



Construction of Versatile and Functional Nanostructures Derived from CO₂-based Polycarbonates**

Yanyan Wang, Jingwei Fan, and Donald J. Darensbourg*

Abstract: The construction of amphiphilic polycarbonates through epoxides/CO₂ coupling is a challenging aim to provide more diverse CO₂-based functional materials. In this report, we demonstrate the facile preparation of diverse and functional nanoparticles derived from a CO₂-based triblock polycarbonate system. By the judicious use of water as chain-transfer reagent in the propylene oxide/CO₂ polymerization, poly(propylene carbonate (PPC) diols are successfully produced and serve as macroinitiators in the subsequent allyl glycidyl ether/CO₂ coupling reaction. The resulting ABA triblock polycarbonate can be further functionalized with various thiols by radical mediated thiol-ene click chemistry, followed by self-assembly in deionized water to construct a versatile and functional nanostructure system. This class of amphiphilic polycarbonates could embody a powerful platform for biomedical applications.

Using the abundant, nontoxic and inexpensive CO₂ as a renewable C1 feedstock, the coupling of CO₂ and epoxides provides an attractive method for preparing polycarbonates. This environmentally more benign approach for polycarbonate synthesis has attracted a lot of attention in both academic and industrial research.^[1] With the recent development of catalytic systems, both heterogeneous and homogeneous, CO₂/epoxides coupling has been commercialized by many companies throughout the world.^[2] A new trend on CO₂-based polycarbonates is the production of poly(propylene carbonate) diols which can undergo condensation reaction with diisocyanate to afford polyurethane.^[3] Nevertheless, the hydrophobic nature and lack of functionalities of the commonly studied CO₂-based polycarbonate have prevented their use in functional materials, especially for biomedical applications.

In order to expand the use of CO₂-based polycarbonates towards improved material performances, it is necessary to synthesize more diverse CO₂-based polymers with functionalities. There are a few reports on the development of

functional aliphatic polycarbonates from CO₂ containing hydroxy, furfuryl, and oligoethylene glycol (OEG) groups.^[4] In these examples, preparation of monomers is usually required and only one type of functional group can be prepared at a time. More importantly, restrained by the reactivity of catalysts available, the type of functionality is usually limited by direct coupling of functional monomers and CO₂. An alternative methodology is to incorporate orthogonal, “click” chemistry into the material design. We and others have employed “thiol-ene” click reactions to successfully anchor various functionalities onto polycarbonates with a vinyl pendant group.^[5]

In the last few decades, amphiphilic block polymers have been extensively studied due to their potential applications in material science and biomedicine. Owing to their unique biodegradability and biocompatibility, aliphatic polycarbonates have received considerable attention in the construction of amphiphilic polymers. To date, most of the amphiphilic block polymers consisting of polycarbonate are based on the ring-opening polymerization of functionalized six-membered cyclic carbonate monomers.^[6] Generally, poly(ethylene glycol) (PEG) is used as a macroinitiator and is the hydrophilic component in the resulting block polymers. To the best of our knowledge, amphiphilic polymers with hydrophobic and hydrophilic components both derived from CO₂-based polycarbonates have not been reported. Compared to the ring-opening polymerization, this alternative route from directive CO₂/epoxides copolymerization eliminates the need for the separate preparation of cyclic carbonates.

Here, we demonstrate the facile preparation of CO₂-based amphiphilic block polycarbonates with different functionalities and charges. To achieve this goal, the first challenge to address is the construction of polycarbonate block polymers. Due to the living nature^[7] of the coupling reaction of epoxides/CO₂ catalyzed by (salen)Co system, we hypothesized that block polymers can be synthesized by a “two step, one-pot” strategy by sequentially adding different monomers. For polymerization of epoxides and CO₂ catalyzed by the (salen)CoX/PPNX (X[−] = Cl[−], AcO[−], Br[−], 2,4-dinitrophenoxide (DNP[−]), etc.) binary catalyst system, it is inevitable for chain-transfer reaction to occur due to trace water impurity.^[8] Thus, the coupling of epoxides and CO₂ gives polymers with differing end groups, OH-PC-OH and OH-PC-X. Upon addition of the second epoxide, an undesired mixture of both ABA and AB block polymers will be produced. To circumvent this problem, a certain amount of water is intentionally added to the system. The resulting hydroxy end-capped polymers can serve as macroinitiators in the subsequent copolymerization reaction.^[9] A (salen)CoTFA^[10]/

[*] Y. Wang, J. Fan, Prof. D. J. Darensbourg
Department of Chemistry, Texas A&M University
3255 TAMU, College Station, TX 77843 (USA)
E-mail: djdarens@chem.tamu.edu

[**] We gratefully acknowledge the financial support of the National Science Foundation (CHE-1057743) and the Robert A. Welch Foundation (A-0923). In addition, grant support to Prof. Wooley (J.F.) through the National Science Foundation (CHE-1410272, DMR-1309724) and the Robert A. Welch Foundation A-0001 is greatly appreciated. The microscopy & imaging center (MIC) at Texas A&M University is also gratefully acknowledged.

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/anie.201505076>.

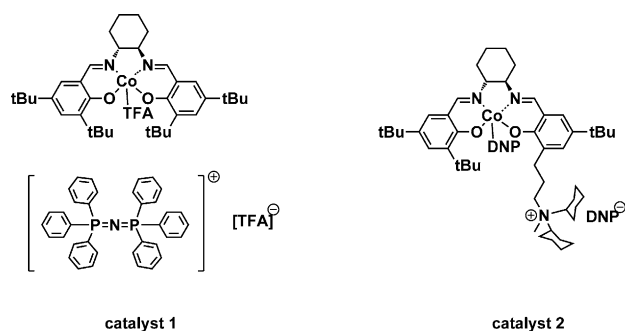


Figure 1. Catalyst systems utilized in copolymerization of epoxides and CO₂. TFA = trifluoroacetic acid, DNP = 2,4-dinitrophenoxide.

PPNTFA (catalyst **1**, Figure 1) catalyst system will be employed due to the fact that trifluoroacetate can undergo hydrolysis more easily and rapidly than other end-groups.^[10a,11]

Since common CO₂-based aliphatic polycarbonates, such as poly(propylene carbonate) and poly(cyclohexene carbonate), are known to be highly hydrophobic, another challenge is to find a candidate for the hydrophilic component of the block polymers. A strategy which can be employed to overcome the hydrophobic nature of the polycarbonate backbone is the introduction of water-soluble functional groups by postpolymerization modification. In our previous report, we demonstrated that water-soluble CO₂-based polycarbonates can be produced employing thiol-ene click chemistry in the postpolymerization functionalization of CO₂/2-vinyloxirane copolymers.^[5a] However, polymerization of 2-vinyloxirane and CO₂ requires the use of a bifunctional catalyst (catalyst **2**, Figure 1) in order to achieve high polymer selectivity. The synthesis of catalyst **2** is quite tedious with low overall yield.^[5a,12] From a practical view, we choose another epoxide, allyl glycidyl ether (AGE), which can couple with CO₂ using easily accessible catalyst **1**. The overall synthetic route for amphiphilic CO₂-based polycarbonate is shown in Figure 2. Two epoxides are employed in the sequential

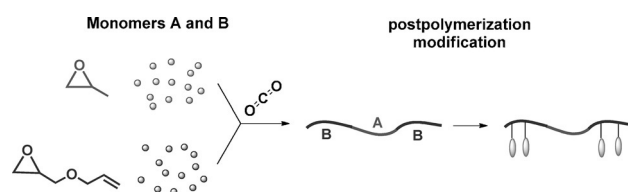


Figure 2. Synthesis of CO₂-based amphiphilic polycarbonates.

polymerization reaction, one is propylene oxide (PO) that leads to the hydrophobic segment, the other is allyl glycidyl ether that carries an alkene functionality for copolymerization followed by modification to the hydrophilic blocks. Related chemistry has been utilized in AGE based polyethers.^[13]

To prepare the triblock polycarbonate, we first examined the copolymerization of PO and CO₂ using catalyst **1** (0.1 mol% loading) in the presence of 20 equiv of water

(to the catalyst). The polymerization reaction was carried out at ambient temperature for 48 h to ensure complete conversion of PO in order to minimize tapering when the second monomer (AGE) is added. Consistent with the result we reported before where a higher catalyst loading was used,^[10a] the resulting polymer shows an extremely narrow polydispersity index (PDI; 1.01) in gel permeation chromatography (GPC) and the MALDI-TOF mass spectrometry showed only one series of signals assigned to two hydroxy end groups (Figure S1 in the Supporting Information). The results indicate that water not only acts as a chain-transfer agent to protonate the anion of the growing polymer chain but also completely hydrolyzes the initiating trifluoroacetate groups at the chain-end.^[10a,11]

Subsequently, after careful release of CO₂, various amounts of AGE was added into the reactor followed by recharging with CO₂. Triblock polycarbonates with different molecular weight and composition were produced. The GPC traces of the resultant copolymers are presented in Figure 3,

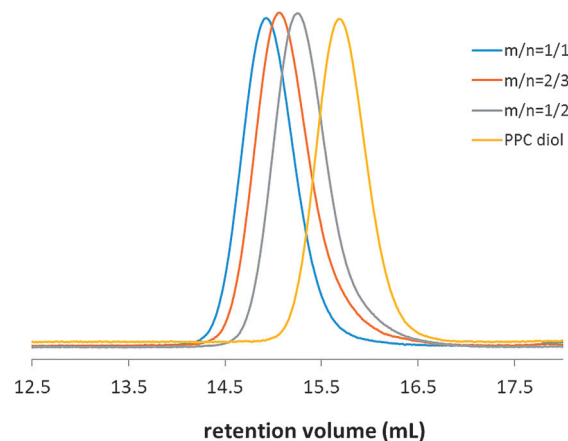


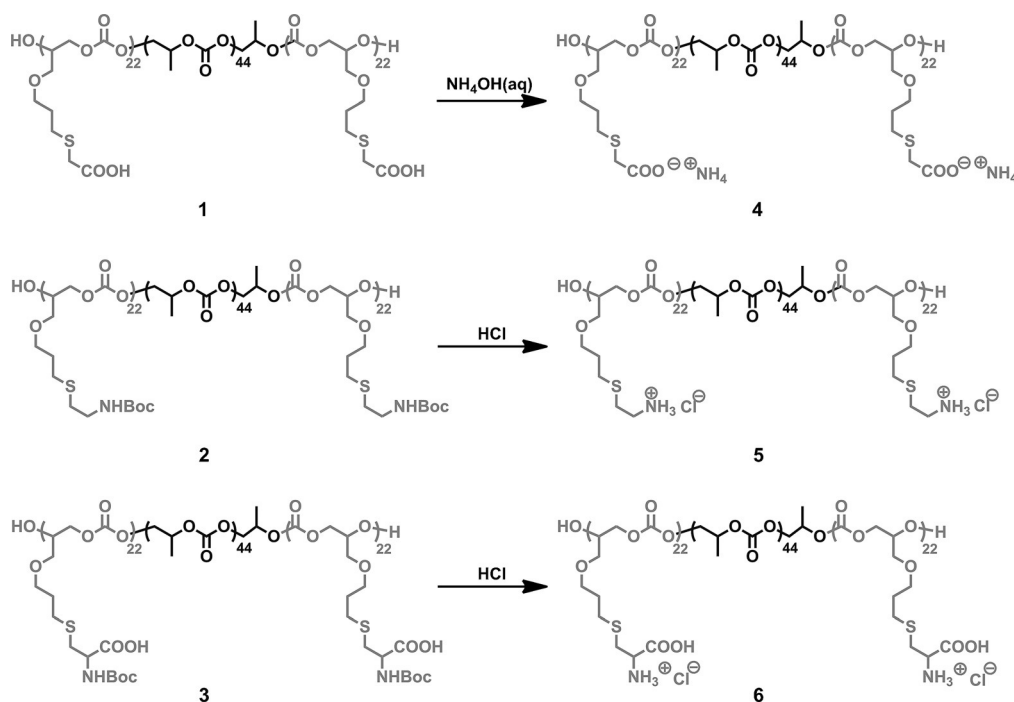
Figure 3. GPC traces of triblock polycarbonates with different composition (Table 1).

which shows an increase in the copolymer's molecular weight with an increase in AGE loading. The fact that the measured M_w is close to the theoretical values (Table 1) together with the narrow PDI of these triblock copolymers confirm that the reaction system maintained its living character during the course of chain extension. Differential scanning calorimetry (DSC) revealed decreasing T_g (glass transition temperature) with a larger poly(allylglycidylether carbonate) (PAGEC)

Table 1: Results from “two-step, one-pot” strategy to prepare ABA triblock polycarbonate.

	$M_{w(\text{in theory})}$ [g mol ⁻¹]	$M_{w(\text{GPC})}^{[b]}$ [g mol ⁻¹]	PDI ^[b]	$T_g^{[c]}$ [°C]
PPC diol	—	4600	1.01	23
$m/n = 1:2$	8100	7000	1.01	7
$m/n = 2:3$	9300	8100	1.01	4
$m/n = 1:1$	11 700	10 300	1.01	−1

[a] See the Experimental Section for the exact procedure. [b] Determined by GPC. $PDI = M_w/M_n$. [c] Determined by DSC.



Scheme 1. Synthesis of amphiphilic block polycarbonates with different charges. Boc = *tert*-butoxycarbonyl.

ratio. This is attributed to the long flexible pendant group of the PAGEC blocks.

The functionalization of PAGEC-*b*-PPC-*b*-PAGEC ($m/n = 1$) triblock polycarbonates was achieved by radical-mediated thiol–ene click reaction with various thiols including mercaptoacetic acid, 2-(Boc-amino)ethanethiol and boc-L-cysteine, to give polymers **1**, **2**, and **3**, respectively (Scheme 1). In order to avoid possible chain–chain coupling reactions, 20 equivalents of thiols to alkene groups were used in the thiol–ene click reaction under UV irradiation with dimethoxy-2-phenylacetophenone (DMPA) as photoinitiator. The resulting polymers were readily purified and their structures were confirmed. The disappearance of the terminal alkene protons in the ^1H NMR spectra of the three resulting polymers confirmed the complete conversion of the alkene groups. GPC analysis of each of these polymers shows a narrow single peak without any tailing at the high-molecular weight portion, confirming the successful suppression of crosslinking side reactions.

In order to provide high hydrophilicity of the end blocks, the deprotonation of the pendant carboxylic acid of polymer **1** and the Boc deprotection of polymer **2/3** were conducted in THF, giving the corresponding negatively charged **4** and positively charged **5/6** triblock amphiphilic polycarbonates.

All three amphiphilic polycarbonates were dissolved in deionized (DI) water by sonication for 10 min at room temperature. The morphology of the resulting nanostructures were characterized by dynamic light scattering (DLS) and transmission electron microscopy (TEM). DLS analysis shows no hydrodynamic diameter distribution for the aqueous solution of polymer **5**, consistent with its ^1H NMR

spectrum in D_2O in which the proton signal from the hydrophobic PPC was only slightly shielded (Figure S13). This result indicates that no shell–core structure was formed. In contrast, the DLS studies of anionic block polymer **4** and cationic polymer **6** showed that they underwent assembly to form nanoparticles with high uniformity, giving a similar intensity-averaged hydrodynamic diameters of 26 ± 15 nm (Figure 4a,b). The formation of micelles can also be confirmed by ^1H NMR spectra of polymers **4** and **6** in D_2O (Figure S11 and S15). TEM images revealed that the morphologies of both nanoparticles formed by **4** and **6** are spherical (Figure 4c,d). The surface

charge densities of the resulting nanoparticles in DI water were characterized by zeta potential analysis. Zeta potential values of -59 mV for polymer **4** and $+28$ mV for polymer **6** indicated the anionic and cationic surface characteristics of these nanoparticles. It is noted that an attempt to make zwitterionic triblock polycarbonate by removal of HCl from polymer **6** resulted in a non-soluble polymer, even in DMSO (dimethylsulfoxide) and DMF (dimethylformamide). This is due to the strong interchain charge interaction between $-\text{CO}_2^-$ and $-\text{NH}_3^+$ which is unbreakable through solvation. Both polymers **4** and **6** displayed a similar critical micelle concentration (CMC) of $66 \mu\text{g mL}^{-1}$ in DI water, determined by pyrene fluorescence measurements at room temperature (Figure S2 and S3).

In summary, we have demonstrated the facile construction of CO_2 -based versatile and functional amphiphilic polymer with negatively and positively charged functionalities from a sequential copolymerization and chemical transformation strategy. By the judicious use of water as a chain-transfer reagent, well-defined ABA triblock polycarbonates were prepared by a “two-step, one-pot” strategy. The living nature of the (salen)CoX catalyst systems for epoxides/ CO_2 coupling enabled the preparation of multiblock polymers with precise control of block chain lengths. Furthermore, the clickable alkene groups were then modified to install different functionalities and charges onto the polymer backbones, yielding amphiphilic CO_2 -based polycarbonates. This emerging class of polycarbonates derived from CO_2 could provide a powerful platform for biomedical applications.

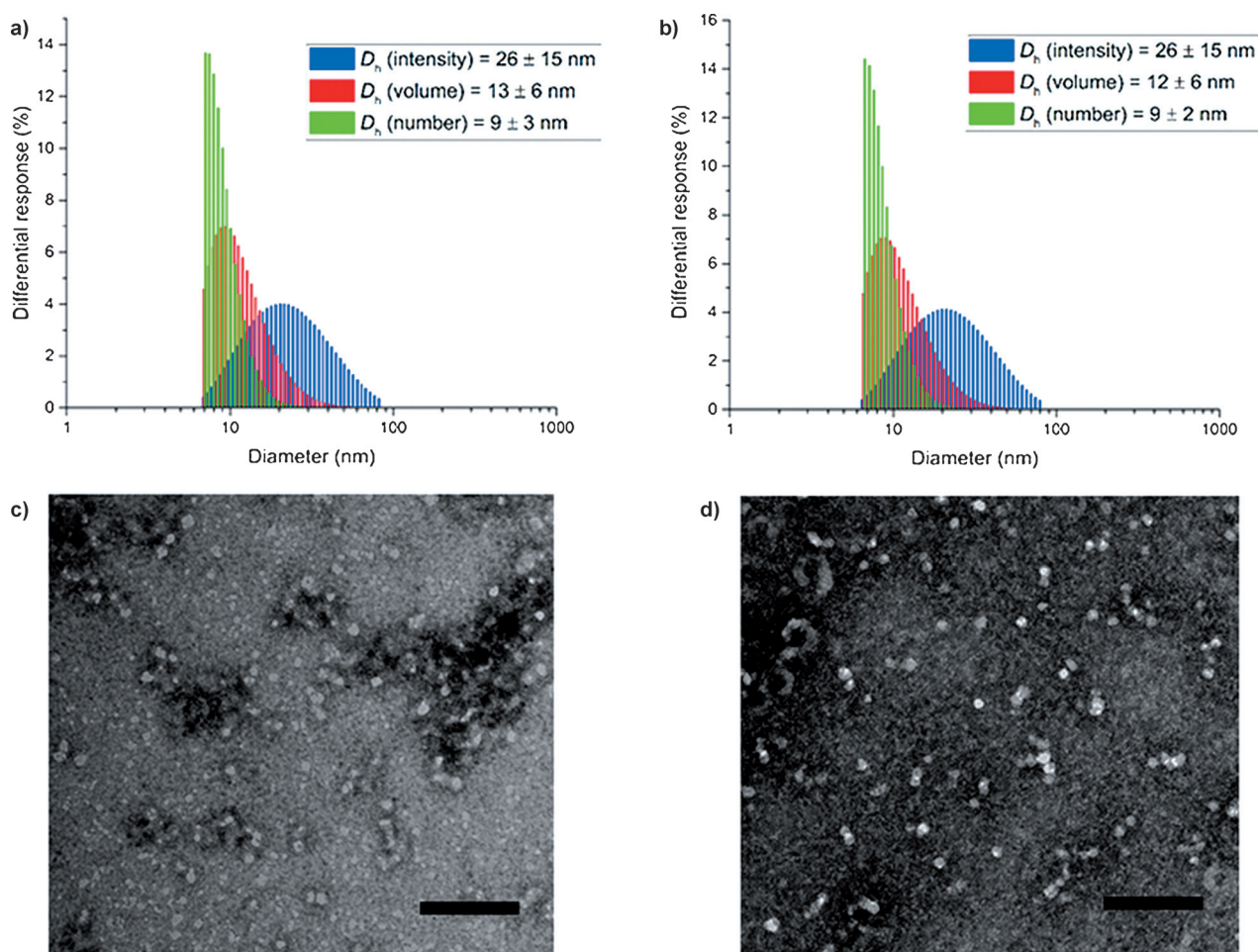


Figure 4. a) DLS results of anionic nanoparticles of **4**: D_h (intensity) = 26 ± 15 nm, D_h (volume) = 13 ± 6 nm, D_h (number) = 9 ± 3 nm. b) DLS results of cationic nanoparticles of **6**: D_h (intensity) = 26 ± 15 nm, D_h (volume) = 12 ± 6 nm, D_h (number) = 9 ± 2 nm. TEM images for c) anionic and d) cationic nanoparticles. The scale bars in both TEM images are 100 nm.

Experimental Section

Materials: All manipulations involving air- or/and moisture-sensitive compounds were carried out in a glovebox or with standard Schlenk technique under an Ar atmosphere. Allyl glycidyl ether (97%, Alfa) and propylene oxide (98%, Alfa) were distilled over CaH_2 under reduced pressure prior to use. 2-aminoethanethiol and dimethoxy-2-phenylacetophenone (DMPA) were purchased from TCI. L-cysteine hydrochloride anhydrous and mercaptoacetic acid were acquired from Amresco and Alfa Aesar, respectively. Di-*tert*-butyl dicarbonate was purchased from Chem Impex Int'l Inc. Tetrahydrofuran (THF), dichloromethane, and toluene were purified using an MBraun manual solvent purification system packed with Alcoa F200 activated alumina desiccant. Bone-dry carbon dioxide supplied in a high-pressure cylinder and equipped with a liquid dip tube was purchased from Scott Specialty Gases.

Representative procedure for the synthesis of PAGEC-*b*-PPC-*b*-PAGEC triblock polycarbonates: (Salen)cobalt(III)X/PPNX (X = trifluoroacetate) (0.0125 mmol), propylene oxide (0.87 mL, 12.5 mmol) and 0.7 mL toluene/ CH_2Cl_2 (1/1 volume ratio) with 20 equiv water were added into a 15 mL autoclave, and pressurized to 2.5 MPa. After 48 h, the CO_2 pressure was slowly released and allyl glycidyl ether was added. The reactor was recharged with CO_2 to 2.5 MPa. The pressure was released after 48 h. The crude polymer was dissolved in CH_2Cl_2 and precipitated from methanol. This process was repeated three times to completely remove the catalyst. The obtained polymer was dried under high vacuum at room temperature.

General procedure of thiol-ene reactions of PAGEC-*b*-PPC-*b*-PAGEC triblock polycarbonate with functional thiols: A solution of ABA triblock polymer (0.30 g, $M_n = 10300 \text{ g mol}^{-1}$, 1.15 mmol alkenes), functional thiol (23 mmol) in 25.0 mL of THF was degassed for 15 min and then refilled with Ar. DMPA (0.1 mmol) was added into the solution followed by UV irradiation (365 nm) for 2 h. The reaction mixtures were precipitated from THF into diethyl ether or hexane to remove excess functional thiols and photoinitiator by-products to give the product polymers.

Keywords: carbon dioxide · epoxide · micelles · nanoparticles · polycarbonates

How to cite: *Angew. Chem. Int. Ed.* **2015**, *54*, 10206–10210
Angew. Chem. **2015**, *127*, 10344–10348

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Received: June 3, 2015

Published online: July 14, 2015