SPECTROSCOPIC STUDY OF 1-CYANOACETYL-2-ALKYLHYDRAZINES AND THEIR RING ISOMERS — 1-ALKYL-5-AMINO-3-PYRAZOLONES

R. É. Valter, É. A. Baumanis, L. K. Stradynya, and É. É. Liepin'sh

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The structures of 1-cyanoacetyl-2-alkylhydrazines and their ring isomers, viz., 1-alkyl-5-amino-3-pyrazolones, to which they are readily cyclized, were investigated by IR, UV, and PMR spectroscopy.

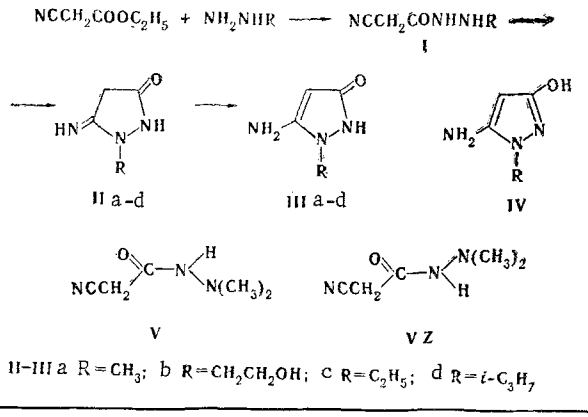
The aim of the present research was a spectroscopic study of the previously obtained [1] products of the cyanoacetylation of alkylhydrazines, to which 1-cyanoacetyl-1-alkyl- and 2-alkylhydrazine structures were assigned on the basis of their chemical properties.

It is known [2] that the acylation of monoalkylhydrazines may lead to both isomers. The data relative to the struture of N-alkylcyanoacethydrazides are contradictory. The problem is complicated by the possibility of their subsequent cyclization, as well as by the tautomeric transformations of the resulting pyrazolones [3, 4]. Thus Weissberger and coworkers [5] in the reaction of cyanoacetic ester with methylhydrazine isolated two compounds, which were identified as products of cyclization of 1-cyanoacetyl-1-methyl- and 2-methylhydrazines, viz., 1-methyl-3-hydroxy-5-pyrazoloneimine and 1-methyl-3-amino-5-pyrazolone. In a systematic study [3, 6, 7] of the reactions of α-alkyl- and α,α-dialkylcyanoacetic esters with hydrazine and substituted hydrazines it was established that α-alkylcyanacethydrazides are isomerized under alkaline catalysis conditions to 3-amino-4-alkyl-5-pyrazolones. 1,4-Dimethyl-5-amino-3-pyrazolone was obtained by acylation of methylhydrazine with 2-cyanopropionic ester [3].

We have found that an intense C=O band (amide I), as well as an amide II band [2] and N—H and C≡N bands, are observed in the IR spectra of 1-cyanoacetyl-2-methyl- and 2-(2-hydroxyethyl)hydrazines (Ia, b), as well as 1-cyanoacetyl-2,2-dimethylhydrazine (V, Table 1).

The PMR spectra of hydrazides Ia, b (Table 1) contain signals of N^1H, N^2H, and CH_2 protons and of an alkyl substituent attached to N^2. On the basis of the PMR spectrum one can make an unambiguous selection between the 1-cyanoacetyl-1-alkyl- and 2-alkylhydrazine structures in favor of the latter, and this confirms the presence of a spin—spin coupling constant between N^2—H and the CH_3 (Ia) or CH_2 (Ib) protons of the alkyl substituent.

The doubling of all of the signals that is observed in the PMR spectrum of 1-cyanoacetyl-2,2-dimethylhydrazine (V), which was used as a fixed model of the open structure, is due [8] to slow (on the PMR time scale) rotation about the CO—NH bond and the existence



II–III a R = CH_3; b R = CH_2CH_2OH; c R = C_2H_5; d R = i-C_3H_7

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TABLE 1. IR and PMR Spectra of 1-Cyanoacetyl-2-methyl-, 2-(2-Hydroxyethyl)-, and 2,2-Dimethylhydrazines

Compound	mp, °C [1]	IR spectrum, cm^{-1}					PMR spectra in d_6-DMSO, ppm			
			C=O	amide II	NH	C≡N	N^1H, 1H, s	N^2H, 1H	CH_2, 2H, s	N^2-Alkyl
Ia	86—87	Nujol	1693	1588 sh 1554, 1528	3318, 3247 sh 3182, 3080	2261	8,76	4,72 q (J=5 Hz)	3,66	2,45 (3H, d, J=5 Hz)
		Dioxane	1701	1530						
		DMSO	1686	1572						
Ib*	91—92	Nujol	1660	1594, 1563, 1524	3288 sh 3246 sh 3170	2260	8,69	4,65 t (J=5 Hz)	3,65	5,25 (1H, s, OH), 3,53 (2H, m, NCH_2), 2,83 (2H, t, J=6 Hz OCH_2)
		DMSO	1688	1578, 1520						
V	115	Nujol	1694 sh 1676	1570	3206	2260	9,05, 8,84	—	3,33, 3,64	2,55 and 2,58 [6H, s, $N(CH_3)_2$]
		Dioxane	1703							

*According to the UV spectrum, this compound contains 12% of ring isomer III.

in solution of two conformers (E and Z). Judging from the intensities of the signals, the E:Z ratio in d_6-DMSO at room temperature is 2:1.

Absorption above 220 nm in the UV spectra of hydrazide Ia and the model compound with an open structure (V) in ethanol is absent.

Thus these data confirm the structure of the previously synthesized hydrazides Ia, b. However, the second group of compounds obtained by acylation of alkylhydrazines with cyanoacetic ester by heating and characterized [1] as 1-cyanoacetyl-1-alkylhydrazines actually have the structure of ring isomers of 1-cyanoacetyl-2-alkylhydrazines.

Two intense bands at 1640 (C=O) and 1575 cm^{-1} (C=C) are observed in the IR spectra of aminopyrazolones IIIa-d in DMSO (Table 2). This picture is in agreement with the data in [9] regarding the absorption of five-membered cyclic aminovinylcarbonyl compounds and makes it possible, in our opinion, to choose between tautomeric forms III and IV in favor of the former. The IR spectra of crystalline IIIa-d at 1500-1700 cm^{-1} and 2600-3400 cm^{-1} have diffuse character with weakly expressed bands; this can be explained by the formation of strong intermolecular hydrogen bonds [4].

Signals of protons of NH_2 and CH groups are observed in the PMR spectra of pyrazolones IIIa-d (Table 2), and this unambiguously excludes the possibility of the existence of the investigated compounds of three of the tautomeric imino forms of the five proposed in [4] for 1-alkyl-5-amino-3-pyrazolones. However, the signal of an N^2H proton is not observed in the spectrum of a solution in d_6-DMSO; this is evidently explained by the relative high NH acidity and rapid proton exchange. Consequently, the PMR spectrum does not make it possible to choose between the III and IV structures.

It should be noted that the compound characterized in [5] as 1-methyl-3-hydroxy-5-pyrazoloneimine has the same melting point (180-182°C) as that of pyrazolone IIIa that we synthesized. They are evidently identical compounds, and the PMR data presented above refutes the imino structure proposed in [5].

An intense absorption maximum at 244 nm is observed in the UV spectra of pyrazolones IIIa-d (Table 2), and this is in agreement with the data in [3] for 1,4-dimethyl-5-amino-3-pyrazolone. This band can be used as an analytical band in the determination of the quantitative composition of the investigated mixtures of isomers.

The I→III isomerization is realized in refluxing ethanol, as well as in a 0.05 M aqueous solution of sodium carbonate or slowly even in an aqueous phosphate buffer solution (pH 7.4) at room temperature. Even recrystallization of hydrazide Ia from ethanol leads to its contamination with ring isomer IIIa.

TABLE 2. IR, UV, and PMR Spectra of 1-Alkyl-5-amino-3-pyrazolones

Compound*		IR spectra, cm^{-1}		UV spectra in ethanol		PMR spectra in d_6-DMSO, ppm		
		bands at 1500-1800 cm^{-1}	NH, OH	λ, nm	lg ε	NH_2, 2H, s	=CH, 1H, s	N-alkyl
IIIa	Nujol	1651, 1527, 1570	3337, 3140, 2790	243	4,16	5,1	4,52	3,19 (3H, s, NCH_3)
	DMSO	1640, 1547, 1520						
IIIb	Nujol	1664, 1593, 1521	3324, 3154, 2844	244	4,18	5,4	4,44	3,56 (4H, s, CH_2CH_2O), 5,4 (OH)
	DMSO	1638, 1564, 1550 sh, 1515						
IIIc	Nujol	1660, 1604, 1564, 1528	3306, 3122, 2834	244	4,21	5,5	4,38	3,47 (2H, q, J=6,8 Hz, NCH_2), 1,09 (3H, t, J=6,8 Hz, CH_3)
	DMSO	1638, 1574, 1548 sh., 1518						
IIId	Nujol	1653, 1600, 1563, 1500	3346, 3146, 2806	244	4,23	5,6	4,36	4,00 (1H, septet, J=6,4 Hz, NCH), 1,08 (6H, d, J=6,4 Hz, $2CH_3$)
	DMSO	1638, 1573 1548 sh., 1512						

*The compounds had the following melting points [1]: IIIa 180-181°C, IIIb 170-171°C, IIIc 247-249°C, and IIId 271-272°C.

Thus hydrazides I are formed in the condensation of cyanoacetic ester with alkylhydrazines in the cold, whereas heating of the reaction mixture leads to the I→III isomerization.

EXPERIMENTAL

The IR spectra of suspensions of the compounds in Nujol or hexachlorobutadiene or $5 \cdot 10^{-2}$ M solutions of the compounds in dioxane and DMSO were recorded with a Specord 75-IP spectrometer. The UV spectra of $2 \cdot 10^{-4}$ M solutions of the compounds in ethanol were recorded with a Specord UV-vis spectrophotometer.* The PMR spectra of 10^{-2} M solutions of the compounds were obtained with a Bruker WH-90/DS spectrometer (90 MHz) with hexamethyldisiloxane as the internal standard.

1-Cyanoacetyl-2-alkyl- and 2,2-Dimethylhydrazines (Ia, b, V). These compounds were obtained by condensation of cyanoacetic ester with alkylhydrazines at −5°C by the method in [1].

1-Alkyl-5-amino-3-pyrazolones (IIIa-d). These compounds were obtained by realization of the above-mentioned condensation in refluxing anhydrous ethanol.

The Ia→IIIa Cyclization. A solution of 1 g of cyanacethydrazide Ia in 20 ml of ethanol was refluxed for 3 h. After 24 h, 0.7 g (70%) of pyrazolone IIIa, with mp 180-181°C, was separated. No difference was observed in the case of a mixed-melting-point determination.

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RESEARCH ON THE CHEMISTRY OF 2-HETARYLBENZIMIDAZOLE.

3.* REACTION OF 1-METHYL-2-(5'-METHYL-2'-HETARYL)BENZIMIDAZOLES WITH ELECTROPHILIC REAGENTS

M. M. El'chaninov, A. M. Simonov, V. P. Kosenko, and L. Ya. Oleinikova

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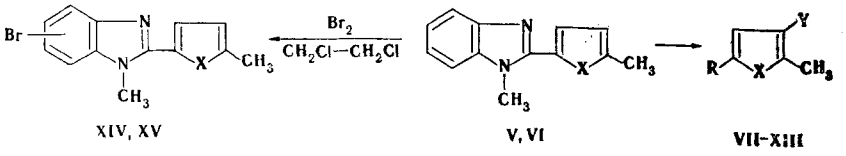
A number of new derivatives of 1-methyl-2-(5'-methyl-2'-hetaryl)benzimidazole were synthesized by electrophilic substitution. The substituent enters the β position of the 4'-hetaryl ring. A furan ring that contains a methyl group in the 5' position undergoes profound destructive oxidation under the influence of acetyl nitrate. Depending on the conditions, bromination leads to the formation of bromo derivatives that are substituted in the benzene or hetaryl ring.

We have previously studied the transformations that occur under the influence of electrophilic reagents on 1-methyl-2-(2'-furyl)- and 1-methyl-2-(2'-thienyl)benzimidazoles (I, II) [1].

We decided to study the effect of a methyl group in the 5 position of the hetaryl ring on the stability of the latter and the orientation of the electrophilic reagent.

2-(5'-Methyl-2'-furyl)- and 2-(5'-methyl-2'-thienyl-benzimidazoles (III, IV) were previously obtained by the reaction of o-phenylenediamine with 5'-methylfurfural and 5-methyl-2-formylthiophene [2]. The products of their methylation (V and VI) were subjected to the action of bromine in dichloroethane and polyphosphoric acid, acetyl nitrate, a mixture of sulfuric and polyphosphoric acids, and paraformaldehyde in the presence of concentrated hydrochloric acid.



XIV, XV V, VI VII-XIII

V, VII—IX, XIV X=O; VI, X—XIII, XV X=S; VII, X Y=Br; VIII, XI Y=SO_3H; IX, XII Y=CH_2OH; XIII Y=NO_2; R=1-methyl-2-benzimidazolyl

In contrast to I, the furan ring in V is considerably less resistant to the action of acetyl nitrate and undergoes profound destructive oxidation, the products of which undergo subsequent conversion to nitro polymers. Compound VI is nitrated relatively smoothly in the 4' position of the thiophene ring, and the product is obtained in 57% yield.

The chloromethylation of V and VI proceeds with great difficulty. Carrying out the reaction at 70-80°C for 20 h gives the chloromethylation products in low yields, and the products, as a consequence of contamination by the starting compounds, can be isolated only in the form of the hydroxymethyl derivatives.

In contrast to chloromethylation, the action of a mixture of sulfuric and polyphosphoric acids on V and VI leads to the 4'-sulfo derivatives in high yields.

*See [7] for Communication 2.

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