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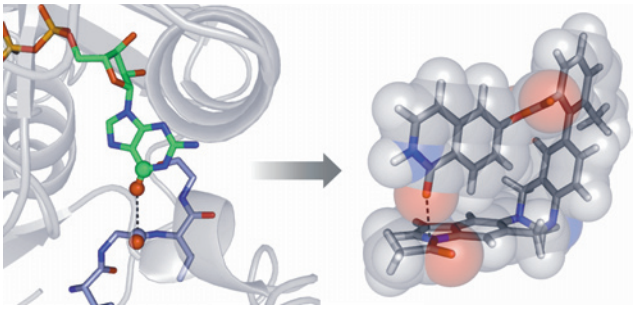
Short Abstracts of Interesting Recent Publications of Swiss Origin

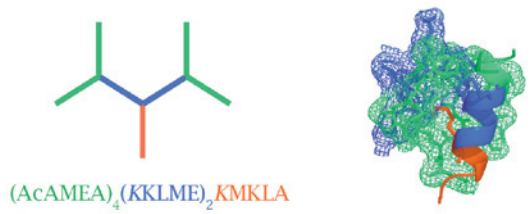
Orthogonal Dipolar Interactions between Amide Carbonyl Groups

F. R. Fischer, P. A. Wood, F. H. Allen, and F. Diederich* *Proc. Natl. Acad. Sci. USA* **2008**, *105*, 17290
ETH Zürich; Cambridge Crystallographic Data Centre
Orthogonal dipolar interactions between amide C=O bond dipoles are commonly found in crystal structures of small molecules, proteins, and protein–ligand complexes. In this article, the authors present the experimental quantification of such interactions in solution using a model system based on a molecular torsion balance. The stabilizing free interaction enthalpies in various apolar and polar solvents amount to –2.73 kJ/mol. These attractive dipolar contacts provide a promising tool for small-molecule crystal design and the enhancement of ligand–protein interactions during lead optimization in medicinal chemistry.



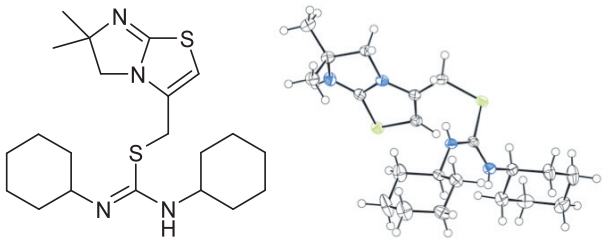
α-Helix Stabilization within a Peptide Dendrimer

S. Javor, A. Natalello, S. M. Doglia,* and J. L. Reymond* *J. Am. Chem. Soc.* **2008**, *130*, 17248
University of Bern; University of Milano-Bicocca
Dendrimers are branched synthetic macromolecules that usually adopt protein-like globular shapes. In this article, the authors show that the introduction of very short 4-residue helical segments based on natural α-helix inducing residues provides a strategy towards more protein-like structures. In particular, dendrimer $(AcAMEA)_4(KKLME)_2KMKLA$ adopts an α-helical conformation that is more stable than the corresponding linear peptide AcAMEAAKLMEAMKLA toward pH-induced unfolding and temperature-induced intermolecular aggregation. The unprecedented stabilization effect is interpreted in terms of an α-helix spanning across two successive branching points of the dendrimer.



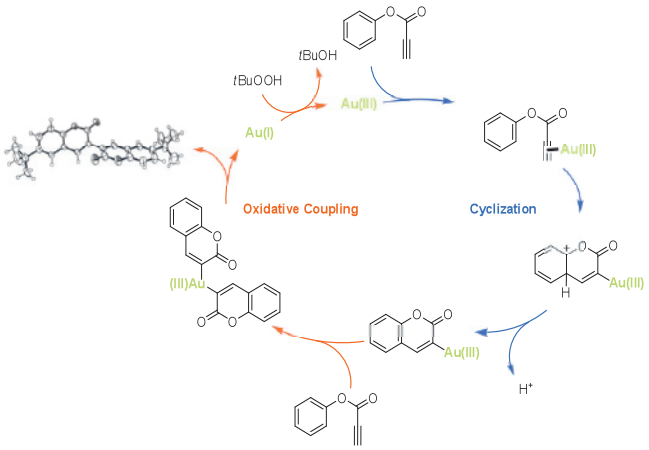
Orally Bioavailable Isothioureas Block Function of the Chemokine Receptor CXCR4 *in vitro* and *in vivo*

G. Thoma*, M. B. Streiff, J. Kovarik, F. Glickman, T. Wagner, C. Beerli, and H.-G. Zerwes, *J. Med. Chem.* **2008**, *51*, 7915
Novartis Institutes for Biomedical Research, Basel
The interaction of the chemokine receptor CXCR4 with its ligand CXCL12 is involved in many biological processes such as hematopoesis, migration of immune cells, as well as in cancer metastasis. CXCR4 also mediates the infection of T-cells with X4-tropic HIV functioning as a coreceptor for the viral envelope protein gp120. In this article, the authors report highly potent selective CXCR4 inhibitors that block, *in vitro* and *in vivo*, the interactions of this receptor with both CXCL12 and the HIV envelope protein gp120.



A New Gold-catalyzed Domino Cyclization and Oxidative Coupling Reaction

H. A. Wegner*, S. Ahles, and M. Neuburger *Chem. Eur. J.* **2008**, *14*, 11310
University of Basel
In this article, the authors report the first example of a gold-catalyzed domino cyclization/oxidative coupling reaction. In this process, the same catalyst promotes the cyclization of the alkyne group in arylpropionic esters onto the arene and the oxidative homocoupling of the bicyclic coumarin adducts as well. The resulting dicoumarins constitute an interesting scaffold present in many natural products.



Prepared by M. Austeri, R. Bach, J. Guin, A. Sharma, F. Toricelli, W. Zeghida, J. Lacour
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