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SYNTHESIS OF 2-AZASTILBENE DERIVATIVES WITH INTRAMOLECULAR CHARGE TRANSFER

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The condensation reaction of 2-cyanomethyl-5-nitropyridine with aromatic aldehydes has been carried out with the aim of preparing 2-azastilbene derivatives having intramolecular charge transfer. The yield of the condensation products can be increased if the reaction is carried out in the medium used for obtaining the starting 2-cyanomethyl-5-nitropyridine without separating or purifying it. The electronic absorption spectra of the compounds show a charge-transfer band, the energy of which increases and the intensity falls with lowering of the electron-donor properties of the substituent in the 4-position. Introduction of the heteroatom into the acceptor part when changing from the stilbene to the 2-azastilbene system is accompanied by a decrease in the energy and increase in the intensity of the charge-transfer electronic transition.

Keywords: pyridine derivatives, intramolecular charge transfer.

A comprehensive theoretical and experimental study of non-linear optical effects in molecules and materials [1-3] has revealed a basic dependence of the change in hyperpolarizibility with the structure and has led to the synthesis of a series of novel chromophoric fragments and compounds. Despite this significant progress as a whole, it should be recognized that the range of compounds studied remains rather narrow, despite the potential of broadening it. The aim of our work is the synthesis of novel compounds with intramolecular charge transfer involving the use of a heterocyclic acceptor part.

The synthesis of 2-cyanomethyl-5-nitropyridine (**8**) [4] and its condensation reaction were carried out according to the scheme given below. This includes the successive introduction of a nitro group at position 5 and halogen at position 2 into the pyridine system with subsequent construction of a carbon chain at position 2 of the 2-chloro-5-nitropyridine obtained. The nitration of 2-aminopyridine gave a mixture of the two isomeric 3-nitro- (**2a**) and 2-amino-5-nitropyridines (**2b**) in the ratio 1:4. In contrast to work in [5] in which a mixture of the isomers **2a** and **2b** was used to prepare compound **3**, we have separated this mixture by the method reported in [6] and it has enabled us to increase the yield of the 2-hydroxy-5-nitropyridine (**3**).

The synthesis of compound **6** and its hydrolysis and decarboxylation in the reaction mixture without separation of the intermediate compound **7** was carried out according to the data in [4]. Compound **8** was purified using column chromatography. Its spectroscopic parameters are given in Table 1. Compound **8** has a low melting point and is difficult to crystallize and this lowers the yield of pure material.

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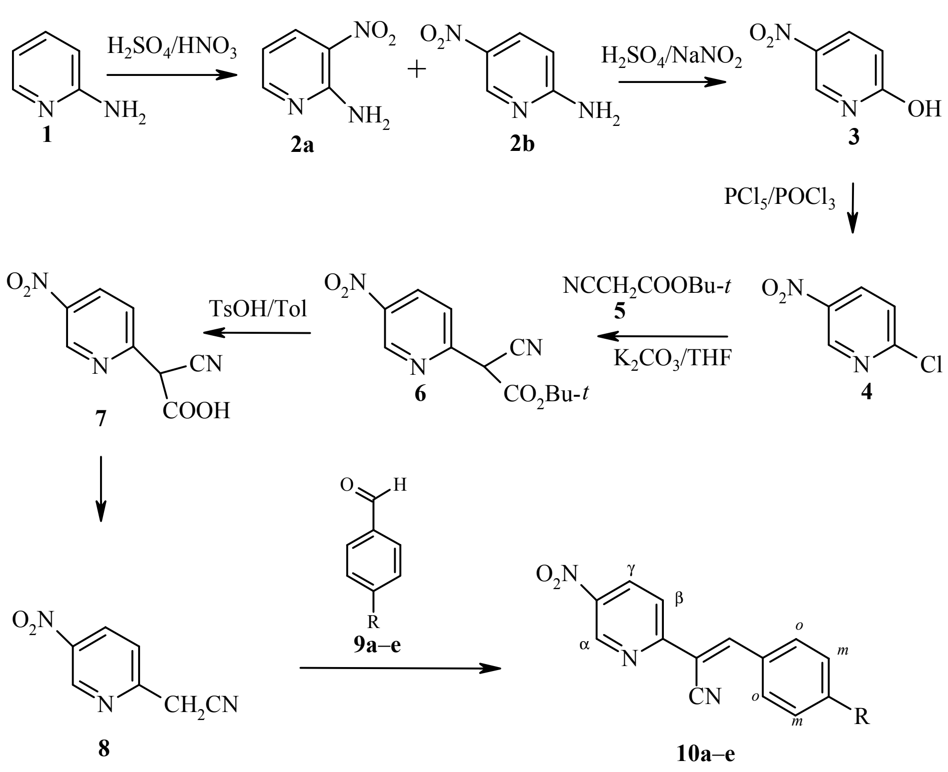

9, **10 a** R = NMe_2, **b** R = OMe, **c** R = Cl, **d** R = H, **e** R = CN

The condensation reaction of compound **8** with different *para*-substituted benzaldehydes **9a-e** gave the 3-(4-R-phenyl)-2-(5-nitro-2-pyridyl)acrylonitriles **10a-e** (see Table 1).

Examination of the solubility of the condensation products showed that compounds **10a-e** are poorly soluble in both polar and non-polar solvents, hence the condensation reaction was carried out without separation of compound **8** from its reaction medium. This led to better yields of the condensation products (see Table 1).

Compounds **10a-e** constitute a donor-acceptor system in which the donor fragment with a changing electron donor ability is bound to a constant electron-acceptor fragment (the 2-(5-nitropyridine)). In the electronic absorption spectra of compounds of this type an absorption band due to intramolecular charge transfer should be observed. The energy of the charge-transfer transition depends on the ionization potential of the donor fragment, i.e. it should correlate with the σ^+-constant for the R substituent.

As might have been expected, intense and non-overlapped long-wavelength absorption bands due to intramolecular charge transfer are observed only in the experimental spectra of compound **10a** (479 nm, 78,400 l/mol·cm) and **10b** (379 nm, 20,200 l/mol·cm). Their intensity rapidly falls with the increase in transfer energy. The long wavelength absorption bands in the spectra of compounds **10c-e** are overlapped by absorption bands at 260 nm and are markedly broadened (half width 7000 cm^{-1}) when compared with the long wavelength absorption band in the spectrum of **10a** (half width 4600 cm^{-1}). Hence, since the electronic spectrum of **10**a shows bands at 280, 300, and 320 nm, it is quite possible that in the case of compounds **10c** and **10d** the charge-transfer bands are overlapped also by the absorption band at 320 nm. All of the experimentally determined band maxima in the spectra of compounds **10c** and **10d** may be considered, with little error, as characteristic of charge-transfer bands since their intensity is decreased when compared with that of the corresponding band in **10b**. The maximum intensity long-wavelength band (327 nm) of compound **10e** is close to that of compound **10b** despite the appreciable increase in transition energy. To all appearances, the charge-transfer band in this case is fully overlapped by the absorption of the other type and the observed band maximum does not characterize the charge transfer energy.

TABLE 1. 5-Nitro-2-pyridylacetonitrile and Its Condensation Products with Aromatic Aldehydes

Compound	Empirical formula	Found, % / Calculated, %		mp, °C	UV spectrum		IR spectrum, ν_{CN}, cm^{-1}	^{1}H NMR spectrum, δ, ppm, *J* (Hz)	Yield, %
		C	H		λ_{max}, nm	log ε			
8	$C_7H_5N_3O_2$	51.26 51.54	3.04 3.09	66			2252	4.00 (2H, s, CH_2); 7.61 (1H, d, *J* = 9, β-H); 8.48 (1H, dd, *J* = 9, *J* = 3, γ-H); 9.33 (1H, d, *J* = 3, α-H)	51
10a	$C_{14}H_{14}N_4O_2$	61.95 62.21	5.13 5.22	225-226	479	4.3	2204	3.07 (6H, s, NMe_2); 6.67 (2H, d, *m*-H); 7.69 (1H, d, *J* = 8, β-H); 7.96 (2H, d, *o*-H); 8.40 (1H, dd, *J* = 8, *J* = 3, γ -H); 8.44 (1H, s, =CH); 9.29 (1H, d, *J* = 3, α-H)	90
10b	$C_{15}H_{11}N_3O_3$	64.16 64.05	4.02 3.94	173-174	379	4.3	2212	3.84 (3H, s, OMe); 6.96 (2H, d, *J* = 9.5, *m*-H); 7.81 (1H, d, *J* = 9, β-H); 8.00 (2H, d, *J* = 9.5, *o*-H); 8.48 (1H, dd, *J* = 9, *J* = 3, γ-H); 8.54 (1H, s, =CH); 9.33 (1H, d, *J* = 3, α-H)	67
10c	$C_{14}H_8ClN_4O_2$	56.17 56.11	2.65 2.69	182-183	339	4.2	2216	7.46 (2H, d, *J* = 9, *m*-H); 7.89 (1H, d, *J* = 9, β-H); 7.96 (2H, d, *J* = 9, *o*-H); 8.53 (1H, dd, *J* = 9, *J* = 3, γ-H); 8.60 (1H, s, =CH); 9.39 (1H, d, *J* = 3, α-H)	56
10d	$C_{14}H_9N_3O_2$	66.71 66.93	3.53 3.61	161-62	335	4.0	2232	7.48 (3H, m, Ph); 7.87 (1H, d, *J* = 10, β-H); 7.98 (2H, m, Ph); 8.50 (1H, dd, *J* = 10, *J* = 2, γ-H); 8.62 (1H, s, =CH); 9.37 (1H, d, *J* = 2, α-H)	24
10e	$C_{15}H_8N_4O_2$	65.03 65.22	2.78 2.92	232-233	334	4.3	2228	7.76 (2H, d, *m*-H); 7.95 (1H, d, *J* = 9, β-H); 8.08 (2H, d, *o*-H); 8.58 (1H, dd, *J* = 9, *J* = 3, γ-H); 8.67 (1H, s, =CH); 9.40 (1H, d, *J* = 3, α-H)	71

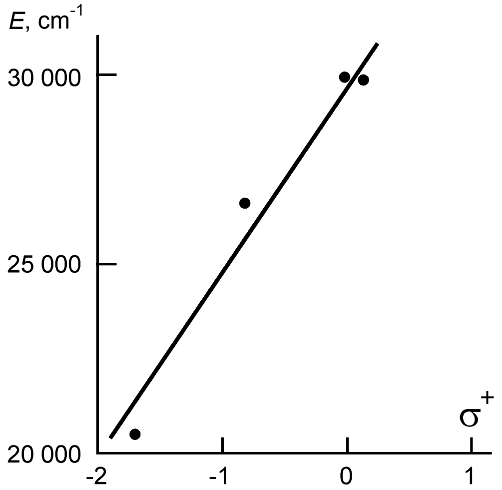

Fig. 1. Dependence of the energy of the long-wavelength transition (E) for compounds **10a-e** on the substituent σ^+-constant.

As seen in Fig. 1, the energy of the long-wavelength transitions of compounds **10a-e** do, in fact, correlate with the substituent σ^+-constant and this confirms the proposals presented above. Comparison of the parameters for compound **10a** and the corresponding stilbene (446 nm, 30,500 l/mol·cm) shows that the introduction of the heteroatom is accompanied by a marked bathochromic shift and increase in band intensity with charge transfer.

EXPERIMENTAL

IR spectra were obtained on a Specord 75-IR spectrometer using paraffin oil and hexachlorobutadiene. UV Spectra were measured on a Specord UV-vis spectrometer for ethanol solutions. ^{1}H NMR spectra were obtained on a Bruker WH-90/DS spectrometer (90 MHz) for solutions in $CDCl_3$ with TMS internal standard. The purity of the synthesized compounds and monitoring of the reaction course was achieved using TLC on Silufol UV-254 plates with the system benzene–ethyl acetate (10:1). The spectroscopic parameters for compounds **8, 10a-e** are given in Table 1.

2-Amino-5-nitropyridine (2b) [7]. 2-Aminopyridine (25.3 g, 0.27 mol) (**1**) was dissolved in conc. H_2SO_4 (50 ml) with constant stirring and maintenance of the temperature below 20°C. The mixture was cooled to 5-10°C and a mixture of conc. H_2SO_4 (20 ml) and 72% HNO_3 (d = 1.42, 20 ml) was added gradually dropwise with the temperature not exceeding 20°C. The reaction mixture obtained was placed on a water bath thermostatted to 46-48°C. An exothermic nitramine rearrangement reaction began at 43-45°C. The reaction mixture was held at this temperature for 12-16 h (until gas bubbling had fully ceased). In the course of the nitramine rearrangement the reaction mixture changed color from light-brown to dark-claret. The mixture obtained was poured onto ice and carefully neutralized using ammonia (200 ml). At pH 5.0-5.5 there appeared a dark-brown precipitate which lightened at pH 5.5-6.0. The filtered precipitate was a mixture of two isomers. For separation of the isomers [5], the mixture was suspended in 50 parts of water and conc. HCl was added to full solution of the precipitate. The dark claret solution was then filtered to remove an oily admixture. The obtained filtrate was taken to pH 4-5 by the addition of 50% NaOH solution and a dark brown precipitate of compound **2b** was formed. When the remaining filtrate was taken to pH 9 a light yellow precipitate of the aminopyridine **2a** appeared. Yield 20.3 g (80%); mp 188°C.

2-Hydroxy-5-nitropyridine (3) [6]. Compound **2b** (23.1 g, 0.166 mol) was dissolved in conc. H_2SO_4 (24.9 ml) and water (358 ml). The solution obtained was filtered, the filtrate cooled to +2-0°C, and ice (89 g) was added with vigorous stirring. A solution of $NaNO_2$ (12.8 g, 0.186 mol) in water (40 ml) was added dropwise with vigorous stirring and cooling. After the addition of all of the $NaNO_2$ the stirring was continued for a further 20-30 min and it was then raised to room temperature. A light brown precipitate was formed which was filtered off. The filtrate was evaporated by two thirds and a light-yellow precipitate of compound **3** was formed. Yield 17.74 g (77%); mp 182-183°C (water).

2-Chloro-5-nitropyridine (4) [6]. $POCl_3$ was added to a mixture of PCl_5 (35 g, 0.168 mol) and compound **3** (11.9 g, 0.085 mol) such as just to cover the mixture and held for 3 h at 110°C. The $POCl_3$ was then distilled of using a water pump vacuum. The residue was poured into water (144 ml). The light brown precipitate was filtered off. Yield 7.9 g (66%); mp 106-107°C (alcohol).

5-Nitro-2-pyridylacetonitrile (8) [4]. A mixture of *tert*-butylcyanoacetate (**5**) (13 ml, 0.090 mol), K_2CO_3 (20.7 g, 0.150 mol) and compound **4** (9.51 g, 0.060 mol) was refluxed in THF (50 ml) for 24 h, after which the THF was distilled off. The residue was poured into a mixture of water (100 ml) and CH_2Cl_2 (100 ml). The aqueous layer was acidified with conc. HCl to pH 1. The organic phase was separated, dried over $MgSO_4$, and evaporated. The orange oil produced was dissolved in toluene (150 ml) and *p*-TsOH (1 g) was added. The reaction mixture was then refluxed for 2 h. A black precipitate was produced during the reflux. The solution was decanted and the precipitate was washed with hot toluene (2 × 50 ml). The combined organic phases were washed with saturated $NaHCO_3$ solution (100 ml), dried over $MgSO_4$, and two thirds of the toluene distilled off. Cooling gave claret crystals of compound **8**. Yield 4.95 g (51%); mp 66°C.

In the subsequent reaction the solution of 5-nitro-2-pyridylacetonitrile in toluene was used without the separation of compound **8** in the condensation reactions.

3-(4-Alkylphenyl)-2-(5-nitro-2-pyridyl)acrylonitriles (10a-e). (General Method). The aldehyde **9a-e** (0.9 mmol), piperidine (1 ml), and acetic acid (1.5 ml) were added to 6 ml of a toluene solution containing compound **8** (~0.9 mmol). The reaction mixture was heated using a Dean and Stark apparatus. When the phase interface became visible, the heating was stopped. Cooling gave the precipitates of compounds **10a-e**.

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