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Tetrahedron: *Asymmetry* 18 (2007) 2016–2020

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Chiral linear polymers bonded alternatively with salen and 1,4-dialkoxy-2,6-diethynylbenzene: synthesis and application to diethylzinc addition to aldehydes

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Received 6 August 2007; accepted 5 September 2007

Abstract—The synthesis of chiral polymers **1** bonded alternatively with salen and 1,4-dialkoxy-2,6-diethynylbenzene was accomplished. These polymers are recyclable and catalyze the Et_2Zn addition to aldehydes with good enantioselectivity.

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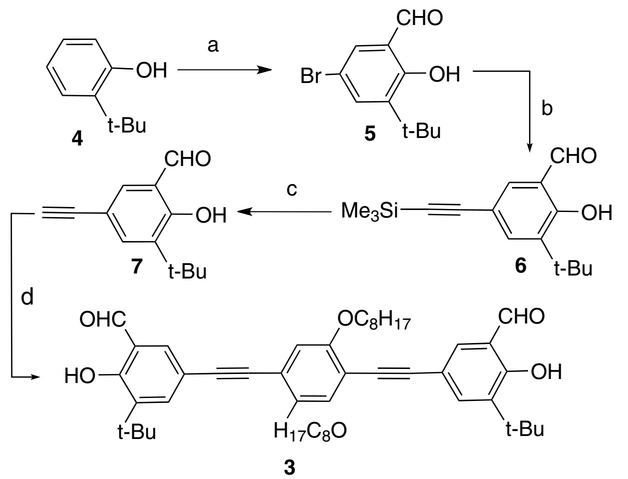
1. Introduction

The application of optically active 1,2-diamine derivatives in asymmetric synthesis has attracted extensive attention.[1] These molecules have demonstrated excellent chiral induction in a number of organic transformations when used either as a chiral auxiliary[2] or a chiral ligand.[3] Subsequently, the synthesis of chiral 1,2-diamine based polymers is developed for asymmetric catalysis to provide simplified product isolation, easy recovery of the catalysts, and potential use in continuous production.[4] From an environmental and economic standpoint, these studies are attractive since the cost and environmental impact (E-factor) of the process can be lowered.[5] Herein, we report the synthesis of new chiral 1,2-diamine based polymers **1** from (1*R*,2*R*)-diamines **2** and dialdehyde **3** by Schiff base formation. These polymers **1** catalyze Et_2Zn addition to aldehydes with up to 70% ee, in a homogeneous process with no additives involved. Polymers **1** can be recovered from the reaction mixture by precipitation using MeOH and recycled without any loss in activity.

2. Results and discussion

The reaction of 2-*tert*-butylphenol **4** with paraformaldehyde in the presence of $SnCl_4$ followed by bromination with Br_2 in $CHCl_3$ afforded 5-bromo-3-*tert*-butylsalicylaldehyde **5** as a yellow solid.[6] Aldehyde **5** was transformed into silyl derivative **6** by coupling with trimethylsilylacetylene using $Pd(PPh_3)_2Cl_2$ and CuI in the presence of Et_3N in THF. Desilylation of **6** with K_2CO_3 in MeOH gave ethynyl derivative **7**, which was coupled with 1,4-dibromo-2,5-dioctyloxybenzene **9** using $Pd(PPh_3)_2Cl_2$ and CuI to afford dialdehyde **3** as a yellow solid (Schemes 1 and 2).



Scheme 1. Reagents and conditions: (a) (i) $(CH_2O)_n$ (2.2 equiv), $SnCl_4$ (0.1 equiv), toluene, 100 °C, 10 h, 85%; (ii) Br_2, AcOH, rt, 1 h, 95%; (b) Me_3SiC_2H (1.1 equiv), $Pd(PPh_3)_2Cl_2$ (3 mol %), CuI (4 mol %), Et_3N (2 equiv), THF, rt, 12 h, 99%; (c) K_2CO_3 (1.5 equiv), MeOH, rt, 6 h, 60%; (d) 1,4-dibromo-2,5-dioctyloxybenene **9** (0.5 equiv), $Pd(PPh_3)_2Cl_2$ (3 mol %), CuI (4 mol %), $(^iPr)_2NH$, THF, reflux, 12 h, 20%.

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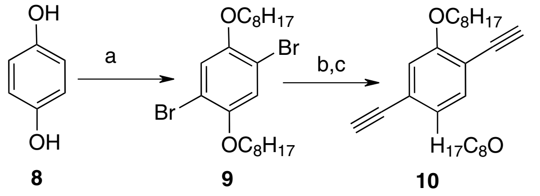
doi:10.1016/j.tetasy.2007.09.004



Scheme 2. Reagents and conditions: (a) (i) $C_8H_{17}Br$ (2.2 equiv), KOH, EtOH, rt, 24 h, 80%; (ii) Br_2, $CHCl_3$, 0 °C, 8 h, 95%; (b) Me_3SiC_2H (2.1 equiv), $Pd(PPh_3)_2Cl_2$ (5 mol %), CuI (5 mol %), $(^iPr)_2NH$, THF, rt, 12 h, 99%; (c) 20% aq KOH, MeOH, THF, rt, 2 h, 90%.

The synthesis of polymers **1** was then accomplished by Schiff base formation between dialdehyde **3**, and amines **2a** and **2b** (Schemes 3 and 4). The products were obtained as yellow colored powder. The specific rotations of **1a**[7] and **1b**[8] are $[\alpha]_D^{25} = +376$ (*c* 0.1, $CHCl_3$) and $[\alpha]_D^{25} = +166$ (*c* 0.1, $CHCl_3$), respectively. GPC analysis employing polystyrene as internal standard and THF as the eluent showed the molecular weights corresponding to ca. 21 repeating units for **1a** ($M_w = 18{,}512$, $M_n = 15{,}242$ and PDI = 1.2) and ca. five repeating units for **1b** ($M_w = 4864$, $M_n = 3441$ and PDI = 1.4). The ^1H NMR spectra recorded at 400 MHz are consistent with their structures. The electronic spectra of both the polymers exhibited very similar absorption.[7] In the UV spectrum of **1a**, λ_{max} were observed at 248, 266, 274, 284, 302, and 333 (br) nm (Fig. 1). Likewise, polymer **1b** showed absorption maximum at 249, 268, 279, 300, and 333 (br) nm. These polymers display very similar cotton effects in circular dichroism spectra (Fig. 2).[9] The CD spectrum of **1a** exhibited weak positive cotton effect with splitting[9b] at 271, 291, 331, 355, 387 nm, and a negative cotton effect at 238 nm showing a positive chirality. Polymer **1b** showed weak positive cotton effect with splitting[9b] at 272, 304, 332, 352 nm and a negative cotton effect at 241 nm showing a positive chirality. We also attempted the synthesis of **1a** by coupling chiral salen

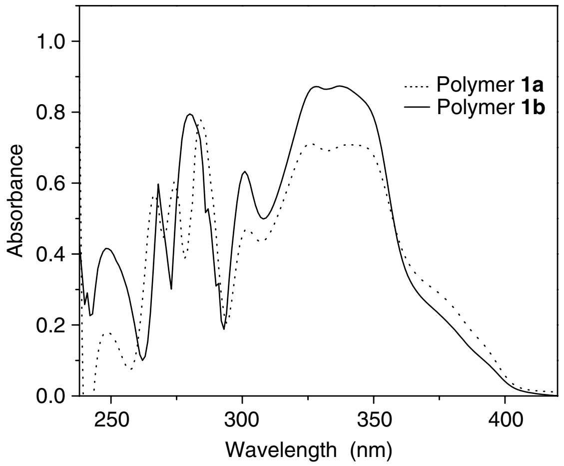


Figure 1. UV–vis spectra of polymers **1** in $CHCl_3$.

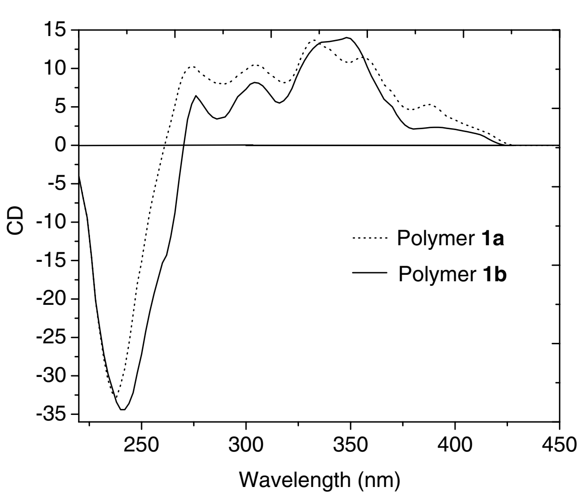
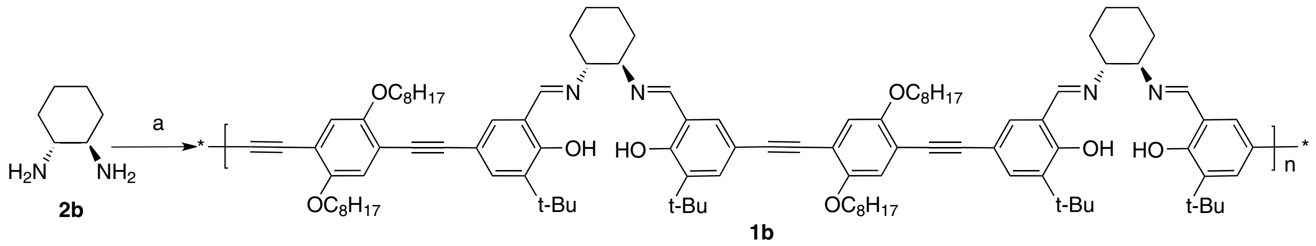
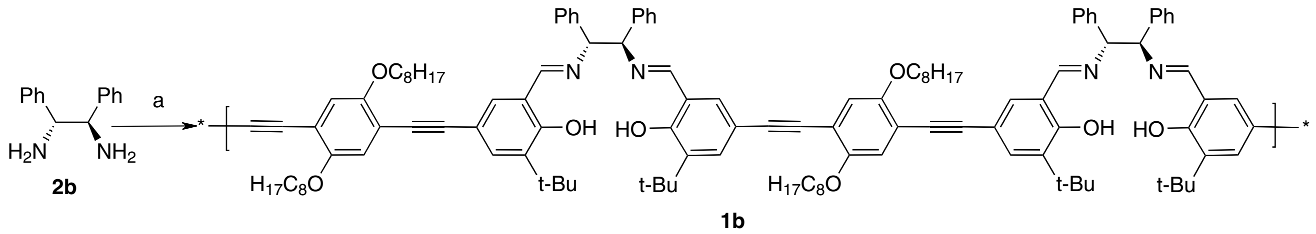


Figure 2. CD spectra of polymers **1** in $CHCl_3$ ($C = 1.99 \times 10^{-5}$ M for **1a** and $C = 8.45 \times 10^{-5}$ M for **1b**) at ambient temperature.

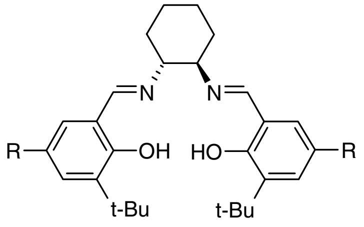


Scheme 3. Reagents and conditions: (a) dialdehyde **3** (1 equiv), $CHCl_3$, 40 °C, 3 h, 76%.



Scheme 4. Reagents and conditions: (a) dialdehyde **3** (1 equiv), $CHCl_3$, 40 °C, 3 h, 70%.

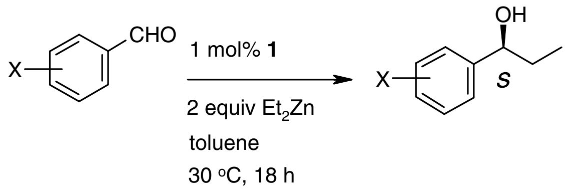
11 with 1,4-dialkoxy-2,6-diethynylbenzene **10** using $Pd(PPh_3)_2Cl_2$ and $Pd(PPh_3)_4$ in combination with CuI in the presence of Et_3N and $^iPr_2NH$ in THF at 25–70 °C.[10] However, this approach was not successful and no cross-coupled polymerized product was observed.



11 R = Br
12 R = t-Bu

Polymers **1** were then studied for Et_2Zn addition to 3-nitrobenzaldehyde (Table 1).[11] We were pleased to find that the reaction occurred to afford the corresponding alcohol with 50% ee, when the reaction was stirred in the presence of 1 mol % of **1a** (with respect to monomeric unit) and 2 equiv of Et_2Zn in toluene at ambient temperature.[12] The enantioselectivity was further increased to 70% ee when the polymer **1b** was employed in the place of polymer **1a**. These reactions did not involve any additive. Benzaldehyde and 4-methoxybenzaldehyde were next reacted with Et_2Zn to provide the corresponding alcohols with 50% and 60% ee, respectively. A similar result has been reported with the monomeric salen complex **12** for Et_2Zn addition to aldehydes.[12d] The advantage of the present system is that polymer **1b** can be recovered from the reaction mixture by adding MeOH and then recycled. The recovered **1b** was used for the fresh reaction of 3-nitrobenzaldehyde with Et_2Zn. As above, the reaction occurred to give the respective alcohol with 70% ee. This study clearly suggests that the polymer is recyclable without any loss in activity or selectivity.

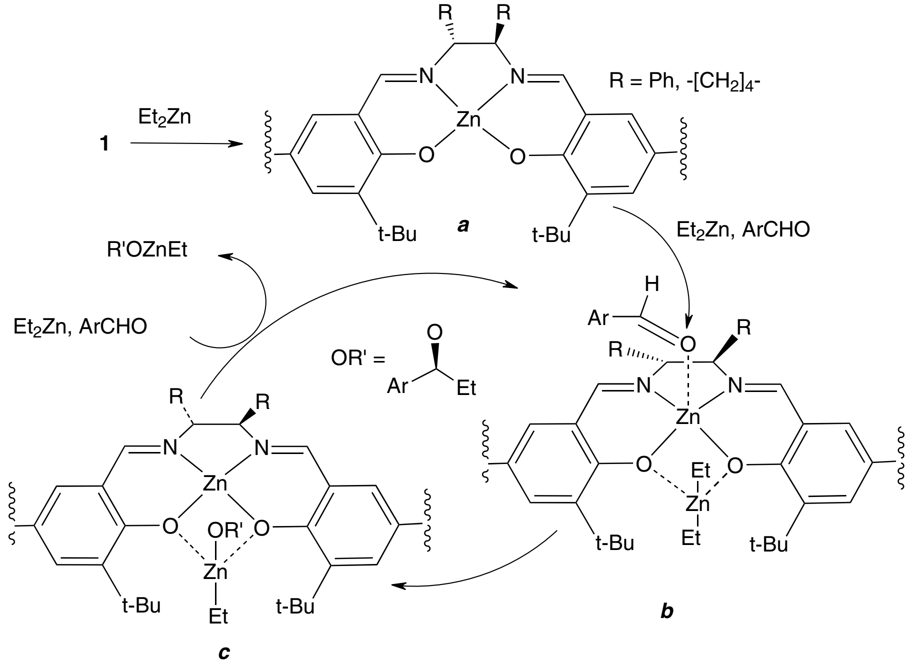
Table 1. Polymer **1** catalyzed Et_2Zn addition to aldehydes



Entry	X	Polymer	Yield[a,b] (%)	ee (%)
1	3-NO_2	**1a**	72	50
2	3-NO_2	**1b**	74	70
3	3-NO_2	**1b**	73	70[c,d]
4	H	**1b**	83	50[e]
5	4-OMe	**1b**	70	60[e]

[a] Aldehyde (1 mmol), Et_2Zn (2 mmol) and polymer **1** (1 mol % with respect to monomeric unit) were stirred at 30 °C in toluene under N_2 atmosphere.
[b] Isolated yield.
[c] Recovered **1b** used.
[d] Determined by HPLC with chiralcel OD-H column using 98:2 hexane–isopropanol.
[e] Determined by HPLC with chiralcel OD-H column using 97:3 hexane–isopropanol.

The proposed catalytic cycle is shown in Scheme 5.[12] The reaction of **1** with Et_2Zn may provide complex **a**, which may transform to intermediate **b** by reaction with Et_2Zn and aldehyde. The transfer of the ethyl group from the coordinated Et_2Zn to the coordinated aldehyde in **b** may give intermediate **c** which on reaction with new Et_2Zn and aldehyde may complete the catalytic cycle.



Scheme 5. Proposed catalytic cycle.

3. Conclusion

In conclusion, the synthesis of chiral polymers **1** was accomplished. These polymers are soluble in common organic solvents; are recyclable and catalyze the Et_2Zn addition to aldehydes with good enantioselectivity. Further study of this reaction is currently underway in our laboratory.

Acknowledgments

We thank Professor Tsutomu Katsuki for CD analysis. This was supported by the Department of Science and Technology, New Delhi, and the Council of Scientific and Industrial Research, New Delhi. We thank Dr. John M. Brown for discussions.

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7. *Polymer* **1a**: To a stirred solution of aldehyde **3** (0.272 mmol, 200 mg) in $CHCl_3$ (3 ml), (1*R*,2*R*)-diaminocyclohexane **2a** (0.272 mmol, 31.8 mg) was added. The resulting solution was stirred at 40 °C for 3 h and cooled to ambient temperature. Methanol was added and the precipitate **1a** collected as a yellow powder with 76% (176.1 mg) yield. GPC: $M_w = 18{,}512$, $M_n = 15{,}242$ (PDI 1.2); ^1H NMR (400 MHz, $CDCl_3$) δ 14.00–14.30 (m, 2H), 8.23 (br s, 2H), 7.39 (s, 2H), 7.18 (s, 2H), 6.94 (s, 2H), 3.95 (t, $J = 6.4$ Hz, 4H), 3.33 (br s, 2H), 1.20–1.99 (m, 50H), 0.83–1.0 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.89, 160.98, 154.03, 149.53, 137.82, 134.17, 133.11, 132.85, 118.31, 118.31, 117.64, 117.08, 113.37, 112.90, 112.74, 94.42, 83.47, 72.47, 70.19, 69.91, 35.17, 33.30, 32.16, 29.99, 29.62, 29.55, 26.41, 26.35, 24.54, 23.00, 14.45; FT-IR (KBr) 3450, 2928, 2857, 1630, 1495, 1467, 1441 cm^{-1}; UV–vis ($CHCl_3$): λ_{max} 248, 266, 274, 284, 302, 333 nm; $[\alpha]_D^{25} = +376$ (*c* 0.1, THF). Anal. Calcd: C, 79.76; H, 8.92; N, 3.44. Found: C, 79.20; H, 9.10; N, 3.40.
8. *Polymer* **1b**: To a stirred solution of aldehyde **3** (0.204 mmol, 150 mg) in $CHCl_3$ (3 ml), (1*R*,2*R*)-diphenylethylenediamine **2b** (0.204 mmol, 43.2 mg) was added. The resulting solution was stirred at 40 °C for 3 h and cooled to ambient temperature. Methanol was added and the precipitate **1b** was obtained as a yellow powder in 70% (135.2 mg) yield. GPC: $M_w = 4864$, $M_n = 3441$ (PDI 1.4); ^1H NMR (400 MHz, $CDCl_3$) δ 14.00–14.30 (m, 2H), 8.27 (m, 2H), 7.45 (m, 2H), 7.25–7.09 (m, 10H), 6.99 (s, 2H), 4.7 (br s, 2H), 3.99 (t, $J = 6.4$ Hz, 4H), 1.9–1.2 (m, 42H),1.0–0.8 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.26, 166.13, 160.80, 154.00, 149.49, 139.09, 139.00, 137.91, 134.41, 133.92, 133.33, 133.20, 128.55, 127.99, 127.89, 118.49, 118.22, 117.59, 113.26, 112.90, 112.77, 94.34, 83.54, 80.22, 70.32, 70.12, 35.23, 32.13, 29.61, 29.54, 26.32, 22.99, 14.46; FT-IR (KBr): 3446, 2928, 2857, 1629, 1456, 1415, 1382, 1262, 1212, 1097, 1028 cm^{-1}; UV–vis ($CHCl_3$) λ_{max} 249, 268, 279, 300, 333 nm; $[\alpha]_D^{25} = +166$ (*c* 0.1, $CHCl_3$). Anal. Calcd: C, 82.09; H, 7.22; N, 3.08. Found: C, 81.88; H, 7.29; N, 3.10.
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11. *General procedure for Et_2Zn addition to aldehydes*: To a solution of polymer **1a** or **1b** (1 mol %) in dry toluene was added Et_2Zn (1 mol %) and the resulting mixture was stirred for 1 h at ambient temperature. This solution was cooled to −40 °C and Et_2Zn (2 mmol) was added. After 5 min, the aldehyde (1 mmol) was added and the stirring was continued for 1 h at −40 °C. The resulting solution was warmed to room temperature and then allowed to stir for an additional 18 h. After the aldehyde was consumed, the reaction mixture was quenched with saturated $NaHCO_3$ solution and extracted with Et_2O. The combined organic layer was concentrated to 1 ml and treated with MeOH to precipitate polymer **1a** or **1b**. The filtrate was evaporated on a rotary evaporator and the residue passed through a short pad of silica gel (60–120 mesh) using ethyl acetate and hexane (1:19) to afford analytically pure alcohols.
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