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Concurrent Hybrid Catalysis at acidic pH for Rare Monosaccharide Production by Combining Aldolase and N-Heterocyclic Carbene Gold Catalysts

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PURPOSE OF THE ABSTRACT

Hybrid catalysis has been increasingly developed in recent years. Indeed, it takes advantage of the robustness and the broad range of applications of the chemical catalysts combined with the high regio, chemo and/or stereoselectivity of the enzymes. Among chemical catalysts, transition-metal complexes are considered as one of the most powerful. Furthermore, metal catalysts working in water are recently emerging, giving opportunities to couple them with enzymes whose natural medium is aqueous. Thus, various examples of combination of biocatalysts and metal-catalysts for linear cascades have been reported, but often in a sequential mode, because of various incompatibilities that could not be solved (for instance: pH, temperature, substrate concentrations, inhibition problems, etc...). Indeed, few one-pot one-step processes, i.e., involving the addition of all the reagents and catalysts from the beginning, without any changes in the operating conditions till the end, are described. The reason is often an incompatibility of the catalysts with each other, or with the operating conditions. Several techniques have overcome these difficulties by compartmentalization using either cells, biphasic systems, artificial metallo-enzymes or supramolecular hosts. Combined with techniques of enzymes evolution, in order to make biocatalysts more robust, in particular with respect to the temperature of the medium or the concentrations of substrates, these methods have made it possible to solve almost all the reasons of incompatibilities of the catalysts between them, except, to our knowledge, when the incompatibility comes from the pH.

In our work, a chemical catalyst, a N-heterocyclic carbene gold complex, only capable of operating at pH 3, was successfully coupled to an aldolase, the Fructose-6-phosphate Aldolase, previously confined in cells to protect it from this extreme pH. The catalyst working better at 60°C, cells were in turn immobilized on Layered Double Hydroxides (LDH), specially designed to resist to pH 3, so as not to degrade cell membranes at this temperature. Finally, to avoid any mutual deleterious interactions between chemical catalyst and the immobilized cells harboring the aldolase, a compartmentalization has been set up thanks to a semi-permeable membrane. Thus, as proof of principle, propargyl alcohol, a cheap and achiral compound, could be hydrated, using a fair range of substrates concentrations (200-500mM) for easier scale-up, and subsequently converted to the corresponding aldol, a high added-value compound with one asymmetric center with fixed configuration, at pH 3 and 60°C, in 70% isolated yield. Interestingly, this process could be exemplified to another concurrent reaction involving an acidic resin catalyzed acetal hydrolysis to the corresponding aldehyde, as aldolase electrophilic substrate, particularly useful in the case of unstable aldehydes. This latter system, even simpler than the previous one, gave the corresponding aldol in 98% yield, with two asymmetric centers with fixed configurations.

FIGURES

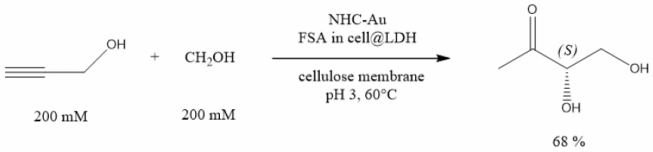

FIGURE 1

Hybrid system

optimized conditions for the one-pot concurrent hydration-aldolisation reaction

FIGURE 2

KEYWORDS

Hybrid catalysis | Layered double hydroxide | Organometallic catalyst | enzyme

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