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SYNTHESIS OF 5-NITROPYRIDIN-2-YLAZO PUSH-PULL DERIVATIVES

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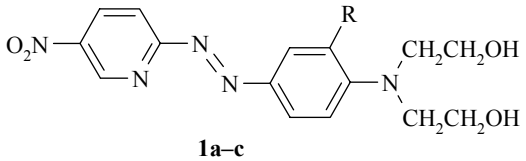
A practical method has been devised for the synthesis of previously unknown push-pull azochromophores with 5-nitropyridin-2-yl acceptor moiety from 2-amino-5-nitro-1-oxypyridine.

Keywords: azo compounds, chromophore, pyridine.

Azo compounds with electron-donating substituents on one side of the molecule and electron-withdrawing groups on the other side, or the so-called push-pull chromophores, are of lasting interest in the field of nonlinear optical materials [1]. Recently, increasing interest has been paid to heterocycle-based push-pull chromophores [2]. Incorporation of π-deficient pyridine conserves the photoactivity of azobenzene and additionally provides the capability of self-assembly through H-bonding or metal coordination [3]. Although a number of investigations have been reported in the literature on pyridin-4-ylazo dyes [3-6], only a few pyridin-2-ylazo dyes have been synthesized [7, 8], and to our knowledge no reports exist on 5-nitropyridin-2-yl-azo push-pull chromophore.

The aim of the present study was to synthesize 5-nitropyridin-2-ylazobenzene derivatives **1a-c** bearing in the electron-releasing part of the molecule a diethanolamino group [$N(CH_2CH_2OH)_2$] and an octyloxy group that efficiently, as our previous research shows [9], improve solubility and are expected to avoid the formation of undesirable centrosymmetric structures in the solid state.



1a–c

a R = H, **b** R = OMe, **c** R = OC_8H_{17}

The usual diazotization-coupling reaction could not be used because of the impossibility to obtain the diazonium salt from 5-nitropyridin-2-ylamine [7]. Three other methods for the synthesis of pyridin-2-ylazo compounds are available: (1) the reaction of pyridin-2-amine with nitrosobenzene in the presence of a strong base (50% NaOH, Bu_4NOH) [10], (2) oxidation of pyridin-2-ylphenylhydrazine [11], and (3) condensation of 2-nitrosopyridine with substituted anilines catalyzed by AcOH [12]. The first two methods were not satisfactory for our purposes owing to the instability of 2-amino-5-nitropyridine (**2**) in concentrated NaOH solutions and

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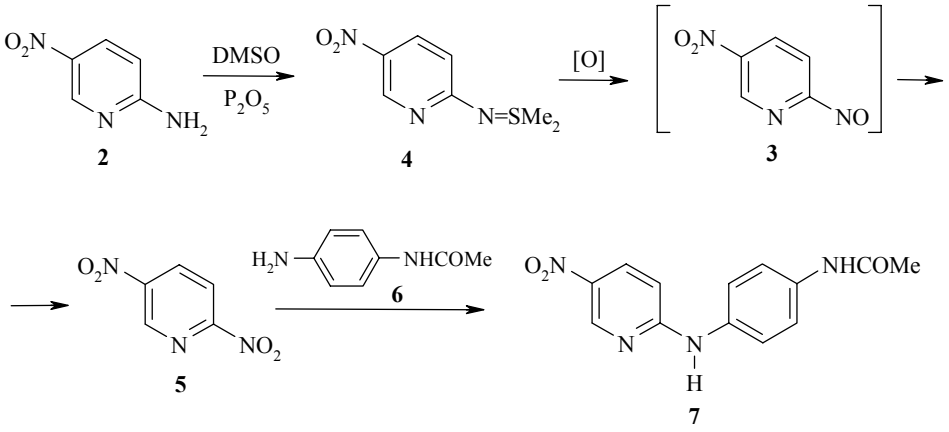
because feasible substituents in the phenyl moiety of hydrazine molecule were limited merely to electron acceptors. To apply the third method, 2-nitroso-5-nitropyridine (**3**) was required, which was unknown. The synthesis is presented in Scheme 1.

Scheme 1



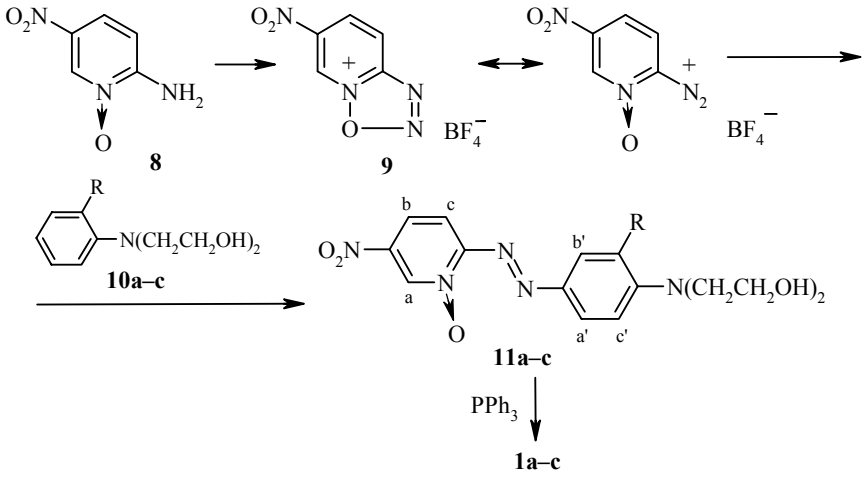
Previously [13] pyridin-2-amine was converted to 2-nitrosopyridine *via* S,S-dimethylsulfylimine. 2 Dimethylsulfylimino-5-nitropyridine (**4**) can be conveniently prepared from compound **2**, DMSO, and P_2O_5 according to [14]. However, oxidation of compound **4** with *m*-chloroperbenzoic acid in methylene chloride at 0°C, i.e. under conditions used for obtaining 2-nitrosopyridine in 44% yield [13], did not proceed. After the temperature was allowed to rise to 20°C, oxidation proceeded, and a yellow crude product **3** was obtained, that, unfortunately, was unstable in the solution and unlike 2-nitrosopyridine did not react with N-acetylphenylene-1,4-diamine (**6**) in the presence of AcOH. When oxidation of compound **4** was conducted in methanol, 2,5-dinitropyridine (**5**) was obtained in 78% yield. This procedure for the synthesis of dinitro compound **5** seems to have advantages over the previous [14], which needs 83% H_2O_2, $(CF_3CO)_2O$, and chromatographic purification. Compound **5** reacted with aniline **6** in AcOH at room temperature and gave the product of nucleophilic displacement of the nitro group, N-[4-(5-nitropyridin-2-ylamino)phenyl]acetamide (**7**) [15] in 85% yield.

As seems likely from these experiments, the procedure [13] elaborated for the direct synthesis of unsubstituted pyridin-2-ylazo compounds, cannot be used for the preparation of azopyridines substituted with strong electron-withdrawing groups in the pyridine moiety: nitroso compound **3** proved to be too unstable to be isolated and a nucleophilic center is expected on α-C rather than the nitrogen atom of the nitroso group.

Further we have investigated the possibility to obtain compound **1** from 2-amino-5-nitropyridine 1-oxide (**8**) by diazotization-coupling with subsequent elimination of the oxygen atom from the pyridine nitrogen according to Scheme 2.

Although generation of diazonium salts from pyridin-2-amine 1-oxide occurs in high yields [16], introduction of the nitro group is expected to substantially lower the stability of diazonium salt **9** promoting substitution with N_2 elimination rather than coupling reaction. The only preparation of azo dye from compound **8** has been recorded in the patent literature [17]: diazotization was performed in H_3PO_4 at -10°C followed by coupling with substituted anilines in buffered aqueous medium (AcONa/AcOH); yields were not given. All our attempts to use this method for the synthesis of compounds **11a–c** were unsuccessful; the yields of azo dyes did not exceed 1%. By examining various combinations of acid for diazotization and solvents and bases for coupling, the best procedure was found: diazonium salt **9** generated in tetrafluoroboric acid at -15 to -20°C and coupling with substituted anilines **10a–c** performed in pyridine solution at the same temperature. Under these conditions the yields are moderate and the azo compounds **11a–c** prepared do not need chromatographic purification. Unreacted anilines **10a–c** can be washed off by diethyl ether.

Scheme 2



a R = H, **b** R = OMe, **c** R = OC_8H_{17}

Azo compounds **11a-c** were obtained as dark blue powders or crystals with golden luster; all are easily soluble in ethanol, **11a**,**b** also in water, but the solubility of compounds **11a-c** in nonpolar solvents, for example toluene, was less than 10^{-6} M. Compounds **11a–c** exhibit two absorption bands (Table 1) near 250 and 600 nm; the latter shows a strong positive solvatochromism (λ_{max} for **11c** in toluene 552 nm).

The long-wave absorption band for compound **11c,** in comparison with push-pull chromophore 4-[N,N-bis-(hydroxyethyl)amino]-4'-nitro-3-octyloxyazobenzene (**12a**) with the same donor unit, is blue shifted by 120 nm (in ethanol λ_{max} of compound **12a** 488 nm [9]) and is very close to **12b** (λ_{max} in ethanol 610 nm [9]).

Therefore, incorporation of the N–O function having strong push-pull properties [18] in *p*-nitrophenyl *ortho*-position to the N=N group substantially enhances the acceptor capacity of the electron-withdrawing moiety of the chromophore and the effect of such action is equal to introduction of two cyano groups in the acceptor moiety.

TABLE 1. Data of elemental analysis, melting points, and UV-vis spectra of azo compounds **1a-c** and **11a-c**

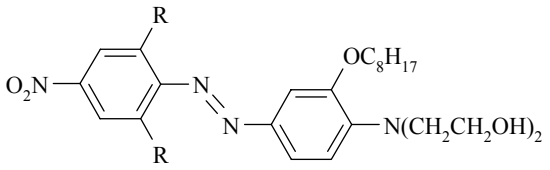
Compound	Empirical formula	Found, % / Calculated, %			mp, °C*	λ_{max}, nm (lg ε), in ethanol	
		C	H	N			
1a	$C_{15}H_{17}N_5O_4$	53.90 / 54.38	5.26 / 5.17	20.85 / 21.14	213-215	289 (3.86)	513 (4.48)
1b	$C_{16}H_{19}N_5O_5$	52.90 / 53.18	5.14 / 5.30	19.08 / 19.38	195-200	288 (3.99)	528 (4.47)
1c	$C_{23}H_{33}N_5O_5$	60.21 / 60.11	7.23 / 7.24	15.20 / 15.24	116-118	290 (3.88)	532 (4.43)
11a	$C_{15}H_{17}N_5O_5$	51.76 / 51.87	5.42 / 4.93	19.83 / 20.15	217-220	268 (4.22)	578 (4.80)
11b	$C_{16}H_{19}N_5O_6$	50.45 / 50.93	5.06 / 5.08	18.32 / 18.56	193-195	241 (4.23)	604 (4.79)
11c	$C_{23}H_{33}N_5O_6$	57.72 / 58.09	6.95 / 6.99	14.55 / 14.73	174-175	240 (4.30)	607 (4.78)

* All azo compounds that are a mixture of *E*/*Z*-isomer do not have sharp mp, temperatures of obvious decomposition of compounds are given.

TABLE 2.[1]H NMR Spectra Characteristics of Synthesized azo compounds **1a-c** and **11a-c**

Com-pound	Chemical shifts of protons, δ, ppm (*J*, Hz)*							
	H_a	H_b	H_c	$H_{a'}$	$H_{b'}$	$H_{c'}$	$H_{d'}$	Other protons
1a	9.20 (s)	8.35 (d, $J_{b,c}$ = 8.8)	7.68 (d, $J_{c,b}$ = 8.8)	7.74 (d, $J_{a',c'}$ = 9.3)	7.74 (d, $J_{b',d'}$ = 8.7)	6.65 (d, $J_{c',a'}$ = 9.3)	6.65 (d, $J_{d',b'}$ = 8.7)	4.62 (2H, br.); 3.61 (4H, m); 3.49 (4H, m)
1b	9.51 (d, $J_{a,b}$ = 2.7)	8.62 (dd, $J_{b,c}$ = 8.8, $J_{b,a}$ = 2.7)	7.92 (d, $J_{c,b}$ = 8.8)	7.78 (dd, $J_{a',c'}$ = 8.2, $J_{a',b'}$ = 1.6)	7.63 (d, $J_{b',a'}$ = 1.6)	7.13 (d, $J_{c',a'}$ = 8.2)	—	3.94 (3H, s); 3.81 (4H, t, *J* = 4.9); 3.61 (4H, t, *J* = 4.9); 2.84 (2H, br.)
1c	9.51 (d, $J_{a,b}$ = 2.7)	8.61 (dd, $J_{b,c}$ = 8.8, $J_{b,a}$ = 2.7)	7.91 (d, $J_{c,b}$ = 8.8)	7.73 (dd, $J_{a',c'}$ = 8.2, $J_{a',b'}$ = 1.6)	7.61 (d, $J_{b',a'}$ = 1.6)	7.12 (d, $J_{c',a'}$ = 8.2)	—	4.09 (2H, t, *J* = 7.1); 3.82 (4H, t, *J* = 4.3); 3.63 (4H, t, *J* = 4.3); 2.94 (2H, br.); 1.86-1.29 (12H, m); 0.88 (3H, t, *J* = 6.5)
11a	9.04 (d, $J_{a,b}$ = 1.9)	8.10 (dd, $J_{b,c}$ = 9.7, $J_{b,a}$ = 1.9)	7.72 (d, $J_{c,b}$ = 9.7)	7.85 (d, $J_{a',c'}$ = 8.7)	7.85 (d, $J_{b',d'}$ = 9.3)	7.01 (d, $J_{c',a'}$ = 8.7)	7.01 (d, $J_{d',b'}$ = 9.3)	4.91 (2H, t, *J* = 4.9); 3.66 (8H, br.)
11b	9.10 (br.)	8.11 (br.)	7.74 (br.)	7.74 (br.)	7.45 (br.)	7.03 (br.)	—	4.8 (br.); 3.83 (3H, s); 3.62 (8H, br.)
11c	9.11 (d, $J_{a,b}$ = 1.9)	8.08 (dd, $J_{b,c}$ = 9.7, $J_{b,a}$ = 1.9)	7.72 (d, $J_{c,b}$ = 9.7)	7.62 (dd, $J_{a',c'}$ = 8.7, $J_{a',b'}$ = 1.9)	7.41(d, $J_{b',c'}$ = 1.9)	7.07 (d, $J_{c',a'}$ = 8.7)	—	4.81 (2H, t, *J* = 4.9); 4.01 (2H, t, *J* = 6.8); 3.67 (8H, m); 1.76 (2H, br.); 1.28 (10H, br.); 0.86 (3H, t, *J* = 6.8)

* Compounds **1a-c** - in $CDCl_3$, **11a-c** – in DMSO-d_6.



12a,b

a R = H, **b** R = CN

Compounds **11a-c** were treated with triphenylphosphine under catalysis [19] of Mo(VI) diethyldithiocarbamate complex, $MoO_2[Et_2NCS_2]_2$, and novel pyridin-2-ylazo dyes **1a-c** as dark red crystals were obtained in 65-80% yield. Their chemical and nonlinear optical properties are under investigation.

The data of elemental analysis, IR, NMR, and UV spectra of all compounds obtained were consistent with their structures (Tables 1, 2).

EXPERIMENTAL

The purity of all compounds was checked by TLC on Merck F_{254} silica plates. The spots were visualized when necessary in UV light and in iodine vapor. Chromatographic separations were carried out on silica gel (Merck, reinst) or basic alumina. Melting points were taken on a Stuart apparatus SMP 10, ^{1}H NMR spectra were obtained on a Varian Mercury BB 200 spectrometer (200 MHz) against TMS as an internal reference, and elemental analysis on a VARIO EL III CHNOS Elemental Analyzer. UV-vis spectra were recorded using the Perkin–Elmer UV-vis spectrometer Lambda 35.

2-Amino-5-nitropyridine 1-oxide (**8**) was obtained from 2-amino-5-nitropyridine by oxidation with *m*-chloroperbenzoic acid in acetone [20], N,N-bis(2-hydroxyethyl)-2-octyloxyaniline (**10c**) was prepared in accordance with [9], and $MoO_2(Et_2NCS_2)_2$ in the reaction of Na_2MoO_4 and Et_2NCS_2Na with HCl [21]. All other starting materials were purchased from Acros.

2,5-Dinitropyridine (**5**). To a suspension of 2-dimethylsulfylimino-5-nitropyridine (1.1 g, 5.5 mmol) in 15 ml of methanol *m*-chloroperbenzoic acid (2.5 g, 11 mmol) in 10 ml of methanol was added slowly within 30 min with stirring. Stirring was continued for additional 30 min, and then the mixture was refrigerated overnight at 0-5°C. The yellow precipitate was filtered off, washed with cold methanol, and dried. Yield 0.72 g (78%), mp 118-118.5°C (methanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.97 (1H, d, *J* = 1.9, H-6); 8.91 (1H, dd, *J* = 1.9, *J* = 9.2, H-4); 8.25 (1H, d, *J* = 9.2, H-3). Found, %: C 35.86; H 1.80; N 25.12. $C_5H_3N_3O_4$. Calculated, %: C 35.52; H 1.79; N 24.85.

N-[4-(5-Nitropyridin-2-ylamino)phenyl]acetamide (**7**). To compound **5** (0.1 g, 0.6 mmol) in AcOH + ethanol (10 ml, 3:2) N-acetylphenylene-1,4-diamine (**6**) (0.09 g, 0.6 mmol) was added with stirring. Stirring was continued for 2 h, and the resulting precipitate was filtered off and washed with ethanol. Yield 0.15 g (95%), mp 238-240°C (ethanol), ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 10.5 (1H, s, NH); 9.47 (1H, d, *J* = 2, H-6 Py); 8.78 (1H, dd, *J* = 2, *J* = 8.8, H-4 Py); 8.04-7.85 (5H, m, H-3 Py, Ph); 2.12 (3H, s, $COCH_3$). Found, %: C 57.76; H 4.62; N 20.73. $C_{13}H_{12}N_4O_3$. Calculated, %: C 57.35; H 4.44; N 20.58.

5-Nitropyridin-2-diazonium 1-oxide tetrafluoroborate (**9**). A solution of compound **8** (2 g, 12.9 mmol) in 16 ml HBF_4 was cooled to -15 to -20°C and $NaNO_2$ (0.88 g, 12.9 mmol) was added with stirring at such rate that the temperature was kept below -15°C (45 min). After the addition was complete, stirring was continued for 1 h at -15 to 20 °C. The yellow suspension was used for azocoupling.

Azo compounds 11a–c were synthesized according to the general procedure illustrated by the synthesis of 4-[N,N-bis(2-hydroxyethyl)amino]-1-(5-nitropyridin-2-yl- azo)-3-octyloxybenzene (**11c**). A suspension of

diazonium salt **9** was added dropwise within 1 h with intensive stirring to the previously cooled to -15°C solution of compound **10c** (4.0 g, 12.9 mmol) in pyridine (12 ml). Stirring was continued for 1 h, allowing the temperature to rise to 0°C. The dark blue reaction mixture was neutralized with a saturated solution of $NaHCO_3$, and the oily precipitate was separated by filtration and washed with diethyl ether. Yield 1.25 g (20%).

Azo compounds 1a–c were synthesized according to the general procedure illustrated by the synthesis of N-(2-hydroxyethyl)-2-[2-octyloxy-4-(5-nitropyridin-2-ylazo)- phenylamino]ethanol (**1c**). Acetone was used instead of $CHCl_3$ for obtaining compound **1a**, the mixture $CHCl_3$ + acetone (3:1) – for preparation of compound **1b**. To the suspension of compound **11c** (1.65 g, 3.45 mmol) in 146 ml of $CHCl_3$ triphenylphosphine (0.91 g, 3.45 mmol) and $MoO_2(Et_2NCS_2)_2$ (0.29 g, 0.70 mmol) were added and the mixture was stirred for 12 h. The solvent was evaporated and the crude product recrystallized from ethyl acetate. Yield 1 g (65%).

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