

AAP China Scholarship Council - CSC 2023 PROJET DE RECHERCHE DOCTORALE (PRD)

Titre du PRD : Catalytic Functionalizations of 5-(Hydroxymethyl)furfural by Selective C–H Activations

DIRECTION de THESE

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Ecole doctorale de rattachement : ED406 - Chimie moléculaire de Paris Centre

Nombre de doctorants actuellement encadrés : 1 + 1 (Soutenance en déc. 2022)

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Ecole doctorale de rattachement : ED406 - Chimie moléculaire de Paris Centre

Nombre de doctorants actuellement encadrés : 2

CO-TUTELLE INTERNATIONALE envisagée : OUI NON

DESCRIPTIF du PRD :

Context. Despite advances in research, fossil resources remain the main source of platform molecules for industrial chemistry. With the increase in global consumption and the demands created by global warming, it is becoming urgent to reduce our dependence on these depletable resources, and thus to rethink the way we design chemistry.¹ One solution to overcome this outcome is the use of renewable biomass, composed in abundance of carbohydrates, which are ideal precursors for the production of environmentally friendly chemicals.² However, this prospect raises questions related to a negative impact on food production, as it could divert food crops to other purposes. In this regard, lignocellulosic materials (cellulose, hemicellulose and lignin), being non-edible, do not suffer from the aforementioned drawbacks. More interestingly, they also represent the most abundant plant dry matter on earth, which can be used as a source of carbon in biorefineries, and is often present in large quantities in agricultural and forestry wastes.³

Today, the valorization of lignocellulosic biomass has therefore become a central strategy for the replacement of fossil resources. For example, versatile synthons such as furfural and 5-(hydroxymethyl)furfural (HMF) can be obtained from hemicellulosic materials after an acid-catalyzed digestion / cyclodehydration sequence (Figure 1).⁴ Their industrial production being considered feasible worldwide from agricultural residues and wastes,⁵ their use seems suitable for fine chemical purposes. The U.S. Department of Energy has thus ranked these two compounds in the "Top 10" most valuable biomass-derived chemicals because of their high reactivity, which allows them to be used as platform compounds for the synthesis of value-added chemicals or biofuels.^{6,7}

Premise and previous results. Studies on the conversion of furfural or HMF into building blocks have highlighted difficulties related to the low stability of the furan ring, which is associated with this low aromaticity. Therefore, specific research on the introduction of stabilizing substituents at the C3, C4, and/or C5 positions of furan-based platforms has become essential to improve the chemical and thermal stability of the furan ring. These functionalizations will solve the important practical problem of furfural instability and will also pave the way for the synthesis of new biomass-derived building blocks and, consequently, for new industrial applications.

In recent years, organic chemists have therefore developed new protocols for the formation of new bonds from furfural derivatives. In particular, their direct functionalization by transition metal catalyzed C–H activation processes has become an area of growing interest where only a few methods have been reported.⁸ Being furan an electron-rich aromatic ring, most examples of reactivity deal with C5-functionalization, which is the most electron-rich site. In contrast, C3–H functionalizations of the formyl-furan unit *via* directing groups, as well as C4–H functionalizations, which circumvent the natural preference at C5, have been much less studied. In the last year, the selective formation of new bonds by a C–H activation process, without modification of the redox state of the formyl function, has become one of our main research axes (J. Oble). We developed a number of functionalizations of the C3–H bond of furfurals, which represented a synthetic challenge. For this purpose, the use of appropriate furfurylimines, allowing a directed C3–H activation of the furanic ring, opened the way to Ru(0)-catalyzed alkylation, arylation, acylation and alkenylation, as well as to Ir(I)-catalyzed silylation (Figure 1).⁹

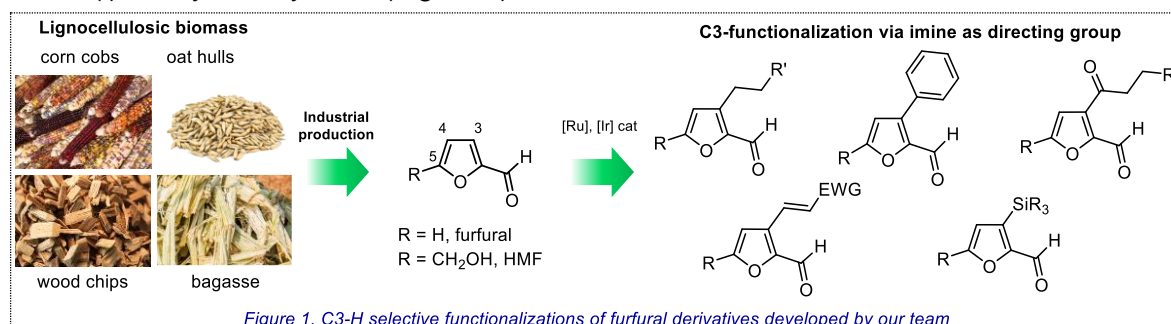
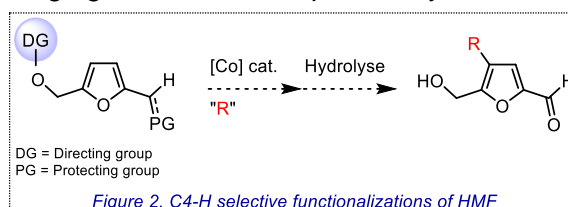


Figure 1. C3-H selective functionalizations of furfural derivatives developed by our team

Objectives. This project is therefore a logical continuation of this work started in 2017 and supported by H2020 funding on the functionalization of biomass derivatives. We now wish to develop innovative strategies for the selective C–H functionalization of the C4 position of the 5-

(hydroxymethyl)furfural. To this purpose, well-designed transient directing groups will be attached to the hydroxymethyl substituent of HMF, and will direct the C–H activation step at the C4 position. The influence and the presence or not of a protective group on the aldehyde function will be carefully studied. It should be noted that, to our knowledge, no C4–H functionalization of HMF has been reported yet. Moreover, in order to go towards the most sustainable processes possible, the use of complexes based on cobalt, a first rank transition metal which is cheap, abundant and rather harmless for the environment, will be considered. This type of complex has indeed shown to be very promising in many C–H activation reactions,¹⁰ as the recent works developed by M. Petit,¹¹ with very good positional selectivity. These strategies will allow us to further decorate the furanic core, in order to access libraries of new emerging molecules with potentially new industrial applications.



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. All the usual techniques of organic and organometallic chemistry will be used: reactions under inert atmosphere, glovebox, handling of organic and organometallic reagents, characterization techniques of organic products (TLC, NMR, IR, UV-Vis, HRMS, HPLC, GC).

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