Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron
Tetrahedron 63 (2007) 11920–11927

Screening of chiral phosphines as catalysts for the enantioselective [3+2] annulations of *N*-tosylimines with allenic esters

Nicolas Fleury-Brégeot, Ludovic Jean, Pascal Retailleau and Angela Marinetti*

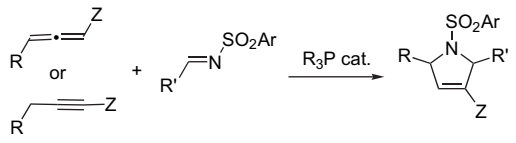
Institut de Chimie des Substances Naturelles, CNRS UPR 2301 1, avenue de la Terrasse, 91198 Gif-sur-Yvette Cedex, France

Received 15 June 2007; revised 10 September 2007; accepted 11 September 2007
Available online 15 September 2007

Abstract—The use of chiral, binaphthyl-based phosphepines as catalysts improves previous results for the enantioselective [3+2] cyclisation reactions between allenic esters and *N*-tosylimines, both in terms of conversion rate and enantioselectivity. Pyrrolines bearing 1-naphthyl, phenyl, *o*-tolyl and *p*-MeO-phenyl substituents on the stereogenic alpha-carbon have been obtained with enantiomeric excesses up to 64–80%.

1. Introduction

The [3+2] annulation between imines and a three-carbon synthon generated from electron poor alkynes or allenes has been introduced in 1997 by Lu[1] as an original method for the synthesis of pyrroline rings (Scheme 1). In principle, any Lewis bases are potential catalysts for this reaction, however, only phosphines have been found to date as suitable promoters, while the nitrogen nucleophiles tested so far led to different products, i.e., either azetidine or dihydropyridine derivatives.[2] Both allenic esters and 2-butynoates have been used as starting materials and are supposed to enter the same catalytic cycle leading to 3-pyrrolines.



Scheme 1. Phosphine-promoted [3+2] annulation of activated allenes or alcynes with imines.

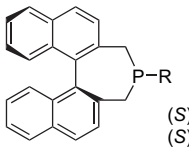
Initial studies involved methyl 2,3-butadienoate and aromatic *N*-tosylimines (R=Ph, *o*- and *p*-MeO-Ph, 1-naphthyl, 2-furyl, etc.) or cinnamaldimine as reaction partners. Later on, the scope of the reaction was extended to imines activated by alternative electron-withdrawing groups (diphenylphosphinyl, *p*-nitrobenzenesulfonyl and β-trimethylsilylethanesulfonyl groups),[1b] to γ-substituted allenoates[2b,3] as well as to alkynoates.[1b,4] Recently the use of an allenic ketone has also been reported.[2b,5] Triphenylphosphine was routinely used as an efficient and highly chemoselective catalyst in the reaction of 2,3-butadienoates with imines, while its rather weak nucleophilicity prevented its use for the activation of 2-butynoates. Tributylphosphine proved to be a more suitable catalyst for reactions involving both acetylenic substrates[1b,4] and sterically hindered γ-substituted allenic esters.[3] As a general trend, increased efficiency is observed when more nucleophilic phosphines were used, however, fine matching of the substrate–Lewis base promoter pairs may be necessary to attain high catalytic activity.[2b]

The synthetic potential of the cycloaddition reaction in Scheme 1 has been substantiated, among others, by its use as a key step in the large scale synthesis of new families of NK1 antagonists based on pyrrolidine moieties (Scheme 2).[6] The synthetic procedure for the preparation of these compounds involves HPLC separation of enantiomers of a pyrroline obtained in the phosphine-catalysed cycloaddition step. This example adequately highlights the usefulness of the method as well as the relevance of a possible enantioselective version of these reactions.

Thus, with the aim of setting an enantioselective [3+2] annulation procedure, we have started a systematic screening of various non-racemic phosphine promoters. Preliminary results have been reported in a previous communication.[7] Herein we wish to report details of these studies, as well as more recent results showing that the efficiency of the annulation reactions can be improved by means of the binaphthyl phosphepine catalysts **A1** and **A2**.[8]

Keywords: [3+2] Cyclisations; Asymmetric organocatalysis; Nitrogen heterocycles; Chiral phosphines; Phosphepines.
* Corresponding author. Tel.: +33 1 69 82 30 36; fax: +33 1 69 07 72 47; e-mail: angela.marinetti@icsn.cnrs-gif.fr

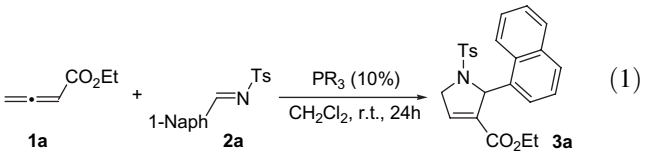
0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.09.022



(*S*)-**A1** R = Ph
(*S*)-**A2** R = t-Bu

2. Results and discussion

The development of enantioselective organocatalysis with phosphorus nucleophiles is at a very early stage[9] and little is known about the structural requirements for efficient catalysts. This is why our studies towards the setting of an asymmetric version of the [3+2] cyclisation reactions above started with the systematic screening of commercially available chiral phosphines. In addition, several monodentate and bidentate chiral phosphetanes from our previous studies (**L** and **M**)[10] have also been included in the screening tests. The annulation of ethyl 2,3-butadienoate with *N*-tosyl-1-naphthaldimine (Eq. 1) was selected as a model reaction. Results obtained with representative phosphines[11] are summarized in Scheme 2.



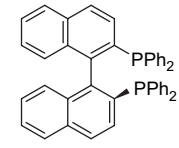
(1)

Atropisomeric diphosphines such as Binap (**B**) and MeO-Biphep (**C**) afforded enantiomeric excesses of about 50%, however, their use is hampered by the rather low catalytic activity, which might be ascribed to the weak nucleophilic character and steric hindrance of these triarylphosphines. For comparison, it is noteworthy that the same cyclisation reaction is efficiently promoted by PPh_3 (80% isolated yield). PhanePHOS (**G**) also displayed a quite low catalytic activity while affording the highest ee of this preliminary screening (64% ee). Higher conversion rates were observed with the atropisomeric triaryl-monophosphines MOP (**D**) and Quinap (**E**), which bear heteroatom donor groups on the aryl moiety, as well as with the Trost ligand (**F**). The possible role of the additional heteroatom is unclear. In the case of Quinap, involvement of nitrogen as the nucleophilic promoter instead of phosphorus could be envisioned, however, it can be reasonably ruled out as isoquinoline itself does not display any catalytic activity under the same reaction conditions.

As expected, a satisfying catalytic activity was observed with the electron-rich di- and trialkyl heterocyclic phosphines bearing phospholane (**H**), phosphetane (**L** and **M**) and phosphepine (**A**) moieties as shown in Scheme 2.

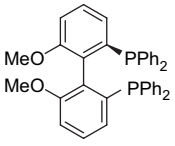
The phospholane-based Me-BPE (**H**) affords a racemic pyrroline product. Together with literature data, this result highlights the rather unpredictable behaviour of BPE in nucleophilic cyclisation reactions. Indeed, if the catalytic activity is generally satisfying, high enantiomeric excesses, up to 72% ee, have been obtained only in the [4+2] annulations of imines with allenes,[9d] while almost racemic products are formed in the [3+2] annulations between allenes and either enones[9g] or imines (this work).

In the ferrocene-derived phosphetanes, **L**[10b,12] and **M**,[10a] tuning of the R-substituents allows to optimize, to some extent, the conversion rates and/or enantioselectivity, with ees up to 48%. In addition to these ferrocene-derived



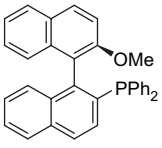
(*S*)-BINAP (**B**)

13% yield, 45% ee



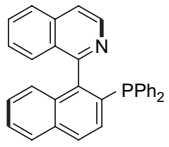
(*R*)-MeO-Biphep (**C**)

22% yield, 53% ee



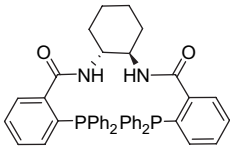
(*R*)-MOP (**D**)

45% yield, 11% ee



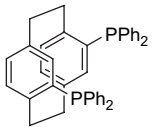
(*R*)-QUINAP (**E**)

61% yield 28% ee



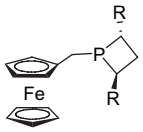
Trost ligand (**F**)

60% yield, 19% ee



(*S*)-PHANEPHOS (**G**)

32% yield, **64% ee**



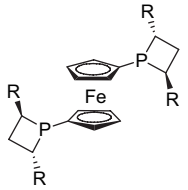
Phosphetane (**L**)

(*S,S*)-**L1** R = *i*-Pr

50% yield, 44% ee

(*S,S*)-**L2** R = Cy

55% yield, **48% ee**



FerroTANE (**M**)

(*R,R*)-**M1** R = Me

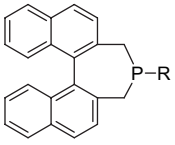
72% yield, 3% ee

(*R,R*)-**M2** R = Et

50% yield, 22% ee

(*S,S*)-**M3** R = *i*-Pr

70% yield, **37% ee**



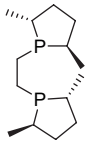
Phosphepine (**A**)

(*S*)-**A1** R = Ph

75% yield, 40% ee

(*S*)-**A2** R = *t*-Bu

70% yield, **54% ee**



(*R,R*)-Me-BPE (**H**)

70% yield, 0% ee

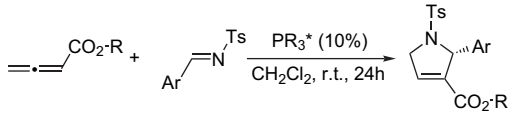
Scheme 2.

phosphetanes, a few other chiral phosphetanes have been tested so far in the same cyclisation reaction, including (*R*,*R*)-2,4-dimethyl-1-phenylphosphetane, (*R*,*R*)-2,4-dimethyl-1-mesitylphosphetane[13] and bis((*S*,*S*)-2,4-dicyclohexylphosphetano)ethane.[14] They afford, however, enantiomeric excesses lower than 10%. Thus it seems that the somewhat higher enantioselectivity observed with phosphetanes **L** or **M** cannot be ascribed to the phosphetane structure itself, it might rather result from specifically combining ferrocene and phosphetane units.

From the work of Fu,[9d,g] the *tert*-butyl-phosphepine **A2** is known to promote the asymmetric [3+2] cycloadditions of allenes with enones and the [4+2] annulations of allenes with imines in very high enantiomeric excesses up to 90% and 98% ee, respectively. Such high enantioselectivity levels have not been observed in the [3+2] cycloadditions of Scheme 2, as a maximum ee of 54% has been obtained. The catalytic activity of **A** proved, however, satisfying when compared to most of the chiral phosphines evaluated so far, with a conversion rate of about 75–80% after 24 h at room temperature. Thus, phosphepines **A** have been selected for more extended screenings where the encouraging preliminary results above have been substantiated by additional tests on different substrates, by varying both the imine substituent and the allene ester group. The main results (conversion rates and enantiomeric excesses) obtained with phosphepines **A1** and **A2** are reported in Table 1, in comparison with those obtained with Et-FerroTANE and Phanephos. The few literature data available so far on the same reactions are also recalled in the table. These data concern the use of the Gladysz organometallic phosphine having metal-centred chirality, Cp(NO)(PPh$_3$)ReCH$_2$PPh$_2$[15]; reaction conditions (8 days at −20 °C with a substrate/catalyst ratio of 20 mol %) are significantly different from those used in our experiments.

All reactions in Table 1 were performed under argon, with equimolar amounts of reactants, 10 mol % catalyst, in dichloromethane at room temperature for 24 h. At first, *N*-tosylimines bearing various aryl groups[16] on the α-carbon have been reacted with ethyl 2,3-butadienoate **1a** to afford pyrrolines **3b–e**. Conversion rates up to 85% have been measured by NMR, the starting imine and small amounts of the corresponding aldehyde being also observed in the final mixtures. With respect to enantioselectivity, the use of the *tert*-butyl-substituted phosphepine **A$_2$** as the catalyst afforded the best results, with enantiomeric excesses up to 79%. The highest ee was obtained in the cyclisation between ethyl 2,3-butadienoate and the electron-rich *p*-anisyl substituted imine **2d**, which gave, however, a rather low conversion rate at room temperature (63%). In the same reaction,

Table 1. Survey of different imines in combination with allenes **1a** and **1b**

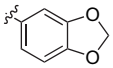


1a, R = Et
1b, R = Cy

2a-g

3b-e
4a-g

Ar = 1-naphthyl (**2a**), *p*-NO$_2$-Ph (**2b**), Ph (**2c**), *p*-MeO-Ph (**2d**), *o*-Me-Ph (**2e**), benzo[1,3]dioxol-5-yl (**2f**), 2-furyl (**2g**)

Product			Phosphepine (*S*)-**A$_1$**		Phosphepine (*S*)-**A$_2$**		Et-Ferrotane (*R*,*R*)-**M$_2$**		PhanePHOS (*S*)-**G**		Ref. 15[b]	
	R	Ar	Conv	ee%[a]	Conv	ee%	Conv	ee%	Conv	ee%	Yield	ee%
3b	Et	*p*-NO$_2$-Ph	70	18	85[d]	43	80	23	38	6	90	***51***
3c	Et	Ph	76	45	72[e]	**71**	88	28	37	26	92	*60*
3d	Et	*p*-MeO-Ph	52	21	63[f]	**79 (86)**[m]		—		—	93	*54*
3e	Et	*o*-Me-Ph	43	25	80[g]	**66**	66	21	18	54		
4a	Cy	1-Naphthyl	>95	**64**[c]	90[h]	41	>95	31				
4b	Cy	*p*-NO$_2$-Ph	78	38	86[i]	43						
4c	Cy	Ph	>95	42	>95[j]	**62**						
4d	Cy	*p*-MeO-Ph	69	53	84[k]	**80**						
4e	Cy	*o*-Me-Ph	>95	**60**	>95[l]	52						
4f	Cy		55	26	91	**62**						
4g	Cy	2-Furyl	78	**48**	80	46						

[a] Enantiomeric excesses have been measured by chiral HPLC.
[b] Conditions: 20 mol % catalyst, chlorobenzene, −20 °C, 8 days.
[c] Isolated yield: 91%. As mentioned in our previous communication, the enantiomeric excess of this pyrroline can be increased by crystallisation, given that the racemate crystallizes preferentially from the mixture.[7]
[d] Isolated yields: 80%.
[e] Isolated yields: 64%.
[f] Isolated yields: 60%.
[g] Isolated yields: 72%.
[h] Isolated yields: 88%.
[i] Isolated yields: 81%.
[j] Isolated yields: 86%.
[k] Isolated yields: 60%.
[l] Isolated yields: 87%.
[m] ee for reaction performed in acetone.

heating at 50 °C allows conversion to be improved from 63 to 75%, with only a small decrease in enantioselectivity (ee=75%). When acetone was used instead of dichloromethane as the solvent, at room temperature, the ee increased up to 86%.

In a second series of experiments, the nature of the allenic ester group has been considered for its possible effects on the reaction rates and enantioselectivity. The preliminary tests already mentioned in our previous communication[7] showed that in the reaction between *N*-tosyl-naphthaldimine **2a** and various allenic esters **1**, promoted by Et-FerroTANE ($\mathbf{M_2}$), increased enantioselectivities were obtained for bulkier alkyls as the ester substituents: pyrrolines[17] having ees of 22%, 2% and 52% were obtained for R=Et, Ph and ^{i}Pr, respectively. However, the practical use of bulky allenic esters is often hampered by their low conversion rates. Unlike this, when cyclohexyl 2,3-butadienoate **1b** was used as the substrate, a high conversion rate, an especially clean reaction and a slightly increased enantiomeric excess, compared to the ethyl ester (31% vs 22%), were observed. Cyclohexyl 2,3-butadienoate **1b** was thus envisioned as a suitable substrate for further evaluation of phosphepines **A**.

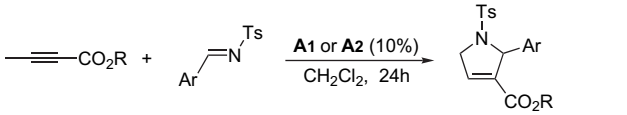
Cyclohexyl 2,3-butadienoate is available from the corresponding phosphorane $Ph_3P{=}CHCO_2Cy$, by Wittig reaction with ketene generated in situ from acetyl chloride and triethylamine,[18] as described in Section 3. In the [3+2] cyclisation reactions with *N*-tosylimines, under the usual conditions above, cyclohexyl butadienoate afforded higher conversion rates than the corresponding ethyl ester. Most substrates, including the *o*-tolyl- and 1-naphthyl-substituted imines **2e** and **2a**, could be converted quantitatively into the corresponding pyrrolines, **4**. In the reaction of **1b** with *N*-tosylbenzaldimine **2c**, promoted by phosphepine $\mathbf{A_1}$, the catalyst amount could be reduced to 5%, which led to **4c** with an 83% conversion rate, in otherwise identical conditions.

Conversion rates were improved to about 85% also for the less reactive electron-rich imine **2d**, and the resulting pyrroline **4d** displayed an 80% enantiomeric excess when the *tert*-butyl-phosphepine $\mathbf{A_2}$ was used as the catalyst.

These results support our previous remark on the particular suitability of the cyclohexyl ester **1b** as the allenic substrate in these cyclisation reactions, as far as conversion rates are considered. Concerning the enantioselectivity levels, the reaction found to be highly substrate dependant and no regular trend is observed when the size of the ester substituent is increased.

Finally, in order to potentially expand the scope and synthetic utility of these [3+2] cyclisation reactions, we considered using acetylenic ester as starting materials, given that butynoates are more easily available substrates, compared to allenic esters. They usually display, however, lower reactivity.

Methyl and cyclohexyl 2-butynoate (**5a**,**b**) were reacted with the *N*-tosylimines **2a** and **2d** to afford the expected pyrrolines **6a** and **4d**, as shown in Scheme 3.



5a R = Me
5b R = Cy

2a
2d

6a, R = Me, Ar = 1-naphthyl
4d, R = Cy, Ar = *p*-MeO-Ph

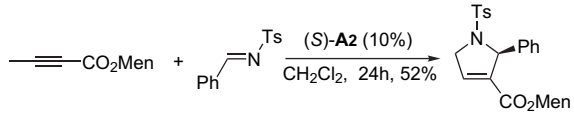
		Phosphepine $\mathbf{A_1}$		Phosphepine $\mathbf{A_2}$	
Product	T	*conv*	Ee%	*conv*	Ee%
6a	r.t.	*75*[a]	51	*25*	**61**
	45°C	-	-	*74*[b]	53
4d	r.t.	-	-	*56*[c]	79

Isolated yields: [a]68%; [b]65%; [c]48%

Scheme 3.

Both phosphepines $\mathbf{A_1}$ and $\mathbf{A_2}$ are suitable catalysts for these reactions. With phosphepine $\mathbf{A_2}$ the reaction between methyl 2-butynoate and **5a** displayed a low conversion rate at room temperature (25% and 61% ee), which could nevertheless be increased to 74% when the reaction was performed at 45 °C. A small decrease in enantioselectivity was observed then. Starting from cyclohexyl 2-butynoate **5b** (Scheme 3), pyrroline **4d** has been obtained with lower conversion rates and comparable enantiomeric excesses with respect to those obtained from the corresponding allene **1b** (Table 1), under as far as possible identical experimental conditions.

The absolute configurations of the final pyrrolines **3**, **4** and **6** are unknown so far. However, the sense of chiral induction from *tert*-butyl-phosphepine (*S*)-$\mathbf{A_1}$ has been inferred from the X-ray crystal structure of pyrroline **7a** obtained from D-menthyl 2-butynoate (Scheme 4). The stereochemical outcome of these reactions is primarily controlled by the chiral phosphine and the menthyl group having only minor effects on chiral induction.[19]



5c, Men = *d*-menthyl

2c

(*S*)-**7a** (+ **7b**)
(78:22 ratio)

Scheme 4.

The major epimer, **7a**, displays an *S*-configuration at the pyrroline carbon atom (Fig. 1).[20]

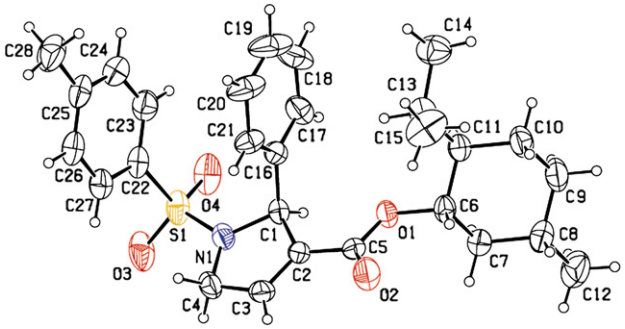


Figure 1. ORTEP drawing for pyrroline **7a**.

On the whole, the use of the phosphepine catalysts **A** improves previous results for the enantioselective [3+2] cyclisation reactions between allenic esters and *N*-tosylimines, both in terms of conversion rate and enantioselectivity. An appropriate choice of the allenic ester, **1a** or **1b**, combined with the suitable phosphepine catalyst, $\mathbf{A_1}$ or $\mathbf{A_2}$, allows enantiomeric excesses up to 64–86% to be obtained for pyrrolines bearing 1-naphthyl, phenyl, *o*-tolyl and *p*-MeO-phenyl substituents on the stereogenic alpha-carbons. Albeit lower conversion rates are observed, 2-butynoates also represent suitable substrates for these cyclisation reactions.

3. Experimental

3.1. General

NMR spectra have been recorded on Bruker Avance 300 or Avance 500 spectrometers. All reactions have been performed under inert atmosphere (argon). *N*-Tosyl-arylimines **2** were prepared via the $BF_3\cdot Et_2O$ catalysed condensation of tosylamine with aldehydes, in a Dean–Stark apparatus, according to the literature method.[21,6a] *N*-Tosyl 1-naphthaldimine, *N*-tosylbenzaldimine, *N*-tosyl *p*-NO_2-benzaldimine, *N*-tosyl *p*-MeO-benzaldimine,[21] *N*-tosyl *o*-Me-benzaldimine[22] *N*-tosyl-2-(2-furyl)imine[23] and *N*-tosyl-2-(benzo[1,3]dioxol-5-yl)imine[23b] are known compounds.

3.2. Cyclohexyl 2,3-butadienoate 1b

A stirred solution of cyclohexyl bromoacetate[24] (7.4 g, 33.6 mmol) and triphenylphosphine (9.7 g, 37.0 mmol) in toluene (100 mL) was heated at 100 °C for 12 h. Filtration of the solution gave the corresponding phosphonium salt (13.3 g, 27.5 mmol, 83% yield). ^{1}H NMR ($CDCl_3$) δ 1.0–1.6 (10H), 4.60 (1H, OCH), 5.45 (d, $^2J_{H-P}$=14.1 Hz, 2H, PCH_2), 7.6–8.0 (15H, Ph); ^{31}P NMR ($CDCl_3$) δ 21 ppm.

A two-layer system of the phosphonium bromide in 70 mL dichloromethane and a 1.2 M solution of NaOH in water (45 mL) were vigorously shaken in a separation funnel, after which the layers were separated. The water layer was washed with dichloromethane. The organic layers were dried over $MgSO_4$ and the solvent was evaporated to yield 10.9 g (27.1 mmol, 98% yield) of cyclohexyl (triphenylphosphoranilydene)acetate. ^{1}H NMR ($CDCl_3$) δ 0.6–2.0 (10H), 2.8 (br d, *J*=23 Hz, 1H, P=CH), 4.56 (1H, OCH), 7.4–7.7 (15H, Ph); ^{31}P NMR ($CDCl_3$) δ 16 and 18 ppm.

A solution of ylide (10.9 g, 27.1 mmol) and triethylamine (3.9 mL, 27.8 mmol) in dichloromethane (90 mL) was stirred at room temperature while a solution of acetyl chloride (2.0 mL, 27.1 mmol) in dichloromethane (10 mL) was added dropwise. The mixture was stirred for 12 h. Dichloromethane was removed under reduced pressure. Pentane was added to the residue and the solid triphenylphosphine oxide was removed by filtration. After evaporation of the solvent, rapid distillation of the residue on a Kugelrohr apparatus (100 °C, 1 mbar) afforded 1.6 g (9.6 mmol, 36%) of the allene. Alternatively, the final product can be purified by column chromatography on silica gel with pentane/ether 90:10 as the eluent (R_f=0.4). ^{1}H NMR ($CDCl_3$) δ 1.3–1.6 (6H), 1.7–1.9 (4H), 4.81 (m, 1H, OCH), 5.19 (d, ^4J=6.6 Hz, 2H, =CH_2), 5.61 (t, ^4J=6.6 Hz, 1H, =CH); ^{13}C NMR ($CDCl_3$) δ 23.6 (CH_2), 25.5 (CH_2), 31.6 (CH_2), 73.1 (OCH), 79.1 (=CH_2), 88.4 (=CH), 165.1 (CO_2–), 215.6 (C) ppm.

3.3. Cyclohexyl 2-butynoate 5b

This compound was prepared in analogy to the procedure of Moyano and co-workers.[25] To a stirred ice-cooled solution containing 2-butynoic acid (1.0 g, 1.19 mmol) and cyclohexanol (1.4 mL, 1.33 mmol) in dichloromethane (12 mL), a solution of dicyclohexylcarbodiimide (2.45 g, 1.19 mmol) and 4-dimethylaminopyridine (0.15 g, 1.19 mmol) in CH_2Cl_2 (12 mL) was added dropwise. The mixture was stirred at 0 °C for 3 h, then warmed up to room temperature. The resulting precipitate was filtered out and washed with dichloromethane. After evaporation of the solvent, Kugelrohr distillation of the crude product (120 °C, 10 mbar) afforded **5b** in 86% yield (1.7 g). ^{1}H NMR ($CDCl_3$) δ 1.2–1.6 (6H), 1.75 (2H), 1.9 (2H), 2.00 (s, 3H, Me), 4.84 (1H, OCH); ^{13}C NMR ($CDCl_3$) δ 3.8 (Me), 23.8 (CH_2), 25.2 (CH_2), 31.4 (CH_2), 72.9 (C), 74.6 (OCH), 84.8 (C), 153.3 (CO_2CH) ppm.

3.4. General procedure for the phosphine-promoted cyclisation reactions

N-Tosylimine **2** (0.3 mmol) and the allenic ester **1** (or alkyne **5**) (0.33 mmol) were dissolved in CH_2Cl_2 (1 mL) under argon. The chiral phosphine (3×10^{-2} mmol) was added and the mixture was stirred at room temperature for about 24 h. After evaporation of the solvent, the residue was chromatographed on silica gel with heptane/ethyl acetate mixtures. Given the small scale of these catalytic tests, the reported yields might not be totally accurate, they are nevertheless consistent with the conversion rates based on ^{1}H NMR analysis of the crude mixtures. Except for the imine derived aldehyde, no other definite side products have been observed in detectable amount. Enantiomeric excesses for pyrrolines **3**, **4** and **6** have been measured by chiral HPLC. Reference sample of racemic pyrrolines have been obtained with either PBu_3 or PPh_3 as the catalyst. The signs of optical rotation for the final 3-pyrrolines have been determined in $CHCl_3$ for enantiomerically enriched samples. The absolute stereochemistry of the cycloadducts was not determined.

3.4.1. Ethyl 2,5-dihydro-2-(1-naphthyl)-1-tosylpyrrole-3-carboxylate 3a. Pale yellow oil; ^{1}H NMR ($CDCl_3$) δ 0.74 (t, *J*=7.2 Hz, 3H, Me), 2.16 (s, 3H, Me), 3.75 (m, 2H, CH_2CH_3), 4.45 (ddd, $^2J_{AB}$=17.1 Hz, ^3J=6.0 Hz, ^4J=1.8 Hz, 1H, NCH_2), 4.64 (dt, $^2J_{AB}$=17.1 Hz, *J*=2.5 Hz, 1H, NCH_2), 6.45 (br, 1H, NCH), 6.8 (3H), 7.1–7.2 (4H), 7.3–7.4 (2H), 7.6–7.7 (2H), 8.11 (d, *J*=8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.6 (Me), 21.4 (Me), 53.5 (NCH_2), 55.1 (OCH_2), 64.8 (NCH), 123.3, 125.0, 125.4, 126.1, 126.8, 126.9, 128.5, 128.6, 129.0, 131.4 (C), 133.6 (C), 135.1 (NCH_2CH=), 135.2 (C), 135.5 (C), 136.8 (C), 143.0 (C-Me), 161.8 (CO_2Et) ppm. HRMS calcd for $C_{24}H_{23}NO_4S\cdot$Na: 444.1245, found: 444.1230. HPLC: Chiracel AD, hexane/isopropanol 80:20, 1 mL/min, 12.0 min [(+)-enantiomer] and 13.6 min. The (*S*)-configurated phosphepines **A** afford the (+)-enantiomer as the major enantiomer.

3.4.2. Ethyl 2,5-dihydro-2-(4-nitrophenyl)-1-tosylpyrrole-3-carboxylate 3b. Pale yellow oil; NMR spectra for compound **3c** in C_6D_6 have been reported in Ref. 15. ^{1}H NMR ($CDCl_3$) δ 1.13 (t, J=7.0 Hz, 3H, Me), 2.40 (s, 3H, Me), 4.0 (m, 2H, CH_2CH_3), 4.50 (dd, J=4.0, 2.5 Hz, 2H, NCH_2), 5.75 (td, J=3.5, 2.5 Hz, 1H, NCH), 6.83 (m, 1H, NCH_2CH=), 7.23 (d, J=8.0 Hz, 2H), 7.46 (d, J=8.5 Hz, 2H), 7.54 (d, J=8.0 Hz, 2H), 8.11 (d, J=8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 14.1 (Me), 21.5 (Me), 55.4 (NCH_2), 61.1 (OCH_2), 68.2 (NCH), 123.5, 127.2, 128.8, 129.8, 134.8 (C), 135.0 (C), 136.6 (NCH_2CH=), 144.1 (C), 147.2 (C), 147.5 (C), 161.3 (CO_2Et) ppm. HRMS calcd for $C_{20}H_{20}N_2O_6S\cdot$Na: 439.0940, found: 439.0954. HPLC: Chiracel OJ, hexane/isopropanol 70:30, 1 mL/min, 27 min [(+)-enantiomer] and 38 min.

3.4.3. Ethyl 2,5-dihydro-2-phenyl-1-tosylpyrrole-3-carboxylate 3c. White solid, mp 115 °C. NMR data for compound **3c** have been reported in Refs. 1b and 15. HRMS calcd for $C_{20}H_{21}NO_4S\cdot$Na: 394.1089, found: 394.1104. HPLC: Chiracel OD, hexane/isopropanol 80:20, 1 mL/min, 9.6 min [(−)-enantiomer] and 12.0 min.

3.4.4. Ethyl 2,5-dihydro-2-(4-methoxyphenyl)-1-tosylpyrrole-3-carboxylate 3d. Pale yellow solid, mp 72 °C; NMR data for **3d** have been reported in Refs. 1b and 15. ^{13}C NMR ($CDCl_3$) δ 13.9 (Me), 21.5 (Me), 54.7 (NCH_2), 55.2 (OMe), 60.8 (OCH_2), 68.5 (NCH), 113.6 ($CH_{o\text{-MeO}}$), 127.1, 128.9, 129.4, 131.7 (C), 135.1 (NCH_2CH=), 135.7, 136.0, 143.1 (C-Me), 159.3 (C-OMe), 161.9 (CO_2Et) ppm. HRMS calcd for $C_{21}H_{23}NO_5S\cdot$Na: 424.1195, found: 424.1199. HPLC: Chiracel AD, hexane/isopropanol 80:20, 1 mL/min, 8.5 and 11.7 min.

3.4.5. Ethyl 2,5-dihydro-2-(*o*-tolyl)-1-tosylpyrrole-3-carboxylate 3e. White solid, mp 110–115 °C; ^{1}H NMR ($CDCl_3$) δ 1.10 (t, J=7.2 Hz, 3H, Me), 2.36 (s, 3H, Me), 2.57 (s, 3H, Me), 4.0 (m, 2H, CH_2CH_3), 4.39 (dd, $^2J_{AB}$=17.1 Hz, ^3J=6.0 Hz, ^4J=2.1 Hz, 1H, NCH_2), 4.58 (dt, $^2J_{AB}$=17.1 Hz, J=2.1 Hz, 1H, NCH_2), 6.08 (1H, NCH), 6.81–6.83 (2H), 6.9 (m, 1H), 7.09–7.13 (4H), 7.34 (d, J=8.1 Hz, 2H, Ts); ^{13}C NMR ($CDCl_3$) δ 13.8 (Me), 19.1 (Me), 21.4 (Me), 54.9 (NCH_2), 60.8 (OCH_2), 64.8 (NCH), 126.0, 127.5, 127.7, 128.0, 129.8, 130.4, 135.1 (NCH_2CH=), 135.9 (C), 136.5 (C), 136.6 (C), 137.5 (C), 143.0 (*C*-Me), 161.8 (CO_2Et) ppm. HRMS calcd for $C_{21}H_{23}NO_4S\cdot$Na: 408.1245, found: 408.1274. HPLC: Chiracel OD, hexane/isopropanol 80:20, 1 mL/min, 9.0 and 11.5 min [(+)-enantiomer].

3.4.6. Cyclohexyl 2,5-dihydro-2-(1-naphthyl)-1-tosylpyrrole-3-carboxylate 4a. White solid, mp 83 °C, NMR data and chiral HPLC analysis for **4a** have been reported in Ref. 7. HRMS calcd for $C_{28}H_{29}NO_4S\cdot$Na: 498.1715, found: 498.1725.

3.4.7. Cyclohexyl 2,5-dihydro-2-(4-nitrophenyl)-1-tosylpyrrole-3-carboxylate 4b. Pale yellow solid, mp 137 °C; ^{1}H NMR ($CDCl_3$) δ 1.0–1.8 (10H), 2.41 (s, 3H, Me), 4.50 (ddd, $^2J_{AB}$=17.0 Hz, ^3J=6.0 Hz, ^4J=2.0 Hz, 1H, NCH_2), 4.54 (dt, J=17.0, 2.5 Hz, 1H, NCH_2), 4.6 (1H, OCH), 5.79 (1H, NCH), 6.86 (1H, NCH_2CH=), 7.22 (d, J=8.0 Hz, 2H), 7.45 (d, J=8.5 Hz, 2H), 7.52 (d, J=8.0 Hz, 2H), 8.13 (d, J=8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.4 (Me), 23.3 (CH_2), 23.4 (CH_2), 25.0 (CH_2), 31.1 (CH_2), 31.3 (CH_2), 55.3 (NCH_2), 68.2 (NCH), 73.8 (OCH), 123.4, 127.1, 128.8, 129.8, 134.8 (C), 135.3 (C), 136.6 (NCH_2CH=), 144.1 (C), 147.2 (C), 147.5 (C), 160.8 (CO_2Cy) ppm. HRMS calcd for $C_{24}H_{26}N_2O_6S\cdot$Na: 493.1409, found: 493.1427. HPLC: AD column, hexane/isopropanol 80:20, 1 mL/min, 18.2 and 28.5 min.

3.4.8. Cyclohexyl 2,5-dihydro-2-phenyl-1-tosylpyrrole-3-carboxylate 4c. Colourless oil; ^{1}H NMR ($CDCl_3$) δ 1.1–1.8 (10H), 2.38 (s, 3H, Me), 4.38 (ddd, $^2J_{AB}$=17.0 Hz, ^3J=6.0 Hz, ^4J=2.0 Hz, 1H, NCH_2), 4.53 (dt, $^2J_{AB}$=17.0 Hz, J=2.5 Hz, 1H, NCH_2), 4.66 (1H, OCH), 5.77 (1H, NCH), 6.82 (1H, NCH_2CH=), 7.14 (d, J=8.5 Hz, 2H, Ts), 7.23 (5H, Ph), 7.40 (d, J=8.5 Hz, 2H, Ts); ^{13}C NMR ($CDCl_3$) δ 21.4 (Me), 23.1 (CH_2), 23.3 (CH_2), 25.2 (CH_2), 30.9 (CH_2), 31.3 (CH_2), 54.8 (NCH_2), 69.0 (NCH), 73.2 (OCH), 127.0, 127.9, 128.2, 129.4, 135.5 (NCH_2CH=), 135.7 (C), 136.4 (C), 139.4 (C), 143.2 (*C*-Me), 161.3 (CO_2Cy) ppm. MS (ESI) *m*/*z* 448 (M+Na). HRMS calcd for $C_{24}H_{27}NO_4S\cdot$Na: 448.1559, found: 448.1536. HPLC: Chiracel AD, hexane/isopropanol 80:20, 1 mL/min, 6.5 min [(+)-enantiomer] and 7.1 min.

3.4.9. Cyclohexyl 2,5-dihydro-2-(4-methoxyphenyl)-1-tosylpyrrole-3-carboxylate 4d. White solid, mp 151 °C; ^{1}H NMR ($CDCl_3$) δ 1.1–1.8 (10H), 2.39 (3H, Me), 3.80 (3H, OMe), 4.35 (ddd, $^2J_{AB}$=17.0 Hz, J=6.0, 2.0 Hz, 1H, NCH_2), 4.50 (dt, $^2J_{AB}$=17.0 Hz, J=2.3 Hz, 1H, NCH_2), 4.67 (1H, OCH), 5.73 (NCH), 6.76 (d, J=9.0 Hz, 2H), 6.78 (1H, NCH_2CH=), 7.14 (4H), 7.42 (d, J=8.0 Hz, 2H, Ts); ^{13}C NMR ($CDCl_3$) δ 21.4 (Me), 23.1 (CH_2), 23.3 (CH_2), 25.2 (CH_2), 31.0 (CH_2), 31.3 (CH_2), 54.6 (NCH_2), 55.3 (OMe), 68.5 (NCH), 73.1 (OCH), 113.6 ($CH_{o\text{-MeO}}$), 127.0, 129.0, 129.4, 131.7 (C), 135.1 (NCH_2CH=), 135.9 (C), 136.4 (C), 143.1 (C-Me), 159.4 (*C*-OMe), 161.4 (CO_2Cy) ppm. HRMS calcd for $C_{25}H_{29}NO_5S\cdot$Na: 478.1664, found: 478.1672. HPLC: Chiracel AD, hexane/isopropanol 80:20, 1 mL/min, 10.5 and 15.8 min.

3.4.10. Cyclohexyl 2,5-dihydro-2-(*o*-tolyl)-1-tosylpyrrole-3-carboxylate 4e. Pale yellow oil; ^{1}H NMR ($CDCl_3$) δ 1.0–1.8 (10H), 2.37 (s, 3H, Me), 2.57 (s, 3H, Me), 4.38 (ddd, $^2J_{AB}$=17.0 Hz, J=6.5, 2.0 Hz, 1H, NCH_2), 4.58 (dt, $^2J_{AB}$=17.0 Hz, J=2.5 Hz, 1H, NCH_2), 4.62 (1H, OCH), 6.07 (1H, NCH), 6.82 (2H), 6.92 (1H), 7.1 (4H), 7.33 (d, J=8.0 Hz, 2H, Ts); ^{13}C NMR ($CDCl_3$) δ 19.2 (Me), 21.4 (Me), 23.5 (CH_2), 23.7 (CH_2), 25.1 (CH_2), 31.0 (CH_2), 31.5 (CH_2), 54.8 (NCH_2), 64.8 (NCH), 73.5 (OCH), 125.9, 126.9, 127.5, 127.6, 129.3, 130.4, 135.1 (NCH_2CH=), 136.6 (C), 136.8 (C), 137.5 (C), 143.0 (C-Me), 161.3 (CO_2Cy) ppm. HRMS calcd for $C_{21}H_{23}NO_4S\cdot$Na: 408.1245, found: 408.1268. HPLC: Chiracel AD, hexane/isopropanol 80:20, 1 mL/min, 4.7 min [(+)-enantiomer] and 5.5 min.

3.4.11. Cyclohexyl 2,5-dihydro-2-(benzo[1,3]dioxol-5-yl)-1-tosylpyrrole-3-carboxylate 4f. Pale yellow solid, mp 118 °C; ^{1}H NMR ($CDCl_3$) δ 1.2–1.8 (10H), 2.40 (s, 3H, Me), 4.36 (ddd, $^2J_{AB}$=17.0 Hz, J=6.0, 2.0 Hz, 1H, NCH_2), 4.50 (dt, $^2J_{AB}$=17.0 Hz, J=2.5 Hz, 1H, NCH_2), 4.69 (1H, OCH), 5.67 (1H, NCH), 5.90 (d, J=1.5 Hz, 1H, OCH_2O),

5.93 (d, J=1.5 Hz, 1H, OCH_2O), 6.58 (1H), 6.70 (d, J=7.5 Hz, 1H), 6.78 (2H), 7.18 (d, J=8.0 Hz, 2H, Ts), 7.47 (d, J=8.0 Hz, 2H, Ts); ^{13}C NMR ($CDCl_3$) δ 20.1 (Me), 23.1 (CH_2), 23.3 (CH_2), 25.2 (CH_2), 31.0 (CH_2), 31.3 (CH_2), 54.7 (NCH_2), 68.7 (NCH), 73.2 (OCH), 101.1 (OCH_2O), 107.8 (CH_{Ar}), 107.9 (CH_{Ar}), 121.9 (CH_{Ar}), 127.1, 129.4, 133.4 (C), 135.2 (NCH_2CH═), 135.8 (C), 136.3 (C), 143.2 (C-Me), 147.3 (C_{Ar}), 147.5 (C_{Ar}), 161.3 (CO_2Cy) ppm. HRMS calcd for $C_{25}H_{27}NO_6S\cdot Na$: 492.1457, found: 492.1467. HPLC: Chiracel OD, hexane/isopropanol 93:7, 1 mL/min, 21.5 and 24.7 min.

3.4.12. Cyclohexyl 2,5-dihydro-2-(furan-2-yl)-1-tosylpyrrole-3-carboxylate 4g. Pale yellow oil; ^1H NMR ($CDCl_3$) δ 1.2–1.8 (10H), 2.40 (s, 3H, Me), 4.30 (ddd, $^2J_{AB}$=17.0 Hz, J=6.0, 2.0 Hz, 1H, NCH_2), 4.48 (dt, $^2J_{AB}$=17.0 Hz, J=2.3 Hz, 1H, NCH_2), 4.75 (1H, OCH), 5.90 (1H, NCH), 6.30 (1H), 6.36 (1H), 6.85 (NCH_2CH═), 7.17 (1H), 7.20 (d, J=8.0 Hz, 2H, Ts), 7.48 (d, J=8.0 Hz, 2H, Ts); ^{13}C NMR ($CDCl_3$) δ 21.5 (Me), 23.1 (CH_2), 23.3 (CH_2), 25.2 (CH_2), 31.0 (CH_2), 31.3 (CH_2), 54.2 (NCH_2), 61.8 (NCH), 73.2 (OCH), 109.1 (CH_{furyl}), 110.4 (CH_{furyl}), 127.0, 129.5, 133.5 (C), 135.7 (C), 136.8 (NCH_2CH═), 142.0 (CH_{furyl}), 143.2 (C), 151.4 (C_{furyl}), 161.1 (CO_2Cy) ppm. HRMS calcd for $C_{22}H_{25}NO_5S\cdot Na$: 438.1351, found: 438.1370. HPLC: Chiracel OD, hexane/isopropanol 90:10, 1 mL/min, 10.9 and 12.4 min.

3.4.13. Methyl 2,5-dihydro-2-(1-naphthyl)-1-tosylpyrrole-3-carboxylate 6a. Pale yellow oil; ^1H NMR data for compound **3m** have been reported previously.[1b] ^{13}C NMR ($CDCl_3$) δ 21.4 (Me), 51.7 (OMe), 55.1 (NCH_2), 65.1 (NCH), 123.2, 125.0, 125.4, 126.1, 126.8, 126.9, 128.5, 128.7, 129.0, 131.3 (C), 133.7 (C), 134.9 (C), 135.4 (NCH_2CH═), 135.4 (C), 136.4 (C), 143.0 (C-Me), 162.2 (CO_2Me) ppm. HRMS calcd for $C_{23}H_{21}NO_4S\cdot Na$: 430.1089, found: 430.1069. HPLC: Chiracel AD, hexane/isopropanol 80:20, 1 mL/min, 13.4 min [(+)-enantiomer] and 16.6 min.

3.4.14. Phenyl 2,5-dihydro-2-(1-naphthyl)-1-tosylpyrrole-3-carboxylate 3f. Pale yellow oil; ^1H NMR ($CDCl_3$) δ 2.28 (s, 3H, Me), 4.65 (ddd, J_{AB}=17.4 Hz, J=6.0, 1.5 Hz, 1H, NCH_2), 4.86 (dt, J_{AB}=17.3 Hz, J=2.7 Hz, 1H, NCH_2), 6.6–6.7 (3H), 6.93 (d, J=8.4 Hz, 2H), 7.1–7.4 (7H), 7.4–7.5 (2H), 7.7–7.8 (2H), 8.23 (d, J=7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1 (Me), 55.2 (NCH_2), 65.0 (NCH), 121.0, 123.2, 125.0, 125.5, 125.9, 126.3, 127.0, 128.6, 128.9, 129.0, 129.2, 131.4 (C), 133.7 (C), 134.8 (C), 135.5 (C), 136.2 (C), 137.2 (NCH_2CH═), 143.1 (C-Me), 149.8 (C_{Ph}), 160.0 (CO_2Ph) ppm. MS (ESI) m/z 492 (M+Na). HPLC: AD column, hexane/isopropanol 80:20, 1 mL/min, 15.0 and 16.5 min.

3.4.15. Isopropyl 2,5-dihydro-2-(1-naphthyl)-1-tosylpyrrole-3-carboxylate 3g. Pale yellow oil; ^1H NMR ($CDCl_3$) δ 0.47 (d, J=6.0 Hz, 3H, Me), 0.89 (d, J=6.3 Hz, 3H, Me), 2.17 (s, 3H, Me), 4.50 (ddd, J_{AB}=16.8 Hz, J=6.0, 2.1 Hz, 1H, NCH_2), 4.56–4.70 (2H, NCH_2+$OCHMe_2$), 6.48 (m, 1H, NCH), 6.8 (3H), 7.1–7.2 (4H), 7.4 (2H), 7.61 (d, J=7.8 Hz, 1H), 7.70 (d, J=7.8 Hz, 1H), 8.13 (d, J=8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 20.9 (Me), 21.3 (Me), 21.4 (Me), 55.0 (NCH_2), 64.5 (NCH), 68.3 (OCH), 123.4, 124.9, 125.4, 126.0, 126.6 (C), 127.0, 128.4, 129.0, 131.5 (C), 133.6 (C), 134.8 (NCH_2CH═), 135.6 (C),137.3 (C), 142.9 (C-Me), 161.3 ($CO_2{}^iPr$) ppm. HRMS calcd for $C_{25}H_{25}NO_4S\cdot Na$: 458.1402, found: 458.1418. MS (ESI) m/z 458 (M+Na). HPLC: WHELK column, hexane/isopropanol 90:10, 1 mL/min, 25 min [(+)-enantiomer] and 28 min.

3.4.16. D-Menthyl 2,5-dihydro-2-(1-phenyl)-1-tosylpyrrole-3-carboxylate 7. The procedure above afforded a 78:22 mixture of **7a+7b**. From this mixture, the major epimer has been obtained in pure form by crystallisation from heptanes/ethyl acetate. Compound **7a**: colourless solid; mp 165 °C; ^1H NMR ($CDCl_3$) δ 0.43 (d, ^3J=7.0 Hz, 3H, $CHMe_2$), 0.56 (d, ^3J=6.8 Hz, 3H, $CHMe_2$), 0.88 (d, ^3J=6.5 Hz, 3H, CHMe), 0.7–1.0 (4H), 1.09 (m, 1H), 1.4 (m, 1H), 1.55 (1H), 1.64 (d, J=12.5 Hz, 1H, CH_2), 1.87 (d, J=11.5 Hz, 1H, CH_2), 2.38 (s, 3H, Me), 4.33 (ddd, $^2J_{AB}$=17.0 Hz, ^3J=6.0 Hz, ^4J=1.5 Hz, 1H, NCH_2), 4.53 (d, $^2J_{AB}$=17.0 Hz, 1H, NCH_2), 4.59 (m, 1H, OCH), 5.77 (1H, NCH), 6.89 (1H, NCH_2CH═), 7.12 (d, J=8.0 Hz, 2H, Ts), 7.2–7.33 (5H, Ph), 7.436 (d, J=8.0 Hz, 2H, Ts); ^{13}C NMR ($CDCl_3$) δ 15.4 (Me), 20.9 (Me), 21.4 (Me), 21.9 (Me), 22.7 (CH_2), 25.0 ($CHMe_2$), 31.3 ($CHMe$), 34.0 (CH_2), 40.8 (CH_2), 46.8 (CH), 54.5 (NCH_2), 68.8 (NCH), 74.8 (OCH), 127.0, 128.0, 128.2, 129.3, 135.9 (C), 136.1 (NCH_2CH═), 136.2 (C), 139.2 (C), 143.1 (C-Me), 161.6 (CO_2Men) ppm. MS (ESI) m/z 504 (M+Na). HRMS calcd for $C_{28}H_{35}NO_4S\cdot Na$: 504.2185, found: 504.2166. Crystals suitable for X-ray diffraction have been obtained by slow crystallisation from an heptane/ethyl acetate mixture.

Acknowledgements

We thank Dr. Thomas Riermeier (Degussa AG, Hanau, Germany) for a generous gift of the chiral phosphines **A1** (catASium®KPh) and **A2** (catASium®KtB).

References and notes

1. (a) Xu, Z.; Lu, X. *Tetrahedron Lett.* **1997**, *38*, 3461–3464; (b) Xu, Z.; Lu, X. *J. Org. Chem.* **1998**, *63*, 5031–5041.
2. (a) Zhao, G.-L.; Huang, J.-W.; Shi, M. *Org. Lett.* **2003**, *5*, 4737–4739; (b) Zhao, G.-L.; Shi, M. *J. Org. Chem.* **2005**, *70*, 9975–9984.
3. Zhu, X.-F.; Henry, C. E.; Kwon, O. *Tetrahedron* **2005**, *61*, 6276–6282.
4. Xu, Z.; Lu, X. *Tetrahedron Lett.* **1999**, *40*, 549–552.
5. Wallace, D. J.; Sida, R. L.; Reamer, R. A. *J. Org. Chem.* **2007**, *72*, 1051–1054.
6. (a) Wager, T. T.; Welch, W.; O'Neill, B. T. WO Patent 2004/110996, Pfizer, 2004; (b) Segelstein, B. E.; Wager, T. T. U.S. Patent 2005/0,272,800, Pfizer, 2005; (c) Humphrey, J. M.; Chappie, T. A. WO Patent 2005/115976, Pfizer, 2005.
7. Jean, L.; Marinetti, A. *Tetrahedron Lett.* **2006**, *47*, 2141–2145.
8. These phosphines are available under the trade name catASium®KPh and catASium®KtB. (a) Gladiali, S.; Dore, A.; Fabbri, D.; De Lucchi, O.; Manassero, M. *Tetrahedron: Asymmetry* **1994**, *5*, 511–514; (b) Chi, Y.; Zhang, X. *Tetrahedron Lett.* **2002**, *43*, 4849–4852; (c) Junge, K.; Oehme, G.; Monsees, A.; Riermeier, T.; Dingerdissen, U.; Beller, M. *Tetrahedron Lett.* **2002**, *43*, 4977–4980.

9. For representative reports see: (a) Zhu, G.; Chen, Z.; Jiang, Q.; Xiao, D.; Cao, P.; Zhang, X. *J. Am. Chem. Soc.* **1997**, *119*, 3836–3837; (b) Chen, Z.; Zhu, G.; Jiang, Q.; Xiao, D.; Cao, P.; Zhang, X. *J. Org. Chem.* **1998**, *63*, 5631–5635; (c) Zhu, X.; Kwon, O. *J. Am. Chem. Soc.* **2003**, *125*, 4716–4717; (d) Wurz, R. P.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 12234–12235; (e) Pereira, S. I.; Adrio, J.; Silva, A. M. S.; Carretero, J. C. *J. Org. Chem.* **2005**, *70*, 10175–10177; (f) Shi, M.; Chen, L.-H.; Li, C.-Q. *J. Am. Chem. Soc.* **2005**, *127*, 3790–3800; (g) Wilson, J. E.; Fu, G. C. *Angew. Chem., Int. Ed.* **2006**, *45*, 1426–1429; (h) MacKay, J. A.; Vedejs, E. *J. Org. Chem.* **2006**, *71*, 498–503; (i) See Ref. 5.
10. (a) Marinetti, A.; Labrue, F.; Genêt, J.-P. *Synlett* **1999**, 1975–1977; (b) Marinetti, A.; Jus, S.; Labrue, F.; Lemarchand, A.; Genêt, J.-P.; Ricard, L. *Synthesis* **2001**, 2095–2104; (c) Marinetti, A.; Carmichael, D. *Chem. Rev.* **2002**, *102*, 201–230.
11. Other well known chiral phosphines including MonoPhos, MandyPhos, Josiphos and PHOX have been evaluated. All afforded very low conversion rates and enantioselectivities.
12. Phosphetane (*S*,*S*)-L2 (R=Cy) is a new compound. It has been prepared according to the procedure reported in Ref. 10b. ^{31}P NMR ($CDCl_3$) δ 22 ppm; ^{1}H NMR ($CDCl_3$) δ 0.5–2 (24H), 2.57 (m, 1H), 2.74 (m, 1H), 2.90 (dd, AB, J_{AB}=14 Hz, J=3.0 Hz, 1H, PCH_2), 2.98 (dd, AB, J_{AB}=14 Hz, J=4.5 Hz, 1H, PCH_2), 4.06 (2H, CH_{Fc}), 4.14 (7H, CH_{Fc}+Cp) ppm. HRMS calcd for $C_{26}H_{37}FeP$: 436.1982, found: 436.2025.
13. Marinetti, A.; Kruger, V.; Buzin, F.-X. *Tetrahedron Lett.* **1997**, *38*, 2947–2950.
14. Marinetti, A.; Jus, S.; Genêt, J.-P.; Ricard, L. *J. Organomet. Chem.* **2001**, *624*, 162–166.
15. Scherer, A.; Gladysz, J. A. *Tetrahedron Lett.* **2006**, *47*, 6335–6337; For other catalytic applications of the same phosphine, see: Seidel, F.; Gladysz, J. A. *Synlett* **2007**, 986–988.
16. Aliphatic imines have not been considered in this first screening. Compared to arylimines, they are known to give sluggish reactions with allenic esters or 2-butynoates: see Ref. 1.
17. Characterisations for the new pyrroline derivatives of this series are reported in Section 3.
18. For analogous reactions see: (a) Lang, R. W.; Hansen, H.-J. *Org. Synth.* **1984**, *62*, 202–209; (b) Pinho e Melo, T. M.; Cardoso, A. L.; Rocha Gonsalves, A. M.; Pessoa, J. C.; Paixão, J. A.; Beja, A. M. *Eur. J. Org. Chem.* **2004**, 4830–4839.
19. Further details and additional experiments will be reported later.
20. Crystallographic data for compound **7a** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC6. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).
21. McKay, W. R.; Proctor, G. R. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2435–2442.
22. Davis, F. A.; Lamendola, J.; Nadir, U.; Kluger, E. W.; Sedergran, T. C.; Panunto, T. W.; Billmers, R.; Jenkins, R.; Turchi, I. J.; Watson, W. H.; Chen, J. S.; Kimura, M. *J. Am. Chem. Soc.* **1980**, *102*, 2000–2005.
23. (a) Harris, J. M.; Padwa, A. *J. Org. Chem.* **2003**, *68*, 4371–4381; (b) Trost, B. M.; Marrs, C. *J. Org. Chem.* **1991**, *56*, 6468–6470.
24. Obtained from bromoacetyl bromide and cyclohexanol in the presence of Et_3N/DMAP. (a) Gryszkiewicz-Trochimowski, E.; Gryszkiewicz-Trichimowski, O.; Lévy, R. *Bull. Soc. Chim. Fr.* **1953**, 462–465; (b) Müller, P.; Fernandez, D.; Nury, P.; Rossier, J.-C. *Helv. Chim. Acta* **1999**, *82*, 935–946.
25. Fonquerna, S.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron* **1995**, *51*, 4239–4254.