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MOLECULAR REARRANGEMENTS WITH CARBOCATION SURROGATES

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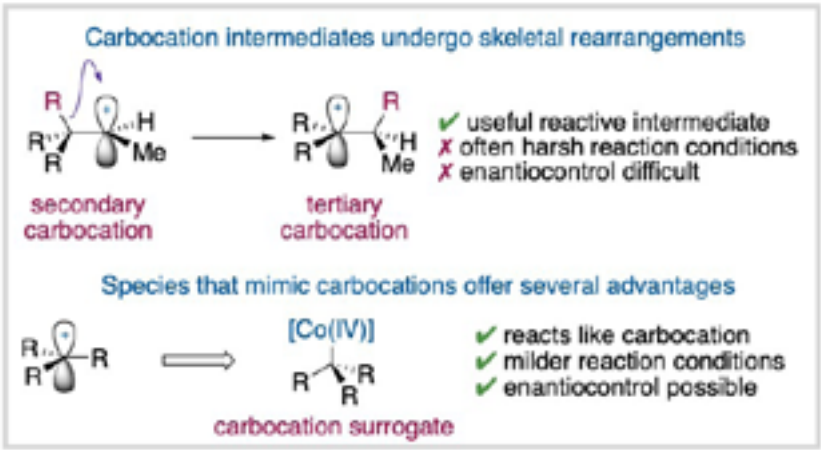
Carbocations are synthetically useful reactive intermediates as they can enable the structural modification of a molecule's carbon framework. However, the generation of these species typically involves harsh electrophiles (e.g. strong acid) and often results in mixtures of isomeric products. Therefore, reactions involving these charged reactive intermediates are inherently limited and often avoided when designing synthetic routes. We have shown that carbocation surrogates, such as alkylcobalt(IV) species, can be used to mimic the reactivity of carbocations in transformations involving the migration of aryl and alkyl-substituents. The conditions for these reactions are generally mild and non-acidic offering improved chemoselectivity and functional group tolerance. Moreover, as the cobalt catalyst is involved during the migration step these transformations can be rendered enantioselective using a suitable chiral ligand.



ORGANOCATALYTIC ASYMMETRIC SYNTHESIS OF α-AMINOPHOSPHINATES

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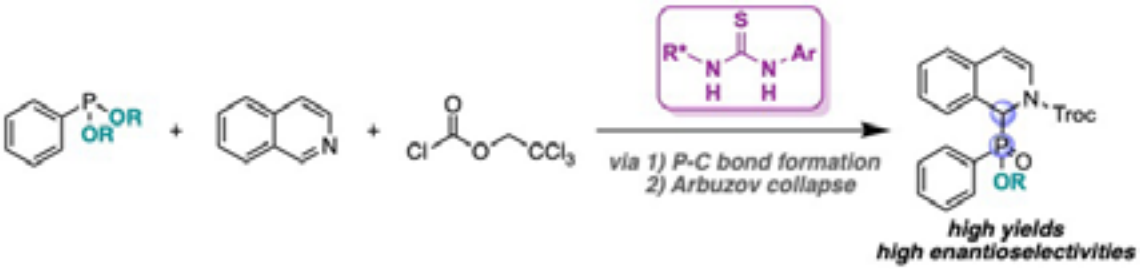
P-Stereogenic organophosphorus compounds have found widespread use as chiral ligands and are important molecules in medicinal and synthetic chemistry. α-Aminophosphinate derivatives are used as surrogates for α-amino acids, so it would be desirable to access *P*-stereogenic aminophosphinates. Jacobsen and co-workers showed that the enantioselective addition to acyl-activated isoquinolines could be achieved through anion-binding catalysis.[1,2] The Mukherjee group successfully applied this method to the synthesis of α-aminophosphonates by using silyl phosphites as nucleophiles in the enantioselective dearomatisation of isoquinolines catalysed by a chiral thiourea. They achieved high enantioselectivities for the C-stereogenic products.[3] Here, we report the organocatalytic additions of prochiral phosphonites to acyl-activated isoquinolines, giving access to α-aminophosphinates which bear both *C*- and *P*-stereogenic centres. An enantiopure chiral thiourea catalyst gave phosphinate products in moderate-to-excellent yields and enantioselectivities. The reactions are suggested to proceed *via* P-C bond formation followed by Arbuzov-type collapse at phosphorus. Our efforts to develop and understand this new route to enantioenriched α-aminophosphinates will be described.



Scheme 1. Organocatalytic synthesis of α-aminophosphinates containing P,C-stereogenic centres.

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(MIS)ADVENTURES IN ORGANOBORANE CATALYSIS: FUNCTIONALISATION AND DECONSTRUCTION OF AMINES

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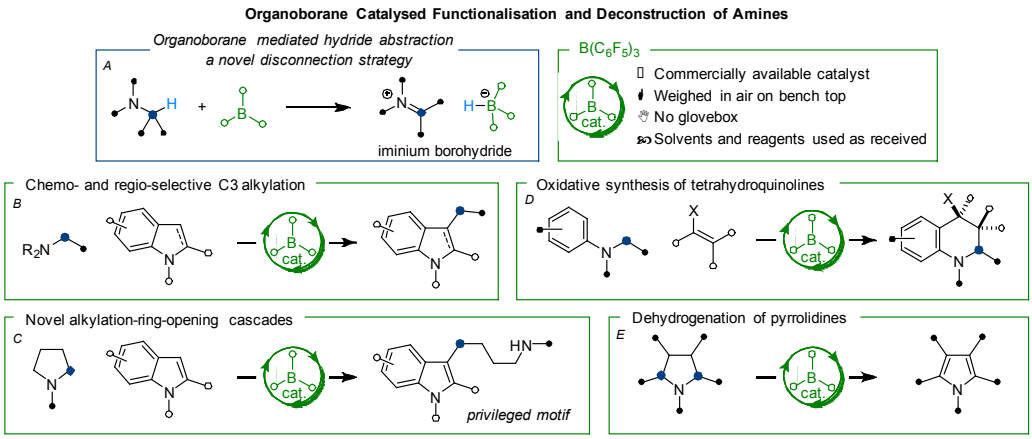
In classic borane chemistry, boron acts as a Lewis acid and activates polarised bonds by interacting with high-energy electron pairs, such as non-bonding electrons or π-bonds. The ability of boranes to interact with σ(C–H) bonds is not often exploited but has unrealised potential in chemical synthesis. When an electron deficient organoborane interacts with an α-*N* C(sp^3)–H bond of an amine, an organoborane mediated hydride abstraction (OBMHA) can occur, resulting in heterolytic cleavage of the C–H bond to form an iminium borohydride ion pair (Scheme A).[1] The Pulis group are using this unique reactivity to mediate unusual catalytic transformations that repurpose common amine starting materials for the generation of molecules relevant to drug discovery. In this talk, we will show how we are using OBMHA to form, functionalise and deconstruct *N*-heterocycles.

The alkylation of indoles and oxindoles generally has poor selectivity (N v C alkylation and over alkylation). Under organoborane catalysis we have shown that amines can be used as unique alkylating agents in the chemo- and regio-selective C3 alkylation of indoles and oxindoles (Scheme B).[2] We have also employed OBMHA in a novel alkylation-ring-opening cascade that rapidly prepares indolebutyl amines, a key motif found in serotonergic/dopaminergic drug molecules (Scheme C).[2] In addition, we are using OBMHA in an oxidative approach to the direct formation of tetrahydroquinolines from readily available anilines and alkenes that does not require stochiometric oxidants (Scheme D).[3] Finally, a novel dehydrogenation process was developed that utilises one of the most common and readily available *N*-heterocycles, pyrrolidines, to directly form pyrroles (Scheme E).[4]

The accessibility and ease of use is a central theme during the development of these processes. Our approaches to the functionalisation and deconstruction of amines use a commercially available organoborane catalyst, $B(C_6F_5)_3$, that can be used as received and weighed in air on an open bench. The reactions are user friendly and straightforward, and do not require the use of a glovebox, specialised glassware, and strictly anhydrous reagents and solvents.



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4. A. Alvarez-Montoya, J. Gillions, L. Winfrey, A. P. Pulis,* *Manuscript submitted*

NFROM SULFONIUM SALTS TO SAMARIUM CATALYSIS: NEW RADICAL CHEMISTRY FOR SYNTHESIS

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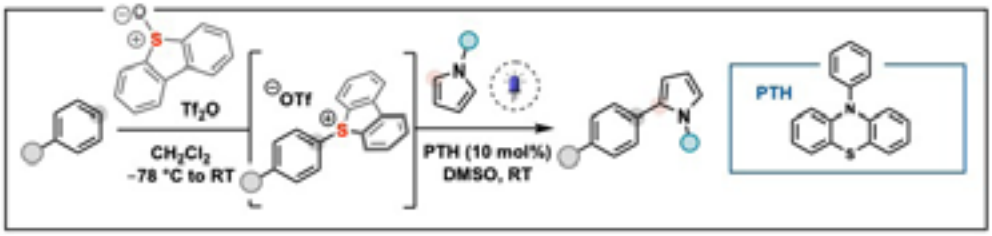
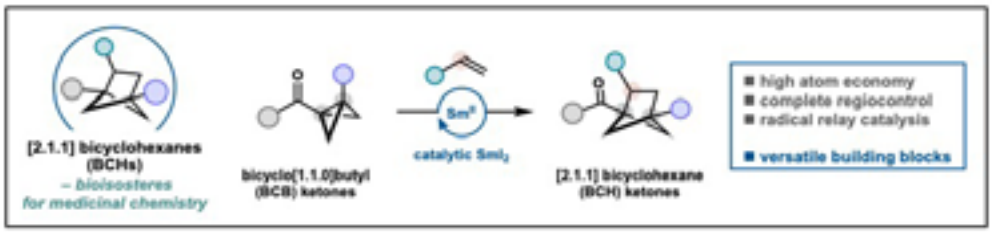
Part I – Our approach to the development of transition metal-free cross-coupling processes is based on the proposal that sulfur can replace metals in activating substrates and generating reactive intermediates for exploitation in C–C bond-formation. In particular, we will describe the exploitation of *in situ* generated aryl sulfonium salts in photocatalytic[1] and photochemical[2] coupling processes involving aryl radicals.



Part II – Samarium(II) iodide is one of the most widely-used single electron transfer reductants in chemistry. We will showcase the reagent's ability to unlock key steps in natural product synthesis[3] and will describe our recent studies on catalysis with SmI_2.[4,5,6]



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