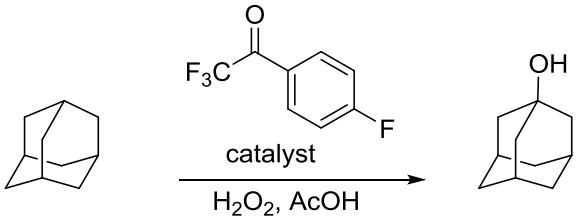
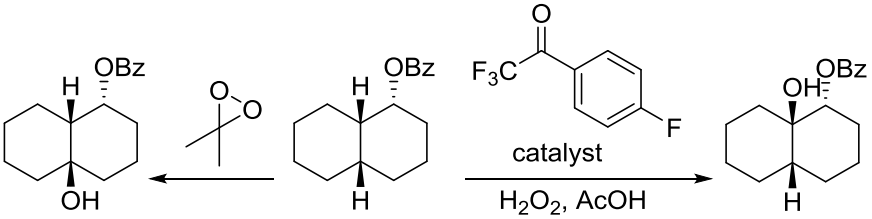
December 8, 2014

Conor J. Pierce and Michael K. Hilinkski. In situ synthesis of dioxiranes for C-H hydroxylation. **DOI:** 10.1021/ol503410e

This week's article focuses on the *in situ* synthesis of reactive dioxiranes using hydrogenperoxide and acetic acid in the presence of a catalytic amount CF3 ketones. The dioxiranes formed via oxidation of the ketone and are then used to hydroxylate activated sp3 centers (either tertiary or electron rich).



In addition to being a nice way to generate the dioxirane *in situ,* this protocol also has complimentary reactivity to classic DMDO conditions; however, the origin of this complimentary activity is under further investigation.

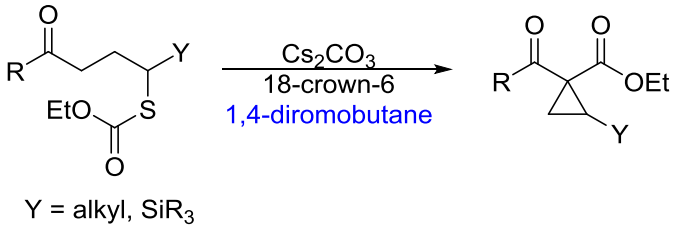


Overall this is a nice reaction to install a hydroxyl group under metal free conditions. Unfortunately the substrate scope seems limited and a large amount of ketone (20 mol %) is still needed for reactivity. However, the ability to easily generate dioxiranes should not be over looked and we're sure the authors will have more advances for this reaction to come. For more information you are invited to read the full article linked at the top of the page.

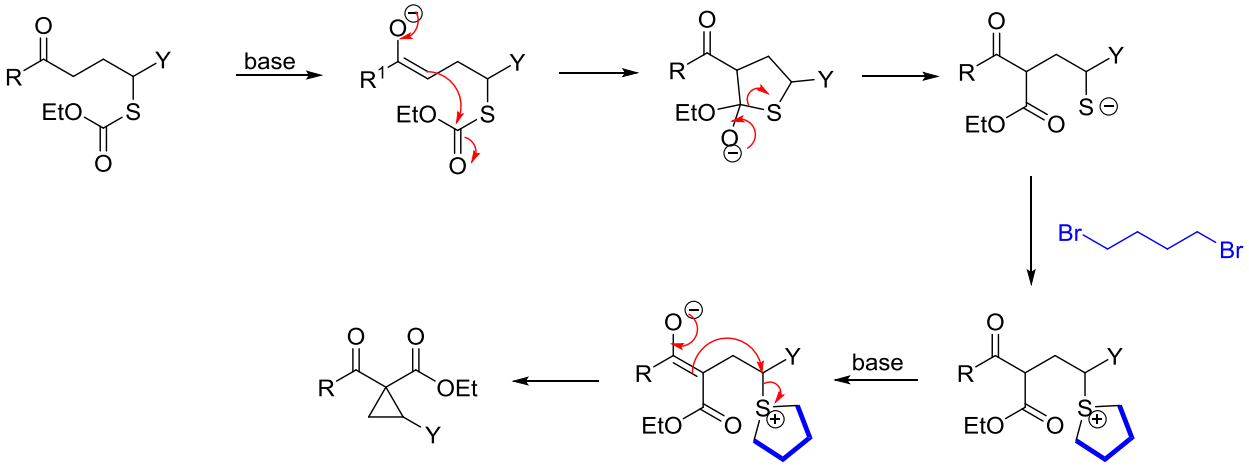
November 25, 2014

Shi-Guang Li and Samir Z. Zard. Synthesis of Cyclopropanes. **DOI:** 10.1021/ol503081b

This week's article focuses on one of my favorite carbaskeletons: the cyclopropane. This new approach by Li and Zard is reminiscent of the Corey-Chaykovsky reaction and the mechansim of the cofactor S-adenosyl methionine (SAM). The researchers approach involves treating functionalized thiocarbonates with base and 1,4-dibromobutane to yield the desired cyclopropane.



Mechanistically, this reaction is simple and complex with a set of enolate additions including one in the product ring forming event (mind you there are a total of 3 rings formed during this reaction and only one survives in the product. Perhaps the most elegant part of this mechansim is when the thiolate anion is trapped by the 1,4-dibromobutane to make a 5-membered sulfanium intermediate that is ultimately dispatched is a tetrahydrothiophene.

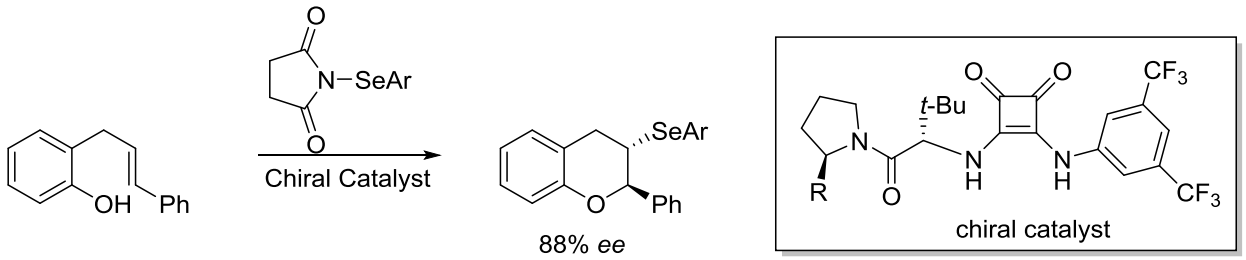


Unfortunately this reaction suffers from non-ideal diastereoselectivity. However, this interesting reaction can be used to make a variety of cyclopropanes from non-classical starting materials. The chemistry to make the thiocarbonate is also of interest and proceeds via a radical insertion of a vinyl silane. For more information on this reaction the reader is encouraged to read the full article linked at the top of the page.

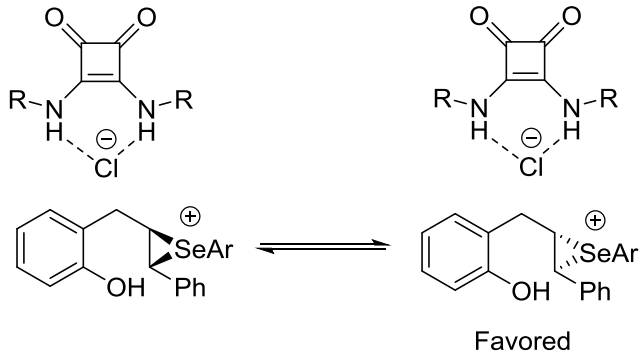
November 18, 2014

Hu Zhang,Song Lin, Eric N. Jacobsen Enantioselective Selenoetherification Reactions. Journal of the American Chemical Society. **DOI:** 10.1021/ja510113s

This week's highlight focus' on work performed by the Jacobsen lab. Having spent a great deal of my early career researching organoselenium chemistry I have a great affection for this type of work. The Jacobsen lab reports using chiral hydrogen bond donor catalysts to promote selenoetherification reactions of the type.



The researchers were able to demonstrate that the enantioselectivity of the reaction is controlled via dynamic kinetic resolution of the intermediate seleniranium ion, which is then 'trapped' during cyclization step.

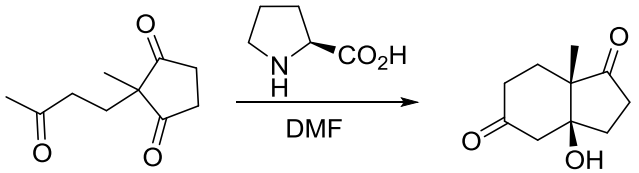


The cyclized products were then further subjected to 'classic' organoselenium chemistry such as diol formation and radical coupling reactions. For more information on this article the reader is encouraged to read the full article linked at the top of the page.

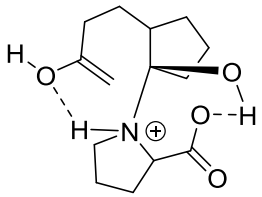
November 11, 2014

Zoltan G. Hajos and David R. Parrish. Asymmetric Synthesis of Bicyclic Compounds Catalyzed by Proline. *Journal of Organic Chemistry*. **1974**, *39*, 1615-1621

This week's highlight is a look back at a historically significant reaction. A reaction that would later go on to be called Hajos-Parrish reaction and then after some controversy the Hajos-Parrish-Eder-Sauer-Wierchert reaction. Although the naming controversy won't be addressed here, this reaction was ahead of it's time and was a 25 year pre-amble to what became the field of organocatalysis. The Hajos-Parrish reaction involves treatment of the triketone drawn below with catalytic proline in a polar aprotic solvent to yield the fused-bicycle product with optical purity >90%.



The mechanism of this reaction has garnered much debate and research since the initial discovery. The evidence at the time of the original report did not support a straight enamine mechanism and Hajos and Parrish put forth a mechanism involving a protonated proline interacting with the substrate through a series of hydrogen bonds (see below). An incredible amount of research has supported that the mechanism is a hybrid of enamine catalysis with the carboxylate on proline engaging in hydrogen bonding with the incoming electrophile.

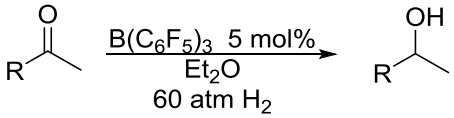


This report is truly an historic article in the history of organic chemistry and should be celebrated nearly 40 years since it was first published. For more information the readers are encouraged to read the full article in the words of Hajos and Parrish themselves linked at the top of the page.

November 04, 2014

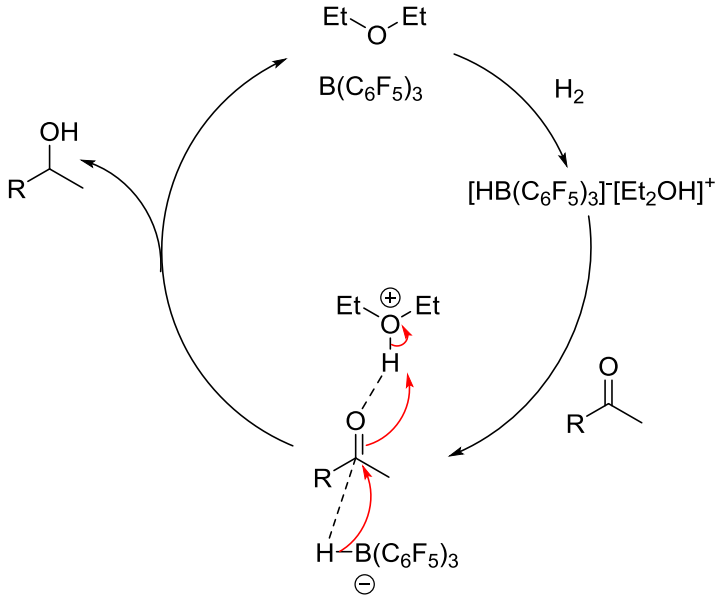
Tayseer Mahdi and Douglas W. Stephan. Catalytic Hydrogenation of Ketones Using Frustrated Lewis Pairs. *Journal of the American Chemical Society*. doi: 10.1021/ja508829x

This week we highlight an article of Douglas Stephan's group on the use of Frustrated Lewis Pairs (FLPs) for catalytic hydrogenation. Most often the use of FLPs has been used for stoichiometric activation of small molecules. This is one of the few examples in the literature where the FLP gets turned over in a catalytic reaction.



This process proved to be general for a a variety of alkyl and aryl ketones, alkyl chlorides were also tolerated during hydrogenation and were left intact. Mechanistically this reaction is similar to other FLP activations where the large Lewis acid B(C6F5)3 is too sterically encumbered to react with the Lewis base, Et2O. The strain from the failure to interact causes an activation of molecular hydrogen and heterolytically pulls the

diatom apart to make an FLP-H2 adduct. This adduct then reacts with the ketone reducing it to an alcohol.

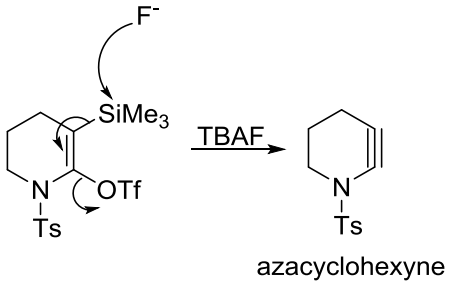


For more information on FLPs and the discussed work the reader is encouraged to read the full article linked above.

October 28, 2014

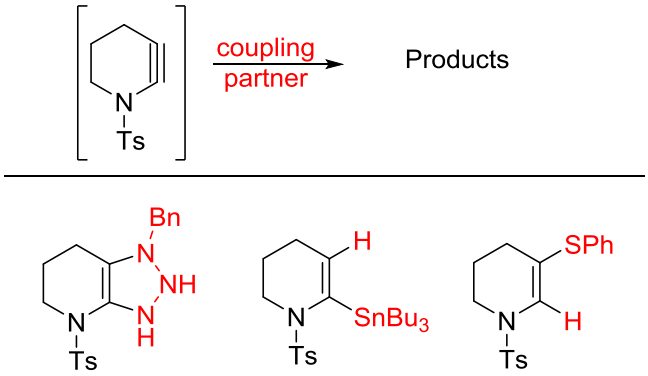
Sami F. Tlais and Rick L. Danheiser. Access to strained azacyclohexynes *Journal of the American Chemical Society*. doi: 10.1021/ja509055r

This week's article is a highlight of work out of the Danheiser group at MIT. The researchers here access a strained azacyclohexyne via fluoride induced elimination of a vinyltosylate. This method has been utilized extensively to access benzynes and recently some cyclohexyne derivatives. However, the authors state that azacyclohexynes have only been accessed one time prior via vacuum pyrolysis.



Although the azacyclohexyne cannot be isolated it could be chemically trapped using a variety of coupling partners including benzylazide, tributyltin hydride, and phenylmercaptan. These reactions are all cousins to coupling reactions that occur with

putative benzyne intermediates, supporting the existence of the proposed azacyclohexyne intermediate.



The researchers are further investigating this mechanistically through computational methods and will report their findings when they are available. For more information on this reaction the reader is encouraged to look at the full article linked at the top of the page.

October 21, 2014

Dudley R. Herschbach "Theodore William Richards: Apostle of Atomic Weights and Nobel Prize Winner in 1914. *Angewandte Chemie International Edition.* doi 10.1002/anie.201407464

This week's article is different from previous highlights. This is a history or science article chronically the life and times of Theodore William Richards. Richards is an alumnus of Haverford College and is the only such alumnus to with the Nobel Prize in Chemistry. He earned is Ph.D. from Harvard at the age of 20 and went on to solve and reassign the atomic weights of many of the elements, and also was one of the first to observe that radioactive materials were different in mass than their 'cold' counterparts. Richards interests extended beyond atomic weight formalizations and later went on to lay the groundwork for what would become the Third Law of Thermodynamics.

Although, by today's standards atomic weight determination may not seem to be the most exciting of enterprises, without fundamental advances in atomic weights, molecular formalisms, and the periodic table, modern chemistry would not exist.

This week, we'll close with a quote from Richards himself that we would all be served to follow:

First and foremost, I should emphasize the overwhelming importance of perfect sincerity and

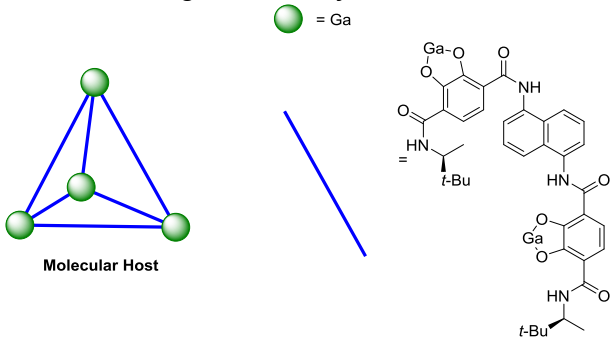
truth: one mustpurge oneself of the very human tendency to look only at thefavorable aspects of his work ... Each step should bequestioned ... then, patience, patience, patience! Only bypersistent, unremitting labor can a lasting outcome bereached"First and foremost, I should emphasize the overwhelming importance of perfect sincerity and truth: one must purge oneself of the very human tendency to look only at the favorable aspects of his work...Each step should be questions...then, patience, patience, patience! Only by persistent, unremitting labor can a lasting outcome be reached."

For more on the life and times of Theodore William Richards you are encouraged to read the full article in Angewandte Chemie linked at the top of the page

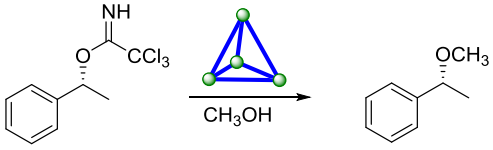
October 14, 2014

Chen Zhao, F. Dean Toste*, Kenneth N. Raymond*, Robert G. Bergman* Substitution Reactions in Molecular Hosts that Give Retention of Stereochemistry. *Journal of the American Chemical Society.* doi. 10.1021/ja508799p

This week's article is a highlight of a recent article by some well-established researchers. Raymond originally reported these molecular hosts in 1998. Since then the Raymond and Bergman groups have shown that they can catalyze several reactions inside these molecular hosts including Nazarov cyclizations and C-H activation chemistry.



This study shows focuses on the stereorentive substitution of trichloroacetimidates with nucleophilic methanol. The researchers show that when using their molecular host catalyst they see 92% retention of stereochemistry as compared to when the reaction is run in solution with a phosphoric acid catalyst (85% inversion) or with no catalyst (80% inversion).

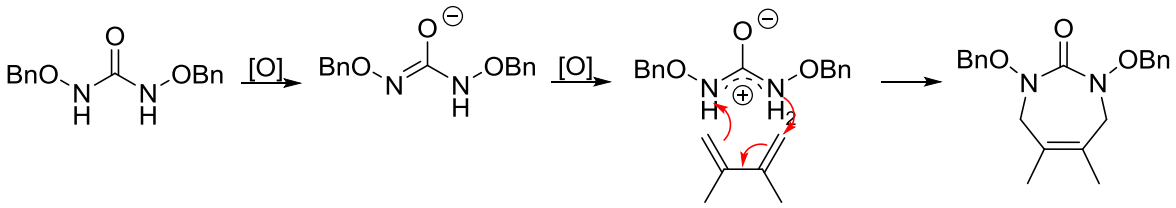


The researchers also show that this works on Cl leaving groups as well. In addition it is hypothesized that this reaction goes through a transient carbocation intermediate that is stabilized via cation-pi interactions with the wall of the molecular host. More work is being carried out to support this claim. For more information you are encouraged to check out the full article at the link above.

October 7, 2014

Devendar Anumandla, Ryan Littlefield, and Christopher S. Jeffrey*, Oxidative 1,4-Diamination of dienes. *Organic Letters.* doi: 10.1021/ol502-460j

The Jeffrey Lab has recently reported the title reaction using simple ureas as the diamine precursor. In their chemistry a urea is treated with 2 equiv. of PhI(OAc)2 as oxidant to yield the depicted diaza-oxyallylcation. This intermediate can then undergo a Woodward-Hoffman allowed [4+3] cycloaddition with a diene. The authors showed that this reaction was general for not just cyclic dienes such as cyclopentadiene and furan, but also acyclic dienes as well.

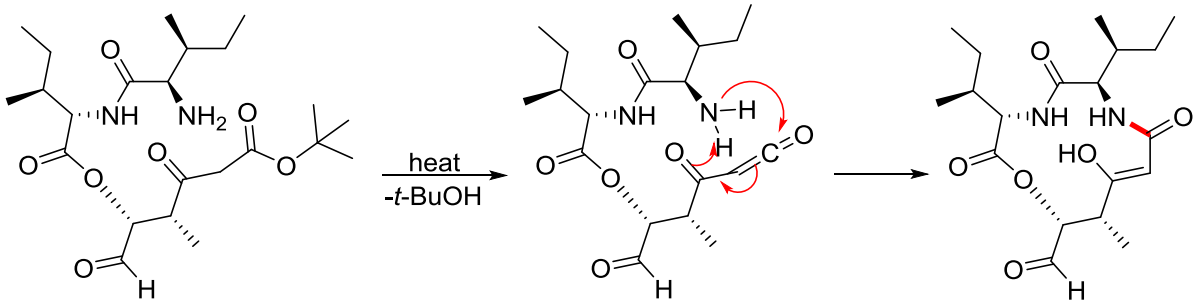


The use of the urea as the diamine precursor is an improvement on previous attempts at 1,4-diamination reactions, in which 2 equivalents of mono-amines were used, which led to poor overall selectivity. Furthermore this reaction tolerates a wide range of functional groups, including unprotected alcohols. For more information on this interesting reaction the you are referred to the full article, linked at the top of the page.

September 30, 2014

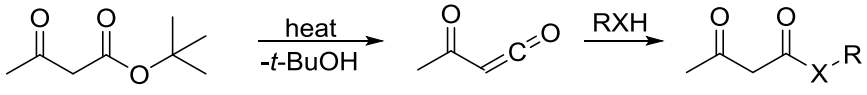
Justine N. deCruyter and William A. Maio*, Synthesis of the Taumycin A Macrocycle. *Organic Letters.* doi: 10.1021/ol5025585

The Maio Lab's synthesis of the title compound culminated in a slick macro-lactam forming reaction involving a ketene intermediate. The ketene was formed via thermal elimination of *t*-BuOH from a 1,3 ketoester. After formation the ketene is primed for intramolecular nucleophilic attack from a pendant amine to form the ring forming the title compound.



Witzeman and Nottingham had previously shown that this ketene formation was general for *tert*-butyl acetoacetate and it could be reacted with a variety of amine and alcohol nucleophiles. This type of amide/ester bond forming reaction is attractive since it avoids

using costly and waste producing common peptide coupling reagents like DCC and EDC.



For more information on the rest of the Maio synthesis of the title compound you are encouraged to referred to the link at the top of the article.