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Synthesis and Photoisomerization of Rhodopsin-Based Molecular Switches

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A new family of switches based on a rhodopsin chromophore is presented. These new photoswitches fulfil most of the required features for an efficient switch to be used in practical applications. The synthetic route is simple and versatile and enables substituents capable of acting as anchoring points to be incorporated. Also, substitution can be used to fine tune the switches' properties. The photostationary state can be reached easily by using low-energy light compatible with complex environments. Thermal reset allows these switches to operate through on/off cycles.

Introduction

The use of light to induce mechanical movement at the molecular level has received considerable attention in recent years.[1] Molecular switches based on *E*/*Z* photoisomerization have been used in various contexts to control diverse properties.[2] Among the different photochemical switches developed, systems based on azobenzene have been used extensively. For instance, azobenzenes have been employed as photoswitches in biological applications,[3] for photomodification of polymers[4] and to induce photomechanical movement in liquid crystals.[5] Azobenzene derivatives absorb light well and photoisomerize efficiently. Also, the isomerization process induces a shape change that is primarily responsible for the photoinduced transformations triggered by this photochemical reaction. Lastly, an enormous range of azobenzene derivatives is synthetically accessible and a detailed knowledge of the relationship between substitution and properties is available. A very different structure and different properties can be obtained by the use of chiral diarylidenes.[6] In these compounds the chirality of the molecule allows for a preferential direction of isomerization. Thus, these compounds can act as molecular rotors or motors. In spite of their unique properties as effective switches, azobenzene derivatives or chiral diarylidenes are just examples of a whole family of compounds capable of performing controlled *E*/*Z* isomerization. Consequently, the preparation and characterization of new switches that differ from these structures in properties such as size, wavelength of absorption, reactivity, polarity and isomerization mechanism represent an attractive research target.

The discovery of new or alternative prototypes could expand the applicability of the switch concept to different and increasingly complex molecular environments.

Inspiration from nature can provide useful insights in the search of new photoswitches. For instance, the retinal protonated Schiff base (PSB) chromophore of rhodopsin[7] constitutes an example of a very efficient *E*/*Z* switch shaped by biological evolution. In bovine rhodopsin (Rh), selective photoisomerization of the 11-*cis* chromophore occurs rapidly (150 fs) through evolution of a single $\pi\rightarrow\pi^*$ excited state (S_1) providing the all-trans ground state (S_0) product with high efficiency (Φ = 67%).[7] These properties make Rh an excellent reference for the design and synthesis of artificial Rh-mimetic molecules. In fact, several families of Rh-based photoswitches have already been synthesized and their properties as photoswitches have been reported (Figure 1).

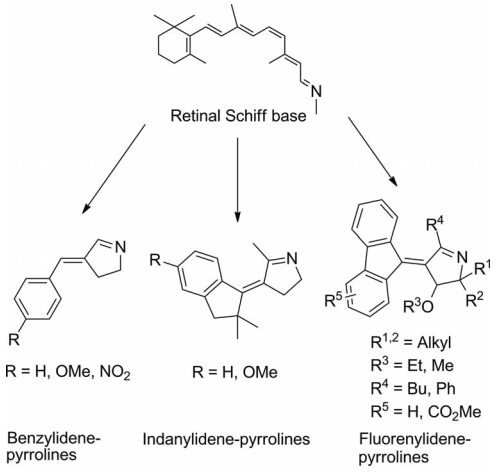

Figure 1. Rhodopsin-based molecular photoswitches.

First of all, a family of benzylidene-pyrroline derivatives was synthesized and analyzed by means of CASSCF// CASPT2 theoretical calculations.[8] Some promising results,

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such as photostability and photostationary state (PSS) dependent on the irradiation wavelength, were overshadowed by the low isomerization quantum yield reported (ca. 10^{-3}). On the other hand, the synthetic route was very limited and only three derivatives could be synthesized. Trying to improve these results, a new generation of Rh-based molecular photoswitches was developed, namely indanylidenepyrrolines.[9] These switches feature a higher isomerization quantum yield (≈ 0.3), increased polarity with respect to azobenzene and a controlled and fast photoisomerization path.[10] Further modification of the substructure allowed the preparation of a dipole-moment switch.[11] However, the synthetic route used was complex and hardly adaptable for switches with different substitution groups. Finally, a different family of Rh-based switches was developed. Fluorenylidene-pyrrolines can be easily synthesized with different substituents within the structure[12] starting from fluorenone imines.[13] These compounds feature even higher isomerization quantum yields (ca. 0.6) and can be operated by using visible light.[14] Unfortunately, it is difficult to vary the composition of the PSS owing to the similar stability and UV absorption of the *E* and *Z* isomers. Despite the promising features of the aforementioned Rh-based photoswitches and the detailed information accumulated by both theoretical calculations and experimental data in solution for isolated molecules, little is known about the practical ability of these systems to act as efficient switches in real applications. In most cases, the reason behind this lack of practical application is the limited available structures that can be incorporated into a complex system.

Any new attempt to build a prototype of an efficient photoswitch should feature (i) an expedient and versatile synthetic route; (ii) anchoring points adequate for linkage; (iii) high isomerization quantum yields and (iv) low-energy absorption bands compatible with complex environments. As explained above, the three precedent Rh-based molecular switches (Figure 1) were synthesized through different synthetic routes but in all cases some experimental problems occurred and one or several of the aforementioned requirements were not met. Thus, we developed a new and versatile entry route to a new family of molecular Rh-based photoswitches that could improve some of the flaws of the previous compounds. It should be noted that the compounds reported here bear some structural differences with the 11-*cis*-retinal. Specifically, these products lack the *cis* configuration in the imine bond and present substituents at the imine carbon. The compound was modified to include a pyrroline ring which would avoid competitive isomerization pathways as discussed previously.[8] This change would also help increase the quantum yield of previous benzylidenepyrrolines switches.[8]

Results and Discussion

These molecular switches based on retinal are analogous to benzylidene-pyrrolines, presenting a substituent R^1 at the C-5 position of pyrroline (Figure 2). We anticipated that a substituent in that position could affect the photoisomerization process. Also, a phenyl ring could substantially increase the UV-absorption and induce a bathochromic shift. After retrosynthetic analysis, we decided to close the pyrroline ring in the last step. Previously, the central double bond could be formed by a Wittig reaction between an aldehyde and a conveniently synthesized phosphonate derivative. This would allow us to independently modify the substituents on both sides of the switch. Also, combinations of different aldehydes and phosphonates would easily yield a complete family of switches. We based our synthetic procedure on a related approach that has been previously reported.[15]

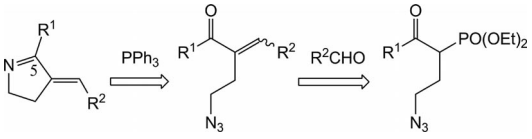
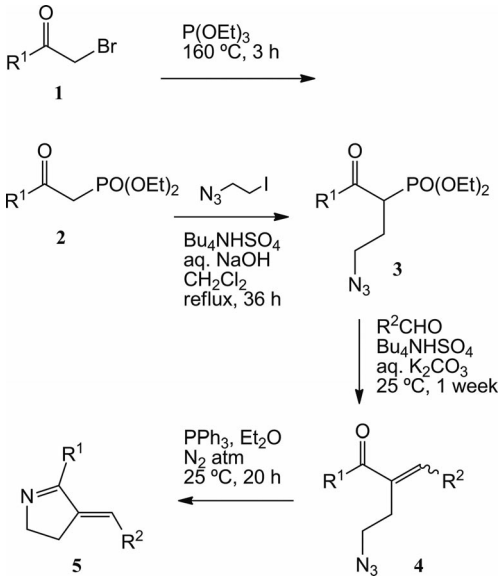


Figure 2. Retrosynthesis of retinal-based photoswitches.

The route (Scheme 1) requires the phosphonates to be synthesized first. Phosphonate **2** with the desired R^1 group may be synthesized from corresponding 2-bromoketone **1**. Next, installation of an ethyl azide side-chain onto **2** by using 2-iodoethylazide by means of a phase-transfer procedure[15] with tetrabutylammonium bisulfate and aqueous sodium hydroxide in CH_2Cl_2 at reflux afforded azido phosphonates **3** in 30–40% yield. Subsequent Horner–Wadsworth–Emmons reaction[15] between the azido-phosphonate and the aldehyde with the corresponding R^2, again by using a phase-transfer procedure with aqueous K_2CO_3 and tetrabutylammonium bisulfate, led to the formation of azido enone in 70% yield. Although a 9:1 mixture of *E* and *Z* isomers of azido enones **4** was obtained, they could be separated by chromatography on silica gel (hexanes/EtOAc, 10:1). However, only the *E* isomer was isolated as final product **5** in 80% yield after carrying out the intramolecular aza-Wittig reaction with triphenylphosphane. It should be noted that both isolated *E* and *Z* isomers of **4** yield the *E* isomer of **5** under the same reaction conditions. Thus, the mixture of isomers of **4** obtained in the reaction crude can be used in the last step without further purification. Monitoring the course of the reaction with ^1H NMR spectroscopy showed that both *Z* and *E* isomers of **5** were formed before consumption of the starting material but isomerization took place under the reaction conditions leading to *E* as the only isolable isomer. Thus, switches **5a**–**o** were obtained as pure *E* forms in all cases.

By using the methodology described above, a complete library of molecular switches were obtained by changing R^1 and R^2 within the structure (see Table 1). It should be highlighted that both alkyl and benzyl aldehydes with different electron withdrawing and donor groups may be used in the synthesis, which constitutes a major advantage over benzylidene- and indanylidenepyrrolines.

Hetero- and polyaromatic aldehydes could also be used to extend the range of molecular switches showing this structure. We also checked the use of ketones with the aim



Scheme 1. Synthetic route to afford the retinal-based photoswitches.

Table 1. Molecular switches synthesized.

R^1	R^2		Absorption[a]	Ratio at PSS[b]	
				E [%]	*Z* [%]
Me	Ph	**5a**	288 (8700)	56	44
Me	*p*-MeC_6H_4	**5b**	287 (7300)	43	57
Me	*p*-$MeOC_6H_4$	**5c**	296 (26600)	47	53
Me	*o*-$MeOC_6H_4$	**5d**	275 (8900)	30	70
Me	$CH_3(CH_2)_4$	**5e**	232 (15000)	85	15
Ph	Ph	**5f**	289 (22200)	76	24
Ph	*p*-MeC_6H_4	**5g**	296 (24800)	72	28
Ph	*p*-$MeOC_6H_4$	**5h**	304 (24900)	75	25
Ph	*o*-$MeOC_6H_4$	**5i**[c]	281 (15200); 317 (14200)	44	56
Ph	*p*-BrC_6H_4	**5j**	282 (47700)	40	60
Ph	*o*-BrC_6H_4	**5k**	282 (18200)	41	59
Ph	*p*-$O_2NC_6H_4$	**5l**	335 (13700)	30	70
Ph	4-pyridyl	**5m**	284 (19300)	80	20
Ph	2-naphthyl	**5n**[c]	265 (25300); 311 (14200)	60	40
p-MePh	*p*-MeC_6H_4	**5o**	294 (20100)	76	24

[a] λ_{max} [nm] (ε [($M^{-1}\,cm^{-1}$)]). [b] By using a Hg lamp after 1–3 h of irradiation. [c] Two different absorption bands were observed.

of obtaining compounds where the number of torsional degrees of freedom of the switch backbone is decreased, especially the potential competitive rotation around the allylic/benzylic single bonds. However, this idea was not possible because it was impossible to carry out the Horner–Wadsworth–Emmons reaction. However, selecting the proper R^1 and R^2 groups it would be possible to obtain a switch with two anchoring points for linkage to complex structures in order to explore the practical applications of PSB-retinal-based molecular switches. Owing to the versatility of the procedure, diverse substituents could be incorporated within the substructure to enable coupling to surfaces, nanoparticles or polymers. For example, the compound could be linked to a selected peptide to enable photocontrol of its conformation and properties, as recently reported.[16]

The *E* isomer of switches **5** is expected to be more stable than the *Z* isomer owing to steric repulsion between substituents R^1 and R^2. Also, the spectroscopic data correlates well with the *E* isomer of similar compounds.[15] In order to confirm the *E* configuration of final compounds **5**, 2-D NMR spectroscopy experiments were carried out (see Supporting Information). From the NOESY spectrum of compound **5d** (Figure 3), it can be seen that there is an NOE signal arising from the proton at the vynilic C-1′ carbon and the methyl at the C-5 of the pyrroline ring, and also between the proton at the aromatic C-3′ carbon and the two protons at the C-3 of the pyrroline ring. Therefore, an *E* configuration for this isomer could be assigned.

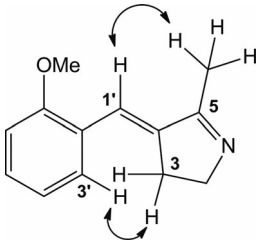


Figure 3. NOESY spectrum of the *E* isomer of switch **5d**.

Further stereochemical information could be obtained from the X-ray diffraction data of compound **5k** (Figure 4). This switch shows an *E* configuration of the central C=C double bond in agreement with the NOESY experiment. Also, X-ray diffraction data reveals that in the solid state the central double bond is almost planar (torsion angle of approximately 6°) whereas both phenyl groups are twisted (approximately 35°) to avoid steric repulsion. Furthermore, the *o*-Br substituent is placed opposite to the pyrroline ring, as the NOESY spectrum showed in the case of the methoxy substituent in **5d**.

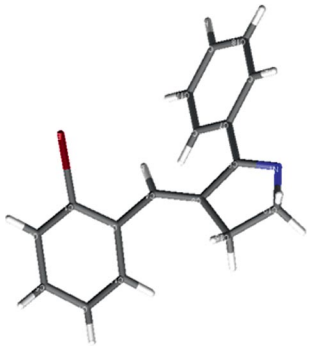


Figure 4. X-ray structure of the *E* isomer of switch **5k**.

After the chemical characterization of the different compounds was performed, their potential as molecular switches was tested. A good molecular switch must be able to reversibly interconvert between two different states by means of an external stimulus.[1a] In this particular case, the two states are the *E* and *Z* isomers. Therefore, these compounds need to isomerize from the *E* form to the *Z* form by irradiation and return from the PSS. First of all, the UV/Vis spectra for all the compounds synthesized were recorded. In all cases, spectra featuring similar absorptions were obtained. The values for the maximum wavelengths

and the extinction coefficients of the bands found for each compound in acetonitrile are shown in Table 1. It should be noted that the maximum of the absorption can be modified by the substituents present within the structure. This could be useful in applications in which the wavelength used to carry out the isomerization process has some restrictions. Thus, by modifying the substituents present, the photophysical properties of the switch could be fine-tuned. A further modification of the photophysical properties could be made by quaternization of the nitrogen atom as previously shown.[8,12] By doing so, the photochemical and photophysical properties of the chromophore can be changed drastically. These modifications are currently under study and will be reported in due course.

A typical UV spectrum for switches **5a**–**o** is shown in Figure 5. The UV spectrum remains almost the same when carried out in polar and non-polar solvents. Thus, photophysical properties, isomerization kinetics and PSS composition would be quite similar in both types of solvent. This fact could allow applications of these switches in both polar and non-polar media, which provides a very wide field of action.

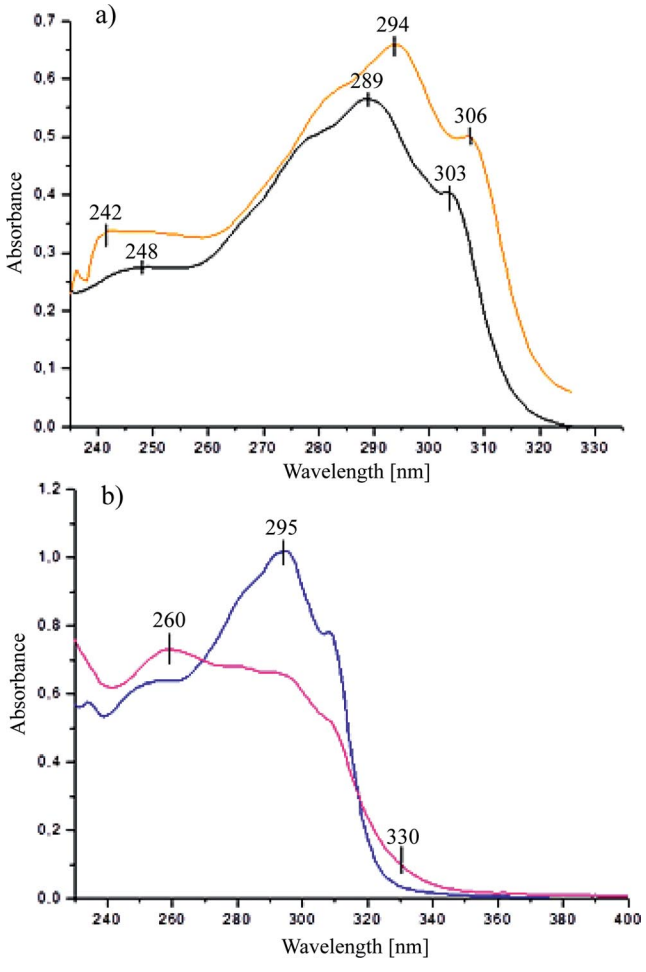


Figure 5. (a) UV/Vis spectrum of a 10^{-5} M solution of **5f** in CH_3CN (black line) and $CHCl_3$ (orange line). (b) UV/Vis of a 10^{-5} M solution of the *E* isomer (blue line) and *Z* isomer (pink line) of **5o** in CH_3CN.

Figure 5 also shows the UV-spectra for both *E* and *Z* isomers of a typical switch, by using **5o** as an example. The *Z* isomer was obtained by separation from the PSS mixture. In all cases, both isomers show only slight differences in the absorption bands; however, these differences could be used to tune the switch behavior under irradiation by using light at an appropriate wavelength. In the two spectra shown in part b of Figure 5, the *E* isomer absorbs preferentially at 295 nm whereas the *Z* isomer features stronger absorption bands at 260 and 330 nm. Thus, varying the light wavelength from 260 to 295 nm the main isomer in the reaction mixture would change. Unfortunately, thermal back-reaction with the current set-up prevented us from confirming the effect of the wavelength in the PSS. Instead, mixtures of different ratios of *Z*/*E* isomers were found when different wavelengths were used and the PSS could not be reached after several hours of irradiation. This suggests the influence of the wavelength in the PSS, as proven for a related compound that was cross-linked to a peptide and thermally more stable.[16] This fact has also some interesting implications in which the average position of the switch could be modified by adjusting only the wavelength of irradiation.

Then, a solution of the *E* isomer of each compound (10^{-2} M) in acetonitrile was irradiated with a 125-W medium-pressure Hg lamp and Pyrex filter (except for compound **5e**, in which quartz was used instead of Pyrex) until the PSS was reached. Isomerization was followed by ^1H NMR spectroscopy because the *E* and *Z* isomers have distinctive signals. Depending on the absorption bands, the mixture took 1–3 h to reach the PSS. The results of the isomer ratio at the PSS for every compound are shown in Table 1 and show some trends. When changing the R^1 group from a methyl group (i.e. **5a**) to a phenyl group (i.e. **5f**) and R^2 remains the same, the percentage of the *Z* isomer obtained at the PSS decreases. This could be due only to steric reasons. On the other hand, when the R^1 and R^2 groups are the same, but R^2 is *ortho* (i.e. **5i**) instead of *para* (i.e. **5h**), the percentage of isomer *Z* increases. Finally, maintaining R^1 but modifying R^2 from H (i.e. **5f**) to an electron-withdrawing group in the *para* position, such as nitro (i.e. **5l**), the percentage of the *Z* isomer increases significantly. As explained previously, the different absorption of the isomers under the reaction conditions given could explain this fact.

Moreover, the same methodology could be employed to introduce the heterocycle **5m** with little effect on both the absorption properties and the PSS. However, the addition of another aromatic ring **5n** increases the percentage of *Z* isomer in the PSS and also displaces the absorption-band maximum. Finally, we checked if having an alkyl group as R^2 in **5e** leads to a similar isomerization process as experienced by the rest of compounds and the results confirmed that an *E*/*Z* isomerization occurs despite the presence of multiple single bonds capable of rotation. Therefore, we conclude that the value of isomers ratio at the PSS can be modified depending on the structure substitution, which is a great advantage over fluorenylidene-pyrroline switches.[12]

We also checked the thermal stability for this family of switches. In every case, the PSS is composed of a mixture

of *E*/*Z* isomers and this rate is stable for some hours at room temp. Also, the equilibrium between the *E* and *Z* isomers can be displaced from the PSS after heating at 50 °C for several hours, eventually reverting to the pure *E* form. Thus, the main isomer can be easily selected by choosing between light and heat. This could be important in practical applications in which on/off switching cycles are necessary. This thermal back-reaction towards the thermodynamically more stable *E* isomer was studied. The rate of this thermal reaction depends on the substituents R^1 and R^2 of the molecule. A few examples are shown in Table 2. The results were obtained after following by ^{1}H NMR spectrum of the thermal back-reaction to recover the *E* isomer of several compounds.

Table 2. Thermal stability.

R^1	R^2	Compound	*E* isomer recovery[a]
Me	Ph	**5a**	12
Me	*p*-MeC_6H_4	**5b**	60
Me	*o*-$MeOC_6H_4$	**5d**	156

[a] Time in hours, in the dark at 25 °C.

From the data in Table 2, we infer that the compound that reverts more readily to the *E* isomer is **5a**, in which the phenyl group in R^2 does not have any substitution. But when the phenyl group in R^2 has a substituent, such as a *p*-methyl (**5b**) or an *o*-methoxy (**5d**), the recovery of *E* is slower, taking a few days. The data in Table 2 shows that the more electron donating the substituent, the slower the return to the thermodynamically stable isomer (*E*). This change is a result of a higher energy barrier for the thermal transition state.

Conclusions

The applicability of molecular switches to photocontrol complex systems requires the availability of a diverse range of compounds with different properties. The choice between different families of compounds could allow a good match to be found for each practical application by taking into account the photophysical properties and experimental performance of the right switch. Fine-tuning of switch properties can only be carried out once a complete set of compounds with different substitution patterns is synthesized. Also, the synthetic route should be simple and versatile enough to allow modifications and incorporation into complex systems. In this paper we have shown how the rhodopsin chromophore can be used as inspiration for the design and synthesis of a new family of molecular photoswitches that fulfill most of the required features. The synthetic route is expedient and versatile, and allows for the presence of several substituents capable of acting as anchoring points suitable for linkage. The PSS can be reached easily after irradiation of the low-energy absorption bands compatible with complex environments. Finally, the switch can be easily reset after heating. Further efforts will be necessary to completely describe the photophysical properties and to test these compounds in practical applications.

Experimental Section

General Details: All commercially available materials were used without further purification. NMR spectra were recorded by using a 300 or 400 MHz NMR Bruker spectrometer. UV/Vis spectra were recorded by a Hewlett–Packard HP 8451A Diode Array UV/Vis spectrophotometer. Quartz cuvettes (1.0 cm path length) were used for the measurements.

Synthesis of Phosphonates 2: When phosphonate **2** was not commercially available with the required R^1 group, it was synthesized by treatment of the corresponding 2-bromo ketone **1** with triethyl phosphite at 160 °C for 3 h.[17]

Synthesis of Azido Phosphonates 3: To a mixture of phosphonate **2** (1 equiv.) and 2-iodoethyl azide (2.5 equiv.) in CH_2Cl_2 (5 mL) a solution of tetrabutylammonium hydrogen sulfate (1 equiv.) in sodium hydroxide (2 equiv., 2 M) was added, and the resulting mixture was heated to reflux for 36 h.[15] Later, it was cooled and treated with water (50 mL) and CH_2Cl_2 (50 mL). The organic layer was separated and concentrated under reduced pressure. The resulting residue was dissolved in Et_2O (100 mL) and the tetrabutylammonium iodide precipitated. The salt was filtered off, and the filtrate was dried (Na_2SO_4) and concentrated under reduced pressure to give a colorless oil. The resulting product was purified by flash chromatography on silica gel (1:1 hexanes/EtOAc) to afford **3** with the required R^1 group in 30–40% yield.

Synthesis of Azido Enones 4: K_2CO_3 (28 equiv.), H_2O (10 mL), tetrabutylammonium hydrogen sulfate (0.2 equiv.) and aldehyde with the required R^2 group (1.5 equiv.) were added to azido phosphonate **3** (1 equiv.) and the resulting mixture was stirred for 1 week at room temperature.[15] The reaction was followed by TLC (5:1 hexanes/EtOAc) until azido phosphonate **3** was consumed. Then, the solvent was removed and water (50 mL) was added before extracting with CH_2Cl_2 (3 × 50 mL). The organic layers were combined, dried (Na_2SO_4), and concentrated under reduced pressure. The residual oil was purified by chromatography on silica gel (5:1 hexanes/EtOAc) to give azido enone **4** as a 9:1 mixture of *E* and *Z* isomers in 70% yield. The two isomers could be separated by chromatography on silica gel (10:1 hexanes/EtOAc); however, it was possible to carry out the next step by using the 9:1 mixture of *E* and *Z* isomers.

General Procedure for the Synthesis of Switches 5a–o: To a solution of **4** (1 equiv.) in dry diethyl ether (20 mL) was added Ph_3P (3 equiv.). The resulting mixture was stirred for 24 h under nitrogen at room temperature and concentrated under reduced pressure. The resulting solid was purified by chromatography on silica gel (1:4 hexanes/EtOAc) to obtain the *E* isomer of (**5a–o**) in 60–85% yield.

(*E*)-4-Benzylidene-5-methyl-3,4-dihydro-2*H*-pyrrole (5a): Brown oil, yield 85%. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.48 (d, J = 7.4 Hz, 2 H), 7.40 (t, J = 7.6 Hz, 2 H), 7.29 (t, J = 13.0 Hz, 1 H), 6.73 (s, 1 H), 4.02 (m, 2 H), 2.89 (m, 2 H), 2.24 (s, 3 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 173.06, 142.99, 137.05, 128.88, 128.74, 127.90, 124.90, 58.97, 29.81, 16.31 ppm. UV/Vis (CH_3CN): λ [nm] 277 (ε = 7640 $M^{-1}cm^{-1}$), 288 (ε = 868 $M^{-1}cm^{-1}$), 303 (ε = 585 $M^{-1}cm^{-1}$). HRMS: calcd. for $C_{12}H_{13}N$ $[M + H]^+$ 172.1121; found 172.1122.

5-Methyl-4-[(*E*)-4-methylbenzylidene]-3,4-dihydro-2*H*-pyrrole (5b): Brown oil, yield 82%. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38 (d, J = 8.1 Hz, 2 H), 7.21 (d, J = 8.0 Hz, 2 H), 6.71 (s, 1 H), 4.02 (m, 2 H), 2.88 (m, 2 H), 2.38 (s, 3 H), 2.23 (s, 3 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 173.30, 142.24, 138.15, 134.44, 129.66, 129.01, 124.99, 59.16, 29.29, 21.59, 16.49 ppm. UV/Vis (CH_3CN):

λ [nm] 287 (ε = 7345 $M^{-1}cm^{-1}$), 300 (ε = 5715 $M^{-1}cm^{-1}$), 305 (ε = 4790 $M^{-1}cm^{-1}$). HRMS: calcd. for $C_{13}H_{15}N$ [M + H]$^+$ 186.1277; found 186.1279.

(*E*)-4-(4-Methoxybenzylidene)-5-methyl-3,4-dihydro-2*H*-pyrrole (5c): Brown oil, yield 80%. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40 (d, *J* = 8.8 Hz, 2 H), 6.91 (d, *J* = 8.8 Hz, 2 H), 6.65 (s, 1 H), 3.98 (m, 2 H), 3.80 (s, 3 H), 2.80 (m, 2 H), 2.20 (s, 3 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 174.39, 159.50, 139.24, 130.45, 129.17, 126.35, 114.14, 57.39, 55.30, 29.65, 15.61 ppm. UV/Vis (CH_3CN): λ [nm] 296 (ε = 26636 $M^{-1}cm$–1). HRMS: calcd. for $C_{13}H_{15}NO$ [M + H]$^+$ 202.1226; found 202.1235.

(*E*)-4-(2-Methoxybenzylidene)-5-methyl-3,4-dihydro-2*H*-pyrrole (5d): Brown oil, yield 80%. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50 (m, 1 H), 7.28 (m, 1 H), 7.11 (s, 1 H), 6.96 (m, 2 H), 3.98 (m, 2 H), 3.88 (s, 3 H), 2.85 (m, 2 H), 2.25 (s, 3 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 173.52, 157.50, 143.02, 131.40, 129.26, 128.19, 120.59, 118.91, 110.74, 58.84, 55.64, 29.76, 16.50 ppm. UV/Vis (CH_3CN): λ [nm] 275 (ε = 8938 $M^{-1}cm^{-1}$), 291 (ε = 6818 $M^{-1}cm^{-1}$), 312 (ε = 4713 $M^{-1}cm$–1). HRMS: calcd. for $C_{13}H_{15}NO$ [M + H]$^+$ 202.1226; found 202.1228.

(*E*)-4-Hexylidene-5-methyl-3,4-dihydro-2*H*-pyrrole (5e): Brown oil, yield 75%. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.80 (s, 1 H), 3.90 (m, 2 H), 2.51 (m, 2 H), 2.14 (m, 2 H), 2.09 (s, 3 H), 1.47 (m, 2 H), 1.35 (m, 4 H), 0.93 (m, 3 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 171.93, 143.31, 126.62, 57.58, 31.71, 30.62, 28.78, 26.89, 22.68, 15.94, 14.18 ppm. UV/Vis (CH_3CN): λ [nm] 232 (ε = 15000 $M^{-1}cm$–1). HRMS: calcd. for $C_{11}H_{19}N$ [M + H]$^+$ 166.1590; found 166.1591.

(*E*)-4-Benzylidene-5-phenyl-3,4-dihydro-2*H*-pyrrole (5f): White solid, yield 82%; m.p. 103–105 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.65 (m, 2 H), 7.40 (m, 7 H), 7.26 (m, 1 H), 6.83 (s, 1 H), 4.21 (m, 2 H), 3.06 (m, 2 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 174.94, 142.12, 137.02, 134.55, 129.63, 128.92, 128.79, 128.60, 128.49, 127.92, 127.76, 59.68, 31.00 ppm. UV/Vis (CH_3CN): λ [nm] 231 (ε = 10059 $M^{-1}cm^{-1}$), 248 (ε = 10806 $M^{-1}cm^{-1}$), 289 (ε = 22232 $M^{-1}cm^{-1}$), 303 (ε = 15717 $M^{-1}cm$–1). HRMS: calcd. for $C_{17}H_{15}N$ [M + H]$^+$ 234.1277; found 234.1284.

4-[(*E*)-4-Methylbenzylidene]-5-phenyl-3,4-dihydro-2*H*-pyrrole (5g): Orange solid, yield 70%; m.p. 64–66 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.64 (m, 2 H), 7.45 (m, 3 H), 7.31 (d, *J* = 8.2 Hz, 2 H), 7.17 (d, *J* = 8.1 Hz, 2 H), 6.80 (s, 1 H), 4.19 (m, 2 H), 3.03 (m, 2 H), 2.35 (s, 3 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 175.06, 141.17, 137.96, 134.63, 134.19, 129.56, 129.34, 128.90, 128.78, 128.45, 127.74, 59.62, 30.97, 21.36 ppm. UV/Vis (CH_3CN): λ [nm] 283 (ε = 21154 $M^{-1}cm^{-1}$), 296 (ε = 24808 $M^{-1}cm^{-1}$), 309 (ε = 1923 $M^{-1}cm$–1). HRMS: calcd. for $C_{18}H_{17}N$ [M + H]$^+$ 248.1434; found 248.1430.

4-[(*E*)-4-Methoxybenzylidene]-5-phenyl-3,4-dihydro-2*H*-pyrrole (5h): Brown oil, yield 83%. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.62 (m, 2 H), 7.42 (m, 3 H), 7.32 (d, *J* = 8.7 Hz, 2 H), 6.87 (d, *J* = 8.8 Hz, 2 H), 6.76 (s, 1 H), 4.16 (m, 2 H), 3.75 (s, 3 H), 2.97 (m, 2 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 174.87, 159.12, 139.66, 134.43, 130.19, 129.42, 129.35, 128.58, 128.25, 127.33, 127.24, 59.28, 55.07, 30.63 ppm. UV/Vis (CH_3CN): λ [nm] 226 (ε = 12467 $M^{-1}cm^{-1}$), 249 (ε = 10345 $M^{-1}cm^{-1}$), 304 (ε = 24934 $M^{-1}cm^{-1}$), 317 (ε = 20689 $M^{-1}cm$–1). HRMS: calcd. for $C_{18}H_{17}NO$ [M + H]$^+$ 264.1383; found 264.1389.

4-[(*E*)-2-Methoxybenzylidene]-5-phenyl-3,4-dihydro-2*H*-pyrrole (5i): White solid, yield 85%; m.p. 111–113 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.69 (m, 2 H), 7.46 (d, *J* = 7.7 Hz, 1 H), 7.38 (m, 3 H), 7.21 (m, 2 H), 6.94 (t, *J* = 7.5 Hz, 1 H), 6.77 (d, *J* = 8.3 Hz, 1 H), 4.08 (m, 2 H), 3.61 (s, 3 H), 2.90 (m, 2 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 174.45, 156.98, 141.42, 134.23, 129.24, 128.91, 128.52, 128.01, 127.93, 125.59, 121.74, 119.92, 110.50, 58.95, 54.72, 30.77 ppm. UV/Vis (CH_3CN): λ [nm] 237 (ε = 13840 $M^{-1}cm^{-1}$), 281 (ε = 15225 $M^{-1}cm^{-1}$), 294 (ε = 13840 $M^{-1}cm^{-1}$), 317 (ε = 14189 $M^{-1}cm$–1). HRMS: calcd. for $C_{18}H_{17}NO$ [M + H]$^+$ 264.1383; found 264.1394.

4-[(*E*)-4-Bromobenzylidene]-5-phenyl-3,4-dihydro-2*H*-pyrrole (5j): White solid, yield 74%; m.p. 120–122 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.63 (m, 2 H), 7.46 (m, 5 H), 7.26 (d, *J* = 8.6 Hz, 2 H), 6.74 (s, 1 H), 4.20 (m, 2 H), 2.99 (m, 2 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 174.74, 142.80, 135.94, 134.33, 131.74, 130.34, 129.71, 128.73, 128.53, 126.47, 121.80, 59.75, 30.82 ppm. UV/Vis (CH_3CN): λ [nm] 282 (ε = 47716 $M^{-1}cm^{-1}$), 295 (ε = 43147 $M^{-1}cm^{-1}$), 311 (ε = 23350 $M^{-1}cm$–1). HRMS: calcd. for $C_{17}H_{14}BrN$ [M + H]$^+$ 312.0382; found 312.0385.

4-[(*E*)-2-Bromobenzylidene]-5-phenyl-3,4-dihydro-2*H*-pyrrole (5k): White solid, yield 77%; m.p. 106–108 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.71 (m, 2 H), 7.57(t, *J* = 9.2 Hz, 2 H), 7.47 (m, 3 H), 7.33 (t, *J* = 7.3 Hz, 1 H), 7.14 (m, 2 H), 4.17 (m, 2 H), 2.95 (m, 2 H) ppm. ^{13}CNMR (300 MHz, $CDCl_3$): δ = 174.28, 143.75, 136.76, 134.10, 132.95, 129.75, 129.07, 128.78, 128.58, 128.44, 127.26, 126.40, 124.99, 59.28, 30.37 ppm. UV/Vis (CH_3CN): λ [nm] 235 (ε = 15015 $M^{-1}cm^{-1}$), 240 (ε = 14114 $M^{-1}cm^{-1}$), 282 (ε = 18182 $M^{-1}cm^{-1}$), 292 (ε = 17117 $M^{-1}cm$–1). HRMS: calcd. for $C_{17}H_{14}BrN$ [M + H]$^+$ 312.0382; found 312.0388.

4-[(*E*)-4-Nitrobenzylidene]-5-phenyl-3,4-dihydro-2*H*-pyrrole (5l): Pale orange solid, yield 76%; m.p. 119–121 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.23 (d, *J* = 8.8 Hz, 2 H), 7.66 (m, 2 H), 7.57 (d, *J* = 8.9 Hz, 2 H), 7.50 (m, 3 H), 6.90 (s, 1 H), 4.30 (m, 2 H), 3.10 (m, 2 H); ^{13}CNMR (300 MHz, $CDCl_3$) ppm. ^{13}CNMR (300 MHz, $CDCl_3$): δ = 174.47, 146.61, 146.19, 143.64, 133.90, 129.96, 129.34, 128.67, 125.51, 125.43, 123.93, 123.87, 60.03, 31.30 ppm. UV/Vis (CH_3CN): λ [nm] 233 (ε = 10150 $M^{-1}cm^{-1}$), 262 (ε = 7026 $M^{-1}cm^{-1}$), 335 (ε = 13684 $M^{-1}cm^{-1}$). HRMS: calcd. for $C_{17}H_{14}N_2O_2$ [M + H]$^+$ 279.1128; found 279.1133.

4-[(*E*)-(2-Phenyl-4,5-dihydro-3*H*-pyrrol-3-ylidene)methyl]pyridine (5m): Brown solid, yield 65%; m.p. 99–101 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.64 (m, 2 H), 7.65 (m, 2 H), 7.51 (m, 3 H), 7.30 (m, 2 H), 6.77 (s, 1 H), 4.29 (m, 2 H), 3.11 (m, 2 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 174.48, 150.19, 146.69, 144.43, 133.93, 130.02, 128.76, 128.72, 125.10, 123.03, 59.98, 31.25 ppm. UV/Vis (CH_3CN): λ [nm] 245 (ε = 10028 $M^{-1}cm^{-1}$), 275 (ε = 18384 $M^{-1}cm^{-1}$), 284 (ε = 19304 $M^{-1}cm^{-1}$), 300 (ε = 12368 $M^{-1}cm$–1). HRMS: calcd. for $C_{16}H_{14}N_2$ [M + H]$^+$ 235.1230; found 235.1232.

4-[(*E*)-Naphthalen-1-ylmethylene]-5-phenyl-3,4-dihydro-2*H*-pyrrole (5n): Yellow solid, yield 60%; m.p. 153–155 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.88 (s, 1 H), 7.83 (m, 3 H), 7.68 (m, 2 H), 7.56 (m, 1 H), 7.49 (m, 5 H), 6.98 (s, 1 H), 4.26 (m, 2 H), 3.18 (m, 2 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 175.16, 142.56, 134.61, 134.59, 133.40, 132.81, 129.64, 128.82, 128.51, 128.41, 128.23, 128.15, 127.88, 127.67, 126.52, 126.47, 126.46, 59.79, 31.12 ppm. UV/Vis (CH_3CN): λ [nm] 245 (ε = 26342 $M^{-1}cm^{-1}$), 266 (ε = 34448 $M^{-1}cm^{-1}$), 275 (ε = 34853 $M^{-1}cm^{-1}$), 311 (ε = 28368 $M^{-1}cm^{-1}$), 324 (ε = 24316 $M^{-1}cm$–1). HRMS: calcd. for $C_{21}H_{17}N$ [M + H]$^+$ 284.1434; found 284.1439.

4-[(*E*)-4-Methylbenzylidene]-5-*p*-tolyl-3,4-dihydro-2*H*-pyrrole (*E*-5o): Orange solid, yield 80%; m.p. 83–85 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 8.0 Hz, 2 H), 7.32 (d, *J* = 8.1 Hz, 2 H), 7.27 (d, *J* = 7.9 Hz, 2 H), 7.19 (d, *J* = 8.0 Hz, 2 H), 6.82 (s, 1 H),

4.19 (m, 2 H), 3.05 (m, 2 H), 2.42 (s, 3 H), 2.36 (s, 3 H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 174.91, 141.27, 139.56, 137.88, 134.29, 131.69, 129.32, 129.14, 128.89, 128.74, 127.68, 59.44, 31.01, 21.47, 21.35 ppm. UV/Vis (CH_3CN): λ [nm] 254 (ε = 12623 $M^{-1}cm^{-1}$), 294 (ε = 20118 $M^{-1}cm^{-1}$), 309 (ε = 15385 $M^{-1}cm^{-1}$). HRMS: calcd. for $C_{19}H_{19}N$ [M + H]$^+$ 262.1590; found 262.1598.

4-[(*Z*)-4-Methylbenzylidene]-5-*p*-tolyl-3,4-dihydro-2*H*-pyrrole (*Z*-5o): Orange solid, yield 15%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.13 (d, J = 8.0 Hz, 2 H), 6.92 (s, 1 H), 6.84 (d, J = 7.8 Hz, 2 H), 6.72 (q, J = 8.2 Hz, 4 H), 4.07 (m, 2 H), 2.96 (m, 2 H), 2.24 (s, 3 H), 2.19 (s, 3 H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 172.94, 140.04, 138.80, 136.58, 133.29, 132.68, 129.31, 128.29, 128.25, 127.95, 126.17, 57.71, 35.88, 21.44, 21.23 ppm. UV/Vis (CH_3CN): λ [nm] 260 (ε = 14600 $M^{-1}cm^{-1}$), 295 (ε = 13400 M^{-1}cm–1). HRMS: calcd. for $C_{19}H_{19}N$ [M + H]$^+$ 262.1590; found 262.1598.

Typical Procedure for Irradiation: A solution of the *E* isomer of each compound **5a**–**o** (10^{-2} M) in CH_3CN was prepared and irradiated at room temperature through Pyrex glass with a 125-W medium-pressure Hg lamp (except for compound **5e**, where quartz was used instead of Pyrex) until the PSS was reached. The isomerization reaction was followed by ^{1}H NMR because *E* and *Z* isomers have distinctive ^{1}H NMR signals. Depending on the absorption bands, the mixture took 1–4 h to reach the PSS.

Supporting Information (see footnote on the first page of this article): Copies of the ^{1}H NMR and ^{13}C NMR spectra for compounds **5**, 2D-NMR experiments of the *E* isomer of switch **5d**.

CCDC-889062 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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