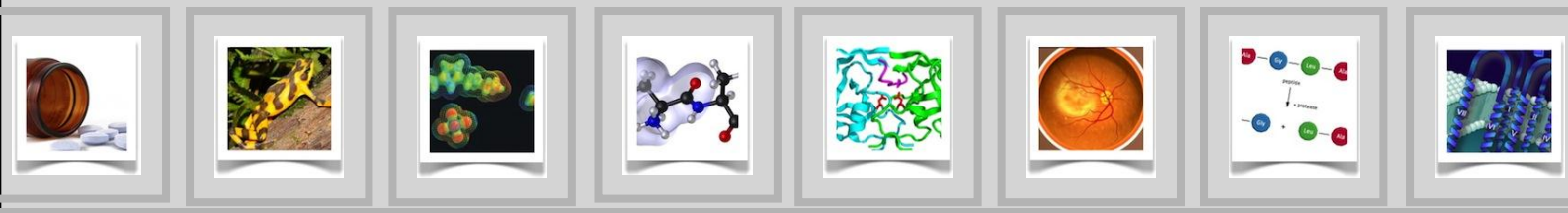

School of Pharmacy PhD Projects 2013

Project Title Accessing novel Therapeutics and Catalysts from common synthetic precursors through the combined use of Ionic liquids and mechanochemistry

Supervisors Dr Marie Migaud and Prof C. Hardacre

Description

Many of the limitations of the current phosphorus-based technologies, for example ligand design for catalysis or novel phosphorus-based therapeutics, stem from the difficulty in controlling the selectivity at the phosphorus centre. Restrictions are linked to the use of standard synthetic protocols which offer no scope for improved chemical control and cannot access fit for purpose chemicals. Functionalisation at the phosphorus centre can generate a vast range of properties in, for example, homogeneous catalysis and masked bisphosphonate pro-drugs. The latter would provide new therapeutic opportunities for medicines which possess poor bioavailability and biodistribution profiles.

Migaud/Hardacre have developed ionic liquid plus mechanical methodologies to effectively access high purity phosphorus-based chemicals. This approach allows the synthesis of a broad range of functionalisable phosphoramidites and phosphodiamidites which will extend their use in catalysis, green chemistry and drug development. These phosphorus reagents have been under-exploited in catalysis due to the lack of structural and functional group diversity. In this project, new technology to effectively prepare novel phosphorus-based catalysts which possess high efficacy and good recyclability, due to improved stability, will be developed and tested for industrially relevant reduction and allylic insertion reactions. Moreover, the phosphoramidites/phosphodiamidites are excellent synthetic precursors to unsymmetrical and masked bisphosphonates. The mechanochemistry plus ionic liquids process allows the synthesis of therapeutically relevant entities in yields and purity greatly exceeding state-of-the-art protocols. The next generation of masked bisphosphonates based on novel phosphoramidites/ phosphodiamidites will improve the bioavailability and therapeutic applications of pyrophosphate analogues for cancer and inflammation research and chemical biology.

Start Date October 2013

Keywords Green chemistry; phosphorus chemistry; ionic liquids; bisphosphonates; catalysis.

Contact Details
pharmacypostgrad@qub.ac.uk

How to Apply

Postgraduate applications should be made using Queen's Online:
http://go.qub.ac.uk/pgapply
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