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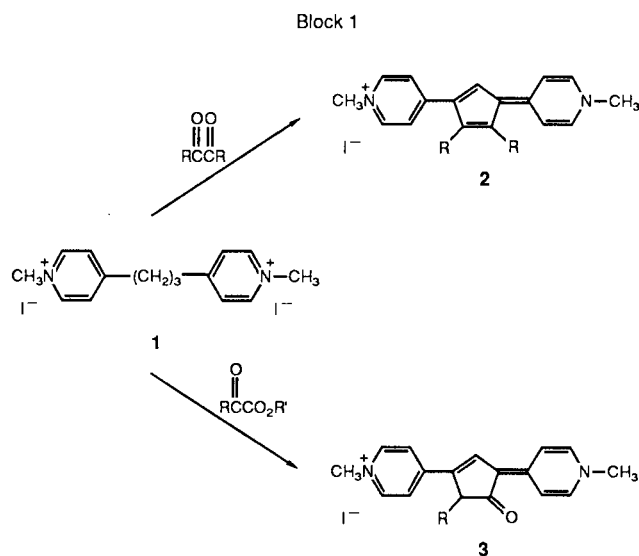
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1,3-Bis(*N*-methyl-4-pyridyl)- and 1,3-bis(*N*-methyl-2-benzothiazolyl)-propane diiodides react with 1,2-cyclohexanedione, tetrachloro-1,2- and -1,4-benzoquinone, 2,3-dichloronaphthoquinone, 3,4-dichloromaleimide and 2,3-dichloroquinoxaline to give novel fused ring bridged cyanine dyes.

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We recently disclosed [1] a simple general synthetic method for the novel bridged cyanines **2** and **3** containing substituents (*e.g.* cyclic and acyclic alkyl, aryl and heteroaryl) attached to a linking cyclopentadiene ring. These deep red bridged cyanine dyes were prepared by condensation of 1,3-bis(*N*-methyl-4-pyridyl)propane diiodide **1** with  $\alpha$ -diketones or  $\alpha$ -ketoesters and have extinction coefficients exceeding  $10^5$ . We now report extensions of this methodology both to the 1,3-bis(2-benzothiazolyl)propane systems and to the preparation of novel fused ring bridged cyanine dyes by using compounds containing two adjacent active chlorine atoms in place of the dicarbonyl compounds.

1,3-Bis(2-benzothiazolyl)propane [2] was prepared in 80% yield from *o*-aminothiophenol and glutaric acid in polyphosphoric acid, and bisquaternized with methyl iodide in dimethylformamide to afford 1,3-bis(*N*-methyl-2-benzothiazolyl)propane diiodide **4** (82%). Condensation of



Scheme 1

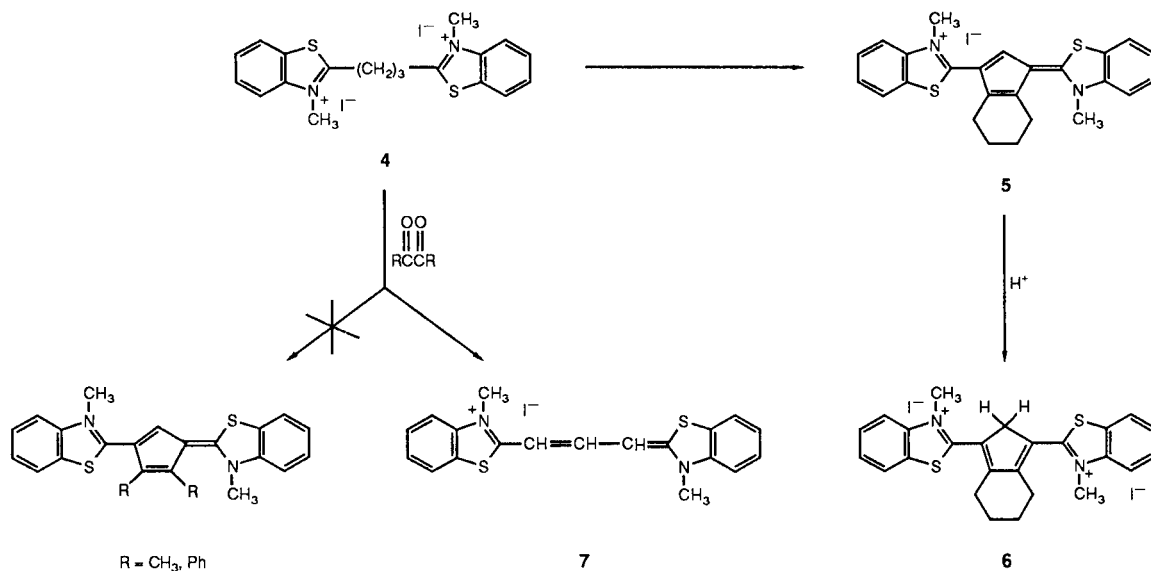


Table I  
Preparation of the Bridged Cyanine Dyes

No.	series	yield %	mp (°C)	crystal [a]	Calcd.			analysis formula	Found		
					C	H	N		C	H	N
5	A	50	241-243	red	53.47	4.40	5.00	C <sub>25</sub> H <sub>23</sub> N <sub>2</sub> S <sub>2</sub> I [b]	53.05	3.99	4.91
8	A	71	226-229	violet	45.63	2.43	4.26	C <sub>25</sub> H <sub>16</sub> N <sub>2</sub> S <sub>2</sub> Cl <sub>3</sub> OI	45.82	2.44	4.18
9	A	60	217-220	violet	54.50	3.13	4.39	C <sub>29</sub> H <sub>20</sub> N <sub>2</sub> S <sub>2</sub> ClOI	54.18	3.08	4.07
10	A	58	180 dec	violet	43.34	2.78	4.61	C <sub>25</sub> H <sub>15</sub> N <sub>2</sub> S <sub>2</sub> Cl <sub>4</sub> I	43.52	2.60	4.29
11	A	65	208 dec	violet	54.91	3.16	6.61	C <sub>29</sub> H <sub>20</sub> N <sub>3</sub> S <sub>2</sub> O <sub>2</sub> I	54.45	3.01	6.25
12	A	49	207-210	violet	54.74	3.57	9.46	C <sub>27</sub> H <sub>21</sub> N <sub>4</sub> S <sub>2</sub> I	55.18	3.50	9.10
13	B	68	>250	blue	51.25	3.56	6.64	C <sub>36</sub> H <sub>30</sub> N <sub>4</sub> Cl <sub>2</sub> I <sub>2</sub>	50.78	3.64	6.33
14	B	70	215-218	violet	55.10	4.04	5.14	C <sub>25</sub> H <sub>20</sub> N <sub>2</sub> ClO [b]	54.69	4.27	4.89
15	B	61	>300	blue	43.30	2.92	4.81	C <sub>21</sub> H <sub>15</sub> N <sub>2</sub> Cl <sub>4</sub> I [b]	42.87	3.15	4.47
16	B	57	240-242	blue	57.58	3.84	8.06	C <sub>25</sub> H <sub>20</sub> N <sub>3</sub> O <sub>2</sub> I	57.91	3.70	7.88
17	B	46	>250	blue	55.44	4.61	11.27	C <sub>23</sub> H <sub>21</sub> N <sub>4</sub> I [b]	55.42	4.22	11.24
18	B	65	208-210	blue	63.97	4.59	5.15	C <sub>29</sub> H <sub>23</sub> N <sub>2</sub> I [b]	64.33	4.83	5.26

[a] Recrystallization from ethanol. [b] Containing one mole of crystallization water.

Table II  
Spectral Data of Bridged Cyanine Dyes

No.	series	Visible spectra $\lambda$ (lg $\epsilon$ )		IR (CHBr <sub>3</sub> , cm <sup>-1</sup> )	<sup>1</sup> H NMR (DMSO-d <sub>6</sub> , $\delta$ , TMS)			
		methanol	1 <i>N</i> HCl		Aromatic H (m)		N-CH <sub>3</sub> (s)	
5	A	484 (4.97)	386 (4.40)	1640, 1460, 1370,	740	7.4-8.35	4.19	
8	A	558 (4.64)	543 (4.08)	1710, 1650, 1530,	750		not soluble	
9	A	558 (4.18)	430 (4.00)	1640, 1525, 1450,	750	7.30-8.45	4.10	
10	A	550 (4.02)	546 (3.87)	1640, 1570, 1440,	750		not soluble	
11	A	558 (4.06)	450 (3.88)	1700, 1500, 1380,	750	7.25-8.10	3.90	
12	A	562 (4.50)	410 (3.90)	3200, 1650, 1550,	740	7.55-8.35	4.00	
13	B	586 (4.51)	465 (4.03)	1660, 1500, 1460,	830	8.20 (d)	9.15 (d)	4.15
14	B	584 (3.89)	405 (3.87)	1670, 1510, 1370,	760	7.30-8.35	8.95 (d)	4.05
15	B	607 (3.90)	460 (3.60)	1650, 1560, 1430,	740		not soluble	
16	B	584 (3.81)	405 (3.51)	1710, 1660, 1630,	1370	7.30-8.30	9.15 (d)	4.12
17	B	590 (4.12)	440 (3.98)	3250, 1640, 1500,	750	7.60-8.45	9.10 (d)	4.10
18	B	601 (4.11)	410 (4.04)	1660, 1600, 1500,	750	7.65-8.55	9.20 (d)	4.15

555 (4.19)

the diiodide **4** with 1,2-cyclohexanedione in methanol and piperidine gave the deep red dyestuff **5** (50%) (Scheme 1), which was confirmed by its spectra and analysis (Tables 1 and 2). Its high extinction coefficient in ethanol (93600) (Table 2), indicates a very strong chromophore with  $\lambda$  max 484 nm; however, it was almost colorless in 1*M* hydrochloric acid (386 nm,  $\epsilon$  = 25000). This dramatic hypochromic shift and hypochromic effect is explained by protonation of the cyanine **5** in a acidic solution to yield dication **6**, in a manner similar to that previously described [1].

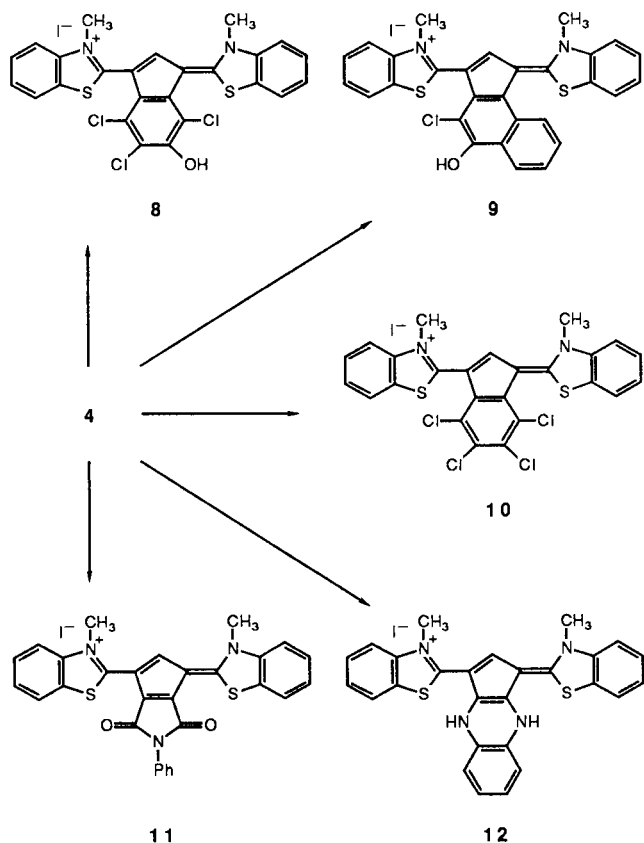
Attempted conversions of diiodide **4** into corresponding bridged cyanines by reactions with butane-2,3-dione, ben-

zil and phenanthrenequinone gave in each case the same deep red thiacyanine dye **7**. In these cases, the  $\alpha$ -diketones do not condense, but instead promote oxidation presumably because of steric hinderance. As thiacyanine **7** was readily produced in 55% yield by stirring **4** with two equivalents of piperidine in methanol without  $\alpha$ -diketone at 50° for 20 minutes, the oxidation presumably occurs by air (Scheme 1). Thiacyanine dye **7** was previously prepared by treating **4** with sodium hydroxide in ethanol or triethylamine in pyridine [3].

Although these attempts to convert 1,3-bis(*N*-methyl-2-benzothiazolyl)propane diiodide **4** into bridged cyanine by

condensation with various  $\alpha$ -diketones failed, we found that reactions with quinones and with compounds with adjacent active chlorine atoms (known to readily undergo nucleophilic substitution [4-5]) allowed the synthesis of novel fused ring bridged cyanines. The reactions of **4** with 2,3-dichloro-1,4-naphthoquinone, tetrachloro-1,2- and -1,4-benzoquinone, 3,4-dichloromaleimide and 2,3-dichloroquinoxaline in dimethylformamide in the presence of tributylamine as base, gave, in 50-70% yields, the cyanine dyes **8** to **12**, respectively (Scheme 2). In the case of tetrachloro-1,4-benzoquinone, a single molecule of the diiodide **4** reacted to form cyanine **8**. In the reaction with 2,3-dichloro-1,4-naphthoquinone to form **9**, the diiodide **4** attacked one carbon quinone having chlorine and the adjacent carbonyl carbon to give an unsymmetrical cyanine dye; this is similar to the previously reported [6-7] products formed from 2,3-dichloro-1,4-naphthoquinone with other bisnucleophiles (e.g. *o*-aminothiophenol and *o*-diaminophenylene). The new cyanine derivatives **8-12** were characterized analytically (Table 1, series A) and by their spectra (Table 2).

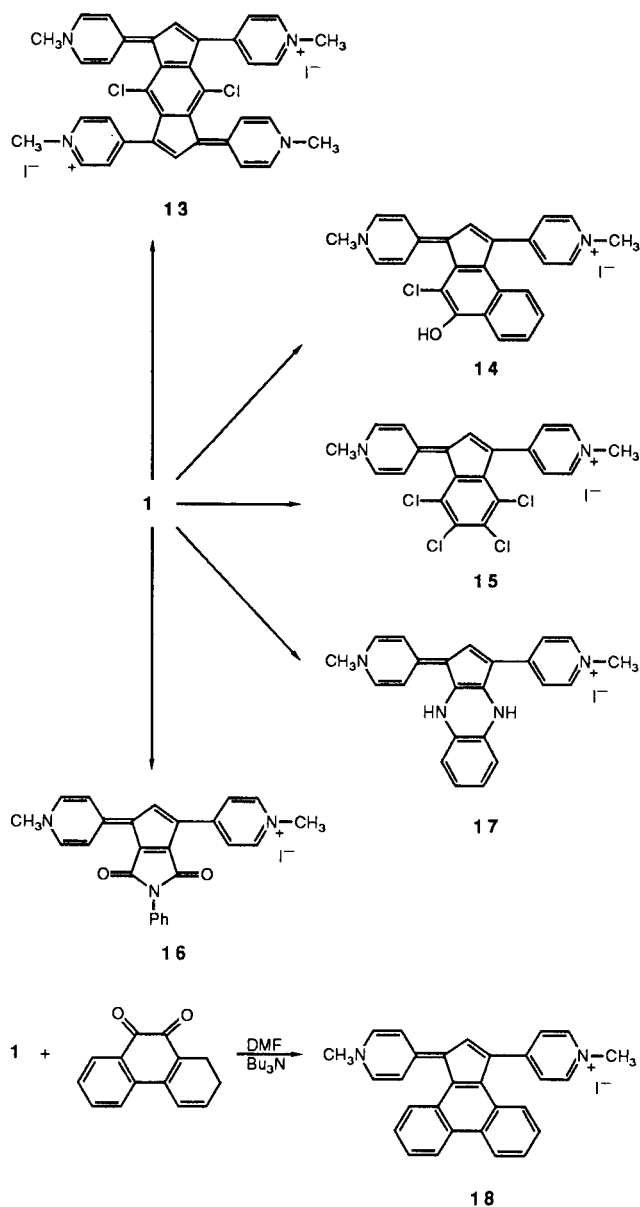
Scheme 2



In a similar manner, 1,3-bis(*N*-methyl-4-pyridyl)propane diiodide **1** reacted with the same quinones and active chlorine compounds in dimethylformamide at 50° in the presence of tributylamine to give similar fused ring bridged

pyridyl cyanine dyes. The reaction with tetrachloro-1,4-benzoquinone yielded **13** in which two of the diiodide molecules had each attacked one carbonyl and one adjacent chlorine atom. 2,3-Dichloro-1,4-naphthoquinone, tetrachloro-1,2-benzoquinone, 3,4-dichloromaleimide and 2,3-dichloroquinoxaline formed **14**, **15**, **16**, and **17**, respectively (Scheme 3). The condensation of **1** with phenanthrenequinone under the same condition afforded the blue dye **18** (Scheme 3). The properties of these novel cyanines **13-18** are summarized in Table 1. They were characterized by <sup>1</sup>H nmr and ir spectra, and by microanalysis (Tables 1 and 2).

Scheme 3



Some of these dyestuffs **5,17,18** crystallize with one mole of water as indicated by microanalysis and the presence of water peaks in the proton nmr spectra at  $\delta$  3.3-3.5 ppm. The CH= signals of the cyclopentadiene usually overlapped those of the aromatic protons. The high-field shift of the N-CH<sub>3</sub> signals in cyanines (both series A and B ~4.0 ppm) compared with the starting diiodide (**4**, 4.45 ppm and **1**, 4.55 ppm) is consistent with the cyanine-type structure. In the infrared spectra of **11** and **16** the two expected characteristic bands were found for  $\nu$  C=C at around 1640 and 1600 cm<sup>-1</sup>, and for  $\nu$  C=O at 1690 cm<sup>-1</sup>. The  $\nu$  NH occurred at 3200 cm<sup>-1</sup> for **12** and **17**. The <sup>13</sup>C nmr spectra of some selected compounds (*e.g.* **5**) also agree well with the assigned cyanine structures.

All these compounds contain benzothiazolyl or pyridyl cyanine chromophores in which the two heterocyclic rings are conjugated through an uneven number of carbon atom, and thus are deep colored (red, purple or blue) in the solid state. The visible absorption spectra were recorded in ethanol and in 1M hydrochloric acid and are listed in Table II. Most of these cyanine dyes showed absorption maximum above 550 nm. The extinction coefficients of these dyes **8-18** are high. The effects of substituents (fused rings) in the cyclopentene ring on both the extinction coefficient and the absorption maximum are significant which is different from the situation reported in our previous paper [1] for dyes of type **2** and **3**. Presumably this is because most of the fused rings in **8-18** are themselves chromophoric and are conjugated with the cyanine system. Again in the strongly acidic solution (*cf.* 1M hydrochloric acid), a dramatic hypsochromic shift (the color was changed to yellow or even colorless) was observed, and this was accompanied by a decrease of the extinction coefficient. The bridged cyanine dyes are evidently protonated in acid at the central cyclopentene ring to form dication, with resulting loss of the cyanine structure.

The protonation of some simple open-chain cyanines in acidic media was studied by Feldman and co-workers [8],

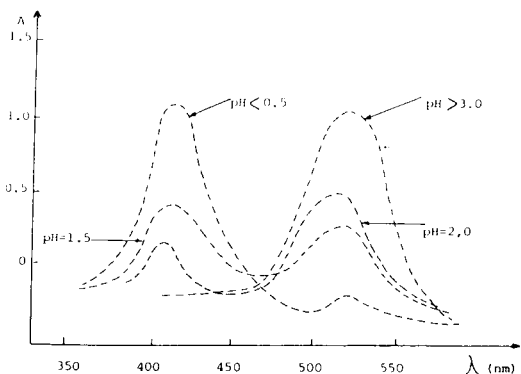


Figure 1. pH dependence of absorption of cyanine dye **18** in aqueous solution.

who calculated the pK<sub>a</sub> values from the pH dependence of the visible spectra. We reported similar studies of our bridged pyridyl cyanine dyes **2** and **3** [1], and have now investigated the protonation behavior and the pK<sub>a</sub> values of our novel fused ring bridged cyanine dyes. Typical visible absorption spectra showing the pH dependence of the cyanine **18** is shown in Figure 1. The absorption at  $\lambda$  527 nm due to the cyanine **18** is formed in weakly acidic as well as in basic aqueous solution, no protonation occurred in the solution with pH > 2. In acidic solutions with pH lower than 2, the absorption at  $\lambda$  527 nm decreases and a new peak at  $\lambda$  410 nm appears, and only the 410 nm absorption is found in strongly acidic solution (pH < 0.5), this is believed to be the absorption of the dication corresponding to **18**. Similarly, the absorption of cyanine dye **5** changed in the range pH = 3.5 to 2.0.

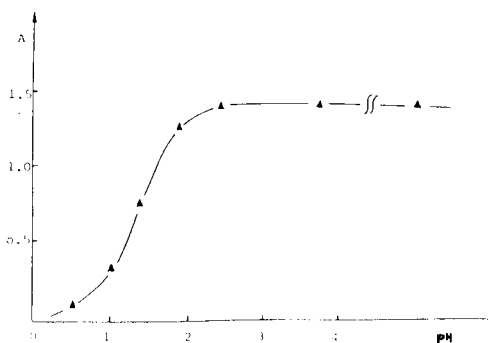


Figure 2. pH dependence of absorption intensity of cyanine dye **18** at  $\lambda$  max 527 nm.

The pK<sub>a</sub> of cyanine dyes **18** and **5** could be evaluated as 1.20 and 3.10 respectively from the pH dependence of the spectra at  $\lambda$  527 nm for **18** (Figure 2) and 456 nm for **5** from the protonation reaction (Scheme 2).

The cyanine dyes **8** and **10** were protonated only in strongly acidic solutions. In the case of **8**, the absorption at  $\lambda$  543 nm does not decrease in hydrochloric acid until 4*N*, and that of **10** at  $\lambda$  546 nm in 2*N* hydrochloric acid.

## EXPERIMENTAL

Melting points were determined using a Thomas-Hoover capillary melting point apparatus without correction. The <sup>1</sup>H spectra were taken on a EM-360L (60 MHz) with TMS as the internal standard and <sup>13</sup>C nmr on JEOL Model JNM-FX 100 (25.05 MHz) spectrometer. The ir spectra were recorded with Perkin-Elmer 283 B instrument. Visible spectra were measured on a Perkin-Elmer 330 spectrophotometer. Elemental analyses were conducted in this department under Dr. R. King.

The following compounds were prepared by the literature method quoted: 1,3-Bis(2-benzothiazolyl)propane, mp 76-78° (lit [2] mp 77-78°); 1,3-bis(*N*-methyl-4-pyridyl)propane diiodide, mp 142-144° (lit [9] mp 141-144°); 3,4-dichloro-*N*-phenylmaleimide, mp 201-203 (lit [4] mp 203°).

### 1,3-Bis(*N*-methyl-2-benzothiazolyl)propane Diiodide **4**.

1,3-Bis(2-benzothiazolyl)propane (31.0 g, 0.1 mole) was heated with excess methyl iodide in dimethylformamide at 80° for 10 hours. The

resulting precipitate was collected by filtration and washed with ethanol. The crude product was recrystallized from ethanol to give **4** (48.7 g, 82%), mp 226-228°; pmr(dimethyl sulfoxide- $d_6$ ): 2.52 (m, 2H, CH<sub>2</sub>), 3.95 (t, 4H, 2CH<sub>2</sub>), 4.45 (s, 6H, N-CH<sub>3</sub>), 8.00-8.55 (m, 8H, ArH); cmr: 180.1, 142.9, 130.5, 129.5, 129.2, 125.7, 118.1, 43.1 (N-CH<sub>3</sub>), 30.5 (CH<sub>2</sub>), 27.4 (CH<sub>2</sub>).

*Anal.* Calcd. for C<sub>19</sub>H<sub>20</sub>I<sub>2</sub>N<sub>2</sub>S<sub>2</sub>: C, 38.38; H, 3.37; N, 4.71. Found: C, 38.26; H, 3.03; N, 4.43.

1-(*N*-Methyl-2-benzothiazolylene)-3-(*N*-methyl-2-benzothiazolinio)-4,5-(1,2,3,4-tetrahydrobenzo)cyclopenta-1,4-diene Iodide **5**.

The reaction mixture of 5 mmoles of **4**, 5 mmoles of 1,2-cyclohexanedi-one and 10 mmoles of piperidine in methanol (20 ml) was stirred at 50° for 5 hours. A deep red solid formed was filtered and washed with ethanol to give **5**; cmr(dimethyl sulfoxide- $d_6$ ): 141.6, 128.1, 127.8, 126.4, 125.8, 122.8, 122.0, 114.8, 114.3, 110.7, 45.1 (NCH<sub>3</sub>), 24.9, 22.7 (see Tables 1 and 2).

1-(*N*-Methyl-2-benzothiazolylinio)-3-(*N*-methyl-2-benzothiazolylene)-1-propene Iodide **7**.

The reaction mixture of 5 mmoles of **4** and 10 mmoles of piperidine in methanol (20 ml) was stirred at 50° for 20 minutes. A deep red precipitate was filtered and washed with methanol to give **7**, 55% yield, mp 273-275°; pmr(dimethyl sulfoxide- $d_6$ ): 8.25-7.45 (m, 8H, ArH), 6.75-6.50 (m, 3H, CH=), 3.90 (s, 6H, N-CH<sub>3</sub>); cmr: 141.5, 127.5, 126.7, 124.9, 124.6, 122.5, 113.2, 106.4, 37.0 (N-CH<sub>3</sub>); ir (bromofrom): 1640, 1550, 1460, 1380, 825, 740 cm<sup>-1</sup>; uv/vis (ethanol): 428 nm (89000).

#### General Procedure for Preparation of Cyanine Dyes **8-18**.

In general, the reaction mixture of 5 mmoles of **4** or **1**, 5 mmoles of the corresponding substrates with active chlorine and 10 mmoles of tributylamine in dimethylformamide (20 ml) was stirred at 40-50° for 5-10 hours.

Addition of ether and filtration afforded a deep colored solid which on recrystallization from ethanol gave cyanine dyes (see Table 1 and 2).

#### Acknowledgements.

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