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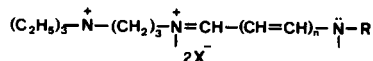
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A series of heterocyclic cyanine dyes were prepared. Unsymmetrical dyes showed self-micellizing properties due to the presence of two positive charges and of a long alkyl chain. Symmetrical dyes, containing three positive charges and not containing the hydrophobic chain, did not give rise to micelles. The physical properties of the dyes and their spectra were briefly discussed. Cationic (HTAB) and anionic (SDS) surfactants gave strong interactions with surface active dyes, leading to deaggregation and solvation phenomena.

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In part one of this work we discussed some properties of heterocyclic cyanine dyes having one or two long alkyl chains including their interactions with anionic and cationic surfactants [2].

Recently, we have reported on the preparation of some amphiphilic cyanines [3-5] and now we extend our work to a new series of dyes. The choice of the general structure I is the result of our previous findings that, to obtain self-micellizing dyes, bis cationic structures are preferable and



sometimes necessary. The introduction of a triethylammonium chain proved to be a satisfactory way towards achieving this goal. In the general structure I, the nitrogen

atoms belong to heterocyclic rings (pyridine, quinoline, benzoxazole, benzothiazole), where *n* is 2, 3 or 4, X<sup>-</sup> is bromide or nitrate, and R is *n*-hexadecyl. The individual structures are detailed in Tables 1 and 2. As an example, the principal steps in the synthesis of symmetrical and unsymmetrical dyes are indicated in the Scheme. Only the unsymmetrical dyes exhibit amphiphilic properties.

The salts **1-4**, according to their structures of bis charged cations, are highly soluble in water. Their behaviour is closely related to the short chain counterparts.

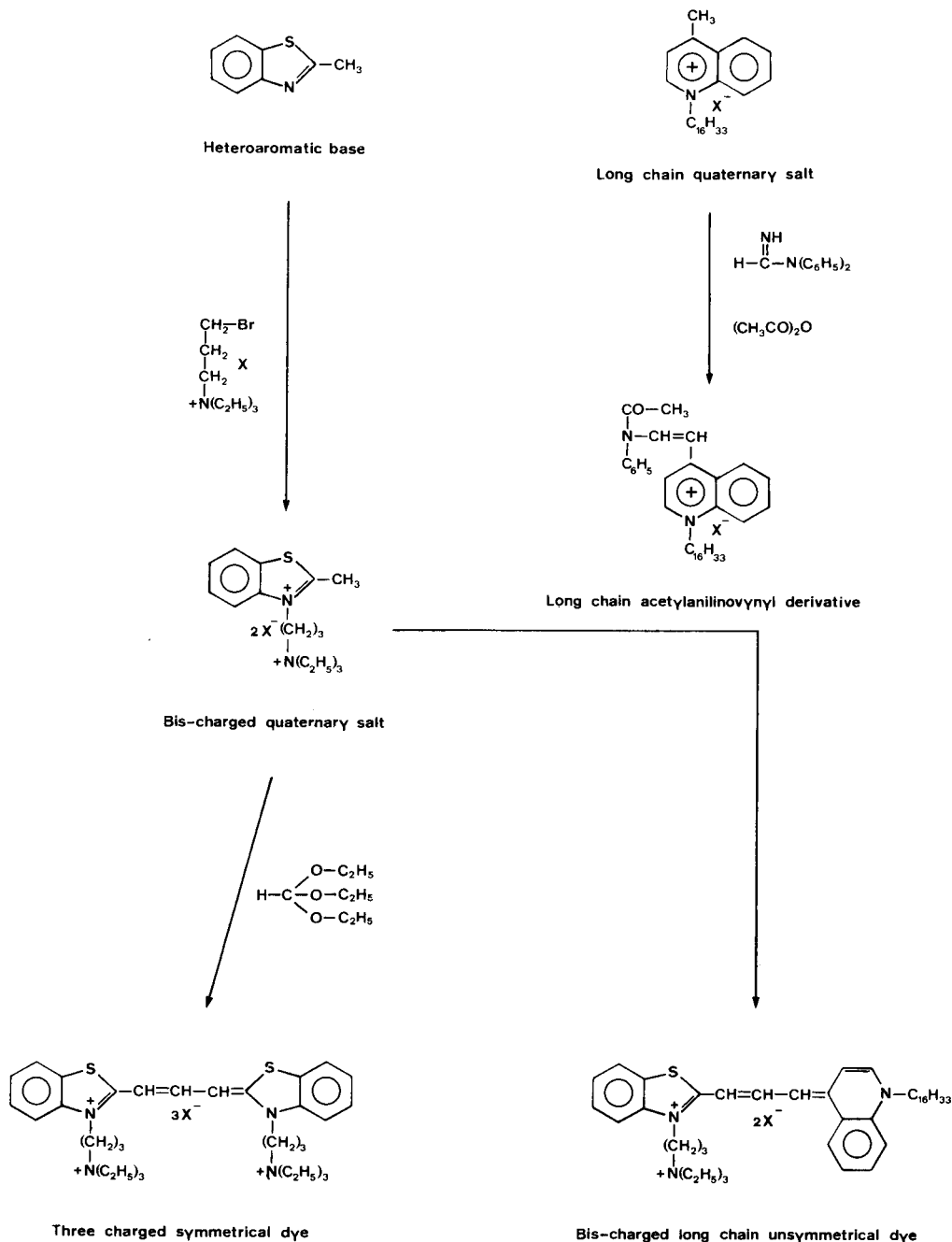
The nmr spectra show complex patterns in both the aliphatic and aromatic regions. The methylene protons of the triethylammonium groups are involved in complex signals, whereas the methyl protons appear as clearly detectable triplets. Other triplets at lower fields are assigned to the methylene protons directly linked to the heterocyclic

Table 1

Characterisation Data of Bis-quaternary Salts

Compound number	X =	Yield %	Mp °C	Empirical formula	Elemental Analyses			Electronic absorption spectra λ max nm (log ε) [a]	NMR (δ)	
					Calcd./Found	C	H		N	≥C-CH <sub>3</sub> [b]
1 [d]	Br <sup>-</sup>	72.1	232-234	C <sub>15</sub> H <sub>28</sub> Br <sub>2</sub> N <sub>2</sub>	45.47	7.12	7.07	256 (3.62)	2.63	4.75
					45.31	7.23	6.98			
2	Br <sup>-</sup>	73.3	208-210	C <sub>19</sub> H <sub>30</sub> Br <sub>2</sub> N <sub>2</sub>	51.13	6.78	6.28	314 (3.93)	3.17	5.82
					51.25	6.62	6.33			
3	Br <sup>-</sup>	55.6	192-193	C <sub>17</sub> H <sub>28</sub> Br <sub>2</sub> N <sub>2</sub> S	45.15	6.24	6.19	278 (3.85)	3.46	4.96
					45.00	6.33	6.04			
4	Br <sup>-</sup>	54.7	213-215	C <sub>17</sub> H <sub>28</sub> Br <sub>2</sub> N <sub>2</sub> O	46.81	6.47	6.42	277 (3.50)	3.60	5.30
					47.03	6.39	6.53			

[a] The λ max and log ε values corresponding to the most intense peak of the long-wavelength band (solvent ethanol). [b] Methyl protons linked to the azine and azole rings. [c] Methylene protons directly linked to the heteroaromatic nitrogens. [d] See also ref [3].



nitrogen. The methyl groups in the azine or azole rings give sharp singlets downfield from the corresponding mono charged salts. This indicates a sensitivity of the chemical shifts to the electron withdrawing effect of the triethylammonium group.

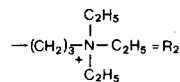
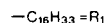
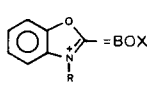
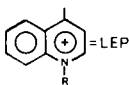
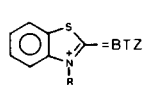
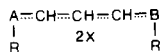
The melting points of the unsymmetrical dyes **5-11** lie distinctly below those of the corresponding starting salts **1-4** owing to the introduction of a long alkyl chain which modifies the ionic interactions between the molecules in the crystalline lattice. The symmetrical dyes **12-14** practically correspond to a redoubling of the starting salts and,

as a consequence, the gap in the melting points is very small.

The absorption maxima of the dyes in ethanol are consistent with predictable data for the classic cyanine-type chromogen and available in the case of dyes with simple substituents [7]. The presence of unusual structure features (*eg.* the triethylammonium cation and the hydrophobic chain) is, however, accompanied by a general bathochromic shift probably arising from different interactions of the dyes with the solvent.

The spectra of the dyes in water follow the general beha-

Table 2  
Characterisation Data of Cyanine Dyes



Compound number	R	Structure [a]				Yield %	Mp °C	Empirical formula	Elemental Analyses			Electronic absorption spectra λ max nm (log ε) [b]
		A	B	R	X				Calcd./Found	C	H	
5	R <sub>1</sub>	BTZ	LEP	R <sub>2</sub>	NO <sub>3</sub> <sup>-</sup>	14.8	196-198	C <sub>44</sub> H <sub>67</sub> N <sub>5</sub> O <sub>6</sub> S	66.55 66.37	8.50 8.61	8.82 8.73	639 (5.14)
6	R <sub>1</sub>	BTZ	BTZ	R <sub>2</sub>	NO <sub>3</sub> <sup>-</sup>	22.1	186-188	C <sub>42</sub> H <sub>65</sub> N <sub>5</sub> O <sub>6</sub> S <sub>2</sub>	63.05 63.17	8.19 8.08	8.75 8.75	562 (5.06)
7	R <sub>1</sub>	BTZ	BOX	R <sub>2</sub>	NO <sub>3</sub> <sup>-</sup>	70.1	124-126	C <sub>42</sub> H <sub>65</sub> N <sub>5</sub> O <sub>7</sub> S	64.34 64.19	8.36 8.35	8.93 9.08	523 (5.01)
8	R <sub>1</sub>	LEP	PYR	R <sub>2</sub>	Br <sup>-</sup>	46.0	209-211	C <sub>42</sub> H <sub>67</sub> Br <sub>2</sub> N <sub>3</sub>	65.19 65.02	8.73 8.81	5.43 5.37	659 (4.76)
9	R <sub>1</sub>	LEP	LEP	R <sub>2</sub>	Br <sup>-</sup>	13.5	129-131	C <sub>46</sub> H <sub>69</sub> Br <sub>2</sub> N <sub>3</sub>	67.06 67.19	8.44 8.37	5.10 5.01	711 (5.25)
10	R <sub>2</sub>	BTZ	LEP	R <sub>1</sub>	Br <sup>-</sup>	22.5	143-145	C <sub>44</sub> H <sub>67</sub> Br <sub>2</sub> N <sub>3</sub> S	63.68 63.69	8.14 8.23	5.06 5.15	626 (5.00)
11	R <sub>2</sub>	BOX	LEP	R <sub>1</sub>	Br <sup>-</sup>	5.0	136-138	C <sub>44</sub> H <sub>67</sub> Br <sub>2</sub> N <sub>3</sub> O	64.94 64.73	8.30 8.28	5.16 5.02	589 (4.55)
12	R <sub>2</sub>	LEP	LEP	R <sub>2</sub>	Br <sup>-</sup>	11.1	203-205	C <sub>39</sub> H <sub>57</sub> Br <sub>3</sub> N <sub>4</sub>	57.01 57.22	6.99 7.04	6.82 6.71	711 (5.05)
13	R <sub>2</sub>	BTZ	BTZ	R <sub>2</sub>	Br <sup>-</sup>	68.7	228-230	C <sub>35</sub> H <sub>53</sub> Br <sub>3</sub> N <sub>4</sub> S <sub>2</sub>	50.43 50.37	6.41 6.43	6.72 6.66	566 (4.96)
14	R <sub>2</sub>	BOX	BOX	R <sub>2</sub>	Br <sup>-</sup>	11.6	182-184	C <sub>35</sub> H <sub>53</sub> Br <sub>3</sub> N <sub>4</sub> O <sub>2</sub>	52.45 52.40	6.66 6.67	6.99 7.04	489 (4.53)

[a] The heterocyclic nuclei are alternatively charged according to the extreme resonance structures: R-A<sup>+</sup>-CH=CH-CH=B-R ↔ R-A=CH-CH=CH-B<sup>+</sup>-R.

[b] Solvent ethanol.

Table 3  
Spectral and Tensiometric Data of Cyanine Dyes

Compound number	λ max (log ε) in ethanol	λ max (log ε) in water		γ (cmc) (dyne/cm)	log cmc	A min (Å <sup>2</sup> )
		2 × 10 <sup>-4</sup> M	2 × 10 <sup>-6</sup> M			
5	639 (5.14)	566 (4.62)	635 (4.87)	60	-4.398	67
6	562 (5.06)	528 (4.59) 559 (4.57)	552 (4.83)	48	-4.065	60
7	523 (5.01)	496 (4.47) 525 (4.45)	519 (4.80)	46	-4.097	76
8	659 (4.76) 712 (4.38)	654 (4.63) 611 (4.62)	651 (4.79)	53	-4.030	72
9	711 (5.25) 653 (4.60)	639 (4.74) 700 (4.67)	703 (4.81) 651 (4.63)	53	-4.097	55
10	626 (5.00)	574 (4.66)	612 (4.85)	51	-4.176	84
11	589 (4.55)	565 (4.58)	585 (4.75)	49	-4.198	51
12	711 (5.05)	701 (4.93)	701 (4.93)			
13	566 (4.96)	557 (4.93)	557 (4.93)			
14	489 (4.55)	482 (4.55)	482 (4.55)			

viour shown in Figure 1 (dye **6**). In very dilute solution the main absorption is accompanied by an unresolved shoulder at shorter wavelength as also observed in alcoholic media. Increasing the concentration, leads to a decrease in the intensity of the transition for unaggregated species, while the other absorptions are consequently strengthened from the prevalence of aggregates; an isosbestic point is

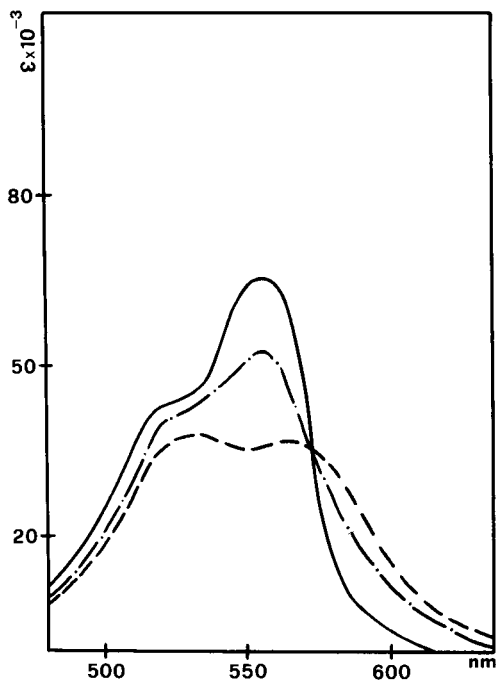


Figure 1. Spectra of dye No. **6** in water: — ( $5 \times 10^{-6}M$ ); -.-.- ( $1 \times 10^{-4}M$ ); --- ( $5 \times 10^{-4}M$ ).

evident (*cf.* Figure 1). Under no circumstances are J aggregates observable. The aggregation results in the formation of micelles, as clearly shown by the sharp variation of the slope in the  $\gamma/\log c$  plots which indicate that a cmc is reached (Figure 2). Using the Gibbs equation (1), where  $\gamma$  is the surface tension and  $m$  is a constant ( $m = 2$ ), one

$$\Gamma = -\frac{1}{mRT} \left( \frac{\delta\gamma}{\delta \ln c} \right)_T \quad (1)$$

can evaluate the surface excess  $\Gamma$ . The reciprocal value of  $\Gamma$  represents the surface requirement per molecule  $A$  (in  $\text{\AA}^2$ ).

Table 3 reports spectral and tensiometric data of dyes **5-11**.

The absence of a long alkyl chain in dyes **12-14** renders them surface inactive and their tensiometric data are consequently omitted. The Beer-Lambert law is obeyed and the spectral patterns are unaltered with changes in concentration. Only a slight hypsochromic shift is detected

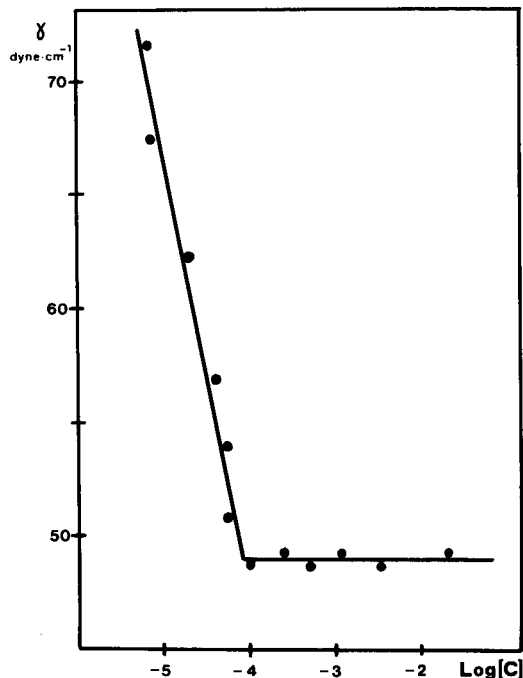


Figure 2. Surface tension ( $\gamma$ ) as a function of the logarithm of the molar concentration of dye No. **6**.

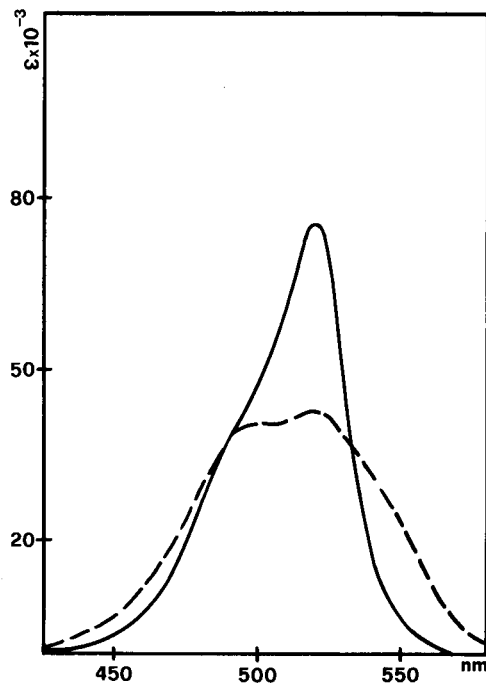


Figure 3. Spectra of dye No. **7** in water: — ( $2 \times 10^{-6}M$ ); --- ( $2 \times 10^{-4}M$ ).

upon changing from alcohol to aqueous media; a similar behaviour, linked to a different degree of solvation, is also shown by the amphiphilic dyes in dilute solutions.

Three dyes were selected for looking into their interac-

tions with organized systems. Dyes **7** and **10** were chosen as representative of self-micellizing structures and dye **13** of not aggregating ones. Cationic (hexadecyltriethylammonium bromide = HTAB) and anionic (sodium dodecylsul-

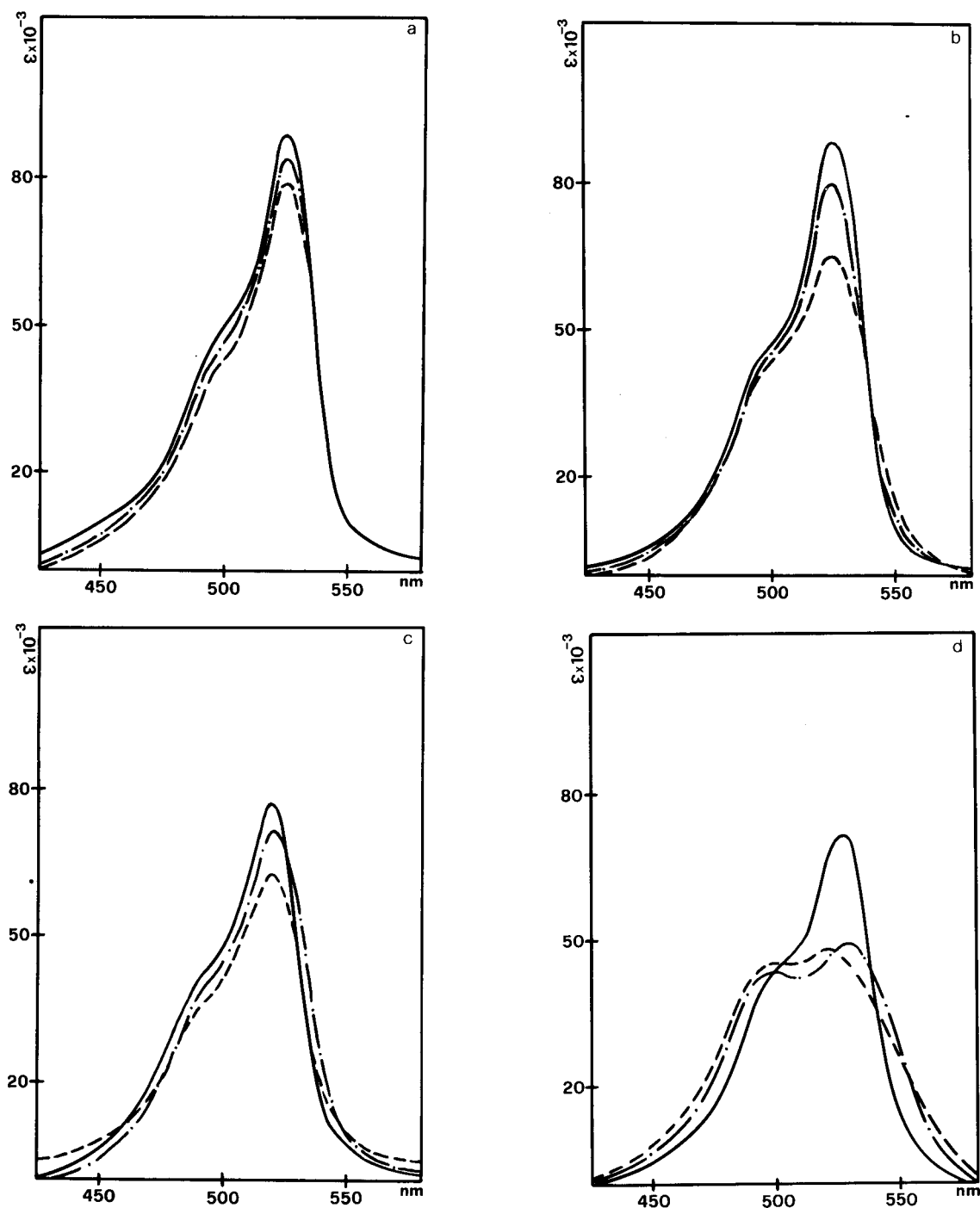


Figure 4. Spectra of dye No. 7: (a) fixed cyanine ( $2 \times 10^{-6}M$ ); variable SDS: — ( $80 \times 10^{-3}M$ ); -·-·- ( $8 \times 10^{-3}M$ ); --- ( $4 \times 10^{-3}M$ ); (b) fixed cyanine ( $2 \times 10^{-4}M$ ); variable SDS: — ( $80 \times 10^{-3}M$ ); -·-·- ( $8 \times 10^{-3}M$ ); --- ( $4 \times 10^{-3}M$ ); (c) fixed cyanine ( $2 \times 10^{-6}M$ ); variable HTAB: — ( $7 \times 10^{-3}M$ ); -·-·- ( $7 \times 10^{-4}M$ ); --- ( $7 \times 10^{-6}M$ ); (d) fixed cyanine ( $2 \times 10^{-4}M$ ); variable HTAB: — ( $7 \times 10^{-3}M$ ); -·-·- ( $7 \times 10^{-4}M$ ); --- ( $7 \times 10^{-6}M$ ).

phate = SDS) surfactants were investigated at different concentrations. Also, the aggregating dyes were studied above and below their cmc.

Figure 3 shows the spectra of dye **7** in water at two different concentrations. In  $2 \times 10^{-6} M$  solution the dye is essentially monomeric, whereas at  $2 \times 10^{-4} M$  solution a strong aggregation occurs. In the presence of SDS, the dye is generally not aggregated although, at the highest concentration of the surfactant, a weak hypochromic effect and band widening become appreciable (Figures 4a-b). At very low SDS concentration (*i.e.*  $8 \times 10^{-5} M$ ) the absorption spectra are broadened, probably due to ion-pair or small aggregate formation. The band maxima are red-shifted (4 nm) in comparison to aqueous solutions and are consistent with maxima in alcohol media. The cationic surfactant has a somewhat reduced deaggregating power towards dye **7** and this is particularly evident in Figure 4d (higher concentration of the dye and HTAB at or below its cmc). For lower concentrations of the dye, the maxima (Figure 4c) occur at the same wavelength as observed in spectra of aqueous solutions of the dye (Figure 3).

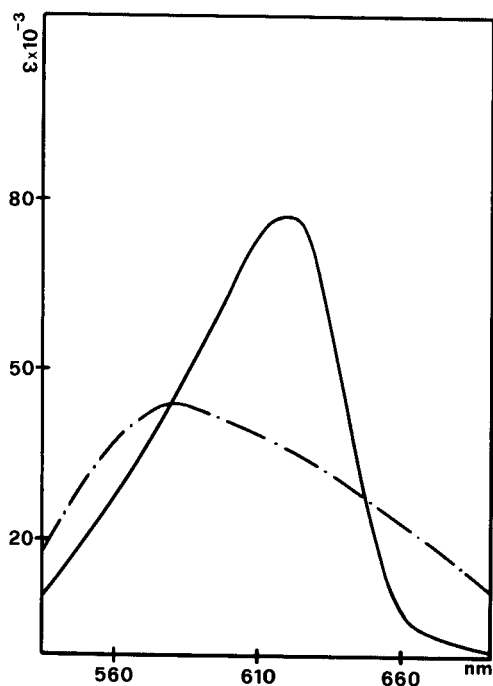


Figure 5. Spectra of dye No. **10** in water: — ( $2 \times 10^{-6} M$ ); -.-.- ( $2 \times 10^{-4} M$ ).

Figure 5 depicts the spectra of dye **10** in water. The dye clearly tends to a stronger aggregation than dye **7**. The deaggregating effect of the tensides is consequently lowered and the higher efficiency of SDS towards HTAB, observed

for dye **7**, is evidenced. Figures 6a-b-c-d clearly illustrate the above statement. The inability of HTAB to produce an efficient deaggregation even if present above its cmc (Figure 6d) is worth noting. The position of the absorption maxima in the presence of SDS closely follows the previous case whereas, in the presence of HTAB, the bands of the monomeric species lie at longer wavelengths than observed in spectra taken in water or ethanol media.

From the above observations we may conclude that the micelles of anionic and cationic surfactants strongly interact with amphiphilic cyanines, exerting both deaggregation and solvation effects.

As evidence of the observed interactions, we tested the dye **13**, in which the hydrophobic chain is removed and three positive charges are present. In water only one curve is reported (Figure 7a) because there is no variation in the shape or position *vs* concentration. The cationic surfactant does not affect the spectra at any concentration (Figure 7b). The presence of SDS (Figure 7a) at the various concentrations affects the spectra giving rise to bathochromic shifts (4 nm for ethanol, 13 nm for water). Evidently, because of a lack of aggregation, only solvation effects are involved between the strongly positive dye and anions or anionic micelles.

## EXPERIMENTAL

The nmr spectra were obtained with a Varian T 60 spectrometer in DMSO- $d_6$  or in deuteriochloroform solution (6%) using TMS as internal standard. Electronic spectra were recorded on a Pye Unicam SP 8-100 spectrophotometer. Surface tension measurements were performed with a Dognon-Abribat tensiometer.

(3-Bromopropyl)triethylammonium bromide was prepared as indicated in reference [7].

Salts **1-4** were prepared treating at  $140^\circ$  for 2 hours  $10^{-2}$  moles of the suitable heteroaromatic base (4-methylpyridine, 4-methylquinoline, 2-methylbenzothiazole or 2-methylbenzoxazole) with (3-bromopropyl)triethylammonium bromide ( $0.5 \times 10^{-2}$  moles). The crude products were slurried in hot acetone and crystallized from 1-butanol.

2-( $\beta$ -Acetylanilinovinyl-3-hexadecyl)benzothiazolium iodide and 4-( $\beta$ -acetylanilinovinyl-1-hexadecyl)quinolinium bromide were prepared as indicated in reference [2] and directly used for the preparation of the dyes.

Dye **5** was prepared reacting 2-( $\beta$ -acetylanilinovinyl-3-hexadecyl)benzothiazolium iodide ( $10^{-2}$  moles) and **2** ( $10^{-2}$  moles), dissolved in 40 ml of absolute ethanol in presence of triethylamine (1.5 ml). After refluxing one hour, the mixture was cooled, treated with ether, filtered and the residue washed with ether. The dinitrate was obtained mixing ethanolic solutions of the dye and of silver nitrate in the dark, removing the silver halide, and adding ether to the solution previously reduced to small volume. The crude product was crystallized from acetonitrile.

Dyes **6** and **7** were similarly prepared, replacing **2** with **3** and **4**, respectively.

Dyes **8** and **9** were obtained by adding (30 minutes) 4-( $\beta$ -acetylanilinovinyl-1-hexadecyl)quinolinium bromide ( $10^{-2}$  moles) dissolved in absolute ethanol (20 ml) to a boiling solution of quaternary salt (**1** or **2**,  $10^{-2}$  moles) in 20 ml of absolute ethanol and 1.5 ml of triethylamine. After refluxing for one hour, the mixture was cooled, treated with ether, filtered and the residue washed with ether. The crude products were crystallized from acetonitrile.

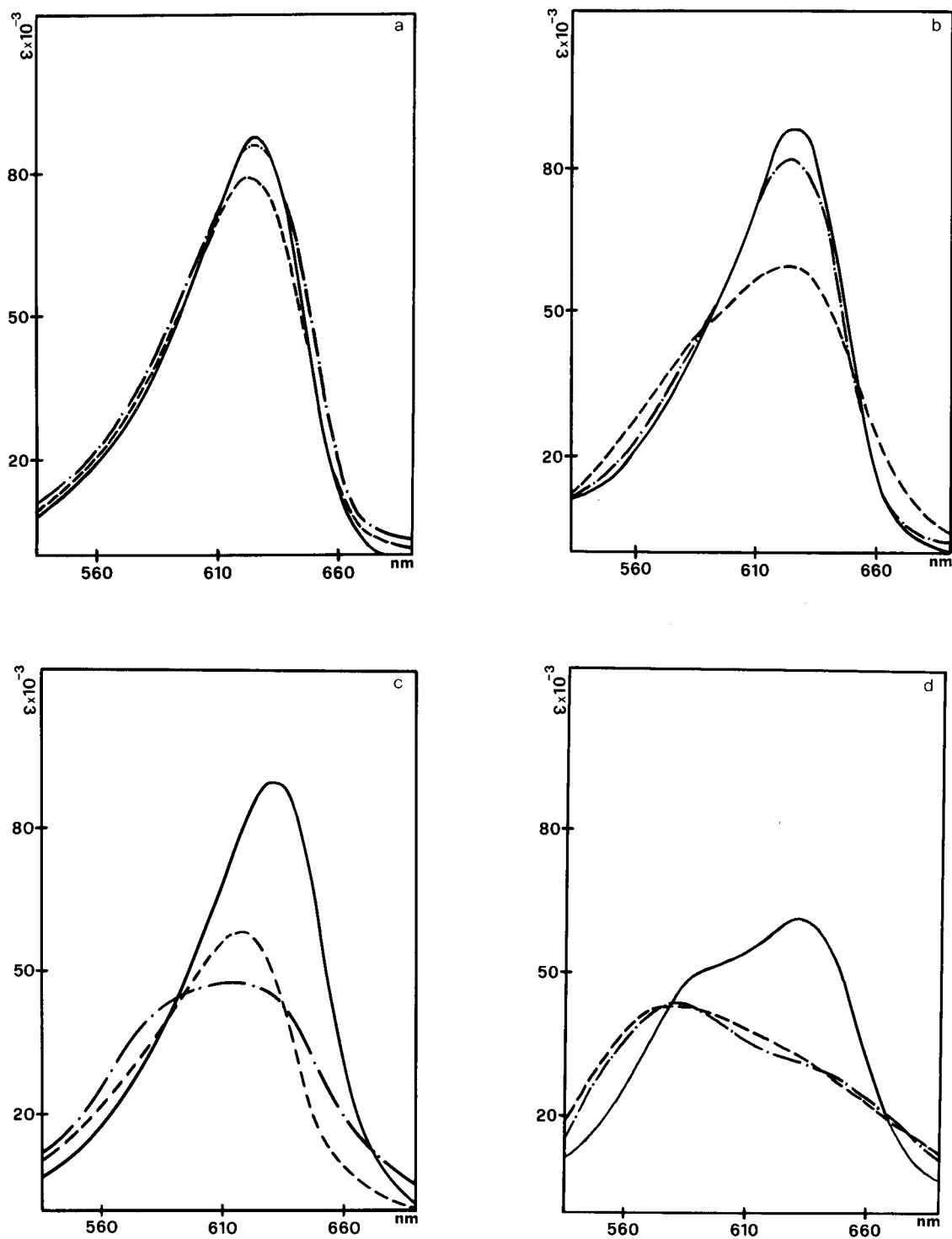


Figure 6. Spectra of dye No. **10**: (a) fixed cyanine ( $2 \times 10^{-6}M$ ); variable SDS: — ( $80 \times 10^{-3}M$ ); - - - ( $8 \times 10^{-3}M$ ); - · - ( $4 \times 10^{-3}M$ ); (b) fixed cyanine ( $2 \times 10^{-4}M$ ); variable SDS: — ( $80 \times 10^{-3}M$ ); - - - ( $8 \times 10^{-3}M$ ); - · - ( $4 \times 10^{-3}M$ ); (c) fixed cyanine ( $2 \times 10^{-6}M$ ); variable HTAB: — ( $7 \times 10^{-3}M$ ); - - - ( $7 \times 10^{-4}M$ ); - · - ( $7 \times 10^{-6}M$ ); (d) fixed cyanine ( $2 \times 10^{-4}M$ ); variable HTAB: — ( $7 \times 10^{-3}M$ ); - - - ( $7 \times 10^{-4}M$ ); - · - ( $7 \times 10^{-6}M$ ).

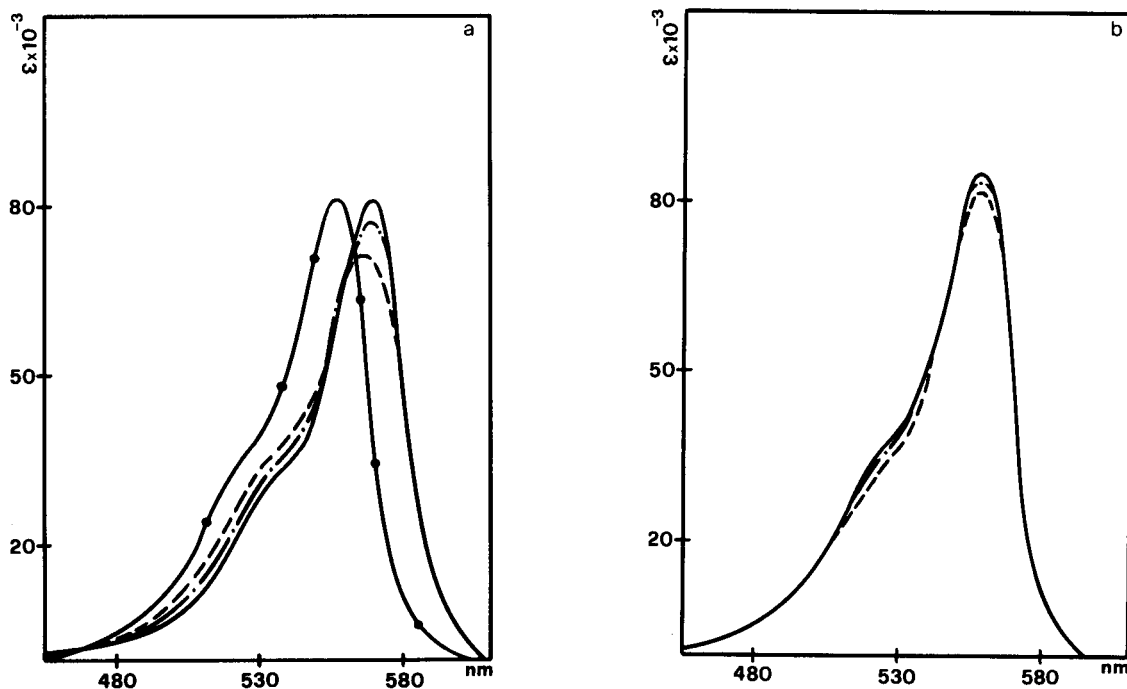


Figure 7. Spectra of dye No. 13: (a) fixed cyanine ( $2 \times 10^{-4}M$ );  $\leftarrow$  in water (tensides absent); variable SDS: — ( $80 \times 10^{-3}M$ ); - - - - ( $8 \times 10^{-3}M$ ); - - - ( $4 \times 10^{-3}M$ ); (b) fixed cyanine ( $2 \times 10^{-4}M$ ); variable HTAB: — ( $7 \times 10^{-3}M$ ); - - - - ( $7 \times 10^{-3}M$ ); - - - ( $7 \times 10^{-6}M$ ).

Dye 10 was prepared refluxing for one hour a solution of bis-quaternary salt 3 ( $10^{-2}$  moles) and 4( $\beta$ -acetylanilinovinyl-1-hexadecyl)quinolinium bromide ( $10^{-2}$  moles) in 30 ml of pyridine. The mixture was cooled, treated with ether, filtered and the residue washed with ether. The crude product was dissolved in 40 ml of boiling water containing potassium bromide (0.5 g). The precipitate was crystallized from acetonitrile.

Dye 11 was obtained refluxing for one hour 4( $\beta$ -acetylanilinovinyl-1-hexadecyl)quinolinium bromide ( $10^{-2}$  moles) and 4 ( $10^{-2}$  moles) in nitrobenzene (15 ml) and triethylamine (3 ml). The mixture was cooled, treated with ether, filtered and the residue washed with ether. The crude product was crystallized from acetonitrile.

Dye 12 was prepared refluxing for 10 hours the bis-quaternary salt 2 ( $10^{-2}$  moles) with triethylorthoformate ( $2.5 \times 10^{-2}$  moles) in pyridine (10 ml) and absolute ethanol (50 ml). The mixture was cooled for 24 hours, treated with ether, filtered and the residue washed with ether. The crude product was crystallized from acetonitrile.

Dyes 13 and 14 were prepared as 12, using respectively the salt 3 and a reduced volume of absolute ethanol (25 ml), the salt 4 in absence of absolute ethanol.

#### REFERENCES AND NOTES

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