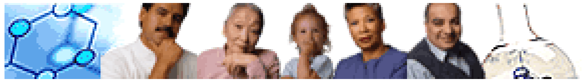

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Heart Cut

March 6, 2006

- Robust chiral macroporous organic materials
- "Telescoping" thioether reactions reduces emissions
- An improved method for C-3-substituted β-lactams
- Catalyze aqueous Diels – Alder reactions with a DNA complex
- Pressure-infused enzymes as enantioselective catalysts
- Use the right particle size in heterogeneous reactions
- Polymer dissolves in a room-temperature ionic liquid
- Prepare homoallylamines efficiently in a one-pot synthesis

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Make robust chiral macroporous organic materials. Macroporous materials made from ordered colloidal templates have attracted much attention because of their potential applications in fields such as photonics, catalysis, and separation. Whereas a wealth of inorganic macroporous materials have been prepared, their organic counterparts have seldom been made. Although organic materials offer great flexibility in structural design, they suffer from such disadvantages as shape instability and environmental susceptibility.

L. Yang and W. Cao* at Peking University (Beijing) used reinforcement methods such as thermosetting and hybridization to fashion robust macroporous organic materials. They prepared 3-D macroporous chiral polyaniline composite materials by using polystyrene beads with an average diameter of ~5.7 mm as sacrificial templates. The macroporous materials were reinforced with diazoresin and TiO_2 as thermosetting and hybridizing agents, respectively. Their pore structures were maintained after template removal.

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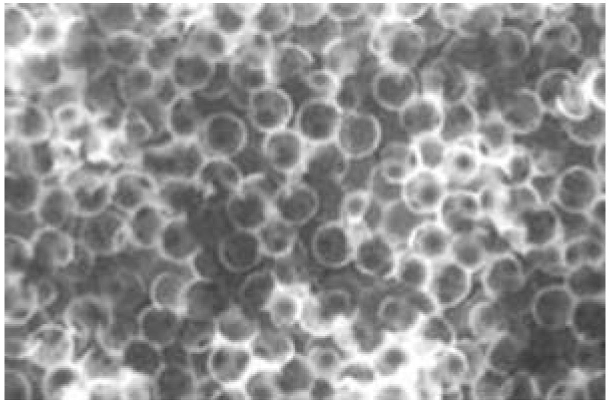
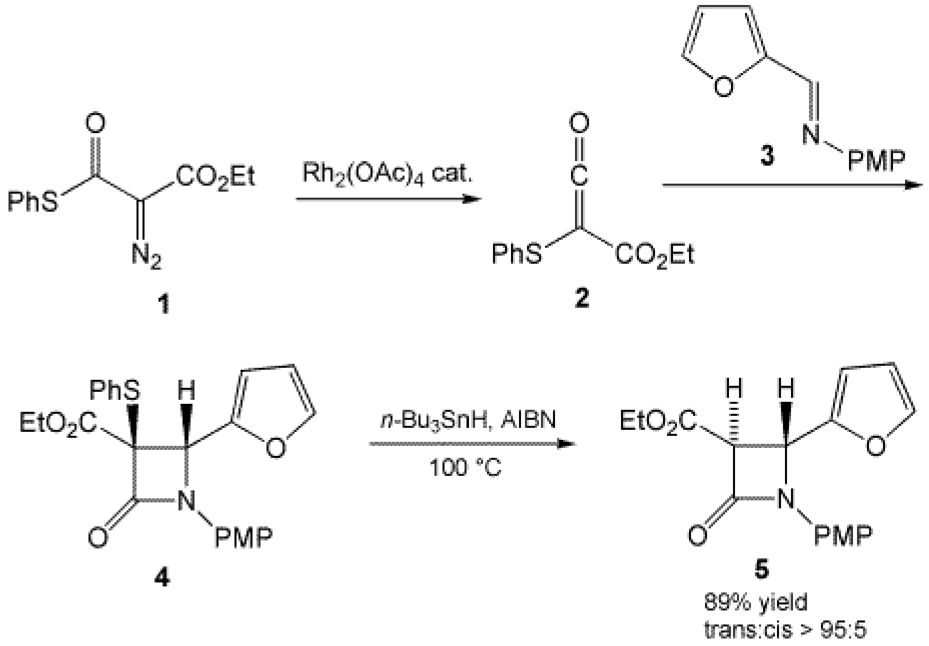


As shown in the photo above, no changes in the shape and size of the pores could be detected, even after the materials were soaked in strongly solvating DMF. The researchers envision that these porous materials may be applied as chiral stationary phases in drug enantioseparation. (*Chem. Mater.* **2006**, *18*, 297 – 300; Ben Zhong Tang) Go to top

"Telescoping" thioether reactions reduces toxic and odorous emissions. The first two reactions in the synthesis of a compound that has potential use for the treatment of neurological or psychiatric disorders are formation of a sulfur ylide from Me_2S and ethyl bromoacetate and insertion of the ylide into the C=C bond of 2-cyclopentenone to form a bicyclic ketone. This sequence requires controlling Me_2S emissions during both steps.

O. M. Rasmy and co-workers at Eli Lilly (Indianapolis and Tippecanoe, IN) show that by "telescoping" these reactions, Me_2S emissions need only be contained during one step. Both reactions can be carried out effectively with MeCN as solvent and 1,8-diazabicyclo[5.4.0]undec-7-ene as base. (*Org. Process Res. Dev.* **2006,** *10,* 28 – 32; Will Watson) Go to top

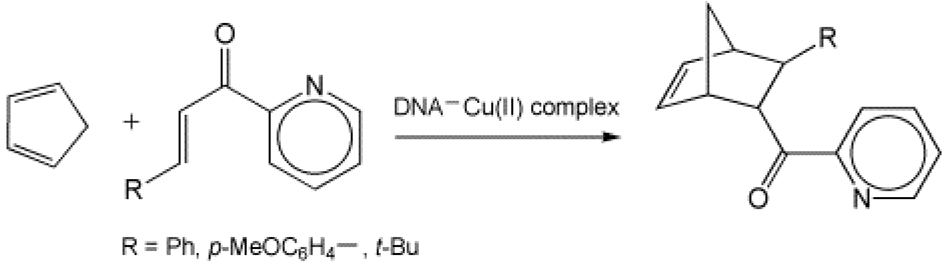
This β-lactam synthesis provides an improved method for substitution at the 3-position. Functionalized β-lactam rings are extremely useful scaffolds for pharmaceutical products. J. Xu and co-workers at Peking University (Beijing) focused on 3-alkoxycarbonyl derivatives and developed an unusual synthesis of these materials using a ketene – imine cycloaddition reaction. This approach gave 3-ethoxycarbonyl-substituted β-lactam product **5** with yields up to 97% and trans/cis isomer ratios up to >95:5.



AIBN is azobisisobutyronitrile; PMP is *p*-methoxyphenyl. The easily prepared phenylthiodiazoacetate (**1**) underwent smooth $Rh_2(OAc)_4$-mediated rearrangement to ketene **2**, which was trapped by imine **3** to give *cis*-β-lactam isomer **4** in high yield. The authors prepared a series of highly stereoselective cis isomers that formed as only a pair of enantiomers. Finally, the thiophenyl group was removed from **4** using the relatively mild *n*-Bu_3SnH – AIBN method to give trans-3-substituted β-lactams (**5**) as the predominant isomers.

This is a mild, versatile method for preparing 3-alkoxycarbonyl trans-disubstituted β-lactam derivatives with good-to-excellent yields and diastereoselectivities. (*J. Org. Chem*. **2006,** *71*, 815 – 818; W. Jerry Patterson) Go to top

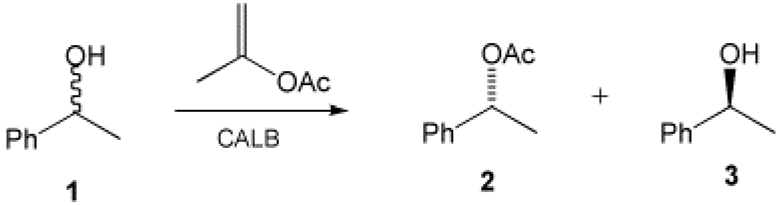
Catalyze Diels – Alder reactions in aqueous solution with a DNA – copper complex. According to G. Roelfes*, A. J. Boersma, and B. L. Feringa* of the University of Groningen (The Netherlands), achiral copper complexes based on bidentate ligands bonded to DNA display high enantioselectivities (up to 99% ee) in aqueous Diels – Alder reactions. The reactive Cu(II) center is brought into close contact with the DNA double helix because the metallic binding site and the DNA base are integrated into one moiety, and a spacer is no longer required. The close contact between DNA and the copper complex allows for a direct transfer of chirality from DNA to the reaction product.



Because the chirality is directly derived from the DNA, the enantioselectivity of the Diels–Alder reaction strongly depends on the precise nature of the interaction between DNA and the Cu(II) complex. The highest enantioselectivity is achieved with a catalyst complex of moderate DNA-binding strength, suggesting that some flexibility in the binding geometry of the complex is beneficial to bind the dienophile in a favorable orientation in the DNA groove. (*Chem. Commun*. **2006,** 635–637; George Xiu Song Zhao) Go to top

Pressure-infused supported enzymes effectively catalyze enantioselective reactions. Y. Han, S. S. Lee, and J. Y. Ying* of the Institute of Bioengineering and Nanotechnology (Singapore) used 3000–5000 psi pressure to introduce enzymes into mesoporous silica supports. This process has an advantage over solvent infusions in that higher and more persistent loadings of enzymes can be achieved.

Mesoporous MCF and FDU-12 forms of silica were chosen for this work because of their relatively large pore sizes (20–50 nm and 10–14 nm, respectively), which can accommodate a wide range of enzymes and are interconnected to facilitate mass transfer. The openings (windows) are smaller than the channels themselves, helping to retain enzymes once they enter the structures.

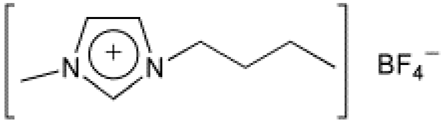


In one example of the chemistry that can be catalyzed by these immobilized enzyme systems, *Candida antarctica* lipase B (CALB) was introduced into MCF supports. The esterification of racemic 1-phenylethanol (**1**) with isopropenyl acetate proceeded with complete conversion of the *R*-isomer to (*R*)-1-phenylethyl acetate (**2**) in >99.7% ee, leaving the *S*-isomer feedstock (**3**) unconverted. (*Chem. Mater.* **2006**, *18,* 643–649; David A. Schiraldi) Go to top

Use the right solid particle size in heterogeneous reactions. J. D. Moseley and coauthors at AstraZeneca (Bristol, Loughborough, and Macclesfield, UK) and Dottikon Exclusive Synthesis AG (Switzerland) carried out the base-catalyzed protection of a pyrimidone N–H bond with a pivaloyloxymethyl group using K_2CO_3 in DMSO. They found that the particle size of the K_2CO_3 was critical to the degree of conversion and the reaction time: Smaller particle sizes gave higher conversions in shorter times.

The particle size was also relevant during the workup, which involved filtering K_2CO_3 from the product solution. Improper combinations of particle size and filter type led to inefficient washing of entrained product from the filter cake. (*Org. Process Res. Dev.* **2006,** *10,* 153 – 158; Will Watson) Go to top

Poly(ethylene oxide) dissolves in a room-temperature ionic liquid. Room-temperature ionic liquids (RTILs) are potential replacements for organic solvents because they are nonvolatile and environmentally friendly. But the limited solubility of many compounds in RTILs prevents widespread use. "RTIL-philic" macromolecules may be the key to making RTILs practical solvents.



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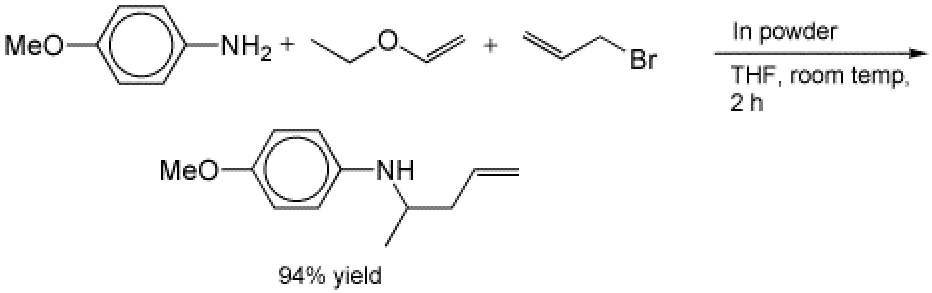
A. Triolo and coauthors at the National Research Council (Messina, Italy), Hahn-Meitner Institute (Berlin), and Paul Scherrer Institute (Villigen, Switzerland) explored the solubility of poly(ethylene oxide) (PEO) in an RTIL, 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF_4], **1**). Small-angle neutron-scattering measurements of dispersions of PEO in **1** were in good agreement with the Debye random-coil dispersion model. No phase separation was observed until the mol fraction of PEO in **1** was ⩾0.23. (*J. Phys. Chem. B* **2006**, *110*, 1513−1515; Sally Peng Li) Go to top

Prepare homoallylamines efficiently using a one-pot synthesis. Y. Kin and coauthors at the Korea Institute of Science and Technology and Korea University (both in Seoul) have devised an exceptionally simple and mild synthesis of *N*-aryl-substituted homoallylamines from a three-component reaction of aromatic amines, enol ethers, and allylic bromides. The reaction is mediated by metallic indium in a one-pot process, which leads to high product yields in many cases. The authors noted that the allylic indium reagent $(CH_2{=}CHCH_2)_3In_2Br_3$ forms in situ from the initial reaction of indium powder and the allyl bromide.



The best choice for the enol ethers was ethyl vinyl ether. Unexpectedly, the use of diethyl ethoxymethylenemalonate as the enol ether did not result in the homoallylamine, but in the corresponding enamine, in quantitative yield. Several electron-deficient and electron-rich anilines gave high yields of homoallylamines. Also, when γ-substituted allylic bromides were used, the reaction showed complete γ-regioselectivity. This gentle procedure may be useful when the goal of the synthesis is homoallylamines with sensitive functional groups. (*Org. Lett.* **2006,** *8*, 195 – 198; W. Jerry Patterson) Go to top

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