CONFORMATIONS OF THE SIDE CHAIN IN $N_{(6)}$-ACETYL- AND $N_{(6)}$-CARBAMOYL-SYDNONEIMINES AND THEIR SALTS

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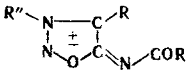
The conformations of the exocyclic group of $N_{(6)}$-acetyl- and $N_{(6)}$-carbamoylsydnoneimines and their salts were studied by means of their vibrational spectra. It is shown that the side chain in compounds that do not contain a bulky substituent in the 4 position of the sydnoneimine ring has primarily a planar syn-s-cis form. When there is a methyl group or a bromine atom in the 4 position, the C=O group deviates from the plane of the ring and enters into conjugation with the unshared pair of electrons of the $N_{(6)}$ atom.

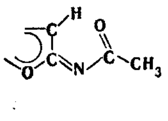
The chemical structures of $N_{(6)}$-acetyl- and $N_{(6)}$-carbamoyl derivatives of sydnoneimines have been previously established by means of their IR spectra [1-3]. However, the conformational states of the exocyclic group, which determine the peculiarities of the conjugation of the C=O and C=N bonds in these molecules, have not yet been investigated.

The carbonyl group in the simplest representative of the above-indicated compounds — $N_{(6)}$-acetyl derivative I — can interact with either the π orbitals of the C=N bond or with the unshared pair of electrons of the $N_{(6)}$ atom. In the first case the C=O and C=N bonds should be coplanar, whereas in the second case they should be situated in mutually perpendicular planes. Thus three conformations of the side chain — s-cis (Ia, Ib), s-trans (Ic, Id), and a nonplanar form in which the C=O and C=N bonds are mutually perpendicular — may exist for each of the possible geometrical isomers — syn or anti.

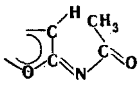


I-V

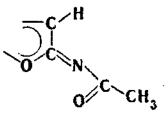
I $R=R''=CH_3$, $R'=H$; II $R=CH_3$, $R'=H$, $R''=C_6H_{11}$ (cyclohexyl); III $R=R'=CH_3$, $R''=C_6H_{11}$; IV $R=NHCH_3$, $R'=H$, $R''=CH_3$; V $R=NHCH_3$, $R'=Br$, $R''=CH_3$



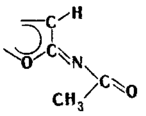
I a



Ic



Ib



Id

An examination of molecular models shows that the syn and anti forms are energetically nonequivalent. Thus anti-s-cis conformation Ib is destabilized due to electrostatic repulsion between the oxygen atoms. A planar orientation of the side chain is hindered in the anti-s-trans conformation because of the nonvalent interactions between the CH_3 group and the $O_{(1)}$ atom; judging from the models, the least steric hindrance is present in the syn-s-cis form Ia.

A choice between the indicated structures can be made by comparison of the vibrational spectra of the corresponding model compounds. With this end in mind we synthesized $N_{(6)}$-acetylsydnoneimines I-III. Replacement of the hydrogen atom in the 4 position of the sydnoneimine ring by a methyl group (or another bulky substituent) should not affect the conformation of the side chain nor, consequently, its characteristic vibrations in any anti form (Ib, Id) or in the case of a nonplanar orientation of the C=O group.

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TABLE 1. Frequencies and Intensities in the IR Spectra of Acetyl and Carbamoyl Derivatives of Sydnoneimines and Their Salts

Compound	Solvent	$\nu_{C=N}\cdot cm^{-1}$	$A_{C=N}\cdot 10^{-4}$, $mole^{-1}\cdot liter\cdot cm^{-2}$	$\nu_{C=O}\cdot cm^{-1}$	$A_{C=O}\cdot 10^{-4}$, $mole^{-1}\cdot liter\cdot cm^{-2}$	$\delta_{NH}\cdot cm^{-1}$	$A_{NH}\cdot 10^{-4}$, $mole^{-1}\cdot liter\cdot cm^{-2}$
I	$CHCl_3$	1558	5,6	1631	3,0	—	—
II	$CHCl_3$	1545sh, 1556	5,9	1631	2,9	—	—
	DMSO	1540sh, 1558	—	1636	—	—	—
III	$CHCl_3$	1570sh, 1598	5,0	1627	3,1	—	—
II · HCl	DMSO	1614	4,5	1730sh, 1740	2.5	1552	3,5
III · HCl	$CHCl_3$	1635	3,9	1740	2,6	—	—
IV	DMSO	1600	2,8	1645	5,5	1520	2,7
V	$CHCl_3$	1638	—	1650	—	1520	—
	DMSO	1635	—	1650	—	—	—

The frequencies and integral intensities of the C=O and C=N bands of $N_{(6)}$-acetylsydnoneimines I and II and 4-methyl analog III are presented in Table 1. It is apparent from Table 1 that the introduction of a methyl group in the 4 position leads to a substantial increase in the frequency of the C=N vibrations (35-40 cm^{-1}), whereas the frequency of the carbonyl group remains virtually unchanged. The intensities of the bands of both groups also change only slightly. This character of the changes in the vibrational spectra makes it possible to conclude that the side chain in $N_{(6)}$-acetylsydnoneimines I and II is planar and has a syn configuration. The low values of the frequencies of the C=N and C=O vibrations and the high integral intensity of the corresponding bands constitute evidence for effective conjugation of the C=O and C=N bonds in this form. Let us note that the $A_{C=N}$ integral intensity values exceed the $A_{C=O}$ values in this case by a factor of almost two. This is evidently the highest intensity that has been observed up to now in the IR spectra for the C=N stretching vibration.

Because of strong nonvalent interactions with CH_3, the C=O group in $N_{(6)}$-acetyl-4-methylsydnoneimine (III) deviates from the plane of the ring; however, the possibility of conjugation of the C=O group with the unshared pair of electrons of the $N_{(6)}$ atom, which should stabilize this form, is created in this case. The existence of n—π conjugation in the III molecule is confirmed by retention of the low C=O frequency vis-à-vis a sharp increase in the C=N frequency.

During the formation of hydrochlorides, the frequency of the carbonyl group in compounds with both planar (I, II) and nonplanar (III) structures increases ∿100 cm^{-1}, whereas the C=N frequency of II increases ∿60 cm^{-1}, as compared with only 35 cm^{-1} in the case of III (Table 1). The close values of the C=O and C=N frequencies and intensities make it possible to assume that these groups are not coplanar in the hydrochlorides of II and III.

In the series of carbamoyl derivatives, $N_{(6)}$-methylcarbamoyl-3-cyclohexyl-4-methylsydnoneimine, which was selected as a model compound, was found to be unstable, and $N_{(6)}$-methylcarbamoyl-4-bromosydnoneimine (V) was therefore synthesized. As in the case of the acetyl derivatives, the introduction of a bulky substituent in the 4 position of the sydnoneimine ring leads to a change in the conformational state of the side chain, during which the frequency of the carbonyl group changes only slightly (Table 1, V). The frequency of the C=N bond increases ∿40 cm^{-1} and turns out to be close to the C=O frequency, as a result of which both vibrations appear in the form of one very broad intense band in the spectrum of a crystalline sample of V. However, they can be resolved in the spectrum of a solution of V in $CHCl_3$. The results show that the side chain in $N_{(6)}$-carbamoylsydnoneimine IV has a planar structure, and this is additionally confirmed by the Raman spectra and data on the transmission of the mutual effect of substituents [3]; when there is a bulky substituent in the 4 position, the C=O group deviates from the plane of the ring and enters into conjugation with the unshared pair of electrons of the $N_{(6)}$ atom.

EXPERIMENTAL

The IR spectra of solutions of the compounds in KBr and CaF_2 cuvettes were obtained with a UR-10 spectrometer. The integral intensities of the bands were determined by measurement of the areas [4]. The UV spectra of 10^{-4}-10^{-5} mole/liter solutions of the compounds (in 1-cm thick cuvettes) were recorded with a Shimadzu MPS-50 spectrophotometer.

N($_6$)-Acetyl-3-methylsydnoneimine (I). A solution of 0.5 g (0.004 mole) of 3-methylsydnoneimine [5] in 15 ml of acetic anhydride was treated with 0.45 g of anhydrous sodium acetate (at 20°C for 3 h), and the resulting precipitate was separated and washed with alcohol. The solvent was removed by evaporation to give 0.35 g (67%) of I with mp 181-183°C (dec., from ethyl acetate) [5].

N($_6$)-Acetyl-3-cyclohexylsydnoneimine (II). This compound, with mp 148-150°C (dec., from ethyl acetate) (mp 147-148°C [7]), was similarly obtained in 65% yield from 3-cyclohexylsydnoneimine [6]. The hydrochloride had mp 134-135°C (dec., from alcohol). Found: Cl 14.5; N 17.0%. $C_{10}H_{15}N_3O_2 \cdot HCl$. Calculated: Cl 14.5; N 17.1%.

N($_6$)-Acetyl-3-cyclohexyl-4-methylsydnoneimine (III). This compound, with mp 92-94°C (dec., from ethyl acetate), was similarly obtained in 75% yield from 1 g (0.005 mole) of 3-cyclohexyl-4-methylsydnoneimine (VI). UV spectrum (in alcohol), λ_{max} (ε): 242 (14,200), and 330 nm (22,000). Found: C 58.4; H 7.6; N 18.5%. $C_{11}H_{17}N_3O_2$. Calculated: C 59.1; H 7.7; N 18.9%. The hydrochloride had mp 142-144°C (from alcohol). Found: Cl 13.8; N 16.2%. $C_{11}H_{17}N_3O_2 \cdot HCl$. Calculated: Cl 13.7; N 16.3%.

N($_6$)-Methylcarbamoyl-3-methyl-4-bromosydnoneimine (V). A 2-g (0.013 mole) sample of bromine was added at 2-4°C to a mixture of 2 g (0.013 mole) of N-methylcarbamoyl-3-methylsydnoneimine (IV) [8] and 2.1 g (0.025 mole) of sodium bicarbonate in 50 ml of dry ether, and the mixture was stirred for 3 h. It was then treated with water and extracted with chloroform. The extract was dried, and the solvent was evaporated to give 0.7 g of V with mp 136-138°C (dec., from alcohol). Found: C 25.1; H 2.9; N 23.8%. $C_5H_7BrN_4O_2$. Calculated: C 25.5; H 3.0; N 23.9%.

3-Cyclohexyl-4-methylsydnoneimine Hydrochloride (VI). A 10-g (0.1 mole) sample of cyclohexylamine and 6.65 g (0.1 mole) of potassium cyanide were added at 10°C to a solution of 14.8 g (0.1 mole) of the sodium bisulfite derivative of acetaldehyde in 150 ml of water. After 3 h, the mixture was worked up to give N-cyclohexylaminoacetonitrile hydrochloride with mp 151-153°C (from isopropyl alcohol). Found: Cl 18.7%. $C_9H_{16}N_2 \cdot HCl$. Nitrosation of 10 g (0.053 mole) of the nitrile by means of 3.66 g (0.053 mole) of sodium nitrite and subsequent cyclization with hydrogen chloride in ether solution yielded 6.3 g (55%) of hydrochloride VI with mp 178-179°C (dec., precipitated from alcohol by the addition of ether). Found: C 49.8; H 7.4; N 19.5; Cl 16.4%. $C_9H_{15}N_3O \cdot HCl$. Calculated: C 49.7; H 7.5; N 19.4; Cl 16.4%.

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