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The design of efficient carbonate interchange reactions with catechol carbonate

T. Tabanelli, E. Monti, F. Cavani* and M. Selva*

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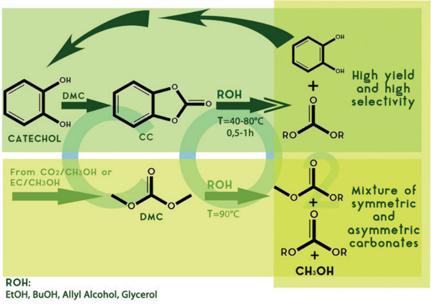

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The design of efficient carbonate interchange reactions with catechol carbonate†

Q2

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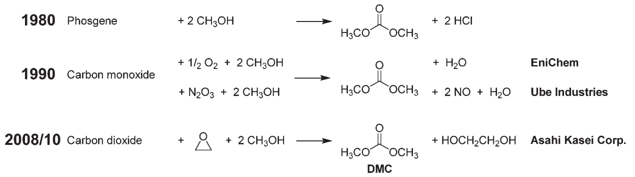
Catechol carbonate (CC) has been investigated as an innovative and highly active reactant for carbonate interchange reactions (CIRs). Under mild conditions (atmospheric pressure, and 60–80 °C), the selective synthesis of symmetric aliphatic carbonates ($ROCO_2R$) has been achieved by the reaction of a slight excess of both primary and secondary alcohols with CC in the presence of NaOMe or MgO as a catalyst. Quantitative conversions have been reached in only 1 hour and products have been isolated in yields of up to 58%. Of note is that the reaction of glycerol with CC also proceeded under similar conditions (40–60 °C, 1 atm) to afford glycerol carbonate (96–98%). The comparison of the reactivity of CC with that of conventional dialkyl carbonates, including dimethyl carbonate (DMC) and ethylene carbonate (EC), proved the superior performance of CC in all the investigated CIR processes. Accordingly, a mechanism has been formulated based on the leaving group ability of a catecholate anion originating from CC.

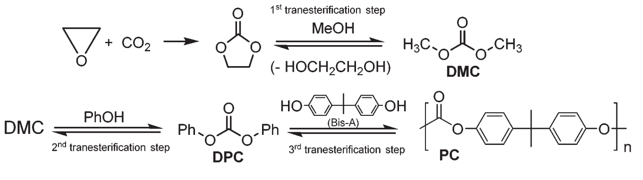
Introduction

Organic carbonates (OCs) are among the most promising green candidates for the replacement of conventional noxious solvents and fuel additives as well as for the development of innovative intermediates in the pharma, lubricant and polymer industries.[1] Such interest in OCs largely results from the effort that, over the years, has addressed the optimization of their synthesis. Consider, for example, the case of the simplest member of the series, dimethyl carbonate (DMC, $MeOCO_2Me$).[2] The early industrial preparation of DMC was based on a reaction involving a lethal chemical: before the 80s, the phosgenation of methanol was the main available process (Scheme 1, top).[3]



Scheme 1 Top: phosgenation of methanol; middle: EniChem and Ube processes; bottom: Asahi process for the production of DMC.

Since then however, the production and use of phosgene have been severely restricted worldwide and, by the end of the 90s, two phosgene-free plants were operative, both based on the oxidative carbonylation of methanol by transition metal catalysis: one developed by EniChem[4] and the other by Ube Industries[5] through the use of oxygen and NOx as oxidants, respectively (Scheme 1, middle). With respect to the phosgenation of methanol, these synthetic routes improved not only the safety of the process, but also the properties of the final product: DMC was classified as a non-toxic flammable liquid. Nonetheless, the use of poisonous gases such as carbon monoxide and methyl nitrite, and chlorine-based catalysts was still a concern. A breakthrough for the preparation of DMC was proposed by the early 2000s,[6] and a few years later, implemented by Asahi-Kasei Corp. in an integrated process for the industrial production of polycarbonate (PC, Scheme 2).[7] Accordingly, DMC was achieved *via* a two-step catalytic sequence composed of the insertion of CO_2 into ethylene oxide to give ethylene carbonate, followed by the transesterification of ethylene carbonate with methanol (Scheme 2, top).



Scheme 2 Innovative green production of polycarbonate by the Asahi Kasei process.

Q3

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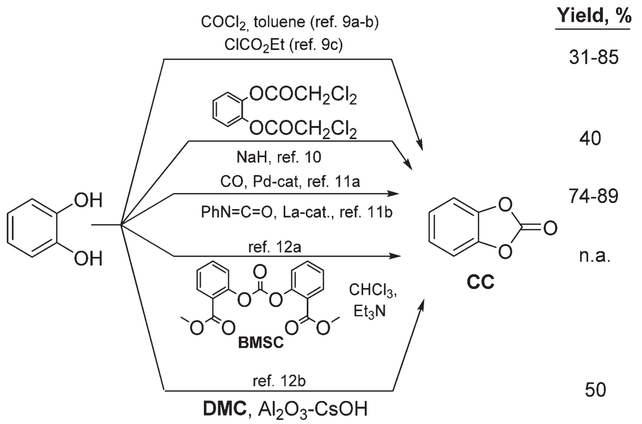
The conversion of DMC into diphenyl carbonate (DPC) and the further reaction of DPC with bisphenol-A (Bis-A) completed the synthesis of polycarbonate (Scheme 2, bottom).

Overall, beyond the activation of carbon dioxide, the Asahi-Kasei procedure is an excellent model to exemplify two other aspects: (i) the role of the transesterification reaction to achieve not only the simplest homologue (DMC, 1st transesterification, top), but also higher carbonates, including the final polymer (DPC and PC: 2nd and 3rd transesterification steps, respectively; bottom); (ii) the tunable reactivity of OCs. Due to the better leaving group ability of phenoxide with respect to the methoxide anion, DPC was suitable for the reaction with Bis-A, while DMC was not.

As a part of our long standing interest in organic carbonates,[8] these considerations prompted us to further investigate the potential of carbonate interchange reactions (CIRs) by using highly active electrophilic species. The attention was focused on a rather unexplored compound, namely catechol carbonate (benzo-1,3-dioxolan-2-one: CC). A literature survey disclosed relatively few methods available for the preparation of CC (Scheme 3). Starting from catechol, they included reactions with phosgene and ethyl chloroformate,[9] an oxidative cleavage of a bis-dichloroacetate compound,[10] cyclocarbonylation processes catalysed by La- and Pd-based systems,[11] and transesterifications with bis-methyl salicyl carbonate (BMSC) or dimethyl carbonate catalysed by Et_3N or alumina loaded with cesium hydroxide, respectively.[12] The majority of these procedures, however (ref. 9, 11*b*, and 12*a*), were either directly or indirectly phosgene-dependent since they used phosgene or its derivatives such as alkylchloroformates, BSMC, and phenyl isocyanate.[13] Other methods also posed safety concerns because they involved stoichiometric amounts of toxic chlorinated compounds (ref. 10) or noxious CO (up to 30 bar, ref. 11*b*).

The most attractive preparation was from the transesterification of DMC (ref. 12*b*), though the moderate yield of the product (50% at 583 K) indicated that there was large room for improvement. Moreover, one of the most active homogeneous catalysts studied for the CIR of DMC with alcohols, namely di-*n*-butyltin oxide (and other similar complexes) shows a complete lack of reactivity with catechol. This is probably due to the formation of a stable cyclic tin ester which is inert to further reaction.[14]



Scheme 3 Synthetic routes for CC. Yield of CC is shown for each procedure (right).

In this context, we were able to demonstrate that an efficient clean synthesis of catechol carbonate could be optimized through a reactive distillation system in which the reaction of catechol with DMC was implemented in the presence of a basic catalyst such as sodium methoxide. CC was achieved in yields as high as 95% under very mild and simple conditions (90 °C, ambient pressure).[15] We wish to report here an innovative application of CC for selective transesterification processes with a variety of alcohols including model primary and secondary substrates such as ethanol, *n*-butanol, allyl alcohol, i-propanol and cyclohexanol, and bio-based derivatives such as solketal (2,2-dimethyl-1,3-dioxolane-4-methanol) and glycerol. The reactions were explored at 40–80 °C and ambient pressure, in the presence of NaOMe and MgO as homogeneous and heterogeneous catalysts, respectively. Also, a comparative analysis of the same processes carried out with DMC and ethylene carbonate (EC) was investigated. The results proved the unprecedented outstanding potential of CC for the synthesis of both dialkyl and alkylene carbonates. Catechol carbonate not only greatly favoured the reaction kinetics, but it also promoted the quantitative formation of symmetric carbonates ($ROCO_2R$), these products being elusive in the CIRs of both EC and DMC.

Experimental

Catalyst preparation and characterisation

Magnesium oxide was synthesized by a precipitation technique: a solution of $Mg(NO_3)_2 \cdot 6H_2O$ in distilled water (1 mol L^{-1}) was added dropwise to a second aq. solution of $Na_2CO_3 \cdot 10H_2O$ (1 mol L^{-1} in distilled water) which was kept under magnetic stirring, at 60 °C. The pH was maintained between 9.8 and 10.2 during the reaction. The obtained magnesium hydroxide was filtered, washed with distilled water and dried overnight at 110 °C. The material was then crushed and calcined at 450 °C for 5 hours.

The MgO powder was characterized by X-ray diffraction, with Ni-filtered Cu Kα radiation (λ = 1.54178 Å) on a Philips X'Pert vertical diffractometer equipped with a pulse height analyzer and a secondary curved graphite-crystal monochromator.

The BET surface area of MgO was determined by N_2 absorption–desorption at the temperature of liquid N_2 using a Sorpty 1750 Fison instrument. A sample of 0.2 g was first outgassed at 150 °C before N_2 absorption. The surface area of MgO was found to be equal to $200 \pm 5 \text{ m}^2 \text{ g}^{-1}$.

Reaction procedure and product analysis

Catalytic tests were carried out in a Pyrex-glass screw-cap 10 mL-vial equipped with a magnetic stirrer. The mild conditions of the investigated transesterification reactions never required more complex equipment.

In a typical experiment, the vial was charged with the selected alcohol (usually from 3 to 9 mmol), the catalyst ($NaOCH_3$ 0.05 mmol or MgO 5 wt% with respect to CC), and CC (1.5 mmol), purged with a nitrogen atmosphere and finally, closed. The mixture was stirred at the desired temperature (40, 60, and 80 °C) for 1 h, and then cooled to rt. Thereafter, it (the mixture) was recovered with acetone (10 mL, HPLC grade, Sigma-Aldrich). The solution was further diluted with acetone (ten volumes) and added to *n*-decane (10 μL) which served as an internal standard. If needed (when an MgO catalyst was used), the resulting mixture was filtered, and it was finally analyzed by using a Thermo Focus gas-chromatograph equipped with a HP-5 capillary column (25 m × 320 μm × 1.05 μm; T_{injector}: 280 °C; split ratio: 30 : 1, nitrogen flow: 1.2 mL min^{-1}). The temperature ramp was: 50 °C for two min, then heating up to 280 °C at 10 °C min^{-1}, and 280 °C for five min. Each compound was calibrated with respect to *n*-decane (the internal standard) to obtain the corresponding response factor in the appropriate range of concentrations. The structure of the products was assigned by ESI-MS and GC-MS, and whenever possible, by comparison with authentic commercial samples.

Most of the catalytic tests were triplicated to check for reproducibility. In the repeated runs carried out under the same conditions, the values of conversion and yields of the products (determined by GC/MS) differed by less than 5% from one reaction to another.

Some model products were also isolated by purifying the reaction mixture through extraction in *n*-hexane or dichloromethane (5–10 mL) and water (20–40 mL), respectively.

Only in the case of glycerol carbonate (GlyC), the product was separated and purified by flash chromatography on silica gel (230–400 mesh; gradient elution: *n*-hexane/ethyl acetate, from 50/50 to 30/70 v/v). The GlyC purity (>99%) was determined by ^1H NMR spectroscopy.

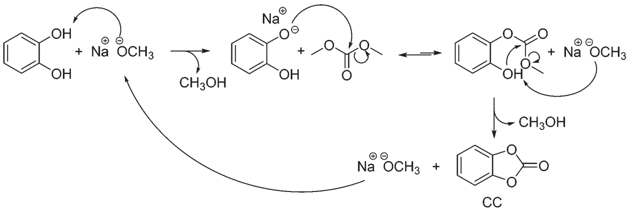
The spectroscopic properties of symmetric carbonate products ($ROCO_2R$) were in agreement with those reported in the literature. Reaction intermediates were also sometimes observed: these compounds were plausibly asymmetric carbonates derived from CC ($ROCO_2R'$) which, due to their high reactivity, could not be isolated. The structures of such products were assigned by GC/MS analyses.

Results and discussion

The synthesis of catechol carbonate

Catechol carbonate (CC, benzo-1,3-dioxolan-2-one) was synthesized by the CIR between DMC and catechol in the presence of the sodium methoxide catalyst (Scheme 4).

DMC, catechol, and the catalyst were used in a 10 : 1 : 0.03 molar ratio, respectively. Experiments were carried out for 24 hours at reflux temperature (90 °C).



Scheme 4 Reaction mechanism of the CIR between DMC and catechol.

The soft nucleophilic character of the catecholate anion did not favour the involved equilibrium processes. Moreover, methanol and DMC formed a low boiling (64 °C, at atmospheric pressure) homogeneous azeotrope in a 85 : 15 molar ratio, respectively.[16] This implied that if the reaction flask was equipped with a conventional distillation system, the co-product azeotrope could be continuously removed, thereby increasing the CC yield. At the same time, however, a sizeable amount of DMC was lost along with MeOH. This drawback was minimized, if not overcome, by implementing a dedicated reactive distillation system (RDS) able to ensure the selective adsorption of methanol over appropriate molecular sieves.[15] Such a RDS and the optimisation of the steps required for the isolation and purification of the product allowed CC to be obtained in a very high isolated yield and selectivity of 90% and 99%, respectively, with satisfactory recycling (up to 60%) of the excess DMC.

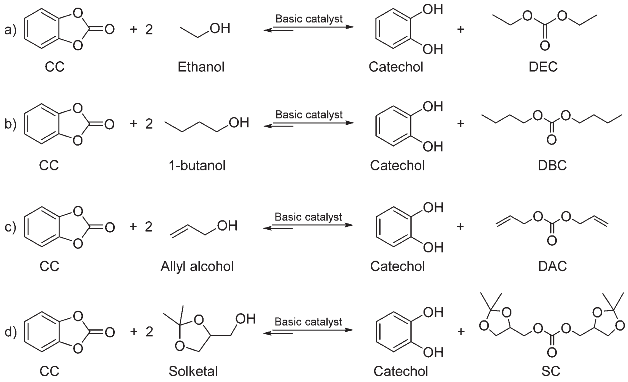
CC: a new and efficient reagent for carbonate interchange processes

The synthesis of symmetric carbonates by CIR with traditional reagents such as DMC or EC includes two consecutive equilibrium reactions, in which two acyl nucleophilic substitutions take place by formal transesterifications and/or disproportionation mechanisms.

This usually requires both long reaction times (up to days) and a large excess of the co-reacting alcohol to shift reaction equilibria rightwards. Moreover, if a polyol like glycerol is used, the reaction selectivity is often elusive since the formation of the desired cyclic carbonate (glycerol carbonate, GlyC) is accompanied by several side-processes which afford oligomers and other heavier glycerol derivatives bearing carbonate-type functions.[17]

By contrast, this investigation demonstrates that CIRs mediated by CC are not only fast and selective processes, but they also proceed with a good mass efficiency.

The reaction of CC with primary aliphatic alcohols. The reactivity of CC for the CIR was initially investigated by using four model alcohols including ethanol, 1-butanol, allyl alcohol, and solketal. The study was aimed at achieving the corresponding symmetric carbonates, *i.e.* diethyl-, dibutyl-, diallyl-, and di-solketal-[bis((2,2-dimethyl-1,3-dioxolan-4-yl)methyl)] carbonate (Scheme 5). Q5

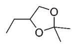


Scheme 5 CIR of CC and primary alcohols to yield symmetric carbonates, in particular: (a) diethyl carbonate (DEC), (b) dibutyl carbonate (DBC), (c) diallyl carbonate (DAC) and (d) bis((2,2-dimethyl-1,3-dioxolan-4-yl)methyl) carbonate. For convenience, the latter compound was named di-solketal carbonate (DSkC).

Each one of these carbonates is characterized by interesting properties and applications. In particular (a) DEC is used as a solvent and a reactant in the manufacture of pharmaceuticals, fertilizers, pesticides, dyes and polymers.[14,18] Moreover, it is a potential fuel additive with superior properties to DMC, because of its higher energy content, lower vapor pressure, and safer hydrolysis products.[19] DEC is mainly produced by the CIR of DMC (or EC) and ethanol: the reaction often leads to mixtures of symmetric and asymmetric methyl ethyl carbonate,[20–22] but DEC yields may be improved (up to 90%), using a RDS apparatus.[23] (b) DBC finds major uses in the production of high-performance polycarbonates and as an eco-lubricant: the good lubricity, wearability, corrosion resistance and high thermal oxidative stability of DBC have literally boosted its market demand over the past decade.[24–26] The synthesis of DBC is usually carried out by the transesterification of DMC or propylene carbonate (PC) with 1-butanol in the presence of a suitable catalyst (ionic liquids, TBD, Fe–Zn cyanide and titanium complexes).[27–30] (c) DAC is an important polyfunctional carbonate mostly used for the fabrication of plastics for optical applications,[30] and as an allylating reagent.[32–34] DAC is mainly prepared by the transesterification of DMC and allyl alcohol in RDS systems. (d) Finally, DSkC has been reported as an intermediate for the synthesis of polyol carbonate and for carbonate based polymers. The synthesis of DSkC has been achieved by the CIR of DEC and solketal in the presence of sodium methoxide as a catalyst: the reaction requires a continuous distillation system to remove the ethanol/DEC azeotrope, followed by extraction with CH_2Cl_2. Under such conditions, however, the isolated yield of DSkC does not exceed 65% even after 20 h.[35]

Such interest in these organic carbonates is fuelling a continuous search for efficient methods for their synthesis; particularly, procedures based on catalytic transesterification processes are still a highly desirable target. In light of these considerations, a study of the reactions shown in Scheme 5 was undertaken. Experiments were carried out at 80 °C by using a mixture of CC, alcohol, and a homogeneous basic catalyst, namely sodium methoxide in a 1 : 2 : 0.03 molar ratio, respectively. The reactions were all performed under an inert atmosphere (N_2) and they were monitored for 1 hour. The results are reported in Table 1 where the conversion of reagents (CC and the alcohol) and the yield of both the desired symmetric carbonates ($ROCO_2R$) and the corresponding asymmetric intermediates ($ROCO_2R'$, Fig. 1) are shown.

Table 1 CIRs of CC with aliphatic alcohols

		Conv. (%)		Products, yield (%)		
Entry	Alcohol (A)	X_{CC}	X_A	R	$ROCO_2R$	$ROCO_2R'$
1	Ethanol	92	33	Et	33	0
2	1-Butanol	89	48.1	*n*-Bu	48	0.1
3	Allyl alcohol	100	53	Allyl	52.7	0.3
4	Solketal	97.3	82.3	 (Sk)	70.7	1.6

[a] Reagents and catalyst molar ratio: CC : A : NaOMe = 1 : 2 : 0.03. Reaction conditions: 1 h, 80 °C, an inert (N_2) atmosphere was always secured. Conversion (X) and yields (Y) were based on CC as the limiting reagent and were evaluated by GC analysis using *n*-decane as an internal standard. Q6

It was noted that particularly the conversion of the reactant alcohol (X_A) was far lower than that expected from the stoichiometry. This was mainly due to the onset of a hydrolysis process of CC back to the parent catechol (Scheme 6).

This side-reaction clearly hindered the formation of the desired symmetrical carbonates whose corresponding yields were only 33–71%. Since the hydrolysis of CC could not be limited even on operating under a N_2 atmosphere, two further expedients were considered. A second set of experiments was devised in which the reactions shown in Scheme 5 were carried out at a lower temperature (60 °C) using excess alcohol (CC : alcohol in a 1 : 6 molar ratio, respectively). For comparison, the same conditions were also applied to conduct the CIR with both DMC and EC in place of CC. The results are described in Table 2.

In the case of CC, the reaction proved successful: the undesired competitive hydrolysis process shown in Scheme 6 was substantially suppressed and good-to-excellent yields (71–98%) of the symmetric carbonates ($ROCO_2R$) could be reached in all cases (entries 1, 4, 7, and 10). No asymmetric carbonates were

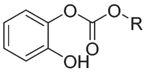
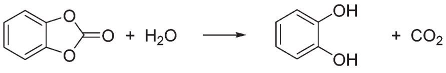


Fig. 1 Asymmetric carbonate in the CIRs of CC.



Scheme 6 CC hydrolysis to catechol.

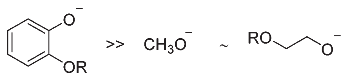
Table 2 Reactivity comparison of CC, EC and DMC in CIRs with ethanol, 1-butanol, allyl alcohol, and solketal[a]

Entry	Carbonyl source (A)	Alcohol (B)	A : B : NaOMe (molar ratio)	Conv. (%)		Products				
						Symmetric: $ROCO_2R$		Asymmetric: $ROCO_2R'$		
				X_A	X_B	Yield (%)	R	Yield (%)	R	R′
1	CC	Ethanol	1 : 6 : 0.03	100	29	93	Et (DEC)	—	Et	Catechol
2	EC			64	33	8		43		CH_2CH_2O–
3	DMC			78	18	21		57		Me
4	CC	1-Butanol	1 : 6 : 0.03	100	28	71	*n*-Bu (DBC)	—	*n*-Bu	Catechol
5	EC			59	10	4		9		CH_2CH_2O–
6	DMC			5	1	—		5		Me
7	CC	Allyl alcohol	1 : 6 : 0.03	100	36	73	Allyl (DAC)	—	Allyl	Catechol
8	EC			61	48	2		5		CH_2CH_2O–
9	DMC			34	7	2		32		Me
10	CC	Solketal	1 : 6 : 0.03	100	36	98	Sk (DSkC)	1.6	Sk	Catechol
11	EC			23	5	2		21		CH_2CH_2O–
12	DMC			79	28	12		67		Me

[a] All reactions were carried out for 1 hour at 60 °C under an inert (N_2) atmosphere in the presence of NaOMe as a catalyst. Sk defined as in Table 1. Conversion (*X*) and yields (*Y*) were evaluated by GC analysis using *n*-decane as an internal standard. Yields were based on the reactant carbonate (CC, EC, and DMC, respectively) as the limiting reagent.

detected under such conditions. Both the temperature and the reactants molar ratio were clearly crucial parameters to steer the reaction selectivity. But even more importantly, experiments highlighted the role of the reactant carbonate: the results left few doubts about the superior outcome of the CC-mediated CIR with respect to the same reactions carried out with DMC or EC. Irrespective of the co-reagent alcohol, carbonates traditionally used for CIRs such as DMC and EC not only were significantly less reactive than CC, but they led to a mixture of products where the desired derivatives ($ROCO_2R$) were obtained in very low yields (8–21%: entries 2–3, 5–6, 8–9, and 11–12). By contrast, sizeable amounts of asymmetric carbonates were noted ($ROCO_2R'$: 5–67%): the structures of such products were assigned by GC/MS analyses. A plausible explanation for such behaviour could be found looking at the involved leaving groups (LGs): the catecholate-like anion released during the reaction of CC was remarkably more stable than the methoxide and glycolate-like species formed as LGs from DMC and EC, respectively (Scheme 7).

Of particular note was the difference between CC and EC: even though both compounds bear the carbonate moiety in a 5-membered cyclic structure, the easier ring opening observed during the transesterification of CC could be ascribed to the simultaneous contribution of the release of steric strain[36] and the leaving group properties (stability) of the catecholate anion. The same (latter) reason also accounted for the choice of diphenyl-rather dimethyl-carbonate for the transesterification of bisphenol-A in the above mentioned Asahi-Kasei method for the production of polycarbonate.[7]



Scheme 7 The stability order of LGs originated in CIRs carried out with CC, DMC, and EC, respectively.

With respect to ethanol and solketal, allyl and butyl alcohols gave lower, but still good yields of the corresponding carbonates (71–73%). No clear explanation could be offered for such a behaviour.

Once the CIRs carried out by CC were complete, an effective purification and separation of symmetric carbonates was achieved by washing the final mixtures with water: while the co-product catechol and unreacted alcohols were rapidly solubilized in the aqueous medium, the desired derivatives ($ROCO_2R$) were not and they were easily isolated in a very high purity by extraction with common hydrophobic solvents (*n*-hexane or dichloromethane). For example, after the reaction of entry 4, the mixture was treated with water/*n*-hexane (30 and 10 mL, respectively) to isolate DBC in a 58% yield (based on 71% GC yield). Moreover, a good recovery of the excess alcohol and catechol (90%) was carried out by distillation of aq. mother liquors. Catechol could then be recycled for the synthesis of CC (Scheme 4). These observations indicated how the low atom economy of CC-mediated CIRs was offset by the practical implementation of the process through efficient steps of reaction, separation, and recycling.

We also tested CC for the CIR with phenol, aimed at the synthesis of diphenylcarbonate (DPC), and for the synthesis of polycarbonates; the results of these experiments are reported in the ESI.† Unfortunately, in the case of the CIR with phenol, despite the high CC conversion, we did not obtain any formation of either DPC or the asymmetric intermediate. This may be due to the steric hindrance which limits the nucleophilic attack of the phenate to CC.

Conversely, preliminary polymerisation tests carried out with CC and 1,4-butanediol led to polycarbonate with a moderate molecular weight – close to 15.000 – and good polydispersity, when the reaction was carried out at 120 °C for 48 h.

To further explore the potential of CC for CIR protocols, additional experiments were performed by replacing NaOMe with a heterogeneous catalyst such as magnesium oxide (MgO: 5 wt% with respect to CC). Preliminary screening tests were carried out under the conditions presented in Table 2 (60 °C, 1 hour, CC : alcohol in a 1 : 6 molar ratio, respectively). It was noted that MgO disfavoured the CIR kinetics with respect to NaOMe. Both the weaker basicity of the oxide and diffusional limitations at the surface of the solid catalyst plausibly accounted for the result. A higher reaction temperature of 80 °C was therefore considered to continue the investigation. The results are reported in Table 3.

The conversion of reactants was not as satisfactory as that obtained with NaOMe (*cf.* Table 2), but the overall reaction outcome was still acceptable: the yields of symmetric carbonates were in the range of 60–72% for DEC, DBC, and DAC, respectively (entries 1–3). Surprisingly, a remarkable drop was observed in the case of DSkC (32%, entry 4); such a result was improved by prolonging the reaction up to 4 hours (69%, entry 5). Although the (case-by-case) optimization of reaction conditions was not further investigated, the results proved the concept, thereby confirming the good performance of CC-mediated CIRs with primary aliphatic alcohols even in the presence of a simple and cheap catalyst such as MgO.

Table 3 CIR of CC with primary alcohols catalysed by MgO[a]

		Conv. (%)		Products, yield (%)		
Entry	Alcohol (A)	X_{CC}	X_A	R	$ROCO_2R$	$ROCO_2R'$
1	Ethanol	94	23	Et	65	9
2	1-Butanol	83	21	*n*-Bu	60	0
3	Allyl alcohol	95	24	Allyl	72	0
4	Solketal	46	27	Sk	31.5	0.5
5[b]	Solketal	74	24	Sk	69	1.1

[a] Reagents molar ratio: CC : A = 1 : 6; MgO was used as a heterogeneous catalyst in 5 wt% with respect to the limiting reagent (CC). [b] The reaction time was increased to 4 hours. Reaction conditions: 1 h, 80 °C, an inert (N_2) atmosphere was always secured. Sk defined as in Table 1, ROCOR′ defined as in Fig. 1. Yields were based on CC and were evaluated by using *n*-decane as an internal standard.

The reaction of CC with secondary aliphatic alcohols. Secondary alcohols are poorer nucleophiles than primary alcohols. Not surprisingly, CIRs involving such (secondary) substrates are often sluggish processes, if occurring at all. Based on the results of Tables 1–3, we wondered whether the peculiar reactivity of CC could be exploited also for the synthesis of less accessible symmetric dialkyl carbonates; in particular, the preparation of diisopropyl carbonate (DiPC) and dicyclohexyl carbonate (DCC) was considered from the reaction of CC with 2-propanol and cyclohexanol, respectively.

The reactions were carried out at 80–100 °C, in the presence of NaOMe as a catalyst (0.06 molar equiv. with respect to CC), and by varying the CC : alcohol molar ratio from 1 : 4 to 1 : 30. The results are reported in Table 4.

Under conditions similar to those used for primary alcohols, the CIR of CC with both i-PrOH and CyOH showed an incomplete CC conversion (86–89%) and it afforded variable amounts of symmetric and asymmetric carbonate products (entries 1 and 4).

However, the progressive increase of the amount of alcohol (up to 30 equiv. excess), the reaction time (2 to 5 hours), and the temperature (up to 100 °C in the case of i-PrOH only) allowed the boosting of the selectivity and the yield of the desired derivatives ($ROCO_2R$) to 100% and 90–99%, respectively (entries 3 and 6). Once the reaction of entry 3 was complete, the mixture was washed with water (20 mL) and extracted with dichloromethane (5 mL). The purification procedure was not further optimized: DiPC was isolated in a 67% yield, while the co-product catechol was quantitatively recovered.

Secondary alcohols clearly required more energy- and mass-intensive reactions with respect to primary substrates. Moreover, it was noticed that 2-propanol was remarkably less reactive than cyclohexanol. Steric reasons plausibly accounted for the comparison between primary and sec-alcohols; less obvious was the different behaviour of the two investigated sec-alcohols. Whichever the case, the results of Table 4 substantiated the capability of CC as a building block also for sterically hindered carbonates.

Table 4 CIR of CC with secondary alcohols (2-propanol and cyclohexanol)

					Conversion (%)		Products, yield (%)		
Entry	Alcohol (A)	CC : A : NaOMe (molar ratio)	*T* (°C)	*t* (h)	X_{CC}	X_A	R	$ROCO_2R$	$ROCO_2R'$
1	2-Propanol	1 : 4 : 0.06	80	1	86	—	i-Pr	10.3	43.3
2	2-Propanol	1 : 10 : 0.06	80	1	86.3	—	i-Pr	56.8	14.5
3	2-Propanol	1 : 30 : 0.06	100[a]	5	100	—	i-Pr	90	0
4	Cyclohexanol	1 : 4 : 0.06	80	1	89.6	25.6	Cy	47.6	14.3
5	Cyclohexanol	1 : 10 : 0.06	80	1	97.2	14.8	Cy	93.9	1.3
6	Cyclohexanol	1 : 30 : 0.06	80	2	98.5	5.9	Cy	98.5	0

All reactions were carried out under a N_2 atmosphere. Yields were calculated based on the limiting reagent and were evaluated by using *n*-decane as an internal standard. ROCOR′ defined as in Fig. 1. [a] Test performed in an autoclave under an autogenous pressure of 2 bar.

The reaction of CC with glycerol: the synthesis of glycerol carbonate (GlyC)

A further aspect of the investigation reported in this paper was devoted to explore the use of CC for the synthesis of alkylene carbonates. Among such cyclic derivatives, glycerol carbonate (4-hydroxymethyl-2-oxo-1,3-dioxolane, GlyC) was chosen as a model product. The preparation of this compound has gained momentum over the last 20 years not only as a strategy for the valorisation of bio-glycerol (from the manufacture of biodiesel), but also for the versatility of GlyC. GlyC in fact is a carbonate species bearing also a free hydroxyl group, a feature which makes it an ambiphilic synthon able to serve (even simultaneously) as an electrophile and a nucleophile.[36] Moreover, GlyC exhibits excellent physicochemical properties: it shows an unusually large liquid range (from −69 °C to 354 °C), a flash point as high as 190 °C, and a high solvency even for inorganic salts. Only to cite a few of its potential applications, glycerol carbonate has been investigated as a component for gas separation membranes, polyurethane foams and surfactants, coatings, and hyperbranched polymers,[38] and as a candidate for green syntheses of glycidol and epichlorohydrin.[39]

The preparation of GlyC has been described from two major reagents: glycidol and glycerol.[40] The value of glycidol-based routes is in the use of safe CO_2 as the carbonate building block; these methods however suffer from the high toxicity and cost of glycidol.

Even more undesirable in this respect are the phosgenation and oxidative carbonylation of glycerol which use highly toxic and corrosive starting materials.[41]

A far more sustainable method is the carbonation of glycerol with CO_2, this being a highly atom economical process (AE: 87%) which involves renewable, safe, and cheap reactants. Though, of the many studies in this field,[39,42,43] the best reported yield of GlyC is only 34% by using Bu_2SnO and methanol as the catalyst and the solvent, respectively.[44] Such a moderate result is due to thermodynamic constraints and it makes the process not yet acceptable for an industrial scale-up. A more promising procedure is the glycerolysis of urea which proceeds with high conversions (>80%) and complete selectivity towards GlyC.[45,46] This process however co-produces sizeable amounts of ammonia as a by-product which limits any large scale implementation of the reaction. A last route for the synthesis of GlyC is the CIR of both cyclic and linear carbonates with glycerol. This reaction has been widely reported in several reviews: although a good conversion is often described, an issue is the selectivity control (and the product separation) due to side-reactions of glycerol forming heavier by-products and oligomers.[38,46,47]

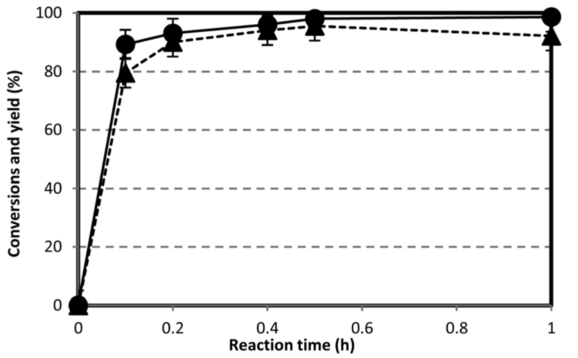


Fig. 2 CIR of CC with glycerol. Conditions: CC : glycerol : $NaOCH_3$ = 1 : 1 : 0.03; N_2 atmosphere; T = 60 °C. ● CC conversion, ▲ GC yield (dashed line).

Glycerol carbonate (GlyC) from CC. In this work, the CIR of CC with glycerol was initially investigated using $NaOCH_3$ as a catalyst. A preliminary test was carried out at 60 °C, under a N_2 atmosphere, and using a mixture of CC, glycerol, and the catalyst in a 1 : 1 : 0.03 molar ratio respectively. The results are reported in Fig. 2.

Even if the reagents were used in the exact stoichiometric proportions, a very fast, quantitative, and selective reaction was observed. It was noticed that the yield of GlyC was as high as 92% after 30 min, and in only just 1 hour, it was further increased up to 98% (Table 5), with an outstanding selectivity >99%. Even more surprisingly, the CIR of CC with glycerol proceeded at a lower temperature of 40 °C: under the conditions of Fig. 2 (CC, glycerol, and NaOMe in a 1 : 1 : 0.03, molar ratio respectively; 1 hour), the desired GlyC was achieved in a yield of 92%, only slightly less than that observed at 60 °C. To the best of our knowledge and considering the very mild reaction conditions used, this was one of the best ever reported results for the synthesis of glycerol carbonate.

The process took place through the initial attack of a primary hydroxyl of glycerol to CC, which plausibly formed a mono-transesterified intermediate (though, this species was never detected); afterwards, a ring-closure reaction afforded GlyC as a stable cyclic derivative (Scheme 8).

In general, the reaction proved rather sensitive to traces of water in the reaction environment. In line to the results of Tables 1–4, a single experiment carried out at 60 °C (conditions of Fig. 2, but in the absence of an inert atmosphere) showed a significant drop in the GlyC yield: this did not exceed 82% after 1 h, because CC was partly hydrolysed to catechol (Scheme 6).

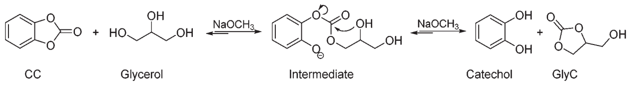
Encouraged by these very good results, additional tests were carried out by replacing NaOMe with MgO as a heterogeneous catalyst (5 wt% with respect to CC). In this case however, a solvent was necessary because the solid catalyst could not be adequately suspended (not even under vigorous stirring) in the highly viscous equimolar mixture of CC and glycerol. Anhydrous THF (1 mL) was used for this purpose. At 60 °C, MgO allowed a comparable outcome to NaOMe: the yield of GlyC was 96% after 1 hour, with no appreciable by-products. The visual inspection of the reaction also showed that the mixture became more and more fluid and easy-to-handle during the progressive formation of GlyC, this compound clearly acts as an effective co-solvent for the unconverted reagents. Once the experiment was complete, the solid catalyst was filtered and the product was purified by flash column chromatography on silica gel (230–400 mesh; gradient elution : *n*-hexane/ethyl

Table 5 The synthesis of GlyC by the CIR of CC with glycerol in the presence of both homogeneous and heterogeneous catalysts[a]

	Homogeneously catalysed reactions (sodium methoxide)					
Entry	Carbonyl source (A)	A : glycerol : NaOMe (molar ratio)	T (°C)	Conversion (%)		Glycerol carbonate, yield (%)
				X_A	$X_{Glycerol}$	
1	CC	1 : 1 : 0.03	60	98.6	99	98
2	EC	1 : 1 : 0.03	60	73	80	69
3	DMC	1 : 1 : 0.03	60	27	30	26

	Heterogeneously catalysed reactions (MgO)[a]						
	Carbonyl source (A)	A : glycerol (molar ratio)	MgO cat. (wt%)[b]	T (°C)	Conversion (%)		Glycerol carbonate, yield (%)
					X_A	$X_{Glycerol}$	
4	CC	1 : 1	5	60	99	96	96
5	EC	1 : 1	5	60	60	95	69
6	DMC	1 : 1	5	60	20	11	1

[a] All reactions were carried out for 1 hour. [b] MgO-catalysed reactions were carried out in the presence of anhydrous THF as a solvent. Yields were based on the reactant carbonate (CC, EC, and DMC, respectively) as the limiting reagent and were evaluated by using *n*-decane as an internal standard.



Scheme 8 CIR of CC with glycerol.

acetate, from 50/50 to 30/70 v/v). Glycerol carbonate was isolated in a 77% yield with a purity grade >99%.

The CIRs of EC and DMC with glycerol were finally investigated to compare the reactivity of such conventional carbonates with that of CC. The reactions were run under the conditions of Fig. 2. The results are reported in Table 5 which, for convenience, also includes the above described data on catalytic tests carried out with CC and glycerol.

Experiments demonstrated beyond any doubt that CC was the best reagent among the tested carbonates. In the presence of the NaOMe catalyst, both EC and DMC led to a limited conversion and the corresponding yields of GlyC were only 69% and 29%, respectively (entries 2 and 3). Moreover, especially in the case of EC, the formation of sizeable amounts of oligomers was noticed, this fact causing a severe loss in the carbon balance of these reactions.

The situation was even worse when MgO was used as a catalyst. In this case, DMC proved completely inefficient for the CIR (yield ~1%; entry 6).

By contrast, irrespective of the catalyst, the reaction of CC with glycerol always offered a quantitative process with complete selectivity towards glycerol carbonate (entries 1 and 4).

The overall behaviour could be accounted for by the leaving group stability described in Scheme 7, thereby confirming the trend already observed for the CIRs of CC, EC, and DMC with primary alcohols (*cf*. Table 2).

In the ESI,† the results presented here are compared with the best literature results for glycerol carbonate synthesis carried out using other procedures.

Conclusions

This investigation describes an inventive protocol for the carbonate interchange reaction based on catechol carbonate (CC). The study provides evidence of the outstanding and never previously reported reactivity of CC with a variety of aliphatic alcohols including primary, secondary and polyfunctional substrates. Even after operating under very mild conditions (more often 40–60 °C and ambient pressure), a very fast kinetics is observed, most of the reactions being complete in only 1 hour in the presence of genuine catalytic amounts of NaOMe (3 mol%) or MgO (5 wt%) as the basic homogeneous or heterogeneous catalysts, respectively. Symmetric carbonate products ($ROCO_2R$) are hence achieved in good-to-excellent yields in the range of 70–99%. By contrast, under the same reaction conditions, conventional model carbonates such as DMC and EC show a much poorer performance (yields ≤15–20%). This difference is plausibly explained by the weaker stability of leaving groups (methoxide and glycolate-like anions) released by both DMC and EC with respect to the catecholate species expelled by CC.

The CC-mediated CIR protocol is characterized by an intrinsically low atom economy and it requires over stoichiometric amounts of reactant alcohols, particularly when moderate nucleophiles such as secondary substrates are involved. However, the implementation of a simple expedient such as the water washing of the final reaction mixtures perfectly separates hydrophobic symmetric carbonates from the water-soluble (unconverted) alcohols and the co-product catechol, thereby allowing not only an easy purification of the desired products, but also the recovery and recycling of residual compounds in the aqueous phase. This implies a remarkable reduction of the reaction wastes and the impact (cost, time, safety) of the work-up procedure.

In addition, the method does not use any solvents and it is suited to the conversion of bio-based alcohols, particularly glycerol. In this respect, the CC-based method has highlighted an extremely promising synthesis of glycerol carbonate which affords a quantitative yield in only 30 min even on operating at 60 °C and with an equimolar mixture of the reactants (CC and glycerol). This being one of the best ever reported results for such a reaction.

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