Producing specific secondary alcohols via ketone catalysis

Jing Wu et al. have synthesized enantiomerically pure secondary alcohols under mild reaction conditions. The stereospecific alcohols, formed by the hydrosilylation of prochiral ketones, are intermediates in the manufacturing of industrial compounds and pharmaceuticals. Previous methods for creating the alcohols have been hampered by the high cost of metal catalysts, low substrate-to-catalyst ratios, and rigorous production conditions. In previous work, the authors developed a system using the atropisomeric dipyridylphosphine ligand P-Phos and its analogs for ruthenium-catalyzed hydrogenation of a broad scope of simple ketones. In the present study, the authors employed the Xyl-P-Phos analog and demonstrated that, in a nitrogen atmosphere, it served as an effective catalyst for the hydrosilylation of acetophenone in the presence of CuF₂. Other copper(I) and copper(II) salts showed diminished reactivities. When the reactions were carried out in air atmosphere and at moderately low temperatures (−20°C), they could produce levels of enantioselectivities for meta- and para-substituted acetophenones of up to 97% and achieve high activities with substrate/ligand ratios of 50,000–100,000. The authors employed their catalyst system in a wide array of asymmetric diaryl ketones without the addition of organic or inorganic bases and found similar selectivities, representing an important advancement in the field.

“Delineation of a unique protein–protein interaction site on the surface of the estrogen receptor” by Eric H. Kong, Nina Heldring, Jan-Åke Gustafsson, Eckardt Treuter, Roderick E. Hubbard, and Ashley C. W. Pike (see pages 3593–3598)
Identifying potential ALS therapeutics

Soumya Ray et al. use a combination of in silico and in vitro methods to identify compounds that may act to inhibit the progression of familial amyotrophic lateral sclerosis (FALS). Previous research has shown that FALS, a genetic form of the degenerative motor neuron disease, is caused by mutations in the gene encoding the enzyme superoxide dismutase 1 (SOD-1). Wild-type SOD-1 protein, a metalloenzyme responsible for scavenging superoxide ions, functions as a homodimer, whereas the mutant protein uncouples and forms insoluble toxic aggregates in affected neurons. The authors employed computational methods to identify drug-like compounds that bind the protein dimerization site and calculated the docking affinities of >1.5 million small molecules. The authors screened the top 100 binders and found that 15 of these compounds significantly slowed in vitro aggregation and denaturation of three FALS-linked SOD-1 variants: A4V, G93A, and G85R. A mutant enzyme having a disrupted binding site was unaffected by the small molecules and continued to form aggregates. Wild-type SOD-1 protein requires zinc and copper to be active, and the authors showed that these compounds stabilized mutant SOD-1 homodimers in both the presence and the absence of metal ions.

“Small-molecule-mediated stabilization of familial amyotrophic lateral sclerosis-linked superoxide dismutase mutants against unfolding and aggregation” by Soumya S. Ray, Richard J. Nowak, Robert H. Brown, Jr., and Peter T. Lansbury, Jr. (see pages 3639–3644)

Wound healing process related to breast cancer survival

In some breast cancers, a set of genes involved in wound healing show distinct expression profiles, and these wound-response signatures can help predict the long-term health of patients, researchers report. Previous work discovered consistent features in the transcriptional response of cells in a simulated wound-healing environment and linked this genetic expression profile to cancer progression in a variety of common epithelial tumors. To explore whether this gene signature could be reliably used to guide clinical decisions and biologic experimentation, Howard Chang et al. turned to an independent data set from 295 breast cancer patients in The Netherlands. The authors found that patients whose tumors expressed the wound-response signature had lower rates of both overall survival and distant metastasis-free survival. The authors then developed a prognostic wound-response score, which quantifies the degree to which a patient’s individual expression pattern matches the canonical wound-response signature found in previous work. This score was a more accurate independent predictor of metastasis and death than the classic risk factors clinicians now use. The authors suggest that this work demonstrates the strengths of a bottom-up approach to gene expression research that involves developing and testing specific hypotheses about the pathogenic mechanisms underlying clinical outcomes, as opposed to top-down methods that fit simple models to global gene expression data.

“Robustness, scalability, and integration of a wound-response gene expression signature in predicting breast cancer survival” by Howard Y. Chang, Dimitry S. A. Nuyten, Julie B. Sneddon, Trevor Hastie, Robert Tibshirani, Therese Sørlie, Hongyue Dai, Yudong D. He, Laura J. van’t Veer, Harry Bartelink, Matt van de Rijn, Patrick O. Brown, and Marc J. van de Vijver (see pages 3738–3743)

Termites choose food by resonant frequency

Termites choose their food carefully, but how they decide which pieces of wood to feed on is not well understood. Different termite species are known to prefer eating particular sizes of wood, presumably to avoid competition with neighboring groups. Theodore Evans et al. investigated exactly how the blind insects measure size after only minimal contact with wood. In large and small blocks of wood, the researchers recorded the foraging sounds of worker drywood termites (Cryptotermes domesticus), which normally prefer to eat small pieces of wood. The authors then broadcast these sound vibrations into fresh wood blocks of equal size and gave them to another group of termites to eat. With only recorded noises to guide their choice of blocks, the termites preferred tunneling into wood with signals from the small block over those with the signal from the large block. Furthermore, the termites could distinguish the recorded foraging sounds from artificially generated signals of the same frequency and from randomly generated pink noise, a filtered variant of white noise. These findings suggest that the termites use the resonant frequency of a block of wood to assess its size and can perhaps discriminate the source of the vibration.

“Termites assess wood size by using vibration signals” by Theodore A. Evans, Joseph C. S. Lai, Emilie Toledano, Lee McDowall, Sandrine Rakotonarivo, and Michael Lenz (see pages 3732–3737)