Notes

Direct Coupling of Cs$_2$CO$_3$ and Alcohols for the Synthesis of Dimethyl, Diethyl, and Various Dialkyl Carbonates

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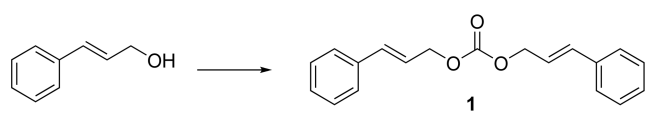*Received September 18, 2013, Accepted November 9, 2013*

Dimethyl carbonate (DMC) has been used in synthetic organic chemistry as a low-toxicity and versatile methylating and carbonylating agent. In industrial processes, DMC is widely used as a fuel additive, electrolyte for lithium ion batteries, and monomer for polycarbonate and polyurethane synthesis.[1] Therefore, an efficient and high-yield synthesis for DMC has been actively investigated. Reaction conditions typically involve either carbon monoxide (CO) or derivatives (*e.g.*, phosgene), or carbon dioxide (CO$_2$) or derivatives (*e.g.*, inorganic carbonates or organic cyclic carbonates). Due to the toxicity and flammability of CO and phosgene, the more environmentally benign and sustainable carbon sources CO$_2$ and derivatives have been actively employed for production of DMC and related acyclic carbonates. The DMC and acyclic carbonate syntheses that have been reported include: 1) transesterification of cyclic carbonates derived from oxirane and CO$_2$;[2] 2) dehydrative condensation of alcohols with CO$_2$;[3] 3) reactions between alkyl halide and metal carbonates;[4] 4) reactions between alcohol, alkyl halide, and CO$_2$;[5] and 5) reactions between alcohol and CO$_2$ in the presence of condensing agents.[6] Other than transesterification of cyclic carbonates, DMC is generated from alcohols or alkyl halide. In terms of chemical cost, use of an alcohol without an extra step for alkyl halide preparation appears more desirable; however, direct coupling of alcohols with CO$_2$ or metal carbonates is challenging. In dehydrative condensation of alcohols with CO$_2$, very efficient dehydrating reagents and metal catalysts are necessary to drive the reaction equilibrium to the product.[3] In direct coupling of alcohols with CO$_2$, alcohol-activation reagents such as the Mitsunobu reagent are required. According to Saito *et al.*, dichloromethane, a common organic solvent, has been used as an alcohol-activating reagent for synthesis of various aliphatic carbonates in the presence of CO$_2$ and Cs$_2$CO$_3$ (base), although synthesis of DMC has not been reported using dichloromethane.[6c] In the present study, we used dibromomethane (CH$_2$Br$_2$) as an alcohol-activating reagent and solvent. Using CH$_2$Br$_2$ and an ionic liquid, direct coupling of alcohols with Cs$_2$CO$_3$ in the absence of CO$_2$ was

achieved. Using Cs$_2$CO$_3$-mediated conditions, various aliphatic carbonates, including DMC and diethyl carbonate (DEC), were prepared with good yields.

Optimization of the synthesis of carbonate **1** is summarized in Table 1. Reaction of cinnamyl alcohol and Cs$_2$CO$_3$ in a mixture of dichloromethane (CH$_2$Cl$_2$) and 1-butyl-3-methylimidazolium hexafluorophosphate (bmimPF$_6$) was carried out at 70 °C. Even in the absence of CO$_2$, carbonate **1** was formed with 71% yield (entry 1). In this reaction, Cs$_2$CO$_3$

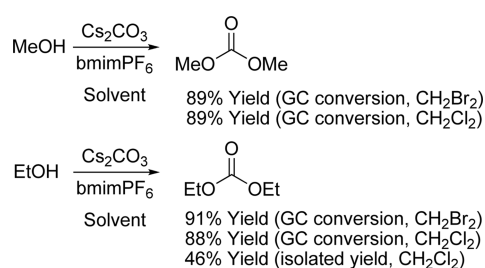**Table 1.** Synthesis of carbonate **1** from cinnamyl alcohol

Entry	Base	Solvent	Temp	Yield
1	Cs$_2$CO$_3$ (2 equiv)	CH$_2$Cl$_2$ (1 mL), bmimPF$_6$ (0.1 mL)	70 °C	71%
2	Cs$_2$CO$_3$ (3 equiv)	CH$_2$Cl$_2$ (1 mL), bmimPF$_6$ (0.1 mL)	70 °C	60%
3	Cs$_2$CO$_3$ (1 equiv)	CH$_2$Cl$_2$ (1 mL), bmimPF$_6$ (0.1 mL)	70 °C	57%
4	Cs$_2$CO$_3$ (2 equiv)	CH$_2$Br$_2$ (1 mL), bmimPF$_6$ (0.1 mL)	70 °C	94% (82%[a])
5	Cs$_2$CO$_3$ (2 equiv)	CH$_2$Cl$_2$ (1 mL), bmimBF$_4$ (0.1 mL)	70 °C	70%
6	Cs$_2$CO$_3$ (2 equiv)	CH$_2$Cl$_2$ (1 mL), bmimCl (1 equiv)	70 °C	66%
7	Cs$_2$CO$_3$ (2 equiv)	CH$_2$Cl$_2$ (1 mL), bmimOMs (1 equiv)	70 °C	59%
8	K$_2$CO$_3$ (2 equiv)	CH$_2$Cl$_2$ (1 mL), bmimPF$_6$ (0.1 mL)	70 °C	5% (59%[b])
9	Cs$_2$CO$_3$ (2 equiv)	CH$_2$Cl$_2$ (1 mL)	70 °C	−%
10	Cs$_2$CO$_3$ (2 equiv)	CH$_2$Cl$_2$ (1 mL), NMP (0.1 mL)	70 °C	−%

Experimental procedure: A mixture of cinnamyl alcohol (0.5 mmol) and Cs$_2$CO$_3$ in the solvent was equipped with a seal tube and stirred for 18 h at 70 °C. [a]The experiment was run in a round-bottomed flask. [b]18-Crown-6 ether (1 equivalent) was added.

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acted as a carbonate source as well as a base. Changing the amount of Cs_2CO_3 to 3 equivalents or 1 equivalent did not significantly improve the yield (entries 2 and 3). Considering the leaving group ability of halogen, the reactivity of CH_2Br_2 was expected to be greater than dichloromethane (CH_2Cl_2). Satisfactorily, **1** was obtained with 94% yield using CH_2Br_2 (entry 4). Because the boiling point of CH_2Br_2 is higher than 70 °C, the reaction was run in a round-bottomed flask, to give **1** in 82% yield, which is slightly lower yield than the reaction equipped with a seal tube. Next, the counter anions (BF_4^-, Cl^-, and ^-OMs) of the ionic liquid were varied, producing similar yield with BF_4^- and lower yields with Cl^-, and ^-OMs (entries 5-7). Rather than Cs_2CO_3, K_2CO_3 was employed, yielding **1** with 5% yield; however, by adding 18-crown-6 ether, the yield of **1** was increased to 59%, implying that the carbonate anion of K_2CO_3 is more tightly bound to the counter cation than that of Cs_2CO_3 in a mixture of CH_2Br_2 and bmimPF$_6$ (entry 8).[7] To figure out the role of the ionic liquid, **1** was subjected to the reaction mixture without bmimPF$_6$, providing no carbonate (entry 9). The ionic liquid is assumed to have increased the nucleophilicity of carbonate, providing **1** in high yield.[8] Replacing bmimPF$_6$ with a polar solvent, *N*-methyl-2-pyrrolidone (NMP), did not promote formation of **1** (entry 10).

Using the optimized conditions, a wide range of alcohols, including benzyl alcohols, allyl alcohols, and aliphatic alcohols, were subjected to these carbonate formation conditions using Cs_2CO_3 (Table 2). Benzyl alcohol and 3-methoxy-substituted benzyl alcohols were converted to carbonates **2** and **3** with 87% and 80% yield, respectively (entries 1 and 2). Compared to 1° alcohols, sterically hindered 2° alcohols reacted with Cs_2CO_3 with slightly lower yields (entries 3 and 4). Aliphatic alcohols were incorporated into acyclic carbonates with comparable yields to benzyl alcohols (entries 5-8). In addition to synthesis of symmetric acyclic carbonates, unsymmetric acyclic carbonates were prepared by using 1 equivalent of benzyl alcohol and 1 equivalent of cinnamyl alcohol (entry 9). As shown in entry 9 of Table 2, 24% yield of **1**, 23% yield of **2**, and 43% yield of **10** were obtained, implying that the degree of self-condensation and cross-condensation of alcohols was similar.

Following synthesis of the non-volatile carbonates, DMC and DEC were prepared under Cs_2CO_3-mediated reaction conditions.[2] Because of the low boiling points of DMC and DEC, conversion from alcohols to carbonates was evaluated by gas chromatographic analysis. As shown in Scheme 1,

Table 2. Synthesis of carbonates from alcohols and Cs_2CO_3

Entry	Reactant	Product	Yield
1	Ph⌒OH	**2**	87%
2	(3-OCH₃ benzyl alcohol)	**3**	80%
3	Ph(CH₃)CHOH	**4**	64%
4	(2-cyclohexenol)	**5**	66%
5	Ph⌒⌒OH	**6**	84%
6	(pentanol)	**7**	70%
7	BnO(CH₂)₂OH	**8**	63%
8	Ph₂CH-CH₂-CH₂OH	**9**	73%
9	Ph⌒OH Ph⌒⌒OH	**1** (R_1,R_2 = CH₂CH=CHPh) 24% **2** (R_1,R_2 = CH₂Ph) 23% **10** (R_1 = CH₂CH=CHPh, R_2 = CH₂Ph) 43%	

Experimental procedure: A mixture of the alcohol (0.5 mmol) and Cs_2CO_3 (1.0 mmol) in dibromomethane was equipped with a seal tube and stirred for 18 h at 70 °C.

methanol was converted to DMC with 89% yield with CH_2Br_2 as a solvent, and with 89% yield with CH_2Cl_2. Conversion of ethanol to DEC proceeds with 91% yield with CH_2Br_2, and with 88% yield with CH_2Cl_2. DEC was isolated

Scheme 1. Synthesis of dimethyl carbonate (DMC) and diethyl carbonate (DEC).
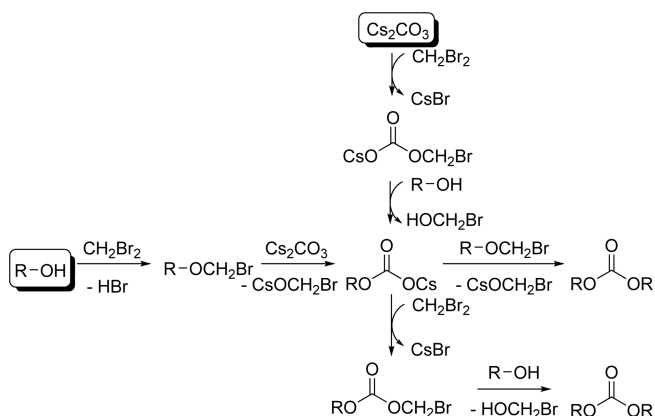
Scheme 2. Plausible mechanisms for Cs_2CO_3-mediated reactions.

in 46% by distillation, showing the lower yield than GC conversion due to the volatility of DEC. Accordingly, low-molecular-weight alcohols can successfully be incorporated into carbonates with good yields using Cs_2CO_3-method.

The reaction mechanism of Cs_2CO_3-mediated carbonate formation was proposed (Scheme 2). An alcohol might react with CH_2Br_2, followed by reaction with Cs_2CO_3 to afford carbonates. Alternatively, Cs_2CO_3 reacts with CH_2Br_2, resulting in a reactive carboxylate, $Cs^{+-}OCO_2CH_2Br$. This reactive carboxylate reacts with alcohols to afford carbonates. Based on previous reports,[6c] the mechanism involving a reactive carboxylate, $Cs^{+-}OCO_2CH_2Br$, would be favorable.

We present here transition-metal-free and efficient acyclic carbonate synthetic protocols using non-toxic carbon sources, Cs_2CO_3. Using CH_2Br_2, direct coupling of alcohols with Cs_2CO_3 was achieved without Mitsunobu-type reagents or separate steps for alkyl halide preparation. A wide range of alcohols, including benzyl alcohols, allyl alcohols, aliphatic alcohols, and low-molecular-weight alcohols (ethanol and methanol), were converted to acyclic carbonates with good yields. In particular, DMC and DEC, which are attractive and versatile compounds for use in a variety of chemical industries, were prepared with good yields.

Experimental

Representative Procedure for Carbonates Synthesis from Cs_2CO_3. A mixture of cinnamyl alcohol (67.1 mg, 0.5 mmol), Cs_2CO_3 (325.8 mg, 1 mmol) and 1-*n*-butyl-3-methylimidazolium hexafluorophosphate (bmimPF_6) (0.1 mL) in dibromomethane (1 mL) was equipped with a seal tube and stirred for 18 h at 70 °C. The reaction mixture was evaporated and purified by flash column chromatography (silica gel) (2% Ether/hexane) to obtain dicinnamyl carbonate (**1**) 69.0 mg (94%).

Representative Procedure for Synthesis of Low-molecular-weight Carbonates (DMC and DEC). A mixture of methanol (16.0 mg, 0.5 mmol), Cs_2CO_3 (325.8 mg, 1 mmol), 1-*n*-butyl-3-methylimidazolium hexafluorophosphate (bmimPF_6) (0.1 mL) and tetradecane (19.8 mg, 0.1 mmol) in dibromomethane (1 mL) was equipped with a seal tube and stirred for 18 h at 70 °C. The yield was determined by GC analysis of the reaction mixture using tetradecane as an internal standard; average of three runs.

Supporting Information. Experimental procedures and ^1H NMR and ^{13}C NMR spectra.

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