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Glycerol carbonate, an innovative alkylating agent for phenyl-glyceryl ethers synthesis

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PURPOSE OF THE ABSTRACT
Organic carbonates (OCs) represent a class of molecules on which both industrial and academic institutions have focussed great attention in the last decade.
The growing interest is based not only on the fact that it is possible to obtain these molecules in a sustainable way from alcohols and CO2, but also on the promising properties that are generally displayed, such as good biodegradability, low toxicity and high solvency. [1]
Glycerol carbonate (GlyC) emerges as one of the most interesting members of OCs for several reasons, starting from its renewable origin and its versatile structure and reactivity. Noteworthy, it represents an interesting candidate for the valorization of glycerol, which is coproduced in high amounts during biodiesel production: it is in fact possible to obtain biobased glycerol carbonate starting from glycerol, through different synthetic routes such as carbonation processes with CO/O2 or directly CO2, or transcarbonation reactions. [2] On the other hand, the simultaneous presence of a cyclic carbonate structure and a primary hydroxyl group, which bring both soft and hard electrophilic sites as well as a nucleophilic centre, allows GlyC to be suitable for a wide plethora of applications, spacing from high-boiling point solvent to uses as electrolyte carrier in batteries, in polymer and pharmaceutical intermediates preparations and so on.
Recently, our group has demonstrated the very peculiar behaviour of GlyC in alkylation reactions on phenolic derivatives, particularly in the synthesis of 2-hydroxymethyl-1,4-benzodioxane (HMB), a key moiety of several APIs, starting from catechol. Through this process, carried out in solventless conditions and in presence of cheap basic catalysts, it has been possible to obtain HMB with high yields and selectivity (i.e. around 88%). [3]
Following these encouraging results, the focus has been moved to the exploitation of glycerol carbonate in the alkylation of phenol and its derivatives to obtain both mono and di-phenyl glyceryl ethers (Scheme 1a). These molecules, generally synthesized through a nucleophilic attack of phenol derivatives onto epichlorohydrin, glycidol or 1-chloroglycerol, are reported to be applied both in pharmaceutical and surfactants field. Nonetheless, the possibility to use GlyC as alkylating agent for phenolics represents an innovative synthetic strategy, scarcely explored in literature. [4] Therefore, this reaction has been studied in liquid phase at atmospheric pressure and batch, solventless conditions over a series of both homogeneous and heterogeneous basic catalysts (e.g. NaOCH3, K2CO3, MgO and Na-mordenite). Moreover, the effect of several reaction parameters such as reaction time, temperature and reagents molar ratio has been investigated in order to better understand the reaction scheme and in this way optimising yield and selectivity toward the target products.
Interestingly, after only one hour of reaction between phenol and GlyC, with the latter in a slight excess, at 170 °C and using K2CO3 as a cheap catalyst (loading 6,6 mol%), a full conversion of both the reagents and good yields in monophenoxy glycerol (3-phenoxy-1,2-propanediol) and diphenoxy glycerol (1,3-diphenoxy-2-propanol) were obtained, with the first displaying the highest selectivity (54%).
Moreover, a multistep process has been investigated to obtain selectively diphenyl glyceryl ethers: by reacting the monophenoxy glycerol, obtained as main product in the one-pot approach, with dimethyl carbonate, it has been possible to obtain 4-(phenoxy)methyl-1,3-dioxolane-2-one (phenoxy glycerol carbonate, PhOGlyC), the key

intermediate for the production of diphenoxy glycerol. Indeed, by reacting this intermediate with phenol in a further step, the desired product has been obtained with a yield as high as 63% (Scheme 1b).

FIGURES

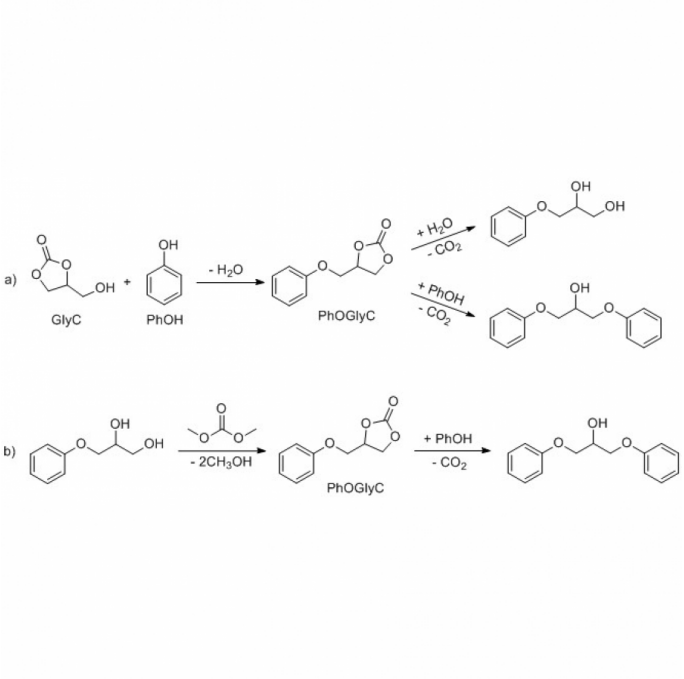

FIGURE 1

Scheme 1:
a) reaction between GlyC and phenol to yield mono- and diphenylglyceryl ethers;
b) multi-step approach for the selective synthesis of diphenylglyceryl ethers.

FIGURE 2

KEYWORDS

Glycerol carbonate | Phenyl glyceryl ethers | Solventless | Basic catalysis

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