University of Birmingham

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Senior Lecturer in Organic Chemistry

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About

Dr Liam Cox is currently a Senior Lecturer in Organic Chemistry and Senior Admissions Tutor at the University of Birmingham. Since joining Birmingham in 1999, he has developed a productive research group, securing funding from a range of bodies (EPSRC, MRC, Wellcome Trust, The Leverhulme Trust, Nuffield Foundation, Royal Society, GSK, Pfizer, Merck Sharp and Dohme, AstraZeneca), publishing 50 papers in the scientific literature and giving over 45 seminars on his research, as well as supervising over 10 PhD students in this time.

His research interests are currently focused around three principal themes. His first research theme is based on a long-standing interest in stereoselective C-C bond-forming processes and is currently focusing on the use of chiral Brønsted acids and chiral anions as organocatalysts for the enantioselective allylation of latent electrophiles.

His second research strand concerns the development of new methods for oligoyne assembly. In this area, the group has pioneered a novel route to oligoynes using β-halovinylsilanes as masked alkynes. A highlight of this work was the synthesis of an aryl end-capped dodecayne, which represents the longest aryl end-capped oligoyne reported to-date.

An increasing interest in chemical biology has opened up a third research theme in his group, which is a highly multidisciplinary project investigating the role of glycolipids in CD1d-mediated immunity. This project is carried out in collaboration with **Prof Del Besra (http://biosciences-people.bham.ac.uk/About/staff_profiles_contact.asp?ID=69)** (Microbiology, Bham) and **Prof Vincenzo Cerundolo (http://www.imm.ox.ac.uk/wimm-research/mrc-human-immunology-unit/vincenzo-cerundolo)** (Immunology, Oxford).

Group webpages (http://chemweb.bham.ac.uk/~coxlr/index.htm)

Qualifications

- Postgraduate Certificate in Learning and Teaching in Higher Education (2002)
- PhD in Organic Chemistry, University of Cambridge (1998)
- BA (Hons) in Natural Sciences, University of Cambridge (1994)
- Member of the Royal Society of Chemistry (2003-present)

Biography

Liam Cox graduated in 1994 from the University of Cambridge (King's College) with a BA (hons) Class I degree in Natural Sciences, specialising in Chemistry. He remained in Cambridge to carry out his PhD, working under the supervision of **Professor Steven Ley FRS CBE (http://www.ch.cam.ac.uk/staff/svl.html)** on the use of π-allyltricarbonyliron lactone complexes in remote asymmetric induction.

On completing his PhD in 1997, he moved to the ETH-Zürich to work as a post-doctoral research fellow in the group of **Professor François Diederich (http://www.diederich.chem.ethz.ch/)** where he developed synthetic approaches to chiral 1,3-diethynylallenes and investigated their use as highly unsaturated monomers for the preparation of helical polymers.

In September 1999, he took up an academic position at the University of Birmingham where he is currently a Senior Lecturer in Organic Chemistry and Senior Admissions Tutor.

Teaching

Dr Cox currently teaches on a range of courses covering core Organic Chemistry on all Chemistry degree programmes.

These include: carbonyl chemistry, nucleophilic substitution and elimination (Level 1 core), aromatic chemistry (Level 2 core), natural product synthesis (Level 4), and biological carbohydrate chemistry (Level 4).

Postgraduate supervision

Research projects in the Cox group provide excellent training for anyone wishing to pursue a career in synthetic organic chemistry or chemical biology.

Potential applicants interested in joining the group are encouraged to contact Dr Cox directly by email.

Research

RESEARCH THEMES AND ACTIVITY

Organic Chemistry focusing on Stereoselective Synthesis and Asymmetric Catalysis
The Cox group has a long-standing interest in stereoselective synthesis and in particular, the allylation reaction, which is one of the most valuable C-C bond-forming processes available to the synthetic chemist. We have shown how employing a temporary silicon connection to tether two reacting moieties can dramatically improve / reverse the stereoselectivity of a subsequent intramolecular allylation [Beignet, J., Jervis, P. J., Cox, L. R., (2008), Temporary Silicon Connection Strategies in Intramolecular Allylation of Aldehydes using Allylsilanes. *J. Org. Chem*., 73: 5462-5475.].

We have also developed intramolecular allylation strategies to synthesise a range of oxygen heterocycles and recently employed our methodology in the first total synthesis of the natural product (-)-aureonitol [Jervis, P. J., Cox, L. R., (2008), Total synthesis of (-)-Aureonitol and 3-*epi*-Aureonitol. Confirmation of Relative Stereochemistry. *J. Org. Chem*., 73: 7616-7624.].

Research has more recently shifted away from substrate-controlled reactions to reagent-controlled processes, with a particular focus on the use of chiral Brønsted acids and chiral anions as organocatalysts for the enantioselective allylation of latent electrophiles.

Carbohydrate Chemistry and Chemical Biology
Carbohydrate chemistry has been a research interest in the group for some time. In recent years, we have begun to employ our synthesis skills in the glycolipid arena as part of a highly multidisciplinary project in association with Prof Del Besra (Microbiology, Birmingham) and Prof Vincenzo Cerundolo (Immunology, Oxford).

This productive interdisciplinary research programme focuses on the CD1d molecule, which is a protein that binds glycolipids. Recognition of the resulting protein-lipid complex by receptors on invariant Natural Killer T cells results in an immune response.

We have synthesised a diverse range of novel glycolipids and shown that the structure of the bound glycolipid determines whether the immune response is activated or suppressed. This opens up the possibility of using these small-molecule regulators of the immune response to treat a range of diseases [Jervis, P. J., Cox, L. R., Besra, G. S. (2011) Synthesis of a Versatile Building Block for the Preparation of 6-*N*-Derivatized α-Galactosyl Ceramides: Rapid Access to Biologically Active Glycolipids. *J. Org. Chem.,* 76: 320-323.].

We are also using labelled analogues to help shed more insight into the mode of action of different glycolipids CD1d agonists [Garcia-Diaz, Y. R., Wojno, J., Cox, L. R., Besra, G. S., (2009), Synthesis of Threitol Ceramide and [^{14}C]Threitol Ceramide, Non-Glycosidic Analogues of the Potent CD1d Antigen α-Galactosyl Ceramide. *Tetrahedron: Asymmetry,* 20: 747-753.].

Oligoynes and related π-Conjugated Molecules
We have developed a conceptually new approach to oligoyne assembly [for a review: Weller, M. D., Cox, L. R., (2009), A Novel Twist on an Old Theme: β-Halovinylsilanes, A New Elimination Approach to Oligoyne Assembly. *C. R. Chimie,* 12: 366-377.], which has culminated in our report of the synthesis of a dodecayne [Simpkins, S. M. E., Weller, M. D., Cox, L. R., (2007), β-Chlorovinylsilanes as Masked Alkynes in Oligoyne Assembly: Synthesis of the First Aryl-End-Capped Dodecayne. *Chem. Commun.,* 4035-4037.] This polyyne, consisting of 24 linearly arranged carbon atoms, represents the longest aryl end-capped oligoyne reported to-date and indeed one of the longest oligoynes ever reported. Oligoyne encapsulation strategies are also being developed in order to access even longer π-conjugated frameworks [Simpkins, S. M. E., Kariuki, B. M., Cox, L. R., (2006), Towards the Synthesis of Insulated Oligoynes: a Ring-Closing-Metathesis Approach to Molecular Encapsulation. *J. Organomet. Chem*., 691:5517-5523.].

Other activities

- Society of Chemical Industry (**www.soci.org/ (http://www.soci.org/)**): Invited member (2003-2008) and Chair (2006-2008) of Young Chemists' Panel of the Society of Chemical Industry.
- 2009-present: invited member of Fine Chemicals Group.

Publications

Jervis, P. J., Cox, L. R., Besra, G. S. (2011), Synthesis of a Versatile Building Block for the Preparation of 6-*N*-Derivatized α-Galactosyl Ceramides: Rapid Access to Biologically Active Glycolipids. *J. Org. Chem.,*76: 320-323.

Jervis, P. J., Polzella, P., Wojno, J., Jukes, J.-P., Ghadbane, H., Garcia Diaz, Y. R., Besra, G. S., Cerundolo, V., Cox, L. R. (2013), Design, Synthesis and Functional Activity of Labeled CD1d Glycolipid Agonists. *Bioconjugate Chem*., 24: 586–594.

Paduraru, C., Bezbradica, J. S., Kunte, A., Kelly, R., Shayman, J. A., Veerapen, N., Cox, L. R., Besra, G. S., Cresswell, P. (2013), Role for lysosomal phospholipase A2 in iNKT cell-mediated CD1d recognition. *Proc. Natl. Acad. Sci. USA*, 110: 5097–5102.

Wojno, J., Jukes, J.-P., Ghadbane, H., Shepherd, D., Besra, G. S., Cerundolo, V., Cox, L. R. (2012), Amide Analogues of Threitol Ceramide and □-Galactosyl Ceramide as CD1d Agonists for Modulating iNKT-cell-Mediated Cytokine Production. *ACS Chem. Biol.*, 7: 847–855.