

## EXTENDED HÜCKEL CONFORMATIONAL ANALYSIS OF NICOTINAMIDE

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Conformation of nicotinamide was studied by means of extended Hückel theory (LCAO-EHMO). Comparison of theoretical electron energies leads to the conclusion that the amidic group is planar and its plane is twisted by the angle of c.  $33^\circ$  from the plane of the heteroaromatic ring, the amino group being closer to the ring nitrogen atom. The contributions of  $\sigma$ - and  $\pi$ -electrons to the total electron energy and the effect of the geometry of the molecule on electron distribution are discussed. The results are confronted with analogous calculations carried out by HMO and SCF methods with the use  $\pi$ -electron approximation. A number of theoretical quantities are compared with experimental data.

Within the framework of the study of applicability of LCAO-MO methods considering all valence shell electrons it was of interest to ascertain to what extent a comparatively simple LCAO-EHMO procedure<sup>1,2</sup> is able to describe geometry of some biologically interesting molecules. In our study we have now chosen nicotinamide which is important for its ability to be incorporated by living organisms into pyridine nucleotides<sup>3,4</sup>.

Recently, similar studies have been reported in which such biochemically interesting molecules as acetylcholine, muscarine and muscarone<sup>5</sup>, nicotine<sup>6</sup>, histamine<sup>7</sup>, serotonin<sup>8</sup>, ephedrine<sup>9</sup>, noradrenaline<sup>10</sup>, oxotremorine<sup>11</sup>, as well as some amino acids<sup>12-14</sup>, peptides<sup>15-17</sup>, steroids<sup>18</sup> and nucleosides<sup>19</sup> were subjected to conformational analysis. From the results obtained it can be concluded that quantum chemical calculations on the basis of EHMO and CNDO/2 can be used to predict most stable forms of molecules.

### EXPERIMENTAL

*Calculations.* The calculation of 42 MO's of nicotinamide was carried out with the use of segmented EHT-program on ICL-4-50 digital computer (one calculation took c. 15 min), following standard procedure reported by Hoffmann<sup>1,2</sup>. The orientation of the molecule in coordinate system is shown in Fig. 1. The interatomic distances determined by X-diffraction<sup>20</sup> were used. The used values of ionisation potentials  $I_s$  and  $I_p$  for states  $s$  and  $p$ , as well as Slater exponents are presented in Table I. Diagonal matrix elements  $H_{ii}$  were approximated by ionisation potential of a given electron state, nondiagonal elements  $H_{ij}$  were obtained from the relation<sup>2</sup>

$$H_{ij} = 0.5K S_{ij}(H_{ii} + H_{jj}),$$

where the empirical constant  $K$  equals to 1.75 and  $S_{ij}$  is the overlap integral. The calculation on the basis of  $9\pi$  MO's was carried out both by simple HMO method<sup>21</sup>, using usual empirical parameters  $h_{\dot{N}} = 0.5$ ,  $h_{\bar{N}} = 1.5$ ,  $h_O = 1.0$ ,  $k_{C-\dot{N}} = 1.0$ ,  $k_{C-\bar{N}} = 0.8$ ,  $k_{C=O} = 1.0$ , and by Pople version<sup>22</sup> of SCF method with exchange integrals  $\beta_{CC} = \beta_{CN} = -2.388$  eV (aromatic),  $\beta_{C-C} = -2.149$  eV and  $\beta_{C=O} = -2.627$  eV. The used ionisation potentials  $I$ , electron affinities  $A$  and Slater Z-values are presented in Table II. Both types of calculations were carried out on El-

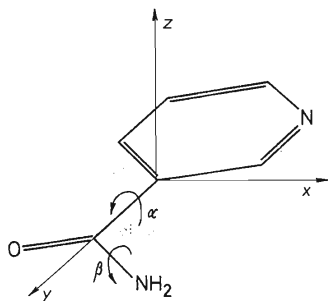


FIG. 1  
Nicotinamide Molecule in Coordinate System

TABLE I  
Data Used in LCAO-EHMO Calculations<sup>25,26</sup>

Atom	$I_s$ , eV	$I_p$ , eV	Slater exponent
H	-13.60	—	1.0
C	-21.01	-11.27	1.625
N	-26.92	-14.42	1.950
O	-32.07	-18.53	2.275

TABLE II  
Data Used in LCAO-SCF-MO Calculations<sup>27</sup>

Atom	$I$ , eV	$A$ , eV	Z-Values
C ( $sp^2$ )	11.22	0.69	3.25
$\dot{N}$ ( $sp^2$ )	14.12	1.78	3.25
$\bar{N}$ ( $sp^2$ )	25.00	10.00	4.00
O ( $sp^2$ )	16.00	2.00	4.25

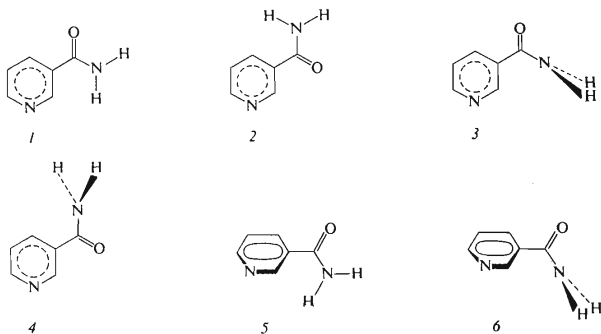
liott 503 digital computer; 11 iterations were necessary to achieve satisfactory self-consistency in the SCF procedure (the calculation times were from 0.5 to 2.5 min). The electronic spectra of nicotinamide were calculated by the limited configurational interaction method (LCI) according to Pariser and Parr<sup>23,24</sup> on the basis of SCF MO's comprising 16 monoexcited configurations. The calculation was carried out on Elliott 503 computer with the use of standard LCI program.

**Spectral Measurements.** The ultraviolet spectrum of nicotinamide (m.p. 129–130°C, acetone) was measured in ethanolic solutions (conc.  $5 \cdot 10^{-5} M$ ) in 1 cm thick cell on Optica Milano CF 4 NI spectrophotometer. The PMR spectrum was recorded with Varian HA-100 instrument (stable frequency 100 Hz), in hexadeuteriodimethylsulfoxide with tetramethylsilane as standard.

## RESULTS

### ELECTRON ENERGY

In order to derive most stable conformations of nicotinamide, the changes in the total electron energy of the corresponding models,  $E_{tot}$ , were followed in dependence on a) the angle  $\alpha$  between the planes of the heteroaromatic ring and of the carbonyl bond and on b) the angle  $\beta$  between the planes of the amino group and of the carbonyl bond (Fig. 1). The minima on the curve  $E_{tot} = f(\alpha)$  were attributed to the most probable and the maxima to the improbable conformations. Variations in angles  $\alpha$  and  $\beta$  lead to six characteristic conformations 1–6. Both planar forms 1 and 2 differ only by orientation of the carbonyl group with respect to the heterocyclic nitrogen. On increasing angle  $\beta$  they are converted into nonplanar conformations 3 and 4. Analogously, on changing angle  $\alpha$  the two planar conformations give the same conformer 5, which by additional change of angle  $\beta$  leads to the form 6.



*Rotation around the C—CO bond:* The curve  $E_{\text{tot}} = f(\alpha)$  for  $\beta = 0^\circ$  is shown in Fig. 2. It is obvious that conformations 1, 2 and one of the forms of type 5, in which the planes of the heteroaromatic ring and the CONH<sub>2</sub> group contain right angle ( $\alpha 90^\circ$ ), are not probable at all. In view of the energy the most suitable have appeared to be another two conformations of type 5 ( $\alpha 33^\circ$  and  $117^\circ$ ), the corresponding projections of which are designated as 5a and 5b, form 5a being most probable. If for this conformation the corresponding value of  $E_{\text{tot}}$  is read from Fig. 2 ( $-20.175.6$  kcal/mol) then theoretical barrier towards the CONH<sub>2</sub> group rotation corresponds to the value of 4.1 kcal/mol (Table III). This value has to be however regarded critically, since surprisingly low value of medium maximum for  $\alpha 90^\circ$  (Fig. 2) may be caused by excessive height of both side maxima, due to overestimation of the effect of nonbonded interaction in LCAO-EHMO procedure<sup>2,14</sup>.

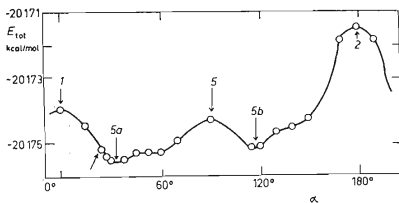
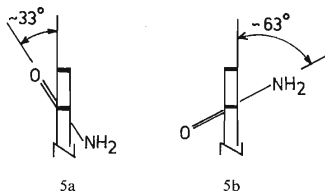


FIG. 2

Dependence of Total Energy of Nicotinamide ( $\beta 0^\circ$ ) on Angle  $\alpha$   
The arrow without denotation means X-ray data.



*Rotation around the C—NH<sub>2</sub> bond:* Table III presents also the values of  $E_{\text{tot}}$  for some conformations of types 3, 4 and 6. It is evident that the rotation of the amino group through the angle  $\beta 90^\circ$  leads to increase in the energy of the molecule which amounts to 14.1 kcal/mol for conformation of type 3, *i.e.* this increase is greater than the already mentioned theoretical barrier towards rotation of the whole amidic group. Also the deviation of the NH<sub>2</sub> group from the carbonyl group plane through the angle  $\beta = \pm 15^\circ$  leads in energetically most suitable conformations, which are close to 5a and 5b ( $\alpha = 33^\circ$  and  $125^\circ$ ), to distinct increase of the energy of the molecule. From the foregoing it can be concluded that for nicotinamide molecule conformations 3, 4 and 6 do not have to be considered, since the CONH<sub>2</sub> group would be always planar. Similar conclusions have been arrived at on the basis of LCAO-EHMO calculations of some peptide-like compounds<sup>15,16,28</sup>.

On the basis of our LCAO-EHMO calculations the most probable conformation of nicotinamide seems to be that designated as 5a. This is in satisfactory agreement with the results of X-ray analysis<sup>20</sup> which also showed that the same form, with the angle  $\alpha$  24°, however, is most probable. The small deviation of our value ( $\alpha$  33°) from that reported may be caused by a) imperfectness of LCAO-EHMO method, b) not strictly coplanar arrangement of  $\sigma$ -bonds in the NH<sub>2</sub> group and c) additional change of the angle  $\alpha$  as the result of formation of dimeric amidic form in crystalline state<sup>20</sup>.

TABLE III  
Total Electron Energy of Some Nicotinamide Conformations (in kcal/mol)

$\alpha$	$\beta$	$-E_{tot}$	$\alpha$	$\beta$	$-E_{tot}$
0°	0°	20 174.0	120°	0°	20 175.2
0°	90°	20 159.9	125°	15°	20 173.6
33°	0°	20 175.6	125°	165°	20 173.8
33°	15°	20 174.9	180°	0°	20 171.6
33°	165°	20 175.1	180°	15°	20 171.0
90°	90°	20 158.5	180°	90°	20 159.2

TABLE IV  
Energies of EHMO's of Nicotinamide in Conformation 5 ( $\alpha = 30^\circ$ )

MO	$E, eV$	Type	MO	$E, eV$	Type	MO	$E, eV$	Type
1	58.2547	$\sigma^*$	15	1.8235	$\sigma^*$	29	-15.6554	$\sigma$
2	43.5622	$\sigma^*$	16	-4.8334	$\pi^*$	30	-16.5048	$\sigma$
3	36.6648	$\sigma^*$	17	-7.2673	$\pi^*$	31	-16.8737	$\sigma$
4	31.8980	$\sigma^*$	18	-8.9393	$\pi^*$	32	-17.4321	n(O)
5	27.3569	$\sigma^*$	19	-9.3910	$\pi^*$	33	-18.6918	n(O)
6	24.0740	$\sigma^*$	20	-12.4348	n( $\dot{N}$ )	34	-18.8535	$\pi(C=O)$
7	22.8840	$\sigma^*$	21	-12.6454	$\pi$	35	-19.4564	$\sigma$
8	15.6066	$\sigma^*$	22	-12.9826	$\sigma$	36	-20.2831	$\sigma$
9	13.7900	$\sigma^*$	23	-13.4961	$\pi$	37	-20.9830	$\sigma$
10	11.7597	$\sigma^*$	24	-14.0294	$\sigma$	38	-25.3498	$\sigma$
11	11.5062	$\sigma^*$	25	-14.7177	$\sigma$	39	-26.7400	$\sigma$
12	7.8276	$\sigma^*$	26	-14.8549	$\pi(C=\dot{N})$	40	-29.0664	$\sigma(\dot{N})$
13	5.4237	$\sigma^*$	27	-15.2654	$\sigma$	41	-31.1242	$\sigma(\dot{N})$
14	2.9119	$\sigma^*$	28	-15.5856	$\pi$	42	-34.2440	$\sigma(O)$

*Effect of  $\sigma$ - and  $\pi$ -electrons on conformations:* Limiting planar conformations 1 and 2 can be interconverted by rotating the amidic group through the angle  $\alpha = 180^\circ$ . In both these forms electron energy levels can be divided into  $\sigma$ -EHMO's and  $\pi$ -EHMO's on the basis of the magnitude of expansion coefficients which indicate localisation of electrons in corresponding AO's of a given MO. In similar way we have also performed analogous formal classification of EHMO's of other transition conformations of type 5. By way of an example, the assignment for the angle  $\alpha = 30^\circ$  is given in Table V. Correlation diagrams between individual forms show that during rotation of the amidic group no crossing of the individual levels given in Table IV is taking place. This

fact allows to dissect single terms in the whole region of angle  $\alpha$  ( $0-180^\circ$ ) on  $\sigma$ - and  $\pi$ -type and thus to express  $E_{tot}$  as the sum of  $E_\sigma$  and  $E_\pi$ , the  $E_\sigma$  term including at the same time energy contributions of the unshaired electron pairs on hetero atoms.

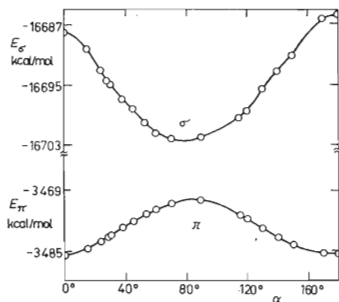


FIG. 3  
Dependence of  $E_\sigma$  and  $E_\pi$  on Angle  $\alpha$

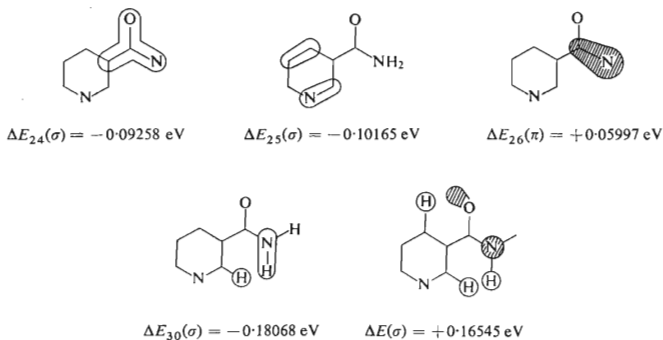


FIG. 4

EHMO's of Nicotinamide, the Energies of Which are Most Dependent on Angle  $\alpha$  (Fig. 1)

The profiles of lobes are proportional to expansion coefficients. Hatched areas correspond to the negative, the other to the positive wave function.  $\Delta E$ 's are the changes of  $E_{EHMO}$  for  $\alpha 30^\circ$  and  $180^\circ$ .

Fig. 3 shows changes of the values of  $E_\sigma$  and  $E_\pi$  caused by the change of angle  $\alpha$ , from which it is apparent that side energy maxima on the  $E_{tot}$  curve (Fig. 2) are due to  $\sigma$ -electron contributions, and that in the main only by terms corresponding to the occupied EHMO's depicted in Fig. 4. On the other hand, the medium maximum (Fig. 2) corresponds predominantly to the increase of  $E_\pi$  brought about by a decreased extent of conjugation at  $\alpha \approx 90^\circ$ . These results of LCAO-EHMO calculation thus speaks for significant nonbonded interaction between  $\sigma$ -electrons of the CONH<sub>2</sub> group and the C—H bonds in positions 2 and 4 of the heteroaromatic ring.

### ELECTRON DISTRIBUTION

Parameters of Mulliken overlap population and atoms charges for most stable conformation 5a are presented in Tables V and VI. The numbering of individual atom centres in molecule of nicotinamide is shown in Fig. 5.

*Rotation around the C—CO bond:* Distribution of electrons on individual atom centres and bonds changes with the change of angle  $\alpha$  in different way (Figs 6 and 7); the two characteristic

TABLE V

Atom Population for Nicotinamide in Conformation 5 ( $\alpha = 30^\circ$ )

Atom <sup>a</sup>	Net charge	Atom <sup>a</sup>	Net charge	Atom <sup>a</sup>	Net charge
N(1)	-1.1204	C(6)	+0.4435	H(11)	+0.3648
C(2)	+0.4589	C(7)	+1.3538	H(12)	+0.0908
C(3)	-0.0385	O(8)	-1.3857	H(13)	+0.0925
C(4)	+0.0891	N(9)	-0.7603	H(14)	+0.0947
C(5)	-0.1228	H(10)	+0.3587	H(15)	+0.0782

<sup>a</sup> The number of position (Fig. 5) is given in parenthesis.

TABLE VI

Mulliken Overlap Population for Nicotinamide Conformation 5 ( $\alpha = 30^\circ$ )

Bond <sup>a</sup>	Overlap populations	Bond <sup>a</sup>	Overlap populations	Bond <sup>a</sup>	Overlap populations
N(1)—C(2)	0.8756	C(6)—N(1)	0.8947	C(4)—H(13)	0.8243
C(2)—C(3)	1.0957	C(3)—C(7)	0.8648	C(5)—H(14)	0.8269
C(3)—C(4)	1.0460	C(7)—O(8)	0.7287	C(6)—H(15)	0.8209
C(4)—C(5)	1.0444	C(7)—N(9)	0.9508	N(9)—H(10)	0.6410
C(5)—C(6)	1.0949	C(2)—H(12)	0.8114	N(9)—H(11)	0.6537

<sup>a</sup> The number of position (Fig. 5) is given in parenthesis.

features can be observed: *a)* different frequency of population changes with the change of angle  $\alpha$ , and *b)* different symmetry of population curves in dependence on angle  $\alpha$ .

According to viewpoint *a)* it seems remarkable that the change of certain parameters of electron distribution is distinctly harmonic. This is especially true for overlap population of the carbonyl group  $C_{(7)}-O_{(8)}$  and the gross electron density on the amidic group bonds. In other cases the harmonicity of the changes is imperceptible and, as a rule, more distinct changes can only be observed for conformations of type 5 for  $\alpha \rightarrow 90^\circ$  (Fig. 7). The greatest changes of population parameters and of charges ( $10^{-2}$  to  $10^{-1}$  of electron) occur for the bonds and atom centres connecting the functional group with the nucleus,  $C_{(3)}$ ,  $C_{(7)}$  and  $C_{(3)}-C_{(7)}$ , further those the mutual distance of which undergoes greatest change on rotation, *i.e.*  $H_{(11)}$ ,  $H_{(12)}$ ,

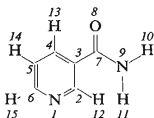


FIG. 5

The Designation of Individual Centres of Nicotinamide in Mulliken Electron Population

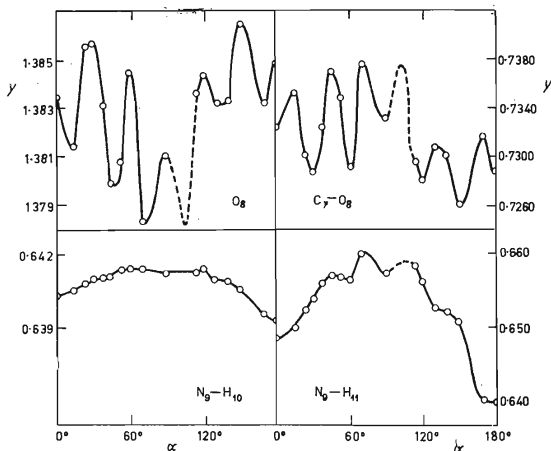


FIG. 6

Differently Developed Harmonicity on the Curves of the Dependence of Mulliken Atom and Overlap Populations  $y$  in Nicotinamide ( $\beta 0^\circ$ ) on Angle  $\alpha$



$H_{(13)}$ ,  $C_{(4)}$ ,  $C_{(6)}$ ,  $C_{(2)}-H_{(12)}$ ,  $C_{(4)}-H_{(13)}$ ,  $C_{(2)}-C_{(3)}$  and  $C_{(3)}-C_{(4)}$ , and also on the carbon *para* with respect to the functional group, *i.e.*  $C_{(6)}$ . On the other hand, the conformation of the amidic group does not affect the distribution on  $H_{15}$  and  $C_{(6)}-H_{(15)}$ , where  $\sigma$ -electrons are exclusively localized. This is in harmony with the assumption that electronic effects are transmitted to more remote parts of the molecule through  $\pi$ -bonds. The other population data change only slightly ( $\sim 10^{-3}$  of electron). In the sense of the criterion *b*) the curves of electron distribution changes are of more or less symmetric character. The first case occurs with atom centres and bonds in unconjugated parts of the molecule, *e.g.*  $H_{10}$ ,  $H_{(13)}$  and  $C_{(4)}-H_{(13)}$ , where electron distribution follows rather changes of the energy of the whole molecule and does not depend much on  $\pi$ -electron distribution. Contrarily, highly symmetric course of population changes can be observed in the cases where  $\pi$ -electrons exert strong effect, depending mainly on the deviation from the planarity of the molecule, *e.g.*  $C_{(3)}$ ,  $C_{(4)}$ ,  $C_{(6)}$ ,  $C_{(7)}$ ,  $O_{(8)}$ ,  $C_{(3)}-C_{(2)}$ , and  $C_{(3)}-C_{(7)}$ .

*Effect of rotation around the C-NH<sub>2</sub> bond:* On the change of angle  $\beta$  from  $0^\circ$  to  $90^\circ$  the changes of electron distribution indicate the expected extinction of the conjugation of unshared electron pair of the NH<sub>2</sub> group. For instance, in conformation I the charge on  $N_{(9)}$  changes from  $-0.7774$  to  $-0.9361$ , that on  $O_{(8)}$  from  $-1.3834$  to  $-1.3727$ , overlap population  $C_{(7)}-N_{(9)}$  from  $0.9511$  to  $0.8315$ , and the charge on  $C_{(7)}$  increases from  $+1.3460$  to  $+1.4588$ . Furthermore, on all the atoms of the heterocyclic ring one can observe a small decrease of the negative and a small increase of the positive charges.

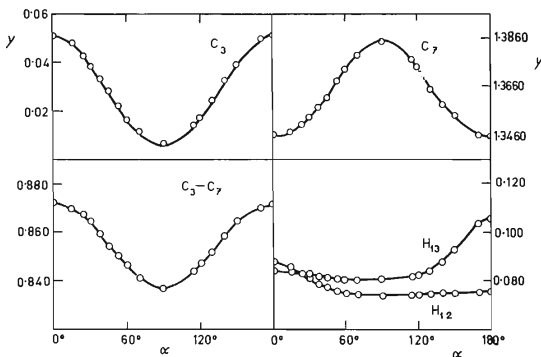


FIG. 7

Different Symmetry of the Curves of the Dependence of Mulliken Atom and Overlap Populations ( $y$ ) in Nicotinamide ( $\beta$   $0^\circ$ ) on Angle  $\alpha$

## DISCUSSION

Quantum chemical calculations of nicotinamide have to date been performed only by HMO method<sup>29,30</sup> and by  $\omega$ -technique<sup>31</sup>. Table VII presents  $\pi$ -electron charges obtained on the basis of HMO's, SCF-MO's and EHMO's for individual centres of planar form 1, which is close in geometry to optimum conformation 5*a*. It is obvious that the minimum localization of electrons is predicted by HMO method and the maximum one by EHMO procedure. All three methods give, however, the same qualitative charge distribution.

The calculated dipole moments for conformations 1–6 attain minimum value for form 1 ( $\alpha$  0°),  $\mu$  (0°) = 4.56 D and the maximum for form 6 ( $\alpha$  180°),  $\mu$  (180°) = 13.53 D, the dependence on angle  $\alpha$  being approximately  $\mu(\alpha) = 9 - 4.5 \cos \alpha$ .

TABLE VII

$\pi$ -Electron Charges Calculated by Various LCAO-MO Procedures for the Model of Nicotinamide 1

Atom	HMO	SCF	EHMO
N(1)	-0.1944	-0.1961	-0.5456
C(2)	+0.0850	+0.0892	+0.2594
C(3)	-0.0095	-0.0259	-0.0158
C(4)	+0.0520	+0.0726	+0.1813
C(5)	-0.0051	-0.0085	-0.0203
C(6)	+0.0773	+0.0992	+0.2404
C(7)	+0.0517	+0.1777	+0.5593
O(8)	-0.1438	-0.4159	-0.8985
N(9)	+0.0869	+0.2077	+0.2423

TABLE VIII

Comparison of Mulliken Overlap Population of C—H Bond with Proton Chemical Shifts in the NMR Spectrum of Nicotinamide

Bond	Overlap populations				Proton	Chemical shift (p.p.m.)
	$\alpha = 0^\circ$	$\alpha = 30^\circ$	$\alpha = 115^\circ$	$\alpha = 180^\circ$		
C <sub>(2)</sub> —H <sub>(12)</sub>	0.804	0.811	0.816	0.815	H <sub>(12)</sub>	9.15
C <sub>(4)</sub> —H <sub>(13)</sub>	0.824	0.824	0.824	0.808	H <sub>(13)</sub>	8.26
C <sub>(5)</sub> —H <sub>(14)</sub>	0.827	0.827	0.827	0.827	H <sub>(14)</sub>	7.40
C <sub>(6)</sub> —H <sub>(15)</sub>	0.821	0.821	0.821	0.821	H <sub>(15)</sub>	8.70

Contrarily, the experimental dipole moments obtained in different solvents were reported<sup>32-34</sup> to be within the range of 3.1–4.2 D. When comparing these data with the dipole moments of pyridine and benzamide, Purcell has arrived at the conclusion<sup>33</sup> that in benzene solution nicotinamide is present from 75% in form *I*. Confrontation of EHMO calculation with this statement does not seem to be reasonable, since theoretical values all are too high and the author has not considered nonplanar forms of type 5. Nevertheless, the results of the calculation are in better agreement with experiment for the lower values of  $\alpha$  considered, which is not at variance with the assumption that conformation *5a* is prevailing.

Chemical shifts of the heteroaromatic protons of nicotinamides were compared with several parameters of Mulliken electron population in the vicinity of the nuclei followed. Table VIII presents the confrontation of these data with the values of overlap population of the corresponding C—H bonds for different angles  $\alpha$  with the planar amidic group. It is obvious that the parameter of population increases with increasing shielding of protons, this trend being roughly followed for angles  $\alpha < 150^\circ$ . The calculated gross electron density on corresponding carbon atoms, *i.e.* C<sub>(2)</sub>, C<sub>(4)</sub>, C<sub>(5)</sub> and C<sub>(6)</sub>, changes analogously, however, over the whole range of  $\alpha$  considered. On the other hand, very slightly changeable charges on hydrogen atoms do not reflect the trend of the changes of the shielding of their nuclei. These facts do not rule out the existence of *5a*, neither do they the forms *5b* and *I*, however. In harmony with the conclusion about the improbable rotation around the C—NH<sub>2</sub> bond, the protons of atoms H<sub>(10)</sub> and H<sub>(11)</sub> appear as magnetically nonequivalent and exhibit two broadened signals at 7.21 and 8.09 p.p.m. In Fig. 8 is compared the experimental extinction curve of nicotinamide in the UV region with the positions and intensities of absorption bands calculated by LCI(PPP) method for the models corresponding

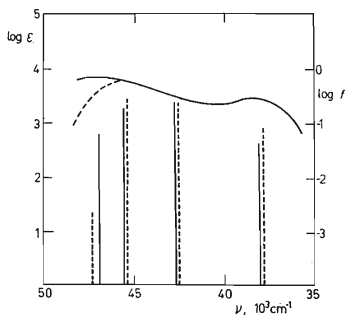


FIG. 8

Comparison of Extinction Curves of Nicotinamide (in Ethanol) with Theoretical Electronic Bands Calculated by LCI(PPP) Method

Full lines were calculated for model *I*, broken ones for model 2; the broken curve represents the presumed course for model 2.

to structures 1 and 2. Theory predicts so small changes in absorption caused by different orientation of the amidic group that from the experimental curve no unambiguous conclusions can be drawn, concerning the predominant conformation of nicotinamide in solution. Nevertheless, the course of the curve in the 45000–47000  $\text{cm}^{-1}$  region seems to correspond rather to theoretical prediction for model 1 which is close to the most suitable conformation 5a, since in the case of conformation 2, which is closer to conformation 5b, a decrease in extinction for  $\lambda \approx 46000 \text{ cm}^{-1}$  has to be expected (broken part of the curve in Fig. 8).

The present results of LCAO-EHMO calculation of the conformation of nicotinamide molecule are in satisfactory agreement with X-ray data<sup>20</sup> and are not also at variance with other physical characteristics. In accordance with the cited calculations<sup>5-19</sup> they further demonstrate the usefulness of Hoffmann method in the study of the geometry of greater biologically interesting molecules.

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