COMPARATIVE EVALUATION OF QUANTUM-CHEMICAL METHODS FOR CALCULATING AROMATIC AND ANTIAROMATIC NITROGEN HETEROCYCLES (RFVIEW)

B. Ya. Simkin and M. N. Glukhovtsev

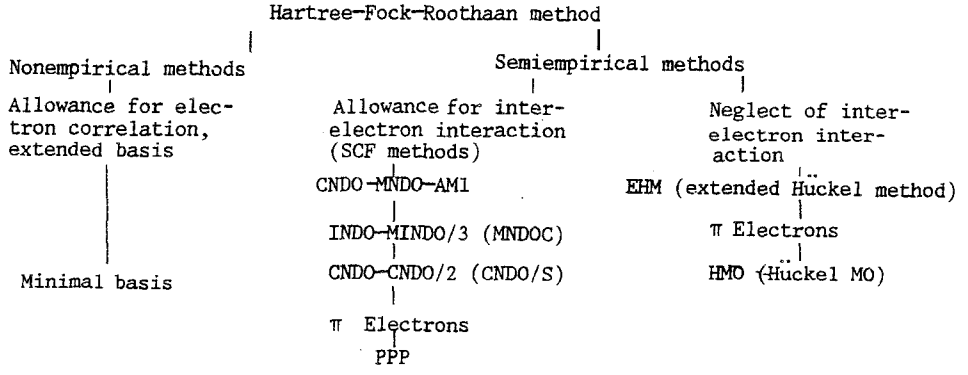
UDC 547.853'852'821'781'771'741.04:519.25:539.192

The possibilities of quantum-chemical methods in the determination of characteristics of aromatic and antiaromatic nitrogen heterocycles such as the thermodynamic stabilities, geometries of the molecules, electron distributions, dipole moments, ionization potentials, electron and proton affinities, energies and geometries of the molecules in the excited states, electronic spectra, and reactivities are discussed.

The aims of quantum-chemical calculations can be arbitrarily divided into two principal types. The first is the interpretation of the experimental data within the framework of a certain theoretical scheme, the construction of a model, and the formulation of the problem for a new experiment in order to verify this model. In a number of cases the calculation can be performed right away, i.e., a chain of the following sort is formed: calculation model → formulation of the experiment → change in the preceding model or construction of a new model. The aims of the second type – perhaps the most widespread at present – reduce to the verification of a number of special positions of a model constructed by the experimenter on the basis of data obtained by him within the framework of already canonized theoretical concepts; the term "verification" is sometimes tacitly understood to mean "confirmation," since otherwise the experimenter is more inclined to doubt the reliability of the computational method than his model. The aim of the present review was to demonstrate whether such doubts are always legitimate and how to select the optimal method of calculation.

The perfection of the computational methods of quantum chemistry makes it possible in a number of cases to obtain results that are not inferior in accuracy to the experimental data. A situation that would appear to be paradoxical 10-15 years ago often arises in this case: data on the physical properties and reactivity of a compound can be obtained by quantum-chemical calculation with the same level of reliability as that obtained as a result of a more expensive experimental investigation [1, 2]. In the present review we give a comparative evaluation of quantum-chemical methods of calculation of nitrogen heterocycles for characteristics such as the thermodynamic stabilities, geometries, electron distributions, dipole moments, ionization potentials, electron and proton affinities, electronic spectra, and reactivities. For illustration we selected primarily examples of calculations of conjugated aromatic and antiaromatic nitrogen heterocycles.

The "hierarchy" of the principal MO LCAO methods [3] can be represented by the scheme below.



Scientific-Research Institute of Physical and Organic Chemistry, Rostov Stata University, Rostov-on Don 344104. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1587-1603, December, 1989. Original article submitted April 11, 1988.

 ©1990 Plenum Publishing Corporation

These methods have been examined in detail [1-11]. In connection with the development of computer techique nonempirical methods of calculation have become increasingly widespread in recent years [1, 2, 10]. However, the progress of ab initio methods should not lead to "chauvinism" [12] with respect to the most perfected semiempirical methods – MINDO/3 [13], MNDO [14], and AM1 [15]. The results of calculations by these methods and nonempirical methods have been frequently compared [12, 16, 17]. For example, in comparing the mean values of the error in the calculation of the heat of formation it is seen that the MNDO and AM1 methods give better results than nonempirical calculations in a minimal basis. Semiempirical methods require fundamentally smaller expenditures of computer time as compared with nonempirical methods [12, 14]. Thus the time necessary for the nonempirical calculation of benzene in the 4-31G basis is greater by a factor of $\sim 10^3$ than with the same computer by means of the MNDO method [12]. Modern computers such as the CRAY and CDC-205 have very high efficiencies, but it should be noted that the cost of computer time also increases in proportion to the efficiency of the computer. Thus an important advantage of semiempirical methods is the significantly smaller expenditures of computer time.

However, semiempirical methods should not be contrasted with nonempirical methods. They are not an alternative but rather a supplement to the latter. The results obtained by the MINDO/3, MNDO, and AM1 methods may serve as a starting point for nonempirical calculations in an extended basis with allowance for electron correlation.

Comparative characteristics of semiempirical methods are presented, for example, in [3, 5-7, 9]. Recommendations for the selection of the basis of a nonempirical calculation are indicated in monographs [1, 2, 10].

In the examination of the applicability of methods of calculation for the description of the structures and electron structures of nitrogen heterocycles it is expedient to single out two aspects. The first aspect involves the limitations of the methods that are also characteristic for the corresponding hydrocarbon molecules. These include the difficulties that are asociated with the description of strained molecules, nonclassical structures, molecules with an open shell, etc. These problems have been previously examined [1, 5, 7-11, 18, 19]. We will therefore direct principal attention to the second aspect, i.e., the problems associated with the presence of nitrogen atoms of the pyrrole or pyridine type. In comparing the results of calculations by the various methods and the experimental data we strove to reveal both the advantages of one or another method and (which, perhaps, is even more important) the increased possibilities of modern quantum-chemical methods of calculation.

Thermodynamic Stabilities. In speaking of the stability of a compound one should be precise about the form of "stability" with which one is dealing. We will examine the thermodynamic stability, i.e., the stability relative to other isomers or decomposition products formed in the absence of other reagents. The so-called hydrolytic stability, for example, is not necessarily concomitant with the thermodynamic stability [20]. Thus sym-triazine is is thermodynamically stable relative to decomposition into three molecules of HCN, which occurs only at high temperatures; however, this compound is easily decomposed by the action of water.

If for the determination of the relative thermodynamic stabilities of isomers it is sufficient to compare, for example, their heats of formation, it is much more difficult to establish which compound, benzene or pyridine, is more stable. In the latter case one must resort to some scheme for the determination of the "stabilization energy." But, first and foremost, we encounter the problem of the sufficiently accurate calculation of the heat of formation (ΔH_f). If there is only one nitrogen atom in the ring in the heterocyclic molecule, quantum-chemical methods satisfactorily reproduce ΔH_f – for example, in the case of pyridine and pyrrole (Table 1).

It is apparent from Table 1 that the best results were obtained when the MINDO/3 method was used. However, the situation changes radically in the case of heterocycles that contain two or more nitrogen atoms of the pyridine type, particularly if these atoms are adjacent. In this case the MINDO/3 method substantially understates the ΔH_f values [24-26]. Underestimation of the repulsion of the unshared electrom pairs (UEP) of nitrogen atoms of the pyridine type is characteristic to a lesser extent for the MNDO and AM1 methods. Let us note that the heats of formation of pyrazole and imidazole calculated by the NDO method [27] are in much better agreement with the experimental data than in the case of diazines (Table 2).

TABLE 1. Calculated and Experimental Heats of Formation (kJ/mole) of Pyridine and Pyrrole

Compound	MINDO/3 [21]	MNDO [22]	MNDOC [23]	AM1 [15]	Exptl.*
Pyridine (I)	142,7	120,1	130,9	134,3	144,8
Pyrrole (II)	123,4	135,6	—	166,9	108,4

*Cited in [15].

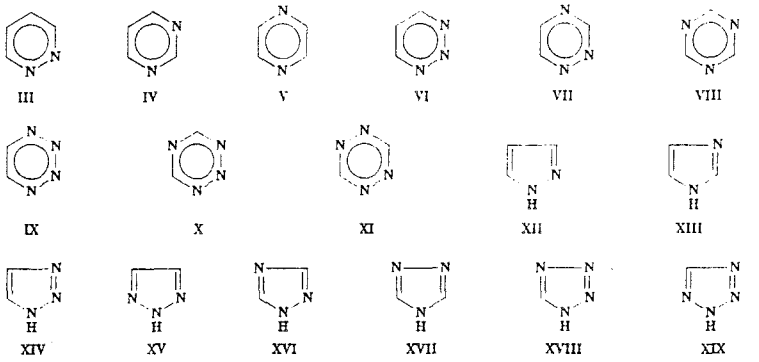
TABLE 2. Calculated and Experimental Heats of Formation (kJ/mole) of Diazines, Pyrazole, and Imidazole

Compound	MNDO [22, 27]	AM1 [15]	Exptl.*
1,2-Diazine (III)	184,9	231,4	278,2
1,3-Diazine (IV)	148,5	183,6	195,8
1,4-Diazine (V)	160,2	186,2	196,2
Pyrazole (VI)	190,0	—	181,2±8,9
Imidazole (VII)	138,9	—	128,0±7,5

*Cited in [15, 27].

It has been assumed that a systematic error that is due to underestimation of the repulsion of the UEP of the nitrogen atoms of the pyridine type arises in calculations by the MNDO method. On the basis of this, corrections of 41-50 kJ/mole for each pair of adjacent nitrogen atoms in azines and 33-41 kJ/mole for each pair of corresponding atoms in azoles have been proposed [28]. The differences in the energies of isomers III-V, VIII-X, XI-XIII, and XIV-XVII corrected in this way are in good agreement with the available experimental data and the results of nonempirical calculations (Table 3).

It is apparent from Table 3 that calculations in the STO-3G basis understate the difference in the energies of imidazole and pyrazole by a factor of almost two (ΔE_{exp} = 53.2 kJ/mole), while the MNDO method gives ΔE = 51.1 kJ/mole. This once again confirms the conclusion of the results of calculations by the semiempirical MNDO and AM1 methods as compared with nonempirical calculations in the minimal basis.



In an insufficiently extended basis ab initio calculations may give qualitatively incorrect estimates of the relative stabilities of isomers. A characteristic example is afforded by 1H- and 2H-tetrazoles XVIII and XIX (Table 3). In addition to the data presented in Table 3, let us note that calculation in the 3-21G basis gives a difference in energies for XIX-XVIII of 4.2 kJ/mole, whereas calculation in the 6-31G basis, leads to a qualitatively different result: ΔE = −4.2 kJ/mole [32]. According to the calculation in the 6-31G**//6-31G basis, this value is −7.1 kJ/mole, which corresponds to the value calculated by the MNDO method with allowance for the corrections proposed in [28] (Table 3).

As an example of the evaluation of the relative energies of tautomers let us examine the 2-pyridone ⇄ 2-hydroxypyridine system, which has been studied in, perhaps, greatest detail both theoretically and experimentally. The existence of data on the relative stabilities of the tautomers in the gas phase makes it possible to thoroughly analyze the accuracy of calculations by different quantum-chemical methods (Table 4).

TABLE 3. Relative Energies (kJ/mole) of Nitrogen-Containing Heterocycles III-XIX from the Results of Calculations

Compound	PPP [29]	MNDO [27, 28]	STO-3G [30, 31]	3-21G [30]	6-31G [30, 31]	6-31G*//6-31G [30, 31]
III	108,3	36.4 (77...87)*1, *2	65,3	122.2	104,6	112,5
IV	0	0	0	0	0	0
V	57,1	11,7*2	11,7	22,6	19,2	26,8
VI	—	51,1*3	28,0	61,9	50,6	54,4
VII	—	0	0	0	0	0
VIII	—	65,7 (148...166)	124,3	230,9	202,5	218,4
IX	—	48,5 (130...150)	77,4	138,9	122,6	138,5
X	—	0	0	0	0	0
XI	—	30,9 (71...80)	57,7	112,5	97,9	105,0
XII	—	0	0	0	0	0
XIII	—	20,8	21,3	34,7	27,6	37,2
XIV	—	40,6 (74...82)	50,6*4	79,1*5	—	—
XV	—	67,0	45,2*4	63,2*5	—	—
XVI	—	15,1	0*4	0*5	—	0
XVII	—	0	20,9*4	21,3*5	—	28,0*6
XVIII	—	0(17)*7	10,5*4	0*5	—	7,1*7
XIX	—	17,6(0)	0*4	0,8*5	—	0

*1 The value corrected in accordance with [28] is indicated in parentheses. According to the experimental data, the difference in the energies of heterocycles III and IV is 82.4 kJ/mole.

*2 Calculation in the 4-31G basis with the geometry optimized by the MNDO method gives a difference in the energies of heterocycles III and IV of 111.7 kJ/mole, as compared with 20.1 kJ/mole for V and IV, respectively. Here and subsequently, calculation in the A basis with the geometry optimized by nonempirical calculation in the B basis or by semiempirical method C is designated as A//B or A//C.

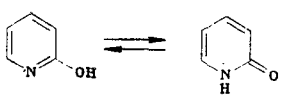
*3 Experimental evaluation 53.2 kJ/mole (see [27]).

*4 Calculation in the STO-3G/INDO basis [33].

*5 Calculation in the DZ basis [32].

*6 $\Delta E_{XVII-XVI}$ = 16.3 (STO-3G), 15.9 (3-21G), and 22.6 (6-31G kJ/mole [30].

*7 $\Delta E_{XIX-XVIII}$ = −6.7 ([28], 4-31G/MNDO), −1.7 ([30], STO-3G), and −3.4 ([30], 6-31G) kJ/mole. Heterocycle XIX predominates in the gas phase [32].



A B

Calculation by the MINDO/2 method and nonempirical calculation in the 3-21G basis lead to a qualitatively incorrect conclusion regarding the greater stability of the B form, while calculations by the PPP, CNDO/2, and MNDO methods an ab initio calculation in the minimal basis give qualitatively correct results: However, they understate the difference in energies, particularly in calculations by the CNDO/2 method. Calculations by the MINDO/3 method prove to be somewhat better. Let us direct attention to the fact that nonempirical calculations both in the 3-21G basis and in the 6-31G basis with the geometry optimized in the 3-21G basis (6-31G//3-21G) lead to results that differ qualitatively from the experimental results. Only calculations in the 6-31G* basis (6-31G*//3-21G) give correct ratios of the stabilities of tautomeric forms A and B.

Agreement with the experimental estimates was also obtained in ab initio (6-31G*) calculations of the relative energies of the tautomers of 4-hydroxypyrimidine [40]. In addition, let us note that the results of calculations by the PPP method of, for example, cytosine tautomers

TABLE 4. Difference in the Energies of 2-Hydroxypyridine (A) and 2-Pyridone (B) ΔEA-B (kJ/mole) Calculated by Different Methods and Experimentally Determined (gas phase)

PPP [34]	CNDO/2 [35]	MINDO/2 [36]	MINDO/6 [35]	NMDO [37]	STO-3G [38]	3-21G [38]	6-31G// 3-21G [38]	6-31G*// 3-21G [39]	Exptl.
−48,5	−141,8	56,9	−15,7	−41,0	−64,4	7,1	8,8	−4,2	−2,6±1,2*[1]

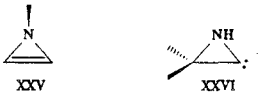
*Cited in [39].

[41] are in agreement with the results of both nonempirical calculations [42] (see the comparison of the results in [41]) and calculations by the MNDO method [43]. Thus it may be assumed that the PPP method [29] retains its value in calculations of tautomers of polyatomic molecules (without steric hindrance and an intramolecular hydrogen bond) that are as yet beyond the limits of the possibilities of methods with a higher level of approximation.

The results of calculations by the MNDO method are in agreement with the results of nonempirical calculations in extended bases not only in the case of five- and six-membered nitrogen heterocycles but also in the case of three- and four-membered heterocycles. For example, for diazirine and its isomers the MNDO method and nonempirical calculations lead to qualitatively identical ratios of the stabilities of isomers (Table 5) [44].

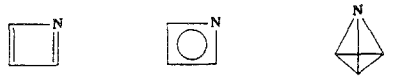
XX XXI XXII XXIII XXIV

As in the case of five- and six-membered rings, satisfactory results can also be obtained when the MINDO/3 method is used when only one nitrogen atom is present in the three-membered heterocycle. The results of calculations by this method of the relative stabilities of 1H-azirine (XXV) and its carbene isomer XXVI are in agreement with the results of nonempirical calculations. The relative energy (in kilojoules per mole) of isomer XXVI as compared with XXV is −37.2 (MINDO/3) [45], −46.0 (STO-4G) [46], and −37.6 (6-31G) [46].



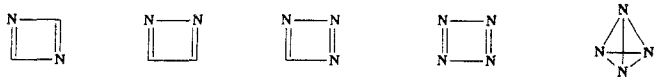
XXV XXVI

The results of calculations of the relative stabilities of azete (XXVII) and its valence isomer azatetrahedrane (XXVIII) by the MINDO/3 method [47] are in agreement with the results of the MNDO method [26, 48] and nonempirical calculations [18, 40]. However, the type of stationary point of the potential energy surface (PES) that corresponds to the C_{2v} structure (XXVIIa) is reproduced incorrectly by the MINDO/3 method [50].



XXVII, C_s XXVIIa, C_{2v} XXVIII, C_{3v}

On the other hand, the results of calculations of azacyclobutadienes, XXVII and XXIX-XXXII by the MNDO method [26, 48, 49] are in good agreement with the results of nonempirical calculations [49-51].


XXIX XXX XXXI XXXII XXXIII

The MNDO method gives results that are close to those obtained by the ab initio method also in calculations of nitrogen heterocycles of the biradical type. Thus, 3-4-didehydropyridine (XXXIV), according to calculations by the MNDO method [52], is more stable than 2,3-didehydropyridine (XXXIVa) by 37.7 kJ/mole. Nonempirical calculations confirm this result (the difference in energies is 56 kJ/mole, 6-31G basis) [53].

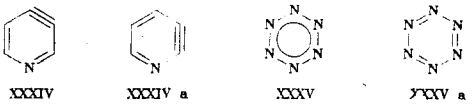

XXXIV XXXIV a XXXV XXXV a

TABLE 5. Calculated Relative Energies of CN_2H_2 Isomers

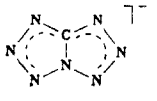
Isomer	E_{rel}, kJ/mole			
	MNDO	3-21G	6-31G*// 3-21G	MP3/6-31G*// 3-21G*[1]
XX	0	0	0	0
XXI	77,7	143,7	—	—
XXII (singlet)	214,3	261,6	386,1	416,8
XXIII	−22,6	−126,1	−41,4	−14,7
XXIV	130,6	−163,2	−21,7	31,8

[1] The abbreviation MP3 pertains to allowance for electron correlation in the Meller–Pleset third-order perturbation theory (see [1]).

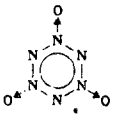
In a comparison of the results of calculations of nitrogen heterocycles by semiempirical (MNDO) and nonempirical methods it has already been noted that in the latter case the selection of the appropriate basis is important. Less accurate results were obtained in calculations in a minimal basis such as the STO-3G basis than by the MNDO method. Let us present two characteristic examples. According to calculations by the MNDO method, tera-azatetrahedrane (XXXIII) has a higher energy (by 156.8 kJ/mole) than the planar structure of tetrazete with D_{2h} symmetry [26]. Nonempirical calculation in the STO-3G basis, on the other hand, indicates higher stability of the T_d tetrahedral structure. However, according to calculation in the 4-31G basis, the N_4 (D_{2h}) planar structure, in conformity with the results of calculations by the MNDO method, is more stable by 187.7 kJ/mole than the N_4 structure with T_d symmetry [26].

Another example involves calculations of hexazine N_6 (XXXV), which have become particularly timely after its experimental fixation in a matrix at low temperatures [54].

According to calculations by the MNDO method, the completely asymmetical D_{6h} structure of hexazine corresponds to the minimum on the potential energy surface (PES) of N_6 [55].* On the other hand, nonempirical calculations in both minimal and extended (DZ) bases show that the minimum on the PES corresponds to a structure of the Kékulé type with D_{3h} structure (XXXV), which corresponds to the transition state of π-valence isomerization of Kékulé D_{3h} structures [56]. However, taking into account polarization functions (DZ + P basis) leads to a result [56] that is in qualitative agreement with the results of calculations by the MNDO method.


XXXVI

XXXVII


XXXVIII

Thus the semiempirical MNDO method satisfactorily communicates the heats of formation of even polyazatheterocycles, and the results of calculations by this method approach in accuracy the results of ab initio calculations in an extended basis. The error in the MNDO method that is associated with underestimation of the repulsion of the ushared electron pairs (UEP) of the nitrogen atoms of the pyridine type [28] is, to a smaller extent, characteristic for a modification of this scheme, viz., the AM1 method, as one can judge from the results of the calculations [15].

This makes it possible to use the MNDO method for the study of polyazaheterocyclic compounds as, for example, in the search for methods for stabilization of polynitrogen heterocycles, particularly the hexazine carcass in the form of 1,3,5-trioxide XXXVIII [58].

However, how does one estimate the relative stabilities of hexazine XXXV and its symtrioxide XXVIII, which are not isomers? Let us examine this question for the simplest example: is pyridine less stable than benzene? The relative stabilizies of these molecules can be determined by comparison of the heats of the isodesmic reactions involving severing of the bonds [59]:

*In [55] the calculated (by the MNDO method) heat of formation of hexazine was refined: ΔH_f = 438.2 kJ/mole instead of the previously obtained ΔH_f = 1352.1 kJ/mole [24]. The abbreviation PES stands for the potential energy surface.

$$\text{Benzene} + 6CH_4 \rightarrow 3CH_3{-}CH_3 + 3CH_2{=}CH_2$$

$$\Delta H_{298}^0 \text{ (exp.)} = 268 \pm 7 \text{ kJ/mole;}$$

$$\Delta E_T \text{ (calc.)} = 293 \text{ (STO-3G) [1]; } 175 \text{ (3-21G) [1];}$$

$$243 \text{ kJ/mole (6-31G*) [60].}$$

$$\text{Pyridine} + 5CH_4 + NH_3 \rightarrow 2CH_3CH_3 + CH_3NH_2 + 2CH_2{=}CH_2 + CH_2{=}NH$$

$$\Delta H_{298}^0 \text{ (exp.)} = 274 \pm 7 \text{ kJ/mole,}$$

$$\Delta E_T \text{ (calc.)} = 293 \text{ (STO-3G) [1]; } 268 \text{ (3-21G) [1];}$$

$$254 \text{ kJ/mole (6-31G*) [60].}$$

However, one should take into account the fact that factors such as a change in the number and type of CC and CN bonds and a change in the number of hydrogen atoms bonded to a given atom make a contribution to the enthalpy of an isodesmic reaction. The heats of homodesmic reactions are a more acceptable criterion [61]:

$$\text{Benzene} + 3CH_2{=}CH_2 \rightarrow 3CH_2{=}CH{-}CH{=}CH_2 \text{ (trans)}$$

$$\Delta H_{298}^0 \text{ (exp.)} = 90 \pm 6 \text{ kJ/mole;}$$

$$\Delta E_T \text{ (calc.)} = 104 \text{ kJ/mole (6-31G*).}$$

$$\text{Pyridine} + 3CH_2{=}CH_2 \rightarrow 2CH_2{=}CH{-}CH{=}CH_2 +$$
$$CH_2{=}CH{-}N{=}CH_2 \text{ (trans)}$$

$$\Delta E_T \text{ (calc.)} = 106 \text{ kJ/mole) (6-31G*).}$$

Thus benzene and pyridine have essentially identical stabilities. One can similarly show the lower stability of hexazine XXXV as compared with its 1,3,5-trioxide XXXVII [58] by comparison of the heats of various reactions involving the cleavage of the rings of these molecules. In a number of cases, in view of the indicated circumstances, the determination of the relative stabilities of molecules on the basis of the heats of isodesmic reactions proves to be impracticable, and one should examine only the heats of homodesmic reactions (see [26] for the example of the relative stabilities of azetes).

The stabilization (destabilization) of a molecule due to aromatic character (antiaromatic character) can be evaluated by calculation of the resonance energies (for example, see a previous review [62] for various schemes for calculation of the resonance energies). Examples of calculation of the resonance energies of nitrogen heterocycles have been examined in a monograph [63] and a review [64]. Let us point out several circumstances that one must bear in mind in carrying out such calculations. The Dewar resonance energy (the PPP method) of hexazine (118.2 kJ/mole) even exceeds the corresponding value for benzene (83.8 kJ/mole) [545]. However, calculation of the Dewar resonance energies of hexazine and benzene by the MNDO method (i.e., taking into account all of the valence electrons) leads to −0.5 kJ/mole and 88.3 kJ/mole [55].

The results of calculations of the heats of atomization of nitrogen heterocycles by the PPP method are, as a rule, in good agreement with the experimenal ΔH_{at} values [3, 27, 65, 66]. For example, for pyrrole ΔH_{at}(exp) = −44.77 eV and ΔH_{at}(calc) = 44.768 eV; for pyridine ΔH_{at}(cxp) = −51.79 eV and ΔH_{at}(calc) = −51.87 eV [29]. However, in calculations of the heats of atomization of antiaromatic molecules for the determination of the Dewar resonance energies one can obtain both singlet-unstable solutions [67-69] (see [70] for the classification of the type of filling of the MO [71]). This leads to artifacts in the results of the calculation of ΔH_{at} and, correspondingly, in the resonance energies.

Molecular Geometries. The experimentally determined geometry of a molecule corresponds to the local minimum on the potential energy surface (PES). The calculated geometry should therefore also correspond to the determined (by calculation) local minimum of the PES, for otherwise the calculated PES is an artifact. An experimentally determined geometry is sometimes used for nonempirical and semiempirical calculations. Strictly speaking, this approach is incorrect, since the experimentally determined geometry also may not correspond to the energy minimum calculated by a given method. However, the geometry of this local minimum on the PES should be close to the experimentally determined geometry, for otherwise the method used is unsuitable for calculations of the PES.

Experimental data on the geometries are known for a limited number of molecules. Quantum-chemical calculations of the molecular geometry that take on special significance in investigations of unstable, highly reactive molecules or ions therefore prove to be important.

TABLE 6. Geometries of Pyridine and Pyrazine Calculated by Various Methods and Determined Experimentally (by microwave spectroscopy in the case of pyridine and by electron-diffraction spectroscopy in the case of pyrazine)

Molecule	PPP [29]	QCFF/PI [74]	MINDO/3 [21, 75]	MNDO [22]	AM1 [15]	3-21G [39]	4-21G [76]	6-31G [31]	Exptl. [77, 78]
Pyridine									
				Ring bond lengths, (pm)					
$N_{(1)}C_{(2)}$	133,8	133,5	133,5	135,3	134,7	133,1	133,3	133,2	133,8
$C_{(2)}C_{(3)}$	139,6	141,9	140,7	141,1	140,8	138,2	138,2	138,6	139,4
$C_{(3)}C_{(4)}$	139,7	140,9	140,6	140,5	139,6	138,3	138,4	138,7	139,2
				Angles (deg)					
$C_{(6)}N_{(1)}C_{(2)}$	—	120,8	119,9	118,2	117,6	—	118,4	118,9	116,9
$N_{(1)}C_{(2)}C_{(3)}$	—	121,2	122,5	122,8	123,4	—	122,8	122,5	123,8
$C_{(2)}C_{(3)}C_{(4)}$	—	119,7	117,8	118,8	118,3	—	118,5	118,6	118,5
$C_{(3)}C_{(4)}C_{(5)}$	—	117,1	119,6	118,6	118,9	—	119,0	118,9	118,4

	PPP [29]	CNDO/2 [79]	STO-3G [79]	4-21G [2]	4-21G [2]	6-31G [31]	Exptl. [20]
Pyrazine							
			Ring bond lengths, (pm)				
NC	133,3	134,5	136,5	133.3	132,6	133.2	133,9
CC	139,8	138,0	139,0	138,1	138,3	138,6	140,3
			Angles (deg)				
NCC	—	123.3	123,0	121,1	122.2	121,0	122.1
CNC	—	113,4	114,1	117,9	115.5	118,1	115.6

There are various methods of optimization of the geometry. A review of them has been presented in, for example, a monograph [8] (also see [72]). Let us note only that inefficient procedures for optimization of the geometry are used in the GAUSSIAN-70 and GAUSSIAN-76 programs of nonempirical calculations that have become widely used, and one must therefore have a cautious attitude toward the results obtained [12]. This inadequacy was surmounted in the GAUSSIAN-80 program, in which optimization of the geometry is carried out by the method of conjugate gradients [73].

The experimental and calculated (by various methods) geometrical parameters of pyridine, pyrazine, pyrrole, and pyrazole are presented in Tables 6 and 7. Of the semiempirical methods, the MINDO/3 and AM1 methods give the best results for pyridine and pyrrole. The lengths of the bonds in the ring, particularly the NN bonds (3-6 pm too high), are overstated appreciably when the STO-3G basis is used. This tendency is less pronounced for CC and CN bonds. Thus nonempirical calculation in the STO-3G basis leads to rings that are not only "larger" but also more distorted as compared with the results obtained in the 6-31G basis. This limitation of calculation in the minimal basis is not surmounted completely on passing to the 3-21G basis [30, 31]. Agreement with the experimental data is achieved only by calculations in the 6-31G basis. In the case of pyrazine in calculations by both semiempirical methods and ab initio methods in the STO-3G basis the size of angle CNC is understated as compared with the experimental value. On the other hand, in the case of pyridine both semiempirical and nonempirical methods for different bases overstate this value (Table 6). Thus, any systematic character of the errors is not manifested in this case.

A variant of the MINDO/3 method with corrected values of the two-center α_{NN} and B_{NN} parameters is known [49]. The bond lengths of polyazaheterocycles obtained by this method differ from the results of nonempirical calculation: nevertheless, the method correctly conveys the peculiarities in the change in the lengths of the CC, CN, and NN bonds as N atoms accumulate.

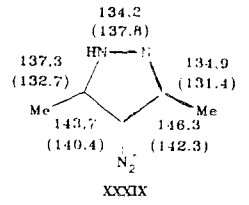
The MNDO method understates the lengths of the NN bonds in pyridine systems to 127-129 pm; the experimental value in the III molecule is 133.0 pm, as compared with 132.1 pm in the XIII molecule [20]. Let us note, however, that calculations with a corrected geometry lead only to a slight change in the ΔH_f values [28].

The example of the calculation by the MNDO method of the geometry of the 1H-3,5-dimethylpyrazole-4-diazonium cation (XXXIX), particularly the length of the N(pyrrole type)—N(pyridine

TABLE 7. Geometries of Pyrrole and Pyrazole Calculated by Various Methods and Determined Experimentally (by microwave spectroscopy)

Molecule	PPP [29]	QCFF/PI [74]	MINDO/3 [21]	MNDO [22, 27]	AM1 [15]	STO-3G [30]	3-21G [30]	4-21G [80]	6-31G [30]	Expt1. [81, 82]
Pyrrole										
Bond lengths (pm)										
$N_{(1)}C_{(2)}$	139,0	134,4	136,8	139,8	139,1	138,9	137.7	137,9	137,3	137,0
$C_{(2)}C_{(3)}$	135,8	138,5	139,1	139,4	140,1	135,1	136,0	135.7	136,3	138,2
$C_{(3)}C_{(4)}$	144,0	143,3	143,3	143,7	143,6	143,2	143,3	143,2	143,0	141,7
Angles (deg)										
$C_{(5)}N_{(1)}C_{(2)}$	—	110,1	—	—	—	108,7	109,2	109,1	109,4	109,8
$N_{(1)}C_{(2)}C_{(3)}$	—	108,9	—	—	—	107,9	108,0	108,0	108,0	107,7
$C_{(2)}C_{(3)}C_{(4)}$	—	106,1	—	—	—	107,8	107,4	107,5	107,3	107.4
Pyrazole										
Bond lengths (pm)										
$N_{(1)}N_{(2)}$	135,6	—	—	133,3	—	138,4	137,8	—	135.1	134,9
$N_{(2)}C_{(3)}$	130,9	—	—	135,4	—	133,0	131.3	—	131.5	133,1
$C_{(3)}C_{(4)}$	142,3	—	—	144,1	—	142,4	142.0	—	141.8	141,6
$C_{(4)}C_{(5)}$	136,9	—	—	139.5	—	135,4	136.3	—	136,7	137,2
$C_{(5)}N_{(1)}$	136,7	—	—	139,8	—	137,9	135,6	—	135,3	135,9
Angles (deg)										
$C_{(5)}N_{(1)}N_{(2)}$	—	—	—	112,9	—	112,3	111,6	—	112.1	113,1
$N_{(1)}N_{(2)}C_{(3)}$	—	—	—	106,2	—	103,2	104,6	—	105,3	104.1
$N_{(2)}C_{(3)}C_{(4)}$	—	—	—	110,3	—	112,5	111,8	—	111.1	111,9
$C_{(3)}C_{(4)}C_{(5)}$	—	—	—	105,1	—	105,4	105,0	—	104,9	104.5
$C_{(4)}C_{(5)}N_{(1)}$	—	—	—	105,6	—	106,6	107,1	—	106,6	106,4

type) bond, is interesting. The results obtained are in good agreement with the results of x-ray diffraction analysis, with the exception of the length of the NN bond (all of the bonds in the ring are elongated somewhat as compared with the experimental values for a crystal of XXXIX chloride, which are indicated in parentheses, while the reverse tendency is characteristic for the NN bond) [83]:



XXXIX

Bond lengths in picometers (pm)

Similarly, for pyrazole the MNDO method overstates, as compared with the experimental values, the lengths of all of the bonds in the ring except the NN bond, which, on the contrary, is understated [27] (Table 7).

In calculations of the geometries of antiaromatic molecules or higher [n]annulenes the selection of the basis and allowance for electron correlation often prove to be fundamentally important. Thus according to nonempirical calculations in the STO-3G basis the structure of [18]-sym-nonazaannulene (XL) with C_{3h} symmetry and alternation of the CN bonds (128.3 and 144.4 pm) is 174.5 kJ/mole more stable than the D_{3h} structure with identical lengths of the CN bonds (135.1 pm). However, calculation in the 4-31G basis decreases this difference to 4.2 kJ/mole [51]. This provides a basis for the assumption that the structure of the ground state of XL has D_{3h} symmetry, and a more flexible basis and allowance for the energy of electron correlation are necessary for the correct reproduction of the geometry [84].

We did not examine the conformational analysis of nitrogen-containing saturated cyclic molecules and the use of methods of molecular mechanics for it. There is a monograph [85] dealing with these questions.

Electron Distributions and Dipole Moments. First of all, let us note the extremely pronounced differences in the π-electron distributions calculated for nitrogen heterocycles by the PPP and HMO methods [65]. Significant differences are observed when one compares the

TABLE 8. Calculated and Experimental Dipole Moments (D) of Azoles and Azines

Molecule	π-SCF*[1] [87]	QCFF/PI [74]	MINDO/3 [21]	MNDO [22, 27]	AM1 [15]	6-31G*//6-31G [30, 31]	Exptl.*[2]
Pyrrole	2,27	1,81	1,99	1,81	1,96	1,85	1,75
Pyrazole	2,53	2,64	—	2,11	—	2,42	2,21
Imidazole	3,95	3,88	—	3,48	—	3,84	3,67
Pyridine	2,21*[3]	1,90		1,97	1,98	2,30	2,22*[4]
Pyrimidine	2,24	1,76	—	—	—	2,40	2,33*[4]
Pyridazine	3,71	3,82	—	—	—	4,42	4,22*[4]

*[1]See [87] for a bonded variant of perturbation theory.
*[2]Cited in [30].
*[3]The dipole moment of pyridine calculated by the HMO method is 2.25 D [88].
*[4]Cited in [20].

charges of the atoms in adenine, guanine, cytosine, uracil, and thymine calculated by the HMO (with allowance for the σ charges by the Del Re method), PPP, EHM, IEHM, CNDO/2, and ab initio methods [86].

The accuracy of the calculated values of the dipole moments can be judged from the data presented in Table 8.

Ionization Potentials (IP) and Electron Affinities (EA). The simplest theoretical method for the determination of IP is based on Koopmans' theorem. However, a number of factors such as the energy of reorganization of the electron shell and the change in the correlation energy are not taken into account in this method [10, 89]. As a result, for example, the use of Koopmans' theorem also leads to a qualitatively incorrect prediction of the ionization potentials of tetrazoles [90], since the π ionization of tetrazole does not lead to the most stable cation radical, although the π orbital is the highest occupied molecular orbital (HOMO). One can use the ΔSCF method for the determination of the IP; the vertical IP in this case is obtained as the difference between the energy of the ion calculated with the geometry of the neutral molecule and the energy of the neutral molecule [10]. To find the IP of, for example, azoles in this way the energies of both the π- and σ-cation radicals are calculated with the geometry of the neutral molecule [30]. It turns out that π ionoization is characteristic for pyrrole, pyrazole (VI), and imidazole (VII), while σ ionization is characteristic for triazoles XIV and XVI and tetrazoles XVIII and XIX. In addition, one should take into account the fact that the values of the vertical IP are underestimated in calculations in the STO-3G basis [32, 91].

In the case of pyridine values of the vertical IP that are qualitatively correct and quantitatively close to the results of photoelectron spectroscopy could be obtained as a result of nonempirical calculation in the DZ basis only when the relaxation energies and electron correlation were taken into account [92]. However, the determination of the IP of pyridine based on Koopman's theorem does not give the correct result [31]. The results of calculations of the IP and EA for pyrrole and pyridine are presented in Table 9.

Proton Affinities. The proton affinities in the gas phase are determined as the difference in the total energies of, for example, azole and the corresponding azolium cation. It is apparent from Table 10 that the MNDO method gives results that are even closer to the exerimental values than nonempirical calculation in the 6-31G* basis. The protonation energies are substantially overstated in calculations in the STO-3G basis [97]. The calculated proton affinities are in agreement with the conclusion regarding the greater basicity of imidazole as compared with pyrazole.

Excited States and Electronic Spectra. Calculations of the electronic spectra of conjugated nitrogen heterocycles by the PPP and CNDO/S semiempirical methods have been examined in detail [3, 5, 6, 11, 65, 88, 89]. Let us note only those peculiarities of the calculations that are caused by the existence of a close-lying excited singlet state. This leads to the development of unstable solutions, in particular those that are unstable relative to the type of filling of the MO [67; 68]. As a result, calculations of the electron transi-

TABLE 9. Calculated and Experimental Vertical Ionization Potentials (IP) and Adiabatic Electron Affinities (EA) (eV)

Molecule	Value	PPP [92]	MNDO [23, 94]	AM1 [15]	STO-3G [30, 31]	6-31G*[1] [30, 31]	Exptl.
Pyrrole	IP	8,69	8,57	8,66	5,6	7,00	8,22*[2]
Pyrrole	EA	−1,88	2,00	—	—	—	2,39*[3]
Pyridine	IP	9,32	9,69	9,93	—	7,99	9,59*[2]
Pyridine	EA	−0,68	0,22	—	—	—	−0,62*[3]

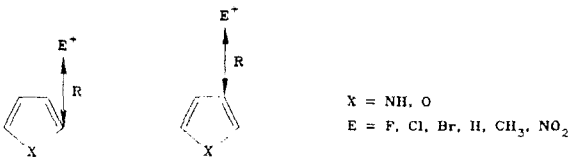
*[1]ΔSCF.
*[2]Cited in [20].
*[3]Cited in [94].

tions for molecules of conjugated heterocycles by the PPP and CNDO/S methods may give negative values of the energies [67-69, 99].

In calculations of excited states by the MINDO/3 and MNDO methods either one uses the "half-electron" scheme (for example, see [8]), or calculations are made within the unrestricted Hartree–Fock (UHF) approximation (the corresponding versions of the MNDO method – MNDO/HE and MNDO/UHF). The energies of the S_1 and T_1 states with the geometry optimized by the MNDO method for the corresponding ground state are determined for the calculation of the energies of the vertical transitions. The parametrization of the MNDO method was realized in such a way as to compensate the effects of the electron correlation in molecules with a closed electron shell. The use of these parameters in the MNDO/UHF scheme in the calculation energy is taken into account twice [100]. As a result, the energies of the singlet states $S_1(n, \pi^*)$ are systematically understated by ∿1 eV.

The MNDO/HE method conveys the energies of the lowest singlet states (π, π^*) of heteroatomic molecules – analogs of the corresponding even-numbered alternant hydrocarbons – quite well [100]. This is due to the fact that in the even-numbered alternant hdyrocarbon the coefficients of the AO in the highest occupied molecular orbitals (HOMO) and lowest vacant molecular orbitals (LVMO) are identical in absolute value and differ only in sign. Consequently, the correlation energies for the S_0 and S_1 states differ only slightly. However, for benzene and pyridine the MNDO/HE method gives unsatisfactory values of the energies of the S_1 states, which in the case of benzene is due to twofold degeneracy of the HOMO and LVMO. As a result, the energy of the S_1 state will be minimal if the unpaired electrons occupy the MO of different pairs. In this case the interelectron repulsion is smaller than when the unpaired electrons are located in the MO of one pair. In other words, benzene differs from other alternate hydrocarbons in that in the S_1 state two unpaired electrons occupy MO that differ in form. The consequence of this is the substantial difference in the energies of the electron correlation for the S_0 and S_1 states. This is also valid for pyridine, in which the degeneracy of both the HOMO and the LVMO is eliminated, but the HOMO and LVMO differ inform, since they correspond to the MO of different HOMO–LVMO pairs of benzene. Thus the MNDO/HE method overestimates the correlation energy, and the energy of the S_1 state of pyridine is therefore understated (Table 11). The energies of the adiabatic transitions calculated by the SINDO 1 method with allowance for configuration interaction (SINDO 1/CI) are also presented in Table 11 [101].

Reactivities. Various reactivity indexes of nitrogen-containing heterocycles have been examined in detail [3, 4, 8, 63-65, 104-106]. At the present time the possibilities of quantum-chemical methods make it possible to obtain a detailed description of the mechanism of a chemical reaction on the basis of calculations of the potential energy surface (PES) and the trajectories of the movement of the reacting particles over it (for example, see [9]). As an example, let us examine calculations of one of the principal types of reactions of conjugated heterocycles – heteroaromatic electropbilic substitution. Calculations of a model reaction pathway have been made by the DNCO/2 method [107]:



X = NH, O
E = F, Cl, Br, H, CH_3, NO_2

TABLE 10. Calculated and Experimental Proton Affinities (kJ/mole)

Molecule	MNDO [27, 95]	AM1 [96]	STO-3G [30, 31]	3-21G [30, 31]	6-31G [30, 31]	6-31G*//6-31G [30, 31]	Expl.*1
Pyrrole	1461	—	—	—	—	—	1509
Pyrazole*2	814	—	1109	976	973	950	845
Imidazole*3	894	—	1186	1041	1033	1005	900
Pyridine	870	900	1159	1010	1011	986	913

*1 Cited in [95].
*2 Protonation at $N_{(2)}$; calculation by the STO-3G/INDO method gies a proton affinity of 1108 kJ/mole for pyrazole [97].
*3 Protonation at $N_{(3)}$; according to calculation by the STO-3G/INDO method, the proton affinity for imidazole is 1185 kJ/mole [97].

TABLE 11. Calculated Energies of the Transitions (eV) to the Lowest Excited Singlet and Triplet States of Pyridine and Pyrazine

Molecule	Vertical transition						Adiabatic transition			
	to S_1			to T_1			to S_1		to T_1	
	CNDO/S [102]	MNDO/HE [100]	Expt1.	CNDO/S [103]	MNDO/HE [100]	MNDO/UHF [100]	SINDO 1/CI [101]	Expt1.	SINDO 1/CI [101]	Expt1.
Pyridine	4,2	4,49	4,81*1	3,44	2,15	1,77	5,5	4,3	3.6	3,7*2
Pyrazine	3,2	—	—	3,11	—	—	5,1	3,8	3,3	3,4

*1 Cited in [100].
*2 Cited in [101].

Primary attention was directed to the question of the existence of steps involving charge transfer as intermediate or transition states of a given reaction. According to [108], for the detection on the pathway of the minimal energy of the reaction the zone in which electron transfer occurs it is sufficient to determine the lowest eigenvalue $t\lambda_+$ (min) of the matrix of the triplet instability of the solutions obtained within the restricted Hartree–Fock (RHF) approximation (see [70] for the instability of the solutions and its types). These calculations made it possible to reveal on the pathway of the minimal energy of the reaction the region of triplet instability of the RHF solutions. An examination of the $t\lambda_+$ values makes it possible to discuss the problem of the relative activities of benzene, furan, and pyrrole in processes associated with one-electron transfer: the benzene molecule should be less active than pyrrole and furan [107]. It was established that both the positional selectivity and the substrate selectivity of pyrrole and furan begin to be determined in the electron-transfer zone.

The important question of the possibility of application of the results obtained to the reaction of reacting molecules in polar solvents, in which electrophilic substitution reactions are usually carried out, has been examined. Taking into account the effect of a polar solvent it was found that the absolute values of $t\lambda_+$ (min) decrease, but the step involving electron transfer remains energically favorable in the reaction of H^+, F^+, Cl^+, and NO_2^+ with pyrrole and furan [107].

Examples of the use of quantum-chemical calculations for obtaining information regarding the mechanisms of the reactions of nitrogen heterocycles are presently not numerous. One of the reasons for this is the demand imposed on the computational method for obtaining reliable results. A second reason, in our opinion, often consists in the absence of the proper formulation of the task on the part of the chemist-experimenter, i.e., the task that would be associated with permissible expenditures of computer time and for which the available experimental expenditures of computer time and for which the available experimental data on the mechanism of a specific reaction would make it possible, on the one hand, to correct the reliability of the results of calculations and, on the other, to construct, taking into account the latter, a detailed reaction scheme. This sort of formulation of the task will serve as a significant stimulus for overcoming difficulties of the first sort.

LITERATURE CITED

1. W. J. Hehre, L. Radom, and P. V. R. Schleyer, Ab initio Molecular Orbital Theory, Wiley, New York (1986).
2. T. A. Clark, Handbook of Computational Chemistry, Wiley, New York (1985).
3. V. I. Minkin, B. Ya. Simkin, and R. M. Minyaev, Theory of Molecular Structure [in Russian], Vysshaya Shkola, Moscow (1979), Chap. 7.
4. G. Del Re, G. Berthier, and J. Serre, Lecture Notes in Chemistry, Vol. 13, Springer, Berlin (1980).
5. H. Klopman and R. Ivans, Semiempirical Methods for the Calculation of Electron Structures [Russian translation], edited by G. Siegal, Mir, Moscow (1980), p. 47.
6. V. A. Gubanov, V. P. Zhukov, and A. O. Litinskii, Semiempirical Molecular Orbital Methods in Quantum Chemistry [in Russian], Nauka, Moscow (1976).
7. G. M. Zhidomirov, P. V. Schastnev, and N. D. Chuvylkin, Quantum-Chemical Calculations of Magnetic-Resonance Parameters, Nauka, Novosibirsk (1978), p. 89.
8. G. M. Zhidomirov, A. A. Bagatur'yants, and I. A. Abronin, Applied Quantum Chemistry [in Russian], Khimiya, Moscow (1979).
9. V. I. Minkin, B. Ya. Simkin, and R. M. Minyaev, The Quantum Chemistry of Organic Compounds [in Russian], Khimiya, Moscow (1986), p. 65.
10. P. Carsky and M. Urban, Lecture Notes in Chemistry, Vol. 16, Sprirger, Berlin (1980).
11. Yu. A. Usynuk (editor), Quantum-Chemical Methods for the Calculation of Molecules [in Russian], Khimiya, Moscow (1980).
12. M. J. S. Dewar, J. Mol. Struct., 100, 41 (1983).
13. R. C. Bingham, M. J. S. Dewar, and D. H. Lo, J. Am. Chem. Soc., 97, 1285 (1975).
14. M. J. S. Dewar and W. Thiel, J. Am. Chem. Soc., 99, 4899 (1977).
15. M. J. S. Dewar, E. G. Zoebisch, E. F. Healy, and J. J. P. Stewart, J. Am. Chem. Soc., 107, 3902 (1985).
16. M. J. S. Dewar, J. Phys. Chem., 89, 2145 (1985).
17. M. J. S. Dewar and D. M. Storch, J. Am. Chem. Soc., 107, 3898 (1985).
18. V. I. Minkin and R. M. Minyaev, Nonclassical Organic Compounds [in Russian], Izd. Rostovsk. Gosundasrstv. Univ., Rostov-on-Don (1985).
19. M. M. Mestechkin, Matrix-Density Method in Molecular Theory [in Russian], Naukova Dumka, Kiev (1977).
20. A. J. Boulton and A. McKillop, Comprehensive Heterocyclic Chemistry, Vol. 2, edited by A. J. Boulton and A. McKillop, Pergamon Press., Oxford (1984), p. 1.
21. R. C. Bingham, M. J. S. Dewar, and D. H. Lo, J. Am. Chem. Soc., 97, 1302 (1975).
22. M. J. S. Dewar and W. Thiel, J. Am. Chem. Soc., 99, 4907 (1977).
23. W. Thiel, J. Am. Chem. Soc., 103, 1413 (1981).
24. M. J. S. Dewar, Pure Appl. Chem., 44, 767 (1975).
25. P. H. Budzelaar, A. J. de Koning, and B. K. G. van Aarssen, J. Chem. Soc., Perkin 2, No. 3, 989 (1983).
26. M. N. Glukhovtsev, B. Ya. Simkin, and V. I. Minkin, Zh. Strukt. Khim., No. 4, 28 (1987).
27. S. Olivella and J. Vilarrasa, J. Heterocycl. Chem., 18, 1189 (1981).
28. E. Fos, J. Vilarrasa, and J. Fernandez, J. Org. Chem., 50, 4894 (1985).
29. M. J. S. Dewar and T. Morita, J. Am. Chem. Soc., 91, 796 (1969).
30. O. Mo. J. L. G. de Paz, and M. Yanez, J. Phys. Chem., 90, 5597 (1986).
31. O. Mo, J. L. G. de Paz, and M. Yanez, THEOCHEM, 35, 135 (1987).
32. M. H. Palmer, I. Simpson, and J. R. Wheeler, Z. Naturforsch., 36A, 1246 (1981).
33. J. Catalan, J. L. G. de Paz, M. Yanez, and J. Elguero, Chem. Scripta, 24, 84 (1984).
34. N. Bodor, M. J. S. Dewar, and A. J. Harget, J. Am. Chem. Soc., 92, 2929 (1970).
35. C. Krebs, H. J. Hoffmnan, H. H. Köhler, and C. Weiss, Chem. Phys. Lett., 69, 537 (1980).
36. H. G. Benson and J. N. Murrell, J. Chem. Soc., Faraday 2, No. 2, 129 (1972).
37. J. Mirek and A. Sygula, THEOCHEM, 3, 85 (1981).
38. H. B. Schlegel, P. Gund, and E. M. Fluder, J. Am. Chem. Soc., 104, 5347 (1982).
39. M. J. Scahlau, I. H. Hiller, and A. A. MacDowell, J. Am. Chem. Soc., 105, 3568 (1983).
40. G. La Manna, THEOCHEM, 37, 83 (1987).
41. B. Ya. Simkin, Khim. Geterotsikl. Soedin., No. 1, 94 (1978).
42. J. D. Goddard, P. G. Mezey, and I. G. Gsizmadia, Theor. Chim. Acta, 39, 1 (1975).
43. A. Buda and A. Sygula, THEOCHEM, 9, 255 (1983).
44. C. Thomson and C. Glidewell, J. Comput. Chem., 4, 1 (1983).
45. M. J. S. Dewar and C. A. Ramsden, Chem. Commun., No. 18, 688 (1973).
46. M. Torres, E. M. Lown, H. E. Gunning, and O. P. Strausz, Pure Appl. Chem. 52, 1623 (1980).

47. R. M. Minyaev and V. I. Minkin, Teor. Éksp. Khim., 16, 659 (1980).
48. B. Ya. Simkin and M. N. Glukhovtsev, Advances in the Chemistry of Nitrogen Heterocycles [in Russian], Rostov-on-Don (1983), p. 198.
49. A. Yu. Shibaev and Yu. V. Puzanov, Zh. Strukt. Khim., 27, 151 (1986).
50. M.N. Glukhovtsev, B. Ya. Simkin, and V. I. Minkin, Zh. Org. Khim., 19, 1353 (1983).
51. R. C. Haddon, Pure Appl. Chem., 54, 1129 (1982).
52. M. J. S. Dewar and G. P. Ford, Chem. Commun., No. 15, 539 (1977).
53. L. Radom, R. H. Nobes, D. J. Underwood, and W.-K. Li, Pure Appl. Chem., 58, 75 (1986).
54. A. Vogler, R. E. Wright, and H. Kunkely, Angew. Chem., 92, 745 (1980).
55. B. Ya. Simkin, M. N. Glukhovtsev, and V. I. Minkin, Zh. Org. Khim., 24, 24 (1988).
56. P. Saxe and H. F. Schaefer, J. Am. Chem. Soc., 105, 1760 (1983).
57. J. A. C. Gorini, J. Farras, M. Feliz, S. Olivella, A. Sole, and J. Vilarrasa, Chem. Commun., No. 12, 959 (1986).
58. M. N. Glukhovtsev, B. Ya. Simkin, and V. I. Minkin, Khim. Geterotsikl. Soedin., No. 2, 250 (1988).
59. W. J. Hehre, R. Ditchfield, L. Radom, and J. A. Pople, J. Am. Chem. Soc., 92, 4796 (1970).
60. P. George, C. W. Bock, and M. Trachtman, Tetrahedron Lett., No. 46, 5776 (1985).
61. P. George, M. Trachtman, C. W. Bock, and A. M. Brett, Theor. Chim. Acta, 38, 121 (1975).
62. M. N. Glukhovtsev, B. Ya. Simkin, and V. I. Minkin, Usp. Khim., 54, 86 (1985).
63. A. F. Pozharskii, Theoretical Foundations of the Chemistry of Heterocycles [in Russian], Khimiya, Moscow (1985).
64. Yu. B. Vysotskii, N. A. Kovach, and O. P. Shvaika, Izv. Sibirsk. Otd. Akad. Nauk SSSR, Ser. Khim., 2, 3 (1980).
65. M. J. S. Dewar, Molecular Orbital Theory in Organic Chemistry [Russian translation], Mir, Moscow (1969).
66. M. J. S. Dewar and N. Trinajstic, Theor. Chim. Acta, 17, 235 (1970).
67. B. Ya. Simkin, M. N. Glukhovtsev, and V. I. Minkin, Chem. Phys. Lett., 71, 284 (1980).
68. M. N. Glukhovtsev, B. Ya. Simkin, and V. I. Minkin, Zh. Strukt. Khim., No. 4, 15 (1980).
69. M. N. Glukhovtsev, M. M. Mestechkin, V. I. Minkin, and B. Ya. Simkin, Zh. Strukt. Khim., No. 2, 14 (1982).
70. M. M. Mestechkin, The Instability of Hartree–Fock Equations and the Stability of Molecules [in Russian], Naukova Dumka, Kiev (1986).
71. M. N. Glukhovtsev and B. Y. Simkin, Zh. Strukt. Khim., No. 3, 31 (1983).
72. F. Bernadi, A. Bottoni, and G. Tonachini, THEOCHEM, 3, 123 (1981).
73. H. B. Schlegel, J. Comput. Chem., 3, 214 (1982).
74. A. Warshell and A. Lappicirella, J. Am. Chem. Soc., 103, 4664 (1981).
75. J. I. Seeman, J. C. Schug, and J. W. Viers, J. Org. Chem., 48, 2399 (1983).
76. F. Pang, P. Pulay, and J. E. Boggs, THEOCHEM, 88, 79 (1982).
77. F. Mata, M. J. Quintana, and G. O. Sorensen, J. Mol. Struct., 42, 1 (1977).
78. L. V. Vilkov, V. S. Mastryukov, and N. I. Sadova, Determination of the Geometrical Structures of Free Molecules [in Russian], Khimiya, Leningrad (1978).
79. F. Billes, THEOCHEM, 34, 289 (1987).
80. F. R. Cordell and J. E. Boggs, THEOCHEM, 85, 163 (1981).
81. C. W. Bird and G. W. H. Cheeseman, Comprehensive Heterocyclic Chemistry, Vol. 4, edited by C. W. Bird and G. W. H. Cheeseman, Pergamon Press, Oxford (1984), p. 1.
82. A. R. Katritzky and J. M. Lagowski, Comprehensive Heterocyclic Chemistry, Vol. 5, edited by K. T. Potts, Pergamon Press, Oxford (1984), p. 1.
83. R. P. Brint, D. J. Coveney, F. L .Lalor, G. Feruson, M. Parvez, and P. Y. Siew, J. Chem. Soc., Perkin 2, No. 1, 139 (1985).
84. H. Baumann, J. Am. Chem. Soc., 100, 7196 (1978).
85. U. Burkert and N. Allinger, Molecular Mechanics [Russian translation], Mir, Moscow (1986), p. 259.
86. N. Olaru and Z. Simon, Rev. Roum. Chim., 32, 83 (1987).
87. Yu. B. Vysotskii, Doctoral Dissertation, Donetsk (1984).
88. T. Peacock, Electronic Properties of Aromatic and heterocyclic Molecules [Russian translation], Mir, Moscow (1979).
89. V. I. Nefedov and V. I. Vovna, Electron Structures of Chemical Compounds [in Russian], Nauka, Moscow (1987).
90. A. P. Mazurek and R. Osman, J. Phys. Chem., 89, 460 (1985).
91. W. Niessen, H. F. Diercksen, and L. S. Cederbaum, Chem. Phys., 10, 345 (1975).

92. T. L. Kunii and H. Kuroda, Theor. Chim. Acta, 11, 97 (1968).
93. N. Bodor and R. Pearlman, J. Am. Chem. Soc., 100, 4946 (1978).
94. M. J. S. Dewar and H. S. Rzepa, J. Am. Chem. Soc., 100, 784 (1978).
95. S. Olivella, F. Urpi, and J. Vilarrasa, J. Compt. Chem., 5, 230 (1984).
96. M. J. S. Dewar and K. M. Dieter, J. Am. Chem. Soc., 108, 8075 (1986).
97. J. Catalan, J. L. G. de Paz, M. Yanez, and J. Elguero, J. Am. Chem. Soc., 106, 6552 (1984).
98. R. L. Ellis, G. Kuehnlenz, and H. H. Jaffe, Theor. Chim. Acta, 26, 131 (1972).
99. B. Ya. Simkin, M. N. Glukhovtsev, and V. I. Minkin, Proceedings of the 9th National Conference on Molecular Spectroscopy (Bulgaria), Albena (1980), p. 44.
100. M. J. S. Dewar, M. A. Fox, K. A. Campbell, C.-C. Chen. J. E. Friedheim, M. K. Holloway, S. C. Kim, P. B. Lieschenski, A. M. Pakiari, T.-P. Tien, and E. G. Zoebisch, J. Comput. Chem., 5, 480 (1984).
101. K. Jug and G. Hahn, J. Compt. Chem., 4, 410 (1983).
102. J. Del Bene and H. H. Jaffe, J. Chem. Phys., 48, 1807 (1968).
103. J. Ridley and M. Zerner, Theor. Chim. Acta, 32, 111 (1973).
104. M. V. Bazilevskii, The Molecular Orbital Methods and the Reactivities of Organic Molecules [in Russian], Khimiya, Moscow (1969).
105. V. I. Ivanskii, The Chemistry of Heterocyclic Compounds [in Russian], Vysshaya Shkola, Moscow (1978).
106. M. J. S. Dewar and R. Daughtery, Molecular Orbital Perturbation Theory in Organic Chemistry [Russian translation], Mir, Moscow (1977).
107. L. G. Gorb, I. A. Abronin, V. A. Korsunov, G. M. Zhidomirov, and V. P Litvinov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 5, 1079 (1984).
108. T. Takabe, K. Takenaka, K. Yamaguchi, and T. Fueno, Chem. Phys. Lett., 44, 65 (1976).

REACTION OF 4-METHYL-3,4-EPOXYTETRAHYDROPYRAN WITH α-AMINO ACIDS

U. G. Ibatullin S. A. Vasil'eva, Z. Kh. Karimova,
I. Z. Latypova, and M. G. Safarov

UDC 547.466'811'812.07

Depending on the conditions, α-amino acids react with 4-methyl-3,4-epoxytetrahydropyran at the amin or carboxy group to give products of opening of the oxirane ring in conformity with the Krasusskii rule.

The reaction of epoxide with various nucleophiles is often used in organic synthesis owing to its high selectivity and the mild conditions under which it is carried out. For example, the corresponding amino alcohols were obtained in this way from epoxides of the tetrahydropyran series by the action of aliphatic amines [1, 2]. α-Amino acids can also be regarded as potential nucleophiles, although they exist in the zwitterionic form in aqueous solutions [3, 4]. However, the situation changes when one uses a certain excess of alkali, which promotes an increase in the pH and conversion of the zwitterion to the conjugate base. Using this, we investigated the reaction of 4-methyl-3,4-epoxytetrahydropyran (I), previously synthesized in [2], with a number of amino acids.

It was found that N-(4-hydroxy-4-methyl-3-tetrahydropyranyl)amino acids IIIa-o are formed in the 60-96% yields (Table 1) when epoxide I is treated with sodium salts of amino acids in aqueous solution at 80°C. An intense absorption band at 1580-1590 cm^{-1}, which is characteristic for stretching vibrations of an NH_2 group, and a band at 1610-1620 cm^{-1}, which corresponds to stretching vibrations of the CO_2^- anion [5], are observed in the IR spectra of products IIIa-o. In the case of the reaction of piperidine with 2-aryl-4-methyl-4,5-epoxytetrahydropyrans the primary formation of one of the stereoisomers – the product of trans-diaxial opening of the epoxide ring – was proved by spectral methods (by means of the chromatographic mass, IR, and PMR spectra) in [6]. This sort of orientation of the amino and hydroxy groups is also characteristic for other epoxides of the pyran series [2, 7]. On the basis of this it might be expected that, when amino acids are used, opening of the epoxide ring

Bashkir State University, Ufa 450074. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1604-1606, December, 1989. Original article submitted April 29, 1988; revision submitted October 25, 1988.

 ©1990 Plenum Publishing Corporation