

***N*-Substituted Indigos as Red-Light Photoswitches with Tunable Thermal Half-Lives**

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In the past years, the field of photoswitches has seen exciting developments and broader applications in material science, biomedical studies and many other disciplines of science. Although numerous works have been done on improving systems, mainly azobenzenes, that are addressable by visible light,^[1] photochromic molecules that can undergo photoisomerization under the irradiation of red light have received relatively less attention. Red-light photoswitches not only would avoid the use of high-energy irradiation source but would also allow for the *in vivo* application due to the constraint of biological window.

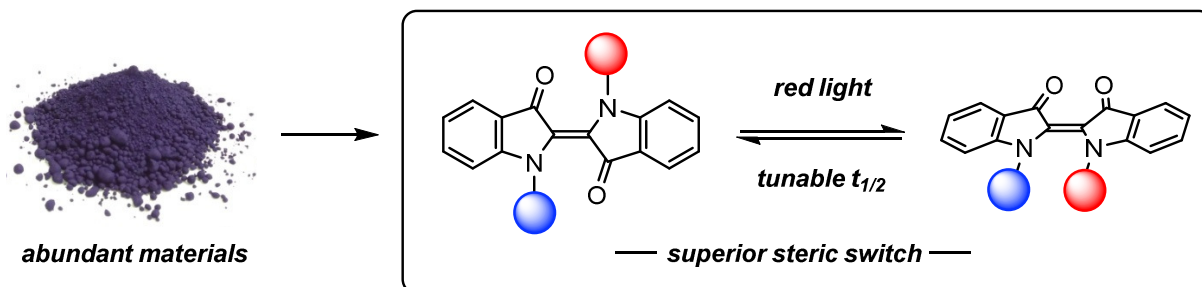


Figure 1. *N*-substitutions of abundant indigo dye generate red light photoswitches whose thermal half-lives can be tuned by modular changes of chemical structures.

To our surprise, indigo, one of the most ancient dyes known to human history, has been left out in this wave of developments, despite the fact that their *E-Z* photoisomerization by red light has been established for more than 50 years.^[2] Photoswitches based on indigos enjoy four advantages. First, they would be prepared from extremely abundant materials. Second, these molecules are intrinsically red-shifted without the need of special derivatization. Furthermore, the *E-Z* isomerization confers greater structural changes and renders them superior steric switches as compared to azobenzenes. Finally, indigo photoswitches demonstrate negative photochromism, which makes them advantageous in many applications. To date, photoswitches based on indigos all show λ_{\max} ranging from 530-670 nm, which unequivocally demonstrates their red-shifted character. However, these compounds suffer from either chemical instability or poor functionalizability, and more importantly, there is not an obvious way to tune their thermal half-lives by modular variations of the molecular structures.

Herein, we report a series of synthetic methods which allow for rapid installation of *N*-alkyl and *N*-aryl substituents on the indigo. Furthermore, through these synthetic modifications, it

is possible to modulate their thermal half-lives in a systematic fashion. How these substituents tune the thermal barrier as well as insights into the transition state structure will be discussed.

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