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ELECTRON STRUCTURES OF AZOLOISOINDOLES WITH A NODAL NITROGEN ATOM.

1. DERIVATIVES OF ISOINDOLOBENZIMIDAZOLE AND IMIDAZO-AND PYRAZOLOISOINDOLES

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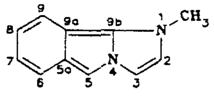
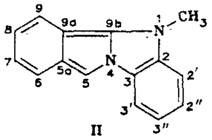
N-Methyl-substituted 1H-imidazo[2,1-a]isoindole, 5H-isoindolo[2,1-a]benzimidazole, and 3H-pyrazolo[5,1-a]isoindole were calculated by the PPP and CNDO/2 methods. On the basis of the canonical and localized MO it was concluded that the examined compounds can, to a first approximation, be regarded as 1,2-disubstituted isoindoles, i.e., 10π-electron systems. The calculated data are in good agreement with the experimental UV spectra and the chemical properties of the investigated compounds.

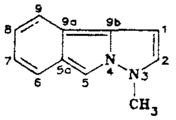
There is a vast group of compounds, viz., azoloisoindoles, among condensed heterocyclic systems with a nodal nitrogen atom. Compounds of this type have found application in practice as medicinal preparations and agents for the protection of plants and are currently under extremely intensive investigation [1]. Soviet chemists have also made a definite contribution to the study of this series of heterocyclic compounds [2-4]. However, all of the previous investigations have basically been experimental in character. We therefore attempted to study the electron structures of three typical representatives of this group, viz., 1H-imidazo[2,1-a]isoindole (I), 5H-isoindolo[2,1-a]benzimidazole (II),* and 3H-pyrazolo[5,1-a]isoindole, by quantum-chemical methods.



I



II



III

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*For the most concise exposition of the material, the numbering of the atoms does not always coincide with the generally accepted numbering.

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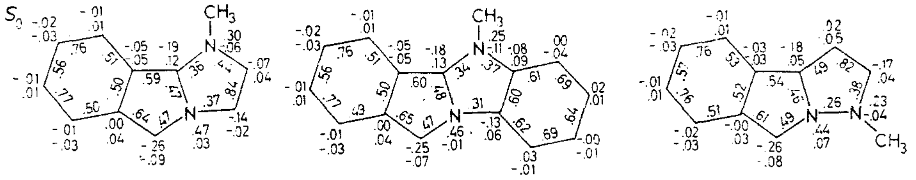

	PPP	CNDO/2	PPP	CNDO/2	PPP	CNDO/2
E_{LVMO}	−192,01	258,48	−202,62	210,14	−206,48	246,13
E_{HOMO}	−812,40	−801,69	−800,83	−800,73	−809,51	−804,01
	$E_\pi = -19\,625{,}90$	$E_{(\sigma+\pi)} = -286\,253{,}9$	$E_\pi = -24\,703{,}83$	$E_{(\sigma+\pi)} = -365\,060{,}8$	$E_\pi = -19\,537{,}10$	$E_{(\sigma+\pi)} = -286\,297{,}0$

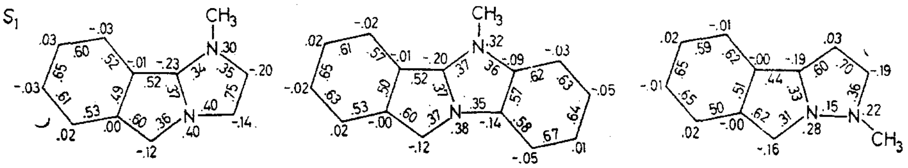

Fig. 1. Orders of the π bonds calculated by the PPP method, π charges on the atoms (upper numbers), and (σ + π) charges (lower numbers) in the ground (S_0) and first singlet excited (S_1) states of I-III. The energies of the lowest vacant molecular orbitals (LVMO) and the highest occupied molecular orbitals (HOMO), the π energies (PPP), and the total electron energies (CNDO/2) are given in kilojoules per mole. Only the data from calculations by the PPP method are presented for the S_1 state.

The calculations were made by the PPP and CNDO/2 methods, and the conclusions regarding the electron structures were based on an analysis of both the canonical and localized MO. In view of the fact that N-methyl-substituted diazoloisoindoles are more accessible than the unsubstituted systems, the calculations by the CNDO/2 method were made precisely for structures I-III.

The bond orders (p_{rs}) in the ground states of the I-III molecules are presented in Fig. 1. Localization of the 6–7 and 8–9 bonds is appreciable in the benzene ring of 1H-imidazo-[2,1-a]isoindole (I). The p_{rs} values are more equalized in the pyrrole part. The 2–3 bond of the imidazole ring is the most localized. An analysis of the localized MO of structure I leads to the same conclusions. The valence activities (VA; see the experimental section) of the two-center fragments that include the 6,7 and 8,9 atoms are lower than those of the adjacent bonds, while the VA of the bonds in the pyrrole ring have close values (Table 1). The VA of the 2–3 bond of the imidazole ring is much lower than the VA of the adjacent bonds. This bond can be assumed to be sufficiently isolated. An analysis of the VA of fragments containing 3–5 atoms (Table 1) indicates that the pyrrole ring is conjugated with the remaining atoms of the benzene ring to a much greater extent than is the imidazole ring. Thus the VA of the pyrrole ring is 2.2, of which 0.8 goes into conjugation with the fragment containing the $C_{(6)}$–$C_{(9)}$ atoms. The VA of the fragment containing the 1–3 atoms is 0.5. The VA of the isoindole fragment has the same value, since the VA of the molecule as a whole is equal to zero. It is interesting that the VA of the 2–3 bond is greater than the VA of the fragment that contains the 1–3 atoms. This means that the 1–2 bond is characterized by greater multiplicity than the 1–9b bond; this is also confirmed by an analysis of the canonical orbitals (see Fig. 1). The conjugation of the free pair of electrons of the nitrogen atom bonded to the methyl group is stronger with the 2–3 multiple bond than with the isoindole part of the molecule. It follows from the information set forth above that, to a first approximation, imidazo[2,1-a]isoindole can be regarded as a 1,2-disubstituted isoindole, i.e., a 10π-electron system, rather than a 14π-electron system, as one should have expected from formula I.

Annelation of the benzene ring along the 2–3 bond of imidazo[2,1-a]isoindole does not lead to substantial changes in the bond orders and VA in the isoindole part of the II molecule as compared with I (see Fig. 1 and Table 1). The 2–3 bond is involved in the aromatic sextet of the benzene ring, the orders of all of the bonds and the VA of the two-center

TABLE 1. π-Valence Activities of Fragments of I-III Calculated by the PPP Method*

No. of atoms entering into the fragment	I		II		III	
	S_0	S_1	S_0	S_1	S_0	S_1
1,2	1,1 (1,15)	1,2	1,2 (1,17)	1,3	0,6 (0,60)	1,0
2,3	0,6 (0,58)	0,8	1,3	1,3	1,1 (1,16)	1,1
3,4	1,4 (1,50)	1,3	1,5	1,3	1,0 (1,06)	0,8
4,5	1,2 (1,30)	1,4	1,2 (1,29)	1,3	1,1 (1,21)	1,3
5,5a	1,1, (1,02)	1,3	1,1 (0,99)	1,3	1,2 (1,18)	1,2
5a,6	1,5 (1,52)	1,4	1,5 (1,54)	1,4	1,5 (1,50)	1,5
6,7	0,8 (0,81)	1,2	0,8 (0,78)	1,2	0,9 (0,82)	1,1
7,8	1,4 (1,49)	1,2	1,4 (1,42)	1,2	1,3 (1,38)	1,2
8,9	0,8 (0,84)	1,3	0,8 (0,81)	1,2	0,9 (0,86)	1,3
9,9a	1,5 (1,45)	1,4	1,5 (1,48)	1,3	1,4 (1,44)	1,2
9a,9b	1,3 (1,27)	1,4	1,2 (1,20)	1,4	1,4 (1,31)	1,6
1,9b	1,2 (1,21)	1,2	1,2 (1,19)	1,2	1,5 (1,57)	1,2
4,9b	1,2 (1,24)	1,3	1,2 (1,22)	1,3	1,2 (1,22)	1,2
5a,9a	1,5 (1,54)	1,5	1,5 (1,57)	1,5	1,5 (1,52)	1,5
2,2′			1,3 (1,22)			
2′,2″			1,0 (1,07)			
2″,3″			1,2 (1,16)			
3′,3″			1,0 (1,08)			
3,3′			1,2 (1,20)			
1,2,3	0,5	1,0			0,6	1,1
6,7,8,9	0,8 (0,81)	1,6	0,8 (0,77)	1,6	0,8 (0,83)	1,6
5,5a,9a,9b	1,5 (1,58)	2,2	1,5 (1,49)	2,2	1,7 (1,67)	2,2
2′,2″,3″,3′			1,0	1,3		
1,2,3,4,9b	1,0 (0,96)	1,6	2,0 (2,05)	2,5	1,0 (1,00)	1,4
4,5,5a,9a,9b	1,2	2,2	1,1	2,1	1,3	2,2
5a,6,7,8,9,9a	1,0 (1,13)	1,8	1,1 (1,20)	1,6	1,0 (1,08)	1,5
2,2′,2″,3″,3′,3			0,4 (0,46)	0,9		
1,2,3,4,5,5a,9a,9b	0,8	2,4			0,8	2,4
1,2,3,4,9b,2′,2″,3″,3′			1,0	1,6		
4,5,5a,6,7,8,9,9a,9b	0,5	2,3	0,4	2,1	0,6	2,1
1,2,2′,2″,3″,3′,3,4,9b			1,0	1,6		
1,2,3,4,5,5a,6,7,8,9,9a,9b	0,0	2,4	1,0	2,9	0,0	2,1
1,2,2′,2″,3″,3′,3,4,5,5a,9a,9b			0,8	2,4		

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*The π-valence activities calculated by the CNDO/2 method are presented in parentheses.

fragments in which have close values. The VA of this ring is lower than the VA of the 2—3 bond in I, i.e., it is more isolated than the multiple bond in imidazo[2,1-a]isoindole.

Knowing the electron density on the nitrogen atom ($Q = 2 - q_\pi$, where q_π is the π charge), one can calculate its VA from the formula [5]

$$\mathrm{VA} = 2Q - Q^2.$$

Comparing the VA of the nitrogen atoms bonded to the methyl groups in I and II (0.51 and 0.44, respectively), one can state that annelation of the benzene ring to I leads to greater isolated character of the free electron pair of the nitrogen atom under consideration. Isoindolo[2,1-a]benzimidazole (II) can then be represented in the form of three weakly interacting fragments: the isoindole part, the electron pair of the nitrogen atom bonded to the methyl group, and the benzene ring annelated along the 2—3 bond.

A similar examination of the p_{rs} values and VA in the III molecule leads to the following conclusions. As compared with the I molecule, the bond orders are somewhat equalized in the pyrrole ring and, to a lesser extent, in the benzene ring, retaining, on the whole, the previous pattern of the electron-density distribution in the isoindole fragment (Fig. 1 and Table 1). The 1—2 bond is relatively autonomous. The VA of the nitrogen atom bonded to the methyl group is 0.41 (from the formula presented above), i.e., it is still lower than in I and II. Consequently, the electron structure of the III molecule can also be characterized by a system made up of three fragments: the isoindole part, the $C_{(1)}$—$C_{(2)}$ double bond, and the free electron pair of the nitrogen atom.

The VA of the nodal nitrogen atoms calculated by the method described above for I-III are 0.72, 0.70, and 0.69, respectively. This indicates significant conjugation of the free electron pair of the nitrogen atom, particularly with the residue of the isoindole fragment, since in all three cases the VA of this fragment on the whole is lower than the values presented above (Table 1). To sum up, it may be noted that there is a common structural element

TABLE 2. Boundary Electron Densities of the Atoms in the HOMO Calculated by the PPP Method

Compound	1	2	3	4	5	5a	6	7	8	9	9a	9b
I	0,16	0,00	0,10	0,00	0,58	0,00	0,28	0,06	0,20	0,20	0,08	0,28
II*	0,24	0.00	0,04	0,00	0.56	0.00	0,26	0,08	0,18	0,20	0,08	0.30
III	0,08	0,24	0,14	0,00	0,56	0,00	0,26	0,04	0,20	0,16	0,08	0,24

*The boundary electron densities on the remaining atoms in II are as follows: 0.04 for 2', 0.00 for 2", 0.04 for 3", and 0.00 for 3'.

in the electron structures of I-III, viz., the isoindole fragment, which is sufficiently isolated, and all of the examined compounds can be regarded as 1,2-disubstituted isoindoles, i.e., to a first approximation, 10π-electron systems. This peculiarity of the electron structure should be reflected in the chemical properties of I-III. It is interesting, in this connection, to compare their electron structures with azinoisoindolines, which, to a first approximation, we regarded as 14π-electron systems [6]. Judging from our observations, the synthesized pyrido[2,1-a]isoindole [6] is more stable than 1,2-dimethylimidazo-[2,1-a]isoindole (see the experimental section). In this case the greater interannular conjugation in the tricyclic system promotes greater stability (the VA of the pyrrole ring in pyrido[2,1-a]isoindole is 1.5, as compared with 1.2 in the I molecule).

A comparison of the π energies (E_π) of positional isomers I and III (Fig. 1) shows that the π-electron system of imidazo[2,1-a]isoindole (I) is more stable than that of pyrazolo-[5,1-a]isoindole (III). The total energies of the electrons [$E_{(\sigma+\pi)}$] for these compounds differ to a smaller extent. Judging from the energies of the HOMO (Fig. 1) calculated by the CNDO/2 method, in accordance with Koopmans' theorem, one may assume an increase in the ionization potentials in the order II < I < III. The investigated compounds can be arranged in the same order with respect to the degree of resistance to oxidation. The order changes when the energies of the HOMO calculated by the PPP method are compared; however, II again proves to be the least resistant to oxidation.

An analysis of the π and σ + π charges on the atoms (Fig. 1) shows that in all of the examined systems the greatest negative charge is located on the free α-carbon atom of the pyrrole ring; this suggests initial electrophilic attack in this position. For I and II this conclusion is also confirmed by the boundary electron densities in the HOMO (Table 2). There are examples of acylation in the 5 position for derivatives of II [4]; this is in agreement with the calculations. Unfortunately, in view of the low stabilities of derivatives of I, electrophilic-substitution reactions have not been investigated for them.

A comparison of the π charges on the atoms of the benzene and diazole rings in I and III shows that the diazole ring should be more reactive with respect to both electrophilic and nucleophilic reagents. In examining electrophilic-substitution reactions this should be taken into account if the 5 position is occupied.

On the basis of the concept of the π-surplus character of heterocycles [7] one can approach its quantitative evaluation for the examined compounds. Taking into account the carbon atoms of only the isoindole fragment shows that the investigated compounds can be arranged in the order I > II ≈ III with respect to increasing π-surplus character. Taking into account all of the carbon atoms in isomers I and III suggests greater π-surplus character of imidazo[2,1-a]isoindole (I).

Since structures I-III can be conceived of as disubstituted isoindoles, it might be assumed that the Diels—Alder reaction would be the most characteristic for them. In the examined compounds one can formally isolate two diene fragments that are capable of reaction with dienophiles in the 5 and 9b or 6 and 9 positions. In addition, the energies of the HOMO of these compounds are in the range that is characteristic for typical dienes [8]. The π charges on the ends of the corresponding fragments are among the static indexes that are used to characterize the reactivities of dienes [9]. Proceeding from this, the diene fragment of the pyrrole ring should be assumed to be more active in the Diels—Alder reaction (Fig. 1). This conclusion is also confirmed by the VA of the fragments that contain the 6, 7, 8, and 9 atoms and the 5, 5a, 9a, and 9b atoms (Table 1).

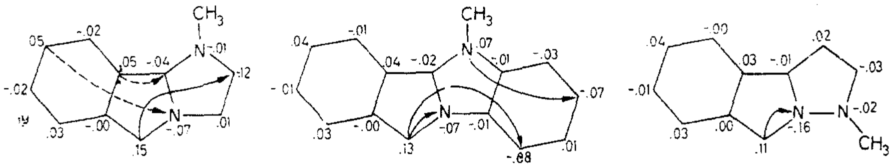

Fig. 2. Change in the π-electron density on the atoms on passing from the ground state to the first singlet excited state.

TABLE 3. Electronic Spectra of I-III

Compound	Calculated			Expt. λ_{max}, nm (log ε)
	λ_{max}, nm (lg ε)	Configuration interaction, %	Polarization M_x/M_y*	
I	204 (4,18)	$\Phi_6^8:\Phi_6^9=17:34$	1,57	206**
	222 (4,09)	$\Phi_5^8:\Phi_7^{10}=37:4$	−1,17	222
	233 (3,06)	$\Phi_7^{11}=79$	−19,89	229
	236 (4,26)	$\Phi_7^{10}=34$	−5,35	274***
	277 (3,88)	$\Phi_6^8:\Phi_7^{10}=55:21$	−49,01	280***
				287
	311 (3,63)	$\Phi_7^9=76$	−0,90	294***
	339 (3,89)	$\Phi_7^8=83$	−0,21	387
II	204 (4,03)	$\Phi_6^{10}:\Phi_8^{11}=38:41$	0.13	
	207 (3,29)	$\Phi_8^{11}=18$	14,63	
	229 (3,96)	$\Phi_9^{14}:\Phi_7^{10}=36:20$	−5,29	215 (4,38)
	232 (4,24)	$\Phi_8^{10}:\Phi_9^{14}=6:49$	−8,34	238 (4,25)
	234 (3,93)	$\Phi_9^{13}=13$	−25,98	249 (4,24)
	253 (2,05)	$\Phi_7^{10}:\Phi_9^{12}=25:18$	6,18	
	273 (4,20)	$\Phi_8^{10}:\Phi_9^{11}=48:20$	5,77	274*** (4,11)
				279 (4,20)
	282 (3,21)	$\Phi_9^{12}:\Phi_8^{10}=52:17$	−3,22	290*** (4,03)
	310 (3,44)	$\Phi_9^{11}:\Phi_9^{12}=71:11$	−3,10	305*** (3,85)
	344 (4,12)	$\Phi_9^{10}=94$	−0,48	414 fs (3,22)
III4*	345 (4,28)	$\Phi_7^8=96$	−1,13	

*The OX axis is directed along the 5a–9a bond, and the OY axis is perpendicular to it with the positive direction toward the benzene ring.

**Spectrum of the 1,2-dimethyl derivative (see the experimental section).

***Inflection.

4*Compound III has not yet been obtained; from the calculated data, therefore, only the long-wave absorption band is presented.

By analyzing the bond orders and VA of the various fragments in the first singlet excited state (Fig. 1, Table 1) one can arrive at the conclusion that in the case of excitation as a whole one observes a tendency for equalization of the bonds and that conjugation is intensified. Equalization of the multiplicities of the bonds occurs most appreciably in the benzene ring of the isoindole fragment.

The change in the charges on the atoms during excitation determines the nature of the electron transition. In imidazo[2,1-a]isoindole (I) the most substantial change in electron density is observed in the free α position of the pyrrole ring and in the 2 position of the imidazole ring; these changes affect the pyrrole nitrogen atom and the 9b position to a lesser extent (Fig. 2). It follows from Fig. 2 that transfer of electron density during excitation is realized to the atoms of the imidazole ring. In the isoindolo[2,1-a]-benzimidazole (II) molecule on passing to the S_1 state the electron density is transferred from the free α position of the pyrrole ring and the nitrogen atom bonded to the methyl group to the pyrrole nitrogen atom and the to 2'' and 3' positions.

Table 3, in which the parameters of the electronic spectra of I-III are presented, provides evidence for the good agreement between the calculated and experimental characteristics. It is interesting that the first electron transition in II is a longer-wave transition than in the case of I. This is in agreement with the fact that in II the distribution of the electron density on the atoms of the benzene ring annelated to the imidazole ring changes appreciably upon excitation. In pyrazolo[5,1-a]isoindole (III) the first electron transition is more localized than in I. Transfer of electron density is realized from the free α position of the pyrrole ring to the adjacent nitrogen atom (Fig. 2).

EXPERIMENTAL

The calculations were made by the PPP [10] and CNDO/2 [11] methods with the standard parametrization in [12]. The geometrical parameters of the I-III molecules were borrowed from studies of related compounds [13, 14]. The localization of the MO was determined by means of the VA [5, 15]. The UV spectra were recorded with a Specord UV-vis spectrophotometer.

1,2-Dimethyl-1H-imidazo[2,1-a]isoindole. A 1-g (3.2 mmole) sample of 1,2-dimethyl-5H-imidazo[2,1-a]isoindolium methylsulfate was placed in a sublimator, and 1 g (18 mmole) of potassium hydroxide was added. A yellow crystalline substance formed on the cooling element at 150°C and 1 mm (mercury column). This substance was sublimed repeatedly at 90°C to give 0.17 g (28%) of the product. The melting point could not be measured, since the substance decomposed extremely readily. The UV spectrum of a solution of the product in ethanol was recorded. Found: C 78.1; H 6.3; N 15.4%. $C_{12}H_{12}N_2$. Calculated: C 78.3; H 6.5; N 15.2%.

5-Methyl-5H-isoindolo[2,1-a]benzimidazole (II). This compound was obtained by the method in [5] and was purified by vacuum sublimation. The UV spectrum of a solution in heptane was obtained.

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