

# Semiempirical MNDO and UV Absorption Studies on Tautomerism of 2-Quinolones

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Semiempirical MNDO calculations with geometry optimization were carried out for seven 4-X-2-quinolone tautomers (X = H, CH<sub>3</sub>, Cl, OCH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub>, COOH, COOCH<sub>3</sub>). The results show that 2-hydroxyquinolines are less stabilized compared to 2-quinolones than 2-hydroxypyridines vs. 2-pyridones. The earlier estimated correction applied to these MNDO results suggests that 4-X-2-quinolones have lower chemical binding energies than the corresponding 4-X-2-hydroxyquinolines by ca. 2.1–3.3 kcal/mol. It is additionally shown that the substituent in position 4 does not influence significantly the relative stabilities of the tautomers. The results of the calculations are verified by UV absorption studies of diluted decane solutions of 2-quinolones at ca. 120°.

CNDO/S-CI-1 calculations based on the optimal MNDO geometries were carried out for 4-X-2-quinolone tautomers. The results generally agree well with the experimental data. A disagreement of the data for 4-COOR-2-quinolones is rationalized.

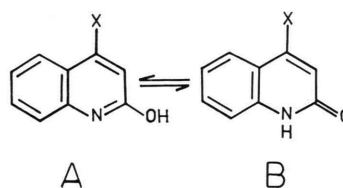
## Introduction

The predominance of the lactam form of 2-quinolone over the lactim form in aqueous solutions is the result of one of the classic studies on tautomerism. As early as in 1899 Hartley and Dobbie compared UV absorption spectra of aqueous solutions of 2-quinolone with the spectra of N-methyl-2-quinolone and 2-methoxyquinoline and concluded that the structure of 2-quinolone is analogous to the structure of N-methyl-2-quinolone [1]. Since then the predominance of the lactam form of 2-quinolone in liquid media has been confirmed by several studies with ultraviolet spectroscopy [2]. Qualitative support for this conclusion has also been provided by infrared spectral data, both in solution and in the crystalline state [3]. The same conclusion has emerged from dipole moment studies of 2-quinolone [4]. A recent structure determination by x-ray crystallography also supports the lactam form of 2-quinolone as favored in the solid [5]. Basicity measurements of 2-quinolone tautomers, with 2-methoxyquinoline and N-methyl-2-quinolone as model compounds, have provided a quantitative estimate of the equilibrium constant  $K_T$  in aqueous solution at ambient temperature as ca. 3000 [6] or ca. 7600 [7] in favour of 2-quinolone.

The above results would suggest that the problem of relative stabilities of 2-quinolone tautomers

has been thoroughly studied and resolved. However, in 1976 Beak and co-workers showed that the well known predominance of the lactam forms of 2- and 4-hydroxypyridines and 2- and 4-mercaptopyridines in condensed phases should be attributed to the differences in solvation and/or association [8]. Comparing their chemical binding energies estimated from UV absorption studies in the vapour, the lactim forms of these compounds appeared to be more stable [8].

The aim of our study was therefore to reinvestigate the problem of relative stabilities of 2-quinolone tautomers excluding solvation and association effects, both by quantum chemical methods and UV absorption spectroscopy under conditions which secure a minimization of intermolecular interactions. These methods were applied to the 4-substituted 2-quinolones (Scheme).



- 1: X = H
- 2: CH<sub>3</sub>
- 3: Cl
- 4: OCH<sub>3</sub>
- 5: N(CH<sub>3</sub>)<sub>2</sub>
- 6: COOH
- 7: COOCH<sub>3</sub>

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The relative stabilities of 4-X-2quinolone tautomers were calculated using the semiempirical MNDO method of Dewar and Thiel with full geometry optimization [9]. It has been shown that MNDO is successful in predictions of such molecular properties as molecular geometries, heats of formation, dipole moments, and ionization potentials [9]. A superiority of the MNDO procedure over the more popular semiempirical methods (i.e. CNDO/2, MINDO/2, and MINDO/3) has been evidenced in predictions of the relative stabilities of monosubstituted pyridine tautomers [10].

The results of our calculations were confronted with the results of UV absorption studies of diluted decane solutions of 4-X-2-quinolones at high temperatures (ca. 120°). As it has been shown previously, the UV absorption spectra of tautomeric heterocyclic systems recorded under these conditions closely resemble the spectra of the systems taken in the vapour phase [11].

## Experimental

### Calculations

The MNDO procedure of Dewar and Thiel (Modified Neglect of Diatomic Overlap) used in our calculations is a semiempirical version of the NDDO approximation of the Roothan-Hall SCF-LCAO-MO method [9]. The calculations were carried out with geometry optimization. The only assumption about the molecular geometries was that the quinoline and quinolone rings were planar in all considered cases because the calculations of the optimal geometries of **1A** and **2A** carried out with full geometry optimization have shown that the rings were planar.

Starting geometries of the tautomers considered by us were as follows: crystallographic data were utilized as the starting geometry of the quinolone ring in the B-type tautomers [5]. Starting geometries of the A-type tautomers were based on standard bond lengths and angles.

Calculations of the total energies of the rotamers of **6A** were carried out with geometry optimization of the carboxy-group whereas the geometry of the quinolone ring was fixed for optimal parameters of the most stable rotamer.

Positions of UV absorption bands were calculated with an employment of the CNDO/S-CI procedure of Del Bene and Jaffe [12]. The optimal MNDO geometries were used as input data for CNDO/S. 50

lowest singly excited states were involved in the CI-1 procedure in all cases.

Calculations were carried out on the CDC CYBER 72 computer in the Regional Computational Center "CYFRONET" in Kraków.

### Materials

The compounds were synthesized and purified by standard methods. All samples were sublimated or distilled immediately before measurements.

### UV Measurements

The measurements were carried out with a VSU-2P Carl Zeiss, Jena, spectrophotometer. Temperature in the cell unit was controlled by a thermocouple within an accuracy  $\pm 0.2^\circ$ . Temperature was maintained with an accuracy  $\pm 1.0^\circ$  during the measurements carried out above 120°. Quartz absorption cells of 1.0–4.0 cm path length were used.

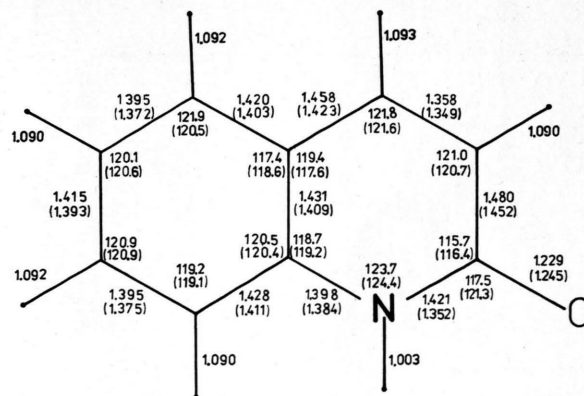
## Results and Discussion

### Optimal Geometries

Comparison of the optimal MNDO bond lengths and angles of 2-quinolone (**1B**) with those found by x-ray crystallography [5] is shown in Figure 1.

As it can be seen from Fig. 1 the bond angles are satisfactory reproduced by MNDO within an error, as a rule, less than  $1^\circ$ , whereas the bond lengths are almost systematically overestimated by ca. 0.02 Å. This difference cannot be rationalized because of lack of structural data for 2-quinolones in the vapour phase.

The most striking disagreement between the calculated and experimental bond lengths is found



in the "amide" part of the heterocyclic ring of 2-quinolone. This is most probably due to the fact that intermolecular hydrogen bonds existing in the solid state of 2-quinolone [5] significantly change bond lengths, especially in the "amide" portion of the molecule, in comparison with an isolated molecule. Such an explanation is additionally supported by the observation that the C=O bond length calculated by MNDO is by 0.016 Å shorter than found in the crystalline state, in contrast to the other bonds which lengths are systematically overestimated by MNDO (Figure 1). In general however, it should be emphasized that the agreement between the calculated and crystallographic geometry parameters for 2-quinolone is satisfactory.

### Relative Stabilities

Table 1 presents heats of formation, dipole moments, and first ionization potentials for tautomers of seven 4-substituted 2-quinolones, as calculated by MNDO.

In all considered cases the values of  $\Delta E$ , defined as  $\Delta H_B^f - \Delta H_A^f$ , are positive. This suggests that the A-type tautomers of 2-quinolones should be more stable by chemical binding energy than the corresponding B-type tautomers. However, as we have previously shown, relative stabilities of hydroxy type tautomers of heterocyclic systems were systematically overestimated by the MNDO method [10, 13]. For 2- and 4-hydroxypyridine tautomers this overestimation has been evaluated to be ca.

8.6 kcal/mol [13, 14]. Assuming that the similar correction should be applied in the case of 2-quinolones tautomers we obtain that  $\Delta E$ 's (i.e. relative stabilities of B-type tautomers versus A-type tautomers) are equal to ca. -2.7, -2.1, -2.5, -3.3, -2.3, -2.2, and -2.3 kcal/mol for **1-7**, respectively. These  $\Delta E$ 's are now all negative. Thus in contrast with 2- and 4-hydroxypyridines the B-type tautomers of 4-X-2-quinolones appear to be more stable by chemical binding energy and should then predominate over A-type tautomers in the vapour phase. This result is in a qualitative agreement with the previously published results of the semiempirical calculations of relative stabilities of parent 2-quinolone tautomers carried out by Dewar et al. [15] and by Fabian [16]. The coincidence, however, does not unambiguously resolve the problem of the most stable tautomer of 2-quinolone because it is known that both the "SCF-MO" method of Dewar and co-workers [15] and the MINDO/2 method [16] predict the B-type tautomers to be more stable also for 2- and 4-hydroxypyridines, in a qualitative disagreement with the vapour phase experiment.

The only experimental attempt of an estimation of the relative stabilities of 2-quinolone tautomers in the gas phase was performed by Beak, based on the gas phase calorimetric measurements of enthalpy difference between 2-methoxyquinoline and N-methyl-2-quinolone [11]. This determination has suggested that 2-hydroxyquinoline was more stable in the vapour phase by ca. 0.3 kcal/mol than 2-quinolone [11]. However, as it has been shown recently, estimation of relative stabilities of tautomers using methyltropic isomers as model compounds may be charged by an error of few kilocalories per mole [17].

Comparison of the relative stabilities of 2-quinolone tautomers with the experimentally found  $\Delta G^0$  of tautomerisation **1A**  $\rightleftharpoons$  **1B** in aqueous solution may be accomplished after consideration of the polar solvent influence on the tautomeric equilibrium. It has been shown recently that an application of the simple solvation model based on the Onsager equation [18] gives a surprisingly realistic estimation of the influence of a polar environment on the relative stabilities of heterocyclic systems tautomers [8]. Application of this model, in the form given by Sinogoglu [19], to the **1A**  $\rightleftharpoons$  **1B** system indicates that **1B** should be additionally stronger stabilized in aqueous solution by ca.

Table 1. MNDO heats of formation, relative stabilities, dipole moments, and first ionization potentials of 4-X-2-quinolone tautomers.

	$\Delta H_f^f \left[ \frac{\text{kcal}}{\text{mol}} \right]$	$\Delta E^a \left[ \frac{\text{kcal}}{\text{mol}} \right]$	$\mu \text{ [D]}$	IP <sup>b</sup> [eV]
1 A	- 9.41	5.87	1.28	8.87
1 B	- 3.54		3.54	8.83
2 A	- 14.80	6.52	1.35	8.86
2 B	- 8.28		3.56	8.81
3 A	- 14.57	6.11	1.09	9.08
3 B	- 8.45		3.46	9.07
4 A	- 47.47	5.31	1.67	8.70
4 B	- 42.16		3.24	8.83
5 A	1.53	6.33	1.33	8.82
5 B	7.86		3.41	8.81
6 A	- 94.87	6.45	1.55	9.12
6 B	- 88.42		3.46	9.06
7 A	- 87.41	6.33	1.75	9.10
7 B	- 81.08		3.54	9.03

<sup>a</sup>  $\Delta E = \Delta H_f^B - \Delta H_f^A$ , where  $\Delta H_f$  denotes the calculated heat of formation for B and A tautomers, respectively.

<sup>b</sup> using the Koopmans' theorem.



2.2 kcal/mol [20]. Bearing in mind that **1B** is also stronger stabilized by chemical binding energy (by ca. 2.7 kcal/mol — see above) and assuming that differences in zero-point energies and molecular entropies of the tautomers are small we obtain an estimation of  $\Delta G_{\text{aq}}^0$  of **1A**  $\rightleftharpoons$  **1B** to be equal to ca. -4.9 kcal/mol. The above value is surprisingly and maybe fortuitously close to the values -4.66 [6] or -5.2 kcal/mol [7] estimated from basicity measurements. This agreement shows that using the "corrected" MNDO method and the simple Onsager model one can predict, at last semiquantitatively, relative stabilities of heterocyclic tautomers also in polar solvents.

Application of the Onsager model to the other 4-X-2-quinolone tautomers indicates that also in these cases the B-type tautomers are stronger stabilized by interactions with water molecules by 1.1–2.0 kcal/mol, compared to the corresponding A-type tautomers. This is of course due to the fact that in all considered cases the B-type tautomers possess a considerably larger dipole moments than the corresponding A-type tautomers (see Table 1).

In addition, it can be seen from Table 1 that the  $\Delta E$ 's obtained by MNDO do not vary significantly with a change of the substituent in the position 4 of 2-quinolone. Since the substituents considered differ drastically in electron donor-acceptor properties (cf.  $-\text{N}(\text{CH}_3)_2$  and  $-\text{COOH}$ ) one can conclude that the electronic influence of these substituents on the tautomeric equilibrium of 4-X-2-quinolones can be neglected in most cases. It appears to us therefore that the results of our investigations of 2-quinolone and its simple 4-X derivatives could be extended to more complicated derivatives, for example quinoline alkaloids, containing the 2-quinolone unit.

#### Dipole Moments and Ionization Potentials

Roger has found that 2-quinolone in dioxane solution possesses a dipole moment equal to 3.45 D, and its methyltropic analogue, N-methyl-2-quinolone — 3.72 D [4]. The calculated MNDO value (3.54 D — Table 1) agrees very well with these experimental determinations.

The very recently published results of UV PES of 2-quinolone, N-methyl-2-quinolone, and 2-methoxyquinoline [22] made possible estimating reality of the molecular orbital energies calculated by MNDO. Comparison of the calculated and experimental

Table 2. Comparison of the calculated (using the Koopmans' theorem) and experimental [22] ionization potentials for **1A** and **1B** (all data in eV).

<b>1A</b>		<b>1B</b>		
MNDO	exp. <sup>a</sup>	MNDO	exp. <sup>b</sup>	exp. <sup>c</sup>
8.87	8.30	8.83	8.25	8.40
9.22	8.70	9.49	9.0	9.13
<b>9.95<sup>d</sup></b>	<b>9.60</b>	<b>9.96<sup>d</sup></b>	<b>9.4</b>	<b>9.45</b>
11.02	10.50	11.17	10.7	10.7
11.48	10.50	11.71	10.8	11.20
<b>12.90</b>	<b>11.70</b>	<b>12.81</b>	11.95	12.2

Ionization energies from  $\sigma$ -type orbitals are boldfaced.

<sup>a</sup> data for 2-methoxyquinoline.

<sup>b</sup> data for N-methyl-2-quinolone.

<sup>c</sup> data for **1B**.

<sup>d</sup> the ionization energies from n-type orbitals are corrected (see. M. J. S. Dewar, Y. Yamaguchi, S. Doraiswamy, S. D. Sharma, and S. H. Suck, Chem. Phys. **41**, 21 (1979).

energies of six higher occupied molecular orbitals of **1A** and **1B** is given in Table 2.

It is apparent from Table 2 that there is a satisfactory agreement between the calculated and experimental values of ionization energies. All MO energies of **1A** and **1B** molecules are reproduced in the correct order and with approximately correct values. This confirms the validity of the MNDO method in interpretation of photoelectron spectra of heterocyclic compounds.

#### UV Absorption Measurements

We have carried out UV absorption measurements of 4-X-2-quinolones in order to confront the results of our calculations with the experiments. The UV spectra were recorded for diluted decane solutions (ca.  $10^{-4}$ – $10^{-5}$  M) at temperature ca. 120°. Such conditions of the experiment were chosen so as to minimize intermolecular solute-solvent and/or solute-solute interactions. UV absorption spectra of 2-pyridone in decane solutions at temperature 120° appear to be similar to the spectra recorded in the vapor phase, indicating that the nonpolar solvent does not affect the tautomeric equilibrium, and that the high temperature breaks up self-association of 2-pyridones [11]. Taking into account that the differences in zero-point energies and in kinetic energies between such tautomers are suggested to be negligible [8], the experimentally found ratio of the tautomer quantities under defined above conditions reflects differences in their chemical binding energies.

Figure 2 shows the UV absorption spectra of methyltropic isomers: N-methyl-2-quinolone and 2-

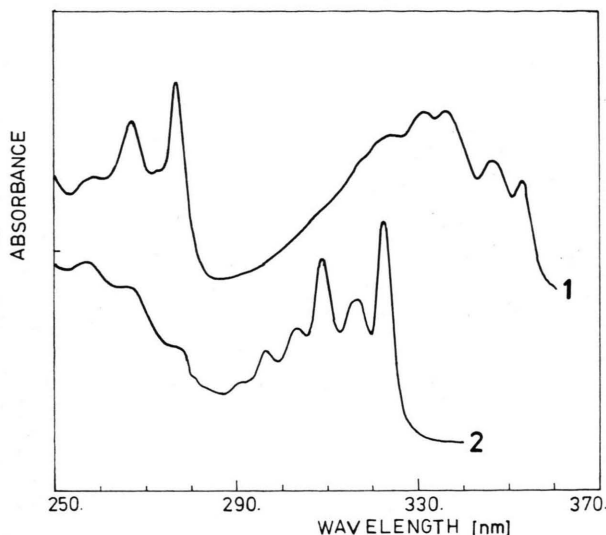


Fig. 2. Ultraviolet spectra of N-methyl-2-quinolone (1) and 2-methoxyquinoline (2) in decane at ambient temperature.

methoxyquinoline, in decane solutions. It can be seen from Fig. 2 that 2-quinolone tautomers should be distinguishable in the region at 290–360 nm. The absorption spectrum of decane solution of 2-quinolone recorded at room Temperature (Fig. 3) is almost identical with the spectrum of N-methyl-2-quinolone. It confirms the known fact of predominance of **1B** in liquid media. This example is also in full analogy with the case of 2-pyridone. In decane solutions (ca.  $10^{-4}$  M), at room temperature, 2-

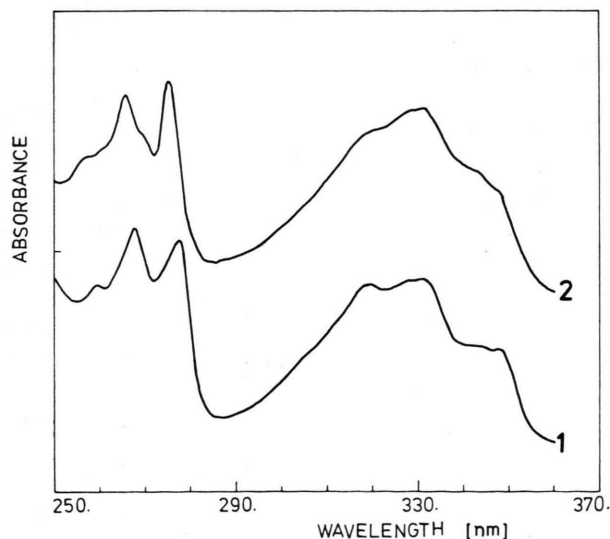


Fig. 3. Ultraviolet spectra of **1A** ⇌ **1B** system in decane (ca.  $10^{-4}$  M) at 22° (1) and 122° (2).

pyridone exists predominately as the **B** tautomer ( $K_T = [B]/[A] > 10$ ), since the **B**-type tautomer is stabilized additionally by self-association, although the **A** tautomer has the lower chemical binding energy [8]. 2-quinolones are also highly dimerized by self-association in nonpolar solvents [23]. However, in contrast to 2-pyridone [7], heating of decane solution of 2-quinolone up to 122° does not change essentially the UV absorption spectrum (Figure 3). Particularly, significant peaks in the 305–325 nm  $\lambda_{\max}$  region, where **1A** should absorb strongly, are not observed. Identical results were obtained for other 4-X-2-quinolones (also for temperatures ca. 20 and ca. 120°) [24]. This is a qualitative experimental evidence showing that 2-quinolones are more stable by chemical binding energies in their **B**-type tautomeric forms.

Further support is obtained from the multi-wavelength analysis [25] of the UV data. We applied this technique to **1A** ⇌ **1B** and **2A** ⇌ **2B** systems, using corresponding N-methyl and 2-methoxy-derivatives as model compounds (**2A** ⇌ **2B** system was chosen because, according to our calculations, this system exhibits the smallest difference in stabilities of the tautomers). The multi-wavelength analysis shows that for both **1** and **2**, the tautomeric equilibrium constants are  $K_T = [B]/[A] > 10$  [26]. This implies that  $\Delta G^0$  value of the tautomerisation is less than  $-1.8$  kcal/mol.

The experimental UV results support therefore the theoretical conclusions that the **B** tautomers of 2-quinolones are more stable than the **A** tautomers, when their chemical binding energies are compared. Also a greater stability of the **B**-type tautomers is in agreement with the very recently published results of mass spectroscopic [27] and UV PES studies [22], which suggest a predominance of the **B** tautomer of 2-quinolone in the vapour phase. This is a supporting evidence for our calculations.

#### CNDO/S Calculations

We carried out CNDO/S CI-1 calculations for six 4-X-2-hydroxyquinolines and 4-X-2-quinolones. Results of the calculations (positions and oscillator strengths of electronic absorption bands) are collected in Table 3. The experimental positions of electronic absorption bands ( $\lambda_{\max}$  in decane solutions, in range 270–420 nm) are also placed in Table 3. The electronic transition of the lowest

Taut-omer	Transition energies		Taut-omer	Transition energies	
	calc. (f <sup>a</sup> )	exp. <sup>b</sup>		calc. (f <sup>a</sup> )	exp. <sup>b</sup>
1 A	3.83 (0.0461)	3.84 <sup>c</sup>		4.36 (0.0000)	
	4.17 (0.0129)	4.01 <sup>c</sup>		4.47 (0.0000)	
	4.54 (0.0818)	4.64 <sup>c</sup>		4.53 (0.1921)	
1 B	3.46 (0.0029)		5 B	3.57 (0.0003)	
	3.87 (0.1696)	3.75		3.91 (0.0781)	3.81 <sup>d</sup>
	4.46 (0.1525)	4.48, 4.63		4.35 (0.0001)	
2 A	3.84 (0.0355)	3.85 <sup>c</sup>		4.46 (0.0857)	4.28 <sup>d</sup>
	4.26 (0.0112)	4.01 <sup>c</sup>	6 A	3.84 (0.0218)	
	4.54 (0.1169)	4.64 <sup>c</sup>		4.02 (0.0001)	
2 B	3.53 (0.0029)			4.31 (0.0001)	
	3.90 (0.1582)	3.77		4.52 (0.0505)	
	4.49 (0.1374)	4.49, 4.65	6 B	3.64 (0.0002)	
4 A	3.85 (0.0154)			3.89 (0.0846)	3.64 <sup>e</sup>
	4.43 (0.0000)			4.26 (0.0000)	
	4.44 (0.1096)			4.49 (0.0939)	4.40 <sup>e</sup>
4 B	3.25 (0.0000)		7 A	3.85 (0.0210)	
	3.68 (0.0000)			4.07 (0.0001)	
	3.91 (0.0477)			4.35 (0.0000)	
	4.17 (0.1430)	4.03		4.53 (0.0505)	
4 B-cont.	4.43 (0.0000)		7 B	3.67 (0.0001)	
	4.55 (0.0000)			3.90 (0.0830)	3.62 <sup>f</sup>
	4.98 (0.2017)	4.88	7 B-cont.	4.28 (0.0001)	
5 A	3.86 (0.0136)			4.49 (0.0941)	4.33 <sup>f</sup>

Table 3. Calculated and experimental positions of electronic absorption bands (in eV) of 4-X-2-quinolones tautomers.

<sup>a</sup> oscillator strengths.<sup>b</sup> decane solutions, 10<sup>-4</sup>–10<sup>-5</sup> M, at ambient temperature, unless otherwise stated.<sup>c</sup> data for 2-methoxy-derivatives.<sup>d</sup> data for (4-(1-piperidine)-2-quinolone.<sup>e</sup> methanol solution.<sup>f</sup> data for 4-carbethoxy-2-quinolone.

energy in A-type tautomers of 2-quinolones, which is of  $\pi \rightarrow \pi^*$  type, may be termed as <sup>1</sup>L<sub>a</sub> band, by analogy with benzenoid aromatics. The calculated positions of this band are almost independent from substituents in position 4 (Table 3), so that it can be predicted that for A-type tautomers of all 2-quinolones considered the UV bands should appear in the region 290–325 nm.

Comparison of the results of the CNDO/S calculations for 1A and 2A with the measured UV absorption band positions of 2-methoxyquinoline and 4-methyl-2-methoxyquinoline, respectively, shows a satisfactory agreement of the data (Table 3). Also for the B-type tautomers the CNDO/S calculations predict UV absorption band positions with an accepted accuracy for interpretation of such spectra. However, as it can be seen from Table 3,

the method overestimates systematically the transition energies by ca. 0.1 eV. It is not surprising bearing in mind that our CNDO/S calculations were based on the optimal MNDO geometries. On the other hand the CNDO/S calculations reproduce satisfactorily changes in positions of the lowest observed transitions of 4-X-2-quinolones with changes of substituents within an accuracy  $\pm 0.02$  eV (Table 4). The only exceptions are the cases of 6B and 7B. It seems that the striking differences between the calculated and experimentally found band positions are caused in these cases at least by two factors:

i) the calculated band position for 7B was compared with the experimental UV spectrum of 4-carbethoxy-2-quinolone. However, differences in the spectra of decane solutions of these compounds should not be significant – the difference in positions of the considered band in ethanol solutions of 7B and 4-carbethoxy-2-quinolone does not exceed 1 nm.

ii) the input geometries of 6B and 7B seem to be therefore responsible mainly for this inconsistency. In the optimal MNDO geometries – COOR groups are perpendicular to the plane of 2-quinolone ring (COOR group could not be coplanar with the ring because of “peri” repulsive interactions with a hydrogen atom in the position 5).

Table 4. CNDO/S and experimental changes of HOMO→LUMO ( $\pi \rightarrow \pi^*$ ) transition energy in 4-X-2-quinolones (relative to the parent 2-quinolone)<sup>a</sup>.

	1 B	2 B	4 B	5 B	6 B	7 B
$\Delta E$ exp.	0.00	0.02	0.28	0.06	– 0.11	– 0.13
$\Delta E$ calc.	0.00	0.03	0.30	0.04	0.02	0.03

<sup>a</sup> All data in eV,  $\Delta E_x$  denotes a difference  $E_x - E_{1B}$ , where  $E_x$  and  $E_{1B}$  are the HOMO→LUMO transition energies of 4-X-2-quinolone and 1B, respectively.

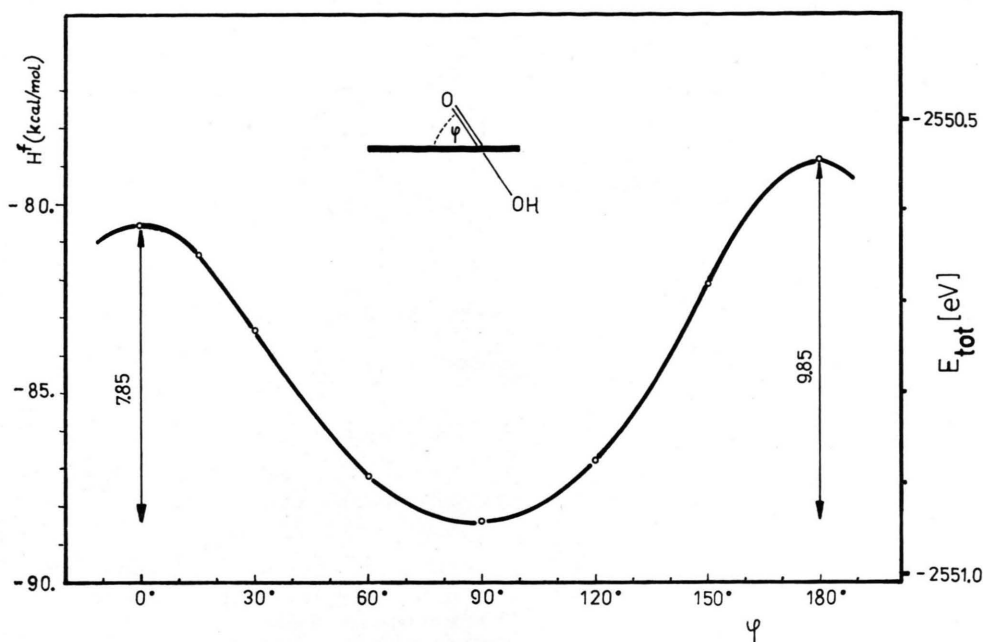


Fig. 4. Conformational MNDO energies of **6B** as a function of the rotation of the COOH group.

Figure 4 shows a dependence of the total MNDO energy of **6B** on the dihedral angle of the carboxy-group and the plane of the 2-quinolone ring. It can be seen from Fig. 4 that:

- there exists a minimum of the total energy for the angle value equal to  $90^\circ$  and, by symmetry,  $270^\circ$ .
- as suspected, there exist two different rotational barriers of the  $-\text{COOH}$  group equal to 7.85 and 9.85 kcal/mol for  $\varphi = 0^\circ$  and  $180^\circ$ , respectively.
- the minima of the considered curve are rather shallow — it means that small changes of the  $\varphi$ -angle value do not cause significant increase of the total energy.

Taking these facts into account one can suggest that although in the vapor phase the  $-\text{COOR}$  group may be perpendicular to the plane of the ring, it may be not in condensed phases. Intermolecular interactions often flatten molecules, so that in solutions  $\varphi$ -value could be less than  $90^\circ$ . In this case a stronger conjugation of the  $\pi$ -electrons of the  $-\text{COOR}$  group with the  $\pi$ -electron system of the 2-quinolone ring decreases the energy of the first  $\pi \rightarrow \pi^*$  (HOMO-LUMO) transition. The calculated CNDO/S energies of the transition carried out for various  $\varphi$ -angle values (3.89, 3.87, 3.81,

and 3.78 eV for  $\varphi = 90^\circ, 60^\circ, 30^\circ$ , and  $0^\circ$ , respectively) confirm the validity of our conclusions that the conformation of the  $-\text{COOR}$  group (in respect to the ring plane) is the main cause of the disagreement between CNDO/S and experimental data. On the other hand, one can expect that 4-COOR-2-quinolones are not completely planar in condensed phases. It has been shown that "peri" interactions caused in  $\alpha$ -naphtholic acid the plane of  $-\text{COOH}$  group to be twisted relatively to the naphthalene ring by ca.  $12^\circ$  even in the solid [28].

A similar problem of an optimal arrangement of a substituent in the position 4 arose in **5B**. Also in this case the plane of the dimethylamino-group is perpendicular to the 2-quinolone ring in its optimal MNDO geometry. However, in contrast with 4-COOR-2-quinolones, comparison of the experimental transition energies of 4-(1-piperidine)-2-quinolone with the data obtained by CNDO/S (based on the MNDO geometry for **5B**) shows a satisfactory agreement (Table 4). This confirms that in 4-(1-piperidine)-2-quinolone a mean plane of the piperidine ring is significantly twisted in respect to the 2-quinolone ring even in condensed phases.

## Conclusions

The MNDO calculations carried out with geometry optimization show that 2-hydroxyquinolines



compared to 2-quinolones are less stabilized than 2-hydroxypyridine vs. 2-pyridone. The earlier estimated correction [10, 13], applied to these MNDO results suggests that 4-X-2-quinolones ( $X = \text{H}, \text{CH}_3, \text{Cl}, \text{OCH}_3, \text{N}(\text{CH}_3)_2, \text{COOH}, \text{COOCH}_3$ ) are more stable tautomers by ca. 2.1–3.3 kcal/mol than the corresponding 4-X-2-hydroxyquinolines. It appears that the substituents in position 4 do not influence significantly the relative stabilities of the tautomers.

Comparison of molecular geometries, dipole moments, and ionization potentials obtained by MNDO with the available experimental results shows a satisfactory agreement of the data. This confirms the validity of the MNDO approximation and parametrization for this type of compounds.

The greater stability of 2-quinolone (B-type) forms was verified by UV absorption studies of diluted decane solutions of 4-X-2-quinolones at ca.

120°. Our results are consistent with the recently published results of mass spectroscopic [27] and UV PES [22] studies, which suggest the predominance of the B-form of 2-quinolone (**1B**) in the vapour phase.

Application of the simple Onsager solvation model to the systems considered reveals that in all cases the B tautomers are additionally stabilized in aqueous solutions by 1.1–2.2 kcal/mol, compared to the corresponding A tautomers. Combination of these results with the “corrected” MNDO predictions for isolated tautomers appears useful in estimating  $\Delta G^0$  of tautomerisation also in aqueous solution.

Energies of UV transitions obtained by CNDO/S-CI-1 calculations based on the optimal MNDO geometries generally agree well with experimental data.

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