



Organic carbonates: sustainable and environmentally-friendly ethylation, allylation, and benzylation reagents



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ARTICLE INFO

Article history:

Received 19 August 2014
Received in revised form 7 October 2014
Accepted 19 November 2014
Available online 25 November 2014

Keywords:

Alkylation
Esterification
Organic carbonates
Phenolic acids
Renewable resources

ABSTRACT

Diallyl, dibenzyl, and diethyl carbonate are shown to be non-toxic, sustainable and efficient reagents for the alkylation of phenols as well as for an esterification of carboxylic acids under microwave irradiation in the presence of sub-stoichiometric quantities of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or potassium carbonate. Comparative studies with diethyl carbonate (DEC), diallyl carbonate (DAC), and dibenzyl carbonate (DBC) were performed for the etherification of phenol. Moreover, the reaction of these organic carbonates with hydrogenated ferulic acid show that ester formation is significantly faster and requires lower temperatures if compared to the etherification. Generally, DBC and DAC show a higher reactivity than DEC. Moreover, the use of DBC and DAC under optimized reaction conditions allowed a selective protection of carboxyl groups in the presence of phenols.

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1. Introduction

Currently, the use of dimethyl carbonate (DMC) as sustainable, non-toxic and environmentally friendly reagent as well as organic solvent is increasing dramatically. In the last years, numerous application possibilities of DMC were described.^{1–3} The most important applications of DMC are the methylation of phenols,^{4,5} anilines, and indoles,^{6,7} as well as α -methylations of substrates having acidic α -methylene groups.⁸ Moreover, DMC is used as reagent for the formation of methyl esters from carboxylic acids under basic conditions.^{9,10} Recently, our group demonstrated that DMC is an excellent activation agent for hydroxamic acids to initiate Lossen rearrangements.^{11,12} By using catalytic amounts of tertiary amine bases, aliphatic hydroxamic acids rearranged to methyl carbamates, while aromatic ones directly yielded anilines. DMC is considered to be a 'green' reagent, since it is accessible via sustainable synthesis procedures.^{1,13,14}

Recently, our group and others reported the use of suitable catalysts for the transesterification of DMC **1** with alcohols to the corresponding dialkyl carbonates.^{15–17} A highly efficient catalyst for these reactions is the strong cyclic guanidine base 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD). TBD was successfully used for the mono and double transesterification of **1** utilizing primary

and secondary alcohols under neat conditions at temperatures between 80 and 130 °C.¹⁷ Applying this procedure, diallyl carbonate (DAC) **3** and dibenzyl carbonate (DBC) **4** can be obtained in a straightforward fashion by transesterification reactions of **1** with two equivalents of allyl alcohol and benzyl alcohol, respectively.

Employing **3**, **4**, and commercially available diethyl carbonate (DEC) **2**, we investigated the applicability of these dialkyl carbonates for alkylation and esterification reactions of phenol **5a** and hydrogenated ferulic acid **9a** as a representative phenolic acid. Numerous procedures describe the alkylation and esterification ability of DMC at different conditions and catalytic systems.^{4–10} Contrary, identical reactions with other dialkyl carbonates are rarely described. Some groups reported the use of DBC and DAC for a benzylation of phenols, indoles, carboxylic acids, or thiol compounds,^{18–20} as well as for a mono-alkylation of anilines.²¹ One reason for the rare use of commercially available DBC and DAC as benzylation or allylation reagents might be their high prices. Thus, the above mentioned transesterification methodology utilizing, e.g., TBD as catalyst offers a cost-efficient possibility for a multi-gram synthesis of these organic carbonates.

Highly efficient, sustainable, and eco-friendly procedures for allylations and benzylations as well as for the corresponding alkoxy-carbonylations are of great interest, since these reactions are commonly used to introduce protecting groups for phenols, alcohols, carboxylic acids, and amines.²² Thus, in our studies we were interested in the different reactivity of DAC, DBC and DEC in alkylation reactions of phenols and the formation of alkyl esters from

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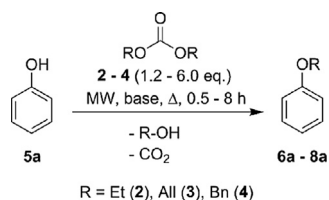
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carboxylic acids. Conventional ethylation,^{23–25} benzylation,^{24–28} or allylation^{24,26,29} reactions utilizing halogenated compounds can be performed at lower temperatures. However, in this typical Williamson type ether synthesis, stoichiometric amounts of bases are necessary and high amounts of waste are formed.^{30,31} Therefore, the alternative catalytic approach using eco-friendly dialkyl carbonates is far more sustainable.

2. Results and discussion

2.1. Alkylations of phenol with dialkyl carbonates

In first experiments, we investigated the alkylation of phenol **5a** with dialkylcarbonates **2–4** under basic conditions applying two different methods: conventional heating in a carousel reactor and reactions performed under microwave irradiation (Scheme 1).



Scheme 1. Alkylation of phenol **5a** with dialkyl carbonates **2–4**.

The reactions were performed under neat conditions with excess of dialkyl carbonates **2–4** (1.2–6.0 equiv) and conversions were monitored by GC–MS relative to an internal standard. It is known from literature that the most efficient basic catalysts for alkylation reactions with dialkyl carbonates are potassium carbonate and DBU.^{4–10} For ethylation reactions of **5a** with DEC **2** (each with 2.0 equiv) at 125 °C performed under conventional heating (Table 1, entry 1–3), long reaction times (>20 h) were needed to obtain moderate to good conversions. A comparative study of potassium carbonate and DBU revealed that higher conversions (up to 88%) were only achieved using potassium carbonate (0.5 equiv) as base. Decreasing the amount of potassium carbonate to 0.2 equiv resulted in a significantly lower conversion (23%). In order to drastically shorten the reaction time, the following experiments were performed in a closed vessel microwave reactor system at higher temperatures and a slightly increased pressure. In this way, alkylation reactions performed at 180 °C at a pressure of ~6.0 bar applying the same amounts of **2** as well as DBU and potassium carbonate, were significantly faster and full conversions were achieved in both experiments after only two hours (Table 1, entry 4 and 5). After purification by column chromatography, ethoxybenzene **6a** was isolated in a yield of 84%. With regard to economic and environmental aspects, reactions with decreased amounts of **2** were investigated. Applying the same conditions using only 1.2 equiv of **2** led to a conversion of 83% after two hours (entry 6). Although potassium carbonate and DBU showed similar activities as catalysts for these alkylation reactions, the following experiments were performed only with DBU as catalyst to guarantee a better handling and reproducibility of the microwave experiments and to simplify the purification of the crude products. If potassium carbonate was used, the reaction mixtures solidified and thus, the reactions were hardly stirrable and a temperature control of the microwave instrument via the IR sensor was not possible (leading to an explosion in one case; be careful!). To enable faster ethylation reactions, the reaction temperature was increased to 220 °C applying 1.5 equiv of **2** (entry 7 and 8). Moreover, utilizing only 0.2 equiv of DBU still yielded good conversions of 90% after 3 h.

Using these optimized reaction conditions, the allylation employing DAC **3** in order to obtain allyl phenyl ether **7a** was

Table 1

Results for the reaction of phenol **5a** with carbonates **2–4** applying different conditions

Entry	Method ^a	Time (h)	Temp (°C)	Carbonate (eq.)	Base (eq.)	Conversion ^b (%)	Product ^b yield (%)
1	A	23	125	2 (2.0)	DBU (0.5)	49	6a (44)
2	A	23	125	2 (2.0)	K ₂ CO ₃ (0.5)	88	6a (88)
3	A	26	125	2 (2.0)	K ₂ CO ₃ (0.2)	23	6a (22)
4	B	2.0	180	2 (2.0)	DBU (0.5)	>99	6a (94)
5	B	2.0	180	2 (2.0)	K ₂ CO ₃ (0.5)	98	6a (90)
6	B	2.0	180	2 (1.2)	K ₂ CO ₃ (0.5)	83	6a (44)
7	B	1.0	220	2 (1.5)	DBU (0.5)	>99	6a (95)
8	B	3.0	220	2 (1.5)	DBU (0.2)	90	6a (87)
9	B	0.5	220	3 (1.5)	DBU (0.5)	>99	7a (80) ^c
10	B	2.0	220	3 (1.5)	DBU (0.3)	>99	7a (76) ^c
11	B	3.0	220	3 (6.0)	DBU (0.5)	>99	7a (62) ^c
12	B	2.0	220	3 (1.5)	DBU (0.2)	>99	7a (77) ^c
13	B	2.5	200	3 (1.5)	DBU (0.5)	93	7a (88) ^c
14	B	8.0	180	3 (1.5)	DBU (0.5)	88	7a (83) ^c
15	B	1.0	220	4 (1.5)	DBU (0.5)	>99	8a (98)
16	B	1.0	200	4 (1.5)	DBU (0.5)	>99	8a (96)
17	B	1.0	180	4 (1.5)	DBU (0.5)	>99	8a (99)

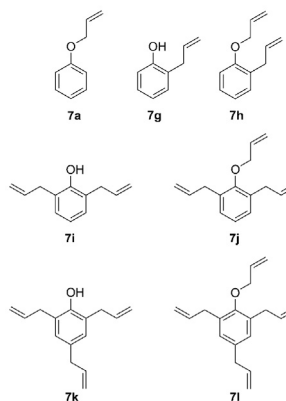
^a Method A: reactions were performed in a carousel reactor under neat conditions. Method B: reactions were performed in a microwave reactor.

^b Conversions and yields of the products were determined via GC–MS using *n*-tetradecane as internal standard.

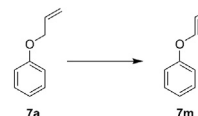
^c Formation of side products was observed (Scheme 3, Table 2).

studied (entry 9–14). Here, the formation of diverse side-products was observed at temperatures above 200 °C (entry 9–12). A detailed analysis via GC–MS and ¹H NMR revealed a mixture of multiple allylated products **7g–7l**, certainly derived from Claisen rearrangements occurring at high temperatures (Scheme 2a, Table 2).^{32–34} Isolation of these side-products by column chromatography was not possible due to their similar retention behavior. Moreover, if the reaction was performed with 6.0 equiv of **3** (entry 11), ¹H NMR and GC–MS revealed traces of vinyl ether **7m** (<2.0%), as a result of double bond isomerization of **7a** (Scheme 2b). Below temperatures of 200 °C, the formation of side-products can be reduced to a minimum (<5.0%), but this requires longer reaction times (up to eight hours) to achieve high conversions (Table 1, entry 13 and 14). The composition of the reaction mixtures is given in Table 2.

a) Allyl phenyl ether **7a** and Claisen rearrangement side-products **7g–7l**



b) Double bond isomerization of **7a** to vinyl ether derivative **7m**



Scheme 2. a) Claisen rearrangement to the side-products **7g–7l** derived by multiple alkylations of phenol **5** with DAC **3** to obtain allyl phenyl ether **7a**. b) Double bond isomerization of **7a** to the vinyl ether derivative **7m**.

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