A Simple, Effective, and Selective Synthesis Route for Difunctional 30-Membered Macrocyclic Ester and Linear Oligoester Derived from Benzoxazine Dimers

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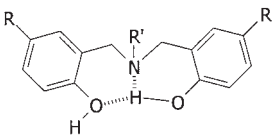
A series of benzoxazine dimer based difunctional 30-membered macrocyclic and linear oligomer esters are selectively obtained in simple and mild condition. The unique intramolecular hydrogen bond of the dimer is a key factor to proceed the ''self-selective reaction'' in esterification between terephthaloyl chloride and benzoxazine dimers. This is a so-called ''simple, effective, and selective synthesis route'' since we can obtain a well-defined structure product in a high yield without using expensive catalysts for multistep reactions in specific conditions.

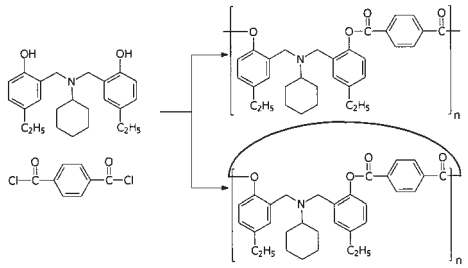
For the past few years, macrocyclic compounds have become new intermediates in engineering thermoplastics since it can overcome the melt flow behavior of classical high molecular weight polymers in the processing, i.e., pultrusion, resin-transfer-molding, or reaction injection molding.[1–3] Recently, we proposed monosubstituted benzoxazine monomers based aza-methylene-phenol macrocyclic compounds via ring opening polymerization.[4,5] The monosubstituted benzoxazines are even more attractive when we found that the ring opening reaction of benzoxazine monomers terminates as soon as the dimers are formed.[6] We clarified that the dimers obtained are stabilized by an imbalanced intramolecular H-bond to give asymmetric compounds inevitably (Scheme 1).[6] Herein, we present a ''self-selective reaction'' of benzoxazine dimer to obtain difunctional 30-membered macrocyclic esters and linear oligoester.

Benzoxazine dimers (Scheme 1), i.e., *N*,*N*-bis(2-hydroxy-5-ethylbenzyl)cyclohexylamine (**1**), *N*,*N*-bis(2-hydroxy-5-methylbenzyl)propylamine (**2**), and *N*,*N*-bis(2-hydroxy-5-methylbenzyl)-cyclohexylamine (**3**), were prepared as reported elsewhere.[4,5] Dimer **1** (1.84 g, 5 mmol) was mixed with triethylamine, Et_3N (1.40 mL, 10 mmol), and dissolved in dichloromethane (100 mL). A solution of terephthaloyl chloride (1.02 g, 5 mmol) in tetrahydrofuran (50 mL) was added dropwise and stirred at room temperature for 8 h. The solution obtained was collected, washed with water, and dried over anhydrous sodium sulfate. The solvent was removed and the crude product was recrystallized from the mixture of isopropanol and dichloromethane (1 : 1) to obtain a clear crystal product (**4**) (Scheme 3) in 40% yield. In the case of sodium hydroxide catalyst, similar procedures were proceeded but using an aqueous solution of NaOH (0.80 g, 20 mmol in 50 mL water) to obtain product (**5**)



1: R = -C_2H_5, R' = -C_6H_{11}
2: R = -CH_3, R' = -C_3H_7
3: R = -CH_3, R' = -C_6H_{11}

Scheme 1.



Scheme 2.

(Scheme 3) in 85% yield.

Esterification by acid chloride on **1** may provide either linear or cyclic product (Scheme 2). Dimer **1** gives peaks at 3251 cm^{-1} (intermolecular H-bond), 3000–2800 cm^{-1} (intramolecular H-bond), 1599 cm^{-1} (N···H-O, intramolecular H-bond)[7] and 1499 cm^{-1} (trisubstituted benzene) (Figure 1(a)). When using Et_3N as a catalyst, the product obtained shows a new peak at 1737 cm^{-1} due to C=O stretching of ester group while the peak at 3251 cm^{-1} disappeared (Figure 1(b)). However, the broad peak at 3000–2800 implies a remained intramolecular H-bond. ^{1}H-NMR gives two different methylene protons at $\delta_H = 3.49$ and 3.68 ppm suggesting that the esterification occurred at two hydroxyl groups belonging to different dimer unit as shown in **4**. Meanwhile, the peak at $\delta_H = 8.27$ ppm corresponding to four equivalent aromatic protons strongly supports that one diacid chloride molecule is reacted onto two dimer units. The structure is precisely confirmed by the matrix-assisted laser desorption ionization time-of-flight mass spectrometer (MALDI-TOF MS). Figure 2 shows the molecular ion signal, $M^+ = 864$ corresponding to **4** consisting of two dimer units and one unit of diacid (Scheme 3). The elemental analysis result confirms the proposed structure **4**. The product obtained is also only a single compound without by-products implying the reaction is successfully proceeded in a selective route.

Referring to our previous studies,[6] the present result may

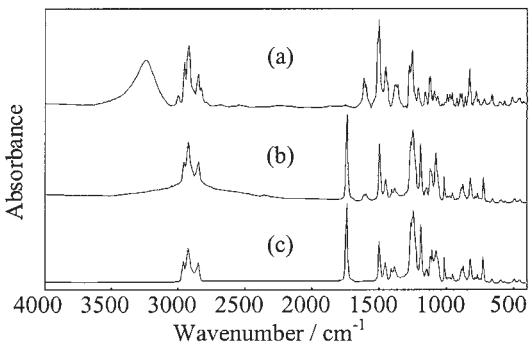


Figure 1. FTIR spectra of (a) Benzoxazine dimer **1**, (b) Compound **4**, and (c) Compound **5**.

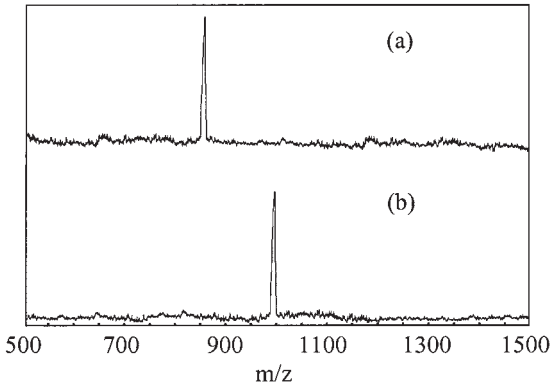
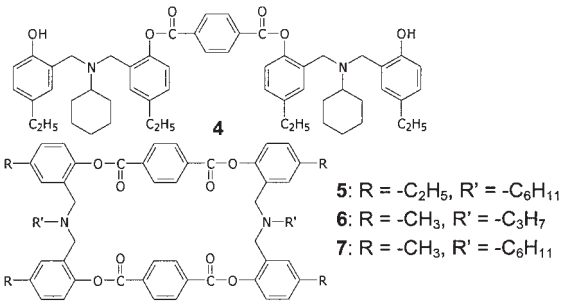


Figure 2. MALDI-TOF mass spectra of (a) Compound **4**, and (b) Compound **5**.



Scheme 3.

imply that the catalytic esterification of diacid chloride by Et_3N may not be effective enough to overcome the intramolecular H-bond. The low yield 40% indicated that the stoichiometry between diacid chloride and the dimer is not 1 : 1 but 1 : 2, which supports our explanation. An attempt to overcome the intramolecular H-bond by using a strong base was done. Although the system is heterogenous when we used NaOH, but it is easy to neutralize the excess acid chloride in aqueous phase after the reaction.

Compound **5** exhibits different structural characterization results from **4**, as given below. Figure 1(c) shows no OH and N$\cdots$H peaks but the ester peak at 1750 cm^{-1}. ^1H NMR shows only one methylene species ($\delta_H = 3.49$ ppm), implying the symmetric structure of aza-methylene linkage. The peak at $\delta_H = 8.27$ ppm assigned to four equivalent aromatic proton suggested that one diacid chloride molecule reacted completely and there was no acid end group left. At present, the product is likely to be a macrocyclic compound as proposed in **5** (Scheme 3). Further analysis was done as outlined below.

The integration ratio of methylene and phenyl (belonging to diacid) in ^1H NMR chart is clarified to be 1 : 1, suggesting that diacid esterification occurred at both hydroxyl groups. In this way, we conclude that the repeating unit of **5** consisted of a unit of dimer and a unit of diacid. However, the combination number of dimer and diacid has to be further investigated. MALDI-TOF MS shows a single molecular ion signal at $M^+ = 994$ (Figure 2). Combining all results, we conclude that the compound obtained is a difunctional 30-membered macrocyclic ester. Moreover, the elemental analysis gives the C, H, N percentage consistent with the proposed structure **5**. It is to our surprise to find that only one type of macrocyclic, i.e., [2 + 2], is generated when benzoxazine dimers were esterified under the strong basic catalyst. We extended the synthesis work for **2** and **3** to obtain **6** and **7** as our expectation. We speculated that the selectivity of [2+2]macrocyclic might come from the template formation between Na^+ and benzoxazine dimer. As a result, the selectivity with high yield (85% for **5**) is obtained. Further studies are in the progress.

Here, the reaction is simple for operating at room temperature, effective for elimination of H-bond of benzoxazine dimer by base catalyst, and selective to obtain only a single species of cyclic or linear compound. The key factor to control the formation of linear or cyclic ester compound might be the elimination of only intermolecular H-bond to produce linear ester or both inter and intramolecular H-bonds to achieve cyclic ester.

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References and Notes

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8 Spectroscopic results of compounds, **4**–**7**, were shown as follows. Compound **4**: 40% yield; mp = 208 °C; FTIR (KBr, cm^{-1}): 3000–2800 (br, OH), 1737 (s, C=O), 1499 (vs, dimer); ^1H NMR (200 MHz, $CDCl_3$, ppm): δ_H 1.1 (4H, m, CH_2), 1.20 (12H, m, CH_3-CH_2-Ar), 1.70 (16H, m, CH_2), 2.18 (2H, m, CH), 2.70 (8H, m, CH_3-CH_2-Ar), 3.49 (4H, s, Ar-CH_2-N), 3.68 (4H, s, Ar-CH_2-N), 6.95 (4H, d, Ar-H, $J_1 = 8.17$ Hz), 7.08 (4H, d, Ar-H, $J_1 = 8.17$ Hz), 7.55 (4H, s, Ar-H), 8.28 (4H, s, CO-Ar-CO). MALDI-TOF MS (m/z): 864. Anal. Calcd for $C_{56}H_{68}N_2O_6$: C, 77.78; H, 7.87; and N, 3.24%. Found: C, 77.82; H, 7.86; and N, 3.21%. Compound **5**: 85% yield; mp = 215 °C; FTIR (KBr, cm^{-1}): 1737 (s, C=O), 1499 (vs, dimer); ^1H NMR (200 MHz, $CDCl_3$, ppm): δ_H 1.1 (4H, m, CH_2), 1.26 (12H, t, CH_3-CH_2-Ar, $J_1 = 7.86$ Hz), 1.45 (8H, m, CH_2), 1.82 (8H, m, CH_2), 2.18 (2H, m, CH), 2.67 (8H, q, CH_3-CH_2-Ar, $J_1 = 7.86$ Hz), 3.49 (8H, s, Ar-CH_2-N), 6.95 (4H, d, Ar-H, $J_2 = 8.17$ Hz), 7.08 (4H, d, Ar-H, $J_2 = 8.17$ Hz), 7.55 (4H, s, Ar-H), 8.28 (8H, s, CO-Ar-CO). MALDI-TOF MS (m/z): 994. Anal. Calcd for $C_{64}H_{70}N_2O_8$: C, 77.26; H, 7.04; N, 2.82%. Found: C, 77.31; H, 7.01; N, 2.85%. Compound **6**: 80% yield; mp = 240 °C; FTIR (KBr, cm^{-1}): 1738 (s, C=O), 1492 (vs, dimer); ^1H NMR (200 MHz, $CDCl_3$, ppm): δ_H 0.87 (6H, t, CH_3-CH_2-CH_2-N, $J_1 = 7.2$ Hz), 1.45 (4H, m, CH_3-CH_2-CH_2-N), 2.45 (12H, s, CH_3-Ar), 2.30 (4H, t, CH_3-CH_2-CH_2-N, $J_2 = 6.79$ Hz), 3.43 (8H, s, Ar-CH_2-N), 6.95 (4H, d, Ar-H, $J_3 = 8.17$ Hz), 7.05 (4H, d, Ar-H, $J_3 = 8.17$ Hz), 7.52 (4H, s, Ar-H), 8.26 (8H, s, CO-Ar-CO). MALDI-TOF MS (m/z): 858. Anal. Calcd for $C_{54}H_{54}N_2O_8$: C, 75.52; H, 6.29; N, 3.26%. Found: C, 75.48; H, 6.32; N, 3.28%. Compound **7**: 85% yield; mp = 270 °C; FTIR (KBr, cm^{-1}): 1734 (s, C=O), 1494 (vs, dimer); ^1H NMR (200 MHz, $CDCl_3$, ppm): δ_H 1.1 (4H, m, CH_2), 1.45 (8H, m, CH_2), 1.82 (8H, m, CH_2), 2.22 (2H, m, CH), 2.39 (12H, s, CH_3-Ar), 3.51 (8H, s, Ar-CH_2-N), 6.95 (4H, d, Ar-H, $J_1 = 8.16$ Hz), 7.05 (4H, d, Ar-H, $J_1 = 8.16$ Hz), 7.50 (4H, s, Ar-H), 8.31 (8H, s, CO-Ar-CO). MALDI-TOF MS (m/z): 938. Anal. Calcd for $C_{60}H_{62}N_2O_8$: C, 76.76; H, 6.61; N, 2.99%. Found: C, 76.73; H, 6.59; N, 2.31%.