Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Novel Polymer-Bound Aminoalcohol Ligands for the Asymmetric Addition of Diethylzinc to Aldehydes

Philip C. Bulman Page [a], Steven M. Allin [a], Suzanne J. Dilly [a] & Benjamin R. Buckley [a]

[a] Department of Chemistry, Loughborough University, Loughborough, Leicestershire, England

Version of record first published: 22 Jun 2007.

To cite this article: Philip C. Bulman Page , Steven M. Allin , Suzanne J. Dilly & Benjamin R. Buckley (2007): Novel Polymer-Bound Aminoalcohol Ligands for the Asymmetric Addition of Diethylzinc to Aldehydes, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 37:12, 2019-2030

To link to this article: http://dx.doi.org/10.1080/00397910701356553

Synthetic Communications®, 37: 2019–2030, 2007

ISSN 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910701356553

Novel Polymer-Bound Aminoalcohol Ligands for the Asymmetric Addition of Diethylzinc to Aldehydes

Philip C. Bulman Page, Steven M. Allin, Suzanne J. Dilly, and Benjamin R. Buckley
Department of Chemistry, Loughborough University, Loughborough, Leicestershire, England

Abstract: The synthesis of several novel polymer-supported aziridine-containing aminoalcohol chiral ligands has been accomplished, and the polymers have been used as ligands for the catalytic asymmetric addition of diethylzinc to benzaldehyde, giving up to 89% ee. Incorporation onto a polymer support prevents the variation of ee with time that is observed in reactions of one unsupported ligand, perhaps as a result of site isolation of the ligand within the polymer, preventing cooperative effects.

Keywords: addition, aldehyde, aminoalcohol, asymmetric dialkyl zinc, ligand

Chiral β-amino alcohols have been well documented as effective ligands for the asymmetric addition of diethylzinc to aromatic aldehydes,[1] and the mechanism has been thoroughly studied over the past few years. The postulated mechanism involves a two-zinc species in the diastereofacially selective step: one zinc atom, bearing one ethyl group, is chelated by the aminoalcohol ligand and is also associated with the aldehyde oxygen atom; a second zinc atom, of a diethylzinc unit, is associated with both the ligand and aldehyde oxygen atoms. Ethyl group transfer then takes place.[2] The incorporation of an aziridine moiety into these ligands allows the reaction to be carried out with up to 99% ee.[3] We have recently reported the

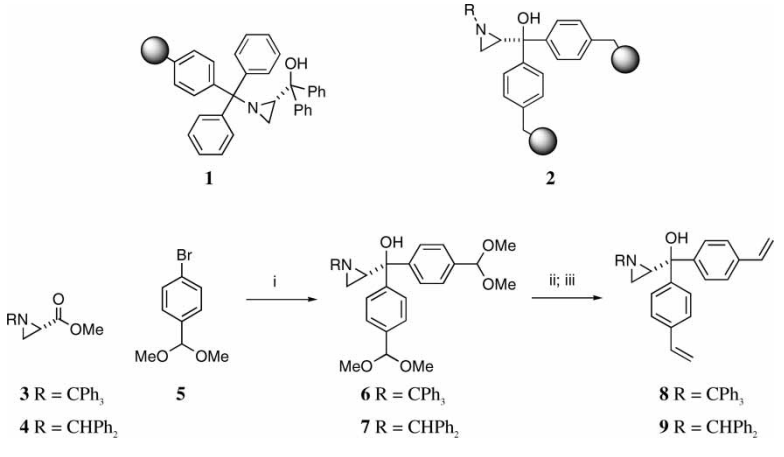
Received in the USA November 7, 2006
Address correspondence to Philip C. Bulman Page, Department of Chemistry, Loughborough University, Loughborough, Leicestershire LE11 3TU, U.K. E-mail: p.c.b.page@lboro.ac.uk

synthesis of a number of aziridine ligands and their use as ligands in the enantioselective addition of diethylzinc to benzaldehyde.[4] We report here the preparation and use of polymer-supported versions of three of these ligands.

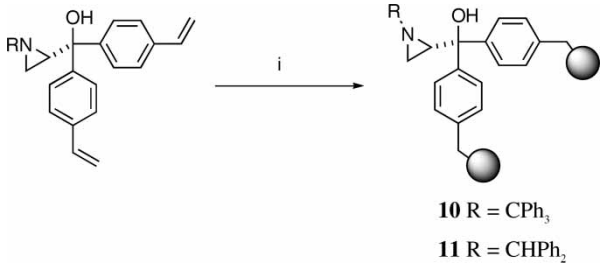
A polymer-supported aziridine ligand **1**, derived from L-serine and supported through the nitrogen substituent, has been shown by Holte et al. to be effective as a ligand in the enantioselective addition of diethylzinc to benzaldehyde, providing (*S*)-1-phenylpropanol in up to 96% ee.[5] In contrast, to allow variation of *N*-substitution in the aziridine ligand framework, we have attached the polymer to our ligands through the tertiary alcohol phenyl ring substituents to give the polymer-supported motif **2**.

The synthesis of the ligand monomers was carried out from aziridinyl esters **3** and **4** and 4-bromobenzaldehyde dimethyl acetal **5** (Scheme 1). The aziridinyl esters **3** and **4** were prepared by the method of Zwanenburg, whereby *N*-protected L-serine methyl ester was treated with methanesulfonyl chloride and subsequently ring-closed to form the aziridine with either trityl or benzhydryl *N*-substitution.[6] The protected 4-bromobenzaldehyde **5** was lithiated, and the anion underwent smooth double addition to give esters **3** and **4**. Deprotection of the aldehyde units was effected with *para*-toluene sulfonic acid and water, and the aldehydes converted into vinyl moieties with methyl Wittig reagent, giving ligand monomers **8** and **9**.

Suspension copolymerization was carried out with styrene and divinyl benzene in the presence of poly(vinyl alcohol) (MW 14000) as an emulsifier, by the method of Far et al.,[7] to produce functionalized copolymers **10** and **11**, each of which was found by elemental analysis to contain a loading of aziridine ligand of 0.1 mmol/g (Scheme 2).



Scheme 1. i) *n*-BuLi, THF, −78°C (R = CPh_3, 75%; R = $CHPh_2$, 62%); ii) *p*TsOH, DCM, H_2O, rt (R = CPh_3, 69%; R = $CHPh_2$, 60%); iii) $MePPh_3Br$, KHMDS, THF, 0°C (R = CPh_3, 81%; R = $CHPh_2$, 80%).

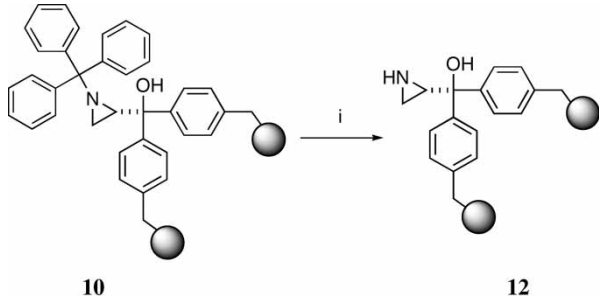


Scheme 2. i) Styrene, divinyl benzene, PhCl, benzoyl peroxide, PVA, NaCl, H_2O, 100°C.

The copolymer **10** containing the *N*-tritylated aziridine was treated with trifluoroacetic acid to achieve detritylation, giving the corresponding NH-functionalized copolymer **11** (Scheme 3).

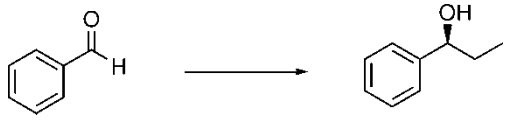
The three styrene copolymers generated were then tested as ligands in the addition of diethylzinc to benzaldehyde. The copolymers were allowed to swell in toluene at room temperature before being cooled to 0°C prior to the addition of benzaldehyde followed by diethylzinc. The reactions were allowed to reach room temperature over a further 24 h. After quenching with aqueous ammonium chloride, the dried crude products were analyzed by GC (Chrompak, Chirasil CB, 140°C, 10 psi) and 250-MHz ^{1}H NMR spectroscopy to obtain the ee and conversions respectively. The results are shown in Table 1. For comparison, our previously reported results for the unsupported ligand analogues are also shown.[4]

In each case, the major product enantiomer was found to have the (*S*)-configuration. We observed the same sense of asymmetric induction with the solution-phase analogues of these ligands, as did Holte et al. with ligand **1**.[5] Compared to the unsupported analogues, however, polymer-supported ligands **10** and **11** both induce slightly reduced enantioselectivities and conversions for the same addition reaction. We were disappointed to note that



Scheme 3. TFA, DCM, MeOH.

Table 1. Addition of diethylzinc to benzaldehyde in the presence of polymeric aziridine ligands[a]



Ligand	Conversion (%)[b]	Ee (%)[c]	Unsupported ligand analogue[4] conversion (%)	Unsupported ligand analogue[4] ee (%)
10	>95	89	>99	95
11	62	88	>99	96
11[d]	3	0	—	—
12	52	84	85	62

[a]Reaction conditions: benzaldehyde (2.0 mmol), ligand (5 mol%), diethyl zinc (4.0 mmol), toluene, 0°C, 24 h.
[b]Conversion after 24 h determined by 250-MHz ^{1}H NMR spectroscopy.
[c]Ee values determined by GC, Chrompak, Chirasil CB.
[d]Recycled polymer.

the reuse of ligand **11** demonstrated the complete loss of enantioselectivity and catalytic ability of the recycled polymer-supported ligand.

It is particularly interesting, therefore, that polymer-supported ligand **12** induces a substantially higher level of enantioselectivity in the addition of diethylzinc to benzaldehyde than does its unsupported analogue in the solution phase after reaction for 24 h at room temperature. Further, we have reported a reduction of ee with time throughout this reaction using the corresponding unsupported ligand from 85% ee after 15 min to 62% ee after 24 h.[4] It is fascinating to note that the reaction using the polymer-supported ligand **12** displays no such variation of ee with reaction time and that the enantioselectivity of the reaction with the polymer-supported ligand is equivalent to that displayed after 15 min of reaction time when using the unsupported analogue. The variation in ee with time during the reaction using the unsupported ligand may be caused by cooperative effects involving more than one ligand molecule in the reaction. We therefore suggest that the use of these polymer-supported ligands restricts this effect, possibly due to site isolation of the ligand within the polymer.

EXPERIMENTAL

General Experimental Detail

All infrared spectra were obtained using a Perkin-Elmer Paragon 1000 FT-IR spectrophotometer; thin-film spectra were acquired using sodium chloride

plates. All ^{1}H and ^{13}C NMR spectra were measured at 250.13 and 62.86 MHz with a Bruker AC 250-MHz spectrometer or at 400.13 and 100.62 MHz with a Bruker DPX 400, in deuteriochloroform solution unless otherwise stated, using TMS (tetramethylsilane) as the internal reference. Mass spectra were recorded using a Jeol-SX102 instrument utilizing electron-impact (EI), fast atom bombardment (FAB), and the EPSRC national mass spectrometry service at the University of Wales, Swansea, utilizing electrospray (ES). Analysis by gas chromatography-mass spectrometry (GCMS) utilized a Fisons GC 8000 series (AS 800), using a 15 m × 0.25 mm DB-5 column and an electron-impact low-resolution mass spectrometer. Melting points were recorded using an Electrothermal-IA 9100 melting-point instrument and are uncorrected. Optical rotation values were measured with an optical activity polAAar 2001 instrument operating at $\lambda = 589$ nm, corresponding to the sodium D line, at the temperatures indicated. Microanalyses were performed on a Perkin-Elmer elemental analyser 2400 CHN. All chromatographic manipulations used silica gel as the adsorbent. Reactions were monitored using thin-layer chromatography (TLC) on aluminium-backed plates coated with Merck Kieselgel 60 F254 silica gel. TLC plates were visualized by UV radiation at a wavelength of 254 nm or stained by exposure to an ethanolic solution of phosphomolybdic acid (acidified with concentrated sulfuric acid), followed by charring where appropriate. Reactions requiring anhydrous conditions were carried out using flame-dried glassware under a nitrogen atmosphere unless otherwise stated. Reaction solvents were used as obtained commercially unless otherwise stated. Light petroleum (bp 40–60°C) was distilled from calcium chloride prior to use. Ethyl acetate was distilled over calcium sulfate or chloride. Dichloromethane was distilled over calcium hydride. Tetrahydrofuran was distilled under a nitrogen atmosphere from the sodium/benzophenone ketyl radical.

(−)-(*S*)-Methyl *N*-Tritylaziridine-2-carboxylate 3

A suspension of L-serine methyl ester (74.0 g, 476.0 mmol) in chloroform (600 mL) was treated with triethylamine (115.5 g, 1140.0 mmol), and the solution was cooled to 0°C. Triphenylmethyl chloride (132.5 g, 476.0 mmol) was added in portions. The reaction mixture was maintained at 0°C for 3 h, allowed to reach room temperature, and washed with water (600 mL) and brine (400 mL). The organic layer was dried over magnesium sulfate. The solution was concentrated to 300 mL and treated with triethylamine (115.5 g, 1140.0 mmol) and 4-dimethylaminopyridine (10 mol%, 5.83 g, 48.0 mmol). Methanesulfonyl chloride (75.8 g, 660.0 mmol) was added dropwise over 90 min. The reaction mixture was heated to reflux for 20 h, allowed to cool to room temperature, and washed with water (600 mL) and brine (500 mL). The organic layer was dried over sodium sulfate and evaporated to dryness. The residue was recrystallized from

ethanol (300 mL) to give the product as pale beige crystals (97.0 g, 59%); mp 122–126°C; $[\alpha]_D^{20} = -85.9$ (*c* 0.40, CH_2Cl_2) (Found: C, 79.9; H, 6.3; N, 3.8; $C_{23}H_{21}NO_2$ requires C, 80.4; H, 6.2; N, 4.1%); ν_{max}/cm^{-1} 2950, 1749, 1448, 1199, 708; δ_H (400 MHz, $CDCl_3$) 1.41 (dd, $J = 1.6$, 6, 1H), 1.89 (dd, $J = 2.4$, 6, 1H), 2.25 (dd, $J = 1.6$, 2.4, 1H), 3.75 (s, 3H), 7.15–7.32 (9H, m), 7.50 (d, $J = 8$, 6H); δ_C (100 MHz, $CDCl_3$) 28.7, 31.7, 52.1, 74.4, 126.9, 127.8, 128.0, 128.7, 129.3, 143.6, 171.9; *m/z* 343.1565 ($C_{23}H_{21}NO_2$ requires 343.1572) 105 (90%), 165 (95%), 244 (100%), 343 (>1%).

(–)-(*S*)-Methyl *N*-Benzhydryl-2-amino-3-hydroxypropanoate

A solution of L-serine methyl ester (5.0 g, 32.0 mmol) in chloroform (50 mL) was treated with triethylamine (7.7 g, 77.0 mmol), and the solution was cooled to 0°C. Benzhydryl chloride (4.4 g, 22.0 mmol) was added dropwise, and the mixture was heated to reflux for 20 h. The mixture was allowed to cool to room temperature, and saturated aqueous ammonium chloride (20 mL) was added. The mixture was extracted into dichloromethane (50 mL), and the organic was later dried over magnesium sulfate and evaporated to dryness. The residue was purified by chromatography on silica gel (eluent 8:1 petroleum ether–ethyl acetate) to give the product as a yellow oil (3.1 g, 49%); $[\alpha]_D = -31.1$ (*c* 0.28, CH_2Cl_2); ν_{max}/cm^{-1} 3447, 1741, 1452, 1204, 1056, 753; δ_H (400 MHz, $CDCl_3$) 3.40–3.43 (m, 1H), 3.64–3.68 (m, 2H), 3.74 (s, 3H), 4.92 (s, 1H), 7.22–7.40 (m, 10H); δ_C (100 MHz, $CDCl_3$) 52.2, 60.4, 63.1, 65.3, 127.3, 127.4, 127.6, 128.6, 128.7, 142.3, 143.5, 173.7; *m/z* 284.1281 found ($C_{17}H_{19}NO_3$ requires 284.1288) 77 (50%), 105 (70%), 167 (100%), 182 (90%), 284 (<1%).

(–)-(*S*)-Methyl *N*-Benzhydrylaziridine-2-carboxylate 4

(–)-(*S*)-Methyl *N*-benzhydryl-2-amino-3-hydroxypropanoate (3.0 g, 10.5 mmol) and 4-dimethylamino pyridine (10 mol%, 0.12 g, 1.1 mmol) were dissolved in chloroform (200 mL), triethylamine (2.54 g, 25.2 mmol) was added, and the solution was cooled to 0°C. A solution of methanesulfonic anhydride (2.4 g, 15 mmol) in chloroform (20 mL) was added dropwise. The mixture was maintained at 0°C for 1 h, allowed to reach room temperature, heated to reflux for 24 h, and allowed to cool to room temperature. Water (50 mL) was added, the mixture was extracted into dichloromethane (100 mL), and the organic layer was dried over magnesium sulfate and evaporated to dryness. The residue was purified by chromatography on silica gel (eluent: 3:1 petroleum ether–ethyl acetate with 1% triethylamine added) to give the product as pale yellow crystals (2.04 g, 73%), mp 84–87°C; $[\alpha]_D = -93.3$ (*c* 0.45, CH_2Cl_2); ν_{max}/cm^{-1} 1744, 1453, 1440, 1120; δ_H (400 MHz, $CDCl_3$) 1.82 (d, $J = 6$, 1H), 2.26 (dd, $J = 3$, 6, 1H), 2.30 (d, $J = 3$, 1H), 3.60 (s, 1H), 3.69 (s, 3H),

7.18–7.42 (m, 10H); δ_C (100 MHz, $CDCl_3$) 34.9, 38.1, 52.1, 77.9, 126.6, 127.1, 127.3, 127.4, 127.5, 127.6, 128.2, 128.4, 128.5, 128.6, 142.4, 171.0; m/z 266.1183 ($C_{17}H_{17}NO_2$ requires 266.1181) 105 (23%), 165 (35%), 167 (100%), 266 (12%), 267 (3%).

(–)-(*S*)-*N*-Tritylaziridin-2-ylDi(4-(dimethoxymethyl)phenyl) methanol 6

A solution of 4-bromobenzaldehyde dimethylacetal **5** (2.8 g, 5.0 mmol) in tetrahydrofuran (12 mL) was cooled to −78°C. A solution of *n*-butyllithium in hexanes (2.5 M, 5.8 mL, 15.0 mmol) was added dropwise to the solution. The reaction mixture was maintained at −78°C for 2 h, and (–)-(*S*)-methyl *N*-tritylaziridine-2-carboxylate **3** (1.0 g, 2.9 mmol) was added. The green suspension was allowed to reach room temperature, stirred for a further 19 h at room temperature, and heated to reflux for 5 h. The resulting orange suspension was quenched with saturated aqueous ammonium chloride (20 mL) and extracted into diethyl ether (50 mL). The organic layer was dried over magnesium sulfate and evaporated to dryness. The residue was purified by column chromatography on silica gel (eluent: 4:1 hexanes–ethyl acetate) to give the product as a yellow oil (1.2 g, 67%); ν_{max}/cm^{-1} 3422, 2935, 447, 1530, 1100, 1053; δ_H (250 MHz, $CDCl_3$) 1.34 (d, $J = 6$, 1H), 2.09 (d, $J = 3$, 1H), 2.35 (dd, $J = 3$, 6, 1H), 3.24 (s, 6H), 3.26 (s, 6H), 4.51 (s, 1H), 5.26 (s, 1H), 5.33 (s, 1H), 7.13–7.48 (m, 23H).

(–)-(*S*)-*N*-Benzhydrylaziridin-2-yl Di(4-(dimethoxymethyl) phenyl)methanol 7

A solution of 4-bromobenzaldehyde dimethylacetal **5** (1.2 g, 5.0 mmol) in tetrahydrofuran (6 mL) was cooled to −78°C. A solution of *n*-butyllithium in hexanes (2.5 M, 3.0 mL, 7.5 mmol) was added dropwise, and the mixture was maintained at −78°C for 2 h. A solution of (–)-(*S*)-methyl *N*-benzhydrylaziridine-2-carboxylate (0.3 g, 1.2 mmol) in tetrahydrofuran (6 mL) was added. The green suspension was allowed to reach room temperature and stirred at room temperature for 19 h. The resulting orange suspension was quenched with saturated aqueous ammonium chloride (10 mL) and extracted into diethyl ether (50 mL), and the organic layer was dried over magnesium sulfate and evaporated to dryness. The residue was purified by column chromatography on silica gel (eluent: 4:1 hexanes–ethyl acetate) to give the product as a yellow oil (0.4 g, 62%); ν_{max}/cm^{-1} 3424, 2937, 1352, 1101, 1053; δ_H (250 MHz, $CDCl_3$) 1.60 (d, $J = 6$, 1H), 2.10 (d, $J = 4$, 1H), 2.72 (dd, $J = 4$, 6, 1H), 3.27 (s, 6H), 3.31 (s, 6H), 3.85 (s, 1H), 3.99 (s, 1H), 5.25 (s, 1H), 5.33 (s, 1H), 6.93–7.41 (m, 18H).

(−)-(*S*)-*N*-Tritylaziridin-2-yl Di(4-formylphenyl)methanol

(−)-(*S*)-*N*-Tritylaziridin-2-yl di(4-(dimethoxymethyl)phenyl)methanol **6** (0.5 g, 0.8 mmol) and *para*-toluenesulfonic acid (50 mg) were dissolved in dichloromethane (20 mL) and water (5 mL). The mixture was stirred vigorously for 4 days. Saturated aqueous sodium hydrogen carbonate (10 mL) was added, the mixture was extracted into dichloromethane (20 mL), and the organic layer was dried over sodium sulfate and evaporated to dryness. The residue was purified by column chromatography on silica gel (eluent: 5:1 petroleum ether–ethyl acetate) to give the product as a colorless oil (0.25 g, 69%); ν_{max}/cm^{-1} 3443, 1699, 1604, 1212, 706; δ_H (250 MHz, $CDCl_3$) 1.37 (d, $J = 6$, 1H), 2.09 (d, $J = 3$, 1H), 2.45 (dd, $J = 3$, 6, 1H), 4.74 (s, 1H), 7.13–7.75 (m, 23H), 9.91 (s, 1H), 9.95 (s, 1H).

(−)-(*S*)-*N*-Tritylaziridin-2-yl Di(4-vinylphenyl)methanol 8

A solution of methyltriphenylphosphonium bromide (0.56 g, 1.6 mmol) in tetrahydrofuran (10 mL) was cooled to 0°C. A solution of potassium bis(trimethylsilyl)amide in toluene (0.5 M, 2.8 mL, 1.4 mmol) was added dropwise, and the resulting bright yellow suspension was maintained at 0°C for 1 h. The suspension was transferred into a solution of (−)-(*S*)-*N*-tritylaziridin-2-yl di(4-formylphenyl)methanol (0.2 g, 0.4 mmol) in tetrahydrofuran (10 mL). The mixture was allowed to reach room temperature over 3 h, quenched with saturated aqueous ammonium chloride (10 mL), and extracted into ethyl acetate (50 mL). The organic layer was dried over sodium sulfate and evaporated to dryness. The residue was purified by column chromatography on silica gel (eluent: 6:1 hexanes–ethyl acetate) to give the product as a colorless oil (0.16 g, 81%); $[\alpha]_D = +13.1$ (*c* 0.09, CH_2Cl_2); ν_{max}/cm^{-1} 3423, 1437, 1191, 1120, 722, 695; δ_H (250 MHz, $CDCl_3$) 1.28 (d, $J = 6$, 1H), 2.08 (d, $J = 3$, 1H), 2.35 (dd, $J = 3$, 6, 1H), 4.34 (s, 1H), 5.10–5.16 (m, 2H), 5.61–5.65 (m, 2H), 6.61–6.65 (m, 2H), 7.14–7.36 (m, 23H); δ_C (100 MHz, $CDCl_3$) 32.1, 47.5, 74.1, 114.2, 114.5, 125.7, 126.1, 126.3, 126.4, 126.9, 127.3, 128.5, 128.8, 135.7, 136.3, 136.7, 137.2, 143.2, 143.4, 146.0, 146.9.

(−)-(*S*)-*N*-Benzhydrylaziridin-2-yl Di(4-formylphenyl)methanol

(−)-(*S*)-*N*-Benzhydrylaziridin-2-yl di(4-(dimethoxymethyl)phenyl)methanol **7** (0.3 g, 0.6 mmol) was dissolved in dichloromethane (20 mL), and *para*-toluenesulfonic acid (50 mg) and water (5 mL) were added. The suspension was stirred at room temperature for 4 days. Saturated aqueous sodium hydrogen carbonate (10 mL) was added, the mixture was extracted into dichloromethane (20 mL), and the organic layer was dried over magnesium sulfate and evaporated to dryness. The residue was purified by column

chromatography on silica gel (eluent: 5:1 petroleum ether–ethyl acetate) to give the product as pale yellow crystals (0.15 g, 60%); ν_{max}/cm^{-1} 3432, 2835, 1698, 1604, 1306, 1212, 1171; δ_H (250 MHz, $CDCl_3$) 1.70 (d, $J = 6$, 1H), 2.15 (d, $J = 3$, 1H), 2.74–2.81 (m, 1H), 3.85 (s, 1H), 4.17 (s, 1H), 6.98–7.31 (m, 10H), 7.22 (d, $J = 8$, 2H), 7.47 (d, $J = 8$, 2H), 7.58 (d, $J = 8$, 2H), 7.81 (d, $J = 8$, 2H), 9.88 (s, 1H), 9.96 (s, 1H).

(–)-(*S*)-*N*-Benzhydryl aziridin-2-yl Di(4-vinylphenyl)methanol 9

A solution of methyltriphenylphosphonium bromide (0.42 g, 1.2 mmol) in tetrahydrofuran (10 mL) was cooled to 0°C. A solution of potassium bis(trimethylsilyl)amide in toluene (0.5 M, 1.4 mL, 0.7 mmol) was added dropwise, and the suspension was maintained at 0°C for 1 h. The suspension was transferred into a solution of (–)-(*S*)-*N*-benzhydryl aziridin-2-yl di(4-formylphenyl)methanol (0.1 g, 0.2 mmol) in tetrahydrofuran (10 mL). The mixture was allowed to reach room temperature over 3 h, quenched with saturated aqueous ammonium chloride (10 mL), and extracted into ethyl acetate (50 mL). The organic layer was dried over sodium sulfate and evaporated to dryness. The residue was purified by column chromatography on silica gel (eluent: 6:1 petroleum ether–ethyl acetate) to give the product as pale yellow crystals (0.05 g, 51%), mp 167–170°C; $[\alpha]_D^{20} = +10.4$ (*c* 0.06, CH_2Cl_2); ν_{max}/cm^{-1} 3424, 2924, 1490, 1447, 706; δ_H (400 MHz, $CDCl_3$) 1.60 (d, $J = 6$, 1H), 2.14 (d, $J = 4$, 1H), 2.70 (dd, $J = 4$, 6, 1H), 3.82 (s, 1H), 3.88 (s, 1H), 5.14–5.20 (m, 2H), 5.59–5.71 (m, 2H), 6.67–6.70 (m, 2H), 6.95–7.44 (m, 18H); δ_C (100 MHz, $CDCl_3$) 31.6, 46.7, 74.3, 77.5, 113.6, 114.1, 125.9, 126.2, 126.3, 126.4, 126.8, 127.4, 128.0, 128.7, 136.0, 135.7, 136.8, 137.0, 142.8, 143.1, 145.0, 146.7.

Polystyrene-Supported (–)-(*S*)-*N*-Tritylaziridin-2-yl Diphenylmethanol 10

(–)-(*S*)-*N*-Tritylaziridin-2-yl di(4-vinylphenyl)methanol **8** (0.12 g, 0.23 mmol), styrene (2.0 g, 19.2 mmol), and divinylbenzene (0.11 g, 0.68 mmol) were dissolved in chlorobenzene (4 mL), and benzoyl peroxide (60 mg) was added. A solution of sodium chloride (0.25 g) and poly(vinyl alcohol) (MW 14000, 80 mg in water (10 mL) was added as an emulsifying agent, and the mixture was stirred to form an emulsion. The emulsion was degassed with dry nitrogen and heated to 85°C for 20 h. The resulting polymer beads were removed by filtration and washed successively with methanol, acetone, water, and tetrahydrofuran (2 × 50 mL each). The polymer was allowed to swell in tetrahydrofuran (50 mL), and the mixture was heated to reflux for 1 h to remove monomeric materials. The solvent was decanted, and methanol (50 mL) was added to induce the polymer to contract. The beads were

collected by filtration and dried under vacuum for 5 days to give the product (2.2 g, 100%) (found: C, 90.4; H, 7.5, N, 0.1%); δ_{max}/cm^{-1} 3446, 3059, 2922, 1718, 1601, 1492, 1451, 1436, 1270, 756, 695, 632. A loading of 0.1 mmol/g was calculated from the percentage of nitrogen present.

Polystyrene-Supported (−)-(*S*)-*N*-benzhydrylaziridin-2-yl Diphenylmethanol 11

(−)-(*S*)-*N*-Benzhydrylaziridin-2-yl di(4-vinylphenyl)methanol **9** (0.1 g, 0.23 mmol), styrene (2.0 g, 19.2 mmol), and divinylbenzene (0.11 g, 0.68 mmol) were dissolved in chlorobenzene (4 mL), and benzoyl peroxide (60 mg) was added. A solution of sodium chloride (0.25 g) and poly(vinyl alcohol) (MW 14000, 80 mg) in water (10 mL) was added as an emulsifying agent, and the mixture was stirred to form an emulsion. The emulsion was degassed with dry nitrogen and heated to 85°C for 20 h. The resulting polymer beads were removed by filtration and washed successively with methanol, acetone, water, and tetrahydrofuran (2 × 50 mL each). The polymer was allowed to swell in tetrahydrofuran (50 mL), and the mixture was heated to reflux for 2 h to remove monomeric materials. The solvent was decanted, and methanol (50 mL) was added to induce the polymer to contract. The beads were collected by filtration and dried under vacuum for 5 days to give the product (2.2 g, 100%) (found: C, 89.9; H, 7.5; N, 0.1%); ν_{max}/cm^{-1} 3448, 3025, 2923, 1719, 1602, 1492, 1451, 1420, 1271, 757, 696, 670. A loading of 0.1 mmol/g was calculated from the percentage of nitrogen present.

Polystyrene-Supported (−)-(*S*)-aziridin-2-yl Diphenylmethanol 12

Polystyrene-supported (−)-(*S*)-*N*-tritylaziridin-2-yl diphenylmethanol **10** (1.2 g, 0.12 mmol) was allowed to swell in dichloromethane (20 mL) for 30 min. Trifluoroacetic acid (0.14 g, 1.2 mmol) was added dropwise. The mixture was stirred at room temperature for 3 h. Triethylamine (0.12 g, 1.2 mmol) was added, and the reaction was stirred at room temperature for a further 1 h. The polymer beads were collected by filtration, and methanol (20 mL) was added to cause the polymer to contract. The polymer beads were washed with acetone (20 mL), water (50 mL), and methanol (50 mL) and dried under vacuum for 5 days to give the product (1.1 g, 100%) (found: C, 90.1; H, 7.6; N, 0.3%); ν_{max}/cm^{-1} 3436, 3024, 2920, 1721, 1682, 1600, 1492, 1451, 1372, 1270, 756, 696.

General Procedure for the Addition of Diethylzinc to Benzaldehyde

To a suspension of polymer-supported ligand (5 mol%) in toluene (8 mL), benzaldehyde (2 mmol) was added. The solution was cooled to 0°C prior to

the addition of diethylzinc (1.1 M solution in toluene, 4 mmol), allowed to reach room temperature, and stirred for a further 24 h. Saturated aqueous ammonium chloride was added, and the mixture was extracted into diethyl ether. The organic layer was dried over sodium sulfate to yield the crude 1-phenyl propanol, which was analyzed by GC (Chrompak, Chirasil CB, 10 psi, 140°C) without further purification.

ACKNOWLEDGMENTS

This investigation has enjoyed the support of Charnwood Molecular Ltd. and the EPSRC. We are also indebted to the EPSRC Mass Spectrometry Service, Swansea, U.K., and to the Royal Society for an industry fellowship.

REFERENCES

1. For recent reviews, see (a) Pu, L. Asymmetric alkynylzinc additions to aldehydes and ketones. *Tetrahedron* **2003**, *59*, 9873–9886; (b) Pu, L. Catalytic asymmetric organozinc additions to carbonyl compounds. *Chem. Rev.* **2001**, *101*, 757–824; For recent papers, see (c) Scarpi, D.; Lo Galbo, F.; Occhiato, E. G.; Guarno, A. Enantioselective addition of diethylzinc to aldehydes using 1,4-aminoalcohols as chiral ligands. *Tetrahedron: Asymmetry* **2004**, *15*, 1319–1324; (d) Barros, M. T.; Maycock, C. D.; Phillips, A. M. F. Novel cyclic 1,2-diacetals derived from (2R,3R)-(+)-tartaric acid: Synthesis and application as N,O ligands for the enantioselective alkylation of benzaldehyde by diethylzinc. *Eur. J. Org. Chem.* **2004**, 1820–1829.
2. (a) Rosner, T.; Sears, P. J.; Nugent, W. A.; Blackmond, D. G. Kinetic investigations of product inhibition in the amino alcohol-catalyzed asymmetric alkylation of benzaldehyde with diethylzinc. *Org. Lett.* **2000**, *2*, 2511–2513; (b) Yamakawa, M.; Noyori, R. Asymmetric addition of dimethylzinc to benzaldehyde catalyzed by (2S)-3-exo-(dimethylamino)isobornenol: A theoretical study on the origin of enantioselection. *Organometallics* **1999**, *18*, 128–133; (c) Yamakawa, M.; Noyori, R. An AB-initio molecular-orbital study on the amino alcohol–promoted reaction of dialkylzincs and aldehydes. *J. Am. Chem. Soc.* **1995**, *117*, 6327–6335; (d) Noyori, R.; Kawai, S. K.; Okada, S.; Kitamura, M. Enantioselective alkylation of carbonyl compounds—From stoiceometric to catalytic asymmetric induction. *Pure Appl. Chem.* **1988**, *60*, 1597–1606; (e) Kitamura, M.; Suga, S.; Niwa, M.; Noyori, R. Self and nonself recognition of asymmetric catalysts—Nonlinear effects in the amino-alcohol-promoted anantioselective addition of dialkylzincs to aldehydes. *J. Am. Chem. Soc.* **1995**, *117*, 4832–4842; (f) Itsuno, S.; Fréchet, J. M. J. Enantioselective addition of diethylzinc to aldehydes catalysed by polymer-supported chiral amino-alcohols—Evidence for a 2 zinc species mechanism. *J. Org. Chem.* **1987**, *52*, 4140–4142.
3. (a) Tanner, D.; Korno, H. T.; Guijarro, D.; Anderson, P. G. Aziridino alcohols as catalysts for the enantioselective addition of diethylzinc to aldehydes. *Tetrahedron* **1998**, *54*, 14213–14232; (b) Tanner, D. Chiral aziridines—Their synthesis and use in stereoselective transformations. *Angew. Chem. Int. Ed.* **1983**, *33*, 599–619;

(c) Hermsen, P. J.; Cremers, J. G. O.; Thijis, L.; Zwanenburg, B. Enantioselective diethylzinc addition to aldehydes using azetidine-derived chiral catalysts. *Tetrahedron Lett.* **2001**, *42*, 4243–4245.

4. Page, P. C. B.; Allin, S. M.; Maddocks, S. J.; Elsegood, M. R. New ligands for asymmetric diethylzinc additions to aromatic aldehydes, demonstrating substrate-dependent nonlinear effects. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2827–2832.
5. Holte, P.; Wijgergangs, J. P.; Thijs, L.; Zwanenburg, B. Polymer-supported N-tritylaziridinyl(diphenyl)methanol as an effective catalyst in the enantioselective addition of diethylzinc to aldehydes. *Org. Lett.* **1999**, *1*, 1095–1097.
6. Willems, J. G. H.; Hersmis, M. C.; Gelder, R.; Smits, J. M. M.; Hammink, J. B.; Dommerholt, F. J.; Thijs, L.; Zwanenburg, B. Synthesis and crystal structure of enantiopure N-tritylaziridin-2-yl-methanols from L-serine and L-threonine. *J. Chem. Soc., Perkin Trans. 1*, **1997**, 963–967.
7. Far, A. R.; Cho, Y. L.; Rang, A.; Rudkevich, D. M.; Rebek, J. Polymer-bound self-folding cavitands. *Tetrahedron* **2002**, *58*, 741–755.