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Tetrahedron Letters	**MOOK**	Matt Stevens

Next Due Date: Wednesday, February 15, 2017

Instructions for Authors (*Volume 1)*

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.

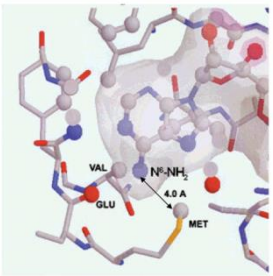
Include a brief textual summary of the article; an example of a completed abstract is shown below. The list of topics and subgroups on the right is useful to highlight which subgroups should pay attention to your abstract and roughly what kind of chemistry the article contains.

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

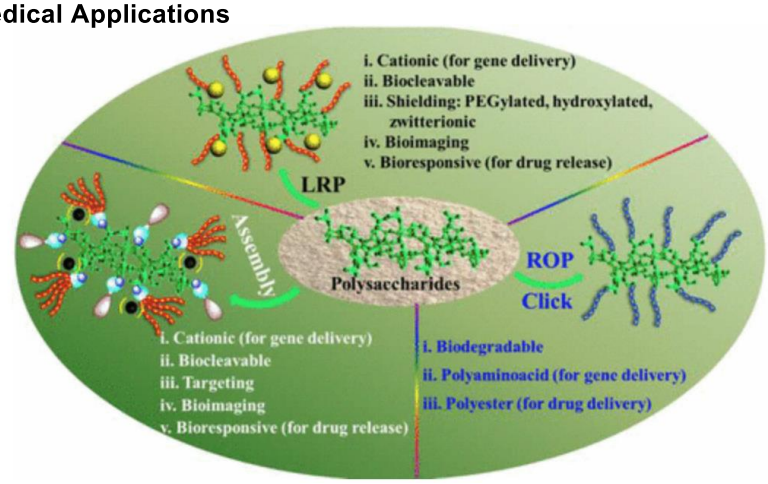
DON'T BE A MOOK!

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: Hu, Y; Li, Y; Xu, F-J.; *Acc. Chem. Res.* **2017**, **ASAP**

Versatile Functionalization of Polysaccharides via Polymer Grafts: From Design to Biomedical Applications



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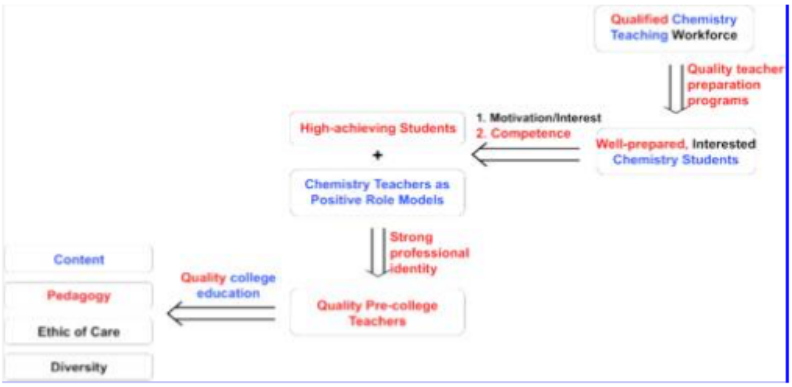
Citation: ACS Cent. Sci. 2016, 2 (11), 825–833 DOI: 10.1021/acscentsci.6b00216.

Setting a Standard for Chemistry Education in the Next Generation: A Retrosynthetic Analysis.



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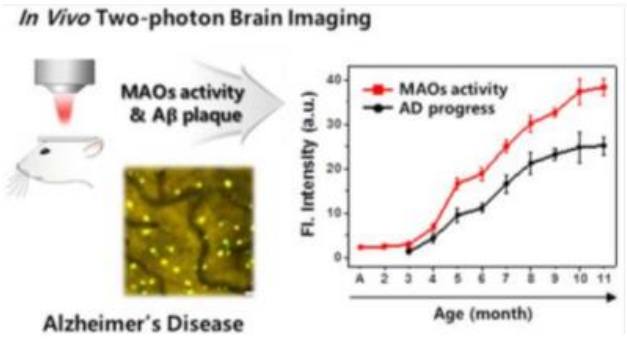
Citation: ACS Cent. Sci. 2016, 2 (12), 967–975 DOI: 10.1021/acscentsci.6b00309.

Close Correlation of Monoamine Oxidase Activity with Progress of Alzheimer's Disease in Mice, Observed by in Vivo Two-Photon Imaging.



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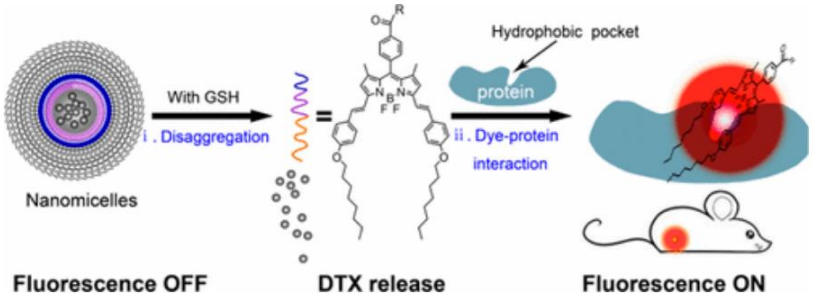
Citation: Liu, X. et. al, *ACS Nano,* **2016**, 10, 11385-11396.

Redox-Activated Light-Up Nanomicelle for Precise Imaging-Guided Cancer Therapy and Real-Time Pharmacokinetic Monitoring



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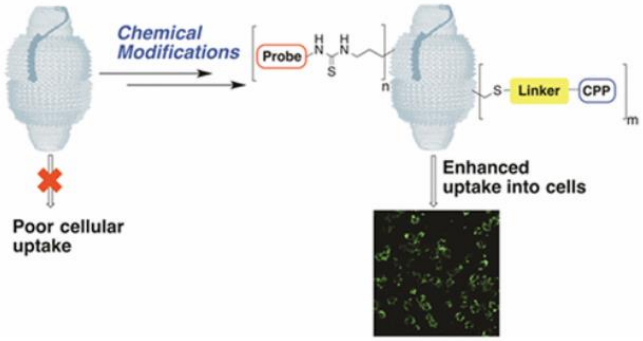
Citation: Benner, N. L.; Zang, X.; Buehler. D. C.; Kickhoefer, V.A.; Rome, M.E.; Rome, L.H.; Wender, P.A. *ACS Nano,* **2017**, *ASAP*

Vault Nanoparticles: Chemical Modifications for Imaging and Enhanced Delivery



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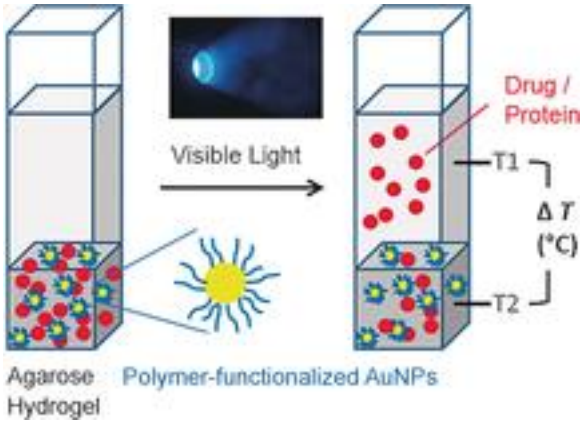
Citation: Basuki, J. S. et al. *Angew. Chem. Int. Ed.* **2017**, *56*, 966 - 971.

Photo-Modulated Therapeutic Protein Release from a Hydrogel Depot Using Visible Light



A light-triggered drug delivery system based on photo-thermal interactions of polymer-coated gold nanoparticles (AuNPs) inside an agarose hydrogel was developed. Localized temperature increase induced by visible-light exposure causes reversible softening of the hydrogel matrix to release the pre-loaded therapeutics. The biological activity of the released biomolecular drug was still highly retained.

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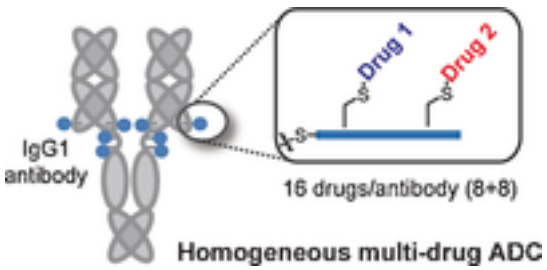
Citation: Levengood, M. R. et al. *Angew. Chem Int. Ed.* **2017**, *56*, 733 - 737.

Orthogonal Cysteine Protection Enables Homogeneous Multi-Drug Antibody–Drug Conjugates



Two is better than one: A general method for the preparation of homogeneous antibody–drug conjugates (ADCs) containing multiple payloads has been developed. This approach utilizes sequential unmasking of cysteine residues to enable site-specific conjugation of each drug. Dual-drug ADCs prepared through this approach had improved anticancer activities compared to single-drug ADCs.

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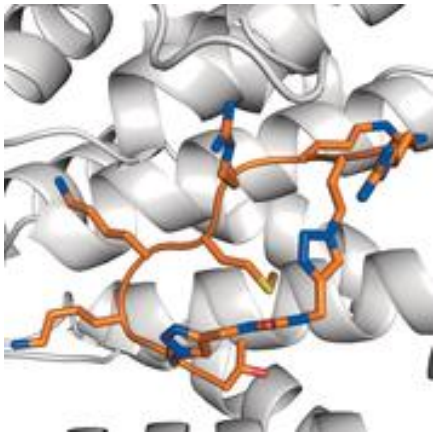
Citation: Wiedmann, M. M. et al. *Angew. Chem Int. Ed.* **2017**, *56*, 524-529.

Development of Cell-Permeable, Non-Helical Constrained Peptides to Target a Key Protein–Protein Interaction in Ovarian Cancer



Import ban: The transcription factor HNF1Œ is ubiquitously overexpressed in ovarian clear cell carcinoma. Guided by X-ray crystallographic data and molecular dynamics simulations, cell-permeable, non-helical constrained proteomimetics (orange) were designed to target the HNF1β-importin, α protein-protein interaction and thereby inhibit the nuclear import of HNF1β. This general approach may be extended to other transcription factors.

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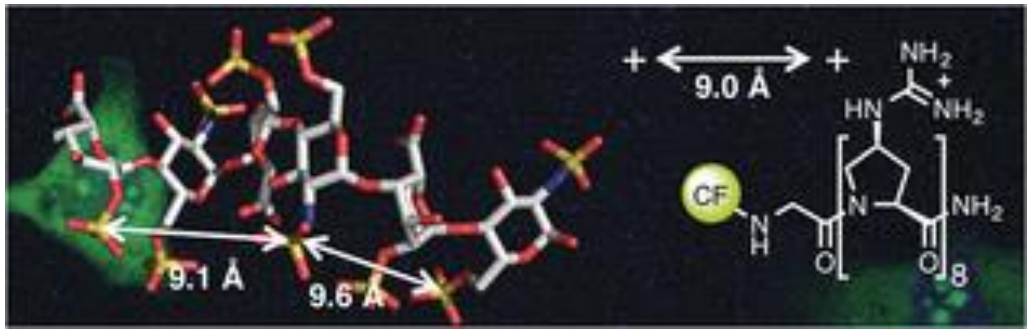
Citation: Nagel, Y. A. et al. *Angew. Chem Int. Ed.* **2017**, *56*, 122 - 126.

Effect of Preorganized Charge-Display on the Cell-Penetrating Properties of Cationic Peptides



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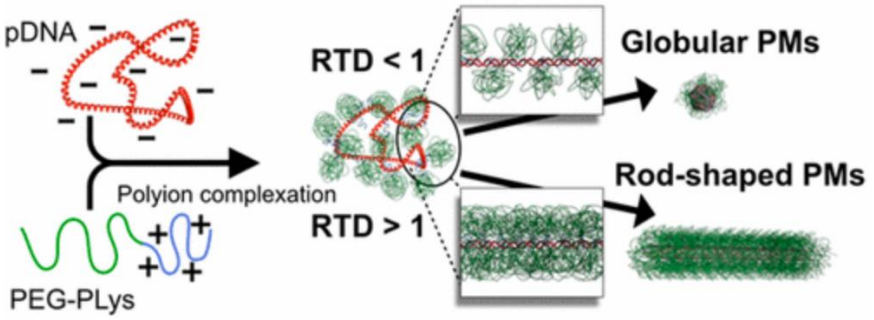
Citation: Takeda, A.M. et al.. *Biomacromolecules* **2017**, 18(1), 36-43

Poly(ethylene glycol) Crowding as Critical Factor To Determine pDNA Packaging Scheme into Polyplex Micelles for Enhanced Gene Expression



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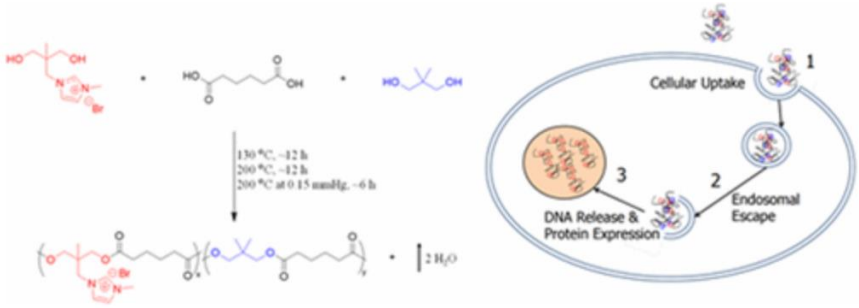
Citation: Nelson, A.M. et al.. *Biomacromolecules* **2017**, 18(1), 68-76

Synthesis of Water-Soluble Imidazolium Polyesters as Potential Nonviral Gene Delivery Vehicles



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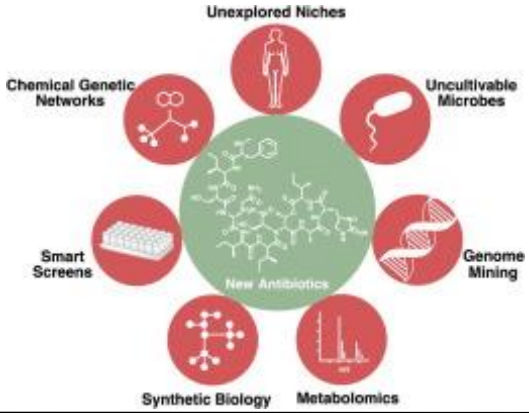
Citation: Wencewicz, T. A. et al. *Bioorg. Med. Chem.* **2016**, *24*, 6227-6252.

New antibiotics from Nature's chemical inventory



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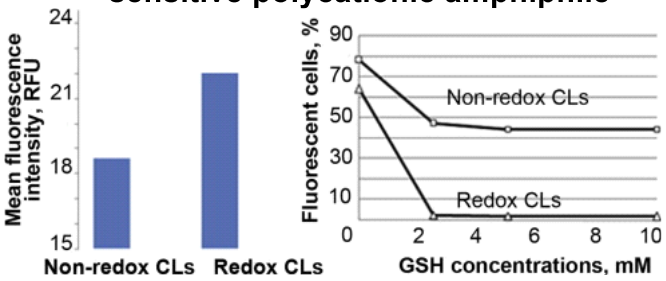
Citation: Puchkov, P. A. *et al*. *Bioorg. Med. Chem. Lett.* **2016**, *26*, 5911.

Design, synthesis and transfection efficiency of a novel redox-sensitive polycationic amphiphile



A novel redox-sensitive polycationic amphiphile with disulphide linkers for nucleic acid delivery was developed. Cationic liposomes (CLs) formed with the helper lipid DOPE demonstrated effective DNA delivery into HEK293 cells with a maximal transfection activity that is superior than both nonredox-sensitive cationic liposomes and Lipofectamine® 2000 at an N/P ratio of 6/1. Redox-sensitivity was tested by experiments with extracellular glutathione which shown the ability of disulphide linker degradation.

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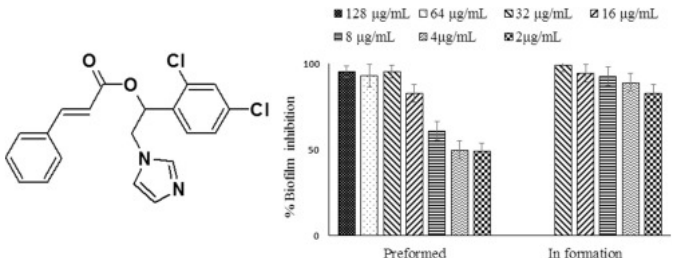
Citation: De Vita, D., *et al*. *Bioorg. Med. Chem. Lett.* **2016**, *26*, 5931.

Exploring the anti-biofilm activity of cinnamic acid derivatives in Candida albicans



The authors synthesized a series of cinnamoyl ester and amide derivatives in order to evaluate them for the activity against *C. albicans* biofilm and planktonically grown cells. The most active compounds showed >50% biofilm inhibition concentrations (BMIC50) of 2 µg/mL and 4 µg/mL respectively, against *C. albicans* biofilm formation.

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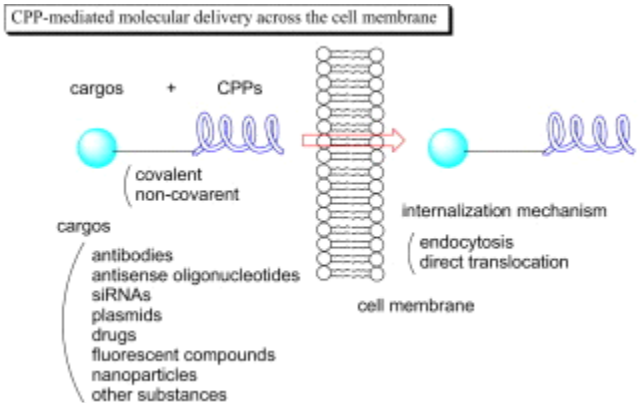
Citation: Tashima, T. *Bioorg. Med. Chem. Lett.* **2017**, *27*, 121.

Intelligent substance delivery into cells using cell-penetrating peptides



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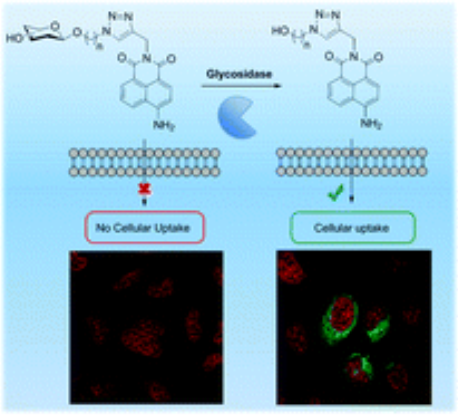
Citation: Calatrava-Perez, E., *et al. Chem Commun.* **2016**, *52,* 13086.

Glycosidase activated release of fluorescent 1,8-naphthalimide probes for tumor cell imaging from glycosylated 'pro-probes'



Glycosylated 4-amino-1,8-naphthalimide derivatives possess a native glycosidic linkage that can be selectively hydrolysed in situ by glycosidase enzymes to release the naphthalimide as a fluorescent imaging or therapeutic agent. In vitro studies using a variety of cancer cell lines demonstrated that the naphthalimides only get taken up into cells upon enzymatic cleavage from the glycan unit; a mechanism that offers a novel approach for the targeted delivery of probes/drugs.

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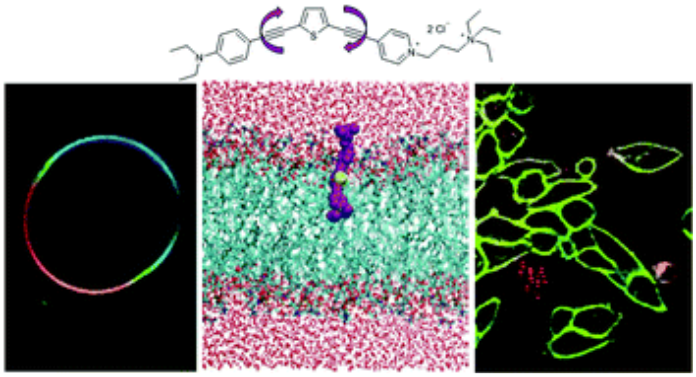
Citation: Dent, M. R. *et al. Chem. Commun.* **2016**, *52,* 13269.

Imaging plasma membrane phase behaviour in live cells using a thiophene-based molecular rotor



Molecular rotors have emerged as versatile probes of microscopic viscosity in lipid bilayers. Here, we investigate the use of a membrane-targeting viscosity-sensitive fluorophore based on a thiophene moiety with equal affinity for ordered and disordered lipid domains to probe ordering and viscosity within artificial lipid bilayers and live cell plasma membranes.

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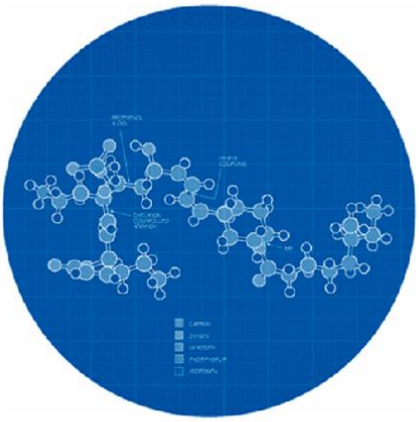
Citation: Trost, B. M.; Knopf, J. D.; Brindle, C. S. *Chem. Rev.* **2016**, *116*, 15035-15088

Synthetic Strategies Employed for the Construction of Fostriecin and Related Natural Products

Fostriecin and related natural products present a significant challenge for synthetic chemists due to their structural complexity and chemical sensitivity. This review will chronicle the successful efforts of synthetic chemists in the construction of these biologically active molecules. Key carbon–carbon bond forming reactions will be highlighted, as well as the methods used to install the numerous stereocenters present in this class of compounds.



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Citation: Takahashi, K.; et al. *Chem. Sci.* **2017**, 8, 101-107

Selective synthesis of unsymmertric dibenzo[a,e] pentalenes by a rhodium-catalysed stitching reaction

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Citation: Pillow, T. H.; et al. *Chem. Sci.* **2017**, 8, 366-370

Decoupling stability and release in disulfide bonds with antibody-small molecule conjugates

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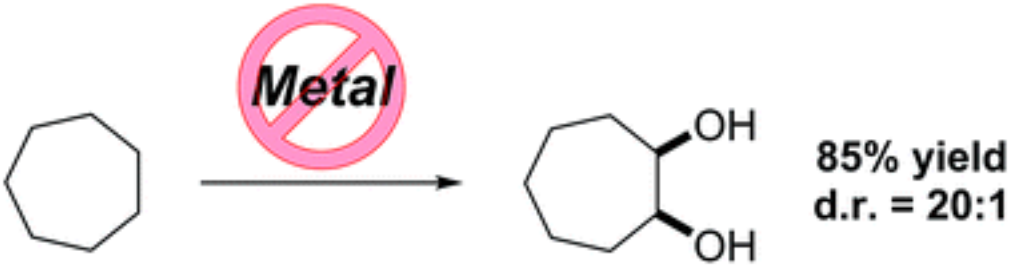
Citation: Bering, L.; et al. *Chem. Sci.* **2017**, 8, 452-457

Selective transition-metal-free vicinal *cis*-dihydroxylation of saturated hydrocarbons



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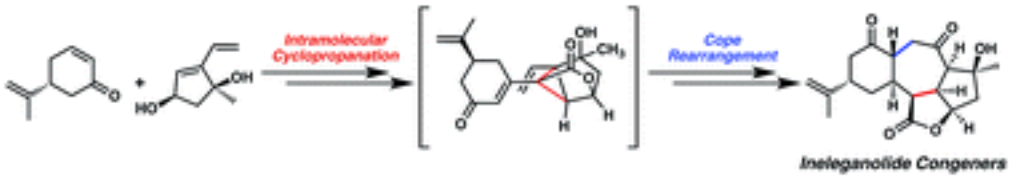
Citation: Craig, R. A.; et al. *Chem. Sci.* **2017**, 8, 507-514

Enantioselective, convergent synthesis of the ineleganolide core by a tandem annulation cascade



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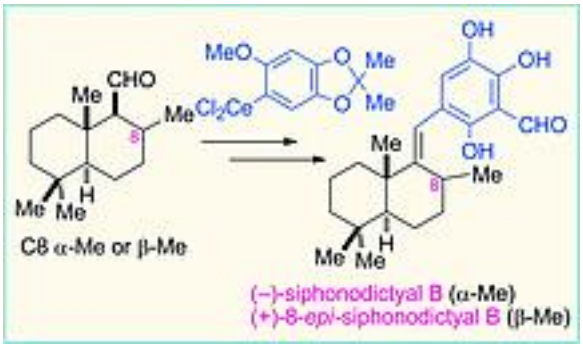
Citation: Kikuchi, T.; et al. *Eur. J. Org. Chem.* **2016**, 34, 5659-5666

Enantioselective Total Synthesis of (-)-Siphonodictyal B and (+)-8-*epi*-Siphonodictyal B with Phosphatidylinositol 3-Kinase α (PI3Kα) Inhibitory Activity



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Citation: Verlinden, S.; et al. *Eur. J. Org. Chem.* **2016**, 35, 5807-5812

Synthesis of Heterocycle-Bridged Peptidic Macrocycles through 1,3-Diyne Transformations

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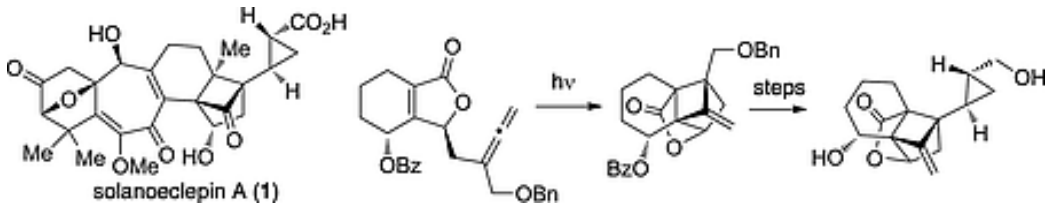
Citation: Lutteke, G.; et al. *Eur. J. Org. Chem.* **2016**, 35, 5845-5854

Enantioselective Approach to the Right-Hand Substructure of Solanoeclepin A



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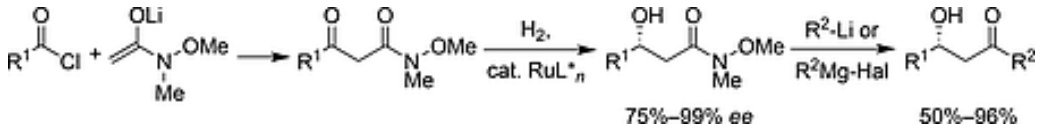
Citation: Diehl, J.; et al. *Eur. J. Org. Chem.* **2017**, 2, 278-286

Synthesis of Enantiomerically Pure β-Hydroxy Ketones via β-Keto Weinreb Amides by a Condensation/Asymmetric-Hydrogenation/Acylation Sequence



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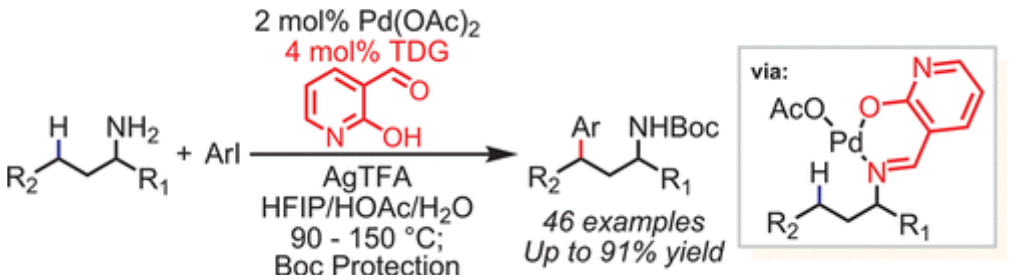
Citation: Yongwei Wu, Yan-Qiao Chen, Tao Liu, Martin D. Eastgate, and Jin-Quan Yu
Journal of the American Chemical Society 2016 138 (44), 14554-14557

Pd-Catalyzed gamma-C(sp3)–H Arylation of Free Amines Using a Transient Directing Group



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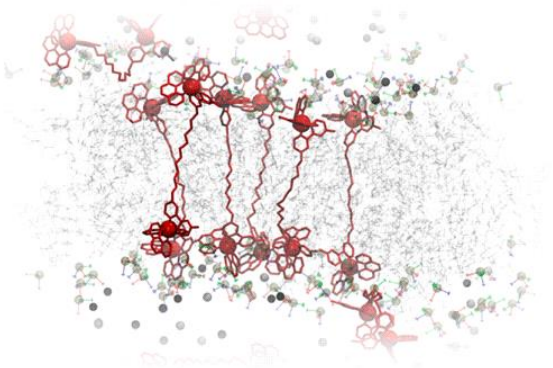
#C-H activation

Citation: Daniel K. Weber, Marc-Antoine Sani, Matthew T. Downton, Frances Separovic, F. Richard Keene, and J. Grant Collins Journal of the American Chemical Society 2016 138 (46), 15267

Membrane Insertion of a Dinuclear Polypyridylruthenium(II) Complex Revealed by Solid-State NMR and Molecular Dynamics Simulation: Implications for Selective Antibacterial Activity



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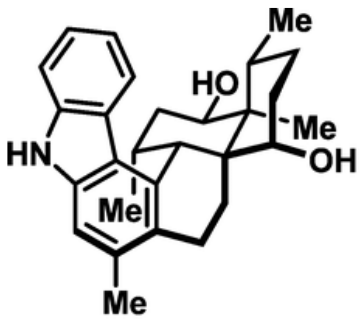
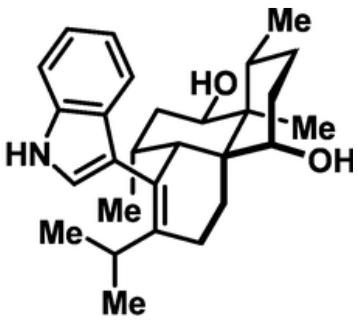
Citation: Hailong Li, Qifeng Chen, Zhaohong Lu, and Ang Li
Journal of the American Chemical Society 2016 138 (48), 15555-15558

Total Syntheses of Aflavazole and 14-Hydroxyaflavinine



aflavazole



14-hydroxyaflavinine

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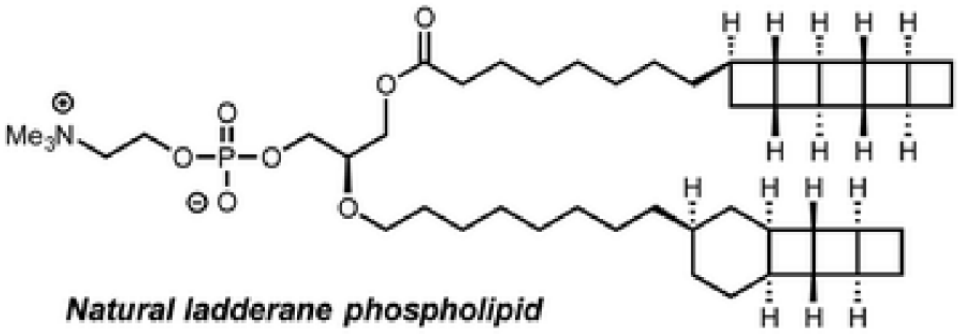
Citation: *JACS,* **2016,** *138,* 15845.

Chemical Synthesis and Self-Assembly of a Ladderane Phospholipid

Burns paper



Natural ladderane phospholipid

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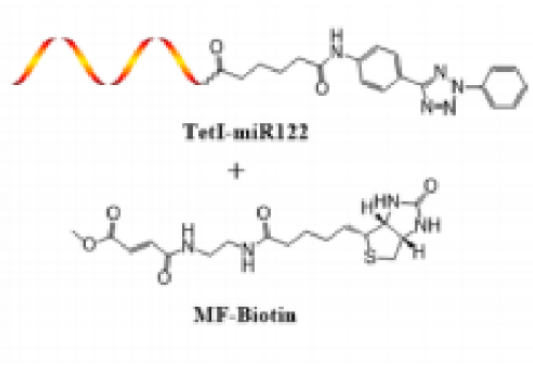
Citation: *JACS*, **2016,** *138,* 15943.

Photoclickable MicroRNA for the Intracellular Target Identifiaciton of microRNAs.



Pretagged miRNAs keep the intracellular function of miRNAs and allow the addition of molecular handles through photoclick reaction. The photoclickable miRNAs upon transfection inside cells were able to form functional complexes with target genes and repress target gene expression. Target genes associated with the photoclickable miRNAs in the complexes were then tagged with the molecular handle through photoclick reaction for upll-down and identification. A biotin handle was atached through a tetrazole-ene photoclick reaction.

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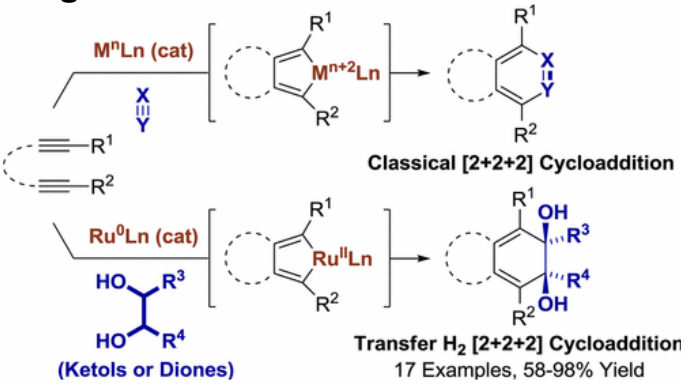
Citation: Hiroki Sato, Matthias Bender, Weijie Chen, and Michael J. Krische
Journal of the American Chemical Society 2016 138 (50), 16244-16247

Diols, a-Ketols, and Diones as 22p Components in [2+2+2] Cycloadditions of 1,6-Diynes via Ruthenium(0)-Catalyzed Transfer Hydrogenation



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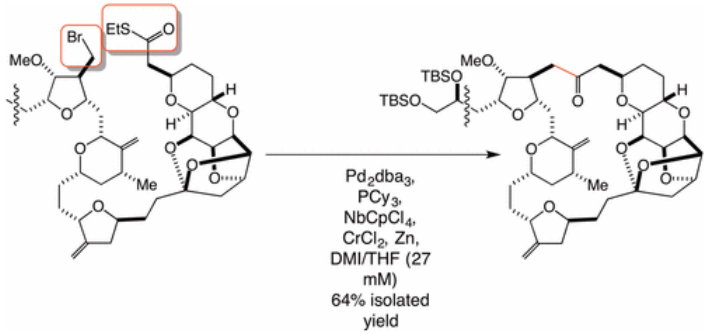
Citation: Jung Hwa Lee, Zhanjie Li, Ayumi Osawa, and Yoshito Kishi
Journal of the American Chemical Society 2016 138 (50), 16248-16251

Extension of Pd-Mediated One-Pot Ketone Synthesis to Macrocyclization: Application to a New Convergent Synthesis of Eribulin



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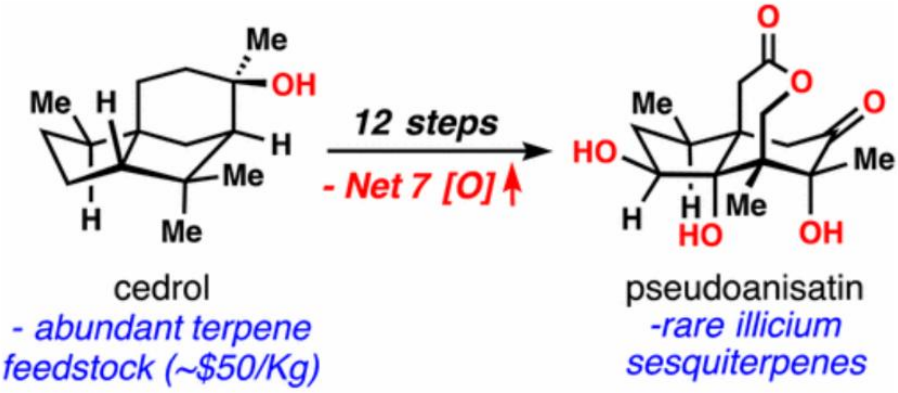
Citation: *JACS*, **2016,** *138*, 16616.

Oxidative Entry into the *Illicium* Sesquiterpenes: Enantionspecific Synthesis of (+)-Pseudoanisatin

Maimone paper



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Citation: ***JAMA.* 2016;316(22):2366-2367**

Artificial Intelligence With Deep Learning Technology Looks Into Diabetic Retinopathy Screening

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Citation: ***JAMA.* 2017;317(1):14-16**

23andMe, Big Data, and the Genetics of Depression

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Citation: Sun, et *al.* *Mor. Pharm.* **2017,** *14*, 81-92

PEGylated Cationic Vectors Containing a Protease-Sensitive Peptide as a miRNA Delivery System for Treating Breast Cancer

This study designed a cationic gene vector containing matrix metalloproteinase-2 (MMP2)-cleavable substrate peptides that specifically target tumor sites where MMP2 levels are high. The targeted delivery system is fabricated by linking enzyme-cleavable polyethylene glycol (PEG) derivatives to cationic beta-cyclodextrin-polyethylenimine conjugates, which reduce the toxicity of polyethylenimine and condense the therapeutic cargo. tumor suppressor microRNA miR-34a, which suppresses onset and progression of many types of cancers, was investigated for its therapeutic potential for treating breast cancer. The PEG coating markedly reduces nonspecific interaction between cationic particles and serum proteins, permitting accumulation at the target site; subsequent peptide cleavage by MMP2 facilitates miR-34a delivery into tumor cells. The nanopreparation shows excellent stability, and its internalization, tumor targeting, and antitumor efficacy in vitro and in vivo are better than those of a nanopreparation containing MMP2-uncleavable peptide.

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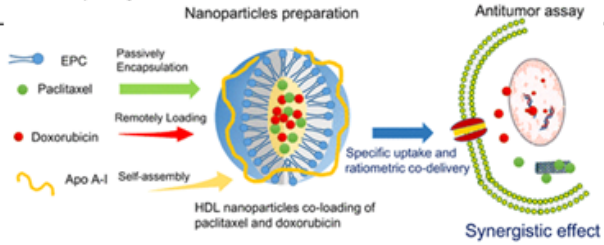
Citation: Xu, et *al.* *Mor. Pharm.* **2017,** *14*, 107-123.

Targeted Biomimetic Nanoparticles for Synergistic Combination Chemotherapy of Paclitaxel and Doxorubicin



The coloaded rHDL was formulated by passively incorporating hydrophobic paclitaxel (PTX), and subsequently remotely loading hydrophilic doxorubicin (Dox) into the same nanoparticles. The resultant rHDL system restored targeted delivery function toward cancer cells via scavenger receptor class B (SR-BI), as confirmed by in vitro confocal imaging and flow cytometry. These coloaded rHDL nanoparticles were remarkably effective in increasing the ratiometric accumulation of drugs in cancer cells and enhancing antitumor response at synergistic drug ratios. In particular, they exhibited more efficacious anticancer effects in an in vitro cytotoxicity evaluation and in a xenograft tumor model of hepatoma compared with free drug cocktail solutions. These results confirm that the coloaded rHDL nanoparticles are promising candidates for the synergistic delivery of drugs with diverse physicochemical properties in cancer treatment integrating efficiency and safety considerations.

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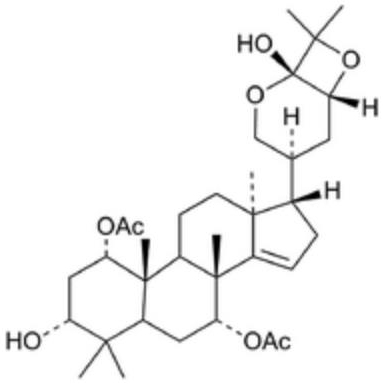
Citation: Hill, R. et al. *Nat. Prod. Rep.*, **2017**, 34, 90-122.

Triterpenoids



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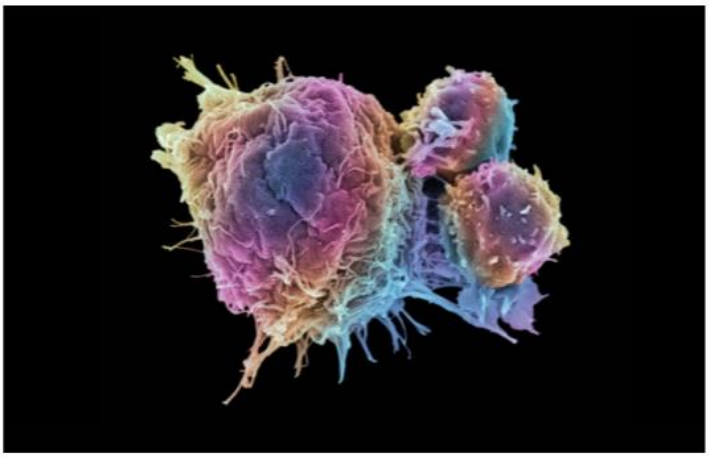
Citation: ***Nature*** **540, 328–329 (15 December 2016) doi:10.1038/540328a**

Algorithms compete to predict recipe for cancer vaccine



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Citation: ***Nature*** **540, 487 (22 December 2016) doi:10.1038/540487a**

Targeting host genes for therapy

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Citation: ***Nature*** **540, 496–499 (22 December 2016) doi:10.1038/540496a**

2016 in news: The science events that shaped the year

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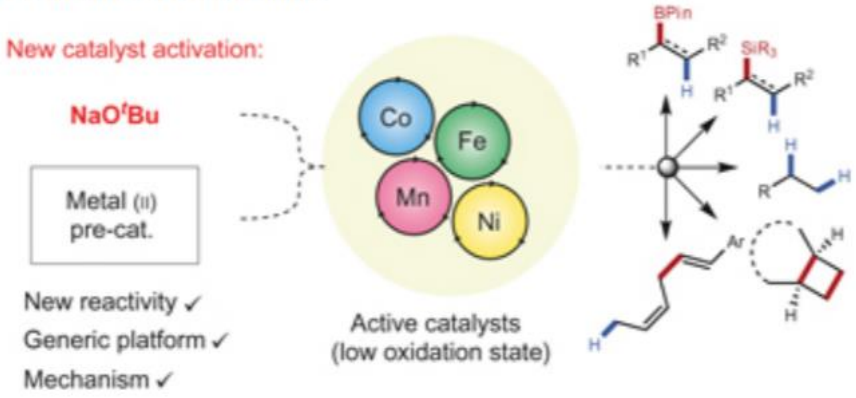
Citation: ***Nature Chemistry*** **(2017) doi:10.1038/nchem.2697**

Activation and discovery of earth-abundant metal catalysts using sodium *tert*-butoxide



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Citation: Over, *et al. Nat. Chem. Bio.* **2016,** *12,* 1065-1074

Structural and conformational determinants of macrocycle cell permeability

Macrocycles are of increasing interest as chemical probes and drugs for intractable targets like protein-protein interactions, but the determinants of their cell permeability and oral absorption are poorly understood. To enable rational design of cell-permeable macrocycles, we generated an extensive data set under consistent experimental conditions for more than 200 non-peptidic, de novo designed macrocycles from the Broad Institute's diversity-oriented screening collection. This revealed how specific functional groups, substituents and molecular properties impact cell permeability. Analysis of energy-minimized structures for stereo- and regioisomeric sets provided fundamental insight into how dynamic, intramolecular interactions in the 3D conformations of macrocycles may be linked to physicochemical properties and permeability. Combined use of quantitative structure ¨Cpermeability modeling and the procedure for conformational analysis now, for the first time, provides chemists with a rational approach to design cell-permeable non-peptidic macrocycles with potential for oral absorption.

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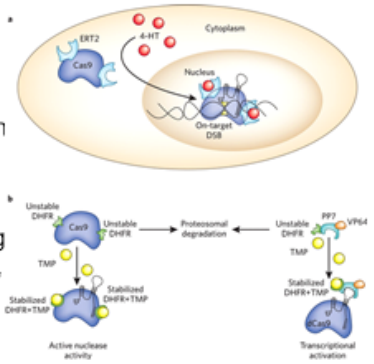
Citation: Hilton, et *al. Nat. Chem. Bio.* **2017,** *13,*

Chemical control for CRISPR editing

New approaches allow tight control over Cas9 activity using chemical induction. These studies expand the ability to rapidly induce and suppress Cas9-mediated nuclease activity and conditionally modulate the multiplex regulation of endogenous gene expression. (a) Liu et al. fused Cas9 to four copies of the hormone-binding domain of the estrogen receptor (ERT2), resulting in exclusion of Cas9 from the nucleus. Upon the addition of 4-hydroxytamoxifen (4-HT), the Cas9-ERT2 fusion protein is imported to the nucleus, where it can complex with guide RNAs (gRNAs) and cleave target genomic DNA. DSB, double-strand break. (b) Maji et al. fused destabilized protein domains, including the dihydrofolate reductase (DHFR) domain from E. coli, to Cas9, leading to proteasomal degradation. The DHFR-Cas9 fusion protein is stabilized by the addition of trimethoprim (TMP), facilitating targeted nuclease activity.



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Citation: Piraner, et *al. Nat. Chem. Bio.* **2017,** *13,*75-80.

Tunable thermal bioswitches for in vivo control of microbial therapeutics

Temperature is a unique input signal that could be used by engineered microbial therapeutics to sense and respond to host conditions or spatially targeted external triggers such as focused ultrasound. To enable these possibilities, we present two families of tunable, orthogonal, temperature-dependent transcriptional repressors providing switch-like control of bacterial gene expression at thresholds spanning the biomedically relevant range of 32-46 C. We integrate these molecular bioswitches into thermal logic circuits and demonstrate their utility in three in vivo microbial therapy scenarios, including spatially precise activation using focused ultrasound, modulation of activity in response to a host fever, and self-destruction after fecal elimination to prevent environmental escape. This technology provides a critical capability for coupling endogenous or applied thermal signals to cellular function in basic research, biomedical and industrial applications.

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Citation: **N Engl J Med 2016; 375:2286-2289**

Drugging the Undruggable Ras — Immunotherapy to the Rescue?

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Citation: **N Engl J Med 2017; 376:86-88**

Targeting Therapeutic Oligonucleotides

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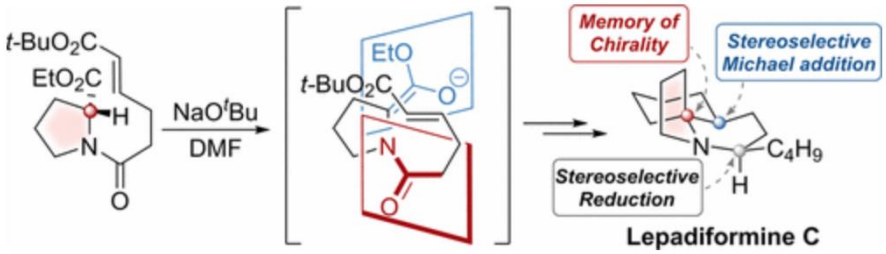
Citation: Lee, S; Bae, M; In, J; Kim, J. H; Kim, S. *Org. Lett.* **2017**, *19*, 254-257.

Asymmetric Total Synthesis of Lepadiformine C Using Memory of Chirality in an Intramolecular Ester Enolate Micheal Addition



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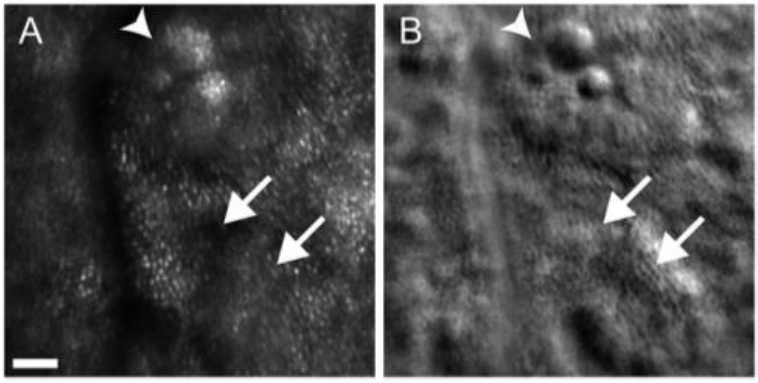
Citation: PNAS 2017, 114 (3), 586–591 DOI: 10.1073/pnas.1613445114.

Imaging Individual Neurons in the Retinal Ganglion Cell Layer of the Living Eye.



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Citation: Harper, K. *Science.* **2016,** *354,* 1384

The aftermath of AIDS in China

By the mid-1990s, the terror of the early AIDS epidemic had subsided in many western countries, as antiretroviral therapy transformed the once-deadly disease into a chronic condition. In China, however, the AIDS epidemic was just getting started. Slipping across the nation's southern borders via injection drug use, the virus went largely undetected until it exploded among tens of thousands of plasma sellers in rural China. HIV/AIDS in China: Beyond the Numbers is a candid account of how the AIDS epidemic forced Chinese leaders into action.When the Chinese government did decide to support prevention and treatment efforts in earnest, it did so with all of its weight. The government's spending on AIDS skyrocketed from a mere US$2 million in 2000 to $600 million in 2015. And between 2010 and 2014, health officials reduced the number of steps between HIV screening and treatment from 4 to 1, thus increasing the percentage of individuals with a confirmed HIV infection who had initiated antiretrovirals from 40% to 90%. Most recently, in February of this year, the government announced that anyone with a confirmed HIV diagnosis can seek free treatment immediately, regardless of CD4 cell count.this book offers a vivid history of China's response to HIV from the pathogen's emergence until the present, and it joins the relatively thin ranks of books that offer first-person accounts of important eras in public health. This is a must-read book for anyone interested in HIV, infectious diseases more generally, or global health.

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Citation: Harms, *et al.* *Science.* **2016,** *354*

Mechanisms of bacterial persistence during stress and antibiotic exposure

The prevailing crisis of antibiotic resistance has therefore raised fears that we are descending into a postantibiotic ¡°era of untreatable infections¡± (9). Already today, however, many patients suffer from bacterial infections that defy massive, long-lasting, and repeated antimicrobial treatment regardless of genetically acquired antibiotic resistance. These infections are often chronic and are never fully cleared by antibiotic treatment because bacteria can persist in biofilms or other protected niches The limited comprehensive understanding of persister formation and survival is a critical issue in controlling persistent infections. However, recent work in the field has uncovered the molecular architecture of several cellular pathways underlying bacterial persistence, as well as the functional interactions that generate heterogeneous populations of persister cells. These results confirm the long-standing notion that persistence is intimately connected to slow growth or dormancy in the sense that a certain level of physiological quiescence is attained. Persister cells are phenotypic variants of regularly growing bacteria and survive lethal antibiotic treatment in a nongrowing, dormant state. Upon termination of treatment, the resuscitation of persister cells can replenish the population. This review focuses on the diverse molecular mechanisms that underlie bacterial persister formation and drive the heterogeneity of these cells. PMF, proton-motive force.

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Citation: Rinaldi, L. *Science.* **2016,** *354,* 1666

Rescuing my time from science

It was a cold autumn day a couple years ago when I first felt that pursuing a Ph.D. was warping my sense of time. I had started working at 8:30 in the morning. By 8 in the evening, when almost everybody else had left, I was still in my office. I had so much work still to do that I reluctantly called my life partner to tell her that I would not be home for dinner. As I finally headed home around midnight, walking down dark, empty corridors and through the deserted university square, I realized that I was living in a sort of time warp¡ªwhich was particularly ironic given that I was studying how daily activities shape our sense of time. Now, though, after years of allowing my work to take over my life, I'm reclaiming my power to decide how to spend my time.

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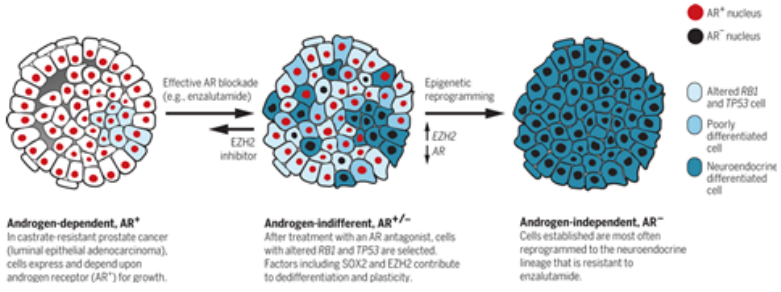
Citation: Kelly, *et al.* *Science.* **2016,** *355,* 29-30

Reprogramming to resist

One means by which cancer cells evade therapies involves their ability to reprogram to a cell type that no longer depends on the cellular pathway being targeted by the treatments. Hormone deprivation therapies that suppress androgen receptor (AR) signaling are the mainstay of treatment for metastatic prostate cancer. However, prostate cancers can become resistant to this approach by losing dependence on androgen hormones.



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