WENDER GROUP
LITERATURE REVIEW

Volume 39 / Issue 10   15 October 2014

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Next Due Date: November 17th 2014

Instructions for Authors (*Volume 39)*

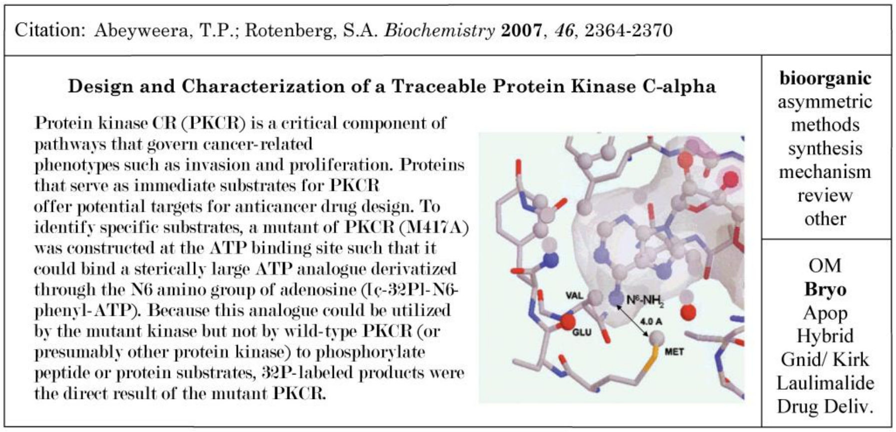
Identify articles to abstract in the journals you have been assigned. Try to pick things that the group (or specific subgroups) would like to read or should be aware of. This does not need to be limited to chemistry! If you encounter interesting pieces of media elsewhere (The Economist being a recent example) don't hesitate to let the group know. If you are splitting a journal with another group member, talk with him/her to be sure you are not reviewing redundantly. If you are not able to cover your journal for some reason, get someone to cover it for you—as if it were your group job.

Create an Abstract

Abstract submissions are usually prepared using ChemDraw. The editors of the *Lit Review* strongly encourage the copying of graphical material from PDF files and wish to point out the following. Graphics stored in PDF files are typically of postscript or >300 dpi quality. When an image is copied into a ChemDraw document, a screen snapshot is taken, and the image is captured at the present screen resolution. If the PDF file is being viewed zoomed-in, this typically results in the transfer of a high quality image. If the PDF is being viewed zoomed-out, a low quality image typically results. Text can be copied from a PDF file and pasted as text using the text select or column select tool. Once pasted, this text behaves as if it were input from the keyboard.

Include a brief textual summary of the article; an example of a completed abstract is shown below. The list of topics and subgroups on the right is useful to highlight which subgroups should pay attention to your abstract and roughly what kind of chemistry the article contains.

Please email the files to sryckbos@stanford.edu. Late abstracts will be included in the Lit Review for the following month**. PCs please send .pdf and macs please send .cdx files.**



Citation: Abeyweera, T.P.; Rotenberg, S.A. *Biochemistry* **2007**, *46*, 2364-2370

Design and Characterization of a Traceable Protein Kinase C-alpha

Protein kinase CR (PKCR) is a critical component of pathways that govern cancer-related phenotypes such as invasion and proliferation. Proteins that serve as immediate substrates for PKCR offer potential targets for anticancer drug design. To identify specific substrates, a mutant of PKCR (M417A) was constructed at the ATP binding site such that it could bind a sterically large ATP analogue derivatized through the N6 amino group of adenosine (Iç-32PI-N6-phenyl-ATP). Because this analogue could be utilized by the mutant kinase but not by wild-type PKCR (or presumably other protein kinase) to phosphorylate peptide or protein substrates, 32P-labeled products were the direct result of the mutant PKCR.

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Citation: Dictionary.com (search term = "mook")	
For those of you who always wanted to know what it meant.... **mook** **Pronunciation Key** (mk) *n. Slang* An insignificant or contemptible person.	***methods*** synthesis

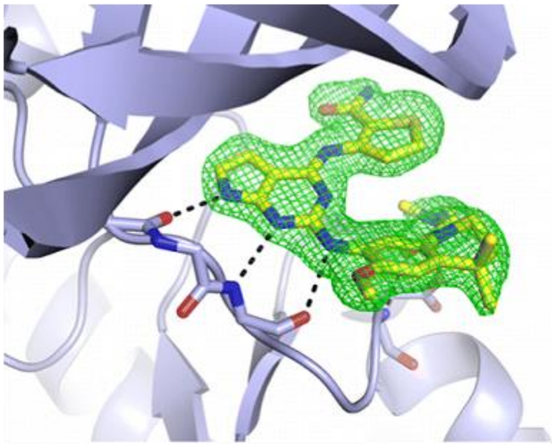
DON'T BE A MOOK!

Lit Review MOOKS include those who:
- fail to submit their abstracts in a timely fashion (or at all), or
- claim there was nothing to abstract in *JACS*, *JOC*, *Org. Lett.*, etc.

Penalties for being a Lit Review MOOK:
- You will get last choice when it's time to pick new journals.

Citation: Homan, K.T.; *et al. ACS Chem. Biol.* **2014,** *Article ASAP.*

Identification and Structure-Function Analysis of Subfamliy Selective G Protein-Coupled Receptor



Most of the identified compounds can be clustered into two chemical classes: indazole/dihydropyrimidine-containing compounds that are selective for GRK2 and pyrrolopyrimidine-containing compounds that potently inhibit GRK1 and GRK5 but with more modest selectivity.

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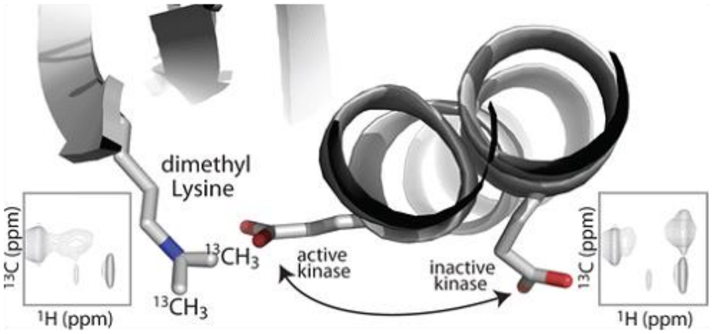
Citation: Xie, Q.; *et al. ACS Chem. Biol.* **2014,** *Article ASAP.*

A Selective NMR Probe to Monitor the Conformational Transition from Inactive to Active Kinase



The authors apply [13C] reductive methylation to chemically introduce NMR-active nuclei into unlabeled protein kinases. The results demonstrate that solution NMR spectroscopy can be used to monitor specific changes in the chemical environment of structurally important lysines in a [13C]-methylated kinase as it shifts from the inactive to active state.

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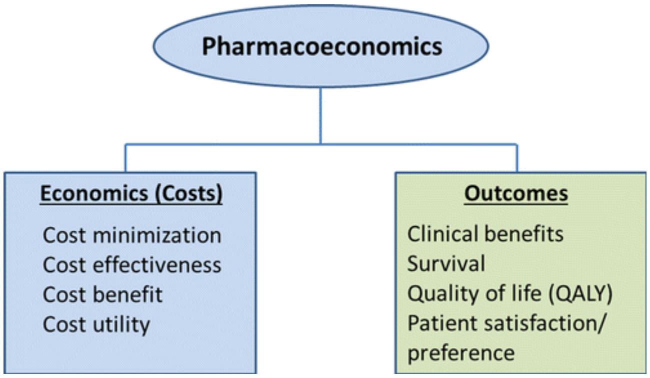
Citation: Lindsley, *ACS Med. Chem Lett.* **2014**, *5,* 1066-1068.

Pharmacoeconomics and the Medicinal Chemist



Pharmacoeconomics is a rational, scientific approach to compare the value (in terms of both cost and patient outcome) of one medication or drug therapy regimen to another. The impact of this new approach on both the practicing medicinal chemist and broader drug discovery efforts is considered.

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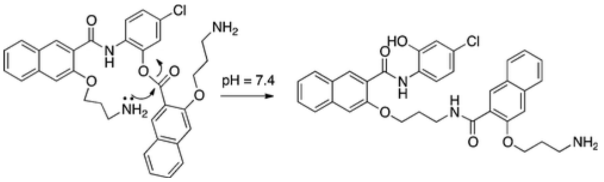
Citation: Li, *et al. ACS Med. Chem Lett.* **2014**, *5*, 1104-1109.

Novel Type of Prodrug Activation through a Long-Range O,N-Acyl Transfer: A Case of Water-Soluble CREB Inhibitor



A water-soluble inhibitor of CREB-mediated gene transcription with in vivo anticancer activity. Unexpectedly, it was found to be a prodrug of compound 12 necessitating an unprecedented long-range O,N-acyl transfer. The rate of this transfer was pH- and temperature-dependent. To the best of our knowledge, this is the first time to show that a long-range O,N-acyl transfer could be exploited as a prodrug activation strategy to improve aqueous solubility. This type of prodrug may be applicable to other structures with spatially arranged hydroxyl amide to improve their aqueous solubility.

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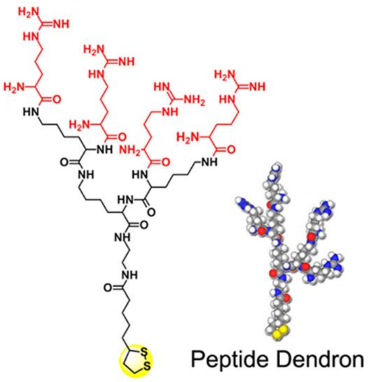
Citation: Xu, X.; Jian, Y.; Li, Y.; Zhang, X.; Tu, Z.; Gu, Z. ACS Nano, 8, 9255–9264 (2014)

Bio-Inspired Supramolecular Hybrid Dendrimers Self-Assembled from Low-Generation Peptide Dendrons for Highly Efficient Gene Delivery

A bio-inspired strategy to develop a supramolecular dendritic system as an analytical and delivery platform is described. This strategy provides a novel supramolecular hybrid dendrimer with well-defined, hierarchical, and stable nanostructure via coordination interactions. This supramolecular strategy self-assembles low-generation PDs, generating highly efficient gene delivery efficiency in vitro and in vivo owing to the arginine-rich surface of the dendritic peptide coronas mimicking viral capsids. This hybrid strategy gives some unique features to SHDs for intracellular tracking, protein expression monitoring, and in vivo bioimaging, which contribute to the comprehensive understanding of gene delivery pathways and the improvement of delivery systems.



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Citation: Eetezadi, S.; *et al. Adv. Drug Deliv. Rev.* **2014,** *In Press.*

The challenges facing block copolymer micelles for cancer therapy: *in vivo* barriers and clinical translation

The application of block copolymer micelles (BCMs) in oncology has benefitted from advances in polymer chemistry, drug formulation and delivery as well as in vitro and in vivo biological models. While great strides have been made in each of these individual areas, there remains some disappointment overall, citing, in particular, the absence of more BCM formulations in clinical evaluation and practice. In this review, the barriers posed by systemic administration and tumor properties are examined. The impact of critical features, such as the size, stability and functionalization of BCMs is discussed, while key pre-clinical endpoints and models are critiqued.

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Citation: Dai, X.; *et al. Adv. Drug Deliv. Rev.* **2014,** *In Press.*

Combination of microRNA therapeutics with small-molecule anticancer drugs: Mechanism of action and co-delivery nanocarriers

MicroRNAs (miRNAs) regulate multiple molecular pathways vital for the hallmarks of cancer with a high degree of biochemical specificity and potency. By restoring tumor suppressive miRNAs or ablating oncomiRs, miRNA-based therapies can sensitize cancer cells to conventional cytotoxins and the molecularly targeted drugs by promoting apoptosis and autophagy, reverting epithelial-to-mesenchymal transition, suppressing tumor angiogenesis, and downregulating efflux transporters. The development of miRNA-based therapeutics in combination with small-molecule anticancer drugs provides an unprecedented opportunity to counteract chemoresistance and improve treatment outcome in a broad range of human cancers. This review summarizes the mechanisms and advantages for the combination therapies involving miRNAs and small-molecule drugs, as well as the recent advances in the co-delivery nanocarriers for these agents.

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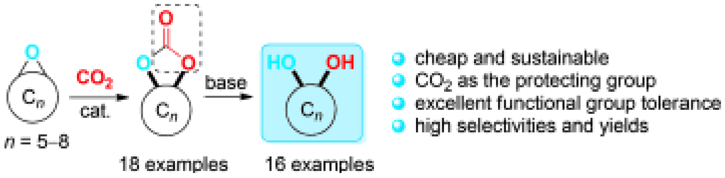
Citation: Kleij, A.; et al. *Angew. Chem. Int. Ed*. **2014**, *53 (39)*, 10416-10419.

Carbon Dioxide as a Protecting Group: Highly Efficient and Selective Catalytic Access to Cyclic cis-Diol Scaffolds

Aminotriphenolate complexes of FeIII and AlIII are highly efficient and selective catalysts for the conversion of functional (multi)cyclic oxiranes into the corresponding cis carbonates. Basic hydrolysis of the latter provides a series of useful cyclic cis-diol scaffolds in high yield. In this process, CO2 acts as both a temporary protecting group and an oxygen donor.



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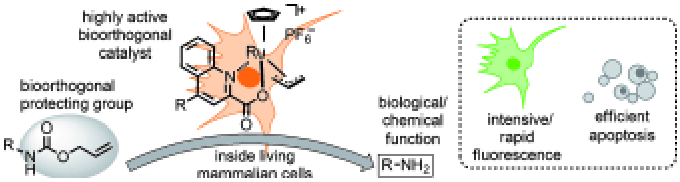
Citation: Meggers, E.; et al. *Angew. Chem. Int. Ed*. **2014**, *53 (39)*, 10536-10540.

Progress towards Bioorthogonal Catalysis with Organometallic Compounds

Organometallic ruthenium complexes have been developed for bioorthogonal catalysis under biologically relevant conditions as well as inside living mammalian cells. The catalysts activate allyl carbamate protected amines with unprecedented high catalytic activity. A fluorescence probe and a caged anticancer drug were efficiently activated within the cellular cytoplasm.



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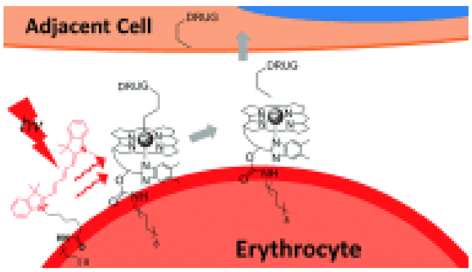
Citation: Lawrence, D.; et al. *Angew. Chem. Int. Ed.* **2014**, *53 (41)*, 10945-10948.

Cell-Mediated Assembly of Phototherapeutics

A wavelength-encoded drug-delivery strategy operates within the optical window of tissue. The photoresponsive system is acquired by the assembly of lipid-cobalamin-drug and lipid-fluorophore constructs on the surface of erythrocytes. The desired wavelength of cobalamin-drug photocleavage is “dialed-in” by simply choosing the appropriate lipid-fluorophore “antenna”.



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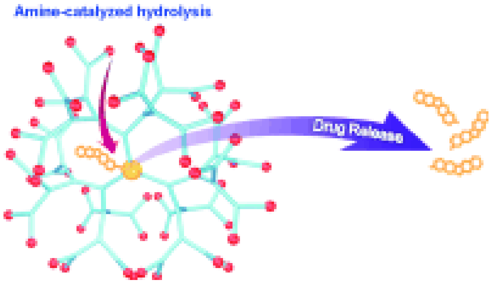
Citation: Murdoch, W.; et al. *Angew. Chem. Int. Ed.* **2014**, *53 (41)*, 10949-10955.

Molecularly Precise Dendrimer–Drug Conjugates with Tunable Drug Release for Cancer Therapy

Polylysine dendrimers with the conjugated drug in the core were synthesized for cancer therapy. The release rates of the camptothecine conjugates were easily tunable by adjusting the dendrimer generation and the peripheral functional groups as well as the pH. Conjugates showing a fast drug release also exhibited a high anticancer activity against intraperitoneal and subcutaneous tumors.



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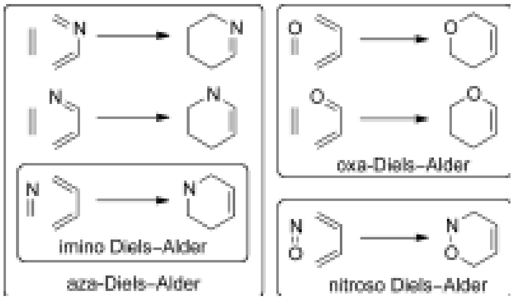
Citation: Waldmann, H.; et al. *Angew. Chem. Int. Ed.* **2014**, *53 (42)*, 11146-11157.

The Asymmetric Hetero-Diels–Alder Reaction in the Syntheses of Biologically Relevant Compounds

The hetero-Diels–Alder reaction is a powerful method for constructing six-membered aza- and oxa-ring systems. This Minireview provides an overview of the application of this reaction in the synthesis of natural products and other biologically relevant small molecules.



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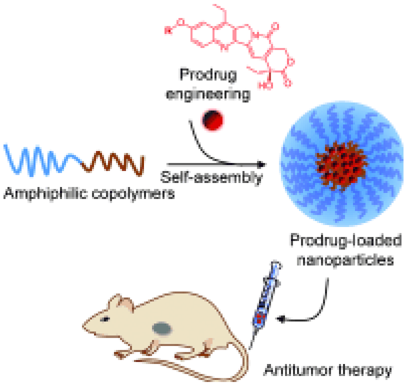
Citation: Zheng, S.; et al. *Angew. Chem. Int. Ed.* **2014**, *53 (43)*, 11532-11537.

Structure-Based Rational Design of Prodrugs To Enable Their Combination with Polymeric Nanoparticle Delivery Platforms for Enhanced Antitumor Efficacy

Lipophilicity enhancement of a chemotherapeutic agent was achieved by the introduction of a variety of hydrophobic moieties. This allows the self-assembly of the generated prodrugs with block copolymers into amphiphilic polymeric nanoparticles, which exhibited excellent antitumor activity compared to a clinically approved prodrug in a colorectal tumor xenograft model



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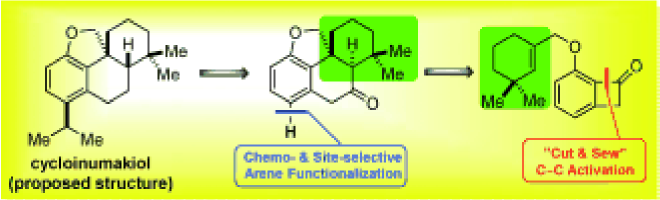
Citation: Dong, G.; et al. *Angew. Chem. Int. Ed.* **2014**, *53 (40)*, 10733-10736.

Coupling of Sterically Hindered Trisubstituted Olefins and Benzocyclobutenones by C-C Activation: Total Synthesis and Structural Revision of Cycloinumakiol

The first total synthesis of the proposed structure of cycloinumakiol has been achieved by rhodium catalysis. In the key step, the coupling of a trisubstituted olefin with a benzocyclobutenone through C-C activation yields the tetracyclic core skeleton. Comparison of the synthetic product to natural cycloinumakiol revealed a misassignment, and the natural compound was unambiguously identified as 19-hydroxytotarol.



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Citation: Joubran, S., et al. *Bioconjugate Chem*. **2014**, 25, 1644-1654

Optimization of Liganded Polyethylenimine Polyethylene Glycol Vector for Nucleic Acid Delivery

Delivery of nucleic acid molecules to cells is a powerful therapeutic approach. There is thus always a need for better, cheaper delivery vehicles for therapeautic DNA or RNA. The authors report the synthesis and characterization of PEGylated linear polyethlyenimine copolymers. They then established they these polymers could be selectively delivered to target cells by conjugating them to antibodies. *In vitro* experiments revealed that these copolymers delivered attached DNA cargo both selectively and effectively.

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Citation: Zhang, X., et al. *Bioconjugate Chem*. **2014**, 25, 1689-1696

Reduction-Sensitive Dual Function Nanomicelles for Improved Delivery of Paclitaxel

Targeted delivery of antitumor agents such as paclitaxel remains a vastly important goal in the fields of chemistry and biology. The authors here report the synthesis of a hydrophilic polyethylene glycol nanocarrier coupled to a Ras antagonist for selective delivery of paclitaxel to tumor cells. Coupling of these two moeites was accomplished via a reduction-sensitive disulfide linker, allowing release of the drug in cells. *In vivo* and *in vitro* experiments demonstrated that this disulfide linked complex demonstrated a higher level of cytotoxicity towards tumor cells than previous complexes lacking disulfide linkers. Importantly, micelles loaded with this nanocarrier system showed higher antitumor activity than the marketed drug Taxol or previous paclitaxel nanocarrier systems lacking disulfide linkers.

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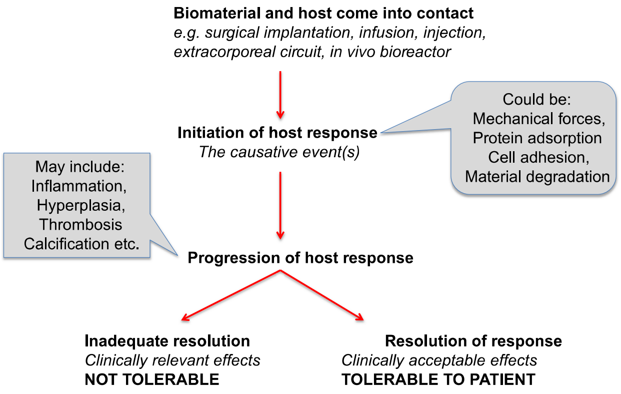
Citation: Biomaterials 2014, 35, 10009–10014.

There Is No Such Thing as a Biocompatible Material



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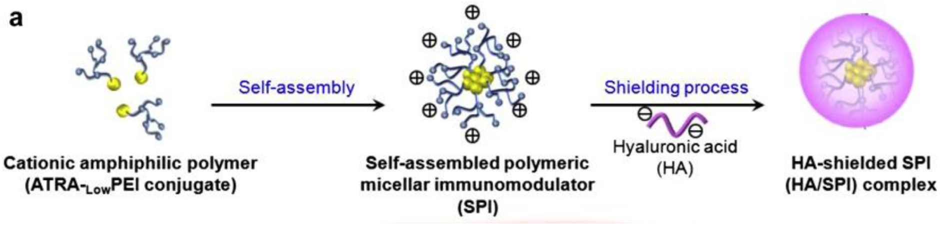
Citation: Biomaterials 2014, 35, 9912–9919.

A Self-Assembled Polymeric Micellar Immunomodulator for Cancer Treatment Based on Cationic Amphiphilic Polymers.



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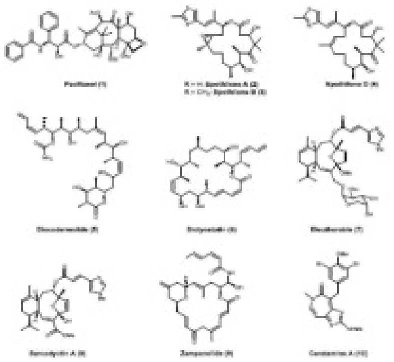
Citation: Brunden, K. R.; et al. *Bioorg. Med. Chem.*, 22, (2014) 5040-5049

Microtubule-stabilizing agents as potential therapeutics for neurodegenerative disease



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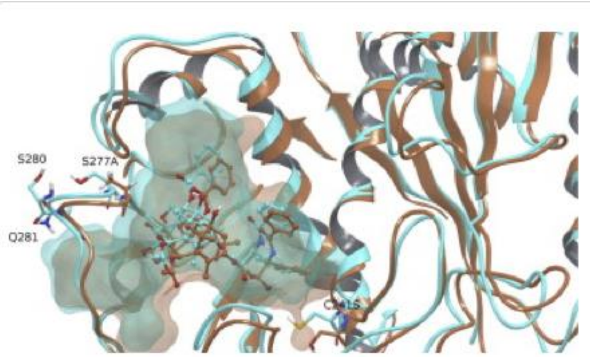
Citation: Matesanz, R. et al, *Bioorg. Med. Chem.*, 22, (2014) 5078-5090

Taxanes with high potency inducing tubulin assembly overcome tumoural cell resistances



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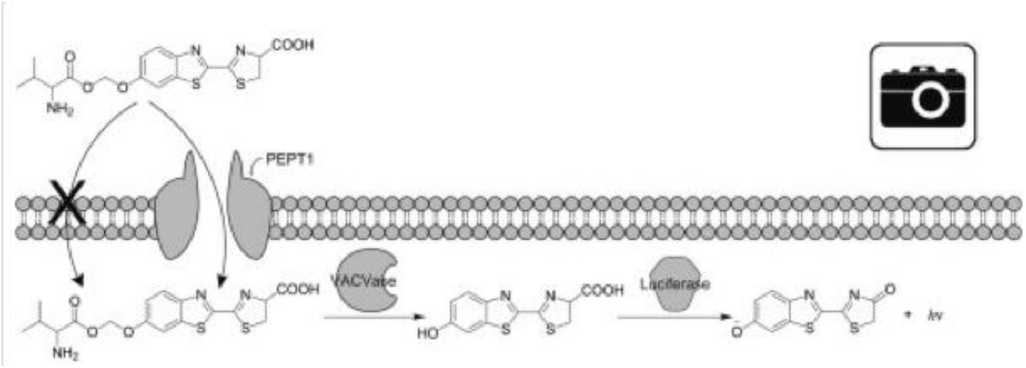
Citation:Walls, Z. F.; et al. *Bioorg. Med. Chem.*, 22, (2014) 4871-4873

Synthesis and characterization of valyloxy methoxy luciferin for the detection of valacyclovirase and peptide transporter



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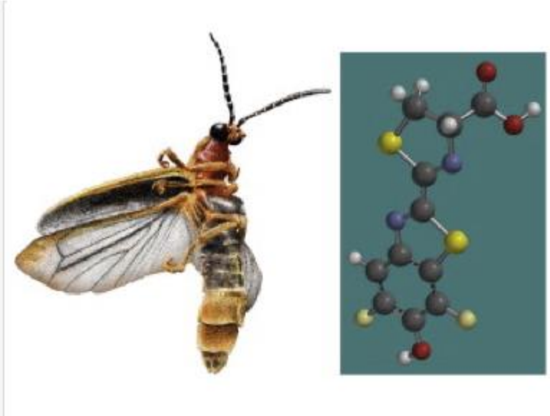
Citation: Pirrung, M. C.; et al. *Bioorg. Med. Chem. Lett.*, 24, (2014) 4881-4883

Synthesis and bioluminescence of difluoroluciferin



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Citation: Yuan, Y.; *et al. Chem. Commun.* **2014**, *50,* 11465.

Targeted theranostic prodrugs based on an aggregation-induced emission (AIE) luminogen for real-time dual-drug tracking

A targeted theranostic delivery system containing two prodrugs with drug tracking and activation monitoring functions was developed for visualizing cancer cell ablation with synergistic anticancer effects.

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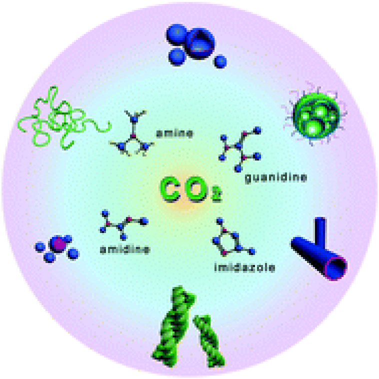
Citation: Yan, Q., Zhao, Y. *Chem. Commun.* **2014**, *50,* 11631.

Block copolymer self-assembly controlled by the "green" gas stimulus of carbon dioxide



The authors review the recent development of using carbon dioxide (CO2) as a stimulus for tuning or controlling block copolymer (BCP) self-assembly and show that a series of CO2-responsive functionalities can easily be incorporated into BCP structures, and that rationally designed BCPs can have their self-assembled structures undergo drastic changes in size, shape, morphology and function, controlled by the amount of CO2 in aqueous solution.

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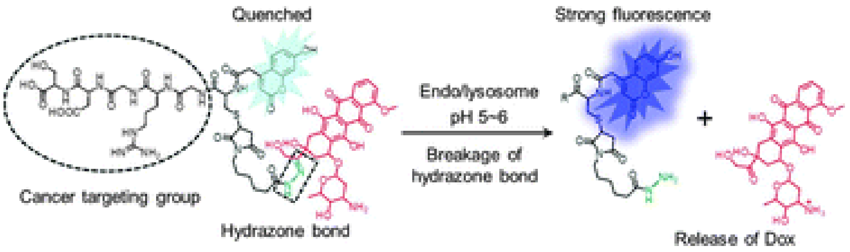
Citation: Li, S.-Y.; *et al. Chem. Commun.* **2014**, *50,* 11852.

A pH-responsive prodrug for real-time drug release monitoring and targeted cancer therapy



A novel cancer targeting and pH-responsive prodrug was successfully designed and synthesized. This M-prodrug was demonstrated to have real-time drug release monitoring capability based on the concept of contact-mediated quenching between doxorubicin and a coumarin derivative.

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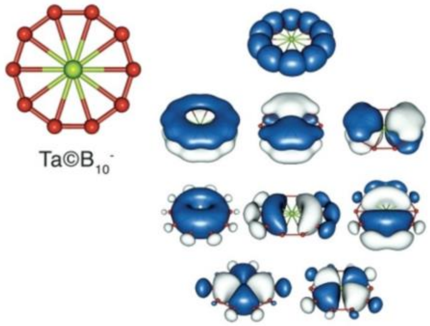
Citation: Ritter, S. *C&EN.* **2014**, 92(38), 10-13.

Pushing The Limits Of Chemical Bonding



Conference highlights how computational and experimental chemists are applying bonding models to more complex systems

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Citation: Wolf, L. *C&EN.* **2014**, 92(38), 28-30.

A Taste Of Wine Science

Researchers zero in on flavor molecules, ponder ways to control them during production

bioorganic
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synthesis
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other

OM
Bryo
DDO
Hybrid
Drug Deliv.
Prostratin

Citation: Jarvis, L. *C&EN.* **2014**, 92(40), 12-19.

The Immune System Fights Back

Reprogrammed T cells show promise at beating blood cancers, but other foes may be tougher to vanquish

bioorganic
methods
synthesis
mechanism
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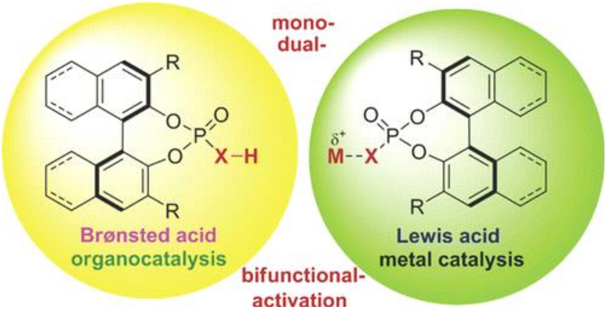
other

OM
Bryo
DDO
Hybrid
Drug Deliv.
Prostratin

Citation: Parmar, D.; Sugiono, E.; Raja, S.; Rueping,M.* Chem. Rev., 2014, 114 (18), pp 9047–9153

Complete Field Guide to Asymmetric BINOL-Phosphate Derived Brønsted Acid and Metal Catalysis: History and Classification by Mode of Activation; Brønsted Acidity, Hydrogen Bonding, Ion Pairing, and Metal Phosphates



bioorganic
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Prostratin

Citation: Pradere, U.; Garnier-Amblard, E.C.; Coats, S.J.; Amblard, F.; Schinazi, R.F.* Chem. Rev., 2014, 114 (18), pp 9154–9218

Synthesis of Nucleoside Phosphate and Phosphonate Prodrugs

bioorganic
methods
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OM
Bryo
Gnid/Kirk
Hybrid
Drug Deliv.
Prostratin

Citation: Sun, C-L.; Shi, Z-J.* Chem. Rev., 2014, 114 (18), pp 9219–9280

Transition-Metal-Free Coupling Reactions

2. Classification of Transition-Metal-Free Cross-Coupling Reactions
3. Base-Promoted HAS-Type Coupling Reactions
4. Transition-Metal-Free Cross-Coupling of Grignard Reagents
5. Transition-Metal-Free Oxidative Coupling Reactions
6. Photochemical Coupling Reactions
7. Transition-Metal-Free Coupling Reactions Involving Aryne Intermediates

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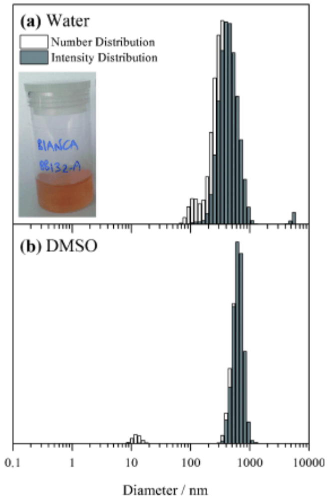
Citation: Blunden, *et al.* *Chem. Eur. J.* **2014,** 20, 12745-12749.

Drug Conjugation to Cyclic Peptide¨CPolymer Self-Assembling Nanotubes

polymeric nanotubes (NTs) based on self-assembled conjugates of polymers and cyclic peptides can be used as an efficient drug carrier. RAPTA-C, a ruthenium-based anticancer drug, was conjugated to a statistical co-polymer based on poly(2-hydroxyethyl acrylate) (pHEA) and poly(2-chloroethyl methacrylate) (pCEMA), which formed the shell of the NTs. Self-assembly into nanotubes (length 200¨C5006¤1nm) led to structures exhibiting high activity against cancer cells.



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DDO
Hybrid
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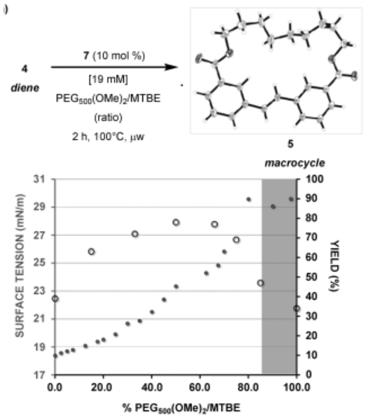
Prostratin

Citation: Raymond, *et al.* *Chem. Eur. J.* **2014,** 20, 12763-12767.

Macrocyclic Olefin Metathesis at High Concentrations by Using a Phase-Separation Strategy

a protocol to promote macrocyclic olefin metathesis, one of the most common synthetic tools used to prepare macrocycles, at relatively high concentrations (up to 606¤1mM) is described by exploitation of a phase-separation strategy. A variety of macrocyclic skeletons could be prepared having either different alkyl, aryl, or amino acids spacers.



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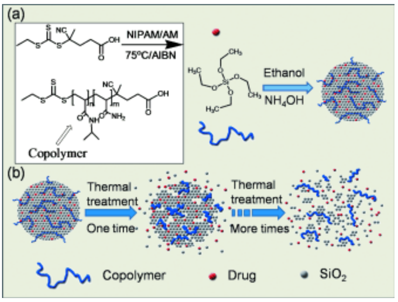
Citation: Li, *et al.* *Chem. Eur. J.* **2014,** 20, 12945-12953.

Thermoresponsive Copolymer/SiO2 Nanoparticles with Dual Functions of Thermally Controlled Drug Release and Simultaneous Carrier Decomposition

These drug carriers were fabricated by incorporation of drug molecules and thermoresponsive copolymer, poly(N-isopropylacrylamide-co-acrylamide), into silica nanoparticles in a one-pot preparation process. The enhanced drug release was primarily attributed to faster molecule diffusion resulting from the particle decomposition triggered by phase transformation of the copolymer upon the temperature change. The decomposition of the drug carriers into small fragments should benefit their fast excretion from the body. In addition, the resulting drug-loaded nanoparticles showed faster drug release in an acidic environment (pH5) than in a neutral one. The controlled drug release of methylene blue and doxorubicin hydrochloride and the self-decomposition of the drug carriers were successfully characterized by using TEM, UV/Vis spectroscopy, and confocal microscopy. Together with the nontoxicity and excellent biocompatibility of the copolymer/SiO2 composite, the features of controlled drug release and simultaneous carrier self-destruction provided a promising opportunity for designing various novel drug-delivery systems.



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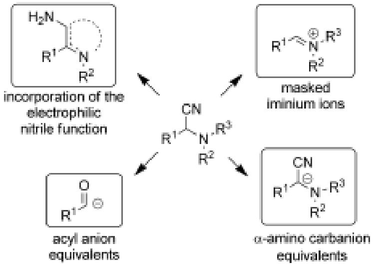
Citation: Otto, *et al. Chem. Eur. J.* **2014,** 20, 13064-13077

Heterocycles from alpha-Aminonitriles

This article focuses on synthetic methodologies using their bifunctional nature which is the basis of their reactivity as ¦Á-amino carbanions and as iminium ions. Reactions exclusively taking place on either the amine or on the nitrile moiety will not be considered.



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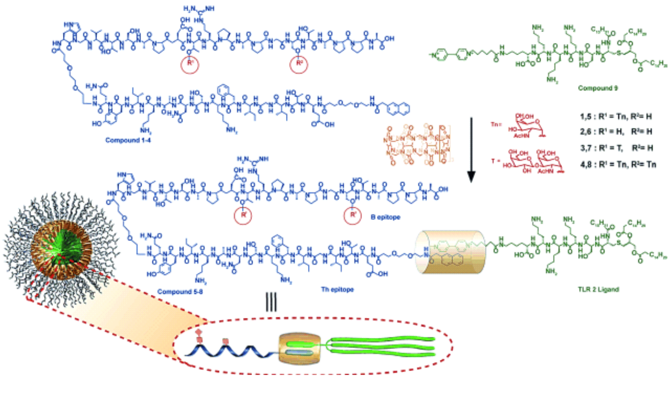
Prostratin

Citation: Gao, *et al. Chem. Eur. J.* **2014,** 20, 13541-13546.

Covalent Bond or Noncovalent Bond: A Supramolecular Strategy for the Construction of Chemically Synthesized Vaccines

A novel noncovalent strategy to construct chemically synthesized vaccines has been designed to trigger a robust immune response and to dramatically improve the efficiency of vaccine preparation. Glycosylated MUC1 tripartite vaccines were constructed through host¨Cguest interactions with cucurbit[8]uril. These vaccines elicited high levels of IgG antibodies that were recognized by transformed cells and induced the secretion of cytokines.This noncovalent strategy with good suitability, scalability, and feasibility can be applied as a universal strategy for the construction of chemically synthesized vaccines.



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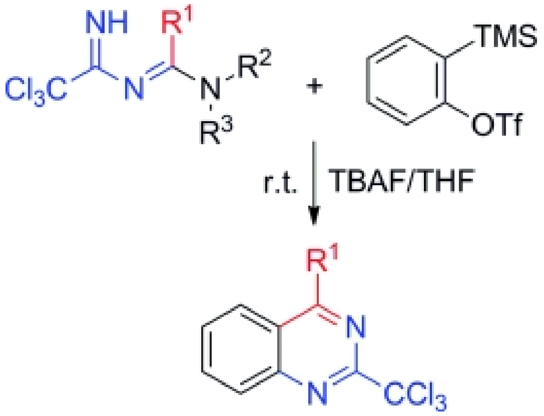
Citation: Romero-Ortega, M. et. al. *Eur. J. Org. Chem.* **2014**, 5910–5913.

Syntheses of 4-Substituted 2-(Trichloromethyl)quinazolines under Mild Conditions by Benzyne [4+2] Cycloaddition

The preparation of 4-aryl-2-(trichloromethyl)quinazolines under mild conditions by cycloaddition of benzyne with 2-(trichloromethyl)-1,3-diazabutadienes is reported. The 4-aryl-2-(trichloromethyl)-1,3-diazabutadienes are prepared by coupling of trichloroacetamidine with Vilsmeier–Haack reagents.



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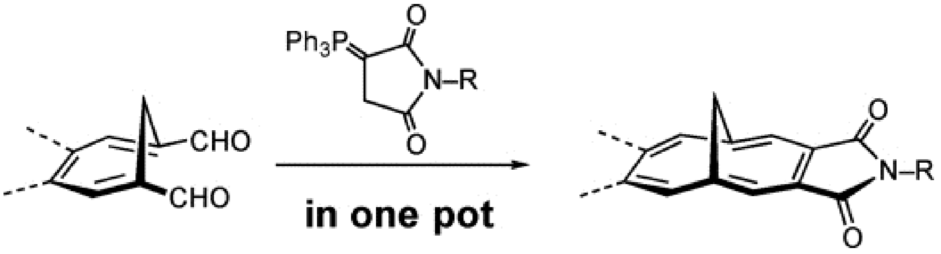
Citation: Osa, M.. et. al. *Eur. J. Org. Chem.* **2014**, 5976–5985.

A Short-Step Synthesis of 1,6-Methano[10]annulene-3,4-dicarboximides and Their Benzene-, Naphthalene-, and Thiophene-Annulated Compounds

A new one-pot procedure for 1,6-methano[10]annulene-3,4-dicarboximides and its arene-annulated compounds is developed. Cyclohepta-1,3,5-triene-1,6-dicarbaldehyde and its arene-annulated dicarbaldehyde analogs react with various phosphorane reagents to give 1,6-methano[10]annulene-3,4-dicarboximides.



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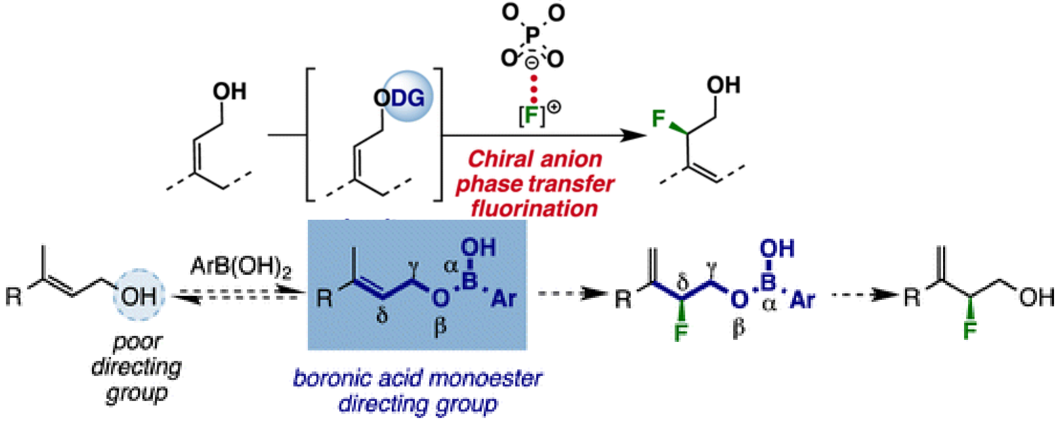
Citation: Zi, W.; Wang, Y.-M.; Toste, F.D. *J. Am. Chem. Soc.*, **2014**, *136* (37), 12864-12867.

An *In Situ* Directing Group Strategy for Chiral Anion Phase-Transfer Fluorination of Allylic Alcohols



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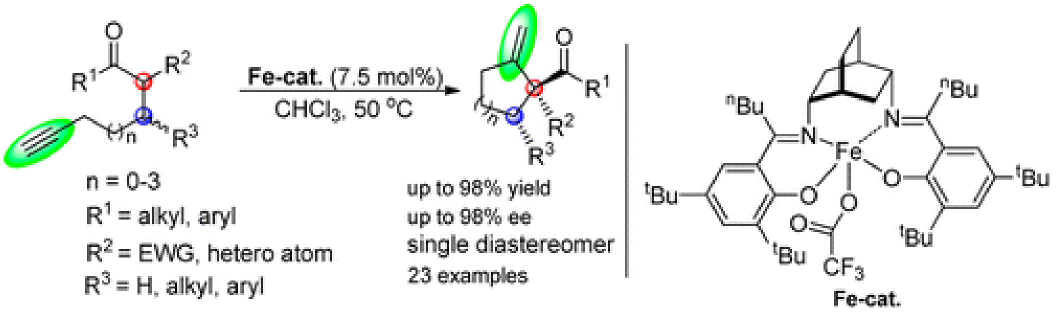
Drug Deliv.
Prostratin

Citation: Shaw, S.; White, J.D. *J. Am. Chem. Soc.*, **2014**, *136* (39), 13578-13581.

A New Iron(III)-Salen Catalyst for Enantioselective Conia-ene Carbocyclization



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Hybrid
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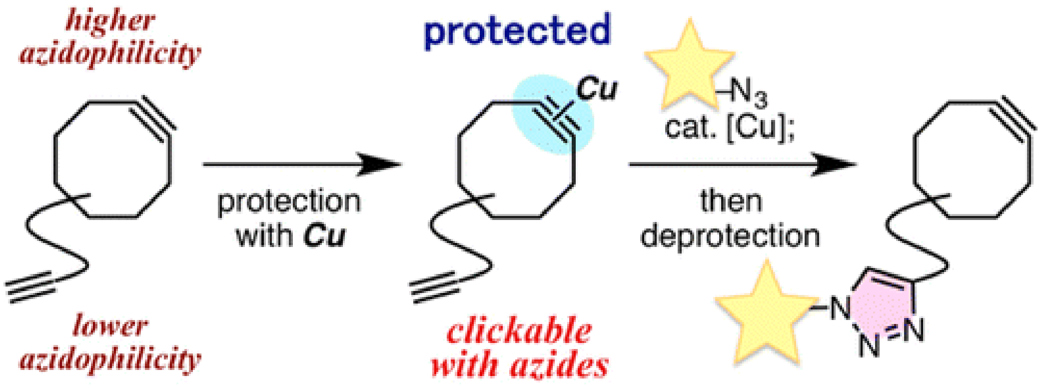
Prostratin

Citation: Yoshida, S.; Hatakeyama, Y.; Johmoto, K.; Uekusa, H.; Hosoya, T. *J. Am. Chem. Soc.*, **2014**, *136* (39), 13590-13593.

Transient Protection of Strained Alkynes from Click Reaction via Complexation with Copper



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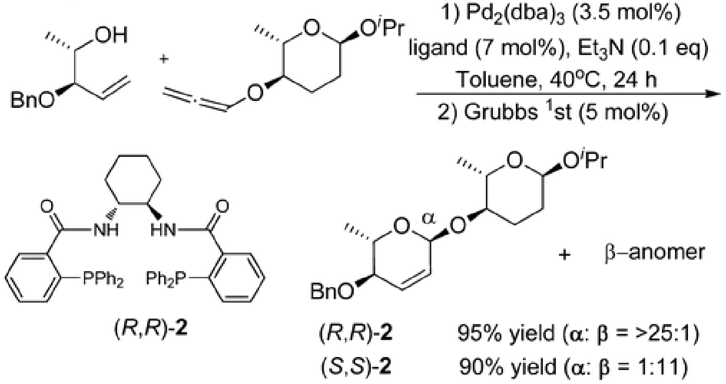
Prostratin

Citation: Lim, W.; Kim, J.; Rhee, Y.H. *J. Am. Chem. Soc.*, **2014**, *136* (39), 13618-13621.

Pd-Catalyzed Asymmetric Intermolecular Hydroalkoxylation of Allene: An Entry to Cyclic Acetals with Activating Group-Free and Flexible Anomeric Control



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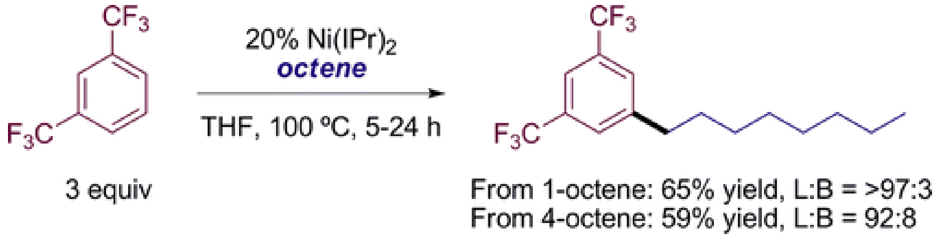
Citation: Bair, J. S. et al. J. Am. Chem. Soc., 2014, 136 (38), pp 13098–13101

Linear-Selective Hydroarylation of Unactivated Terminal and Internal Olefins with Trifluoromethyl-Substituted Arenes



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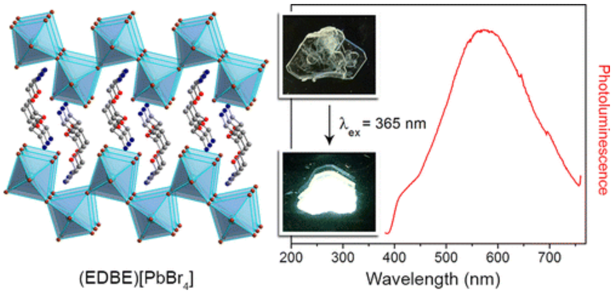
Prostratin

Citation: Dohner, E. R. et al. J. Am. Chem. Soc., 2014, 136 (38), pp 13154–13157

Intrinsic White-Light Emission from Layered Hybrid Perovskites (Congratulations to Hema's Lab!)



This study reports on the second family of layered perovskite white-light emitters with improved photoluminescence quantum efficiencies (PLQEs).These hybrids provide a tunable platform for combining the facile processability of organic materials with the structural definition of crystalline, inorganic solids.

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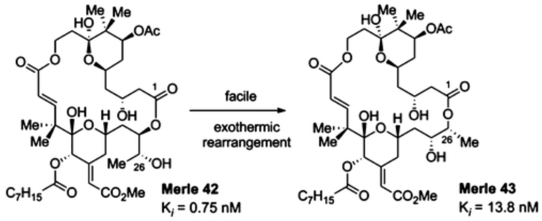
Citation: Kraft, M. B. et al. J. Am. Chem. Soc., 2014, 136 (38), pp 13202–13208

Synthesis of a des-B-Ring Bryostatin Analogue Leads to an Unexpected Ring Expansion of the Bryolactone Core



The des-B-ring bryostatin analogue was found to undergo an unexpected ring expansion of the bryolactone core to generate the corresponding 21-membered macrocycle. The parent analogue and the ring-expanded product both displayed nanomolar binding affinity for PKC. Despite containing A-ring substitution identical to that of bryostatin 1 and displaying bryostatin-like biological function, the des-B-ring analogues displayed a phorbol-like biological function in cells. These studies shed new light on the role of the bryostatin B-ring in conferring bryo-like biological function to bryostatin analogues.

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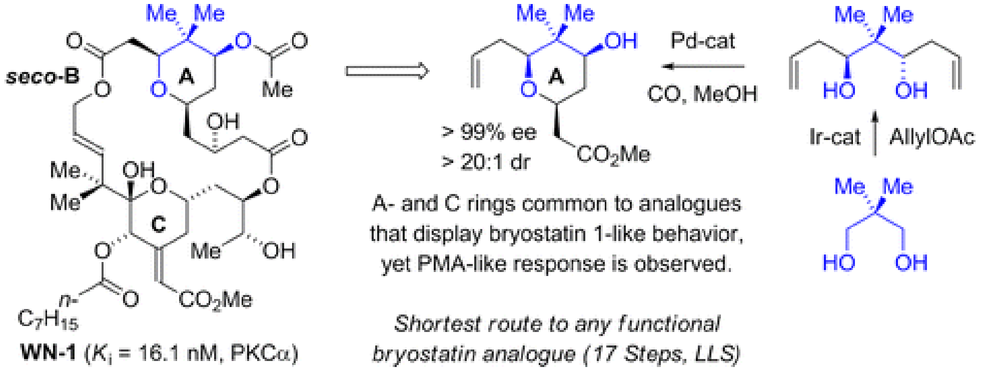
Citation: Andrews, I. P. et al. J. Am. Chem. Soc., 2014, 136 (38), pp 13209–13216

Synthesis of seco-B-Ring Bryostatin Analogue WN-1 via C–C Bond-Forming Hydrogenation: Critical Contribution of the B-Ring in Determining Bryostatin-like and Phorbol 12-Myristate 13-Acetate-like Properties



WN-1 (K_i = 16.1 nM, PKCα)

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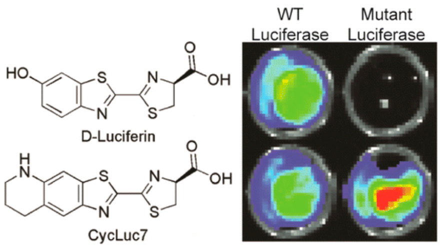
Citation: Mofford, D. M. et al. J. Am. Chem. Soc., 2014, 136 (38), pp 13277–13282

Aminoluciferins Extend Firefly Luciferase Bioluminescence into the Near-Infrared and Can Be Preferred Substrates over D-Luciferin



Firefly luciferase adenylates and oxidizes D-luciferin to chemically generate visible light and is widely used for biological assays and imaging. Here we show that both luciferase and luciferin can be reengineered to extend the scope of this light-emitting reaction. D-luciferin can be replaced by synthetic luciferin analogues that increase near-infrared photon flux >10-fold over that of D-luciferin in live luciferase-expressing cells. Firefly luciferase can be mutanted to accept and utilize rigid aminoluciferins with high activity in both live and lysed cells yet exhibit 10000-fold selectivity over the natural luciferase substrate. These new luciferin analogues thus pave the way to an extended family of bioluminescence reporters.

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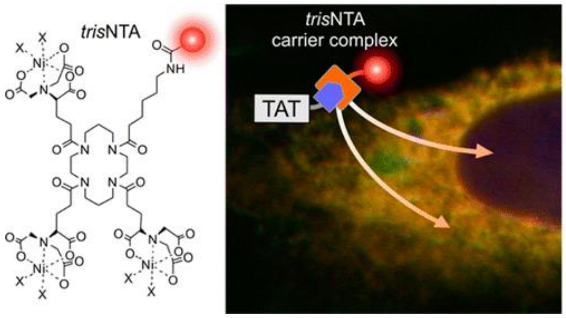
Citation: Wieneke, R. et al. J. Am. Chem. Soc., 2014, 136 (40), pp 13975–13978

Live-Cell Targeting of His-Tagged Proteins by Multivalent N-Nitrilotriacetic Acid Carrier Complexes



This study reports the site-specific, rapid, and efficient labeling of endogenous and recombinant histidine-tagged proteins in distinct subcellular compartments using cell-penetrating multivalent chelator carrier complexes. In vivo labeling was followed in real time in living cells, demonstrating a high specificity and high degree of colocalization in the crowded cellular environment.

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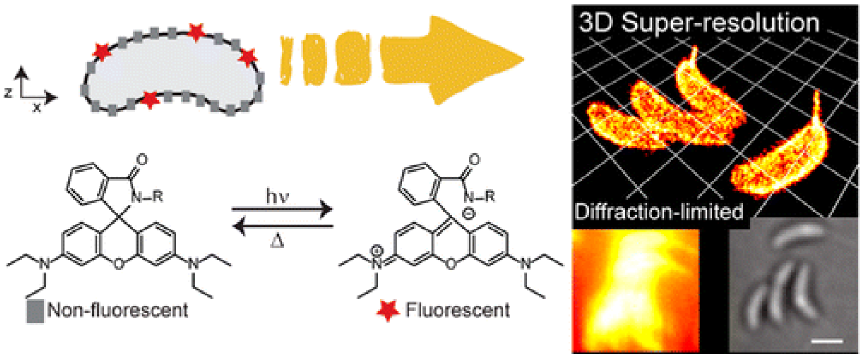
Citation: Lee, M. K. et al. J. Am. Chem. Soc., 2014, 136 (40), pp 14003–14006

Small-Molecule Labeling of Live Cell Surfaces for Three-Dimensional Super-Resolution Microscopy (The masterpiece of our Nobel Laureate W.E.)



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DDO
Hybrid
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Citation: Gibbs, A. C. *J. Med. Chem.* **2014**, *57* (19), 7819.

Elements and Modulation of Functional Dynamics

Drug discovery is beginning to take into account functional dynamics and conformational entropy as a driving force of protein function and intermolecular recognition. Conformational dynamics (a proxy of conformational entropy) impacts the degree of protein (dis)order and the constitution of the conformational ensemble, the mechanisms of allostery and drug resistance, and the free energy of ligand binding.

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Drug Deliv.
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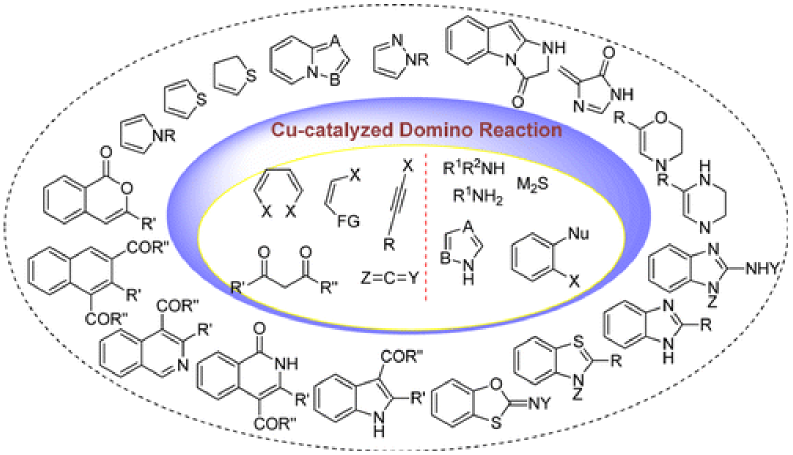
Citation: Liao, Q.; Yang, X.; Xi, C. *JOC,* **2014**, *79,* 8507-8515.

Copper-Catalyzed Domino Reactions for the Synthesis of Cyclic Compounds



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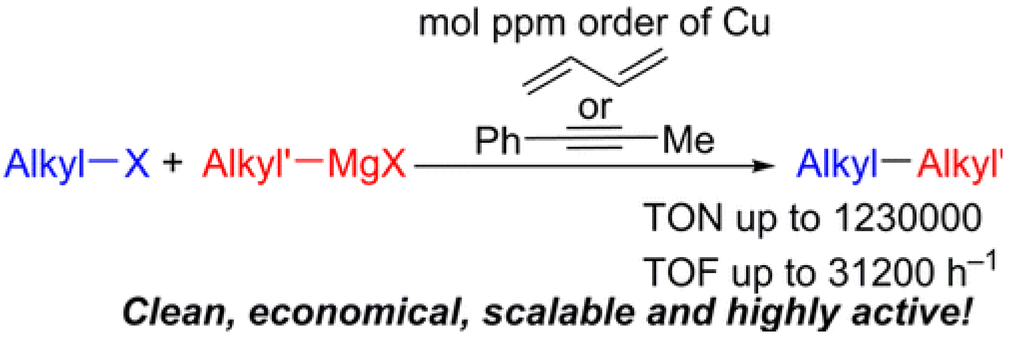
Citation: Kambe, N.; *et al. JOC,* **2014**, *79*, 8522-8532.

Copper-Catalyzed Alkyl–Alkyl Cross-Coupling Reactions Using Hydrocarbon Additives: Efficiency of Catalyst and Roles of Additives



I am not so sure about this one...

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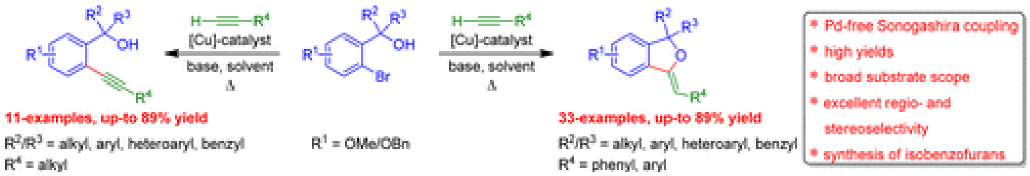
Citation: Satyanarayana, G.; *et al. JOC,* **2014**, *79*, 8566-8576.

[Cu]-Catalyzed Domino Sonogashira Coupling Followed by Intramolecular 5-exo-dig Cyclization: Synthesis of 1,3-Dihydro-2-benzofurans



Substrate scope is somewhat limited. Only aryl substrates cyclize. R2 and R3 are always both substituted.

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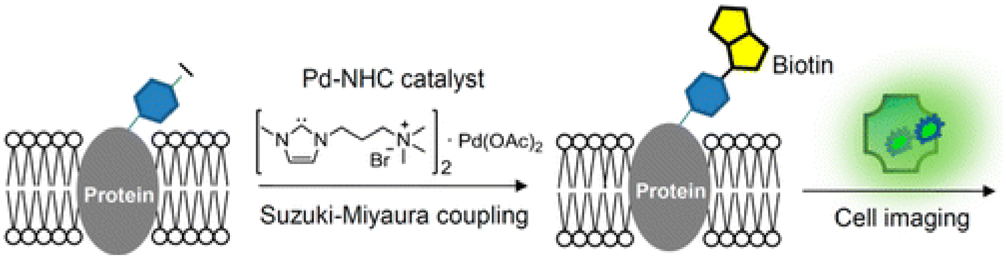
Citation: Ma, X.; Wang, H.; Chen, W. *JOC,* **2014**, *79,* 8652-8658.

N-Heterocyclic Carbene-Stabilized Palladium Complexes as Organometallic Catalysts for Bioorthogonal Cross-Coupling Reactions



"A small library of water-soluble N-heterocyclic carbene (NHC)-stabilized palladium complexes was prepared and applied for cross-couplings of biomolecules under mild conditions in water. Pd–NHC complexes bearing hydrophilic groups were demonstrated to be efficient catalysts for the Suzuki–Miyaura coupling of various unnatural amino acids and proteins bearing p-iodophenyl functional groups. We further utilized this catalytic system for the rapid bioorthogonal labeling of proteins on the surfaces of mammalian cells. These results demonstrated that NHC-stabilized metal complexes have potential utility in cellular systems."

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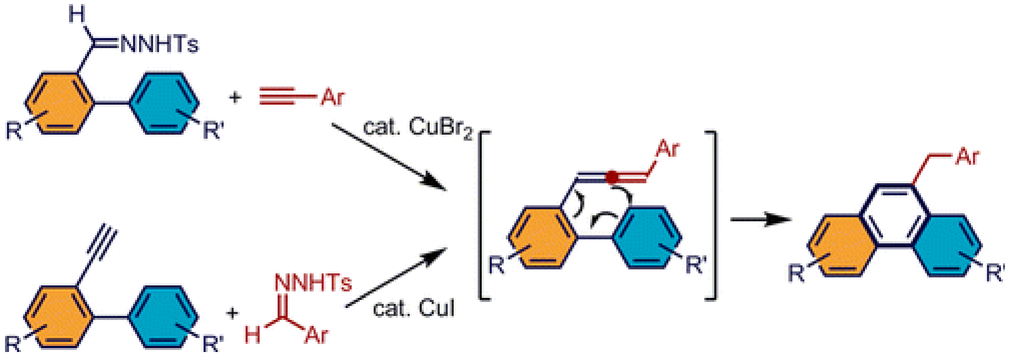
Citation: Wang, J.; *et al. JOC,* **2014**, *79*, 8689-8699.

Synthesis of Phenanthrenes through Copper-Catalyzed Cross-Coupling of *N*-Tosylhydrazones with Terminal Alkynes



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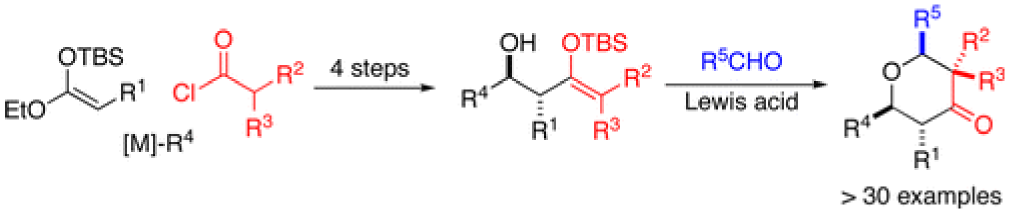
Citation: Tay, G.C.; Huang, C.Y.; Rychnovsky, S.D. *JOC,* **2014**, *79*, 8733-8749.

Silyl Enol Ether Prins Cyclization: Diastereoselective Formation of Substituted Tetrahydropyran-4-ones



This looks like a pretty robust strategy, although R2 and R3 are usually methyl groups and they lose some of the R4-R5 cis relationship when they are not. Interesting nonetheless.

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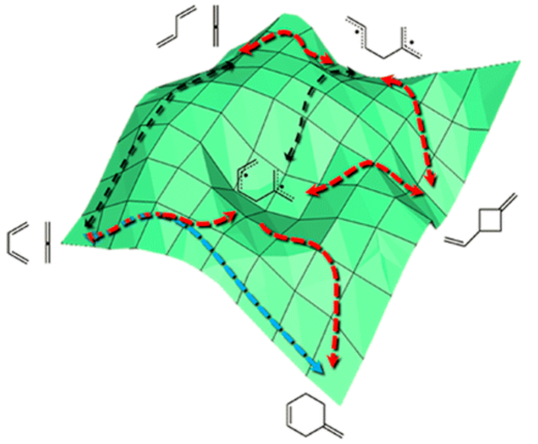
Citation: Pham, H.V.; Houk, K.N. *JOC*, **2014**, *79*, 89698976.

Diels-Alder Reactions of Allene with Benzene and Butadiene: concerted, Stepwise, and Ambimodal Transition States

Not too much to say about this one. The differences between allene's reactivity with butadiene and benzene are pretty cool though.



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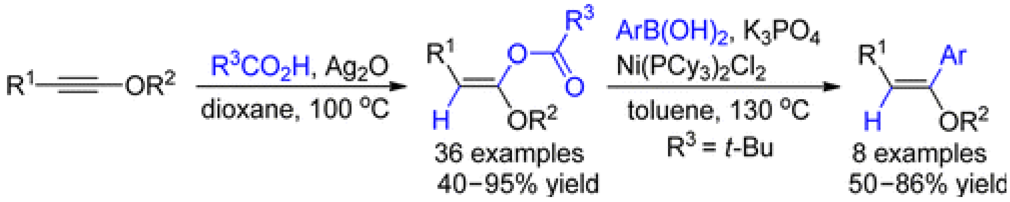
Citation: Yin, J.; Mao, M.; Zhu, G. *JOC*, **2014**, *79*, 9179-9185.

Silver-Catalyzed Regio- and Stereoselective Addition of Carboxylic Acids to Ynol Ethers



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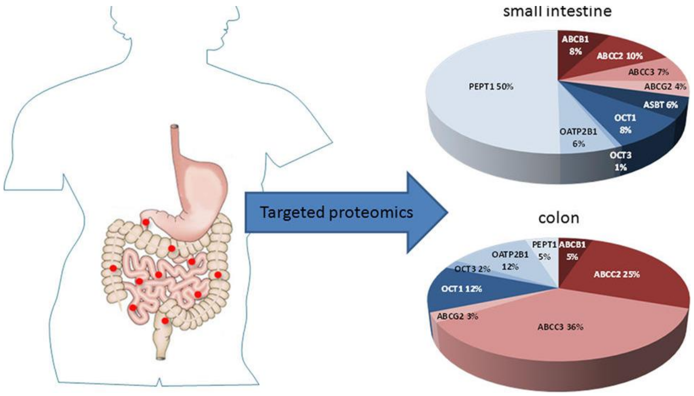
Citation: Mol. Pharmaceutics 2014, 11, 3547–3555.

Protein Abundance of Clinically Relevant Multidrug Transporters along the Entire Length of the Human Intestine.



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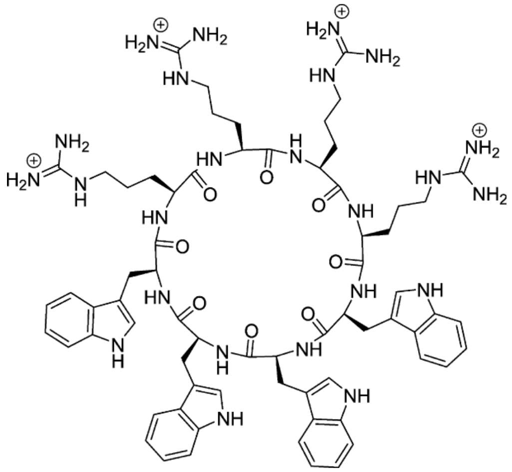
Citation: Mol. Pharmaceutics 2014, 11, 3528–3536.

Antibacterial Activities of Amphiphilic Cyclic Cell-Penetrating Peptides against Multidrug-Resistant Pathogens



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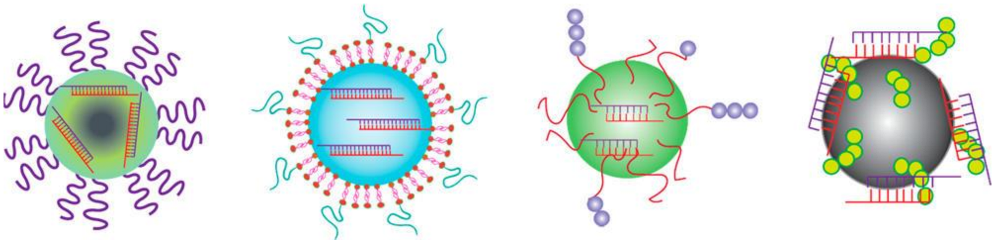
Citation: Mol. Pharmaceutics 2014, 11, 3395–3408.

Peptides Used in the Delivery of Small Noncoding RNA



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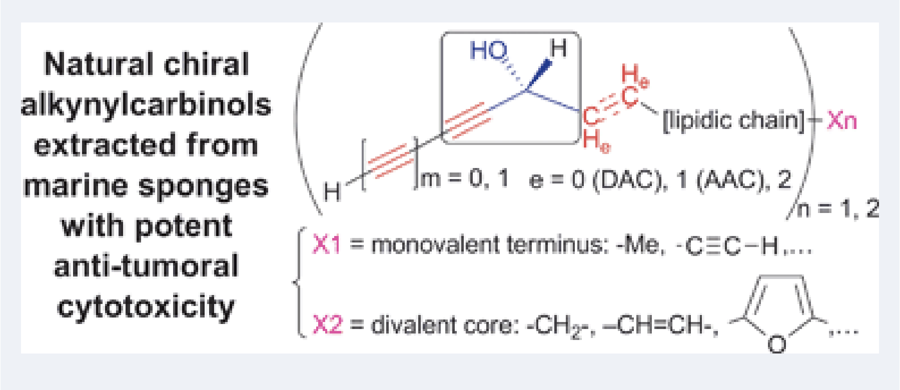
Citation: Listunov, D. et al, *Nat. Prod. Rep.* (2015) *Advance Article*

Chiral alkynylcarbinols from marine sponges: asymmetric synthesis and biological relevance



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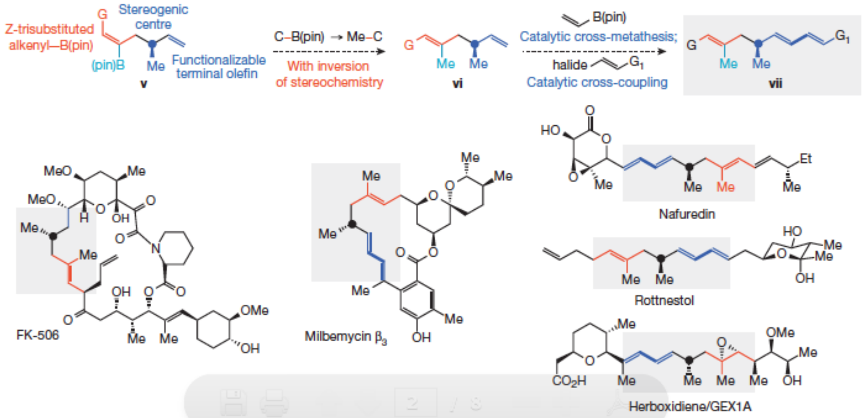
Citation: Meng, F.; McGrath, K. P.; Hoveyda, A. H. *Nature*. **2014**, *513*, 367.

Multifunctional organoboron compounds for scalable natural product synthesis



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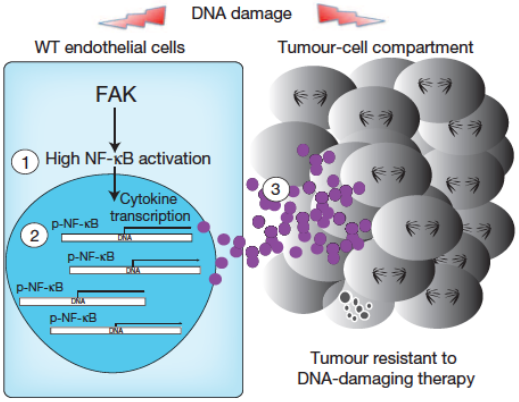
Citation: Tavora, B. et al. *Nature*. **2014**, *514*, 112.

Endothelial-cell FAK targeting sensitizes tumours to DNA-damaging therapy



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Citation: Suez, J. et al. *Nature*. **2014**, *514*, 181.

Artificial sweeteners induce glucose intolerance by altering the gut microbiota

Non-caloric artificial sweeteners (NAS) are among the most widely used food additives worldwide, regularly consumed by lean and obese individuals alike. NAS consumption is considered safe and beneficial owing to their low caloric content, yet supporting scientific data remain sparse and controversial. Here we demonstrate that consumption of commonly used NAS formulations drives the development of glucose intolerance through induction of compositional and functional alterations to the intestinal microbiota. These NAS-mediated deleterious metabolic effects are abrogated by antibiotic treatment, and are fully transferrable to germ-free mice upon faecal transplantation of microbiota configurations from NAS-consuming mice, or of microbiota anaerobically incubated in the presence of NAS. We identify NAS-altered microbial metabolic pathways that are linked to host susceptibility to metabolic disease, and demonstrate similar NAS-induced dysbiosis and glucose intolerance in healthy human subjects. Collectively, our results link NAS consumption, dysbiosis and metabolic abnormalities, thereby calling for a reassessment of massive NAS usage.

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Citation: Collins, K.D. Gensch, T.; Glorius, F. Nature Chemistry 6, 859–871 (2014)

Contemporary screening approaches to reaction discovery and development

New organic reactivity has often been discovered by happenstance. Several recent research efforts have attempted to leverage this to discover new reactions. In this Review, we attempt to unify reported approaches to reaction discovery on the basis of the practical and strategic principles applied. We concentrate on approaches to reaction discovery as opposed to reaction development, though conceptually groundbreaking approaches to identifying efficient catalyst systems are also considered. Finally, we provide a critical overview of the utility and application of the reported methods from the perspective of a synthetic chemist, and consider the future of high-throughput screening in reaction discovery.

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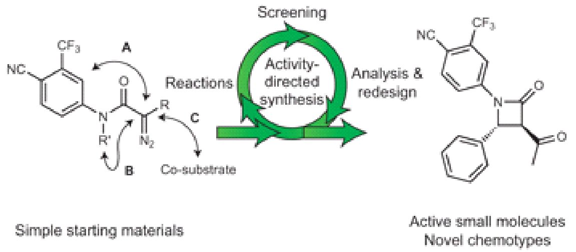
Citation: Karageorgis,G.; Warriner, S.; Nelson, A. Nature Chemistry 6, 872–876 (2014)

Efficient discovery of bioactive scaffolds by activity-directed synthesis



Here, we describe a discovery approach—which we term activity-directed synthesis—in which reactions with alternative outcomes are steered towards functional products. Arrays of catalysed reactions of a-diazo amides, whose outcome was critically dependent on the specific conditions used, were performed. The products were assayed at increasingly low concentration, with the results informing the design of a subsequent reaction array.

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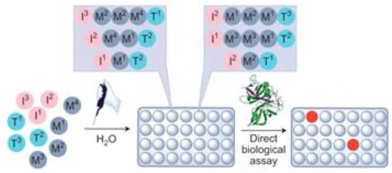
Citation: Huang, Y-L.; Bode, J.W. Nature Chemistry 6, 877–884 (2014)

Synthetic fermentation of bioactive non-ribosomal peptides without organisms, enzymes or reagents



Microbial fermentation can rapidly provide potent compounds that can be easily screened for biological activity, and the active components can be isolated. Its success in drug discovery has inspired extensive efforts to modulate and control the products. In this Article, we document a ‘synthetic fermentation’ of bioactive, unnatural peptides ‘grown’ from small building blocks in water using amide-forming ligations. No organisms, enzymes or reagents are needed. The sequences, structures and compositions of the products can be modulated by adjusting the building blocks and conditions. No specialized knowledge of organic chemistry or handling of toxic material is required to produce complex organic molecules.

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Citation: Chaikuad, A., et al. *Nature Chem. Bio.* **2014**, 10, 853-860

A Unique Inhibitor Binding Site in ERK1/2 Is Associated with Slow Binding Kinetics

Because protein kinases are upstream regulators of copious cell signaling pathways, their activation or inhibition by small molecules is of incredible interest in the field of bioorganic chemistry. The authors here describe the utility of a small molecule in binding selectively to and inhibiting ERK1/2, a protein kinase that plays a great role in cancer regulation. Importantly, this small molecule showed slow binding kinetics and ERK supression was maintained even after removal of the small molecule from cell medium. The authors claim that this discovery paves the way for a new generation of ERK1/2 kinase inhibitors.

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Citation: http://www.nytimes.com/2014/10/04/health/italy-child-thought-to-be-rid-of-hiv-suffers-a-relapse.html

Italy: Child Thought to Be Rid of H.I.V. Suffers a Relapse

A child in Milan treated early and aggressively with AIDS drugs after being born with H.I.V. suffered a rebound of the virus soon after stopping the drugs, indicating that early treatment had not wiped out all the reservoirs of virus. (Similar story to the Mississippi baby)

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Citation: http://www.nytimes.com/2014/10/11/business/harvoni-a-hepatitis-c-drug-from-gilead-wins-fda-approval.html

Harvoni, a Hepatitis C Drug From Gilead, Wins F.D.A. Approval

The first complete treatment for hepatitis C that requires taking only a once-a-day pill won approval Friday from the Food and Drug Administration.

The drug, called Harvoni from Gilead Sciences, could shorten the duration of treatment and provide the first all-oral regimen for many patients.

The new drug also appears to be a bit less expensive for some patients than Gilead's existing blockbuster hepatitis C drug, Sovaldi, which has become the poster child for those complaining that the cost of medicines is out of control.

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Citation: *The Onion*, http://goo.gl/jn7GHe

Pfizer Releases Vintage Cask-Aged Robitussin

GROTON, CT—Touting the new offering's full-bodied flavor and bold, fruit-forward bouquet, pharmaceutical giant Pfizer unveiled a vintage cask-aged variety of its popular cold medicine Robitussin on Friday. Labeled as Robitussin Reserve, the high-end over-the-counter cough remedy is reportedly being marketed toward a more affluent segment of consumers with acute upper respiratory symptoms. Company officials confirmed the select Cough & Cold blend has been prepared in a limited run of 100 barrels and retails for $39.95 a bottle.

"This is an upscale product for the cold and flu sufferer with a discerning palate," said Pfizer spokesman Mark Dumont. "This fine vintage provides multi-symptom relief while satisfying the tastes of even the most refined connoisseur. It is well-balanced, elegant, and loosens phlegm and mucus with minimal drowsiness."

"You're going to want to save this Robitussin for a very special cold," Dumont continued. "We recommend pairing it with soup, saltines, and plenty of fluids."

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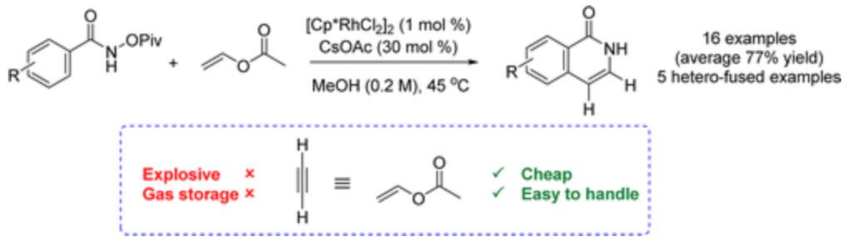
Citation: Webb, N.; *et al*. *Org. Lett.* **2014**, 16 (18), 4718-4721

Rhodium(III)-Catalyzed C-H Activation/Annulation with Vinyl Esters as an Acetylene Equivalent



The behavior of electron-rich alkenes in rhodium-catalyzed C–H activation/annulation reactions is investigated. Vinyl acetate emerges as a convenient acetylene equivalent, facilitating the synthesis of sixteen 3,4-unsubstituted isoquinolones, as well as select heteroaryl-fused pyridones. The complementary regiochemical preferences of enol ethers versus enol esters/enamides is discussed.

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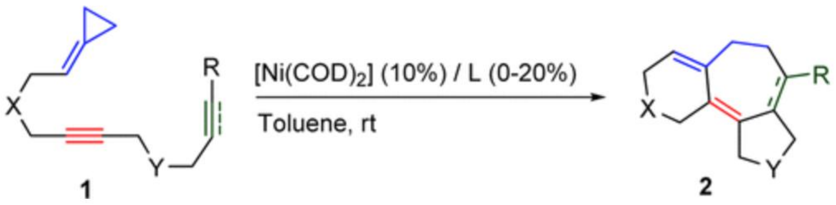
Citation: Saya, L. *et al*. *Org. Lett.* **2014**, 16 (19), 5008-5011.

Nickel-Catalyzed Intramolecular [3 + 2 + 2] Cycloadditions of Alkylidenecyclopropanes. A Straightforward Entry to Fused 6,7,5-Tricyclic Systems



A highly diastereo- and chemoselective intramolecular nickel-catalyzed cycloaddition of alkene- and alkyne-tethered alkynylidenecyclopropanes is reported. The method constitutes the first fully intramolecular [3 + 2 + 2] alkylidenecyclopropropane cycloaddition occurring via a proximal cleavage of the cyclopropane and makes it possible to build relevant 6,7,5-tricyclic frameworks in a single-pot reaction. Importantly, the reaction outcome is highly dependent on the characteristics of the nickel ligands.

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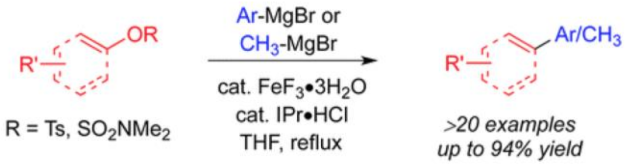
Citation: Agrawal, T.; Cook, S. *Org. Lett.* **2014**, 16 (19), 5080-5083

Iron-Catalyzed Coupling of Aryl Sulfamates and Aryl/Vinyl Tosylates with Aryl Grignards



- Fe-catalyzed biaryl coupling of C-O-based electrophiles now possible
- Low levels of homocoupling of aryl Grignard regardless of Fe source
- Works well on gram scale

The iron-catalyzed coupling of aryl sulfamates and tosylates with aryl Grignard reagents is reported for the first time. The methodology employs air-stable, low-cost $FeF_3·3H_2O$ and the N-heterocyclic carbene ligand IPr·HCl as the preligand to form a long-lived catalyst upon treatment with aryl Grignards. The reaction provides a range of cross-coupled products in good-to-excellent yields. In contrast to previous reports with aryl chlorides, these reactions proceed with low levels of Grignard homocoupling regardless of the iron source.

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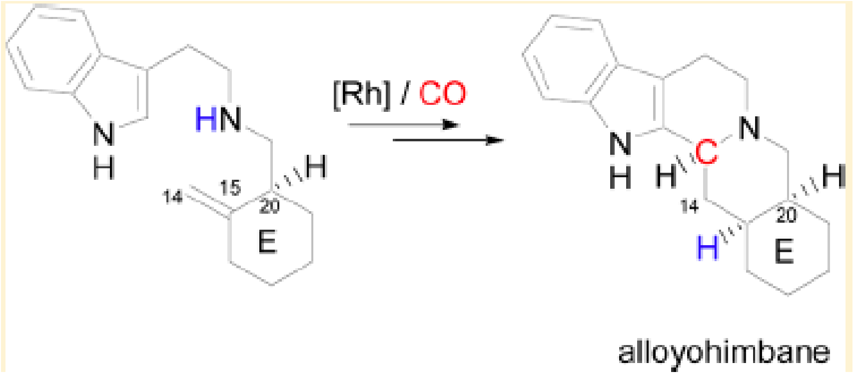
Citation: Chiou, W. -H.; Wang, Y. -W.; Kao, C. -L.; Chen, P. -C.; Wu, C. -C. *Organometallics*. **2014**, *33*, 4240.

Rhodium-Catalyzed Hydrocarbonylation of a Homoallylamine via N-H Activation and Application for Synthesis of Yohimbane Alkaloids



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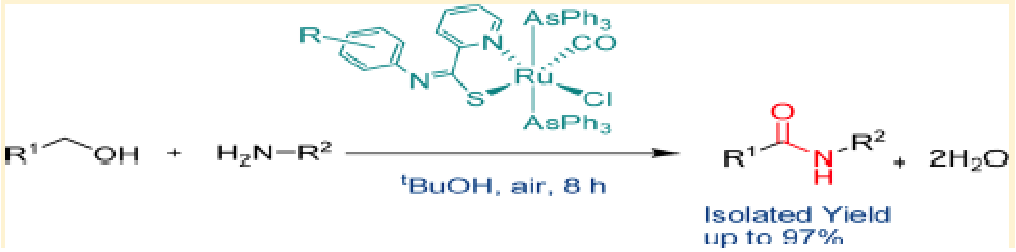
Citation: Sindhuja, E.; Ramesh, R.; Balaji, S.; Liu, Y. *Organometallics*. **2014**, *33*, 4269.

Direct Synthesis of Amides from Coupling of Alcohols and Amines Catalyzed by Ruthenium(II) Thiocarboxamide Complexes under Aerobic Conditions



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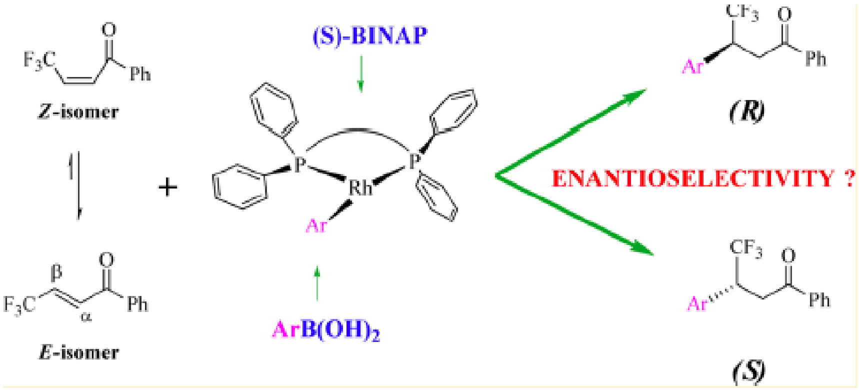
Citation: Boz, E.; Haslak, Z. P.; Tuzun, N. S.; Konuklar, F. A. S. *Organometallics*. **2014**, *33*, 5111.

A Theoretical Study on Rh(I) Catalyzed Enantioselective Conjugate Addition Reactions of Fluoroalkylated Olefins



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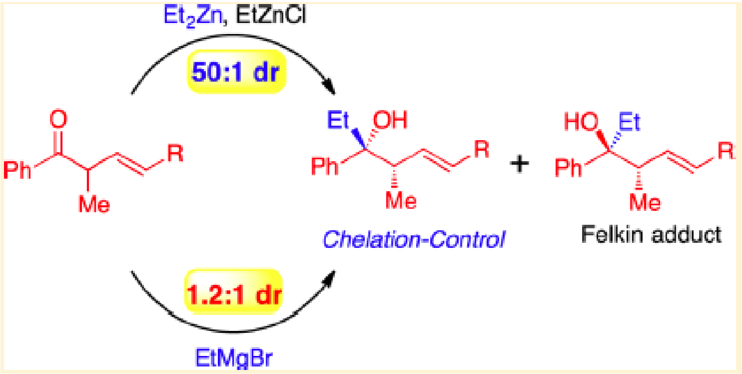
Citation: Raffer, L.; Gutierrez, O.; Stanton, G. R.; Kozlowski, M. C.; Walsh, P. J. *Organometallics*. **2014**, *33*, 5371.

Alkenes as Chelating Groups in Diastereoselective Additions of Organometalics to Ketones



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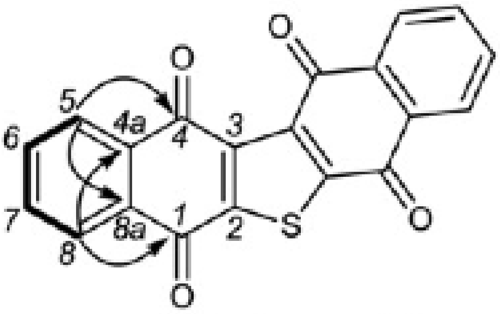
Citation: PNAS | October 14, 2014 | vol. 111 | no. 41 | 14687–14692

Seriniquinone, a selective anticancer agent, induces cell death by autophagocytosis, targeting the cancer-protective protein dermcidin

This is a previously undiscovered NP from a marine sponge that coincidentally is a reported molecule that was previously synthesized in a materials science program. It and simple derivatives are shown to have potent anticancer activity.



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Citation: PNAS | September 16, 2014 | vol. 111 | no. 37 | 13481–13486

Clearance of pathological antibodies using biomimetic nanoparticles

PLGA nanoparticles coated with antigen-bearing cell membranes deplete autoimmune disease-causing Abs, protecting red blood cells from opsonization, without deleterious effects to a patient's immune system.

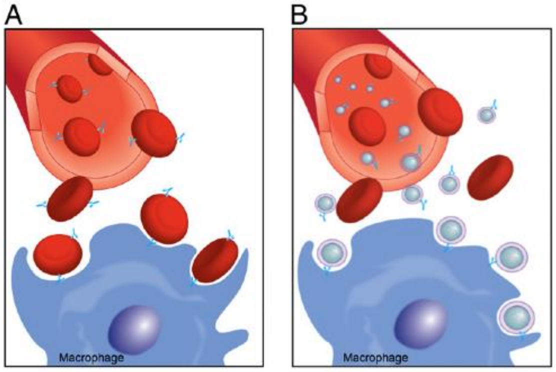

Fig. 1. Schematic representation of RBC-ANS neutralizing anti-RBC antibodies (anti-RBCs). (*A*) Anti-RBCs opsonize RBCs for extravascular hemolysis, via phagocytosis, as observed in AIHA and DIA. (*B*) RBC-ANS absorbs and neutralizes anti-RBCs, thereby protecting RBCs from phagocytosis.

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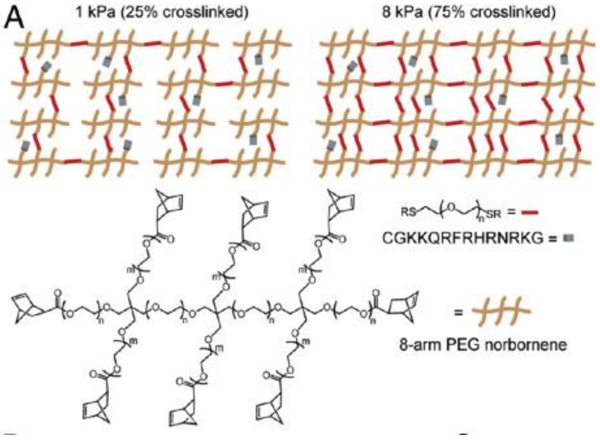
Citation: Kiessling, et al. PNAS | September 23, 2014 | vol. 111 | no. 38 | 13805–13810



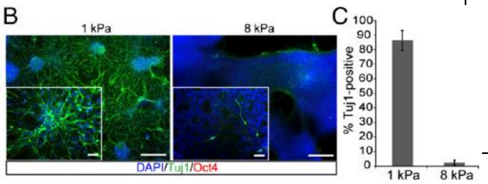


Fig. 5. hES cell differentiation on PEG hydrogels of varying elasticity. (*A*) Schematic of compliant (1 kPa, 25% cross-linked) and stiff (8 kPa, 75% cross-linked) PEG hydrogels. (*B*) Microscopy images of hES cells (H9 line) differentiated for 2 wk on compliant or stiff PEG hydrogels. Cells were immunostained for pluripotency marker Oct4 (red) and neuronal marker Tuj1 (green), and counterstained for DAPI (blue). (*C*) Quantification of neuronal differentiation efficiency on compliant and stiff PEG hydrogels. Error bars denote SD of the mean (*n* = 4). [Scale bars: *B*, 250 μm; *B* (*Insets*), 50 μm.]

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Citation: Nuno R. Faria *et al.*, *Science* **2014,** *346,* 56-61.

The early spread and epidemic ignition of HIV-1 in human populations

Thirty years after the discovery of HIV-1, the early transmission, dissemination, and establishment of the virus in human populations remain unclear. Using statistical approaches applied to HIV-1 sequence data from central Africa, we show that from the 1920s Kinshasa (in what is now the Democratic Republic of Congo) was the focus of early transmission and the source of pre-1960 pandemic viruses elsewhere. Location and dating estimates were validated using the earliest HIV-1 archival sample, also from Kinshasa. The epidemic histories of HIV-1 group M and nonpandemic group O were similar until ~1960, after which group M underwent an epidemiological transition and outpaced regional population growth. Our results reconstruct the early dynamics of HIV-1 and emphasize the role of social changes and transport networks in the establishment of this virus in human populations.

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Citation: Bach, T.et. al *Synthesis* **2014**, *46(19)*: 2663Bach, T.et. al *Synthesis* **2014**, *46(19)*:

[2+2] Photocycloaddition Studies on Complex Tetronic Acid Esters Related to the Synthesis of Cembranoid Diterpenes

Twelve different tetronic acid esters bearing two potentially reactive olefinic groups were prepared and subjected to [2+2] photocycloaddition reactions by irradiation at ? = 254 nm in tert-butanol (5 mM). The diastereoselectivity and regioselectivity of the reaction was studied with regard to the synthesis of cembranoid diterpenes. When the tetronic acid core carried an alk-3-enyl substituent in the ?-position and an alk-3-enyloxy substituent in the ß-position, the undesired ?-products prevailed and were formed in 48–81% yield. Altering the ?-alk-3-enyl substituent into an alk-3-ynyl or alk-2-ynyl substituent, resulted in formation of the desired ß-photocycloaddition products. The latter products were obtained in yields of 56–88%, with two out of three products exhibiting very high regio- and diastereoselectivity.

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Citation: Wang, Z. et. al *Synlett* **2014**, *25(16)*: 2260-2264

Tandem Diels–Alder [4+2] Cycloadditions and Intramolecular [3+2] Cross-Cycloadditions of Dienylcyclopropane 1,1-Diesters

A novel tandem reaction by combination of Diels–Alder [4+2] cycloaddition and [3+2] IMCC (intramolecular cross-cycloaddition) of dienylcyclopropane 1,1-diesters has been successfully developed. In this reaction, three new rings and four new stereocenters were generated in one-pot. This supplies a strategy for rapid construction of 6,6- and 6,7-fused carbocyclic skeletons which are common cores in many biologically important natural products.

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Citation: Snieckus, V. et. al *Synlett* **2014**, *25(16)*: 2258-2259

Activated Cyclopropanes: A Remarkable Breadth of Recent Chemistry

The reactions of cyclopropanes activated by electron-withdrawing groups and electron-donating groups – donor–acceptor (DA) cyclopropanes – and with alkenyl or alkylidene substituents has been an area of recent intense research activity. This Cluster contains contributions from many of the leading research groups in this area, and provides a concise introduction to the rich ring-opening, ring-expansion, dimerization, and cycloaddition chemistry of these compounds.

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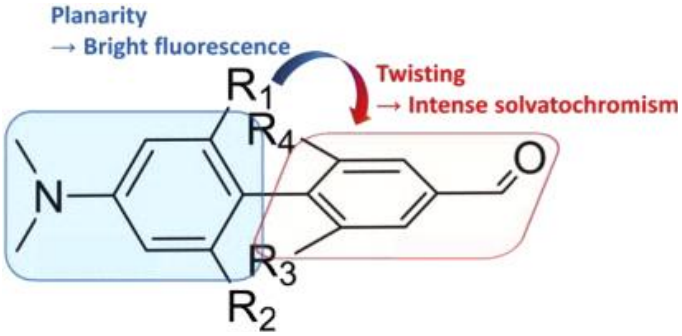
Citation: Shunsuke Sasakia, Gen-ichi Konishi, et al. (**2014**) *Tetrahedron*, 70(41), 7551

Design of donor–acceptor geometry for tuning excited-state polarization: fluorescence solvatochromism of push–pull biphenyls with various torsional restrictions on their aryl–aryl bonds



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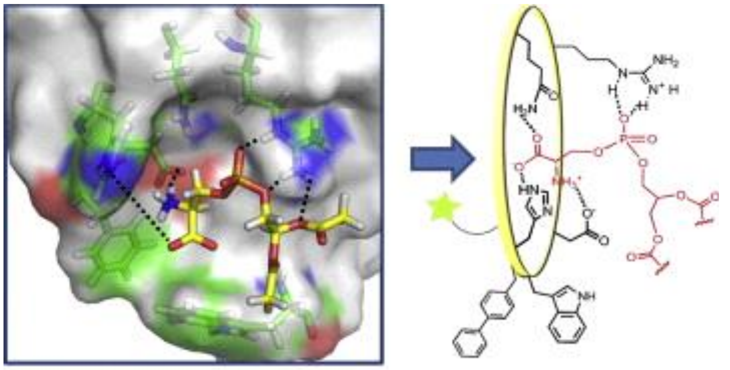
Citation: Azade S. Hosseini, Hong Zheng, Jianmin Gao. (**2014**). *Tetrahedron*, 70(42), 7632

Understanding lipid recognition by protein-mimicking cyclic peptides



Mimicking Protein for Lipid Recognition

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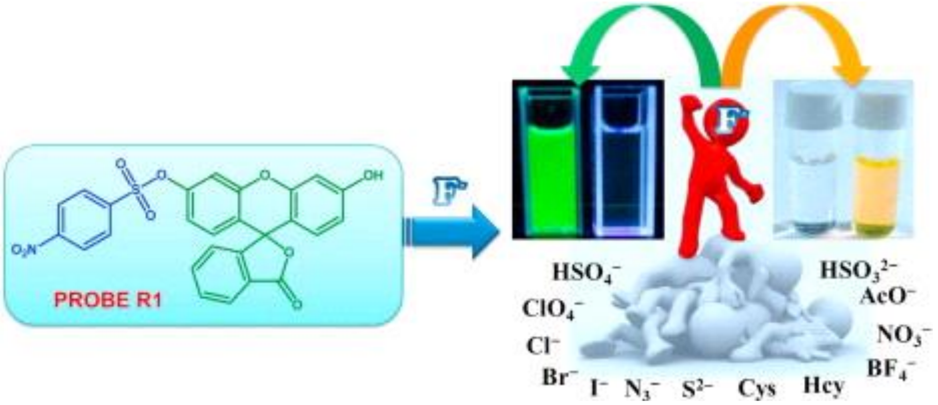
Citation: Sharad Kumar Asthana, Ajit Kumar, Neeraj, K.K. Upadhyay. (**2014**). *Tetrahedron Letters*, 55(43), 5988

A reaction based chromofluorogenic turn-on probe for specific detection of fluoride over sulfide/thiols



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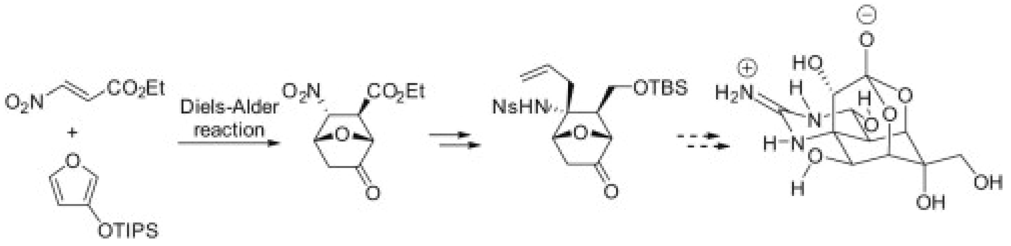
Citation: Atsushi Manabe, Yasufumi Ohfune, Tetsuro Shinada. (**2014**). *Tetrahedron Letters*, 55(44), 6077

Toward the total synthesis of tetrodotoxin: stereoselective construction of the 7-oxanorbornane intermediate



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