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FORMAZANS IN THE SYNTHESIS OF HETEROCYCLES

I. SYNTHESIS OF AZOLES (REVIEW)

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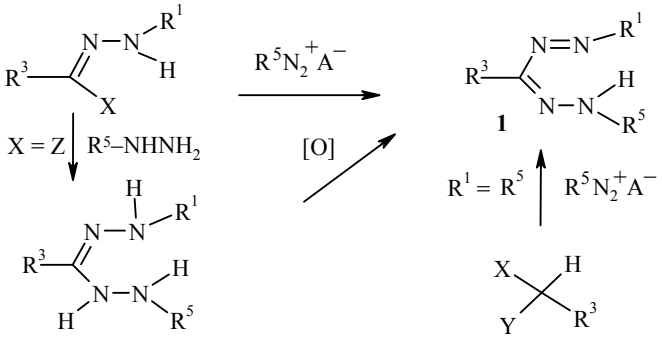
The review covers the use of formazans in the synthesis of azoles.

Keywords: azoles, carbazone, heterocycles, annelated and mesoionic heterocycles, dehydrodithizone, dithizone, indazole, pyrazole, polyazaheteroenes, polyazapolyenes, tetrazole, tetrazolium salts, tetrazolium-5-aminide, tetrazolium-5-methylide, tetrazolium-5-olate, tetrazolium-5-thiolate, 1,3,4-thiadiazole, thiazole, 1,2,3-triazole, 1,2,4-triazole, formazans, 3-HX-formazans (X = S, O, NR, CRR[1]), pericyclic and electrocyclic reactions.

Formazans **1** represent a readily available class of organic compound. They have found wide use as dyes, luminophores, thermo- and photochromic substances, chelating agents, etc. Their use has been particularly fruitful in biochemistry, medicine, and analytical chemistry. The great variety of formazans according to type of substituents (here and subsequently the numbering of the substituents coincides with the numbering of the N and C atoms to which they are attached), their synthetic (see Sheme 1 and [1-17]) and commercial availability draw

Scheme 1



R^1, R^5 = Ar, Het, C(=O)R, C(=O)NRR'; R^3 = Alk, Ar, Het, NO_2, RC(=O), COOR, RSO_2, CN, Cl, Br, CF_3, OR, SR, RC=NOH, RC=NNHAr, $P(=O)(OR)_2$, $P(=O)(NRR')_2$, Ph_3P^+; X or Y = H, COOH, $CONH_2$, HC=O, Ac, Bz, RC(=O), COOR, CN, RSO_2 ; Z = Cl, Br, NO_2

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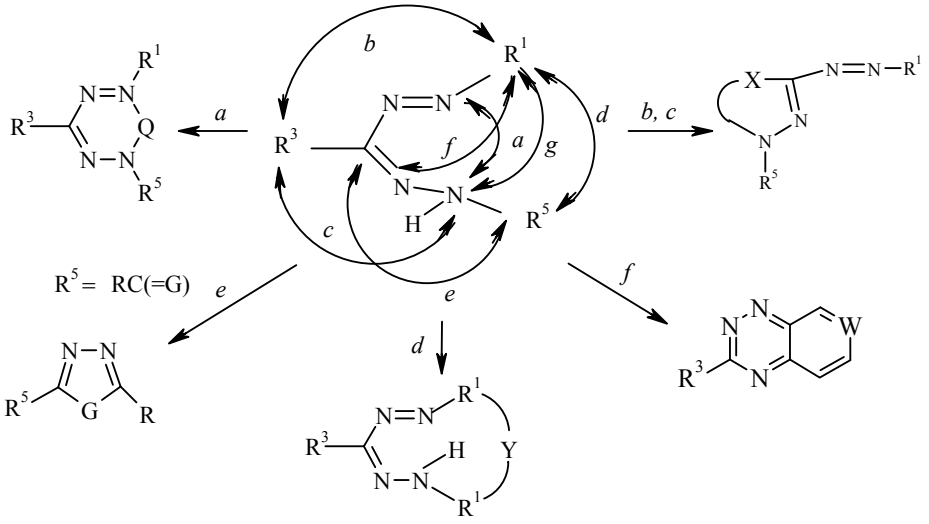
attention to them as starting compounds for the production of various heterocyclic systems. Nevertheless the potential of formazans as precursors in the synthesis of heterocycles has not yet been sufficiently investigated. Thus, unlike other types of arylhydrazones they have not been used in the Fischer indole synthesis. There are no examples of the production of 1,2,3-triazole derivatives by 1,3-dipolar cycloaddition of accessible 3-azidoformazans to various dipolarophiles (C=C, C=S, C=O, etc.) and in many other reactions. The bis-, tris-, and tetrakisformazans have only been used for the synthesis of the corresponding tetrahydrotetrazinyl free radicals.

A very large number of papers, reviews, and books (e.g., [1-16] and the references therein) and even patent reviews [17] have been devoted to the synthesis of formazans, study of their physical and chemical properties, and identification of practically useful compounds among them, but there has been no separate analysis of the possibilities of using formazans in the synthesis of heterocycles, and this has provided the motivation for writing the present review.

The principles of the construction of various heterocyclic systems from formazans (Scheme 2) are based on the ability of the formazan group to be included fully or only partially in the ring that forms. The first of them is realized in the synthesis of derivatives of tetrazole, tetrahydro-1,2,4,5-tetrazine, 1,2,3,5,6-boratetrazine, and macrocycles, including those based on metathesis reactions [18] (Scheme 2, paths *a* and *d*), but there as yet no examples of cyclizations by path *g*.

Scheme 2



The pericyclic reactions of the 1,2,4-triazabuta-1,3-diene system of the formazan fragment and other polyazapolyene fragments (including the π-systems of aryl and heteryl substituents) and very many intramolecular substitution or addition reactions between the various substituents make it possible to realize the second principle of the heterocyclization of formazans and to synthesize azacyclic systems of practically any size with the retention of two or three nitrogen atoms (Scheme 2, paths *b*, *c*, *e*, and *f*).

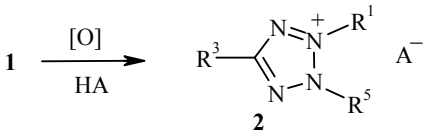
A considerable part of the large amount of experimental data concerns the transformation of formazans into five- or six-membered azacycles, and this gives rise to the separation of the data into two parts.

1. DERIVATIVES OF TETRAZOLE

1.1. Tetrazolium Salts

The synthesis of tetrazole derivatives and of 2,3-di- and 2,3,5-trisubstituted tetrazolium salts **2** in particular by the oxidation of formazans **1** (Scheme 3) is the most studied and most useful reaction of the latter (see [1, 2, 4-6, 13-15, 19-30] and the references therein). It is easy to see that the formazan group is fully included in the heterocycle that forms (path *a*, Scheme 2).

Scheme 3



R^3 = H, Alk, *cyclo*-Alk, Ar, Het, 1-RHet$^+$, RC(=O), HOOC, ROC(=O), PhNHC(=O), RR'NC(=O), Cl, Br; N=NAr, RR'N, $(AlkO)_2P(=O)$; R^1, R^5 = Ar, Het

The colorless tetrazolium salts **2** are very easily reduced to the strongly colored formazans (from red to blue), due to which the "formazan–tetrazolium salt" system has found unusually wide use in medicine, biology, biochemistry, cytochemistry, histochemistry, and photography, and this has stimulated further research in this field [1, 2, 4-6, 8, 13-26]. Tetrazolium salts are used in organic [23, 24] and inorganic [24, 27, 28] analysis, in the study of oxidation–reduction processes, in the synthesis of verdazyl radicals [19], in radiochemistry, and for the determination of Re, Hg, and many other metals, amines, proteins and alcohols, small concentrations of sugars, ascorbic acid, steroids, isoniazid, and other substances in biological liquids [21, 24, 29].

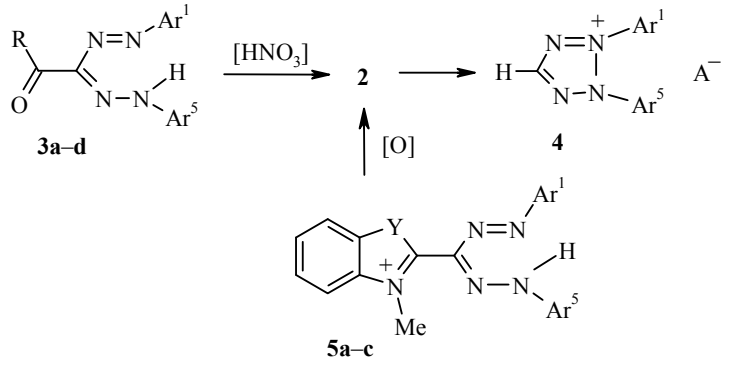
The tetrazolium salts **2** are produced smoothly by the oxidation of 1,5-diaryl-, 1(5)-aryl-5(1)-heteryl-, and 1,5-diheterylformazans [1, 2, 4, 7, 8, 21, 22, 25, 26] and various types of bis- and trisformazans [1, 2, 7, 8]. At the *meso* position of formazan (R^3) there can be alkyl, cycloalkyl, aryl, acyl, and heterocyclic substituents, sugar residues, halogens, arylazo, nitrile, ester, dialcoxyphosphoryl, alkyl(aryl)oxy, alkyl(aryl)sulfanyl, amide, and 1,5-diphenylformazyl groups, or a hydrogen atom [1, 2, 9, 13, 22, 23, 30-33]. Macrocyclic formazans containing a spacer between the N-aryl groups are also easily converted into bicyclic tetrazolium salts.

Practically the whole range of oxidizing agents have been used as oxidizing agents [1, 2, 4, 7, 8, 13, 14, 21, 30, 34, 35]. Amyl nitrite has been used from the day of discovery of this reaction up to the present time. The salts of Pb, Ta, Fe, Cu, Co, and other metals, oxides of Cr, Pb, and Mn, $PhPbO_2$, persulfates and permanganates, $K_3Fe(CN)_6$, Pb_3O_4, chromic and nitric acids, N-haloacylamides, *t*-BuOCl, NaOCl, Cl_2 and Br_2, $NOBF_4$, atmospheric oxygen and singlet oxygen, $SOCl_2$, boron trifluoride etherates, and electrochemical oxidation have been used. Hydrogen peroxide is only effective in the presence of F(3+) or VO_2 salts.

It must be emphasized that there is no universal oxidizing agent for the oxidation of all types of formazans and that a preference for any one of them can always arise [2-4, 8, 13, 20, 21]. The choice of oxidizing agent can therefore be based on the nature of the substituents in the formazan or a problem in the isolation of the salts **2** from the reaction medium [2, 8, 21, 22, 36]. For example, $PhPbO_2$ in AcOH is more effective than PbO_2 and $KMnO_4$ under the conditions of phase-transfer catalysis [22, 36]. It is advisable to use chlorine dry in an organic solvent and to control the temperature regime. With N-haloamides it is possible to conduct the oxidation under mild conditions, which is important when the precursors, such as certain 3-hetarylformazans, have insufficient stability. Nitric acid is most suitable for the oxidation of formazans containing a quaternized aza ring at position 3 and 1,3,5-triarylformazans, but it gives rise to decarboxylation of

the ester or carboxyl groups and to profound decomposition of carbohydrate and amino groups and also benzothiazole substituents at position 3. The removal of 3-Ac, 3-COOH, and 3-COOAlk groups was also observed during the oxidation of formazans **3** with $Pb(OAc)_4$ or copper salts. Here the tetrazolium salts **4** not substituted at the carbon atom are formed (Scheme 4). To protect carbohydrate *meso* substituents they are first acylated [2-5, 8]. Similar detachment of groups with substitution by a hydrogen atom was observed during the oxidation of the formazans **5a-c** containing a quaternized azacycle in the *meso* position. On account of the good availability of formazans of types **3** and **5** these reactions have acquired synthetic significance. The salts **4** are reduced quantitatively to 3-H-formazans, making them accessible precursors in the synthesis of 3-X-formazans with heteroatomic substituents at the *meso* position: X = Cl, NO_2, Br, Ar–N=N–, CH_2NR_2.

Scheme 4

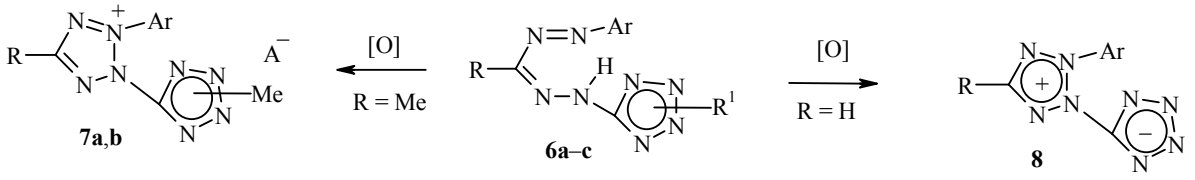


3 a R = OH, **b** R = OAlk, **c** R = Me, **d** R = Ph; **5 a** Y = O, **b** Y = S, **c** Y = NMe

Much attention has been paid to the effect of substituents in formazans not only from the chemical standpoint [2, 4, 8, 12-16, 21, 22, 25, 26, 33, 34, 36] but also in the light of the demands of biochemists to the characteristics of the tetrazolium salts [24] (particularly the water solubility, color and spectral characteristics, redox potential, etc.). The presence of accepting substituents at all positions of formazan requires a stronger oxidizing agent. Donating substituents in C- and/or N-arylformazans facilitate the formation of the salts **2** right up to spontaneous oxidation in alkaline solutions. The nature of the substituents at position 3 of formazan plays a more substantial role than at the nitrogen atoms. 3-Alkylformazans are oxidized more easily than 3-arylformazans, and during the oxidation of 3-(hydroxyalkyl)- and 3-(hydroxyphenyl)formazans the yield of the salts **2** is reduced. The effect of substituents at the *meso* position of formazan on this reaction decreases in the following order [4]: CN, Ph, COOAlk, Br, PhN=N, Ac, Me, COOH, H.

Study of the oxidation reactions of 1(5)-aryl-5(1)-hetaryl- and 1,5-dihetarylformazans started much later than study of 1,5-diarylformazans [7, 8]. This imbalance has now been rectified, and in biological investigations 2-(2-thiazolyl)tetrazolium salts, for example, are more popular than all the previously employed 2,3,5-triaryl-tetrazolium salts [14, 15, 24, 37, 38]. The nature of the heterocycle at the nitrogen atoms can also exhibit its own features. Thus, 5-(1- and 2-methyl-5-tetrazolyl)formazans **6a**,**b** readily form the corresponding salts **7a**,**b** (Scheme 5), while 5-(1-H-tetrazol-5-yl)formazans **6c** are transformed into the mesoionic heterocycles **8**.

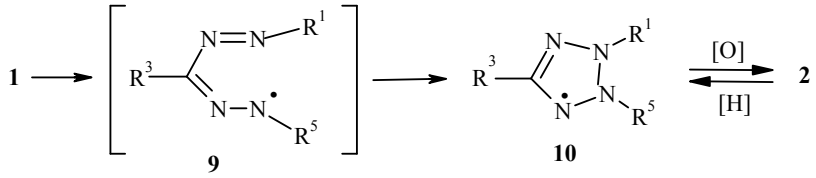
Scheme 5



6 a R^1 = 1-Me, **b** R^1 = 2-Me, **c** R^1 = H

The transformation of the formazans **1** into the tetrazolium salts **2** may include various intermediates depending on the nature of the substituents and the nature of the oxidizing agent [2, 4, 8, 19, 20]. In most cases, including the synthesis of 2,3-diaryl-5-pyridyltetrazolium trichlorocobaltates or trichlorocuprates [13], a radical mechanism is realized for this reaction (Scheme 6). Spectral methods recorded not formazanyl radicals **9** but tetrazolyl radicals **10**, which can also be obtained during one-electron reduction of the salts **2**.

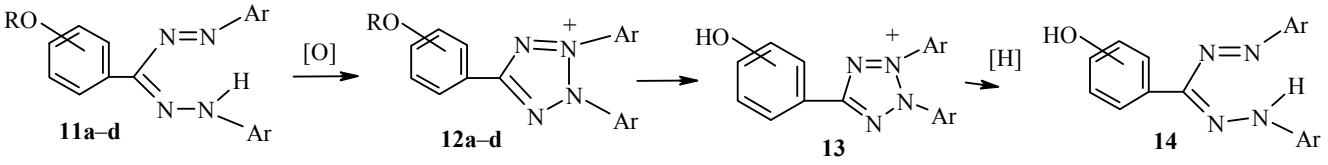
Scheme 6



In addition to the radical mechanism for the formation of the salts **2** other mechanisms determined by the nature of the oxidizing agent were examined [2, 4, 8, 20, 35]. Thus, an ionic mechanism was proposed for the oxidation of formazans by bromine. The almost quantitative yield of the salts **2** with the use of N-haloamides is explained by the formation of intermediate 1,5-diaryl-5-bromoformazans and bis(arylazo)-hydroxyperoxides during oxidation by singlet oxygen. In cases where Pb and Ta acetates were used complexes with nitrogen–metal bonds were detected as intermediates.

On account of their availability and extremely easy reduction to formazans the tetrazolium salts **2** are used in organic synthesis as precursors and as protecting groups [2, 4, 8, 29, 34]. For example, the salts **12a-d** are formed during the oxidation of 3-(alkoxyphenyl)- and 3-(acetoxyphenyl)formazans **11a-d** (Scheme 7). Demethylation of the salts **12a-c** is realized by the action of BF_3. The acyl protection in the O-acylated salts **12d** is removed even more easily. The obtained salts **13** with a free OH group are easily reduced to 3-(hydroxyphenyl)formazans **14**, the synthesis of which from hydroxybenzaldehyde arylhydrazones is complicated by azo-coupling reactions in the hydroxyphenyl ring. On account of this the formazans **14** have become accessible for various syntheses at the free OH group, including the synthesis of podands with a terminal chromogenic grouping [34].

Scheme 7



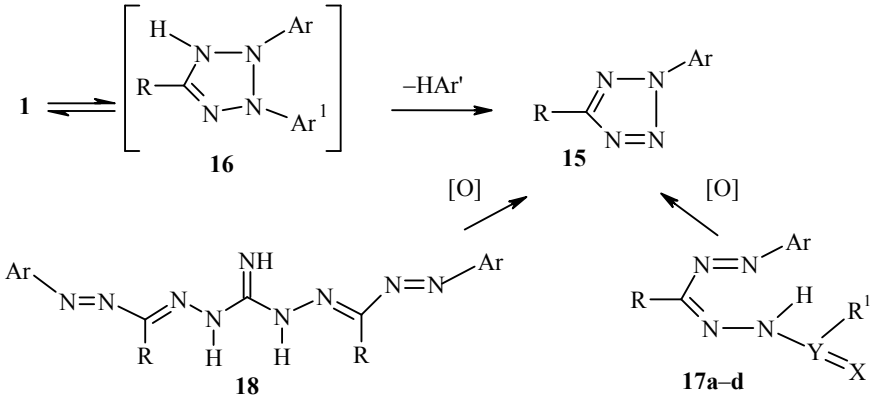
11, 12 a RO = 2-MeO, **b** RO = 3-MeO, **c** RO = 4-MeO, **d** RO = 4-AcO

1.2. 2,5-Disubstituted Tetrazoles

Formazans are extremely popular as precursors in the synthesis of 2,5-disubstituted tetrazoles **15** ([1, 2, 4-8, 19] and the references therein). This is due to the ease of cleavage of the N–R^5 bond in certain formazans **1** or in the tetrazolium salts **2**. During the thermolysis of formazans the reaction may take place through the cyclic tautomer **16**, particularly in the case of heterylformazans (Scheme 8). The formation of the tetrazoles **15** was described during heating or oxidation of 5-carbamoyl- (**17a**), 5-amidino- (**17b**), 5-acyl- (**17c**), and 5-tosyl-formazans (**17d**) and also of certain N(5),N(5')-(iminomethylene)bisformazans **18** (Scheme 8). The carbamoyl-

formazans **17a** represent a unique group of 5-acylformazans, which can be obtained by the azo coupling of arenediazonium salts with 4,4-disubstituted aldehyde semicarbazones. Since the latter are extremely accessible compounds this reaction can be competitive in the synthesis of 2,5-disubstituted tetrazoles **15**.

Scheme 8

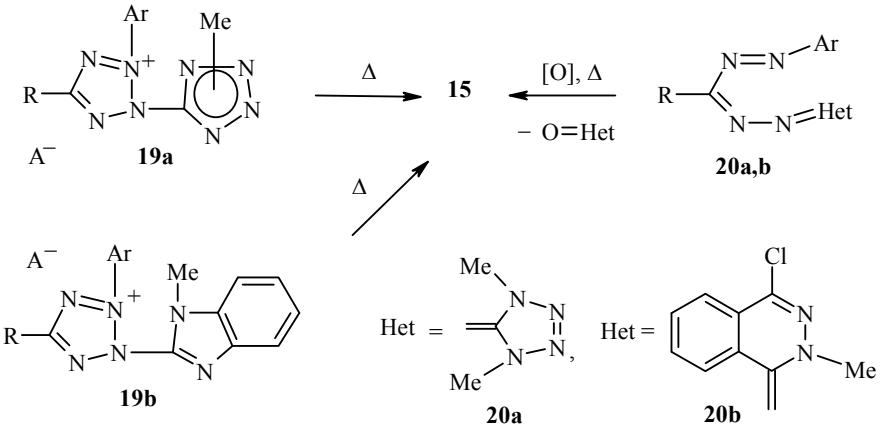


17 a $R^1Y{=}X$ = C(=O)NHR, **b** $R^1Y{=}X$ = C(=NH)NHR, **c** $R^1Y{=}X$ = RC(=O)–, **d** $R^1Y{=}X$ = RSO_2; R = Alk, Ar

5-Amidino-1-hetarylformazans (guanylformazans) **17b** (Ar = Het) can undergo similar transformations [1, 2, 4, 6, 8, 20], but unlike the aryl analog **17b** the nature of the heteryl fragment can manifest itself quite unexpectedly [7, 8]. Thus, 5-guanyl-3-phenyl-1-(5-tetrazolyl)formazan is oxidized by $KMnO_4$ to 5-phenyl-2-(5-tetrazol-yl)tetrazole, while 3-bromo-6-phenyl-1,2,4,5-tetrazine was isolated during the action of bromine.

During the heating or oxidation of the tetrazolium salts **19a**,**b** containing N-methyltetrazolyl or 1-methylbenzimidazolyl fragments the corresponding heterocycle splits off, and the tetrazoles **15** are formed (Scheme 9). The same happens with 1-aryl-5-heterylideneformazans **20a**,**b** during their oxidation by metal oxides or during heating in acetic acid (Scheme 9).

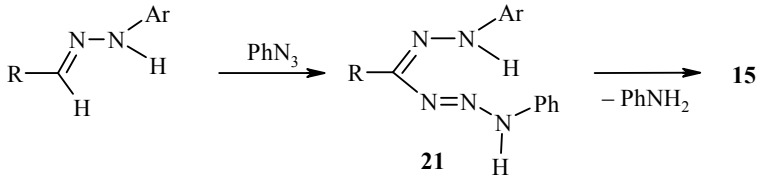
Scheme 9



In spite of the lack of study and the low stability the 5-aryl-3-R-1-arylaminoformazans **21** are prospective starting compounds for the synthesis of 2,5-disubstituted tetrazoles **15**, since they are produced by the reaction of the extremely readily available aldehyde arylhydrazones with aryl azides [2, 4, 8]. The

formazans **21** with R = Me, COOH can be isolated, but those with R = Ph cannot. Even during preparation such formazans are completely transformed into 2-aryl-5-phenyltetrazoles (Scheme 10). The transformation of the formazans **21** into 2-aryl-5-R-tetrazoles proceeds with quantative yield and is a convenient method for synthesis of the latter. The examples of the participation of heterylhydrazones or heteryl azides in a reaction similar to that presented in Scheme 10 were not found in the literature.

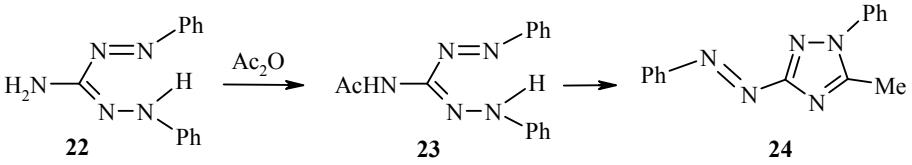
Scheme 10



2. 1,2,4-TRIAZOLES AND ANNELATED 1,2,4-TRIAZOLES

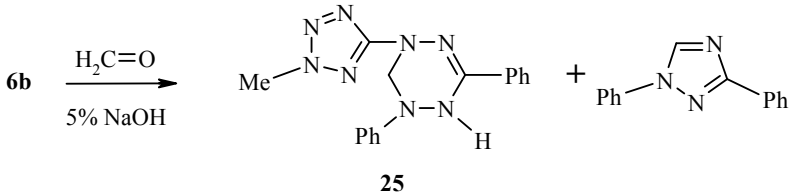
The extremely accessible 3-amino-1,5-diarylformazans are one of the types of amidrazones that number among the most widely used precursors in the synthesis of 1,2,4-triazoles [2, 4, 6, 8, 31, 39]. They are easily obtained from 3-chloro(bromo, fluoro)-, 3-nitro-, 3-alkoxy-, 3-alkylsulfanyl-, and 3-(arylazo)formazans. The amidrazone fragment of 3-amino-1,5-diarylformazans is more reactive than the formazan fragment, but there are as yet few examples of the production of 1,2,4-triazoles by this method. Thus, during the acylation of 3-amino-1,5-diphenylformazan (**22**) the amino group at position 3 is acylated and not the 1-NH group as in other types of formazans (Scheme 11). Like other N(3)-acylamidrazones, the 3-(acylamino)formazans of type **23**, formed with high yields, are easily transformed into 1,2,4-triazoles similar to 5-methyl-1-phenyl-3-(phenylazo)-1,2,4-triazole (**24**) [6, 8, 39]. Unfortunately, examples of the participation of unsymmetrically substituted 3-amino-1,5-diarylformazans ($Ar^1 \neq Ar^5$) in this reaction have not been described, and the problem of competition of the reaction centers at the cyclization stage is still not resolved.

Scheme 11



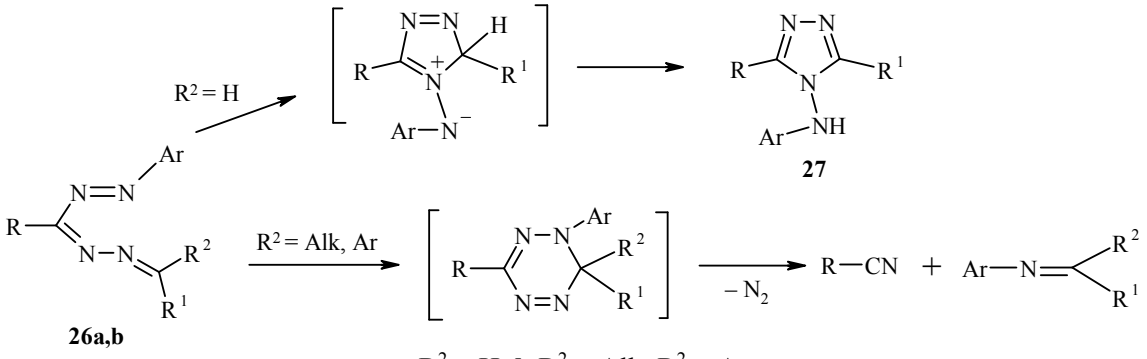
Derivatives of 1,2,4-triazole are sometimes formed from certain unsymmetrical 1-aryl-5-heteryl-formazans although such reactions do not yet have preparative significance. Thus, during the treatment of 5-(2-methyl-5-tetrazolyl)-1,3-diphenylformazan (**6b**) with formaldehyde in addition to 1,2,3,4-tetrahydro-1,2,4,5-tetrazine **25** a litle of 1,3-diphenyl-1,2,4-triazole was isolated although its yield from the isomeric 5-(1-methyl-5-tetrazolyl)-1,3-diphenylformazan (**6a**) under the same conditions amounted to 46% (Scheme 12).

Scheme 12



Derivatives of 4-amino-1,2,4-triazole **27** are formed with good yields from 1,3-diaryl-5-ylideneformazans **26a**,**b** (formazenes [7, 8]) (Scheme 13). The formazenes **26** are accessible on account of the reactions of the arylhydrazones of acyl halides with N,N-unsubstituted hydrazones, the alkylation of (2-azaheteryl)formazans, or the oxidative condensation of the hydrazones of 2-oxyheterocycles [7, 8]. It must be stressed that the derivatives of 4-amino-1,2,4-triazole **27** are only obtained from the aldoformazenes **26a** that partly undergo nitrile imine cleavage. The ketoformazenes **26b** only undergo nitrile imine cleavage, often at the moment of production (Scheme 13). Such a transformation is not characteristic of 5-heterylideneformazans of type **20** [7, 8].

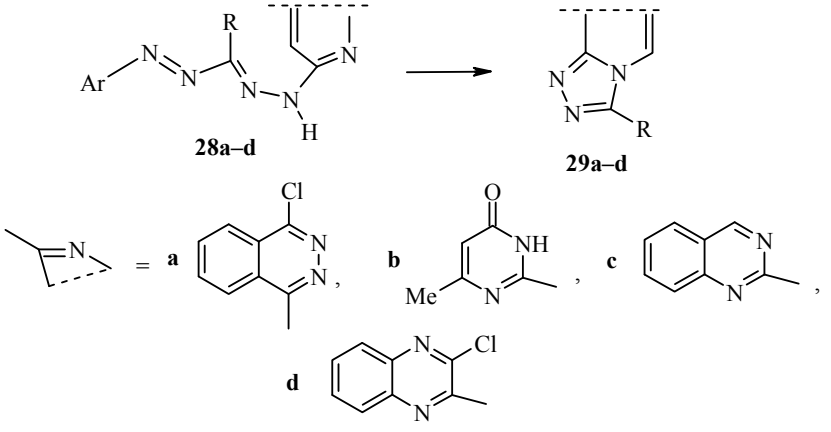
Scheme 13



a R^2 = H, **b** R^2 = Alk, R^2 = Ar

When heated in polar solvents or in the presence of acids 1-aryl-5-(2-azaaryl)formazans **28a-d** and 1,5-bis(2-azaaryl)formazans are easily converted into annelated 1,2,4-triazoles **29**, and this was realized in the series of 5-(2-pyrimidinyl)-, 5-(2-quinazolinyl)-, 5-(2-quinoxalinyl)-, and 5-(1-phthalazinyl)formazans [7, 8] (Scheme 14). In many cases such a synthesis of 1,2,4-triazolo[3,4-*a*]azacycles gives a good yield and may be preferred to other methods by virtue of the ready availability of the respective heterylformazans and particularly 1,5-diheterylformazans.

Scheme 14

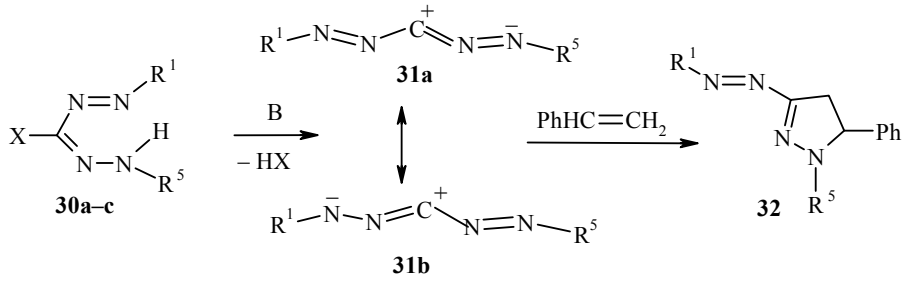


The mechanism of formation of triazolo[1,2,4-*a*]pyrimidines from 1,5-diaryl-3-chloro- or 1,5-diaryl-3-nitroformazans and derivatives of 2-thiouracils is probably more complicated [40].

3. PYRAZOLES AND INDAZOLES

The formazans **30a-c**, containing at position 3 characteristic groups with clearly defined nucleofugic characteristics (Cl, Br, NO_2, etc.), are convenient precursors for the generation of 1,3-dipolar reagents – N-aryl-C-(arylazo)nitrile imines **31** [6, 8, 41, 42]. In the presence of dipolarophiles (styrenes, enols, etc.) 1,3-dipolar cycloaddition occurs with the formation of 3-(arylazo)pyrazolines **32** (Scheme 15). As in the case of other nitrile imines the reaction of (arylazo)nitrile imines **31** with monosubstituted ethylenes takes place regiospecifically – only to the 5-isomers of 3-(arylazo)pyrazolines **32**. In the case of 3-nitroformazans **30c**, as a rule, the NO_2 group exhibits the characteristics of an oxidizing agent, and the formed pyrazolines **32** are dehydrogenated to the corresponding pyrazole derivatives.

Scheme 15



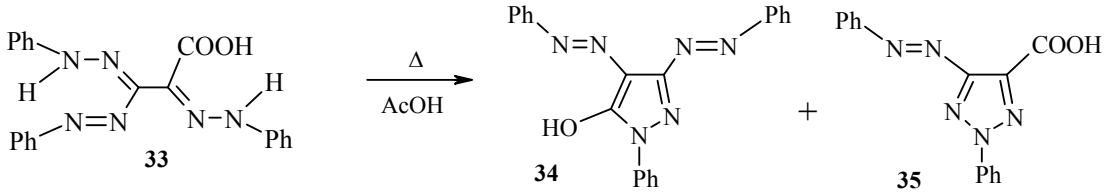
30 a X = Cl, **b** X = Br, **c** X = NO_2

In spite of the great synthetic potential the discussed reactions are clearly used insufficiently. Other reactions such as [3+3]-dimerizations, rearrangements, and reactions with compounds of the RXH type containing a mobile hydrogen atom have also not been studied. The 3-(arylazo)pyrazolines **32** formed in these reactions are themselves suitable precursors for the synthesis of 3-(arylazo)pyrazoles, 3-aminopyrazolines, 3-aminopyrazoles, and other valuable reagents. The N-aryl-C-(arylazo)nitrile imines **31** have also been studied insufficiently in theoretical respects. In the case where there are different substituents at positions 1 and 5 of the initial formazans **30a-c** one of the two possible nitrile imines can prevail: **31a** or **31b**. Accordingly, the structure of the final products will be determined by rivalry in the reactivity of these isomers. It is quite difficult to predict whether the relationships characteristic of the initial formazans (the 1-R_D-5-R_A isomer is preferred to the 1-R_A-5-R_D isomer, where R_D is the donor and R_A the acceptor substituent) [8, 9] are retained in this case.

The 3-X-formazans **30a-c** were brought more often into reaction with the Na derivatives of 1,3-dicarbonyl compounds (DCC) [4, 6, 8, 41, 42]. It was supposed that in these cases substitution of the group X by the corresponding C-nucleophile with the formation of formazans of type **30** (X = Ac(Y)CH, Y = Ac, COOEt, CN, PhNHC(O), $PhSO_2$] takes place initially, and their intramolecular cyclization supposedly leads to the pyrazoles. However, such formazans are stable compounds and only undergo cyclization in an acidic medium (e.g., see [2, 4, 8]). The fact that 1,3-DCCs with many Huisgen reagents and in neutral media form products from cycloaddition at the C=C bond of the enolic forms [8, 41, 42] makes it possible to propose the same mechanism for the formation of the pyrazole derivatives in the examples involving the participation of C-(arylazo)nitrile imines **31** described above.

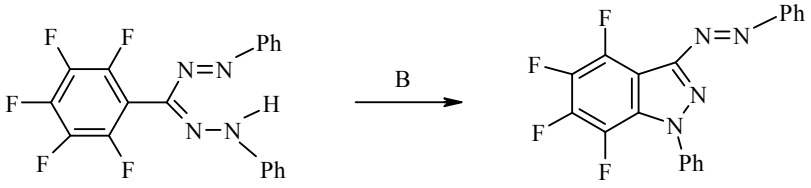
If there is an electrophilic center capable of reacting with the hydrazone group in the *meso* substituent of the formazans **1**, depending on its position derivatives of various heterocycles, including pyrazole, can form as a result of an intramolecular reaction (path *c* in Scheme 2) [3, 4, 8]. Here, the formation of the pyrazole ring is sometimes preferred. For example, the ozoformazans **1** (R^3 = RC=NNHAr) usually cyclize to derivatives of 1,2,3-triazole (see below), but during the cyclization of osoformazancarboxylic acid **33** the yield of the pyrazole **34** was considerably higher than the yield of the triazole **35** (Scheme 16).

Scheme 16



4,5,6,7-Tetrafluoro-1-phenyl-3-(phenylazo)indazole (**37**) (Scheme 17) was synthesized on the basis of intramolecular arylation by the pentafluorophenyl fragment of formazan **36** also according to path *c* (Scheme 2). The number of examples of such syntheses is still small although this methodology can be used for the synthesis of many heterocyclic systems with five or more atoms, including annelated systems.

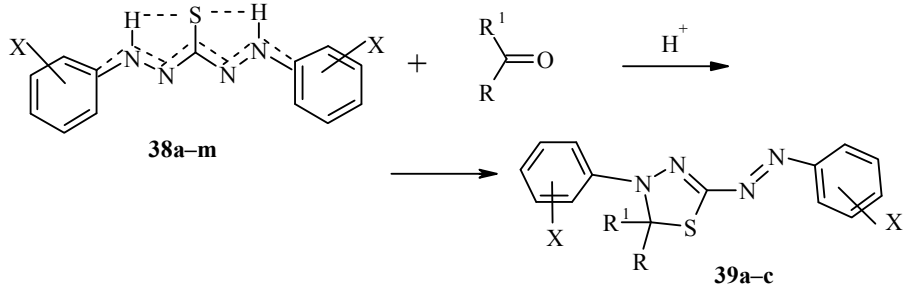
Scheme 17



4. 1,3,4-THIADIAZOLES

In an acidic medium 1,5-diaryl-3-sulfanylformazans (dithizone (**38a**) and its *p*-methyl and *p*-methoxy analogs **38b**,**c**) enter into cyclization with aldehydes and ketones (Scheme 18). In contrast to the reactions of the usual formazans, in these cases the derivatives of 1,3,4-thiadiazole **39a-c** are formed instead of 1,2,3,4-tetrahydro-1,2,4,5-tetrazines (see part II of this review*). Other analogs of dithizone **38d-m** have not yet been used in this reaction.

Scheme 18

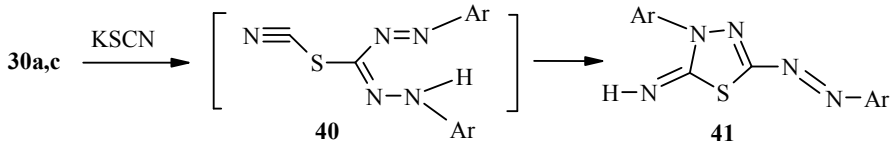


a X = H, **b** X = 4-Me, **c** X = 4-MeO, **d** X = 2-F, **e** X = 2-Cl, **f** X = 2-MeO, **g** X = 4-F, **h** X = 3-Cl, **i** X = 2-Me, **j** X = 4-Me, **k** X = 3-MeO, **l** X = 1-Naphth, **m** X = 2-Naphth; R = H, Me, Ph; R^1 = H, Me

*Part II of the review will be published in a future issue of the journal.

1,5-Diaryl-3-(cyanosulfanyl)formazans **40**, obtained from the respective 3-chloro- or 3-nitroformazans **30a**,**c** and KSCN, actually undergo intramolecular nucleophilic addition of the NH group at the nitrile bond under the reaction conditions with the formation of 3-aryl-5-(arylazo)-2-imino-2,3-dihydro-1,3,4-thiadiazoles **41** (Scheme 19).

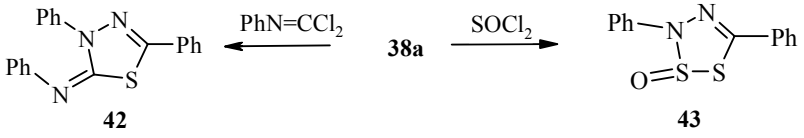
Scheme 19



40, **41** Ar = 4-Tol, 4-ClC_6H_4

The reaction of 1,*n*-dihaloalkanes with the dithizone **38a** begins with attack on the sulfur atom, while one of the terminal nitrogen atoms acts as a second nucleophilic center. Thus, only 3-phenyl-5-(phenylazo)-2,3-dihydro-1,3,4-thiadiazole (**39a**) (R = R^1 = X = H) is formed with a high yield during the reaction of methylene diiodide with dithizone (Scheme 18). The dithizone **38a** reacts in a similar way with the phenylimine of phosgene and with thionyl chloride (Scheme 20) with the formation of derivatives of 1,3,4-thiadiazolines **42** and, accordingly, 1,2,3,4-dithiadiazol-2-ones **43** [43].

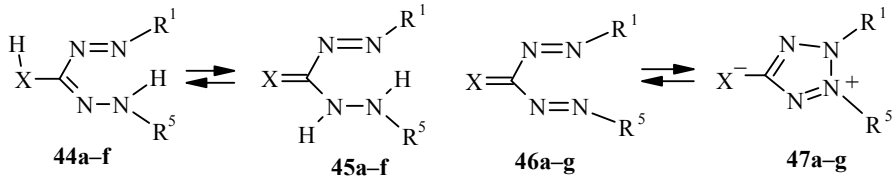
Scheme 20



5. DEHYDROGENATION OF 3-HX-FORMAZANS IN THE SYNTHESIS OF AZOLES

Formazans **44a**-**d**, containing a functional group of the HX type (X = S, O, NR, and even certain CRR' groups, Scheme 21) at position 3, have a series of specific characteristics [8, 9, 20, 31-33]. Thus, depending on the nature of the atom X, they can exist in the crystals and in solutions as formazan tautomers **44** (mostly formazans with X = CRR' **44d**), hydrazide tautomers **45** (e.g., **45b**, X = O, Scheme 21], or betaine salts **38a**-**m** (Scheme 18). Unfortunately, the tautomeric transformations of 3-aminoformazans **44c** (X = NR) and formazans **44d**, having a methine group with strongly accepting substituents (X = $CR_AR'_A$), have not been studied, and the 3-hydroselenoformazan **44c** (X = Se) and 3-phosphinylformazan **44f** (X = PR) have not been described. The tautomeric transformations of the vinylogs of 3-HX-formazans **44**, i.e., 3-HX(A=B)$_n$-formazans, in which the HX group is separated from the *meso* carbon atom by some system of multiple bonds (A=B can be C=C, C=N, N=C, OC_6H_4, SC_6H_4, $N(R)C_6H_4$, and others, *n* = 1, 2, 3, and more) are little known, and many have not been described [8, 9, 11].

Scheme 21



44–47 a X = S, **b** X = O, **c** X = NR, **d** X = CRR'; **e** X = Se, **f** X = PR;
46, **47 g** X = PR_3

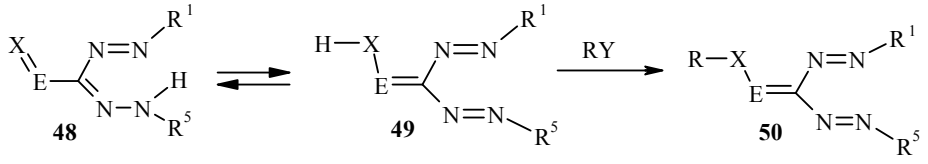
Unlike the monodehydrogenation of 3-R-1,5-diaryl- and 3-R-1(5)-aryl-5(1)-heterylformazans (R = Alk, Ar, Het, RC=O, Cl, CN, O_2SR, etc.), which leads to the tetrazolium salts **2**, the dehydrogenation of the 3-HX-formazans **44a-d** takes place in a different way, irrespective of their tautomeric form. Here 1,1-bis-(arylazo)ethenes or -heteraethenes **46**, which tend to exist partly or entirely in the form of the cyclic mesoionic isomers **47** depending on the nature of the atom X, are formed (Scheme 21).

Few examples of the dehydrogenation of formazans in which the HX group is separated from the C(3) atom by a system of multiple bonds $(A=B)_n$ with a view to synthesizing the vinylogs of compounds **46** have been described. Only hydrazono-substituted formazans **44d** – osoformazans (HX–A=B = ArNHN=C(R)–) have been studied in somewhat greater detail in this respect [2-4, 8]; and one of Neugebauer's papers describes the dehydrogenation of 3-(hydroxyiminomethyl)-1,5-diphenylformazan (HX–A=B = HON=CH–) [33].

1,1-Bis(arylazo)heteraethenes **46a**,**b** (X = S, O) and 1,1-bis(arylazo)ethylenes **46d** (X = CRR') are capable of undergoing various intramolecular and intermolecular pericyclic processes. As a result the polyenes **46** and their vinylogs (imino analogs, etc.) are of considerable interest for the synthesis of various heterocyclic systems. Their isomeric tetrazolium-5-ylides **47** belong to the mesoionic heterocycles [31, 32]. They are capable of rearrangements and of new cyclocondensations, including the formation of complex heterocyclic systems.

Formazans of type **48**, containing a 3-diheteraethenyl or heteravinyl substituent, are potentially capable of existing in the tautomeric forms **49**. As a result of various reactions it is possible to synthesize 1,1-bis-(arylazo)heteraethenes and -diheteraethenes **50** (X–E = S–C, O–C, O–N, R'N–N, etc.), the analogs of polyenes **46** containing one more heteroatomic substituent at the double bond (Scheme 22). Unfortunately, as an example of such syntheses it is only possible to cite the same paper of Neugebauer (X = E = O=CH) [33], although the synthetic potential of these reactions is very high. More distant vinylogies also have not yet been described.

Scheme 22



Depending on the nature of the atom X, the 1,1-bis(arylazo)heteraethenes **46** can be stable compounds (phosphoranes **46g**, X = PR_3), exist in equilibrium with the cyclic form of the betaine (X = S), or exist exclusively in the mesoionic form (X = O). Reliable data on the structure and synthesis of the bis(arylazo)imines **46c** (X = NR) either by dehydrogenation of the corresponding 3-aminoformazans **44c** or by other methods have evidently not yet been described although their cyclic isomers **47c** (X = NR) have been mentioned in the literature [31, 32].

Compounds **46**, the products from the dehydrogenation of 3-HX-formazans, have for a long time attracted the attention of both synthetic and theoretical chemists (e.g., see [31, 32]). They are of great interest both as prospective precursors in the synthesis of various heterocyclic systems and as subjects for structural chemistry and for the theory of pericyclic reactions (the dependence of the equilibrium with their cyclic isomers **47** on the nature of the heteroatom X and the substituents at the nitrogen atoms, particularly when they are nonequivalent).

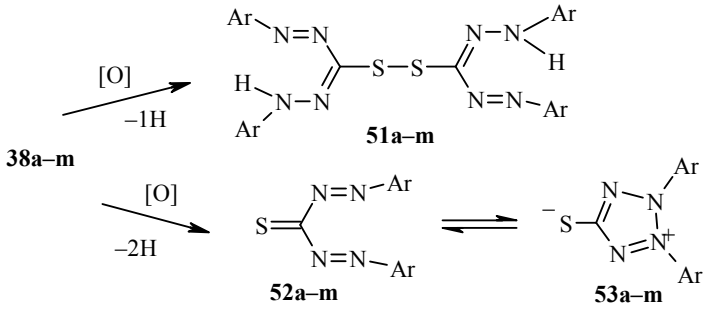
The dehydrogenation reactions of 3-HX-formazans **44a-d** and the following heterocyclization processes have so far unfortunately been studied in detail for the case of the dithizone **38a** and its aryl (but not heteryl) analogs **38b-m** and have been discussed little in reviews.

5.1. Dehydrodithizone in the Chemistry of Azoles

Dithizone **38a** is the parent of a large group of readily obtainable 1,5-diaryl-, 1-aryl-5-hetaryl-, and 1,5-dihetaryl-3-sulfanylformazans (**38b-m**, etc., Scheme 18) [4, 6, 8, 44-49]. In the crystals and in solutions the dithizone exists not in the thiol or thione form but as a mesoionic inner salt **38a** [8, 9, 11, 46, 49]. The same situation is observed in the symmetrically substituted analogs **38b-m**.

During investigation of the structure of the products from the oxidation of dithizone **38a** there were no fewer problems than during the investigation of the structure of the dithizone itself. Beginning with the work of E. Fischer and H. Fischer a great deal of effort has been expended on analyzing the color range of the isolated products and their structure in relation to the nature of the oxidizing agent and the conditions of the reaction [8, 47, 48]. Mild dehydrogenation (atmospheric O_2, oxidation by Au, Tl, or Mn salts, SeO_2, iodine, or electrochemical) takes place with the loss of only one hydrogen atom and leads to the formation not of tetrazolium salts but of the yellow di(1,5-diphenylformazan-3-yl) disulfide (**51a**) (Scheme 23, see [8, 45, 48, 50] and references therein). The oxidation of dithizone with H_2O_2 in a strongly alkaline medium leads to purple crystals (1,5-diphenylformazan-3-yl)sulfonic acid **44** (HX = SO_3H, R^1 = R^5 = Ph). The action of stronger oxidizing agents (MnO_2, etc.) leads to fuller dehydrogenation of the dithizone with loss of two hydrogen atoms and the formation of the red dehydrodithizone (see [8, 31, 32, 47, 49, 51] and the references therein). For the synthesis of dehydrodithizone $K_3[Fe(CN)_6]$ and $K_4[Fe(CN)_6]$, atmospheric O_2 in an alkaline medium, and even dialkoxy disulfides AlkOSSOAlk were used [31, 48, 52]. The formation and isolation of dehydrodithizone were observed during attempts at the production of complexes of dithizone with many metals such as molybdenum, gold, manganese, and other metals [49, 53].

Scheme 23



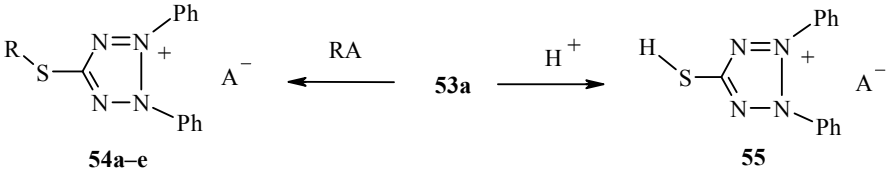
a–**k** Ar = RC_6H_4 (**a** R = H, **b** R = 3-Me, **c** R = 4-MeO, **d** R = 2-F, **e** R = 2-Cl, **f** R = 2-MeO, **g** R = 4-F, **h** R = 3-Cl, **i** R = 2-Me, **j** R = 4-Me, **k** R = 4-MeO); **l** Ar = 1-Naphth; **m** Ar = 2-Naphth

The results from the oxidation of dithizone and its analogs are determined not only by the nature of the oxidizing agent but also by the reaction conditions. Here mixtures of diformazyl disulfide **51** and dehydrodithizone are often formed. The synthesis of dehydrodithizones can further be complicated by the fact that the formed disulfide (e.g., **51a**) quickly disproportionates to dehydrodithizone and the initial dithizone even at room temperature.

Initially dehydrothizone was assigned the structure of linear 1,5-diphenyl-3-thioxo-1,2,4,5-tetra-azapenta-1,4-diene (**52a**) and then the cyclic isomer 2,3-diphenyl-1,2,3,4-tetrazolium-5-thiolate (**53a**) and even the two products of their thermal rearrangements. The efforts of many chemists showed that in the crystals dehydrodithizone only exists in the cyclic form **53a**, and in some solutions the latter can be fixed in equilibrium with a small portion of the linear form **52a**. In spite of the fact that the cyclic form is energetically only a

little more stable than the linear form it always predominates in the solutions [31, 32, 45, 54-56]. The higher the polarity of the solvent, the larger the portion of the tetrazolium thiolate **53a**. Thus, in DMSO only it is detected by ^{13}C and ^{14}N NMR methods. Its characteristics in the UV spectra coincide with those of 5-(methylsulfanyl)-2,3-diphenyltetrazolium iodide (**54a**) (Scheme 24) [47, 51]. Here, with increase in the polarity of the solvents there is a hypsochromic shift of the maximum of the absorption band of the dehydrodithizone (e.g., 465 nm in $CHCl_3$ and 405 nm in MeOH) [51]. It was not reported whether this is due to the transition to the linear isomer.

Scheme 24



54a–e **55**

54 a R = Me, **b** R = Et, **c** R = Bn, **d** R = CH_2COOH, **e** R = CH_2CH_2COOH

The introduction of substituents into the phenyl rings of dehydrodithizone, even at the *ortho* position, has little effect on the geometric parameters of the tetrazolium thiolates **53**. For example, in the 2,2'-dimethoxy derivative **53f** only the rotation of the aryl rings in relation to the heterocycle is increased (63.1° and 57.1° respectively) in comparison with the unsubstituted compound **53a** (both 44.8°) [49, 52].

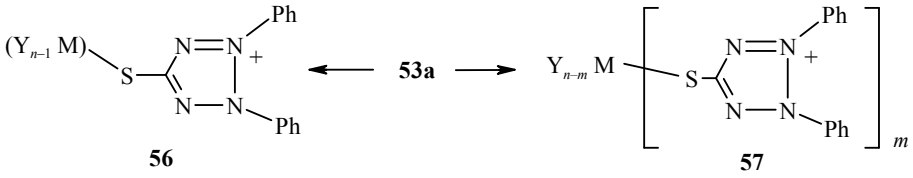
The dehydrothizones **53a-m** and others are widely used in analytical chemistry and in the synthesis of metal complexes and five- and six-membered heterocyclic systems, including annelated compounds [31, 32, 44, 45, 47-50, 53, 57]. The readily obtainable tetrazolium thiolate **53a** was proposed for the modification of polymers for use in hydrometallurgy [58] and in the production of photomaterials. The production of dehydrodithizones **53a-h** from the corresponding 1,5-diarylthiocarbazides in a single stage increases their synthetic potential.

Being a weak base with high polarizability [51, 54], dehydrodithizone enters into reaction with electrophilic reagents only at the sulfur atom [31, 32, 55, 56, 58-60]. Here the cyclic form **53a** is always secured. On this basis the alkylation of dehydrodithizone was proposed as a novel preparative method for the synthesis of tetrazolium salts **54a-e** (Scheme 24) and from them the formazans **1** (3-R^3 = RS) [8, 47]. The alkylation of dehydrodithizone was also realized with polymers containing chloromethyl groups with the aim of producing immobilized tetrazolium salts and formazanyl-containing polymers (see [58, 59] and the references therein).

During the protonation of dehydrodithizone **53a** and its analogs **53b-e** the corresponding tetrazolium salts of type **55** are formed (Scheme 24) [8, 31, 32, 55, 56]. The position of protonation at the sulfur atom is confirmed not only by calculations [54, 60] but also by the fact that the spectral characteristics of the obtained salts **55** (hydrochlorides, acetates, trifluoroacetates) are close to those of 5-alkylsulfanyltetrazolium salts, e.g., **54a-e**, obtained both during alkylation of dehydrodithizone (Scheme 24) and during oxidation of the corresponding formazans [47].

During the formation of the metal complexes of dehydrodithizone both the cyclic form **53a** and the linear form **52a** can be realized [45, 48, 53, 57, 60]. Thus, during its reaction with $HgCl_2$, $AuCl_3$, or $K_2[PdCl_4]$ the 1:1 complexes **56** with the [S–M–Cl_n] coordination unit, formed with the participation of the cyclic isomer **53a**, were isolated (Scheme 25). Complexes of type **56** [**(53a)**AuX, X = Cl, Br], containing Au(I), were also synthesized by the reaction of $[NBu_4][AuX_4]$ with dithizone [50]. Here the metal was reduced with simultaneous dehydrogenation of the dithizone, and it is difficult to determine the order of the stages in the complex formation and cyclization of the ligand. The complexes of the metal pentacarbonyls with composition [**(53a)**$M(CO)_5$)], obtained from tetrazolium thiolate **53a** or nickel complex of dithizone, have similar structure [48].

Scheme 25

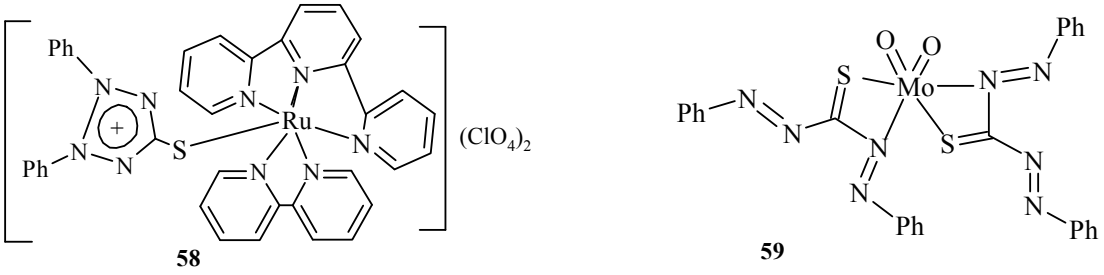


$(Y_nM) = AuCl_3$, AuCl, HgCl, $Cr(CO)_5$, $Mo(CO)_5$, $W(CO)_5$ etc.

Complexes of dehydrodithizone of type **57** with metal–ligand ratios of 1:2 or 1:3, in which the metal (Hg, Co, Zn, Cd, Zn) are also coordinated only with the sulfur atoms of the cyclic isomer **53a**, were also described (Scheme 25). In contrast to selenium the As(III), Sb(III), and Bi(III) cations also form complexes of type **57**, having the compositions $[(\mathbf{53a})_5M(ClO_4)_3]$ and $[(\mathbf{53a})_2MX_3]$ (M = As, Sb, and Bi), with dehydrodithizone.

Tetrazolium thiolate **53a** can also become embedded in polyligand complexes. Thus, the more complicated ruthenium complex **58** $[Ru(trpy)(bpy)(\mathbf{53a})](ClO_4)_2$, in which the dehydrodithizone is also a monodentate ligand with coordination at the sulfur atom, was obtained from the complex $[Ru(trpy)(bpy)Cl]Cl^-$ (where trpy = 2,2',6',2''-tripyridyl and bpy = 2,2'-bipyridyl) (Scheme 26) [57]. The bond lengths and bond angles of the thiolate ring in the complex **58** differ little from the parameters of the tetrazolium thiolate **53a** itself [49, 57]. In the oxomolybdate complexes **59** the bicyclic coordination unit $[(MoO_2)SN^2]$ (Scheme 26) is formed but with participation of the linear isomer **52a** and with bidentate coordination at the S and N(2) atoms.

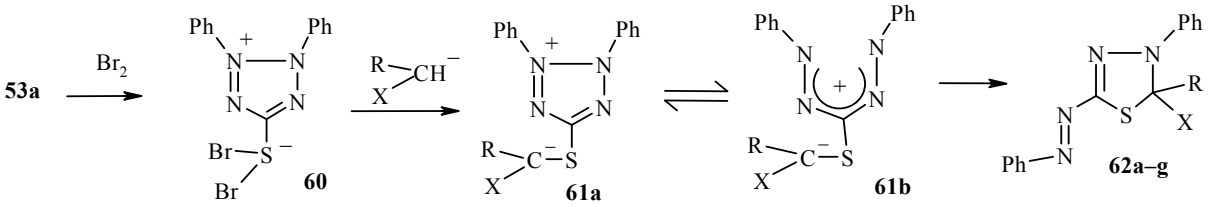
Scheme 26



With bromine dehydrodithizone forms a stable complex, which was assigned the tetrazolium structure **60** (Scheme 27). The complex **60** reacts vigorously with nucleophiles and, for example, with the anions of CH-active compounds forms zwitterionic heterocycles **61a** (Scheme 27). The stability of the latter is determined by the nature of the substituents in the nucleophile. With R = COOEt and X = 4-Tos such salts were isolated in the form of crystals. In other cases the reaction results in the production of a good yield of derivatives of 2-(phenylazo)-1,3,4-thiadiazol-2-ines such as **62a-d**. It was suggested that they are formed through the stage of the linear zwitterion **61b** (Scheme 27) [44].

Dehydrodithizone is also active in reaction with carbenes (from $RHC=N_2$) and with carbenoids from $Fe_2(CO)_{10}$ [31, 32, 43]. Derivatives of 1,3,4-thiadiazoline **62e**,**f** were also obtained in the first case, and 1,3,4-thiadiazolin-5-one **62g** in the second (Scheme 27). The formation of these products can be explained by cheletropic reaction of the carbenes with the Ph–N=N–C=S fragment of the linear form of dehydrodithizone **52a**. The accessibility of dithizone and its analogs makes this method for the production of 2-arylazo-1,3,4-thiadiazolines **62**, which have significant synthetic and biological potential, extremely productive (cf. [43]).

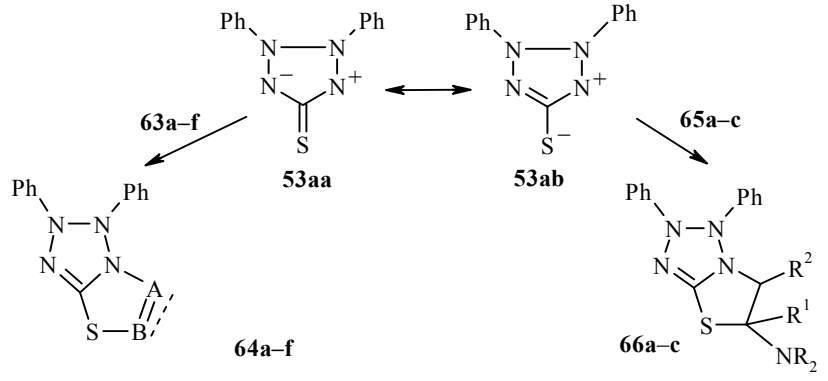
Scheme 27



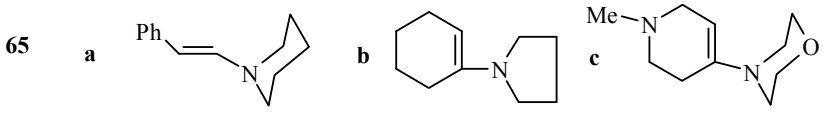
61, **62 a–e** R = COOEt, **a** X = 4-TolSO$_2$, **b** X = COOEt, **c** X = CN, **d** X = Ac, **e** X = H; **f** R = Ph, X = H; **g** R+X = O

Dehydrodithizone enters into pericyclic reactions with unsaturated compounds. Initially it was assumed that dehydrodithizone behaves in these reactions as a Huisgen 1,3-dipole, but unlike other mesoionic heterocycles [31, 32] not in the form of a cyclic dipole **53aa** but in the form of an exocyclic mesoion **53ab** (Scheme 28). Here the products of its reaction with all dipolarophiles were assigned similar structures, characteristic of 1,3-dipolar cyclocondensation: with electron-deficient derivatives of acetylene and ethylene **63a-f** – structures **64a-f** – and with electron-excessive enamines **65a-c** – structures **66a-c** (Scheme 28).

Scheme 28



63 a MeOOCC≡CCOOMe, **b** PhC(=O)C≡CC(=O)Ph, **c** (NC)$_2$C=C(CN)$_2$, **d** dehydrobenzene, **e** tetraphenylcyclopentadienone, **f** tetraphenylcyclopentadienethione;

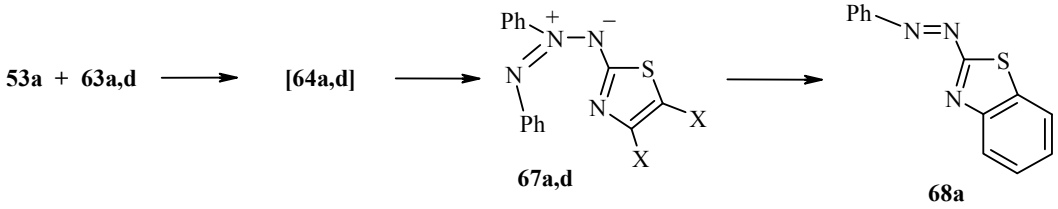


Later on it was shown that the structure of the products isolated in these cases depends very strongly on the electronic and steric characteristics of the ethylenes and acetylenes. Thus, it was established by X-ray diffraction that the product **67a** is produced in the reaction of dehydrodithizone with acetylenedicarboxylic esters **63a** (Scheme 29). Its formation is explained by the fact the 1,3-dipolar cycloaddition product **64a** arising

at the first stage soon undergoes further transformations. As a result of retro-1,5-electrocyclic reaction the N–N bond of the bridging nitrogen atom is cleaved, and a new reagent **67a** (of the Huisgen azoimine type) containing a triazolyl substituent is formed.

In the analogous reaction with dehydrobenzene **63d** as dipolarophile 2-(phenylazo)benzothiazole **68a**, formed as a result of one more consecutive reaction, was isolated (Scheme 29). Phenylnitrene is split off from the dipole **67d**, and this then dimerizes to azobenzene.

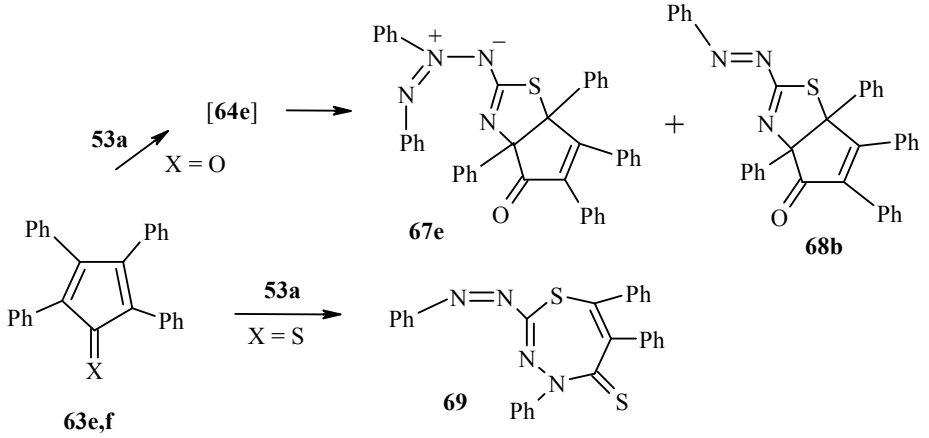
Scheme 29



a X = COOMe, **d** X = –CH=CH–

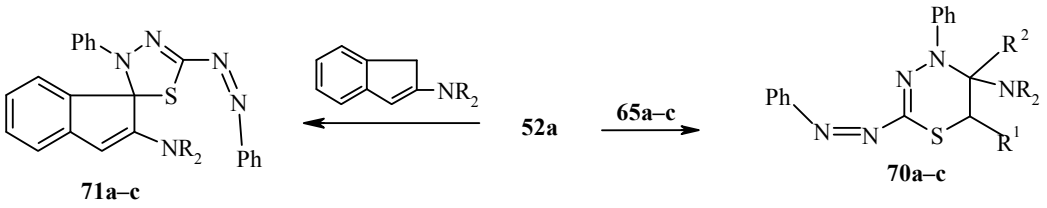
A similar situation was described for sterically hindered cyclic dienones and dienethiones (Scheme 30). In the molecule of tetraphenylcyclopentadienone **63e** only one double bond enters into reaction with the dehydrodithizone **53a**. In contrast to the previous reactions, here two products (**67e** and **68b**) were isolated. They are formed from the initial adduct **64e** as a result of similar successive reactions. The reaction with tetraphenylcyclopentadienethione **63f** concludes also with the loss of 1,2-diphenylacetylene and the formation of 4,6,7-triphenyl-2-(phenylazo)-1,3,4-thiadiazepine-5(4H)-thione (**69**) (Scheme 30).

Scheme 30



Later it was established that the reactions with electron-excessive ethylenes and acetylenes also take place in a different way [31, 32]. Here the variety of products, which depends on the nature of the enamines and ynamines, demonstrates the dual reactivity of the dehydrodithizone. Thus, the products of the reaction with the enamines **65a-c** were derivatives of 2-(arylazo)-5,6-dihydro-1,3,4-thiadiazine **70a-c** (Scheme 31) and not derivatives of thiazolo[3,2-*d*]tetrazole **66a-c** as previously supposed (Scheme 28). Here the reaction is regiospecific in all cases. The formation of the thiadiazines can probably be explained more simply by the participation of the (arylazo)thione fragment Ph–N=N–C=S of the open form of dehydrodithizone **52a** in a Diels–Alder reaction with the enamines (Scheme 31) than by complex transformations of the potential 1,3-dipolar cycloaddition products **66a-c**.

Scheme 31

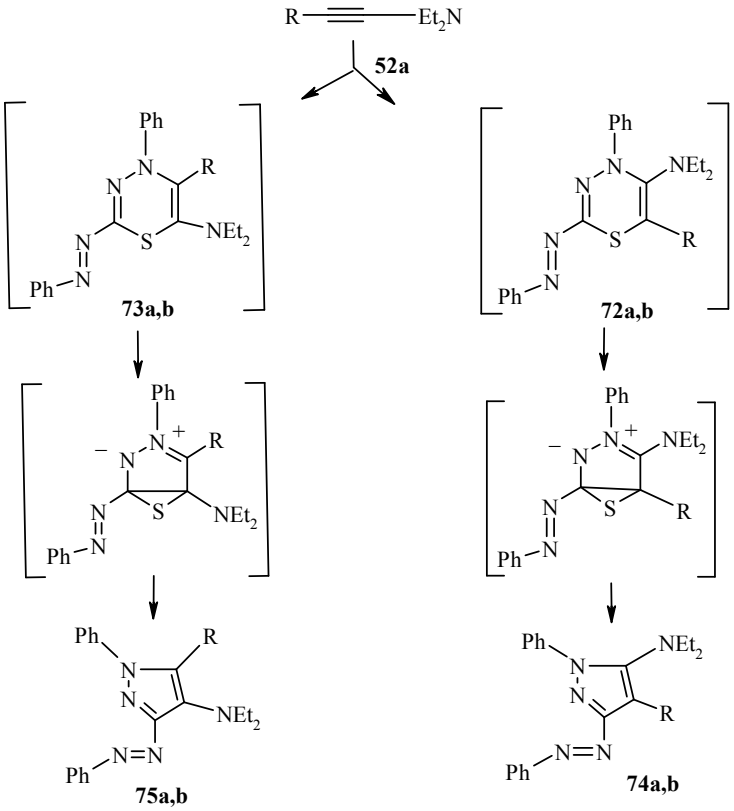


70 a $NR_2 = N(CH_2)_5$, R^1 = Ph, R^2 = H; **b** $NR_2 = N(CH_2)_4$, $R^1+R^2 = (CH_2)_4$; **c** $NR_2 = N(CH_2)_4O$, $R^1+R^2 = CH_2NCH_2CH_2$; **71 a** $NR_2 = N(CH_2)_4$, **b** $NR_2 = N(CH_2)_5$, **c** $NR_2 = N(CH_2)_4O$

Still more unexpected was the reaction of dehydrodithizone with 2-pyrrolidino-, 2-piperidino-, and 2-morpholinoindenes, as a result of which the spiro compounds **71a-c** were isolated (Scheme 31). The structure of spiro[indene-3,2-thiadiazoline] **71a** was proved by X-ray diffraction, but it is difficult to present suitable paths for its formation in view of the removal of the two hydrogen atoms.

Only [4+2] cycloaddition products are formed too with electron-excessive acetylenes such as 1-(diethylamino)propyne and 1-(diethylamino)-2-phenylacetylene, although regioselectivity was not observed in these reactions (Scheme 32). Unlike the dehydrogenated analogs **70**, the derivatives of the isomeric 1,3,4-4H-thiadiazines **72a**,**b** and **73a**,**b**, like other antiaromatic 8*n*π-electron systems [61], quickly undergo rearrangement with ejection of the sulfur atom and the formation of 3-(phenylazo)pyrazoles **74a**,**b** and **75a**,**b** as reaction products.

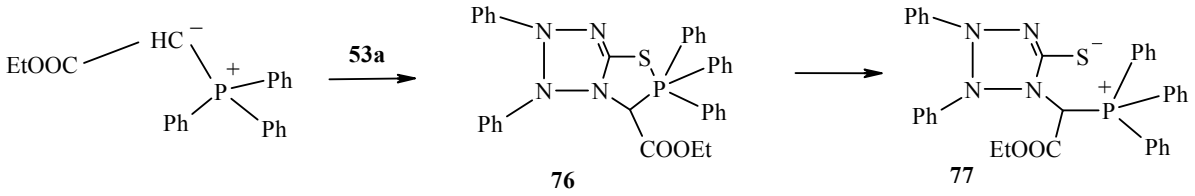
Scheme 32



a R = Me, **b** R = Ph

Of the ylides only one, ethoxycarbonylmethylidenetriphenylphosphorane, was brought into reaction with dehydrodithizone. The suggestion that the 1,3-cycloaddition product **76**, which opens to the 1,5-zwitterionic compound **77** (Scheme 33), is formed at the first stage requires elaboration since the bicycle **76** would most likely split off $Ph_3P=S$ as a result of retro [3+2] cycloaddition.

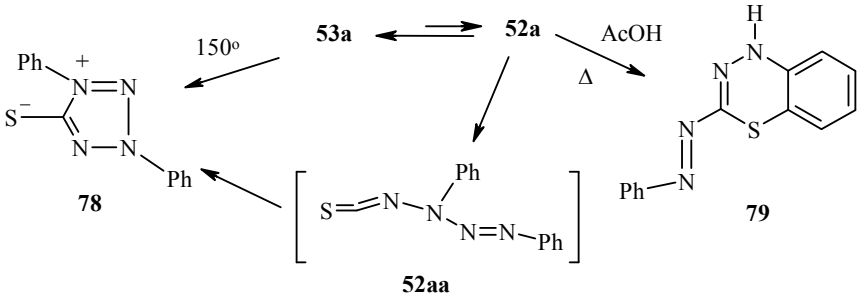
Scheme 33



Above the reactions in which the inner framework of atoms in the dehydrodithizone molecule is preserved were examined. In addition, two rearrangements where the isomeric products have cyclic structures of a different type have been described. One of the rearrangements is typical of the cyclic form of dehydrodithizone **53a** and characteristic of many mesoionic heterocycles [31, 32, 62], and the other is of the linear form **52a**.

At elevated temperature (120-150°C) dehydrodithizone isomerizes to the mesoionic isomer **78** (1,3-diphenyltetrazolium-5-thiolate) (Scheme 34). Such rearrangements have been explained by a 1,2-shift of the phenyl group in the cyclic thiolate **53a** [32], although the process can be explained by a C–N shift of the phenylazo group in the bis(phenylazo) thioketone **52a** and subsequent cyclization of its isomer the tetrazene **52aa** that forms to the 1,3-diphenyltetrazolium-5-thiolate (**78)** (Scheme 34). This reaction is of interest not only for theoretical chemistry but also with appropriate modification for organic synthesis. For example, the 1,3-diphenyl isomer **78** reacts just as easily as dehydrodithizone with electrophilic reagents [32]. Moreover, the method under discussion for the synthesis of 1,3-diaryltetrazolium-5-thiolates is preferred to other methods (cf., for example, their synthesis from 3-aryl-1,2,3,4-thiatriazolium-5-aminides).

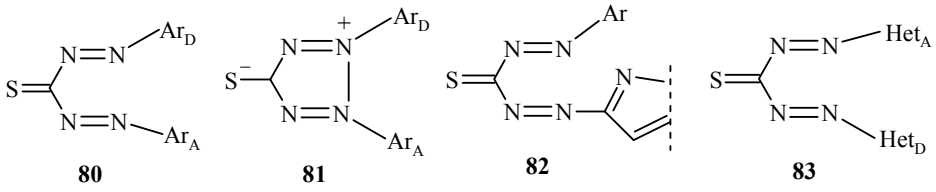
Scheme 34



In solutions of dehydrodithizone the fraction of the linear isomer **52a** can increase, particularly on heating. Here it is capable of entering into many reactions as a polyazapolyene system, including pericyclic rearrangements. Thus, when solutions of dehydrodithizone in acetic acid are boiled 1,6-electrocyclization of the 1-thia-3,4-diazahexa-1,3,5-triene system of its linear isomer (with participation of the π-system of the phenyl ring) occurs (Scheme 34). A subsequent 1,5-prototropic shift leads to the formation of the purple 2-(arylazo)-1,3,4-benzothiadiazine **79** [31, 44]. 1,3,4-Benzothiadiazine derivatives of type **79** are interesting as biologically active compounds and as precursors, while at the same time their synthesis in other ways is extremely difficult [43, 44]. The oxidation and cyclization stages can be combined, and the precursors of dehydrodithizone, e.g., thiazine and even 1,5-diphenylthiocarbohydrazide, can be brought into the reaction.

The dehydrogenation reactions of substituted dithizones **38b-m** and the properties of the substituted dehydrodithizones **52(53)b-m** obtained from them, including their rearrangements, have unfortunately been studied little. For example, the cyclic structure of 2,2'-dimethoxydehydrodithizone **53f** was only confirmed for the crystalline state [52]. Of all the physical characteristics only the solvatochromism of substituted dehydrodithizones **52(53a)a-i** was studied in greater detail. Many theoretical and practical issues remain unanswered. In the case of the dehydrogenation of the unsubstituted dithizones **38** ($Ar^1 \neq Ar^5$) the corresponding unsymmetrical dehydrodithizones **80** ($Ar^1 \neq Ar^5$) should be formed (Scheme 35).

Scheme 35



In these cases it will be difficult to predict which of their isomeric forms, the linear **52** or cyclic **53** analog, will be more stable. It is even more difficult to predict which of the two arylazo fragments will take part preferentially in the reactions described above. For example, in the molecules of the dehydrodithizones **80** with donor and acceptor substituents in the various aryl fragments will their cyclic isomer **81** be more stable and how many of the isomeric forms (one or two) will be realized in solutions with different polarity? And which isomers of the rearrangement products (from the two possible 1,3-thiolates **78** or 2-(arylazo)benzo-1,3,4-thiadiazines **79** will be realized (Scheme 34)? Moreover, according to calculations, in the molecule of 2,3-diphenyl-2H-tetrazolium-5-thiolate (**53a**) the positive charge is located only on the phenyl fragments, and the negative charge on the sulfur atom and in the tetrazole ring [54, 60]. Of course, the insertion of various types of substituents into the phenyl rings can substantially affect the distribution of electron density, especially in the unsymmetrically substituted derivatives of dehydrodithizones **80** with substituents differing greatly in electronic characteristics. In the case of the 1-aryl-5-heteryl derivatives **82** competition between the aryl and heteryl fragments and the various (C- or N-) centers of the heterocycle is possible. The last situation is even more likely in the case of the two different heterocyclic substituents in the diheteryl analogs **83** (Scheme 35); for example, there is competition between the electron-excessive (Het_D) and electron-deficient (Het_A) residues. Competition is also possible for various heterodiene and heterotriene systems in various pericyclic reactions, and this is typical of polyazapolyene systems [63, 64].

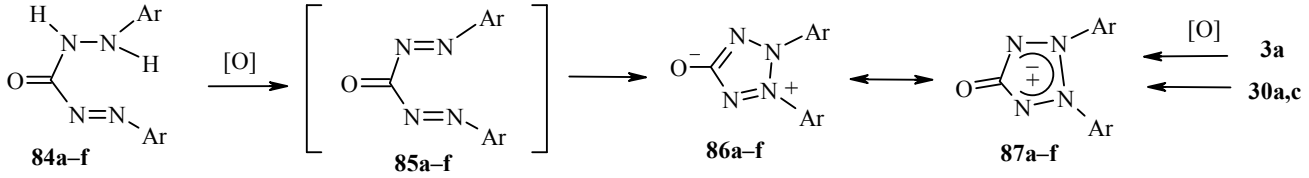
5.2. Hetero Analogs of Dehydrodithizone in the Chemistry of Azoles

Unlike the dithizone (**38a**), in the crystals and in solutions 3-hydroxy-1,5-diphenylformazan (**44b**, X = O, $R^1 = R^5$ = Ph, Scheme 21) exists only in the tautomeric form of the phenylhydrazide of (phenylazo)carboxylic acid (**84a**) (Scheme 36) [4, 6, 8, 9]. It is well known as the analytical reagent "1,5-diphenylcarbazone" [65] and is used not only for the determination of metal cations but also for chloride ions [66], which is due to the ease of its dehydrogenation,

In spite of the availability of 1,5-diphenylcarbazone **84a** and its analogs **84d-f** (and others) their dehydrogenation has been studied significantly less than the dehydrogenation of the dithizones **38**. Here there is very little information on the bis(arylazo) ketone form **85a**. Most of the data relate to the production and study of the characteristics of 2,3-diphenyltetrazolium-5-olate **86a** (Scheme 36). Only a few examples of the synthesis of other 2,3-diphenyltetrazolium-5-olates (**86b-f**) etc. are known [8, 31, 32, 47, 55, 56, 67-69].

2,3-Diphenyl-1,2,3,4-tetrazolium-5-olate (**86a** Bamberger's betaine) was first obtained from 3-nitro-1,5-diphenylformazan (**30c**) during treatment with alkali or pentyl nitrite [8, 31, 32, 47]. It is also formed readily during the action of HNO_3 on diphenylcarbazide, diphenylcarbazone, dithizone (**38a**), diphenylthiocarbazone, and their salts and also during the oxidation of 3-chloro-1,5-diphenylformazan or 1,5-diphenylformazan-3-carboxylic acid (**3a**) (Scheme 36) [8, 23, 31]. On account of its ready availability the tetrazolium-5-olate **86a** has found use in analytical chemistry and biochemistry and as yet only a little in organic synthesis [23, 31, 32, 47, 67, 69].

Scheme 36



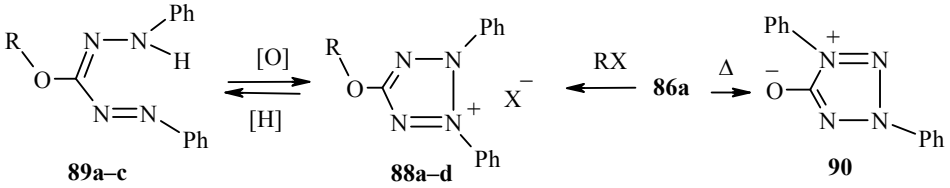
84a–f **85a–f** **86a–f** **87a–f**

84–87 Ar = RC_6H_4 (**a** R = H, **b** R = 4-Me, **c** R = 4-MeO, **d** R = 4-NO_2, **e** R = 4-Cl, **f** R = 4-Br)

The bis(phenylazo)ketone form **85a** of the product from oxidation of the carbazone **84a** is evidently even less stable than the linear form of dehydrodithizone **52a**. They are either not formed during the methods used for the synthesis of tetrazolium-5-olate **86a** or change into the cyclic form so quickly that they are not detected even by spectral methods. In many instances the possibility of its realization is not even discussed, e.g., during study of the dependence of the position of the maximum of the absorption bands in the UV spectra of the tetrazolium-5-olates **86a-f** on the polarity of the solvent or during determination of the pK_{BH^+} values of their conjugate acids.

The tetrazolium olate structure **86a** of the crystalline samples of the products from the oxidation of diphenylcarbazone and 3-nitro- and 3-chloroformazans was confirmed by X-ray diffraction. The bond lengths C–N (1.378 Å) and N–NPh (1.311 Å) in the molecule of the tetrazolium-5-olate **86a** are equal in pairs, and the length of the C–O bond (1.237 Å) is close to that in amides; the structure of this compound is probably represented more accurately by the formula **87a** (Scheme 36). This view is confirmed by the fact that its IR spectrum contains a strong absorption band at 1665 cm^{-1} [55, 68], which is characteristic of amides. The cyclic structure of tetrazolium-5-olate **86a** in solutions in DMSO was confirmed by ^{13}C and ^{15}N NMR methods [67]. The characteristics of the UV spectra of the tetrazolium-5-olates **86a-f**, containing various substituents in the aryl fragments, coincide with those of the corresponding 5-alkoxy-2,3-diaryltetrazolium salts (**88a-d** etc., Scheme 37), indicating that the cyclic structure of the dehydrocarbazones **86a-f** in various types of solvents is stable.

Scheme 37



89a–c **88a–d** **90**

a R = Me, **b** R = Et, **c** R = $PhCH_2$, **d** R = H; X = I, Br, Cl, OSO_2Tol

2,3-Diphenyltetrazolium-5-olate **86a** is protonated at the exocyclic oxygen atom and forms stable 5-hydroxy-2,3-diphenyltetrazolium salts **88d** (Scheme 37). It can be easily alkylated to the corresponding 5-alkoxytetrazolium salts **88a-c**, which are easily reduced to the corresponding 3-alkoxy-1,5-diphenylformazans **89a-c**. A combination of the described reactions provides a convenient method for the synthesis of certain types of formazans inaccessible by other methods (Scheme 1) [8, 19, 47, 55].

2,3-Diphenyltetrazolium-5-olate **86a** undergoes thermal rearrangement to 1,3-diphenyltetrazolium-5-olate (**90**) more readily than the dehydrodithizone **53a** (Scheme 37) [31, 32, 47, 62]. The isomeric 1,3-diphenyltetrazolium-5-olate **90** and its aryl analogs are widely used in the synthesis of other mesoionic 1,3-diaryltetrazolium-5-ylides [31, 32, 49, 64]. The method for the production of the isomeric 1,3-diphenyl-tetrazolium-5-olate **90** by the discussed rearrangement is preferred to other methods on account of the availability of the initial tetrazolium-5-olate **86a**.

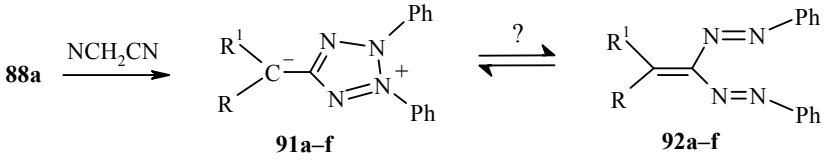
The accessible alkoxytetrazolium salts **88a-c** (and others), capable of substitution of the alkoxy groups by various nucleophiles, have also been used for the synthesis of 2,3-diphenyltetrazolium-5-olates **86a**,**c**, the isomeric 1,3-diphenyltetrazolium-5-olates **90**, and other tetrazolium ylides. They are therefore of interest as precursors in such syntheses. Thus, with Na_2S they form tetrazolium thiolates **53** with preparative yields, and the tetrazolium methylide **91a** was obtained from the methoxy-substituted salt **88a** with malononitrile (Scheme 38).

Examples of the participation of 2,3-diaryltetrazolium-5-olates **86a-f** and their 1,3-isomers (**90**, etc.) in complexation and cyclocondensation were not found. Unfortunately, representatives of the 5(1)-aryl-1(5)-heteryl-3-hydroxy- and 1,5-diheteryl-3-hydroxyformazans, like the corresponding analogs of dithizone, have likewise not yet been used as precursors in the dehydrogenation and cyclocondensation reactions under discussion.

Surprisingly, there are no data on the selenium analogs of dehydrodithizone **46e** and **47e** (X = Se, Scheme 21), and data on 1,5-diphenylselenocarbazone **44e** or **45e** (X = Se) have been presented only in two patents.

It was also not possible to find information on the dehydrogenation of formazans of type **44d** (HX = CHRR', Scheme 21) having an active methine group attached to a *meso* carbon atom. The expected oxidation products (of types **46** and **47**) were obtained in other ways. Thus, the cyclic structure of tetrazolium ylide **91a** was assigned to the product of the reaction of 5-methoxytetrazolium salt **88a** with malononitrile (Scheme 38 [67]), while the linear isomers of 1-aryl-2,2-bis(arylazo)-1-R-ethylenes **92a-f** were obtained by azocoupling of arenediazonium salts with alkyl-, 1-aryl-, or 1-(aryloxy)styrenes [67, 70-72].

Scheme 38



91a–f **92a–f**

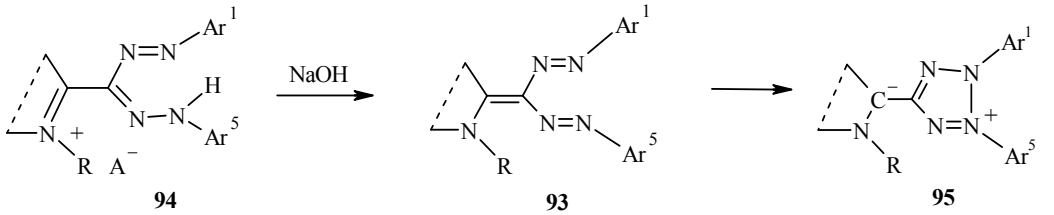
a R = R^1 = CN, **b** R = R^1 = Ph, **c** R = Ph, R^1 = Me; **d** R = R^1 = 4-$MeOC_6H_4$;
e R = 4-MeC_6H_4, R^1 = Me; **f** R = 4-$MeOC_6H_4O$, R^1 = Me

The possibility of the existence of cyclic isomers **91b-f** for the products **92b-f** was not even discussed, even in well known reviews on the chemistry of mesoionic heterocycles ([31, 32] and references therein). However, the open structure of the tetraazatrienes **92b-f** requires additional confirmation since their analog containing two nitrile groups in the ylidene fragment, according to ^{13}C NMR data, has the cyclic structure of 5-dicyano-2,3-diphenyltetrazolium methylide (**91a)** in DMSO-d_6 [67]. The strong dependence of the position of the long-wave absorption maximum in the UV spectrum of this compound on the polarity of the solvent [67] does not exclude equilibrium between its open **92a** and cyclic **91a** forms (Scheme 38), which may be due to the presence of the strong electron-withdrawing nitrile groups.

Apart from the tetraazatrienes of type **92** several of their analogs, differing in the structure of the ylidene fragment $RR^1C=$, are known. First of all, there are a considerable number of well known azacyanine dyes **93**, in which the fragment analogous with the $RR^1C=$ in compounds **92** is the residue of a substituted

α-azacycle (indole, isoquinoline, benzimidazole, benzothiazole, benzoxazole, benzoselenazole, etc.) (Scheme 39). 2-[Bis(arylazo)methylene]-heterocycles **93** are easily obtained during treatment of the extremely accessible formazans of type **94**, containing the corresponding heterocyclic cation with a quaternized α-nitrogen atom at position 3, with bases (see [4, 8, 19] and the references therein). From bisformazans with two similar fragments more complicated heterocyclic dyes, containing two tetraazatrienes fragments, were obtained. However, it was not possible to find data on the ability of tetraazatrienes dyes of type **93** or their bis-analogs to undergo transformations to tetrazolium-5-ylides of type **95**.

Scheme 39

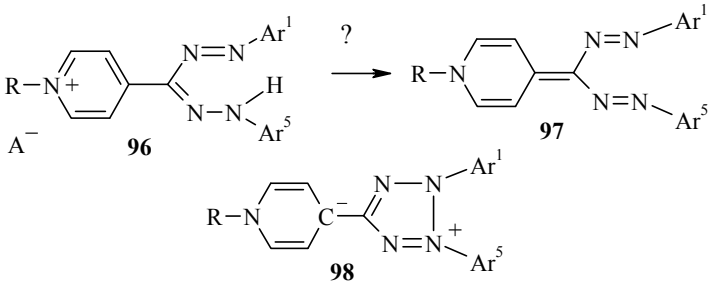


94 **93** **95**

R = Me, Et, $PhCH_2$, Ph;  = indole, isoquinoline, benzimidazole, benzothiazole, benzoxazole, benzoselenazole, etc. residue

Compounds **96** with a formazyl substituent at the γ-position to the quaternized heteroatom are also known (Scheme 40), although they are not so widely represented as their α-analogs **94**. Examples of the production of tetraazatrienes, such as 4-[bis(arylazo)methylidene]-heterocycles of type **97** or their cyclic isomers **98**, from them were not found [2, 4, 6-8]. The structure of the tetraazatrienes **93** and **96** and their analogs with two formazan groups was not studied in detail, but they are probably not susceptible to transition to the bicyclic mesoionic structures of types **95** and **98**.

Scheme 40



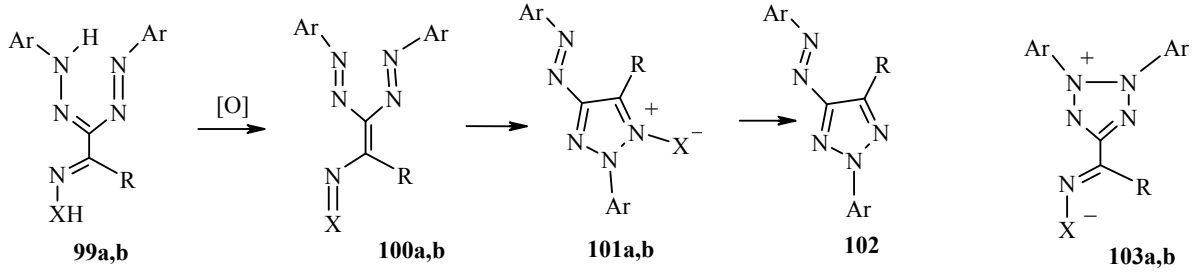
96 **97** **98**

Another type of tetraazatriene analogs of type **92** is produced during the dehydrogenation of 1,5-diarylformazans **99a**,**b** containing at position 3 oxime (formazan **99a**, X = O) or arylhydrazone groups (osoformazans **99b**, X = NAr, including the osoformazans of sugars) (Scheme 41) [3, 8, 33]. However, these reactions take place in a complicated manner, they are multistage processes, and the structure of the isolated heterocycle depends on the nature of the substituents in the formazan and, in particular, on the reaction conditions. Accepting substituents in the N-aryl rings of the osoformazans **99b** hinder the process, and stronger oxidizing agents, higher temperatures, and increased reaction times are therefore required. The stability of the obtained polyazapolyenes of type **100a**,**b** is determined by the nature of the terminal heteroatom [1-6, 8, 33]. It was possible to isolate

polyazapolyenes of type **100** in a small quantity only during the oxidation of the oxime **99a** in a mixture with the 1,2,3-triazole derivatives **101a** or **102**, which are formed as a result of 1,5-electrocyclization of the initially formed oxapentaazatetraene **100a** (X = O, Scheme 41) [8, 33]. During dehydrogenation of the oxime **99a** with acetic anhydride in acetic acid the triazole **102** is the dominant product.

In comparison with the dehydrogenation of 3-HX-formazans **84a**,**b** the competing process of electrocyclization of the other unsaturated system in the molecule of the polyheteropolyenes **100**, leading to the formation of a triazole (**101**, **102**) and not a tetrazole ring (**103**), is observed in this transformation.

Scheme 41



a X = O, **b** X = NAr

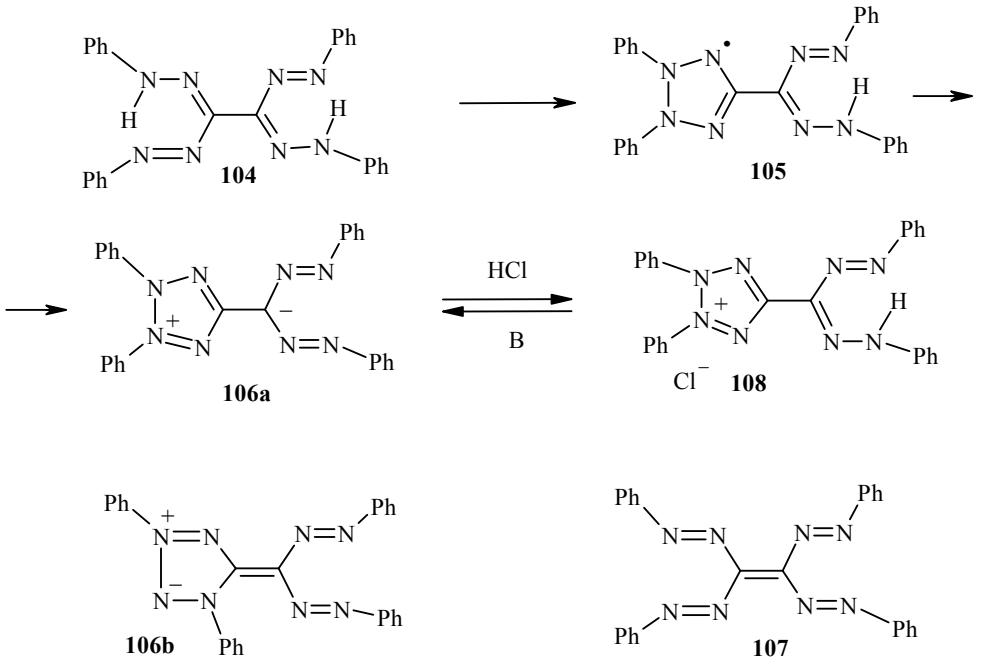
During dehydrogenation of the ozoformazans **99b** the initial oxidation products were not isolated. Like the 1,2-bis(phenylazo)ethylenes (the products from dehydrogenation of the osazones) [3-6, 8, 33, 73-76], the expected 1,1,2-tris(phenylazo)ethylenes **100b** (analogs of the ethylenes **92**) quickly undergo 1,5-electrocyclization to 1,2,3-triazolium-1-aminides **101b**, which in certain cases can be isolated (Scheme 41). The aminides **101b** much more often eliminate the arylnitrene. Here derivatives of 1,2,3-triazole **102** are usually obtained, although more complicated transformations have been described [8, 32, 73, 74]. Consequently, in these cases too the other competing process of electrocyclization of the polyheteropolyenes **100b**, leading to the formation of triazole derivatives **101b** and **102** and not the tetrazole system of the expected ylide **103b**, predominate.

In spite of the widespread use of these reactions in the synthesis of 1,2,3-triazoles (Scheme 41) it is not yet possible to give the full picture of the competing effect of the various substituents in the initial 3-imidoylformazans **99a**,**b** on the nature of the final product. In most cases the osoformazans **99b** with identical aryl substituents, most often with phenyl groups, were used. Usually the 1,1,2-tris(phenylazo)ethylenes **100b** (Ar = Ph) were not isolated, and other paths for the transformation of the formazans **99b** into the triazoles **102** were therefore proposed: through a ring–chain tautomer or the initial formation of radicals by the action of one-electron oxidizing agents (MnO_2, etc.). In these cases too it is assumed that the successive stages of the process include the formation of 1,2,3-triazolium-1-aminides **101b** and not the zwitterions **103**.

It is possible to regard bis(1,5-diphenylformazan-3-yl) **104** (Scheme 42) as an analog of the osoformazans **99b** (R = –N=NPh) (Scheme 41) and to expect similar behavior. However, during its dehydrogenation Neugebauer and Fischer recorded the initial formation of tetrazolyl radicals **105** [33] (Scheme 42). Further dehydrogenation leads to the formation of a product which, according to ^{1}H NMR data, has an unsymmetrical structure, and this enabled the authors to assign it the structure of the mesoionic compound **106a** and not the expected symmetrical tetrakis(phenylazo)ethylene **107** or its cyclic mesoionic 1,2,3-triazole isomer of type **101b** (R = N=NPh).

During the action of HCl the oxidation product **106a** forms the tetrazolium salt **108**, which is stable (Scheme 42). The tetrazolium salt **108** can be regarded as an analog of salt formazans of type **94** and **96**, but with a β-quaternized nitrogen atom, and the reverse reaction of conversion of this salt into the mesoionic product **106a** by alkalis is similar to the reaction leading to the production of the stable [bis(arylazo)-methylene]azacycles **93** and **97**.

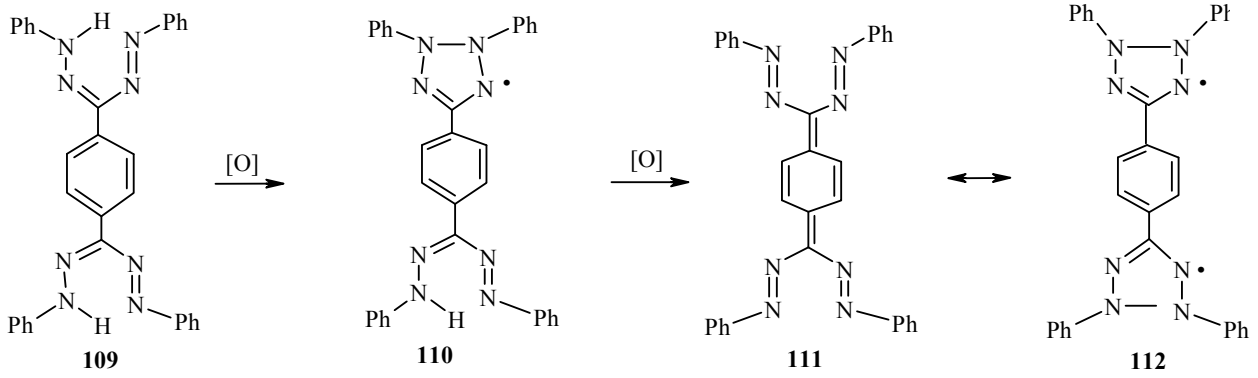
Scheme 42



It must be emphasized that the history of the synthesis of the bisformazan **104** is rich in contradictions. For a long time this structure was assigned to another compound, which proved to be the 1,3-diphenyl isomer **106b** of tetrazolium-5-ylide **106a** (Scheme 42) (see [8, 33] and the references therein).

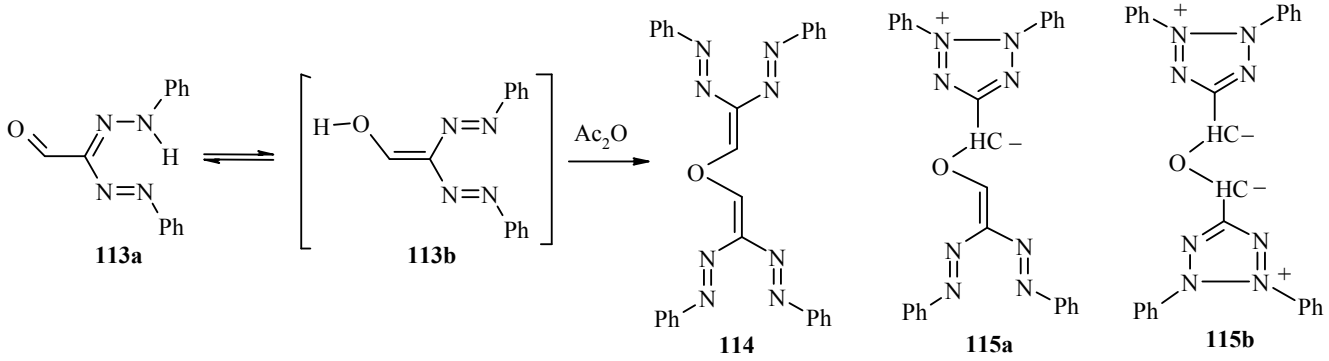
The dehydrogenation of 1,4-bis(1,5-diphenylformazan-3-yl)benzene **109** by the action of PbO_2 was restricted to the generation of the initial tetrazolinyl radical **110** (Scheme 43), the ESR spectrum of which was similar to the spectrum of the product from oxidation of the 1,3-isomer. The structure of the products from further oxidation was not discussed. The question of the greater stability of the quinodimethane products **111**, analogs of 1,1-bis(phenylazo)ethylenes **92**, or diradicals **112** remains open.

Scheme 43



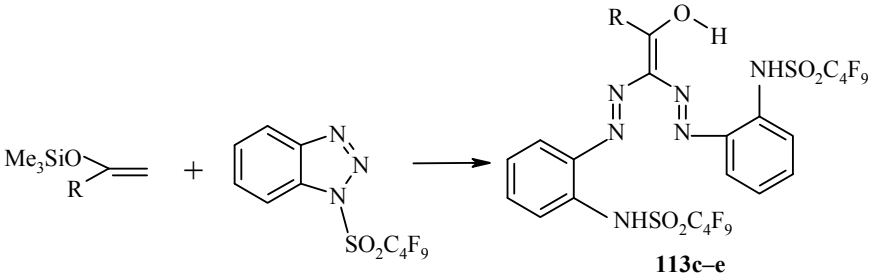
Another type of 1,1-bis(phenylazo)ethylenes, similar to the heteropolyenes **92**, was obtained during the action of acetic anhydride on 3-formyl-1,5-diphenylformazan **113a**. Instead of the expected product from acylation at the NH group of the formazan **113a** or at the OH group of the tautomer **113b** 2,2,2',2'-tetrakis-(phenylazo)divinyl ether (**114**) was isolated (Scheme 44) [33]; its possible existence in cyclic ionic forms such as **115a** or **115b** was also not discussed.

Scheme 44



The formation of the ether **114** was explained by the possibility of the existence of the formazan **113a** in the enolic form **113b** [33]. This suggestion was recently confirmed by the isolation in crystalline form of the enols **113c-e** of similar type during the azocoupling of 1-R-1-(trimethylsilyloxy)ethylenes with 1-(nonafluoro-butylsulfoxy)benzotriazole, which acts as a synthetic equivalent of the diazo salt (Scheme 45) [77].

Scheme 45

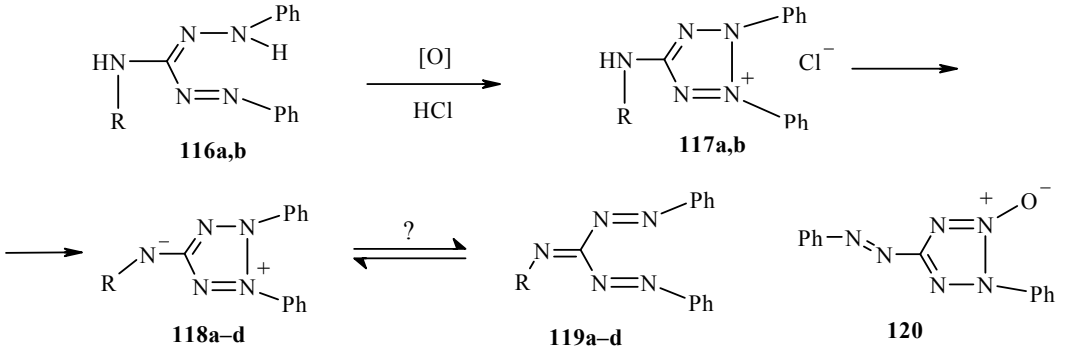


c R = Me, **d** R = Et, **e** R = Ph, etc.

In spite of the accessibility of 3-(R-amino)formazans **44c** (X = RN, Scheme 21) there are very few examples of their dehydrogenation with a view to synthesizing the corresponding polyazapolyenes of type **46c** or their cyclic isomers of type **47c**. In all the reviews and books only one paper by Bamberger et al. is mentioned [78]. By oxidizing 3-amino-1,5-diphenylformazan (**116a**) with amyl nitrite in hydrochloric acid they synthesized 5-amino-2,3-diphenyltetrazolium chloride (**117a**) (Scheme 46). In their opinion the action of Ag_2O on it gave 2,3-diphenyl-1,2,3,4-tetrazolium-5-aminide (**118a**) (R = H), the treatment of which with benzol chloride as they considered gave the benzoylated analog **118b** (R = Bz). It was later shown that this product was 3-(benzoylamino)-1,5-diphenylformazan (**116b**) ([31] and references therein). Other structures proposed by Bamberger et al. were also reexamined. Thus, it was later argued ([31] and references therein) that 2,3-diphenyltetrazolium-5-(N-nitroso)-aminide (**118c**) is obtained during the nitrosation of the salt **117a**; this compound, unlike the dehydrodithizone **53a** and the olate analog **86a**, rearranges during heating not to the 1,3-diphenyl isomer but is converted through the open isomer **119c** into 3-phenyl-5-(phenylazo)tetrazolium 2-oxide (**120**) (Scheme 46). On the basis of this

example it is possible to conclude that the possibility of the existence of tetrazolium-5-aminides of type **118** and the possibility of their conversion into open isomers of type **119** are confirmed. In the latter two pericyclic processes can compete: the usual cyclization of the 1,1-bis(phenylazo)imine system to the tetrazolium-5-aminide **118** and in the case of the corresponding substituents at the exocyclic nitrogen atom cyclization of the other heteroene system (in this case the O=N–N=C–N=N– fragment) to the tetrazolium oxide **120**, which is a mesoionic product of a different type. Unfortunately, the structure of these products have not yet been studied further, and it is difficult to reach unambiguous conclusions (see the reviews [31, 32], the electronic bases "Scopus", "Scirus," and "Beilstein" on 03.03.2009) although their 1,3-diaryl isomers were studied by ^{13}C, ^{14}N, and ^{15}N NMR spectroscopy in a fair amount of detail [79]. In the light of the lower stability of the mesoionic compounds with the anionic center at the exocyclic nitrogen atom it seems that for the compounds under discussion it is impossible to exclude also the possible stability of open structures of type **119a**,**b**. Indirect evidence for this is the fact that an open structure is always assigned to the well known 1,5-diaryl-3-(arylazo)formazans **119d** (R = ArNH) [4-6, 8, 30]. The UV spectra of the formazans **119d** are similar to those of other groups of 3-R-1,5-diarylformazans, which does not provide grounds for supposing that they may exist in the cyclic forms **118d**. However, since the spectral characteristics of tetrazolium aminides of type **118** and **119** were not studied the question of the preference for the isomeric forms **118** and **119** can be considered open.

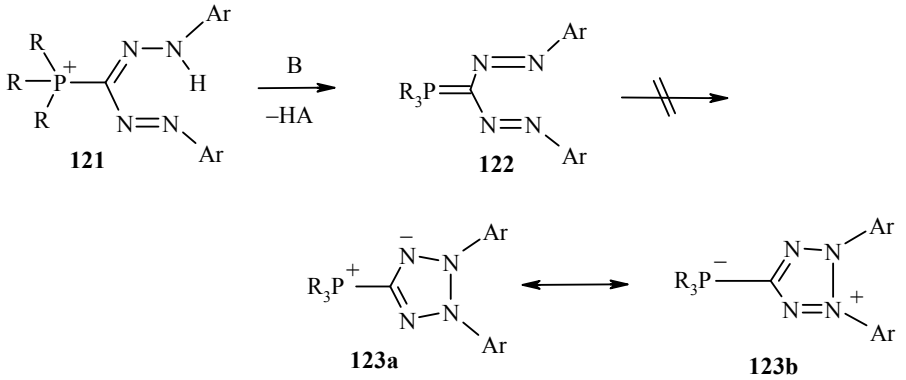
Scheme 46



a R = H, **b** R = PhC(=O), **c** R = ON–N; **d** R = ArNH

1,5-Diarylformazans **121**, containing a quaternized phosphorus atom at position 3 (Scheme 47), are produced by the action of arenediazonium salts or 1-(arylsulfonyl)benzotriazoles (the synthetic equivalent of diazo salts) on methylenetriphenylphosphonium salts or on the zwitterionic triphenylphosphonium acetate [6, 80, 81].

Scheme 47



R = Ph; Ar = Ph, 4-Tol, 4-$O_2NC_6H_4$, 2-$F_9C_4(SO_2)NHC_6H_4$

Formazans of type **121** are easily transformed into brightly colored phosphoranes **122** by the action of the weakest bases or even during isolation (Scheme 47), e.g., during the azocoupling of 1-(nonafluorobutylsulfoxy)benzotriazole with triphenylphosphonium acetate [80, 81]. The specific nature of the electronic structure of the phosphorus atoms in the phosphoranes makes it possible to understand why they do not tend to change into cyclic structures of type **123a**,**b**.

REFERENCES

1. W. Ried, *Angew. Chem*., **64**, 391 (1952).
2. A. W. Nineham, *Chem. Rev.*, **55**, 355 (1955).
3. H. S. El Kadem, *Adv. Carbohydr. Chem*., **59**, 135 (2004).
4. R. Pütter, in: E. Müller (editor), *Methoden der organischen Chemie (Houben-Weyl),* Stuttgart, Thieme (1965), Vol. 10/3, p. 627.
5. A. Banciu, *Rev. Roum. Chim*., **37**, 575 (1992).
6. Yu. P. Kitaev and B. I. Buzykin, *Hydrazones* [in Russian], Nauka, Moscow (1974), 415 pp.
7. N. P. Bednyagina, I. Ya. Postovskii, A. D. Garnovskii, and O. A. Osipov, *Usp. Khim.*, **44**, 1052 (1975).
8. B. I. Buzykin, G. N. Lipunova, L. P. Sysoeva, and L. I. Rusinova, *Formazans* [in Russian], Nauka, Moscow (1992), 376 pp.
9. G. N. Lipunova, N. B. Ol'khovikova, B. I. Buzykin, and G. I. Segeikin, *Zh. Nauch. Prikl. Foto- i Kinematografii*, **48**, 5 (2003).
10. Y. A. Ibrahim, A. A. Abbas, and A. H. M. Elwahy, *J. Heterocycl. Chem.*, **41**, 135 (2004).
11. G. I. Segeikin, G. N. Lipunova, and I. G. Pervova, *Usp. Khim.*, **75**, 980 (2006).
12. A. R. Katritzky, S. A. Belyakov, Dai Cheng, and H. D. Durst, *Synthesis*, 577 (1995).
13. N. A. Frolova, S. Z. Vatsadze, A. I. Stash, R. D. Rakhimov, and N. V. Zyk, *Khim. Geterotsikl. Soedin.*, 1682 (2006). [*Chem. Heterocycl. Comp.*, **42**, 1444 (2006)].
14. I. V. Růzičková, J. Slouka, and T. Gucky, *Acta Univ. Palacki. Olomuc. Fac. Rerum Nat., Chem.*, **44**, 55 (2005).
15. I. Fryšová, J. Slouka, and J. Hlavka, *ARKIVOC*, ii, 207 (2006).
16. D. E. Berry, R. G. Hicks, and J. E. Gilroy, *J. Chem. Educ.*, **86**, 76 (2009).
17. T. F. DeRosa, *Advances in Synthetic Organic Chemistry and Methods Reported in US Pat.*, Elsevier (2006), 686 pp.
18. Y. A. Ibrahim, H. Behbehani, M. R. Ibrahim, and N. M. Abrar, *Tetrahedron Lett.*, **43**, 6971 (2002).
19. O. M. Polumbrik, *Chemistry of Verdazyl Radicals* [in Russian], Naukova Dumka, Kiev (1984), 252 pp.
20. R. N. Butler, in: A. R. Katritzky, Ch. W. Rees, and E. F. V. Scriven (editors), *Comprehensive Heterocyclic Chemistry, II*, (1996), vol. 4, Pt. 4–17, p. 621.
21. A. B. Zhivich, G. I. Koldobskii, and V. A. Ostrovskii, *Khim. Geterotsikl. Soedin.*, 1587 (1990). [*Chem. Heterocycl. Comp*., **26**, 1319 (1990)].
22. G. I. Koldobskii, Yu. E. Myznikov, A. B. Zhivich, V. A. Ostrovskii, and V. S. Poplavskii, *Khim. Geterotsikl. Soedin.*, 754 (1992). [*Chem. Heterocycl. Comp*., **28**, 626 (1992)].
23. I. Wiedermannova, J. Slouka, and K. Lemr, *J. Heterocycl. Commun*., **8**, 479 (2002).
24. *Biolog Redox Dye Mixes for Enumerating Mammalian Cells in Proliferation and Chemosensitivity Assays, Catalogs Biolog.: Inc.* (2006).
25. Y. A. Ibrahim, *Tetrahedron*, **53**, 8507 (1997).
26. I. Fryšová, J. Slouka, and T. Gucky, *ARKIVOC*, xv, 30 (2005).
27. M. Kamburova, T. Popov, and D. Nikitova, *Zh. Analit. Khim.*, **47**, 799 (1992).

28. K. B. Gavazov, A. N. Dimitrov, and V. D. Lekova, *Usp. Khim.*, **76**, 187 (2007).
29. I. Kulich, P. Adamek, A. B. Zhivich, G. I. Koldobskii, and Yu. E. Myznikov, *Zh. Obshch. Khim.*, **60**, 2370 (1990).
30. V. V. Kozlov, Yu. M. Kulikov, and Yu. A. Kolesnik, *ZhVKhO D. I. Mendeleeva*, **21**, 323 (1976).
31. W. D. Ollis and Ch. A. Ramsden, *Adv. Heterocycl. Chem.*, **19**, 1 (1976).
32. Ch. Newton and Ch. A. Ramsden, *Tetrahedron*, **38**, 2965 (1982).
33. F. A. Neugebauer and H. Fischer, *Chem. Ber.*, **113**, 1226 (1980).
34. A. R. Katritzky, S. Belyakov, O. V. Denisenko, U. Maran, and N. S. Dalal, *J. Chem. Soc.*, *Perkin Trans. 2*, 661 (1998).
35. R. N. Butler, *Chem. Rev*., **84**, 249 (1984).
36. I. V. Nikonova, G. I. Koldobskii, A. B. Zhivich, and V. A. Ostrovskii, *Zh. Obshch. Khim.*, **61**, 2104 (1991).
37. D. Wolde Meskel, G. Abate, M. Lakew, S. Goshu, A. Selassie, H. Miorner, and A. Aseffa, *Ethiop. J. Health Dev.*, **19**, 51 (2005).
38. T. Riss and R. Moravec, *Promega Notes Magazine*, No. 59, 19 (1996).
39. P. J. Garratt, in: A. R. Katritzky, Ch. W. Rees, and E. F. V. Scriven (editors), *Comprehensive Heterocyclic Chemistry, II*, (1996), Vol. 4, p. 127.
40. A. S. Shawali, A. H. Elghandour, and A. R. Sayed, *Synth. Commun.*, **31**, 731 (2001).
41. A. Padwa (editor), *1,3-Dipolar Cycloaddition Chemistry*, 1983, vol. 1, 817 pp; vol. 2, 704 pp.
42. L. M. Harwood and R. J. Vickers, in: A. Padwa and W. H. Pearson (editors), *The Chemistry of Heterocyclic Compounds*, John Wiley and Sons, New York,Vol. 59, (2002), p. 169.
43. G. I. Kornis, in: A. R. Katritzky, Ch. W. Rees, and E. F. V. Scriven (editors), *Comprehensive Heterocyclic Chemistry II*, (1996), Vol. 4, p. 379.
44. R. K. Smalley, in: A. R. Katritzky, Ch. W. Rees, and E. F. V. Scriven (editors), *Comprehensive Heterocyclic Chemistry*, *II*, 1996, vol. 6, p. 737.
45. H. M. M. H. Irving, *Dithizone*. *Analytical Science Monographs*, The Chemical Society, London, Vol. 5, (1977), 106 pp.
46. T. Schönherr, R. Linder, U. Rosellen, and V. Schmid, *Int. J Quantum Chem.*, **86**, 90 (2002).
47. R. N. Hanley, W. D. Ollis, C. A. Ramsden, and I. S. Smith, *J. Chem. Soc.*, *Perkin Trans. 1*, 744 (1979).
48. A. A. Pasynskii, A. I. Blokhin, S. S. Shapovalov, and Yu. V. Torubaev, *Zh. Neorgan. Khim.*, **52**, 939 (2007).
49. T. V. Koksharova, *Zh. Struktur. Khim.*, **45**, 361 (2004).
50. F. Mirkhalaf, D. Whittaker, and D. J. Schiffrin, *J. Electroanal. Chem.*, **452**, 203 (1998).
51. A. Taha and A. M. Kiwan, *New J. Chem*., **25**, 502 (2001).
52. K. G. von Eschwege and A. Muller, *Acta Crystallogr.*, **E65**, o2 (2009).
53. I. G. Santos, A. Hagenbach, and U. Abram, *J. Chem. Soc.*, *Dalton Trans*., 677 (2004).
54. F. Jian, P. Zhao, L. Zhang, and Yuxia Hou, *J. Org. Chem.*, **70**, 8322 (2005).
55. W. Kozminski, J. Jaźwiński, L. Stefaniak, and G. A. Webb, *Magn. Reson. Chem.*, **28**, 1027 (1990).
56. J. Jaźwiński, *Bull. Polish Acad. Sci.*: *Chemistry*, **46**, 79 (1998).
57. J. L. Walsh, R. McCrackin, and A. T. McPhail, *Polyhedron*, **17**, 3221 (1998).
58. M. Grote, M. Sandrock, and A. Kettrup, *Reactive Polymers*, **13**, 267 (1990).
59. M. Grote and A. Kettrup, *Reactive Polymers. Ion Exchangers*, *Sorbents*, **6**, 337 (1986).
60. P.-S. Zhao, F.-L. Bei, X.-J. Yang, X. Wang, L.-D. Lu, F.-F. Jian, and Y.-X. Hou, *Jiegou Huaxue*, **23**, 1117 (2004)**.**
61. R. N. Butler, A. M. Evans, E. M, McNeela, G. A. O'Holloran, P. O'Shela, D. Cunningham, and P. McArdle, *J. Chem. Soc.*, *Perkin Trans. 1*, 2527 (1990).
62. D. Moderhack, *J. Prakt. Chem./Chem. Zeitung*, **340**, 687 (1998).

63. V. V. Zverev and B. I. Buzykin, *Izv. Akad. Nauk, Ser. Khim.*, 1459 (1995).
64. Yu. B. Vysotskii, B. I. Buzykin, and V. S. Bryantsev, *Khim. Geterotsikl. Soedin.*, 373 (2006). [*Chem. Heterocycl. Comp*., **42**, 331 (2006)].
65. O. A. Zaporozhets, T. E. Keda, L. E. Seletskaya, and V. V. Sukhan, *Zh. Analit. Khim.*, **55**, 635 (2000).
66. J. Novak and P. Vyhlidka, Inventor's Certificate CSFR No. 269928; *Ref. Zh. Khim.*, 4G197 (1992).
67. Sh. Araki, J. Mizuya, and Y. Butsugan, *J. Chem. Soc.*, *Perkin Trans. 1*, 2439 (1985).
68. M. V. Farrar, *J. Chem. Soc.*, 906 (1964).
69. J. Thiem and T. Wiemann, *Angew. Chem*., **103**, 1184 (2006).
70. V. V. Razumovskii and E. F. Rychkina, in: *Zh. Obshch. Khim.*, Coll. 2, 1953, p. 1005.
71. V. V. Razumovskii and E. F. Rychkina, *Zh. Obshch. Khim.*, **27**, 3143 (1957).
72. E. P. Nesynov and T. F. Aldokhina, *Zh. Obshch. Khim.*, **49**, 1087 (1979).
73. R. N. Butler, F. A. Lysaght, and L. A. Burke, *J. Chem. Soc.*, *Perkin Trans. 2*, 1103 (1992).
74. Ch. H. Suresh, D. Ramaiah, and M. V. George, *J. Org. Chem.*, **72**, 367 (2007).
75. Wei-Qiang Fan and A. R. Katritzky, in: A. R. Katritzky, Ch. W. Rees, and E. F. V. Scriven (editors), *Comprehensive Heterocyclic Chemistry*, *II*, 1996, vol. 4, p. 1.
76. V. P. Krivopalov and O. I. Shkurko, *Usp. Khim.*, **74**, 369 (2005).
77. M. Uhde and T. Ziegler, *Synthesis*, 1190 (2009).
78. E. Bamberger, R. Padova, and E. Ormerod, *Liebigs Ann. Chem*., **446**, 260, 297 (1926).
79. J. Jaźwiński, *Polish J. Chem.*, **46**, 1719 (1999).
80. R. H. Lowack and R. Weiss, *J. Am. Chem.*, *Soc*., **112**, 333 (1990).
81. X. A. Micó, R. G. Bonbarelli, L. R. Subramanian, and T. Ziegler, *Tetrahedron Lett*., **47**, 7845 (2006).