MONO- AND DISUBSTITUTED PSORALENS FOR INTERCALATION AND PHOTOADDITION INTO DNA

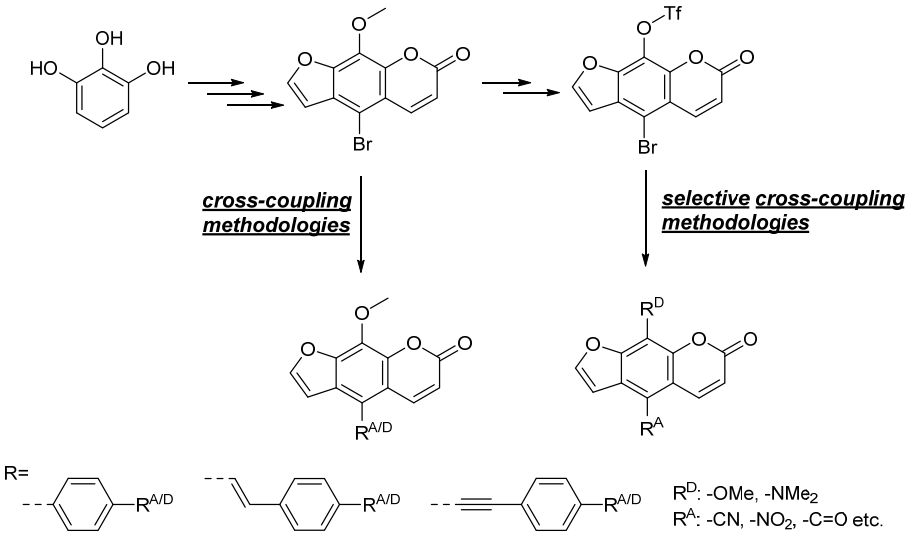
Sarah R. Geenen, Thomas J. J. Müller*

Institute of Organic Chemistry and Macromolecular Chemistry,
Heinrich Heine University Düsseldorf, D-40225 Düsseldorf, Germany

Psoralens are DNA intercalators and undergo photoreactions causing hampered DNA replication and transcription. With this respect the PUVA (psoralen + UV-A-light) therapy offers advantages in treatment of cancer and several skin diseases.[1,2] To study the crosslinking photocycloadditions with DNA the electronic structure of the psoralens has to be controlled and optimized. Furthermore, the goal of this project is to establish structure-property relationships by synthesizing different psoralen derivatives.

A diversity-oriented approach leads to a new generation of mono- and disubstituted psoralens. Simultaneously, structure-property relationships of the photoreactivity of psoralens with DNA are investigated. Starting from commercially available pyrogallol, an efficient route to pivotal coupling partners was employed.[3,4]

Hence, mono- or disubstituted psoralens are synthesized by site-selective cross-coupling methodologies, such as Suzuki, Sonogashira and Heck reactions. Introduction of donor groups at the 8-position causes a bathochromic shift of the absorption maxima. Furthermore, substituted psoralens fluoresce in solution and in the solid state.



Scheme 1: Conceptual synthetic route to 5-acceptor-8-donor substituted psoralens.

[1] J. W. Tessman, S. T. Isaacs, J. E. Hearst, *Biochemistry* **1985,** *24,* 1669-1676.

[2] T. F. Anderson, J. J. Voorhees, *Annu. Rev. Pharmacol. Toxicol.* **1980,** *20,* 235-257.

[3] R. A. Leão, P. F. de Moraes, M. C. Pedro, *Blucher Chemistry Proceedings* **2013,** *1,* 72-72.

[4] J. Timonen, K. Vuolteenaho, T. Leppänen, R. Nieminen, E. Moilanen, P. Aulaskari, J. Jänis, *J. Heterocycl. Chem.* **2015,** *52,* 1286-1295.