ELECTROPHILIC SUBSTITUTION IN N-ARYL-2-PYRAZOLINES: REACTIONS WITH 1,3-DITHIOLES

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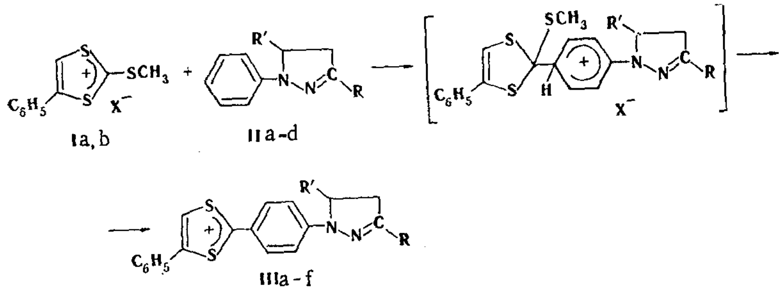
Dyes that absorb at 525-580 nm were obtained by the reaction of derivatives of 1,3-dithiolium iodide (or perchlorate) with 1-phenyl-3,5-di-R-2-pyrazolines, N,N-dimethylaniline, and benzaldehyde N-methylphenylhydrazone. It was demonstrated by alternative synthesis that the reaction takes place in the para position of the N-phenyl group. Dyes can be obtained in two steps from 2-dimethylamino-1,3-dithioles and activated aromatic compounds with subsequent oxidation of the intermediate leuco compounds with air oxygen.

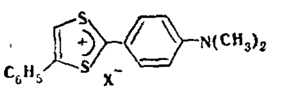
Convenient preparative methods for the production of 1,3-dithioles [1, 2] that have paved the way for their extensive use have been developed as a result of intensive research on the synthesis of tetrathiofulvalene, which is an effective π donor. It was recently shown [3, 4] that 1,3-dithiolium cations or 2-alkoxydithioles may react with various activated aromatic compounds (arylamines and phenols), during which they act as mild electrophiles. We directed our attention to this characteristic of 1,3-dithioles during a search for new highly polarized pyrazoline compounds [5].

In the present paper we set forth the results of a study of the reaction of 1,3-dithioles with arylpyrazolines, for which calculations [6] predict significant activation of the N-aryl substituent. Dyes IIIa-f were obtained in the reaction of 2-methylthio-4-phenyl-1,3-dithiolium salts (Ia, b) with 2-pyrazoline derivatives:

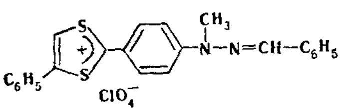


I a $X=ClO_4^-$; b $X=I^-$; II a $R=CH_3$, $R'=C_6H_5$; b $R=C_6H_5$, $R'=H$; c $R=R'=C_6H_5$; d $R=C_6H_5CH=CH$, $R'=C_6H_5$; III a $R=CH_3$, $R'=C_6H_5$, $X^-=I^-$; b $R=CH_3$, $R'=C_6H_5$, $X^-=ClO_4^-$; c $R=C_6H_5$, $R'=H$, $X^-=I^-$; d $R=R'=C_6H_5$, $X^-=C_6H_5$; e $R=R'=C_6H_5$, $X^-=ClO_4^-$; f $R=C_6H_5CH=CH$, $R'=C_6H_5$, $X^-=ClO_4^-$

In addition, model compounds IVa, b and V, respectively, were obtained by condensation of I with N,N-dimethylaniline and benzaldehyde N-methylphenylhydrazone:



IVa, b



V

a $X=I$; b $X=ClO_4$

Compounds III-V were characterized by the results of elementary analysis and data from the IR and UV spectra (Table 1). It follows from the results of analysis that the ratio of the reacting substances is 1:1 in all cases. The presence in the IR spectra of the compounds

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TABLE 1. Characteristics of the Dyes

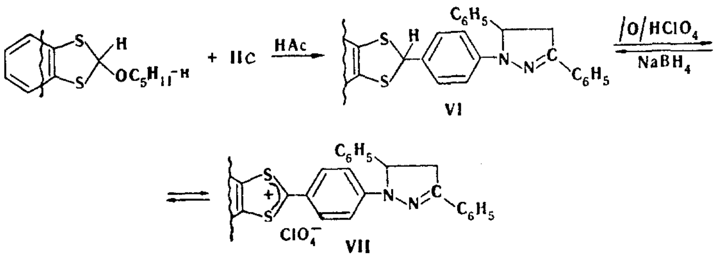
Compound	mp, °C	λ_{max}, nm ($\varepsilon \cdot 10^{-3}$), in CH_3CN	CH_3CN[a] + $NaBH_4$	$\nu_{C=N}$, cm^{-1}	N (S) found, %	Empirical formula	N (S) calc., %	Yield, %
IIIa	230—232	560 (47,1), 365 sh, 296 (11,6), 272 sh, 246 (28,3)	303	1594	5,0 (11,8)	$C_{25}H_{21}IN_2S_2$	5,2 (11,9)	81
IIIb	236—238	556 (56,3), 270 (12,8), 248 (16,8)	305	1593	5,4	$C_{25}H_{21}ClN_2O_4S_2$	5,5	85
IIIc	237—239	587 (42,4), 246 (21,4)	365	1595	5,2 (12,2)	$C_{24}H_{19}IN_2S_2$	5,3 (12,2)	67
IIId	218—219	576 (46,6), 364 (10,7), 296 sh, 244 (30,2)	360	1590	4,8 (10,5)	$C_{30}H_{23}IN_2S_2$	4,6 (10,6)	75
IIIe	228—230	573 (51,0), 305 sh, 244 (31,0)	361	1590	4,8	$C_{30}H_{23}ClN_2O_4S_2$	4,9	79
IIIf	255—257	580 (51,8), 305 sh, 248 (20,1)	380	1591	4,6	$C_{32}H_{25}ClN_2O_4S_2$	4,7	48
IVa	240—242	543 (40,4), 360 sh, 280 sh, 245 (16,0)	338	—	3,2 (15,0)	$C_{17}H_{16}INS_2$	3,3 (15,1)	87
IVb[b]	218—220	536 (48,1), 302 (11,4), 244 (21,4)	—	—	—	—	—	90
V	231—233	525 (3,7), 371 (16,1), 275 (12,8), 240 (25,7)	330	1589	5,7	$C_{23}H_{18}ClN_2O_4S_2$	5,8	84
VII	248—250	570 (48,3), 336 (6,5), 295 (6,5), 264 sh, 235 sh	364	1594	5,1	$C_{28}H_{21}ClN_2O_4S_2$	5,1	63
IX	251—253	577 (52,3), 333 (6,6), 298 (5,4)	365	1591	5,1	$C_{29}H_{23}ClN_2O_4S_2$	5,0	17

[a] These are the λ_{max} bands of the leuco forms. [b] According to the data in [15], this compound has mp 219-220°C.

obtained of characteristic absorption at 1590-1595 cm^{-1} ($\nu_{C=N}$) constitutes evidence for retention of the pyrazoline ring in IIIa-f or the azomethine group in V.

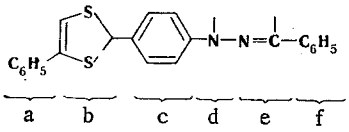
The related character of the electronic absorption spectra of the compounds obtained (Table 1) makes it possible to assume that electrophilic substitution takes place in the N-phenyl group in all cases. Both a quantum-chemical calculation of the ground state of 1,3-diphenylpyrazoline [6], according to which the electron density on the 1-phenyl ring is an order of magnitude higher than that on the 3-phenyl ring, and the literature data on the specificity of the related-in-character formylation [7, 8], diazo coupling [9], and bromination [10] of pyrazolines are in agreement with this assumption. These data make it possible to assume that the para position of the N-phenyl ring is the preferred site for attack by the 1,3-dithiole.

To obtain experimental evidence for this specificity of the process we investigated in greater detail the reaction of 2-amyloxybenzo-1,3-dithiole [11] with 1,3,5-triphenyl-2-pyrazoline (IIc), which takes place extremely smoothly but, in contrast to 2-alkylthio-1,3-dithiolium salts, stops at the step involving the formation of leuco compound VI.



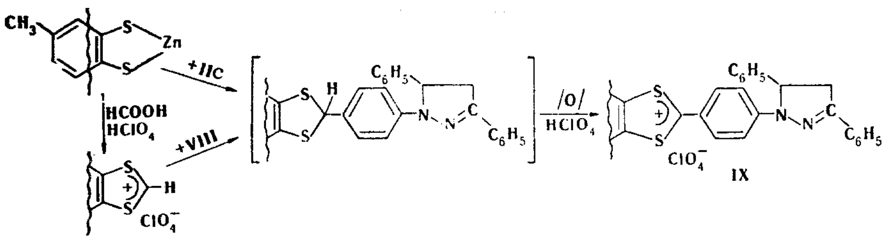
Compound VI undergoes quantitative oxidation to dye VII by air oxygen in the presence of $HClO_4$ (it was shown by means of the electronic absorption spectra that $NaBH_4$ reduces VII to VI in quantitative yield). The electronic absorption spectra of dyes VII and III-V are identical in character (Table 1), and this makes it possible to state that their structures are similar. Since VI is the benzodithioacetal of the known 1-(4-formylphenyl)-3,5-diphenyl-2-pyrazoline (VIII) [8], we attempted to cleave it by known methods (by means of chloramine T and mercury salts [12]). The expected VIII was detected among the products of hydrolysis in the presence of Hg^{2+} salts by thin-layer chromatography (TLC).

TABLE 2. Distribution of the Effective Charges in the Ground [$S_0(q_0)$] and First Excited [$S_1(q_1)$] States and Localization Numbers of the 0–1 Electronic Transition (L, %) in the Fragments:

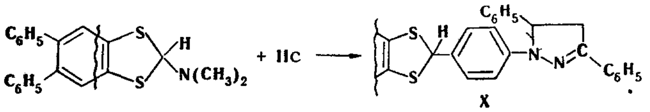


Compound	λ_{max}, nm		Property	Fragments of the molecule					
	theor.	exptl.		a	b	c	d	e	f
IV	521	543	q_0	+0,025	+0,586	−0,022	+0,411	—	—
			q_1	+0,181	+0,359	−0,068	+0,528	—	—
			L	11	55	26	8	—	—
IIIa	536	556	q_0	+0,025	+0,573	−0,022	+0,480	−0,246; +0,190	—
			q_1	+0,138	+0,345	−0,065	+0,653	−0,254; +0,183	—
			L	8	49	26	16	1	—
IIIc	548	575	q_0	+0,023	+0,552	−0,031	+0,488	−0,282; +0,192	+0,058
			q_1	+0,121	+0,238	−0,061	+0,742	−0,284; +0,171	+0,073
			L	7	44	27	19	2	1

We obtained a more reliable confirmation of the structures of the synthesized substances by synthesizing dye IX by two independent methods, viz., on the basis of the accessible zinc dithiolate and IIc and on the basis of VIII (the intermediates were not isolated):



The above-noted ability of alkoxydithioles to react with activated aromatic rings to give the same products as in the reactions with 1,3-dithiolium cations is due, in our opinion, to the fact that these compounds are capable of generating cations under the conditions of general acid catalysis. Similar behavior should have been expected for 2-dialkylamino- and 2-alkylthio-1,3-dithioles, since it is known [2] that, like alkoxydithioles, they are converted to 1,3-dithiolium salts in quantitative yields in an anhydrous medium in the presence of strong acids. One might have assumed that dialkylamino-1,3-dithioles, which in a number of cases are more accessible and stable during storage than their OR and SR analogs, would react with activated aromatic rings. In fact, 2-dimethylamino-4,5-diphenyl-1,3-dithiole reacts with IIc to give leuco compound X.



All of the synthesized dyes have low solubilities in solvents with low polarities. When they are dissolved in alcohols, they undergo solvolysis accompanied by decolorization of the solutions; the autonomous absorption of the corresponding arylpyrazoline fragments of the molecules (∿360 nm) appears distinctly in the electronic spectra of these solutions. Acetonitrile proved to be the most suitable solvent for the spectral measurements.

A characteristic feature of the absorption spectra of III-V, VII, and IX is the presence of an intense symmetrical absorption band with $\nu_{1/2}$ ∿ 2300 cm^{-1} at 500-600 nm. The weak absorption at 300-400 nm due to the small percentage of the dye base, which finally disappears when I^- is replaced by ClO_4^-, is retained in the spectra of the iodo derivatives.

To achieve a detailed analysis of the spectra obtained we calculated the electronic characteristics of the ground and excited states of a number of molecules by the MO LCAO self-consistent-field (SCF) configuration-interaction (CI) method in the Pariser—Parr—Pople (PPP) variant. The 0—1 electronic transition is of particular interest, since it basically determines the color of the dye. To evaluate the contributions of the individual fragments of the molecules to it we used the localization numbers proposed in [13]. It is apparent from Table 2 that although the electronic transition under discussion involves the entire molecule, it is primarily localized on the p-dithiolylaniline fragment; the remaining groups have only a slight perturbing effect. Shortening and lengthening the entire π system in the dyes both on the pyrazoline ring side (compare IIIe with IIIb and IV) and on the dithiole side (compare IIIe with VIII and IX) therefore have little effect on λ_{max} of the long-wave absorption (Table 1). At the same time, even the slight steric effects created by the introduction of a phenyl group in the 5 position of the pyrazoline ring, which have virtually no effect on the spectra of 1,3-diphenyl- and 1,3,5-triphenyl-2-pyrazolines (358 and 360 nm, respectively, in isooctane [14]), are manifested in the investigated dye molecules as a hypsochromic shift of the long-wave band (compare IIIc with IIId, Table 1). The spectral data obtained supplement the concept developed in [5] that the incorporation of a carbonium center as a powerful electron acceptor in conjugation with the N-phenyl group suppresses the crossconjugation character of the pyrazoline system.

In conclusion, we must make one remark. According to [15], compounds of the IV type are protonated in trifluoroacetic acid. In addition, the long-wave absorption of these compounds is identical in both CF_3COOH and CH_3COOH (535-540 nm [15]) and in an aprotic solvent, viz., acetonitrile (536 nm, Table 1). Moreover, the data in [16] clearly show that the absorption of the 2-(p-R-phenyl)dithiolium cation becomes regularly deeper as the electron-donor properties of the substituents in the aryl ring become more pronounced [for R = H, CH_3, OCH_3, and $N(CH_3)_2$ the λ_{max} values are 390, 402, 432, and 536 nm, respectively, in acetonitrile]. Thus this set of data constitutes unambiguous evidence for the erroneousness of the conclusion [15] that dye IV possibly undergoes protonation at the nitrogen atom in trifluoroacetic acid.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were measured with a UR-20 spectrometer. The UV spectra of solutions of the compounds in acetonitrile were recorded with a Specord UV-vis spectrophotometer. The electronic states of the III dye molecules were calculated by the MO LCAO self-consistent-field (SCF) configuration-interation (CI) method in the Pariser—Parr—Pople (PPP) variant with the standard set of parameters.

Reaction of the 2-Methylthio-4-phenyl-1,3-dithiolium Ion with N-Phenylpyrazolines. A 0.2-mmole sample of Ia or Ib was dissolved in 20 ml of glacial acetic acid, 0.21 mmole of the corresponding pyrazoline IIa-g was added, and the solution was heated at 100°C for 30 min, after which it was allowed to stand at 20°C for 18 h. The resulting precipitate was separated, dried in air, and chromatographed with a column (on SiO_2, elution with $CHCl_3$).

Compounds IIIa-f were obtained by this method, while IVa, b and V, respectively, were obtained from N,N-dimethylaniline and benzaldehyde N-methylphenylhydrazone (see Table 1).

2-[4-(3,5-Diphenyl-2-pyrazolin-1-yl)phenyl]-4,5-benzo-1,3-dithiole (VI). This compound was obtained by the method presented above from 1 g (3.30 mmole) of IIc and 0.9 g (3.7 mmole) of 2-amyloxybenzo-1,3-dithiole [11]. To isolate the desired product the reaction mixture was poured into water, and the precipitate was separated and dried in air to give 1.25 g (86%) of VIII with mp 183-185°C (from ethyl acetate). IR spectrum: 1607 cm^{-1} (C=N). UV spectrum, λ_{max} (ε): 367 nm (28000). Found: N 6.3; S 14.3%. $C_{28}H_{18}N_2S_2$. Calculated: N 6.3; S 14.4%.

2-[4-(3,5-Diphenyl-2-pyrazol-1-yl)phenyl]-4,5-benzo-1,3-dithiolium Perchlorate (VII). A 0.3-g sample of leuco compound VI was dissolved in 30 ml of glacial acetic acid, 5 ml of 70% $HClO_4$ was added, and the solution was allowed to stand in an open beaker for 3-4 days. It was then poured into 200 ml of water, and the precipitate was separated, dried in air, and purified by chromatography with a column filled with SiO_2 (elution with $CHCl_3$) to give 0.23 g (63%) of VII (Table 1).

2-[4-(3,5-Diphenyl-2-pyrazolin-1-yl)phenyl]-4,5-(4-methylbenzo)-1,3-dithiolium Perchlorate (IX). A) A 0.2-g sample of crude zinc dithiolate was dissolved in 30 ml of glacial acetic acid, 3 ml of 70% $HClO_4$ and 0.3 g of VIIIc were added, and the resulting solution was heated at 100°C for 30 min, after which it was allowed to stand for 18 h. The solution was then poured into 200 ml of water, and the product was extracted with chloroform (three 50-ml portions). The extract was dried over $CaCl_2$ and evaporated, and the residue was chromatographed with a column filled with SiO_2 [elution with $CHCl_3$—C_2H_5OH (1:1)] to give 0.08 g of dye IX with mp 251-253°C (Table 1).

B) A mixture of 1 g of the zinc dithiolate and 5 ml of HCOOH was heated for 10 min, 3 ml of 70% $HClO_4$ was added, and heating was continued until the solid material dissolved completely. A 1.36-g sample of IIc was added, and the solution was refluxed for 20 min, after which it was allowed to stand for 12-18 h. The reaction mixture was then worked up as in method A to give 0.45 g (17%) of dye IX. No melting-point depression was observed for a mixture of samples of the products obtained by methods A and B.

2-[4-(3,5-Diphenyl-2-pyrazolin-1-yl)phenyl]-4,5-diphenyl-1,3-dithiole (X). This compound was obtained from 0.6 g (2.0 mmole) of 2-dimethylamino-4,5-diphenyl-1,3-dithiole [20] and 0.5 g (1.8 mmole) of IIc by the method used to prepare VI. Workup gave 0.68 g (74%) of a product with mp 183-185°C. IR spectrum: 1601 cm^{-1} (C=N). UV spectrum, λ_{max} (ε): 368 nm (30400). Found: N 5.0; S 11.6%. $C_{36}H_{28}N_2S_2$. Calculated: N 5.1; S 11.6%.

LITERATURE CITED

1. E. Campaigne and R. D. Hamilton, Quart. Rep. Sulfur Chem., 5, 275 (1970).
2. M. Narita and C. U. Pittman, Jr., Synthesis, No. 8, 489 (1976).
3. J. Nakayama, K. Fujiwara, and M. Hoshino, Bull. Chem. Soc. Jpn., 49, 3567 (1976).
4. J. Nakayama, Synthesis, No. 3, 171 (1975).
5. V. D. Orlov and A. I. Roberman, Dokl. Akad. Nauk SSSR, 246, 888 (1979).
6. V. D. Orlov, A. I. Roberman, A. I. Rybachenko, and V. F. Lavrushin, Khim. Geterotsikl. Soedin., No. 11, 1538 (1977).
7. A. F. Plue, U.S. Patent No. 2976295; Chem. Abstr., 55, 16569 (1961).
8. L. A. Kutulya, A. E. Shevchenko, and Yu. N. Surov, Khim. Geterotsikl. Soedin., No. 2, 250 (1975).
9. G. F. Duffin and J. D. Kendall, J. Chem. Soc., No. 1, 408 (1954).
10. L. Szucs and A. Bradlerova, Z. Chem., 15, 477 (1975).
11. J. Nakayama, Synthesis, No. 1, 38 (1975).
12. J. Degani and R. Fochi, J. Chem. Soc., Perkin Trans. I, No. 17, 1886 (1976).
13. A. V. Luzanov, A. A. Sukhorukov, and V. É. Umanskii, Teor. Éksp. Khim., 10, 456 (1974).
14. L. A. Kutulya, V. F. Morina, A. E. Shevchenko, and Yu. N. Surov, Zh. Prikl. Khim., 27, 76 (1977).
15. E. Campaigne and R. D. Hamilton, J. Org. Chem., 29, 1711 (1964).
16. K. Hirai, Tetrahedron, 27, 4003 (1971).
17. R. Zahradnik and R. Polak, Fundamentals of Quantum Chemistry [Russian translation], Mir, Moscow (1977), p. 230.
18. E. Faughanel, J. Prakt. Chem., 317, 123 (1975).
19. E. Campaigne and N. W. Jacobsen, J. Org. Chem., 29, 1703 (1964).
20. K. M. Pazdro and W. Polaczkowa, Rocz. Chem., 45, 811 (1971).