295. Studies on Heterocyclic Colouring Matters Part II[1]: $\Delta^{2,2'}$-Bi (2*H*-1,4-benzothiazines)

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(3. IX. 74)

Summary. A novel one-step 'Inverse Indigo Synthesis' of the $\Delta^{2,2'}$-bi(3,4-dihydro-3-oxo-2*H*-1,4-benzothiazine) chromophore is described. Structure, substitution reactions, mechanism of formation, colour and other relevant properties of this system have been investigated in relation to known thioindigos. A synthesis of the basic skeleton of one of the 'Trichosiderins', the colouring matters of human red hair, is reported.

Introduction. – 'INDIGOID' nomenclature has been proposed for a group of colouring matters possessing the common chromophoric systems shown in *Scheme 1* [3].

Scheme 1

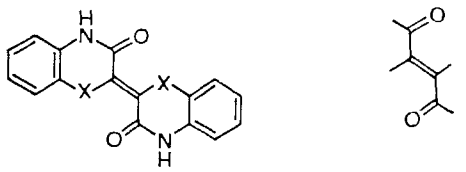
trans *cis*

X = NH, S etc.

Indigoid Chromophore

Beginning with *Baeyer*'s & *Friedländer*'s celebrated syntheses of indigo and thioindigo[2]), respectively [4], such colouring matters have been invariably obtained by a multi-step process. The initial steps involve the synthesis of the constituent heterocyclic monomeric units, followed by the oxidative/condensative coupling of these units to the desired indigoid system [5].

Scheme 2



1 **2**

[1]) Part I see ref. [1]. Presented in part at the 5th International Colour Symposium in Basle, September 23–30, 1973; see ref. [2] for the abstract.

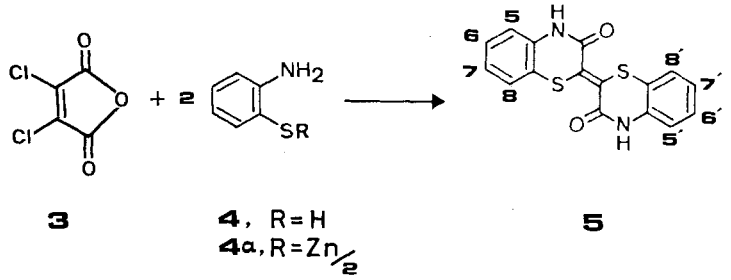
[2]) Chemical Abstracts nomenclature: respectively, [$\Delta^{2,2'}$-Biindoline]-3,3'-dione and [$\Delta^{2,2'(3H,3'H)}$-Bibenzo[*b*]thiophene]-3,3'-dione.

As part of a general programme of synthesis of organic pigments containing amide functions within the chromophore, we now have prepared the novel indigoids of type **1** by constructing the molecule about the central conjugated enedione skeleton **2**.

We have designated this approach to the preparation of indigoid systems as 'Inverse Indigoid Synthesis' since it involves the concomitant formation of both the constituent heterocyclic units and the connecting carbon-carbon double bond. This paper deals with the sulfur derivative of **1** (*i.e.*, X = S).

Synthesis[3]) and Structure. – Treatment of 1 mol of 2,3-dichloromaleic anhydride (**3**) with 2 mol of 2-aminobenzenethiol (**4**) or its zinc salt **4a** in boiling acetic acid, resulted in the formation of an extremely insoluble orange-red compound (*Scheme 3*). This product was assigned the *trans*-2,2'-bis(4*H*-1,4-benzothiazine)-indigo[4]) structure **5** on the basis of elemental and spectral analysis.

Scheme 3



3 **4**, R = H; **4a**, R = Zn/2 **5**

Thus, the mass spectrum showed the molecular ion peak at *m/e* 326. The fragmentation ions at *m/e* 308 (–H_2O), 298 (–CO), 293 (–SH), 284 (–NCO), etc. are presumably the results of complex rearrangements tentatively formulated in *Scheme 4*.

The NMR. spectrum in $(CD_3)_2SO$–NaOD solutions [1] was suggestive of a single, symmetrical *ortho*-disubstituted benzenoid structure[5]) with protons H_a and H_d each appearing as a singly *ortho*-coupled and singly *meta*-coupled quartet at 6.75[6]) and 6.95 respectively. The octet absorptions (doubly *ortho*-coupled and singly *meta*-coupled) due to protons H_b and H_c were discernible at 6.84 and 6.675, respectively. The IR. spectrum (Nujol) showed a single carbonyl band at 1648 cm^{-1}, expected for a molecule with C_{2h}-symmetry and hence the transoid configuration [8].

Mechanism of Formation. – A possible mechanism for the formation of **5** is shown in *Schemes 5* and *6*. It is proposed that the reaction is initiated by the addition of one mol of thiol **4** to one of **3** to form the succinic anhydride derivative **6**. The

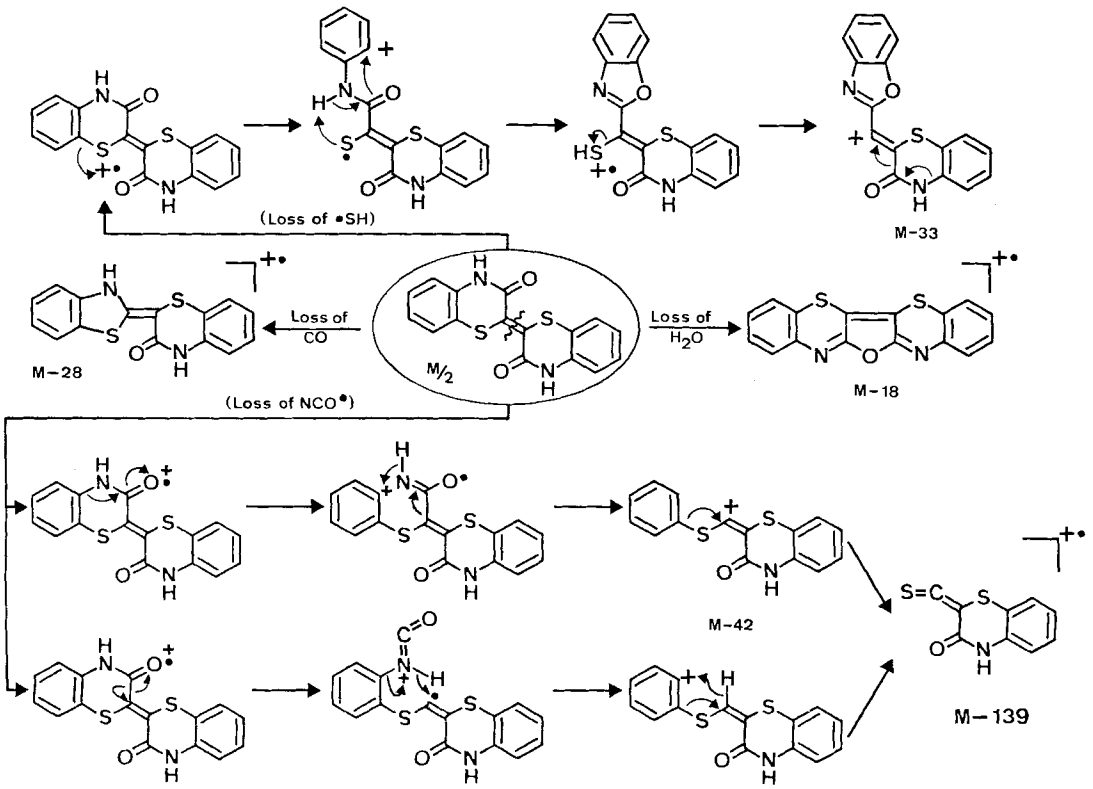
[3]) Based on our patent, see ref. [6].

[4]) According to the system of nomenclature proposed by *Jacobson* & *Friedländer* and generally adopted in textbooks [7]. The Chemical Abstracts name, however, would be: $\Delta^{2,2'}$-bi(3,4-dihydro-3-oxo-2*H*-1,4-benzothiazine).

[5]) The symmetry of **5** permits the following proton designations: H_a = H–C(5) and H–C(5'), H_b = H–C(6) and H–C(6'), H_c = H–C(7) and H–C(7'), and H_d = H–C(8) and H–C(8').

[6]) All chemical shifts are reported in δ ppm.

Scheme 4

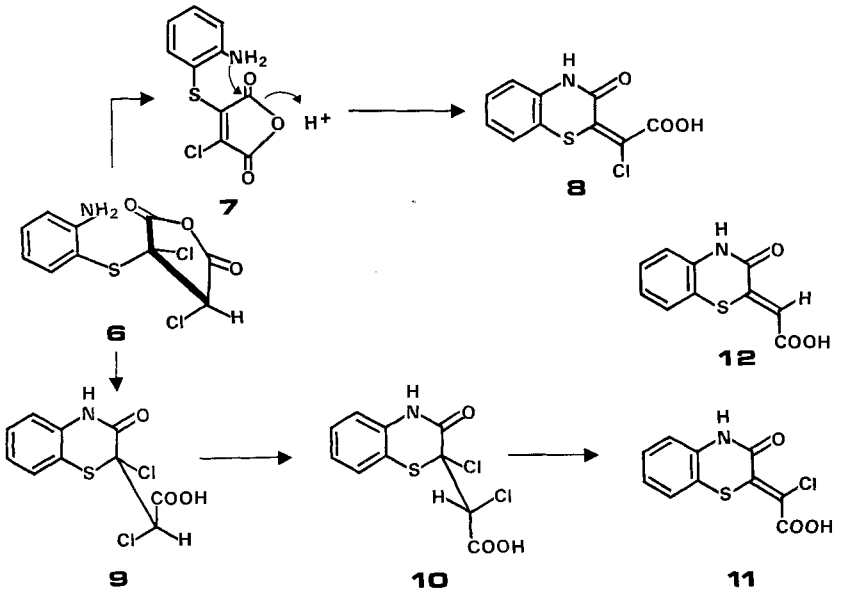


addition, which probably occurs transversely, is the precedented reaction of thiols, in general, with activated double and triple bonds [9] and, in particular, that of **4** with maleic anhydride and its derivatives [10], and with acetylenedicarboxylic acid/esters [11]. The adduct **6** can undergo *cis*-elimination of hydrochloric acid to lead to **7** and then to 3,4-dihydro-3-oxo-2*H*-1,4-benzothiazine-$\Delta^{2,\alpha}$-chloroacetic acid (**8**) as indicated. Alternatively, **6** may first cyclize to **9** and then undergo *trans*-elimination of hydrochloric acid *via* **10** to **11**, the *trans*-isomer of **8**.

The operation of the former mechanism is suggested by the observation that, when the reaction of **3** with **4** is carried out in a molar proportion of 1:1, the main product of the reaction is **8**[8]). Assignment of the structure **8** rather than **11** to this product is based on IR. evidence. The compound showed two carbonyl bands, one at 1700 cm^{-1} (COOH) and the other at 1670 cm^{-1} (CONH). In 3,4-dihydro-3-oxo-2*H*-1,4-benzothiazine-$\Delta^{2,\alpha}$-acetic acid (**12**), obtained by the interaction of acetylene-

[8]) We have considered the alternative formation of **8** *via* the β-chloro-enol **13**, (*i.e., Michael*-addition), but have ruled out this possibility on the following grounds: a) Since maleic anhydride undergoes 1,2-addition of **4**, **3** will be more likely to do so. The inductive effect of chlorine would be expected to result in an increase in the stability of the carbanionic centre (and the site of protonation) in **14** compared with that in **15**; b) In the reaction of 2,3-di-

Scheme 5



dicarboxylic acid with **3** (*trans*-addition), bands due to both the carboxyl and amide carbonyl groups appear at 1670 cm^{-1} [13].

Compound **8** would be expected to react readily with the second mol of **4** *via* such intermediate stages as **17** and **18** to lead ultimately to **5**, as depicted in *Scheme 6*[9]).

Thus, the formation of **5** is assumed to occur by the *trans*-addition of **4** to the available activated double bonds in both steps but by the *cis*-elimination of hydrochloric acid in the first step and its *trans*-elimination in the second. Intramolecular lactonization processes, required for the derivation of benzothiazine rings, take place during the course of the reaction or in the last step. The cause of this dual mode of

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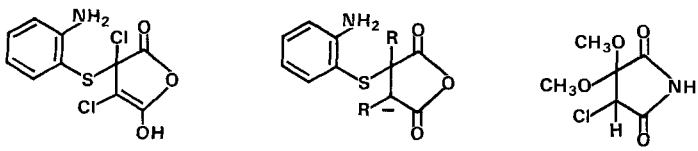
chloromaleimide with 2 mol of sodium methoxide, exclusive formation of the ketal succinimide **16** has been reported [12].

These observations seem to suggest that 1,2-addition is favoured over both the elimination and 1,4-addition reactions in such systems.

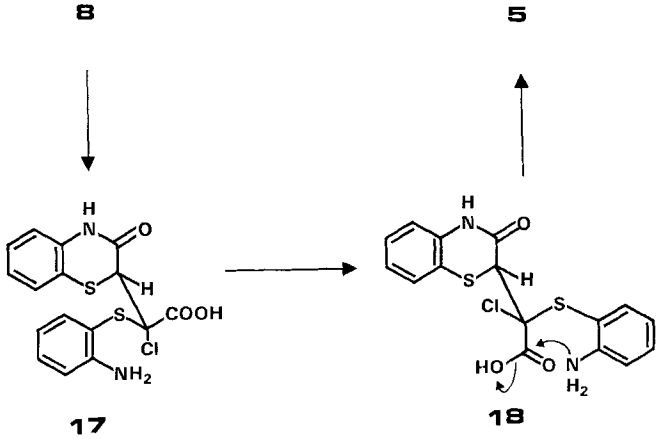
Scheme 5a



13 **14**, R = Cl; **15**, R = H **16**

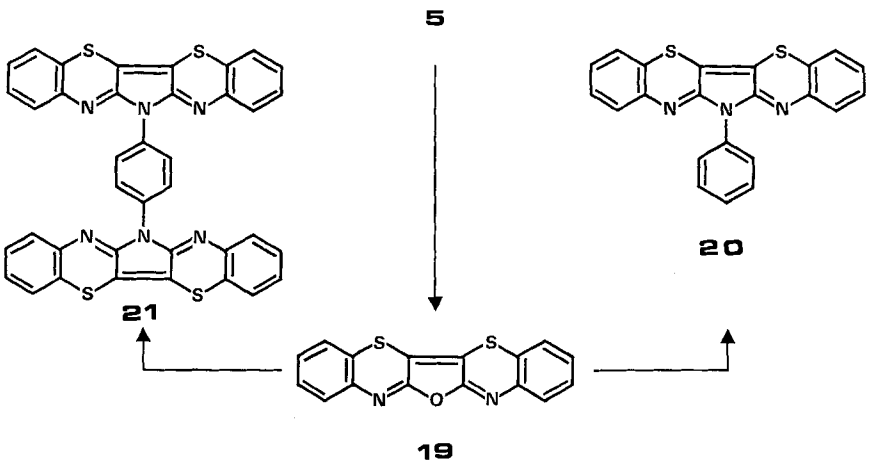
[9]) For the addition of **4** to a system related to **8** see ref. [14].

Scheme 6



elimination is understandable. In the first step, only *cis*-elimination (from **6**) is both possible and favoured[10]. In the second, both modes of elimination are possible but the *trans* would be favoured[11].

Scheme 7



Reactions of Benzothiazine-indigos. – Reaction of **5** with thionyl chloride in dimethylformamide resulted in the exothermic formation of the new heterocycle furo[3,2-*b*:4,5-*b'*]bis[1,4]benzothiazine (**19**).

Furan **19** could be further treated with primary aromatic monoamines, *e.g.*, aniline, to give 6-phenyl-6*H*-pyrrolo[3,2-*b*:4,5-*b'*]bis[1,4]benzothiazine (**20**)[12], or

[10] In five-membered cyclic systems, eliminations can occur from a *syn*-periplanar (or eclipsed) conformation, over a dihedral angle of 0°, a conformation rare in non-cyclic systems [15].

[11] For the discussion see ref. [16].

[12] For a list of amines thus condensed with **19**, see ref. [17]. For an alternative synthesis of **20** and **21**, see ref. [18].

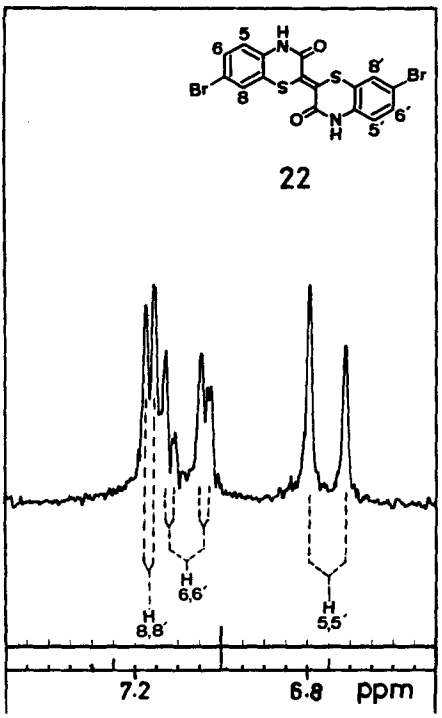


Fig. 1. *NMR. spectrum of* **22** *in* $(CD_3)_2SO$—*NaOD*

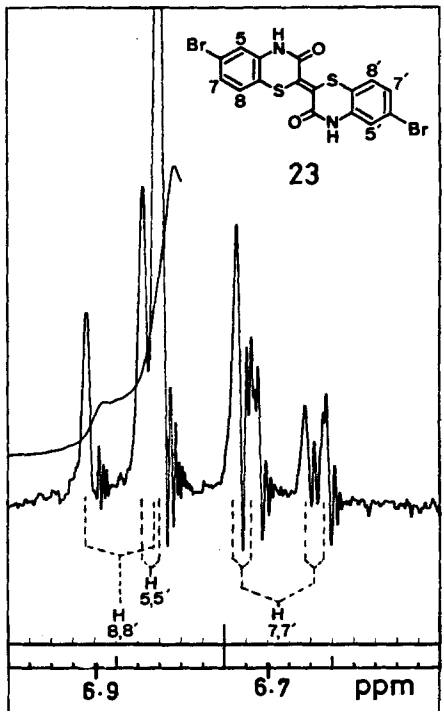
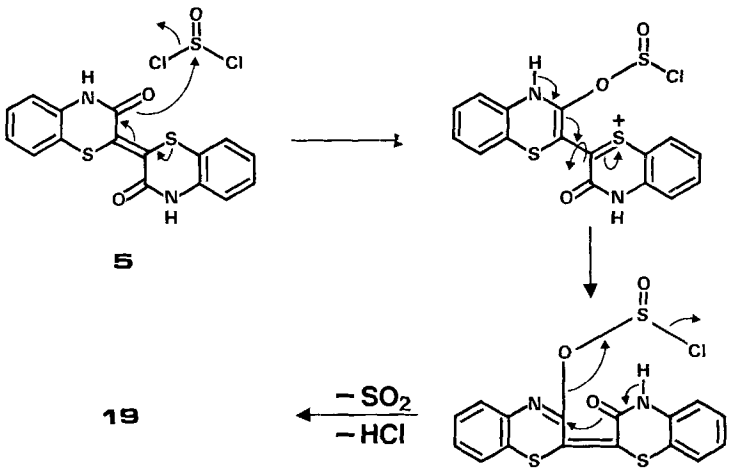


Fig. 2. *NMR. spectrum of* **23** *in* $(CD_3)_2SO$—*NaOD*

with aromatic diamines, *e.g.*, *p*-phenylenediamine, to give 6,6'-(1,4-phenylene)-bis(6*H*-pyrrolo[3,2-*b*:4,5-*b*']bis[1,4]benzothiazine) (**21**).

The transformation of **5** to **19** may occur by the sequence of reactions proposed in *Scheme 8*.

Scheme 8

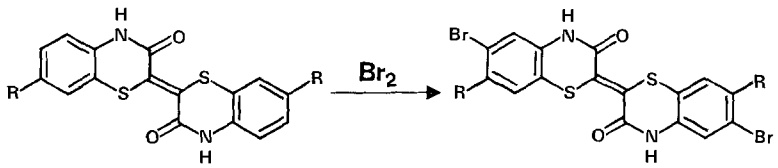


Exposure of **5** to the action of bromine in sulfuric acid or nitrobenzene[13]) resulted in the formation of its dibromo derivative, whose NMR. spectrum was suggestive of a single, symmetrical 1,2,4-trisubstituted benzenoid structure. Such symmetry can be found in both the 7,7'-dibromo (**22**) and 6,6'-dibromo (**23**) derivatives.

Authentic **23** was obtained by an unambiguous synthesis from **3** and the zinc salt of 2-amino-4-bromo-benzenethiol. A direct NMR. comparison between **23** and our dibromo product clearly indicated their dissimilarity (Fig. 1 and 2). Thus the bromination product was assigned structure **22**.

It should be noted that, when the positions *para* to nitrogen atoms are occupied as in 7,7'-diethoxy (**24**), 7,7'-dimethoxy (**25**) and 7,7'-dimethyl (**26**) derivatives, bromination occurs exclusively in positions *para* to sulfur atoms to give 6,6'-dibromo-7,7'-diethoxy- (**27**), 6,6'-dibromo-7,7'-dimethoxy- (**28**) and 6,6'-dibromo-7,7'-dimethyl-2,2'-bis(4*H*-1,4-benzothiazine)-indigo (**29**), respectively[14]). The NMR. spectra (in $(CD_3)_2SO$–NaOD) of all these brominated products contained a pair of singlets in the aromatic region. This is consistent with their assigned 1,2,4,5-tetrasubstituted benzenoid structures.

Scheme 9



R		
24	OC_2H_5	**27**
25	OCH_3	**28**
26	CH_3	**29**

Trichosiderins. – Colouring matters containing the $\Delta^{2,2'}$-bi(2*H*-1,4-benzothiazine) chromophore have been isolated from red human hair and are known under the trivial name 'Trichosiderins' [20] (*Scheme 10*). The synthesis of $\Delta^{2,2'}$-bi(3-aryl-2*H*-1,4-benzothiazines) by self-oxidative coupling (conventional indigo synthesis) has been reported recently [21]. We now have synthesized the basic *cis*-[$\Delta^{2,2'}$-bi(2*H*-1,4-benzothiazine)]-3(4*H*)-one skeleton **30** of one of these trichosiderins (**31**), exploiting our inverse indigo reaction scheme. The synthesis involves the reaction of **4** with 'mucochloric' (= *cis*-2,3-dichloro-3-formyl-acrylic) acid (**32**) in *o*-dichlorobenzene in the presence of sodium carbonate to yield **30** directly.

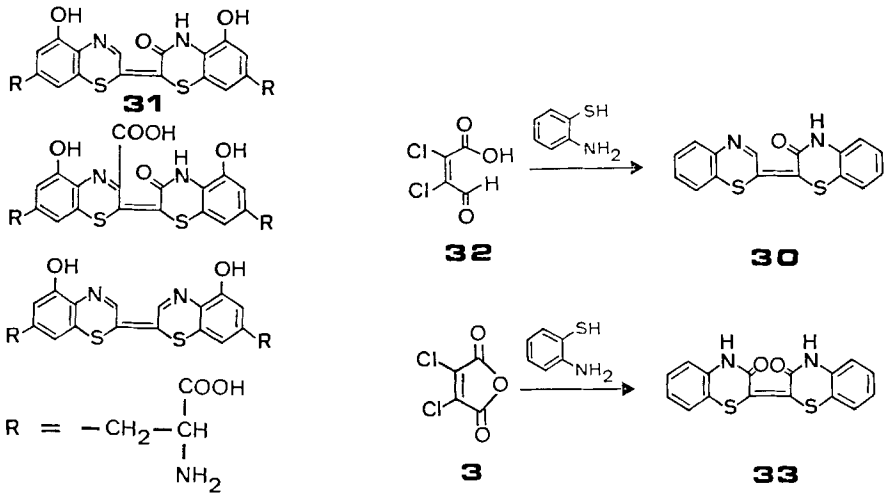
Under similar conditions, **3** reacts with **4** to give *cis*-2,2'-bis(4*H*-1,4-benzothiazine)-indigo **33**. A possible sequence of reactions leading to **33** is depicted in *Scheme 11*[15]).

[13]) Technically employed mediums for the bromination of indigoid compounds [19].

[14]) The orientation of bromination may also be influenced by group R.

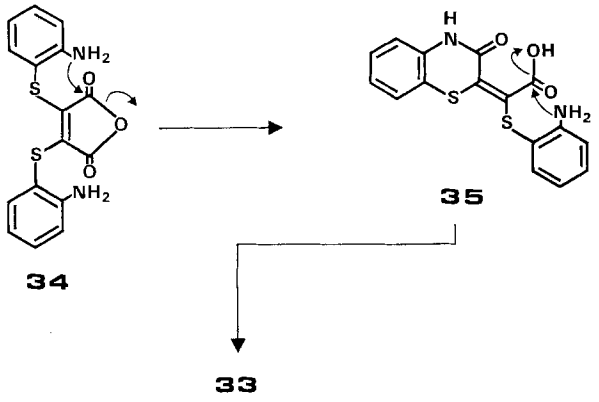
[15]) *I.e.*, the successive displacement of both chlorines in **3** by **4** to give **34** (as **3** normally behaves towards nucleophiles in the presence of a base [22]), and the subsequent stepwise cyclization of **34** to **33** *via* **35**.

Scheme 10



TRICHOSIDERINS

Scheme 11

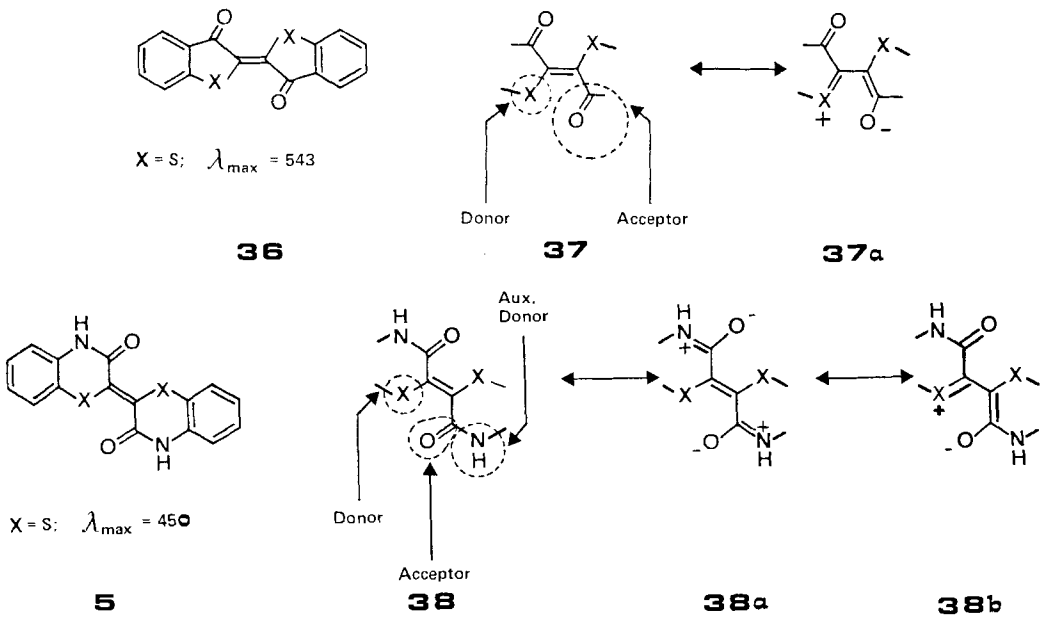


Some major differences between the *cis*-isomer **33** and the *trans*-product **5** include: i) **33** has poor thermal stability and is transformed on heating to **5**; ii) **33** is yellow, **5** is orange-red; iii) the IR. spectrum of **33** (Nujol) shows two carbonyl bands at 1680 cm^{-1} (weak) and 1650 cm^{-1} (strong), expected for a molecule with C_{2v} symmetry.

Colour and Chemical Constitution. – Compared with thioindigo (**36**), benzothiazine-indigo **5** absorbs at shorter wavelength. In order to understand this distinctive character of these two systems, one should perhaps look at the very basic chromophore responsible for their respective absorptions.

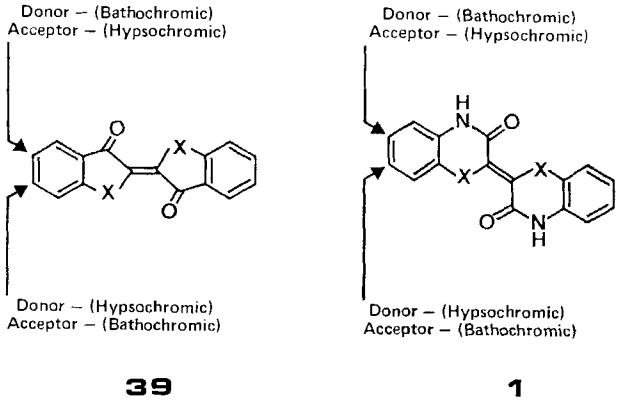
According to *Lüttke* the basic indigoid chromophore is **37** (*cf. Scheme 1*), in which the carbonyl groups act as electron acceptors, and the donor group X can be sulfur,

Scheme 12



NH, oxygen, selenium, etc. [3]. The conjugation between the donor and the acceptor groups through their connecting C,C double bond is then probably responsible for the longest wavelength absorption due to their $\pi - \pi^*$ transitions [23]. In other words the contribution of the polarized structure of type **37a** is important. If this donor-acceptor interaction is somehow interfered with, *i.e.* diminished or enhanced, the colour (or the shade) of the resulting (indigoid) system would be expected to respond accordingly to such interpolation. The central skeleton **38** of the indigoid system reported herein contains, besides the main donor and acceptor groups, an auxiliary donor group. The function of this auxiliary donor group is to reduce the

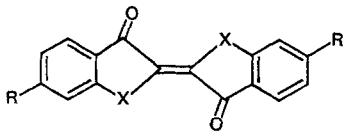
Scheme 13

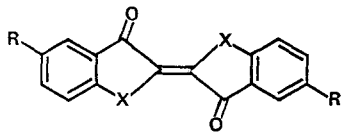


effective conjugation between the main donor and the acceptor groups by self-conjugation with the carbonyl moiety. In other words the contribution of zwitter ion **38a** occurs at the expense of the colour generating canonical structure **38b** and hence the hypsochromic shift.

If this explanation is valid, it would also be expected that the electron donor groups in the positions *para* to both the C=O in the known indigoid systems **39** and the NH in system **1** would cause a hypsochromic shift by depriving the keto group of its acceptor ability. Conversely, electron withdrawing groups would produce a bathochromic shift by enhancing the acceptor ability of the carbonyl groups. Similar considerations suggest that the effect of these substituents in positions *para* to the donor groups would be reversed, *i.e.* a donor group would increase the donor ability of the group X and the acceptor group would deprive it of its donor ability. As can be seen from Tables 1 and 2, the absorption spectra of the known substituted indigoid systems and of the systems reported herein confirm these predictions.

Table 1. Absorption Spectra of Indigos and Thioindigos[1])





λ_{max} [nm]			λ_{max} [nm]	
X = NH	X = S	R	X = NH	X = S
635	567	NO_2 [2])	580	513
	558	SO_2CH_3		519
605	543	H	605	543
590	539	Cl	620	556
	531	SC_2H_5		573
		OCH_3	645	
570	515	OC_2H_5		584
	490	NH_2		638

Hypsochromic Shift ↓ Bathochromic Shift ↓

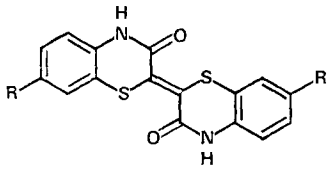
1) Taken from Ref. [25]
2) Taken from Ref. [28]

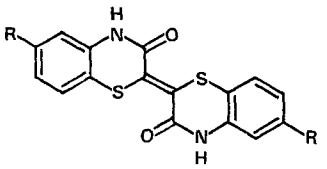
Further support is also provided by the observation that, unlike *cis*-thioindigo, **33** is stable at room temperature[16]), and needs rather extreme conditions for trans-formation into the corresponding *trans*-isomer **5**. Increased double bond character of the central C=C bond, as a consequence of the contribution of non-colour generating structure **38a**, would account for this behaviour.

It should be noted that, as the band at *ca.* 450 nm in the spectra of the system **1** (*cf.* Table 2) undergoes a bathochromic shift, the band at *ca.* 300 nm undergoes a

[16]) *cis*-Thioindigo has a half-life of several hours at room temperature [24], whereas **33** is still unaltered three years after its synthesis.

Table 2. Absorption Spectra of Benzothiazineindigos





Compound	λ_{max} [nm]			R	Compound	λ_{max} [nm]		
	$(CH_3)_2SO$		PVC [1]			$(CH_3)_2SO$		PVC [1]
	Band A	Band B				Band A	Band B	
				CF_3	41	319	438	520
5	295	450	535	H	5	295	450	535
22	298	448	535	Br				
				Cl	42	295	450	538
26	300	445	533	CH_3	43	290	456	545
24	318	440		OC_2H_5				
25	318	440	530	OCH_3	44	285	470	562

[1] Longest wavelength absorption determined from their transmission spectra as dispersions in polyvinyl chloride. λ_{max} of thioindigo measured similarly was found to be 544 nm.

hypsochromic shift, and *vice versa*. The shorter wavelength band is presumably due to $n \rightarrow \pi^*$ transitions of the amide resonance structure **38b**, whose contribution obviously increases or decreases at the expense of the canonical structure **38b**, which in turn is responsible for the absorption at *ca.* 450 nm.

The theory now proposed[17]) by us to explain the colour-structure relationship of indigoid dyestuffs is a compromise between the rule-of-thumb 'Chromophorenverteilung' theory of *Wizinger* [25], and the modern concepts of colour and chemical constitution [26].

Experimental Part

General. – The melting points (m.p.) were determined on a *Kofler* block and are uncorrected. The IR. spectra were recorded on a *Perkin-Elmer* model 21 spectrophotometer, the UV./VIS. on a *Beckman* DK-2, and the NMR. on a *Varian* HA-100 spectrometer, using sodium 3-trimethylsilyl-propanesulfonate as an internal lock. The mass spectra (MS.) were measured by direct insertion technique with a *CEC* 21-110B instrument (70 eV) (results in *m/e*). TLC. was carried out on F_{254} silica (*E. Merck*).

Starting materials. – Commercial 'mucochloric acid' (**32**) (*BASF*), 2,3-dichloromaleic anhydride (**3**) (*Fluka*) and 2-aminobenzenethiol (**4**) (*Fluka*) were used directly without further purification. The zinc salt of 2-aminobenzenethiol (**4a**) was prepared from **4** according to the method of *Nodiff & Hausman* [29]. The zinc salts of 2-amino-5-ethoxy-, 2-amino-5-methoxy- and 2-amino-5-methyl-benzenethiols were prepared, respectively, from 2-amino-6-ethoxy-, 2-amino-6-methoxy- and 2-amino-6-methyl-benzothiazoles [30]. The zinc salts of all other 2-aminobenzenethiols were prepared as follows: Appropriately substituted 2-chloronitrobenzene was converted into the corresponding bis(2-nitrophenyl) disulfide [31] which then was reduced to the desired zinc salt of the 2-aminobenzenethiol by the previously described procedure [29].

[17]) This theory has proved to be very general in character and can be used to explain the colour-structure relationship of many of the chromophoric systems examined by us [27].

***trans*-2,2'-Bis(4*H*-1,4-benzothiazine)-indigos.** – All of the benzothiazineindigos in Table 3 were prepared from **3** and the zinc salt of a 2-aminobenzenethiol by essentially the same procedure. The following experiment illustrates the general method:

A mixture of 8.35 g (0.05 mol) of **3**, 0.055 mol[18]) of zinc salt of the appropriate 2-aminobenzenethiol, and 200 ml of glacial acetic acid was stirred at 116° for 20 h. The precipitated crystalline pigment was collected by filtration at 100°. After washing with glacial acetic acid, till the washings were almost colourless, the product was washed with ethyl alcohol and water, and dried at 120°. For elemental analysis and spectral measurements, a sample was crystallized from a large excess of dimethylformamide.

Table 3. trans-*2,2'-Bis(4*H*-1,4-benzothiazine)-indigos*[1])

2-Amino-benzene-thiol[2])	Prod-uct	Appearance (yield %)	Formula (Mol Wt)		Analysis C	H	N	O	S	Halogen
unsub-stituted	**5**	orange-red (77)	$C_{16}H_{10}N_2O_2S_2$ (326.396)	Calc.	58.9	3.1	8.6	9.8	19.6	–
				Found	58.7	3.1	8.6	9.8	19.7	–
4-Br	**23**	orange-red (80)	$C_{16}H_8Br_2N_2O_2S_2$ (484.198)	Calc.	39.7	1.7	5.8	6.6	13.2	33.0
				Found	40.1	1.9	5.4	6.5	12.9	33.1
5-OC_2H_5	**24**	orange (58)	$C_{20}H_{18}N_2O_4S_2$ (414.282)	Calc.	58.0	4.4	6.8	15.4	15.5	–
				Found	58.2	4.6	7.0	15.9	15.4	–
5-OCH_3	**25**	orange (62)	$C_{18}H_{14}N_2O_4S_2$ (386.448)	Calc.	55.9	3.7	7.2	16.6	16.6	–
				Found	54.9	3.7	7.4	16.6	16.9	–
5-CH_3	**26**	orange (68)	$C_{18}H_{14}N_2O_2S_2$ (354.45)	Calc.	61.0	3.4	7.9	9.0	18.1	–
				Found	61.0	3.4	8.2	9.4	17.9	–
4-CF_3	**41**	yellow (23)	$C_{18}H_{14}F_6N_2O_2S_2$ (462.39)	Calc.	46.8	1.7	6.1	6.9	13.9	24.7
				Found	47.1	1.7	6.2	7.4	13.8	25.0
4-Cl	**42**	yellowish-red (50)	$C_{16}H_8Cl_2N_2O_2S_2$ (395.286)	Calc.	48.6	2.0	7.0	8.1	16.2	18.0
				Found	48.0	1.8	7.4	8.5	15.8	18.0
4-CH_3	**43**	red (83)	$C_{18}H_{14}N_2O_2S_2$ (354.45)	Calc.	61.0	3.4	7.9	9.0	18.1	–
				Found	60.5	4.0	7.9	9.5	18.2	–
4-OCH_3	**44**	red violet (87)	$C_{18}H_{14}N_2O_4S_2$ (386.448)	Calc.	55.9	3.7	7.2	16.6	16.6	–
				Found	55.0	3.6	7.1	17.0	17.0	–

[1]) None of the products melted below 330°.
[2]) Zinc salt.

Compound **5** was also synthesized by the following alternative procedure: To a stirred solution of 83.5 g (0.5 mol) of **3** in 800 ml of glacial acetic acid at room temp. was added 125 g (1 mol) of 2-aminobenzenethiol over a period of 15 min. The mixture was stirred at room temp. for another 15 min and thereafter under reflux for 12 h. The precipitated crystalline orange-red pigment was collected by filtration at room temp., washed with glacial acetic acid and ethyl alcohol, and dried. The yield was 85.9 g (52.7%).

*3,4-Dihydro-3-oxo-2*H*-1,4-benzothiazine-$\Delta^{2,\alpha}$-chloroacetic acid* (**8**). To a stirred solution of 16.7 g (0.1 mol) of **3** in 150 ml of glacial acetic acid at room temp. a solution of 12.5 g (0.1 mol) of **4** in 50 ml glacial acetic acid was added over a period of 2 h. The mixture was then stirred at room temp. for 1 h and under reflux for 2 h. The precipitated product was collected by filtration at room temp., washed with a little acetic acid and water, and dried at 100° in vacuum. The yield was 19.1 g (74.7%). The product was boiled with 600 ml of 96% ethyl alcohol and filtered

[18]) Corresponding to 0.11 mol of the free benzenethiol.

hot. The insoluble orange-red fraction (0.76 g) was identified as **5**. The alcohol extract, on cooling to room temp., deposited pale-yellow crystals which were collected by filtration, washed with alcohol and dried (yield 9.1 g). The product was homogeneous on TLC. (chloroform/acetone 4:1, *v/v*), m.p. 232–233°.

$C_{10}H_6ClNO_3S$	Calc.	C 47.0	H 2.4	Cl 13.9	N 5.5	O 18.8	S 12.5%
(255.679)	Found	,, 47.0	,, 2.5	,, 13.8	,, 5.8	,, 18.7	,, 12.7%

The mother liquor was diluted with water and the crystalline pale-yellow product was collected by filtration, washed with water and dried. The yield was 6.7 g, m.p. 232–233°. The product was analytically and spectroscopically identical with that crystallized from alcohol.

General procedure for the bromination of trans-*2,2'-bis-(4H-1,4-benzothiazine)-indigos* (*cf.* Table 4). To a stirred mixture of 0.03 mol of the appropriate benzothiazine-indigo and 300 ml of nitrobenzene at room temp. was added 8 ml of bromine over a period of 1 h. Thereafter, the mixture was stirred at room temp. for 1 h and at 100° for 1 h. The brominated product was collected by filtration at 100°, washed with nitrobenzene and ethyl alcohol, and dried at 120° in vacuum. – The resulting products were much less soluble in dimethylformamide than their corresponding starting materials and were purified as follows: 10 g of the pigment was stirred in 500 ml of dimethylformamide and heated to reflux temp. The mixture was stirred under reflux for 1 h, filtered hot, washed with dimethylformamide and ethyl alcohol, and dried at 120° in vacuum.

Table 4. *Bromination Products of* trans-*2,2'-Bis(4H-1,4-benzothiazine)-indigos*[1])

Product	Appearance (yield %)	Formula (Mol Wt)		Analysis C	H	N	O	S	Halogen
22	yellowish-red	$C_{16}H_8Br_2N_2O_2S_2$	Calc.	39.7	1.7	5.8	6.6	13.2	33.0
	(60)	(484.198)	Found	39.8	1.9	6.0	7.0	13.2	33.7
27	orange-red	$C_{20}H_{16}Br_2N_2O_4S_2$	Calc.	42.0	2.8	4.9	11.2	11.2	27.9
	(80)	(572.304)	Found	42.3	2.9	4.9	11.3	11.3	27.2
28	orange-red	$C_{18}H_{12}Br_2N_2O_4S_2$	Calc.	39.7	2.2	5.1	11.8	11.8	29.4
	(83)	(544.25)	Found	39.2	2.2	5.4	11.6	11.7	29.2
29	orange-red	$C_{18}H_{12}Br_2N_2O_2S_2$	Calc.	42.2	2.4	5.5	6.2	12.5	31.2
	(86)	(512.252)	Found	42.6	2.5	5.6	6.3	12.7	31.2

[1]) None of the products melted below 330°.

Compound **22** was also prepared as follows: To a stirred solution of 9.6 g (0.029 mol) of **5** in 290 ml of conc. sulfuric acid was added 25.6 g (0.16 mol) of bromine over a period of $^1/_2$ h. The mixture was stirred further at room temp. for 1 h and then poured on about 2 kg of ice. The precipitated yellowish-red pigment was collected by filtration, then washed with water until free of acid, and dried at 120° in vacuum. The yield was almost quantitative.

Furo[3,2-*b*:4,5-*b'*]bis[1,4]benzothiazine (19). – A mixture of 30 g of **5**, 100 ml thionyl chloride and 750 ml dimethylformamide was stirred at room temp. for 15 min and heated with stirring to *ca.* 80°. The heating oil bath was then removed and the temp. of the reaction mixture rose to 100–110° (external cooling is recommended if the reaction becomes too violent). The mixture was stirred at 80° for 2 h. During this time, **5** went into solution and the yellow-orange crystals of **19** started to precipitate out. The mixture was cooled to room temp. and the product collected by filtration. After washing with dimethylformamide and carbon disulfide, it was dried at 120°. The yield was 18.8 g (66.3%). The product could be recrystallized from *o*-dichlorobenzene; m.p. > 300°. – MS.: 308, 280, 279, 276, 256, 248, 194, 192, 178, 160, 154 etc. A chloroform solution of the product showed an intense greenish-yellow fluorescence under UV. light.

$C_{16}H_8N_2OS_2$	Calc.	C 62.3	H 2.6	N 9.1	O 5.2	S 20.8%	
(308.381)	Found	,, 61.9	,, 2.6	,, 9.0	,, 5.2	,, 20.8%	

6-Phenyl-6*H*-pyrrolo[3,2-*b*:4,5-*b*']bis[1,4]benzothiazine (20). – A mixture of 6.16 g (0.02 mol) of **19**, 1.86 g (0.02 mol) of aniline, 0.11 g of *p*-toluenesulfonic acid and 65 ml of *o*-dichlorobenzene was heated with stirring to reflux temp. and stirred thereafter for 24 h. The water of condensation was allowed to distil off, along with some solvent which was replaced from time to time. The mixture was allowed to cool to room temp., and the crystallized product was collected by filtration, washed with *o*-dichlorobenzene, ethyl alcohol and water, and dried at 120° in vacuum. The yield was 5.1 g (66.5%). The product was recrystallized from dimethylformamide; m.p. > 300°.

$C_{22}H_{13}N_3S_2$	Calc.	C 68.9	H 3.4	N 11.0	S 16.7%
(383.495)	Found	,, 68.8	,, 3.3	,, 10.8	,, 16.7%

6,6'-(1,4-Phenylene)-bis(6*H*-pyrrolo[3,2-*b*:4,5-*b*']bis[1,4]benzothiazine) (21). – This compound was prepared by the same procedure as for **20**, using 1.08 g (0.01 mol) of *p*-phenylenediamine in place of aniline and 1,2,4-trichlorobenzene in place of *o*-dichlorobenzene as reaction medium. The yield was 5.6 g (81.3%) and the product was purified by the same procedure as adopted for the purification of compounds in Table 4.

$C_{38}H_{20}N_6S_4$	Calc.	C 66.3	H 2.9	N 12.2	S 18.6%
(688.876)	Found	,, 66.9	,, 2.9	,, 12.3	,, 18.5%

***cis*-$\Delta^{2,2'}$-Bi(2*H*-1,4-benzothiazine)-3(4*H*)-one (30).** – To a stirred mixture of 16.9 g (0.1 mol) of 'mucochloric acid', 10.6 g (0.1 mol) of sodium carbonate and 300 ml of *o*-dichlorobenzene at room temp. a solution of 26 g (0.21 mol) of **4** in 100 ml of *o*-dichlorobenzene was added over a period of 2 h. The mixture was then stirred at 100° for 2 h and at 150° for 2 h. Thereafter, the mixture was allowed to cool to room temp. The crystallized brownish-yellow product was collected by filtration, washed with alcohol and water, and dried at 120° in vacuum. The yield was 4.9 g (15.8%). TLC. examination (chloroform/acetone 19:1, *v/v*) showed the presence of a very minor fast moving impurity[19]. After recrystallization from 1,2,4-trichlorobenzene, the product was practically homogeneous[20] and showed the following characteristics: Appearance: yellow; Rf 0.4; m.p. > 300°. – IR. (Nujol): lactam carbonyl absorption at 1665 cm^{-1}, identical with that of the dimethyl ester of **31** (1663 cm^{-1}) [32]. – MS.: 310, 282, 268, etc. – A chloroform solution of the product showed greenish fluorescence under UV. light, of less intensity than that of **19**.

$C_{16}H_{10}N_2OS_2$	Calc.	C 61.9	H 3.2	N 9.0	O 5.2	S 20.7%
(310.397)	Found	,, 61.8	,, 3.4	,, 9.0	,, 5.0	,, 20.6%

***cis*-2,2'-Bis(4*H*-1,4-benzothiazine)-indigo (33).** – To a stirred mixture of 8.35 g (0.05 mol) **3**, 5.3 g (0.05 mol) sodium carbonate and 100 ml of *o*-dichlorobenzene at room temp. was added 13 g (0.104 mol) of **4** over a period of 2 h. The reaction was conducted and worked up as for **30**, to yield 13.6 g (83.4%) of a reddish-yellow product having m.p. > 300°.

$C_{16}H_{10}N_2O_2S_2$	Calc.	C 58.9	H 3.1	N 8.6	O 9.8	S 19.6%
(326.396)	Found	,, 58.6	,, 3.2	,, 8.5	,, 9.9	,, 19.5%

Transformation of **33** *into the* trans *form* **5**. A mixture of 1 g of **33** and 100 ml of 1,2,4-trichlorobenzene was heated to reflux. The product slowly went into solution and the orange-red crystals of **5** started to appear. The heating was continued for 15 min and **5** was collected by filtration. After washing with trichlorobenzene and alcohol the product was dried at 120° in vacuum. The product was both analytically and spectroscopically identical with **5**.

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[19] Probably the stereoisomer of **30**.

[20] The high thermal stability of **30** is surprising, which might raise doubt about its assigned *cisoid* structure. However, since the lactam carbonyl absorption in the IR. spectrum of **30** appears almost exactly where it does in **31**, it is assumed that both possess the same stereochemistry. The configurational assignments remain open.

REFERENCES

[1] *R. H. Altiparmakian, H. Bohler, B. L. Kaul & F. Kehrer,* Helv. *55,* 85 (1972).
[2] *B. L. Kaul,* Chimia *27,* 653 (1973).
[3] *H. Hermann & W. Lüttke,* Chem. Ber. *101,* 1715 (1968); *G. M. Wyman & B. M. Zarnegar,* J. physic. Chemistry *77,* 831 (1973).
[4] *A. Baeyer,* Ber. deutsch. chem. Ges. *13,* 2254 (1880); *P. Friedländer, ibid. 39,* 1060 (1906); see also *H. E. Fierz-David* «Künstliche organische Farbstoffe», siebzehntes Kapitel, Verlag von Julius Springer, Berlin 1926.
[5] *P. Rys & H. Zollinger* in 'Fundamentals of the Chemistry and Application of Dyes', p. 119, Wiley-Interscience, London 1972.
[6] *Sandoz AG.,* Deutsche Offenlegungsschrift 2151723.
[7] *K. Venkataraman,* 'The Chemistry of Synthetic Dyes', Vol. II, Chap. 33, Academic Press, New York 1952; *A. J. Johnson* in 'The Chemistry of Synthetic Dyes and Pigments' (ed. by *H. A. Lubs*), Chap. 8, Reinhold Publishing Corporation, New York 1955.
[8] *H. Hermann & W. Lüttke,* Chem. Ber. *104,* 499 (1971).
[9] *W. A. Pryor* in 'Mechanisms of Sulfur Reactions' pp 71 & 72 (and the references cited therein), McGraw-Hill book Company, Inc. 1962.
[10] *B. Dmuhovsky, B. D. Vineyard & F. B. Zienty,* J. Amer. chem. Soc. *86,* 2874 (1964); *S. M. Kalbag, N. D. Nair, P. Ragagopalan & C. N. Jalaty,* Tetrahedron *23,* 1911 (1967); French Pat. 1443917.
[11] *Y. Maki & M. Suzuki,* Chem. pharm. Bull. (Japan) *20,* 832 (1972), and the references cited therein.
[12] *D. M. Lynch & A. J. Crovetti,* J. heterocycl. Chemistry *9,* 1027 (1972).
[13] *R. T. Coults, S. T. Matthias* & (in part) *E. Mah & N. J. Pound,* Canad. J. Chemistry *48,* 3727 (1970).
[14] *H. Nagase,* Chem. pharm. Bull. (Japan) *22,* 42 (1974).
[15] *C. H. DePuy, R. D. Thurn & G. F. Morris,* J. Amer. chem. Soc. *84,* 1314 (1962); *C. H. DePuy, G. F. Morris, J. S. Smith & R. J. Smat, ibid. 87,* 2421 (1965).
[16] *J. March* in 'Advanced Organic Chemistry' Chap. 17, McGraw-Hill book Company, New York 1968.
[17] *Sandoz AG.,* Deutsche Offenlegungsschrift 2152257.
[18] *BASF,* Brit. Pat. 1221503.
[19] *J. Martinet,* «Matières Colorantes: les Indigoïdes», p. 192, Baillière, Paris 1934.
[20] *R. H. Thomson,* Angew. Chem. *86,* 355 (1974), and the references cited therein.
[21] *F. Giordano, L. Mazzarella, G. Prota, C. Santacroce & D. Sica,* J. chem. Soc. (C) *1971,* 2610.
[22] *E. L. Martin, C. L. Dickinson & J. R. Roland,* J. org. Chemistry *26,* 2036 (1961).
[23] *M. Klessinger,* Tetrahedron *22,* 3355 (1966); see also Ref. [3].
[24] *G. M. Wyman & W. R. Brode,* J. Amer. chem. Soc. *73,* 1487 (1951).
[25] *R. Wizinger,* Chimia *19,* 339 (1965).
[26] *S. F. Mason* in 'The Chemistry of Synthetic Dyes' (ed. by *K. Venkataraman*), Vol. III, Chap. IV; see also Ref. [5], p. 5.
[27] *B. L. Kaul,* unpublished results.
[28] *N. S. Dokunikhin & Yu. E. Gerasimenko,* Ž. obšč. Chim. *31,* 1927 (1961).
[29] *E. A. Nodiff & M. Hausman,* J. org. Chemistry *31,* 625 (1966).
[30] *M. Schubert,* Liebigs Ann. Chem. *557,* 10 (1947).
[31] *Th. Wohlfahrt,* J. prakt. Chem. [2] *66,* 553 (1902); see also Ref. [10], French Pat.
[32] *R. A. Nicolaus, G. Prota, C. Santacroce, G. Scherillo & D. Sica,* Gazz. chim. ital. *99,* 323 (1969).