CHAPTER IV

AN ELEGANT; -SIMPLE, EFFECTIVE, AND SELECTIVE-, SYNTHESIS ROUTE FOR DIFUNCTIONAL 30-MEMBERED MACROCYCLIC ESTER AND LINEAR OLIGOESTER DERIVED FROM BENZOXAZINE DIMERS

Abstract

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 "elegant 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.

Introduction

For the past few years, macrocyclic compounds have become a 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 mono-substituted benzoxazine monomers based aza-methylene-phenol macrocyclic compounds via ring opening polymerization.[4-5] The mono-substituted benzoxazines are even more attractive when we found that the ring opening reaction of benzoxazines 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 I).[6] Herein, we present a "self-selective reaction" of benzoxazine dimer to obtain difunctional 30–membered macrocyclic esters and linear oligoester.

Experimental

Benzoxazine dimers (Scheme I), i.e., *N*,*N*-bis(2-hydroxy-5-ethylbenzyl)cyclo hexylamine **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 dropwisely and stirred at room temperature for 8 h. The solution obtained was collected, washed by water, and dried over anhydrous sodium sulfate. The solvent was removed and the crude product was recrystallized in the mixture of isopropanol and dichloromethane (1:1) to obtain a clear crystal product **4** at 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** at 80% yield.

Results and Discussion

Esterification by acid chloride on **1** is possible to provide either linear or cyclic product (Scheme II). 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} (tri-substituted benzene) (Fig. 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 (Fig. 1(b)). However, the broad peak at 3000-2800 implies a remaining intramolecular H-bond. ^{1}H-NMR gives two different methylene protons at δ_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 δ_H = 8.27 ppm corresponding to four equivalent aromatic protons strongly supports that one diacid chloride molecule has reacted with two dimer units. The structure is 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 III). 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] this can be explained that the catalytic esterification of diacid chloride by Et_3N may not be effective enough to overcome the intramolecular H-bond. The low yield of 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, 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 follows. Figure 1(c) shows no OH and N---H peaks but the ester peak is seen at 1750 cm^{-1}. ^{1}H NMR shows only one methylene species (δ_H = 3.49 ppm), implying the symmetric structure of aza-methylene linkage. The peak at δ_H = 8.27 ppm refers to four equivalent aromatic proton suggesting that one diacid chloride molecule reacted completely and there was no acid end group left. At present, the product is

likely to be considered as a macrocyclic compound as proposed in **5** (Scheme III). Further analysis was done as below.

The integration ratio of methylene and phenyl (belonging to diacid) in ^{1}H NMR chart is found to be 1:1, suggesting 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 (Fig. 2). Combining all results, we conclude that the compound obtained to be a difunctional 30-membered macrocyclic ester. Moreover, the elemental analysis gives the C, H, N percentage as 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**.

Here, we claim our synthesis route as an elegant pathway to obtain linear and cyclic esters which are inevitably controlled from the dimer structure.[6] The reaction is simple for operating in 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 due to 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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6. A. Laobuthee, S. Chirachanchai, H. Ishida, and K. Tashiro, *J. Am. Chem. Soc.* **123**, 9947-9955 (2001).

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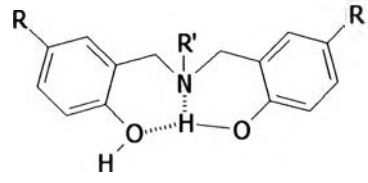
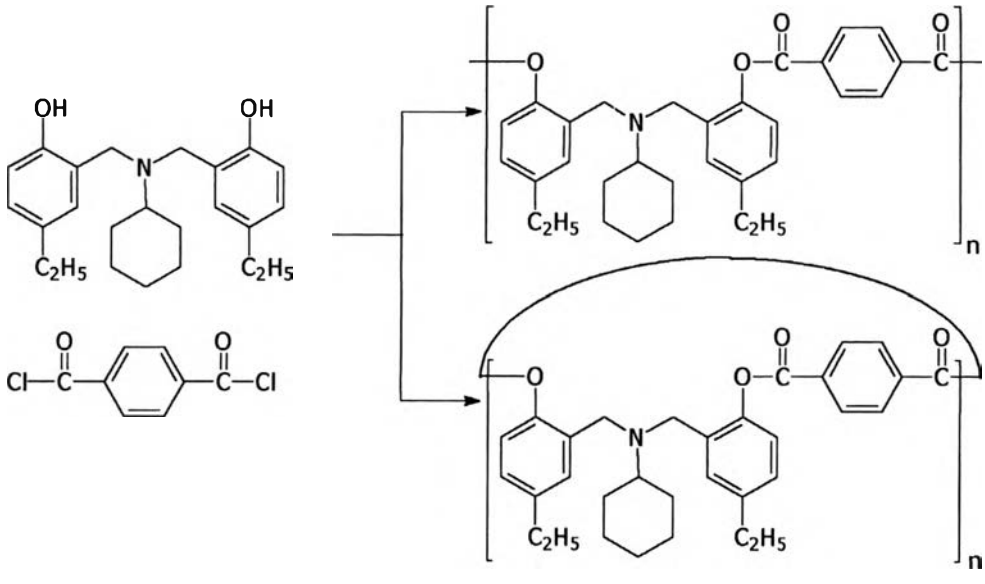
8. Spectroscopic results of compounds, **4**-**7**, were shown as follows. Compound **4**: 40 % yield; mp = 208°C; FTIR (KBr, cm^{-1}): 3000-2800 (br, OH), 1737 (s, C=O), 1499 (vs, dimer); ^1H NMR (200 MHz, $CDCl_3$, ppm): δ_H 1.1 (4H, m, CH_2), 1.20 (12H, m, **CH_3**-CH_2-Ar), 1.70 (16H, m, CH_2), 2.18 (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), 6.64 (2H, d, Ar-**H**, J_1 = 8.19 Hz), 6.78 (2H, s, Ar-**H**), 6.95 (2H, d, Ar-**H**, J_1 = 8.19 Hz), 7.08 (2H, d, Ar-**H**, J_2 = 8.22 Hz), 7.18 (2H, d, Ar-**H**, J_2 = 8.22 Hz), 7.25 (2H, 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; and N, 2.82. Found: C, 77.31; H, 7.01; and 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; and N, 3.26. Found: C, 75.48; H, 6.32; and N, 3.28. Compound **7**: 85% yield; mp = 270°C; FTIR (KBr, cm^{-1}): 1734 (s, C=O), 1494 (vs,

dimer); ^{1}H 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; and N, 2.99. Found: C, 76.73; H, 6.59; and N, 2.31.

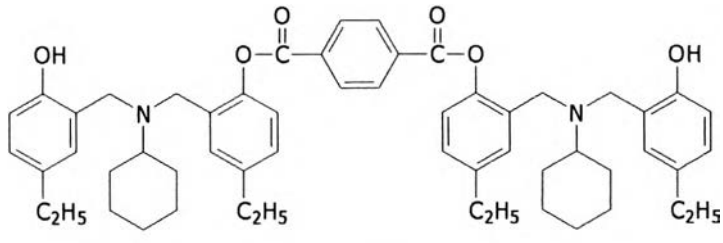


1: R = $-C_2H_5$, R' = $-C_6H_{11}$
2: R = $-CH_3$, R' = $-C_3H_7$
3: R = $-CH_3$, R' = $-C_6H_{11}$

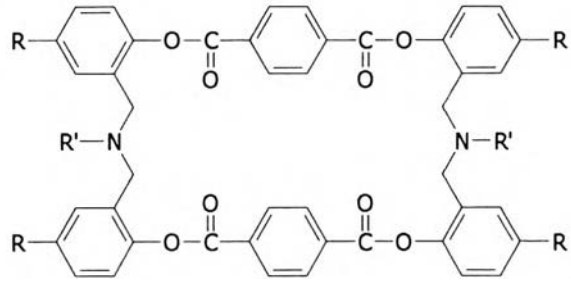
Scheme I. (Apirat et al.)



Scheme II. (Apirat et al.)



4



5: R = $-C_2H_5$, R' = $-C_6H_{11}$
6: R = $-CH_3$, R' = $-C_3H_7$
7: R = $-CH_3$, R' = $-C_6H_{11}$

Scheme III. (Apirat et al.)

Figure Captions

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**.

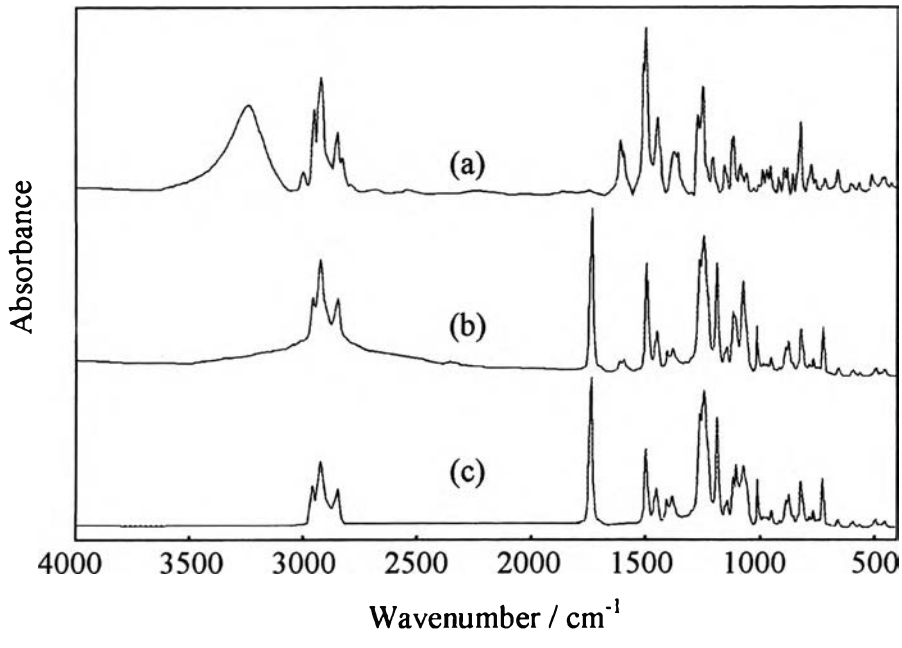


Figure 1. (Apirat et al.)

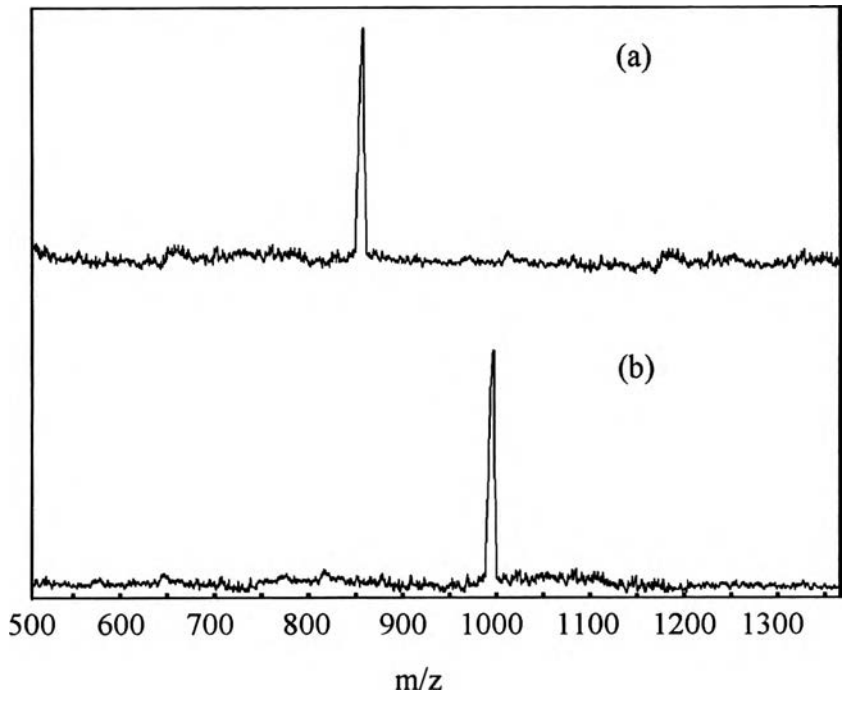


Figure 2. (Apirat et al.)