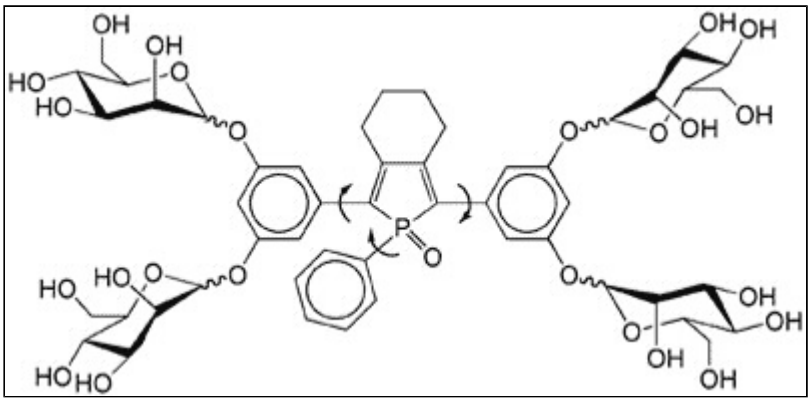
Noteworthy Chemistry

March 23, 2009

Sugar–phosphole oxide conjugates are fluorescence "turn-on" biosensors for lectins. Lectins are selective sugar-binding proteins that occur ubiquitously in nature. The term "lectin" is derived from the Latin word *legere* that means "to select". Because of lectins' essential biological role and widespread use in biochemistry and medicine, T. Sanji*, K. Shiraishi, and M. Tanaka* at the Tokyo Institute of Technology developed rapid, sensitive, selective biosensors for these proteins.

The authors previously found that phosphole oxides do not emit in solution but emit as aggregates because aggregate formation restricts intramolecular rotation of their phenyl groups. The sugar–lectin interactions involved in molecular recognition are typically found in aggregates, so the researchers hypothesized that sugar–phosphole oxide conjugates would emit strongly when supramolecular aggregates form via these interactions. They designed and synthesized conjugates such as compound **1** in the figure, and they used concanavalin A (Con A) as a model lectin for studying the biosensing behavior of the conjugates.



Conjugate **1** is nonemissive in aqueous buffer but becomes emissive in the presence of Con A. After filtration, the buffer becomes nonemissive again, demonstrating that the emission is "turned on" by the formation of **1**–Con A aggregates. The detection process is rapid and sensitive; the increase in fluorescence intensity in the presence of trace amounts of Con A (~0.2 μM) reaches a final value within a few seconds. The sensing is also selective: Con A-recognition is not affected by interferants such as peanut agglutinin. (*ACS Appl. Mater. Interfaces* **2009,** *1,* 270–273; Ben Zhong Tang)

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Placing nanoparticles inside carbon nanotubes enhances catalytic performance. The concept of using the inner cavity of a carbon nanotube (CNT) as a nanoreactor has been the subject of much research, but selective confinement of discrete nanoparticles within the CNT cavity is still a challenge. P. Serp and co-authors at CNRS (Toulouse and Strasbourg, France) and the University of Toulouse report a simple, efficient way to selectively confine bimetallic Pt–Ru nanoparticles (NPs) within these cavities. The scope of their study also includes the effect of this process on the resulting catalytic efficiency of the CNTs.

The first step is a controlled preparation of NPs stabilized by a ligand that has two functionalities: one with an affinity for the NP surface and the other for the CNT graphite layers. To accomplish this, they used 4-(3-phenylpropyl)pyridine as the ligand structure on the assumption that it can coordinate to the NPs via the nitrogen atom of the pyridine group and interact with the CNT surface through the phenyl ring. They also functionalized the CNT external surfaces by using carboxylic acid and amide groups bearing long alkyl chains.

The authors facilitated the entry of NPs into the CNT cavities by ball-milling the CNTs to open both ends of the nanotubes. They used two methods to prepare 5–23 wt% Pt–Ru–CNT samples: impregnation of the CNTs with THF mixtures containing the bimetallic nanoparticles and co-decomposition of platinum and ruthenium precursors in the presence of the ligand and CNTs. In a sample from the first method, they estimated that ~30% of the Pt–Ru NPs were located inside the CNT cavity. In products from the second method, the NPs agglomerated in large aggregates on the external CNT surfaces.

The catalytic efficiency of the modified CNTs was evaluated by using selective hydrogenation of cinnamaldehyde. Control experiments at 20 bar hydrogen and 70 °C showed no activity for unmodified CNTs. However, CNTs with NPs located primarily inside the nanotubes showed high selectivity for forming cinnamyl alcohol. Increasing the NP loading to the maximum level (23 wt%) promoted the selectivity for cinnamyl alcohol to 100%.

These nanocatalysts seem to show exceptional catalytic performance because of the confinement of the active phase and the reactants in the inner cavity of the CNTs. (*Angew. Chem., Int. Ed.* **2009,** *48,* **2529–2533**; **W. Jerry Patterson**)

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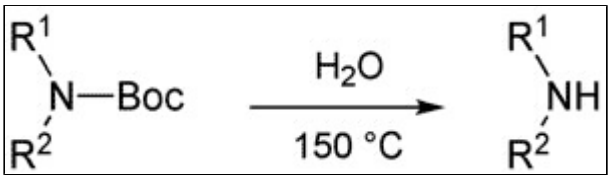
Deprotect *N*-Boc-amines in water without a catalyst. The *tert*-butoxycarbonyl (Boc) group is widely used as a protecting group in organic synthesis and peptide chemistry because of its stability and resistance to hydrogenation, alkaline conditions, and nucleophilic reactions. Current deprotection protocols use strong Brønsted acids or Lewis acids as catalysts in the presence of organic solvents.

X. Jia and co-workers at Shanghai University report the catalyst-free, water-mediated *N*-Boc deprotection of aromatic and aliphatic amines. They chose *N*-Boc-aniline as a model protected amine; their best results were attained at higher temperatures (150 °C) and a 4-h reaction time. The amount of water used also influenced the results: The best H_2O/substrate ratio was 1 mL:1 mmol. The experiments were conducted in a poly(tetrafluoroethylene)-lined stainless steel bomb.



The authors explain the enhancement of yield at high temperature by noting that subcritical water (>150 °C) contains higher H^+ and OH^- concentrations than water at lower temperatures. They verified the role of water as a catalyst in the *N*-Boc-aniline deprotection reaction by showing that no reaction occurs under the same conditions in the absence of water.

Aromatic amines with electron-releasing substituents are deprotected more rapidly than those with electron-withdrawing substituents. N-protected amino acids can also be deprotected by this method. The authors note that *N*-Boc amino acid esters are deprotected and hydrolyzed in one step; this reaction may be valuable for peptide synthesis. (*Tetrahedron Lett.* **2009,** *50,* **1438–1440**; **José C. Barros**)

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The structures of hydrogel scaffolds control cell-spreading characteristics. S. Khetan, J. S. Katz, and J. A. Burdick* at the University of Pennsylvania (Philadelphia) used several schemes for cross-linking acrylated hyaluronic acid (AHA) to form 3-D hydrogels that regulate cellular spreading. They formed 3-wt% hydrogels by adding cleavable peptide units, photo-cross-linking, or sequential application of addition and photo-cross-linking. As expected, the swelling, mechanical, and degradation behaviors of the gels were a function of the mode and degree of cross-linking.

For example, the compressive modulus and swelling ratio of hydrogels formed sequentially by addition polymerization (assuming 50% acrylate) followed by photopolymerization were between the values obtained for hydrogels generated solely by either method. The covalent cross-links in photo-cross-linked hydrogels prevented significant enzymatic degradation. A comparison of the spreading of cells encapsulated in radically cross-linked or sequentially cross-linked gels revealed that cell spreading occurred in addition-cross-linked hydrogels but was inhibited in sequentially cross-linked gels. The inhibition was a function of the degree of acrylate modification. Viability of the cells was maintained for both types of cross-linked hydrogels.

The authors confirmed that adhesion and cleavable sites are necessary for cell shaping. In a proof-of-concept study, they demonstrated that a stratification of spread characteristics is possible within a single hydrogel and may lead to advances in spatial control of cellular growth. (*Soft Matter* **2009,** *5,* Advance Article DOI: **10.1039/b820385g**; **LaShanda Korley**)

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Speed up *N,N'*-carbonyldiimidazole-mediated amide couplings. *N,N'*-Carbonyldiimidazole (CDI)-mediated couplings of aromatic amines with carboxylic acids can be slow, but J. P. Gilday and co-workers at AstraZeneca (Bristol, UK) describe the use of imidazole hydrochloride as an additive that significantly enhances the reaction rate. They believe that the weakly acidic imidazole salt assists in the proton transfer step and may help to protonate the intermediate carbonylimidazolide to make it more reactive. The net result is that reactions that normally take days to go to completion can now be carried out in a few hours. (*Org. Process Res. Dev.* **2009,** *13,* **106-113**; **Will Watson**)

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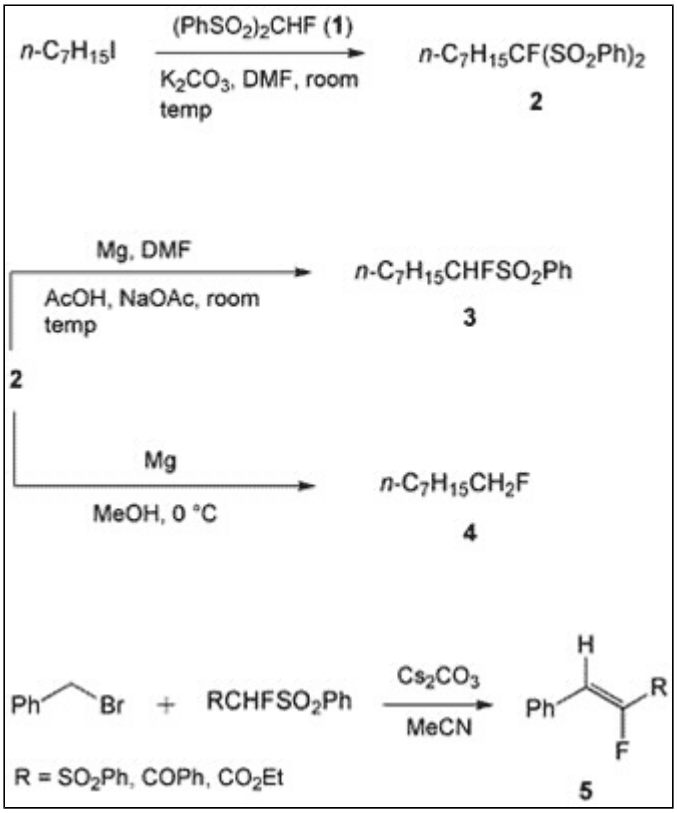
Here's an efficient fluoromethylation of alkyl and benzyl halides. Introducing a monofluoromethyl group into organic molecules leads to several biologically important compounds. According to G. K. S. Prakash, G. A. Olah, and co-workers at the University of Southern California (Los Angeles), α-fluorobis(phenylsulfonyl) methane (**1**) is a versatile reagent for the nucleophilic fluoromethylation of alkyl and benzyl halides. The reaction of **1**



with alkyl halides is carried out under straightforward, mild conditions, and it leads to an efficient new method for preparing alkylated α-fluorobis(phenylsulfonyl)alkanes (e.g., **2**) with a range of alkyl chain lengths.

These geminal bis-sulfones are versatile intermediates in organic synthesis; they allow easy deprotonation and use in nucleophilic substitution and cyclizations. The authors developed a simple protocol for the stepwise desulfonation of **2**. Reductive monodesulfonylation of **2** can be carried out by using a Mg–HOAc–NaOAc

system to give compound **3**. Compounds such as **2** can also be treated with magnesium and MeOH for complete conversion to the monofluoromethyl-substituted compound **4** with no detectable monodesulfonylated impurities in the product.

Alternatively, benzyl halide substrates can be treated with **1** to provide a stereospecific synthesis of α-fluorovinyl compounds such as **5**. By using other α-substituted fluoro(phenylsulfonyl)methane derivatives in place of **1**, a variety of densely functionalized vinyl fluorides can be prepared. The authors stress the value of these fluorinated products as potential intermediates for pharmaceutical compounds. (*Org. Lett*. **2009,** *11*, **1127–1130**; **W. Jerry Patterson**)

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