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Syntheses of Some Cyanine Dyes of Bunte Salt Type

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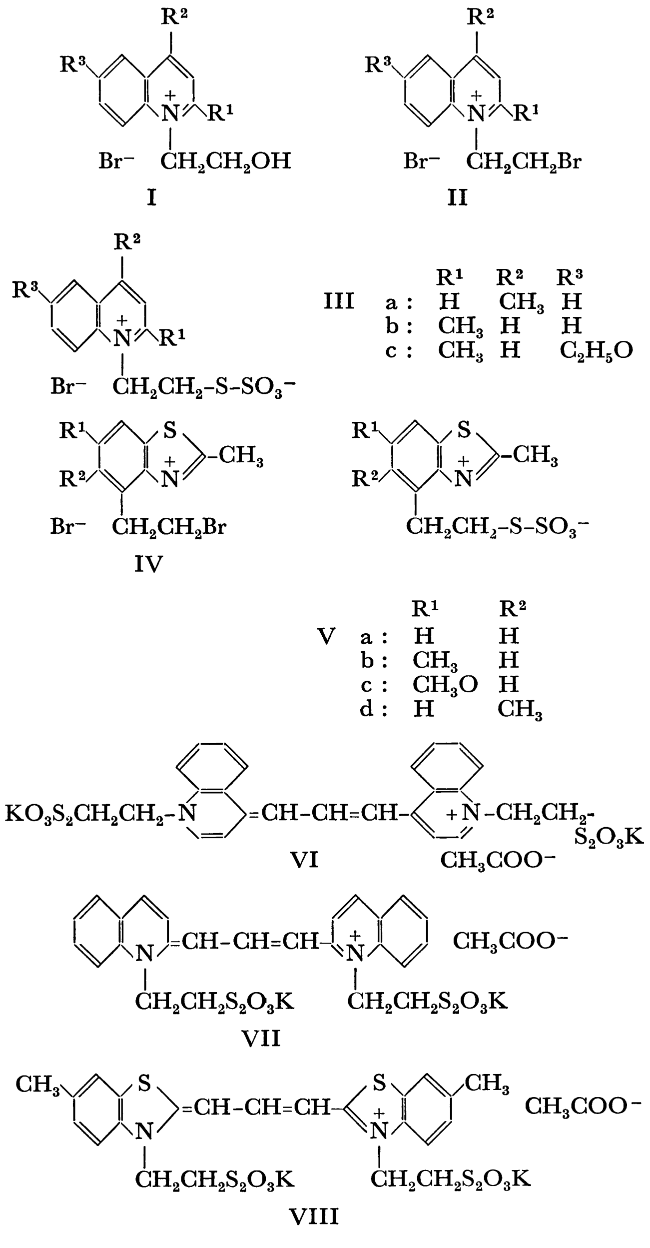
In order to investigate the photosensitivity of compounds such as photosensitizing dyes of Bunte salt type which have not been synthesized yet, the following compounds were prepared: 1,1′-di-(2-potassiumsulfothioethyl)-4,4′-tricarbocyanine acetate (VI), 1,1′-di-(2-potassiumsulfothioethyl)-2,2′-tricarbocyanine acetate (VII), 6,6′-dimethyl-3,3′-di-(2-potassiumsulfothioethyl)dithiacarbocyanine acetate (VIII), and 3-(2-bromoethyl)-3′-(sulfothioethyl)-5,6,5′,6′-tetramethoxydithiacarbocyanine (XII).

Three kinds of substituted 1-(2-bromoethyl)quinolinium bromide(II) (4-methyl (a), 2-methyl- (b), and 6-ethoxy-2-methyl- (c)) were subjected to reaction with sodium thiosulfate to yield the corresponding thiosulfates (IIIa, b, and c), respectively. Similarly, four kinds of substituted 4-(2-bromoethyl)benzothiazolium bromides (IV) (2-methyl- (a), 2,6-dimethyl-, (b), 6-methoxy-2-methyl- (c), and 2,5-dimethyl- (d)) gave the corresponding thiosulfates (Va, b, c, and d).



I II III IV V VI VII VIII

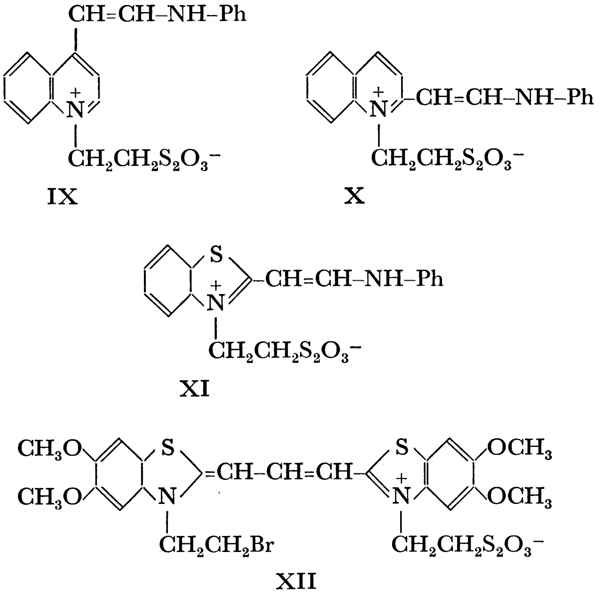
III	R^1	R^2	R^3
a:	H	CH_3	H
b:	CH_3	H	H
c:	CH_3	H	C_2H_5O

V	R^1	R^2
a:	H	H
b:	CH_3	H
c:	CH_3O	H
d:	H	CH_3

Fig. 1.

IIIa, IIIb and Vb yielded the corresponding cyanine dyes (VI, VII and VIII) in low yields on being heated[1] with aniline and ethyl orthoformate, followed by heating with acetic anhydride and potassium acetate. IIIa, IIIb, and Va gave their thiosulfates (IX, X and XI) by heating with aniline and ethyl orthoformate. In order to introduce a thiosulfate group into the carbocyanine dye, 3,3′-di-(2-bromoethyl)-5,6,5′,6′-tetramethoxydithiacarbocyanine bromide (XIV) was derived from the corresponding hydroxyethyl compound (XIII). However, it was found that only one bromoethyl group in XIV was converted into the sulfothioethyl group with sodium thiosulfate.

An attempt to obtain 1,1′-di-(2-potassiumsulfothioethyl)-2,4′-tricarbocyanine acetate by heating a mixture of IX and IIIb in the presence of acetic anhydride and potassium acetate gave a powder, which had an absorption maximum in the visible region, λ(MeOH)[2]



IX X XI XII

Fig. 2.

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[1] T. Ogata, *Rikwagaku Kenkyu-jo Iho*, **13**, 501, 549 (1934).

[2] Indicated in nm.

673—674 (ν(KBr)[3] 1209 and 1025). Reaction of IIIa with 1-(2-hydroxyethyl)-4-(phenylaminoethenyl)quinolinium bromide, expected to form 1-(2-hydroxyethyl)-1′-(2-potassiumsulfothioethyl)-4,4′-tricarbocyanine acetate, gave a powder possessing an absorption maximum in the visible region, λ(MeOH) 728 (ν(KBr) 1232, 1195, and 1021). An attempt to prepare 3,3′-di-(2-potassiumsulfothioethyl)dithiacarbocyanine acetate as in the formation of VIII yielded a crystal which showed an absorption maximum in the visible region, λ(EtOH) 556—557 (ν (KBr) 1221—1208 and 1024).

Experimental[4]

1-(2-Bromoethyl)-4-methylquinolinium Bromide (IIa). A mixture of 10.0 g of 1-(2-hydroxyethyl)-4-methylquinolinium bromide (I) and 8.0 g of phosphorus tribromide was heated at 110 °C for 10 min. The reaction mixture was triturated repeatedly with ether, and the solid was recrystallized from ethanol to give 11.4 g of colorless crystals, mp 205 °C (decomp.).

S-*[2-(4-Methylquinolinium-1-yl)ethyl]thiosulfate (IIIa).* A mixture of 10.0 g of IIa and 8.0 g of sodium thiosulfate in 120 ml of water was heated on a water bath for 2.5 hr and then kept in a refrigerator. The crystals fromed were collected, washed with 30 ml of ethanol and finally recrystallized from water to yield 8.4 g of colorless crystals, mp 216—218 °C (decomp.), ν(KBr) 1230, 1215, and 1027.

Found: C, 50.73; H, 4.48; N, 4.81%. Calcd for $C_{12}H_{13}NO_3S_2$: C, 50.87; H, 4.59; N, 4.95%.

S-*[2-(2-Methylquinolinium-1-yl)ethyl]thiosulfate (IIIb).* A mixture of 10.6 g of IIb and 8.1 g of sodium thiosulfate in 130 ml of water was heated on a water bath for 1 hr. After being left to stand at room temperature, the crystals deposited were recrystallized from water to give 7.9 g of colorless crystals, mp 227—228 °C (decomp.). ν(KBr) 1247, 1233, 1224, 1208, and 1022.

Found: C, 50.97; H, 4.47; N, 4.76%. Calcd for $C_{12}H_{13}NO_3S_2$: C, 50.87; H, 4.59; N, 4.95%.

S-*[2-(6-Ethoxy-2-methylquinolinium-1-yl)ethyl]thiosulfate (IIIc).* A mixture of 5.0 g of IIc and 3.4 g of sodium thiosulfate in 30 ml of water was heated on a water bath for 1 hr, and then kept in a refrigerator. The resulting crystals were recrystallized from water to give 1.5 g of colorless crystals, mp 223 °C (decomp.). ν(KBr) 1234—1217 and 1022.

Found: C, 51.51; H, 5.59; N, 3.90%. Calcd for $C_{14}H_{17}NO_4S_2$: C, 51.34; H, 5.20; N, 4.28%.

S-*[2-(2-Methylbenzothiazolium-3-yl)ethyl]thiosulfate (Va).* A mixture of 5.6 g of IVa and 4.1 g of sodium thiosulfate in 20 ml of water was heated at 80—90 °C for 10 min. The crystals formed on standing were collected and recrystallized from water to give 2.9 g of colorless crystals, mp 191—193 °C (decomp.). ν(KBr) 1240, 1228, 1221, 1208, 1193, and 1023.

Found: C, 41.28; H, 3.37; N, 4.61%. Calcd for $C_{10}H_{11}NO_3S_3$: C, 41.50; H, 3.80; N, 4.84%.

S-*[2-(2,6-Dimethylbenzothiazolium-3-yl)ethyl]thiosulfate (Vb).* A mixture of 7.0 g of IVb and 5.0 g of sodium thiosulfate in 10 ml of water was treated as for Va. Yield, 3.9 g of colorless crystals, mp 203—204°C (decomp.), ν(KBr) 1246, 1230, 1209, 1021, and 1011.

Found: C, 43.12; H, 4.22; N, 4.37%. Calcd for $C_{11}H_{13}NO_3S_3$: C, 43.54; H, 4.29; N, 4.62%.

S-*[2-(6-Methoxy-2-methylbenzothiazolium-3-yl)ethyl]thiosulfate (Vc).* A mixture of 7.3 g of IVc and 5.0 g of sodium thiosulfate in 10 ml of water was treated as for Va. Yield, 4.6 g of colorless crystals, mp 206—207 °C (decomp.). ν(KBr) 1245, 1220, 1204, and 1016.

Found (dried at 130°C, 3 hr): C, 40.84; H, 4.08; N, 4.44%. Calcd for $C_{11}H_{13}NO_4S_3$: C, 41.35; H, 4.07; N, 4.39%.

S-*[2-(2,5-Dimethylbenzothiazolium-3-yl)ethyl]thiosulfate (Vd).* A mixture of 7.0 g of IVd and 5.0 g of sodium thiosulfate in 10 ml of water was treated as for Va. Yield, 4.0 g of colorless crystals, mp 192—194 °C (decomp.). ν(KBr) 1237, 1220 (shoulder), 1213, and 1020.

Found (dried at 120°C, 3 hr): C, 42.63; H, 4.04; N, 4.41%. Calcd for $C_{11}H_{13}NO_3S_3$: C, 43.54; H, 4.29; N, 4.62%.

1,1′-Di-(2-potassiumsulfothioethyl)-4,4′-tricarbocyanine Acetate (VI). A mixture of 1.3 g of finely-powdered IIIa, 0.80 g of aniline and 0.35 g of ethyl orthoformate was heated at 88 °C under stirring for 20 min. 3.0 g of acetic anhydride and 1.5 g of potassium acetate were added to the mixture, which was then heated at 110—120 °C for 10 min. The reaction mixture was triturated three times with ether, methanol, and water successively, and then finally with 50 ml of hot water. The residue was then extracted three times by refluxing with a 500 ml-portion of methanol each time. The combined methanolic solution was concentrated to 300 ml, passed through a column (cellulose powder) maintained at 50—55 °C, and then eluted with 2 l of hot methanol. A blue-colored fraction of the eluate was concentrated to 50 ml and set aside to yield 30 mg of crystals, mp 241—242 °C (decomp.). Soluble with difficulty in water and most organic solvents. λ (MeOH) 728 (ε 2.05×10^5). ν (KBr) 1234, 1200, and 1028—1019.

Found: C, 45.36; H, 4.39; N, 3.75%. Calcd for $C_{27}H_{26}K_2N_2O_8S_4$: C, 45.46; H, 3.68; N, 3.93%.

1,1′-Di-(2-potassiumsulfothioethyl)-2,2′-tricarbocyanine Acetate (VII). A mixture of 0.50 g of finely-powdered IIIb, 0.40 g of aniline and 0.25 g of ethyl orthoformate was heated at 120 °C for 9 min under stirring. To this were added 0.80 g of acetic anhydride and 0.80 g of potassium acetate, and the mixture was heated at 140 °C for 9 min. The reaction mixture was successively triturated and decanted with ether, ethanol, and water. The residue was refluxed twice with a 500 ml-portion of methanol, transferred to a Soxhlet apparatus and further extracted with methanol to give 140 mg of crystals, mp 236—237 °C (decomp.). Soluble with difficulty in water and most organic solvents. λ (MeOH) 625 (ε 1.51×10^5). ν (KBr) 1236, 1214, and 1027.

Found: C, 45.08; H, 3.42; N, 3.96%. Calcd for $C_{27}H_{26}K_2N_2O_8S_4$: C, 45.46; H, 3.68; N, 3.93%.

6,6′-Dimethyl-3,3′-di-(2-potassiumsulfothioethyl)dithiacarbocyanine Acetate (VIII). A mixture of 0.60 g of Vb, 0.20 g of aniline and 0.30 g of ethyl orthoformate was heated at 100°C for 5—10 min. To this were added 0.20 g of acetic anhydride and 0.27 g of potassium acetate, and heating was continued for 5—10 min at 160 °C. The reaction mixture was successively triturated with hot ethanol and hot water, and the residue was extracted three times with a 100 ml-portion of hot methanol each time. The combined methanolic solution was passed through a column (cellulose powder) maintained hot, and eluted with hot methanol. A red-colored fraction of the eluate was again passed through

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[3] Indicated in cm^{-1}.

[4] IR peaks appearing only in the regions 1200—1230 (strong) and 1020 (strong) and considered to be characteristic of the thiosulfate group of Bunte salt are given.

the column. The red fraction of the eluate gave 45 mg of crystals on concentration, mp 223—225 °C (decomp.). Soluble with difficulty in water and most organic solvents. λ (MeOH-H_2O (19 : 1)) 570 (ε 2.6×10^4). ν (KBr) 1240—1203, and 1027.

Found: C, 39.78; H, 3.68; N, 3.89%. Calcd for $C_{25}H_{26}K_2N_2O_8S_6$: C, 39.86; H, 3.46; N, 3.72%.

S-[*2-(4-Phenylaminoethenylquinolinium-1-yl)ethyl*]*thiosulfate (IX).* A mixture of 1.15 g of IIIa, 0.60 g of aniline and 0.70 g of ethyl orthoformate was heated at 123 °C for 10 min under stirring. The reaction mixture was triturated successively with ether, ethanol, and hot water. The residue was recrystallized from DMF–DMSO (1 : 1) to give 1.25 g of crystals, mp 252—253 °C (decomp.). λ (MeOH) 492. ν (KBr) 1227, 1220, and 1014.

Found (dried at 120 °C, 3 hr): C, 58.40; H, 5.03; N, 7.27%. Calcd for $C_{19}H_{18}N_2O_3S_2$: C, 59.05; H, 4.67; N, 7.25%.

S-[*2-(2-Phenylaminoethenylquinolinium-1-yl)ethyl*]*thiosulfate (X).* A mixture of 0.28 g of IIIb, 0.30 g of aniline and 0.40 g of ethyl orthoformate was heated at 120 °C for 15 min under stirring. The reaction mixture was triturated successively with ether, ethanol, and hot water. The residue was dissolved in methanol, and the solution was passed through a column (cellulose powder). Concentration of a yellow-colored fraction of the eluate yielded crystals, which were recrystallized from methanol. Yield, 80 mg, mp 240—241 °C (decomp.). λ (MeOH) 451. ν (KBr) 1245, 1235, 1227, 1024 (shoulder), and 1019.

Found: C, 57.10; H, 5.12; N, 6.49%. Calcd for $C_{19}H_{18}N_2O_3S_2\cdot CH_3OH$: C, 57.39; H, 5.30; N, 6.69%.

S-[*2-(2-Phenylaminoethenylbenzothiazolium-3-yl)ethyl*]*thiosulfate (XI).* A mixture of 3.7 g of Va, 1.0 g of aniline and 0.80 g of ethyl orthoformate was heated at 100 °C for 10 min under stirring. The reaction mixture was triturated with ethanol and decanted. The residue was dissolved in methanol and passed through a column (cellulose powder). Concentration of a yellow-colored fraction of the eluate gave crystals, which were then recrystallized from methanol. Yield, 1.4 g, mp 250—252 °C. λ (MeOH) 420. ν (KBr) 1244, 1232, 1203, and 1022.

3,3'-Di-(2-hydroxyethyl)-5,6,5',6'-tetramethoxydithiacarbocyanine Bromide (XIII). A mixture of 2.0 g of 3-(2-hydroxyethyl)-5,6-dimethoxy-2-methylbenzothiazolium bromide, 0.60 g of anilline, and 0.90 g of ethyl orthoformate was heated at 115 °C for 7 min under stirring. To this were added 1.8 g potassium acetate and 0.70 g of acetic acid, and heating was continued at 160 °C for 7 min. The reaction mixture was triturated successively with ether, ethanol, and water. Recryatallization of the residue from methanol–ether gave crude crystals, which were dissolved in methanol. The methanolic solution was passed through a column (cellulose powder), and eluted with methanol. The crystals from the eluate on concentration were similarly treated twice. Yield, 1.6 g, mp 259—260 °C. λ (MeOH) 605.

Found: C, 50.65; H, 4.99; N, 4.69%. Calcd for $C_{25}H_{29}BrN_2O_6S_2$: C, 50.25; H, 4.86; N, 4.69%.

3,3'-Di-(2-bromoethyl)-5,6,5',6'-tetramethoxydithiacarbocyanine Bromide (XIV). A mixture of 0.50 g of XIII and 3.8 g phosphorus tribromide was kept at room temperature for 5 hr. The reaction mixture was triturated with benzene, and the residue was recrystallized from methanol–ether (1 : 1). The crystals formed were dissolved in methanol, treated chromatographically as for XIII, and finally recrystallized from methanol. Yield, 0.43 g, mp 226—228 °C. λ (MeOH) 605.

Found: C, 41.12; H, 3.69; N, 3.75%. Calcd for $C_{25}H_{27}Br_3N_2O_4S_2$: C, 41.50; H, 3.74; N, 3.87%.

3-(2-Bromoethyl)-3'-sulfothioethyl-5,6,5',6'-tetramethoxydithiacarbocyanine (XII). A mixture of 1.0 g of XIV and 0.90 g of sodium thiosulfate in 300 ml of methanol was heated under reflux for 20 hr. The reaction mixture was carefully concentrated by distilling methanol until XII began to crystallize (otherwise, excess sodium thiosulfate deposited.) The crystals, after recrystallization once from methanol–ether, were dissolved in methanol, passed through a column (cellulose powder), and eluted with DMF. The crystals obtained from the eluate were finally recrystallized from methanol. Yield, 0.70 g, mp 213—215 °C, λ (MeOH) 610 ε 6.24×10^4). ν (KBr) 1270—1223 and 1025.

Found: C, 41.25; H, 4.41; N, 4.07; S, 16.55%. Calcd for $C_{25}H_{27}BrN_2O_7S_4\cdot 3H_2O$: C, 41.14; H, 4.53; N, 3.84; S, 17.59%. Found (dried at 145 °C, 7 hr): C, 44.17; H, 4.57; N, 4.06%. Calcd for $C_{25}H_{27}BrN_2O_7S_4$: C, 44.43; H, 4.00; N, 4.15%.

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