AMINE—IMINE TAUTOMERISM OF 2-AMINOTHIAZOLINES

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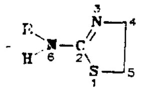
UDC 547.789.1:543.422.4'25:
541.623:519.25

The MNDO method was used to calculate the geometrical parameters and relative energy of the terminal tautomeric structures of 2-aminothiazoline and 2-iminothiazolidine. The hydrogen bond energy and barrier to proton transfer in the cyclic dimers of these molecules were evaluated. The amino and imino structure were assigned for a series of phenyl-, alkyl-, and alkenyl-2-aminothiazolines using IR and PMR spectroscopy.

The tautomerism of five- and six-membered cyclic amidine systems, including guanidines [1, 2], aminoimidazoles [1], 1,3-thiazines, and thiazolines [1, 3, 4] has been discussed by many workers. The nature of this tautomeric equilibrium has been evaluated using the position and intensity of the electronic absorption bands, ^{13}C and ^{15}N NMR chemical shifts [1-5] and the IR bands for the stretching vibrations of the exocyclic and endocyclic C=N bonds [6-8].



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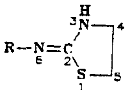

B

These criteria are not unequivocal. Thus, electronic absorption [8], IR [7, 9], and PMR spectroscopy [9, 10] and mass spectrometer [10, 11] indicate that sulfur-containing five-membered cyclic amidines exist in amino form A. According to subsequent ^{1}H NMR spectral studies [5], imino form (B) (thiazolidines) is predominant in the aryl-substituted derivatives. However, ^{15}N NMR spectroscopy was used to conclude that 2-phenylaminothiazoline and its six-membered thiazine analog in chloroform solution form a mixture of the imino and amino tautomers [4]. Cholpankulova et al. [6] used IR and PMR spectroscopy to propose that derivatives of these compounds with an aryl substituent at the exocyclic nitrogen atom exist only in amino form A. Further contradictory results could be given if we included earlier studies [12].

Having synthesized a broad range of aminothiazoline derivatives, containing various substituents [13, 14] (Table 1), we undertook a theoretical and experimental analysis of the structure and possible tautomeric transformations of these compounds.

An MNDO calculation was carried out for the relative energy of forms A and B [15]. The geometrical parameters of the crystallographic structures were used as the starting parameters [16, 17] (Table 2). This calculation showed that, for this geometry, imino structure B is more stable than amino structure A by approximately 20 kcal/mole. The stabilities of forms A and B were also evaluated with optimization of the structures. The calculated values of the optimized geometrical parameters are compared with the experimental values in Table 2.

The calculation results for structure B are in much better accord with the experimental data than for structure A. The reason for these discrepancies undoubtedly lies in the circumstance that the experimental parameters of the amino form given by Toth et al. [16], as in the work of Kalmann et al. [17, 18], were taken for a thiazolidinone molecule (2-amino-5-phenyl-4-thiazolinone). This accounts for the anomalous shortening of the $C(_4)$—$C(_5)$ and $C(_4)$—$N(_3)$ bonds and levelling of the $C(_2)$—$N(_3)$ and $C(_2)$—$N(_6)$ bonds of experimental geometry A. Such a strained role proved energetically unfavorable. Table 2 shows that optimization of the geometrical parameters leads to a virtually unstrained amino structure with an extended

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Institute of Biophysics. Health Ministry of the USSR, Moscow 123182. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 981-988, July, 1989. Original article submitted January 4, 1988.

0009-3122/89/2507-0824$12.50

exocyclic nitrogen—carbon bond and shortened endocyclic nitrogen—carbon bond. The energy of this structure coincides with that of the imino form within 1 kcal/mole.

Thus, the calculation showed the possible existence of an unstrained amino structure, which is virtually isoenergetic with the imino structure. The lack of strain in this case is apparently related to the presence of a sulfur atom in the ring. The greater value of the C—S bond lengths and $C_{(5)}$—$S_{(1)}$—$C_{(2)}$ bond angle (∿90°) permit a planar unstrained structure. The differences in the energies between the two forms may be greater upon the replacement of the sulfur atom by carbon in ordinary amidines.

PMR spectroscopy showed that the existence of a double bond in the five-membered ring for cyclic amidines [1, 9] in DMSO and $CHCl_3$ solution leads to deshielding of the $CH_2(4)$ methylene group protons by 0.3-0.6 ppm. Our results for model alkyl (I, II) and phenyl derivatives (III, IV) are in accord with this tendency. In model amino derivative V, having a methyl group at $C_{(5)}$, only one of the inequivalent $CH_2(4)$ protons is deshielded by 0.3-0.5 ppm (Table 3). Since the bulky $CH_3(5)$ substituent most likely has equatorial orientation, the axial CH(4) proton with J^{vic} = 6.8 Hz should be deshielded and the equatorial CH(4) proton with J^{vic} = 4.3 Hz should be shielded (J^{gem} = 12.5 Hz for the $CH_2(4)$ protons).*

Thus, at least one of the $CH_2(4)$ methylene protons for structure A in comparison with form B, independently of the presence of a methyl substituent $C_{(5)}$, should be deshielded by 0.3-0.6 ppm.

For VII-XIII, in which the position of the C═N double bond is unknown, the chemical shifts of the $CH_2(4)$ protons are closer to that of the analogous protons for the model amino form. For the unsubstituted (VII and VIII) and alkyl-substituted compounds (IX-XI), this is observed both in DMSO and $CDCl_3$ solution and in inert C_6D_{12}. The signal for the $CH_2(4)$ protons in the phenyl derivatives (XII and XIII) is shifted upfield upon going from DMSO and $CDCl_3$ to C_6D_{12} to occupy a position intermediate between the signals of the $CH_2(4)$ protons for the terminal structures.

This experimental observation, in our opinion, indicates the necessity of taking into account not only the solvent effect but also, the predominant effect of the solvent at the cyclic $N_{(3)}$ atom on the chemical shift of the $CH_2(4)$ protons. If we assume that VII-XIII have imino form B, the chemical shift difference $\Delta\delta CH_2(4)$ of 0.2-0.6 ppm for these compounds and imino models I-IV may be attributed to the difference in the effect of the substituent at $N_{(3)}$ (comparable, for example, with N-methylperazine, for which the chemical shifts of the α- and β-methylene protons differ by about 0.5 ppm).

The chemical shifts of the NCH_3 group protons in XI, XIV, and XV (solutions in $CDCl_3$) have values of 2.92, 2.91, and 2.88 ppm, respectively, which are intermediate between the chemical shift values of the $-NCH_3$ and $=NCH_3$ groups protons in I (2.86 and 3.03 ppm).

Thus, the chemical shift data do not permit an unequivocal assignment of VII-XIII to either form.

The experimental IR spectral data for the aryl and alkyl derivatives and compounds with rigid structures were obtained in CCl_4 (an inert solvent), $CHCl_3$ (a weak proton donor), acetonitrile (a polar solvent), and DMSO and CD_3OD, which have weak and stronger hydrogen bonds. The frequencies obtained for the C═N stretching bands under these conditions are given in Table 1. Comparison of the data for compounds with proven imino (I-IV) and amino structure (V and VI) shows that higher $\nu_{C=N}$ values of usually 20-40 cm^{-1} than for the C═N bond in the ring correspond to the exocyclic double bond. This behavior was noted in our previous work [6]. The absolute values of these frequencies by themselves, especially in the crystalline state, clearly cannot be an unequivocal criterion as assumed in our previous work [6]. On the basis of only the indicated values, we should propose imino form B in CCl_4 and amino form A in the crystalline state for III and IV with rigid imino structure. The significant decrease in the $\nu_{C=N}$ values for phenylthiazolidines III and IV in the solid phase is apparently related to strong intermolecular interactions of the phenyl ring and the $N\overset{\cdots}{-}C\overset{\cdots}{-}N$ system, which may

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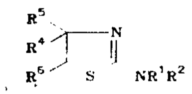
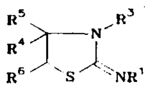
*The J^{gem} and J^{vic} constants for the $CH_2(4)$ and $CH_2(5)$ protons of VIII, X, XI, and XIII do not differ by more than 0.1 Hz from the analogous constants for V (J^{vic} = 6.5-6.8 Hz for I-IV), which may indicate approximately equal mobility of this fragment in both forms.

TABLE 1. Frequencies of C═N Stretching Bands (cm^{-1}) in the IR Spectra of Thiazolines and Thiazolidines





Compound	R^1	R^2	R^3	R^4	R^5	R^6	KBr (neat)	CCl_4	$CHCl_3$	CH_3CN	DMSO	CD_3OD	Δ*1
I	CH_3	—	CH_3	H	H	H	(1642)	1650	1640	1642	1640	1631	19
II	$CH_2{=}CHCH_2$	—	CH_3	H	H	H	—	1650 1640 d	—	—	—	—	
III	C_6H_5	—	CH_3	H	H	H	1616 1581*2	1633 1591	1626 1591	1628 1595	1622 1589	1618 1595	15
IV	C_6H_5	—	$C_6H_5CH_2$	H	H	H	1613 1620 1585*2	1633 1598	1626 1595	1630 1640sh. 1595	1622 1591	1618 1595	15
V	CH_3	CH_3	—	H	H	CH_3	(1612)*3 v.br	1613	1609	1612	1610	1605	8
VI	CH_3	C_6H_5	—	H	H	CH_3	—	1616	1610	1612	1614	1608	8
VII	H	—	H	H	H	H	1647*4 1600 sh.	1655	1648	1652	1650	1627	28
VIII	H	—	H	H	H	CH_3	1670 . . . 1550*4 v.br.	1645 1655 sh	1640	1645 1660sh	1645 1660 sh.	1620	25
IX	$CH_2{=}CHCH_2$	—	H	H	H	H	1620	1635	1628	1632	1622	1617	18
X	$CH_2{=}CHCH_2$	—	H	H	H	CH_3	1615 v.br. 1640 sh	1632	1625	1627	1625	1611	21
XI	CH_3	—	H	H	H	CH_3	1627 1640 sh.	1634 1650sh.	1626	1630	1627	1612	22
XII	C_6H_5	—	H	H	H	H	1625 1585*2	1640 1591	1632 1590	1634 1595	1630 1595	1620 1598	20
XIII	C_6H_5	—	H	H	H	CH_3	1632 br. 1640, 1660sh. 1597*2	1642 1590	1635 1595	1634 1592	1630 1592	1620 1598	22
XIV	CH_3	—	H	H	C_2H_5	H	1610 1630	1637	1628	1631	1628	1618	19
XV	CH_3	—	H	CH_3	CH_3	H	1610 1625	1636	1628	1629	1628	1618	18
XVI	C_2H_5	—	H	CH_3	CH_3	H	1605 1625	1635	1624	1628	1626	1611	24
XVII	C_2H_5	—	H	H	C_2H_5	H	1625 v.br.	1636	1627	1629	1628	1614	20
XVIII	$C_6H_5CH_2$	—	H	CH_3	CH_3	H	1620 1605	1632	1628	1629	1622	1611	21
XIX	$C_6H_5CH_2$	—	H	H	C_2H_5	H	1628	1634	1627	1629	1627	1610	24

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*1Difference in the $\nu_{C=N}$ frequencies in CCl_4 and CD_3OD, cm^{-1}.

*2Benzene ring lines.

*3Unresolved doublet.

*4The band halfwidth was about 100 cm^{-1}. br) Broad, v. br) very broad, sh) shoulder, d) double.

TABLE 2. Experimental* and Calculated Geometrical Parameters and Bond Orders in 2-Methylaminothiazoline (A) and 2-Methyliminothiazolidine (B)

Bond	Bond length, Å (bond order)				Bond angles (°)				
	calculation		experiment		Angle	calc.		experiment	
	A	B	A	B		A	B	A	B
$C_{(2)}$—$S_{(1)}$	1,75 (0,54)	1,74 (0,54)	1,75	1,77	$C_{(5)}$—$S_{(1)}$—$C_{(2)}$	91	96	89	93
$C_{(2)}$—$N_{(3)}$	1,29 (0,73)	1,38 (0,60)	1,33	1,37	$N_{(3)}$—$C_{(2)}$—$S_{(1)}$	117	109	119	110
$N_{(3)}$—$C_{(4)}$	1,44 (0,48)	1,44 (0,51)	1,39	1,42	$C_{(2)}$—$N_{(3)}$—$C_{(4)}$	115	119	111	117
$C_{(4)}$—$C_{(5)}$	1,55 (0,53)	1,54 (0,55)	1,47	1,54	$N_{(3)}$—$C_{(4)}$—$C_{(5)}$	110	108	112	111
$C_{(5)}$—$S_{(1)}$	1,79 (0,44)	1,77 (0,45)	1,78	1,78	$C_{(4)}$—$C_{(5)}$—$S_{(1)}$	107	108	108	109
$C_{(2)}$—$N_{(6)}$	1,37 (0,62)	1,29 (0,78)	1,32	1,27					

*The experimental values for thiazolidine were taken from data for the structure of 2-phenylaminothiazolidine, while such values for thiazoline were taken from data on 2-amino-5-phenyl-4-thiazolinone [16, 17]. The mean deviations of the calculated values from the experimental data are 0.037 and 0.015 Å for the amino and imino forms, respectively and 2° for the bond angles in both structures.

TABLE 3. Chemical Shifts of the $CH_2(4)$ Protons, δ, ppm, in the PMR Spectra of the Compounds Studied

Compound	Solvent		
	DMSO-d_6	$CDCl_3$	C_6D_{12}
I	3,36	3,41	
II	3,42*	—	3,28
III	3,59*	3,55	—**
IV	3,50	—	—
V	3,90; 3,52	4,06; 3,70	3,92; 3,58***
VII	3,80*	3,90	3,84
VIII	3,89; 3,45	4,04; 3,64	—
IX	3,80	3,99	3,84
X	3,82; 3,46	3,99; 3,60	3,87; 3,51
XI	3,84; 3,46	4,04; 3,67	3,90; 3,56
XII	3,95*	3,77	—
XIII	3,90; 3,60	3,80; 3,36	3,70; 3,28

*Acetone-d_6 was the solvent.

**Low solubility in cyclohexane.

***In the case of a large number of NS accumulations = 4000.

lead to charge transfer and delocalization of the electron density in this fragment. The $\nu_{C=N}$ frequencies in unsubstituted VII and VIII in all solvents are high.* This finding indicates that the electronic structure of these compounds is closer to the imino form. The broad bands at 2900-3400 cm^{-1} in the IR spectra of VII and VIII in nonpolar solvents even upon very high dilution indicate that a significant portion of these molecules remain associated under these conditions.

Let us now consider cases, in which there is an alkyl or alkenyl substituent (IX-XI) or phenyl substituent (XII and XIII) at the exocyclic nitrogen atom, while the position of the proton is unknown. The $\nu_{C=N}$ frequencies for phenyl derivatives XII and XIII are in the range characteristic for imino form B both in polar and nonpolar solvents as well as in the solid phase. The lower $\nu_{C=N}$ frequencies of XII and XIII in the crystalline state in comparison with these values in solution, precisely as in the case of III and IV, may be attributed to the same factors. The same behavior holds true for solutions of IX-XI. Additional evidence for the localization of the proton in the ring may be found in the value of the NH stretching band frequency (3440-3470 cm^{-1}) and the solvent effect. Table 1 shows a characteristic large decrease in $\nu_{C=N}$ values for rigid imino structures B (I-IV) in CD_3OD solution in comparison with CCl_4 solution (20 cm^{-1}) and a much smaller decrease (8 cm^{-1})

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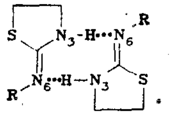
*The high intensity and small halfwidth of these bands excludes their assignment to NH_2 deformation vibrations.

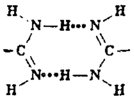
is found for the known amino forms (V and VI). The corresponding decrease in $\nu_{C=N}$ in IX-XI and XII-XIX is about 18-22 cm^{-1}, while it is approximately 28 cm^{-1} for VII and VIII. The latter is apparently related to a change in the form of the corresponding normal mode in these molecules upon replacing the hydrogen atom by a deuterium one. Thus, the polar properties of VII-XIX are close to those for the imino structure.

Comparative analysis of these IR spectra (Table 1) shows that the effect of solvent polarity and the capacity of the solvent to form hydrogen bonds, leading to some additional redistribution of electron density in the amidine fragment, does not produce however, a radical change in structure. The compounds with imino form in solution in nonpolar solvents retain the imino form in all other cases. We reemphasize that the absolute values of the C=N stretching band frequencies by themselves cannot be used for structure assignment. Thus, the low $\nu_{C=N}$ values in IX and X in CD_3OD (Table 1) do not at all indicate transition to the amino form. These values would be lower in the case of such a transition than in rigid structures V and VI and would be found below 1600 cm^{-1}. The experimental results indicate that the actual difference in the energies of structures A and B is somewhat greater than the theoretical estimate. A difference of 2 kcal/mole (which is within the error limits of the calculation) may prove completely sufficient to shift the equilibrium toward the imino form. The IR spectral results for VII-XIX are in better accord with proton localization on $N(_3)$, i.e., with a shift of π-electron density toward the exocyclic bond. Additional evidence for this conclusion is found in the lack of coupling of the NH proton with the CH_2 or CH_3 protons of the same substituent ($J_{HNCH_2} \sim 0.05$ Hz) in the PMR spectra of IX-XI as observed in compounds with an NHAlk fragment [13]. Furthermore, splitting of the signal of the NCH_3 group to a doublet with J = 5.5 Hz is observed upon the protonation of XI in trifluoroacetic acid.

The capacity to form hydrogen bonds is an important property of the compounds examined. According to x-ray diffraction structural data [20], 2-phenyliminothiazolidines in the crystal cell form strong dimers with $N(_3)...N(_6)$ and $N(_3)H...N(_6)$ distances equal to 2.98 and 2.17 Å, respectively.



Our data show that such associated species also exist in dilute solutions in nonpolar solvents. Since the $N(_3)H...N(_6)$ distances in the dimeric species are small, the barrier for intermolecular transfer should be much lower than the barrier for intramolecular transfer. An MNDO/H calculation was carried out for the cross-section of the potential energy surface for synchronous transfer of two amidine fragments using the geometrical parameters



given in Table 1. The optimal N...H—N distance was 2.9 Å. According to our calculation, the energy of the two hydrogen bonds in this system is 12 kcal/mole and the height of the activation barrier for transfer of two protons is about 4 kcal/mole, which is less than for carboxylic acid dimers [21].

The authors express their gratitude to V. Yu. Kovtun for a helpful discussion of this work.

EXPERIMENTAL

The IR spectra were taken on a Perkin—Elmer 398 spectrometer for KBr pellets and solutions in standard cells. The PMR spectra were taken on a Bruker WM-250 spectrometer with TMS as the internal standard. The MNDO calculations were carried out using our program.

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NITROGEN—TELLURIUM-CONTAINING HETEROCYCLES.

3*. REACTION OF 2-PHENYLBENZOTELLURAZOLE AT THE HETEROATOMS

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UDC 547.789.9.04

Reactions of 2-phenylbenzotellurazole at both heteroatoms are studied. σ-Telluranes and molecular complexes with mercury and palladium salts are prepared. Exchange of a tellurium atom by sulfur is achieved. Alkylation of a heteroatom of the pyrrole type, the tellurium atom, is achieved in a series of benzazoles for the first time.

If in benzoxazoles (-thiazoles and -selenazoles) the main reaction centers are the nitrogen atom and the ring annelated to the heterocyclic benzene, then in benzotellurazoles the tellurium atom is added to these reaction centers. It should be noted that tellurium-containing heterocycles are probably unique heterocycles for which a wide variety of reactions is characteristic. These occur at the heteroatom of the pyrrole type, the tellurium atom [2, 3]. The present work reports results of a study of reactions of 2-phenylbenzotellurazole (I) at both heteroatoms, the tellurium and nitrogen.

Reactions at the tellurium atom in this heterocycle, as in others, are caused by the ease of transition of the dicoordinated tellurium atom into tetra- and tricoordinated forms. Similar to other derivatives of dicoordinated tellurium [4], including the heterocyclics of [2, 3], 2-phenylbenzotellurazole is converted with high yields under the action of halogens under mild conditions into the corresponding σ-telluranes, 1,1-dihalo-2-phenylbenzotellurazoles (IIa-c). Another σ-tellurane, 1,1-dinitro-2-phenylbenzotellurazole (IId) is formed upon treatment of compound I with dilute nitric acid. The reaction probably occurs through intermediate formation of the corresponding telluroxide, interaction of which with excess

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*For Communication 2, see [1].

Scientific-Research Institute of Physical and Organic Chemistry, Rostov State University, Rostov-on-Don 344104. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 989-993, July, 1989. Original article submitted January 6, 1988.

0009-3122/89/2507-0829$12.50