SYNTHESIS OF SUBSTITUTED PYRIDINES BY REACTION OF TETRACYANOETHYLATED KETONES WITH HYDROCHLORIC AND HYDROBROMIC ACIDS

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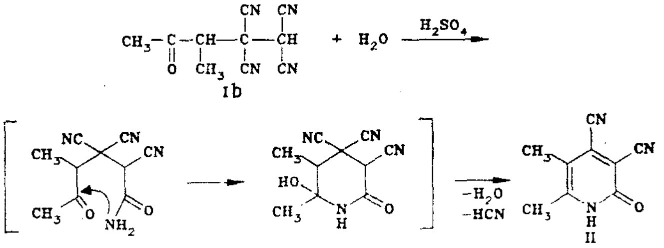
Previously unknown derivatives of pyridine have been synthesized by reaction of tetracyanoethylated ketones with concentrated aqueous solutions of hydrochloric and hydrobromic acids. The unique course of the reaction of 4,4,5,5-tetracyano-2-pentanone with gaseous hydrogen chloride has been demonstrated.

We have previously demonstrated that sym-tetracyanoethane reacts with hydrogen halides in more than one way. Thus, with HI it forms a substituted pyrrole [1], while with HCl it forms a polyfunctional butadiene [2]. Moreover, in [3] it was reported that when it was reacted with HBr, 2-amino-3,4-dicyano-5-bromopyrrole was formed in low yield. At the same time, when sym-tetracyanoethane is reacted with aqueous solutions of halogen derivatives and mineral acids a tarry mass of complex composition is formed, from which it is not possible to isolate any pure substances [4].

Continuing the study of the reaction of sym-tetracyanoethane and its monosubstituted analogs, we investigated the reaction of tetracyanoethylated ketones [5-9] Ia-f with mineral and hydrogen halide acids.

Heating of these ketones with 50% sulfuric acid gives, as a rule, a very tarry reaction mixture, from which pure compounds cannot be isolated. Only in the case of ketone Ib was a compound obtained in 10% yield, which was identical in properties to the previously reported [10] 5,6-dimethyl-3,4-dicyano-2(1H)-pyridone. Its formation is evidently due to hydrolysis of one of the nitrile groups to an amide group with subsequent cyclization and dehydrocyanation and dehydration of the 2-piperidinone formed:



Reaction of ketones Ia-f with concentrated hydrochloric and hydrobromic acids at 20°C proceeds more specifically and gives 2-halo-3,4-dicyanopyridines (IIIa-f) in 60-80% yield. Evidently the reaction starts with the addition of a hydrogen halide molecule to one of the cyano groups, which is characteristic of sym-tetracyanoethane [2], and there is subsequent cyclization and loss of a hydrocyanic acid molecule.

Conducting the reaction at raised temperatures (up to 100°C) leads to a sharp increase in tar formation. When ketones Ia-f were treated with hydriodic acid, we failed to isolate pure compounds.

In the IR spectra of cyanopyridines IIIa-f (Table 1) vibrational bands from the cyano groups occur in the region 2242-2250 cm^{-1}. The ^{13}C NMR spectra of these compounds are characterized by singlets in the region 112-113 ppm from the carbon atoms of the two cyano groups and by singlets from the carbon atoms of the pyridine ring: $C_{(3)}$ (108-112 ppm) $C_{(4)}$ (121-126

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TABLE 1. Properties of 2-Chloro(bromo)-3,4-dicyanopyridines III

Compound	mp, °C	IR spectrum, cm^{-1}		Found, %			Empirical formula	Calculated, %			Yield, %
		C≡N	ring vibrations	C	H	N		C	H	N	
IIIa	98—100	2242	1560, 1540	54,2	2,0	23,8	$C_8H_4ClN_3$	54,1	2,2	23,6	73
IIIb	72—74	2250	1560, 1538	56,3	2,9	22,1	$C_9H_6ClN_3$	56,4	3,1	21,9	84
IIIc	103—104	2248	1565, 1537	45,9	2,4	17,6	$C_9H_6BrN_3$	45,7	2,5	17,8	61
IIId	104—106	2245	1558, 1530	45,9	2,8	18,0	$C_9H_6BrN_3$	45,8	2,5	17,8	71
IIIe	77—79	2250	1580, 1553	59,2	2,8	20,5	$C_{10}H_6ClN_3$	58,9	2,9	20,6	70
IIIf	95—96	2245	1558, 1540	60,7	3,5	19,1	$C_{11}H_8ClN_3$	60,7	3,7	19,3	62

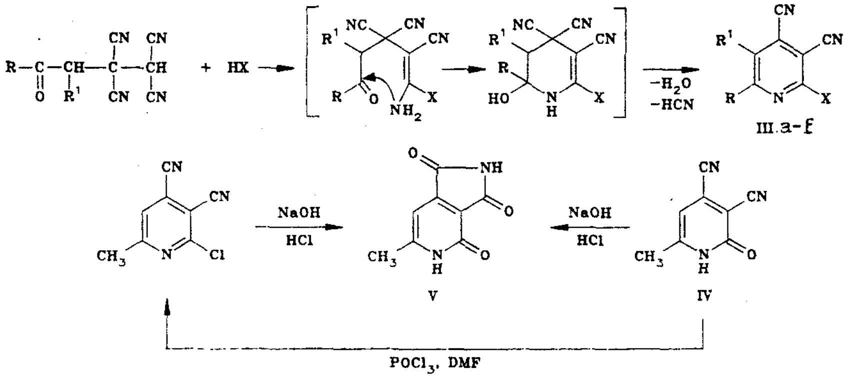
ppm), and $C_{(5)}$ (135.4-135 ppm). Signals from the $C_{(2)}$ atoms occur in the region 148-151 ppm specifically for the chloro derivatives, and at 139.5 ppm for the bromo-substituted compounds. It should be noted that in the case of the more strained 5,6-trimethylenedicyanochloropyridine IIIe, not only the signals from the $C_{(5)}$ and $C_{(6)}$ atoms but also the signal from the $C_{(2)}$ atom are shifted downfield. Such chemical shift values in ^{13}C NMR spectra are typical for pyridine derivatives, in particular cyano- and halopyridines [11]. The mass spectrometric decomposition of compound IIId proceeds somewhat unusually, whereby its molecular ion initially eliminates a molecule of HBr and the fragment with m/z 155 formed in the process subsequently eliminates a cyano group and two HCN molecules.

$$\underset{\text{III}d}{M^{+}} \xrightarrow{-HBr} 155\ (100) \xrightarrow{-CN^{\cdot}} 129\ (88) \xrightarrow{-HCN} 102\ (57) \xrightarrow{-HCN} 75\ (21)$$

The peak intensities in percent are given in brackets.

Chloropyridine IIIa was obtained by counter synthesis from reaction of the previously reported pyridone IV with phosphorus oxychloride (Scheme 1). It is interesting to note that alkaline hydrolysis of both chloropyridine IIIa and pyridone IV gives one and the same previously reported [10] imide V.

Scheme 1

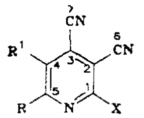


a R=CH_3, R¹=H, X=Cl; b R=R¹=CH_3, X=Cl; c R=R¹=CH_3, X=Br; d R=C_2H_5, R¹=H, X=Br; e R=R¹=(—CH_2—)₃, X=Cl; f R=R¹=(—CH_2—)₄, X=Cl

In contrast to tetracyanoethane the reaction of tetracyanoethylated ketones with gaseous hydrogen chloride takes place with considerable tar formation. Only in the case of ketone Ia in diethyl ether was it possible to obtain from the reaction mixture a crystalline compound, in the IR spectrum of which there were absorption bands due to an amino group at 3390, 3280, and 3190 cm^{-1} and from conjugated double bonds at 1597 and 1590 cm^{-1}; carbonyl group absorption bands were absent. In the mass spectrum the molecular ion peak appeared with m/z 197/195.

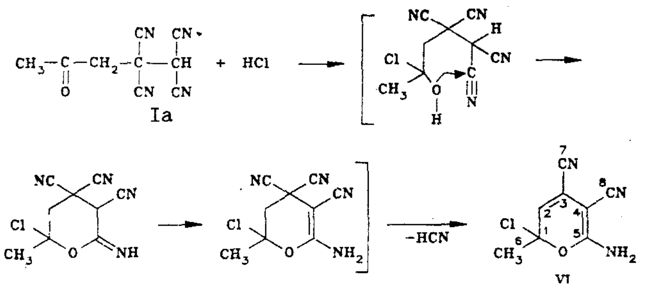
It is likely in this case (Scheme 2) that a competing addition of HCl to the carbonyl group takes place with subsequent cyclization and separation of hydrocyanic acid. The structrue of 2-chloro-2-methyl-4,5-dicyano-6-amino-2-pyran (VI) is confirmed by the data of the ^{13}C NMR spectra. The chemical shifts of the carbon atoms are: $C_{(1)}$ 69.90; $C_{(2)}$ 94.52; $C_{(3)}$ 136.25; $C_{(4)}$ 148.18; $C_{(5)}$ 165.19; $C_{(6)}$ 23.86; $C_{(7,\ 8)}$ 112.03, 115.64 ppm.

TABLE 1. Chemical Shifts in ^{13}C NMR Spectra of Carbon Atoms of Ring and Nitrile Groups in Compounds III (δ, ppm)



Compound	$C_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6,7)}$
IIIa	148,84	108,74	125,93	135,68	162,62	112,76, 112,46
IIIb	148,98	108,82	125,67	135,38	165,21	113,03, 112,81
IIIc	139,48	113,83	125,41	135,44	165,16	112,86, 111,95
IIId	139,51	113,94	125,25	135,49	165,19	112,43, 112,00
IIIe	151,30	107,98	121,28	141,13	173,70	113,08, 112,67
IIIf	148,79	108,74	126,03	135,65	165,54	112,49, 112,30

Scheme 2



EXPERIMENTAL

The course of the reactions and the purity of the products synthesized were monitored on Silufol UV-254 plates. IR spectra were recorded in a suspension of petrolatum oil on a UR-20 instrument. Mass spectra were run on a Varian MAT-212 instrument with ionization energy 70 eV. ^{13}C NMR spectra were recorded on a Bruker WH-90 instrument with acetone-d_6 as solvent.

2-Chloro(bromo)-3,4-dicyanopyridines (IIIa-f). A 0.05-mole amount of tetracyanoethylated ketone in 50-70 ml of hydrochloric or hydrobromic acid was agitated in a closed flask with a high-power magnetic stirrer at 20°C continuously for 15-20 h. The color of the reaction mass changed several times during this period. On completion of the reaction (TLC) 200 ml of water was added, the crystalline products were filtered off, washed thoroughly with water, and recrystallized from isopropanol with hot filtration required.

2-Chloro-2-methyl-4,5-dicyano-6-amino-2-pyran (VI). A 5-g (0.026 mole) sample of 4,4,5,5-tetra-cyano-2-pentanone was suspended in 20 ml of diethyl ether and gaseous hydrogen chloride was bubbled through with agitation. After 35 min the reaction mass became homogeneous, there was then the formation of a white precipitate, which was filtered off and dried. The product was recrystallized from an acetone–hexane mixture. Yield 4.5 g (86%), mp 202-204°C. Found: C 49.2; H 3.3; N 21.3%. $C_8H_9ClN_3O$. Calculated: C 49.1; H 3.0; N 21.5%.

2-Chloro-6-methyl-3,4-dicyanopyridine from 6-Methyl-3,4-dicyano-(1H)-pyridone. A mixture of 3 g of 6-methyl-3,4-dicyano-2(1H)-pyridone, 10 g of phosphorus oxychloride, 50 ml of chlorobenzene, and 1.5 g of dimethylformamide was agitated for 5 h at the boiling point until the pyridone had disappeared (TLC). The reaction mass was cooled, chlorobenzene and excess phosphorus oxychloride were distilled off under vacuum, and the residue was treated with water. A 19-g amount of a dark crystalline substance was obtained, from which was isolated 0.28 g of chloropyridine IIIa after repeated recrystallization from isopropanol. Hydrolysis of chloropyridine to imide V was carried out under the conditions given in [10].

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1-(FLUOREN-2-YL)-2-(2-AZAFLUOREN-3-YL)ETHENE AND 1-(FLUOREN-2-YL)-2-(2H,2-METHYLINDENO[2,3-c]PYRIDINE)ETHENE

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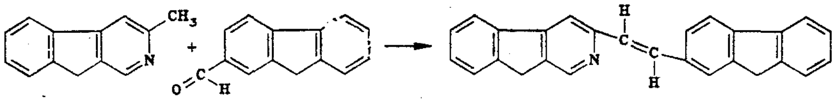
Condensation of 3-methyl-2-azafluorene with 2-formylfluorene results in the formation of a compound containing a polyconjugated system and two acidic CH centers, namely, 1-(fluoren-2-yl)-2-(2-azafluoren-3-yl)ethene. The conversions of this compound upon treatment with alkali have been studied by electronic absorption spectroscopy. The methyl iodide derivative of this base was used as an intermediate in the preparation of a pseudo-azulene, 1-(fluoren-2-yl)-2-(2H, 2-methylindeno[2,3-c]pyridine)ethene.

In order to prepare polyconjugated systems containing fluorene and azafluorene fragments, and to study their optical properties, we have carried out the condensation of 3-methyl-2-azafluorene [1] with 2-formylfluorene. 1-(Fluoren-2-yl)-2-(2-azafluoren-3-yl)ethene (I) was obtained in 30% yield and isolated chromatographically in pure form as light yellow crystals, mp 190-192°C. The IR spectrum of compound (I) exhibited the C=C stretching vibration and out-of-plane deformation bands at 1675 and 965 cm^{-1}, respectively, which confirms the trans-configuration about the double bond. In the electronic absorption spectrum of compound (I) (Fig. 1a), the long-wavelength band at λ_{max} 346 nm (log ε 4.42) is shifted bathochromically by 46 nm relative to the corresponding band in 3-methyl-2-azafluorene (Fig. 2, 1), which may be explained in terms of an increase in the degree of conjugation in compound (I).



I

Compound (I) is a di-CH-acid (active methylene groups of the fluorenyl and azafluorenyl fragments), and we thus investigated the conversions of this compound upon treatment with

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