Issue 13 | October 2016

# Key Organics Newsletter

Chemistry | Innovation | Quality

**In July 2016 we celebrated our 30th year in business!** Much has changed within the industries we serve, but our focus on excellence in customer services, quality and providing value has remained consistent. Our proprietary collection of BIONET products has grown to over 100,000 and includes intermediates, screening compounds, fragments and biochemicals, we continue to invest and innovate through internal R&D and collaborations with selected partners. Our collaboration with the University of Nottingham continues to generate new and innovative products as exemplified herein.

During 2016 we also launched our novel and proprietary fluorine fragment library that has been designed and verified in collaboration with the Broad Institute in Boston and NMX Research (Montreal, Canada). Within our BIONET Intermediate product group, we continue to add new products and profile a range of new reagents through our collaboration with Squarix.

Our staff interview is with Andy Dusntan who joined us last year from Novartis UK.

BIONET Fragment Libraries

## Announcing our New Fluorine Fragment Library

**We are pleased to announce the launch of our new Fluorine Fragment Library that has been constructed using "Rule of Three and other industry-standard substructure filtering including "PAINS" analysis. Our Diversity selection also utilizes methods in shape, scaffold, fingerprint and predicted property space such that our library is highly refined and unique.**

$^{19}$F NMR experimental profiling has also been used to carefully select highly soluble and well behaved fragments with desirable physicochemical and stability properties. This experimental curation has enabled us to minimise sources of false positive hits (due to aggregation) and attrition for fragment screening. Our provision of $^{19}$F NMR spectral data in aqueous buffer solution enables the practitioner to rapidly build "fragment pools" and initiate screening that saves valuable time and costs.

### All fragments in the Fluorine Fragment Library will be analyzed by NMR for:

- Structure verification
- Purity
- Aqueous Solubility
- Aggregation

### Physiochemical Properties of the library:

- Heavy atoms ≤16
- logP ≤3,
- Hydrogen bond donors ≤3
- Hydrogen bond acceptors ≤3
- Polar surface area ≤60
- Rotatable bonds ≤3

### Substructure Filtering:

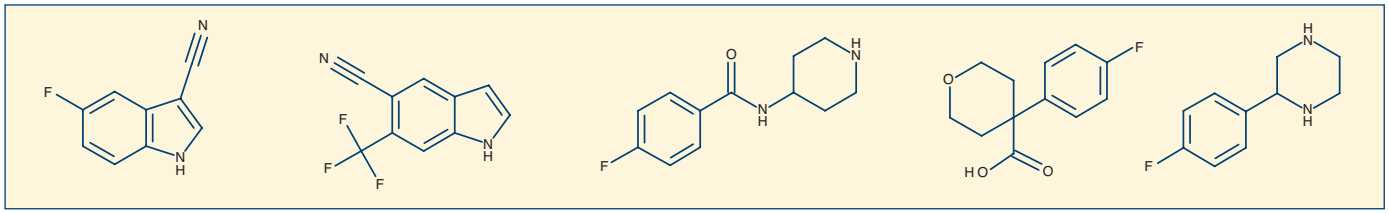
- Lilly MedChem Rules[1]
- PAINS[2]
- BMS[3]

### DMSO Solubility:

All Fragments are soluble in DMSO at 200mM

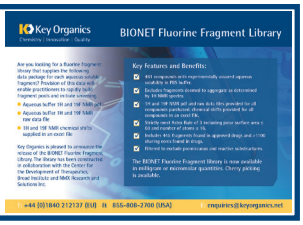
### All customers will be supplied with the following data package for each aqueous soluble fragment purchased:

- $^{19}$F NMR pdf and Raw data files
- $^{1}$H NMR pdf and Raw data files
- NMR chemical shifts supplied in an excel file



References:
1. Bruns, R. F.; Watson, I. A. *J. Med. Chem.* **2012**, 55 (22), 9763–9772.
2. Baell, J. B.; Holloway, G. A. *J. Med. Chem.* **2010**, 53 (7), 2719–2740.
3. Pearce, B. C.; Sofia, M. J.; Good, A. C.; Drexler, D. M.; Stock, D. A. *J. Chem. Inf. Model.* **2006**, 46 (3), 1060–1068.

**Our new fragment information brochure is now available, please contact Andrew Lowerson for more details; e: andrewl@keyorganics.net**




**FREE SHIPPING* on orders over £100/$150/€130 during 2016 to existing and new customers.**

**This offer is not available to resellers, agents or intermediaries and cannot be combined with any other offer of discount that may be in operation.*

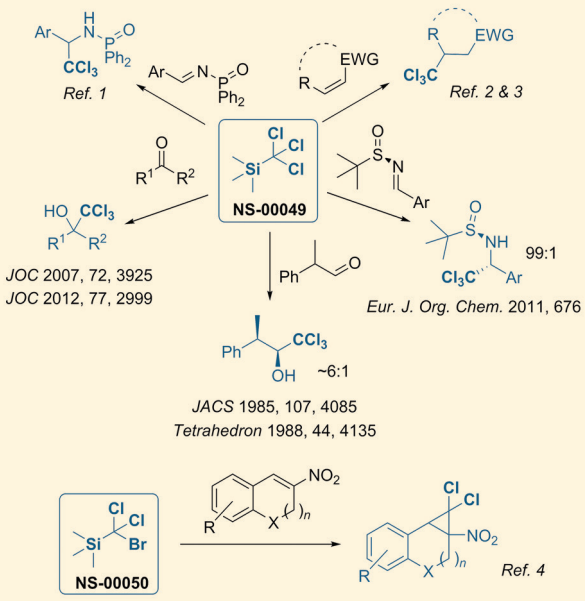
# BIONET Pioneering Reagents for R&D

## TMS-Haloforms: reagents for $CCl_3$-additions and dichlorocyclopropanation

With the expansion of our co-marketing collaboration with the University of Nottingham come new reagents from Prof. Simon Woodward's lab: trimethyl(trichloromethyl)silane (TMS-$CCl_3$) and (bromodichloromethyl)trimethylsilane (TMS-$CCl_2Br$). Both have been recently added to BIONET Reagents and can serve an excellent tool for 1,2- and 1,4 additions[1-4] followed by chosen types of rearrangements,[3] eliminations, and cyclopropanations[4] (*Figure 1*). As developed by the Woodward group, analytically pure trimethylsilane-haloforms can be now prepared in large quantities[1,4] which allow us to offer you these equivalents of halogenated carbanions to accelerate your research.

**Please contact us if you need more information about our new additions to the BIONET collection.**

**Figure 1.** Examples of synthetic utility of TMS-haloforms.




References:

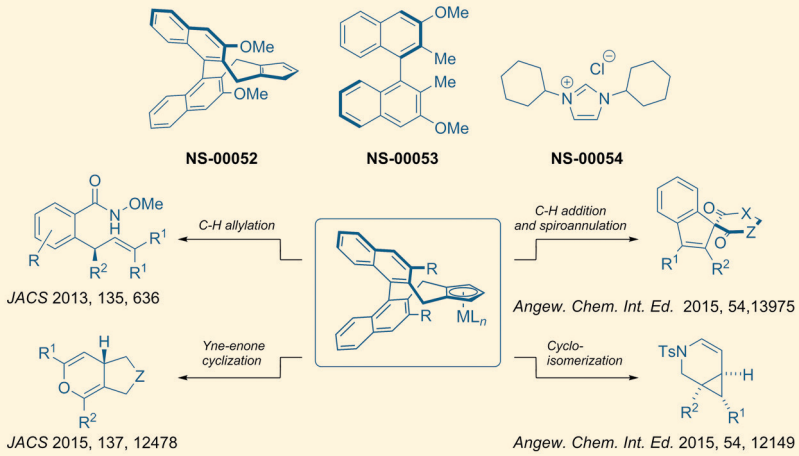

1. Wahl, B.; Cabré, A.; Woodward, S.; Lewis, W. *Tetrahedron Letters* **2014**, *55*, 5829.
2. Wu, N.; Wahl, B.; Woodward, S.; Lewis, W. *Chemistry – A European Journal* **2014**, *20*, 7718.
3. Wahl, B.; Lee, D. S.; Woodward, S. *European Journal of Organic Chemistry* **2015**, *2015*, 6033.
4. Lee, D. S.; Durán-Peña, M. J.; Burroughs, L.; Woodward, S. *Chemistry – A European Journal* **2016**, DOI: 10.1002/chem.201600607.


## The first chiral BINOL-derived cyclopentadienyl ligand on the market!

In continuation of growing the BIONET collection, we are pleased to announce that we have now on offer the first on the market chiral binaphthyl-derived cyclopentadienyl ligand ($Cp^x$) *via* our collaboration with the University of Nottingham. Research of Prof. Hon Wai Lam focuses on the design of new metal-catalysed reactions which led to an improved synthesis[1] of the $Cp^x$ ligand **1** for metal complexes that, among others, has been used worldwide in various enantioselective transformations.[2] Since the first report in 2013 by Cramer and co-workers,[3] chiral $Cp^x$ ligands of type **1** have been complexed with rhodium,[1,3] ruthenium,[4] iridium,[5] and even scandium,[6] to successfully catalyse high-ee yielding reactions such as C-H bond functionalisation[1,2,3,6] and spiroannulation.[1] From Lam's laboratory we have also on offer a BINOL-derived intermediate **2** and a precursor **3** for *N*-heterocyclic carbene (NHC) catalysis.[7]

**Please contact us if you need more information about our new additions to the BIONET catalogue.**

**Figure 2.** New additions and applications of $Cp^x$

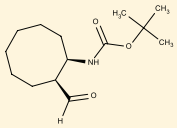


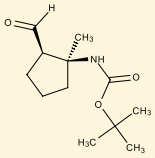

References:

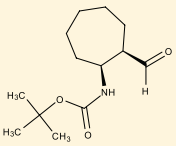

1. Reddy Chidipudi, S.; Burns, D. J.; Khan, I.; Lam, H. W. *Angew. Chem., Int. Ed.* 2015, 54, 13975.
2. Newton, C. G.; Kossler, D.; Cramer, N. *J. Am. Chem. Soc.* 2016, 138, 3935.
3. Ye, B.; Cramer, N. *J. Am. Chem. Soc.* 2013, 135, 636.
4. Kossler, D.; Cramer, N. *J. Am. Chem. Soc.* 2015, 137, 12478.
5. Dieckmann, M.; Jang, Y.-S.; Cramer, N. *Angew. Chem., Int. Ed.* 2015, 54, 12149.
6. Song, G.; O, W. W. N.; Hou, Z. *J. Am. Chem. Soc.* 2014, 136, 12209.
7. Díez-González, S., N. Marion, and S.P. Nolan, *Chem. Rev.* 2009, 109, 3612.

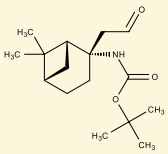
# New BIONET Products

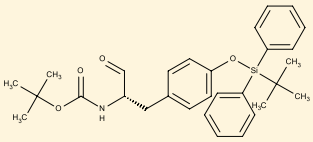
## A sample of Boc Aldehydes

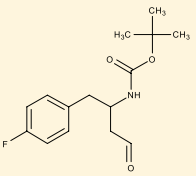

TS-7003


TS-7008

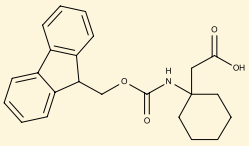

TS-7011

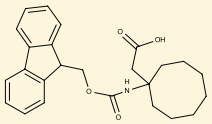

TS-7031

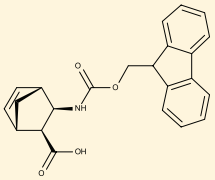

TS-7042

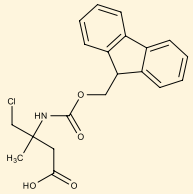

TS-7055

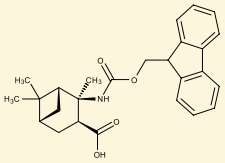
## A sample of FMOC Amino Acids


TS-7097

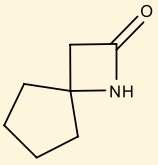

TS-7101

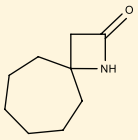

TS-7119

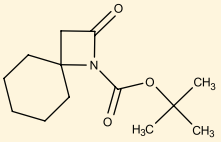

TS-7152

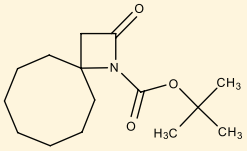

TS-7167

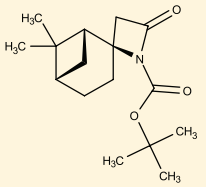
## A sample of Spiro compounds


TS-7305

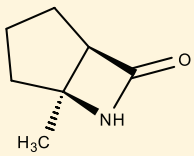

TS-7323

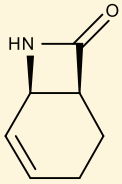

TS-7340

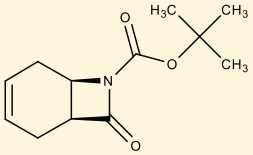

TS-7357

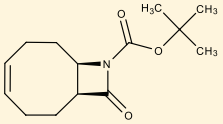

TS-7366

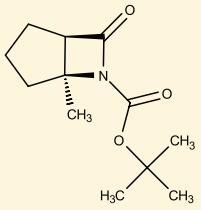
## A sample of Azabicycles


TS-7303

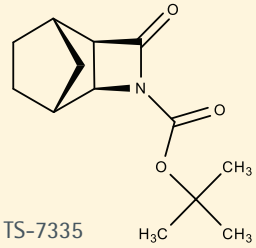

TS-7309

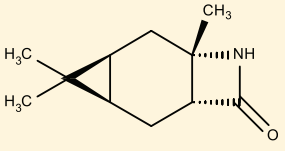

TS-7341

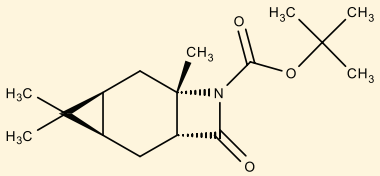

TS-7344


TS-7337

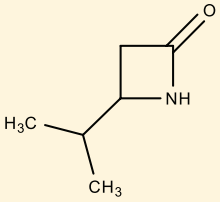
## Azatricycles

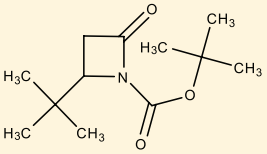

TS-7335

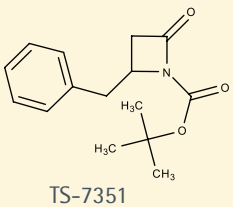

TS-7364

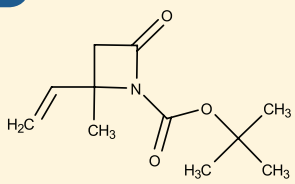

TS-7369

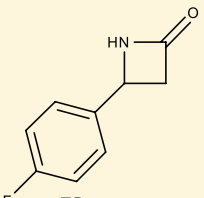
## A sample of Azetidin-2-ones


TS-7317


TS-7349


TS-7351


TS-7358


TS-7367

We will be exhibiting and/or attending the following exhibitions and conferences in the coming months:

| | | |
|---|---|---|
| October 6th | The Chemistry of Collaboration: Oxford | Oxford, UK TBC |
| October 9th - 12th | Fragment-based Lead Discovery Conference 2016 | Cambridge, MA, USA TBC |
| October 13th - 14th | Drug Discovery 2016 | Liverpool, UK Poster Delegate |
| October 18th | Synthesis in Drug Discovery and Development, 4th Symposium | Liverpool, UK TBC |
| November 16th | Plugging the Antibiotics Gap: A Medicinal Chemist's Perspective | Alderley Edge, Cheshire, UK TBC |
| December 6th - 7th | University of St Andrews – Second Annual Postgraduate Symposium | St Andrews, UK TBC |

# Staff Interview Andy Dunstan, Organic Chemist

**Q: Please tell us a bit about yourself?**

A: I was born and brought up in Truro, Cornwall, and after 3 years away studying Natural Sciences at the University of Cambridge, my first job was back in Cornwall as a chemist with Maybridge. After a couple of years I got caught by the lure of the big city, and I moved to London and a position in the medicinal chemistry department at what was then Sandoz, which later became part of Novartis. I spent over 20 years with them, first in London in the pain research group, and later in Horsham working mostly on respiratory disease, and developing an interest in parallel synthesis, automation and new technologies. Sadly Novartis closed the Horsham site in 2014 and I was made redundant. Misfortune turned to opportunity though, as before long I was lucky enough to be offered a position at Key Organics, and the chance to return to Cornwall was too good to miss!

In my spare time I am a keen amateur photographer and enjoy exploring Bodmin Moor and the South-West Coast Path with a camera over my shoulder. I'm also very interested in Cornish history and culture, and have been studying the Cornish language for the last few years; I'm far from fluent but I can just about hold up a simple conversation!

**Q: What is your role within Key Organics?**

A: As a member of the synthetic chemistry team, it's a very hands-on lab-based role, which is just how I like it. The work is very varied; at any one time I could be working with a client on an FTE basis, or doing a custom synthesis, or re-stocking intermediates and the projects span the whole gamut of the chemical industry from pharmaceuticals and agrochemicals to the petrochemical industry and more.

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

A: I've always loved chemistry ever since having a chemistry set when I was about 10 years old. The variety of the work here at Key keeps things interesting and I'm working with a great team of dedicated and enthusiastic chemists with a wide range of backgrounds and experience. There's a nice friendly atmosphere here, and of course it's been lovely to be able to move back to Cornwall.

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

A: A good reputation for delivering high quality goods and services, achieved through having an excellent team of dedicated, hard-working people with a wealth of experience and knowledge.

Key Organics

Chemistry | Innovation | Quality

For more information, please contact us at:


**Key Organics Ltd.,**
Highfield Road Industrial Estate,
Camelford,
Cornwall PL32 9RA,
UK

T: +44 (0)1840 212137
F: +44 (0)1840 213712
E: enquiries@keyorganics.net

**Key Organics Inc.,**
Suite 100,
55 North Road,
Bedford,
MA 01730

Toll Free No: 855 808-2700
Or: 781 280-5000
E: enquiries@keyorganics.net

www.keyorganics.net

Acknowledgements: *Design by* David Anthony, AK Design (Scotland) Ltd.