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Swiss Science Concentrates

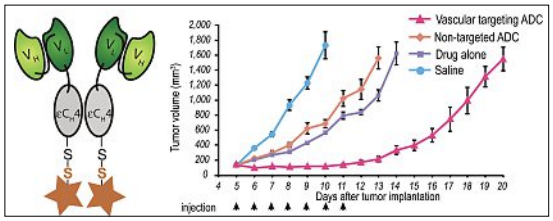
A CHIMIA Column

Short Abstracts of Interesting Recent Publications of Swiss Origin

A Traceless Vascular-Targeting Antibody-Drug Conjugate for Cancer Therapy

G. J. L. Bernandes, G. Casi, S. Trüssel, I. Hartmann, K. Schwager, J. Scheuermann, and D. Neri* *Angew. Chem. Int. Ed.* **2011**, *51*, 941.
ETH Zurich

Delivering a drug selectively to its target is an attractive approach in the struggle for efficient cancer treatment. Antibody–Drug conjugates (ADCs) display excellent targeting capabilities, but suffer from the need for tumor cell internalization for the delivery of their drug load. A new strategy based on non-internalizing vascular targeting ADCs has been shown to mediate strong antitumor activity *in vivo*. The human antibody F8, used in a small immune protein (SIP) format, was selectively modified at its terminal cysteine residue as a mixed disulfide with a derivative of the potent cytotoxic drug cemadotin. Upon initiated tumor cell death, reducing agents – such as cysteine and glutathione – are released into the extracellular matrix and lead in a self-amplifying process to the traceless cleavage of the cytotoxic payload.



Composites Reinforced in Three Dimensions by Using Low Magnetic Fields

R. M. Erb, R. Libanori, N. Rothfuchs, and A. R. Studart*, *Science*, **2011**, *335*, 199.
ETH Zurich

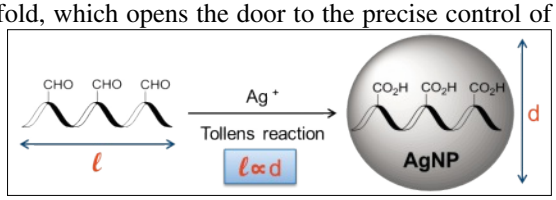
Lightweight and strong composite materials have found widespread application in load-bearing applications, *e.g.* in the aerospace sector. Common polymer-based composites rely on one- or two-dimensional arrays of reinforcing fibers or webbings. A 3D reinforcement would strongly enhance material properties. The authors now report a method to align and position reinforcing particles in three dimensions within polymers by using low magnetic fields (1 to 10 mT). To this end, micron-sized alumina platelets were coated with superparamagnetic nanoparticles. An ultra high magnetic response was achieved by rational design of the microparticle's dimensions and the density of the superparamagnetic coating. Composite materials with increased mechanical strength, as well as tunable wear resistance and localized reinforcements were realized thus demonstrating the versatility of this concept.

Cross-section of a synthetic composite showing enhanced control over the position and orientation of stiffer elements (aluminum oxide platelets, dark color) within a softer material (epoxy resin, light color).

Oligoprolines as Scaffolds for the Formation of Silver Nanoparticles in Defined Sizes – Correlating Molecular and Nanoscopic Dimensions

G. Upert, F. Bouillère, and H. Wennemers*, *Angew. Chem. Int. Ed.* **2012**, *51*, DOI: 10.1002/anie.201107183.
University of Basel and ETH Zurich

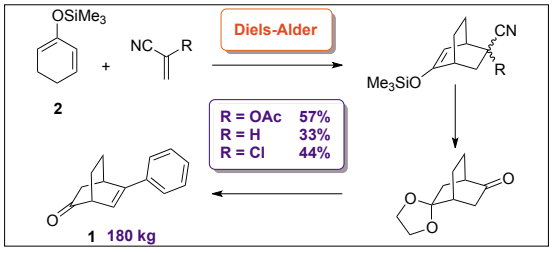
Silver nanoparticles (AgNPs) display great potential in various applications, which include – among others – imaging, catalysis, and antimicrobial coatings. Precisely controlling the size and shape of AgNPs is crucial as these parameters directly affect the targeted properties of the nanoparticles. Thus, methods that allow for the reliable preparation of AgNPs with defined dimensions are of great value. The authors report that aldehyde-functionalized oligoprolines are well suited to control the size of AgNPs which are formed during the *Tollens* reaction starting from silver ions. The aldehyde groups are oxidized to carboxylic acids, which stabilize the nanoparticles through coordination. The size of the resulting nanoparticles correlates linearly with the length of the peptide scaffold, which opens the door to the precise control of the size of metal nanoparticles.



Design and Scale up of Diels–Alder Reactions for the Practical Synthesis of 5-Phenylbicyclo [2.2.2]oct-5-en-2-one

J.-A. Funel, G. Schmidt, and S. Abele*, *Org. Process Res. Dev.* **2011**, *15*, 1420.
Actelion Pharmaceuticals Ltd.

Several synthetic pathways towards racemic 5-phenylbicyclo[2.2.2]oct-5-en-2-one **1** have been devised starting with a Diels–Alder reaction of (cyclohexa-1,5-dien-1-yloxy)trimethylsilane **2** and α-acetoxyacrylonitrile, acrylonitrile, or α-chloroacrylonitrile (R = OAc, H, Cl). The first 'fit-for-purpose' route relied on α-acetoxyacrylonitrile as a dienophile and rapidly delivered kilogram amounts of **1**. Process safety data then triggered the development of a scalable Diels-Alder reaction using α-chloroacrylonitrile as the dienophile. This practical and volume-efficient route delivered **1** in 44% yield in six chemical steps with two isolated intermediates. Notably, neither chromatography nor distillation was required for the multi-kilogram synthesis of **1**, all intermediates being oils. A total of 180 kg of **1** was produced with this route.



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