Optically Active Polycarbonates: Asymmetric Alternating Copolymerization of Cyclohexene Oxide and Carbon Dioxide

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Catalytic asymmetric synthesis polymerization is of much interest as an efficient method to produce optically active polymers from achiral monomers.[1] Chiral catalysts create new chiral centers in the main chain of the resulting polymers with control of the absolute configuration. Precedents for such a methodology are ring-opening polymerization of epoxide or episulfide,[2] cyclopolymerization of α,ω-dienes,[3] polymerization of unsymmetrical dienes[4] or cyclic olefins,[5] and alternating copolymerization of α-olefins with carbon monoxide.[6,7] Here, we report the first example of asymmetric synthesis copolymerization of meso epoxide **1** with CO_2, initiated by a chiral Zn catalyst.[8] Since the ring-opening of epoxides involves configurational inversion at one of the two chiral carbons,[14] meso epoxides **1**, achiral by nature, produce copolymers **2**, including chiral diol units −O−CHR−CHR−O−. One intriguing feature of polycarbonates **2** is their easy degradation into diols **3** and CO_2 by alkali treatment, which enables the unambiguous determination of the degree of asymmetric induction.[15] In this paper, we describe the synthesis of completely alternating copolymer **2a** from cyclohexene oxide

Table 1. Asymmetric Alternating Copolymerization of Epoxide 1 and Carbon Dioxide[a]

run	epoxide	4/Zn, mol/mol	temp, °C	time, h	yield of 2,[b] %	Mn (Mw/Mn)[c]	yield of 3[d] %	% ee of 3[e]
1	1a	1.00	60	24	>99	13000 (3.6)	85	51 (R,R)[f]
2	1a	1.00	60	12	89	13000 (4.3)	95	57 (R,R)[f]
3	1a	1.00	60	8	92	12000 (2.9)	87	58 (R,R)[f]
4	1a	1.00	60	4	49	11000 (3.7)	98	59 (R,R)[f]
5	1a	1.00	60	2	37	9800 (2.7)	88	68 (R,R)[f]
6	1a	1.00	40	12	85	13000 (1.9)	94	70 (R,R)[f]
7	1a	1.00	40	4	20	8400 (2.2)	93	73 (R,R)[f]
8	1a	0	60	48	0			
9	1a	0.60	60	48	41	77000 (7.5)	79	3 (R,R)[f]
10	1a	0.80	60	48	71	43000 (13.7)	76	11 (R,R)[f]
11	1a	1.10	60	24	>99	18000 (1.7)	82	23 (R,R)[f]
12	1a	1.20	60	48	98	13000 (1.7)	85	22 (R,R)[f]
13	1b	1.00	60	68	66	12000 (3.9)	83	24 (R,R)[g]
14	1c	1.00	60	48	8	20000 (2.0)	70	34 (R,R)[f]

[a] Meso epoxide (**1**, 10 mmol) was treated with carbon dioxide (30 atm) in the presence of a mixture of an amino alcohol **4** (0.50 mmol) and Et_2Zn (1.25 M in hexane, 0.50 mmol) in toluene (17 mL). After aqueous workup, the resulting copolymer was precipitated with MeOH, filtered, and eluted by $CHCl_3$. [b] Calculated based on **1**. [c] Estimated by size-exclusion chromatography analysis using a polystyrene standard. [d] Calculated based on **2**. [e] Absolute configuration is shown in parentheses. [f] Determined by GLC analysis with a chiral column (Chrompack, CHIRASIL-DEX CB). [g] The product **3b** was derivatized into its dibenzoate, and the % ee was determined by HPLC analysis with a chiral column (Daicel, CHIRALCEL OJ).

(**1a**) and CO_2, using Et_2Zn−chiral amino alcohol **4**. Enantiomeric excess of 70%, determined as **3a**, has been achieved.
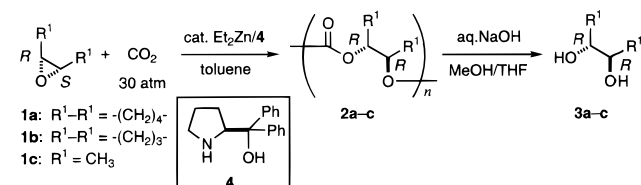
Copolymers **2** were obtained by treatment of meso epoxides **1** with 30 atm of CO_2 in the presence of a mixture of Et_2Zn and chiral amino alcohol **4**.[16] The representative results are summarized in Table 1. Using a 1:1 mixture of Et_2Zn and (*S*)-α,α-diphenylpyrrolidine-2-yl-methanol (**4**),[17] copolymer **2a** was given in a quantitative yield from cyclohexene oxide (**1a**) (run 1). The completely alternating nature of **2a** was manifested by ¹H NMR, as shown in Figure 1. The peak assigned to the methine proton is observed at δ 4.60 (for carbonate, −CH−OCO₂CH−);[18] no peak was observed at δ 3.45 (for ether, −CH−OCH−) attributable to a homopolymer of **1a**.

Hydrolysis of **2a** with aqueous NaOH gave (1*R*,2*R*)-cyclohexane-1,2-diol {(*R*,*R*)-**3a**} of 51% ee in 85% isolated yield.[15] With shorter reaction time, the percent ee of (*R*,*R*)-**3a** was slightly improved (runs 1−5), and at lower reaction temperature, 40 °C, the enantiomeric excess of (*R*,*R*)-**3a** was raised to 70% (run 6). In all runs, *meso*-**3a** {(1*R**,2*S**)-**3a**} was not obtained, which confirms the completely S_N2-type ring-opening of **1a** during the copolymerization.[14]

The ¹³C NMR of the sample of run 6 (Figure 2 (i)) raises a question regarding the reported assignment of syndiotactic and

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(2) Spassky, N.; Momtaz, A.; Kassamaly, A.; Sepulchre, M. *Chirality* **1992**, *4*, 295 and references cited there in.
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(4) (a) Pino, P. *Adv. Polym. Sci.* **1965**, *4*, 393. (b) Natta, G.; Farina, M.; Donati, M. *Makromol. Chem.* **1961**, *43*, 251. (c) Tsunetsugu, T.; Fueno, T.; Furukawa, J. *Makromol. Chem.* **1968**, *112*, 220.
(5) (a) Okamoto, Y.; Nakano, T.; Kobayashi, H.; Hatada, K. *Polym. Bull.* **1991**, *25*, 5. (b) Onimura, K.; Tsutsumi, H.; Oishi, T. *Chem. Lett.* **1998**, 791.
(6) Nozaki, K.; Hiyama, T. *J. Organomet. Chem.* **1999**, *576*, 248 and references cited therein.
(7) For helix-sense selective polymerization of achiral monomers, see ref 1a. Enantiomer selective polymerization is also known, for example: Spassky, N.; Pluta, C.; Simic, V.; Thiam, M.; Wisniewski, M. *Macromol. Symp.* **1998**, *128*, 39. See also refs 1a and 2.
(8) Since the pioneering work by Inoue and Tsuruta using a mixture of Et_2Zn and H_2O,[9] mixtures of Et_2Zn with alcohols, carboxylic acids, or phenols were applied as an achiral catalyst to the copolymerization of epoxide and CO_2.[10] Recent elegant works by Darensbourg[11] and Coates[12] provided new types of catalysts with well-defined structures, with which much higher catalytic activities and smaller molecular-weight distribution were achieved. Reaction in super-critical CO_2 also improved the catalytic activity.[13]
(9) Inoue, S.; Koinuma, H.; Tsuruta, T. *J. Polym. Sci., Part B* **1969**, *7*, 287.
(10) Review articles, for example: (a) Rokicki, A.; Kuran, W. *J. Macromol. Sci., Rev. Macromol. Chem.* **1981**, *21*, 135. (b) Inoue, S. *Carbon Dioxide as a Source of Carbon*; Aresta, M., Forti, G., Eds.; Reidel Publishing Co.: Dordrecht, 1987; p 331. (c) Darensbourg, D. J.; Holtcamp, M. W. *Coord. Chem. Rev.* **1996**, *153*, 155. (d) Beckman, E. J. *Science* **1999**, *283*, 946.
(11) (a) Darensbourg, D. J.; Holtcamp, M. W. *Macromolecules* **1995**, *28*, 7577. (b) Darensbourg, D. J.; Niezgoda, S. A.; Draper, J. D.; Reibenspies, J. H. *J. Am. Chem. Soc.* **1998**, *120*, 4690. (c) Darensbourg, D. J.; Holtcamp, M. W.; Struck, G. E.; Zimmer, M. S.; Niezgoda, S. A.; Rainey, P.; Robertson, J. B.; Draper, J. D.; Reinbenspies, J. H. *J. Am. Chem. Soc.* **1999**, *121*, 107.
(12) Cheng, M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **1998**, *120*, 11018.
(13) (a) Super, M.; Berluche, E.; Costello, C.; Beckman, E. *Macromolecules* **1997**, *30*, 368. (b) Super, M.; Beckman, E. J. *Macromol. Symp.* **1998**, *127*, 89.
(14) Using achiral Zn catalysts, the ring-opening has been reported to proceed in a completely S_N2 fashion.[15]
(15) Inoue, S.; Koinuma, H.; Yokoo, Y.; Tsuruta, T. *Makromol. Chem.* **1971**, *143*, 97.
(16) The experimental procedure is submitted as Supporting Information.
(17) The structure of the active species is not clear at this moment. Addition of amino alcohol **4** to Et_2Zn (in hexane−toluene-d_8) at 20 °C was followed by ¹H NMR which implies that both of the ethyl groups of Et_2Zn might be protonated. The charts are available in the Supporting Information.
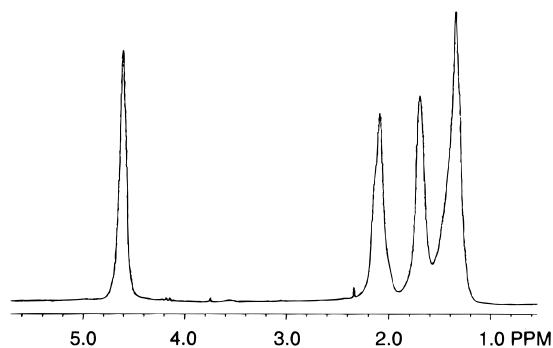(18) Koinuma, H.; Hirai, H. *Makromol. Chem.* **1977**, *178*, 1283.

Figure 1. ^{1}H NMR of the copolymer **2a** obtained in run 1 of Table 1. Methine protons geminal to oxygens give peaks at δ 4.60, assigned to carbonates. The absence of any peak at δ 3.45 (less than 0.01% of the peak at δ 4.60) attributed to an ether bond clearly demonstrates that the polymerization has proceeded in a completely alternating fashion of **1a** and CO_2 with no homopolymerization of **1a**. All products from **1a** in Table 1 show the same peak patterns unless otherwise stated.
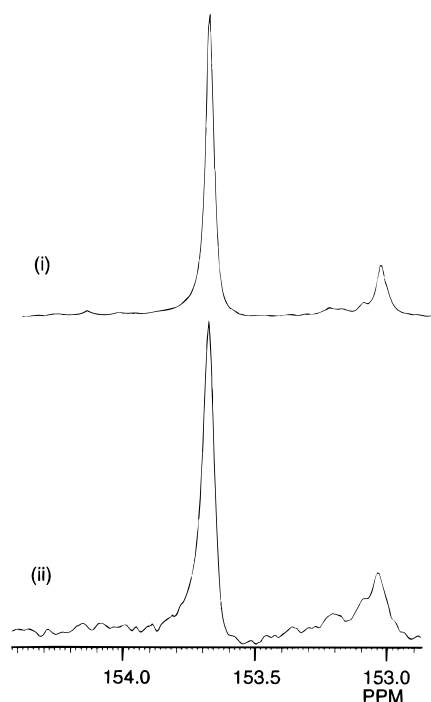

Figure 2. The carbonyl region of ^{13}C NMR of (i) the sample of Table 1, run 6, and (ii) run 1. In (i), the reported assignment for δ 153.7 and 153.1, as syndiotactic and isotactic diad, respectively, gives the syndio-tactic/isotactic = 83/17 ratio, the result contradicting the possible maximum syndioselectivity of 40% calculated from 94% yield and 70% ee of **3a**.

isotactic diads. In a syndiotactic diad, two diol units with the opposite absolute configuration are connected through a carbonate bond. The same two enantiomers afford an isotactic diad. Thus, for a 94% yield of (*R,R*)-**3a** with 70% ee, the possible maximum content of the syndiotactic diad and the possible minimum content of the isotactic diad in copolymer **2a** can be calculated to be 40% and 60%, respectively.[19] However, if we follow the literature characterization,[20,21] the 83:17 ratio of peaks at δ 153.7 and 153.1 in Figure 2(i) would be interpreted as syndiotactic (the former, 83%) and isotactic (the latter, 17%). The contradiction between the two sets of values suggests that *the signal due to the isotactic diad is included in a peak at δ 153.7 but not in that at δ 153.1*. Similarly, the sample of run 1 (51% ee, namely, a mixture of 75.5% of (*R,R*)-**3a** and 24.5% of (*S,S*)-**3a**) shows a similar peak pattern with a peak ratio of 78:22 for δ 153.7 and 153.1, respectively.

Chain transfer reactions are suggested to exist by the experiments with varying reaction times (runs 1−5). It should be noted that the ratio of **4**/Et$_2$Zn is essential to achieve the highest activity and selectivity. As shown in runs 1 and 8−12, a slight change in the ratio caused drastic loss of the catalytic activity and/or selectivity. Hence, although the structure of the real active species is unknown at this moment,[17] it seems that the species consists of **4** and Et$_2$Zn in a 1:1 ratio.

The use of cyclopentene oxide (**1b**) and *cis*-2-butene oxide (**1c**) as substrates gave the corresponding completely alternating copolymer **2b** and **2c**, respectively; however, the percent ee's of **3b** and **3c** were both lower than that of **3a** (runs 13 and 14).

In conclusion, the asymmetric synthesis polymerization of cyclohexene oxide (**1a**) and CO_2 gave completely alternating copolymer **2a** in which the percent ee of the chiral diol unit **3a** was controlled to be 70%, or at least 60% (*R,R*).[19] Thus, highly isotactic copolymer **2a** has been prepared in an optically active form, for the first time. This work provides a new aspect of asymmetric synthesis polymerization with the unambiguous determination of enantiomeric excess of the chiral units. Meanwhile, the overall transformation from **1a** to **3a** may be considered as a new route for asymmetric hydrolysis of **1a**.[22] Further studies are focused on the determination of the precise structure of the active species.

Supporting Information Available: Experimental details, ^{1}H NMR charts of **4**/Et$_2$Zn, and ^{13}C NMR charts of polymers obtained in runs 1 and 6 of Table 1 (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

(19) The sample of run 6, (*R,R*)-**3a** with 70% ee, is an 85:15 mixture of (*R,R*)-**3a** and (*S,S*)-**3a**. On the basis of 94% yield of **3a** from **2a**, one might assume that the unrecovered diol units (corresponds to 6%) are all the minor enantiomer, (*S,S*)-**3a**. In this case, the enantiomeric excess of the diol unit in **2a** would be at least $\{85 \times 0.94 - (15 \times 0.94 + 6)\}/\{85 \times 0.94 + (15 \times 0.94 + 6)\} \times 100 = 60\%$ ee, corresponding to (*R,R*):(*S,S*) = 80:20. Thus, if all the (*S,S*)-diol unit is involved in syndiotactic diads, (i) the possible maximum content of the syndiotactic diad would be 40%, and (ii) the possible minimum content of the isotactic diad would be 60%. The values contradict the 83:17 of the syndio:iso ratio derived from the literature assignment.
(20) Kuran, W.; Listos, T. *Macromol. Chem. Phys.* **1994**, *195*, 977.
(21) Hasebe, Y.; Tsuruta, T. *Makromol. Chem.* **1987**, *188*, 1403.
(22) Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. *Science* **1997**, *277*, 936.