Swiss Science Concentrates

A CHIMIA Column
Short Abstracts of Interesting Recent Publications of Swiss Origin

Cell-Permeant and Photocleavable Chemical Inducer of Dimerization


Time-resolved localization of proteins is key to unravel and control the complexity of intracellular processes. Chemical inducers of dimerization (CIDs) enable intracellular delocalization of proteins of interest (POI) by chemical linking through genetically encoded fusion tags, if one of the cargo proteins carries a membrane anchor. A CID where a SNAP-tag and a Halo-tag substrate are linked via a photocleavable group has been developed, which allows the release of a model protein with subcellular precision by means of a scanning laser at irradiation times of <1 s. If required, the linkage can also be cleaved by global illumination. This new type of CID holds great promise for various applications, not least the validation of CID-linked protein complexes.

Iron-Catalyzed 1,2-Addition of Perfluoroalkyl Iodides to Alkenes and Alkynes


The authors present an iron-catalyzed method for synthesis of perfluoroalkylated organic compounds starting from readily available alkenes and alkynes. In a first step, perfluoroalkyl iodides are activated by cesium carbonate affording radical intermediates. These subsequently react with alkenes and alkynes, which in turn are activated by iron, to the respective 1,2-addition products. Various functional groups are well tolerated and trifluoromethylation is feasible. The synthetic utility of the obtained 1,2-addition products was demonstrated for several cross coupling reactions.

Distance Dependence of Bidirectional Concerted Proton–Electron Transfer in Phenol-Ru(2,2'-bipyridine)$_3^{2+}$ Dyads


Concerted Proton-Electron transfer (CPET) plays a fundamental role in numerous enzymatic redox-transformations, including in photosystem II. By incrementally increasing the separation between a covalently linked phenolic donor moiety and a [Ru(bpy)$_3$]$^{2+}$ acceptor moiety, Wenger and coworkers were able to determine the distance dependence of the CPET rates. The system was designed such that the proton and the electron migrate in opposite directions thus offering a powerful means to create a charge gradient across a membrane. Interestingly, the distance dependence does not differ significantly from that observed for ordinary electron transfer. This finding predicts that CPET should be possible for up to a 20 Å distance.

A Small-Molecule Drug Conjugate for the Treatment of Carbonic Anhydrase IX Expressing Tumors


Carbonic Anhydrase IX (CAIX) is overexpressed in various cancer forms and thus is an attractive target for the delivery of payloads. Neri and coworkers present a strategy whereby a CAIX inhibitor is linked to cleavable cytotoxic payload (maytansinoid, DM1). They demonstrate that such small molecule drug conjugates are i) accessible by organic synthesis ii) display good tissue penetration properties, iii) non immunogenic and iv) lead to preferential payload uptake at the tumor site. This design thus offers a viable alternative to antibody drug conjugates for the treatment of solid tumors.

Prepared by Christophe Daeppen, Adrian von der Höh, Valentin Köhler, Raphael Reuter, Mariana Spulber and Thomas R. Ward

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Please contact thomas.ward@unibas.ch