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Isolation of the Intermediate in the Tricyanovinylation of Indole and *N*-Methylindole

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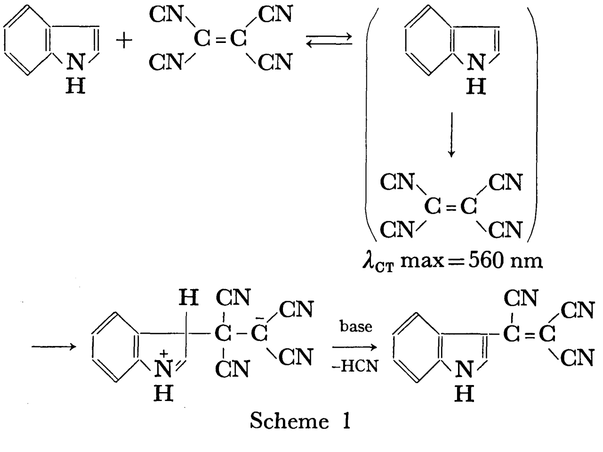
The intermediate has been isolated in the tricyanovinylation of indole and *N*-methylindole. The neutral adduct structure at the 3-position is assigned on the basis of spectroscopic as well as chemical evidence. The mechanism for tricyanovinylation is discussed.

The tricyanovinylation of aromatic amines at either N-position or *para*-position by the reaction with tetracyanoethylene is well known.[1] Indole and its derivatives are also known to undergo tricyanovinylation at the 3-position.[2,3] In these tricyanovinylation reactions tetrahydrofuran, dimethylformamide or pyridine has usually been used as the solvent. Kinetic studies in chloroform or in dichloromethane have shown that the reaction involves three steps:[4,5] (a) rapid formation of a 1: 1 charge-transfer complex (π-complex), (b) formation of a zwitterionic σ-complex, (c) elimination of hydrogen cyanide from the σ-complex to form the final product. In the process of hydrogen cyanide elimination which is the rate-determining step, the



Scheme 1

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[1] B. C. Mckusick, R. E. Heckert, T. L. Cairns, D. D. Coffman, and H. F. Mower, *J. Amer. Chem. Soc.*, **80**, 2806 (1958).

[2] G. N. Sausen, V. A. Engelhardt, and W. J. Middleton, *ibid.*, **80**, 2815 (1958).

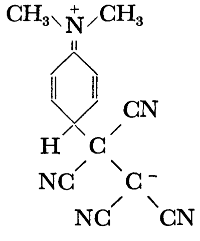
[3] W. E. Noland, W. C. Kuryla, and R. F. Lange, *ibid.*, **81**, 6010 (1959).

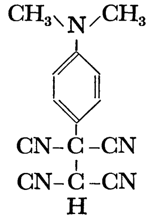
[4] Z. Rappoport, *J. Chem. Soc.*, **1963**, 4498.

[5] R. Foster and P. Hanson, *Tetrahedron*, **21**, 255 (1965).

amine or indole is suggested to act as a proton-abstractor. The proposed mechanism with indole is shown as an example in Scheme 1.

Concerning the above mechanism it should be mentioned that while the formation of the charge-transfer complex is visually observable, the intermediacy of the σ-complex was inferred by indirect evidence.[6] Recently Farrell *et al.* have succeeded in isolating an intermediate from the tetracyanoethylene-*N*,*N*-dimethylaniline reaction by changing the solvent. The structure of the isolated intermediate had first been assigned to the zwitterionic σ-complex (1),[7] but later the neutral adduct structure (II) was shown to be the correct one.[8] Rappoport and Shohamy have also achieved the isolation of intermediates in the tricyanovinylation of several primary aromatic amines by introducing the *ortho*-substituents to the amino group.[9] In this case tricyanovinylation occurs at the *para*-position instead of the N-position owing to steric crowding. It has been claimed that the *ortho*-substituted amine is too bulky to be very effective as a proton-abstractor from the intermediate, thus increasing its lifetime and enabling its isolation. Neutral adduct structure like II is assigned from the spectroscopic evidence.


(I)

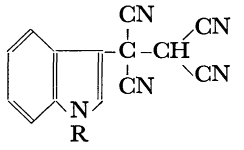

(II)

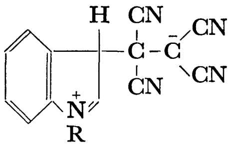
Indole and its derivatives are less basic than aromatic amines, and thus less effective as a proton-abstractor since the unpaired electrons on nitrogen atom participate in the aromatization. It was therefore expected that under favorable conditions isolation of the intermediate would be possible.[10] In the present study we have isolated the intermediate in the tricyanovinylation of indole and *N*-methylindole. Spectroscopic evidences are presented to indicate the neutral adduct structure (III), and the mechanism for tricyanovinylation is discussed.

Results and Discussion

When a half equimolar amount of tetracyanoethylene was mixed with *N*-methylindole in benzene at room temperature, a blackish purple color characteristic of the charge-transfer complex developed immediately. The solution was left at room temperature for 24 hr, during which time the initial blackish purple color slowly faded away to become slighlty reddish yellow. White crystalline solids were precipitated from the solution, collected by filtration and recrystallized from benzene to give white needles. Removal of the solvent *in vacuo* gave additional white solids together with recovered *N*-methylindole. When equimolar amounts of tetracyanoethylene and *N*-methylindole were refluxed in benzene for 7 hr, white needles and the final tricyanovinylated compound, *N*-methyl-3-tricyanovinylindole (VIIa), were obtained simultaneously. The isolated white needles were almost quantitatively converted into VIIa with a loss of hydrogen cyanide when heated in methanol for a few hours. The molecular ion peak of the isolated white needle is observed at m/e 259 in the mass spectrum. From these results and from other spectral evidences described below together with the elemental analysis, the isolated white needle was concluded to be the intermediate adduct between *N*-methylindole and tetracyanoethylene, which led to the final substitution product VIIa. The yields of the isolated intermediate were 97% in the reaction at room temperature and 65% in the reaction under reflux. Simultaneous formation of VIIa under reflux appears to result from a thermal decomposition of the isolable intermediate.

The intermediate in the tricyanovinylation of indole was similarly isolated. A benzene solution of indole was added to a solution of a half equimolar amount of tetracyanoethylene in benzene. The initial blackish purple color faded slowly and after 24 hr the solution turned reddish orange. From this solution the intermediate adduct and the final tricyanovinylated compound, 3-tricyanovinylindole (VIIb), were obtained in 83% and 16% yields, respectively. When the reaction solution was refluxed for 7 hr, the main product isolated was VIIb (54%), the intermediate adduct being obtained only in a 14% yield. The isolated intermediate from the reaction of indole was likewise con-


IIIa R=CH_3
IIIb R=H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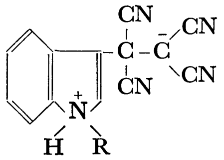
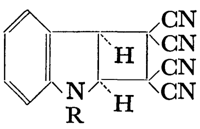
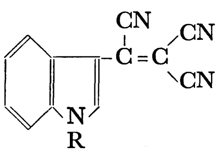
IVb R=H


Va R=CH_3
Vb R=H


VIa R=CH_3
VIb R=H


VIIa R=CH_3
VIIb R=H

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[6] The appearance of the final substitution product is much slower than a decay of the chage-transfer complex.

[7] P. G. Farrell, J. Newton, and R. F. M. White, *J. Chem. Soc., B*, **1967**, 637.

[8] P. G. Farrell and R. K. Wojtowski, *ibid., B*, **1970**, 1390.

[9] Z. Rappoport and E. Shohamy, *ibid., B*, **1969**, 77.

[10] Before kinetic studies of the tricyanovinylation reaction were made by Rappoport,[4] and Foster and Hanson,[5] Noland *et al.*[3] had reported in their synthetic studies of tricyanovinylated compounds from indole and its derivatives that in one case, with 2-methylindole, the intermediate was isolated and found to be the adduct tetracyanoethane based on a brief characterization.

verted almost quantitatively into VIIb when heated in methanol. The elementary analysis of the intermediate was in good agreement with the adduct structure between indole and tetracyanoethylene.

Both of the isolated intermediates are relatively stable and can be stored for several days when kept dry below room temperature. The intermediate derived from indole is less stable than that derived from *N*-methylindole, which is also reflected in the results of their preparative reactions described above. They are almost insoluble in carbon tetrachloride but soluble in acetone or tetrahydrofuran. On contact with moisture or basic solvent they slowly turn through pink to red to form the final tricyanovinylated compounds.

The follwing possible structures from IIIa and IIIb to VIa and VIb are conceivable for the isolated intermediates which lead to the final substitution products VIIa and VIIb. Of these structures IIIa and IIIb were assigned from the sepctral evidences.

Infrared Spectra. The infrared spectrum of the isolated intermediate from *N*-methylindole in KBr disk shows a sharp strong absorption at 2900 cm^{-1} which is characteristic of the intermediate and assignable to the aliphatic tertiary C–H stretching vibration. The absorption at 2900 cm^{-1} in the intermediate corresponds to that observed at 2900 cm^{-1} in tetracyanoethane and in *N,N*-dimethyl-4-(1,1,2,2,-tetracyanoethyl)aniline (II).[9] While a sharp absorption characteristic of the conjugated C≡N group appears at 2200 cm^{-1} in VIIa, only a very weak absorption of the unconjugated C≡N group appears at 2260 cm^{-1} in the isolated intermediate. Similarly the spectrum of the intermediate derived from indole in KBr disk shows the characteristic absorption at 2900 cm^{-1}. In this case a very weak absorption at 2260 cm^{-1} and a sharp absorption at 2200 cm^{-1} are observed in the cyano-band region. It is suspected that the intermediate decomposed partly to VIIb during the preparation of the disk as suggested from its reddish orange color. When the spectrum is taken in Nujol mull with a freshly prepared sample, no absorption appears at 2200 cm^{-1}, although in VIIb a sharp strong band appears at 2200 cm^{-1} due to the conjugated C≡N group. The absorption of the unconjugated C≡N group of the intermediate at 2260 cm^{-1} is so weak as to be hardly detectable in Nujol mull. It is generally accepted that cyano-compounds with electron-withdrawing substituents at the α-position frequently show only weak absorption or sometimes no absorption of the C≡N group.[11] It should also be noted that many compounds containing $^{-}C(CN)_2$ moiety are reported to show two medium bands at the unsaturated cyano-band region.[12] In the spectrum of the intermediate derived from indole a single, rather strong band of the secondary N–H stretching vibration appears at 3300 cm^{-1} as observed in indole and in VIIb at 3380 and 3200 cm^{-1}, respectively. No absorption ascribable to the $-\overset{+}{N}H_2$ or $C=\overset{+}{N}H$ group is observed in the regions, 2780—2500 cm^{-1} or 2500—2325 cm^{-1}, respectively[13,14] in both intermediates. The infrared spectra eliminate the σ-complex structures such as IV or V for the isolated intermediates, thus favoring structure III.

NMR Spectra. The NMR spectra of the isolated intermediate were measured in hexadeuterioacetone as soon as possible after the solutions were prepared. The intermediate derived from *N*-methylindole shows a singlet at τ 6.0 due to *N*-methyl protons, a singlet at τ 3.75 and multiplets at τ 1.9—2.8 due to aromatic protons including the proton at the 2-position in the indole ring, the relative ratios being 3: 1: 5. The singlet peak at τ 3.75 is reasonably attributed to the methine proton of the dicyanomethyl moiety in structure IIIa from consideration of the chemical shift value of τ 4.19 for tetracyanoethane.[9] The peak due to the *N*-methyl protons appears as a singlet at τ 6.63 (in $CDCl_3$) in *N*-methylindole[15] and at τ 5.84 in VIIa. Similarly the spectrum of the intermediate derived from indole exhibits a singlet at τ 3.74 and multiplets at τ 1.9—2.8 in the relative ratios of 1: 6. In the latter the indole ring protons and the N-H proton are included. The NMR spectra exclude the cyclo-adduct structure VI with two methine protons which should couple with each other. Structures IV and V are also unlikely from the position and the relative intensity of the signals. In these structures the methine proton at the 3-position should be coupled with the neighboring carbon-bound hydrogen at the 2-position.[14] Thus the isolated intermediates leading to the tricyanovinylated compounds VIIa and VIIb are assigned to structures IIIa and IIIb, respectively, from both the infrared and NMR spectra.

Electronic and Mass Spectra. The electronic spectra of the intermediates IIIa and IIIb in benzene show maxima at 282 nm (log ε 3.62) and 279 nm (log ε 3.76), respectively.

Although the mass spectrum is of no particular use for distinguishing between the adduct structures, it is briefly described. Both intermediates IIIa and IIIb show very low molecular ion peaks at *m/e* 259 and *m/e* 245, respectively. The base peak appears at *m/e* 232 in IIIa and at *m/e* 218 in IIIb, which corresponds to the loss of hydrogen cyanide from the molecular ion. The position and relative intensity of the peaks below *m/e* 232 in IIIa and *m/e* 218 in IIIb are almost the same as those of the tricyanovinylated compounds VIIa and VIIb, respectively, except for the peaks at *m/e* 195 (very low intensity) and *m/e* 194 in IIIa and *m/e* 181 (very low intensity) and *m/e* 180 in IIIb. The characteristic peaks at *m/e* 195 and *m/e* 194 in IIIa and at *m/e* 181 and at *m/e* 180 in IIIb which are absent in the spectra of VIIa and VIIb correspond to the direct loss of $:C(CN)_2$ and $\cdot CH(CN)_2$ from the molecular ion, respectively. Other fragments below *m/e* 232 in IIIa and *m/e* 218 in IIIb are suggested to be formed by the fragmentation of VIIa and VIIb. The main peaks over *m/e* 180 observed in IIIa and IIIb are listed in the Table and the fragmentation course from the molecular ion to the ion of

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[11] L. J. Bellamy, "The Infra-Red Spectra of Complex Molecules," 2nd ed., Methuen, London, (1958), p. 265.

[12] Z. Rappoport and S. Gertler, *J. Chem. Soc.*, **1964**, 1360, and references cited therein.

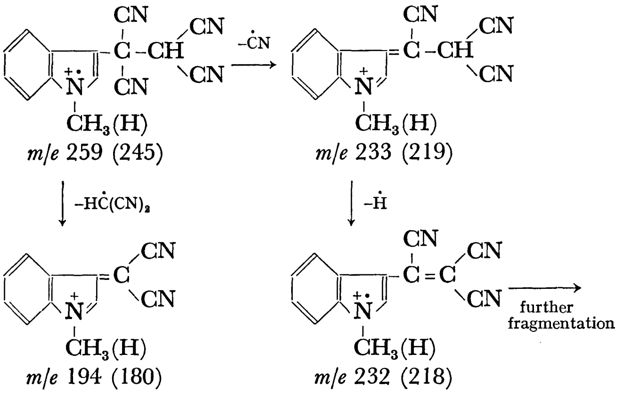
[13] L. J. Bellamy, "The Infra-Red Spectra of Complex Molecules," 2nd ed., Methuen, London, (1958), p. 259.

[14] R. L. Hinman and J. Lang, *Tetrahedron Lett.*, **1960**, 12.

[15] L. A. Cohen, J. W. Daly, K. Kny, and B. Witkop, *J. Amer. Chem. Soc.*, **82**, 2184 (1960).

Table 1. Fragmentation of IIIa and IIIb in the mass spectra

			IIIa			
m/e	259	233	232	205	194	190
Abundance	1.6	15.6	100	14.4	9.5	8.6
Assignment	P	M-CN	M-HCN	M-2HCN	M-CH(CN)$_2$	M-2HCN-Me
			IIIb			
m/e	245	219	218	191	180	
Abundance	3.6	16.2	100	41.5	7.2	
Assignment	P	M-CN	M-HCN	M-2HCN	M-CH(CN)$_2$	



Scheme 2

the tricyanovinylated compound is depicted in Scheme 2.

Mechanism for Tricyanovinylation. It was shown from kinetic studies that the tricyanovinylation of aromatic amines or indole by tetracyanoethylene proceed in three steps as shown with indole in Scheme 1. However, a neutral adduct tetracyanoethane has recently been isolated as an intermediate in the tricyanovinylation of aromatic amines, and a general mechanism as shown in Scheme 3 has been proposed by Rappoport and Shohamy[9] for the tricyanovinylation of aromatic amines. In the present study a similar adduct tetracyanoethane has been isolated as an intermediate in the tricyanovinylation of indole and *N*-methylindole. Consequently, the same general mechanism as has been proposed for the tricyanovinylation of aromatic amines may be written also for the tricyanovinylation of indole and its derivatives.

$$\begin{tikzcd}[column sep=small] \text{Reactants} \arrow[r, shift left] & \text{Charge-transfer Complex } (\pi\text{-Complex}) \arrow[l, shift left] & \\ \arrow[r] & \text{Zwitterionic } \sigma\text{-Complex} \arrow[r, shift left] \arrow[d] & \text{Neutral Adduct} \arrow[l, shift left] \arrow[dl] \\ & \text{Final Substitution Product} & \end{tikzcd}$$

Scheme 3

Although the neutral adduct intermediate was isolated under the present reaction conditions, it should be noted that there might be a possibility that the reaction proceeds as described in Scheme 1 under different reaction conditions. Especially, in strongly basic solvents such as pyridine or dimethylformamide it is likely that the tricyanovinylated compound is formed directly from the σ-complex, the basic solvent abstracting a proton from the 3-position in the σ-complex. Whether the final tricyanovinylated compound is formed *via* the neutral adduct intermediate or directly from the σ-complex under the given reaction conditions, where the intermediate can not be isolated, can be seen by examining the hydrogen isotope effect, the presence of which is expected in the elimination of hydrogen cyanide from the σ-complex (IV) owing to the relatively low acidity of the hydrogen at the 3-position.[16]

Experimental

Materials. Indole was obtained commercially and purified by recrystallization from *n*-hexane three times, mp 52°C. *N*-methylindole was prepared from indole as described by Potts and Saxton.[19] Crude distilled product was contaminated with unreacted indole as revealed by the N-H absorption in the infrared spectrum. Chromatograph over alumina and subsequent two distillations *in vacuo* yielded pure *N*-methylindole, bp 128—129°C/25 mmHg (lit.[19] bp. 133°C/26 mmHg). Tetracyanoethylene was obtained commercially, recrystallized from chlorobenzene and sublimed twice *in vacuo*, mp 201°C. Benzene was purified and dried in the usual way, and distilled from sodium wire immediately before use.

Spectra. Infrared spectra were taken with Hitachi EPI-G2 and Jasco IR-G infrared spectrophotometers. Electronic spectra were taken with a Hitachi 124 spectrophotometer. NMR spectra were obtained with a Japan Electron Optics Laboratory JNM 3H-60 spectrometer. Mass spectra were recorded with a Hitachi RMU-6E mass spectrometer by means of a direct inlet with an ionization energy of 70 eV.

Isolation of N-*methyl-3-(1,1,2,2-tetracyanoethyl)indole (IIIa).* Reaction 1. To a solution of tetracyanoethylene (0.64 g, 0.005 mol) in 40 m*l* benzene was added *N*-methylindole (1.31 g, 0.01 mol) dissolved in 5 m*l* benzene. A blackish purple color appeared immediately and the solution was left at 20°C for 24 hr. During that time the initial characteristic color of the charge-transfer complex slowly faded to a slightly reddish yellow. From the solution were precipitated white crystalline solids (IIIa), which were collected by filtration. Evaporation of the solvent *in vacuo* gave additional IIIa together with recovered *N*-methylindole (0.34 g). The total yield of IIIa was 1.26 g (97%). It was recrystallized from dry benzene to give a white needle. Prolonged heating or repeated recrystallization caused its partial decomposition to *N*-methyl-3-tricyanovinylindole (VIIa). On heating it gradually turned through pink to red above 100°C accompanied by its decomposition to VIIa, and melted at *ca.* 210°C.

Found: C, 70.07; H, 3.48; N, 26.22%. Calcd for $C_{15}H_9N_5$: C, 69.49; H, 3.50; N, 27.02%.

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[16] A kinetic hydrogen isotope effect was observed with a k_H/k_D value of 3.6 in the tricyanovinylation of *N,N*-dimethylaniline in chloroform owing to the relatively low acidity of *para*-hydrogen in I, while no isotope effect was found in the amine-catalyzed elimination of hydrogen cyanide from II due to the more acidic hydrogen in II[17,18]

[17] P. G. Farrell and J. Newton, *Tetrahedron Lett.*, **1964**, 189.

[18] P. G. Farrell and J. Newton, *J. Chem. Soc.*, *B*, **1970**, 1630.

[19] K. T. Potts and J. E. Saxton, "Organic Synthesis," Vol. 40, (1960), p. 68.

Reaction 2. Solutions of tetracyanoethylene (1.28 g, 0.01 mol) and *N*-methylindole (1.31 g, 0.01 mol) were mixed and refluxed in 45 m*l* benzene for 7 hr. In this case the color of the solution remained black at the end of the reaction. Purple solids were obtained on cooling of the reaction solution. Evaporation of the solvent from the mother liquor also gave additional solids. They were collected and 50 m*l* of benzene was again added and reheated. The hot benzene solution was filtered to separate the insoluble red solids (VIIb, 0.23 g, 10%), which were recrystallized from methanol to give red fine needles. Cooling of the filtrate gave slightly pinkish white needles (IIIb, 1.69 g, 65%).

Isolation of 3-(1,1,2,2-tetracyanoethyl) indole (IIIb). Reaction 1. To a solution of tetracyanoethylene (0.77 g, 0.006 mol) in 40 m*l* benzene was added indole (1.41 g, 0.012 mole) in 5 m*l* benzene and left at 20°C for 24 hr. The initial blackish purple color faded slowly to a deep bluish purple and then to yellow and after 24 hr the solution turned reddish orange. The precipitated reddish pink solids were collected and dissolved rapidly in warm benzene. Insoluble red solids (VIIb) were separated (0.2 g, 16%) and from the filtrate was obtained IIIb as slightly pinkish white needles on cooling. The yield of IIIb was 1.23 g (83%). When heated to determine the mp, it gradually turned pink above 50°C and bove 100°C it turned reddish brown, decomposing to VIIb, mp *ca* 273—278°C. IIIb is less stable than IIId and prolonged heating or repeated recrystallizations from benzene caused considerable decomposition to VIIb.

Found: C, 68.29; H, 2.74; N, 28.50%. Calcd for $C_{14}H_7N_5$: C, 68.56; H, 2.88; N, 28.56%.

Reaction 2. Indole (1.17 g, 0.01 mol) dissolved in 5 m*l* benzene was added to a benzene solution (40 m*l*) of tetracyanoethylene (1.28 g, 0.01 mol) and refluxed for 7 hr. The solution was then cooled to 20°C and the precipitated blackish purple-colored solids were filtered off. Benzene (50m*l*) was again added, reheated to boiling for several minutes and filtered to separate the insoluble red solids (VIIb, 1.18 g, 54%). When the filtrate was cooled, slightly pinkish white needles (IIIb, 0.34 g, 14%) precipitated. In addition, small amounts of brown-colored solids were obtained from the initial mother liquor, which appeared to be *N*-tricyanovinylindole, since N–H absorption disappeared and strong conjuagted C≡N absorption was observed at 2200 cm^{-1} in the infrared spectrum.

Decomposition of IIIa and IIIb to VIIa and VIIb. IIIa or IIIb was heated in methanol for a few hours. The solution gradually turned red, and on cooling red fine needles VIIa or VIIb precipitated. The decomposition of the neutral adduct tetracyanoethane to the final substitution product was almost quantitative in each case.

Identification of VIIa and VIIb. VIIa: mp 226—226.5°C (recryst. from MeOH), (lit.[3]) mp 218—219°C). IR: $\nu_{C\equiv N}$ 2200 cm^{-1}. Mass: M$^+$ *m/e* 232 (calcd 232). NMR: (in acetone) τ 5.84 (3H, singlet, N–CH$_3$), τ 1.9—2.8 (5H, multiplet, aromatic protons). UV and V: λ_{max} (in MeOH), 252 (log ε 3.91), 286 (log ε 3.99), and 460 nm (log ε 4.39). [lit.[3]) in 95% EtOH. 262 (log ε 4.11), 280 (log ε 3.97), and 465 nm (log ε 3.91).]

Found: C, 71.89; H, 3.29: N, 24.06%. Calcd for $C_{14}H_8N_4$: C, 72.40; H, 3.47; N, 24.13%.

VIIb: mp 273—275°C (recryst. from MeOH), (lit.[3]) mp 268—270°C). IR: $\nu_{C\equiv N}$ 2200 cm^{-1}, ν_{N-H} 3200 cm^{-1}. Mass: M$^+$ *m/e* 218 (calcd 218). NMR: (in acetone), τ 1.9—2.8 (multiplets, N–H proton and aromatic protons), UV and V: λ_{max} (in MeOH), 249 (log ε 3.95), 284 (log ε 4.00), and 454 nm (log ε 4.34). [lit.[3]) in 95% EtOH, 251 (log ε 3.86), 285 (log ε 3.90), 357 (log ε 4.08), and 464 nm (log ε 4.33).]

Found: C, 71.84; H, 2.36; N, 25.11%. Calcd for $C_{13}H_6N_4$: C, 71.56; H, 2.57; N, 25.69%.