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TETRAHEDRON: *ASYMMETRY*

Enantioselective allylic alkylation using polymer-supported palladium catalysts

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Abstract

Chiral 2′-(4′′,5′′-dihydro-2′′-oxazolyl)-6′-(1-hydroxyalkyl)pyridines were grafted via ester-linkages directly to cross-linked polystyrene and to polyethyleneglycol-containing resins TentaGel and ArgoGel functionalized with carboxylic acid groups or via spacers containing a carboxylic acid group. The polymeric ligands were used in the palladium-catalyzed substitution of *rac*-1,3-diphenyl-2-propenyl acetate with dimethyl malonate. The enantioselectivities (up to 80% ee) were similar to those observed employing an analogous monomeric catalyst.

1. Introduction

In recent years the interest in using functionalized polymers has been constantly growing. The development of solid-supported reagents and catalysts[1] has been stimulated by the preparation of new types of polymeric supports, such as graft-copolymers of gel-type polystyrene and polyoxyethylene,[2] which have complemented the traditionally used polystyrene–divinylbenzene resins.[3] Reagents bound to the new types of resins can be used in solvents with a wider range of polarity and are more easily analyzed by spectroscopic methods in the solvent-swollen state.

Solid phase asymmetric metal catalysts have attractive properties as they can be easily separated from the reaction mixture after the catalytic reaction, thereby facilitating the purification of the product. Occasionally such catalysts may also be recovered and reused in the catalytic process.[4] The palladium-catalyzed allylic alkylation is a synthetically important process in that new carbon–carbon bonds are formed.[5] With chiral catalysts, high enantioselectivities have often been observed.[5a] Pyridinooxazolines **1** are highly useful ligands in the reaction.[6] The selectivity is highly dependent on the structure of the substituent in the 6-position of the pyridine ring; ees ranging from 15 to >99% have been observed.[6a] In addition, pyridinooxazolines are known to induce chirality in various metal-mediated processes such as

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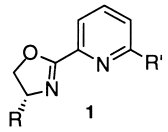
Rh[7]- and Co-catalyzed[8] hydrosilylations, Diels–Alder reactions,[9] Cu-catalyzed allylic acyloxylations,[10] Meerwein arylation of activated olefins,[11] 1,4-additions,[12] epoxidations,[13] additions of diethylzinc[14] and of allylsilanes[15] to aldehydes, monophenylation of *meso*-diols[16] and in π-complexation.[17]



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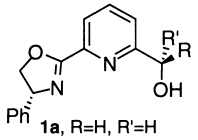
A polymeric pyridinooxazoline has previously been prepared and employed in Rh-catalyzed hydrosilylations.[18] The polymeric ligand was prepared via reaction of the pyridinooxazoline with lithiated 2% cross-linked polystyrene, resulting in substitution primarily at the 6-position of the pyridine ring. Since we have found that pyridinooxazolines containing 1-alkoxymethyl or 1-hydroxymethyl groups in the 6-position of the pyridine ring (**1**, R′=CH(OR^1)R^2) induce high selectivity in catalytic reactions as a result of restricted rotation around the pyridine carbon–carbinol carbon bond,[19] attachment of 6-hydroxymethyl derivatives of **1** (R′=CH_2OH) was preferred. In principle, immobilization of such derivatives to a polymer can be achieved by substitution of the pyridine ring or via functionalization of the substituent in the oxazoline ring (R) or of the substituent in the pyridine ring (R′). A route involving functionalization at oxygen was expected to yield suitable polymeric derivatives and was therefore chosen.

We present here the preparation of pyridinooxazolines supported on appropriately functionalized 1% cross-linked polystyrene, TentaGel and ArgoGel. The new polymers have been assessed in the palladium-catalyzed allylation of dimethyl malonate.[20] The results are compared to those obtained employing monomeric analogs as catalysts.

2. Results and discussion

2.1. Preparation of polymeric ligands

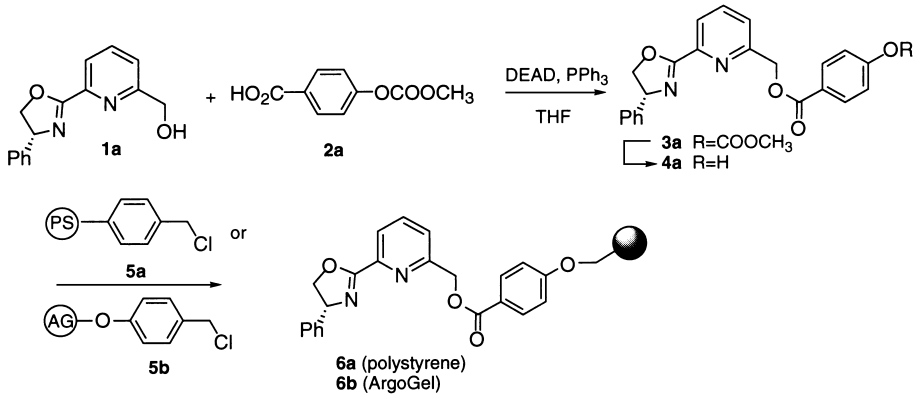
(4″*R*)-2′-(4″,5″-Dihydro-4″-phenyl-2″-oxazolyl)-6′-(hydroxymethyl)pyridine[6b] **1a**, (4″*R*,2*R*)-2′-(4″,5″-dihydro-4″-phenyl-2″-oxazolyl)-6′-(2,2-dimethyl-1-hydroxypropyl)pyridine (*R*,*R*)-**1b** and (4″*R*,2*S*)-2′-(4″,5″-dihydro-4″-phenyl-2″-oxazolyl)-6′-(2,2-dimethyl-1-hydroxypropyl)pyridine (*R*,*S*)-**1b** were selected as suitable ligands for attachment to polymeric supports, either via a spacer containing a carboxylic acid group or directly to a polymer functionalized with carboxylic acid groups.



1a, R=H, R'=H
(*R*,*R*)-**1b**, R=^{t}Bu, R'=H
(*R*,*S*)-**1b**, R=H, R'=^{t}Bu

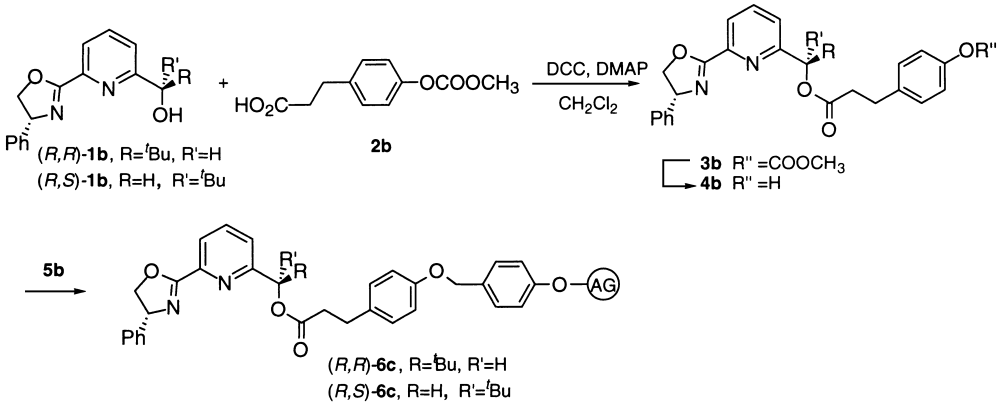
Since phenolic compounds react readily with chloromethylated polymers,[21] reaction of **1a** with a spacer containing a protected phenolic residue was considered as an appropriate strategy for the preparation of the polymer-supported ligand. Carbonate **2a** was selected as a suitable compound for this purpose,[22] as the carbonate group can be deprotected under mild conditions after reaction with the pyridinecarbinol, to yield the desired phenol. Chloromethylated polystyrene–1% divinylbenzene (**5a**, 1.6 mmol chloromethyl groups/g resin) and ArgoGel™–Wang–Cl (**5b**, 0.35–0.45 mmol chloromethyl groups/g resin) were chosen as polymeric supports.

Since esterification of **2a** with the model alcohol 2-(hydroxymethyl)pyridine using DCC/DMAP[23] resulted in a low yield (20%) of product, Mitsunobu coupling[24] of **1a** and **2a** was employed, affording the desired **3a** (Scheme 1) as a crude product which was used in the next step without further purification. Deprotection with aqueous ammonia yielded phenol **4a** (56% over two steps), which was treated with chloromethylated polystyrene–1% divinylbenzene **5a** and ArgoGel™–Wang–Cl **5b** in DMF in the presence of K_2CO_3 to afford polymers **6a** and **6b**, respectively. The increase in weight of the polystyrene resin **6a** indicated a conversion of about 57%, which was in agreement with the elemental analysis (1.78% N, corresponding to 51% conversion). The signal at δ 46.29 (CH_2Cl) in the ^{13}C NMR spectrum of the ArgoGel resin **6b** disappeared completely, but the resin was shown to contain merely 0.56% N by elemental analysis (corresponding to ca 55% conversion).



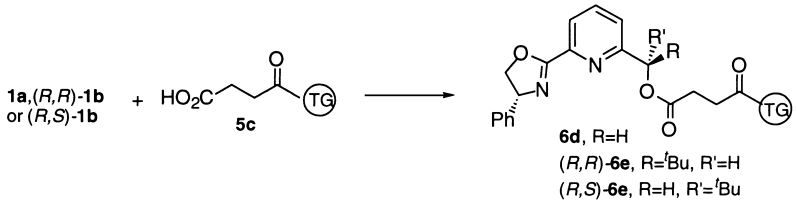
Scheme 1.

Ligands (*R,R*)-**1b** and (*R,S*)-**1b** (Scheme 2) were also grafted on an ArgoGel resin. Attempts to react a model compound containing a secondary alcohol group, *rac*-2-(2,2-dimethyl-1-hydroxypropyl)pyridine, with **2a** under Mitsunobu conditions were unsuccessful. The sterically less hindered carbonate **2b**, containing two carbon atoms between the carboxylic acid function and the aromatic ring, was also unreactive under the same conditions, but reacted with (*R,R*)-**1b** and (*R,S*)-**1b** in the presence of DCC and DMAP to yield (*R,R*)-**3b** (65%) and (*R,S*)-**3b** (58%), respectively. Subsequent deprotection (to give (*R,R*)-**4b**, 93%, and (*R,S*)-**4b**, 95%) and reaction with ArgoGel™–Wang–Cl (**5b**) gave the desired polymers (*R,R*)-**6c** and (*R,S*)-**6c** (0.42% and 0.43% N, respectively, corresponding to ca 40% conversion).



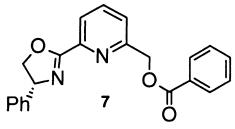
Scheme 2.

A TentaGel resin containing carboxylic acid group **5c** was also used as a solid support in order to allow direct attachment of the ligand to the polymer. Ligand **1a** was thus reacted with **5c** in the presence of DCC/DMAP to yield, according to ^{13}C NMR spectroscopy, the desired polymer **6d** (Scheme 3). From ligands (*R*,*R*)-**1b** and (*R*,*S*)-**1b** polymers (*R*,*R*)-**6e** and (*R*,*S*)-**6e**, respectively, were prepared using the same procedure. According to elemental analysis, essentially complete conversion to the products **6d** and (*R*,*R*)-**6e** took place. Polymer (*R*,*S*)-**6e** was formed in about 80% yield.



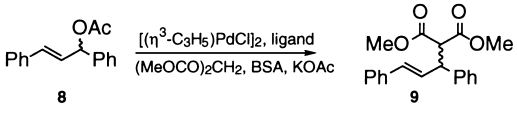
Scheme 3.

Finally, in order to allow comparison of the reactivity and selectivity of the polymeric catalysts with a monomeric analog, ester **7** was prepared from **1a** and benzoic acid.



2.2. Catalytic reaction

Polymer-supported ligands **6d**, (*R*,*R*)-**6e** and (*R*,*S*)-**6e**, which were conveniently obtained in high yields, and monomer **7**, were assessed in the palladium-catalyzed allylic substitution of *rac*-1,3-diphenyl-2-propenyl acetate **8**. The reactions were performed in CH_2Cl_2 at room temperature in the presence of a (π-allyl)palladium–ligand complex generated in situ from 2.0 mol% of bis[(π-allyl)palladium chloride] and ca 6 mol% of the appropriate ligand. The nucleophile was generated from dimethyl malonate in the presence of *N*,*O*-bis(trimethylsilyl)acetamide (BSA) and a catalytic amount of KOAc (Scheme 4).[25]



Scheme 4.

The reactions were slow, requiring about seven days reaction time. All ligands (i.e. polymers **6d**, **6e** and monomer **7**) gave the product **9** of *R* absolute configuration with similar enantioselectivities (Table 1). Very low yields of **9** were observed when the sterically bulky ligands **6e** were employed. The yields of **9** using **6d** and **7** varied considerably (60–100%) but the enantioselectivity was always reproducible.

In contrast to previous investigations,[6a] only minor differences in the enantioselectivity exhibited by diastereomeric ligands were observed in the present study. However, the low yields of products obtained using ligands (*R*,*R*)-**6e** and (*R*,*S*)-**6e** do not allow definite conclusions regarding the selectivity, which has previously been shown to depend on the conformational preferences of the ligands.[26]

Table 1
Alkylation of *rac*-1,3-diphenyl-2-propenyl acetate with dimethyl malonate[a]

Catalyst	Polymer	Yield[b] (%)	ee[c] (%)
6d	TentaGel	60-100	80
(*R*,*R*)-**6e**	TentaGel	4	66
(*R*,*S*)-**6e**	TentaGel	3	61
7	-	76-98	77

[a] Solvent: CH_2Cl_2; reaction time: 7 days; catalyst: 2 mol% $[(\eta^3\text{-}C_3H_5)PdCl]_2$; 6 mol% ligand. [b] Values from 2-4 reactions. [c] Determined by HPLC analysis using a chiral column (Chiracel-OD-H)

3. Conclusion

Chiral polymer-supported pyridinooxazolines have been prepared and assessed in the palladium-catalyzed substitution of *rac*-1,3-diphenyl-2-propenyl acetate. The use of a polymer obtained in high yield from (4′′*R*)-2′-(4′′,5′′-dihydro-4′′-phenyl-2′′oxazolyl)-6′-(hydroxymethyl)pyridine **1a** and TentaGel HL-COOH® resulted in high yield and good enantioselectivity (80% ee).

4. Experimental

4.1. General

^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 400 and 100.6 MHz, respectively, unless otherwise stated. Enantiomeric excesses were determined by HPLC using a chiral column (Chiralcel OD-H). Merck Kieselgel 60H was used for flash chromatography. Three different polymeric supports were used: chloromethylated[27] SX1, which is a polystyrene resin cross-linked with 1% divinylbenzene from Bio-Rad, **5a**, ArgoGel™–Wang–Cl **5b** from Aldrich, bead size ca 170 μm and TentaGel HL-COOH® **5c** from Fluka, bead size ca 110 μm, which are graft-copolymers of a gel-type polystyrene (cross-linked with 1% divinylbenzene) and polyoxyethylene. The palladium-catalyzed allylations were performed as described previously.[6a]

4.2. Compound *1a*. Imidate

To a solution of 2-cyano-6-(hydroxymethyl)pyridine (0.25 g, 1.83 mmol) in methanol (6 mL) was added sodium methoxide (10 mg, 0.19 mmol). The mixture was stirred for 1 day at room temperature and the solvent removed under pressure to give the expected product as a yellow solid, which was used without further purification: ^1H NMR δ 9.31 (1H, NH, s), 7.77–7.83 (2H, aromatic, m), 7.35–7.41 (1H, aromatic, m), 4.83 (2H, CH_2, s), 4.01 (3H, CH_3O).

To the above imidate (0.29 g, 1.72 mmol) in CH_2Cl_2 (7 mL) was added a solution of (*R*)-2-phenylglycinol (0.24 g, 1.72 mmol) in CH_2Cl_2 (2.5 mL). A few drops of conc. H_2SO_4 were added, the mixture was stirred at reflux for 3 days, and then saturated aqueous Na_2CO_3 (8 mL) was added. The phases were separated, the aqueous layer was extracted with CH_2Cl_2 (3×8 mL), and the combined

organic phases were dried over $MgSO_4$. Evaporation of the solvent in vacuo gave **1a** (0.43 g, 91%) as an oil, according to ^{1}H NMR identical to **1a** prepared previously in lower yield using another method.[6b]

4.3. 4-(Methoxycarbonyloxy)benzoic acid *2a*

4-Hydroxybenzoic acid (2.03 g, 14.6 mmol) was added to a slurry of sodium hydroxide (1.69 g, 42.3 mmol) in water (45 mL) at −10°C under vigorous stirring. The reaction mixture was allowed to warm to −5°C and methyl chloroformate (2.22 g, 23.3 mmol) was added over a period of 10–15 min. The reaction was allowed to warm to room temperature, then stirred overnight and quenched by adding a mixture of HCl:H_2O, 1:1, until a pH of 3 was reached, which resulted in the formation of a thick white precipitate. The white solid was filtered off, washed with water and finally dried to yield **2a** (2.83 g, 99%): mp 163–168°C; ^{1}H NMR δ 8.16 (2H, aromatic, d, *J*=8.5 Hz), 7.31 (2H, aromatic, d, *J*=8.5 Hz), 3.94 (3H, CH_3O, s); the acidic proton was not observed.

4.4. Compound *3a*

Spacer **2a** (69.3 mg, 0.353 mmol) and DEAD (diethyl azodicarboxylate, 55 μL, 0.346 mmol) were added to a solution of ligand **1a** (88.1 mg, 0.347 mmol) in THF (2.5 mL). PPh_3 (92.2 mg, 0.551 mmol) was added to the resulting yellow solution, whereby the color of the solution faded with time. After 3.5 h of stirring at room temperature, the solvent was evaporated under reduced pressure. The product was extracted from the oil with 4×5 mL of a mixture of hexane:EtOAc, 80:20. The combined organic layers were filtered through glasswool and then concentrated to give **3a** (190 mg) as a slightly yellow oil. The crude product was used for the next step without further purification.

4.5. Compound *4a*

An aqueous solution of NH_3 (25%, 1.5 mL) was slowly added to a solution of **3a** (179 mg of the crude product described above) in absolute ethanol (4 mL). After stirring at room temperature for 4 h, the solvent was removed under reduced pressure to give a yellow oil, which was purified by flash chromatography on silica gel (3.5×2 cm column, hexane:EtOAc, 60:40, and hexane:EtOAc, 30:70) to yield **4a** (24 mg, 56% yield based on **1a**) as a colorless oil: $[\alpha]_D^{20}$ +26.9 (*c* 0.48, CH_2Cl_2); ^{1}H NMR δ 8.10 (1H, aromatic, d, *J*=7.6 Hz), 7.94 (2H, aromatic, d, *J*=8.6 Hz), 7.83 (1H, aromatic, app t, *J*=7.9 Hz), 7.58 (1H, aromatic, d, *J*=7.6 Hz), 7.27–7.40 (5H, aromatic, m), 6.83 (2H, aromatic, d, *J*=8.6 Hz), 5.49 (2H, CH_2, s), 5.47 (1H, oxazoline, dd, *J*=10.1, 8.6 Hz), 4.92 (1H, oxazoline, dd, *J*=10.1, 8.6 Hz), 4.42 (1H, oxazoline, t, *J*=8.6 Hz); the acidic proton was not observed. ^{13}C NMR δ 163.91, 160.65, 156.91, 146.14, 141.57, 137.68, 132.11, 128.89, 127.91, 126.86, 124.12, 123.54, 121.81, 115.44, 76.29, 76.06, 75.59, 70.22, 66.81.

4.6. Polymer-supported ligand *6a*

K_2CO_3 (21 mg, 0.153 mmol) was added in one portion to a suspension of chloromethylated polystyrene **5a** (1.6 mmol of chloromethyl groups/g of polymer, 53.5 mg, 0.085 mmol) and **4a** (35 mg, 0.094 mmol) in dry DMF (1.2 mL) in a dry round-bottomed flask. The reaction mixture was stirred overnight under a nitrogen atmosphere at 60°C. The polymer was filtered off and washed in succession with MeOH (2 mL), THF:H_2O, 1:1 (2 mL), H_2O (2 mL), acetone (2 mL), CH_2Cl_2 (2 mL) and MeOH (2 mL). The polymer was dried at room temperature in vacuo overnight, resulting in 70.4 mg of **6a** containing 1.78%

N, corresponding to 0.64 mmol of ligand/g of polymer (51% conversion). Due to poor resolution we were not able to assign the signals in the ^{13}C NMR spectrum.

4.7. Polymer-supported ligand **6b**

This polymer was prepared according to the procedure described for **6a** starting from ArgoGel™–Wang–Cl **5b** (0.35–0.45 mmol of chloromethyl groups/g of polymer, 0.179 g, 0.072 mmol), **4a** (29.6 mg, 0.079 mmol), K_2CO_3 (17.9 mg, 0.130 mmol) and dry DMF (1 mL). The polymer was dried at room temperature in vacuo overnight, resulting in 170 mg of **6b** containing 0.56% N, corresponding to 0.20 mmol of ligand/g of polymer (ca 54% conversion, assuming 0.40 mmol/g of functional groups in **5b**): ^{13}C NMR δ 163.70, 158.91, 156.92, 141.83, 137.63, 131.93, 131.64, 129.28, 128.86, 128.50, 127.83, 126.91, 123.50, 114.87, 114.70, 114.53, 75.54, 69.75–71.41 (several signals), 67.56, 66.85.

4.8. 3-(4-Methoxycarbonyloxyphenyl)propionic acid **2b**

This compound was prepared according to the procedure described for **2a** starting from 3-(4-hydroxyphenyl)propionic acid (0.395 g, 2.38 mmol), a solution of sodium hydroxide (0.276 g, 6.9 mmol) in water (7 mL) and methyl chloroformate (0.364 g, 3.85 mmol). The thick white precipitate obtained after lowering the pH to 3 was filtered off and washed with water, and then dissolved in CH_2Cl_2. The resulting solution was dried over $MgSO_4$. Evaporation followed by drying in vacuo afforded **2b** (0.322 g, 60%): mp 66°C; ^1H NMR δ 7.22 (2H, aromatic, d, *J*=8.3 Hz), 7.09 (2H, aromatic, d, *J*=8.3 Hz), 3.90 (3H, CH_3O, s), 2.97 (2H, CH_2, t, *J*=7.6 Hz), 2.68 (2H, CH_2, t, *J*=7.6 Hz); the acidic proton was not observed.

4.9. Compound (R,R)-**3b**

DCC (1,3-dicyclohexylcarbodiimide, 35 mg, 0.17 mmol) was added to a solution of (*R*,*R*)-**1b** (47 mg, 0.15 mmol), **2b** (34 mg, 0.15 mmol) and DMAP (4-dimethylaminopyridine, 1.8 mg, 0.015 mmol) in CH_2Cl_2 (0.1 mL). The resulting mixture, which became thick and white, was stirred for 4.5 h at room temperature, then diluted with Et_2O (5 mL) and filtered through a glass filter. Evaporation of the filtrate in vacuo afforded a yellow oil which was purified by flash chromatography on silica gel (3.5×2 cm column, hexane:EtOAc, 60:40) to give (*R*,*R*)-**3b** (50 mg, 65%) as a colorless oil: $[\alpha]_D^{20}$ +17.9 (*c* 0.69, CH_2Cl_2); ^1H NMR δ 8.06 (1H, aromatic, d, *J*=7.7 Hz), 7.68 (1H, aromatic, t, *J*=7.7 Hz), 7.28–7.40 (5H, aromatic, m), 7.06–7.21 (3H, aromatic, m), 7.07 (2H, aromatic, d, *J*=8.6 Hz), 5.71 (1H, CHO, s), 5.42 (1H, oxazoline, app t, *J*=9.5 Hz), 4.88 (1H, oxazoline, dd, *J*=10.1, 8.6 Hz), 4.36 (1H, oxazoline, app t, *J*=8.6 Hz), 3.90 (3H, OCH_3), s), 2.98 (2H, CH_2, app t, *J*=7.6 Hz), 2.74 (2H, CH_2, td, *J*=7.6, 2.5 Hz), 0.95 (9H, $C(CH_3)_3$, s).

4.10. Compound (R,R)-**4b**

An aqueous solution of NH_3 (25%, 370 μL) was slowly added to a suspension of (*R*,*R*)-**3b** (30.5 mg, 0.059 mmol) in absolute ethanol (1 mL). After stirring at room temperature for 4 h, the solvent was removed under reduced pressure to give (*R*,*R*)-**4b** (25 mg, 93%) as a colorless oil: $[\alpha]_D^{20}$+30.8 (*c* 0.83, CH_2Cl_2); ^1H NMR δ 8.05 (1H, aromatic, d, *J*=7.9 Hz), 7.65 (1H, aromatic, t, *J*=7.9 Hz), 7.25–7.38 (5H, aromatic, m), 7.16 (1H, aromatic, d, *J*=7.9 Hz), 7.02 (2H, aromatic, d, *J*=8.4 Hz), 6.69 (2H, aromatic,

d, *J*=8.4 Hz), 5.70 (1H, CHO, s), 5.43 (1H, oxazoline, app t, *J*=9.5 Hz), 5.15 (1H, OH, s), 4.88 (1H, oxazoline, dd, *J*=10.1, 8.5 Hz), 4.37 (1H, oxazoline, t, *J*=8.5 Hz), 2.89 (2H, CH_2, app t, *J*=7.4 Hz), 2.69 (2H, CH_2, app t, *J*=6.9 Hz), 0.95 (9H, $C(CH_3)_3$, s).

4.11. *Polymer-supported ligand (*R,R*)-**6c***

The same procedure as that used for the preparation of **6a** was followed, starting from **5b** (0.35–0.45 mmol of chloromethyl groups/g of polymer, 0.120 g, 0.048 mmol), (*R,R*)-**4b** (24.2 mg, 0.053 mmol), K_2CO_3 (11.9 mg, 0.086 mmol) and dry DMF (800 μL). Polymer (*R,R*)-**6c** was obtained as yellow beads (116 mg) containing 0.42% N, corresponding to 0.15 mmol ligand/g of polymer (ca 40% conversion, asumming 0.40 mmol/g of functional groups in **5b**): ^{13}C NMR δ 171.98, 164.20, 158.87, 158.27, 142.06, 136.46, 133.88, 132.64, 130.09, 129.18, 128.83, 128.50, 127.76, 126.88, 123.53, 123.16, 114.96, 114.78, 114.62, 83.41, 75.56, 70.5–70.9 (several signals), 69.8, 67.55, 64.59, 46.30, 42.81, 36.14, 35.10, 30.14, 26.13.

4.12. *Compound (*R,S*)-**3b***

This compound was prepared according to the procedure described for (*R,R*)-**3b**, starting from DCC (35 mg, 0.17 mmol), (*R,S*)-**1b** (48 mg, 0.15 mmol), **2b** (35 mg, 0.15 mmol), DMAP (1.9 mg, 0.015 mmol) and CH_2Cl_2 (0.1 mL). The colorless oil obtained after chromatography was dried at room temperature in vacuo overnight, resulting in 46.7 mg of (*R,S*)-**3b** (58%): $[\alpha]_D^{20}$ +47.3 (*c* 0.60, CH_2Cl_2); ^{1}H NMR δ 8.07 (1H, aromatic, d, *J*=7.8 Hz), 7.69 (1H, aromatic, t, *J*=7.8 Hz), 7.26–7.38 (5H, aromatic, m), 7.17–7.20 (3H, aromatic, m), 7.07 (2H, aromatic, d, *J*=8.6 Hz), 5.71 (1H, CHO, s), 5.43 (1H, oxazoline, dd, *J*=4.7, 4.7 Hz), 4.89 (1H, oxazoline, dd, *J*=10.1, 8.6 Hz), 4.36 (1H, oxazoline, app t, *J*=8.6 Hz), 3.90 (3H, OCH_3, s), 2.98 (2H, CH_2, app t, *J*=7.6 Hz), 2.74 (2H, CH_2, td, *J*=7.6, 2.5 Hz), 0.95 (9H, $C(CH_3)_3$, s).

4.13. *Compound (*R,S*)-**4b***

The same procedure as that used for the preparation of (*R,R*)-**4b** was followed, starting from (*R,S*)-**3b** (41.9 mg, 0.081 mmol), NH_3 (aq, 25%, 505 μL) and absolute ethanol (1.4 mL). A white solid was obtained, which was dried in vacuo overnight, resulting in 35.7 mg of (*R,S*)-**4b** (95%): mp 208–210°C; $[\alpha]_D^{20}$ +44 (*c* 0.63, CH_2Cl_2); ^{1}H NMR δ 8.06 (1H, aromatic, d, *J*=7.8 Hz), 7.67 (1H, aromatic, t, *J*=7.8 Hz), 7.21–7.38 (5H, aromatic, m), 7.20 (1H, aromatic, d, *J*=9.5 Hz), 7.04 (2H, aromatic, d, *J*=8.5 Hz), 6.70 (2H, aromatic, d, *J*=8.5 Hz), 5.71 (1H, CHO, s), 5.43 (1H, oxazoline, app t, *J*=9.3 Hz), 4.90 (1H, oxazoline, app t, *J*=7.9 Hz), 4.64 (1H, OH, s), 4.37 (1H, oxazoline, t, *J*=8.5 Hz), 2.91 (2H, CH_2, app t, *J*=7.6 Hz), 2.69 (2H, CH_2, td, *J*=7.6, 2.8 Hz), 0.95 (9H, $C(CH_3)_3$, s).

4.14. *Polymer-supported ligand (*R,S*)-**6c***

The same procedure as that used for the preparation of **6a** was followed, starting from **5b** (0.35–0.45 mmol of chloromethylated groups/g of polymer, 0.178g, 0.071 mmol), (*R,S*)-**4b** (35.7 mg, 0.078 mmol), K_2CO_3 (17.9 mg, 0.127 mmol) and dry DMF (1.1 mL). Polymer (*R,S*)-**6c** was obtained as yellow beads (185 mg) containing 0.43% N, corresponding to 0.15 mmol ligand/g of polymer (41%, assuming 0.40 mmol/g of functional groups in **5b**): ^{13}C NMR (125.7 MHz) δ 172.3, 164.6, 159.3, 159.2, 136.8, 136.5, 135.7, 134.3, 130.5, 129.6, 129.2, 128.9, 128.1, 127.3, 127.0, 123.6, 121.4, 115.2, 115.1, 115.0, 83.7, 83.2, 78.0, 70.2–71.8 (several signals), 67.9, 65.0, 53.9, 46.7, 43.2, 40.8, 36.5, 35.5, 30.5, 26.5.

4.15. Polymer-supported ligand **6d**

DCC (22.8 mg, 0.111 mmol) was added to a suspension of TentaGel HL-COOH® **5c** (0.40–0.60 mmol of acid groups/g of polymer, 0.225 g, 0.090 mmol), **1a** (25.3 mg, 0.099 mmol) and DMAP (2.0 mg, 0.016 mmol) in dry CH_2Cl_2 (1.5 mL). The reaction mixture was stirred for 22 h at room temperature. The polymer was filtered off and washed in succession with MeOH (2 mL), EtOH (2 mL), THF:H_2O, 1:1 (2 mL), H_2O (2 mL), acetone (2 mL), CH_2Cl_2 (2 mL) and MeOH (2 mL), and then dried at room temperature in vacuo overnight, resulting in 238.4 mg of **6d** containing 1.29% N, corresponding to 0.46 mmol ligand/g of polymer (100%, assuming 0.50 mmol/g of functional groups in **5c**): ^{13}C NMR δ 172.3, 171.31, 163.64, 156.50, 146.24, 141.82, 137.63, 133.76, 131.90, 128.85, 127.80, 126.88, 123.44, 75.48, 70.6–75.5 (several signals), 69.78, 66.67, 39.40, 30.73, 29.50.

4.16. Polymer-supported ligand (R,R)-**6e**

The same procedure as that used for the preparation of **6d** was followed, starting from **5c** (0.40–0.60 mmol of acid groups/g of polymer, 0.231g, ca 0.092 mmol), (*R,R*)-**1b** (31.4 mg, 0.101 mmol), DMAP (1.1 mg, 0.009 mmol), dry CH_2Cl_2 (1.5 mL) and DCC (21.1 mg, 0.101 mmol). Polymer **6e** was obtained as beads (244 mg) containing 1.15% N, corresponding to 0.41 mmol ligand/g polymer (93%, assuming 0.50 mmol/g of functional groups in **5c**): ^{13}C NMR (125.7 Hz) δ 172.20, 171.61, 164.22, 158.92, 154.55, 145.57, 142.13, 136.68, 128.95, 127.90, 126.98, 124.14, 123.33, 83.47, 75.61, 70.8–69.9 (several signals), 54.78, 39.48, 35.25, 32.52, 31.27, 30.77, 29.95, 29.72, 26.31, 25.70, 24.92.

4.17. Polymer-supported ligand (R,S)-**6e**

This polymer was prepared in the same manner as **6d** starting from **5c** (0.278 g, ca 0.111 mmol), (*R,S*)-**1b** (38.0 mg, 0.122 mmol), DMAP (1.4 mg, 0.011 mmol), dry CH_2Cl_2 (1.8 mL) and DCC (25.4 mg, 0.122 mmol). Polymer (*R,S*)-**6e** was obtained as beads (292 mg) containing 1.02% N, corresponding to 0.36 mmol ligand/g polymer (82% assuming 0.50 mmol/g of functional groups in **5c**): ^{13}C NMR (125.7 Hz) δ 172.18, 171.67, 164.31, 158.95, 154.57, 145.58, 142.19, 136.71, 128.98, 127.93, 127.01, 124.15, 123.40, 83.48, 75.62, 70.8–69.9 (several signals), 54.75, 39.46, 35.29, 32.50, 31.19, 30.75, 29.92, 29.68, 28.30, 26.30, 24.91.

4.18. Compound **7**

The procedure used for the preparation of (*R,R*)-**3b** was followed. Starting from **1a** (33.2 mg, 0.131 mmol), benzoic acid (16.5 mg, 0.135 mmol), DMAP (1.8 mg, 0.015 mmol) and DCC (27.5 mg, 0.152 mmol) in 200 μL CH_2Cl_2 afforded 35 mg of **7** (75%) as a white solid after purification by flash chromatography on silica gel (4×1.5 cm column, hexane:EtOAc, 40:60): $[\alpha]_D^{20}$ +57.3 (*c* 0.59, CH_2Cl_2); mp 98–102°C; ^{1}H NMR δ 8.13 (2H, aromatic, app d, *J*=7.3 Hz), 7.84 (1H, aromatic, app t, *J*=7.9 Hz), 7.59 (1H, aromatic, app t, *J*=7.3 Hz), 7.47 (1H, aromatic, app t, *J*=7.5 Hz), 7.3–7.4 (8H, aromatic, m), 5.61 (2H, CH_2, s), 5.46 (1H, oxazoline ring, app t, *J*=9.3 Hz), 4.92 (1H, oxazoline ring, app t, *J*=9.5 Hz), 4.42 (1H, oxazoline ring, app t, *J*=8.7 Hz); ^{13}C NMR δ 166.14, 163.68, 156.65, 146.45, 141.78, 137.60, 133.34, 129.87, 129.79, 128.86, 128.53, 127.83, 126.89, 123.62, 123.56, 75.54, 70.40, 67.12. Anal. calcd for $C_{22}H_{18}N_2O_3$: C, 73.73; H, 5.06; N, 7.82. Found C, 73.06; H, 4.92; N, 7.55. The product probably contained approximately 0.1 equiv. of water which we were unable to get rid of: calcd for $C_{22}H_{18}N_2O_3 \cdot 0.1H_2O$: C; 73.36; H, 5.09; N, 7.78.

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References

1. (a) Proceedings of the 6th International Conference on Polymer Supported Reactions in Organic Chemistry: *React. Funct. Polym.* **1995**, *26*, 1. (b) Noyori, R. In *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994; Chap. 8.
2. (a) Barany, G.; Albericio, F.; Kates, S. A.; Kempe, M. *ACS Symposium Series*, 680; Harris, J. M.; Zalipsky, S., Eds.; Poly(ethylene glycol) Chemistry and Biological Applications. Am. Chem. Soc., 1997. (b) Bayer, B. *Angew. Chem., Int. Ed. Engl*. **1991**, *30*, 113. (c) Li, W.; Yan, B. *J. Org. Chem*. **1998**, *63*, 4092.
3. See, for instance: (a) Garrou, P. E.; Gates, B. C. In *Syntheses and Separations Using Functional Polymers*; Hodge, P.; Sherrington, D. C., Eds.; Wiley: Chichester, 1988; Chap. 3. (b) Takaishi, N.; Imai, H.; Bertelo, C. A.; Stille, J. K. *J. Am. Chem. Soc*. **1976**, *98*, 5400. (c) Pittman Jr., C. U.; Hannes, R. M. *Ibid*. **1976**, *98*, 5402. (d) Pittman Jr., C. U. In *Comprehensive Organometallic Chemistry*; Wilkinson, G.; Stone, F. G. A.; Abel, E. W., Eds.; Pergamon Press: Oxford, 1982; Vol. 8, Chap. 55.
4. (a) Shuttleworth, S. J.; Allin, S. M.; Sharma, P. K. *Synthesis* **1997**, 1217, and references cited therein. For a catalytic application, see: (b) Nagel, U.; Leipold, J. *Chem. Ber*. **1996**, *129*, 815.
5. (a) Trost, B. M.; Van Vranken, D. L. *Chem. Rev*. **1996**, *96*, 395. (b) Williams, J. M. J.; Howarth, J.; Frost, C. G. *Tetrahedron: Asymmetry* **1992**, *3*, 1089.
6. (a) Nordström, K.; Macedo, E.; Moberg, C. *J. Org. Chem*. **1997**, *62*, 1604. (b) Bremberg, U.; Rahm, F.; Moberg, C. *Tetrahedron: Asymmetry* **1998**, *9*, 3437. (c) Bremberg, U.; Larhed, M.; Moberg, C.; Hallberg, A. *J. Org. Chem*. **1999**, *64*, 1082. (d) Chelucci, G. *Tetrahedron: Asymmetry* **1997**, *8*, 2667. (e) Chelucci, G.; Medici, S.; Saba, A. *Tetrahedron: Asymmetry* **1997**, *8*, 3183. (f) Chelucci, G.; Medici, S.; Saba, A. *Tetrahedron: Asymmetry* **1999**, *10*, 543.
7. (a) Brunner, H.; Störiko, R.; Nuber, B. *Tetrahedron: Asymmetry* **1998**, *9*, 407. (b) Brunner, H.; Henrichs, C. *Tetrahedron: Asymmetry* **1995**, *6*, 653. (c) Brunner, H.; Huber, C. *Z. Naturforsch.* **1991**, *46b*, 1145. (d) Brunner, H.; Brandl, P. *Tetrahedron: Asymmetry* **1991**, *2*, 919. (e) Brunner, H.; Brandl, P. *J. Organomet. Chem*. **1990**, *390*, C81. (f) Brunner, H.; Obermann, U. *Chem. Ber*. **1989**, *122*, 499.
8. Brunner, H.; Amberger, K. *J. Organomet. Chem*. **1991**, *417*, C63.
9. Davies, D. L.; Fawcett, J.; Garratt, S. A.; Russell, D. R. *Chem. Commun*. **1997**, 1351.
10. Clark, J. S.; Tolhurst, K. F.; Taylor, M.; Swallow, S. *J. Chem. Soc., Perkin Trans. 1* **1998**, *7*, 1167.
11. Brunner, H.; Blüchel, C.; Doyle, M. P. *J. Organomet. Chem.* **1997**, *541*, 89.
12. Takemoto, Y.; Kuraoka, S.; Hamaue, N.; Aoe, K.; Hiramatsu, H.; Iwata, C. *Tetrahedron* **1996**, *52*, 14177.
13. Yang, R.; Dai, L. *J. Mol. Catal*. **1994**, *87*, L1.
14. Macedo, E.; Moberg, C. *Tetrahedron: Asymmetry* **1995**, *6*, 549.
15. Angell, R. M.; Barrett, A. G.; Braddock, D. C.; Swallow, S.; Vickery, B. D. *Chem. Commun*. **1997**, 919.
16. (a) Brunner, H.; Chuard, T. *Monatsh. Chem*. **1994**, *125*, 1293. (b) Brunner, H.; Obermann, U.; Wimmer, P. *Organometallics* **1989**, *8*, 821. (c) Brunner, H.; Obermann, U.; Wimmer, P. *J. Organomet. Chem*. **1986**, *316*, C1.
17. Koelle, U.; Bücken, K.; Englert, U. *Organometallics* **1996**, *15*, 1376.
18. Brunner, H.; Brandl, P. *Z. Naturforsch*. **1992**, *47b*, 609.
19. Moberg, C.; Adolfsson, H.; Wärnmark, K.; Norrby, P.-O.; Marstokk, K.-M.; Møllendal, H. *Chem. Eur. J*. **1996**, *2*, 516.
20. A chiral polymer-supported palladium catalyst was recently used in the reaction: Uozumi, Y.; Danjo, H.; Hayashi, T. *Tetrahedron Lett.* **1998**, *39*, 8303. For an achiral analog, see: Uozumi, Y.; Danjo, H.; Hayashi, T. *Tetrahedron Lett.* **1997,** *38*, 3557.
21. Levacher, V.; Moberg, C. *React. Polym*. **1995**, *24*, 183.
22. Chin, E.; Goodby, J. W. *Mol. Cryst. Liq. Cryst*. **1986**, *141*, 311.
23. Moore, J. S.; Stupp, S. I. *Macromolecules* **1990**, *23*, 65.
24. Mitsunobu, O. *Synthesis* **1981**, 1.
25. Leutenegger, U.; Umbricht, G.; Fahrni, C.; von Matt, P.; Pfaltz, A. *Tetrahedron* **1992**, *48*, 2143.
26. Svensson, M.; Bremberg, U.; Hallman, K.; Csöregh, I.; Moberg, C. Accepted for publication in *Organometallics*.
27. Warshawsky, A.; Deshe, A.; Gutman, R. *Br. Polym. J*. **1984**, *16*, 234.