HETEROCYCLIC NITRO COMPOUNDS

IV. Acid–Base Properties of Nitro Derivatives of 1,2,4-Triazole

L. I. Bagal and M. S. Pevzner

The acidity of a number of nitro derivatives of 1,2,4-triazole has been determined. The acidity indices correlate well with Hammett's σ_I and σ_{meta} constants and somewhat less well with the σ_{para} constants. The high values of ρ show the great sensitivity of the system to the influence of substituents. The acidities of the conjugate acids of 3-nitro-1,2,4-triazole and its C- and N-methyl derivatives have also been determined. Hammett's postulate is not observed for these compounds, and the amide scale of acidity, H_A, is more suitable for calculating their acidity indices than H_O.

As is well known, 1,2,4-triazoles unsubstituted on the nitrogens exhibit amphoteric properties and, depending on the pH of the medium, can give up or add a proton.

The acid-base properties of some derivatives of 1,2,4-triazole have been studied previously [2-7]. Recently the applicability of Hammett's equation to the triazole ring has been shown [3, 4] and a good correlation between the pKa values of the triazoles and the σ_{meta} constants of the substituents have been found.

The present work was devoted to a study of the acid-base properties of nitro derivatives of 1,2,4-triazole. The ionization constants of the nitrotriazoles unsubstituted on the nitrogen atoms were determined at 20°C by the potentiometric method, with the exception of 3,5-dinitro-1,2,4-triazole, which proved to be a strong acid. For this compound, the ionization constants were determined spectrophotometrically (Table 1).

Table 1. Acidity of Nitro Derivatives of 1,2,4-Triazole at 20°C

Compound	Name	pK_{A_1}	pK_{A_2}
I	3-Nitro-1,2,4-triazole	6,05±0,05	—
II	5-Methyl-3-nitro-1,2,4-triazole	6,75±0,05	—
III	5-Ethyl-3-nitro-1,2,4-triazole	6,65±0,05	—
IV	3-Nitro-5-n-propyl-1,2,4-triazole	6,60±0,05	—
V	3-Nitro-5-phenyl-1,2,4-triazole	5,65±0,05	—
VI	3-Nitro-5-(4-nitrophenyl)-1,2,4-triazoie	4,20±0,05	—
VII	3-Nitro-5-(3-nitrophenyl)-1,2,4-triazole	4,40±0,05	—
VIII	3-Nitro-1,2,4-triazole-5-carboxylic acid	<2	6,10±0,05
IX	5-Methoxycarbonyl-3-nitro-1,2,4-triazole	3,55±0,05	—
X	3,5-Dinitro-1,2,4-triazole	−0,66±0,10	—
XI	Bis(3,3'-dinitro-1,2,4-triazole-5-yl)	3,30±0,05	5,35±0,05
XII	Bis(3,3'-dinitro-1,2,4-5-yl)methane	4,15±0,05	6,30±0,05
XIII	1,2-Bis(3,3'-dinitro-1,2,4-triazol-5-yl)ethane	5,00±0,10	6,60±0,10

*A spectroscopic determination gave pK_A = 6.03.

For compound VIII, which has two degrees of ionization, two ionization variants are possible:
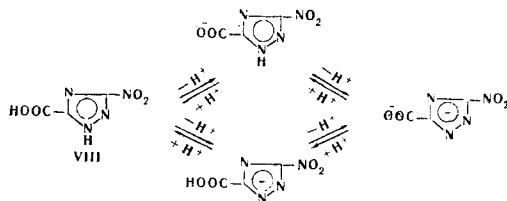
A comparison of the UV spectra at various pH values of the nitro acid VIII (Fig. 1) and of 1-methyl-5-nitro-1,2,4-triazole-3-carboxylic acid (XIV) (Fig. 2) with the spectra of compound I and of the N-methylated nitrotriazoles XV-XVII (Table 2) has shown that the splitting off of a proton attached to a hetero nitrogen atom causes a marked bathochromic shift in the UV spectrum (by 50 nm) while dissociation at the carboxyl group (Fig. 2) leads to only a very small bathochromic shift (by 5 nm). In compounds not containing imine hydrogen (XV-XVIII, Table 2), no changes are observed in the UV spectra on passing to an alkaline medium.

Table 2. Maxima of the Absorption Bands and Their Intensities for the Nitrotriazoles

Compound	Name	Medium	Form*	λ_{max}, nm	log ε
I	3-Nitro-1,2,4-triazole	pH 1	NM	230	3,73
		pH 13	A	290	3,81
		83,4% H₂SO₄	SA	<220	3,80
II	5-Methyl-3-nitro-1,2,4-triazole	pH 1	NM	258	3,61
		pH 13	A	298	3,70
		76,1% H₂SO₄	SA	235	3,80
XV	1-Methyl-5-nitro-1,2,4-triazole	pH 7	NM	270	3,66
		83,4% H₂SO₄	SA	245	3,70
XVI	1-Methyl-3-nitro-1,2,4-triazole	pH 7	NM	255	3,74
		83,4% H₂SO₄	SA	230	3,75
XVII	4-Methyl-3-nitro-1,2,4-triazole	pH 7	NM	260	3,75
		62,3% H₂SO₄	SA	225	3,78
X	3,5-Dinitro-1,2,4-triazole	40% H₂SO₄	NM	255	3,79
		water	A	285	3,90

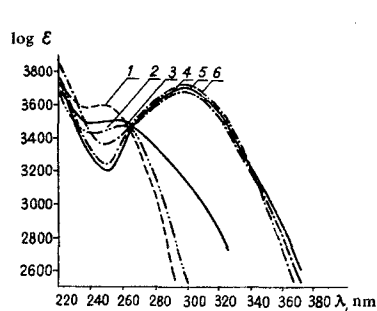*NM) neutral molecule; A) anion; CA) conjugate acid (cation).

Fig. 1   Fig. 2

Fig. 1. UV spectrum of 3-nitro-1,2,4-triazole-5-carboxylic acid: 1) pH 1.00; 2) 3.95; 3) 4.40; 4) 6.88; 5) 9.30; 6) 13.0.
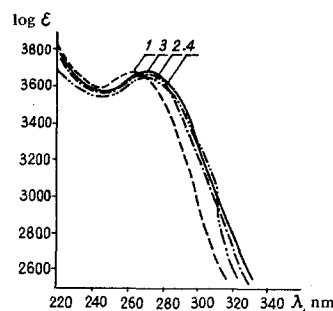
Fig. 2. UV spectrum of 1-methyl-5-nitro-1,2,4-triazole-3-carboxylic acid: 1) pH 1.00; 2) 3.95; 3) 4.60; 4) 9.30.

Thus, the changes in the UV spectrum of compound VIII that take place on passing from pH 4 to pH 10 are due to the splitting off of the imine hydrogen and, consequently, the pK_{A_2} value of 6.10 (Table 1) must relate to dissociation at the imino group and that of pK_{A_1} to dissociation at the carboxyl group. In this connection, it is an interesting fact that the opposite pattern is found in diazotriazocarboxylic acid [8], i.e., dissociation of the imino group at the N−H bond takes place first and then dissociation at the carboxyl group.

A comparison of the acidities of the nitrotriazoles I-X with the σ constants of the substituents in position 5 has shown that the pK_a values of the nitrotriazoles correlate well with the σ_{meta} constants and with the induction constants σ_I (the correlation coefficients r are, respectively, 0.990 and 0.993) and correlate somewhat worse with σ_{para} (r =0.975). The values of σ were taken from the literature [9].

The correlation equations have the form:

$$pK_A = -8{,}92 \ \sigma_{meta} + 5{,}95;$$
$$pK_A = -10{,}53 \ \sigma_I \ + 6{,}27;$$
$$pK_A = -7{,}23 \ \sigma_{para} + 5{,}84.$$

The high value of ρ shows the great sensitivity of the acid properties of the triazoles to the influence of substituents the induction influence apparently playing a somewhat greater role.

We studied the protonation of the neutral molecules of the nitrotriazoles in the case of 3-nitro-1,2,4-triazole (I), 5-methyl-3-nitro-1,2,4-triazole (II), and all the isomeric N-methyl-substituted nitrotriazoles: 1-methyl-5-nitro-1,2,4-triazole (XV), 1-methyl-3-nitro-1,2,4-triazole (XVI), and 4-methyl-3-nitro-1,2,4-triazole (XVII).

The addition of a proton to the neutral molecule of a nitrotriazole causes a hypsochromic shift of the absorption maximum in the UV spectrum by 25-35 nm (Table 2).

A study of the degree of protonation of compounds I, II, XV, XVI, and XVII in sulfuric acid solutions of various concentrations has shown that the nitrotriazoles do not obey Hammett's postulate [10]. As can be seen from Fig. 3, the slopes of the straight lines expressing log (BH^+/B) as a function of H_0 are less than 1, namely 0.55-0.65, for all the compounds studied.
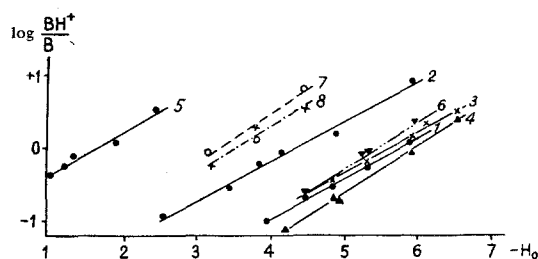

Fig. 3. Log (BH^+/B) as a function of H_0: 1) I; 2) II; 3) XVI; 4) XV; 5) XVII; 6) 1-methyl-4,5-dinitroimidazole [12]; 7) 2-methyl-4,5-dinitroimidazole [12]; 8) 1,2-dimethyl-4,5-dinitroimidazole [12].

Without going into a discussion of the causes of the deviation from Hammett's postulate (on this question see, in particular, [10, 11]) we may mention only that this circumstance does not enable us to obtain a constant pK_{BH^+} by using the H_0 scale. Table 3 gives an example of the calculation of pK_{BH^+} for compound II.

Table 3

% H_2SO_4	H_0	$\lg \dfrac{\varepsilon_B - \varepsilon}{\varepsilon - \varepsilon_{BH^+}}$	pK_{BH^+} on the H_0 scale	pK_{BH^+} on the H_A scale
39.90	−2.54	−0.92	−3.46	−2.90
50.38	−3.45	−0.53	−3.98	−2.99
54.25	−3.84	−0.16	−4.00	−2.86
57.31	−4.19	−0.04	−4.23	−2.94
62.54	−4.89	+0.20	−4.69	−3.04
64.84	−5.16	+0.26	−4.90	−3.14
70.34	−5.97	+0.96	−5.01	−2.80

The same pattern is observed for the other nitrotriazoles. The same factors apparently explain the large scatter of the values of pK_{BH^+} for some nitroimidazoles [12].

Figure 3 gives log (BH^+/B) as a function of H_0 for some nitro derivatives of imidazole (6,7,8) plotted on the basis of the work of Epishina et al. [12]. It can be seen from the figure that Hammett's postulate is not observed for these compounds (slopes 0.65-0.7).

In order to have the possibility of marking a quantitative comparison and an evaluation of the acidity of the conjugate acids of the nitrotriazoles not satisfying Hammett's postulate, we decided to use for calculating their acidity indices the amide scale of acidities H_A, proposed by Yates et al. [13].

We started from the existence of some structural analogy between triazoles and amides:
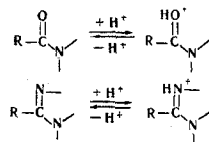
This analogy probably explains the similar solvation interactions of the two classes of compounds with sulfuric acid and this, in its turn, leads to similar values of the slopes of the straight lines expressing log (BH$^+$/B) as a function of H_0. For amides the slope is 0.7 [13]. The use of the H_A scale led to a far greater constancy of the pK_{BH^+} values at various concentrations of acid (Table 3).

It is an interesting fact that the H_A function has also been successfully used to calculate the pK_{BH^+} values of conjugated carbonyl compounds [14].

Table 4 shows that the introduction of a methyl group into position 1 or 2 of the triazole ring has little effect on its basicity: the pK_{BH^+} values of compounds I, XV, and XVI are similar to one another. At the same time, the introduction of a methyl group into position 4 (compound XVII) leads to a marked rise in basicity. This phenomenon is due to the fact that in compounds I, XV, and XVI the addition of a proton takes place at the N_4 heteroatom, and in XVII at the N_1 heteroatom. The ratio of the possible 1 H and 4 H tautomers of 3-nitro-1,2,4-triazole can be evaluated from a comparison of the pK_{BH^+} values of compounds XVI and XVII; this is equal to the ratio K_{1-Me}/K_{4-Me} [15] and is about 180, i.e., the predominant isomer is 3-nitro-1-H-1,2,4-triazole*.
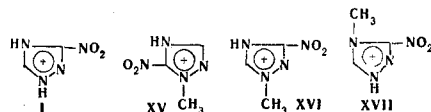
The introduction of a nitro group increases this tautomeric ratio by a factor of 20-40 as compared with the unsubstituted 1,2,4-triazole [3].

Table 4. Ionization Constants (pK_{BH^+}) of the Conjugate Acids of the Nitrotriazoles at 20°C on the Amide Scale

Compound	λ, nm	pK_{BH^+}	Concentration of H_2SO_4 at the half-ionization point
I	250	-3.70 ± 0.15	69.6
II	260	-2.93 ± 0.20	57.6
XV	270	-3.88 ± 0.20	71.8
XVI	255	-3.56 ± 0.13	67.7
XVIII	260	-1.31 ± 0.10	26.7

It can be seen from a comparison of the pK_{BH^+} values of compounds I and II that the introduction of a methyl group into position 5 (adjacent to the reaction center) leads to a considerable increase in basicity (a rise in pK_{BH^+} by ~0.8 unit). This confirms the hypothesis of the existence of an influence of the inductive effect of the substituent on the reaction center in prototropic reactions of the nitrotriazoles.

EXPERIMENTAL (with the participation of N. I. Sheludyakova).

All the nitro compounds used in the work were obtained by published methods [17, 18] and were additionally recrystallized. The potentiometric measurements were carried out on a LPM-60M potentiometer by the standard method [19].

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*The position of the proton on the N_1 heteroatom and not on N_2 was shown by measuring the dipole moment of compound I by the method of Halverstadt and Kumler [16]. The determination was carried out by I. N. Shokhor and E. Ya. Fedorova, for which the authors express their thanks to them.

The ultraviolet spectra were taken on an SF-4A instrument. The conditions for recording the spectra are given in Table 2.

REFERENCES

1. L. I. Bagal, M. S. Pevzner, and V. Ya. Samarenko, KhGS [Chemistry of Heterocyclic Compounds], 6, 269, 1970.
2. G. Dedichen, Ber., 39, 849, 1906.
3. C. F. Kröger and W. Freiberg, Z. Chem., 5, 381, 1965.
4. W. Freiberg and C. F. Kröger, Chimia, 21, 159, 1967.
5. L. I. Bagal, M. S. Pevzner, and V. A. Lopyrev, KhGS [Chemistry of Heterocyclic Compounds], 2, 440, 1966.
6. W. Freiberg, C. F. Kröger, Chimia, 21, 161, 1967.
7. J. Schmidt and H. Gehlen, Z. Chem., 5, 304, 1965.
8. A. N. Frolov, M. S. Pevzner, I. N. Shokhor, A. G. Gal'kovskaya, and L. I. Bagal, KhGS [Chemistry of Heterocyclic Compounds], 6, 1970 (in press).
9. Yu. A. Zhdanov and V. I. Minkin, Correlation Analysis in Organic Chemistry [in Russian], 85, 191, 1966.
10. E. M. Arnett, Modern Problems of Physical Organic Chemistry [Russian translation], Mir, Moscow, 202, 1967.
11. Yu. L. Khaldna, Reaktsionnaya sposobnost' organicheskikh soedinenii, 5, 489, 1968.
12. L. V. Epishina, V. I. Slovetskii, O. V. Lebedev, L. I. Filippova, L. I. Khmel'nitskii, V. V. Sevost'yanova, and T. S. Novikova, KhGS [Chemistry of Heterocyclic Compounds], collection 1, 102, 1967.
13. K. Yates, J. B. Stevens, and A. R. Katritzky, Canad. J. Chem. 42, 1957, 1964.
14. R. I. Zalewski and G. E. Dunn, Canad. J. Chem., 46, 2469, 1968.
15. S. F. Mason, J. Chem. Soc., 674, 1958.
16. J. F. Halverstadt and W. D. Kumler, J. Am. Chem. Soc., 64, 2988, 1942.
17. L. I. Bagal, M. S. Pevzner, A. N. Frolov, and N. I. Sheludyakova, KhGS [Chemistry of Heterocyclic Compounds] 6, 259, 1970.
18. L. I. Bagal, M. S. Pevzner, N. I. Sheludyakova, and V. M. Kerusov, KhGS [Chemistry of Heterocyclic Compounds], 6, 265, 1970.
19. A. Albert and E. Serjeant, Ionization Constants of Acids and Bases [Russian translation], Khimiya, Moscow, 1964.

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Lensovet Leningrad Technological Institute