Pergamon

SCIENCE DIRECT®

Tetrahedron: *Asymmetry* 14 (2003) 1517–1527

TETRAHEDRON: *ASYMMETRY*

Polymer-supported phosphoramidites: highly efficient and recyclable catalysts for asymmetric hydrogenation of dimethylitaconate and dehydroamino acids and esters

Simon Doherty,[a,*] Edward G. Robins,[a,b] Ibolya Pál,[a] Colin R. Newman,[a] Christopher Hardacre,[a] David Rooney[b] and Damian A. Mooney[b]

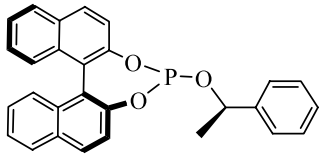
[a]*School of Chemistry, David Keir Building, Queens University, Belfast BT9 5AG, UK*
[b]*Department of Chemical Engineering, David Keir Building, Queens University, Belfast BT9 5AG, UK*

Received 10 February 2003; accepted 12 March 2003

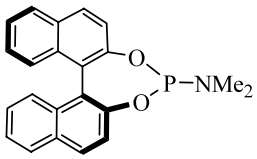
Abstract—Several novel phosphoramidites have been prepared by reaction of the primary amines *para*-vinylaniline, *ortho*-anisidine, 2-methoxyphenyl(4-vinylbenzyl)amine, 8-aminoquinoline and 3-vinyl-8-aminoquinoline with (*S*)-1,1′-bi-2-naphthylchlorophosphite, in the presence of base. Rhodium(I) complexes of these phosphoramidites catalyse the asymmetric hydrogenation of dimethylitaconate and dehydroamino acids and esters giving ee values up to 95%. Soluble non-cross linked polymers of the *para*-vinylaniline and 3-vinyl-8-aminoquinoline-based phosphoramidites have been prepared by free radical co-polymerisation with styrene in the presence of AIBN as initiator. The corresponding $[Rh(COD)]^+$ complexes serve as recyclable catalysts for the asymmetric hydrogenation dimethylitaconate and dehydroamino acids and esters to give ee values up to 80%.

1. Introduction

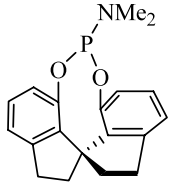
Although the enantioselective hydrogenation of prochiral alkenes has been extensively studied, the design of efficient chiral ancillary ligands for homogeneous transition metal-catalysed hydrogenation still continues to receive much attention. Since the development of (*R*,*R*)-DIOP in 1971,[1] it has generally been accepted that a conformationally rigid symmetric bidentate diphosphine is required to achieve effective asymmetric induction,[2] even though the P-chiral monodentate phosphines phenyl-*o*-anisylmethylphosphine (PAMP) and cyclohexyl-*o*-anisylmethyl phosphine (CAMP) were shown to be highly efficient ancillary ligands for the asymmetric hydrogenation of dehydroamino acid derivatives, the former giving up to 90% ee.[3] In fact, soon after the development of PAMP, Knowles prepared its diphosphine counterpart, DIPAMP, which was more efficient as a chiral ancillary ligand than its monophosphine equivalent.[4] Since these pioneering studies, an immense number of P-chelate ligands have been prepared including the bidentate phosphines Chiraphos,[5] DuPHOS,[6] BICP,[7] BINAP,[8] Norphos[9] TangPhos[10] and various ferrocenyl-based ligands such as Josiphos and FerroPHOS[11] as well as bidentate phosphites,[12] phosphinites[13] and phosphonites,[14] many of which form highly enantioselective hydrogenation catalysts. Despite encouraging performances by many of these bidentate P-chelates, the past few years have witnessed a renewed interest in the development of chiral monodentate phosphorus-containing ligands for use in rhodium-catalysed asymmetric hydrogenation reactions.[15] Pringle was among the first to demonstrate that monodentate phosphonites derived from 2,2′-binaphthol and 9,9′-biphenanthrol can outperform their chelating analogues in the asymmetric hydrogenation of methyl-2-acetamido acrylate.[16] Following this, a number of closely related reports appeared which detail the use of monodentate phosphine,[17] phosphonite,[18] phospholane,[19] and phosphite[20] ligands for the rhodium-catalysed asymmetric hydrogenation of dehy-



1



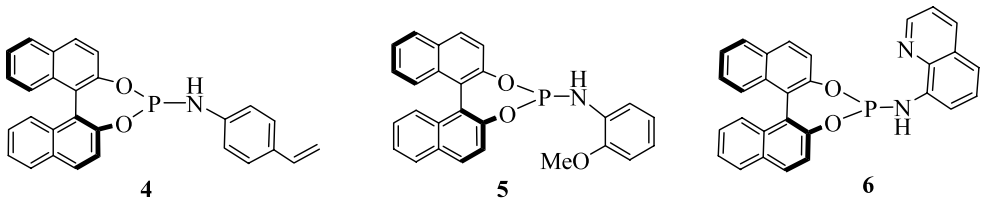
2



3

* Corresponding author. E-mail: s.doherty@qub.ac.uk

0957-4166/03/$ - see front matter © 2003 Elsevier Science Ltd. All rights reserved.
doi:10.1016/S0957-4166(03)00253-2



droamino acid derivatives. Among the most successful of these are complexes of monodentate phosphites **1**[21] and phosphoramidites **2**[22] based on axially chiral 2,2′-binaphthol and phosphoramidites **3**[23] containing a 1,1′-spirobiindane backbone (SIPHOS), which gives ee values in excess of 99%.

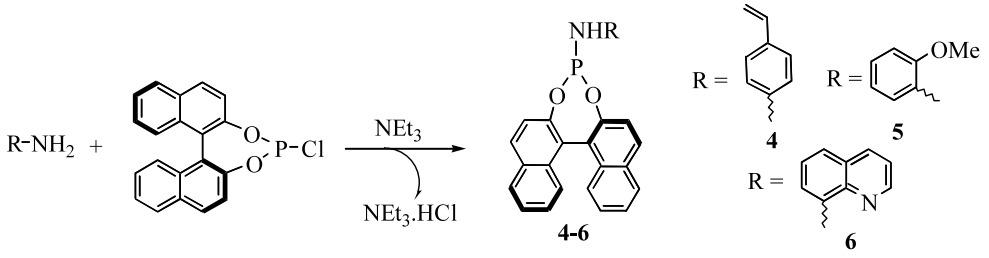
There is also considerable interest in the recycling and reusability of chiral transition metal catalysts since the metal is often relatively expensive and the ligand synthesis often involves a multi-step procedure that requires expensive reagents. One of the most straightforward approaches to recycle a catalyst is immobilisation on an inert support. Ideally, the immobilised catalyst should have an activity and selectivity comparable to that of its homogeneous counterpart and be easily recovered from the reaction mixture by filtration. Unfortunately, loss of activity due to leaching is a common problem for supported catalysts and the selectivity is often lower than that obtained with its unsupported homogeneous counterpart. Monodentate phosphoramidites are ideal candidates for immobilisation since they are highly efficient chiral ancillary ligands for rhodium-catalysed asymmetric hydrogenations but are relatively expensive in metal and ligand. Polymer resins such as polystyrene are finding increasing use in organic synthesis[24] and are rapidly becoming the support of choice for catalyst immobilisation.[25] Whilst insoluble cross-linked polystyrene has been most commonly employed, non-cross-linked polystyrene (NCPS) is often soluble and combines the advantages of solution phase properties with ease of product purification and separation.[26] Herein we report the synthesis of novel phosphoramidites based on the axially chiral 2,2′-binaphthol backbone and their application to the homogenous and soluble polymer-supported rhodium-catalysed hydrogenation of dimethylitaconate and dehydroamino acid derivatives.

2. Results and discussion

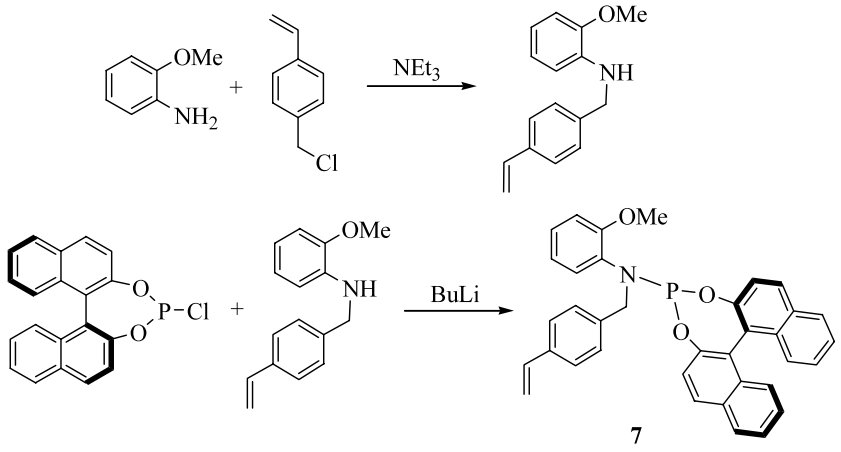
2.1. Synthesis of phosphoramidites

To the best of our knowledge there have been no reports of the use of polymer-supported phosphoramidites for the rhodium-catalysed asymmetric hydrogenation of dehydroamino acid derivatives, although polymer-bound phosphoramidites have been successfully employed in copper-mediated enantioselective conjugate addition reactions.[27] With the aim of preparing polymer-supported phosphoramidites it was first necessary to identify, prepare and evaluate the performance of monomers that can either undergo direct co-polymerisation or be easily modified to incorporate a polymerisable vinyl substituent. Firstly, phosphoramidite **4** was chosen since it can be prepared from commercially available 4-vinylaniline and can be tethered to a polymer support by co-polymerisation with styrene. Phosphoramidite **5** was prepared as it contains an *ortho* methoxy group similar to that present in the chiral monodentate phosphines PAMP and CAMP,[3] which form highly efficient hydrogenation catalysts. It has been suggested that the high selectivity of these catalysts may result from the formation of a hemilabile chelate via coordination of the methoxy group. In this regard, **5** is also potentially capable of forming a hemilabile six-membered chelate as is phosphoramidite **6** via coordination through phosphorus and the quinoline nitrogen atom. Phosphoramidite **2**, reported earlier by Feringa and co-workers,[22] was chosen as the benchmark with which to compare ligands **4**–**6** since it is relatively straightforward to prepare and is an excellent chiral ancillary ligand for rhodium-catalysed hydrogenations.

Phosphoramidite **2** was prepared from (*S*)-1,1′-bi-2-naphthol and hexamethylphosphorus triamide according to the literature procedure[22] and phosphoramidites **4**–**6** were prepared according to the general procedure outlined in Scheme 1. The chiral chlorophosphite (*S*)-1,1′-bi-2-naphthyl chlorophosphite was prepared by slow addition of a THF solution of phosphorus trichloride to a solution of (*S*)-1,1′-bi-2-naphthol and triethylamine in THF, according to the modified procedure of Osborne.[28] Dropwise addition of a toluene solution of the appropriate primary amine to an ice-cooled toluene solution of (*S*)-1,1′-bi-2-naphthyl chlorophosphite and base gave high yields of the desired phosphoramidites **4**–**6**, as air-stable spectroscopically pure solids after purification by flash column chromatography.



Scheme 1. Synthesis of phosphoramidites **5** and **6**.



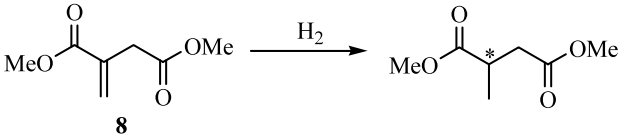
Scheme 2. Synthesis of phosphoramidite **7**.

Phosphoramidite **7**, containing a *p*-styrenyl substituent was identified as a monomer that could be converted into a soluble non-cross linked polymer-supported version of the *ortho*-methoxy substituted phosphoramidite **5**. Although **7** could not be prepared using the procedure outlined above for **4**–**6**, reaction of (*S*)-1,1′-bi-2-naphthyl chlorophosphite with lithium 2-methoxyphenyl(4-vinylbenzyl)amide, generated in situ by deprotonation of the corresponding secondary amine with butyl lithium, gave the desired product in reasonable yield. Purification of the crude reaction mixture by flash chromatography on silica gel afforded phosphoramidite **7** as an air-stable spectroscopically pure material (Scheme 2).

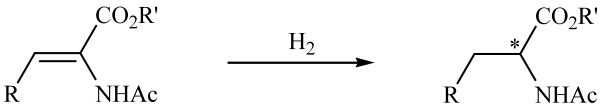
2.2. Rhodium-catalysed enantioselective hydrogenation of dimethylitaconate and dehydroamino acid derivatives

The efficiency of phosphoramidites **2**, **4**, **5** and **7** as chiral ancillary ligands for rhodium-catalysed asymmetric hydrogenations has been investigated. The cationic rhodium catalysts $[RhL_2(COD)][BF_4]$ (L = **2**, **4**, **5**, **7**) were typically prepared in situ by reaction of 2 equiv. of the appropriate phosphoramidite with $[Rh(COD)_2][BF_4]$ in dichloromethane at room temperature. The results for the asymmetric hydrogenation of dimethylitaconate **8** (Eq. (1)) and dehydroamino acid derivatives **9**–**12** (Eq. (2)) catalysed by $[RhL_2(COD)][BF_4]$ under ambient conditions (rt, 1 bar H_2, 20 h), are given in Table 1.

Under our conditions the rhodium-catalysed hydrogenation of dimethylitaconate **8** proceeds to completion for all catalysts studied with phosphoramidite **5** giving an ee of 91% (entry 3), compared to that of 85% for the benchmark phosphoramidite **2** (entry 2). While phosphoramidite **2** catalysed the hydrogenation of dehydroamino esters **9** and **11** to give ee's in excess of 99% (entries 5 and 13) reduction of the corresponding acids **10** and **12** was markedly less selective. Surprisingly, in our hands the $[Rh(\mathbf{2})_2(COD)][BF_4]$ catalysed hydrogenation of substrate **12** gave an ee value of 67% (entry 17), which is significantly lower than that reported earlier by Feringa under similar conditions.[22] Reassuringly though, the enantioselectivities obtained for hydrogenation of substrates **8**–**11** were comparable to those reported for the benchmark phosphoramidite **2**. While phosphoramidite **5** was more selective for the rhodium-catalysed hydrogenation of esters **10** and **12** than their corresponding acids, phosphoramidite **4** was slightly more selective for the hydrogenation of acid **12** compared with its ester **11** (entries 14 and 18). In this regard, Chan has noted on several occasions that the rates and enantioselectivities of hydrogenation of (*Z*)-acetamido-3-arylacrylic acids are lower than those obtained for the hydrogenation of their corresponding esters.[13e,f] Despite the promising selectivities obtained for hydrogenations based on **5**, introduction of an additional *p*-vinylbenzyl group on nitrogen, i.e. phosphoramidite **7**, resulted in a dramatic reduction in catalyst performance. Indeed, for all substrates exam-



8 (1)



(2)

9 : R = H, R' = Me; **10** : R = H, R' = H

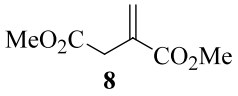
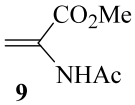
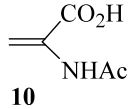
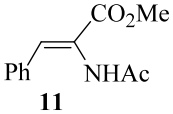
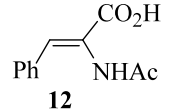
11 : R = Ph, R' = Me; **12** : R = Ph, R' = H

ined, phosphoramidite **7** gave significantly lower ee's values (entries 4, 8, 12, 16 and 20) than those obtained with **5** (entries 3, 7, 11, 15 and 19). Such a reduction in enantioselectivity with increasing steric bulk at nitrogen parallels closely the reduced selectivity observed in the asymmetric hydrogenation of enamides with diethyl and diisopropyl spiro-phosphoramidites.[23]

With regard to catalyst performance, Orpen and Pringle have proposed that two sterically demanding *cis*-coordinated binaphthol derived phosphonites adopt a stable rigid conformation around the metal such that the two biaryl fragments adopt an edge-on arrangement which is highly effective for transfer of chiral information,[16] in much the same manner as the alternating edge/face arrangement of chiral diphosphines. The pre-catalyst $[Rh(\mathbf{1})_2(COD)][BF_4]$ is also clearly capable of forming a similar conformationally rigid framework and in this regard the high enantioselectivities for these substrates is not surprising (Table 1).

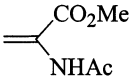
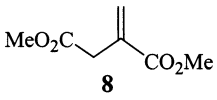
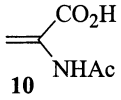
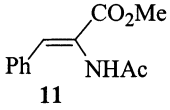
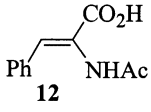
In general, the performance of catalysts prepared in situ from 2 equiv. of monodentate phosphoramidites **2**, **4**, **5** or **7** and $[Rh(COD)_2][BF_4]$ were comparable to that obtained with pre-formed complexes of the type $[Rh(L)_2(COD)][BF_4]$. In contrast, precatalyst prepared by reaction of $[Rh(COD)_2][BF_4]$ with 2 equiv. of phosphoramidite **6**, showed no activity for hydrogenation of substrates **8**–**12**. Since phosphoramidite **6** is capable of coordinating to rhodium in a bidentate manner, as a P,N chelate, the absence of activity for catalyst mixtures based on a Rh:ligand ratio of 1:2 could be due to formation of the inactive bischelate $[Rh(\mathbf{6})_2][BF_4]$. In this regard, bischelate complexes have previously been reported to be inactive for olefin hydrogenation.[4a] The bis(chelate) complex $[Rh(\mathbf{6})_2][BF_4]$ (δ 146.8 ppm, d,

Table 1. Homogeneous rhodium-catalysed hydrogenation of dimethylitaconate **8** and dehydroamino acid derivatives **9**–**12**[a]

Entry	Substrate	Ligand	%Conv	%ee	Confign.
1	 **8**	2	100	85	*S*
2		4	100	76	*S*
3		5	100	91	S
4		7	100	29	*R*
5	 **9**	2	100	>99	*R*
6		4	100	72	*R*
7		5	100	76	*R*
8		7	100	37	*S*
9	 **10**	2	100	97	*R*
10		4	100	73	*R*
11		5	100	67	*R*
12		7	100	46	*R*
13	 **11**	2	100	>99	*R*
14		4	100	79	*R*
15		5	100	82	*R*
16		7	100	33	*R*
17	 **12**	2	100	67	*R*
18		4	100	84	*R*
19		5	100	63	*R*
20		7	100	39	*S*

[a]The reaction was performed at room temperature under ambient H_2 pressure for 20 h [substrate (0.2 mmol, 0.04 M):$[Rh(COD)_2]BF_4$:ligand = 1:0.05:0.10]. Enantioselectivities were determined by GC using a CHROMPAK Chirasil-L-Val (25m x 0.25mm) column and/or specific rotation.

Table 2. Homogeneous rhodium-catalysed hydrogenation of dimethylitaconate **8** and dehydroamino acid derivatives **9–12** using phosphoramidite **6**[a]

Entry	Substrate	Catalyst	%Conv	%ee[c]	Confign[d]
1		$[Rh(COD)_2]BF_4$	100	0	-
2	 **9**	1:1 $[Rh(COD)_2]BF_4$/**6**	100	69	*R*
3		1:2 $[Rh(COD)_2]BF_4$/**6**	0	0	-
4		[Rh(**6**)(COD)]BF_4	100	84	*R*
5	 **8**	[Rh(**6**)(COD)]BF_4	100	95	*S*
6	 **10**	[Rh(**6**)(COD)]BF_4	49	63	*R*
7[e]		[Rh(**6**)(COD)]BF_4	74	54	*R*
8	 **11**	[Rh(**6**)(COD)]BF_4	100[b]	78	*R*
9	 **12**	[Rh(**6**)(COD)]BF_4	98	75	*R*

[a]The reaction was performed at room temperature under ambient H_2 pressure for 20 h, unless otherwise stated [substrate (0.2 mmol, 0.04 M):$[Rh(COD)_2]BF_4$:ligand = 1:0.05:0.05]. [b]Reaction time of 4 h. [c]Enantioselectivities were determined by GC with a CHROMPAK CP-Chirasil-L-Val (25m x 0.25mm) column and/or specific rotation. [d]Determined by comparison with reference compounds or by the sign of the specific rotation. [e]Hydrogenation conducted at 30 °C.

$J_{RhP}=271$ Hz) has been prepared by reaction of 2 equiv. of phosphoramidite with $[Rh(COD)_2][BF_4]$, isolated by crystallisation from a dichloromethane solution layered with hexane, and shown to be catalytically inactive. A molecular ion peak at 1020 amu in the electrospray mass spectrum of $[Ru(\mathbf{6})_2][BF_4]$ is consistent with this bischelate formulation. Our suggestion that **6** acts as a bidentate ligand is also supported by the recent studies of Buono and co-workers who have demonstrated that the related diastereomerically pure (2*R*,5*S*)-3-phenyl-2-(8-quinolinoxy)-1,3-diaza-2-phosphabicyclo-[3.3.0]octane (QUIPHOS) coordinates to palladium in a bidentate chelating manner.[29] Reduction of the Rh:ligand combination to a ratio of 1:1 gave a catalyst mixture that was active for the hydrogenation of substrate **9**, giving complete conversion and a modest enantioselectivity of 69% (entry 2). Full details of the asymmetric hydrogenation of dimethylitaconate **8** and dehydroamino acid derivatives **9–12** catalysed by rhodium complexes of phosphoramidite **6** are given in Table 2. Under identical conditions, preformed catalyst [Rh(**6**)(COD)][BF_4] showed a marked increase in enantioselectivity to give an ee value of 84% for the same substrate (entry 4). In an attempt to glean insight in to the origin of these disparate enantioselectivities ^{31}P NMR spectroscopy was used to examine the nature of the solution species formed by mixing $[Rh(COD)_2][BF_4]$ and phosphoramidite **6** in a 1:1 ratio. The $^{31}P\{^1H\}$ NMR spectrum of this reaction mixture revealed the presence of two major phosphorus-containing species $[Rh(\mathbf{6})_2][BF_4]$ (δ 146.8 ppm) and [Rh(**6**)(COD)][BF_4] (δ 131.7 ppm, d, $J_{RhP}=247$ Hz) in approximately 3:2 molar ratio, respectively. In comparison the ^{31}P NMR spectrum of isolated precatalyst, purified by crystallisation, showed one major component, a doublet at δ 131.7 which corresponds to [Rh(**6**)(COD)][BF_4]. Under ambient conditions, $[Rh(COD)_2][BF_4]$ is also active for the hydrogenation of methyl-2-acetamidoacrylate **9** and

gives quantitative conversion to racemic product. Thus, the most likely origin of the lower enantioselectivity obtained during the hydrogenation of **9** with in situ generated catalyst is competing hydrogenation by unreacted achiral $[Rh(COD)_2][BF_4]$, which could account for up to 40% of the reaction mixture.

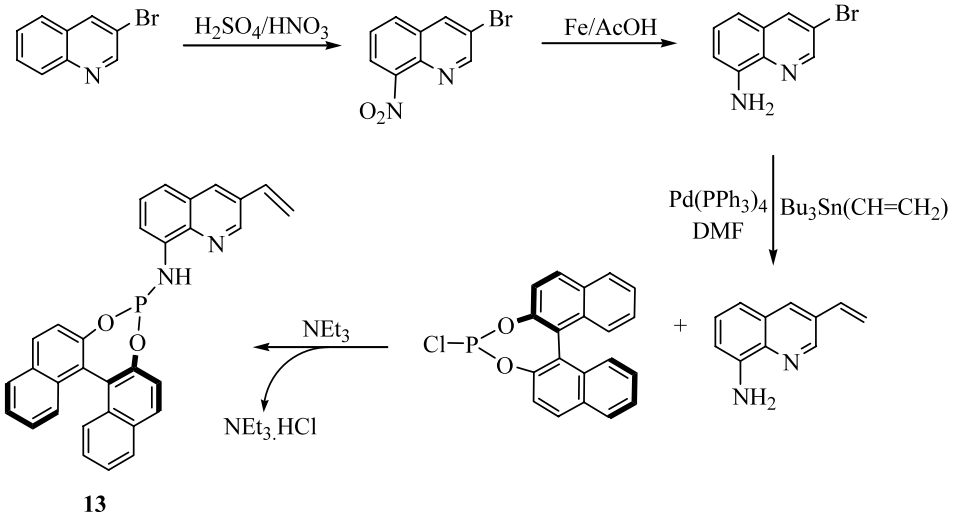
Although hydrogenation of substrates **9** and **11**–**12** with [Rh(**6**)(COD)][BF_4] gave conversions and enantioselectivities similar to those obtained with phosphoramidites **4** and **5**, dehydroamino acid **10** gave less than 50% conversion, although the ee value of 63% was only marginally lower. As expected the conversion improved to 74% when the hydrogenation of **8** was conducted at 30°C, although the enantioselectivity was slightly lower with an ee value of 54%. Encouragingly, [Rh(**6**)(COD)]-[BF_4] showed excellent enantioselectivity for the hydrogenation of **8** giving quantitative conversion to dimethyl-(*S*)-methylsuccinate with an ee of 95%, a marked improvement compared with the performance of benchmark phosphoramidite **2**, which gave an ee of 85% under identical conditions.

2.3. Polymer-supported catalysis

In order to synthesise a styrene co-polymer incorporating the same functionality as **6**, phosphoramidite **13** was prepared from 3-bromoquinoline according to the procedure outlined in Scheme 3. Nitration of 3-bromoquinoline followed by Fe-mediated reduction in 50% acetic acid afforded a 9:1 mixture of 8-amino-3-bromoquinoline and 5-amino-3-bromoquinoline, which was purified by crystallisation to give the desired 8-amino-substituted product. The polymerisable vinyl substituent was introduced by a Pd(0) mediated Stille cross-coupling reaction between 8-amino-3-bromoquinoline and tributylvinyltin to give 3-vinyl-8-aminoquinoline, which was subsequently converted into phosphoramidite **13** by reaction with (*S*)-1,1′-bi-2-naphthyl chlorophosphite in the presence of triethylamine.

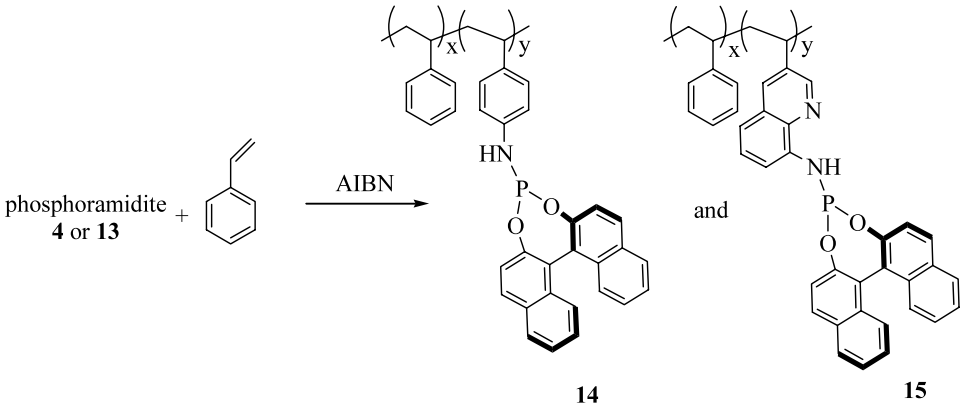
The objective of preparing soluble, non-cross-linked styrene-based co-polymers of **4** and **13** was to generate functionalised resins that combine the solubility of homogeneous catalysts with the ease of separation of heterogeneous supports.[17] Co-polymers **14** and **15** were prepared by suspension co-polymerisation of styrene with phosphoramidite monomers **4** and **13**, respectively, in toluene in the presence of 2,2′-azobis(2-methyl)propionitrile (AIBN) as radical initiator (Scheme 4). The resulting co-polymers were isolated as off-white powders by precipitation with methanol followed by exhaustive drying to remove residual solvent. The phosphorus content was obtained by elemental analysis (C, H, N and P) and the polydispersities of **14** and **15** were measured by gel permeation chromatography (GPC). Both polymers **14** and **15** were found to have a unimodal molecular weight distribution with similar polydispersities $M_W/M_N = 1.7$ and 1.6, respectively, although their average molecular weights (M_W) differed ($M_W = 20{,}100$ Da. for **14** and $M_W = 10{,}200$ Da. for **15**). The supported complexes **14[Rh]** and **15[Rh]** were prepared by stirring a dichloromethane solution of **14** and **15** with $[Rh(COD)_2][BF_4]$ at room temperature for 24 h and isolated as yellow/orange powders by precipitation with dry methanol. The rhodium loading in **14[Rh]** and **15[Rh]** was determined by inductively coupled plasma atomic emission (ICP-AES) analysis of a sample of polymer digested in refluxing aqua.

Rhodium-loaded polymers **14[Rh]** and **15[Rh]** catalyse the enantioselective hydrogenation of dimethylitaconate **8** and dehydroamino acid derivatives **9**–**12** under the same conditions as rhodium complexes of phospho-



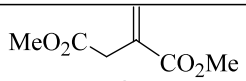
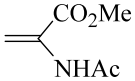
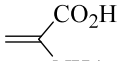
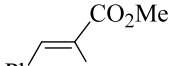
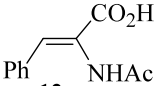
13

Scheme 3. Synthesis of phosphoramidite **13**.



Scheme 4. Polymerisation of phosphoramidite monomers **4** and **13**.

Table 3. Hydrogenation results for metal-loaded phosphoramidite co-polymers **14[Rh]** and **15[Rh]**

Entry	Substrate	Polymer	%Conv	%ee[b]	Config.[c]
1	 **8**	**14[Rh]**	100	67	*R*
2		**15[Rh]**	57	49	*S*
3	 **9**	**14[Rh]**	100	75	*R*
4		**15[Rh]**	96	65	*R*
5	 **10**	**14[Rh]**	100	70	*R*
6		**15[Rh]**	23	57	*R*
7	 **11**	**14[Rh]**	100	80	*R*
8		**15[Rh]**	100	64	*R*
9	 **12**	**14[Rh]**	100	74	*R*
10		**15[Rh]**	100	49	*R*

[a]The reaction was performed at room temperature under ambient H_2 pressure for 20 h [substrate (0.2 mmol, 0.04 M):$[Rh(COD)_2]BF_4$:ligand = 1:0.05:0.05]. [b]Enantioselectivities were determined by GC with a CHROMPAK CP-Chirasil-L-Val (25m x 0.25mm) column and/or specific rotation. [c]Determined by comparison with reference compounds or by the sign of the optical rotation.

ramidites **2** and **4**–**7** (ambient temperature, 1 bar H_2 in dichloromethane, 5 mol% [Rh]), the results of which are summarised in Table 3. Following the reaction, the solvent was removed and the product isolated by extracting the resulting residue with methanol. The polymer that remained was redissolved in the minimum volume of dichloromethane, precipitated with methanol, filtered, dried and recycled (vide infra). Hydrogenation of **8**–**12** in the presence of **Rh[14]** gave quantitative conversions for all substrates and enantio-

selectivities that were comparable to those obtained with phosphoramidite **4**. In fact, **Rh[14]** gave slightly higher enantioselectivities for the hydrogenation of dehydroamino esters **9** and **11** than catalyst generated from $[Rh(COD)_2][BF_4]$ and **4**. Specifically, **14[Rh]** gave ee's of 75 and 80% for the hydrogenation of **9** and **11**, respectively, while $[Rh(COD)_2][BF_4]$/**4** gave ee values of 72 and 79%, respectively. In contrast, [Rh(**6**)(COD)]-$[BF_4]$ clearly outperforms its polymer-supported counterpart **15[Rh]** for the asymmetric hydrogenation of substrates **8**–**12** with the most dramatic difference manifested in the hydrogenation of dimethylitaconate **8**, which gave 100% conversion and an ee of 95% compared with 57% conversion and 49% ee with **15[Rh]**.

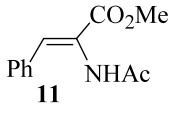
The results listed in Table 3 clearly show that co-polymer **14[Rh]**, containing the monodentate ligand **4**, consistently outperforms **15[Rh]**, which contains the P,N chelating ligand **6**. In the case of **14[Rh]** the random co-polymerisation and low phosphoramidite content (2.5–3.5%) is likely to preclude *cis*-coordination of two phosphoramidites and thus **14[Rh]** would be expected to behave/perform in much the same manner as a 1:1 Rh:ligand combination. In this regard, while the rhodium-catalysed hydrogenation of substrates **8**–**12** with the $[Rh(COD)_2][BF_4]$/**4** combination were typically run at a Rh:ligand ratio of 1:2, catalysts generated with a Rh:ligand ratio of 1:1 gave comparable enantioselectivities and conversions. Given that enantioselectivity does not depend markedly on the Rh:ligand ratio it is not surprising that the **14[Rh]** catalysed hydrogenation of substrates **8**–**12** (Table 3) gave ee values that were either comparable to or higher than those achieved with $[Rh(\mathbf{4})_2(COD)][BF_4]$. Although efficient transfer of chirality appears unlikely for a complex of a single monophosphorus ligand, Reeetz and Mehler have shown that simple BINOL-based monophosphites are excellent ancillary ligands for the rhodium-catalysed hydrogenation of dimethylitaconate giving ee values as high as 99.6% with a Rh:ligand ratio of 1:1. Moreover, this variable did not influence enantioselectivity over a range of Rh:ligand combinations from 1:1 to 1:4. Similarly, Chan has used monodentate phosphoramidites, derived from enantiopure H_8-BINOL and dimethylamine, for the rhodium-catalysed hydrogenation of methyl (*Z*)-acetamidocinnaminate and found that the Rh:L ratio does not significantly effect enantioselectivity, although a marked drop in conversion was noted between the 1:2 and 1:1 Rh:ligand combination.[30]

The major advantages of polymer-supported catalysts are the ease of separation and product purification and the ability to recycle and reuse expensive catalysts a number of times. Rhodium-loaded phosphoramidite co-polymer **14** was chosen for catalyst recycling studies since the conversions and enantioselectivities achieved with this catalyst were comparable to those of its unsupported counterpart. The results for the hydrogenation of methyl-2-acetamidocinnamate **11** catalysed by **14[Rh]** and recycled over four runs are given in Table 4. After each run the dichloromethane solvent was removed under reduced pressure and the polymer precipitated by addition of methanol to give near quantitative recovery of orange-yellow catalyst (ca. 95%) after filtering and drying, with less than 14% losses due to manual transfer over four catalyst recycles. The results shown in Table 4 clearly demonstrate that recycling of **14[Rh]** results in negligible loss of activity and enantioselectivity over four recycles and ICP-AES analysis of the methanol washings showed no sign of rhodium leaching after each run. However, significant losses in activity and selectivity were observed for catalysts requiring longer reaction times and for these substrates only three catalyst recycles were possible.

3. Conclusions

In summary, several phosphoramidite ligands have been prepared which give ee values as high as 95% for the asymmetric hydrogenation of prochiral olefins. We have demonstrated the straightforward synthesis and practical application of soluble non-cross-linked styrene-phosphoramidite co-polymers as suitable supports for the rhodium-catalysed asymmetric hydrogenation of prochiral olefins. In some cases the performance of the polymer-supported catalyst is comparable to or better than that of the corresponding unsupported catalyst. These catalysts have been successfully recycled with no significant loss of activity or selectivity over short reaction times. Investigations are currently underway in our laboratory to improve and optimise catalyst performance through ligand modification and determine the nature of the active catalyst and the factors that deter-

Table 4. Asymmetric hydrogenation of **11** with recycling of polymer-supported catalyst **14[Rh]**

Run	Substrate	Time/h	%Conv	%ee	Confign.
1	 **11**	4	100	80	*R*
2		4	100	82	*R*
3		4	100	80	*R*
4		4	95	80	*R*

mine selectivity. Ultimately, we intend to examine the processibility and engineering properties of these polymer-supported catalysts in order to identify polymers suitable for fibre extrusion and/or coating of high surface area substrates.

4. Experimental

4.1. General procedures

All manipulations involving air/moisture sensitive materials were carried out using standard Schlenk techniques under an inert atmosphere of nitrogen or argon. Toluene was distilled from sodium metal, diethyl ether and hexane were distilled from potassium/sodium alloy, tetrahydrofuran was distilled from potassium, dimethylformamide (DMF) and dichloromethane were distilled from calcium hydride and methanol distilled from magnesium methoxide. Deuteriochloroform was pre-dried from calcium hydride, then vacuum transferred and stored over 4 Å molecular sieves. ^{1}H, $^{13}C\{^{1}H\}$ and $^{31}P\{^{1}H\}$ NMR spectra were recorded on a Bruker 300 MHz spectrometer, gas chromatography was performed using a Varian Gas Chromatograph CP-3800 with a CP7495 Chirasil-L-Val column (25 m×0.25 mm id) using He as a carrier gas. Bis(1,5-cyclooctadiene)rhodium tetrafluoroborate,[31] 3-bromo-8-aminoquinoline[32] and phosphoramidite **2**[22] were prepared according to literature procedures.

4.2. Synthesis of amines

4.2.1. Synthesis of 2-methoxyphenyl-(4-vinylbenzyl)-amine. An ice-cooled solution of triethylamine (4.58 mL, 32.85 mmol) in toluene (20 mL) was treated with a toluene (10 mL) solution of *ortho*-anisidine (1.85 mL, 16.43 mmol) followed by a toluene (10 mL) solution of *para*-vinylbenzyl chloride (2.32 mL, 16.43 mmol) before being heated at reflux overnight. After this time, the mixture was cooled to room temperature and diluted with water (150 mL) and diethyl ether (150 mL). The organic phase was separated, washed with water (3×50 mL) and the aqueous phase extracted with diethyl ether (3×50 mL). The organic phases were combined, dried over anhydrous magnesium sulfate and the solvent removed under vacuum to afford a crude orange solid which was recrystallised from boiling hexane to give 2-methoxyphenyl-(4-vinylbenzyl)amine as a white crystalline solid in 61% yield (2.40 g). ^{1}H NMR ($CDCl_3$): δ 7.36 (m, 4H, Ar), 6.81 (m, 2H, Ar), 6.69 (m, 2H, Ar), 6.57 (dd, 1H, $J=17.6$ Hz, 10.9 Hz), 5.73 (d, 1H, $J=17.6$ Hz), 5.22 (1H, $J=10.9$ Hz), 4.62 (br. s, 1H, NH), 4.34 (s, 2H, -CH_2-), 3.84 (s, 3H, -OCH_3); $^{13}C\{^{1}H\}$ ($CDCl_3$): δ 47.8, 55.4, 109.4, 110.1, 113.6, 116.7, 121.3, 126.4, 127.7, 136.6, 138.1, 139.3, 146.8.

4.2.2. Synthesis of 3-bromo-8-nitroquinoline. To a solution of 3-bromoquinoline (5.0 g, 24.0 mmol) in conc. H_2SO_4 (10 mL) cooled in a water/ice bath was added dropwise 8 mL of a conc. H_2SO_4/conc. HNO_3 mixture (6:2). The reaction mixture was maintained at low temperature, stirred rapidly and monitored by thin layer chromatography until all the 3-bromoquinoline had been consumed (ca. 2 h). The mixture was diluted with water (50 mL) and NaOH added until the solution reached pH 10–11. The resulting solution was extracted with diethyl ether (2×50 mL), the organic phase dried over anhydrous magnesium sulfate and the solvent removed under reduced pressure to give a 9:1 mixture of 3-bromo-8-nitroquinoline and 3-bromo-5-nitroquinoline, respectively. Recrystallisation from ethylacetate afforded 5.0 g of. 3-bromo-8-nitroquinoline. ^{1}H NMR ($CDCl_3$): 3-bromo-8-nitroquinoline δ 9.26 (dd, 1H, $J=2.2$ Hz, 0.7 Hz), 9.04 (d, 1H, $J=6.5$ Hz), 8.44 (m, 2H), 7.86 (pseudo t, 1H).

4.2.3. Synthesis of 3-vinyl-8-aminoquinoline. A DMF (15 mL) solution of 3-bromo-8-aminoquinoline (0.500 g, 2.24 mmol) and tetrakis(triphenylphosphine) palladium(0) (0.129 g, 0.112 mmol, 5 mol%), shielded from the light, was treated with 1.1 equiv. of tributyl-(vinyl)tin (0.72 mL, 2.47 mmol) and the resulting mixture heated to 60°C overnight, after which time it was cooled to room temperature and quenched by addition of saturated aqueous potassium fluoride (100 mL). The organic phase was extracted with diethyl ether (4×50 mL), separated, dried over anhydrous magnesium sulfate and the solvent removed under reduced pressure to afford the crude product as a pale orange solid. Purification by chromatography over silica gel using diethyl ether as eluent afforded 3-vinyl-8-aminoquinoline as a pale orange/yellow solid in 66% yield (0.251 g). ^{1}H NMR ($CDCl_3$): δ 9.00 (d, 1H, $J=2.1$ Hz), 8.07 (br. s, 1H), 7.50 (m, 2H), 6.85 (dd, 1H, $J=17.7$ Hz, 11.1 Hz), 6.79 (m, 1H), 5.96 (d, 1H, $J=17.7$ Hz), 5.43 (d, 1H, $J=11.1$ Hz), 4.25 (br. s, 2H); $^{13}C\{^{1}H\}$ ($CDCl_3$): δ 149.2, 148.8, 142.8, 134.4, 130.3, 129.3, 126.7, 120.4, 118.7, 116.2, 110.9.

4.3. Synthesis of phosphoramidites

4.3.1. Synthesis of phosphoramidite 4. A toluene (10 mL) solution of triethylamine (0.69 mL, 4.95 mmol) and (*S*)-1,1′-bi-2-naphthyl chlorophosphite (0.868 g, 2.48 mmol) was cooled to 0°C and treated dropwise with a toluene (10 mL) solution of 4-aminostyrene (0.29 mL, 2.48 mmol). The resulting solution was heated at 80°C overnight, cooled to room temperature, filtered through celite and concentrated under vacuum. The crude product was extracted into a minimum volume of dichloromethane and purified by flash chromatography over silica gel (60–120 mesh, 9:1 hexane/diethylether) to give **1** as a white, air stable solid (0.69 g, 55%). $^{31}P\{^{1}H\}$ ($CDCl_3$): δ 148.2; ^{1}H NMR ($CDCl_3$): δ 7.85 (m, 4H, Ar), 7.46–7.16 (m, 10H, Ar), 6.86 (m, 2H, Ar), 6.57 (dd, 1H, $J=17.6$ Hz, 10.9 Hz), 5.53 (d, 1H, $J=17.6$ Hz), 5.03 (m, 2H, vinyl CH, NH). Anal. calcd for $C_{28}H_{20}NO_2P$: C, 77.59; H, 4.65; N, 3.23. Found: C, 78.01; H, 4.79; N, 3.51%. $[\alpha]_D=+7.52$ (*c* 0.05, $CHCl_3$).

4.3.2. Synthesis of phosphoramidite 5. A toluene solution of *ortho*-anisidine (0.26 mL, 2.31 mmol) was added dropwise to an ice-cold solution of triethylamine (0.64 mL, 4.62 mmol) and (*S*)-1,1′-bi-2-naphthyl chlorophosphite (0.810 g, 2.31 mmol) in toluene (10 mL). The

resulting reaction mixture was heated at 80°C and stirred overnight after which time it was cooled to room temperature and filtered through celite. The solvent was removed and the crude product purified by column chromatography over silica gel (1:1 hexane/dichloromethane) to give **2** as a white air-stable solid in 59% yield (0.600 g). $^{31}P\{^1H\}$ ($CDCl_3$): δ 148.8; ^1H NMR ($CDCl_3$): δ 7.84 (m, 4H), 7.24 (m, 4H), 7.18 (m, 4H), 6.78 (m, 4H), 5.89 (br s, 1H), 3.68 (s, 3H). Anal. calcd for $C_{27}H_{20}NO_3P$: C, 74.14; H, 4.61; N, 3.20. Found: C, 74.44; H, 4.91; N, 3.43%. $[\alpha]_D = +96.9$ (*c* 0.05, $CHCl_3$).

4.3.3. Synthesis of phosphoramidite 6. A solution of 8-aminoquinoline (597 g, 4.14 mmol) in toluene (10 mL) was added dropwise to an ice-cold toluene solution containing triethylamine (1.15 mL, 8.27 mmol) and (*S*)-1,1′-bi-2-naphthyl chlorophosphite (1.450 g, 4.14 mmol) in toluene (10 mL). The reaction mixture was heated at 80°C overnight then cooled to room temperature and filtered through celite. The solvent was removed from the colourless filtrate to afford phosphoramidite **3** as a white solid, which needed no further purification (1.365 g, 72%). $^{31}P\{^1H\}$ ($CDCl_3$): δ 147.2; ^1H NMR ($CDCl_3$): δ 8.55 (m, 1H), 7.83 (m, 6H), 7.38–7.12 (m, 12H), 5.18 (br s, 1H). Anal. calcd for $C_{29}H_{19}N_2O_2P$: C, 75.98; H, 4.18; N, 6.11. Found: C, 76.23; H, 4.29; N, 6.53%. $[\alpha]_D = -43.4$ (*c* 0.05, $CHCl_3$).

4.3.4. Synthesis of phosphoramidite 7. A THF (25 mL) solution of 2-methoxyphenyl-(4-vinylbenzyl)amine (1.100 g, 4.60 mmol) was cooled to −78°C and a 2.5 M solution of butyllithium in hexanes (1.84 mL, 4.60 mmol) added carefully. The resulting mixture was stirred for 30 min, after which time a THF (20 mL) solution of (*S*)-1,1′-bi-2-naphthyl chlorophosphite (1.612 g, 4.60 mmol) was added dropwise. The reaction mixture was stirred at low temperature for a further 1.5–2 h before being allowed to warm to room temperature. The solvent was removed under reduced pressure and the resulting off-white solid purified by flash chromatography over silica gel (9:1 hexane/diethyl ether) to give phosphoramidite **5** as a white solid in 63% yield (1.60 g). $^{31}P\{^1H\}$ ($CDCl_3$): δ 142.2; ^1H NMR ($CDCl_3$): δ 7.93 (m, 4H), 7.63 (m, 2H), 7.40 (m, 4H), 7.27 (m, 2H), 7.12 (m, 3H), 6.95 (m, 4H), 6.72 (m, 1H), 6.56 (dd, 1H, $J = 17.6$ Hz, 10.9 Hz), 5.59 (dd, 1H, $J = 17.6$ Hz, 1.0 Hz), 5.11 (dd, 1H, $J = 10.9$ Hz, 1.0 Hz), 4.33 (dd, 1H, $J = 14.6$ Hz, $J_{HP} = 2.4$ Hz), 3.98 (s, 3H), 3.95 (dd, 1H, $J = 14.6$ Hz, $J_{HP} = 1.9$ Hz). Anal. calcd for $C_{36}H_{28}NO_3P$: C, 78.11; H, 5.10; N, 2.53. Found: C, 78.38; H, 2.66; N, 2.61%. $[\alpha]_D = +96.9$ (*c* 0.05, $CHCl_3$).

4.3.5. Synthesis of phosphoramidite 13. A toluene (10 mL) solution of triethylamine (0.59 mL, 4.23 mmol) and (*S*)-1,1′-bi-2-naphthyl chlorophosphite (0.741 g, 2.12 mmol) was cooled in an ice bath and treated with a solution of 3-vinyl-8-aminoquinoline (0.360 g, 2.12 mmol) in a THF/toluene (5 mL/15 mL) before being heated 60°C overnight, after which the mixture was filtered through celite and concentrated under reduced pressure to yield a bright orange solid. The product was extracted into a minimum volume of dichloromethane and purified by flash chromatography over silica gel (1:1 diethyl ether/hexane) to afford phosphoramidite **11** as an off-white solid in 61% yield (0.627 g). $^{31}P\{^1H\}$ ($CDCl_3$): δ 147.3; ^1H NMR ($CDCl_3$): δ 9.00 (d, 1H, $J = 2.0$ Hz), 7.92 (m, 6H), 7.52 (m, 7H), 7. 30 (m, 3H), 6.79 (dd, 1H, $J = 17.7$ Hz, 11.1 Hz), 5.91 (d, 1H, $J = 17.7$ Hz), 5.70 (d, 1H, $J_{PH} = 4.6$ Hz), 5.42 (d, 1H, $J = 11.1$ Hz). Anal. calcd for $C_{31}H_{21}N_2O_2P$: C, 76.85; H, 4.37; N, 5.78. Found: C, 77.10; H, 4.59; N, 5.97%. $[\alpha]_D = -39.2$ (*c* 0.05, $CHCl_3$).

4.4. General procedure for co-polymerisation of phosphoramidite monomers with styrene

A Schlenk flask was charged with phosphoramidite monomer **4** or **13** (0.73 mmol, 2.5 mol%) and styrene (28.47 mmol, 97.5 mol%). The mixture was degassed by three vacuum/nitrogen cycles and diluted with toluene (30 mL) before being treated with 2 mol% 2,2′-azobis(2-methylpropionitrile (AIBN) and heated at 65°C overnight. The solvent was concentrated under reduced pressure to give a viscous paste, which was triturated with hexane (60 mL) to yield the co-polymer as a fine powder. The phosphoramidite–styrene co-polymers were isolated by filtration and dried under reduced pressure. Co-polymer **14**: $^{31}P\{^1H\}$ ($CDCl_3$): δ 148.4; Polydispersity (M_W/M_N) = 1.7, Average molecular weight (M_W) = 20,100 Da. Anal. calcd for $C_{340}H_{332}NO_2P$: C, 90.84; H, 7.44; N, 0.31; P, 0.69. Found: C, 89.90; H, 7.72; N, 0.83; P, 0.68%. $[\alpha]_D = +4.84$ (*c* 0.10, $CHCl_3$). Co-polymer **15**: $^{31}P\{^1H\}$ ($CDCl_3$): δ 147.0; Polydispersity (M_W/M_N) = 1.6, Average molecular weight (M_W) = 10,200 Da. Anal. calcd for $C_{343}H_{333}N_2O_2P$: C, 90.62; H, 7.38; N, 0.62; P, 0.68. Found: C, 89.33; H, 7.78; N, 0.92; P, 0.74%. $[\alpha]_D = +13.72$ (*c* 0.10, $CHCl_3$).

4.5. Synthesis of rhodium-loaded polymers

In a typical procedure, polymer **14** or **15** (0.087 mmol phosphoramidite) was added to a solution of $[Rh(COD)_2][BF_4]$ (0.031 g, 0.0764 mmol) in dichloromethane (10 mL). The resulting solution was allowed to stir for 1 h after which time the polymer was precipitated by addition of methanol, filtered and washed exhaustively with *n*-hexane. The rhodium loadings of **14[Rh]** and **15[Rh]** were determined as 0.32 and 0.26% Rh by wt, respectively, by inductively coupled plasma atomic emission analysis.

4.6. General hydrogenation procedure

Hydrogenation reactions were performed using standard Schlenk techniques and conducted under ambient H_2 pressure at room temperature for 20 h (4 h for the hydrogenation of methyl-2-acetamidocinnamate). Homogeneous catalytic reactions were performed with 0.2 mmol substrate in dichloromethane (5 mL, 0.04 M) and a substrate:$[Rh(COD)_2]BF_4$:phosphoramidite ratio of 1:0.05:0.10. Polymer-supported reactions were performed using 0.2 mmol substrate in dichloromethane (5 mL, 0.04 M) and a substrate:polymer ratio of 1:0.05. Amino acids were converted to the corresponding

methyl esters by reaction with diazomethane prior to analysis by gas chromatography with a CP7495 Chirasil-L-Val column. Enantiomeric excesses were determined by gas chromatography for the hydrogenation of amino acid derivatives as their methyl esters. For *N*-acetylalanine methyl esters: initial $T=80$°C held for 4 min, ramping to 100°C at 4°C/min. For *N*-acetylphenylalanine methyl esters: initial $T=120$°C, ramping to 160°C at 8°C/min, held for 2.5 min and then ramped to 190°C at 4°C/min. For dimethyl-methylsuccinate ee's were determined by optical rotation relative to dimethyl-(*R*)-methylsuccinate standard (99%). Absolute configurations were determined by comparison with reference compounds and literature values.

Acknowledgements

We gratefully acknowledge the Queens University of Belfast (SD) and the EPSRC (EGR) for financial support of this work and Johnson Matthey for loans of palladium salts.

References

1. (a) Dang, T.-P.; Kagan, H. B. J. C. S. *Chem. Commun.* **1971**, 481; (b) Kagan, H. B.; Dang, T.-P. *J. Am. Chem. Soc.* **1972**, *94*, 6429.
2. (a) Ohkuma, T.; Kitamura, M.; Noyori, R. In *Catalytic Asymmetric Synthesis*, 2nd ed.; Ojima, I., Ed.; Wiley: New York, 2000; Chapter 1; (b) Burk, M. J. Bienewald, F. In *Transition Metals for Organic Synthesis*; Beller, M.; Bolm, C., Eds.; Wiley-VCH: Weinham, 1998; Vol. 2, Chapter 1.1.2; (c) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994; Chapter 2.
3. Knowles, W. S.; Sabacky, M. J.; Vineyard, B. D. *J. Chem. Soc., Chem. Commun.* **1972**, 10.
4. (a) Vineyard, B. D.; Knowles, W. S.; Sabacky, M. J.; Bachman, G. L.; Weinkauff, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 5946; (b) Knowles, W. S.; Sabacky, M. J.; Vineyard, B. D.; Weinkauff, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 2657; (c) For an informative account, see: Knowles, W. S. *Angew. Chem., Int. Ed.* **2002**, *41*, 1998.
5. Fryzuk, M. D.; Bosnisch, B. *J. Am. Chem. Soc.* **1977**, *99*, 6262.
6. (a) Burk, M. J. *J. Am. Chem. Soc.* **1991**, *113*, 8158; (b) Burk, M. J.; Feaster, J. E.; Nugent, W. A.; Harlow, R. L. *J. Am. Chem. Soc.* **1993**, *115*, 10125.
7. Zhu, G.; Cao, P.; Jiang, Q.; Zhang, X. *J. Am. Chem. Soc.* **1997**, *119*, 1799.
8. Miyoshita, A.; Yosuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7932.
9. Brunner, H.; Pieronczyk, W.; Schönhammer, B.; Streng, K.; Bernal, I.; Korp, J. *Chem. Ber.* **1981**, *114*, 8265.
10. (a) Tang, W.; Zhang, X. *Angew. Chem., Int. Ed.* **2002**, *41*, 1612; (b) Tang, W.; Zhang, X. *Org. Lett.* **2002**, *4*, 4159; (c) Tang, W.; Zhang, X. *Org. Lett.* **2003**, *5*, 205.
11. (a) Togni, A.; Breutel, C.; Schnyder, A.; Spindler, F.; Landert, H.; Tijani, A. *J. Am. Chem. Soc.* **1994**, *116*, 4062; (b) Kang, J.; Lee, J. H.; Ahn, S. H.; Choi, J. S. *Tetrahedron Lett.* **1998**, *39*, 5523.
12. Reetz, M. T.; Neugebauer, T. *Angew. Chem., Int. Ed.* **1999**, *38*, 179.
13. (a) Chan, A. S. C.; Hu, W.; Pai, C.-C.; Lau, C. P. *J. Am. Chem. Soc.* **1997**, *118*, 9570; (b) Zhu, G.; Zhang, X. *J. Org. Chem.* **1998**, *63*, 3133; (c) Zhou, Y. G.; Zhang, X. *Chem. Commun.* **2002**, 1124; (d) Zhang, X. *J. Am. Chem. Soc.* **2002**, *124*, 4952; (e) Zhang, F. Y.; Kwok, W. H.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2001**, *12*, 2337; (f) Guo, R.; Au-Yeung, T. T.-L.; Wu, J.; Choi, M. C. K.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2002**, *13*, 2519.
14. Reetz, M. T.; Gosberg, A.; Goddard, R.; Kyung, S. H. *Chem. Commun.* **1998**, 2077.
15. Komarov, I. V.; Borner, A. *Angew. Chem., Int. Ed.* **2001**, *40*, 1197.
16. Claver, C.; Fernandez, E.; Gillon, A.; Heslop, K.; Hyett, D. J.; Martorell, A.; Orpen, A. G.; Pringle, P. G. *Chem. Commun.* **2000**, 961.
17. Junge, K.; Oehme, G.; Monsees, A.; Riermeier, T.; Dingerdissen, U.; Beller, M. *Tetrahedron Lett.* **2002**, *43*, 4977.
18. Reetz, M. T.; Sell, T. *Tetrahedron Lett.* **2000**, *41*, 6333.
19. (a) Guillen, F.; Rivard, M.; Toffano, M.; Legros, J.-Y.; Daran, J.-C.; Fiaud, J.-C. *Tetrahedron* **2002**, *58*, 5895; (b) Fiand, J.-C.; Guillen, F. *Tetrahedron Lett.* **1999**, *40*, 1939.
20. (a) Chen, W.; Xiao, J. *Tetrahedron Lett.* **2001**, *42*, 2897; (b) Chen, W.; Xiao, J. *Tetrahedron Lett.* **2001**, *42*, 8737.
21. Reetz, M. T.; Mehler, G. *Angew. Chem., Int. Ed.* **2000**, *39*, 3889.
22. van den Berg, M.; Minnaard, A. J.; Schudde, E. P.; van Esch, J.; de Vries, A. H. M.; de Vries, J. G.; Feringa, B. L. *J. Am. Chem. Soc.* **2000**, *122*, 11539.
23. (a) Fu, Y.; Xie, J.-H.; Hu, A.-G.; Zhou, H.; Wang, L.-X.; Zhou, Q.-L. *Chem. Commun.* **2002**, 480; (b) Hu, A.-G.; Fu, Y.; Xie, J.-H.; Zhou, H.; Wang, L.-X.; Zhou, Q.-L. *Angew. Chem., Int. Ed.* **2002**, *41*, 2348.
24. Shuttleworth, S. J.; Allin, S. M.; Sharma, P. K. *Synthesis* **1997**, 1217.
25. Leadbeater, N. E.; Marco, M. *Chem. Rev.* **2002**, *102*, 3217.
26. Dickerson, T. J.; Reed, N. N.; Janda, K. D. *Chem. Rev.* **2002**, *102*, 3325.
27. Huttenloch, O.; Laxman, E.; Waldmann, H. *Chem. Commun.* **2002**, 673.
28. Sablong, R.; Newton, C.; Dierkes, P.; Osborn, J. A. *Tetrahedron Lett.* **1996**, *37*, 4933.
29. Brunel, J. M.; Constantieux, T.; Buono, H. *J. Org. Chem.* **1999**, *64*, 8940.
30. Zeng, Q.; Liu, H.; Mi, A.; Jiang, Y.; Li, X.; Choi, M. C. K.; Chan, A. S. C. *Tetrahedron* **2002**, *58*, 8799.
31. Schenck, T. G.; Downes, J. M.; Milne, C. R. C.; Mackenzie, P. B.; Boucher, T. G.; Whelan, J.; Bosnich, B. *Inorg. Chem.* **1985**, *24*, 2334.
32. Hauser, C. R.; Bloom, M. S.; Breslow, D. S.; Adams, J. T.; Amore, S. T.; Weiss, M. J. *J. Am. Chem. Soc.* **1946**, *68*, 1544.