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Chiral 8-amino substituted 2-phenyl-5,6,7,8-tetrahydro-6,6-dimethylmethanoquinolines as chiral ligands for enantioselective catalysis: palladium catalysed allylic substitution and addition of diethylzinc to benzaldehyde

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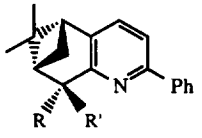
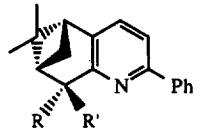
Abstract: Diastereomerically pure 8-amino substituted (5S,7S)-2-phenyl-5,6,7,8-tetrahydro-6,6-dimethylmethanoquinolines were prepared and assessed in the enantioselective palladium catalysed allylic substitution of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate and addition of diethylzinc to benzaldehyde. Enantioselectivities up to 68% were obtained. © 1997 Published by Elsevier Science Ltd

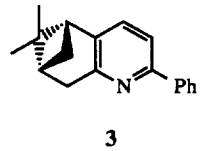
Recently, we and others found that the pyridyl alcohol **1** and the phenylthiopyridine **2**, both prepared from the 2-phenyl-5,6,7,8-tetrahydro-6,6-dimethylmethanoquinoline **3**, were effective ligands for the enantioselective addition of diethylzinc to benzaldehyde[1] and the palladium catalysed allylic alkylation of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate.[2]



1a: R=OH, R'=H
1b: R=H, R'=OH



2a: R=SPh, R'=H
2b: R=H, R'=SPh



3

Continuing our interest in the synthesis and application of chiral pyridine derivatives as ligands for metal complexes in enantioselective catalysis[3] we have been evaluating the potential utility of the 8-amino derivatives of the tetrahydroquinoline **3** as chiral controllers for asymmetric synthesis.[4]

In this paper we report the synthesis of some diastereomerically pure 8-amino substituted 2-phenyl-5,6,7,8-tetrahydro-6,6-dimethylmethanoquinolines and the results obtained with these new ligands in the enantioselective palladium catalysed allylic substitution of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate and addition of diethylzinc to benzaldehyde.

We decided to prepare primary and secondary amine derivatives of **3** because a very good enantioselectivity in the addition of organozinc compounds to aldehydes can be achieved using organometallic reagents modified by protic chiral ancillaries.[5] Moreover, also in palladium catalysed allylic substitutions secondary amines have been found effective ligands giving very high enantiomeric eccess.[6] It is appropriate to note at this point that the ligands **1** and **2** provided a level of stereodifferentiation depending from the configuration at the C_8 carbon. In the enantioselective addition of diethylzinc to benzaldehyde the *cis*-alcohol **1a** gave a better enantioselectivity than its *trans*-epimer,[1] whereas a reverse result was obtained in the palladium catalysed allylic substitutions. In this case the best stereochemical outcome was obtained by the *trans*-phenylthiopyridine **2b**.[2] Therefore, we devoted our efforts to obtain both epimers of amine derivatives of **3**.

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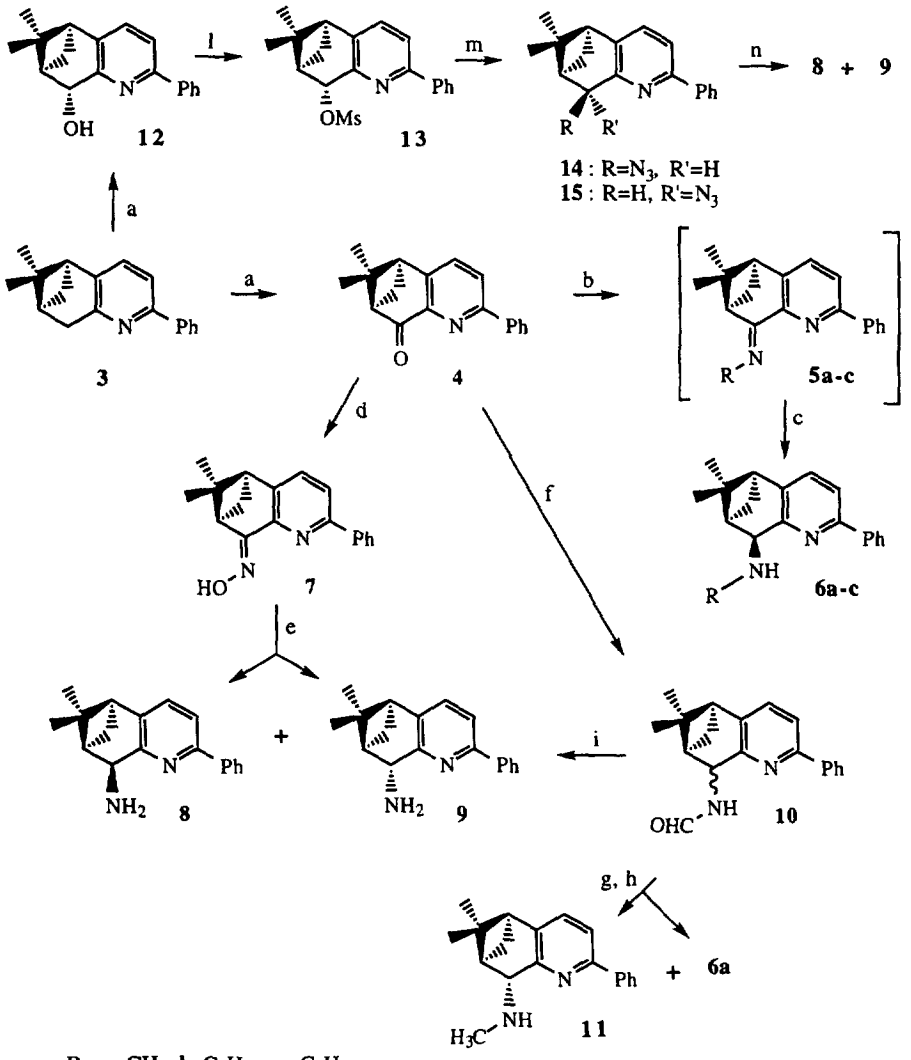
Our investigation for the synthesis of secondary amines derivatives of **3** started from the 2-phenyl-5,6,7,8-tetrahydro-6,6-dimethylmethano-8-quinolone **4** which was accessible from the tetrahydroquinoline **3**[7] following a literature procedure[1,8] (Scheme 1). Thus, the reaction of the proper amine with the ketone **4**, followed by sodium borohydride reduction of the corresponding unisolated imines gave secondary amines **6a–c** in satisfactory yield. The reduction was stereospecific and in all cases the *cis*-stereoisomer was obtained. Then, we turned our attention to the possibility to prepare both epimeric primary amines, from which to obtain the desired N-alkylamino derivative. The synthesis of the primary amines **8** and **9** was accomplished following two ways. Treatment of the ketone **4** with hydroxylamine hydrochloride afforded the corresponding oxime which by reduction with lithium aluminium hydride gave an 8:2 mixture of the *cis* and *trans*-amines **8** and **9**, respectively. This mixture was separated by column chromatography on silica gel to give the diasteromerically pure amines **8** and **9** in overall yield of 48 and 12%, respectively. Also in this case the *cis*-epimer was prevalent. In the latter approach the ketone **4** was transformed with formic acid and formamide (Leuckart reaction) into an 8:2 diastereomeric mixture of formamides **10** (51% yield). This mixture was not separable and then used in the next step without further characterisation. Hydrolysis of **10** under basic conditions, to remove the N-formyl group, afforded the primary amines **8** and **9** in approximately a 2:8 diastereomeric ratio but in very poor yield (7 and 27%, respectively). Although this route does not appear useful to obtain the primary amines **8** and **9**, it allows ready access to the *trans*-N-methylamine **11** which cannot be obtained through the above described reductive amination procedure. In fact, lithium aluminium hydride reduction of **10** gave the methylamine **11** along with its epimer **6a**. The ratio of **11**:**6a** was 65:35 which is fairly different from that of formamides **10**. It is likely that equilibration of the amides **10**, *via* their enol tautomers, occurs during the basic conditions of the lithium aluminium hydride reduction.[9]

A third way to obtain the diastereomerically pure *cis*- or *trans*-amine **8** or **9** from the corresponding diastereomerically pure *trans*- or *cis*-alcohols was also evaluated. In this approach the sequence alcohol-mesylate-azide-amine was followed. Thus, (5S,7S,8R)-8-hydroxy-5,6,7,8-tetrahydro-6,6-dimethyl-2-phenyl-5,7-methanoquinoline **12**[1] was converted into the corresponding mesylate which was treated with sodium azide in DMF. The reaction occurred only at 90°C (24 h)[10] to afford with the azide **14** its unexpected epimer **15** in a 85:15 ratio, respectively (32% overall yield from the alcohol). The formation of an intermediate carbocation, which probably occurs during the nucleophilic displacement of the mesyloxy group by the azido group, explains the stereochemical outcome (formation of the mixture of epimeric azides) and the low yield (owing to isomerization phenomena). Reduction of this unseparable mixture of azides by hydrogen on Pd/C gave the expected amines **8** and **9** in very poor yield and in a 73:27 ratio. It is possible that also in this case a process similar to that previously observed occurs.

With ligands **6a–c**, **8**, **9**, **11** in hand we examined the ability of new ligands to provide asymmetric induction in the palladium catalysed allylic alkylation of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate[11] and in the enantioselective addition of diethylzinc to benzaldehyde.[5]

Allylic alkylation of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate (Table 1)

C_2-symmetric bidentate nitrogen-ligands have been employed successfully to control the enantioselectivity in palladium-catalysed asymmetric allylic substitutions.[11,12] In these ligands the two nitrogens have identical stereoelectronic properties. Since not only steric but also electronic properties effect both rate and stereoselectivity[13] we decided to examine in this catalytic process these new aminopyridines which have two significantly different donor atoms. It should be noted that so far no data has been reported on the use of aminopyridines in palladium-catalysed asymmetric allylic substitutions.[14] Allylic substitutions were carried out employing Trost's procedure which used $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ as procatalyst and a mixture of dimethyl malonate, N,O-bis(trimethylsilyl)acetamide (BSA) and potassium acetate in methylene chloride.[15] Amines provided insufficiently reactive palladium catalysts at room temperature therefore all reactions were carried out at reflux temperature. Under

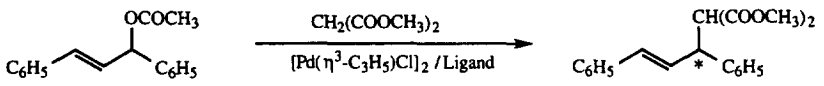


a: literature; b: R-NH_2, catalytic BF_3, benzene, reflux; c: $NaBH_4$, EtOH, r.t.;
d: NH_2OH, EtOH; e: $LiAlH_4$, Et_2O, reflux; f: HCOOH/$HCONH_2$, 120 °C, 7h;
g: $LiAlH_4$, THF, reflux; h: Chromatographic separation; i: KOH, EtOH, reflux, 4h.
l: MsCl, Et_3N, DMAP, CH_2Cl_2, 24h; m: NaN_3, DMF, r.t., 24h; n: Pd/C, H_2, MeOH, 24h.

Scheme 1.

these conditions a complete conversion was achieved in all cases after 48 h to give the reaction product in good yield and in low to moderate enantiomeric excess. A comparison between epimeric amines shows that the *cis*-amine **6a** gave a more reactive palladium catalyst that its *trans*-epimer **11**. Moreover, these ligands gave a similar level of stereodifferentiation but opposite configuration of dimethyl 1,3-diphenylprop-2-enylmalonate indicating that the steric course of the reaction depends on the stereogenic centre bonded to the nitrogen and it is insensitive to the other stereocentres (including the stereogenic centre on the nitrogen atom); therefore, they behave as pseudoenantiomers.[2] Finally, in the *cis*-amine series a higher enantioselectivity is recorded with ligands containing a large substituent on the nitrogen atom.

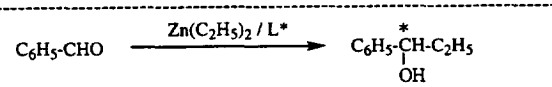
Table 1. Allylic alkylation of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate[a]



Ligand	React. time, h	Yield[b]	% Ee[c]	Conf.[d]
6a	24	95	21	R
6b	20	91	68	R
6c	28	85	40	R
11	48	88	12	S

[a]Reaction of the ligand (10 mol %) and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (2.5 mol %) with 1,3-diphenylprop-2-enyl acetate (0.4 mmol), $CH_2(COOMe)_2$ (1.2 mmol), N,O-bis(trimethyl silyl)acetamide (BSA) (1.2 mmol) and KOAc (3.5 % mol) in CH_2Cl_2 (2 ml) at reflux temperature. [b]Isolated yields. [c]Determined by ^{1}H-NMR using Eu(hfc)3 as chiral shift reagent. [d]The assignement is based on the sign of the specific rotation: Leutenegger, U.; Umbricht, G.; Fahrni, C.; Matt, P.V.; Pfaltz, A. *Tetrahedron*, **1992**, *48*, 2143.

Table 2. Enantioselective addition of diethylzinc to benzaldehyde[a]



Ligand	Time (h)	Yield.[b] (%)	Ee (%)[c]	Conf.[d]
6a	26	81	21	R
6b	5	84	48	R
6c	44	91	22	R
8	30	85	62	R
9	20	87	0	-
11	35	92	9	S

[a]Reaction carried out at 0 °C in hexane/toluene with a molar ratio Et_2Zn/aldehyde/ligand= 2/1/0.05. [b]GLC yield of the crude products.[c]Determined by chiral GC (30 m Beta Dex-120 column, Supelco).[d]Determined from the specific rotation of (S)-1-phenylpropanol: $[\alpha]^{25}_D$ -47.6 ($CHCl_3$): Kitamura, M., Suga, S., Kawai, R., Noyori, R. *J. Am. Chem. Soc.*, **1986**, 108, 6071.

Asymmetric addition of diethylzinc to benzaldehyde[4,16]

The reactions were carried out in hexane–toluene solution in the presence of 5 mol% of ligands at 0°C (Table 2). All catalysts gave 1-phenyl-1-propanol in good yield and in low to moderate enantioselectivities. An examination of Table 2 indicates that the stereochemical outcome depends on the stereogenic centre bonded to the nitrogen. The *trans*-isomers show a lower catalytic activity and enantioselectivity with respect to their *cis*-epimers. Our findings are in accord with the results obtained in the same catalytic process with the epimeric 8-hydroxytetrahydroquinolines **1a** and **1b**.

In summary, we have prepared chelating ligands of the desired type and demonstrated that chiral amino-pyridines can be used as ligands in enantioselective palladium catalysed allylic substitutions. Further studies aimed at the modification of ligand design and application to other catalytic asymmetric reactions are in progress.

Experimental section

General

Melting points were determined on a Buchi 510 capillary apparatus and are uncorrected. The ^{1}H NMR (300 MHz) spectra were obtained with a Varian VXR-300 spectrometer. Optical rotations were measured with a Perkin–Elmer 241 polarimeter in a 1 dm tube. Elemental analyses were performed on a Perkin–Elmer 240 B analyser. Gas chromatographic analyses were performed by a Perkin–Elmer 8600 chromatograph using He_2 as a carrier gas. A 30 m Beta Dex-120 column (Supelco) was employed.

Materials

(5S,7S)-5,6,7,8-Tetrahydro-6,6-dimethyl-2-phenyl-5,7-methano-8-quinolinone **4**[1] ($[\alpha]^{25}_D$ +175.8 (*c* 1.3, $CHCl_3$)) and (5S,7S,8R)-8-hydroxy-5,6,7,8-tetrahydro-6,6-dimethyl-2-phenyl-5,7-methano-quinoline **12**[1] ($[\alpha]^{25}_D$ +5.15 (*c* 0.9, $CHCl_3$)) were prepared according to reported procedures.[7]

*(5S,7S,8S)-8-Alkyl-5,6,7,8-tetrahydro-6,6-dimethyl-2-phenyl-5,7-methanoquinoline, **6a–c***

Compounds **6a–c** were prepared by condensation of the tetrahydroquinolinone **4** with the proper amine (cyclohexylamine or phenylamine) in a Dean–Stark apparatus (benzene, catalytic BF_3, 24 h) followed by sodium borohydride reduction of the crude imine intermediate.[17] The methylimine **5a** was obtained by reaction of **4** with a 33% ethanolic solution of methylamine in a sealed tube at 60°C for 24 h.

*(5S,7S,8S)-8-Methylamino-5,6,7,8-tetrahydro-6,6-dimethyl-2-phenyl-5,7-methanoquinoline, **6a***

This compound was obtained as an oil in 52% overall yield after chromatography on silica gel (petroleum ether:ethyl acetate/7:3): $[\alpha]^{25}_D$ +96.7 (*c* 1.8, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 8.02 (d, 2H), 7.52–7.24 (m, 5H), 3.95 (s, 1H), 2.77 (overlapping, 2H), 2.72 (s, 3H), 2.63 (m, 1H), 1.45 (s, 3H), 1.41 (overlapping, 1H), 0.75 (s, 3H). *Elem. Anal.*, found % (calcd. for $C_{19}H_{22}N_2$) C, 81.77 (81.97); H, 7.91 (7.97); N, 10.26 (10.06).

*(5S,7S,8S)-8-Cyclohexylamino-5,6,7,8-tetrahydro-6,6-dimethyl-2-phenyl-5,7-methanoquino line, **6b***

This compound was obtained in 76% overall yield after chromatography on silica gel (petroleum ether:ethyl acetate/7:3): mp 73–74°C; $[\alpha]^{25}_D$ +82.6 (*c* 1.2, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 8.04 (d, 2H), 7.49–7.30 (m, 4H), 7.24 (d, 1H), 4.20 (s, 1H), 2.92 (m, 1H), 2.71 (m, 2H), 2.49 (m, 1H), 2.08 (m, 2H), 1.96 (m, 1H), 2.80 (m, 1H), 1.94 (m, 1H), 1.46–1.11 (m, 6H), 1.45 (s, 3H) 0.77 (s, 3H). *Elem. Anal.*, found % (calcd. for $C_{24}H_{30}N_2$) C, 83.37 (83.19); H, 8.64 (8.73); N, 8.26 (8.08).

*(5S,7S,8S)-8-Phenylamino-5,6,7,8-tetrahydro-6,6-dimethyl-2-phenyl-5,7-methanoquinoline, **6c***

This compound was obtained in 56% overall yield after chromatography on silica gel (petroleum ether:ethyl acetate/9:1): mp 164–5°C; $[\alpha]^{25}_D$ +90.6 (*c* 1.1, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 8.05 (d, 2H), 7.57 (d, 1H), 7.49–7.20 (m, 6H), 6.90–6.71 (m, 3H), 4.83 (s, 1H), 4.71 (s, 1H), 2.83 (m, 3H), 1.60 (d, 1H), 1.45 (s, 3H), 0.77 (s, 3H). *Elem. Anal.*, found % (calcd. for $C_{24}H_{24}N_2$) C, 84.47 (84.67); H, 7.22 (7.11); N, 8.16 (8.23).

*(5S,7S,8S)- and (5S,7S,8R)-8-Amino-5,6,7,8-tetrahydro-6,6-dimethyl-2-phenyl-5,7-methanoquinoline, **8 and 9***

Compounds **8** and **9** were prepared by condensation of the tetrahydroquinolinone **4** with hydroxylamine hydrochloride followed by lithium aluminium hydride reduction of the crude oxime intermediate, according to a known procedure.[18] The reduction gave a 8:2 mixture of epimeric amines **8** and **9** which were separated by chromatography on silica gel eluting with ethyl acetate:petroleum ether:ethyl ether/7:3:2.

*(5S,7S,8S)-8-Amino-5,6,7,8-tetrahydro-6,6-dimethyl-2-phenyl-5,7-methanoquinoline, **8***

This compound was obtained as oil in 48% overall yield: $[\alpha]^{25}_D$ +117.9 (*c* 1.1, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 8.03 (d, 2H), 7.52–7.24 (m, 5H), 4.24 (s, 1H), 2.77 (m, 2H), 2.52 (m, 1H), 2.15 (s, 2H), 1.47 (s, 3H), 1.41 (m, 1H), 0.79 (s, 3H). *Elem. Anal.*, found % (calcd. for $C_{18}H_{20}N_2$) C, 81.96 (81.77); H, 7.47 (7.63); N, 10.44 (10.60).

*(5S,7S,8R)-8-Amino-5,6,7,8-tetrahydro-6,6-dimethyl-2-phenyl-5,7-methanoquinoline, **9***

This compound was obtained as oil in 12% overall yield: $[\alpha]^{25}_D$ +23.3 (*c* 0.4, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 8.01 (d, 2H), 7.55–7.22 (m, 5H), 4.20 (s, 1H), 2.83 (m, 1H), 2.64 (m, 1H), 2.39 (m, 1H), 1.96 (s, 2H), 1.45 (m, 3H), 1.41 (m, 1H), 0.72 (s, 3H). *Elem. Anal.*, found % (calcd. for $C_{18}H_{20}N_2$) C, 81.98 (81.77); H, 7.41 (7.63); N, 10.56 (10.60).

*8-N-Formylamino-5,6,7,8-tetrahydro-6,6-dimethyl-2-phenyl-5,7-methanoquinoline, **10***

A solution of ketone **4** (1.58 g, 0.6 mol), formamide (15.8 ml) and formic acid (9.5 ml) was heated at 120°C for 7 h. The cooled solution was alkalised with a 5% sodium hydroxide solution and extracted with ethyl ether. The separated organic phase was dried over anhydrous Na_2SO_4, evaporated and the residue purified by flash chromatography (eluent: petroleum ether/ethyl acetate:1/1). The mixture of compounds which corresponded to a spot on TLC with Rf=2.3–2.5 (SiO_2, petroleum ether/ethyl acetate:1/1) was collected. This mixture (0.9 g) was used in the next step without further characterization.

*Hydrolysis of **10***

A solution of the formamide **10** (0.41 g) in ethanol (3.3 ml) and a 10% molar solution of potassium hydroxide (0.33 ml) was heated under reflux for 4 h. The mixture was diluted with water and extracted with ethyl ether. The separated organic phase was dried over anhydrous Na_2SO_4, evaporated and the residue purified in usual way to give pure **8** (25 mg, 7%, 3.6% from **4**) and **9** (101 mg, 27%, 14% from **4**).

*(5S,7S,8R)-8-Methylamino-5,6,7,8-tetrahydro-6,6-dimethyl-2-phenyl-5,7-methanoquinoline **11***

A solution of the formamide **10** (0.45 g) was added dropwise to a suspension of lithium aluminium hydride (134 mg) in THF (10 ml) and the mixture heated under reflux for 30 min. The mixture was cooled, water was carefully added and the mixture extracted with CH_2Cl_2. The separated organic phase was dried over anhydrous Na_2SO_4, evaporated and the residue purified by chromatography on neutral aluminium oxide (eluent: ether/petroleum ether/ethyl acetate:2/6/7) to give pure **11** (130 mg, 32%) and **6a** (70 mg, 17%). Compound **11** was obtained as an oil: $[\alpha]^{25}_D$ +168.0 (*c* 0.8, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 8.00 (d, 2H), 7.53–7.23 (m, 5H), 3.89 (s, 1H), 2.79 (t, 1H), 2.69–2.45 (m, 3H), 2.64 (s, 3H), 1.51 (d, 1H), 1.47 (s, 3H), 0.72 (s, 3H). *Elem. Anal.*, found % (calcd. for $C_{19}H_{22}N_2$) C, 81.76 (81.97); H, 7.81 (7.97); N, 10.11 (10.06).

*(5S,7S,8R)- and (5S,7S,8R)-8-Azido-5,6,7,8-tetrahydro-6,6-dimethyl-2-phenyl-5,7-metha noquinoline, **14** and **15***

Methanesulfonyl chloride (1.15 g, 10 mmol) in CH_2Cl_2 (7 ml) was added at 0°C to a solution of **12** (1.77 g, 6.68 mmol), triethylamine (2.14 ml), 4-(dimethylamino)pyridine (95 mg) in CH_2Cl_2 (20 ml). The resulting solution was stirred at 0°C for 10 min and then at room temperature for 24 h. The reaction mixture was poured into a $NaHCO_3$ solution, the organic phase separated, washed with H_2O, dried on Na_2SO_4 and the solvent removed under reduced pressure. The obtained mesylate (^{1}H-NMR ($CDCl_3$): δ 7.94 (d, 2H), 7.60 (d, 1H), 7.49–7.38 (m, 4H), 5.83 (d, 1H), 4.41 (s, 3H), 2.85 (t, 1H), 2.73 (m, 2H), 1.72 (d, 1H), 1.52 (s, 3H), 0.72 (s, 3H)) was used in the next step without further purification. The crude mesylate was taken up in N,N-dimethyl formamide (13 ml) and sodium azide (1.3 g) was added a portion. After 24 h at 90°C the solvent was evaporated under reduced pressure and the residue purified by chromatography on silica gel (CH_2Cl_2) to afford a 85:15 mixture of unseparable

diastereomeric azides in 32% overall yield from the alcohol: ^{1}H-NMR ($CDCl_3$, selected data): (major diastereomer) δ 5.04 (s, 1H), 1.45 (s, 3H), 0.79 (s, 3H); (minor diastereomer) δ 4.90 (s, 1H), 1.42 (s, 3H), 0.72 (s, 3H).

*Reduction of azides **14** and **15***

A mixture of **14** and **15** (0.6 g) and 10% Pd/C (50 mg) in methanol (10 ml) was reduced by H_2 at atmospheric pressure and room temperature for 24h. The solvent was evaporated under reduced pressure and the residue purified in usual way to give pure **8** (120 mg, 22%; 7% from **12**) and **9** (44 mg, 8%; 3% from **12**).

Allylic alkylation of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate: general procedure

A solution of ligand (0.04 mmol, 10 mol%) and [{Pd(η^3-C_3H_5)Cl}$_2$] (4 mg, 2.5 mol%) in dry CH_2Cl_2 (2 ml) was stirred at room temperature for 15 min. This solution was treated successively with a solution of *rac*-(E)-1,3-diphenyl-2-propenyl acetate (0.4 mmol) in CH_2Cl_2 (1 ml), dimethyl malonate (1.2 mmol), N,O-bis(trimethylsilyl)acetamide (1.2 mmol) and anhydrous potassium acetate (3.5 mol%). The reaction mixture was stirred for the appropriate time (see Table 1) until conversion was complete as shown by TLC analysis [light petroleum:ether/3:1]. The reaction mixture was diluted with ether (25 ml), washed with ice-cold saturated aqueous ammonium chloride. The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash chromatography [light petroleum:ether/3:1] to afford dimethyl 1,3-diphenylprop-2-enylmalonate. The enantiomeric excess was determined from the ^{1}H-NMR spectrum in the presence of enantiomerically pure shift reagent Eu(hfc)$_3$; splitting of the signals for one of the two methoxy groups was observed.

Addition of diethylzinc to benzaldehyde: typical procedure

A solution of ligand (0.15 mmol) in toluene (3 ml) was cooled at 0°C. A 1 M solution of diethylzinc in hexane (6 ml, 6 mmol) was added over a period of 5 min. The mixture was stirred at room temperature for 20 min, cooled at 0°C, added with benzaldehyde (0.3 ml, 0.323 g, 3 mmol) and then stirred at room temperature for the appropriate time (see Table 2). The reaction mixture was quenched with 10% H_2SO_4 (5 ml) and extracted with ether. The organic layer was washed with 10% H_2SO_4, saturated $NaHCO_3$, and dried (Na_2SO_4). The solvent was evaporated and the residue purified by flash chromatography to afford pure (GLC) 1-phenylpropanol.

Acknowledgements

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