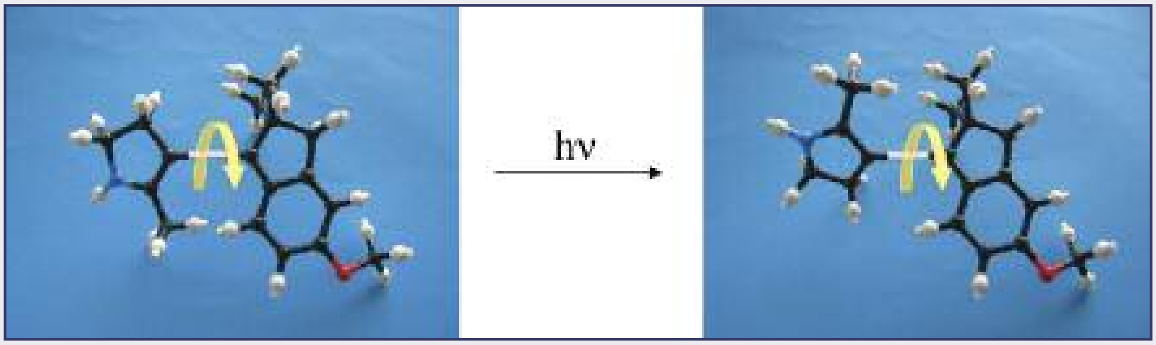

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# BIOMIMETIC PHOTOSWITCHES

***The search for new and more efficient artificial molecular machines, among which molecular switches, is of great interest in the field of nanotechnology and a fascinating challenge for chemists. In this context, light-driven molecular switches called photoswitches, that use light as fuel, are of particular importance. In this review, a brief introduction on the most common photoswitches and some examples of their possible applications are presented. Moreover, the recent achievements on the design, preparation and characterization of a novel biomimetic photoswitch, the N-alkylated indanylidene pyrroline (NAIP) switch, are reported.***

The design and development of new devices and machines at the molecular level, having the dimension of $10^{-9}$ m (nm), are guidelines for the modern and multidisciplinary field of nanotechnology. Using the *bottom-up* approach, molecules are used as building blocks for nanodevices able to perform a specific and useful function. Examples of molecules that can be assembled to build up such molecular-level structures are molecular switches.

Molecular switches are a special type of molecular machines[a] that can be switched between (at least) two distinct stable forms by the application of a chemical, electrochemical, photochemical, or thermal stimulus [1-3]. Among others, *photoswitches* are molecular switches where the different forms of a molecule can be inter-converted by means of a photochemical reversible process [1-3].

Several other building blocks for nanoscale devices such as molecular propellers, brakes, turnstiles, shuttles, scissors, elevators, rotating modules, muscles, rotors, ratchets and catalytic self-propelled objects are known [4]. Their assembly has already resulted in molecular systems in which switching, translational or rotary motion, or a change in shape or assembly is controlled by means of external stimuli [4]. If one considers the design and realization of artificial nanodevices with such functions, nature is a primary source of inspiration. Among the most marvellous examples in nature are the DNA/RNA replication system, the porphyrin arrays in the light-harvesting complex, the muscle linear and ATPase rotary motors and the retinal *cis-trans* photoisomerization in the process of vision [5].

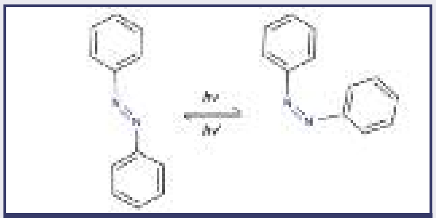
With such an inspiration chemists together with physicists and biologists are constructing a wide variety of *biomimetic switches*, mimicking or hopefully outperforming the elegant switches found in nature. Several exciting examples of the incorporation of switches in devise applications in the areas of microelectronics and material sciences are already available [1, 4, 6].

## Photoswitches

Within molecular switches, photochromic compounds [7] are particularly interesting. Photochromic molecules are a special type of photoswitches that undergo a reversible transformation by absorption of electromagnetic radiation between two stable forms (photochemical bistability) having different absorption spectra.

A very important advantage of using light as energy source of these light-driven systems is that, using modern lasers, one can simultaneously control spatial and temporal characteristics of light at the nanometer and femtosecond levels, respectively. This control can be transferred to molecular functions by means of these photoresponsive molecules [8].

Several exciting examples of photoreversible compounds including azobenzenes, diarylethenes, fulgides, sterically overcrowded alkenes, spiropyrans, salicylideneimines, viologens, and azulenes are described in literature [1-3]. The photochromic processes involved are typically *cis-trans* isomerization, photocyclization, photoinduced electron transfer and keto-enol tautomerism. A brief discussion on some of available *photoswitches* and their possible applications will be given below.



Scheme 1 - Trans (left) - Cis (right) isomerization of the azobenzene chromophore

## Azobenzenes

The azobenzene (Ab) and Ab-based molecules represent the most extensively studied molecular switches [9] whose switching process is based on a *cis-trans* isomerization (Scheme 1). Ab-based molecules have been successfully applied to control ion complexation [10], electronic properties [11] and catalysis [12], to modify organization in monolayers and thin films [13], to trigger folding/unfolding of oligopeptide chains [14] but also to construct photoresponsive amphiphiles [15] and membranes [16]. As a drawback, most known Ab derivatives are achiral and suffer from the low thermal stability of the energetically less favorable *cis*-isomer, leading to thermal isomerization back to the *trans*-state.

## Spiropyrans

The photochromism of spiropyrans is based on the interconversion of the closed spiropyran form and the open zwitterionic merocyanine form (Scheme 2). UV irradiation leads to the open form, which reverts to the closed form either thermally or by irradiation with visible light.

Due to the achiral nature of the merocyanine form, the photochromic process will always lead to racemization. By the introduction of a stereogenic center at position 3 vicinal to the spiro carbon, photochemical switching of optical activity could be accomplished [17].

The photochromism of spiropyrans forms the basis for photochemical memory devices [18]. Spiropyrans are also employed as light filters in sunglasses.

## Diarylethenes

The switching mechanism of photochromic diarylethenes is based on a photocyclization under UV light irradiation of the colorless open form resulting in colored closed form, which can undergo ring-opening again with visible light [19] (Scheme 3).

The presence of various substituents on the tiophene moieties eliminates the low thermal stability of open form, which would limit the applicability of their reversible photocyclization. Bridging the central alkene bond, to prevent unwanted *cis-trans* isomerization, is another key structural improvement. The introduction of a perfluorocyclopentene moiety makes the photoswitch thermally and chemically stable [20]. These types of systems have been used as phototriggers of liquid crystalline phase transitions.

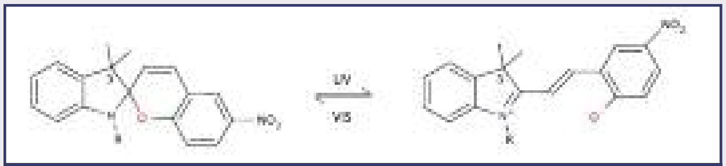
## Fulgides

The bistability of fulgides is based on the reversible photochemical conrotatory electrocyclization of the 1,3,5-hexatriene moiety. The introduction of alkyl substituents suppressed undesired sigmatropic hydrogen shifts [21] and the thermal reverse reaction could be avoided by using a variety of heterocyclic derivatives such as furoyl- and indolylfulgides. A typical chiral example is the indolylfulgide of Scheme 4 [22]. The photochromic reaction involves the open-colorless and conformational mobile *trans*-form (often in equilibrium with the *cis*-form) and the closed-colored and rigid form (Scheme 4). All three isomers are chiral as a result of a stereogenic center in the closed form and a helical conformation in the open (*trans* and *cis*) structures.

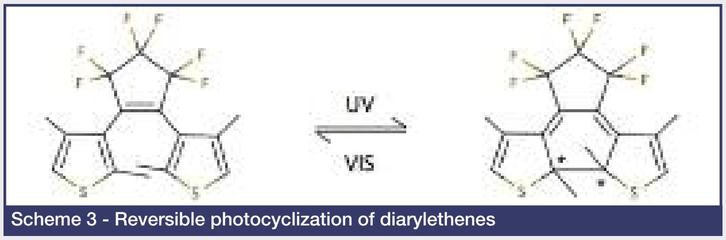
Following the discovery of the photochromic behavior of fulgides by Stobbe [23] at the beginning of the previous century, there has been considerable interest in these molecules as potential candidates for organic optical memory systems [24]. The use of a fulgide as a chiral switch in a polymeric liquid crystal has also been described [25].

## Overcrowded alkenes

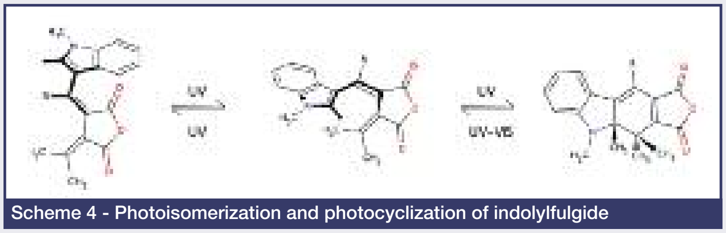
The basic molecular structure of an overcrowded alkene (Scheme 5) consists of an unsymmetrical upper part (tetrahydrophenanthrene or 2,3-dihydronaphtho(thio)pyran) connected via a double bond to a symmetric lower part (xanthene, thioxanthene, fluorene). The chirality in these alkenes, denoted with M and P for left- and



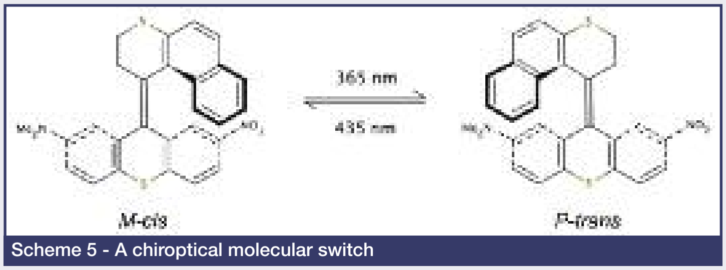
Scheme 2 - Interconversion of the closed spiropyran form (left) and the open merocyanine (right)



Scheme 3 - Reversible photocyclization of diarylethenes



Scheme 4 - Photoisomerization and photocyclization of indolylfulgide

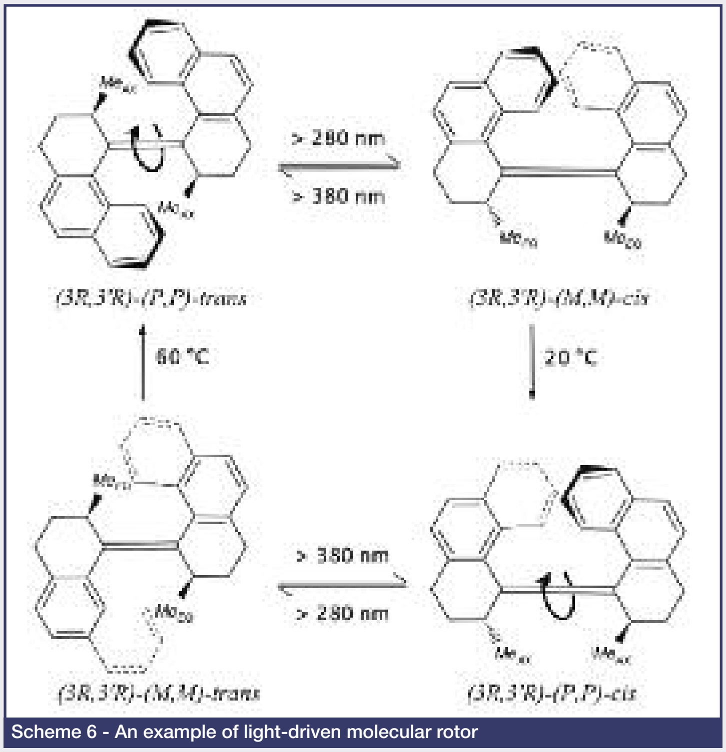


Scheme 5 - A chiroptical molecular switch

right-handed helices respectively, originates from unfavorable steric interactions around the central olefinic bond that forces the molecules to adopt a helical shape. These *pseudoenantiomeric*[b] chiroptical switches undergo, upon irradiation, a *cis-trans* isomerization associated to a change in the helicity of the molecule.

Overcrowded alkenes are also frameworks for the design of light-driven unidirectional molecular rotors [1, 2, 26]. In the field of nanotechnology, a rotor is defined as a device that can convert energy into controlled rotary motion that should eventually be translated into work. In designing a molecular rotor the major objective is to generate controlled full rotary motion (i.e. a 360° unidirectional rotation) different from random Brownian thermal motions.

Feringa and coworkers have demonstrated that in the sterically overcrowded alkene *(3R,3'R)-(P,P)-trans*-1,1',2,2',3,3',4,4'-octahydro-3,3'-dimethyl-4,4'-biphenanthrylidene (Scheme 6) where two methyl-substituents adopt, due to steric effects, an energetically favored axial orientation, it is possible to achieve unidirectional rotation with a full light driven 360° rotation of one (rotor) half of the molecule relative to the other (stator) half. The controlled and repetitive full 360° unidirectional rotation is achieved in two photochemical steps and two thermal steps. The driving forces in this rotary process are the two photoinduced isomerization processes that, in both cases, force the methyl-substituents to adopt an energetically unfavorable equatorial orientation. Helix inversion releases the energy in a unidirectional manner to form the stable isomers with methyl in axial orientation. The direction of this rotation is controlled solely by the configuration at the stereogenic centers. By using circular dichroism spectroscopy, the unidirectionality of the rotor was established. Every step of the rotary motion could be identified spectroscopically.



Scheme 6 - An example of light-driven molecular rotor

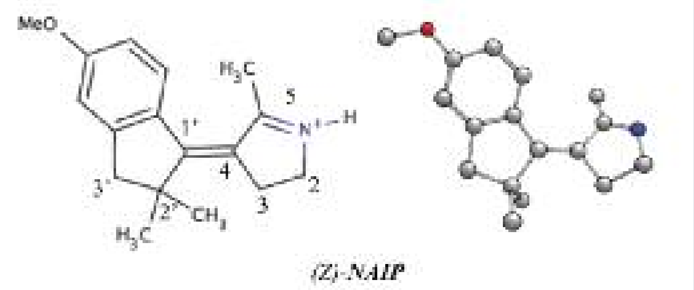
A major drawback is the thermal energy required for helix inversion especially in case of the *trans*-isomer. Improved systems have already been developed in Feringa's group [27].

## A novel biomimetic photoswitch at LCPP[c]

Design and preparation of novel switches with the aim of obtaining novel building blocks to be employed in different molecular environments is desirable. In this section we summarize the results of a multidisciplinary research effort where *state-of-the-art* computational methods and retrosynthetic analysis, together with spectroscopical and photochemical characterization, have contributed to prepare a *novel* designed molecule that can act as *photoswitch* [28-31], the N-alkylated indanylidene pyrroline (NAIP) switch (Scheme 7).

This artificial light-driven NAIP switch is a *biomimetic photoswitch* since, as we have established with our work, it is able to mimic various aspects of the photoisomerization of the protonated Schiff base of retinal (PSB11), the chromophore of the visual pigment Rhodopsin (Rh) (Fig. 1). In Rh a selective unidirectional photoisomerization of the 11-cis PSB11 occurs via the evolution of a single $\pi \rightarrow \pi^*$ excited state that has a lifetime of only 150 fs and decays to the all-trans ground state product with a quantum yield of 0.67 [32].

Indeed the photoisomerization of PSB11 can be seen as extremely efficient because is stereoselective, unidirectional, ultrafast and occurs with high quantum yield. While these properties make Rh an excellent reference for the design of *cis-trans* photoisomerizable switches, irradiation of the PSB11 chromophore in solution [33] features an unselective isomerization and an excited state lifetime in the picosecond range thus prompting a search for artificial rhod-



Scheme 7 - 2D (left) and 3D (right) molecular models of N-alkylated indanylidene pyrroline (NAIP) switch in its Z form

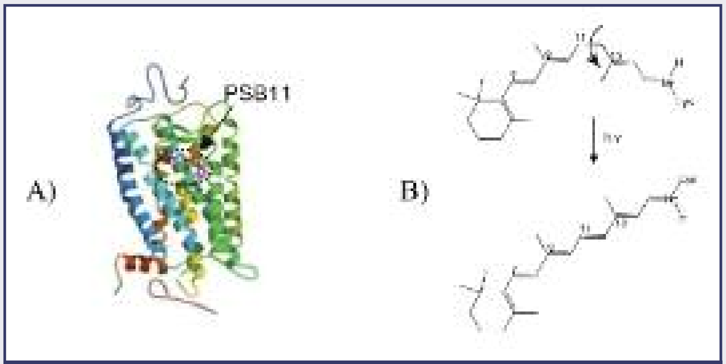


Fig. 1 - A) The rhodopsin molecule. In evidence the seven $\alpha$-helices and the chromophore (PSB11), in purple. B) A scheme of the "primary event" in vision: the photoinduced isomerization of the 11-cis PSB11 to all-trans PSB11

mimetic molecules. In other words, while it has been established that the complex protein environment enhances the efficiency of the PSB11 reaction, one may always try to design an unnatural protonated Schiff base that, in solution phase, replicates the excited-state properties of the protein-embedded chromophore and that can be switched efficiently and in both direction via light irradiation. A simple-minded idea is to design molecular switches that are hybrids of the retinal chromophore and of the light-driven molecular rotors biphenantrylidene of Scheme 6 that are molecules able to rotate around a single isomerizable bond upon irradiation. This idea led to the design of the NAIP switches displaying a single exocyclic double bonds (Fig. 2).

In particular, NAIPs have unique features[d] (i) synthetic flexibility, (ii) a potentially very efficient photoisomerization, (iii) $\lambda_{max}$ can be modulated as a function of $G_1$ and $G_2$ (340-420 nm) (Fig. 2), (iv) a positively charged framework, (v) the possibility to be used as either steric switches (like azobenzenes) or dipole moment switches[e] (like spiropyranes) and (vi) a size of the conjugated $\pi$-system that allows the prediction/simulation of their spectral and photochemical properties using *ab initio* multiconfigurational quantum chemical tools.

This last feature appears to provide a unique opportunity for the modeling of NAIP because the study of photochemical processes by means of modeling makes possible insights at the microscopic level of what happens to a molecule after absorption of a photon. The control of these molecular events that may follow light energy absorption (i.e. energy wastage or energy exploitation) can be considered as a basic requirement for the rational design of molecular *photoswitches*, novel photoresponsive materials, light-activated molecular devices and molecular level machines, efficient photochemical reactions or artificial photosynthetic systems.

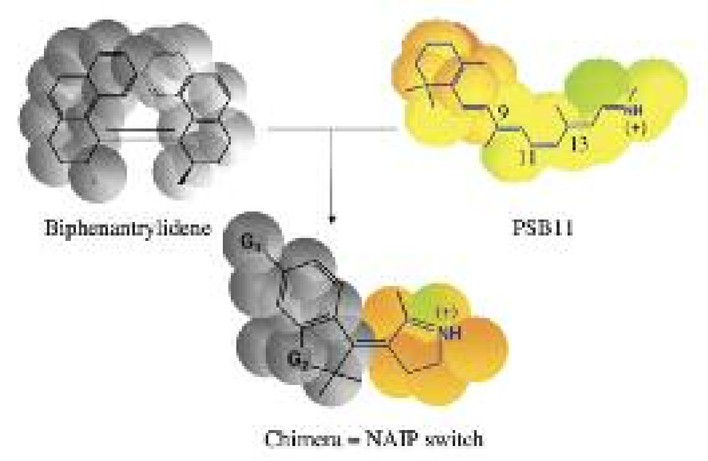


Fig. 2 - Chimera of biphenantrylidene and PSB11 featuring a single reactive double bond as in the biphenantrylidene switch and the same electronic structure of PSB11

The success of *in silico* approaches to these problems depends on advances in methodology and in computer hardware. Furthermore, the ability to treat large and complex systems using methods of reasonable accuracy and cost is a prerequisite for computational studies in this field. Nowadays the most popular approach for this task is to employ the so-called hybrid quantum mechanics/molecular mechanics (QM/MM) methods. The basic idea of the QM/MM approach is to combine the accuracy of a quantum chemical treatment of the chromophore with a molecular mechanics (i.e., parameterized) description of its environment. In this way the effect that the surroundings exert on the chromophore reactivity can be evaluated. Spectroscopic parameters like absorption and fluorescence maxima can be computed, providing a benchmark for the accuracy of the QM/MM scheme. When explor-

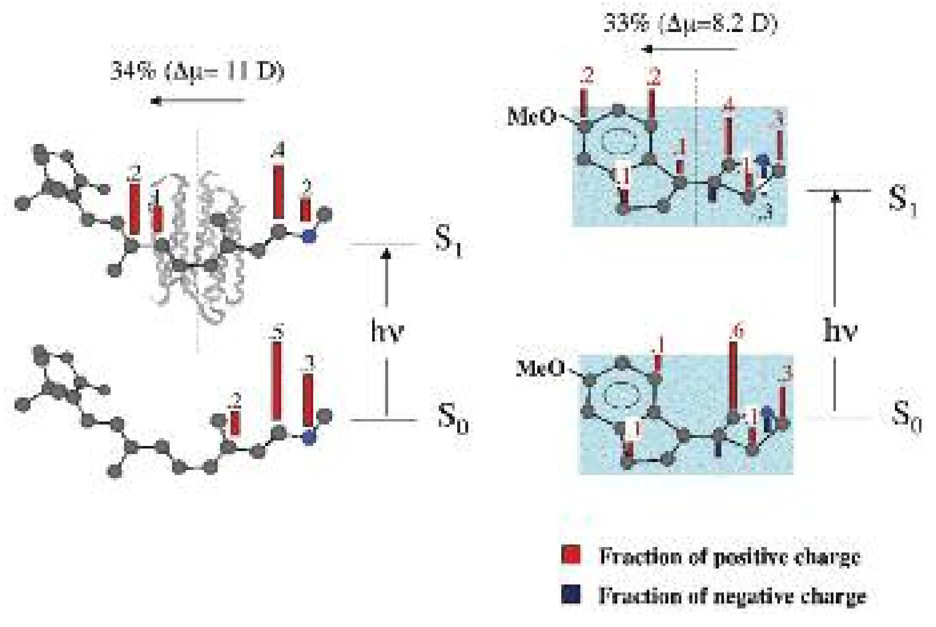


Fig. 3 - Change in the charge distribution along the backbone of Rh-embedded PSB11 (left) and in NAIP switch (right) in methanol solution, upon vertical ground state (S0) → excited state (S1) excitation. Partial charges are given in atomic units

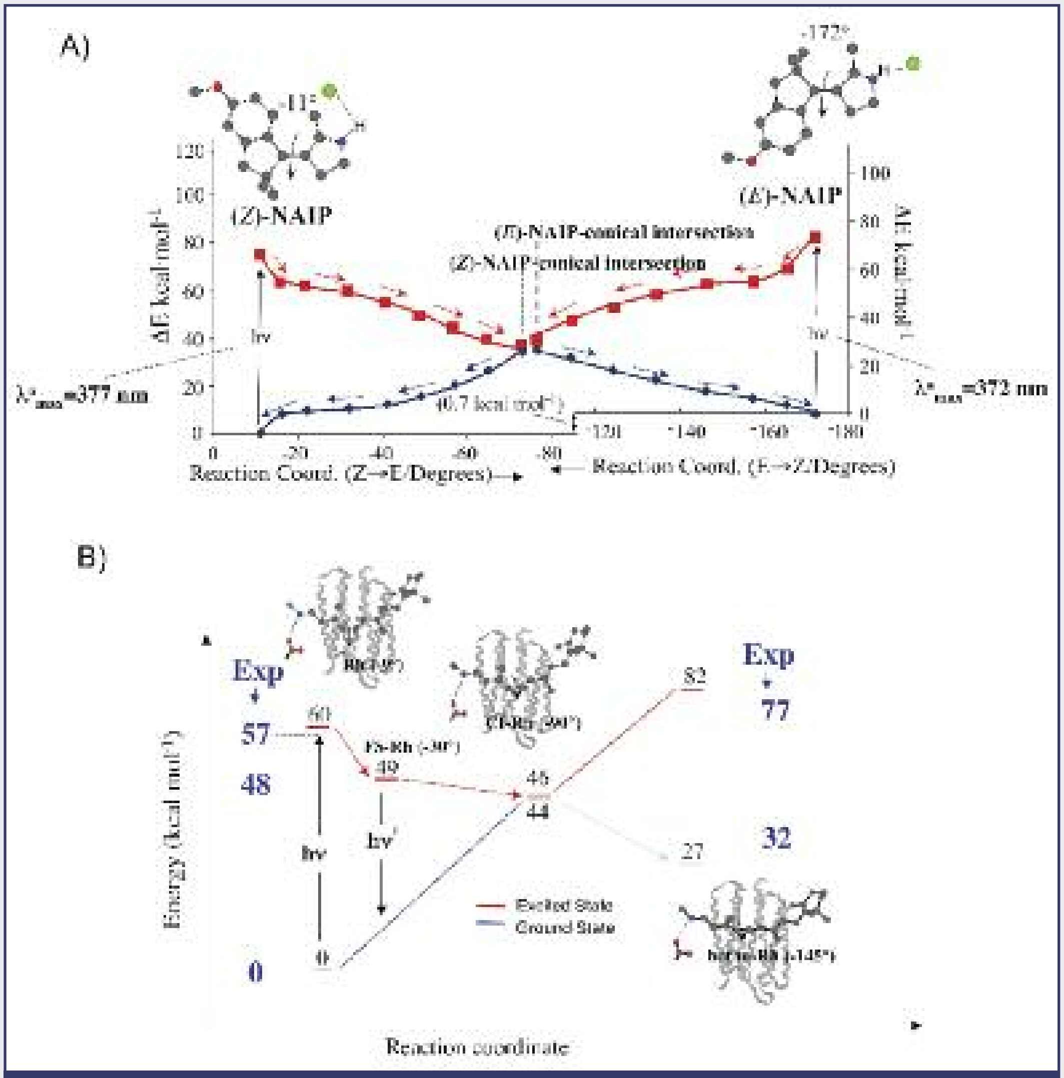


Fig. 4 - CASPT2//CASSCF/6-31G*/AMBER energy profiles along the photoisomerization coordinate of A) (Z)-NAIP and (E)-NAIP. The absorption maxima ($\lambda^a$max) of Z- and E-NAIP are 377 nm and 372 nm, respectively; B) Rh→bathoRh (only few critical points are shown). Rh, rhodopsin; FS-Rh, fluorescent intermediate; CI-Rh, the lowest lying $S_1/S_0$ Conical Intersection; bathoRh, bathorhodopsin (the first stable ground state intermediate); Adapted from [36]

ing a photochemical reaction mechanism, it is crucial to follow the global evolution of the system in the excited state. It is especially important to be able to study the mechanism through which the system eventually returns to the ground state, thereby completing the photochemical transformation. Obtaining a quantitative QM/MM description of a photochemical reaction mechanism is currently a substantial undertaking. While the capability offered by static QM/MM methods for locating key molecular species of photochemical reaction mechanisms and to evaluate the overall reaction energetics has far-reaching implications, the dynamic effects also need to be addressed through comparisons with experimental results from electronic and vibrational spectroscopy studies, often employing time-resolved techniques.

Recently [35] the LCPP lab has implemented the ab initio CASPT2//CASSCF protocol (where equilibrium geometries and electronic energies are determined at the CASSCF and CASPT2 levels respectively) in a QM/MM scheme allowing for the evaluation of the excitation and emission energy of neutral or charged chromophores (treated quantum mechanically) embedded in protein or solution environments (described by the AMBER force field) with a few kcal mol$^{-1}$ errors [31, 36-38]. Using such CASPT2//CASSCF/AMBER protocol we were able to show that the observed absorption and fluorescence maxima of NAIP switch can be reproduced within few kcal mol$^{-1}$ [28, 31].

The computational characterization of the NAIP switch started investigating its first excited state electronic structure in methanol solution. In Rh this corresponds to the structure of a charge transfer state characterized by a large charge translocation from the C=N region towards the region of the hexocyclic ring. Such a charge translocation is also responsible for the large change in dipole moment upon vertical excitation. Interestingly we found that the NAIP switch taken with a *p*-methoxy (electron releasing group) in solution and in the presence of chloride as the counterion, displays a similar charge traslocation (towards the byciclic ring) and change in dipole moment of Rh (Fig. 3). It is worthwhile to notice that instead, PSB11 in solution only displays a 21% charge translocation and 6 D for the change in dipole moment.

These positive results encouraged the computational investigation of the full photoisomerization path for both the (Z)-NAIP → (E)-NAIP and for (E)-NAIP → (Z)-NAIP[f] reactions in order to look for analogies with the photoisomerization of the PSB11 chromophore. Very interestingly and similarly to PSB11 in Rh, the existence of substantially barrier-less paths featuring an excited state to ground state decay at a conical intersection[g] funnel was found. The computed CASPT2//CASSCF/A***MBER*** photoisomerization path for Rh and for the structure of the Z → E (and also E → Z) photoisomerization path of the NAIP switch are compared in Fig. 4.

The successful synthesis of (Z)-NAIP (yields >80%) and its proved photochemical conversion to (E)-NAIP allowed for the spectroscopic characterization of (Z)-NAIP and for the experimental investigation of its photoisomerization efficiency. As mentioned before, this allowed the verification that the QM/MM computational strategy

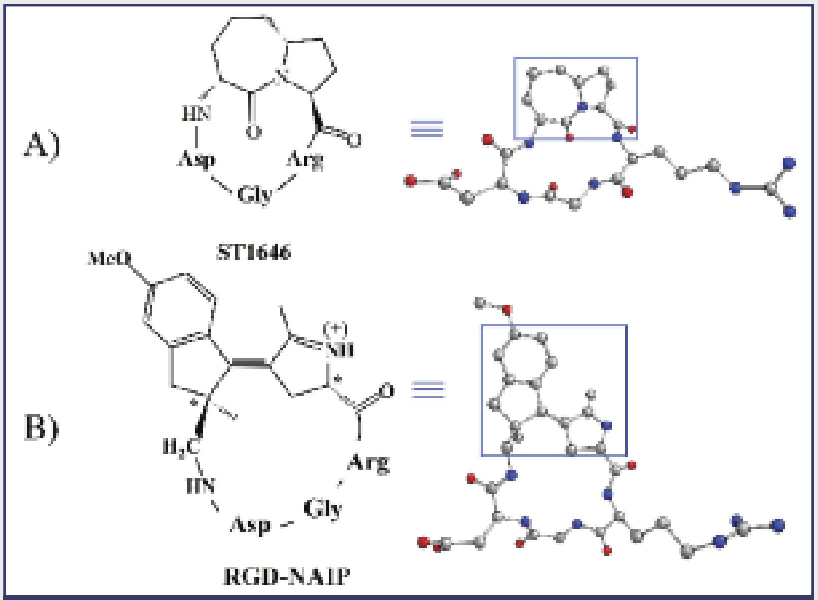


Fig. 5 - a) Cyclic RGD pseudopentapeptide incorporating a bicyclic lactam (ST1646); b) Cyclic photoswitchable RGD-NAIP

provides realistic predictions (within few kcal $mol^{-1}$) of the absorption maxima ($\lambda_{max}$) of both isomers of the switch in methanol. Furthermore, measurements of the quantum yields in methanol gave 0.20 and 0.35 values for the Z → E and for E → Z processes respectively, thus confirming that the NAIP switch provides a realistic alternative to other switches such as Ab that features quantum yields of the similar magnitudes [9].

The barrierless path suggests that the switch has a short excited-state lifetime and, thus, a very weak fluorescence. Such a path is usually associated with short excited state lifetimes and efficient photoisomerization processes (as a consequence of the Landau-Zener model for impulsive radiationless deactivation at a conical intersection) and, therefore, to moderate-to-high product quantum-yields. Actually, time-resolved spectroscopy results show that, similar to Rh, the isomerization occurs on a 0.3 ps time scale and is followed by <10 ps cooling and solvation. The entire (2-photon-powered) Z→E→Z switch cycle was traced by following the evolution of its infrared spectrum. These measurements indicate that the cycle can be completed within 20 ps [31].

The photochemical study has also demonstrated the potential use of Z-NAIP as a light-driven switch by investigating the wavelength dependent composition of the photostationary state (PSS). The basic photocycle for the proposed class of switches implies that, at a given wavelength, the difference in extinction coefficients that is approximately the differences in absorption maximal intensities of the Z and E forms can be exploited to control the PSS composition. Tab. 1 shows that by changing the irradiation wavelength from 360 to 440 nm the Z/E ratio can be inverted. In particular, at 440 nm, the E form becomes dominant. However, due to a low E → Z thermal isomerization barrier, the generated ratio returns rapidly to the original 98:2 mixture (the composition of the thermally equilibrated solution) when the irradiation is interrupted at room temperature.

The property of inverting the composition of the photostationary state upon irradiation at a given wavelength figured out different applications of the indanylidene pyrroline switch, where the control of the percentage in solution of the two forms is needed.

## Design and computational characterization of a photoswitchable cyclic oligopeptide

When integrated into a biopolymer backbone or residue, *photoswitches* allow control of the conformational space, favoring or disfavoring the associated biological activity. Examples include the photo-modulation of redox activity [39], integrin-binding activity [40], DNA triplex formation and binding [41], various enzymatic activities [42], ion channel permeability [43] and secondary structure (this last has provided detailed information about the kinetics of peptide folding [44]).

In basically all applications, the light-energy induced motion results in a permanent or transient conformational change of a molecular scaffold bound to the switch. As already mentioned in section "Azobenzenes", Ab-based switches have already been used to trigger folding/unfolding of oligopeptides chains [14]. On the other hand, it has also been pointed out that Ab has properties that limit its applicability in certain fields related to the conformational control of peptides.

NAIP exhibits several properties that make it a promising alternative to Ab and, at the same time, a proper scaffold for the development of functional cyclic peptidomimetics: i) it has a high polarity (NAIP is a cation) and so it is suitable for applications in highly polar environment (while Ab has a limited dipole moment value); ii) the length of the NAIP framework is shorter than that of the di-para-functionalized Ab switch, so NAIP may be more easily integrated in a peptide backbone (NAIP is isosteric to a dipeptide); iii) NAIP is rigid (the isomerization mechanism only involves twisting about the exocyclic double bond) and its photoisomerization is controlled exclusively by the $\pi$-$\pi^*$ excited state while Ab has both twisting and inversion mechanism and reacts through both the n-$\pi^*$ and $\pi$-$\pi^*$ states; iv) NAIP is synthetically flexible, so it can be used as a starting point to create libraries of compounds.

| λ (nm) | Z-NAIP | E-NAIP |
|---|---|---|
| 360 | 1 | 0.28 |
| 293 | 1 | 0.34 |
| 420 | 1 | 0.74 |
| 430 | 1 | 0.90 |
| 440 | 1 | 1.44 |

Tab. 1 - Composition of the photostationary state (irradiation for 9 h) of NAIP in methanol solution as a function of the irradiation wavelength

In the following we revise the results of a recent feasibility study for the design and computational chracterization of a cyclic peptidomimetic formed by the NAIP switch conjugated to the biologically active RGD-peptide in order to photomodulate its conformation [45]. The RGD motif can be found in proteins of the extracellular matrix and constitutes the recognition sequence for integrin receptors, which play a major role in cell/cell and cell/matrix adhesive interactions [46].

In order to explore the conformational modifications of the peptide domain induced by the presence of the photomodulable unit, we considered as a template a cyclic RGD pseudopentapeptide incorporating a bicyclic lactam (ST1646, Fig. 5a) that has been found to display an high affinity for the integrin receptor $\alpha_v\beta_3$. We replaced the rigid bicyclic skeleton with a derivative (conveniently functionalized to permit the cyclization of the molecule) of our NAIP switch, synthetically accessible and already available in our laboratory (Fig. 5b).

We have carried out an investigation of the structural properties of the photoswitchable cyclic RGD-peptide (RGD-NAIP, Fig. 5b) in aqueous solution using molecular dynamics (MD) simulations. The analysis of MD trajectories has revealed that, for each diastereoisomer (E or Z), different conformations of the peptide backbone are stabilized.

Electrostatic and spectroscopic properties have been evaluated by means of QM/MM (CASPT2//CASSCF/6-31G*/AMBER) method. The vertical excitation energy calculated for the Z- and E- form of the chromophore attached to the RGD unit proves to be different so that the composition of the PSS can be potentially modulated by irradiation at different wavelengths. This strategy can be pursued to create photoswitchable inhibitors that can be activated or inactivated by irradiation, with the possibility to use them in the control of cellular adhesion or other biological activities mediated by integrins.

## Final remarks

Searching for *novel* designed *photoswitches* calls for a detailed comprehension of molecular events that may follow light energy absorption. The molecular modeling and simulation of these photochemical processes represent valuable tools for the rational design of such novel materials. Using *ab initio* multiconfigurational quantum chemical methods available at LCPP, combined with retrosynthetic analysis, it has been possible to prepare a *novel biomimetic photoswitch* [28-31], the NAIP switch, which is able to mimic various aspects of the extremely efficient photoisomerization of the chromophore of the visual pigment Rhodopsin. Recently, the NAIP switch has been used for the design of a photomodulable cyclic oligopeptide, formed by NAIP conjugated to the RGD recognition sequence for integrins, that can potentially act in the control of cellular adhesion. These encouraging results make NAIP *photoswitches* interesting candidates for relevant and future technological or bio-technological applications.

## Notes

[a] Molecules that react to a certain external signal by displacing, usually reversibly, one or more of their parts.

[b] Pseudoenantiomers are defined as two isomers that show close resemblance and exhibit opposite -mirror-image- chiral properties, yet are not real enantiomers.

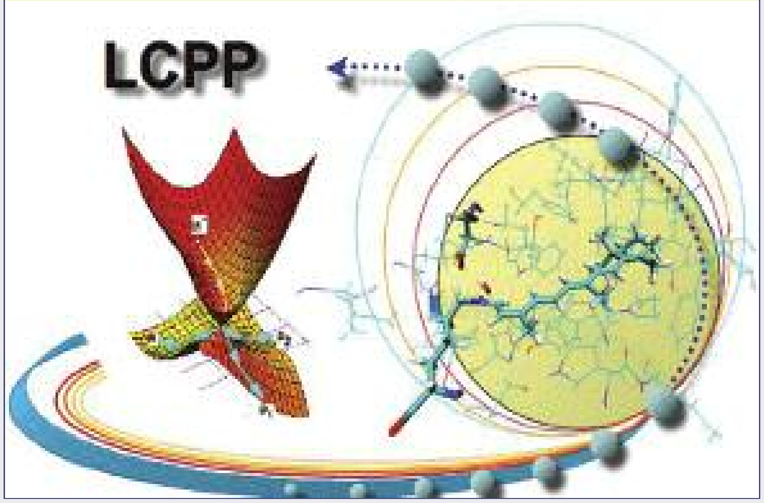
[c] The Laboratory for Computational Photochemistry and Photobiology (LCPP) is a bi-national lab, directed by Prof. M. Olivucci, which exploits the computer facilities both at the Department of Chemistry, University of Siena, Italy and at the Center for Photochemical Sciences, Department of Chemistry, Bowling Green State University, Ohio. The research at LCPP is devoted to the development of tools for mapping excited state potential energy surfaces and for the characterization of the photochemical reactivity of different classes of organic and biological chromophores. Visit Our Web Site @ http://www.lcpp.unisi.it/

[d] See later in the text for more details.

[e] Recently we have designed, synthesized and characterized a NAIP switch incorporating a permanent zwitterionic head. This system constitutes the first photochemical switch displaying, with respect to its own molecular scaffold, a photoinduced dipole moment change of ca. 30 Debye (V. [34]).

[f] See Fig. 4 for the structures of the two Z and E forms of NAIP.

[g] Conical intersections are special molecular structure that define points (or regions) of the excited state energy surface where there is an extremely high rate of internal conversion.



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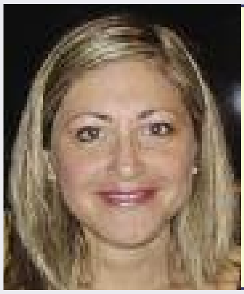

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## RIASSUNTO

### *Interruttori fotochimici e biomimetici*

*La progettazione e lo sviluppo di nuovi dispositivi e macchine di dimensioni nanometriche ($10^{-9}$ m) hanno un ruolo fondamentale nel campo delle nanotecnologie. Tra questi nanodispositivi possiamo includere gli interruttori molecolari i quali possiedono due forme stabili interscambiabili mediante l'applicazione di uno stimolo chimico, elettrochimico, fotochimico o termico. In questa review sono discussi alcuni esempi di interruttori molecolari fotochimici più comuni nonché i risultati della progettazione in silico, successiva sintesi e applicazione di un nuovo interruttore molecolare guidato dalla luce e biomimetico in quanto ispirato al gruppo prostetico dei recettori visivi (rodopsine). Tale interruttore è stato recentemente inserito come unità fotomodulabile all'interno di un pentaptide ciclico che ha un potenziale impiego nel controllo dell'adesione cellulare. Mediante metodologie ibride computazionali QM/MM (quantomeccanica/meccanica molecolare) è stato possible studiare i cambiamenti conformazionali del polipeptide indotti dal movimento del dispositivo molecolare.*