Tetrahedron Letters 55 (2014) 133–136

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Room temperature synthesis of glycerol carbonate catalyzed by *N*-heterocyclic carbenes

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ARTICLE INFO

Article history:
Received 20 September 2013
Revised 23 October 2013
Accepted 28 October 2013
Available online 4 November 2013

Keywords:
N-Heterocyclic carbenes
Organocatalysis
Room temperature
Glycerol carbonate
Dimethyl carbonate

ABSTRACT

N-Heterocyclic carbenes were used as efficient organocatalysts for the synthesis of glycerol carbonate from glycerol and dimethyl carbonate. The reaction takes place in a liquid mixture of reactants without solvent at room temperature. It provides glycerol carbonate in high yield using 2.6–4 mol % of catalyst in a reaction period of 20–30 min.

An important goal for sustainable chemistry is the development of synthetic methodology that minimizes or eliminates the use of solvents, reduces the consumption of energy, and generates minimal wasted chemicals and by-products. Catalysts can play a central role in achieving these goals. The transformation of renewable resources such as glycerol into useful products through catalytic methods is one example. Glycerol, a triol, is obtained from fats and oils by saponification, hydrolysis, or transesterification. The production of biodiesel has increased glycerol surplus. The production of 1000 kg of biodiesel yields roughly 110 kg of crude glycerol.

Glycerol is a useful and inexpensive material that can be transformed into several useful chemicals such as glycerol carbonate,[1–3] acrolein,[1,2,4] and dihydroxyacetone,[1,2,5] among others. Glycerol carbonate applications are increasing because it has low flammability, and is water-soluble, nontoxic, and biodegradable.[1–3,6,7]

The direct conversion of glycerol and carbon dioxide into glycerol carbonate is difficult; yields are low and the reaction conditions are harsh.[6,8] However, the transesterification between glycerol and dimethyl carbonate is a good alternative that yields glycerol carbonate in high yields.[3c,5a] The reaction can be catalyzed by potassium carbonate,[3a] enzymes,[9] and other catalysts.[10]

It has been reported that imidazolium carboxylates can catalyze the transesterification between glycerol and dimethyl carbonate, providing good yields of glycerol carbonate in 30 min at 74 °C.[11] Imidazolium carboxylates generated from *N*-heterocyclic carbenes (NHC) and carbon dioxide and other methods,[12,13] can transfer NHC to metals forming the corresponding complexes.[12] Imidazolium carboxylates are prone to thermal decarboxylation, they decompose almost completely above 80 °C,[12,13] and the free NHC is likely to be the catalyst for the transesterification reaction between dimethyl carbonate and glycerol at 74 °C.[11]

Transesterifications for the synthesis of glycerol carbonate using dimethyl carbonate are attractive because of its low toxicity, it can be readily synthesized from CO_2 and renewable resources, and avoids the use of toxic reagents such as phosgene.[14] Drawbacks of current syntheses of glycerol carbonate from dimethyl carbonate and glycerol include prolonged heat, long reaction times, and environmental impact. The use of NHCs as catalysts appears to offer improvement. NHCs have been used as organocatalysts[15] in transesterification,[17] polymerization,[17b,18] asymmetric synthesis,[15a] and other processes.[15] We report herein results for the transesterification of dimethyl carbonate and glycerol catalyzed by *N*-heterocyclic carbenes at room temperature.

Our findings for other organocatalyzed reactions showed that NHC precursors with *N*-alkyl and *N*-xylyl substituents on the imidazolium core are more effective than imidazolium salts with two *N*-alkyl substituents.[16] The NHC precursors were synthesized by alkylation of the known 1-(2,6-dimethylphenyl)-1*H*-imidazole (**1**), prepared from 2,6-dimethylaniline by a reported method.[19a,b] The NHC precursor **2** was used for the development of reaction conditions, Figure 1.

The NHC was generated in dimethyl carbonate by deprotonation of the imidazolium salt precursor with potassium *tert*-butoxide. Dimethyl carbonate served as reagent and solvent, to which glycerol was subsequently added. Initially, equimolar amounts of

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http://dx.doi.org/10.1016/j.tetlet.2013.10.135

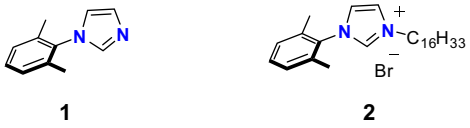


Figure 1. Structures of 1-(2,6-dimethylphenyl)-3-hexadecylimidazolium bromide **2** and its imidazole precursor.

glycerol and dimethyl carbonate were treated with 5 mol % of the NHC catalyst generated in situ as described above. The reaction afforded glycerol carbonate in 72.5%, after 40 min at room temperature without evidence of by-products detectable by proton NMR.

Reported syntheses of glycerol carbonate by transesterification of glycerol and dimethyl carbonate with other catalysts have used molar ratios from 1:3 to 1:3.5.[3a,11] The reaction is reversible and we monitored the conversion by proton NMR. By varying the amount of catalyst **2** with equimolar amounts of glycerol and dimethyl carbonate, the reaction gives a conversion profile as shown in Figure 2. With adequate catalyst load and reaction time, the reaction gives a plateau at 72.5% conversion, which represents the equilibrium concentration of the product. The reactions at 20 min give conversions lower than the equilibrium yield when the catalyst precursor **2** loading is less than 4%. Higher catalyst loads afford faster attainment of equilibrium but do not change the equilibrium composition. A catalyst load of 4 mol % and 20 min of reaction time is adequate to reach equilibrium condition.

Data for the reaction at 20 min are shown in Table 1 with results for additional experiments aimed at investigating catalyst **2** performance. The first six entries show the effect of catalyst loading on the progression toward equilibrium that is shown in Figure 2. No reaction occurs in the absence of catalyst (entry 1). The NHC generated from **2** and KO*t*-Bu is more active as catalyst than KO*t*-Bu by itself, Table 1 (entries 6 and 7). It has been reported that molecular sieves improve the yields of other transesterification reactions by absorbing the methanol by-product.[17a] In our case, however, molecular sieves deactivate the catalyst, providing no glycerol carbonate after 60 min, (entry 8).

The results in Table 2 show the effect of different molar ratios of glycerol to dimethyl carbonate on the equilibrium yield of glycerol carbonate. These experiments were conducted using 4 mol % of NHC catalyst generated from **2** and KO*t*-Bu, at room temperature

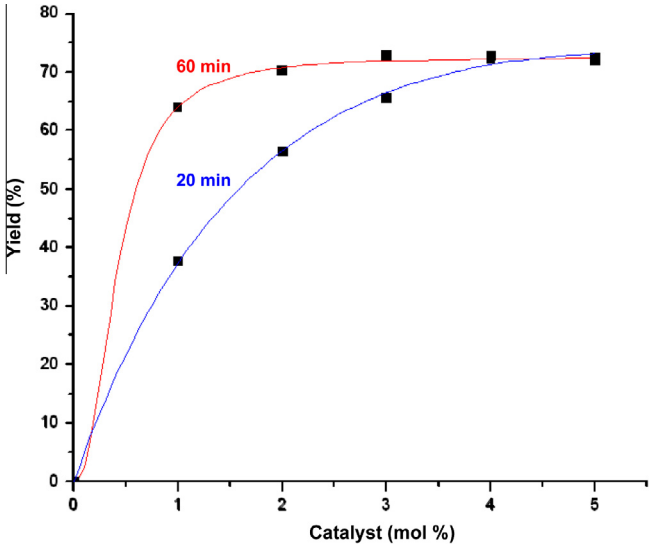
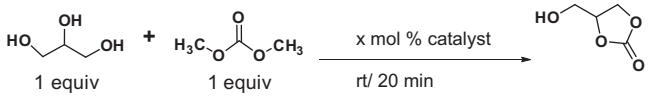


Figure 2. Profile of conversion into glycerol carbonate at 20 and 60 min reaction time as a function of catalyst amount; glycerol:dimethyl carbonate molar ratio is 1:1.

Table 1
Development of reaction conditions for synthesis of glycerol carbonate.



Entry[a]	Mole % of catalyst	Yield of GC (%)[b]
1	**0**	0.0
2	**1**	37.7
3	**2**	56.5
4	**3**	65.6
5	**4**	72.5
6	**5**	72.5
7[c]	**5**	59.6
8[d]	**5**	0.0

[a] Reactions were carried out with a molar ratio of glycerol to dimethyl carbonate of 1:1, and x mol % of catalyst, and 20 min of reaction time at room temperature; the catalyst was prepared reacting x mol % of 2 with x mol% of K-OtBu.
[b] Average of two experiments, determined by proton NMR integration with an internal standard.
[c] No imidazolium salt was used, only 5 mol % of KOt-Bu was used as catalyst.
[d] With 5 mol % of catalyst in the presence of 25 mg of powdered 4 Å molecular sieves/60 minutes.

Table 2
Influence of molar ratio gycerol:dimethyl carbonate (DMC) in the yield of glycerol carbonate (GC).

Entry[a]	Molar ratio Glycerol: DMC	Yield of GC (%)[b]
1	1	72.5
2	2	87.7
3	2.5	88.1
4	3	92.3
5	3.5	93.5
6	4.5	95.7

[a] Reactions were carried out with 4 mol % of (2/K-OtBu) and 20 min of reaction time at room temperature.
[b] Average of two experiments, determined by proton NMR integration with an internal standard.

during 20 min. A molar ratio of glycerol:dimethyl carbonate of 1:3 gives a yield of 92.3% (entry 4) and higher ratios improved the yield only slightly (entries 5 and 6).

The influence of catalyst structure on the reaction was also studied; findings are shown in Table 3. Catalysts with *N*-xylyl and *N*-alkyl groups of variable chain length *N*-alkyl were investigated. The yields of glycerol carbonate correlated with the length of the alkyl chain. The highest yields of glycerol carbonate occurred with the catalyst having the longest *N*-alkyl substituent. We do not know why the longer alkyl chains make the catalysts more effective, and we are investigating the effect. It is also clear that catalysts bearing an *N*-xylyl substituent perform better than those with a *N*-methyl substituent (entries 5–8).

The *N*-aryl group plays an important role in the reactivity and selectivity of reactions catalyzed by NHCs.[20] Reactions with α-functionalized aldehydes catalyzed by NHCs occur faster when they have an *N*-mesityl group.[21] NHCs bearing and *N*-mesityl group had better selectivity and enantioselectivity, and also faster rates of reaction. It appears that di-ortho substituents in the *N*-mesityl group make the addition of the NHC to the carbonyl nearly irreversible, thereby accelerating the formation of the Breslow intermediate.[21] It is likely that the *N*-xylyl group in our NHCs also shows the di-ortho effect and is the cause of better performances of the catalyst precursors having an *N*-xylyl substituent.

A catalytic cycle has been proposed for the NHC organocatalyzed ring opening polymerization of ε-caprolactone.[18] By analogy,