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Synthesis of Aminophosphines Containing a Chiral Dinaphthoazepine Entity and their Use in Asymmetric Catalysis

P. Wimmer and **M. Widhalm***

Institut für Organische Chemie, Universität Wien, A-1090 Wien, Austria

Summary. Three azaphospha ligands with a chiral dinaphthoazepine subunit were prepared and used in asymmetric carbon-carbon bond forming reactions. The nickel catalyzed *Grignard* cross coupling reaction of 1-phenylethyl magnesium chloride and vinyl bromide afforded the product in up to 47% ee. The palladium catalyzed allylic substitution of 1,3-substituted propenylacetates with dimethyl malonate and the coupling of allylacetate with methyl N-(diphenylmethylene)-glycinate resulted in asymmetric inductions of up to 97% ee and 51% ee, respectively.

Keywords. Chiral ligands; Cross coupling; Allylic substitution.

Synthese von Aminophosphinen mit einer chiralen Dinaphthoazepineinheit und ihre Anwendung in der asymmetrischen Katalyse

Zusammenfassung. Drei Azaphospha-Liganden mit einer chiralen Dinaphthoazepineinheit wurden dargestellt und in asymmetrischen Kohlenstoff-Kohlenstoff-Verknüpfungsreaktionen eingesetzt. Bei der nickelkatalysierten *Grignard*-Crosskupplung von 1-Phenylethylmagnesiumchlorid mit Vinylbromid erhielt man das Kupplungsprodukt mit bis zu 47% ee. Die palladiumkatalysierte allylische Substitution von 1,3-substituierten Propenylacetaten mit Dimethylmalonat und die Kupplung von Allylacetat mit Methyl-N-(diphenylmethylen)-glycinat zeigten asymmetrische Induktionen von bis zu 97% bzw. 51% ee.

Introduction

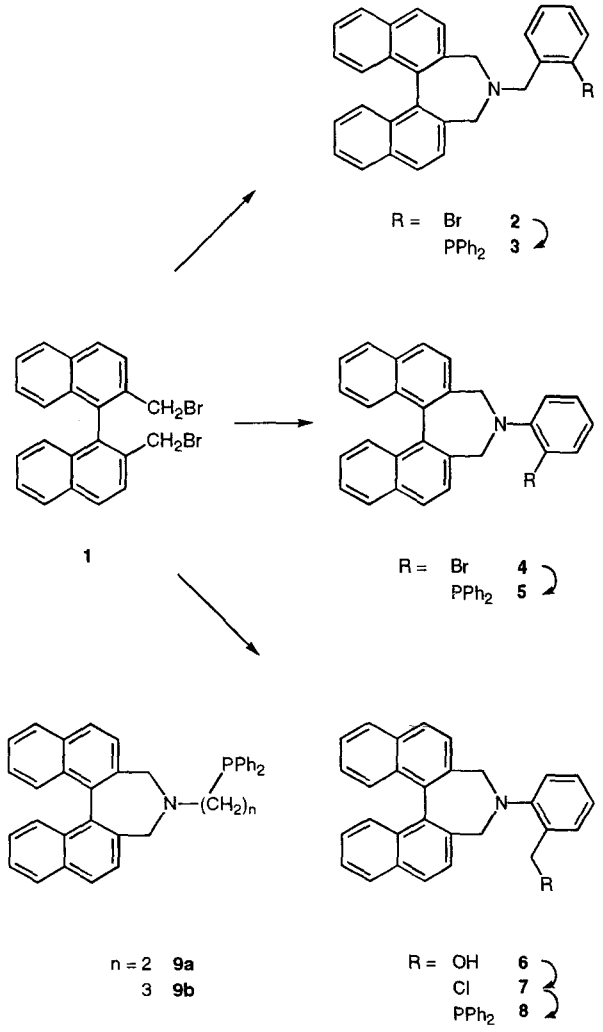
Numerous binaphthyl derivatives have been employed as chiral auxiliaries in stoichiometric and catalytic reactions [1]. The discovery of 2,2′-*bis*-(diphenylphosphino)-1,1′-binaphthyl (*BINAP*) which proved to be an extremely successful ligand [2] stimulated synthetic efforts in order to access both C_2- and C_1-symmetrical binaphthyls in racemic [3] and optically active form [4]. Mixed bidentate ligands with phosphorus and nitrogen complexation sites have been used in asymmetric carbon–carbon coupling reactions, frequently showing higher reactivity and/or enantioselectivity than diphospha or diaza ligands [5].

The ease of formation of dibenzo- and dinaphtho-azepines from 2,2′-*bis*-(bromomethyl) precursors [6] and their successful use in asymmetric transformations

[7] encouraged us and others to prepare aminophosphines **3**, **5**, and **8** [8] and **9a**, **b** [9] in which N and P donor atoms are connected by a bridge of two or three carbon atoms. Their use in catalytic asymmetric hydrogenation reactions and carbon-carbon bond forming reactions has been reported briefly [8]. In this paper, we give full details of the synthesis of **3**, **5**, and **8** together with a more comprehensive study on their use in allylic substitution reactions to show scope and limitations.

Results and Discussion

Aminophosphines **3** and **5** were accessible in two steps from 2,2′-*bis*-(bromomethyl)-1,1′-binaphthyl (**1**) which was refluxed with 2-bromo-benzylamine or 2-bromoaniline in toluene/triethylamine to give azepines **2** and **4** in 80% and 48% yield, respectively. Lithiation with *n*-BuLi in *THF* at −40 °C and subsequent treatment with chlorodiphenylphosphine afforded ligands **3** and **5** in 71% yield in both cases.



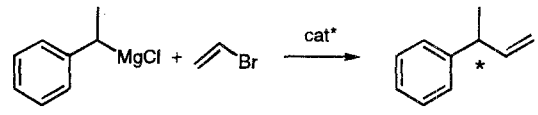
Scheme 1

Aminophosphine **8** was accessible *via* the benzyl alcohol **6**. The hydrochloride of **6** could easily be converted to the benzyl chloride **7** (81%). Reaction of lithium diphenylphosphide with **7** at 0 °C yielded ligand **8** (65%). Optically active compounds were prepared in a similar manner starting from optically pure enantiomers of **1** [10].

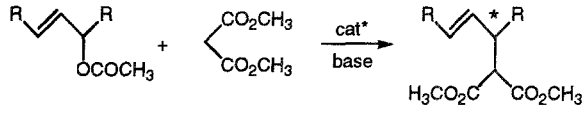
All ligands were isolated as crystalline solids or foams which proved to be largely stable towards oxidation. They have been stored in ampouls at −20 °C for months without noticeable decomposition. Even in solution, **3** and **5** can be handled for short periods without precautions; only **8** was found to be partly oxidized after hours. Attempts to isolate nickel(II) or palladium(II) complexes of the aminophosphine ligands failed. NMR spectra were not conclusive, and their poor resolution precluded structural information; nevertheless, the formation of several species was evident.

In a recent publication we briefly reported on catalytic asymmetric hydrogenations and carbon-carbon coupling reactions using ligands **3**, **5**, and **8**. The attractivity of the enantioselective formation of carbon-carbon bonds prompted us to investigate the efficiency of our ligands in some typical reactions (Scheme 2), varying substrates and reaction conditions.

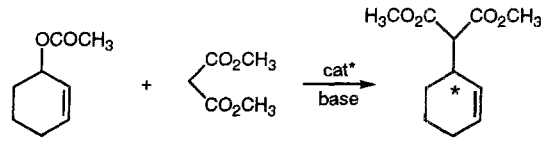
Model reactions (1)–(3) have been selected with respect to their different mechanistic features: with or without kinetic resolution of the educt, entrance of an electron-rich carbon species from outside without interaction with the transition metal center ((2) and possibly (3)) or through a reductive elimination at the



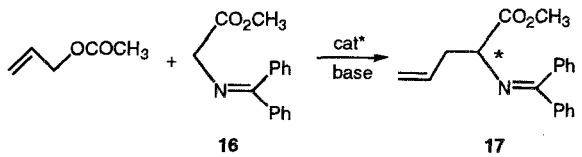
(1)



R = Ph **10** R = Ph **12** (2a)
CH3 **11** CH3 **13** (2b)



14 **15** (2c)



16 **17** (3)

Scheme 2

Table 1. Ni catalyzed cross coupling reaction (Scheme 2, (1))

entry[a]	ligand	temp. (°C)	isol. yield (%)	ee (%)[b]	config.[c]	formation of styrene (%)[d]
1	(*S*)-**3**	10	78	42	*R*	5
2	(*S*)-**3**	0	67	46	*R*	2
3	(*S*)-**3**	−10	44	47	*R*	1
4	(*S*)-**5**	0	55	9	*R*	28
5	(*S*)-**8**	0	13	3	*S*	34

[a] 0.5 mol% of catalyst, *L*/$NiCl_2$ (1:1), in Et_2O, 24 h; [b] estimated by GC on derivatized β-cyclodextrin (Lipodex C® [20]); [c] deduced from the sign of the optical rotation [18]; [d] estimated by NMR integration

carbon-carbon bond-forming step (1), *via* π-allyl ((2) and (3)) or σ-alkyl intermediates (1), etc. Detailed investigations on the reaction mechanisms have been carried out by numerous groups [11–13]. Scheme 2 shows three reactions which have been investigated. The cross coupling reaction between 1-phenylethyl magnesium chloride and vinyl bromide (1), the palladium catalyzed allylic substitution of prochiral substrates with a symmetric nucleophile (2), and the allylic substitution of the achiral allyl entity with a prochiral nucleophile (3). In all cases, catalysts were prepared *in situ*.

The *Grignard* cross coupling (1) afforded 3-phenyl-1-butene in up to 47% ee when using **3**/$NiCl_2$ (1:1) (Table 1). Only a slight temperature dependence was observed concomitant with a decrease of chemical yield. In contrary, **5** and **8** showed low reactivity and enantioselectivity. In all cases, styrene – probably formed from coordinated 1-phenylethyl *via* β-hydride elimination – was produced as a by-product. Its amount was found to be inversely proportional to the asymmetric induction. The use of palladium complexes resulted in excessive formation of styrene.

For the allylic substitution (2), three substrates (**10**, **11**, and **14**) were chosen which all form mixtures of symmetrically substituted π-allyl intermediates (Fig. 1). Although the enantiomeric purity of the products may be influenced by different reaction rates of the enantiomers of the (racemic) educt (kinetic resolution) [14], equilibrium of stereoisomeric η^3-allyl complexes, and differences in the reaction rate of the nucleophilic attack on these intermediates, the ratio of allyl complexes in equilibrium will dominate the enantioselectivity if (*a*) the attack of the nucleophile is rate determining, (*b*) *Curtin-Hammett* conditions are fulfilled, and (*c*) the reaction proceeds under reactant control [12b]. If the reactivity of the allyl termini is similar (*i.e.* in *cis*-diphosphine palladium complexes), the regioselectivity of the nucleophilic attack will also contribute to the stereochemical outcome of the reaction. In the present case, however, it seems very probable that the nucleophile should be introduced at the allylic carbon *trans* to phosphorus (and *cis* to nitrogen).

For the reaction of dimethyl malonate with 1,3-diphenyl-prop-2-ene-1-yl acetate (**10**), ligands **3** and **5** gave the coupling product **12** with similar enantiopurity

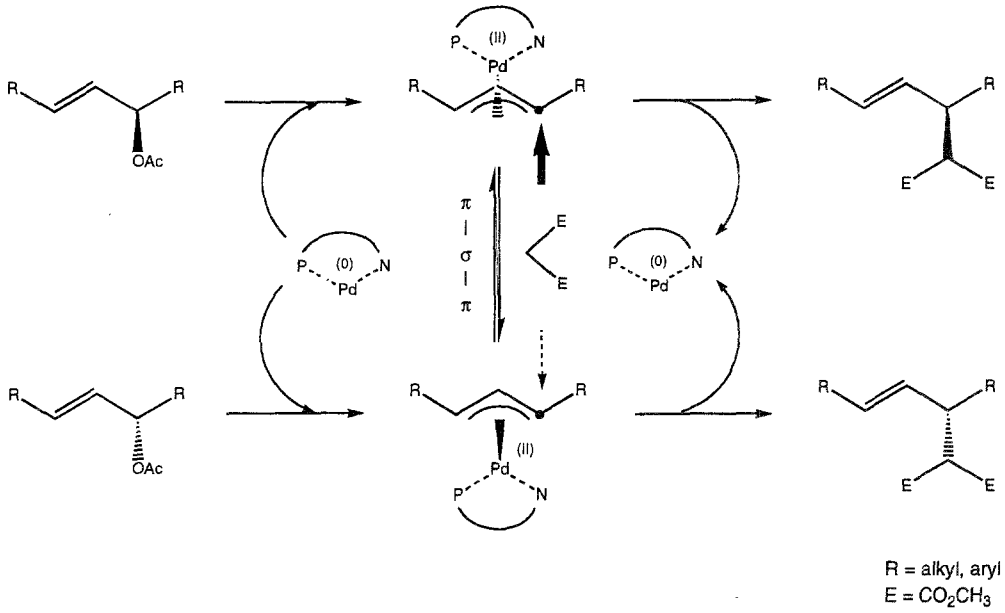


Fig. 1

(95–98% ee if N,O-*bis*-trimethylsilylacetamide (*BSA*) was employed as a base. The reactivity was found to be excellent at room temperature with 1 mol% of catalyst (Table 2). In contrast, ligand **8** afforded **12** with only 16% ee. If sodium dimethyl malonate in *THF* was used, the results were uneffected for **5** but decreased to 80% ee for **3** and increased to 19% ee for **8**, accompanied by inversion of configuration of the product in the latter case. Lowering the temperature to 0 °C affected only the rate of the conversion, whereas the effect on stereoselectivity was small. These reactions were found to be rather insensitive to solvent changes, and also the dependence on the ligand/palladium ratio was small and pointed to the operation of thermodynamically stable 1:1 complexes. The use of *BSA* in CH_2Cl_2 at room temperature and 1 mol% of a 1:1 Pd-ligand complex gave the best results. Merely for **8** the sodium hydride method gave slightly better results, but ee never exceeded 19% ee under various conditions. This might be a consequence of the preferred monodentate complexation mode of **8** which was recently observed for corresponding rhodium(I) complexes [15].

To vary substrate structure, the dimethyl analogue **11** and 3-acetylcyclohex-1-ene (**14**) were also investigated. Only the more promising ligands **3** and **5** were tested for their efficiency, but both substrates showed a disappointing low asymmetric induction of only 6 and 31% ee, respectively (Table 3).

Reaction (3) represents the attack of a prochiral nucleophile (**16**) on a η^3-allyl complex with the allyl moiety being achiral. In this case also an isomeric mixture of allyl complexes will be present, but their ratio will not be reflected directly by the enantiomeric composition of the product **17**. Both the differences in the reactivity of the allyl complexes and the formation of a non-racemic nucleophile caused by the chiral environment will influence the enantioselectivity.

Table 2. Pd catalyzed allylic substitution of 1,3-diphenyl-prop-1-en-3-yl acetate (**10**) with dimethyl malonate (Scheme 2. (2a))

entry[a]	ligand	Pd precursor	L/Pd	base	solvent	temp. (°C)[b]	time (h)[c]	isol. yield (%)	ee (%)[d]	config.[e]
1	(*S*)-**3**	$Pd(OAc)_2$	2:1	NaH	*THF*	r.t.	4.0	93	76	*S*
2	(*S*)-**3**	$Pd(OAc)_2$	2:1	NaH	*THF*	0	49	45	72	*S*
3	(*S*)-**3**	$Pd(OAc)_2$	1.3:1	NaH	*THF*	r.t.	5.5	88	79	*S*
4	(*S*)-**3**	$Pd_2(dba)_4$	1:1	NaH	*THF*	r.t.	4.0	90	81	*S*
5	(*S*)-**3**	$[PdC_3H_5Cl]_2$	1:1	BSA	CH_2Cl_2	r.t.	4.0	92	97	*S*
6	(*S*)-**3**	$[PdC_3H_5Cl]_2$	1:1	BSA	toluene	r.t.	17	59	97	*S*
7	(*S*)-**5**	$Pd(OAc)_2$	2:1	NaH	*THF*	r.t.	4.0	95	95	*S*
8	(*S*)-**5**	$Pd(OAc)_2$	2:1	NaH	*THF*	0	22	79	95	*S*
9	(*S*)-**5**	$Pd(OAc)_2$	1:1	NaH	*THF*	r.t.	4.0	99	97	*S*
10	(*S*)-**5**	$Pd_2(dba)_4$	1:1	NaH	*THF*	r.t.	4.0	90	96	*S*
11	(*S*)-**5**	$[PdC_3H_5Cl]_2$	1:1	NaH	CH_3CN	r.t.	4.0	82	94	*S*
12	(*S*)-**5**	$Pd_2(dba)_4$	2:1	BSA	CH_2Cl_2	r.t.	92	26	97	*S*
13	(*S*)-**5**	$[PdC_3H_5Cl]_2$	1:1	BSA	CH_2Cl_2	r.t.	4.0	99	97	*S*
14	(*S*)-**5**	$[PdC_3H_5Cl]_2$	1:1	BSA	toluene	r.t.	17	–	95	*S*
15	(*S*)-**8**	$Pd(OAc)_2$	2:1	NaH	*THF*	r.t.	4.0	96	19	*S*
16	(*S*)-**8**	$Pd(OAc)_2$	1:1	NaH	*THF*	r.t.	4.0	91	19	*S*
17	(*S*)-**8**	$Pd(OAc)_2$	0.5:1	NaH	*THF*	r.t.	4.0	88	16	*S*
18	(*S*)-**8**	$Pd_2(dba)_4$	1:1	NaH	*THF*	r.t.	4.0	95	19	*S*
19	(*S*)-**8**	$[PdC_3H_5Cl]_2$	1:1	BSA	CH_2Cl_2	r.t.	4.0	92	16	*R*
20	(*S*)-**8**	$[PdC_3H_5Cl]_2$	1:1	BSA	toluene	r.t.	17	84	13	*R*

[a] For experimental details see Ref. [5f]; [b] "r.t." corresponds to 20–23 °C; [c] the reaction was followed by TLC (first time after 4 h); reactions were stopped either after no starting material could be detected or if no further progress could be observed; [d] determined by HPLC on a Chiralcel OD-H® column (250 × 4.6 mm, 2-PrOH/*n*-hexane 2:98) and using a chiral shift reagent ($Eu(hfc)_3$ in $CDCl_3$); both methods yielded consistent results (±1%); [e] deduced from the sign of optical rotation [21]

Table 3. Pd catalyzed allylic substitution of 1-methylbut-2-enyl acetate (**11**) and 3-acetoxycyclohex-1-ene (**14**) with dimethyl malonate (Scheme 2, (2b, c))

entry[a]	ligand	substrate	base	solvent	temp. (°C)[b]	time (h)	isol. yield (%)	ee (%)[c]	prevailing config.
1	(*S*)-**3**	**11**	*BSA*	CH_2Cl_2	r.t.	18	92	3	(+)-**13**
2	(*S*)-**3**	**11**	*BSA*	toluene	0	18	78	4	(+)-**13**
3	(*S*)-**5**	**11**	*BSA*	CH_2Cl_2	r.t.	18	84	7	(+)-**13**
4	(*S*)-**3**	**14**	*BSA*	CH_2Cl_2	r.t.	18	86	28	(R)-**15**
5	(*S*)-**3**	**14**	*BSA*	toluene	r.t.	18	54	31	(R)-**15**
6	(*S*)-**5**	**14**	*BSA*	CH_2Cl_2	r.t.	18	13	n.e.	–

[a] 1 mol% of catalyst prepared *in situ*, for experimental details see Refs. [5d, f]); [b] "r.t." corresponds to 20–23 °C; [c] determined by GC on derivatized γ-cyclodextrin (**13**: FS, 50% *octakis*-(6-O-methyl-2,3-di-O-pentyl)-γ-cyclodextrin, 25 m × 0.25 mm, 0.5 bar H_2, 55 °C) and on the basis of the highest reported value of the specific rotation ((−)-(*S*)-**15**: $[\alpha]_D^{20} = -46.1$ (*c*: 2.86, $CHCl_3$) [22])

Table 4. Pd catalyzed allylic substitution of allyl acetate with the benzophenone imine of methyl glycinate (**16**) (Scheme 2, (3))

entry[a]	ligand	Pd precursor	L/Pd	base	solvent	temp. (°C)[b]	time (h)[c]	isol. yield (%)	ee (%)[d]	config. of **17**[e]
1	(*S*)-**3**	$[PdC_3H_5Cl]_2$	2:1	*BSA*	CH_2Cl_2	r.t.	20	76	41	*S*
2[f]	(*S*)-**3**	$[PdC_3H_5Cl]_2$	2:1	*BSA*	CH_2Cl_2	r.t.	20	70	42	*S*
3	(*S*)-**3**	$[PdC_3H_5Cl]_2$	2:1	*BSA*	CH_2Cl_2	−20	110	57	45	*S*
4	(*S*)-**3**	$[PdC_3H_5Cl]_2$	2:1	*BSA*	toluene	−20	110	81	51	*S*
5[f]	(*S*)-**3**	$[PdC_3H_5Cl]_2$	2:1	*BSA*	toluene	−40	170	<5	–	–
6	(*S*)-**3**	$Pd(OAc)_2$	2:1	Li*HMDS*	*THF*	−40	20	67	36	*S*
7	(*S*)-**5**	$[PdC_3H_5Cl]_2$	1:1	*BSA*	CH_2Cl_2	r.t.	40	45	11	*S*
8	(*S*)-**5**	$[PdC_3H_5Cl]_2$	2:1	*BSA*	CH_2Cl_2	r.t.	20	66	11	*R*
9	(*S*)-**5**	$Pd(OAc)_2$	2:1	Li*HMDS*	*THF*	−40	20	52	0	–

[a] For experimental details see Refs. [5f, 19]; [b] "r.t." corresponds to 20–23 °C; [c] the reaction was followed by TLC (first time after 20 h); reactions were stopped either if no starting material could be detected or if no further progress was observed; [d] determined by HPLC on a Chiralcel OD-H® column (2-PrOH/*n*-hexane 1:99); [e] deduced from the sign of the optical rotation [19b]; [f] instead of acetate, the corresponding carbonate was used as the substrate

Lithium hexamethyldisilazid (Li*HMDS*) or *BSA* were employed as bases (Table 4). Only ligand **3** afforded **17** in good chemical yield and 51% ee if the reaction was conducted at −20 °C in toluene with *BSA*. Lowering the temperature further caused precipitation of the educt and resulted in a sharp drop of reactivity even when the more reactive carbonate was used. The use of Li*HMDS* gave lower chemical and optical yields (36% ee).

Conclusions

The usefulness of the easily accessible aminophosphines **3** and **5** with a chiral subunit near to the N-complexation site has been demonstrated for C–C coupling reactions proceeding *via* palladium-allyl intermediates. Nucleophiles attacking the allyl complex from "outside" will receive efficient asymmetric interaction from those parts of the chiral ligand which is located near to the complexation plane [16]. Nevertheless, the importance of the preference of a single coordination geometry becomes evident in the case of substrates **10** *vs.* **11** and **14**. Preliminary molecular modelling experiments pointed to positive interactions of one of the P-phenyl rings with one phenyl ring of the substrate [12b, 17]. A detailed study is presently under progress.

Experimental

NMR spectra were recorded on a Bruker AM 400 WB instrument in $CDCl_3$ if not otherwise noted. Chemical shifts (δ) are reported in parts per million (ppm) *vs.* internal tetramethylsilane (*TMS*) (^{1}H,

$^{13}C\{^1H\}$, J-modulated ^{13}C) and external 85% H_3PO_4 ($^{31}P\{^1H\}$). Mass spectra were obtained with a MAT-CH7. Optical rotations were measured on a Perkin-Elmer polarimeter 241 (1 dm cell, thermostated). Melting points (mp) were obtained on a Kofler melting point apparatus (uncorrected). Elemental analyses were performed at Mikroanalytisches Laboratorium der Universität Wien.

All reactions with air- or moisture sensitive materials were carried out at an argon line using standard *Schlenk* techniques. *THF* was distilled from potassium benzophenone ketyl. Chlorodiphenylphosphine (Aldrich) was distilled under reduced pressure and stored under argon. *o*-Bromoaniline (Aldrich) was purified by *Kugelrohr* distillation. All other chemicals were analytical grade and used as purchased.

4-(2-Bromobenzyl)-4H-dinaphth[2,1-c:1',2'-e]azepine ((±)-**2** *and* (*R,S*)-**2**)

A mixture of 4.50 g (10 mmol) of (±)-**1**, 2.73 g (12 mmol) of *o*-bromobenzylamine hydrochloride, and 7 ml (50 mmol) of triethylamine in 70 ml of toluene was refluxed under argon for 24 h. The suspension was cooled to room temperature, and the solvent was evaporated under reduced pressure. The residue was extracted with water and CH_2Cl_2. The organic layers were washed with brine, dried (Na_2SO_4), and evaporated. The remaining oil was chromatographed on silica gel with *PE*/ethyl acetate (*EE*) (95:5) to give 3.302 g (80%) of (±)-**2** as a white foam. Optically pure **2** was prepared essentially the same way starting from (*R*)- or (*S*)-**1**.

(*S*)-**2**: $[\alpha]_\lambda^{20}$ ($c = 1.2$, CH_2Cl_2) = +217 (589 nm), +226 (587 nm), +254 (546 nm), +337 (436 nm); ^1H NMR: $\delta = 3.28$ (d, 2H, $J = 12.2$ Hz), 3.57 (d, 1H, $J = 14.5$ Hz), 3.65 (d, 2H, $J = 12.3$ Hz), 3.86 (d, 1H, $J = 14.5$ Hz), 7.11 (dt, 1H, $J = 7.7$, 1.6 Hz), 7.23 (ddd, 2H, $J = 8.4$, 8.4, 1.4 Hz), 7.32 (dt, 1H, $J = 7.6$, 1.1 Hz), 7.43 (ddd, 2H, $J = 8.1$, 8.1, 1.1 Hz), 7.47 (d, 2H, $J = 8.4$ Hz), 7.55 (d, 2H, $J = 8.3$ Hz), 7.56 (dd, 1H, $J = 7.9$, 1.0 Hz), 7.62 (dd, 1H, $J = 7.7$, 1.5 Hz), 7.93 (d, 2H, $J = 7.9$ Hz), 7.94 (d, 2H, $J = 8.2$ Hz) ppm; ^{13}C NMR: $\delta = 55.21$ (CH_2), 58.44 (CH_2), 124.50 (C), 125.36 (CH), 125.70 (CH), 127.27 (CH), 127.46 (CH), 127.85 (CH), 128.26 (CH), 128.35 (CH), 128.39 (CH), 130.83 (CH), 131.41 (C), 132.81 (CH), 133.13 (C), 133.66 (C), 135.05, 138.41 (C) ppm; MS (170 °C): $m/z = 463$ (M^+, 14%); $C_{29}H_{22}BrN$; calc.: C 75.00, H 4.78, N 3.02; found: C 74.71, H 5.01, N 2.96.

4-(2-Bromophenyl)-4H-dinaphth[2,1-c:1',2'-e]azepine ((±)-**4** *and* (*R/S*)-**4**)

A solution of 3.00 g (6.8 mmol) of (±)-**1**, 1.29 g (7.5 mmol) of *o*-bromoaniline, and 4.7 ml of triethylamine in 45 ml of toluene was refluxed under argon for 48 h. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure. The residue was shaken with water and CH_2Cl_2, the organic layer was separated, washed with brine and dried over Na_2SO_4. The solution was concentrated to approx. 100 ml and diluted with petroleum ether (*PE*). The crystalline precipitate was filtered off, washed with diethyl ether, and dried to give 1.14 g (37%) of **4**. Chromatography of the mother liquor on silica gel with *PE*/CH_2Cl_2 (75:25) yielded a further crop of 0.34 g (11%) of (±)-**4**; mp. 270–272 °C. Optically pure **4** was prepared essentially the same way starting from (*R*)- or (*S*)-**1**; the whole amount of crude product was chromatographed to yield 1.92 g (63%) of (*R/S*)-**4**; mp: 196–198 °C.

(*S*)-**4**: $[\alpha]_\lambda^{20}$ ($c = 1.1$, CH_2Cl_2) = −41.1 (589 nm), −45.6 (578 nm), −64.6 (546 nm), −317.0 (436 nm); ^1H NMR: $\delta = 3.94$ (AB-system, 2H, $J = 12.3$ Hz), 4.09 (AB-system, 2H, $J = 12.3$ Hz), 6.90 (m, 2H), 7.14 (dt, 1H, $J = 7.6$, 1.5 Hz), 7.28 (ddd, 2H, $J = 8.4$, 8.4, 1.5 Hz), 7.47 (m, 4H), 7.51 (d, 2H, $J = 8.4$ Hz), 7.62 (dd, 1H, $J = 7.9$, 1.5 Hz), 7.93 (d, 2H, $J = 7.9$ Hz), 7.94 (d, 2H, $J = 7.9$ Hz) ppm; ^{13}C NMR: $\delta = 54.82$ (CH_2), 119.44 (C), 122.18 (CH), 123.95 (CH), 125.55 (CH), 125.85 (CH), 127.47 (CH), 127.66 (CH), 127.73 (CH), 128.29 (CH), 128.81 (CH), 131.33 (C), 133.18 (C), 133.46 (C), 134.00 (CH), 134.99 (C), 149.93 (C) ppm; MS (110 °C): $m/z = 449$ (M^+, ^{79}Br, 15%); $C_{28}H_{20}BrN$ calc.: C 74.67, H 4.48, N 3.11; found: C 74.43, H 4.50, N 3.02.

General Procedure for the Preparation of Aminophosphines **3** *and* **5**

To a degassed solution of 2 mmol of bromide **2** or **4** in 25 ml of *THF* (except of racemic **4**, which was suspended in 50 ml of *THF*) stirred at −40 °C, 1.6 ml (2.6 mmol) of *n*-BuLi (1.6 *M* solution in *n*-hexane) were added dropwise. After stirring for 2.5 h, 1.08 ml (6 mmol) of chlorodiphenylphosphine was slowly added to the mixture at −78 °C. The mixture was warmed to room temperature overnight. After removing the solvent under vacuum, the residue was quenched with water, and the aqueous suspension was extracted with three portions of CH_2Cl_2. The combined organic extracts were successively washed with water and brine, dried, and evaporated.

4-((2-Diphenylphosphino)-benzyl)-4H-dinaphth[2,1-c:1',2'-e]azepine (**3**)

The residue was chromatographed on silica gel (deactivated with 13% of water). Elution with *PE/EE* (96:4) gave 809 mg (71%) of **5** as a white foam. An analytical sample of (±)-**5** was recrystallized from CH_2Cl_2/*n*-hexane; mp: 216–218 °C. The optically active ligand was prepared analogously.

(*S*)-**3**: $[\alpha]_\lambda^{20}$ ($c = 1$, CH_2Cl_2) = +211 (589 nm), +219 (578 nm), +245 (546 nm), +339 (436 nm); ^{1}H NMR: $\delta = 2.77$ (AB-system, d, 2H, $J_{AB} = 12.2$ Hz), 3.37 (AB-system, d, 2H, $J_{AB} = 12.3$ Hz), 3.67 (A'B'-system, d, 1H, $J_{A'B'} = 13.6$ Hz), 3.78 (A'B'-system, d, 1H, $J_{A'B'} = 13.3$ Hz), 6.98 (m, 4H), 7.11 (m, 5H), 7.23 (m, 8H), 7.32 (m, 4H), 7.41 (m, 1H), 7.76 (d, 2H, $J = 8.2$ Hz), 7.82 (d, 2H, $J = 7.8$ Hz) ppm; ^{13}C NMR: $\delta = 54.07$ (CH_2), 58.23 (CH_2, $J_{CP} = 16.1$ Hz), 125.18 (CH), 125.51 (CH), 127.24 (CH), 127.43 (CH), 127.91 (CH), 127.97 (CH), 128.01 (CH, $J_{CP} = 7.2$ Hz), 128.20 (CH), 128.24 (CH), 128.40 (CH, $J_{CP} = 6.7$ Hz), 128.53 (CH), 129.24 (CH, $J_{CP} = 5.8$ Hz), 131.31 (C), 132.98 (C), 133.60 (CH, $J_{CP} = 19.5$ Hz), 133.77 (CH, $J_{CP} = 17.9$ Hz), 133.83 (C), 134.58 (CH), 134.80 (C), 137.62 (C, $J_{CP} = 16.6$ Hz), 137.80 (C, $J_{CP} = 9.2$ Hz), 138.48 (C, $J_{CP} = 10.8$ Hz), 144.02 (C, $J_{CP} = 23.2$ Hz) ppm; ^{31}P NMR: $\delta = -14.70$ ppm; MS (240 °C): $m/z = 569$ (M^+, 5%); $C_{41}H_{32}NP$; calc.: C 86.44, H 5.66, N 2.46; found: C 85.78, H 5.82, N 2.35.

4-((2-Diphenylphosphino)-phenyl)-4H-dinaphth[2,1-c:1',2'-e]azepine (**5**)

The crude oily product was purified by column chromatography (SiO_2, deactivated with 13% of water, eluent: *PE*/CH_2Cl_2, 80:20). Racemic and optical active aminophosphine **5** were obtained as a white foam in 71% yield (789 mg).

(*S*)-**5**: $[\alpha]_\lambda^{20}$ ($c = 0.9$, CH_2Cl_2) = +33.9 (589 nm), +33.3 (578 nm), +28.7 (546 nm), +117.8 (436 nm); ^{1}H NMR: $\delta = 3.63$ (AB-system, 2H, $J_{AB} = 12.3$ Hz), 3.75 (AB-system, 2H, $J_{AB} = 12.1$ Hz), 6.79 (m, 1H), 6.87 (m, 1H), 7.06 (m, 3H), 7.19 (m, 1H), 7.25 (m, 3H), 7.29–7.34 (m, 6H), 7.38–7.47 (m, 7H), 7.86 (d, 2H, $J = 8.2$ Hz), 7.93 (d, 2H, $J = 8.7$ Hz) ppm; ^{13}C NMR: $\delta = 55.22$ (CH_2), 124.58 (CH), 125.32 (CH), 125.8 (CH), 125.61 (CH), 127.48 (CH), 127.92 (CH), 128.20 (CH), 128.29, 128.30, 128.37, 128.40, 128.43, 129.27 (CH), 131.33 (C), 133.05 (C), 133.20 (CH), 133.82 (CH, d, $J_{CP} = 20.6$ Hz), 133.88 (C), 134.33 (CH, d, $J_{CP} = 20.6$ Hz), 134.81 (C), 137.54 (C, d, $J_{CP} = 6.9$ Hz), 138.18 (C, d, $J_{CP} = 12.7$ Hz), 138.46 (C, d, $J_{CP} = 10.7$ Hz), 155.36 (C, d, $J_{CP} = 17.8$ Hz) ppm; ^{31}P NMR: $\delta = -11.5$ (s) ppm; MS (170 °C): $m/z = 555$ (M^+, 97%); $C_{40}H_{30}NP$; calc.: C 86.46, H 5.44, N 2.52; found: C 86.18, H 5.67, N 2.50.

4-((2-Hydroxymethyl)-phenyl)-4H-dinaphth[2,1-c:1',2'-e]azepine (**6**)

A degassed suspension of 2.00 g (4.5 mmol) of (±)-**1**, 1.12 g (9.1 mmol) of *o*-aminobenzyl alcohol, and 3.20 ml (22.5 mmol) of triethylamine was refluxed under argon for 20 h. CH_2Cl_2 and water were added to the cooled reaction mixture, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were washed with brine, dried, and evaporated. The residue was recrystallized from CH_2Cl_2/CH_3OH. The crystals were separated, washed with methanol, and dried *in vacuo* to give 1.44 g (79%) of (±)-**6**; mp: 205–208 °C. (*S*)-**6** was prepared in an analogous way; mp: 157–159 °C.

(*S*)-**6**: $[\alpha]_\lambda^{20}$ ($c = 1.2$, CH_2Cl_2) = +161 (589 nm), +166 (578 nm), +184 (546 nm), +191 (436 nm); ^{1}H NMR: $\delta = 3.92$ (AB-system, 2H, $J_{AB} = 12.1$ Hz), 4.00 (AB-system, 2H, $J_{AB} = 12.1$ Hz), 4.75 (A'B'-system, 1H, $J_{A'B'} = 13.3$ Hz), 5.03 (A'B'-system, 1H, $J_{A'B'} = 13.3$ Hz), 5.29 (br s, 1H), 6.95 (m, 1H), 7.14 (m, 2H), 7.29 (m, 3H), 7.50 (m, 4H), 7.54 (d, 2H, $J = 8.9$ Hz), 7.98 (d, 4H, $J = 7.9$ Hz) ppm; ^{13}C NMR: $\delta = 55.17$ (CH_2), 64.68 (CH_2), 123.09 (CH), 124.91 (CH), 125.68 (CH), 125.95 (CH), 127.42 (CH), 127.55 (CH), 127.86 (CH), 128.30 (CH), 128.69 (CH), 128.99 (CH), 131.32 (C), 132.91 (C), 133.24 (C), 135.00 (C), 135.86 (C), 150.38 (C) ppm; MS (210 °C): $m/z = 401$ (M^+, 83%); $C_{29}H_{23}NO$; calc.: C 86.75, H 5.77, N 3.49; found: C 86.31, H 5.85, N 3.39.

4-((2-Chloromethyl)-phenyl)-4H-dinaphth[2,1-c:1',2'-e]azepine (**7**)

To a suspension of 1.00 g (2.5 mmol) of **6** in 5 ml of ethanol, 1.5 ml of concentrated hydrochloric acid were slowly added. The solvent and excess of HCl were carefully removed under reduced pressure. The residue was taken up in 5 ml of benzene and cooled to 0 °C. An excess of thionyl chloride (1.5 ml) was added dropwise with stirring. After stirring for 1 h, the mixture was evaporated and the residue was triturated with benzene/CH_2Cl_2 to remove thionyl chloride, and the crude hydrochloride of **7** was recrystallized from CH_2Cl_2/*PE*. The crystals were collected, washed with *PE*, and after heating to 100 °C *in vacuo* (to liberate hydrochloric acid), 0.85 g (81%) of **7** were obtained; mp: 203–213 °C (dec.). (*S*)-**7** was prepared in an analogous way; mp: 217–224 °C (dec.).

(*S*)-**7**: $[\alpha]_\lambda^{20}$ ($c = 1.0$, CH_2Cl_2) = +90 (589 nm), +92 (578 nm), +98 (546 nm), +23 (436 nm); ^{1}H NMR: $\delta = 3.99$ (AB-system, 4H, $J_{AB} = 12.6$ Hz), 4.83 (A'B'-system, 1H, $J_{A'B'} = 11.3$ Hz), 4.87 (A'B'-system, 1H, $J_{A'B'} = 11.3$ Hz), 6.92 (dd, 1H, $J = 7.9$, 1.2 Hz), 7.13 (dt, 1H, $J = 7.4$, 1.5 Hz), 7.18 (dt, 1H, $J = 7.6$, 2.0 Hz), 7.29 (ddd, 2H, $J = 8.4$, 8.4, 1.5 Hz), 7.50 (m, 7H), 7.97 (d, 4H, $J = 8.4$ Hz) ppm; ^{13}C NMR: $\delta = 43.27$ (CH_2), 55.66 (CH_2), 122.64 (CH), 124.22 (CH), 125.55 (CH), 125.86 (CH), 127.48 (CH), 127.70 (CH), 128.29 (CH), 128.81 (CH), 129.08 (CH), 131.33 (CH), 131.36 (C), 132.64 (C), 133.17 (C), 133.46 (C), 134.93 (C), 151.32 (C) ppm; MS (120 °C): $m/z = 419$ (M^+, 33%); $C_{29}H_{22}ClN$; calc.: C 82.94, H 5.28, N 3.34; found: C 82.74, H 5.31, N 3.35.

Hydrochloride of **7**

^{1}H NMR: $\delta = 4.49$ (br s, 4H), 5.14 (AB-system, 2H, $J_{AB} = 12.8$ Hz), 5.63 (br AB-system, 2H, $J_{AB} = 11.8$ Hz), 6.92 (d, 1H, $J = 7.4$ Hz), 7.25 (m, 1H), 7.31 (m, 2H), 7.40 (t, 1H, $J = 7.1$ Hz), 7.45 (d, 2H, $J = 8.4$ Hz), 7.54 (m, 2H), 7.56–7.67 (d + very br d, 3H), 7.98 (d, 2H, $J = 8.4$ Hz), 8.01 (d, 2H, $J = 8.4$ Hz).

4-((2-Diphenylphosphinomethyl)-phenyl)-4H-dinaphth[2,1-c:1',2'-e]azepine (**8**)

The preparation of **8** and its work-up were carried out with degassed solvents under argon. To 56 mg (8.0 mmol) of lithium wire in 4 ml of *THF*, 360 µl (2.0 mmol) of chlorodiphenylphosphine were added at room temperature. The mixture was refluxed for 1 h to give a cherry-red solution of the desired lithium phosphide. After cooling to room temperature, the excess of lithium wire was removed using a spatula. 562 mg (1.3 mmol) of **7** dissolved in 15 ml of *THF* were added dropwise at 0 °C. The mixture was warmed up to room temperature overnight. The solvent was removed under reduced pressure, and 5 ml of water followed by 10 ml of CH_2Cl_2 were added with stirring. The organic layer was separated, repeatedly washed with water, and dried (Na_2SO_4). The solution was filtered through a short silica gel column and concentrated to approx. 3 ml. After addition of methanol, **8** crystallized at −25 °C. The crystals were collected, washed with methanol, and dried to give 495 mg (65%) of **8**; mp: 156–159 °C. (*S*)-**8** was prepared from (*S*)-**7**; mp: 184–186 °C.

(*S*)-**8**: $[\alpha]_\lambda^{20}$ ($c = 1.2$, CH_2Cl_2) = +43.6 (589 nm), +43.7 (578 nm), +42.4 (546 nm), −64.8 (436 nm); ^{1}H NMR: $\delta = 3.50$ (AB-system, 1H, $J_{AB} = 13.3$ Hz), 3.72 (AB-system, 1H, $J_{AB} = 13.3$ Hz, $J_{HP} = 2.5$ Hz),

3.81 (A'B'-system, 2H, $J_{A'B'} = 12.1$ Hz), 3.89 (A'B'-system, 2H, $J_{A'B'} = 12.1$ Hz), 6.84 (d, 1H, $J = 7.9$ Hz), 6.92 (dt, 1H, $J = 7.4$, 1.0 Hz), 7.01 (br m, 1H), 7.15 (br td, 1H, $J = 5.9$, 1.1 Hz), 7.23–7.31 (m, 8H), 7.37–7.51 (m, 10H), 7.94 (d, 2H, $J = 7.9$ Hz), 7.95 (d, 2H, $J = 7.4$ Hz) ppm; ^{13}C NMR: $\delta = 31.12$ (CH_2, d, $J_{CP} = 15.0$ Hz), 55.63 (br CH_2), 123.03 (CH), 123.93 (CH), 125.43 (CH), 125.75 (CH), 126.47 (CH, d, $J_{CP} = 2.7$ Hz), 127.50 (CH), 127.89 (CH), 128.24 (CH, d, $J_{CP} = 6.1$ Hz), 128.26 (CH), 128.27 (CH, d, $J_{CP} = 6.9$ Hz), 128.41 (CH), 128.46 (CH), 128.64 (CH), 130.76 (CH, d, $J_{CP} = 10.4$ Hz), 131.39 (C), 132.96 (CH, d, $J_{CP} = 19.0$ Hz), 132.98 (CH, d, $J_{CP} = 18.5$ Hz), 133.10 (C), 133.72 (C, d, $J_{CP} = 8.5$ Hz), 133.86 (br C), 134.91 (C), 138.85 (C, d, $J_{CP} = 16.5$ Hz), 139.09 (C, d, $J_{CP} = 16.1$ Hz), 151.22 (C, d, $J_{CP} = 4.3$ Hz) ppm; ^{31}P NMR: $\delta = -8.25$ ppm; MS (> 300 °C): $m/z = 570$ (M^+, 87%): $C_{41}H_{32}NP$; C 86.44, H 5.66, N 2.46; found: C 85.78, H 5.45, N 2.40.

Catalytic reactions

The *Grignard* cross coupling reaction (1) and the allylic alkylation (2a–c) were conducted as described elsewhere [5f, 12a, 18].

Allylic substitution of allyl acetate with methyl N-(diphenylmethylene)glycinate (Typical procedure, Table 4, entry 4)

A 10 ml *Schlenk* tube was charged with 1 ml of dry toluene and degassed by three freeze-pump-thaw cycles. $[Pd(C_3H_5)Cl]_2$ (1.8 mg, 1 mol%) and ligand (*S*)-**3** (11.7 mg, 2 mol%) were added, and the pale yellow solution was stirred at room temperature. After 10 min, allylacetate (100 mg, 1 mmol) was added and stirring was continued for 20 min. Then, methyl N-(diphenylmethylene)glycinate (**16**; 256 mg, 1 mmol), *BSA* (203 mg, 247 µl, 1 mmol), and a catalytic amount of KOAc were added subsequently. The resulting solution was degassed once more and kept at −20 °C for 110 h. The reaction was quenched with 10 ml of sat. NH_4Cl solution and extracted with ether (3 × 20 ml). The combined extracts were washed with brine and dried (Na_2SO_4). After evaporation the crude product was purified by chromatography (column: 25 × 2.2 cm, ether/petroleum ether, 15:85) to give **17** as a colorless oil. The enantiomeric excess was estimated by HPLC (Chiralcel OD-H, 250 × 4.6 mm, 2-PrOH/*n*-hexane (1:99)).

Entries 6 and 9: preparations according to a reported procedure [19].

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