An integrated approach to the study of the tautomerism of 4-((Phenylimino)methyl) naphthalene-1-ol

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ABSTRACT: The aim of the current report is to shed light on the tautomerism of 4-((Phenylimino)methyl) naphthalene-1-ol in solution, which was studied by UV–Vis spectroscopy and quantum chemical calculations. It was found that this compound does not have the typical tautomeric behavior of its analog 4-Phenylazo-naphthalen-1-ol. The complicated equilibrium between the enol- and keto-like forms and two kinds of dimers that can exist in solution, is strongly dependent on the proton acceptor/donor abilities of the solvent. Using advanced data treatment quantitative information about the tautomeric and dimeric equilibrium constants was obtained. Copyright © 2007 John Wiley & Sons, Ltd.

KEYWORDS: tautomerism; solvent effect; Schiff base; chemometrics

INTRODUCTION

Although the tautomerism in 4-Phenylazo-naphthalen-1-ol (compound **1** in Scheme 1) was discovered more than a century ago,[1] the number of studies dealing with these tautomeric compounds is rising continuously. This is not surprising, because on one hand tautomerism lies at the base of many elementary processes in living systems, and advanced technological applications,[2–4] and on the other hand it remains of substantial fundamental interest for method development in molecular spectroscopy,[5] since in most of the cases the individual tautomers cannot be physically separated.

It is well-known that the position of the tautomeric equilibrium in solution can be shifted by changing environmental factors such as temperature, and solvent properties, and the corresponding spectra can be recorded, but not analyzed by means of classical spectrophotometry.[5] Recently we have developed a chemometric approach for processing complicated absorption spectra,[6] which leads to quantitative information about the molar fractions of the tautomers and their individual spectra. For instance, the tautomeric equilibria of species **1–5** in Scheme 1 were studied intensively[7–10] and the quantitative information obtained allowed effects of the solvents[11,12] and temperature[13] to be elucidated.

It was found that the tautomeric equilibrium of compound **1** can be strongly affected by the solvent due to the lack of intramolecular hydrogen bonding such as present in compounds **2–5**. However, this hydrogen bond is relatively weak in the azonaphthols **2** and **3** compared to the Schiff bases **4** and **5**, which determines different thermochromic behaviors.[13] In the light of these facts 4-((Phenylimino)methyl)naphthalene-1-ol (compound **6**) represents an interesting object for investigation and comparison with compound **1**. Quite surprisingly (compound **6** is the structural analog of the most intensively studied tautomeric dye **1**), to the best of our knowledge there is no information available about its tautomeric properties.

The general aim of the current report is to shed light on the tautomerism of compound **6** in solution using UV–Vis spectroscopy combined with quantum chemical calculations. Particular attention is given to solvent effects and to the comparison of the spectral properties of **6** with those of **1** on one hand and of **4–5** on the other.

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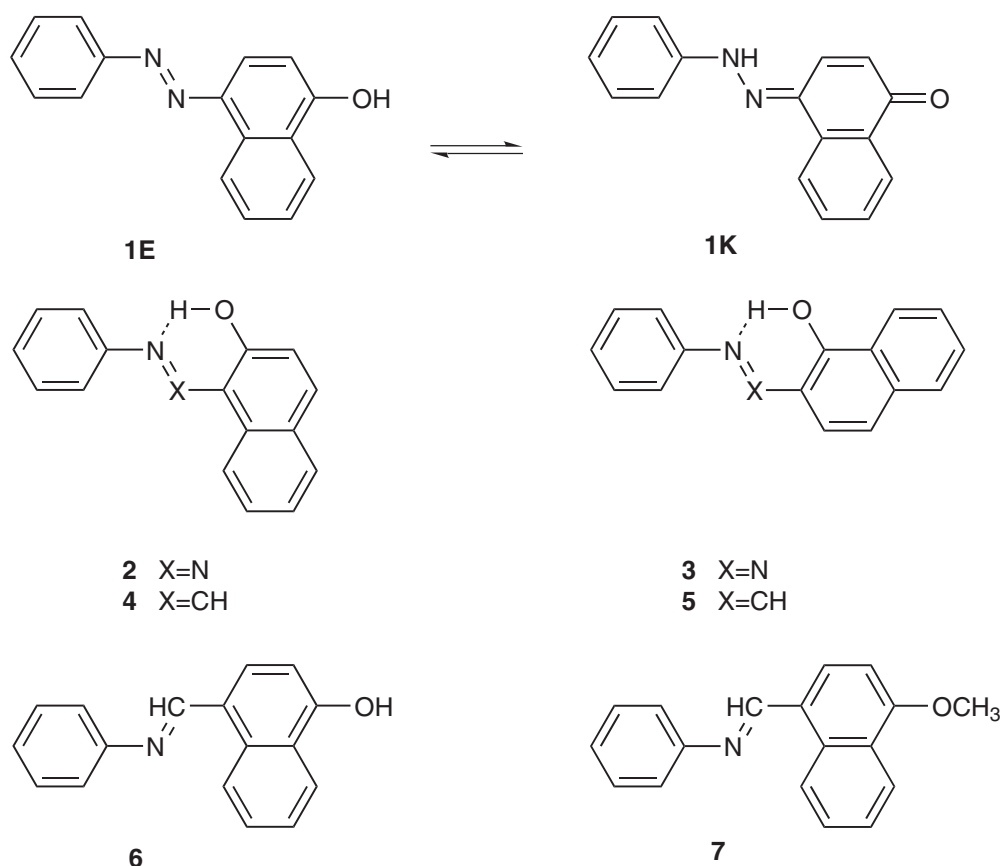
Scheme 1

EXPERIMENTAL PART

Synthesis

1-Methoxynaphthalene, 1-naphthol, aniline, benzene, absolute ethanol, dichloromethane, and ethyl acetate were supplied by Aldrich and used as received. Silica gel Kieselgel 60 type Merck was supplied by Fluka. 4-Methoxy-1-naphthaldehyde[14] and 4-hydroxy-1-naphthaldehyde[15] were prepared according to methods in the literature. Melting points were determined on a Gallenkamp MF-370 apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz NMR (Bruker) spectrometer (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR), in CDCl$_3$ using tetramethylsilane (TMS) as internal reference. Fast-atom bombardment (FAB) mass spectra were recorded on a Jeol JMS-HX 110A mass spectrometer.

Preparation of 4-(Phenylimino-methyl)-1-naphthol (compound 6).

A modified method was used for this preparation. 4-hydroxy-1-naphthaldehyde (1.72 g; 10 mmol) was suspended in water (50 ml) and heated for 30 min while stirring. The mixture was cooled to room temperature and treated with aniline (0.931 g;

10 mmol). Then the mixture was stirred at 25°C for 3 h. The light orange precipitate was filtered off, washed with water and subsequently with n-hexane, and dried in a vacuum oven at 50°C. This solid was purified by column chromatography on silica, using dichloromethane-ethyl acetate (10:1) as an eluent. Evaporation of the solvent produced a solid residue which was recrystallized from benzene to give orange–brown crystals, m.p. 135–136°C; ^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.95 (m, 2H), 7.28 (m, 3H), 7.41 (m, 2H), 7.53 (m, 1H), 7.87 (d, 1H), 8.55 (d, 1H), 9.22 (d, 1H), 10.07 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 108.1, 120.9, 122.6, 123.7, 124.5, 125.9, 126.5, 126.9, 127.6, 128.1, 130.2, 141.6, 154.8, 161.5; m/z (FABMS): 247.3 (M^{+1}).

Preparation of 4-Methoxy-1-(N-phenyl)iminomethylnaphthalene (compound 7).

A solution of 4-methoxy-1-naphthaldehyde (1.86 g; 10 mmol) in absolute ethanol (20 ml) was treated at room temperature with aniline (0.931 g; 10 mmol). The clear solution was refluxed for 3 h. The mixture was cooled and a creamy solid was deposited. The solid was filtered and recrystallized twice from ethanol to give light-cream leaflet shaped crystals; m.p. 84–85°C. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 4.05 (s, 1H), 6.88 (d, 1H), 7.25

(m, 3H), 7.41 (m, 2H), 7.53 (m, 1H), 7.65 (m, 1H), 7.98 (d, 1H), 8.35 (d, 1H), 8.94 (s, 1H), 9.16 (d, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 55.8$, 120.99, 124.4, 125.3, 125.5, 125.7, 128.1, 129.2, 132.6, 139.4, 142.6, 153.1, 158.4, 160.2; m/z (FABMS): 261.2 (M^{+1}).

Spectroscopy and data processing

Absorption spectra at room and higher temperatures (25–70°C) were recorded on a Jasco V-570 UV-Vis-NIR spectrophotometer equipped with a Julabo ED5 thermostat (precision 1°C). Low temperature spectra (100–300 K) were recorded on a home-built spectrophotometer using a specially constructed 6 mm thick cell cooled by a Cryodyne (CTI Cryogenics) model 21 closed-cycle helium cryostat. An ordinary deuterium lamp was used as light source, the signal was detected by a PC2000 Miniature Fiber Optic Spectrometer (Ocean Optics Inc.) and initially processed by OOIBase 32 (Ocean Optics Inc.) software. All spectra were corrected for solvent density changes with the temperature according to a procedure described in the literature.[16] All solvents used were of spectral grade.

The recorded spectral data sets with different tautomeric ratios were processed by the Fishing-Net Algorithm implemented in the MULTIRES software for quantitative analysis of undefined mixtures.[17] The mathematical background of the procedure was described elsewhere.[6,18]

Quantum chemical calculations

Ab initio (HF/6-31G** basis set) calculations were done by the Gaussian 98 program suite.[19] Bulk solvent effects were estimated by single-point calculations using the polarized continuum model (PCM).[20,21] The tautomeric structures shown in Scheme 2 were optimized without restrictions and were then characterized as true minima by vibrational frequency calculations. The dimers and tautomer-solvent complexes were optimized keeping the already optimized structures of the individual tautomers fixed and optimizing only the intermolecular geometry. Considering this fact the obtained stabilization and relative energies are the minimal possible values at this level of theory.

RESULTS AND DISCUSSION

The tautomeric equilibrium of compound **1** in nonpolar solvents without substantial proton donor or proton acceptor properties, was shifted toward enol-like **E**-form[22] due to its substantially lower dipole moment. The tautomeric constant (K_T), defined as [**K**]/[**E**] ratio, in cyclohexane (CH) was estimated to be 0.09.[13] Accord-

1

6

6
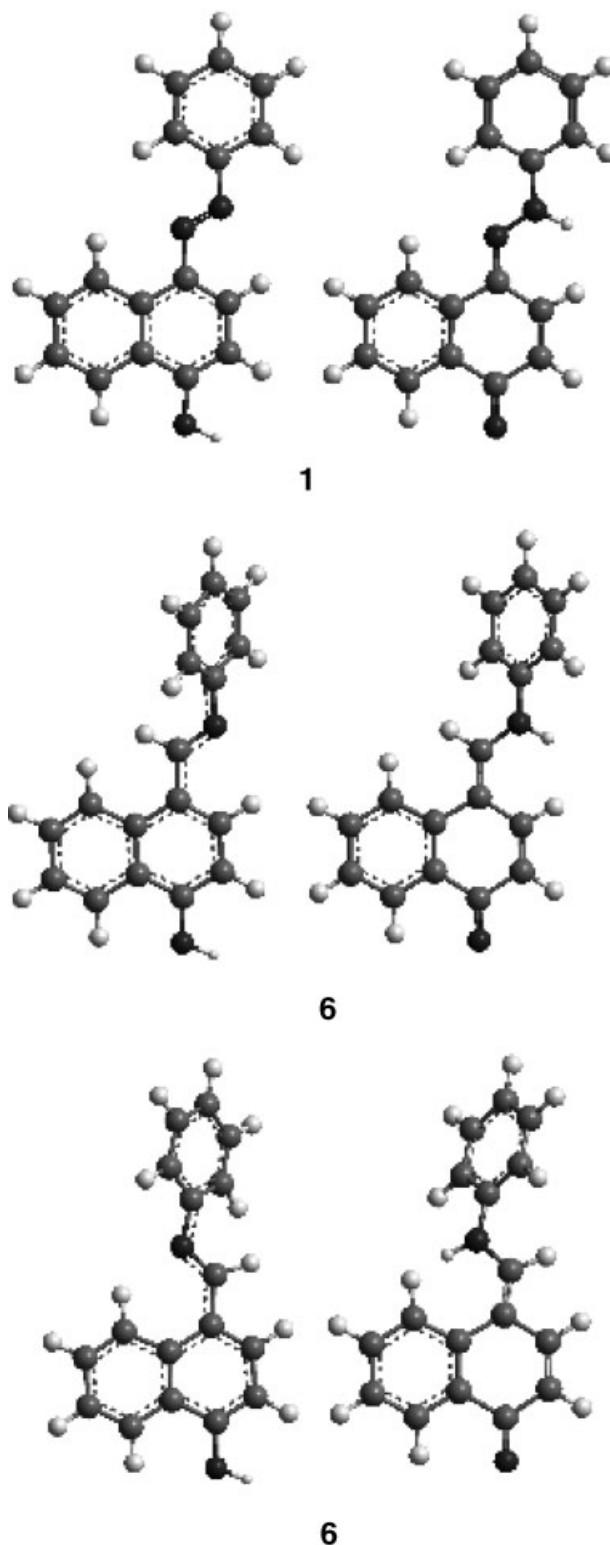
Scheme 2

ingly, a similar situation was expected for **6**, but the recorded spectra in toluene at different temperatures (Fig. 1) show an atypical behavior. Firstly, there is no evidence for the existence of **6E**, which should absorb around 350 nm, where its model compound **7** absorbs.
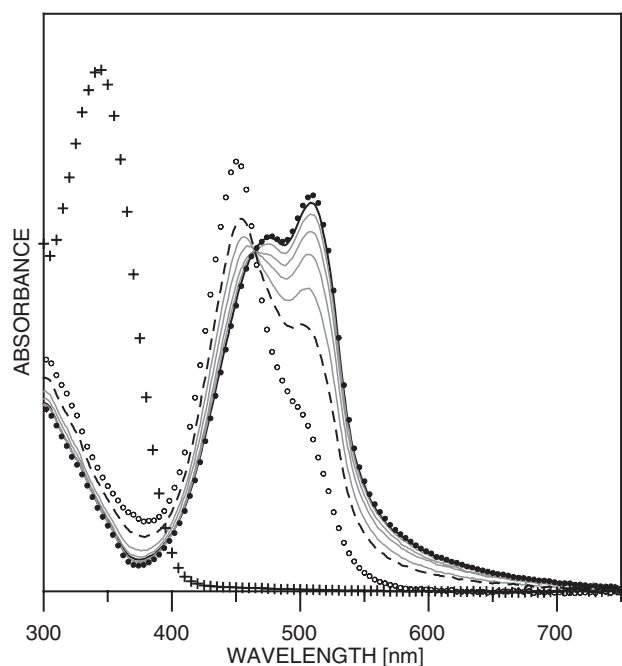
Figure 1. Absorption spectra of **6** ($c = 6.92 \cdot 10^{-5}$ M) in toluene as a function of T: from 25 (black solid line) to 70°C (dashes) along with the calculated spectra of **6K-SD** (filled circles) and **6K-HTD** (empty circles). The absorption spectrum of **7** (+++) is given for comparison

Fig. 1 proved the existence of a two-component mixture. In addition, decrease of the temperature down to 100 K did not cause an essential change in comparison with the room temperature curve.

Quantum chemical calculations (Scheme 2 and Table 1) show a substantial difference in the optimized structures of the tautomeric forms of compounds **1** and **6**. In the case of **1** both tautomeric forms are essentially planar[24] and exist as only one stable isomer (trans) with respect to the N—C$_{naphtalene}$ bond. In the case of **6** each tautomer has two possible isomers with almost the same energy (see Table 1), which is caused by the steric repulsion between the azomethine H-atom and the near naphthalene hydrogen (structure **6′**). This repulsion also exists in **4** and **5**, but in that case it is compensated by the strength of the intramolecular hydrogen bond, and the azomethine group remains in the plane of the naphthalene fragment [9]. In both isomers **6** and **6′** the phenyl ring is twisted, which is typical for the Schiff bases, including **4** and **5**.[9,10] The most important aspect to be noted in the more stable **6** is that the tautomeric H-atom lies out of the plane of the naphthalene ring in the **K** form (the same is observed in **6′**), giving possibilities for out-of-plane interactions. As a result of this behavior two stable dimeric forms of **6K** exist—head-to-tail and sandwich (Scheme 3, Table 1).[25] For **6E** no stable dimers were found in the calculations, which is supported experimentally by the lack of spectral changes in the spectral region of the **E**-form (Fig. 1). This is probably due to the fact that the tautomeric proton remains in the plane of the molecule, which hampers the intermolecular interactions. Although keto form aggregation was reported for Schiff bases derived from hydroxybenzaldehyde,[26,27] no such

Secondly, there are substantial spectral changes in the area of absorbance of the **K**-form with increase of temperature: an increase of the intensity at 450 nm and a decrease at 520 nm. Factor analysis[23] of the curves from

Table 1. Main quantum-chemical (HF/6-31G^b) results

| Structure	E (a.u.)	μ (D)	ΔE (kcal/mol)	
			Definition	Value
1E	−796.6322304	1.18	E$_{1K}$–E$_{1E}$	1.5^c
1K	−796.6297890	3.48		
6E	−780.6703713	2.98	E$_{6K}$–E$_{6E}$	3.8
6K	−780.6641951	6.69		
6E′	−780.6694753	1.36	E$_{6E′}$–E$_{6E}$	0.5
6K′	−780.6640154	6.81	E$_{6K′}$–E$_{6K}$	0.1^d
6K-HTD^a	−1561.3404305	9.01	2. E$_{6K}$–E$_{6K-HTD}$	8.8
			2. E$_{6K}$–E$_{6K-SD}$	7.5
			E$_{6K-HTD}$–E$_{6K-SD}$	1.3
6K-SD^b	−1561.3425661	0		
6E + DMSO^e	−1332.2373853	6.59	E$_{6E}$ + E$_{DMSO}$–E$_{6E+DMSO}$	12.4
6K + DMSO^e	−1332.2272989	6.60	E$_{6K}$ + E$_{DMSO}$–E$_{6K+DMSO}$	9.9
			E$_{6K+DMSO}$–E$_{6E+DMSO}$	6.3
6K-HTD + DMSO^e	−2112.9023340	11.45	E$_{6K-HTD}$ + E$_{DMSO}$–E$_{6K-HTD+DMSO}$	9.2

^{a} Head-to-tail dimmer.
^{b} Sandwich dimmer.
^{c} $K_T = 0.11$ in i-octane.[22]
^{d} The rotation barrier (N–C$_{naphtalene}$) between **6K** and **6K′** is 34 kcal/mol.
^{e} Molecule DMSO added.
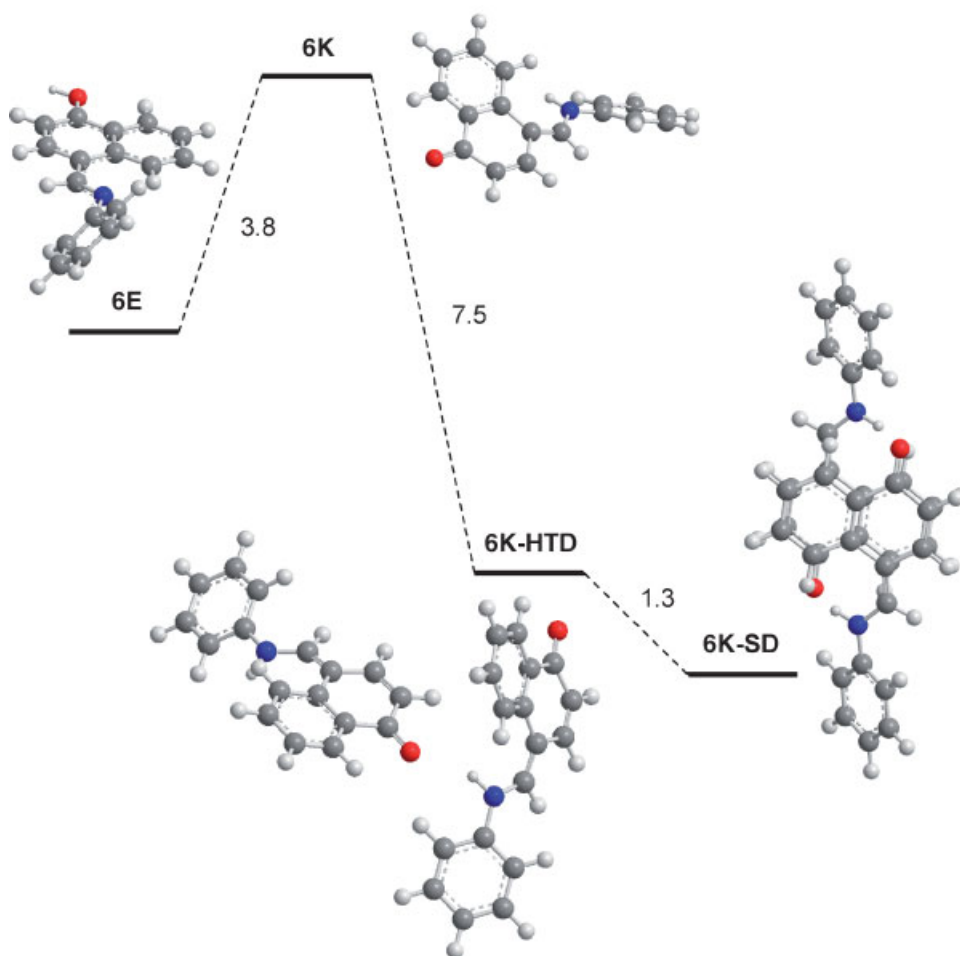
Scheme 3. Energy diagram in gas phase

behavior was observed in the case of derivatives of hydroxynaphthaldehyde, at least not in the concentration range used in UV–Vis spectroscopy.

The energy diagram derived from the quantum chemical calculations (Scheme 3) explains in a reasonable way the observed spectral changes in Fig. 1. Obviously they correspond to an equilibrium between dimers with relatively close lying energies. The forms **6E** and **6K** are not present in the solution because if **6K** were present it would be transformed to the less polar and more stable (by 3.8 kcal/mol) **6E** with an absorption maximum at ∼350 nm. In support of this we could mention that in compound **1** the energy difference between the tautomeric forms was calculated (Table 1) to be 1.5 kcal/mol in favor of **1E** and in that case the content of the **1K** was less than 10%.

The spectral data from Fig. 1 were analyzed using MULTIRES software,[6] which gives the individual spectra of the dimers as well as the molar fractions as function of temperature. As can be seen from Fig. 1, with increase of the temperature the equilibrium shifts toward **6K-HTD** (to 68% at 75°C), but at room temperature the less polar **6K-SD** prevails (96%) although the quantum chemical calculations in toluene (Scheme 4, Table 2) show that both forms are almost equally stable. Hence, at lower
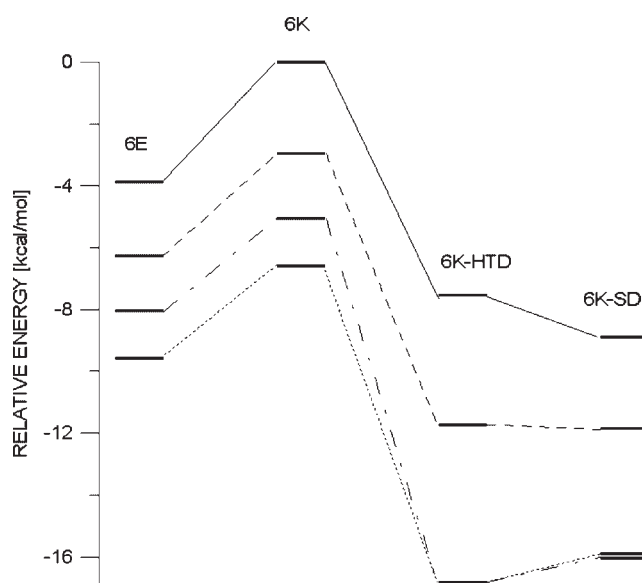
Scheme 4. Energy diagram in various bulk solvents (PCM model): solid line – gas phase, dashes – toluene, dot-dashes – DMSO, dots – acetonitrile. The values are collected in Table 2

Table 2. Relative energies (**6K** in gas phase taken as zero point) in various solvents (PCM)

Solvent	Structure			
	6E	**6K**	**6K-HTD**	**6-SD**
Gas phase	−3.8	0.0	−7.5	−8.8
DMSO	−8.0	−5.0	−16.8	−16.0
Acetonitrile	−9.5	−6.5	−16.8	−15.9
Toluene	−6.2	−2.9	−11.7	−11.8
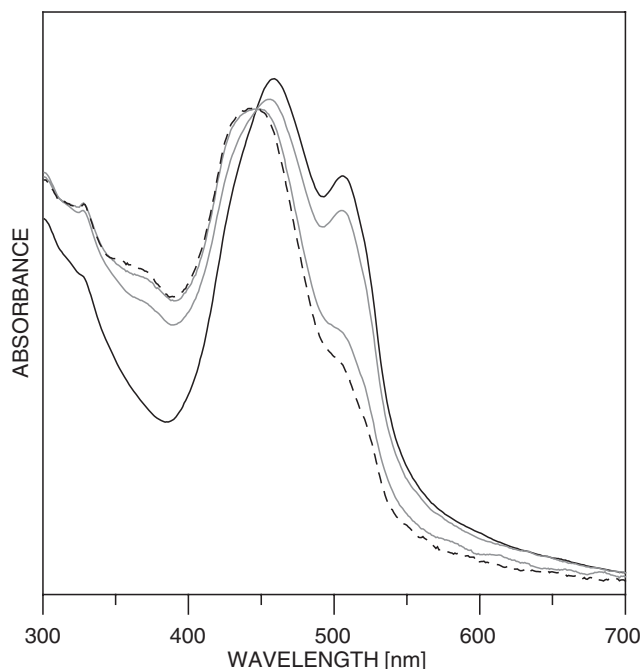
Figure 2. Absorption spectra of **6** in acetonitrile with different concentrations (keeping c.l = constant): from $2.5 \cdot 10^{-4}$ M (solid line) to $5.5 \cdot 10^{-5}$ M (dashes)

temperature it is expected that only **6K-SD** exists, which is in agreement with the lack of spectral changes below 270 K. The known molar fractions of the dimers lead to an estimate of the thermodynamic parameters for the equilibrium **6K − HTD ⇌ 6K − SD**, as follows: $\Delta H = -5.62$ kcal/mol, and $\Delta S = -16.6$ cal/mol·K.
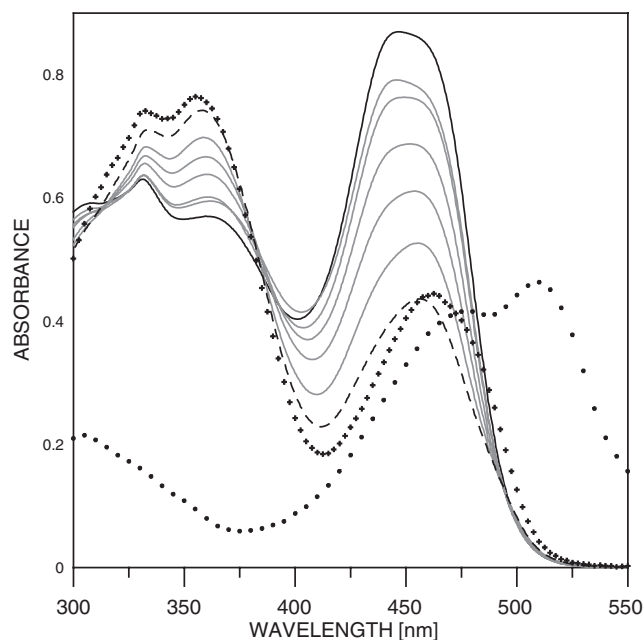
The absorption spectra of **6** in toluene at room temperature are concentration independent (full transformation to the dimers), but in polar solvents the relative stabilities of the dimers and monomers (**6E** and **6K**) might change as suggested by Scheme 4. It is clearly seen from Fig. 2 that in acetonitrile the dimers (and especially **6-SD**) are partially converted to monomers. As a result the spectra are concentration dependent and absorption bands of **6E** (∼360 nm) and **6K** (∼430 nm) can be seen. Acetonitrile is a polar solvent with relatively weak proton donating and substantial proton acceptor properties,[11] which leads on one hand to stabilization of the more polar **6-HTD** (Scheme 4), but on the other to further

stabilization of the individual tautomers through specific interactions with the solvent. It is difficult from Fig. 2 to judge what the ratio is between the dimers since their spectra are strongly overlapping with the **6K** absorption maximum, but the existence of isosbestic point clearly shows that an overall equilibrium exists[28] in the form:

$$26E \rightleftharpoons 26K \rightleftharpoons 6K − HTD \rightleftharpoons 6K − SD$$

However, this equilibrium scheme does not allow the data of Fig. 2 to be processed as a four component mixture, but rather as a two component one (monomers-dimers), since the tautomeric and dimer-dimer equilibrium constants are concentration independent. The results give for the most concentrated solution a value of 14% for the monomer (**6E** + **6K**) and 86% for the dimers. The use of the individual spectra of both dimers in toluene gives one an estimate of 20% for **6K-HTD** and 66% for **6-SD**, that is, the polar solvent shifts the equilibrium in accordance with Scheme 4. In the most diluted solution the percentage of the monomeric tautomers rises to 28%.

Concentration effects were also observed in DMSO and acetone, where the sandwich dimer was totally absent. From Fig. 3, in pure DMSO, the lack of absorption for **6K-SD** is evident. Increase of the toluene content in the binary solvent leads to two effects: increase of amount of **6E** (the less polar tautomer) and rise of the maxima of the dimers (especially to **6K-HTD**). This means that the initial quantity of the **K**-form (∼430 nm), formed as a result of the proton acceptor action of DMSO, is now gradually transformed to both **K**-dimers and enol

Figure 3. Absorption spectra of **6** ($c = 7.9 \cdot 10^{-5}$ M, $l = 1$ cm) in DMSO/toluene solvent mixtures as follows (in volume %): 100% DMSO (solid black line), 10% DMSO (dashes), 1% DMSO (++++), 100% Toluene (filled circles). The curve in toluene is underestimated due to the low solubility of **6**
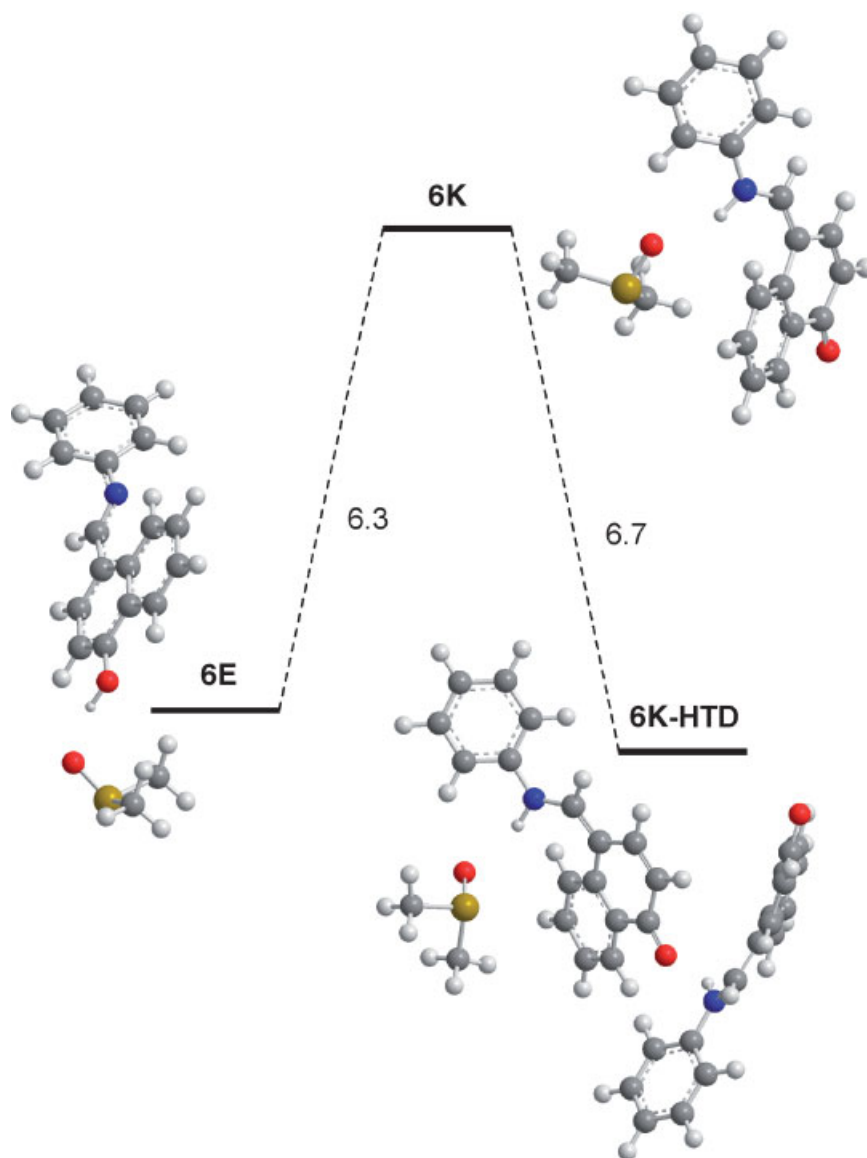
Scheme 5. Energy diagram in DMSO

tautomer as expected from the energy diagrams (Schemes 3 and 5). Comparison between the curves in 100% toluene and 99% toluene shows that the dimer equilibrium crucially depends on specific solute–solvent interactions.

The effect of the temperature in DMSO is demonstrated in Fig. 4. Taking into account the spectral changes in Fig. 3 a three-component equilibrium ($2\mathbf{6E} \rightleftharpoons 2\mathbf{6K} \rightleftharpoons \mathbf{6K} - \mathbf{HTD}$) can be assumed. Obviously temperature elevation leads to a decrease of the dimer and increase of **6E**. However, from the spectral curves it is difficult to find visual confirmation for these changes. The curves were processed using the Fishing-Net Algorithm[6,18] and the individual spectra of the species were estimated, along with the molar fractions. It was found that at room temperature the amounts of **6E**, **6K**, and **6K-HTD** are as follows: 10%, 42%, and 48%, which yields values of $K_T = 0.23$ and $\log K_D = 5.6$.[29] At 70°C the **6E** and **6K** amounts increase to 23% and 46%,

respectively. The molar fractions as a function of the temperature allowed estimation of ΔH and ΔS for both these processes:

$$\mathbf{6E} \rightleftharpoons \mathbf{6K} : \Delta H_T = 3.47\,\text{kcal/mol and}\,\Delta S_T$$
$$= 8.89\,\text{cal/mol} \cdot \text{K}$$

$$2\mathbf{6K} \rightleftharpoons \mathbf{6K} - \mathbf{HTD} : \Delta H_D$$
$$= -9.88\,\text{kcal/mol and}\,\Delta S_D = -7.72\,\text{cal/mol} \cdot \text{K}$$

As can be seen, both processes are really competitive and the enthalpy values are in reasonable agreement with the relative energies obtained by the quantum chemical calculations.

The individual spectra of **6K** and **6E**, shown in Fig. 4, need some additional comment: in compounds **4** and **5** the intensity of the keto form is about 1.5–2 times higher than that of the enol form.[9,10] In the case of **6** they are
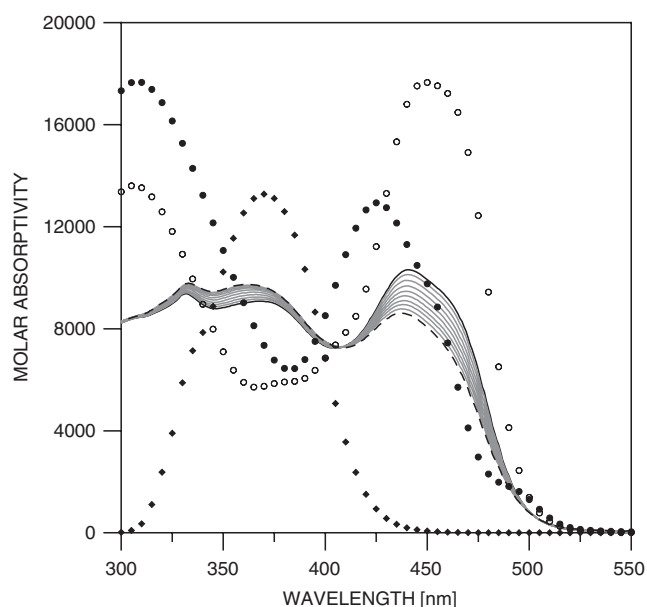
Figure 4. Absorption spectra of **6** in DMSO ($c = 6.4 \cdot 10^{-5}$ M, $l = 1$ cm) at different temperatures: from 25°C (black solid line) to 70°C (dashes). Calculated spectra of the **K**- (filled circles) and **E**- (rhombs) forms and the head-to-tail dimer (empty circles)

approximately the same, which could be associated with the limited planarity of **6K**.

Acknowledgements

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28. If a system: **6E ⇌ 6K**, **26K ⇌ 6K – HTD**, **26K ⇌ 6K – SD** were assumed, different concentration effects would exist in these two aggregation processes and there should not be an isosbestic point.
29. Defined as: $K_D = (x_{VIK–HTD})/(2 \cdot c_o \cdot x_{VIK}^2)$, where x are the molar fractions and c_o is the total solute concentration.