# Working as a Student and Employee in Pharmaceutical Research

*Dr Robert Law*

*GSK*

# Overview

- My background and education
- My career path into pharmaceutical research
- The GSK/University of Strathclyde Collaborative PhD Programme
- Working as a medicinal chemist
- Summary

# My Background and Education

- University of Bristol 2008-2012; MSci Chemistry with Industrial Experience
- Industrial Placement year with AstraZeneca, Alderley Park
  - A 12 month full time placement in an industrial lab
  - Working on organic synthesis for medicinal chemistry
- Final year project focussing on natural product analogue synthesis
- Career goal of working as an industrial organic chemist
- But which route to take?

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# GSK/University of Strathclyde Collaborative PhD Programme

- Collaborative PhD with GSK and Strathclyde University
- Research conducted primarily at GSK Stevenage with a 3-6 month secondment at Strathclyde
- Co-supervisors from both institutions
- Research focuses on medicinal, process or computational chemistry
- Courses on chemistry theory delivered by leading academics, with formal interim assessments
- Worked within project teams, and independently on the development of bromodomain inhibitor chemical probes and boron-mediated cross-couplings

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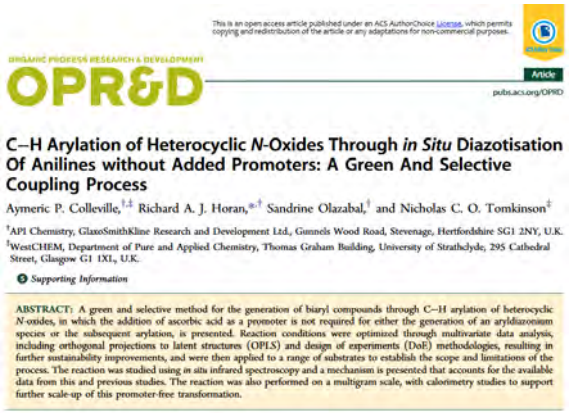
# GSK/University of Strathclyde Collaborative PhD Programme

- Over 100 candidates and GSK staff enrolled to date
- Over 40 publications and 37 conference prizes



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ORGANIC PROCESS RESEARCH & DEVELOPMENT

OPR&D

Article

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**C–H Arylation of Heterocyclic *N*-Oxides Through *in Situ* Diazotisation Of Anilines without Added Promoters: A Green And Selective Coupling Process**

Aymeric P. Colleville,[†,‡] Richard A. J. Horan,[*,†] Sandrine Olazabal,[†] and Nicholas C. O. Tomkinson[‡]

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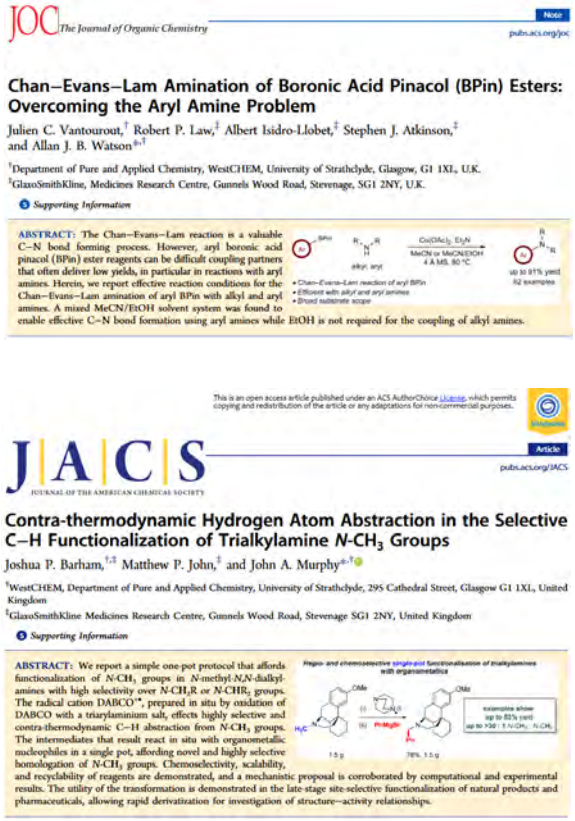
Supporting Information

ABSTRACT: A green and selective method for the generation of biaryl compounds through C–H arylation of heterocyclic *N*-oxides, in which the addition of ascorbic acid as a promoter is not required for either the generation of an aryldiazonium species or the subsequent arylation, is presented. Reaction conditions were optimized through multivariate data analysis, including orthogonal projections to latent structures (OPLS) and design of experiments (DoE) methodologies, resulting in further sustainability improvements, and were then applied to a range of substrates to establish the scope and limitations of the process. The reaction was studied using *in situ* infrared spectroscopy and a mechanism is presented that accounts for the available data from this and previous studies. The reaction was also performed on a multigram scale, with calorimetry studies to support further scale-up of this promoter-free transformation.



JOC The Journal of Organic Chemistry

Note

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**Chan–Evans–Lam Amination of Boronic Acid Pinacol (BPin) Esters: Overcoming the Aryl Amine Problem**

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Supporting Information

ABSTRACT: The Chan–Evans–Lam reaction is a valuable C–N bond forming process. However, aryl boronic acid pinacol (BPin) ester reagents can be difficult coupling partners that often deliver low yields, in particular in reactions with aryl amines. Herein, we report effective reaction conditions for the Chan–Evans–Lam amination of aryl BPin with alkyl and aryl amines. A mixed MeCN/EtOH solvent system was found to enable effective C–N bond formation using aryl amines while EtOH is not required for the coupling of alkyl amines.



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JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Article

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**Contra-thermodynamic Hydrogen Atom Abstraction in the Selective C–H Functionalization of Trialkylamine *N*-$CH_3$ Groups**

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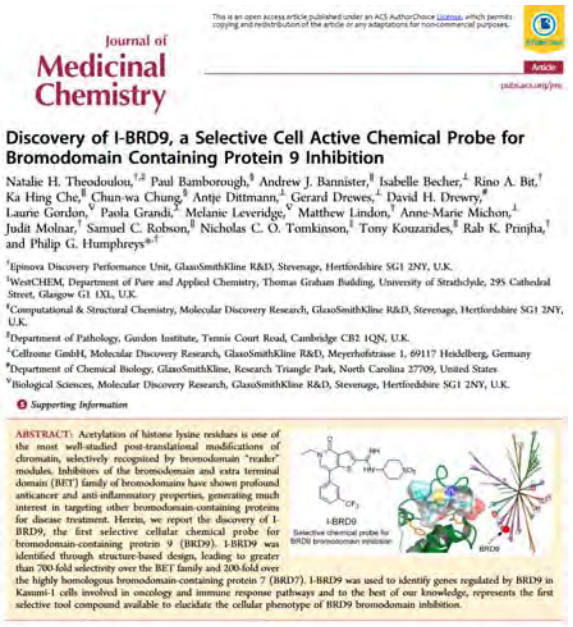
Supporting Information

ABSTRACT: We report a simple one-pot protocol that affords functionalization of *N*-$CH_3$ groups in *N*-methyl-*N*,*N*-dialkylamines with high selectivity over *N*-$CH_2R$ or *N*-$CHR_2$ groups. The radical cation DABCO$^{\bullet+}$, prepared in situ by oxidation of DABCO with a triarylaminium salt, effects highly selective and contra-thermodynamic C–H abstraction from *N*-$CH_3$ groups. The intermediates that result react in situ with organometallic nucleophiles in a single pot, affording novel and highly selective homologation of *N*-$CH_3$ groups. Chemoselectivity, scalability, and recyclability of reagents are demonstrated, and a mechanistic proposal is corroborated by computational and experimental results. The utility of the transformation is demonstrated in the late-stage site-selective functionalization of natural products and pharmaceuticals, allowing rapid derivatization for investigation of structure–activity relationships.



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Journal of Medicinal Chemistry

Article

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**Discovery of I-BRD9, a Selective Cell Active Chemical Probe for Bromodomain Containing Protein 9 Inhibition**

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Supporting Information

ABSTRACT: Acetylation of histone lysine residues is one of the most well-studied post-translational modifications of chromatin, selectively recognized by bromodomain "reader" modules. Inhibitors of the bromodomain and extra terminal domain (BET) family of bromodomains have shown profound anticancer and anti-inflammatory properties, generating much interest in targeting other bromodomain-containing proteins for disease treatment. Herein, we report the discovery of I-BRD9, the first selective cellular chemical probe for bromodomain-containing protein 9 (BRD9). I-BRD9 was identified through structure-based design, leading to greater than 700-fold selectivity over the BET family and 200-fold over the highly homologous bromodomain-containing protein 7 (BRD7). I-BRD9 was used to identify genes regulated by BRD9 in Kasumi-1 cells involved in oncology and immune response pathways and to the best of our knowledge, represents the first selective tool compound available to elucidate the cellular phenotype of BRD9 bromodomain inhibition.

# Working as a Student in Pharmaceutical Research

- Studentships in chemistry research are an excellent opportunity to enhance your skills
- Chemistry roles are typically lab-based, providing lots of practical experience
- Students gain exposure to unfamiliar areas of science and industry
- Gain expertise and knowledge through group meetings, seminars and mentoring
- Students work within project teams and are valued members of the department
- Contribute to high-level research projects, while also being given ownership of work packages
- People are always willing to support students and share their skills

# Working as a Medicinal Chemist in Pharmaceutical Research

- Currently employed as a medicinal chemist at GSK, in the Protein Degradation DPU
- Designing and synthesising novel molecules as potential therapeutic agents

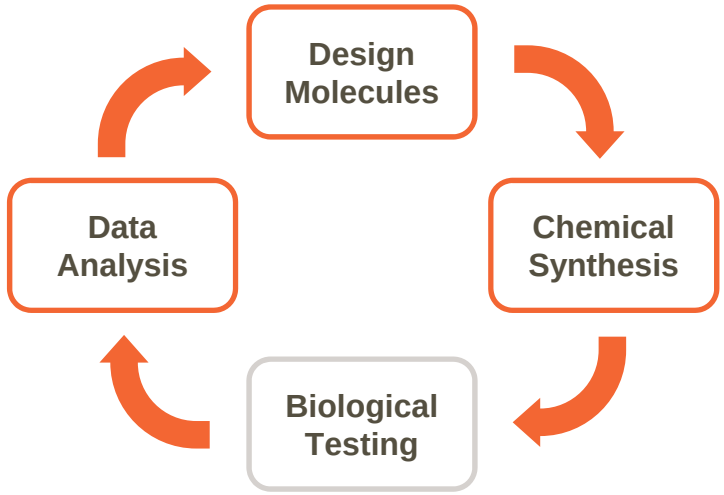
Using biological data, structural information and team knowledge to develop a hypothesis

Designing new compounds which test that hypothesis and aim to improve activity or properties

Collating and analysing data from multiple sources

Elucidation of structure-activity relationships

Using computational tools to analyse large data sets




Developing and executing synthetic routes for new targets

Optimising the synthesis of key compounds

Adapting literature methodology and developing new reactions

Working with CROs

Working closely with Biological Sciences to generate useful data

Assessing compound performance against isolated proteins, cell lines and in animal models

# Working as a Medicinal Chemist in Pharmaceutical Research

- Intellectually and practically challenging – something different every day!
- Cutting edge research focussed on patients
- Working closely with biologists, computational and analytical chemists in a close team and integrated R&D community
- Strong focus on personal development and career progression
- Opportunities to develop transferrable skills outside the lab
- Helping others develop - involved in interviews, mentoring and supervision of students

# Is a Job in Pharmaceutical Research for You?

- Working in a multi-disciplinary team to solve stimulating scientific problems
- Exciting, patient-focussed science
- Strong emphasis on personal development

- What does GSK look for?
  - Excellent scientific skills
  - Teamwork
  - Mental agility and the ability to adapt to new challenges
  - Communication skills

# Summary

- Studentships in industrial chemistry are an excellent way to improve practical and theoretic scientific skills, explore potential careers and network
- Pharmaceutical research provides an engaging science-based career with a strong focus on your personal and career development
- Publication of work can be slower due to intellectual property considerations, but other avenues for recognition and sharing science are available

- My key reflections from my career so far:
  - Find something you enjoy doing and are passionate about
  - Embrace new challenges and opportunities to expand your skills
  - Assistance from inspirational people has shaped my career path - ask for guidance and experience as much as you can