Playing with corn

Dr Roger Herger and **Dr Ivo Hubacek** of **Dottikon Exclusive Synthesis** look at isosorbide as a renewable platform for novel applications

Biobased plastics from renewable sources are no longer an oxymoron. In fact, a recent study suggested the production volume of bioplastics will nearly quintuple from 1.2 to 5.8 million tonnes/year by 2016. Growth will be mainly driven by non-biodegradable plastics that are based on renewable raw materials and are used as alternatives to bulk plastics like PE or PET.

In addition, new bio-monomer based plastics have been in the focus of recent R&D work. In this context, isosorbide is a paradigm-shifting renewable chemical platform for novel and green applications, not only in biobased polymer materials but also in a variety of other applications within different industries.

The first part of this article focuses on the versatile chemical and physical properties of the isosorbide building block and applications, while the second will shed light on the needs across different markets by comparing the requirements of the pharmaceuticals and material performance-oriented industries. We also outline the current paradigm change necessary for innovators to establish strategic chemical development and manufacturing partnerships.

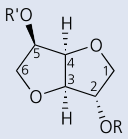
Production & applications

The production of isosorbide from biomass is of economic interest as source materials like straw or wood contain some 35-50% cellulose, in addition to hemicellulose and lignin. It also offers the potential not to compete with food production. The multi-step conversion process from biomass to isosorbide contains several biotechnological process steps, including depolymerisation, hydrogenation and dehydration. Thus, a variety of new companies are financed and formed to commercialise processes to produce chemicals from carbohydrates rather than from fossil resources.

Isosorbide (1,4:3,6-dianhydro-D-sorbitol) is a V-shaped bicyclic intramolecular diether with two secondary hydroxyl groups in the 2- and 5-positions (Figure 1). It has been suggested that the 5-hydroxyl group in *endo* configuration forms intramolecular hydrogen bonds, leading to higher reactivity because of the more nucleophilic character of the oxygen at the 5-position.

Choosing different reaction conditions, the less sterically hindered *exo* 2-hydroxyl group may be more reactive; certainly the two secondary hydroxyl groups are not of equivalent reactivity. The two other isomers, isomannide (2/5 = *endo*/*endo*) and isoidide (2/5 = *exo*/*exo*) are less selective in terms of reactivity and not directly accessible via plant biomass, respectively, explaining the interest in isosorbide as a renewable chemical to study functionalisation and use as monomer and building block.

Figure 1 - Isosorbide & derivatives

Structure	R/R'	Application
	H	• Replacement for diol monomers (e.g. ethylene glycol) • Replacement for bisphenol A • New polyamides and polyimides • Chiral auxiliary
	Ethers	• Pharmaceutical, non-toxic solvent • Cosmetics • High boiling (co-)solvent • Phase transfer reagent • Energy storage devices • Surfactants and rheology design • Fuel additives • Hydrotopes and coalescents
	Alkyl/aryl esters	• Plasticisers • Solvents • Fuel additives • Tensides • Chiral building blocks (monoesters) • Chiral dopants • UV stabilisers
	Sulphates or phosphates	• Tensides for personal care • Foamers

Isosorbide applications

Professor Mike Jaffe of the New Jersey Institute of Technology has investigated the utility of isosorbide in thermoplastics and thermosets. Proprietary isosorbide polyester technology, based on stereochemical and stoichiometric control, allows the synthesis of new, semi-crystalline homo- and co-polyesters with improved processability and thermal stability.

Controlling the hydrophilicity of isosorbide derivatives allows the high water uptake of isosorbide ether compounds to be overcome, leading to bisphenol A-free epoxides with acceptable Tg and mechanical properties.

Jaffe therefore believes that isosorbide derivatives will become a significant component of thermoplastic and thermoset resins, bringing both improved performance and cost-effectiveness to many polymer applications.

Isosorbide and its functionalised derivatives have a broad spectrum of potential applications, according to Professor Mike Jaffe of the New Jersey Insititute of Technology (*see box story*). These include use as a monomer (co-)building block in polymers, partially replacing diols such as ethylene glycol or bisphenol A. Polyisosorbide terephthalates and polyethylene-co-isosorbide terephthalates are of particular technological interest due to the high glass transition temperature (Tg, i.e. the temperature of transition from an amorphous glassy and brittle to a molten or rubber-like state). These enhanced thermal properties increasingly find new applications in friction bearings, rollers, gaskets, etc. in the engineering, textile and automotive industries.

Other examples include heat- and shock-resistant materials for glass or aerospace applications. Moreover, the addition of isosorbide as (co-)monomer lowers the polymer degradation rate $dX/dt = f(X)k(T)$ defined by Friedman's model, where $f(X)$ represents the net result of a series of elementary degradation steps and their individual activation energies, and $k(T)$ is the Arrhenius rate constant.

Life science uses

An isosorbide derivative, the alkyl ether dimethyl isosorbide (DMI), has recently attracted significant interest due to its versatility in pharmaceutical, cosmetic and technical applications, such as surfactants, fuel additives and energy storage devices. Moreover, the ongoing miniaturisation of electronic devices offers new applications for DMI in the production of semiconductors.

For life science purposes, DMI is increasingly being used as a non-toxic (co-)solvent, for instance in topical applications to transport active ingredients through the dermis into living tissue. It is also under investigation as solvent for injectable formulations by several research groups.

This wide range of applications is partly due to DMI's high chemical and physical versatility as an amphiphilic, polar, aprotic H-bridge acceptor molecule. Its commercial availability in high volumes and meeting the highest quality demands, i.e. >99.5% purities, further boosts the use of the molecule made from renewable sources. When these factors meet, widespread use of DMI as a performance chemical in advanced life science applications becomes economically interesting.

Figure 2a-b shows the effect of Dottisol*, Dottikon's proprietary DMI when used in crop science applications in cuticular leaf penetration tests. These tests used astomatous tomato cuticles at low and high relative humidity (RH) and with $CaCl_2$ at concentrations of

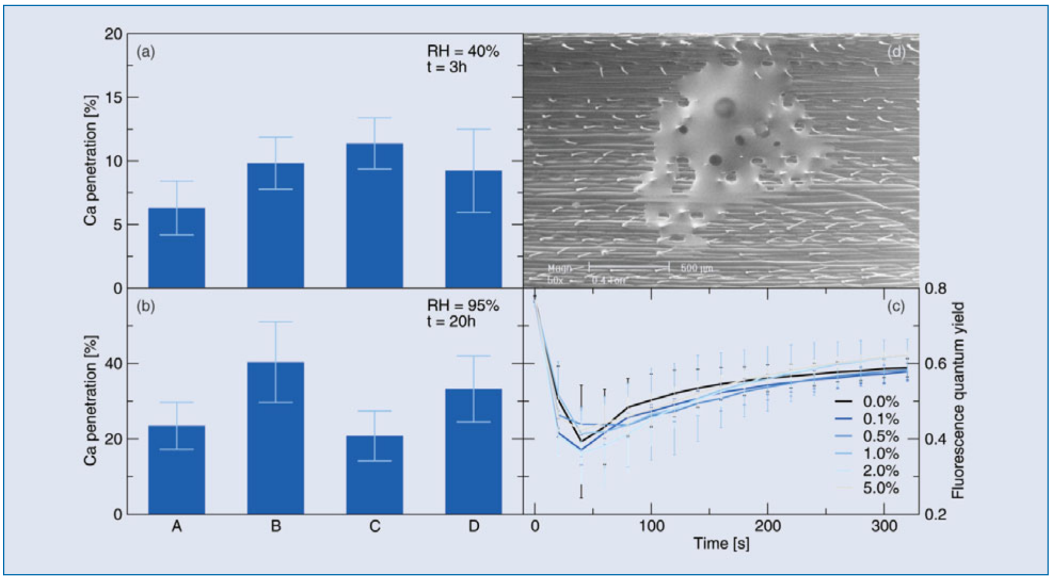


Figure 2 - Cuticular leaf penetration, surface & fluorescence tests

1.0% and 1.5% in water as a hydrophile model substance respectively.

Comparison of the $CaCl_2/H_20$ reference (**A**) with 0.5% Dottisol (**B**), 0.05% organomodified trisiloxane (**C**, the current industry standard) and a wax-like, long-chain aliphatic adjuvant (**D**) showed Dottisol to be among the best-in-class penetration promoter both at low and high RH, based on statistical analysis by the Duncan multiple range test ($p \leq 0.05$).

Moreover, organomodified trisiloxanes show phytotoxicity at concentrations of around 0.05% or lower and wax-like adjuvants often cannot interact effectively with new generations of biodegradable, biocompatible and highly active agrochemical ingredients. Additional measurements of the surface tension illustrate the absence of stomata penetration for Dottisol-containing spray systems, indicating that Dottisol is more suitable for topical crop applications.

Figure 2c shows the results of the chlorophyll fluorescence measurements that are typically used to measure the stress on a plant organism. The quantum yield of fluorescence increases under stress induced by spray applications, while the plant decreases its photosynthesis rate.

For different concentrations of Dottisol up to 5%, however, no such effect can be observed by using pulse-amplitude modulated chlorophyll fluorescence on leaves of sweet pepper. In addition, scanning electron micrographs confirm the close interaction of Dottisol and the plant surfaces (Figure 2d). Details in the micrographs indicate that Dottisol might retain a higher content of water at the interface of the spray droplet.

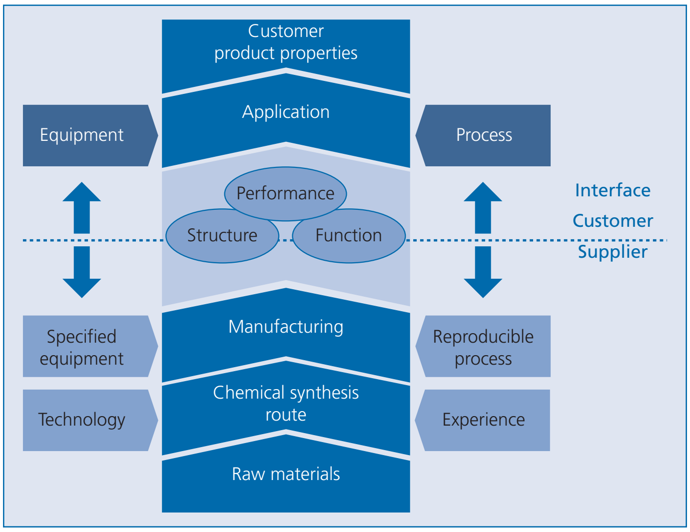


Figure 3 - Chemical product process design paradigm

Finding partners

As shown above, there are many applications where isosorbide and its derivatives are of potential technological interest. The challenge is to find the proverbial needle in the haystack. In order to do this, exchange is needed among a broad spectrum of collaboration partners, ranging from the R&D and technical units of chemical manufacturers to existing and future customers and application-oriented departments at universities and research institutes.

It needs to be kept in mind that, however difficult it is to find the needle in the haystack, it is even more challenging subsequently to develop the application to resolve technological problems. Today, highly specialised business partners interact and it is no longer obvious where the interface for development between the two lies.

Figure 3 shows this paradigm change for suppliers of traditional actives and intermediates to become strategic development and manufacturing partners. For pharmaceutical applications, the drugs company provides a chemical structure that has already proved to have a physiological effect in the patient's body. Ideally, it has also initiated process development work to scale up from lab to commercial quantities. It is aware of the chemistry and the functionalisation of the compound.

Well-defined specifications are available to meet performance requirements. A custom manufacturer supplies raw materials, challenges and develops the synthesis route and uses technology and its experience in validated equipment to develop a reproducible process for multi-tonne quantities. In short, the interface is well defined below the chemical layer.

However, customers outside the pharmaceuticals industry experience increasing quality demands and enhanced performance requirements as well. Hence, they need a well-defined and qualified production environment, too. They both need a strategic partner for product development, launch, manufacturing and life-cycle management.

In the case of material performance-oriented players, the interface gets fuzzier. Instead of a defined functionality, chemical structure and specifications, the customer is looking for a product performance because he has a specific application in mind. He may no longer have the in-depth chemical expertise in-house assisting him in the chemical development of his product.

In fact, many innovators are start-ups and have limited chemical experience. That is why they need a reliable, flexible, strategic and highly interactive development and manufacturing partner to help them improve product or application performance rapidly and to launch new products. This way, the tailor-made chemistry delivers the performance needed.

Where the interface actually lies is no longer important, as the product is developed jointly by the two partnering companies. This joint venture attitude of two production partners - as opposed to previous finance-production ventures - enables innovative new applications to be developed with chemicals from renewable or other sources.

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