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

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Abstract: Various cavitand based polyphenols were prepared from cheap and accessible aldehyde and resorcinol/pyrogallol reagents giving their respective resorcin[4]- or pyrogallol[4]arenes. The pre-organization of the phenolic units allows for intra- and intermolecular hydrogen bond (HB) networks affecting both the reactivity and stability of these HB donor catalysts. Unexpectedly, we found that resorcin[4]arenes show cooperative catalysis behavior compared to parent resorcinol in the catalytic coupling of epoxides and CO₂ with significantly higher turnover. At elevated reaction temperatures, the resorcin[4]arene based catalyst **3d** displays the best catalytic performance with both very high turnover numbers and frequencies combining increased reactivity and stability compared to pyrogallol, and ample substrate scope. This type of polyphenol structure thus illustrates the importance of a new, highly competitive organocatalyst design for devising sustainable CO₂ conversion processes.

Introduction

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

Organocatalysis has recently appeared on the radar of synthetic chemists representing a sustainable alternative for metal based approaches in CO₂ conversion catalysis.^[7] In particular, the catalytic coupling of epoxides and CO₂ has been studied extensively and can be regarded as a benchmark process for new catalyst development in non-reductive CO₂ couplings. Progress in this area has been considerable with the development

of efficient catalyst systems based on binary or bifunctional systems comprising of azaphosphatranes,^[8] polyphenols,^[9] phosphonium or ammonium alcohols,^[10] silane diols^[11] and fluorinated alcohols.^[12] Parallel to these activities other promising organocatalytic systems have been recently communicated presenting new catalyst designs based on the host-guest complexation of nucleophilic reagents,^[13] the use of phosphorus ylides^[14] and hydroxy-functionalized mono- and bis-imidazolium bromides.^[15]

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

We have become interested in the use of (natural) polyphenols such as pyrogallol and tannic acid (see Figure 1; **1b** and **2**) 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 activation of the epoxide towards the formation of key intermediates, and consequently lower kinetic barriers

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allowed for either low temperature conversions (45°C)^[9b,c] or the use of 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 formation of relatively inactive phenolate groups cannot be fully avoided preventing the efficient recycling of these phenolic additives and thus restricts the total turnover number (TON).^[9a,c]

Figure 2. Intra- and intermolecular hydrogen-bonding networks in cavitand based structures. Part of this figure has been reprinted with permission from reference 19. Copyright (2013) American Chemical Society.

In our quest to develop thermally more robust polyphenol based catalysts while maintaining high reactivity and privileged substrate scope, we considered that cavitand structures (Figure 1, structures **3**)^[16] may deliver the appropriate combination of activity and thermal/chemical stability. These cavitand structures, including resorcin[4]arenes (**3**: X = H) and pyrogallol[4]arenes (**3**: X = OH), give rise to pre-organized supramolecular structures, often being hexameric in nature, in solution and solid state through *inter*-molecular, water-assisted HB interactions (Figure 2, right).^[17] At the same time, the bowl shape of monomeric cavitand molecules is also controlled through *intra*-molecular HBs between adjacent resorcinol/pyrogallol units typically expressed in solvent media such as alcohols and acetonitrile (Figure 2, left).^[18] These latter, *intra*-molecular HB patterns suggest a similar potential for catalytic activation^[19] of epoxides compared to pyrogallol/tannic acid (Figure 1) with stabilization of key intermediate transition states through multiple HB interactions being more efficient than in the absence of such HB donors.

In this contribution we will show that cavitand based polyphenols are excellent HB activators in the formation of cyclic carbonates from epoxides and CO₂ 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, which also 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 CO₂ into value added chemicals.

Results and Discussion

Resorcin[4]arenes **3a–e**, pyrogallol[4]arenes **3f–i** and the octahydroxypyridine[4]arene **3j** (Scheme 1) were prepared according to previous reported procedures (Experimental Section) and their molecular identity was established by ¹H/¹³C NMR and mass analysis: these analyses were in accordance with the literature data (Supporting Information for details). Compounds **3a–3i** 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 methylethyl ketone (MEK) as solvent (Table 1).

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

Table 1. Screening of conditions using a polyphenol/TBAX binary catalyst in the coupling of 1,2-epoxyhexane and CO₂ to afford cyclic carbonate **4b**.^[a]

Entry	Polyphenol	Amount [mol %]	NBu ₄ X [mol %]	T [°C]	MEK [mL]	Yield 4b [%] ^[b]
1	3b	1.5	I, 5.0	45	2.5	81
2	3b	1.5	I, 5.0	50	2.5	91
3	3b	1.5	I, 5.0	50	5.0	65
4	3b	1.5	Cl, 5.0	50	2.5	31
5	3b	1.5	Br, 5.0	50	2.5	65
6	–	0	I, 5.0	50	2.5	4
7	3b	1.5	0	50	2.5	0
8	1a	6.0	I, 5.0	50	2.5	47
9	1a	6.0	I, 5.0	50	5.0	24
10	1b	4.0	I, 5.0	50	2.5	99

[a] Reaction conditions: 1,2-epoxyhexane 1.0 mmol, *p*(CO₂) = 10 bar, 18 h, polyphenol amount normalized with respect to [OH] groups, *p*(CO₂)⁰ = 1.0 MPa, 18 h. [b] NMR yields based on mesitylene as internal standard, selectivity for **4b** was >99%.

We first tested resorcin[4]arene **3b**/NBu₄I as a binary catalyst for the synthesis of organic carbonates from epoxides and CO₂ under conditions closely related to those previously probed for a binary pyrogallol based system (entry 1).^[9c] At 45°C, a NMR yield of 81% was already achieved, and raising 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 leading 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 noted showing the imperative role of both catalyst components in this coupling reaction. Comparison of the efficiency of resorcin[4]arene **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 dilute conditions (*cf.*, entries 3 and 9). Pyrogallol **1b**, a triphenol, gave virtually quantitative yield (entry 10, 99%) under these conditions. The remarkable yield of **4b** in the presence of resorcin[4]arene **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.

Table 2. Screening of cavitand/TBAI binary catalysts **3** in the coupling of 1,2-epoxyhexane and CO₂ to afford cyclic carbonate **4b**.^[a]

Entry	Cavitand	Amount [mol %]	NBu ₄ I [mol %]	T [°C]	R	Yield 4b [%] ^[b]
1	3a	1.5	5.0	50	Me	93
2	3b	1.5	5.0	50	Et	91
3	3c	1.5	5.0	50	Bu	94
4	3d	1.5	5.0	50	Non	98
5	3e	1.5	5.0	50	Ph	27
6	3f	1.0	5.0	50	Me	78
7	3g	1.0	5.0	50	Et	84
8	3h	1.0	5.0	50	Bu	87
9	3i	1.0	5.0	50	Non	93

[a] 1,2-epoxyhexane 1.0 mmol, polyphenol amount normalized with respect to [OH] groups, MEK 2.5 mL, $p(\text{CO}_2)^0 = 1.0$ 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%.

We then screened a series of nine cavitands (**3a–3i**, Scheme 1) in the coupling of 1,2-epoxyhexane **4a** and CO₂ (Table 2) to investigate the role of the pendent R groups. Within the series of resorcin[4]arenes **3a–3e** (entries 1–5), the highest

yield of **4b** was achieved with **3d** (R = nonyl), a trend that was also observed within the series of pyrogallol[4]arenes **3f–3i** (entries 6–9).^[20]

Figure 3. Comparative kinetics in the formation of carbonate **4b** from 1,2-epoxyhexane and CO₂ using resorcinol **1a**, pyrogallol **1b**, resorcin[4]arene **3d** and pyrogallol[4]arene **3i**. The polyphenol amount was normalized with respect to the [OH] groups. Conditions used: 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, $p(\text{CO}_2)^0 = 10$ bar, 50°C.

The best-performing nonyl-substituted polyphenols **3d** and **3i** were then more closely examined and compared with the parent resorcinol **1a** and pyrogallol **1b**: the kinetic profiles of each binary catalyst (upon combining with NBu₄I) were determined (Figure 3). Interestingly, the pyrogallol[4]arene **3i** shows inferior catalytic performance with respect to resorcin[4]arene **3d**. The reason for this behaviour is likely the competing self-assembly of the individual cavitand molecules of **3i** into larger aggregates (*i.e.* hexamers, *cf.* Figure 2). Cohen et al. compared the stability of undecyl-substituted resorcin[4]arenes and pyrogallol[4]arenes.^[21] Titration studies involving these cavitand molecules demonstrated that upon increasing the polarity of the medium 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 CD₃OD were required in the case of the resorcin[4]arene in line with a stronger self-assembly behaviour of the pyrogallol[4]arene. Therefore, under the reaction conditions reported in Table 2 and Figure 3, the poorer performance of **3f–3i** compared to the resorcin[4]arene series **3a–3d** is thus explained in terms of a stronger competing self-assembly. This behaviour competes with hydrogen bonding between the epoxide and the phenolic groups, and thus slows down the reaction. In order to further support the view that competitive HB interactions can slow down the catalytic reaction, octahydroxypyridine[4]arene **3j** (Scheme 1)^[22] was also tested as a HB donor system in the synthesis of carbonate **4b**. The 2,6-dihydroxypyridine subunits in **3j** are known to induce

intramolecular N...HO hydrogen bonds, and the significant lower yield after 18 h (1.5 mol%, 60%) than observed for resorcin[4]arene **3d** (1.5 mol%, 98%) is a clear testament of competitive H-bonding. Thus, the best catalytic performance among the cavitand structures at 50°C is noted for **3d**.

In an effort to further increase the reactivity, the coupling of 1,2-epoxyhexane and CO₂ was carried then out at 80°C using resorcin[4]arene **3d**, pyrogallol[4]arene **3i** and pyrogallol **1b** (Table 3, Figure 4). Under these conditions the nucleophilic additive NBu₄I alone produces poor catalysis (entry 1, 17% yield of **4b**). Various combinations of cavitand/nucleophile were probed (entries 2–5) while maintaining a similar ratio between both catalyst components (ratio NBu₄I/[OH] groups ~ 3.3). For the resorcin[4]arene **3d** based catalyst, the conditions reported in entry 3 still produced quantitative yield of **4b**, whereas further lowering the amount of catalyst to 0.25 mol% **3d**/ 0.8 mol% NBu₄I showed a modest decrease in yield to 80% (entry 4). For comparison, upon using a similar amount of catalyst derived from pyrogallol[4]arene **3i** (cf., entries 3 and 5), a very high though not quantitative yield of **4b** was noted. Remarkably, under these latter conditions, the pyrogallol **1b** based catalyst produced a markedly lower yield of **4b** (77%; cf. entries 3 and 7) showing the superior performance of the resorcin[4]- and pyrogallol[4]arene based catalysts at 80°C.

Table 3. Catalytic coupling of 1,2-epoxyhexane and CO₂ at 80°C to afford cyclic carbonate **4b**.^[a]

Entry	Polyphenol	Amount [mol %]	NBu ₄ I [mol %]	T [°C]	Yield 4b [%] ^[b]
1	–	0	1.6	80	17
2	3d	0.75	2.5	80	>99
3	3d	0.50	1.6	80	>99
4	3d	0.25	0.8	80	80
5	3i	0.33	1.6	80	93
6	1b	2.0	3.2	80	>99
7	1b	1.3	1.6	80	77
8	1b	0.66	0.8	80	55

[a] 1,2-epoxyhexane 1.0 mmol, polyphenol amount normalized with respect to [OH] groups, MEK 2.5 mL, $p(\text{CO}_2)^0 = 1.0$ MPa, 18 h. [b] NMR yields based on mesitylene as internal standard, selectivity for **4b** was >99%.

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 (see Figure 4). The pyrogallol catalyst system reaches a plateau conversion of around 70% after 6 h which

thereafter barely increases. This is in line with our previous results using either pyrogallol **1b** or tannic acid **2** as catalysts components; both systems show inferior stability at this elevated temperature causing side-reactions that involve the deprotonation of the polyphenolic unit and replacement thereof by NBu₄.^[9a,b] The formation of (deprotonated) phenolate groups causes a decrease in the ability to form extended HB networks as to stabilize catalytic intermediates, which results in higher kinetic barriers and thus slower reactions. Consequently, both the nucleophile and polyphenol concentration is negatively affected and the catalysis is shut down in the case of pyrogallol. On the contrary, both cavitand based catalysts based on **3d** and **3i** retain catalytic activity after prolonged use and therefore are more effective systems for cyclic carbonate preparation under elevated temperature conditions with **3d** performing slightly better than **3i** in the reported time span. Importantly, comparing the pK_a values of resorcinol **1a** (9.20)^[23] and pyrogallol **1b** (9.01)^[24] shows that the pyrogallol unit is more acidic and likely to undergo deprotonation more facilely. This is likely causing a (much) shorter lifetime of the catalyst whereas the resorcin[4]arene based system **3d** shows comparatively a longer lifetime. This results in better potential for obtaining higher turnover numbers at elevated reaction temperatures. Interestingly, the preorganization of less active resorcinol units (cf., Figure 3, **1a** versus **1b**) in the cavitand significantly increases their catalytic potential as compared with the pyrogallol based one underlining the importance of the catalyst structure for effective turnover.

Figure 4. Comparative kinetics in the formation of carbonate **4b** from 1,2-epoxyhexane and CO₂ at 80°C using pyrogallol **1b** (1.3 mol%), resorcin[4]arene **3d** (0.50 mol%) and pyrogallol[4]arene **3i** (0.33 mol%). Conditions used: 1,2-epoxyhexane 1.0 mmol, NBu₄I 1.6 mol%, 2.5 mL, $p(\text{CO}_2)^0 = 10$ bar, 80°C. Note that in all reactions the same molar amount of phenol groups was used.

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 carried with resorcin[4]arene **3d** and pyrogallol **1b** in the synthesis of carbonate **4b** (Table 4; scale 10 mmol of **4a**). Solvent-less (neat) conditions were employed to favour kinetics and the use of nucleophile alone again showed considerably

lower yield of **4b** (entries 1 and 2; 7 and 32%, respectively) compared with the use of both **3d** and NBu₄I combined (entries 2 and 4; 46 and 74%, respectively). Under these conditions, the TON based on the total of phenol active sites amounted to 1225 (entry 5). Higher turnover numbers were thus simply achieved by prolonging the reaction showing 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 as defined above after 18 h further confirming the favourable stability features of the cavitand structure **3d** at elevated temperature. Thus the combination of the cooperative action of the resorcinol units in **3d** with a higher chemical stability compared to pyrogallol **1b** makes this system among the most efficient organocatalyst reported to date with very high TON. The turnover frequency of the binary catalyst system based on **3d** and NBu₄I was estimated after 1 h (entry 3, 46%) considering the much lower conversion (entry 1, 7%) in the absence of **3d**. When correcting 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/h/[OH] group = 488 h⁻¹), reporting thus the highest (initial) activity for a binary organocatalyst in this area.

Table 4. Comparison between resorcin[4]arene **3d**/NBu₄I and pyrogallol **1b**/NBu₄I as binary catalysts in the coupling of 1,2-epoxyhexane and CO₂ at 80°C to afford cyclic carbonate **4b**. N.a. stand for non-applicable.^[a]

Entry	Cat. [mol%] [a]	OH units [mol%]	t [h]	Yield 4b [%] ^[c]	TON ^[d]	TON _c [e]	TOF _c [f]
1	–	–	1	7	–	–	–
2	–	–	18	32	–	–	–
3	3d , 0.010	0.080	1	46	575	488	488
4	3d , 0.010	0.080	18	74	925	525	29
5	3d , 0.010	0.080	30	98	1225	n.a.	n.a.
6	1b , 0.026	0.080	18	60	750	350	19
7	1b , 0.026	0.080	30	66	825	n.a.	n.a.

[a] 1,2-epoxyhexane 10.0 mmol, polyphenol amount normalized with respect to [OH] groups (see third column), neat conditions, $p(\text{CO}_2) = 1.0$ MPa, NBu₄I 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/h using the measured background conversions, see entries 1 and 2.

Motivated by these results, we then examined a wide scope of epoxide substrates (**4a–22a**) in the formation of their cyclic

carbonates **4b–22b** in the presence of CO₂. In order 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 solidification of the reaction mixture and incomplete conversion of the substrate: for the internal epoxides **18a–22a** neat conditions were used.

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

At 50°C and 1 MPa of pressure terminal epoxides **4a–17a** were smoothly converted into their carbonates **4b–17b** in high conversion (>99%) and isolated yields (92–99%). The temperature and pressure conditions are comparatively very mild considering the use of an organocatalyst system, and prompted us to examine more challenging internal epoxides (**18a–22a**) as reaction partners. To date limited progress has been achieved

using such epoxide substrates in organocatalytic approaches. One promising example was recently reported by Tassaing *et al.*^[12b] who used a fluorinated alcohol as HB donor and achieved at 100°C and 2 MPa a conversion of 73% of cyclohexene oxide (CHO; **18a** in Figure 5) after 5 h. Werner *et al.* reported on the use of bifunctional phosphonium salts that were effective for internal epoxide conversion at temperatures in the range 90–120°C and 1 MPa.^[10a] For CHO specifically, the best results in terms of yield were obtained at 120°C and 4 MPa (40 bar) producing the carbonate **18b** in 69% yield after 6 h.

We first screened potential conversion of CHO **18a** at 50°C and 1 MPa but this afforded the carbonate **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 significantly increased to 89% (isolated yield 85%) using neat conditions. As a control experiment, the reaction in the absence of **3d** was also carried out and gave only 8% yield (duplo experiment) showing the importance of the cavitand **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 including cyclic and acyclic substrates. Whereas the 3,4-epoxyfuran **21a** was converted in high conversion (84%) and yield (79%), the corresponding 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** showing the more general potential of **3d**/NBu₄I as a binary organocatalyst in the conversion of more challenging internal epoxides. All epoxides **18a–22a** were converted with full retention of configuration (*cis* >99% for **18b**, **20b** and **21b** or *trans* >99% for **22b**) except for **19a** (*cis/trans* = 8:2). Such loss of stereo-chemical 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 initially formed in the ring-opening of the epoxide by NBu₄Br.

Conclusions

The use of easily accessible and modular cavitand structures such as resorcin[4]arenes and pyrogallol[4]arenes constitute interesting HB donor binary catalysts in combination with ammonium halide salts. The pre-organization of the phenolic units within the resorcin[4]arenes was proven to be beneficial for the catalytic efficiency in organic carbonate formation from epoxides and CO₂, and resulted in cooperative effects (for **3d**) leading to significantly higher conversion rates compared to resorcinol **1a**. Upon raising the reaction temperature from 50 to 80°C in order to improve the overall reactivity, the cavitand structures showed higher chemical stability than pyrogallol **1b** making these former systems more suitable for achieving both very high TONs. Also, 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°C, 1 MPa). Further to this, six di-substituted epoxides (**16a** and **18a–22a**) were also screened as reaction partners and efficiently converted under neat conditions at 80°C providing good to excellent isolated yields of 79–94%. Compared with the state-of-the-art in organocatalytic CO₂/epoxide coupling chemistry this is a remarkable result. Hence, cavitand based binary organocatalysts have proven to be sustainable, versatile and highly reactive alternatives for 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

Methyl ethyl ketone (MEK, Aldrich ACS reagent >99%) and carbon dioxide (purchased from PRAXAIR) 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 are commercially available at Aldrich and were used as received. ¹H and ¹³C{¹H} NMR spectra were recorded on 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 [DMSO]-D₆ (δ = 2.50 ppm). Mass analyses were carried out by the High Resolution Mass Spectrometry Unit at the ICIQ in Tarragona, Spain.

Cavitand synthesis

Typical experiment: a solution of one equivalent of resorcinol/pyrogallol (6 mmol) in a solution of ethanol (95%, 75 mL) and concentrated hydrochloric acid (25 mL) was cooled to 2 °C. Then the aldehyde reagent (6 mmol, 1 eq.) dissolved in ethanol (95% 50 mL) was added drop-wise to the reaction mixture. The resulting solution was stirred at 75°C during a period of 18 h up to 72 h depending on aldehyde substrate. Upon cooling to rt, the precipitate that separated was washed repeatedly with cold water and methanol and finally dried: the compounds were recrystallized from acetonitrile. Analysis details of all cavitand structures **3a–3j** can be found in the Supporting Information.

Catalytic experiments

Typical procedure: the organic cyclic carbonate synthesis from epoxides and CO₂ was carried out in a 30 mL steel autoclave using 1,2-epoxyhexane (1 mmol, 1 eq), cavitand structure (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 content stirred for 18 h. Hereafter, 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. Analytical details of all organic carbonates **4b–22b** can be found in the Supporting Information.

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Keywords: carbon dioxide • cooperativity • organocatalysis • pyrogallenes • resorcinarenes

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Organize yourself ! Cavitand based polyphenols in combination with NBu_4X ($\text{X} = \text{I}, \text{Br}$) are excellent organocatalysts for the synthesis of organic carbonates showing interesting cooperative behaviour and high chemical stability. The catalytic results demonstrate a combination of high initial TOFs with an exclusive substrate scope that includes several internal epoxides. These new metal-free, cheap and modular cavitand based binary catalysts showcase the importance of a pre-organization of functional groups for maximum catalytic efficiency.

- 50-80°C, 1 MPa, 19 examples
- including internal epoxides
- cooperative behavior & robust
- very high initial TOFs

Luis Martínez-Rodríguez, Javier Otalora Garmilla and Arjan W. Kleij*

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