HETEROCYCLIC ANALOGS OF PLEIADIENE

XXXIII.* TAUTOMERISM OF 2-ACETAMIDOPERIMIDINES AND THEIR IMIDAZOLE ANALOGS

A. F. Pozharskii, A. A. Konstantinchenko, and I. S. Kashparov

UDC 547.856.7: 781.785: 543.422.4

It was established by IR and PMR spectroscopy that 2-acylamino-1-alkylperimidines and 2-acetamido-1-methylnapth[2,3-d]imidazole exist in the nonaromatic acylimino form in the crystalline state and in solution. 2-Acetamido-4,5-diphenylimidazole exists in the acylamino form in the solid state and in solution. 2-Acetamido derivatives of 1-methylbenzimidazole and 1-methyl- and 3-methylnapth[1,2-d]imidazoles, for which a shift to favor the acylimino form is observed only in solution, occupy an intermediate position. It is concluded that the relative aromaticities of the heterosystems and the strength of the intramolecular hydrogen bond in the imino form affect the position of the tautomeric equilibrium.

2-Aminoperimidines differ from other N-heteroaromatic amines with respect to the extremely high (~ 2% in solution) percentage of the imino form in their tautomeric mixtures [2]. One therefore might have expected that their N-acetyl derivatives would exist completely in the imino form, in contrast to the other amines, for which it is usually necessary to introduce a haloacetyl group to effect a complete shift of the equilibrium to favor the imine [3, 4]. In this connection, in the present research we studied the tautomerism of 2-acetamido- and 2-benzamido derivatives of perimidine. In addition, for comparison we studied the tautomerism of 2-acetamido derivatives of naphth[2,3-d]imidazole, naphth[1,2-d]imidazoles, benzimidazole, and 4,5-diphenylimidazole.

2-Acetamidoperimidines

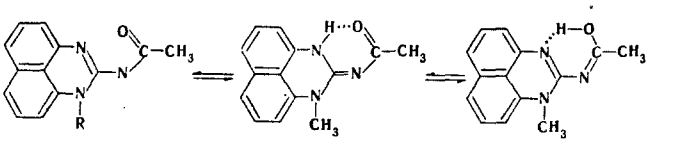
1-Alkyl-2-acetamidoperimidines (I-III) theoretically can exist in three tautomeric forms: the acetamido (Ia-IIIa), acetimido, (Ib-IIIb), and imidol (Ic-IIIC) forms. The data from the IR (Table 1) and PMR (Table 2) spectra make it possible to unambiguously exclude the Ia form. In fact, the bands of stretching vibrations of free and even associated NH groups are absent in the IR spectrum of 1-methyl-2-acetamidoperimidine (I) in both the crystalline state and in a dilute solution in chloroform (Fig. 1, spectra a and b); this constitutes evidence for very strong chelation of the NH proton, which is possible only in the Ib or Ic form. The low-field position of the chemical shift of this proton in the PMR spectrum of I in $CDCl_3$ (δ 13.45 ppm; the signal vanishes when a drop of D_2O is added to the solution) also speaks in favor of chelation of this type. Another characteristic feature of the IR spectrum of I is the strong shift of the $\nu_{C=O}$ band to the low-frequency side. The spectrum of I contains three peaks at 1500-1700 cm^{-1}. The peak of medium intensity at 1650 cm^{-1} evidently belongs to the stretching vibrations of the C=N bond in the Ib form. The bands at 1610 and 1590 cm^{-1} have high intensities. The first band is typical for 2,3-dihydroperimidine structures [1], such as that of the Ib form, and most likely is related to the stretching vibrations of aromatic C=C bonds activated by peri-amino groups. Thus the band at 1590 cm^{-1} in the spectrum of I can be assigned to $\nu_{C=O}$.

We synthesized fixed model forms IV and V, which correspond to tautomers Ia and Ib. The $\nu_{C=O}$ band in the IR spectrum of IV is found at 1690 cm^{-1} (Fig.1), i.e., in the usual region for amides of this type [3, 4]. On the other hand, the intense peak at 1510 cm^{-1} in the spectrum of fixed acetylimine V evidently belongs to the $\nu_{C=O}$ vibrations (Fig. 1). The $\nu_{C=O}$ bands in the spectra of 1,3-dimethyl-2-acetimidobenzimidazoline [5] and 1,3-dimethyl-2-acetimido-4,5-diphenylimidazoline (XI) are found in precisely this region (Table 1).

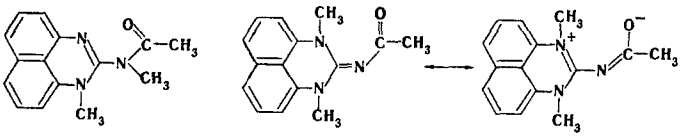
*See [1] for communication XXXII.

Rostov State University. Scientific-Research Institute of Physical and Organic Chemistry, Rostov-on-Don 344006. Novocherkassk Polytechnic Institute, Novocherkassk 346400. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 113-121, January, 1978. Original article submitted January 26, 1977.

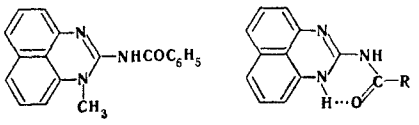
0009-3122/78/1401-0093$07.50



I-III a I-III b I-III c



IV Va Vb



VI VII, VIII

I, VII R=CH_3; II R=C_2H_5; III R=CH_3; VIII R=C_6H_5

Such a pronounced shift of the carbonyl absorption to the low-frequency region is explained [5] by the considerable contribution of dipolar structures of the Vb type to the resonance hybrid. The contribution of a limiting structure of the Vb type in structure Ib is evidently smaller because of the hydrogen atom attached to the endocyclic N atom, and the $\nu_{C=O}$ band in the spectrum of Ib therefore occupies a position intermediate between the $\nu_{C=O}$ bands in the spectra of IV and V.

The differences in the chemical shifts of the aromatic ring protons in the spectra of I, IV, and V are extremely characteristic. The 4-H and 9-H protons give two quartets with markedly different chemical shifts in the PMR spectrum of model acylamino form IV (Table 2); this is typical for 1-substituted perimidines [6]. The 4-H and 9-H protons in the PMR spectrum of acetylimine V are chemically and magnetically equivalent and give one quartet with an intensity of two proton units. These protons also give one quartet in the spectrum of I, i.e., although they are chemically nonequivalent, their magnetic environments are almost identical. This fact makes it possible to exclude the Ia structure and evidently the Ic structure for 1-methyl-2-acetamidoperimidine, leaving only chelated imine structure Ib as the correct structure.

The IR spectra of II and III, as well as 1-methyl-2-benzamidoperimidine (VI) and 1-methyl-2-acetamidoaceperimidine [7], differ little from the spectrum of I. Weak absorption at 2700-3200 cm^{-1} is observed only for the spectra of solutions of III and IV in chloroform; this indicates less chelation of the proton in these cases.

A study of the tautomerism of 2-acetamido- (VII) and 2-benzamidoperimidine (VIII) led to somewhat unexpected conclusions. Solutions of these compounds (Fig. 1 and Table 1) give bands of both associated (2600-3350 cm^{-1}) and free (ν_{NH} 3435 and 3440 cm^{-1} for VII and VIII, respectively) NH groups; the position of the latter is typical for 2-amino- [2] and 2-alkylaminoperimidines [8] but differs from the position in the spectrum of 1,3-dimethyl-2-imino-2,3-dihydroperimidine (ν_{NH} 3375 cm^{-1}) [2]. In addition, the $\nu_{C=O}$ band in the spectrum of VII is found at 1702 cm^{-1}, as compared with 1640 cm^{-1} for VIII. On the basis of this, it may be concluded that VII and VIII exist in the amino form. There is no doubt that the latter is realized owing to an intramolecular hydrogen bond (IHB) between the pyrrole NH group and the carbonyl oxygen atom. In 1-alkyl-2-acetamidoperimidines (I-III, VI) the loss in energy on passing to the nonaromatic imino form is evidently more than compensated for by the gain in energy due to the formation of a strong IHB. In VII and VIII there is a possibility for the formation of IHB with the simultaneous retention of the aromatic structure of the ring, and this also ensures their existence in the amino form.

Interesting conclusions regarding the structure of 2-acetamidoperimidines can be drawn on the basis of their color. It is known that perimidines are bright-yellow compounds, whereas 2,3-dihydroperimidines are colorless compounds. Colorless 2-aminoperimidines constitute the only exception in the perimidine series [2, 7, 8]. We have previously expressed the opinion that the low-intensity band at 400 nm, which is responsible for the color of perimidines but does not follow Beer's law, is due to the formation of intermolecular aggregates of the CTC (charge-transfer complex) type [9]. In these aggregates charge is transferred from the negatively charged naphthalene fragment of one molecule of the corresponding perimidine to the effectively positively charged heteroring of another molecule and vice versa (perimidines are the strongest π donors and

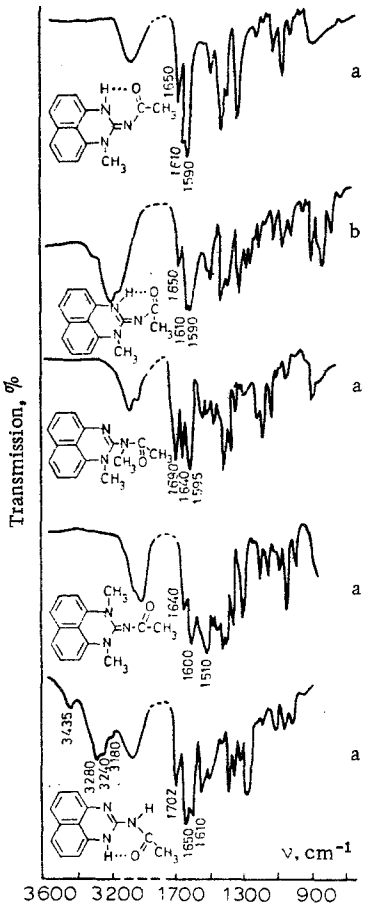


Fig. 1. IR spectra of 2-acetamidoperimidines: a) in chloroform; b) in mineral oil.

good electron acceptors [6, 10]). The disappearance of color in the case of 2-aminoperimidines can be explained by the fact that the positive charge of the heteroring in them is reduced substantially because of the ^{+}M effect of the amino group, which prevents intermolecular charge transfer. The fact that IV is yellow provides evidence in favor of this explanation. It is logical to imagine that the N-acetyl group in IV prevents migration of the pair of electrons of the N atom to the heteroring, as a result of which positive charge sufficient for the formation of a CTC is retained in the latter. Compounds VII and VIII are also yellow; this, in the light of what we have said above, constitutes additional evidence in favor of their amino structure. On the other hand, all of the 1-alkyl-2-acylaminoperimidines (I-III, V, VI) are colorless; this is explained by their existence in the imino form, since they are derivatives with a 2,3-dihydroperimidine structure (2-acetamidoaceperimidines constitute an exception, since virtually all aceperimidines are yellow because of the effect of the CH_2-CH_2 bridge). The absence of color probably makes it possible to exclude for I-III the imidol structure (Ic-IIIc), which, since it is an azomethine structure, most likely would be colored, in analogy with 2-benzylideneamino-perimidines [7].

2-Acetamidoimidazoles

According to the IR spectroscopic data (Fig. 2, spectrum a), 1-methyl-2-acetamido-4,5-diphenylimidazole in chloroform solution exists exclusively in the acylamino form (IXa), to which the intense $\nu_{C=O}$ band at 1732 cm^{-1} and the band of stretching vibrations of free NH groups at 3425 cm^{-1} correspond. The $\nu_{C=O}$ band of model acylamino form X is found in the same region (1690 cm^{-1}), whereas the $\nu_{C=O}$ band in the IR spectrum of fixed acylimino form XI is considerably lower (1550 cm^{-1}) (Table 1). Somewhat unexpectedly, two $\nu_{C=O}$ bands are present in the IR spectrum of a crystalline sample of IX (Fig.2, spectrum b). Judging from their position (1745 and 1700 cm^{-1}), they both belong to the aromatic acylamino form of IX and most likely characterize two types of bonding of the acylamino groups (XII and XIII) due to intermolecular hydrogen

TABLE 1. IR Spectra of 2-Acetamido Derivatives

Compound	ν_{NH}		$\nu_{C=O}$		$\nu_{C=N}$		$\nu_{C=C}$	
	in $CHCl_3$	in mineral oil	in $CHCl_3$	in mineral oil	in $CHCl_3$	in mineral oil	in $CHCl_3$	in mineral oil
I	—	—	1590 v.s.[a]	1590 v.s	1650 m	1650m	1610 s	1610 s
II	—	—	1590 v.s	1590 v.s	1650 m	1650m	1610 s	1610 s
III	—	—	1588 v.s	1585 v.s	1645 m	1645m	1610 s	1610 s
IV	—	—	1690 s	1680 m	1640 s	1650m	1595 s	1590 s
V	—	—	1510 s	1510s	1640 m	1640m	1600 s	1600 s
VI	3230—2800 w	—	1590 v.s	1620 s	1650 s	1650 m	1610 s	1600 s 1560 s
VII	3435 w 3275 w 3240 w 3180 w	—	1702 m	—	1650 s	—	1610 s 1555 m	—
VIII	3440 w 3280 w	—	1640 s	—	(1640)[b]	—	1610 s 1590 s	—
IX[c]	3425 w	3470 w 3200 w	1732 s	1745 m 1700 s			1610 s 1570 m	1610 1540 m
X	—	—	1690 v.s	1690 v.s			1610 m 15.0 s	1610 m 1530 s
XI	—	—	1550 s	1550 v.s			1610 s	1600 s
XIV	3300 w	3150 w 3050 w	1563 v.s 1715 w	1700 v.s	1632 m	1630 m	1600 s	1600 w 1575 s
XV	3420 w 3270 w	3260 w 3180 w	1710 m 1560 s	1700 s	1635 m	1630 m	1595 s	1610 s 1570 s
XVI	3420 w 3240 w	3460 w 3370 w 3150 w	1710 m 1565 v.s	1690 s	1640 w	1640 w	1595 s	1600 m 1560 m
XVII	3300 w	3280 w	1580 v.s	1580 v.s	1650 w	1650 w	1605 s	1590 s

[a]Abbreviations: v.s is very strong, s is strong, m is medium, and w is weak.

[b]The $\nu_{C=O}$ bands is covered. [c]In contrast to the perimidine derivatives, the bands of the stretching vibrations of the C=N bond in the spectra of IX-XI do not show up distinctly, and they are therefore not noted in the table.

TABLE 2. Chemical Shifts of the Protons in the PMR Spectra

Compound	δ, ppm (в $CDCl_3$)			
	N—CH_3	$COCH_3$	NH	aromatic ring protons
I	3,33	2,13	13,45	6,37 (q, 4- and 9-H); 7,13 (m)
IV	3,08; 3.1	2.12	—	6,15 (q, 9-H); 6,72 (q , 4-H); 7,1 (m)
V	3.42	2,17	—	6,62 (q, 4- and 9-H); 7,22 (m)
VII	—	2,05	—	6,37 (q, 4- and 9-H); 7,07 (m)
X	3,22	1,85	—	7,12 (m)
XI	3,30	2,14	—	7,20 (m)
XIV	3,55	2,20; 2,23 (6 : 1)	9.60	7,10 (m)
XVI	3,70	2.22	—	7,47 (m)
XVII	3,59	2,20	—	7,38 (m)

bonds during packing of the molecules in the crystal lattice. Association of the XII type is well known for substituted amides [11], while dimers of the XIII type may develop owing to the presence in the molecule of a highly basic pyridine heteroatom. It should be noted that none of the acylamines investigated by us (which exist in the amino form) displayed two $\nu_{C=O}$ bands in the solid form. We ascribe this to the increased basicity of the imidazole ring in 4,5-diphenylimidazole (pK_a 5.90) as compared with benzimidazole (pK_a 5.50) and naphthimidazoles (pK_a 5.2-5.3) [12], for which only an association of the XII type is characteristic because of this. Since the $\nu_{C=O}$ band for solid samples of XIV-XVII is found at 1700 cm^{-1}, the less intense $\nu_{C=O}$ band at 1745 cm^{-1}, in the spectrum of IX can be ascribed to XIII aggregates.

According to the IR spectroscopic data (Fig. 2, spectra a and b), 1-methyl-2-acetamidobenzimidazole exists in the crystal state in acylamino form XIVa ($\nu_{C=O}$ 1700 cm^{-1}) [4]; however, we have established that in solution imino form XIVb, the $\nu_{C=O}$ band of which can be observed at 1563 cm^{-1}, becomes the dominant form. The imino form evidently is in equilibrium with a small amount of amino tautomer XIVa in solution, since a low-intensity band that is difficult to assign to any other absorption is observed at 1715 cm^{-1}. The shoulder at 3420 cm^{-1}, which can be ascribed to the band of free stretching vibrations of the NH group in XIVa, also provides evidence in favor of the presence of the amino form in solution. This shoulder is found on a broad band centered at 3300 cm^{-1}, which belongs to the NH group of acylimino form XIVb with an IHB. However, the

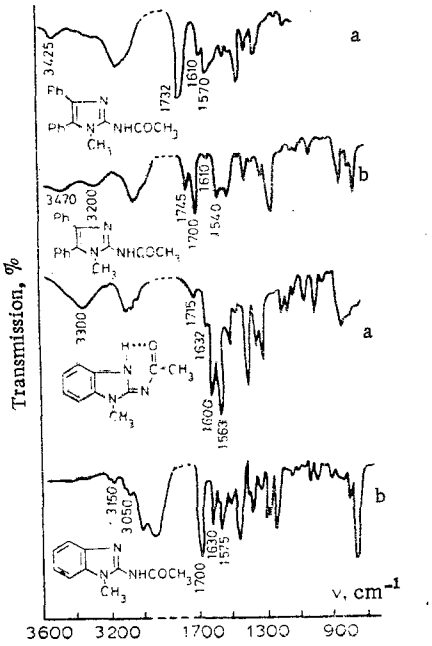


Fig. 2

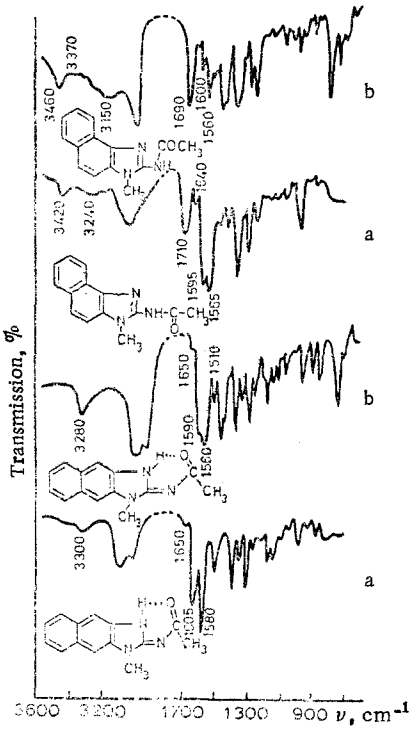


Fig. 3

Fig. 2. IR spectra of 2-acetamido derivatives of 4,5-diphenylimidazole and benzimidazole: a) in chloroform; b) in mineral oil.

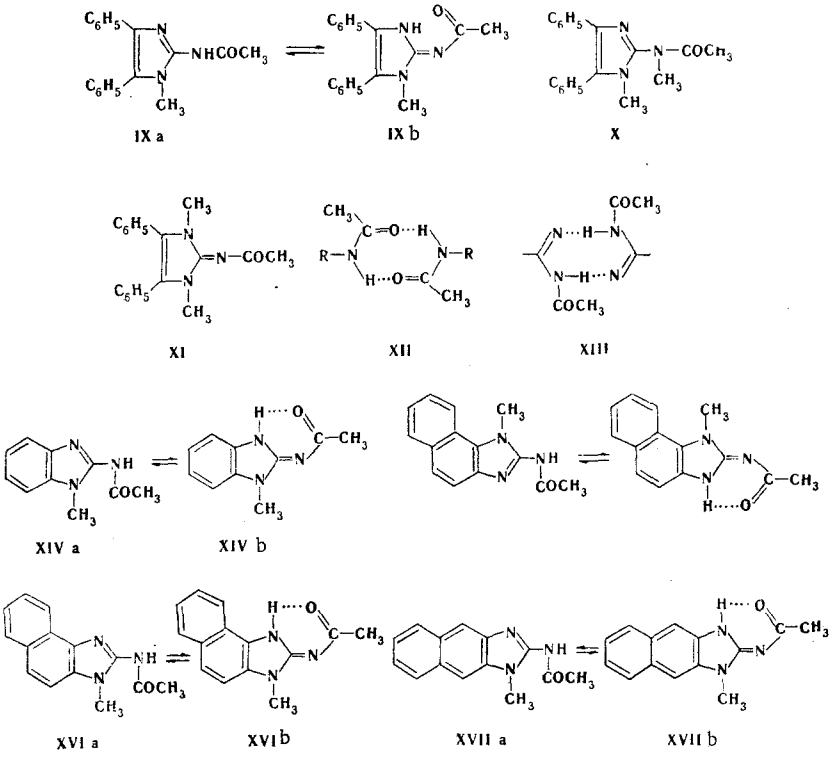
Fig. 3. IR spectra of 2-acetamido derivatives of naphthimidazoles: a) in chloroform; b) in mineral oil.

TABLE 3. Synthesized Compounds

Compound	mp, °C (solvent)	Found, %			Empirical formula	Calc., %			Yield, %
		C	H	N		C	H	N	
I	219 (water)		—	—	$C_{14}H_{13}N_3O$	—	—	—	91
II	207 (water)	71.0	6.0	16.4	$C_{15}H_{15}N_3O$	71,1	6,0	16.6	90
III	152 (water)	71,8	6,2	15.9	$C_{16}H_{17}N_3O$	71,9	6,4	15,7	93
IV	94 (octane)	71,3	6,1	16.2	$C_{15}H_{15}N_3O$	71,1	6,0	16,6	72
V	187 (ethyl acetate)	71.2	6,1	16,3	$C_{15}H_{15}N_3O$	71,1	6,0	16,6	75
VI	212 (toluene)	75,9	4,9	13,7	$C_{19}H_{15}N_3O$	75,7	5,0	13,9	80
VII	221 (toluene)	69.5	5,0	18,6	$C_{13}H_{11}N_3O$	69,3	4,9	18,7	71
VIII	236 (toluene)	74,9	4,7	14.8	$C_{18}H_{13}N_3O$	75,2	4,6	14,6	73
IX	198 (aqueous alcohol)	—	—	—	$C_{18}H_{17}N_3O$	—	—	—	90
X	161 (octane)	74,8	6.2	14,0	$C_{19}H_{19}N_3O$	74,7	6,3	13,7	80
XI	174 (octane)	74.9	6,2	13.9	$C_{19}H_{19}N_3O$	74,7	6,3	13,7	50
XIV	182 (methanol)	—	—	—	$C_{10}H_{11}N_3O$	—	—	—	90
XV	237 (ethyl acetate)	70,2	5.5	17,6	$C_{14}H_{13}N_3O$	70,3	5,5	17,5	90
XVI	190 (ethyl acetate)	70,1	5,3	17,3	$C_{14}H_{13}N_3O$	70,3	5,5	17,5	90
XVII	240 (ethyl acetate)	70,4	5.5	17,6	$C_{14}H_{13}N_3O$	70,3	5,5	17,5	90

position of this band (3300 cm^{-1}) and the PMR spectrum of XIV indicate weak chelation of the proton in imine XIVb: The chemical shift of this proton in the spectrum of a solution in $CDCl_3$ is 9.6 ppm. An interesting feature of the PMR spectrum of XIV is the splitting of the signal of the methyl protons of the $COCH_3$ group into two peaks at δ 2.20 and 2.23 ppm with a relative intensity of 7:1. These signals can also be ascribed to the acylamino and acylimino forms, respectively, but the closeness of the chemical shifts of the CH_3 and $COCH_3$ groups of the two tautomeric forms (Table 2) does not make it possible to consider this conclusion to be sufficiently reliable, although it is in agreement with the IR spectroscopic data. (See Scheme on the following page).

Judging from their IR spectra (Fig. 3 and Table 1), the 2-acetamido derivatives of 1-methyl- (XV) and 3-methylnaphth[1,2-d]imidazoles (XVI) exist in the acylamino form (XVa and XVIa) in the crystalline state,



whereas equilibrium with a certain predominance of the imino form (2 : 1) is established in solution. The presence of two $\nu_{C=O}$ signals in the spectra of solutions [for example, at 1710 cm^{-1} (the XVIa form) and 1565 cm^{-1} (the XVIb form) for XVI] constitutes evidence for this conclusion. The region of stretching vibrations of the NH group contains a band at 3420 cm^{-1}, which can be assigned to a nonassociated NH group in tautomer XVIa, and a diffuse band at 3100-3350 cm^{-1}, which is probably related to the bonded (by an IHB) NH proton in imine XVIb. We were unable to establish the signal of this proton in the PMR spectrum of XVI, evidently because of its weak chelation and the low solubility of the compound. We also did not note the splitting of the signals of the methyl groups that corresponds to the presence of two tautomers in solution. However, as we stated above, the absence of this splitting is not solid evidence for the absence of tautomerism, since the chemical shifts of the CH_3 protons in the spectra of the two tautomers are very close.

Of all the investigated imidazole compounds, 2-acetamido-1-methylnaphth[2,3-d]imidazole (XVII) (Fig. 3), which exists in imino form XVIIb with a relatively weak IHB (ν_{NH} 3300 cm^{-1}) in both the crystalline state and in solution, is closest to 2-acetamidoperimidines with respect to the character of the tautomeric transformations. Unfortunately, its insufficient solubility did not enable us to observe a PMR signal from the NH proton in its spectrum.

Thus the ratio of tautomers of 2-acetamido derivatives of perimidine and imidazoles varies over an extremely wide range: from 2-acetamido-4,5-diphenylimidazoles, which exist in the aromatic acylamino form in solution and in the crystalline state, to 2-acetamido derivatives of 1-alkylperimidines and 1-alkylnaphth[2,3-d]imidazoles, which exist in the nonaromatic acylimino form. 2-Acetyl derivatives of benzimidazole and the angular naphthimidazole, which are converted to imines only in solution, occupy an intermediate position. The chief factor that determines the position of the tautomeric equilibria of the investigated compounds is evidently the different aromaticities of the corresponding heterosystems. Thus the REPE (resonance energy per π electron) indexes showed that the aromaticities change in the following order: benzimidazole > naphth[1,2-d]imidazole > naphth[2,3-d]imidazole > perimidine [13]. This order is in good agreement with the tendency of 2-acetamido derivatives of the above heterocycles to undergo conversion to the nonaromatic imino form.

The strength of the intramolecular hydrogen bond, which stabilizes one or another tautomer, should be considered to be another important factor that affects the tautomerism. For example, this factor explains the existence of 1-unsubstituted 2-acylaminoperimidines in the amino form.

EXPERIMENTAL

The IR spectra of the compounds were recorded with a UR-20 spectrometer. The PMR spectra were recorded with a Tesla BS-467 spectrometer (60 MHz) with hexamethyldisiloxane as the internal standard.

Compounds I-III, IX, and XIV-XVII were obtained by the method that we previously described for the synthesis of I [7]. The properties of the compounds and the results of elementary analysis are presented in Table 3.

1-Methyl-2-(N-methylacetamido)perimidine (IV). A mixture of 2.1 g (0.01 mole) of 1-methyl-2-methylaminoperimidine [13] and 2 ml (0.02 mole) of acetic anhydride was stirred at 100°C for 2 h, after which it was cooled and treated with 20 ml of water and potassium carbonate. The liberated oil was extracted with 30 ml of chloroform, and the extract was dried and passed through a column filled with Al_2O_3 (elution with chloroform). The first (yellow) fraction was collected and worked up, and the residue (a yellow oil) was crystallized from octane. The yield was 1.8 g (72%).

2-Acetimido-1,3-dimethyl-2,3-dihydroperimidine (V). A solution of 1 g (5 mmole) of 2-imino-1,3-dimethyl-2,3-dihydroperimidine [7] in 3 ml (30 mmole) of acetic anhydride was heated at 100°C for 1 h, after which it was diluted with water and neutralized with potassium carbonate. The precipitated crystals of a mixture of V and 1,3-dimethylperimidone [14] were removed by filtration, washed with water, and dried. Compound V was isolated by chromatography (on Al_2O_3, elution with $CHCl_3$); the second fraction was collected (the process was monitored by TLC). The yield was 0.9 g (75%).

2-Acetamidoperimidine (VII). A mixture of 1.83 g (0.01 mole) of 2-aminoperimidine [8] and 2 ml (0.02 mole) of acetic anhydride was stirred at 100°C for 1 h, after which it was cooled, diluted with 20 ml of water, and neutralized with potassium carbonate. The resulting precipitate was removed by filtration, washed with water, and dried. The product was purified by chromatography with a column filled with Al_2O_3 (elution with chloroform). The first (yellow) fraction was collected and worked up to give 1.6 g (71%) of bright-yellow crystals of VII.

2-Benzamidoperimidines (VI and VIII). A mixture of equimolar amounts of the corresponding 2-aminoperimidine and benzoic anhydride was stirred at 100°C for 2 h, after which it was cooled and triturated with 10% potassium carbonate solution. The solid material was removed by filtration, washed with water, and dried. The benzamido derivatives were purified by two crystallizations from toluene.

1-Methyl-2-(N-methyl-N-acetyl)amino-4,5-diphenylimidazole (X). A mixture of 1.25 g (5 mmole) of 1-methyl-2-methylamino-4,5-diphenylimidazole, obtained by methylation of 2-amino-4,5-diphenylimidazole in the presence of sodium amide by the method in [15], and 1 ml (10 mmole) of acetic anhydride was heated at 100°C for 2 h, after which it was cooled, diluted with 20 ml of water, and made alkaline to pH 8 with solid sodium bicarbonate. The liberated oil was extracted with chloroform, and the extract was dried. The solvent was removed from the extract by evaporation, and the residue was crystallized from octane containing activated charcoal. The yield of X was 1.2 g (80%).

2-Acetimido-1,3-dimethyl-4,5-diphenyl-2,3-dihydroimidazole (XI). A mixture of 2.8 g (0.01 mole) of 2-acetamido-4,5-diphenylimidazole [16] and 1.3 g (0.01 mole) of dimethyl sulfate was heated at 120-130°C for 4 h, after which it was cooled and triturated with 30 ml of water. The aqueous mixture was treated with solid sodium bicarbonate, and the liberated oil was extracted with chloroform. The extract was dried and passed through a column filled with Al_2O_3. Elution with ethyl acetate gave 1.3 g (46%) of the starting compound; subsequent elution with chloroform gave 1.5 g (50%) of XI.

LITERATURE CITED

1. V. A. Anisimova, A. F. Pozharskii, L. E. Nivorozhkin, and V. I. Minkin, Khim. Geterotsikl. Soedin., No. 1, 108 (1978).
2. A. F. Pozharskii, I. S. Kashparov, Yu. P. Andreichikov, A. I. Buryak, A. A. Konstantinchenko, and A. M. Simonon, Khim. Geterotsikl. Soedin., No. 6, 807 (1971).
3. Yu. N. Sheinker, E. M. Peresleni, N. P. Zosimova, and Yu. I. Pomerantsev, Zh. Fiz. Khim., 33, 2096 (1959).
4. Yu. N. Sheinker, A. M. Simonon, Yu. M. Yutilov, V. N. Sheinker, and E. I. Perel'shtein, Zh. Org. Khim., 2, 917 (1966).
5. O. E. Shelepin, V. G. Sayapin, N. K. Chub, and A. M. Simonov, Khim. Geterotsikl. Soedin., No. 5, 674 (1970).

6. A. F. Pozharskii, I. S. Kashparov, P. J. Halls, and V. G. Zaletov, Khim. Geterotsikl. Soedin., No. 4, 543 (1971).
7. G. N. Pershin, A. F. Pozharskii, I. S. Kashparov, N. S. Bogdanov, N. A. Novitskaya, and A. L. Mikerina, Khim.-Farm. Zh., No. 2, 5 (1973).
8. I. V. Komissarov, A. A. Konstantinchenko, A. F. Pozharskii, I. T. Filippov, and I. S. Kashparov, Khim.-Farm. Zh., No. 7, 28 (1976).
9. A. F. Pozharskii, T. I. Vinokurova, and V. G. Zaletov, Khim. Geterotsikl. Soedin., No. 4, 539 (1976).
10. A. V. Lizogub, A. F. Pozharskii, and V. I. Sokolov, Zh. Obshch. Khim., 36, 680 (1976).
11. L. Bellamy, Infrared Spectra of Complex Molecules, Methuen (1958).
12. Outline of the Chemistry of Azoles [in Russian], Izd. Rostovsk. Univ., Rostov-on-Don (1965), p. 17.
13. A. I. Belyashova, N. I. Zatsepina, E. N. Malysheva, A. F. Pozharskii, L. P. Smirnova, and I. F. Tupitsyn, Khim. Geterotsikl. Soedin., No. 11, 1544 (1977).
14. A. F. Pozharskii, É. A. Zvezdina, I. S. Kashparov, Yu. P. Andreichikov, V. M. Mar'yanovskii, and A. M. Simonov, Khim. Geterotsikl. Soedin., No. 9, 1230 (1971).
15. O. Christmann, Chem. Ber., 98, 1282 (1965).
16. A. M. Simonov, and Yu. P. Andreichikov, Zh. Org. Khim., 5, 779 (1969).
17. T. Pyl, S. Melde, and H. Beyer, Lieb. Ann., 663, 108 (1963).
18. Yu. Andriechkov, Master's Dissertation, Rostov-on-Don (1970), p. 96.
19. A. M. Simonov and N. D. Vitkevich, Zh. Obshch. Khim., 30, 590 (1960).

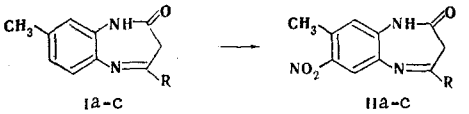
NITRATION OF 7- AND 8-METHYL-4-R-1H-2,3-DIHYDRO-1,5-BENZODIAZEPIN-2-ONES

Z. F. Solomko, T. S. Chmilenko, P. A. Sharbatyan, N. I. Shtemenko, and S. I. Khimyuk

UDC 547.892.07:542.941.7'958.1

4-R-8-Methyl-2,3-dihydro-1H-1,5-benzodiazepin-2-ones are nitrated in the 7 position, whereas their 7-methyl analogs are nitrated in the 1, 8, or 9 position. The nitration of 4,8-dimethyldihydrobenzodiazepinone proceeds as primary substitution at the N_1 atom of the amide group. The resulting N_1-nitroamide undergoes prototropic rearrangement to the 9-nitro isomer in strongly acidic media.

In the nitration of 1,5-benzodiazepin-2-ones the nitro group enters the 7 position, i.e., the para position relative to the amide grouping [1, 2]. In the present research we established that the introduction of a CH_3 group in the 8 position does not change the orientation (although one might have expected the formation of the 9-nitro isomer). The corresponding 7-nitro compounds (IIa-c) are formed in 78-93% yields from 4-substituted 8-methyl-2,3-dihydro-1H-1,5-benzodiazepin-2-ones (Ia-c) by nitration with potassium nitrate in concentrated sulfuric acid.



Ia-c IIa-c

I, II a R=CH_3; b R=C_6H_5; c R=$C_6H_4OCH_3$-*p*

The PMR spectrum of IIa contains two singlets of the 6-H and 9-H aromatic protons (7.56 and 8.57 ppm), and the observed shift of 0.77 ppm of the singlet of the methyl group of the benzene ring as compared with the signal in the spectrum of the starting benzodiazepinone Ia is in agreement with the usual shift under the in-

Dnepropetrovsk State University, Dnepropetrovsk 320625. M. V. Lomonosov Moscow State University, Moscow 117234. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 122-126, January, 1978. Original article submitted April 18, 1977.

 0009-3122/78/1401-0100$07.50