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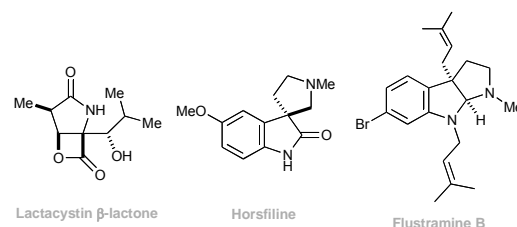
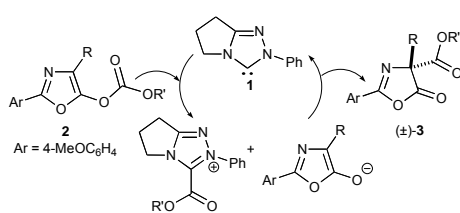
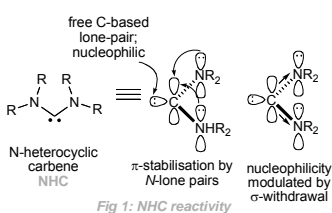
Research Interests: Organic synthesis, asymmetric synthesis, organocatalysis, natural product synthesis



Organocatalysis uses simple organic molecules rather than metal-based complexes to catalyse synthetic transformations. Our research seeks to develop new organocatalytic reactions and novel asymmetric synthesis methodologies for the preparation of enantiomerically pure building blocks. Current projects include the use of N-heterocyclic carbenes (NHCs) as nucleophilic catalysts and the development of new amine based organocatalysts. We also seek a fundamental mechanistic understanding of the new reactions developed within our laboratory in order to generate efficient asymmetric catalysts, and seek to apply these strategies to the synthesis of natural product targets.

N-heterocyclic carbenes (NHCs) as nucleophilic catalysts: Carbenes are electron deficient species and are usually treated as reactive intermediates. NHCs incorporate two N-substituents adjacent to the carbene centre, which drastically increase their chemical stability due to electronic stabilisation from the adjacent N-lone pairs, leaving a carbon based lone pair (Fig 1). NHCs show nucleophilic properties due to the availability of this lone pair and our research uses this characteristic to catalyse organic transformations. For example, NHC **1** promotes the rearrangement of amino acid derived O-acyl carbonates **2** to their corresponding (\pm)-C-acylated isomers **3** with high efficiency. This process requires low catalyst loadings (generally <1 mol% of NHC) while generating a C-C bond and a quaternary stereogenic centre. A simplistic mechanism for these transformations uses NHC **1** as a nucleophilic catalyst (Fig 2), although crossover experiments indicate an *intermolecular* reaction step and product stability experiments show that the C-C bond-forming step is *irreversible*. We are currently investigating diastereo- and enantioselective versions of this reaction. We are also interested in probing other novel applications of NHCs as catalysts for a range of processes and developing a range of chiral NHC catalysts for a variety of uses in asymmetric synthesis.

Natural Product Synthesis: Our synthetic target structures are chosen on the basis of containing challenging structural motifs and interesting biological properties. A number of our current molecular targets are illustrated below (Fig 3).



For further information on research projects visit the Smith Group website at <http://chemistry.st-and.ac.uk/staff/ads/group/> or contact us directly.

SELECTED RECENT PUBLICATIONS

1. Efficient N-Heterocyclic Carbene Catalysed O- to C-acyl transfer; J. E. Thomson, K. Rix and A. D. Smith; *Org. Lett.*, 2006, **8**, 3785.
2. Lithium Amide Conjugate Addition for the Asymmetric Synthesis of 3-Aminopyrrolidines; S. G. Davies, A. C. Garner, E. C. Goddard, D. Kruchinin, P. M. Roberts, A. D. Smith and H. Rodriguez-Solla; *Chem. Commun.*, 2006, 2664
3. Highly enantioselective organocatalysis of the Hajos-Parrish-Eder-Sauer-Wiechert Reaction by the β -amino acid cispentacin; S. G. Davies, R. L. Sheppard, A. D. Smith and J. E. Thomson; *Chem. Commun.*, 2005, 3802
4. Ammonium directed dihydroxylation of *N,N*-dibenzylaminocyclohex-2-ene: metal-free syntheses of the diastereoisomers of 3-dibenzylamino-1,2-dihydroxycyclohexane; S. G. Davies, M. J. C. Long and A. D. Smith; *Chem. Commun.*, 2005, 4536.