Synthesis of Dyes with the Neocyanine Structure Presented by Brooker, and Related Dyes. IV. Structure of the Dyes Obtained by the Condensation of 3-Ethyl-2-methylbenzothiazolium Iodide with Nitrone or Anil Derivatives

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It has been shown in the preceding paper¹⁾ that the condensation of phenylnitrone of 3-ethyl-2-formylbenzothiazolium iodide and 3-ethyl-2-methylbenzothiazolium iodide in pyridine gave four kinds of dyes and their structures were deduced from analytical values and absorption spectra.

In order to examine the formation process of these dyes, the anil I and 3-ethyl-2-methylbenzothiazolium iodide were reacted by refluxing for a short time (8~15 min.) in pyridine and, in this case, 3, 3-diethyl-9-(3-ethyl-1-thia-3-azoniainden-2-yl)thiacarbocyanine diiodide (VI) alone was obtained. This result shows that

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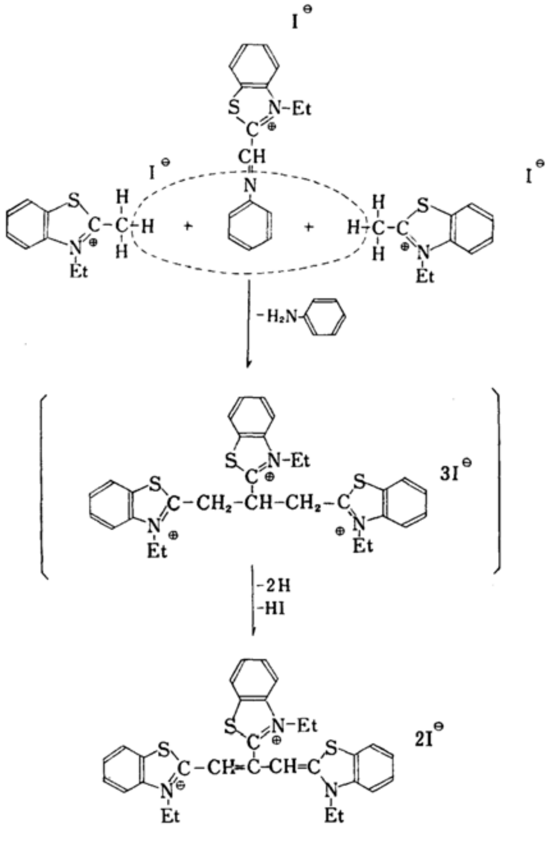
1) S. Kimura, This Bulletin, 33, 872 (1960).

this dye VI is initially formed in the early stage of this reaction and its formation mechanism is considered to be as follows:

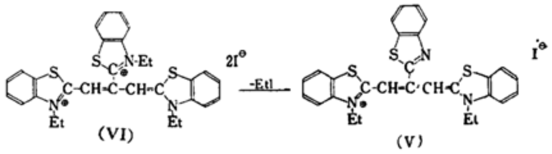


(VI)

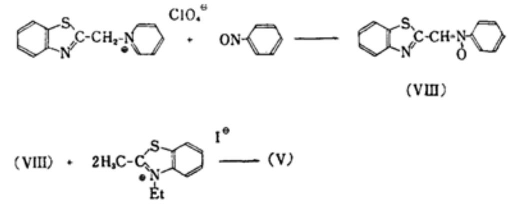
Dehydrogenation of cyanines in pyridine had been observed already by Mills[2] and the present reaction was considered to be of similar mechanism. The dye VI obtained earlier was isolated as an anhydrous salt, but the same dye obtained in the present series of experiments possessed 2 mol. of water of crystallization. The same dye VI was also obtained on replacing the anil I with the nitrone II but the yield of the dye was better when the anil was used.

Tanabe synthesized dyes of this structure and reported the formation of 3-ethyl-2-trichloromethylbenzothiazolium chloride as an intermediate during the reaction of 3-ethyl-2-methylbenzothiazolium iodide and thionyl chloride. On following this reaction, a substance of m. p. 124°C (decomp.), identical with that reported in the literature, was obtained in a good yield. The elemental analytical values, however, did not correspond to those of the objective intermediate and further, iodine was detected besides the chlorine atom. Therefore, this product was not considered to be 3-ethyl-2-trichloromethylbenzothiazolium chloride as reported in the literature. Further, an attempt was made to prepare a dye with this intermediate but a single dye of m. p. 85°C as given in the literature was not obtained and in its stead, a crude dye of m. p. 185°C (decomp.) was obtained. This dye was submitted to paper chromatography and dye spots of yellow, magenta, and purple were separated on the chromatogram, showing the dye to be a mixture. Although further examination of this crude dye mixture was not made, it is certain that the dye VI obtained in the present series of experiments is not the same as the dye obtained by Tanabe.

This dye VI was heated at 130°C for about 12 hr. in the Abderhalden apparatus for the purpose of determining the water of crystallization and the loss in weight was more than that calculated. Therefore, the dried sample was examined by paper chromatography and it was found that the dye VI had changed into the structurally unknown dye V described in the preceding paper. Consideration of this phenomenon showed the necessity of assuming the liberation of ethyl iodide and analytical results supported this assumption. Therefore, the structure of this dye V must be 3, 3′-diethyl-9-(2-benzothiazolyl)thiacarbocyanine iodide.



In order to clarify the structure of this dye V an attempt was made to synthesize it by a different route. With reference to the report of Ried and others[3], iodine was applied to 2-methylbenzothiazole in pyridine, and the *N*-(benzothiazol-2-ylmethyl)pyridinium perchlorate obtained therefrom was reacted with nitrosobenzene to form the phenylnitrone VIII of 2-formylbenzothiazole. Condensation of VIII with 2 mol. of 3-ethyl-2-methylbenzothiazolium iodide in pyridine afforded the same dye as V. This fact proves the correctness of the structure of 3, 3′-diethyl-9-(2-benzothiazolyl)thiacarbocyanine iodide for V.



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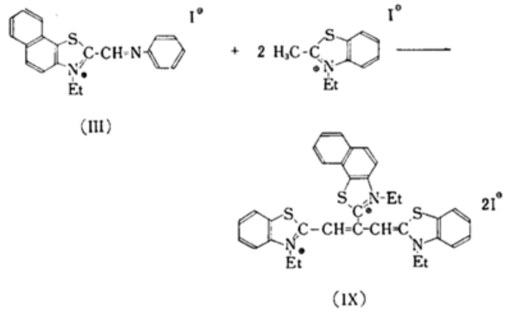
[2] W. H. Mills, *J. Chem. Soc.*, **121**, 455 (1922).

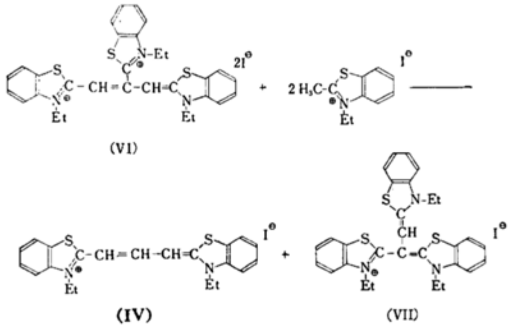
[3] W. Ried and H. Bender, *Ber.*, **89**, 1893 (1956).

With the identification of the structure of the dye V, the structure of the dye VI also became certain and conversion of this dye VI into V was experimentally proved by refluxing in pyridine for about 2 hr.

Condensation of the anil III of 3-ethyl-2-formylnaphtho-[2, 1-*d*] thiazolium iodide with 2 mols. of 3-ethyl-2-methylbenzothiazolium iodide in pyridine afforded, as anticipated, 3,3′-diethyl-9-(3-ethyl-1-thia-3-azoniacyclopenta-[*a*] naphth-2-yl) thiacarbocyanine diiodide (IX). It was thereby found that this process can be recommended as a general method for the synthesis of dyes of this type.

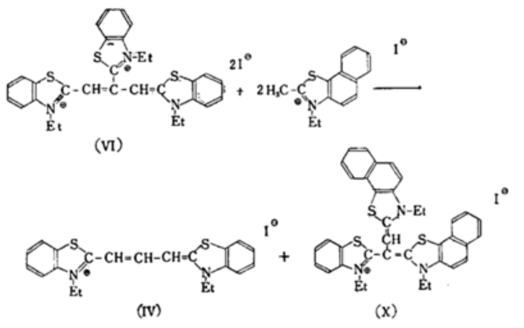


The foregoing experiments have revealed the course of formation of the dyes V and VI in the reaction described in the preceding paper and, consequently, formation of the dyes thought to be 3, 3′-diethylthiacarbocyanine iodide (IV), and 3, 3′-diethyl-8-(3-ethyl-2-benzothiazolinylidenemethyl) thiacyanine iodide (VII) was found to occur through the reaction of 3-ethyl-2-methylbenzothiazolium iodide with 3, 3′-diethyl-9-(3-ethyl-1-thia-3-azoniainden-2-yl)-thiacarbocyanine diiodide (VI) in pyridine.



The structure of the dye VII was merely presumed from its analytical values and absorption spectrum, and unequivocal establishement of this structure has not succeeded as yet, but it is certain that the dye VI is cleaved at the 9-position to liberate the substituent group to form the dye IV. In order to ascertain this cleavage reaction, the dye VI was refluxed with 3-ethyl-2-methylnaphtho [2, 1-*d*] thiazolium iodide in pyridine and the same dye (IV) was found to be formed. Whether the dye X formed at the same time is the anticipated 3, 3′-diethyl-8-(3-ethyl-2-naphtho [2, 1-*d*] thiazolinylidenemethyl)-6′, 7′-benzothiacyanine iodide or not is still uncertain since, although the analytical values of the dye X are comparatively close to the theoretical values, its absorption maximum is in a longer wavelength region (650 mμ), and this is unthinkable in the case of monomethine dyes.

Therefore, structural determination of these dyes VII and X must await further studies.



Experimental

Reexamination of Synthetic Method Tanabe's for the So-called 3, 3′-Diethyl-9-(3-ethyl-1-thia-3-azoniainden-2-yl) thiacarbocyanine Diiodide.—The experiments followed Tanabe's report[4]. To 6.1 g. (0.02 mol.) of 3-ethyl-2-methylbenzothiazolium iodide, 24 ml. of thionyl chloride was added dropwise with cooling, by which the iodide turned black and dissolved gradually. Ether was added to this reaction mixture and the yellow precipitate thereby formed was collected to 7 g. of a solid, m. p. 100°C. This was dissolved in thionyl chloride, reprecipitated with ether, and 5 g. (yield, 79%) of yellow powder, m. p. 124°C (decomp.), was obtained. This substance agrees with the so-called 3-ethyl-2-trichloromethylbenzothiazolium chloride, m. p. 125°C (decomp.), reported by Tanabe, but he had assumed this structure from the analytical value of the chlorine alone, and elemental analyses in the present series of experiments gave results which were inconsistent with this structure.

Found: C, 30.81; H, 3.43; N, 3.70. Calcd. for $C_{10}H_9NCl_4S$: C, 37.85; H, 2.84; N, 4.42%.

A solution of 1 g. (0.0032 mol.) of this intermediate product and 2 g. (0.0057 mol.) of 3-ethyl-2-methylbenzothiazolium iodide dissolved in 2.5 ml. of acetic anhydride, added with 1 g. of anhydrous potassium acetate, was heated in an oil bath at 120~130°C for 10 min., cooled, and ether was added to this reaction mixture. The crude dye that precipitated out was collected by filtration washed with water, and the powdery dye so obtained was recrystallized from acetone to 0.5 g. of pale purplish brown powder, m. p. 185°C (decomp.). This dye

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[4] Y. Tanabe, *J. Pharm. Soc. Japan*, **74**, 814 (1954).

is different from that of m. p. 85°C reported in the literature and was found to be a mixture of three kinds of dyes, giving spots colored violet, pink, and yellow by paper chromatography. R_f values were 0.54 (violet), 0.72 (pink), and 0.81 (yellow) (butanol : water = 6 : 1). This dye was also different from the dye VI obtained in the present series of experiments.

Results of this reexamination indicated that there is some doubt about the structure of this intermediate and the dye produced in the present series of experiments was never identical with that reported in the literature. Therefore, this examination was not followed further.

Formation of 3, 3′-Diethyl-9-(2-benzothiazolyl)-thiacarbocyanine Iodide (V) by Liberation of Ethyl Iodide from 3, 3′-Diethyl-9-(3-ethyl-1-thia-3-azonia-inden-2-yl) thiacarbocyanine Diiodide (VI). — The dye VI was heated in the abdelhalden apparatus at 120∼130°C in 20 mmHg for 12 hr. and the loss in weight amounted to 12.22%. The values calculated for 2 mol. of water of crystallization is 4.41%. This dried dye was developed by paper chromatography by which it separated into two kinds of dyes : one a violet zone of R_f 0.44 and the other of reddish violet zone of R_f 0.89 (butanol : water = 6 : 1). The violet zone was that of the starting dye VI and the reddish violet zone agrees with R_f 0.89 of the dye V.

On boiling this dye VI in pyridine for 2 hr., the dye VI completely changed into V and the unity of this dye was proved by the reddish violet single zone of R_f 0.90 in the paper chromatogram.

The fact that the chromatographic purification of the mixture of four kinds of dyes through alumina column only afforded three kinds of dyes, IV, V and VII, as described in the preceding paper, indicates that VI had transited into V.

Preparation of the Phenylnitrone VIII of 2-Formylbenzothiazole. — To a solution of 6.52 g. (0.02 mol.) of *N*-(benzothiazolyl-2-methyl)-pyridinium perchlorate and 2.14 g. (0.02 mol.) of nitrosobenzene dissolved in 40 ml. of pyridine, 20 ml. of 2 N sodium hydroxide solution was added and the mixture was stirred, by which process exothermic reaction took place. The mixture was allowed to cool and crystals separated out after 2 hr. The crystals were collected by filtration, washed with ethanol, and 3 g. of yellowish brown needles, m. p. 160∼167°C, was obtained. Recrystallization from ethanol afforded 1.1g. (yield, 21.6%) of pale yellowish brown needles, m. p. 163∼164°C.

Found: C, 66.28; H, 4.17; 10.82. Calcd. for $C_{14}H_{10}ON_2S$: C, 66.15; H, 3.98; N, 11.02%.

Preparation of 3, 3′-Diethyl-9-(2-benzothiazolyl)-thiacarbocyanine Iodide (V).—A solution of 0.254 g. (0.001 mol.) of the phenylnitrone VIII of 2-formylbenzothiazole and 0.61 g. (0.002 mol.) of 3-ethyl-2-methylbenzothiazolium iodide in 3 ml. of pyridine was refluxed in an oil bath of 120°C for 10 min. The color of the reaction mixture changed from the initial yellow through green to purple. Ether was added to the reaction mixture to precipitate the dye formed which was collected by decantation and washed with wather to 0.4 g. of crystalline powder, m. p. 192∼195°C (decomp.). Recrystallization from ethanol afforded 0.1 g. (yield, 16%) of green needles, m. p. 266°C (decomp.): λ_{max} 580mμ. Paper chromatogram : R_f 0.89 (butanol : water = 6 : 1) : single spot of violet, indicating the substance to be identical with dye V among the four kinds of dyes isolated from a mixture.

Synthesis of 3, 3′-Diethyl-9-(3-ethyl-1-thia-3-azoniacyclopenta[*a*]naphth-2-yl)thiacarbocyanine Diiodide (IX).—A mixture of 2.2 g. of the anil III of 3-ethyl-2-formylnaphtho[2, 1-*d*]thiazolium iodide and 3.0 g. of 3-ethyl-2-methyl-benzothiazolium iodide in 30 ml. of pyridine was heated in an oil bath of 130°C for 25 min., cooled, and ether was added to this mixture. The precipitate thereby formed was separated by decantation, washed with ether and water, and warmed with a small amount of ethanol. On allowing this solution to cool, navy-blue crystalline powder was obtained which melted once at 185°C, resolidified, and again melted with decomposition at 245°C. Two recrystallizations from ethanol failed to change this mode of melting. Paper chromatogram exhibited a single zone of bluish purple color at R_f 0.51, λ_{max} 585 mμ. The analytical values agreed with those calculated as a monohydrate.

Found: C, 48.06; H, 4.07; N, 5.08; I, 29.54. Calcd. for $C_{34}H_{31}N_3I_2S_3 \cdot H_2O$: C, 48.06; H, 3.89; N, 4.95; I, 29.95%.

Formation of 3,3′-Diethylthiacarbocyanine Iodide (IV) and 3, 3′-Diethyl-8-(3-ethyl-2-benzothiazolinylidenemethyl)thiacyanine Iodide (VII) from the Dye VI and 3-Ethyl-2-methylbenzothiazolium Iodide.— A mixture of 0.1 g. of VI and 0.075 g. of 3-ethyl-2-methylbenzothiazolium iodide in 30 ml. of pyridine was boiled and an aliquot of this reaction mixture was periodically examined by paper chromatography (butanol : water = 6 : 1) to find the formation of dyes. After 30 min., the starting dye still appeared as a spot at R_f 0.35, but this disappeared after 60 min., and the reaction solution contained three kinds of dyes, one of reddish pink zone at R_f 0.75 (dye IV), one of violet zone at R_f 0.86 (dye V), and one of brown zone at R_f 0.93 (dye VII).

Formation of 3,3′-Diethylthiacarbocyanine Iodide (IV) and 3, 3′-Diethyl-8-(3-ethyl-2-naphtho[2, 1-*d*]-thiazolinylidenemethyl)-6′, 7′-benzothiacyanine Iodide (X) from the Dye VI and 3-Ethyl-2-methyl-naphtho[2, 1-*d*]thiazolium Iodide. — A mixture of 1 g. of IV and 0.9 g. of 3-ethyl-2-methylnaphtho[2, 1-*d*]-thiazolium iodide in 300 ml. of pyridine was boiled at 130°C for 4 hr., pyridine was removed under a reduced pressure, and the residue was washed with 2 portions of ether. The residue was dissolved in acetone and the solution was developed through an alumina column by which the product separated into three bands of greenish black, reddish pink, and violet, from bottom to top. The reddish pink band was eluted with acetone, acetone solution was evaporated, and the residue was treated with ether, affording 0.1 g. of a crude dye, m. p. 200°C (decomp.) : λ_{max} 580 mμ : paper chromatogram : R_f 0.74 (butanol : water = 6 : 1). This was identified with the dye IV.

The greenish black zone was eluted with acetone and the residue obtained on evaporation of acetone was treated with ether, affording greenish black crystalline powder, m. p. 192°C (decomp.). Recrystallization from methanol gave 0.5 g. of a dark green crystalline powder, m. p. 195°C (decomp.) : $\lambda_{\max}$ 470 and 650 mμ. Paper chromatogram : a single spot of dark green color at R_f 0.94 (butanol : water=6 : 1).

Found : C, 59.75 ; H, 4.56 ; N, 6.00. Calcd. for $C_{37}H_{32}N_3IS_3$: C, 59.90 ; H, 4.32 ; N, 5.67%.

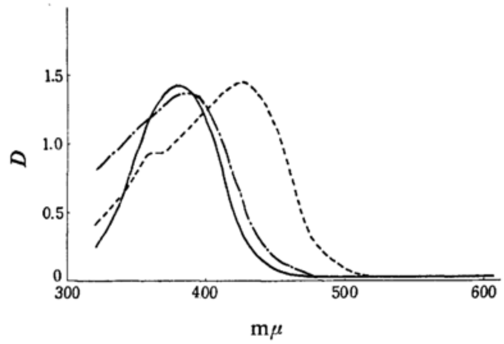

Fig. 1. Absorption spectral curves of I, II and III (in ethanol).
—·— (I), —— (II), ---- (III)

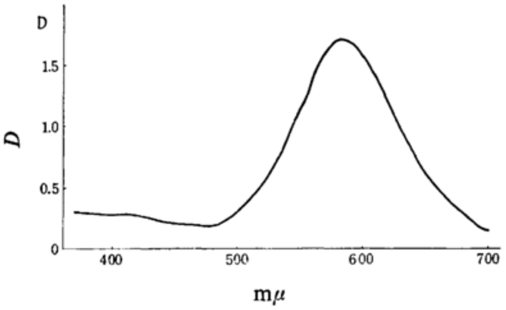

Fig. 2. Absorption spectral curve of IX (in ethanol).

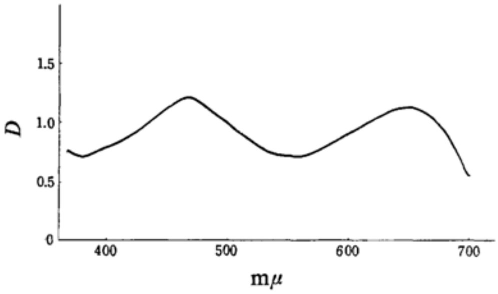

Fig. 3. Absorption spectral curve of X (in ethanol).

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