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# APPLICATION OF AM1 METHOD IN STUDYING TAUTOMERIC CONVERSIONS OF 1,3-DIIMINOISOINDOLINE AND ITS NITRO AND AMINO DERIVATIVES

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*The semiempirical method AM1 was used to calculate transition states corresponding to conformational and tautomeric conversions of 1,3-diiminoisoindoline, and also its nitro and amino derivatives. Tautomeric conversions through an intermolecular mechanism involving a protic solvent have a lower energy barrier than in the case of intramolecular proton transfer. Substitution in the benzene ring of 1,3-diiminoisoindoline does not have any significant effect on the energy barriers of the conformational transitions and tautomeric conversions. Calculated IR and electronic spectra of 1,3-diiminoisoindoline are in satisfactory agreement with the experimental spectra.*

1,3-Diiminoisoindoline and its derivatives are finding extensive applications in the synthesis of phthalocyanines and macroheterocyclic compounds [1-3]; however, many questions regarding the features of its structure (stereoisomerism, tautomerism, and the influence of substitution on these processes) have not been studied adequately. On the basis of electronic absorption spectra of solutions of isoindoline derivatives, it was concluded in [4, 5] that these compounds exist in isoindoline and isoindolenine forms; this conclusion was subsequently confirmed by means of IR spectroscopy [6].

Theoretical study of the stereoisomeric conversions of 1,3-diiminoisoindoline and its derivatives has been limited to calculations of the tautomers by the Hückel method (Zaitsev et al. [7]). In that work, on the basis of an examination of energy and electronic indexes, the investigators concluded that the isoindoline form is more stable than the isoindolenine.

Investigation of the stereochemistry of 1,3-diiminoisoindoline and its derivatives is an important task from the standpoint of examining the reactivities of these compounds. The work reported here was aimed at investigating conformational and tautomeric conversions of 1,3-diiminoisoindoline, and also the influence of substituents and the choice of solvent on the energetics of the isomer transitions.

Calculations of the stationary points on the potential energy surfaces were performed by the AM1 method, using the MOPAC-7 program package [8] with full optimization of geometric parameters. The saddle points corresponding to transition states were found by means of the SADDLE procedure with subsequent optimization (NLLSQ) and testing for correspondence to critical conditions [9]. The calculations were performed at the Krakow Computer Center on a CONVEX C3220 computer and at the Ivanovo State Chemical Technology Academy on a DX2 computer (Intel 486 processor).

1,3-Diiminoisoindoline can be represented in the form of three geometric isomers identified as I, II, and III in the following scheme. Calculated heats of formation of compounds I-III are listed under the structural formulas.

Structure I is the most favorable energetically. The transition I → II encounters a barrier higher than 600 kJ/mole, so that this transition is improbable. In contrast, the transition between the isomers I and III encounters only a relatively low potential barrier, 92.6 kJ/mole.

The structure of the transition state I → III is shown in Fig. 1. Characteristic for this structure is a decrease of the $N_{10}$–$H_{13}$ bond length to 0.96 Å (from 0.99 Å in the original structure I), and also a change of the $C_{(1)}$–$N_{(10)}$–$H_{(13)}$ angle from 117.13° to 173.46°.

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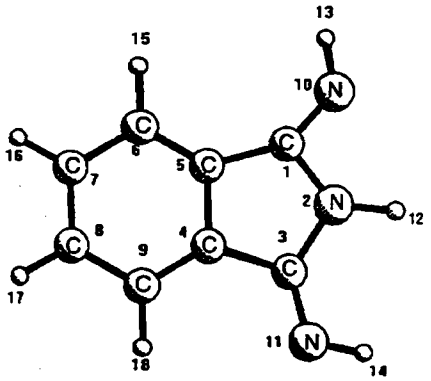
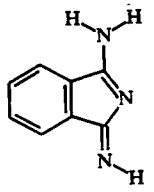


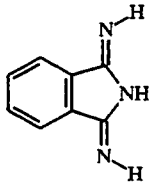
Fig. 1. Structure of transition state I → III.



IV

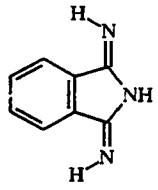
$\Delta H_f$ = 356,2 kJ/mole

The transition from the isoindoline structure to the isoindolenine structure (1-amino-3-iminoisoindolenine IV) can be represented as intramolecular transfer of a proton from the cyclic nitrogen atom to an exocyclic nitrogen atom, with the participation of the unshared pair of electrons of the exocyclic atom.



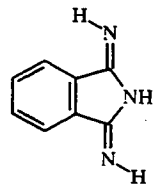
I

$\Delta H_f$ = 339,9 kJ/mole



II

$\Delta H_f$ = 359,5 kJ/mole



III

$\Delta H_f$ = 348,1 kJ/mole

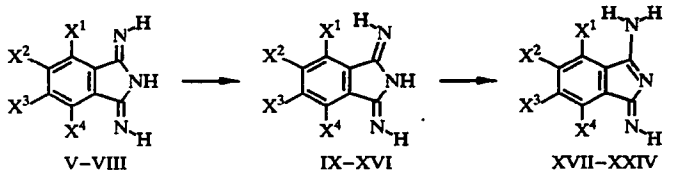
From the standpoint of conformance to stereoelectronic requirements, structure III is preferred over structure I. Calculations of transition states for the conversions I → IV and III → IV have shown that the activation energy of the first transition is greater than 600 kJ/mole; i.e., the transition is improbable. For the transition III → IV, the energy barrier is 303.9 kJ/mole, which is in good agreement with the results from *ab initio* calculations (4-31G basis) for formamidine, where a value of 248.0 kJ/mole was found for the barrier [10]. The structure of the transition state III → IV is shown in Fig. 2.

In the transition state, the $H_{(12)}$ migrating proton is in the field of the nitrogen atoms $N_{(2)}$ and $N_{(10)}$. The distances $N_{(2)}$–$H_{(12)}$ and $N_{(10)}$–$H_{(12)}$ are approximately equal (1.40 and 1.42 Å, respectively).

Thus, the most energetically favorable is the conversion of the indoline form I to the indolenine form IV through the structure III.

With the aim of evaluating the influence of substitution on transitions between isomers and tautomeric conversions, we calculated the isoindoline structures V-XVI and isoindolenine structures XVII-XXIV of 4-nitro, 5-nitro, and amino derivatives, and also transition states corresponding to possible interconversions. The structures under consideration and the values of the heat of formation and activation barrier are listed in Tables 1 and 2. From the data of Table 2, it follows that the introduction of the electron-accepting nitro group lowers the energy barrier of both the conformational and tautomeric conversions. The amino group has the opposite effect.

TABLE 1. Calculated Heats of Formation of Nitro and Amino Derivatives of Diiminoisoindoline (V-XVI) and Corresponding Isoindolenines (XVII-XXIV)



V–VIII IX–XVI XVII–XXIV

| Compound | $x^1$ | $x^2$ | $x^3$ | $x^4$ | $\Delta H_f$, kJ/mole | Compound | $x^1$ | $x^2$ | $x^3$ | $x^4$ | $\Delta H_f$, kJ/mole |
|---|---|---|---|---|---|---|---|---|---|---|---|
| V | $NO_2$ | H | H | H | 379,97 | XV | H | $NH_2$ | H | H | 339,70 |
| VI | $NH_2$ | H | H | H | 323,97 | XVI | H | H | $NH_2$ | H | 339,07 |
| VII | H | $NO_2$ | H | H | 362,54 | XVII | $NO_2$ | H | H | H | 382,54 |
| VIII | H | $NH_2$ | H | H | 330,37 | XVIII | H | H | H | $NO_2$ | 396,77 |
| IX | $NO_2$ | H | H | H | 382,38 | XIX | $NH_2$ | H | H | H | 347,23 |
| X | H | H | H | $NO_2$ | 391,08 | XX | H | H | H | $NH_2$ | 341,16 |
| XI | $NH_2$ | H | H | H | 342,88 | XXI | H | $NO_2$ | H | H | 376,60 |
| XII | H | H | H | $NH_2$ | 331,79 | XXII | H | H | $NO_2$ | H | 380,28 |
| XIII | H | $NO_2$ | H | H | 372,33 | XXIII | H | $NH_2$ | H | H | 350,16 |
| XIV | H | H | $NO_2$ | H | 373,92 | XXIV | H | H | $NH_2$ | H | 346,73 |

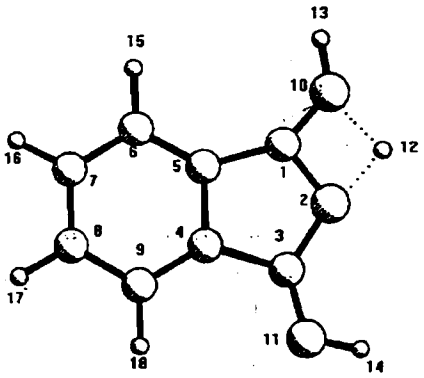



Fig. 2. Structure of transition state III → IV.

The synthesis of 1,3-diiminoisoindoline and its subsequent conversions are performed in solutions; therefore, it was of interest to investigate the influence of the medium on the processes of imine–amine tautomerism. Any accounting for all types of interaction between an organic molecule and a solvent is a task that requires major expenditure of machine time; in the present work, therefore, we have made an evaluation of the influence of specific solvation on tautomerization. Using the supermolecule approach [11], we calculated proton transfer in the molecule of 1,3-diiminoisoindoline with the participation of a solvent molecule (water or methanol).

The calculation showed that double proton migration between molecules of the diiminoisoindoline isomer III and water results in a lowering of the activation barrier when the transition is made to the isoindolenine structure, down to 223.7 kJ/mole (structures XXV, XXVa, XXVI). These data are in qualitative agreement with the results obtained in *ab initio* calculations (6-31G basis) for intermolecular proton transfer in the formamidine hydrate, for which $E_{act}$ = 87 kJ/mole [12].

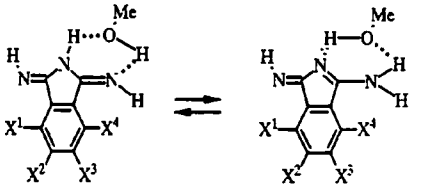
Since the formation and subsequent conversions of 1,3-diiminoisoindoline are carried out in alcohol media, we carried out calculations of intermolecular proton transfer with the participation of a methanol molecule (XXVII, XXVIIa, XXVIII). The energy barrier in this case is lowered by 32.8 kJ/mole, down to 190.9 kJ/mole.

With the aim of evaluating the influence of substitution on the magnitude of the potential barriers of tautomerization, we carried out a calculation of intermolecular proton transfer involving a methanol molecule, in 4-nitro-, 5-nitro-, and amine-substituted diiminoisoindolines. As can be seen from Table 3, the introduction of the amino group into position 4 or 5 of the

TABLE 2. Energy Barriers of Conformational and Tautomeric Transitions in Nitro and Amino Derivatives of Diiminoisoindoline

| Conformational transitions 1,3(E)-1(Z),3(E) | | Tautomeric transitions imino-amino | |
|---|---|---|---|
| transition | $E_{act}$, kJ/mole | transition | $E_{act}$, kJ/mole |
| V—IX | 83,30 | IX—XVII | 291,67 |
| V—X | 91,76 | X—XVIII | 302,71 |
| VI—XI | 99,37 | XI—XIX | 298,70 |
| VI—XII | 93,55 | XII—XX | 305,60 |
| VII—XIII | 89,75 | XIII—XXI | 301,54 |
| VII—XIV | 91,50 | XIV—XXII | 303,84 |
| VIII—XV | 94,10 | XV—XXIII | 306,23 |
| VIII—XVI | 94,14 | XVI—XXIV | 302,08 |

TABLE 3. Activation Barriers of Intermolecular Proton Transfer in Substituted Diiminoisoindolines



XXIX-XXXVI XXXVII-XLIV

| Compound | $X^1$ | $X^2$ | $X^3$ | $X^4$ | Transition | $E_{act}$, kJ/mole |
|---|---|---|---|---|---|---|
| XXIX, XXXVII | $NO_2$ | H | H | H | XXIX—XXXVII | 201,79 |
| XXX, XXXVIII | $NH_2$ | H | H | H | XXX—XXXVIII | 188,61 |
| XXXI, XXXIX | H | $NO_2$ | H | H | XXXI—XXXIX | 203,09 |
| XXXII, XL | H | $NH_2$ | H | H | XXXII—XL | 184,72 |
| XXXIII, XLI | H | H | $NO_2$ | H | XXXIII—XLI | 201,04 |
| XXXIV, XLII | H | H | $NH_2$ | H | XXXIV—XLII | 190,33 |
| XXXV, XLIII | H | H | H | $NO_2$ | XXXV—XLIII | 194,56 |
| XXXVI, XLIV | H | H | H | $NH_2$ | XXXVI—XLIV | 184,14 |

TABLE 4. Values of $\lambda_{max}$ (nm) of Long-Wave Absorption Band of 1,3(E)-diiminoisoindoline I and 1-Amino-3-Iminoisoindolenine IV

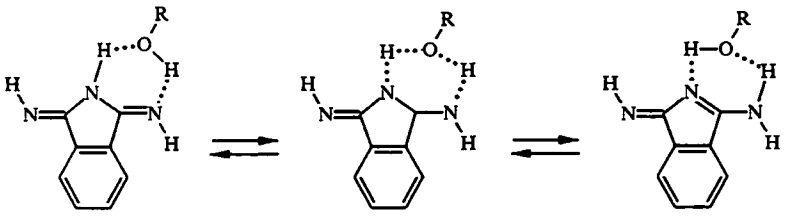
| Compound | Calculation | | Experiment [13] | |
|---|---|---|---|---|
| | $\lambda_{max}$ | Oscillator strength, f* | $\lambda_{max}$ (MeOH) | $\varepsilon$ |
| I | 297,8 (292,0) | 0,052 (0,074) | 303 | 4600 |
| IV | 319,2 (357,0) | 0,041 (0,086) | — | — |

*Data from [14] are listed in parentheses.

TABLE 5. Frequencies of Stretching Vibrations ($cm^{-1}$) of N–H Bonds of 1,3(E)-diiminoisoindoline I and 1-Amino-3-iminoisoindolenine IV

| Compound | Calculation | | Experiment [14] |
|---|---|---|---|
| | $\nu$ ($NH_2$) | $\nu$ (NH) | $\nu$ (NH) |
| I | — | 3432 | 3440 |
| IV | 3491; 3514 | 3417 | — |

1,3-diiminoisoindoline molecule lowers the energy barriers for the transitions to the isoindolenine form. The nitro group, when introduced into the same positions, increases the magnitude of the activation barrier.



XXV, XXVII XXVa, XXVIIa XXVI, XXVIII

R = H, Me

According to [4-6], the spectral characteristics of the isoindoline and isoindolenine forms of 1,3-diiminoisoindoline are substantially different. In this connection, we carried out the calculation of IR and electronic spectra of 1,3(E)-diiminoisoindoline I and 1-amino-3-iminoisoindolenine IV.

The parameters of the electronic absorption spectra were calculated by means of the HYPERCHEM program with an accounting for configuration interaction 5/5. It can be seen from the data of Tables 4 and 5 that the calculated and experimental values of $\lambda_{max}$ of the long-wave absorption band, and also the frequencies of stretching vibrations of the imino group, are in satisfactory agreement for the indoline form I.

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