. While **3f** and Safranine T (3,7-diamino-2,8-dimethyl-5-phenazinium chloride), as well as the picrate from **3f**, produce as a main signal that of the molecular ion of the safranine base, no signal of this type was observed in the cases under study. The destabilizing effect of the hydroxyl groups seems to be especially strong when these are situated on both alkyl substituents; in the case of **3a**, all peaks observed were of low molecular number, indicating extensive fragmentation. With one hydroxyalkyl substituent (**3b**, **3d**) weak signals of higher mass number, corresponding to partial or full elimination of the substituents, appeared in the mass spectra of the respective picrates.

In the determination of the identity of the products, determination of the molecular weights of the corresponding picrates by a spectrophotometric procedure[13] was undertaken. In principle, the method used implies quantitative determination of the anion, which is one of the possible approaches in determination of basic dyes discussed in the literature.[14] The results obtained are shown in Table 1, in comparison with the expected values of molecular weights. In all cases, experimental and theoretical values coincide within the limits of error (±2%). This result confirms the constitution of **3a–e** expected on synthetic grounds.

Table 2 contains some physical characteristics of **3a–e** and of the respective picrates. Data for **3f** are included for comparison. The electron

TABLE 1
Molecular Weights of the Picrates Obtained from **3a–f** Determined by Measurements of Light Absorption at 360 nm With Molar Absorption Coefficient ε_M = 16 840

Picrate from	*Molecular formula*	*Molecular weight*		*Error (%)*
		Expected	*Found*	
3a	$C_{28}H_{25}N_7O_9$	604	609	+0·8
3b	$C_{27}H_{23}N_7O_8$	573	567	−1·0
3c	$C_{30}H_{29}N_7O_{11}$	664	665	+0·1
3d	$C_{28}H_{25}N_7O_9$	604	602	−0·3
3e	$C_{29}H_{27}N_7O_{10}$	634	628	−0·6
3f	$C_{28}H_{25}N_7O_7$	572	573	+0·2

absorption maxima presented are due to the cationic moieties. In the UV region, picrates and chlorides exhibit an absorption maximum at 275 nm. The picrates have their specific absorption maximum at 360 nm, which has been the wavelength chosen for spectrophotometric determination of the molecular weights. The spectroscopic characteristics of chlorides and picrates were recorded on the purest samples available. The molar absorption coefficients (ε_M) were measured with picrates, in view of their purity, and in ethanol because of their extremely low solubility in water. As seen in the table, picrate and chlorides exhibit the same absorption maximum in ethanol. Changing this solvent to water, a hypsochromic shift from 3 to 8 nm with **3a–e** occurs. Even greater shifts in the same direction were observed in the case of safranines with nonsubstituted amino groups: 12 nm with phenosafranine (3,7-diamino-5-phenylphen-

TABLE 2
Some Spectral and Chromatographic Characteristics of **3a–f** and the Respective Picrates

Substance	*Visible light absorption (λ_{max}, nm ($\varepsilon \times 10^{-4}$))*			*Rf TLC on silicagel, EtOH–conc. HCl (0·25% vol.)*
	In ethanol		*In water (chloride)*	
	picrate	*chloride*		
3a	554 (7·3)	554	549	0·56
3b	552 (7·5)	551	548	0·54
3c	556 (7·15)	556	548	0·50
3d	553 (7·3)	553	549	0·57
3e	555 (7·3)	556	550	0·61
3f	554 (7·8)	554	554	0·66

azinium chloride) and 14 nm (literature: 10 nm[15]) with Safranine T. In contrast, **3f** shows one and the same absorption maximum in both solvents.

The R_F values in Table 2 refer to TLC of the chlorides under the conditions used for their purification.

2 EXPERIMENTAL

Unless otherwise stated, commercially available reagent-grade substances were used in this work.

3.1 *N,N*-Dialkylanilines with hydroxyl groups in one or both of the alkyl substituents (1a–e)

A mixture of 1 mol aniline or N-monosubstituted aniline and (2·5 mol), 1·25 mol chlorohydrin respectively was refluxed for 4 h with gradual addition of 2, or 1 mol, respectively, of NaOH (10% solution in water). The isolation of the product depended on its solubility. In the case of **a**, **b** and **d**, two layers were formed on cooling the reaction mixture to room temperature. With **1a** and **1b**, extraction with diethyl ether was the most effective for isolation of the product, which was finally subjected to vacuum distillation. With **1d**, which crystallized readily, vacuum distillation was not necessary. By washing the organic layer with water, crystallization in ethanol and washing with a small amount of ether, a practically pure product was obtained.

In the case of **1c**, and **1d**, which are too soluble in water to be extracted, water was removed under vacuum, the oily residue was treated with absolute ethanol, the alcoholic solution was filtered to remove NaCl, ethanol was evaporated, and the residue was vacuum-distilled. Essentially pure **1a–e** (TLC on silica gel with ether as eluent) were thus obtained in 50 to 80% yields. On further purification, the physical characteristics described in the literature[10,16–19] were obtained.

3.2 *N,N*-Disubstituted *p*-nitrosoaniline hydrochlorides (2a–e)

These were obtained[20] by the addition of an aqueous solution of sodium nitrite to a solution of **1** in concentrated hydrochloric acid at low temperature. After 1 h stirring of the reaction mixture, further treatment depended on the solubility of the product. Compound **2b** precipitated on cooling overnight and was isolated by filtration (50% yield of hydrochloride crystals). On adjusting the reaction mixture to pH 8 by dropwise addition of 10% NaOH at 10 to 20°C, **2a** precipitated as a base, and after 1 h stirring, it was filtered off, washed with cold water and air-dried (81%

yield, m.p. 132–137°C, lit.[20] 137–138°C). Compounds **2c–e** could not be isolated and the respective reaction solutions were used in the next stage of synthesis after a spectrophotometric check of the yield of *p*-nitrosoaniline on a Unicam 800 UV/VIS spectrophotometer (Unicam, Cambridge, UK). A standard solution containing 1 g/litre **2f** was prepared using *N,N*-diethyl-*p*-nitrosoaniline (Fluka puriss; Buchs, Switzerland), conc. hydrochloric acid (Merck *pro analysi*; Darmstadt, Germany) and distilled water. Aliquot portions of this solution were diluted in 2 M hydrochloric acid to draw the calibration curve by absorption measurements at λ_{max} = 350 nm. The molar absorption coefficient was found to be $\varepsilon_M = 20\,600$. This value was used to determine the yield of **2c–e** by the absorption of aliquot samples of the reaction solutions diluted in 2 M HCl, measured at the absorption maximum ($\lambda_{max} \approx 350$ nm). In all three cases, nitrosation yields above 80% were thus found.

3.3 *N,N*-Dialkylsafranines containing OH groups in the alkyl substituents (3a–e)

To 400 ml of water, the following ingredients were consecutively added: **2** (0·027 mol), aniline 5·3 g (0·057 mol), $ZnCl_2$ 2·2 g (0·16 mol) and ZnO 5·5 g (0·067 mol). In the case of **3a**, the base of **2** and the equivalent amount of hydrochloric acid were consecutively added. In the case of **3c–e**, **2** was introduced as the hydrochloride solution obtained from the respective reaction mixture (see the preceding paragraph) after neutralization to pH 5 by 10% NaOH. The volume was adjusted to 400 ml, etc. The mixture was then heated, with stirring, at 80 to 90°C.

During the course of the reaction, the mixture changed colour from yellow to red, and finally violet (over 1 h). The consumption of the nitrosoaniline derivative was verified by a drop of the reaction mixture spread on to filter paper; when the yellow ring around the violet spot was no longer observed, $Na_2Cr_2O_7.2H_2O$, 5·4 g (0·18 mol), dissolved in 40 ml of H_2O was added and the mixture was heated for a further hour. Calcium carbonate 5·7 g (0·057 mol), was then cautiously added (small portions, stirring), the chromium salts were removed by filtration of the hot mixture, washed with hot water and the conjoint filtrate was treated according to the solubility of the product. The usual way of isolation of safranines, viz., by salting out (NaCl 250 g/litre, $ZnCl_2$ 5–10 g/litre) was still effective with **3a**, **3b** and **3d**, although the residues obtained were sticky, hardening with time. In the case of the more soluble **3c** and **3e**, water was removed under vacuum, the residue was treated with absolute ethanol and the mixture was filtered, giving **3** on evaporation of the solvent. About 4 g of crude **3a–e** was obtained, i.e. a yield of 35 to 40%.

3.3.1 Purification of 3a–e

Preparative TLC of **3** was performed on Merck Silica gel 60 G spread on 20 cm × 20 cm glass plates. Each plate was charged with 0·010 to 0·015 g of **3** dissolved in ethanol. The chromatograms were developed in ethanol–concentrated hydrochloric acid (0·25% vol.), after which the main coloured band was scraped off and extracted in ethanol; the procedure was repeated with the concentrated extract. Prior to TLC, the samples of **3a**, **3b** and **3d** were precipitated with ethyl acetate from ethanol to remove coloured impurities of lower polarity; for the same purpose, aqueous solutions of **3c** and **3e** were treated with chloroform and with ether.

3.3.2 Picrates from 3a–f

The ethanolic solutions obtained after twofold preparative TLC of **3a–e** were treated with an 8% ethanolic solution of picric acid to precipitate the respective picrates. A sample of **3f** was subjected to the same procedure after fivefold crystallization in water. After twofold crystallization in ethanol or ethanol–water, the picrates were found to be chromatographically pure (Merck silica gel precoated aluminium sheets, mobile phase ethanol–conc. HCl 0·25% vol.).

3.3.3 Mass spectra

All mass spectra were recorded on a JMS D 300 mass spectrometer by (1) ionization by electron impact (70 eV) or (2) chemical ionization (isobutane).

3a (picrate): **(1)** 229 (4·5%, M^+ of picric acid), 209 (5·4%), 199 (100%), 182 (4·5%); **(2)** 240 (4·5%), 224 (3·4%), 200 (100%), 180 (10·3%).

3b (picrate): **(1)** 314 (1%, elimination of $HOCH_2$ from M^+ of the base), 299 (0·5%), 287 (2·4%), 209 (4·5%), 199 (100%); **(2)** 224 (7·5%), 210 (19·4%), 200 (100%), 180 (31·3%), 170 (19·4%).

3d (picrate): **(1)** 299 (6%, elimination of $HOCH_2CH(OH)CH_2$), 286 (3·5%), 272 (1·7%), 258 (1·7%), 199 (55·2%), 59 (100%).

3f (picrate): **(1)** 342 (62·1%, M^+ of the base, which is 100% with the chloride), 327 (17·2%, elimination of CH_3), 298 (13·8%, the former fragment minus CH_3CH_2), 199 (100%).

Safranine T: **(1)** 314 (100%, M+ of the base), 286 (13·8%), 239 (27·6%).

3.4 Spectrophotometric characterization of 3a–f and the respective picrates

Measurements of λ_{max} were performed on a Unicam SP 800 spectrophotometer calibrated against holmium. A Beckman 5270 spectrophotometer (Fullerton, CA, USA) was used for more exact absorption

TABLE 3
Molar Absorption Coefficients of Picrates of Known Bases and of Picric Acid at 360 nm

Substance	*Sample m.p. (°C)*	*Lit. m.p. (°C)*	ε_M *found*
Piperidine picrate	152–153	151–152[21]	16 710
Morpholine picrate	148–151	146–148[22]	16 740
N,*N*-Bis(2-hydroxyethyl) aniline picrate	121–122	118[23]	17 070
Picric acid	122–123	122·5[24]	16 700

measurements (±1%), by which the molecular weights (Table 1) and the molar absorption coefficients ε_M (Table 2) were determined.

The hypsochromic shifts (in water) concerning Safranine T and phenosafranine (as mentioned in Section 2) are the differences between the absorption maxima measured: 533 nm (lit. 530) in EtOH against 519 nm (lit. 520) in H_2O for Safranine T and 532 nm in EtOH against 520 nm in water for phenosafranine.

3.5 Determination of the molecular weights of the picrates obtained from 3a–f

The spectroscopic method used[13] relies on the independence of the absorption of picrates in the 350 to 400 nm region on the respective bases. The molar absorption coefficients of three picrates of known bases were determined by absorption measurements at 360 nm (Table 3), and the average $\bar{\varepsilon}_M$ was used to determine the molecular weights of the picrates obtained from **3a–f**. The picrates of the known bases were obtained in the usual way (precipitation in ethanol) and purified by recrystallization. About 0·010 g samples of the picrates were quantitatively weighed, transferred into a 100 ml measuring flask, brought to volume in ethanol and diluted (1 : 25) in the same solvent. The absorbance *A* of the diluted solutions was measured in a 1 cm quartz cell. The average value obtained was $\bar{\varepsilon}_M = 16\,840$. The molecular weights of the picrates from **3a–f** were evaluated as $M = \bar{\varepsilon}_M C.1/A = 16\,840 C/A$, the absorbance being measured under the above experimental conditions, except for the dilution, which was 2 : 25 in this case.

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