

Welcome to our new quarterly newsletter which serves to inform our established and prospective customers of news and developments at Key Organics. The newsletter will include details of new products and services introductions, together with updates on our conference and exhibition attendance throughout the year. In this first edition, we profile new additions to our staff, our outlook for 2013 and an interesting article covering the synthesis of some novel spiro compounds that are now part of our Intermediates collection.

News & Outlook

Some recent developments at Key Organics have included changes to our management team, sales force and chemistry staff which, together with new product and service offerings, form part of our growth strategy for 2013.

We are pleased to report that Dr **Joe Carey** was appointed as our new Managing Director in August 2012. Joe originally trained as a physical-organic chemist with Shell Research and then completed his BSc at the University of Sussex and his D.Phil at the University of Oxford in asymmetric synthesis. He then joined Pfizer Central Research Ltd. as a Scientist where he managed a team of graduate analysts working on process related impurities in drug substance. Thereafter he held various commercial roles, initially as a co-founder of the chiral technology company ChiroTech where he spent five years growing their chiral services and products businesses. Following senior commercial roles at BTG plc and Encap Drug Delivery, he most recently held the position of Director of Manufacturing Services at Tillotts Pharma AG and was based in Switzerland.

In January 2013, we welcome **Steve Brough** as our new Sales Manager, who joins us from Asynt, where he managed their technical sales within the UK. Steve has an extensive background in medicinal chemistry, having spent 15 years within various technical functions at AstraZeneca plc. Prior to that, he held senior technical roles at Fisons and Boots Pharmaceuticals. Steve brings valuable experience in medicinal chemistry, working on inflammation, respiratory and cardiovascular projects, scale-up, library synthesis and solid state drug properties. He has contributed to a number of patents and publications in discovery and medicinal chemistry as well as in lead optimisation. Steve will be field-based, managing the growth of European sales of our growing BIONET product range and further promoting our increasing range of Services offerings.

Within our Services Chemistry Team, we extend a warm welcome to **Dr Nathan Bartlett**, who joins us fresh from the completion of his Ph.D. on '*The total synthesis of Luminacin D*' with Dr Bruno Linclau at the University of Southampton. We also welcome back to Key Organics **Dr Dominic Guly**, who had previously started his career with us following completion of his Ph.D. at the University of Bristol before moving to Evotec (UK) Ltd for five years. We were delighted to welcome Dominic back home in September and he features in our first staff interview (rear page). To our Research Intermediates Team we welcome **Melia Burdon**, who recently acquired her MChem degree from the University of Southampton.

As well as extending our product and service offerings, we will also launch our new website by the end of January. This will include a new and more functional shop that allows customers to search for BIONET products more quickly and to purchase products more easily.



Fragment Libraries

Our New BIONET CNS Fragment Library

We have recently launched our new CNS fragment library that builds upon our previously successful and popular fragment collections. Important features of this new collection include:

- ✓ Rule of Two/Three compliant
- ✓ Measured solubility in PBS buffer (1mM)
- ✓ Purity $\geq 95\%$. NMR and/or LC-MS available for each fragment
- ✓ Chemically clean – filtered to remove toxic and reactive groups
- ✓ High diversity – Diversity coefficient = 0.73

Our BIONET CNS Fragment Library consists of 700 carefully selected fragments with high purity ($\geq 95\%$), experimentally assured aqueous solubility (1mM) and excellent diversity.

Please contact our sales team for more information at: fragments@keyorganics.net or call us on: +44 (0)1840 212137

Looking for New and Novel Fragment Libraries?

With over 26 years' experience in the design and synthesis of novel screening compounds and building blocks, let Key Organics build your new fragment collection. Please contact us for more information.

Small and Niche, but part of a Special Family...

Sadly the global pharmaceutical industry continues to go through further rationalisation and downsizing. Not surprisingly, competition amongst chemistry service providers has also increased, whereby the 'survival of the fittest' concept continues to conform to Darwin's famous evolutionary theory. Just under five years ago, North Cornwall hosted a variety of chemistry-based service providers that included Maybridge, Tripos and Key Organics. At that time, the population density of organic chemists was amongst the highest in the



UK. Key Organics is now the sole survivor and we are fortunate to be part of Tennants Consolidated Ltd (TCL), a family-owned chemicals conglomerate whose UK business interests date back to the 1700s. In 2011 TCL had a global turnover in excess of £409 million (£18.9M profit) and currently employs 974 staff. So although we are relatively small, we are part of a financially stable, secure and growing group of companies.

Expanding our Products and Services

Key Organics is focussed on providing an increasing range of products and services to its customers across the life-sciences sector, further building on our capabilities in synthetic organic chemistry. Over the last 26 years we have worked on and solved some of the most challenging problems in medicinal chemistry, process R&D and analytical chemistry. This provides us with a unique and diverse skill set that we now build upon through offering customers new products and services to include Process R&D/Scale-up and Consultancy Services (figure 1).

Our consultancy services will include a range of technical and commercial areas including;

- Research & Development
- Outsourcing
- Sales & Market Analysis
- Technology Due Diligence

We are able to support projects with additional 'bolt-on' practical chemistry services. Our experienced team can offer bespoke services on a day-rate basis or fully-costed for a specific assignment. We have a proven track record in working with a broad range of public and private organisations covering the following sectors:

- Pharmaceutical and biotechnology
- Agrochemical and Petrochemical
- Universities and Government Research Bodies
- Venture Capital and Investment Banks
- Private individuals and investment consortia

To help us remain a customer-focussed company we continually seek to address the changing needs of our customer base. During 2013 we will be adding new technologies, products and services. Our future newsletters and flyers will be used to communicate these and we therefore actively encourage your feedback.

Product Areas	Service Offerings
	
<ul style="list-style-type: none">• Intermediates• Fragment Libraries• Biochemicals• Screening Compounds	<ul style="list-style-type: none">• Collaborative R&D• FTE Services• Custom Synthesis• Process R&D/Scale-up • Analytical Chemistry• Consultancy 

Figure 1. Key Organics Extended Product Areas and Services Offerings

During Q1 2013 our newly-refurbished kilo lab will be equipped with 20 litre vessels and will be capable of low temperature process development work that extends our capabilities to a wider range of chemistries. Following process validation, we are able to take technology transfer process chemistry to larger GMP partners for both key intermediates and drug substance. Please contact us for more information.

We have traditionally offered chemistry consultancy service to our customers and we are now pleased to announce that this will be extended to cover analytical as well as formulation development, technology due diligence, drug product development and project management. **Please contact us at consultancy@keyorganics.net for more information.**

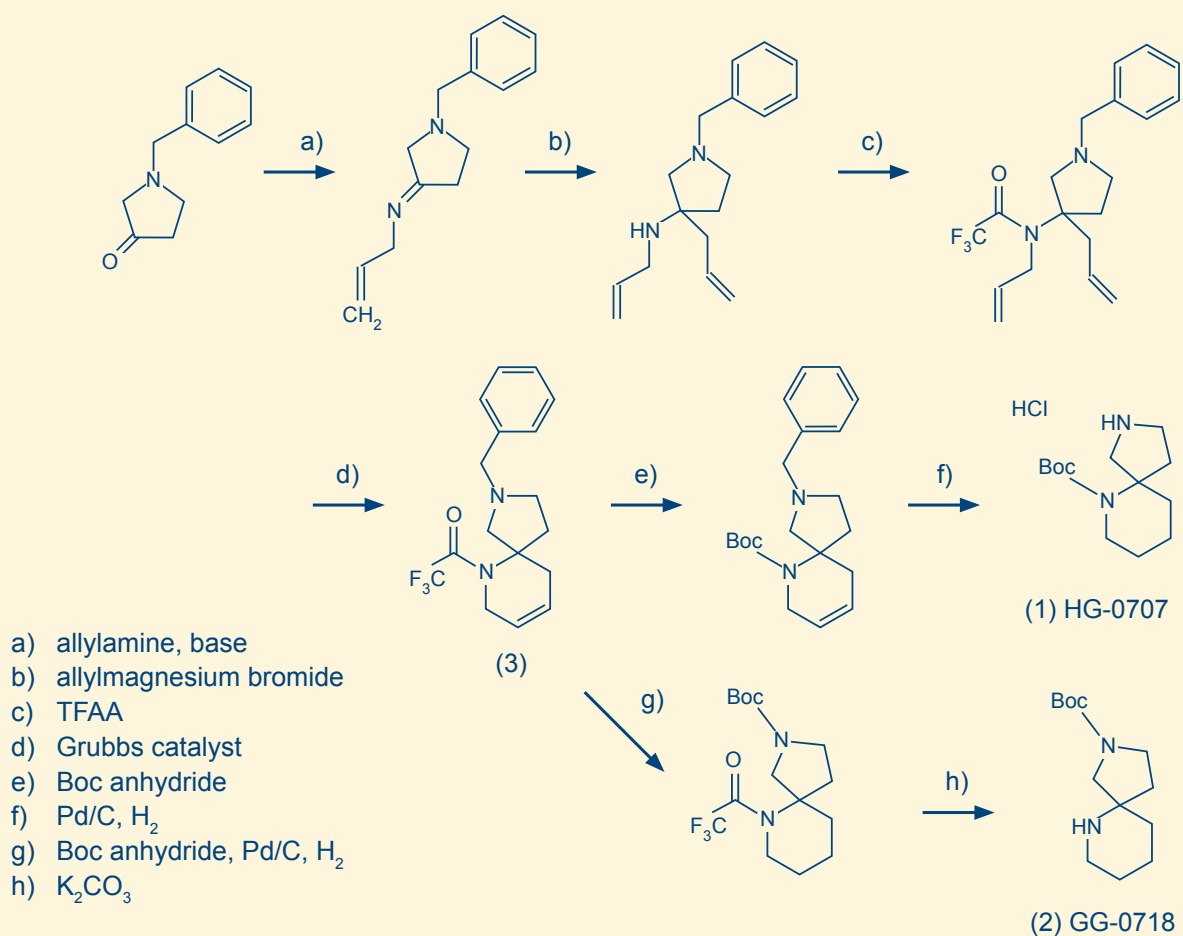
Chemistry Focus:

Novel Diazaspiro[4.5]decane Scaffolds

Spiro compounds can be defined as cyclic molecules containing at least two rings joined together by a single atom. This unique structural feature has been observed in natural products and is arguably among the most challenging structural motifs to synthesise.

Recent patents^{1,2} have reported the closely related diazaspiro[5.5]undecane derivatives having activity as neurokinin NK1, NK2, NK3 antagonists and orexin receptor antagonists, which are considered to be useful in the treatment of disorders including anxiety and depression, irritable bowel syndrome, COPD, sleeping disorders, eating disorders and substance related disorders.

Inspired by published literature methodology³ we set about synthesising two novel diazaspiro[4.5]decane compounds (1) HG-0707 and (2) GG-0718, which would be useful in the design and synthesis of targeted lead generation libraries.



Starting from commercially available 1-benzyl-3-pyrrolidinone, treatment with allylamine gave the imine in high yield (91%), however reaction with allylmagnesium bromide in the subsequent step was poor yielding (28%). TFA protection and ring closure with 1st generation Grubbs catalyst gave the core intermediate (3). Yields were modest and variable with 1st generation Grubbs and may have been improved with 2nd Gen catalyst but this was not investigated further. Protecting group manipulation of intermediate (3) gave the desired spiro compounds with alternate Boc-protection.

These compounds are useful scaffolds for library design and are available from stock in gram quantities.

References

- [1] JANSSEN PHARMACEUTICA N.V. Patent: WO2005/97795 A1, 2005
- [2] NOVARTIS AG; BADIGER, Patent: WO2011/76747 A1, 2011
- [3] Ian D. Jenkins et al; J Org Chem. 2009, 74, 1304-1313

Let's Have Coffee..

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



19 - 20 March 2013

Discovery Chemistry Congress

Munich, Germany

For more information please visit:
www.selectbio.com

14 - 16 May 2013

BioTrinity

Newbury, UK

For more information please visit:
www.biotrinity.com

22 - 24 October 2013

CPhI

Frankfurt, Germany

For more information please visit:
www.cphi.com/event-calendar



Chemistry | Innovation | Quality

For more information, please contact us at:

Key Organics Ltd.,
Highfield Road Industrial Estate,
Camelford,
Cornwall PL32 9RA,
United Kingdom

T: +44 (0)1840 212137

F: +44 (0)1840 213712

E: enquiries@keyorganics.net

www.keyorganics.net

Staff Interview

In this edition we interview
Dr Dominic Guly.



Q: Please tell us a bit about yourself?

A: I grew up in West Devon, not far from our laboratories in Camelford. I studied at Imperial College London before moving to the University of Bristol for my PhD, which involved developing methodology for heterocyclic chemistry.

I started my career at Key Organics in 2004 and initially spent several years working on a large collaboration with a major pharmaceutical company. I then joined Evotec (UK) Ltd as a Senior Scientist where I worked on several medicinal chemistry projects. In September 2012 I returned to Key Organics as a Synthetic Organic Chemist.

Key Organics is based in North Cornwall, a perfect location for people who love the outdoor life. When not doing chemistry I enjoy fishing, kayaking, and photography.

Q: What is your role within Key Organics?

A: I am a chemist in the Custom Synthesis Team. When a customer orders a compound, I am responsible for designing an efficient synthetic route, carrying out the synthesis, and purifying the final compound to the customer's requirements. All our work is done to deadlines and the customer is kept fully informed about the progress of their compound.

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

A: There is a great sense of team spirit among the chemists at Key Organics. We all love a challenge and take great pride in successfully completing a project. Another aspect of our work that I enjoy is the wide diversity of synthetic chemistry we carry out. I don't think there has ever been a day when I haven't learnt something. The company is also growing, adding new technologies and capabilities so it is good to be a part of a company making progress.

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

A: There is an enormous wealth of experience among the staff at Key Organics, which has been established for over 26 years. We also have access to all the major chemical databases and an electronic laboratory notebook (ELN) system. I think that this gives us, as a company, the confidence to solve complex synthetic problems in order to provide our customers with a reliable service.