

TETRAZOLE DERIVATIVES.

26.* 2-ARYL-3-(p-DIMETHYLAMINOPHENYL)-5-PHENYL-TETRAZOLIUM

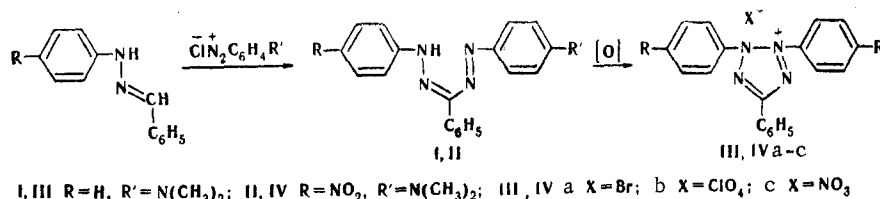
SALTS

V. P. Shchipanov

UDC 547.796.1

Deeply colored tetrazolium salts were obtained by oxidation of triarylformazans containing a p-dimethylamino group in the N-phenyl substituent with bromine or nitrous acid.

We have previously demonstrated that 2-(1- or 2-methyl-5-tetrazolyl)-3,5-diaryltetrazolium salts may have deep and intense coloration when strong electron-donor substituents are present in the phenyl group attached to the N₃ atom [2]. To ascertain the general principles of the coloration of tetrazolium salts, in the present research we have realized the synthesis of a number of triaryl-tetrazolium salts and have investigated their electronic spectra.



Tetrazolium bromides (IIIa, IVa) are obtained in good yields in the reaction of formazans I and II† with bromine in chloroform in the presence of an equimolar amount of pyridine. Tetrazolium perchlorates (IIIb and IVb) were obtained by oxidation of the formazans with nitrous acid in acetic acid by the method in [2] with the subsequent addition of perchloric acid. In the case of oxidation of formazan II by this method we were able to isolate an intermediate that proved to be a tetrazolium nitrate (IVc). The formation of nitrate IVc is, in all likelihood, due to the participation of air oxygen in the oxidation of nitrous acid or the products of its transformation. The tetrazolium salts, viz., the bromides and the nitrate, are readily soluble in water, while the perchlorates are only very slightly soluble in water, and this facilitates their isolation considerably.

A long-wave band at 440-475 nm is observed in the electronic spectra of the tetrazolium salts (Table 1). As compared with the analogous salts that contain hetaryl substituents attached to the N₂ atom [2-(1- or 2-methyl-5-tetrazolyl)-3-(p-dimethylaminophenyl)-5-phenyl-tetrazolium perchlorates (V, VI) with λ_{max}, nm (log ε): 530 (4.12) and 495 (4.09), respectively] [2], the triaryl-tetrazolium salts absorb in the shorter-wave region and with decreased intensity. With allowance for the principle of shifting of the long-wave band in the spectra of N-tetrazolyl-containing tetrazolium salts [2, 5] (a bathochromic shift occurs as the acceptor capacity of the substituent in the 2 or 5 position increases), the shorter-wave absorption of tetrazolium salts IIIa, b might have been associated with the lower degree of electron-acceptor character of the phenyl group attached to N₂ as compared with the 1- and 2-methyltetrazolyl substituents in tetrazolium salts V and VI. However, the p-nitrophenyl substituent in tetrazolium salts IVa, b is more of an acceptor group than the 1-methyltetrazolyl grouping. This follows from the lower basicity of p-nitroaniline as compared with the basicity of 1-methyl-5-aminotetrazole (pK_a 1.02 [6] and 1.82 [7], respec-

*See [1] for communication 25.

†The structure of formazans I and II presented in the scheme follows from the data in [3], in which it was shown that the hydrogen atom in unsymmetrical formazans is attached to the nitrogen atom bonded to the more electron-acceptor substituent.

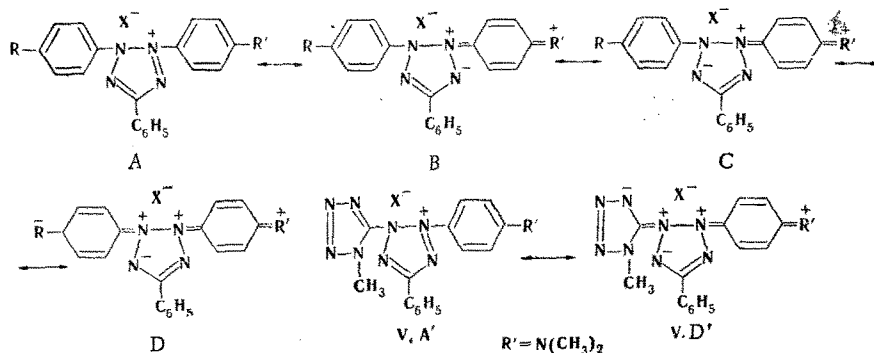
Lenin Komsomol Tyumen Industrial Institute, Tyumen 625036. Translated from *Khimiya Geterotsiklicheskikh Soedinenii*, No. 7, pp. 987-990, July, 1981. Original article submitted June 18, 1980.

TABLE 1. Properties of Formazans I and II and Tetrazolium Salts III and IV

Com- pound	mp, °C	Crystallization solvent	Electronic spectra in ethanol, λ_{\max} , nm (log ϵ)	Found, %			Calculated, %			Yield, %
				C	H	N	C	H	N	
I	190—191 ^a	Dimethylformamide— propanol (1:5)	268 (3,84), 546 (4,00), 578 (3,99)	64,7	5,0	21,7	64,9	5,2	21,6	83
II	203—204	Dimethylformamide— propanol (2:3)	230 (4,04), 438 (4,11), 606 (4,37)	55,3	4,8	15,2	55,0	5,3	15,3	98
III a	163—165	Water	244 (4,28), 270 (4,21), 440 (3,87)	57,4	4,7	15,6	57,1	4,6	15,8	81 ^b
III b	133—135	Propanol	243 (4,41), 268 (4,34), 440 (3,93)							71 ^b
IV a	177—179	Water	257 (4,00), 473 (3,40)	52,9	3,9	17,5	52,9	4,2	17,6	93 ^c
IV b	249—250 (dec.)	Water	257 (3,85), 475 (3,25)	51,6	4,0	17,1	51,8	3,9	17,3	76 ^b
IV c	217—218 (dec.)	Ethanol—water 1:2	259 (4,51), 472 (3,84)	56,2	4,4	21,7	56,1	4,3	21,8	92 ^b 98 ^c

^aAccording to [4], this compound had mp 192—193°C. ^bObtained by oxidation of the formazan with nitrous acid with the subsequent addition of HClO₄. ^cObtained by the addition of HClO₄ to a solution of the corresponding tetrazolium bromide.

tively). Let us note that the pK_{α} of aniline is 4.58 [6]. It is therefore apparent that allowance for some donor-acceptor properties of the substituents is not sufficient to explain the differences in the coloration of aryl- and hetaryl-containing tetrazolium salts.



One might have assumed that the long-wave band in the spectra of the colored tetrazolium salts is due to a polar transition associated with charge transfer in the excited state from the phenyl group attached to the N_3 atom not only to the central tetrazole ring [2, 5] but also to the aryl or hetaryl substituent attached to the N_2 atom. In this case the energy of the $A \rightarrow D$ transition with the formation of a quinoid structure for the phenyl group attached to the N_2 atom should be greater than, for example, the energy of the analogous $A' \rightarrow D'$ transition of tetrazolium salt V. This is due to the much greater difficulty involved in the formation of quinoid structures by benzene derivatives as compared with heterocycles [8, 9].

It should be noted that the contribution of structure D to the excited state with the development of significant positive charges on the N_2 and N_3 atoms that weaken the bond between these atoms explains the ability of tetrazolium salts to undergo reduction to formazans under the influence of light [10] or ultrasound [11].

The decrease in the intensity of the long-wave band in the spectra of triaryltetrazolium salts as compared with salts V and VI is due, in all likelihood, to a decrease in the coplanarity of the phenyl ring attached to the N_3 atom relative to the tetrazole ring because of steric hindrance experienced by the phenyl groups attached to the N_2 and N_3 atoms [12].

EXPERIMENTAL

The electronic spectra of solutions of the compounds in ethanol (from $1.25 \cdot 10^{-5}$ to 10^{-4} mole/liter) were recorded with a Specord UV-vis spectrophotometer. The melting points were determined with a PTP-1 apparatus.

1-(p-Dimethylaminophenyl)-3,5-diphenylformazan (I). A solution of the diazonium salt obtained from 4.68 g (20 mmole) of N,N -dimethyl-*p*-phenylenediamine sulfate, 3.5 ml of concentrated HCl, 60 ml of water, and 1.38 g (20 mmole) of NaNO_2 in 8 ml of water was added in the course of 30 min at 2°C to a solution of 3.92 g (20 mmole) of benzaldehyde phenylhydrazone in 150 ml of dimethylformamide (DMF)-ethanol (1:1) and 10 ml of a 45% solution of NaOH, and the resulting mixture was allowed to stand for 30 min. The precipitate was removed by filtration, washed with water and alcohol, and dried. Formazan II (Table 1) was similarly obtained.

2,5-Diphenyl-3-(p-dimethylaminophenyl)tetrazolium Bromide (IIIa). A 0.23-ml (2.9 mmole) sample of pyridine and 5.8 ml (2.9 mmole) of a solution of bromine in chloroform (0.5 mole/liter) were added to a solution of 0.9 g (2.6 mmole) of formazan I in 30 ml of chloroform, after which the flask was sealed tightly and maintained at 20°C for 18 h. The solvent was then evaporated *in vacuo*, and 60 ml of boiling water was added to the residue. The mixture was then filtered, and the filtrate was cooled to precipitate the tetrazolium salt. An additional amount of tetrazolium salt IIIa was isolated when the mother liquor was concentrated. Bromide IVa was similarly obtained (Table 1).

2-(p-Nitrophenyl)-3-(p-dimethylaminophenyl)-5-phenyltetrazolium Nitrate (IVc). A 0.86-ml (3.5 mmole) sample of a 25% solution of NaNO_2 was added at 10°C to a solution of 1 g (2.58 mmole) of formazan II in 80 ml of acetic acid, and the mixture was allowed to stand

for 1 h. It was then concentrated, and the residue was treated with 120 ml of boiling water. The aqueous mixture was filtered, and the filtrate was cooled to precipitate tetrazolium salt IVc.

Preparation of Tetrazolium Perchlorates (IIIb, IVb). A) Concentrated HClO_4 (~10 ml) was added dropwise to the hot aqueous solution obtained after oxidation of formazans I and II by the action of NaNO_2 in acetic acid (see the preceding synthesis) until the perchlorate had precipitated completely. The precipitate was removed by filtration and washed with water and alcohol (Table 1).

B) Concentrated HClO_4 was added to a saturated aqueous solution of the tetrazolium bromide (IIIa, IVa), and the precipitated perchlorate (IIIb, IVb) was isolated. The compounds obtained did not depress the melting points of the perchlorates synthesized by the preceding method.

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