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1,3-THIAZEPINES. 6*. UV SPECTROSCOPIC AND THEORETICAL STUDY OF THE ELECTRONIC STRUCTURES OF 2-AMINOTETRAHYDRO- AND 2-IMINOTETRAHYDRO-1,3-THIAZEPINES

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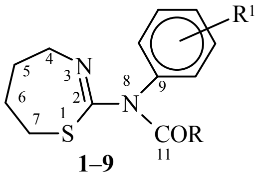
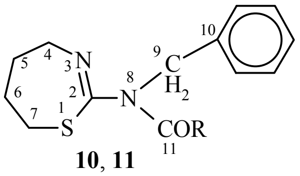
On the basis of studies of the electronic absorption spectra and quantum-chemical calculations of the energies and bond orders of a series of N-acetyl-N-aryl substituted 2-amino-4,5,6,7-tetrahydro-1,3-thiazepines and N-aryl substituted 2-iminohexahydro-1,3-thiazepines it has been concluded that the reason for the weak basicity of the ring nitrogen atom of the former is the acceptor properties of the amide carbonyl which obstructs the interaction of the unshared pair (USP) of this atom with the phenyl ring; in the case of the derivatives of hexahydroazepine the strengthening of the basic properties of the exocyclic nitrogen atom is associated with the conjugation of its USP with the π-electrons of the benzene ring, which is strengthening by delocalisation of the USP of the sp^3-hybridized ring nitrogen atom into the azomethine bond.

Keywords: 2-aminotetrahydro-1,3-thiazepines, acyl derivatives, 2-iminohexahydro-1,3-thiazepines, quantum-chemical calculations, unshared electron pair, UV spectra.

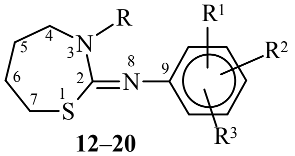
The principal factor which determines the basic properties of nitrogen bases is the hybrid state of the unshared electron pair (USP) of the nitrogen atom. It is considered that the basicity of amines increases with increasing *p*-character of the USP of this atom [2-4].



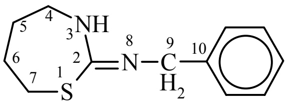
1–9



10, **11**



12–20



21

1–7, **12–14** $R^1 = R^2 = R^3 = H$; **8**, **15** $R^1 = 4\text{-}Me_2N$, $R^2 = R^3 = H$; **9**, **16** $R^1 = 3\text{-}CF_3$;
17 $R^1 + R^2 = 2,3\text{-}CH{=}CH{-}CH{=}CH{-}$; **18**, **20** $R^1 = H$, $R^2 = 2\text{-}Me$, $R^3 = 3\text{-}Me$; **19** $R^1 = 2\text{-}Me$, $R^2 = 4\text{-}CH_3$, $R^3 = 6\text{-}Me$,
1, **9**, **10**, **13** R = Me; **2** R = Ph; **3**, **8**, **11** R = PhNH; **4** $R = 2\text{-}BrC_6H_4$; **5** $R = 3\text{-}BrC_6H_4$; **6** $R = 4\text{-}BrC_6H_4$; **7** $R = 4\text{-}O_2NC_6H_4$;
12, **15–19** R = H; **14**, **20** $R = MeOOCCH_2CH_2$

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* For Communication 5, see [1].

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TABLE 1. UV Spectra of Compounds 1-21*

Compound	λ_{max}, nm	Compound	λ_{max}, nm	
			I	II
1	226, 290	**12**	276	253
2	227	**13**	251	238
3	228	**14**	251	238
4	227	**15**	295	311
5	228	**16**	282	250
6	230	**17**	297	283
7	248, 282	**18**	238	244
8	230, 258	**19**	240	245
9	230, 282	**20**	238	240
10	240	**21**	240	240
11	237, 240			

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* The UV spectra of compounds **1-11** were recorded in ethanol or in a mixture of ethanol+HCl, while those of compounds **12-21** were recorded in ethanol, a mixture of ethanol–HCl–NaOH (I), or a mixture of ethanol+HCl (II).

In a continuation of the study of the spectroscopic properties of derivatives of 2-amino-1,3-thazepine [1, 5], with the aim of clarifying the peculiarities of the electronic structure of the USP of the sp^2-hybridized endocyclic and exocyclic nitrogen atoms, we have in the present work investigated the electronic absorption spectra of 2-(N-acylamino-N-aryl-)-4,5,6,7-tetrahydro-1,3-thiazepines (**1-11**) and 2-aryliminohexahydro-1,3-thiazepines (**12-21**) in media of different pH (Table 1).

Analysis of the results obtained showed that the electronic absorption spectra of compounds **1-11** taken in ethanol solution did not change on the addition of 0.1 N HCl no matter what the nature of Ar and the substituent R on the carbonyl of the amide (Fig. 1). The identity of the UV spectra of the ethanolic and acid ethanolic solutions shows the absence of protonization of atom N(3) of the 2-acylamino- and 2-ureido derivatives of tetrahydro-1,3-thiazepines **1-11**, which is in agreement with chemical experiments.

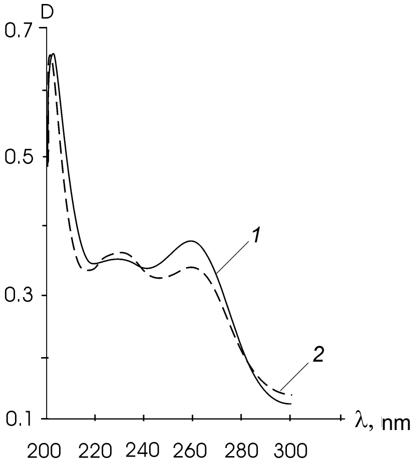


Fig. 1.

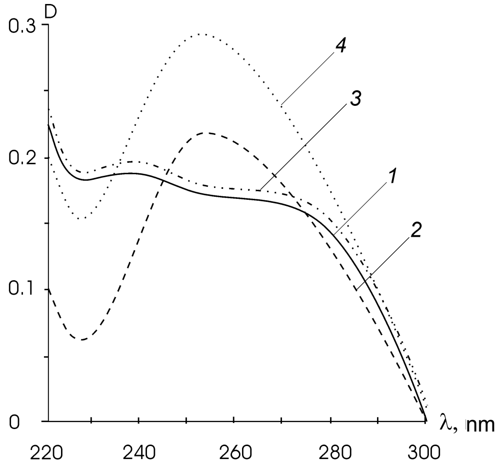


Fig. 2.

Fig. 1. UV spectra of compound **1** in ethanol (*1*) and after addition of 0.1 N HCl (2).

Fig. 2. UV spectra of compound **12** in ethanol (*1*), after addition of 0.1 N HCl (*2*), after addition of 0.1 N NaOH to the acidic ethanolic solution (*3*). Spectrum of the ethanolic solution of compound **12**×HCl (*4*).

However, addition of 0.1 N HCl to ethanolic solutions of the imino compounds **12-20** caused a bathochromic or hypsochromic shift (depending on the donor or acceptor properties of the aryl substituent) of the maximum of the bands at 256 nm, which is a result of the symmetry forbidden nature of the transition $A_{1g}\rightarrow B_{2u}$ [6] (see Fig. 2 and 3). The shift of the maximum of this band to longer wavelength in the case of donor aryl substituents (compounds **15**, **18**) and to shorter wavelength observed for compounds with acceptor aryl substituents (**12-14**, **18**, **17**) indicates changes in the electronic properties of the exocyclic nitrogen atom, N(8), of 2-aryliminohexahydro-1,3-thiazepines. Moreover, on addition of 0.1 N NaOH solution to the acidic ethanolic solutions of compounds **12-20** the spectra observed are identical to those of the neutral solutions. This account, and also the similarity of the spectra of ethanolic solutions of experimentally prepared hydrochlorides of compounds **12**, **13**, **16**, and **20** to that corresponding electronic spectra of acidic ethanolic solutions of the bases confirms the process of protonization and not solvation of atom N(8) of the amines discussed.

TABLE 2. Calculated Values of the Bond Orders in the Compounds Studied

Compound	Bond order					
	C(2)–N(3)	N(3)–C(4)	C(2)–N(8)	N(8)–C(9)	N(8)–C(11)	C(9)–C(10)
1	0.93	0.04	0.03	0.04	0.15	—
3	0.93	0.05	0.08	0.05	0.06	—
8	0.93	0.05	0.07	0.05	0.06	—
9	0.95	0.04	0.05	0.04	0.15	—
10	0.95	0.05	0.06	0.03	0.17	0.03
11	0.88	0.05	0.08	0.03	0.05	0.03
12	0.10	0.03	0.88	0.08	—	—
13	0.07	0.03	0.95	0.08		
15	0.10	0.03	0.88	0.08	—	—
16	0.10	0.03	0.87	0.08	—	—
21	0.05	0.03	0.97	0.04	—	0.03

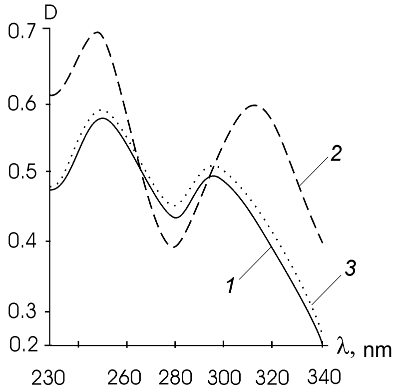


Fig. 3.

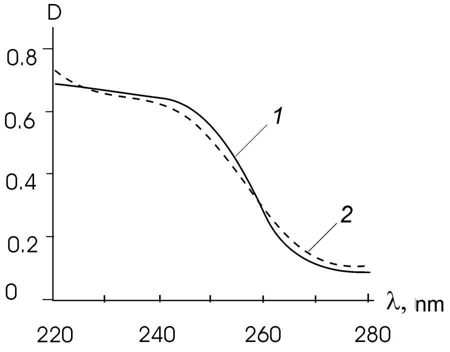


Fig. 4.

Fig. 3. UV spectra of compound **15** in ethanol (*1*), after addition of 0.1 N HCl (*2*), and after addition of 0.1 N NaOH to the acidic ethanolic solution (*3*).

Fig. 4. UV spectra of compound **21** in ethanol (*1*) and after addition of 0.1 N HCl (*2*).

Compound **21**, in which atom N(8) is separated by a methylene group from the phenyl nucleus, behaves quite differently. The absence of a band in the 250-256 nm region indicates the absence of conjugation between USP of this atom and the phenyl ring, and the identity of the UV spectra of the neutral and acidic ethanolic solutions in the 230-256 nm region allows the conclusion that protonization of atom N(8) in compound **21** does not occur (Fig. 4).

Hence it can be proposed on the basis of the UV spectroscopic study that the increase in delocalisation of the USP in the sp^2-hybridized exocyclic nitrogen atom into the delocalized system of the aryl substituent leads to an increase in the *p*-character of the USP in the planar transition state of the molecule and consequently to an increase in the protonization energy of this atom in 2-aryliminohexahydro-1,3-thiazepines [3, 7].

The absence of protonization of the cyclic unsaturated atom N(3) in compounds **1-11** is probably connected to the influence of the acceptor substituent in the amino group which hinders the interaction of the USP of this atom with the benzene ring which leads to a notable contribution of *s*-electrons to the USP of atom N(3) and a corresponding decrease of its basicity in the heterocycles **1-11**.

To confirm the conclusions reached as a result of the study of the electronic spectra, the bond orders and energies of some bonds (Tables 2 and 3) were calculated by the semiempirical LCAO MO method in the PM3 approximation, and the localized molecular orbitals of atoms N(8) and N(3) which form bonds with the neighbouring carbon atoms were examined for a number of the discussed amines and imines (Table 4). The results in the Tables indicate the higher bond order and bond energies in bond N(8)–C(9) in the imines **12**, **13**, **15**, and **16** than in the amines **1**, **3**, **8**, **9**. For example, the bond order and energy of the N(8)–C(9) bond for compound **12** are 0.078 and 14.43 eV respectively, whereas for compound **1** they are 0.038 and 13.84 eV. An analogous picture is observed on comparing the quantum-chemical parameters for compounds **15** and **8**, and **16** and **9** (see Tables 2 and 3).

Data on the interaction of the USP of the nitrogen atoms with neighbouring carbon atoms (Table 4) also indicates delocalisation of the USP of N(8) onto the neighbouring atom C(9) in the thiazepines **12**, **13**, and **15**. It is also observed that this interaction strengthens the conjugation of the USP of atom N(3) with the π-electrons of the azomethine bond C(2)=N(8) in compounds **12**, **13**, **15**, and **16**. On the basis of the discussion above it may be concluded that the redistribution of the electron density in the molecules of the studied imines **12-20** occurs in the following direction:

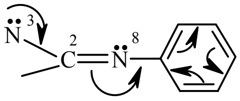


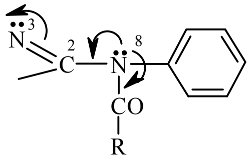
TABLE 3. Energies of Some Bonds in the Compounds Studied (*E*)

Compound	*E*, eV				
	C(2)–N(3)	C(2)–N(8)	N(8)–C(9)	N(8)–C(11)	C(9)–C(10)
1	21.92	13.83	13.84	14.00	—
3	22.02	14.20	13.97	13.24	—
8	22.02	14.11	14.01	13.24	—
9	22.02	13.73	13.83	14.10	—
10	22.18	13.86	13.04	14.44	14.17
11	21.36	13.91	13.06	12.96	14.17
12	14.43	21.74	14.43	—	—
13	13.76	22.28	14.47	—	—
15	14.21	21.69	14.44	—	—
16	14.48	21.54	15.52	—	—
21	13.51	22.44	13.24	—	14.14

TABLE 4 Composition of the USP of Atoms N(3) and N(8)

Compound	Localized orbital	Atom fraction, %				
		N(3)	N(8)	C(2)	C(9)	C(11)
1	N(3)	97.47	—	1.11	—	—
	N(8)	—	91.83	—	—	4.41
3	N(3)	96.96	1.18	1.34	—	—
	N(8)	—	93.42	1.89		1.39
8	N(3)	96.97	1.02	1.33	—	—
	N(8)	—	93.57	1.43	—	—
9	N(3)	97.24	—	1.22	—	—
	N(8)	—	91.14	—	—	4.56
10	N(3)	96.88	—	1.33	—	—
	N(8)	—	90.83	1.07	—	5.06
12	N(3)	94.65	1.85	2.58	—	—
	N(8)	—	96.15	—	1.26	—
13	N(3)	96.28	—	1.34	—	—
	N(8)	—	96.07	—	1.28	—
15	N(3)	94.65	1.85	2.58	—	—
	N(8)	—	96.14	—	1.27	—
16	N(3)	94.50	1.80	2.74	—	—
	N(8)	—	96.16	—	—	—
21	N(3)	97.97	—	—	—	—
	N(8)	—	97.73	—	—	—

At the same time in the 2-(N-acylamino-N-aryl)tetrahydro-1,3-thiazepines **1**, **3**, **8**, **9**, and **11** the USP of atom N(8) is delocalized onto the C atom of the amide carbonyl C(11), and also onto the neighbouring atom C(2) of the azomethine bond C(2)=N(3), but does not interact with atom C(9) of the aryl substituent. Thus, the redistribution of electron density in the investigated amines **1-9** and their benzyl analogs **10** and **11** takes the form:



These electron redistributions, bond orders, and bond energies of the N(8)-C(9) bonds confirm the absence of conjugation of the USP of atom N(3) with the phenyl group, i.e., the localized nature of the USP of this nitrogen atom in compounds **1-11**.

Comparison of the values of the bond order and bond energy of the C(9)-C(10) bond in compounds **21** (0.03, *E* 14.14 eV), **10** and **11** (0.03, *E* 14.17 eV), which have a methylene bridge between atom N(8) and the phenyl ring, indicate the absence of conjugation between the USP of this atom and the aromatic ring in compound **21**. This is confirmed by the date in Table 4 which show the localized nature of the USP of atom N(8).

Thus it can be concluded on the basis on the studied electronic absorption spectra and the quantum-chemical calculations of the bond energies and bond orders that the reason for the weakly basic nature of the endocyclic nitrogen atom in the acyl derivatives **1-11** is the acceptor properties of the amide carbonyl which prevents interaction of the USP of this atom with the phenyl group. On the other hand, conjugation of the USP of the exocyclic atom N(8) with the π-electrons of the benzene ring strengthens the delocalisation of the USP of the sp^3-hybridized N(3) atom onto the azomethine bond, which leads to an increase of the contribution of the π-electrons to the USP of the N(8) atom and consequently to the increase of its basicity in compounds **12-20**.

Compounds **1-8, 10-21** were synthesized by known methods [1, 5, 8-10]. Compound **9** was made by treatment of 2-(*m*-trifluoromethylphenylimino)tetrahydro-1,3-thiazepine with acetyl chloride.

EXPERIMENTAL

UV spectra of ethanol solutions in 1 cm cuvettes were recorded with a Perkin-Elmer Lambda-16 spectrometer. To change the pH of the solutions 0.1 ml of 0.1 N HCl or NaOH was added. Quantum-chemical calculations using the PM3 method [11] were carried out using the MOPAC 7.0 suite [12, 13] with complete optimization of the molecular geometry.

Conditions for obtaining ^{1}H NMR, IR, and mass spectra were analogous to those described in [9].

2-[N-Acetyl-N-(*m*-trifluoromethylphenyl)amino]-4,5,6,7-tetrahydro-1,3-thiazepine (9). Triethylamine (0.25 g, 2.5 mmol) was added to a solution of 2-*m*-trifluoromethylphenyliminohexahydro-1,3-thiazepine (0,6 g, 2.2 mmol) in dry benzene (8 ml). Acetyl chloride (0.2 g, 2.5 mmol) in benzene (2 ml) was then added dropwise with stirring at 5-10°C. The reaction mixture was kept for 3 days at room temperature with occasional shaking, evaporated in the air, washed with 5% HCl solution, then with water, and chromatographed on a 100/160 silica gel column, with successive elution with hexane and 20:1 hexane–acetone to give compound **9** (0.5 g, 72%) as a yellow sticky oil, R_f 0.67 (Silufol UV-254, 2:1 benzene–acetone). IR spectrum (KBr), ν, cm^{-1}: 1690 (CO), 1615 (C=N). Mass spectrum, *m/z* (I_{rel}, %): 316 [M$^+$] (72), 301 $[M-CH_3]^+$ (6), 273 $[M - COCH_3]^+$ (100), 241 (37), 186 (37), 145 (31), 87 (60). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.88 (4H, m, $2CH_2$), 2.32 (3H, s, CH_3), 2.84 (2H, t, CH_2S), 3.80 (2H, t, CH_2N), 6.85-7.60 (4H, m, H arom). Found, %: C 53.41, H 4.85, N 8.68. $C_{14}H_{15}F_3N_2OS$. Calculated, %: C 53.15, H 4.78, N 8.86.

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