TETRAZOLE DERIVATIVES.

24.* 1- AND 2-METHYLTETRAZOLYL-CONTAINING TETRAZOLIUM SALTS.

NATURE OF THE COLOR OF TETRAZOLIUM SALTS

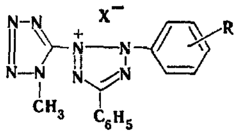
V. P. Shchipanov

UDC 547.796.1

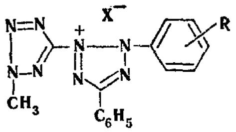
It is shown that the frequencies of the long-wave band in the electronic spectra of tetrazolium salts correlate with Brown's electrophilic σ^+ constants. The color of the tetrazolium salts is due to a polar transition associated with transfer of charge from the phenyl ring attached to the N_3 atom to the central tetrazole ring.

It has been previously established that 1-(5-tetrazolyl)-3,5-diarylformazans that contain strong electron-donor substituents are converted by oxidation to deeply colored tetrazolium salts with betaine structures [2, 3]. Among tetrazolium salts that are arylformazan derivatives, most of which are colorless or pale yellow [4], examples of brightly colored salts [4-6] and betaines [7] are also known. However, the reasons for their color have not been established.

To ascertain the nature and the extent to which this phenomenon occurs we investigated the electronic spectra of a number of tetrazolium salts that contain 1- and 2-methyltetrazolyl residues.



I a-h



II a-g

a R=H, b R=p-CH_3, c R=o-CH_3, d R=p-OH, e R=p-OCH_3, f, f' R=p-$N(CH_3)_2$, g R=p-NO_2, h R=m-NO_2; X=Cl (I a-c), ClO_4 (Id-h, IIa-g), picrate (If')

It was found that tetrazolium salts are obtained in good yields by oxidation of the corresponding formazans in acetic acid under the influence of nitrous acid. The subsequent addition of hydrochloric or perchloric acid leads to the isolation of tetrazolium salts in the form of chlorides or perchlorates (Table 1). The tetrazolium salts in the form of chlorides or perchlorates (Table 1). The tetrazolium salts are converted quantitatively to the starting formazans under the influence of mild reducing agents of the hydrazine hydrate type.

The salts obtained are colorless or light-yellow substances; however, when a dimethylamino group is present, they are intensely colored (more deeply colored than the starting formazans [1]). Two absorption bands, viz., a long-wave band (300-530 nm) and a short-wave band (245-250 nm), are observed in the electronic spectra of tetrazolium salts I, II(a-f) in ethanol.

Tetrazolium salts that contain an OH group (Id and IId) are yellow in the crystalline state but turn violet in solution [in alcohols and dimethylformamide (DMF)] because of partial dissociation of the hydroxy group, which intensifies its donor effect. Two long-wave bands corresponding to compounds with an ionized (540 and 520 nm) and nonionized (395 and 372 nm) OH group are observed in the spectra of these salts in ethanol.† Tetrazolium salts

---

*See [1] for Communication 23.

†A similar pattern was observed in the case of a tetrazolium salt with a betaine structure that contains a hydroxy group [2].

Lenin Komsomol Tyumen Industrial Institute, Tyumen 625036. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 111-114, January, 1980. Original article submitted January 10, 1979; revision submitted May 18, 1979.

0009-3122/80/1601-0094$07.50

TABLE 1. 2-(1-Methyl-5-tetrazolyl)-3-(R-phenyl)-5-phenyltetrazolium (Ia-h) and 2-(2-Methyl-5-tetrazolyl)-3-(R-phenyl)-5-phenyltetrazolium (IIa-g) Salts

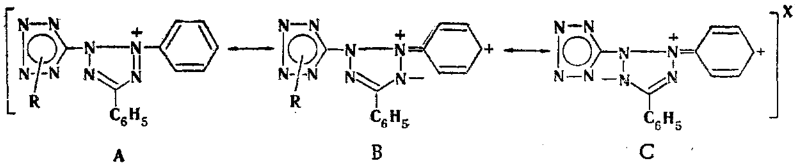
Compound	mp, °C (dec.)[a]	Electronic spectra in ethanol, λ_{max}, nm (log ε)	Empirical formula[b]	N, %		Yield, %
				found	calc.	
Ia	176 (176[8])	249 (4,49), 320 (3,68)				96
Ib	169—170	245 (4,45), 330 (3,77)	$C_{16}H_{15}ClN_8$	31,4	31,6	76
Ic	163—164	250 (4,46), 325 (3,86)	$C_{16}H_{15}ClN_8$	31,6	31,6	98
Id	180—181	245 (4,44), 395 (3,75), 542 (3,78)	$C_{15}H_{13}ClN_8O_5$	26,4	26,6	83
Ie	165—166	246 (4,35), 290 (4,16), 380 (3,81)	$C_{16}H_{15}ClN_8O_5$	25,6	25,8	63
If	161—162	245 (4,40), 530 (4,12)	$C_{17}H_{18}ClN_9O_4$	28,0	28,2	95
If'	161—162	245 (4,75), 345 (4,35), 397 (3,91), 530 (4,03)	$C_{23}H_{20}N_{12}O_7$	28,7	29,1	96
Ig	156—157	250 (4,49), 300 (4,09)	$C_{15}H_{12}ClN_9O_6$	28,6	28,0	51
Ih	170—171	244 (4,36)	$C_{15}H_{12}ClN_9O_6$	28,4	28,0	78
IIa	198—199	250 (4,60), 295 (3,88)	$C_{15}H_{13}ClN_8O_4$	27,7	27,7	93
IIb	212—213	245 (4,44), 312 (3,78)	$C_{16}H_{15}ClN_8O_4$	26,8	26,8	70
IIc	239—240	249 (4,48), 310 (3,65)	$C_{16}H_{15}ClN_8O_4$	26,7	26,8	65
IId	173	245 (4,37), 372 (3,61), 520 (3,52)	$C_{15}H_{13}ClN_8O_5$	26,2	26,6	95
IIe	193—194	245 (4,45), 357 (4,03)	$C_{16}H_{15}ClN_8O_5$	26,2	25,8	64
IIf	203	245 (4,44), 495 (4,09)	$C_{17}H_{18}ClN_9O_4$	28,3	28,2	78
IIg	230—231	250 (4,56)	$C_{15}H_{12}ClN_9O_6$	28,0	28,0	89

---

[a] The compounds were recrystallized: Ia and Ic from propanol, Ib from water, IIg from ethanol—chloroform (2:1), and the remaining compounds from ethanol. [b] Compounds If and If' are violet, IIf is red, Id, Ie, IId, and IIe are yellow, and the remaining compounds are colorless.

of this type are not stable in acidic and, particularly, alkaline media [8]. When alcohol solutions of salts Id and IId are made alkaline with sodium or ammonium hydroxide, an increase in the intensity of the color due to an increase in the degree of dissociation of the hydroxy group therefore is observed initially, after which the intensity of the color decreases gradually. Dissociation of the hydroxy group is suppressed when alcohol solutions of salts Id and IId are acidified with concentrated hydrochloric acid (the concentration of the acid in solution was raised to 0.1 N): the color and, correspondingly, the long-wave band vanish immediately, and the absorption at 370-390 nm increases. However, the intensity of this band soon decreases rapidly as a consequence of destruction of the tetrazolium salt.

The frequencies of the long-wave maxima in the spectra of the tetrazolium salts correlate satisfactorily with the electrophilic substituent constants σ^+ (Fig. 1) in accordance with the equation $\Delta\nu = \nu_R - \nu_H = \rho\sigma^+$ (in reciprocal centimeters). The correlation parameters for the 1-methyl derivatives are $\rho = -7516$ cm^{-1}, $r = 0.995$, and $n = 5$, and the correlation parameters for the 2-methyl derivatives are $\rho = -8171$ cm^{-1}, $r = 0.999$, and $n = 5$. It is noteworthy that the linear dependence encompasses both compounds that contain substituents with unshared pairs of p electrons and compounds that do not contain a substituent or in which the substituent is a methyl group. This constitutes evidence for a



monotypic character of the origin of the long-wave band in the spectra of the tetrazolium salts. This band is due in all likelihood to intramolecular charge transfer from the N-aryl residue to the central tetrazole ring.

It is apparent that donor substituents in the ortho or para positions of the phenyl group attached to the N_3 atom will facilitate this transfer.

One's attention is directed to the unusually high ρ value, which indicates extremely strong interaction of the substituent with the system of conjugated bonds of the tetrazole ring and also attests to the high polarity of the excited state.

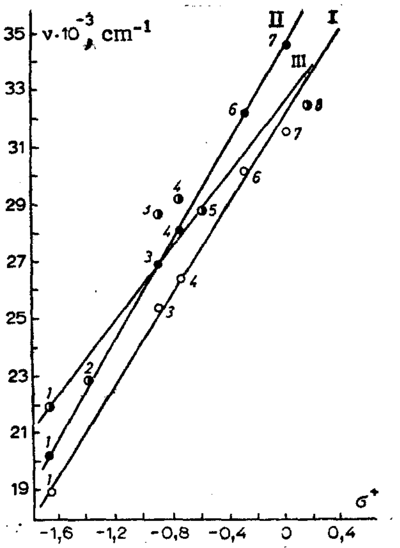


Fig. 1. Correlation of the frequencies of the long-wave absorption bands in the spectra of: ○) 2-(1-methyl-5-tetrazolyl)-3-(p-R-phenyl)-5-phenyltetrazolium salts (I); ●) 2-(2-methyl-5-tetrazolyl)-3-(p-R-phenyl)-5-phenyltetrazolium salts (II); ◑) 2-(5-tetrazolyl)-3-(p-R-phenyl)-5-phenyltetrazolium betaines (III) [R = $N(CH_3)_2$ (1), NH_2 (2), OH (3), OCH_3 (4), $NHCOCH_3$ (5), CH_3 (6), H (7), and I (8)].

The long-wave absorption maximum of tetrazolium salts that contain a 1-methyltetrazolyl substituent is shifted bathochromically 15-35 nm as compared with salts that contain a 2-methyltetrazolyl substituent. This is a consequence of the high degree of electron-acceptor character of the 1-methyltetrazolyl residue [9], which evidently more effectively promotes delocalization of the negative charge in the excited state (C, D), thereby lowering the energy of this transfer. The absorption of tetrazolium salts that contain 1- and 2-methyltetrazolyl substituents occurs in the longer-wave region as compared with the tetrazolium salts with a betaine structure [2], in which the degree of acceptor character of the tetrazolyl anion is even smaller, probably for the same reason.

A correlation in accordance with the equation presented above is also realized for tetrazolium betaines [2, 10], although less successfully: $\rho = -6325.7\ cm^{-1}$, $r = 0.981$, and $n = 6$ (Fig. 1).

EXPERIMENTAL

The electronic spectra of $2.5 \cdot 10^{-5}$ to 10^{-4} M solutions of the compounds in ethanol were recorded with an SF-4A spectrophotometer. The melting points were determined with a PTP-1 apparatus. The preparation of the starting formazans was described in [1].

2-(2-Methyl-5-tetrazolyl)-3-(p-dimethylaminophenyl)-5-phenyltetrazolium Perchlorate (IIf). A 1-ml (1.45 mmole) sample of 10% $NaNO_2$ solution was added to a solution of 0.5 g (1.43 mmole) of 1-(2-methyl-5-tetrazolyl)-3-phenyl-5-(p-dimethylaminophenyl)formazan in 40 ml of acetic acid, and the mixture was allowed to stand for 24 h. It was then concentrated to a volume of 10 ml, and concentrated $HClO_4$ was added dropwise until precipitation was complete. The precipitate was removed by filtration and washed with water to give 0.5 g of tetrazolium perchlorate IIf. The product was soluble in chloroform and alcohol, slightly soluble in water, and insoluble in benzene. Salts Id-f and IId, e were similarly obtained; a threefold to fivefold excess of $NaNO_2$ was used in the synthesis of salts I, II(a-c, g, h), and the oxidation time was shortened to 2-3 h.

The tetrazolium chlorides were readily soluble in water, but the perchlorates were only slightly soluble.

The synthesis of picrate If' was accomplished by reaction of the acetic acid solution obtained after oxidation of the formazan with an equimolar amount of a saturated aqueous solution of picric acid.

The characteristics of the tetrazolium salts are presented in Table 1.

LITERATURE CITED

1. V. P. Shchipanov, L. G. Surovtsev, I. I. Mudretsova, and N. I. Khizhnyak, Zh. Org. Khim., 15, 2207 (1979).
2. V. P. Shchipanov and G. F. Grigor'eva, Khim. Geterotsikl. Soedin., No. 2, 268 (1974).
3. V. P. Shchipanov, Zh. Org. Khim., 13, 209 (1977).
4. A. W. Nineham, Chem. Rev., 55, 355 (1955).

5. G. Maerkl. Z. Naturforsch., 17, 782 (1962).
6. K. S. Tsou and H. C. F. Su, J. Med. Chem., 6, 693 (1963).
7. H. Pechmann and E. Wedekind, Chem. Ber., 28, 1688 (1895).
8. V. P. Shchipanov, S. A. Nagovskaya, and L. S. Podenko, Khim. Geterotsikl. Soedin., No. 2, 266 (1977).
9. R. N. Butler, Adv. Heterocycl. Chem., 21, 323 (1977).
10. V. P. Shchipanov, K. I. Krashina, and A. A. Skachilova, Khim. Geterotsikl. Soedin., No. 11, 1570 (1973).