Identity Double-Proton Transfer in (3*Z*)-3-Hydroxy-1,4-di(quinolin-2-yl)-but-3-en-2-one

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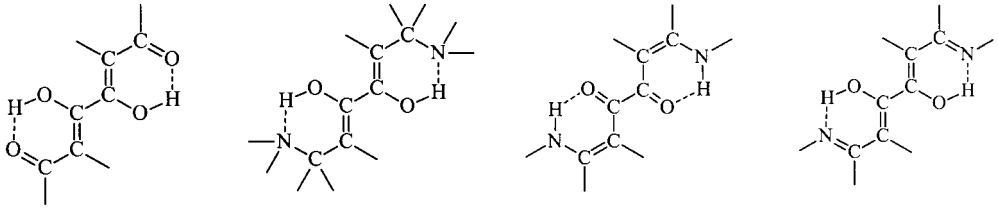
Abstract: Although there is a very fast (on the NMR timescale) double-proton transfer in (1*Z*,3*Z*)-3-hydroxy-4-quinolin-2-yl-1-quinolin-2(1*H*)-ylidenbut-3-en-2-one (the product of the condensation of ethyl oxalate with 2-lithiomethylquinoline), it is the only species present in chloroform solution. Comparison of the product of condensation of ethyl oxalate with 2-lithiomethyl derivatives of pyridine (recent studies) and quinoline (present studies) shows that benzoannulation considerably affects the tautomeric equilibrium. The observed changes are not only quantitative but also qualitative. Moreover, contrary to the proton transfer in the pyridine tautomers, this process is fast in the quinoline tautomers. Comparison of the experimental and ab initio/DFT GIAO-calculated ^{13}C and ^{15}N chemical shifts for the transition states in the proton-transfer reactions between (1*Z*,3*Z*)-3-hydroxy-4-quinolin-2-yl-1-quinolin-2(1*H*)-ylidenbut-3-en-2-one and its tautomers support the theory that a concerted identity reaction takes place between the enolimine-enaminone and enaminone-enolimine tautomeric forms. As a consequence, the most stable tautomeric form, (1*Z*,3*Z*)-1,4-di(quinolin-2-yl)buta-1,3-diene-2,3-diol, is not present in the tautomeric mixture.

Keywords: ab initio calculations · annulation · identity reaction · NMR spectroscopy · tautomerism

Introduction

The formation of strong hydrogen bonds in 3,4-dihydroxy-2,4-hexadiene-1,6-dione (**a**) is expected to be responsible for its stabilization as compared to the respective 1,3,4,6-hexanetetraone.[1–3] On the other hand, it is noteworthy that resonance interactions are not necessary to stabilize enols. Thus, some dihydroxydiallylamines (**b**) are known.[4] Although the respective dienaminedione tautomer (**c**) was found to be present in solution,[5] additional proofs are needed to distinguish it from diiminedienol (**d**).

Steric hindrance in 1,3,4,6-tetraones, $RCOCH_2COCOCH_2COR$ (R = alkyl or aryl), is believed to be responsible for the lack of this form in solution.[6] Instead, there is a fast proton exchange between diketodienediols (**a**) and 2-hydroxy-2-acylmethyl-3(2*H*)-furanone (the minor tautomer).[6] 1,4-Di(pyridin-2-yl)-2,3-butanedione is the diimine derivative of the respective 1,3,4,6-tetraone. These two compounds are isoelectronic. Recently[7] we found that proton transfer takes place in 1,4-di(pyridin-2-yl)butane-2,3-dione and that the highly conjugated dienol, (1*Z*,3*Z*)-1,4-di(pyridin-2-yl)buta-1,3-diene-2,3-diol, predominates over other tautomeric forms



a **b** **c** **d**

in chloroform. This tautomer is additionally stabilized by two strong intramolecular hydrogen bonds. It is the only form present in the crystal.[7] Knowing that benzoannulation may affect the tautomeric equilibrium both qualitatively and quantitatively,[8–14] we were very much interested to discover how it affects the tautomeric preferences of 1,4-di(pyridin-2-yl)butane-2,3-dione. Its tautomers and rotamers are shown in Scheme 1.

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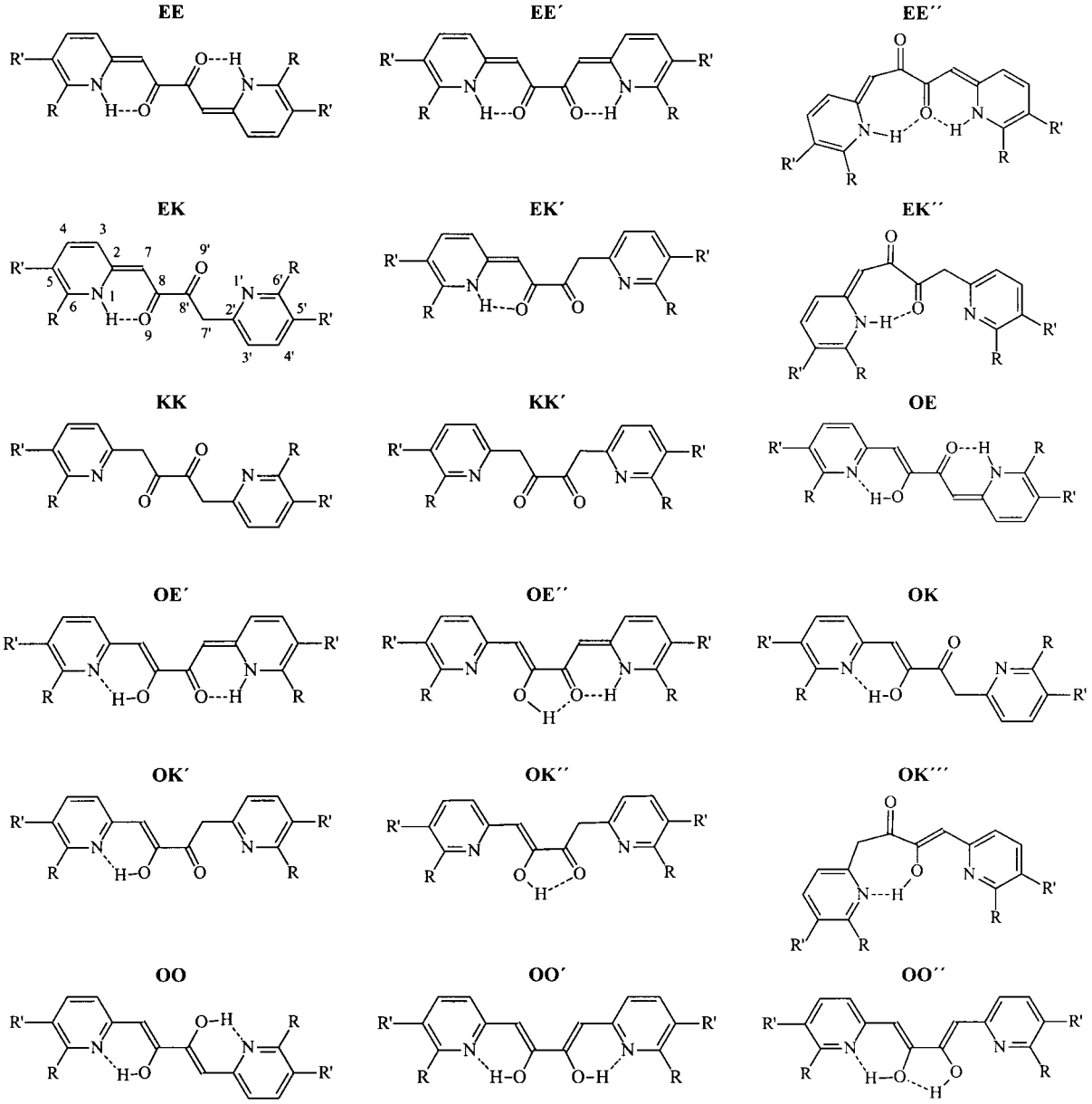


Scheme 1. The tautomers and rotamers of 1,4-di(pyridin-2-yl)butane-2,3-dione. **1**: R = R′ = H; **2**: R,R′ = benzo. The numbering of positions in the molecule is exemplified for the **2EK** form.

Results

Experimental spectral data: An IR spectrum of the product of the reaction of 2-lithiomethylquinoline with ethyl oxalate in chloroform shows the broad band of the C=O stretching vibrations at ~1720 cm^{-1} and three bands in the 3250–3600 cm^{-1} region (O–H[15] and N–H[16] stretching vibrations).

Complete experimental NMR chemical shifts (δ) for **2** (0.1–0.2 M solution in $CDCl_3$ at 303 K) are: ^{1}H: 6.45 (1H), 6.96 (1H), 7.26 (1H), 7.5–7.6 (3H), 7.72 (1H), 15.73 (1H); ^{13}C: 90.29, 118.70, 121.66, 123.14, 123.40, 126.68, 130.00, 135.71, 137.91, 154.46, 177.21; ^{15}N: –209.3. No other, even very weak, signals can be seen in the spectra.

Ab initio calculations: B3LYP/6-311++G** GIAO calculations on the geometry obtained with the RHF/3-21G level may help to assign the ^{15}N signals. The calculated chemical shifts of the different forms are presented in the Discussion. Those of the transition states between different tautomers are also included there. The B3LYP/RHF method for different basis sets was used to calculate the ^{1}H and ^{13}C NMR chemical shifts (δ) for **2OO**, **2EE**, and **2OE** (Table 1).

The relative energies of the different tautomers and rotamers **2** were calculated at the MP2/6-31G**//RHF/6-31G** level to see which of them is expected to be present in the tautomeric mixture (Table 2).

The RHF/6-31G** method was used to calculate the optimized geometries of the different tautomers **2**. The dihedral angles in their molecules are presented in Table 3.

Calculations at the MP2/6-31G**//RHF/6-31G** level and PCM model of solvation were used to show the dependence between the energy of some tautomers and their geometries. The results are presented in the Discussion.

Table 1. ^{1}H and ^{13}C NMR chemical shifts (δ) for **2OO**, **2EE**, and **2OE** calculated with the B3LYP/RHF method for different basis sets.

Tautomer		6-311G//3-21G	6-311G//6-31G**	6-311G**//6-31G**
2OO	C2/C2′	158.15	162.20	163.74
	C3/C3′	123.37	128.99	128.17
	C4/C4′	135.62	140.85	141.85
	C5/C5′	126.50	131.27	131.27
	C6/C6′	145.08	149.88	151.87
	C7/C7′	100.32	105.18	102.91
	C8/C8	161.06	163.50	164.53
	H3/H3′	6.47	7.31	7.37
	H4/H4′	7.03	7.84	8.09
	H9/H9′	11.90	10.72	11.39
2EE	C2/C2′	149.18	153.06	155.67
	C3/C3′	126.05	132.17	132.23
	C4/C4′	134.35	138.98	139.60
	C5/C5′	123.37	128.18	128.05
	C6/C6′	137.10	142.10	144.02
	C7/C7′	89.37	93.76	91.12
	C8/C8′	186.37	188.92	188.58
	H1/H1′	12.02	11.39	12.22
	H3/H3′	5.97	6.72	6.75
	H4/H4′	6.43	7.18	7.27
2OE	C2	158.49	162.55	164.22
	C2′	149.06	152.99	155.63
	C3	123.77	129.33	128.60
	C3′	125.83	131.79	131.71
	C4	135.60	140.70	141.64
	C4′	134.64	139.22	139.99
	C5	126.59	131.27	131.24
	C5′	123.66	128.28	128.15
	C6	145.17	149.98	151.97
	C6′	137.03	141.97	143.82
	C7	99.12	103.96	102.50
	C7′	91.58	96.39	93.11
	C8	163.39	166.37	167.08
	C8′	183.15	185.00	184.71
	H3	6.51	7.35	7.43
	H3′	5.95	6.72	6.75
	H4	7.05	7.84	8.08
	H4′	6.48	7.21	7.31
	H9	11.75	10.63	11.25
	H1′	12.21	11.58	12.46

Table 2. Calculated relative energies [kJ mol^{-1}] at the MP2/6-31G**//RHF/6-31G** level for different tautomers/rotamers **2**.

Tautomer	in vacuo	in chloroform
EE	23.67	20.68
EE′	50.19	43.41
EE″	55.93	54.64
EK	20.59	16.85
EK′	47.12	38.71
EK″	58.00	56.69
KK	27.99	24.04
KK′	52.65	44.17
OE	11.43	9.65
OE′	32.27	27.08
OE″	54.99	48.33
OK	8.97	7.05
OK′	28.31	22.29
OK″	53.44	47.82
OK‴	85.61	80.86
OO	0.00	0.00
OO′	19.79	17.08
OO″	61.86	56.40
[a]	− 1104.645914	− 1104.646175

[a] Energy [a.u.] of the most stable tautomer.

Discussion

Treatment of 2-lithiomethylquinoline with one equivalent of alkyl benzoate leads to 2-phenacylquinolines, which in solution are in equilibrium with 1,2-dihydro-2-benzoyl-methylenequinolines.[11] Diesters, such as oxalate, may react with two molecules of the lithium derivative. This should result in formation of the respective α-diketone, 1,4-di(quinolin-2-yl)butane-2,3-dione, **2KK** (Scheme 1). By analogy with the pyridine derivative,[7] it can be anticipated that in solution this diketone is predominated by (1*Z*,3*Z*)-1,4-di(quinolin-2-yl)-buta-1,3-diene-2,3-diol (**2OO**), and (3*Z*)-3-hydroxy-1,4-di-(quinolin-2-yl)but-3-en-2-one (**2OK**, Scheme 1).

The IR spectrum confirms that both enolimine, **O**, and enaminone, **E**, forms are present in solution. Thus, it may contain a mixture of **2OX** and **2EX** (**X** = **K**, **O** or **E**) or **2OE** (Scheme 1).

Table 3. RHF/6-31G** optimized dihedral angles [°] in different tautomers **2** (initial angles in parentheses).[a]

Tautomer	N1C2C7C8	C2C7C8O9	O9C8C8′O9′	C2′C7′C8′O9′	N1′C2′C7′C8′
EE	0.00(0)	0.00(0)	179.91(0)	0.00(0)	0.00(0)
EE′	1.23(0)	− 1.84(0)	61.81(0)	− 1.84(0)	1.23(0)
EE″	0.00(0)	179.98(180)	179.91(180)	0.00(0)	0.00(0)
EK	0.27(0)	− 0.55(0)	− 173.36(180)	− 5.45(− 15.51)	− 112.37(− 135.38)
EK′	0.00(0)	0.00(0)	0.18(0)	4.24(0)	117.24(135.38)
EK″	0.00(0)	180.00(180)	180.00(180.00)	− 0.9(0)	− 103.63(− 86.95)
KK	108.85(106.59)	6.96(115.10)	167.63(150.01)	6.96(115.10)	108.85(106.59)
KK′	112.89(106.6)	13.68(15.77)	− 0.86(0)	12.65(14.25)	113.35(106.65)
OE	0.00(0)	0.00(0)	180.0(180)	0.00(0)	0.00(0)
OE′	1.32(0)	− 0.58(0)	38.38(0)	1.27(0)	0.79(0)
OE″	− 0.01(0)	0.00(0)	− 0.04(0)	− 0.01(0)	0.00(0)
OK.	− 0.24(0)	0.19(0)	176.27(180)	5.11(9.64)	113.43(133.66)
OK.′	0.11(0)	− 0.08(0)	0.39(0)	6.02(9.17)	116.12(133.77)
OK.″	2.95(0)	0.11(0)	− 0.45(0)	6.42(0)	112.62(72.21)
OK.‴	0.00(0)	0.00(0)	179.97(180)	− 179.99(− 180)	0.04(0)
OO	0.00(0)	0.00(0)	180(180)	0.00(0)	0.00(0)
OO′	− 0.29(0)	0.99(0)	43.08(0)	0.99(0)	− 0.29(0)
OO″	0.00(0)	0.00(0)	0.00(0)	0.00(0)	− 0.07(0)

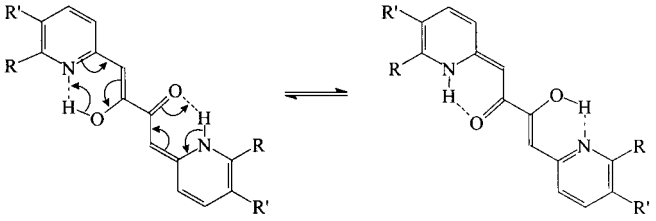
[a] In the asymmetric forms, for example **EK**, the primed positions are these in the latter part of the molecule (**K**).

The position of the signal at $\delta = 6.45$ is comparable with that for H7 in the spectrum of (1*Z*,3*Z*)-1,4-di(pyridin-2-yl)buta-1,3-diene-2,3-diol (**1OO**).[7] The chemical shift of the acidic proton seen in the ^{1}H NMR spectrum is $\delta = 15.73$, but the positions of the other NMR signals show that the tautomer present is not of the **2OO** type. Both the broad singlet at $\delta = 15.73$ in the ^{1}H NMR spectrum and another signal at $\delta = 177.21$ in the ^{13}C NMR spectrum show it could be 1,4-di-[quinolin-2(1*H*)-ylidene]butane-2,3-dione, **2EE**. On the other hand, the position of the latter signal is different from the typical chemical shift of the carbonyl carbon atom in the enaminone form.[11] It is also noteworthy that the value of 177.21 ppm is not a result of the vicinity of the two carbonyl groups in α-diketones.[17] The ^{15}N chemical shift (-209.3) is also different from that of enaminones.[11] Indeed, it is intermediate between the ^{15}N chemical shifts seen in the NMR spectra of enaminones[11] and enolimines.[8]

The experimental ^{13}C NMR chemical shifts of **2** are also averaged typical signal positions of the enaminone[11] and enolimine forms.[8] This shows that, in solution, a fast proton exchange may take place between two tautomers that contain the **O** and **E** moieties, for example, **2OK** $\rightleftharpoons$ **2EO** or **2OE** $\rightleftharpoons$ **2EE**. Double-proton transfer is required to transform **2OO** and **2EE** into each other. The difference in energy between **2OO** and **2EE** is equal to 20.68 kJ mol^{-1} (Table 2). On the other hand, this difference between **2OO** and **2OE** is only 9.65 kJ mol^{-1}. Moreover, interconversion of these two forms requires only a single-proton transfer. Since this process is also expected to be fast on the NMR timescale, the observed chemical shifts for the tautomeric mixture should also be the average of those for the respective tautomeric forms present in solution. When comparing different forms **1** and **2**, one should bear in mind that there are at least two tautomeric forms in their solutions. On the other hand, in contrast with equilibrium between **1OO** and **1OK**, the proton exchange between tautomers **2** is seen to be fast on the NMR timescale. This explains the significant differences between the NMR spectra of **1** and **2**: these contains the separate and averaged signals of each tautomeric form, respectively.

We found recently that B3LYP/6-311++G** GIAO calculations at the geometry obtained with the RHF/3-21G level gave reliable ^{15}N chemical shifts.[18] For the nitrogen atom in the conserved (enaminone) part of the molecule in the transition state of the **2EE** $\rightarrow$ **2OE** reaction, it is equal to -284.1 ppm (NH$\cdots$O). On the other hand, such a shift for another nitrogen atom is -240.5 ppm (N$\cdots$H$\cdots$O). The ^{15}N chemical shift for the transition state of the **2EE** $\rightarrow$ **2OO** process (N$\cdots$H$\cdots$O) is equal to -221.2 ppm (-221.7 ppm). This value is comparable with the ^{15}N chemical shift of the nitrogen atom in the nonconserved part of the molecule during the **2OO** $\rightarrow$ **2OE** process (-220.2 ppm). On the other hand, $\delta(^{15}\mathrm{N})$ for another nitrogen atom in this transition state is -134.3 ppm (N$\cdots$HO), which is comparable with the ^{15}N chemical shift in the NMR spectra of enolimines.[7] The calculated chemical shifts for the transition states during the **2OO** $\rightarrow$ **2OE** $\rightarrow$ **2EE** processes (~ -220 ppm) are comparable with the experimental $\delta(^{15}\mathrm{N})$ value for **2** (-209.3 ppm). This shows that a fast proton exchange between the **2OO**, **2OE**, and/or **2EE** tautomers may take place or that there is a permanent transition state between these forms (a similar phenomenon has been studied earlier[19–21]).

Theoretical calculations at the MP2/6-31G**//RHF/6-31G** level (Table 3) show that the **2OO** $\rightarrow$ **2OE** and **2OE** $\rightarrow$ **2EE** transition states are planar. The relative energies of **2OE** and **2EE** in a vacuum (referenced to that of **2OO**) are equal to 15.34 and 27.20 kJ mol^{-1}, which are further decreased by the solvent (chloroform) to 14.31 and 24.77 kJ mol^{-1}, respectively. However, it is noteworthy that the energy barrier (energy of the respective transition state) in the reaction **2OO** $\rightarrow$ **2OK** is much lower, that is, 12.35 or 12.29 kJ mol^{-1} in a vacuum or in solution, respectively. The question arises why **2OK** is not present in chloroform. It has to be mentioned that, following the **O** $\rightarrow$ **E** reaction path, the distance that the proton jumps is only 96 pm. It is 307.8 pm for **O** $\rightarrow$ **K**, and the quinolyl moiety is forced to rotate about the C2–C7 single bond during this process. Thus, that distance is extremely short for the **2EO** $\rightarrow$ **2OO** $\rightarrow$ **2OE** proton transfers (due to the high energy of **2EE**, the option **2EO** $\rightarrow$ **2EE** $\rightarrow$ **2OE** was not considered). Since proton transfer of the N$\cdots$H-O $\rightleftharpoons$ N-H$\cdots$O type is known to be relatively fast,[22] one may conclude that there is a very fast reversible intramolecular rearrangement between **2OE** and **2EO**. Such a doubly degenerate intramolecular proton transfer has an identity-reaction character.[23, 24] Both configuration and conformation of the molecule enables two simultaneous proton transfers (Scheme 2). The presence of two identical species in the tautomeric mixture (being both the reactant and product) gives a statistical factor of 2, which increases the entropy of this species relative to a single tautomer. Comparison of **1** and **2** shows that benzoannulation considerably affects the electron-density distribution in the molecule during the proton transfer.



2OE **2EO**

Scheme 2. Intramolecular proton transfer between **2OE** and **2EO**. **1**: R = R′ = H; **2**: R, R′ = benzo.

The observed double-proton transfer may be synchronous by character as it is in the dimers of carboxylic acids.[25] No kinetic studies have been done by us, but the MP2/6-31G**//RHF/6-31G** calculations show that the distance that the proton jumps during the **2EO** $\rightarrow$ **2OE** process is exceptionally short (96 pm), and thus, this proton transfer can be governed by the tunneling effect. Such processes play a key role in the catalytic activity of some enzymes.[26] Tunneling-mediated intramolecular double-proton transfers were found to take place in 2,5-dihydroxy-1,4-benzoquinone[27] and *N*,*N*′-bis-(salicylidene)-*p*-phenylenediamine, which is very similar to **2**.[28] It was also found to control the concerted multiple-proton

transfer in the cyclic oligomers of numerous compounds[29–35] and in the dimers of amidines[36] and carboxylic acids[37] in their crystalline states. In solution, the intermolecular double-proton transfer probably also takes place in the dimers of 2-nitrimino-1,2-dihydropyridines, the tautomers of 2-nitraminopyridines.[38–40]

The energetic dependence of **1OO** on the O–H bond length (calculations at the MP2/6-31G**//RHF/6-31G** level and PCM model of solvation) shows that the molecule has the minimum energy for $d_{OH} = 100.3$ pm.[7] It is noteworthy that lengthening of the O–H bond to 120.0 pm causes a relatively small increase in energy: $\Delta E = 39.16$ kJ mol^{-1}. Such a correlation between the energy and d_{OH} for **2OO** is very similar to that of **1OO**. The minimum is observed at 100.6 pm, and lengthening of the O–H bond length to 120.0 pm causes a 30.98 kJ mol^{-1} increase in the energy (in chloroform). On the other hand, an energetic minimum at $d_{NH} = 102.5$ pm was found for **2EE** in chloroform (Figure 1). It is noteworthy, however, that for longer N–H bonds the energy increases (maximum at 114.8 pm) and then decreases. In consequence $E(120.0\text{ pm}) < E(114.8\text{ pm})$.

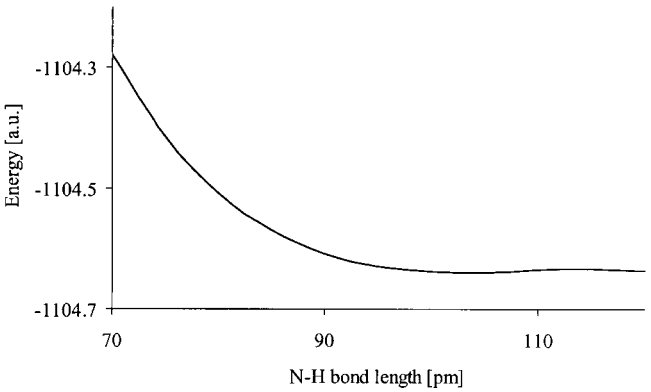
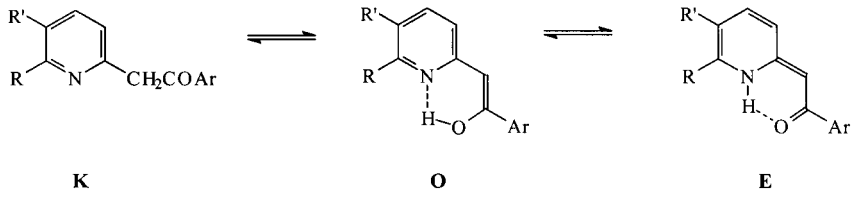


Figure 1. Energetic dependence of **2EE** on the N–H bond length.

Experimental ^{1}H, ^{13}C, and ^{15}N NMR chemical shifts are certainly helpful in distinguishing between different tautomeric forms.[8] GIAO-RHF/DFT calculations afford additional support, especially if one is going to see which conformer predominates in the tautomeric mixture.[41] Such data for some tautomers **2** are shown in Table 1. It can easily be seen that the experimental chemical shifts of 90.29, 137.91, 154.46, and 177.21 ppm for **2** are the averaged signal positions found in the spectra of **2OO** and **2EE** (**2OE**) (Table 1). It is noteworthy that the experimental chemical shifts for two consecutive single-proton transfers **2OE** $\rightleftharpoons$ **2OO** (or **2EE**) $\rightleftharpoons$ **2EO** should differ from those averaged for **2OO** and **2EE** (in such a case there is an additional statistic contribution from the symmetrical intermediate). This finally proves that interconversion between **2OE** and **2EO** is a result of simultaneous double-proton transfer.

It is known that 2-phenacyl derivatives of pyridine and quinoline (**K**) may equilibrate with **3O** [(*Z*)-2-(2-hydroxy-2-phenylvinyl)pyridine] and **4E** [*(Z)*-1,2-dihydro-2-benzoylmethylene-quinoline] (Scheme 3).[8, 11] Except for **3K** (2-phenacylpyridine), only the **O** and **E** forms were detected in



K **O** **E**

Scheme 3. Equilibrium of the 2-phenacyl quinoline derivative **K**. **3**: R = R′ = H; **4**: R, R′ = benzo.

chloroform for R = R′ = H and R,R′ = benzo, respectively.[8, 11] Benzoannulation is responsible for the remarkable stability of the **4E** form.[11] The loss of aromatic character of **4E** (as relative to that of **4K**) is efficiently compensated for by the extended conjugation in its molecule.[11] It is also noteworthy that **4E** is additionally stabilized by the strong intramolecular hydrogen bond. Since the stability of **1OO** [(1*Z*,3*Z*)-1,4-di(pyridin-2-yl)buta-1,3-diene-2,3-diol] is much higher than that of **1OE** [(1*Z*,3*Z*)-3-hydroxy-4-pyridin-2-yl-1-pyridin-2(1*H*)-ylidenbut-3-en-2-one], no **1OE** and **1EO** tautomers were detected in chloroform.[7] Instead, an insignificant amount of **1OK** [(3*Z*)-3-hydroxy-1,4-di(pyridin-2-yl)-but-3-en-2-one] is present. One would expect benzoannulation to stabilize the **2EE** form;[11] however, this is not the case.

Optimization of the geometries of different tautomers (Scheme 1) with the ab initio (RHF/6-31G**) method shows that the diketo form **2KK** is significantly twisted around the C2–C7 bond (Table 3). The O9C8C8′O9″ and C2C7C8O9 dihedral angles in **2KK** are not 180°. Twisting around the C2′–C7′ and C7′–C8′ bonds can be also seen in the keto fragment of asymmetric forms such as **2EK** and **2OK**. On the other hand, the **E** fragments are planar. The initial C8C8′O9H angle in **2OE**″ was set to 0° in order to enable formation of the intramolecular >C=O···H-O- hydrogen bond. Note that the respective pyridine derivatives have similar geometries.[7]

Strong repulsion between the two carbonyl oxygen atoms in the s-*cis*-**2EE**′ rotamers results in a significant twist around the C8–C8′ bond. Energetic preferences also cause twisting around the C8–C8′ bond in **2OE**′ and **2OO**′. Note that conformation of the quinoline moieties with respect to the central part of the molecule was also subjected to the geometry optimization procedure.

Calculations including both electron correlation (MP2/6-31G**) and solvent effect (PCM model of solvation) show that the **2OK** and especially highly conjugated **2OO** forms are expected to predominate in the tautomeric mixtures both in chloroform and in vacuo (Figure 2 and Table 2). The ketimine-enolimine form **2OK**‴ was found to have the highest energy. The relative energy of **1EE**″ was equal to 96.46 or 89.68 kJ mol^{-1} in a vacuum or in solution, respectively.[7] These values are 55.93 and 54.64 kJ mol^{-1} for **2EE**″ (Table 1). Benzoannulation seems to be responsible for the lower energy of **2EE**″ relative to that of **1EE**″. The data in

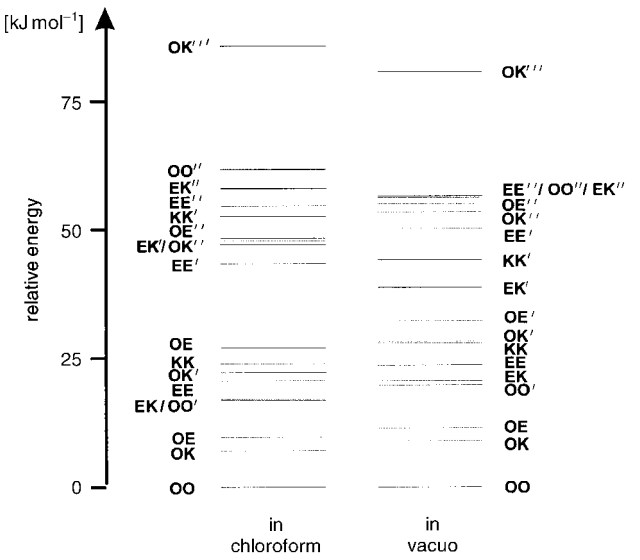


Figure 2. Relative energies of different tautomers/rotamers **2** in vacuo and in chloroform, calculated with the MP2/6-31G** method at the geometry obtained with the RHF method and the same basis sets.

Table 1 show that the energy of **2OK** is higher in vacuo than in solution. The energy of **2OK** in chloroform is equal to 7.05 kJ mol^{-1} (it was 3.63 kJ mol^{-1} for **1OK**[7]). The third energetically lowest form is **2OE** (relative energy 11.43 and 9.65 kJ mol^{-1} in vacuo and in solution, respectively).

Theoretical calculations[7] show that, for solutions in chloroform, **1OO** has the lowest energy among the different tautomers **1** and that **1OE** and **1EE** are less or significantly less preferred. Tautomer **2OO** is also favored among the different tautomers of **2** (Figure 2 and Table 1) but **2OE** and **2EE** have energies significantly lower than the respective tautomers **1** ($E_{\mathbf{1EE}} = 56.33$ kJ mol^{-1} and $E_{\mathbf{2EE}} = 20.68$ kJ mol^{-1}).

The presence of (1*Z*,3*Z*)-3-hydroxy-4-quinolin-2-yl-1-quinolin-2(1*H*)-ylidenbut-3-en-2-one in chloroform does not authorize anyone to name the solid product. Due to their size, the crystals obtained cannot be used to identify the species present there by X-ray experiment. Since the structure of the solid **2** is not known, no name is used in the Experimental Section for the product of the condensation of ethyl oxalate with 2-lithiomethylquinoline.

Conclusion

It has been pointed out that the difficulties met in determining the structures of the different tautomers under a fast dynamic exchange can be overcome by modern NMR spectroscopic and computational approaches. The GIAO-calculated NMR chemical shifts for the transition states in the proton-transfer reactions are a very helpful tool in identifying the contributing tautomers in a fast equilibrium. In chloroform, there is a fast double-proton transfer in (1*Z*,3*Z*)-3-hydroxy-4-quinolin-2-yl-1-quinolin-2(1*H*)-ylidenbut-3-en-2-one. Benzoannulation of the condensation product of ethyl oxalate with 2-lithiomethylpyridine considerably affects the content of the tautomeric mixture. Moreover, contrary to proton transfer in the respective pyridine tautomers, for the quinoline derivatives this process is fast on the NMR timescale.

Experimental Section

Compound **2** (m.p. 218–220 °C) was obtained by treating 2-lithiomethylquinoline (two molar excess) with ethyl oxalate. The synthetic procedure was that used recently.[7, 8] The crude product precipitated from the reaction mixture was further purified by recrystallization from aqueous ethanol. Satisfactory analytical data (±0.3 % for C, H, and N) were obtained for the formula $C_{22}H_{16}N_2O_2$.

All NMR spectra were recorded for solutions in at $CDCl_3$ (0.1–0.2 M) at 303 K with a Bruker Avance DRX500 FT NMR spectrometer equipped with an inverse detection 5 mm diameter broad-band probe head and z-gradient working at 500.13 MHz (^{1}H), 125.76 MHz (^{13}C), or 50.59 MHz (^{15}N). The ^{1}H NMR chemical shifts are referenced to the (trace) signal of $CHCl_3$ ($\delta = 7.26$ from int. TMS), and the ^{13}C NMR chemical shifts to the signal of solvent $CDCl_3$ ($\delta = 77.00$ from int. TMS). In order to distinguish the spin systems belonging to different rings and tautomeric forms as well as to assign the ^{1}H NMR spectra reliably, 2D double-quantum-filtered (DQF) ^{1}H,^{1}H COSY[42, 43] experiments were run. 2D pulsed-field z-gradient (PFG) selected ^{1}H,^{13}C HMQC[44, 45] and ^{1}H,^{13}C HMBC[46] experiments were also run to reliably assign the ^{13}C NMR spectra. In order to determine the ^{15}N NMR chemical shifts, z-PFG ^{1}H,^{15}N HMBC spectra with a 100 ms evolution delay for spin–spin couplings were recorded. The ^{15}N NMR chemical shifts were referenced to an external nitromethane ($\delta = 0.0$) sample in a 1 mm diameter capillary tube inserted coaxially inside the 5 mm NMR sample tube. Other experimental details are available in our recent paper.[7]

IR spectra were recorded on a Bruker Vector 22 FTIR spectrophotometer with samples at room temperature as solutions in chloroform.

Ab initio calculations were carried out with the GAUSSIAN 98[47] program by using the 6-31G** basis set at the RHF and MP2 levels. All calculations were performed with the PCM model of solvation.[48, 49]

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