Cavitand-Based Polyphenols as Highly Reactive Organocatalysts for the Coupling of Carbon Dioxide and Oxiranes

Luis Martínez-Rodríguez,^[a] Javier Otalora Garmilla,^[a] and Arjan W. Kleij*^[a, b]

A variety of cavitand-based polyphenols was prepared from cheap and accessible aldehyde and resorcinol/pyrogallol reagents to give the respective resorcin[4]- or pyrogallol[4]arenes. The preorganization of the phenolic units allows intraand intermolecular hydrogen bond (HB) networks that affect both the reactivity and stability of these HB-donor catalysts. Unexpectedly, we found that the resorcin[4]arenes show cooperative catalysis behavior compared to the parent resorcinol in the catalytic coupling of epoxides and CO_2 with a significantly

Introduction

One of the biggest challenges associated with CO₂ conversion is the design of appropriate catalyst systems that show good reactivity and selectivity.^[1] To date, most attention in the area of CO₂ catalysis has been focused on (homogeneous) catalysts based on metal complexes of various kinds that show high reactivity and unusual scope and/or selectivity in a few cases.^[2] Metal catalysts based on abundant metals such as Zn,^[3] Fe,^[4] Al,^[5] and Co^[6] have received much attention to allow for significant evolution in both catalyst design as well as the improvement of the product portfolio that can be accessed from CO₂, which represents a renewable and cheap carbon feedstock for chemical synthesis.

Recently, organocatalysis has appeared on the radar of synthetic chemists as it is a sustainable alternative to metal-based approaches in the catalysis of CO_2 conversion.^[7] In particular, the catalytic coupling of epoxides and CO_2 has been studied extensively and can be regarded as a benchmark process for new catalyst development in nonreductive CO_2 coupling. Progress in this area has been considerable with the development of efficient catalyst systems based on binary or bifunctional systems that comprise azaphosphatranes,^[8] polyphenols,^[9] phosphonium or ammonium alcohols,^[10] silane diols,^[11] and flu-

-	
[a]	L. Martínez-Rodríguez, J. Otalora Garmilla, Prof. Dr. A. W. Kleij Institute of Chemical Research of Catalonia (ICIQ)
	The Barcelona Institute of Science and Technology
	Av. Països Catalans 16
	43007 Tarragona (Spain)
	E-mail: akleij@iciq.es
[b]	Prof. Dr. A. W. Kleij
	Catalan Institute of Research and Advanced Studies (ICREA)
	Pg. Lluís Companys 23
	08010 Barcelona (Spain)
	Supporting information for this article can be found under http:// dx.doi.org/10.1002/cssc.201501463.

higher turnover. At elevated reaction temperatures, the resorcin[4]arene-based catalyst **3d** displays the best catalytic performance with very high turnover numbers and frequencies, combining increased reactivity and stability compared to pyrogallol, and an ample substrate scope. This type of polyphenol structure thus illustrates the importance of a new, highly competitive organocatalyst design to devise sustainable CO_2 conversion processes.

orinated alcohols.^[12] Parallel to these activities, other promising organocatalytic systems have been communicated recently that present new catalyst designs based on the host–guest complexation of nucleophilic reagents,^[13] the use of phosphorus ylides,^[14] and hydroxy-functionalized mono- and bisimida-zolium bromides.^[15]

We have become interested in the use of (natural) polyphenols such as pyrogallol and tannic acid (1 b and 2, respectively; Figure 1) for the conversion of epoxides through hydrogen bond (HB) activation. Their transformation into cyclic carbonates in the presence of CO₂ takes advantage of the extended HB network that arises upon the activation of the epoxide towards the formation of key intermediates. Consequently, lower kinetic barriers allow either low-temperature conversions (45 °C)^[9b,c] or the use of a reduced polyphenol loading for effective catalytic turnover.^[9a] Nonetheless, there are still challenges to be met upon using such polyphenols as at higher reaction temperatures (i.e., 80°C) some catalyst degradation through deprotonation and the formation of relatively inactive phenolate groups cannot be fully avoided, which prevents the efficient recycling of these phenolic additives and thus restricts the total turnover number (TON).^[9a,c]

In our quest to develop thermally more robust polyphenolbased catalysts with a high reactivity and a privileged substrate scope, we considered that cavitand structures (Figure 1; 3)^[16] may deliver the appropriate combination of activity and thermal/chemical stability. These cavitand structures, which include resorcin[4]arenes (**3**: X = H) and pyrogallol[4]arenes (**3**: X = OH), give rise to preorganized supramolecular structures that are often hexameric in nature in solution and in the solid state through intermolecular, water-assisted HB interactions (Figure 2, right).^[17] At the same time, the bowl shape of monomeric cavitand molecules is controlled through intramolecular





Figure 1. Schematic structures of resorcinol (1 a), pyrogallol (1 b), tannic acid (2), and cavitand-based polyphenols (3).



Figure 2. Intra- and intermolecular HB networks in cavitand-based structures. Part of this figure is reprinted with permission from Ref. [19]. Copyright (2013) American Chemical Society.

HBs between adjacent resorcinol/pyrogallol units typically expressed in solvent media such as alcohols and acetonitrile (Figure 2, left).^[18] These intramolecular HB patterns suggest a similar potential for the catalytic activation^[19] of epoxides as for pyrogallol/tannic acid (Figure 1) as the stabilization of key intermediate transition states through multiple HB interactions is more efficient than in the absence of such HB donors.

CHEMSUSCHEM Full Papers

In this contribution we will show that cavitand-based polyphenols are excellent HB activators in the formation of cyclic carbonates from epoxides and CO_2 with unprecedented turnover numbers and frequencies. Catalytic data in combination with several control experiments support a cooperative catalytic effect when using the resorcin[4]arene systems; the latter show the best combination of activity and stability at elevated temperatures. In combination with the easy access to these modular and cheap polyphenolic structures and catalytic scope, these cavitands represent a new and powerful type of organocatalyst for the conversion of CO_2 into value-added chemicals.

Results and Discussion

Resorcin[4]arenes **3** a–e, pyrogallol[4]arenes **3** f–I, and octahydroxypyridine[4]arene **3** j (Scheme 1) were prepared according to procedures reported previously (Experimental Section) and their molecular identity was established by ¹H and ¹³C NMR spectroscopy and MS: these data were in accordance with the



Scheme 1. Resorcin[4]arenes 3 a-e, pyrogallol[4]arenes 3 f-i, and the octahydroxypyridine[4]arene 3 j.

literature data (Supporting Information). Compounds **3ai** were initially tested in combination with NBu₄X (X = halide) as binary catalysts in the coupling of 1,2-epoxyhexane (**4a**) and CO₂ at 50 °C using methyl ethyl ketone (MEK) as the solvent (Table 1).

We first tested **3 b**/NBu₄I as a binary catalyst for the synthesis of organic carbonates from epoxides and CO₂ under conditions closely related to those tested previously for a binary pyrogallol-based system (Table 1, entry 1).^[9c] At 45 $^{\circ}$ C, a yield of 81% (measured by NMR spectroscopy) was already achieved, and an increase of the temperature to 50°C increased this yield to 91% (entry 2). Dilution of the reaction mixture (entry 3) or changing the nature of the nucleophile (entries 4 and 5) gave poorer kinetics, which led to lower yields of 4b. In the absence of **3b** (entry 6; 4%) or nucleophile (entry 7; 0%) very low to no conversion of the epoxide substrate was observed, which shows the imperative role of both catalyst components in this coupling reaction. A comparison of the efficiency of 3b (entry 2) with that of the parent building unit resorcinol (1a; entry 7) showed a much higher yield of carbonate 4b for the cavitand-based system despite the use of a similar concentration of diphenol units. This effect was maintained under more

Table 1. Screening of conditions using a polyphenol/TBAX binary catalyst in the coupling of 1,2-epoxyhexane and CO_2 to afford $4b$. ^[a] nBu nBu_4X nBu MEK, CO_2 $4a$						
Entry	Polyphenol	Amount [mol %]	NBu₄X [mol%]	<i>T</i> [°C]	MEK [mL]	Yield of 4 b ^[b] [%]
1	3 b	1.5	l, 5.0	45	2.5	81
2	3 b	1.5	l, 5.0	50	2.5	91
3	3 b	1.5	l, 5.0	50	5.0	65
4	3 b	1.5	Cl, 5.0	50	2.5	31
5	3 b	1.5	Br, 5.0	50	2.5	65
6	-	0	l, 5.0	50	2.5	4
7	3 b	1.5	0	50	2.5	0
8	1a	6.0	l, 5.0	50	2.5	47
9	1a	6.0	l, 5.0	50	5.0	24
10	1 b	4.0	l, 5.0	50	2.5	99
[a] Reaction conditions: 1,2-epoxyhexane 1.0 mmol, $p(CO_2) = 10$ bar, 18 h,						

polyphenol amount normalized with respect to [OH] groups, $p(CO_2) = 1.0$ MPa, 18 h. [b] NMR yields based on mesitylene as internal standard, selectivity for **4b** was >99%.

dilute conditions (cf. entries 3 and 9). Pyrogallol (1b), a triphenol, gave a virtually quantitative yield (entry 10, 99%) under these conditions. The remarkable yield of 4b in the presence of 3b suggests a cooperative effect between the 1,3-diphenol sites in the catalytic activation of the epoxide and/or more efficient stabilization of the intermediates of the carbonate formation reaction.

We then screened a series of nine cavitands (3a-i;Scheme 1) in the coupling of 4a and CO_2 (Table 2) to investigate the role of the pendent R groups. Within the series of 3a-e (entries 1–5), the highest yield of 4b was achieved with 3d (R=nonyl), a trend that was also observed for 3f-i (entries 6–9).^[20]

Table 2. Screening of cavitand/TBAI binary catalysts 3 in the coupling of1,2-epoxyhexaneand CO_2 toaffordcycliccarbonate4b. ^[a] nBu_{4l}^{0} NBu_{4l}^{0} NBu_{4l}^{0} nBu_{4b}^{0} nBu_{4b}^{0} nBu_{4b}^{0}						
Entry	Cavitand	Amount [mol%]	NBu₄l [mol%]	<i>Т</i> [°С]	R	Yield 4 b ^[b] [%]
1	3 a	1.5	5.0	50	Me	93
2	3 b	1.5	5.0	50	Et	91
3	3 c	1.5	5.0	50	Bu	94
4	3 d	1.5	5.0	50	Non	98
5	3 e	1.5	5.0	50	Ph	27
6	3 f	1.0	5.0	50	Me	78
7	3 g	1.0	5.0	50	Et	84
8	3 h	1.0	5.0	50	Bu	87
9	3i	1.0	5.0	50	Non	93
[a] 1.2-Enovybeyane 1.0 mmol polyphenol amount normalized with re-						

[a] 1,2-Epoxyhexane 1.0 mmol, polyphenol amount normalized with respect to [OH] groups, MEK 2.5 mL, $p(CO_2) = 1.0$ MPa, 18 h; abbreviations: Me=methyl, Et=ethyl, Bu=*n*-butyl, Non=*n*-nonyl, Ph=phenyl. [b] NMR yields based on mesitylene as internal standard, selectivity for **4b** was >99%.

The best-performing nonyl-substituted polyphenols **3d** and **3i** were examined more closely and compared with the parents **1a** and **1b**, and the kinetic profiles of each binary catalyst (in combination with NBu₄I) were determined (Figure 3). In-



Figure 3. Comparative kinetics in the formation of **4b** from 1,2-epoxyhexane and CO_2 using **1a**, **1b**, **3d**, and **3i**. The amount of polyphenol was normalized with respect to the concentration of OH groups. Conditions: 4 mol% **1b**, 5 mol% **1a**, 1.5 mol% **3d**, and 1.0 mol% **3i**. For all reactions: 1,2-epoxyhexane 1.0 mmol, NBu₄I 5 mol%, MEK 2.5 mL, $p(CO_2) = 10$ bar, 50 °C.

terestingly, 3i shows an inferior catalytic performance to 3d. The reason for this behavior is likely the competing self-assembly of the individual cavitand molecules of 3i into larger aggregates (i.e., hexamers, cf. Figure 2). Avram and Cohen compared the stability of undecyl-substituted resorcin[4]arenes and pyrogallol[4]arenes.^[21] Titration studies on these cavitand molecules demonstrated that if the polarity of the medium was increased by adding CD₃OD to a solution of the cavitand in CDCl₃, the hexameric, aggregated state was fully disrupted for both types of cavitand. However, essentially much lower amounts of CD_3OD were required in the case of the resorcin-[4] arene in line with a stronger self-assembly behavior of the pyrogallol[4]arene. Therefore, under the reaction conditions reported in Table 2 and Figure 3, the poorer performance of 3 fi compared to 3a-d is thus explained in terms of a stronger competing self-assembly. This behavior competes with hydrogen bonding between the epoxide and the phenolic groups and thus slows down the reaction. To further support the view that competitive HB interactions can slow down the catalytic reaction, octahydroxypyridine[4]arene (**3j**; Scheme 1)^[22] was tested as a HB-donor system in the synthesis of 4b. The 2,6-dihydroxypyridine subunits in 3j are known to induce intramolecular N-HO hydrogen bonds, and the significantly lower yield after 18 h (1.5 mol%, 60%) than that observed for 3d (1.5 mol%, 98%) is a clear testament for competitive H-bonding. Thus, the best catalytic performance among the cavitand structures at 50 °C is observed for **3 d**.

In an effort to further increase the reactivity, the coupling of 1,2-epoxyhexane and CO_2 was performed at 80 °C using **3d**, **3i**, and **1b** (Table 3, Figure 4). Under these conditions, the nucleophilic additive NBu₄I alone leads to poor catalysis (entry 1, 17% yield of **4b**). Various combinations of cavitand and nucle-

ChemSusChem	2016	9	749 – 755	
circinsuscricin	2010,	γ,	747 755	



Table 3. Catalytic coupling of 1,2-epoxyhexane and CO ₂ at 80 °C to afford cyclic carbonate 4 b. ^[a] P_{Bu}						
Entry	Polyphenol	Amount [mol%]	NBu₄l [mol%]	Т [°С]	Yield 4b ^[b] [%]	
1	-	0	1.6	80	17	
2	3 d	0.75	2.5	80	>99	
3	3 d	0.50	1.6	80	>99	
4	3 d	0.25	0.8	80	80	
5	3i	0.33	1.6	80	93	
6	1 b	2.0	3.2	80	>99	
7	1 b	1.3	1.6	80	77	
8	1 b	0.66	0.8	80	55	
[a] 1,2-Epoxyhexane 1.0 mmol, polyphenol amount normalized with re-						

spect to [OH] groups, MEK 2.5 mL, $p(CO_2) = 1.0$ MPa, 18 h. [b] NMR yields based on mesitylene as internal standard, selectivity for **4b** was >99%.



Figure 4. Comparative kinetics in the formation of **4b** from 1,2-epoxyhexane and CO₂ at 80 °C using **1b** (1.3 mol%), **3d** (0.50 mol%), and **3i** (0.33 mol%). Conditions: 1,2-epoxyhexane 1.0 mmol, NBu₄l 1.6 mol%, 2.5 mL, $p(CO_2) = 10$ bar, 80 °C. Note that in all reactions the same molar amount of phenol groups was used.

ophile were tested (entries 2–5) and a similar ratio was maintained between the catalyst components (ratio NBu₄I/[OH] groups \approx 3.3). For the catalyst based on **3 d**, the conditions reported in entry 3 still produced a quantitative yield of **4 b**, whereas a further decrease of the amount of catalyst to 0.25 mol% **3 d**/0.8 mol% NBu₄I showed a modest decrease in yield to 80% (entry 4). For comparison, we used a similar amount of catalyst derived from **3 i** (cf., entries 3 and 5), and a very high though not quantitative yield of **4 b** was observed. Remarkably, under these conditions, the catalyst based on **1 b** produced a markedly lower yield of **4 b** (77%; cf. entries 3 and 7), which shows the superior performance of the resorcin[4]and pyrogallol[4]arene-based catalysts at 80 °C.

To investigate this in more detail, the full kinetic profiles for each of the catalyst systems reported in entries 3, 5, and 7 (Table 3) were determined (Figure 4). The pyrogallol catalyst system reaches a plateau in the conversion of around 70% after 6 h, which barely increases thereafter. This is in line with our previous results using either **1b** or **2** as catalyst components; both systems show inferior stability at this elevated temperature, which causes side-reactions that involve the deprotonation of the polyphenolic unit and its replacement by NBu₄.^[9a,b] The formation of (deprotonated) phenolate groups causes a decrease in the ability to form extended HB networks to stabilize catalytic intermediates, which results in higher kinetic barriers and thus slower reactions. Consequently, both the nucleophile and polyphenol concentration is affected negatively and the catalysis is shut down in the case of pyrogallol. Conversely, both the catalysts based on 3d and 3i retain their catalytic activity after prolonged use and, therefore, are more effective systems for cyclic carbonate preparation at elevated temperatures; compound 3d performs slightly better than 3i in the reported time span. Importantly, a comparison of the pK_a values of **1a** (9.20)^[23] and **1b** (9.01)^[24] shows that the pyrogallol unit is more acidic and likely to undergo deprotonation more easily. This causes a (much) shorter lifetime of the catalyst, whereas the system based on **3d** shows a comparatively longer lifetime. This results in a better potential to obtain higher TONs at elevated reaction temperatures. Interestingly, the preorganization of less active resorcinol units (cf., Figure 3, 1 a vs. 1 b) in the cavitand increases their catalytic potential significantly compared with the pyrogallol-based system, which underlines the importance of the catalyst structure for effective turnover.

The influence of the time frame on the performance of the polyphenol to act as an efficient HB donor in the activation of epoxides was investigated with 3d and 1b in the synthesis of 4b (Table 4; scale 10 mmol of 4a). Solvent-free (neat) conditions were employed to favor the kinetics, and the use of nucleophile alone again showed a considerably lower yield of 4b (entries 1 and 2; 7 and 32%, respectively) compared with the use of both 3d and NBu₄I in combination (entries 2 and 4; 46)



= 1.0 MPa, NBu₄| 1.6 mol%. [b] Total amount of OH (phenol) units. [c] NMR yields based on mesitylene as internal standard, selectivity for **4b** was >99%. [d] TON=total turnover number based on molar amount of phenol groups. [e] Corrected TON using the measured background conversions, see entries 1 and 2. [f] Corrected average TOF per hour using the measured background conversions, see entries 1 and 2.



and 74%, respectively). Under these conditions, the TON based on the total number of phenol active sites was 1225 (entry 5). Higher TONs were thus achieved simply by prolonging the reaction to give virtually full conversion after 30 h. The pyrogallol-based catalyst (entries 6 and 7) showed lower efficiencies with only a modest increase in the TON after 18 h; this further confirms the favorable stability of **3 d** at elevated temperatures. Thus, the combination of the cooperative action of the resorcinol units in **3d** with a higher chemical stability than **1b** makes this system among the most efficient organocatalysts reported to date with a very high TON. The turnover frequency of the binary catalyst system based on **3d** and NBu₄I was estimated after 1 h (entry 3, 46%) by considering the much lower conversion (entry 1, 7%) in the absence of 3d. If we corrected for this background conversion, still a significant part of it may be attributed to the binary catalyst (39%, TON=488 based on phenol group molar concentration, TOF per hour/[OH] group = 488 h^{-1}), which is the highest (initial) activity for a binary organocatalyst in this area.

Motivated by these results, we then examined a wide range of epoxide substrates (**4a–22a**) in the formation of their cyclic carbonates **4b–22b** in the presence of CO₂. To produce synthetically useful yields, 1.5–3.0 mol% of **3d** was used together with 5 mol% of NBu₄X (X=I, Br) in MEK (2.5 mL). The use of solvent was in some cases warranted to prevent the solidification of the reaction mixture and incomplete conversion of the substrate. Neat conditions were used for the internal epoxides **18a–22a**.

At 50 °C and under 1 MPa of pressure, terminal epoxides 4a-17a were converted smoothly into the carbonates 4b-17b with high conversions (>99%) and isolated yields (92-99%). The temperature and pressure conditions are comparatively very mild for an organocatalyst system, which prompted us to examine more challenging internal epoxides 18a-22a as reaction partners. To date, limited progress has been achieved with the use of such epoxide substrates in organocatalytic approaches. One promising example was reported recently by Tassaing et al.^[12b] who used a fluorinated alcohol as a HB donor and achieved a conversion of 73% of cyclohexene oxide (**18a** in Figure 5) after 5 h at 100° C and 2 MPa. Werner et al. reported the use of bifunctional phosphonium salts that were effective for internal epoxide conversion at temperatures in the range 90–120 $^\circ\text{C}$ and 1 MPa. $^{[10a]}$ For $18\,a$ specifically, the best results in terms of yield were obtained at 120 $^\circ\text{C}$ and 4 MPa (40 bar) and produced 18b in 69% yield after 6 h.

We first screened the potential conversion of **18a** at 50° C and 1 MPa, but this afforded **18b** in only 6% yield after 18 h. We were pleased to find that upon increasing the temperature to 80° C and using 3 mol% of cavitand **3d**, the conversion of **18b** could be increased significantly to 89% (isolated yield 85%) under neat conditions. As a control experiment, the reaction in the absence of **3d** was also performed and gave only 8% yield (duplicate experiment), which shows the importance of **3d** to achieve a high yield of **18b** under similar conditions.

Other internal epoxides **19a–22a** (Figure 5) were then also subjected to these latter conditions to test cyclic and acyclic substrates. Although 3,4-epoxyfuran (**21a**) was converted with

CHEMSUSCHEM Full Papers



Figure 5. Substrate scope in the conversion of various terminal and internal epoxides **4a–22a** into cyclic carbonates **4b–22b** using **3d**/NBu₄I as the catalyst. General conditions: epoxide 1 mmol, 1.5 mol% **3d**, 5 mol% NBu₄I, 18 h, 1 MPa, 50 °C, 2.5 mL of MEK. *With the use of 3 mol% of **3d**, 5 mol% NBu₄Br, 80 °C 18 h, neat.

a high conversion (84%) and yield (79%), cyclopentene oxide (20a) gave a much lower (reproducible) yield (38%). The acyclic epoxides 19a and 22a were also converted into their carbonates 19b and 22b, which shows the general potential of 3 d/NBu₄I as a binary organocatalyst in the conversion of more challenging internal epoxides. All epoxides 18a–22a were converted with the full retention of configuration (*cis* > 99% for 18b, 20b, and 21b and *trans* > 99% for 22b) except for 19a (*cis/trans* = 8:2). Such a loss of stereochemical information with this substrate in the formation of its carbonate product in the presence of CO₂ has been observed before^[25] and may be related to a partial S_N1 character of the nucleophilic attack of the linear carbonate intermediate onto the C–Br bond formed initially in the ring-opening of the epoxide by NBu₄Br.



Conclusions

Easily accessible and modular cavitand structures such as resorcin[4]arenes and pyrogallol[4]arenes constitute interesting hydrogen-bond-donor binary catalysts in combination with ammonium halide salts. The preorganization of the phenolic units within the resorcin[4]arenes was beneficial for the catalytic efficiency in organic carbonate formation from epoxides and CO₂ and resulted in cooperative effects (for **3 d**) that led to significantly higher conversion rates compared to resorcinol (1 a). If the reaction temperature was increased from 50 to $80 \,^\circ C$ to improve the overall reactivity, the cavitand structures showed a higher chemical stability than pyrogallol (1b), which makes these former systems more suitable to achieve very high turnover numbers. Furthermore, resorcin[4]arene 3d combined with NBu₄I shows very high initial turnover frequencies of almost 500 h⁻¹ at 80 °C. This improved and unparalleled reactivity was shown to be beneficial in the formation of 19 different carbonates under comparatively mild reaction conditions (50-80 °C, 1 MPa). Moreover, six disubstituted epoxides (16a and 18a-22a) were also screened as reaction partners and were converted efficiently under neat conditions at 80 °C to provide good to excellent isolated yields (79-94%). Compared with the state-of-the-art in organocatalytic CO₂/epoxide coupling chemistry, this is a remarkable result. Hence, cavitandbased binary organocatalysts are sustainable, versatile, and highly reactive alternatives to metal-based systems in the catalytic coupling of epoxides and CO₂. Further attention is now on the combination of cooperative and bifunctional concepts to develop organocatalytic processes with improved reactivity under ambient conditions.

Experimental Section

General

MEK (Aldrich ACS reagent > 99%) and CO₂ (purchased from PRAX-AIR) were used as received without further purification or drying. All the resorcin[4]arenes and pyrogallol[4]arenes were synthesized following the classical condensation of aldehydes in the presence of acid.^[18] All other (polyphenolic) chemicals were commercially available from Aldrich and were used as received. ¹H and ¹³C{¹H} NMR spectra were recorded by using a Bruker Avance 500 NMR spectrometer at 297 K. Chemical shifts are reported in ppm relative to the residual solvent peaks in CDCl₃ (δ = 7.26 ppm) and [D₆]DMSO (δ = 2.50 ppm). MS was performed at the High Resolution Mass Spectrometry Unit at the ICIQ in Tarragona, Spain.

Cavitand synthesis

Typically, a solution of one equivalent of resorcinol/pyrogallol (6 mmol) in a solution of ethanol (95%, 75 mL) and concentrated HCl (25 mL) was cooled to 2° C. Then the aldehyde reagent (6 mmol, 1 equiv.) dissolved in ethanol (95% 50 mL) was added dropwise to the reaction mixture. The resulting solution was stirred at 75 °C for 18–72 h, which depended on the aldehyde substrate. Upon cooling to RT, the separated precipitate was washed repeatedly with cold water and methanol and dried, and the compounds

were recrystallized from acetonitrile. Characterization details of **3 a-j** are given in the Supporting Information.

Catalysis experiments

Typically, the synthesis of organic cyclic carbonates from epoxides and CO₂ was performed in a 30 mL steel autoclave using 1,2-epoxyhexane (1 mmol, 1 equiv.), cavitand (1.0–1.5 mol%), NBu₄I (5 mol%), and MEK (2.5 mL). The autoclave was then subjected to three cycles of pressurization and depressurization with CO₂. Finally the autoclave was charged with 1 MPa (10 bar) of CO₂, heated to 50 °C, and the contents was stirred for 18 h. Thereafter, the autoclave was cooled to RT and carefully depressurized. The volatiles were removed under reduced pressure, and the product was purified by flash column chromatography (1:1 hexane/ethyl acetate as eluent) to afford the pure cyclic carbonate. Characterization details of **4b–22b** are given in the Supporting Information.

Acknowledgements

We thank ICIQ, ICREA, and the Spanish Ministerio de Economía y Competitividad (MINECO) through project CTQ-2014–60419-R and the Severo Ochoa Excellence Accreditation 2014–2018 through project SEV-2013–0319. Dr. Noemí Cabello, Sofía Arnal, and Vanessa Martínez are acknowledged for the MS analyses. L.M.R. thanks ICIQ for a predoctoral fellowship.

Keywords: cavitands • cooperitivity • hydrogen bonds • organocatalysis • polyphenols

- For some general reviews: a) M. Aresta, A. Dibenedetto, A. Angelini, *Chem. Rev.* 2014, 114, 1709–1742; b) Q. Liu, L. Wu, R. Jackstell, M. Beller, *Nat. Commun.* 2015, 6, 5933; c) M. Cokoja, C. Bruckmeier, B. Rieger, W. A. Herrmann, F. E. Kühn, *Angew. Chem. Int. Ed.* 2011, 50, 8510–8537; *Angew. Chem.* 2011, 123, 8662–8690; d) M. Peters, B. Köhler, W. Kuckshinrichs, W. Leitner, P. Markewitz, T. E. Müller, *ChemSusChem* 2011, 4, 1216–1240; e) M. H. Beyzavi, C. J. Stephenson, Y. Liu, O. Karagiaridi, J. T. Hupp, O. K. Farha, *Front. Energy Res.* 2015, 2, 63; f) R. Martín, A. W. Kleij, *ChemSusChem* 2011, 4, 1259–1263.
- [2] a) N. Kielland, C. J. Whiteoak, A. W. Kleij, Adv. Synth. Catal. 2013, 355, 2115–2138; b) C. Martín, G. Fiorani, A. W. Kleij, ACS Catal. 2015, 5, 1353–1370; c) Y. Tsuji, T. Fujihara, Chem. Commun. 2012, 48, 9956–9964; d) B. Yu, L.-N. He, ChemSusChem 2015, 8, 52–62; e) J. W. Comerford, I. D. V. Ingram, M. North, X. Wu, Green Chem. 2015, 17, 1966–1987.
- [3] Selected examples: a) M. R. Kember, P. D. Knight, P. T. R. Reung, C. K. Williams, Angew. Chem. Int. Ed. 2009, 48, 931–933; Angew. Chem. 2009, 121, 949–951; b) M. A. Fuchs, C. Altesleben, S. C. Staudt, O. Walter, T. A. Zevaco, E. Dinjus, Catal. Sci. Technol. 2014, 4, 1658–1673; c) A. Decortes, A. W. Kleij, ChemCatChem 2011, 3, 831–834; d) A. Decortes, M. M. Belmonte, J. Benet-Buchholz, A. W. Kleij, Chem. Commun. 2010, 46, 4580–4582; e) R. Ma, L.-N. He, Y.-B. Zhou, Green Chem. 2016, 18, 226–231; f) O. Hauenstein, M. Reiter, S. Agarwal, B. Rieger, A. Greiner, Green Chem. 2016, 18, 760–770; g) S. Kissling, M. W. Lehenmeier, P. T. Altenbuchner, A. Kronast, M. Reiter, P. Deglmann, U. B. Seemann, B. Rieger, Chem. Commun. 2015, 51, 4579–4582; h) C. M. Byrne, S. D. Allen, E. B. Lobkovsky, G. W. Coates, J. Am. Chem. Soc. 2004, 126, 11404–11405; i) M. A. Fuchs, S. Staudt, C. Altesleben, O. Walter, T. A. Zevaco, E. Dinjus, Dalton Trans. 2014, 43, 2344–2347.
- [4] Selected examples: a) A. Buchard, M. R. Kember, K. G. Sandeman, C. K. Williams, *Chem. Commun.* 2011, 47, 212–214; b) A. Buonerba, A. De Nisi, A. Grassi, S. Milione, C. Capacchione, S. Vagin, B. Rieger, *Catal. Sci. Technol.* 2015, 5, 118–123; c) M. A. Fuchs, T. A. Zevaco, E. Ember, O. Walter, I. Held, E. Dinjus, M. Döring, *Dalton Trans.* 2013, 42, 5322–5329; d) C. J. Whiteoak, E. Martin, M. M. Belmonte, J. Benet-Buchholz, A. W.



Kleij, Adv. Synth. Catal. 2012, 354, 469–476; e) M. Taherimehr, S. M. Al-Amsyar, C. J. Whiteoak, A. W. Kleij, P. P. Pescarmona, Green Chem. 2013, 15, 3083–3090; f) X. Frogneux, O. Jacquet, T. Cantat, Catal. Sci. Technol. 2014, 4, 1529–1533.

- [5] Selected examples: a) T. A. Zevaco, A. Janssen, J. Sypien, E. Dinjus, *Green Chem.* 2005, *7*, 659–666; b) W. Clegg, R. Harrington, M. North, R. Pasquale, *Chem. Eur. J.* 2010, *16*, 6828–6843; c) J. Martínez, J. A. Castro-Osma, A. Earlam, C. Alonso-Moreno, A. Otero, A. Lara-Sánchez, M. North, A. Rodríguez-Diéguez, *Chem. Eur. J.* 2015, *21*, 9850–9862; d) J. A. Castro-Osma, M. North, X. Wu, *Chem. Eur. J.* 2014, *20*, 15005–15008; e) L. P. Carrodeguas, J. González-Fabra, F. Castro-Gómez, C. Bo, A. W. Kleij, *Chem. Eur. J.* 2015, *21*, 6115–6122; f) V. Laserna, G. Fiorani, C. J. Whiteoak, E. Martin, E. Escudero-Adán, A. W. Kleij, *Angew. Chem. Int. Ed.* 2014, *53*, 10416–10419; *Angew. Chem.* 2014, *126*, 10584–10587; g) C. J. Whiteoak, N. Kielland, V. Laserna, E. C. Escudero-Adán, E. Martin, A. W. Kleij, *J. Am. Chem. Soc.* 2013, *135*, 1228–1231; h) Y. Qin, H. Guo, X. Sheng, X. Wang, F. Wang, *Green Chem.* 2015, *17*, 2853–2858.
- [6] Selected examples: a) C. T. Cohen, T. Chu, G. W. Coates, J. Am. Chem. Soc. 2005, 127, 10869–10878; b) G.-P. Wu, D. J. Darensbourg, X.-B. Lu, J. Am. Chem. Soc. 2012, 134, 17739–17745; c) D. J. Darensbourg, S. J. Wilson, J. Am. Chem. Soc. 2011, 133, 18610–18613; d) K. Nakano, S. Hashimoto, M. Nakamura, T. Kamada, K. Nozaki, Angew. Chem. Int. Ed. 2011, 50, 4868–4871; Angew. Chem. 2011, 123, 4970–4973; e) M. R. Kember, A. J. P. White, C. K. Williams, Macromolecules 2010, 43, 2291–2298.
- [7] a) G. Fiorani, W. Guo, A. W. Kleij, *Green Chem.* 2015, *17*, 1375–1389;
 b) M. Cokoja, M. E. Wilhelm, M. H. Anthofer, W. A. Herrmann, F. E. Kühn, *ChemSusChem* 2015, *8*, 2436–2454; c) A. Tlili, E. Blondiaux, X. Frogneux, T. Cantat, *Green Chem.* 2015, *17*, 157–168.
- [8] a) B. Chatelet, L. Joucla, J.-P. Dutasta, A. Martinez, K. C. Szeto, V. Dufaud, J. Am. Chem. Soc. 2013, 135, 5348-5351; b) B. Chatelet, L. Joucla, J.-P. Dutasta, A. Martinez, V. Dufaud, Chem. Eur. J. 2014, 20, 8571-8574.
- [9] a) S. Sopeña, G. Fiorani, C. Martín, A. W. Kleij, *ChemSusChem* **2015**, *8*, 3248–3254; b) C. J. Whiteoak, A. H. Henseler, C. Ayats, A. W. Kleij, M. A. Pericàs, *Green Chem.* **2014**, *16*, 1552–1559; c) C. J. Whiteoak, A. Nova, F. Maseras, A. W. Kleij, *ChemSusChem* **2012**, *5*, 2032–2038.
- [10] a) H. Büttner, J. Steinbauer, T. Werner, *ChemSusChem* 2015, *8*, 2655–2669; b) C. Kohrt, T. Werner, *ChemSusChem* 2015, *8*, 2031–2034; c) T. Werner, H. Büttner, *ChemSusChem* 2014, *7*, 3268–3271.
- [11] A. M. Hardman-Baldwin, A. E. Mattson, ChemSusChem 2014, 7, 3275 3278.
- [12] a) S. Gennen, M. Alves, R. Méreau, T. Tassaing, B. Gilbert, C. Detrembleur, C. Jerome, B. Grignard, *ChemSusChem* 2015, *8*, 1845–1849; b) M. Alves, B. Grignard, S. Gennen, R. Mereau, C. Detrembleur, C. Jerome, T. Tassaing, *Catal. Sci. Technol.* 2015, *5*, 4636–4643.

- [13] A. Mirabaud, J.-C. Mulatier, A. Martinez, J.-P. Dutasta, V. Dufaud, ACS Catal. 2015, 5, 6748–6752.
- [14] H. Zhou, G.-X. Wang, W.-Z. Zhang, X.-B. Lu, ACS Catal. 2015, 5, 6773–6779.
- [15] M. H. Anthofer, M. E. Wilhelm, M. Cokoja, M. Drees, W. A. Herrmann, F. E. Kühn, ChemCatChem 2015, 7, 94–98.
- [16] For some illustrative examples of extended, functional cavitands: a) A. Gissot, J. Rebek, Jr., J. Am. Chem. Soc. 2004, 126, 7424–7425; b) D. Ajami, J. Rebek, Jr., Nature. Chem. 2009, 1, 87–90; c) L. Martínez-Rodríguez, N. A. G. Bandeira, C. Bo, A. W. Kleij, Chem. Eur. J. 2015, 21, 7144–7150.
- [17] a) L. R. MacGillivray, J. L. Atwood, *Nature* **1997**, *389*, 469–472; b) L. Avram, Y. Cohen, *J. Am. Chem. Soc.* **2002**, *124*, 15148–15149.
- [18] L. M. Tunstad, J. A. Tucker, E. Dalcanale, J. Weiser, J. A. Bryant, J. C. Sherman, R. C. Helgeson, C. B. Knobler, D. J. Cram, J. Org. Chem. 1989, 54, 1305–1312.
- [19] The use of parent, nonfunctionalized cavitand structures in catalytic applications remains rare, see: Q. Zhang, K. Tiefenbacher, J. Am. Chem. Soc. 2013, 135, 16213–16219.
- [20] Notably, the Ph-substituted cavitand structure 3e showed incomplete dissolution in the reaction medium, which thereby affected catalytic turnover. Larger R groups are known to influence the preorganization of these structures and are thus beneficial for the selective formation of cavities; these effects are particularly known and well studied for related calix[4]arenes. Note also the recent work from Dufaud et al.^[13] who studied extended cavitands that can engage with tetraalkyl ammonium halides.
- [21] L. Avram, Y. Cohen, Org. Lett. 2003, 5, 3329-3332.
- [22] T. Gerkensmeier, J. Mattay, C. Näther, Chem. Eur. J. 2001, 7, 465-474.
- [23] S. E. Blanco, M. C. Almandoz, F. H. Ferretti, Spectrochim. Acta Part A 2005, 61, 93–102.
- [24] Dissociation Constants of Organic Acids in Aqueous Solution (Eds.: G. Kortum, K. Andrussow), International Union of Pure and Applied Chemistry, Buttersworth, London, **1961**; Kim et al. used voltametric measurement to determine the pK_a of pyrogallol (8.94), see: H.-S. Kim, T. D. Chung, H. Kim, J. Electroanal. Chem. **2001**, 498, 209–215.
- [25] a) J. Langanke, L. Greiner, W. Leitner, *Green Chem.* 2013, *15*, 1173–1182;
 b) C. J. Whiteoak, E. Martin, E. Escudero-Adán, A. W. Kleij, *Adv. Synth. Catal.* 2013, *355*, 2233–2239.

Received: October 28, 2015 Revised: November 26, 2015 Published online on February 23, 2016