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Enantioselective Palladium-Catalysed Allylation of 1,5-Dimethylbarbituric Acid

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Allylation of 1,5-dimethylbarbituric acid (**BS**) with allyl acetate using in situ catalysts of palladium(II) acetylacetonate and chiral phosphane imine ligands results in the enantioselective formation of 5-allyl-1,5-dimethylbarbituric acid (**ABS**) as the main product with up to 34% *ee* and 3,5-diallyl-1,5-dimethylbarbituric acid (**AABS**) as a possible by-product, also with up to 34% *ee*. This reaction is a type of allylic alkylation, the stereoselectivity of which is difficult to control because the new stereocenter is formed in the nucleophile attacking from the side opposite to the metal atom. Classical optically active ligands do not give any enantioselectivity in this palladium-catalysed reaction. Chiral phosphane imine ligands, however, are a successful class of compound, synthesized by Schiff base condensation of 2-formylphenyl(diphenyl)phosphane with optically active primary amines. An optimisation of this ligand type showed that the substituents at the stereogenic center in the imine part should be a hydroxymethyl group and a bulky alkyl group, with the best ligand being the L-*tert*-leucinol derivative. A screening of other types of chiral ligand, e.g. phosphane amines and phosphane trisimines, has also been performed. NMR experiments and a molecular modelling study of the cation $[(\eta^3\text{-allyl})\text{Pd}(\mathbf{2a})_2]^+$ were carried out (tripos force field). The enantioselectivity of the phosphane imine ligands is explained by an interaction of the chiral side arm of one of the ligands, which extends to about 3 Å above the allyl plane, with the incoming nucleophile.

Introduction

The enantioselective palladium-catalysed allylic alkylation is one of the most studied subjects in stereoselective synthesis[2][3][4][5]. Usually the new stereogenic center is formed at one of the carbon atoms of the allylic system. The enantioselectivity of this type of allylic alkylation can be controlled by optically active phosphane ligands bound to the Pd catalyst, which forms an intermediate η^3-allyl complex in the catalytic cycle. High optical inductions have been obtained for systems, in which the new asymmetric center is generated in the allylic moiety[2][3][4][5][6][7][8][9][10][11][12][13][14][15]. However, there is an unsolved problem in the palladium-catalysed allylic alkylation involving the creation of an asymmetric center in the nucleophile, usually a carbanion, which attacks the η^3-allyl system in the C−C bond forming step. Control of the enantioselectivity of this type of allylic alkylation is difficult because the nucleophile approaches the (η^3-allyl)Pd complex from the side opposite to the metal atom (and its optically active ligand). By using special nucleophiles, such as the benzophenoneimine of methyl glycinate[18][19] or 2-acetylcyclohexanone[3], enantioselectivities of 62 and 81% *ee*, respectively, were obtained in the alkylation of allyl acetate.

The enantiomers of chiral barbituric acids show different effects inside the organism[20][21][22][23][24]. These optically active barbituric acids are synthesized by the resolution of racemates[20][25][26] or by regioselective condensation of *N*-methylurea with optically active cyanoacetates[21][22][24]. Although interest in barbituric acids acting as sedative/hypnotic and antiepileptic agents is decreasing, this is not true for barbituric acids which function as short time anesthetics. An important example is Methohexital (Brevimytal®)[20][27][28][29][30][31][32][33][34], an allylated barbituric acid, the synthesis of which in principle could be attempted by stereoselective palladium-catalysed allylic alkylation. An achiral allylation of the unsubstituted barbituric acid has been reported[35].

As a model system for the synthesis of Methohexital by allylic alkylation, we chose the reaction of 1,5-dimethylbarbituric acid with allyl acetate as the allylic component, which we introduced in 1994 together with the pertinent enantiomer analysis[36]. In these previous studies we showed that classical ligands, such as (−)-Diop, (−)-Prophos and (−)-Norphos, only gave the allylated product 5-allyl-1,5-di-

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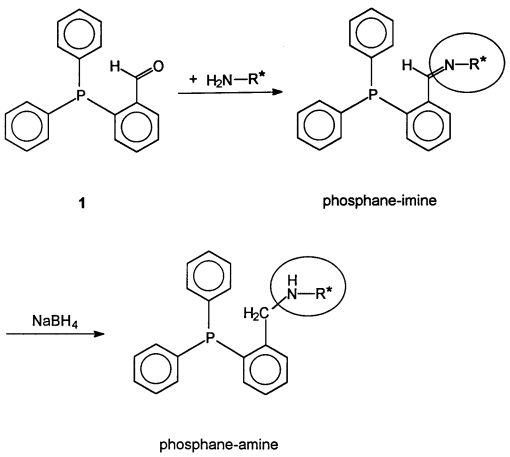
methylbarbituric acid in racemic form[36], whereas with the phosphane imine ligands **2a**, **2b**, and **11**, an enantiomeric excess of 10 to 13% was obtained[36].

In this paper we describe our investigations into the enantioselective palladium-catalysed allylation of 1,5-dimethylbarbituric acid with allyl acetate in which we varied the base, solvent, temperature, concentration, Pd/ligand ratio and ligand type[37]. In all, 134 different chiral ligands have been tested[37][38]. We present an explanation for the enantioselectivity of the phosphane imine ligands in the (η^3-allyl)Pd complex[37]. The preparation of new optically active phosphane imine, phosphane amine, and phosphane trisimine ligands is reported[37].

Synthesis of New Optically Active PN Ligands

In the previous studies the phosphane imine ligands **2a**, **2b,** and **11** had given the best results in the Pd-catalysed allylation of 1,5-dimethylbarbituric acid with allyl acetate[36]**.** The synthesis of the new PN ligands described here was carried out bearing in mind information gained from the enantioselectivities obtained in the catalytic model reaction between 1,5-dimethylbarbituric acid/allyl acetate. Schiff base condensation (Scheme 1) of 2-formylphenyl(diphenyl)phosphane **1**[39][40][41] with the optically active primary amines (*R*)-(−)-2-amino-1-butanol, (*S*)-(+)-2-amino-1-butanol, L-alaninol, L-valinol, L-leucinol, (2*S*,3*S*)-(+)-2-amino-3-methyl-1-pentanol (L-isoleucinol), (*S*)-(+)-2-amino-3,3-dimethyl-1-butanol (L-*tert*-leucinol), D-α-phenylglycinol, L-phenylalaninol, L-norephedrine, (1*S*,2*S*)-(+)-2-amino-1-phenyl-1,3-propanediol, L-*tert*-butyl *tert*-leucinate and (+)-dehydroabietylamine in refluxing methanol and dichloromethane, respectively, gave the corresponding phosphane imines **2**−**13** (Scheme 2). Recrystallisation of the dry residues from petroleum ether (boiling range 40−60°C) provided colourless or white-yellow crystals and powders, except in the case of **6**, which is a colourless oil.

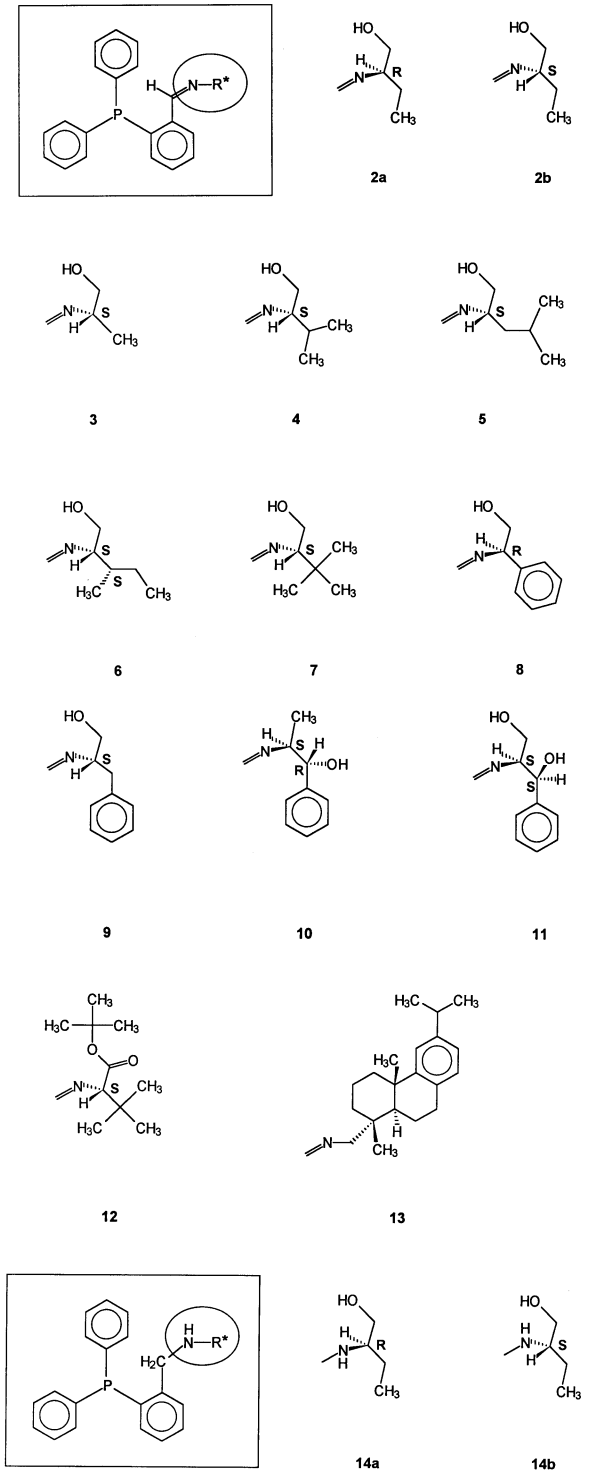
Scheme 1. Synthesis of phosphane imines and phosphane amines

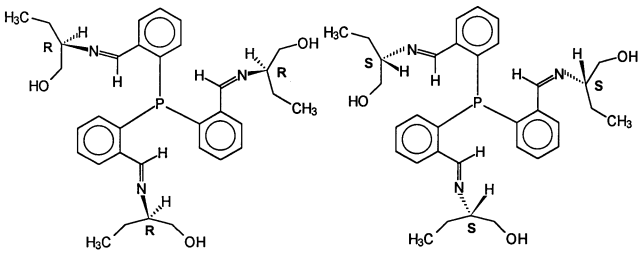


Reduction of the phosphane imines **2a** and **2b** with sodium borohydride at −10°C in methanol (Scheme 1) gave the phosphane amines **14a** and **14b** (Scheme 2).

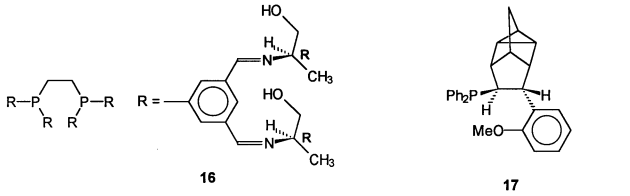
The phosphane trisimines **15a** and **15b** (Scheme 2) were prepared by Schiff base condensation of tris(2-formylphenyl)phosphane[40][41][42] with an excess of (*R*)-(−)-2-amino-1-butanol and (*S*)-(+)-2-amino-1-butanol, respectively, in refluxing dichloromethane. **15a** and **15b** were isolated as yellow crystalline solids after recrystallisation from petroleum ether (boiling range 40−60°C). The crystals were suitable for X-ray analysis. Figure 1 shows the molecular struc-

Scheme 2. The phosphane imines **2-13**, the phosphane amines **14a**, **14b**, the phosphane trisimines **15a**, **15b**, the osphane octaimine **16**, the deltacyclanephosphane **17** and the osphane oxazolines **18-20**

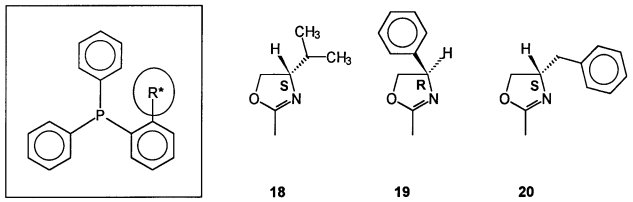




15a **15b**



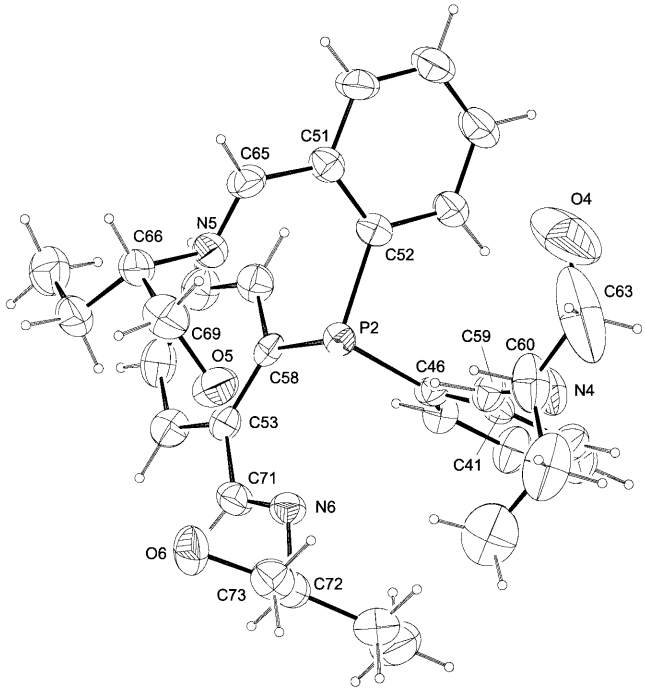
16 **17**



18 **19** **20**

ture of one of the two independent phosphane trisimine molecules **15b** in the unit cell. For details and the CSD number see Experimental Section.

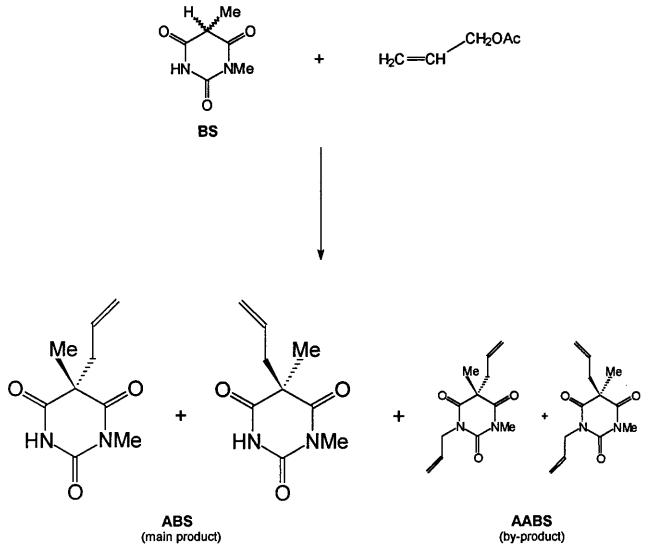
Figure 1. Molecular structure of one of the two independent phosphane trisimine molecules **15b** as ORTEP plot (thermal ellipsoids are depicted with 50% probability)



Standard Reaction: The Allylation of 1,5-Dimethylbarbituric Acid

In the catalytic model reaction, 1,5-dimethylbarbituric acid (**BS**) is allylated with allyl acetate to give 5-allyl-1,5-dimethylbarbituric acid (**ABS**) as the main product and 3,5-diallyl-1,5-dimethylbarbituric acid (**AABS**) as a possible by-product (Scheme 3).

Scheme 3. Enantioselective palladium-catalysed allylation of 1,5-dimethylbarbituric acid (**BS**) with allyl acetate



In dichloromethane **BS** is deprotonated with a small excess of a base, such as DBU or NEt_3. To the clear solutionwas added 1 mol% of palladium(II) acetylacetonate, $[Pd(acac)_2]$, 4 mol% of a monodentate optically active phosphane imine ligand and a mixture of dichloromethane and toluene. The addition of allyl acetate starts the reaction. Typically, the clear solution is stirred at 38°C for 24, 48 or 72 hours. A qualitative TLC test (silica 60, Merck; dichloromethane/acetonitrile 25:1) shows how much **ABS**, **AABS** and allyl acetate are present at a specific point of conversion (yellow spots after dipping into a dilute $KMnO_4$ solution). The reaction is stopped with 0.2 M hydrochloric acid. In ordert to remove the excess base, base/acetic acid adduct, and the unreacted **BS**, the organic layer is treated with 0.2 M hydrochloric acid and washed three times with water. Evaporation to dryness removes the excess allyl acetate. Due to the slight water-solubility of **ABS**, about 3% of the yield of **ABS** is lost in the work-up procedure described. This loss, however, cannot be avoided because repeated extraction of the organic layer with hydrochloric acid and water is necessary to remove **BS** quantitatively, as this compound would be detected as a broad peak below the (−)-**ABS** peak in the GC analysis with a Chirasil-Val-L column.

The enantiomeric excess of monoallylated barbituric acid **ABS** and diallylated barbituric acid **AABS** was determined by GC on a Chirasil-Val-L column and on a Lipodex E column, respectively. The first peak detected on the Chirasil-Val-L column was assigned to (−)-**ABS** (configuration unknown) by correlation with an enantiomerically enriched sample (see below). For **AABS**, the symbols (1.) and (2.),

respectively, indicate whether the first or the second detected peak of the two **AABS** enantiomers on the Lipodex E column was in excess. Chemical yields of **ABS** and **AABS** were determined on the same Chirasil-Val-L column using the internal standard benzil. In some cases, e.g. if the chemical yield was below 3%, the by-product 5-chloromethyl-1,5-dimethylbarbituric acid was detected. This compound results from the reaction of the carbanion of **BS** with the solvent dichloromethane[37].

Samples of optically active **ABS** dissolved in dichloromethane did not change their enantiomeric excess after half a year. In a racemisation test under standard catalytic conditions at 25°C, (+)-**ABS** (12.4% *ee*) was dissolved in dichloromethane and then [Pd(acac)$_2$] and PPh_3 were added. After 72 h a sample was examined by GC [12.2% *ee* (+)]. The base DBU was then added. After 48 h, work-up using the usual procedure gave 11.8% *ee* (+) (GC reproducibility about ±0.5% *ee*). Thus, **ABS** is configurationally stable during catalysis.

An enantiomerically enriched sample of (−)-**ABS** was obtained by recrystallisation from water/ethanol (175:1). After this recrystallisation the *ee* in crystals had diminished, whereas it increased in the mother liquor. A crystal of 17.4% *ee* (−)-**ABS** had the optical rotations $[\alpha]_D^{25} = -0.36$ and $[\alpha]_{436}^{25} = -2.4$ (c = 5, CH_2Cl_2). An extrapolation to optical purity gives $[\alpha]_D^{25} = \pm 2.1$ and $[\alpha]_{436}^{25} = \pm 13.8$ for the enantiomers of **ABS**.

The Diallylated 1,5-Dimethylbarbituric Acid AABS

The formation of **AABS** depends on the reaction conditions. When the catalysis is carried out with a 3-fold excess of the base DBU and a 21-fold excess of allyl acetate, **AABS** is produced in 98% yield in refluxing THF after 24 h. After 6 h a yield of 34% **ABS** and 32% **AABS** is obtained in this experiment. The formation of **AABS** depends on the ligand used in the catalyst, although a correlation between the ligand structure and the amount of **AABS** cannot be found. Under standard conditions (25°C or 38°C) the 134 ligands tested give the by-product **AABS** in yields ranging from 0 to 19%[37][38]. Ligands which form 7- to 9-membered chelate rings containing a dioxolane structural element[37][38] (e.g. Diop) give, in all cases, **AABS**, due to the high catalytic activity of their complexes. For example, with the ligand (1*S*,2*S*)-1,2-bis[2′-(diphenylphosphanyl)phenyl]-1,2-dimethoxyethane[43], the reaction was almost complete after 1 h, yielding 78% **ABS** and 8% **AABS**. However, in the case of the the phosphane imine ligand **2a**, formation of **ABS** and **AABS** had not even begun after 1 h[37]. Interestingly, a mixture of the starting material **BS** and the diallylated product **AABS**, in the absence of allyl acetate, under catalytic conditions gave the monoallylated product **ABS**, i.e. the formation of the diallylated product **AABS** is reversible[37].

Catalyses with the Ligand PPh_3

When the catalysis was attempted with [Pd(acac)$_2$] without a ligand, there was no turnover. Addition of triphenylphosphane in dichloromethane at 25°C (base DBU) gave 64% **ABS** and traces of **AABS** (Table 1, entry 1). Thus, the palladium-catalysed allylation of **BS** is an ideal example of a ligand accelerated catalysis[44]. Under the same conditions, but at −17°C, a yield of only 4% **ABS** was obtained after 72 h[37]. The use of [(η^3-allyl)PdCl]$_2$ in place of [Pd(acac)$_2$] afforded 60% **ABS** along with 11% **AABS**, the doubly allylated product (entry 2). Nickel dichlorophosphane complexes (1 mol% of catalyst) gave yields below 2% for **ABS**. With 10 mol%, yields of up to 29% for **ABS** were obtained[38]. Therefore, only Pd-catalysed reactions with 1 mol% of [Pd(acac)$_2$] were investigated further.

Variation of the base, i.e. replacement of DBU by triethylamine, at 38°C in dichloromethane yielded 98% **ABS**, and these conditions are close to those chosen as the standard conditions described later (entry 3). The use of BSA [*N*,*O*-bis(trimethylsilyl)acetamide] as the base in equimolar quantities with respect to **BS**, in dichloromethane at 25°C, gave 63% of **ABS** (entry 4), and this is comparable with the results obtained using DBU (entry 1). When a 1.5 M LDA·THF solution in cyclohexane was added to **BS** dissolved at −72°C in THF (colourless precipitate), low yields of **ABS** and **AABS** were obtained[37]. Stirring a mixture of **BS**, NBu_4OH, the catalyst, and allyl acetate in a two-phase system for 72 h at 25°C gave 59% **ABS** and 6% **AABS** (entry 5). Presynthesis of the tetrabutylammonium salt of **BS** (**NBu_4**BS) makes the addition of a base unnecessary[37]. Thus, **NBu_4**BS in a dichloromethane/toluene mixture (5:1) at 25°C (homogeneous solution) afforded a yield of 44% **ABS** and 1% **AABS** after 24 h (entry 6).

The optically active bases (−)-quinine, (+)-quinidine, (−)-cinchonidine and (+)-cinchonine, in combination with the achiral ligand triphenylphosphane, induced an enantiomeric excess of up to 6% *ee* in **ABS,** with the yields varying from 71 to 90% (entry 7)[37]. 2-Formylphenyldiphenylphosphane (**1**) is the parent compound of the imines **2**−**13**. As this compound could be formed on hydrolysis of these imines, it was tested as a ligand in the catalytic allylation. Indeed, **1** in combination with (−)-quinine as a base induced 6% *ee* (+) for **ABS** (81% yield) and 4% **AABS** (entry 8).

Catalyses with the Phosphane-Imine Ligands 2a and 2b

With a 1:2 ratio of [Pd(acac)$_2$]/**2a** in 10 ml of dichloromethane at 25°C, a yield of 14% and an enantiomeric excess of 8% of (+)-**ABS** was obtained (Table 2, entry 1). Increasing the Pd/ligand ratio to 1:4 and the amount of dichloromethane to 15 ml increased the enantiomeric excess to 10% *ee* and 13% *ee* for (+)-**ABS**, respectively (entries 2, 3). At a reaction temperature of 38°C the yield improved significantly to 63% **ABS** and 9% **AABS** without loss of enantioselectivity (entry 4). With 15 ml of a mixture of dichloromethane/toluene (2:1) as the solvent, the enantiomeric excess rose to 20% *ee* for (+)-**ABS** and 20% *ee* (2.) for **AABS** (entry 5), with the yield being 66% **ABS** and 12% **AABS** (typical standard conditions). The use of triethylamine and (−)-quinine as bases did not improve the enantiomeric excess[37]. Little or no enantioselectivity with ligand **2a** was observed in solvents such as acetonitrile, methanol, tetra-

Table 1. Palladium-catalysed allylation of 1,5-dimethylbarbituric acid (**BS**) with allyl acetate using PPh_3 and **1** as achiral ligands

Entry[a]	Ligand[b]	Base	[ml] Solvent	Temp. [°C]	Time [h]	Yield[c] **ABS** [%]	*ee* [%][d] **ABS** config.	Yield[c] **AABS** [%]
1	PPh_3	DBU	10 CH_2Cl_2	25	24	64	0	0
2[e]	PPh_3	DBU	10 CH_2Cl_2	25	24	60	0	11
3	PPh_3	NEt_3	15 CH_2Cl_2	38	24	98	0	0
4	PPh_3	BSA[f]	6 CH_2Cl_2	25	24	63	0	0
5	PPh_3	NBu_4OH solution in MeOH	5 H_2O + 20 toluene	25	72	59	0	6
6	PPh_3	none; substrate **NBu_4**BS	25 CH_2Cl_2 + 5 toluene	25	24	44	0	1
7	PPh_3	(−)-quinine	10 CH_2Cl_2 + 5 toluene	38	24	73	6 (+)	1
8	**1**	(−)-quinine	10 CH_2Cl_2 + 5 toluene	38	24	81	6 (+)	4

[a] 1 Mol% [$Pd(acac)_2$] was used as procatalyst. − [b] Pd:ligand ratio = 1:4. − [c] Yields were determined by GC on a Chirasil-Val-L column, yields < 0.5% are given as 0%. − [d] The *ee* of **ABS** was measured by GC on a Chirasil-Val-L column. − [e] 0.5 Mol% [(η^3-allyl)PdCl]$_2$ was used as procatalyst. − [f] **BS**:BSA ratio = 1:1 + ≈ 1 mg KOAc.

hydrofuran, chloroform and hexamethylphosphoric triamide (base DBU)[37]. Thus, the best solvent for the allylation of **BS** is a dichloromethane/toluene mixture. As **BS** is only sparingly soluble in toluene, the toluene content is limited in order to keep the reaction mixture homogeneous.

The ligand **2b**, the enantiomer of **2a**, verified with 19% *ee* for (−)-**ABS** and 20% *ee* (1.) for **AABS** the reproducibility of the catalysis and the product analysis under the standard reaction conditions (entry 6). Double stereoselection came into play for the optically active base (−)-quinine in combination with the enantiomeric phosphane imines **2a** and **2b**. Thus, **2a** provided 16% *ee* (+)-**ABS** (78% yield) and **2b** 12% *ee* (−)-**ABS** (entries 7, 8). With (+)-quinidine in combination with **2a**, 3% *ee* was obtained for (+)-**ABS** under the standard conditions[37]. The bases (−)-cinchonidine and (+)-cinchonine, together with ligand **2a**, induced 9% *ee* and 10% *ee* (+)-**ABS** and yields of 87 and 82%, respectively, in a reaction which started as a suspension in a 6:1 mixture of dichloromethane and toluene and which became clear after 41 h under standard conditions. The bases BSA and LDA·THF with ligand **2a** afforded low **ABS** yields[37]. With **NBu_4**BS and the ligands **2a** and **2b**, 12% *ee* (+)- and (−)-**ABS** was obtained, but with a yield of only 20 and 17%, respectively, in a dichloromethane/toluene mixture of 5:1 under the standard reaction conditions[37].

Optimisation of the Lead Structure of 2a

As already mentioned, the phosphane imine ligand **2a** gave an enantioselectivity of 20% *ee* (+)-**ABS** and 20% *ee* (2.) **AABS** using the base DBU in the solvent mixture dichloromethane/toluene (Table 2, entry 5; Table 3, entry 1), and this is superior to all the classical ligands. Therefore, the structure of **2a**, which carries a hydroxymethyl group and an ethyl group at the stereogenic center in its imine substituent in the *ortho* position of one of its phenyl rings, seems to be a lead structure for catalytic allylation in which the new stereocenter is formed at the carbanionic center of the deprotonated nucleophile **BS**. Therefore, we set out to optimize this lead structure.

Ligand **3** is similar to ligand **2b**, having a methyl group instead of an ethyl group and the same hydroxymethyl group in the ligand side arm, and this gives rise to an enantiomeric excess of 9% for (−)-**ABS** with DBU (entry 2) and of 8% for (−)-**ABS** with triethylamine . Thus, a decrease in the size of the alkyl group in the ligand side arm reduces the enantioselectivity. Therefore, we increased the size of the alkyl group in the ligands **4**−**7**, a strategy which turned out to be successful. The phosphane imine **4**, carrying an isopropyl group instead of the ethyl group in **2b**, gave 21% *ee* for (−)-**ABS** and 21% *ee* (1.) for **AABS** with DBU

Table 2. Palladium-catalysed allylation of 1,5-dimethylbarbituric acid (**BS**) with allyl acetate using the phosphane imine ligands **2a** and **2b**

Entry[a]	Ligand	Pd/ligand ratio[a]	Base	[ml] Solvent	Temp. [°C]	Time [h]	Yield[b] **ABS** [%]	*ee* [%][c] **ABS** config.	Yield[b] **AABS** [%]	*ee* [%][c] **AABS** config.
1	**2a**	1:2	DBU	10 CH_2Cl_2	25	72	14	8 (+)	0	−
2	**2a**	1:4	DBU	10 CH_2Cl_2	25	72	26	10 (+)	0	−
3	**2a**	1:4	DBU	15 CH_2Cl_2	25	72	22	13 (+)	0	−
4	**2a**	1:4	DBU	15 CH_2Cl_2	38	72	63	13 (+)	9	12 (2.)
5	**2a**	1:4	DBU	10 CH_2Cl_2 + 5 toluene	38	72	66	20 (+)	12	20 (2.)
6	**2b**	1:4	DBU	10 CH_2Cl_2 + 5 toluene	38	72	66	19 (−)	7	20 (1.)
7	**2a**	1:4	(−)-quinine	10 CH_2Cl_2 + 5 toluene	38	24	78	16 (+)	1	−
8	**2b**	1:4	(−)-quinine	10 CH_2Cl_2 + 5 toluene	38	48	80	12 (−)	3	−

[a] 1 Mol% [$Pd(acac)_2$] was used as procatalyst. − [b] Yields were determined by GC on a Chirasil-Val-L column, yields < 0.5% are given as 0%. − [c] The *ee* of **ABS** was measured by GC on a Chirasil-Val-L column, *ee* of **AABS** was measured by GC on a Lipodex E column.

(entry 3), which is slightly better than the enantioselectivity of **2b** (Table 2, entry 6). Triethylamine and (−)-quinine, respectively, in combination with **4** afforded 18% *ee* for (−)-**ABS** with 89 and 75% yield, respectively[37]. Further enlargement of the alkyl group, i.e. to an isobutyl group in ligand **5**, provided 28% *ee* for (−)-**ABS** and 28% *ee* (1.) for **AABS** with DBU (entry 4). Triethylamine and (−)-quinine, respectively, together with **5** gave 24% *ee* and 23% *ee* for (−)-**ABS**[37]. The ligand **6**, bearing a *sec*-butyl group, gave a similar result for (−)-**ABS** with 26% *ee* with DBU (entry 5) and 20% *ee* with triethylamine (yield 97%)[37]. The best enantiomeric excess in the palladium-catalysed system **BS**/allyl acetate was obtained with the phosphane imine **7**, which contains a *tert*-butyl substituent. **7** induced 34% *ee* for (−)-**ABS** with 77% yield and 1% yield for **AABS** [(34% (1.)] with DBU (entry 6). Ligand **7** with triethylamine as a base afforded 29% *ee* and 89% yield of (−)-**ABS** and 1% yield of **AABS** with 30% *ee* (1.) (entry 7).

nantly (−)-**ABS**, whereas the ligands with the (*R*) configuration (**2a**, **8**) give (+)-**ABS** (bases DBU and triethylamine).

Screening of the Ligands 12−20

Under standard conditions, nitrogen, nitrogen/oxygen and nitrogen/sulfur ligands [e.g. 2,2′-bipyridine, (−)-sparteine, pyridine-oxazolines, etc.] only give yields below 1% for **ABS** in the Pd-catalysed allylation of 1,5-dimethylbarbituric acid[38]. Therefore, the ligand screening concentrated on phosphane ligands[37][38]. Here, we only report representative results.

The phosphane imines **12** and **13**, the phosphane amines **14a** and **14b**, the phosphane trisimines **15a** and **15b**, the phosphane octaimine **16**, the deltacyclanephosphane **17** and the phosphane oxazolines **18**−**20** (Scheme 2) were tested in the standard palladium-catalysed allyllation of 1,5-dimethylbarbituric acid (**BS**) with allyl acetate.

Table 3. Palladium-catalysed allylation of 1,5-dimethylbarbituric acid (**BS**) with allyl acetate using the phosphane imine ligands **2a**−**11**

Entry[a]	Ligand[a]	Base	Solvent	Time [h]	Yield[b] **ABS** [%]	*ee* [%][c] **ABS** config.	Yield[b] **AABS** [%]	*ee* [%][c] **AABS** config.
1	**2a**	DBU	10 CH_2Cl_2 + 5 toluene	72	66	20 (+)	12	20 (2.)
2	**3**	DBU	15 CH_2Cl_2 + 5 toluene	72	74	9 (−)	7	−
3	**4**	DBU	10 CH_2Cl_2 + 5 toluene	48	75	21 (−)	2	21 (1.)
4	**5**	DBU	15 CH_2Cl_2 + 5 toluene	72	71	28 (−)	6	28 (1.)
5	**6**	DBU	15 CH_2Cl_2 + 5 toluene	72	82	26 (−)	4	26 (1.)
6	**7**	DBU	15 CH_2Cl_2 + 5 toluene	72	77	34 (−)	1	34 (1.)
7	**7**	NEt_3	10 CH_2Cl_2 + 5 toluene	72	89	29 (−)	1	30 (1.)
8	**8**	DBU	10 CH_2Cl_2 + 5 toluene	72	40	12 (+)	0	−
9	**9**	DBU	10 CH_2Cl_2 + 5 toluene	48	41	11 (−)	0	−
10	**10**	DBU	15 CH_2Cl_2 + 5 toluene	24	67	2 (−)	4	−
11	**11**	(−)-quinine	10 CH_2Cl_2 + 5 toluene	24	71	6 (+)	1	−

[a] 1 Mol% [$Pd(acac)_2$] was used as procatalyst, Pd : ligand ratio = 1:4 at 38°C. − [b] Yields were determined by GC on a Chirasil-Val-L column, yields < 0.5% are given as 0%; [c] The *ee* of **ABS** was measured by GC on a Chirasil-Val-L column, *ee* of **AABS** was measured by GC on a Lipodex E column.

We subsequently replaced the alkyl group at the stereogenic center with a phenyl and a benzyl group while retaining the hydroxymethyl substituent (ligands **8** and **9**). Phosphane-imine **8** induced 12% *ee* and 13% *ee* for (+)-**ABS** with DBU (entry 8) and triethylamine, respectively. Similar results were obtained with the ligand **9** (entry 9). The results with the ligands **8** and **9** show that phenyl and benzyl substituents in the ligand side arm are not as efficient as alkyl groups. Ligand **10** differs slightly from ligand **3** in that it has a hydroxybenzyl group instead of a hydroxymethyl group, and this gave only 2% *ee* for (−)-**ABS** with DBU (entry 10) and 2% *ee* for (+)-**ABS** with (−)-quinine. Thus, the hydroxymethyl substituent, essential for the optical induction, cannot be replaced by a hydroxybenzyl substituent. With ligand **11**, which compared to **2b** contains a second hydroxy group and an additional phenyl substituent in its chiral side arm, no enantioselectivity was found for **ABS** using DBU[37]. With (−)-quinine and ligand **11**, 6% *ee* (+)-**ABS** was induced (entry 11).

Uniformly, within the phosphane imine ligand family **2**−**11**, the ligands with the (*S*)-configuration of their *N*-bound stereogenic center (**2b**−**7**, **9**−**11**) induce predomi-

Though resembling the phosphane imine ligands **2**−**11**, ligand **12**, a *tert*-butyl *tert*-leucinate, gave only 1% *ee* for (−)-**ABS** with DBU and triethylamine, respectively. Ligand **13** bears the alkylaromatic system of (+)-dehydroabietylamine with no hydroxy group in its side arm, and this afforded racemic **ABS** with DBU and 4% *ee* (+)-**ABS** with (−)-quinine. With 2−3% *ee* for (+)- and (−)-**ABS**, the phosphane amine ligands **14a** and **14b** were much less enantioselective than the corresponding phosphane imine ligands **2a** and **2b**. The change from one-arm phosphane imines **2a** and **2b** to the three-arm phosphane trisimines **15a** and **15b** did not lead to an improvement in the optical induction of **ABS**. With **15a** an enantiomeric excess of 6% *ee* and a yield of only 2% for (−)-**ABS** was found with the base DBU. Interestingly, with **15a** **ABS** was formed with the inverse configuration in comparison to **2a**. Ligand **15b** in combination with (−)-quinine provided (−)-**ABS** with 3% *ee* and in only 1% yield.

With the phosphane octaimine **16**[45], which bears D-alaninol in its eight side arms, an enantiomeric excess of 11% *ee* for (+)-**ABS** was obtained. The incorporation of (*R*)-(−)-2-amino-1-butanol, L-valinol, L-leucinol, L-phenylalan-

inol in the ligand arms and changing the ligand backbone to the 1,2-disubstituted phenylene bridge decreased the enantioselectivity for **ABS**[37]. The deltacyclanephosphane **17**[46] gave 8% *ee* for (+)-**ABS** with DBU. The combination of **17** with (−)-quinine led to an improvement to 11% *ee* for (+)-**ABS** (double stereoselection). The phosphane oxazoline ligands **18**−**20**[47][48] induced up to 99% *ee* in allylations in which the stereogenic center is formed in the allylic system and up to 13% *ee* in allylations in which the stereogenic center is formed in the nucleophile[49][50]. In the catalytic allylation of **BS** with allyl acetate, an enantiomeric excess of only about 1% *ee* for (+)-**ABS** was obtained. Phosphane-oxazoline **20** in combination with (−)-quinine provided 4% *ee* for (+)-**ABS**, probably an effect of (−)-quinine.

A Model for the Catalytically Active Phosphane-Imine Pd Complex

The in situ system consisting of the dimeric (η^3-allyl)palladium chloride and the phosphane imine **2a** was investigated by $^{31}P\{^1H\}$-NMR spectroscopy. In dichloromethane using a Pd/**2a** ratio of 1:1, signals at δ = 36.34 (broad) (0.6 P), 32.81 (0.1 P), 32.63 (0.1 P) and 21.82/21.74 (0.2 P) were observed, the most intense of which could be due to a Pd complex containing **2a** as a P−N chelating ligand similar to the Pd complexes of the phosphane oxazoline ligands[8][9][11][13]. On changing from a Pd/**2a** ratio of 1:1 to a ratio of 1:4, all the signals present in the 1:1 experiment disappeared. Two new doublets of equal intensity arose at δ = 45.86 and 18.67 (coupling constant 341.8 Hz), belonging to the complex [(η^3-allyl)Pd(**2a**)$_2$]Cl. Excess **2a** exhibited a singlet at δ = −9.92 with double the intensity compared to the signals of the coordinated **2a**. In addition there were small signals at δ = 33.28 (oxide of **2a**), 23.27 and 15.20 (broad) (CH_2Cl_2/CD_2Cl_2, external 85% H_3PO_4, 162 MHz, 21°C). After seven days the signal at δ = 15.20 had disappeared and that at δ = 33.28 had increased (increasing oxidation). Thus, using a Pd to ligand ratio of 1:4, a (η^3-allyl)Pd complex formed containing two inequivalent phosphane imine ligands **2a**.

Based on X-ray studies[51][52][53][54][55] and calculations[56] of (η^3-allyl)Pd complexes a molecular modelling study of an (η^3-allyl)Pd complex with two phosphane imine ligands **2a** was carried out using the tripos force field. Figure 2 shows a conformation of this complex obtained on energy minimisation.

The two phosphane imine ligands **2a** turn out to be different. The hydroxy group of one phosphane imine extends to about 3 Å above the allyl plane, whereas the hydroxy group of the other phosphane imine remains below the allyl plane in accord with their NMR inequivalence (Figure 2). Furthermore, a substituted and an unsubstituted phenyl ring, one from each of the two phosphane imines, form a π-stacking pair which participates in the conformational organisation of the two monodentate ligands. Taking into account this phenyl/phenyl interaction, the two monodentate ligands in the (η^3-allyl)Pd complex can be considered a ″chelating″ ligand. The hydroxy group, which is about 3 Å above the allyl plane, can influence the incoming 1,5-dimethylbarbiturate anion (Figure 2), e.g. by forming hydrogen bonds, thus differentiating the N−H and the N−Me side of the **BS** anion (Figure 3), which explains the enantioselectivity of long-arm ligands of the type **2a**.

Figure 2. Conformation of the (η^3-allyl)Pd complex containing two phosphane imine ligands **2a** after energy minimisation

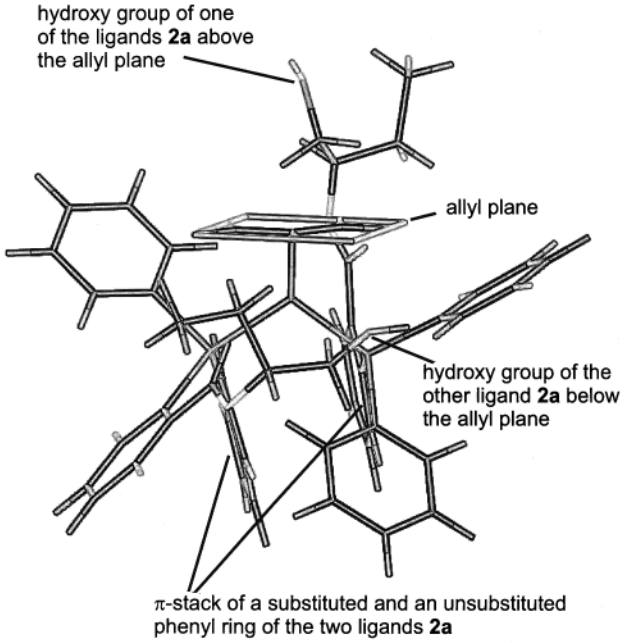
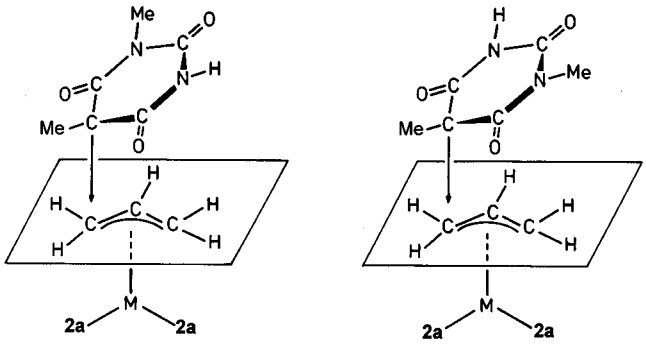


Figure 3. Differentiation between the N−H and the N−Me side of the incoming 1,5-dimethylbarbiturate anion in the formation of the new stereogenic center



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Experimental Section

NMR spectra were recorded on a Bruker WM 250 or on a Bruker ARX 400 instrument. Chemical shifts (δ) are reported in parts per million (ppm) vs. internal tetramethylsilane (TMS) (^1H) and external 85% H_3PO_4 ($^{31}P\{^1H\}$). − FD mass spectra were obtained on a Finnigan MAT 95, and for EI mass spectra a Varian MAT 311A was used. − Gas chromatography measurements were carried out on a Fisons Instruments GC 8000 series 8130. For integration of gas chromatograms a Spectra-Physics SP 4270 was used. − Infra red spectra were recorded on a Beckman Gitterspektro-

meter IR 4240. − Optical rotations were measured on a Perkin-Elmer polarimeter 241 (1-dm cell). − Melting points were obtained on a Büchi SMP 20 (uncorrected). The X-ray structure analysis was carried out on a AED II diffractometer.

(−)-Quinine, (−)-cinchonidine, and (+)-cinchonine were purchased from Merck, (+)-quinidine from Fluka, (*R*)-(−)-2-amino-1-butanol, (*S*)-(+)-2-amino-1-butanol, (1*S*,2*S*)-(+)-2-amino-1-phenyl-1,3-propanediol, (+)-dehydroabietylamine, L-*tert*-butyl *tert*-leucinate from Merck, L-alaninol, L-valinol, L-leucinol, D-α-phenylglycinol, L-phenylalaninol, L-norephedrine from Fluka, (2*S*,3*S*)-(+)-2-amino-3-methyl-1-pentanol (L-isoleucinol) from Aldrich, (*S*)-(+)-2-amino-3,3-dimethyl-1-butanol (L-*tert*-leucinol) from Sigma or Fluka and used without further purification. 2-Formylphenyl(diphenyl)phosphane (**1**)[39][40][41] and tris(2-formylphenyl)phosphane[40][41][42] were prepared as described in the literature. New analytical data are reported for **1**. The phosphane octaimine **16**[45], the deltacyclanephosphane **17**[46] and the osphane oxazolines **18**−**20**[47][48] were prepared using procedures described in the literature. All the syntheses and catalytic reactions were carried out with dried solvents under a nitrogen atmosphere using standard Schlenk techniques.

2-Formylphenyl(diphenyl)phosphane (**1**): Yellow crystals, m.p. 115−116°C. − IR (KBr): $\tilde{\nu}$ = 1701, 1679 cm^{-1} (C=O). − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 10.50 (d, ^4J_P = 5.4 Hz, 1 H, aldehyde), 7.97 (ddd, ^4J = 1.8 Hz, ^4J_P = 3.7 Hz, ^3J = 7.2 Hz, 1 H, Ar−H^3), 7.51−7.43 (m, 2 H, Ar−H^4 and Ar−H^5), 7.37−7.25 (m, 10 H, Ar−H), 6.99−6.95 (m, 1 H, Ar−H^6). − ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ = −10.99 (s). − $C_{19}H_{15}OP$ (290.30): calcd. C 78.61, H 5.21; found C 78.66, H 5.07.

General Procedure for the Preparation of the Phosphane Imines **2**−**13**. − *Variant A*: 3.45 mmol of the optically active primary amine was dissolved in 10 ml of methanol. 2-Formylphenyl(diphenyl)phosphane (**1**) (3.45 mmol; 1.00 g) and 10 ml of methanol were added to the above solution with stirring and the mixture refluxed for 3 h. After cooling to room temp. the methanol was removed and the resulting residue was dried and recrystallized as described for the individual phosphane imines.

Variant B: 3.45 mmol (or 4.14 mmol) of the optically active primary amine was dissolved in 30 ml of dichloromethane. 2-Formylphenyl(diphenyl)phosphane (**1**) (3.45 mmol; 1.00 g), 1 g of Na_2SO_4, and 10 ml of dichloromethane were added to the above solution with stirring and the mixture refluxed for 3 h. After cooling to room temp. the Na_2SO_4 was filtered off and washed with dichloromethane. The dichloromethane was removed and the resulting residue was treated as in variant A.

(+)-2-[N-(R)-1′-Hydroxybut-2′-ylcarbaldimino]phenyl(diphenyl)phosphane (**2a**): Variant A with 3.45 mmol (307 mg, 325 µl) of (*R*)-(−)-2-amino-1-butanol. Recrystallisation from 50 ml of petroleum ether (boiling range 40−60°C): colourless needles (1.02 g, 82%), m.p. 84.5−85°C. − $[\alpha]_D^{25}$ = +73 (*c* = 1, EtOH). − IR (KBr): $\tilde{\nu}$ = 1639 cm^{-1} (C=N). − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.68 (d, ^4J_P = 4.0 Hz, 1 H, azomethine), 7.80 (ddd, ^4J = 1.5 Hz, ^4J_P = 3.8 Hz, ^3J = 7.7 Hz, 1 H, Ar−H^3), 7.41 (pseudo dt, ^4J = 1.2 Hz, ^3J = 7.6 Hz, 1 H, Ar−H^4 or Ar−H^5), 7.35−7.20 (m, 11 H, Ar−H), 6.88 (ddd, ^4J = 1.2 Hz, ^3J_P = 4.5 Hz, ^3J = 7.6 Hz, 1 H, Ar−H^6), 3.52 (d, ^3J = 5.4 Hz, 2 H, NCH−C*H*$_2$−OH), 3.09 (ddt, ^3J = 4.8 Hz, ^3J = 8.5 Hz, ^3J = 5.4 Hz, 1 H, CHH′−NC*H*−CH$_2$), 1.82 (s br, 1 H, O*H*), 1.42 (dqd, ^3J = 4.8 Hz, ^3J = 7.4 Hz, ^2J = 13.7 Hz, 1 H, NCH−C*H*H′−CH$_3$), 1.30 (qdd, ^3J = 7.4 Hz, ^3J = 8.5 Hz, ^2J = 13.7 Hz, 1 H, NCH−CH*H*′−CH$_3$), 0.62 (pseudo t, ^3J = 7.4 Hz, 3 H, CHH′−C*H*$_3$). − ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ = −9.69 (s). − $C_{23}H_{24}NOP$ (361.42): calcd. C 76.44, H 6.69, N 3.87; found C 76.15, H 6.76, N 3.95.

(−)-2-[N-(S)-1′-Hydroxybut-2′-ylcarbaldimino]phenyl(diphenyl)phosphane (**2b**): Variant A with 3.45 mmol (307 mg, 325 µl) of (*S*)-(+)-2-amino-1-butanol. Recrystallisation analogous to **2a** (946 mg, 76%), m.p. 84.5−85°C. − $[\alpha]_D^{25}$ = −73 (*c* = 1, EtOH). − IR, ^{1}H NMR, ^{31}P{^{1}H} NMR analogous to **2a**. − $C_{23}H_{24}NOP$ (361.42): calcd. C 76.44, H 6.69, N 3.87; found C 76.19, H 6.84, N 3.91.

(−)-2-[N-(S)-1′-Hydroxyprop-2′-ylcarbaldimino]phenyl(diphenyl)phosphane (**3**): Variant A with 3.45 mmol (259 mg) of (*S*)-(+)-2-amino-1-propanol (L-alaninol). Recrystallisation from 50 ml of petroleum ether (boiling range 40−60°C): colourless crystals (995 mg, 83%), m.p. 62−63°C. − $[\alpha]_D^{25}$ = −19 (*c* = 1, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 1646 cm^{-1} (C=N). − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.72 (d, ^4J_P = 4.0 Hz, 1 H, azomethine), 7.80 (ddd, ^4J = 1.5 Hz, ^4J_P = 3.8 Hz, ^3J = 7.6 Hz, 1 H, Ar−H^3), 7.40 (pseudo dt, ^4J = 1.3 Hz, ^3J = 7.5 Hz, 1 H, Ar−H), 7.35−7.21 (m, 11 H, Ar−H), 6.89 (ddd, ^4J = 1.2 Hz, ^3J_P = 4.5 Hz, ^3J = 7.7 Hz, 1 H, Ar−H^6), 3.51−3.34 (m, 3 H, NC*H*−C*HH*′−OH), 1.89 (s br, 1 H, OH), 0.96 (d, ^3J = 6.3 Hz, 3 H, NCH−C*H*$_3$). − ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ = −9.86 (s). − MS (FD, CH_2Cl_2); *m*/*z* (%): 347.0 (100) [M$^+$]. − $C_{22}H_{22}NOP$ (347.40): calcd. C 76.06, H 6.38, N 4.03; found C 75.74, H 6.28, N 3.98.

(−)-2-[N-(S)-1′-Hydroxy-3′-methylbut-2′-ylcarbaldimino]phenyl(diphenyl)phosphane (**4**): Variant A with 3.45 mmol (356 mg) of (*S*)-(+)-2-amino-3-methyl-1-butanol (L-valinol). Recrystallisation from 50 ml of petroleum ether (boiling range 40−60°C): colourless crystals (795 mg, 61%), m.p. 51−53°C. − $[\alpha]_D^{25}$ = −68 (*c* = 1, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 1643 cm^{-1} (C=N). − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.61 (d, ^4J_P = 3.8 Hz, 1 H, azomethine), 7.78 (ddd, ^4J = 1.5 Hz, ^4J_P = 3.8 Hz, ^3J = 7.6 Hz, 1 H, Ar−H^3), 7.42 (pseudo dt, ^4J = 1.2 Hz, ^3J = 7.5 Hz, 1 H, Ar−H), 7.35−7.20 (m, 11 H, Ar−H), 6.89 (ddd, ^4J = 1.2 Hz, ^3J_P = 4.4 Hz, ^3J = 7.7 Hz, 1 H, Ar−H^6), 3.60 (ddd, ^3J = 5.7 Hz, ^3J = 7.4 Hz, ^2J = 11.1 Hz, 1 H, NCH−C*H*H′−OH), 3.54 (ddd, ^3J = 3.4 Hz, ^3J = 8.2 Hz, ^2J = 11.1 Hz, 1 H, NCH−CH*H*′−OH), 2.87 (pseudo dt, ^3J = 3.4 Hz, ^3J = 7.2 Hz, 1 H, CHH′−NC*H*−CH), 1.80 (ddd, J_P = 3.3 Hz, ^3J = 5.7 Hz, ^3J = 8.2 Hz, 1 H, CHH′−O*H*), 1.68 (pseudo oct., ^3J = 6.8 Hz, 1 H, CH$_3$−C*H*−CH$_3$′), 0.81 (d, ^3J = 6.8 Hz, 3 H, CH−C*H*$_3$), 0.58 (d, ^3J = 6.8 Hz, 3 H, CH−C*H*$_3$′). − ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ = −9.33 (s). − MS (FD, CH_2Cl_2); *m*/*z* (%): 375.1 (100) [M$^+$]. − $C_{24}H_{26}NOP$ (375.45): calcd. C 76.78, H 6.98, N 3.73; found C 76.47, H 6.99, N 3.77.

(−)-2-[N-(S)-1′-Hydroxy-4′-methylpent-2′-ylcarbaldimino]phenyl(diphenyl)phosphane (**5**): Variant A with 3.45 mmol (404 mg) of (*S*)-(+)-2-amino-4-methyl-1-pentanol (L-leucinol). Recrystallisation analogous to **4**: colourless needles (962 mg, 72%), m.p. 68−69°C. − $[\alpha]_D^{25}$ = −81 (*c* = 1, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 1637 cm^{-1} (C=N). − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.71 (d, ^4J_P = 4.3 Hz, 1 H, azomethine), 7.81 (ddd, ^4J = 1.3 Hz, ^4J_P = 3.8 Hz, ^3J = 7.6 Hz, 1 H, Ar−H^3), 7.41 (pseudo dt, ^4J = 1.2 Hz, ^3J = 7.5 Hz, 1 H, Ar−H), 7.35−7.20 (m, 11 H, Ar−H), 6.87 (ddd, ^4J = 1.1 Hz, ^3J_P = 4.5 Hz, ^3J = 7.6 Hz, 1 H, Ar−H^6), 3.50 (m, 2 H, NCH−C*H*$_2$−OH), 3.31 (ddt, ^3J = 3.9 Hz, ^3J = 9.4 Hz, ^3J = 5.4 Hz, 1 H, CH$_2$−NC*H*−CH$_2$), 1.85 (s br, 1 H, OH), 1.30 (ddd, ^3J = 4.1 Hz, ^3J = 9.4 Hz, ^2J = 12.8 Hz, 1 H, NCH−C*H*H′−CH), 1.21−1.09 [m, 1 H, CHH′−C*H*(CH$_3$)$_2$], 1.08 (ddd, ^3J = 3.9 Hz, ^3J = 9.1 Hz, ^2J = 12.8 Hz, 1 H, NCH−CH*H*′−CH), 0.72 (pseudo t, ^3J = 6.6 Hz, 6 H, *H*$_3$C−CH−C*H*$_3$′). − ^{31}P{^{1}H} NMR ($CDCl_3$, 162 MHz): δ = −10.05 (s). − MS (FD, CH_2Cl_2); *m*/*z* (%): 389.1

(100) [M$^+$]. − $C_{25}H_{28}NOP$ (389.48): calcd. C 77.10, H 7.25, N 3.60; found C 77.02, H 7.27, N 3.55.

(−)-2-[N-(S)-1′-Hydroxy-(3′S)-methylpent-2′-ylcarbaldimino]phenyl(diphenyl)phosphane (**6**): Variant A with 3.45 mmol (404 mg) of (2*S*,3*S*)-(+)-2-amino-3-methyl-1-pentanol (L-isoleucinol). Recrystallisation analogous to **4**: colourless crystals at −20°C, which form a highly viscous oil at room temp. (798 mg, 59%). − $[\alpha]_D^{25}$ = −72 (*c* = 1, CH_2Cl_2). − IR (film): $\tilde{\nu}$ = 1648 cm^{-1} (C=N). − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.61 (d, ^4J_P = 4.0 Hz, 1 H, azomethine), 7.78 (ddd, ^4J = 1.5 Hz, ^4J_P = 3.8 Hz, ^3J = 7.6 Hz, 1 H, Ar−H^3), 7.42 (pseudo dt, ^4J = 1.2 Hz, ^3J = 7.5 Hz, 1 H, Ar−H), 7.35−7.20 (m, 11 H, Ar−H), 6.89 (ddd, ^4J = 1.2 Hz, ^3J_P = 4.4 Hz, ^3J = 7.7 Hz, 1 H, Ar−H^6), 3.63 (dd, ^3J = 7.3 Hz, ^2J = 11.2 Hz, 1 H, NCH−C*H*H′−OH), 3.54 (dd, ^3J = 3.4 Hz, ^2J = 11.2 Hz, 1 H, NCH−CH*H*′−OH), 2.97 (pseudo dt, ^3J = 3.4 Hz, ^3J = 7.3 Hz, 1 H, CHH′−NC*H*−CH), 1.90 (s br, 1 H, OH), 1.50−1.39 (m, 1 H, CH−C*H*H′−CH_3), 1.10 (dqd, ^3J = 3.8 Hz, ^3J = 7.3 Hz, ^2J = 13.2 Hz, 1 H, CH−CH*H*′−CH_3), 0.83−0.71 (m, 1 H, H_3C−C*H*−CHH′), 0.77 (d, ^3J = 6.9 Hz, 3 H, *H*$_3$C−CH), 0.67 (pseudo t, ^3J = 7.3 Hz, 3 H, CHH′−C*H*$_3$). − $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz): δ = −9.36 (s). − MS (FD, CH_2Cl_2); *m/z* (%): 389.2 (100) [M$^+$]. − $C_{25}H_{28}NOP$ (389.48): calcd. C 77.10, H 7.25, N 3.60; found C 76.88, H 7.48, N 3.75.

(−)-2-[N-(S)-1′-Hydroxy-3′,3′-dimethylbut-2′-ylcarbaldimino]phenyl(diphenyl)phosphane (**7**): Variant A with 3.45 mmol (404 mg) of (*S*)-(+)-2-amino-3,3-dimethyl-1-butanol (L-*tert*-leucinol). Recrystallisation analogous to **4**: colourless needles (969 mg, 72%), m.p. 85−86°C. − $[\alpha]_D^{25}$ = −66 (*c* = 1, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 1648 cm^{-1} (C=N). − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.59 (d, ^4J_P = 3.8 Hz, 1 H, azomethine), 7.78 (ddd, ^4J = 1.4 Hz, ^4J_P = 3.8 Hz, ^3J = 7.7 Hz, 1 H, Ar−H^3), 7.42 (pseudo dt, ^4J = 1.2 Hz, ^3J = 7.5 Hz, 1 H, Ar−H), 7.35−7.20 (m, 11 H, Ar−H), 6.89 (ddd, ^4J = 1.1 Hz, ^3J_P = 4.3 Hz, ^3J = 7.7 Hz, 1 H, Ar−H^6), 3.64 (ddd, ^3J = 3.2 Hz, ^3J = 10.4 Hz, ^2J = 11.0 Hz, 1 H, NCH−C*H*H′−OH), 3.54 (ddd, ^3J = 3.9 Hz, ^3J = 9.2 Hz, ^2J = 11.0 Hz, 1 H, NCH−CH*H*′−OH), 2.86 (ddd, ^6J_P = 0.8 Hz, ^3J = 3.2 Hz, ^3J = 9.2 Hz, 1 H, NC*H*−CHH′), 1.46 (pseudo td, J_P = 3.9 Hz, ^3J = 3.9 Hz, ^3J = 10.4 Hz, 1 H, CHH′−O*H*), 0.74 [s, 9 H, C(C*H*$_3$)$_3$]. − $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz): δ = −9.59 (s). − MS (FD, CH_2Cl_2); *m/z* (%): 389.1 (100) [M$^+$]. − $C_{25}H_{28}NOP$ (389.48): calcd. C 77.10, H 7.25, N 3.60; found C 77.12, H 7.25, N 3.52.

(+)-2-[N-(R)-1′-Hydroxy-2′-phenyleth-2′-ylcarbaldimino]phenyl(diphenyl)phosphane (**8**): Variant A with 3.45 mmol (473 mg) of (*R*)-(−)-2-amino-2-phenyl-1-ethanol (D-α-phenylglycinol). Recrystallisation analogous to **4**: yellowish solid (884 mg, 63%), m.p. 47−49°C. − $[\alpha]_D^{25}$ = +141 (*c* = 1, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 1649 cm^{-1} (C=N). − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.65 (d, ^4J_P = 3.5 Hz, 1 H, azomethine), 7.71 (ddd, ^4J = 1.3 Hz, ^4J_P = 3.8 Hz, ^3J = 7.6 Hz, 1 H, Ar−H^3), 7.41 (pseudo dt, ^4J = 1.2 Hz, ^3J = 7.5 Hz, 1 H, Ar−H), 7.38−7.23 (m, 11 H, Ar−H), 7.19−7.15 (m, 3 H, Ar−H), 6.96−6.92 (m, 3 H, Ar−H), 4.41 (dd, ^3J = 5.2 Hz, ^3J = 7.4 Hz, 1 H, NC*H*−CHH′), 3.70−3.62 (m, 2 H, NCH−C*HH*′−OH), 2.46 (s br, 1 H, OH). − $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz): δ = −8.37 (s). − MS (FD, CH_2Cl_2); *m/z* (%): 409.2 (100) [M$^+$]. − $C_{27}H_{24}NOP$ (409.47): calcd. C 79.20, H 5.91, N 3.42; found C 78.98, H 5.96, N 3.19.

(−)-2-[N-(S)-1′-Hydroxy-3′-phenylprop-2′-ylcarbaldimino]phenyl(diphenyl)phosphane (**9**): Variant B with 3.45 mmol (522 mg) of (*S*)-(−)-2-amino-3-phenyl-1-propanol (L-phenylalaninol). Recrystallisation from 90 ml of pentane: yellowish solid (1.01 g, 69%), m.p. 42−43°C. − $[\alpha]_D^{25}$ = −167 (*c* = 1, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 1652, 1641 cm^{-1} (C=N). − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.29 (d, ^4J_P = 3.8 Hz, 1 H, azomethine), 7.59 (ddd, ^4J = 1.4 Hz, ^4J_P = 3.8 Hz, ^3J = 7.6 Hz, 1 H, Ar−H^3), 7.38 (pseudo dt, ^4J = 1.3 Hz, ^3J = 7.5 Hz, 1 H, Ar−H), 7.35−7.10 (m, 14 H, Ar−H), 6.95−6.92 (m, 2 H, Ar−H), 6.89 (ddd, ^4J = 1.2 Hz, ^3J_P = 4.3 Hz, ^3J = 7.7 Hz, 1 H, Ar−H^6), 3.61−3.51 (m, 2 H, NCH−CH_2−OH), 3.45−3.37 (m, 1 H, CH_2−NC*H*−CHH′), 2.71 (dd, ^3J = 5.3 Hz, ^2J = 13.4 Hz, 1 H, NCH−C*H*H′−Ph), 2.48 (dd, ^3J = 8.3 Hz, ^2J = 13.4 Hz, 1 H, NCH−CH*H*′−Ph), 2.12 (s br, 1 H, OH). − $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz): δ = −9.14 (s). − MS (FD, CH_2Cl_2); *m/z* (%): 423.2 (100) [M$^+$]. − $C_{28}H_{26}NOP$ (423.49): calcd. C 79.41, H 6.19, N 3.31; found C 79.12, H 6.37, N 3.32.

(+)-2-[N-(1′R,2′S)-1′-Hydroxy-1′-phenylprop-2′-ylcarbaldimino]phenyl(diphenyl)phosphane (**10**): Variant B with 3.45 mmol (522 mg) of (1*R*,2*S*)-(−)-2-amino-1-phenyl-1-propanol (L-norephedrine). Recrystallisation from 18 ml of petroleum ether (boiling range 40−60°C)/THF (5:1): colourless crystals (918 mg, 63%), m.p. 74.5−75°C. − $[\alpha]_D^{25}$ = +8, $[\alpha]_D^{25}$ = +50 (*c* = 1, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 1649 cm^{-1} (C=N). − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.72 (d, ^4J_P = 4.0 Hz, 1 H, azomethine), 7.82 (ddd, ^4J = 1.3 Hz, ^4J_P = 3.8 Hz, ^3J = 7.6 Hz, 1 H, Ar−H^3), 7.41 (pseudo dt, ^4J = 1.2 Hz, ^3J = 7.5 Hz, 1 H, Ar−H), 7.37−7.19 (m, 16 H, Ar−H), 6.89 (ddd, ^4J = 1.1 Hz, ^3J_P = 4.6 Hz, ^3J = 7.8 Hz, 1 H, Ar−H^6), 4.63 (d, ^3J = 3.6 Hz, 1 H, NCH−*H*COH−Ph), 3.49 (dq, ^3J = 3.6 Hz, ^3J = 6.5 Hz, 1 H, H_3C−NC*H*−HCOH), 3.15 (s br, 1 H, OH), 0.77 (d, ^3J = 6.5 Hz, 3 H, *H*$_3$C−NCH). − $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz): δ = −9.80 (s). − MS (FD, CH_2Cl_2); *m/z* (%): 423.1 (100) [M$^+$]. − $C_{28}H_{26}NOP$ (423.49) · 0.5 THF: calcd. C 78.41, H 6.58, N 3.05; found C 78.16, H 6.73, N 3.30.

(+)-2-[N-(1′S,2′S)-1′,3′-Dihydroxy-1′-phenylprop-2′-ylcarbaldimino]phenyl(diphenyl)phosphane (**11**): Variant A with 3.45 mmol (577 mg) of (1*S*,2*S*)-(+)-2-amino-1-phenyl-1,3-propanediol. Recrystallisation from 150 ml of petroleum ether (boiling range 40−60°C): microcrystalline colourless solid (1.24 g, 82%), m.p. 64−66°C. − $[\alpha]_D^{25}$ = +88 (*c* = 1, EtOH). − IR (KBr): $\tilde{\nu}$ = 1650 cm^{-1} (C=N). − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.30 (d, ^4J_P = 3.2 Hz, 1 H, azomethine), 7.60 (ddd, ^4J = 1.4 Hz, ^4J_P = 3.8 Hz, ^3J = 7.6 Hz, 1 H, Ar−H^3), 7.43 (pseudo dt, ^4J = 1.2 Hz, ^3J = 7.5 Hz, 1 H, Ar−H), 7.38−7.19 (m, 16 H, Ar−H), 6.93 (ddd, ^4J = 1.2 Hz, ^3J_P = 4.5 Hz, ^3J = 7.7 Hz, 1 H, Ar−H^6), 4.66 (d, ^3J = 5.3 Hz, 1 H, NCH−*H*COH−Ph), 3.61−3.34 (m, 3 H, NC*H*−CH_2−OH), 2.76 (s br, 1 H, OH), 1.70 (s br, 1 H, OH). − $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz): δ = −5.69 (s). − $C_{28}H_{26}NO_2P$ (439.49): calcd. C 76.52, H 5.96, N 3.19; found C 75.70, H 5.96, N 3.38.

(−)-2-[N-(S)-3′,3′-Dimethyl-tert-butyloxy-2′-butyrylcarbaldimino]phenyl(diphenyl)phosphane (**12**): Variant B with 4.14 mmol (775 mg) of (*S*)-(+)-2-amino-3,3-dimethyl-*tert*-butyloxybutyric acid (L-*tert*-butyl *tert*-leucinate). Recrystallisation analogous to **4**: yellowish crystals (1.37 g, 86%), m.p. 94−95°C. − $[\alpha]_D^{25}$ = −99 (*c* = 1, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 1742 cm^{-1} (C=O), 1643 (C=N). − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.88 (pseudo qd, *J* = 0.6 Hz, ^4J_P = 5.4 Hz, 1 H, azomethine), 8.18 (ddd, ^4J = 1.4 Hz, ^4J_P = 4.0 Hz, ^3J = 7.8 Hz, 1 H, Ar−H^3), 7.38 (pseudo ddt, *J* = 0.6 Hz, ^4J = 1.3 Hz, ^3J = 7.5 Hz, 1 H, Ar−H), 7.36−7.23 (m, 11 H, Ar−H), 6.85 (dddd, *J* = 0.6 Hz, ^4J = 1.3 Hz, ^3J_P = 4.7 Hz, ^3J = 7.7 Hz, 1 H, Ar−H^6), 3.43 [d, *J* = 0.6 Hz, 1 H, OOC−NC*H*−C(CH$_3$)$_3$], 1.40 [s, 9 H, COOC(C*H*$_3$)$_3$], 0.87 [s, 9 H, NCH−C(C*H*$_3$)$_3$]. − $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz): δ = −14.11 (s). − MS (FD, CH_2Cl_2); *m/z* (%): 459.2 (100) [M$^+$]. − $C_{29}H_{34}NO_2P$ (459.60): calcd. C 75.79, H 7.46, N 3.05; found C 75.79, H 7.32, N 3.03.

(+)-2-[N-(1′R,11′R,12′S)-Dehydroabietylcarbaldimino]phenyl(diphenyl)phosphane (**13**): Variant B with 4.14 mmol (1.18 g)

of (+)-dehydroabietylamine. Recrystallisation from 50 ml of ethanol/methanol (3:2): colourless crystals (1.36 g, 71%), m.p. 74−75°C. − $[\alpha]_D^{25}$ = +13 (*c* = 1, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 1638 cm^{-1} (C=N). − ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.87 (d, ^4J_P = 5.1 Hz, 1 H, azomethine), 7.99 (ddd, ^4J = 1.1 Hz, ^4J_P = 3.9 Hz, ^3J = 7.7 Hz, 1 H, Ar−H^3), 7.37−7.20 (m, 12 H, Ar−H), 7.15 (d, ^3J = 8.2 Hz, 1 H, Ar−H), 6.97 (dd, ^4J = 1.7 Hz, ^3J = 8.2 Hz, 1 H, Ar−H), 6.85−6.82 (m, 2 H, Ar−H), 3.38 (d, ^2J = 11.9 Hz, 1 H, N−C*H*H′), 3.26 (dd, *J* = 1.0 Hz, ^2J = 11.9 Hz, 1 H, N−CH*H*′), 2.81 (sept., ^3J = 6.9 Hz, 1 H, $H_3C-CH-CH_3$), 2.77−2.62 (m, 2 H, Ar−CH_2−CH_2), 2.18 (d, $^3J_{axial}$ = 12.8 Hz, 1 H, C_3C-H), 1.83−1.15 (m, 8 H, 4 CH_2), 1.22 (d, ^3J = 6.9 Hz, 6 H, $H_3C-CH-CH_3$), 1.18 (s, 3 H, C_3C-CH_3), 0.92 (s, 3 H, C_3C-CH_3). − $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz): δ = −13.82 (s). − MS (EI, 70 eV); *m/z* (%): 557.3 (29) [M^+], 542.2 (24) [$M^+ - CH_3$], 303.2 (100) [$Ph_2P(C_6H_4)CHNHCH_2^+$], 302.1 (75) [$Ph_2P(C_6H_4)CHNCH_2^+$], 288.1 (64) [$Ph_2P(C_6H_4)CHN^+$]. − $C_{39}H_{44}NP$ (557.76): calcd. C 83.98, H 7.95, N 2.51; found C 83.62, H 7.99, N 2.58.

Synthesis of the Phosphane amines **14a** *and* **14b**: 750 mg (2.08 mmol) of **2a** (or **2b**) was dissolved in 30 ml of methanol at −10°C followed by the addition of 100 mg (2.64 mmol) of $NaBH_4$. The solution was allowed to come to room temp. within 4 h and heated for 2 h at 50°C. After removal of the methanol, 25 ml of water and 120 ml of dichloromethane were added to the residue. The dichloromethane layer was extracted twice with 25 ml of water and dried with Na_2SO_4. After filtration the dichloromethane was removed and the resulting oil was recrystallized with 20 ml of petroleum ether (boiling range 40−60°C) to give colourless crystals at −20°C. At room temp. the crystals of **14a** (or **14b**) became a highly viscous oil. Yield: 665 mg (88%).

(+)-N-[2-(Diphenylphosphanyl)benzyl]-N-[(R)-1′-hydroxybut-2′-yl]amine (**14a**): $[\alpha]_D^{25}$ = +11, $[\alpha]_{365}^{25}$ = +75 (*c* = 1, CH_2Cl_2). − ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.41 (ddd, ^4J = 1.2 Hz, ^4J_P = 4.5 Hz, ^3J = 7.6 Hz, 1 H, Ar−H^3), 7.36−7.23 (m, 11 H, Ar−H), 7.18 (pseudo dt, ^4J = 1.2 Hz, ^3J = 7.6 Hz, 1 H, Ar−H), 6.92 (ddd, ^4J = 1.2 Hz, ^3J_P = 4.5 Hz, ^3J = 7.6 Hz, 1 H, Ar−H^6), 4.10 (s very br, 2 H, OH and NH), 3.98 (dd, ^4J_P = 1.6 Hz, ^2J = 12.6 Hz, 1 H, Ar−C*H*H′−NH), 3.95 (dd, ^4J_P = 1.2 Hz, ^2J = 12.6 Hz, 1 H, Ar−CH*H*′−NH), 3.60 (dd, ^3J = 3.8 Hz, ^2J = 10.9 Hz, 1 H, NCH−C*H*H′−OH), 3.24 (dd, ^3J = 5.9 Hz, ^2J = 10.9 Hz, 1 H, NCH−CH*H*′−OH), 2.51 (pseudo dq, ^3J = 3.8 Hz, ^3J = 6.3 Hz, 1 H, CHH′−NC*H*−CH_2), 1.36−1.27 (m, 2 H, NCH−CH_2−CH_3), 0.82 (t, ^3J = 7.4 Hz, 3 H, CH_2-CH_3). − $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz): δ = −15.44 (s). − MS (FD, CH_2Cl_2); *m/z* (%): 363.1 (100) [M^+]. − $C_{23}H_{26}NOP$ (363.44): calcd. C 76.01, H 7.21, N 3.85; found C 74.70, H 7.10, N 3.82.

(−)-N-[2-(Diphenylphosphanyl)benzyl]-N-[(S)-1′-hydroxybut-2′-yl]amine (**14b**): $[\alpha]_D^{25}$ = −11, $[\alpha]_{365}^{25}$ = −75 (*c* = 1, CH_2Cl_2). − ^1H NMR, $^{31}P\{^1H\}$ NMR and MS analogous to **14a**. − $C_{23}H_{26}NOP$ (363.44): calcd. C 76.01, H 7.21, N 3.85; found C 75.72, H 7.28, N 3.82.

Synthesis of the Phosphane trisimines **15a** *and* **15b**: 3.79 ml (40.4 mmol, 3.60 g) of (*R*)-(−)-2-amino-1-butanol [or (*S*)-(+)-2-amino-1-butanol] was dissolved in 10 ml of dichloromethane and 1 g (7 mmol) of Na_2SO_4 was added. A solution of 0.70 g (2.0 mmol) of tris(2-formylphenyl)phosphane[40][41][42] in 10 ml of dichloromethane was added dropwise during 15 min. After 16 h reflux the yellow solution was filtered and the dichloromethane was evaporated. The excess amine was removed by heating under high vacuum at 100°C for 6 h. The resulting yellow oil was dissolved in 50 ml of dichloromethane, stirred for 15 min and filtered. The clear solution was evaporated to dryness. Recrystallisation from 90 ml of petroleum ether (boiling range 40−60°C) afforded yellow crystals of **15a** (or **15b**). Yield 0.90 g (80%).

(+)-Tris[2-(N-(R)-1′-hydroxybut-2′-ylcarbaldimino)-phenyl]phosphane (**15a**): M.p. 106.5−107°C. − $[\alpha]_D^{25}$ = +105 (*c* = 1, EtOH). − IR (KBr): $\tilde{\nu}$ = 1647 cm^{-1} (C=N). − ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.45 (d, ^4J_P = 2.0 Hz, 3 H, azomethine), 7.65−7.59 (m, 3 H, Ar−H^3), 7.38 (pseudo dt, ^4J = 1.2 Hz, ^3J = 7.5 Hz, 3 H, Ar−H), 7.16 (pseudo t, ^3J = 7.4 Hz, 3 H, Ar−H), 6.92 (ddd, ^4J = 1.2 Hz, ^3J_P = 3.8 Hz, ^3J = 7.7 Hz, 3 H, Ar−H^6), 3.76 (s br, 3 H, OH), 3.51−3.37 (m, 6 H, NCH−C*H*H′−OH), 3.02−2.94 (m, 3 H, CHH′−NC*H*−CHH′), 1.25−1.10 (m, 3 H, NCH−C*H*H′−CH_3), 0.92−0.78 (m, 3 H, NCH−CH*H*′−CH_3), 0.41 (pseudo t, ^3J = 7.3 Hz, 9 H, CHH′−CH_3). − $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz): δ = −10.12 (s). − MS (EI, 70 eV); *m/z* (%): 559.2 (100) [M^+], 486.3 (95) [$M^+ - C_4H_8OH$], 470.3 (39), 459.3 (15) [$M^+ - CHNC_4H_8OH$]. − $C_{33}H_{42}N_3O_3P$ (559.69): calcd. C 70.82, H 7.56, N 7.51; found C 70.38, H 7.64, N 7.45.

(−)-Tris[2-(N-(S)-1′-hydroxybut-2′-ylcarbaldimino)-phenyl]phosphane (**15b**): M.p. 106.5−107°C. − $[\alpha]_D^{25}$ = −105 (*c* = 1, EtOH). − IR, ^1H NMR, $^{31}P\{^1H\}$ NMR and MS analogous to **15a**. − $C_{33}H_{42}N_3O_3P$ (559.69): calcd. C 70.82, H 7.56, N 7.51; found C 70.68, H 7.55, N 7.53.

X-ray Structure Analysis of **15b**: $C_{33}H_{42}N_3O_3P$ (559.69); crystal dimensions 0.30 × 0.45 × 0.50 mm; two independent molecules in the unit cell; crystal system triclinic; space group *C*1/1, *P*1, (1); unit cell dimensions *a* = 10.068(6), *b* = 11.611(7), *c* = 15.125(9) Å, α = 88.08(5), β = 73.55(5), γ = 70.35(5)°, *V* = 1593.3 Å^3; *Z* = 2; density $d_{calcd.}$ = 1.17g/cm^3; μ(Mo-K_α) = 0.12 mm^{-1}; 3.0° < 2θ < 50.5°; total no. of reflections 8224, unique reflections 7653, unique reflections with $I > 2.5\sigma(I)$ 6037; *F*(000) = 600; diffractometer AED II; temp. −70°C. The structure was solved by direct methods using the SHELXTL PLUS version 4.2/800 program system. Hydrogen atoms were calculated by the HFIX program; R = 0.044; R_w = 0.033; residual electron density max. 0.36 e/Å^3, min. −0.39 e/Å^3. Further details of the crystal structure investigation may be obtained from the Fachinformationszentrum Karlsruhe, D-76344 Eggenstein-Leopoldshafen (Germany), on quoting the depository number CSD-407358.

1,5-Dimethylbarbituric Acid (**BS**): Handling of **BS** has been described in the literature[57][58][59][60], but a synthesis and characterisation was not given. 16.6 g (0.722 mol) of sodium was dissolved under reflux in 230 ml of absolute ethanol under a nitrogen atmosphere. After cooling to about 60°C, 25.9 g (0.350 mol) of *N*-methylurea and 20 ml of ethanol and, after 15 min, 59.8 ml (0.350 mol, 61.0 g) of methylmalonic acid diethyl ester were added (colourless precipitate). After 2 h reflux the solvent was removed. The dry residue was dissolved in 400 ml of hot water and, with vigorous stirring, 100 ml of conc. hydrochloric acid was added. After cooling to room temp. the precipitated product was filtered off and washed with 400 ml of cooled diethyl ether. Recrystallisation from 600 ml of absolute ethanol/methanol (3:1) provided colourless crystals, which were washed with petroleum ether (boiling range 40−60°C) and dried under high vacuum at 60°C for several days. Yield 34.7 g (63%), m.p. 170−171°C. − IR (KBr): $\tilde{\nu}$ = 1703 cm^{-1} (C=O). − ^1H NMR ([D$_6$]DMSO, 250 MHz): δ = 11.27 (s, 1 H, NH), 3.72 (q, ^3J = 6.9 Hz, 1 H, *H*CCH$_3$), 3.06 (s, 3 H, N−CH$_3$), 1.34 (d, ^3J = 6.9 Hz, 3 H, HCC*H*$_3$). − $C_6H_8N_2O_3$ (156.14): calcd. C 46.15, H 5.16, N 17.94; found C 46.21, H 5.18, N 17.90.

Enantioselective Palladium-Catalysed Allylation of 1,5-Dimethylbarbituric Acid (**BS**) *with Allyl Acetate:*150 mg (0.961 mmol) of **BS** and 1.01 mmol of base were dissolved in 10 ml of dichlorometh-

ane at 38°C under a nitrogen atmosphere. The following bases were used: DBU (150 µl, 153 mg), triethylamine (140 µl, 102 mg), BSA (247 µl, 205 mg), 1.5 M LDA·THF solution in cyclohexane (673 µl), NBu_4OH solution in methanol (12.5%) (2.59 ml, 2.10 g), (−)-quinine (328 mg), (+)-quinidine (328 mg), (−)-cinchonidine (297 mg) and (+)-cinchonine (297 mg). **BS** and base can be replaced by 382 mg (0.961 mmol) of **NBu_4BS**. After 5 min stirring 2.93 mg (0.0096 mmol) of palladium(II) acetylacetonate, 0.0384 mmol of a monodentate ligand or 0.0192 mmol of a bidentate ligand and 10 ml of a 1:1 mixture of methylene choride/toluene were added to the clear solution. After 2.0 min the reaction was started by the addition of 115 µl (1.07 mmol, 107 mg) of allyl acetate. The solution was stirred for 24, 48 or 72 h at 38°C. For work-up the solution was diluted with 10 ml of dichloromethane and extracted successively with 10 ml and 5 ml of 0.2 M hydrochloric acid and three times with 5 ml of water. The organic layer was dried with Na_2SO_4. The solid was filtered off and washed with 10 ml of dichloromethane. Removal of the solvent from the filtrate left the dry product ready for GC analysis. To the product was added about 25 mg of benzil (GC standard) and 6 ml of dichloromethane. This solution was used to determine the enantiomeric excess of **ABS** and the yield of **ABS** and **AABS** by GC on a Chirasil-Val-L column. Furthermore, a chromatographic analysis of 3 ml of the solution on alumina was carried out in a Pasteur pipette, in which only **AABS** and benzil eluted. The eluate was used for the determination of the enantiomeric excess of **AABS** on a Lipodex E column.

Conditions: 25 m *Chirasil-Val-L* fused silica capillary column (0.25 mm inner diameter, 0.12 µm film thickness, from Chrompack), column temp. 130°C, He pressure 1.2 bar, injector temp. 250°C, detector temp. 230°C [flame ionisation], retention times: (±)-**AABS** 4.24 min, standard benzil 17.10 min, (−)-**ABS** 19.09 min, (+)-**ABS** 20.33 min, separation factor $\alpha_{[(+)\text{-ABS}/(-)\text{-ABS}]} = 1.07$, resolution $R_{[(+)\text{-ABS}/(-)\text{-ABS}]} = 1.80$, mass correlation factors: $f_{\text{benzil/ABS}} = 1.77$ and $f_{\text{benzil/AABS}} = 1.50$; retention times for the enantiomers of 5-chloromethyl-1,5-dimethylbarbituric acid were 34.74 and 35.32 min, respectively. − 50 m *Lipodex E* fused silica capillary column (0.25 mm inner diameter, coated with octakis(2,6-di-*O*-pentyl-3-*O*-butyryl)-γ-cyclodextrine, from Macherey-Nagel), column temp. 110°C (after 45 min the column temp. was raised by 12°C/min to 170°C), H_2 pressure 2.07 bar, injector temp. 250°C, detector temp. 240°C (flame ionisation), retention times: (1.)-**AABS** 42.45 min, (2.)-**AABS** 43.84 min, standard benzil 65.0 min, separation factor $\alpha_{[(2.)\text{-AABS}/(1.)\text{-AABS}]} = 1.03$, resolution $R_{[(2.)\text{-AABS}/(1.)\text{-AABS}]} = 1.74$.

5-Allyl-1,5-dimethylbarbituric Acid (**ABS**): Main product of catalysis under standard reaction conditions. Maximum yield 184 mg (98%) (Table 1, entry 3). Recrystallisation from water/ethanol 175:1 provided colourless crystals, m.p. 131−131.5°C. − IR (KBr): $\tilde{\nu}$ = 1758, 1716, 1680 cm^{-1} (C=O). − ^1H NMR ($CDCl_3$, 400 MHz): δ = 9.03 (s, 1 H, NH), 5.60 (tdd, ^3J = 7.5 Hz, $^3J_{cis}$ = 10.1 Hz, $^3J_{trans}$ = 17.0 Hz, 1 H, $CH_2-CH{=}CHH$), 5.14 (md, $^3J_{trans}$ = 17.0 Hz, 1 H, $CH_2-CH{=}CHH_{trans}$), 5.11 (md, $^3J_{cis}$ = 10.1 Hz, 1 H, $CH_2-CH{=}CH_{cis}H$), 3.28 (s, 3 H, $N-CH_3$), 2.71 (d, ^3J = 7.5 Hz, 2 H, $CH_2-CH{=}CHH$), 1.57 (s, 3 H, $C-CH_3$). − GC-MS (EI, 70 eV); *m/z* (%): 195.9 (6) [M^+], 180.9 (100) [$M^+ - CH_3$], 41.0 (32) [$C_3H_5^+$]. − $C_9H_{12}N_2O_3$ (196.21): calcd. C 55.09, H 6.16, N 14.28; found C 55.09, H 6.23, N 14.09.

3,5-Diallyl-1,5-dimethylbarbituric Acid (**AABS**): By-product of catalysis under standard reaction conditions (yield 0−19%). To produce **AABS**, the standard catalysis was carried out with a 3-fold excess of the base DBU (450 µl) and a 21-fold excess of allyl acetate (2.20 ml) in refluxing THF (10 ml) with a reaction time of 24 h (ligand PPh_3). The THF was removed and 30 ml of dichloromethane was added followed by standard work-up. The resulting liquid was dissolved in dichloromethane and filtered through aluminia to remove traces of **ABS**. For further purification a bulb to bulb distillation was carried out to give a colourless liquid at 130°C and 3 Torr. Yield 222 mg (98%), b.p. ≈ 80°C at 3 Torr. − IR (film): $\tilde{\nu}$ = 1689 cm^{-1} (C=O). − ^1H NMR ($CDCl_3$, 400 MHz): δ = 5.82 (pseudo tdd, ^3J = 6.0 Hz, $^3J_{cis}$ = 10.2 Hz, $^3J_{trans}$ = 17.1 Hz, 1 H, $N-CHH'-CH{=}CHH$), 5.54 (tdd, ^3J = 7.5 Hz, $^3J_{cis}$ = 10.1 Hz, $^3J_{trans}$ = 17.0 Hz, 1 H, $C-CH_2-CH{=}CHH$), 5.28 (pseudo qd, $^{2/4}J$ = 1.3 Hz, $^3J_{trans}$ = 17.1 Hz, 1 H, $N-CHH'-CH{=}CHH_{trans}$), 5.21 (pseudo qd, $^{2/4}J$ = 1.3 Hz, $^3J_{cis}$ = 10.2 Hz, 1 H, $N-CHH'-CH{=}CH_{cis}H$), 5.10 (md, $^3J_{trans}$ = 17.0 Hz, 1 H, $C-CH_2-CH{=}CHH_{trans}$), 5.08 (md, $^3J_{cis}$ = 10.1 Hz, 1 H, $C-CH_2-CH{=}CH_{cis}H$), 4.50 (pseudo tdd, ^4J = 1.3 Hz, ^3J = 6.0 Hz, ^2J = 14.6 Hz, 1 H, $N-CHH'-CH{=}CHH$), 4.44 (pseudo tdd, ^4J = 1.3 Hz, ^3J = 6.0 Hz, ^2J = 14.6 Hz, 1 H, $N-CHH'-CH{=}CHH$), 3.30 (s, 3 H, $N-CH_3$), 2.69 (d, ^3J = 7.5 Hz, 2 H, $C-CH_2-CH{=}CHH$), 1.55 (s, 3 H, $C-CH_3$). − GC-MS (EI, 70 eV); *m/z* (%): 236.0 (100) [M^+], 221.0 (99) [$M^+ - CH_3$], 194.9 (17) [$M^+ - C_3H_5$], 138.0 (90), 41.0 (59) [$C_3H_5^+$]. − $C_{12}H_{16}N_2O_3$ (236.27): calcd. C 61.00, H 6.83, N 11.86; found C 60.95, H 7.04, N 11.63.

5-Chloromethyl-1,5-dimethylbarbituric Acid: Found in catalyses with yields of **ABS** <3%. − $C_7H_9ClN_2O_3$ (204.61). − GC-MS (EI, 70 eV); *m/z* (%): 204.0 (14) [M^+], 189.0 (30) [$M^+ - CH_3$], 169.0 (100) [$M^+ - Cl$], 155.1 (6) [$M^+ - CH_2Cl$], 69.0 (62), 40.9 (27).

Molecular Modelling: The calculations were carried out with the program Sybyl 6.1 using the standard tripos force field on a Silicon Graphics Indigo workstation (tripos metal file with standard geometries and van der Waals parameters of transition metal atoms). After establishment of the geometry of the (η^3-allyl)Pd system and the two P atoms, the P substituents were attached in their standard geometries, the *ortho*-substituent being oriented towards the allyl plane. A conformational analysis with energy minimisation was carried out.

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