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Agrochemical intermediates

Shackles on innovation

Agrochemical innovation is more necessary than ever, yet has never been more costly and difficult to do. We report from Informex USA 2010

Simply the pest

Are we on the verge of a new kind of chemistry in pest control? Elisabeth Jeffries reports

More from less in agrochemicals

Dr Susan Brench and Dr Chris Rainford review how Pentagon Chemicals streamlines the introduction of new agrochemical products and optimises the performance of existing processes

Leather & textile chemicals

So long, solvents

Plasma technology is perfect for giving fabrics a water-repellent nano-coating, so why is the textiles industry only just beginning to see its value, asks Emma Davies?

Eco & economical advantages of anti-soiling leather protection

Dr Michael Franken of Lanxess looks at the thinking behind the Aquaderm X-Shield technology

Electronic chemicals

Additives for copper electroplating in microelectronics

Dr Marco Arnold and Dr Cornelia Röger show how BASF develops key compounds for even smaller node sizes

Developments in chemistry for printed electronics

Dr Peter Harrop of IdTechEx takes a brief look at the role of the chemicals industry in the next electronic revolution

Sustainability

Keeping things going

Sustainability was the theme of Wacker Chemie’s international press briefing earlier this year

Getting to the point

Dennis McGrew of Genomatica outlines the case for directly produced, drop-in bio-based replacements for traditional manufacturing methods

Designing the next generation of biorefineries

Professor Franck Dumeignil of the Université Lille Nord de France presents the concept and the objectives of the EuroBioRef project

Osmium chemistry

Reactions & scope of osmium chemistry: An overview

James Thomson of Ceimig looks at the chemistry of the heaviest of the metallic elements

Outsourcing Special Publication

– Bound between pages 22 & 23
Out of the woods?

There are many positive indicators, but is it too soon to talk of recovery?

Following the worst economic crisis in living memory - even allowing for the fact that living memory seems to amount to about five years among the bankers who got us into this mess and subsequently arranged it that everyone else could pay their way out of it - there could only be one direction to go in.

After all, life went on, most of us still work, earn and consume. It was inevitable that at some point some common sense would find its way back into Western society after the panic. Just as inevitable, in fact, as that manufacturing industry would take more than its fair share of the pain and less than its fair share of the rewards. Some things don’t change.

The mood has generally been much better since one of the latest and most glorious springs Europe has enjoyed in decades. (Maybe not entirely a coincidence? Just a thought.) The indications for the chemicals industry have also been much more positive, both in terms of the predictions put out by industry bodies and the views of the financial markets.

In June, CEFIC put out its forecasts for growth in the chemicals industry, pharmaceuticals omitted, over the next 18 months. After the staggering slump in demand from Q4 2008 into 1H 2009, it said, demand had already seen “an equally sharp rebound” in 2H as the previous liquidation of supply chains was reversed, though this was nowhere near enough to make up for the previous drop. Overall, 2009 saw a fall of 11.3% in output.

The recovery in output levels continued in early 2010 at a rate well in excess of what CEFIC itself anticipated when it had looked at trends in November 2009. This is likely to continue well into the year. Overall, CEFIC forecasts year-on-year production growth of 9.5% this year.

For 2011, however, growth is forecast to fall sharply back to a more modest 2%. CEFIC warned that the recovery still looks fragile and that capacity utilisation within the industry still remains below normal levels. The industry would be vulnerable to any economic shocks arising from external factors, most worrying the prospect of sovereign debt defaults.

To look at in a wider perspective, from its peak of 110.5 (based on the year 2005 = 100) in Q1 2008, the fall to the trough in Q1 2009 was a staggering 20.2% to 88.2. The following 14.9% rise, to 101.3 in Q1 2010, still means that the industry is barely back to where it was in 2005 and will probably not reach 2008 levels again before 2013.

Both decline and rebound were sharpest at the commodity end of the market. Basic inorganics, polymers and petrochemicals saw falls of 18.5%, 16.4% and 8.9% respectively in 2009, followed by projected rebounds of 11.0%, 14.5% and 11.0% in 2010. For speciality chemicals, there was an 8.2% fall followed by a 8.5% rise. This sector, however, is forecast to see relatively strong 2.5% growth in 2011.

At more or less the same time, Moody’s Investors Service confirmed a stable outlook for the chemicals industry, which, it said, is “in a sustained rebound in Asia, Europe and the Americas”, aided by improving demand, low raw materials prices and strong balance sheets. Credit conditions are reasonably good and likely to remain so.

Moody’s industrial production figures for Europe differ very sharply from CEFIC’s - 2.3% growth this year, rising to 3.4% next - though the terms of reference are probably somewhat different. They are also well below what was projected for the US: 4.3% this year, falling to 4.1% next.

Moody’s also expected M&A activity in the industry to rise substantially in 2010. True, it was unlikely to go any lower after such a quiet year, but this view has been echoed by other leading analysts, such as Peter Young of Young & Partners and Dmitry Silverstein of Longbow Research.

More interestingly, many believe that a disproportionate amount of the deal-making would take place in speciality chemicals. The sector is less capital-intensive than basic chemicals and more affected by raw materials costs, which typically account for 60-80% of the cost-of-goods-sold at speciality chemicals companies. These have been a relatively benign factor since the slump took the sting out of previous hikes.

Moreover, as we documented in the April edition of SCM, even while delivering eye-wateringly bad results for last year, speciality chemicals companies have become rather good at conserving cash. Many generated record free cash flows in 2009, some of which has been used to pay down debt. Some of the rest must be available for acquisitions - and not just at the fire-sale prices that prevailed sometimes last year.

Right on cue, as we report this month, BASF has since agreed to buy Cognis in a deal that appears well-priced on both sides (page 6) and which - unusually - was well received, even in the short term, in the financial markets. Ironically, this will be the last of the major buys initiated by CFO Kurt Bock, who will become chairman of the management board next year.

What next? The process by which two industry behemoths, BASF itself and Dow, have transformed themselves into mainly speciality players is substantially complete although some of the latter’s commodity businesses still have ‘For Sale’ sign notices out. Who will drive forward the next wave of transformations that will reshape the industry?

And what will be the role of private equity? For some time during the downturn when cash was king, the companies who once seemed poised to take over the industry appeared a spent force. Now there are signs that they are back.

May saw the takeover of Mallinckrodt Baker by New Mountain Capital. And, more unusually still, even the labour unions, who often (correctly) regard private equity as asset-sweaters, were enthusiastic. Of course, it might not have happened but for the chance that Dow had made the former CEO of Rohm and Haas available to New Mountain - but this is, as we all know, a small world.

Dr Andrew Warmington
Editor - Speciality Chemicals Magazine
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BASF acquires Cognis for €3.1 billion

GERMANY

BASF has agreed to acquire Cognis from Permira Funds, GS Capital Partners and SV Life Sciences for an equity purchase price of €700 million in cash, €503 in pension obligations and extra debt to give a total enterprise value of €3.1 billion, or 7.3 times EBITDA. This should be completed by November, subject to regulatory approval.

This acquisition continues BASF’s recent strategic move from commodity to specialty chemicals, as well as adding over 5% to its sales and confirming it as the world’s largest chemicals company. A sale had been in the pipeline for some months; the three funds had tried to sell Cognis in 2006 but failed to secure the price they wanted, then considered an IPO only to abandon it as the European stock market slid down.

According to analysts, Cognis’s owners had hoped to get about €3.5 billion, while BASF was reluctant to pay over €3.0 billion, as it now believes that it overpaid for Ciba Specialty Chemicals last year. €3.2-3.3 billion was widely touted as the likely range. Lubrizol reportedly offered more, but only via a partly-share financed offer that did not interest the owners, and BASF became the preferred bidder.

Cognis employs about 5,600 people, almost 40% fewer than when it became the preferred bidder. Six billion was widely touted as the likely price range. Lubrizol reportedly offered more, but only via a partly-share financed offer that did not interest the owners, and BASF became the preferred bidder.

The Monnheim-based company has a supplier of products and services based on renewable raw materials for the health, nutrition, cosmetics, detergents and cleaning industries, as well as making products for mining, lubricants, coatings and agriculture.

The company’s position in home and personal care ingredients will be particularly boosted via Cognis’s strength in chemicals based on natural raw materials such as palm kernels and coconut oil. The Care Chemicals division has sales of €3.4 billion/year and was already targeting such areas as hair care, sun screen and thickeners.

The purchase was well received among financial analysts, giving a mild boost to BASF’s shares. Peter Spengler of DZ Bank called the price “reasonable”, adding that “BASF has a good track record in adding new segments”.

BASF’s credit rating will probably come down a notch because of the extra debt it has taken on - an extra €1.9 billion at the end of 2009. This will add to €13 billion in existing net debt. However, because BASF generates €3.5 billion/year in free cash flow, it does not need to take on extra loans.

This news came only a month after BASF announced that CEO Kurt Bock would succeed Dr Jürgen Hambrecht as chairman of the board of executive directors at the next AGM. Bock had been the architect of the €13 billion on purchases BASF has spent in the past seven years, most notably Engelhard and Ciba, but this will be the last major acquisition in the foreseeable future, according to Hambrecht.

Separately, BASF and Astra Polymer Compounding of Saudi Arabia are abandoning plans for a joint venture to produce customer-specific antioxidant blends (CSBs) in the Middle East. This had been agreed between Astra and the Plastic Additives business of the former Ciba. An existing tolling agreement with Astra covering CSBs is unaffected.

John Frijns, senior vice-president for plastic additives in the Europe/EAWA region, stressed that BASF is still “convinced of the strategic importance of the Middle East Region and the need for a local production unit for customer-specific blends”. However, he said, an evaluation of the Ciba legacy had revealed new options that will offer better value to BASF and its customers.

Investment options are now being evaluated.

Earlier, the Intermediates division of BASF had announced that it is working with RWI International, a research institute based in Research Triangle Park, North Carolina, to develop a cost-effective technology to capture CO2 from waste gases emitted by coal-fired power plants and other industrial sources. This is sponsored to the tune of €1.6 million by the US Department of Energy as part of its stimulus-funded initiative on energy-related research projects. With RTI, which will add its engineering and research capabilities, BASF plans to work on novel non-aqueous solvent systems that can be recycled and which would use 40% less energy than conventional amine-based processes. It already supplies its aMDEA (‘activated methyldiethanolamine’) brand of technologies to remove acid gases like hydrogen sulphide (H2S) and CO2 to some 200 ammonia, natural gas, syngas and liquefied petroleum gas facilities worldwide.

Since 2007, BASF has worked with RWE Power and Linde in Germany to develop a process for capturing CO2 from flue gases emitted by coal-fired power plants. These account for 50% of all electricity generation and 36% of all CO2 emissions in the US.

Finally, BASF is merging its Swiss group companies BASF Orgamol Pharma Solutions and BASF Fine Chemicals Switzerland into a single firm called BASF Pharma (Evionnaz). This is based at the former Orgamol site in Evionnaz and forms part of the BASF Pharma Ingredients & Services Business Unit.

Martin Widmann, general manager of the former BASF Fine Chemicals Switzerland, who has been named president of the new firm, said that this “reduces complexity at our site and simplifies processes”, the two firms having already worked together for years.

The former BASF Orgamol Pharma Solutions companies at Evionnaz and Saint-Vulbas in France were both renamed BASF Pharma in April. None of the name changes has any effect on the number of or existing contracts with employees or on relationships with suppliers and customers.
Bio-succinic acid JV formalised as new technique is launched

**NETHERLANDS-FRANCE**

DSM and Roquette Frères, the French-based starch and starch-derivatives company, have signed a joint venture agreement for the production, commercialisation and market development of bio-based succinic acid. A new 50-50 joint venture, Reverdia, is being set up in the Netherlands for this purpose.

This follows a co-operation between the two firms since early 2008 to develop a suitable fermentation technology. Test volumes of the product have already been made at a demonstration plant in Lestrem, eastern France, which was built last year, and have been used in polymers, resins and other products.

DSM subsequently unveiled a technical breakthrough for the manufacture of bio-based succinic acid from starch that it and Roquette had made at the 7th Annual World Congress on Industrial Biotechnology. This, the company said, is based on two separate innovations, one in enzyme technology and the other in advanced yeast technology.

DSM focused its R&D on a fungal organism that typically thrives in compost heaps or on fallen trees, enabling it to find enzymes that are able to break down biomass into its constituent sugars much more efficiently than conventional enzymes and which can also function at higher temperatures. These properties facilitate lower enzyme dosage, better contamination control during fermentation, increased feedstock loadings, reduced energy consumption and shorter processing times.

Via classical strain improvement combined with metabolic engineering, DSM claims to have developed an advanced yeast strain that is capable of converting all of the major fermentable six- and five-carbon sugar components in biomass to ethanol, the most common current biofuel. This could double yields compared to the standard yeasts in use now, which typically only consume six-carbon sugars and are consequently less efficient.

DSM added that it is has a totally different approach to market development for second generation biofuels. Instead of remotely producing and bulk-selling enzymes and yeasts, it is “working with customers and partners to develop more localised, on-site production”. It believes this to be the most sustainable way forward in the long run, “because it bypasses long and expensive global supply chains and truly integrates conversion technology into the biofuel process itself”.

The two companies will expand their joint capacity to meet demand, adding that many customers already intend to take shipments from the joint venture when it starts. The initial focus will be on products such as 1,4-butanediol, polyurethane resins and biopolymers such as polyhydroxybutyrate succinate for applications in paints and coatings, automotive and textiles, among others.

**CHINA-GERMANY**

Lanxess has announced that its yellow iron oxide pigments site at Jinshan near Shanghai can now run at full capacity of 28,000 tonnes/year. This follows the completion of another step in the company’s ‘technical improvement drive’. The company has also revealed that production of Bayferrox iron oxide pigments at its Krefeld-Uerdingen site in Germany has hit an all-time high. The Jinshan site, which is the largest yellow iron oxide pigments facility in Asia, opened in 2007. Since then, various different measures have been implemented to increase production efficiency, such as consolidating steam generation in one boiler house operation with an advanced off-gas cleaning system. In a second phase, which will see €6 million invested up to 2011, Lanxess will further optimise the site’s environmental protection facilities, notably by upgrading the drainage system. It will also shift the water supply and the fire-fighting system to piping above the ground for greater availability and easier monitoring.

Jörg Hellwig, head of the Inorganic Pigments business unit, said that Lanxess plans further growth in the field. “We are confident in the growth opportunities offered by the APAC region and want in particular to serve rising market demand in China for high-quality pigments in the long term,” he added.

Meanwhile, Krefeld-Uerdingen, which at 280,000 tonnes/year capacity is the largest of its kind in the world, produced about 25,000 tonnes of Bayferrox in May. Of this, 85% was exported. This was the largest monthly total in the site’s 85-year history. Between January and May, total production was up by about one third over the same period of 2009.

Between Krefeld-Uerdingen, Jinshan and Porto Feliz in Brazil, Lanxess has some 350,000 tonnes/year capacity of Bayferrox. It is continuing to implement process and logistical optimisation, efficiency increases and plant expansions to increase capacity as demand for premium iron oxide pigments grows world-wide, investing a total of about €20 million at all three sites this year.

**In Brief**

**Dow Kokam breaks ground**

Dow Kokam, a joint venture between Dow and TK Advanced Battery, has broken ground at the first phase of a facility to make large-format lithium-ion batteries for electric and hybrid electric vehicles at Midland, Michigan. This will employ 320 people and produce 600 million watt hours of batteries, supported by a €128 million grant under the American Recovery & Reinvestment Act. Ultimately, the company plans a world-scale, 75,000 m² plant employing 800, with double the current capacity.

**Borregaard closes Ravenna**

Borregaard Synthesis is to close its Borregaard Italia production plant in Ravenna, with the loss of 40 jobs. This mainly produces cetearyl and hydroquinone for flavours and fragrances, agrochemicals, pharmaceuticals and other industrial applications. The former has been and will remain in overcapacity, giving the plant little prospect of returning to profitability, and the company had failed to find alternative solutions for it.

**Aesica buys R5**

Aesica Pharmaceuticals has acquired the Nottingham-based R&D company R5, which develops and manufactures new medicines and clinical trial materials, particularly pharmaceutical dosage forms. This buy, the third in the UK after two large former Big Pharma manufacturing sites near London, will “complement Aesica’s existing formulation capability and enable it to significantly consolidate and enhance its portfolio of pharmaceutical and biotechnology clients”, the company said.

**Evonik licenses Elevance**

Elevance Renewable Sciences of Bolingbrook, Illinois, has taken a licence to Evonik Industries’ US patent portfolio related to metathesis technology, not including the CatMETium RF range. It will use them in its processes to make specialty chemicals, notably oils, lubricant additives and antimicrobials, from natural oils such as soybean, canola, corn, sunflowers, palm, rapeseed, algae and Jatropha. Terms were not disclosed.

**Speciality Chemicals Magazine July 2010**

www.specchemonline.com
Three power up in batteries

The growing demand for new materials for high-technology batteries is creating major interest among specialty chemicals firms. Within the past month, Germany’s Süd-Chemie, Thomas Swan of the UK and Chemetall Foote in the US have all made important announcements in the field.

Süd-Chemie is investing about €60 million to build a new facility for the production of lithium iron phosphate (LFP), a high performance energy storage material used in batteries for electric vehicle drives and other applications. This will come onstream in 2012 at the firm’s Canadian subsidiary, Phostech Lithium, in Candiac, Quebec.

Capacity will be 2,500 tonnes/year, on top of 300 tonnes/year of existing capacity at the Moosburg site in Germany - enough for 50,000 all-electric or up to 500,000 hybrid electric vehicles. The new site will produce LFP via a proprietary wet chemistry process.

Süd-Chemie’s Life Power-brand LFP is said to combine high energy density with superior safety, a long service life, a favourable manufacturing cost profile and excellent cycle stability. The company already supplies LFP for power tools, starter batteries and electric scooters.

Meanwhile, under a new long-term agreement, Thomas Swan will supply carbon nanotubes, first in R&D quantities and ultimately in commercial volumes to US-based battery technology development company Vendum Batteries, on an exclusive basis “at a preferential price”.

Vendum has a pending patent on its eponymous carbon nanotube-cellulose-based, lightweight and very thin battery. This, it says, contains none of the toxic elements used in conventional batteries and is entirely biodegradable.

The firm plans to develop this from its current low power capacity to meet growing demand for greener products in the €50 billion/year market for personal batteries in applications like mobile phones, iPods and human implants.

Membranes in, white out for Kemira

Kemira has begun a two-year R&D cooperation with the Singapore Membrane Technology Centre at Nanyang Technological University (NTU). The stated aim of this is “to design a more efficient water production process with a higher recovery rate, lower energy consumption and less waste volume”, in support of Kemira’s own Centre of Water Efficiency Excellence in Finland, which was launched in March.

“Kemira will develop together with NTU an improved-used water reclamation process with higher recovery rates. By contributing our vast experience in water treatment chemistry, we aim to work with NTU to produce more clean and usable water with less energy and waste,” said Kaj Jansson, vice president of R&D and technology.

Like many countries in South-East Asia, Singapore depends on reclaimed and desalinated water sources. In 2006, the government identified the environment and water industry as a strategic key growth area and committed €189 million to develop Singapore as a ‘global hydrohub’. Now some 70 water companies operate regional headquarters, manufacturing and R&D activities here.

Earlier, Kemira had agreed to sell its global fluorescent whitening agents (FWAs) business, which it acquired as part of Lanxess’s former paper chemicals interests, to Catec, a German firm with financial backing from Fong Heng Beteiligungen. The deal covers production plant in Leverkusen, the global sales network and the associated support functions.

Petri Helsky, head of the Paper segment at Kemira, said that the company “is focusing according to its strategy on products and services that enhance the water quality and quantity management in the water-intensive industries, such as pulp and paper”. Exiting from FWAs is in line with this. About 100 people will transfer when the agreement closes, which is expected to be in August, and negotiations are in progress with the Works Council. Kemira added that this transaction will not have any significant impact on its financial figures and it is not disclosing the transaction price.
The slimming down of Big Pharma has continued apace, with both GlaxoSmithKline (GSK) and Sanofi-Aventis selling sites in the past month, to Aptuit and Covance respectively. Further changes may be in the pipeline after Merck & Co. announced that it would sell or close eight manufacturing sites and eight R&D sites worldwide.

Aptuit, a global pharmaceutical services company headquartered in the US, has reached an agreement to acquire GSK’s Medicines Research Centre in Verona, Italy. No time-frame or financial terms were disclosed. GSK is also rumoured to be selling its GSK Chemical Development site in Tonbridge, UK, to Cherokee Pharmaceuticals of the US.

This will bring Aptuit 500 new staff, who will continue to supply GSK with R&D services from the facilities. Tim Tyson, chairman and CEO of Aptuit, described the transaction “an example of the developing new model of outsourced R&D collaborations”.

This brings to 19 the total number of locations of Aptuit, which is owned by private equity firm Welsh, Carson, Anderson & Stowe and now offers development and manufacturing services to some 800 pharmaceuticals and biotechnology companies. It will combine its existing capabilities with the Verona site’s expertise in drug discovery, lead optimisation, API development and manufacturing and pre-clinical and clinical drug development.

The deal was said to have financial support from the Italian government and the approval of the local unions. GSK had decided in February to stop all discovery research in certain neurosciences areas such as pain and depression, which meant that its need for the Verona facility was greatly reduced.

Philadelphia-based Cherokee, which is widely believed to be on the verge of acquiring GSK’s Tonbridge site, is owned by PRW Services and manages the former Merck site at Riverside, Pennsylvania, which it acquired in January 2008. This site, which employs 390, now offers contract manufacturing services for APIs as well as having a five-year continuing supply agreement with Merck.

Cherokee has been actively looking for more sites to buy, so taking on Tonbridge would not come as a great surprise. Moreover, the company president is John Elliot, who had previously sold GSK’s site at Montrose in Scotland to Akzo Nobel Diosynth in 2002, when he was senior vice-president of GSK Primary Manufacturing.

Separately, Sanofi-Aventis has revealed plans to sell two R&D facilities in Porcheville, France, and Alnwick, UK, to the multinational giant CRO Covance under a non-binding memorandum. Terms were not disclosed. This came a year after the company said that it would sell some of its sites. Talks reportedly began in late 2009.

Whether the two sites would continue to supply Sanofi-Aventis under a long term contract, as is often the case in such acquisitions, is still unclear. Both are focused on pre-clinical trials. Porcheville, which dates back to 1976, works mainly in chemistry and toxicology, while Alnwick is focused on drug safety assessment.

This transaction would result in some 330 employees transferring when the deal closes, which is expected to be by the end of the year. Covance had previously acquired Eli Lilly’s pre-clinical research facility in Greenfield, Illinois, in August 2008, in what is widely seen as the model for such transactions between Big Pharma and CROs.

Merck, meanwhile, has announced that it will fully or partially close or sell eight manufacturing plants and eight R&D laboratories as it seeks to shrink the R&D and manufacturing base following the completion of the mega-merger with Schering-Plough in November 2009.

This gave Merck a total of 91 facilities. Coupled with previous closures, this will now come down to 77, including 29 animal health facilities which are not affected. In this field, Merck is merging its Intervet Schering-Plough subsidiary with Sanofi-Aventis’s Merial.

The cuts are expected to reduce the workforce by 15%, while saving costs of €2.1-2.4 billion/year. The first phases of the programme, however, will cost Merck some €2.8-3.4 billion. The company is focusing on seven therapeutic areas of: cardiovascular disease; diabetes and obesity; infectious disease; oncology; neuroscience and ophthalmology; respiratory and immunology; and, women’s health and endocrine diseases.

On the chopping board, therefore, are manufacturing locations at Azcapotzalco and Coyoacan, Mexico, Santo Amaro, Brazil, Mirador, Argentina, chemical production at the existing Merck site in Singapore (though pharmaceutical manufacturing will continue there and at the Schering-Plough site), Comazzo, Italy, Cacem, Portugal and Miami Lakes. Mirador and Miami Lakes are specifically earmarked for sale.

In addition, relatively small R&D sites at Montreal, Canada, Oss, Schaijk and the Nobilion facility at Boxmeer in the Netherlands, Odense, Denmark, Waltrop in Germany, Newhouse in Scotland and Cambridge, Massachusetts, will all go. This will reduce the number of R&D labs from 24 to 16, though Merck will retain clinical and regulatory affairs expertise in all major regions.

### In Brief

**JM buys X-Zyme**

Johnson Matthey has acquired X-Zyme of Düsseldorf, which develops and makes enzymes for the manufacture of chiral alcohols, particularly oxidoreductases, chiral diols and chiral amines for pharmaceuticals and fine chemicals. This, it said, will complement its Catalysis & Chiral Technologies (CCT) business unit’s expertise in chemocatalysis based on chiral ligands for asymmetric hydrogenation, platinum group metal-based and Spong Nickel catalysts, plus related services.

**AkzoNobel sharpens focus**

AkzoNobel has agreed to sell National Starch, which makes food ingredients and speciality starches for industrial use, to Corn Products International for €1,030 million. The deal should close at the end of Q3, subject to regulatory approval. CEO Hans Wijers said that this “marks the strong focus on our core business and confirms AkzoNobel’s transformation into the world’s largest global coatings and speciality chemicals company”.

**ISP to work with Vivimed**

ISP has concluded a manufacturing alliance with cosmetic active ingredients maker Vivimed Labs of Hyderabad, India. The two will "work together to optimise manufacturing assets dedicated to UV absorbers", jointly marketing certain UVA and UVB protection products for consumer sprays and lotions via its global sales, marketing and technical service teams, with ISP adding Vivimed’s products to its own Escalol brand portfolio from October.

**Squeeze out agreed**

Altana shareholders agreed at their AGM in June to transfer the remaining shares to the company’s main shareholder Skion, a vehicle by which owner Susanne Klatten is taking the company private after 33 years on the German stock exchange. Skion already owns 95.04% of the shares. Once this ‘squeeze out’ has been entered into the Commercial Register, the remaining shares will be transferred to Skion in return for a cash compensation of €15.01/share.
Rhodia in Chinese surfactant maker buy

**CHINA-FRANCE**

Rhodia, which is a major player in surfactants via its Novecare enterprise is to acquire an 87.5% stake in Feixiang Chemicals (Zhangjiagang) (ZJG), China’s largest producer of amines and surfactants. It believes that the €387 million deal, which is expected to close in 2H 2010, subject to approval from the Chinese authorities, will be accretive to earnings from the first year.

Chairman and CEO Jean-Pierre Clamadieu said: “This acquisition is a key step in the implementation of our profitable growth strategy. Through the integration of ZJG, we significantly strengthen our leadership positions in the surfactant business, while enhancing our footprint in the world’s fastest growing region.” Once this is complete, around one third of Rhodia’s sales will be in Asia.

Based in the city of Zhangjiagang, 110 kilometres from Shanghai in Jiangsu province, ZJG employs about 650 people. It has been enjoying 20% year growth in recent years, as well as increasing profitability, selling a complete range of fatty amines and specialty amines.

Via ZJG, Rhodia will be able to integrate specialty amine technologies into Novecare’s business portfolio, adding capacity to its own expertise in formulation and end-market applications in specialty surfactants for home and personal care, agrochemicals, oilfield and general industrial applications. It plans to double the size of the acquired business within the next five years.

Separately, Rhodia has agreed to support the Chair of Pine Chemistry & Natural Resources at the new University of Bordeaux Foundation. The stated aim is to expand the role of plant-based raw materials in the chemical industry, notably pine tree products, which are superabundant in France and which Rhodia already uses in surfactants and ingredients for paints and varnishes.

Rhodia is present in the Bordeaux region through its Laboratory of the Future, a joint research centre with the CNRS and the University of Bordeaux. Via this new partnership, it will work with the university’s laboratories on new products. 10% of its raw materials are already plant-based.

Chemtura files Plan of Reorganisation

**US**

Chemtura and 26 of its US affiliates have filed a Joint Plan of Reorganisation and a Disclosure Statement with the US Bankruptcy Court for the Southern District of New York, which is expected to consider approval of the statement shortly. This could enable the company to emerge from Chapter 11 bankruptcy protection within a few months.

Chairman, president and CEO Craig Rogerson described filing the plan as “a significant milestone in the Chapter 11 process, demonstrating Chemtura’s progress toward emerging as a stronger, leaner, global enterprise. It is a testament to the outstanding progress we have made in restructuring our finances and operations,” he added.

The plan, as described recently, is for all worldwide operations of Chemtura and its subsidiaries to continue in business. Some ‘treatment’ is envisaged for funded debt obligations, trade claims and litigation claims, including those related to diacetyl, and for all creditors to be paid in cash or common stock of a reorganised and publicly traded company at or near the full value of their claims.

This is supported by Chemtura’s official committee of unsecured creditors and an ad hoc committee of bondholders. The company had revealed in late May that it was in the process of finalising agreements with both on the subject. It will continue to work with the official committee on any concerns they may have about the plan, which, it said, “provides the potential to satisfy all creditors’ claims in full, as well as offering value to equity holders”.

The disclosure statement includes a historical profile of the company, a description of proposed distributions to creditors and equity holders, and details of the ‘new’ Chemtura, plus many of the technical matters required for the solicitation process, such as descriptions of who will be eligible to vote on the plan. Both documents can be viewed online at www.kccllc.net/chemtura.

**Corrections**

In the May edition of SCM, a figure in the article by GAB Consulting incorrectly had ‘No Safe Use’ rather than ‘Safe Use’ in part of a flow chart showing the steps to the authorisation of a biocidal product under the Biocidal Products Directive due to a production error. The correct figure is shown here (below).

In addition, in the March edition, the structure of Smopex 101 was shown incorrectly in the article by Johnson Mattey; it contains SO3, not SO2. The figure above shows the correct structure.
Shackles on innovation

Agrochemical innovation is more necessary than ever, yet has never been more costly and difficult to do. We report from Informex USA 2010

Agrochemicals, crop production and global food supply: these were the themes of two breakfast meetings during Informex USA 2010, which took place in San Francisco in February. With the almost simultaneous release of a new study commissioned by the US and European trade associations on the R&D costs of new crop protection products, a number of key issues were brought into sharp focus.

It was appropriate, said one speaker at Informex, Mary-Ann Warmerdam, director of the California Department of Pesticide Regulation, to be discussing such issues in California. This is not only the US’s number one farming state, accounting for 11% of all farm revenues, but it also has the most extensive pesticides regulatory regime in the US and possibly in the world.

Session moderator Jay Vroom, president and CEO of CropLife America, the US trade association, observed that crop protection is and will remain essential; indeed, “the wise use of scientific technology is the reason we can feed over 6 billion people and our only hope to feed 9 billion by 2050.” Plant science technologies help farmers grow more food on less land, while crop protection prevents the loss of 40-80% the crop to pests, weeds and diseases.

Innovation is expensive

According to a study commissioned by CropLife America and the European Crop Protection Association (ECPA), the costs associated with the discovery, development and registration of new crop, pest and disease agents increased by 64.8% to €256 million (€189 million) between 1995 and 2005-8. This is in large part because of the regulatory burden on the industry.

The report, which was carried out by consultants Phillips McDougall, looked at R&D costs among 14 agrochemicals companies, including four of the ‘Big Six’ R&D-based producers - Syngenta, Bayer CropScience, DuPont, Dow, BASF and Monsanto - and some generics producers. Their total R&D costs in 2007 amounted to €1,701 million, or 6.7% of their agrochemical sales.

Breaking costs down at each stage of the process showed clearly that the increase has mainly come in the ‘D’ phase of R&D, where costs have increased by 84.8% to $146 million, whereas the costs of the ‘R’ phase have actually fallen since 2000 (Figure 2). The most significant rise of all came in the costs of environmental chemistry and toxicology, which are 63.4% up to $67 million.

This, says Phil Newton of the ECPA, can be directly related to the regulatory environment, especially that in Europe. Changes that were made to the Plant Protection Products Directive, 91/414/EC, in 2009 but which are only being implemented now have meant a switch from risk-based to hazard-based assessment criteria, on top of the costs of registration effectively reducing the number of products on the market from over 1,000 to nearer 300, in most cases because the cost of pre-registration was not deemed worthwhile.

“The key thing is that cost of a credible risk-based assessment was increasing anyway because of product safety and environmental effect issues, but in a legitimate way,” Newton says. “Now, it is going over the edge into a situation where a product can be banned outright based on a hazard assessment or effectively banned because of unreasonable standards.”

No other chemical-based industry in Europe, adds Newton, is regulated this way. Cosmetics, for example, are regulated on explicitly risk-based criteria. And yet, pesticides are more needed than ever, not least because pests’ life-spans are so short and a new form of immunity is found somewhere every year.

Field trials have also become more costly. This reflects not so much the effects of regulation as the consequence of combinatorial chemistry and high-throughput screening generating vast quantities of leads. The number of compounds going into initial research every year is about 140,000, of which one or two might make it to market.

Time pressures - it takes an average of 9.8 years from first tests to product registration - mean that it is no longer possible to do all the necessary screening of lead compounds before getting into research. Trials are increasingly taking place during the development phase, so more has to be invested in products that will ultimately fail.

Agrochemical intermediates and actives were not covered per se in the report, notes author Matthew Phillips. Broadly speaking, though, industry trends for producers of intermediates and actives have meant that the volumes are positive but the spread of products has narrowed a lot and this trend is expected to continue.

Overall, the ECPA argues that agrochemical R&D in the EU is becoming increasingly hard to justify, despite the urgent need for innovation to address global mega-trends. The best thing the EU can do, it adds, “is to establish a science-based regulatory framework and develop policy grounded in the reality of agriculture and what R&D can actually achieve”.

“There is still room to implement this sensibly,” says Newton. “If it is not, the hammer could fall anywhere.”
Intermediate action

According to consultant Jan Ramakers of the Jan Ramakers Fine Chemical Consulting Group, who was also speaking at the Informex breakfasts, agrochemicals account for 2.5% of a total world chemicals market of $2.5 trillion, with base chemicals accounting for 43%, pharmaceuticals 28% and others 27%.

This gives it a total value of $40-42 billion this year, following a steady increase from $28 billion in 2000 and particularly strong growth in the last two years. About 30% of the agrochemicals market, he said, is still proprietary - that is, subject to IP protection and/or exclusivity rights - 40% is made up of proprietary off-patent products, which are not subject to such rights but which are only made by one company, and 30% are true generics.

“This is a very concentrated industry,” Ramakers noted. “There has been a lot of M&A activity in the last 20 years: the top six originators have 73% of total sales and the top six generics producers have a further 18%, so the top 12 together have more than 90% of the market.”

Of the total $87.7 billion market for fine chemicals in 2008, Ramakers estimates that pharmaceutical intermediates accounted for 63%. Agrochemical intermediates were a further 8%, the same as flavours and fragrances. Dyes accounted for 5%, the remaining 16% being split among many others (Figure 3).

This market has seen strong growth in the past decade. It was worth a little under $60 billion in 2000 and particularly strong growth this year, following a steady increase from $28 billion in 2000, it had reached around $6.5 billion in 2006, then saw two years of much stronger growth to reach its current level of $71 billion.

Another speaker in San Francisco, David Frabotta, editor of Farm Chemical International, attributed the strong growth in 2006-8 to an “explosion in companion chemistry” that accompanied the mass uptake of biotechnology in farming, particularly for herbicides. By 2008, he noted, 125 million hectares of transgenic crops in 25 countries, with soybeans leading the way, ahead of corn, cotton and canola.

With more muted forecast growth of 1-2%/year, the world agrochemical intermediates market should reach $77.7-78 billion in 2013, said Ramakers. Further market growth for both agrochemicals and their intermediates and active ingredients seems likely because of the global mega-trends: population growth; growing food demand; increases in biofuel crops; and, higher food prices. In part because agrochemicals generate fewer new active ingredients, the generics sector is seeing - and will continue to see - relatively fast growth.

There has also been a tendency for agrochemical intermediate production to be switched into converted plants, mostly cGMP, that were built in the - unfilled - expectation of ever-growing demand for pharmaceutical intermediates. However, these are rarely well suited to agrochemical intermediate production, for reasons of cost, regulatory issues and the risk of cross-contamination.

“Because of this and the increasing market share of Asian producers, a lot of agrochemical intermediate production capacity has been taken out of the market,” Ramakers said. “Now there are relatively few Western producers left”. KemFine, Albemarle, BASF, Saltigo, Lonza and DSM are among the most important.

There are three areas of opportunity for producers of agrochemical intermediates, Ramakers concluded: the growth of generic and proprietary off-patent products, outsourcing opportunities from the ‘Big Six’ and the growth of older established products.
Plant health (stress tolerance, yield increase & food quality)
New approaches in biological crop protection & diagnostics

These are all built on the major technology platforms of chemistry, biochemistry and biology, genomics and bioinformatics, high-throughput screening and combinatorial chemistry. The company, Lubosch added, plans to increase its R&D spend by 16% from €649 million in 2008 to about €750 million in 2016.

Of this, crop protection, one of Bayer CropScience’s three pillars alongside environmental science and bioscience, will account for about €500 million. Seeds and biotechnology will take a further €200 million, environmental science the rest, but they will certainly not be replacing crop protection in Bayer’s armoury.

“We have a strong commitment to chemistry,” Lubosch commented. Indeed, the company has launched 23 new active ingredients since 2000. Sales of new active ingredients increased by 31% from €1,384 million in fiscal 2007 to €1,808 million in 2008.

Meanwhile, the share of new active substances grew from 25.4% to 30.5%. Nine more herbicides, fungicides and insecticides with sales potential of up to €150 million/year each are coming through the pipeline to 2012.

Marlin for his part highlighted a few emerging technologies that could bring plant potential to life, both increasing productivity and/or reducing carbon emissions. Tropical sugar beet, corn amylase and the use of no-till production all offer extraordinary opportunities, he said. Syngenta itself is developing the Moddus stress management chemistry, which can greatly improve water use efficiency.

“Films like ‘Food, Inc.’ have shown the downside. We need to show the huge benefits chemistry and mechanisation have brought in enabling us to feed a massively increased population,” said Dyer. “We proved Malthus wrong once, but we have to do it all over again. The mega-trends are here to stay and the challenge for the crop science industry is to develop the technology that will help us to deal with them all.”

As ever, perception is a big part of the issue. Vroom showed some results of surveys by Charlton Research in the US. Predictably, these showed strongly negative connotations by 3:1 majority in peoples’ minds for ‘pesticides’, whereas ‘crop protection’ scored a nearly 2:1 favourable response.

There was a strong general sense among those surveyed that organic is best. Even so, education on the issues showed that a solid majority of all groups surveyed, including the general US public, agricultural officials and health, science and environmental experts, could be swung behind the use of pesticides.

Dyer added that much of the regulation of pesticides in Europe in the last two years has been driven by NGOs’ demonisation of them and of GM technology. This must be tackled, he said, because we could lose 30-40% of all crops without them. Combined with the rising population, a continuation could lead to a total catastrophe and the EU in general has been slow to address the problem.

Seeing organic labelling as the solution, said Dyer, “is not just wrong, but very, very dangerous. Agrochemicals have a key role to play and companies need to know they will be able to market products before they spend €200 million over ten years to bring them to market. GM is not a replacement for agrochemicals, they complement each other. Agrochemicals will be an important tool for years to come.”
Simply the pest

Are we on the verge of a new kind of chemistry in pest control? **Elisabeth Jeffries** reports

**S**trategies devised by worried farmers and pesticide producers to fight off aphids, potato scab and other pests plaguing them all over the world were dealt a blow in 2008. A group of South German honey bee farmers reported a wave of bee deaths which they connected to the use of the neonicotinoid pesticide clothianidin.

The German government responded by banning eight seed treatment products that used neonicotinoids, a family of pesticides that was discovered in the 1970s and which are similar to the pesticidal compounds produced by the tobacco plant. Wildlife news has hummed with reports of bee disorders ever since.

This is not, of course, the first time that pesticide companies have come under attack. DDT, perhaps the most vilified pesticide ever produced, was banned for agricultural use after similar rows erupted in the 1960s and 1970s. Even if some of the more toxic pesticides have been outlawed, pests have in any case become smarter at fighting back at the many still in use. A natural selection of increasingly smart products has been the result as this war progresses on many of the insect class, not to mention the nematodes, fungi and other organisms that may ruin farmers’ livelihoods.

Pesticides that target particular plants or attack particular pests, potent pesticides that are only needed in low quantities, pesticides that confuse an insect and make it fly away - these are just a few of the products to have been developed since the scandals in North America nearly 50 years ago caused by the indiscriminate spraying of chemicals.

Synthetic pyrethroids were among the most brilliant innovations in the field in the 1960s and 1970s, evolving in the laboratories of the pioneer chemist Michael Elliott at Rothamsted Research in the UK. His inventions showed that it was possible to respond to public concern by creating new insecticides that can be less harmful to the environment.

Elliott identified the most active components of pyrethrum extract, a natural product found in the pyrethrum plant, *Tanacetum cinerariifolium*, a member of the daisy family which has insecticidal properties, and he started to synthesise analogues. He and his team developed several sets of compounds which would revolutionise pesticide development in the 1980s and which still account for one third of the global insecticides market.

Having synthesised approximately 1,500 chemicals based on pyrethrin, Elliott invented five market leaders in pesticide sales. Some, such as deltamethrin, are still at the front of insect control today.

Not the least of his achievements was to synthesise a relatively small number of chemicals, as plant pathology and microbiology at Rothamsted Research, acknowledges: “There have been incremental improvements but not a new paradigm shift.”

That said, one potentially significant innovation may have emerged. Dr Peter Lümmen, a biochemist at Bayer CropScience in Germany, argues that a new product, flubendiamide, only discovered five years ago by researchers from Nihon Nohyaku in Japan, could yield a whole class of new insecticides. It was first approved for use in the US in 2008.

“We can justifiably say that the phthalic acid diamides, to which flubendiamide belongs, have blockbuster potential,” Lümmen claims.

Bayer CropScience indicates that the innovative character of flubendiamide lies in its ability to target a molecule found in insects without creating major damage elsewhere. It could be used to kill *Heliothis virescens*, the tobacco budworm that eats fruit, vegetables and other plants and eventually turns into a moth, and is also generally a potential insecticide against lepidoptera.

Unlike other pesticides, flubendiamide aims at the muscles rather than directly at the nervous system; this, too, is an innovative feature. The membrane-bound molecule targeted by the substance, known as the ryanodine receptor, plays a part in muscle contraction and calcium concentration in insect muscles and has already been the subject of chemical trials for years.

These, however, failed due to the toxicity of the chemicals used in relation to other organisms too. The flubendiamide innovation relates to the fact that it targets a previously undiscovered part of the ryanodine receptor.

Ryanodine receptors in humans and in other vertebrates do not react in the same way to flubendiamide, according to Bayer CropScience, which has stated that it “wants to take advantage of these structural variations in the ryanodine receptors to develop other insecticides based on phthalic acid diamide in the future.” These could act on other insect pests.

Synthetic pheromones have made a fair contribution to pesticide development. Shin-Estu Chemical of Japan has been a significant player in this field, developing in 2006, for example, synthetic compounds of dodecyl acetate, a sex pheromone in the moth *Heliothis* (Scribograplopsis solanivora), which attacks potatoes in South America.

Placed in a dispenser, the compound disrupts mating behaviour by interfering with communication between males and females, camouflaging the female signal and possibly reducing male responsiveness through sensory imbalance. This of course prevents the moth from reproducing at a normal pace.
Farms that prefer integrated pest management have often altered mating behaviour using synthetic pheromones, seeing it as a more benign way of controlling plant pests. Curiously, they have not been the most widely used control tool in agriculture.

In Europe, pheromones’ more marginal role may be about to change as Directive 2009/128/EC on the sustainable use of pesticides comes into force. This establishes a framework to achieve a sustainable use of pesticides by reducing the risks and impacts of pesticide use on human health and the environment and promoting the use of integrated pest management and alternative approaches or techniques, including non-chemical alternatives to pesticides.

EU Member States are required to draw up action plans to cut the risks to humans and the environment and to encourage integrated pest management by 2012. So some pesticide producers’ efforts to come up with new products may be thwarted. Not only do insects battle them by evolving new modes of resistance but European authorities are imposing a risk-based approach. “It’s a huge step forward in integrated pest management in the UK,” remarks Nick Mole, a campaigner at the Pesticides Action Network, an NGO.

Concerns about the impacts of chemical pesticides are, perhaps, one of the factors affecting scientists’ attention to other methods for controlling or managing pests. But Lucas says that one of the most important areas of research at the moment is to work out how pests develop resistance to existing chemistry.

“The stewardship of current chemicals so they don’t lose their effectiveness is the ‘now’ issue,” he comments, adding that this problem is “a moving goalpost”. Understanding the evolution of resistance and the genes responsible can then help them design molecules that get around it.

In the longer term, researchers are likely to use genomics more and more to understand why some insects are damaging to crops in the first place and possibly to subsequently develop new chemicals. They can already, for instance, interrogate the genome of aphids, which was first sequenced in May 2010.

“Identifying the genes involved that made them a problem means that you can identify new targets for intervention,” explains Lucas. Scientists can devise new chemicals that interfere with a key enzyme by designing a molecule that prevents a toxin from being synthesised. Nevertheless, the increasingly strict regulatory limits placed on pesticide chemical development mean that this is a challenging and long term option.

However, genomics could be of use in helping manage pests by improving insights into their behaviour. Lucas points out that scientists are now sequencing genomes in an afternoon - a huge step from the major endeavours of the earlier part of the last decade.

“This gives us a hugely powerful compensating resource, allowing us to compare different strains and variants,” he explains. This could help to improve intelligence relating to the whereabouts and spread of a particular virus, for example.

“Extrapolating ten or twenty years ahead, we might have smart biosensors and more rapid communications, but whether we manage using different methods is another matter.” In the mean time, it is likely that major chemical innovations from crop protection companies will become even rarer.
More from less in agrochemicals

Dr Susan Brench and Dr Chris Rainford review how Pentagon Chemicals streamlines the introduction of new agrochemical products and optimise the performance of its existing processes.

With the global population estimated to grow from the current 6 billion to around 9 billion by 2050, there has never been a greater need for increased crop productivity to use the limited natural resources available fully. One of the key enablers for this is the targeted use of a combination of herbicides, insecticides and fungicides to ensure that the maximum yield is derived from each planting. This philosophy - of getting more from less - is one that Pentagon Chemicals, as a supplier of active agrochemical ingredients and intermediates, has incorporated into its ways of working.

Pentagon’s fine chemicals operations at Halebank, UK were purchased in December 2003 as part of a strategy to mix organic growth with the acquisition of complementary technologies and access to new markets. The site brought with it a long history of new product development in the life sciences, adding bromination, chlorination, cyanation, phosphonation and sodium dispersion chemistries to the existing core technologies of maleic anhydride derivatives and Grignard reagents.

In addition to widening the available technology toolbox, the integration of Halebank with the existing site at Workington enabled teams from the two businesses to identify and select individual best working practices with a view to establishing a fully integrated programme of continuous improvement for existing manufacturing processes, as well as new product introductions.

Products & process development

The first step was to ensure that all employees across the sites were fully engaged. At the heart of this objective was the concept of the product team - a multi-disciplinary group formed from representatives from all departments charged with ensuring the delivery of each customer’s expectations, in particular a safe and sustainable operating environment, as well as the development and production of the right products at the right time and to the desired quality within the cost boundaries agreed.

For the fine chemicals business, the focus on productivity improvements yielded immediate benefits with increased output, higher yield and reduced waste achieved on many key products. When the concept was expanded to include customers in the teams in order to provide greater integration of objectives and transparency of progress, even further advances in process development were realised.

At the core of each product team is a member from the Pentagon technology group, who is tasked with employing a consistent methodology to help determine the most effective method of delivering improvements.

The process chosen to advance the understanding of the chemistry uses a Six Sigma approach to help define key product and process outputs, identify the main drivers necessary in achieving these objectives, analysing their impact on performance before finally optimising them and ensuring successful incorporation into the manufacturing procedures. This (Figure 2) employs the five-step methodology of define, measure, analyse, improve, control, as discussed below.

Five steps

Recently, Pentagon developed a two-stage process to produce a novel agrochemical intermediate using its proprietary sodium dispersion technology, a unique method of safely generating 5-10 µm particles of highly reactive sodium to produce an alkoxide moiety which could then be coupled to a halogenated substrate, as shown in Figure 3.

As in all highly regulated markets, product quality is of vital importance to ensuring a successful outcome, not only for us but for our customers as well. In this instance, the product team’s close collaboration with the customer enabled...
a detailed product specification to be created and its parameters, including the identity and maximum limits of all critical impurities, to be set.

With a clear timetable agreed for development work and trial manufacture, Pentagon’s technologists considered which factors would potentially determine the formation of the impurities and used the methodology to design a series of experiments that enabled the maximum amount of information to be extracted from a minimum set of experiments. The potential critical process parameters were identified by the design team as the stoichiometry of reactants A and B, concentration, temperature and the feed rate of reactant C. In order to study each of the factors, a two-level factorial experiment was designed. This resulted in a total of only 11 experiments being carried out. Since each experiment took over two days to complete, significant savings were made in time and resource when set against a full factorial study consisting of 32 experiments.

The results of the experimental design were analysed using JMP software and the key controlling factor was identified as reaction temperature. In this instance, indications were that lower temperatures favoured reduced levels of the critical impurities.

Next, a targeted set of experiments were run at the lower temperature setting to demonstrate that the process was capable of producing material with the required impurity profile (the CpK was 1.2, well above the target of ≥1.3). This gave us and our customer the confidence to move forward to main plant manufacture without the need for intermediate pilot plant trials - a crucial factor in meeting the customer’s objectives.

Using the information obtained from the laboratory work, the team then ensured that all the necessary controls were in place for a successful scale-up. In this case arrangements were made for a clearly documented manufacturing procedure to be produced, as well as provision for additional training and support to the operations teams running the process.

Greater automation of the plant was also introduced to ensure that the process remained within the identified operating parameters. The trial successfully produced material at a larger scale than all other sources and analysis of results from the production batches clearly demonstrated that the process was robust with respect to the key impurities.

**Conclusion**

Pentagon has found that the product team concept to be an excellent platform for providing teams with the necessary focus and cross functional co-operation to deliver high performance in improving existing processes, as well as introducing new products. This framework can be further enhanced by closer ties with customers in order to provide greater understanding of their needs.

Clearly defined project outputs and consistent use of process improvement methodology then makes possible more efficient use of development resources, shorter cycle time from laboratory to plant, greater confidence in laboratory data and scale-up from laboratory to plant without the need for a pilot plant stage.

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So long, solvents

Plasma technology is perfect for giving fabrics a water-repellent nano-coating, so why is the textiles industry only just beginning to see its value, asks Emma Davies?

Stephen Coulson says that he has yet to find a material that he cannot put an invisible water-repellent coating on using plasma technology. It is not for want of trying. After all, he is chief technology officer at P2i, a UK company specialising in liquid-repellent nano-coatings.

Wood, leather, ceramics, glass, metal and paper can all be given a nano-coat using P2i’s plasma process, but these tests were just to show how versatile the technology is. The company is currently reaping rewards from a plasma process that can make shoes and boots instantly waterproof by coating them with a polymer layer that is tens of nanometres thick, invisible to the naked eye.

Plasma is ionised gas which can be created by passing a current between two electrodes. The plasma ions ‘activate’ other molecules, such as monomers, so they attach to the surface that is to be coated, paving the way for polymer chains to grow out and give a permanent coating.

Plasma technology has long been used in packaging and to coat architectural glass, microelectronics and car components. The technology’s main selling point is that it requires no solvents. This is a big deal for the textiles industry, which currently consumes huge volumes of water, often in parts of the world where it is scarce, but which has been slow to adopt the process.

The standard way to coat fabrics is to dip them in aqueous solutions of chemicals which have been specially formulated for the particular type of textile being coated. This is a successful process, but it has its drawbacks. “For some materials it is very difficult to find the solution-based process which will put the functionality on the surface,” explains Coulson.

Trying to apply water-based solutions to fabrics that are inherently hydrophobic is also tricky and often ineffective. For plasma technology, by contrast, anything goes; it does not matter what the surface being treated is.

Utterly repellent

Fabrics that are inherently hydrophobic can be given a plasma treatment to make them hydrophilic before they undergo chemical treatment, reducing the volume of water needed for the dyeing process and giving a better colour fastness.

P2i focuses on making materials liquid-repellent but is now looking at ways to use plasma to give anti-microbial or fire-retardant nano-coatings. The company, which was spun out of the UK Ministry of Defence’s Defence Science & Technology Laboratory at Porton Down in 2004, having developed a plasma process to make liquid-repellent military apparel, is building on existing anti-microbial knowledge, particularly in the area of quaternary ammonium salts, and has patented new related monomers.

“What we were looking for was the highest level of repellency for a whole variety of liquids, not just water: petrol, oils, lubricants, and also chemical challenges that you may see on the battlefield, such as nerve agents or mustard gas - liquids with a substantial vapour pressure,” explains Coulson.

At the time, many in the plasma community thought that it would be very difficult to make the plasma process - which operates in a low vacuum - cost-effective, but Coulson says that P2i has done this and has signed up brands such as Nike, Adidas, Hi-Tec and Ecco.

About 40% of its business is now in textiles, with the rest in coatings for electronics. The company is currently securing its next round of funding to take it through a “rapid growth patch”.

P2i’s successful entry into clothing and footwear is something of an exception in the plasma world although it is far from alone in targeting the textiles industry. Belgian company Europlasma has made plasma machines for coating textiles for ten years but has had little interest from clothing textile manufacturers, despite major take-up by other industries, including medical device manufacturers.

“The clothing industry is very conservative and difficult to penetrate,” says Peter Martens, product manager at Europlasma. “We have been trying to get into the clothing business for the past two years but it is not easy.”

Dirk Hegemann, from EMPA, a Swiss governmental research institute which works closely with industry, can see where the industry’s reluctance to adopt plasma comes from. “The textiles industry has invested a lot in wet chemical processes. A dry process - plasma technology - is new for them. They would not only need new equipment, they would also need new know-how.”

The new equipment needed generally incorporates a chamber to create the low vacuum required for most commercial plasma processes. This effectively puts a size restraint on the fabric that can be treated.

The low-pressure plasma processes have the advantage of being tried and tested for many years by other industries. P2i, Europlasma and EMPA have all opted for these, quoting reliability and low-running costs. EMPA has developed low-vacuum plasma processes for an Austrian textile company called Grabber, which uses a ‘roll-to-roll plasma coater’, and for Tersuisse, a Swiss company that treats individual fibres using plasma technology.

In principle, atmospheric pressure plasma technology would be far easier to incorporate into production lines - no vacuum is required and it promises high throughput rates - but Hegemann is not aware of any companies using atmospheric pressure plasma to treat fabrics.

The technology is not that different from the corona (electrical discharge) treatment that the textiles industry has been using for over 30 years to activate textiles before applying chemicals. Atmospheric plasma treatment simply takes the process further, activating and coating a material in one step.

“In the early days a lot of people believed that you could only do plasma processing of fabrics at atmos-
dispersion, and you atomise it in a plasma atmosphere,” explains Arjan Giaya, vice-president of technology at Triton.

The precursor and substrate are activated simultaneously at atmospheric pressure and room temperature so that the precursor polymerises and bonds to the activated substrate to create a coating with a thickness of 10-200 nm. “You don’t have a heating source or a vacuum pump so the energy consumption is very, very low,” says Giaya.

The drawback of the system, he admits, is that it needs to be done in an expensive inert gas atmosphere of, say, helium or argon. If the system were to operate in air, the corresponding high-temperature plasma would degrade the precursors. APPLD retains the original properties of the liquid precursor.

Triton has spoken to textile companies with a view to sub-licensing the technology. Many are apprehensive about investing in new equipment in the current economic climate but some are keen to adopt the technology when they can afford to invest.

The company is out to identify areas where ASSET is better than anything else available and it has high hopes for speciality textiles, especially high-end synthetic fibres. It currently offers a range of coatings, including the standard hydrophilic, water-repellent and oil-repellent ones, but also claims to be able to mix polymers to give multi-functional surfaces.

“You can mix different active ingredients in the precursor stream and use them at the same time or you can do a different treatment on each side of the fabric,” explains Giaya. “So you could have a fabric that is hydrophobic on one side and hydrophilic on the other or one that is both antimicrobial and water-repellent.”

Add to this work that Hegemann is doing at Empa on coating fibres with silver, in which the metal is sputtered by plasma, and there are some interesting processes being developed. Metallised fibres could be used to incorporate electrical wiring into textiles, he says, bringing the possibility of clothes that could perhaps measure your pulse.

Such progress may be a leap too far for the textiles industry but plasma coating companies can perhaps be cautiously optimistic about the textiles industry adopting its technology. As water usage becomes more of an issue, plasma may become the only choice.

Breaking the mould

Dow Corning has developed atmospheric plasma technology called atmospheric pressure plasma liquid deposition (APPLD), which it claims can treat 3D objects. It has licensed this to Triton Systems, a coatings company based in Massachusetts, which is combining APPLD with its own chemistry and formulation expertise in what it calls ASSET (advanced solutions in surface engineering technology).

What is unusual about APPLD is that it sprays tiny droplets of a liquid precursor such as a monomer into the plasma; other processes use gas or vapour deposition. “Based on the functionality you want for your textile, you choose a liquid or even a particle
Dr Michael Franken of Lanxess looks at the thinking behind the Aquaderm X-Shield technology

Demand for leather in light colours is increasing, especially in the upholstery sector. From both aesthetic and psychological points of view, car manufacturers are tending to use more light brown, beige and even white leather seats, especially in the luxury segment. Even furniture leather for dining room chairs and lounge suites is increasingly being marketed in lighter colours.

Today, light-coloured upholstery leather has about a 20% share of the total upholstery market. Approximately 41.8 million m² of furniture leather and 29.7 million m² of automotive leather are produced in light colours.

**Ecological & economical aspects**

The lifetime of a lounge suite upholstered with light-coloured leather depends very much on the anti-soiling and the cleanability performance of the leather employed - and bright colours are, of course, more sensitive by nature to soiling and staining.

This fact is also very important from the environmental point of view. Modern life cycle assessments of articles of leather furniture evaluate more than the manufacturing process of the leather and subsequent furniture production. They also look at the lifetime and final disposal of the article and these aspects are likely to play an even more important role in the future.

This highly complex topic can be put quite simply: if the working lifetime of an article can be doubled, its environmental impact is reduced by 50%. Compared to the effort needed to improve a manufacturing process in order to achieve a better life-cycle rating, efforts in development are often much more efficient.

Since a positive environmental profile for an article is more and more valued, from our point of view it is worthwhile to establish and develop further best practice technologies in terms of anti-soiling and cleanability. With light-coloured leather, this means that high performance chemicals and additives are needed.

Such products are true speciality chemicals, which may noticeably increase the cost of a finished formulation. However, if one weighs the additional performance versus the additional cost, the consumer’s willingness to spend more money on such high quality products should not be underestimated.

The market price of a high quality leather lounge suite ranges from approximately €3,000 up to about €10,000. A typical SUV vehicle fitted out with leather costs approximately between €2,000-8,000 more than a standard textile edition. Comparing the additional cost of some €5-10 per lounge suite or car seat for a best possible anti-soiling and cleaning performance, the enhanced longevity of such articles with the commercial value of those items, the cost can be considered of minor importance.

Today it is possible to produce leather with a long lasting anti-soiling and cleanability performance which remains or can be kept clean over an extended period of time, thus maintaining its initial value. Promotional packages which include, for example, warranties for the final consumer would compensate for the additional cost of such articles and improve the image of leather as a durable material substantially.

**Best practice technology:**

Based on this economical and ecological assessment, Lanxess has dedicated significant R&D resources in the field of anti-soiling and cleanability in recent years. New chemicals have been developed, formulations have been screened and optimised and test procedures have been established. The resulting products and the application technology are marketed under the brand Aquaderm X-Shield.

During these studies, it became clear that a perfect anti-soiling and cleanability performance is not just an additional criterion which can be achieved by simply adding certain chemicals into a top coat formulation. As described in the literature, anti-soiling and anti-staining performance must be distinguished, because different contaminants have different impacts on the degree of damage they may cause on leather.\(^1\, ^3\)

Soiling is the constant and regular exposure of leather to contaminants through daily use. The most common contaminants are dust, carbon compounds, oils and dyestuffs from textiles. Staining means the accidental and occasional contamination of leather goods by, say, wine, coffee, lipstick, pens or a myriad of other substances, which can contribute to a significant loss in value for, or even destroy, precious leather goods.

Because of this, Lanxess thought it important to develop different testing methods focusing on the required performance characteristics of the respective leather articles. In the case of staining, the contaminants are applied directly onto the leather and wiped off after a certain residence time with common household cleaners, after which their cleaning efficiency is evaluated.

In the case of soiling, which is an important issue in the automotive industry, standardised fabrics contaminated with different pollutants are rubbed over the leather by means of the Martindale abrasion tester. The degree of colour change is measured after 2,000 cycles, then the dirt is wiped off by means of common leather cleaners and the colour change is measured again.

During the development phase of the Aquaderm X-Shield system, it became clear that such a wide variety of potential contaminants, along with an even bigger number of different leather properties, requires individual anti-soiling systems. Our goal was to achieve the best possible spectrum of efficacy.

Although a ‘one-size-fits-all’ system does not exist, we found that polymers with built-in tetrafluoroethene (TFE)
units were the most suitable substances for such applications, as they have a performance profile which is very similar to polytetrafluoroethene (PTFE). This is essentially because PTFE:

- Provides hydrophobic and oleophobic effects at the same time
- Is thermostable at temperatures from -200°C to +260°C
- Is chemically inert and resistant to UV radiation
- Provides low friction and excellent release properties
- Has extremely low surface energy

In practice there are two ways of using this chemistry in the leather field namely the so-called comb polymers or via linear copolymers. Comb polymer-based products containing TFE side chains, such as Aquaderm X-Shield L, are used as an additive in special top coats and provide outstanding dirt repellency and cleanability.

Analysis of leather finished with Aquaderm X-Shield L has proved that neither perfluorocetyl sulphonic acid (PFOS) nor perfluorooctanoic acid (PFOA), which both present environmental issues, is present. Nevertheless, there is a drawback to comb polymers in that cross-linking is only partly possible, which limits the durability of such systems.

In the case of linear TFE-copolymers, such as Aquaderm X-Shield G and M2, the TFE groups are permanently built into the polymer backbone. Combined with additional functional groups, such products offer a versatile application field to the leather industry, adding durability to the excellent dirt repellency and cleanability of comb polymers.

In cooperation with Daikin, Lanxess has been able to develop a water-based linear TFE copolymer for use in leather applications. Finishing systems based on this unique chemistry can be pigmented and cross-linked with isocyanate, which leads to an excellent film formation. At the same time, different gloss levels can be adjusted and suitable feel agents can be added.

By these means a superior and long lasting anti-soiling resistance along with an outstanding cleanability performance can be achieved. Figure 1 shows the linear polymer structure of these systems.

**Conclusion**

Aquaderm X-Shield technology can provide leather articles with outstanding performance in terms of anti-soiling and long term cleanability, generally summarised under the term ‘anti-soiling’. Depending on the requirements, formulations can and must be customised for each individual purpose.

Specially developed high performance polymers based on fluorocarbon are used in carefully balanced recipes provide anti-soiling performance without sacrificing other physical requirements. The additional cost for this chemistry is not negligible, but it gives additional value to the consumer because it extends the life of a high performance article.

References:

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5th October 2010 | Beach Rotana Hotel | Abu Dhabi, U.A.E.
Dr Marco Arnold and Dr Cornelia Röger show how BASF develops key compounds for ever smaller node sizes*.

Every microchip comprises a base layer of transistors with several layers of wiring stacked above to connect the transistors to each other and finally to the rest of the computer (Figure 1a). These interconnects are today based upon copper and form a complex three-dimensional network of horizontal and vertical lines, called trenches and vias, with a total length of up to several kilometres.

The first copper-based microprocessor was manufactured by IBM in 1997 using a completely new integration scheme called the damascene process (Figure 1b). This had to be developed because copper cannot be patterned by a reactive ion etching process.1

First, the formation of a barrier layer is required, preventing the diffusion of copper into the dielectric material. Currently a Ta/TaN barrier is deposited via a physical vapour deposition (PVD) process on a patterned dielectric layer.

The creation of a copper seed layer in the following step provides the whole wafer with a conductive surface, facilitating the subsequent electrochemical deposition (ECD) of copper. Finally, a chemical mechanical planarisation (CMP) process is required to remove the excess copper layer as well as the barrier layer from the top of the dielectric.

Since the semiconductor market demands ever faster chips with higher power density and lower energy consumption, the race to fabricate devices with an increasing transistor density continues.2 With each new chip generation (technology node), not only the transistor dimensions but also the feature sizes of interconnects have to shrink.

Hand-in-hand with the decreasing feature size, the requirements to the electroplating chemicals used in the damascene process are more and more challenging. For example, the feature openings of the 32 nm technology node show a width of merely 20 nm after seed layer deposition.

**Role of additives**

The quality of copper interconnects determines the lifetime and electrical performance of an integrated circuit. Thus, it is essential to avoid defects inside the copper lines. However, if a substrate is electroplated without additives, voids are formed, due to a higher copper deposition rate at the wafer surface and feature opening compared to the feature bottom (Figure 2a).1

Perfectly filled structures can only be obtained if the copper deposition rate is high at the feature bottom and slow at its upper edges and at the top of the wafer. This superfilling process is realised by adding an accelerator and a suppressor to the plating bath.

Suppressors are polyalkylene glycol (PAG) polymers. The suppressing behaviour of PAGs can be explained by their adsorption on the wafer surface. The adsorbed polymer film acts as a physical barrier for copper ions, due to the formation of PAG-Cu(I)-chloride complexes, and for accelerator molecules, as well by limiting their access to the wafer surface. The most common accelerator used in industry is bis(3-sulphopropyl)-disulphide (SPS).

The superfill mechanism is caused by a sophisticated interplay of additive transport and adsorption kinetics.3,4,5 When a structured wafer is immersed into the plating solution, both additives are uniformly distributed in the solution (Figure 2b). When a structured wafer is immersed into the plating bath, both additives are uniformly distributed in the solution (Figure 2b). Due to its high adsorption rate, the polymeric suppressor additive is rapidly consumed by film formation on the wafer surface. Since the wafer rotates in the plating solution, a constant convectional flow of electrolyte to the wafer surface is
induced, providing fresh supply of suppressors and resulting in the formation of a compact suppressor film on top of the wafer.

By contrast, the transport of additives into the feature is diffusion-controlled. Only a small fraction of the inner feature surface is covered by the suppressor, caused by the low suppressor diffusion rate and a large surface to volume ratio (Figure 2c).

For this reason, the deposition rate at the feature bottom is much higher compared to the wafer surface. There, the accelerator molecules are accumulated due their higher diffusion rate (Figure 2d).

The key function of the accelerator is to keep the feature bottom free of adsorbed suppressor and to maintain a locally high deposition rate (Figure 2e). Furthermore, during the superfill the accelerator deactivates the suppressor film at the upper walls of the feature by decomposing the PAG-Cu(I)-chloride complexes, resulting in a void-free filled feature (Figure 2f).

**Suppressor synthesis**

Until now, few structural variations of PAG derivatives have been published for use as suppressing agents. Established additive formulation providers very often purchase commercially available PAGs that have not been developed specifically for an electronic application. However, as the technology nodes decrease down to 32 nm and even smaller, the likelihood of finding a commercial PAG derivative matching the challenging criteria to provide a fast and defect-free superfill becomes increasingly slim.

Since BASF has strong expertise in R&D into and in the production of PAG, it has successfully commercialised this class of polymers for many different applications, such as washing and cleaning, as ingredients for cosmetic formulations, raw materials for polyurethanes and construction chemicals, as well as agrochemical adjuvants. Recently, the company used its expertise in developing structure-property relationships in the field of PAGs, designing tailor-made suppressor additives for current and future copper plating technologies.

In addition to commercially available PAGs, an enormous structural variety of these polymers is accessible. Synthesis can be carried out by cationic, anionic or coordinative polymerisation mechanisms, using ethylene oxide (EO) as a key monomer. In addition, propylene oxide and higher alkylene oxides serve as additional components to synthesise statistical or block copolymers, while alkylene oxides carrying functional groups as substituents allow further fine-tuning of the PAG’s properties.

Many different molecules can start the polymerisation reaction, i.e. alcohols or amines, but other nucleophilic compounds have also been employed. This further multiplies the structural variety of PAGs (Figure 3). A broad range of such PAG structures was synthesised to gain access to suppressors showing a huge spectrum of different physical and electrochemical properties.

The handling of alkylene oxides, especially EOs, requires special safety measures and well-trained technical staff. EO has an extremely high ring tension, leading to a very high reactivity, for example with traces of nucleophilic and acidic residues, and self-decomposition at elevated temperature, which can be catalysed even by traces of rust. Thus, handling obviously has to be done using advanced safety equipment.

**Suppressor screening**

To investigate the suppressor properties of numerous newly synthesised PAG derivatives, a fast and efficient screening method is required. Potential transients from galvanostatic copper deposition experiments are suitable to select promising suppressors for further wafer plating experiments.

For these investigations an electrochemical cell equipped with a platinum rotating disk is used. Copper is deposited from a so-called low acid electrolyte (10 g l⁻¹ H₂SO₄, 50 ppm Cl⁻, 40 g l⁻¹ Cu²⁺) under constant current conditions.

At the beginning of each experiment, a thin copper film is freshly plated without additives. Afterwards the additives are injected in particular sequences into the plating bath (Figure 4a). The corresponding change of the cathodic overpotential is a direct measure for the impact of the additives on the copper deposition process.

Upon suppressor injection, the cathodic overpotential is increased in order to maintain the predefined current. The larger the potential difference compared to the copper dep-
position from an additive-free plating solution (ΔU), the stronger the suppression by the PAG derives. Compounds showing the largest increase in overpotential were expected to be the most promising candidates to show good filling results in 32 nm and following node features.

However, to predict a good superfilling behaviour the competitive action of suppressor and accelerator must also be taken into account. This is simulated by injecting the accelerator into a suppressor-containing plating bath. For the superfilling mechanism it is indispensable that the accelerator should be able to deactivate the suppressor film.

Thus, after the addition of the accelerator to the solution a decrease of the cathodic overpotential is expected. Accordingly, only PAG derivatives showing the overpotential sequence shown in Figure 4a have been selected as promising suppressor candidates. SEM images of 32 nm test structures plated with a weak and a strong suppressor demonstrate that a strong suppression results in void-free filling (Figure 4b).

**Leveller additives**

It has been demonstrated that defect-free filling of 32 nm features can be observed by using a combination of a tailor-made PAG derivative and SPS. However, to observe the desired plating result a third additive, the so-called leveller, is required.

When the feature is filled, the accelerator species concentration is locally very high on top of the features, leading to a significantly higher copper thickness over dense lines compared to an unstructured area (Figures 5a & 5c). Leveller molecules interact with the negatively charged accelerator compound. This deactivates the accelerator molecules, thus prohibiting the mounding phenomenon after superfilling (Figures 5b & 5c).

The addition of a leveller is essential, since mounding can greatly disturb the subsequent CMP process. Besides its main function of generating a homogeneous thickness distribution, the leveller must provide a low surface roughness and a mirror-finish appearance in the plated copper over the entire wafer. Without a proper leveller, a rough surface is obtained and the wafer appears hazy.

The challenge in developing leveller compounds for ≤ 32 nm technologies is to find the right balance between good levelling behaviour and a low interference with the superfill. Typically, leveller molecules are positively charged monomeric or polymeric nitrogenous compounds such as dodecyltriethylenemmonium chloride, polyethyleneimine or polyvinylpyrrolidone.\(^7,8,9\)

New generation leveller candidates were tested for their levelling behaviour in the presence of an optimised suppressor and SPS. The experiment revealed several that did not show any substantial interference with the superfill (Figure 5f) and provided excellent levelling properties (Figure 5d). For comparison, Figures 5c and 5e show the fill results of an additive package containing an inappropriate leveller, causing void formation within the trenches and unwanted mounding.

In conclusion, synthesis and step-wise screening of a huge variety of tailor-made suppressor and leveller compounds resulted in the appropriate additive packages fulfilling the requirements for the 32 nm and 22 nm technology. Based on our previous results, we are now developing additive packages for even smaller technology nodes.

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**References:**

3. A. Flügel, Copper Damascene Process: From the Wafer to the Atomic Scale, DFG Frühjahrstagung, Regensburg 2010
5. P. Broekmann, Adsorptive SPS Dissociation within the c(2 × 2)-Cl Matrix on Cu(100) Under Reactive Conditions, ECS 217th Meeting, Vancouver, 2010
Dr Peter Harrop of IDTechEx takes a brief look at the role of the chemicals industry in the next electronic revolution

Imagine helicopters dropping biodegradable smart dust on that oil slick to monitor all the animals and pollution in detail. It self-organises electronically like the internet to send the information back and each speck gets its electricity from the sun and waves without batteries.

Imagine superwoman, created by smart textiles and implants. Or dream of an electric car that is completely coated with transparent layers. These variously act as solar cells creating electricity, batteries storing it and electronics and electrics managing everything required by the car.

You have entered the world of printed electronics and there is more, much more, to come, even bending light to make things invisible. Then we have mimicking the synapses of the human brain with the printed TiO2 'memristors' first demonstrated last year and making edible and stretchable electronics.

Recently, many patents have been registered on these capabilities, based on actual demonstrations. More important than the silicon chip 40 years ago, this new electronics potentially includes printed electronics and electrics. What is thin film today is printed tomorrow. And the chemists are holding things up.

There are many successes on the way to what will be a $300 billion business, incorporating at least a $100 billion materials business 20 years from now. Printed silver already gives us waterproof, roll-up, membrane keyboards, complex antennae moulded into the plastic of cars and sensors that record which tablet you took and when from your blister pack.

Together with printed resistors, we get the battery tester in the Duracell battery. Conductive printed polyanilene and polythiophene provide antistatic and RF shielding on plastic film.

Recent progress

In the last year, three companies have announced ways of printing very conductive copper without problems from the insulating oxide. That will save money and avoid the need to use a biocide. Manganese-doped zinc sulphide AC electroluminescent layers are printed to give us huge, flexible, screen-printed, animated posters and the T-shirt that flashes a sequence of images when you enter a WiFi zone.

This technology is now being used in reprogrammable posters that have light-emitting moving images, sound and even the emission of an aroma when you approach. Partially printed electrochromic displays, based on carbon, TiO2 and glycerine, need no electricity unless the image is being altered, so they have been the basis of e-readers, shelf-edge displays and even wristwatches.

Flexible versions with printed polythiophene transistor arrays on the back are coming to market this year. InGaZnO semiconductors are the basis of transparent printed transistor circuits and we are printing ZnO nanowires and lead zirconate titanate piezoelectric to generate electricity for small printed electronic devices. Carbon nanotube inks form superb semiconductors, conductors and other layers in the laboratory and some are transparent. C60 buckyballs enhance the performance of printed organic photovoltaics (OPV).

Most of the potential market for the new electronics is for flexible and conformal things, such as the large display that will unroll from your mobile phone then snap back when it is not needed. Photovoltaics (PV) must be pasted across the bumpy, angled outside and inside of buildings.

Organic materials are attractive for much of this but the polythiophenes and other chemicals they employ are still very reactive and inefficient in converting light to electricity. For example, the new printed organic solar bags that charge your phone have only a one-year guarantee. Printed inorganic versions based on CdTeCdSe, GaAsGe or copper indium gallium diselenide or TiO2 and ruthenium-based dye and iodine-based electrolyte are more enduring but possibly more expensive to make. Organic light-emitting diodes (OLEDs) are a thin film form of display with no pollutants, very low voltage for safety and superb moving colour images. These light-emitting displays are successful in some mobile phones and available in a tiny number of television sets but they are tediously made by vacuum processes sandwiched in glass.

We are trying to move from monomers to soluble oligomers and polymers for flexible OLEDs. When printed on plastic film, their life is often only a few weeks yet we need the lower cost of printing and the flexible displays that result. They will go on billions of medical disposables and trillions of consumer packaged goods.

Chemists need to produce more stable active materials in these displays and better barrier layers (typically one oxide or nitride layer, then an organic layer for planarisation, these ‘dyads’ being repeated if necessary. Can they have gettering action as well as impermeability?). Barrier layers are also needed to make OPV on buildings, boats and aircraft a long-lived success.

Thin film and fully printed batteries are finding uses as back-up and energy harvesting power supplies, for example. NEC is bringing a transparent, flexible organic battery to market in Japan.

The polymer developed by the researchers consists of a simple polystyrene backbone with aryl pendant groups known as ‘galvinoxyl’ groups.
These support an oxygen radical, which gives up its electron under redox conditions. When it is placed in a battery arrangement with an electron-accepting polymer, electrons can flow around the circuit to provide power.

In 2009, initial tests in a cell with a lithium anode revealed that the galvinoxyl polymer’s performance was stable for at least 500 charge-discharge cycles. Such batteries, printed on polyester film can be charged in one minute. Redox reactions are also the basis of printed electrochromic displays but their life needs to improve.

Role of chemistry

Let us now summarise the trends, challenges and future of this exciting new opportunity for the chemicals industry. Here we have a huge number of opportunities for premium priced speciality chemicals and associated services but also for high volume materials. This is mainly a story about inorganic materials today but there will be a more even split of organic, inorganic and composite materials in the future. Chemicals companies with the necessary virtuosity will have an advantage in terms of pollution, price, morphology and materials.

Carcinogens and alleged endocrine-disrupting materials used in the manufacture of some organic inks are troublesome too.

The new electronics often employs materials where there are ample crustal resources but extraction is troublesome leading to price hikes. Think silver conductors (copper is not the whole answer; it is no longer approved for all contact with food and it poisons an OLED), indium (ITO transparent electrodes are currently used for most forms of display and PV, printed CIGS PV and so on), neodymium (thin film magnets and motors) and lanthanum (NiMH batteries).

Almost all forms of printing are employed in printed electronics. Often, several printing technologies are employed to produce one device. Each calls for a different morphology and rheology.

Fully dissolved metals are sometimes used for inks but they need to be more affordable. Nanosilver ink can be annealed at low temperature so that low cost plastic films or paper substrates suffice.

Its price premium may now have fallen to the point where the resulting conductive pattern is lower cost than that printed conventionally, because less silver is used, but more progress would be welcome. PVDF derivatives are favoured for printed ferroelectric memory but better technical parameters would be welcome, even the avoidance of destructive read write.

Flexible smart substrates are increasingly used to leverage the printed circuits on them. For example, the New University of Lisbon makes the paper substrate of a printed InGaZnO transistor double as the gate dielectric. Other substrate films at ITRI Taiwan act as ultrasound emitters and detectors when printed with electronics. New smart substrates are welcome and there should certainly be more work on paper. For example, Kimberley Clark has carbon-loaded paper that acts as a heating element or sensor network.

Even dumb substrates need improvement. The favourite substrate for printed electronics is biaxially oriented, surface-treated polyester film but PEN or something similar is needed where greater dimensional stability and temperature range are vital, if only to tolerate the annealing of sub-optimal inks. However, its price multiple needs to come down.
Sustainability was the theme of Wacker Chemie’s international press briefing earlier this year.

The company has been involved in the Responsible Care initiative since it started in 1991 and joined the UN’s Global Compact in 2006. This is now the world’s largest sustainability initiative, with over 4,700 member companies and participants from 130 countries committing themselves to promoting human rights, labour standards and environmental protection and to fighting corruption.

Like health and safety, Krey continued, environmental protection is a core component of all Wacker’s processes. It begins at the product development and planning stages and, in line with Responsible Care principles, involves taking measures that go beyond what is legally required. The company aims to conserve resources and decouple energy consumption and waste generation from production volumes.

As part of its product stewardship responsibility, Wacker ensures that the findings of risk assessments are implemented speedily and provides material safety data sheets (MSDSs) on all of its products - a total of some 54,000 MSDSs in 32 languages - even though only 40% of the products require them by law. It has also pre-registered over 7,000 substances under REACH and submitted 45 registration dossiers to the ECHA in 2009.

Workplace, plant & transport safety “form the basis for uninterrupted production”, Krey said. This involves extensive safety and risk analyses of plants from the design stage to commissioning and regular seminars on plant and work safety and explosion protection. More specifically, Wacker launched its ‘Fresh Impetus for Work’ initiative in 2007, with the aim of reducing workplace accidents and extended this to non-German sites last year.

There is still some way to go, since last year the company had 4.0 accidents/million hours worked, slightly above the ICCA’s world average of 3.65. However, this was well below the German average of 9.1, while Burghausen’s rate of reportable accidents in 2009 - 1.3 per 1,000 employees was well below the chemical industry rate of 14.7 in 2007.

In terms of transport, sustainability means ensuring that hazardous goods are transported by rail wherever possible and that hazardous goods vehicles are always checked before loading, with non-compliant ones not being loaded. Shippers of hazardous goods for Wacker are audited very strictly and, in line with Responsible Care principles, involves taking measures that go beyond what is legally required. The company aims to conserve resources and decouple energy consumption and waste generation from production volumes.

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Finally, as well as corporate citizenship activities, Krey cited the steps Wacker takes to create the right conditions for all employees to develop their abilities to the full through training and advancement programmes and initiatives to balance work with family life. The company has a significantly lower employee fluctuation rate than most - 0.7%/year in Germany and 2.3%/year worldwide.

Burghausen, as site communications manager Klaus Millrath pointed out, is the largest chemicals site in Bavaria. It employs nearly 10,000 people in about 130 production facilities, which offers ecological as well as economic benefits in terms of the immediate reuse and recycling of materials, production intermediates and by-products. Figure 2 illustrates the loop.

Four starting materials - silicon, methanol, hydrogen and sodium chloride - are used to make over 3,000 silicone products, pyrogenic silica and polysilicon at the site, while...
the integrated ethylene system generates organic intermediates, polymer dispersions and dispersible powder polymers. Likewise, HCl, which is used to make many chlorine-containing intermediates is recovered and returned to the production loop.

Energy is another critical element of production sustainability, Blum continued. The chemicals industry is one of the most energy-intensive of all industries, accounting for 20% of all industrial power consumption in Germany, while Burghausen alone consumes 1.7 billion kWh/year, about as much as a mid-sized city. Efficient use of electricity is vital for climate protection and competitiveness.

For this reason, Wacker launched its ‘Power Plus’ initiative at Burghausen and the other main German site at Nünchritz in 2006, striving for a 10% reduction in specific energy consumption by 2009. Today, 35 plants at the two sites have been examined and potential savings in electrical energy and steam identified of 14.3% and 22.8% at Burghausen and 18% and 50% at Nünchritz. The initiative’s programme has now been extended to the Cologne site.

Both Burghausen and Nünchritz have combined heat and power plants, which are 80% fuel-efficient, far more than most power generators. Burghausen also takes 270 million kWh/year of hydroelectric power generated by a Wacker subsidiary company, Alzweber, on a nearby river, thereby saving 58,700 tonnes of natural gas consumption and preventing 162,000 tonnes of CO₂ emissions.

Combined, these power sources generated 1.4 million MWh of electricity in 2008, about 60% of total electricity needs at the two sites. Burghausen also uses ion exchange membrane electrolysis in chlorine manufacture, using 25% less energy than the mercury or asbestos processes.

Other key issues at Burghausen include water and waste disposal. Biological treatment is used to purify waste water, while technological improvements in the cooling water system have saved some 4,700 m³/year of water. In 2008, Nünchritz developed a new method for recycling some 1,000 tonnes/year of pyrogenic silica that used to be landfilled for use as a building additive.

Because the North Sea ports of Hamburg and Bremerhaven are some 400 km away, Wacker uses the Schütz container system to reduce shipments. In addition, 600,000 km³/year of transport needs have been eliminated by having the supplier open a plant near Burghausen.

There were also presentations from most of the operating divisions of Wacker at the briefing. Each of these, the company claims, contributes in different ways to sustainability in their production at Burghausen and other sites and, more importantly, to much wider sustainability issues in the world.

Perhaps foremost among them is Wacker Polysilicon, which is one of the world’s largest makers of hyper-pure photovoltaic (PV) silicon. As senior marketing manager Dr Wolfgang Storm pointed out, we must make increasing use of PV if we are to rely more on renewable energy in order to put a lid on global warming while meeting ever-increasing energy demand.

Mono- or multi-crystalline silicon (c-Si) cells represent by far the most important technology on the PV market, Storm added, and will remain so. This had 86% of the total in 2008 and is edging out a- and µ-Si on cost grounds. Cadmium telluride (CdTe) is the only serious competitor but the cost advantages it seemed to offer at first are levelling off; CIGS and organic PV are still in the development phase.

By, for example, improving process efficiency, cutting costs and introducing its advanced polysilicon deposition technology, Wacker has contributed to making solar panels more economically viable. The payback period for the initial investment is now about one year for products with an expected lifetime of 25-35 years.

The energy required to produce polysilicon is the single largest portion of energy usage by it. In this context, Storm said, Wacker’s success in reducing by 50% the energy needed to make a tonne of it is a “significant contribution”. Net energy generation has risen to 7,000 kWh/tonne of polysilicon, while some 6,000 tonnes of CO₂ are saved compared to the cost of burning coal to generate electricity.

In addition, the cost of PV systems have fallen by 50% in the past three years. As a result, ‘consumer grid parity’, the point at which the cost of generating solar energy is the same as buying it, has been reached in some sunny areas, notably Italy and Hawaii, and is looming close in others.

Virtually all major countries, with Russia the only notable exception, are supporting the growth of the PV industry via feed-in tariffs or preparing to. The industry association forecasts that solar energy markets will grow by 45%/year from 2007 to 2013, creating millions of jobs as well as contributing to sustainable development.

Dr Bernd Pachaly, vice-president of engineering silicones at Wacker Silicones, described the use of silicone elastomers, which represent about 20% of the global silicones market, in high-tech applications. Their properties, he said, “make them interesting for a wide range of sustainable applications” – notably their heat stability, low glass transition temperature, long-term flexibility and stability, biocompatibility, physiological inertness and low flammability.

Silicone elastomers are increasingly used in the production of LEDs, the use of which can massively reduce energy consumption and CO₂ generation. Thanks to their heat- and UV-resistance and allowing lead-free soldering at over 260°C. Certain Wacker grades are already used to encapsulate LED chips and produce lenses, while the new high performance Lumisil silicones enable optical lenses for LEDs to be produced directly onto the chip in a single step for the first time.

In a similar vein, said Pachaly, Elastosil Solar 3210 was designed specifically for optical lenses and mouldings in high-concentrated PV systems. These are an alternative to conventional PV technology in which the sunlight is bundled and focused onto highly efficient cells via crystal-clear silicone Fresnel lenses.

Silicone elastomers are also used in power generation, transmission and distribution, in applications ranging from insulation to coatings, arresters,
cables and transformer fluids. Silicone rubber composite insulators consume 50% less energy and release 75% less CO₂ than comparable porcelain insulators, making them an increasingly attractive option.

Finally, Wacker has recently developed a new generation of UV-activated silicone elastomers, which addition-cure rapidly with minimal energy input at room temperature. This means that their reactivity can be controlled within a broad time slot and processing window, without depending on the intensity or duration of the UV radiation, thus allowing shorter cycle times and higher productivity.

“The use of silicones can often greatly boost the efficiency of production processes, both economically and ecologically,” Pachaly concluded. “The durability of silicone elastomers makes a considerable contribution towards the efficient use of resources.”

The construction industry is another major consumer of energy and generator of CO₂, as well as a major client of several divisions of Wacker, according to Peter Summo, vice-president of construction polymers at Wacker Polymers, and Bernd Judas, vice-president of construction silicones at Wacker Silicones.

The mega-trends of urbanisation and megacities, combined with increasing population and pressure on resources mean that more sustainable building is vital. Summo and Judas noted figures from a Deutsche Bank study suggesting that emissions from buildings account for 40% of all emissions and that applying energy efficiency measures could save five times more energy than that produced by all the nuclear power plants in Germany in 2007.

In this context, Vinnapas dispersible polymer powders have a major role to play. Such polymeric binders are vital to the use of external insulation and finish systems (EIFs) in both new and refurbished buildings. These, said Summo, “are the simplest and most reliable method of conserving energy for buildings over the long term”, because better insulation means less energy is needed to create a comfortable indoor climate, whatever the conditions outside.

Polymer-modified sealing slurries are also based on Vinnapas powders. These are easy to use and protect structures from water damage by both preventing water ingress and conserving water in impregnated water channels and reservoirs.

Finally, Vinnapas powders make possible the thin-bed technique of laying tiles, using 3 kg of dry mortar/m² instead of the 10 kg of adhesive used in the thick-bed technique that still prevails in the developed world. Thus tilers can work faster while saving on material consumption and reducing CO₂ emissions by 50%. Many Wacker customers, notably BASF, Henkel and Mapei, are already working on product development based on these sustainable offers.

Silicones also play a part in the functional coating systems that protect modern façade coatings against moisture and harmful environmental influences, according to Judas. Indeed, silicone resin emulsion paints (SREPs) are among the most effective of all, because they form a hydrophobic film on the façade that is also water vapour-permeable, ensuring that damp masonry dries faster.

Dr Christopher Winterhalter, director of chewing gum at Wacker Biosolutions - recently renamed Wacker Fine Chemicals - looked at sustainable biotech products and processes. His main emphasis was on the use of two corn-based products, cyclodextrins and the natural amino acid cysteine, in both of which the company is a world market leader.

A major recent innovation, he said, was the development of an “extremely efficient and environmentally compatible” fermentative production method for cysteine from plant-based raw materials using E. coli bacteria. This is increasingly replacing the extraction of cysteine from human hair, pigs’ bristles and poultry feathers.

The new technique enables 90% of the bacterial cysteine to end up in the final product, as opposed to 60%. The amount of hydrochloric acid needed to extract it is reduced by 96% from 2.7 kg/kg of final product to 1. Fractional crystallisation and electrodialysis are no longer needed and boiling temperatures are reduced to 30-35°C.

The final product, said Winterhalter, is vegetarian-grade, kosher and halal. It is also ideal for food and pharmaceutical applications because any risk of contamination by human or animal pathogens is avoided. In addition, the residues, of which there are fewer, can now be used as fertilisers.

White biotechnology in general, added Dr Fridolin Starry, senior vice-president of corporate R&D, is “a key technology for innovative and sustainable products and processes in the chemicals industry”. This includes chemical products based on biomass, the increasing use of biocatalysis in process chemistry and processing of the by-products of biorefineries.

With rising petrochemical prices and improvements in technology, “more and more processes will become economically competitive for bulk chemicals” based on such superabundant resources as glucose, straw and ethanol. Indeed, they already are for some high value products like vitamin B2, antibiotics, cyclodextrins and cysteine.

Wacker has therefore implemented several R&D projects for the biotech production of bulk chemicals. It looked at three routes to biogenic acetic acid and is now operating 500 tonnes/year pilot plant that uses the ACEO process to ferment bioethanol directly via gas phase oxidation. This was preferred to the more indirect routes via fermentation to butanediol and homoacetoacetate fermentation.

The process, Starry said, achieves excellent yields and selectivities yet is still completely energy-autarkic. Moreover, it can use low quality feed-stocks with >25% EtOH. In the six months of operation, it has exceeded expectations in terms of:

- An efficient and robust process
- No need for exotic engineering materials
- Known scale-up engineering data
- Low capex requirements
- High variability for different ethanol quantities
- Bioethanol costs strongly influencing production costs

Production from this route means that the refinery can be located anywhere while still being competitive on price. Finally, the bioethylene obtained could be suitable for Wacker’s vinyl acetate ethylene and vinyl acetate monomer (VAM) production. VAM is, indeed, another bulk chemical that the company is evaluating for biotech production routes.

Above all, Wacker feels that sustainability makes sense at every level. “Chemistry makes a vital contribution to global progress and sustainable development,” Krey said. At present, it is saving two tonnes of greenhouse gas emissions for every tonne emitted and that ratio should be 4:1 by 2030.

Moreover, he concluded, sustainable chemistry also makes economic sense. “Mega-trends such as energy, urbanisation, construction, digitisation and rising living standards will increasingly stimulate demand for sustainable products and technologies.” The BRIC countries alone will generate a compound annual growth rate of 3.7%/year over the next 25 years for such products, so the potential is vast.

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Getting to the point: Direct bio-basing replacements for traditional manufacturing methods

Dennis McGrew of Genomatica outlines the case for directly produced, drop-in bio-based replacements for traditional manufacturing methods

In the last 18 months, the chemicals industry has made significant strides toward more bio-based production. One year ago, a survey conducted by Genomatica and ICIS showed that 57% of industry executives said their companies should reduce their exposure to the petroleum-based commodity market. Companies also acknowledged that their customers have expressed real interest in chemicals based on renewable materials.

More than half of the executives in the survey, however, said that cost was the most prohibitive part of a sustainable chemicals programme. Consumer attitudes, volatile petroleum markets and global demand contraction have converged for a unique moment of interest and demand for sustainable chemicals, but cost continues to be the key barrier to adoption.

If capacity rebounds in the next three to five years, as some analysts predict, it will present an interesting opportunity to introduce new process technologies that use renewable feedstocks to manufacture chemicals. These new processes can drive the start of a transformation of the chemicals industry.

However, helping the industry to transition from petroleum-based feedstocks to renewable feedstocks will not happen overnight. As shown in the survey, common wisdom holds that transitioning to a more sustainable industry will raise costs and further squeeze tight margins.

Making the industry more environmentally sustainable at the cost of economic viability is not an option. Genomatica believes strongly that sustainability must come at a lower cost and that innovative biotechnology can deliver sustainable solutions for lower costs, especially when direct production routes eliminate as many intermediate processing steps as possible and the resulting materials are equivalent to conventional ones used today, enabling them to be dropped into existing downstream value chains.

**Metabolic engineering platform**

To fulfill this daunting goal of low-cost sustainability, our research teams have explored hundreds of routes to dozens of products. Genomatica’s core technologies for metabolic engineering, combined with our laboratory and process engineering capabilities, have enabled us to explore a broad portfolio of processes to generate a range of chemical intermediates.

Early assessment and IP around platform molecules like succinic acid and 3HP were de-emphasised in favour of more direct production routes to existing, large chemical intermediates like 1,4-butanediol (BDO). Our other ongoing efforts also include various acrylates, polyamide (PA, or nylon) intermediates, solvents and surfactants. Published patent applications demonstrate the breadth of routes available, with development priority given to those with the best opportunity to deliver breakthrough cost reductions of >25% over the best available conventional technology in large, growing chemical intermediate markets.

**Challenges with indirect routes**

In August 2004, the US Department of Energy (DOE) published a study intended to evaluate and compare more than 300 molecules from the point of view of technological feasibility, size of potential market and interest to the chemicals industry. It identified priorities for the top 12 chemicals of greatest interest.

These 12 are often called platform molecules, because they may serve as a platform for producing a variety of derivatives. However, they generally provide an indirect route to the chemical intermediates that are large consumers of fossil fuels today. Such routes face several potential challenges that may ultimately affect economics.

Unwanted by-products are often generated that impact not only costs, but also the process’s environmental footprint, while additional processing steps typically require more unit operations with the inherent added capital, energy and operating expense, as well as creating the potential for yield losses.

Finally, the chemical intermediates purportedly derived from these platform molecules often have substantially larger markets than the platform chemicals themselves, requiring large infrastructure investments to reach sufficient economies of scale to make a significant impact on fossil fuel use.

**Unintended consequences**

A concern, especially for larger-scale chemical intermediate production, is the potential for undesirable co-products from indirect production routes. Organic acids, some considered as potential platform molecules, are an example of this. Lactic acid can be produced from bio-based feedstocks through fermentation but requires direct acidification, esterification and hydrolysis through reactive distillation to purify and provide a useful chemical intermediate. Direct acidification produces large quantities of gypsum co-product, which may not be pure enough for industrial use.

As processes scale up, even a relatively minor waste stream can become problematic, adding disposal costs and reducing yield. Improvements in technology may substantially reduce undesirable co-products, but will likely not eliminate them entirely.

Platform chemical routes like organic acids may be effective for some small speciality chemicals or...
niche ‘green’ markets, but for larger volume chemical intermediates like 1,4-BDO, acrylates or nylon intermediates, the waste products could become problematic.

Lactic acid also shows the challenge of multiple unit operations required to isolate and purify it as a raw material for subsequent chemical conversion to the targeted chemical intermediates (Figure 1). Further, impurities associated with its production can be problematic for downstream products, affecting yields and separations, especially as one strives for lower costs. These challenges may also manifest themselves for other organic acids developed as platform chemicals.

**Keeping it simple**

Whilst platform molecules may indeed provide bio-based routes to various chemical intermediates, the additional necessary steps run counter to the goal of a low-cost solution. To foster widespread adoption of sustainable chemicals, the new processes must cost less than traditional methods.

We see our direct production route to 1,4-BDO (Figure 2) as a prime example, eliminating the need for the isolation and purification of succinic acid and the subsequent high-temperature and high-pressure steps for BDO conversion via catalytic hydrogenation. We estimate that the additional processing steps between succinic acid and butanediol could add at least 20 cts/lb ($0.36/kg) to the cost of the final product.

In both academic journals and media outlets, there is concern that succinic acid production has not yet reached economic competitiveness with traditional production methods. Most sources say the cost of separating and purifying it from the fermentation broth is the largest barrier to economic production for most applications.

For the large global PA market, we have filed a patent application for bio-based direct route to several intermediates, potentially opening up fully bio-based PA 6 and PA 6,6. We typically file patents on a range of routes, but pursue only the most direct ones, those that can be achieved in a single organism and the simplest possible process. We achieve this through metabolic engineering and genetic modification.

By contrast, many of the other approaches for pursuing bio-based nylon routes are indirect production routes through platform chemicals including lysine, a common bio-based amino acid. For instance, researchers at Michigan State University have patented a process for converting L-lysine from natural materials to ε-caprolactam, a precursor to PA 6, in a handful of processing steps with a yield of about 75%. The ε-caprolactam is then polymerised into PA 6, which has a huge global market. Genomatica’s proposed routes have significantly fewer steps and those steps are simpler, especially in the separations of intermediates and desired end-products (Figure 3).

Industrial inertia dictates that a simpler replacement technology will spread faster through the industry where the simplicity leads to lower costs. Building replacement processes with the minimum number of unit operations for current large-market chemical intermediates is vital. Instead of requiring additional processing steps and additional capital investments, more direct production route will ease adoption when compared to indirect methods.

**Leveraging infrastructure**

The effective and rapid transformation of the chemicals industry toward greater production of bio-based materials will require leveraging existing infrastructure to the greatest extent possible. Historically, substitutes for existing chemical intermediates or polymers have required substantial changes in existing infrastructure or downstream derivative production.

These changes can create barriers to market adoption, extending time for speed-to-scale of new products and offsetting economies gained with bio-based production. Success critically relies on performance advantages due to these barriers.

We feel that an approach with chemically identical, performance-equivalent chemicals and polymers at lower cost than conventional processes will be required to drive the large-scale transformation of the chemicals industry. Instead of developing new markets for chemicals or requiring new infrastructure or supply chains, direct production of existing chemical intermediates can quickly drop into current markets and leverage substantial downstream infrastructure that is already in place globally.

At present, succinic acid serves a relatively small world market of about 40,000 tonnes/year. Proponents contend that the market could grow 100-fold if the bio-based variety is made at a lower price than the petrochemical method. Whilst the global market for lysine is substantially larger than succinic acid at more than 700,000 tonnes/year, it remains far smaller than the 4,000,000 tonnes/year market for caprolactam.

It is difficult to believe that economical production of large-scale chemical intermediates can be driven through these indirect routes, as a significant amount of capital will need to be invested for the platform molecule, in addition to capital for conversion to target chemical intermediates.

Chemicals producers are making important strides to serve this sustainable market demand and allow the industry to diversify away from petrochemical feedstocks. Several processes are nearing commercialisation, as small demonstration facilities start up and industry leaders, including BASF and DSM, have announced the commercialisation of bio-based succinic acid in the coming years.

However, most industry efforts appear focused on lower volume specialties, green niches, like deicing fluids, and potentially new polymers, like polybutylene succinate, rather than as a platform molecule for the production of BDO. While these efforts establish more important examples of successful bio-based processes, we believe the path to open large chemical intermediate markets is through drop-in, low-cost alternatives via the most direct production method possible.

The International Sugar Organisation’s (ISO) first industrial bio-products market study, ‘Market Potential of Sugarcane & Beet Bio-products’,

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**Figure 2 - Succinic acid (a) & direct (b) routes to BDO**

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Acidification | BDO
---|---
BDO | Separations
Separations | BDO
Sugar | Fermentation | Acidification | Separations | Hydrogenation | BDO
Simultaneously, we are reducing by-products and gm/litre titres in 30 litre fermentations.

Our research teams have focused on increasing titre and other key metrics of bio-based chemical production. They understand the keys to viable production and recognise both our process and the organism as critical to success.

If the fermentation process can produce more quickly, that lowers the overall cost of production. Genomatica uses genetic engineering and adaptive evolution to improve the rate of production from fermentation processes.

Our research teams have focused on increasing titres as we move toward commercialisation. This spring, they achieved an important milestone with BDO's large market size, it adds, combined with Genomatica’s process, gives bio-based BDO several advantages over bio-based succinic acid, which has a significantly smaller market and requires additional conversion to create chemicals such as BDO, with yield losses and cost increases in the process.

Direct to 1,4-BDO

If a process is to produce the target chemicals directly, a microorganism must be engineered to produce the chemical and serve as an effective biocatalyst. Driving the titre, productivity and yield of the process are some of the most important metrics to produce an economically viable, sustainable chemical, and organism performance is critical to success.

If the fermentation process can produce more quickly, then we are reducing, combined with Genomatica’s process, gives bio-based BDO several advantages over bio-based succinic acid, which has a significantly smaller market and requires additional conversion to create chemicals such as BDO, with yield losses and cost increases in the process.

Unlike many organisms that make a targeted chemical as a by-product of their own growth, our technology platform allows us to link the organism’s growth to the production of the target chemical. We genetically knock out the pathways to the other by-products, so the organism must produce our target chemical to survive. All of these advances are important and our economic models estimate that our process is now at least cost-competitive with traditional methods of manufacturing.

We continue to refine the process and we are confident that we can achieve a significant cost advantage through an even higher titre and improved yield. In less than two and a half years, we moved from the first detectable quantities of BDO ever shown in a fermentation to over 80 gm/litre from raw sugar (sucrose). This threshold matches the cost of current petroleum-based BDO production, and we are well on our way to the next threshold, which will give us a strong cost advantage.

We find that traditional chemicals producers are becoming more knowledgeable and comfortable about titre and other key metrics of bio-based chemical production. They understand the keys to viable production and recognise both our progress and the power of our integrated development process.

Next steps

Looking to the future, a few more key milestones will mark the industry’s progress toward a more sustainable future. We have scaled our flagship BDO process up 100-fold, as part of the preparation for a demonstration plant in 2011, and have recently shown equivalent fermentation performance at both 30 and 3,000 litre scales.

Our initial engagements with existing BDO consumers and producers indicate that our bio-based BDO is promising from both analytical and application standpoints. Pilot-scale production and the demonstration plant will allow for further large-scale sampling and downstream conversion testing to demonstrate effective use in key derivative products, including PBT, PTMEG and TPU.

A wide range of companies are innovating to make the chemicals industry more sustainable and to allow for the use of other feedstocks. Many different bio-based applications will find a range of niche markets, but a truly widespread revolution will require lower costs and simple conversion. Direct, cost-effective production has greater potential to revolutionise the chemicals industry, expanding sustainability more quickly and bringing increased profitability at the same time.

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References:
3. wwwisosugar.org/PDF%20files/MECAS(09)17;%20MECAS(09)18;%20MECAS(09)19.pdf

Figure 3 - Lysine-based (a) & direct 6-ACA-based (b) routes to PA 6
Designing the next generation of biorefineries

Professor Franck Dumeignil of the Université Lille Nord de France presents the concept and the objectives of the EuroBioRef project*

Within a future sustainable society, biomass is expected to become one of the major renewable resources for the production of food, cattle feed, materials, chemicals, fuels, power and/or heat. To realise this vision, a combined coherent package of measures is necessary: higher overall energy efficiency, reduced raw material consumption, a decrease in the cost of goods and the framework to make the large-scale transition towards a bio-based sustainable economy possible.

Such a transition requires completely new approaches in R&D. The biological and chemical sciences will play a leading role in building the industries of the 21st century, while new synergies must be developed and established between the agricultural, biological, physical, chemical and technical sciences. This will be combined with logistics, media and IT, economy, policy and social sciences. Specific requirements will be placed on both industry and R&D with regards to the efficiency and sustainability of raw materials and product lines. The development of biorefineries is the key to initiate this new approach in R&D and will allow access to integrated production of the chemicals, materials, goods and fuels of the future.

Integrating biorefineries

The development and implementation of biorefinery processes, i.e. the sustainable processing of biomass to a spectrum of marketable products and energy, is an absolute necessity and key to meeting the vision of a bio-based economy.

This means using the available biomass as efficiently as possible and with the lowest possible environmental impact, energy consumption, manufacturing costs and CO₂ footprint. It also requires redefining transformation routes and changing product specifications according to the performances and the limitations of the new processes.

Biorefineries can use various combinations of feedstock and conversion technologies to produce a variety of products. However, most of the existing biorefinery concepts use limited feedstocks and technologies and produce only ethanol or biodiesel. They also focus essentially on producing biofuels, with the consequence of substantially reducing the added value of the biomass chain.

Economic and production advantages increase with the overall level of integration in the biorefinery. The benefits of this derive mostly from the diversification in feedstocks and marketable final products, which is missing from most current biorefinery concepts.

Continuous developments in the areas of feedstocks and conversion processes (biochemical, chemical and thermochemical), combined with their integration with powerful downstream separations, will mean more economically and environmentally sustainable options for integrated biorefineries. Such an approach will also make it possible to spread biorefineries across the whole of Europe, while adapting them to local conditions and resources.

Moreover, as different studies show, biobased industrial products can only compete through biorefinery systems where new value chains are developed and implemented. This means that new marketable products, like high-value-added chemical or biochemical products, and specific high value-added biofuels, like high-energy aviation biofuels, could enhance the viability and interest of biomass.

Such is the thinking behind the European Multilevel Integrated Biorefinery Design for Sustainable Biomass Processing (EuroBioRef) project, of which I am the co-ordinator. EuroBioRef was launched on 1 March 2010 for a duration of four years, supported by €23 million in funding from the EU’s 7th Framework Programme.

EuroBioRef deals with the entire process of biomass transformation, from fields to final commercial products. It involves 28 partners from 14 different countries into a highly collaborative work.

The 28 include producers of biomass and advanced biomass, such as lignocellulosic and oil crops, as well as suppliers of pre-treatment services, thermochemical reactions, catalysts and advanced enzymes, process designers and engineers and final chemical and biochemical producers and end-users.

Also involved are an aviation fuel refinery and a jet-engine maker, both in Poland. The sustainability of the whole project will be analysed and optimised by socioeconomic, life cycle and civil organisation analysts and project management specialists.

EuroBioRef will focus on developing and deploying a highly integrated and diversified concept with feedstocks, technologies and processes that can be bundled to facilitate and define a new interwoven value chain with integrated flexible biorefinery facilities. These will help to develop optimised production processes yielding high-value-added products that could be also adapted to large and/or dedicated small production for application in wider regions throughout Europe.

EuroBioRef concept

The watchwords of the EuroBioRef project - ‘flexibility’, ‘adaptability’ and ‘multi-dimensional integration’ - show its high ambitions. The basic concept uses a new and flexible approach of combining ‘virtual integration’ with proximity to both feedstock sources and product markets, so as to address fully:

![Figure 1 - EuroBioref concept](image-url)

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The variety of available biomass feedstocks, matched with a variety of pre-processing options to pre-treat them into viable pre-products, which are subject to logistical optimisation

- The variety of markets for bio-based products, matched with a variety of integration options to combine several conversion modules with pre-treated feedstock availability, thus avoiding excessive transportation of inputs and outputs
- The flexibility of conversion routes, which makes it possible to integrate key modules with existing facilities in order to reduce investment risks
- Proximity to both adapted feedstocks and expected markets, which can be combined with integration into existing or specifically adapted facilities, selecting suitable sites through system analysis

The ‘standard’ biorefinery concepts use massive economies of scale at one dedicated site to achieve higher performance and optimise along few product lines (e.g. liquid biofuels and electricity, or basic bio-chemicals plus ethanol or biodiesel). These are risky investments, as logistical requirements drastically increase with the size of a single plant and market dynamics may turn simplistic product output optimisation into a dead end.

To avoid these risks, the EuroBioRef approach is deliberately non-selective in nature. It achieves integration along the whole system, from feedstock through conversion to markets, thus taking into account overall logistics, feedstock and product diversification to reduce risks, and internal integration of multiple conversion routes, which are subjected to the regionally available (pre-processed) feedstocks, and the prospective (regional) markets for the possible outputs.

The concept thus adapts to regional conditions, integrating with existing infrastructure and minimises risks, both for the investors and operators and for the feedstock suppliers as well as for downstream market partners. This chain integration is fundamental to the concept and can be extended through ‘virtual integration’ along logistical chains to cover larger regions.

The process integration starts with the feedstock options, their potential pre-treatment, biochemical, chemical and thermochemical conversion, combinations of them, the use of conversion residues as inputs for other internal or external value chains (such as renewable electricity and syngas production) and output optimisation with regard to downstream markets.

This concept makes it possible to widen biorefinery implementation to the full geographical range of Europe, adapting to local conditions and resources. It also offers better opportunities to export biorefinery technology ‘packages’ to more local markets and feedstock ‘hot spots’ in developing countries and economies in transition.

Concept principles
The new proposed concept is based on several principles that must be included in the new biorefinery to bridge the gap between agriculture and the chemicals industries by providing a stream for a variety of bio-mass feedstocks and producing a menu of finished green chemical products adapted to the future sustainable bio-based European society.

More specifically, biomass raw materials can come from a large variety of sources from northern and southern Europe but also from other parts of the world. They can be sourced from agricultural and forest residues and dedicated non-food crops, which do not compete with food crops in terms of agricultural land use as they can grow on less fertile fields, with low water and fertiliser requirements.

Secondly, integrated biorefinery production should be adapted to such a variety of sustainable biomass sources in the various regional and European contexts by a combination of adapted logistics, flexible processes and socio-economic viability.

In addition, the diverse biomass sources should be pre-treated efficiently and produce a variety of fractions (cellulose, hemicellulose, lignin, refined non-edible oils, seed-meal, glycerine, fatty acids/esters, solid residues, etc.). For these, separation has to be optimised and used in the most added-value, eco-efficient and optimised way for the production of marketable products.

The development of an original variety of eco-efficient chemical, biochemical and thermochemical routes is the key for the production of marketable high-value added chemicals, biofuels, polymers and materials in a competitive way. An intelligent crossroad design can combine these routes in a way that optimises them and uses their by-products.

Moreover, the by-products of the different routes have to be reintroduced into the integrated process as reactants or energy or even transformed in products in order to obtain a zero-waste biorefinery. Finally, life cycle, economic and socio-economic analysis will ensure that the whole production chain is optimised in a sustainable way.

The EuroBioRef integrated concept (Figure 1) is thus based on a diversified, flexible and zero waste approach. This includes an integrated cluster of biotechnological and chemical industries, using a variety of different technologies to produce a wide range of valuable commodities and end-products from diverse sources of biomass pre-treated raw materials in an eco-efficient way.

Integration aspects will be treated simultaneously, making possible the integration of: different feedstocks to produce the targeted molecules; different transformation pathways to convert biofeedstocks efficiently; of bioreactions and separations in order to generate new efficient processing technologies; and, sustainable and flexible process designs that take socio-economic and regional contexts into consideration. The project will develop and then demonstrate at the industrial scale the closer to the market a socio-economic viable process of the EuroBioRef biorefinery concept.

Objectives
The aim of the EuroBioRef concept is to make possible the large-scale research, testing, optimisation and demonstration of processes in the production of a wide range of products, while using all of the fractions of the various biomasses and exploiting their potential to produce the highest added value possible in an eco-efficient and sustainable way.

The project also seeks to overcome the fragmentation of the efforts of the whole biomass value chain, notably land use, agriculture, second generation biomass treatment, thermo- and biochemical conversion, new green marketable products, bio-aviation fuels, socio-economic sustainable development.
It therefore requires greater networking, coordination and cooperation among a large variety of actors from agriculture and the biochemicals and chemicals industries, including SMEs, and the scientific biomass knowledge chain, as well as actors from sustainable development and policy rules advisors.

The new EuroBioRef design will adopt a flexible and modular process design that should be adaptable in large- and small-scale production units for installation in multiple European regions, depending on site-specific biomass resources and needs. The overall efficiency of this approach will clearly exceed existing pathways and will consider sustainable options in order to:

- Produce and use a large diversity of sustainable biomass adapted to various European regions but also for sustainable development in third countries
- Produce high energy (42 MJ/kg) bio-aviation fuels that could replace traditional fuels
- Produce multiple products (chemicals, polymers and materials) in a flexible and optimised way that takes advantage of the differences in biomass components and intermediates while maximising the value derived from the biomass feedstock
- Improve cost-efficiency by 30% through improved reaction and separation effectiveness (e.g. reduced separation and waste disposal costs), reduced capital investments (e.g. novel integrated processes and reactor concepts), improved plant and feedstock flexibility and reduced production time and logistics
- Produce zero waste and rationalise the use of raw materials, reducing feedstock consumption by at least 10%
- Reduce by 30% the energy needed to manufacture the desired products and operate specific processes using land more efficiently, using less energy-consuming reactions and producing the heat and power needed by the biorefinery
- Reduce time-to-market by 30% by developing new biorefinery manufacturing processes adapted in particular regional contexts through intelligent conceptual process design methods

**EuroBioRef approach**

The key challenge for the new biorefinery process design is its capacity to apply its potential towards significant improvement of total biomass efficiency, which will benefit producers, the environment, industry and end users. This will be obtained through the proposed multi-level integrated approach, involving a large number of key points (Figure 2).

The first is efficient and adapted biomass production for Europe and the integration of sustainable development in Third World countries. This can be achieved by several transition paths, notably improving the efficiency of using existing residual forms of biomass and sustainable improvement of the yield and quality of biomass crops, especially non-food crops.

Also vital is transversal activity to rationalise the whole process by combining assessments on the optimisation of crop culture rotation logistics with aspects of the whole biomass value chain, flexible process design and consideration of life cycle analysis, socio-economic and policy aspects.

Second generation advanced pretreatment of biomass for the sustainable production of lignocellulosic materials is also important. This involves the cross-integration of a bio-oil route with a lignocellulosic route, which offers original perspectives for cross-valorisation of derived primary products (notably cellulose and oils) including by-products (glycerine and lignin), while in parallel developing original applications inherent to each route.

Enzymatic and catalytic transformations, both homogeneous and heterogeneous, will need to be interwoven. When necessary, they will also have to be integrated with new separation techniques and/or reactor technologies.

This must yield a very large variety of products with - high value-added - niche applications and large volume applications, including bio-aviation fuels, chemicals, solvents and others that must be kept confidential for the moment. These must either have very fast access to the market, because they are substituting homologous petrochemical-derived products, or be very innovative, with high potential for larger downstream developments.

The technical and economic feasibility and efficiency of the different steps and building blocks, as well as of the majority of applications and some subprocesses, will be demonstrated in pilot plants and the units will work either in a centralised or a decentralised way. This will ensure design flexibility, adapting the most rational system to each local and global economical constraint.

Zero waste will be generated by several means: the implementation of applications for each type of by-products with reutilisation in the global loop; implicitly, by optimising the catalytic processes for reducing feedstock consumption by at least 10%.

Finally, the project involves setting up new definitions for product quality, taking into account the biomass-issued product specificity that are thus specifically suitable for biorefinery-dictated applications. Quality by design, in other words.

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James Thomson of Ceimig looks at the chemistry of the heaviest of the metallic elements

In 1803, Smithson Tennant (1761-1815) wrote "fusion with alkali of the black residue remaining after treatment of native platinum with aqua regia followed by extraction and acidification of the melt gave a pungent and peculiar smell ... from the extrication of a very volatile metal oxide, and, as this smell is one of its most distinguishing characters, I should on that account incline to call this metal Osmium".1

This moment in the history of chemical discovery recorded the first transaction of one of the most mysterious elements of the periodic table. From the colour of the metal sponge being an impressive blue, its high density, its ability to form one of the highest oxidation states of all the metals - only ruthenium and osmium give VIII oxidation states - the high volatility and toxicity of osmium tetroxide, all give this metal a unique mystique. This article will review some of the chemical properties and applications of this element and hopefully invigorate researchers to the interesting world of osmium chemistry.

The principle oxidation states of osmium are 0, II, III, IV, VI, and VIII. Its density is 4.906 g/cm³; its melting point is 40.6°C; and its boiling point is 130°C. Osmium is known to achieve the (VIII) oxidation state with fluorine or iodine and the (III) oxidation state with dioxygen and difluorine, the (IV) oxidation state with nitrogen and chlorine. Osmium tetroxide melts at 2.7°C.

Osmium tetroxide is moderately soluble in water, giving a yellow solution, this colour being consistent with the osmium (VIII) oxide structure being tetrahedral. The solubility at STP of crystalline OsO₄ in water is limited, at 7.2 wt%. Solutions are usually supplied commercially as 2 or 4 wt% but can be anything up to around 6 wt%.

Owing to the low solubility of OsO₄ in water, it is sometimes more convenient to generate it in situ. This is achieved by using potassium osmate (K₂[OsO₄(OH)₂]). In strong alkaline solutions, the yellow colour of OsO₄ gives a deep red solution from which red K₂[OsO₄(OH)₂] is formed. This is a convenient material to give osmium (VIII) oxide, in the which the solvated anion undergoes an acid-catalysed dehydration step to form OsO₄ in situ:

$$2K_2[OsO_4(OH)_2]\rightarrow 2H^+\rightarrow 2H_2OsO_4 + 4KOH \rightarrow OsO_2 + OsO_4 + 4KOH + 4H_2O$$

The OsO₄ thus generated is then available to undergo a typical Sharpless osmylation (Figure 1).

**Cis-hydroxylation of π-bonds**

A valuable use of OsO₄ solution is the oxidation of olefinic bonds. The reaction is highly selective, giving cis-hydroxylation of the π-bond to yield glycols. The demand from the pharmaceuticals and agrochemicals industries for chiral 1,2-diols requires a suitable oxidative catalyst.

The formation of 1,2-diols by OsO₄ has been extensively studied. It is unsurpassed in its ability to catalyse syn-diols from alkenes. The cis-hydroxylation of olefins is reported to be faster in the presence of pyridine as the solvent.

When OsO₄ is heated to 175°C in xylenne together with carbon monoxide at 190 bar in an autoclave, dodecacarbonyl tris-osmium (Os₃(CO)₁₂) is produced. This reaction in xylene giving Os₃(CO)₁₂ reacts in situ with triphenylphosphine and is a convenient route to tris(Os₃(CO)₁₂)(PPh₃)₃. The supercritical CO₂ has been used for the dihydroxylation of olefins in the presence of ionic liquids. This procedure was used to prepare chiral vicinal diols as precursors for biological active intermediates and ee's of 90-97 were achieved using N-methylmorpholine oxide as a co-oxidant with potassium permanganate. The mechanism is consistent with the addition of O=Os=O to the C=C bond. The hydroxylation reaction of olefins is catalytic when OsO₄ is used in the presence of hydrogen peroxide or perchlorate ion. The oxidation of olefins to 1,2-diols is by a two step sequence: epoxidation of an olefin followed by peroxide or peracetic acid. The hydrosis of the resulting peroxide.

The osmium-catalysed route to 1,2-diols is the most efficient, reliable and atom-efficient method.

OsO₄ is used to hydroxylate the olefin to the diol catalytically in the presence of a secondary oxidant (e.g. hydrogen peroxide). Studies of the reaction as a function of pH have shown that the oxidative reaction is better performed in acidic solutions and citric acid performs well as a suitable pH buffer. Recent work has also shown that the addition of co-catalysts such as N-methylmorpholine (NMO) together with flavin markedly improves the re-oxidative properties, promoting OsVIII back to OsVIII by the hydrogen peroxide-catalysed osmylation of OsO₄.

Using ligands such as hydroquinidine 1,4-phthalazinediyldi-(DHQD)₂-PYR, (DHQD)₂-PHAL, (DHQD)₂-AQN and (DHQD)₂-PHAL gave high ee values in conjunction with osmium (VIII) oxide.

**Microencapsulation of OsO₄**

The high toxicity associated with OsO₄ in conjunction with its volatility is particularly important for its use in large-scale processes - hence the development of a microencapsulation route using an insoluble polymer-supported osmylate beads, together with a suitable solvent.

This procedure involves the immobilisation of OsO₄ onto a polystyrene-based polymer. When...
Osmium chemistry

Biochemistry applications

Osmium (VIII) oxide as a 2 wt% solution in aqueous form is used for fixing and staining cell and biological tissue for use in microscopy and electron microscopy studies. The fixation of cells by osmium (VIII) tetroxide is a non-destructive method to lock the cellular organisation of the biological material.

The staining method involves the pre-treatment of the biological material with a suitable aldehyde followed by immersing the treated material in 2 wt% OsO4 solution. Alternatively the biological material may be exposed to the vapours of osmium tetroxide following by washing, staining, embedding the biological material in resin and slicing, followed by microscopy examination. The staining process involves attacking the lipid and unsaturated bonds contained in the lipid material, forming osmate (VI) esters and/or dioxo bridges.

Osmium (VIII) oxide is also used in glucose sensing. During the late 1980s, the development of mediator-coated electrodes led to an amperometric approach to the determination of concentrations of glucose in biological fluids.

The sensor measures the transfer of electrons between the enzyme and the electrode through the use of a multivalent co-ordination complex known as a mediator. Fluoranil, chloroanil, polyvinylalcohol and ferrocene are common and available mediator complexes. The efficiency and speed of glucose sensing depends on the mediator used.

Co-ordination complexes of transition metal cations, usually iron, ruthenium or vanadium, are used as the variable reduction/oxidation electron centres. Some of the mediators are volatile, photoactive, reactive to molecular oxygen and subject to hydrolysis, such as ferrocene. The photoactivity and hydrolytic nature of ferrocene results in the degradation of the material, so suitable storage criterion is a pre-requisite for long term use.

Osmium-bis-(N,N'-1,2-bipyrindyl-N'-pyridine-4-yl-methyl-1,6-pyrrrole-1-yl-hexylamine dichloride

and analogous osmium-pyridyl complexes have been shown to be suitable electron transfer reagents in oxygen insensitive glucose biosensors. The bipyrindyl osmium complex is prepared from potassium hexachloroosmate and the entrapped oxygen induces a glucose dehydrogenase reaction. Tris(4,4'-dihydroxy-2,2'-bipyridine) osmium (Figure 2a) is chemically stable, yet reactive to glucose reduction. It gives an electrode response of +150 mV (at pH 1, calomel reference electrode) and -1V at pH 13. Investigations have led to the preparation of (4,4'-dimethoxy-2,2'-bipyridine) osmium (Figure 2b), while bis(4,4'-dimethyl-2,2'-bipyridine) derivatives of osmium have been used as mediators, resulting in good glucose potential.

Electronic applications

Osmium (II) complexes have been shown to be efficient organic light-emitting diodes (OLEDs). Chelating 3-(trifluoromethyl)-5-12-2pyridylpyrazole or the corresponding 3-(tert-butyl triazole) with the osmium (II) cation in the equatorial positions and phosphine donors at the axial locations balances the overall charge on the molecule. Recently, phosphine ligation has been replaced with methyl diphenyl phosphine and the results show high luminescence properties in methylene chloride at h max values of 617, 632 and 649 nm. This osmium (II) phosphor is a red emitter and has received intensive study.

The preparation of these red-emitting OLEDs followed the preparative methods described for the blue-emitting carbonyl analogues, 3-trifluoromethyl-5-12-2pyridylpyrazole or 3-tert-butyl triazole osmium (II) dicarbonyl. These blue emitters have the carbonyl ligands in an axial and equatorial position respectively of the octahedral structure.

The h max for the carbonyl osmium complexes described is about 340 nm and this is attributed to the MLCT properties of the complex. These carbonyl osmium (II) OLEDs show a depreciation in the activity of the OLED as a function of time, owing to the cationic nature of the molecular structure.

The loss in activity has been attributed to a low energy bonding between the osmium (II) centre and the counterions within the crystalline matrix - hence the synthesis of the phosphor analogues where the osmium (II) phosphor complex is in a neutral charge state. This neutral charge over the molecule appears to stabilise the phosphor from deactivation.

These studies show that the emission spectra from carbonyl osmium complexes are sensitive to the coordination ligands associated with the axial or equatorial positions of the osmium octahedra. This work offers great interest in the study of OLED devices and the structural coordination chemistry of carbonyl osmium complexes.

Homogeneous catalysis

K2[OsO4(OH)3] catalysed reactions with phtha-lazine ligands have proved surprisingly efficient in the preparation of ee’s of >90 in olefinic dihydroxylation. A mixture of K2[OsO4(OH)3], potassium ferricyanide and potassium carbonate was mixed with 1,4 bis-(9-O-dihydroquinolyl)phthalazine (IDHOD2PHAL) or 1,4 bis-(9-O-dihydroquinolyl)phthalazine (IDHQ2PHAL). The OsO4 shows an ability to turn over 400 olefin molecules/OsO4 to give extremely high ee values.

Osmium co-ordination compounds have found uses in hydride shift catalysis by phosphorus co-ordination complexes. Phosphino-catalyzed hydridocarbonyl osmium (II) complexes like OsHCl(CO)(PPh3)3 have been shown to be active by a pseudo-first order law in the homogeneous hydrogenation of trans-cinnamaldehyde using isopropanol as the hydrogen donor.

These co-ordination complexes of osmium have also been shown to be active by a pseudo-first order rate law in the homogeneous hydrogenation of propionaldehyde to propan-1-ol in toluene at 110°C under 20 bar dihydrogen.

Comparative analysis of ligand effects have shown PPh2PFe(C5H4-η5)PPh > PPh2PCH2J2PPh2 > PPh2PCH2J2PPh2 > PPh2PCH2J2PPh2. The results indicate that the presence of the chelating ring results in a higher catalytic performance than the carbonyl complex OsHCl(CO)(PPh3)3.

Applications are also found in nitrogen co-ordination. In aqueous solutions with pH of >8, macrocyclic amine complexes of osmium (trans-I0sV1, 1,4,8,11-tetra-methyl-1,4,8,11-tetraazacyclotetradecane)O32+ undergoing a reversible one-electron oxidation to osmium (trans-I0sV1, 1,4,8,11-tetra-methyl-1,4,8,11-tetraazacyclotetradecane)O32+ in acidic solutions the electrochemical reduction of osmium (trans-I0sV1, 1,4,8,11-tetra-methyl-1,4,8,11-tetraazacyclotetradecane)O32+ is a reversible three-electron three-proton transfer in the activity of the OLED as a function of time, owing to the cationic nature of the molecular structure.
process. These amine complexes of osmium seem inert to ligand exchange processes.

Heterogeneous catalysis

Jacobs made the first reports of a heterogeneous diolation reaction, describing what was effectively a reversed heterogeneous catalysis procedure. The group immobilised a tetraolefin to a silica support via covalent bonds. This heterogeneous phase was then reacted with OsO₄ solution to give a osmyl diolate ester that is hence fixed to the silica support.

The catalytic process then takes place at the co-ordinatively unsaturated osmium environments. Next, the group demonstrated the feasibility of this procedure by the diolation of mono and disubstitution of aromatic olefins using NMO as the co-oxidant.

Choudary developed this approach by designing an ion-exchange column where the osmium was immobilised onto silica supported on an organic resin. The work demonstrated the asymmetric dihydroxylation of trans-stilbene with an ee of about 96%, in which the reactivity was superior to that of a potassium osmate benchmark. Choudary prepared a silica gel-supported titanium silicate phase, upon which (DHQD)₂PHAL-OsO₄ reacted with an appropriate alkaloid. NMO was used as the co-oxidant.

References:
1. Smithson Tennant, Phil. Trans. 1804, 94, 411
2. W.P. Griffiths, Platinum Metals, Rev. 1974, 18, 94-96
26. The work demonstrated the asymmetric dihydroxylation of trans-stilbene with an ee of about 96%, in which the reactivity was superior to that of a potassium osmate benchmark. Choudary prepared a silica gel-supported titanium silicate phase, upon which (DHQD)₂PHAL-OsO₄ reacted with an appropriate alkaloid. NMO was used as the co-oxidant.

Immobilation of the reactant has also been shown to give good results for the asymmetric aminohydroxylation of olefins. This approach also anchors the ligand onto an insoluble polymer (PEG) to which cinchona-derived alkaloids, 1,4 bis-O-dihydroquinindinylphthalazine [(DHQD)₂PHAL] or 1,4 bis-O-dihydroquininyphthalazine (IDHQ)₂PHAL, were bonded, where N-chlorocarbamate was used under Sharpless reaction conditions. The reaction gives α-amino alcohols with high ee values.

*Also contributing were M.J. Duncan & C.A. McGowan, also of Ceimig. The author would like to thank colleagues at Ceimig for their respective support and assistance in the preparation of a wide range of osmium complexes and in particular the preparation of osmium (VIII) oxide crystal.
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