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Synthesis and Properties of Some Naphtho (Quinolino)-Quinone Heterocyclic Dimethine Cyanine Dyes

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ABSTRACT

Some new asymmetrical naphtho-/quinolinoquinone [2, 3-d]-thiazole-4, 9-dione and/or [2, 3-e] oxadiazine 5, 10-dione dimethine cyanine dyes have been prepared. Their solvatochromic and spectral behaviour in buffer solutions has been utilized to select the optimum solvent and pH value at which they might be applied as photosensitizers. Some of the dyes have been tested for their antimicrobial activity.

1 INTRODUCTION

As an extension to our earlier work on the synthesis and properties of cyanine dyes,[1] some new heterocyclic quinone cyanine dye moieties have been synthesised in view of the applicability of such compounds as photosensitizers[2], textile dyes[3] and bactericidal agents.[4] Naphtho-/quinolino-quinone [2,3-*d*] thiazole-4,9-dione (**1a,1b**) and naphthoquinone [2, 3-*e*]-oxadiazine-5, 10-dione (**5**) were used as intermediates for the dye synthesis. Details are given in Scheme 1.

2 RESULTS AND DISCUSSIONS

2.1 Synthesis

The asymmetrical dimethine cyanine dyes (**3a–3e**) were obtained by selective SeO_2 oxidation of the previously prepared 2-methyl naphtho-/quinolino-quinone [2,3-*d*]thiazole-4,9-diones (**1a, 1b**) in dioxane to afford the 2-formyl

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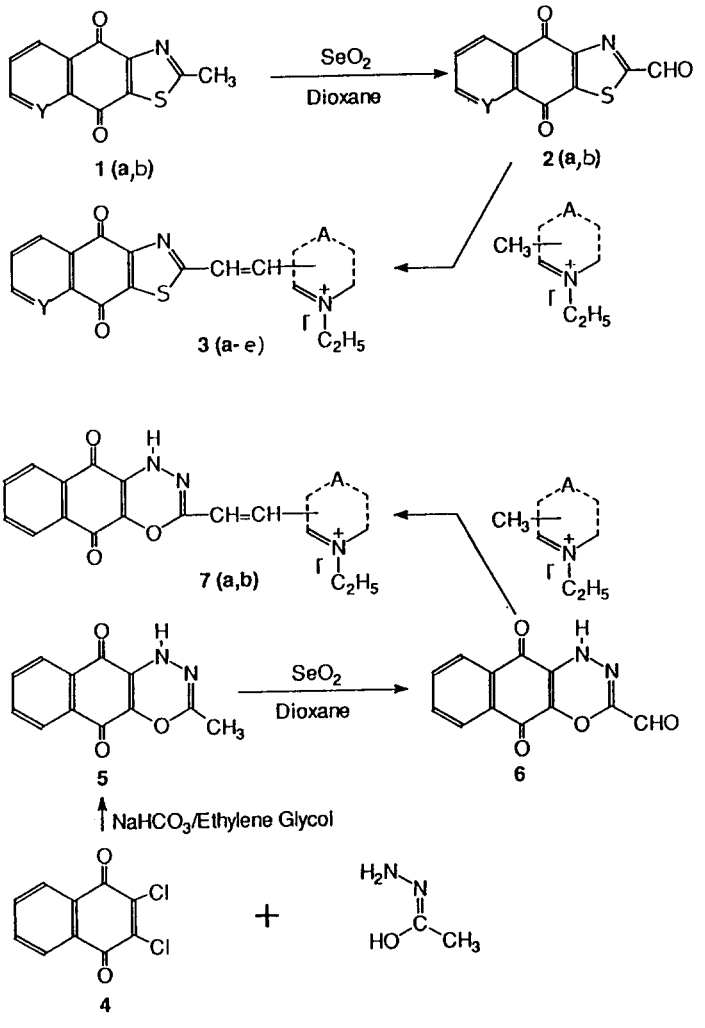

1(a,b) and 2(a,b) Y = CH a,
Y = N b.

3 (a-e)
Y = CH , A = 1-Ethyl pyridinium-2yl salt (a)
Y = CH , A = 1-Ethyl quinolinium-2yl salt (b)
Y = CH , A = 1-Ethyl quinolinium-4yl salt (c)
Y = CH , A = 1-Ethyl pyridinium-4yl salt (d)
Y = N , A = 1-Ethyl quinolinium-2yl salt (e)

7 (a,b) A = 1-Ethyl pyridinium-2yl salt (a)
A = 1-Ethyl quinolinium-2yl salt (b)

Scheme 1

derivatives (**2a, 2b**). Reaction of **2a, 2b** with methyl quaternary salts under base catalysis conditions then gave the corresponding asymmetrical dimethine cyanine dyes (**3a–3e**). 2-Methyl naphthoquinone [2, 3-*e*]-oxadiazine-5,10-dione (**5**) was also prepared as intermediate for the synthesis of other asymmetrical dimethine cyanines incorporating a naphthoquinone [2, 3-*e*] oxadiazine moiety. It was obtained by interaction of 2, 3 dichloro-1,4-naphthoquinone (**4**) with acetic acid hydrazide in the presence of ethylene glycol as solvent and sodium bicarbonate.[6] Selective SeO_2 oxidation of **5** gave the corresponding 2-formyl derivative (**6**) in satisfactory yield and further reaction of (**6**) with methyl quaternary salts gave the asymmetrical dimethine cyanine dyes **7a** and **7b**.

2.2 Spectra and solvatochromic behaviour

Electronic spectra of the dimethine cyanines in 95% ethanol showed absorption bands which became more intense and with a strong bathochromic shift on increasing the conjugation of the quaternary heterocyclic residue (A). Thus, the absorption spectra of dyes **3a** and **7a**, which contain a pyridinium salt moiety showed absorption to be hypsochromically shifted by 255–275 nm and 230 nm respectively compared with the analogous dyes **3b** and **7b** containing the quinolinium moiety (Table 1). This can be attributed to the more extensive π-delocalisation within the respective quaternary heterocyclic system.

Additionally, changing the linkage position of the heterocyclic quaternary residue from a 2yl-salt to a 4yl-salt resulted in a red shift. Thus, comparison of **3b** and **3c** or of **3a** and **3d** shows that the 4yl-linkage not only results in a bathochromic shift of 5–10 nm respectively, but also enhances the band intensity (Table 1).

The absorption bands of dye **3e**, which contains a quinolinoquinone nucleus was hypsochromically shifted with respect to the naphthoquinone analogue (**3b**); this can be attributed to the antagonistic effect of the N-atom in the quinolinoquinone nucleus with respect to electron mobility in the dye system.

Comparison of the spectrum of dye **3b**, containing a naphthoquinone [2,3-*d*] thiazole-4, 9 dione residue, with that of **7b**, which contains a naphthoquinone [2,3-*e*] oxadiazine-5,10-dione residue, shows that the absorption of the former is the more bathochromic, presumably due to the greater electron-withdrawing ability of the oxadiazine nucleus.

The absorption spectra of some selected dyes in different solvents were examined in order to evaluate their solvatochromic behaviour. Thus, dyes **3b** and **3c** were investigated in solvents of different electric permittivity, viz water (78·54), dimethylformamide (DMF) (36·70), ethanol (24·3), chloroform (4·806), carbon tetrachloride (2·238) and dioxane (2·209)[7] (Table 2).

TABLE 1
Characterization data for Dimethine Cyanine Dyes

Comp. no.	*M.p. (°C)*	*Yield (%)*	*Colour*	*Molecular formula (Mol. wt.)*	*Analytical data Calcd (found)*			*Absorption in 95% ethanol*	
					C	*H*	*N*	$\lambda_{max}(nm)$	$\epsilon_{max}(cm^2\,mole^{-1})$
3a	180	13	Deep red	$C_{20}H_{15}N_2O_2SI$ (474)	50·63 (50·03)	3·16 (3·30)	5·91 (5·87)	315, 425	5700, 3000
3b	195	53	Deep violet	$C_{24}H_{17}N_2O_2SI$ (524)	54·96 (54·83)	3·24 (4·09)	5·34 (5·24)	570, 610-615, 700	8600, 13600 5200
3c	245	39	Brown green	$C_{24}H_{17}N_2O_2SI$ (524)	54·96 (54·93)	3·24 (3·22)	5·34 (5·39)	460, 582, 705	10400, 6800, 4200
3d	105	9·4	Red	$C_{20}H_{15}N_2O_2SI$ (474)	50·63 (50·41)	3·16 (3·03)	5·91 (5·88)	435	5460
3e	205	14	Deep violet	$C_{23}H_{16}N_3O_2SI$ (525)	52·57 (52·42)	3·05 (3·02)	8·00 (8·09)	430, 539, 620	5700, 8200, 2400
7a	240	42	Reddish-brown	$C_{20}H_{16}N_3O_3I$ (473)	50·74 (50·18)	3·38 (4·05)	8·88 (8·60)	360	5800
7b	235	30	Violet	$C_{24}H_{18}N_3O_3I$ (523)	55·06 (55·32)	3·44 (3·93)	8·03 (8·21)	515, 555, 590	4600, 4000, 2600

In ethanolic medium, these two dyes show three absorption bands in the visible region. The bands located above 400 nm are relatable to electronic transitions involving the whole molecule and are associated with intramolecular charge transfer.[8] This charge transfer (CT) appears to originate from the thiazole sulphur atom as a source to either the positively charged heterocyclic quaternary (N) atom or the oxygen of the carbonyl quinone as a sink.[9]

From the data in Table 2, it is apparent that the bands corresponding to n-π^* and CT transitions exhibit a blue shift in ethanolic medium relative to DMF, dioxane, chloroform and carbon tetrachloride which can be attributed to the following:

(a) the red shift occuring in DMF relative to ethanol is a result of the increased solvent polarity of DMF.
(b) the high blue shift in ethanol relative to dioxane, chloroform and carbon tetrachloride is a result of the solute–solvent interaction through intermolecular hydrogen bond formation.

The H-bond formation between ethanol and the lone pair of electrons of the thiazole nitrogen atom or of the oxygen atom of the carbonyl quinone slightly decreases the electron density in the thiazole nucleus and consequently decreases to some extent the electron mobility through the conjugated pathway.

On the other hand, the CT transition of **3b** and **3c** in water shows an unexpected hypsochromic shift relative to ethanol, and this can be ascribed to the interaction of water molecules with the thiazole hetero atoms or the naphthoquinone oxygen atoms.

2.3 Acid-base properties

Ethanolic solutions of the dimethine cyanine dyes show a permanent colour in basic medium, which discharges on acidification. Their spectral behaviour in different universal buffer solutions was therefore evaluated in order to investigate their acid-base properties and suitable pH when applied as photosensitizers.

The spectra of dyes **3b** and **7b** in aqueous buffer solutions of different pH values (1·35–12·5) show regular changes with increasing pH of the medium, especially in the n-π^* and CT bands (Table 3). It was observed that the absorption was bathochromically shifted in alkaline medium and hypsochromically shifted in acidic medium. The bathochromic shift is essentially due to the relatively increased negative charge densities of the thiazole and oxadiazine nuclei in these compounds and the hypsochromic shift is attributable to protonation of the thiazole and oxadiazine nitrogen or oxygen atoms in an acidic medium.

TABLE 2
Electronic Absorption Spectral Data for the Dimethine Cyanines (**3b** and **3c**)

Comp. no.	*Water*		*DMF*		*Ethanol*		$CHCl_3$		CCl_4		*Dioxane*	
	λ_{max} (*nm*)	ϵ_{max} (m^{-1} cm^2)	λ_{max} (*nm*)	ϵ_{max} (m^{-1} cm^2)	λ_{max} (*nm*)	ϵ_{max} (m^{-1} cm^2)	λ_{max} (*nm*)	ϵ_{max} (m^{-1} cm^2)	λ_{max} (*nm*)	ϵ_{max} (m^{-1} cm^2)	λ_{max} (*nm*)	ϵ_{max} (m^{-1} cm^2)
	—	—	575	8400	570	8600	572	8000	600*sh*	7800	573	7800
3b	600	6400	620	12400	615	13600	620	11200	640	8600	621	10000
	632	7200	715	4200	700	5200	705	4400	705	4000	715	3600
	460	9600	465	12000	460	10400	465	4200	470	8800	465	10600
3c	—	—	585	6400	582	6800	591	5600	590	5200	585	5800
	—	—	709	2800	705	4200	712	3200	715	2800	712	4600

TABLE 3
Absorbance (λ_{max}) for Dimethine Cyanines **3b** and **7b** in Different Universal Buffer Solutions

λ_{max} (*nm*) \ *pH*		*1·35*	*1·50*	*3·12*	*3·95*	*4·98*	*5.48*	*5·90*	*6·50*	*7·36*	*8·37*	*9·41*	*10·45*	*11·85*	*12·50*	*pKa*
Abs.	**3b** λ_{570}	0·04	0·06	0·24	0·42	0·50	0·56	0·64	0·64	0·60	0·56	0·64	—	—	—	3·2 7·3
	7b λ_{555}	0·10	0·08	0·18	0·26	0·32	0·36	0·38	—	0·30	—	0·52	0·52	0·48	0·44	3·7 6·6 8·4

The acid dissociation or protonation constants of **3b** and **7b** were determined in order to ascertain the optimum pH for possible application of the dyes as photosensitizers. These values were measured by plotting the variation of absorbance with pH, using the spectrophotometric half-height limiting absorbance and Collete methods.[10] The effectiveness of the compounds as photosensitizers increases when they are present in the ionic forms which have higher planarity.[8]

The spectra at pH > 1·50 for **3b** and at pH > 3·12 for **7b** represent the absorption of the ionic (non-protonated) forms, whereas those at lower pH are due to the non-ionic (protonated) species. On decreasing the pH of the medium, the absorbance of the band due to the ionic or non-protonated forms decreases in intensity, whereas that of the non-ionic or protonated forms increases. The pK_a values of compound **7b** (3·7, 6·6, 8·4) are higher than those of **3b**, pK_a = 3·2, 7·3 (Table 3). This can be explained in terms of the higher planarity and greater stability of the thiazole nucleus in **3b**, which favours intramolecular charge transfer. This results in a lower negative charge density on the nucleus, resulting in weaker bonding of the proton. Dyes of this type are therefore concluded to be more potentially sensitive as photosensitizers in acidic and basic media at pH > 1·50.

2.4 Biological activity

Selected dyes (**3b, c, e** and **7b**) were chosen to study biological activity relationships in these compounds. The dimethine cyanines incorporating a quinoline moiety 2-or 4-linked in the naphthoquinone [2,3-*d*]-thiazole nucleus, i.e. **3b, c**, had some activity for all the bacteria tested, but showed fungicidal activity only on *Alternaria sp.*.

Replacing the naphthoquinone[2,3-*d*]thiazole nucleus in dye **3b** by the quinolinoquinone[2,3-*d*]thiazole nucleus in dye **3e** resulted in only slight bactericidal properties and no fungicidal activity. However, the naphthoquinone [2,3-*e*]oxadiazine-5,10-dione dimethine cyanine dye (**7b**) had strong antimicrobial activity, much higher than that of the naphthoquinone [2,3-*d*]-thiazole-4,9-dione analogue **3b**. (Table 4).

3 EXPERIMENTAL

All melting points are uncorrected. Elemental analyses were carried out at the microanalytical centre of Cairo University.

IR spectra were determined on a Perkin Elmer Infrared 127 Spectrophotometer (Cairo University) and electronic spectra on a Shimadzu UV VIS

TABLE 4
Antimicrobial Screening of Dimethine Cyanine Dyes (**3b,c,e & 7b**)

Organism used	*Compound tested (100 ppm)*			
	3b	**3c**	**3e**	**7b**
A. Bacterial species:				
1–*Bacillus Stearot-hermophillus*	++	++	++	+++
2–*Serratia Sp.*	++	++	+	++
3–*Pseudomonas Sp.*	++	+	+	++
B. Fungi. species:				
1–*Penicillium Sp.*	–ve	–ve	–ve	+
2–*Alternaria Sp.*	++	+	–ve	+

+++ (high activity), ++ (medium activity), + (lower activity) and –ve (no activity).

240 spectrophotometer (Faculty of Science, Aswan). The ^{1}H NMR spectra were obtained using an EM-390 Spectrometer (Cairo University).

3.1 Syntheses

*3.1.1 Synthesis of 2-methyl naphtho-/quinolino-quinone [2,3-*d*]-thiazole-4,9-dione (***1a, b****)*
Compounds **1a** and **1b** were prepared in a way similar to that described in Ref. 5.

*3.1.2 Synthesis of 2-methyl naphthoquinone [2,3-*e*] oxadiazine-5, 10-dione (***5****)*
A mixture of an ethylene glycol solution of 2,3-dichloro-1,4-naphthoquinone (**4**, 0·01 mole) and mono-acetyl hydrazine (0·01 mole) was refluxed for 1 h; a reddish-brown solution resulted. $NaHCO_3$ (5 ml of 20% aq. solution) was added and refluxing continued for 2 h. The reaction mixture was cooled, diluted with aqueous ethanol and the product was collected and crystallized from acetic acid to give compound **5** as brown crystals; m.p. 170°C, yield 63%. Data for $C_{12}H_8N_2O_3$: Calcd (found): C, 63·16 (63·38); H, 3·51 (3·02); N, 12·28 (12·00),

IR (KBr): 3500–3300 (NH), 1680 (quinone C=O), 1600 (C=N), 1170–1070 (C-O-C cyclic) and 760 cm^{-1} (benzene disubstituted).
^{1}H NMR δ ppm: in $CDCl_3$:8·3–7·4 (m,4 H,Ar (het)-H) 2·9–2·1 (m, 4H for NH and CH_3 groups).

*3.1.3 Synthesis of 2-formyl naphtho/quinolino quinone [2,3-*d*] thiazole-4,9-dione (***2a, b***) and/or naphthoquinone-[2,3-*e*]oxadiazine-5,10-dione (***6***)*
2-Methyl naphtho/quinolino-quinone [2,3-*d*] thiazole-4,9-dione and/or [2,3-*e*] oxadiazine-5,10-dione (0·01 mole) were refluxed for 8–15 h with SeO_2 (0·02 mole) in 20 ml dioxane. The reaction mixture was filtered hot from selenium metal. The filtrate was allowed to cool and refiltered. The filtrate was concentrated and the separated product was filtered off after cooling, washed, and crystallized from ethanol.

Data for **2a**, Y=CH; $C_{12}H_5NO_3S$. Calcd (found): C, 59·26 (59·31); H, 2·05 (2·01); N, 5·76 (5·79); buff crystals, m.p. 135°C, yield 50%. IR: 1615 (νC=N) of thiazole, 1120–1110 (ν-thiazole C–S–C).

Data for **2b**, Y=N, $C_{11}H_4N_2O_3S$. Calcd (found) C, 54·098 (53·5); H, 1·64 (1·44); N, 11·48 (11·57); green crystals, m.p. 120°C, yield 21%.

Data for **6**, $C_{12}H_6N_2O_4$. Calcd (found) C, 59·50 (59·00); H, 2·48 (3·00); N, 11·57 (11·99), brown crystals, m.p. 191°C, yield 42%. IR (νKBr cm^{-1}) 3500 (NH), 1740 (νC=0 for quinone), 1680 (ν CHO), 1600 (νC=N), 1140–1080 (C–O–C cyclic) and 760–720 (benzene disubstituted). ^1H NMR ($CDCl_3$) δ ppm: 7·6–7·1 (m, 4H, Ar-H), 9·5 (s, 1H, CHO), 3·6 (s, 1H, NH exchangeable with D_2O).

*3.1.4 Synthesis of asymmetrical naphtho/quinolino-quinone[2,3-*d*]thiazole-4,9-dione and/or [2,3-*e*] oxadiazine-5,10-dione 2[2(4)]-dimethine cyanine dyes (***3a–e*** & ***7a, b***)*
Equimolar amounts of **2a**, **2b** or **6** and the appropriate 2-or 4-methyl quaternary salt (0·01 mole) were dissolved in ethanol (30 ml), and piperidine (3–5 drops) added. The reaction mixture was refluxed for 6–8 h, filtered hot, concentrated, cooled and acidified with acetic acid. The precipitated products after dilution with water were collected and crystallized from aqueous ethanol. Relevant data are shown in Table 1.

3.2 Solvatochromism and acid-base properties

The solvents used were of spectroscopic grade or were purified according to the recommended methods.[11]

A stock solution (10^{-3}M) of the dyes was diluted to appropriate volume in order to obtain the required concentrations. A series of buffer solutions with pH values ranging from 1·35 to 12·5 was prepared as recommended by Britton.[12]

The appropriate aliquot of the stock solution was added to 5 ml of buffer solution and made up to 10 ml with distilled water; all pH values were checked before spectral measurements.

3.3 Biological activity

Anti-microbial activity of selected dyes was tested using two methods.

3.3.1 Filter paper disc method (Ref. 13)
All the compounds used were dissolved in ethylene glycol. The bacteria used in the experiments were previously found among several soil micro-organisms tested to be susceptible (see Table 4).

3.3.2 Bacterial suspension
This was prepared by adding 10 ml of sterile distilled water to a ten-day-old culture of the test bacteria grown on nutrient agar (NA).[14] (Beef extract 10 g l^{-1}, peptone 5 g l^{-1} sodium chloride 5 g l^{-1}, Agar 17 g l^{-1}, pH $\simeq$ 7·4). One-millilitre aliquots of the bacterial suspension were added to NA Petri dishes. The excess liquid was removed and two filter paper discs (6 mm diameter) containing the test compound were placed on each plate. Plates were then incubated at 37°C and the diameter of the inhibition zones was measured after 24 h. These experiments were repeated three times and the results were averaged and listed in Table 4.

REFERENCES

1. El-Maghraby, M. A., Koraiem, A. I. M. & Khalafalla, A. K., *J. Chem. Tech. Biotechnol.*, **33A** (1983) 71–9.
2. Osman, A. M. & Khalil, Z. H., *J. Appl. Chem. Biotechnol.*, **25** (1975) 683.
3. Kendall, J. D. & Duffin, G. F. to Ilford Ltd, *British Patent* 432628, 1993.
4. Opanasenko, E. P., Palli, G. K. & Prisyazhynuk, P. V., *Kim. Farm. Zh.*, **8** (1974) 18.
5. Hammam, A. S. & Bayoumy, B. E., *J. Collection Czechoslovak Chem. Commun.*, **50** (1985) 71–9.
6. Hammam, A. S. & Osman, A. M., *J. Prakt Chemie*, Band 319, Heft 2 (1977) 254–8.
7. *CRC Handbook of Chemistry and Physics*, 61st edn, 1980–81, p. 56.
8. Mahmoud, M. R., Khalil, Z. H. & Issa, R. M., *Acta Chim. Acad. Sci. Hung.*, **87** (2) (1975) 121.
9. Bhutra, M. P. & Tandon, S. P., *Z. Naturforsch.*, **25b** (1970) 36.
10. Collete, J. C., *Ann. Chim. (France)*, **5** (1960) 415.
11. Reddick, J. A. & Banger, W. B., *Techniques of Chemistry*, ed. A. Weissberger, 3rd edn. Wiley, 1970, Vol. 2.
12. Britton, H. T. S., *Hydrogen Ions*, 4th edn. Chapman and Hall, London, 1952, p. 313.
13. Loo, Y. H., Skell, P. S., Thorabery, H. H., Ehrlich, J., Meguire, J. L., Savage, G. M. & Sylvester, J. C., *J. Bact.*, **50** (1954) 701.
14. Knudsen, E. T. & Rolinson, G. W., *Lancet* (1945) 1105–9.