# *Synthesis of Dyes with the Neocyanine Structure Presented by Brooker, and Related Dyes. III. Condensation of 3-Ethyl-2-methylbenzothiazolium Iodide and Nitrosobenzene, and the Dyes Obtained from its Condensates*

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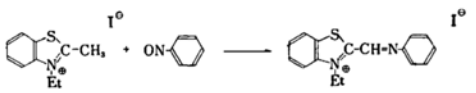
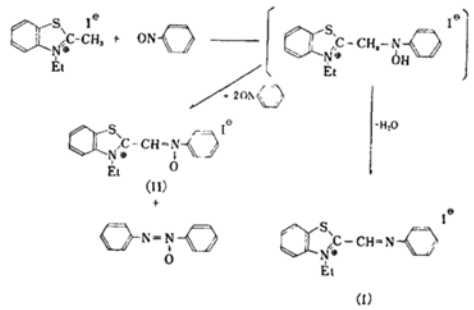
The synthetic process for the "Brooker-type dyes" described in the preceding paper[1] could possibly be improved with regard to the yield and by-product formation. The present series of experiments was carried out in order to obtain some fundamental concept of this reaction. An attempt was first made to prepare the 2-aldehyde anil derivative I of 3-ethyl-2-methyl-benzothiazolium iodide by the condensation of 3-ethyl-2-methylbenzothiazolium iodide and nitrosobenzene. In accordance with the report Katayanagi[2], the condensation of 3-ethyl--2-methylbenzothiazolium iodide and nitrosobenzene was carried out in ethanol with piperidine as a condensation agent. The product of this reaction was obtained as dark purple-needle crystals, m. p. 213–214°C (decomp.) $\lambda_{max}$ 390 m$\mu$ which became bluish purple prisms, m. p. 215°C (decomp.), when recrystallized from acetic anhydride. But this was not the expected anil I and was found to be a nitrone II.



(I)

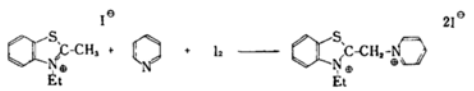
The basic condensation reactions of active methyl and nitroso compounds in general has been known from olden times as the Ehrlish-Sachs reaction[3]. It has been clarified in recent years that this reaction is accompanied by an oxidative reaction to form a nitrone as a by-product, besides the anil. It is also known that these two products are difficult to separate. The nitrone obtained in the present series of experiments was not completely pure and rather difficult to separate. When the impure nitrone was boiled with nitrosobenzene in ethanol, a dark purple substance was obtained which crystallized in reddish brown needles, m. p. 219°C (decomp.). Its analytical values were closer to those of the phenylnitrone. Then a mixture of 1 mol. of 3-ethyl-2-methyl-benzothiazolium iodide and 3 mol. of nitroso-benzene in ethanol was reacted with the addition of piperidine and reddish brown needles, m. p. 219°C (decomp.) were obtained. This was found to be pure nitrone II from its analytical values. The mechanisms of this reaction were shown by the following scheme:



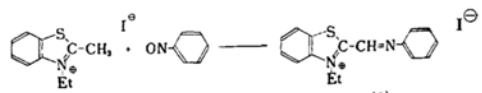
(II)

(I)

Synthesis of the phenylnitrone was also attempted with reference to the general method of synthesis by Kröhnke and others[4] for the phenylnitrone of 1-methyl-2-formylpyridinium iodide, and preparation of *N*-(3-ethyl-1-thia-3-azoniainden-2-ylmethyl) pyridinium diiodide was undertaken, but the product seemed to be labile and the objective was not attained.



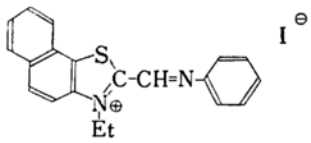
A purely synthetic preparation of the anil from heterocyclic ammonium salts has recently been reported by Mcgookin[5]. This process was applied to 3-ethyl-2-methylbenzothiazolium iodide and pure anil I of 3-ethyl-2-formyl-benzothiazolium iodide was obtained. In this case, equimolecular amounts of 3-ethyl-2-methylbenzothiazolium iodide and nitroso-benzene were reacted in absolute ethanol, with anhydrous potassium carbonate as the condensation agent, and red needles, m. p. 199°C (decomp.) were obtained.



(I)

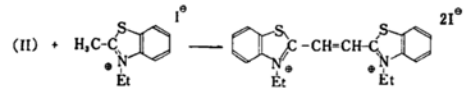
1) S. Kimura, *Bull. Soc. Sci. Phot. Japan*, **9**, 45 (1959).
2) M. Katayanagi, *J. Pharm. Soc. Japan*, **69**, 38 (1949).
3) P. Ehrlich and F. Sachs, *Ber.*, **32**, 2341 (1899).
4) F. Kröhnke and H. Leister, ibid., **71**, 2583 (1938).
5) A. Mcgookin, *J. Appl. Chem.*, **5**, 65 (1955).

Similarly, condensation, of 3-ethyl-2-methylnaphtho[2, 1-*d*]-thiazolium iodide and nitrosobenzene afforded the anil III of 3-ethyl-2-formylnaphtho[2, 1-*d*] thiazolium iodide.

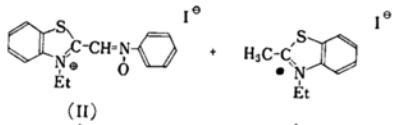


(III)

We then attempted the synthesis of 3, 3′-diethyl-2, 2′-vinylidendibenzothiazolium diiodide as a clue to the synthesis of "Brooker-type dyes", by the condensation of 3-ethyl-2-methylbenzothiazolium iodide with these nitrone derivative obtained above. Unexpectedly, however, this reaction was found to be much more complicated than was anticipated.



By refluxing an equimolar mixture of this phenylnitrone of 3-ethyl-2-formylbenzothiazolium iodide and 3-ethyl-2-methylbenzothiazolium iodide in pyridine for 30 min., a mixture of four kinds of dyes was obtained: the dyes were purified by fractional crystallization from acetone according to the scheme shown:



(II)

refluxed in pyridine for 30 min.
$Et_2O$ added, and washed with water

Dark pinkish purple needles m. p. 141～150° with decomp. p. 181°C

Waste liquor

recrystallized from acetone

Tan needles with copper luster m. p. 255～256°C (decomp.)

Filtrate

concn.

Dark green crystals m. p. 243～245°C (decomp.)

Filtrate

concn.

recrystd. from MeOH

recrystd. from MeOH, then from acetone

Filtrate

Green needles m. p. 266°C (decomp.) $\lambda_{max}$ 580 mμ (V)

Filtrate

Dark tan crystal with copper luster, m. p. 187～194°C (decomp.)

Waste liquor

recrystd. from MeOH

Copper-colored crystals. m. p. 265°C (decomp.) $\lambda_{max}$ 580 mμ (VI)

concd.

Solid

recrystd. from MeOH

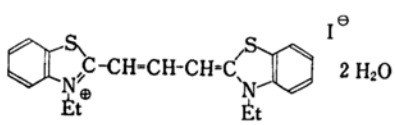
Bluish violet needles, m. p. 265°C (decomp.) $\lambda_{max}$ 560 mμ (IV)

recrystd. from acetone then twice from MeOH

Dark brown crystals, m. p. 218°C (decomp.) $\lambda_{max}$ 457 mμ (VII)

These dyes were also examined by paper chromatography and exactly the same four kinds of dyes were found to have been formed.

The structures of these four kinds of dyes

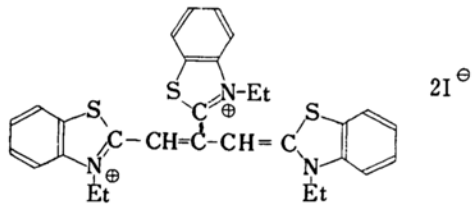


(IV)

were examined from their analytical values and absorption spectra and IV was identified with the known 3,3′-diethylthiacarbocyanine iodide dihydrate by comparison with the dyes prepared by a known route.

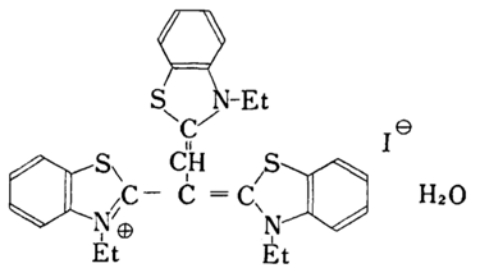
The analytical values of V were very close to those of the known trinuclear carbocyanine, 3, 3′-diethyl-9-(3-ethyl-2-benzothiazolinylidenemethyl)thiacarbocyanine iodide, but the absorption spectra and physical characteristics were entirely different and no presumption could be made of its structure. The analytical

values of VI suggested it to be a diiodide, and accordingly a trinuclear carbocyanine, 3,3'-dietyl-9-(3-ethyl-1-thia-3-azoniainden-2-yl)-thiacarbocyanine diiodide, was presumed. The dye with this structure had earlier been synthesized by Tanabe[6] who recorded the melting point of 85°C and $\lambda_{max}$ 545 m$\mu$, but these data are entirely different from those of VI and definite conclusion can be drawn. Its 8-substituted isomer was synthesized by Anish[7] and shwos entirely different physical properties.




(VI)

VII was assumed to be a monomethine from its absorption spectrum and analytical values suggested the structure of a trinuclear monomethinecyanine, 3,3'-diethyl-8-(3-ethyl-2-benzothiazolinylidenemethyl)thiacyanine iodide monohydrate.




(VII)

Chemical evidences for the structure of these four dyes will be discussed in the following paper.

## Experimental

**Preparation of the Phenylnitrone II of 3-Ethyl-2-formylbenzothiazolium Iodide.**—A solution of 50 g. of 3-ethyl-2-methylbenzothiazolium iodide and 18 g. of nitrosobenzene dissolved in 500 ml. of ethanol with warming on a water bath, added with 7 drops of piperidine, was stirred thoroughly and allowed to stand for about 2 hr. The dark purple crystals that separated out were collected by filtration, washed with water and methanol, and 21 g. (yield, 33%) of a dye, m. p. 156~164°C (decomp. at 174°C), was obtained. Recrystallization of this dye from 200 ml. of methanol afforded 7 g. (yield, 11%) of dark purple needles, m. p. 213~214°C (decomp.). Approximately the same result was obtained on repeating this experiment several times.

These dyes were boiled with about 40 volumes of acetic anhydride for 30 min. and the dark bluish purple prismatic crystals thereby formed were collected by filtration. After washing with ether the dye melted at 215°C with decomposition and its analytical value supported the nitrone structure.

Found: C, 46.56; H, 4.07; N, 6.62; I, 29.93. Calcd. for $C_{16}H_{15}ON_2IS$: C, 46.82; H, 3.66; N, 6.83; I, 30.98%.

**Condensation of the Phenylnitrone II of 3-Ethyl-2-formylbenzothiazolium Iodide and 3-Ethyl-2-methylbenzothiazolium Iodide.**—A solution of 6 g. of the phenylnitrone II of 3-ethyl-2-formylbenzothiazolium iodide and 4.8 g. of 3-ethyl-2-methylbenzothiazolium iodide in about 100 ml. of pyridine was refluxed for 30 min. and the major part of pyridine was distilled off under reduced pressure. About 100 ml. of ether was added to the residue, the dark purple crystals that precipitated out were washed with several 300 ml. portions of ether. The residue was mixed with 50 ml. of water, filtered, and the precipitate on the filter was washed with water. The dark pinkish violet crystals, m. p. 141~150°C (decomp. at 181°C) so obtained were dissolved in ca. 1 l. of acetone, concentrated to 400 ml., and 0.5 g. of dark tan crystals with copper luster, m. p. 255~256°C (decomp.) was obtained. Concentration of its mother liquor afforded 0.3 g. of dark green crystals, m. p. 243~245°C (decomp.). Further concentration of its mother liquor to about 50 ml. separated an oily substance which crystallized upon addition of ca. 50 ml. of ether. The crystals were collected by filtration and washed with ca. 30 ml. of ether, affording 0.4 g. of dark tan crystals with copper luster, m. p. 187~197°C (decomp.). These three kinds of crude dyes were purified through fractional crystallization and four kinds of pure dyes were isolated.

**Purification of the Dark Tan Crystals, M. P. 255~256°C (Decomp.).**—A solution of 0.5 g. of the crude dye dissolved in 50 ml. of methanol was concentrated to about 30 ml. and 0.35 g. of green needles, m. p. 260~262°C, separated. This substance was recrystallized twice from methanol to 0.18 g. of green needles V m. p. 266°C (decomp.) $\lambda_{max}$ 580 m$\mu$.

Found: C, 53.31; H, 4.06; N, 6.95; I, 20.53. Calcd. for $C_{28}H_{24}N_3IS_3$: C, 53.75; H, 3.84; N, 6.72; I, 20.25%.

The initial filtrate left after separation of the green crystals was concentrated and the copper-colored crystals m. p. 258°C (decomp.), so formed were recrystallized from methanol to clustered crystals VI m. p. 265°C (decomp.) $\lambda_{max}$ 580 m$\mu$.

Found: C, 45.80; H, 4.29; N, 5.22. Calcd. for $C_{30}H_{29}N_3I_2S_3$: C, 46.10; H, 3.70; N, 5.38%.

**Purification of Dark Green Crystals, M. P. 243~245°C (Decomp.).**—A solution of 0.3 g. of the crude dye dissolved in 60 ml. of methanol was concentrated to about 30 ml. and a mixture of green and bulish purple needle crystal was obtained. The green crystals were comparatively sparingly soluble in acetone and, therefore, the bluish purple crystals

6) Y. Tanabe, *J. Pharm. Soc. Japan*, 74, 814 (1954).
7) A. W. Anish, U. S. Pat. 2,427,177 (1944).

dissolved out with 100 ml. of acetone, leaving 0.1 g. of green needles, m. p. 262°C (decomp.). The acetone solution was concentrated to 80 ml. and 0.05 g. of the same green crystals, m. p. 265°C (decomp.) separated. These green crystals were found to be identical with the dye V described above. The acetone mother liquor was concentrated to 20 ml. and 0.04 g. of bluish purple needles, m. p. 260°C (decomp.), was obtained. This was recrystallized from a small amount of methanol to 0.01 g. of bluish purple needles IV m. p. 265°C (decomp.) $\lambda_{max}$ 560 m$\mu$.

Found: C, 48.03; H, 4.55; N, 5.52; I, 25.61. Calcd. for $C_{21}H_{21}N_2IS_2 \cdot 2H_2O$: C, 47.70; H, 4.73; N, 5.31; I, 24.03%.

**Purification of the Dark Tan Crystals with Copper Luster, M. P. 187~194°C (Decomp.).** —A solution of 0.4 g. of the crude dye dissolved in 300 ml. of acetone was concentrated to 50 ml. and 0.3 g. of dark brown needles, m. p. 210~211°C (decomp.) was obtained. This was mixed with a small amount of bluish purple crystals which were removed and the rest was recrystallized twice from methanol to 0.12 g. of dark brown needles, VII, m. p. 218°C (decomp.) $\lambda_{max}$ 457 m$\mu$.

Found: C, 52.25; H, 4.55; N, 6.c9; I, 19.65. Calcd. for $C_{29}H_{28}N_3IS_3 \cdot H_2O$: C, 52.80; H. 4.55; N, 6.37; I, 19.28%.

**Separation of Dye Mixture by Chromatography.** —Instead of the fractional crystallization as described above, the precipitate obtained from the pyridine reaction mixture was purified through chromatography. A solution of 2 g. of this mixture was dissolved in ca. 200 ml. of acetone concentrated to about 100 ml. and allowed to stand overnight. About 400 ml. of acetone was added to this mixture to dissolve the crystals but sparingly soluble crystals V remained undissolved. The green crystals were removed by filtration, the filtrate was concentrated about 200 ml., and the solution was passed through a column of alumina (Merck), requiring about 1.5 hr., the adsorbed layers separated into pale orange, violet, and pink bands. Each of these bands was eluted with acetone, the acetone elute was concentrated, and separated crystals were recrystallized from methanol. Dark brown needles VII m. p. 216°C(decomp.) $\lambda_{max}$ 457 m$\mu$. were obtained from the pale orange band, green needles V m. p. 260°C (decomp.), $\lambda_{max}$ 580 m$\mu$, from the violet band, and bluish purple needles IV m. p. 267~268°C (decomp.), $\lambda_{max}$ 560 m$\mu$, from the pale pink band. The dye VI obtained by fractional crystallization, was not isolated from this chromatographic separation.

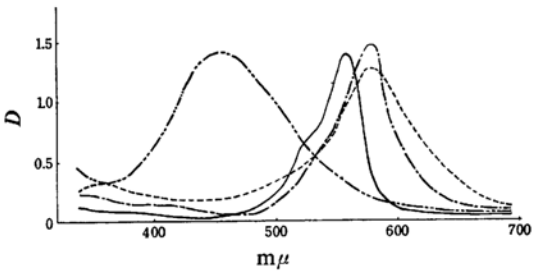



Fig. 1. Absorption spectral curves of IV, V, VI and VII (in ethanol).
—— (IV) —— (V) ---- (VI)
—— (VII)

Chemical evidences for the structure of these four dyes will be discussed in the following paper.

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