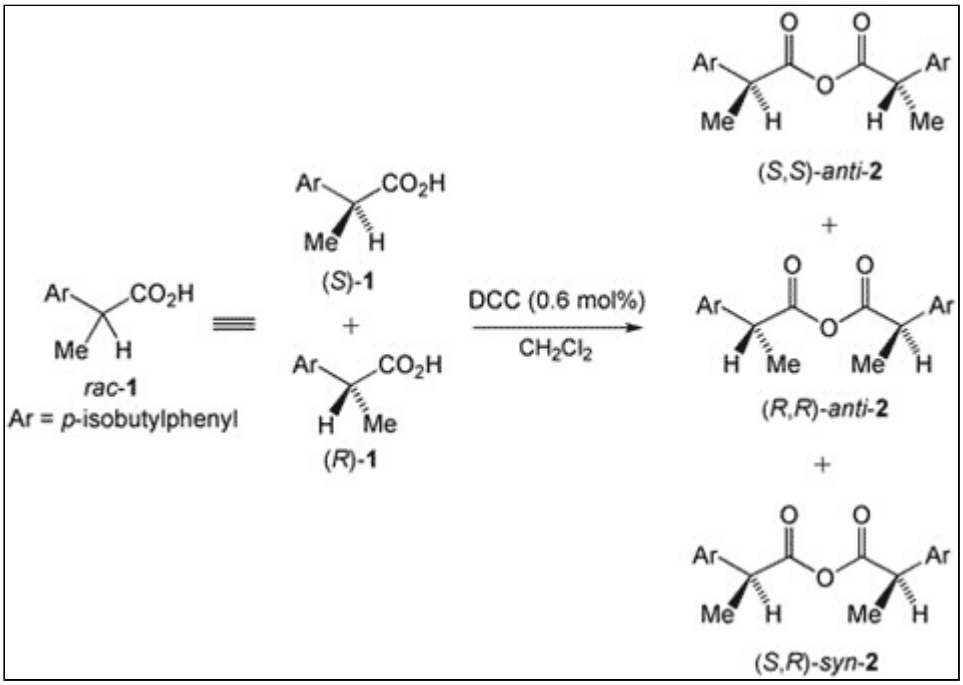
Noteworthy Chemistry

May 25, 2009

A self-coupling method determines the enantiomeric purity of profens. Current methods to determine the enantiomeric purity of profens (2-phenylpropionic acid and related compounds) usually require derivatization, chiral HPLC, or NMR with chiral shift reagents. E. Coulbeck and J. Eames* at the University of Hull (Kingston upon Hull, UK) report a new way to determine enantiopurity by using a profen self-coupling reaction.

The coupling reaction is mediated by *N,N'*-dicyclohexylcarbodiimide (DCC). When a racemic mixture of profens (e.g., *rac*-**1**) is coupled, the product consists of a 1:1 mixture of chiral and meso anhydrides. The chiral products are (*S*,*S*)-*anti*-**2** and (*R*,*R*)-*anti*-**2**; the meso product is (*S*,*R*)-*syn*-**2**. The diastereomeric ratio of the anhydrides, determined by NMR without chiral shift reagents, can be related to the enantiomeric purity of the parent carboxylic acids.



The authors showed that the coupling reaction is enantiospecific by treating enantiomerically pure (*S*)-**1** with DCC to give only (*S*,*S*)-*anti*-**2**. The reaction is stereorandom; the diastereoselectivity is independent of the conversion percentage and the amount of remaining unreacted carboxylic acid.

To test the robustness of the method, the authors subjected a series of enantioenriched mixtures of **1** to the self-coupling reaction. The product diastereoselectivity levels compared well with theoretical values. The original carboxylic acids can be obtained by alkaline hydrolysis of the anhydrides. (*Tetrahedron: Asymmetry* **2009,** *20,* **635–640**; **José C. Barros**)

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A polymer membrane protects anticancer drugs from premature release. In cancer research, emulsion-based drugs and drug carriers are attractive because of their compatibility with body fluids. F. Caruso and co-workers at the University of Melbourne (Victoria, Australia) developed a way to produce monodisperse micelles (*Chem. Mater.* **2008,** *20,* 2063–2065); they have now applied this technique to the production of anticancer drug carriers. The drug particles are designed to be encapsulated in hydrophilic shells made by attaching thiol groups to poly(methacrylic acid) (PMA). The shells prevent the drugs from migrating into body fluids.

Uniform-size silica particles are used as the sacrificial template; they are enclosed in sequential poly(*N*-vinylpyrrolidone) (PVP) and PMA layers via intermolecular hydrogen bonding. The silica core and PVP inner layer are then removed. To prevent the shell from decomposing, PMA molecules are cross-linked with thiol groups. The resulting hollow polymeric shells entrap the drug particles to form blood-inert micelles that can enter cancer cells without interference. After the polymer shield decomposes within the cell, the anticancer drug is released. (*Adv. Mater.* **2009,** *21,* **1820–1824**; **Sally Peng Li**)

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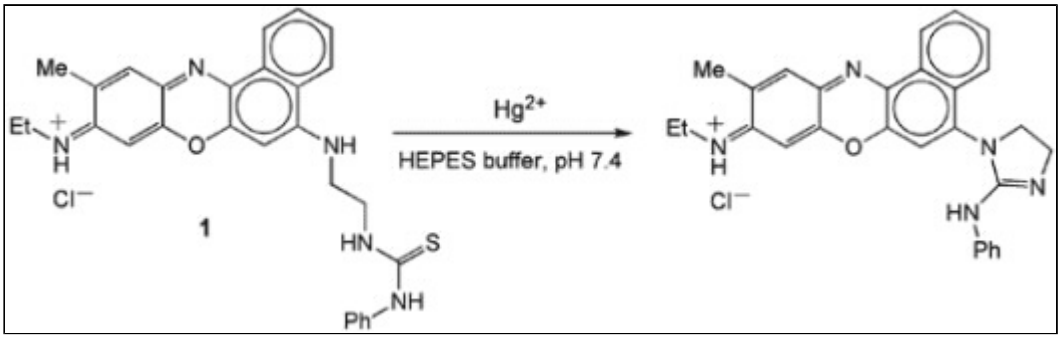
Nile blue chemical sensors detect nanomolar mercuric ion. The ingestion and inhalation toxicity of mercury is well established and makes selective and sensitive methods for detecting it in biological samples critically important. One approach to this problem is using a chemodosimeter, which selectively reacts with a particular metal ion to produce a unique spectroscopic change. Several such techniques, based on the mercury desulfurization reaction, have been developed for Hg^{2+} ion-selective detection. However, their usefulness in biological samples is hampered by poor water solubility or modest sensitivity.

C. Kang, J. S. Kim, and coauthors at Korea University (Seoul), Sungkyunkwan University (Suwon, Korea), and Kyung Hee University (Yongin, Korea) developed a new derivative of Nile blue dye (**1**). This compound absorbs and emits at 630 and 652 nm, respectively, with a high quantum yield. Its hydrochloride salt is highly soluble in water. Its reaction with Hg^{2+} results in a desulfurization-based cyclization that leads to a shift in the absorption and emission of **1**. The reaction is completed in a practical time frame of <1 min.



The authors found that neither selectivity nor sensitivity of **1** toward Hg^{2+} is compromised by the presence of high concentrations of Na^+, K^+, Ca^{2+}, or Mg^{2+}. In addition, **1** retains a high Hg^{2+}-selective chemodosimetric response even in the presence of Zn^{2+}, Cd^{2+}, Co^{2+}, Fe^{2+}, Ba^{2+}, and Ni^{2+}. The detection of Hg^{2+} is apparent to the naked eye in the presence of other cations and is useful over a pH range of 2–9.

The researchers confirmed the sensitivity of **1** by developing a fluorescence profile versus Hg^{2+}. The profile clearly demonstrates that **1** can respond to <1.0 ppb of aqueous Hg^{2+}—below the 2.0-ppb limit of Hg^{2+} in drinking water mandated by the US Environmental Protection Agency.

As a further indication of practical use, the authors detected Hg^{2+} in deproteinized blood plasma that contained 5.0 μM of Hg^{2+}. The blue shift of the emission band of **1** changed immediately, verifying that **1** can detect Hg^{2+} in human blood samples in the micromolar range. They also tested the system in the presence of highly concentrated bovine serum albumin, the most abundant plasma protein in human blood serum. Under these conditions, the fluorescence of **1** selectively changed in the presence of the Hg^{2+} ion, demonstrating its value as a chemodosimeter for biological samples. (*Org. Lett.* **2009,** *11,* **2101–2104**; **W. Jerry Patterson**)

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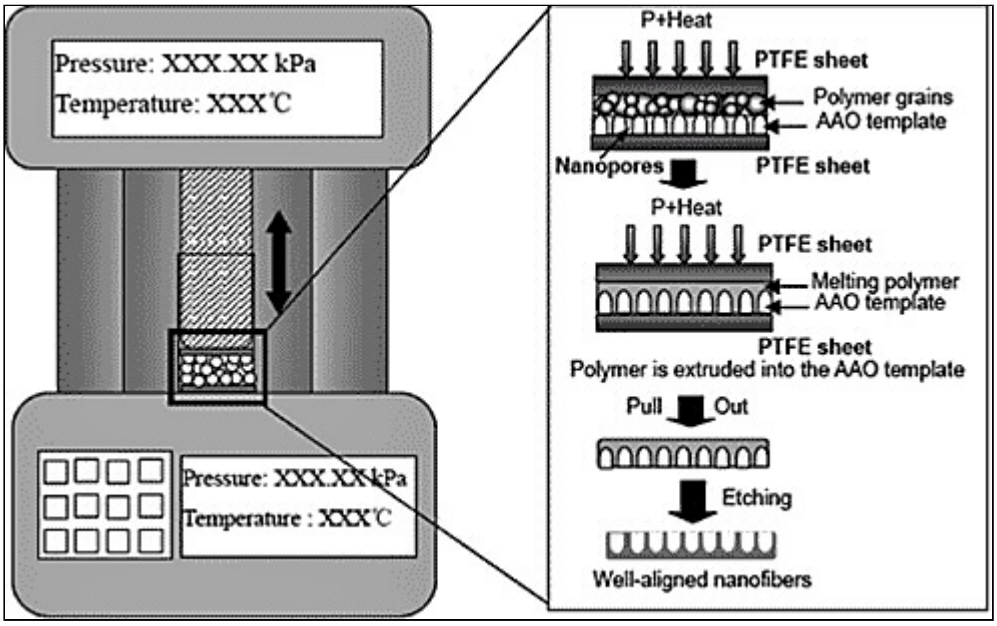
Nanoextrusion process yields superhydrophobic surfaces with variations in wetting adhesion. X. Sheng at Inner Mongolia Agriculture University (Hohhot, China) and J. Zhang* at the Aerospace Research Institute of Material and Processing Technology (Beijing) report a simple, reproducible nanotemplate extrusion process for developing superhydrophobic surfaces from high-density poly(ethylene) (HDPE) nanofiber arrays. They made large-area (16 mm x 1.8 mm) HDPE nanostructured arrays by extrusion through straight-channel anodic aluminum oxide (AAO) nanoporous templates and subsequent etching.



The diameters and lengths of the HDPE nanofibers were tuned by varying the AAO template diameter (~27, ~136, and ~218 nm) and the extrusion temperature and pressure. The HDPE nanoarrays were not completely straight; the authors attributed this to the etching and cleaning processes and to self-aggregation and deformation from strong capillary forces. For example, the smaller diameter HDPE nanofibers formed 5–30 μm diam bundles that generated pores on the array surface, whereas no bundles of HDPE nanofibers derived from ~136- and ~218-nm AAO templates were observed.

As expected, the nanostructured assemblies directly affected the wetting dynamics of the HDPE nanoarrays. The maximum contact angle (CA) was obtained on the HDPE nanofibers templated from ~136-nm AAO. The high-CA surfaces also exhibited low sliding angles. The authors suggest that the pore structure generated by nanofiber HDPE bundling at the smallest template diameter results in a large sliding angle (~90°), high wetting hysteresis (e.g., reduction in CA value), and strong wetting adhesion. In contrast, low wetting adhesion with significant rebound upon drop impact occurs on the HDPE nanofiber surface with ~136-nm pore diam, but the CA remains relatively constant. (*Langmuir* **2009,** *25,* Article ASAP DOI: **10.1021/la9002077**; **LaShanda Korley**)

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Beware of new cocrystalline phases! A synthesis of 6-nitro-1-indanol, to be used to make a muscarinic receptor antagonist, started from a commercially available 4:1 mixture of 6- and 4-nitro-1-indanone. Separating the nitroindanone mixture is tedious, so the mixture was reduced with $NaBH_4$ to give the corresponding mixture of 6- and 4-nitro-1-indanols. Crystallization of the nitroindanol mixture efficiently rejected the unwanted 4-nitro-1-indanol.

M. M. Hansen and co-workers at Eli Lilly (Indianapolis) scaled up the crystallization in a pilot plant. In the first two batches, the products contained 1.2% of the 4-nitro isomer. The third batch, however, produced material with 20.1% of the 4-nitro isomer. This new cocrystalline phase was thermodynamically more stable than the 6-nitroindanone crystals, and the original separation could no longer be repeated. (*Org. Process Res. Dev.* **2009,** *13,* **198–208**; **Will Watson**)

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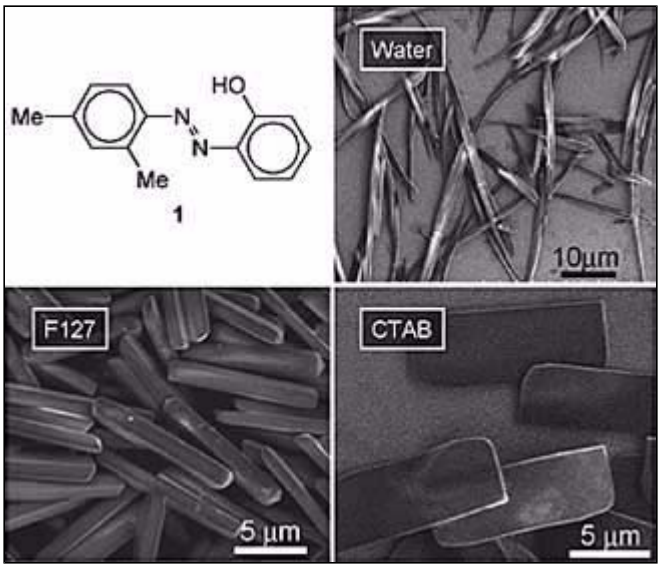
Control morphological structure and enhance luminescence efficiency of organic microcrystals.

Materials scientists all over the world are attempting to make organic low-dimensional microstructures with controlled morphologies and advanced functionalities. H. Yu and L. Qi* of Peking University (Beijing) have developed a system that accomplishes these goals.



The researchers made micro-sized ribbons, rods, and plates by precipitating THF solutions of the organic dye Sudan II (**1**) in water, Pluronic F127 solution, and cetyltrimethylammonium bromide (CTAB) solution. Pluronic F127 is an amphiphilic triblock copolymer of ethylene and propylene oxides. Whereas the THF solution of Sudan II is nonemissive, its microstructured aggregates are highly luminescent. Unique 1-D and 2-D waveguiding effects are observed in the precipitated luminogen microcrystals.

The authors foresee that microcrystals with defined morphological structures and unique optical effects may be used as building blocks for miniaturized photonic devices. (*Langmuir* **2009,** *25,* Article ASAP DOI: **10.1021/la900296y**; **Ben Zhong Tang**)

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