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Lipase-Catalyzed Glucose Fatty Acid Ester Synthesis in Ionic Liquids

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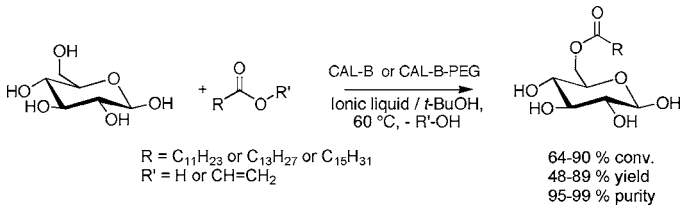
ABSTRACT



Glucose fatty acid ester synthesis with poly(ethylene glycol)-modified *Candida antarctica* lipase B (CAL-B) was performed in pure 1-butyl-3-methyl imidazolium tetrafluoroborate [BMIM][BF_4] (30% conversion) and in pure 1-butyl-3-methyl imidazolium hexafluorophosphate [BMIM]-[PF_6] (35% conversion). In a solvent system composed of ionic liquid and 40% *t*-BuOH conversions up to 90% and isolated yields of up to 89% were achieved using fatty acid vinyl esters as acyl donors and commercial CAL-B.

Sugar fatty acid esters are nonionic surfactants widely used in the pharmaceutical, cosmetic, and food industry. A synthesis directly from sugar and fatty acid is preferred, but this is difficult to achieve because of the low solubility of sugars in organic solvents. Only a few solvents (e.g., pyridine) are able to dissolve the highly polar sugar and the nonpolar fatty acid.[1] Major disadvantages are denaturation of most lipases and incompatibility of the solvents for products used in food applications. Alternatively, solubility was increased by using protected sugars (e.g., isopropylidene, phenylboronic acid derivatives)[2] or alkyl glycosides.[3] However, either this requires extra protecting and deprotecting steps or the products show different properties compared to nonderivatized sugar fatty acid esters. Another method described by our group is based on a solid-phase system,[4] which enabled up to quantitative sugar ester yields. However, problems arise during up-scaling and reactions cannot be run continuously.

Ionic liquids[5] have no measurable vapor pressure and are able to dissolve compounds of varying polarity.[6] In addition, it was shown that lipase-catalyzed reactions can take place in ionic liquids.[7] Kazlauskas and Park observed that lipase-catalyzed acylation of glucose with vinyl acetate proceeded with substantially higher regioselectively compared to conventional solvents.[8] Kim and co-workers described the selective enzymatic acylation of alkyl glycosides in ionic liquids and noticed enhanced reactivity and regioselectivity.[9] However, contradictory reports were published, in which the same lipase was found active or inactive in ionic liquids, making their straightforward application somehow unpredictable.[10]

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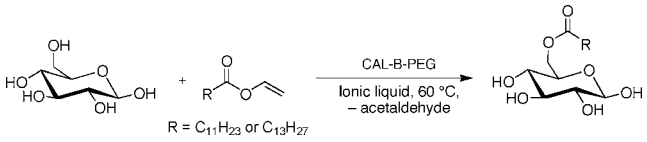
We here describe for the first time that glucose fatty acid esters can be obtained directly from glucose and fatty acids (or their corresponding vinyl esters) using ionic liquids as solvent (Scheme 1).

Scheme 1. Glucose Fatty Acid Ester Synthesis Using CAL-B−PEG in Ionic Liquids



Initially, we tested several imidazolium-based ionic liquids as reaction media for sugar ester synthesis using lipase B from *Candida antarctica* (CAL-B). The enzyme was chosen because it was identified as the most active enzyme in sugar ester synthesis in previous studies.[4] Unfortunately, starting directly from glucose and lauric acid vinyl ester, no enzyme activity was found using pure ionic liquids. Thus, various immobilization methods were investigated, as we assumed that the type of carrier could contribute to enzyme activity in ionic liquids. Indeed, it turned out that activity could be obtained upon immobilization of CAL-B with PEG.[11] Conversions of 30% in the presence of pure [BMIM][BF_4] and 35% for [BMIM][PF_6] could be observed using lauric and myristic acid vinyl ester as substrate. Still, no sugar ester synthesis took place using free fatty acids as substrate.

It was already known from the literature that, in principle, *t*-BuOH could be used as solvent for sugar ester synthesis. However, the solubility of glucose is very low (0.34 mg/mL at 25 °C), and only in the solid-phase system could acceptable conversion be achieved.[4a] Nevertheless, addition of *t*-BuOH to the ionic liquid was studied, and it turned out that even with commercial CAL-B (Chirazyme L2 C2) glucose fatty acid ester synthesis could be observed in [BMIM][BF_4] containing 40% *t*-BuOH (Scheme 2). Moreover, free fatty acids also reacted, and substantially higher conversion and isolated yield were achieved (Table 1).

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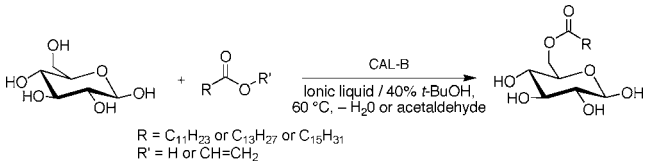
Table 1. Preparative Scale Reactions using a Mixture of [BMIM][BF_4] and 40% *t*-Butanol[a]

substrates [glucose +]	conversion [%]	yield [%]	purity [%]
lauric acid vinyl ester	90	75	99.8
myristic acid vinyl ester	89	89	95.1
palmitic acid	64	48	99.8

[a] 5 mmol glucose, 10 mmol fatty acid (vinyl ester). Enzyme: Chirazyme L2 C2 (CAL-B).

Similar results were found using [BMIM][PF_6]. NMR analysis confirmed that the 6-*O*-monoester was formed exclusively.

Scheme 2. CAL-B-Catalyzed Synthesis of Glucose Fatty Acid Esters in a Two-Solvent System



Thus, we could demonstrate that a lipase-catalyzed synthesis of glucose fatty acid esters is possible in the presence of ionic liquids, allowing for almost quantitative conversion in *t*-BuOH. Both solvents are considered safe and should be appropriate for an application of sugar esters, e.g., as emulsifiers in food applications. In contrast to a solid-phase system, which gives similar conversion and purity, this process should be easy to scale up and could also be run in a continuous manner.

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Supporting Information Available: Experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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