

Polymer-Supported *N*-Tritylaziridinyl(diphenyl)methanol as an Effective Catalyst in the Enantioselective Addition of Diethylzinc to Aldehydes

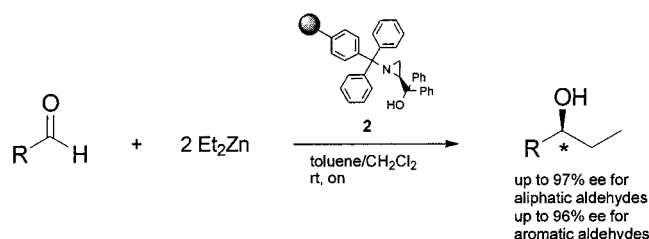
Peter ten Holte, Jan-Piet Wijgergangs, Lambertus Thijs, and Binne Zwanenburg*

Department of Organic Chemistry, NSR Institute for Molecular Structure, Design and Synthesis, University of Nijmegen, Toernooiveld, 6525 ED Nijmegen, The Netherlands

zwanenb@sci.kun.nl

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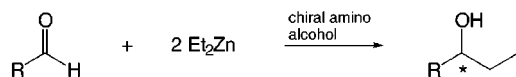
ABSTRACT



Novel polymer-supported *N*-tritylaziridino alcohol **2** was utilized as chiral ligand in the asymmetric addition of diethylzinc to aldehydes. High enantioselectivities were obtained for both aromatic and aliphatic aldehydes. The catalyst was successfully recycled and employed in subsequent additions with retention of high enantioselectivity.

Chiral β -amino alcohols have been proven to be extremely successful catalysts in the enantioselective addition of diethylzinc to aldehydes (see Scheme 1).

Scheme 1. Enantioselective Addition of Diethylzinc to Aldehydes Catalyzed by a Chiral Amino Alcohol



These ligands allow an efficient addition reaction and give rise to high ee's, as has been demonstrated for several examples.^{1,2} Attachment of such β -amino alcohol ligands to a polymeric support offers important advantages such as

(1) For reviews, see: (a) Soai, K.; Niwa, S. *Chem. Rev.* **1992**, 92, 833. (b) Noyori, R.; Kitamura, M. *Angew. Chem., Int. Ed. Engl.* **1991**, 30, 49.

facilitated workup procedures, easy recovery, and reuse of the catalyst in successive additions.³ However, only few of these immobilized amino alcohols display a high enantioselectivity for both aromatic and aliphatic aldehydes. Recently, an exceptional class of amino alcohols, viz. the aziridinylmethanols, has been successfully applied as catalyst in the asymmetric addition of diethylzinc to aldehydes.⁴ It

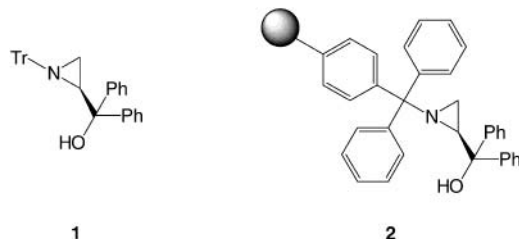
(2) (a) Reddy, K. S.; Solà, L.; Moyano, A.; Pericàs, M. A.; Riera, A. *J. Org. Chem.* **1999**, 64, 3969. (b) Cho, B. T.; Chun, Y. S. *Tetrahedron: Asymmetry* **1998**, 9, 1489. (c) Shi, M.; Satoh, Y.; Makihara, T.; Masaki, Y. *Tetrahedron: Asymmetry* **1995**, 6, 2109. (d) Soai, K.; Ookawa, A.; Kaba, T.; Ogawa, K. *J. Am. Chem. Soc.* **1987**, 109, 7111.

(3) (a) Vidal-Ferran, A.; Bampos, N.; Moyano, A.; Pericàs, M. A.; Riera, A.; Sanders, J. K. M. *J. Org. Chem.* **1998**, 63, 6309. (b) Liu, G.; Ellman, J. A. *J. Org. Chem.* **1995**, 60, 7712. (c) Watanabe, M.; Soai, K. *J. Chem. Soc., Perkin Trans. 1* **1994**, 837. (d) Soai, K.; Watanabe, M.; Yamamoto, A. *J. Org. Chem.* **1990**, 55, 4832. (e) Itsuno, S.; Fréchet, J. M. J. *J. Org. Chem.* **1987**, 52, 4140.

(4) (a) Tanner, D.; Kornø, H. T.; Guijarro, D.; Andersson, P. G. *Tetrahedron* **1998**, 54, 14232. (b) Lawrence, C. F.; Nayak, S. K.; Thijs, L.; Zwanenburg, B. *Synlett* **1999**, in press.

is worth noting that the aziridinylmethanols belong to the class of β - as well as γ -amino alcohols. We showed that especially *N*-tritylaziridinyl(diphenyl)methanol **1** (see Chart 1) is an excellent chiral catalyst in the solution-phase

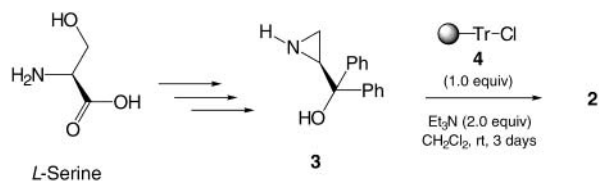
Chart 1. *N*-Tritylaziridinyl(diphenyl)methanol **1** and Its Polymer-Supported Analog **2**, Tr = Trityl



enantioselective addition of diethylzinc to both aromatic and aliphatic aldehydes.^{4b} These recent findings, and taking into account the advantages of immobilized catalysts over homogeneous ones, have prompted us to develop polymer-supported *N*-tritylaziridinyl(diphenyl)methanol **2** (see Chart 1) as the chiral catalyst in diethylzinc additions to aldehydes. These investigations are part of our continuing studies on functionalized small-ring heterocycles.⁵

In this paper, we describe the immobilized aziridino alcohol **2**, which is a highly potent catalyst in the asymmetric addition of diethylzinc to both aliphatic and aromatic aldehydes. Polymer-supported ligand **2** was obtained by attachment of aziridino alcohol **3** to polymer-bound triphenylchloromethane **4** (1.1 mequiv/g)⁶ as is depicted in Scheme 2. The coupling of **3** to the trityl chloride resin took

Scheme 2. Synthesis of Polymer-Supported *N*-Tritylaziridino Alcohol **2** from *L*-Serine



place in a yield of 70% as was determined by gravimetric analysis. Optically pure (*S*)-aziridinylmethanol **3** was readily obtained from *L*-serine.^{5b} The polymeric chloride moieties that remained unreacted in the attaching step were capped with methoxy groups.⁷

(5) (a) Starmans, W. A. J.; Thijs, L.; Zwanenburg, B. *Tetrahedron* **1998**, *54*, 629. (b) Willems, J. G. H.; Hersmis, M. C.; de Gelder, R.; Smits, J. M. M.; Hammink, J. B.; Dommerholt, F. J.; Thijs, L.; Zwanenburg, B. *J. Chem. Soc., Perkin Trans. 1* **1997**, 963 and references therein. (c) Zwanenburg, B.; Thijs, L. *Pure Appl. Chem.* **1996**, 735 and references therein.

(6) Triphenylchloromethane polymer bound, cross-linked with 1% DVB; 100–200 mesh, Fluka Chemika.

(7) The resin was stirred for 15 min in a mixture of DCM/MeOH (1/1) containing an excess of base, according to a procedure by Barlos et al.: Barlos, K.; Chatzi, O.; Gatos, D.; Stavropoulos, G. *Int. J. Peptide Protein Res.* **1991**, *37*, 513.

The addition of diethylzinc to benzaldehyde in the presence of 10 mol % of polymer-supported catalyst **2** gave the corresponding (*S*)-alcohol in a high yield (92%) and an enantiomeric excess of 96%. It is noteworthy that the solvent system does not only affect the yield of the reaction to a great extent but also has a considerable impact on the enantioselectivity. The best result was obtained in a 1/1 (v/v) mixture of toluene and dichloromethane (see Table 1).

Table 1. Enantioselective Addition of Diethylzinc to Aromatic and Aliphatic Aldehydes Employing Polymer-Supported Catalyst **2**

aldehyde	solvent (toluene/CH ₂ Cl ₂)	yield (%)	ee ^a (%)	config ^d
benzaldehyde	100/0	88	93 ^b	<i>S</i>
benzaldehyde	75/25	91	96 ^b	<i>S</i>
benzaldehyde	50/50	92	96 ^b	<i>S</i>
benzaldehyde	0/100	72	91 ^b	<i>S</i>
<i>p</i> -chlorobenzaldehyde	50/50	88	96 ^b	<i>S</i>
anisaldehyde	50/50	88	95 ^b	<i>S</i>
cyclohexanecarboxaldehyde	50/50	90	97 ^c	<i>S</i>
isovaleraldehyde	50/50	77	81	<i>S</i>
undecylic aldehyde	50/50	80	77 ^c	<i>S</i>

^a Determined by chiral GC (Beta-DEX). ^b Determined by optical rotation. ^c Determined by ¹⁹F NMR of Mosher's ester.⁸ ^d Determined by comparison with absolute optical rotation given in the literature.

The presence of dichloromethane is essential for swelling of the polymer and making the aziridino alcohol ligands accessible for the substrates.

In this toluene/dichloromethane (1/1, v/v) mixture, other aromatic aldehydes such as *p*-chlorobenzaldehyde and anisaldehyde also underwent highly enantioselective addition of diethylzinc (96 and 95% ee, respectively) in the presence of ligand **2** (Table 1). An enantiomeric excess of 97% was observed for the addition of diethylzinc to cyclohexanecarboxaldehyde (cy 90%) using polymer-bound ligand **2**. This is a remarkably high enantioselectivity for a heterogeneously catalyzed asymmetric addition of diethylzinc to an aliphatic aldehyde. Likewise, addition of diethylzinc to other aliphatic aldehydes, such as isovaleraldehyde, took place with good enantioselectivity in the presence of catalyst **2** (see Table 1).

The catalytic capability of our polymer-supported ligand (**2**) was retained in successive addition cycles (see Table 2). Addition of diethylzinc to benzaldehyde in the presence of chiral ligand **2** occurred in the second reaction cycle with an ee of 95% and in the third cycle with an ee of 94%. These results demonstrate that in addition to highly facilitated workup procedures, polymer-supported catalyst **2** shows the advantage of easy recovery and utilization in consecutive asymmetric diethylzinc additions.

In summary, we have demonstrated that catalyst **1** is suitable for immobilization and that polymer-supported

(8) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

Table 2. Enantioselective Addition of Diethylzinc to Benzaldehyde Using Recycled Polymer Supported Catalyst **2**

aldehyde	run (no.)	yield (%)	ee ^{a,b} (%)
benzaldehyde	1	92	96
benzaldehyde	2	92	95
benzaldehyde	3	92	94

^a Determined by chiral GC (Beta-DEX). ^b Determined by optical rotation.

aziridino alcohol **2** is a highly efficient chiral ligand for asymmetric addition of diethylzinc to aromatic as well as aliphatic aldehydes.

Typical procedure for the addition of diethylzinc to benzaldehyde, catalyzed by polymer-bound ligand **2**: Benzaldehyde (0.21 g, 2.0 mmol) was added to a cooled (0 °C) suspension of polymer-bound ligand **2** (0.28 g, 0.2 mmol) in a mixture of dichloromethane and toluene (1/1, v/v, 16 mL), followed by gradual addition of diethylzinc (4.1 mL of a 1 M solution of diethylzinc in *n*-hexane), and the mixture was stirred at ambient temperature overnight. A saturated,

aqueous solution of ammonium chloride (25 mL) was added, and the mixture was stirred for 15 min. The resin was removed by filtration and washed with dichloromethane (5 × 5 mL) the organic layer was dried (MgSO₄) and concentrated under reduced pressure, and the product was purified by column chromatography to give 0.25 g (92%) of (1*S*)-1-phenyl-1-propanol.

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Supporting Information Available: Experimental procedures for polymer bound catalyst **2**. FT-IR spectrum of **2**. General procedure for the enantioselective addition of diethylzinc to aldehydes catalyzed by **2**. Chiral GC spectrum of racemic and enantiomeric 1-(4-chlorophenyl)-1-propanol. ¹⁹F NMR spectrum of Mosher's ester of racemic and enantiomeric 1-cyclohexyl-1-propanol. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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