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Glycerol carbonates as an innovative alkylating agents for phenolics

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PURPOSE OF THE ABSTRACT

Organic carbonates (OCs) are an important class of molecules with a wide range of applications, such as aprotic polar solvents, monomers, surfactants, plasticizers and electrolytes to name a few. OCs peculiarities are the non-toxicity and a good biodegradability.1 Because of these reasons their importance as chemical intermediates is continuously increasing. Nowadays, cyclic carbonates (e.g ethylene and propylene carbonate) are synthesized from the corresponding epoxides and CO2 by a cycloaddition reaction.2 On the other hand, the utilisation of glycidol, a toxic and carcinogenic compound, as a starting material for the synthesis of glycerol carbonate (GlyC) is not desirable. For this reason, we have recently proposed the utilisation of catechol carbonate (CC) as an alternative, extremely efficient carbonate source for the selective synthesis of a wide plethora of both cyclic alkylene or symmetric dialkyl carbonates, by the reactions with the parent aliphatic alcohols or polyols. Indeed, starting from a stoichiometric amount of glycerol and CC, in the presence of a basic catalyst (e.g. NaOCH3 or MgO), the results obtained in very mild reaction conditions (40-60°C, ambient pressure) and low reaction time (30 to 60 minutes), proved an unprecedented outstanding potential of CC, that promoted the quantitative, selective, formation of GlyC and of course catechol as co-product of the reaction. 3 For this reason, the so-formed GlyC was tested as a pioneering alkylating agent for catechol, by only increasing the temperature from the previous step in a one-pot strategy. Indeed, only a few works in literature have investigated the possibility of using GlyC as an alkylating agent for the derivatization of aromatic compounds. 4 In this way, 2-hydroxymethyl-1,4-benzodioxane (HMB), has been selectively synthesized, without requiring any reaction solvent nor halogenated compounds, in the presence of both homogeneous (NaOCH3) or heterogeneous (MgO, Na-Mordenite) basic catalysts (Scheme 1). HMB is a key intermediate for pharmaceutical industries because its moiety is present in many active principles of antidepressant (e.g. Doxasozin), antihypertensive, anxiolytic, and antithrombotic drugs, in addition to cardiovascular agents, to name a few. Currently, HMB synthesis required a multistep sequence of reactions and the use of toxic solvents (DCM and DMF) and reagents (glycidol derivatives, pyridine etc.).5 In our optimized conditions, a slight excess of GlyC has been reacted with catechol in the presence of a homogeneous basic catalyst (NaOCH3) at 170°C for just one hour; both reagents have been quantitatively converted with a HMB yield up to 88%. Notably, the main side product, the HMB isomer, may be an interesting intermediate for the synthesis of calone analogues, which are important scaffolds used in fragrances. Moreover, a detailed mechanistic study, supported by kinetics, GC-MS, and HMBC NMR has been performed, underscoring the unique behaviour of GlyC compared to other organic carbonates (e.g. propylene carbonate) and the importance of GlyC as a multifunctional structure, in particular of the free aliphatic -OH group. The latter plays a fundamental role in obtaining the reactive carbonate intermediate responsible for the intramolecular cyclization aimed at the selective formation of HMB, with only water and carbon dioxide as benign coproducts. The reported results represent a completely innovative and greener synthesis pathway to benzodioxanes.6

Finally, the reaction of glycerol carbonate and phenol has been investigated tuning the reaction conditions with

the aim of optimizing the synthesis of mono or di-phenylglyceryl ethers or their more valuable derivatives.

FIGURES

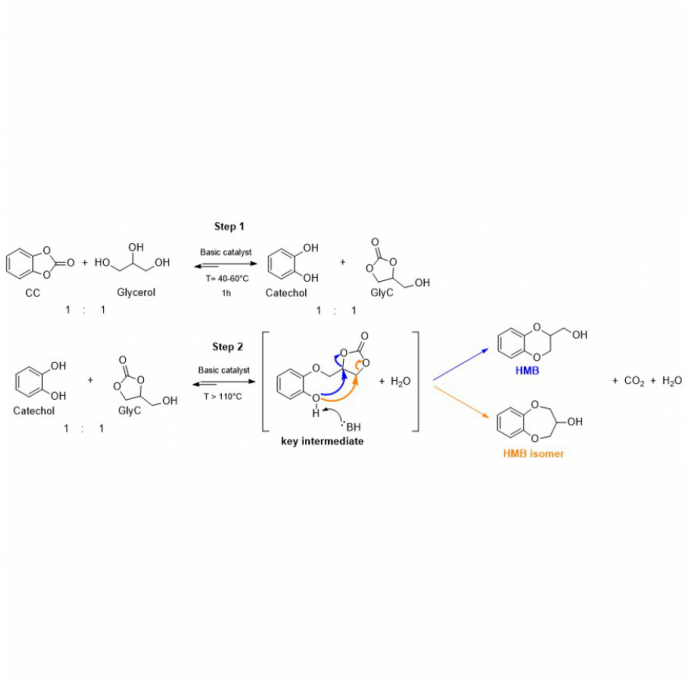

FIGURE 1

Scheme 1

HMB innovative synthetic pathways from glycerol and catechol carbonate

FIGURE 2

KEYWORDS

Glycerol carbonate | 2-hydroxymethyl-1,4-benzodioxane (HMB) | Catechol | basic catalyst

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