



## Swiss Science Concentrates

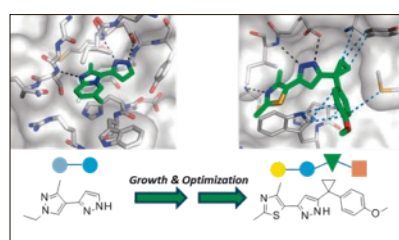
A CHIMIA Column

Short Abstracts of Interesting Recent Publications of Swiss Origin

### Design of Potent and Druglike Nonphenolic Inhibitors for Catechol *O*-Methyltransferase Derived from a Fragment Screening Approach Targeting the *S*-Adenosyl-L-methionine Pocket

C. Lerner, R. Jakob-Roetne, B. Buettelmann, A. Ehler, M. Rudolph, and R. M. Rodríguez Sarmiento\*, *J. Med. Chem.* **2016**, *59*, 10163. F. Hoffmann-La Roche AG, Basel

Catechol *O*-methyltransferase (COMT) catalyzes the Mg<sup>2+</sup> dependent methyl transfer from its cofactor *S*-adenosyl-L-methionine (SAM), to one of the hydroxyl groups of endogenous neurotransmitters, such as dopamine and noradrenaline, terminating their biological activity. Rodríguez Sarmiento and co-workers designed a fragment screening targeting specifically the SAM pocket of COMT followed by X-ray guided fragment optimization. This allowed the identification of potent and novel inhibitors that bind to the SAM pocket of COMT and do not require a catechol or phenol like motif for high potency. The

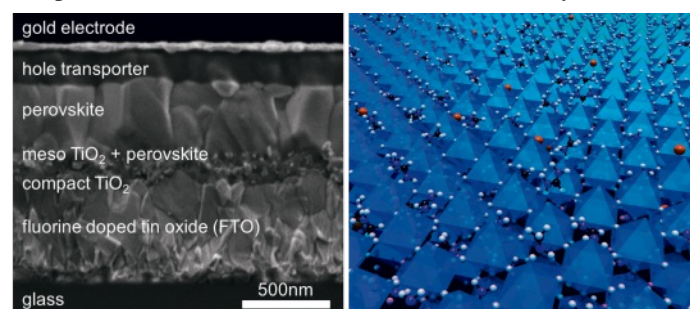


derivatives may serve as lead compounds for the treatment of Parkinson's disease, as adjuncts in levodopa based therapies, or schizophrenia.

### Incorporation of Rubidium Cations into Perovskite Solar Cells Improves Photovoltaic Performance

M. Saliba\*, T. Matsui, K. Domanski, J.-Y. Seo, A. Ummadisingu, S. M. Zakeeruddin, J.-P. Correa-Baena, W. R. Tress, A. Abate, A. Hagfeldt, and M. Grätzel\*, *Science* **2016**, *354*, 206. EPF Lausanne

Low-cost perovskite solar cells have achieved certified power conversion efficiencies of 22.1%. Inherent stability problems of organic-inorganic perovskites, however, represent a major drawback for their use in photovoltaic cells. Saliba, Grätzel and coworkers now demonstrate that the small, oxidation-stable Rb<sup>+</sup> can be used to create perovskite materials with efficiencies of up to 21.6% and an electroluminescence of 3.8% external quantum efficiency. The open-circuit voltage of 1.24 volts at a band gap of 1.63 electron volts leads to a loss-in-potential of 0.39 V, which compares well with commercial silicon cells. Polymer-coated



cells maintained 95% of their initial performance at 85 °C for 500 hours under full illumination and maximum power point tracking.

### One-Pot Three-Component Synthesis of Vicinal Diamines via *in Situ* Amino Formation and Carboamination

U. Orce and J. Waser\*, *Angew. Chem. Int. Ed.* **2016**, *55*, 12881. EPF Lausanne

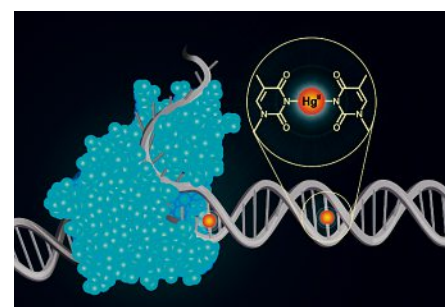
Vicinal diamines are of utmost importance in natural products, agrochemicals, drugs, and as chiral ligands. Hence, tremendous efforts have been invested to develop new methods for efficient access. Orce and Waser report the synthesis of vicinal diamines by *in situ* amino formation and carboamination of allyl amines. The use of highly electron-poor trifluoromethyl aldimines in their stable hemi-aminal form enables both a fast and complete amino formation as well as the palladium-catalyzed carboamination step. The reaction conditions allow the introduction of a wide variety of regioselectivity and high diastereoselectivity. The imidazolidine products can be selectively N-protected; alternatively, the free diamines are obtained by amino cleavage under mild conditions.



### Fluorescent Base Analogue Reveals T-Hg<sup>II</sup>-T Base Pairs Have High Kinetic Stabilities That Perturb DNA Metabolism

O. P. Schmidt, G. Mata, and N. W. Luedtke\*, *J. Am. Chem. Soc.* **2016**, *138*, 14733. University of Zurich

Some of the cytotoxic and mutagenic activities of Hg<sup>II</sup> could be the result of direct mercury-DNA binding interactions. Hg<sup>II</sup> stoichiometrically binds to T-T mismatches in duplex DNA to give T-Hg<sup>II</sup>-T base pairs. Luedtke and co-workers used the new fluorescent thymidine analogue <sup>DMAT</sup> to conduct the first detailed kinetic and thermodynamic analyses of site-specific T-Hg<sup>II</sup>-T binding reactions in duplex DNA. This high-affinity binding interaction is characterized by very slow association and dissociation kinetics. This causes the inhibition of dynamic processes including DNA strand displacement and primer extension by DNA polymerases that resulted in premature chain termination of DNA synthesis. These results demonstrate that T-Hg<sup>II</sup>-T base pairs have a high potential to disrupt DNA metabolism *in vivo*.



Prepared by Caroline D. Bösch, Mariusz Kownacki, Yuliia Vyborna, Simon M. Langenegger and Robert Häner\*

Do you want your article to appear in the SWISS SCIENCE CONCENTRATES highlight?

Please contact robert.haener@dcb.unibe.ch