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Solvatochromism of Heteroaromatic Compounds: XX.[1] 4(5)-Nitroimidazole

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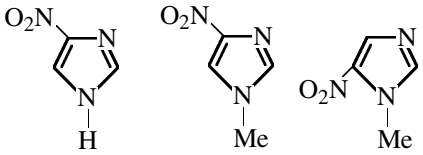
Abstract — 4(5)-Nitroimidazole in solution is stabilized as the 5-nitro isomer due to formation of hydrogen bond with an aprotic protophilic solvent. Amphiprotic medium favors displacement of the tautomeric equilibrium toward the 4-nitro isomer via formation of a solvate complex where 4-nitroimidazole acts as hydrogen bond acceptor. The observed specific solvatochromic effect in the UV spectrum of 4-nitroimidazole and related heterocyclic nitro compounds is determined by the electronic configuration of the excited π,π^*-state.

The results of studying the specific solvatochromic effect of NH-containing aromatic and heteroaromatic nitro compounds in aprotic protophilic solvents showed that this effect depends on both the structure of hydrogen bond donor and electronic configuration of the excited state [2–8]. If the π,π^* transition corresponding to intermolecular charge transfer does not change the orbital electron density on the nitrogen atom of the N–H bond involved in formation of solvate H-complex, specific solvatochromic effect is weak or is absent at all [7]. Therefore, while studying structure–property relations, the nature of absorption bands in the spectra of solvatochromic reference compounds and parameters of the corresponding electronic transitions must be taken into account. Otherwise, it is difficult to understand (in terms of the orbital approximation) fine details of hydrogen bonding for electronically excited states and to reveal any general relations between specific solvatochromic effect and molecular parameters of the dissolved substance, though some attempts to reveal these were made [9]. In the series of five-membered heterocycles, no explanation was given to the change of specific solvatochromic effect observed for the long-wave absorption band of 4-nitropyrazole, 3-nitropyrazole, and 3-nitropyrrole [3, 5]. It is known that pyrrole and 1,2-diazole molecules are characterized by different orbital structures; however, the number of studied heterocyclic nitro compounds is very limited. Therefore, it seems reasonable to examine solvatochromism of the long-wave absorption band in the UV spectrum of 4(5)-nitroimidazole (**I**) which is related to the corresponding pyrrole in the orbital structure. In order to obtain reliable data on the specific solvatochromic effect it was necessary to estimate the effect of the medium on the relative stability of tautomeric forms of 4(5)-nitroimidazole (**I**) over a wide series of organic solvents.

Effect of the medium on tautomeric properties of 4(5)-nitroimidazole. According to the experimental data, the 5-nitro isomer is stable in the gas phase, while in aqueous solution the 4-nitro isomer prevails (99%) [10, 11]. 4-Nitroimidazole was also found to predominate in crystal [12]. It was presumed that the displacement of the tautomeric equilibrium in highly polar media toward 4-nitroimidazole is explained in terms of a large difference in the dipole moments (μ) of the 4- and 5-nitro isomers [10, 13], i.e., the former is stabilized by nonspecific solvation. The dipole moments of 4(5)-nitroimidazole and its *N*-methyl derivatives which are models of possible tautomers were measured in 1,4-dioxane [10].



μ, D (25°C)	7.38	7.36	4.07

It is seen that the dipole moment of the unsubstituted compound is closer to that found for 1-methyl-4-nitroimidazole. Equation (1) given below was derived on the basis of theoretical calculations (HF/6–31G*) and experimental data for pyrrole, pyrazole, imidazole, 1,2,4-triazole, and 1-methylimidazole. This equation makes it possible to estimate the

[1] For communication XIX, see [1].

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Table 1. Relative energies (ΔE_T) and dipole moments of 4-nitroimidazole (**I**), 5-nitroimidazole (**IV**), and their 1 : 1 and 1 : 2 solvate H-complexes, calculated by the nonempirical HF/6–31G* method

Comp. no.	H-bond acceptor[a]	ΔE_T, kJ/mol	$\Delta E_T(T\rightarrow 0)$,[b] kJ/mol	μ, D	Comp. no.	H-Bond donor[a]	ΔE_T, kJ/mol	μ, D
I	–	0	0	7.97	**I**	–	0	7.97
IV	–	0.46	0.46	3.85	**IV**	–	0.46	3.85
I	Dimethyl ether	0	–	10.83	**I**	Water	0	8.96
IV	"	–0.88	–	4.55	**IV**	"	2.10	2.96
I	1,4-Dioxane	0	0	9.50	**I**	Metanol	0	6.77
IV	"	–0.96	–0.92	4.38	**IV**	"	1.76	2.66
I	THF	0	0	11.56	**I**	Metanol[c]	0	10.19
IV	"	–1.89	–1.89	4.77	**IV**	"	1.09	

[a] 1 : 1 Complexes; the data refer to the most stable H-complexes with water and methanol. [b] With account taken of zero-point vibration energy (0 K). [c] 1 : 2 Complexes.

dipole moments for 4- and 5-nitroimidazoles from the μ value calculated for the isolated molecule [10]:

$$\mu_d = 0.45 + 0.807\mu_{6-31G^*}. \quad (1)$$

The corresponding values were 7.51 and 3.87 D, and it was concluded that only the 4-nitro isomer is stable in dioxane. However, this conclusion should be revised, for it is based on the assumption that 4(5)-nitroimidazole is not solvated by dioxane in a specific mode. Such an assumption is inadmissible in principle. Both dioxane and other related proton-acceptor solvents are known to form NH···O hydrogen bonds with *C*-nitroazoles [3, 5, 8]. HF/6–31G* nonempirical calculations showed that complex formation with 4(5)-nitroimidazole affects not only μ values but also energy parameters of the tautomeric process: the stability of solvate H-complexes of the 5-nitro isomer increases as the proton-acceptor power of a protophilic solvent rises (Table 1). Therefore, specific solvation mechanism should necessarily be taken into account while considering effect of the medium on the state of tautomeric equilibrium. Moreover, nonspecific solvation in a protophilic medium involves not a molecule but a 1 : 1 solvate H-complex in which the solvent acts as hydrogen-bond acceptor.

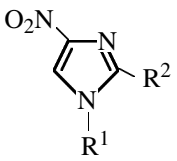
Table 2. Experimental (μ_d; dioxane, 25°C) and calculated (HF/6–31G*) dipole moments of isolated *C*-nitroazole molecules (μ_i) and their 1 : 1 H-complexes with dioxane (μ_c)

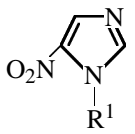
Comp. no.	μ_d,[a] D	μ_c,[b] D	μ_i,[b] D	Comp. no.	μ_d,[a] D	μ_i,[b] D
I	8.03[c]	9.50	7.97	**II**	7.30,[b] 7.36	8.55
IV	3.83[c]	4.38	3.85	**III**	7.64[b]	8.70
VI	6.19	7.12	6.90	**V**	4.07	4.44
VIII	4.87	6.04	5.00	**VII**	6.20	7.26
IX	4.96	5.80	4.85	**X**	4.83	5.69
XIV	6.74	8.13	7.43	**XI**	4.89	5.47
XV	7.19	8.49	7.94	**XII**	4.19	4.77
XVI	7.26[b]	9.08	7.87	**XVII**	6.78	8.03
XXI	1.59	1.96	1.15	**XVIII**	6.05	7.13
XXII	1.40	1.49	1.77	**XIX**	4.96	5.55
				XX	3.30	3.59

[a] Data of [8, 10, 16–19]. [b] This work. [c] Calculated by Eq. (2).

It should be noted that the results of calculations performed with no account taken of electronic correlations (for its effect on the energy parameters of tautomeric transformations, see, e.g., [14, 15]) do not agree perfectly with the experimental data obtained for the gas phase [10, 11]. In this connection, the energy parameters given in Table 1 must be regarded as those characterizing the above tendency. According to the higher-level calculations (V3LYP/6–31G*), the isolated 5-nitroimidazole molecule is preffered over its 4-nitro isomer by 3.27 kJ/mol.

Before proceeding to the estimation of the dipole moments of specifically solvated 4- and 5-nitroimidazole molecules by Eq. (1), it was interesting to elucidate how specific solvation affects the polarity of H-complexes derived therefrom. For this purpose, we used the data given in Table 2, which include published and newly measured dipole moments of *C*-nitroazoles **I**–**XXIII** in dioxane (μ_d), as well as the calculated (HF/6–31G*) values for the isolated molecule (μ_i) and its 1 : 1 H-complex with dioxane (μ_c). The values given for *C*-nitropyrazoles and


I–III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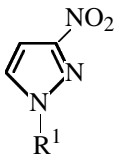
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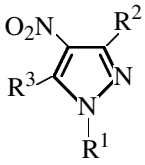
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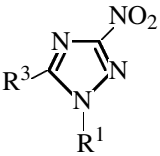
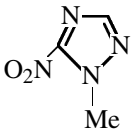
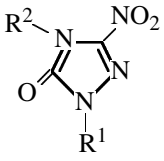
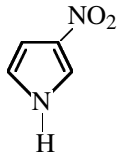
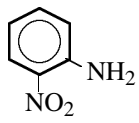

XIV–XIX


XX


XXI–XXII


XXIII


XXIV

I, **IV**, **VI**, **VIII**, **IX**, **XIV**–**XVI**, **XXI**, R^1 = H; **II**, **III**, **V**, **VII, X**, **XI**, **XIII**, **XVII**–**XIX**, **XXII**, R^1 = Me; **XII**, R^1 = CH_2=CH; **I**, **II**, **VIII**, **X**, **XIII**, **XIV**, **XVII**, **XXII**, R^2 = H; **III**, **IX**, **XI**, **XII**, **XV**, **XXI**, R^2 = H; **XVI**, R^2 = Pr; **XVIII**, R^2 = Cl; **XIX**, R^2 = NO_2; **VIII**, **X**, R^3 = H; **IX**, **XI**, **XII**, R^3 = Me; **XIII**, R = NH_2.

C-nitro-1,2,4-triazoles refer to the previously established tautomeric forms [8, 10, 16–19].

Linear regression analysis of the calculated (μ_{6-31G^*}) and experimental dipole moments (μ_d) of nitroazoles was performed using the theoretical values for isolated molecules of N-substituted azoles and those calculated for 1 : 1 H-complexes with dioxane for NH compounds. As a result, general correlation (2) was obtained:

$$\mu_d = (0.24 \pm 0.13) + (0.82 \pm 0.02)\mu_{6-31G^*};$$
$$r = 0.995,\ s = 0.19,\ n = 19. \quad (2)$$

The parameters of linear regression (2) differ considerably from the parameters of Eq. (1). Equation (2) covers the values corresponding to both nonspecifically solvated molecules and solvate H-complexes. We can conclude that H-complexes with dioxane are analogous to N-substituted compounds in the effect of nonspecific solvation on their dipole moment. Equation (2) gives μ = 8.03 and 3.83 D, respectively, for the H-complexes of 4- and 5-nitroimidazoles with dioxane. Comparison with the experimental dipole moment shows that 4-nitroimidazole predominates in dioxane with a population of 80%.

Tautomeric equiblria in other organic solvents were studied on a qualitative level using the positions of the long-wave absorption band in the UV spectra of 4(5)-nitroimidazole. From the previous data it follows that the 4-nitro isomer prevails in aprotic protophilic solvents whose polarity is comparable to or higher than the polarity of dioxane. Therefore, as model structures we used 1-methyl-4-nitroimidazole (**II**) and 1,2-dimethyl-4-nitroimidazole (**III**). Their solvatochromic properties (Table 3) are described by Eqs. (3) and (4), respectively.

$$\nu^{pr}_{max} = (35\,340 \pm 70) - (3830 \pm 100)\pi^*;$$
$$r = 0.995,\ s = 100,\ n = 19; \quad (3)$$
$$\nu^{pr}_{max} = (34\,950 \pm 80) - (3450 \pm 110)\pi^*;$$
$$r = 0.994,\ s = 100,\ n = 15. \quad (4)$$

Here, ν^{pr}_{max} is the wave number corresponding to the long-wave absorption maximum in protophilic medium, and π^* is the Kamleta–Taft parameter characterizing the solvent polarity/polarizability (Table 3). Taking into account that 4(5)-nitroimidazole gives rise to H-complexes in aprotic protophilic solvents, its solvatochromism was described by three-parameter Eq. (5), where β is a parameter characterizing the ability of a solvent to act as proton acceptor in an H-complex with the solute, and ξ is the relative measure of covalent character of the coordination bond (Table 3). However, we failed to obtain a satisfactory correlation for all the examined aprotic solvents. This fact alone suggests tautomeric heterogeneity of 4(5)-nitroimidazole. Further on, we applied a procedure based on the shifts of the long-wave absorption maxima relative to those of the model compounds ($\Delta\nu_n$).

4(5)-Nitroimidazole: $\nu'_{max} = \nu'_0 - s'\pi - b\beta - e\xi$; (5)

Models: $\nu_{max} = \nu_0 - s\pi^*$;

$\Delta\nu_n = \Delta\nu_0 - \Delta s\pi - b\beta - e\xi$;

Here, $\Delta\nu_n = \nu'_{max} - \nu_{max}$, $\Delta\nu_0 = \nu'_0 - \nu_0$, $\Delta s = s' - s$; ν'_0 and ν_0 are free terms of the solvatochromic equations; and s, s', b, and e are regression coefficients.

Taking into account Eqs. (3) and (4), the quantity Δs may be assumed approximately constant. There-

Table 3. Solvatochromism of nitroimidazoles **I**–**III** and 3,5-dimethyl-4-nitropyrazole (**IX**) in aprotic media

No.	Solvent	Kamlet–Taft parameters[a]			$\nu^{pr}_{max} \times 10^{-3}$, cm^{-1}				No.	Solvent	π^{*a}	$\nu^{in}_{max} \times 10^{-3}$, cm^{-1}	
		π^*	β	ξ	**I**	**II**	**III**	**IX**				**II**	**IX**
1	Triethylamine	0.14	0.71	1.0	35.50	35.00		36.15	1	Hexane	–0.08	35.75	37.60
2	Dibutyl ether	0.24	0.46	0.2	34.55	34.45	34.15	36.55	2	Pentane	–0.08	35.70	37.60
3	Diethyl ether	0.27	0.47	0.2	34.55	34.20	34.00	36.45	3	Heptane	–0.02	35.55	37.60
4	Diisopropyl ether	0.27	0.49	0.2	34.55	34.40			4	Cyclohexane	0.00	35.45	37.50
5	Butyl acetate	0.50	0.45	0.0	35.05	33.40	33.20		5	Octane	0.01	35.55	37.50
6	1,2-Dimethoxy-ethane	0.53	0.41	0.2	34.55	33.00	32.95		6	Decane	0.03	35.35	37.40
7	1,4-Dioxane	0.55	0.37	0.2	34.55	33.20	33.05	36.10	7	Carbon tetra-chloride	0.28	34.75	37.00
8	Ethyl acetate	0.55	0.45	0.0	34.90	33.20	33.20	36.10	8	Butyl chloride	0.39	33.85	
9	THF	0.58	0.55	0.2	34.65	33.10	33.00	35.90	9	Butyl bromide	0.48	33.55	
10	Ethyl trichloro-acetate	0.61	0.25	0.0	34.95	33.00[b]			10	Chloroform	0.58	33.30	36.50
11	Ethyl chloro-acetate	0.70	0.35	0.0	34.65	32.65		36.00	11	Pentachloro-ethane	0.62		36.50
12	Acetonitrile	0.75	0.31	0.1	34.35	32.50	32.30	35.90	12	1,2-Dibromo-ethane	0.75	32.70	
13	Propylene carbonate	0.83	0.40	0.0	34.00	32.05	32.00	35.60	13	1,2-Dichloro-ethane	0.81	32.70	36.20
14	Tetramethylurea	0.83	0.80	0.0	33.70	32.20	32.20		14	Methylene dichloride	0.82	32.65	36.20
15	γ-Butyrolactone	0.87	0.49	0.0	33.85	32.00			15	1,1,2,2-Tetra-chloroethane	0.95	32.40	36.10
16	HMPA	0.87	1.05	–0.2	33.55	32.00	32.00						
17	DMF	0.88	0.69	0.0	33.60	32.00	31.85	35.25					
18	*N*,*N*-Dimethyl-acetamide	0.88	0.76	0.0	33.55	31.95	31.75						
19	1-Methylpyrrol-idin-2-one	0.92	0.77	0.0	33.45	31.95	31.85	35.05					
20	DMSO	1.00	0.76	0.0	33.15	31.60	31.55	34.90					

[a] Data of [20, 21]. [b] Calculated by Eq. (3).

fore, we expected that the dependence of $\Delta\nu_n$ will be contributed mainly by β and ξ. Figure 1 shows a graphical representation of the dependence of $\Delta\nu_n$ (determined relative to model compound **II**) upon β. It is seen that such solvents as triethylamine, dibutyl ether, diethyl ether, diisopropyl ether, 1,2-dimethoxy-ethane, and 1,4-dioxane (nos. 1–4, 6, 7; Table 3) must be excluded. These solvents deviate from the linear $\Delta\nu_n$—β dependence plotted in Fig. 1. The absorption maximum shifts by 400–1600 cm^{-1} toward lower frequency relative to the predicted position ($\Delta\Delta\nu_n$, Fig. 1), i.e., toward the 5-nitro isomer [22–24]. Subsequent consideration of the parameter ξ allowed us to determine solvents in which 4-nitroimidazole overwhelmingly predominates over 5-nitroimidazole. These include all aprotic protophilic solvents with $\pi^* \geq 0.58$ (nos. 9–20; Table 3). The solvatochromic equation for 4-nitroimidazole in protophilic solvents looks as follows:

$$\nu^{pr}_{max} = (37410 \pm 100) - (3620 \pm 130)\pi^* - (860 \times 70)\beta - (920 \pm 170)\xi;\ r = 0.995,\ s = 40,\ n = 12. \quad (6)$$

Dimethyl sulfoxide is among solvents which stabilize the solvate H-complex of 4-nitroimidazole. Previous ^{13}C and ^{15}N NMR studies of solutions of 4(5)-nitroimidazole in DMSO-d_6, as well as in a 3 : 1 DMSO–acetone mixture, showed the presence of only 4-nitroimidazole in these systems [25, 26].

The fact that Eq. (6) describes solvatochromism of the 4-nitro isomer is additionally supported by comparison of the free terms in solvatochromic equations like (5) for a series of *C*-nitroazoles in aprotic protophilic media (ν_0^{pr}) with the frequencies of their low-energy π,π^* transitions, which were calculated by the semiempirical AM1(CI) method (ν_{AM1}; Table 4). In order to extend the range of variation of ν_0, the data for 5-amino-1-methyl-4-nitropyrazole (**XIII**), 3-nitropyrrole (**XXIII**), and 2-nitroaniline (**XXIV**) are also included (Table 4).

The long-wave absorption maxima in the UV spectra of compound **XXIV** in inert aprotic media (ν_{max}^{in}) were taken from [29–32]. Correlation analysis of the averaged ν_{max}^{in} values gave Eq. (7):

$$\nu_{max}^{in} = (26\,560 \pm 20) - (1660 \pm 40)\pi^*;$$
$$r = 0.996,\ s = 70,\ n = 17. \quad (7)$$

Insofar as solvatochromism in aprotic protophilic and inert solvents should be considered separately [19], correlations for each solvent series were found for 4-nitropyrazole (**VIII**) on the basis of the available data [3]. Equations (8) and (9) differ only slightly from each other and from the general relation [3]:

$$\nu_{max}^{in} = (38\,950 \pm 20) - (1900 \pm 40)\pi^*;$$
$$r = 0.998,\ s = 50,\ n = 11; \quad (8)$$

$$\nu_{max}^{pr} = (38\,970 \pm 100) - (1870 \pm 90)\pi^* - (1840 \pm 160)\beta;$$
$$r = 0.985,\ s = 70,\ n = 11. \quad (9)$$

We measured new values in hexane (ν_{max} = 39 150 cm^{-1}) and octane (ν_{max} = 38 950 cm^{-1}). Also, additional data for 3-nitropyrazole (**VI**) in diisopropyl ether (ν_{max} = 40 450 cm^{-1}), THF (ν_{max} = 39 200 cm^{-1}), butyl acetate (ν_{max} = 39 900 cm^{-1}), ethyl chloroacetate (ν_{max} = 39 300 cm^{-1}), acetonitrile (ν_{max} = 39 300 cm^{-1}), and butyrolactone (ν_{max} = 38 800 cm^{-1}) were obtained. With account taken of these new data, the known [5] solvatochromic Eq. (10) almost does not change.

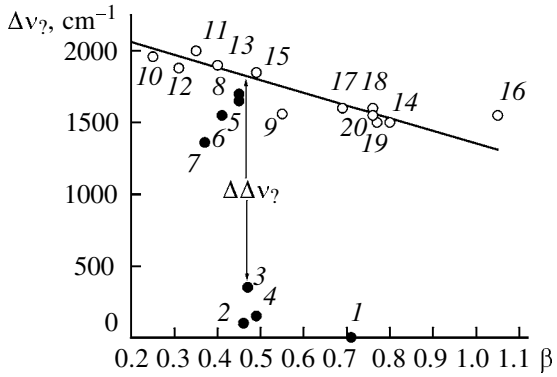


Fig. 1. Graphical analysis of solvatochromism of 4(5)-nitroimidazole in aprotic protophilic solvents (for solvent numbering, see Table 3); black circles refer to the solvents in which tautomeric equilibrium affects the UV spectrum.

$$\nu_{max}^{pr} = (42\,300 \pm 100) - (3310 \pm 140)\pi^*$$
$$- (1520 \pm 130)\beta - (1650 \pm 140)\xi;$$
$$r = 0.985,\ s = 100,\ n = 16. \quad (10)$$

Table 3 contains new experimental data on the effect of the medium on the position of the long-wave absorption maxima of compounds **II** and **IX**. Quantitative treatment of these data gave Eqs. (11)–(13):

Compound **II**: $\nu_{max}^{in} = (35\,450 \pm 60) - (3470 \pm 120)\pi^*;$
$r = 0.993,\ s = 160,\ n = 14.$ (11)

Compound **IX**: $\nu_{max}^{in} = (37\,480 \pm 20) - (1560 \pm 40)\pi^*;$
$r = 0.997,\ s = 50,\ n = 12.$ (12)

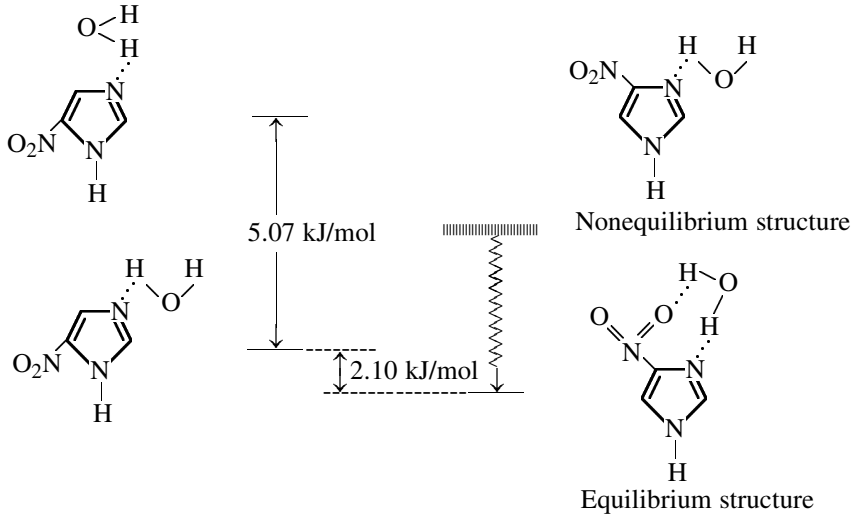
$\nu_{max}^{pr} = (37\,600 \pm 50) - (1740 \pm 70)\pi^*$
$(1230 \pm 70)\beta - (330 \pm 70)\xi;$
$r = 0.994,\ s = 40,\ n = 12.$ (13)

Table 4. Calculated [AM1(CI)] wave numbers (ν_{AM1}) for low-energy π,π^* transitions and free terms in solvatochromic equations for a series of nitro compounds in protophilic (ν_0^{pr}) and inert (ν_0^{in}) media (cm^{-1})[a]

Comp. no.[b]	ν_{AM1}	ν_0^{pr}	ν_0^{in}	Comp. no.[c]	ν_{AM1}	ν_0^{pr}	ν_0^{in}
I	34400[d]	37410[e]		**II**	34200[d]	35340[e]	35450[e]
VI	38300, 34600	42300[e]	40190	**III**	33700[d]	34950[e]	
VIII	36400	38970[e]	38950[e]	**VII**	37500[d], 35400[d]	39300	39510
IX	35300[d], 33200[d]	37600[e]	37480[e]	**X**	36300[d], 35800[d]	37430	37660
XXIII	32500	34700	34700	**XI**	34800, 33700	36340	36310
XXIV	28300	26560	26590[e]	**XIII**	31600	31820	

[a] The transition energies and their assignment were given in [3, 5, 7, 27, 28]. [b] Compounds containing an N–H bond. [c] *N*-Methyl-substituted nitro compounds. [d] Our present data. [e] The complete solvatochromic equation is given in the text.

Scheme 1.



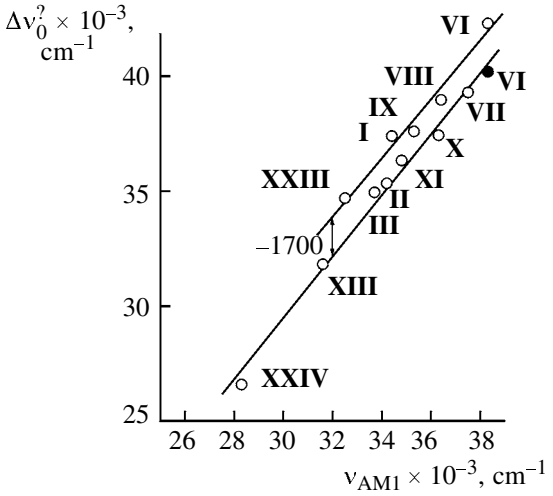


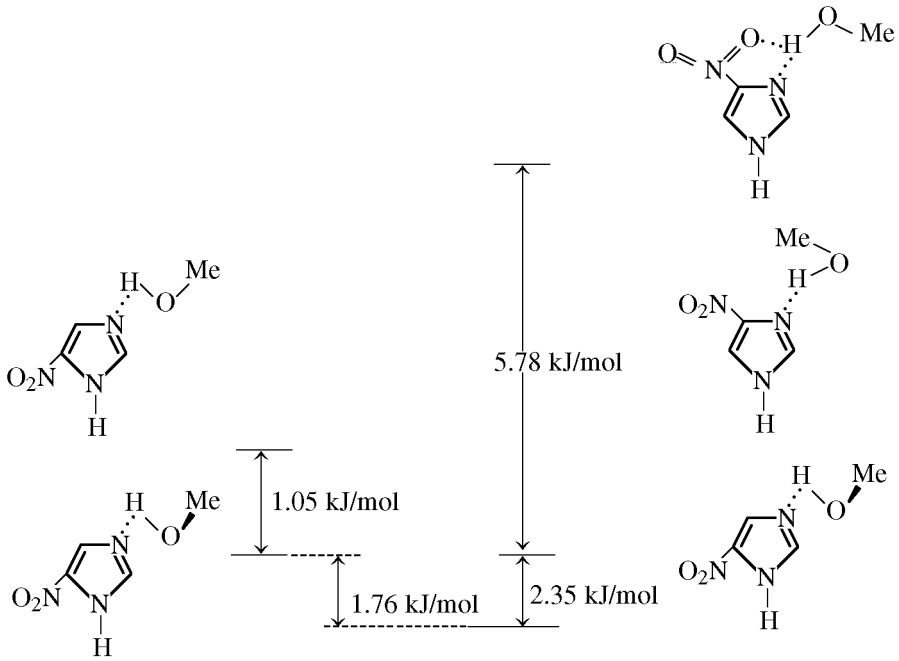
Fig. 2. Correlation between the wave numbers of low-energy π,π^*-transitions (ν_{AM1}) of nitro compounds, calculated in the AM1(CI) semiempirical approximation, and their absorption maxima (ν_0^{pr}) in a medium with $\pi^* = \beta = \xi = 0$; the dark circle corresponds to ν_0^{pr} of 3-nitropyrazole.

Analysis of the ν_0^{pr} and ν_0^{in} values for nitroazoles (Table 4) shows a weak effect of the solvent nature. Therefore, ν_0^{pr} may be related to ν_{AM1}. An exception is 3-nitropyrazole (**VI**), for which $\Delta\nu_0 = \nu_0^{pr} - \nu_0^{in} \approx 2100$ cm^{-1}. This difference was explained by displacement of the global absorption maximum as a result of redistribution of its vibrational components [5]. The relation between ν_0^{pr} and ν_{AM1} is illustrated by Fig. 2 which shows the existence of two regression lines at a distance of ~1700 cm^{-1} from each other. The lower plot corresponds to *N*-methylazoles and 2-nitroaniline. It includes the point belonging to 3-nitropyrazole (**VI**) (ν_0^{in}). The upper plot includes NH-azoles, 4-nitroimidazole (**I**) among them. Thus, comparison of the theoretical and experimental data indicates that in protophilic media with $\pi^* \geq 0.58$ the tautomeric equilibrium of 4(5)-nitroimidazole is displaced almost completely toward the 4-nitro isomer and that replacement of hydrogen at the pyrrolic nitrogen atom in nitro derivatives of five-membered heterocycles by alkyl group (and, in some cases, complex formation involving the N–H bond) could induce intensity redistribution of vibrational components of the absorption band corresponding to electronic transition with intramolecular charge transfer.

The data on solvatochromism of 4(5)-nitroimidazole, model compound **III**, and some other N-substituted nitroazoles in amphiprotic media are collected in Table 5. Contrary to expectations, there were no difficulties while analyzing these data. Direct comparison of the ν_{max}^{am} values for compounds **I** and **III** revealed an excellent linear correlation between them at $\pi^* > 0.45$. In other words, the range of existence of the 4-nitro isomer in amphiprotic medium has extended to π^* ~0.45. This fact is readily explained by increased relative stability of the solvate in which 4-nitroimidazole acts as proton acceptor, and solvent, as proton donor. Let us consider some relevant theoretical data. Scheme 1 shows the relative energies (kJ/mol) and configurations of 1 : 1 H-complexes formed by 4- and 5-nitroimidazoles and water, determined by the HF/6–31G* nonempirical calculations.

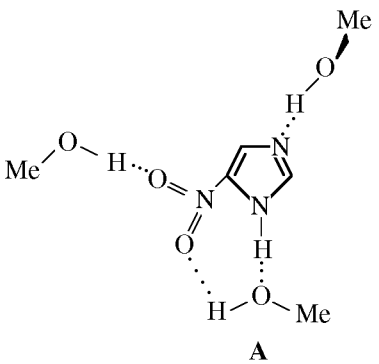
Unlike the NH···O hydrogen bond which stabilizes the 5-nitro isomer (Table 1), the N···HO hydrogen bond with water stabilizes the 4-nitro structure. Therefore, a qualitative agreement is observed between the

Scheme 2.

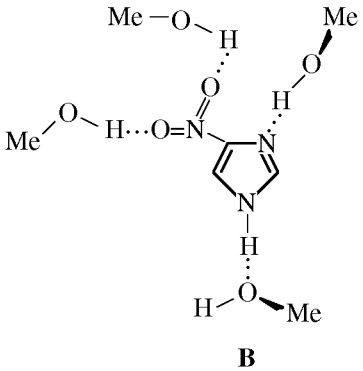


theoretical and experimental data for H-complexes with water. However, the increased stability of hydrated 4-nitroimidazole may be a particular case due to formation of an additional hydrogen bond involving the nitro group in the most energetically favorable configuration of the solvate complex. For that reason and also for the sake of simplicity and generality, we chose methanol as hydrogen-bond donor. The structures of the corresponding 1 : 1 solvate complexes and their energies (HF/6–31G*) are given in Scheme 2. According to the calculations, methanol, as well as water, increases the relative stability of the 4-nitro isomer via N···HO hydrogen bonding. However, real solvate H-complexes have a more complicated structure, as follows from the data of calorimetric and dielcometric titration. For example, compounds **III** and **XI** were found to give 1 : 1, 1 : 2, and 1 : 3 complexes with methanol in benzene (on successive increase of the methanol concentration). This means that the data obtained for 1 : 1 H-complexes cannot form the basis for final conclusions.

Also, it seems unreasonable to use for the above purpose theoretical energies of formation of tautomers with the optimal number and location of solvent molecules in the first coordination sphere of their solvate shell.



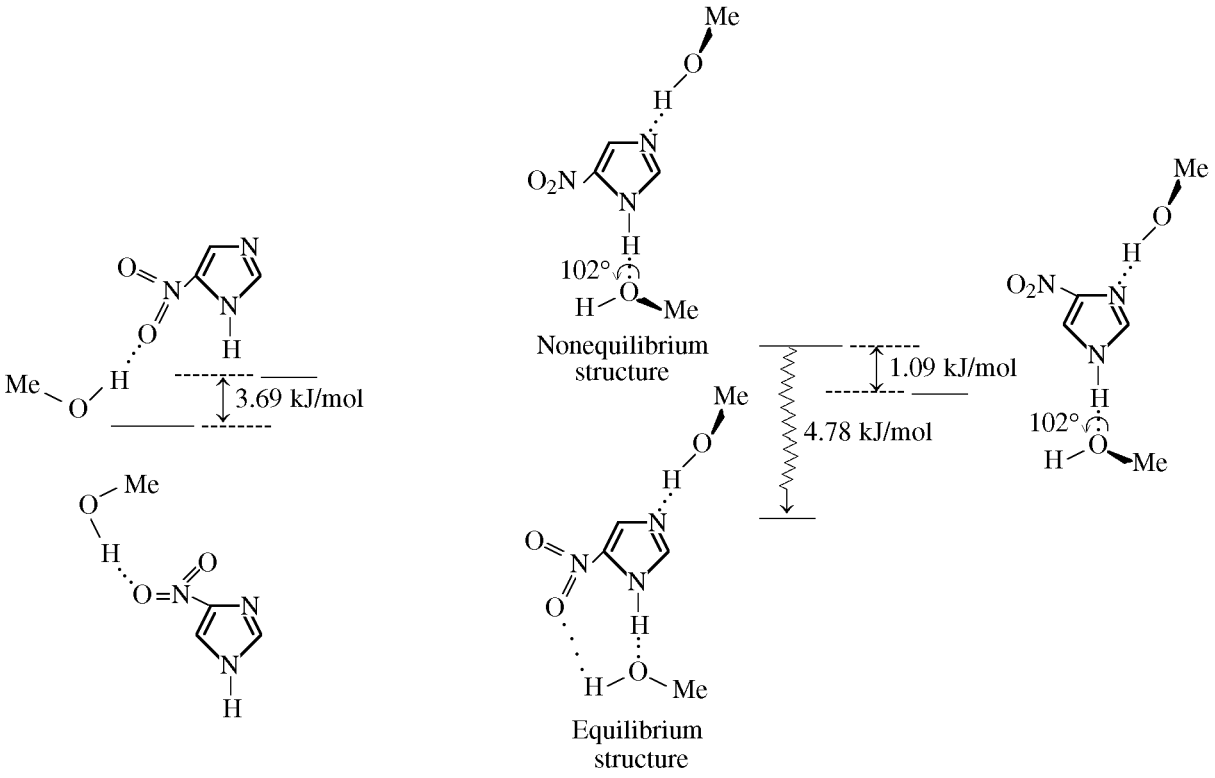
A



B

H-Complexes **A** and **B** have different compositions. Therefore, it is necessary to take into account the basis set superposition error (BSSE) which is comparable with the difference in the energies of formation of the solvates. Specific solvation with participation of the nitro group makes 4-nitroimid-

Scheme 3.



azole more stable, but its contribution to the energy of stabilization of tautomeric forms of 4(5)-nitroimidazole by the solvent is small. On a qualitative level, it becomes possible to compare complexes with two hydrogen bonds (N···HO and NH···O) and similar orientations of the methanol molecules (Scheme 3). The results obtained in such a way (Table 1) confirm the higher stability of the 4-nitro isomer in amphiprotic solvents.

Table 5. Solvatochromism of nitroazoles **I**, **III**, **VII**, **X**, and **XI** in amphiprotic (ν_{max}^{am}) solvents

Solvent	Kamlet–Taft parameters[a]			$\nu_{max}^{am} \times 10^{-3}$, cm^{-1}				
	π^*	β	α	**I**	**III**	**VII**	**X**	**XI**
1-Octanol	0.37	0.97	0.62		33.30			
1-Heptanol	0.39	0.96	0.64	34.90	33.30	37.70	36.65	35.60
1-Hexanol	0.41	0.94	0.67		33.25			
2-Methyl-2-propanol	0.41	1.01	0.68	34.55	33.20	37.70	36.65	35.60[b]
1-Pentanol	0.44	0.92	0.70		33.25			
1-Butanol	0.47	0.88	0.79	35.00	33.25	37.70	36.60	35.50[b]
2-Propanol	0.48	0.95	0.76	34.90	33.10	37.70	36.60	35.60
1-Propanol	0.52	0.83	0.78	34.85		37.65	36.55	35.50
Ethanol	0.54	0.77	0.83	34.75	33.00	37.50	36.50	35.40[b]
Methanol	0.60	0.62	0.93	34.80		37.55	36.45	35.40[b]
Acetic acid	0.64	0.45	1.12	35.15	33.25	37.70	36.70	35.60[b]
Ethylene glycol	0.92	0.52	0.90	33.80	32.00	36.80	35.80	34.60
Formamide	0.97	0.60	0.71	33.10	31.50	36.30	35.25	34.10[b]
Water	1.09	0.18 (0.47)[c]	1.17	33.65	31.70	36.65	35.65	34.30[b]

[a] Data of [20, 21]. [b] Data of [3]. [c] Parameter of polymeric water.

Table 6. Parameters of solvatochromic equations for nitro azoles in amphiprotic ($\nu_{max}^{am} = \nu_0 - s\,\pi^* + a\,\alpha$) and aprotic protophilic media ($\nu_{max}^{pr} = \nu_0 - s\,\pi^* - b\,\beta$)

Comp. no.	ν_0, cm^{-1}	s, cm^{-1}	a (b), cm^{-1}	r	s	n
			Amphiprotic medium			
I	34920±130	3380±110	2100±160	0.992	70	9
III	33590±80	3260±100	1490±140	0.992	60	12
VII	37850±90	2500±90	1310±130	0.988	60	11
X	36690±90	2440±90	1390±130	0.987	60	11
XI	35870±110	2740±110	1270±160	0.985	70	11
			Aprotic protophilic medium			
I[a]	37410±100	3620±130	(860±70)	0.995	40	12
VI[b]	42300±100	3310±140	(1520±130)	0.985	100	16
VIII[c]	38970±100	1870±90	(1840±160)	0.985	70	11
IX[d]	37600±50	1740±70	(1230±70)	0.994	40	12
XVI[e]	41610±90	3760±150	(200±150)	0.991	90	9
XXIII[c, f]	34690±30	3290±70	(800±100)	0.999	50	7

[a] The coefficients were calculated with account taken of the term –(920±170)ξ. [b] The coefficients were calculated with the use of the data additional to those given in [5] (see text) with account taken of the term –(1650±140)ξ. [c] On the basis of the data of [3]. [d] The term –(330±70)ξ was included. [e] Data of [8]. [f] The results of processing of the experimental data for inert, protophilic, and amphiprotic solvents.

Specific solvatochromic effect in aprotic and amphiprotic media. Specific solvatochromic effect arising from interaction with an amphiprotic solvent is among the factors determining spectral shifts of both N-substituted nitroimidazole **III** and solvate H-complex of compound **I** (involving NH···O hydrogen bond. In the established range of variation of π^* ($\pi^* > 0.45$), Eq. (14) including the parameter β for liquid water was found to be valid for 4-nitroimidazole.

$$\nu_{max}^{am} = (35\,120 \pm 480) - (3440 \pm 180)\pi^* - (140 \pm 300)\beta + (2020 \pm 250)\alpha;\ r = 0.991,\ s = 70,\ n = 9. \quad (14)$$

Here, α is the Kamlet–Taft parameter which characterizes the proton-donor power of the solvent in an H-complex with the solute. Unlike Eq. (6), the regression coefficient standing before β in Eq. (14) is statistically insignificant. This means that the NH···O hydrogen bond equally contributes to the energies of stabilization by amphiprotic solvent of the ground electronic and Franck–Condon excited states.

The two-parameter (π^* and α) description of the solvatochromism of azole **I** gives much smaller errors in the determination of the free term and regression coefficients (Table 6). The positive sign of the coefficient a at the parameter α indicates weakening of the N···HO hydrogen bond upon electronic excitation of the solvate complex. The value of a for 4-nitroimidazole is appreciably larger than those for N-substituted nitro azoles (Table 6). Thus, the total specific solvatochromic effect at the long-wave UV absorption band of 4-nitroimidazole is a nonadditive quantity.

Quantitative comparison of the solvatochromic parameters of 4-nitroimidazole and N-substituted nitro azoles **III**, **VII**, **X**, and **XI** (Table 6) indicates a close analogy between the NH···O solvate complex and molecules which interact with amphiprotic solvent through the pyridine-like nitrogen atom (the role of nitro azole solvation at the nitro group was discussed in [3].

As noted above, it is very important to consider the nature of electronic transition while analyzing specific solvatochromic effect in protophilic ($\Delta\nu_n = b\,\beta$) and protophobic solvents ($\Delta\nu_n = a\,\alpha$). It was determined in terms of the AM1(CI) and CNDO/S semiempirical calculations [33, 34], for nonempirical calculations, e.g., HF/6–31G*(CI), afford a large disagreement between the theoretical and experimental frequencies. The results of calculations showed that the nature of electronic transition changes in the series of *C*-nitro derivatives of 1,2- and 1,3-diazoles (Fig. 3). The reason is a sharp variation of the energy gap separating the HOMO-1 and HOMO-2 levels upon isoelectronic replacement of the CH group in position *2* or *3*(*4*) of the five-membered ring by pyridine-like nitro-

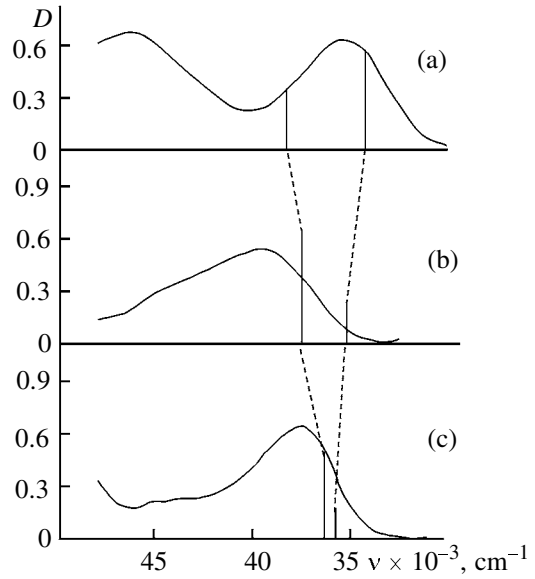


Fig. 3. Experimental and theoretical electronic absorption spectra of compounds (a) **II**, (b) **VII**, and (c) **IX**. Bands corresponding to the low-energy π,π^* transitions were recorded in cyclohexane. The transition energies were calculated in the AM1(CI) semiempirical approximation, and the intensities (relative units), in the CNDO/S approximation.

gen atom (Fig. 4). The difference in the orbital energies of nitro azoles **I**–**III**, calculated by the HF/6–31G* method, is 1.88, 1.71, and 1.89 eV, respectively; the corresponding difference for nitropyrazoles **VI** and **VIII** is 0.67 and 0.51 eV, respectively. An analogous trend is observed for the differences in the first and second ionization potentials determined by photoelectron spectroscopy. These differences are 1.20 and 1.10 eV for nitroimidazoles **II** and **IV** and 0.38 and 0.35 eV for nitropyrazoles **IX** and **XI** [10, 11]. Variation of the difference between the HOMO-1 and HOMO-2 levels is also favored by the different degrees of mixing of low-symmetry orbitals which are transformed according to irreducible representations (b_1 and a_2) of the C_{2v} point symmetry group. The long-wave absorption band of 4-nitroimidazole and 3-nitro-1,2,4-triazole (which is related to the former in the arrangement of occupied π orbitals) correspond to one-electron π,π^* transition leading to the $...\pi_4^2\pi_5^1\pi_6^1$ charge-transfer electronic configuration. The low-energy electronic transition in 3- and 4-nitropyrazoles is multielectron (see, e.g., [5]), and the $...\pi_4^1\pi_5^2\pi_6^1$ electronic configuration is responsible for charge redistribution (electron density transfer from the heteroring to the nitro group; Fig. 4). In the

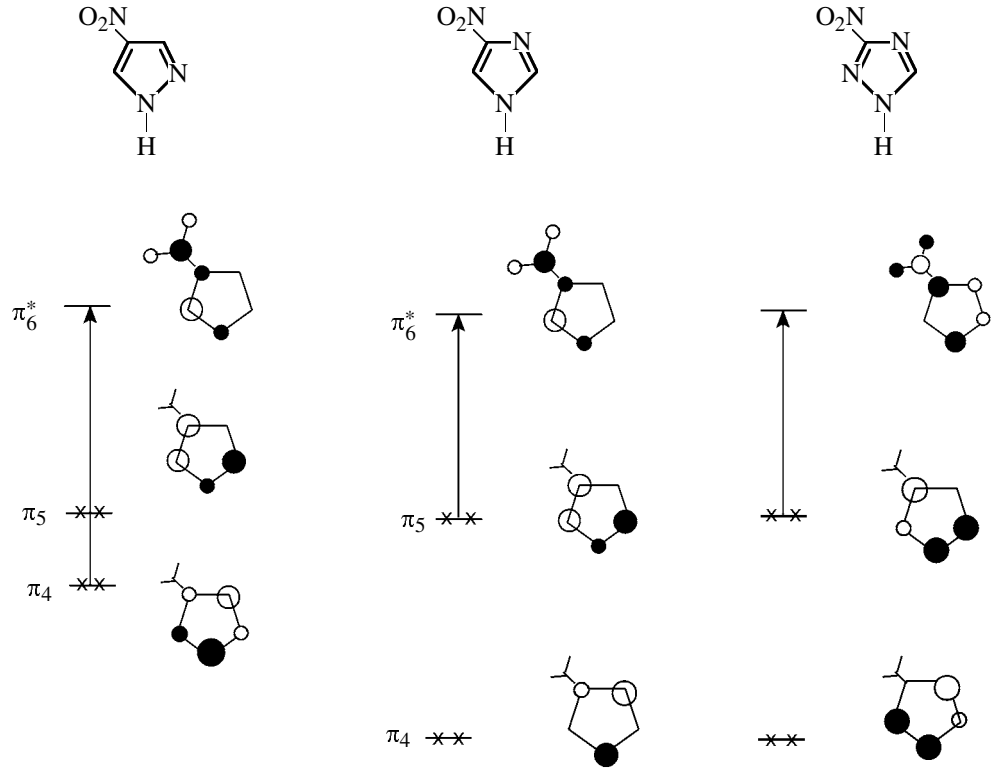


Fig. 4. Orbital diagrams for 4-nitropyrazole, 4-nitroimidazole, and 3-nitro-1,2,4-triazole. Shown are electronic transitions responsible for the position and intensity of the observed absorption band. The energy levels are arranged in a qualitative agreement with the results of HF/6–31G* nonempirical calculations and data of photoelectron spectroscopy (see text).

first case, the orbital electron density is transferred mainly from the carbon atom in position *2* of the five-membered ring, and in the second, from the pyrrole-like nitrogen atom and C^3 (Fig. 4).

According to the Franck–Condon principle, the geometry of H-complex does not change upon absorption of a quantum of light. Therefore, while considering the role of hydrogen bond in the ground electronic and Franck–Condon excited states, only electronic parameters of the solute molecule should be taken into account. Let us analyze NH···O solvate complexes, keeping in mind that excitation of the $\pi_4^2\pi_5^1\pi_6^1$ and $\pi_4^1\pi_5^2\pi_6^1$ electronic configurations differently affects the total charge on the pyrrole-like nitrogen atom. Decrease of the electron density just on that atom in *C*-nitropyrazoles in the electronically excited state should induce additional polarization of the N–H bond and should thus enhance electrostatic interactions. This means that the Franck–Condon state of the complex should be stabilized to a greater extent than the ground electronic state. Excitation of 4-nitroimidazole and 3-nitro-1,2,4-triazole at the long-wave absorption band is accompanied by orbital electron density transfer from the carbon atom neighboring to the N–H bond, and its polarization should be weaker. In keeping with the above stated, we expected that specific solvatochromic effect ($b\,\beta \approx W_e - W_g$, where W_g and W_e are the heats of formation of the H-complex in the ground and excited states, respectively) will be greater for nitropyrazoles than for 4-nitroimidazole or 3-nitro-1,2,4-triazole. In fact, the regression coefficient *b* (Table 6) is not constant, and it decreases in the series **VIII** > **VI** > **XXIII** and **IX** ≫ **XVI**. By contrast, excitation of both configurations ($\pi_4^2\pi_5^1\pi_6^1$ and $\pi_4^1\pi_5^2\pi_6^1$) does not change the total charge on the pyridine-like nitrogen atom of *C*-nitro azoles to an appreciable extent but reduces the electron density on the neighboring carbon atom, i.e., polarization of the C=N bond increases. Thus, we can presume that electronic excitation of H-complexes with N···HO hydrogen bond approximately equally destabilizes their Franck–Condon charge-transfer state. As follows from the data in Table 6, the regression coefficients *a* for *N*-methyl derivatives of nitro azoles are approximately similar.

EXPERIMENTAL

4-Nitroimidazole was synthesized by the procedure described in [35], mp 182–183°C (decomp.). The procedures for preparation of compounds **II** and **III** were reported in [36, 37]; mp 133–134°C (decomp.) (**II**), 308–310°C (decomp.) (**III**). Compounds **I**–**III** were purified by recrystallization from water and ethanol. Their purity was checked by physicochemical methods.

The UV spectra were recorded on a Specord UV-Vis spectrophotometer at 22–25°C. The dielectric permittivities of solutions were measured with the aid of a Sh2-5 instrument (Experimental Design Office of Automation Joint–Stock Company, Angarsk) at a frequency of 1 MHz. The dipole moments were calculated according to Higashi [38]. Quantum-chemical calculations of the electronic transition energies were performed in the AM1 approximation [33] with inclusion of configurational interactions. Total of 200 configurations arising from electronic excitation from six occupied molecular orbitals to six vacant orbitals were considered. Nonempirical calculations (HF/6–31G*) of the energy parameters and dipole moments of the initial azoles anf their H-complexes with solvents were performed using the GAUSSIAN 98 software package [39].

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