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TETRAZOLE DERIVATIVES

XIII.* SYNTHESIS AND PROPERTIES OF 1-(1-METHYL-5-TETRAZOLYL)-3,5-DIPHENYLFORMAZAN, A TETRAZOLIUM SALT, AND THE VERDAZYL RADICAL

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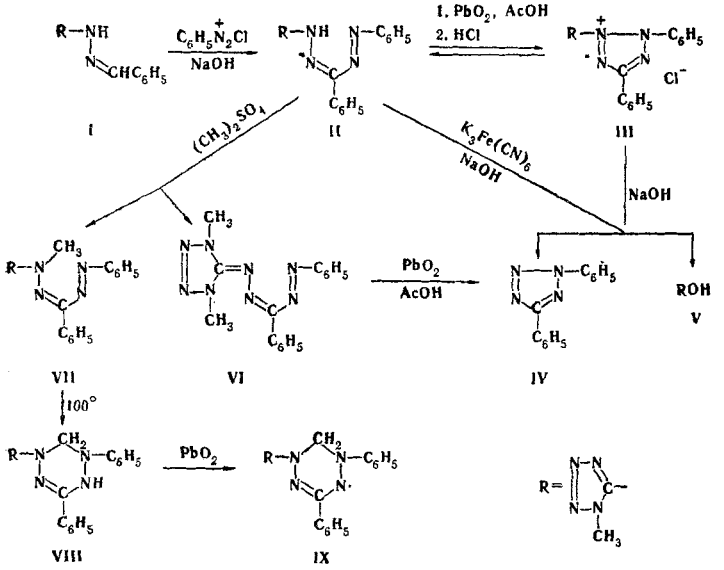
The formazan named in the title and its corresponding tetrazolium salt were synthesized. It is shown that both of these compounds are capable of cleavage to give two tetrazole fragments. Reaction products involving the ring and exocyclic nitrogen atoms are formed in the methylation of the formazan. The product from the exocyclic nitrogen atom on heating is converted to a leucoverdazyl radical, which is capable of undergoing oxidation to give the 1-(1-methyl-5-tetrasolyl)-3,5-diphenylverdazyl radical.

One of the characteristic peculiarities of formazans and verdazyl radicals containing a tetrazole residue attached to the $N_{(1)}$ atom is their ability to readily undergo oxidation to give the corresponding tetrazolium [2] and verdazylium [3] salts with betaine structures. In order to exclude the possibility of the formation of betaines, we attempted to obtain a formazan and a verdazyl radical containing a tetrazole residue with a methyl group in the 1 position.



*See [1] for communication XII.

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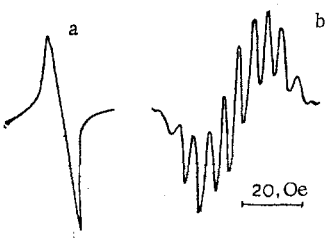

Fig. 1. ESR spectra of 1-(1-methyl-5-tetrazolyl)-3,5-diphenylverdazyl radical (IX): a) crystals, $g_0 = 2.0036 \pm 0.0003$; b) solution in benzene (10^{-3} M) deoxygenated in vacuo (10^{-5} mm), $g_0 = 2.0031 \pm 0.0003$.

Formazan II, obtained by diazo coupling of benzaldehyde (1-methyl-5-pyrazolyl)hydrazone (I) with benzenediazonium chloride, is resistant to autoxidation but under the influence of potassium ferricyanide readily undergoes destruction to give 2,5-diphenyltetrazole (IV) and 1-methyl-5-hydroxytetrazole (V). A tetrazolium salt, which was isolated in the form of the chloride (III), is obtained in good yield by oxidation of II with lead dioxide in acetic acid. The properties of III differ markedly from those of the previously described tetrazolium salts of the betaine type [2]. It is quite soluble in water (betaines are insoluble) and displays much higher chemical activity. In contrast to betaines, salt III is capable of cleavage but is more stable than tetrazolium salts with other hetaryl residues, for example, benzoxazole, [4], benzimidazole [5], and pyrimidine [6], which undergo decomposition at the instant of their formation. When III is heated in concentrated HCl at 100°, for 3 h, it undergoes decomposition, evidently via the usual scheme for tetrazolium salts [4]: 2,5-diphenyltetrazole (IV) is formed. The other possible reaction product – 1-methyl-5-chlorotetrazole – cannot be isolated. The decomposition of III can also occur in the crystalline state: heating at 100° for 5 h leads to complete decomposition of III to give IV. Under the influence of alkali or ammonium hydroxide III is cleaved to give two tetrazole fragments – IV and V. This is the first time that this sort of cleavage of a tetrazolium salt has been observed. However, under the influence of hydrazine hydrate, hydroquinoline, or ascorbic acid, salt III is reduced quantitatively to formazan II. These reactions were used to monitor the completeness of decomposition of the tetrazolium salt during thermal and acidic decomposition. Thus tetrazolium salt III undergoes reduction much more readily than betaines, for which this sort of process takes place only in alkaline media [2].

The reaction of formazan II with dimethyl sulfate in dimethylformamide (DMF) in the presence of sodium hydroxide leads to the formation of methylation products involving the ring (VI) and exocyclic (VII) nitrogen atoms. Methylation at a higher temperature promotes an increase in the yield of VI. For example, at 0° the ratio of VI and VII is 1:1, whereas at 25° it is 2:1. The two compounds are almost equally soluble in various solvents, and this hinders their separation. The isolation of the individual products was based on the difference in their chemical properties. Thus when the reaction mixture is refluxed in heptane, VII undergoes cyclization to colorless leucoverdazyl radical VIII, the solubility of which differs markedly from that of VI; this makes it possible to isolate VI and VIII in pure form. It is interesting to note that VI, which has a ketoformazene structure, is extremely stable, while ketoformazenes that contain only aryl and no heteroaromatic residues are extremely unstable substances, particularly at high temperatures [7]. In addition, VI and VII behave differently with respect to oxidation. Under the influence of lead dioxide in acetic acid, VI undergoes oxidative cleavage: 2,5-diphenyltetrazole (IV) is isolated from the reaction mixture in quantitative yield, whereas the other fragment – the presumed 1,4-dimethyl-5-tetrazolone – could not be isolated. Compound VII is resistant to oxidation under these conditions. Oxidation of the reaction mixture under the above conditions therefore destroys VI and makes it possible to isolate VII in the individual state.

Oxidation of leucoverdazyl radical VIII with lead dioxide gives an intensely green paramagnetic solution, from which crystalline dark-green verdazyl radical IX is isolated by concentration. The intense ν_{NH} band at 3170 cm^{-1} previously present in the spectrum of leucoverdazyl VIII vanishes in the IR spectrum of IX. The ESR spectrum of a solution of IX (Fig. 1) is similar to the spectrum of the 1-(5-tetrazolyl)-3,5-diphenylverdazyl radical [3], but the spectrum of crystals differs with respect to its asymmetrical character and sharp contraction of the absorption line (singlet widths 2.7 and 15.4 Oe, respectively); this is due to the large exchange interaction in crystals of verdazyl radical IX.

EXPERIMENTAL

The electronic spectra were recorded with an SF-4A spectrophotometer. The IR spectra of KBr pellets of the compounds (2 mg of the compound in 800 mg of KBr) were recorded with a UR-20 spectrometer. The

ESR spectra were recorded with an EPR-3 spectrometer. The individuality of the products was monitored by thin-layer chromatography (TLC) on Silufol UV-254; the R_f values are presented for chloroform–acetone system (100 : 5).

1-(1-Methyl-5-tetrazolyl)-3,5-diphenylformazan (II). A diazonium solution, prepared from 1.96 ml (20 mmole) of aniline, 4.8 ml (56 mmole) of concentrated HCl, 60 ml of water, and 1.4 g (20 mmole) of $NaNO_2$ in 16 ml of water, was added at 0-2° to a solution of 4.04 g (20 mmole) of hydrazone I in 200 ml (80 mmole) of 1.6% NaOH, after which the mixture was allowed to stand at room temperature for 1 h. It was then filtered, and the filtrate was acidified with 1 M HCl. Workup gave 5.4 g (88%) of long dark-claret needles of II with mp 158° (from ethanol) and R_f 0.44. UV spectrum, λ_{max} (log ε): in ethanol 270 (4.19) and 408 (3.93); in dioxane 277 (4.36) and 420 (4.26); in 0.1 M NaOH 250 (4.08) and 450 nm (4.58). IR spectrum: 1586 cm^{-1} (vs) (C = N, C = C). Found: N 36.3%. $C_{15}H_{14}N_8$. Calculated: N 36.6%. Complexes with transition metals [λ_{max}, nm, in ethanol; ligand-metal composition determined by the isomolar series method; instability constants (K_i) determined by the method in [8] in 72% (by weight) ethanol in the presence of an ammonia–acetic acid buffer (pH 7.0)]: Cu^{2+}, 570 nm; 1 : 1, $10.30 \cdot 10^{-7}$; Ni^{2+}, 556 nm; 2 : 1, $2.18 \cdot 10^{-7}$; Co^{2+}, 516 nm; 2 : 1; $0.82 \cdot 10^{-7}$.

1-(1,4-Dimethyl-5-tetrazolyl)-3,5-diphenylformazene (VI), 1-Methyl-1-(1-methyl-5-tetrazolyl)-3,5-diphenylformazan (VII), and 1-(1-Methyl-5-tetrazolyl)-3,5-diphenyl-1,4,5,6-tetrahydro-sym-tetrazine (VIII). A 10-g (0.25 mole) sample of NaOH was added to a solution of 3.06 g (0.01 mole) of II in 100 ml of DMF, and the mixture was stirred for 10 min, after which it was cooled to 0°, and a mixture of 24 ml (0.025 mole) of dimethyl sulfate and 25 ml of DMF were added dropwise at 0-2°. The mixture was allowed to stand for 10 min, after which 120 ml of water was added in the course of 20 min. The resulting orange precipitate was separated to give 2.5 g of a mixture of VI and VII. A 1-g sample of the mixture was refluxed in 50 ml of heptane for 20 min, and the hot mixture was filtered. Workup of the filtrate gave 0.4 g of VIII with mp 153-155°. Two crystallizations from ethanol gave colorless plates with mp 158° and R_f 0.18. UV spectrum in ethanol, λ_{max} (log ε): 234 (4.18) and 298 nm (4.00). IR spectrum: 3170 m (NH), 1630 m, and 1580 cm^{-1} s (C = N, C = C). Found: N 34.7%. $C_{16}H_{16}N_8$. Calculated: N 35.0%.

Workup of the cooled filtrate obtained after isolation of VIII gave 0.5 g of VI as elongated orange prisms with mp 141° (from ethanol) and R_f 0.50. UV spectrum (in ethanol), λ_{max} (log ε): 280 (4.17) and 400 nm (4.60). IR spectrum; 1608 s and 1555 m cm^{-1} (C = N, C = C). Found: C 59.7; H 5.0; N 35.1%. $C_{16}H_{16}N_8$. Calculated: C 60.0; H 5.0; N 35.0%.

A 1-g (3.1 mmole) sample of the mixture of VI and VII was dissolved in 20 ml of glacial acetic acid, 4 g (16.7 mmole) of lead dioxide was added, and the mixture was stirred vigorously for 30 min. It was then filtered, and 40 ml of water was added to the filtrate to precipitate 0.5 g of light-orange elongated prisms of VII with mp 106° (from ethanol) and R_f 0.21. UV spectrum (in ethanol), λ_{max} (log ε): 285 (4.13) and 390 nm (3.85). IR spectrum: 1578 cm^{-1} br (C = N, C = C). Found: N 34.7%. $C_{16}H_{16}N_8$. Calculated: N 35.0%. The filtrate after isolation of VII was concentrated and worked up to give 0.1 g of 2,5-diphenyltetrazole (IV) with mp 101-102° (from alcohol). Tetrazine VIII was obtained in 95% yield by refluxing a 2% solution of VII in heptane.

1-(1-Methyl-5-tetrazolyl)-3,5-diphenylverdazyl (IX). A 2.6-g (11 mmole) sample of PbO_2 was added to a solution of 0.5 g (1.55 mmole) of tetrazine VIII in 35 ml of acetone, after which the mixture was shaken for 10 min and filtered. The filtrate was concentrated and worked up to give 0.45 g (90%) of IX with mp 142° (dark-green plates from acetone) and R_f 0.57. UV spectrum (in benzene), λ_{max} (log ε): 370 (3.82) and 696 nm (3.50). IR spectrum : 1630 s and 1585 cm^{-1} s (C = N, C = C). Found: 35.2%. $C_{16}H_{15}N_8$. Calculated: N 35.1%.

Oxidation of Formazan II in Alkaline Media. Approximately 214 ml (13 mmole) of a 2% solution of $K_3Fe(CN)_6$ was added dropwise to a solution of 2 g (6.5 mmole) of formazan II in 200 ml (100 mmole) of 2% NaOH solution until it became colorless, and the resulting precipitate was separated to give 1.45 g (100%) of 2,5-diphenyltetrazole (IV) with mp 101° (from ethanol) [9]. The filtrate after isolation of IV was evaporated to dryness, and the residue was acidified with concentrated HCl and extracted with acetone. The extract was evaporated to give 0.4 g (61.5%) of 1-methyl-5-hydroxytetrazole (V) with mp 121° (from benzene) [10].

2-(1-Methyl-5-tetrazolyl)-3,5-diphenyltetrazolium Chloride (III). A 5-g (21 mmole) sample of lead dioxide was added to a solution of 1 g (3.3 mmole) of formazan II in 25 ml of acetic acid, and the mixture was stirred vigorously until it became colorless. It was then filtered to remove the sediment, and the filtrate was evaporated. The resinous residue was treated with 40 ml of water, and the mixture was acidifed with concentrated HCl. The precipitated lead salt was removed by filtration, and the filtrate was concentrated to 10 ml and worked up to give 0.9 g (81%) of tetrazolium chloride III with mp 176° (light-yellow prisms from

propanol). UV spectrum (in ethanol), λ_{max} (log ε): 249 (4.49) and 320 nm (3.68) shoulder. Found: Cl 10.6; N 32.5%. $C_{15}H_{13}ClN_8$. Calculated: Cl 10.4; N 32.9%.

Oxidation of 1-(1,4-Dimethyl-5-tetrazolyl)-3,5-diphenylformazene (VI). A 4-g (16.7 mmole) sample of PbO_2 was added to a solution of 1.15 g (3.5 mmole) of VI in 45 ml of acetic acid, and the mixture was shaken for 10 min. It was then filtered to remove the sediment, and half the solvent was removed from the filtrate by distillation. Water (50 ml) was added to the concentrate, and the mixture was worked up to give 0.79 g (99%) of 2,5-diphenyltetrazole (IV) with mp 102°. Evaporation to dryness of the filtrate after isolation of IV led to a resinous unidentifiable solid.

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