

In our second quarterly newsletter, we focus upon chirality and new additions to our >65,000 BIONET compound collection that contains an increased variety of new single enantiomer Intermediates, Fragments and Screening Compounds. In March we also launched our new Biochemicals catalogue, available on request in hard copy and pdf formats. We will continue to add new BIONET products on a monthly basis and updates will be available on our recently launched new website, with improved 'search & buy' functionality as well details on new products and services. See www.keyorganics.net for our new look!

The provision of customer-centric chemistry services continues to be a focus for Key Organics and herein we present our capabilities for real-time, global project delivery and how we are keeping ahead with the introduction of new initiatives such as our 'Contur iLabber' e-lab notebooks. On our back page we interview Steve Brough, our new Sales Manager who joined us in January. We also present the conferences and events that we will be attending or exhibiting at during 2013. We hope to meet you at one!

Chirality – A Continued Focus for Drug Discovery

In May 1992 the US Food and Drug Administration introduced new regulations in relation to the development and registration of new single isomer pharmaceuticals. This represented a historical and substantial regulatory milestone in drug development and transformed the way in which New Chemical Entities (NCE's) with stereochemical properties are now developed. A recent review of launched drugs alongside pharmaceutical development pipelines undertaken by Key Organics confirms that the shift to chiral NCE's has continued to grow (Figure 1).

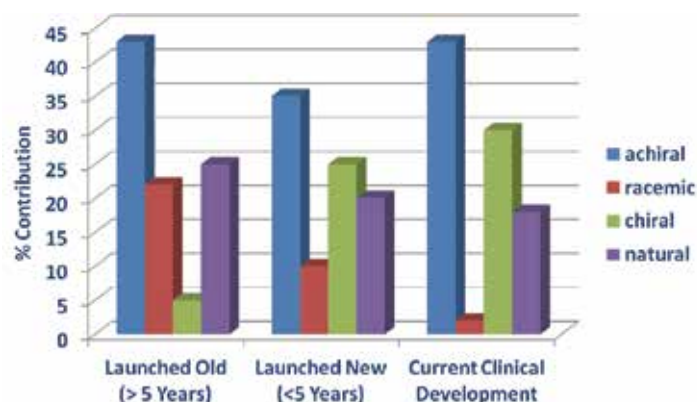
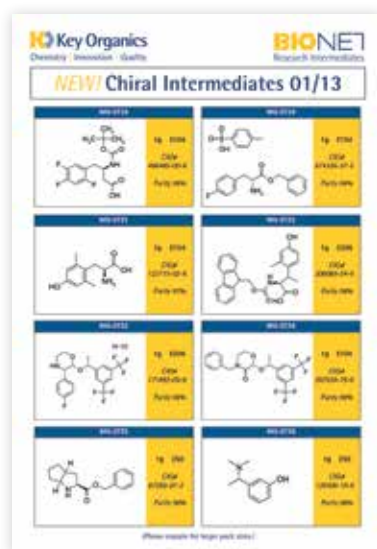


Figure 1. Increased Focus on Chiral Pharmaceuticals

The increased availability of new and novel chiral molecules has been undoubtedly driven by the availability of new asymmetric synthetic methodologies as well as the rapid and continued advances in chiral analytical chemistry. Fragment-based drug design is also showing strong evidence in support of this trend where greater selectivity and specificity that has been achieved through the inclusion of 3D fragments in screening and/or lead candidate optimisation studies. At the recent RSC-BMCS Fragment-based Drug Discovery meeting at the STFC Rutherford Appleton Laboratory (5th - 6th March) in Harwell, a theme emerged with respect to both the increased use of, and demand for more diverse 3D or chiral fragments and intermediates with compelling case studies from Astex Pharmaceuticals and others as to the benefits.



Key Organics continues to meet its customers' needs through offering an increasing number and diversity of new chiral intermediates and fragments as well as working with our customers to meet their needs for specific, novel compounds and tailored fragment libraries. During our 26 year history, we have proactively contributed to innovations in new fragment design and this has continued with the recent launch of our new CNS fragment library that is:

- ✓ Rule of 3 Compliant
- ✓ Highly Diverse: All with a Diversity Coefficient of 0.73
- ✓ Guaranteed Purity of >95%: Supported with NMR and/or LC-MS analytical data and measured solubility

Following the launch of our new CNS Fragment Library, we recently showcased our new 'Premium Fragment Library' at the Discovery Chemistry Congress in Munich. We can now offer customers a bespoke fragment library design service and deliver this in a variety of formats to suite needs. Please contact us for more information.



Key Organics Services: Meeting the Needs of Our Global Customer Base



Figure 2. Benefits of Contur iLabber e-Notebooks

With an increased emphasis on global collaborative R&D and the need to share data and information in real-time, Key Organics has invested in the implementation of Contur iLabber e-lab notebooks which offer several key advantages in customer communication and service provision (Figure 2). For the IT-savvy, it is noteworthy that the iLabber Server and iLabber Cloud is based on the same ELN technology which has been used by 1000s of users worldwide in the life sciences industry, hence its robustness has been well proven with respect to security and operational effectiveness.

Dr Matthew Stent heads up Key Organics' Services Division and recently attained his Registered Practitioner Certification in PRINCE2®. Matthew manages a team of 15 scientists and chemists delivering our Global Chemistry Services with an increased focus on complex chemistry projects in drug discovery, medicinal chemistry as well as new route/process development. Our team contains an experienced and diverse skill set of staff with excellence in customer service which enables us to integrate quickly and effectively into our customers' R&D teams. Key Organics undertakes a range of services for global clients within the life sciences sector (Figure 3).



Figure 3. Key Organics Extended Services Offerings

Whilst most of our projects are undertaken in strict confidentiality, we do have a selection of case studies for unclassified projects that profile our capabilities in many diverse areas of synthetic organic, process R&D and analytical chemistry. We also offer consultancy services which cover technology and business asset due diligence as well as mainstream synthetic organics and analytical chemistry. During the remainder of 2013 we plan investment initiatives to increase the size of our team and implement new equipment and technologies, so please watch this space!

Looking for New Biochemicals? Our New Catalogue is now available!

The recently launched Key Organics 2013 Biochemical's catalogue contains a wide selection of over 900 bioactive compounds from our BIONET Biochemical's collection. It includes APIs, metabolites, peptides and hormones together with a new collection of 21 Deuterated APIs which can be employed as Medicinal Chemistry tools for Research. Deuterium offers a subtle yet powerful medicinal chemistry tool which, when applied to compounds with well understood therapeutic utility can be used to create new drugs that address unmet medical needs. We continue to add more compounds to our collection and monthly updates are available directly from our website or upon request in pdf or sdf file formats.



Your Introduction to Key Organics New Products and New Services!

Key Organics continues to offer its customers value through building a more extensive range of products and services to meet every demanding need. Our new brochure profiles our BIONET product lines as well as our Custom and Contract Services that now extend to Process R&D and Consultancy.

Please also contact us for new products that are not listed which we can make through our Custom Services.



For either publication, please visit the Key Organics website to download your own pdf version, alternatively email: enquires@keyorganics.net or call us on +44(0)1840 212137 to request a hardcopy.

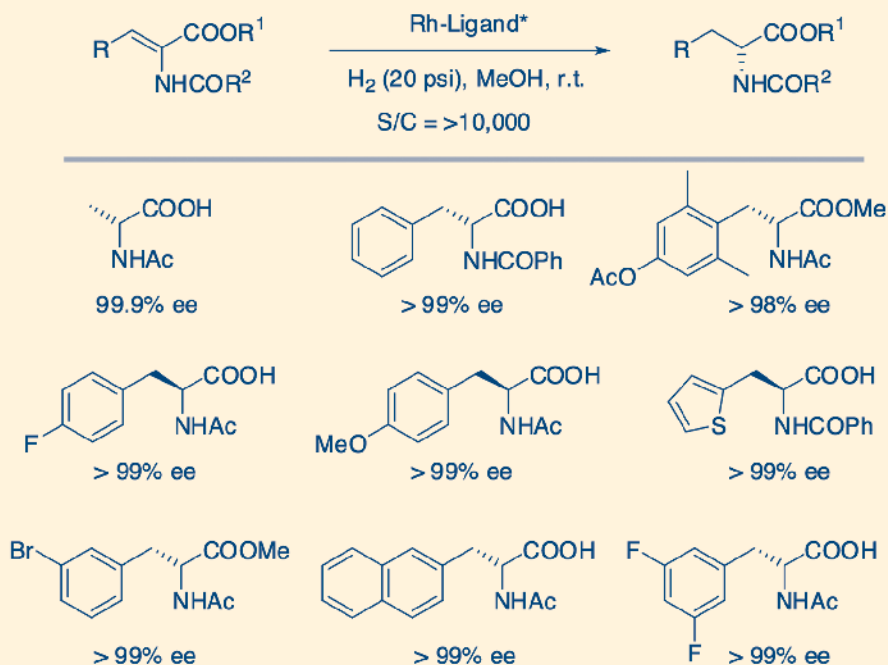
Asymmetric Synthesis: The Application of Catalytic Asymmetric Hydrogenation

Our Managing Director, Dr Joe Carey profiles Key Organics' continued investment into providing new chiral compounds within our BIONET collection and the implementation of new synthetic methodologies to our expanding chemistry capabilities.

Arriving at Key Organics on my first day, I came across a copy of the Strem Chemicals catalogue that allowed me to appreciate the impressive innovations that have been made in new chiral ligand and catalyst design since I completed my D.Phil in asymmetric catalysis with Professor John M. Brown, FRS back in 1991. Equally, the application of catalytic asymmetric hydrogenation in pharmaceutical manufacturing has progressed substantially following my days establishing ChiroTech Ltd. where we scaled up and commercialised the *DuPhos* and *ChiraPhos* range of ligands and catalysts developed by Dr Mark Burk that were licensed to ChiroTech by DuPont Inc. for non-agrochemical applications.

Fortunately, the patents relating to these and other versatile bisphosphine ligands, catalysts and their applications have expired which now provides us all with freedom to operate. Indeed, at Key Organics we try to only use systems that are not subject to IP protection and thereby avoid royalty payments, or restrictions on their use and application(s).

Of note in catalytic asymmetric hydrogenation, is the diversity of α -amino acids that can be made at commercial scale using rhodium[chiral bisphosphine] catalysis (*Scheme*).



Scheme: A Selection of α -Amino Acids made using Asymmetric Catalytic Hydrogenation



In our experience, the main cost driver for commercial manufacture of these products is typically attributed to the substrate cost, especially given the mild reaction conditions, high substrate to catalyst (S/C) ratios that can now be routinely achieved, again due to the availability and structural diversity of new chiral bisphosphine ligands

and their derived rhodium catalysts. We have strong capabilities in developing efficient and cost effective chemistries to pro-chiral substrates and predictive profiling of eventual commercial costs.

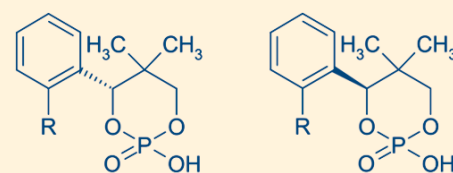
We have well equipped laboratory and development scale, 1 & 4 ltr stainless steel and a 0.5, 2 & 4 ltr Hastelloy autoclaves. These are routinely used for a range of chemistries that includes; catalytic hydrogenation, nitro- and nitrile-reductions, de-benzylations, and carbonylations. All our autoclaves are fitted with pressure gauges to monitor internal pressure/gas uptake and internal thermocouples.

At Key Organics, we are particularly focussed on increasing the diversity of our BIONET compound collection such that we can offer our customers a wider selection of new chiral intermediates, fragments and screening compounds that reduce time and costs. We can also offer our FTE or Collaborative Services to develop applications for new compounds that can be scaled up at our own, or partner facilities or transferred back to our customer. We have a well equipped and resourced analytical department to support this.

In January we launched our new chiral intermediates and will be launching a more extensive collection of new compounds at the Chiral Europe conference in Edinburgh (13th – 15th May). Please contact us for more information.

NEW! Chlocyphos Chiral Phosphoric acid Resolving agents:

Key Organics now offers all six of Chlocyphos chiral phosphoric acid resolving agents at gram or multi-Kg, commercial volume.



R=H; Phencyphos, SS-2994 (R) & SS-2996 (S)
R=Cl; Chlocyphos, SS-2995 (R) & SS-2997 (S)
R=OCH₃; Anicyphos, SS-2992 (R) & SS-2993 (S)

All six items are available with purity >99% and >99% ee in g to Kg quantities.

Please contact us for more information.

Let's Have Coffee..

Key Organics will be attending the following events and would be delighted to meet with you.



25 April 2013

24th Symposium on Medicinal Chemistry in Eastern England
Fielder Centre, Hatfield, UK

30 April 2013

BioScotland 2013
University of Strathclyde, Glasgow, Scotland

13 – 15 May 2013

Chiral Europe 2013
Radisson Blu Hotel, Edinburgh, Scotland

14 – 16 May 2013

BioTrinity 2013
Newbury Racecourse, UK

10 – 11 June 2013

14th Annual Drug Discovery Summit 2013
Geneva, Switzerland

22 – 25 July 2013

Synthesis in Organic Chemistry – 23rd International Symposium
St Catherine's College, University of Oxford, UK

 **Key Organics**
Chemistry | Innovation | Quality

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Staff Interview

In this edition we interview
Steve Brough.



Q: Please tell us a bit about yourself?

A: I grew up in Nottinghamshire, where I am still based and I started my career at Boots in Nottingham as a Lab Technician, working in the laboratories that now are home to BioCity. After studying part time for my HNC in Chemistry at Nottingham Trent University, I moved down the road to Fisons in Loughborough where I completed my BSc in Applied Chemistry, again, part time at NTU.

Fisons R&D then became part of Astra then subsequently AstraZeneca, during my time there, I worked on many multidisciplinary Medicinal Chemistry projects and was also heavily involved in the combinatorial chemistry initiative and early roll out of new technologies in chemistry and purification. After leaving AZ, I spent a couple of years working for Asynt, where I gained my first commercial experience which ultimately led to my current role here at Key.

One of the advantages of still being based in Nottinghamshire is that I get to follow my hometown football team, Mansfield Town, the other big advantage is the nearby Peak District where I enjoy walking, usually followed by a pub lunch!

Q: What is your role within Key Organics?

A: I am the Sales Manager in the Business Development team, my chief role is to be out and about, meeting customers, seeking ways Key can help their projects and programs move forward with our synthesis expertise. This is really enjoyable as I'm always keen to discuss chemistry and as the chemistry world is so small, I usually find I either know the people or we have a common connection.

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

A: Team spirit and a sense of common purpose, everyone is pulling in the same direction, whether it's the synthetic chemists taking pride in solving problems and delivering projects, the front office staff providing first rate customer service or the facilities and compound management group, turning round orders rapidly.

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

A: In two words, synthetic chemistry, since I joined I've been very impressed with the wide range of synthesis skills within the company which comes from many years of experience working on a very wide range of chemistries, it's a skill that is sometimes undervalued in big Pharma but it's crucial for us, something we take pride in and I'm sure our customers appreciate. I think this expertise will be the major driver to growth during an interesting and rapidly changing time in the industry.