

# Dr Alison Hulme

## Senior Lecturer in Organic Chemistry

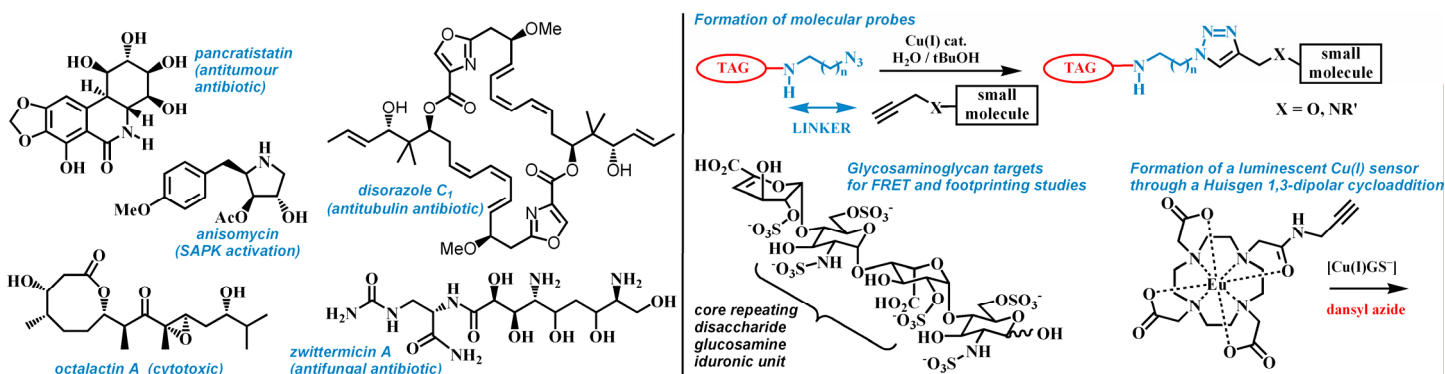
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Research Interests: natural product synthesis, asymmetric synthetic methodology, chemical biology, tagging and imaging in biological systems, historical dyestuffs



The Hulme group's research interests in natural products chemistry cover diverse fields, from synthetic organic chemistry and chemical biology, to historic textile dyestuffs. The group has a particular interest in the synthesis of natural products which interact with their biological targets through several, or many, chiral groups. Using a stereocontrolled glycolate aldol reaction, we have completed the synthesis of a number of iminosugars and the protein synthesis inhibitor anisomycin. We are also investigating the chemical synthesis of members of other classes of natural products, including: polyketides such as octalactin A; tetrahydroisoquinoline antibiotics such as pancratistatin; and products of mixed PKS-NRPS biosynthetic pathways, such as the C<sub>2</sub>-symmetric di-lactone, disorazole C<sub>1</sub>, and the unusual aminopolyol zwittermicin A. In each case we have developed new synthetic methodology to construct these targets, and this has allowed us to design analogues which we are able to test in collaboration with other research groups.



The Hulme group also has a strong interest in the design and synthesis of small molecule probes to investigate the interactions of biomolecules both *in vivo* and *in vitro*. We have synthesised a focused library of compounds to determine a detailed structure activity relationship of the pyrrolidine anisomycin which is frequently used as a tool by biochemists to activate the stress kinase (SAPK) pathways. [These pathways are implicated in a wide range of conditions including inflammatory diseases, ischemic injury and Alzheimer's disease.] Using "click" chemistry, we have designed probes based on biotinylated and fluorescence labeled anisomycin which we are testing in collaboration with Prof. P. Cohen FRS (MRC Unit, Dundee) to determine the anisomycin cellular receptor(s). We are also applying this expertise to the synthesis of probes based on steroids implicated in immunosenescence, which we are testing in collaboration with Prof. J. M. Lord (Medical Sciences, Birmingham). In a separate project, we are investigating the selective dual functionalisation of glycosaminoglycans, GAGs, in order to study them using fluorescence resonance energy transfer (FRET) and NMR footprinting techniques. These studies will allow us to determine the shape of GAGs and their binding modes with proteins.

### SELECTED RECENT PUBLICATIONS

1. Biotinylated Anisomycin: A Comparison of Classical and "Click" Chemistry Approaches, I. A. Inverarity, R. F. H. Viguier, P. Cohen, A. N. Hulme, *Bioconj. Chem.* 2007, **18**, 1593-1603.
2. DMT-MM Mediated Functionalisation of the Non-Reducing End of Glycosaminoglycans, E. Gemma, A. N. Hulme, A. Jahnke, L. Jin, R. Müller, D. Uhrin, *Chem. Commun.*, 2007, 2686-2688.
3. Marked Small Molecule Libraries: A Truncated Approach to Molecular Probe Design, I. A. Inverarity, A. N. Hulme, *Org. Biomol. Chem.* 2007, **5**, 636-643.
4. An Evans-Tishchenko – Ring Closing Metathesis Approach to Medium Ring Lactones, J. I. Aird, A. N. Hulme, J. W. White, *Org. Lett.* 2007, **9**, 631-634
5. Achieving High Selectivity and Facile Displacement with a New Thiol Auxiliary for Boron Mediated Aldol Reactions, S. Fanjul, A. N. Hulme, J. W. White, *Org. Lett.* 2006, **8**, 4219-4222.
6. A Sensitized Europium Complex Generated by Micromolar Concentrations of Copper(I): Towards the Detection of Copper(I) in Biology, R. F. H. Viguier, A. N. Hulme, *J. Am. Chem. Soc.* 2006, **128**, 11370-11371.
7. The Natural Constituents of Historical Textile Dyes, E. S. B. Ferreira, A. N. Hulme, H. McNab, A. Quye, *Chem. Soc. Rev.* 2004, **33**, 329-336.