

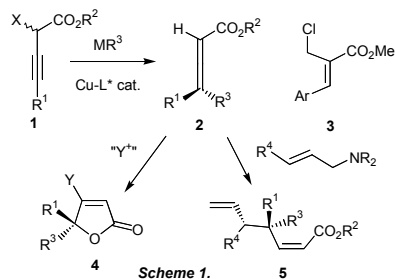
Summaries of the INDAC-CHEM studentships

- **Research**

The key element of the research training will be in synthetic organic chemistry and advanced catalysis. These skills will be gained through investigation of projects 1-8. Details of the skills gained will be recorded on a standardised Fellow Skills Record card across the whole Consortium.

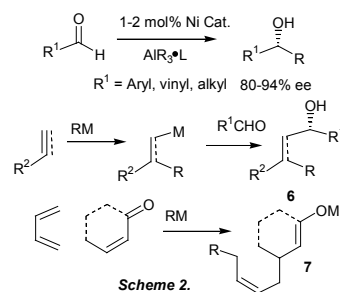
Scientific Details of the Eight Ph.D. Research Training Programmes.

Ph.D. Project 1: S_N2' additions to propargylic systems (Lead Host: Nottingham; Partner Host: Dortmund; Industrial Partner: GlaxoSmithKline). Training in asymmetric catalysis at Nottingham will centre around the development of a kinetic resolution, through the addition of $ZnEt_2$, AlR_3 , to propargylic **1** affording allenes **2** (Scheme 1). The new process will use the known reactivity of **3** where high stereoselectivity is known (80-90% ee, Woodward).

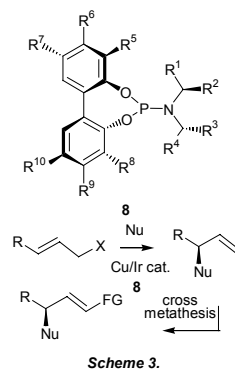


The fragments **2** will demonstrate potent transfer of chirality in subsequent reactions (to be explored in Dortmund and GSK; just two potential examples are shown). **[Objectives:** training in catalysis/synthesis; scope of new routes to bio-active heterocycles determined. **Milestones:** 1st and 2nd year reports, industrial visit report (year 2). **Deliverables:** >2 new selective processes developed].

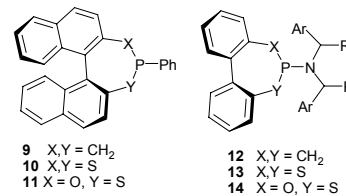
Ph.D. Project 2. Enabling organometallic reagents in asymmetric copper and nickel catalysis (Lead Host: Nottingham; Partner Host: Geneva; Industrial Partner: Radleys DT [SME]). Expertise in selective cascade reactions will be gained based on highly selective aldehyde addition chemistry already under development at Nottingham (Scheme 2). This chemistry will be teamed with the cascade approaches of Montgomery and Jamison to enable the synthesis of complex chiral fragments in one-pot operations (the examples of **6** and **7** are representative). The industrial partner will collaborate with the academics to offer training in high-throughput screening with the aim of making this available to the whole consortium through remote visual learning. **[Objectives:** training in catalysis/synthesis; development of new 'cascade' reactions. **Milestones:** 1st and 2nd year reports, development of remote visual learning (including technology transfer to industry, year 2). **Deliverables:** Commercial utility of 2 new processes to high value fine chemicals determined].



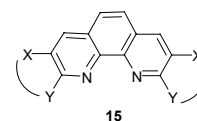
Ph.D. Project 3. Innovative Ligand design for asymmetric conjugate addition and S_N2' chemistry (Lead Host: Geneva; Partner Host: Nottingham; Industrial and other Partners: BASF/LIGBANK, Sassari). Research training in the library preparation of novel phosphoramidites **8** (Scheme 3) will be provided. Further training in high-throughput screening against copper and iridium-catalysed S_N2' chemistry will be realised. The ligands will also be tested in asymmetric conjugate addition reactions of air-stable $Me_3Al(DABCO)$, and related chemistry, during the stay at Nottingham. **[Objectives:** training in catalysis/synthesis; scope an utility of ligands determined. **Milestones:** 1st and 2nd year reports, integration of Alexakis group as an associate member of LIGBANK, year 1). **Deliverables:** >10 new ligands prepared, >100 catalyst trials carried out.].



Ph. D. Project 4. Novel chiral amines in asymmetric synthesis (Lead Host: Geneva; Partner Host: Dortmund; Industrial Partner: Firmenich). A Ph.D. programme in the field of chiral amine synthesis will be undertaken using methodology based on that in place in the Alexakis group. Both 1,2 C₂-chiral diamines (including 2,2'-bipyrrrolodine and heterocyclic carbenes derived from them will be prepared). Both of these species will be tried a ligands for binding Au(III) for potential application in asymmetric gold catalysis (see also project 7). [**Objectives:** training in synthesis; development of new carbene and organo catalysis. **Milestones:** 1st and 2nd year reports, industrial visit report (year 2). **Deliverables:** >10 new amines and carbenes prepared, scope of their catalytic utility defined].



Ph. D. Project 5. Biaryl ligands for superlative asymmetric catalysis (Lead Host: Sassari; Partner Host: Nottingham; Industrial Partner: Avecia). Ph.D. training through research will be in the area of phosphanes (**9**, **12**) and thiaphosphoamidites (**10-11**, **13-14**).

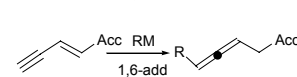
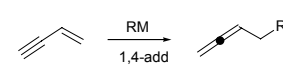
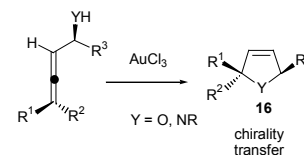


Scheme 4.

These ligands can be expected to be of utility in a wide range of asymmetric processes (catalytic cascades will be tried in Nottingham) based on the utility of the Feringa, BINEPINE and related ligand types. [**Objectives:** training in synthesis; development of new carbene and organo catalysis. **Milestones:** 1st and 2nd year reports, industrial visit report (year 2). **Deliverables:** >10 ligands prepared and their catalytic efficacy tested].

Ph. D. Project 6. Highly original chiral nitrogen heterocycles and their applications in catalysis (Lead Host: Sassari; Partner Host: Dortmund; Industrial Partners: Synkola/Tau-Chem [SMEs] coordinated by Prof. Stefan Toma Commenius University, Bratislava, Slovakia; LIGBANK). Both asymmetric and achiral substituted 1,10-phenanthrolines will be prepared (based on the general structure **15**, Scheme 4, X,Y = natural product derived chiral fragment or ferrocenyl unit). These ligand will be screened in gold-catalysed processes in the Krause group. [**Objectives:** training in catalysis/synthesis; scope an utility of ligands determined. **Milestones:** 1st and 2nd year reports, integration of Gladiali group as an associate member of LIGBANK, year 1). **Deliverables:** >5 new heterocyclic ligands prepared, their metal coordination and catalytic promotion effects defined].

Ph. D. Project 7. Utility of gold-catalysed reaction in organic synthesis (Lead Host: Dortmund; Partner Host: Sassari; Industrial Partner: Solvias). Ph.D. Training in the newly emerging area of organogold catalysis will concentrate on cycloisomerisation of α -heteroatom allenes to 3-pyrrolines **16** (Scheme 5). [**Objectives:** training in catalysis/synthesis; scope of new routes to bio-active heterocycles determined. **Milestones:** 1st and 2nd year reports, industrial visit report (year 2). **Deliverables:** >5 new catalyst systems to high value bioactive compounds defined.].



Scheme 5.

Ph. D. Project 8. Preparation and utilisation of enatio-enriched allenes (Lead Host: Dortmund; Partner Host: Nottingham; Industrial Partners: LIGBANK [FP6 STREP/SME], Schering). New approaches to the preparation of chiral allenes *via* either, S_N2', 1,4 or 1,6 additions of organometallic reagents will form the core of the Ph.D. training (Scheme 5). Chirality transfer in reactions of the products will be investigated. [**Objectives:** training in catalysis/synthesis; scope of ligand effects determined. **Milestones:** 1st and 2nd year reports, industrial visit report (year 2) **Deliverables:** Scope of processes defined.].