DNA-Templated [2+2] Photocycloaddition: A Straightforward and Bio-Inspired entry into the Aplysinopsin Family of Natural Products

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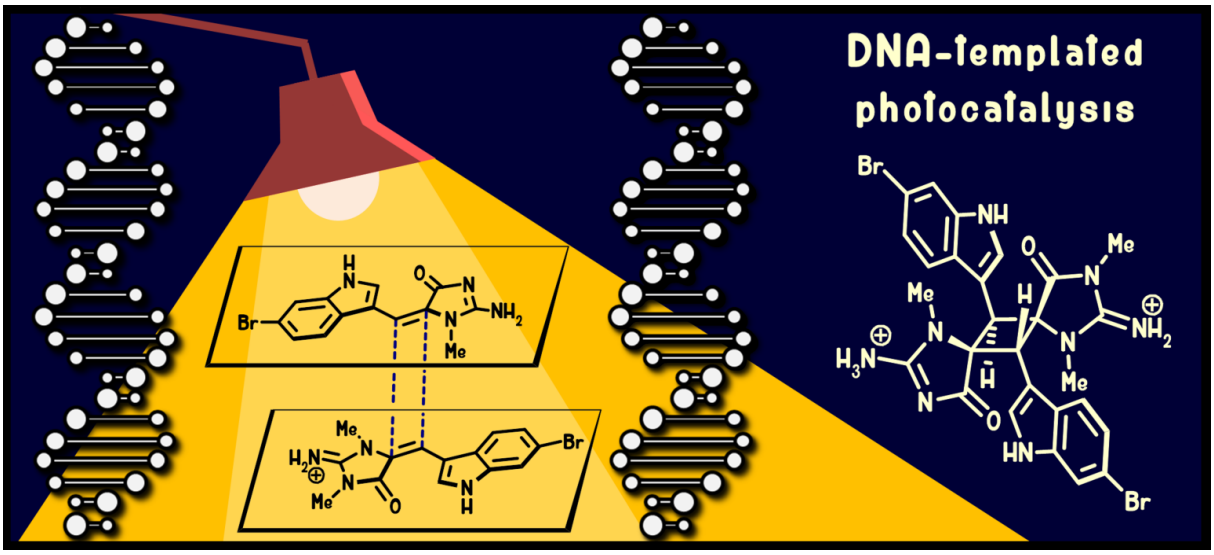
Biosynthetic considerations inspired us to harness the template properties offered by DNA to promote [2+2] photo-induced cycloadditions. The method was developed based on the dimerization of (*E*)-aplysinopsin, which was shown to be unproductive in solution. In contrast, exposure of this tryptophan-derived olefin to light in the presence of DNA reproducibly afforded the corresponding homo-dimerized spiro-fused cyclobutane in excellent yields. Biophysical studies revealed that DNA provides unique templating interactions enabling a singular mimic of the solid-state aggregation necessary for the [2+2] photo-cycloaddition to occur. This method was ultimately used to promote the prerequisite dimerizations leading to both dictazole B and tubastrindole B, thus constituting the first example of a DNA-templated transformation to be applied to the total synthesis of a natural product.[1]



[1] N. Duchemin, A. Skiredj, J. Mansot, K. Leblanc, J.-J. Vasseur, M. A. Beniddir, L. Evanno, E. Poupon, M. Smietana, S. Arseniyadis, *Angew. Chem. Int. Ed.* **2018** (*DOI: 10.1002/anie.201806357*).