Synthesis of 6-membered cyclic carbonates from 1,3-diols and low CO₂ pressure: a novel mild strategy to replace phosgene reagents†

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Low pressure carbon dioxide is used as the carbonation agent in a simple, safe and efficient procedure for the synthesis of 6-membered cyclic carbonates from 1,3-diols. Using readily available reagents and proceeding at room temperature, this route offers a novel mild alternative to phosgene derivatives.

Unlike aromatic polycarbonates, aliphatic polycarbonates (APCs) have been little explored commercially. However, their low toxicity and biodegradability make them excellent candidates for biomedical applications. Recently, they have also been investigated as thermoplastics, binders for photovoltaics, polymer electrolytes and adhesives.

Part of this renewed attention stems from the possibility to obtain APCs via the copolymerisation of CO₂ and epoxides, an attractive reaction which uses an abundant and virtually free source of carbon, but is limited by the scope of usable epoxides. APCs can also be synthesised by polycondensation of diols with phosgene derivatives or dialkyl carbonates, but the control of the polymer molecular weight is highly sensitive to the reaction conditions. Hence, Ring-Opening Polymerisation (ROP) of cyclic carbonates has become the method of choice for APC synthesis, as the development of ROP catalysts has enabled controlled polymerisation of highly functionalised monomers under mild conditions (usually 6-, 7- or strained 5-membered rings).

A common preparation of cyclic carbonate monomers involves the transesterification of diols with phosgene, a toxic reagent synthesised from CO and Cl₂ in an energy intensive process. Nevertheless, phosgene is still widely employed due to its efficiency and the lack of a more versatile and sustainable alternative. Safer phosgene derivatives include di-tert-butyl dicarbonate, 1,1’-carbonyldiimidazole and aromatic carbonates, but these reagents all derive from phosgene, and can lead to unwanted side reactions, low reactivity and difficult workups.

Alternative methods, such as the Pd-catalysed oxidative carboxylation of diols using CO pressure, or the catalytic coupling of CO₂ with oxetanes, have also been reported. The latter however, is limited by the availability of oxetanes. Transesterification of diols with urea, industrially produced from CO₂, is also described but with moderate success.

Using CO₂ as a C₁-carbonation agent is an attractive goal for phosgene related emissions mitigation and direct CO₂ utilisation. The direct coupling of CO₂ with diols, where water is the sole by-product, would be an attractive process. However, the reaction is generally not kinetically and thermodynamically favoured. Therefore, a catalyst and an efficient stoichiometric dehydrating strategy (e.g. nitriles, zeolites, orthoesters, or Mitsunobu reagents) are necessary for the reaction to proceed. Despite recent advances, such as the use of CeO₂ catalyst in tandem with a large excess of 2-cyanoypyridine as a dehydrating agent, or the in situ introduction of a leaving group based on dibromomethane, high CO₂ pressures (10-50 bar) and high temperatures (70-140 °C) are still required, particularly for the synthesis of 6-membered rings.

Herein, we report a safe and efficient one-pot procedure for the synthesis of 6-membered cyclic carbonates directly from 1,3-diols, which uses CO₂ as the carbonation agent instead of phosgene derivatives. This methodology proceeds at room conditions.
temperature, needs only 1 atm of CO2 and common lab reagents (Scheme 1), and does not require the preliminary preparation of oxetanes or chloroalcohols.25

In 2005, Jessop and coworkers reported the reversible carbonation of alcohols with CO2 promoted by 1,8-diazabicyclo[5.4.0]-unde-7-ene (DBU).26 The conversion was later found to depend on the choice of solvent with almost full conversion of 1-hexanol being achieved in CDCl3.27 Inspired by these reports, we investigated the selective mono-insertion of CO2 into one alcohol moiety of 1,3-diols in various solvents. The slow addition of DBU under 1 atm of CO2 to solutions of (±)-1,3-butanediol (1a) was monitored and the conversion to alkyl carbonate species was assessed by 1H NMR (Table 1). Regardless of the solvent used, the carbonation of 1a by CO2 proceeded quickly at low pressure and room temperature, with good selectivity towards the mono-insertion products (ca. 90% of products). A slight preference for the primary alcohol moiety was also observed, in agreement with DFT calculations (see ESI Fig. S4†). In neat diol, the conversion was limited by the increased viscosity upon CO2 insertion (Table 1, Entry 1), but even in solution and with the addition of ionic liquid bmimPF6, as used by Lim et al. (Table 1, Entry 5),24 full conversion of 1a was not observed with only one DBU equivalent. Apolar toluene-d8 gave less conversion than more polar solvents, whereas more dicarbonated product was obtained in acetonitrile-d3 (Table 1, Entry 2 and 4). Overall, optimal results were obtained in CDCl3, and despite it not being a desirable solvent which should be replaced in the future, chloroform was used in the rest of our study. Addition of DBU at low temperature resulted in no further improvement in mono-insertion selectivity (Table 1, Entry 7), while increasing the temperature promoted decarboxylation. A lower concentration of diol slightly decreased the amount of disubstituted product (Table 1, Entry 6) but did not affect the global conversion. The use of stronger base 1,5,7-diazabicyclo[4.3.0]-unde-7ene (TBD) in place of DBU resulted in less conversion, which is attributed to an increased sensitivity to moisture (Table 1, Entry 8). The use of triethylamine resulted in no carbonation of 1a.

Further DFT calculations showed that the direct coupling of 1a and CO2 to form cyclic carbonate 2a is slightly thermodynamically disfavoured (ΔG = +3.0 kcal mol⁻¹). Following the DBU-aided insertion of CO2, the activation barriers are then too high for the cyclisation of 1aII (or 1aII) to proceed under mild conditions (61.1 and 42.2 kcal mol⁻¹ via an S2,2 or addition/elimination mechanism, respectively) (see Fig. S4†). An in situ leaving group strategy was thus applied experimentally to overcome the kinetic as well as the thermodynamic limitation of the reaction. After the selective mono-insertion of CO2 into 1a in CDCl3, at low concentration, 1 equivalent of tosyl chloride and triethylamine were added to the reaction mixture and stirred at room temperature overnight. Rapidly, the cyclic carbonate 2a was detected by 1H NMR (addition of triethylamine alone did not result in any product). The pure product was later isolated by column chromatography in a 44% yield, i.e. 60% conversion based on the mono-CO2 inserted products (Table 2, Entry 1). A higher concentration of diol (1.7 M), despite being slightly detrimental to the first step of the procedure, proved to lead to a higher isolated yield of cyclic carbonate (68%, i.e. 99% conversion based on CO2 mono-insertion, Table 2, Entry 2). This compares well with the traditional phosgene-based method (50%),28 as well as oxidative carboxylation methods (45%),18a the procedure was found to be robust: CO2 from sublimed dry ice could be used and yielded cyclic carbonate 2a, albeit in lower yield (48%, Table 2, Entry 3). The reaction also proceeded without solvent (30% yield). Investigation into the scope of the procedure was carried out with various 1,3-diols. The cyclisation step proceeded efficiently from the CO2-mono insertion products and all cyclic carbonates were isolated in moderate yields (Table 2), comparative with phosgene-based and alternative methods. For example, the isolation of 2d from 2,2-dimethyl-1,3-propanediol (53%, Table 2, Entry 8) was previously reported using phosgene derivatives (60%),29 oxidative carboxylation (50%),18b and metal free cyclisation (50%).24 O-isopropyldiendiyxylene was also successfully transformed, though isolation proved challenging (11%, Table 2, Entry 12).

As cyclisation happens readily, reaction intermediates could not be isolated, but DFT calculations on model compound (R)-1a and additional experiments with optically active diols were carried out to investigate the reaction mechanism. After insertion of CO2, tosylation can occur at the carbonate or at the remaining alcohol group, so that cyclisation proceeds via either an addition/elimination or a S2,2 pathway, leading to retention or inversion of stereochemistry (see Scheme 2). However, the exclusive formation and isolation of (R,R)-cyclic carbonate 2b from (R,R)-2,4-pentanediol, as well as the optical activities of the cyclic carbonates obtained from enantiopure (R) and (S)-1,3-butanediol (Table 2, Entries 4–6),28 both indicated an addition/
Table 2  Synthesis of various cyclic carbonates from 1,3-diols and CO₂

| Entry | Substrate | % Yield<sup>a</sup> [conv.<sup>1</sup>→<sup>2</sup>]<sup>b</sup> | Product |
|-------|-----------|-----------------|--------|
| 1<sup>c</sup> | 1a | 44 [60] | 2a |
| 2 | 1a | 68 [99] | 2a |
| 3<sup>d</sup> | 1a | 48 | 2a |
| 4 | (R)-1a | 68 | (R)-2a |
| 5 | (S)-1a | 70 | (S)-2a |
| 6 | 1b | 53 [71] | 2b |
| 7 | 1c | 55 [96] | 2c |
| 8 | 1d | 53 [82] | 2d |
| 9 | 1e | 49 [78] | 2e |
| 10 | 1f | 46 [71] | 2f |
| 11 | 1g | 41 [70] | 2g |
| 12 | 1h | 11 | 2h |

<sup>a</sup> Isolated yield based on starting diol.<br><sup>b</sup> Spectroscopic conversion of CO₂ mono-insertion products 1→ cyclic carbonate 2. <sup>c</sup> [Diol] = 0.1 M. <sup>d</sup> CO₂ from the sublimation of dry ice was used.
On-going work is now aiming at replacing chloroform for a more environmental benign solvent and making the procedure catalytic in order to reduce the amount of salts produced.

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Notes and references

† Typical procedure for the synthesis of cyclic carbonate monomers: under a CO₂ atmosphere, DBU (1 equiv.) was added dropwise to a stirring solution/suspension of diol (0.5 g, 1 equiv.) in dry chloroform (1.7 M). After stirring at room temperature for 2 hours, triethylamine (1 equiv.) was added. The mixture was stirred slowly and the mixture stirred overnight. Removal of volatiles in vacuo afforded an oily residue, which was purified by column chromatography.

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