**EPSRC DLA PhD Studentship**

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**Section 2 – *Project Information***

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| **Project Title** | New Approaches for Hydrogen Isotope Exchange Catalysed by Organoboranes |
| **Project Summary** | |
| Deuterium- and tritium-labelled organic compounds are crucial throughout academic and industrial research. They are utilised in the investigation of reaction mechanisms, neutron scattering, and in the drug discovery process from target identification to clinical trials. For example: (1) Receptor binding studies rely on the use of tritium-labelled molecules; (2) deuterium-labelled MS standards aid identification of metabolites from animal and human studies; (3) deuterium-labels serve as simple bioisosteres for hydrogen and can alter ADME properties, and; (4) regulatory authorities often require radiolabelled (i.e. tritium) in vivo metabolism studies. Approved deuterium-containing medicines are increasing in prevalence, and deuterium-derivatives offer the opportunity for new chemical entities, but no clear regulatory framework has yet been established. Therefore, synthetic methods that allow for precise control of regio-, chemo- and stereoselectivity will be of strategic importance and a late-stage incorporation approach via direct exchange (ie the direct replacement of hydrogen for deuterium or tritium in a complex molecule) avoids the need for costly and time consuming *de novo* synthesis.    The project will build on the Pulis’ group expertise in main group catalysis,[1-3] and will utilise the unusual and unique ability of organoboranes to activate α-amino C(*sp3*)−H bonds in the development of a new approach to late-stage deuterium- and tritium-labelling of amine-containing pharmaceutical compounds. The new methodology will be regioselective and deliver high levels of isotope incorporation that is suitable for a variety of different industrial and academic research applications.  The project borders on the traditional realms of organic and inorganic synthesis and therefore provides a unique training opportunity suitable for careers in industry (e.g. pharmaceutical, agrochemical, etc) and academia. You will receive high level training in synthetic organic chemistry and catalysis, including relevant analytical techniques (primarily NMR spectroscopy and Mass Spectrometry). There will be opportunities to go beyond these activities, and these may include synthesis and study of new catalysts, mechanistic investigations, and utilisation of new technologies, such as flow chemistry, to enable wider application of the novel methods that will be developed. In addition, we will work closely with established partners from the pharmaceutical industry to ensure that the methodology developed is suitable for industrial applications, and this may include performing late-stage-tritiation at an industrial site.  Informal enquiries are welcome and should be sent to Alex directly ([a.pulis@leicester.ac.uk](mailto:a.pulis@leicester.ac.uk)) | |
| **References** | |
| [1] Alvarez-Montoya, Gillions, Winfrey, Hawker, Singh, Ortu, Fu, Li, Pulis, *ACS Catal.* **2024**, *14*, 4856.  [2] Basak, Alvarez-Montoya, Winfrey, Melen, Morrill, Pulis, *ACS Catal*. **2020**, *10*, 4835.  [3] Basak, Winfrey, Kustiana, Melen, Morrill, Pulis, *Chem. Soc. Rev.* **2021**, *50*, 3720. | |