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Enol Forms of 1,3-Indanedione, Their Stabilization by Strong Hydrogen Bonding, and Zwitterion-Assisted Interconversion

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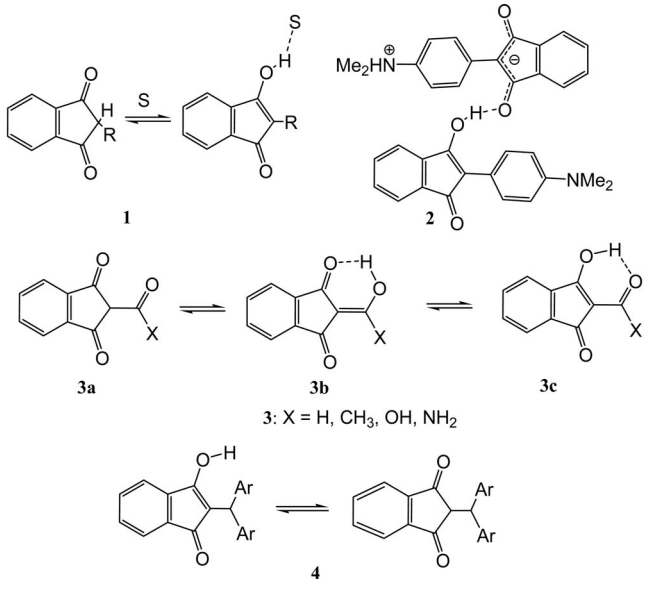
By analyzing NMR spectroscopic data, and supported by IR, UV/Vis, Raman, dielectrometry, and DFT techniques, a comprehensive study of the 1:2 adducts of picolinaldehyde and 1,3-indanediones is presented. The parent indanedione derivative **5** exists in an equilibrium between all-keto and enol forms, the latter being stabilized by an intramolecular O–H···N hydrogen bond. Only the all-keto form was observed in the 5,6-dimethoxy compound **6**, whereas solely the enol tautomer was observed with its 5,6-dichloro analogue **7**. Polar solvents and low temperatures shift the equilibrium towards the enol tautomer in **5**. The structure of adduct **8**, formed with isonicotinaldehyde, prevents the formation of intramolecular O–H···N hydrogen bonds and thus it exists in the all-keto form in low polar solvents. However, in DMSO solutions it adopts a zwitterionic form with a strong anionic O⁻···H···O hydrogen bond. Thus, the enol form in indanedione adducts was unequivocally characterized in solution and the factors that determine the keto–enol tautomerism, namely electronic effects, solvent, temperature, and intramolecular hydrogen bonds, have been methodically studied by spectroscopic and quantum mechanical methods.

Introduction

Cyclic β-diketones are an important class of organic compound. Among them, 1,3-indanedione [1*H*-indene-1,3(2*H*)-dione] attracts the interest of researchers as a valuable synthetic precursor. 1,3-Indanedione and its derivatives have been employed in the synthesis of drugs,[1] in forensic chemistry for fingerprint detection,[2] in dyes and pigments,[3] and in semi- and photosemiconductors.[4] Like all β-diketones, 1,3-indanedione can exist in equilibrium between the diketo and enol forms. However, in low-polarity solvents like cyclohexane or dichloromethane, only the diketo form (**1**, R = H) was observed experimentally. According to ^{1}H and ^{13}C NMR spectroscopic data, 1,3-indanedione exists in the diketo form even in DMSO.[5] However, substitution of the parent molecule may significantly affect the tautomeric equilibrium. For example, 2-phenyl-1,3-indanedione was the first compound for which the existence of the enol form was postulated about a century ago.[6] The driving force for enol formation in solution is generally considered to be the formation of a hydrogen bond between the enol OH groups and the basic solvent molecules S (**1**, R = Ph).[7]



Curiously, up to now, scarce experimental studies on the enol form of **1** or other 1,3-indanedione derivatives in solution have been reported. This is in sharp contrast to acyclic 1,3-diketones for which the keto–enol tautomerism is the subject of numerous publications. According to previous NMR studies reported in the literature,[8] 95% of 2-phenyl-1,3-indanedione (**1**, R = Ph) appears as the diketo form in chloroform and 75–80% is found as the enol in DMSO. However, the ^{1}H NMR spectra in the polar solvent were not analyzed in detail and the symmetrical spectral pattern

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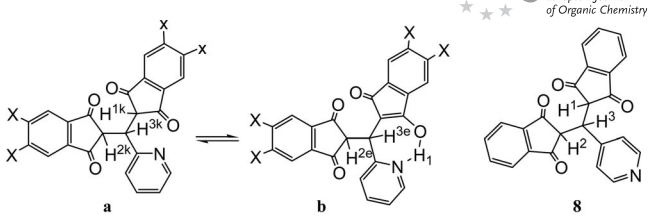
of the enol form (which may be indicative of the presence of the enolate anion) was not discussed. Moreover, the significant and characteristic signal of the hydrogen-bonded OH was not observed, probably because low-temperature spectra in other polar solvents were not recorded. Thus, enolization in solution[8] was not fully analyzed. Nevertheless, according to the X-ray data, in the black crystals of 2-[4(-dimethylamino)phenyl]-1,3-indanedione (**2**) the enol form coexists with the zwitterionic form of the molecule and these two tautomers are stabilized and bonded to each other by strong ionic O⁻···H···O hydrogen bonds (O···O distance is 2.53 Å).[9] Recently, theoretical and spectroscopic studies of 2-carbonyl derivatives of 1,3-indanedione (**3**) showed that the formyl derivative (R = H) exists in the diketo form **3a**, the exocyclic enol form **3b** predominates in the acetyl derivative (R = CH_3), and an equilibrium between **3b** and **3c** is formed in the case of 2-carbamido-1,3-indanedione (R = NH_2) by fast proton exchange.[10] Sterically crowded enols are highly stable species, as has been shown for mesityl-substituted ethenols.[11] In accordance with this, the enol forms of 2-diarylmethyl-1,3-indanediones **4** have been observed in solution[12] for compounds with bulky di-*ortho*-substituted aryl substituents, which is the only unambiguous report of the enol form of a 1,3-indanedione derivative in solution.

The above brief description of the literature data led us to assume that the enol form of sterically uncrowded 1,3-indanediones may be stabilized in solution by strong intramolecular hydrogen bonds and this prompted us to synthesize suitable model compounds for a detailed investigation of the keto–enol tautomerism in this series. Herein, we present the synthesis and careful study of indanedione compounds by extensive analytical tools such as NMR, IR, Raman, and UV spectroscopy, dielectrometry, and density functional theory calculations to gain an understanding of the behavior of this basic tautomeric equilibrium and the means to influence it.

Results and Discussion

2,2′-(Pyridin-2-ylmethylene)bis[1*H*-indene-1,3(2*H*)-dione] (**5**) and its 5,5′,6,6′-tetramethoxy- (**6**) and 5,5′,6,6′-tetrachloro- (**7**) derivatives were readily obtained by Michael addition of the corresponding 1,3-indanediones to 2-pyridinecarbaldehyde.[13] For the sake of comparison, 2,2′-(pyridin-4-ylmethylene)bis[1*H*-indene-1,3(2*H*)-dione] (**8**) was chosen as a model compound in which the electronic and spatial influence of the heteroaryl substituent is similar but intramolecular hydrogen bonding with the pyridine nitrogen atom is prevented. Compounds **5** and **8** have been described previously,[13] but their NMR spectra were recorded only in DMSO at room temperature and many interesting thermodynamic features remained undisclosed. Compounds **6** and **7** have been synthesized for the first time in this study (Scheme 1).



5 (X = H), **6** (X = MeO), **7** (X = Cl)

Scheme 1. Compounds **5**–**7** and **8** studied in this work (subscripts k and e corresponds to all-keto and keto–enol forms, respectively).

^{1}H NMR Spectra: Temperature and Solvent Dependence

The ^{1}H NMR spectrum of **5** in CD_2Cl_2 at 300 K (Figure 1a) exhibits two sets of broad signals that narrow on lowering the temperature to 260 K (Figure 1, b), which indicates the presence of both tautomeric forms **5a** and **5b**. The characteristic peaks that allowed the structure of the two forms in the equilibrium to be established at 260 K are the two doublets at 3.75 (1 H) and 5.12 ppm (1 H) (J = 3.2 Hz), which correspond to the indanedione proton 2e-H and the bridge proton 3e-H, respectively, in the enol form **5b**, and the doublet at 3.95 ppm (2 H) and triplet at 4.55 ppm (1 H) (J = 6.4 Hz), which correspond to two indanedione protons 1k-H and 2k-H, and the methine proton 3k-H, respectively, in the all-keto form **5a**. In the NOESY exchange spectrum of **5** at 300 K (Figure 2) there are cross-peaks between the signals at 5.12 and 4.55 ppm, which correspond to the bridge protons 3-H in **5a** and **5b**, and between the signals at 3.75 and 3.95 ppm, which correspond to the indandione 2-H protons in **5a** and **5b**. The **5a**/**5b** ratio varies from 1:1 at 300 K to 0.5:1 at 260 K, and 0:1 at 220 K (Figure 1, a–c). In addition, a broad signal of the hydrogen-bonded enol OH group (δ = 13.13 ppm) appears at 260 K and narrows at lower temperatures (top inset, Figure 1, c). These changes are reversible and subsequent heating of the sample restores the original spectrum.

The aromatic protons in both tautomeric forms (Figure 3) were fully assigned through a 2D COSY analysis of **5** at 260 K (Figure S1) and by comparison of their chemical shifts with those of model compound **8** and acetylbindone **9**.[14] In all cases, the aromatic protons of the diketo moiety resonate in the range 7.7–8.2 ppm. As expected, the chemical shifts of the aromatic protons of the enol fragment are displaced upfield to about 7.3 ppm, similarly to the acetylated enol fragment of **9** (except for one at δ = 9.16 ppm, shifted downfield due to the spatial proximity of the carbonyl oxygen). As a result of the molecular asymmetry in **5b**, all the protons of the 1,3-indanedione fragment are nonequivalent at every temperature studied, whereas the protons belonging to the enol moiety show a symmetrical AA′BB′ spectrum at 260 K and above. For an explanation of this observation, see below. Likewise, the chemical shifts of the pyridine protons are strongly influenced by the hydrogen bond formed.

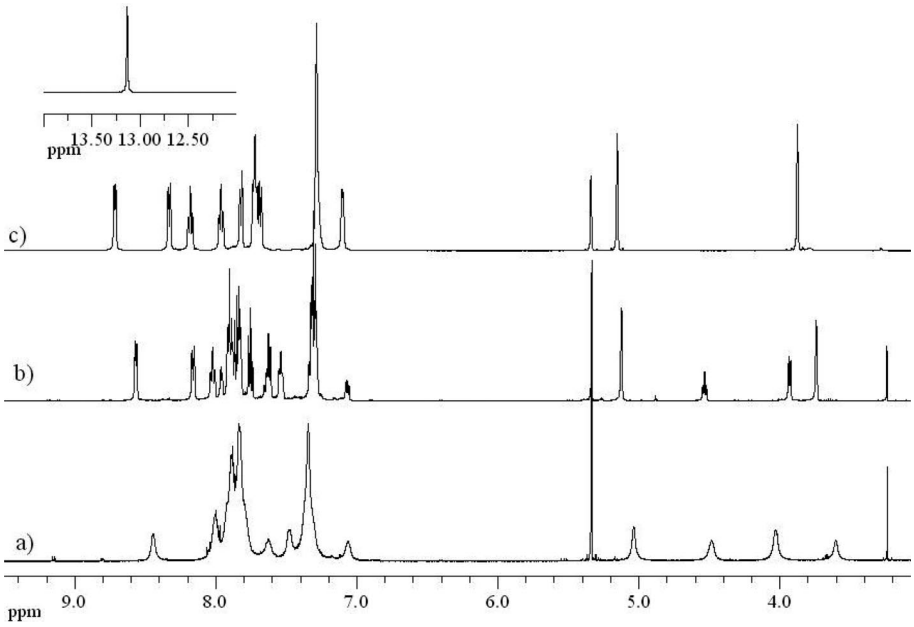


Figure 1. ^{1}H NMR spectra of **5** at (a) 300, (b) 260, and (c) 180 K.

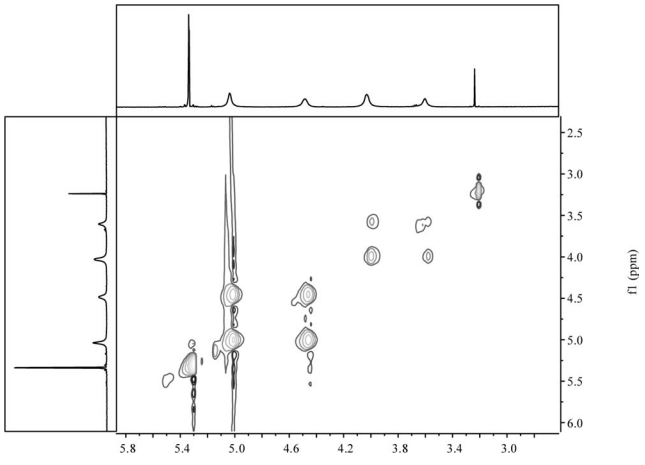


Figure 2. NOESY spectrum of **5** at 300 K.

The ^{13}C NMR spectra of **5** in CD_2Cl_2 at 180 K and of solid **5** at room temperature are very similar (Figure S2), which suggests that the same monoenolic structure **5b** exists both in solution and in the solid state.

The ^{1}H NMR spectra of **6** and **7** (Figure 4) reveal the existence of only one tautomeric form for each compound. In the case of **6**, similar to **5a**, the doublet at δ = 4.08 ppm and the triplet at δ = 4.27 ppm (J = 6.9 Hz) indicate the prevalence of the all-keto form **6a**. The spectrum of **6** does not change upon lowering the temperature to 180 K. On the other hand, all the signals in the ^{1}H NMR spectrum of **7** are broadened at 300 K, but become resolved at 260 K. The aliphatic part of the spectrum of **7**, which is similar to that of **5b**, exhibits two doublets at δ = 3.87 and 5.18 ppm (J = 1.8 Hz), which suggests that, at this temperature, **7** exists entirely as the enol form **7b**.

Model compound **8**, which has no O–H···N hydrogen bond exists in CD_2Cl_2 as the all-keto form and, as expected, its NMR spectra does not undergo any temperature-induced changes.

Because keto–enol tautomeric transformations are extremely sensitive to media properties, we studied the effect of solvent on the spectra of **5** and **8**. The solvents chosen were [D_2]dichloromethane (see above), [D_5]toluene, [D_6]-DMSO, and [D_5]pyridine. These solvents cover a wide polarity range thereby allowing a thorough analysis of hydrogen-bonding interactions and their effect on the structures. For measurements at temperatures below the melting points of pyridine and DMSO (235 and 290 K, respectively), [D_2]-dichloromethane was used as a cosolvent, which allowed the samples to be cooled to 200 K. In both cases, the ratio of dichloromethane to polar solvent was 4:1 by volume.

The shift in the tautomeric equilibrium **5a** ⇆ **5b** to the enol in more polar and basic solvents is illustrated by the data in Table 1.

The ^{1}H NMR spectrum of **5** in [D_8]toluene at 295 K presented a tautomeric distribution similar to that observed in CD_2Cl_2. However, in toluene the spectrum was better resolved, which indicates a slower tautomeric exchange.

The equilibrium **5a** ⇆ **5b** in [D_5]pyridine is strongly shifted towards **5b** even at 300 K. Moreover, the signal of the hydrogen-bonded OH becomes visible only at much lower temperatures than in CD_2Cl_2 (below 200 K). At 180 K, a new weak signal appeared at δ = 19.2 ppm (Figure 5), which indicates the existence of an additional minor tautomeric form (see below).

The ^{1}H NMR spectrum of **5** in [D_6]DMSO at 300 K exhibits relatively narrow signals corresponding to the pyridine ring protons and the 3-H bridge proton and very broad unresolved signals arising from the indanedione aro-

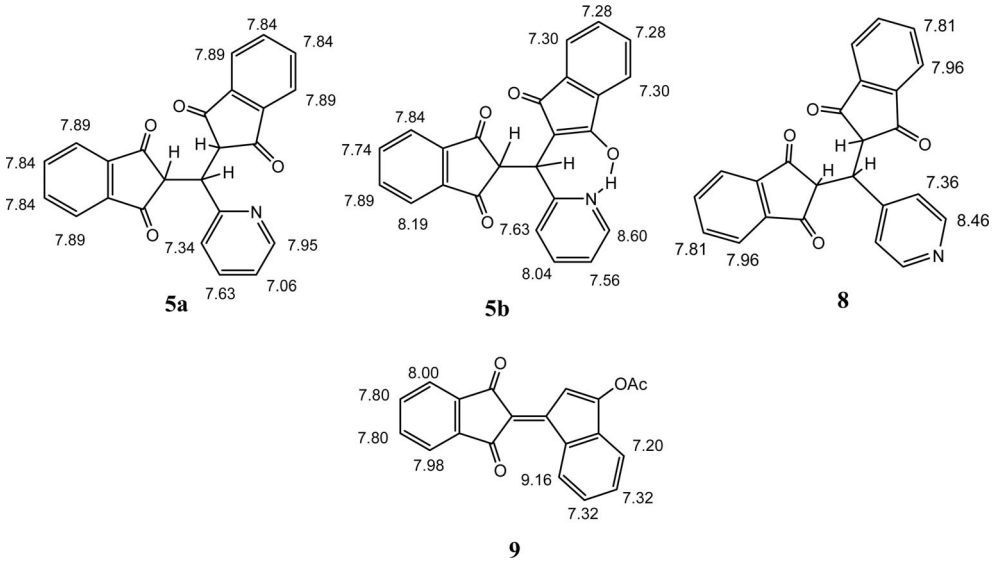


Figure 3. ^{1}H NMR chemical shifts of **5a** and **5b** and the model compounds **8** and **9** in CD_2Cl_2.

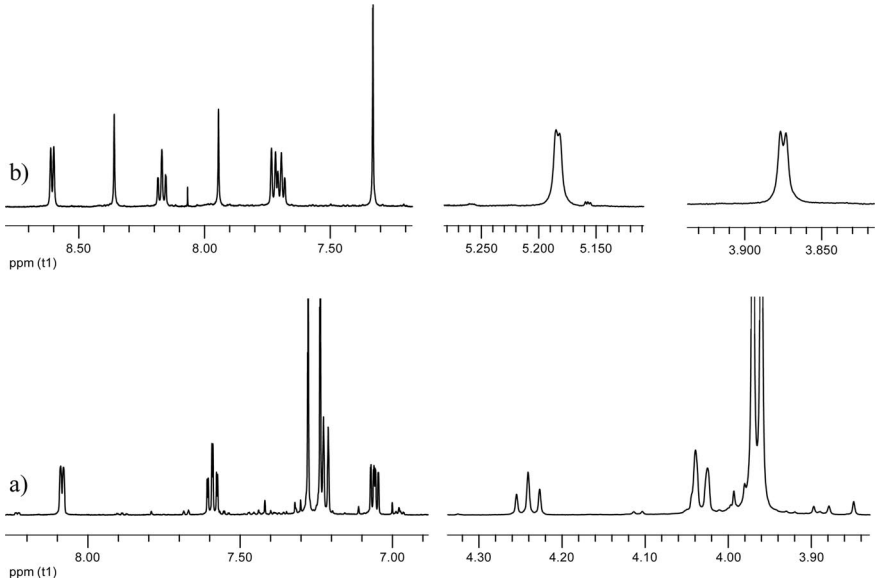
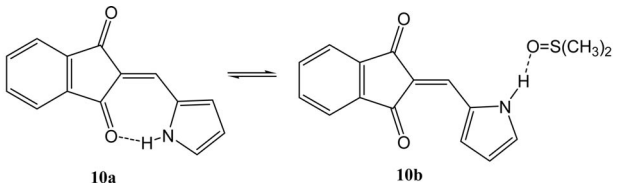


Figure 4. Expanded ^{1}H NMR spectra of (a) **6** at 300 K and (b) **7** at 260 K.

Table 1. Tautomeric equilibrium of compound **5** at 260 K in different solvents.

Solvent	Enol [%]	[Enol]/[Keto]
[D_8]Toluene	60	1.5
CD_2Cl_2	71	2.4
[D_6]Acetone	83	4.9
[D_6]DMSO/CD_2Cl_2	87	6.7
[D_5]Pyridine	93	13.3

matic protons. Upon cooling the solution of **5** in [D_6]-DMSO/CD_2Cl_2 the signals became narrow revealing the existence of the enol form **5b** (Figure 6). At 220 K, the spectrum resembles that of **5** in CD_2Cl_2, except that the enolic OH and the pyridine 6-H signals are shifted upfield by 0.53 ppm and downfield by 0.7 ppm, respectively. We recently observed a similar upfield shift of the hydrogen-bonded NH of 2-(pyrrol-2-ylmethylene)-1,3-indanedione (**10**) in DMSO, which we explained by an equilibrium between the two conformers **10a** and **10b** with and without an intramolecular hydrogen bond, respectively.[15]



The ^{1}H NMR spectra of model compound **8** in [D_6]-DMSO and [D_5]pyridine were significantly different to the ^{1}H NMR spectrum in CD_2Cl_2 (Figure 7). In the solid state

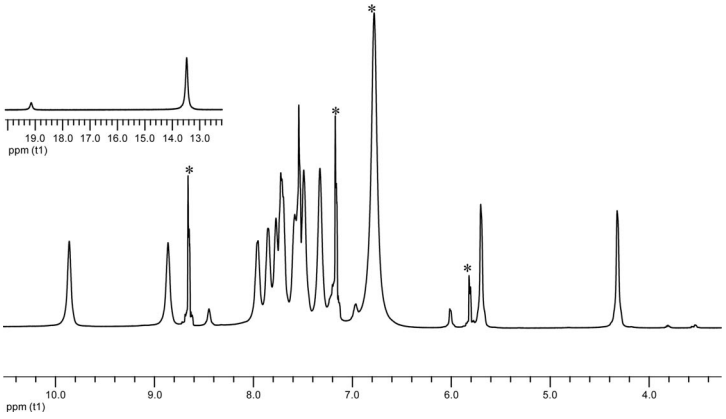


Figure 5. ^{1}H NMR spectrum of **5** in [D_5]pyridine/CD_2Cl_2 at 180 K. The signals from water and residual nondeuteriated solvent are marked with asterisks.

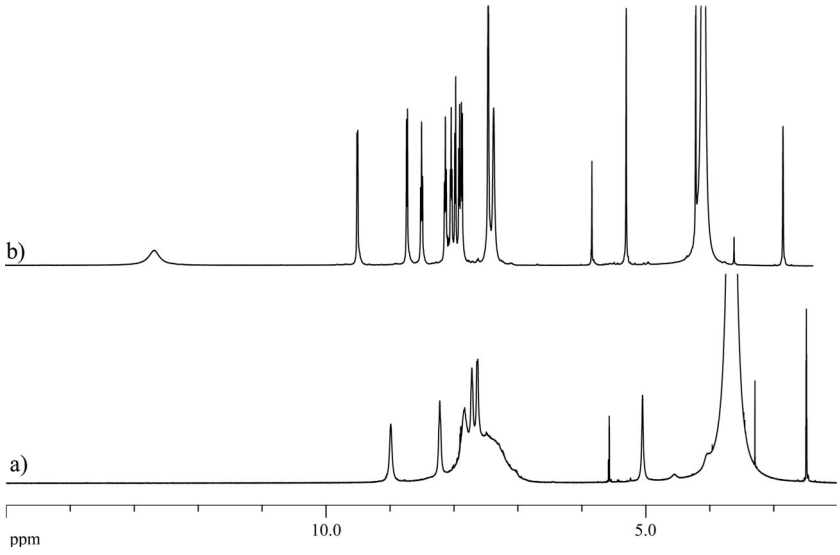


Figure 6. ^{1}H NMR spectra of **5** in [D_6]DMSO/CD_2Cl_2 at (a) 300 and (b) 220 K.

and in CD_2Cl_2 solution **8** is colorless, whereas its solutions in the two polar solvents are yellow. The doublet arising from the OC–CH–CO indanedione protons disappears, whereas the triplet from the bridge proton becomes a singlet and is shifted downfield by 1.5–2 ppm. At the same time, the aromatic indanedione protons are shifted to 7.2 ppm from 7.9 ppm and their spectral pattern becomes simpler (two relatively narrow A_2B_2-type multiplets instead of a complex ABCD spin system). Lowering the temperature of **8** in [D_5]pyridine/CD_2Cl_2 and [D_6]DMSO/CD_2Cl_2 resulted in a spectral pattern similar to those obtained at room temperature. Notably, a new signal appeared at about 18 ppm in both solvent mixtures on cooling to 220 K. Such a low-field shift is characteristic of protons involved in strong ionic hydrogen bonds, for example, as seen in the hydrogen maleate anion **11** (δ =21.5 ppm).[16] Also, in DMSO solutions, a broadened signal at δ = 15.5 ppm appeared.

Thus, in this case one indanedione fragment is ionized, which leads to the enolization of the neighboring indanedione fragment and subsequent stabilization of the enol formed by an ionic hydrogen bond. Note that the 4-chlorophenyl analogue **12** behaved differently; its DMSO solution contained only the all-keto form **12a**. Only upon addition of a strong base such as DBU or tetrabutylammonium hydroxide did enolization to **12b** occur, induced by deprotonation and manifested by the appearance of a low-field hydrogen-bonded OH at δ = 18.2 ppm (Figure S3). This finding reveals the key role of the pyridine nitrogen atom, which acts as a base to afford zwitterion **8a**. The structure of **8a** is strongly supported by the new signal at δ = 15.5 ppm (in DMSO), which corresponds to a NH^+ proton, and by the ^{15}N NMR spectrum of **8** in DMSO, which exhibits a signal at δ = –170 ppm, which corresponds to an *N*-protonated pyridine.[17] Based on these findings, we

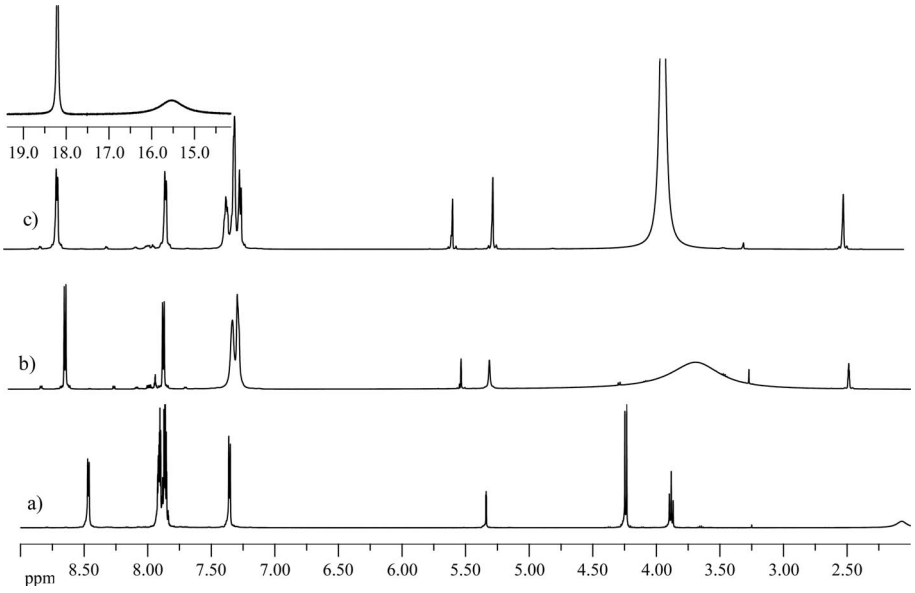
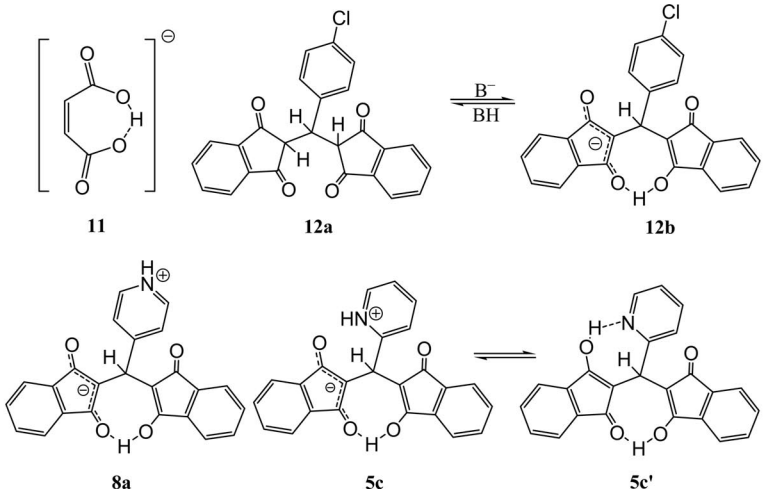


Figure 7. ^{1}H NMR spectra of **8** in (a) CD_2Cl_2 at 300 K, (b) [D_6]DMSO/CD_2Cl_2 at 300 K, and (c) [D_6]DMSO/CD_2Cl_2 at 220 K.



propose that zwitterion **8a** is stabilized in the form of a solvate complex with DMSO, as supported also by dielectrometry and theoretical calculations (see below).

In the light of these considerations, the minor form observed for **5** in pyridine solution at low temperatures and exhibiting a weak signal at δ = 19.2 ppm may be assigned to the zwitterionic structure **5c**, similar to the one observed for **8a**. The **5b**/**5c** ratio is 10:1.

As already mentioned, the ^{1}H NMR spectrum of **5** in CD_2Cl_2 is temperature-dependent. Lowering the temperature shifts the equilibrium towards the more stable hydrogen-bonded enol form **5b**. Moreover, it also strongly affects the shape of the multiplets of the aromatic protons belonging to the enol form. The signals broaden and their spin system changes from AA′BB′ to ABCD (Figure 8). In the ^{13}C NMR spectra of **5**, all the signals corresponding to the enol moiety at 118.5, 130.6, 138.3, and 188.2 ppm broaden and split into two signals.

Similar changes with temperature are observed for the much simpler spectral pattern of the enol fragment in compound **7**. In this case the singlet at δ = 7.33 ppm decoalesces into two separated singlets, whereas the rest of the signals remain unchanged (Figure 9).

The reason for these line-shape changes is hydrogen exchange between the hydroxy and carbonyl oxygen atoms of the enol moiety. Unlike the acyclic 1,3-diketones in which an intramolecular C–O–H···O=C hydrogen bond facilitates hydrogen exchange and leads to a symmetrical system, a similar intramolecular exchange in cyclic W-shaped 1,3-diketones is impossible and an auxiliary external base must be present to abstract the proton. Appealingly, the 2-pyridyl substituent may serve as a "proton shuttle" to facilitate proton transfer from one oxygen atom to the other. The most probable mechanism for this hydrogen exchange is by intramolecular proton transfer from the enol OH to the pyridine nitrogen followed by rotation around the C–C bond and

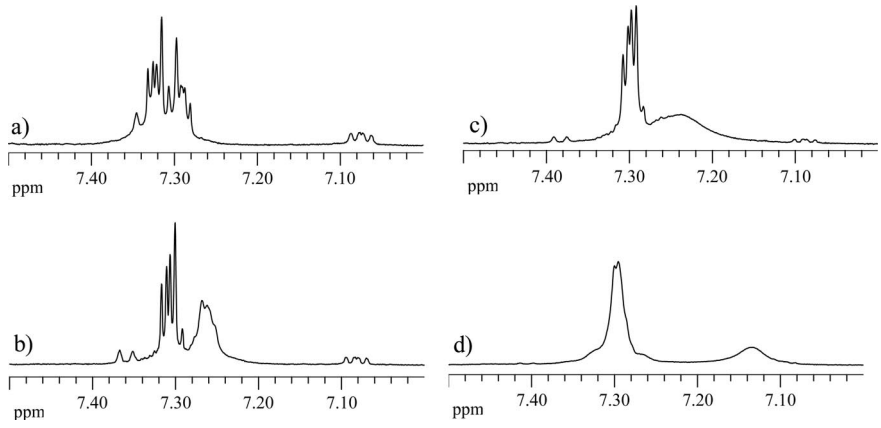


Figure 8. Variable-temperature ^{1}H NMR spectra of **5** at (a) 260, (b) 240, (c) 220, and (d) 200 K.

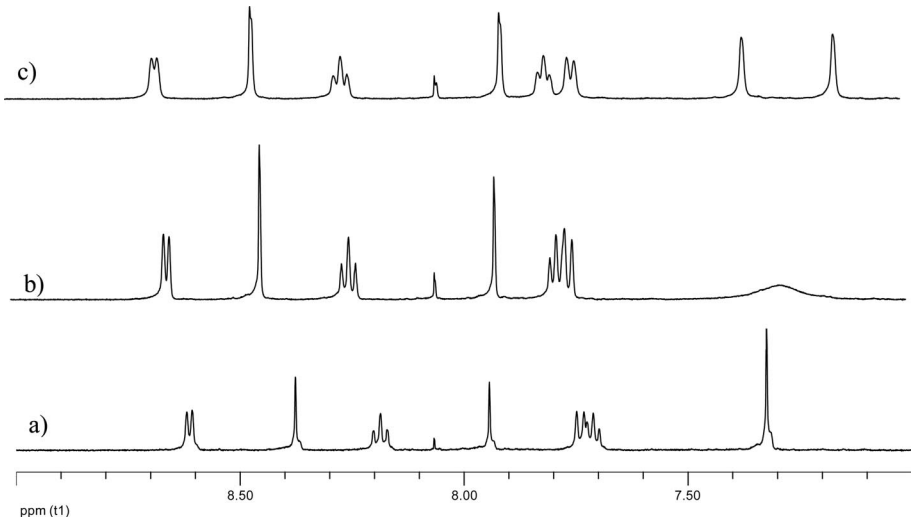
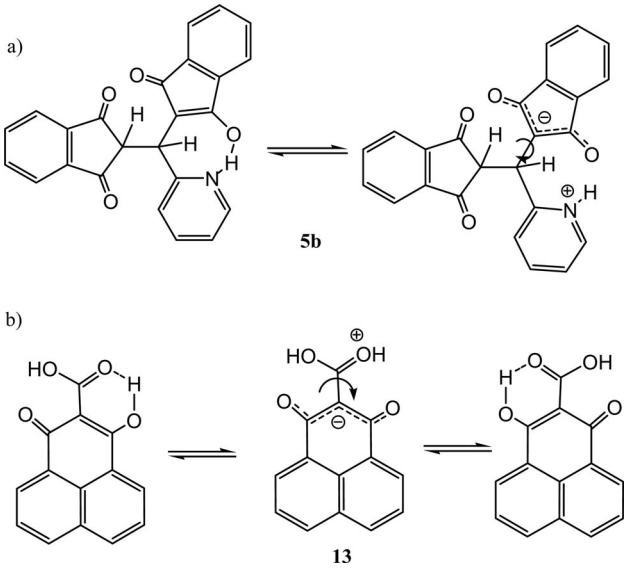


Figure 9. ^{1}H NMR spectra of **7** at (a) 260, (b) 220, and (c) 180 K.

subsequent protonation of the adjacent carbonyl oxygen atom by the pyridinium moiety (Scheme 2).

Note that hydrogen exchange between the oxygen atoms must occur to explain the NMR results. The spectral changes with temperature were used to quantitatively estimate the proton transfer energy. The spectral pattern of the proton signals in **5** was too convoluted and required a complex full line-shape analysis. Alternatively, the free energy of this dynamic process was estimated from the temperature of decoalescence of the ^{13}C NMR signals of the enol fragment at δ = 118.5 and 130.6 ppm, which was found to be 9.6 kcal/mol. Strictly speaking, this value includes both the proton-transfer energy and the energy of the indanedione rotation itself, but an individual estimation of these factors requires further study. Notably, a very similar estimate (9.4 kcal/mol) was obtained by treatment of the decoalescing signals in the spectra of **7**.

In the case of **8** in [D_5]pyridine/CD_2Cl_2, the signals of the aromatic indanedione protons underwent broadening and decoalescence at low temperatures. The same transformations were observed for the signals of the indanedione carbon atoms in the ^{13}C NMR spectrum (Figure S4). The free



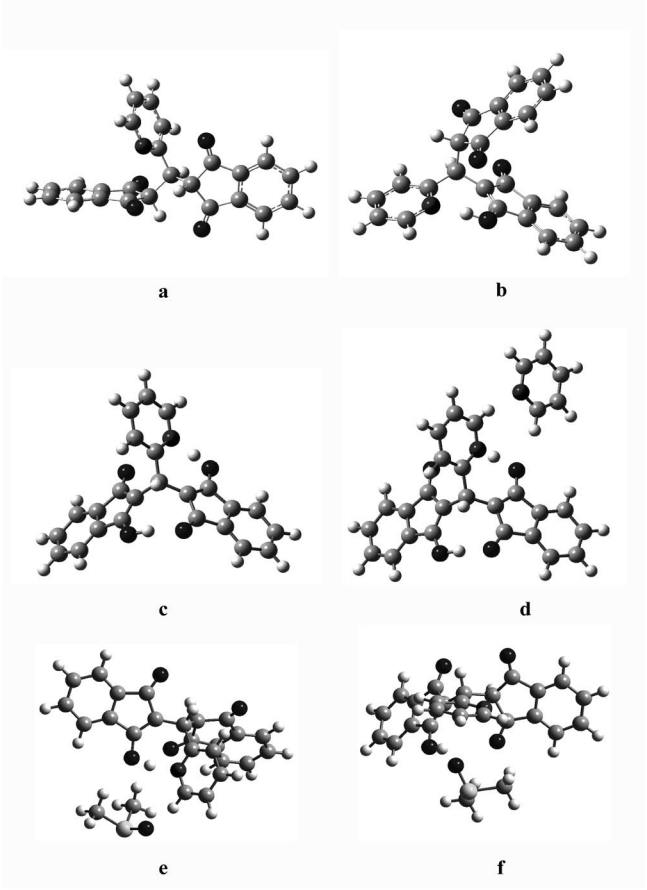
Scheme 2. Proposed proton-transfer mechanism for **5b** and a similarly observed transfer in model 2-carboxy-3-hydroxy-1-phenalenone (**13**).[18]

energy of the dynamic process at the coalescence temperature was determined to be 10.4 kcal/mol.

An important difference to be emphasized between the dynamic processes observed in **5** and **8a** is that in the first case the exchange occurs in a single enol fragment of the molecule such that the second indanedione moiety remains unchanged, whereas in the second case the two indanedione fragments are identical and can be differentiated only at low temperatures. This latter observation is indicative of a fast proton exchange between all four oxygen atoms in **8a** accompanied by the rupture of a hydrogen bond and rotation of both indanedione moieties.

DFT Calculations

To establish the structures and estimate the relative stabilities of the possible tautomers of the studied compounds, quantum chemical calculations were performed at the DFT level of theory (B3LYP) using the 6-311G** basis set. The calculations revealed the presence of three main structures of interest for compound **5** (Scheme 3) as minima on the potential energy surface (PES). The most stable is the highly polar enol tautomer **5b** with the OH group forming a short hydrogen bond of 1.716 Å with the pyridine ring. The next lowest-energy structure is the dienol tautomer **5c′** (see above) with one OH group forming a very short hydrogen bond with the pyridine ring of 1.584 Å and the opposite OH group closing to form an eight-membered ring with the neighboring keto oxygen atom with a bond length of 1.688 Å. The dienol **5c′** is notably less polar and is only 0.48 kcal/mol higher than monoenol **5b**. The all-keto form **5a** has the lowest dipole moment and is 1.05 kcal/mol higher in energy than **5b**. The latter is not only the most stable but also the most polar species, therefore, taking into account the effect of nonspecific solvation can only redouble its energetic preference. Dienol **5c′**, despite the fact that it has a lower energy than **5a**, is not observed in the NMR spectra in low polar solvents. The minor form observed for **5** in pyridine solution and which is supposed to be the zwitterionic tautomer **5c** is, in fact, very similar to **5c′**, with the main geometric difference between the two being the position of the hydrogen atom between the N and O atoms and the distance between the oxygen atoms in the O···H···O fragment. Moreover, the calculations prove that **5c** is not a minimum on the potential energy surface and after proton transfer from nitrogen to oxygen the structure is optimized to dienol **5c′**. Partial optimization of the zwitterion with a fixed N–H bond (1.02 Å) gives a structure that is 9.6 kcal/mol higher in energy than the enol tautomer **5b**. The formation of the complex with one molecule of pyridine leads to the stabilization of zwitterion **5c**. The N–H and O–H distances are 1.10 and 1.46 Å compared with 1.59 and 1.03 Å, respectively, in the complex (**5c** + pyridine) and the dienol **5c′** and the length of hydrogen bond O···H···O (2.58 Å) is shorter than that in **5c′** (2.65 Å). The other bond lengths also show indications of charge delocalization in the indanedione fragments.



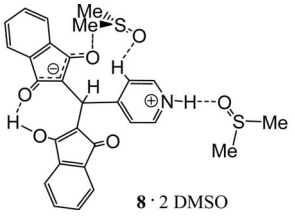
Scheme 3. Optimized geometries of the main tautomers of **5** and their complexes with bases. a) **5a**, μ = 1.44 D; b) **5b**, μ = 6.13 D; c) **5c′**, μ = 2.58 D; d) **5c** + pyridine, μ = 6.35 D; e) **5b** + DMSO (O–H···N bond), μ = 5.01 D; f) **5b** + DMSO (O–H···O=S bond), μ = 8.08 D. A color version is presented in the Supporting Information.

The calculated similar complex enol (**5b** + pyridine) has a shorter hydrogen bond than the free molecule **5b** (N···H distances are 1.650 and 1.716 Å, respectively) and its total energy is only 0.53 kcal/mol lower than that of (**5c** + pyridine). Thus, these calculations explain fairly well the behavior of **5** in pyridine. The color version of the scheme is presented in the Supporting Information.

In attempts to account for the NMR spectral peculiarities of **5** in DMSO solution (see above) we calculated two complexes of **5b** with one molecule of DMSO and found two minima on the PES (Scheme 3). In the more stable complex (Scheme 3, e), stabilized by short contacts C–H···O, the intramolecular O–H···N hydrogen bond is retained and is even shorter (N···H distance is 1.61 Å) than in the free enol. In the isomeric complex (Scheme 3, f), which is 2.07 kcal/mol higher in energy and has an intermolecular hydrogen bond with DMSO (H···O distance is 1.68 Å), the intramolecular hydrogen bond is ruptured. However, taking into account its higher polarity, one can suppose that in polar media this difference will be attenuated. The equilibrium between these two complexes in solution accounts for the observed NMR behavior of **5** in DMSO.

For the 4-pyridyl isomer **8**, which cannot be stabilized by an intramolecular O–H···N hydrogen bond, the most stable tautomer in the gas phase is the all-keto form **8c**, in agreement with the NMR spectroscopic data determined in the nonbasic solvent CD_2Cl_2. Another tautomer found on the PES is the enol tautomer **8b** stabilized by the intramolecular hydrogen bond O–H···O=C similar to that in **5c′**. In spite of an even shorter H···O distance (1.662 Å) than that in **5c′**, the enol tautomer **8b** lies 0.57 kcal/mol higher in energy than the all-keto form **8c**. The latter, in turn, is 3.15 kcal/mol less stable than the corresponding 2-pyridyl isomer **5a**.

The ^1H and ^{15}N NMR spectra of compound **8** in basic solvents undoubtedly prove its zwitterionic structure **8a** in these media (see above). However, the formation of the zwitterion by intramolecular proton transfer in the all-keto form **8c** requires 19.0 kcal/mol and the same process in the keto–enol tautomer **8b** is only slightly less endothermic (15.1 kcal/mol). Therefore it is reasonable to assume that zwitterion **8a** is stabilized by hydrogen bonding with an external base. One can suppose that the zwitterion is stabilized by a hydrogen bond between the pyridine NH^+ and the DMSO molecule (formation of the complex **8a**·DMSO). The keto–enol tautomer **8b** forms a weak complex with DMSO, the oxygen atom of the latter being slightly coordinated to the 2-H atom of the pyridine ring and the methyl groups to the oxygen atoms of the O–H···O fragment. Its energy of formation is only 5.3 kcal/mol. In the corresponding zwitterion with a similar coordination of the base, the energy of complex formation increases to 15.7 kcal/mol, but coordination of the DMSO molecule to the NH^+ proton results in its further increase to 17.7 kcal/mol. As shown by dielectrometry measurements (see below), zwitterion **8a** forms a 1:2 complex with DMSO. Its structure was suggested by calculation of several possible configurations with one DMSO molecule coordinated to the N^+–H group and another either to the intramolecularly bonded O–H···O hydrogen or to the central C_{sp^3}–H hydrogen atom. No coordination to the base occurs through the O–H···O proton: the DMSO molecule during optimization moves apart from the zwitterion, and the distance (S)=O···H exceeds 3.3 Å. The complex with the DMSO molecule coordinated to the central C–H hydrogen is finally optimized to the structure given below (**8a**·2DMSO) with the base coordinated to the 3-H hydrogen atom of the protonated pyridine ring. The N–H···O=S hydrogen bond is very strong (1.683 Å), but the C–3-H···O=S hydrogen bond should also be considered as strong (2.062 Å). The complex is additionally stabilized by short contacts (2.30–2.32 Å) between the hydrogen atoms of the two methyl groups of DMSO and the free oxygen atom of the anionic indanedione moiety. The energy of complex formation is 33.0 kcal/mol.



8 · 2 DMSO

The calculated order of energy nicely reproduces the experimentally observed predominance of either the all-keto or the enol tautomer for compounds **6** and **7**, respectively. For the tetramethoxy-substituted compound **6** the experimentally observed all-keto form is 1.0 kcal/mol more stable than its enol tautomer, whereas for the tetrachloro-substituted compound **7** it is 2.3 kcal/mol less stable than the experimentally observed enol tautomer (both energy values are not ZPE-corrected). It is interesting to compare these results with the effect of the α substituent on the keto–enol equilibrium examined for the system $ArC(O)CHR_2 \leftrightarrows ArC(OH)=CR_2$ by Nadler and Rappoport,[19] who found a linear correlation between the equilibrium constant K and the electrophilic constants σ^+ of the substituents in Ar with a ρ^+ value of 0.65. Taking into account the fact that one of the substituents is *para* and another is *meta* with respect to the enolized carbonyl group in **6** or **7** and by using the values of $\sigma_p^+(OMe) = -0.648$, $\sigma_m^+(OMe) = 0.047$, $\sigma_p^+(Cl) = 0.035$, and $\sigma_m^+(Cl) = 0.399$ and assuming $\rho^+ = 0.65$,[19] we obtained the value of $K = 0.4$ for X = OMe (ca. 28% of enol) and $K = 1.7$ for X = Cl (ca. 63% of enol). These values are close to those reported by Nadler and Rappoport[19] but seem to contradict the experimental observation of the complete predominance of only one tautomer in the keto–enol equilibrium. This can be rationalized by taking into account the fact that the substituents in molecules **6** and **7** affect not only the enolized carbonyl group but also the second carbonyl group, which is in direct polar conjugation with the enol hydroxy HO–C=C–C=O. The latter effect should be even more pronounced than the former, substantially increasing the K value for X = Cl and decreasing it for X = OMe.

IR and Raman Spectroscopic Study

According to the NMR spectroscopic data, five different carbonyl groups can be observed in compound **5** that can be assigned to the dicarbonyl fragments in the all-keto form **5a** and the monoenol **5b**. The IR spectrum of compound **5** in CH_2Cl_2 solution at room temperature shows three stretching vibration bands arising from the C=O groups (Figure 10, b). The major peaks at 1713 and 1746 cm^{-1} correspond to asymmetric $\nu_{as}C=O$ and symmetric $\nu_sC=O$ vibrations, as is typical of cyclic diketones.[20] The reversal of the ratio of intensities of these $\nu_sC=O$ and $\nu_{as}C=O$ bands in the Raman spectrum (Figure 10, a) supports the assignment.

The νC=O band of intermediate frequency at 1731 cm^{-1} in both the IR and Raman spectra has a low intensity at room temperature but its IR intensity increases on cooling (Figure 10, c), as expected for the νC=O band of the enol form of compound **5**. Also, in the more polar acetonitrile solvent, the νC=O enol signal displays a higher intensity signal (and hence content), as anticipated. When the solvent

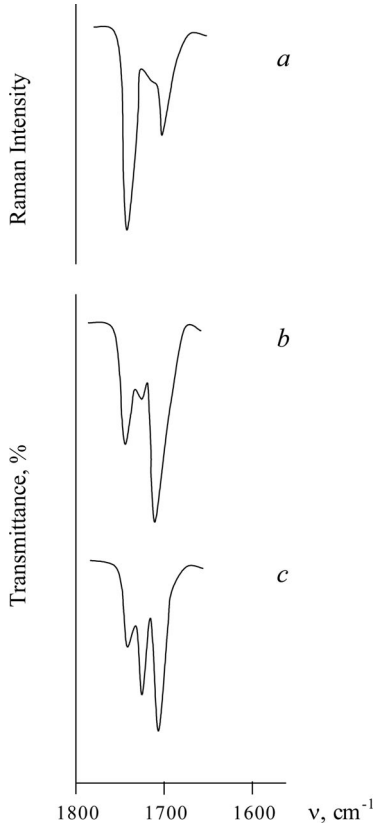


Figure 10. Overlapped Raman and IR spectra of **5** in CH_2Cl_2. (a) Raman spectrum at 300 K and IR spectra at (b) 300 and (c) 230 K.

is changed to the less polar benzene, the fraction of the enol form diminishes and only the two bands (ν_sC=O 1752 and ν_{as}C=O 1721 cm^{-1}) corresponding to tautomer **5a** may be observed in the IR spectrum.

No absorption is registered in the characteristic region of OH vibrations (3000–4000 cm^{-1}) in the IR spectrum of compound **5** in CH_2Cl_2 at room temperature. This might indicate the formation of a strong O–H···N hydrogen bond resulting in a large low-frequency shift of the νOH band, its broadening, and a concomitant sharp decrease in the peak intensity. At low temperatures, the νOH signal appears as a wide band with an averaged maximum at 3350 cm^{-1}.

The IR spectrum of crystalline compound **5** in vaseline oil or KBr exhibits an intense single νC=O band at a frequency of 1715 cm^{-1} (lower than in CH_2Cl_2 solution) and a wide νOH band at 2500–2700 cm^{-1} belonging to hydroxy groups involved in the formation of OH···N hydrogen bonds, indicative of the enol form. The νC=O band also remains single in the Raman spectrum of this compound, allowing its assignment to the νC=O vibrations of enol **5b**.

The IR spectrum of the 4-pyridyl isomer **8** in the crystal is characterized, similarly to the solution of compound **5** in CH_2Cl_2, by the bands of asymmetric and symmetric vibrations of the carbonyl groups. An intense ν_{as}C=O band at 1708 cm^{-1} has a flexion on the low-frequency wing and there is a weak ν_sC=O band, which appears as a doublet, with maxima at 1744 and 1752 cm^{-1}. This may be a result of conformational inhomogeneity or Fermi resonance. The Raman spectrum of compound **8** in the solid state displays two νC=O bands as singlets and, similarly to compound **5**, the ratio of their intensities is reversed when compared with the IR spectrum.

In the IR spectrum of compound **8** in CH_2Cl_2, the absorption bands ν_{as}C=O at 1711 cm^{-1} and ν_sC=O at 1744 cm^{-1} as well as the absence of νOH absorption bands are indicative of the existence of the molecule in the all-keto form. The spectrum in [D_6]DMSO solution exhibits a νNH^+ absorption band at 2400–2700 cm^{-1} as a result of intramolecular proton transfer to the pyridine nitrogen atom (see above). The zwitterion formed is stabilized by the formation of the solvate complex with DMSO, as proved by dielectrometric titration (see below). The formation of the zwitterion is followed by a substantial decrease in the relative intensity of the two νC=O bands and an increase in the intensity of the νC=C bands.

Dielectrometry

The calculated dipole moments of the all-keto form **5a** and the enol form **5b** are 1.44 and 6.13 D, respectively. The dipole moment (μ) of compound **5** measured in benzene at 50 °C is 3.33 D, which suggests the presence of both tautomers in solution. The fraction of the more stable tautomer **5b** increases as the temperature decreases, as shown by the higher μ values of 3.57 D at 25 °C and 5.14 D at 10 °C. At 10 °C the dipole moment is dependent upon the concentration of the solute, decreasing from 5.14 to 3.69 D when the concentration is increased from 3 to 7 mM. This may be due to the formation of intermolecular associates involving the hydroxy groups of enol **5b**.

In dioxane, the measured dipole moment is substantially larger, 5.73 D, apparently due to the "dioxane effect".[21–23] Note that this last value is much closer to the calculated dipole moment of 6.13 D. Dielectrometric titration of **5** with [D_6]DMSO did not show any variation in the dipole moment, which suggests no complex formation with the external base.

The dipole moment of compound **8** measured in dioxane (because of its poor solubility in benzene) is not temperature-dependent and is equal to 3.99 and 3.95 D at 50 and 25 °C, respectively. The calculated dipole moment of **8** is 3.68 D, which is consistent with the experimental values. As distinct from compound **5**, titration of a dioxane solution of **8** with [D_6]DMSO at 25 °C showed a bend in the titration curve (ε vs. **8**/DMSO) corresponding to a 1:2 composition of complex **8**:2[D_6]DMSO. Note, no bend is observed in the titration curve at **8**/DMSO = 1. The measured dipole moment of the 1:2 solvate complex formed is 7.5 D, which is twice as large as that of compound **8** alone in dioxane.

UV Spectra

The UV spectrum of compound **5** in CH_3CN solution exhibits two intense bands at 225 and 248 nm correspond-

ing to π→π* transitions. These bands are not shifted relative to the UV spectra of 1,3-indanedione and its substituted derivatives[24–26] because of the absence of conjugation between the 2-pyridyl residue and the carbonyl-containing moieties of the molecule. The absorption bands corresponding to the π→π* transitions in the 2-pyridyl moiety are much less intense[27] and appear in the spectrum of compound **5** as a shoulder (262 nm) on the red wing of the absorption band with λ_{max} = 248 nm. The longest wavelength band (λ_{max} = 395 nm) in the UV spectra of solutions of **5** in acetonitrile and dichloromethane may be associated with n→π* transitions in the all-keto form **5a** as well as with the presence of the enol tautomer **5b**. Thus, for example, the intensity of absorption in the UV spectra of solutions of 2-aryl-1,3-indanediones in the range of 410–460 nm is used for quantitative determination of the enol content in these compounds.[24] In our case, the largest increase in the intensity of the band at 395 nm occurs for the solution of compound **5** in DMSO.

The UV spectrum of compound **8** in acetonitrile, similarly to that of its isomer **5**, exhibits π→π* bands with maxima at 228 and 248 nm. The relative intensity of the n→π* transitions in its all-keto form in the range of 360–400 nm is substantially less than in the spectrum of compound **5**. In dry DMSO compound **8** gives an intense cherry-colored solution and its UV spectrum exhibits a long-wave absorption band at 500 nm. This band appears to arise from intramolecular charge transfer in the solvate complex **8**·2DMSO (see above).

Conclusions

2,2′-(Pyridin-2-ylmethylene)bis[1*H*-indene-1,3(2*H*)-dione] (**5**), its 5,5′,6,6′-tetramethoxy (**6**) and 5,5′,6,6′-tetrachloro (**7**) derivatives, as well as 2,2′-(pyridin-4-ylmethylene)bis-[1*H*-indene-1,3(2*H*)-dione] (**8**) have been extensively studied by NMR, IR, Raman, and UV spectroscopy, dielectrometry, and quantum mechanical calculations. The parent compound **5** at room temperature exists as an equilibrium mixture of the all-keto and keto–enol forms, the latter being stabilized by strong intramolecular O–H···N hydrogen bonds involving the pyridine nitrogen atom. The ratio of these forms is strongly dependent on the temperature and solvent. Low temperature and polar solvents stabilize the enol form. At 180 K, as well as in the solid state, the enol is the sole tautomer of **5**. The equilibrium in compound **6** is entirely shifted towards the all-keto form, whereas in **7** only the keto–enol form is observed at any temperature. In **5** and **7** intramolecular proton transfer between the hydroxy and carbonyl groups of the enol moiety takes place, which is probably facilitated by the 2-pyridyl substituents as a "proton shuttle".

Compound **8** in the solid state and low-polar solvents exists as the all-keto tautomer, but in DMSO it is ionized to form a zwitterionic structure containing a strong ionic O–H···O$^-$ hydrogen bond and a protonated pyridine nitrogen NH$^+$. This zwitterion, according to a dielectrometric study, forms a strong charge-transfer complex with two DMSO molecules.

The structures and the relative stabilities of the possible tautomers of the compounds studied are in agreement with those estimated by quantum chemical calculations at the DFT level of theory (B3LYP/6-311G**).

Experimental Section

^{1}H and ^{13}C NMR spectra were recorded with a Bruker DMX-500 spectrometer at working frequencies of 500.13 (^{1}H) and 125.76 (^{13}C) MHz. The ^{1}H and ^{13}C NMR chemical shifts are reported in parts per million relative to TMS. The ^{15}N NMR spectrum of compound **8** in DMSO was obtained with a DPX-400 spectrometer at 40 MHz. The ^{15}N NMR chemical shift is reported in parts per million relative to CH_3NO_2. Temperature measurements were carried out by using a BVT 3000 unit with a temperature stability ±0.2°. The IR and Raman spectra of compounds **5** and **8** in the solid state and in solution were obtained with a Bruker Vertex 70 spectrometer and the UV spectra of solutions with a Perkin–Elmer Lambda 35 UV/Vis spectrometer.

The dielectric permeabilities of compound **5** in benzene and of compound **8** in dioxane were measured with an Epsilon instrument (Angarsk, AO OKBA) at 1 MHz. The dipole moments were calculated by the second Debye method using the Higashi extrapolation formula.[28]

ESI-MS data were collected with a Bruker Daltonics Ion Trap MS Esquire 3000 Plus spectrometer equipped with APCI (atmospheric pressure chemical ionization) or with a mass spectrometer with an ESI source (Thermo Fisher Scientific), with which spectra were collected in the positive ion mode and analyzed by using Xcalibur software (Thermo Fisher Scientific).

The compounds studied were synthesized according to the general procedure described previously[13] by stirring 1 equiv. of 2- or 4-pyridinecarbaldehyde with 2 equiv. of the corresponding 1,3-indanedione in absolute ethanol. The reaction proceeded at room temperature and in the absence of catalyst except for compound **6**. In this case one drop of piperidine was added to the reaction mixture, which was refluxed for 30 min. The precipitated solid was filtered and washed with ethanol.

2,2′-(Pyridin-2-ylmethylene)bis[1*H*-indene-1,3(2*H*)-dione] (5): 1,3-Indanedione (1.46 g) was treated with 2-pyridinecarbaldehyde (0.6 g) in ethanol (50 mL); yield 1.7 g (90%). Yellow solid, m.p. 158–160 °C (decomp.). ^{1}H NMR (CD_2Cl_2, 260 K): δ = 13.14 (s, 1 H, OH), 5.73 [d, ^3J(H,H) = 2.4 Hz, 1 H, 3e-H], 4.54 (t, $^3J_{H,H}$ = 6.4 Hz, 1 H, 3k-H), 3.94 (d, $^3J_{H,H}$ = 6.4 Hz, 2 H, 1,2k-H), 3.75 (d, $^3J_{H,H}$ = 2.4 Hz, 1 H, 2e-H) ppm (see Scheme 1 for labeling of k and e H atoms; for the chemical shifts of the aromatic protons see Figure 3). ^{13}C NMR (CD_2Cl_2, 260 K): **5a** and **5b**: δ = 199.06, 198.47, 198.17, 188.23, 158.54, 156.83, 147.70, 146.26, 143.97, 142.38, 141.74, 138.92, 138.28, 137.85, 136.58, 136.33, 135.71, 135.39, 135.28, 133.44, 130.60, 125.37, 125.25, 124.02, 123.68, 123.08, 122.92, 122.83, 122.18, 118.54, 103.29, 60.10, 53.01, 43.72, 39.15 ppm. MS: *m*/*z* = 382.08 [M]$^+$.

2,2′-(Pyridin-2-ylmethylene)bis[5,6-dimethoxy-1*H*-indene-1,3(2*H*)-dione] (6): 5,6-Dimethoxy-1,3-indanedione (103 mg) was treated with 2-pyridinecarbaldehyde (28 mg) in ethanol (5 mL); yield 85 mg (57%). White solid, m.p. 250–252 °C (decomp.). ^{1}H NMR (500 MHz, CD_2Cl_2, 300 K): δ = 8.09 (br. d, $^3J_{H,H}$ = 4.8 Hz, 1 H, 6′-H), 7.54 (dt, $^3J_{H,H}$ = 7.7, $^4J_{H,H}$ = 1.8 Hz, 1 H, 4′-H), 7.22 (br.

d, $^3J_{H,H}$ = 7.8 Hz, 1 H, 3′-H), 7.06 (ddd, $^3J_{H,H}$ = 7.3, $^3J_{H,H}$ = 4.8, $^4J_{H,H}$ = 1.0 Hz, 1 H, 5′-H), 7.28 (s, 2 H, 5,6-H), 7.28 (s, 2 H, 5,6-H), 4.24 (t, $^3J_{H,H}$ = 7.2 Hz, 1 H, 3k-H), 4.03 (d, $^3J_{H,H}$ = 7.2 Hz, 2 H, 1k-H, 2k-H), 3.97 (s, 6 H, MeO), 3.96 (s, 6 H, MeO) ppm. ^{13}C NMR (CD_2Cl_2, 300 K): δ = 197.75, 197.61, 157.62, 155.73, 155.62, 147.92, 137.14, 135.87, 123.59, 121.88, 103.04, 102.98, 56.46, 53.84, 44.80 ppm.

5,6-Dichloro-2-[(5,6-dichloro-3-hydroxy-1-oxo-1*H*-inden-2-yl)(pyridin-2-yl)methyl]-1*H*-indene-1,3(2*H*)-dione (7): 5,6-Dichloro-1,3-indanedione (215 mg) was treated with 2-pyridinecarbaldehyde (54 mg) in ethanol (5 mL); yield 157 g (60%). Yellow solid, m.p. 170–173 (decomp.) MS: *m*/*z* 519.97, 517.95, 515.97 (M^+). ^{1}H NMR (CD_2Cl_2, 260 K): δ = 8.60 (d, $^3J_{H,H}$ = 6.0 Hz, 1 H, 6′-H), 8.17 (t, $^3J_{H,H}$ = 8.2 Hz, 1 H, 4′-H), 7.72 (d, $^3J_{HH}$ = 8.2 Hz, 1 H, 3′-H), 7.69 (t, $^3J_{H,H}$ = 7.0 Hz, 1 H, 5′-H), 8.36 (s, 1 H, HAr), 7.94 (s, 1 H, HAr), 7.36 (s, 2 H, HAr) ppm.

2,2′-(Pyridin-4-ylmethylene)bis[1*H*-indene-1,3(2*H*)-dione] (8): 1,3-Indanedione (1.46 g) was treated with 4-pyridinecarbaldehyde (0.6 g) in ethanol (50 mL); yield 1.45 g (78%). White solid, m.p. 180–182 °C (decomp.). ^{1}H NMR (CD_2Cl_2, 300 K), δ = 4.24 (d, $^3J_{H,H}$ = 7.3 Hz, 2 H, 1,2-H), 3.88 (t, $^3J_{H,H}$ = 7.3 Hz, 1 H, 3-H) ppm (for the chemical shifts of the aromatic protons see Figure 3). ^{13}C NMR (CD_2Cl_2, 300 K): δ = 198.80, 197.67, 149.72, 148.59, 141.72, 141.61, 136.07, 135.90, 124.18, 123.19, 53.50, 40.50 ppm. MS: *m*/*z* = 382.08 $[M]^+$.

Supporting Information (see also the footnote on the first page of this article): Spectral data of the experimentally studied compounds and optimized geometries of the model compounds.

Acknowledgments

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