Volume 36 / Issue 06 15 June 2011

Next Due Date: Friday, 15 July 2011

Instructions for Authors (*Volume 36*)

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 (CNN 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.

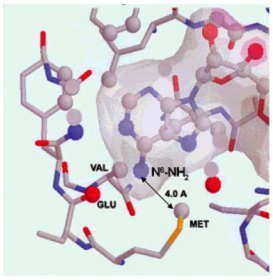
Include a brief textual summary of the article; an example of a completed abstract is shown below. The list of topics and subgroups on the right is useful to highlight which subgroups should pay attention to your abstract and roughly what kind of chemistry the article contains.

Please email the files to lmieuli@stanford.edu. Late abstracts will be included in the Lit Review for the following month. **PC Users should submit their abstracts as PDFs** or purchase a Mac.

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 (1ç-32Pl-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
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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 not receive a printed copy of the Lit Review.
- You will get last choice when it's time to pick new journals.
- We will crack your corn (clean in half)

Citation: Olson, J. A.; Shea, K. M. *Acc. Chem. Res.* **2011**, *44* (5), 311.

Critical Perspective: Named Reactions Discovered and Developed by Women

Interesting investigation into the female chemists behind various named reactions.

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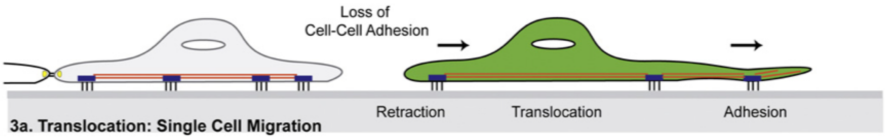
Citation: Palmer, T.D.; Ashby, W.J.; Lewis J.D.; Zijlstra, A.
Adv. Drug Delivery Rev., **2011**, *ASAP* DOI:10.1016/j.addr.2011.04.008

Targeting tumor cell motility to prevent metastasis

Metastasis is a major problem and a leading cause of death among cancer patients. The cause of metastasis is the motility of tumor cells; however, few treatments directly inhibit the process. In this review, the molecular events that control tumor cell motility are elucidated, and suggestions are given as to how each step might be inhibited. Although clinical treatments that contain tumors by targeting motility are not yet widespread, the authors conjecture that this will be a useful way to curb metastasis and curb mortality rates in cancer patients.



3a. Translocation: Single Cell Migration

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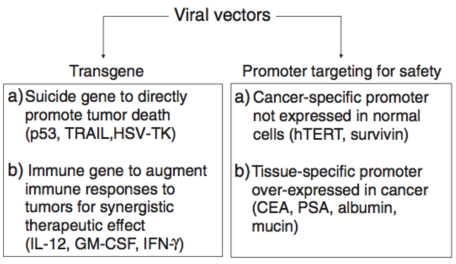
Citation: Wu, T. and Zhou, D.
Adv Drug Delivery Rev., **2011**, *ASAP* DOI:10.1016/j.addr.2011.05.005

Viral delivery for gene therapy against cell movement in cancer



Viral delivery for gene therapy has come a long way in recent years. By choosing appropriate transgenes and promoters, it is possible to introduce reproducing-competent viral vectors into patients for the treatment of cancer. Generally, these are used in combination with more traditional chemotherapies, but the result is significant knockdown of tumor growth and metastasis.

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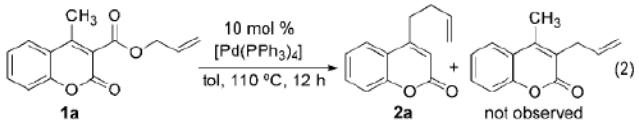
Citation: Jana, R.; Xie, C.; Partridge, J.; Tunge, J. *Angew Chem (Int Ed)*. **2011**, *50 (22)*, 5157-5161.

Migratory Decarboxylative Coupling of Coumarins: Synthetic and Mechanistic Aspects

Decarboxylative coupling of allyl 4-methyl-3-carboxycoumarins provides the products of γ-allylation of the methyl group rather than the typical regiospecific α-allylation. Mechanistic studies show that intramolecular proton transfer from the 4-methyl group to the 3-carboxylate allows allylation of the remote methyl group. The resulting 4-butenyl-3-carboxyl coumarin undergoes Pd^0-catalyzed decarboxylation to provide the observed products.



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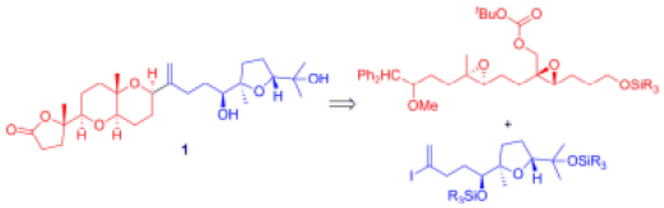
Citation: Clausen, D.; Wan, S.; Floreancig, P. *Angew Chem (Int Ed)*. **2011**, *50 (22)*, 5178-5181.

Total Synthesis of the Protein Phosphatase 2A Inhibitor Lactodehydrothyrsiferol

The squalene-derived polyether lactodehydrothyrsiferol (1) has been prepared through a convergent sequence that features an epoxide-opening cascade to construct the tetrahydrofuran and tetrahydropyran subunits. Additional features include a stereodivergent diene diepoxidation, a monodeoxygenation of a triol, and complex fragment couplings through Suzuki and Nozaki–Hiyama–Kishi reactions.



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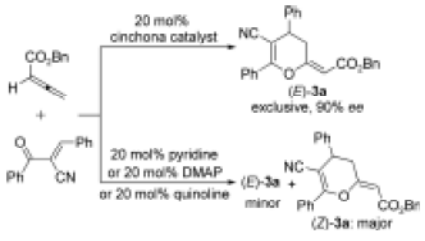
Citation: Wang, X.; Fang, T.; Tong, X. *Angew Chem (Int Ed)*. **2011**, *50 (23)*, 5361-5364.

Enantioselective Amine-Catalyzed [4+2] Annulations of Allenoates and Oxo-dienes: An Asymmetric Synthesis of Dihydropyrans

Biologically significant polysubstituted dihydropyrans have been prepared in high to excellent yields and enantioselectivities. The interaction between functional groups in the zwitterionic intermediate, which is generated by addition of the amine catalyst to the allenoate substrate, is thought to play a crucial role in the stereochemical outcome.



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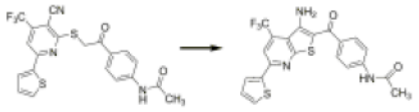
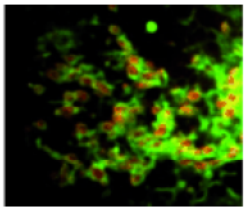
Citation: Kawazoe, T.; et. al. *Angew Chem (Int Ed)*. **2011**, *50 (24)*, 5478-5481.

A Mitochondrial Surface-Specific Fluorescent Probe Activated by Bioconversion

Cell-based image screening of 12 000 small molecules with aromatic groups was carried out, and 31 were identified as having potential as fluorescent probes for living cells. One candidate is the first fluorescent probe that specifically stains mitochondrial surfaces. Spectroscopic analyses indicate that the molecule undergoes bioconversion to be fluorescent within cells.





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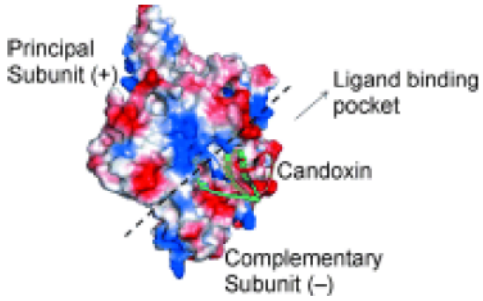
Citation: Zhan, C.; et. al. *Angew Chem (Int Ed)*. **2011**, *50 (24)*, 5482-5485.

Micelle-Based Brain-Targeted Drug Delivery Enabled by a Nicotine Acetylcholine Receptor Ligand

A 16-residue peptide (CDX) that is derived from candoxin binds with a high affinity to nicotinic acetylcholine receptors, which are highly expressed on the blood–brain barrier. In vivo biodistribution and the anti-glioblastoma effect indicate the potential of CDX as a ligand to enable brain-targeted drug delivery.



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Citation: Lehmann, C. *Angew Chem (Int Ed)*. **2011**, *50 (25)*, 5616-5617.

Crystal Structure Prediction—Dawn of a New Era

Improved methodology has led to recent progress in predicting crystal structures of organic molecules. The combination of tailor-made force fields and most importantly dispersion-corrected density functional theory calculations are key factors for successful structure predictions.

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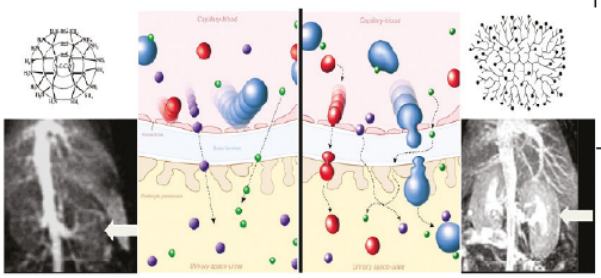
Citation: M. R. Longmire, M. Ogawa, P. L. Choyke, and H. Kobayashi *Bioconjugate Chem.* **2011**, 22, 993.

Biologically Optimized Nanosized Molecules and Particles: More than Just Size

The expanded biological and medical applications of nanomaterials place a premium on better understanding of the chemical and physical determinants of in vivo particles. Nanotechnology allows us to design a vast array of molecules with distinct chemical and biological characteristics, each with a specific size, charge, hydrophilicity, shape, and flexibility.



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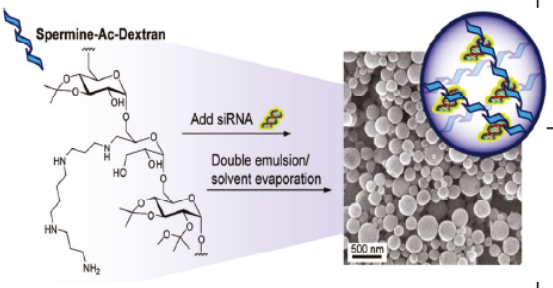
Citation: J. L. Cohen, S. Schubert,† P. R. Wich, L. Cui, J. A. Cohen, J. L. Mynar, J. M. J. Frechet *Bioconjugate Chem.* **2011**, 22, 1056.

Acid-Degradable Cationic Dextran Particles for the Delivery of siRNA Therapeutics

A new acid-sensitive, biocompatible, and biodegradable microparticulate delivery system, spermine modified acetalated-dextran (Spermine-Ac-DEX), which can be used to efficiently encapsulate siRNA is reported. These particles demonstrated efficient gene knockdown in HeLa-luc cells with minimal toxicity. This knockdown was comparable to that obtained using Lipofectamine, a commercially available transfection reagent generally limited to in vitro use due to its high toxicity.



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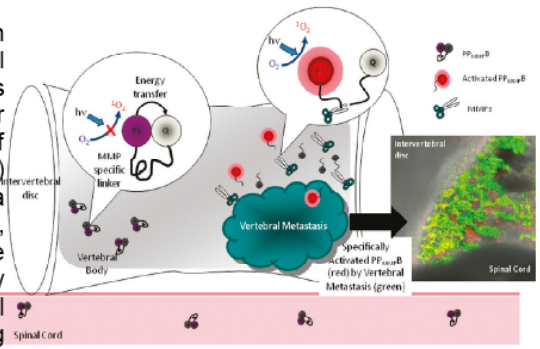
Citation: T. W. Liu, M. K. Akens, J. Chen, L. Wise-Milestone, B. C. Wilson, G. Zheng, *Bioconjugate Chem.* **2011**, 22, 1021.

Imaging of Specific Activation of Photodynamic Molecular Beacons in Breast Cancer Vertebral Metastases

Approximately 85% of patients with advanced cases will develop spinal metastases. The vertebral column is the most common site of breast cancer metastases, where overexpression of matrix metalloproteinases (MMPs) promotes the spread of cancer.Using a clinically relevant metastatic model, fluorescent imaging establishes the specific activation of PPMMPB by vertebral metastases versus normal tissue (i.e., spinal cord) demonstrating the specificity of these beacons.



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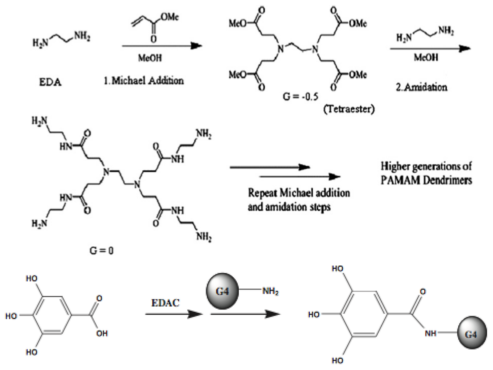
Citation: Sharma, A.; Gautam, S.P.; Gupta, A.K.
Bioorg. Med. Chem., **2011**, *19*, 3341-46.

Surface modified dendrimers: Synthesis and characterization for cancer-targeted delivery

PAMAM (polyamidoamine) dendrimers can be used to either conjugate or encapsulate an anti-tumor therapeutic. Ideally, this therapeutic agent will only attack tumor cells. This is where gallic acid (GA) comes in. Known for its anti-tumor promoting properties, this group functionalizes the surface of their dendrimers to achieve a "cancer-targeted" delivery method. Efficacy dat is in early stage, but these conjugates have been identified as a "promising nano-platform for...treatment and cance diagnosis."



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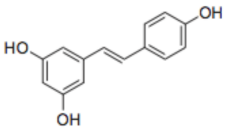
Citation: Huber, K. and Superti-Furga, G.
Bioorg. Med. Chem., **2011**, *19*, 3616-24.

After the grape rush: Sirtuins as epigenetic drug targets in neurodegenerative disorders

Resveratrol and related compounds have received much attention lately in their ability to prevent neurodegnerative disorders such as Alzheimer's, Parkinson's, and Huntington's. Resveratrol and related compounds modulate the expression of sirtuins, which in turn provides the therapeutic benefit. This review summarizes what is known about activators and inhibitors of the sirtuins. The final sentence of the paper makes it well worth the read: "Thus and to conclude, in case anyone wonders if the 'magnificent seven' targets discussed in this review will be of future importance in the treatment of neurodegenerative disor- ders, the tempting answer is 'almost SIRTainly.'"



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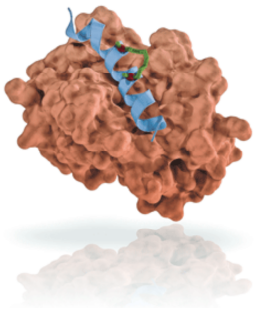
Thayer, A. M. *Chemical & Engineering News.* **2011**, *89* (22), 13-20.



Improving Peptides

Indeed, more large companies are evaluating peptides as part of their drug development strategy, says Joseph A. Yanchik III, CEO of Cambridge, Mass.-based Aileron Therapeutics. "They understand that if you can unlock certain fundamental limitations of peptide therapeutics you might have the largest superclass of drugs that the industry has ever generated." As a result, small firms have attracted investors and large R&D deals. "Clearly the pharma partners are trying to accelerate this development," Yanchik adds.

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Mukhopadhyay, R. *Chemical & Engineering News*. **2011**, *89* (22), 42.

Capturing Carbon Dioxide

Researchers and lawmakers alike are looking for ways to reduce the amount of carbon dioxide released into the atmosphere because of its contribution to global climate change. Work to develop feasible carbon capture and sequestration (CCS) technologies is still ongoing, and methods to turn the CO_2 into a resource for other industrial applications, such as enhanced oil recovery, are years away from becoming reality. This was the less than satisfying message delivered to senators during a hearing earlier this month.

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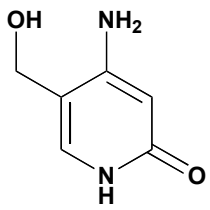
Everts, S. *Chemical & Engineering News*. **2011**, *89* (23), 40-41.

New Base on the Block



The sixth base in life's blueprint is 5-hydroxymethylcytosine (5-hmC), a cytosine decorated with a methylene and a hydroxyl group. For decades, scientists had observed 5-hmC in bacterial viruses, but it was generally thought to be an experimental artifact or random DNA damage in mammalian cells. "5-hmC was pretty much ignored—until two years ago," explains Chuan He, a chemist at the University of Chicago. "That's when two labs independently showed to everybody's huge surprise that 5-hmC was found in genomic DNA from both brain and stem cells."

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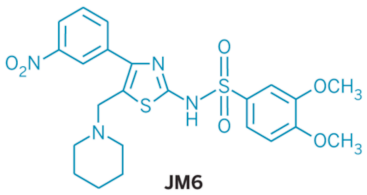
Borman, S. *Chemical & Engineering News*. **2011**, *89* (23), 8.

Compound Prevents Neurodegeneration

Researchers have identified and tested a compound that reverses and prevents symptoms of neurodegenerative diseases like Alzheimer's and Huntington's in animal models (*Cell*, DOI: 10.1016/j.cell.2011.05.020; *Curr. Biol.*, DOI: 10.1016/j.cub.2011.04.028). Neurodegeneration, the breakdown or death of neurons, causes losses in one's ability to think, move, and communicate, often leading to death.

The compound, JM6, offers new hope for treating these diseases, for which new medications are urgently needed. Still, JM6's safety and efficacy have yet to be confirmed in clinical trials.



JM6

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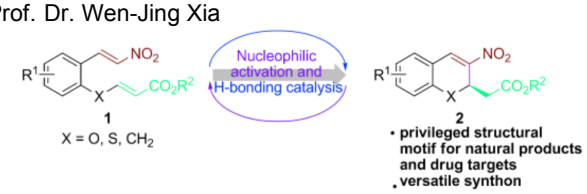
Citation: Chemistry - A European Journal Volume 17, Issue 23, pages 6484–649

Enantioselective Intramolecular Crossed Rauhut–Currier Reactions through Cooperative Nucleophilic Activation and Hydrogen-Bonding Catalysis: Scope and Mechanistic Insight

Xu-Fan Wang, Liang Peng, Jing An, Chao Li, Qing-Qing Yang, Liang-Qiu Lu, Prof. Dr. Feng-Long Gu, Prof. Dr. Wen-Jing Xia



Cooperative nucleophilic activation and hydrogen-bonding catalysis allow a highly efficient and enantioselective intramolecular crossed Rauhut–Currier (RC) reaction of nitroolefins with tethered enonates (≤98% *ee*, 98% yield; see scheme). Computational investigations indicate that the stereoselectivity of the RC reaction is determined by the intramolecular Michael addition and the rate-determining step is a *retro*-aza-Michael addition reaction.

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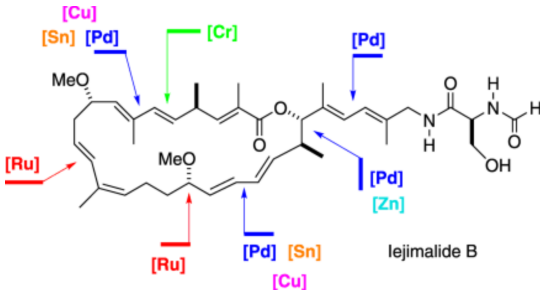
Citation: Chemistry - A European Journal Volume 17, Issue 25, pages 6964–6972

Gram-Scale Synthesis of Iejimalide B

Dr. Julien Gagnepain, Dr. Emilie Moulin, Prof. Alois Fürstner



The delicacy of the polyunsaturated framework of iejimalide B (see figure), a powerful cytotoxic agent of marine origin, made several rounds of careful optimization necessary before the original laboratory synthesis could be scaled up to provide gram amounts of this valuable material. A panopticum of transition-metal-catalyzed transformations made this success possible, amongst which the selective activation of two out of ten different alkenes of the cyclization precursor with the aid of a Grubbs catalyst is most noteworthy.

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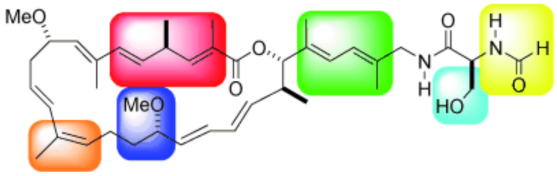
Citation: Chemistry - A European Journal Volume 17, Issue 25, pages 6973–6984

Molecular Editing and Assessment of the Cytotoxic Properties of Iejimalide and Progeny

Dr. Julien Gagnepain, Dr. Emilie Moulin, Dr. Cristina Nevado, Dr. Mario Waser, Dr. Armin Maier, Dr. Gerhard Kelter, Prof. Heinz-Herbert Fiebig, Prof. Alois Fürstner,



An interplay between systematic molecular editing and biological screening led to a series of fully synthetic iejimalide analogues, which show impressive tumor selectivity and a remarkable potency in a tumor-colony assay. Although IC_{50} values as low as ≤1 nM could be reached, preliminary in vivo studies indicate a possible metabolic instability and hence the need for further structural modification.

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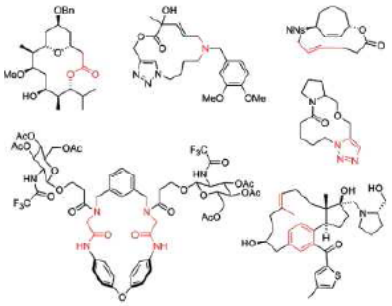
Citation: Masden, C. M.; Clausen, M. H. *European J. Org. Chem.* **2011**, 3107-3115.

Biologically Active Macrocyclic Compounds – from Natural Products to Diversity-Oriented Synthesis

Macrocyclic compounds are attractive targets when searching for molecules with biological activity. The interest in this compound class is increasing, which has led to a variety of methods for tackling the difficult macrocyclization step in their synthesis. This microreview highlights some recent developments in the synthesis of macrocycles, with an emphasis on chemistry developed to generate libraries of putative biologically active compounds.



Examples of synthetic macrocyclic compounds created with various cyclization strategies. This microreview features some recent approaches to the formation of libraries of macrocyclic compounds for biological screening.

The functional groups formed in the macrocyclization step are highlighted in red.

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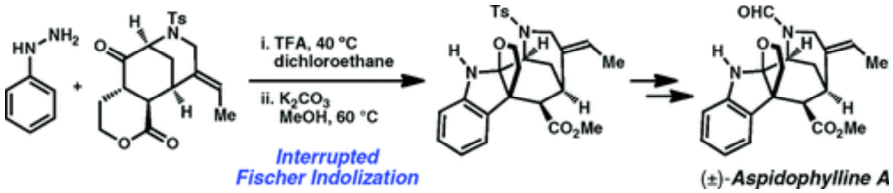
Drug Deliv.
Prostratin

Zu, L.; Boal, B. W.; Garg, N. K. *J. Am. Chem. Soc.* **2011**, *133*, 8877-8879.

Total Synthesis of (±)-Aspidophylline A



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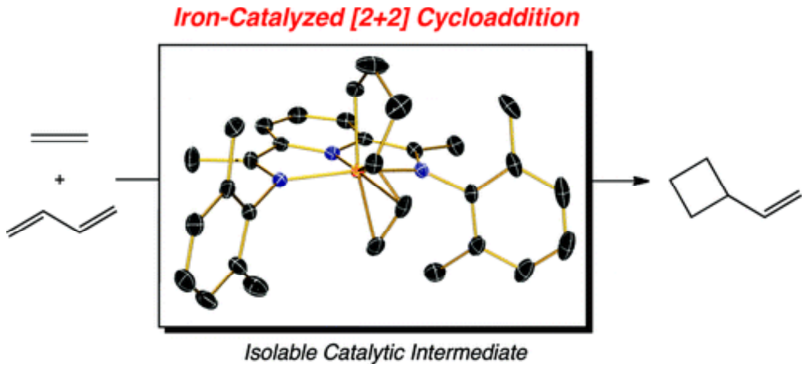
Drug Deliv.
Prostratin

Russell, S. K.; Lobkovsky, E.; Chirik, P. J. *J. Am. Chem. Soc.* **2011**, *133*, 8858-8861.

Iron-Catalyzed Intermolecular [2π + 2π] Cycloaddition



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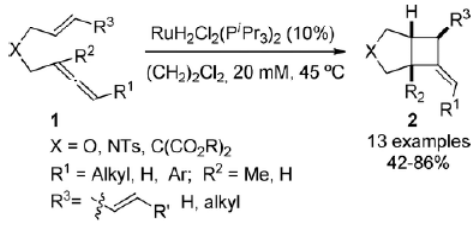
Drug Deliv.
Prostratin

Citation: Gulias,M.; Collado, A.; Trillo, B.; Lopez, F.; Onate, E.; Esteruelas, M.A.; Mascarenas, J.L. *J. Am. Chem. Soc.*, **2011**, *133* (20), pp 7660–7663

Ruthenium-Catalyzed (2 + 2) Intramolecular Cycloaddition of Allenenes



We report a ruthenium-catalyzed (2 + 2) intramolecular cycloaddition of allenes and alkenes. We have found that the use of the ruthenium complex $RuH_2Cl_2(PiPr_3)_2$, which has previously gone unnoticed in catalytic applications, is crucial for the observed reactivity. The reaction proceeds under mild conditions and is fully diastereoselective, providing a practical entry to a variety of bicyclo[3.2.0]heptane skeletons featuring cyclobutane rings.

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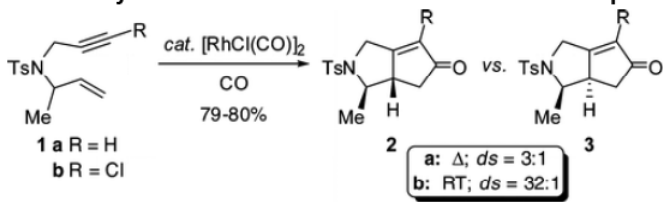
Hybrid
Drug Deliv.
Prostratin

Citation: Baik, M.-H.; Mazumder, S.; Ricci, P.; Sawyer, J.R.; Song, Y.-G.; Wang, H.; Evans, P.A. *J. Am. Chem. Soc.*, **2011**, *133* (20), pp 7621–7623

Computationally Designed and Experimentally Confirmed Diastereoselective Rhodium-Catalyzed Pauson-Khand Reaction at Room Temperature



The computational analysis of the rhodium-catalyzed Pauson-Khand reaction indicates that the key transition state is highly charge-polarized, wherein different diastereoisomers have distinctively different charge polarization patterns. Experimental studies demonstrate that chloro-enynes provide the optimal σ-electron-withdrawing group to promote polarization and thereby reduce the activation barrier to provide a highly diastereoselective reaction at room temperature.

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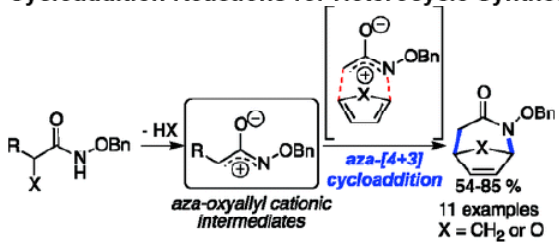
Drug Deliv.
Prostratin

Citation: Jeffrey*, C.S; Barnes, K.L.; Eickhoff, J.A.; Carson, C.R. *J. Am. Chem. Soc.*, **2011**, *133* (20), pp 7688–7691

Generation and Reactivity of Aza-Oxyallyl Cationic Intermediates: Aza-[4 + 3] Cycloaddition Reactions for Heterocycle Synthesis



Aza-[4 + 3] cycloadditions of putative aza-oxyallyl cationic intermediates and cyclic dienes are reported. The intermediate is generated by the dehydrohalogenation of α-haloamides. The reaction is general to a variety of α-haloamides and is diastereoselective. Computational and experimental data suggest that an N-alkoxy substituent stabilizes the aza-oxyallyl cationic intermediate.

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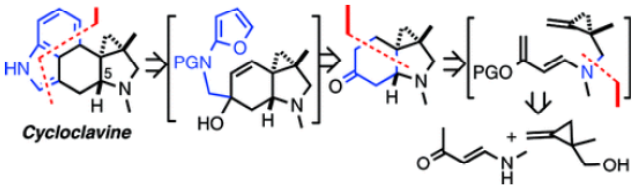
Prostratin

Citation: Petronijevic, F.R.; Wipf, P.* *J. Am. Chem. Soc.*, **2011**, *133* (20), pp 7704–7707

Total Synthesis of (±)-Cycloclavine and (±)-5-epi-Cycloclavine



Key features include the rapid construction of the heterocyclic core segments by two Diels–Alder reactions. An indole annulation was accomplished by a late-stage intramolecular Diels–Alder furan cycloaddition, and a methylenecyclopropane dienophile was used for a stereoselective intramolecular [4 + 2] cycloaddition to give the cyclopropa[c]indoline building block present in cycloclavine.

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Gnid/ Kirk
Laulimalide
Drug Deliv.

Citation: Larsen, A.T.; May, E.M.; Auclair, K. *J. Am. Chem. Soc.*, **2011**, *133* (20), pp 7853–7858

Predictable Stereoselective and Chemoselective Hydroxylations and Epoxidations with P450 3A4

We demonstrate here the utility of a chemical auxiliary to control the selectivity of CYP3A4 reactions. W
linked to substrates, inexpensive, achiral theobromine directs the reaction to produce hydroxylation or
epoxidation at the fourth carbon from the auxiliary with pro-R facial selectivity. This strategy provides a
versatile yet controllable system for regio-, chemo-, and stereoselective oxidations at inactivated C–H
and demonstrates the utility of chemical auxiliaries to mediate the activity of highly promiscuous enzym

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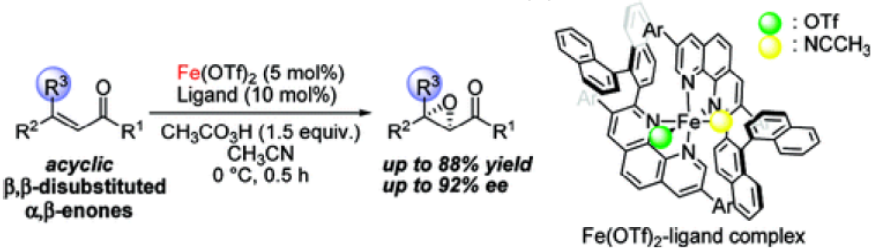
Citation: Nishikawa, Y.; Yamamoto, H.* *J. Am. Chem. Soc.*, **2011**, *133* (22), pp 8432–8435

Iron-Catalyzed Asymmetric Epoxidation of β,β-Disubstituted Enones



The combination of $Fe(OTf)_2$ and novel phenanthroline ligands enables the catalytic asymmetric epoxidation of acyclic β,β-disubstituted enones, which have been a heretofore inaccessible substrate class. The reaction provides highly enantioenriched β,β-epoxyketones (up to 92% ee) that can be further converted to functionalized β-ketoaldehydes with an all-carbon quaternary center.

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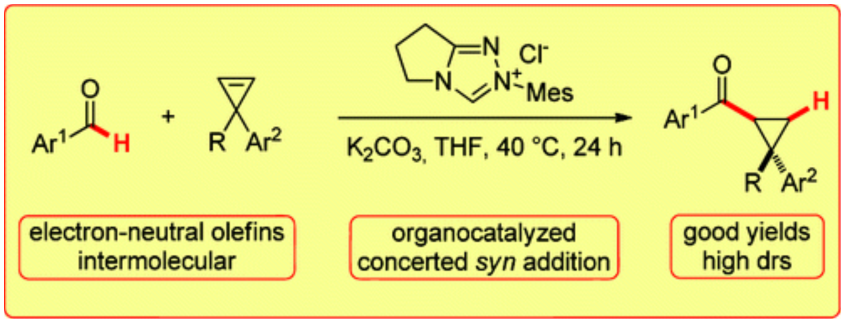
Bugaut, X.; Liu, F.; Glorius, F. *J. Am. Chem. Soc.* **2011**, *133*, 8130-8133.

N-Heterocyclic Carbene (NHC)-Catalyzed Intermolecular Hydroacylation of Cyclopropenes



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Nicolaou, K. C.; Totokotsopoulos, S.; Giguere, D.; Sun, Y. P. *J. Am. Chem. Soc.* **2011**, *133*, 8130-8133.

Total Synthesis of Epicoccin G

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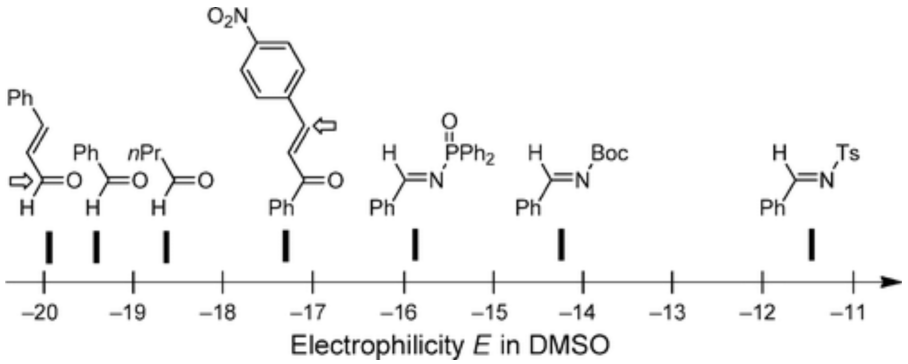
Appel, R.; Mayr, H. *J. Am. Chem. Soc.* **2011**, *133*, 8240-8251.

Quantification of the Electrophilic Reactivities of Aldehydes, Imines, and Enones



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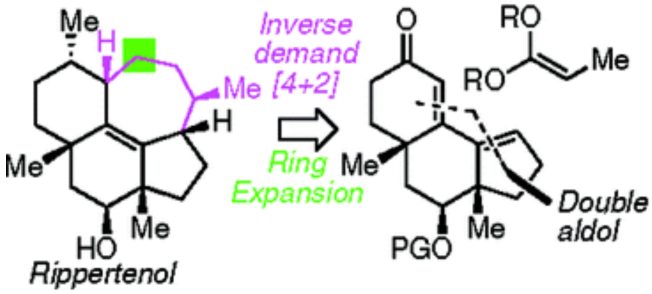
Snyder, S. A.; Wespe, D. A.; von Hof, J. M. *J. Am. Chem. Soc.* **2011**, *133*, 8850-8853.

A Concise, Stereocontrolled Total Synthesis of Rippertenol



- Functionally-deficient terpene synthesized in 19 linear steps
- Highly efficient
- Effective diastereocontrol

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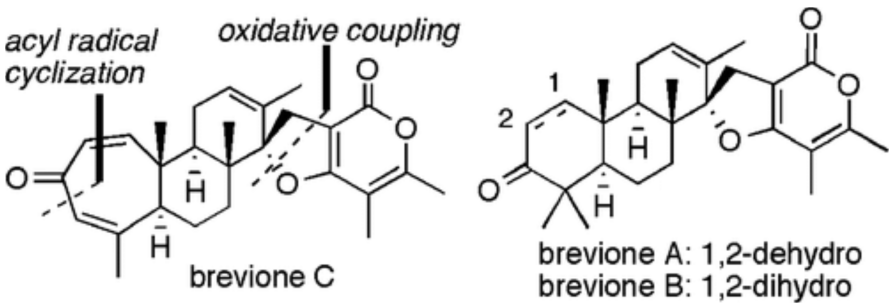
Yokoe, H.; Mitsuhashi, C.; Matsuoka, Y.; Yoshimura, T. *J. Am. Chem. Soc.* **2011**, *133*, 8854-8857.

Enantiocontrolled Total Syntheses of Breviones A, B, and C



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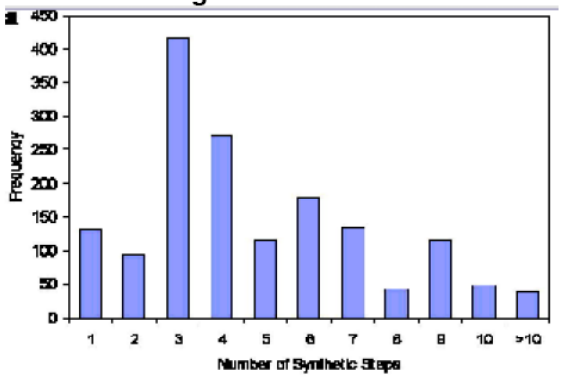
Citation: Roughly, S. D.; Jordan, A. M. *J. Med. Chem.* **2011**, *54* (10), 3451.

The Medicinal Chemist's Toolbox: An Analysis of Reactions Used in the Pursuit of Drug Candidates



Analysis of published reactions from pharmaceutical R&D laboratories at AstraZeneca, GlaxoSmithKline, and Pfizer, spanning a total of 3566 compounds. The reactions were classified based on reaction type, functional groups in the synthesized compounds, and molecular complexity.

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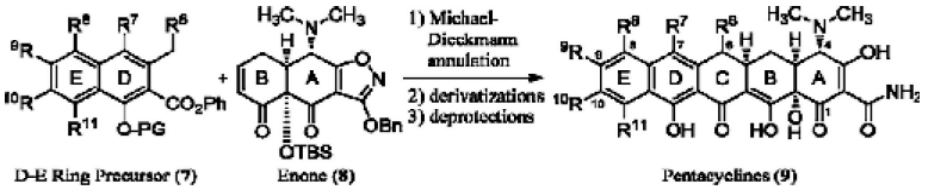
Citation: Sun, C., *et al. J. Med. Chem.* **2011**, *54* (11), 3704.

Synthesis and Antibacterial Activity of Pentacyclines: A Novel Class of Tetracycline Analogs



An efficient total synthetic approach enabled the synthesis and evaluation of novel pentacycline derivatives. Several of the analogs displayed potent activity both *in vitro* and *in vivo*, especially against Gram-positive organisms.

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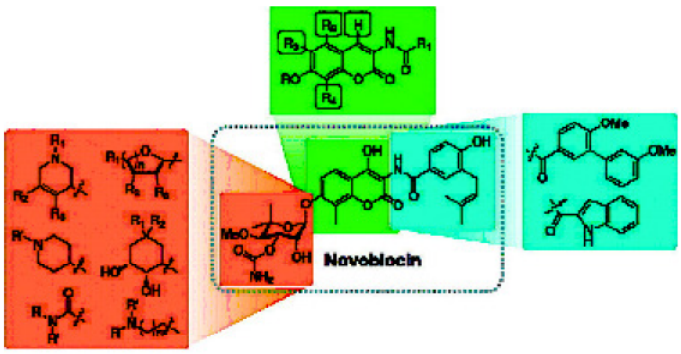
Citation: Zhao, H.; **Donnelly, A. C.**; *et al. J. Med. Chem.* **2011**, *54* (11), 3839.

Engineering an Antibiotic to Fight Cancer: Optimization of the Novobiocin Scaffold to Produce Anti-proliferative Agents



Work done by our own Alison Donnelly! Novobiocin was developed into a selective Hsp90 inhibitor through structural modifications to the amide side chain, coumarin ring, and sugar moiety.

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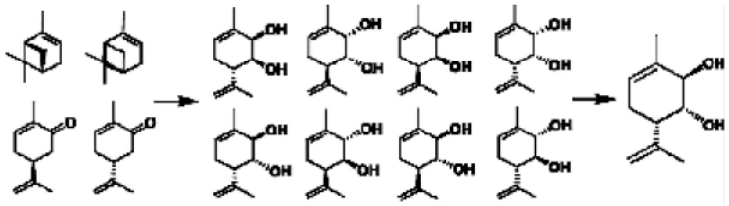
Prostratin

Citation: Ardashov, O. V. *et al. J. Med. Chem.* **2011**, *54* (11), 3866.

Highly Potent Activity of (1*R*, 2*R*, 6*S*)-3-Methyl-6-(prop-1-en-2-yl) cyclohex-3-ene-1,2-diol in Animal Models of Parkinson's Disease



(1R,2R,6S)-3-Methyl-6-(prop-1-en-2-yl)cyclohex-3-ene-1,2-diol possesses potent antiparkinsonian activity in both MPTP and haloperidol animal models. All eight of its stereoisomers have been synthesized and the influence of the absolute configuration on antiparkinsonian activity was shown.

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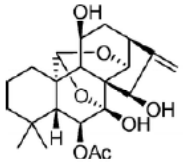
Citation: Zhao, W.; et. al. *J. Nat. Prod*. **2011**, *74*, 1213-1220.

Structure and Cytotoxicity of Diterpenoids from *Isodon adenolomus*

Twelve new diterpenoids, isoadenolins A–L (**1–12**), and 24 known ones were isolated from the aerial parts of *Isodon adenolomus*. Their structures were identified using spectroscopic data, and the absolute configurations of **1** and **14** were determined by single-crystal X-ray diffraction. Selected compounds were evaluated for their in vitro cytotoxicity against human tumor HL-60, SMMC-7721, A-549, MCF-7, and SW-480 cell lines. Compounds **9, 13–16,** and **21** showed significant inhibitory effects on all five cells, with IC_{50} values in the range 0.7–9.7 μM.



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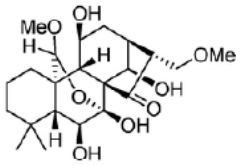

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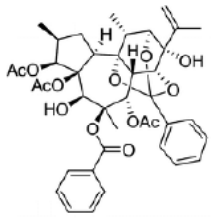
Citation: Dong, S.-H.; Zhang, C.-R.; Xu, C.-H.; Ding, J.; Yue, J.-M. *J. Nat. Prod*. **2011**, *74*, 1255-1261.

Daphnane-Type Diterpenoids from *Trigonostemon howii*

Nine new daphnane-type diterpenoids (**1–9**), named trigohownins A–I, and four known analogues were isolated from *Trigonostemon howii*. Their structures were elucidated on the basis of extensive NMR and MS analyses. Trigohownins A (**1**) and D (**4**) exhibited moderate cytotoxic activity against the HL-60 tumor cell line, with IC_{50} values of 17.0 and 9.3 μM, respectively.



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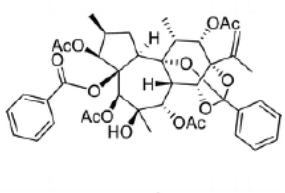

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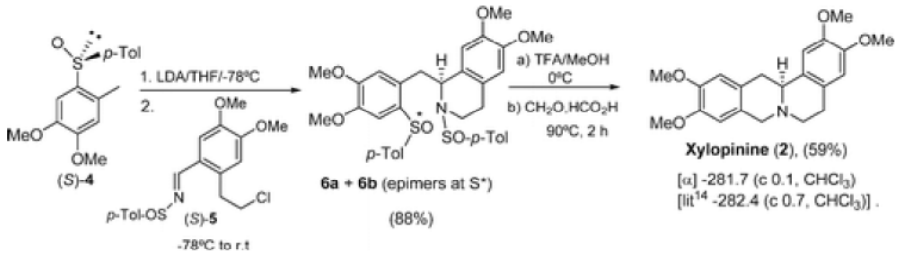
Citation: Virginia M. Mastranzot et al, *J. Org. Chem.*, **2011**, *76* (12) 5036.

Asymmetric Synthesis of (S)-(-)-Xylopinine. Use of the Sulfinyl Group as an Ipso Director in Aromatic SE



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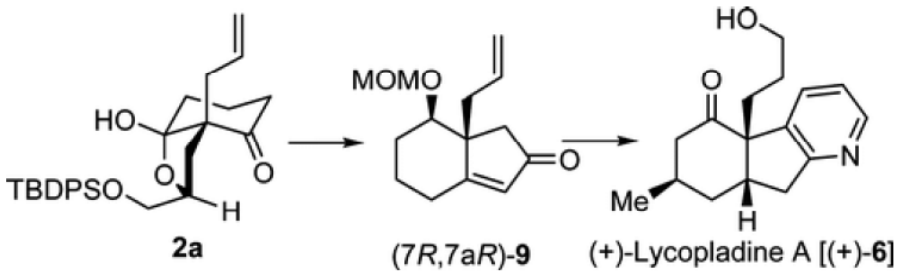
Citation: Kou Hiroya et al, *J. Org. Chem.*, **2011**, *76* (11) 4522.

Total Synthesis of Optically Active Lycopladine A by Utilizing Diastereoselective Protection of Carbonyl Group in a 1,3-Cyclohexanedione Derivative



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mechanism
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Gnid/Kirk
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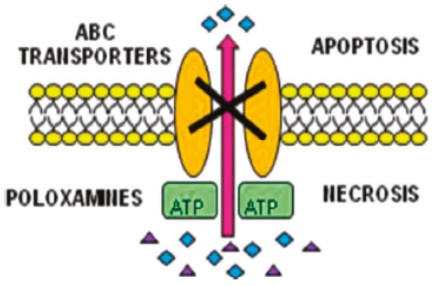
Drug Deliv.
Prostratin

Citation: M. L. Cuestas, A. Sosnik, V. L. Mathet, *Mol. Pharmaceutics* **2011**, ASAP, 10.1021/mp2000132.

Poloxamines Display a Multiple Inhibitory Activity of ATP-Binding Cassette (ABC) Transporters in Cancer Cell Lines

The aim of this study was to investigate the inhibitory effect of different concentrations of pH- and temperature-responsive X-shaped poly(ethylene oxide)-poly(propylene oxide) block copolymers (poloxamines, Tetronic, PEO-PPO) showing a wide range of molecular weights and EO/PO ratios on the functional activity of three different ABC proteins, namely P-glycoprotein (P-gp or MDR1), breast cancer resistance protein (BCRP), and multidrug resistance-associated protein MRP1, in two human hepatocarcinoma cell lines, HepG2 and Huh7.



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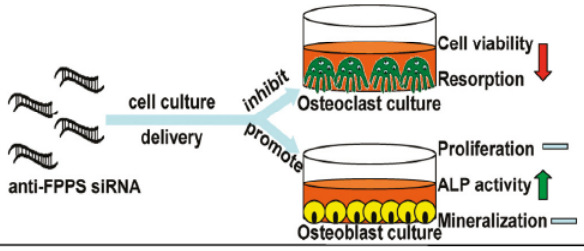
Bryo
Gnid/Kirk
Hybrid
Drug Deliv.
Prostratin

Citation: Y. Wang, A. Panasiuk, D. W. Grainger, *Mol. Pharmaceutics* **2011**, ASAP, 10.1021/mp100374n

Small Interfering RNA Knocks Down the Molecular Target of Alendronate, Farnesyl Pyrophosphate Synthase, in Osteoclast and Osteoblast Cultures

Farnesyl pyrophosphate synthase (FPPS), an enzyme in the mevalonate pathway, is the inhibition target of alendronate, a potent FDA-approved nitrogen-containing bisphosphonate (N-BP) drug, at the molecular level. Alendronate not only inhibits osteoclasts but also has been reported to positively affect osteoblasts. This study assesses the knockdown effects of siRNA targeting FPPS compared with alendronate in both osteoclast and osteoblast cultures.



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Bryo
Gnid/Kirk
Hybrid
Drug Deliv.
Prostratin

Citation: Hudson, J.J.; Kara, D.M.; Smallman, I.J.; Sauer, B.E.; Tarbutt, M.R.; Hinds, E.A. *Nature* **2011**, *473*, 493-495.

Improved Measurement of the Shape of the Electron

I had never really thought about the shape of an electron or considered it to be anything other than spherical... and I guess according to this study with their precise measurements it is.

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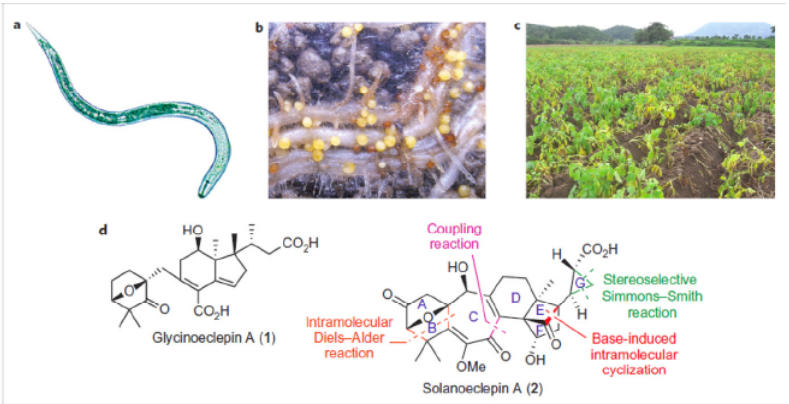
Citation: Tanino and Miyashita, et al *Nature Chem* **2011**, 484

Total synthesis of solanoeclepin A



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Bryo
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Carbazole
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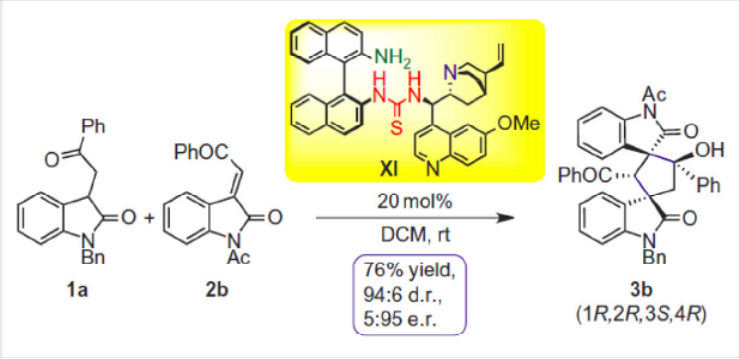
Drug Delivery
INITIALS

Citation: Barbas, C. F. et. al. *Nature Chem* **2011**, 473

Construction of bispirooxindoles containing three quaternary stereocentres in a cascade using a single multifunctional organocatalyst



bioorg
asymmetric
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synthesis
mechanism
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Bryo
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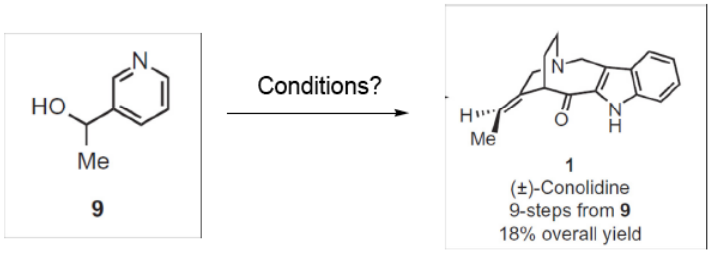
Carbazole
Apop
Gnid/ Kirk
Drug Delivery
INITIALS

Citation: Micalizio, G. C. et. al. *Nature Chem.* **2011**, 449

Synthesis of conolidine, a potent non-opioid analgesic for tonic and persistent pain



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Bryo
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Apop
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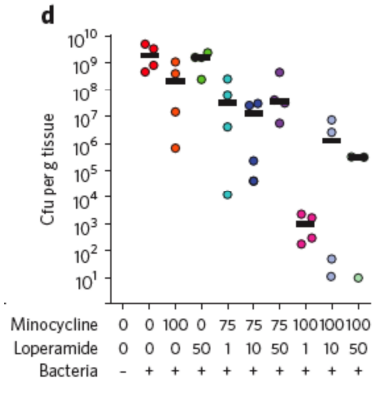
Drug Delivery
INITIALS

Citation: Linda Ejim, Maya Farha, Shannon Falconer, Mike Tyers, Eric Brown & Gerard Wright *et al.* *Nature Chem. Biol.* **2011**, *7*, 348.

Combinations of antibiotics and nonantibiotic drugs enhance antimicrobial efficacy

Combinations of antibiotics are commonly used in medicine to broaden antimicrobial spectrum and generate synergistic effects. Alternatively, combination of nonantibiotic drugs with antibiotics offers an opportunity to sample a previously untapped expanse of bioactive chemical space. We screened a collection of drugs to identify compounds that augment the activity of the antibiotic minocycline. Unexpected synergistic drug combinations exhibited *in vitro* and *in vivo* activity against bacterial pathogens, including multidrug–resistant isolates.



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Drug Deliv.
Prostratin

Citation: http://www.nytimes.com/2011/06/14/health/research/14patterns.html?_r=1&src=me&ref=health

Patterns: Prenatal Vitamins May Ward Off Autism

"A new study reports mothers of children with autism and autism spectrum disorders were significantly less likely than mothers of children without autism to have taken prenatal vitamins three months before conception and in the first month of pregnancy."

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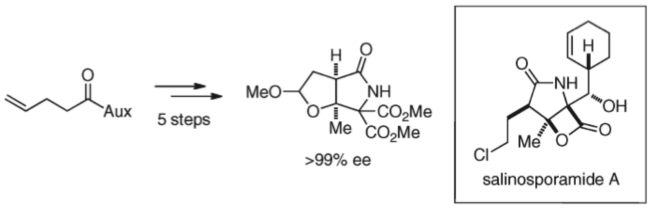
Satoh, N.; Yokoshima, S.; Fukuyama, T. *Org. Lett.* **2011**, *13*, 3028-3031.

Total Synthesis of (-)-Salinosporamide A



A concise and stereoselective total synthesis of (-)-salinosporamide A (**1**), a potent inhibitor of the 20S proteasome that is in clinical development as an anticancer drug candidate, has been accomplished in 14 steps with 19% overall yield from 4-pentenoic acid. Our synthesis features a stereoselective alkylation utilizing a chiral auxiliary, formation of a pyrrolidine unit, and oxidation of the pyrrolidine to a γ-lactam. To demonstrate the scalability of our synthesis, (-)-salinosporamide A has been synthesized on a gram scale.

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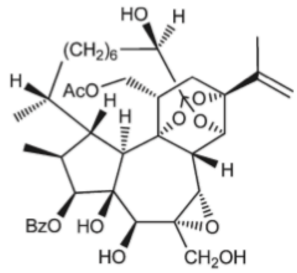
Asada, Y.; *et al*. *Org*. *Lett*. **2011**, *13*, 2904-2907.

Stelleralides A-C, Novel Potent Anti-HIV Daphnane-Type Diterpenoids from *Stellera chamaejasme* L.



4 Stelleralide A

Three novel 1-alkyldaphnane-type diterpenes, stelleralides A–C (**4**–**6**), and five known compounds were isolated from the roots of *Stellera chamaejasme* L. The structures of **4**–**6** were elucidated by extensive spectroscopic analyses. Several isolated compounds showed potent anti-HIV activity. **Compound 4 showed extremely potent anti-HIV activity (EC_{90} 0.40 nM)** with the lowest cytotoxicity (IC_{50} 4.3 μM) and appears to be a promising compound for development into anti-AIDS clinical trial candidates.

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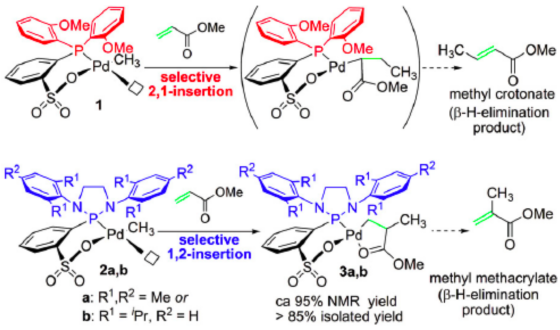
Drug Deliv.
Prostratin

Citation: Philipp Wucher, Lucia Caporaso, Philipp Roesle, Francesco Ragone, Luigi Cavallo, Stefan Mecking, *et al.* *Proceedings of the National Academy of Sciences,* **2011**, *108*, 8955.

Breaking the regioselectivity rule for acrylate insertion in the Mizoroki–Heck reaction



In modern methods for the preparation of small molecules and polymers, the insertion of substrate carbon–carbon double bonds into metal–carbon bonds is a fundamental step of paramount importance.In a combined experimental and theoretical study, we now report that, by destabilizing the transition state of 2,1-insertion via steric interactions, the regioselectivity of methyl acrylate insertion into palladium–methyl and phenyl bonds can be inverted entirely to yield the opposite "regioirregular" products in stoichiometric reactions.

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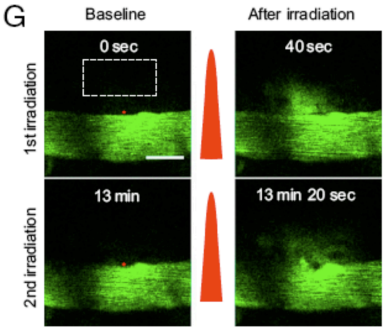
Citation: Myunghwan Choi, Taeyun Kub, Kyuha Chong, Jonghee Yoon, and Chulhee Choi *Proceedings of the National Academy of Sciences,* **2011**, *108*, 9256.

Minimally invasive molecular delivery into the brain using optical modulation of vascular permeability

Systemic delivery of bioactive molecules in the CNS is hampered by the blood–brain barrier, which has bottlenecked noninvasive physiological study of the brain and the development of CNS drugs. Here we report that irradiation with an ultrashort pulsed laser to the blood vessel wall induces transient leakage of blood plasma without compromising vascular integrity. By combining this method with a systemic injection, we delivered target molecules in various tissues, including the brain cortex. This tool allows minimally invasive local delivery of chemical probes, nanoparticles, and viral vectors into the brain cortex.



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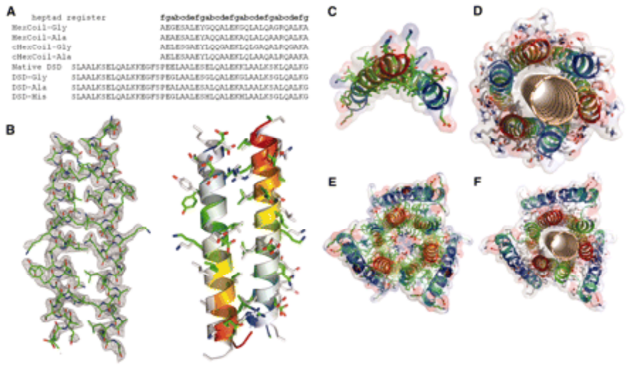
Citation: Grigoryan, G.; DeGrado, W.F. *et al. Science* **2011**, *332*, 1071-1076.

Computational Design of Virus-Like Protein Assemblies on Carbon Nanotube Surfaces



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Citation: Wolfe-Simon, F.; Oremland, R.S. *et al. Science* **2011**, *332*, 1163-1166.

A Bacterium That Can Grow by Using Arsenic Instead of Phosphorus

This is that article about bacteria that can grow in arsenic and incorporate it into their genetic material... it took a long time to come out because of the surrounding controversy. What do you think? Is it for real?

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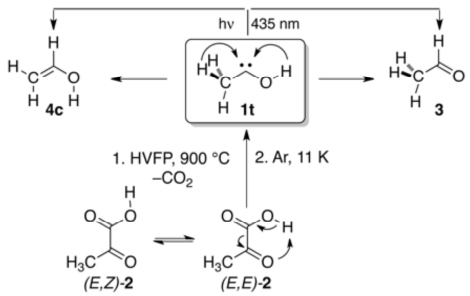
Citation: Schreiner, P.R.; Reisenauer, H.P.; Ley, D.; Gerbig, D.; Wu, C.; Allen, W.D. *Science* **2011**, *332*, 1300-1303.

Methylhydroxycarbene: Tunneling Control of a Chemical Reaction



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Citation: Nakagawa-G.; K., Crimmins, M. T., *Syn*. *Lett*. **2011**, 1413-1418.

Formal Synthesis of the Bryostatin Northern Hemisphere: Asymmetric Synthesis of the B ring and C1-C9 Fragment

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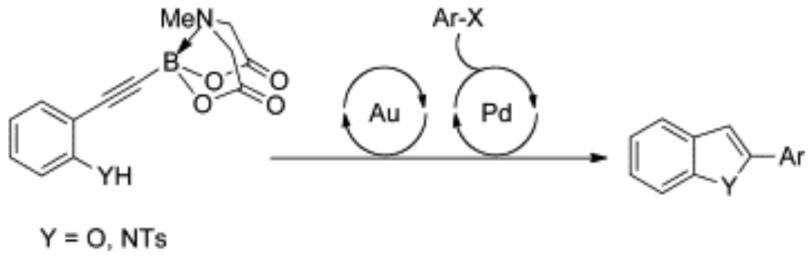
Citation: Chan, J. M. W.; Amarante, G. W.; Toste, F. D., *Tetrahedron*. **2011**, 67, 4306-4312.

Tandem cycloisomerization/Suzuki coupling of arylethynyl MIDA boronates



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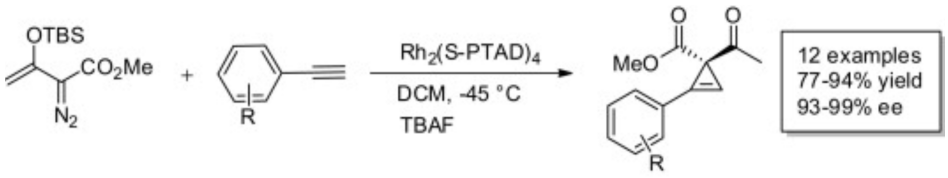
Citation: Briones, J. F.; Davies, H., M. L., *Tetrahedron*. **2011**, 67, 4312-4317..

Rh_2(S-PTAD)$_4$-catalyzed asymmetric cyclopropenation of aryl alkynes



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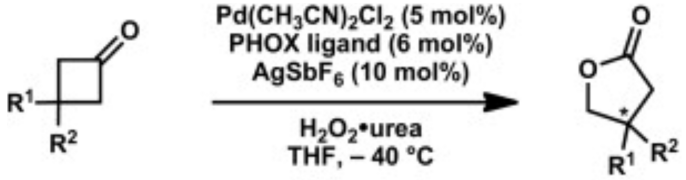
Citation: Petersen, K. S.; Stoltz, B. M., *Tetrahedron*. **2011**, 67, 4352-4357

Palladium-Catalyzed, asymmetric Baeyer-Villiger oxidation of prochiral cyclobutanones with PHOX ligands



ee up to 81%
yield up to 99%
(ee ≥93% after recrystallization)

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Citation: Denmark, S. E.; Smith, R. C.; Chang, W-T. T., *Tetrahedron*. **2011**, 67, 4391-4396.

Probing the electronic demands of transmetalation in the palladium-catalyzed cross-coupling of arylsilanolates

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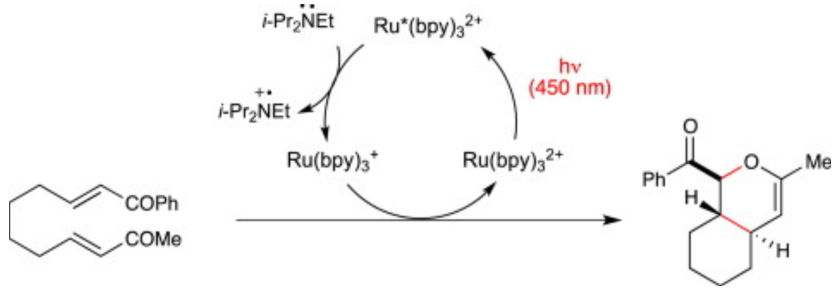
Citation: Hurtley, A. E.; Cismesia, M. A.; Ischay, M. A.; Yoon, T. P., *Tetrahedron*. **2011**, 67, 4442-4448

Visislbe light photocatalysis of radical anion hetero-Diels-Alder cycloadditions



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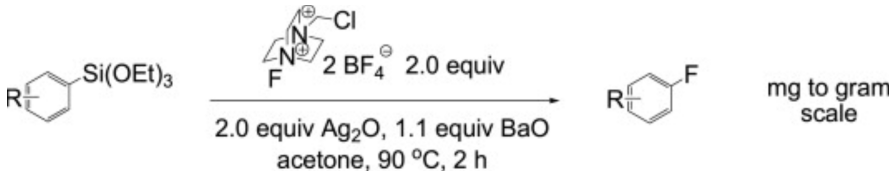
Citation: Tang, P.; Ritter, T., *Tetrahedron*. **2011**, 67, 4449-4454.

Silver-Mediated fluorination of aryl silanes



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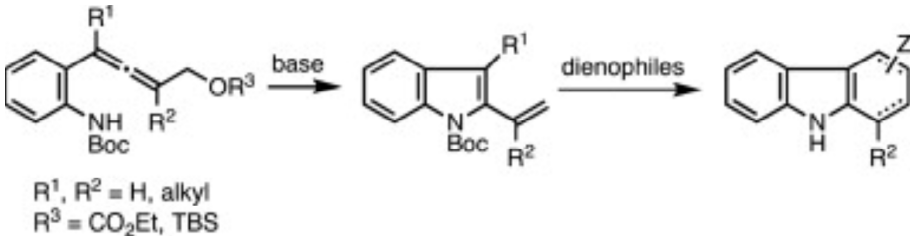
Hybrid
Drug Deliv.
Prostratin

Citation: Mohamed, Y. S. M.; Inagaki, F.; Takahashi, R.; Mukai, C., *Tetrahedron*. **2011**, 67, 5133-5141.

A new procedure for the preparation of 2-vinylindoles and their [4+2] cycloaddition reaction



R^1, R^2 = H, alkyl
R^3 = CO_2Et, TBS

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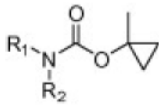
Citation: Erick J. Snider, Stephen W. Wright, *Tetrahedron Lett.* **52** (2011) 3171.

The (1-methyl)cyclopropyloxycarbonyl (MPoc) carbamate: a new protecting group for amines



The (1-methyl)cyclopropyl carbamate (MPoc) group represents a new and useful protecting group for amines. It is orthogonal to the commonly used BOC, Cbz, and FMOC groups. It is cleaved by exposure to hypobromous acid or upon hydrogenolysis over palladium at 80 °C.

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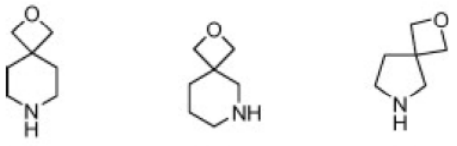
Citation: Ruo Xu et al. *Tetrahedron Lett.* **52** (2011) 3266.

An improved synthesis of 2-oxa-7-azaspiro[3,5]nonane and analogs as novel reagents in medicinal chemistry



1a **2a** **3a**

A detailed synthesis of novel spirocyclic oxetane analogs is described for the first time.

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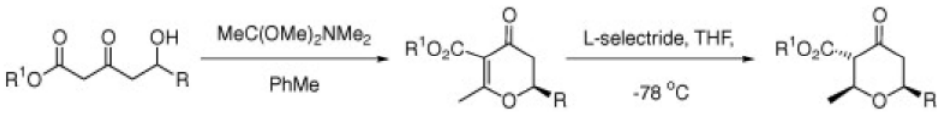
Citation: Paul A. Clarke et al, *Tetrahedron Lett.* **52** (2011) 3654.

Diastereoselective synthesis of functionalized 2-methyltetrahydropyran-4-ones



A simple procedure for the synthesis of functionalized 2-methyl-2,3-dihydropyran-4-ones, based on the Maitland–Japp reaction, and their diastereoselective conversion into functionalized 2-methyltetrahydropyran-4-ones has been developed. This allows access to a structural unit present in a large number of biologically active natural products, and has been successfully applied to the synthesis of the molecule found in Civet cat secretion.

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