

# Applied chemistry

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## Conversion of CO<sub>2</sub> from air into methanol

Carbon dioxide captured from air can, for the first time, be directly converted to CH<sub>3</sub>OH in relatively high yields (ca79%) (J. Kothandaraman, A. Goepfert, M. Czaun, G. A. Olah, G. K. Surya Prakash; *J. Amer. Chem. Soc.*, 2016, **138**, 778).

The highly efficient homogeneous catalyst system utilises pentaethylenhexamine and Ru-Macho-BH at 125–165°C in an ethereal solvent (initial turnover frequency = 70h<sup>-1</sup> at 145°C). The CH<sub>3</sub>OH can be easily separated by simple distillation from the reaction mixture.

The robustness of the catalytic system was shown by recycling the catalyst over five runs without significant loss of activity (turnover number > 2000). Various sources of CO<sub>2</sub> can be used for this reaction including air, despite its low CO<sub>2</sub> concentration (400 ppm).

## Hydrocarbon synthesis

A one-step, gas-phase photothermocatalytic process for the synthesis of hydrocarbons, including liquid alkanes, aromatics, and oxygenates, with carbon numbers (C<sub>n</sub>) up to C<sub>13</sub>, from CO<sub>2</sub> and water has been demonstrated in a flow photoreactor operating at elevated temperatures (180–200°C) and pressures (1–6bar) using a 5% cobalt on TiO<sub>2</sub> catalyst and under UV irradiation (W. Chanmanee, M. F. Islam, B. H. Dennis, F. M. MacDonnell; *PNAS*, 2016, 2579).

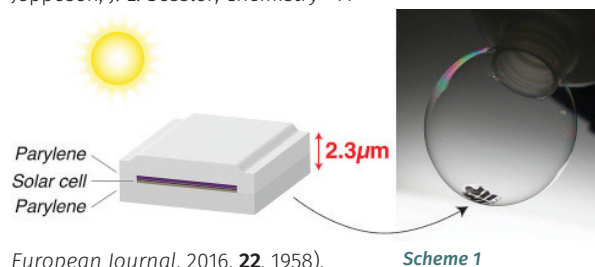
Temperatures in excess of 160°C are needed to obtain the higher C<sub>n</sub> products in quantity and that the product distribution shifts toward higher C<sub>n</sub> products with increasing pressure. When optimised over 13% by mass of the products, C<sub>5</sub>+ hydrocarbons and some of these, ie, octane, are drop-in replacements for existing liquid hydrocarbons fuels. Dioxygen is detected in yields ranging between 64% and 150%.

In principle, this tandem photochemical–thermochemical process, fitted with a photocatalyst better matched to the solar

spectrum, could provide a cheap and direct method to produce liquid hydrocarbons from CO<sub>2</sub> and water via a solar process that uses concentrated sunlight for both photochemical excitation to generate high-energy intermediates and heat to drive important thermochemical carbon-chain-forming reactions.

## Explosive detector

Scientists have created a supramolecular polymeric material that turns fluorescent if there are molecules from explosives in the vicinity (S. Bähring, L. Martín-Gomis, G. Olsen, K. A. Nielsen, D. S. Kim, T. Duedal, Á. Sastre-Santos, J. O. Jeppesen, J. L. Sessler; *Chemistry – A*



*European Journal*, 2016, **22**, 1958).

The new explosive detector comprises a short supramolecular oligomeric system based on two hetero-complementary subunits, a tetrathiafulvalene-functionalised calix[4]pyrrole (TTF-C[4]P) and a glycol diester-linked bis-2,5,7-trinitro-dicyanomethylene-fluorene-4-carboxylate (TND CF). When mixed in organic solvents, such as CHCl<sub>3</sub>, CH<sub>2</sub>ClCH<sub>2</sub>Cl, and methylcyclohexane, supramolecular aggregation takes place to produce short oligomers stabilised by hydrogen bonding and donor–acceptor charge-transfer (CT) interactions.

The fluorescence emitting properties of TND CF are quenched under conditions that promote the formation of supramolecular aggregates containing TTF-C[4]P and TND CF. However, in the presence of substrates in the form of anions, ie chloride, and nitroaromatic explosives, ie 1,3,5-trinitrobenzene, mixtures of TTF-C[4]P and TND CF produce a fluorescence ‘turn-on’ response.

The discovery could improve, for example, airport security – and also it gives us an insight into a rather chaotic micro-world where molecules and atoms constantly are responding to their surroundings.

## Invisibility cloak

In recent years, there has been a surge of interest in invisibility cloaks, made from light-bending structures known as metamaterials. Since invisibility cloaks are currently limited to microwaves, the next best option could be a form of adaptive camouflage based on a reflective display, like the sort used in e-book readers. Some of these displays can generate a variety of colours, but to do so they currently need heavily layered structures, which reduce overall reflectivity and give a dull appearance.

Plasmonic metal nanostructures could be the answer. If light falling on these materials has the right wavelength – that is, the right colour – it meets a collective oscillation of charge known as a plasmon that forces it to reflect. Tuning the size and composition of the nanostructures controls the colour of light that is reflected, but normal methods of fabrication leave the structures fixed.

Scientists from the US and China have developed a way to produce colour-tuneable plasmonic metal nanostructures (G. Wang, X. Chen, S. Liu, C. Wong, S. Chu; *ACS Nano*, 2016, **10**, 1788).

They consist of a layer of nano-sized gold domes coated with a gel containing silver ions, all of which are sandwiched between two electrodes. Applying a positive voltage between the electrodes binds the silver ions to the gold domes, changing the characteristic plasmon reflectivity from red to green and finally blue; reversing the voltage takes the reflectivity back to the red end of the spectrum.

To demonstrate the colour-shifting effect, the researchers attached lots of their cells to a mechanical chameleon that had colour sensors for eyes. As the chameleon rolled in front of a striped background, the sensors detected the stripe colour and tuned the cells’ colours automatically.

## Production of polyamides from sugar

Biorefineries aim to convert biomass into a spectrum of products ranging from biofuels to specialty chemicals.

To achieve economically sustainable conversion, it is crucial to streamline the catalytic and downstream processing steps. A route that combines bio- and electrocatalysis to convert glucose into bio-based unsaturated nylon-6,6 has been reported (M. Suastegui, J. E. Matthiesen, J. M. Carraher, N. Hernandez, N. R. Quiroz, A. Okerlund, E. W. Cochran, Z. Shao, J.-P. Tessonnier; *Angew. Chem. Int. Ed. Engl.*, 2016, **55**, 2368).

An engineered strain of *Saccharomyces cerevisiae* was used as the initial biocatalyst for the conversion of glucose into muconic acid, with the highest reported muconic acid titer of 559.5 mg L<sup>-1</sup> in yeast. Without any separation, muconic acid was further electrocatalytically hydrogenated to 3-hexenedioic acid in 94% yield despite the presence of biogenic impurities. Bio-based unsaturated nylon-6,6 (unsaturated polyamide-6,6) was finally obtained by polymerisation of 3-hexenedioic acid with hexamethylenediamine.

### Room temperature catalytic hydrogenation of olefins

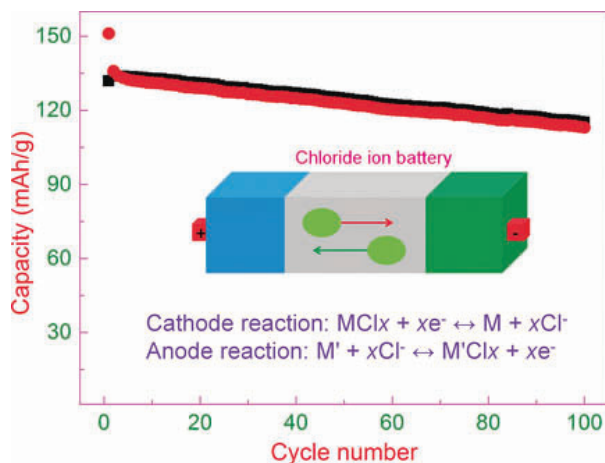
Incorporation of palladium nanocubes (NCs) into the metal-organic framework ZIF-8 affords the composite Pd NCs@ZIF-8, which acts as an efficient catalytic hydrogenation of olefins at room temperature under light irradiation (Qihao Yang, Qiang Xu, Shu-Hong Yu and Hai-Long Jiang; *Angew. Chem. Int. Ed. Engl.*, 2016, **53**, 3685).

The superior catalytic performance is due to the plasmonic photothermal effects of Pd NCs and the multiple roles (H<sub>2</sub> enrichment, size sieving, and Pd stabilisation) of the ZIF-8 shell. Remarkably, the catalytic efficiency of a reaction under 60 mW cm<sup>-2</sup> full-spectrum or 100 mW cm<sup>-2</sup> visible-light irradiation at room temperature is comparable with that of a process driven by heating at 50 °C.

### Lightweight solar cells

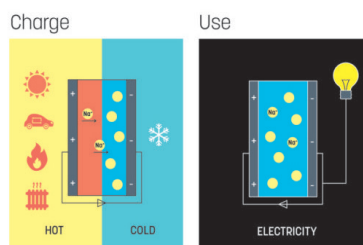
Solar cells that are so thin and lightweight they can be draped over the surface of a soap bubble have been fabricated by researchers in the US (J. Jean, A. Wang and V. Bulović; *Org. Electron.*, 2016, **31**, 120) (Scheme 1).

The key to producing such thin (1.3 μm thick) solar cells, weighing just 3.6 g/m<sup>2</sup>, is the fabrication process, which uses vapour deposition to manufacture the supportive substrate



**Scheme 2 Key:**  
(green) Cl<sup>-</sup>  
(blue) MCl<sub>x</sub> (cathode),  
(green) M' (anode)  
→ (red) discharging  
← green charging

and a protective overcoat (both made of poly(p-xylylene), a polymer which can be made into thin, flexible sheets) together with the light-



**Scheme 3**

absorbing components in a single process, rather than making each layer separately and then assembling them. They are produced within a vacuum chamber at room temperature, and no solvents are used, which avoids the cells becoming contaminated with substances that could reduce their performance.

In this case, the solar cells themselves were organic – based on tetraphenylidibenzoperiflanthene (DBP) – but the team say the manufacturing process could be compatible with other materials such as perovskites or quantum dots. While the solar cells are not particularly efficient, in terms of power-to-weight ratio they outperform commercially available solar panels, with an output of 6 W/g – around 400 times higher than a typical silicon-based solar module with a heavy glass cover.

### Rechargeable chloride ion battery

A novel room temperature rechargeable battery with VOCl cathode, lithium anode, and chloride ion transporting liquid electrolyte has been reported (P. Gao, M. Reddy, X. Mu, T. Diemant, L. Zhang, Z. Zhao-Karger, V. S. K. Chakravadhanula, O. Clemens, R. J. Behm, M. Fichtner; *Angew. Chem. Int. Ed. Engl.*, 2016, **55**, 4285).

The cell is based on the reversible

transfer of chloride ions between the two electrodes (Scheme 2). The VOCl cathode delivers an initial discharge capacity of 189 mAh g<sup>-1</sup>. A reversible capacity of 113 mAh g<sup>-1</sup> can be retained even after 100 cycles when cycled at a high current density of 522 mA g<sup>-1</sup>.

This is the first known high cycling stability in chloride ion batteries, demonstrating the practicality of the system beyond a proof of concept model.

### Thermoelectric supercapacitor

In the future, we could have a completely new type of energy storage, charged by heat energy, for example, during the day when the sun shines, or by waste heat from an industrial process, thanks to the research of scientists based in Sweden (D. Zhao, H. Wang, Z. U. Khan, J. C. Chen, R. Gabrielsson, M. P. Jonsson, M. Berggren, X. Crispin; *Energy Environ. Sci.*, doi: 10.1039/C6EE00121A) (Scheme 3).

The ionic thermoelectric supercapacitor (ITES), fabricated from inexpensive and non-hazardous fluid electrolytes consisting of ions and conductive polymers, has patents pending, and it should be fully possible to manufacture it on an industrial scale.

The ITES is in essence an energy storage device: a type of battery that consists of an electrolyte of charged particles – ions – between two electrodes. The charge is stored next to the electrodes in carbon nanotubes. When exposed to a temperature gradient – that is, one end is warm and the other cold – the ions rush towards the cold side of the supercapacitor and an electric current arises (Soret effect).

Since positively-charged ions are small and quick, while the negatively-charged polymer molecules are large and heavy, when one end is heated and the other one cooled down, the small, quick ions rush towards the cold side while the heavy polymer chains stay where they are.

Since they are ions, and not electrons, they stick to the metal electrodes. The charge that then arises is stored in carbon nanotubes next to the metal electrodes, and can be discharged whenever the electricity is needed.

The researchers claim that the ITES can convert and store 2,500 times more energy than the best of today's supercondensers linked to thermoelectric generators.

# Biomedical

Kevin Burgess Texas A&M University, US

## Exomes in cancer

A massive coordinated effort to investigate the behavior of integrin-expressing exosomes in cancer is under way. Cells release small (30 – 100 nm) vesicles into fluids that surround them. In doing so, the cells are not excreting junk, but instead are sending targeted messages that may perturb the function of other cells they encounter.

In this study, the exosomes are from various types of cancer cells, the targeting groups (analysed using MS and proteomics techniques) are integrins, and the messages may be RNA fragments (*Nature*, 2015, **527**, 329). The findings begin to answer some fundamental questions.

For instance, why do tumors that originate in particular organs, tend to selectively metastasize to some other organs in preference to others?

The answer that may be extrapolated from this study is that some endosomes may express integrins, and their targets may express the corresponding integrin receptors. By isolating endosomes from particular types of cancer cells, labeling them with near-IR dyes, and injecting them into mice, these researchers show how endosomes can 'prime' certain organs to be the victims of metastatic spread of tumor cells from other organs, induced after the priming sequence. These effects are mitigated by simultaneous treatment with appropriate integrin ligands.

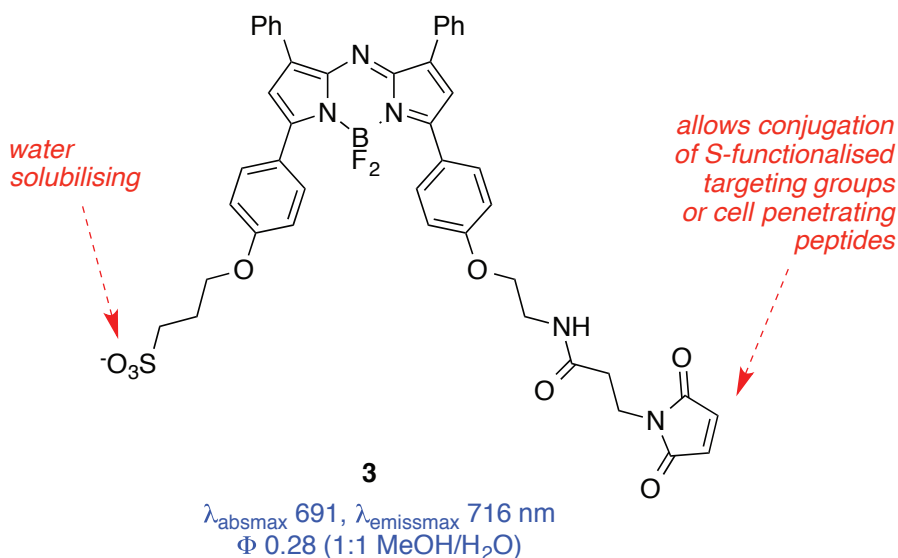
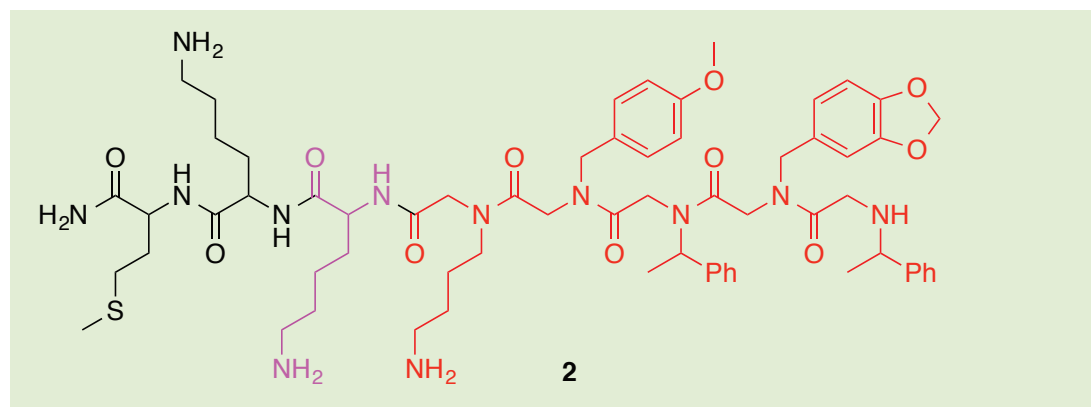
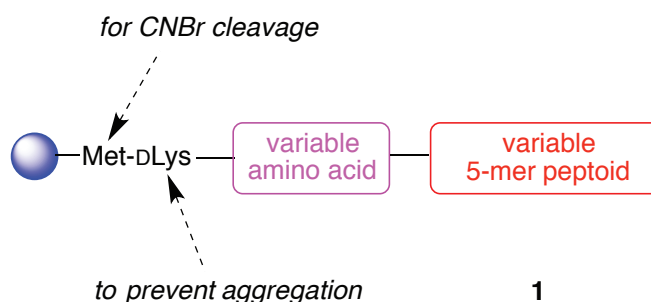
## Peptide-peptoids to target cancer

Udugamasooriya and co-workers at UT Southwestern made a supported library of the type **1** and screened it to find ligands that selectively bound lung cancer cells over bronchial epithelial cells from the same patient (*ACS Chem. Biol.*, doi acschembio.5b00592).

They did this by staining the cancerous cells red and the normal cells green, then incubating them with the beads; only three beads out of 400,000 associated with exclusively red-stained cells. Analysis of those beads showed they bore similar

structures, of which **2** is illustrative. Compound **2** bound the cancerous cells with an affinity of 5 – 7  $\mu$ M.

Curiously, a dimer of **2** showed moderate ( $IC_{50}$  >15  $\mu$ M) only to the cancer cells. *In vivo*, a biotinylated



form of the dimer was shown to accumulate in tumors (analysis via streptavidin-Cy3 after snap freezing and organ removal), but the maximum tolerated dose was low (1 – 5 mg/kg).

## Aza-BODIPY imaging agents

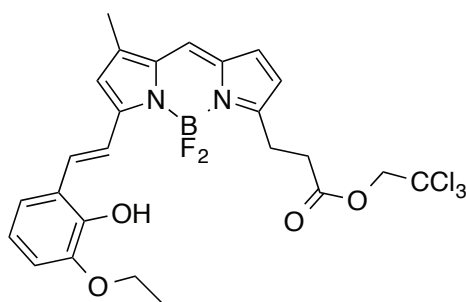
Aza-BODIPY dyes have some appealing characteristics for *in vivo* fluorescence and photodynamic therapy, but they tend to be poorly water soluble, prone to aggregation, and must be engineered to

accommodate peripheral functional fragments. O'Shea and co-workers have found a nice way to do this (*Chem. Commun.*, 2015, **51**, 16667).

They produced fluor **3** that is somewhat hydrophilic, and can be selectively conjugated thiol functionality (over which are more abundant in proteins) to attach targeting groups or cell penetrating peptides. A conjugate of **3** with an RGD-based targeting group was introduced intravenously into mice implanted with subcutaneous human esophageal cancer.

#### A $\beta$ -Oligomer specific probes

Young-Tae Chang and co-workers in NUS, Singapore, have had tremendous success derived from testing large libraries of fluorescent dyes against cells via high throughput screening techniques. In an illustrative effort, they selected five fluors from 3500 that gave greater fluorescence in 7PA2 than CHO cells (*J. Am. Chem. Soc.*, doi: jacs.5b06190).



**BD-Oligo**  
a probe for prefibrillar A $\beta$ -oligomers  
in Alzheimer's disease

The clever aspect of this is that 7AP2's putatively have enriched levels of A $\beta$ -oligomers whereas the CHO cells from which they are derived do not. These five hits were filtered to find leads via *in vitro* assays featuring stabilised A $\beta$ -oligomers, the corresponding monomers, and fibrils.

BD-Oligo showed the best contrast amongst these three A $\beta$ -states, and that correlated with responses to

antibodies that are known to be selective (or not) for prefibrillar oligomers. The dye had an apparent  $K_d$  for A $\beta$ -oligomers of 0.48  $\mu$ M. BD-Oligo treated samples showed increased fluorescence as prefibrillar oligomers formed, then decreased as mature fibrils dominated later.

Predictably, DFT calculations indicate the dye binds exposed hydrophobic patches on the prefibrillar oligomers, which are apparently less abundant as fibril formation proceeds. When injected *ip*, BD-Oligo showed some permeation into the brains of mice of the type commonly used as models for Alzheimer's disease, and stained specific regions.

Overall, this work is significant because literature (including some Highlighted previously in this column) indicates the special role of prefibrillar A $\beta$ -oligomers in the progress of Alzheimer's disease, and the difficulties in monitoring these entities *in vivo*.

# Organic chemistry

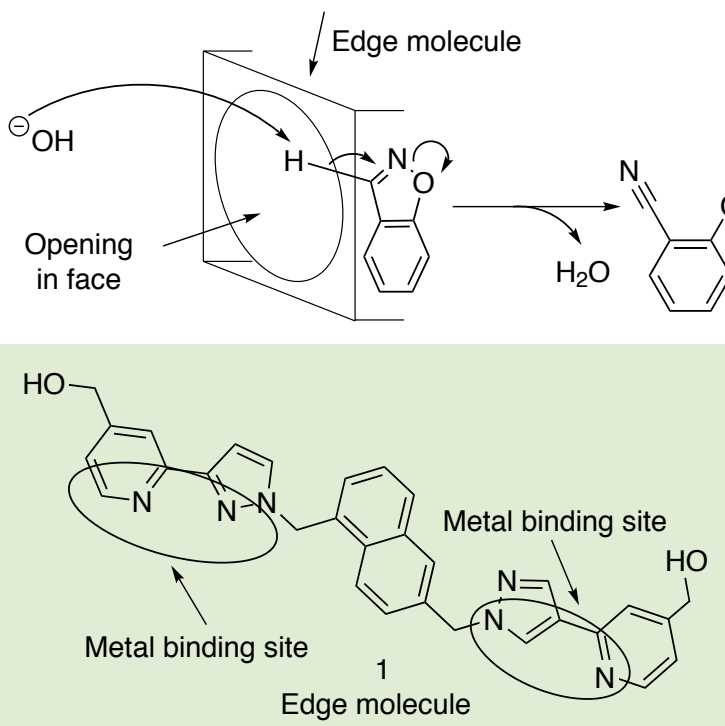
G. Richard Stephenson University of East Anglia, UK

#### Reactions in cages

The idea that macromolecular assemblies can encompass other molecules, or, potentially more significantly, the transition states for their reactions, is not new but in recent months, the precision by which this is performed is becoming far more sophisticated.

An excellent example has been described in a paper that showcases the octacobalt cube-like cages that can be built from tetracoordinating molecular rods (eg **1**) with a bidentate metal binding site at each end (W. Cullen, M. C. Misuraca, C. A. Hunter, N. H. Williams, M. D. Ward; *Nature Chem.*, 2016, **8**, 231).

The volume of a cube is determined by its edge dimension, so the internal binding capacity of these coordination cages is a consequence of the length of the tetracoordinate rods. In this case, encompassed within the cage is the Kemp elimination (Scheme 1)



**Scheme 1** Hydroxide ion accesses the benzisoxazole substrate through an opening in the face of a coordination chemistry cube-like cage (box: the tetracoordinate molecule that forms each edge of the cube)

in which the heterocyclic ring of a benzisoxazole is opened by an E2 process initiated by deprotonation at the  $-\text{CH}=\text{N}-$  position by hydroxide ion to form a 2-cyanophenolate.

The fit between this substrate and the cavity was initially predicted by computational modeling and confirmed by an X-ray crystallographic experiment in which the benzisoxazole was introduced into the preformed cube.

This approach provides important information. It establishes that the guest can enter the cage, *ie* the cage need not be built up around the guest in a stoichiometric directed-assembly fashion, and also reveals the orientation of the guest in the cage, which in this case leaves the CH bond directed towards one of openings that are in the center of each face. Since the coordination chemistry at the corners of these cubes uses  $\text{Co(II)}$ , the assembled cube is a 16+ cationic structure which attracts the hydroxide catalyst to the faces of the cube, increasing the effective concentration of the catalyst.

This is a novel example of a rate-enhancement process mediated by supramolecular chemistry.

#### Hirao-Chiba reduction uses NaH alkali metal composites

Sodium borohydride and lithium aluminium hydride are classic organic hydride donor reducing agents, and in organic chemistry, sodium hydride is well known and a powerful irreversible base.

A recent paper is set to change that by demonstrating novel hydride donor chemistry using an  $\text{NaH.LiI}$  or  $\text{NaH.NaI}$  composite reagent (P. C. Too, G. H. Chan, Y. L. Tnay, H. Hirao, S. Chiba; *Angew. Chem. Int. Ed.* 2016, **55**, 3719).

This is the type of development that is on track to become a new named reaction (the Hirao-Chiba

reduction?) if it proves to be general in its application. In this example, the  $\text{NaH}$  alkali metal composite reagent was used initially for the reductive decarbonylation of  $\text{MePh}_2\text{CCN}$ , but was then applied to reduce amides and lactams to secondary amines.

#### Trimetallic macrocyclic calcium sensors

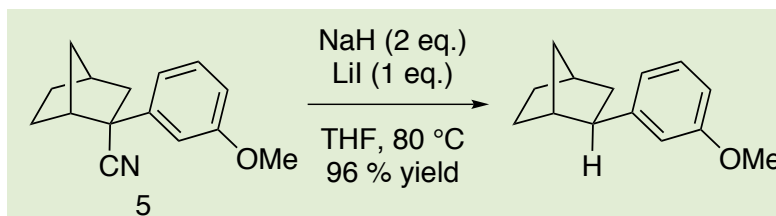
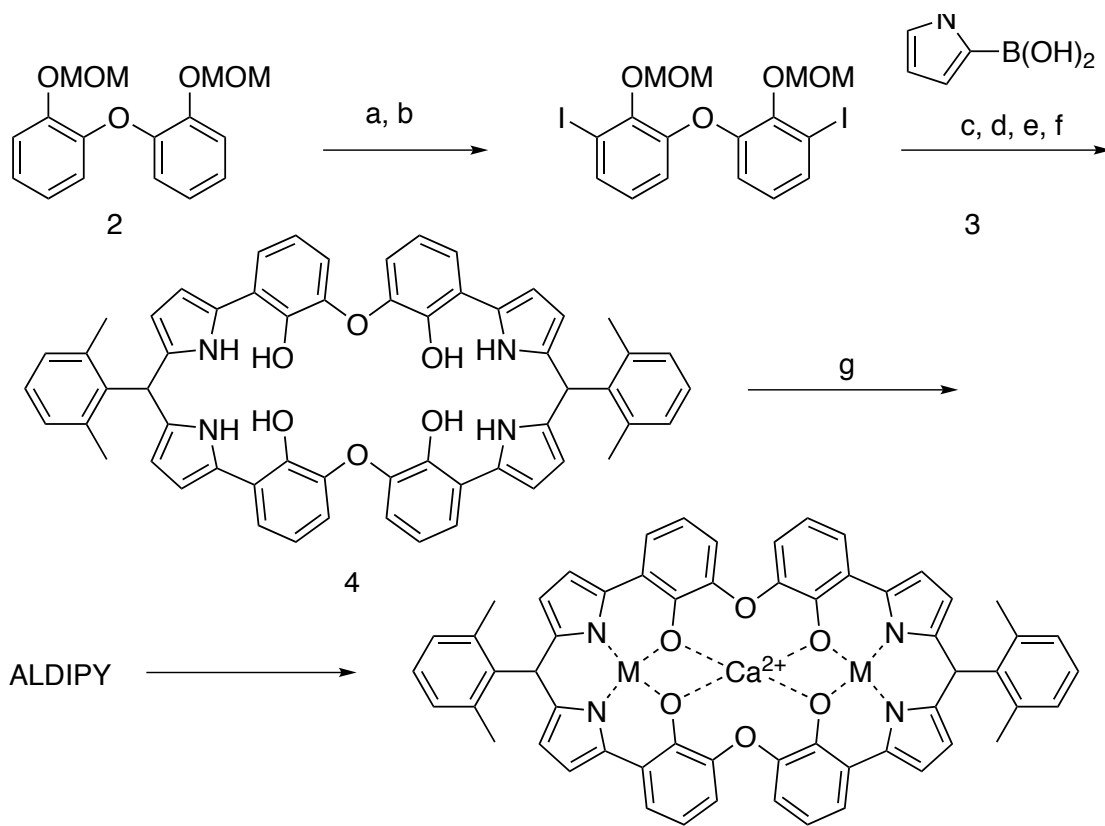
Developments of macrocycle host-guest metal binding to provide multiple metal binding site is a similarly transformative approach. An example uses dipyrin binding sites set in what is nowadays a relatively conventional macrocyclic ligand, built up by directed metallation of the diaryl ether (**2**), and iodination to prepare for Suzuki coupling with a 2-boronate pyrrole derivative (**3**) (M. Saikawa, M. Daicho, T. Nakamura, J. Uchida, M. Yamamura, T. Nabeshima;

*Scheme 2*, top, **a**:  $n\text{-BuLi}$ , THF,  $0^\circ\text{C}$  to rt, 2h, then **b**:  $\text{I}_2$ ,  $-40^\circ\text{C}$  to rt, 2.5 h, 58% yield; **c**:  $\text{Pd(PPh}_3)_4$ ,  $\text{Na}_2\text{CO}_3$ , THF/water, reflux, 25h, then  $\text{NaOMe}$ , rt 16.5h, 75% yield; **d**:  $\text{HCl aq.}$ , 2.5h; **e**:  $\text{MsCHO}$ , TFA, rt, 71h then **f**: DDQ, 6h, 11% overall yield from the product of Suzuki coupling step;  $\text{Al(Oi-Pr)}_3$ ,  $\text{NEt(OPr)}_3$ ,  $\text{CHCl}_3/\text{MeOH}$ , reflux, 36h, 37%; **g**: sensing application [ $\text{Ca(ClO}_4)_2$ ,  $\text{CH}_3\text{OH}/\text{H}_2\text{O}$  (9:1 v/v)]

*Chem. Commun.*, 2016, **52**, 4014) (Scheme 2).

The product has reactive pyrroles at each site, which allow cyclodimerisation with mesitaldehyde to form the macrocycle (**4**), which then binds two  $\text{Al(OMe)}_2\text{s}$  to produce 'ALDIPY'.

This is efficient and modern synthetic approach based on a well established (2,3-dimethoxyphenyl)-2-pyrrole/mesitaldehyde approach, but the true value of the 'ALDIPY' product is its ability to bind a further metal ion inside the central crown-like hexa-oxa region, which exploits two simple diaryl ether oxygen atoms and four aluminium-bound oxygens as the coordination centers. This turns out to provide an extremely powerful binding site for  $\text{Ca}^{2+}$ , which allows excellent performance in colorimetric and fluorometric sensing applications.



**Scheme 3** An example showing reduction of (**5**) with retention of stereochemistry. The reaction was performed in a sealed tube