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The Structure of Hydrazones

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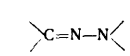
The review surveys the present state of research on the conformation, isomerism, and intramolecular interactions of molecules of the immense class of organic compounds containing a hydrazone group. A list of 221 references is included.

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I. INTRODUCTION

Compounds whose molecules contain the hydrazone grouping



(I)

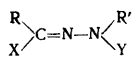
belong to the huge class of azomethines and are distinguished from other members of this class (imines, oximes, etc.) by the presence of two interlinked nitrogen atoms.

Being very readily available substances, hydrazones have found wide application in synthetic chemistry for the preparation of compounds of most diverse structure, and in analytical chemistry for the identification and isolation of carbonyl compounds, and for the detection of a large number of metal cations. Their application has been reported as plasticisers and stabilisers for polymers, polymerisation initiators, antioxidants, etc. However, the most valuable property of hydrazones is, perhaps, their great physiological activity. Among them are found herbicides, insecticides, nematocides, rodenticides, and plant growth regulators. The value of hydrazones in fighting tuberculosis is well known. Substituted hydrazones have been found to exhibit spasmolytic activity, hypotensive action, and activity against leukaemia, sarcomas, and other malignant neoplasms. The possibility is being investigated of using substituted hydrazones for the treatment of schizophrenia, leprosy, and other illnesses.

An attempt is made in the present review to consider on a uniform basis compounds in which the hydrazone group (I) is present in an open chain, and only the outermost atoms of the system can form part of rings. For

convenience we shall henceforward term the nitrogen atom in the azomethine group the imine nitrogen, and the other atom the amine nitrogen.

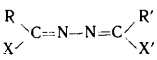
The triatomic hydrazone group is characteristic of a large number of organic compounds of the type



(II)

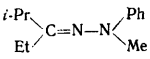
where R, R′, X, and Y can vary widely. We will use the term "hydrazones" as a general name for compounds having the structure (II). When R′ = Y = H we have "unsubstituted hydrazones"; when R′ = Alk(Ar, Az) and Y = H, "alkyl(aryl, acyl)hydrazones", and when R′ = Alk (Ar, Alk, Alk) and Y = Alk(Ar, Ar, Az) "dialkyl(diaryl, alkylaryl, acylalkyl, etc.)hydrazones"; and also with X = H we have an "aldehyde hydrazone", with X = Alk, Ar, Az a "ketone hydrazone", and so on. If R′ = NH_2CO the compounds (II) are semicarbazones, and if R′ = NH_2CS they are thiosemicarbazones. Dihydrazones of α-dicarbonyl compounds are usually termed "osazones".

Where X = Hal, NO_2, OAlk, OAr, the compounds are α-halogeno-hydrazones† or α-nitro(alkoxy, aryloxy)-hydrazones; when X = N : NR they are formazans, X = NHNHR hydrazidines, X = NH_2, NHR, NRR′ amidrazones; and with X = OH, SH hydrazides and thiohydrazides are formed. Furthermore, R′ and Y may together constitute the residue of a carbonyl compound, in which case the structure (II) acquires the form (III), and compounds of this class are termed "azines":



(III)

with R = R′ and X = X′ they are symmetrical, or simply azines of the carbonyl compounds (aldazines, ketazines); and when R ≠ R′ and X ≠ X′ we have mixed azines. Thus in naming the hydrazone we first state the name of the carbonyl compound and then name the substituents attached to the nitrogen atom together with the word "hydrazone", e.g. ethyl isopropyl ketone methylphenylhydrazone‡



(IV)

In present-day chemical literature there is an increasing tendency to name hydrazones more briefly and independently—aromatic arylhydrazones (II: R = R′ = Ar; X, Y = H or Ar), aliphatic arylhydrazones (II: R = Alk; R′ = Ar; Y = H or Ar; X = H or Alk), aldhydrazones (R′ = X = Y = H), ketohydrazones (R and X = Ar, Alk, etc.; R′ = Y = H), keto-acylhydrazones (R and X = Ar, Alk, etc.; R′ = Az; Y = H), etc.—although a special nomenclature has not yet been developed.

It is undoubtedly impossible to give in a single paper an exhaustive review of the literature on the structure and the chemistry of hydrazones, and therefore the authors have not pursued this aim. However, the absence of generalisations of the numerous fresh results on the structure of hydrazone molecules has led us to make an attempt at a systematic discussion. Still, individual aspects of the structure and especially the chemistry of certain types of hydrazones have already been considered many times in special reviews[1-18] or incidentally in reviews concerned mainly with other classes of compounds[19-26].

†σ-Halogeno-hydrazones are often termed "halogeno-hydrazides" or "hydrazones of acid halides".

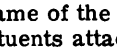
‡A better and more succinct name would be "2-methylpentan-3-one methylphenylhydrazone" (Ed. of Translation).

Henceforward we shall usually give references to papers in which earlier results are often critically discussed. The large number of publications on various aspects of the chemistry of hydrazones makes it necessary to examine separately the structure, the chemical properties, methods of preparation, and the application of hydrazones.

II. GENERAL INFORMATION

Unsubstituted hydrazones, alkylhydrazones and certain arylhydrazones, and azines of simple aliphatic aldehydes and ketones are colourless or very slightly coloured liquids possessing a characteristic odour[4,27,28]. The boiling point rises with increase in the molecular weight of R, X, R′, or Y (II). Alkylhydrazones having a branched carbon chain possess lower boiling points than their analogues having a straight chain. The phenylhydrazones of aromatic and heterocyclic aldehydes and ketones are solids, mostly slightly coloured. Several arylhydrazones, especially the 4-nitro- and 2,4-dinitro-derivatives, have a well-developed crystal structure and sharp melting points, so that they are convenient for identifying carbonyl compounds. Carbazones, semicarbazones and thiosemicarbazones, and sometimes azines are used for this purpose.

Unsubstituted hydrazones, alkylhydrazones and certain arylhydrazones, and azines are bases, forming salts with acids. Increase in the electron-acceptor character of R′ and Y is accompanied by a fall in basic strength, *p*-nitrophenylhydrazones being acidic substances[29]. 2,4-Dinitrophenylhydrazones are weak acids, in which the value of pK_a varies with the nature of R and X [30].

Crystallographic analysis indicates[31-33] that the grouping  in hydrazones possesses a planar structure, although the coplanarity may break down in certain sterically hindered molecules[31]. The length of the C=N bond in hydrazones depends on the nature of the substituents R, R′, X, and Y, varying between 1.27 and 1.35 Å [31-33], which somewhat exceeds the values of 1.24 [34] and 1.255 Å [35] for aliphatic imines, in which the order of this bond is closer to 2.[35] The presence of a lone pair of electrons on the amine nitrogen atom in hydrazones, capable of conjugation with π-electrons, leads to a decrease in the order of the C=N bond and hence an increase in its length. In 1966 Bayer and Häfelinger[35] correlated the stretching frequences ν with the carbon–nitrogen bond length *l* and also order *p* (Fig. 1), which provided a fairly easy method for estimating the variation in length and order of the bond with change in the character of the substituents[14].

Although Bayer and Häfelinger's constructions involved certain assumptions, they yield results which agree quite well with calculations[14] of the bond order by the LCAO-MO method. On the basis of spectroscopic data the latter method of calculation gives estimates of 1.80–1.90 for the order of the C=N bond in hydrazones[9,14].

Less attention has, of course, been paid to the length of the N–N bond in hydrazones, which varies between 1.38 and 1.41 Å [31-33], being rather shorter than in hydrazine (1.46 Å [36]). It is difficult to make any definite statement on the order of the N–N bond, since existing data are insufficient for valid comparisons and conclusions. Calculations by the LCAO-MO method show[9] that this bond order approximates to 1.2 in semicarbazones. The length of the N–C bond (between the amine nitrogen atom

and carbon in a substituent R′) is close[31-33] to the values for a C–N single bond (1.47 Å) [37], but it decreases, of course, when conjugation is present between the hydrazone group and the R′ or Y radical, and in methylglyoxal bisamidinohydrazone, for example, it is 1.35 Å.[32] The C=N–N angle is often close to the theoretical value (120°), although cases of substantial deviations are known. In methylglyoxal bisamidinohydrazone and in ribose *p*-bromophenylhydrazone, for example, this angle is 117° [31,32], but in anisaldehyde azine it is 111.2° [33]. Other angles in the hydrazone group are mostly close to the theoretical values, although the observed deviations differ with different types of hydrazones[31-33].

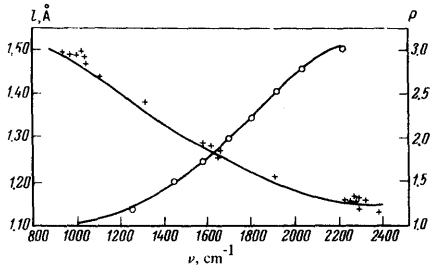


Figure 1. Variation of ν with l and p for the carbon–nitrogen bond[35].

Because of the specific character of the azines (III) coplanarity of the azine group may be destroyed by rotation of the imine fragments about the N–N bond (Fig. 2) [38,39]. Calculations based on dipole moments show that the angle of deflection of the planes of the imine fragments is $\theta = 60-70°$ in most aliphatic and alicyclic aldazines and ketazines. In benzylideneazine this angle $\theta = 20°$, whereas the molecule of the azine of salicylaldehyde is planar as a consequence of intramolecular hydrogen bonding[39].

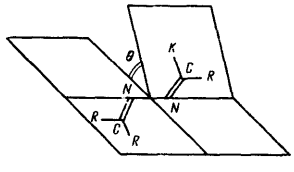


Figure 2. Conformation of azine grouping[39].

It is not possible to estimate the energies of the bonds in the hydrazone group, or to examine the effect of the structure of the molecule on them, since the literature does not contain the necessary data on the group as a whole, while available values of bond energies for the fragments are quite contradictory. The energy of the C=N bond has been given as 94, 132, and 139.5 kcal mole^{-1} by Pauling, Palmer, and Syrkin respectively (see bibliography[34]). The energy of the N–N bond depends greatly on the nature of the radicals attached to the nitrogen atoms, and varies from 57 kcal mole^{-1} in hydrazine to 22 kcal mole^{-1} in hydrazobenzene[40], but has not been determined in hydrazones. This evidently applies also to the energy of the C–N bond in the hydrazone group; the values found for amines lie in the ranges 70–80 and 80–90 kcal mole^{-1} in aliphatic and aromatic amines respectively[40]. Even from these data it can be concluded that the N–N bond is the weakest in the hydrazone group. The energy of internal rotation about the $=N-N\diagup$ bond in the dialkylhydrazones of cyclic ketones appears from the nuclear magnetic resonance spectra to be ~11 kcal mole^{-1} [41].

The group moment has not been determined for hydrazones, values for the individual bonds being used in the additive vectorial calculation of dipole moments[9,14,39,42,43]. The difference in electronegativity between carbon and nitrogen atoms causes polarisation of the C=N and N–C bonds in the direction of the more electronegative nitrogen atom. Values of μ for the C=N bond in the earlier papers—0.9, 2.40, 2.27, 2.5 D—are extremely contradictory[42,43]. From the dipole moments of aliphatic aldimines Everard and Sutton found that $\mu_{C=N} = 1.4-1.5$ D.[44] Kitaev and his coworkers[43] used the experimental dipole moments of various azomethines to obtain a mean value of 1.5 D. A monograph[45] gives the values $\mu_{C=N} = 1.4$ D, $\mu_{C-N} = 0.45$ D, and $\mu_{H-N} = 1.31$ D.

It is also fairly difficult to reach any conclusion on the group refraction, and calculations are based on values of R for the component atoms of the hydrazone group or on the bond refractions $R_D = 3.67$, 1.57, 1.99, and 1.76 for the C=N, C–N, N–N, and N–H bonds respectively[46]. Different authors give values of 8.205, 8.45, and 8.277 [4,46,47] for R_D of the group =N–N= in aliphatic ketazines. Kost and Grandberg[47,48] give such values as

$$=N-N\diagup_{(H)} \quad R_D = 5.871, \quad =N-N\diagup_{(Alk)} \quad R_D = 6.245.$$

for the hydrazone group in pyrazolines, which can be regarded as cyclic hydrazones.

Considerably more work has been done on the infrared spectra of hydrazones. The hydrazone group does not possess a characteristic absorption band, observations usually being based on that of the C=N bond, and with the monosubstituted compounds also on the N–H bond. Depending on the structure of the surrounding radicals, absorption of moderate intensity by C=N lies in the range 1570–1680 cm^{-1} [9,14,27,28,35,39,49-75] (see Table 1), and the N–H stretching band in unsubstituted and monosubstituted hydrazones is located in the range 3150–3400 cm^{-1} [9,43,53,59,69,72,76-78].

In the region of 1600 cm^{-1} arylhydrazones show superimposition of the absorption frequency due to the azomethine group on that due to the aromatic ring[14,28,53,55,59]. If steric conditions in the hydrazone molecule do not prevent $p-\pi$ conjugation, the frequency of the C=N bond shifts to longer wavelengths[14,28,39,58,61,62,69,70,73]. In alkylhydrazones the structure of the alkyl radicals has little effect on the C=N frequency, whereas the structure of the radicals in the carbonyl component has a substantial effect[69]. The C–N absorption band in hydrazones lies in its usual range, and is considered only in a complete interpretation of the spectrum[59,72]. In this connection the band in the range 1525–1550 cm^{-1}, which sometimes produces a different interpretation[54], has recently been assigned to N–H deformation vibrations alone or together with C–N vibrations[51,68,72].

Table 1.

No.	Type of hydrazone	Infrared $\nu_{C=N}$, cm^{-1}	Refs.	Raman $\nu_{C=N}$, cm^{-1}	Refs.	Ultraviolet λ, nm	Refs.
1	Unsubstituted hydrazones	1650	9,51	1645—1650	14,39,79,80	210—230,265—340	87,93
2	Alkylhydrazones	1650—1635	55,69	1640	80	230—245,270—350	55,87,93,94
3	Dialkylhydrazones	1570—1590 1590—1640	52,56 52,55,74	1650	79	210—250,260—320	55,87,93,94
4	Aliphatic aldazines and ketazines	1635—1665	14,39,49,51	1610—1630	14,39,79	205—210,210—215	84
5	Aromatic aldazines and ketazines	1610—1630	14,39,49,51,64	—	—	300—305,310—315	84
6	Arylhydrazones of aldehydes	1600—1610	14,53,59	1620—1630	14,80	250—275	28,57
7	Arylhydrazones of ketones	1635—1645	14,50,59,73	1630—1640	14,80	240—260,325—370	85
8	2,4-Dinitrophenylhydrazones	—	—	—	—	360—400	85,86,88,90
9	Alkylarylhydrazones	1610—1645	57,59	1635—1645	—	250—275	57
10	Acylhydrazones	1610—1630	63,72	—	14,80	225—230,320—325	76,92
11	Semicarbazones	1610—1670	14,51,58,60—62,72	1610—1660	9,14,81	220—250,260—330	87,89,91,96
12	Thiosemicarbazones	1610—1660	14,51,58	1610—1660	9,14,81	230—280,300—360	89,96,98
13	Bis- and tris-phenylhydrazones of vicinal di- and tri-carbonyl compounds	1630—1645	68	—	—	360—400*	88
14	*o*-Chloroarylhydrazones	1595—1670	65	—	—	235—240,350—375	65
15	*o*-Nitro(and sulpho)arylhydrazones	1590—1680	66,67	—	—	240—250,340—400	66,67,97
16	Formazans	1590—1610	75	—	—	220—290,280—450, 420—500	2,75

* Bis-2,4-dinitrophenylhydrazones of α-dicarbonyl compounds.

Considerably less work has been done on the Raman spectra than on the infrared spectra of hydrazones. Lines attributable to C=N absorption occur in the range 1610–1660 cm^{-1} in the Raman spectra (see Table 1) [14,39,53,79-83]. These spectra enable absorption due to C=N in arylhydrazones to be distinguished from that due to the aryl ring system, which, as already mentioned, is not possible from the infrared spectra.

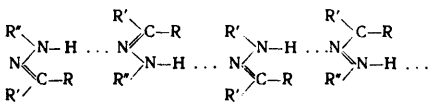
In the near ultraviolet hydrazones usually have two absorption bands, but sometimes a third may appear, or even only one band (Table 1) [14,28,49,57,65-67,76,84-98].

The presence of unsaturated groups capable of conjugation—in any radical of the hydrazone structure—results in a bathochromic shift in the absorption maximum (Table 1). The introduction of electron-acceptor substituents into the phenyl ring of the hydrazones of aromatic aldehydes and ketones has an analogous effect, which is most clearly developed with *para*-substitution [49,84,87,89,93-96,99]. Only a slight bathochromic displacement of λ_{max} but a very considerable increase in intensity of absorption occur [88] on passing from the mono- to the bis-2,4-dinitrophenylhydrazones of α-dicarbonyl compounds.

Nuclear magnetic resonance has been applied many times and extremely usefully to study of the structure of hydrazones [28,100-102]. Without discussing in detail the proton magnetic resonance spectra of hydrazones, we note merely that the chemical shift due to the aldehyde proton in the hydrazones of aldehydes (I: X = H) is $\tau = 3.2-3.8$ ppm, and that due to the NH proton in monosubstituted and unsubstituted hydrazones is considerably more affected by surrounding groups [38,100-102].

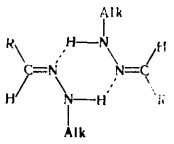
III. HYDROGEN BONDING

The presence of C=N and N–H groups in monosubstituted and unsubstituted hydrazones makes intermolecular hydrogen bonding possible. Several alkylhydrazones and phenylhydrazones are in fact associated in the liquid state, and in solutions molecules of the solvent are involved in the association [69,99-108]:

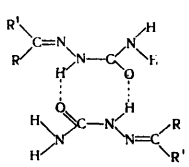


where R, R′ = Alk and R″ = Alk, C_6H_5. The stability of the resulting complexes depends both on the structure of the hydrazone and on the nature of the solvent. With phenylhydrazones, for example, the stability diminishes in the sequence of solvents—dimethyl sulphoxide > acetone > pyridine > nitrobenzene > chlorobenzene > isodurene [102].

It has been suggested that dimers are formed by intermolecular hydrogen bonding of the *syn*-form



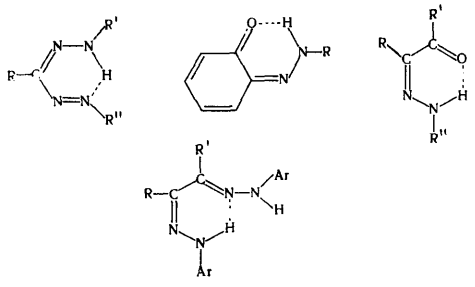
in solutions of the alkylhydrazones of aliphatic aldehydes [69]. The formation of dimeric together with linear association complexes is observed in solutions of semicarbazones



the former being the more stable [9].

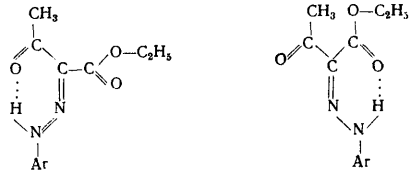
A strong intramolecular hydrogen bond is present in formazans [1,2,109], osazones [110], and monoarylhydrazones of *o*-quinones, semicarbazones, thiosemicarbazones,

alkylhydrazones, and arylhydrazones of keto-acids[9,14,50, 53,54,99], and in bisphenylhydrazones of α-dicarbonyl compounds[111]



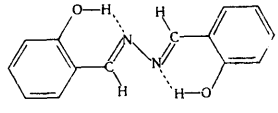
where the hydrogen bond results in formation of a stable chelate system.

Arylhydrazones of ethyl αβ-dioxobutyrate are present in solutions as a mixture of roughly equal quantities of isomers containing an intramolecular hydrogen bond formed by the hydrazone proton with a keto-group or the ester grouping[99]: i.e. both possible alternatives



are realised in this case.

A hydrogen bond is formed in hydrazones also when a hydroxy-group is present and appropriately located in the carbonyl or hydrazine portion. Thus in the azines of *o*-hydroxybenzaldehydes a hydrogen bond is responsible for their luminescence[112], and also for the coplanarity of the atoms in the azine group[39]

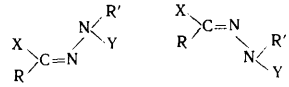


IV. ISOMERISM OF HYDRAZONES

Hydrazones include examples of both stereoisomerism and structural isomerism, while in some cases tautomeric equilibrium of two or even three forms is observed. Isomerism of the skeleton and metamerism are due to the possibility of preparing hydrazones from both isomeric hydrazines and isomeric carbonyl compounds—to the possibility of wide variation in R, R′, X, and Y in (II)—and is of no special interest. Cases of stereoisomerism (geometrical and optical) and position isomerism in the hydrazone group (conversion into azo-compounds or into alkenylhydrazines), with the tautomeric equilibrium of the isomeric forms involved in these changes, are considerably more interesting. Quite often isomeric transitions and tautomeric equilibrium of the various forms of hydrazones are combined, which makes it more difficult to solve the problem.

V. GEOMETRICAL ISOMERISM

The geometrical isomerism of the hydrazones of aldehydes and unsymmetrical ketones is a particular case of isomerism in the $\rangle C{=}N-Z$ system. By analogy with oximes, the isomer in which the substituted or unsubstituted amino-group and the hydrogen atom in the aldehyde derivatives (X = H) or the smaller radical in the ketone derivatives (X < R) are in the *cis*-position with respect to the C=N bond is usually termed the *syn*-isomer (V), and that in which they are in the *trans*-position the *anti*-isomer (VI)[11,100]:



(V) *syn*-isomer (VI) *anti*-isomer

When R and X are complicated it is necessary, in order to avoid confusion, to indicate which isomer is regarded as *syn* and which as *anti*: this is sometimes effected by stating after the type of isomer the group which occupies the given position relative to the amino-group, e.g. the *syn*-phenyl isomer of acetophenone 2,4-dinitrophenylhydrazone[113].

Geometrical isomerism was postulated in hydrazones by analogy with oximes, and very many papers have been devoted to this question. However, some of the earlier papers must be treated with caution, and the designations α- and β-forms must be accepted for the compound having the lower and higher melting point respectively, since only in a few cases were geometrical isomers actually isolated[11,13].

The matter is complicated by the fact that many hydrazones, especially those containing a nitroaryl substituent, tend to exhibit polymorphism. Thus acetaldehyde *syn*-2,4-dinitrophenylhydrazone exists in four polymorphic modifications, having melting points of 145–146°, 157–158°, 160–161°, and 165–166°C respectively[13,101]. Polymorphism may be the reason for the appearance of different colours in a hydrazone, even if the two modifications have the same melting point and identical ultraviolet and infrared spectra. Only by means of X-ray examination has it been possible to establish that 1-phenylpropane-1,2-dione bis-2,4-dinitrophenylhydrazone, which crystallises from acetic acid as orange-yellow and from nitrobenzene as red needles, is present in different crystalline modifications[114].

Hydrazones are characterised also by phototropy. On standing in sunlight benzaldehyde phenylhydrazone acquires an orange-red colour, which disappears when kept in the dark for a long time. The loss of colour is slower than its appearance[11].

In addition, arylhydrazones are able to form mesomorphic phases. Transition of the phenylhydrazones of *p*-nonyloxy- and *p*-decyloxy-benzaldehydes into the nematic state takes place at 94–95° and at 91–92°C respectively, the transition from the nematic into the liquid state occurring at 97–98° and 93–94°C [115].

Many problems in the stereochemistry of hydrazones have been solved during recent years by the application of the most modern physical methods. The nuclear magnetic resonance spectra as well as the infrared and ultraviolet spectra are widely used for these purposes, but a combination of several methods has proved the most fruitful. The existence of geometrical isomers has been recorded in unsubstituted hydrazones[106], methyl-[27,107], dimethyl-[108,116],

methylphenyl-[105,117], aryl-[11,77,102,113], and 2,4-dinitrophenyl-hydrazones[13,100,101,113,118,119], and in thiosemicarbazones[13,77,100,119-121], azines[122-126], acylhydrazones[127,128], formazans[1,2,109], α-nitroarylhydrazones[129], 2,4-dinitrophenylhydrazones of quinones[130], and arylhydrazones of α-dicarbonyl compounds[88,131].

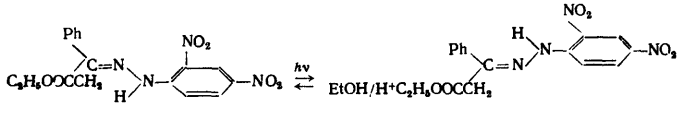
The *syn*-configuration of hydrazones is the more stable. If neither substituent attached to the amine nitrogen atom (R′ or Y) is a hydrogen atom, hydrazones of aldehydes (X = H) are formed, and exist solely in the *syn*-configuration not only in the solid but also in the liquid state and in solutions. A bulky substituent (R′ or Y) produces the same effect even by itself, but equilibrium between *syn*- and *anti*-forms can then be observed in solutions. Thus the dimethyl-, methylphenyl-, and 2,4-dinitrophenylhydrazones and the semicarbazones of aldehydes exist in the *syn*-configuration[101,105,108,119,120]. Equilibrium is slowly established in solutions of 2,4-dinitrophenylhydrazones and semicarbazones, but the process can be accelerated by adding a catalyst, e.g. sulphuric acid. The relative proportions of *syn*- and *anti*-forms depends on the nature of the solvent, as indicated by the following values from the nuclear magnetic resonance spectra of acetaldehyde 2,4-dinitrophenylhydrazone[101]:

in dibromomethane and nitrobenzene	2 : 1
in pyridine, acetone, and dimethylformamide	4 : 1
in tetramethylurea and dimethyl sulphoxide	7 : 1

The rate of isomerisation is fairly low, only a small quantity of the *anti*-isomer being formed during recrystallisation of the *syn*-isomer. This enables the *anti*-form to be isolated or at least enriched by fractional crystallisation of the equilibrium mixture. Acetaldehyde 2,4-dinitrophenylhydrazone containing 85% of the *anti*-isomer has been prepared[101] by crystallising the equilibrium mixture containing only 33%. The size of the radicals in the carbonyl component (R, X) also affects the position of equilibrium between the isomeric forms: when one of them becomes larger, the percentage of the *syn*-form increases. Branching of the carbon chain at the α-position relative to the hydrazone group displaces the equilibrium towards the *syn*-form more than does lengthening the straight chain by the same number of carbon atoms. The various hydrazones of isobutyl [?t-butyl] methyl ketone are present in the *syn*-form in any state[100,103,105-108] (see Table 2).

However, not all hydrazones form equilibrium mixtures in solution. Acetophenone phenylhydrazone is obtained in the *syn*-form, which is preserved in solution[102]. A hydrogen bond usually stabilises the *anti*-form[11].

One isomer can be converted into the other in various ways. The stable *syn*-2,4-dinitrophenylhydrazone of ethyl benzoylacetate (VII) obtained from the reaction passes, on prolonged illumination in benzene solution, into the labile *anti*-form (VIII), which can be changed back into the *syn*-form by heating an alcoholic solution in the presence of catalytic quantities of hydrochloric acid[132]:



(VII) *syn*-isomer — (VIII) *anti*-isomer

m.p. 161.5–163.5°C — m.p. 121–121.5°C

A similar situation is found with ω-bromoacetophenone 2,4-dinitrophenylhydrazone[133].

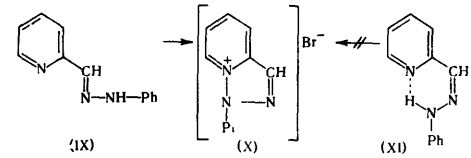
Isomerisation of the geometrical forms of hydrazones can be caused not only by hydrochloric acid and irradiation but also by iodine, sulphur dioxide, hydrogen sulphide, yellow mercuric oxide, caustic potash, sodium ethoxide, sulphur, acetic and other acids, heating to the melting point, etc.[11,113]. Interconversion of the geometrical forms is observed also during the chemical reactions of bromination[116], acylation[134], saponification, and esterification[46]. The explanation of isomerisation during a reaction is that in the *anti*-isomer, for example, the mobility of the methine hydrogen atom (X = H) exceeds that in the *syn*-isomer, perhaps for steric reasons[116].

Table 2. Content (%) of *syn*-form of hydrazone of type (II) (liquid or in solution)[100-103,105-108].

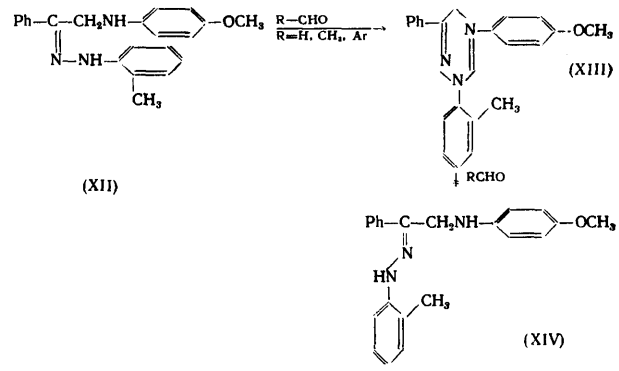
R	X	R′=H Y=H	R′=CH₃ Y=H	R′=CH₃ Y=CH₃	R′=Ph Y=H	R′=Ph Y=CH₃	R′=2,4-(NO₂)₂C₆H₃ Y=H	R′=C(=O)NH₂ Y=H
H	CH_3	51	73	100	65[a]	100	100[b], 66[a]	—
H	C_2H_5	64	83	100	89	100	100[b], 78[a]	—
CH_3	C_2H_5	78	83	82	80	86	80[a]	75[a]
CH_3	$CH(CH_3)_2$	93	96	93	94	94	90[a]	90[a]
CH_3	$C(CH_3)_3$	100	100	—	100	100	100[a]	100[a]
CH_3	Ph	—	—	—	100[a]	100[a]	63[a]	—

(*a*) In solution in dibromomethane or in chloroform.
(*b*) In the initial stages (immediately after dissolution).

Although interconversion of the geometrical forms can be observed, it is not yet possible to establish chemically the structure of each form of a hydrazone. Pyridine-2-aldehyde *syn*-phenylhydrazone (IX) is converted by the action of *N*-bromosuccinimide into 1-phenyl-1,2-diaza-8-azoniaindene bromide (X), whereas the *anti*-isomer (XI), in which the atoms are more favourably arranged for ring closure, does not yield (X):

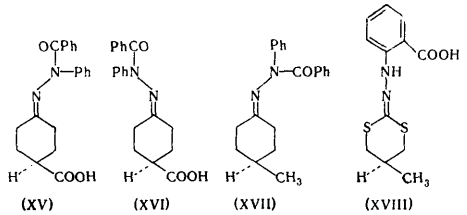


Nevertheless, ω-*p*-methoxyanilinoacetophenone *syn*-*o*-tolylhydrazone (XII) reacts with aldehydes to form triazine derivatives (XIII), whereas the *anti*-isomer (XIV) does not undergo this reaction[135]:



Pearson et al.[136] suggested that geometrical isomers of hydrazones could be identified by their rearrangement into amides, but unfortunately this yields a mixture of amides, which makes the problem more difficult to solve. Khromov-Borisov[113] suggested the genetic relation with pyrazolone as a criterion for establishing the stereochemical structure of a hydrazone. In this case the corresponding pyrazolone must be hydrolysed, decarboxylated, or subjected to other reactions, which greatly limits the range of application, and furthermore introduces the possibility of isomerisation during such operations. The *anti*-structure was attributed[137] to one of the forms of the phenylhydrazone and the bisphenylhydrazone of benzil on the basis of their ability to form a complex with tin(IV) chloride.

The hydrazones (XV), (XVII), and (XVIII) could be resolved into enantiomers[138], their optical activity being explained by molecular asymmetry, as is shown in the case of (XV) and (XVI):

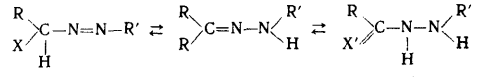


(XV) (XVI) (XVII) (XVIII)

The hypothesis of these workers[138] (repeated by others[11,39]), that the third valency of the imine nitrogen atom in compounds (XV)–(XVIII) does not lie in the C=N plane, is inconsistent with the results of modern X-ray[31-33] and conformational analysis[39,120] of hydrazones. This is a case of atropoisomerism, resulting from the absence of a plane of symmetry in the isomeric forms.

VI. ISOMERISM OF THE TYPE HYDRAZONE ⇌ AZO-COMPOUND

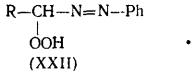
The molecular structure of monosubstituted hydrazones (II: Y = H) has been most often discussed in the literature. It is accepted that three forms—hydrazone (XX), azo-compound (XIX), and alkenylhydrazine (XXI)—are possible:



(XIX) (XX) (XXI)

It is well known that hydrazones and the isomeric azo-compounds are able to exist independently, and also that azoalkanes and arylazoalkanes can be converted into hydrazones[9,11,13,14,42,43,56-58,62,63,81,98,99,102,103,131]. Thus many examples are known of the conversion into hydrazones of azo-compounds formed by coupling arenediazonium salts with aliphatic compounds[20], and also in the Japp–Klingemann reaction[21,140,141]. Diarylazo-compounds, formed by coupling monosubstituted hydrazones with arenediazonium salts, change into formazans either spontaneously or under the influence of alkalis[142,143]. It has been reported that azoalkanes, arylazoalkanes, arylazosteroids, and other azo-compounds are converted into hydrazones under the influence of acids[141,144-146], alkalis[144,147,148], and free radicals[144]. Dondoni and his coworkers have shown[147] that the catalytic activity of tertiary amines in converting azo-compounds into hydrazones in benzene solution is proportional to their pK_a-value in water. Furthermore, the catalytic activity of the amines depends on the type of solvent, diminishing in the sequence—anisole > chlorobenzene > dioxan > benzene—in the case of triethylamine. Several workers[145,147] have observed also the spontaneous transformation of azo-compounds into hydrazones: thus on prolonged storage methylazobenzene rearranges into benzaldehyde methylhydrazone[145].

Considerably greater divergence of views among investigators has been found on the question of the isomerisation of hydrazones into azo-compounds (see Refs. 3, 11, 13, 14, 57, 144, 145, and 149–157 and references in these papers). Baly and Tuck's communication[154] on the possibility of the conversion of phenylhydrazones into phenylazoalkanes by the ultraviolet irradiation of their solutions was criticised by Stobbe and Nowak[155]. Soon after this Busch and Dietz[156] isolated, instead of the expected azo-tautomer, a product of the autoxidation of the phenylhydrazone, which has since been found[149-153,158] to be an azo-hydroperoxide



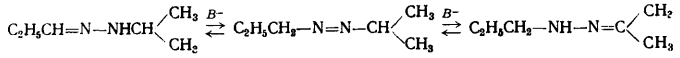
(XXII)

The azo-hydroperoxide (XXII) differs from the azo-tautomer (XIX: X = H) in the presence of the HOO group attached to the carbonyl carbon, which, however, does not entail any great changes in the ultraviolet spectra of these compounds, studied for evidence of isomeric transitions. Therefore Grammaticakis[159] in 1948 and later O'Connor[57], both of whom used ultraviolet spectroscopy to study the changes undergone by arylhydrazones in solutions, reached the erroneous conclusion that the isomerisation hydrazone → azo-compound took place in solution. In fact, however, several investigations have shown[149-153,158] that autoxidation with formation of an azo-hydroperoxide (XXII) occurs under these conditions. O'Connor and Henderson's statement[152] that oxygen may not only take part in forming the hydroperoxide (XXII) but also catalyse the transition (XX) → (XIX) evidently requires verification, since repeated attempts to use this method to convert cyclohexanone phenylhydrazone into phenylazocyclohexane have been unsuccessful[13]. However, the possibility of the isomerisation of hydrazones into azo-compounds is supported by the formation of phenylazomethane when the product of the reaction between phenylhydrazine and formaldehyde is distilled in steam[154]. The use of alkali as catalyst for this reaction enables the azo-compound to be obtained as the main product[160].

Final confirmation of the isomerisation of hydrazones into azo-compounds has been given in a series of publications by Ioffe and his coworkers[28,145,161-163]. In 1965 they accomplished the isomerisation of alkylhydrazones of aliphatic aldehydes and ketones in the presence of an alkaline catalyst, the more volatile azo-compound being distilled off at the same time[161]. They later reported a series of such conversions[145,162], of alkylhydrazones of aromatic aldehydes[163] among others, and also the isomerisation of formaldehyde phenylhydrazone into phenylazomethane[28]. The rate of isomerisation of alkylhydrazones of aromatic carbonyl compounds is lower than that of aliphatic alkylhydrazones, evidently because the conjugated chain is considerably shorter in the latter than the chain of $\pi-\pi-p$ conjugation in the former molecules[163]. The possibility of the isomerisation (XX) → (XIX) is indicated also by the formation of diarylazo-compounds when

arenediazonium salts are coupled with monosubstituted hydrazones[142,143]. Thus evidence for the isomerisation (XX) → (XIX) in the hydrazones is as indisputable as that for the isomerisation (XIX) → (XX). Only the phenylhydrazones of aliphatic carbonyl compounds have not yet proved capable of isomerisation, because of their tendency to Fischer cyclisation and nitrile cleavage[28], but even these difficulties can evidently be overcome by choosing appropriate conditions.

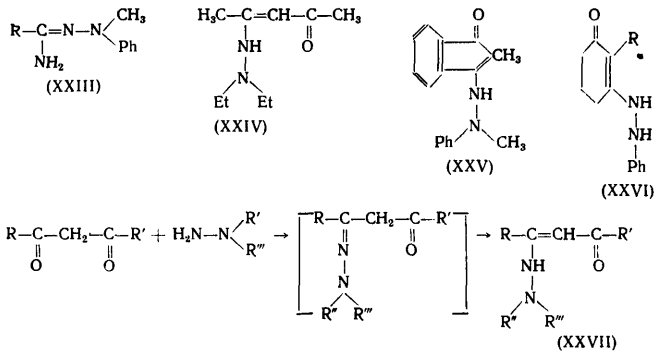
The occurrence of the isomeric transformations (XIX) → (XX) and (XX) → (XIX) indicated the possibility of the tautomeric equilibrium (XIX) ⇌ (XX). Numerous investigations have established that arylhydrazones, alkylhydrazones, semicarbazones, and thiosemicarbazones of aliphatic and aromatic aldehydes and ketones exist in the hydrazone form[9,11,13,14,18-20,38,42,56,58,81-84,102,144,145,149-151,158] and that the above tautomeric equilibrium is not established in the absence of a catalyst[157,162,163]. In 1967 Simon and Moldenhauer[157] noticed, while investigating hydrogen exchange in preparations labelled with tritium, that the equilibrium (XIX) ⇌ (XX) can be observed with phenylhydrazones and semicarbazones if alkali is added to their alcoholic solutions. From kinetic measurements the content of the azo-tautomer in an alkaline alcoholic solution of benzaldehyde phenylhydrazone has been estimated[107] as ~10^{-9}%. Ioffe[162,163] has shown that the content of the azo-form present in the equilibrium mixture in the presence of alkali is considerably higher with the alkylhydrazones of aliphatic and aromatic carbonyl compounds. The most probable explanation of this difference is the breakdown, on the isomerisation of benzaldehyde phenylhydrazone, in the length of the $\pi-\pi-p-\pi$ conjugation chain, which is absent in aliphatic alkylhydrazones[162]. The position of tautomeric equilibrium in alkaline solutions of alkylhydrazones depends on the structure of the substituents in both hydrazine and carbonyl portions of the hydrazone. The content of the azo-tautomer is greater in the alkylhydrazones of aldehydes than in those of ketones. Branching of the alkyl group of the hydrazine shifts the equilibrium towards formation of (XIX) [162]. Unsymmetrical azo-compounds can be obtained from various isomeric hydrazones, and three forms may then be present in equilibrium [157], for example[162]



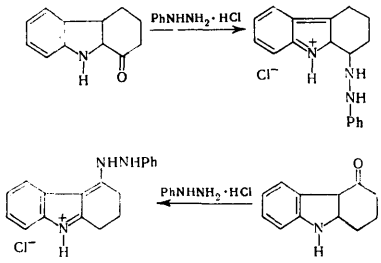
VII. ISOMERISM OF THE TYPE HYDRAZONE ⇌ ALKENYLHYDRAZINE

The concept of the hydrazone ⇌ alkenylhydrazine type of isomerism has considerable value for the interpretation of the mechanisms of certain reactions undergone by hydrazones, primarily the Fischer–Arbuzov reaction, and this isomerism has long been the subject of many investigations, very often being studied at the same time as the hydrazone ⇌ azo-compound isomerism. At an early stage Freer[164] drew attention to the ready oxidisability of some phenylhydrazones and the relative stability of others, and suggested that the former had an alkenylhydrazine structure; in confirmation he was able to establish differences in the chemical behaviour of the two groups of phenylhydrazones on reaction with oxygen, benzoyl chloride, etc. Subsequently the use of various chemical and physicochemical methods has shown that arylhydrazones, alkylhydrazones, disubstituted hydrazones, semicarbazones, thiosemicarbazones[9,14,56,58,102,103,157], and ω-methyl-ω-phenylamidrazones (XXIII) [165], as noted above, are present in the hydrazone form both in the solid state and in solutions. Quantum-chemical calculations have shown[96] that, for example, the semicarbazone form is energetically more advantageous than the alkenylhydrazine form by 15 kcal mole^{-1}. The hypothetical existence of the alkenylhydrazine form in solutions of arylhydrazones of aliphatic aldehydes and ketones, based on polarographic data[166], could not subsequently be confirmed[13,14].

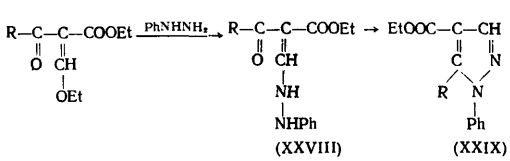
The alkenylhydrazine structure has been established for dialkylhydrazones (XXIV) [167], methylphenylhydrazones (XXV) [168], and monoarylhydrazones (XXVI) [11,169,170] of β-dicarbonyl compounds, derivatives of pentane-2,4-dione, cyclohexane-1,3-dione, indane-1,3-dione, 1-phenylpropane-1,3-dione, etc. The molten phenylhydrazone of ethyl acetoacetate is also regarded as having the alkenylhydrazine structure (XXVII) [170].

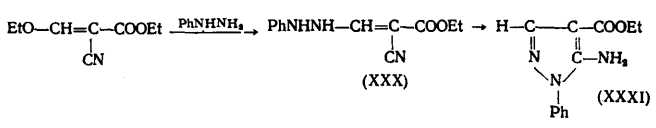


The reaction of 1,2,3,4-tetrahydro-1(and 4)-oxocarbazoles with phenylhydrazine hydrochloride yields products, to which the alkenylhydrazine structure has been assigned on the basis of their infrared spectra[171]:

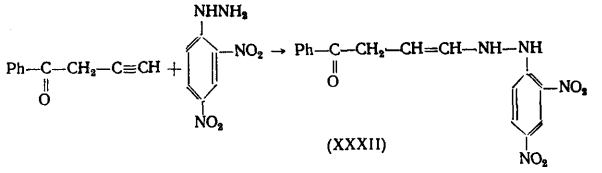


The alkenylhydrazine structure is possessed by the hydrazones of 5-formylbarbituric acids[172] and by compounds (XXVIII) and (XXX), which are prepared as follows[173-175]:



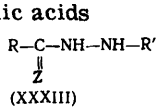


Alkenylhydrazines of type (XXVII) can sometimes be formed by the reaction of acetylene derivatives with arylhydrazines[176]:



(XXXII)

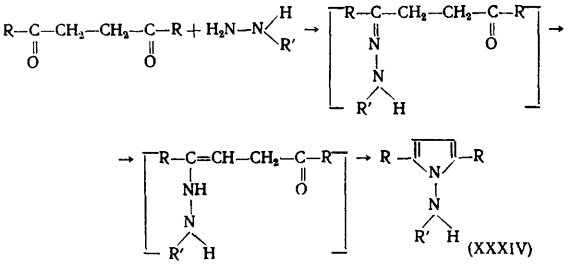
Unsubstituted and β-substituted hydrazides and thiohydrazides of carboxylic acids



(XXXIII)

(where Z = O, S and R′ = H, Alk, Ar, Az) represent a kind of alkenylhydrazine (cf. II, XX, XXI) in which the α-carbon atom has been replaced by a heteroatom.

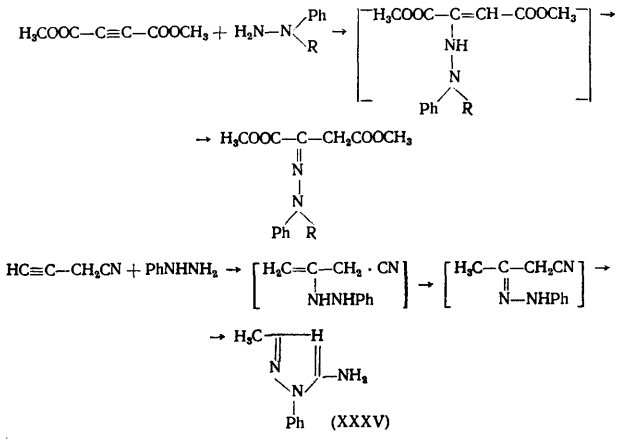
The possibility of the isomerisation hydrazone → alkenylhydrazine (XX → XXI) is suggested by the numerous examples of the formation of 1-aminopyrroles when γ-dicarbonyl compounds react with hydrazine hydrate and with the hydrazides of formic, acetic, benzoic, isonicotinic, phthalic, and other acids[11,177,178]:



(XXXIV)

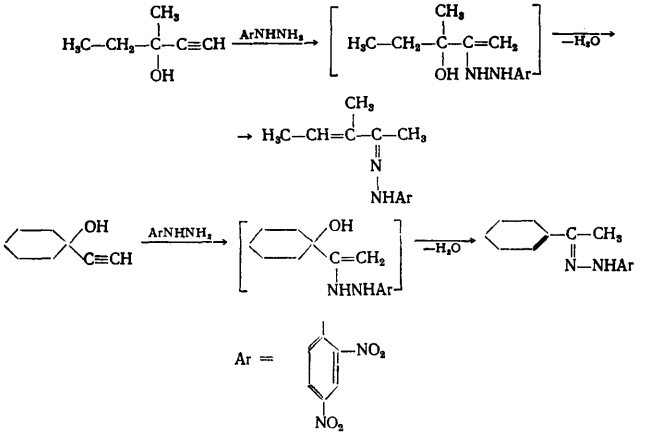
It is supposed that formation of the compounds (XXIV)–(XXVII) also passes through a hydrazone stage. The concept of the isomerisation (XX) → (XXI) is widely used in explaining the mechanism of the Fischer–Arbuzov preparation of indoles from arylhydrazones[5-7,15]. Similar isomerisation had been suggested earlier[179] to explain the formation of osazones from α-hydroxycarbonyl compounds and hydrazine derivatives, and has been confirmed by the most recent investigations[180].

Isomerisation of alkenylhydrazines into hydrazones (XXI → XX) can be observed when arylhydrazines react with acetylene derivatives. The alkenylhydrazines can be isolated only in certain cases (e.g. XXXII [176]), the reaction usually yielding arylhydrazones or products of their further conversion[11,181]:



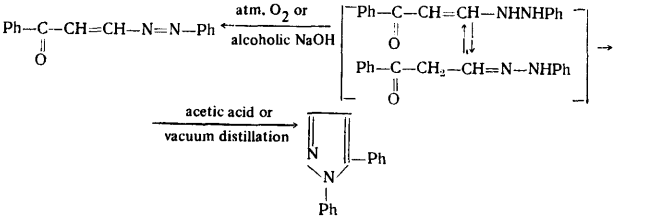
(XXXV)

With derivatives of prop-2-ynol the reaction is accompanied by dehydration[182]:

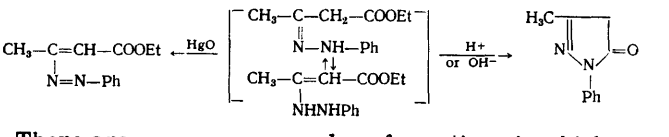


When heated in acetic acid the alkenylhydrazines (XXVIII) and (XXX) are converted into the corresponding pyrazole derivatives (XXIX) and (XXXI), which apparently involves an intermediate stage of isomerisation into the hydrazones [174,175].

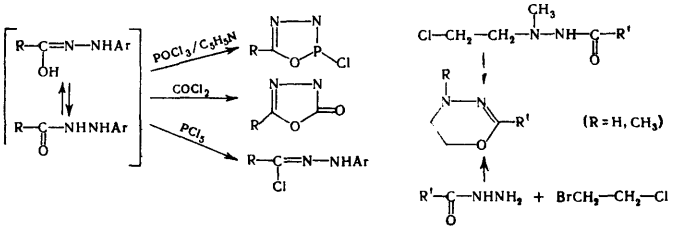
The possibility of the tautomeric equilibrium hydrazone ⇌ alkenylhydrazine (XX ⇌ XXI) is probably suggested by the dual reactivity of the arylhydrazones of β-dicarbonyl compounds and of the hydrazides, thiohydrazides, and hydrazones of certain heterocyclic compounds, e.g. pyrimidine derivatives, etc.[11,19,22]. Aryl hydrazones of β-dicarbonyl compounds (XXIV–XXVII): R″ = H) are converted by oxidants into azoalkenes, but when distilled or heated in acetic acid they are cyclised into pyrazole derivatives[11,169]:



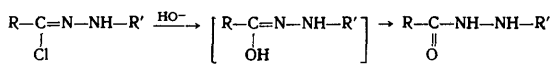
Similar behaviour is shown by the unstable phenylhydrazone of ethyl acetoacetate, obtained in ethereal solution from the ester and phenylhydrazine. When heated with mercury(II) oxide in alcohol it forms ethyl phenylazocrotonate, but in acid and alkaline media it cyclises into 3-methyl-1-phenylpyrazolone[183]:



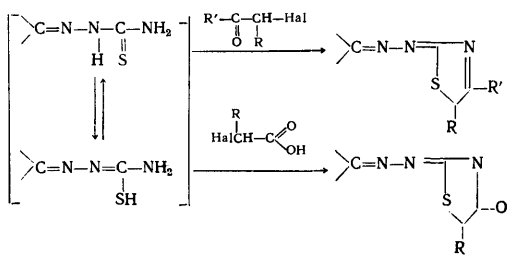
There are numerous examples of reactions in which hydrazides, thiohydrazides, and diacylhydrazines behave as compounds having an α-hydroxy-hydrazone structure[11,19,22,184,185]:



And conversely, the hydrolysis of α-halogeno-hydrazones results in separation of a hydrazide[11,186], instead of the α-hydroxy-hydrazone, which is also an example of the isomerisation (XX) → (XXI):

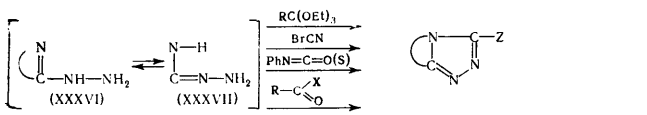


The widely known[187-194] condensations of thiosemicarbazides and thiosemicarbazones with α-halogeno-carbonyl compounds and α-halogeno-carboxylic acids to form thiazoline derivatives are based on their capacity for thione ⇌ thiol tautomerism[98], which in this case is a further variety of the hydrazone ⇌ alkenylhydrazine tautomerism:

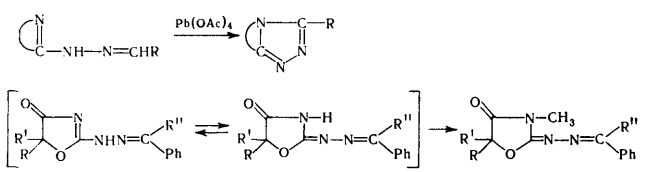


An analogous reaction is characteristic of selenocarbazide and selenocarbazones[195].

Examples of dual reactivity are widely known also with heterocyclic hydrazines containing the grouping (XXXVI) (cyclic amidrazones). They undergo not only reactions characteristic of the hydrazine structure but also reactions characteristic of the hydrazone form (XXXVII)[11,17,196]. Tautomerism of the given type is usually assumed[197]:



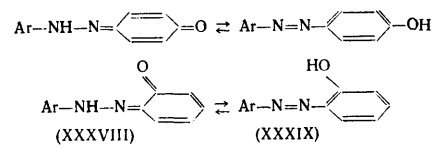
(X = Hal, OAlk, OH, OCOR); Z = R, NH_2, Ph, OH, SH)



However, dual reactivity merely suggests the possibility of the transitions (XX) → (XXI) and (XXI) → (XX), but does not prove the establishment of tautomeric equilibrium, although the occurrence of tautomerism is very often deduced from this fact[5-7,11,15,140,198,199]. Although dual reactivity may be a consequence not of tautomerism but of migration of the reactive centre in the system, it is very likely that equilibrium is actually established in several cases. Thus Razumov et al.[200] have recently reported occurrence of the tautomerism (XX) ⇌ (XXI) in the hydrazides of phosphorylated carboxylic acids, and a paper already referred to[157] has reported establishment of the above tautomeric equilibrium in certain semicarbazones in alkaline alcoholic solutions, although it is very greatly displaced towards the hydrazone tautomer. But the above papers still do not permit any final or general conclusions to be drawn, and the question of the occurrence of the hydrazone ⇌ alkenylhydrazine tautomerism has not yet been finally settled.

VIII. OTHER TYPES OF ISOMERISM OF HYDRAZONES

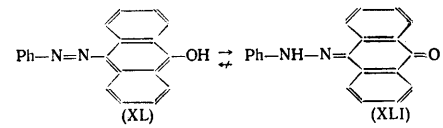
Prototropic isomerism of the quinone arylhydrazone ⇌ hydroxyazobenzene type, which is closely similar to the hydrazone ⇌ azo-compound type, has been known for a long time, widely studied, and discussed repeatedly[11,13,201,202]. Whereas the isomerisation (XX) ⇌ (XIX) involves 1,3-migration of a hydrogen atom, the isomerisation of arylhydrazones of quinones involves 1,7-migration of a proton in derivatives of *p*-benzoquinone and 1,5-migration in those of *o*-benzoquinone. In view of the above and several other peculiarities, this isomerism is usually considered individually, most often in relation to the structure of azo-dyes[202]. These changes were studied considerably earlier and in greater detail than the isomerism (XX) ⇌ (XIX). Detailed investigations have been made of the transitions (XXXVIII) → (XXXIX) and (XXXIX) → (XXXVIII), and also of cases of the tautomerism



(XXXVIII) (XXXIX)

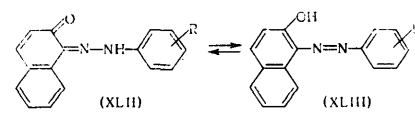
The numerous papers on this problem have been summarised in a review by Ershov and Nikiforov[25].

Whereas benzoquinone derivatives exist in the azo-form even in solution, certain substituted derivatives of naphthaquinone and anthraquinone exhibit a tautomeric equilibrium of the type (XXXVIII) ⇌ (XXXIX) in solution, and 10-phenylazoanthrol (XL) exists only in the hydrazone form (XLI) (see bibliography in Ref. 25):



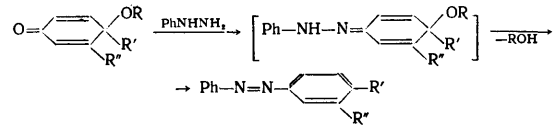
(XL) (XLI)

Substituents in both parts of the molecule have a substantial effect on the position of equilibrium. Accumulation of azo and hydroxyl groups in the quinone ring tends to shift the equilibrium towards the hydrazone form[25,203-205]. The influence of substituents in the phenyl ring of the hydrazine component on the position of the equilibrium (XXXVIII) ⇌ (XXXIX) is illustrated by Table 3[206] for the series 1-R-phenylazo-2-naphthol (solution in deuterated chloroform).



(XLII) (XLIII)

Derivatives of *p*-quinones react comparatively readily with substituted hydrazines, but the resulting hydrazones are converted under the reaction conditions into azobenzenes, with the loss e.g. of an alcohol molecule[207]:



Prototropic isomerism, closely similar to the alkenylhydrazine → hydrazone type of isomerism, was observed by Ioffe and Kochetov with allylhydrazones,

which in the presence of alkalis are converted into mixed azines [208]:

$$AlkCH{=}N{-}NH{-}CH_2{-}CH{=}CH_2 \xrightarrow{HO^-} AlkCH{=}N{-}N{=}CH{-}CH_2{-}CH_3$$

Another type of isomerism, in which the double bond migrates from the nitrogen atom into the aliphatic chain (beyond the α-position), was reported by Abramovitch and Spenser [53], though for cyclic hydrazones:

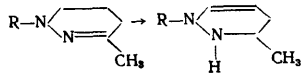
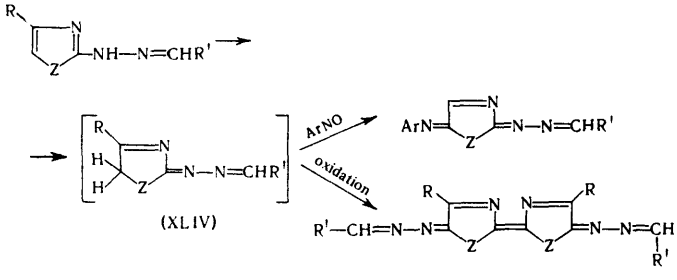


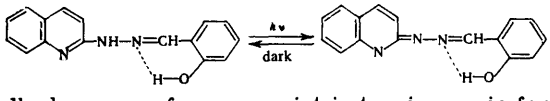
Table 3. Content of hydrazone form in the system (XLII) ⇌ (XLIII) [206].

R	(XLII), %	R	(XLII), %
4-CN	97	H	79
3-CN	91	4-HCl	78
3-Cl	81		
3-OMe	81	4-Me	69
3-Me	80	4-OMe	52

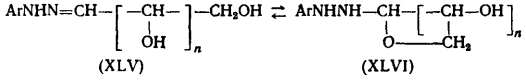
Thiazol-2-ylhydrazones [209] and selenazol-2-ylhydrazones [195] behave in certain reactions probably in the isomeric form (XLIV), which is formed by migration of a hydrogen atom from the hydrazone group to the 5-position in the ring:



Wong and Bruscato [210] invoke analogous migration of a hydrogen atom into a heterocyclic ring to explain the photochromism of quinolylhydrazones, which had previously been explained [24] by hydrazone ⇌ azo-compound isomerisation:

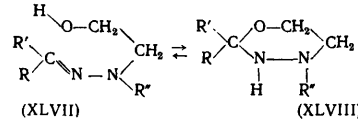


Arylhydrazones of sugars exist in two isomeric forms: in the hydrazone (XLV) the carbohydrate radical has an open chain; the hydrazine (XLVI) contains the carbohydrate residue in a cyclic configuration [31,36,211-214]:



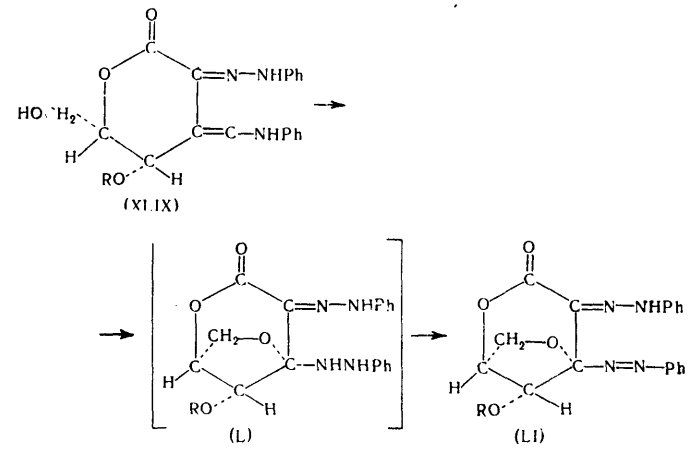
X-Ray examination indicates that ribose *p*-bromophenylhydrazone exists in the crystalline state in the hydrazone form [31], whereas arabinose *p*-bromophenylhydrazone is present in the hydrazine form [36], and many similar examples are known. Open-chain products are formed when (XLVI) is acylated [211]. This suggests that the isomerisation (XLVI) → (XLV) takes place, which is confirmed by a study of the polarographic behaviour of arabinose phenylhydrazone [212], this compound existing in the solid state in the form (XLVI). The tautomeric equilibrium (XLV) ⇌ (XLVI) may be established in solutions of the arylhydrazones of sugars, as is confirmed by spectral data [213,214].

Whereas the tautomerism (XLV) ⇌ (XLVI) is established in the hydrazones of sugars by addition at the C=N bond of a hydroxy-group present in the carbonyl component, Ioffe and Potekhin [215,216], simultaneously with Dorman [217], described a new type of ring–chain tautomerism, involving addition at the C=N bond in the hydrazone of a hydroxy-group present in the hydrazine component:

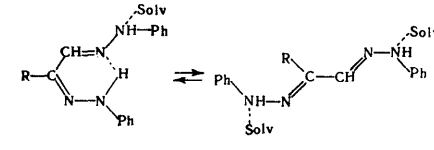


This tautomeric equilibrium is established both in solutions and in the pure substances (liquids) in the case of derivatives of aliphatic carbonyl compounds. Increasing the temperature, the polarity of the solvent, and the molecular weights of the radicals R and R′ and decreasing the molecular weight of R″ tend to increase the content of the hydrazone form (XLVII). Unsubstituted 2-hydroxyethylhydrazones (R″ = H) [215] and also the derivatives (XLVII) of aromatic aldehydes exist in the hydrazone form [216].

The conversion of (XLIX) into (LI) by the action of a periodate, described by El Khadem and El Ashry [218], is easily explained on the assumption that (L) is formed as an intermediate product:

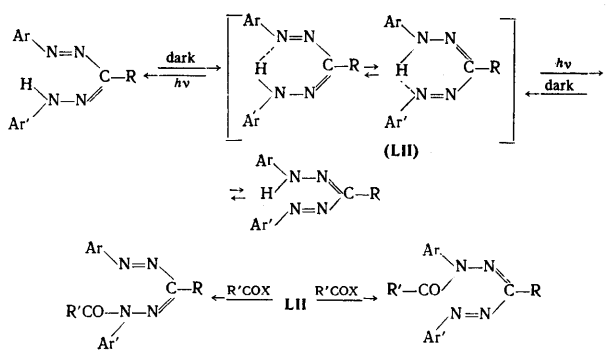


Bisphenylhydrazones of α-dicarbonyl compounds are known to exist in a chelate form [110,111], which is present in solutions in equilibrium with the isomeric open-chain form [111]:



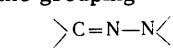
Formazans are in general capable of the interconversions indicated below, and a tautomeric equilibrium is

apparently established in solution, as is indicated by the results of acylation, when both possible acylformazans are obtained from (LII)[1,2,10]:



IX. INTRAMOLECULAR INTERACTIONS

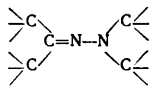
The presence of the grouping

 (I)

makes hydrazones a convenient model for studying $\pi-p$ conjugation[9,14,27,28,39,56,59,60,70,79-85,93,94,163,219-221]. The chief condition for interaction to occur between the π-electrons of the C=N bond and the lone pair of electrons on the amine nitrogen atom is that the hydrazone fragment (I) should be planar[31-33], which permits appropriate orientation of the p- and π-orbitals. The development of the $\pi-p$ type of conjugation in the molecules of hydrazones has been observed in studies of the infrared[59,60,69,70], Raman[79,81,82], ultraviolet[84,85,93,94], and nuclear magnetic resonance[219] spectra and also the optical properties of these compounds[27,28,56,94,220,221]. When conjugation is present, the electronic spectra of hydrazones show a bathochromic shift in the band corresponding to the $\pi \rightarrow \pi^*$ transition[84,85,93,94]. In the vibrational spectra $\pi-p$ conjugation leads to a lowering of the C–N stretching frequency[59,60,70,79,81,82]; in such hydrazones the C–N frequency lies in the range 1590–1620 cm^{-1}, whereas in aliphatic imines it lies between 1650 and 1670 cm^{-1} [34]. The higher the degree of conjugation the larger is $\Delta\lambda$ or $\Delta\nu$. The simple mono- and di-alkylhydrazones of saturated and unsaturated aldehydes and the phenylhydrazone of formaldehyde show high exaltation of molecular refraction, which indicates a considerable degree of conjugation in these systems[27,28,56,220,221]. Whereas in unsaturated hydrazones and alkylhydrazones, in semicarbazones and thiosemicarbazones, $\pi-p$ conjugation occurs within the hydrazone group[27,81,82,94], in arylhydrazones the π-system of the benzene ring is involved in conjugation, $\pi-p-\pi$ conjugation now being observed[28,59,60,81], and in alkylhydrazones of aromatic and unsaturated aldehydes $\pi-\pi-p$ conjugation is present[56,94,163,220,221].

A specific effect of conjugation in hydrazones is an increase in intensity of the C=N absorption band in the Raman spectra on passing from unsubstituted hydrazones to alkylhydrazones[14] and an increase in the exaltation of molecular refraction on passing from mono- to di-alkylhydrazones of $\alpha\beta$-unsaturated aliphatic aldehydes[220]. These facts indicate an increase in degree of conjugation, which can be explained by a change in the hybridisation of the electron orbitals of the amine nitrogen atom in the hydrazone group. In unsubstituted hydrazones the hybridisation of this atom is close to sp^3, and the orbital of its p-electrons is not parallel to that of the π-electrons of the C=N bond, although partial overlapping is already possible. Substitution on the amine nitrogen changes the pyramidal configuration of its bonds into a planar arrangement, as a consequence of which the hybridisation of the nitrogen atom approaches sp^2, which increases the overlapping of p- and π-orbitals[14].

Steric hindrance is one factor affecting the degree of $\pi-p$ conjugation in the hydrazone group. A considerable diminution in the conjugation effect is noticeable in the methylphenylhydrazones of aldehydes[59], and conjugation of the given type is almost completely absent in the methylphenylhydrazones and dialkylhydrazones of ketones[60,93,94]. The reason for the decrease in and even complete absence of $\pi-p$ conjugation when an alkyl group is introduced into a monosubstituted hydrazone of a ketone is that, owing to steric hindrance, the grouping



cannot be planar, as is readily evident when the structure of these compounds is examined with Briegleb–Stuart models: the groups are deflected about the N–N bond, which destroys the appropriate orientation of π- and p-orbitals.

Kitaev and his coworkers[39] have remarked that in azines, in which a considerable conjugation effect had been reported earlier[79], the $\pi-p$ type of conjugation is more strongly developed than the $\pi-\pi$ type, as might have been expected from the planar structure of azine molecules (III). The deflection of the C=N groups about the N–N bond (Fig. 2) is confirmed by spectroscopic data[38,39,51] and by the results of an investigation of the structure of azines by means of the dipole moments[39]. The conditions for $\pi-\pi$ conjugation are destroyed by the deflection, and at a certain angle of rotation ($\theta = 60-70°$) the π-orbitals of one C=N group become able to interact with the p-orbital of the nitrogen atom in the other C=N group[39].

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