TETRAZOLE DERIVATIVES

IX.* 1-(5-TETRAZOLYL)-3-PHENYL-5-ARYLFORMAZANS WITH ELECTRON-DONOR SUBSTITUENTS

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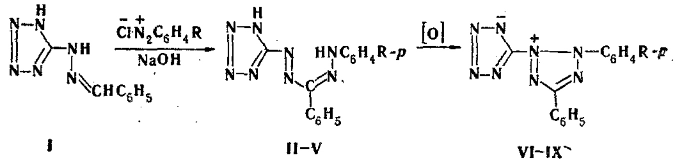
A series of 1-(5-tetrazolyl)-3-phenyl-5-arylformazans, which are readily oxidized to brightly colored 2-(5-tetrazolyl)-3-aryl-5-phenyltetrazolium betaines in alkaline media, are obtained by coupling of arenediazonium salts containing strong electron-donor groups with 5-tetrazolylhydrazones. The formazans form deeply colored complexes with Ni^{2+}, Cu^{2+}, and Co^{2+} salts.

To ascertain the general principles in the properties of formazans, it seemed of interest to synthesize a series of compounds with strong electron-donor substituents.



Considerable difficulties are always encountered in the preparation of formazans containing electron-donor groupings [2]. However, the high reactivity of benzaldehyde 5-tetrazolylhydrazone (I) in azo coupling with arenediazonium salts in aqueous alkaline media makes it possible to obtain such compounds (II-V, Table 1) in high yields. The introduction of a strong electron donor into the tetrazolylformazan molecules changed their properties substantially: the substances became extremely sensitive to the action of oxidizing agents, particularly in alkaline media, in which formazans III-V readily undergo autooxidation. The oxidation of II proceeds under the influence of $K_3Fe(CN)_6$.

Formazans II-V have deep color in the crystalline state and in solution and are readily soluble in aqueous alkali with deepening of the color. Dissolving of II in 0.1 N sodium carbonate solution leads to a considerable hypsochromic shift of the absorption maximum to 387 nm; in more alkaline media (0.1 N NaOH), λ_{max} is 480 nm. The family of curves of the UV spectra of formazan II at different pH values passes through an isopiestic point (Fig. 1); this makes it possible to conclude that equilibrium between two forms – the monoanion and the dianion – exists in alkaline solution.

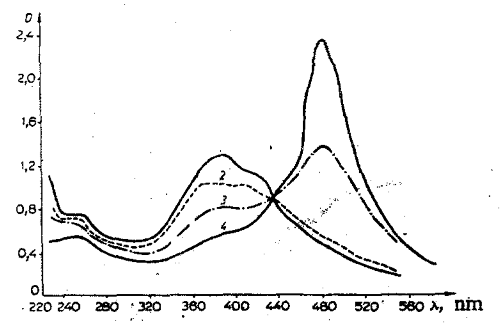
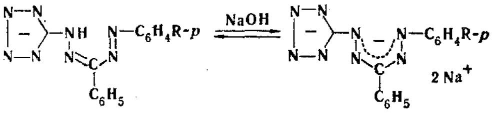


Fig. 1. UV spectra of II at various solution pH values: 1) pH 11.0; 2) pH 11.6; 3) pH 12.0; 4) pH 12.3.



In contrast to II, formazans that contain stronger electron-donor groups of the NH_2 and $N(CH_3)_2$ type absorb at

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*See [1] for communication VIII.

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TABLE 1. 1-(5-Tetrazolyl)-3-phenyl-5-arylformazans (II-V)

Compound	R	mp, deg C[a]	Empirical formula	N, %		Electronic spectra, λ_{max}, nm (log ε)						Yield, %
				found	calc.	alcohol	0,1 N NaOH	0,1 N Na_2CO_3	complexes in alcohol			
									$NiCl_2$	$CuSO_4$	$CoCl_2$	
II	OCH_3	156	$C_{15}H_{14}N_8O$	34,9	34,8	430 (4,11)	480 (4,85)	387 (4,59)	570	610	640	96
III	OH	188	$C_{14}H_{12}N_8O$	36,4	36,4	460 (4,12)	472 (4,66)	490 (4,36)	560	615	640	72
IV	NH_2	200—202	$C_{14}H_{13}N_9$	40,7	40,1	465 (4,25)	496 (4,66)	436 (4,25)	560	456	666	55
V	$N(CH_3)_2$	135—136	$C_{16}H_{17}N_9 \cdot C_2H_5OH$b	33,3	33,1	480 (4,37)	496 (4,44)	480 (4,26)	580	480	684	81

Note. [a]With decomposition; II, III, and V were recrystallized from ethanol, while IV was recrystallized from 70% ethanol. [b]Found, %: C 56.4; H 5.7. Calculated, %: C 56.7; H 6.1.

TABLE 2. 2-(5-Tetrazolyl)-3-aryl-5-phenyltetrazolium Betaines (VI-X)

Compound	R	mp (dec.), deg C[a]	Empirical formula	N, %		Yield, %[b]
				found	calc.	
VI	OCH_3	188	$C_{15}H_{12}N_8O$	34,7	35,0	94
VII	OH	238	$C_{14}H_{10}N_8O$	37,0	36,6	72
VIII	NH_2	230	$C_{14}H_{11}N_9$	41,6	41,3	88
IX	$N(CH_3)_2$	193	$C_{16}H_{11}N_9$	38,0	37,8	94
X	$NHCOCH_3$	213	$C_{16}H_{13}N_9O \cdot H_2O$ c	34,0	34,5	—

Note. [a]Compounds VI, IX, and X were recrystallized from ethanol, while VII and VIII were recrystallized from aqueous dimethylformamide (1 : 1). [b]Betaine VIII was obtained by autooxidation, while the remaining betaines were obtained by means of $K_3Fe(CN)_6$. [c]Found, %: C 52.5; H 4.0. Calculated, %: C 52.5; H 4.1.

TABLE 3. Electronic Spectra of Betaines VI-X

Compound	Medium	λ_{max}, nm (lg ε)
VI	a	235 (4,26), 250d (4,23), 345 (3,67)
	c	240 (4,34), 260 (4,40), 370 (3,92)
VII	a	240 (4,40), 350 (3,78), 485 (2,68)
	b	255 (4,46), 280d (4,24), 490 (4,43)
	c	245 (4,41), 360 (3,81)
VIII	a	245 (4,42), 440 (3,98)
	c	250 (3,87)
IX	a	245 (4,37), 460 (4,10)
	c	247 (4,35)
X	a	255 (4,73), 350 (3,98)
	c	257 (5,02), 350 (4,23)

Note: [a]Ethanol. [b]0.1 N alcohol solution of NaOH. [c] 6 N HCl. [d]Shoulder.

much longer wavelengths (436 and 480 nm, respectively) in Na_2CO_3 solution. We suppose that this is a consequence of equalization of the electron-donor characteristics of the substituents attached to the 1-N and 5-N atoms; this leads to an increase in the symmetry of the electron density on the formazan grouping. Hydroxy derivative III, in which the OH group may be ionized in addition to the tetrazole ring under these conditions, should also be considered from these same positions.

Formazans II-V readily form deeply colored complexes with the cations of transition metals; complexing of IV and V with Cu^{2+}, accompanied by an increase in the color, stands out significantly in the examined series of formazans and metal cations.

The tetrazolium salts (betaines) obtained by oxidation of formazans II-V have colors from light yellow (VI, VII) to intense red (IX) (Table 2). This distinguished them from the colorless tetrazolium betaines containing acceptor or weakly donor groupings in the phenyl group attached to 3-N [1]. It should be noted that examples of brightly colored salts [3,4] and betaines [5,6] are known among tetrazolium salts that are derivatives of aryl- and hetarylformazans, most of which are colorless or pale-yellow; except for [6], the reasons for the color of the compounds have not been established.

In contrast to tetrazolium betaines with acceptor groupings, which are readily reduced in alkaline media [1], compounds VI-X are extremely resistant to reduction. Their reduction to a formazan, the appearance of which is detected from a positive test for complexing with $CoCl_2$, occurs only on heating in an alkaline aqueous alcohol solution in the presence of hydroquinone.

Only one band at 250 nm (log ε 4.4) is observed in the electronic spectra of colorless tetrazolium betaines [1] of the VI-IX type (R = H, CH_3). In comparison with this, a band at 345-350 nm (Table 3) appears in the spectra of betaines that contain OH and OCH_3 groups; absorption is observed at still longer wavelengths (440-460 nm) in compounds with NH_2 and $N(CH_3)_2$ groupings.

Heating betaine VIII in acetic anhydride gives the corresponding acyl derivative (X), the second band in the UV spectrum of which is shifted to the shorter-wave region (350 nm) as compared with starting VIII. Dissolving of betaines VIII and IX in concentrated mineral acids decolorizes them and leads to the disappearance of the long-wave band; this is apparently due to protonation at the amino group. In acidic media, the long-wave band in the spectra of VI and VII undergoes a small bathochromic shift. The nitrogen atom of the tetrazolium ring is probably protonated in this case to give the normal tetrazolium salt A. In the case of protonation at the oxygen atom, one should have expected the disappearance of this band. Similar behavior in acidic media is also characteristic for betaine X. The starting colored salts are isolated unchanged when solutions of VI-X in acid are diluted with water.

Dissolving of betaine VII in aqueous or alcoholic alkali leads to a sharp deepening of the color (λ_{max} 490 nm) with a considerable increase in the extinction. If one considers that betaine VII in neutral alcohol solution displays weak absorption in the same region (485 nm), the connection between this band and the ionized hydroxyl group is obvious. It might be assumed that the long-wave band in the spectra of VI-X is due to a transition of the $l \rightarrow a_\pi$ type, which is usually displayed when an electron-donor substituent containing unshared pairs of electrons is introduced [7]. However, additional studies are necessary to discover the nature of this phenomenon in the case of colored tetrazolium salts.

EXPERIMENTAL*

The UV spectra were recorded with SF-4A and SF-10 spectrophotometers. The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer.

Method for the Recording of the UV Spectra at Different Solution pH Values. A solution of formazan II ($3.33 \cdot 10^{-5}$ M) in 0.1 N Na_2CO_3 was titrated with a 1 N NaOH solution at 20°, during which the pH of the solution was determined with an LPM-60M titrometer. Samples for spectrophotometry were selected at definite solution pH values.

1-(5-Tetrazolyl)-3-phenyl-5-(p-methoxyphenyl)formazan (II) (Table 1). A diazonium salt solution obtained from 1.2 g (0.01 mole) of p-anisidine, 2.6 ml of concentrated hydrochloric acid, 40 ml of water, and 0.7 g of $NaNO_2$ in 8 ml of water, was added at 0-2° to a solution of 1.88 g (0.01 mole) of hydrazone I in 100 ml of 1.6% NaOH, after which the mixture was filtered, and the filtrate was acidified with 10 ml of acetic acid to give 3.1 g of dark-cherry-red precipitate of formazan II. Compound V (Table 1) was similarly obtained.

1-(5-Tetrazolyl)-3-phenyl-5-(p-hydroxyphenyl)formazan (III) and 2-(5-Tetrazolyl)-3-(p-hydroxyphenyl)-5-phenyltetrazolium Betaine (VII) (Tables 1 and 2). Coupling of a diazonium salt solution obtained from p-aminophenol hydrochloride with hydrazone I under the conditions of the preceding synthesis gave 2.65 g of a product from which 2.2 g of formazan III (fine red-brown prisms) and 0.25 g of betaine VII (light-yellow needles, only slightly soluble in ethanol) were isolated by fractional crystallization.

1-(5-Tetrazolyl)-3-phenyl-5-(p-aminophenyl)formazan (IV) and 2-(5-Tetrazolyl)-3-(p-aminophenyl)-5-phenyltetrazolium Betaine (VIII) (Tables 1 and 2). A solution of 0.69 g of $NaNO_2$ in 8 ml of water was added at 6-8° to a solution of 1.08 g (0.01 mole) of p-phenylenediamine in 3 ml of concentrated hydrochloric acid and 30 ml of water. The diazonium solution was added at 0-2° to 1.88 g of hydrazone I in 100 ml of 1.6% NaOH, and the precipitated VIII was separated (0.52 g of light yellow-orange needles). The filtrate was acidified with acetic acid to give 1.68 g of formazan IV (dark-brown plates). IR spectrum (cm^{-1}): IV ν_{NH} 3380 s, 3320 s, 3190 m, δ_{NH} 1630 s, $\nu_{C=N,N=N}$ [8, 9] 1605 s, 1520 m, 1450 w, 1355 m, ν_{C-N} [9] 1310 s, 1240 m, 1150 s; vibrations of the tetrazole ring [8, 10] at 1080 m, 1020 m, 990 m, 845 m, 780 w, 700 w; VIII ν_{NH} 3400 s, 3340 m, 3220 m, δ_{NH} 1650 m, $\nu_{C=N,N=N}$ [8, 11] 1530 m, 1515 m, 1490 w, 1460 m, 1415 w, 1390 w, 1355 m, ν_{C-N} [11] 1270 w, 1175 m, 1150 m; vibrations of the tetrazole ring [8-11] at 1010 w, 990 m, 840 m, 785 w, 720 w, 690 w.

2-(5-Tetrazolyl)-3-(p-dimethylaminophenyl)-5-phenyltetrazolium Betaine (IX) (Table 2). A solution of 0.5 g of formazan V in 50 ml of 1 N NaOH was allowed to stand in a Petri dish overnight. The resulting

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*With the participation of M. A. Kurmaeva.

precipitate was removed by filtration to give 0.45 g (92%) of betaine IX with mp 193° (dec.) (bright-red needles from alcohol). Formazans III and IV were similarly oxidized.

2-(5-Tetrazolyl)-3-(p-methoxyphenyl)-5-phenyltetrazolium Betaine (VI) (Table 2). A solution of 1.65 g (5 mmole) of $K_3Fe(CN)_6$ in 10 ml of water was added to a solution of 0.8 g (2.5 mmole) of formazan II in 50 ml of 1 N NaOH, and the precipitate was removed by filtration and washed with water and alcohol to give 0.75 g of betaine VI (pale-yellow needles from alcohol). Compounds IX and VII (Table 2) were similarly obtained. To isolate betaine VII, the reaction mixture was acidified with concentrated hydrochloric acid.

2-(5-Tetrazolyl)-3-(p-acetamidophenyl)-5-phenyltetrazolium Betaine (X) (Table 2). A 0.5-g sample of betaine VIII in 10 ml of acetic anhydride was refluxed for 1 h, after which the solution was cooled, and the precipitated light-orange X was removed by filtration to give 0.32 g (56%) of yellow-orange needles. The product was only slightly soluble in alcohol and dimethylformamide. IR spectrum, ν, cm^{-1}: NH 3225 m, 3120 m; C=O 1710 s.

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