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Photoswitchable intramolecular hydrogen bonds in 5-phenyl-azopyrimidines revealed by *in situ* irradiation NMR spectroscopy

Eliška Procházková,* [a] Lucie Čechová,[a] Jonas Kind,[b] Zlatko Janeba,[a] Christina M. Thiele,[b] Martin Dračínský* [a]

Abstract: NMR spectroscopy with *in situ* irradiation uncovered unique photoswitchable intramolecular hydrogen bonds (IMHBs) in 5-phenylazopyrimidines with two hydrogen bond donors. These compounds form two stable rotamers, each with one IMHB, and the rotamer ratio changes reversibly upon UV or visible light irradiation. Strong substituent dependence of photo-induced structural changes was observed; using suitable substituents, orthogonal photoswitching can be achieved. For example, while UV irradiation caused switching between the two rotamers of the *trans* isomer of a compound with electron-donating methoxy substituent, visible light enabled to obtain the *cis* photoisomer. No *cis* isomer was detected for compounds with electro-neutral or electron-accepting substituents, but photoswitching between the two *trans* isomers was observed. On the other hand, compounds without hydrogen-bond donors or with one donor only formed stable *cis* isomers. A mechanism of the photoswitching was proposed by DFT computations.

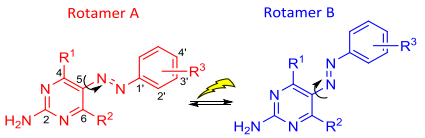
Introduction

5-Phenylazopyrimidine derivatives are structurally similar to the well explored photosensitive azobenzenes whose photoswitching is based on reversible *trans–cis* isomerisation[1] accompanied by a significant change of the molecular shape, dipole moment and electronic distribution. Azobenzene-based compounds have found a wide range of applications in optochemical genetics,[2] photopharmacology,[3] molecular biology,[4] biochemistry,[5] molecular devices,[6] smart remote-controlled materials[7] or catalysis.[8] In azopyrimidines, one of the aromatic phenyl rings is replaced by pyrimidine and such molecules may obtain new prominent properties, such as keto/enol tautomerism, protonation sites leading to changes of acidobasic properties,[9] higher polarity and biocompatibility[10] or formation of intermolecular hydrogen bonds similar to those between natural bases in nucleic acids.

The formation of intramolecular hydrogen bonds (IMHBs) significantly influences molecular physico-chemical properties of compounds, such as reactivity, lipophilicity, solubility, membrane permeability,[11] acidity or biocompatibility.[12] Five- or six-membered pseudorings stabilized by IMHBs are frequently formed when hydrogen-bond donor and acceptor are suitably arranged.[13] These pseudorings have been shown to mimic aromatic rings and they have been successfully exploited in the design of novel drugs.[14] For example, 5-nitrosopyrimidine derivatives have been proposed to work as purine mimics.[15] 5-Phenylazopyrimidines with two hydrogen-bond donors able to form six-membered pseudorings with one of the azo nitrogen atom were investigated in our recent work.[16] It was shown that substitution in *para* position of the phenyl ring does not affect the hydrogen-bond strength, but influences significantly the barrier of rotation around the bond between carbon C5 of the pyrimidine ring and the azo nitrogen.

It has been shown that the formation of IMHBs in azobenzene derivatives dramatically changes their photochemical properties and effectively hampers the formation of the *cis* isomer.[17] Therefore, we decided to explore the photochemical behavior of 5-phenylazopyrimidines with IMHBs.

Herein, we report on unique photoswitchable IMHBs in azopyrimidines with two hydrogen bond donors (rotamer A and B in Fig. 1) by UV/Vis irradiation. While a formation of two stable rotamers of the *trans* isomer in compounds with two hydrogen bond donors has already been studied, photoswitching between them has not been reported so far. The photo-induced structural changes were monitored by NMR spectroscopy with *in situ* irradiation,[18] where a light emitting diode (LED)[19] was used as the source of light. The LED was coupled to the optical fiber to guide the light directly into the NMR tube.[20] This prominent technique allowed investigating the effects of IMHBs on the stability and interconversion of both rotamers and/or the formation of the *cis* isomer in real time. Furthermore, DFT computations were employed to explain the photoswitching behavior.



	R^1	R^2	R^3
1	OCH_3	OCH_3	H
2	NH_2	OCH_3	H
3	NH_2	$NHCH_3$	H
4	NH_2	$NHCH_3$	4'-OCH_3
5	NH_2	$NHCH_3$	4'-Cl
6	NH_2	$NHCH_3$	4'-CN
7	NH_2	$NHCH_3$	4'-NO_2
8	NH_2	$NHCH_3$	3'-NO_2

Figure 1. Structures and numbering of the azopyrimidine derivatives studied.

Results and Discussion

To investigate the effect of IMHBs on the *trans-cis* photoisomerization, we first studied the photochemical behavior of three types of compounds: without (**1**), with one (**2**) and with two (**3**) hydrogen bond donors in the pyrimidine ring in the neighboring positions (C4, C6) with respect to the 5-phenylazo moiety. Based on the interesting photoswitchable IMHBs found in compound **3** (the derivative with two hydrogen bond donors),

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we investigated the photoswitching behaviour in derivatives **4**–**8** differing in the substitution on the phenyl ring.

UV/Vis spectroscopy

There are significant differences in UV/Vis absorption spectra of compounds **1**–**3** (Fig. 2). In compound **1**, where no IMHB can be formed, two absorption maxima are observable (356 and 450 nm). As 20% of the *cis* isomer is detected in thermal equilibrium in ^{1}H NMR spectra (Fig. 3), the shoulder at 450 nm is assigned to the *cis* isomer. Observations of similar concentrations of the *cis* isomer have been described for some azobenzene derivatives.[21] In compound **2**, one strong IMHB is formed, which destabilizes the *cis* isomer significantly and no shoulder/maximum corresponding to the *cis* isomer is observed in the UV/Vis spectrum. Similarly, no *cis* isomer was detected in the spectrum of compound **3**, which has two stable rotamers of the *trans* isomer.

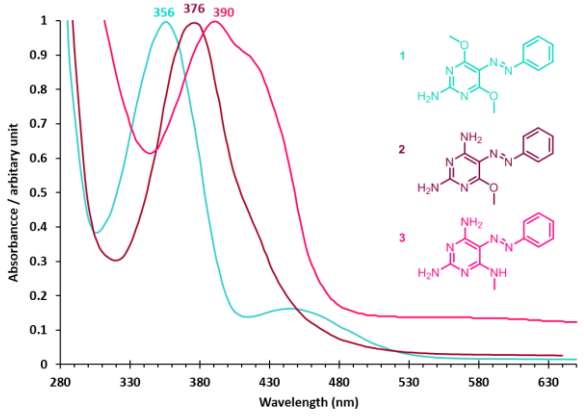

Figure 2. The effect of IMHBs on the absorption wavelengths of azopyrimidine derivatives in UV/Vis spectra. Normalized absorption spectra of compounds **1**–**3** in DMF at room temperature (25 °C).

NMR spectroscopy with *in situ* irradiation

In situ irradiation of compounds **1**–**3** with UV light (365 nm) during NMR experiments (2 mM solutions in DMF-d_7) at room temperature (25 °C) revealed immense differences in their photochemical behavior. Compound **1**, which cannot form any IMHB, provided a very stable *cis* isomer within 10 minutes of irradiation (Fig. 3 left) and the thermal fading occurred monoexponentially with a half-life $\tau_{1/2}$ of ca. 11.5 days in the dark (Fig. S5 in the Supporting Information). The *cis* isomer is easily recognized in ^{1}H NMR spectra by an upfield shift (to lower chemical shift values) of all signals caused by mutual shielding of the pyrimidine and phenyl rings (Fig. 3 left). In derivative **2**, where one IMHB stabilizes rotamer B (Fig. S6), the *cis* isomer was formed within 10 minutes of irradiation as well (Fig. 3 right). In contrast to **1**, thermal relaxation back to the *trans* isomer of **2** was significantly faster with a half-life $\tau_{1/2}$ of ca. 5 h in the dark (Fig. S8). Free energy barriers of the *cis* to *trans* conversion were calculated from the observed rate constants of thermal fading. The energy barrier was higher by 2.4 kcal/mol for derivative **1** than for **2** (Table 1).

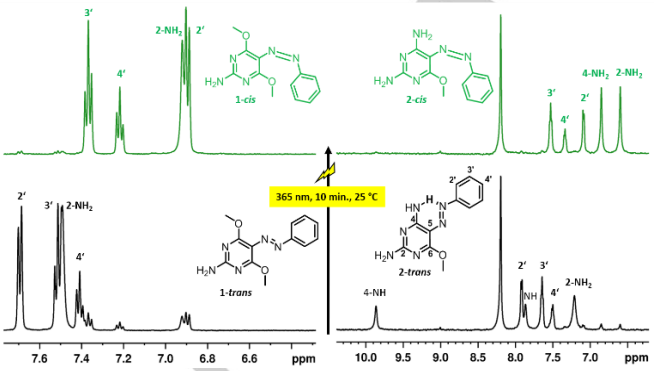

Figure 3. Part of ^{1}H NMR spectra of compounds **1** (left) and **2** (right) prior to (black) and upon irradiation (green) in DMF-d_7. In compound **2**, the signal corresponding to the 4-NH proton participating in an IMHB in the *trans* isomer is shifted downfield significantly (to ca. 10 ppm).

Compound **3** with two hydrogen bond donors exists as a mixture of two rotamers (A and B), each with one IMHB (Fig. 4), and thus, two sets of NMR signals can be observed at low temperatures. At room temperature, fast conformational exchange gives rise to one set of broad signals. Compound **3** does not form detectable concentrations of *cis* isomer upon irradiation even at –55 °C. To accumulate the *cis* isomer in detectable concentrations, irradiation was repeated at lower temperatures to supress thermal *cis*-*trans* isomerization. We speculated that a significantly lower temperature is required for its stabilization. Therefore, a 50% DMF-d_7/CD_2Cl_2 solvent mixture was used to enable NMR measurements with *in situ* irradiation below –100 °C.

Table 1. The effect of the number of hydrogen bond donors on the free energy barrier of the *cis*-to-*trans* thermal relaxation of 5-azopyrimidines in DMF-d_7.

No. of IMHB donors	Cpd	$\Delta G^{\ddagger}_{exp}$ (kcal/mol) [a]	$\Delta G^{\ddagger}_{calc}$ (kcal/mol) [c]
0	**1**	25.9	28.2
1	**2**	23.5	24.2
2	**3**	– [b]	16.4

[a] 2 mM solutions in DMF-d_7, thermal fading monitored at 25 °C after 10 min. irradiation at 365 nm
[b] No *cis* isomer detected even after 3 h irradiation (365 nm) at –105 °C
[c] M06X/6-31+G** with polarizable continuum model of DMF solvation

When compound **3** was irradiated at –105 °C, surprisingly, still no *cis* isomer was detected but the ratio of A and B rotamers changed significantly. Prior to irradiation, rotamer A was the predominant component (62%), while upon irradiation, rotamer B became the predominant form (over 60%). After switching the LED off and leaving the sample inside the NMR spectrometer (in the dark at –105 °C), the rotamer ratio reached the initial equilibrium state (38% B) with a half-life $\tau_{1/2}$ of ca. 0.9 h (Fig. 4). Monitoring the thermal fading, we extracted the rate constant and calculated the energy barrier of interconversion between the

rotamers $\Delta G^{\ddagger}_{B\text{-}A}$ (see the procedure in the SI). The barrier is 12.5 kcal/mol, which is in excellent agreement with the rotamer interconversion barrier recently estimated using line shape analysis of variable temperature ^{1}H NMR spectra.[16] Thus, in addition to variable temperature NMR, the rotational barrier can also be obtained from thermal fading of the photoinduced rotamer ratio change. More importantly, these findings ask for a deeper investigation of factors influencing the novel photoinduced structural changes.

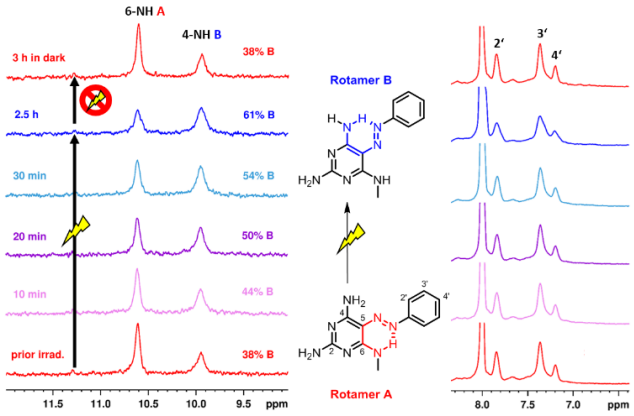

Figure 4. NH (left) and aromatic (right) region of ^{1}H NMR spectra of compound **3** (2 mM solution in 50% DMF-d_7/CD_2Cl_2) prior to and upon UV irradiation (365 nm) at –105 °C. The LED was switched off after 2.5 h. While the NH region changes upon irradiation, no cis isomer has been detected in the aromatic region. For detailed assignment of all signals see the SI.

Photoswitchable IMHBs

Encouraged by these interesting observations of hydrogen bond switching in compound **3**, we prepared a series of compounds **4**–**8** (Fig. 1) with two hydrogen bond donors. The compounds differ in the electronic properties of the substituent R^3 on the phenyl ring. The ratio of rotamers A and B in equilibrium was ca. 6:4 in all cases. The changes in rotamer ratio upon UV irradiation (2 mM, –105 °C, 2.5 h irradiation at 365 nm) were monitored and a substantial substituent dependence on the switching behavior of the compounds as well as on the thermal fading to the initial state was observed (Fig. 5).

Compound **4** with an electron-donating methoxy group (R^3 = 4'-OCH_3) did not allow to obtain rotamer B as the major component (37–40% only) at –105 °C (λ=365 nm). We believe that this is due to a faster thermal fading to the rotamer equilibrium than for the other compounds. This has been confirmed by an irradiation experiment at –115 °C, where we obtained significantly higher amount of rotamer B (more than 50%) within 10 min. Unfortunately, the signals were too broad to integrate them properly (Fig. S15). Furthermore, even at –125 °C no *cis* isomer was detected at 365 nm irradiation wavelength.

Derivative **5** (R^3 = 4'-Cl) behaves like a decent photoswitch (Fig. 5). Within 2.5 h of irradiation at –105 °C, rotamer B was obtained as the predominant component (55%) and then, after switching the light off, the system relaxed back to the initial state with a half-life $\tau_{1/2}$ of ca. 2 h. The rotational barrier of the rotamer interconversion $\Delta G^{\ddagger}_{B\text{-}A}$ was determined to be 12.7 kcal/mol.

Irradiation of derivatives **6** and **7** with electron-withdrawing substituents (R^3 = 4'-CN and 4'-NO_2, respectively) also leads to significant changes of rotamer ratio (rotamer B becomes more abundant, ca. 55%) but the thermal relaxation to the initial equilibrium is very slow at –105 °C. This is caused by the higher rotational barrier between rotamers A and B.[16] When the irradiation experiment is performed at –80 °C, the rotamer ratio also changes (55% B) and the relaxation is sufficiently fast to determine the rotamer interconversion barrier (14.7 and 15.0 kcal/mol, respectively) in a reasonable time (Fig. S16). These findings are an experimental manifestation of push-pull interactions between electron-donating (NH_2) and electron-accepting (CN, NO_2) substituents, which have been shown to lead to higher bond order and rotational barrier of exocyclic substituents in pyrimidines.[22]

In compound **8**, in which the NO_2 substituent is in *meta* position (C3') instead of *para* (C4' in **7**), the push-pull interaction is weaker, which is nicely reflected in the rotamer exchange behaviour (Fig. 5). The $\Delta G^{\ddagger}_{B\text{-}A}$ barrier of the *meta*-substituted derivative **8** was found to be lower (13.5 kcal/mol) than that in *para*-substituted derivative **7** (15.0 kcal/mol).

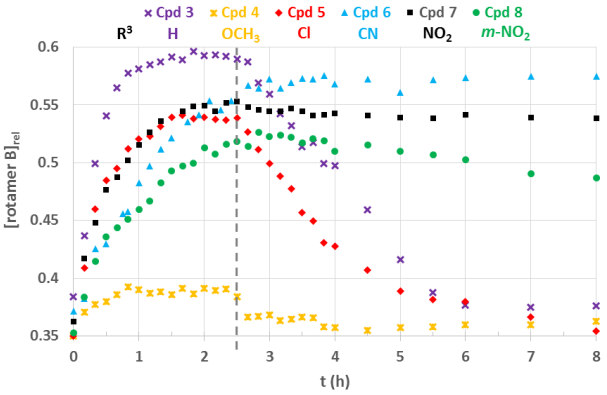

Figure 5. Substituent effect on photoswitching behaviour. Superposition of kinetic curves of compounds **3**–**8** measured under the same conditions: 2 mM solutions in 50% DMF-d_7/CD_2Cl_2, –105 °C. The LED (365 nm) was switched off after 2.5 h of irradiation (dashed line).

Visible light irradiation

Due to different absorption wavelengths of compounds **3**–**8** (Fig. S2), these were also irradiated at 405 and 470 nm. For compound **3** a lower amount of rotamer B is observed at higher wavelengths (Fig. S18). The rotamer ratio changes are slightly different for compound **5** and **8** when irradiated at different wavelengths (Fig. S19 and S21, respectively). For **6** and **7** the highest amount of rotamer B is observed at 405 nm (Fig. S20). Furthermore, and more importantly, upon irradiation at 405 nm (visible light) the *cis* isomer of compound **4** was detected at –105 °C. During the *cis* isomer formation, IMHBs are disturbed and NMR signals corresponding to the NH protons bound in IMHBs disappeared from the ^{1}H NMR spectra (Fig. 6 left).

Simultaneously, new NMR signals corresponding to the *cis* isomer in aromatic region appeared (Fig. 6 right). After switching the light off, the *trans* isomer is formed in the dark within 1.5 h. Unfortunately, no *cis* isomer of compounds **3** and **5–8** was observed. This is probably due to a fast *cis*-to-*trans* isomerization (low $\Delta G^{\ddagger}_{cis\text{-}trans}$ confirmed by DFT, see below).

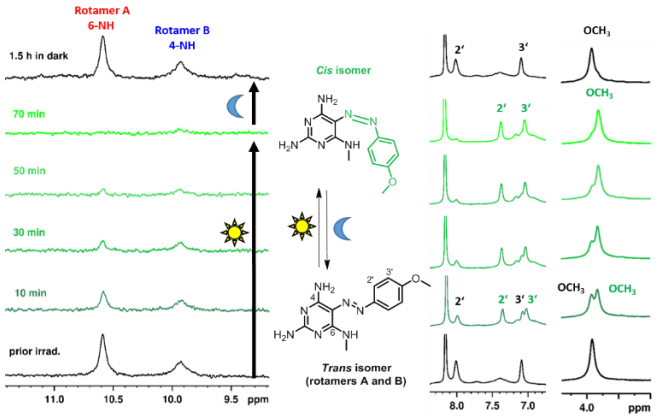

Figure 6. The *cis* isomer formation of compound **4** upon visible light irradiation at 405 nm. NH (left) and aromatic (right) region of ^{1}H NMR spectra of **4** (2 mM solution in 50% DMF-d_7/CD_2Cl_2 at –105 °C).

The mechanism of the photoswitching

To gain insight into the different processes involved, we conducted DFT computations using the M062x functional for the *cis-trans* isomerization as well as for the photoinduced change in rotamer ratios. Four different mechanisms have previously been suggested for the thermal *cis*-to-*trans* isomerization of azobenzene derivatives: inversion, rotation, concerted inversion and inversion-assisted rotation.[21] Our search for transition-state structures for the thermal isomerization of compound **1** (without intramolecular hydrogen bond) revealed true transition state structures (with one imaginary frequency) only for the inversion mechanism. However, the inversion at the nitrogen atom closer to the phenyl ring (TS1) or closer to the pyrimidine ring (TS2) is possible (Fig. S22). The inversion *via* TS1 is associated with an energy barrier lower by 0.1 kcal/mol. This barrier (28.2 kcal/mol) agrees reasonably well with experiment (25.9 kcal/mol). It should be also noted that the transition-state structure optimization with the B3LYP functional led to a slightly lower reaction barrier (23.6 kcal/mol).

The mechanism of the *cis*-to-*trans* thermal isomerization is substantially different in the case of compound **2** with one hydrogen bond donor (R^1=NH_2) next to the 5-phenylazo moiety leading to one IMHB. The transition state TS1 involving inversion at the nitrogen atom attached to the phenyl ring was not found, but a different transition state corresponding to the rotation around the N=N bond was found (TS3) together with TS2. However, both transition states TS2 and TS3 have too high energy (energy barriers for the isomerization reaction of 26.6 and 27.9 kcal/mol, respectively) in comparison with the experimental reaction barrier (23.5 kcal/mol). Therefore, a completely different mechanism for the isomerization process was considered. Both *cis* and *trans* isomers of 5-phenylazopyrimidines bearing amino substituent(s) may exist in two stable tautomeric forms: the amino-azo and imino-hydrazo forms (see in Figs. 7 and S25). There is formally a single bond between the two nitrogen atoms in the imino-hydrazo form and hence, the rotation around this bond should be a low barrier process. Indeed, several transition state structures connecting the *cis* and *trans* isomers of the imino-hydrazo tautomer of compound **2** can be found (Fig. S23). The energy barrier for this isomerization (TS4, 24.2 kcal/mol) is significantly lower than the barrier found for the amino-azo tautomer and it is in excellent agreement with the experimental value (23.5 kcal/mol).

Similar transition state structures TS2, TS3 and TS4 were found also for compounds **3–8**. Because of the presence of two hydrogen bond donors in positions C4 and C6, all these transition states have two possible geometries (orientation of the phenyl ring towards NH_2 or $NHCH_3$ group). The lowest energy barrier of compound **3** (16.4 kcal/mol) was found for TS4 involving the imino-hydrazo tautomer and, importantly, the TS4 structure leading to rotamer B of the *trans* isomer of compound **3** is associated with a lower energy than the transition state structure leading to rotamer A, which may explain the observed rotamer ratio changes. The proposed mechanism of the photoinduced hydrogen bond switching then involves: photoisomerization of both rotamers to the *cis* isomer, imino-hydrazo tautomer formation, rotation around the N–N bond leading to rotamer B and amino-azo tautomer formation of rotamer B (Fig. 7). The calculated energy barrier for the isomerization process is significantly lower than that found for compound **2**.

The structure of the lowest energy transition state depends on the substitution of the phenyl ring; TS4 has the lowest energy in compounds **3–5** whereas TS3 has lower energy in compounds **6–8** with electron-withdrawing substituents (Table 2). At the same time, the height of the isomerization barrier decreases significantly when electron-withdrawing substituents are attached to the phenyl ring, for example, the barrier for compound **7** (4'-NO_2 substituent) is by 10 kcal/mol lower than that for compound **4** (4'-OCH_3). This can explain why the *cis* isomer could be observed for compound **4** (at –105 °C) only; the other compounds isomerize quickly back to the *trans* isomer and the *cis* isomer cannot be detected by NMR spectroscopy.

Table 2. Computed free energy barriers of *cis*-to-*trans* isomerization in compounds **3–8**.

Compound	Substituent	*Calc.* $\Delta G^{\ddagger}_{cis\text{-}trans}$ (kcal/mol)	Transition state structure
3	H	16.4	TS4
4	4'-OCH_3	19.3	TS4
5	4'-Cl	17.0	TS4
6	4'-CN	12.5	TS3
7	4'-NO_2	9.2	TS3
8	3'-NO_2	15.2	TS3

The energy of the imino-hydrazo transition state TS4 is always lower for the structure leading to rotamer B of compounds **3**–**8**, which can explain the observation of increasing rotamer B concentration upon irradiation. However, as the *cis* isomers of compounds (**3** and **5**–**8**) are not experimentally observed, other reaction mechanisms cannot be excluded. For example, it has been shown that an ultra-fast proton transfer may occur in excited state of 2-hydroxyazobenzene derivatives.[23] Geometry optimization of first excited states of compounds **3**–**8** leads to conical intersections with structures similar to those of TS3. After quenching to the ground state and subsequent geometry optimization, *cis* isomers of compounds **3** and **4**, and *trans* isomers of compounds **5**–**8** were obtained. Nevertheless, the energies of the conical intersections of compounds **5**–**8** were always lower for structures leading to *trans*-rotamer B. These calculations suggest that the irradiation-induced rotamer interconversion may proceed even without passing the *cis* isomer.

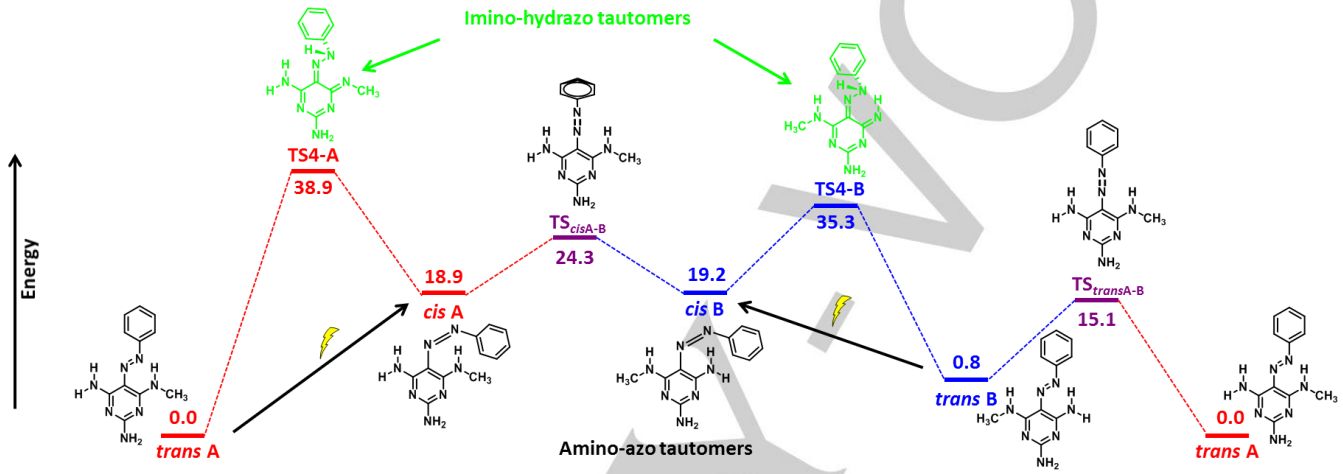

Figure 7. Schematic energy diagram and relative free energies (kcal/mol) of compound **3** showing the proposed mechanism for the photoinduced rotamer ratio change in compounds **3**–**8**. UV irradiation leads to the formation of the *cis* isomer (rotamers A and B with a low barrier of their interconversion TScisA-B). Thermal *cis*-to-*trans* back-isomerization preferentially leads to rotamer B (*via* TS4-B). The rotamer ratio is equilibrated to the initial relative concentrations of A and B rotamers in the dark *via* the TStransA-B transition state.

Conclusions

In conclusion, we described unique photoswitchable intramolecular hydrogen bonds in 5-phenylazopyrimidines with two competing hydrogen bond donors (in compounds **3**–**8**), which are able to form two stable IMHBs differing in the overall azopyrimidine geometry. NMR spectroscopy with *in situ* irradiation was employed as a suitable tool to monitor the photoswitching of the IMHBs and their thermal relaxation to the initial equilibrium. The formation of the *cis* isomer upon irradiation was detected for compounds **1**, **2** and **4**. The effect of hydrogen bond donors on the stability of the *cis* isomer is enormous. We proved that the IMHBs in these compounds do not serve as a lock of photoisomerization, although they dramatically decrease the energy barrier of the *cis*-to-*trans* isomerization. The experimental data were supported by DFT computations and a mechanism for the photoswitching behavior was proposed. These extraordinary photoswitchable azopyrimidines might find diverse applications in drug design as well as in the development of smart materials enabling orthogonal photoswitching (*trans*/*cis* and rotamer A/B).

Experimental Section

Synthesis of the studied compounds, their characterization and HR-MS and NMR spectra can be found in the SI.

NMR spectra were recorded on a Bruker Avance III spectrometer with a broad-band cryo probe with ATM module (5 mm CPBBO BB-^{1}H/^{19}F/^{15}N/D Z-GRD) operating at 500 MHz for ^{1}H and 125.7 MHz for ^{13}C and Bruker Avance III 600 MHz spectrometer with a 5 mm TBI probe (^{1}H, ^{31}P, BB) equipped with a z-gradient coil at a corrected temperature of 25 °C. Low temperature measurements were performed on a Bruker Avance II spectrometer with a triple resonance broad-band probe (5 mm TBO BB-^{1}H/^{19}F/D Z-GRD) operating at 499.9 MHz for ^{1}H and 125.7 MHz for ^{13}C. For NMR signal assignment, standard Bruker pulse sequences for 1D (^{1}H, ^{13}C-APT) as well as 2D (COSY, ROESY, HSQC, HMBC) NMR experiments at corrected temperature 25 °C or –55 °C were employed and all samples were measured in DMF-d_7. Low temperature measurements have been done in 50% DMF/CD_2Cl_2 (a mixture of DMF-d_7 and CD_2Cl_2 1:1 vol.) at –105 °C and –80 °C. All NMR data were interpreted using Topspin 3.5. As a reference, solvent signals were used: 1. DMSO-d_6: 2.50 (^{1}H) and 39.7 (^{13}C) ppm and 2. DMF-d_7: 2.92 (^{1}H) and 34.9 (^{13}C) ppm.

For NMR experiments with *in situ* irradiation, light emitting diodes (LEDs) with 365 nm, 405 nm and 470 nm emission wavelength

from Thorlabs, Germany were used. The light was guided into the NMR spectrometer, directly into the NMR tube, with a multimode silica optical fiber with 1 mm diameter, 0.39 NA, high amount of OH from Thorlabs, Germany.

UV/Vis spectra were measured on a BioTek™ Cytation™ 3 Cell Imaging Multi-Mode Reader using a 96-well transparent plate. The freshly prepared samples were measured as 0.12 mM solutions in DMF or 50% DMF/CH_2Cl_2 at room temperature (25 °C).

All studied structures were subjected to geometry optimization at DFT level, using the M062x functional,[24] standard 6-31+G(d,p) basis set and polarizable continuum model used for implicit dimethylformamide solvation.[25] The Gaussian16 program package was used throughout this study.[26] The QST3 optimization method[27] was applied in the search for the transition state structures of the reaction; that is the structures of the reactant, product, and estimated transition state were used as input for the TS search. The vibrational frequencies and free energies were calculated for all of the optimized structures, and the stationary-point character (a minimum or a first-order saddle point) was thus confirmed. All calculated energies in the manuscript and the SI are free energies (ΔG). The entropy term was obtained by thermochemistry analysis of calculated second derivatives of electronic energy performed for all studied compounds and transition-state structures.

Acknowledgements

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Keywords: azopyrimidines • intramolecular hydrogen bonds • *in situ* irradiation • NMR spectroscopy • photoswitching

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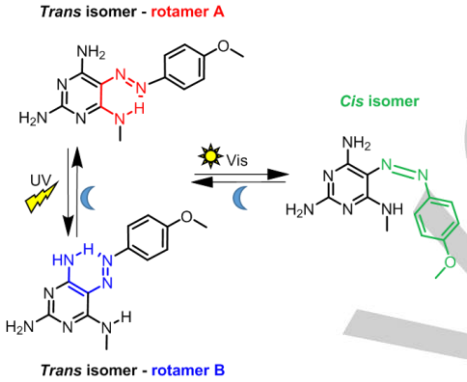
Layout 1:

FULL PAPER

Bond, Hydrogen Bond: NMR spectroscopy with *in situ* UV/Vis irradiation revealed inter-conversion between two stable rotamers in 5-phenylazo-pyrimidines based on strong intramolecular hydrogen bonds triggered by light. The speed and extent of forward and backward hydrogen bond switching can be finely tuned by installing suitable substituents and by the irradiation wavelength.



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Photoswitchable intramolecular hydrogen bonds in 5-phenylazo-pyrimidines revealed by *in situ* irradiation NMR spectroscopy