COMPARISON OF NON-EMPIRICAL AND SEMIEMPIRICAL SCF MO CALCULATIONS OF NON-SUBSTITUTED DIHYDROPYRIDINES*

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Results of *ab initio* MO calculations of the dihydropyridine molecules *I*– *V* are confronted with analogous CNDO/2 and MINDO/3 calculations. The molecular energies calculated by means of the 4-31G base predict the *6pi*-electron isomers *I* and *II* to be the most stable dihydropyridine forms in contrast to the STO-3G and CNDO/2 data preferring the *4pi*-electron isomers *III*– *V*. The charge distributions calculated non-empirically and semiempirically show different characteristic features.

The five isomeric compounds *I* – *V* represent basic heterocyclic systems for a number of significant dihydropyridine derivatives[1,2]. So far, out of them it was possible to isolate and characterize spectroscopically in unambiguous way[3,4] only 1,4-dihydropyridine (*II*) representing a not very stable substance. The existence of the 1,2-isomer *I* is presumed[5,6] in mixtures with 1,4-dihydropyridine (*II*) produced by reductions of pyridine with hydrides. Only 1-methyl-1,2-dihydropyridine was prepared[7] as an extremely labile substance. No experimental evidence is available so far concerning the existence of the other isomers *III* – *V*. Therefore, quantum-chemical calculations of the molecular structures can be considered interesting, since they promise to enable estimates of relative stability and, hence, synthetic accessibility of these compounds. Besides simple HMO calculations[1] concerning only the isomers *I* and *II* there exists an extensive MINDO/3 study by Bodor and Pearlman[8] involving not only all the isomers *I* – *V* but also some 1-methyl derivatives, bicyclic analogues and ionized forms. The authors[8] do not give the calculated molecular energies, but on the basis of semiempirical heats of formation they arrived at the following stability order: *II* > *IV* > *I* > *V* > *III*. This conclusion is particularly interesting with respect to the relative preference of the 3,4-isomer *IV*, because on the basis of the existing derivatives it is usually presumed[1] that the both *6pi*-electron structures *I* and *II* should be energetically preferred to the *4pi*-electron structures *III* – *V* due to more extensive conjugation. With the aim to find the extent to which the used MO approximation affects the prediction of relative stabilities of the com-

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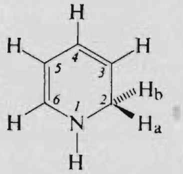
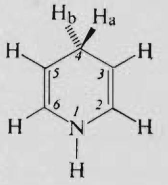
pounds *I*–*V* we have now carried out the *ab initio* STO-3G and 4-31G as well as semiempirical CNDO/2 calculations and compared the calculated energy characteristics and electron distributions with the mentioned[8] MINDO/3 calculations. The results obtained are given in the present communication.



I



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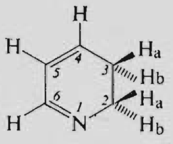

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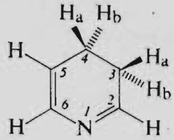

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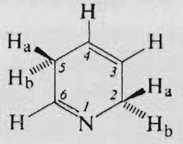

V

CALCULATIONS

All the non-empirical calculations were carried out with a Cyber 172 computer using a standard version of the Gaussian-76 program. As the precise molecular geometries of the structures *I*–*V* are not known, and their non-empiric optimization is not technically feasible for us so far, the geometries used in the calculations are those obtained by semiempirical optimization. In the series A the geometries used were optimized with respect to all degrees of freedom by the gradient method[9] on the basis of the CNDO/2 wave functions. In the series B we used the published[8] geometries *I*–*V* obtained similarly on the basis of the MINDO/3 wave functions. The molecular energies obtained in the series B by the STO-3G calculation for the model *I*–*V* were invariably somewhat lower than those in the series A (Table I). Therefore, the more time-consuming calculations were only carried out in the series B which is closer to physical reality according to the mentioned criterion.

A closer comparison of the calculated geometry parameters in the series A and B shows, that whereas in the series B the heterocycles in the molecules *I*–*V* have plane arrangement[8], in the series A the CNDO/2 calculation results in disturbed planarity of the rings (boat or twist boat), the bond geometry at the tetrahedral carbon centres being closer to the classical sp^3 hybridization. The differences between the series A and B with respect to bond lengths and the other angles are, however, minimum, the following systematical deviations being observed: in the series A the bond lengths type $C^2_{sp}-C^2_{sp}$ $C^2_{sp}-C^3_{sp}$, $C^3_{sp}-C^3_{sp}$, and $C^3_{sp}-N^2_{sp}$ are always somewhat smaller, whereas the bonds $C^2_{sp}-N^3_{sp}$ are somewhat longer. These differences are obviously due to detailed differences between the energy hypersurfaces of CNDO/2 and MINDO/3 wave functions in the region of the deepest energy minimum.

RESULTS AND DISCUSSION

Energy characteristics and stability of the molecules. Table I gives the semi-empirically and non-empirically calculated molecular energies. Similar to the MINDO/3 calculations[8], their relative values E_{rel} are particularly low with the *ab initio* data, so that any energy preferences in the series of the non-substituted dihydropyridines *I – V* can hardly be considered significant, and they do not exclude the existence of any isomer under suitable conditions. However, the found orders of the overall energies E_{SCF} are noteworthy. Regardless of the chosen series of the starting geometry parameters (A or B), the CNDO/2 and STO-3G energies predict a higher reversible (thermodynamic) stability of the 4*pi*-electron dihydropyridines as compared with the 6*pi*-electron isomers *I* and *II* (*V* > *III* > *IV* > *II* > *I* and *IV* > *V* > > *III* > *II* > *I* in the series A; *V* > *III* > *IV* > *I* > *II* and *V* > *IV* > *III* > *II* > *I* in the series B). On the contrary, the 4-31G calculations, using the starting valence-split function, prefer unambiguously the 6*pi*-electron isomers *I* and *II* to all other forms *III – V* and show thus the critical role of the used base in application of the *ab initio* calculations to estimation of energy stability of isomeric molecules. At this point of interpretation of our calculations, however, a possible influence of correlation energy (whose contributions to the overall molecular energies, of course, were not calculated within the used one-electron SCF approximations) should not be neglected. If (due to the present available computer capacity) we limit ourselves to qualitative considerations, we can expect higher contributions of the correlation energy with the isomers *I* and *II* because of their more extensive 6*pi*-electron delocalization. That means that the involvement of the correlation energy E_{corr} could result in a more marked decrease of the overall molecular energy of these particular molecules *I* and *II*, which could change (in the case of the CNDO/2 and STO-3G calculations) the order of the values $E_{SCF} + E_{corr}$ in favour of greater energy preference of 6*pi*- (*I*, *II*) to 4*pi*-electron isomers (*III – V*). On the contrary, in the case of 4-31G calculations the involvement of the E_{corr} term could only result in extension of energy span between the molecules *I*, *II* and *III – V*, so that in this case the preference of 1,2- and 1,4-isomers *I* and *II* can be considered physically justified on the basis of mere E_{SCF} values. This interpretation of the 4-31G calculations, obviously, does not contradict the conclusions by Bodor and Pearlman[8] made on the basis of the MINDO/3 heats of formation, and, furthermore, it eliminates the unexpected preference of the 3,4-isomer *IV* to the 1,2-isomer *I*. However, the latter fact is not considered significant, if considerable probability of the prototropic enimine-dienamine tautomerism $III \rightleftharpoons I \rightleftharpoons V$ and $II \rightleftharpoons IV$ is taken into account in which the equilibria should be generally shifted in favour of the 6*pi*-electron tautomers *I* or *II* according to both the 4-31G calculations and the mentioned authors[8]. Although the tautomerism $II \rightleftharpoons IV$ has not yet been found with the synthetized[3,4] compound *II*, it cannot be excluded as one of reasons of the observed lability of *II*. These considerations of tautomerism are also

TABLE I

The calculated energies of MO models of the compounds *I*–*V*[a]. The E_{SCF} data are non-dimensional values $E_{tot} . E_h^{-1}$, where $E_h = 4{\cdot}3598 . 10^{-18}$ J, the E_{rel} values in kJ mol^{-1}

Isomer	CNDO/2(A)		CNDO/2(B)		STO-3G(A)		STO-3G(B)		4-31G(B)	
	E_{SCF}	E_{rel}	E_{SCF}	E_{rel}	E_{SCF}	E_{rel}	E_{SCF}	E_{rel}	E_{SCF}	E_{rel}
I	−52·5213	38·28	−52·5074	36·63	−244·758352	30·93	−244·762448	50·47	−247·448596	11·22
II	−52·5258	26·54	−52·5019	51·09	−244·763216	18·15	−244·765330	42·90	−247·452865	0·00
III	−52·5339	5·12	−52·5179	8·99	−244·767889	5·87	−244·778162	9·17	−247·441415	30·09
IV	−52·5332	7·00	−52·5162	13·48	−244·770121	0·00	−244·779983	4·39	−247·441688	29·37
V	−52·5359	0·00	−52·5214	0·00	−244·768999	2·95	−244·781652	0·00	−247·445952	18·17

[a] The symbols in brackets refer to the initial geometry — see Calculations.

supported by the fact that simpler alkyl derivatives of dihydropyridines *III* and *V* could so far be prepared[1,10-13] mainly in the cases when character of substituents in the heterocyclic skeleton prevented migration of the proton to nitrogen atom accompanied by the corresponding shift of double bond (geminal 2,2- or 3,3-dialkyl derivatives). The found coexistence[14] of 2,6-ditertbutyl derivatives of the compounds *II* and *IV* can also be connected with the mentioned tautomerism.

Generally, dihydropyridines are considered to be *pi*-electron donors[1], and, therefore, their chemical stability can largely be connected with ionization potential (IP). Our calculated IPs of the compounds *I* – *V* are compared (Table II) with the analogous MINDO/3 values[8]. Obviously none of the CNDO/2, STO-3G, and 4-31G calculations for the 1,4-isomer *II* approaches to the experimental[3] IP = 7·45 eV as close as the MINDO/3 calculation[8] does which, however, is parametrized for these purposes[15]. The *ab initio* calculations carried out give the IP values which are evidently too low, whereas the CNDO/2 method generally leads to too high IPs. However, in general the data of Table II agree in that they show that the energetically more stable 6*pi*-electron isomers *I* and *II* should be better *pi*-donors and, hence, more labile to reactions involving ionization or splitting off of an electron (protonation and oxidation).

Character of the frontier orbitals. Within the geometrical models of the series B both the HOMO and the LUMO are strictly of *pi*-type with all the isomers *I* – *V*. Character of the mentioned MOs depends little on the way of the MO calculation,

TABLE II
The calculated ionization potentials for the compounds *I* – *V*[a]

Isomer	IP, eV					
	CNDO/2(A)	CNDO/2(B)	MINDO/3(B)[b]	STO-3G(A)	STO-3G(B)	4-31G(B)
I	10·26	9·74	7·50	5·41	4·95	6·68
II	10·77	9·72	7·48	6·00	5·02	6·84
III	11·33	11·67	8·43	7·29	7·27	8·84
IV	11·27	11·54	8·52	7·01	7·15	8·59
V	11·72	11·99	8·52	7·09	7·83	9·26

[a] According to the Koopmans theorem, the symbols in brackets refer to the starting geometry (see Calculations); [b] taken from ref.[8].

TABLE III

Comparison of the charge distributions in isomers *I*—*V* calculated by various MO methods (series B)

Method	The charge at the position											
	N(1)	C(2)	C(3)	C(4)	C(5)	C(6)	H(1)	H(2)	(H3)	H(4)	H(5)	H(6)
					1,2-dihydropyridine (*I*)							
CNDO/2	—0·161	0·158	—0·048	0·038	—0·094	0·141	0·097	—0·053	—0·005	—0·006	—0·000	—0·015
MINDO/3[a]	—0·117	0·258	—0·116	0·091	—0·168	0·167	0·066	—0·090	0·008	0·010	0·018	—0·017
STO-3G	—0·352	0·022	—0·071	—0·053	—0·124	0·081	0·193	0·040	0·049	0·060	0·046	0·070
4-31G	—0·923	—0·003	—0·225	—0·139	—0·320	0·220	0·362	0·146	0·171	0·190	0·173	0·204
					1,4-dihydropyridine (*II*)							
CNDO/2	—0·140	0·109	—0·075	0·076	—0·083	0·112	0·093	—0·010	0·001	—0·038	0·003	—0·013
MINDO/3[a]	—0·067	0·120	—0·146	0·200	—0·157	0·124	0·054	—0·008	0·020	—0·078	0·024	—0·012
STO-3G	—0·350	0·058	—0·092	—0·094	—0·089	0·056	0·198	0·066	0·049	0·040	0·049	0·068
4-31G	—0·974	0·191	—0·246	—0·329	—0·245	0·191	0·366	0·200	0·172	0·149	0·171	0·204
					2,3-dihydropyridine (*III*)							
CNDO/2	—0·157	0·105	0·007	0·033	—0·038	0·118	—	—0·017	—0·004	—0·004	—0·001	—0·021
MINDO/3[a]	—0·187	0·173	0·056	0·027	—0·063	0·170	—	—0·042	—0·034	—0·007	—0·004	—0·012
STO-3G	—0·253	—0·015	—0·108	—0·039	—0·084	0·053	—	0·069	0·057	0·063	0·060	0·069
4-31G	—0·531	—0·115	—0·392	—0·118	—0·251	0·098	—	0·186	0·175	0·194	0·194	0·200
					3,4-dihydropyridine (*IV*)							
CNDO/2	—0·150	0·122	—0·004	0·041	—0·029	0·074	—	—0·025	0·003	—0·011	0·001	—0·014
MINDO/3[a]	—0·155	0·146	0·031	0·117	—0·075	0·090	—	—0·016	—0·026	—0·042	0·004	—0·006
STO-3G	—0·261	0·072	—0·112	—0·100	—0·050	0·012	—	0·065	0·062	0·058	0·064	0·068
4-31G	—0·560	0·140	—0·389	—0·346	—0·174	0·028	—	0·191	0·186	0·175	0·188	0·200
					2,5-dihydropyridine (*V*)							
CNDO/2	—0·154	0·105	—0·023	0·007	—0·001	0·118	—	—0·014	0·001	—0·011	0·008	—0·030
MINDO/3[a]	—0·168	0·189	—0·048	—0·002	0·060	0·141	—	—0·045	0·003	—0·012	—0·026	—0·020
STO-3G	—0·248	—0·026	—0·067	—0·057	—0·119	0·066	—	0·070	0·060	0·055	0·067	0·062
4-31G	—0·504	—0·164	—0·185	—0·160	—0·408	0·117	—	0·188	0·186	0·179	0·188	0·186

[a] Taken from ref.[8].

only the absolute values of coefficients of AOs being different in the various used methods. Similar to the MINDO/3 calculations[8] the HOMOs show an important bonding contribution of antisymmetrical combination of 1s AOs of hydrogen atoms of methylene groups expressing thus the operation of hyperconjugation and homoaromacity effects in the electronic structure of the studied molecules. The LUMOs of the models *I* and *III*–*V* show analogous non-bonding contributions of ls AOs, wherefrom it can be concluded that electron excitation will result in weakening of bonds in the methylene groups and, hence, in tendency to aromatization of the dihydropyridine skeleton. It is noteworthy that the energetically most stable 1,4-isomer *II* shows practically no such participation of the methylene group in the LUMO according to the 4-31G calculation.

Charge distribution. The atomic charges obtained by the CNDO/2 and STO-3G calculations differ little in the series A and B. Therefore, Table III only compares the charge distributions in the series B, *viz.* those calculated semiempirically (CNDO/2 and MINDO/3) and non-empirically (STO-3G and 4-31G). Both these basic types of calculation lead obviously to qualitatively and quantitatively different results but with overall identical features in all the isomers *I*–*V*. The semiempirical data show, first of all, little realistic negative charges at many hydrogen centres. Furthermore, they overestimate localization of positive charges at the tetrahedral carbon centres, and, on the other hand, they underestimate localization of negative charges at the nitrogen centres. The non-empirical calculations show, besides, the known tendency to the overall higher charge localization with increasing *sp* base, *i.e.* on transition from the STO-3G to the 4-31G calculations. The latter give the charge distributions of the molecules *I*–*V* which are probably closest to physical reality.

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