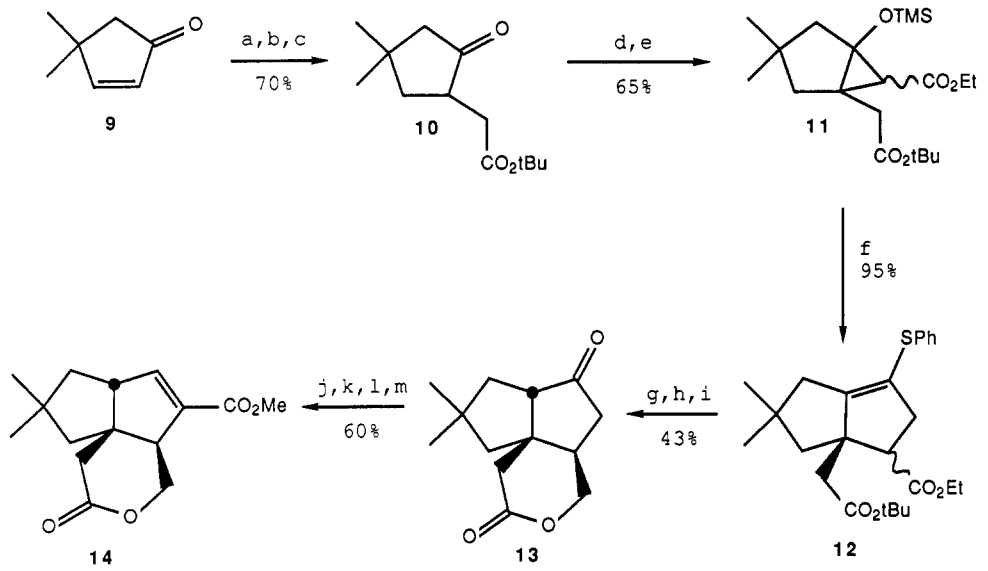
Scheme II[a]



[a] (a) Et_3SiH, $RhCl(PPh_3)_3$, PhH;[6] (b) (2.5 equiv) N_2CHCO_2-*t*-Bu, $CuSO_4$, PhH;[6] (c) Et_3NHF, THF, 25 °C; (d) Me_3SiCl, Et_3N, DMF, 135 °C; (e) 4 equiv of N_2CHCO_2Et, $CuSO_4$, PhH; (f) (2 equiv) **3**, (5 equiv) KF, (0.1 equiv) 18-crown-6, CH_3CN, 82 °C;[2] (g) $NaOH/H_2O$, MeOH, THF, 60 °C; (h) $ClCO_2Et$, Et_3N, THF; $NaBH_4$, THF/H_2O, room temperature; (i) TFA, $CHCl_3$; (j) C_4H_9N, *p*-TSA, PhH, 80 °C; (k) (10 equiv) $ClCO_2Me$, PhH, 80 °C; (l) (3 equiv) $NaCNBH_3$, MeOH, HCl, room temperature; (m) (1.1 equiv) MCPBA, CH_2Cl_2; K_2CO_3, THF, room temperature.

borohydride via its mixed anhydride.[10] Treatment of the resulting alcohol with trifluoroacetic acid in chloroform converts the vinyl sulfide to the ketone, hydrolyzes the *tert*-butyl ester, and catalyzes the lactonization to the crystalline ketolactone[11] **13**. The overall conversion of cis **12** to **13** can be effected in 75% yield.

While ketolactone **13** is a new precursor to pentalenolactone E methyl ester, a similar cyclopentanone was converted previously[4a] to the unsaturated methyl ester by a reduction-dehydration sequence in only 40% yield. We found that the most convenient route to the unsaturated ester[12] **14** involved the following sequence: (1) conversion to pyrrolidine enamine; (2) carbomethoxylation;[13] (3) conjugate reduction with sodium cyanoborohydride;[14] and (4) elimination of the pyrrolidine via its N-oxide in base.[15] The overall sequence was accomplished in 60% isolated yield. Compound **14** had been previously prepared by Paquette[4d] and converted to pentalenolactone E methyl ester[16] by methoxymagnesium carbonate followed by formalin in dimethylamine.

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Registry No. **3**, 69442-54-2; **9**, 22748-16-9; **10**, 109719-46-2; **11**, 109719-47-3; *cis*-**12**, 109719-48-4; *trans*-**12**, 109719-49-5; *cis*-**12** (acid), 109719-50-8; *trans*-**12** (acid), 109719-51-9; **13**, 109719-52-0; **14**, 83648-43-5.

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(10) Perron, Y. G.; Crast, L. B.; Essery, J. M.; Fraser, R. R.; Godfrey, J. C.; Holdrege, C. T.; Minor, W. F.; Neubert, M. E.; Partyka, R. A.; Cheney, L. C. *J. Med. Chem.* **1964**, *7*, 483.

(11) 300-MHz ^1H NMR of **13** ($CDCl_3$): δ 0.90 (s, 3 H), 1.07 (s, 3 H), 1.75 (AB, 2 H, J_{AB} = 13.1 Hz), 1.80–1.86 (m, 1 H), 1.90 (ddd, 1 H, J = 13.1, 4.2, 1.1 Hz), 2.44 (ddd, 1 H, J = 18.0, 7.9, 1.9 Hz), 2.50–2.62 (m, 2 H), 2.63 (AB, 2 H, J_{AB} = 15.0 Hz), 2.75 (dd, 1 H, J = 18.0, 9.0 Hz), 4.11 (dd, 1 H, J = 11.9, 5.3 Hz), 4.44 (dd, 1 H, J = 11.9, 4.2 Hz); mp 108–109 °C.

(12) 300-MHz ^1H NMR of **14** ($CDCl_3$): δ 1.02 (s, 3 H), 1.06 (s, 3 H), 1.37 (dd, 1 H, J = 13.0, 5.9 Hz), 1.74 (AB, 2 H, J_{AB} = 13.5 Hz), 1.87 (dd, 1 H, J = 13.0, 9.4 Hz), 2.60 (AB, 2 H, J_{AB} = 14.4 Hz), 3.07–3.14 (m, 1 H), 3.17–3.20 (m, 1 H), 3.74 (s, 3 H), 4.44 (dd, 1 H, J = 11.8, 4.3 Hz), 4.50 (dd, 1 H, J = 11.8, 4.2 Hz), 6.83–6.84 (m, 1 H).

(13) Stork, G.; Brizzolara, A.; Landesman, H.; Szmuszkovicz, J.; Terrell, R. *J. Am. Chem. Soc.* **1963**, *85*, 207.

(14) Hutchins, R. O.; Rotstein, D.; Natale, N.; Fanelli, J. *J. Org. Chem.* **1976**, *41*, 3328.

(15) Cram, D. J.; Sahyun, M. R. V.; Knox, G. R. *J. Am. Chem. Soc.* **1962**, *84*, 1734.

(16) We have converted compound **14** to pentalenolactone E methyl ester employing methoxymagnesium carbonate and Eshenmosher's salt in yields between 40% and 50%. Our synthetic pentalenolactone methyl ester possessed ^1H NMR and ^{13}C NMR spectral data identical with literature[3] values.

Enantioselective Addition of Diethylzinc to Aldehydes Catalyzed by Polymer-Supported Chiral Amino Alcohols. Evidence for a Two Zinc Species Mechanism

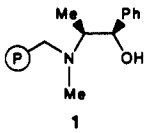
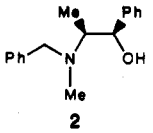
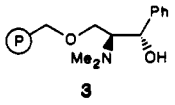
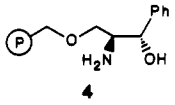
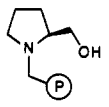
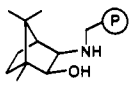
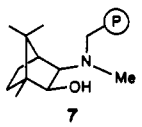
Summary: Polymer-bound chiral amino alcohols (in particular, (dialkylamino)isoborneol) are excellent heterogeneous recyclable catalysts in the enantioselective alkylation of aromatic aldehydes with dialkylzinc.

Sir: The catalytic asymmetric alkylation of carbonyl compounds is a potentially important method for the preparation of enantiomerically pure alcohols. Oguni and Omi have recently reported[1] that the addition of diethylzinc to benzaldehyde was catalyzed by amines or alcohols such as (*S*)-leucinol to afford (*R*)-1-phenylpropanol in 48% ee. In our continuing studies[2-5] of

(1) Oguni, N.; Omi, T. *Tetrahedron Lett.* **1984**, *25*, 2823.

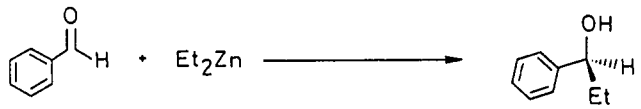
0022-3263/87/1952-4140$01.50/0

Table I. Catalytic Asymmetric Addition of Diethylzinc to Aldehyde in Toluene at 0 °C

aldehyde	catalyst	time/h	% yield	% ee	config
benzaldehyde	 1	48[a]	95	74	*R*
benzaldehyde		62	96	80	*R*
benzaldehyde		62[b]	93	81	*R*
benzaldehyde	 2	15	91	86	*R*
benzaldehyde	 3	72	85	9.5	*S*
benzaldehyde	 4	170	76	9.2	*R*
benzaldehyde	 5	65	93	24	*R*
benzaldehyde	 6	75	90	10	*R*
benzaldehyde	 7	73	91	92	*S*
o-methoxybenzaldehyde	7	24	88	93	
o-ethoxybenzaldehyde	7	24	92	95	

[a] Room temperature. [b] Recycled polymer.

Scheme I



polymers as chiral auxiliaries in asymmetric syntheses, we have demonstrated that polymer attachment facilitates the recovery of often valuable chiral auxiliaries while placing them in a special microenvironment and allowing their use in flow systems.

We now report the use of several polymeric amino alcohols in the addition of diethylzinc to benzaldehydes (Scheme I) and in the elucidation of the likely mechanism of the reaction. While our work was in progress, several reports on similar reactions with soluble catalysts appeared.[6,7] Noyori et al.[6] used (−)-3-*exo*-(dimethylamino)isoborneol (DAIB) as catalyst, and Wynberg[7] studied the same addition of diethylzinc to benzaldehyde using cinchona alkaloids as catalysts. While Wynberg speculates on the mechanism of the reaction, the insolubility of our polymeric catalyst greatly facilitates the understanding of the observed high stereoselectivity and provides evidence to support a mechanism which is quite different from that proposed by Wynberg.

The results we obtained in the addition of diethylzinc to benzaldehydes using a variety of polymeric acid alcohols are shown in Table I. At the present time our best results (95% ee) have been obtained by using a polymeric catalyst derived from N,N-dialkylated (−)-3-*exo*-aminoisoborneol.

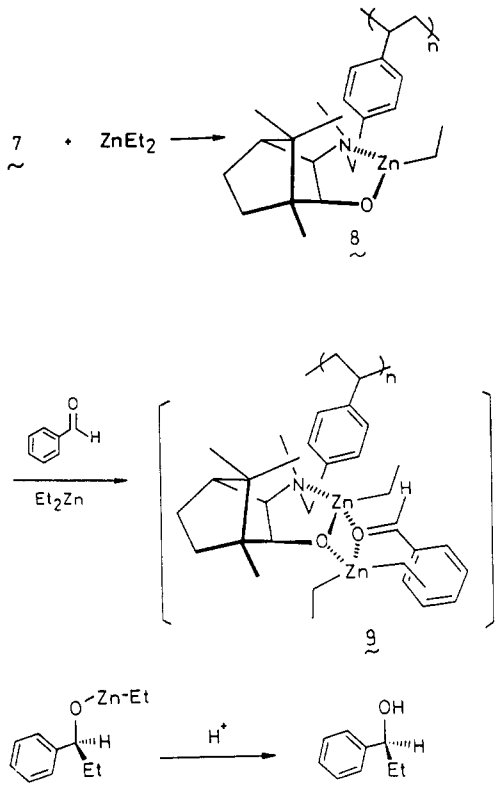
The polymeric catalysts (**1**, **3**–**7**) are prepared through chemical modification of 1–2% crosslinked partly chloromethylated polystyrene under conditions which lead exclusively to amination rather than quaternization.[2,5] In a typical addition procedure, a suspension of **1** (0.43 g, 0.5 mmol) in toluene (10 mL) is treated with a solution of diethylzinc in toluene (10 mL, 15 mmol) at 0 °C under nitrogen. After 30 min of stirring, benzaldehyde (1.0 g, 10 mmol) is added and the mixture is stirred for 60 h at 0 °C. The mixture is quenched with 1 N HCl, and the polymer is filtered off prior to extraction workup and bulb-to-bulb distillation to afford (*R*)-1-phenylpropanol (1.3 g, 96%) in 80.4% ee. The chiral polymer is recovered quantitatively.

As is seen in Table I, best results are obtained with the more hindered polymer **7** which contains bound aminoisoborneol moieties.

Our observations with the polymeric catalysts do not support the reaction mechanism proposed by Wynberg.[7] Ethane evolution is observed as diethylzinc is added to 1 equiv of **1** suspended in toluene at 0 °C. This is in

(2) Fréchet, J. M. J.; Bald, E.; Lecavalier, P. *J. Org. Chem.* **1986**, *51*, 3462.
(3) Itsuno, S. *J. Synth. Org. Chem. Jpn.* **1987**, 101.
(4) Itsuno, S.; Nakano, M.; Ito, K.; Hirao, A.; Owa, M.; Kanda, N.; Nakahama, S. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2887.
(5) Lecavalier, P.; Bald, E.; Jiang, Y.; Fréchet, J. M. J. *React. Polym.* **1985**, *3*, 315.
(6) Kitamura, M.; Suga, S.; Kawai, K.; Noyori, R. *J. Am. Chem. Soc.* **1986**, *108*, 6071.
(7) Smaardijk, A. A.; Wynberg, H. *J. Org. Chem.* **1987**, *52*, 135.
(8) $[\alpha]_D$ +22.6° (neat); lit. $[\alpha]_D$ +28.1° (neat) for pure compound: MacLeod, R.; Welch, F. J.; Mosher, H. S. *J. Am. Chem. Soc.* **1960**, *82*, 876.

Scheme II



agreement with the reported[9] formation of stable organozinc alkoxides from alcohols and diorganozinc. If the alkoxide group bound to zinc contains another electron-rich ligand, as is the case with **1** which possesses a dialkylamino group, a chelate is formed.[10] While benzaldehyde does not react with diethylzinc alone at 0 °C, the 1:1 chelate of **1** and diethylzinc reduces benzaldehyde slowly to afford a low yield of benzyl alcohol. In contrast, the presence of a *catalytic* amount of **1** was sufficient to afford the addition product in 74% ee even at room temperature. The same result is obtained by using a 1:2 mixture of **1** and diethylzinc. Filtration of the polymer after reaction affords the *soluble* chiral zinc alkoxide which can be hydrolyzed to (*R*)-1-phenylpropanol in good yield and ee. Meanwhile the filtered unhydrolyzed chiral polymeric zinc chelate can be used over and over again in further asymmetric reactions at room temperature without requiring regeneration. These observations show clearly that the chiral alkoxide produced by the reaction is *not* bound covalenty to the initially formed polymeric zinc complex and suggest that transfer of ethyl occurs from the excess free diethylzinc in solution. The polymer-bound zinc serves to activate the carbonyl function of benzaldehyde in a chiral environment but does not participate directly in the ethylation. This was confirmed by a study in which a polymer-bound butylzinc alkoxide complex was formed by reaction of polymer **1** with dibutylzinc (1:1) and then used with excess diethylzinc and benzaldehyde in a process which, at room temperature, affords the desired *ethylated* product in 79% ee (vs. 74% ee for the ethylated catalyst). Similarly, if diisobutylzinc is used to form the initial polymer-bound complex, subsequent reaction with benzaldehyde and free diethylzinc affords the ethylated alcohol in 80% ee.[11]

These observations support the formation of chiral chelate complexes such as **8** in Scheme II. The polymer-bound zinc acts to coordinate the aldehydic oxygen to form a chirally fixed transition state such as **9**. Using polymer **7**, this would afford a final product having the *S* configuration (Table I) as the unbound ethyl of diethylzinc would attack the *si* face of benzaldehyde. The alternate mechanism[7] proposed by Wynberg involving transfer of ethyl from the chiral complex would not account for our observations.

This mechanism does not account for the observed stereochemical outcome of reactions involving polymers **4** or **6** for which the presence of additional labile hydrogens on the amino functionality may cause the reaction to proceed through a different intermediate.

(9) Coates, G. E.; Ridley, D. *J. Chem. Soc.* **1965**, 1870. Boersma, J. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Ed.; Pergamon: New York, 1982; Chapter 16.

(10) Boersma, J.; Noltes, J. G. *J. Organomet. Chem.* **1986**, *13*, 291. Coates, G. E.; Ridley, D. *J. Chem. Soc. A* **1966**, 1064.

(11) It should be noted that using excess diisobutylzinc for the reaction results in reduction of benzaldehyde to benzyl alcohol due to the greater activity of the β-hydrogens of diisobutylzinc.

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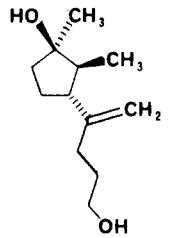
Homochiral Ketals in Organic Synthesis. Enantioselective Synthesis and Absolute Configuration of (-)-Chokol A[1]

Summary: An enantioselective synthesis of (-)-chokol A from 2-methyl-2-cyclopenten-1-one is described.

Sir: Chokol A (**1**) is a fungitoxic modified sesquiterpene recently isolated from stroma of the timothy *Phleum pratense* infected by the fungus *Epichloe typhina*.[2] The



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gross structure and relative stereochemistry initially assigned from spectroscopic measurements[2] were recently confirmed by synthesis of racemic chokol A.[3] Left in doubt was the absolute stereochemistry of the natural product, which we have now established by means of the enantioselective synthesis described below.[4]

Ketalization of 2-methyl-2-cyclopenten-1-one[5a] using 1,4-di-*O*-benzyl-L-threitol[5b] (PPTS, C_6H_6, reflux, 340 h)

(1) Presented in part at the 192nd National Meeting of the American Chemical Society, Anaheim, CA, September 1986; ORGN 33.

(2) Yoshihara, T.; Togiya, S.; Koshino, H.; Sakamura, S.; Shimanuki, T.; Sato, T.; Tajimi, A. *Tetrahedron Lett.* **1985**, *26*, 5551–5554.

(3) Oppolzer, W.; Cunningham, A. F. *Tetrahedron Lett.* **1986**, *27*, 5467–5470. This synthesis gave racemic chokol A in 3% overall yield over 13 steps.

(4) All yields refer to isolated and purified compounds. Satisfactory IR, ^1H NMR, ^{13}C NMR, and HRMS data were obtained for all compounds.

(5) (a) Gassman, P. G.; Pascone, J. M. *J. Am. Chem. Soc.* **1973**, *95*, 7801–7813. (b) Ando, N.; Yamamoto, Y.; Oda, J.; Inouye, Y. *Synthesis* **1978**, 688–690.

0022-3263/87/1952-4142$01.50/0