TAUTOMERISM OF 2-AMINOPERIMIDINES

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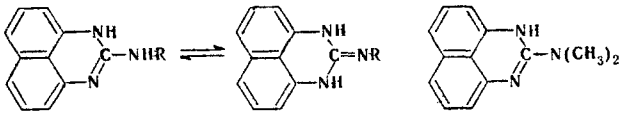
2-Aminoperimidine and substituted 2-aminoperimidines were synthesized, and their amine–imine tautomerism was studied by IR and UV spectroscopy. It is shown that 2-aminoperimidine exists in virtually only the amine form, whereas its acyl derivatives exist largely in the imine form. A complete shift of the tautomeric equilibrium is observed for the chloroacyl derivatives, which exist in the imide form in both the solid state and in solution.

The tautomerism of 1-methyl-2-aminoperimidine and 1-methyl-2-acylaminoperimidines was investigated in [1, 2]. We have studied the tautomeric forms of 2-aminoperimidine (Ia) and substituted 2-aminoperimidines (Ib-g, II) that do not have substituents in the 1 position.



I a-g II

I a R=H; b R=$(CH_2)_3CH_3$; c R=$COCH_3$; d R=$CO(CH_2)_2CH_3$; e R=COC_6H_5; f R=$COCH_2Cl$; g R=$COCCl_3$

Compound Ia was obtained by reaction of 2-chloroperimidine with ammonia via our modification of the method in [3]. The reaction was carried out in phenol with passage of dry ammonia through the reaction mixture. The acylation of 2-aminoperimidine with acid chlorides in acetone in the presence of triethylamine leads to acyl derivatives (Ic-g), the structures of which were confirmed in the case of 2-benzamidoperimidine (Ie), which was also obtained by condensation of 1,8-naphthalenediamine with benzoylcyanamide [4]. 2-Butylaminoperimidine was obtained by reaction of 2-chloroperimidine with butylamine in alcoholic HCl.

The presence of two groups of absorption bands at 230 and ~300 nm is characteristic for the UV spectra of Ia and N-substituted derivatives Ib-g (see Fig. 1). Intense absorption bands in the same spectral regions are also observed for model compounds with a fixed amine (II, 1-methyl-2-dimethylaminoperimidine [1]) or imine structure (1,3-dimethyl-2-iminoperimidine (III) [1]). It is apparent from Fig. 1 that the maxima of the absorption bands of the imine form are shifted hypsochromically as compared with the spectrum of the amine.* The band at 300 nm, which, according to [5], is related to a π,π^* transition, undergoes a large shift (~14 nm).

The position of the maxima of the bands in the UV spectrum of Ia, while differing from the position in the spectra of the model molecules, nevertheless is closer to the spectrum of an amine. These results show that in the case of Ia the equilibrium is shifted to favor the amine form, although one cannot exclude the possibility of the presence of small amounts of the imine form with respect to the UV spectral data. The UV spectrum of Ib also differs from the spectrum of model amine II. However, in this case also the UV spectra do not make

*The differences in the positions of the UV bands of the model amines and the imine cannot be substantially ascribed to the certain difference in the conditions under which the spectra of II (solution in ethanol) and III (solution in methanol) were measured, since these differences are also retained in the case of comparison of the spectra of imine III and 1-methyl-2-dimethylaminoperimidine obtained under identical conditions [1].

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it possible to speak confidently of a substantial shift of the tautomeric equilibrium to favor the imine form.

Distinct differences are observed between the UV spectra of 2-acetamidoperimidine, 2-butyrylaminoperimidine, and 2-benzamidoperimidine, on the one hand, and the spectra of both 2-dimethylaminoperimidine and 1,3-dimethyliminoperimidine, on the other. These differences are substantially greater than one might have expected within the framework of a simple additive scheme as a consequence of variation of the substituent attached to the amino group. The differences in the UV spectra can evidently be interpreted as being the result of a substantial shift in the equilibrium to favor the imine form and the presence in solution of comparable amounts of both tautomeric forms. In addition, one cannot exclude the possibility of interaction of the substituent and the perimidine ring through the "nitrogen bridge," which, although it should not determine the general form of the spectrum, may have an effect on it (see the review in [6]). The UV spectra of the chloro- and trichloroacyl derivatives of Ia and the model imine evidently differ for this reason, although according to [7], one might have expected a complete shift of the tautomeric equilibrium to favor the imine form in the case of If,g. Thus, an examination of only the UV spectral data does not make it possible to solve the problem unambiguously.

Bands at 3460, 3440, and 3350 cm^{-1} are observed in the IR spectrum of a chloroform solution of Ia in the region of NH vibrations, and bands at 1660, 1638 cm^{-1}, etc., are observed in the region of multiple bond vibrations. Partial deuteration leads to a significant decrease in the intensities of the bands at 3460, 3440, 3350, and 1660 cm^{-1}. In addition to new bands in the 2400 cm^{-1} region that are characteristic for ND vibrations, a band appears at 3400 cm^{-1}. According to [8], the presence of this sort of band in the spectrum of the partially deuterated product is due to the NHD group and serves as evidence for affiliation of the band at 3460 cm^{-1} with the asymmetrical stretching vibrations of the NH_2 group and of the band at 3350 cm^{-1} with the symmetrical stretching vibrations of the NH_2 group (the band at 3440 cm^{-1} is affiliated with the "pyrrole" NH group). The substantial effect of deuteration on the intensity of the band at 1660 cm^{-1} makes it possible to assign it to an NH_2 in-plane deformation vibration. The band at 1638 cm^{-1} in the spectrum of Ia remains unchanged when the compound is deuterated. It may therefore be asserted that it is due to the endocyclic amide C=N bond.* Bands of the absorption characteristic for an imide could not be detected in the IR spectrum of Ia. The data obtained in this study make it possible to estimate the possible upper limit of the percentage of the imine form (which does not exceed 5%) in samples of Ia and to confirm the above conclusion regarding the existence of Ia primarily in the amine form. This is in agreement with the quantitative results found for 1-methyl-2-aminoperimidine [1], which, however, Pozharskii and co-workers regard as approximate. Thus the presence of a substituent in the 1 position evidently does not have a substantial effect on the tautomeric equilibrium of 2-aminoperimidine.

According to the data in [7], acylation of the amino group shifts the tautomeric equilibrium to favor the imine form. In fact, two bands at 1643 and 1632 cm^{-1} are observed in the IR spectra of N-acetyl-, N-butyryl-, and N-benzoylperimidines in the region of the frequencies of C=N vibrations. According to [1], the first band can be assigned to the vibration of the endocyclic C=N bond of the amine form, and the second can be assigned to the exocyclic C=N bond of the imine. The presence of comparable amounts of both tautomers in solutions of acyl derivatives of Ia also follows from an examination of the frequencies of the carbonyl absorption. According to [9], the more intense band at 1680 cm^{-1} is characteristic for the amide group present in the amine form. The band of vibrations of a C=O group conjugated with the C=N bond, which is characteristic for the imine form, also lies at lower frequencies in the spectra of Ic and Id and is less intense. The intensity ratio is reversed for the spectrum of Ie. The low value of the C=O frequency of the imine form in the series of investigated compounds (see Table 1) makes it possible to assume the possibility of the formation of a hydrogen bond between the amino group of the perimidine ring and the carbonyl substituent, including an intramolecular hydrogen bond. Evidence in favor of the existence of this bond in the case of 1-methyl-2-acetamidoperimidine has been presented [2];

*The frequencies of the vibrations of the C=N bonds in and outside of the ring differ. The band corresponding to the vibration with greatest participation of the C=N bond of the perimidine ring lies at a higher frequency (according to [1], at ~1640 cm^{-1}).

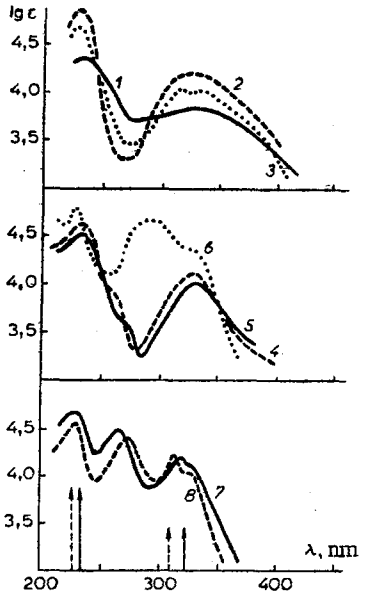

Fig. 1. UV spectra of 2-aminoperimidine and N-substituted 2-aminoperimidines: 1) Ia; 2) Ib; 3) II; 4) Ic; 5) Id; 6) Ie; 7) If; 8) Ig. The arrow indicates the position of the maxima of the absorption bands of 1-methyl-2-dimethylaminoperimidine, and the dashed-line arrow indicates the position of the maxima of 1,3-dimethyl-2-iminoperimidine, according to the data in [1] (for solutions in methanol). The heights of the arrows reflect the ratios of the intensities of the corresponding absorption bands.

in this case the absorption band of the NH group that participates in the intramolecular bond is shifted to ~3000 cm^{-1} or below; its half width increases significantly, and this creates identification difficulties. Only one band will also be observed for the imine form in this case in the region of the usual values of the frequencies of the NH stretching vibrations.

Thus the IR spectral data indicate a shift in the tautomeric equilibria in the case of acyl derivatives of aminoperimidine to favor the imine form as compared with Ia or its N-alkyl derivatives; the amine form predominates somewhat in the case of Ic and Id, whereas the imine form predominates in the case of Ie. The latter is also indicated by the presence of only one band in the region of the NH stretching vibrations in the spectrum of Ie, whereas two bands are observed for other acyl derivatives of aminoperimidine even in very dilute solutions in $CHCl_3$ (in the case of the imine form both NH groups are found in the same environment, and the frequencies of their vibrations should consequently coincide; in the case of the amine form the NH groups lie in different environments and consequently should have different vibrational frequencies, i.e., two absorption bands should appear in the spectrum).

An almost complete shift of the tautomeric equilibrium to favor the imine form is observed in the case of the chloroacyl derivatives (If,g). The IR spectra of these compounds contain only one intense C=N band. The C=O band appears in the form of a shoulder at 1630 cm^{-1}, the position of which does not change when the amino group is deuterated. The preponderance of the imine form in the case of If and Ig is also confirmed by the presence of only one band in the region of the NH stretching vibrations under conditions for which intermolecular association is excluded.

Thus the spectral data show a clearly expressed tendency of N-acylaminoperimidines to undergo conversion to the imine form. This tendency increases in the order R = H, Alk < COAlk < COPh < $COCH_2Cl$, $COCCl_3$.

EXPERIMENTAL

The IR spectra of KBr pellets and chloroform solutions of the compounds were measured with a UR-20 spectrometer. The UV spectra of ethanol solutions of the compounds were recorded with a Specord UV-vis spectrophotometer. Deuteration was carried out directly by prepara-

TABLE 1. Frequencies of the Stretching Vibrations of the NH, C=N, and C=O Groups of 2-Aminoperimidine and Substituted 2-Aminoperimidines

Compound	Vibration frequencies of the groups,[a] cm^{-1}				
	NH[b]	C=N		C=O	
		exocyclic	endocyclic	NH—CO—X	C=N—CO—X
Ia	3460, [3440], 3350	—	1638	—	—
Ib	3443	—	1639	—	—
Ic	3426, 3275	1632	1643	1675	[1635]
Id	3423, 3250	1630	1643	1680	[1635]
Ie	3430	1632	1643	1675	1622
Ig	3425	1624	—	—	[1632]
If	3420	1623	—	—	[1630]
II	3447	—	1638	—	—
IIIc	3375	1630	—	—	—

[a]The position of the maximum of the incompletely resolved band (shoulder) is given in brackets. [b]These are the values for dilute solutions of the compounds in chloroform. [c]Data from [1] (suspensions in mineral oil).

tion of solutions of the compounds in D_2O-saturated chloroform (preliminary experiments showed that saturation of the chloroform solution with water has only a slight effect on the IR spectrum).

2-Aminoperimidine (Ia). Ammonia was bubbled with stirring at 140-145°C into a mixture of 10.3 g (0.051 mole) of 2-chloroperimidine and 50 g of phenol for 3 h, after which the mixture was cooled to 20°C and treated with 300-400 ml of ether. The hydrochloride of Ia was isolated by the addition of alcoholic HCl solution. Workup gave 8.9 g (80%) of a product with mp 278-280°C (from water). Found: Cl 16.5; N 18.6%. $C_{11}H_{10}ClN_3$. Calculated: Cl 16.2; N 19.1%. 2-Aminoperimidine had mp 239-240°C (mp 239-240°C [3]).

2-Butylaminoperimidine (Ib). A 1-ml (0.01 mole) sample of butylamine was added to a suspension of 2.02 g (0.01 mole) of 2-chloroperimidine in 10 ml of alcoholic HCl solution (0.005 M HCl), and the mixture was refluxed with stirring in a stream of nitrogen for 9 h. It was then cooled and diluted with water, and the precipitate (perimidone) was removed by filtration. The filtrate was made alkaline to pH 9 with 10% NH_4OH, and the precipitated Ib was removed by filtration to give 1.17 g (73%) of a product with mp 100-101°C (from water). The hydrochloride of Ib was obtained by heating the base with 10% hydrochloric acid. Workup gave colorless crystals with mp 258-260°C. Found: C 65.8; H 6.8; Cl 13.2; N 15.5%. $C_{15}H_{17}N_3 \cdot HCl$. Calculated: C 65.4; H 6.6; Cl 12.9; N 15.2%.

2-Acylaminoperimidines (Ic-g). A) A solution of 0.01 mole of the appropriate acid chloride in acetone was added slowly dropwise with stirring to a solution of 0.01 mole of freshly crystallized Ia and 0.01 mole of triethylamine in 100 ml of acetone, after which the mixture was allowed to stand at room temperature for 2 h. The precipitated triethylamine hydrochloride was removed by filtration, and the acetone was removed from the mother liquor *in vacuo*. The residue was extracted with ether, and the undissolved solid was removed by filtration. In the case of Ic-f the ester was removed, and the residue was crystallized from aqueous alcohol. Compound Ig was isolated from the extract by chromatography with a column filled with Al_2O_3 [elution with chloroform—acetone (1:1)] (see Table 2). Compounds Ic-g were yellow crystalline substances that were soluble in organic solvents but insoluble in water.

B) 2-Benzamindoperimidine (Ie). A 15-ml sample (0.05 mole of HCl) of a 3.5 N solution of hydrochloric acid was added dropwise with stirring to 7.9 g (0.05 mole) of thoroughly pulverized 1,8-diaminonaphthalene, and the mixture was heated to 80°C and treated with 7.3 g (0.05 mole) of benzoylcyanamide in portions in the course of 25 min. The solution became clear, and a voluminous precipitate formed after 15 min. The precipitate was removed by filtration and washed with water to give 12.5 g (87%) of a product with mp 231-233°C (from aqueous alcohol). Found: N 14.7%. $C_{18}H_{13}N_3O$. Calculated: N 14.6%.

TABLE 2. Characteristics of the Acyl Derivatives (Ic-g) of 2-Aminoperimidine

Compound	mp, °C	Found, %				Empirical formula	Calc., %				Yield, %
		C	H	Cl	N		C	H	Cl	N	
Ic	219—221	69,8	5,3	—	18,4	$C_{13}H_{11}N_3O$	69,4	4,9	—	18,7	60
Id	143—145	71,2	6,2	—	17,1	$C_{15}H_{15}N_3O$	71,2	6,0	—	16,6	45
Ie	231—233	75,4	4,7	—	14,6	$C_{18}H_{13}N_3O$	75,2	4,7	—	14,6	70
If	207 (dec.)*	60,2	3,9	13,6	16,1	$C_{13}H_{10}ClN_3O$	60,2	3,9	13,7	16,2	50
Ig	214	47,5	3,1	32,9	12,8	$C_{13}H_8Cl_3N_3O$	47,6	2,4	32,4	12,8	40

*The melting point was determined with a Meltemp apparatus; the capillary was introduced into the apparatus at 180°C.

2-Dimethylaminoperimidine (II). This compound, with mp 186-188°C (in the case of rapid heating) (mp 185-187°C [10]), was obtained in 86% yield by reaction of 1.1 g of 1-trichloromethyldimethylamine (isolated from the reaction of tetramethylthiuram disulfide with chlorine) with 1,8-diaminonaphthalene.

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