Pergamon

Tetrahedron: Asymmetry Vol. 5, No. 2, pp. 277-282, 1994
Elsevier Science Ltd
Printed in Great Britain
0957-4166/94 $6.00+0.00

0957-4166(94)E0026-7

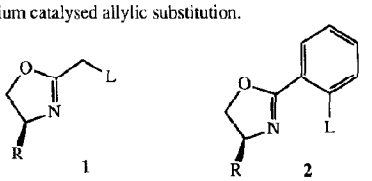
Enantiomerically Pure Oxazolines Tethered to Alcohols. Preparation and Use in Asymmetric Catalysis

Joanne V. Allen and Jonathan M. J. Williams*

Department of Chemistry, Loughborough University of Technology, Loughborough, Leicestershire, LE11 3TU, UK.

Abstract: A series of enantiomerically pure oxazolines tethered to alcohols have been prepared. The use of these oxazolines has been demonstrated in the catalysed addition of diethylzinc to aromatic aldehydes to afford the corresponding secondary alcohols with modest levels of asymmetric induction.

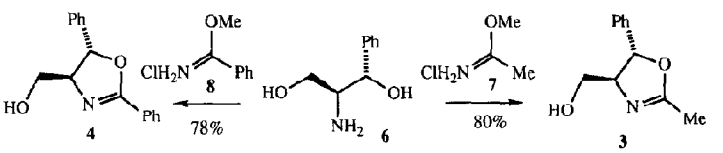
We have recently reported the preparation of enantiomerically pure oxazolines tethered to phosphines and sulphides.[1,2] Thus, ligands of type **1** and **2** have been shown by this group and others[3,4] to provide excellent asymmetric induction for palladium catalysed allylic substitution.



1 **2**

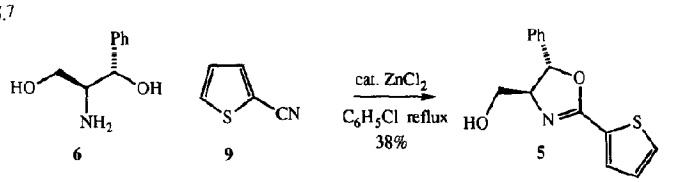
In a preliminary communication,[5] we have outlined the preparation of oxazolines **3** - **5**, and we now wish to detail the preparation of a range of oxazolines tethered to alcohols. Additionally, we report the use of these oxazolines as catalysts for the asymmetric addition of diethylzinc to aromatic aldehydes.

Initially, we prepared oxazolines in which the alcohol was tethered to the 4-position of the oxazoline group. Treatment of (1S,2S)-(+)-2-amino-1-phenyl-1,3-propanediol **6** with the imidate ester hydrochlorides **7** and **8** in dichloromethane at 20 °C for 12 hours afforded the corresponding oxazolines **3** and **4**.[6]



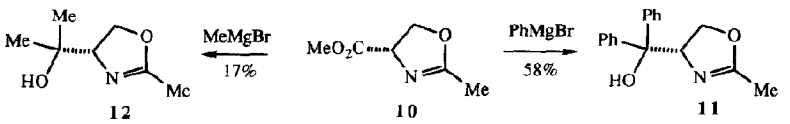
4 **6** **3**

In an alternative procedure, the reaction of (1S,2S)-(+)-2-amino-1-phenyl-1,3-propanediol **6** with thiophene 2-carbonitrile **9** in refluxing chlorobenzene in the presence of catalytic zinc chloride afforded the oxazoline **5**.[7]



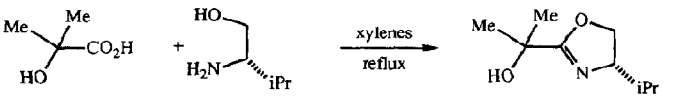
6 **9** **5**

Oxazoline **10** was prepared according to the literature procedure of Meyers and co-workers.[8] Treatment of oxazoline **10** with either phenylmagnesium bromide or methylmagnesium bromide afforded the corresponding alcohols **11** and **12**. Compound **12** was prone to hydrolysis, and was generally used shortly after preparation.



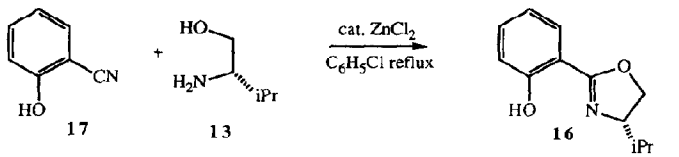
12 **10** **11**

The alcohol could alternatively be tethered to the 2-position of the oxazoline group. Based on the method of Pridgen and Miller,[9] valinol **13** was treated with 2-hydroxyisobutyric acid **14** in refluxing xylene for 16 hours to afford the oxazoline **15**.



14 **13** **15**

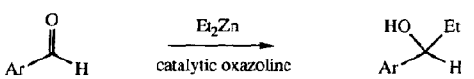
Finally, (*o*-hydroxyphenyl)oxazoline **16**, which has previously been reported by Bolm and co-workers was prepared by the reaction of *o*-cyanophenol **17** with valinol **13** in refluxing chlorobenzene in the presence of catalytic zinc chloride.[7]



17 **13** **16**

Having prepared these oxazolines, we examined their ability to catalyse the addition of diethylzinc to aromatic aldehydes. In the last few years there have been a great number of reports describing the use of amino alcohols as catalysts for the addition of diethylzinc to aldehydes, often with high levels of asymmetric induction.[10] Herein we report that oxazolines tethered to alcohols are also effective catalysts, but that only moderate levels of enantioselectivity have been obtained with these reagents.

Treatment of aryl aldehydes **18** with diethylzinc in the presence of catalytic amounts the oxazolines afforded the corresponding alcohols **19**. In a typical run, the aldehyde and catalyst were stirred in hexane for 30 minutes, followed by the addition of two equivalents of diethylzinc (6 mol%). The reaction was stirred for the time indicated in the Table, followed by a conventional work-up.



18 **19**

The enantiomeric excess obtained under a variety of conditions is summarised in the Table. The enantiomeric excess of the product was determined either by chiral hplc or chiral gc, and the absolute configuration determined by comparison with reported optical rotation data.[11]

With the exception of the oxazolines **11** and **12** (which are derived from serine), all of the oxazoline catalysts provide the same sense of asymmetric induction in the product. The oxazolines all possess the same relative configuration as each other, except for oxazolines **11** and **12**.

The oxazolines **3**, **4**, and **5** derived from (1S,2S)-(+)-2-amino-1-phenyl-1,3-propanediol proved to be better catalysts than the other oxazolines examined in terms of stability, and the yield and enantioselectivity provided in the ethylation of aryl aldehydes. Initially, we had anticipated that by replacing the hydroxymethyl substituent with a bulkier tether (as for oxazolines **11** and **12**) that superior enantioselectivities could be obtained. However, from the results indicated, it seems that this is not the case. It is possible that in the reaction of oxazoline **10** with the Grignard reagents that some racemisation may occur prior to alkylation, which would afford a catalyst which was not enantiomerically pure. However, due to the hydrolytic susceptibility of these ligands, we did not explore this possibility any further.

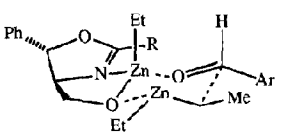
Previously, the use of the lithium salt of amino alcohols has been reported to enhance the enantioselectivity of the catalysed reaction for some systems. However, treatment of oxazoline **3** with one equivalent of butyllithium afforded a catalyst which provided identical levels of enantioselectivity, although the yield of product was seen to increase slightly.

Table: Reaction of arylaldehydes with diethylzinc in the presence of catalysts

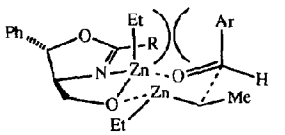
Catalyst	*Substrate: Ar*	*Time (hr)*	*Yield (%)*	*ee*
3	C_6H_5-	18	60	50 (S)[a]
3	2-$MeOC_6H_4$-	18	86	67 (S)[b]
3	4-$MeOC_6H_4$-	18	75	58 (S)[b]
3[d]	4-$MeOC_6H_4$-	18	87	58 (S)[b]
4	C_6H_5-	18	65	57 (S)[a]
4[e]	C_6H_5-	18	48	47 (S)[a]
4	2-$MeOC_6H_4$-	18	78	59 (S)[b]
4	4-$MeOC_6H_4$-	18	86	25 (S)[b]
5	C_6H_5-	18	93	57 (S)[a]
5	4-$MeOC_6H_4$-	18	71	49 (S)[b]
11	C_6H_5-	4	27	30 (R)[c]
11	4-$MeOC_6H_4$-	4	35	23 (R)[c]
12	C_6H_5-	35	46	7 (R)[c]
12	4-$MeOC_6H_4$-	35	61	14 (R)[c]
15	4-$MeOC_6H_4$-	35	37	25 (S)[c]
16	4-ClC_6H_4-	67	92	23 (S)[a]
16	C_6H_5-	22	8	14 (S)[b]

[a] Determined by chiral hplc using a Chiralcel OB column. [b] Determined by optical rotation. [c] Determined by chiral hplc using a Cydex B column. [d] The catalyst was employed as the lithium salt - see the text.
[e] The amount of catalyst was reduced from 6 mol% to 2 mol%

The following transition state is consistent with the observed sense of asymmetric induction, and also with previously proposed models.[11] In the absence of crystallographic data, these models are purely speculation, but are nevertheless consistent with the observed experimental outcome in terms of the sense of asymmetric induction obtained.



Favoured



Disfavoured

In summary, we have investigated the use of enantiomerically pure oxazolines tethered to alcohols as catalysts for the asymmetric addition of diethylzinc to aromatic aldehydes. Good catalytic activity was observed, but only modest levels of asymmetric induction have been achieved.

We are currently investigating applications of these ligands in other processes.

EXPERIMENTAL

Reactions with diethylzinc were performed in a dry nitrogen atmosphere. Commercially available solvents and reagents were purified by standard methods. For column chromatography, Merck Kieselgel 60H was used. ^{1}H and ^{13}C NMR spectra were recorded using Bruker AC-250 and WH-400 (SERC NMR Spectroscopy Centre, Warwick) instruments. High and low resolution mass spectra were recorded on a Kratos MS80 instrument or on a VG Analytical ZAB-E instrument (SERC mass spectroscopy service, Swansea). Infra-red spectra were recorded in the range 4000-600 cm^{-1} using a Nicolet FT-205 spectrometer, with internal calibration. Spectra were recorded as solutions in chloroform or as thin films. Optical rotations were carried out on an Optical Activity AA100 polarimeter. HPLC analyses were carried out on a Waters liquid chromatograph, using a Diacel Chiralcel OB column; solvent, 10-25% isopropanol : hexane; flow rate, 0.5 ml. min^{-1}; 254 nm detection. GC analyses were carried out on a Pye Unicam Series 204 Chromatograph, using an SGE Cydex-B 0.25 chiral capillary column; injector temperature, 200°C; detector temperature, 250°C; oven temperature, 120°C; helium carrier gas (10 lb / in^2); detector, F.I.D. In each case, the (R)-enantiomer is detected first.

(4S,5S)-2-methyl-4-hydroxymethyl-5-phenyl-1,3-oxazoline **3**

(1*S*, 2*S*)-(+)-2-Amino-1-phenyl-1,3-propanediol **6** (9.03 g, 54 mmol) was added in one portion to a solution of imino ether hydrochloride **7** (54 mmol) in dry dichloromethane (30ml) at 0°C. The mixture was warmed to room temperature and stirred for 12 h. The white turbid mixture was poured into ice water (50g). The dichloromethane layer was separated and the aqueous layer extracted with dichloromethane (2 x 20 ml). The combined organic layers were dried ($MgSO_4$) then concentrated *in vacuo* to give a colourless oil which solidified on standing. Crystallisation from ether by cooling to -78°C gave crystalline **3** (8.25g, 80%).

M.p. 62-63°C (lit.[12] (64-65°C). υ_{max} / cm^{-1} 1670(C=N). δ_H (400 MHz, $CDCl_3$) 2.08(3H, s, CH_3), 3.63 (1H, dd, J=4.0, 11.9 Hz, CHHOH), 3.92 (1H, dd, J=3.4, 11.9 Hz, CHHOH), 3.99-4.03 (1H, m, CHN), 5.33 (1H, d, J=7.8 Hz, CHPh), 7.25-7.39 (5H, m, ArH). δ_C (100 MHz, $CDCl_3$) 13.8 (CH_3), 62.9 (CH_2OH), 76.1 (CHN), 82.8 (ArCH), 125.6 (ArCH) 125.7 (ArCH), 127.5 (ArCH), 128.2 (ArCH), 128.7 (ArCH), 140.1(ArC), 166.1(C=N). *m/z* (FAB) 192 (MH+, 100%), 162 (10), 85 (9), 68 (6). $[\alpha]_D^{25}$ -174.6 (c=10.5, $CHCl_3$).

(4S,5S)-2-phenyl-4-hydroxymethyl-5-phenyl-1,3-oxazoline **4**

Using an identical procedure, we prepared **4**.(10.7g, 78%). M.p. 127-129°C. (Found : C, 76.06; H, 5.71; N, 5.98. $C_{16}H_{15}NO_2$ requires C, 75.86; H, 5.97; N, 5.53%). υ_{max} / cm^{-1} 1670(C=N). δ_H (400 MHz, $CDCl_3$) 3.77 (1H, dd, J=3.7, 12.0 Hz, CHHOH), 4.11 (1H, dd, J=3.4, 11.9 Hz, CHHOH), 4.22 (1H, dt, J=3.5 Hz, CHN), 5.56 (1H, d, J=8.0 Hz, CHO), 7.32-7.89(10H, m, ArCH). δ_C (100 MHz, $CDCl_3$) 63.2 (CH_2OH), 77.2 (CHN), 82.6 (CHO), 125.7 (ArCH), 128.2 (ArCH), 128.3 (ArCH), 128.5 (ArCH), 128.7 (ArCH), 128.8 (ArCH), 131.5 (ArC), 140.3 (ArC), 164.7 (C=N). *m/z* (FAB) 254 (MH^+, 100%), 224 (16), 147 (8), 121 (9), 105 (11). $[\alpha]_D^{25}$ -44.6 (c=5.4, $CHCl_3$).

(4S, 5S)-4-hydroxymethyl-5-phenyl-2-(2-thiophenyl)-1,3-oxazoline **5**

In a 50ml Schlenk flask, zinc chloride (68mg, 0.5 mmol) was melted under high vacuum and cooled under nitrogen. After cooling to room temperature, chlorobenzene (30 ml) was added followed by 2-thiophene carbonitrile **9** (10 mmol) and (1*S*,2*S*)-(+)-1-phenyl-2-amino-1,3-propanediol **6** (13 mmol). The mixture was heated under reflux for 24 hours. The solvent was removed under reduced pressure to give an oily residue, which was dissolved in dichloromethane (30 ml). The solution was extracted three times with water (20 ml) and the aqueous phase with dichloromethane (30 ml). The combined organic phases were dried (Na_2SO_4), and the solvent removed *in vacuo*. The residue was purified by flash chromatography (light petroleum/ether 3:1) to afford the **5** (1.0 g, 38 %) as an off-white crystalline solid.

M.p. 160-162°C. (Found : C, 65.00; H, 5.01; N, 5.39. $C_{14}H_{13}NO_2S$ requires C, 64.85; H, 5.06; N, 5.41%). υ_{max} / cm^{-1} 1670(C=N). δ_H (400 MHz, $CDCl_3$) 3.76 (1H, dd, J=3.2, 11.9 Hz, CHHOH), 4.02 (1H, br s,

OH), 4.11 (1H, dd, J=3.2, 12.0 Hz, CHHOH), 4.21 (1H, dt, J=3.2 Hz, CHN), 5.60 (1H, d, J=8.1 Hz, CHO), 7.00 (1H, ap t, J = 4.2, 4.6 Hz, thiophene CH), 7.31-7.40 (5H, m, ArCH), 7.42 (1H, d, J = 5.0, thiophene CH), 7.57 (1H, d, J = 3.7, thiophene CH). δ_C (100 MHz, $CDCl_3$) 62.9 (CH_2OH), 76.7 (CHN), 83.0(CHO), 125.8 (ArCH), 127.5 (ArCH), 128.3 (ArCH), 128.7 (ArCH), 129.4 (ArCH), 130.3 (ArCH), 130.9 (ArCH), 140.0 (ArC), 160.4(C=N). *m/z* (CI) 260 (MH^+, 100%), 230 (27), 111 (9). $[\alpha]_D^{25}$ +50.0 (c=1.02, $CHCl_3$).

General procedure for the addition of diethylzinc to aromatic aldehydes using catalysts **3**, **4**, and **5**.

(S)-(-)-1-Phenylpropanol :

Benzaldehyde (106 mg, 1.0 mmol) and catalyst **3** (11.4 mg, 0.06 mmol) as a solution in hexane (5 ml) were placed in a flame dried flask which had been purged with nitrogen. After stirring at room temperature for 0.5 h, diethylzinc (2 ml, 2.0 mmol) was added. After the indicated time, the reaction was quenched with hydrochloric acid (1 M, 2 ml) and the mixture was extracted into dichloromethane (3 x 20 ml). The dichloromethane extract was dried ($MgSO_4$) and concentrated *in vacuo* and the residue was purified by column chromatography (silica : dichloromethane) to give the corresponding alcohol as a pale yellow oil.

1-Phenylpropanol

δ_H (250 MHz; $CDCl_3$) 0.82 (3 H, t, J = 7.4, CH_3), 1.56-1.82 (2 H, m, CH_2), 2.09 (1 H, br s, OH), 4.48 (1H, t, J = 6.6, CH), 7.24 (5H, s, ArCH). δ_C (62.9 MHz; $CDCl_3$), 10.10 (CH_3), 31.76 (CH_2), 75.83 (CH), 125.99 (CH), 127.31 (CH), 128.26 (CH).

2-Methoxyphenylpropanol

δ_H (250 MHz; $CDCl_3$), 0.96 (3H, t, J = 7.4, CH_3), 1.76-1.88 (2H, m, CH_2), 2.62 (1H, br s, OH), 3.85 (3H, s, OCH_3), 4.79 (1H, t, J = 6.6, CH), 6.87-7.00 (2H, m, ArCH), 7.22-7.33 (2H, m, ArCH). δ_C (62.9 MHz, $CDCl_3$),10.42 (CH_3), 30.10 (CH_2), 55.17 (OCH_3), 72.25 (CHOH), 110.42 (CH), 120.61 (CH), 126.99 (CH), 128.11 (CH), 132.33 (CH).

4-Methoxyphenylpropanol

δ_H (250 MHz; $CDCl_3$), 0.89 (3H, t, J = 7.4, CH_3), 1.17-1.28 (1H, m, CH_2), 2.31 (1H, br s, OH), 3.75 (3H, s, OCH_3), 4.53 (1H, t, J = 6.6, CH), 6.84-6.91 (2H, m, ArCH), 7.23-7.30 (2H, m, ArCH). δ_C (62.9 MHz; $CDCl_3$) 10.15 (CH_3), 31.69 (CH_2), 55.16 (OCH_3), 75.47 (CH), 113.63 (ArCH), 127.15 (ArCH).

4-Chlorophenylpropanol

δ_H (250 MHz, $CDCl_3$), 0.86 (3H, t, J = 7.4, CH_3), 1.61-1.81 (2H, m, CH_2), 2.66 (1H, br s, OH), 4.51 (1H, t, J = 6.6, CH), 7.20-7.32 (4H, m, ArCH). δ_C (62.9 MHz, $CDCl_3$), 9.91 (CH_3), 31.82 (CH_2), 75.15 (CHOH), 127.31 (CH), 128.19 (CH), 128.40 (CH), 128.53 (ArC), 128.85 (ArC).

(4S)-4-hydroxydiphenyl-2-methyl-1,3-oxazoline **11**

To phenylmagnesium bromide (2.0 ml, 3M in diethyl ether) at -78 °C , a solution of **10**[8] (250 mg, 1.75 mmol) in THF (4 ml) was added dropwise. The reaction was maintained at -78 °C for 2 h then allowed to warm to room temperature overnight (16 h). The reaction mixture was poured onto ammonium chloride (sat. soln., 15 ml) and extracted with diethyl ether (3 x 10 ml). The combined organic extracts were dried (K_2CO_3), filtered and concentrated to a yellow oil (810 mg). Purification by column chromatography (petroleum ether - petroleum ether : diethyl ether (3 :1)) yielded **11** as a colourless oil (270 mg, 1.01 mmol, 58 %).

υ_{max}/cm^{-1}; δ_H (250MHz, $CDCl_3$) 1.97 - 1.98 (3H, s, CH_3), 4.03 - 4.15 (2H, m, CH_2O), 5.31 (1H, ap t, J = 8.7, 10.0 Hz, CHN), 7.17 - 7.61 (ArCH). δ_C (62.9MHz, $CDCl_3$) 14.01 (CH_3), 69.09 (CH_2O), 72.50 (CHN), 125.47 (ArCH), 126.47 (ArCH), 127.05 (ArCH), 127.93 (ArC), 128.27 ArC). Susceptabiliy to hydrolysis prevented further characterisation

(4S)-4-hydroxydimethyl-2-methyl-1,3-oxazoline **12**

To methylmagnesium iodide (3.5 ml,.3M in diethyl ether) at -78 °C, a solution of **10** (500 mg, 3.5 mmol) in THF (8ml) was added dropwise. The reaction was maintained at this temperature for a further hour before allowing to warm to R.T. overnight (~16 h.). The reaction mixture was poured onto ammonium chloride (sat. soln., 15 ml) and extracted with diethyl ether (10 ml). The organic layer was dried (K_2CO_3), filtered and concentrated to yield crude **52** as an orange/brown oil (60 mg, 0.42 mmol, 17 %). υ_{max} /cm^{-1} 1673. δ_H

(250MHz, $CDCl_3$), 1.14 (3H, s, CH_3), 1.28 (3H, s, CH_3), 2.00 (3H, s, CH_3), 3.97 (1H, t, J = 10.0 Hz, CHN), 4.12-4.26 (2H, m, CH_2O). δ_C (62MHz, $CDCl_3$), 13.76 (CH_3), 25.01 (CH_3), 26.67 (CH_3), 68.65 (CH_2O), 75.24 (CHN). Susceptibiliy to hydrolysis prevented further characterisation

(4S)-2-hydroxydimethyl-4-isopropyl-1,3-oxazoline **15**

To a solution of 2-hydroxyisobutyric acid **14** (415mg, 3.99mmol) in xylene (12ml) was added (S)-(+)-2-amino-3-methyl-1-butanol (valinol) **13** (415mg, 4.02mmol) and the reaction was brought to reflux in a Dean-Stark trap. After 30 h, no more water was produced. The solvent was removed by evaporation to yield **15** as a colourless oil (625mg, 3.65mmol, 92%). (found M+, 171.1168, $C_9H_{17}NO_2$ requires M+, 171.1259) υ_{max} / cm^{-1} 3391 (OH), 1661 (C=N). δ_H (400 MHz, $CDCl_3$) 0.95 (6H, dd, J = 6.8, 12.2 Hz, 2 x CH_3), 1.46 (6H, d, J = 7.6 Hz, 2 x CH_3), 1.87-1.95 (1H, m, CH), 4.03-4.10 (1H, ap.t, J = 8.2, 9.3 Hz, CHN), 4.20-4.27 (2H, d, J = 5.5 Hz, CH_2O) .δ_C (100 MHz, $CDCl_3$) 18.29 (CH_3), 19.28 (CH_3), 27.22 (CH_3), 27.64 (CH_3), 32.24 (CH), 65.61 (CH_2O), 71.18 (CHN). *m/z* (E.I.) 171 (M+, 4%), 128 (41), 98 (100). $[\alpha]_D^{25}$ -102.3 (c=0.42, $CHCl_3$).

(4S)-2-(Hydroxyphenyl)-4-isopropyl-2-oxazoline **16**

To 2-amino-3-methyl-1-butanol (valinol) **13** (453 mg, 4.40 mmol) in chlorobenzene (10 ml) was added 2-cyanophenol **17** (520 mg, 4.37 mmol) and a catalytic amount of zinc chloride (11 mg, 0.08 mmol). The reaction was brought to reflux for 18h. The chlorobenzene was removed by evaporation to yield a brown oil. The residue was chromatographed on a silica gel column with dichloromethane as eluent to yield **16** as a colourless oil (483 mg, 2.36 mmol, 54%). (found M+, 205.1105, $C_9H_{17}NO_2$ requires M+, 205.1103) υ_{max}/cm^{-1} 1644 and 756. δ_H (250 MHz, CDCl3) 0.92 (3H, d, 6.7 Hz, CH_3), 0.995 (3H, d, 6.7 Hz, CH_3), 1.80 (1H, m, isopropyl CH), 4.06 - 4.16 (2H, m, CH_2O), 4.35 - 4.49 (1H, m, CHN), 6.81 (1H, t, J = 7.65 Hz, ArCH), 6.98 (1H, d, 8.2 Hz, ArCH), 7.31 - 7.36 (1H, m, ArCH), 7.61 (1H, dd, 1.7, 7.9, Hz, ArCH). δ_C (62.9 MHz, CDCl3).18.57 (CH_3), 18.67 (CH_3), 33.01 (CH, isopropyl), 69.84 (CH_2), 71.51 (CHN), 110.70 (ArC), 116.67 (CH), 118.52 (CH), 127.97 (CH), 133.23 (CH), 159.98 (C=N), 165.06 (ArC). *m/z* (EI) 205 (M+, 57%), 162 (100), 134 (34), 107 (28). $[\alpha]_D^{25}$ -35.4 (c=1.07, $CHCl_3$)

Procedure using lithium salt of trans-(4S, 5S)-2-methyl-4-hydroxymethyl-5-phenyl-1,3-oxazoline **3**

Reaction of *n*-butyllithium (200µl, 0.32mmol) with oxazoline **3** (61mg, 0.32mmol) in hexane / toluene (1:1, 4ml) at 0 °C yielded the lithium salt of **3** *in situ*. At this temperature 4-methoxybenzaldehyde (680mg, 5.0mmol) was added and the reaction flask then allowed to warm to room temperature before the addition of diethylzinc (1M soln. in hexanes, 10ml, 10mmol). The pale yellow reaction mixture was stirred for a further 36 h at room temperature. The reation was quenched with hydrochloric acid (1M, 2ml) and the mixture extracted into dichloromethane (3 x 20ml). The combined dichloromethane extracts were dried ($MgSO_4$) and concentrated *in vacuo* to give the corresponding alcohol as a pale yellow oil (88%)

Acknowledgment: We are grateful to the SERC for an earmarked studentship (to JVA).

References and Notes:

1. G. J. Dawson, C. G. Frost, J. M. J. Williams and S. J. Coote, *Tetrahedron Lett.*, 1993, **34**, 3149.
2. G. J. Dawson, C. G. Frost, C. J. Martin, J. M. J. Williams and S. J. Coote, *Tetrahedron Lett*, 1993, **34**, 7793.
3. P. von Matt and A. Pfaltz, *Angew. Chem. Int. Ed. Engl.*, 1993, **32**, 566
4. J. Sprinz and G. Helmchen, *Tetrahedron Lett.*, 1993, **34**, 1769.
5. J. V. Allen, C. G. Frost and J. M. J. Williams, *Tetrahedron: Asymmetry*, 1993, **4**, 649.
6. A. I. Meyers, G. Knaus, K. Kamata and M. E. Ford, *J. Am. Chem. Soc.*, 1976, **98**, 567. (b) Formation of oxazolines from nitriles; D. P. Schumacher, J. E. Clark, B. L. Murphy and P. A. Fischer, *J. Org. Chem.*, 1990, **55**, 5291.
7. C. Bolm, K. Weickhardt, M. Zehnder and T. Ranff, *Chem. Ber.*, 1991, **124**, 1173.
8. A. I. Meyers, W. Schmidt, M. J. McKennon, *Synthesis*, 1993, 250.
9. L. N. Pridgen and G. Miller, *J. Heterocyclic Chem.*, 1983, **20**, 1223.
10. For a useful review on the enantioselective addition of organozinc reagents to aldehydes, see; K. Soai and S. Niwa, *Chem. Rev.*, 1992, **92**, 833.
11. For each of the products described here, a negative rotation indicates the (S)-enantiomer. (a) K. Soai, S. Yokoyama and T. Hayasaka, *J. Org. Chem.*, 1991, **56**, 4264. (b) M. Watanabe, S. Araki, Y. Butsugan and M. Uemura, *J. Org. Chem.*, 1991, **56**, 2218.
12. A. I. Meyers, G. Knaus, K. Kamata, and M. E. Ford, *J. Am. Chem. Soc.*, 1976, **98**, 567.

(*Received in UK* 21 *December* 1993)