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TAUTOMERISM AS AN ELEMENTAL MECHANISM FOR SIGNAL TRANSFER IN MOLECULAR DEVICES

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The dissertation contains **190** pages, **79** figures, **15** tables, **37** schemes and **193** literature sources.

The dissertation was discussed and proposed for defense of a meeting of the Colloquium on "*Functional Materials, Computer Modeling and Technologies*" at the Institute of Organic chemistry with the Centre of phytochemistry - BAS (Protocol № /……..).

Scientific Jury:

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The thesis defense will consist on …… 2020 from …… ..h. at the Institute of organic chemistry with the Centre of phytochemistry - BAS, Acad. G. Bonchev str, bld. 9, Hall 111.

The thesis materials are available to the interested in the office of IOCCP-BAS, Acad. G. Bonchev str., bld. 9, r. 206.

INTRODUCTION

The improved efficiency of electronic devices is largely a result of the miniaturization of their components, which will eventually reach the inevitable physical limit. One of the possibilities for future development is the production of molecular electronic components, where the use of single molecules is the limit of miniaturization. The concept of molecular device design is based on the idea of using single molecules as "hardware" elements (wires, switches, logic gates, rectifiers, etc.), which can then be assembly into working devices using chemical bonding and/or nonbonding interactions.

The switch is one of the simplest components of an electrical circuit. In molecular electronics, this term is used to define a molecular "structure" capable of reversibly switching between two or more stable states in response to external stimuli, such as changes in pH, light, temperature, electric current, microenvironment, or in the presence of ions. In addition, this term can be used to denote a structure that transmits a signal in response to changes in its environment.

The main requirement in the design of molecular switches is to provide fast and clean interconversion between structurally different molecular (*on*- and *off*-) states. The tautomerism coud be a possible elemental process, because the change in the tautomeric state is accomplished by a fast proton transfer reaction between two or more structures, each of them with clear and different properties.

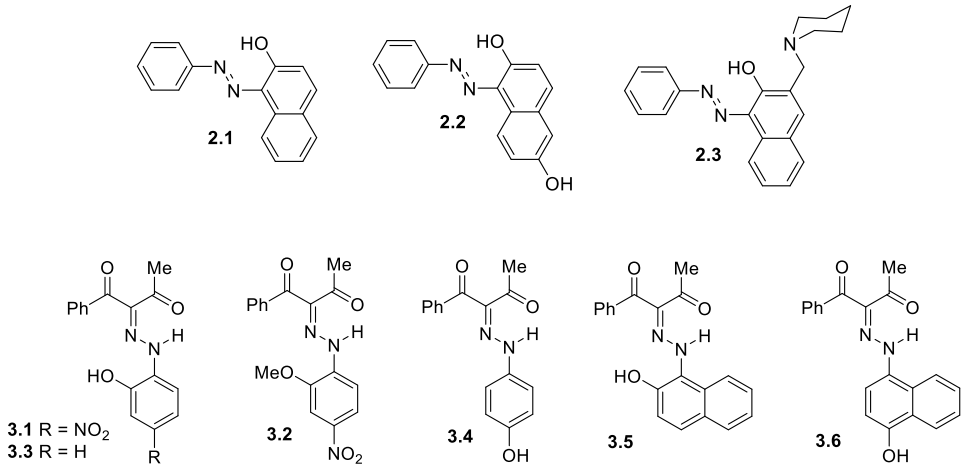
One of the possible promising platforms for the development of switching systems are systems with controllable tautomerism as a rotary switches (molecules, defined parts: "rotor-axis-stator") or molecular cranes (called "small molecules with robotic arms") that deliver cargo from one part of the molecule to another). The action is based on intramolecular, acid - catalysed, proton transfer. In the rotary switches exhibit three major weaknesses, which have to be solved in order to achieve real applicability: a) inability to provide conditions for pure isomeric forms in solution; b) slow rotation of the rotor; and c) uncontrollable rotation of the stator.

AIM AND TASKS

In the present dissertation the attention is focused on the research of two types of compounds - azo dyes (**2.1-2.3**), with possible controllable tautomerism and rotary switches (**3.1-3.6**), in which the influence of the additional tautomeric OH group is considered

(compound **3.2** is chosen as model) and the change of the stator, on the rotation of the molecular rotor.

The aim of this dissertation is to investigate the possible tautomerism and its effect on the switching action of the following dyes:



In order to achieve this goal it is necessary to solve the following **tasks**:

1. Using absorption UV-Vis spectroscopy to study the spectral behavior of 2.1-3.4 in different solvents to assess the position of the tautomeric equilibrium;

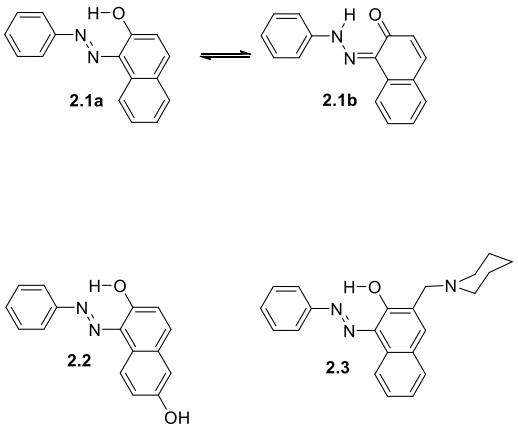
2. Using absorption UV-Vis spectroscopy to investigate the possibilities for controlled displacement of the tautomeric equilibrium under the influence of acids, bases and water (at 2.1-3.4);

3. To explain the observed spectral changes using quantum chemical calculations.

RESULTS AND DISCUSSIONS

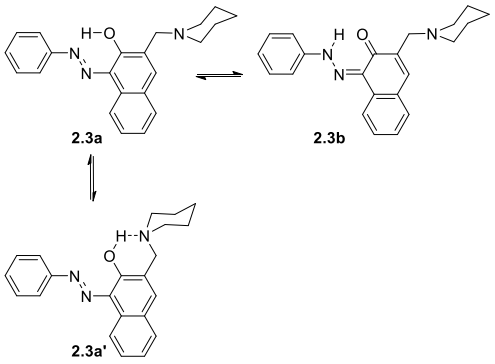
1. Molecular switching in structurally modified Sudan I

Aromatic azo derivatives are one of the largest and the most important classes of colorants. Their practical and theoretical importance has been reflected in textiles, food, paper printing, nonlinear optical devices and liquid crystalline displays. Most of the azodyes are tautomeric ones, and therefore the study of their tautomerism is of practical and fundamental significance, beacause they can be used to develop new systems for molecular electronics.



Scheme 1. *Tautomeric equilibrium in **2.1** and structures of the investigated compounds **2.2** and **2.3.** .*

For example, Sudan I (1-(phenyldiazenyl)naphthalen-2-ol, **2.1**), which is used as a food coloring, exists as a tautomeric mixture in solution. Previous studies have shown [1,2] that due to existence of an intramolecular hydrogen bond, the solvent polarity plays an important role - in non-polar solvents (such as *i*-octane and tetrachloromethane) **2.1a** (enol, azo) form predominates, while in more polar solvents (like methanol) the opposite effect is observed and form **2.1b** (keto-hydrazo) prevails (**Scheme 1**). For this reason, it was interesting investigate how structural modifications (additional OH group **2.2** or sidearm (piperidine unit) **2.3**) in **2.1** can influence its tautomerism (**Scheme 2**). Compounds **2.2** and **2.3** are new and have not been studied until now.



Scheme 2. *Possible equilibria in **2.3**.*

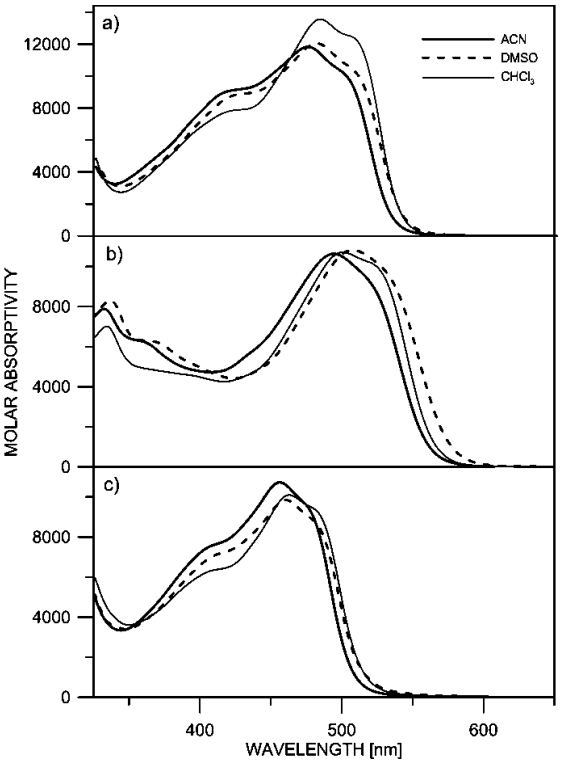


Fig. 1. *Absorption spectra of a) **2.1**, b) **2.2** and c) **2.3** in various solvents.*

The absorption spectra of compounds **2.1**–**2.3** (**Fig. 1**), clearly show the presence of the tautomeric mixture in solution, irrespective of the solvent used, with absorption maxima of the enol form in the range 410–430 nm (420 nm for **2.1**, 430 nm for **2.2** and 420 nm for **2.3**)[1] and red shifted keto form absorbance around 500 nm. It is clearly observed from **Fig. 1** that the quantity of the enol form in **2.1** and **2.2** decreases from acetonitrile to chloroform and DMSO. This conclusion is supported by the NMR results.

The absorption spectra of **2.3** are similar as shape of the curve and position of the absorption maxima as those in **2.1**, proving that the sidearm chain does not influence the position of the tautomeric equilibrium.

The presence of the tautomeric mixture in **2.2** and **2.3** can be confirmed by the addition of water. As shown on **Fig. 2**, in both compounds, the addition of water leads to a decrease of the maximum of the enol form and correspondingly increase of the band belonging to the keto tautomer. If only the keto form is presented in solution, no spectral shifts could be observed. In **2.2**, after the addition of water, a complete shift of equilibrium to the keto tautomer is observed.

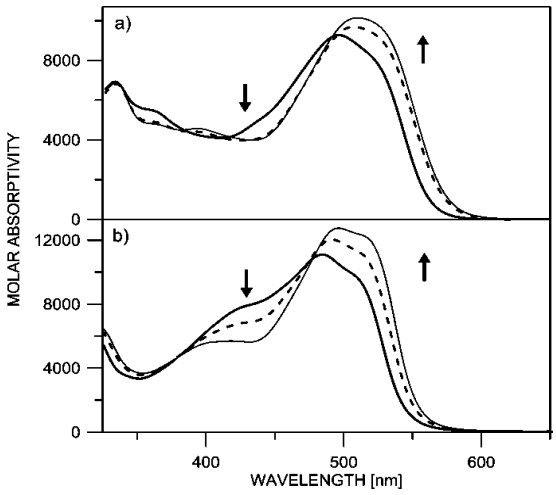


Fig. 2. *Absorption spectra of a) **2.2** in ACN and b) **2.3** in DMSO, upon water addition: (— without water addition; — final spectrum upon water addition).*

[1] *Detailed information can be found in the second derivative spectra.*

The coexistence of the tautomers in the studied compounds is confirmed by the theoretical calculations as well. The moderate energy gap between the enol and the keto tautomeric forms, suggests that compound **2.1** always exists as a tautomeric mixture (**2.1a** and **2.1b**, **Fig. 3**, left) in solution as it is actually observed.

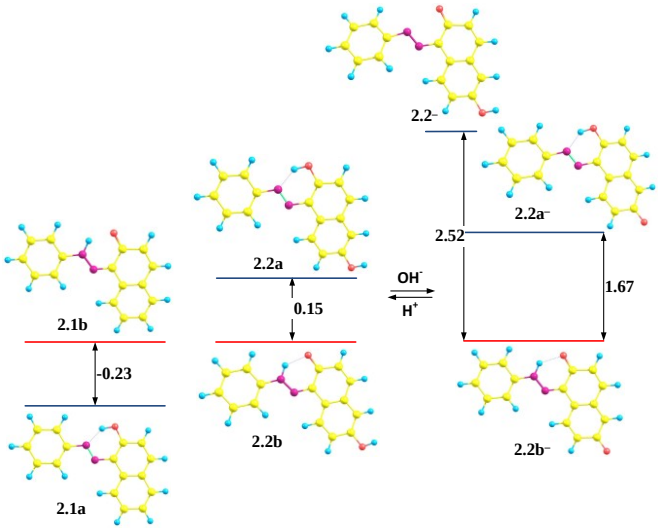


Fig. 3. *Relative energies (M06–2X/TZVP, in kcal/mol) in ACN of the tautomers of **2.1** (left), neutral tautomers (centre) and deprotonated forms of **2.2** (right).*

The implementation of an additional non-tautomeric hydroxyl group (**2.2**) shifts the tautomeric equilibrium towars the keto form **2.2b** (**Fig. 3**, center), however the energy difference between the two forms remained very small and does not substantially change the situation.

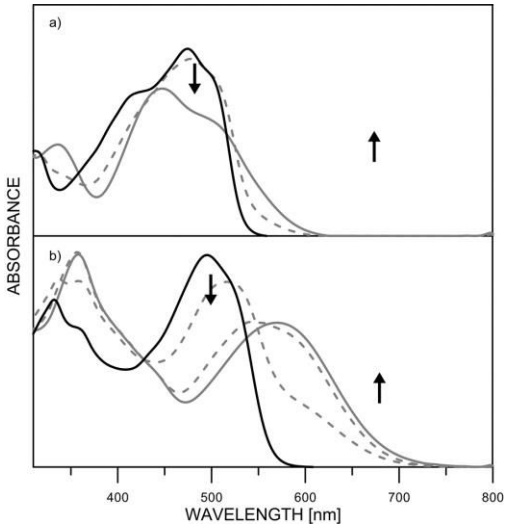


Fig. 4. *Absorption spectra of a) **2.1** and b) **2.2** in ACN, upon base addition: (— without base addition; — final spectrum upon base addition).*

Equilibrium can be affected by the addition of a base, as compound **2.2** has two OH groups that can be deprotonated: (a) loss of the tautomeric proton giving non-tautomeric anion **2.2**$^-$; (b) deprotonation of the additional OH group, which could affect the tautomeric equilibrium (**2.2a**$^-$ vs **2.2b**$^-$, **Fig. 3**, right). As seen from the calculations, the anion **2.2**$^-$ is energetically unfavourable, which means that the deprotonation occurs at the additional OH group. As a result, the tautomeric equilibrium between **2.2a**$^-$ and **2.2b**$^-$ is almost fully shifted to the keto tautomer **2.2b**$^-$ with an energy gap of 1.67 kcal/mol.

From **Fig. 4**, which compares the deprotonation of **2.1** and **2.2**, is observed that the addition of base to the solution of **2.2** leads to a decrease in the keto form maximum at 500 nm and the appearance of a new band at 600 nm. This additional band, which is not observed at **2.1**,

indicates that at **2.2** the additional hydroxyl group is deprotonated, as predicted by theoretical calculations.

Compound **2.3** possesses an option for competitive hydrogen bonding in the enol form, where the tautomeric proton interacts either with the nitrogen from the azo group (**2.3a**, **Scheme 2**), or with the nitrogen atom from the piperidine unit (**2.3a'**). As seen from **Fig. 5** left, the structure **2.3b** is preferred.

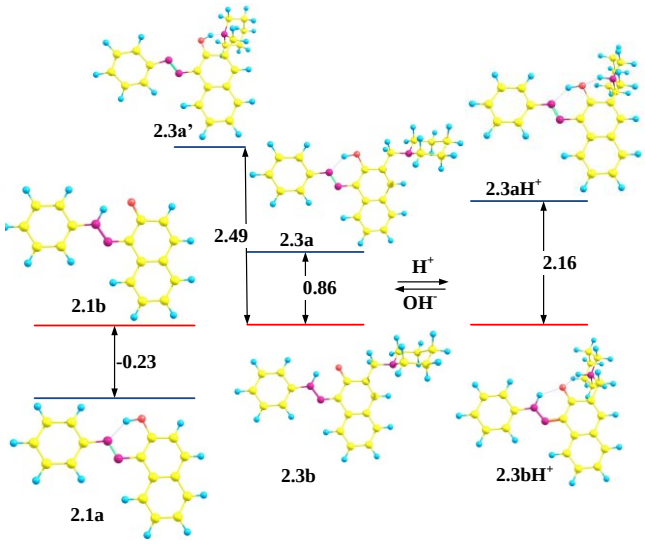


Fig. 5. *Relative energies (M06–2X/TZVP, in kcal/mol) of the neutral tautomers of **2.3** (centre) and the protonated species in ACN (right).*

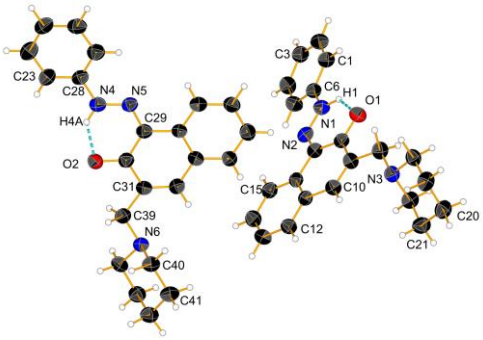


Fig. 6.*Crystal structure of **2.3**.*

Actually, there is no competition for the tautomeric proton, between the nitrogen atom from the chromophore backbone and the nitrogen atom from the piperidine unit (energy gap of 2.5 kcal/mol between **2.3a'** and **2.3b**). Although the overall effect of the existence of the sidearm stabilizes the keto tautomer **2.3b** (in comparison with **2.1**), a substantial amount of **2.3a** could be expected in solution as the energy gap of 0.86 kcal/mol suggests.

Obviously, the sidearm acts as a simple alkyl substituent, because when the whole sidearm is replaced by a methyl group the energy gap between tautomers **2.3a** and **2.3b** remains almost the same - 0.7 kcal/mol. The X-ray analysis of compound **2.3** (**Fig. 6**), as will be shown below, clearly indicates that compound **2.3** exists as the keto form **2.3b** in the solid state and the nitrogen atom from the piperidine unit is far from the tautomeric backbone, as predicted by the theoretical calculations (**Fig. 5**). Equilibrium in **2.3** can be affected by the addition of acid. As seen from **Fig. 5** right, the acid addition is a suitable stimulus for switching the

tautomeric equilibrium to the pure keto form, because the protonated piperidine nitrogen atom, participates in additional intramolecular hydrogen bond formation, which further stabilizes the keto form, shifting the equilibrium fully towards the keto form.

As seen from **Fig. 7**, the addition of acid leads to gradual shift of the tautomeric equilibrium in **2.3** to the keto form, which can be monitored with the decreasing absorption maxima of the enol form and raise of the red shifted absorption of **2.3b**. The process is reversible upon base addition, which shows that the tautomerism in **2.3** can be controlled. The calculated positions of the absorption maxima of the corresponding enol and keto forms of the neutral compounds collected in **Table 1** logically follow the spectral changes in solution. The calculated absorption maxima of the enol and keto forms respectively in compounds **2.1** and **2.3**, coincide, as observed by the experiment. In case of **2.2**, the calculated absorption maximum of the enol form is slightly red shifted, compared to **2.1** and **2.3**, and the position of the keto form absorbance is not affected.

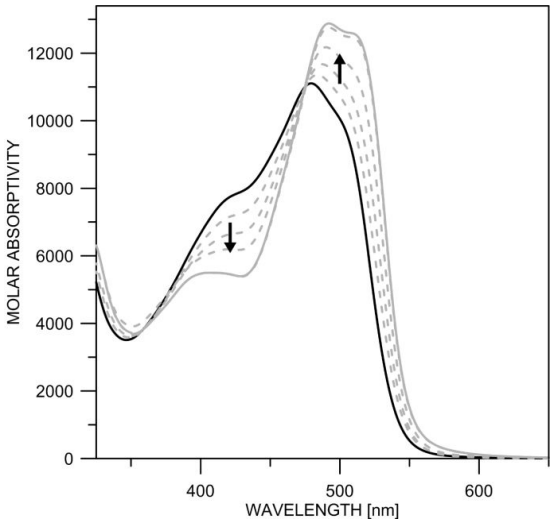


Fig.7. *Absorption spectra of **2.3** in ACN, upon acid addition: (— without acid addition; — final spectrum upon acid addition).*

Table 1. *Predicted absorption maxima of the neutral forms of **2.1**–**2.3** and ionized forms of **2.2** and **2.3** in acetonitrile (see **Fig. 1**).*

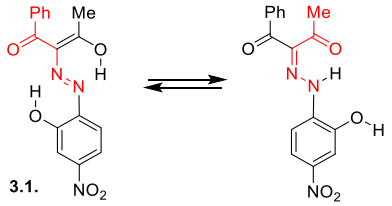
Neutral forms			**Ionized forms**	
Compound	λ_{max}, f* enol	λ_{max}, f keto	λ_{max}, f enol	λ_{max}, f keto
2.1	374; 0.63	405; 0.61	-	-
2.2	390; 0.51	405; 0.61	537; 0.13	569; 0.28
2.3	376; 0.64	404; 0.62	372; 0.63	418; 0.63

**f – oscillator strength.*

As seen from **Table 1**, the deprotonation of **2.2** leads to red shift in the maxima of both enol and keto tautomers, while the protonation of **2.3** does not bring substantial effect, which is logical having in mind that the protonated nitrogen atom from the piperidine unit is not conjugated to the chromophore system.

2. Molecular rotary switches

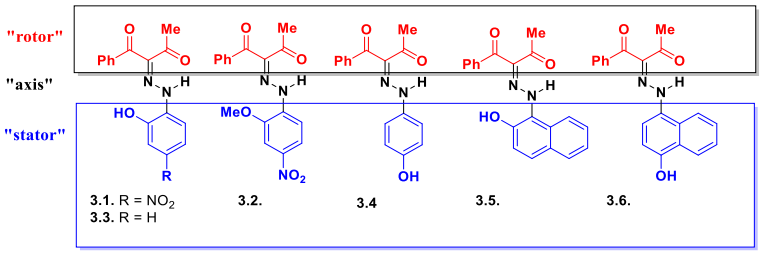
It is known from the literature (*Mahmudov et al. [3,4]),* that 2-(2-(2-hydroxy-4-nitrophenyl) hydrazono)-1-phenylbutane-1,3-dione **3.1** is an interesting example of a potential rotary switch because exists in the form of a tautomeric mixture between enol-azo and hydrazo forms (**Scheme 3**).



Z-anol-azo form hydrazo form

Scheme 3. *Tautomeric equilibrium in **3.1**.*

Critically analyzing the already existing results for **3.1** and providing new experimental and theoretical data, we would like to explain the effect of the additional OH group (**3.3-3.6**) in the stator on the tautomeric properties of this system (**Scheme 4**). Discussion was facilitated by the use of model compound **3.2**, in which the OH group was displaced by methoxy. It is well-known that the azo-hydrazo tautomerism is solvent dependent even when the proton is transferred through an intramolecular hydrogen bond. Therefore the change in the absorption spectra, when the solvent is changed, is the first sign of existence of a tautomeric equilibrium. In the case of **3.1** spectral changes are not observed (λ = 420 nm) in most solvents, only in strong proton-acceptors (such as DMSO and DMF) an additional red shifted band appears (λ = 550 nm) (**Fig.8**). As it is known from the literature that phenols are easily deprotonated in solution, especially if a strong electron-acceptor substituent is present in the aromatic ring, as is the case with compound **3.1**, it was necessary to confirm whether the observed long-wavelength peak was at the deprotonated form. As seen from **Fig. 9** the addition of acid in DMSO leads to disappearance of the band at 550 nm, while the deprotonation with base strengthens it. Spectral data clearly show that there is no evidence of a tautomeric equilibrium in **3.1** for the solvents used, and the compound most likely exists as a mixture of neutral and deprotonated form, depending on the solvent and concentration. The spectra of **3.2** are solvent and concentration independent and no additional band is seen in the solvents listed in **Fig. 8**. The deprotonation of **3.2** in DMSO has not been observed at the same basicity of the solution as in **3.1**.



Scheme 4. *Structure of investigate compounds.*

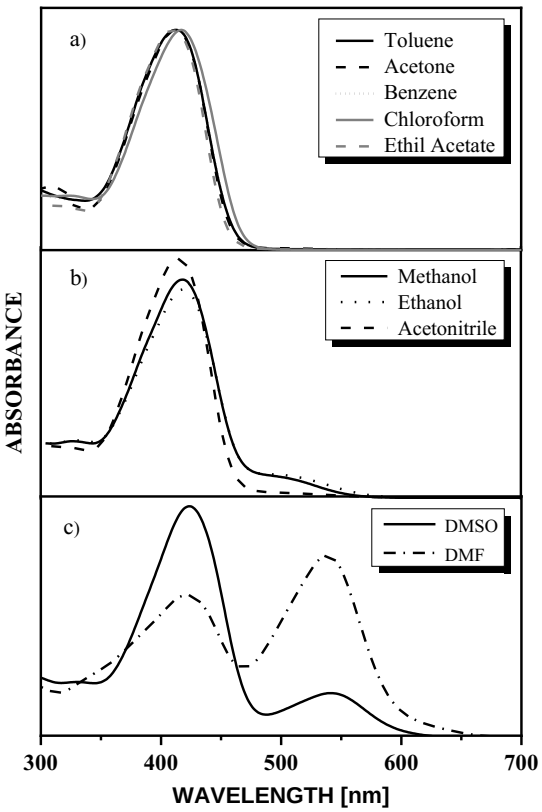


Fig. 8. *Absorption spectra of **3.1** in different solvents at the same concentration.*

Both compounds **3.1** and **3.2** have been investigated by NMR in a series of solvents. The most important solvent is DMSO-d_6 because the results can be compared with those shown in the literature [3].

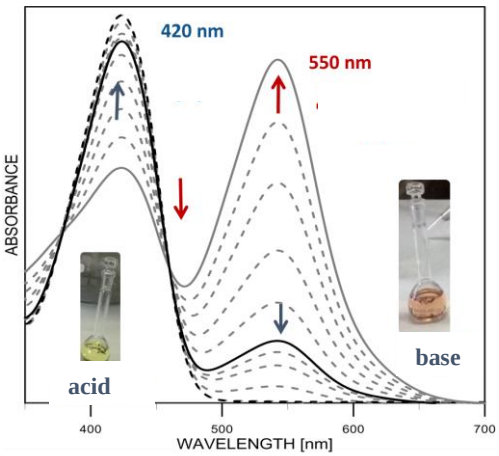


Fig. 9. *Absorption spectra of **3.1** in DMSO upon addition of acid and base.*

From both the ^1H *NMR* spectra of **3.1** and **3.2** in DMSO-d_6 (**Fig. 10-11**), it is obvious that two species are present in different ratios in the following called major and minor form. A comparison of data for **3.1** and **3.2** indicates very similar structures. The NH and phenolic OH chemical shifts for the major species in DMSO-d6 are found at 14.14 ppm and 11.52 ppm; from the minor species (11.70 ppm) and OH resonance of the minor species (11.34 ppm). The apparent contradiction between the *UV-Vis* data (single neutral compound) and *NMR* results (two neutral components) can be explained by the theoretical calculations, performed in DMSO as media. After optimization of all possible tautomeric structures and their conformational isomers, it is predicted, that tautomer **3.1(I)** is substantially more stable and the energy difference to the nearer as stability forms (**3.1**(**III**) and **3.1**(**IV**)) excludes their existence in measurable amounts in solution (**Table 2**).

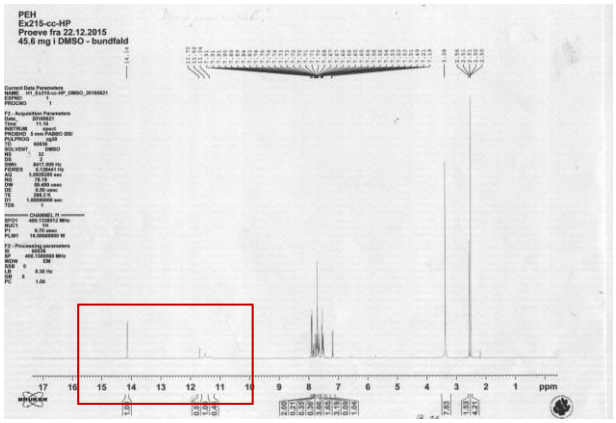


Fig. 10. *^{1}H NMR spectrum of **3.1** in DMSO-d_6.*

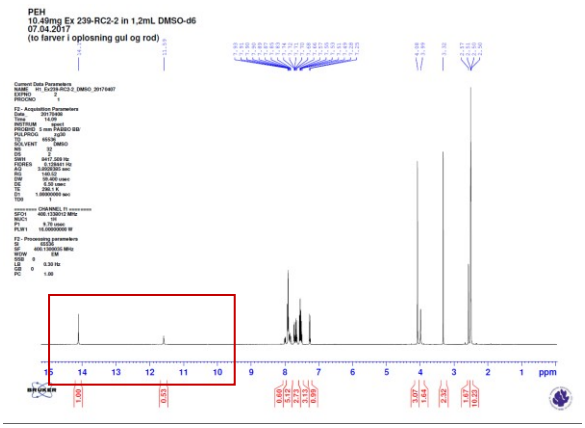
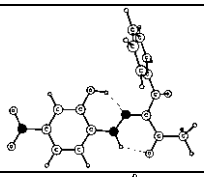
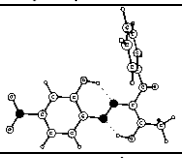
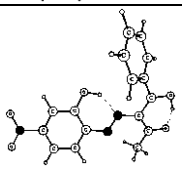


Fig. 11. *^{1}H NMR spectrum of **3.2** in DMSO-d_6.*

Table 2[2]**.** *The most stable isomers of **3.1** in DMSO and their predicted absorption maxima (as position* and oscillator strength).*

	Structure	ΔE [kcal/mol]	Dipole moment [D]	Long-wavelength absorption	
				λ_{max} [nm]	*f*
3.1(I)		0.00	6.0	357 355	0.056 0.735
3.1(III)		6.32	6.0	367	0.704
3.1(IV)		7.42	5.4	442 354	0.012 0.590

** Taking into account that TD-M06-2X systematically underestimates the band positions these values should not be considered as absolute values, but as indication of a spectral shift.*

All three of these most stable structures, according to theoretical calculations, have close dipole moment values and are stabilized by an intramolecular hydrogen bond, which means that changing the solvent as a medium (PCM model) will not significantly change the relative stability.

[2] *All other tautomeric structures are given in detail in the dissertation.*

Even if there are specific interactions with the solvent, which the solvation model does not take into account, structures **3.1(I)**, **(III)** and **(IV)**, could be inert to proton-acceptor solvents and with similar possibility to interact with proton-donor solvents. Therefore, assuming that the order of relative stability is the same in the used solvents and in DMSO (**Fig.8)** one should look not for tautomers, but for isomers from the group of **3.1(I).**

In **Fig. 12** there are four isomers with relative energy, which suppose that they are presented in solution. In order to simplify the further discussion, these four structures will be referred to as **E** and **Z**/ **E'** and **Z'**. As seen **3.1E** should be dominating (~75%) with substantial contribution of **3.1E'** (~20%), followed by minor amounts of **3.1Z'** and **3.1Z**. A careful consideration allows grouping these structures based on their ability to interact with DMSO. On one side in **3.1Z** and **3.1E** the OH proton is involved in an intramolecular hydrogen bonding, which makes it not

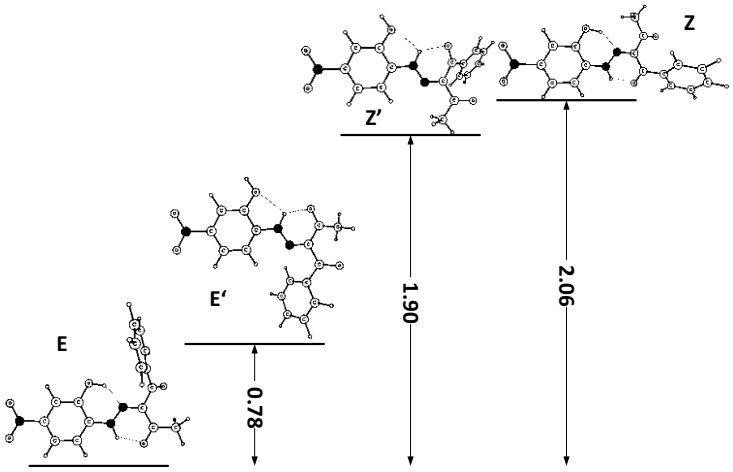


Fig. 12. *Relative energies (in kcal/mol units) of the most stable isomers of **3.1(I)** in DMSO. The corresponding values in other solvents are: 1.13, 2.73, 3.05 (toluene); 0.94, 2.44, 2.54 (chloroform); 0.79, 1.93, 2.07 (acetonitrile); 0.79, 1.94, 2.08 (methanol).*

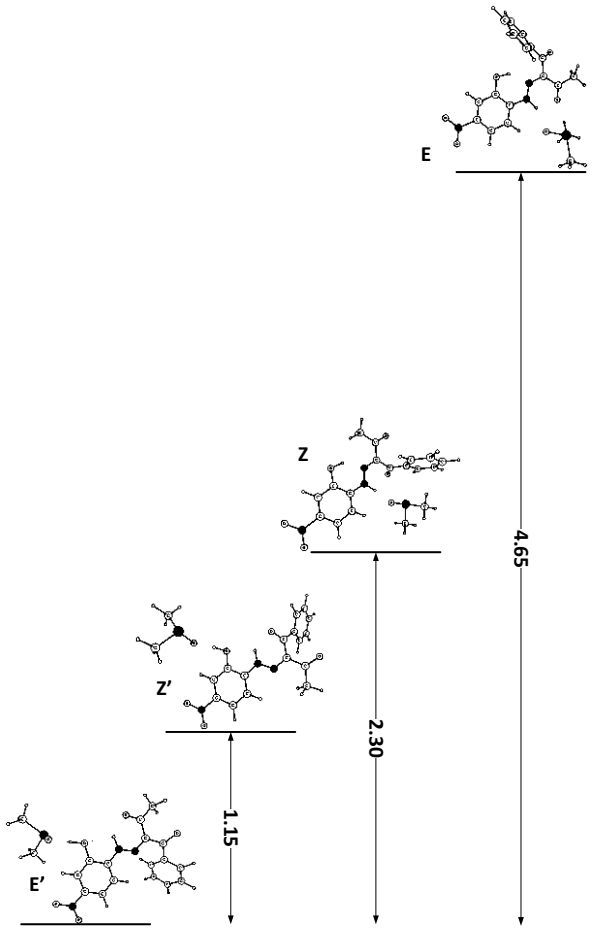


Fig. 13. *Relative energies (in kcal/mole units) of the most stable isomers of **3.1(I)** in DMSO taking specific interactions into account.*

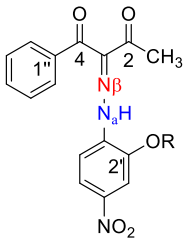
accessible for interaction with the solvent. On the other side in the couple **3.1Z'/3.1E'** the proton can interact with DMSO, which could lead to further stabilization The actual effect of taking the specific solute-solvent interactions into account by adding a DMSO molecule in the DMSO solvent field is shown in **Fig. 13**. As a result the **3.1E'** conformer is strongly stabilized, followed by **3.1Z'** (10-15%). The remaining two could not be presented in a DMSO solution.

Table 3. *Theoretically predicted absorption bands* of the most stable conformational isomers of **3.1** in DMSO.*

Conformer	Dipole moment [D]	S_0-S_1		S_0-S_2	
		λ_{max} [nm]	*f*	λ_{max} [nm]	*f*
3.1E	6.0	357	0.055	355	0.735
3.1E'	2.9	365	0.032	353	0.865
3.1Z'	4.1	369	0.236	356	0.782
3.1Z	7.0	365	0.470	355	0.516
3.1E$^-$, OH deprotonated		478	0.547		
3.1(E')$^-$, OH deprotonated		472	0.475		
3.1(E')$^-$,NH deprotonated				419	0.944

** Here it should be taken into account that the used theory M06-2X/TZVP systematically underestimates the positions of the bands. The values have to be considered not as absolute ones, but more as a qualitative tendency.*

From the view point of *UV-Vis* spectroscopy the structures **3.1E'** and **3.1Z'** could hardly be distinguished. The conjugated system is the same and, correspondingly, their spectra should be very similar (see **Table 3**), which is the reason to see a single spectral envelop and no measurable changes after dissolution in non-polar solvents, as observed by NMR.After optimization of all possible structures at **3.2** (analogous to **3.1**), the isomer types **3.2E'** and **3.2Z'** are the most stable structures (the second higher in energy by 1.08 kcal/mol in DMSO). The structures of the major form of 1 in polar solvents are clearly very similar as judged from the NH and OH chemical shifts (**Table 4**). In the non-polar solvents, $CDCl_3$ and toluene-d_8 the OH chemical shift (**Table 4**) indicates either no hydrogen bonding in line with a structure in which the C=O groups points away from the aromatic ring marked



Scheme 5. *Numbering of the carbon atoms in **3.1** (R=H) and **3.2** (R=CH_3).*

Table 4. *NH, OH, CH_3 and H-6' chemical shifts for **3.1** and **3.2**.*

Compound	NH	OH	CH_3	H-6'	Solvent
3.1 (major form)	14.76	8.42	2.66	7.13	**$CDCl_3$**
3.1 (minor form)	12.42	7.00	2.59	~ 7.84	
3.1 (major form)	14.14	11.52	2.50	7.20	**DMSO-d_6**
3.1 (minor form)	11.70	11.34	2.56	7.75	
3.1 (major form)	14.31	11.94	2.58	7.38	**DMF-d_7**
3.1 (minor form)	11.94	11.94	2.57	~7.8	
3.1 (major form)	14.31	6.97		6.47	**Toluene-d_8**
3.1 (minor form)	12.30	*	*		
3.1 (major form)	14.26	10.58	2.56	7.23	**Acetonitrile-d_3**
3.1 (minor form)	11.93	10.58	2.59	*	
3.2 (major form)	14.40	-	2.63	7.40	**$CDCl_3$**
3.2 (minor form)	12.14	-	2.625	7.78	
3.2 (major form)	14.11	-	2.57	7.27	**DMSO-d6**
3.2 (minor form)	11.58	-	2.57	7.86	
3.2 (major form)	14.40	-	2.55	7.30	**Acetonitrile -d_3**
3.2 (minor form)	11.75	-	2.58	*	
3.2 (major form)	14.32	-	2.54	7.40	**Tetrahydrofuran - d_8**
3.2 (minor form)	11.85	-	2.56	7.85	

** - no signal was observed*

(‘). This is supported by the H-6‘ chemical shift (**Scheme 5**). For the minor form the situation is much the same. The following structures are possible, namely **E, E', Z, Z'** in **3.1** and **E', Z'** in **3.2**. A major difference between the major and the minor species is the chemical shift of H-6'. As the major compound is assigned to **3.1E'**, the minor compound could be found by exclusion. On one side, **3.1E'** and **3.1E** are rotamers and the barrier to rotation around the single C-N bond is low.

As seen from **Fig. 14** the barrier of rotation in **3.1** is 8.14 kcal/mol without to account the specific interaction with the solvent. If it is accounted, the energy of **3.1E** will rise (see **Fig. 13**) and the transition state, where the OH proton can interact with DMSO molecule, would be stabilized, which will even more decrease the rotation barrier. For this reason **3.1E'** and **3.1E** would not show too different sets of signals. The barrier of transition from **3.1E'** to **3.1Z'**, as shown in **Fig. 15**, is sufficient to measure separate signals.

The combined assignment of existing forms in solution could answer the question of the effect of the additional OH group in the stator of the potential rotary switch **3.1**. Obviously, at least in DMSO, the OH group as presented in **3.1E'** and **3.1Z'** does not interact with the rotor and consequently cannot play a direct role in the rotation process. It could be expected to act as an electron acceptor substituent, influencing together with the nitro group the neighboring hydrazone nitrogen atom from the axle.

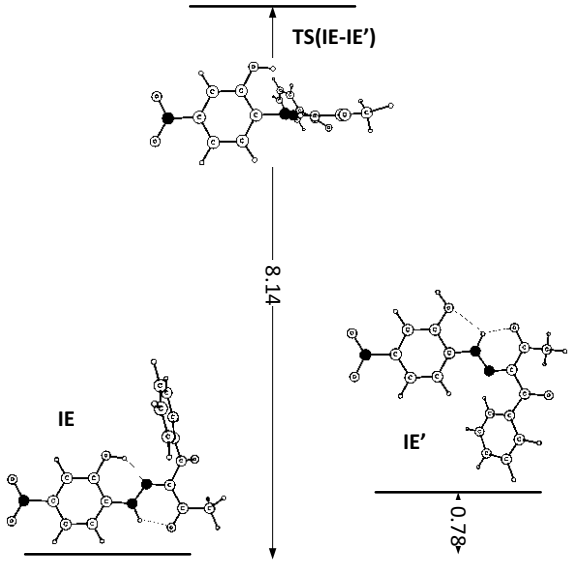


Fig.14. *Schematic diagram for transition from **IE** to **IE'** and back in **3.1** in DMSO (the values are in kcal/mol).*

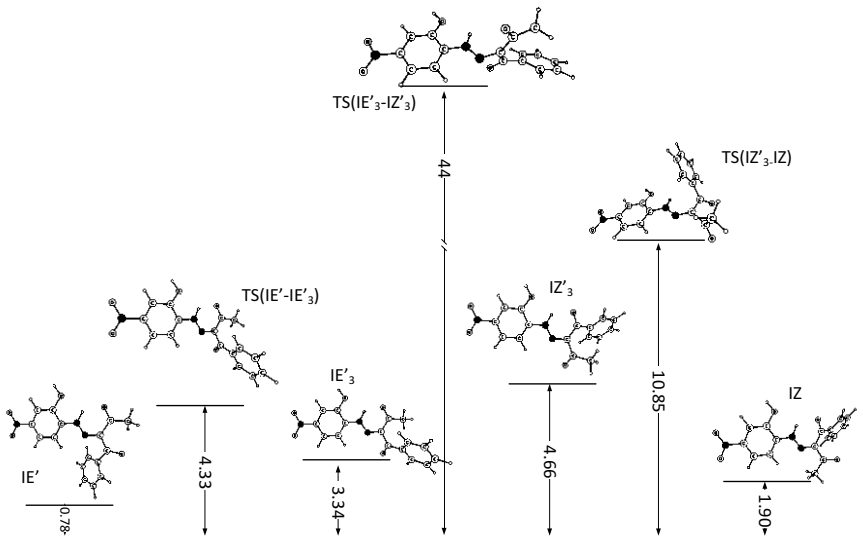


Fig.15. *Schematic diagram for transition from **3.1E'** to **3.1Z'** and back in **3.1** in DMSO (the values are in kcal/mol).*

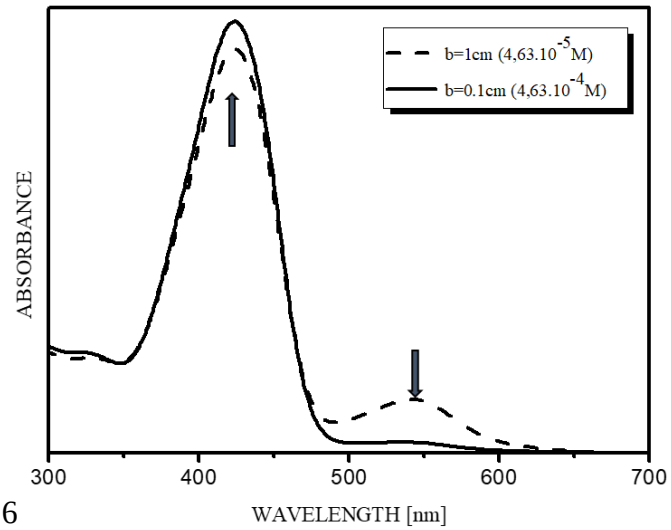


Fig. 16. *Concentration dependence of the absorption spectrum of **3.1** in DMSO. The product of cell thickness and concentration (b x c= 4.63 .10-5 M).*

Two additional factors influence the specific processes in **3.1** in solution, namely the concentration and the water content. The spontaneous deprotonation shown in **Fig. 8** is concentration dependent. The increase of the concentration leads to disappearing of the deprotonated form, which happens at relatively low concentrations. For instance, in DMSO at ~5. 10^{-4} mol/l only neutral form is observed (see **Fig. 16**).

This behaviour suggests that in the NMR concentration scale no deprotonated form exists. The increase of the temperature causes a slight rise of the band at 550 nm and correspondingly decreases the intensity of the neutral form band (**Fig. 17**). Most probably **3.1E'** and **3.1Z'** aggregate in solution and with dilution the monomers are deprotonated by the solvent. The OH deprotonated forms exist in the same ratio (**3.1E'**)$^-$ is more stable with 1.2 kcal/mol comparing to (**3.1Z'**).

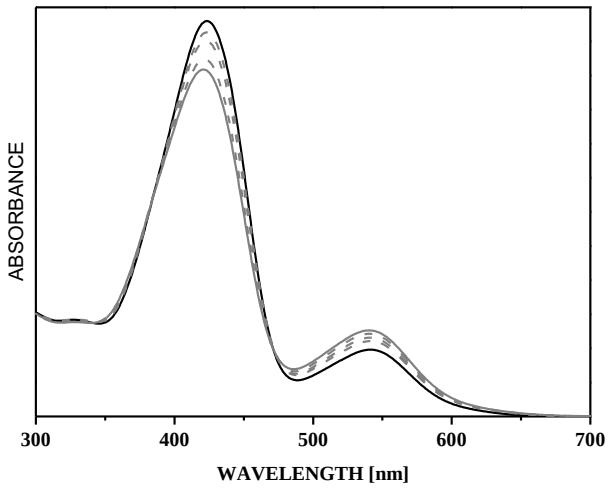


Fig. 17. *Absorption spectrum of **3.1** in DMSO as function of the temperature: 20°C (black solid line), 70°C (grey solid line).*

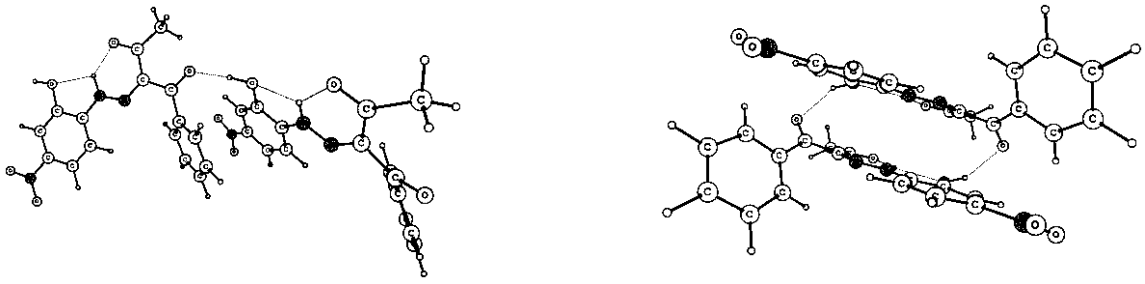


Fig. 18. *Theoretically predicted border cases of dimers of **3.1**: linear (left) and sandwich (right).*

Their spectra are very similar (**Table 3**) and again cannot be distinguished by *UV-Vis* spectroscopy. It could be expected that the OH proton, not involved in an intramolecular hydrogen bonding, is responsible for the aggregation behaviour. On Fig. 18 the border cases of the possible dimers of **3.1E'**are shown.

Although the "*sandwich*" dimer is shown to be almost 8 kcal/mol more stable by the calculations, this value should be considered with care, because no basis set superposition error correction is taken into account. The more important fact is that in both cases OH···O=CPh is the preferred interaction, which defends the OH group from deprotonation.

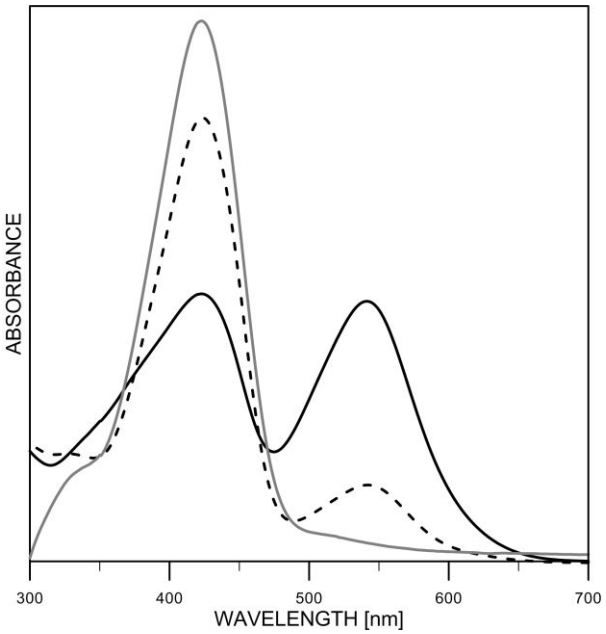


Fig. 19. *Absorption spectra of **3.1** in: dry DMSO (solid black line), DMSO as purchased (dashes), DMSO with further addition of water (20% water to the commercial DMSO, solid gray line).*

The water content is another important factor influencing the absorption spectra. The effect is well illustrated on **Fig. 19**. It is clear that the addition of water leads to disappearance of the deprotonated specie(s). According to the calculations the DMSO molecule forms more stable complexes with the **1E'/1Z'** compared to the water molecule (stabilization energy 13 kcal/mol against 9 kcal/mol, the complexes are shown in **Fig. 20**).

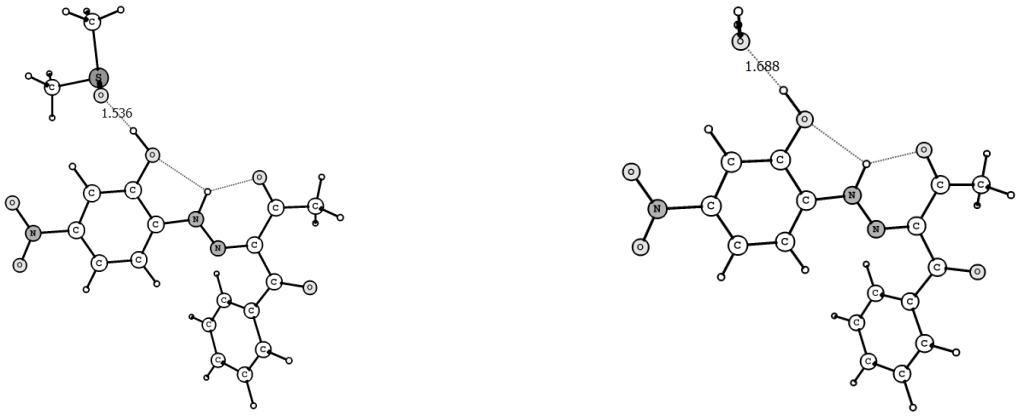
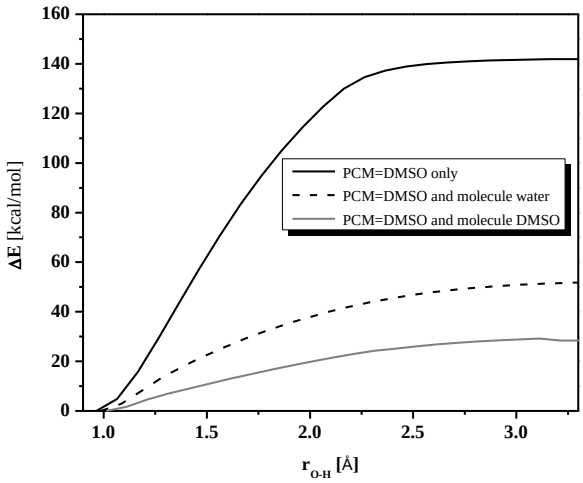


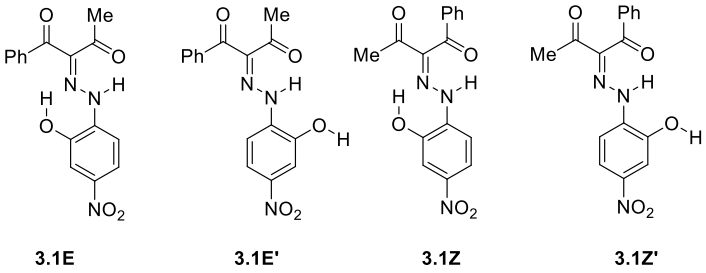
Fig. 20. *Complexes of **3.1E'** with DMSO (left) and with water (right). The optimizations are performed in a DMSO solvent (PCM=DMSO).*

According to the NMR data, discussed above, the water molecules do not interact with the dye directly, but through the DMSO molecule. DMSO is stronger proton acceptor solvent, which could form more stable solute solvent complex and deprotonate the OH group easier (see **Fig. 21**). In turn, the water molecule being proton donor returns the deprotonated dye in its neutral state.

Fig. 21. *Modeling the deprotonation of **3.1E'** through gradual change of the OH distance.*



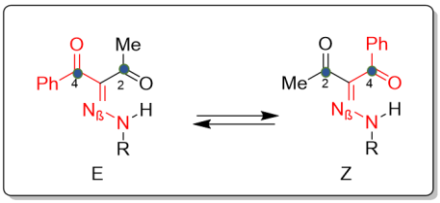
All these studies left one main question open - "What is the reason for the stabilization of the E' and Z' conformational isomers (**Scheme 6**), in which the OH group exists that is unengaged in intramolecular hydrogen bonding?"



Scheme 6. *Possible isomers of the hydrazone form of **3.1**.*

The possible answers are based either on the formation of complexes with proton-acceptor solvents, or traces of water, or aggregation in all solvents.

It is known [5] that *^{15}N NMR* can be used as a method to distinguish the conditional **E** and **Z** conformational isomers based on the orientation relative to the double C = N (**Scheme 7**). Using the ^{2}J ($^{15}N_{\beta}$, ^{13}C) constants, it is possible to determine which carbonyl group is closer to the free electron pair of N_{β}, since the values are sufficiently large.



Scheme 7. *Conformational equilibrium of **3.1**.*

These trends are reproduced theoretically and are summarized in **Table 5**. Theoretically predicted ^{2}J ($^{15}N_{\beta}$, ^{13}C-4) constants are very big in the case of **E(E')** and negligible for **Z(Z')** ones. The exactly opposite is true for $^{2}J(^{15}N_{\beta},^{13}C$-2). The obtained trends and values confirm reasonably well the experimental data. Although it is known that ^{13}C-^{15}N couplings over two or three bonds are generally small, we have calculated ^{2}J ($^{15}N\alpha,^{13}C$) couplings. As

can be seen, the ^{2}J ($^{15}N\alpha$,^{13}C) constants allow distinctions between **E/Z** and **E'/Z'**, i.e they prove the orientation of the conformational isomers with respect to the C_1'-N_α bond. This indicates the presence of ' - conformational isomers. Consequently the combined use of $^{2}J(^{15}N_\alpha,^{13}C)$ and $^{2}J(^{15}N_\beta,^{13}C)$ confirms the availability of **3.1E′** as a major component and **3.1Z′**, as a minor ones, in solution.

Table.5. *Predicted (B3LYP/6-311+G(2d,p)//M06-2X/TZVP) and experimental ^{15}N NMR parameters of selected atoms of **3.1** in DMSO.*

Structure	δ(^{1}H), ppm			δ(^{15}N), ppm		$^{2}J(^{15}N_\beta,^{13}C)$, Hz		$^{2}J(^{15}N_\alpha,^{13}C)$, Hz	
	OH	**NH**	**H-6'**	**N_α**	**N_β**	**C-2**	**C-4**	**C-2'**	**C-6'**
E	9.15	14.54	7.34	-208.7	-35.9	-0.4	8.2	-0.3	2.9
Z	10.12	12.96	7.35	-217.4	-46.1	8.3	-0.6	-0.2	2.8
E'	5.28	14.35	7.74	-219.3	-16.2	-0.1	9.0	1.0	-0.1
Z'	5.24	12.73	8.34	-227.6	-26.1	9.3	-0.4	1.0	-0.1
E-DMSO complex	9.43	14.69	8.83	-200.7	-39.0	-0.3	8.5	-0.3	2.8
Z-DMSO complex	10.22	13.30	7.78	-215.2	-54.9	8.1	-1.2	-0.3	2.9
E'-DMSO complex	13.71 (10.94)*	14.35 (14.31)*	7.63 (7.65)*	-215.0	-13.7	-0.1	9.0	1.1	-0.1
Z'-DMSO complex	13.71 (10.92)*	12.95 (12.84)*	8.24 (8.27)*	-223.0	-23.4	9.3	-0.4	1.1	-0.1
E'-E' aggregate	10.34	14.49	7.49	-216.5	-14.6	-0.2	10.0	1.1	-0.1
Z'-Z' aggregate	8.95	12.82	8.16	-225.0	-24.3	9.7	-0.4	1.0	-0.1
Major form (E')**,***	11.52	14.14	7.20	-220.9 ***	-21.3 ***	<1 ***	11.9 ***	1.6 ***	
Minor form (Z')**,***	11.34	11.70	7.75	−229.7 ***	-29.8 ***	12.5 ***	<1 ***	1.5 ***	

** Water complex in DMSO;** Experimentally measured (**Table 4**), also in (**Fig. 10**); *** Taken from literature, relative error ± 0.3 Hz for ^{2}J constants.*

In the general context of the study of isomerization of similar rotary switches, the use of the combination of these two ^{2}J constants ($^{2}J(^{15}N_\beta,^{13}C)$ and $^{2}J(^{15}N_\alpha,^{13}C)$) gives a good opportunity

to distinguish between **E** and **Z** and their corresponding **E′** and **Z′** analogues: $^{2}J(^{15}N_{\alpha},^{13}C\text{-}2')$ is defined by the N_{α}-*C-1'*rotation, while $^{2}J(^{15}N_{\beta},^{13}C\text{-}2)$ is a function of the N_{β}-*C-1* bond rotation. As a result each of the four isomers, shown in **Scheme 6**, can be presented as a unique logical combination (small/large) of the ^{2}J constants and the assignment can be easily done based on the experimental data (**Table 5**).

The crystal structure of **3.1** is shown in **Fig. 22**. Two conclusions can be drawn from it: the studied compound exists as **E′** isomer in the solid state, which confirms conclusions made above for its dominance in proton acceptor solvents or in solvents with mixed nature like methanol or water (see relative stability in water in **Table 6**); as predicted by the theoretical calculations, **3.1E′** is stabilized by formation of linear aggregates.

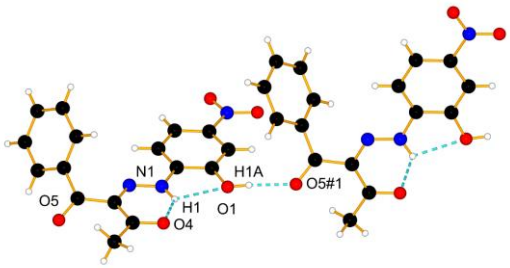


Fig. 22. *Crystal structure of **3.1**.*

This particular structure of the aggregate excludes effective overlapping of the electronic density of the monomers and, consequently, no substantial spectral changes could be observed in the absorption spectra. The theoretically predicted absorbance in both monomer and dimer, is located in the range 352–365 nm. Most probably, the experimental spectra of both species are also almost identical and strongly overlaps, which could not bring *UV–Vis* spectral evidences for the selfassociation. The evidences are indirect: in the experimentallymeasured *UV–Vis* spectra (**Fig. 16**) the observed changes are related only to the process of deprotonation in proton acceptor solvents at low concentrations (10^{-5}M and lower) as a result of the aggregates' destruction according to the general equilibrium scheme:

Aggregates⇔Monomers⇔Anions

Table 6. *Relative energies (M06-2X/TZVP) of the isomers of **3.1*** in various solvents in kcal/mol units.*

Species	Isomer	Solvent (PCM model)	ΔE
Monomer	**E**	chloroform	0.00
	Z		2.44 (1.62) 1.83**
	E'		0.94 1.26**
	Z'		2.54 2.72**
	E	acetonitrile	0.00
	Z		2.07 (1.13) 1.48**
	E'		0.79 1.07**
	Z'		1.93 2.14**
	E	DMSO	0.00
	Z		2.06 (1.11) 1.46**
	E'		0.78 1.07**
	Z'		1.90 2.12**
Monomer-DMSO complex***	**E**		4.65 7.96**
	Z		2.30 7.85**
	E'		0.00
	Z'		1.15 0.89**
Dimer	**E'-E'**		0.00
	Z'-Z'		1.43 1.75**

** Relative energies in the case of **3.2** are given in brackets. ** Relative energies in the case of **3.1** using B3LYP/6-311+G(2d,p)//M06-2X/TZVP; *** The corresponding water complexes in water environment have the following relative energies (following the same order from **E** to **Z'**): 3.25, 3.59, 0.0, 1,07 kcal/mol.*

The assumed scheme brings up the question of what actually happens in proton acceptor solvents (like DMSO and DMF) at the concentration range used in the *NMR* measurements. As was proven, the deprotonation is a result of the formation of solute-solvent (monomer-solvent) complexes at low concentrations. Following the scheme, a rise of the concentration should thus reduce the monomers in favor of the aggregates, which brings a concern about the existence of the solute-solvent complexes as a whole at the NMR concentrations. Looking at the X-ray structure (**Fig. 22**), the H-3′ to H-2″ or H-6″ (from he neighbor molecule in the aggregate) distances are 3.49 and 3.67 Å.

In the calculated dimers, they are similar with 3.4 and 3.8 Å. These distances should allow observation of *NOESY* cross peaks if the complex is also present in solution. The *NOESY* spectrum, presented in **Fig. 23**, a cross-peak is seen between OH at 11.52 to H-3′ at 7.72 ppm. From **Fig. 24** can be seen a cross peak with water was seen to H-3′ and it was suggested that the hydrogen bond partner was DMSO. The observation of cross peaks from H_2O to H-3′ suggests a complex with a water molecule.

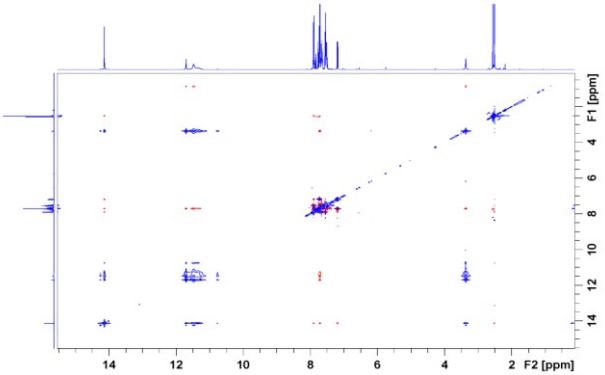


Fig. 23. *NOESY spectrum of **3.1** in DMSO.*

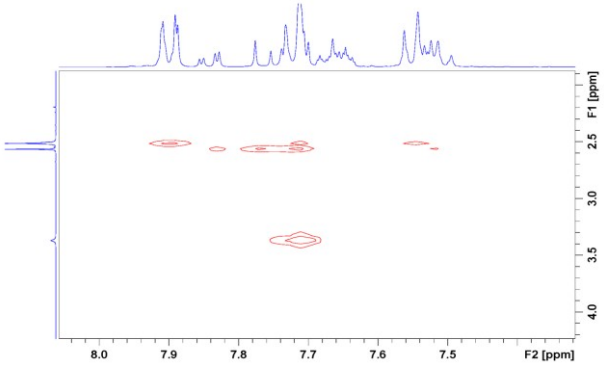


Fig. 24. *NOESY spectrum of **3.1**, showing a correlation peak with water at 3.38 to H-3´ at 7.76 ppm.*

However, the calculations suggest that the DMSO molecule is involved as shown in **Fig. 25**. Actually the formation of this kind of associate in presence of water explains very well why the deprotonation is suppressed in presence of water. The deprotonation needs free monomers to interact directly with DMSO, which deprotonates them, while the water molecules stabilize the aggregates.

In dry DMSO as, shown in **Fig. 19** the compound is substantially deprotonated. The calculated structure as shown in **Fig. 25** has reasonable distances between H-3′ and H-2″, H-6″ to enable the observation of a *NOE* cross peak and the OH group is in the vicinity of H-3′ and is also hydrogen bonded indirectly to DMSO. The observed chemical shift for the OH proton should near the predicted value for the water complex, which is observed in **Table 5**.

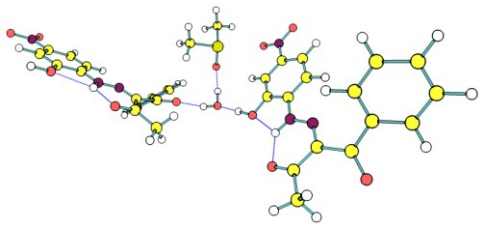
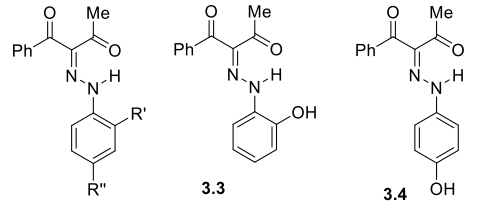


Fig. 25. ***E'-E'** complex, including the water molecule as a linker.*

It is an interesting question whether the lack of tautomerism, the existence of the " ' " isomers and the side effects could be attributed to the strong electron acceptor ability of the nitro group. To answer it, we have studied compounds **3.3** and **3.4,** in which two effects could be clarified: the role of the existence of a nitro group (**3.3** vs **3.1**) and of the position of the OH

group by itself (**3.3** vs **3.4**) (**Scheme 8**). No such comparative study of **3.1**, **3.3** and **3.4** has been performed before.



3.1 R'=OH; R''=NO_2
3.1a R'=H; R''=NO_2
3.1b R'=R''=H
3.1c R'=OMe; R''=H
3.1d R'=H; R''=OMe
3.1e R'=H; R''=COOH

Scheme 8. *Structure of the investigated potential rotary switches **3.3** and **3.4**. For comparison are used compounds **3.1a**-**3.1e**.*

By analogy with **3.1**, all possible tautomeric structures and conformational isomers for compounds **3.3** and **3.4** are optimized. Calculations confirm that there is no tautomeric equilibrium for either compound. They exist in the form of an enol tautomer (type **I** tautomer) stabilized as a mixture of **E** and **Z** conformers.

As can be seen from the results presented in **Fig. 26**, the **E**-form dominates and is followed by **E'** in **3.3**. With an energy difference of more than 2 kcal/mol, the presence of **Z**-form in a solution can be excluded. In **3.4**, the calculations predict an equilibrium between the **E**-(most stable) and **Z**-forms (**Fig. 27**).

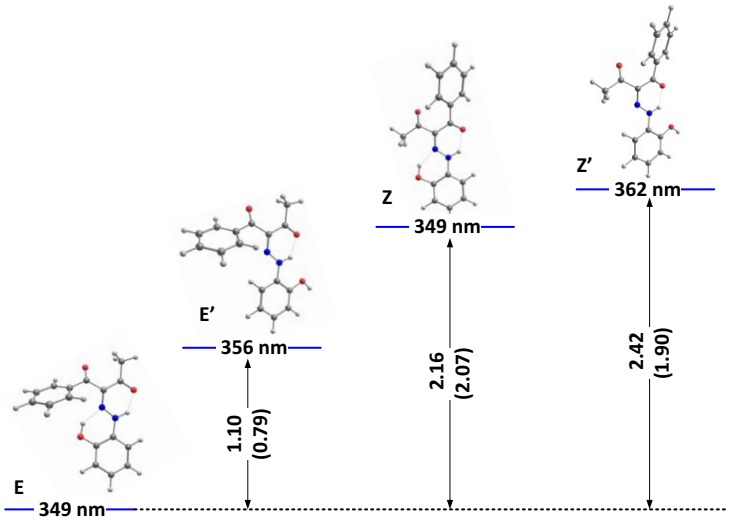


Fig. 26. *Relative energies (in kcal/mole units) and predicted positions of the long-wavelength bands of the most stable isomers of **3.3(I)** in ACN. The corresponding relative energies for **3.1** are given in brackets.*

The theoretical result shows, that the stabilization is a result of the strength of the formed intramolecular hydrogen bonds. While better proton-attracting ability of MeCO through the NH..OMe determines a better stabilization of the **E**-isomer, additional stabilization through OH..N bonding makes the **E/Z** pairs more stable compared to **E'/Z'** in **3.1** and **3.2**.

The effect of the nitro group in **3.1** leads to an overall weak stabilization in the **E/Z** forms and a more pronounced stability of the " ' " isomers. In the case of **3**, the effect of the OH group is limited to a non-hydrogen bonding substituent and leads to stabilization of the **Z**-isomer. The predicted stabilization effect in the series **3.1a**, **3.1b** and **3.4**, follows the experimentally

observed trend for a destabilization of the *Z* isomer (molar fractions of 15%, 10% and 5%, correspondingly) going from electron acceptor to electron donor substituents in *para* position in the stator [6]. Most probably, the absence of the OH..N hydrogen bonding in **E'/Z'** of **3.3** and in **3.4** reduces the steric hindrance between the rotor and the stator, leading to an overall stabilization of the corresponding isomers.

The solvation model used so far describes the solvent as a dielectric medium and does not take into account the possible specific solute–solvent interactions. The model of this specific solvent effect is illustrated in **Fig. 28** and **29**, showing the most stable complexes with DMSO. As can be seen, the interaction between the solvent molecule and the free OH proton in **E'** and **Z'** leads to their stabilization.

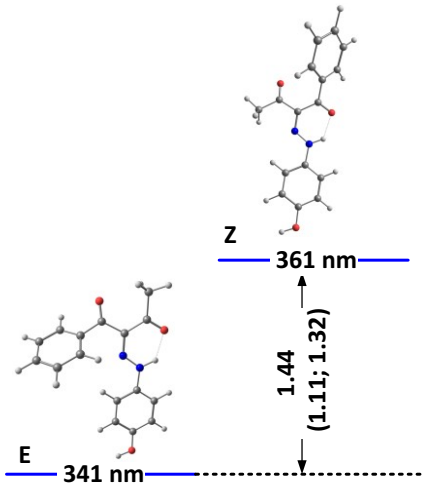


Fig. 27. *Relative energies (in kcal/mole units) and predicted positions of the long-wavelength bands of the most stable isomers of **3.4**(I) in DMSO. The corresponding relative energies for **3.1a** and **3.1b**, are given in brackets.*

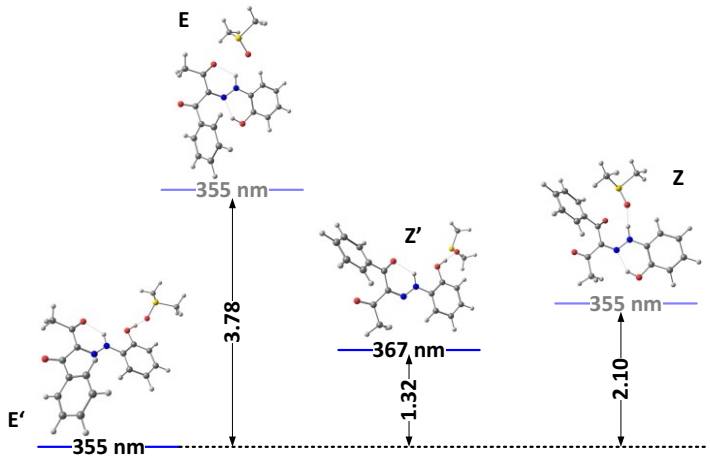


Fig. 28. *Relative energies (in kcal/mole units) and predicted positions of the long-wavelength bands of the most stable isomers of **3.3**(I) in DMSO, accounting for the specific solute–solvent interactions.*

Moreover, in **3.3E** and **3.3Z**, there are no conditions for the formation of any OH..O = SMe_2 hydrogen bond, and the formed NH…O = SMe_2 is weak due to the low acidity of the NH proton and steric effect from adjacent functional groups (**Fig. 28**). The changes in the case of **3.4** are caused by reducing the electron donor ability of the OH group and hence to a rise in the polarization of the N-H bond, leading finally to the stabilization of the **Z**-isomer.

In addition to the relative stability of the isomers, the predicted positions of the long-wavelength bands in the absorption spectra are shown in **Fig. 26–29** as well. The absolute values should be considered with care due to the systematic blue shift of the used M06-2X functional. The relative changes indicate, as expected, that it is practically impossible to distinguish between the most stable isomers by means of *UV-Vis* spectroscopy. The absorption spectra of **3.3** and **3.4**, shown in **Fig. 30**, indicate that there are no substantial changes in the spectral

shape upon changing the solvent. This figure strongly supports the hypothesis, in analogy to **3.1**; there is no tautomeric equilibrium.It is seen that the observed long-wavelength absorption band (~ 400 nm) consists of two sub-bands[3], whose intensity slightly varies with the solvent. They can be associated with the most stable isomers according to the theoretical predictions. However, the strong overlapping between them does not allow either precise estimation of the positions of the bands by derivative spectroscopy nor a quantitative estimation of the isomers' molar fractions [7].

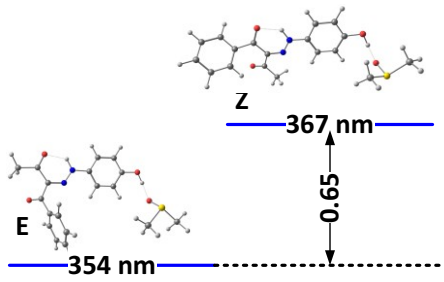


Fig. 29. *Relative energies (in kcal / mol) of the most stable conformational isomers of **3.4** in DMSO, taking into account the specific interaction.*

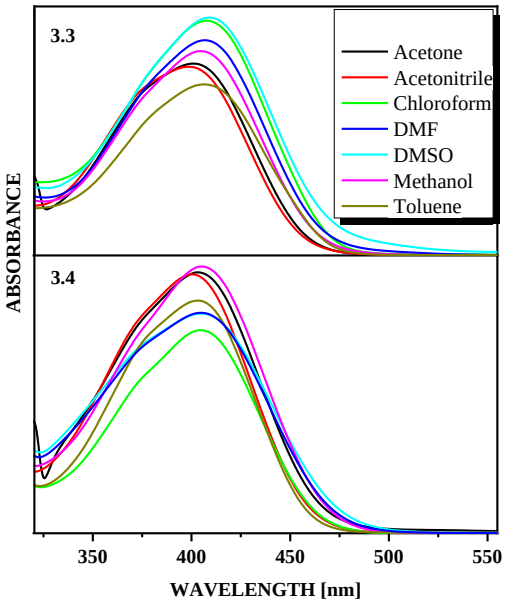


Fig. 30. *Experimental absorption spectra of **3.3** and **3.4** in various solvents.*

[3]*The exact position of the maxima was estimated from the second derivatives of the absorption curves.*

The conformational isomers existing in solution can be identified and quantified using NMR. The corresponding ^{1}H NMR spectra of **3.3** and **3.4** in DMSO-d_6 are shown in **Fig. 31** and **32**.

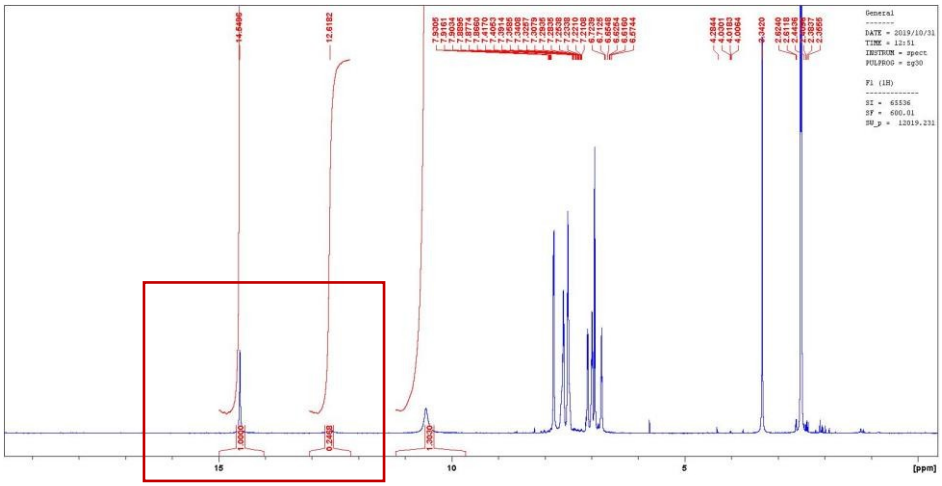


Fig. 31. *^{1}H NMR spectrum of **3.3** in DMSO-d_6.*

The obtained data for chemical shifts can be compared with those for **3.1**.

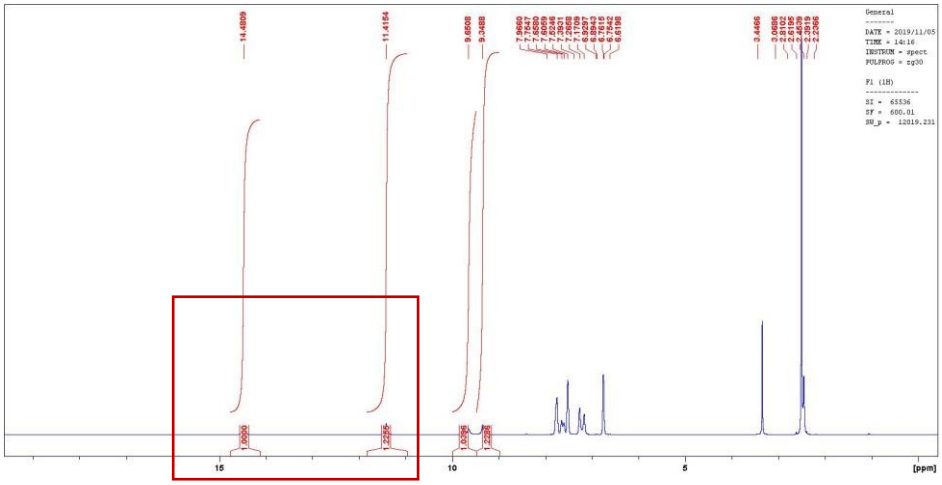


Fig. 32. *^{1}H NMR spectrum of **3.4** in DMSO-d_6.*

From the *^{1}H NMR* spectra of **3.3** and **3.4**, it can be seen that, in both cases, two isomers are present in DMSO-d_6. The chemical shifts in DMSO-d_6 for NH for the major and minor form of **3.3** are at 14.55 ppm and 12.62 ppm, and for **3.4** at 14.48 ppm and 11.42 ppm. Based on the NH signals, the ratio between the isomers is 80%/20% and 45%/55%, respectively for **3.3** and **3.4** (65%/35% for **3.1**), which corresponds to ΔG values (RT) of 0.36, 0.82 and −0.11 kcal/mol for **3.1**, **3.3** and **3.4**. In analogy to **3.1** and following the theoretically predicted relative stabilization, it can be concluded that in DMSO there is an equilibrium between **E'** (major) and **Z'** (minor) forms in **3.3** and between **E** and **Z** of **3.4**. The theoretically predicted values for the chemical shifts of the NH proton of the major and minor form at **3.3** and **3.4**,

respectively, are 14.61 ppm (**3.3E'**) and 13.67 ppm (**3.3Z'**) and 14.51 ppm (**3.4E**) and 13.44 ppm (**3.4Z**), i.e., the theoretical results are consistent with the experimental ones. Although the NMR determined Gibb's free energies are lower comparing the predicted relative energies (Δ**E**), the latter correctly predict the general trend of stabilization of the **Z'** isomers (**3.4** > **3.1** > **3.3**) with a good linearity **(ΔG=1.28 x ΔE – 0.98, R^2=0.92**).

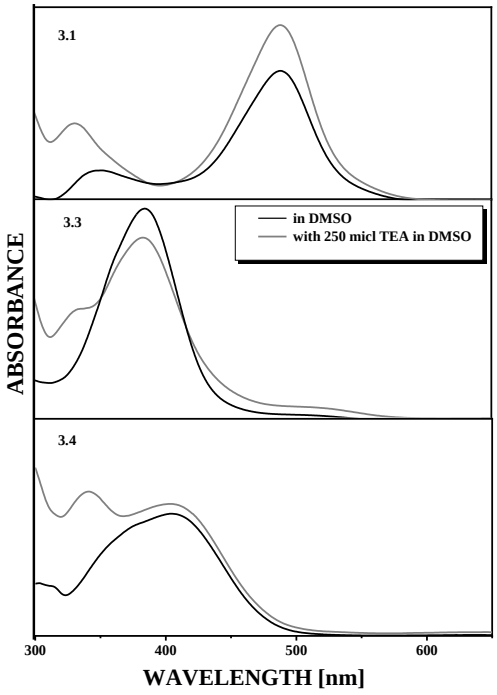


Fig. 33. *Change in the absorption spectra of **3.1**, **3.3** and **3.4** in DMSO upon addition of **TEA** (250 μl **TEA** corresponds to 4x103 eqv).*

Three additional factors influence the conformational equilibrium in **3.3** and **3.4** in solution, namely the temperature, the concentration and the water content of the used solvent. As previously shown in the case of **3.1**, a spontaneous deprotonation (loss of OH proton) occurs in diluted solutions of dry proton acceptor solvents, leading to a new red-shifted band. Actually, **3.1** is almost fully deprotonated in dry DMSO (**Fig. 33**), while, as seen in **Fig. 30** and **33**, deprotonation in **3.3** is weak and negligible in **3.4**. Obviously, the effect of the nitro group is decisive in this case. Upon addition of water, the equilibrium is fully shifted towards the neutral isomers (**Fig. 34**). According to the theoretical calculations (**Table 7**), deprotonation does not substantially change the isomers' ratios.

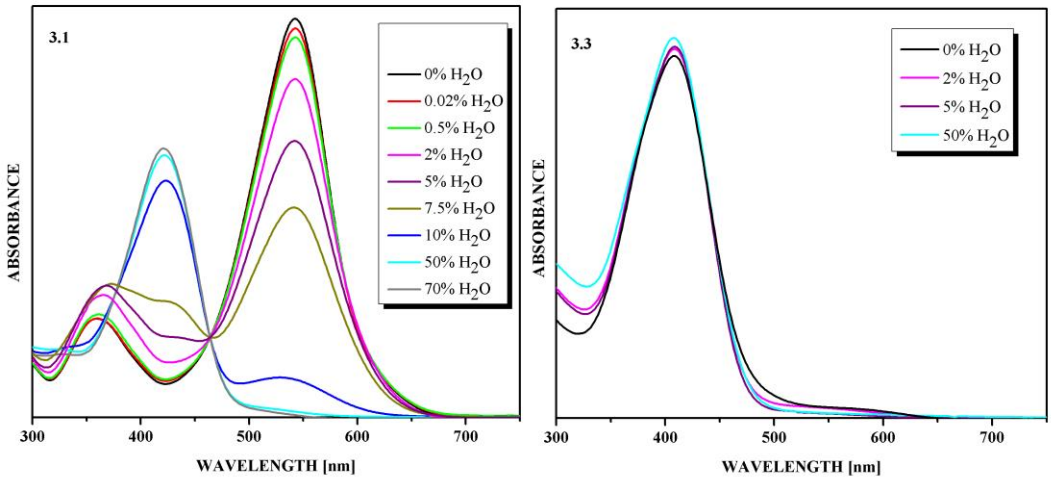
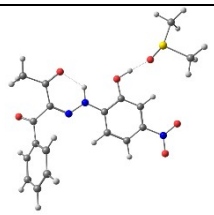
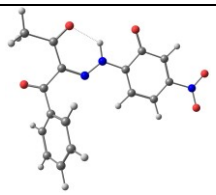
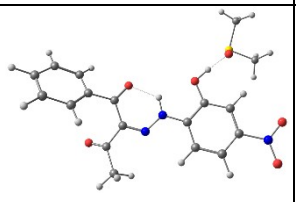
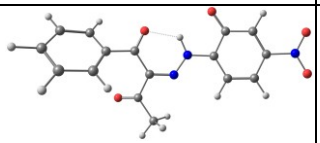
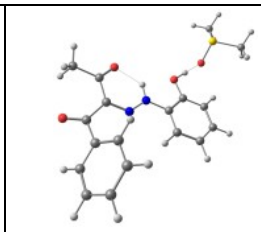
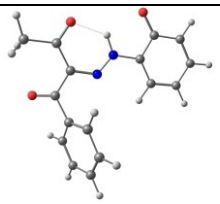
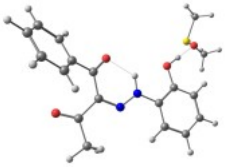
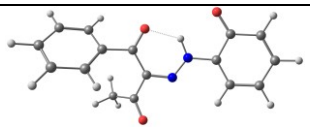
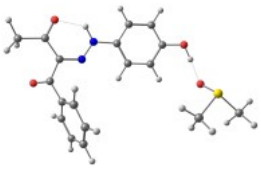
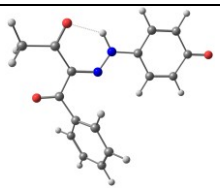
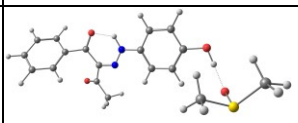
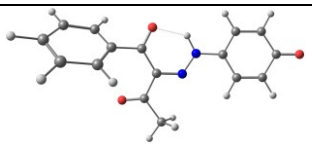


Fig. 34. *Change in the absorption spectra of* ***3.1*** *and* ***3.3*** *in DMSO upon addition of water.*

Table 7. *Relative energies of the most stable neutral and deprotonated forms for compounds* ***3.1***, ***3.3*** *and* ***3.4*** *in kcal/mol.*

Compound	Neutral form			Deprotonated form		
	Isomer	Optimized structure	ΔE [kcal/mol]	Isomer	Optimized structure	ΔE [kcal/mol]
3.1	**E'**		0.00	**(E')$^-$**		0.00
	Z'		1.15	**(Z')$^-$**		1.20

3.3	**E'**		0.00	**(E')$^-$**		0.00
	Z'		1.32	**(Z')$^-$**		1.31
3.4	**E**		0.00	**(E)$^-$**		0.00
	Z		0.65	**(Z)$^-$**		1.53

The concentration is an essential factor determining the deprotonation of the investigated compounds. In **3.3**, as in **3.1**, the increase in the concentration leads to a decrease in the content of the deprotonated form, as shown in **Fig. 35**. No such effect is observed in **3.4**.

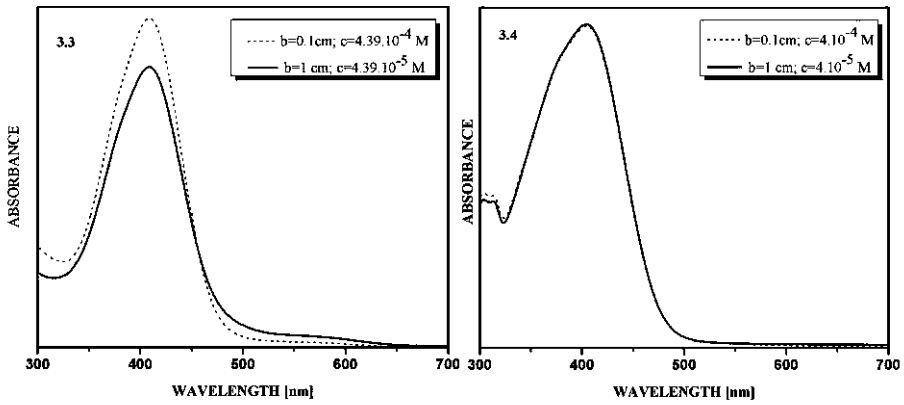


Fig. 35. *Experimental absorption spectra of **3.3** and **3.4** in DMSO as a function of the concentration, keeping the cell thickness (b) × concentration (c) constant.*

The results indicate that the association is a possible reason for the observed changes. The theoretical calculations and X-ray data (**Fig. 36** and **Scheme 9**) suggest that cyclic aggregates are formed in the case of **3.3**.

In the solid state, compound **3.3** exists as an *E'* conformer, stabilized via a cyclic dimer. The major difference with **3.1** is in the shape of the aggregate—again, the **E'** form is stabilized in **3.1**, but in form of a linear aggregate.

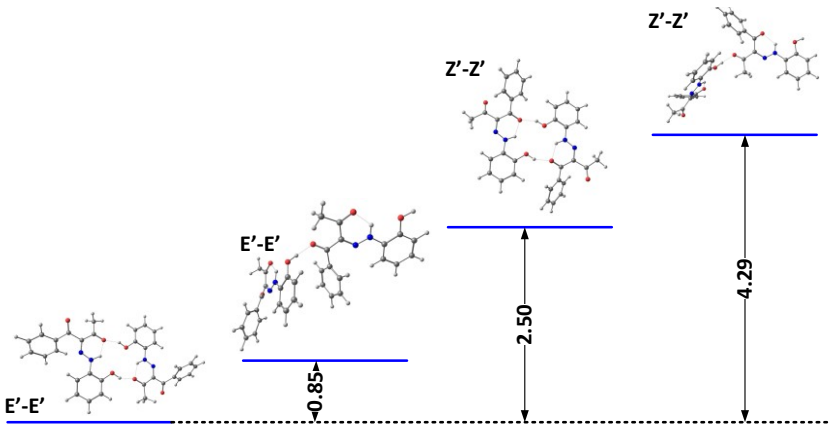
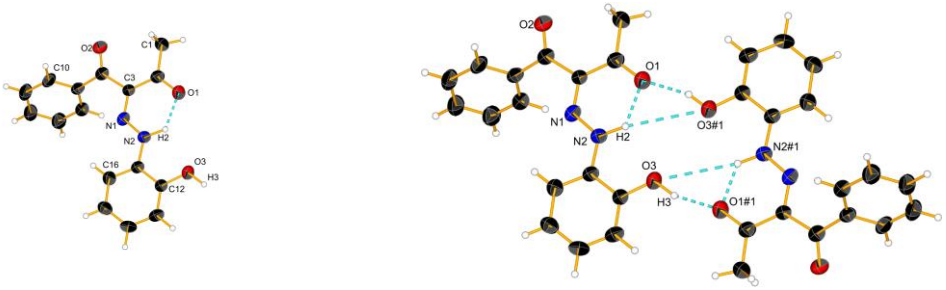


Fig. 36. *Relative energies (in kcal/mol) of the most stable dimers of **3.3** in DMSO.*

The stability of the **E'-E'** cyclic dimer in **3.3** is probably due to the stronger proton acceptor properties of the CH_3CO group compared to the PhCO moiety of **3.1**. The formation of aggregates, as in **3.1**, limits the deprotonation, which explains the observed concentration effects.



Scheme 9. *Crystal structure of **2** and a cyclic dimer model via an intermolecular hydrogen bond.*

The increase in the concentration did not lead to significant spectral changes in **3.4** (**Fig. 35**). This is also expected since the OH group is not polar enough in this particular case, but some linear aggregation cannot be excluded.

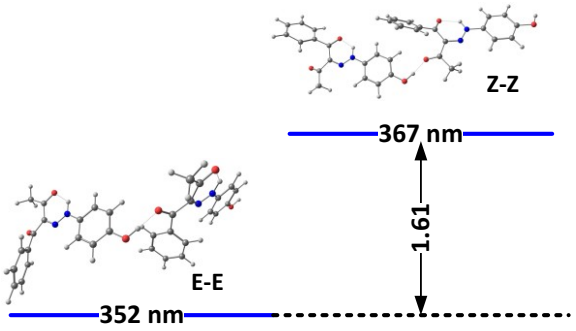
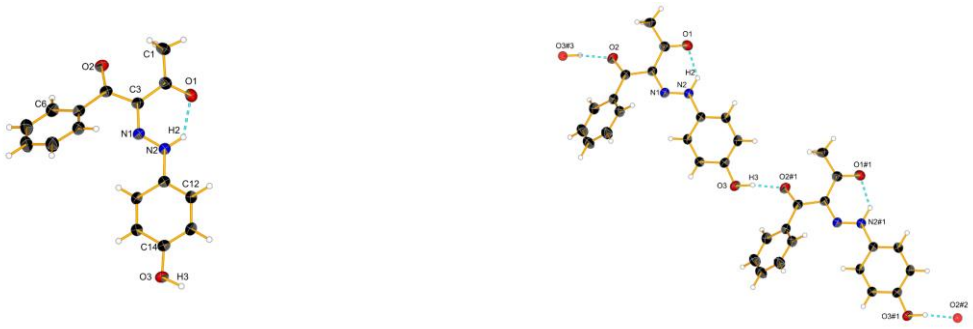


Fig. 37. *Relative energies (in kcal / mol) of the most stable dimers of **3.4** in DMSO.*

According to the theoretical simulations (**Fig. 37**) and the crystal structure (**Scheme 10**), linear **E-E** aggregates are expected in solution



Scheme 10. *Crystal structure of **3.4** and a cyclic dimer model via an intermolecular hydrogen bond.*

The availability of crystallographic data for the series **3.1**, **3.1a-e**, **3.3**, **3.4** allows qualitative estimation of the strength of the existing intra- and intermolecular hydrogen bonding according to *Steiner* and *Jeffrey* [8]. The corresponding bond length and angles are collected in **Table 8**. According to the classification in [9], the existing N-H…O hydrogen bonds are classified as moderate ones using the H…A and D….A distances and the D-H…A angle. It seems that the strength (at least in solid state) of this bond is almost independent on the substitution in the stator. In the cases where this bond is bifurcated, namely **3.1**, **3.1c** and **3.3**, the contribution from N-H…O(=C) is the dominant one. This explains why, according to the theoretical calculations using the solvent only as media, the *E* and *Z* isomers are always more stable compared to the " ‘ " ones. The data in **Table 8** show clearly that the formation of associates through intramolecular hydrogen bonding with strong directionality (D-H…A angle > 160°) has a noticeable stabilizing effect.

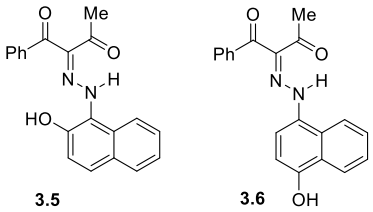
Table 8. *Parameters of the hydrogen bonds of the studied compounds, taken from their crystallographic data.*

Compound	Type D-H…A Bond		Distances [Å]			Д-H…A Angle, [°]
			D-H	H…A	D….A	
3.1 [10]	intramolecular	N-H…O(=C)	0.896(9)	1.890(7)	2.565(1)	130.6(7)
	intermolecular	N-H…O(-H)		2.266(9)	2.619(1)	103.1(6)
	(linear dimer)	O-H…O(=C)	0.85(2)	1.89(2)	2.738(1)	176(1)
3.3	intramolecular	N-H…O(=C)	1.03(3)	1.79(2)	2.567(4)	128(1)
	intermolecular	N-H…O(-H)		2.242(8)	2.609(4)	99(1)
	(cyclic dimer)	O-H…O(=C)	0.92(6)	1.79(7)	2.677(4)	161(6)

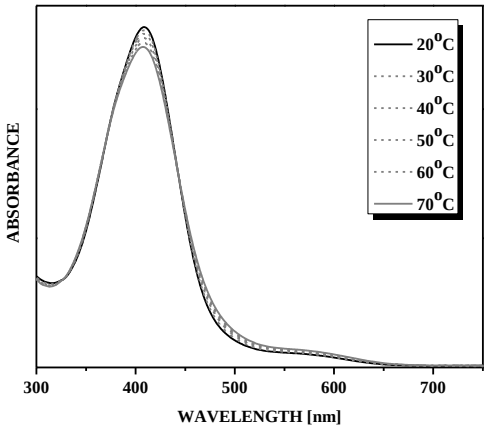
3.3 [11]	intramolecular	N-H…O(=C)	0.873	1.898	2.572(1)	132.5
	intermolecular	N-H…O(-H)		2.257	2.617(1)	104.5
	(complex with water)	O-H…OH_2	0.908	1.736	2.678	170.2
3.4	intramolecular	N-H…O(=C)	0.95(2)	1.83(2)	2.565(2)	132(2)
	intermolecular (linear dimer)	O-H…O(=C)	0.93(3)	1.75(3)	2.667(2)	168(2)
3.1b [12]	intramolecular	N-H…O(=C)	0.82(2)	1.93(2)	2.581(2)	135(2)
3.1c [12]	intramolecular	N-H…O(=C)	0.91(2)	1.85(2)	2.561(2)	133(2)
		N-H…O(-Me)		2.26(2)	2.609(2)	102(1)
3.1d [12]	intramolecular	N-H…O(=C)	0.86(3)	1.89(3)	2.559(3)	133(2)
3.1e [13]	intramolecular	N-H…O(=C)	0.935	1.866	2.594(2)	132(8)

The absorption spectra of **3.3** and **3.4** in DMSO in the temperature range of 20–70 °C are shown in **Fig. 38** and **39**. In both compounds, it can be seen that with increasing temperature, the absorption maximum of the neutral form (~400 nm) decreases slightly, while the amount of the deprotonated form absorbing at ~500 nm increases. The result can be interpreted in analogy to **3.1**. Increasing the temperature leads to the destruction of existing aggregates, which subsequently facilitates the deprotonation of the monomers. The temperature effect was strongest in **3.1** (**Fig. 17**), followed by **3.3** (**Fig. 38**) and lowest for **3.4** (**Fig. 39**). This indicates that **3.1** has the highest tendency to aggregate again related to the effect of the nitro group.

It was interesting to see how increasing the number of rings in the stator, could affect the conformational equilibrium between the conditions **E** and **Z**. Therefore, a theoretical study was performed in compounds **3.5** and **3.6**, where the phenyl ring is replaced by naphthalene and again has a different position of the OH group.



Scheme 11. *Structure of the investigated potential rotary switches **3.5** and **3.6**.*



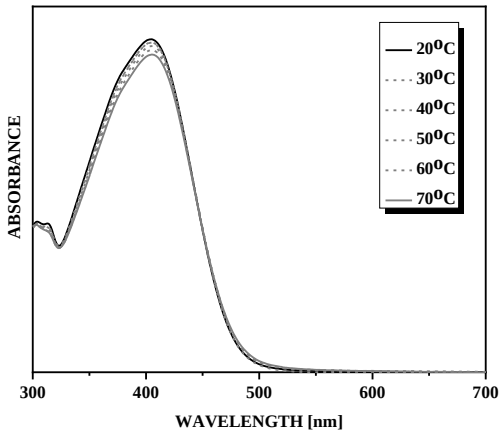


Fig. 38 and 39. *Absorption spectra of **3.3** (left) and **3.4** (right) in DMSO at a temperature range of 20°C - 70°C.*

Respectively, **3.5** can be considered as an analogue of **3.3**, and **3.6** - of **3.4**. Both compounds (**3.5** and **3.6**) are new and have not been studied so far (**Scheme 11**). According to theoretical calculations, **3.4** would be a potential rotary switch in a polar aprotic solvent, since the energy difference between the two conformational isomers (conditional **E** and **Z**) is over 2 kcal / mol (**Fig. 40**).

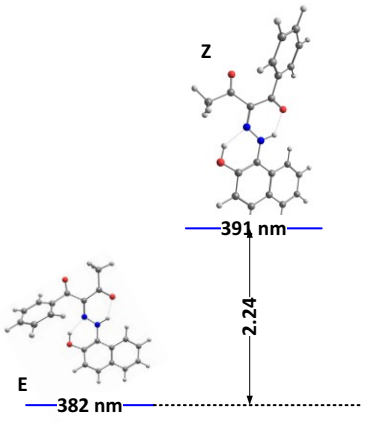


Fig. 40. *Relative energies (in kcal / mol) of the most stable conformational isomers of **3.5** in acetonitrile.*

However, the situation has changed when taking into account the specific interaction with the solvent (**Fig. 41**).

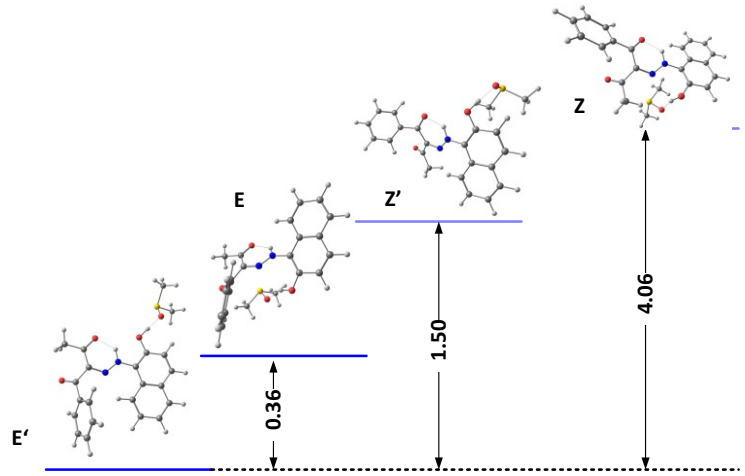


Fig. 41. *Relative energies (in kcal / mol) of the most stable conformational isomers of **3.5** taking into account the specific interation with the solvent DMSO.*

Compared to **3.3** energy difference between **E'-Z'** almost does not change, which shows that increasing the number of aromatic rings, does not lead to additional stabilization of one of the isomers. The higher values of the energy difference in **3.6** between the isomers taking into account the influence of the solvent (**Fig. 42** and **Fig. 43**) can be explained by the absence of the stabilizing effect of intramolecular hydrogen bonds in **3.5**.

This means, that the increase of the aromatic rings in **3.5** and **3.6** does not significantly affect the conformational equilibrium.

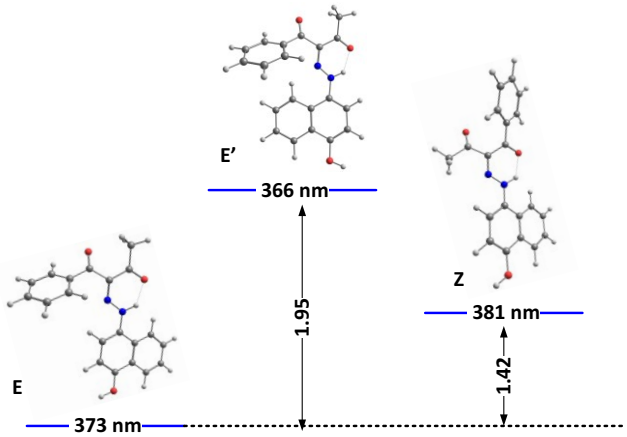


Fig. 42. *Relative energies (in kcal / mol) of the most stable conformational isomers of **3.6** in acetonitrile.*

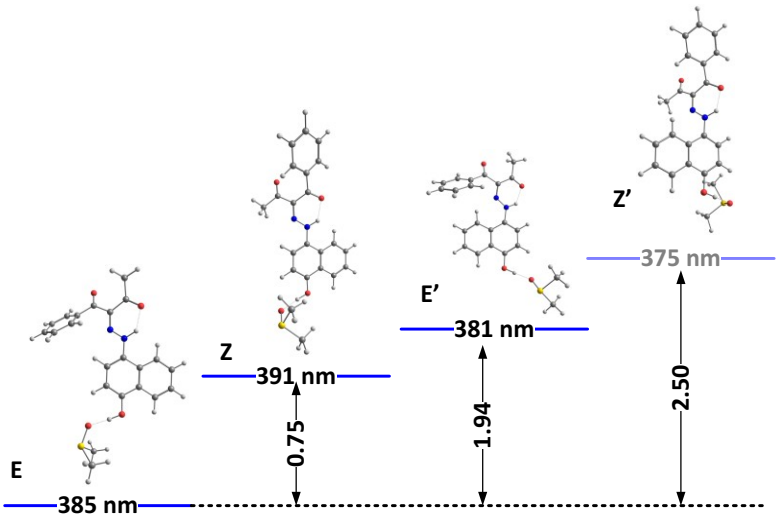


Fig. 43. *Relative energies (in kcal / mol) of the most stable conformational isomers of **3.6** taking into account the specific interaction with DMSO.*

IV. CONCLUSIONS

Based on what is described in this dissertation, the following **conclusions** can be made:

1. Using *UV-Vis* and *NMR* spectroscopy, and quantum chemical calculations, it has been shown that compounds **2.1-2.3** exist as tautomeric mixtures in solution. This information is new for compounds **2.2** and **2.3**.

2. The structural changes in **2.2** and **2.3** make it possible to control the position of the tautomeric equilibrium in solution. In **2.2**, the shift of equilibrium can be achieved by deprotonation of the additional hydroxyl group, while in **2.3**, the protonation of piperidine nitrogen stimulates the transition to the keto tautomer. Both processes are reversible.

3. Compound **2.3** is suitable for a tautomeric switch because the piperidine fragment is not conjugated to the tautomeric unit and the protonation process does not directly affect the absorption spectra. In this way, the piperidine fragment acts as an antenna that transmits the action of the external stimulus (acid / base) to the tautomeric process.

4. According to previous studies by *Mahmudov et al*. [3], compound **3.1** is presented in solution as a several tautomeric forms. Our spectral studies in DMSO and other solvents, as well as quantum chemical calculations, prove that the dye exists as a mixture of two isomers of one of the tautomers. The detailed reference to the NMR signals showed that the interpretation made by *Mahmudov et al.* was incorrect. In recent studies, the same authors have adopted our interpretation [14].

5. Having in mind that **3.1** is a potential rotory switch, it can be expected that the additional OH group will affect the rotation process or stabilize one of the conformational

isomers by forming an intramolecular hydrogen bond. Instead, it forms hydrogen bonds with the solvent, which leads to deprotonation in dilute solutions and to aggregation in concentrated solutions.

6. Based on experimental data published by *Lycka* [5], we have shown that it is possible to distinguish the conformational isomers of **3.1** and structurally similar compounds using ^{2}J constants in ^{15}N *NMR* spectra. This approach confirms that the major form in the solutions of **3.1** and **3.2** is **E´**, which in the case of **3.1** is stabilized by the formation of a linear aggregate. In DMSO, in the presence of water, an associate was observed, including water and DMSO, which explains experimentally the stabilization of the neutral forms. Crystallographic data confirm very well the theoretically predicted structure of aggregates as a way of interaction between individual molecules.

7. The effect of the solvent, temperature, concentration, presence of water and base is less express in compound **3.3**, which showed that the contribution of the NO_2 group to the stabilization of the **E'**-form is large. In **3.4**, the hydroxyl group has small effect on the rotation.

8. The effect of increasing the number of aromatic rings in the stator (**3.5** and **3.6**) was studied for the first time theoretically. Quantum chemical calculations predict that **3.5** would be a suitable rotary switch in a polar aprotic solvent. The increase in the number of aromatic rings in **3.5** and **3.6** does not significantly affect the conformational equilibrium.

V. C O N T R I B U T I O N

1. A concept is defined for stimulated proton transfer by introducing an unconjugated functional group into the molecule, which transfers the action of external stimuli on the tautomeric fragment.

2. Based on theoretical and experimental studies, we found that the previous results of *Mahmudov et al.* were not correctly interpreted.

3. It has been shown that the use of ^{2}J constants in rotary switches (**E, E ', Z, Z'**) in solutions makes it possible to distinguish each of the isomers. Because each of them can be represented as a unique logical combination of ^{2}J constants.

A P P E N D I X 1

PUBLICATIONS

1. **S.Hristova**, F.S.Kamounah, N.Molla, P.E.Hansen, D.Nedeltcheva, L.Antonov, *The possible tautomerism of the potential rotary switch 2-(2-(2-Hydroxy-4-*

nitrophenyl)hydrazono)-1-phenylbutane-1,3-dione, Dyes and Pigments, **144**, (2017), 249; **IF: 3.76; Q1 (2/24 Materials science); Number of citations: 2**;

2. **S.Hristova,** V.Deneva, M.Pittelkow, A.Crochet, F.S.Kamounah, K.M.Fromm, P.E.Hansen, L. Antonov, *A concept for stimulated proton transfer in 1-(phenyldiazenyl)naphtalen-2-ols*, Dyes and Pigments, **156**, (2018), 91-99; **IF: 3.76; Q1 (2/24 Materials science); Number of citations: 2**;

3. **S.Hristova**, F.S.Kamounah, A.Crochet, P.E.Hansen, K.M.Fromm, D.Nedeltcheva, L.Antonov, *Isomerization and aggregation of 2-(2-(2-hydroxy-4-nitrophenyl)hydrazono)-1-phenylbutane-1,3-dione: Recent evidences from theory and experiment*, Journal Of Molecular Liquids, **283**, (2019), 242–248; **IF: 4.51; Q1 (6/37 Molecular and chemical physics); Number of citations: 1**.

4. **S. Hristova**, F.S.Kamounah, A.Crochet, N.Vassilev, K.M.Fromm, L.Antonov, *OH Group Effect in the Stator of β-Diketones Arylhydrazone Rotary Switches*, Chemistry, **2(2)**, (2020), 374–389.

APPENDIX 2

LIST OF CITATIONS:

1. S.Hristova, F.S.Kamounah, N.Molla, P.E.Hansen, D.Nedeltcheva, L.Antonov, *The possible tautomerism of the potential rotary switch 2-(2-(2-Hydroxy-4-nitrophenyl)hydrazono)-1-phenylbutane-1,3-dione*, Dyes and Pigments, 144, (**2017**), 249		
1.	1.	Lyčka, A. ^{15}N NMR study of (E)- and (Z)-2-(2-(2-hydroxy-4-nitrophenyl)hydrazono)-1-phenylbutane-1,3-diones. A suitable method for analysis of hydrazone isomers, Dyes and Pigments, 150, 181-184 (**2018**).
2.	2.	Kumar, S.S., Sreepriya, R.S., Biju, S., Sadasivan, V., Synthesis, crystal structure and spectroscopic studies of trivalent Fe(III) and mixed valent ion-pair Co(II,III) complexes with 5-(2-(2-hydroxyphenyl)hydrazono)-2,2-dimethyl-4,6-dione, Journal of Molecular Structure, 1197, 235-243 (**2019**)
2. S.Hristova, V.Deneva, M.Pittelkow, A.Crochet, F.S.Kamounah, K.M.Fromm, P.E.Hansen, L.Antonov, *A concept for stimulated proton transfer in 1-(phenyldiazenyl)naphtalen-2-ols*, Dyes and Pigments, 156, (**2018**), 91-99;		
3.	1.	Liu J., Zhong X., Wu Sh., Li Y., Xu Y., Zeng H., Green synthesis and characterization for 8-hydroxyquinoline magnesium Materials Research Express, 6, 5 (**2019**)
4.	2.	Chen Z. Li Y., Guan Y., Li H., Rational design of the nonlinear optical materials dinaphtho[2,3-b:2′,3′-d]thiophene-5,7,12,13-tetraone (DNTTRA) and its

		phenyldiazenyl derivatives using first-principles calculations, Journal of Computational Electronics, 18 (1), 6–15 **(2019**)
	3. S.Hristova, F.S.Kamounah, A.Crochet, P.E.Hansen, K.M.Fromm, D.Nedeltcheva, L.Antonov, *Isomerization and aggregation of 2-(2-(2-hydroxy-4-nitrophenyl)hydrazono)-1-phenylbutane-1,3-dione: Recent evidences from theory and experiment*, Journal Of Molecular Liquids, 283, (**2019**), 242–248.	
5.	1.	Gurbanov V., Mahmudov K., Kuznetsov L., Demukhamedova D., Aliyeva N., Godjaev M., etc, *Role of substituents on resonance assisted hydrogen bonding vs. intermolecular hydrogen bonding* (**2020**).

APPENDIX 3

REPORTING TO SCIENTIFIC FORUMS OF SCIENTIFIC RESULTS ON THE TOPIC OF THE DISSERTATION

1. Lectures

✓ *"Молекулни устройства на базата на тавтомерни ефекти",* ***„Докторантски чай" на Физически факултет към Софийски университет "Св. Климент Охридски"***, Sofia, Bulgaria, 06.04.2017.

✓ *"Molecular Rotors based on tautomeric processes",* ***"International Meeting on Medicinal and Bio(in)organic Chemistry"***, Vrnjačka Banja, Serbia, 26-31.08.2017.

✓ *"Дизайн на роторни превключватели: проблеми и перспективи"*- ***XVII Национална конференция по химия за студенти и докторанти****, Факултет по Химия и Фармация на Софийски Университет,* Sofia, Bulgaria, 16-18.05.2018.

✓ *„β-diketones based rotary switches: molecular spectroscopy and computational chemistry playing together"* - ***Young researchers meet molecular spectroscopy,*** Pisa, Italy, 04-05.04.2019.

✓ *"Smart molecules" - the future of electronic devices in the light of intramolecular motion"* - ***"Science without Borders: Alexander von Humboldt's Concept in Today's World"***, Varna, Bulgaria, 18-21.09.2019.

2. Poster participations

✓ *„10-hydroxybenzo[h]quinoline: switching between single- and double-well proton transfer through structural modification" и „Tautomeric molecular rotors",* ***Summer School Supramolecular Chemistry – Ideas, Design and Methods for Investigations*** Borovets, Bulgaria, 16-18.06.2016.

✓ *„2-(2-(2-hydroxy-4-nitrophenyl)hydrazono)-1-phenylbutane-1,3-dione: a potencial rotory switch“,* ***X Научна конференция по Химия с международно участие,*** *Plovdiv, Bulgaria*, 09-11.10.2016.

✓ *“The possible tautomerism of the rotary switch 2-(2-(2-hidroxy-4-nitrophenyl) hydrazono)-1-phenylbutane-1,3-dione”,* ***International spring school “Supramolecular Chemistry Methods, Concepts and Applications”,*** *Plovdiv, Bulgaria*, 19-21.04.2017.

✓ ***„****Experimental investigations and theoretical calculations: Molecular rotors based on ground state proton transfer“****, Joint Training School - “New avenues in molecular theories: From the lab to beyond the Earth”,*** Belgrade, Serbia, 31.08-06.09.2017.

✓ *”Rotary switches as a perspective platform for development of molecular motors”****, Четвърта научна конференция за студенти, докторанти и млади учени „Предизвикателства в Химията“,*** *Plovdiv, Bulgaria*, 10-11.11.2017.

✓ „*Theoretical design and spectral investigations of tautomeric rotary switches“*- ***24th IUPAC International Conference on Physical Organic Chemistry***“, Faro, Portugal, 01-06.07.2018.

✓ „*A concept for stimulated proton transfer in 1-(phenyldiazenyl)naphthalen-2-ols*“ - ***International Summer school - “Supramolecular Chemistry in Medicine and Technology: Advances and Challenges”****,* Albena, Bulgaria, 30.08-03.09.2018.

✓ „*Effect of the tautomeric functionality and aromaticity of the stator in rotary switches*“ - ***XI Научна конференция по Химия с международно участие****, Plovdiv, Bulgaria*, 11-13.11.2018.

✓ *„Детайлно изследване на действието на роторни превключватели“* - ***Втори интердисциплинарен докторантски форум****, Borovets, Bulgaria*, 29-31.08.2019.

✓ *„Factors influencing the switching process of different β-diketones“* - ***Пета научна конференция за студенти, докторанти и млади учени „Предизвикателства в Химията“****, Plovdiv, Bulgaria*, 22-23.11.2019.

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[11] Kopylovich, M. N.; Mahmudov, K. T.; Haukka, M.; Luzyanin, K.V.; Pombeiro, A.J.L. (E)-2-(2-(2-Hydroxyphenyl)Hydrazono)-1-Phenylbutane-1,3-Dione: Tautomery and Coordination to Copper(II). Inorg. Chim. Acta. 2011; 374; 175–180.
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