Selective C–H Functionalization of Furfural and its Derivatives

Thesis Direction. Dr Julie Oble

Context of the project.

In order to develop an ever more eco-compatible synthetic chemistry, it is nowadays essential to synthesize intermediates and value-added chemical compounds starting from biomass derivatives rather than from fossil resources. Furfural 1 and the related compound 5-(hydroxymethyl)furfural (HMF) 2 are one of the most promising bio-based molecules. Obtained by dehydrating lignocellulosic biomass from agricultural residues and dedicated crops, these molecules have great potential as a renewable platform for the sustainable production of fine chemistry products. In particular, the direct functionalization of furfural derivatives by selective C–H activation is an emerging field that is attracting considerable interest. However, the main difficulty in developing a catalytic system for functionalization of biomass-derived furfurals is the low stability of furans. Therefore, a special quest for stabilizing substituents at C3 and/or C4 positions of furanic platforms is essential in order to improve chemical and thermal stability of the furanic core. This will help solving the important practical problem of furans instability and will pave the way for the synthesis of new biomass derived building block and in turn new industrial applications.

Previous results.

Within a broad project directed towards the sustainable C–H functionalizations of furfural derivatives, the selective formation of new bonds through the direct transition metal (TM) catalyzed C–H activation process without modification of the redox state of the aldehyde function, has become one of our recognized research areas (J. Oble in collab. with G. Poli). In the last years, we have developed a number of directed Ru(0)-catalyzed C3 functionalizations of furfurylimines, such as the alkylation (eq. A without CO), arylation, alkenylation (eq. B) and acylation (eq. A with CO), that involved the directed C–H activation of the furan ring. In addition, we also performed a directed Ir-catalyzed C3–H silylation of furfuryl imines with various silanes (eq. C). This transformation gives access to even more versatile platforms which have allowed for additional derivatizations relying on original C–Si bond functionalization chemistry developed through collaborative work within the ROCS group (collab. with A. Perez-Luna). These include Pd-catalyzed cross-coupling reactions (arylation or alkenylation), Ag-mediated halogenation or Cu-mediated alkylation.
Objectives of the project.

In order to extend further the synthetic utility of these processes, we now plan to develop alternative reactions involving the addition of silanes (R₂SiH₂) onto furfural 1 (eq. D) or onto HMF 2 (eq. E) after acetalisation of the aldehyde function. The formation of hydridosilyl ether intermediates followed by a catalytic intramolecular dehydrogenative cyclization in C3 or C4 position could lead to oxasilole derivatives having C–Si bonds poised for further derivatizations.⁹

Another study will be devoted to the directed borylation.¹⁰ We will focus first on Ir(I) or Ru(0)-catalyzed protocol with B₂pin₂ under standard conditions previously developed on aromatic aldimines (eq. F).¹¹ Then, after acid hydrolysis, we will modify the boronic acids with anthranilamide (aam), which could serve as directing agent for transition-metal-catalyzed C4-H functionalizations such as, for example, silylation (eq. F). This will provide a highly versatile platform bearing two modular units: the boron and the silicon groups.¹²

All these processes will be also extended to pyrrole 2-carboxaldehydes,⁷ which can also be considered as a biomass-derived building block, given their accessibility from furfurals in one step (or three steps).

Finally, a special attention will be given to the use of these silyl- and boryl-furfural synthons as nucleophilic partners in Pd-catalyzed cross-couplings, which could be envisioned in a domino sequence.¹³ These couplings will lead to a variety of C3-substituted (or C4-substituted) furfurals, which will in turn grant access to an even broader range of polyfunctionalized synthons via rapid post-functionalization protocols.

Requested Profile. Master and/or chemical engineer degree (obtained at latest by the end of the present academic year). Good knowledge of molecular chemistry and catalysis is essential. The candidate must be motivated, curious and rigorous in order to carry out this project.

Location. Sorbonne Université, IPCM (Institut Parisien de Chimie Moléculaire), ROCS team (Réactivité Organométallique et Catalyse pour le Synthèse).

Contact. julie.oble@sorbonne.universite.fr (01 44 27 41 14)

References

3 Karlinskii, B. Y.; Ananikov, V. P. ChemSusChem 2021, 14, 558.


7 Unpublished results (PhD Sebastien Curpanen in progress – end 2021).


