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Synthesis and first applications of a new family of chiral monophosphine ligand: 2,5-diphenylphosphospholanes

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Abstract—The cyclic phosphinic acid 1-hydroxy-1-*r*-oxo-2*c*,5-*t*-diphenylphospholane was synthesized and resolved into enantiomers through fractional crystallization of the quinine salts. The *P*-phenyl, *P*-methyl and *P*-benzyl tertiary phosphine oxides were obtained from the secondary phosphine oxide, reduction of the oxides afforded the corresponding tertiary *P*-phenyl and *P*-benzyl phosphines. Hydrogenation of prochiral enamides were performed with Rh/(*S*,*S*)-1-1,2*c*,5-*t*-triphenylphospholane catalytic system. Methyl (*Z*)-*N*-acetyl dehydrocinnamate was hydrogenated to give the *N*-acetyl phenylalaninate in 93% ee. © 2002 Published by Elsevier Science Ltd.

The elaboration of new chiral ligands is important for the improvement of both reactivities and enantioselectivities of transition metal-catalyzed asymmetric syntheses. Phosphines are among the most widespread used ligands in catalytic organometallic transformations.[1] Owing to their chelating properties, chiral diphosphines were the most widely and successfully investigated in many reactions such as Rh-, Ru-, Ir-catalyzed hydrogenation of olefinic and carbonyl compounds and Pd-catalyzed allylic substitutions among others.

It appears however that for some reactions, the suggested turnover-determining or enantiodetermining step involve complexes bearing a monodentate-P ligand. Indeed in such reactions both reactivities and/or selectivities (enantio-, regio-) displayed by diphosphines are often lower than with monophosphines.[2] This has been shown for Pd-catalyzed hydrosilylation of olefins[3] and 1,3-dienes,[4] Pd-catalyzed hydrovinylation,[5] Pd-catalyzed allylation of organometallics[6] and stabilized carbanions[7] with allylic carboxylates, Pd-catalyzed reduction of allylic esters,[8] 1,4-hydroboration of 1,3-eneynes,[9] rhodium(I)-catalyzed hydrogenation of 2-acetamido cinnamate[10] and nickel-catalyzed [2+2+2] cocyclization of triynes.[11]

Moreover, chiral basic monophosphines have been recognized as useful asymmetric nucleophilic catalysts in kinetic resolution of racemic secondary alcohols through acylation,[12] in cycloaddition of dienoates with electron-deficient olefins[13] and imines,[14] and in γ-addition reactions to acetylenic esters.[15]

The chiral, 2,5-disubstituted phospholane framework, first synthesized by Burk,[16] was the motif of the successful diphosphine ligands DuPHOS [1,2-bis(2,5-dialkylphospholanyl)-benzene], BPE [1,2-bis(2,5-dialkylphospholanyl)-ethane] and related diphosphines. In those compounds, the chiral 2,5-phospholane ring was built by a double substitution of the stereochemically well-defined di-mesylates[4a,16] or cyclic sulfates[17] with dilithiated arylphosphide compounds. The 2,5-dimethyl-1-phenylphospholane **1** showed an interesting catalytic activity in acylation-mediated resolution of secondary alcohols.[12]

However the above method does not permit the synthesis of 2,5-diarylphospholanes, owing to the sensitivity of the corresponding dimesylate or cyclic sulfate towards elimination in basic conditions. The synthesis of 2,5-diarylphospholanes, whose steric, electronic and chelating properties could be fine-tuned by varying the substitution of the aryl rings, would be highly desirable. We reported yet 10 years ago the synthesis of the chiral 1,2-*c*,5-*t*-triphenylphospholane **2a**, through the resolution by chiral liquid chromatography, then the reduction of the corresponding oxide **3a**.[18] Since the resolution procedure of this phosphine oxide was not practical on a preparative scale, we turned to an other synthetic approach based on the synthesis and resolution of the intermediate phospholanic acid 1-hydroxy-*r*-1-oxo-*c*-2,*t*-5-diphenylphospholane (or *trans*-2,5-diphenylphospholanic acid) **4**.

Keywords: phosphinic acid; phosphine; catalysis; enantioselection.

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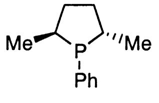

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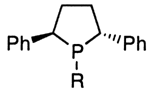
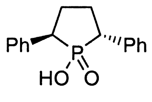


2a R = Ph
2b R = Bn



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The present paper describes details for the preparation of a set of new, enantiomerically pure 2,5-diphenylphospholanes, including 1,2-*c*,5-*t*-triphenylphospholane **2a**[9] and 1-*r*-benzyl-2-*c*, 5-*t*-diphenylphospholane **2b**.

1. Synthesis and resolution of 1-hydroxy-1-*r*-oxo-2-*c*,5-*t*-diphenylphospholane 4

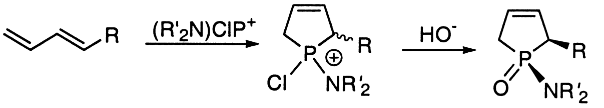
The target compound 1-hydroxy-1-*r*-oxo-2-*c*,5-*t*-diphenylphospholane **4** has been previously described as a byproduct in the reaction of the 1,4-diphenylbutane-1,4-dione with diphenylphosphine.[20] The low yield of phosphinic acid along with the inconvenience of the reaction protocol prompted us to devise a new synthesis of the phospholanic acid **4**.

Only a limited number of methods are known for the preparation of cyclic phosphinic acids or derivatives. A low-yielding method involved an intramolecular nucleophilic attack on a phosphonyl dichloride.[21] Better yields were obtained through the double Arbusov reaction between bis (trimethylsilyloxy)phosphine (BTSP) and dielectrophiles:[22] 2-methylphospholanic acid has been produced using this route. However, on reaction with BTSP the 1,4-dibromo-1,4-diphenylbutane did not give in our hands the desired 2,5-diphenylphospholanic acid, but elimination products instead.

The reaction of diorganometallics with dichlorophosphites has also been used for the synthesis of phospholanic acids. Indeed, the reaction of the di-Grignard reagent from 1,4-dibromobutane or from 2,5-dibromohexane with ethyl phosphorodichloridate afforded ethyl phospholanate[23] or a mixture of diastereoisomeric ethyl 2,5-dimethylphospholanates,[24] respectively. However, the di-Grignard or di-lithio compound from 1,4-diaryl-1,4-dihalobutane are not readily available.

More recently, cyclic phosphinates could be obtained through RCM of diallylphosphinates.[25] The reaction is however sensitive to the steric crowding of the substrates and the yields are reduced when using α-P-substituted phosphinates.

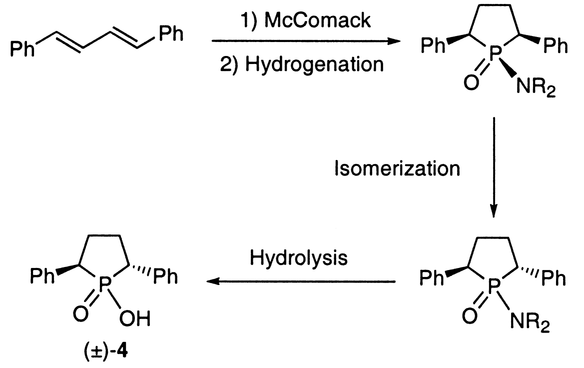
More interestingly, phospholanes may result from hydrogenation of phospholenes obtained by McCormack cycloaddition reaction between 1,3-dienes and P(III) reagents, i.e. dihalophosphines,[26] 2-ethyldichlorophosphite[27] or phosphenium cations.[28] Aminochlorophosphenium ions react with dienes below room temperature to give the corresponding 1-amino-1-oxophospholene (Scheme 1).



Scheme 1. Synthesis of 1-aminophospholenes.

Polniaszek used this latter strategy for the synthesis of 2-alkyl substituted phospholanic acids: hydrogenation of the 1-amino-1-oxophospholene followed by hydrolysis of the P–N bond gave access to the desired phospholanic acid.[29] In this study, Polniaszek showed that the hydrolysis of the intermediate chlorophospholenium salt afforded mainly the *trans* isomer of the 2-alkyl-1-amino-1-oxophospholene, and that the *trans*/*cis* ratio increased with the steric bulk of the substituents to reach 100% for a *t*-butyl substituent.

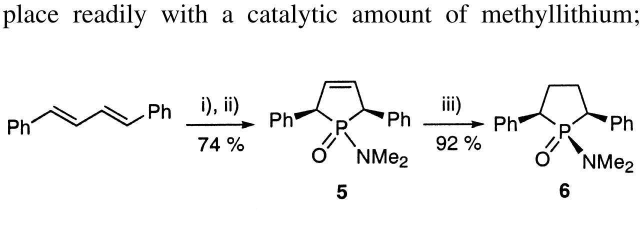
We therefore devised a strategy for the synthesis of 1-hydroxy-1-*r*-oxo-2-*c*,5-*t*-diarylphospholanes based on the McCormack reaction between the corresponding 1,4-diarylbutadiene and an aminophosphenium cation, followed, after hydrogenation of the intermediate *cis*-phospholene, by an isomerization step[18] to give the *trans*-1-amino-1-oxophospholene. Hydrolysis of the later should give the desired *trans*-diarylphospholanic acid **4** (Scheme 2).



Scheme 2. Synthesis of the *trans*-diarylphospholanic acid **4**.

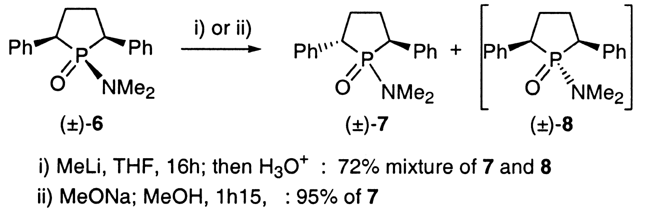
We found that the reaction of the commercially available (*N*,*N*-dimethylamino)dichlorophosphine with 1,4-diphenylbutadiene in the presence of aluminium trichloride afforded, after hydrolysis, the desired *meso* 1-(*N*,*N*-dimethylamino)-1-*r*-oxo-2-*t*,5-*t*-diphenylphosphol-3-ene **5** as the sole diastereomer. The carbon–carbon double bond of **5** was then catalytically hydrogenated over Pd on carbon to give the corresponding *meso* 1-(*N*,*N*-dimethylamino)-1-*r*-oxo-2-*t*,5-*t*-diphenylphospholane **6** (Scheme 3).

Isomerization of **6** into the more stable *trans* isomer **7** took place readily with a catalytic amount of methyllithium;



i) Me_2NPCl_2, $AlCl_3$, CH_2Cl_2, 0°C ; ii) $NaHCO_3$ / EDTA, 0°C
iii) Pd/C, 50 bar H_2, MeOH

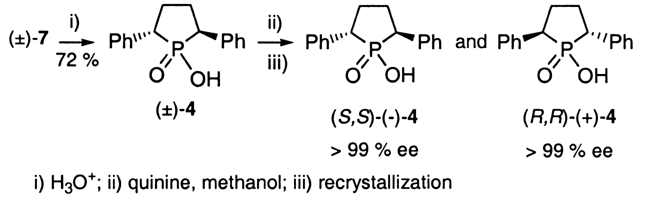
Scheme 3. Synthesis of the 1-(*N*,*N*-dimethylamino)-1-*r*-oxo-2-*t*,5-*t*-diphenylphospholane **6**.



Scheme 4. Isomerization of 1-(*N*,*N*-dimethylamino)-1-*r*-oxo-2-*t*,5-*t*-diphenylphospholane **6**.

however careful monitoring of the reaction is needed to minimize the formation of the even more stable *cis* isomer **8** (Scheme 4). More conveniently, the use of an excess sodium methoxide in methanol afforded only the *trans* isomer **7**.

The stereochemistries of the compounds **5** and **6** were assigned according to Polniaszek,[23] whereas the 2,5-*trans* relationship in compound **7** is clearly indicated by the loss of the symmetry plane in ^{13}C NMR. Moreover, the comparison of the chemical shifts of the benzylic protons in compounds **6–8** shows the characteristic deshielding of the protons in 1,2-*cis* relationship with the oxygen of the P=O bond (δ=3.45–3.65 ppm) in compound **6** as compared to the *trans* proton in compounds **7** and **8** (δ=3.20–3.40 ppm). Subsequent acid-hydrolysis of the resulting phosphinamide **7** delivered the 1-hydroxy-*r*-1-oxo-*c*-2,*t*-5-diphenylphospholane **4**, which was readily resolved by fractional crystallization of its diastereomeric quinine salts from methanol. Both enantiomers of **4** could thus be obtained in high enantiomeric purity (>99% ee) (Scheme 5).



Scheme 5. Synthesis and resolution of 1-hydroxy-*r*-1-oxo-*c*-2,*t*-5-diphenylphospholane **4**.

The enantiomeric purity could be checked by analysis (chiral HPLC) of the corresponding methyl phosphinate **10**, obtained by reaction of the phosphinic acid **4** with diazomethane or trimetylsilyldiazomethane.

2. X-Ray crystal structure of 1-hydroxy-1-oxo-2,5-*trans*-diphenylphospholane 4

The crystal data was collected using a Stoe IPDS diffractometer operating at 180(2) K. Intensities were collected with graphite monochromatized Mo Kα radiation (λ=0.71073), using a ϑ scan technique. Cell parameters were refined using 8000 selected reflections.

A molecular view with atom labeling scheme is shown in Fig. 1. The molecule has a twisted conformation with puckering parameters Q=0.455 Å, Φ=−101.9(2)°.[30]

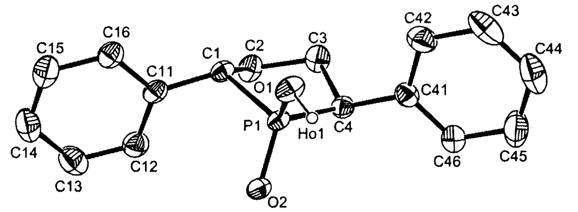


Figure 1. Molecular view of 1-hydroxy-1-oxo-2,5-*trans*-diphenylphospholane **4**.

Each molecule of phosphinic acid interacts with a neigbour through a strong hydrogen bond (O(1)–H(1) 1.04 Å; H(1)···O(2) 1.43 Å; O(1)···O(2) 2.45 Å; O(1)–H(1)···O(2) 167.4°) to form helicoïdal catemer chain parallel to the *b* axis (Fig. 2). The distances within the phospholane ring are identical within experimental errors to related structures.[31]

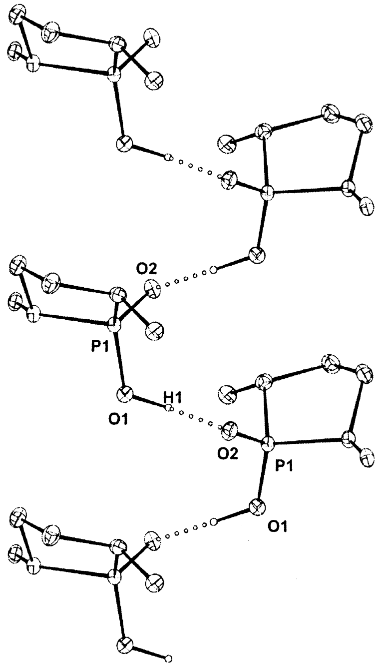
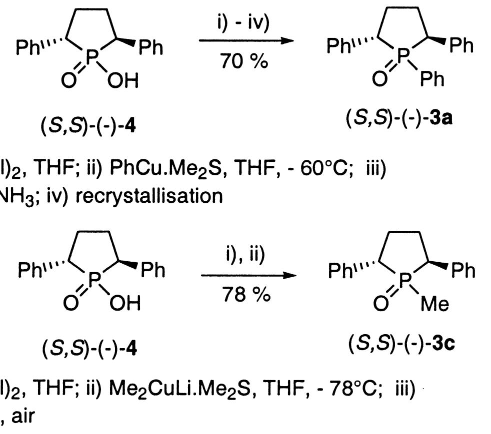


Figure 2. Helicoïdal catemer chain in **4**.

It is then anticipated that in solution, the phosphinic acid molecules could associate through this type of hydrogen-bonding, resulting in reduced solubility of this material. The phosphinic acid **4** is indeed only sparingly soluble in THF, dichloromethane and more soluble in methanol.

3. Synthesis of the 1-oxo-2-*c*,5-*t*-diphenylphospholanes

The functionalization at the phosphorus atom by an alkyl or aryl group may be carried out either by electrophilic or nucleophilic substitution. The substitution of phosphinic acid derivatives by organometals (mainly organolithium and Grignard reagents) has been widely used for the synthesis of phosphine oxides,[32] especially P-chiral tertiary phosphine oxides.[33] However Polniaszeck showed that phospholanates are mostly inactive toward Grignard reagents.[29] On comparison of the behavior of phosphinoyl chlorides and carboxylic chlorides towards organometals



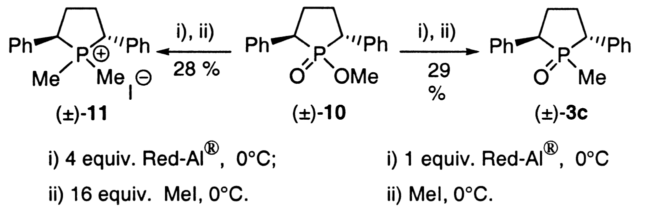
i) $(COCl)_2$, THF; ii) $PhCu.Me_2S$, THF, - 60°C; iii) NH_4Cl/NH_3; iv) recrystallisation

i) $(COCl)_2$, THF; ii) $Me_2CuLi.Me_2S$, THF, - 78°C; iii) NH_4OH, air

Scheme 6. Synthesis of the tertiary phosphine oxide via nucleophilic substitution.

(for which a number of organometals have been reported),[34] one could anticipate that the reaction of the phosphinic chloride **9** with a phenyl organometallic reagent would produce the corresponding tertiary phosphine oxide. Care should be taken however not to use too basic organometallic reagents in order to avoid epimerization at the stereogenic carbons atoms of the phospholane ring. In that respect should the use of organolithiums being precluded. However, neither the Grignard reagents nor the less basic ceric organometallics[35] succeeded in the clean substitution of the chloride atom of **9**. Phenyl copper and lithium dimethyl cuprate were successful in producing the corresponding phosphine oxide **3a** and **3c**, respectively, in satisfactory yields (Scheme 6).

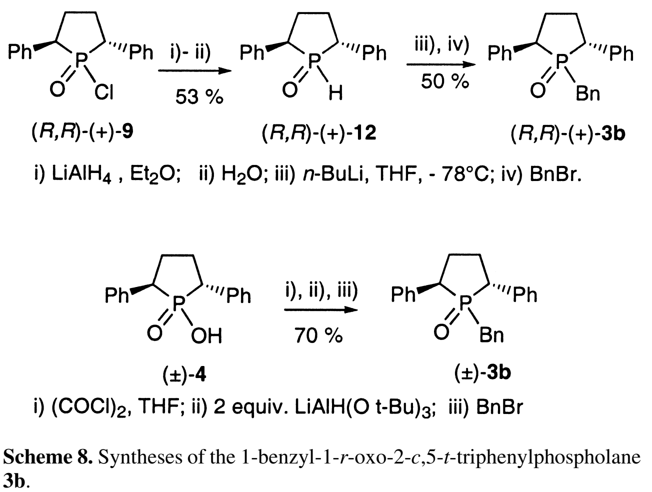
Preparation of tertiary phosphine oxides has been reported through reduction of phosphinates followed by reaction with alkyl halides.[36] Treatment of methyl phosphinate **10** successively with Red-Al, then methyl iodide gave either the methyl phospholanyl oxide **3c** or the dimethyl phosphonium **11**, according to the reaction conditions used (Scheme 7).



i) 4 equiv. Red-Al®, 0°C; ii) 16 equiv. MeI, 0°C.

i) 1 equiv. Red-Al®, 0°C ii) MeI, 0°C.

Scheme 7. Alkylation of the 1-methoxy-l-oxo-2,5-*trans*-diphenylphospholane.



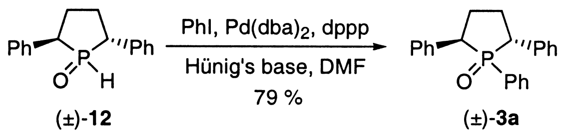
i) $LiAlH_4$, Et_2O; ii) H_2O; iii) *n*-BuLi, THF, - 78°C; iv) BnBr.

i) $(COCl)_2$, THF; ii) 2 equiv. $LiAlH(O\ t\text{-}Bu)_3$; iii) BnBr

Scheme 8. Syntheses of the 1-benzyl-1-*r*-oxo-2-*c*,5-*t*-triphenylphospholane **3b**.

1-*r*-Oxo-1-benzyl-2-*c*,5-*t*-diphenylphospholane **3b** could be obtained from the secondary phosphine oxide **12** by deprotonation with butyllithium followed by treatment with benzyl bromide. Better results were obtained with the anion produced in situ by $LiAlH(OtBu)_4$ reduction of the phosphinoyl chloride **9** (Scheme 8). Treatment of the chloride **9** with SmI_2 and benzyl chloride (the SmI_2-promoted coupling of alkyl halides and chlorophosphinites)[37] gave less satisfactory results.

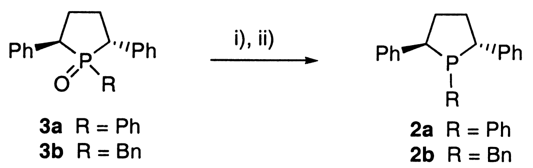
A second way for the production of phospholanyl oxide **3a** is shown in Scheme 9. Palladium-catalyzed coupling of the secondary phosphine oxide **12** with phenyl iodide afforded **3a** in good yield.



Scheme 9. Synthesis of **3a** via a Pd-catalyzed coupling reaction.

4. Synthesis of the 2-*c*,5-*t*-diphenylphospholanes

A number of procedures have been tried to reduce the phosphine oxides to phosphines. Reduction of the oxides into phospholanes was carried out according to Imamoto.[38] Treatment of the phosphine oxides **3a** and **b** with methyl triflate, followed by $LiAlH_4$ afforded the phosphines **2a** and **b**, respectively, and quantitatively (Scheme 10).



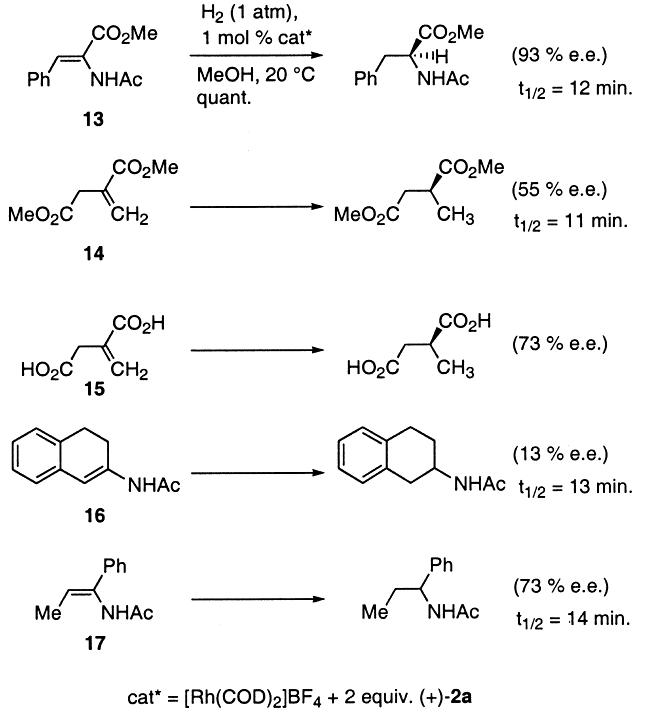
i) MeOTf, DME; ii) 1,5 equiv. $LiAlH_4$

Scheme 10. Reduction of the tertiary phosphine oxides.

5. Enantioselective reduction of olefinic compounds

Preliminary results[19] indicated that triphenylphospholane **2a** could induce asymmetry (84%) in the rhodium-catalyzed hydrogenation of *N*-acetyl dehydrocinnamic ester **13**. We report now that the asymmetric induction can reach 93% using the same catalytic system, when the catalyst precursor is prepared under rigorous exclusion of oxygen (Scheme 11).

The results of the asymmetric hydrogenation of dimethyl itaconate **14** and itaconic acid **15** are indicated in Scheme 11. In every case hydrogenation took place at room temperature, under atmospheric pressure of hydrogen at



Scheme 11. Catalytic asymmetric hydrogenation using **2a**–Rh complex.

high rate ($t_{1/2}<15$ min in all cases). The catalytic system showed also good activity in the hydrogenation of electron-rich *N*-acetyl enamides **16** and **17** ($t_{1/2}=14$ min for **16**); however for the cyclic enamide **16** the asymmetric induction is poor.

6. Conclusion

A new chiral phospholane ligand has been developped. The preliminary assays indicate that ligand **2a** affords excellent activity and enantioselectivity in Rh-catalyzed asymmetric hydrogenation of trisubstituted acyclic enamides. Further ligand modifications and applications in asymmetric catalysis are currently underway.

7. Experimental

7.1. General procedures

NMR spectra were recorded on a Bruker AC 250 spectrometer at 250 MHz (^{1}H), 62.9 MHz (^{13}C) and 101.2 MHz (^{31}P). Chemical shifts (δ) are reported in ppm relative to internal tetramethylsilane for ^{1}H and ^{13}C and to external 85% H_3PO_4 for ^{31}P. Carbon and phosphorus NMR spectra were recorded with complete proton decoupling. Flash column chromatography was performed using silica gel Merck (0.04–0.063 μm). Optical rotations were recorded at the sodium D line with a Perkin–Elmer 341 polarimeter. High-resolution mass spectra were obtained with a MAT 95 spectrometer.

Analytical HPLC was performed with a single wavelength UV detector (254 nm). Chiral analytical HPLC was carried out on a Regis Pirkle(*S*,*S*)-Whelk-O1 column or a Chiralcel OD-H column.

All reactions were carried out in Schlenk tubes under an argon atmosphere. All solvents were distilled from appropriate drying agents prior to use.

The crystal data was collected using a Stoe IPDS diffractometer operating at 180(2) K. Intensities were collected with graphite monochromatized Mo Kα radiation ($\lambda=0.71073$), using a ϑ scan technique. Cell parameters were refined using 8000 selected reflections.

The structure was solved by direct methods (SIR97[39]) and refined by least-squares procedures on F^2 using SHELXL-97.[40] All H atoms attached to carbon were introduced in calculation in idealized positions (d(CH)=0.96 Å, d(OH)=0.82 Å) and treated as riding models. The drawing of the molecule (Fig. 1) was realized with the help of ORTEP32[41] and the view of the hydrogen bond catemer (Fig. 2) with CAMERON.[42] Final refinement allowed the fraction contribution of the inverted enantiomer to vary (Bernardinelli and Flack, 1985; Flack, 1983)[43] the Flack's parameter quoted being the refined value of this contribution. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 171981. Copies of the data can be obtained free of charge on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

7.1.1. 1-[(*N*,*N*)-Dimethylamino]-1-*r*-oxo-2-*t*,5-*t*-diphenylphosphol-3-ene 5.

N,*N*-dimethylaminophosphinodichloridite (12 g, 82.2 mmol) was added to a stirred suspension of aluminium chloride (10.4 g, 77.7 mmol) in 100 mL anhydrous CH_2Cl_2 under argon. After 45 min, the greenish solution was placed in an ice bath and a pre-cooled solution of 1,4-diphenylbutadiene (15.4 g, 75 mmol) in 250 mL anhydrous CH_2Cl_2 was slowly added. The reaction mixture was then stirred at 0°C under argon for 16 h, then poured in a mixture of 400 mL of aqueous EDTA (0.2 M) and 200 mL of an aqueous saturated solution of $NaHCO_3$ cooled to 0°C. The biphasic mixture was then vigorously stirred for 4 h at 0°C, then filtered on celite, decanted and the aqueous layer extracted with CH_2Cl_2 (2×100 mL). The organic layers were washed with saturated $NaHCO_3$ (200 mL), 1 M HCl (200 mL) and brine (200 mL), then dried over $MgSO_4$ and concentrated under vacuum at room temperature. The resulting yellow oil was triturated with ether (50 mL), and the slightly yellowish precipitate of 1-[(*N*,*N*)-dimethylamino]-1-*r*-oxo-2-*t*,5-*t*-diphenylphosphol-3-ene (14.5 g) collected by filtration. Partial concentration of the ether solution, followed by cooling to 0°C allowed the recovery of an additional 2.0 g of product, for a total amount of 16.5 g (55.6 mmol, 74%) that was used without further purification in the following step. A recrystallization from cold acetone/hexane gave an analytical sample of phospholene **5** as white crystals (mp 105–115°C, dec.). Anal. calcd for $C_{18}H_{20}NOP$ (297.33): C, 72.71; H, 6.78; P, 10.42. Found: C, 72.63; H, 7.45; P, 10.53. ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=7.35$–7.10 (10H, m), 6.52 (2H, d, $J=29.3$ Hz), 4.27 (2H, d, $J=18.6$ Hz), 1.85 (6H, d, $J=8.3$ Hz). ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta=135.7$ (d, $J=8.0$ Hz), 130.6 (d, $J=16.7$ Hz), 128.4 (d, $J=2.4$ Hz), 127.0 (d, $J=4.8$ Hz), 126.7 (d, $J=2.8$ Hz), 49.1 (d, $J=71.9$ Hz), 35.8 (d, $J=1.9$ Hz). ^{31}P NMR (101.2 MHz, $CDCl_3$): $\delta=69.0$.

7.1.2. 1-[(*N*,*N*)-Dimethylamino]-1-*r*-oxo-2-*t*,5-*t*-diphenylphospholane 6. A pressure reactor was charged with 1-[(*N*,*N*)-dimethylamino]-1-*r*-oxo-2-*t*,5-*t*-diphenylphosphol-3-ene **5** (16.08 g, 54.1 mmol), Pd–C (10%, 0.5 g) and methanol (75 mL). The reactor was purged with hydrogen, then pressurized to 50 bar of hydrogen. After 16 h, the reaction mixture was filtered through celite and the solvent removed in vacuo, giving 15.4 g of colorless oil, which crystallized upon addition of ether. A recristallization in an AcOEt/hexane mixture gave 14.9 g (50 mmol, 92%) of 1-[(*N*,*N*)-dimethylamino]-1-*r*-oxo-2-*t*,5-*t*-diphenylphospholane **6** as colorless crystals (mp 114–115°C). Anal. calcd for $C_{18}H_{22}NOP$ (299.35): C, 72.22; H, 7.41; P, 10.35. Found: C, 72.04; H, 7.41; P, 10.39. MS (El) *m/z* (rel. int.): 77 (15), 91 (20), 104 (base), 206 (45), 299 ($M^{+\cdot}$, 47). ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=7.3–7.0$ (10H, m), 3.65–3.45 (2H, m), 2.5–2.3 (4H, m), 1.75 (6H, d, $J=8.3$ Hz). ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta=136.6$ (d, $J=5.7$ Hz), 128.1 (d, $J=2.4$ Hz), 126.6 (d, $J=5.0$ Hz), 126.0 (d, $J=2.6$ Hz), 45.3 (d, $J=72.7$ Hz), 34.9 (d, $J=2.4$ Hz), 26.4 (d, $J=13.1$ Hz). ^{31}P NMR (101.2 MHz, $CDCl_3$): $\delta=67.3$.

7.1.3. MeLi-mediated isomerization of 6. Methyllithium (0.12 mL of a 1.6 M solution in hexane, 0.19 mmol) was slowly added at room temperature to a stirred solution of 1-[(*N*,*N*)-dimethylamino]-1-*r*-oxo-2-*t*,5-*t*-diphenylphospholane **6** (1.12 g, 3.75 mmol) in anhydrous THF (6 mL) under argon. After 16 h at room temperature, the orange solution was hydrolyzed with aqueous HCl (1 M, 5 mL), extracted with toluene (2×20 mL) and the organic layers washed with water (10 mL), brine (10 mL), then dried over anhydrous $MgSO_4$ and the solvent removed in vacuo. A flash chromatography over silica gel (AcOEt/MeOH 95/5) afforded 0.81 g (2.7 mmol, 72%) of 1-[(*N*,*N*)-dimethylamino]-1-*r*-oxo-2-*c*,5-*t*-diphenylphospholane **7** as a white crystalline solid. A similar reaction carried out with 5.0 g (16.7 mmol) of **6** and 0.52 mL (0.83 mmol) of MeLi in 20 mL of anhydrous THF afforded, after silica gel column chromatography, 3.05 g (10.2 mmol, 61%) of *dl*-**7** and 1.71 g (5.7 mmol, 34%) of *meso*-**8**.

7.1.4. 1-[(*N*,*N*)-Dimethylamino]-1-*r*-oxo-2-*c*,5-*t*-diphenylphospholane 7. Mp 141–142°C. Anal. calcd for $C_{18}H_{22}NOP$ (299.35): C, 72.22; H, 7.41; P, 10.35. Found: C, 72.41; H, 7.45; P, 10.97. MS (El) *m/z* (rel. int.): 44 (31), 91 (22), 104 (98), 206 (43), 256 (43), 299 ($M^{+\cdot}$, base). ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=7.35–7.1$ (10H, m), 3.58 (1H, ddd, $J=7.7$, 12.1, 23.4 Hz), 3.24 (1H, dt, $J=7.1$, 12.7 Hz), 2.6–2.0 (4H, m), 2.27 (6H, d, $J=8.8$ Hz). ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta=136.7$ (d, $J=4.8$ Hz), 136.0 (d, $J=5.2$ Hz), 128.5 (d, $J=5.2$ Hz), 128.2 (d, $J=1.7$ Hz), 128.1 (d, $J=2.1$ Hz), 126.9 (d, $J=5.2$ Hz), 126.4 (d, $J=2.4$ Hz), 126.2 (d, $J=2.6$ Hz), 47.0 (d, $J=75.3$ Hz), 42.1 (d, $J=78.0$ Hz), 35.6 (d, $J=2.4$ Hz), 29.4 (d, $J=11.9$ Hz), 27.2 (d, $J=9.3$ Hz). ^{31}P NMR (101.2 MHz, $CDCl_3$): $\delta=59.9$.

7.1.5. 1-[(*N*,*N*)-Dimethylamino]-1-*r*-oxo-2-*c*,5-*c*-diphenylphospholane 8. Mp 153–154°C. Anal. calcd for $C_{18}H_{22}NOP$ (299.35): C, 72.22; H, 7.41; P, 10.35. Found: C, 72.21; H, 7.39; P, 10.83. MS (El) *m/z*(rel. int.): 44 (7), 91 (14), 92 (15), 104 (base), 206 (23), 299 ($M^{+\cdot}$, 12). ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=7.4–7.1$ (10H, m), 3.4–3.2 (2H, m), 2.63 (6H, d, $J=9.5$ Hz), 2.45–2.25 (4H, m). ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta=137.5$ (d, $J=6.2$ Hz), 128.7 (d, $J=5.5$ Hz), 128.5 (d, $J=1.9$ Hz), 126.5 (d, $J=2.1$ Hz), 41.4 (d, $J=78.0$ Hz), 36.2 (d, $J=2.2$ Hz), 29.4 (d, $J=11.9$ Hz). ^{31}P NMR (101.2 MHz, $CDCl_3$): $\delta=57.8$.

7.1.6. One pot isomerization-hydrolysis of 6. Sodium methoxide (11.3 g, 209 mmol) was added to a solution of 1-[(*N*,*N*)-dimethylamino]-1-*r*-oxo-2-*t*,5-*t*-diphenylphospholane **5** (12.5 g, 41.8 mmol) in methanol (100 mL). The resulting suspension was stirred at room temperature for 1 h 15 min, at which time the GC analysis of an aliquot showed 99% conversion into the *trans* isomer. The reaction mixture was then poured into 250 mL of 6N aqueous HCl and stirred for 4 h. The white precipitate was then collected by filtration and recrystallized in methanol to give 10.6 g (39 mmol, 93%) of racemic 1-hydroxy-1-oxo-2,5-*trans*-diphenylphospholane **4** as a white crystalline solid (mp 227–228°C). Anal. calcd for $C_{16}H_{17}O_2P$ (272.27): C, 70.58; H, 6.29; P, 11.38. Found: C, 70.48; H, 6.33; P, 11.08. MS (El) *m/z* (rel. int.): 78 (21), 91 (20), 104 (base), 168 (7), 272 ($M^{+\cdot}$, 54). ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=7.3–7.05$ (10H, m), 4.5 (1H, large s), 3.2–3.0 (2H, m), 2.5–2.2 (2H, m), 2.1–1.9 (2H, m). ^{13}C NMR (62.9 MHz, CD_3OD): $\delta=138.0$ (d, $J=5.7$ Hz), 129.7 (d, $J=5.5$ Hz), 129.5 (d, $J=1.9$ Hz), 127.7 (d, $J=2.4$ Hz), 47.0 (d, $J=87.0$ Hz), 30.2 (d, $J=11.9$ Hz). ^{31}P NMR (101.2 MHz, CD_3OD): $\delta=66.0$.

7.1.7. Hydrolysis of 7. 48 mL (144 mmol) of a 3 M aqueous HCl solution were slowly added at room temperature to a solution of 1.16 g (3.88 mmol) of 1-[(*N*,*N*)-dimethylamino]-1-*r*-oxo-2-*c*,5-*t*-diphenylphospholane **7** in 20 mL of ethanol. After 16 h at room temperature, the cloudy solution was made alkaline by careful addition of a 4 M aqueous NaOH solution and extracted by 2×30 mL of dichloromethane. The organic phase was discarded and the aqueous layer made acidic by careful addition of concentrated HCl. The precipitated phospholanic acid extracted by 5×50 mL of dichloromethane and the organic phase was washed withe brine (50 mL), dried over anhydrous magnesium sulfate and the solvent removed in vacuo to afford 0.88 g (3.23 mmol, 83%) of phospholanic acid *dl*-**4** as a white solid.

7.1.8. Resolution of 1-hydroxy-1-oxo-2,5-*trans*-diphenylphospholane 4. Racemic 1-hydroxy-1-oxo-2,5-*trans*-diphenylphospholane **4** (2.72 g, 10 mmol) was dissolved in the minimum amount of refluxing methanol. Quinine (3.25 g, 10 mmol) was then added; after cooling to room temperature, the white precipitate was collected, dissolved in dichloromethane, then decomposed with 100 mL of 2N aqueous NaOH. After decantation, the organic layer was washed with 2N NaOH solution (3×10 mL), then with brine, dried over $MgSO_4$ and the solvent was evaporated to offered the quinine. The aqueous phase was collected and treated with concentrate HCl solution to give the precipitated phospholanic acid **4**. Recrystallization in methanol afforded 1.18 g (4.34 mmol, 87% of the theoretical amount for one enantiomer) of (*S*,*S*)-(−)-1-hydroxy-1-oxo-2,5-*trans*-diphenylphospholane **4** as white crystals (mp 269–270°C).

$[\alpha]_D=-102.7$ ($c=0.6$, CH_2Cl_2). The enantiomeric excess was found to be >99.6% by chiral HPLC ((*S*,*S*)-Whelk 01, CH_2Cl_2/Hexane/MeOH 80/20/1) of the methyl ester derivative **10**.

The filtrate was evaporated and decomposed following the same procedure to give 1.15 g (4.23 mmol, 85% of the theoretical amount for one enantiomer) of (*R*,*R*)-(+)-1-hydroxy-1-oxo-2,5-*trans*-diphenylphospholane **4** (>99.6% ee).

Crystal data for ***4***. $C_{16}H_{17}O_2P$; $M_r=272.27$; monoclinic; space group *I*2; $a=11.3405(12)$, $b=5.7054(5)$, $c=22.323(3)$ Å, $V=1402.5(3)$ Å^3, $Z=4$, $\rho_{calcd}=1.289$ g mm^{-3}, $\mu=0.191$ mm^{-1}; 2θmax=52.3°; reflections collected unique used, 6977 2675($R_{int}=0.0276$) 2613 ($I>2\sigma(I)$); parameters refined, 176; $R/wR2$ (all data)=0.0249/0.0660; GOF=1.082; $\Delta/\sigma_{max}=0.001$; $[\Delta\rho]_{min}=[\Delta\rho]_{max}=-0.18$, 0.18 e Å^{-3}; Flack's parameter=−0.08(7).

7.1.9. (*R*,*R*)-(+)-1-Methoxy-1-*r*-oxo-2-*c*,5-*t*-diphenylphospholane 10. A solution of (*R*,*R*)-(+)-1-hydroxy-1-oxo-2,5-*trans*-diphenylphospholane **4** (705 mg, 2.59 mmol) in CH_2Cl_2 (50 mL) was treated at room temperature by a solution of diazomethane in ether, until persistence of the yellow color. The excess diazomethane was quenched by acetic acid, and the resulting solution concentrated in vacuo, to give 740 mg (2.58 mmol, 99%) of (*R*,*R*)-(+)-1-methoxy-1-*r*-oxo-2-*c*,5-*t*-diphenylphospholane **10** as a white solid. $[\alpha]_D=+76.4$ (CH_2Cl_2, $c=1.03$). MS (EI) *m*/*z* (rel. int.): 78 (26), 91 (20), 104 (base), 182 (14), 286 ($M^{+\cdot}$, 94). ^1H NMR (250 MHz, $CDCl_3$): $\delta=7.4$–7.2 (10H, m), 3.5–3.3 (1H, m), 3.25–3.1 (1H, m), 3.14 (3H, d, $J=10.2$ Hz), 2.6–2.4 (4H, m). ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta=136.1$ (d, $J=4.6$ Hz), 135.5 (d, $J=6.9$ Hz), 128.7–128.4 (m), 127.9 (d, $J=4.7$ Hz), 126.85 (d, $J=2.6$ Hz), 126.8 (d, $J=2.4$ Hz), 51.7 (d, $J=7.4$ Hz), 46.3 (d, $J=82.8$ Hz), 44.9 (d, $J=87.4$ Hz), 30.4 (d, $J=13.4$ Hz), 27.7 (d, $J=11.6$ Hz). ^{31}P NMR (101.2 MHz, $CDCl_3$): $\delta=65.9$.

7.1.10. (*S*,*S*)-(−)-1-Chloro-1-*r*-oxo-2-*c*,5-*t*-diphenylphospholane 9. A Schlenk tube was charged with (*S*,*S*)-(−)1-hydroxy-1-oxo-2,5-*trans*-diphenylphospholane **4** (272 mg, 1 mmol), then purged with argon. Anhydrous THF (5 mL) was then added, and the resulting suspension cooled to 0°C in an ice bath. Oxalyl chloride (0.4 mL, 4 mmol) was then slowly added. After 5 min, the ice bath was removed and the stirring continued for 2 h. The THF and excess oxalyl chloride were then removed under high vacuum, and the 1-chloro-1-*r*-oxo,2-*c*,5-*t*-diphenylphospholane obtained as 276 mg (0.95 mmol, 95%) of a white, moisture sensitive solid. ^1H NMR (250 MHz, $CDCl_3$): $\delta=7.4$–7.1 (10H, m), 3.9–3.6 (2H, m), 2.65–2.5 (1H, m), 2.45–2.15 (3H, m). ^{31}P NMR (101.2 MHz, $CDCl_3$): $\delta=80.3$.

7.1.11. (*S*,*S*)-(−)-1-*r*-Oxo-1,2-*c*,5-*t*-triphenylphospholane 3a through organocuprate substitution of 9. To a Schlenk tube containing a suspension of the CuBr–dimethylsulfide complex (1.5 g, 7,3 mmol) in 20 mL THF and cooled to −40°C in an acetone/dry ice bath was added 7.4 mL (7.4 mmol) of a 1 M phenyllithium solution in ether. The resulting yellow solution was stirred for 10 min (−40°C), then 5 min (0°C). After cooling down to −60°C, the phenylcuprous solution was added to a precooled (−60°C) solution of phosphinoyl chloride (*S*,*S*)-**9**, prepared as above from 2 g (7.34 mmol) of (*S*,*S*)-(−)-1-hydroxy-1-oxo-2,5-*trans*-diphenylphospholane **4**. The mixture was stirred for 1.15 h at −60°C, whereas the solution turned deep yellow. The reaction was quenched at −60°C with acetic acid (2.5 mL), and after 5 min stirring at this temperature, the colorless solution was treated in open air with 50 mL of a 1/1 mixture of a concentrated aqueous solution of ammonia and saturated NH_4Cl aqueous solution under vigorous stirring. The mixture was diluted with dichloromethane and allowed to heat to room temperature. The blue solution was extracted with dichloromethane, the organic layer washed with brine, dried over anhydrous magnesium sulfate and concentrated. The white solid was subjected to chromatographic purification (dichloromethane/methanol, 95/5) on silica gel, to obtain 2.15 g (6.47 mmol, 88%) of a white solid. A recrystallization from AcOEt/hexane gave 1.70 g (70% from **4**) of (*S*,*S*)-(−)-1-*r*-oxo-1,2-*c*,5-*t*-triphenylphospholane **3a**, mp 202–204°C (racemic compound: 171–173°C). The enantiomeric excess of **3a** was found to be >99.5% by chiral HPLC analysis (Chiralcel OD-H, eluent hexane/*i*PrOH 3/1). $[\alpha]_D=-130$ (MeOH, $c=1.01$). Anal. calcd for $C_{22}H_{21}OP$ (332.36): C, 79.25; H, 6.44; P, 9.15. Found: C, 79.09; H, 6.61; P, 9.32. ^1H NMR (250 MHz, $CDCl_3$): $\delta=7.5$–7.3 (2H, m), 7.3–7.1 (8H, m), 6.9–6.1 (5H, m), 3.83 (1H, ddd, $J=7.1$, 12.9, 25.5 Hz), 3.48 (1H, dt, $J=12.9$, 8.1 Hz), 2.75–2.4 (3H, m), 2.25–2.1 (1H, m). ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta=135.3$ (d, $J=3.6$ Hz), 135.7 (d, $J=5.5$ Hz), 131.5 (d, $J=2.8$ Hz), 131.1 (d, $J=8.3$ Hz), 130.6 (d, $J=88.9$ Hz), 128.8 (d, $J=5.0$ Hz), 128.6 (d, $J=1.9$ Hz), 128.2 (d, $J=2.4$ Hz), 128.0 (d, $J=11.4$ Hz), 127.1 (d, $J=5.0$ Hz), 127.0 (d, $J=2.1$ Hz), 126.3 (d, $J=2.6$ Hz), 51.0 (d, $J=61.5$ Hz), 46.7 (d, $J=62.0$ Hz), 31.5 (d, $J=7.4$ Hz), 27.9 (d, $J=8.6$ Hz). ^{31}P NMR (101.2 MHz, $CDCl_3$): $\delta=53.5$. MS (EI) *m*/*z* (rel. int.): 78 (16), 91 (40), 104 (46), 206 (20), 227 (35), 228 (33), 332 (base, $M^{+\cdot}$).

7.1.12. (*R*,*R*)-(+)-1-Benzyl-1-*r*-oxo-2-*c*,5-*t*-diphenylphospholane 3b. (*R*,*R*)-(+)-1-Chloro-1-*r*-oxo-2-*c*,5-*t*-diphenylphospholane **9** (3.68 mmol, from 1 g of (*R*,*R*)-(+)-1-hydroxy-1-oxo-2,5-*t*-diphenylphospholane **4**) were suspended in 30 mL of freshly distilled ether after sonication and cooled at 0°C. Lithium tri-*ter*-butoxyaluminohydride (12 mmol, prepared from 455 mg (12 mmol) of lithium aluminium hydride and 2.66 g (36 mmol) of *t*-butanol) in suspension in ether were then added via cannula and the mixture was allowed to reach room temperature. When gas evolution had ceased, 1 mL (8.5 mmol) of benzyl bromide was added and the resulting mixture was stirred overnight. After dilution with EtOAc/dichloromethane (60/40), the mixture was hydrolyzed with aqueous 1N HCl. The aqueous layer was extracted with EtOAc and the combined organic layers were washed with aqueous saturated K_2CO_3 then distilled water and dried over $MgSO_4$. Recrystallization from EtOAc/dichloromethane afforded 900 mg (2.60 mmol, 70%) of the phosphine oxide (*R*,*R*)-(+)-**3b** as a white solid (mp 212–216°C). $[\alpha]_D=+33.6$ (MeOH, $c=1.02$). ^1H NMR (250 MHz, $CDCl_3$): $\delta=7.45$–7.35 (4H, m), 7.35–7.05 (7H, m), 7.05–6.95 (2H, d, $J=3$ Hz), 6.85–6.75 (2H, d, $J=5.3$ Hz), 3.8–3.6 (1H, m), 3.1–2.8 (2H, m), 2.6–2.4 (2H, m), 2.4–2.1 (2H, m), 2.1–1.85 (1H, m). ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta=136.5$ (d, $J=5.4$ Hz), 136.2 (d, $J=3.6$ Hz), 131.6 (d,

J=7.2 Hz), 130.3 (d, J=5.3 Hz), 129.3 (d, J=5.1 Hz), 129.1 (d, J=5.1 Hz), 128.9 (d, J=2.1 Hz), 128.6 (d, J= 1.5 Hz), 127.6 (d, J=4.6 Hz), 127.4 (d, J=2.6 Hz), 127.1 (d, J= 2.6 Hz), 126.9 (d, J=2 Hz), 49.8 (d, J=57.6 Hz), 44.6 (d, J=60.4 Hz), 36.4 (d, J=56.4 Hz), 32.4 (d, J= 7.5 Hz), 26.8 (d, J=9.3 Hz). ^{31}P NMR (101.2 MHz, $CDCl_3$): δ= 58.8. HRMS (EI) calcd for $C_{23}H_{23}OP$: 346.1487, found: 346.1482.

7.1.13. (*S*,*S*)-(−)-1-Methyl-1-*r*-oxo-2-*c*,5-*t*-diphenylphospholane 3c. To a Schlenk tube containing a suspension of the CuBr–dimethylsulfide complex (185 mg, 0.9 mmol) in 4 mL THF and cooled (−78°C) in a bath was added 1.12 mL (1.8 mmol) of a solution of 1.6 M methyllithium in ether. The resulting yellow solution was stirred for 30 min (−78°C). The dimethylcuprate solution was added to a precooled (−78°C) solution of phosphinic acid chloride (*S*,*S*)-**9**, prepared as above from 246 mg (0.9 mmol) of (*S*,*S*)-(−)-1-hydroxy-1-oxo-2,5-*trans*-diphenylphospholane **4** and 0.4 mL of oxalyl chloride in 4 mL THF. The mixture was stirred for 2 h at −78°C, whereas the solution turned deep yellow. The reaction was quenched at −78°C with acetic acid (0.2 mL), and after 5 min stirring at this temperature, the mixture was allowed to heat to room temperature. The colorless solution was treated in open air with 10 mL of a 1/9 mixture of a concentrated aqueous solution of ammonia and saturated NH_4Cl aqueous solution under vigorous stirring. The blue solution was stirred for 15 min then extracted with dichloromethane, and the organic layer washed with brine, dried over anhydrous magnesium sulfate and concentrated to give 191 mg of a white solid. A recrystallization from AcOEt/hexane gave 169 mg (0.63 mmol, 69%) of (*S*,*S*)-(−)-1-methyl-1-*r*-oxo-2-*c*,5-*t*-diphenylphospholane **3c** as slim needles, mp 160–162°C; the ee was assayed to >98% through ^{31}P NMR of the compound in the presence of the chiral solvating agent (*R*)-*N*-(1-phenylethyl)-3,5-dinitrophenylamide. $[\alpha]_D=-67.5$ ($CHCl_3$, c=1.04). ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.4–7.2 (10H, m), 3.61 (1H, ddd, J=25, 12.5, 7.2 Hz), 2.95 (1H, dt, J=12.9, 7.5 Hz), 2.65–2.25 (3H, m), 2.1–1.9 (1H, m), 1.14 (3H, d, J=12.4 Hz). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ= 136.5 (d, J=3.8 Hz), 136.0 (d, J=5.2 Hz), 128.9 (d, J= 2.6 Hz), 128.8 (d, J=5.0 Hz), 128.6 (d, J=1.9 Hz), 127.2 (d, J=4.5 Hz), 127.0 (d, J=2.4 Hz), 126.9 (d, J=2.8 Hz), 49.5 (d, J=60.8 Hz), 47.4 (d, J=61.5 Hz), 31.9 (d, J= 7.2 Hz), 27.3 (d, J=8.8 Hz), 13.9 (d, J=63.4 Hz). ^{31}P NMR (101.2 MHz, $CDCl_3$): δ=61.3 (63.1 in the presence of (*R*)-*N*-(1-phenylethyl)-3,5-dinitrophenylamide). MS (EI) *m*/*z* (rel. int.): 91 (60), 103 (44), 104 (61), 165 (70), 166 (70), 270 ($M^{+\cdot}$, base).

7.1.14. 1,1-Dimethyl-2,5-*trans*-diphenylphospholanium iodide 11. To a solution of 1-methoxy-1-oxo-2,5-*trans*-diphenylphospholane **10** (143 mg, 0.5 mmol) in 5 mL of THF were added at 0°C, 0.60 mL (2.1 mmol) of a solution of Red-Al® (3.5 M in toluene). The solution was stirred for 15 min at 0°C, then 1 h at room temperature. To the resulting bright yellow mixture cooled in an ice-bath iodomethane (0.5 mL, 8 mmol) was added. After 5 min, 20 mL of an aqueous solution of sodium acetate (10 g L^{-1}) were added, the mixture stirred for 30 min, the THF removed in vacuo and the aqueous phase extracted with dichloromethane (4×50 mL). The organic phases were dried ($MgSO_4$), concentrated to give 147 mg of a white solid. A chromatographic purification (silica gel, CH_2Cl_2/MeOH 95/5) afforded 102 mg (0.26 mmol, 51%) of **11** as a white powder. ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.6–7.45 (4H, m), 7.4–7.2 (6H, m), 5.1–4.95 (2H, m), 2.9–2.7 (3H, m), 2.6–2.5 (1H, m), 1.74 (6H, d, J=13.4 Hz). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=131.9 (d, J=5.2 Hz), 129.4 (d, J=2.9 Hz), 128.5 (d, J=5.2 Hz), 128.4 (d, J=3.8 Hz), 42.8 (d, J=46.5 Hz), 30.8 (d, J=6.9 Hz), 7.4 (d, J=48.2 Hz). ^{31}P NMR (101.2 MHz, $CDCl_3$): δ=47.3.

7.1.15. (*S*,*S*)-(−)-1-*r*-Oxo-2-*c*,5-*t*-diphenylphospholane 12. *Method A*. To a suspension obtained after sonication of (*S*,*S*)-(−)-1-chloro-1-*r*-oxo-2-*c*,5-*t*-diphenylphospholane **9** (0.95 g, 3.68 mmol) in dry ether (50 mL) were added portionwise 180 mg (4.73 mmol) of lithium aluminium hydride. The reaction mixture turned yellow then purple and finally gray. The suspension was stirred overnight then hydrolyzed with 1N aqueous HCl. The aqueous layer was extracted with EtOAc and the combined organic layers washed with saturated K_2CO_3, water and dried over $MgSO_4$. The solvent was removed in vacuo and the phosphine oxide **12** was recovered almost quantitatively as a smelly white solid.

Method B. To a suspension of anhydrous cerium chloride (296 mg, 1.2 mmol) in 10 mL anhydrous THF was added at room temperature a solution of (*S*,*S*)-(−)-**9** prepared from 272 mg (1 mmol) of phosphinic acid (*S*,*S*)-(−)-**4** dissolved in 5 mL THF. After 0.5 h stirring, $LiAlH_4$ (76 mg, 2.0 mmol) was added portionwise. The resulting mixture was stirred for 20 min at room temperature, then hydrolyzed with a minimum amount of water. The granular precipitate was filtrated, the solvent removed in vacuo and the yellow solid obtained dissolved in 20 mL toluene. To this solution were added 0.23 mL (3.5 mmol) of 30% H_2O_2 diluted in 5 mL of water, and the biphasic mixture was stirred for 2 h at room temperature. After decantation, the organic layer was thoroughly extracted with 6×10 ml of water, dried over anhydrous magnesium sulfate et concentrated in vacuo. Flash chromatography (eluent CH_2Cl_2/AcOEt 9/1 then CH_2Cl_2/MeOH 19/1) followed by a recrystallization in AcOEt/hexane afforded 146 mg (0.57 mmol, 57%) of (*S*,*S*)-(−)-1-*r*-oxo-2-*c*,5-*t*-diphenylphospholane **12** as a white solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.5–7.0 (10H, m), 7.15 (1H, dq, J=470, 2.9 Hz), 3.55 (1H, dddd, J=23.4, 11.8, 7.8, 3.9 Hz), 3.26 (1H, dtd, J=12.3, 7.6, 2.9 Hz), 2.75–2.25 (3H, m), 2.1–1.85 (1H, m). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=136.2 (d, J=3.3 Hz), 135.0 (d, J=6.0 Hz), 129.0 (d, J=0.7 Hz), 128.9 (d, J=2.6 Hz), 128.7 (d, J=1.4 Hz), 127.3 (d, J=5.9 Hz), 127.2 (d, J= 2.9 Hz), 127.1 (d, J=2.1 Hz), 48.6 (d, J=60.6 Hz), 45.3 (d, J=59.8 Hz), 32.8 (d, J=7.2 Hz), 28.4 (d, J=11.0 Hz). ^{31}P NMR (101.2 MHz, $CDCl_3$): δ=54.5. MS (EI) *m*/*z* (rel. int.): 78 (28), 91 (70), 104 (base), 117 (26), 134 (14), 152 (20), 256 ($M^{+\cdot}$, 45).

7.1.16. (*S*,*S*)-(−)-3a Through palladium-catalyzed coupling of (*S*,*S*)-12 with iodobenzene. Pd(dba)$_2$ (30 mg, 0.05 mmol) and 1,3-bisdiphenylphosphinopropane (23 mg, 0.056 mmol) were placed in a Schlenk tube under an argon atmosphere. Anhydrous DMF (2 mL) was added and the solution was stirred for 15 min at room temperature. To the yellow solution was added 134 μL (0.6 mmol) of iodobenzene. After 15 min stirring, to the orange mixture was added a solution of 350 μL (2 mmol) of diisopropylethylamine and 178 mg (0.5 mmol) of 2,5-*trans*-diphenylphospholane oxide **12** in 2 mL of anhydrous DMF. The resulting solution was heated to 100–105°C for 16 h. The solvent was then removed and the brown oil taken into 10 mL dichloromethane. The organic phase was washed with 5% aqueous $NaHCO_3$ (2×10 mL), brine (10 mL), dried over $MgSO_4$, and concentrated in vacuo. The brown solid was subjected to chromatographic purification (dichloromethane/methanol 95/5), to obtain 131 mg (0.395 mmol, 79%) of 1-*r*-oxo-1,2-*c*,5-*t*-triphenylphospholane **3a**.

7.1.17. (*S*,*S*)-(−)-1-*r*-,2-*c*,5-*t*-Triphenylphospholane 2a. To 665 mg (2 mmol) of phosphine oxide **3a** dissolved in 10 mL of freshly distilled DME, 250 μL (2.2 mmol) of methyl trifluoromethanesulfonate were added dropwise at room temperature under an argon atmosphere. After 2 h, the mixture was cooled down to 0°C and 115 mg (3 mmol) of lithium aluminium hydride were added. The heterogeneous mixture was allowed to warm to room temperature and stirred for additional 1.5 h. After hydrolysis with a minimum amount of water, the mixture was filtered under argon through Celite via cannula. The solvent was removed in vacuo and the phospholane **2a** was obtained as a white solid and stored in a glove box without further purification. $[\alpha]_D=-35.5$ (CH_2Cl_2, $c=0.85$). ^1H NMR (250 MHz, $CDCl_3$): $\delta=7.4-7.2$ (4H, m), 7.2–7.0 (9H, m), 6.87 (2H, d, $J=6.8$ Hz), 4.04 (1H, dt, $J=10.8$, 7.8 Hz), 3.8 (1H, ddd, $J=17.8$, 12.0, 5.7 Hz), 2.8–2.7 (1H, m), 2.3–2.2 (2H, m), 2.15–2.0 (1H, m). ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta=144.6$ (d, $J=18.9$ Hz), 138.6 (s), 135.8 (d, $J=29.1$ Hz), 133.2 (d, $J=18.5$ Hz), 128.6 (s), 128.1 (d, $J=30.9$ Hz), 127.8–127.5 (m), 126.0 (d, $J=2.2$ Hz), 125.4 (d, $J=1.8$ Hz), 48.8 (d, $J=17.4$ Hz), 46.8 (d, $J=15.6$ Hz), 36.6 (s), 32.7 (d, $J=3.6$ Hz). ^{31}P NMR (101.2 MHz, $CDCl_3$): $\delta=21.3$.

7.1.18. (*S*,*S*)-(−)-1-*r*-Benzyl-2-*c*,5-*t*-diphenylphospholane 2b. To 1.8 g (5.2 mmol) of phosphine oxide **3b** dissolved in 7 mL of freshly distilled DME, 600 μL (5.7 mmol) of methyl trifluoromethanesulfonate were added dropwise at room temperature under an argon atmosphere. After 2 h, the mixture was cooled down to 0°C and 500 mg (13 mmol) of lithium aluminium hydride were added. The heterogeneous mixture was allowed to warm to room temperature and stirred for additional 1.5 h. After dilution with 25 mL of dry and degassed diethyl ether, the mixture was filtered under argon through silica via cannula. The solvent was removed in vacuo and the phospholane **2b** was obtained as a white solid and stored in a glove box without further purification. $[\alpha]_D=-197$ ($CDCl_3$, $c=1.12$). ^1H NMR (250 MHz, $CDCl_3$): $\delta=7.35-7.3$ (4H, m), 7.2–7.0 (7H, m), 7.0 (2H, d, $J=7.9$ Hz), 6.85 (2H, d, $J=7.9$ Hz), 3.8–3.6 (1H, m), 3.3–3.2 (1H, m), 2.65–2.3 (5H, m), 2.05–1.85 (1H, m). ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta=144.7$ (d, $J=17$ Hz), 139.3 (s), 138 (d, $J=7.4$ Hz), 129.7 (d, $J=6$ Hz), 128.9–128.5 (m), 128.0–127.7 (m), 126.3 (s), 126.0 (d, $J=4.8$ Hz), 48.8 (d, $J=18.5$ Hz), 47.2 (d, $J=17$ Hz), 36.5 (s), 32.3 (d, $J=32$ Hz), 32.2 (s). ^{31}P NMR (101.2 MHz, $CDCl_3$): $\delta=18.4$.

7.2. Rhodium-catalyzed asymmetric hydrogenation: general method

A Schlenk tube placed in a glove box was charged with (−)-**2a** (15.2 mg, 24 μmol) and bis(cyclooctadiene)-rhodium tetrafluoroborate (8.4 mg, 10 μmol). The tube was then taken out of the glove box and charged with 10 mL of degassed, anhydrous methanol. The mixture was stirred for 20 min, and the yellow solution obtained was canulated into a Schlenk tube containing 2 mmol of the chosen enamide under a hydrogen atmosphere. The uptake of hydrogen began immediately upon stirring. After completion of the reaction (no further hydrogen uptake), the resulting solution was concentrated in vacuo, taken up in dichloromethane (10 mL) and stirred with activated carbon for 1.5 h. Filtration over celite and removal of the solvent afforded the hydrogenated product. Enantiomeric excesses were determined by chiral HPLC on a Chiralcel OD-H column, with hexane/*i*-PrOH 9/1 as eluent.

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