Welcome to this edition of the Camida review which is brought to you by the Technical Sourcing Team at Camida. Sourcing has long been recognised by the Chemical & Pharmaceutical industries as a critical step in effective procurement of raw materials and all of us that work in the area know there are no “magical” solutions to the problems facing our industries in these unprecedented times.

The Pharmaceuticals sector is currently facing one of the biggest waves of drug patent expirations in history, a phenomenon we have come to know as the “patent cliff” and companies are fighting fierce competition to protect their markets as a significant number of the top-selling drugs of all time reach the end of their period of exclusivity. As a result R&D groups are looking to alternative Drug routes and second generation drugs, and Purchasing departments are focussing on Raw Material Sources. Now, more than ever before, an expert Sourcing partner is vital to the industry.

Camida’s Sourcing Department, as managed by Lisa Daniels, is an integral part of the customer service offered to our customers. Our team consists of Technical Sourcing Specialists Eileen McAree, Siobhan Clarke, Aoife Moloney, Hannah Gilligan and newest recruit Alice O’Regan. As well as working with our Pharma & Life Science customers we also work very closely with customers in the Industrial and Ingredient sectors on a daily basis and we have built up expertise and knowledge pertinent to each respective industry sector. We receive and work on over 3,000 enquiries per year from our customers and while cost is often a fundamental concern for companies it is frequently a technical or logistical aspect that is the driving factor behind our customer enquiries.

We invite enquiries from all industry sectors: if you require a cost-of-goods calculation for a new manufacturing route, need to assess alternative sources for your current Raw materials, or if you have a technical or logistical issue that your current source cannot accommodate please send your query to Camida and we’ll dedicate our time and experience to offering a solution.

You never know we might just be able to work a little magic too!

THE SOURCING TEAM!
Vitride - sodium dihydrobis (2-methoxyethoxy) aluminate, the structure of which is shown below - is a reducing agent that is an excellent substitute for Lithium Aluminum Hydride (LAH) and related hydrides such as Diisobutyl Aluminum Hydride (DiBAl). It is chemically equivalent to LAH but does not share the same drawbacks as LAH, such as a pyrophoric nature, a short shelf life and limited solubility. Moreover, it has similar flexibility in reducing power to that of DiBAl.

**Vitride:**
- Is thermally stable to 170°C
- Does not crystallise even at -60°C
- Is not oxygen sensitive
- Is not pyrophoric in nature
- Has found use in many APIs in particular in Generic markets
- Has use in many Flavour and Fragrance materials

Carbonyl, carboxyl (eg ester), amide, alkene, alkyne, nitrile and a number of other functional groups are reduced with Vitride in aprotic solvents, (for full details see contact below).

Solvent polarity generally does not affect the final yield. The solubility of the organic compound is not a necessity in most cases, and reductions can be carried out as heterogeneous reactions as well as the expected homogeneous reactions.

Unlike other hydrides, Vitride almost always forms a complex, or intermediate, which is exceptionally soluble. Thus, many compounds insoluble in toluene are easily reduced in this solvent.

The sequence of addition is an important factor, sometimes determining directly the extent of reduction and thus the type of product obtained.

There are two logical modes of addition:

a) Normal addition, in which the organic compound is added into an excess of Vitride and an excess of active hydrogen is maintained, which means the reduction will proceed as far as it can – so this mode is useful for reducing amides to amines or esters to alcohols. Examples are shown:

b) Inverse addition, where Vitride is added into the organic compound and an excess of active hydrogen is avoided; this gives kinetic control and the most reactive functionality is reduced first – so this mode is useful for reducing esters to aldehydes or lactones to lactols as is required for Gemcitabine shown:

Vitride is used extensively in the pharmaceutical industry as a replacement for LAH, particularly in India for generic products, requiring a differing range of functional groups to be reduced. Vertellus® supplies Vitride in several different pack sizes, from 1kg Lab samples, to 18kg packs for small scale trials to 200kgs drums, or even 1000kgs pressurised containers.

Vertellus® offers a comprehensive supply chain management with stocks around the world and offers a full technical back up and advice and technical packages for many of the reduction steps in the products in which it is used. We have solved many customer selectivity issues based on our intimate knowledge and understanding of this versatile metal hydride reducing agent.

Typical products where Vitride is used include many APIs in the pharmaceutical industry, many products in F&F and some Agrochemicals as well as an anionic polymerisation initiator in polyamide to give higher molecular weight and a greater degree of crystallinity resulting in higher strength.

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For further information on Vitride by Vertellus, please contact Camida
+353 52 6125455 or info@camida.com.
Camida are pleased to announce our recent collaboration with NCEC Part of Ricardo – AEA who will provide Camida’s Emergency Response Service: Carechem 24. Carechem 24 is a multilingual telephone advice service providing access to a team of trained responders 24 hours a day, 365 days a year and will provide emergency product support to our customers all over the world in the event of a Hazmat incident.

Camida are in the process of updating all relevant documents. In the interim period, existing Camida ERS numbers are also operational and will connect you to the Carechem team.

Camida Emergency Response
+ 44 1865 407333 (Carechem 24)

Improved Document Availability
Camida have developed a secure web based storage and retrieval system for documents.

This means each customer can have dedicated secure access to documents relating to their business with Camida.

This may include, as appropriate, Specifications, Safety Data Sheets, Certificates of Analysis, BSE/TSE Certificates.

If interested, please contact Deirdre McGrath at Camida to discuss further +353 52 6125455 or deirdre.mcgrath@camida.com.

Industry / Academia Collaboration
My name is Amanda Kunaka, I am a third year student studying Chemical and Pharmaceutical Sciences in DCU. I am currently doing my INTRA placement at Camida. The INTRA (INtegrated TRAining) Work Placement programme is an accredited and highly valued part of student learning at DCU. DCU works in partnership with organisations to create positions and relationships that will benefit both the student and the organisation.

I have been working here in Camida for 6 months in the sourcing department, working primarily with John McNeille, Senior Sales Manager and I have really enjoyed my time here.

INTRA student Amanda Kunaka and DCU President Professor Brian MacCraith at recent PharmaChemical Ireland dinner held in Westin Hotel, Dublin.
TETRAKIS DMA4B2
A New Borylation Reagent

Transition metal catalyzed C-C coupling reactions are some of the most versatile transformations in synthetic organic chemistry. Among them, the Suzuki Reaction of a boronic acid and an aryl or vinyl halide sticks out as being particularly regio- and stereoselective as well as tolerating a broad range of functional groups.

While standard boronic acid building block can be synthesised by an organometallic route (fig. 1),

more advanced building blocks call for more advanced boronation reagents (fig. 2).

While reagents like Pinacolborane (PINB) or Bis-pinacolatodiboron (Pin2B2) extend the toolkit of the organic chemist significantly, there is still a need for more flexible and capable boronation reagents. Particularly, the hydrolysis of the pinacol ester of the boronic acid prior to the coupling step can be cumbersome and often leads to poor yields and/or by-product formation. Also, PINB and Pin2B2 are limited to electron poor and electron rich aromatic systems, respectively. Overall, there is limited flexibility in optimising boronation reactions.

This limited flexibility can be overcome by the use of Tetrakis-dimethylamino-diboron (DMA4B2), BASF’s new boronation reagent. Other than the previously mentioned reagents, DMA4B2 offers full flexibility not only with respect to solvents suitable but also with respect to the diol used (fig. 3).

Most noteworthy, the boronation reagent is generated in situ without the need for further purification. Dimethylamine generated in the process generally doesn’t interfere with the coupling reaction and can be removed, e.g. by a gentle purge of nitrogen. Another feature of DMA42 is the possibility of running borylation reactions in high concentrations or even solventless, thus increasing reactor output significantly.

Overall, BASF’s new product DMA4B2 stands out from existing reagents due to the additional flexibility it gives by the free choice of diol. Also, it is suitable for both electron rich and electron poor reaction partners, unlike PINB and Pin2B2. What is more, being a liquid, DMA4B2 can be handled much more easily on a technical scale, offering the possibility to run reactions without any solvent at all.

For further information on DMA4B2 by BASF, please contact Camida
+353 52 6125455 or info@camida.com.
CAMIDA FAMILY DAY

Fun for the kids (of all ages)

Camida Families and Friends enjoying a recent visit from Mickey and Minnie Mouse.
Hot Diggety Dog!

GUESS WHO’S TURNING 25?

25th Birthday Greetings will soon be heard in Clonmel as Camida will celebrate a landmark Birthday,
More to follow ……

CONGRATULATIONS!

… to Orla Heenan on her gorgeous new arrival and a big Camida Welcome to baby Ayana

CLONMEL JUNCTION FESTIVAL

The Animals and Children took to the Streets

1927 Theatre Company performing our sponsored show ‘The Animals and Children took to the Streets’ at the Junction Festival this year
BASFs NMP Life Science can offer higher yields and efficiencies in the manufacture of pharmaceutical peptides and membranes

N-Methylpyrrolidone (NMP) is a high boiling, non-corrosive, aprotic and highly polar solvent with excellent dissolving properties and high chemical stability. It is often used as an inert reaction medium in the synthesis of organic intermediates and building blocks for pharmaceuticals. In addition, NMP is completely miscible with water and many organic solvents. This property is particularly useful when a solubiliser is sought for non-polar organic compounds in water-based formulations. This is the basis for the use of NMP as reaction medium for the synthesis of active ingredients for crop protection and pharmaceutical applications and in the manufacture of synthetic membranes. Other industrial applications include the coatings sector and industrial cleaning.

NMP contains trace amounts of amines as a by-product of the production process. Although they are typically in the ppm range, even traces of amines can have an adverse effect in certain applications. NMP Life Science was specially designed for life science applications where a greatly reduced amine content leads to substantial improvements in the synthesis or production process. Significant advantages have been demonstrated, particularly in the synthesis of therapeutically active peptides and the production of high-performance filtration membranes for blood dialysis and water purification.

In solid-phase peptide synthesis (SPPS) a N-protected amino acid derivative is coupled to the reactive N-terminal amino-group of a peptide which is covalently bound to a solid polymer support. NMP is efficiently used in this process to rinse off excess reagents and synthesis by-products not bound to the support after each coupling cycle on the growing peptide chain. Hence, NMP is the solvent of choice for rinsing and filtration steps in SPPS due to its unique solvent characteristics, polarity and its favorable effect on the swelling behavior of the solid support. Amine impurities in NMP are critical because of their side reactions with the coupling reagent, inhibiting the growth of the peptide chain and increasing the overall consumption of the coupling reagent. Thus, BASF’s amine reduced NMP Life Science ensures higher yields in SPPS, lower consumption of the expensive coupling reagent and simpler purification of the final peptide. BASF has proven that NMP Life Science improves the yield of hydrophobic therapeutically active peptides by up to 15% compared to conventional NMP grades and by 5% for semi-hydrophobic peptides.

Another field of application for NMP Life Science is the phase inversion process for the production of synthetic membranes for ultra- and nanofiltration which are used for blood dialysis or the purification of water. In the continuous production process using polysulfone, polyethersulfone and polyvinylpyrrolidone out of BASF’s broad portfolio of polymers, the exceptionally low amine content of NMP Life Science has proven to be advantageous for the swelling behavior of the membrane polymers and the resulting pore distribution. The recovery of the polar solvent after the phase separation step between water and the polymer-rich phase is an important issue during production and the low amine content has shown a positive effect on the recycling efficiency and thus the cost-efficiency of the entire production process.

BASF’s patented high-purity solvent NMP Life Science is due to its elaborate production process characterised by low moisture content (< 0.03%), more than ten times lower amine level (< 1 ppm monomethylamine, dimethylamine and trimethylamine) compared to conventional NMP grades and low pH-value (6 – 8 in a 10% solution). Its unique product quality has advantages for the manufacture of membrane films and pharmaceuticals, like therapeutically active peptides, by improving the recycling efficiency and the product yield. A preliminary purification step of NMP Life Science is unnecessary and thus saves time and costs, and this NMP grade significantly contributes to the quality assurance of a chemical synthesis process.

BASF’s Intermediates portfolio also includes other solvents like tetrahydrofuran (THF), dimethylformamide (DMF) and N,N-dimethylacetamide (DMAC) as well as recently added glymes and 1,3-dioxolane. Speciality bases, such as pharma-grade diazabicycloundecene (DBU P), Hünig’s base and various amines complement BASF’s broad pharma portfolio as do chiral amines and amino alcohols combined under the ChiPros® brand.

For further information on NMP by BASF, please contact Camida +353 52 6125455 or info@camida.com.