The following Communications have been judged by at least two referees to be “very important papers” and will be published online at www.angewandte.org soon:

K. Moehle, Z. Athanassiou, K. Patora, A. Davidson, G. Varani, J. A. Robinson**
Design of β-Hairpin Peptidomimetics That Inhibit Binding of α-Helical HIV-1 Rev Protein to the Rev Response Element RNA

*P. A. Chase, G. C. Welch, T. Jurca, D. W. Stephan**
Metal-Free Catalytic Hydrogenations

*J. A. Teprovich, Jr., M. N. Balili, T. Pintauer, R. A. Flowers II**
Mechanistic Studies of Proton-Donor Coordination to Samarium Diiodide

*E. B. Hadley, A. M. Witek, F. Freire, A. J. Peoples, S. H. Gellman**
Thermodynamic Analysis of a β-Sheet Secondary Structure By Backbone Thioester Exchange

*G. E. Veitch, E. Beckmann, B. J. Burke, A. Boyer, S. L. Maslen, S. V. Ley**
The Synthesis of Azadirachtin: A Long But Successful Journey

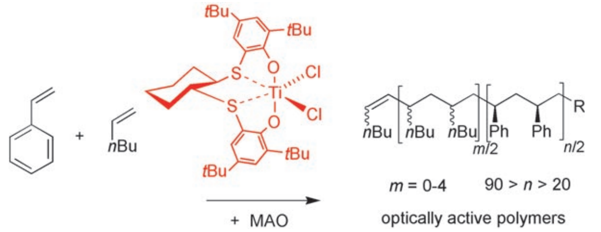
*G. E. Veitch, E. Beckmann, B. J. Burke, A. Boyer, C. Ayats, S. V. Ley**
A New Relay Route for the Synthesis of Azadirachtin

News

Books

Highlights

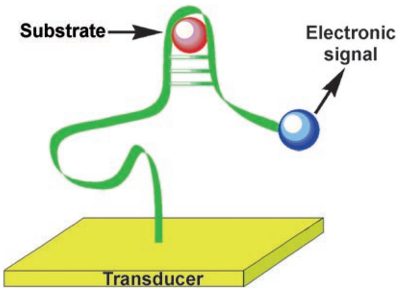
Optically Active Polymers



Ziegler–Natta revival: Enantiomerically pure, isotactic oligo/polystyrenes have been prepared by titanium-based single-site catalysis. The optical activity of these polystyrenes was shown to be measurable up to a degree of polymerization of 45, providing a discrete border for the appearance of “cryptochirality” for larger macromolecules. MAO = methylaluminoxane.

Minireviews

Bioelectronics



How apt these sensors are! Electronic aptamer-based sensors (aptasensors) hold great promise as analytical devices for the detection of low-molecular-weight substrates or proteins. The Minireview highlights the advantages of electronic transduction of aptasensor systems and discusses the latest developments in the design of electrochemical, field-effect transistor, and piezoelectric aptasensor systems.

Contents

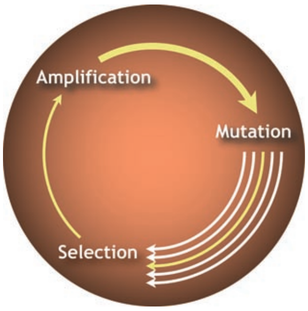
Reviews

Molecular Evolution

G. F. Joyce* ———— **6420 – 6436**

Forty Years of In Vitro Evolution

Darwinian chemistry was first practiced by Spiegelman and colleagues in 1967 when they carried out the Darwinian evolution of RNA molecules in a test tube. In the following 40 years, the directed evolution of RNA has become a highly fruitful area of research and has deepened our understanding of evolutionary processes at the molecular level.



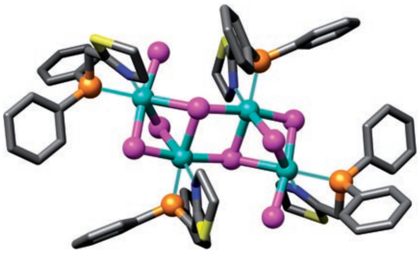
Communications

Coordination Chemistry

A. Kermagoret, R. Pattacini,
P. Chavez Vasquez, G. Rogez, R. Welter,
P. Braunstein* ———— **6438 – 6441**

Unprecedented Tetranuclear Complexes with 20-Electron Ni^{II} Centers: The Role of Pressure and Temperature on Their Solid-State and Solution Fragmentation

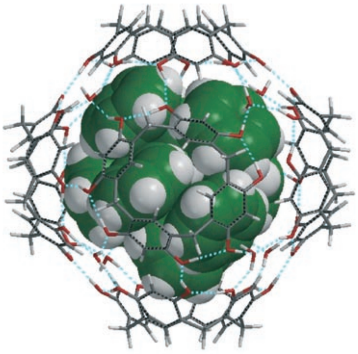
Complexes under pressure! The complexes $[\{NiCl_2(PN)\}_4]$ (PN = 2-diphenylphosphinomethyl-2-oxazoline or -2-thiazoline; see picture; Ni green, Cl pink, P orange, S yellow, N blue, C gray) have an unprecedented, centrosymmetric Ni_4Cl_8 core with 20-electron metal centers and undergo pressure-induced fragmentation into the mononuclear, square-planar 16-electron complexes $[NiCl_2(PN)]$, which are in equilibrium with the respective tetramer in solution.



Supramolecular Chemistry

S. Shimizu,* T. Kiuchi,
N. Pan ———— **6442 – 6445**

A “Teflon-Footed” Resorcinarene: A Hexameric Capsule in Fluorous Solvents and Fluorophobic Effects on Molecular Encapsulation



$(\mathbf{1}^F)_6\supset(C_6H_6)_8$

A slippery character: Cyclooligomerization of resorcinol with a highly fluorinated aldehyde afforded a “teflon-footed” resorcinarene **1**^{F}, which is soluble in wet fluorous solvents through formation of a hexameric capsule. The supramolecular capsules in fluorous solvents exhibited more selective and/or enhanced properties as a result of fluorophobic effects on molecular encapsulation (such as encapsulating eight molecules of benzene, see picture).

For the USA and Canada:
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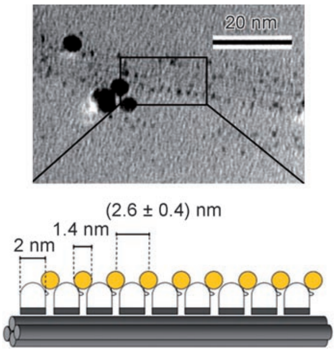
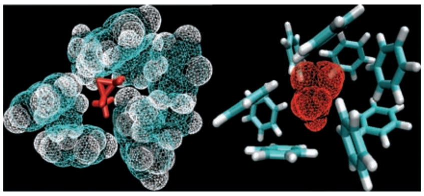
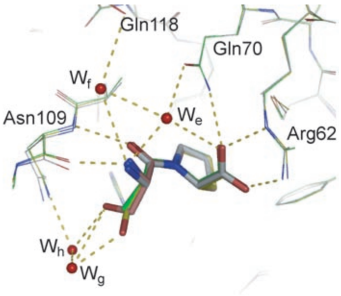


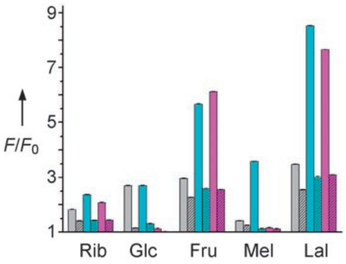
Spread them out: A hierarchically ordered material in which gold nanoparticles are positioned along carbon nanotubes with a spacing of 2.6 nm is described. The organization is achieved by self-assembly and relies on the functionality of a surfactant protein called HFBI (a hydrophobin).

Solvent or solute dissymmetry? The dissymmetric ordering of solvent molecules around the chiral solute (see picture) contributes to the chiroptical signature. Indeed, the solvent can dominate the chiroptical response, as shown for (*S*)-methyloxirane in benzene.

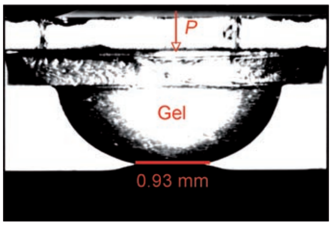




Gaze into the crystal: A crystallographic approach for determining and analyzing free energy not only provides a way of measuring binding energy, it also provides a detailed picture identifying, at the atomic level, which interactions are responsible for changes in binding affinity (picture: superposition of dipeptide–cyclophilin 3 structures; $W_{e\text{–}h}$ are conserved water molecules e–h).



That's discrimination! An array of boronic acid appended bipyridinium salts (BBVs) as receptor units is able to distinguish twelve saccharides in aqueous solution and at neutral pH values by a fluorescent-indicator displacement assay. The picture shows the fluorescence increase of a fluorescent dye with BBV receptors after adding saccharides (D-ribose (Rib), D-glucose (Glc), D-fructose (Fru), melibiose (Mel), and lactulose (Lal)).



Make up and break up: A pH-responsive system that displays switchable adhesion in situ is described. Polyacid gels and polybases grafted to a substrate (brushes) strongly adhere in water, but in an acidic environment, the gel and brush dissociate. Adhesion can be controlled by environmental acidity and the process can be repeated several times. Such adhesion may be used in actuators, microfluidics, drug delivery, or personal-care products.

Polyelectrolytes

R. La Spina, M. R. Tomlinson, L. Ruiz-Pérez, A. Chiche, S. Langridge, M. Geoghegan* **6460 – 6463**

Controlling Network–Brush Interactions to Achieve Switchable Adhesion

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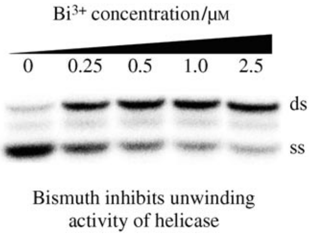
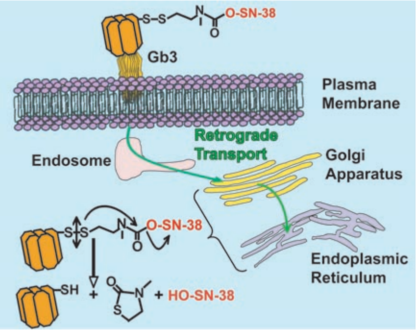
Hold tight: Bismuth complexes including ranitidine bismuth citrate effectively inhibit the nucleoside triphosphate hydrolase and DNA unwinding activities of the SARS coronavirus (SCV) helicase and dramatically reduce SCV replication levels in infected cells. This suggests that bismuth-based drugs should be further evaluated for the treatment of SCV infections in vivo. ss = single-stranded DNA, ds = duplex DNA.



Metalloantiviral Agents

N. Yang, J. A. Tanner, B. J. Zheng, R. M. Watt, M. L. He, L. Y. Lu, J.-Q. Jiang, K. T. Shum, Y. P. Lin, K. L. Wong, M. C. M. Lin, H. F. Kung, H. Sun,* J. D. Huang* **6464 – 6468**

Bismuth Complexes Inhibit the SARS Coronavirus



A retrograde strategy: An innovative cancer-cell delivery concept exploits the naturally evolved characteristics of the Shiga toxin B-subunit (STxB) for the intracellular activation of a newly synthesized prodrug at the level of the biosynthetic/secretory pathway (see picture). Retrograde prodrug targeting allows its slow release, which should sustain the presence of the active principle in dividing tumor cells.

Chemical Biology

A. El Alaoui, F. Schmidt,* M. Amessou, M. Sarr, D. Decaudin, J.-C. Florent, L. Johannes **6469 – 6472**

Shiga Toxin-Mediated Retrograde Delivery of a Topoisomerase I Inhibitor Prodrug

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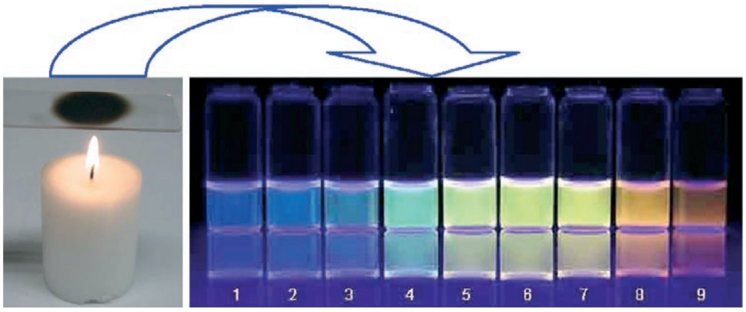


Flame and fluorescence: Water-soluble, multicolor fluorescent carbon nanoparticles are prepared by refluxing candle soot with nitric acid (see picture). The starting materials are easily accessible and inexpensive.

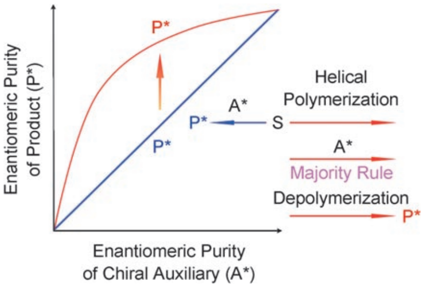
Fluorescent Nanoparticles

H. Liu, T. Ye, C. Mao* **6473 – 6475**

Fluorescent Carbon Nanoparticles Derived from Candle Soot

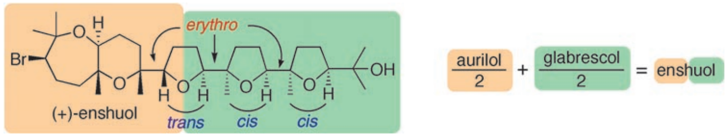
Contents

Chiral Amplification



Majority rules: "Chiral amplification" in asymmetric transformations can be realized if a helical supramolecular polymer, derived from the substrate (S), obeys the "majority rule" in determining its handedness. This concept works properly for the asymmetric transformation of a chirality-memorizing D_2-symmetric saddle-shaped porphyrin.

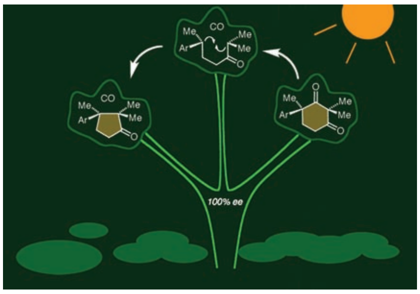
Structure Elucidation



Finding its true identity: The complete stereostructure of the marine pentacyclic triterpene polyether (+)-enshuol is shown. Asymmetric total synthesis confirmed the configuration predicted on the basis of NMR spectroscopic data of the previously synthesized natural products aurilol and glabrescol, substructures of which are present in enshuol, and disproved an earlier prediction based on biogenetic considerations.

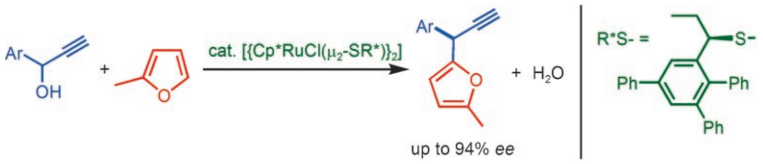
Solvent-Free Synthesis

Photo[Organic]synthesis: Irradiation of well-designed crystalline ketones can result in the solvent-free generation of compounds having adjacent quaternary stereogenic centers, as illustrated for the enantiospecific synthesis of the natural products (+)- and (−)-(α)-cuparenone (see picture).



Asymmetric Catalysis

VIP

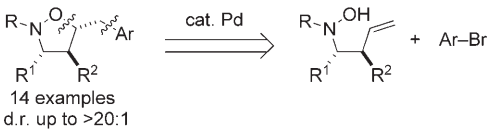


High enantioselectivity was achieved in the Ru-catalyzed propargylation of furans and *N*,*N*-dimethylaniline derivatives to afford the propargylated aromatic compounds. This first asymmetric propargylation of aromatic compounds provides a novel protocol for the asymmetric Friedel–Crafts alkylation using propargylic alcohols as a new type of electrophile. $Cp^* = C_5Me_5$

Isoxazolidine Synthesis

M. B. Hay, J. P. Wolfe* **6492 – 6494**

Stereoselective Synthesis of Isoxazolidines through Pd-Catalyzed Carboetherification of *N*-Butenylhydroxylamines

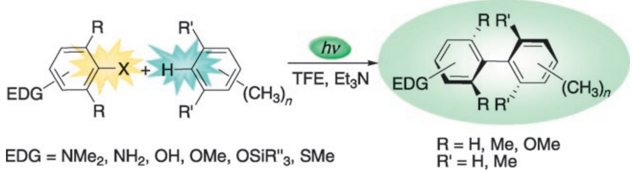


Pd ploy to isoxazolidines: Carboetherification reactions of *N*-butenylhydroxylamines with aryl bromides afford substituted isoxazolidines in good yield with up to > 20:1 d.r. These transformations provide a new strategy for the construction of isoxazolidines and allow for the synthesis of isoxazolidine stereoisomers that cannot be prepared with existing methods.

Photochemical Synthesis

V. Dichiarante, M. Fagnoni,*
A. Albini **6495 – 6498**

Metal-Free Synthesis of Sterically Crowded Biphenyls by Direct Ar–H Substitution in Alkyl Benzenes



Four's definitely a crowd: The chemoselective activation of Ar–H bonds in methylbenzenes by treatment with photogenerated phenyl cations allowed the synthesis of sterically crowded biphenyl compounds, including tetra-*ortho*-substituted biphenyls, by intermolecular cross-coupling (see scheme). This method is an appealing metal-free alternative to widely used transition-metal catalysis. TFE = 2,2,2-trifluoroethanol.

Gas Complexes

A. G. Grechin, H.-J. Buschmann,*
E. Schollmeyer **6499 – 6501**

Supramolecular Solid–Gas Complexes: A Thermodynamic Approach

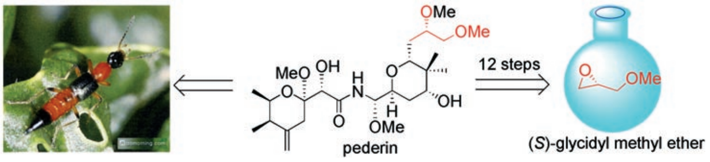
$$\begin{tikzcd} \text{Host}_{(\text{solid})} \arrow[d, "\Delta Y_s(\text{Host})"] & + & \text{Guest}_{(\text{gas})} \arrow[d, "\Delta Y_s(\text{Guest})"] & \Leftrightarrow & \text{Complex}_{(\text{solid})} \arrow[d, "\Delta Y_s(\text{Complex})"] \\ \text{Host}_{(\text{aq})} & + & \text{Guest}_{(\text{aq})} & \Leftrightarrow & \text{Complex}_{(\text{aq})} \end{tikzcd}$$

Phasing up to complex problems: A thermodynamic approach based on solution data has been proposed for the determination of the stability of gas complexes and elucidation of the selectivity of gas binding. Stability constants, reaction enthalpies, and entropies for the complexation of gaseous guests (*n*-alkylamines) by solid macrocyclic hosts (β-cyclodextrin, cucurbit[6]uril) were calculated by using the Born–Haber type cycle (see picture).

Natural Products

J. C. Jewett, V. H. Rawal* **6502 – 6504**

Total Synthesis of Pederin



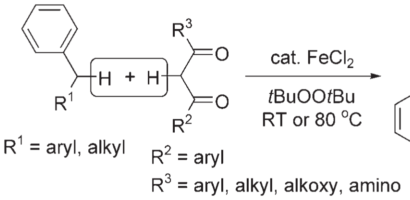
Blisteringly fast: The potent cytotoxic blistering agent pederin has been synthesized (see scheme). The synthesis is diastereoselective and concise (just 12 steps for the longest linear sequence), and features a formal hetero-Diels–Alder reaction of a hindered diene, a Mukaiyama–Michael reaction to set two additional stereocenters, and a Curtius rearrangement to stereospecifically introduce the aminal functionality.

Contents

C–C Bond Formation

Z. Li,* L. Cao, C.-J. Li* ______ **6505 – 6507**

FeCl$_2$-Catalyzed Selective C–C Bond Formation by Oxidative Activation of a Benzylic C–H Bond



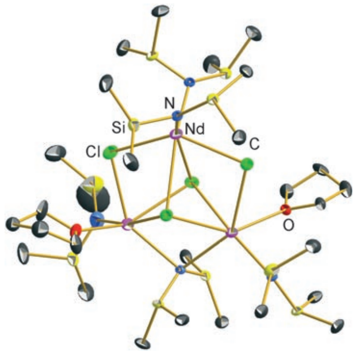
Any old iron: Readily available and nontoxic FeCl$_2$ effectively catalyzes C–C bond formation by oxidative activation of benzylic C–H bonds in the presence of *tert*-butyl peroxide as a stoichiometric oxidant (see scheme). The mild reaction conditions, good yields, low catalyst cost, and easy operation are the major advantages of this cross-dehydrogenation coupling reaction.

Polymerization Catalysts

C. Meermann, K. W. Törnroos, W. Nerdal, R. Anwander* ______ **6508 – 6513**

Rare-Earth Metal Mixed Chloro/Methyl Compounds: Heterogeneous–Homogeneous Borderline Catalysts in 1,3-Diene Polymerization

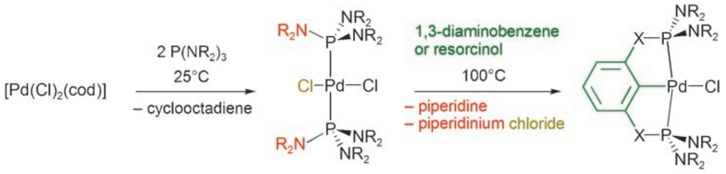
On the right path: A chlorination–alkylation sequence involving the reaction of preformed mixed amido/chloro complexes (see structure) with trimethylaluminum causes precipitation of $[\{Ln_aAl_bMe_cCl_d\}_n]$, which for Ln = Nd polymerizes isoprene in greater than 99% *cis* stereospecificity ($M_n/M_w = 1.76$); the catalyst performance is comparable to that observed following a "detour" alkylation–chlorination sequence employing $[Nd(AlMe_4)_3]/Et_2AlCl$.



C–C coupling

J. L. Bolliger, O. Blacque, C. M. Frech* ______ **6514 – 6517**

Short, Facile, and High-Yielding Synthesis of Extremely Efficient Pincer-Type Suzuki Catalysts Bearing Aminophosphine Substituents

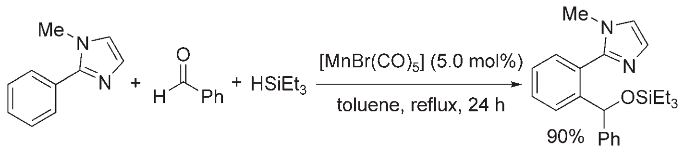


Feeling the pinch: Aryl bromides can be coupled with phenylboronic acid quantitatively within a few minutes by using pincer-type catalysts bearing aminophosphine substituents. $[Pd(Cl)_2P(NR_2)_3]$ has been used as a template for the pincer core directly on the metal center (see scheme, NR$_2$ = piperidinyl, X = NH or O), which makes the independent synthesis and purification of the air- and moisture-sensitive ligand systems unnecessary.

C–H Activation

Y. Kuninobu,* Y. Nishina, T. Takeuchi, K. Takai* ______ **6518 – 6520**

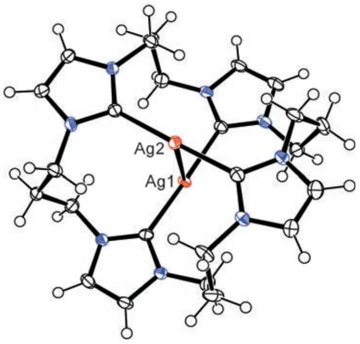
Manganese-Catalyzed Insertion of Aldehydes into a C–H Bond



Mn gets in the game: In the presence of a manganese catalyst and a stoichiometric amount of hydrosilane, aldehydes insert into C–H bonds of aromatic rings of compounds with directing groups (see scheme). This first example of a manganese-catalyzed chemical transformation through C–H bond activation gives silyl ethers in good to excellent yields and can also be applied to asymmetric transformation.

Cheap and safe: An iron-catalyzed cross-coupling reaction between alkyl halides and alkenyl Grignard reagents is described. This C–C bond coupling reaction is promoted by the cheap and nontoxic $FeCl_3$ and displays good tolerance against various functional groups.

Homogeneous Catalysis



Two ways about it: The first metal N-heterocyclic carbene complexes derived from a cyclic tetraimidazolium salt show a remarkable versatility of ligand conformation and coordination geometry. With Pd^{II}, a mononuclear square-planar complex is obtained, but with Cu^{I} and Ag^{I}, an unprecedented dinuclear motif with a short metal–metal interaction is observed (see structure; N blue, C white ellipsoids, H white circles).

Macrocyclic Carbene Ligands

Fluorine makes the difference: FIBX (see structure), the tetrafluoro derivative of the hypervalent iodine reagent, is more soluble and has higher reactivity than its nonfluorinated counterpart. An efficient synthesis of FIBX and initial reactions are presented. Some of these reactions can be conducted in standard organic solvents. Owing to the increased reactivity, new transformations and catalytic reactions may be possible.

FIBX

Hypervalent Compounds

$$Me_3MPPh_2 \;+\; RX \xrightarrow[\text{2) } H_2O_2]{\text{1) radical initiator}} RP(O)Ph_2$$

57-94%

A transition-metal-free radical phosphonation using Me_3SnPPh_2 and the less toxic Me_3SiPPh_2 is reported. These readily available reagents react highly efficiently with primary and secondary alkyl radicals. Moreover, aryl radicals and tertiary alkyl radicals are phosphonated with Me_3SnPPh_2 (see scheme; R = aryl, alkyl, vinyl; X = I, Br, OC(S)imidazolyl). DFT calculations provide insights into the mechanism of the reaction.

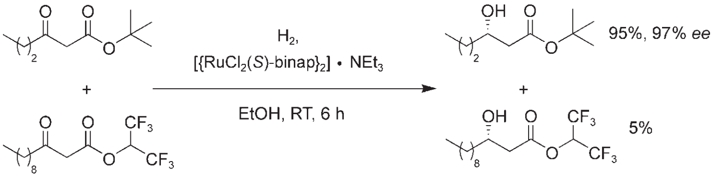
Synthetic Methods

Contents

Asymmetric Catalysis

R. Kramer, R. Brückner* ____ **6537 – 6541**

Discrimination of β-Ketoesters by Ruthenium(II)–Binap-Catalyzed Asymmetric Hydrogenation

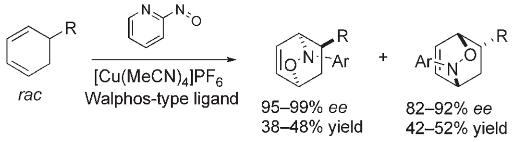


Please, after you... β-Ketoesters in mixtures underwent Noyori reduction one by one at room temperature under 4 bar of hydrogen pressure in the presence of a catalyst formed from Ru^{II} and (*S*)-binap (see example). The rate of the asymmetric hydrogenation and hence the selectivity for a particular β-ketoester was found to depend on the Lewis basicity of the ester group. Binap = 2,2′-bis(diphenylphosphanyl)-1,1′-binaphthyl.

Asymmetric Catalysis

C. K. Jana, A. Studer* ______ **6542 – 6544**

Divergent Reactions for Racemates: Catalytic, Enantioselective, and Regiodivergent Nitroso Diels–Alder Reactions



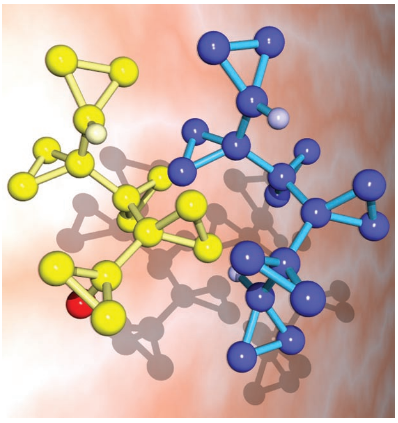
Two products out of eight possible isomers are obtained from the [CuPF$_6$-(MeCN)$_4$]-catalyzed, highly enantioselective, and regiodivergent nitroso Diels–Alder reactions of 6-substituted 1,3-cyclohexadienes (see scheme; R = phenyl, alkyl; Ar = 2-pyridyl). These divergent reactions of racemic cyclohexadienes deliver valuable compounds for the synthesis of biologically interesting carbasugars. In a first application peracetylated 2-*epi*-validamine was synthesized.

Oligocyclopropanols

T. Kurahashi, S. I. Kozhushkov, H. Schill, K. Meindl, S. Rühl, A. de Meijere* ____________ **6545 – 6548**

1,1′-Linked Cyclopropane Derivatives: The Helical Conformation of Quinquecyclopropanol

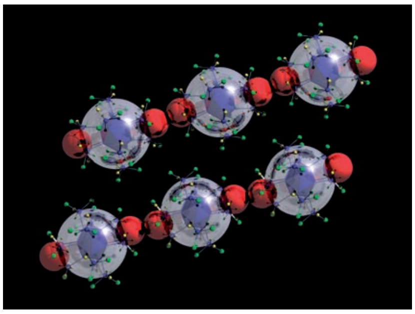
In a twist: 1,1′-Linked oligocyclopropanols have been obtained by an iterated reaction of a cyclopropaneboronate with in situ generated lithium bromocyclopropylidenoid and subsequent oxidation. As predicted by DFT computations for sexicyclopropane (shown in blue) in the gas phase, the quinquecyclopropane unit in the 3,5-dinitrobenzoate of quinquecyclopropanol (yellow, dinitrobenzoyl group omitted for clarity) adopts a helical conformation in the crystal.



Gallium Clusters

J. Hartig, F. Klöwer, J. Rinck, A.-N. Unterreiner, H. Schnöckel* ____________ **6549 – 6552**

Ga$_{24}$Br$_{18}$Se$_2$: A Highly Symmetrical Metalloid Cluster and Its One-Dimensional Arrangement in the Crystalline State as a Model for the Photoconductivity of Solid GaSe



Cluster on cluster: [Ga$_{12}$Ga$_{12}$(Br$_{18}$Se$_2$)]·12 THF units with a platonic polyhedral substructure are ordered through the crystal in straight lines by Se–Se contacts in an arrangement resembling superatoms (see picture). According to topological, spectroscopic, and energetic findings, these chains of clusters can be interpreted as a model for the lattice structure of photoconducting GaSe.

Supporting information is available on the WWW (see article for access details).

A video clip is available as Supporting Information on the WWW (see article for access details).

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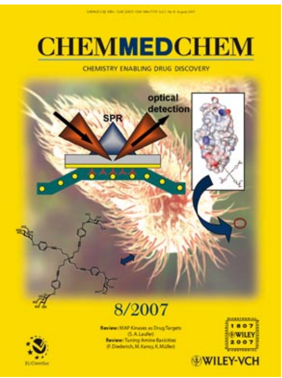

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