The department is pleased to announce that **Professor P. Andrew (Andy) Evans** has accepted an appointment in the Department of Chemistry at Queen’s as Alfred R. Bader Chair in Organic Chemistry. Andy succeeds Victor Snieckus in this important highly and honoured position, and it is clear that Queen’s Chemistry has once again recruited a magnificent talent to the Bader Chair. The Alfred R. Bader Chair in Organic Chemistry was endowed in 1993 by Alfred R. Bader, an alumnus of Queen’s who received a B.Sc. (Engineering Chemistry) in 1945, a B.A. (History) in 1946, an M.Sc. (Chemistry) in 1947 and an Honorary LLD in 1985. Dr. Bader’s subsequent chemical research at Harvard earned an M.A. in 1948 and a Ph.D. in 1949. He has been a staunch supporter and benefactor of Queen’s for many years.

Born June 20, 1964, in Llangollen, Wales, Andy obtained his B.Sc. (Hons.) in 1987 at Newcastle Polytechnic and his Ph.D. in 1990 at the University of Cambridge under the guidance of Andrew B. Holmes, FRS. Andy moved on to a NATO Postdoctoral Fellowship at the University of Texas at Austin (1991-1993; Philip D. Magnus, FRS), and subsequently joined the chemistry departments at first the University of Delaware and then at Indiana. He returned to the UK in 2006, assuming the position of Professor of Chemistry and Heath Harrison Chair of Organic Chemistry at the University of Liverpool. The Heath Harrison Chair is one of the most prestigious chairs in the UK, and has been held by a number of extremely prominent organic chemists.

Andy has won numerous awards and has been extremely active in the community. For example, he was awarded an NIH First Award (1997); Zeneca Pharmaceuticals Excellence in Chemistry Award (1997); Francis Alison Outstanding Young Scholar Award (1997); Eli Lilly Grantee Award (1998); Camille Dreyfus Teacher-Scholar Award (1998); GlaxoWellcome Chemistry Scholar Award (1999); Novartis Pharmaceuticals Academic Achievement Award (2000); Pfizer Distinguished Michigan Lecturer (2000); French Chemical Society Organic Division SFC-Rhodia Lecturer (2000); Johnson and Johnson Focused Giving Award (2001); Pfizer Creativity in Organic Chemistry Award (2002); Board of Consulting Editors, Tetrahedron and Tetrahedron Letters (2003-Present); ACS Division of Organic Chemistry Member-at-Large (2003-2005); US Associate Editor, Chemical Communications (2005-2007); National Organic Symposium Executive Officer (2005-2007); Royal Society Wolfson Research Merit Award (2006-11); Letters in Organic Chemistry Editorial Advisory Board (2006-Present); NIH Study Section Member (2006-2008); Novartis Chemistry Lectureship (2007); Chem. Comm. Editorial Board (2008-2010); RSC Pedler Award (2009); Synlett and Synthesis
Editorial Board (2009-2010); ACS Division of Organic Chemistry Chair (2010); ACS Fellow (2011); Associate Editor for Synthesis (2010-Present); ACS-DOC Councilor (2012-Present).

Andy has published more than 100 papers, articles, reviews and monographs. He has also presented over 450 plenary and invited lectures at international conferences, symposia, universities, research institutes and companies.

**Brief Description of Research**

Our research focuses on the development of novel synthetic transformations that permit the expeditious total synthesis of complex bioactive natural products. A unique and striking feature of our program is the ability to access new chemical reactivity, which in conjunction with detailed mechanistic studies allows the development of sophisticated multi-component processes that permit the stereoselective construction of complex molecular architectures. The following synopsis highlights three such areas of investigation, which have advanced the fundamental understanding of these types of processes and provided new synthetic strategies for synthesis.

The metal-catalysed allylic substitution reaction with acyclic unsymmetrical allylic alcohol derivatives has proven one of the most challenging metal-catalysed reactions to perform in a selective manner. Significantly, we demonstrated that the rhodium-catalysed version of this transformation provides unprecedented levels of regio- and stereospecificity, due to the intermediacy of a putative enyl ($\sigma^{+}\pi$) organorhodium intermediate. Indeed, this catalytic system remains the most versatile and selective method for acyclic allylic cross-coupling reactions to date. This is evident from the scope of the transformation, which is tolerant to a variety of pronucleophiles that had historically proven challenging. For example, we were the first to demonstrate a regio- and stereospecific allylic amination of acyclic chiral nonracemic unsymmetrical allylic carbonates, which provide an array of enantiomerically enriched allylic amine derivatives. We employed an adaptation of this protocol, using a dihydropyrimidin-2(1H)-one as the nitrogen pronucleophile, to complete the expeditious total synthesis of the marine alkaloid, (–)-batzelladine D (14 steps). More recently, we have extended the allylic amination reaction to aza-ylides, which constitute an entirely new class of nitrogen pronucleophiles. This work represents the first example of an ylide being employed in a metal-catalysed cross-coupling reaction, which is important given the functional group provides opportunities for further functionalisation. In the context of unstabilised carbon and heteroatom nucleophiles, the rhodium-catalysed allylic variant has challenged much of the longstanding dogma. For example, we demonstrated that copper alkoxides of secondary and tertiary alcohols provide unprecedented levels of regio- and enantiospecificity, which circumvents the challenges associated with the high basicity of these nucleophiles in conventional reactions. Indeed, the allylic
etherification is particularly significant, given it provides a convenient alternative to the venerable *Williamson Ether Synthesis*. The synthetic utility of this process was further enhanced by its combination with ring-closing metathesis to facilitate the construction of a variety of disubstituted cyclic ethers, which was employed in the first total synthesis of the mosquito deterrent, guar acid. In a related study, we demonstrated that acyclic copper enolates also serve as versatile nucleophiles, and that prochiral ketones provide exquisite levels of acyclic diastereoccontrol. The extension of the rhodium-catalysed allylic substitution to unstabilised carbanions, which are arguably the most challenging nucleophiles, represents an even more impressive accomplishment. This work demonstrated that aryl zinc reagents undergo allylic alkylation in a regio- and stereospecific fashion with inversion of absolute configuration. Interestingly, this remains the only example of a hard nucleophile providing good selectivity in an unsymmetrical system.

Transition metal-catalysed higher-order carbocyclisation reactions represent a very important class of reactions due to their ability to construct complex polycyclic systems in a highly selective and atom-economical fashion. Our work has contributed significantly to the development and understanding of these transformations. For example, in early studies we combined the rhodium-catalysed allylic substitution with the Pauson-Khand carbocyclisation, using temperature to modulate the catalytic activity. This was the first example of a single-pot transition metal-catalysed reaction, which does not involve the *in situ* combination of metathesis with hydrogenation. This work has prompted an array of related studies, since the ability to circumvent the isolation of intermediates provides an opportunity to develop new reaction sequences that reduce the number of synthetic operations in a synthetic sequence. We additionally demonstrated that the origin of diastereoccontrol in the Pauson-Khand is a consequence of the ligand coordination number on the metal center, which has widespread implications for related processes that proceed through similar metallacycle intermediates. More recently and quite significantly, we demonstrated that the oxidative addition of a 1,6-enyne can be tailored to permit a room temperature reaction, which overcomes the problem with poor stereocontrol. Interestingly, DFT calculations indicate the oxidative addition proceeds through a polarized transition state in a manner akin to Woodward-Hoffman cycloadditions, which has exciting implications for reactions that proceed through metallacycle intermediates. In a related programme, we have begun to examine the merit of alkenylidene cyclopropanes, which provide a convenient route for the diastereoselective synthesis of bicycloheptadienes applicable to an array of important bioactive targets. A critical issue in all carbocyclisation reactions is the ability to combine the $\pi$-components in a chemo- and stereoselective manner. In this context, we demonstrated a regiodivergent ligand-controlled rhodium-catalysed $\left[2+2+2\right]$ carbocyclisation of 1,6-enynes with activated alkynes to provide the constitutional isomers of bicyclobutadienes in a
highly selective manner. This work represents the first example of a regiodivergent higher-order carbocyclisation reaction, which again provides important insight into the factors that control selectivity. We have also developed the homologue of this process, namely the rhodium-catalysed [4+2+2] carbocyclisation of tethered 1,6-enynes with 1,3-butadienes to provide bicyclic octanoids. The problems encountered with controlling diastereoccontrol prompted combined theoretical/computational studies to demonstrate the process proceeds through a novel metallacycle intermediate. This inspired the development of the first metal-catalysed higher-order carbocyclisation with an $N$-heterocyclic carbene (NHC) ligand, which obviates the problems encountered with the triorganophosphine complexes. Additional challenges with the ability to incorporate substituted dienes motivated the development of the intramolecular temporary silicon-tethered carbocyclisation reaction. Although temporary silicon-tethered reactions have been widely employed in conventional reactions, the metal-mediated variants were primarily restricted to stoichiometric reactions prior to our contributions in this area. For example, we devised the temporary silicon-tethered ring-closing metathesis strategy as a new homo- and cross-coupling reaction. This provided an opportunity to devise a novel strategy for Long-Range Stereochemical Induction exploiting prochiral dienes to prepare cis- and trans-silaketals. The temporary silicon-tethered ring-closing metathesis reaction of unsymmetrical allylic alcohols provided the key reaction in the concise total synthesis of the potent antitumor agent, (–)-mucocin (12 steps). Interestingly, the insights afforded by the diastereoselective studies provided an opportunity to develop several variants. This strategy now provides the most concise approach to the non-adjacent acetogenins, thereby making it an important and timely contribution to the construction of these important antitumor agents.

In the last theme of the program, we have developed a series of bismuth-mediated reductive and two-component etherification reactions, which provide a conceptually new approach to the development of cascade reactions. A critical feature with these reactions is the decomposition of the bismuth(III) salt and the ability to control the rate of protodesilylation to orchestrate a cascade event. For example, the bismuth(III) salts furnish the requisite Brønsted acid and bismuthoxy halide upon hydrolysis, in which the latter is critical for internally buffering the two-component etherification reaction. In contrast, the reductive etherification reaction provides the Bronsted acid and bismuth metal. This process was utilised in the preparation of the 2,3,6-trisubstituted tetrahydropyran required to complete the total synthesis of the complex acetogenin, (–)-mucocin. More recently, we have developed a series of intramolecular kinetic oxa-conjugate addition reactions. Insights from these studies were utilised to combine a sequential the two-component etherification with an in situ oxa-conjugate addition to install the key 1,5-bis-tetrahydropyran in the total synthesis of (–)-leucascandrolide A macrolactone (14 steps). Although there are at
least thirteen approaches to this important intermediate, this strategy provides the shortest and most efficient sequence developed to date.

Overall, we have developed a number of new synthetic transformations, which in combination with mechanistic studies provide the necessary insight to devise a series of novel multi-component reactions. The application of these new transformations to challenging synthetic targets illustrates the far-reaching implications of these contributions for the development of practical total syntheses of several classes of challenging biologically important natural products.