TETRAZOLE DERIVATIVES

VIII.* SYNTHESIS AND PROPERTIES OF 5-ARYL-3-PHENYL-1-(TETRAZOL-5-YL)FORMAZANS

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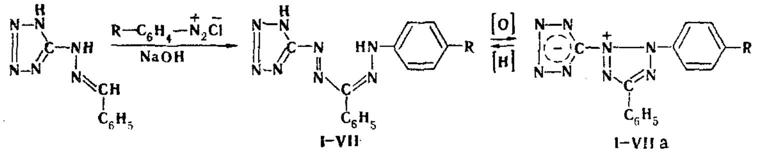
A series of 5-aryl-3-phenyl-1-(tetrazol-5-yl)formazans has been obtained by the azo coupling reaction. In an aqueous alkaline medium they are oxidized to tetrazolium salts with a betaine structure. Information is given on the electronic spectra of the formazans and the tetrazolium salts and the acidic properties and complex-forming capacity of the formazans.

Continuing investigations on the chemistry of tetrazoles [1], we have undertaken the study of formazans containing tetrazole as a substituent, and the tetrazolium salts corresponding to them. In the literature there is only a brief report of the synthesis of 3,5-diphenyl-1-(tetrazol-5-yl)formazan [2, 3] and its oxidation with bromosuccinimide to a tetrazolium salt with a betaine structure [2].

The present communication considers the preparation and some properties of tetrazole formazans differing by the substituents in the para position of a phenyl radical attached to the N_5 atom (Table 1).



I, I a R=H; II, II a R=CH_3; III, III a R=Cl; IV, IV a R=Br; V, V a R=I; VI, VI a R=NO_2;
VII, VII a R=m-NO_2

The most suitable method for preparative purposes, ensuring almost quantitative yields of the formazans (I-VII) is the azo coupling of the corresponding arenediazonium salt with benzaldehyde tetrazol-5-ylhydrazone in an aqueous alkaline medium. The independent synthesis of (I) by the azo coupling of diazotized 5-aminotetrazole with benzaldehyde phenylhydrazone in pyridine led to the identical formazan. It is interesting to note that in an attempt to obtain the same substance by a similar method of synthesis but in an acid medium 1,3,5-triphenylformazan was obtained instead of (I) [4].

The individuality of the compounds was checked by chromatography in a thin layer of alumina (Table 1). The substances are characterized by strong sorption on Al_2O_3 and exhibit adequate chromatographic mobility only in a sorbent of activity grade V. No direct relationship between the R_f values and the acid properties of the formazan was observed.

In the crystalline state, all the substances have intense colorations of dark red shades. In the electronic spectra of the formazans (III-VII), containing acceptor substituents, a slight bathocromic displacement of the long-wave maximum (by 18-38 nm) as compared with the unsubstituted formazan (I) is observed.

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*For Communication VII, see [1].

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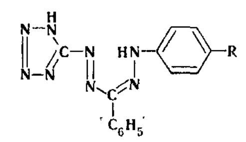
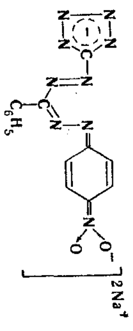
TABLE 1



Compound	R	Decomp. pt., °C	Empirical formula	Found, %			Calc., %			Ethanol		NaOH 0,1 N		λ_{max}, nm, complexes in ethanol			R_f	pK_a	Yield, %
				C	H	N	C	H	N	λ_{max}	lg ε	λ_{max}	lg ε	Ni^{2+}	Cu^{2+}	Co^{2+}			
I	H	147*	$C_{14}H_{12}N_8$	57,4	4,4	38,3	57,5	4,1	38,2	442	3,82	486	4,48	570	596	634	0,86	5,10	91
II	CH_3	156	$C_{15}H_{14}N_8$	59,3	4,7	36,8	58,8	4,6	36,6	445	4,00	486	4,52	560	610	630	0,82	5,25	100
III	Cl	144	$C_{14}H_{11}ClN_8$	49,3	2,9	34,3	49,9	3,3	34,6	470	3,78	490	4,57	580	616	640	0,86	4,85	100
IV	Br	145	$C_{14}H_{11}BrN_8$	44,5	3,1	29,8	44,1	2,9	30,2	480	4,32	498	4,69	580	616	640	0,84	4,70	100
V	I	134	$C_{14}H_{11}IN_8$	39,7	2,8	26,4	39,3	2,6	26,9	460	3,96	494	4,66	590	620	650	0,81	—	100
VI	NO_2	119	$C_{14}H_{11}N_9O_2$	49,3	3,0	36,9	49,8	3,3	37,4	480	4,02	568	4,55	630	644	670	0,92	3,45	74
VII	m-NO_2	103	$C_{14}H_{11}N_9O_2$	50,1	3,1	37,2	49,8	3,3	37,4	460	3,78	496	4,60	596	614	654	0,92	4,10	85

*According to the literature [2], decomp. pt. 143°C; [3], mp 147°C.

Compounds (I-VII) are readily soluble in aqueous solutions of alkalis with some deepening of the color and a two- to threefold increase in the intensity of absorption. The particularly pronounced bathochromic effect of salt formation in the case of the p-NO_2 derivative (88 nm) is probably due to the appearance of a structure with the aci-nitro form. In the m-nitro derivative, where the possibility of the formation of such a structure is excluded, the shift is small (36 mm).



The formazans possess two mobile hydrogen atoms – in the tetrazole and in the formazan grouping. Because of the considerable acidity of tetrazole (pK_a in water 4.89 [5]), the constants of the first degree of acid dissociation of the formazans, which characterize the splitting off of a proton from the tetrazole group, had to be determined indirectly, by potentiometric titration (Table 1).

In ethanolic solution at room temperature, compounds (I-VII) instantaneously form deeply colored complexes with bivalent metal ions of the 3rd series, with a progressive deepening of the coloration in the sequence $Ni^{2+} < Cu^{2+} < Co^{2+}$ (Table 1). The properties and structures of the complexes will be reported separately.

Compounds (I-VII) are oxidized in aqueous alkaline solution under the action of $KMnO_4$ or $K_3Fe(CN)_6$ with good yield to the tetrazolium salts (Ia-VIIa) (Table 2). The compounds obtained, in contrast to the analogous derivatives of other heterocycles [6], are stable substances. Thus, (Ia) withstands being boiled in concentrated HCl for 6 h without change. The salts are sparingly soluble in water and far more soluble in organic solvents – chloroform, ethanol, acetone. Substances (Ia-Va) are colorless, while (VIa) and (VIIa) have a faint yellow tinge. The electronic spectra of ethanolic solutions of the salts are characterized by a strong absorption maximum in the 245-255-nm region which depends little on the nature of the substituent, and by inflection in the 300-340-nm region which changes in the case of the p-I derivative (Va) into a distinct band with a maximum at 310 nm. On being heated in an aqueous ethanolic solution of alkali, and in the presence of a reducing agent of the type of hydroquinone, even in the cold, the salts are converted into the initial formazans. The tetrazolium salts with strong acceptor substituents – (VIa) and (VIIa) – are reduced with particular ease.

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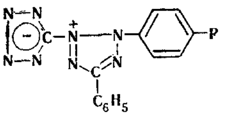
*When compounds (I) were oxidized with bromosuccinimide by the method of Kuhn and Kainer [2], compounds (Ia) were obtained with a yield of 25%.

TABLE 2



Compound	R	Decomp. pt., °C	Empirical formula	N, % found	N, % calc.	λ_{max}, nm, (log ε)	Yield, %
Ia	H	209[a]	$C_{14}H_{10}N_8$	38,9	38,7	245 (4,39)[d]	97
IIa	CH_3	203[b]	$C_{15}H_{12}N_8$	36,5	36,8	250 (4,38)[d]	85
IIIa	Cl	194[b]	$C_{14}H_9ClN_8$	34,3	34,5	247 (4,21)[d]	81
IVa	Br	202[b]	$C_{14}H_9BrN_8$	30,1	30,3	245 (4,71)[d]	72
Va	I	210[c]	$C_{14}H_9IN_8$	26,8	26,9	245 (4,50) 310 (3,93)	86
VIa	NO_2	155[b]	$C_{14}H_9N_9O_2$	37,6	37,6	255 (4,18)[d]	44
VIIa	*m*-NO_2	182[b]	$C_{14}H_9N_9O_2$	37,3	37,6	251 (4,86)[d]	95

Note: a) From pyridine. b) From ethanol. c) From a mixture of dimethylformamide and water (2 : 1). d) There is an inflection in the 300–340-nm region.

EXPERIMENTAL*

The spectra in the UV and visible region were taken on SF-4A and SF-10 spectrophotometers. The pK_a values were determined by a graphical method as the pH at the half-neutralization point in each case. The titration of $5 \cdot 10^{-3}$ M solutions of the substances in 72% ethanol was performed at 25°C with a 0.1 N solution of carbonate-free caustic potash with glass and calomel electrodes on an LPM-60M instrument. For chromatography in a thin layer of alumina (activity grade V), acetone–chloroform–acetic acid (78 : 20 : 2) was used as eluent.

Typical Procedure for the Synthesis of 5-Aryl-3-phenyl-1-(tetrazol-5-yl)formazans (I-V, VII). Over 10-15 min, a solution of diazonium salt obtained from 0.01 mole of the appropriate amine, 2.4 ml of concentrated HCl, 30 ml of water, and 0.69 g (0.01 mole) of $NaNO_2$ in 8 ml of water was added to a solution of 1.88 g (0.01 mole) of benzaldehyde tetrazol-5-ylhydrazone in 100 ml of 5% NaOH at 1-2°C. After the mixture had been stirred at room temperature for 1 h, 500 ml of water was added and it was acidified to pH 2 with 1 N HCl. The formazan that had separated out was filtered off, washed with water, crystallized from ethanol, and dried at 80°C over P_2O_5 in vacuum.

Independent Synthesis of 3,5-Diphenyl-1-(tetrazol-5-yl)formazan(I). At −3 to 0°C, 0.69 g (0.01 mole) of $NaNO_2$ in 8 ml of water was added to a solution of 1.03 g (0.01 mole) of 5-aminotetrazole in 2.4 ml of concentrated HCl and 40 ml of water. The resulting mixture was kept at a temperature of −1 to 0°C for 20 min and was then added in small portions to a solution of 1.96 g (0.01 mole) of benzaldehyde phenylhydrazone in 50 ml of pyridine cooled to −7°C. After an hour, the mixture was diluted with 100 ml of water, 50 ml of concentrated HCl was added, and the (I) was isolated. Yield 2.1 g (72%), decomp. pt. 146°C. A mixture with the (I) obtained by the method described above gave no depression of the melting point. λ_{max}, nm (log ε (, in ethanol: 445 (3.78), R_f 0.86.

5-p-Nitrophenyl-3-phenyl-1-(tetrazol-5-yl)formazan (VI) was obtained in a similar manner to (I-V), but in 1.6% caustic soda at 8-10°C. After isolation, the formazan was treated with 10 ml of glacial acetic acid, filtered off, washed with ethanol, and dried. Yield 2.5 g (74%). It crystallized from ethanol at a temperature of 45-50°C. Compound (VII) was isolated and purified similarly.

2,5-Diphenyl-3-(tetrazol-5-yl)tetrazolium Betaine (Ia). A solution of $K_3Fe(CN)_6$ was added to a solution of 2.5 g of (I) in 40 ml of 1% NaOH until this solution had become decolorized. The precipitate that deposited was filtered off, washed with water to neutrality, and then with ethanol. This gave 2.39 g (97%) of (Ia). Decomp. pt. 209°C (from pyridine); according to the literature [2], decomp. pt. 209-210°C. Compounds (IIa-Va and VIIa) were obtained similarly (Table 2). On heating, all the salts decomposed vigorously, sometimes explosively, which complicates their analysis for C and H.

2-p-Nitrophenyl-5-phenyl-3-(tetrazol-5-yl)tetrazolium Betaine (VIa). A solution of 0.32 g of $KMnO_4$ in 10 ml of water was added to 1 g of (VI) in 50 ml of 1% NaOH. The precipitate was filtered off and was washed successively with water, 0.1 N HCl, and water again, and it was then extracted with ethanol. The extracts were concentrated, giving 0.45 g (44%) of (VIa).

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*With the participation of T. V. Eremina.

Reduction of (Ia). A suspension of 1.45 g (0.005 mole) of (Ia) in 100 ml of ethanol and 5 ml of 2 N NaOH was treated with 0.66 g (0.006 mole) of hydroquinone. The mixture was stirred until the solid matter had dissolved completely and was then concentrated, diluted with water, acidified, and filtered. The yield of (I) was 1.2 g (80%), decomp. pt. 147°C (from ethanol). The product was identical with the (I) described above.

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