Issue 4 | October 2013

Key Organics Newsletter

Chemistry | Innovation | Quality

On 1st September 2013 we announced our new alliance with Advanced Molecular Technologies Pty Ltd., (AMT) based in Melbourne, Australia. AMT have appointed Key Organics as their exclusive European partner for the supply of an increasingly large range of organoboron and organosilicon products including the highly versatile HOMSi® reagents that we have profiled herein. Both companies will continue to collaborate in order to further grow their differentiated technology and service offerings to customers within the life sciences sector.

We are seeing increased traffic and gaining positive feedback from users on our new website that allows customers to quickly search our growing BIONET collection and expediently complete purchases for next-day delivery. See www.keyorganics.net for further details. We also interview Ian Bennington who recently joined Key Organics as a senior analyst and is currently in the process of unpacking his new gas chromatograph!

BIONET | Innovative New Products for R&D and beyond...

Now available at the click of a mouse!

Our new BIONET shop (*Figure 1*) has been designed to facilitate ease of information access, increased functionality and expedient BIONET product purchasing/transaction. We continue to add hundreds of new products each month to our BIONET collection that now contains over 65,000 and growing stock items of intermediates, fragments, biochemicals and screening compounds. These can be downloaded as an SD or PDF, alternatively we can send monthly updates directly to you via email following the registration of your details with us.

Benefits & Advantages of Buying Direct

At Key Organics we manufacture over 90% of our 65,000 and growing, BIONET products! Buying direct from us can save you up to 150% on agent and re-seller prices; we provide an assured quality guarantee, next-day delivery and excellent front, and back-end customer support.

All products are available in a variety of pack sizes and we can offer many products at development scale using our new scale-up facility. cGMP material can be supplied through our partnership network where we have access to facilities in the UK, mainland Europe, North America, Asia and Australasia.

Figure 1. Our New BIONET shop

New & Versatile Organoboron and Organosilicon Compounds

Following our recent agreement with Advanced Molecular Technologies Pty Ltd., (AMT) of Melbourne, Australia, we are proud to announce the addition to our catalogue of a range of organoboron and organosilicon compounds, and "click chemistry" building blocks. The Suzuki and popular Hiyama coupling reactions being the mainstay of today's synthetic chemistry, demand for evermore diverse building blocks containing active boron and silicon functionality is increasing. Likewise, the Huisgen 1,3-dipolar cycloaddition of azides and alkynes (click chemistry) is a mild and high-yielding route to 1,2,3-triazoles, a structural feature familiar to synthetic and medicinal chemists. Consequently our fast growing range of azide and alkyne building blocks suitable for click chemistry (many of which possess dual functionality allowing further elaboration beyond the click step) will be of interest to our customers. Key Organics is now able to supply these compounds expediently to customers within Europe with next-day delivery; in addition we are able to offer a wide range of chemistry services to downstream products, process-related impurities and degradation products that is supported by our state-of-the-art analytical chemistry capability.

The palladium-catalysed Hiyama coupling reaction is a carbon-carbon bond forming reaction between organosilicons and organohalides (*Figure 2*), similar to the better-known Suzuki-Miyaura reaction. Dimethylsilanols react with aryl halides under mild conditions affording the desired products in high yields. Dimethylsilanols are prone to dehydration and formation of disiloxanes under unfavourable storage conditions. Sodium and potassium salts of dimethylsilanols are immune to this undesired process, are excellent Hiyama coupling partners, and do not require additional base to be used in the reaction.

Figure 2. Examples of the classical Hiyama reaction

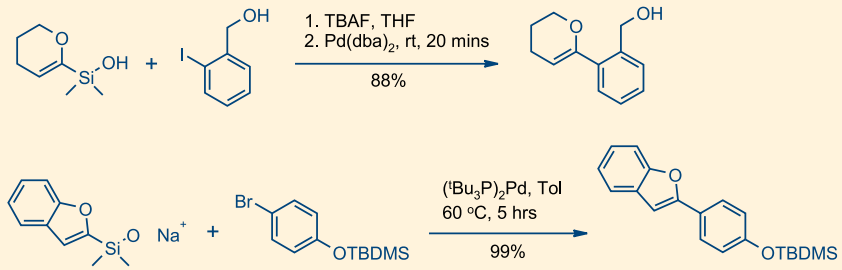
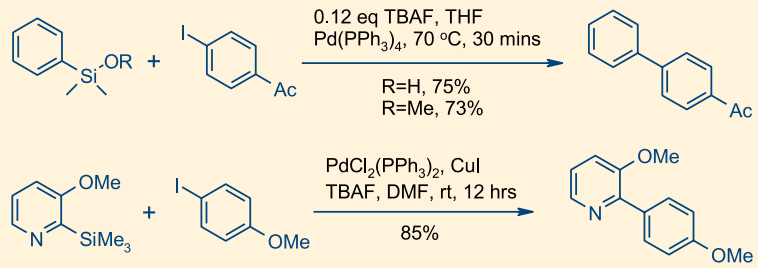


Figure 3. Examples of more recently developed silicon substrates for the Hiyama coupling reaction



Methyl ethers of dimethylsilanols and substituted pyridyl-2-trimethylsilanes are a more recent addition to the silicon cross-coupling toolkit: they are competent Hiyama coupling partners and do not suffer from disiloxane formation on storage (*Figure 3*).

A serious drawback of the classical Hiyama coupling is the need for fluoride activation of the silicon atom. Fluoride will remove silyl ethers commonly used as protecting groups and may interfere with acidic protons or other base-sensitive functional groups. Among our new product offering is a range of HOMSi® reagents originally developed by Hiyama, Nakao and co-workers, which circumvent this drawback. HOMSi® reagents for use in Hiyama cross-couplings show high functional group tolerance (amino, cyano, hydroxyl, ester, ketone, nitro, etc.), react with a wide variety of halides (iodides, bromides and chlorides), do not require fluoride activation, a mild base such as potassium carbonate is generally sufficient for the reaction to proceed, and the organosilicon by-product can be recycled if required (*Figure 4*). Two additional features of HOMSi® reagents are their compatibility with pinacol esters of aryl boronates and the ability to turn the silicon "on" or "off" for coupling as required by protecting the hydroxymethyl oxygen.

A sample of AMT's HOMSi® reagents now available from Key Organics is shown in *Figure 5*.

Figure 4. Examples of the versatility of HOMSi® reagents

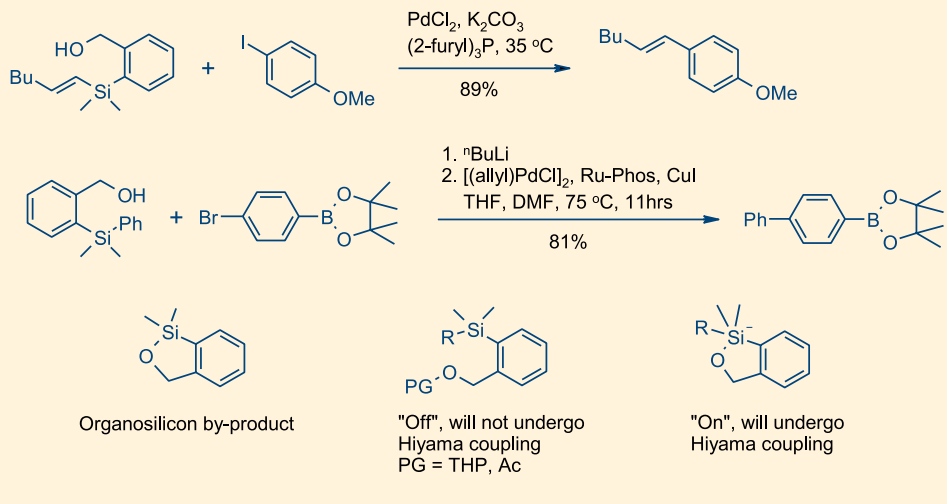
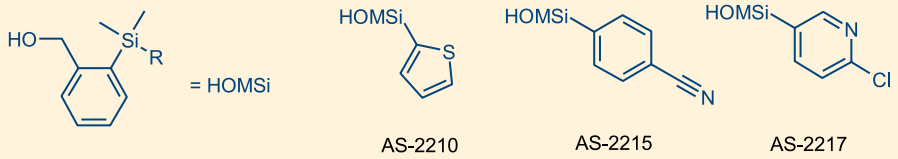
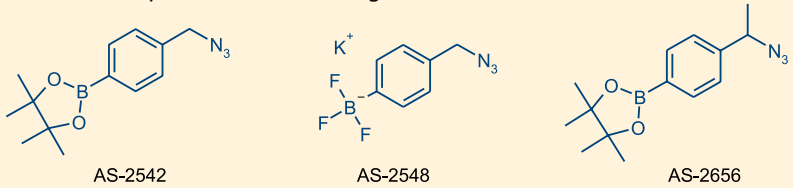


Figure 5. Examples of HOMSi® reagents

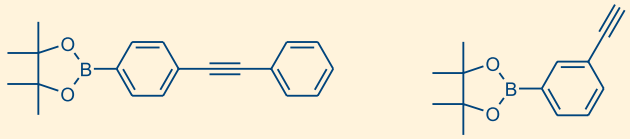


AS-2210 AS-2215 AS-2217

Figure 6. New alkyne and azide building blocks



AS-2542 AS-2548 AS-2656



AS-2407 AS-2418

The Huisgen 1,3-dipolar cycloaddition is a mild and high-yielding route to 1,2,3-triazoles and the best known example of the concept of click chemistry introduced by Sharpless in 2001. One of the requirements for click chemistry characteristics is the ready availability of starting materials and reagents. To this end, AMT offer a growing range of functionalised alkyne and azide building blocks which are suitable for click chemistry applications. Many of these have dual functionality, thus allowing for further chemistry prior or after the click step. A sample of compounds now available from Key Organics is shown in *Figure 6.*

Case Studies and Information Sheets

New case studies and Information Sheets are now available for download from our website that profile the versatility of our new range of organoboron and organosilicon reagents.

Please visit: **http://www.keyorganics.net/downloads/**

Key Organics Selected by Sprint Bioscience to supply Fragments for their Discovery Research

Key Organics has been selected to supply fragments from its BIONET Fragment Library to support the discovery research activity at Sprint Bioscience, Stockholm, Sweden.

The BIONET Premium and CNS Fragment Libraries comprise of carefully selected fragments with high purity (≥95%), experimentally assured aqueous solubility (1mM) and excellent diversity. BIONET Premium and CNS Fragments were selected based on rule of three criteria, chemical tractability and potential for fragment evolution. Diversity and Clustering analysis has demonstrated that the majority of compounds are singletons and the libraries have excellent diversity.

About Sprint Bioscience

Sprint Bioscience is a privately-owned Swedish drug development company with a mission to speed up development of novel therapies exploiting cancer metabolism.

With the proprietary The Gene2Lead™ platform and a lean and flexible company structure, Sprint Bioscience can move in just months from target selection to compounds ready for testing in cell-based assays. This approach provides early pharmacological validation of new and highly relevant targets and builds up a valuable project portfolio. Sprint Bioscience establishes early collaboration to ensure that projects are developed with a focus on current market needs from the start.

Jenny Viklund is a Computational Medicinal Chemist with 11 years experience in the pharmaceutical industry, working for Sprint Bioscience and AstraZeneca. She is a co-author of 7 scientific publications and co-inventor of 11 patents/patent applications and her specialty is lead generation.

Sprint Bioscience

Jenny Viklund comments:

"We can recommend Key Organics for being very service minded and professional in customer relationships, and for fast and reliable deliveries of high quality, price worthy fragments for our lead generation projects".

New Satellite Offices, Let's Meet-up!

We are now able to meet with customers at our new satellite offices at BioCity Nottingham and BioCity Scotland.

Events that we will attend during 2013

9 – 11 October Yokohama, Japan	**BioJapan 2013** www.ics-expo.jp/biojapan
22 – 24 October Frankfurt, Germany	**CPhI Pharma Ingredients Event** www.cphi.com/home
29 - 30 October Amsterdam, The Netherlands	**Crop World** www.cropworld-global.com
26 - 27 November London, UK	**Pharma Integrates** www.lifesciencesindex.com

Staff Interview

with
Ian Bennington, Senior Analyst

Q: Please tell us a bit about yourself?

A: I grew up in Huddersfield, in Yorkshire, and studied at the University of Huddersfield and gaining a GRSC Part 1 qualification from the Royal Society of Chemistry. I'm proud of my Yorkshire roots and I'm an avid follower of my hometown football team, Huddersfield Town and Huddersfield Giants rugby league team. Since graduating, I've worked for a number of pharmaceutical companies, large and small, moving from Yorkshire to Cambridgeshire in 2001 and then to the South West of England. I joined Key Organics in July of this year.

I now live in North Cornwall, on the edge of Bodmin Moor which is very reminiscent of the area of Yorkshire where I grew up. North Cornwall is a great place to live if you enjoy the great outdoors and being close to the coast, as much as I do.

Q: What is your role within Key Organics?

A: As Senior Analyst in the analytical department, my role is to oversee the day to day running of the department and to expand our analytical capabilities. We will soon be adding GC analysis to our current offerings of NMR, LCMS, HPLC, Preparative LC and Solubility Profiling. I am able to draw upon my many years of experience in analytical method development to tackle more complex analytical challenges, including identification of process/synthesis related impurities. Sixteen years in industrial analytical chemistry, validation and technical roles has given me a solid understanding of the broader analytical needs of our customers, and a strong sense of commercial awareness.

Q: What do you enjoy about working at Key Organics?

A: My role provides challenges aplenty and a lot of scope for professional development, but I also get the opportunity to be 'hands-on' in the laboratory which I believe is crucial to keeping pace with the latest analytical techniques. It's great to be able to do those things in such a friendly environment, where a strong team spirit is so evident.

Q: What do you think is Key Organics' greatest strength?

A: Flexibility and adaptability; being a smaller company gives us the agility to meet customers' changing requirements in a way experience has shown me larger companies can find difficult to do.

Key Organics

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