

A Study of Azo-Hydrazone Tautomerism in 3-Phenyl-4-arylaazo-5-isoazolones by ¹H-NMR Spectra of ¹⁵N-Labeled Compounds and HMO Method

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Abstract □ The tautomerism in 3-phenyl-4-arylaazo-5-isoazolones **1** was examined by ¹H-NMR spectra of ¹⁵N-labeled compound and by HMO method. Both spectra data (¹H-NMR and IR) and bonding energies are in support of the assignment of the hydrazone structure to such compounds. It is further shown that intermolecular and intramolecular hydrogen bondings favor the hydrazone tautomer.

Keywords □ 3-Phenyl-4-arylaazo-5-isoazolones, azo-hydrazone tautomerism, HMO method, NMR spectra.

In continuation of our studies of azo-hydrazone tautomerism in the diazonium coupling products of active methylene compounds¹⁻⁹, we became interested in the tautomeric form of 3-phenyl-4-arylaazo-5-isoazolones **1** for which four possible tautomeric structures can be written (Scheme 1). The latter compounds are of interest because of the uses of their 3-alkyl analogs **2** as agricultural fungicides¹⁰ and in controlling a number of plant pathogenic micro-organisms¹². Also, as the mechanism of aminolysis of **1** is under current investigation in our laboratory, the knowledge of their true tautomeric form was felt important in understanding their chemical behaviour.

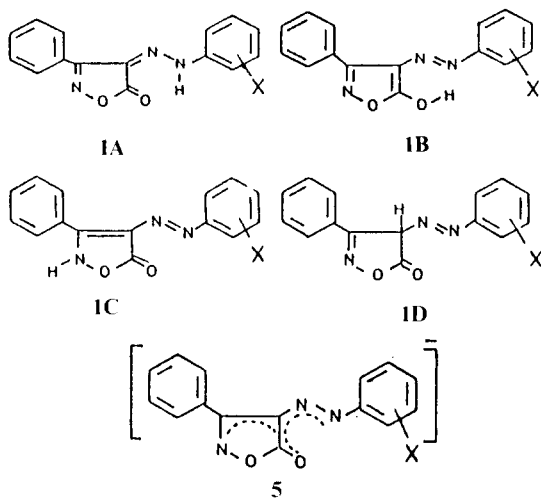
The tautomerism of the related 3-methyl-4-arylaazo-5-isoazolones **2** had been studied by two groups who reached different conclusions. Summers *et al.*¹¹⁻¹³ suggested, on the basis of UV, IR and ¹H-NMR studies, that such compounds exist in the hydrazone form **2A**. However, Cum *et al.*^{14,15} favor the NH form **2C**. The latter authors drew their conclusion on the basis of a comparative IR and ¹H-NMR study of the methyl compounds **2a** (R=CH₃)¹⁴, but they confused one of the methylated derivatives **3** with an isomeric triazole **4** formed during the reaction¹³. Their arguments were considered not

convincing by others, however¹⁶.

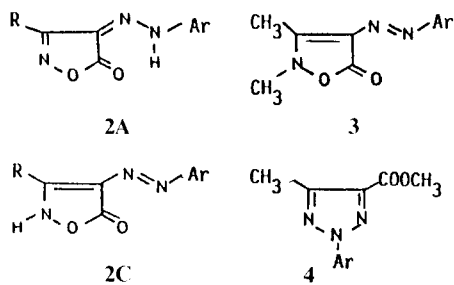
To provide an unambiguous proof of the tautomeric form of the compounds **1** in question, we examined the ¹H-NMR spectrum of **1a'** labeled with ¹⁵N adjacent to the phenyl group of the 4-arylaazo-moiety. Since only the hydrazone tautomer **1A** could exist with hydrogen attached to ¹⁵N, a splitting of the proton resonance would be a conclusive proof of the existence of the hydrazone form. In addition the ¹H-NMR spectra of the unlabeled compounds **1a-i** were also examined. In order to obtain further insight into the tautomeric structure of such compounds, the relative stabilities of the tautomeric forms of **1a** and the effects of hydrogen bonding have been investigated by Hückel Molecular Orbital (HMO) method. The use of both the ¹H-NMR spectra^{17,18} and HMO method^{5,7,8,19} in solving the tautomeric structure problems in the diazonium coupling products of active methylene compounds is well established.

EXPERIMENTAL

The infrared spectra of the compounds **1a-i** in potassium bromide were obtained using Zeiss infrared spectrophotometer model IMT 16. The ¹H-NMR



- a. X=H b. X=3-CH₃ c. X=4-CH₃
 d. X=3-CH₃O e. X=4-CH₃O f. X=3-Cl
 g. X=4-Cl h. X=3-NO₂ i. X=4-NO₂



Scheme 1

spectra were obtained in deuterated chloroform with a Varian EM 390-90 MHz spectrometer. ¹⁵N-Aniline (96.8% isotopic purity) was purchased from Merck Sharp and Dohme of Canada.

Compounds **1a**, **1a'**, **1h** and **1i** were prepared by low temperature diazotization of the appropriate aniline followed by coupling of the diazonium salt with 3-phenyl-5-isoxazolone in ethanol in the presence of sodium acetate at low temperature 5-10°C as previously described^{29,30}. The other compounds **1b-g** in the series studied were prepared by refluxing ethyl α -arylaminoacetate with hydroxylamine hydrochloride in the presence of pyridine following a literature procedure^{29,30}. All compounds were crystallized from acetic acid before recording their spectra. Their physical constants agreed with those reported^{13,14}. The physical properties of **1a'** were identical with those of the unlabeled compound **1a**.

Table I. ¹H-NMR and IR spectral Data of 3-Phenyl-4-arylamino-5-isoxazolones **1a-i**

Compound	$\bar{\nu}$, cm ⁻¹	δ , ppm ^a
1a	3185, 1719	13.4 (s, 1H)
1b	3185, 1719	13.4 (s, 1H), 2.4 (s, 3H)
1c	3181, 1720	13.2 (s, 1H), 2.35 (s, 3H)
1d	3169, 1719	13.1 (s, 1H), 4.1 (s, 3H)
1e	3190, 1718	13.2 (s, 1H), 4.0 (s, 3H)
1f	3176, 1717	13.5 (s, 1H)
1g	3190, 1724	13.5 (s, 1H)
1h	3190, 1722	13.6 (s, 1H)
1i	3190, 1725	13.6 (s, 1H)
1a'	3190, 1719	13.4 (d, $J=96$ Hz, 1H)

^aAll compounds exhibit aromatic proton multiplet in the region 7.0-8.2 ppm.

RESULTS AND DISCUSSION

As shown in Table I, the unlabeled compounds **1a-i** in deuterated chloroform exhibit a broad singlet in the 13.4 \pm 0.2 ppm region. This signal is undoubtedly corresponds to the hydrazone NH proton resonance. The far-down field position of the NH peak suggests that the proton is involved in strong hydrogen bond in chloroform solution. Absorption in this region has been observed in the spectra of the related 1,3-diphenyl-4-phenylazo-5-pyrazolone and was assigned to the same hydrazone NH group²⁰. This conclusion was supported by the ¹H-NMR spectrum of the labeled ¹⁵N compound **1a'**. The latter compound was prepared by diazotization of ¹⁵N aniline followed by coupling with 3-phenyl-5-isoxazolone. The possibility of diazonium scrambling under these mild conditions is nil^{23,24}. The spectrum of **1a'** in deuterated chloroform revealed a doublet centered at δ 13.4 ppm with a large coupling constant ($J=96$ Hz). This finding indicates that the proton is attached to ¹⁵N and not to either the ring nitrogen or to the oxygen atom as in **1C** and **1B**, respectively. Furthermore, the presence of only one ¹⁵N-induced doublet in the spectrum of **1a'** and only singlet in the spectra of the unlabeled compounds **1a-i** indicate that such compounds have in chloroform solution one geometric isomer of the hydrazone form namely the intramolecularly hydrogen bonded Z-form.

The foregoing conclusion is further substantiated by the infrared data of the compounds studied. The

ir spectra of **1a-i** revealed the presence of bands due to NH and carbonyl groups in the regions 3169-3185 and 1717-1725 cm^{-1} respectively. The intensity and the position of the NH band were independent of the concentration when spectrum was recorded in chloroform solution. This suggests that such group is involved in chelated ring structure.

To establish the relative stability of the three tautomeric forms **1A-C** within the framework of the HMO method²¹, the pi bonding energy, BE, defined by the equation: $\text{BE} = E_n - \sum \alpha_i n_i$, where E_n is the total pi energy of the system, n_i is the number of pi electrons contributed by atom i to the system, and α_i is the coulomb integral of the atom i ²⁵, was calculated for each tautomeric form of **1a** using standard HMO heteroatom parameters²⁶. The values of BE for the three forms **1A-C** were as follows: 24.894, 24.747 and 24.689 β , respectively. These data indicate that the order of stability of such form is **1A** (hydrazone) > **1B** (Azo OH) > **1C** (Azo NH). This conclusion is supported further by comparison of these values with the bonding energy calculated for the common resonance stabilized anion **5** which these three forms would give in alkaline medium. The value obtained for the bonding energy of **5** is 23.186 β . The difference between this value and the bonding energies of the tautomers **1A-C** are as follows: $\Delta\text{BE}(\mathbf{1A-5}) = 1.708$, $\Delta\text{BE}(\mathbf{1B-5}) = 1.561$ and $\Delta\text{BE}(\mathbf{1C-5}) = 1.503\beta$. Such values indicate that the hydrazone form is the least acidic. Because in acid-base equilibria of various tautomers, the tautomer with higher acidity is considered to be less stable¹⁹. It is reasonable to conclude that the hydrazone form **1A** is the most stable one of the three tautomeric forms **1A-C**. It should be pointed out that changes in the values of the coulomb and resonance integrals used in the calculation by ± 10 -25% do not affect the foregoing order of stability of the three tautomers **1A-C**.

The effects of intermolecular hydrogen bonding with a protic solvent upon the stability of the three tautomeric forms **1A-C** were next studied. For this purpose the parameters used for the centers XH and Y interacting with the solvent are: $\alpha_{\text{XH} \cdots \text{SH}} = \alpha_x - 0.2\beta$ and $\alpha_{\text{YHS}} = \alpha_y + 0.2\beta$. Such an approach to solvent effects has been used to correlate the difference in ESR spectra of semiquinone radicals seen in various solvents²⁷. Table II gives the bonding energies of the hydrogen bonded tautomers.

Table II. Effects of Intermolecular and Intramolecular Hydrogen Bondings on the Bonding Energies of Tautomeric Forms of **1a**

Tautomer	BE, β	
	no H-Bond	Intramolecular H-bond
1A	24.894	25.134
1B	24.747	24.864
1C	24.689	25.871

The results show that intermolecular hydrogen bonding with protic solvent increases the stability of the three tautomeric forms **1A-C**, the stabilization is more pronounced in the case of the azo NH form **1C** than in the case of the hydrazone form **1A**.

As additional step we have considered the effect of intramolecular hydrogen bonding on the stabilities of the two forms **1A** and **1B**. For this purpose the treatment developed by Pullman *et al.*²⁸ for intramolecular hydrogen bond was adopted. According to that treatment, the HMO parameters for the centers in the hydrogen bonded system $\text{X-H} \cdots \text{Y}$ are: $\alpha_{\text{XH}} = \alpha_x - 0.2\beta$, $\alpha_y = \alpha_y + 0.2\beta$ and $\beta\text{X(H)Y} = 0.2\beta$. The results of the calculations are given in Table II. The data show that intramolecular hydrogen bonding increases the stability of the hydrazone tautomer **1A** and the azo OH form **1B**. However, the stabilization of **1A** is more than twice larger than that of **1B**. This finding suggests also that the hydrazone form **1A** has the Z configuration in agreement with the spectral data.

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