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Cyclization Reactions of 1,2-Bis(2-cyanophenyl)propionitriles. I. Structure of the"Red Pigment" formed by the Base-catalyzed Cyclization of 1,2-Bis(2-cyano-3-methoxyphenyl)propionitrile in the Presence of Diethyl Carbonate[1]

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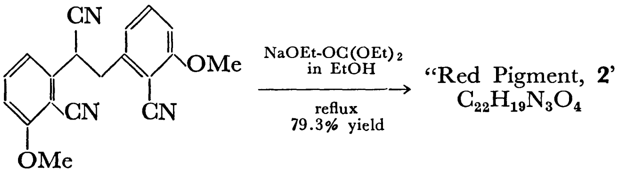
The reaction of 1,2-bis(2-cyano-3-methoxyphenyl)propionitrile (**1**) with diethyl carbonate and sodium ethoxide gave a red pigment **2**, $C_{22}H_{19}N_3O_4$ in 79% yield. It afforded 5-amino-4,7-dimethoxy-11*H*-indeno[1,2-*c*]isoquinolin-11-one (**4**) on treatment with alkaline hydrogen peroxide. The "red pigment" has been confirmed to have a novel 5*H*-indeno[1,2-*c*]isoquinoline structure which transforms into colorless 11*H*-indeno-[1,2-*c*]-isoquinoline form in an acidic medium. The mechanism of the formation of **2** from **1** imparts an interesting problem as regards carbanion reactivity.

In the course of synthetic studies[1,2] of compounds related to sclerin, a plant growth hormone,[3] we happened to treat 1,2-bis(2-cyano-3-methoxyphenyl)propionitrile (**1**) with diethyl carbonate and sodium ethoxide in ethanol solution at refluxing temperature. When the brownish black reaction mixture was poured into ice-water, a red pigment **2** was obtained in 79% yield. The reaction was found to be reproducible. This led us to study the structure of **2** and investigate this reaction. In this paper we deal with the structure elucidation of **2**.



Scheme 1

The red pigment **2**, $C_{22}H_{19}N_3O_4$, is slightly soluble in chloroform and dichloromethane, and practically insoluble in other common organic solvents. It is easily soluble in strong acids such as trifluoroacetic acid or ethanolic hydrochloric acid giving a yellow solution with strong blue fluorescence. When this solution was neutralized or diluted with a large amount of water, **2** was recovered, indicating that compound **2** is a weak base. **2** is also soluble in sodium hydroxide, indicating it to be amphoteric in nature. The infrared spectrum indicates the presence of an imino or a hydroxyl group (3340 cm^{-1}), a cyano group (2166 cm^{-1}) and a carbonyl group (1705 cm^{-1}) in **2**. The imino or the hydroxyl group in **2** was found to be inactive on acetylation. It should be noted that the band due to a cyano group appears at unusually low frequency, compared to the normal range 2260—2210 cm^{-1}.[4] Because of the lack of a suitable neutral solvent, the NMR spectrum of **2** was taken in trifluoroacetic acid solution, showing the signals due to an ethoxy group, two methoxy groups and six aromatic protons. An additional signal was observed at δ 5.61 (1H). This could be tentatively assigned to be the methine proton which has a strongly deshielding environment. The results in conjunction with the molecular composition of **2** suggest that **2** is formed from **1** through a complex intramolecular cyclization, incorporating one mole of diethyl carbonate.

Upon alkaline hydrolysis under exlcusion of oxygen and the following treatment with dilute hydrochloric acid, **2** afforded a pale yellow amine hydrochloride **3**, $C_{19}H_{16}N_3O_2Cl$: ν_{max} 3300, 3080—2760 ($-NH_3^+$) and 2245 cm^{-1} (-CN); δ 4.13 ($-OCH_3$), 4.34 ($-OCH_3$) and 5.30 (1H). The IR and NMR spectra of **3** indicate that **3** is the amine hydrochloride formed by hydrolytic cleavage of the carbethoxyamide group originally present in **2**. The transformation of the cyano group in **2** was carried out using alkaline hydrogen peroxide in aqueous ethanol at 55 °C. The product **4** obtained in 92.5% yield exhibited absorption bands at 3460 3280, 3170 and 1670 cm^{-1} in the IR region, showing no band due to the cyano group. The NMR spectrum of **4** showed signals due to two methoxy groups and six aromatic protons, no signals due to ethoxy and groups being observed. In contrast to **2**, **4** was sufficiently basic to give the hydrochloride **5** and monoacetate **6**. The orange-red colored acetate **6** exhibited a UV spectrum similar to that of **4**. The peak in the IR spectrum of **6** were observed at 3330 and 1675 cm^{-1}. From the analytical values for **5** and **6**, **4** was concluded to have a molecular formula of $C_{18}H_{14}N_2O_3$ although the combustion analyses did not give a satisfactory result. This indicates that **4** is not a product of mere hydrolysis but a degraded product with the loss of one carbon, most probably corresponding to the cyano group in **2**. The formation of **5** and **6**, and the band at 3330 cm^{-1} in the IR spectrum of **6** suggest the presence of a primary amino group in **4**, though this compound is resistant to the diazotization reaction. Treatment of **4** with 6 M aqueous ethanolic potassium hydroxide solution under refluxing yielded an orange-red colored product **7**, $C_{18}H_{13}NO_4$, which no longer basic and showed IR peaks at 3380, 1690 and 1665 cm^{-1}, suggesting the presence of a lactam and an additional carbonyl group. Methylation of **7** with sodium methoxide and methyl iodide produced a monomethylation product **8**. The UV spectrum of **8** was similar to that of the strating material **7**. In the IR spectrum of **8**, the NH stretching band present in **7**

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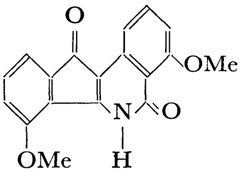
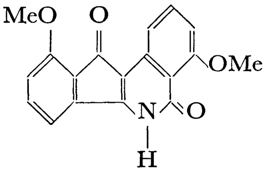
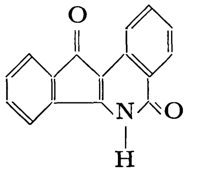


7a



7b



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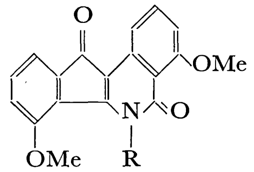
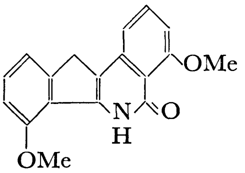


7 R=H
8 R=Me

disappeared and the carbonyl frequency was found at 1670 cm^{-1}. Three methyl singlets appeared at δ 3.92, 3.99 and 4.04 in the NMR spectrum. Thus the nitrogen atom of the lactam grouping in **7** is methylated in **8**. The only possible formula for **7**, in line with the above evidence would be **7a** or **7b**, provided that no rearrangement invoving carbon-carbon bonds occurs during the derivation of **7**. The parent compounds this ring system, 5,6-dihydro-11*H*-indeno[1,2-*c*]isoquinoline-5,11-dione (**9**), has been reported to be orange-red colored crystals but no description was of the electronic spectral data.[5] The choice **7a** or **7b** was possible by the consideration of the NH stretching band in **7**. This band was observed as a sharp peak at 3380 cm^{-1} in contrast to that of **9** as a broad band at 3226—2700 cm^{-1}. This would be interpreted by assuming that the intermolecular hydrogen bond existing in **9** becomes difficult in **7** owing to steric hindrance. Thus **7a** turned out to be the more acceptable structure for **7**. Accordingly formula **8** was assigned to the methylation product. In order to verify the structure for **7**, the reduction of the conjugated cyclopentanone group was investigated by treating with zinc dust in refluxing aqueous acetic acid. Two colorless products, **10**, $C_{18}H_{15}NO_3$ and **11**, $C_{18}H_{15}NO_4$ were obtained. When the reduction was carried out with glacial acetic acid, **10** was formed in a good yield. The UV spectra of of **10** and **11** were similar, indicating the presence of the same conjugated system in both products. The former shows the IR peaks at 3420 and 1650 cm^{-1} (lactam group), and NMR signals at δ 3.74 ($>CH_2$). Thus in **10** the ketonic group of **7** has been transformed into a methylene group. On the other hand **11** is found to be the product in which the ketonic group in **7** was reduced to a hydroxyl group, showing the IR peaks at 3420 (sh., -OH), 3380 (-NH) and 1654 cm^{-1} (-NHCO-). On the basis of the established structure for **7**, three formulas **4**, **4a** and **4b** are taken for the precursor **4**. When **4** was treated with zinc in glacial acetic acid in the same way as for **7**, the reduction product **12**, $C_{18}H_{16}N_2O_2$, was obtained in 70.5% yield. The IR spectrum of **12** revealed the disappearance of the carbonyl group in **4** and the NMR spectrum indicated the formation of the methylene group in **12**. Production of **12** from **4** is compatible only with the assignment of structure **4** for the latter and hence the formula for the reduction product **12**, the hydrochloride **5** and the acetylation product **6** are depicted as shown.



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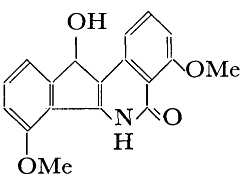

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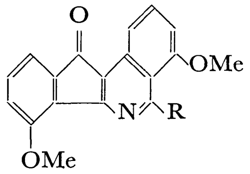
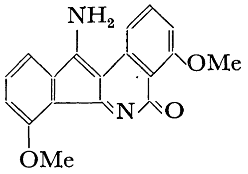
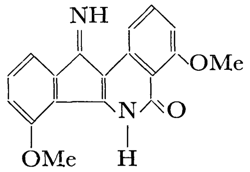


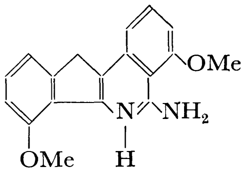
4 R=-NH_2
5 R=-$NH_3^+Cl^-$
6 R=-$NHCOCH_3$



4a



4b



12

The disclosure of the structure for **4**[6] allows us to discuss the constitution of the "red pigment" **2**. The UV spectrum of the amine hydrochloride **3** closely resembles that of 5-amino-4,7-dimethoxy-11*H*-indeno[1,2-*c*]isoquinoline (**12**), a reduction product of **4** (Fig. 1), indicating the presence of the same chromophore in both compounds. Thus the only position available for the attachment of the cyano group in **3** would be the C-11 of 11*H*-indeno[1,2-*c*]isoquinoline nucleus, suggesting the structure **3** for the hydrochloride. When **3** was catalytically hydrogenated in the presence of palladium-on-charcoal in acetic acid containing hydrochloric acid, two products were obtained (Scheme 2). One product **13**, $C_{19}H_{18}N_2O_2$, was separated easily

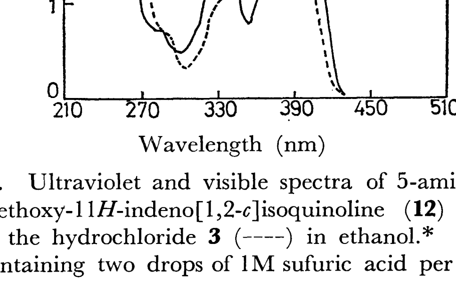
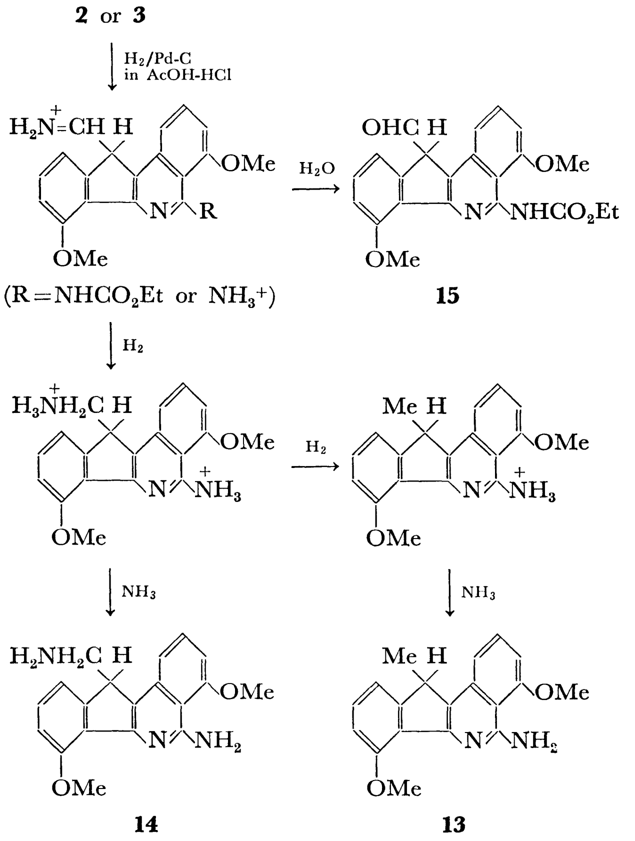


Fig. 1. Ultraviolet and visible spectra of 5-amino-4,7-dimethoxy-11*H*-indeno[1,2-*c*]isoquinoline (**12**) (——) and the hydrochloride **3** (----) in ethanol.*
* containing two drops of 1M sufuric acid per 10 ml.



Scheme 2

from the other by treatment as hydrochloride with chloroform since only the former was soluble in this solvent. In the IR spectrum of **13** the band due to the cyano group in **3** has disappeared. A marked feature in the NMR spectrum of **13** is the appearance of the signals due to a secondary methyl groups. The UV spectrum of **13** resembles closely that of **3** and **12** (Fig. 1). This indicates that the secondary cyano group in **3** was transformed into a methyl group during the course of hydrogenation, confirming the position of the cyano group in the indenoisoquinoline skeleton of **3**. Another product obtained as an oil shows the absorption bands at 3460 and 3360 cm^{-1} in the IR spectrum. Insolubility of its hydrochloride in chloroform suggests that it could be the diamine **14** an intermediate product to **13**. Hydrogenation of **2** in the same way as **3** gives rise to the secondary aldehyde **15** though this compound could not be obtained in a pure state. Upon acetylation with acetic anhydride and concd. sulfuric acid, the hydrochloride **3** yielded a red colored acetate **16**. The UV spectrum of **16** resembles markedly that of the "red pigment" **2** (Fig. 2). This indicates that **2** and **16** have a common structure except for the acyl substituents on the primary amino group. For the sake of explanation it would be reasonable to assume that **2** and **16** have an iminoindene structure **17** which is transformed into colorless indenoisoquinoline skeleton **18** on salt formation with an acid. Thus the coloration in **2** and also in **16** is understandable.[7] In this respect the ketimine form **19** might also be taken into consideration.[8] In the IR spectrum of **2** a strong absorption band is observed at 2166 cm^{-1}, which is considerably out of the normal range for the cyano group. Although available data for the IR absorption of ketimines are very much limited, this structure appears to have the absorption band at 2040—2000 cm^{-1}.[9,10] Thus the IR peak of **2** in question would be in favor of a cyano group (conjugated). The chemical stability of the responsible group in **2** on addition reactions[9–13] precludes the ketimine structure.[14] The unusual lowering of the cyano frequency could be attributed to the contribution of the canonical formula like **20**.[15] The low-field singlets in the NMR spectra of **2** and **16** (δ 5.61 and 5.53 respectively) in the acidic conditions are assigned to the methine protons attached to the carbon atoms bearing cyano groups in the indenoisoquinoline structures. The solubility of **2** in alkali to form a light yellow solution with fluorescence is explainable by the formation of the anion **21**. In order to obtain the free amine, **3** was treated with ammonia to afford a product **22**, which has a somewhat dim red color compared to that of **2**. In the IR spectrum **22** exhibits broad bands due to the amino group at 3440 and 3300 cm^{-1} and a strong absorption due to cyano group at 2160 cm^{-1}. The product is presumed to be a tautomeric mixture of the iminoindeno derivative **22a** and the indenoisoquinoline compound **22b**. Fur-

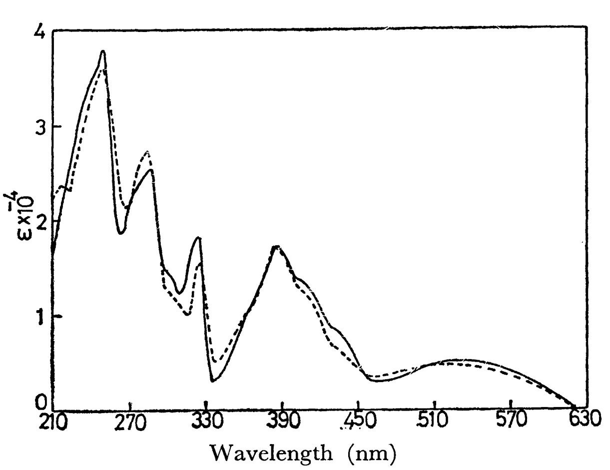
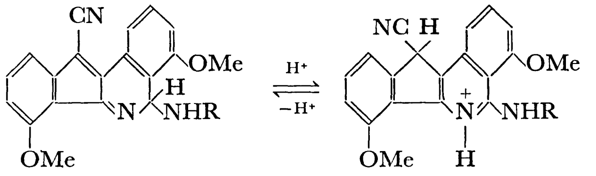
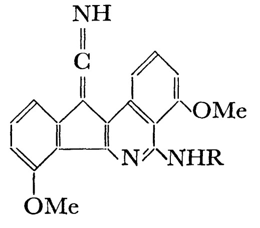


Fig. 2. Ultraviolet and visible spectra of the "red pigment" **2** and the acetate **16** in ethanol.



17 **18**

Scheme 3



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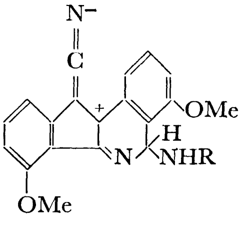

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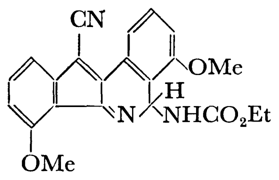
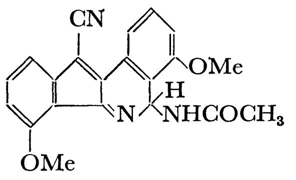


2



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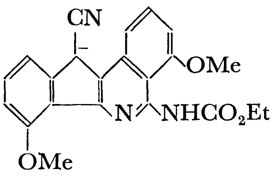

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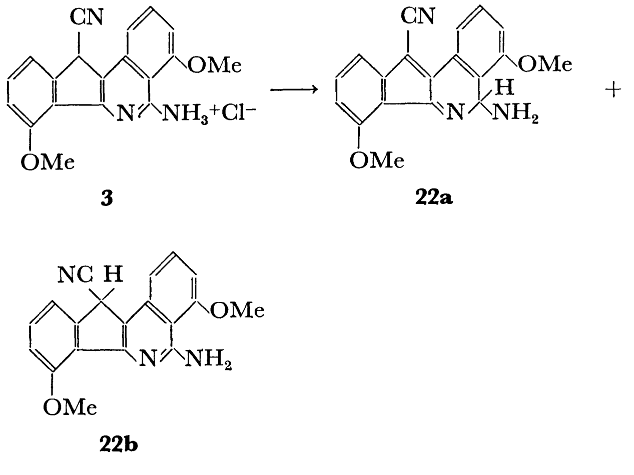
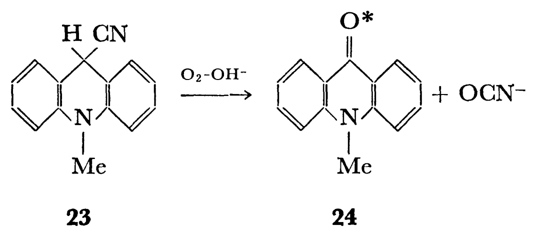
ther characterization was difficult since it was quite unstable in the air and converted into the same oxidation product **4** obtained from **2**.

The easy oxidative degradation of **2** by treatment with alkaline hydrogen peroxide to form **4** should be noted in terms of the established formula for **2**. In this connection Happ *et al.*[16] have reported that *N*-methyl-9-cyanoacridane **23** is oxidized by molecular oxygen in alkaline medium to afford *N*-methylacridone **24** with



Scheme 4

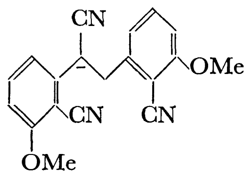


Scheme 5

chemiluminescence in which a carbanion electron transfer mechanism involving *N*-methyl-9-cyanoacridanyl radical is postulated. The reactions of **2** might proceed in the manner depicted in Scheme 6. The autoxidation of the free amine **22** to **4** could be interpreted similarly.

To our best knowledge, the 5*H*-indeno[1,2-*c*]isoquinoline system is a novel heterocycle. The relative stability of the iminoindene ring system in **2** over the tautomeric indenoisoquinoline would be a subject of interest in view of structural organic chemistry.[7]

Formation of the "red pigment" **2** from **1** provides a fascinating problem also from the side of the reaction mechanism. In the first sight the base-catalyzed reaction of **1** would be anticipated to proceed *via* a Thorp type path initiated by the anion **25**, produced by the removal of the most acidic hydrogen in **1**.[17] However the formation of **2** is accounted for only by the assumption of the path including the anion **26** (Scheme 7). The cyclization of **26** would take place involving the two cyano groups to afford the intermediate **27**, which is transformed into **2** by the redistribution of the double bonds. The reason why **26** mainly participates in the reaction instead of **25** seems to deserve further scrutiny.



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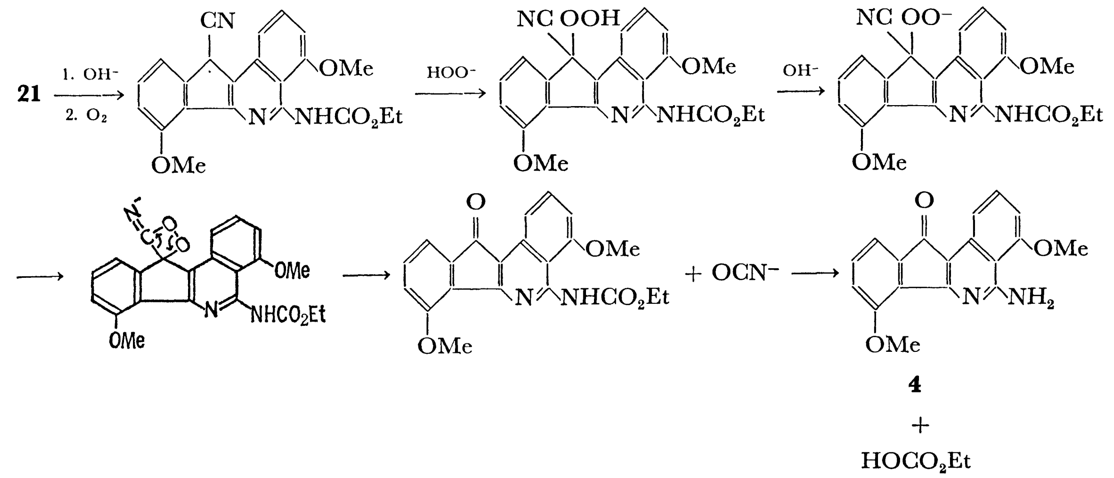
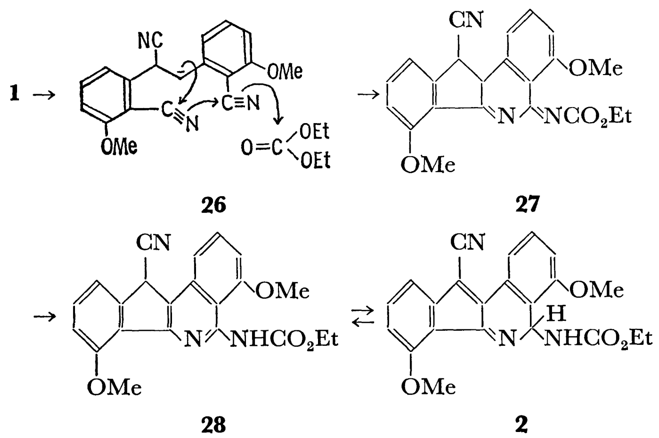


Scheme 6



Scheme 7

Experimental

Melting points were uncorrected. The IR spectra were measured, unless specified, on Nujol mull on a Nippon Bunko IR-S spectrometer and the electronic spectra on a Hitachi EPS-2 spectrometer. Chemical shifts are reported in δ-values, using TMS as internal references.

*Formation Reaction of the Red Pigment **2**.* A solution of sodium ethoxide in ethanol (prepared from 600 mg of sodium and 11 ml of abs. ethanol) was added to a mixture of 1,2-bis-(2-cyano-3-methoxyphenyl)propionitrile (**1**)[2] (3.6 g) and diethyl carbonate (26 ml) under stirring, and the mixture was refluxed for 2 hr. The reacting solution rapidly turned brownish black. The mixture was poured onto ice-water, providing **2** as red precipitate. Dilute acid may be added when necessary for the completion of precipitation. Recrystallization from chloroform afforded pure **2** as needles, mp 272 °C (dec.), 3.5 g (79.3% yield): $\lambda_{\max}^{\text{EtOH}}$ 249 (ε 37900), 283 (27100), 325 (18200), 387 (17100) and 528 nm (5200); $\nu_{\max}$ 3340 (-NH), 2166(strong, -CN) and 1705 cm^{-1} (-NHCO$_2$R); δ(CF$_3$CO$_2$H), 1.57(3H, t, J=7.5 Hz, -OCH$_2$-C$\underline{\text{H}}_3$), 4.33 (3H, s, -OCH$_3$), 4.42(3H, s, -OCH$_3$), 4.76(2H, q, J=7.5 Hz, -OC$\underline{\text{H}}_2$CH$_3$), and 5.61(1H, s, ⩾CH). Found: C, 67.88; H, 5.04; N, 10.76%. Calcd for $C_{22}H_{19}N_3O_4$: C, 67.85; H, 4.92; N, 10.79%.

*Alkaline Hydrolysis of the Red Pigment **2**.* A mixture of **2** (300 mg) with sodium hydroxide (630 mg), water (12 ml) and ethanol (12 ml) was refluxed under nitrogen atmosphere for 3 hr. After cooling the reaction mixture was acidified with dil. hydrochloric acid. The solution, initially yellow, temporarily yielded a red precipitate which redissolved itself and then finally produced a white precipitate. This was filtered and washed with small amount of ethanol to afford almost pure **2**, 237 mg (87.2% yield). The analytical specimen was recrystallized from methanol: mp 249 °C (dec.); $\lambda_{\max}^{\text{H}_2\text{SO}_4\text{-EtOH}}$ 220(ε 32500), 239(sh., 17400), 263(19600), 287(sh., 7050), 332(sh., 10300), 344(13200), 380(16300) and 398 nm(1500); $\nu_{\max}$ 3300, 3080—2760(-NH$_3^+$) and 2245 cm^{-1} (-CN); δ(CF$_3$CO$_2$H), 4.13(3H, s, -OCH$_3$), 4.34(3H, -OCH$_3$), 5.30(1H, s, ⩾CH), and 7.20—8.27(6H, m, ArH). Found: C, 64.15; H, 4.76; N, 11.72%. Calcd for $C_{19}H_{16}N_3O_2Cl$: C, 64.50; H, 4.56; N, 11.88%.

*Oxidative Degradation of the Red Pigment **2** with Alkaline Hydrogen Peroxide.* Hydrogen peroxide (3%) (100 ml) was added to a solution of **2**(980 mg) in ethanol (200 ml) and 10% aq. sodium hydroxide solution (10 ml) under stirring for 15 min. The reaction mixture gradually turned red and finnally gave a red precipitate, mp 288 °C(dec.), 750 mg (92.5% yield). Recrystallization from chloroform provided pure **4**, mp 289—290 °C; $\lambda_{\max}^{\text{dioxane}}$ 224.5 (ε 22300), 235 (sh., 19000), 290(29700), 350(19600), 364(sh., 10800), 375 (sh., 6880), and 470 nm(3310); $\nu_{\max}$ 3460, 3280, 3170 (-NH$_2$), and 1670 cm^{-1} ($>$CO); δ(CF$_3$CO$_2$H), 3.65(3H, s, -OCH$_3$), 3.79(3H, s, -OCH$_3$), and 6.72—7.94(6H, m, ArH). *Hydrochloride* **5** was prepared by stirrring a mixture of **4** (30 mg), ethanol (50 ml) and concd. hydrochloric acid (5 ml). Evaporation of the mixture to dryness and recrystallization of the residue from ethanol yielded **5**, mp 300 °C (dec.); $\nu_{\max}$ 3320, 3000 (-NH$_3^+$), and 1705 cm^{-1} ($>$CO). Found: C, 63.15; H, 4.50; N, 8.16%. Calcd for $C_{18}H_{15}N_2O_3Cl$: C, 63.07; H, 4.41; N, 8.17%. Acetylation of **4** (187 mg) with acetic anhydride (50 mg) and anhyd. pyridine (25 ml) was carried out overnight at room temperature. The resulting orange red precipite (128 mg) was filtered and washed with ethanol. Recrystallization from chloroform afforded *the acetate* **6**, mp 270—273 °C; $\lambda_{\max}^{\text{EtOH}}$ 222(ε 21500), 275(33900), 355(19500), 368(sh., 12300), 380(sh., 6650), and 485 nm (2850); $\nu_{\max}$ 3330(-NH) and 1675(-NHCO- and $>$CO) cm^{-1}; δ(CF$_3$CO$_2$H), 2.72(3H, s, -COCH$_3$), 4.25(3H, s, -OCH$_3$), 4.35(3H, s, -OCH$_3$), and 7.23—8.13 (6H, m, ArH).

*Alkaline Hydrolysis of **4**.* A mixture of **4**(2.0 g), 6M potassium hydroxide solution(300 ml) and ethanol (360 ml) was refluxed for 20 hr, and filtered while hot. The filtrate, after concentration *in vacuo*, was acidified with hydrochloric acid to give almost pure **7** as a red precipitate (1.65 g, 82.% yield), which was recrystallized from ethanol: mp 295.5 °C; $\lambda_{\max}^{\text{EtOH}}$ 235(ε 26600), 269(33300), 291(19600), 353(18500), 372(sh., 13100), and 475 nm(3270); $\nu_{\max}$ 3380 (sharp, -NH), 1690(CO), and 1665 cm^{-1} (-CONH-); δ(CF$_3$CO$_2$H), 4.16 (3H, s, -OCH$_3$), 4.36(3H, s, -OCH$_3$) and 7.26—9.00(6H, m, ArH). Found: C, 70.35; H, 4.24; N, 4.53%. Calcd for $C_{18}H_{13}NO_4$: C, 70.35; H, 4.26; N, 4.56%.

*Methylation of **7**.* Sodium methoxide (4.05 g) and methyl iodide (5.1 ml) was alternatively added in three portions to a refluxing solution of **7** (150 mg) in abs. methanol (300 ml) for two days. After removal of most of the solvent, water was added. The red precipitate (200 mg) thus obtained was chromatographed on a column of silica gel (5 g) and the methylated product **8** (128 mg) was isolated from the chloroform eluate in 81.5% yield. Recrystallization from chloroform provided pure **8**, mp 241—242 °C; $\lambda_{\max}^{\text{EtOH}}$ 237 (ε 21800), 272(28900), 293(sh., 18200), 355(19500), 374 (sh., 11600) and 485 nm(1490); $\nu_{\max}$ 1670 cm^{-1} (-CON$<$ and $>$CO); δ(CDCl$_3$), 3.92, 3.99, 4.04(each 3H, s, -OCH$_3$) and 6.85—8.50(6H, m, ArH). Found: C, 71.06; H, 4.75; N, 4.35%. Calcd for $C_{19}H_{15}NO_4$: C, 71.02; H, 4.71; N, 4.36%.

*Zinc Dust Reduction of **7**.* *a) In Aqeous Acetic Acid*: A mixture of **7**(1.05 g), glacial acetic acid (400 ml), water (15 ml) and zinc dust (2.1 g) was refluxed for 1.5 hr. The reaction mixture was filtered. After concentration *in vacuo*, water (700 ml) was added. The resulting white precipitate (940 mg) was chromatographed on a column of silica gel (30 g). Elution with chloroform yielded 5,6-dihydro-4,7-dimethoxy-11*H*-indeno[1,2-*c*]isoquinolin-5-one (**10**) (306 mg) and subsequent elution with 2% methanol-chloroform gave 5,6-dihydro-11-hydroxy-4,7-dimethoxy-11*H*-indeno[1,2-*c*]isoquinolin-5-one (**11**) (286 mg). **10**(from methanol), mp 275—276 °C; $\lambda_{\max}^{\text{EtOH}}$ 215(ε 33900), 255(21200), 274(sh., 5920), 305(sh., 5380), 325(sh., 11200), 353(14300), 369(19700) and 388 nm(16700); $\nu_{\max}$ 3420($>$NH) and 1650 cm^{-1}(-CONH-); δ(CDCl$_3$), 3.74(2H, s, $>$CH$_2$), 3.80(3H, s, -OCH$_3$) and 3.82 (3H, s, -OCH$_3$). Found: C, 73.57; H, 5.21; N, 4.78%. Calcd for $C_{18}H_{15}NO_3$: C, 73.70; H, 5.15; N, 4.78%. **11** (from chloroform-methanol): mp 249—250 °C(dec.); $\lambda_{\max}^{\text{EtOH}}$ 217(ε 26200), 258(22000), 278(sh., 5300), 312(sh., 3440), 358(14500), 376(19100) and 396 nm (16700); ν_{max} 3420(sh., –OH), 3380(⟩NH) and 1654 cm^{-1}(-NHCO–). Found: C, 69.46; H, 4.95; N, 4.52%. Calcd for $C_{18}H_{15}NO_4$: C, 69.89; H, 4.89; N, 4.53%.

b) In Glacial Acetic Acid: A mixture of **7**(140 mg), zinc dust (560 mg) and glacial acetic acid (14 ml) was refluxed for 30 min. After working up as above, only **10** (110 mg) was obtained in 82% yield.

*Zinc Dust Reduction of **4**.* **4**(270 mg), zinc dust (550 mg) and glacial acetic acid (10 ml) were mixed and refluxed for 2 hr. The insoluble material was removed by filtration. Water (10 ml) was added to the filtrate, which was then made basic by the addition of ammonia solution under ice-cooling. The precipitate, mp 218—221 °C(dec.) (182 mg, 70.5% yield) was recrystallized from methanol to give pure 5-amino-4,7-dimethoxy-11*H*-indeno[1,2-*c*]isoquinoline **12**, mp 229—230 °C(dec.); $\lambda_{max}^{H_2SO_4}$ 220(ε 36900), 239(sh., 17600), 259 (21300), 289(6960), 328(13500), 342(16200), 386(17600)and 405 nm(16500); ν_{max} 3500 and 3370 cm^{-1} (each –NH_2); δ(CF_3CO_2H), 3.75(2H, s, ⟩CH_2), 4.03(3H, s, –OCH_3) and 4.13(3H, s, –OCH_3). Found: C, 73.73; H, 5.63; N, 9.35%. Calcd for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52; N, 9.58%.

*Ammonia Treatment of the Hydrochloride **3**.* When an aq. solution of 3 (72 mg) was neutralized by dropwise addition of ammonia, red precipitate **22** (52 mg), not as vivid in color as the "red pigment" was obtained. ν_{max} 3440, 3300(broad) and 2160 cm^{-1}. However, attempts to purify **22** failed since it was so unstable that it changed completely to **4** within a few days on standing in air.

*Catalytic Hydrogenation of the Hydrochloride **3**.* A solution of the hydrochloride **3** (100 mg) in acetic acid (8 ml) was stirred for 18 hr under hydrogen atmosphere with 10% palladium-on-charcoal (150 mg) and 2M HCl (8 ml), until the starting material was consumed completely. After the removal of the catalyst by filtration, the filtrate was diluted with water and the product was extracted three times with chloroform. The organic layer was treated with ammonia. After being washed with water and dried, the solvent was evaporated to leave an oil (30 mg) which was crystallized from methanol to afford **13**, mp 189—190 °C; $\lambda_{max}^{H_2SO_4\text{-}EtOH}$ 221(ε 36600), 239(sh., 17100), 260(20500), 289 (7230), 328(13400), 387(17100) and 406 nm(16700); $\nu_{max}^{CHCl_3}$ 3460 and 3360; ν_{max}^{Nujol} 3544 and 3408 cm^{-1}; δ($CDCl_3$), 1.52 (3H, d, J=7 Hz, ⟩$CHC\underline{H}_3$), 3.93(3H, s, –OCH_3), 3.99(1H, q, J=7 Hz, ⟩$C\underline{H}CH_3$), 4.00(3H, s, –OCH_3) and 6.63—7.63 (6H, m ArH). Found: C, 74.19; H, 5.93; N, 9.08%. Calcd for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92; N, 9.15%. The aq. layer was made alkaline by the addition of ammonia and extracted with chloroform. The evaporation of the solvent gave **14** as an oil. $\nu_{max}^{CHCl_3}$ 3460 and 3360 cm^{-1}.

*Catalytic Hygrogenation of the "Red Pigment" **2**.* A solution of **2** (100 mg) in acetic acid (3 ml) and 1 M HCl (2 ml) was hydrogenated over 10% palladized charcoal (60 mg) for 24 hr at room temperature. After removal of the catalyst by filtration, the filtrate was treated with ammonia. The resulting precipitate (80 mg) was crystallized from chloroform to give a red colored product **15** (18 mg), mp 208 °C (dec.); ν_{max}^{Nujol} 3340 (⟩NH) and 1710 cm^{-1} (⟩CO); δ(CF_3CO_2H), 1.54(3H, t, J=7 Hz), 4.24(3H, s), 4.32(3H, s), 4.64(2H, q, J=7 Hz), 5.34(1H, d, J=3 Hz), 6.68—8.16 (6H, m) and 9.42(1H, d, J=3 Hz). The compound was contaminated with another product as revealed by the presence of smaller signals in the NMR spectrum of δ 1.57 (t, J=7 Hz), 4.06(s), 4.34(s) and 4.60(q, J=7 Hz). Attempts to separate both compounds were unsuccessful.

*Acetylation of the Hydrochloride **3**.* To a mixture of **3** (190 mg) and acetic anhydride (15 ml) was added five drops of concd. H_2SO_4 and the total mixture was swirled until an homogeneous yellow solution was obtained. After being left to stand at room temperature overnight, the mixture was poured onto ice-water (200 g) and the resulting red precipitate was recrystallized from chloroform to yield the acetate **16**, mp 292—293 °C(dec.), 120 mg (62.2% yield): λ_{max}^{EtOH} 217(ε 23800), 250(36200), 279(sh., 24300), 286(25400), 325(15300), 384(17100) and 520 nm(4480); λ_{max}^{Nujol} 3300, 2165 and 1680 cm^{-1}; δ(CF_3CO_2H), 2.73(3H, s, –$COCH_3$), 4.27(3H, s, –OCH_3), 4.37(3H, s, –OCH_3), 5.53(1H, s, ⋟CH) and 7.20—8.40(6H, m, ArH). Found: C, 69.84; H, 4.86; N, 11.77%. Calcd for $C_{21}H_{17}N_3O_3$: C, 70.18; H, 4.77; N, 11.69%.

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6) This structure was confirmed by a total synthesis, which constitutes the subject of Part II of this study.

7) The SCF-MO calculation on the tautomeric structure of **2** has been unertaken in collaboration with Dr. K. Nishimoto and Mr. H. Tomono of Osaka City University. The result corroborates the assignment of the iminoindene structure for **2**.

8) For references on the tautomerism between the nitrile and ketenimine forms, *cf.* J. Casanova, Jr., "The Chemistry of the Cyano Group," ed. by Z. Rappoport, Interscience, New York, N. Y. (1970), p. 894.

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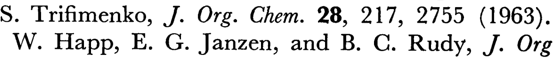
14) For example, it has been reported[9] that, though an acetone solution of diphenylketene-*p*-tolylimine reacts only slowly with water, the hydrolysis is complete in a few seconds by the addition of a small amount of hydrochloric acid to give *N*-(*p*-tolyl)diphenylacetamide in 86% yield. The treatment of **2** with a mixture of dil. hydrochloric acid and ethanol even at refluxing temperature merely resulted in the recovery of the starting material.

15) Trofimenko has reported[12] the value 2170 cm^{-1} for the IR absorption of the cyano group in the metal salt of tricyanomethane which has the structure



$$\left[\begin{matrix}NC\\NC\end{matrix}\!\!>C^{-}-C\equiv N \longleftrightarrow \begin{matrix}NC\\NC\end{matrix}\!\!>C=C=N^{-}\ \textit{etc.}\right]M^{+}.$$

cf. also S. Trifimenko, *J. Org. Chem.* **28**, 217, 2755 (1963).

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17) We have found that cyclization by way of this path does also occur but to a lesser extent and this subject will be dealed with in the forthcoming publications.