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Formazans and their metal complexes

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Abstract. The current data on the structure of formazans in crystals and in solutions are considered and some problems of tautomeric and conformational equilibria are discussed. Some novel classes of formazans synthesised over the past decade are presented. The results of structural studies of formazan complexes with various types of metal coordination are generalised. Examples of synthesis of formazan-containing polymers are given. Special emphasis is placed on analytical and practical applications of formazan derivatives. The bibliography includes 155 references.

I. Introduction

Studies into tautomerism and complexation of heterocyclic compounds are among the main lines of research at the Urals school of organic chemists founded by I Ya Postovsky. The main results and achievements in the chemistry of formazans have been surveyed.[1, 2]

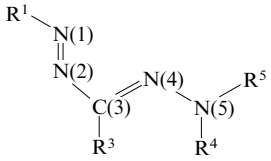
Formazans were first synthesised over a century ago, but still attract attention of chemists, biologists, technologists and other specialists. The presence in formazans of a mobile π-system, the ease of redox reactions typical of these compounds, their ability for isomerisation and tautomeric transformations and enhanced acidity and basicity have determined the main areas of their practical applications. Formazan derivatives are widely used as dyes for different purposes, charge-generating compounds, biochemical markers for redox processes, analytical reagents, photo- and thermochromic materials and synthons for the synthesis of heterocyclic compounds. The data on the structures, properties and applications of the known formazans and methods for their synthesis published before 1992 are generalised in a monograph.[2] However, the results of recent studies allow the consideration of problems of tautomerism and isomerism of this class of compounds at a higher level. Despite the large number of novel formazan derivatives synthesised over the last years, the number of publications devoted to the examination of chemical properties of these compounds is very limited. The interest of investigators was mainly focused on the description of different modes of coordination of formazans with metals and their novel applications. Therefore, the aim of the present review is to elucidate the state-of-the-art in theoretical and applied aspects of the chemistry of formazans.

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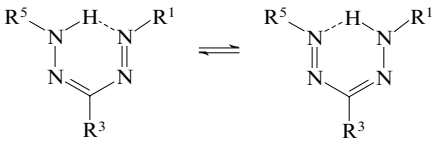
II. Structure of formazans

Formazans represent compounds with an azohydrazone system of bonds:



This review is confined exclusively to the consideration of formazan derivatives with R^4 = H among which 1,3,5-trisubstituted formazans have been studied in especially great detail. Traditionally, substituents at the N(1) and N(5) atoms are designated as R^1 and R^5, and those at C(3) (which is also referred to as the *meso* position), as R^3. Substituents in the formazan fragment are enumerated in the ascending order of the atom numbers in the azohydrazone chain; if the position of the substituents at the N(1) and N(5) atoms is not exactly known, they are additionally designated by numbers in parentheses. These rules will be followed in this review.

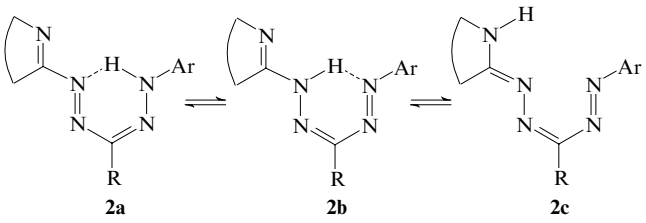
The molecules of all currently known formazans manifest extremely high conformational and tautomeric mobilities, the types of their isomerism being dependent on the nature of the substituents, first of all, those at the N(1) and N(5) atoms. Thus *N*,*N*′-diarylformazans **1** are characterised by prototropic tautomerism of the type R^5NH (compound **1a**) $\rightleftharpoons$ R^1NH (**1b**).



1a **1b**

R^1, R^5 = Ar.

If an α-azaheterocyclic substituent is linked to one of the nitrogen atoms of a formazan (compound **2**), an additional amine – imine tautomerism is observed, which involves the nitrogen atom of the heterocycle (**2a** ⇌ **2b** ⇌ **2c**).



2a **2b** **2c**

Some types of formazans, *e.g.,* the well-known analytical reagent dithizone (1,5-diphenyl-3-mercaptoformazan), are subject to autoprotonation. *N*(5)-Acylformazans are also characterised by the presence of rotamers due to hindered rotation around the N(5) – C = O amide bond. Besides, the system of double and single nitrogen – nitrogen and carbon – carbon bonds is responsible for different spatial arrangement of the fragments relative to one another, which determines the existence of geometric isomers.

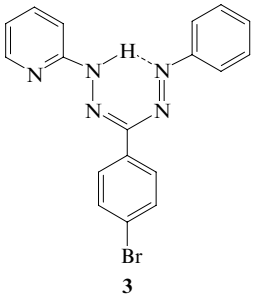
Thus, structural studies of formazans consist in elucidating the prototropic equilibrium between possible tautomeric forms and analysing configurational isomerism.

1. Spatial structure of formazans

The presence in the formazan chain of two multiple bonds and the N(5) atom with a lone electron pair brings about the formation of an overall conjugated system. This leads to an increase in the order of the N(2) – C(3) and N(4) – N(5) bonds and in the height of the rotation barrier around them. Therefore, the configurations of all the bonds in the formazan fragment are designated in terms of the *Z*,*E* nomenclature.[2]

X-Ray diffraction studies of a large series of formazans revealed[3] three configurational combinations in the azohydrazone chains in the crystals, *viz*., *EZZ*, *EEZ* and *EEE* [hereinafter, this refers to the bond sequences N(1) – N(2), N(2) – C(3) and C(3) – N(4), respectively] (Scheme 1).

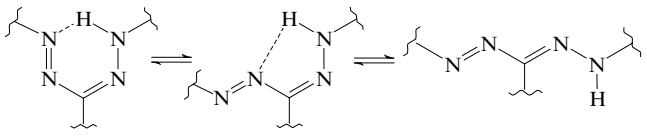
The configuration of formazans is largely determined by the steric effect of the substituent at the *meso*-carbon atom. Thus *EZZ* isomers (structure **A**) are characteristic of formazans with a bulky substituent R^3 (Ph, Bu^t, NO_2, *etc*.).[3,4] For example, the chain of 1-phenyl-3-(4-bromophenyl)-5-(2-pyridyl)formazan (**3**) in crystals has an *EZZ* configuration.[5]



3

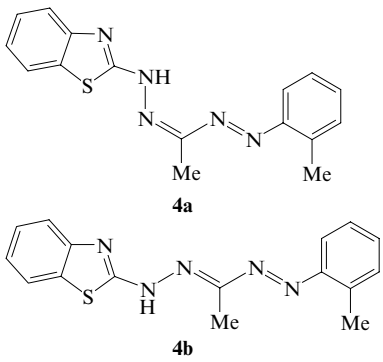
If the *meso*-carbon atom of formazan contains an alkyl substituent, the crystals can adopt both the *EEE* (structure **C** in Scheme 1) and *EEZ* (structure **B**) configurations. This can be attributed to the fact that the steric demands of these substituents and the phenylazo group are comparable. X-Ray diffraction data

Scheme 1



A (*EZZ*) **B** (*EEZ*) **C** (*EEE*)

for formazans[3] suggest that these compounds exist in crystals exclusively as individual geometric isomers. However, co-crystallisation of 1-(*o*-tolyl)-3-methyl-5-(benzimidazol-2-yl)-formazan *Z* (**4a**) and *E* isomers (**4b**) relative to the C=N bond (Fig. 1) has been observed.[6]



4a **4b**

In the crystal lattices, both isomers form dimers, where the molecules are linked by an intermolecular H-bond between the hydrogen atom at the N(5) atom and the nitrogen atom of the heterocycle; in addition, the molecule of compound **4a** contains an intramolecular H-bond with a length of 2.234 Å (see Fig. 1).

It is of note that formazans devoid of substituents at the C(3) atom exist in crystals exclusively in the form of *EEE* isomers.[2]

The configuration of the azohydrazone chain in crystals of formazans is determined not only by the bulk of the substituent at the carbon atom, but, to a large extent, by the possibility of hydrogen bonding which stabilises their geometric structures.

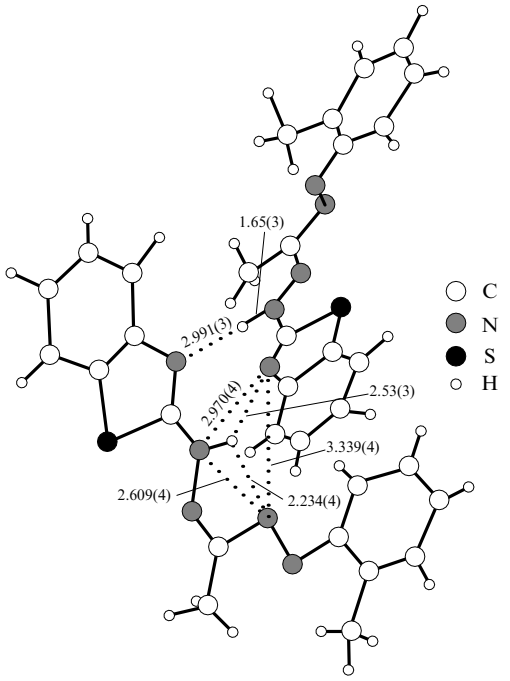
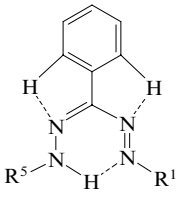


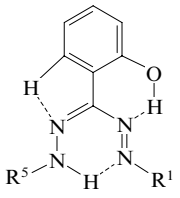
Figure 1. Molecular structure of compound **4**.

Thus the *EZZ* configuration of formazans is stabilised by the intramolecular N(1)···HN(5) hydrogen bond in the six-membered ring (see structure **A** in Scheme 1), the *EEZ* isomer is stabilised by the N(2)···HN(5) bond in the five-membered ring (see structure **B**), while the *EEE* form is stabilised by intermolecular H-bonds. In *N*-azaheterocyclic formazans, which crystallise in the imino tautomeric form, the intramolecular N(4)···HN(heterocycle) H-bond provides additional stabilisation.[7]

A prominent role in stabilisation of one or another configuration of the formazan molecule is played by H-bonds with atomic groups in peripheral substituents. These include not only NH, OH or SH groups, but also CH groups. π-Interactions of aromatic rings with the heteroatom are also possible. For example, a significant role in stabilisation of the *EZZ* form of 3-arylformazans is played by two CH···N hydrogen bonds between the *ortho*-protons of the aryl fragment and the nitrogen atoms of the formazan chain (structure **5**). The replacement of the naphthalene rings ($R^1 = R^5$ = 1-naphthyl) at positions 1 and 5 of compound **5** ($R^1 = R^5$ = Ph) with benzene rings did not influence the configuration of the molecule (the *EZZ* form), while the passage from 3-phenyl- to 3-naphthylformazans resulted in a shift of the tautomeric equilibrium towards the formation of an open form.[2] At the same time, the introduction of a hydroxy group into the *ortho* position of the *meso*-phenyl substituent (compound **6**) provided additional stabilisation of the *EZZ* isomer due to formation of an intramolecular H-bond.[8]



5



6

It is noteworthy that no compounds with the *EZE* configuration of the formazan chain are known so far. Apparently, such isomers would be energetically unfavourable due to repulsion between the lone electron pairs at the N(1) and N(4) atoms, whereas this configuration is rather common in metal complexes of formazans.[2]

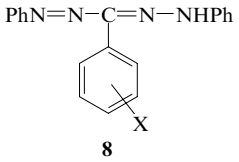
Recently, theoretical data on the structures of unsubstituted and 3-nitro-substituted formazans, which are unstable under ordinary conditions and could not be prepared experimentally, have been obtained.[9] The results of *ab initio* quantum-chemical calculations of all possible conformations of these compounds suggest that the *EZZ* configuration is the most stable (at least, in the gas phase). To a large extent, this structure is stabilised by a bridging N—H···N hydrogen bond in the six-membered chelate ring where proton transfer is possible. However, according to X-ray diffraction data, 3-unsubstituted 1,5-diphenylformazan (**7**) has the *EEE* configuration in crystals.[3] Evidently, the formation of the crystal lattice is controlled by other factors the effects of which have not been taken into account in the quantum-chemical calculations.

The knowledge of spatial structures of arylformazans in solutions had long been confined to recognition of the ability of these compounds to exist in two forms which can conventionally be designated as 'red' (chelated) and 'yellow' (open) forms. It is the transitions from one form to another that underlie the well-established red–yellow photochromism of 1,3,5-triarylformazans. However, until very recently their structures have been a debated topic.[2]

Structural analysis of the 'red' form proved unequivocally this to be the *EZZ* isomer. The majority of formazans with this structure are characterised by the lack of absorption bands (ν_{NH}) in their IR spectra at 3100–3500 cm^{-1}, but manifest the presence of a low-field signal of NH in the ^1H NMR spectra and an intense absorption band around 480–500 nm in the electronic spectra irrespective of the nature of the solvent. The chemical shift of the *meso*-carbon atom in ^{13}C NMR spectra of these compounds is at δ 148–151.[10]

In the absence of irradiation, 'yellow' forms of 1,3,5-triarylformazans are unstable, the long-wavelength band at 410–420 nm in the electronic spectra being their only spectral characteristics. Other spectral features of 1,3,5-triarylformazans do not allow their unambiguous structural identification.

Conformations of arylformazans were calculated using different quantum-chemical methods including DFT (density functional theory).[11] The effects of substituents on the spectral characteristics of 1,5-diphenylformazans **8** with a substituted phenyl group at position 3 have been described.[12].



8

X = 2-NO_2, 3-NO_2, 4-NO_2, 2-CO_2H, 3-CO_2H, 4-CO_2H.

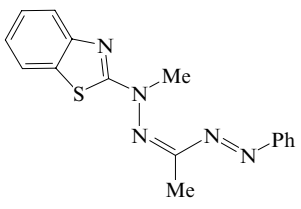
A good correlation was found between the absorption maxima in the electronic spectra and the Hammett constants of the substituents in the benzene ring; however, this correlation was not related to the spatial structures of the formazans under study.

The 'chelate' structure of the *EZZ* isomer is also typical of 1,3-diaryl-5-hetarylformazans. However, the chelate ring with the intramolecular N(1)···HN(5) hydrogen bond appeared to be less stable in solution in comparison with 1,3,5-triarylformazans. The ring is easily opened in proton-acceptor solvents, which resulted in an equilibrium between the *EZZ* and *EEZ* forms; their ratio depends on the nature of the heterocycle and the solvent.[13] This was manifested in the dependence of the position of the δ_{NH} signal in the ^1H NMR spectrum on the solvent polarity as well as in the presence of weak and moderate ν_{NH} bands at 3300–3340 cm^{-1} in the IR spectra.

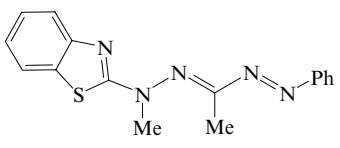
1,5-Diarylformazans devoid of aryl substituents at the C(3) atom are often unable to preserve the configuration of the azohydrazone chain upon dissolution. The transition between their isomeric forms occurs spontaneously and is catalysed by Brønsted acids or by irradiation of solutions with visible light. Such a conformational lability of 1,5-diarylformazans hampers the elucidation of their structures in solutions and identification of spectral 'diagnostic' markers.[2]

The electronic spectra of substituted diarylformazans in organic solvents of different polarity and the effects of solvents on the position of the intramolecular charge-transfer band have been studied.[14] The results of calculations of molecular orbitals (MO) by the MPDP/PM3 method point to the *EEZ* configuration of the formazan chain as the most preferrable geometry of the diarylformazan molecule.

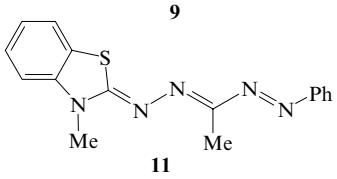
The problem of establishing spatial structures of 1-aryl-3-alkyl-5-(benzothiazol-2-yl)formazans in solutions was successfully solved[15] using *N*-alkylated 3-methylformazans **9**–**11** as the



9



10



11

model compounds. The fixed configurations of the double bonds in these formazans rule out the formation of intra- and intermolecular H-bonds and their tautomerism.

In-depth studies of these compounds using a combination of modern physicochemical methods (X-ray diffraction, ^{1}H and ^{13}C NMR, electronic spectroscopy, dipole moment measurements) with consideration of the published spectral data for 1,5-diaryl-3-alkylformazans enabled establishing 'diagnostic' markers for determination of the configuration of the azohydrazone chain:

(1) The *EEZ* Isomers absorb visible light in a longer-wavelength region than compounds with the *EEE* configuration. The bathochromic shift of the absorption maxima (λ_{max}) of formazans containing an alkyl substituent at the *meso*-carbon atom on going from polar to nonpolar solvents (the so-called negative solvatochromism) is due to an increased content of *Z* isomers as regards substituents at the C(3)=N(4) bond ($Z^{3,4}$). The *EEE* isomer with the absorption maximum around 400 nm is predominant in polar solvents.

(2) The chemical shift (δ ^{13}C) of the *meso*-carbon atom in the ^{13}C NMR spectra of *EEE* isomers is observed at lower field (δ ^{13}C = 155.0–162.9) in comparison with the *EEZ* isomers (δ ^{13}C = 150.3–156.0). The carbon atoms of alkyl substituents at the C(3) atom (R^3) of the *EEE* isomers resonated at higher field in comparison with the *EEZ* isomer, the difference between them being equal to 5.4–9.5 ppm.[16,17] The dependence of the chemical shift on the concentration of the solute is characteristic of only the carbon atoms that are directly linked to the C(3) atom.

Analysis of the spectral data for 1-aryl-3-alkyl-5-(benzothiazol-2-yl)formazans with consideration of the observed regularities made it possible to calculate the ratio of the *EEE* to *EEZ* isomers in solution. An increase in the length of the alkyl substituent at the C(3) atom results in the predominance of the $Z^{3,4}$-isomer in solution, while an increase in its bulk (*e.g.*, for R^3 = Pr^i) stabilises the *EEZ* configuration with a five-membered chelate ring (structure **B** in Scheme 1) irrespective of the nature of the solvent. The ratio of the $E^{3,4}$ to $Z^{3,4}$ isomers of compounds studied in solution depends on both the nature of the solvent (polar protic solvents stabilise the *Z* form, while non-polar solvents stabilise the *E* form) and on conditions of isolation and purification of formazans.[16]

The configurations and electronic structures of several novel 3-furyl-, 3-thienyl- and 3-pyrrolylformazans have been studied.[18] The electron density distribution in these molecules was studied by the PPDP/2 method and related to the electronic structures of the substituents and the nature of the heteroatom in the heterocycle.

2. Tautomerism of formazans

It is believed that the tautomerism of triarylformazans containing identical substituents at the N(1) and N(5) atoms ($R^1 = R^5$) is an intramolecular process occurring between two degenerate forms. In 1,3,5-triphenylformazan with the *EZZ* configuration (structure **A** in Scheme 1), the proton forms covalent bonds alternately with the N(1) and N(5) atoms in the course of intrachelate proton transfer with the lifetime of the tautomers of about 10^{-3} s. The position of the hydrogen atom in the azohydrazone chain is important for formazans with different substituents R^1 and R^5.

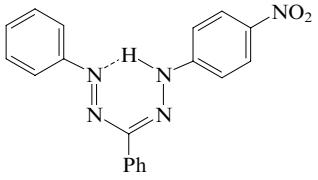
The tautomeric ratio in solution of a formazan is determined by the electronic characteristics of the substituents at the N(1) and N(5) atoms. The introduction of a strong electron-withdrawing (*e.g.*, acyl , nitro or dinitrophenyl) or an electron-donating group may lead to only one tautomer. The levelling of the electronic characteristics of the terminal substituents (*e.g.,* if R^1 and R^5 are different aromatic groups) results in a tautomeric equilibrium $R^1NH \rightleftharpoons R^5NH$; the position of the latter is judged upon by a number of features established from the analysis of ^{1}H and ^{13}C NMR spectra (see Refs 2 and 3).

The changes in the chemical shifts of the signals for the carbon atoms of the aryl substituent linked to the N(1) or N(5) atom in the ^{13}C NMR spectrum relative to the signal for the carbon atom of benzene or its derivative ($\Delta\delta$ ^{13}C) are the most informative. A method for the quantitative evaluation of the tautomeric equilibrium of formazans[3,19] allowed determination of the percentage of one of the tautomers [*e.g.,* that containing a proton at the N(5) atom] according to the formula:

$$P_{R^5NH} = \left(\frac{\Delta\delta_{R^5} - \Delta\delta_{R^5N=N}}{\Delta\delta_{R^5NH} - \Delta\delta_{R^5N=N}}\right) \times 100\%,$$

where $\Delta\delta_R{}^5$ is the experimental change of the chemical shift (δ ^{13}C) of the carbon atoms of substituent R^5 relative to that in substituent R^5H; $\Delta\delta_R{}^5{}_{NH}$ is the change of the δ ^{13}C of the carbon atoms of substituent R^5 relative to that in R^5H calculated for the R^5NH tautomer and $\Delta\delta_R{}^5{}_{N=N}$ is the difference calculated for the R^1NH tautomer.

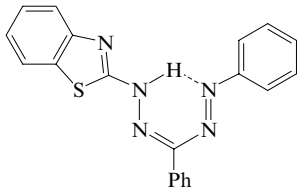
The nitrophenylhydrazone group of 1,3-diphenyl-5-(*p*-nitrophenyl)formazan (**12**) was used as a model of the R^5NH tautomer, while its azophenyl fragment, as a model of the R^1NH tautomer. It is considered[19] that compound **12** exists in solution in the form of nitrophenylhydrazone.



12

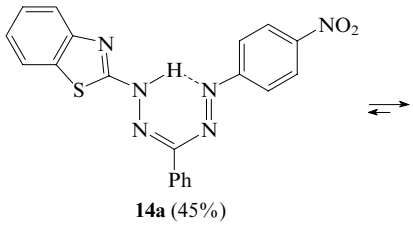
The most characteristic changes in δ ^{13}C induced by the azo or the hydrazone fragment were observed for the carbon atoms in the *ipso*, *ortho* and *para* positions. The calculations took into account the changes in the chemical shifts of these atoms.

At present, this method is considered to be the most convenient and reliable procedure for determininging the percentage of tautomeric forms of different types of formazans. For example, a comparison of δ ^{13}C in R^1NH and R^5NH tautomers of 1,3-diphenyl-5-(benzothiazol-2-yl)formazan (**13**) suggests that this compound exists almost exclusively in the form of a PhN(1) tautomer irrespective of the solvent polarity.[3]

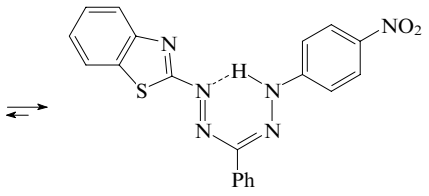


13

The enhancement of the electron-withdrawing properties of the aryl substituent at the N(5) atom (introduction of the *p*-nitrophenyl group, formazan **14**), leads to co-existence of azoaryl tautomer **14a** with a considerable amount of the arylhydrazone tautomer **14b**.



14a (45%)

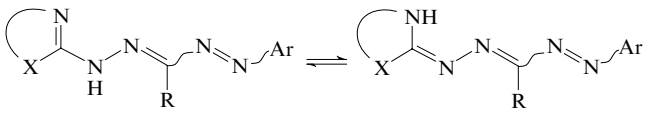


14b (55%)

Quantitative evaluation of the tautomeric equilibrium in solutions of formazan revealed that, unlike the gas phase, the effect of the electronic characteristics of substituents R^1 and R^5 on the position of the tautomeric equilibrium is very pronounced. In 1,3,5-triarylformazan solutions, the equilibrium is fully shifted towards the form where the proton is localised at the nitrogen atom linked to the substituent with the strongest electron-withdrawing properties.[2,3]

Similar conclusions were made in studies on the tautomerism of 3-furyl(thienyl, pyrrolyl)formazans by mass spectrometry.[18,20]

In addition to the aforementioned prototropic equilibrium ($R^1NH \rightleftharpoons R^5NH$), the amino – imino (formazan – formazene) tautomerism, which involves the nitrogen atom of the azaheterocyclic substituents, is observed for 1-aryl-5-hetarylformazans.[2] Quantitation of the isomer ratio in the gas phase of hetarylformazans by mass spectrometry presents a problem due to identical masses of the fragment ions of the imino (**15a**) and amino (**15b**) tautomers of the heterocycles.



15a **15b**

However, the predominant localisation of the proton at the endocyclic nitrogen atom (the imine form of the type **15a**) of 1,3-diphenyl-5-(benzothiazol-2-yl)formazan (**13**) could be established on the basis of electron impact and chemical ionisation mass spectrometry and using semiempirical calculations.[21]

The position of the ν_{NH} band in the IR spectra of *N*-hetarylformazans has long remained the only spectral criterion of the amino – imino tautomerism in solutions. The imino form manifests a characteristic band around 3420 – 3460 cm^{-1}, while the band around 3330 – 3360 cm^{-1} is more typical of the amino form.

^{13}C NMR spectroscopy is the most informative method for studying the amino – imino tautomerism in solutions. These conversions strongly affect the chemical shifts of the carbon atoms in azaheterocycles. The use of fixed models of different isomeric forms of 1-phenyl-3-methyl-5-(benzothiazol-2-yl)formazans **9** – **11** as examples revealed[15] that the differences in the chemical shifts (δ ^{13}C) of individual atoms in the benzene rings of the heterocycle range from 7 to 11 ppm. A comparison of the δ ^{13}C values in the ^{13}C NMR spectra of model compounds and the corresponding formazans enabled quantitative determination of the ratios of amino to imino tautomers in solutions of trisubstituted 1(5)-aryl-5(1)-(benzothiazol-2-yl)formazans.[13,16] It was found that the concentration of the imino tautomer in a non-polar solvent decreases with an increase in the bulk of the substituent at the C(3) atom and the ability of formazans to exist in a 'folded' state stabilised by intramolecular H-bonds. Thus in $CDCl_3$ the contribution of the imino tautomer of formazans **13** (the *EZZ* isomer) and **4b** (the *EEZ* isomer) could not be reliably established because its percentage did not exceed 5%, whereas that of the imino tautomer of *EEE* formazan **4a** was 20% – 25% [calculated from signals for the C(4), C(8) and C(9) atoms of the heterocycle]. In proton-acceptor solvents, the percentage of the imino tautomer increases (in some cases, up to 44% – 76%).

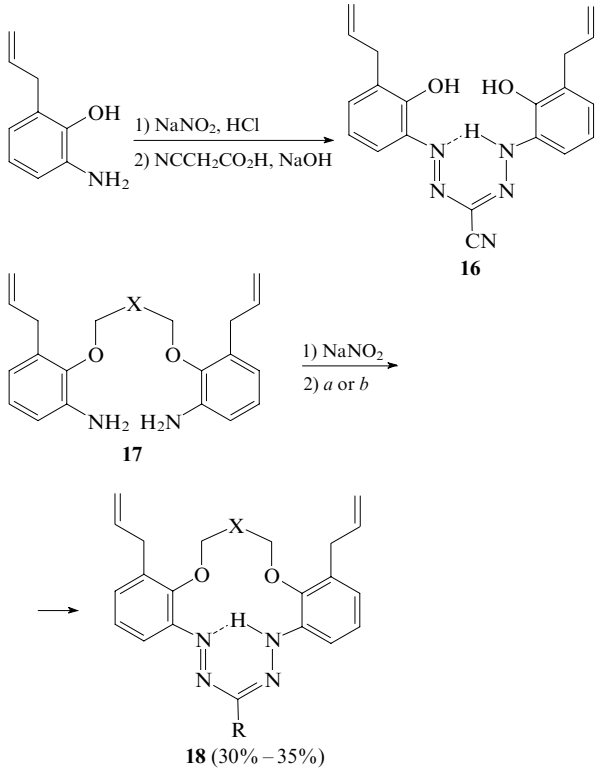
A comparison of the tautomeric compositions of solutions of 1-aryl-3-phenyl-5-hetarylformazans differing in the substituents at the N(5) atom demonstrated that the contribution of the imine structure increases with an increase in the basicity and a decrease in the aromaticity of the heterocycle. Thus in formazans containing thiazole, benzothiazole and benzoxazole rings the position of the tautomeric equilibrium in non-polar solvents was close to that for triarylformazans, *i.e.*, both classes of compounds exist predominantly in the amine form. In contrast, their benzimidazole analogues exist exclusively as imino tautomers with the *EEE* configuration.[3]

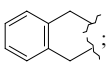
The preferable tautomeric forms of *N*-pyrazolyl-*C*,*N*-diarylformazans were established on the basis of a comparative analysis of quantum-chemical calculations and spectroscopic data.[22]

III. Synthesis and properties of formazan derivatives

The majority of recent studies aimed at the synthesis of novel formazans are directed at the design of substances with valuable properties. Most often, the known approach to the synthesis of formazans is used, which is based on reactions of aryl(hetaryl)hydrazones with diazo compounds, non-traditional compounds being used as amine, hydrazine or aldehyde components in recent years. Thus the introduction, into the azohydrazone chain, of new heterocycles that play the role of additional addends for complexation and such metal-coordinating groups as podands, crown ethers, *etc.*, allows preparation of metal chelates with improved characteristics.

Allyl-substituted macrocyclic crown-formazans as non-traditional intermediates for the design of polymeric macrocycles have been synthesised.[17] Thus bisphenol **16** was prepared by a reaction of diazotised 6-allyl-2-aminophenol with cyanoacetic acid. Diazotisation of diamine **17** and its subsequent azo coupling with compounds containing a reactive CH group have led to a vast variety of the corresponding macrocyclic formazans **18**.

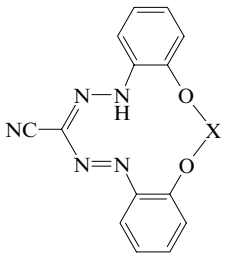


X = $(CH_2)_3$ or ;

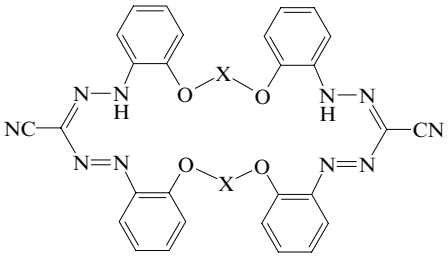
(*a*) $NCCH_2CO_2H$, Py, Cu(II) (for R = CN);
(*b*) $PhCH_2C(O)CO_2H$, NaOH, H_2O (for R = Ph).

The synthesis of 14- and 15-membered crown-formazans and estimation of the prospects of their use for spectrophotometric determination of lithium have been described.[23] These compounds were shown to be highly selective chelating agents for this ion. Some of these formazans were assayed as selective neutral conductors for caesium ion-selective electrodes.[24] Thus formazan containing a 4-pyridine *N*-oxide residue at the C(3) atom manifested the highest selectivity with respect to caesium ions with low selectivity for potassium and ammonium ions.

Crown formazans **19a–c** as well as 28- and 30-membered bisformazans **20a–c** have been synthesised in low yields.[25]



19a–c



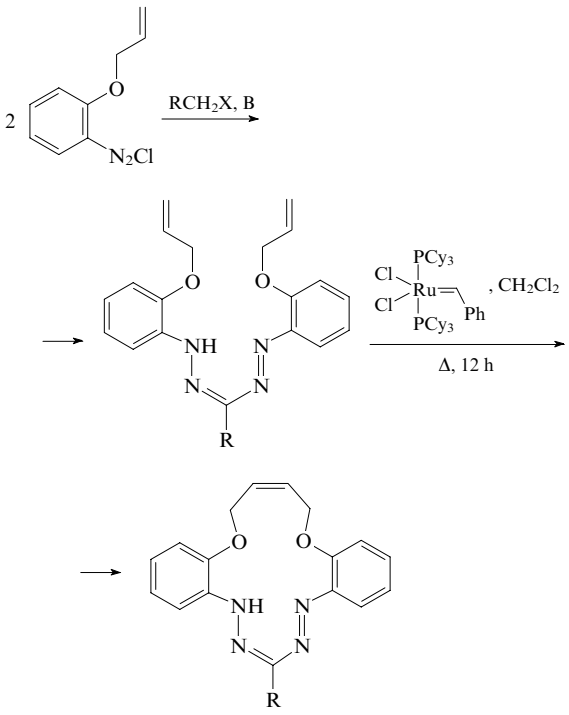
20a–c

X = $CH_2C(=CH_2)CH_2$ (**a**), $(CH_2)_3$ (**b**), $(CH_2)_4$ (**c**).

Mixtures of formazans **19** and **20** were separated into individual components by TLC.

Ozonolysis of compound **19a** at low temperature yielded ketone **19d**; reduction of the latter with sodium borohydride gave alcohol **19e**. The condensation of ketone **19d** with 1,3-diaminopropane yielded bisformazan **21** (Scheme 2).

A highly stereoselective synthesis of 15-membered macrocyclic crown formazans **22** with *Z* configuration of the C=C bond (the *Z* : *E* ratio varied from 90 : 10 to 97 : 3) has been carried out.[26]



22 (60% – 95%)

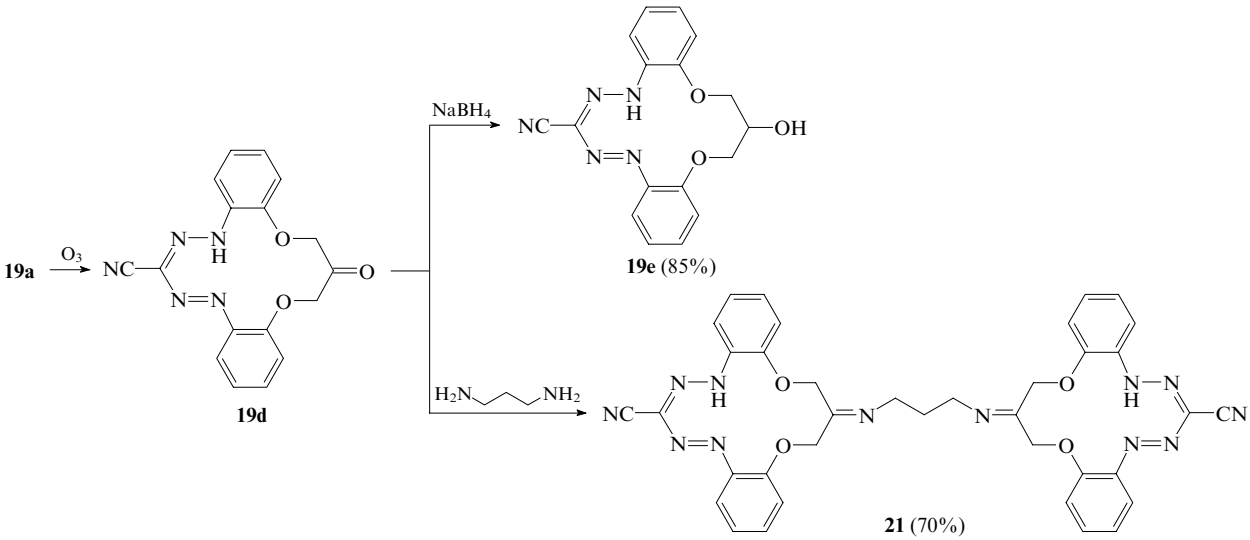
R = CN, Ph, 4-ClC_6H_4, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-$C_5H_5N^+O^-$, $PhSO_2$; X = CO_2H or $C(O)CO_2H$; Cy = cyclo-C_6H_{11}.

The introduction of podands containing oligooxyethylene bridges of various lengths between two formazan fragments afforded new classes of bisverdazyls (**23**) and bisverdazylium salts (**24**) (Scheme 3).[27]

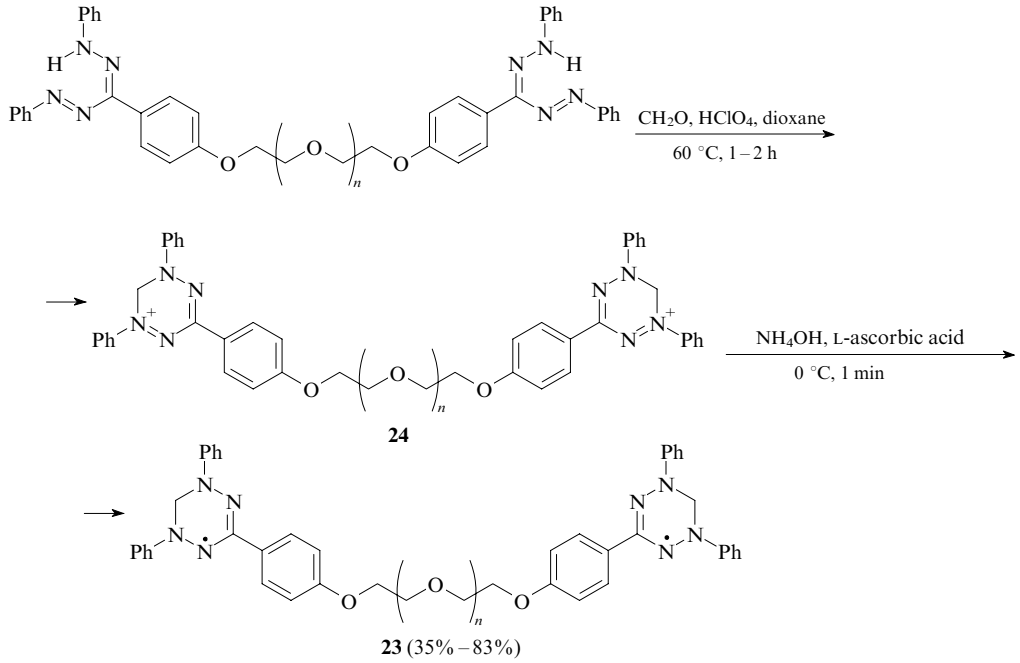
Bisverdazyls **23** represent a novel class of stable biradicals: solid samples decompose at room temperature only after several days, while their solutions in organic solvents do not change optical densities over a course of several weeks. The calculated distances between the spin centres agree well with experimental values.[28] These compounds are good models for the study of 'host – guest' interactions.

Podands can be used as amine (like the aforementioned compounds **18–22**) or aldehyde components in the synthesis of formazans (in the latter case, the role of the azo component is played by diazonium salts). The synthesis of benzothiazolylfor-

Scheme 2



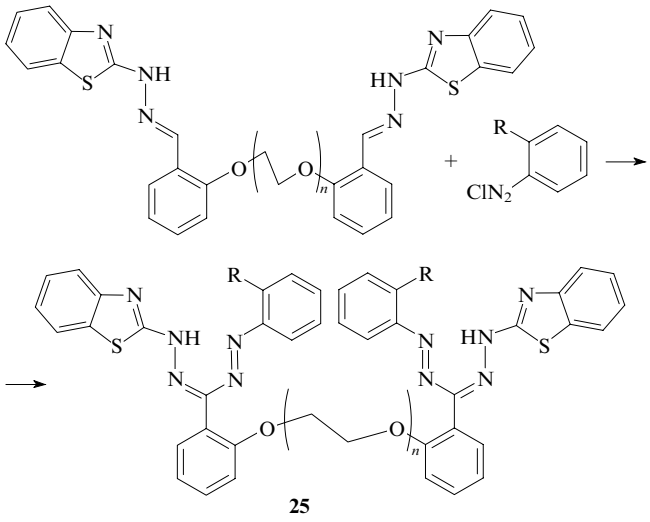
Scheme 3



24

23 (35% – 83%)

mazans **25** containing oxyethylene groups (n = 1 – 3) has been described.[29] Cross-linked salicylaldehyde benzothiazol-2-yl-hydrazones and diazonium salts prepared from aniline or *o*-anisidine served as the starting compounds in the synthesis of podands **25**.



25

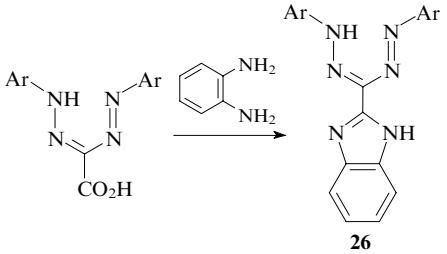
R = H (n = 1 – 3), OMe (n = 2, 3).

The complexation ability of nickel(II), cadmium(II), zinc(II) and lead(II) ions toward compounds **25** has been investigated. Formazans **25** formed mono- and binuclear complexes with these metals. The introduction of an oxyethylene bridge not only expanded the range of the coordinated metals, but also conferred novel properties on the formazan complexes. Thus the binuclear lead(II) – formazan **25** complex (R = OMe, n = 2) shows photochromic properties.[29] After sunlight irradiation, the blue colour of a solution of the complex in ethanol changed into orange; the original colouring was restored in the dark. Such interconversions occur repeatedly with no change in the absorption intensity in the electronic spectra. The reaction of formazan **25** (R = H, n = 3) with solid metal salts yielded coloured complexes only with zinc(II) and cadmium(II) ions, which can be used for the extraction of these metals from mixtures. Some specific features of the behaviour of zinc and cadmium formazanates with respect to sunlight were established.

A recently published review [30] devoted to macrocyclic formazans describes methods for the synthesis and properties of crown formazans, discusses elucidation of their structures by NMR, IR and UV spectroscopy and mass spectrometry and presents data on their reactivities and applications.

The synthesis of 1,5-diphenylformazans carrying a substituted benzene ring at the C(3) atom has been described.[31] The structures of formazans were studied by IR, ^{1}H and ^{13}C NMR spectroscopy. A good correlation was found between the absorption maxima in the electronic spectra and the Hammett constants of the substituents in the benzene ring. Tetrazolyl-substituted formazans were prepared from (tetrazol-1-yl)acetohydrazide and *p*-chloro- or *m*-nitrobenzaldehyde.[32] The condensation was induced by microwave irradiation. The hydrazone formed was then treated with a diazonium salt to give a high yield of 1,3-diaryl-5-[(tetrazol-1-yl)acetyl]formazan.

The condensation of 1,5-diaryl-3-carboxyformazan with *o*-phenylenediamine yielded 1,5-diaryl-3-(benzimidazol-2-yl)formazans **26**.[33]



26

Reductive cleavage of these compounds yielded benzimidazole-2-carboxamide arylhydrazones.

The ability of formazans to form complexes with metal ions is among their most salient properties. Thus 1,5-bis(2-carboxyphenyl)-3-(2-furyl)formazans gave complexes with zinc(II), cadmium(II), mercury(II) and lead(II) ions and mixed-ligand complexes of these formazans and 2,2′-bipyridyl with cadmium(II), mercury(II) and lead(II).[34] The structures and properties of the synthesised compounds were studied by IR, electronic and ^{1}H NMR spectroscopy; their thermal analyses were carried out.

The synthesis and spectroscopic analysis of 1-aryl-3-(n-heptyl)-5-benzothiazolylformazans and their complexes with metal

ions have been carried out.[35] It was found that these formazans form 1 : 1 complexes with silver(I) ions and 1 : 2 complexes with nickel ions. The ligands of some compounds of this series formed stable complexes with lead and rare-earth ions. In aprotic solvents (*e.g.,* acetonitrile), formazans manifested specific, *e.g.,* complexing, properties. For example, the *m*-nitro group in an aryl substituent at the N(1) atom is involved in the coordination to the metal.

The dependence of complexation of formazans with metals on the nature of the solvent has been studied.[36] A comparison of complexing properties of aryl- and hetarylformazans in acetonitrile revealed that the efficiency of the complexation depends on the ionic strength of the solutions and the donor-acceptor properties of the substituents in the ligand molecule.

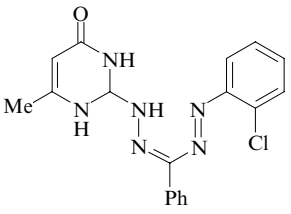
Some recently published papers were devoted to practical applications of formazans as analytical reagents for the determination of microquantities of metals in various objects. Thus 1,5-bis(2-carboxyphenyl)-3-phenylformazan was used for spectrophotometric determination of copper ions in the presence of other metal ions.[37] The highly sensitive colour reaction of 1-(2-hydroxy-5-sulfophenyl)-3-(2-hydroxyphenyl)-5-(3,5-dibromo-2-pyridyl)formazan with copper ions for the determination of the copper content in ores has been studied.[38] Simple, rapid and accurate methods for the spectrophotometric determination of divalent cobalt, copper and palladium ions based on the formation of coloured complexes of these metals with 1-(2-arsenophenyl)- (Ref. 39) and 1-(2-carboxyphenyl)-3-benzoyl-5-phenylformazan (**27**) have been developed and employed for the quantitation of copper ions in alloys.[40] Carboxyphenylformazan **27** was recommended as an indicator in spectrophotometric titration of cobalt, copper and palladium by ethylenediaminetetraacetic acid (EDTA). In the series of hetarylformazans, 1-(2-hydroxy-5-nitrophenyl)-3-isopropyl-5-(benzoxazol-2-yl)formazan was found as a new extractant for preconcentration and determination of scandium(III) ions.[41] This compound was highly selective with respect to Sc(III) in the presence of different metals. Its lower homologue, *viz*., 1-(2-hydroxy-5-nitrophenyl)-3-ethyl-5-(benzoxazol-2-yl)formazan, proved to be a selective reagent for the photometric determination and preconcentration of lead.[42]

Formazans are used more and more often in flow injection analysis (FIA). This method in combination with spectrophotometric detection of multicomponent mixtures can be used for simultaneous determination of cobalt, copper and zinc ions (in the concentration range 0.2–1.9 μg ml^{-1}) with 1-(2-carboxyphenyl)-3-phenyl-5-(2-hydroxy-5-sulfophenyl)formazan as the chromogenic reagent.[43] This procedure was employed for the determination of copper and zinc in blood sera, veterinary preparations[43] and plants.[44] Formazans were also proposed as sorbents for flow sorption–atomic absorption determination of metals in solutions.[45]

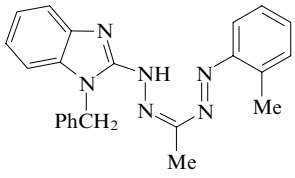
A spectrophotometric procedure for the determination of copper ions in water using 1,5-bis(2-hydroxy-5-sulfophenyl)-3-cyanoformazan has been developed.[46] A rapid spectrophotometric method was described[47] for the determination of zinc in biological materials and pharmaceutical preparations using 3-acetyl-1,5-diarylformazans as ligands in the presence of cetylpyridinium chloride.

The ability of formazans to form complexes with metals is also used in some electrochemical analytical techniques. Thus the electrochemical behaviour of seven hetarylformazans used as components of carbon-containing inks of thick-film screen-printed electrodes was studied.[48,49] The compositions of complex compounds formed on the electrode surface and their stability constants were determined. It was shown, for example, that 1-(2-chlorophenyl)-3-phenyl-5-(6-methyl-4-oxo-3,4-dihydropyrimidin-2-yl)formazan (**28**) provides high sensitivity of graphite-containing modified electrodes, low detection limits with respect to Cu(II), Pb(II), Cd(II) and Zn(II) ions and high reproducibility of the results of analysis.

A mercury-free thick-film graphite-containing electrode modified with 1-(*o*-tolyl)-3-methyl-5-(1-benzylbenzimidazol-2-yl)formazan (**29**) was proposed for the determination of Mn(II) ions by the cathodic inverse voltammetric method.[50] The determination limit of manganese(II) with this electrode was 0.04 μg $litre^{-1}$; the preconcentration time was 60 s. The dependence of the analytical signal of Mn(II) on its concentration in solution was linear in the range from 0.1 to 30 μg $litre^{-1}$. This procedure was used for the analysis of natural and drinking waters for the detection of manganese(II) ions.



28

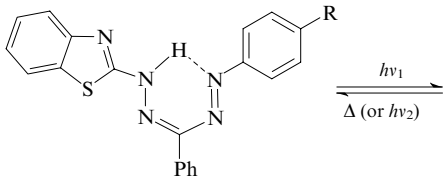


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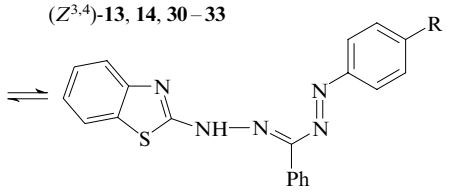
Gas-phase oxidation and reduction of 1-(benzothiazol-2-yl)-3,5-diphenylformazans as well as complex formation with transition metals under laser ionisation were studied.[51] The data obtained suggest that formazan molecules are photoionised to molecular radical ions, which are further involved in ion-molecular reactions. Formazans give singly charged metal formazanates with the composition 1 : 2. Anionic metal complexes of formazans were also studied by capillary electrophoresis–mass-spectrometry.[52]

Photochromic properties of formazans have been known since long ago and were repeatedly discussed in the literature. However, detailed mechanisms of their photochromic conversions still remain obscure. Therefore, the number of publications on this subject is steadily increasing. For instance, the dependence of spectral-kinetic characteristics of photochromic arylformazans on their structures was investigated.[53] It was found that enhancement of the electron-donor properties of substituents was accompanied by a bathochromic shift of the absorption bands of the original chelate structure, the positions of the absorption maxima of the photoinduced form being determined by the properties of the tautomeric structures. As for the kinetic characteristics, they depend exclusively on the thermal relaxation of the photoinduced form into the original state, the rate of this process being related to the nature of the substituents.

The photothermochromic conversions of 1-aryl-3-phenyl-5-(benzothiazol-2-yl)formazans **13**, **14** and **30**–**33** were studied under conditions of steady-state photolysis.[54]



($Z^{3,4}$)-**13**, **14**, **30**–**33**



($E^{3,4}$)-**13**, **14**, **30**–**33**

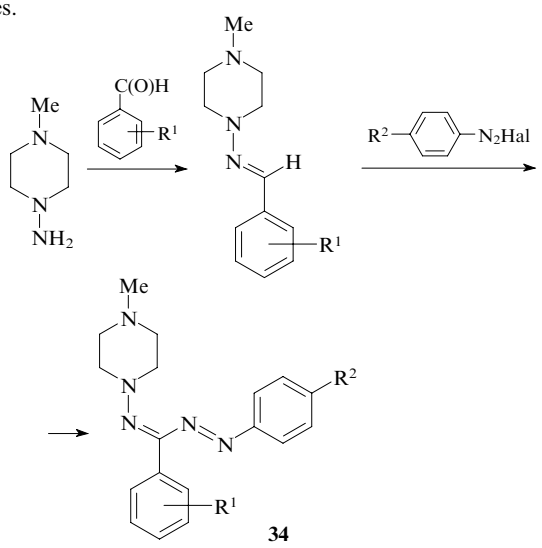
R = H (**13**), NO_2 (**14**), Cl (**30**), Br (**31**), NMe_2 (**32**), CO_2Me (**33**).

Irradiation of solutions of these compounds in toluene at λ = 578 nm resulted in changes of the colour of the solution from red and blue (for R = NO_2 and CO_2Me) to yellow. The relaxation of the photoinduced form into the original state takes place both as a result of either thermal dark reaction or irradiation

(λ = 436 nm). In this case, the *E*,*Z* isomerisation of the C=N bond becomes the major photochemical reaction. The reverse reaction proceeds at a higher rate in comparison with triphenylformazan due to the presence of a weaker intramolecular hydrogen bond in the original forms of formazans **13**, **14** and **30**–**33**. Kinetic studies of photo conversions and thermal conversions of compounds **14** and **33** revealed the presence of an isosbestic point in their absorption spectra. This suggests that the lifetimes of their intermediate forms were significantly shorter than those of the starting compounds and the final products. The photothermal conversions of formazans **13**, **30**–**32** were accompanied by the formation of long-lived intermediate species.

Variation of substituents in the formazan molecule was aimed at a search for biologically active substances. Thus a series of 1-aryl-3-(3,4,5-trimethoxyphenyl)-5-(3-nitrobenzoyl)formazans were synthesised and assayed for antibacterial, antituberculosis and antifungal activities.[55] It was found that formazans comprising 2-chlorophenothiazine could be employed as antiinflammatory agents.[56]

The synthesis of formazans **34** containing the piperazine fragment was described and their biological activities were investigated.[57] Compounds **34** were prepared by a reaction of *N*-amino-4-methylpiperazine with salicylaldehyde or vanillin with subsequent condensation of the hydrazones with aryldiazonium halides.



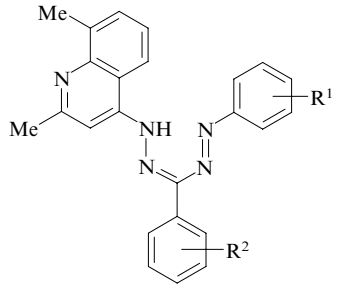
34

R^1 = 2-OH, 3-OMe-4-OH; R^2 = 2-OMe, 3-OH, 4-OH, 4-OMe.

Some formazans **34** manifest bactericidal activity against S*taphylococcus aureus* and *Mycobacterium* $H_{37}R_v$.

The synthesis of formazans containing the 1,8-naphthyridinyl fragment was described and the antibacterial effects of these compounds against Gram-positive and Gram-negative bacteria were investigated.[58]

Several quinolinyldiarylformazans **35** were assayed for tuberculostatic (*Mycobacterium* $H_{37}R_v$) and antibacterial (*E. coli*, *B. subtilis*, *S. paratyphi* B) activities.[59]

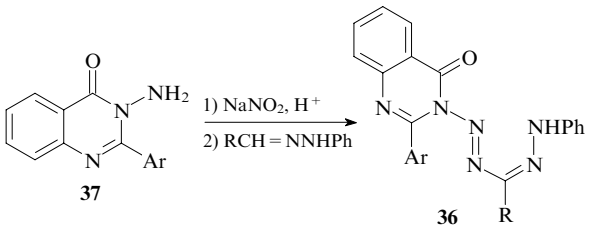


35

R^1 = 4-OMe, 2-Cl; R^2 = 2-OMe, 4-OMe, 4-OEt, 4-OH, 3-OH.

Some of recently synthesised formazans containing a *p*-toluenesulfamide fragment possess high fungicidal activity.[60]

A series of 1-[2-aryl-4-oxo-(3*H*)-quinazolin-3-yl]-5-phenylformazans **36** have been synthesised.[61] *N*-Aminoquinazolinones **37** prepared by condensation of the corresponding benzoxazinone with hydrazine hydrate served as the starting compounds in the synthesis of formazans **36**. Diazotisation of compounds **37** and condensation of the diazonium salts with aldehyde phenylhydrazones gave quinazolinylformazans **36**. The latter manifest moderate activity against *Vaccinia* virus.



37 **36**

R = Ph, PhCH=CH.

Antiviral, antibacterial and fungicidal effects of formazan derivatives and the respective tetrazolium salts† have been studied.[62–64]

In some cases, directed synthesis of formazans designed for biological studies was achieved through introduction of various pharmacophore groups into formazan molecules. 1-Phenyl-3-[2-methoxy-4-*N*,*N*-bis(2-cyanoethyl)aminophenyl]-5-arylformazans were assayed for anticancer and anti-HIV activities.[65] In a more recent study,[66] a series of 3-[2-methyl-4-*N*,*N*-bis(2-cyanoethyl)-aminophenyl]-containing formazans were assayed for the same activities. Formazans containing *p*-tolylhydrazine residues were also synthesised,[67,68] but they were found to be inactive.

A series of formazans containing benzenesulfamido groups were synthesised[69] and their properties including the fungicidal activity were investigated.

It was found[70] that hetarylformazans containing the indole fragment at position 3 possess contraceptive properties. Reactions of 6-substituted indole-3-carbaldehydes with (1-naphthyl)acetohydrazide and their subsequent coupling with aryldiazonium salts yielded indol-3-ylformazans[71] possessing weak antiviral activity.

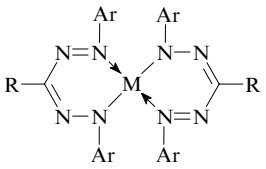
The above-mentioned examples unequivocally demonstrate that formazans hold little promise as basic materials for medicinal drugs. Unfortunately, the papers cited did not provide any information about the relationship between the results obtained and the nature of the substituents in the formazan fragment.

IV. Formazan complexes with metals: structures and applications

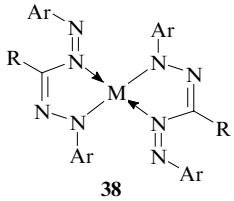
Complex compounds based on formazans constitute a well-known class of tetraaza-coordinated metal chelates.[2,72] These ligands attract attention by virtue of stable intense colour of their metal complexes. Variation of substituents at positions 1, 3 and 5 of the formazan fragment enables the introduction of additional complexing groups which increases the denticity of the formazan ligands.

Reactions of 1,5-diarylformazans with metals yield three types of bicyclic compounds. Those containing two six-membered metallacycles (structure **37**) belong to the first type, two five-membered rings (structure **38**), to the second and one six-membered and one five-membered rings (structure **39**), to the third type.

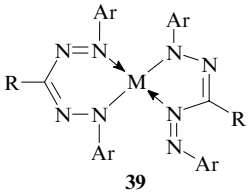
† Tetrazolium salts are formed upon oxidation of 1,5-di- and 1,3,5-trisubstituted formazans.[2]



37



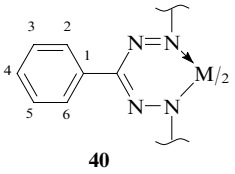
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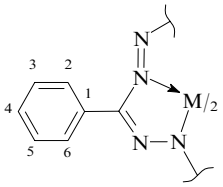
39

The calculation of relative stabilities of systems **37**–**39** by the molecular mechanics method using the PCMODEL software revealed [73] that their strain energies are very close, *viz*., −915, −859 and −976 kJ mol^{-1}, respectively. It is noteworthy that six-membered metallacycles implemented in crystals are far from being energetically favourable. The loss of strain energy of these rings is compensated by intermolecular interactions. If metallacycles contain the same number of fragments, the type of the coordination polyhedron of the complex is determined by the structure of the substituent at the C(3) atom and the nature of the metal complexing agent.

Five- and six-membered rings in diamagnetic formazan complexes with transition metals can be identified by ^{13}C NMR spectroscopy.[72] The transition from the ligand to the metal complex (structure **40**) is accompanied by shielding of the C(1) atom of the phenyl ring at position 3 with a concomitant change in the chemical shift $\Delta\delta$ = 2.4–5.5 ppm and deshielding of the C(2) and C(6) atoms ($\Delta\delta$ = 2.9–4.0 ppm). Contrariwise, deshielding of the C(1) atom ($\Delta\delta$ = 1.6–3.0 ppm) and virtually unchanged chemical shifts of the atoms in the *ortho* position of the benzene ring are more characteristic of structure **41**.



40

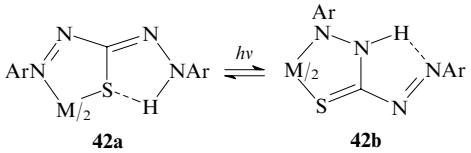


41

In the majority of metal formazanates, the ligand exists as an anion. Only in the Cu(I)–1,5-diphenylformazan complex (compound **7**) is the copper atom coordinated by a neutral molecule (X-ray diffraction data).[72] This complex presents interest as a new example of a molecular adduct based on a chelating formazan ligand.

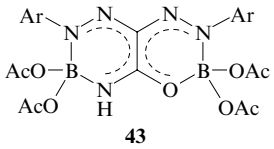
The introduction of additional complexing groups into the formazan molecules not only expands the range of metals able to form complexes with formazans, but also results in formation of new coordination sites. Thus the coordination units of the majority of metal chelates of 1,5-diaryl-3-mercaptoformazans (**42**) contain both nitrogen and sulfur atoms.[2,72]

Metal complexes **42** are characterised by intrachelate bond isomerism, which underlies their photochromism. The changes in the colour of a substance from orange (or red) to blue (violet) upon irradiation are due to proton transfer and subsequent rearrangement of the π-electron system. It is structure **42b** that corresponds to the photocoloured form. Novel photochromic materials were designed based on such metal complexes.



42a **42b**

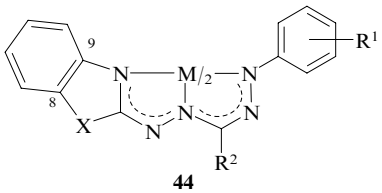
Boron chelates with 1,5-diarylformazans that contain amide groups at position 3 able to bind to the boron atom have been described.[74,75] For example, in compounds **43** the formazan molecule is involved in the formation of two six-membered heterocycles.



43

The ability of formazans containing hydroxy, carboxy, *etc*., groups in the *ortho* position of the aryl substituents at the N(1) and N(5) atoms to coordinate metals, which is accompanied by the formation of five- or six-membered metallacycles, is especially pronounced. Such formazans play the role of tri- or tetradentate ligands.[72]

The introduction of an α-azaheterocycle into the formazan molecule is equivalent to the presence of an aryl substituent with an additional coordinating group; as a result, the ligands acquire a tridentate character. The structures of hetarylformazan complexes were established by ^{13}C, ^{15}N, ^{199}Hg and ^{113,111}Cd NMR spectroscopy and X-ray diffraction.[76–78] These studies demonstrated that Zn-, Cd- and Hg-containing benzazolylformazanates have pseudo-octahedral structures in solutions. The ligand in such complexes is coordinated through the N(1) and N(4) atoms of the formazan fragment and the nitrogen atom of the heterocycle. The changes in the chemical shifts of the heterocyclic substituent (similar to those observed for the transition from the amino to the imino tautomer) and the values of the spin-spin coupling constants of the carbon atoms in the benzene ring fused to the heterocycle [C(8) and C(9) atoms in structure **44**] were used as characteristic criteria for the identification of this coordination mode.[76]



44

X = S, O; M = Ni, Co, Zn, Cd, Hg, Fe, Mn.
R^1 = H, OMe, Bu^n; R^2 = Pr^i, Bu^n, Ph.

The chemical shifts in the ^{199}Hg and ^{113,111}Cd NMR spectra and the spin–spin coupling constants of these nuclei with the ^{13}C nuclei of the ligand were measured.[78] For the first time, ^{14}N NMR spectroscopy was used [77] in structural studies of zinc and cadmium complexes **44**, in the first place, with regard to the ^{14}N nuclei in the coordination units.

It should be noted that independently of the isomeric form of the starting formazan, the complexes formed contained only an imino tautomer in the *EZZ* configuration. The results of X-ray diffraction studies of complexes **44** [M = Ni, X = S, R^1 = 4-Bu^n, R^2 = 4-Bu^n; M = Co, X = S, R^1 = 4-Bu^n, R^2 = Ph; M = Fe(II), X = O, R^1 = H, R^2 = Pr^i; M = Fe(II), Mn(II): X = S, R^1 = H, R^2 = Ph][79–82] suggest unequivocally the involvement of the nitrogen atom of the benzazole system in the formation of the metallacycle. The configuration of the metal bonds in these

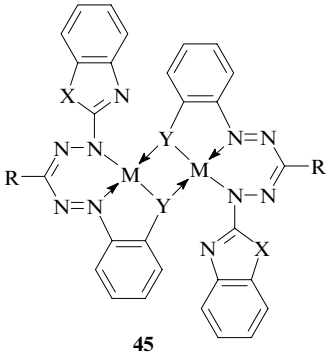
complexes represents a distorted octahedron with an MN_4 coordination unit.

Complexes similar to compounds **44** were also prepared on the basis of formazans containing azine fragments.[2,72]

The geometry of metal hetarylformazanates is represented by only one type of a polyhedron, *viz*., a distorted octahedron; the degree of distortion and the coplanarity of the metallacycles depend on the nature of the metal and the structure of the ligand. In contrast to their aromatic analogues, hetarylformazan complexes contained predominantly five-membered metallacycles.[83]

It was found [82] that reactions of 1,3-diphenyl-5-(benzothiazol-2-yl)formazan (**13**) with Fe(III) and Mn(III) ions result in the reduction of metal ions to the oxidation state 2+ and, as a consequence, in the oxidation of the formazan to the tetrazolium salt. The complex compounds formed had a composition L_2M; the iron complex was diamagnetic. The structures of the formazanates were confirmed by X-ray diffraction data. At the same time, Fe(III) and Mn(III) ions retained a high oxidation state in reactions with 1-(2-carboxyphenyl)-3-alkyl-5-(benzothiazol-2-yl)formazan; the corresponding iron complex was paramagnetic. In the authors' opinion, in the latter case this was due to the involvement of the carboxy group in the complexation with the metals.

Indeed, 1-hetaryl-5-arylformazans with a hydroxy or a carboxy group in the *ortho* position of the aryl substituent at the N(1) atom can be regarded as tetradentate ligands that form complexes **45** with metals.[72,84]

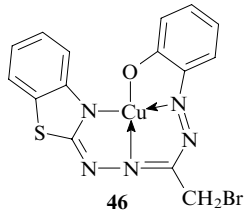


45

X = NH, NAlk, S; Y = O, OC(O); M = Ni, Zn; R = Alk, Ar.

It is noteworthy that depending on the position of the nitro group in the *N*-aryl fragment in complexes **45** (M = Zn) with 1-[2-hydroxy-4(5)-nitrophenyl]-5-(benzazol-2-yl)formazan the ligand is coordinated to the zinc atom either in the hydroxyazo (similar to nickel complexes) or in the quinone–hydrazone form.[84] In contrast to nickel formazanates, zinc complexes readily undergo ligand exchange reactions with amines. Owing to this property, such complexes have been used for the design of thermochromic systems with positive and negative thermoinduction effect.

The compositions and structures of coordination units in Cu(II)–benzothiazolylformazan complexes were studied by EPR spectroscopy.[85] It was found that depending on the nature of the substituents at the N(1) atom, the copper atom acquires a square-planar or a pseudo-tetrahedral configuration. For L_2Cu complexes prepared in an excess of a ligand, the coordination unit CuN_4 formed contained the N(1) and N(5) atoms of formazan (see structure **37**). 1-(2-Hydroxyphenyl)-5-(benzothiazol-2-yl)formazan gave copper complex **46** (LCu) the copper atom in which is coordinated to the nitrogen atoms of the heterocycle, to the N(1) and N(4) atoms of the formazan chain and to the oxygen atom of the hydroxy group (the coordination CuN_3O unit).



46

Mono- and binuclear metal formazanates present interest as catalysts for diverse chemical reactions. Thus benzazolylformazan–nickel complexes manifest high catalytic activity in the dimerisation of ethylene.[86] The synthesis of novel homo- and heterobimetallic catalysts based on 1,5-diaryl-3-ferrocenylformazan complexes has been described.[87]

The structures and properties of thorium(IV), uranium(VI) and REE 3-acetyl- and 3-cyano-1,5-diarylformazanates have been studied.[88–91] It was found that the stabilities of REE 1,3,5-triphenylformazanates correlated with the basicity of the ligand as well as with the ionisation potential, electronegativity and the ionic radius of the metal.

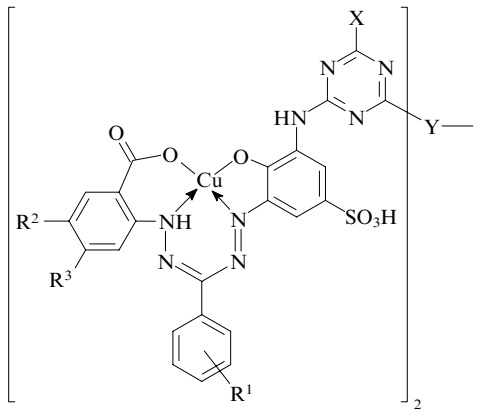
Ligands containing two formazan fragments were used in the synthesis of polymetallic complexes.[92] Tetranuclear complexes with cobalt, nickel, copper, manganese, zinc, cadmium and mercury ions were prepared from bis[1-phenyl-3-(2-hydroxyphenyl)formazanyl]phenyl ether. The results of spectroscopic and magnetic studies suggest that Co(II)-, Cu(II)- and Mn(II)-containing complexes have an octahedral or a distorted octahedral structure; Ni(II) derivatives have a planar structure, while Zn(II), Cd(II) and Hg compounds have a tetrahedral structure. Palladium complexes with formazans containing a heterocyclic fragment (pyrrole and 1-methylpyrrole) were synthesised [93] and their properties were investigated.

Potentiometry, conductometry, IR spectroscopy, thermogravimetry and measurements of electroconductivity and magnetic susceptibility were used for the study of complexation of praseodymium, neodymium, samarium, gadolinium, holmium, erbium, thulium and ytterbium ions with symmetric 1,5-diphenyl-3-cyanoformazan.[94] In a study [95] of complexation of benzazolylformazans with uranyl ions and some REE, it was demonstrated that uranyl complexes have mainly the composition $L(UO_2)$ in solution and in the crystalline state, while benzazolylformazan–REE coordination complexes have the composition L_2M.

The same authors [96] studied the complexing properties of 1-(2-hydroxyphenyl)-5-benzazolylformazans with respect to scandium(III) ions in the pH range 3–10. The composition of scandium formazanates (L_2Sc) was confirmed by IR and electronic spectroscopy and the ligand exchange method, while the structure of the coordination unit depends on the nature of the heterocycle.

The fluorescence properties of formazan–REE complexes were studied in solutions and in monolayers.[97] For the first time, fluorescence in the IR spectral region of complexes of 1-aryl-3-alkyl-5-benzothiazolylformazans devoid of additional complexing groups was detected. It was found that the efficiency of fluorescence depends on the structure of formazans, nature of the metals and state of the surface of Langmuir–Blodgett films as supports.

Many properties of formazan–metal complexes (in the first place, their catalytic, photochemical and thermochromic properties) are connected with conversions that involve the metal chelate unit. However, only functional groups of the ligand can be involved in reactions of metal formazanates without affecting the nearest environment of the metal centre. These reactions include acylation of peripheral groups by acid derivatives (including those of the heterocyclic series), alkylation, reactions with azines (most commonly, introduction of pyrimidine and *sym*-triazine), *etc*.[2] These reactions are usually employed for the preparation of active metal-containing formazan dyes, which have long been used for the dyeing of miscellaneous materials. The main advantages of such dyes include high water and light resistance, good colour characteristics, *etc*. The methods for their preparation and dyeing technologies are usually covered by patents.[98] For example, a vast variety of copper complexes based on polydentate triarylformazans (structure **47**) are used as dyestuffs for cellulose materials.[99]



47

R^1 = H, SO_3H, OH, Cl, OMe, C(O)Alk; R^2, R^3 = H, SO_3H;

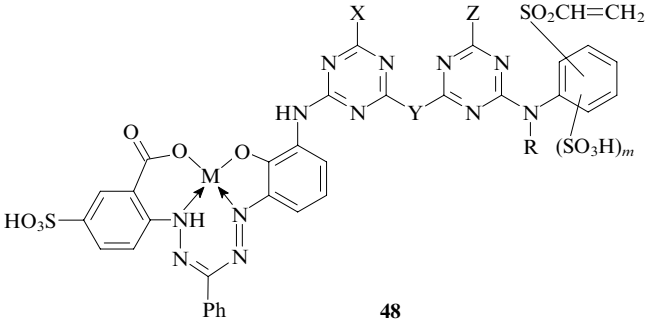
X = N(CH$_2$CH$_2$)$_2$O, $NHCH_2CH_2OH$, $N(CH_2CH_2OH)_2$;

Y = HN–C$_6$H$_4$–C$_6$H$_4$–NH, HN–C$_6$H$_3$(OMe)–C$_6$H$_3$(OMe)–NH.

The synthesis of metal complexes with aryl- and hetarylformazans containing a vast variety of substituents in different positions as promising pigments for cellulose tissues, cotton and synthetic fibres was patented.[100–103] All these dyes contain sulfo groups and triazine fragments able to bind to fibres, whereas copper, nickel or cobalt ions usually play the role of metal centres, which made it possible to attain various shades of blue or green colour.

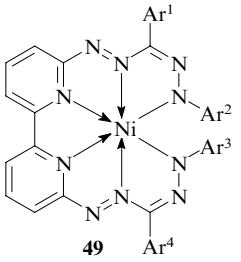
The use of formazan complexes **48**, which represent active dyes with good colour properties, as dyestuff for natural and synthetic cotton and hemp has been patented.[104]

The use of a mixture of nickel–1,3-diaryl-5-(2-pyridyl)formazan complexes **49** as a dye has been studied.[105] By varying aryl substituents, one can obtain dyes with different colour gamut.



48

M = Cu, Ni; X, Z = F, Cl, Br; Y = $NH(CH_2)_nNH$, *etc*.



49

Dyeing entails the use of mixtures of various classes of dyes. For example, formazan–cyanine copolymer dyes for the preparation of optical self-recording layers and sensors contain up to 70%–100% of molecular fragments of the general formula:

$$-\left[\left(F-Z-W-Z\right)_i\left(G-Z-W-Z\right)_g\right]_n-,$$

where F is the fragment of the formazan dye; G is the fragment of the cyanine dye; W is the (cyclo)alkylene, arylene, *etc*., bridging group and Z is the residue of a carbonic acid derivative, urea, an ester or an amide.[106]

The use of composites containing formazans, azo dyes and benzoxazines carrying different substituents in each fragment, has been patented.[107] Such mixtures are distinguished for high colourability and high stability and are used as dyestuff for cellulose fibres. Mixtures of azo and formazan dyes, or pure formazan dyes manifest a synergistic effect in the formation of the colour gamut.[108, 109]

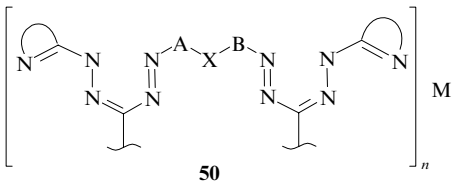
A mixture based on cellulose triacetate, a formazan derivative and an organic solvent was proposed for the manufacture of light- and thermally inhibited films.[110] Here, the nickel complex of 1-(1-methylbenzimidazol-2-yl)-3-methyl-5-(*p*-sulfamidophenyl)-formazan was used as the dyestuff.

The use of formazans, *e.g*., Zincone [1-(2-hydroxy-5-sulfophenyl)-3-phenyl-5-(2-carboxyphenyl)formazan], for staining proteins in polyacrylamide gels [111] demonstrated their advantages over traditional staining reagents, *e.g*., Brilliant Green.

An increasing attention in the past decade was given to the development and application of environmentally safe dyes. Formazan complexes with metals were synthesised where chromium, cobalt and copper ions were replaced by, *e.g*., iron ions.[112, 113] Iron complexes based on 1,5-diaryl-3-cyanoformazans with the composition Fe : L = 1 : 2 were also synthesised.[114] The structures of these compounds and their colour characteristics were studied by ^{1}H NMR, FAB (Fast Atom Bombardment Mass Speectrometry) and electronic spectroscopy. The complexes were used as acid dyestuffs for wool and polyamide fibres. A recently published review [115] is devoted to the chemistry of this type of dyes.

Yet another trend in the practical application of metal complexes based on formazans is their use as materials for registration, recording and storage of information.[116–118] The structures and properties of metal formazanates as optical recording media are described in a series of Japanese patents.[119–122] It is of note [119] that the recording layer contains a dye with the absorption maximum at 700–750 nm, is characterised by high photo and storage stability and is used for recording information on CD carriers.

Metal complexes **50**, which contain two formazan fragments with residues of nitrogen heterocycles, are described in a patent.[123] They were synthesised from formazans directly linked through methylene or sulfonyl bridges.



50

A, B is arylene; X = CH_2, SO_2; M is a divalent metal.

The material based on complexes **50** manifests high light resistance and good storage stability and is used for recording DVD.

There is an increasing number of patents devoted to the use of metal formazanates as optical elements (see, *e.g*., Refs 124–130). The use of a mixture consisting of cyanine or phthalocyanine and formazan derivatives for the manufacture of materials with high photo and storage stability has been described.[124, 130] Such elements are usually employed in the commercial production of CD.

Yet another area of application of formazan-based metal chelates is worth noting, *viz*., a method for the manufacture of thermosensitive materials for lithographic boards based on complexation of formazans.[131]

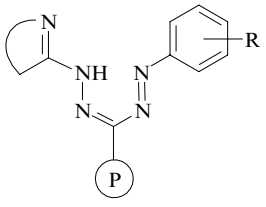
V. Formazan-containing polymers

The advent and development of modern technologies brought forth the necessity of a search for novel materials endowed with desired properties. To such materials one can relate, in particular, formazan-containing polymers including high-molecular-mass metal complexes that have already found wide practical application. Several approaches to the synthesis of such polymers have been developed.

The simplest method includes introduction, into the formazan molecule, of polymerisable fragments. The preparation and properties of polymeric materials containing formazan units are described in a review.[132] Formazans containing a styrene residue at positions 1 and 3 were subjected to anionic (or radical) polymerisation.[132] The polyformazans thus prepared were used for the preparation of polymeric metal complexes, polyverdazyl radicals and polytetrazolium salts. The main advantage of this approach to the synthesis of polyformazans and their complexes is that the composition of the polymer formed and the structure of the metal chelate unit correspond to those of the original monomer. However, its practical application is limited due to possible complications during polymerisation.

The synthesis of polyformazans by polymer-analogous transformations was more successful. Thus numerous formazans containing polymeric fragments at position 1 were obtained from poly(*m*-aminostyrene). Polyacrolein and poly(*p*-formylstyrene) were used for the synthesis of formazans containing polymeric fragments at position 3. Such polymeric formazans were used for the synthesis of chelates with the coordination unit MN_4.[132] Some poly(acroleinphenylformazans) are efficient selective ion-exchangers for extraction of heavy metals: under certain conditions they bind Cu(II) and UO_2(II) ions and do not react with Ni(II) and Co(II) ions. Analogously, poly(styrene–divinylbenzene) with an aldehyde group was transformed to hetarylformazan employed for the preparation of novel adsorbents.[133] The sorption properties of such polymers with respect to heavy metals and the possibility of selective extraction of copper ions were investigated.

Modification of cellulose by hetarylformazans is described in a monograph by V M Ostrovskaya *et al.*[134] This work deals with the description of different methods for immobilisation of formazan-containing reagents and provides examples of their practical applications. Many cellulose derivatives of hetarylformazans **51** were prepared by a reaction of aldehyde-cellulose with hetarylhydrazones and subsequent coupling with aromatic diazo compounds.



51

(P) is cellulose; R = H, OMe, SO_3H, CO_2H, Cl;



2,6- and 4,6-disubstituted pyrimidines, thiazole, pyrazole, benzazoles, *etc.*

It was found [135] that the cellulose backbone exerts the same effect on the chromaticity of formazans as the alkyl substituent at position 3. The bathochromic colour reactions of formazans attached to modified α-cellulose at position 6 with ions of some heavy, precious and rare-earth metals were studied. Irregular polydentate 1-aryl-5-(benzazol-2-yl)formazan-6-α-celluloses were used for the manufacture of reagent test papers (RTP).[135] Formazans covalently grafted to cellulose exceed formazans adsorbed on cellulose in both selectivity and stability, presumably due to higher structural rigidity. Cellulose benzoxazolylformazans are promising analytical reagents for determination of metals by test methods.

Several approaches have recently been developed to the quality control of copper(II) test reagents based on irregular polydentate α-celluloses including those containing 1-(4-methyl-6-methoxypyrimidin-2-yl)-5-phenyl-, 1-(4-methyl-6-methoxypyrimidin-2-yl)-5-(2-carboxyphenyl)- and 1,5-bis(4-methyl-6-methoxypyrimidin-2-yl)formazan units.[136] The efficiency of such materials used as tubes and multilayer test reagents is usually determined from the contrast of their colour reactions with copper(II), which are accompanied by liberation of equivalent amounts of hydrogen ions and formation of chelates.

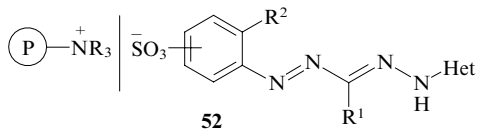
Celluloses modified by benzothiazolyl-, benzoxazolyl- and 4,6-dimethylpyrimidinylformazans were studied in detail [137–140] and characterised by diffuse reflectance spectroscopy. The complexation of these polymers with copper, nickel, cadmium, zinc, lead, silver and mercury ions revealed certain differences in their sorption capacities. The efficiency of extraction of metal ions depends on both the structure of the immobilised formazan group and the complexation conditions. Certain formazan-containing polymers can be used as reagents for the concentration of metal ions, *e.g.,* Cu(II), Ni(II), Pd(II), Hg(II); these polymers served as the basis for the development of novel RTP for the analysis of drinking water.

Sorption of heavy metals by membranes prepared by modification of sheet cellulose with formazan derivatives is accompanied by profound colour transitions.[138] Such membranes have the shape of coloured paper discs and are used, in particular, for purification of distilled and tap water from trace amounts of heavy metals and iron (the metal content in the membranes is determined by visual inspection and X-ray fluorescence analysis). Studies of sorption and chromogenic complexing properties of these membranes with respect to palladium and silver ions and some REE resulted in the development of a procedure for measuring palladium(II) concentrations in process solutions using 1-phenyl-5-(4,6-diphenylpyrimidin-2-yl)formazan-6-α-cellulose.[139] Hetarylformazanyl-6-α-celluloses, which supplemented the database of novel indicator materials, are among promising highly sensitive chromogenic ion-exchange polymeric reagents.[140] They are characterised by a combination of reversible complexation colour and redox reactions.

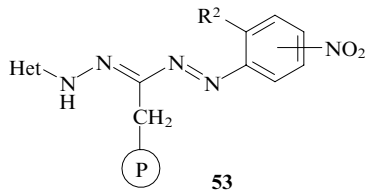
At present, formazans fixed on solid substrates by physical or chemical forces have found wide application as sorbents. The fixation is achieved by covalent immobilisation, ion exchange or physical sorption.[132] The first experiments aimed at immobilisation of formazans on polymeric substrates employed compounds containing amide fragments at position 3 of the formazan chain. Sorbents obtained by immobilisation of aminophenyl-containing formazan on chloromethylated polystyrene manifested anion-exchange properties and high selectivity with respect to noble metals. They allowed isolation of trace amounts of Pd(II) from ammoniacal solutions containing a 10-fold excess of Ni(II). A modified ion-exchange sorbent for the separation of Ag(I) from a 1000-fold excess of Cu(II) was prepared by immobilisation of sulfoformazans on an aminomethylated polystyrene support. The use of silica gel as a substrate for immobilisation of sulfoformazans allowed preparation of an efficient ion-exchanger for preconcentration and separation of Ag(I) ions from Pd(II) and Pt(II) ions.

Selective sorbents for Hg(II) from aqueous media were prepared by fixation of sulfoformazans on cellulose and immobilisation of dithizone on a polyurethane foam.[132] These sorbents are used for the isolation of mercury from domestic and industrial waste waters in a broad range of pH.

Several papers [141–145] describe the results of immobilisation of hetarylformazans on anion-exchangers. Modified ion-exchangers **52** and **53** were prepared by ion-exchange and condensation.



52



53

(P) is a polymer; R^1 = Me, Et, Pr^i, Ph; R^2 = H, OH.

The cross-linked amino-containing ion-exchanger AN-20 and commercial ion-exchangers AV-17, AN-18 and AN-31 differing in basicities were used as polymeric supports. Benzothiazole, benzoxazole and benzimidazole fragments and 4,6-disubstituted pyrimidine were used as heterocyclic components of formazans. The stabilities of the reagents synthesised in different media were found to depend on the basicity of the anion-exchanger. The sorption characteristics of the modified ion-exchangers with respect to a broad range of metals were investigated. They were used for the qualitative detection of trace elements in natural and waste waters and selective isolation of copper and scandium ions from solutions containing accompanying elements. For example, benzoxazolylformazan-modified anion-exchangers **52** selectively bind Sc(III) ions from solutions also containing Ti(IV) and Zr(III). The soprtion properties of modified ion-exchangers depend on the structure of formazans immobilised, nature of the metal and sorption conditions. Representatives of compounds **52** and **53** can be used for efficient separation of copper and nickel in low-concentration acidic solutions, for selective isolation of mercury(II) in the presence of zinc(II) and cadmium(II) and for separation of silver(I) from nickel(II) and cobalt (II) and of zinc(II) from cadmium(II). Some of these polymers were proposed for separation of REE mixtures and preconcentration of lead(II) ions.

Analytical sorption-spectroscopic and test methods are based on the use of the known formazans in a new quality, *viz*., in immobilised form, are actively developed of present. Fibrous materials and ion-exchange tissues are popular solid-phase supports for their immobilisation. Especially promising is a flow-through method for the preconcentration of chromium(VI) compounds on polyacrylonitrile discs filled with finely dispersed strongly basic anion-exchangers. Treatment of the disc with a solution of 1,5-diphenyl-3-hydroxyformazan in a dynamic mode ensures binding of chromium in a complex in the solid phase; metal ions are detected by the diffuse reflectance method.[146] Reagents preimmobilised on the surface of the support have got the name flow sensor systems.

Dithizone is widely used for this purpose. A test method for semi-quantitative determination of zinc by its sorption from alkaline borate solutions onto tissue discs has been developed.[147] Subsequent detection of zinc ions was carried out by visual inspection following treatment with dithizone solutions from the appearance of crimson colour. In another study,[148] the same authors studied colour reactions of zinc ions with dithizone on vinylpyridinium-containing tissues and fibrous materials filled with anion-exchangers using diffuse reflectance spectroscopy. Sensitive optical sensors based on immobilised dithizone for the presence of uranium(VI), mercury(II) and lead(II) compounds have been developed.[149] The use of these materials for direct determination of mercury in various waters revealed that the most sensitive reaction was observed in the case of immobilisation of dithizone on polyamide (*e.g*., caprone, capropore or halipore) membranes.

Non-covalent immobilisation of benzazolyl- and pyrimidinylformazans on polyacrylonitrile fibres filled with the anion-exchange resin AV-17 was carried out and the effects of various factors on the soprtion properties of the polymers synthesised with respect to some heavy metal ions were investigated.[150] Among these compounds, selective sorbents were found for the isolation of copper ions in the presence of nickel, zinc and cadmium ions. Different hetarylformazans were immobilised on polyacrylonitrile fibres filled with the anion-exchanger AN-31 by covalent binding, ion exchange and physical sorption.[151] Studies of the properties of these sorbents demonstrated that they can be used for sorption-spectroscopic determination of heavy metals.

Metallopolymeric systems have been prepared on the basis of immobilised formazans. High efficiency of such products is due to strong multipoint fixation of the metal as the complex with a formazan. Thus the aforementioned hetarylformazan-modified anion-exchangers **52** and **53** were used as ligands in the synthesis of polymeric metal complexes.[152] Copper complexes of these materials prepared by sorption of Cu(II) ions from copper sulfate solutions were studied by EPR.[153] By varying the conditions of synthesis (chemical nature of the formazan, concentration ratio, method of synthesis of metal complexes on solid supports), one can obtain formazanates with different compositions (CuN_4, CuN_3 or CuN_3O) and structures of the coordination metal centre. Polymeric metal complexes were also synthesised [84] by immobilisation of preformed Cu(II) or Fe(II) complexes with sulfobenzothiazolylformazan on an ion-exchanger. In this case, structural features of the coordination sphere of the monomeric analogues are retained.

Formazan-containing polymers were examined as catalysts of decomposition of aqueous solutions of H_2O_2 and liquid-phase oxidation of sulfides and hydrogen sulfide. The analysis of catalytic properties of copper- and iron-containing sorbents based on benzazolylformazan-modified anion-exchangers demonstrated [154, 155] that the best results were obtained at the maximum saturation of the coordination unit of the metal chelate. In the case of copper complexes, the catalytic activity depends on both the content of copper ions and the structure and composition of the metal chelate unit. For example, the activity with respect to decomposition of H_2O_2 decreased on going from copper complexes (CuN_4) with a distorted square-planar coordination mode to mixed nitrogen – oxygen-containing complexes with a square-planar coordination mode.

* * *

The formazan systems considered in this review manifest extremely high tautomeric and conformational flexibilities. The use of such chelating ligands makes it possible to obtain complex compounds that present interest as subjects for solution of the problem of competitive coordination and effect of the nature of the polyhedra on the number of units in the metallacycle. It is noteworthy that in parallel with traditional applications of formazans and their metal chelates as dyes and photochromic agents some new areas emerge, *e.g*., for their application as optical filtres, thermosensitive elements, catalysts, optical sensors, test reagents and modified polymeric materials.

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[i] — *Russ. Chem. Bull., Int. Ed. (Engl. Transl.)*
[j] — *Mendeleev Chem. J. (Engl. Transl.)*
[k] — *Russ. J. Coord. Chem. (Engl. Transl.)*
[l] — *Polym. Sci. (Engl. Transl.)*
[m] — *Russ. J. Appl. Chem. (Engl. Transl.)*