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Hetarylformazans†

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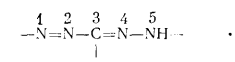
The literature data on the synthesis, structure, and properties of formazans containing heteroaromatic substituents (hetarylformazans) have been reviewed and arranged sytematically. Hetarylformazans have been compared with arylformazans in characteristic reactions such as oxidation to tetrazolium salts, alkylation, and conversion into stable verdazyl radicals. Special attention has been devoted to the coordination chemistry of formazan-containing systems and to the consideration of the characteristic features introduced by hetaryl substituents into the structure of the complexes. Various aspects of the practical applications of hetarylformazans and their derivatives (dyes, bioindicators, ligands, analytical reagents) and the prospects for the development of their chemistry have been examined.
The bibliography includes 221 references.

CONTENTS

I.	Introduction	493
II.	Syntheses of hetarylformazans	493
III.	The structure of formazans	497
IV.	The properties of hetarylformazans	501
V.	Coordination compounds of hetarylformazans	502

I. INTRODUCTION

Formazans[1-5] are compounds with the characteristic azohydrazone group



The compounds unsubstituted in the 1- and 5-positions and also 1,5-dialkylformazans are so far unknown. The 3-position (the *meso*-position) can contain various substituents (hydrogen, alkyl, aryl, hetaryl, halogens, CN, SH, OH, etc.).

Aromatic formazans—1,5-diphenyl and 1,3,5-triphenyl derivatives—were first described by von Pechmann and Bamberger in 1892.[1,2] However, the chemistry of formazans and the tetrazolium salts obtained from them did not begin to develop vigorously until the 1940s when Kuhn and Jerchel[6] found applications for tetrazolium salts in biochemistry and histology as indicators for oxidation-reduction processes. The successful use of formazans as dyes[3,5], ligands in complex formation reactions[7-12], and analytical reagents[5] played an important role in the development of the chemistry of formazan-containing systems.

While arylformazans have been known since the end of the past century, the first representative of hetarylformazans was described in 1951 by Ludolfy[13], who synthesised a $C_{(3)}$-substituted formazan of the pyridine series by combining a diazonium salt with uracil-4-aldehyde. However, this synthesis constituted merely an episode in a series of studies on the preparation of arylformazan derivatives and a series of systematic studies on heterylformazans was initiated by the investigations of Ried and coworkers[14-18]. These studies were stimulated by the search for blue formazans and new tetrazolium salts which might serve as indicators for the investigation of redox processes in blood[17-21]. Subsequently valuable dyes, analytical reagents, ligands, and other practically important compounds were found among hetarylformazans. All these factors led to a considerable development of the chemistry of hetarylformazan systems. During the last fifteen years (mainly in 1963–1972), more than 200 studies were published on the synthesis, physicochemical properties, structure, complex-forming capacity, and analytical applications of hetarylformazans. This review deals with these studies and includes the literature up to 1974.

† We have given the name hetarylformazans to formazans containing heteroaromatic substituents in the 1-, 5-, or 3-positions in the formazan group.

II. SYNTHESES OF HETARYLFORMAZANS

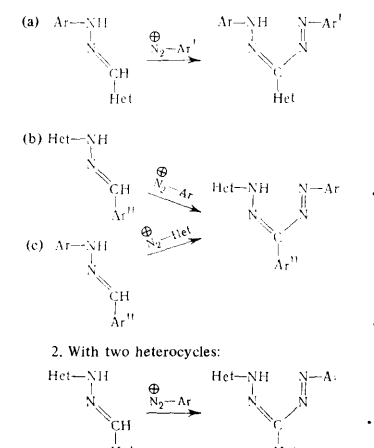
1. The Coupling of Diazo-compounds with Hydrazones (Ried's Method)[1]

The most widely used method for the synthesis of formazans is the coupling of diazonium salts with hydrazones in an alkaline medium[1-5]. Ried developed an amost exhaustive scheme of synthetic pathways for all possible hetarylformazans based on the coupling of aryl- or hetaryl-diozonium salts with various hydrazones (Scheme 1).

Scheme 1

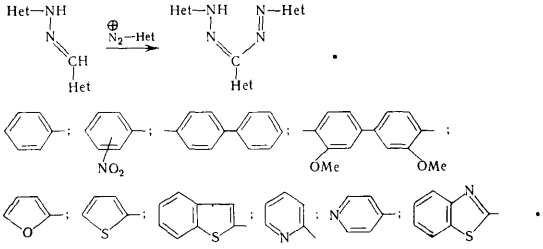
Ried's syntheses of hetarylformazans

1. With one heterocycle:



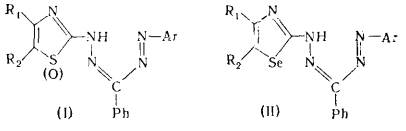
2. With two heterocycles:

3. With three heterocycles:



The syntheses of formazans containing a heterocycle at the meso-carbon atom, i.e. based on heterocyclic aldehydes (method 1 in Ried's scheme), were developed further. Thus, in order to investigate the biological activity of formazan and tetrazolium salts, Cottrell et al.[22] obtained a group of formazans containing 4-pyridyl, 2-furyl, and 2-phenyl-2,1,3-triazolyl substituents in the *mesc*-position. Pyridine derivatives were synthesised to test them as potential antitubercular agents, since there is some structural similarity between 3-pyridylformazans and 5-pyridyltetrazolium salts on the one hand, and isonicotinic acid hydrazide (isoniazide) on the other.

The syntheses of 1-hetarylformazans developed extensively on the basis of Ried's studies (methods 1b and 2 in Scheme 1). Beyer, Pyl, and coworkers[23-26] described 1-azolylformazans containing thiazole, oxazole (I), and selenazole (II) residues. In their study of the properties of heterocyclic hydrazino-derivatives, they synthesised benzylidenehydrazones and then, via coupling the latter with aryldiazonium salts, they obtained formazans. 1-Thiazolylformazans were also obtained by specific synthesis from thiazolyldiazonium salts and aromatic hydrazones:



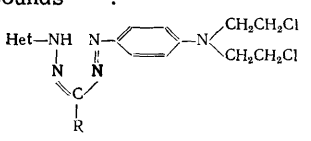
(I) (II)

R_1 and R_2 = H, Me, Ph; R_1 = Ph, Me; R_2 = Ph, COOEt

In the study of formazans of this type, the main aim was the preparation of tetrazolium salts suitable for the investigation in enzymohistology.

In order to study the relation between the structure and properties of formazan-containing systems, 1-(1-alkylbenzimadazol-2-yl)-3-methyl-5-phenylformazans with different substituents in the benzene ring[27], 1-benzothiazolyl- and 1-benzoxazolyl-formazans[28-31], and also derivatives containing tetrazole[32-36], triazole[37], or naphthothiazole[38, 39] residues in the 1-position of the formazan group were obtained.

Heterocyclic formazans containing cytotoxic and bis-(β-chloroethylamino)-groups were obtained as potential antitumour compounds[40-41]:

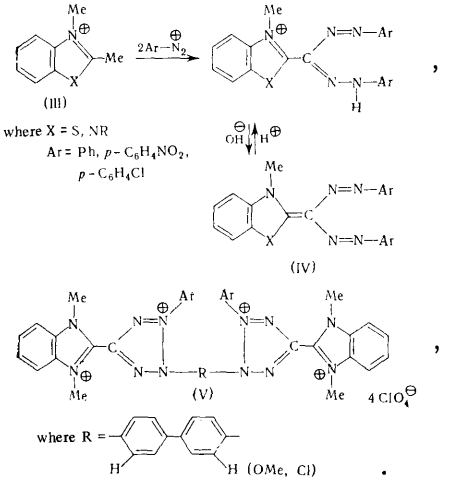


where Het = phenyltetrazolyl, 1-methylbenzimidazol-2-yl, or 1,5,6-trimethylbenzimidazol-2-yl and R = Me or Ph.

To investigate their antibacterial and complex-forming properties, formazans derived from benzimidazole with a sulphamoyl group in the phenyl substituent were synthesised[42]. 1-Benzazolyl-3-methyl-5-phenylformazans containing a sulpho-group in the phenyl residue, introduced to increase the solubility of the compound in water, can be used as analytical reagents[43]. 1-Hetaryl-3,5-diphenylformazans (hetarylthiazoloyl, benzothiazolyl, α-pyridyl, nitropyridyl, and other derivatives) were synthesised and investigated[44-46] as reagents for the determination of a number of metal ions. A series of 1-benzothiazolyl-3,5-diphenylformazans with halogeno-, methyl, and alkoxy-groups as substituents in the 6-position of the heterocyclic ring were synthesised for this purpose[47,48].

2. Azo-coupling with Compounds Containing an Active Methyl Group (the Wahl-Le Bris Method[3])

3-Hetarylformazans can be synthesised not only from aldehydes, but also from heterocycles in which the methyl group has been activated by the quaternisation of the nitrogen atom of the heterocycle[3]. Thus Wahl and Le Bris[49-52] used in the synthesis of 3-benzazolylformazans the quaternary ammonium salts of 2-methylbenzothiazole or 2-methylbenzimidazole (III), which yielded hydrazones (one mole) or "pseudoformazans" (IV) (2 moles) on coupling with diazonium salts. In an acid medium the pseudoformazans exhibited all the properties of formazans, gave rise to deeply coloured chelate complexes with metals, and on oxidation were converted into colourless tetrazolium salts. Bisformazans, obtained by the successive coupling of 1,2-dimethylbenzimidazolium methiodide, initially with phenyldiazonium salts and then with bisdiazobenzidine, had a blue colour and were readily oxidised to colourless bistetrazolium salts (V).[53,54] The authors proposed these salts as histochemical reagents.

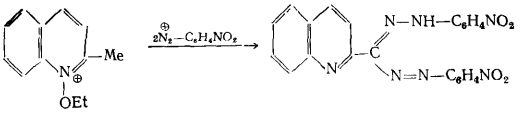


(III) (IV) (V)

where X = S, NR; Ar = Ph, p-$C_6H_4NO_2$, p-C_6H_4Cl

where R = H (OMe, Cl)

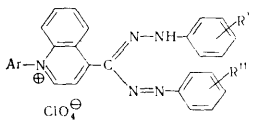
Using the mobility of the hydrogen atoms in the α-methyl groups of the heterocycles (the Porai-Koshits rule), Mishina and Efros[55] obtained a group of 3-hetarylformazans (VI). The quaternary salts of quinaldine or lepidine N-oxide were introduced into the azo-coupling reaction:



(VI)

The ability of the quaternary salts of *N*-oxides to enter into the azo-coupling reaction depends on the structure and basicity of the heterocycle. Thus the quaternary salts of α- and γ-picoline *N*-oxides proved to be incapable of reacting in this way. 9-Methylacridine and its *N*-oxide form only the hydrazone on coupling with diazonitroaniline, while 9-methylphenanthridine is readily converted into 3-phenanthridinylformazan[55].

Pilyugin and coworkers[56-62] synthesised and investigated a series of 3-hetarylformazans (VII). 1-Aryl-lepidinium or arylquinaldinium perchlorates undergo azo-coupling with various diazo-compounds, yielding formazans. On the other hand, the reaction with 1-alkyl-lepidinium salts stops at the hydrazone stage. The structure of the resulting formazans (VII) was demonstrated by the stepwise synthesis of asymmetric formazans (R′ ≠ R″):

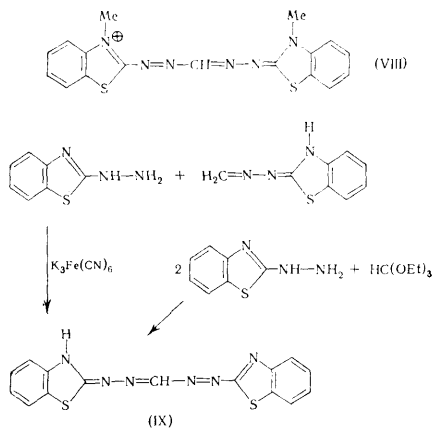


(VII) ,

where R′ and R″ are groups with different electronic effects in the *ortho*-, *meta*-, or *para*-positions.

3. Oxidative Azo-coupling (the Hünig Method[63])

Symmetrical 1,5-dihetarylformazans, which are missing from Ried's scheme, appeared at the beginning of the 1960s. Hünig quotes the synthesis of 1,5-dibenzothiazolylformazan as an example of oxidative azo-coupling. The Hünig reaction is based on the fact that, in an acid medium in the presence of $K_3Fe(CN)_6$ as an oxidant, amidrazone systems (hydrazine derivatives in the hydrazone form) can undergo the electrophilic coupling reaction with azo-components, forming azodyes, or tetraazapentamethine-cyanine dyes (VIII). Numerous studies by Hünig and coworkers, begun in 1957, have been summarised in a review[63]:



In 1963 Hünig[64] obtained the product of the oxidative coupling of 2-hydrazinobenzothiazole and its formaldehyde hydrazone (IX), which was called 1-(benzothiazol-2-yl)-5-(benzothiazolin-2-ylidene)-1,2,4,5-tetraazapenta-1,3-diene. The structure of the compound was demonstrated by a specific synthesis from 2-hydrazinobenzothiazole and orthoformic ester. However, Hünig does not describe studies on the tautomerism and properties of this compound in relation to the properties of formazans and hence its characteristics as a 1,5-dibenzothiazolylformazan.

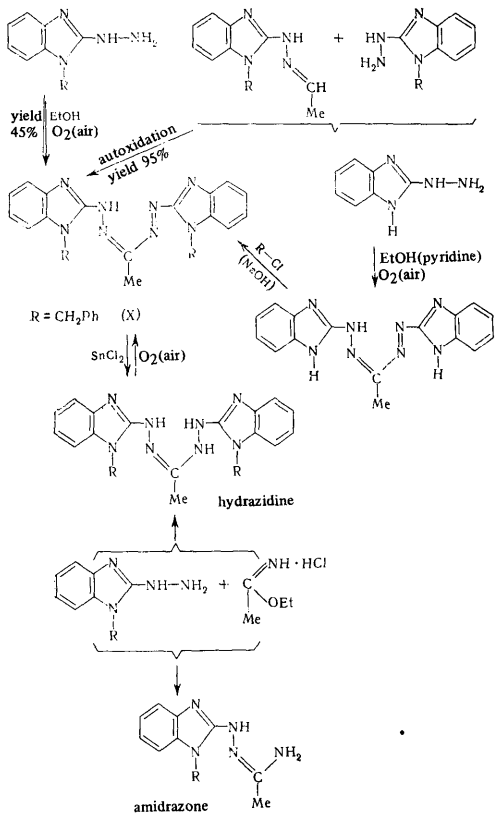
4. Autoxidation of Hetarylhydrazines (the Bednyagina–Postovskii Method[66,70])

Simultaneously with Hünig's studies, the syntheses of 1,5-dibenzimidazoylformazans were described. It was observed in 1960 [65] that alcoholic solutions of 1-alkyl-2-hydrazinobenzimadazoles become dark-violet in air and on standing give rise to large violet crystals of unknown dyes with a green lustre. In the study of the molecular structures of the dyes considerable difficulties arose owing to their ability to form stable solvates with water and alcohol. On varying the 1-alkyl-2-hydrazinobenzimidazoles employed (alkyl = methyl, ethyl, benzyl, or phenyl) and the primary alcohols taken for the autoxidation (methanol, ethanol, and 1-butanol), a series of dyes were obtained. The involvement of the alcohol in the formation of the dye molecule was established and it was shown that the dyes have the structure of the hitherto unknown 1,5-di-(1-alkylbenzymidazol-2-yl)-3-alkylformazans[66]. The autoxidation probably involves several reactions with different mechanisms. Thus oxygen is absorbed rapidly (in the first 30 min) and the colour develops slowly (in 24 h). The rate-limiting stage (the autoxidative coupling) is nucleophilic, since it is catalysed by bases (pyridine) and is inhibited by Lewis acids. Thus, despite its outward similarity to the Hünig reaction, the autoxidation reaction differs significantly from it as regards conditions and mechanism.

The first group of symmetrical 1,5-dibenzimidazolylformazans containing an alkylated or arylated benzimidazole ring was described in 1964.[66,67] 2-Hydrazinobenzimidazole unsubstituted at the nitrogen atom is more acidic and resistant to autoxidation. Formazans based on it can all be obtained by autoxidation in an alcohol–pyridine medium[68]. Formazans unsubstituted at the *meso*-carbon atom have been obtained in two ways to confirm their structure: by autoxidation in methanol and by condensation of hetarylhydrazines with orthoformic ester[66,67]. One of the alkyl-substituted formazans, namely 1,5-di-(1-benzylbenzimidazol-2-yl)-3-methylformazan (X), was obtained by several independent syntheses (Scheme 2), in addition to the autoxidation reaction, which left no doubt about its structure[69,70]. When 1-benzyl-2-hydrazinobenzimidazole was allowed to react with the hydrochloride of acetimidoethyl ether, colourless products—a hydrazidine (in the presence of a deficiency of the iminoether) and an amidrazone (for a 1 : 1 reactant ratio)—were isolated (similarly to the reaction in the series of arylhydrazines[71,72]) in addition to the formazans. It was shown that, the formazan ⇌ hydrazidine oxidation-reduction transitions take place fairly readily.

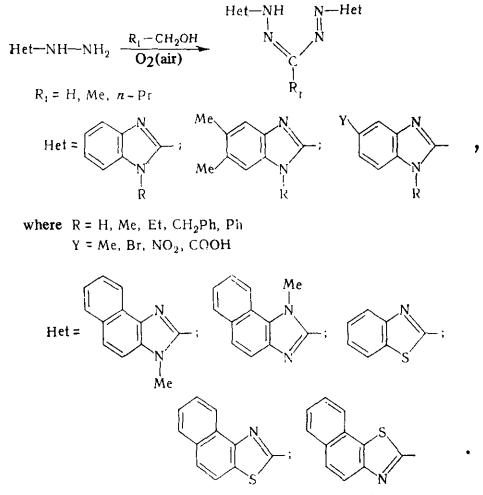
Scheme 2

Syntheses of 1,5-di(1′-benzylbenzimidazol-2′-yl)-3-methylformazan



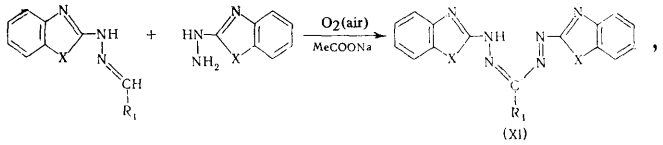
Scheme 3

Synthesis of 1,5-dibenzazolylformazans and 1,5-dinaphthazolylformazans



Other hydrazinobenzazoles or hydrazinonaphthazoles are also capable of spontaneous oxidation and conversion into the corresponding 1,5-dibenzazolylformazans or 1,5-dinaphthazolylformazans (Scheme 3). Thus 2-hydrazinonaphtho[1,2-*d*]imidazole and its 1-methyl- or 3-methyl-substituted derivatives yielded the corresponding 1,5-dinaphthimidazolylformazans in methanol, ethanol, or 1-butanol solutions[73]. 1,5-Di{naphtho[2,1-*d*]thiazolyl}-3-methylformazan was obtained from 2-hydrazinonaphtho-[2,1-*d*]thazole in ethanol[38]. The autoxidation of 2-hydrazinobenzimadazoles substituted in the 5-position proceeds smoothly. 1,5-Di-(1-benzylbenzimazol-2-yl)-3-methylformazans containing methyl, bromo-, methoxy-, nitro-, or carboxy-groups in the benzene rings were obtained in this way[74]. On autoxidation in ethanol, 2-hydrazino-1,5,6-trimethylbenzimidazole or 1-benzyl-2-hydrazino-5,6-dimethylbenzimadazole give rise to beautiful large violet crystals of 1,5-di[1,5,6-trimethylbenzimadazol-2-yl]3-methylformazan or 1,5-di-[1′-benzyl-5,6-dimethylbenzimadazol-2-yl]-3-methylformazan[75,76].

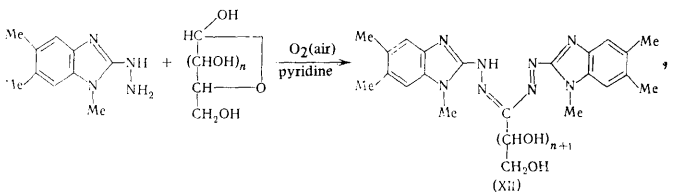
The yields of formazans do not usually exceed 40%. Deeply coloured resins are formed as side products. 1-Alkylbenzimidazoles can be always isolated in 10% yield from the colourless products of the autoxidation of 1-alkyl-2-hydrazinobenzimidazoles. In autoxidation in an alkaline medium (NaOH, pH > 10) nitrogen is evolved and the yield of 1-alkylbenzimidazole rises to 50%. Since 1-alkylbenzimidazolones were not detected among the side products, the formation of an intermediate diazohydrate appears to be unlikely. It is suggested that 2-benzimidazolyldiimine and a hydrazone, produced as a result of the oxidation of the alcohol to the aldehyde, are formed as intermediates[70]. The experimental observation that 1-alkyl-2-hydrazinobenzimidazole and its hydrazone with acetaldehyde, taken in equimolecular proportions, give rise to a formazan in a nearly quantitative yield constitutes convincing proof that the autoxidation reaction proceeds via a stage in which a hydrazone is produced. This reaction was extended to other heterocyclic and aromatic hydrazones. A convenient method for the synthesis of 1,5-dibenzalolylformazans (XI) was developed[77]. It consists in the joint autoxidation of 2-hydrazinobenzazoles with their aldehyde-hydrazones in solution in the alcohol corresponding to the aldehyde to which sodium acetate had been added:



where R_1 = H, Me, or n-Pr and X = NH, NMe, NEt, NCH_2Ph, NPh, or S.

In certain cases it is possible to employ a version of the method which involves the joint autoxidation of the hydrazino-derivative and the aldehyde, without the isolation of the intermediate hydrazone, in pyridine solution.

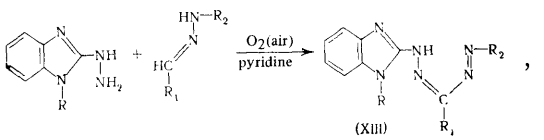
Symmetrical benzimidazolylformazans (XII) containing sugar residues in the 3-position were obtained in this way[78]. The formazans are of interest as structural fragments of vitamin B_{12}:



(XII)

where the sugar is D-ribose, L-arabinose, or glucose.

1-Alkyl-2-hydrazinobenzimidazoles, which undergo autoxidation particularly readily, can undergo autoxidative coupling in pyridine–water solutions with a wide variety of hydrazones, including aromatic hydrazones[79]. Mono-, di-, and tri-hetarylformazans (XIII), including asymmetric formazans, containing various benzazole residues in the 1- and 5-positions (benzimidazole–benzothiazole or benzimidazole–benzoxazole) were obtained in this way:



(XIII)

where R_1 = Me, Ph, or quinoxalin-2-yl and R_2 = Ph, *p*-$C_6H_4NO_2$, benzothiazol-2-yl, benzoxazol-2-yl, or 1-phenyltetrazol-5-yl.

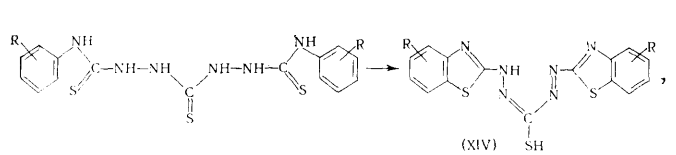
Symmetrical benzazoyl formazans containing the phenyl group in the 3-position were synthesised in the same way[80]. However, autoxidative coupling of 1-benzyl-2-hydrazinobenzimidazole with arylhydrazones of nitroformaldehyde led to the formation of 1-(1-benzylbenzimidazol-2-yl)-5-arylformazans unsubstituted at the *meso*-carbon atom instead of the expected 3-nitroformazans[81].

Thus the syntheses of 1-hetaryl- or 1,5-dihetarylformazans can be based on 2-hydrazinobenzimidazoles, 2-hydrazinobenzothiazoles, or the corresponding naphtho-derivatives, which are all capable of autoxidation. The range of hydrazines capable of autoxidation can probably be extended.

5. Other Methods

Formazans containing non-aromatic heterocycles in the 3-position can be obtained by the introduction of the heterocycle into the finished formazan. Thus, 3-piperidinyl- and 3-morpholinyl-formazans were synthesised from 3-chloro-1,5-diphenylformazan[82] and pyrrolidino-, piperidino-, and morpholino-methyl derivatives were obtained from arylformazans[83] or 1,5-dibenzimidazolylformazans[67] unsubstituted in the *meso*-position.

Pel'kis and coworkers[84,85] obtained 1,5-dibenzothiazol-yl-3-mercaptoformazans (XIV) by the closure of the benzothiazole ring in the almost completed formazan molecule:



(XIV)

where R = H, Me, OEt, or Cl.

The oxidative cyclisation of 1,5-di(phenylthiocarbamoyl) thiocarbonyldihydrazides was carried out in alcoholic alkaline solutions by treatment with potassium hexacyanoferrate(III). The compounds obtained are deeply coloured crystalline substances (λ_{max} = 530–550 nm). They can exist in several tautomeric forms, but on methylation with methyl iodide they give rise to *S*-methyl derivatives. 1,5-Dibenzothiazolyl-3-mercaptoformazan is of interest as the first heterocyclic analogue of dithizone described in the literature.

It follows from the data quoted above that reliable methods have now been developed for the preparation of $N_{(1,5)}$ and $C_{(3)}$-substituted hetarylformazans. Methods involving the coupling of diazo-compounds with hydrazones and the autoxidation of hetarylhydrazines are the most general for the synthesis of hetarylformazans. While the former method is convenient for the preparation of 1(5)-hetaryl- and 1,3-dihetaryl-formazans, the latter can be used to synthesise symmetrical 1,5-dihetarylformazans. At the same time a modification of the second method, making use of the capacity of the readily oxidised hydrazinobenzazoles to undergo oxidative coupling with hydrazones[79], makes it possible to obtain asymmetric formazans, and, what is particularly important, derivatives with various heterocycles in the 1- and 5-positions of the formazan group.

The Wahl–Le Bris and Hünig methods are of limited applicability: the former can be used to prepare $C_{(3)}$-hetaryl-substituted derivatives and the latter is mainly employed for the synthesis of *NN*-dihetaryl-substituted formazans.

Five-membered monoheteraromatic systems (thiophen, furan), six-membered heterocycles (pyridine, quinoline, azines[86,87]), azoles, and their benzo-analogues have been introduced into the formazan group as hetaryl substituents.

III. THE STRUCTURE OF FORMAZANS

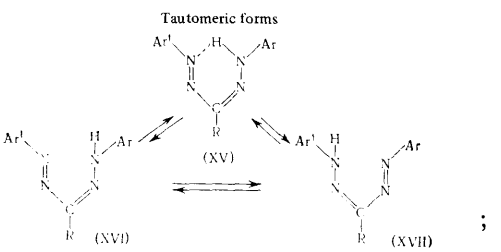
1. Arylformazans

A number of studies have been made on the tautomerism, stereoisomerism, and the state of the hydrogen bond in arylformazans[88–95]. Special studies have been carried out on the infrared spectroscopy of arylformazans[96–106], including a systematic comparative investigation of the infrared spectra of triarylformazans in relation to hydrazones, tetrazolium salts, complexes, and verdazyl radicals[102–104]. The relations between the structure and colour of formazans have been studied[107,108]. Quantum-mechanical calculations on the π-electron systems and the electronic spectra of formazans have been published[109–114].

The isomerism of arylformazans presupposes the existence of three tautomeric (XV–XVII) and four stereoisomeric (XVIII–XXI) forms (*cis-trans* with respect to the N–N bond and *syn-anti* with respect to the C–N bond) (Scheme 4).

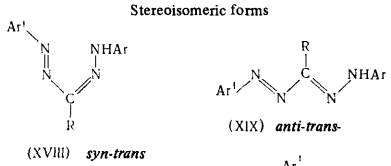
Scheme 4

Tautomeric forms



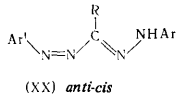
(XV) (XVI) (XVII)

Stereoisomeric forms

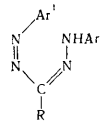


(XVIII) *syn-trans*

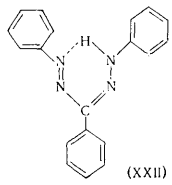
(XIX) *anti-trans-*



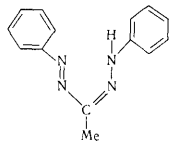
(XX) *anti-cis*
(R = Ph; Me; H)



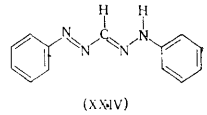
(XXI) *syn-cis*



(XXII)



(XXIII)



(XXIV).

The structure of the formazan chain is influenced significantly by the substituent R in the *meso*-position. The phenyl group usually promotes the fixation of the chelate form. The alkyl substituent (other than t-butyl[115]) weakens the hydrogen bond and leads to the opening of the chelate ring, while hydrogen stabilises the *anti-trans*-structure.

Triphenylformazan has a quasiaromatic chelate ring (XXII) with a strong intramolecular hydrogen bond[88,93,94,116], which is confirmed by the absence of the ν(NH) band in the region 2500–3200 cm^{-1} from the infrared spectra of both crystals and solutions.

The ring is so stable that it is not opened even in alkaline medium although the introduction of a nitro-group in the 1- or 5-position in the phenyl group leads to a weakening of the intramolecular hydrogen bond, which is manifested in a capacity to be converted into the sodium salt[108]. The (XVI) $\rightleftharpoons$ (XVII) tautomerism of such asymmetric formazans has been demonstrated by an isotopic method[117].

3-Methyl-1,5-diphenylformazan has an "open" structure, is more coloured than triphenylformazan [λ_{max} = 430 nm for (XXIII) and 494 nm for (XXII)], its infrared spectrum contains the ν(NH) band (3360 cm^{-1} in chloroform), and it readily forms a sodium salt in solution[2]. According to Zeif et al.[111], it has the *cis-trans*-configuration in solution without an intramolecular hydrogen bond [structure (XXIII)].

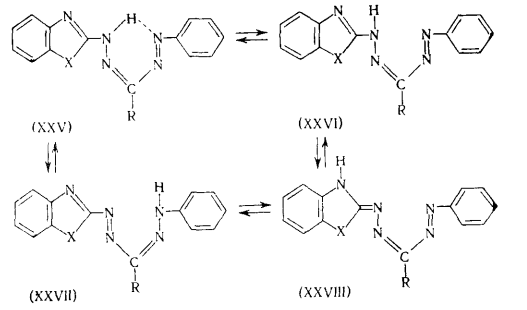
The configuration of the molecule and the nature of the hydrogen bond in diphenylformazan were recently determined by X-ray diffraction[118]. It was found that in the crystalline phase diphenylformazan has an open *anti-trans*-structure with intermolecular hydrogen bonds; according to other data[110,111], diphenylformazan retains the *anti-trans*-structure (XXIV) also in solutions.

Triphenylformazan has the chelate *syn-trans*-structure (XXII) both in solutions and apparently in the crystalline state. This is indicated by the experimental hydrogen bond energies[119] (7 kcal $mole^{-1}$ for triphenylformazan and 2.7 kcal $mole^{-1}$ for diphenylformazan) determined experimentally from the heats of combustion and also from the electronic spectra[111] and the calculation of the energy of the stabilisation of the ring by the hydrogen bond in solution (8.7 kcal $mole^{-1}$).

2. Hetarylformazans

The structure of 1-benzazolylformazans has been studied systematically in the series of hetarylformazans[27-31,108-112,120-122]. The number of possible tautomeric and isomeric forms in the series of hetarylformazans is greater than in the aromatic series. Thus the tautomeric forms (XXV)–(XXVIII) (Scheme 5) are possible for the asymmetric 1-benzazolyl-5-phenylformazans. On the other hand, the number of theoretically possible stereoisomers increases to 16 (on the assumption that the molecule is coplanar). Among these, account has been taken[110,111] of the most probable *syn-trans*- (with or without allowance for the intramolecular hydrogen bond) and linear *anti-trans*-structures.

Scheme 5



(XXV) (XXVI) (XXVII) (XXVIII).

The state of tautomeric equilibrium involving benzazolylformazans depends both on the *meso*-substituent and on the nature of the heterocycle (acidity, basicity, aromaticity) (Table 1).

Table 1. Spectroscopic characteristics and acid pK_a values of 1-benzazolyl-3-R-5-methylformazans.

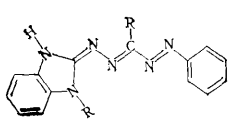
Compound	X	R	ν(NH), cm^{-1} (in CCl_4)	λ_{max}, nm (in n-heptane)	pK_a
(XXIX)	N—$CH_2C_6H_5$	Me	3450	452	12.5
(XXX)	N—$CH_2C_6H_5$	Ph	3445	454	12.1
(XXXI)	S	Ph	absent	492	11.1
(XXXII)	O	Ph	absent	475	11.2
(XXXIII)	S	Me	3450; 3360	445	9.1
(XXXIV)	O	Me	3450; 3370	415	9.7

The ν(NH) bands in the infrared spectra have been assigned on the basis of experimental[109,120] and calculated[110] (Hückel's molecular orbital method) data [correlation between π-electronic charge on the nitrogen atom linked to the proton and the ν(NH) wavenumber]: the high-frequency band (~3450 cm^{-1}) was assigned to the imino-form (XXVIII) and the low-frequency band [~3360 cm^{-1}, coinciding with ν(NH) for 3-methyl-1,5-diphenylformazan] was assigned to the amino-form (XXVI). The ν(C=N) infrared bands, with wavenumbers in the range 1510–1630 cm^{-1} for the chelate forms of formazans and 1555–1580 cm^{-1} for the open-chain forms[103,110,112], are also striking [following Kukushkina et al.[105] these bands were assigned to ν_{as}(–N=C–N)].

The long-wavelength band in the visible spectrum in the range 400–500 cm ($\pi \rightarrow \pi^*$ transition) constitutes a convenient criterion for the comparison of the structures of formazans. In the series of benzazolylformazans the chelate forms (XXXI) and (XXXII) have a deeper colour to the extent of 50–60 nm (Table 1) than the corresponding open-chain forms (XXXIII) and (XXXIV). It has been established[110,111] that in the spectra of formazans with the *anti-trans*-configuration this band exhibits a higher extinction, although it is displaced towards shorter wavelengths compared with the chelate forms.

Calculations (by the Pariser–Parr–Pople method) on the π-electron system of formazans (XXIX)–(XXXIV),[111,112] comparison of the experimental and calculated spectra (the energies and oscillator strengths of various electronic transitions), and the determination of the relations between the reactivity indices, the spectra, and the properties of formazans led to the following conclusions.

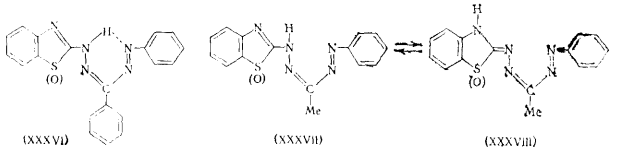
(a) Regardless of the *meso*-substituent, 1-benzimidazolyl-3-methyl(phenyl)-5-phenylformazans (XXIX) and (XXX) have (in heptane, dioxan, and carbon tetrachloride) the open-chain imino-structure and the *anti-trans* chain configuration (XXXV).



(XXXV)

The exceptional behaviour of 1-benzimidazolylformazans (the lack of an effect of the *meso*-substituent on the tautomeric shift) has been explained by the greater basicity of benzimidazole and a tendency towards the transition to imino-systems with an exocyclic double bond.

(b) Benzothiazolyl- and benzoxazolyl-formazans (XXXI)–(XXXIV) exhibit the behaviour discovered in the series of arylformazans, i.e. compounds (XXXI) and (XXXII) with a phenyl substituent in the *meso*-position have a chelate structure, like triphenylformazan. In heptane they assume the *syn-trans*-amino-configuration (XXXVI) with a weak intramolecular hydrogen bond, which dissociates even as a result of the solvating action of solvents [ν(NH) = 3200 cm^{-1} in dioxan]. A *syn-trans*-configuration with a rapid proton transfer and equilibrium between the amino- and imino-forms (XXXVII) $\rightleftharpoons$ (XXXVIII), is characteristic of the formazans (XXXIII) and (XXXIV) with the methyl group in the *meso*-position in heptane or carbon tetrachloride solutions:



(XXXVI) (XXXVII) (XXXVIII)

The changes in acidity[120] are consistent with the above conclusions. As was to be expected, the benzimidazolylformazans (XXIX) and (XXX) have pK_a values of the same order of magnitude (Table 1). In the series of benzothiazolyl- and benzaxolyl-formazans (XXXI)–(XXXIV) the proton mobility depends on the *meso*-substituent. Hydrogen bound in the intramolecular hydrogen bond is less mobile and the chelate formazans (XXXI) and (XXXII) differ from the non-chelate forms (XXXIII) and (XXXIV) by having an acid strength weaker by one–two orders of magnitude (Table 1). The *meso*-substituent has similar effects on the structure of the formazan chain in 5-aryl-1-(1-phenyltetrazolyl)formazans[32,35] and 1-naphthothiazolyl-5-phenylformazans[38,39]

The influence of the nature of the heterocycle on the colour of 1-hetarylformazans is different in the series of "open-chain" and chelate structures[70]. The colour of the "open-chain" 1-benzazolyl-3-methyl-5-phenylformazans (in benzene or heptane) depends on the basicity of the heterocycle, while in chelate formazans the determining factor is the aromaticity of the heterocycle. Formazans with the chelate structure have in general a deeper colour than those with an "open-chain" structure (Tables 1 and 2).

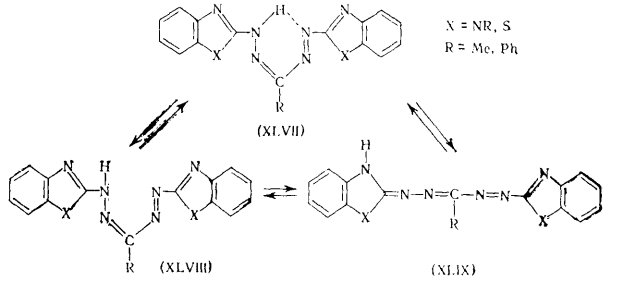
Table 2. Characteristics of 1-benzazolyl-3-R-tolylformazans.

Compound	R	X	Tolyl	M.p., °C	ν(NH), cm^{-1} (in CCl_4)	λ_{max}, nm (in alcohol)
(XXXIX)	Me	NCH_2Ph	*para*	121—124	3445	460
(XL)	Me	NCH_2Ph	*ortho*	85—87	3445	456
(XLI)	Me	S	*para*	136—137	3435; 3340	414
(XLII)	Me	S	*ortho*	81—87	3435; 3340	414
(XLIII)	Me	O	*para*	115—116	3440; 3355	400
(XLIV)	Me	O	*ortho*	80—82	3440; 3355	400
(XLV)	Ph	S	*ortho*	195—198	3425	470
(XLVI)	Ph	O	*ortho*	182—184	3421; 3321	432

The *ortho*-substituent in the benzene ring (methyl[30], halogen[31]) does not affect the structure of the formazan chain in the series of "open-chain" 3-methyl-substituted derivatives. Thus the *ortho*- and *para*-isomers of 1-benzazolyl-3-methyl-5-tolylformazans are spectroscopically indistinguishable (Table 2). However, steric hindrance by the *ortho*-substituent affects the complex-formation reactions[30] or the conversion into tetrazolium salts[31]. In contrast to this, in the series of chelate 3-phenylformazans the steric hindrance of the *ortho*-substituent is clearly manifested in the opening of the chelate ring of (XLV) and (XLVI).[123] The naphthyl residue has an effect similar to that of the *ortho*-tolyl substituent[123].

The introduction of an electron-donating (NMe_2) or an electron-accepting (NO_2) substituent into the *para*-position of the benzene ring has a particularly marked influence on the structure and colour of formazans[124]; a bathochromic effect is observed in both cases.

In the series of symmetrical 1,5-dibenzazolylformazans three tautomeric forms are possible: the chelate form (XLVII) and the "open-chain" amino-form (XLVIII) and imino-form (XLIX):

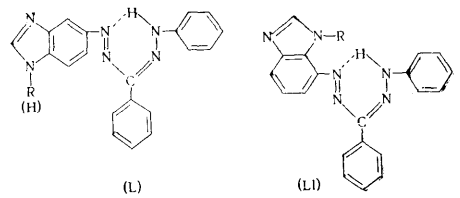


(XLVII) (XLVIII) (XLIX)

Regardless of the substituent in the 3-position (methyl, phenyl), the tautomeric imino-form of 1,5-dibenzimidazolylformazan (XLIX) has been detected in solutions [ν(NH) = 3420 and 3468 cm^{-1} in chloroform].[80] The infrared spectra of benzothiazolylformazans do not contain the ν(NH) band and they probably have the chelate structure (XLVII). Thus in the series of both symmetric and asymmetric

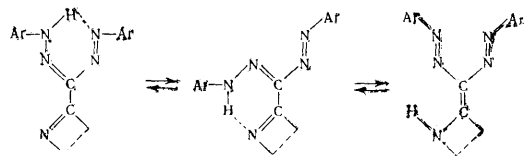
formazans benzothiazolyl derivatives exhibit a greater tendency towards the formation of chelate forms, while benzimidazolyl derivatives tend to form the open-chain imino-forms. The alkyl groups in the benzimidazole ring as well as those at the *meso*-carbon atom of 1,5-dibenzimidazolylformazans do not have a significant influence on the structure and colour of the formazan[66,125]. The mobility of the proton in these formazans is greater than in the asymmetric compounds (pK_a = 9.5–10.5). They are amphoteric and also exhibit a considerable basicity (pK_a = 4–5). The contribution of the imino-form with a cyanine chain is also responsible for the greater dipole moment of 1,5-di-(1-benzylbenzimidazol-2-yl)-3-methylformazan (4.9 D) compared with 1-(benzylbenzimidazol-2-yl)-3-methyl-5-(*p*-tolyl)formazan (2.7 D) or the chelate triphenylformazan (1.73 D).[70,126]

The structure of hetarylformazans in which the benzazole ring is not involved in tautomeric transformations is analogous to that of arylformazan derivatives. 1-(Benzimidazol-5-yl)-3,5-diphenylformazan (L) and 1-(1-benzylbenzimidazol-7-yl)-3,5-diphenylformazan (LI) have a chelate structure like 1,3,5-triphenylformazan (XXII).[127,128]



The replacement of the phenyl group in the *meso*-position by the methyl group leads to the opening of the chelate ring. When the benzimidazole ring is unsubstituted, the hydrogen atom attached to the pyrrole nitrogen atom can participate in intermolecular hydrogen bonds (L, R = H) and can form an intramolecular hydrogen bond with a nitrogen atom of the formazan group (LI, R = H).[128]

The tautomerism and isomerism in the series of 3-hetarylformazans has not been studied. Nevertheless in this case too there is a possibility of the existence of a series of tautomeric forms, for example:



The –N=C– fragment can form part of the pyridyl, benzazolyl, or another heterocyclic substituent with a "pyridine" nitrogen atom.

3-Benzothiazolyl-1,5-diphenylformazan does not form a sodium salt and the spectra of its solutions do not contain the ν(NH) band[29,122,129]. The data quoted, although limited, confirm that 3-hetarylformazans do not belong to systems with rapid proton transfer and in all probability give rise to chelate forms.

Thus the structure and tautomerism of hetarylformazans are mainly determined by the mode of fixation and position of the heterocyclic substituent in the formazan ring. 2-Benzazolylformazans are involved in complex tautomeric transformations, in which the state of equilibrium depends not only on the nature of the *meso*-substituent, but also on the nature and properties (basicity, acidity, and aromaticity) of the heterocycle. Similar features should probably be observed also for hetarylformazans, containing azoles and six-membered heteroaromatic systems (pyridines, azines, etc.) as the heterocyclic substituents, while the structure of hetarylformazans derived from five-membered systems with one heteroatom (furan, thiophen, pyrrole, and their benzo-analogues) should be close to those of arylformazans. However, there are virtually no experimental data concerning the tautomerism of these types of hetarylformazans.

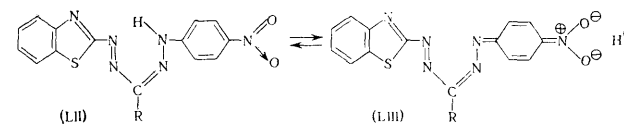
3. Photochromism and Thermochromism

Aryl- and hetaryl-formazans can in many cases isomerise by photoinduction or thermoinduction with proton transfer, which entails a change in the chromophoric system and the colour of the compound. The photochromism of arylformazans has been described by Kuhn and coworkers[89–94]. When a benzene solution of triphenylformazan is illuminated with visible light, the red chelate *syn-trans*-form (XV) (λ_{max} = 495 nm) undergoes reversible isomerisation to the yellow *anti-trans*-form (XIX) (406 nm). The transformation proceeds via the unstable *syn-cis*-form (XXI) and *anti-cis*-form (XX). Negative red-yellow photochromism of this type has also been observed for benzene solutions of compounds (L), which are analogues of triphenylformazan[127].

The photochromism of 1-benzimidazolyl-5-phenylformazans (XXIX) and (XXX), which occurs in chloroform or carbon tetrachloride solutions, is of a different type[120,130]. Here positive red–blue photochromism with a large (up to 200 nm) bathochromic photoinduction effect is observed. The reverse dark transition is difficult, but the initial form can be quantitatively isolated when a more polar solvent is added to the chloroform solution of the blue form. The ease of the reconversion into the initial formazan, the change in the nature of the infrared spectrum of the irradiated form, and steric hindrance by the *ortho*-substituent in the 5-phenyl group suggested[120] that photoinduction is accompanied by intermolecular proton transfer and the formation of dimeric structures.

The photochromism of mercury and zinc dithiozonates, which has been described[131,132], can also be accounted for by a change in the chromophoric system of the ligand (isomerisation and proton transfer). The isomerisation of the formazan chain similarly explains the photochromism of 5-alkyldithizones[133,134].

Substances exhibiting both negative[135,136] and positive[135,137] thermochromism have been found among the benzazolylformazans. The group of 1-benzothiazolyl-5-nitrophenylformazans (LII) has been studied in greater detail:



It has been established that the repeated reversible thermochromic transitions of alcoholic solutions from the initial red form (LII) to the thermally induced blue form are due to dissociation and conversion into the anionic form (LIII), whose spectrum is identical with that of the sodium salt of the formazan. The formazan with R = Me has pK_a = 8.20 and therefore in aqueous and alcoholic solutions (pK_a = 8.15) dissociation proceeds readily as a result of thermoinduction. The formazans with R = Ph

and $CHMe_2$ are less acidic (pK_a = 8.94 and 9.53) and therefore they exhibit thermochromism in buffer solutions at pH values close to the pK_a of the formazans.

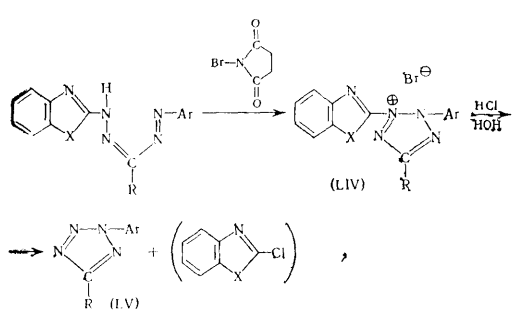
IV. PROPERTIES OF HETARYLFORMAZANS

The characteristic reactions of formazans (reversible oxidation-reduction transitions to tetrazolium salts, alkylation and conversion into verdazyl radicals, and salt and complex formation with metal ions) proceed in a specific manner in the series of hetarylformazans. 1(5)-Hetaryl- and 1,5-dihetaryl-formazans are much more labile and reactive than aryl- or 3-hetarylformazans. 1,5-Dihetarylformazans exhibit a tendency towards transitions to cyanine systems.

1. Oxidation to Tetrazolium Salts

The only method for the preparation of tetrazolium salts is oxidation of formazans. In the series of hetarylformazans the oxidation and formation of tetrazolium salts of 3-hetarylformazans has been most thoroughly investigated[1,6]. Since the stabilities of these formazans and their tetrazolium salts are comparable to those of aromatic compounds, it is possible to employ here the same oxidants, namely mercury(II) oxide, isopentyl nitrite, and lead tetraacetate. A convenient method for the oxidation by nitric acid has been proposed for 3-arylquinaldinium- and 3-aryllepidinium-formazans (VII).[58]

The oxidation-reduction properties of 1-hetarylformazans and their tetrazolium salts have so far been inadequately investigated. Owing to the instability of these formazans in an acid medium, their conversion into tetrazolium salts is carried out by Kuhn's method[138] under the influence of bromosuccinimide. Tetrazolium salts derived from thiazolyl-, oxazolyl-, and selenazolyl-formazans[24,25] and also from 1-benzozolylformazans[29,31,139] were obtained in this way. They differ from aryltetrazolium salts (LIV) by their instability, which becomes more pronounced with increase of the electronegativity of the heterocycle (on going from benzothiazole to benzoxazole). Benzoxazolyltetrazolium bromides have not been isolated at all: they are immediately cleaved with formation of 2,5-disubstituted tetrazoles[29,123] (LV). The more stable benzothiazolyltetrazolium bromides[123] and benzimidazolyltetrazolium bromides[140] are readily cleaved in acid hydrolysis, yielding the same disubstituted tetrazoles and 2-chlorobenzazoles (isolated in the case of benzimidazole[140]):

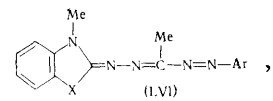


where R = Me of Ph, Ar = Ph or $\alpha(\beta)$-naphthyl, and X = NMe, S, or O.

Symmetrical, 1,5-dibenzimidazolylformazans are readily brominated by bromosuccinimide[139], but instead of tetrazolium salts they probably form bromoamines, which are themselves capable of brominating toluene or acetone.

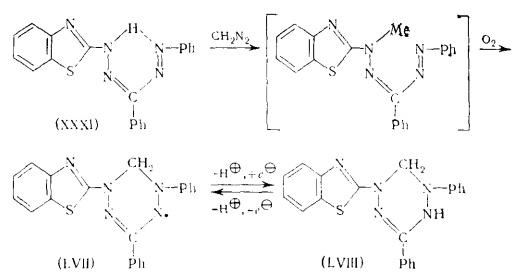
2. Alkylation and Preparation of Verdazyl Radicals

Methylation of 5-aryl-1-benzazolyl-3-methylformazans by methyl iodide in an alcoholic alkaline medium with the aim of investigating the tautomeric shifts and reactivities of asymmetric hetarylformazans led[141,142] to the formation of methyl derivatives (LVI) containing the methyl group in the benzazole ring, i.e. to the fixation of the tautomeric imino-form:



where X = NR, S, or O.

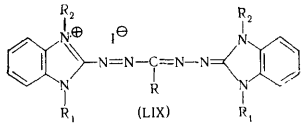
In the light of the studies of Kuhn and coworkers[143,144] and Neugebauer and coworkers[145,146] on the oxidative methylation of triarylformazans and the formation of deeply coloured stable free radicals (verdazyl radicals), the methylation of chelate hetarylformazans is of special interest. However, it was found that in the series of hetarylformazans capable of the amine–imine tautomerism, the possibility of the formation of verdazyl radicals is limited. Thus methylation of compounds (XXXI) and (XXXII) by methyl iodide yielded[142] the methyl derivatives (LVI). Only in the case of compound (XXXI), i.e. the formazan with the most aromatic heterocycle (benzothiazole) was it possible to obtain a crystalline dark-green paramagnetic substance by methylation with a benzene solution of diazomethane and autoxidation in air. Analysis, spectra (ESR and ultraviolet), and properties [capacity for the leuco-base (LVIII) ⇌ verdazyl (LVII) oxidation-reduction transitions] confirmed the structure of the compound as 1-benzothiazolyl-3,5-diphenylverdazyl (LVII):



Presumably, wider possibilities for the synthesis of verdazyl radicals will become apparent also in the series of 3-hetarylformazans or hetarylformazans in which the heterocycle is not involved in tautomerism [compounds (L) and (LI)].

Alkylation of symmetrical 1,5-dibenzimidazolylformazans proceeds in an altogether different manner. When the formazan is acted upon by an alkyl iodide in dimethylformamide, well-crystallised deeply coloured (violet) substances are formed, analysis of which shows them to be the iodides of the alkyl derivatives, while their spectra in

the visible region hardly differ from those of the hydrochlorides of the same formazans. It has been established[141] that these products are tetraazapentamethinecyanines derived from benzimidazole (LIX) and resemble Hünig's azacyanines (VIII):[69]

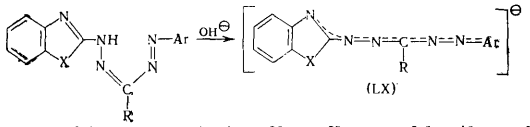

(LIX)

where R = H or Me and R_1 and R_2 = Me, Et, or CH_2Ph.

3. Acid-Base Properties and Capacity for Complex Formation

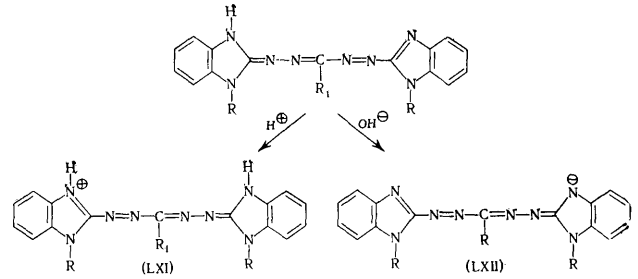
Benzazolylformazans are much more amphoteric than arylformazans. Their basicity increases owing to the presence of the benzazole ring (the "pyridine" nitrogen atom) and the acidity increases owing to tautomerism.

Like arylformazans, asymmetric 1-benzazolylformazans are unstable in acid media, where, after a deepening of the colour (conversion into the cation), the solution undergoes a reversible decolorisation after several minutes (cleavage, oxidation)[70]. Formazans are stable in alkaline media. The conversion into the aryl (LX) is accompanied by a bathochromic shift due to salt formation, which depends on the structure of the formazan. For each formazan, the pH at which the proton is abstracted can be readily determined spectrophotometrically (the most convenient method for the determination of approximate values of pK_a).


(LX)

The colour of the anion is hardly influenced by the substituent R in the *meso*-position. But, since the initial formazans (derived from benzothiazole and benzoxazole) have different colours depending on the *meso*-substituent, the bathochromic effect of the abstraction of a proton from the more deeply coloured chelate formazans (R = Ph) is smaller (50–60 nm), while for the "open-chain" (R = Me) compounds it is greater (100–110 nm). The colour of the anion is determined by the nature of the heterocycle (X = NR, 530–540 nm; X = S, 516–520 nm; X = O, 490–500 nm). The substituents in the benzene rings of the phenyl groups have different effects on the colour of the anion: the sulpho-group (in both *meta*- and *para*-positions) hardly alters the colour[43], while the nitro-group causes a sharp bathochromic shift[124]; the ortho-effect of substituents (methyl, halogen) is not shown[30,31].

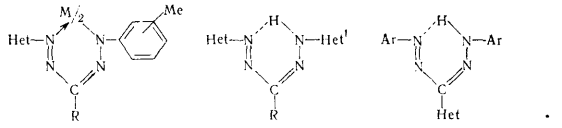
The symmetrical 1,5-dibenzimidazolylformazans are stable over a wide pH range. They form well-crystallised salts with both hydrogen halides (monohydrohalides) and with sodium hydroxide (monosodium salts)[147]. The similarity of the absorption spectra in the visible region of the hydrochlorides and sodium salts is striking. When formazans (λ_{max} = 530–540 nm) are converted into salts, a bathochromic shift of the absorption band maximum, an increase in its intensity, and its splitting are observed (570–580 and 600–610 nm for the cation and 560–570 and 600–614 nm for the anion). It has been established[125,147] that these formazans behave in salt formation like cyanine bases and on addition or abstraction of a proton are converted into systems analogous to the onium (cation) or acihalochromic (anion) cyanine dyes. The similarity of the structures of the cation (LXI) and the anion (LXII) is responsible for their identical colour.


(LXI) (LXII)

The formation of complexes by 1-hetaryl- and 1,5-dihetaryl-formazans with metal ions of the 3-α-series in aqueous organic solutions proceeds just as readily as salt formation. The large bathochromic effect (100–200 nm), high sensitivity, and virtually instantaneous complex formation make these formazans (particularly benzazolylformazans) promising reagents for spectrophotometry. By varying the heterocyclic residues in the formazan molecule or by introducing additional complex-forming groups, it is possible to influence the selectivity of the ligand, the bathochromic shift, and the stability of the complex.

V. COORDINATION COMPOUNDS OF HETARYLFORMAZANS

The capacity for the formation of complexes with metals is virtually the most characteristic property of formazans. The interaction of hetarylformazans with metals leads to the formation of molecular complexes or chelate complexes with an MN_4 coordination unit. The latter has been attracting continued attention not only owing to the specific action of the ligand environment on the stereochemistry of the polyhedra of the complexes but also owing to its exceptional role in biologically important objects[70,148–153].


(LXIII) (LXIV) (LXV)

The molecular complexes $MCl_n.mL$ (n = 2 or 4, m = 1 or 2, L = formazan; M/2 can be also a hydrogen atom) were synthesised by the interaction in the cold between metal chlorides and 1(5)-hetarylformazans in acetone (MX_2) or carbon tetrachloride (MCl_4).[156] At the same time molecular complexes of $C_{(3)}$-hetarylformazans (LXV) with cobalt(II) chloride have been isolated[129] from hot ethanol. This solvent, together with acetone and dimethylformamide, has been widely used to prepare metal chelates[152–155,157–173].

The choice of salts for the synthesis of chelate complexes depends on the complex-forming metal: for copper(II), cobalt(II), and zinc(II), the best result was achieved when chlorides were employed, and for nickel, nitrates were most successful. On the other hand, bearing in mind the continued applications[148,152,153] in the synthesis of different classes of chelate complexes the method based on the interaction of metal acetates in ethanol or methanol, it should be recommended for wide-scale employment also in the synthesis of metal chelates

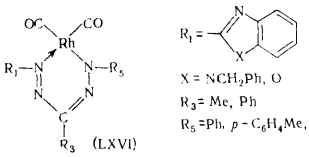
derived from formazans. We see the advantages of this method, which has already been used in a few instances[155,174] in a series of formazan-containing systems and yielded satisfactory results, also in the possibility of avoiding the formation of molecular adducts of the type $M(L-H)_2.nMX_2$, which accompanies the formation of copper chelates[162]. The formation of adducts greatly complicates the isolation of pure $Cu(L-H)_2$ complexes and requires repeated crystallisation of $Cu(L-H)_2.nCuCl_2$ from aqueous pyridine[162]. In this case pyridine apparently play the role not so much of a solvent as of an effective complex-forming agent:

$$Cu(L-H)_2 \cdot n\,CuCl_2 + n\,C_5H_5N \rightarrow Cu(L-H)_2^{+}\,n(C_5H_5N \rightarrow CuCl_2)\ .$$

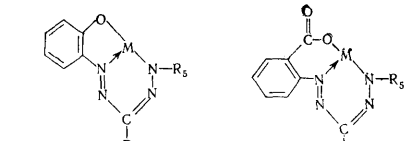
The type of complex (molecular or chelate) depends on the nature of MX_n and the conditions of synthesis.

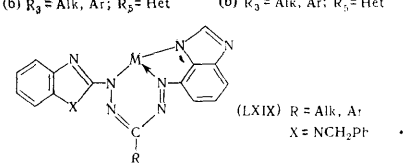
The tetrachlorides of Group IV metals form the molecular complexes $MX_4.L_n$ (n = 1 or 2).[156] Cobalt[129] and zinc[155] dichlorides give rise to complexes of a similar type under mild conditions. Bivalent transition metal and uranyl nitrates and acetates tend to form preferentially metal chelates of the type $M(L-H)_2$ or $M(L-H_2)$. At the same time, depending on the conditions of the synthesis, it is possible in a few instances to obtain complexes of both types indicated above for the same MX_n. Thus zinc chloride forms not only molecular complexes but also chelate complexes (in aqueous acetone or aqueous alcoholic media at pH in excess of 7).[70,155]

Complexes with mixed ligands may occupy a special place among formazan complexes. So far there has been only one report on this subject: dicarbonylhetarylformazanrhodium complexes (LXVI) were synthesised and their infrared absorption spectra were obtained[175].

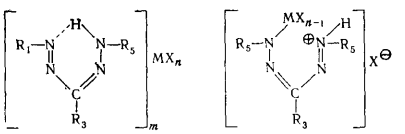


In most cases the molecular complexes have the composition $MX_n.L$ [129,153,155,156] (with the exception of the complexes of tin tetrachloride—$SnCl_4.2L$),[156] while the metal chelates have the composition $M(L-H)_2$.[152-156,162,163,166-168,174,176-178] However, an extremely characteristic feature of hydroxy- and *o*-carboxy-hetarylformazans, like that of 1-(benzimidazol-2-yl)-5-(benzimidazol-4-yl)formazan derivatives, is the formation, together with 2:1 chelate complexes[129,157-160,164,176], of 1:1 metal chelates $(ML-H)_2$ [129,157,164,165,169,172,173] [compounds (LXVII)–(LXIX) respectively].

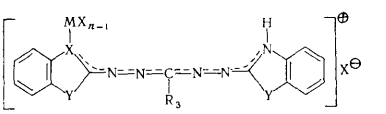




The structure of the molecular complexes was studied mainly by spectroscopic methods[70,153,155,156], while that of metal chelates was investigated in addition by the dipole moment and magnetochemical methods[153,163,166,168,174,177,178]. The compositions $MX_n.L$ and $MX_n.2L$ do not by themselves indicate the nature of the complexes formed, since ionogenic compounds such as the salts (LXXI) or the cyanines (LXXII) can have the same elemental composition as the products (LXX) of the addition of MX_n to formazans[156].



m = 1, 2; n = 2, 4;
M = Ti, Sn, Zn



Y = O, S, NR; M = Ti, Sn, Zn; X = Cl

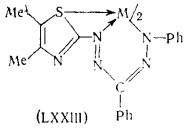
The choice between the above structures in favour of (LXX) [156] for MCl_4 and (LXXII) [155] for $ZnCl_2$ was based on ultraviolet and infrared spectroscopic data and dipole moments. The infrared spectra of $MCl_4.L$ and $MCl_4.2L$ do not contain the absorption bands of the immonium group (NH^+), which would have been expected for the ionic structure of (LXXI). The dipole moments of the compounds (8–10 D) also support molecular complexes of type (LXX).[156] On the other hand, the $ZnCl_2$ complexes with bisazolylformazans have ultraviolet spectra resembling those of the hydrochlorides and sodium salts of the initial formazans (two maxima in close proximity in the spectrum).[155] This factor suggests that the structure of $ZnCl_2.L$ is analogous to that of the cyanine dyes (LIX).[147,155]

Hetarylformazans are ambident systems[179,180], containing several potential electron-donating centres: the nitrogen atoms of the formazans and azole rings and the O and S atoms of the benzothiazole and benzoxazole rings respectively. Therefore in the study of the molecular complexes (LXX) the problem of the location of the coordinate bond in the hetarylformazan system (competitive coordination) was solved[179]. In agreement with the results of quantum-chemical calculations[112], the infrared spectra[156] led to the conclusion that MX_n is coordinated to the $N_{(3)}$ atom of the azole fragment, and, in complexes having the composition $2TiCl_4.L$, to the $N_{(2\ or\ 4)}$ atom of the formazan ring[156].

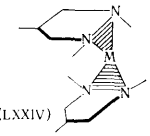
A square planar configuration is most characteristic of the chelate complexes of bivalent metals with the MN_4 coordination unit, to which the metal chelates of hetarylformazans also belong[148,152,181-184]. However, it has been shown for the chelate complexes of hetarylformazans[153,163,166-168,174,177,178] that the metal chelates with an MN_4 coordination unit can also have a non-planar structure: polymeric octahedral in the condensed phase and tetrahedral in solution.

In 1966 two independent investigations[163,174] showed that the nickel chelate complexes of *N*-azolylformazans are paramagnetic, in contrast to the analogous planar metal chelates of the aromatic series[10,88,185], and therefore have non-planar structures. The authors explained in different ways the appearance of paramagnetism in the nickel chelate complexes of formazans of the azole series: three

of the present authors[163] attributed it to a polymeric octahedral configuration of the complexes (MN_6) in the crystalline phase and a tetrahedral configuration (MN_4) in solutions; Pyl and Meyer[174] attributed it to an intramolecular octahedral configuration (LXXIII) containing the MN_4S_2 coordination unit.



(LXXIII)



(LXXIV)

In order to establish how general is the above change in the structure of the MN_4 coordination unit on passing from *N*-aryl to *N*-azolyl complexes in formazans, a study was made of the magnetic and polar properties of a large series of copper, nickel, and cobalt chelates of formazans of the azole series and the following observations were made:

(1) Nickel complexes of *N*-azolylformazans are of the high-spin type in both the crystalline phase and in solution regardless of the structure of the ligand (except for *o*-hydroxy- and carboxy-phenylformazan chelate complexes[164,165]).

(2) The cobalt chelate complexes of hetarylformazans are of the low-spin type, in the condensed phase, while in benzene and carbon tetrachloride solutions they are of the high-spin type.

(3) The copper, nickel, cobalt, and zinc chelate complexes in benzene, dioxan, and carbon tetrachloride solutions have polar structures with dipole moments in the range 1.7–2.5 D.

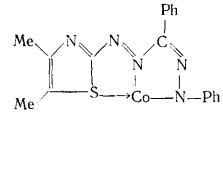
These data made it possible to ascribe a tetrahedral structure to metal chelates of hetarylformazans in solution, in agreement with the results of cryoscopic studies (the existence of the complexes as monomeric species in benzene and dioxan solutions)[153,163,167,177,178]. The polarity of the externally symmetrical (regardless of the type of polyhedron) chelate complexes of *NN*-diazolylformazans merits particular attention[153,167,168,177,178]. The polar model of a tetragonal pyramid with the metal atom above the plane of the metal-containing ring (cf. Garnovskii and coworkers[153,186]) conflicts with magnetochemical data. Therefore the most probable structure of the metal chelates of *NN'*-diazolylformazans, capable of explaining their magnetic and polar properties, we believe to be, by analogy with the complexes of other externally symmetrical *NN'*-disubstituted derivatives[187], the tetrahedral structure (LXXIV) with the metal-containing rings bent along the *N–N'* line at an angle α. This hypothesis is also supported by the finding that the nickel complexes of *NN'*-diarylformazans are paramagnetic in solution and have a dipole moment of 1.2 D.[177,178] The results (particularly for bivalent cobalt chelate complexes of hetarylformazans[167]) make it possible to reject the intramolecular octahedral structure (LXXIII) with M–N and M–S bonds.[174]

A polymeric octahedral configuration has been attributed to the metal chelates of formazans of heterocyclic series in the crystalline phase. It is consistent with the results of magnetochemical measurements and the high tendency of azoles to form intermolecular M–N bonds[152,153]. The explanation of the low-spin nature of the cobalt chelate complexes of hetarylformazans involves certain difficulties from this point of view[167,174,177]: their effective magnetic moments are of the order of 1.3–2 Bohr magnetons (B.M.) and can be attributed to the planar model, which is not inconsistent with theoretical and structural‡ considerations[185,188,189], or a spin-paired octahedron, which is comparatively rarely encountered. For this reason, X-ray diffraction data are necessary to reach a final conclusion about the structure of the chelate complexes of hetarylformazans in the crystalline phase. A preliminary report on the problem[190] still does not allow a definite conclusion.

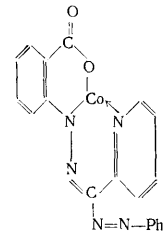
In contrast to the chelate complexes discussed above, the nickel chelates of *N*-(*o*-carboxyphenyl)-*N'* hetarylformazans (LXVIIIb)[164,165] as well as the analogous complexes of *o*-carboxyarylformazans[191–193] are diamagnetic (planar structure). The coordination saturation in complexes of this type [compounds (LXVIIIb)] probably involves the participation of the carbonyl oxygen. However, since there is reason to believe[192] that the chelates (LXVIIIb) have a structure in which the nickel is joined by a double bond, in this case too X-ray diffraction data will prove extremely useful. The metal chelates (LXIX) should probably also be planar[169].

The purely synthetic study by Seyhan[157,161,170–173], who first began to investigate 3-hetarylformazan complexes in 1954, stand alone from the standpoint of modern coordination chemistry. He did not employ any physical research techniques and therefore his structures of the complexes are open to serious objection. This applies particularly to the 2:1 metal chelates, to which the author attributes the structure of 1:1 complexes with an added ligand molecule[158,160,172,173].

In connection with the problem discussed above, the formulae of the cobalt complexes of hetarylformazans proposed by Pearse[194] [structure (LXXV)] and Beffa et al.[195] [structure (LXXVI)] are of very great interest:



(LXXV)



(LXXVI)

Whereas the first structure (LXXV) gives rise to doubts in connection with the possible involvement of the sulphur atom of the thiazole ring in coordination interaction[152,153,179], the second structure (LXXVI) appears to be fully justified.

Thus the introduction of the azole ring induces a preferential tetrahedral coordination of the chelate complexes of the formazan series (compared with the metal chelates of arylformazans) or leads to polymeric octahedral structures. Experimental results have shown[148,152,153,196,197] that both these effects are characteristic not only of metal chelates of the azole series with the MN_4 coordination unit, but also of MN_2O_2 and MN_2S_2.

The properties of the chelate complexes of hetarylformazans have been comparatively little investigated. There are isolated data on their stability[70,154,176] and their infrared spectra[70,122,156,164–166].

The dependence of the ν(C=N) shifts in the spectra of formazans on the structure of the ligand and the nature of the metal is a striking feature of the infrared spectroscopic data[166]. For formazans with the chelate structure, the transition from the chelate with a hydrogen-bond bridge

‡ By analogy with the structure of the nickel complexes of 3-methyl-1-phenyl-5-(*p*-tolyl)formazan[185].

to one of the inner complex type does not entail an appreciable change in the position of the band. On the other hand the ν(C=N) wavenumbers for the metal chelates of formazans with an open-chain structure are significantly reduced compared with the corresponding bands of the non-coordinated formazans[70,166]. The changes in the above infrared bands as a function of the metal are such that the shift $\Delta\nu$(C=N) is a maximum for the cobalt complexes.

In connection with the development of studies on the use of the complexes as ligands[179], the adducts of hetaryl-formazans with $CuCl_2$,[70,162] MCl_4,[156] and $Zn(OH)_2$[155] are of some interest. The number of MX_n molecules attached to the metal chelate of the hetarylformazan depends mainly on the nature of the metal and the ligand. Thus in the case of $CuCl_2$ it is determined by the number of azole rings[70,162] and in the case of MCl_4 (M = Sn or Ti) by the number of potential electron-donating centres (including the nitrogen atoms of the formazan ring)[153,156,179].

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The prospects for the further development of studies in the field of hetarylformazans are determined, apart from their theoretical interest (the problems of complex tautomeric equilibria, photochromic and thermochromic transformations, structure, colour, etc.), by the possibility of using them in various branches of science and engineering. In the introduction and in the description of the methods ofsynthesis, we already mentioned above certain practical applications. Now we shall emphasise particularly the use of tetrazolium salts obtained on the basis of formazans of the heterocyclic series as bioindicators. The tetrazolium salts derived from 1-hetaryl-formazans, which readily form complexes, are converted by enzymatic reduction into formazans forming deeply coloured complexes with the metal (cobalt) of the enzyme. The use of tetrazolium salts {particularly 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide[23,198]} in histochemistry for the determination of the activities of oxidation-reduction enzymes is based on this reaction[194].

Hetarylformazans and their derivatives are of considerable interest as dyes[3,5]. The azacyanines derived from benzothiazole[63], benzimidazole[141], and indazole[199,200] are dyes resembling the pentamethinecyanine dyes. The deeply coloured inner complexes of formazans containing OH and COOH groups have been patented by the Ciba[201] and Geigy[202,203] Companies as dyes for natural silk. Stable colours on cellulose fibres are produced by the copper complexes of formazans containing dichloropyrimidinyl substituents[204,205]. Hetarylformazans can be of interest as photochromic and thermochromic dyes[130,135] and also as pH indicators[70].

The study of the applications of hetarylformazans in analytical chemistry has been developing rapidly in recent years. Whereas in the series of arylformazans it is necessary to introduce additional groups into the formazan ring for this purpose (the SH group in dithizone[206], the hydroxy- and carboxy-groups in zincon[207], cyanoformazan-II,[208] etc.[5]), among 1-hetarylformazans capable of tautomerism there are extensive possibilities for the selection of effective analytical reagents.

The studies in the field are being carried out mainly by two groups of chemists: Japanese[44,45,209-213] and Soviet[214-220]. Spectrophotometric studies of the formation of bivalent nickel, copper, cobalt, zinc, and cadmium complexes with 1-hetaryl-3,5-diphenylformazans (hetaryl= thiazolyl, benzothiazolyl, selenazolyl, oxazolyl, and pyridyl) were described in reports by the first group. In the studies of the second group of investigators effective analytical reagents for copper, silver, nickel, zinc, lead, mercury, cadmium, and thallium were found among 1-benzazolyl- and 1,5-dibenzimidazolylformazans. The results concerning the application of 3-ethoxycarbonyl-1,5-di(tetrazol-2-yl)formazan as an excellent reagent for the colorimetric determination of copper and nickel[221] are also of interest.

All the foregoing considerations leave no doubt about the necessity for the intensification of research on hetaryl-formazans and their derivatives (particularly tetrazolium salts, verdazyl radicals, and complex compounds).

REFERENCES

1. W. Ried, Angew. Chem., 64, 391 (1952).
2. A. W. Nineham, Chem. Rev., 55, 355 (1955).
3. H. Wahl and M. T. Le Bris, in "Recent Progress in the Chemistry of Natural and Synthetic Colouring Matters and Related Fields", Edited by T. S. Gore, Acad. Press, New York, 1962.
4. R. Pütter and Houben-Weyl, Methoden der organischen Chemie, 10, No. 3, 631 (1965).
5. R. Price, in "Chemistry of Synthetic Dyes" (by K. Venkataraman) (Translated into Russian), Izd. Khimiya, Leningrad, 1974, p. 2013.
6. R. Kuhn and D. Jerchel, Ber., 74, 941, 949 (1941).
7. L. Hunter and L. B. Roberts, J. Chem. Soc., 820, 823 (1941).
8. R. Wizinger and V. Biro, Helv. Chim. Acta, 32, 901 (1949).
9. R. Wizinger, Z. Naturforsch., 9b, 729 (1954).
10. H. Irving, J. B. Gill, and W. R. Cross, J. Chem. Soc., 2087 (1960).
11. H. R. Tabel and R. Wizinger, see Ref. 5, p. 495.
12. R. Wizinger, Chimia (Switz.), Supple, 82 (1968).
13. E. Ludolfy, Ber., 84, 385 (1951).
14. W. Ried and H. Gick, Annalen, 581, 16 (1953).
15. W. Ried and R. Hoffschmidt, Annalen, 581, 29 (1953).
16. W. Ried, H. Gick, and G. Quertal, Annalen, 581, 29 (1953).
17. W. Ried and H. Hillenbrand, Annalen, 581, 44 (1953).
18. W. Ried and M. Wilk, Annalen, 581, 49 (1953).
19. H. Seiler and H. Schmid, Helv. Chim. Acta, 37, 1 (1954).
20. S. Karmarkar, J. Barnett, M. Nachlas, and A. Seligman, J. Amer. Chem. Soc., 81, 3771 (1959).
21. A. Altmann and P. Frank, Histochemie, 17(4), 319 (1969).
22. H. J. Cottrell, D. L. Pain, and R. Slack, J. Chem. Soc., 2968 (1954).
23. H. Beyer and Th. Pyl, Ber., 87, 1505 (1954).
24. H. Beyer and E. Bulka, Z. Chem., 2, 321 (1962).
25. E. Bulka, G. Rodekirch, and H. Beyer, Ber., 95, 658 (1962).
26. T. Pyl, Z. Chem., 6, 260 (1966).
27. Yu. A. Rybakova and N. P. Bednyagina, Khim. Geterotsikl. Soed., 421 (1965).
28. N. P. Bednyagina, N. V. Serebryakova, and G. N. Lipunova, Khim. Geterotsikl. Soed., 342 (1967).
29. N. P. Bednyagina and G. N. Lipunova, Khim. Geterotsikl. Soed., 902 (1968).
30. N. P. Bednyagina, N. V. Serebryakova, R. I. Ogloblina, and I. I. Mudretsova, Khim. Geterotsikl. Soed., 541 (1968).

31. G. A. Mokrushina and N. P. Bednyagina, Khim. Geterotsikl. Soed., 1080 (1969).
32. N. P. Bednyagina, A. P. Novikova, and I. Ya. Postovskii, Khim. Geterotsikl. Soed., 456 (1966).
33. F. L. Scott, D. A. O'Sullivan, and J. Reilly, J. Amer. Chem. Soc., **75**, 5309 (1953).
34. R. Kuhn and H. Kainer, Angew. Chem., **65**, 442 (1953).
35. A. P. Novikova, N. P. Bednyagina, and I. Ya. Postovskii, Khim. Geterotsikl. Soed., **1**, 195 (1967).
36. V. P. Shchipanov, A. I. Krashina, and A. A. Skachilova, Khim. Geterotsikl. Soed., 1570 (1973).
37. A. P. Novikova, I. Ya. Postovskii, and I. L. Shegal, Khim. Geterotsikl. Soed., 459 (1966).
38. G. N. Tyurenkova and N. P. Bednyagina, Khim. Geterotsikl. Soed., 913 (1967).
39. G. N. Tyurenkova and N. P. Bednyagina, Khim. Geterotsikl. Soed., 1198 (1970).
40. N. P. Bednyagina, Yu. A. Sedov, I. Ya. Postovskii, and Yu. A. Rybakova, "Puti Sinteza i Izyskaniya Protivoopukholevykh Preparatov" (The Syntheses and Applications of Antitumour Preparations), Izd. Meditsina, Moscow, 1967, p. 45.
41. Yu. A. Sedov, N. P. Bednyagina, and I. Ya. Postovskii, Khim. Geterotsikl. Soed., **1**, 191 (1967).
42. Yu. A. Sedov and I. Ya. Postovskii, Khim. Farm. Zhur., 2(7), 16 (1968).
43. G. M. Petrova, N. P. Bednyagina, T. G. Malkina, and V. N. Podchainova, Khim. Geterotsikl. Soed., 709 (1968).
44. A. Uchiumi, J. Chem. Soc. Japan, 90(11), 1133 (1969); Chem. Abs., 72, 55 308y (1970).
45. M. Kiyokawa and A. Kawase, Japan Analyst, **21**, 244 (1972); Chem. Abs., 74, 13 515m (1972).
46. L. M. Shegal, L. P. Sidorova, N. P. Bednyagina, and I. L. Shegal, Khim. Geterotsikl. Soed., 1379 (1972).
47. L. M. Shegal, I. L. Shegal, and N. P. Bednyagina, Khim. Geterotsikl. Soed., 35 (1972).
48. L. M. Shegal and I. L. Shegal, Khim. Geterotsikl. Soed., 1330 (1970).
49. H. Wahl and M. T. Le Bris, Bull. Soc. chim. France, 587 (1954).
50. H. Wahl and M. T. Le Bris, Compt. rend., **241**, 1143 (1955).
51. H. Wahl and M. T. Le Bris, Compt. rend., **241**, 1585 (1955).
52. M. T. Le Bris and H. Wahl, Bull. Soc. chim. France, 2653 (1959).
53. M. T. Le Bris and H. Wahl, Compt. rend., **250**, 136 (1960).
54. M. T. Le Bris, Bull. Soc. chim. France, 1158 (1960).
55. I. M. Mishina and L. S. Efros, Zhur. Obshch. Khim., **32**, 2217 (1962).
56. G. T. Pilyugin and S. V. Shinkorenko, Zhur. Obshch. Khim., **28**, 1313 (1958).
57. G. T. Pilyugin, S. V. Shinkorenko, and O. M. Stashkevich, Khim. Geterotsikl. Soed., 408 (1966).
58. G. T. Pilyugin, S. V. Shinkorenko, and O. M. Stashkevich, Khim. Geterotsikl. Soed., 311 (1968).
59. G. T. Pilyugin, T. S. Zueva, V. V. Stashkevich, S. V. Shinkorenko, and O. M. Stashkevich, Zhur. Obshch. Khim., **38**, 1392 (1968).
60. O. M. Stashkevich, G. T. Pilyugin, S. V. Shinkorenko, and V. V. Stashkevich, Khim. Geterotsikl. Soed., 152 (1968).
61. O. M. Stashkevich, G. T. Pilyugin, and V. V. Stashkevich, Khim. Geterotsikl. Soed., 1104 (1970).
62. S. V. Shinkorenko, G. T. Pilyugin, and G. B. Finkel', Zhur. Obshch. Khim., **42**, 2551 (1972).
63. S. Hünig, Angew. Chem., **74**, 818 (1962).
64. S. Hünig, F. Brühne, and E. Breitner, Annalen, **667**, 72 (1963).
65. N. P. Bednyagina and I. Ya. Postovskii, Zhur. Obshch. Khim., **30**, 1431 (1960).
66. N. P. Bednyagina, G. N. Tyurenkova, and Yu. A. Rybakova, Zhur. Obshch. Khim., **34**, 1288 (1964).
67. G. N. Tyurenkova and N. P. Bednyagina, Zhur. Org. Khim., 136 (1965).
68. Yu. A. Rybakova and N. P. Bednyakina, Zhur. Org. Khim., Symposium, "Problemy Organicheskogo Sinteza" (Problems of Organic Synthesis), 1965, p. 210.
69. Yu. A. Rybakova and N. P. Bednyagina, Khim. Geterotsikl. Soed., 287 (1965).
70. N. P. Bednyagina, Doctoral Thesis, The Urals Polytechnic Institute, Sverdlovsk, 1968.
71. H. Voswinkel, Ber., **36**, 2483 (1903).
72. D. Jerchel and H. Fischer, Annalen, **574**, 85 (1951).
73. I. N. Getsova and N. P. Bednyagina, Khim. Geterotsikl. Soed., 284 (1965).
74. G. A. Mokrushina and N. P. Bednyagina, Khim. Geterotsikl. Soed., 1401 (1970).
75. N. P. Bednyagina, G. N. Tyurenkova, and I. V. Panov, Zhur. Obshch. Khim., **34**, 1575 (1964).
76. N. N. Vereshchagina, I. Ya. Postovskii, and N. P. Bednyagina, Khim. Geterotsikl. Soed., 1967, Symposium 1, p. 162.
77. N. P. Bednyagina, G. M. Petrova, and N. V. Serebryakova, USSR P. 199 900; Byul. Izobret., No. 16 (1967).
78. Yu. A. Sedov, N. P. Bednyagina, and I. Ya. Postovskii, Zhur. Obshch. Khim., **37**, 139 (1967).
79. N. P. Bednyagina, Yu. A. Sedov, G. M. Petrova, and I. Ya. Postovskii, Khim. Geterotsikl. Soed., 390 (1972).
80. N. P. Bednyagina, G. N. Lipunova, and G. M. Petrova, Khim. Geterotsikl. Soed., 699 (1973).
81. R. I. Ogloblina, N. P. Bednyagina, and N. M. Gulemina, Khim. Geterotsikl. Soed., 393 (1972).
82. M. O. Lozinskii and P. N. Pel'kis, Zhur. Obshch. Khim., **33**, 113 (1963).
83. M. I. Ermakova and I. Ya. Postovskii, Zhur. Obshch. Khim., **34**, 2855 (1964).
84. R. G. Dubenko, I. M. Bazavova, and P. S. Pel'kis, Khim. Geterotsikl. Soed., 598 (1970).
85. R. G. Dubenko, I. M. Bazavova, and P. S. Pel'kis, USSR P. 225 177; Byul. Izobret., No. 16 (1968).
86. I. Ya. Postovskii, A. P. Novikova, and V. A. Ershov, Zhur. Org. Khim., **6**, 1104 (1970).
87. Yu. A. Sedov, A. I. Zabolotskaya, and N. V. Koba, Khim. Geterotsikl. Soed., 1705 (1973).
88. M. I. Ermakova, E. I. Krylov, and I. Ya. Postovskii, Zhur. Obshch. Khim., **30**, 849 (1960).
89. J. Hausser, D. Jerchel, and R. Kuhn, Ber., **82**, 195 (1949).
90. J. Hausser, D. Jerchel, and R. Kuhn, Ber., **82**, 515 (1949).
91. I. Hausser, D. Jerchel, and R. Kuhn, Ber., **84**, 651 (1951).
92. K. Hausser, Naturwiss, **36**, 313 (1949).
93. R. Kuhn and H. Weitz, Ber., **86**, 1199 (1959).
94. D. Shulte-Frolinde, R. Kuhn, W. Münzig, and W. Ottig, Annalen, **622**, 43 (1959).
95. G. R. Burns and J. F. Duncan, Chem. Comm., **4**, 116 (1966).
96. D. Jerchel and W. Edler, Ber., 88, 1287 (1955).

97. R. J. Le Fevre, J. B. Sousa, and R. L. Werner, Austral. J. Chem., 9, 151 (1956).
98. A. Foffani, C. Pecile, and S. Ghersetti, Tetrahedron Letters, 16 (1959).
99. A. Foffani, C. Pecile, and S. Ghersetti, Adv. Mol. Spectroscopy, 2, 769 (1962).
100. C. Schiele, Annalen, 689, 197 (1965).
101. C. Schiele and G. Arnold, Tetrahedron Letters, 4103 (1966).
102. G. Arnold and C. Schiele, Spectrochim. Acta, 25A, 671 (1969).
103. G. Arnold and C. Schiele, Spectrochim. Acta, 25A, 685 (1969).
104. G. Arnold and C. Schiele, Spectrochim. Acta, 25A, 697 (1969).
105. I. I. Kukushkina, E. N. Yurchenko, M. I. Ermakova, and N. I. Latosh, Zhur. Fiz. Khim., 46, 176 (1972) [Russ. J. Phys. Chem., No. 1 (1972)].
106. I. I. Kukushkina, E. N. Yurchenko, D. V. Arkhipenko, and B. A. Orekhov, Zhur. Fiz. Khim., 46, 1677 (1972) [Russ. J. Phys. Chem., No. 7 (1972)].
107. H. Ziegler, Ind. chim. Belge., 22, 533 (1957).
108. N. P. Bednyagina, A. P. Novikova, N. V. Serebyakova, I. I. Mudertsova, and I. Ya. Postovskii, Zhur. Org. Khim., 4, 1613 (1968).
109. N. P. Bednyagina, G. N. Lipunova, A. P. Novikova, A. P. Zeif, and L. N. Shchegoleva, Zhur. Org. Khim., 6, 619 (1970).
110. A. P. Zeif, N. N. Shchegoleva, G. N. Lipunova, A. P. Novikova, and N. V. Bednyagina, Zhur. Org. Khim., 6, 1332 (1970).
111. A. P. Zeif, G. N. Lipunova, N. P. Bednyagina, L. N. Shchegoleva, and L. I. Chernyavskii, Zhur. Org. Khim., 6, 2590 (1970).
112. G. N. Lipunova, A. P. Zeif, N. P. Bednyagina, and L. N. Shechegoleva, Zhur. Org. Khim., 8, 1757 (1972).
113. E. N. Yurchenko and I. I. Kukushkina, Zhur. Strukt. Khim., 10, 706 (1960).
114. I. I. Kukushkina, E. N. Yurchenko, M. I. Ermakova, G. P. Sadakova, and N. I. Latosh, Zhur. Strukt. Khim., 11, 341 (1971).
115. F. A. Neugebauer and H. Trischman, Annalen, 706, 107 (1967).
116. G. Tiers, S. Plovan, and S. Searles, J. Org. Chem., 25, 285 (1960).
117. W. Ottig and F. Neugebauer, Ber., 102, 2520 (1969).
118. Yu. A. Omel'chenko, Yu. D. Kondrashev, S. L. Ginzburg, and M. G. Neigauz, Zhur. Strukt. Khim., 14, 574 (1973).
119. A. P. Novikova, L. P. Kozina, D. N. Shigorin, and I. Ya. Postovskii, Zhur. Obshch. Khim., 38, 934 (1968).
120. N. P. Bednyagina and G. N. Lipunova, Khim. Geterotsikl. Soed., 877 (1969).
121. E. N. Yurchenko, K. V. Aglitskaya, N. P. Bednyagina, E. P. Darienko, and I. I. Kalinichenko, Zhur. Fiz. Khim., 40, 1313 (1966) [Russ. J. Phys. Chem., No. 6 (1966)].
122. G. N. Lipunova, K. V. Aglitskaya, and N. P. Bednyagina, Izv. Akad. Nauk SSSR, Sibir, Otd., No. 4, 50 (1967).
123. G. N. Lipunova, E. P. Motyleva, and N. P. Bednyagina, Khim. Geterotsikl. Soed., 831 (1971).
124. N. V. Serebryakova, G. N. Lipunova, N. P. Bednyagina, and L. F. Lipatova, Khim. Geterotsikl. Soed., 1403 (1970).
125. G. A. Sereda, R. I. Ogloblina, V. N. Podchainova, and N. P. Bednyagina, Zhur. Anal. Khim., 23, 1224 (1968).
126. V. T. Panyushkin, A. D. Garnovskii, N. P. Bednyagina, and O. A. Osipov, "Tezisy Vsesoyuznoi Konferentsii Svyaz' Stroeniya i Svoistv v Ryadu Azotsoderzhashchikh Geterotsiklicheskikh Soedininenii, Sverdlovsk, 1967" (Abstracts of Reports at the All-Union Conference on the Relation Between Structure and Properties in the Series of Nitrogen-containing Heterocyclic Compounds, Sverdlovsk, 1967).
127. L. P. Sidorova, N. P. Bednyagina, and T. A. Koznetsova, Khim. Geterotsikl. Soed., 1136 (1971).
128. L. P. Sidorova and N. P. Bednyagina, Khim. Geterotsikl. Soed., 1138 (1972).
129. M. Seyhan, Ber., 88, 646 (1955).
130. N. P. Bednyagina, G. N. Lipunova, and G. A. Mokrushina, USSR P. 241 442; Byul. Izobret., No. 14 (1969).
131. L. S. Meriwether, E. S. Breitner, and C. L. Sloan, J. Amer. Chem. Soc., 87, 4441 (1965).
132. L. S. Meriwether, E. S. Breitner, and N. B. Colthup, J. Amer. Chem. Soc., 87, 4448 (1965).
133. P. S. Pel'kis and R. G. Dubenko, Dokl. Akad. Nauk SSSR, 110, 798 (1956).
134. P. S. Pel'kis and R. G. Dubenko, Ukrain. Khim. Zhur., 23, 64 (1957).
135. Yu. A. Rybakova, G. N. Lipunova, and N. P. Bednyagina, USSR P. 296 791; Byul. Izobret., No. 9 (1971).
136. Yu. A. Rybakova and N. P. Bednyagina, Khim. Geterotsikl. Soed., 970 (1971).
137. G. N. Lipunova, N. N. Gulemina, A. P. Zeif, and N. P. Bednyagina, Khim. Geterotsikl. Soed., 493 (1974).
138. R. Kuhn and W. Münzig, Ber., 86, 858 (1953).
139. N. P. Bednyagina, N. P. Serebryakova, and Yu. K. Rybakova, Khim. Geterotskikl. Soed., 750 (1967).
140. Yu. A. Sedov and I. Ya. Postovskii, Zhur. Org. Khim., 5, 781 (1969).
141. Yu. A. Rybakova and N. P. Bednyagina, Khim. Geterotsikl. Soed., 287 (1966).
142. G. N. Lipunova and N. P. Bednyagina, Khim. Geterotsikl. Soed., 882 (1969).
143. R. Kuhn and H. Trischmann, Monatsh., 95, 457 (1964).
144. R. Kuhn, F. A. Neugebauer, and H. Trischmann, Monatsh., 97, 846 (1966).
145. F. A. Neugebauer and H. Trischmann, Monatsh., 98, 713 (1967).
146. F. A. Neugebauer, Angew. Chem., 85, 485 (1973).
147. N. P. Bednyagina and Yu. A. Rybakova, Khim. Geterotsikl. Soed., 283 (1966).
148. H. Hennig, Z. Chem., 11, 81 (1971).
149. S. Trofimenko, Chem. Rev., 72, 497 (1972).
150. A. Eschenmoser, Pure Appl. Chem., 20, 1 (1969).
151. D. St. C. Black and A. J. Hartshorn, Coord. Chem. Rev., 9, 219 (1973).
152. A. D. Garnovskii, O. A. Osipov, L. A. Kuznetsova, and N. N. Bogdashev, Uspekhi Khim., 42, 177 (1973) [Russ. Chem. Rev., No. 2 (1973)].
153. A. D. Garnovskii, Doctoral Thesis, Rostov University, Rostov-on-Don, 1972.
154. E. N. Yurchenko, Yu. A. Rybakova, N. P. Bednyagina, E. P. Daryenko, and I. I. Kalinichenko, "Primenenie Molekulyarnoi Spektroskopii v Khimii" (Chemical Applications of Molecular Spektroscopy), Izd. Nauka, Moscow, 1967, p. 69.

155. R. I. Ogloblina, N. P. Bednyagina, and A. D. Garnovskii, Zhur. Obshch. Khim., **40**, 367 (1970).
156. V. T. Panyushkin, A. D. Garnovskii, O. A. Osipov, N. P. Bednyagina, and R. I. Nikitina, Zhur. Obshch. Khim., **38**, 1161 (1968).
157. M. Seyhan, Ber., **87**, 399 (1954).
158. M. Seyhan, Ber., **87**, 1124 (1954).
159. M. Seyhan, Ber., **88**, 212 (1955).
160. M. Seyhan and W. C. Fernelius, Ber., **90**, 220 (1957).
161. M. Seyhan and W. C. Fernelius, J. Org. Chem., **22**, 219 (1957).
162. N. P. Bednyagina and Yu. A. Rybakova, Khim. Geterotsikl. Soed., 425 (1965).
163. A. D. Garnovskii, V. T. Panyushkin, N. P. Bednyagina, and O. A. Osipov, Zhur. Strukt. Khim., **8**, 247 (1967).
164. N. P. Bednyagina, G. M. Petrova, and K. V. Aglitskaya, Zhur. Obshch. Khim., **38**, 529 (1968).
165. G. M. Petrova and N. P. Bednyagina, Zhur. Obshch. Khim., **39**, 887 (1969).
166. G. N. Lipunova, E. I. Krylov, N. P. Bednyagina, and V. A. Sharov, Zhur. Obshch. Khim., **39**, 1293 (1969).
167. A. D. Garnovskii, O. A. Osipov, N. P. Bednyagina, L. I. Kuznetsova, R. I. Ogloblina, V. P. Kurbatov, and L. S. Kostromina, Zhur. Obshch. Khim., **39**, 1620 (1969).
168. A. D. Garnovskii, N. P. Bednyagina, L. I. Kuznetsova, V. T. Panyushkin, O. A. Osipov, R. I. Ogloblina, and A. P. Novikova, Zhur. Neorg. Khim., **14**, 1576 (1969) [Russ. J. Inorg. Chem., No. 6 (1969)].
169. L. P. Sidorova, E. P. Darienko, L. P. Davydenkova, and N. P. Bednyagina, Zhur. Obshch. Khim., **42**, 571 (1972).
170. M. Seyhan, Ber., **88**, 1454 (1955).
171. M. Seyhan, Monatsh., **86**, 545 (1955).
172. M. Seyhan and N. Sargin, Ber., **99**, 2072 (1966).
173. M. Seyhan and B. Ocacioglu, Monatsh., **101**, 829 (1970).
174. T. Pyl and P. Meyer, Z. Chem., **6**, 264 (1966).
175. Yu. S. Varshavskii, T. G. Cherkasova, O. A. Osipov, N. P. Bednyagina, A. D. Garnovskii, R. I. Ogloblina, G. K. Mitina, and G. N. Lipunova, Zhur. Neorg. Khim., **17**, 1401 (1972) [Russ. J. Inorg. Chem., No. 5 (1972)].
176. I. I. Shevlina, L. P. Sidorova, V. N. Podchainova, and N. P. Bednyagina, Zhur. Obshch. Khim., **42**, 2546 (1972).
177. A. D. Garnovskii, O. A. Osipov, N. P. Bednyagina, L. I. Kuznetsova, A. S. Kostromina, V. P. Kurbatov, V. T. Panyushkin, R. I. Ogloblina, and N. N. Serebryakova, Dokl. Akad. Nauk SSSR, **184**, 1132 (1969).
178. A. D. Garnovskii, N. P. Bednyagina, L. I. Kuznetsova, V. T. Panyushkin, O. A. Osipov, R. I. Ogloblina, and A. P. Novikova, Zhur. Obshch. Khim., **38**, 2119 (1968).
179. A. D. Garnovskii, O. A. Osipov, and S. P. Bulgarevich, Uspekhi Khim., **41**, 648 (1972) [Russ. Chem. Rev., No. 4 (1972)].
180. O. Yu. Okhlobystin, A. D. Garnovskii, and N. S. Erdyneev, Izv. Severo-Kavkazskovo, Tsentra Vysshei Shkoly (Ser. Khim. i Fiz), 3 (1973).
181. P. W. Selwood, "Magnetochemistry" (Translated into Russian), Inostr. Lit., Moscow, 1958, p. 248.
182. E. A. Shugam and L. A. Shkol'nikova, "Kristallokhimiya, Itogi Nauki" (Crystal Chemistry. Advances in Science), Izd. VINITI, Akad. Nauk SSSR, Moscow, 1967, p. 62.
183. M. A. Porai-Koshits and E. A. Gilinskaya, "Kristallokhimiya, Itogi Nauki" (Crystal Chemistry. Advances in Science), Izd. VINITI, Akad. Nauk SSSR, Moscow, 1966, p. 112.
184. A. B. Neiding, in "Magnetokhimiya, Itogi Nauki" (Magnetochemistry. Advances in Science), Izd. VINITI, Akad. Nauk SSSR, Moscow, 1970.
185. D. Dale, J. Chem. Soc. (A), 278 (1967).
186. A. D. Garnovskii, N. F. Krokhina, T. A. Zayakina, and L. I. Kuznetsova, Zhur. Neorg. Khim., **17**, 2302 (1972) [Russ. J. Inorg. Chem., No. 8 (1972)].
187. V. P. Kurbatov, S. V. Serbina, and O. A. Osipov, Zhur. Neorg. Khim., **18**, 2662 (1974) [Russ. J. Inorg. Chem., No. 8 (1974)].
188. E. N. Yurchenko, V. I. Avdeev, and I. I. Kalinichenko, Teor. Eksper. Khim., **3**, 552 (1957).
189. R. S. Nyholm, Uspekhi Khim., **32**, 354 (1963) [Russ. Chem. Rev., No. 3 (1963)].
190. Z. A. Starikova, N. P. Bednyagina, and E. A. Shugam, Zhur. Strukt. Khim., **14**, 572 (1973).
191. R. Wizinger and H. Herzog, Helv. Chim. Acta, **36**, 531 (1953).
192. W. Freisleben and F. Grun, Chimia (Switz.), **II**, 276 (1957); Helv. Chim. Acta, **41**, 574 (1958).
193. M. Kral, Collect. Czech. Chem. Comm., **32**, 1698 (1967).
194. A. G. E. Pearse, "Theoretical and Applied Histochemistry", Churchill Ltd., London, 1960 (Quoted after Ref. 174).
195. F. Beffa, P. Lienhard, and G. Schetty, Helv. Chim. Acta, **46**, 1369 (1963).
196. O. A. Osipov, V. I. Minkin, A. D. Garnovskii, V. A. Kogan, V. P. Kurbatov, L. E. Nivorozhkin, L. S. Minkina, I. Ya. Kvitko, and S. G. Kochin, "Tezisy XV Mezhdunarodnoi Konferentsii po Koordinatsionnoi Khimii, Moskva, 1973" (Abstracts of Reports at the Fifteenth International Conference on Coordination Chemistry, Moscow, 1973), p. 160; Izv. Severo-Kavkazskogo Tsentra Vysshei Shkoly (Ser. Khim. i Fiz.), No. 3 (1974).
197. V. P. Kurbatov, A. D. Garnovskii, O. A. Osipov, L. S. Minkina, and I. Ya. Kvitko, Zhur. Obshch. Khim., **45**, 202 (1975).
198. A. G. Pearse, J. Histochem. Cytochem., **5**, 515 (1957).
199. R. Surean and G. Kremer, French P. 1 353 497 (1964); Chem. Abs., **61**, 3242a (1964).
200. R. Surean, G. Kremer, and H. Dupre, Belg. P. 609 146 (1962); Chem. Abs., **59**, 1791g (1963).
201. Ciba Ltd., Swiss P. 246, 475 (1947); Chem. Abs., **43**, 5198 (1949).
202. I. R. Geigy A. G., Belg. P. 650 328 (1965); Chem. Abs., **63**, 13 454f (1965).
203. I. R. Geigy A. G., French P. 1 560 653 (1969); Chem. Abs., **73**, 100 039v (1970).
204. Sandoz Ltd., B. P. 1 022 043 (Quoted after Ref. 5, p. 2021).
205. I. R. Geigy S. A., B. P. 950 861 (Quoted after Ref. 5, p. 2022).
206. G. Ivantscheffi, "Dithizon und seine Anwendung in der Mikro- und Spurenanalyse" (Translated into Russian), Inostr. Lit., Moscow, 1961.
207. M. B. Johnson, A. J. Barnard, and W. C. Brood, Rev. Univ. Ind. Santander., **4**, 43 (1962); Chem. Abs., **57**, 4002f (1963).
208. M. I. Ermakova, N. L. Vasil'eva, and I. Ya. Postovskii, Zhur. Anal. Khim., **16**, 8 (1961).
209. A. Kavase, Japan Analyst., **16**, 1364 (1967).

210. A. Uchiuma, J. Chem. Soc. Japan, Pure Chem. Sect., 90, 1133 (1969).
211. T. Matsuchima and A. Kawase, Japan Analyst, 20, 1310 (1971).
212. A. Kawase, Japan Analyst, 21, 578 (1972).
213. A. Uchiumi, Repts. Govt. Chem. Ind. Res. Inst., Tokyo, 67, 170 (1972).
214. S. A. Lomonosov, Yu. A. Rybakova, V. N. Podchainova, and N. P. Bednyagina, Zhur. Anal. Khim., 19, 1062 (1964).
215. L. V. Kholevinskaya, G. N. Kipunoya, and N. P. Bednyagina, Zhur. Anal. Khim., 24, 1756 (1969).
216. V. N. Podchainova and L. F. Dubinina, Zhur. Anal. Khim., 27, 242 (1972).
217. V. N. Podchainova and L. F. Dubinina, Zavod. Lab., 1322 (1972).
218. V. N. Podchainova and I. N. Serebrennikova, Zhur. Obshch. Khim., 44, 618 (1974).
219. V. N. Podchainova, T. G. Malkina, N. P. Bednyagina, and G. M. Petrova, "Tezisy II Vsesoyuznogo Soveshchaniya po Primeneniyu Organicheskikh Reaktivov v Analiticheskoi Khimii, Saratov, 1966" (Abstracts of Reports at the Second All-Union Conference on the Applications of Organic Reagents in Analytical Chemistry, Saratov, 1966), p. 56.
220. "Tezisy Dokladov Simpoziuma po Khimii i Primeneniyu Formazanov" (Abstracts of Reports at a Symposium on the Chemistry and Applications of Formazans), Ural'sk Politekh. Inst., Sverdlovsk, 1968.
221. H. B. Jonassen, V. C. Chamblin, and V. L. Wagner, Anal. Chem., 30, 1660 (1958).

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