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Polymer-supported Chiral Lewis Acids as Asymmetric Catalysts for Diels-Alder Reactions of Methacrolein with Cyclopentadiene

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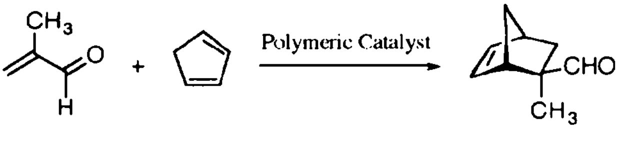
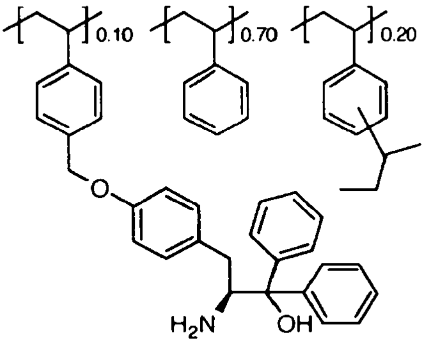
Abstract: *Insoluble polymer-supported chiral Lewis acids were prepared from monobromoborane or borane with crosslinked polymers having a chiral moiety such as an amino alcohol, diol, or N-sulfonylamino acid. These polymers were used as chiral catalysts for Diels-Alder reactions of methacrolein with cyclopentadiene to give optically active cycloadduct.*

The asymmetric Diels-Alder reaction using chiral Lewis acid catalysts has been the subject of intensive research in recent years.[1] Various chiral Lewis acids have been prepared from Lewis acids including aluminum, titanium or boron atoms modified by chiral ligands such as amino alcohol,[2] diol,[3] binaphthols,[4] N-sulfonylamino acid,[5] bis-sulfonamide[6] and α-hydroxy acid.[7] On the other hand, polymers containing pendant chirality are finding a number of interesting applications in organic chemistry. The use of polymers as chiral auxiliaries in asymmetric induction reactions offers interesting properties as the chiral polymers may have some unique advantages over their low-molecular-weight counterparts. For example, the polymers, being insoluble, offer a well documented purification advantage; the polymers can be recycled repeatedly, and the polymers may provide a unique microenvironment for the reactions, which in favorable cases may result in enhanced stereoselectivities. In a continuing effort to prepare effective polymeric catalysts for asymmetric transformations,[8] new polymeric chiral Lewis acids have been employed to explore the possibility of using them in the model Diels-Alder reaction of methacrolein with cyclopentadiene. We now wish to report the preliminary results of the asymmetric reaction obtained by the use of these chiral polymeric catalysts derived from the suitable combinations of boron based Lewis acids and the chiral polymers containing several types of chiral moieties such as amino alcohol, diol and N-sulfonylamino acid.



The chiral polymers used in this study were easily prepared using suspension polymerization techniques in water. The chiral polymers **1**[9] and **4**[10] were prepared by copolymerization of the corresponding chiral monomer with styrene and divinylbenzene (DVB) as crosslinking agent. The chiral polymers **2** and **3** were obtained by copolymerization of styrene with the chiral monomers having two polymerizable vinylbenzyl groups which also act as crosslinking agent.[11] Insoluble swellable polymers were obtained in high yield without DVB in these cases. Treatment of these polymers having chiral bifunctional moieties with borane gave the polymeric Lewis acids, presumed to be metallacycles, which were used for the Diels-Alder reaction of cyclopentadiene with methacrolein.



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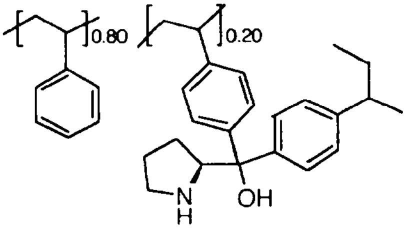

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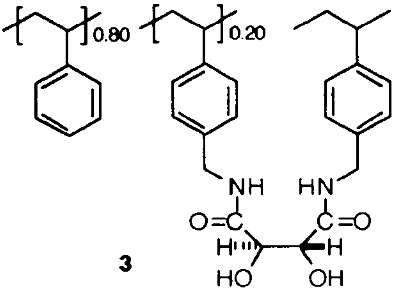

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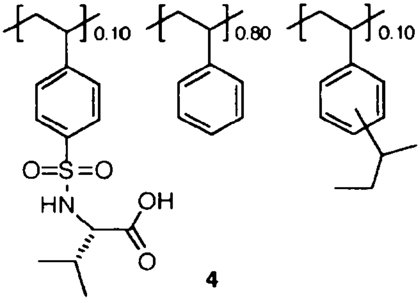

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In a previous paper, we described that the polymeric chiral oxazaborolidines derived from amino alcohol polymers **1** and **2** with borane were very effective catalysts for the asymmetric reduction of ketones, oximes and imines.[9,11,12] These polymers unfortunately did not catalyze the Diels-Alder reaction and no desired cycloadduct was obtained. On the other hand, the reaction proceeded smoothly in the presence of polymeric catalyst generated in situ from monobromoborane and **1** or **2**. The corresponding cycloadduct was obtained at -78°C in this case in high chemical yield and high exo/endo ratio (Table I, entry 1, 2). However, although **1** and **2** are quite effective chiral auxiliaries in some asymmetric reactions including reductions[13] and alkylations,[12a] the polymeric catalysts derived from monobromoborane offered low level of asymmetric induction in the Diels-Alder reaction. Chiral diols derived from tartaric acid have been also reported as efficient ligand of the catalyst for Diels-Alder reactions,[14] whereas the chiral Lewis acid generated from monobromoborane and the polymeric analog **3** gave only low enantioselectivity (entry 3). Several examples of this asymmetric Diels-Alder reaction using insoluble polymeric chiral catalyst are shown in Table 1.

Helmchen's investigation[5a,b] of chiral Lewis acids prepared by reacting sulfonamides of (*S*)-valine with borane for Diels-Alder reactions prompted us to prepare the polymeric version of the catalyst. By using polymeric Lewis acid catalyst prepared from **4** and monobromoborane the Diels-Alder adduct was obtained in 99% yield with almost perfect exo selectivity and the optical yield of the exo form was improved to 44% ee.

Polymeric catalyst generated from **4** and borane also catalyzed the reaction efficiently to afford the adduct in 57%ee, which is higher enantioselectivity than that obtained using Helmchen's soluble catalyst in dichloromethane. The effect of solvent used on enantioselectivity was reported to be important in this reaction.[5a] Addition of donor solvent such as THF resulted in higher enantioselectivity. All of the Diels-Alder reactions gave predominantly the adduct having *R* configuration determined by the sign of optical rotation.[15] The use of insoluble polymeric catalysts facilitates greatly the separation of the chiral adduct which is obtained in solution from the solid catalyst. The chiral polymer was recovered quantitatively by simple filtration and could be reused at least for several times without any loss of enantioselectivity.

Table I Asymmetric Diels-Alder Reaction of Cyclopentadiene with Methacrolein Using Polymeric Catalyst[a]

Entry	Polymer	Borane	Solvent	Yield[b] %	endo/exo[c]	% ee[d]	$[\alpha]_D$ (c 5.0, EtOH)
1	**1**	BH_2Br	CH_2Cl_2	96	8 : 92	16	- 3.73
2	**2**	BH_2Br	CH_2Cl_2	98	4 : 96	25	- 5.83
3	**3**	BH_2Br	CH_2Cl_2	88	11 : 89	17	- 3.96
4	**4**	BH_2Br	CH_2Cl_2	99	<1 : 99	44	- 10.31
5	**4**	BH_3	CH_2Cl_2	95	<1 : 99	57	- 13.29
6	**4**	BH_3	CH_2Cl_2/THF	89	<1 : 99	65	- 15.08
7[e]	**4**	BH_3	CH_2Cl_2/THF	93	<1 : 99	65	- 15.14

[a] All reactions were carried out in the presence of 15 mol% polymeric boron catalyst. [b] Isolated yields. [c] Determined by ^1H NMR. [d] The optical purity of the exo isomer was calculated by the observed optical rotation on the basis of the rotation reported by Koga.[15] Determined to be *R* configuration based on the optical rotation. [e] Recycled polymer was used.

The following experiment is typical: To a stirred suspension of 0.94g (0.75 mmol) of polymer-supported N-sulfonylated valine **4** (0.8 mmol/g) in 10 ml of THF under nitrogen atmosphere was added 0.75 mmol of BH_3•DMS (1 M solution in dichloromethane) at 0 °C. After stirring for 2 hours at room temperature methacrolein (5 mmol) and cyclopentadiene (7.5 mmol) were successively introduced at -78°C. The mixture was stirred at -78°C for 2 hours, and then quenched with sodium hydrogen carbonate. After removal of the polymer by filtration usual workup gave the desired Diels-Alder adduct.

Further investigations on scope and limitation of this catalytic asymmetric Diels-Alder reaction as well as application of the polymeric catalysts to continuous flow system are now in progress.

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REFERENCES AND NOTES

1. Narasaka, K. *Synthesis* **1991**, 1. Lohray, B. B., Bhushan, V. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 729, and references cited therein.
2. Kobayashi, S., Murakami, M., Harada, T., Mukaiyama, T. *Chem. Lett.* **1991**, 1341.
3. Devine, P. N., Oh, T. *J. Org. Chem.* **1992**, *57*, 396. Narasaka, K., Iwasawa, N., Inoue, M., Yamada, T., Nakashima, M., Sugimori, J. *J. Am. Chem. Soc.* **1989**, *111*, 5340. Chapuis, C., Jurczak, J. *Helv. Chim. Acta* **1987**, *70*, 436.
4. Maruoka, K., Murase, N., Yamamoto, H. *J. Org. Chem.* **1993**, *58*, 2938. Maruoka, K., Itoh, T., Shirasaka, T., Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 310. Bao, J., Wulff, W. D. *J. Am. Chem. Soc.* **1993**, *115*, 3814.
5. a) Sartor, D., Saffrich, J., Helmchen, G., Richards, C. J., Lambert, H. *Tetrahedron:Asymmetry*, **1991**, *2*, 639. b) Sartor, D., Saffrich, J., Helmchen, G. *Synlett*, **1990**, 197. c) Takasu, M., Yamamoto, H. *Synlett* **1990**, 194. d) Corey, E. J., Loh, T. -P., Roper, T. D., Azimioara, M. D., Noe, M. C. *J. Am. Chem. Soc.* **1992**, *114*, 8290. e) Corey, E. J., Loh, T. -P. *J. Am. Chem. Soc.* **1991**, *113*, 8966.
6. Corey, E. J., Imwinkelried, R., Pikul, S., Xiang, Y. B. *J. Am. Chem. Soc.* **1989**, *111*, 5493.
7. Furuta, K., Shimizu, S., Miwa, Y., Yamamoto, H. *J. Org. Chem.* **1989**, *54*, 1481. Furuta, K., Miwa, Y., Iwanaga, K., Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 6254.
8. Itsuno, S. in *Macromolecules 1992* Kahovec, J. Ed. VSP: Utrecht, **1993**, p.413-422.
9. Itsuno, S.; Sakurai, Y.; Ito, K.; Hirao, A.; Nakahama, S. *Polymer* **1987**, *28*, 1005.
10. Polymer **4** was obtained as follows; To a well stirred solution of poly(vinyl alcohol) (degree of polymerization : 2000, degree of saponification: 78-82% hydrolyzed) in 230 ml of water was added a solution of 10 mmol of the chiral monomer, p-styrenesulfonamide of (*S*)-valine, prepared from p-styrenesulfonyl chloride and (*S*)-valine, 10 mmol of DVB, 80 mmol of styrene and benzoyl peroxide (1 mmol) as radical initiator in benzene/THF at 0°C. Obtained suspension was stirred at 0°C for 30 min and the temperature was raised to 80°C and the reaction mixture was stirred vigorously for 24 hours. The resulting polymer beads were filtered and washed with water, water-methanol, THF, methanol followed by drying under reduced pressure at 40°C afforded **4**. The N-sulfonylamino acid content is determined by elemental analysis.
11. Itsuno, S., Ito, K. in *Trends in Organic Chemistry*, Councile of Scientific Research Integration, Research Trends: **1991**, p.199-211.
12. a) Itsuno, S., Sakurai, Y., Ito, K., Maruyama, T., Nakahama, S., Fréchet, J. M. J. *J. Org. Chem.*, **1990**, *55*, 304. b) Itsuno, S. *J. Synth. Org. Chem., Jpn.* **1987**, *45*, 101.
13. Itsuno, S., Sakurai, Y., Ito, K. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1859.
14. Maruoka, K., Sakurai, M., Fujiwara, J., Yamamoto, H. *Tetrahedron Lett.* **1986**, *27*, 4895.
15. Hashimoto, S., Komeshima, N., Koga, K. *J. Chem. Soc., Chem. Commun.* **1979**, 437.

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