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Synthesis of Polymer-Supported Fesulphos Ligands and their Application in Asymmetric Catalysis

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Dedicated to Prof. M. Yus on occasion of his 60th birthday.

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Abstract: The synthesis of two Fesulphos-based chiral ligands and their immobilization on a polystyrene support is described. These supported chiral ligands act as very efficient catalysts in 1,3-dipolar cycloaddition and allylic substitution reactions providing the products with excellent enantioselectivities (91 to >99% *ee*). Filtration of the catalyst from the reaction mixtures allows simple product isolation. The polymer-supported Cu complex of chiral ligand PS-**8** can be recycled without further addition of a copper salt in 1,3-dipolar cycloaddition reactions.

Keywords: allylic substitution; asymmetric catalysis; copper; cycloaddition; immobilization; palladium

Introduction

The development of more efficient and environmentally friendly methodologies in asymmetric catalysis is a very important area of research in chemistry. An alternative that has received a great deal of attention in recent years is the immobilization of a chiral catalyst on a non-soluble support (polystyrene resins, silica gel, zeolites, etc), thereby creating a chiral heterogeneous catalyst. Unlike homogeneous catalysts, these supported complexes can be recovered from the reaction mixture by simple filtration, and can be easily recycled.[1]

We have previously described a sterically and electronic tunable family of bidentate 1,2-disubstituted ferrocenyl ligands[2] bearing phosphorus and sulphur heteroatoms as coordinating groups, and the presence of planar chirality as the only element of chirality (Figure 1). These sulfenylphosphinoferrocenes, named Fesulphos ligands,[3a] have proven to be excellent chiral ligands in a variety of highly enantioselective Pd-catalyzed and Cu-catalyzed reactions, such as allylic substitution, formal aza-Diels–Alder reactions of *N*-sulphonylimines, ring-opening of *meso*-heterobicyclic alkenes, 1,3-cycloaddition of azomethine ylides, and Mannich-type reactions of *N*-sulphonylimines.[3]

To increase the synthetic utility and practicability of these ligands in enantioselective metal-catalyzed transformations, we have now focussed on the synthesis of a Fesulphos-type ligand that could be attached to polymeric supports. Furthermore, although many examples of supported ligands based on P/P, N/N, O/O or P/N coordination modes can be found in the literature,[1,4] to the best of our knowledge, there are no examples of supported bidentate P/S ligands. In addition, only few reports of ferrocene chiral ligands immobilized *via* covalent[5] or non-covalent interactions[6] have been published. Here we report the synthesis of polymer-supported Fesulphos-type ligands and their application in two enantioselective transformations, the Cu(I)-catalyzed 1,3-dipolar cycloaddition of azomethine ylides and the Pd(II)-catalyzed allylic substitution reaction.

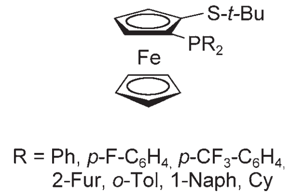


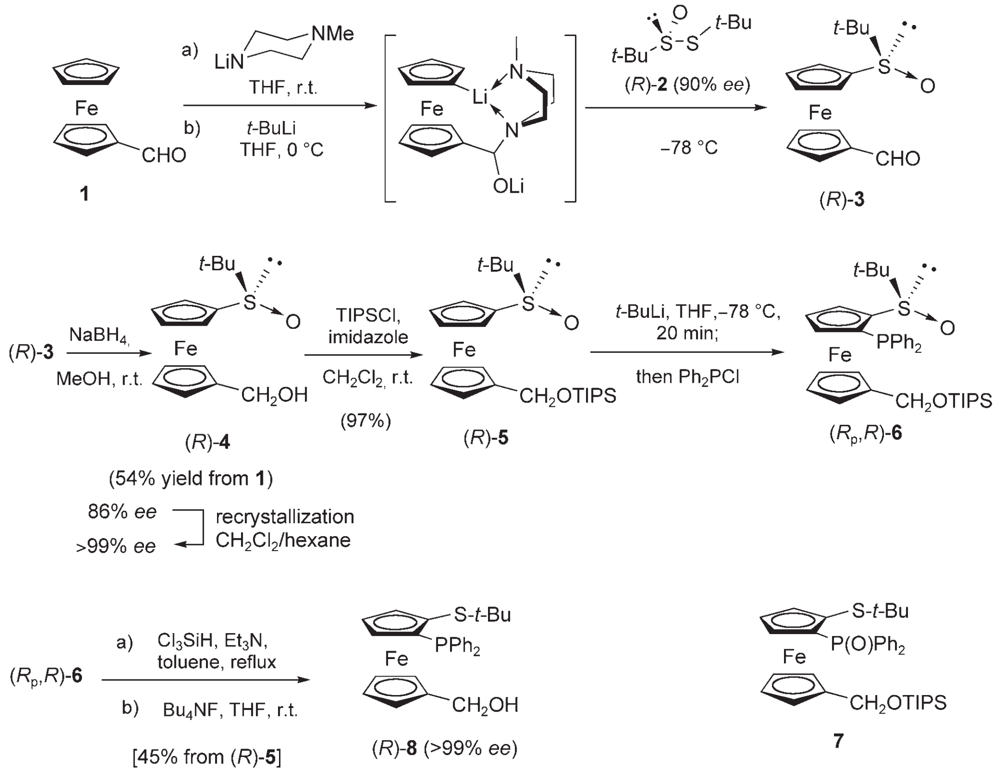
Figure 1. Fesulphos ligands.

Results and Discussion

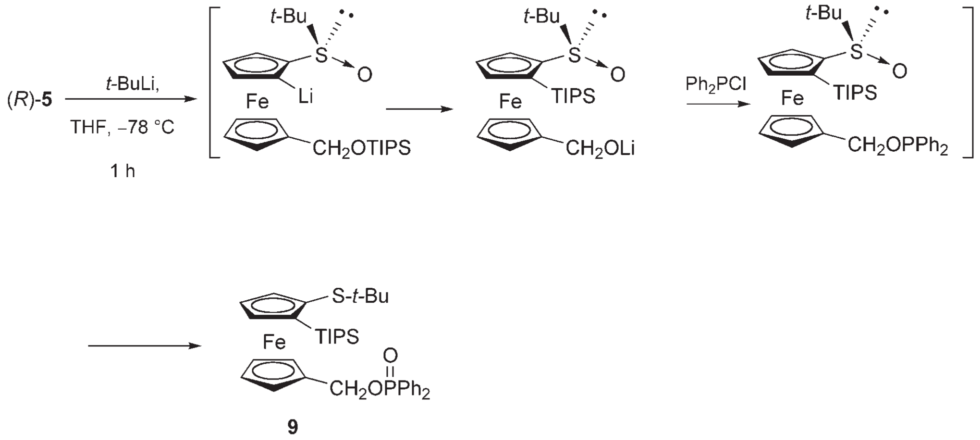
Synthesis and Immobilization of Chiral Fesulphos-Type Ligands

To incorporate the Fesulphos ligand into a polymer, an additional functional group on the ferrocene moiety was required. In order to minimize steric interactions that could result in a lower reactivity and/or selectivity in the catalytic reaction, we chose to attach the polymer to the Cp ring that does not contain the coordinating phosphine and sulphur groups. We started the synthesis from ferrocenecarboxaldehyde (**1**) and introduced a sulphinyl group on the unsubstituted Cp ring using the methodology developed by Manoury and Balavoine for the selective functionalization of the 1′-position of ferrocenecarbaldehyde.[7] They reported that treatment of **1** with the lithium salt of *N*-methylpiperazine forms an aminal anion which, upon treatment with *t*-BuLi followed by reaction with an electrophile, affords a mixture of 1,1′- and 1,2-disubstituted ferrocene compounds, with the former as the major regioisomer (>90:10). Indeed, when (*R*)-*tert*-butyl *tert*-butanethiosulphinate (90% *ee*) (**2**)[8] was used as the electrophile, 1,1′-sulphinylferrocenecarboxaldehyde (**3**) was obtained in 86% *ee* (Scheme 1). In order to avoid a significant loss in the enantioselectivity, this sulphinylation step must be carried out by addition *via* cannula of the dilithiated species to a cooled solution of **2** (−78 °C).[9] Aldehyde (*R*)-**3** decomposes on standing, thus it was immediately reduced to the corresponding alcohol [(*R*)-**4**] (54% overall yield from **1**) by treatment of the reaction mixture with NaBH$_4$. After purification and recrystallization, (*R*)-**4** was obtained in >99% *ee*. Protection of the alcohol function afforded sufoxide (*R*)-**5** in almost quantitative yield. Diastereoselective *ortho*-lithiation of (*R*)-**5** at low temperature for a short period of time (≤20 min), followed by treatment with Ph$_2$PCl gave sulphoxide (*R*$_P$,*R*)-**6**. Intermediate (*R*$_P$,*R*)-**6** spontaneously isomerizes to phosphine oxide **7**. This unwanted transformation can be avoided by fast treatment of the crude mixture containing (*R*$_P$,*R*)-**6** with Cl$_3$SiH and Et$_3$N. Finally, deprotection of the silyl group with Bu$_4$NF provided enantiopure (*R*)-**8** in 45% yield from (*R*)-**5**.

If, during the synthesis of (*R*)-**8**, the *ortho*-lithiated intermediate formed from (*R*)-**5** is left at −78 °C for prolonged reaction times (1 h instead of 20 min) before adding Ph$_2$PCl, a by-product is formed. We thought its formation arises from a retro-Brook rearrangement[10] of the triisopropylsilyl group (Scheme 2). Its ^{1}H NMR spectrum shows the presence of a triisopropylsilyl group which remains even after treatment of the reaction mixture with Bu$_4$NF, while its ^{31}P NMR spectrum shows a resonance at +25 ppm. In sharp contrast, ferrocenes bearing a phosphine group, such as (*R*$_P$,*R*)-**6** and (*R*)-**8**, show singlets at



Scheme 1.



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Scheme 2.

around –25 ppm in their ^{31}P NMR spectra.[11] Based on the spectroscopic data, in particularly on the ^{31}P NMR and mass spectra, the structure of this byproduct has been tentatively assigned as the diphenylphosphinate **9**. Typically, the ^{31}P NMR spectra of diphenylphosphinates show resonances at around +30 ppm, whereas phosphinites show resonances at >100 ppm.[12] The oxidation of the phosphinite intermediate to phosphinate is believed to take place *via* an intramolecular process, such as that proposed for the formation of **7** (*vide supra*).

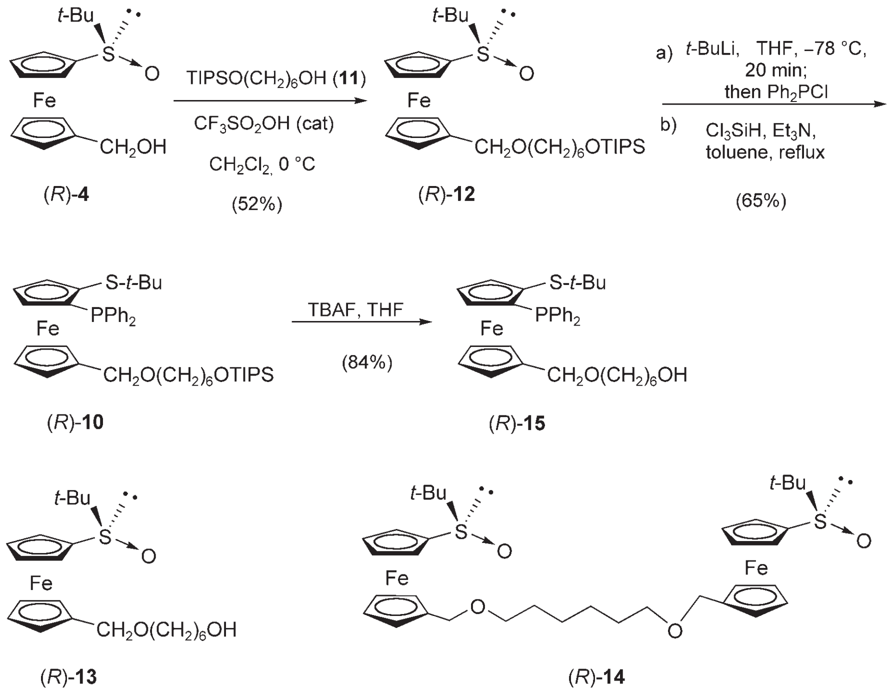
First we tried the attachment of ligand (*R*)-**8** to a polystyrene resin without using any linkage. However, when (*R*)-**8** was treated with a catalytic amount of triflic acid in the presence of trichloroacetimidate Wang resin, only less than 10% of polymer-supported ligand could be obtained, the remaining (*R*)-**8** being decomposed. We thought that decomposition may occur through the formation, in the presence of acid, of a favourable ferrocenylmethyl carbocation from the starting alcohol (*R*)-**8**. Thus, we focussed our attention on the introduction of a linkage with the aim of avoiding decomposition under the acidic conditions required for the attachment. Direct alkylation of (*R*)-**8** with Br$(CH_2)_6$OTIPS[13] gave the TIPS-protected alcohol **10**, albeit in low yield (44%). Alternatively, one can take advantage of the easy formation of ferrocenylmethyl carbocations from ferrocenylmethanol derivatives in the presence of acid. The carbocation could be trapped with a nucleophile present in the reaction media. To our delight, treatment of sulphoxide (*R*)-**4** with monoprotected diol **11**, in the presence of a catalytic amount of triflic acid, afforded sulphoxide (*R*)-**12** (52% yield, 99% *ee*) together with the alcohol derived from removal of the TIPS protecting group [(*R*)-**13**, *ca.* 4%], and dimer **14** (17%). From (*R*)-**12**, a similar synthetic route to that shown in Scheme 1 (*ortho*-lithiation/phosphination/sulphoxide reduction) yielded enantiopure alcohol (*R*)-**15** (Scheme 3).

Ferrocene (*R*)-**15** was treated with trichloroacetimidate Wang resin [copoly(styrene-1% DVB), 200–400 mesh, 0.6 mmol/g resin] in the presence of triflic acid, affording polymer-supported (*R*)-**15** (PS-**15**) in good yield (80%). We also directly supported ligand (*R*)-**8** by *O*-alkylation with a chloro Merrifield resin (1% cross-linked, 200–400 mesh, 2 mmol Cl/g resin) in the presence of an excess of NaH and a catalytic amount of NaI (Scheme 4). In this case, the yield of polymer-supported (*R*)-**8** (PS-**8**) was 40% [>90% based on recovered starting material, unreacted (*R*)-**8** could be easily recovered by filtration]. The yields were calculated from elemental analyses of the polymer-supported ferrocene derivatives. Unfortunately, all attempts to immobilize ferrocene (*R*)-**15** into the Merrifield resin failed or resulted in very low yields.

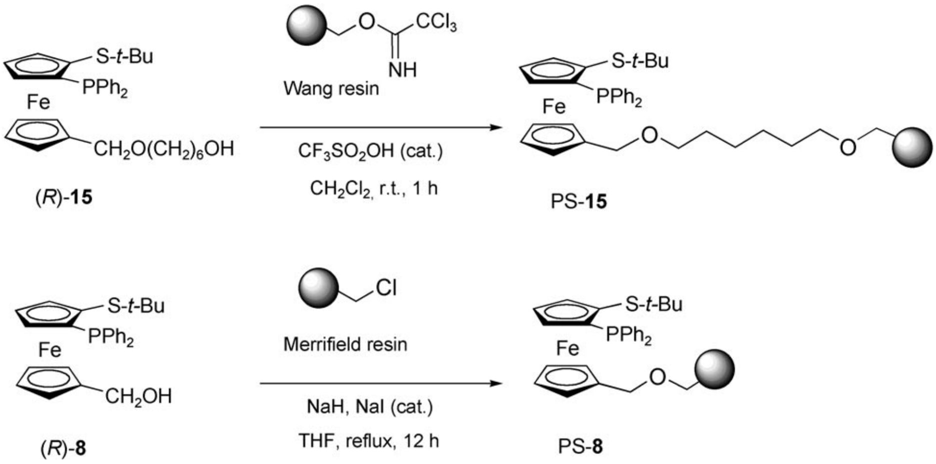
Cu(I)-Catalyzed 1,3-Dipolar Cycloaddition of Azomethine Ylides

We had previously reported that Fesulphos ligand (R=Ph, see Figure 1) shows excellent performance in the Cu(I)-catalyzed enantioselective 1,3-dipolar cycloaddition of azomethine ylides (Scheme 5).[3e,14] Very high levels of reactivity, enantioselectivity, and *endo/exo* selectivity were obtained in very short reaction times.

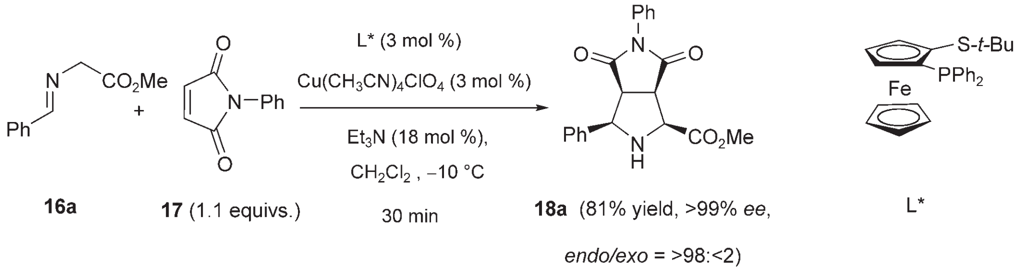
In order to find out whether the introduction of substituents on the lower Cp ring of the chiral ligand has any influence on the outcome of the reaction, we first tested ligands **8** and **15** in the Cu(I)-catalyzed 1,3-dipolar cycloaddition reaction between imine **16a** and *N*-phenylmaleimide (**17**). We were delighted to see that both ligands, **8** and **15**, afforded results very similar to those shown in Scheme 5: cycloadduct **18a** was obtained in >92% yield with complete *endo* selectivity and >99% *ee*. Thus, we turned our attention to the use of polymer-supported ferrocenes PS-**8** and



Scheme 3.



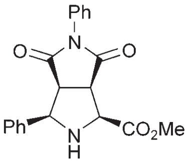
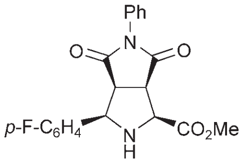
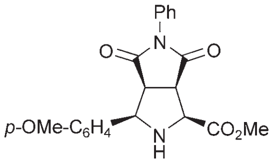
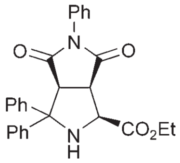
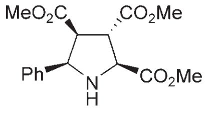
Scheme 4.



Scheme 5.

PS-**15** as chiral catalysts for this transformation. It is important to note that Cu(I) complexes not bearing a chiral ligand can catalyze the formation of racemic cycloadducts. Thus, for a successful enantioselective 1,3-dipolar cycloaddition, it is necessary that the Cu(I) is coordinated to the chiral ligand prior to the addition of the reactants, and that the reaction catalyzed by this chiral complex is faster than the reaction catalyzed by Cu(I) complexes not bearing the chiral ligand, which may be present in the reaction mixture. Although our preliminary attempts failed, a detailed study led us to the conclusion that coordination of Cu(I) to the polymer-supported ligands is slow: whereas formation of the Cu(I)-Fesulphos complex takes place within seconds in CH_2Cl_2 at ambient temperature, the formation of the polymer-supported chiral complex is rather slow. Thus, a suspension of PS-**8** or PS-**15** and $Cu(CH_3CN)_4ClO_4$ (2 mol%) has to be stirred for one hour at room temperature before adding the remaining reagents to ensure the formation of the supported copper complex. Interestingly, PS-**8** showed a much better catalytic performance than PS-**15**: reaction of *N*-benzylidenglycine methyl ester (**16a**) with *N*-phenylmaleimide (**17**) afforded only 55% of cycloadduct **18a** in 98% *ee* after 24 h when PS-**15** (*ca.* 15 mol%) was used (Table 1, entry 1), while PS-**8** (*ca.* 6.5 mol%) provided **18a** in 98% yield and >99% *ee* after only 4 h at room temperature (Table 1, entry 2). The *endo* selectivity was complete (*endo/exo* = >98%:<2%) as in the case of

Table 1. 1,3-Dipolar cycloaddition of azomethine ylides catalyzed by immobilized Fesulphos-type ligands.[a]

Entry	Imine	Dipolarophile	PS-L*	Product		Time [h]	Yield [%][b]	*ee* [%][c]
1	**16a**	**17**	PS-**15**[d]		**18a**	24	55[e]	98
2	**16a**	**17**	PS-**8**		**18a**	4	98[e]	>99
3	**16b**	**17**	PS-**8**		**18b**	9	92[e]	>99
4	**16c**	**17**	PS-**8**		**18c**	9	95[e]	>99
5	**16d**	**17**	PS-**8**		**18d**	7	95[e]	99
6	**16a**	**19**	PS-**8**		**20**	2	92[f]	98[g]
7	**16a**	**19**	PS-**15**[d]		**20**	24	15[h]	98[g]

[a] Unless otherwise noted, a suspension of the polymer-supported ligand PS-**8** (ca. 6.5 mol%) and $Cu(MeCN)_6ClO_4$ (2 mol%) in CH_2Cl_2 (1 mL) was stirred for 1 h at ambient temperature. Then, a solution of the imine (**16a–d**, 0.198 mmol) in CH_2Cl_2 (0.5 mL) was added, followed by Et_3N (18 mol%) and by a solution of the dipolarophile (**17** or **19**, 0.18 mmol) in CH_2Cl_2 (0.5 mL).

[b] Isolated yield.

[c] Determined by HPLC.

[d] *Ca.* 15 mol% of PS-**15**.

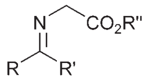
[e] *endo/exo* = >98%:<2%.

[f] Isolated yield of a mixture of *endo/exo* = 80:20.

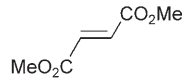
[g] *ee* of *endo* adduct.

[h] Isolated yield of a mixture of *endo/exo* = 78:27.

the non-supported Fesulphos ligand.[3e] Encouraged by these excellent results, we tested the reaction of a variety of arylimines of glycine methyl ester (**16b–d**) with two dipolarophiles, *N*-phenylmaleimide (**17**) and methyl fumarate (**19**), under similar reaction conditions.



16a, R = Ph, R' = H, R'' = Me
16b, R = *p*-F-C_6H_4, R' = H, R'' = Me
16c, R = *p*OMe-C_6H_4, R' = H, R'' = Me
16d, R = Ph, R' = Ph, R'' = Et



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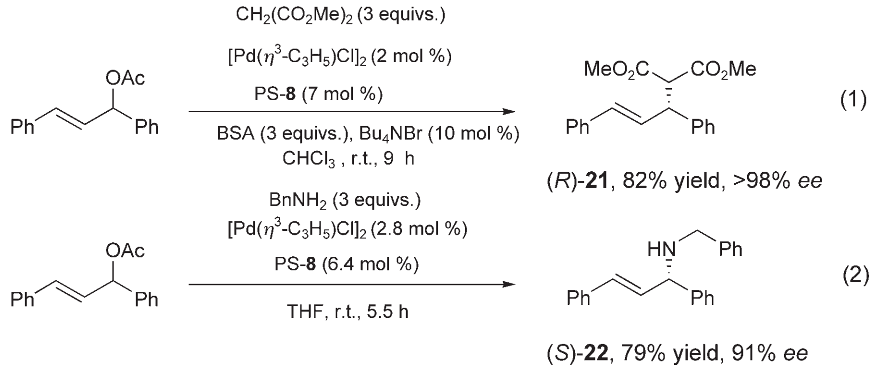
N-Benzylidenglycine methyl ester bearing both electron-withdrawing and electron-donating groups gave excellent results, yielding in 9 h the corresponding cycloadducts (**18b–c**) in excellent yields and enantioselectivities (Table 1, entries 3 and 4, respectively). The incorporation of an extra substituent at the α position of the azomethine ylide was not detrimental to the *ee* or the yield: the 1,3-dipole derived from the ketimine of benzophenone (**16d**) reacted with *N*-phenylmaleimide (**17**) affording cycloadduct **18d** in 95% yield and 99% *ee* (Table 1, entry 5). On the other hand, the reaction of *N*-benzylidenglycine methyl ester (**16a**) with methyl fumarate (**19**) catalyzed by PS-**8** afforded cycloadduct **20** in 92% yield with an *endo/exo* selectivity of 80:20 (Entry 6). The major *endo* adduct was obtained with 98% *ee* and the *exo* adduct with 86% *ee*. In this reaction, the catalyst PS-**15** proved to be, once again, much less reactive (15% yield, entry 7), although the *endo* selectivity and enantioselectivity were similar to that obtained with PS-**8**. For entries 2–6, purification of the products was performed by filtration and addition of hexane to the filtrate until precipitation of the cycloadducts occurred. No further purification by column chromatography was required.

Pd-Catalyzed Allylic Substitutions

We had previously reported very high enantioselectivities (up to >99% *ee*) in the palladium-catalyzed allylic substitution reaction of allylic acetates with carbon and nitrogen nucleophiles using Fesulphos ligands.[3b] Encouraged by the excellent results obtained in the 1,3-dipolar cycloadditions (*vide supra*), we decided to test the catalytic performance of the polymer-supported Fesulphos ligands in enantioselective palladium-catalyzed allylic substitution reactions.[15] The reaction of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate in chloroform at room temperature using *N*,*O*-bis(trimethylsilyl)acetamide (BSA) as base, and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (2 mol%)/PS-**8** (*ca.* 6.5 mol%) as catalyst system is shown in Scheme 6 [Eq. (1)]. The substitution product (*R*)-**21** was obtained in 82% yield after 9 h in very high *ee* (98%). Although the yield is slightly lower than that obtained when using the non-supported Fesulphos ligand (82% *vs.* 92%), the enantioselectivity is higher (98% *vs.* 93% *ee*).[3b] Similarly, when benzylamine was used as nucleophile the substitution product (*S*)-**22**[3b,16] [Scheme 6, Eq. (2)] was obtained in 79% yield and good enantioselectivity (91% *ee*), albeit somewhat lower than from the unsupported Fesulphos ligand (97% *ee*).[3b]

Recovery and Reuse of PS-8

Finally, we studied the recovery and reuse of the heterogeneous chiral catalyst PS-**8**. As a test reaction, we chose the 1,3-dipolar cycloaddition of *N*-benzylideneglycine methyl ester (**16a**) with *N*-phenylmaleimide (**17**) (Table 1, entry 2). To make the reuse of the heterogeneous chiral catalyst more efficient, we used a bigger resin particle for these experiments (1% cross-linked, 70–90 mesh, 1 mmol Cl/g). In our first attempt, once the cycloaddition was over, we simply filtered off the resin and rinsed it with CH_2Cl_2, but we observed a great depletion of the enantioselectivity in the second run (from 99% *ee* in the first run to 80%



Scheme 6.

ee in the second cycle). This lower enantiopurity could be due to a partial oxidation of the supported PS-**8**-copper complex when filtering off under an air atmosphere, which may produce achiral Cu(I) particles able to catalyze the formation of racemic product. We confirmed this hypothesis by analyzing PS-**8** before and after use in the reaction. While the ^{31}P solid state MAS NMR spectrum of a sample of freshly prepared PS-**8** showed a peak at −25.9 ppm, the ^{31}P solid state MAS NMR spectrum of PS-**8** after one run showed two peaks at −25.9 and +27.8 ppm. The latter peak is characteristic for phosphine oxide compounds.[12] To our delight, excellent results were obtained when the catalytic system was filtered and reused under a rigorously inert atmosphere.[9] Thus, as shown in Table 2, the catalyst derived from PS-**8** and $Cu(MeCN)_6ClO_4$ could be recycled up to three times without further addition of Cu(I). Both catalyst activity and reaction rate were typically unaffected up to the third consecutive run (Table 2). Attempts to reuse metal-free PS-**8** were also tried. Thus, after a first run, the polymer was washed with a solution of *o*-phenanthroline to remove the Cu atoms. Unfortunately, the use of this resin in the second run afforded a mixture of racemic *endo/exo* cycloadducts.

Conclusions

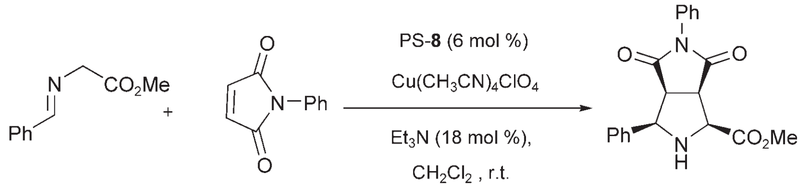
In summary, we have developed an efficient method for the synthesis of chiral 1,2,1′-trisubstituted Fesulphos-type ligands. These ligands have been successfully attached to polystyrene resins and used as heterogeneous chiral ligands in enantioselective Cu(I)-catalyzed 1,3-dipolar cycloadditions of azomethine ylides and enantioselective Pd-catalyzed allylic substitution reactions. Excellent catalytic activities and enantioselectivities were obtained in all cases (91 to >99% *ee*). Furthermore, the polystyrene-supported Fesulphos ligand PS-**8** can be recovered and reused in successive catalytic 1,3-dipolar cycloadditions without further addition of Cu(I) maintaining excellent enantioselectivity in up to three runs.

Experimental Section

General Remarks

All reactions were carried out under dry nitrogen atmosphere in oven-dried glassware. Solvents were dried under MS 4 Å. Flash chromatography was carried out on 60 Å (35–70 μm) silica gel. ^{1}H and ^{13}C NMR spectra were recorded at 300 MHz and and 75 MHz, respectively. Enantiomeric excess and diastereomeric excess were determined by HPLC. Imines **16a–c** were prepared as already described.[3e] *N*-Phenylmaleimide (**17**), methyl fumarate (**19**), imine **16d**, benzylamine, dimethyl malonate, *N,O*-bis(trimethylsilyl)acetamide (BSA), $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$, and Merrifield's peptide resin (1% cross-linked, 70–90 mesh, 1 mmol Cl/g or 1% cross-linked, 200–400 mesh, 2 mmol Cl/g) were purchased from Sigma–Aldrich and used without further purification. Trichloroacetimidate Wang resin [copoly(styrene-1% DVB), 200–400 mesh, 0.6–1.00 mmol/g resin] was purchased from Novabiochem, Merck, and washed with THF and filtered to dryness before use. The *endo/exo* ratios of **18a–d**[3e,17] and **20**[18] were established by comparison of the corresponding ^{1}H NMR with those previously reported. The absolute configurations of **18a–d** and **20** were assigned by comparison of the optical rotation values with those previously reported in

Table 2. Catalyst recycling experiments.[a]



16a (1.1 equivs.) **17** **18a**

Run	Cu(I) [mol%]	Time [h]	Yield [%][b]	*endo/exo*[c]	*ee* [%][d]
1	2	4	99	>98%:<2%	98
2	0	4	87	>98%:<2%	99
3	0	5	99	>98%:<2%	99

[a] Reaction conditions: A suspension of the polymer-supported ligand PS-**8** (*ca.* 6.5 mol%) and $Cu(MeCN)_6ClO_4$ (2 mol%) in CH_2Cl_2 (1 mL) was stirred for 1 h at ambient temperature. Then, a solution of imine **16a** (0.198 mmol) in CH_2Cl_2 (0.5 mL) was added, followed by Et_3N (18 mol%) and by a solution of dipolarophile **17** (0.18 mmol) in CH_2Cl_2 (0.5 mL). After 4 h, the resin was filtered off under N_2 atmosphere and rinsed with CH_2Cl_2 and immediately suspended in 1 mL of CH_2Cl_2. After stirring 20 min, the reactants were added as indicated before. The same resin was used for each entry.

[b] Isolated yield.

[c] Determined by ^{1}H NMR spectroscopy.

[d] Determined by HPLC.

the literature.[3e] 1,3-Diphenyl-2-propenyl acetate was prepared as previously described.[19]

(*R*)-1′-(*tert*-Butylsulphinyl)ferrocenecarboxaldehyde [(*R*)-3] and (*R*)-1′-(*tert*-Butylsulphinyl)ferrocenemethanol [(*R*)-4]

To a solution of *N*-methylpiperazine (1.55 mL, 14.0 mmol) in dry THF (20 mL) was added *t*-BuLi (8.2 mL, 14.0 mmol, 1.7 M in pentane), at room temperature under a nitrogen atmosphere. The resulting mixture was stirred for 30 min before adding a solution of ferrocenecarboxaldehyde (**1**, 2.75 g, 12.85 mmol) in dry THF (25 mL). After 2 h at room temperature, the mixture was cooled down to 0 °C and *t*-BuLi (8.9 mL, 15.2 mmol, 1.7 M in pentane) was slowly added. After three hours, the mixture was added *via* cannula to a solution of di-*tert*-butyl thiosulphinate [(*R*)-**2**, 90% *ee*, 4.48 g, 23.13 mmol] in dry THF (25–30 mL) at −78 °C. The reaction mixture was left stirring at −78 °C overnight. After extractive work-up (EtOAc/H_2O) and chromatography (SiO_2, hexane/EtOAc, 1:1) (*R*)-**3** was obtained as a dark red solid; yield: 2.21 g (54%); mp 96–98 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 10.01$ (s, 1H), 4.97 (d, $J = 4.1$ Hz, 2H), 4.78 (s, 3H), 4.48 (s, 3H), 1.10 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 193.69$, 88.65, 80.66, 75.00, 74.82, 71.57, 71.24, 71.02, 70.76, 66.87, 55.26, 22.69 (3C); EI-MS (70 EV): *m/z* (%) = 318(23) [M^+], 262 (100), 214 (27), 166 (47), 121 (19).

Aldehyde (*R*)-**3** decomposes on standing. Isolation of (*R*)-**3** is not necessary. Treatment of the reaction mixture with MeOH (10 mL) and addition of an excess of $NaBH_4$ (938 mg, 24.6 mmol) at 0 °C gives after 2 h complete conversion to alcohol (*R*)-**4**. Extractive work-up (EtOAc/H_2O) and chromatography (SiO_2, hexane/EtOAc, 3:2) afforded (*R*)-**4** as a yellow solid; yield: 54% (from **1**, 86% *ee*; >99% *ee* after recrystallization in hexane/CH_2Cl_2): mp 118.2 °C; $[\alpha]_D^{20}$: −300 (*c* 0.30, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 4.93$ (t, $J = 6.8$ Hz, 1H), 4.46 (s, 1H (OH)), 4.31 (d, $J = 3.6$ Hz, 2H), 4.24 (d, $J = 6.6$ Hz, 4H), 4.18 (s, 1H), 4.13 (s, 1H), 4.06 (s, 1H), 0.96 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 93.48$, 86.03, 70.17, 69.67, 69.31, 68.89, 68.70, 68.29, 67.39, 66.53, 59.59, 55.26, 22.72 (3C); EI-MS (70 EV): *m/z* (%) = 320 (40) [M^+], 264 (100), 198 (22), 168 (34), 121 (9), 78 (49); HPLC conditions: AS-H column (Chiral Daicel); 0.7 mL min^{-1}; 90:10 (hexane:2-propanol): (*S*): 21.4 min, (*R*): 23.5 min.

(*R*)-1-*tert*-Butylsulphinyl-1′-(triisopropylsilyloxymethyl)ferrocene [(*R*)-5]

To a solution of (*R*)-**4** (150 mg, 0.468 mmol) and imidazole (64 mg, 0.94 mmol) in dry CH_2Cl_2 (7 mL) was added triisopropylsilyl chloride (180 mg, 0.936 mmol) at ambient temperature under a nitrogen atmosphere. The resulting mixture was stirred at room temperature overnight. After extractive work-up (CH_2Cl_2/H_2O) and chromatography (SiO_2, hexan/EtOAc, 3:1), (*R*)-**5** was obtained as dark yellow oil; yield: 216 mg (97%): ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 4.60$ (m, 1H), 4.48 (m, 2H), 4.37–4.29 (m, 7H), 1.05 (m, 21H), 1.00 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 65.81$, 60.98, 54.87, 22.78 (3C), 18.08 (6C), 12.06 (3C).

(*R*)-1-*tert*-Butylsulphinyl-2-diphenylphosphino-1′-(triisopropylsilyloxymethyl)ferrocene [(R_p,*R*)-6] and (*R*)-1-*tert*-Butylsulphenyl-2-diphenylphosphino-1′-hydroxymethylferrocene [(*R*)-8]

To a solution of (*R*)-**5** (329 mg, 0.69 mmol) in dry THF (10 mL) was slowly added *t*-BuLi (600 μL, 1.04 mmol, 1.7 M in pentane) at −78 °C under a nitrogen atmosphere. The mixture was stirred for 20 min at the same temperature before adding diphenylphosphine chloride (228 mg, 1.04 mmol). The reaction mixture was stirred for 1 h at −78 °C. After extractive work-up (Et_2O/H_2O), (R_p,*R*)-**6** was obtained as a brown thick oil. ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 7.67$–7.58 (m, 2H), 7.36–7.20 (m, 8H), 4.62 (dd, $J = 2.2$, 3.6 Hz, 1H), 4.56 (dd, $J = 2.5$, 2.6 Hz, 1H), 4.50 (m, 2H), 4.43 (dd, $J = 1.3$, 2.6 Hz, 1H), 4.26–4.25 (m, 2H), 4.18 (m, 1H), 3.94 (dd, $J = 2.2$, 3.7 Hz, 1H), 3.81–3.80 (m, 1H), 1.05–1.03 (m, 21H), 1.02 (s, 9H).

The crude mixture containing (R_p,*R*)-**6** was dissolved in toluene (10 mL). Then, triethylamine (1.4 g, 13.8 mmol) and trichlorosilane (935 mg, 6.9 mmol) were added at room temperature under a nitrogen atmosphere. The reaction mixture was left stirring under reflux overnight. After cooling down to room temperature, the mixture was poured into a conical flask containing CH_2Cl_2 (50 mL), and a solution of 1 N NaOH (50 mL) was slowly added. The organic phase was washed with brine, dried over $MgSO_4$ and evaporated to dryness. The product can be used in the next step without further purification. Alternatively, purification by flash chromatography (SiO_2, hexane/EtOAc, 3:1) yields (*R*)-1-(*tert*-butylsulphenyl)-2-diphenylphosphino-1′-(triisopropylsilyloxymethyl)ferrocene. ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 7.60$–7.34 (m, 2H), 7.30–7.23 (m, 5H), 7.16–7.14 (m, 3H), 4.61 (dd, $J = 2.2$, 3.6 Hz, 1H), 4.15 (m, 3H), 4.07 (dd, $J = 1.3$, 2.6 Hz, 1H), 3.98 (dd, $J = 2.2$, 3.8 Hz, 1H), 3.77 (s, 2H), 0.97 (m, 21H), 0.92 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 140.24$ (d, $^1J_{CP} = 10.4$ Hz, C_{ipso} PPh_2), 138.47 (d, $^1J_{CP} = 9.3$ Hz, C_{ipso} PPh_2), 135.32 (d, $^2J_{CP} = 21.9$ Hz, CH_o PPh_2), 133.91 (d, $^2J_{CP} = 19.2$ Hz, CH_o PPh_2), 129.06 (CH, PPh_2), 128.08 (d, $^3J_{CP} = 8.2$ Hz, CH_m PPh_2), 127.88 (d, $^3J_{CP} = 6.6$ Hz, CH_m PPh_2), 127.83 (CH, PPh_2), 89.93, 83.73, 83.28, 81.00 (d, $^3J_{CP} = 2.2$ Hz, C_5H_3), 73.73 (d, $^2J_{CP} = 4.4$ Hz, C_5H_3), 72.67, 71.50, 70.61 (d, $^2J_{CP} = 4.9$ Hz, C_5H_3), 69.08, 60.73, 46.00, 31.09 (3C), 18.09 (6C), 12.01 (3C); ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta = -27.03$; EI-MS (70 EV): *m/z* (%) = 644(100) [M^+], 587 (6), 467 (22), 423 (15), 336 (37), 302 (9), 226 (11), 170 (7).

The crude mixture of (*R*)-1-(*tert*-butylsulphenyl)-2-diphenylphosphino-1′-(triisopropylsilyloxymethyl)ferrocene was dissolved in THF (50 mL) and Bu_4NF (1.04 mmol, 1.04 mL, 1 M in THF) was added at 0 °C. The resulting reaction mixture was stirred for 1 h at room temperature. Evaporation of the solvent and purification by column chromatography (SiO_2, hexane/EtOAc, 4:1) afforded (*R*)-**8** (>99% *ee*) as a yellow solid; yield: 150 mg [45% from (*R*)-**5**]: mp 115.2 °C; $[\alpha]_D^{20}$: −300 (*c* 0.24, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 7.60$–7.54 (m, 2H), 7.31–7.23 (m, 5H), 7.19–7.15 (m, 3H), 4.66 (dd, $J = 2.8$, 3.6 Hz, 1H), 4.44 (dd, $J = 2.4$, 2.5 Hz, 1H), 4.17 (m, 3H), 4.09 (dd, $J = 1.3$, 2.6 Hz, 1H), 4.05 (dd, $J = 0.9$, 1.1 Hz, 1H), 3.83 (dd, $J = 2.4$, 3.6 Hz, 1H), 3.63 (dd, $J = 2.4$, 3.6 Hz, 1H), 2.47 (t, $J = 6.7$, Hz, OH), 0.93 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 139.91$ (d, $^1J_{CP} = 9.9$ Hz, C_{ipso} PPh_2), 138.08 (d, $^1J_{CP} = 9.4$ Hz, C_{ipso} PPh_2), 135.21 (d, $^2J_{CP} =$

22.6 Hz, CH_o PPh_2), 132.96 (d, $^{2}J_{CP}=19.8$ Hz, CH_o PPh_2), 129.17 (CH_p PPh_2), 128.19 (CH_p PPh_2), 128.04 (d, $^{3}J_{CP}=7.2$ Hz, PPh_2), 127.96 (d, $^{3}J_{CP}=9.9$ Hz, PPh_2), 91.39, 83.47, 83.03, 81.28 (d, $^{2}J_{CP}=5.5$ Hz, C_5H_3), 80.32 (d, $^{3}J_{CP}=2.2$ Hz, C_5H_3), 73.36, 71.83, 70.49 (d, $^{1}J_{CP}=12.6$ Hz, C_5H_3), 70.02, 68.11, 59.59, 46.70, 31.06 (3C); ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta=-26.50$; EI-MS (70 EV): *m/z* (%) = 488(100) [M^+], 414 (18), 336 (78), 302 (23), 258 (5), 226 (13), 170 (18); HPLC conditions: AS-H column (Chiral Daicel); 0.5 mL min^{-1}; 80:20 (hexane:2-propanol): (*R*): 13.29, (*S*): 19.32 min. The structure was confirmed by ^{1}H-^{13}C (HMQC) correlations.

[1-*tert*-Butylsulphenyl-2-triisopropylsilyl]ferrocenyl-1′-methyl Diphenylphosphinate (9)

When the *ortho*-lithiated intermediate formed from (*R*)-**5** is left at −78 °C for prolonged reaction times (1 h) before adding Ph_2PCl, a retro-Brook rearrangement of the silyl group gives rise to the formation of ferrocene **9**. ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=7.90$–7.80 (m, 4H), 7.49–7.41 (m, 6H), 4.77–4.76 (dd, $J=1$, 1.1 Hz, 1H), 4.48–4.45 (m, 2H), 4.41–4.30 (m, 4H), 4.24 (dd, $J=1$, 1.1 Hz, 1H), 4.08 (dd, $J=2.7$, 3.1 Hz, 1H), 1.06 (m, 21H), 0.89 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=135.08$ [d, $^{1}J_{CP}=9.9$ Hz, C_{ipso} $P(O)Ph_2$], 133.67 [d, $^{1}J_{CP}=8.8$ Hz, C_{ipso} $P(O)Ph_2$], 132.09 [d, $^{2}J_{CP}=9.3$ Hz, CH_o $P(O)Ph_2$], 131.67 [d, $^{2}J_{CP}=9.3$ Hz, CH_o $P(O)Ph_2$], 131.24 [CH_p $P(O)Ph_2$], 128.07 [d, $^{3}J_{CP}=3.3$ Hz, CH_m $P(O)Ph_2$], 127.91 [d, $^{3}J_{CP}=3.8$ Hz, CH_m $P(O)Ph_2$], 90.79, 81.98–75.20 (several peaks overlapping), 72.81 (d, $^{3}J_{CP}=2.2$ Hz, C_5H_4), 72.68, 71.53, 71.34, 69.19, 60.63, 46.27, 31.02 (3C), 18.09 (6C), 12.00 (3C) [one C signal for CH_p $P(O)Ph_2$] is missing due to overlapping); ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta=+25.03$; EI-MS (70 EV): *m/z* (%) = 660 (19) [M^+], 526 (100), 483 (32), 449 (7), 397 (11), 352 (85), 228 (8).

6-Triisopropylsilyloxy-1-hexanol (11)

To a solution of 1-bromo-6-hexanol (100 mg, 0.55 mmol) and imidazole (56 mg, 0.83 mmol) in dry CH_2Cl_2 (1.4 mL) was added triisopropylsilyl chloride (116 mg, 0.60 mmol) at room temperature under a nitrogen atmosphere. The resulting mixture was stirred at room temperature overnight. The residue was washed with H_2O (×4) and extracted with CH_2Cl_2. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (SiO_2, hexane/EtOAc, 3:1) affording **11** as a colourless; yield: 104 mg (69%). ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=3.66$ (t, $J=6.4$ Hz, 2H), 3.60 (t, $J=6.6$ Hz, 2H), 2.19 (s, OH), 1.55–1.35 (m, 8H), 1.04–1.03 (m, 21H).

Ferrocene (*R*)-12

To a solution of (*R*)-**4** (200 mg, 0.63 mmol) in dry CH_2Cl_2 (1.2 mL) a solution of trifluoromethanesulphonic acid (1.9 mg, 0.0125 mmol) in dry Et_2O (0.2 mL) was added, followed by a solution of $TiPSO(CH_2)_6OH$ (**11**) (343 mg, 1.25 mmol) in dry CH_2Cl_2 (0.8 mL) at 0 °C under a nitrogen atmosphere. The reaction mixture was left stirring overnight at room temperature. After evaporation of the solvent and purification by flash chromatography (SiO_2, hexane/EtOAc, 1:1), (*R*)-**12** was obtained as a dark brown oil; yield: 199 mg (52%). ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=4.63$ (m, 1H), 4.44 (dd, $J=1.7$, 1.9 Hz, 2H), 4.39–4.33 (m, 5H), 4.31 (d, $J=1.7$ Hz, 1H), 3.66 (t, $J=6.6$ Hz, 2H), 3.43 (t, $J=6.6$ Hz, 2H), 1.58–1.49 (m, 4H), 1.40–1.25 (m, 4H), 1.12 (s, 9H), 1.09–1.01 (m, 21H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=86.07$, 71.45, 71.09, 70.44, 70.38, 70.34, 70.31, 69.89, 68.40, 65.95, 63.42, 54.99, 32.99, 29.76, 26.03, 25.69, 22.78 (3C), 18.05 (6C), 11.99 (3C); EI-MS (70 EV): *m/z* (%) = 576 (15) [M^+], 520 (30), 476 (5), 329 (10), 303 (5), 246 (100), 196 (11), 131 (50), 83 (61); HPLC conditions: AS-H column (Chiral Daicel); 0.5 mL min^{-1}; 95:5 (hexane:2-propanol): (*S*): 6.4 min, (*R*): 7.2 min.

Ferrocene (*R*)-10

To a solution of (*R*)-**12** (500 mg, 0.87 mmol) in dry THF (20 mL) was slowly added *t*-BuLi (765 μL, 1.3 mmol, 1.7 M in pentane) at −78 °C under a nitrogen atmosphere. The mixture was stirred for 20 min at −78 °C before adding diphenylphosphine chloride (287 mg, 1.3 mmol). The mixture was stirred for 3 h at −78 °C. After evaporation of the solvent the mixture was dissolved in dry toluene (16 mL). Then Et_3N (876 mg, 8.67 mmol) and Cl_3SiH (1.7 g, 13 mmol) were added at room temperature under a nitrogen atmosphere. The reaction mixture was left stirring under reflux overnight. The flask was cooled to room temperature and a 1 N solution of NaOH (20 mL) was added. The organic phase was washed with brine and (*R*)-**10** was isolated by flash chromatography (SiO_2, hexane/EtOAc, 3:1) as a dark brown oil; yield: 421 mg (65%). Alcohol **13** (*ca.* 4%) and dimer **14** (17%) were also formed in this transformation.

(*R*)-**10**: ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=7.60$–7.55 (m, 2H), 7.37–7.22 (m, 5H), 7.15–7.14 (m, 3H), 4.56 (d, $J=1.3$ Hz, 1H), 4.38 (t, $J=2.5$ Hz, 1H), 4.14–4.13 (m, 1H), 4.06 (dd, $J=1.3$, 2.5 Hz, 1H), 3.96–3.97 (m, 1H), 3.92 (s, 1H), 3.86–3.85 (m, 1H), 3.80 (d, $J=1{,}1$ Hz, 1H), 3.73 (s, 1H), 3.58 (t, $J=6.5$ Hz, 2H), 3.21 (t, $J=6.5$ Hz, 2H), 1.50–1.40 (m, 3H), 1.25–1.19 (m, 4H), 1.12–1.10 (m, 21H), 0.92 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=140.12$ (d, $^{1}J_{CP}=9.9$ Hz, C_{ipso} PPh_2), 138.40 (d, $^{1}J_{CP}=9.4$ Hz, CH_{ipso} PPh_2), 135.37 (d, $^{2}J_{CP}=22.6$ Hz, CH_o PPh_2), 132.87 (d, $^{2}J_{CP}=19.3$ Hz, CH_o PPh_2), 129.12 (CH_p PPh_2), 128.13 (d, $^{3}J_{CP}=7.7$ Hz, CH_m PPh_2), 127.89 (d, $^{3}J_{CP}=6.6$ Hz, CH_m PPh_2), 85.27, 84.02, 81.11 (d, $^{2}J_{CP}=5.5$ Hz, C_5H_3), 80.70 (d, $^{3}J_{CP}=2.2$ Hz, C_5H_3), 73.60 (d, $^{2}J_{CP}=4.9$ Hz, C_5H_3), 72.18 (d, $^{3}J_{CP}=3.8$ Hz, C_5H_3), 71.80, 71.47, 71.06, 71.04, 67.98, 63.41, 40.07, 32.98, 31.10 (3C), 29.70, 25.99, 25.68, 18.04 (6C), 12.01 (3C) (two peaks are missing due to overlapping); EI-MS (70 EV): *m/z* (%) = 760 (39) [$M^+ + 16$], 717 (10), 626 (78), 430 (15), 352 (100), 298 (5), 229 (7), 201 (12), 131 (32), 83 (39).

13: ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=4.57$ (dd, $J=1.1$, 1.2 Hz, 1H), 4.37–4.23 (m, 9H), 3.56 (t, $J=6.6$ Hz, 2H), 3.37 (dt, $J=3.4$, 6.5 Hz, 2H), 2.35 (s, OH), 1.54–1.26 (m, 8H), 1.06 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=84.66$, 76.60 (2C), 76.25, 70.81 (2C), 70.13 (2C), 69.92 (2C), 68.69, 62.88, 53.40, 44.93, 32.70, 30.65 (3C), 29.64, 25.95, 25.53. EI-MS (70 EV): *m/z* (%) = 420 (16) [M^+], 364 (17), 246 (100), 198 (10), 171 (15), 121 (6).

14: ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=4.60$ (dd, $J=1.1$, 1.2 Hz, 2H), 4.41–4.27 (m, 18H), 3.39 (t, $J=3.4$ Hz, 4H), 1.54–1.28 (m, 8H), 1.10 (s, 18H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=86.10$ (2C), 71.36 (2C), 71.03 (2C), 70.49 (2C), 70.35 (2C), 70.27 (4C), 70.00 (2C), 69.88 (2C), 68. 35 (2C), 65.91 (2C), 53.42 (2C), 29.66 (2C), 25.98 (2C), 22.76 (6C); FAB-MS (70 EV): *m/z* (%)=722 (24) [M^+], 622 (33), 475 (2), 375 (11), 247 (100), 136 (12).

Ferrocene (*R*)-15

To a solution of (*R*)-**10** (200 mg, 0.35 mmol) in dry THF (2.2 mL) was added Bu_4NF (520 µL, 0.52 mmol, 1 M in THF) at 0 °C under a nitrogen atmosphere. The resulting reaction mixture was stirred for 1 h at room temperature. The solvent was evaporated and the product purified by flash chromatography (SiO_2, hexane/EtOAc, 6:1 and then 2:1). (*R*)-**15** was obtained as a dark yellow oil; yield: 173 mg (84%); $[\alpha]_D^{20}$: −240 (*c* 0.20, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ=7.60–7.62 (m, 2H), 7.37–7.16 (m, 8H), 4.63 (d, *J*=1.3 Hz, 1H), 4.45 (t, *J*=2.6 Hz, 1H), 4.20 (m, 1H), 4.14 (m, 1H), 4.04–4.00 (m, 2H), 3.93 (s, 1H), 3.87 (m, 1H), 3.81–3.77 (m, 1H), 3.62 (dt, *J*=4.9, 6.5 Hz, 2H), 3.28 (t, *J*=6.5 Hz, 2H), 2.35 (s, OH), 1.58–1.48 (m, 4H), 1.33–1.31 (m, 4H), 0.99 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=135.38 (d, $^1J_{CP}$=9.9 Hz, C_{ipso} PPh_2), 138.39 (d, $^1J_{CP}$=9.9 Hz, CH_{ipso} PPh_2), 135.38 (d, $^2J_{CP}$=22.5 Hz, CH_o PPh_2), 132.88 (d, $^2J_{CP}$=19.2 Hz, CH_o PPh_2), 129.14 (CH_p PPh_2), 128.14 (d, $^3J_{CP}$=8.2 Hz, CH_m PPh_2), 127.91 (d, $^3J_{CP}$=6.6 Hz, CH_m PPh_2), 85.27, 83.60, 81.15 (d, $^2J_{CP}$=54.9 Hz, C_5H_3), 80.71 (d, $^3J_{CP}$=2.7 Hz, C_5H_3), 73.61 (d, $^2J_{CP}$=5.5 Hz, C_5H_3), 72.21 (d, $^3J_{CP}$=9.3 Hz, C_5H_3), 71.82, 71.48, 71.08, 71.08, 69.90, 68.04, 62.95, 46.11, 32.70, 31.10 (3C), 29.63, 25.95, 25.54 (two peaks are missing due to overlapping); EI-MS (70 EV): *m/z* (%)=588 (100) [M^+], 487 (10), 414 (11), 338 (51), 302 (16), 259 (6), 226 (26), 170 (15); HPLC conditions: AS-H column (Chiral Daicel); 0.7 mL min^{-1}; 93:7 (hexane:2-propanol): (*R*)=12.0 min, (*S*)=13.9 min.

Polymer-Supported (*R*)-8: PS-8

To a suspension of NaH (51 mg, 0.75 mmol, 60% in mineral oil) in THF (2 mL) a solution of (*R*)-**8** (75 mg, 0.15 mmol, > 99% *ee*) in THF (2 mL) was added under a nitrogen atmosphere. After 10 min, Merrifield's peptide resin (64 mg, 1% cross-linked, 70–90 mesh, 1 mmol Cl/g) and NaI (4 mg) were added to the reaction mixture and it was stirred overnight at 40 °C. MeOH (5 mL) was added to the flask. The insoluble material was filtered off, and washed with MeOH, CH_2Cl_2 and hexane, and dried under vacuum. PS-**8** was obtained as a yellow solid (110 mg). By elemental analysis it was calculated that 1 g of PS-**8** contains *ca.* 0.6 mmol of chiral ligand.

Polymer-Supported (*R*)-15: PS-15

To a suspension of trichloroacetimidate Wang resin (188 mg, 0.11 mmol) and (*R*)-**13** (100 mg, 0.17 mmol, > 99% *ee*) in dry CH_2Cl_2 (3 mL) a solution of trifluoromethanesulphonic acid (8.6 mg, 0.06 mmol) in dry Et_2O (600 µL) was added at room temperature and under a nitrogen atmosphere. The mixture was left stirring for 1 h before filtering off. The insoluble material was washed with MeOH, acetone, CH_2Cl_2 and hexane, and dried under reduced pressure. The average immobilization (determined by elemental analysis) was 80%. By elemental analysis it was calculated that 1 g of PS-**8** contains *ca.* 0.47 mmol of chiral ligand.

General Procedure for the 1,3-Dipolar Cycloaddition of Azomethine Ylides Catalyzed by PS-8

A suspension of polymer-supported ligand PS-**8** (*ca.* 6.5 mol%) and $Cu(MeCN)_6ClO_4$ (2 mol%) in CH_2Cl_2 (1 mL) was stirred for 1 h at ambient temperature. Then, a solution of imine **16a** (0.198 mmol) in CH_2Cl_2 (0.5 mL) was added, followed by Et_3N (18 mol%) and by a solution of dipolarophile **17** (0.18 mmol) in CH_2Cl_2 (0.5 mL). After 4 h, the resin was filtered off. The filtrate was concentrated under reduced pressure, and hexane was added until precipitation of the cycloadducts occurred. The precipitated was filtered and dried. Cycloadduct **18a**[3e,17] was obtained as a white solid; yield: 62 mg (98%), *endo/exo*= > 98%: < 2%, > 99% *ee.* ^1H NMR ($CDCl_3$, 200 MHz): δ=7.50–7.32 (m, 8H), 7.17–7.12 (m, 2H), 4.63 (dd, *J*=8.6, 5.1 Hz, 1H), 4.16 (dd, *J*=6.5, 5.1 Hz, 1H), 3.88 (s, 3H), 3.78–3.71 (m, 1H), 3.58 (t, *J*=8.2 Hz), 2.55–2.50 (m, 1H). HPLC conditions: Daicel Chiralpak AS-H, hexane/2-propanol, 50:50, flow 0.8 mL min^{-1}, t_R: 13.6 min (1*S*,3*R*,3a*S*,6a*R*)-**18a** and 29.2 min (1*R*,3*S*,3a*R*,6a*S*)-**18a** (not detected), 220 nm.

General Procedure for the Enantioselective Allylic Substitution Reaction Catalyzed by PS-8

A suspension of polymer-supported ligand PS-**8** (*ca.* 7 mol%), $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (1.3 mg, 0.0035 mmol), and Bu_4NCl (4.8 mg, 0.017 mmol) in $CHCl_3$ (0.5 mL) was stirred for 1 h at ambient temperature. Then, a solution of 1,3-diphenyl-2-propenyl acetate (44.5 mg, 0.176 mmol) in $CHCl_3$ (1 mL) was added, followed by *N,O*-bis(trimetilsilyl)acetamide [BSA] (131 µL, 0.530 mmol) and dimethyl malonate (61 µL, 0.530 mmol). The mixture was stirred at ambient temperature for 9 h. After work-up (CH_2Cl_2/H_2O), and purification by column chromatography (SiO_2, hexane/EtOAc, 6:1), (*R*)-**21** was obtained as a colourless oil; yield: 47 mg (82%); 98% *ee*);[20] $[\alpha]_D^{20}$: +21 (*c* 1.60, $CHCl_3$), 98% *ee*; Lit:[19] (*S*)-**21** $[\alpha]_D$: −22.4 (*c* 1.80, $CHCl_3$). ^1H NMR ($CDCl_3$, 200 MHz): δ=7.34–7.20 (m, 10H), 6.49 (d, 1H, *J*=16.1 Hz), 6.33 (dd, 1H, *J*=15.6, 8.1 Hz), 4.27 (dd, 1H, *J*=10.7, 8.1 Hz), 3.96 (d, 1H, *J*=10.7 Hz), 3.71 (s, 3H), 3.52 (s, 3H).

Recycling Experiments

Reactions were performed as above except in a 10-mL Schlenk-type flask fitted with a sintered glass filter disk. A suspension of the polymer-supported ligand PS-**8** (ca. 6.5 mol%) and $Cu(MeCN)_6ClO_4$ (2 mol%) in CH_2Cl_2 (1 mL) was stirred for 1 h at ambient temperature. Then, a solution of imine **16a** (0.198 mmol) in CH_2Cl_2 (0.5 mL) was added, followed by Et_3N (18 mol%) and by a solution of dipolarophile **17** (0.18 mmol) in CH_2Cl_2 (0.5 mL). After 4 h, the resin was filtered off under N_2 atmosphere and rinsed with CH_2Cl_2 and immediately suspended in 1 mL of CH_2Cl_2. After stirring 20 min, the reactants were added as indicated before. The same resin was used for each entry, and no further copper salt was added. Isolation of the cycloadduct **18a** was performed as stated before (*vide supra*).

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