

MNDO and AM1 Quantum-Chemical Study of Tautomerism of 2-Substituted 1,3-Indandiones

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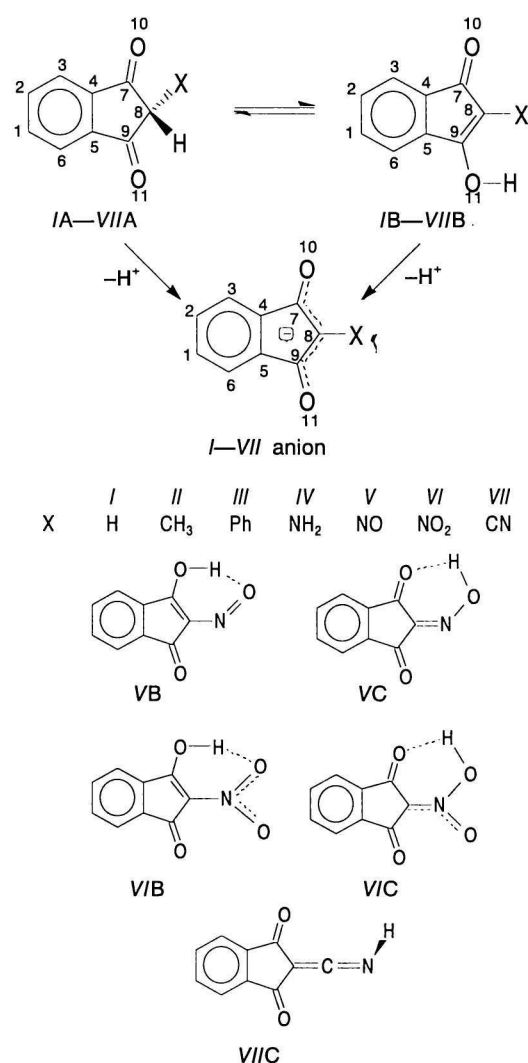
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The reliability of the semiempirical quantum-chemical methods AM1 and MNDO for the treatment of the tautomerism of 2-substituted 1,3-indandiones is tested. The effect of the substituents (H, CH₃, Ph, NH₂, NO, NO₂, CN) on the tautomerization energies is considered. It is shown that the AM1 results are in agreement with the available experimental data. The deprotonization enthalpy and the structural changes of the tautomers in the process of anion formation are discussed.

1,3-Indandione is biologically inert but its 2-substituted derivatives are of practical interest because they are physiologically active. They influence the central nervous system or show anticoagulant action. The derivatives of 1,3-indandione are also of technological interest as inhibitors of autooxidation processes in the liquid phase, stabilizing agents for polymers [1], dyes and organic semiconductors [2]. The 2-heteroaryl derivatives (phthalones) are good complexation agents [2–4]. They are photochemically stable compounds while 2-aryl-1,3-indandiones photoisomerize to compounds which are effective luminophores [5, 6]. The coloured activated esters, obtained on interaction of *N*-protected amino acids with 2-hydroxyimino-1,3-indandione [7] or 2-aryl-1,3-indandione [8], can react with amines and esters of amino acids [9]. The betaines of 2-(1-pyridyl)-1,3-indandiones are of interest as electron-donating components for CT complexes [10] and as objects for the study of intramolecular charge transfer [11]. Masaaki [12] claimed that 2-(*N,N*-dimethylamino)-1,3-indandione is an effective absorber of UV radiation. Recently the synthesis of various novel 2-substituted phenylazo-1,3-indandiones, which are potential dyestuff, has been reported [13]. The investigations on the 1,3-indandiones are summarized in the monograph [14], the paper by Ploguin *et al.* [15] and the reviews by Gudrinence [16, 17]. In some recent papers [18, 19] mainly IR, ¹H and ¹³C NMR studies on 2-substituted 1,3-indandiones have been made. Quantum-chemical calculations of betaine, 2-pyridyl-1,3-indandione, and 2-aryl-1,3-indandione by means of CNDO/S and INDO methods have also been performed [20–22]. Theoretical calculation of the electron spectrum of the 1,3-indandione has been performed at the INDO/S-CI level [23].

The 1,3-indandiones can exist in diketo form A, enol form B or as anion (Scheme 1). In the solid state



Scheme 1

most indandiones exist in diketo form (colourless or yellow substances). In nonpolar aprotic solvents

mostly diketo form is present while in polar solvents there is a mixture of diketo and enol forms. The substituents in the second position influence the enolization of 1,3-indandiones. The aim of this work is to study the influence of different substituents in position 2 of 1,3-indandiones on the relative stability of the different tautomeric forms.

CALCULATIONS

In this investigation the semiempirical AM1 and MNDO methods were chosen to study tautomeric equilibria of the compounds shown in Scheme 1. Recently, the reliability of these methods for the treatment of tautomeric equilibria was tested for a series of heterocyclic compounds [24, 25] and it was shown that with the exception of compounds with adjacent pyridine-like lone pairs they give quite reliable predictions. For a discussion of the merits and shortcomings of MNDO [26] and AM1 [27] Hamiltonians see literature [28–31]. MNDO and AM1 calculations were carried out with the AMPAC program package [32] using the PRECISE option. Geometries of the neutral molecules and anions were completely optimized without any restrictions using the Davidon–Fletcher–Powell [33] procedure.

RESULTS AND DISCUSSION

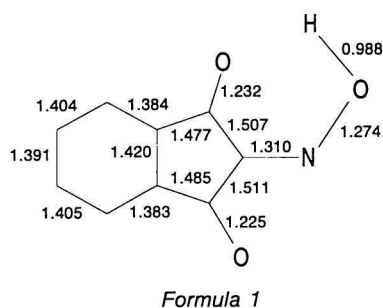
Relative Stabilities and Structure of the Tautomers

In nonpolar solvents (*e.g.* cyclohexane) the diketo form of 2-aryl-1,3-indandiones predominates; according to [14] the ratio is $w_r(A-B) = 94 : 6$. *Burdett* and *Rodgers* [34] have shown that neither 1,3-indandione nor 2-phenyl-1,3-indandione shows evidence of enolization in solvents such as chloroform, benzene, dioxane or dichloroethane. In polar protic solvents like ethanol, the enol form prevails ($w_r(A-B) = 44 : 56$) [14]. The calculated heats of formation and relative stabilities of the compounds I–VII are listed in Table 1. More complicated cases of tautomerism (see compounds V–VII, Scheme 1) are also considered.

As can be seen from Table 1 the AM1 method predicts the keto form A as the most stable for all studied compounds. The only exception is 2-nitroso-1,3-indandione. From the three tautomeric forms [35] of this compound the oximino form C is the most stable. This fact is in agreement with experimental results for nonpolar solvents and in crystal [36]. The AM1-calculated structure (bond lengths numerical values ($\text{Å} \cdot 10^{10}/\text{m}$)) of 2-hydroxyimino-1,3-indandione VC is shown in Formula 1. According to the MNDO

Table 1. Heats of Formation of the Tautomers HB of Compounds I–VII and Their Anions B[−] and Deprotonization Enthalpy DPE

Tautomer	AM1			MNDO		
	$\Delta_f H(\text{HB})$ kJ mol ^{−1}	$\Delta_f H(\text{B}^-)$ kJ mol ^{−1}	DPE kJ mol ^{−1}	$\Delta_f H(\text{HB})$ kJ mol ^{−1}	$\Delta_f H(\text{B}^-)$ kJ mol ^{−1}	DPE kJ mol ^{−1}
<i>I</i> 1,3-Indandione						
A	− 144.9 (0.0)	− 246.8	1434.4	− 188.1 (0.0)	− 287.6	1436.8
B	− 76.0 (68.9)		1365.6	− 152.2 (35.9)		1400.9
<i>II</i> 2-Methyl-1,3-indandione						
A	− 162.3 (0.0)	− 280.1	1418.6	− 202.5 (0.0)	− 338.6	1400.3
B	− 110.5 (51.8)		1366.8	− 189.9 (12.6)		1387.7
<i>III</i> 2-Phenyl-1,3-indandione						
A	− 13.2 (0.0)	− 182.3	1367.2	− 56.6 (0.0)	− 216.5	1367.5
B	26.4 (39.6)		1327.7	− 55.3 (1.3)		1375.2
<i>IV</i> 2-Amino-1,3-indandione						
A	− 104.3 (0.0)	− 239.0	1401.7	− 158.9 (4.5)	− 302.3	1392.9
B	− 76.7 (27.6)		1374.1	− 163.4 (0.0)		1397.4
<i>V</i> 2-Nitroso-1,3-indandione						
A	− 68.1 (1.1)	− 290.5	1314.0	− 145.3 (15.2)	− 364.6	1317.1
B	− 51.4 (17.8)		1297.3	− 142.8 (17.7)		1314.6
C	− 69.2 (0.0)		1315.1	− 160.5 (0.0)		1332.4
<i>VI</i> 2-Nitro-1,3-indandione						
A	− 78.9 (0.0)	− 319.3	1296.0	− 99.1 (0.0)	− 342.5	1229.9
B	− 61.5 (17.4)		1278.0	− 93.6 (5.5)		1287.4
C	− 54.3 (24.6)		1271.4	− 96.5 (2.6)		1290.3
<i>VII</i> 2-Cyano-1,3-indandione						
A	20.8 (0.0)	− 177.7	1337.8	− 30.6 (1.5)	− 239.3	1327.7
B	58.6 (37.8)		1300.0	− 32.1 (0.0)		1329.1
C	78.3 (57.5)		1280.4	28.8 (60.9)		1272.2



calculations the enol form is most stable for substituents $R = \text{NH}_2$ and CN . In all the other cases AM1 and MNDO are in qualitative agreement. There are quantitative differences for the relative stabilities of the studied tautomers and these differences vary significantly with the method used. In all cases MNDO predicts considerably smaller energy differences in the relative stabilities of the compounds studied.

For the enol tautomer of 2-phenyl-1,3-indandione *II*B the MNDO-calculated dihedral angle between the indandione fragment and the phenyl ring is 86° while the AM1-calculated one is 36° . For the enol tautomer of 2-amino-1,3-indandione *IV*B, MNDO and AM1 predict that the amino group is twisted relative to the indandione moiety at 58° and 75° , respectively. It should be mentioned that MNDO predicts large values for the torsion angles in such cases while AM1 gives more reasonable ones.

The AM1-calculated bond lengths (in 10^{-10} m) in the tautomers A and B of 1,3-indandione are listed in Table 2. For the keto tautomer A under the influence of the substituent X the C-7—C-8 and C-8—C-9 bond lengths numerical values are elongated: C-7—C-8 to 1.527 (X = CH_3), 1.535 (X = Ph), 1.538 (X = NO, CN), and 1.545 (X = NO_2 , NH_2), respectively; C-8—C-9 to 1.527 (X = CH_3), 1.531 (X = Ph), 1.538

Table 2. AM1-Calculated Bond Lengths for Keto A and Enol B Tautomers of 1,3-Indandione and Its Anion

Bond length	$a \cdot 10^{10}/\text{m}$		
	A	B	Anion
C-1—C-2	1.392	1.387	1.388
C-2—C-3	1.404	1.409	1.408
C-3—C-4	1.384	1.377	1.378
C-4—C-5	1.420	1.432	1.425
C-5—C-6	1.384	1.378	1.378
C-1—C-6	1.404	1.410	1.408
C-4—C-7	1.483	1.500	1.517
C-7—C-8	1.519	1.491	1.425
C-8—C-9	1.519	1.366	1.425
C-5—C-9	1.483	1.480	1.517
C-9—O-11	1.228	1.356	1.248
C-7—O-10	1.228	1.227	1.248
C-8—H	1.119	1.087	1.083
C-8—H'	1.119		
O-11—H		0.971	

(X = CN), 1.541 (X = NO), 1.546 (X = NO_2), and 1.549 (X = NH_2), respectively. The C-4—C-7 bond length numerical value almost does not change except for X = Ph when it is shortened to 1.431 (X = Ph). For the enol form B the C-7—C-8 and C-8—C-9 bond lengths numerical values are also elongated under the influence of the substituent: C-7—C-8 to 1.370 (X = CH_3), 1.376 (X = Ph), 1.378 (X = CN), 1.380 (X = NH_2), 1.393 (X = NO_2), and 1.395 (X = NO), respectively; C-8—C-9 to 1.498 (X = CH_3 , Ph, NO_2 , CN), 1.502 (X = NO), and 1.512 (X = NH_2), respectively. For X = NO or NO_2 the C-7—O-10 bond length numerical value is shortened to 1.341 and 1.336, respectively.

It can be seen that the substituent X (donor or acceptor) in position 2 of the tautomer A always increases the C-7—C-8 and C-8—C-9 bond lengths in comparison to those in the unsubstituted compound. Probably this is due to steric effects. The substituent X influences significantly the C-8—C-9 bond length for enol tautomer B: for example when X = NO or NO_2 . There are intramolecular hydrogen bonds in these cases. The AM1-optimized distances O—H...O for the tautomers *VB* and *V/B* were calculated to be 2.246×10^{-10} m, and 2.086×10^{-10} m, respectively. For 2-hydroxyimino-1,3-indandione *VC* the distance O...H—O (Formula 1) was calculated to be 2.169×10^{-10} m.

The AM1- and MNDO-calculated dipole moments of the tautomers of compounds *I*—*VII* are listed in Table 3. The available experimental values [37] for

Table 3. MNDO- and AM1-Calculated Dipole Moments μ_r (μ/μ^D) for the Tautomers of the Compounds *I*—*VII*

Tautomers	μ_r (AM1)	μ_r (MNDO)	Tautomers	μ_r (AM1)	μ_r (MNDO)
<i>IA</i> ^a	2.60	2.65	<i>VA</i>	4.20	4.28
<i>IB</i>	2.86	2.77	<i>VB</i>	5.55	5.43
			<i>VC</i>	4.72	4.48
<i>IIA</i>	2.44	2.53			
<i>IIB</i>	2.54	2.80	<i>VIA</i>	7.06	7.00
			<i>V/B</i>	7.50	7.57
<i>IIIA</i> ^b	2.50	2.28	<i>V/C</i>	4.82	2.64
<i>IIIB</i>	2.55	2.71			
			<i>VIIA</i>	5.22	5.12
<i>IVA</i>	3.65	3.40	<i>VII/B</i>	5.63	5.58
<i>IVB</i>	1.92	2.26	<i>VII/C</i>	1.45	1.98

a) $\mu_r(\text{INDO/S-CI}) = 3.71$ [23]; $\mu_r(\text{exp.}) = 2.72$ [37]. b) $\mu_r(\text{exp.}) = 2.90$ [37].

the keto tautomers of 1,3-indandione *IA* and 2-phenyl-1,3-indandione *IIIA* are also given. The calculated and experimental values are in good agreement. For *IA* the MNDO-calculated dipole moment is closer to the experimental value, while for *IIIA* the AM1-calculated one is in better agreement with experiment.

Anion Formation and Deprotonization Enthalpy

In water at pH = 12 the equilibrium shown in Scheme 1 is strongly shifted to the anion form. Although the MNDO and AM1 methods were parametrized to reproduce ground-state properties of neutral closed-shell molecules, they also give good results for positive and negative ions [38, 39]. An exception are the ions where the charge is concentrated on one atom [31]. The deprotonization enthalpy DPE of compound HB is the heat of the reaction of loss of a proton and a formation of a conjugated base, and is determined by the expression

$$\text{DPE} = \Delta_f H(\text{H}^+) + \Delta_f H(\text{B}^-) - \Delta_f H(\text{HB}) \quad (1)$$

In eqn (1) $\Delta_f H(\text{B}^-)$ and $\Delta_f H(\text{HB})$ are calculated by the MNDO or AM1 methods, and for $\Delta_f H(\text{H}^+)$ the experimental value 1536.4 kJ mol⁻¹ is used.

It can be seen from the results given in Table 1 that for compounds I–V the enol tautomers B have lower DPE than the keto tautomers A. An exception are the MNDO-calculated DPE for compound IV. In more complex cases of tautomerism for compounds VI and VII AM1 predicts the lowest DPE for tautomer C (Scheme 1).

The structural changes which occur as a result of the deprotonization of A or B to the anion are expressed in lengthening of the bonds C-4—C-7 and C-5—C-9 (Scheme 1 and Table 2) and shortening and equalizing of the C-7—C-8 and C-8—C-9 bonds as well. For all anions AM1 predicts planar structure with the exception of the anion of the 2-amino-1,3-indandione where the torsion angle between the amino group and the indandione moiety was calculated to be 61°. Under the influence of the substituent X the C-7—C-8 = C-8—C-9 bond lengths numerical values (in 10⁻¹⁰ m) are elongated to 1.430 (X = CH₃), 1.442 (X = NH₂, CN), 1.446 (X = Ph), 1.456 (X = NO₂), and 1.461 (X = NO), respectively. MNDO also predicts planar structure for all anions studied except the anions of the 2-amino-1,3-indandione and 2-phenyl-1,3-indandione. The torsion angle between the indandione fragment and amino group is calculated to be 56°, while that between the indandione moiety and the phenyl ring is computed to be 52°.

In conclusion, it seems that AM1 yields more reliable results than MNDO for ground-state geometries and relative stabilities of tautomeric species. Besides, the AM1 provides qualitatively correct hydrogen bond geometries as well.

REFERENCES

- Moiseev, V. V. and Poluektov, I. T., *Usp. Khim.* 42, 471 (1973).
- Neilands, O. and Katzen, J. J., *Khim. Geterotsikl. Soedin.* 1975, 435.

- Miteva, M., Bontchev, P., Enchev, V., Minchev, S., and Kashchieva, M., *J. Prakt. Chem.* 327, 516 (1985).
- Miteva, M., Bontchev, P. R., Zheglova, E., Mechandjiev, D., Minchev, S., and Kashchieva, M., *J. Prakt. Chem.* 332, 99 (1990).
- Zechner, J., Getoff, N., Timtcheva, I., Fratev, F., and Minchev, S., *Z. Naturforsch., A* 38, 1337 (1983).
- Timtcheva, I., Nikolov, P., Zechner, J., Getoff, N., and Minchev, S., *Z. Naturforsch., A* 43, 59 (1988).
- Minchev, S., Nedev, H., and Enchev, V., *Liebigs Ann. Chem.* 1987, 375.
- Minchev, S., Derdowska, J., and Kupryszewski, G., *Pol. J. Chem.* 54, 443 (1980).
- Nedev, H., Rolka, K., Minchev, S., Kupryszewski, G., Kolasa, K., and Kleinrok, Z., *Pol. J. Pharmacol. Pharm.* 40, 303 (1988).
- Kampars, V. and Neilands, O., *Izv. Akad. Nauk Latv. SSR, Ser. Khim.* 1975, 727.
- Kampars, V., *Izv. Akad. Nauk Latv. SSR, Ser. Khim.* 1984, 585.
- Masaaki, I., *Eur. Pat. Appl.* 22,647 (1981).
- Hocaoglu, N., Uyar, T., and Turker, L., *Dyes Pigments* 12, 1987 (1990).
- Neilands, O., Stradins, J., Silins, E., Balode, D., Valtere, S., Kadysh, V., Kalinina, S., Kampars, V., Mazeika, I., and Taure, L., in *Structure and Tautomerism of β -Dicarbonyl Compounds*. (Gudrinence, E., Editor.) Publishing House Zinatne, Riga, 1976.
- Ploguin, J., Sparfel, L., Baut, G. Le, Floch, R., and Letourneux, Y., *J. Heterocycl. Chem.* 17, 961 (1980).
- Gudrinence, E., *Izv. Akad. Nauk Latv. SSR, Ser. Khim.* 1980, 645.
- Gudrinence, E., *Izv. Akad. Nauk Latv. SSR, Ser. Khim.* 1986, 3.
- Petrova, M., Leipinis, E., Paulins, J., Gudele, I., and Gudrinence, E., *Izv. Akad. Nauk Latv. SSR, Ser. Khim.* 1987, 601.
- Boháč, A., Perjéssy, A., Loos, D., and Hrnčiar, P., *Monatsh. Chem.* 122, 943 (1991).
- Kampaar, V., Bruvers, V., and Neilands, O., *Khim. Geterotsikl. Soedin.* 1981, 658.
- Benders, J., Fleisher, M., Gavars, R., and Stradins, J., *Izv. Akad. Nauk Latv. SSR, Ser. Khim.* 1985, 61.
- Kampaar, V., Bruvers, Z., Adamsone, B., Kampare, R., and Neilands, O., *Izv. Akad. Nauk Latv. SSR, Ser. Khim.* 1986, 496.
- Galasso, V. and Pappalardo, G. C., *J. Chem. Soc., Perkin Trans. 2* 1976, 574.
- Fabian, W. M. F., *J. Comput. Chem.* 12, 17 (1991).
- Fabian, W. M. F., *Z. Naturforsch., A* 45, 1328 (1990).
- Dewar, M. J. S. and Thiel, W., *J. Am. Chem. Soc.* 99, 4899, 4907 (1977).
- Dewar, M. J. S., Zoebisch, E., Healy, E., and Stewart, J. J. P., *J. Am. Chem. Soc.* 107, 3902 (1985).
- Baird, N. C. and Hadley, G. C., *Chem. Phys. Lett.* 128, 31 (1986).
- Dewar, M. J. S. and O'Connor, B. M., *Chem. Phys. Lett.* 138, 141 (1987).
- Thiel, W., *Tetrahedron* 44, 7393 (1988).
- Voityuk, A. A., *Zh. Strukt. Khim.* 29, 138 (1988).
- Stewart, J. J. P., *AMPAC, Quantum Chemistry Program Exchange*, program 506.
- Fletcher, R. and Powell, M. J. D., *Comput. J.* 6, 163 (1963); Davidon, W. C., *Comput. J.* 10, 406 (1969).
- Burdett, J. L. and Rodgers, M. T., *J. Am. Chem. Soc.* 86, 2105 (1964).
- Otsuji, Y., Yabune, H., and Imoto, E., *Bull. Chem. Soc. Jpn.* 41, 1745 (1968).
- Minchev, St., Enchev, V., and Nedev, H., *Z. Naturforsch., B* 45, 543 (1990).
- Mazeika, I., Stradins, J., and Gribeshok, M., *Izv. Akad. Nauk Latv. SSR, Ser. Khim.* 1973, 589.
- Halim, H., Henrich, N., Koch, W., Schmidt, J., and Frenking, G., *J. Comput. Chem.* 7, 93 (1986).
- Dewar, M. J. S. and Dieter, K. M., *J. Am. Chem. Soc.* 108, 8075 (1986).