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Synthesis of novel polyethers with abundant reactive sites and diverse skeletons based on the ring-opening reaction of D–A cyclopropanes†

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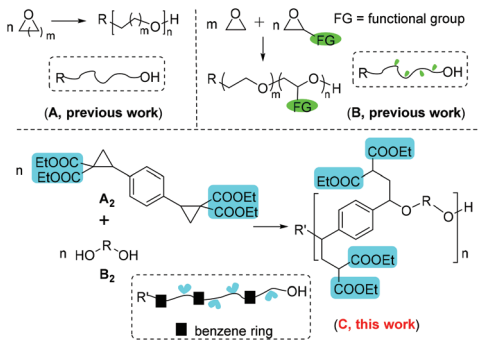
Based on the ring-opening reaction of D–A cyclopropanes, a facile synthesis of novel polyethers is developed with molecular weights up to 17.7 kg mol^{-1}. The resulting polymers possess diverse skeletons and abundant reactive *gem*-diester groups, which could be conveniently transformed into polyethers with a novel topology or bearing carboxylic acid groups.

Polyethers possess excellent water solubility, biocompatibility and stealth properties, and thus attract enormous interest from synthetic chemists, materials scientists and biologists.[1–7] Polyethers are generally synthesized *via* the ring-opening polymerization of epoxides (**A**, Scheme 1).[8–10] The commonly used monomers include ethylene oxide (EO), oxetane, tetrahydrofuran and their derivates.[11–14] Conventional polyethers simply contain alkoxy repeating units and hydroxyl groups at the chain end. The need for highly functional polyethers has motivated intense interest in synthesizing novel components, either *via* appropriate initiators and terminating agents or *via* functional epoxide building units,[15,16] which can be homopolymerized or copolymerized with EO to yield multifunctional polyethers (**B**, Scheme 1).[17–22] For example, carboxylic acid groups at the polyether backbone are desirable to generate polyether-based polyelectrolytes and possess the potential to act as adsorbents and moisturizing materials, and have hardly been investigated to date. In this context, the copolymerization of EO with functional epoxides has been exploited to generate a platform for post-polymerization modification, including allyl glycidyl ether,[22] ethoxyethyl glycidyl ether[13] and epicyanohydrin.[21] However, the efficiency of these methods and the density of functional groups introduced need to be improved. Besides, the polyethers synthesized by all the above-described approaches have a very similar skeleton structure. It is necessary to develop new methods for synthesizing polyethers to expand the potential applications *via* enriching the skeleton structure and reactive sites.

Donor–acceptor (D–A) cyclopropanes have emerged as versatile synthons for natural products and molecules with biological activity.[23–26] Our group has realized a series of highly enantioselective ring opening/cyclization reactions of D–A cyclopropanes with various nucleophiles.[27–31] For example, the catalytic system of oxazoline/Cu(II) achieves the asymmetric ring-opening reaction of D–A cyclopropanes with alcohols, obtaining high yields (up to 99%) under mild conditions for various cyclopropane and alcohol substrates.[32] The high efficiency endows the reaction potential to evolve into a polymerization reaction for synthesizing novel polyethers. The skeleton of the resulting polyether can be conveniently regulated by modifying the monomer structure, including the A_2 monomer containing two cyclopropane groups combined with the B_2 monomer (diols) (**C**, Scheme 1) and the AB monomer bearing both hydroxyl and cyclopropane groups. Moreover, this kind of polyether contains plentiful reactive *gem*-diester



Scheme 1 The synthesis of polyethers.

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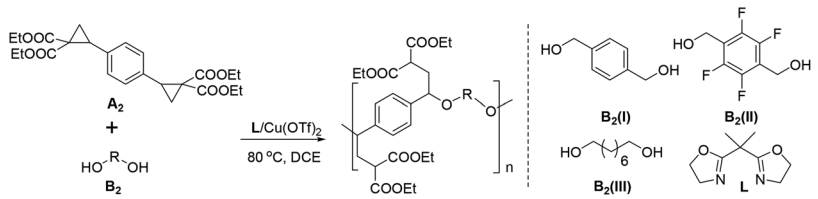
Table 1 The polymerizations of A_2 and B_2 using different diols[a]



Run	B_2	Conv.[b] (cyclopropane)	Conv.[b] (OH)	$M_{n,NMR}$[c] (kg mol^{-1})	M_n[d] (kg mol^{-1})	M_w[d] (kg mol^{-1})	PDI[d]	T_g[e] (°C)	T_{d5}[f] (°C)
1	B_2(I)	100%	94%	4.7	5.3	16.5	3.1	15	277
2	B_2(II)	87%	79%	1.6	1.2	2.3	2.0	32	248
3	B_2(III)	100%	—[g]	—[g]	2.1	12.2	5.7	−24	312

[a] Conditions: 2.5 mL DCE, 1 mmol monomers, c(Cat.) = 0.02 M, n(Cu(OTf)$_2$)/n(L) = 1/1.2, c(A_2 or B_2) = 0.4 M, oil bath 80 °C, 24 h. [b] Determined by ^{1}H NMR. [c] Determined by ^{1}H NMR. [d] Determined by GPC. [e] Determined by DSC. [f] 5% weight loss temperature determined by TGA. [g] It cannot be calculated because of the overlap of the resonance peak.

groups, which facilitate the generation of polyethers with a novel topology and high-density carboxylic acid groups.

We first attempted the polymerizations of B_2(I) and A_2 monomers (0.4 M). Similar to asymmetric catalysis, the Cu(OTf)$_2$/bioxazoline (BOX) complex was utilized as the catalytic system. Considering that a very fast conversion rate is necessary to reduce the probability of side reactions and so as to achieve a high molecular weight, a high reaction temperature of 80 °C and a simple BOX ligand with low steric hindrance were employed, as shown in Table 1. After 24 hours, the GPC measurement shows that the obtained polymer possesses a weight average molecular weight (M_w) of 16.5 kg mol^{-1} and a PDI of 3.1 (run 1), demonstrating the feasibility of the design. The conversion of the hydroxyl group is calculated to be 94%,[33] while cyclopropane groups are completely consumed, which indicates that the side reactions involving the cyclopropane group[34–36] should be the main factor limiting the increase of the molecular weight. According to the literature,[34–36] D–A cyclopropanes (2-arylcyclopropane-1,1-dicarboxylates) might isomerize into the corresponding propenes or γ-butyrolactone derivatives under the polymerization conditions (in the presence of Lewis acid and at 80 °C), which might result in some low molecular weight components and relatively high PDI values. As suggested by the signal "g" in the ^{1}H NMR spectrum (Fig. 1a) of the purified polymer, the resulting polyether possesses a terminal hydroxyl group. Based on the content of terminal hydroxyl and the assumption that each polymer chain contains one hydroxyl, the number average molecular weight (M_n) of the polymer is calculated to be 4.7 kg mol^{-1},[33] which is consistent with that measured by GPC (5.3 kg mol^{-1}). This result confirms that each macromolecule contains approximately one hydroxyl terminal, and it is unlikely to have ring-shaped and crosslinked structures.

Next, different diols were used as B_2 monomers to enrich the skeleton structure of polyethers. As shown in Table 1, all the three B_2 monomers can be polymerized with cyclopropane monomer A_2, resulting in polyethers with different skeletons. In addition, the structure of diol monomers affects the molecular weight of polymers. Under the same conditions, the polymerization using the B_2(I) monomer with the aromatic ring achieves a M_w of 16.5 kg mol^{-1} and a PDI of 3.1, while the polymer of aliphatic diols B_2(III) possesses a lower M_w of 12.2 kg mol^{-1} and a wider PDI of 5.7. The B_2(II) monomer bearing four fluorine groups in the benzene ring leads to an even lower M_w of 2.3 kg mol^{-1}, suggesting a very strong electronic effect. The polymerization of A_2 and B_2(II) is so slow that cyclopropane groups are retained in the system after 24 hours and the conversion of hydroxyl is only 79%. The ^{1}H NMR spec-

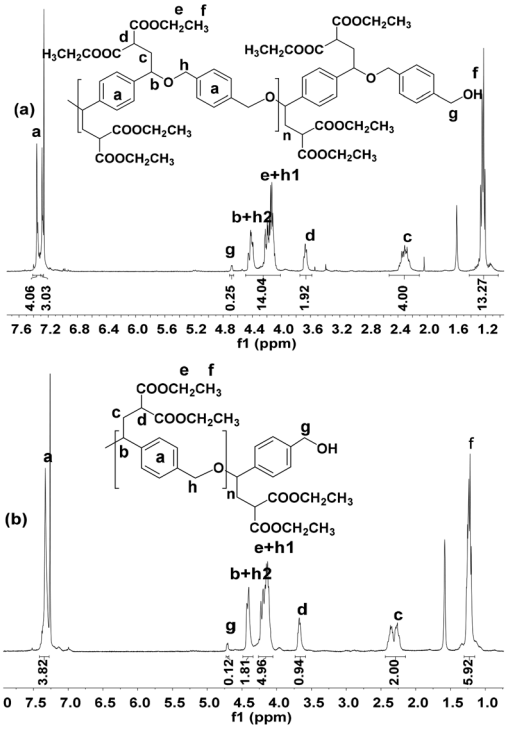


Fig. 1 ^{1}H NMR spectra (CCl_3D, 30 °C) of the polymer of the A_2 monomer with the B_2(I) monomer (a, Table 1, run 1) and the polymer of the AB monomer (b, Table 2, run 3).

trum (Fig. S2†) suggests that the polymers of B_2(II) also contain terminal hydroxyl but not cyclopropane ends. As expected, polyethers with different structures exhibit different thermodynamic properties. The more benzene rings in the main chain, the higher the glass transition temperature (T_g) of the polymer (run 1 *vs.* 3, Fig. S4 and S5†). The introduction of fluorine in the benzene ring further increases the T_g value, might be due to the hydrogen-bonding effect (run 2, Fig. S6†). However, the thermostability of the polymers shows an opposite trend (Fig. S8–S10†). The polyether of A_2/B_2(III) without the benzene ring shows the highest thermal stability, with a 5% weight loss temperature (T_{d5}) of 312 °C. While, the T_{d5} values for the polymers of A_2/B_2(I) and A_2/B_2(II) are 277 °C and 248 °C, respectively. Besides, all the resulting polyethers are poorly soluble in water and easily soluble in common organic solvents, such as dichloromethane, ethyl acetate, chloroform, tetrahydrofuran, *N*,*N*-dimethylformamide and dimethyl sulfoxide.

Subsequently, the polymerizations of A_2 and B_2(III) were conducted at different monomer and catalyst concentrations (Table S2†). The M_w declines from 13.9 kg mol^{-1} to 3.0 kg mol^{-1}, as the catalyst concentration gradually decreases from 0.02 M to 0.004 M while the monomer concentration is fixed as 0.4 M. Similarly, the M_w decreases from 5.4 kg mol^{-1} to 3.1 kg mol^{-1} when the concentrations of A_2 and B_2(II) are reduced from 0.4 M to 0.2 M while the catalyst concentration is set as 0.008 M. The higher concentrations of catalysts and monomers might accelerate the intermolecular polymerization, which reduces the probability of side reactions, mainly those involving the cyclopropane group. Therefore, a higher molecular weight is obtained at higher concentrations of monomers and catalysts.

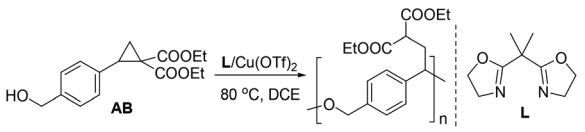
Compared to A_2/B_2 monomers, the AB monomer (Table 2) has good solubility and can guarantee the initial 1 : 1 concentration ratio of hydroxyl and cyclopropane groups. The polymerizations of the AB monomer were carried out under the optimal conditions of the A_2/B_2 polymerizations. The monomer concentration was initially set as 0.8 M, equivalent to the 0.4 M of each monomer in the A_2/B_2 system. With 0.02 M catalyst, the polymerization achieves a M_w of 11.5 kg mol^{-1} and a PDI value of 2.9 (run 1, Table 2). The increase of AB concentration is also conducive to achieve high molecular weights. At a lower AB concentration of 0.4 M, a lower M_w of only 3.9 kg mol^{-1} is achieved, while a much higher M_w of 17.7 kg mol^{-1} is achieved when the AB concentration is increased to 1.6 M (runs 2 and 3, Table 2). In the three polymerization reactions, all the cyclopropane groups are converted, while the conversion of hydroxyl is improved from 88% to 94% with an increase of monomer concentration. The ^{1}H NMR spectrum (Fig. 1b) shows that the isolated polymer of AB (run 3, Table 2) possesses hydroxyl at the chain end but no terminal cyclopropane group is found. According to the content of the terminal hydroxyl, the M_n is calculated to be 2.1–5.7 kg mol^{-1}, which is consistent with that measured by GPC, confirming that each polymer chain contained approximately one terminal hydroxyl. These results reveal that the side reaction involving the cyclopropane group[34–36] should also be the primal reason that restricts a further increase of the molecular weight for the system of the AB monomer. The polyether of AB possesses a T_g value of 14 °C (Fig. S7†), which is similar to that of the polyether of A_2/B_2(I), probably due to these two polymers having similar structures. However, the polymer of AB has a higher thermal stability than the polyether of A_2/B_2(I), with T_{d5} values of 304 °C *versus* 277 °C (Fig. S8 and S11†).

The polymerization of the AB monomer (run 1, Table 2) was tracked by ^{1}H NMR measurement. Based on the NMR spectra (Fig. S1†), the $M_{n,NMR}$ as well as the conversion of hydroxyl and cyclopropane groups are calculated and the values are listed in Table S3.† The $M_{n,NMR}$ continues to increase in the initial 3 hours, and then levels off. It is found that the cyclopropane group is converted faster than hydroxyl, and the M_n stops increasing at the time when all the cyclopropane groups are consumed. This confirms our hypothesis that the side reaction of the cyclopropane group[34–36] limits the increase in the molecular weight of the polymer.

In order to further confirm the structure of the polyethers, the polymer of the AB monomer was subjected to MALDI-TOF-MS measurement using AgOAc as the cationization agent. As shown in Fig. S12,† the *m*/*z* value in the spectrum is distributed in an arithmetic sequence close to (108 + 292 n), where 108 is the relative molecular mass of a silver ion while the difference of 292 between each peak is equal to the relative molecular mass of the AB monomer. These results demonstrate that the polyether formed *via* the reaction of hydroxyl with cyclopropane in the AB monomer, ruling out the possibility that impurities, such as water, initiate the ring-opening of cyclopropanes to form macromolecules.

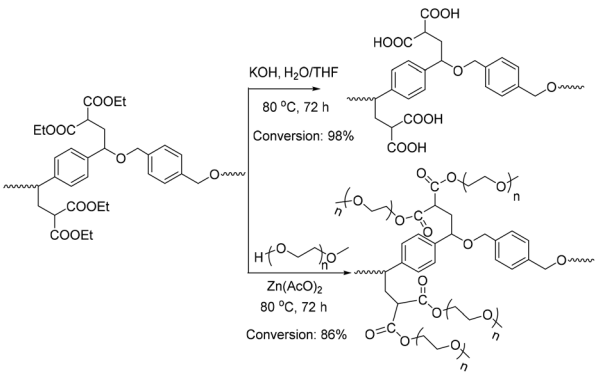
Next, as shown in Scheme 2, we conducted some macromolecular reactions towards the polyether obtained from the polymerization of A_2 with B_2(I) (run 1, Table 1). The ethyl ester group of the polyether is transformed into the carboxylic acid group through the hydrolysis reaction, with a conversion of 98%. From the ^{1}H NMR spectrum of the transformation

Table 2 Polymerizations of the AB monomer[a]



Run	c(M) (M)	Conv.[b] (OH)	$M_{n,NMR}$[c] (kg mol^{-1})	M_n/M_w[d] (kg mol^{-1})	PDI[d]	T_g[e] (°C)	T_{d5}[f] (°C)
1	0.8	93%	4.2	4.0/11.5	2.9	14	304
2	0.4	88%	2.5	2.1/3.9	1.9	—	—
3	1.2	94%	4.9	5.7/17.7	3.1	—	—

[a] Conditions: 1 mL DCE, 0.02 mmol $Cu(OTf)_2$, 0.024 mmol ligand, oil bath 80 °C, 24 h. [b] Determined by ^{1}H NMR. [c] Determined by ^{1}H NMR. [d] Determined by GPC. [e] Determined by DSC. [f] 5% weight loss temperature determined by TGA.



Scheme 2 Macromolecular transformation.

product (Fig. S13†), it is found that after the reaction the signal of the carboxylic acid proton (i′) is present, while the signal peaks attributed to the ethyl ester group (e and f) nearly disappear. Through the transesterification reaction of ester groups, PEG with a low molecular weight and monohydroxyl is linked to the polyether of A_2/B_2(I), yielding branched polyethers with a conversion of 86%. The ^{1}H NMR spectrum (Fig. S14†) of the grafting product indicates that after the reaction most of the original signals attributed to the ethyl ester group (f) disappear, while the signal peaks (i′) of the PEG segment are observed. These results demonstrate the potential of the resulting polyether for functional group transformation and topological modification based on the reactivity of the *gem*-diester group.

In summary, we have developed a new method to synthesize novel polyethers, based on the ring-opening reaction of D–A cyclopropanes. A series of polyethers with novel skeletons are synthesized by employing different monomers. The M_w of the resulting polyester is up to 17.7 kg mol^{-1}. The hydrolysis reaction and the transesterification reaction were conducted towards the reactive ester groups in the obtained polyether, which realized the convenient transformation of functional groups and the modification of topology. This work provides a strategy for the design and synthesis of novel polymers. In order to reduce the probability of side reactions and to improve the molecular weight of the polymer for practical applications, it is necessary to further optimize the reaction conditions, such as the types of catalysts and monomers. Besides, in the A_2/B_2 system, the molecular weight might be improved *via* slowly and continuously adding the cyclopropane monomer A_2, which is prone to side reactions. Another approach to increase the molecular weight is to graft other terminally functionalized polymers onto the resulting polyether, which acts as the skeleton. The relevant research is underway.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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