PERKIN 1

# Phosphane ligands with two binding sites of differing hardness for enantioselective Grignard cross coupling†

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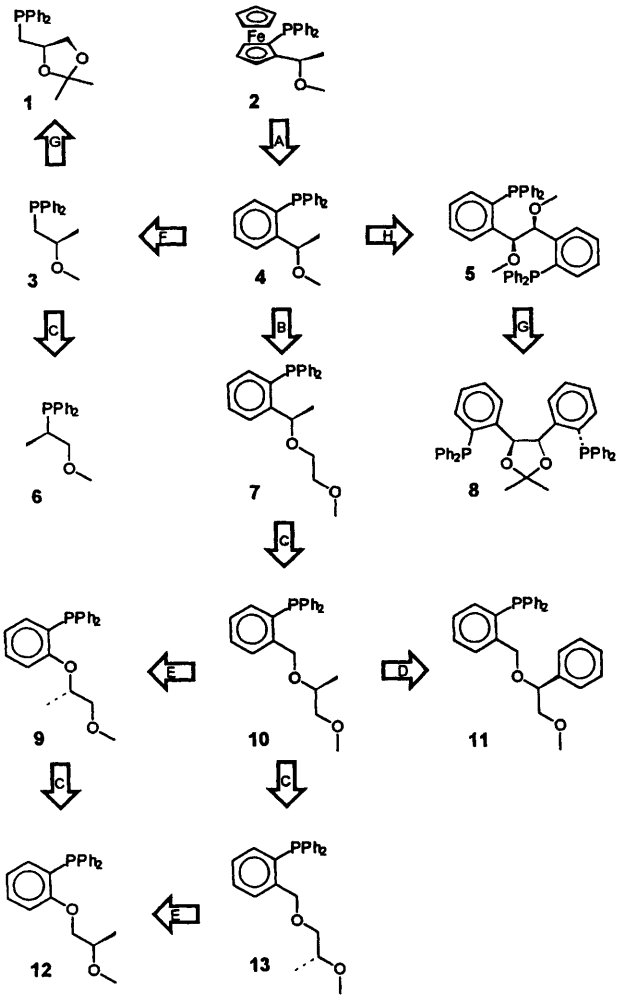
**A series of new, chiral phosphanes is presented, individual members of which were designed to serve as ligands in transition-metal mediated asymmetric Grignard cross coupling reactions. These ligands are characterized by a side chain containing one or two oxygen atoms with the capacity to act as binding sites for the incoming Grignard reagent. A number of structural parameters for the compounds was varied to learn about the reaction mechanism. Most of the ligands were tested in two cross coupling reactions, the formation of 3-phenylbut-1-ene and of 2,2′-dimethyl-1,1′-binaphthyl, respectively. Although both systems gave modest enantiomeric excesses it was not possible to make a comparison of their respective abilities.**



Grignard cross coupling offers the possibility of combining two large molecular fragments *via* carbon–carbon bonds, the resulting stereochemistry of which can be controlled by the use of chiral modified transition-metal catalysts.[1–3] These catalysts often consist of a nickel(II) halide and a chiral phosphane ligand which form *in situ* the active $Ni^0$ species. The mechanism of this reaction is well elucidated.[4] The choice of ligand for a particular Grignard cross coupling reaction is still empirical, little being known about the structural and electronic demands for individual members. Recently, Hayashi reported very good enantioselectivities in the formation of atropisomeric binaphthyls when oxygen-containing ferrocenyl phosphanes such as PPFOMe **2** (Scheme 1) were used as co-catalysts.[5] Oxygen-free homologues of these ligands resulted in a significant decrease of the enantioselectivities (from 95 to 1% ee). This is explained in terms of the formation of a complex not only with the nickel atom but also with the Grignard reagent, resulting in a pre-reaction approach. This result also suggested that the origin of the stereochemistry is the chirality of the side chain rather than the chirality of the ferrocene moiety.

This background led us to synthesize a series of new, easily accessible oxygen-containing phosphanes, the chirality of which would be either of natural origin or obtained by highly efficient asymmetric syntheses to avoid tedious resolution procedures. Our goal was controlled variation of the binding properties of the new ligands towards nickel and magnesium to give a more detailed insight into the mechanism of chirality transfer. Thus, starting from Hayashi's most efficient ligand PPFOMe, the first step was a switch from the ferrocene backbone to a benzene moiety (step **A**, Scheme 1).

Since this results in the loss of the planar chirality, chiral information is only available from the stereogenic carbon atom in the side chain of **4**. Elongation of the alkoxy side chain to a diether moiety (step **B**) should increase the binding constant in **7** towards Grignard reagents. In this elongated chain, the chiral centre was shifted to each of the positions possible (step **C**, ligands **10**–**13**) to gather information about the influence of the distance of the stereogenic centre from the nickel atom. In addition, ligand **11** bearing a phenyl group instead of a methyl group on the stereogenic centre, was synthesized (step **D**) together with the two ligands **9** and **12** with shortened diether side chains (step **E**). In a further reduction of the ligand backbone, the omission of the benzene moiety (step **F**) should



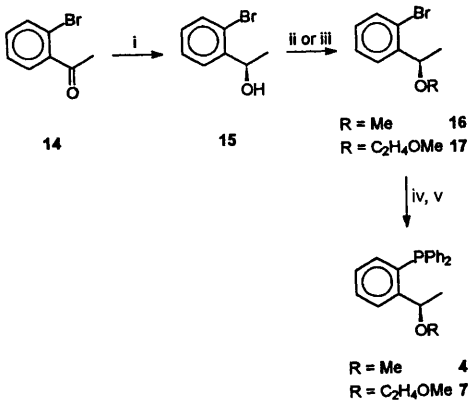

**Scheme 1** Genealogy of the phosphanes presented in this paper. PPFOMe **2** is a very efficient ligand described in literature. The letters within the arrows characterize the topological transformations (not chemical reactions). **A** = Substitution of the ferrocene moiety by a benzene ring; **B** = increase of the binding properties of the 'hard' binding site by elongation; **C** = shift of the stereogenic centre; **D** = substitution of the relatively small methyl group by the larger phenyl group; **E** = shortening of the distance 'hard'–'soft' binding site; **F** = omission of the arene moiety; **G** = rigidization of the molecule and increase of the donor capability of the oxygen atoms; **H** = increase of the complex formation constant by formal doubling of the molecule.

† Enantioselective catalyses. Part 99. For part 98, see H. Brunner, J. Bügler and B. Nuber, *Tetrahedron: Asymmetry*, 1995, **6**, 1699.

lead to an increase in the electron density at the phosphorus atom together with a reduction of the ligand cone angle.[6] Two of these ligands, **3** and **6**, bearing the stereogenic centre in the two positions possible, were prepared. In addition, the known ligand glyphos **1**[7] was tested. This ligand has a structure similar to that of **3**, although the oxygen atoms have higher donor capability as a result of their position within a five-membered ring (step **G**). A further approach to favour complex formation is the use of bidentate ligands investigated by a formal doubling of ligand **4** (step **H**). Conformational rigidity, and thus more defined transition states, in addition to the increased basicity of the oxygen atoms should be introduced in **8** by the formation of a dioxolane using the backbone of **5** (step **G**).

### Preparation of the ligands

The synthesis of compound **4** started with the enantioselective hydrogenation of 2-bromophenyl methyl ketone **14** in the presence of a Ru(binap) catalyst, as described by Takaya and Noyori,[8] yielding 1-(2′-bromophenyl)ethanol **15** in an optical purity of 60–80% ee (Scheme 2).




**Scheme 2** i, 100 bar $H_2$, 80 °C, Ru(R)BINAP, 75%; ii, $(MeO)_2SO_2$, KOH, DMSO, 91%; iii, $MeOC_2H_4OTos$ **18**, KOH, DMSO, 97%; iv, Mg; v, $ClPPh_2$, (70% for **4**, 77% for **7**)

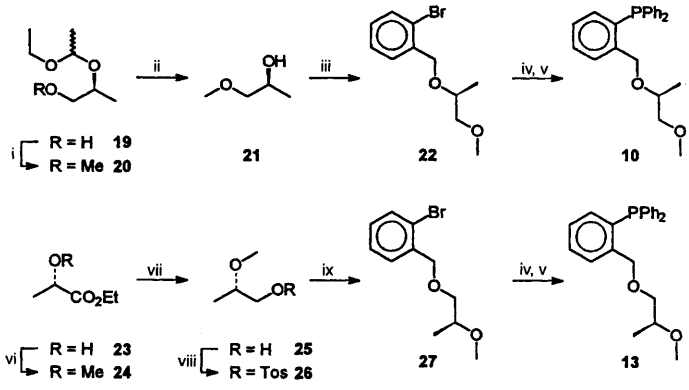
Since compound **15** crystallized as a conglomerate from light petroleum, it was easily enriched to enantiopurity by two crystallizations. Thus, when solutions were seeded with the enantiomerically pure major isomer, the mother liquors were enriched in the minor enantiomer. In a typical preparation, the crude product with an optical purity of 60% gave, after two crystallizations, the optically pure product in a chemical yield of 75%. Nevertheless, attempts to separate racemic 1-(2′-bromophenyl)ethanol (a liquid) by this procedure have not yet been successful.

Both enantiomers of **15** were etherified using a modified Williamson synthesis[9,10] to yield 91% of the methyl ethers **16** without racemization. In this modified procedure[9,10] the alkoxide was generated by the use of an excess of powdered potassium hydroxide in dimethyl sulfoxide (DMSO) at room temperature, followed by the addition of an alkylating agent, such as an alkyl halide, sulfonate or sulfate. After a short reaction time the product could be extracted either directly or, after dilution with water, with light petroleum, a solvent which did not dissolve significant amounts of DMSO. In contrast to most of the common etherification procedures, this operation yielded the desired products in high yields and, after a short column filtration, in high purity, without any racemization of neighbouring stereogenic centres. Diols may be monoalkylated in good yields by the use of only 1 equiv. of the alkylating agent. The reaction is limited to substrates without hydrolysable groups, *e.g.* esters, and acidic protons other than alcoholic OH protons, which can also be alkylated. Benzyl halides have to be used at temperatures < 20 °C to avoid Kornblum reactions.

The methyl ether **16** was treated with magnesium to form the corresponding Grignard reagent, which was quenched with chloro(diphenyl)phosphane to give 70% of the desired phosphane **4** as large crystals after two crystallizations from methanol.

The preparation of ligand **7** with a diether side chain proceeded analogously (Scheme 2). 2-Methoxyethyl toluene-*p*-sulfonate **18** (obtained from methoxyethanol and tosyl chloride in 65% yield) was used in the etherification of **15** resulting in 97% of the diether **17**. Since separation of the product **17** from the sulfonate **18** proved difficult, the latter was converted into volatile 1,2-dimethoxyethane by adding an excess of methanol to the reaction mixture before work-up. The transformation of **17** to the phosphane **7** *via* the Grignard reagent was carried out as in the case of **4** to give a 77% yield of colourless crystals (from methanol). In this context, it is noteworthy that while the magnesium salts formed during the phosphanylation of **4** were precipitated as a white solid, in the synthesis of the diether product **7** the reaction mixture stayed clear. This phenomenon demonstrates that compared with simple ethers diether ligands form more stable complexes with magnesium reagents.

To obtain the diether ligands **10** and **13** with stereogenic centres in the 3- and 4-position respectively, the chiral starting materials were lactic acid derivatives from the natural chiral pool. The synthesis of the enantiomers of **10** started with the transformation of lactic acid esters into the respective propane-1,2-diols **19** protected in the 2-position by an acetal group, following a literature procedure.[11] Methylation of the remaining alcohol group in **19** utilizing the KOH–DMSO procedure resulted in good yields of the desired ether **20**. Losses may occur in this step owing to the unlimited miscibility of the product in water. Removal of the protecting acetal group by acid hydrolysis gave the chiral ether alcohol **21** which was alkylated with 2-bromobenzyl bromide under the conditions described above (Scheme 3). The yield of the product **22**

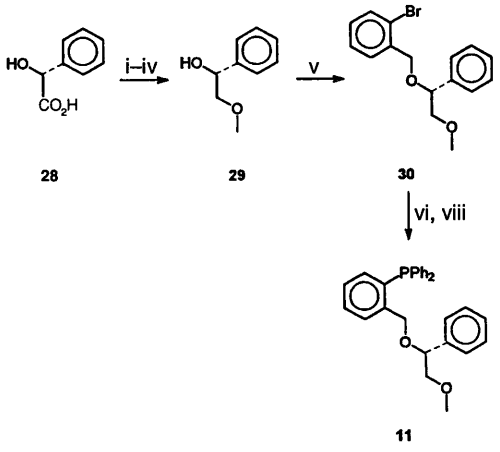



**Scheme 3** i, $(MeO)_2SO_2$, KOH, DMSO (73–89%); ii, $H_2O$, $H^+$, (79–85%); iii, 2-$BrC_6H_4CH_2Br$, KOH, DMSO (52%); iv, Mg; v, $ClPPh_2$ (84% for **10**, 82% for **13**); vi, NaH, $(MeO)_2SO_2$, 83–91%; vii, $LiAlH_4$, 77%; viii, TosCl, py, 96%; ix, 2-$BrC_6H_4CH_2OH$, KOH, DMSO, 52%

was only 52% owing to side reactions of the benzyl halides mentioned above. The conversion of **22** into the ligand **10** *via* the Grignard reagent gave an 84% yield of product (colourless oil).

The synthesis of ligand **13** began with the *O*-methylation of ethyl lactate **23** (Scheme 3). In this case the KOH–DMSO method could not be used owing to hydrolysis of the ester function (*vide infra*). The generation of the alkoxide ion with sodium hydride and its reaction with methyl iodide or dimethyl sulfate according to standard Williamson procedures led to more or less complete racemization because of the relatively high acidity of the proton in the α-position to the carboxy group. In this case, a method developed by Seebach *et al.*[12] for the etherification of tartaric acid esters demonstrated its efficacy. The addition of a mixture of (*S*)-ethyl lactate and

dimethyl sulfate to a suspension of sodium hydride in diethyl ether at −10 to −5 °C led to (2*S*)-ethyl 2-methoxy-propanoate **24** in good yields without any detectable loss in enantiopurity.‡ This ester was reduced with lithium aluminium hydride to give (2*S*)-2-methoxypropanol **25** in 77% yield. Interestingly, the optical rotation of this product was reproducibly almost double that of the highest rotation reported in the literature.[13] The transformation into the toluene-*p*-sulfonate **26** gave nearly quantitative yields of a colourless oil, which was used to alkylate 2-bromobenzyl alcohol in the presence of KOH to yield **27** in 93% yield. The substitution of the bromine atom by the diphenylphosphino group to **13** (Scheme 3) proceeded in 82% yield (colourless oil). The formation of ligand **11** bearing the phenyl group at the stereogenic centre proceeded according to that of **10**. Instead of lactic acid esters, the chiral synthon was mandelic acid **28**, which was fully protected by means of ethyl vinyl ether (Scheme 4). Reduction with lithium aluminium



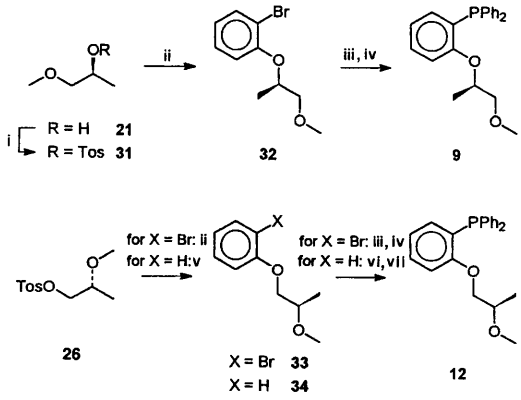

**Scheme 4** i, $EtOC_2H_3$, $H^+$; ii, $LiAlH_4$; iii, $(MeO)_2SO_2$ KOH, DMSO; iv, $H_2O$, $H^+$ (91% from **28**); v, 2-$BrC_6H_4CH_2Br$, KOH, DMSO, 82%; vi, Mg; vii, $ClPPh_2$ (50%)

hydride without prior purification yielded the monoprotected diol which was not purified either. Methylation of the alcohol function using the KOH–DMSO method, and hydrolysis of the acetal function resulted after a single distillation in the chemically and optically pure ether alcohol **29** in a 91% yield. This alcohol was alkylated with 2-bromobenzyl bromide as described for **22**, followed by the usual bromine–diphenylphosphane exchange giving **11** as a yellowish syrup.

For the preparation of ligands **9** and **12** with the shortened diether side chain the building blocks **31** and **26**, derived from lactic acid, were utilized. Thus, the alcohol **21** was first transformed into its toluene-*p*-sulfonate **31** and then etherified with 2-bromophenol in DMF using potassium *tert*-butoxide as base (Scheme 5). The exchange of the bromine in **32** by the diphenylphosphino moiety proceeded in the usual manner, yielding the phosphane **9** (colourless oil).

The isomeric phosphane **12** was obtained similarly by alkylation of 2-bromophenol with the tosylate **26** and the usual Br–$PPh_2$-substitution (Scheme 5). The phosphane **12** crystallized from methanol in the form of colourless needles. A further point of entry into this class of phosphane ligands has been tested. To avoid the use of the relatively expensive *ortho*-brominated arenes, such as 2-bromophenol or 2-bromobenzyl bromide, *ortho*-lithiation was checked as an alternative approach (Scheme 5). Thus, the diether **34** was synthesized by coupling phenol with **26**. The lithiation of the arene of **34** with butyllithium–TMEDA followed by addition of chloro-(diphenyl)phosphane resulted in the regioselective formation

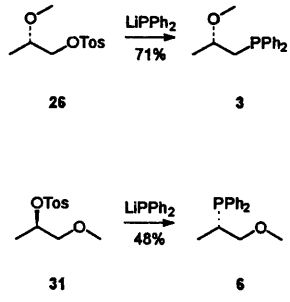
‡ The (*S*)-ethyl lactate used had an optical purity of 94%. Thus, all phosphanes derived from it had only this enantiomeric excess. An exception was **12**, which could be crystallized to enantiopurity.




**Scheme 5** i, TosCl, py (84–91%); ii, 2-$BrC_6H_4OH$, $KOBu^t$, DMF (68% for **32**, 81% for **33**); iii, Mg; iv, $ClPPh_2$ (79% for **9**, 65% for **12**); v, $C_6H_5OH$, $KOBu^t$, DMSO (87%); vi, BuLi, TMEDA; vii, $ClPPh_2$ (48%)

of **12** in 48% yield. For future work in this area, especially on the preparation of bulk amounts, this approach would be preferred.

The syntheses of the alkyldiarylphosphane ligands **3** and **6** proceeded by reaction of lithium diphenylphosphide with the tosylates **26** and **31**, respectively. Both phosphanes were obtained in satisfying yields (71 and 48%) in the form of colourless, very air-sensitive liquids (Scheme 6). The formation

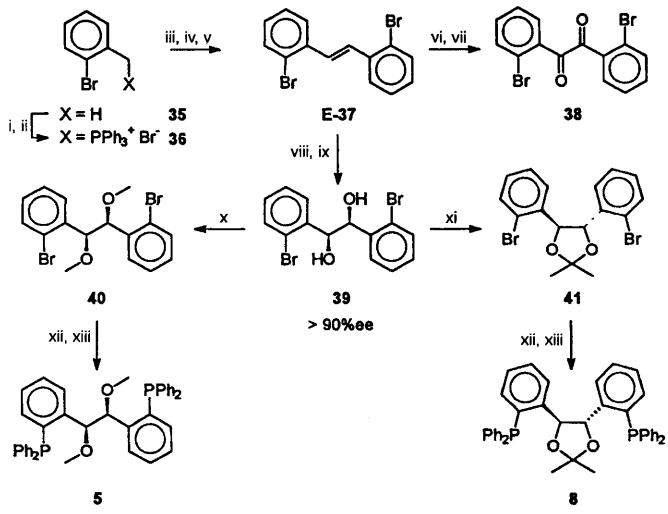



**Scheme 6**

of **6** is thought to occur by Walden-inversion, but since no solid derivative of this substance could be obtained of a quality sufficient for use in X-ray analysis, the stereochemical assignment of **6** remains tentative (retention of configuration due to a double $S_N2$-reaction because of the neighbouring group effect of the methoxy moiety would be the alternative).

For the syntheses of the chelating phosphanes **5** and **8** no appropriate starting material was available from the chiral pool. Consequently, these ligands had to be obtained by asymmetric synthesis. The enantioselective dihydroxylation (ADH) developed by Sharpless is a method for the production of chiral 1,2-diols starting from alkenes of *E* configuration with high enantiopurity.[14] Thus, the dibromo substituted diol **39** (Scheme 7) could be prepared by catalytic, asymmetric dihydroxylation of (*E*)-2,2′-dibromostilbene *E*-**37**.[15] This stilbene was synthesized by a Wittig reaction of 2-bromobenzyl(triphenyl)phosphonium bromide **36** with 2-bromobenzaldehyde as described in the literature[15] (Scheme 7). Compound **36** was obtained in 88% yield by bromination of 2-bromotoluene **35** followed by quaternization with triphenylphosphane without intermediate purification. In contrast to the usual systems, which result in exclusive formation of the (*E*)-stilbenes,[16] this Wittig reaction yielded a 3:7 mixture of *E*- and *Z*-product (*E*-**37** and *Z*-**37**, respectively). The components *E*-**37** and *Z*-**37** can be separated by fractional crystallization from methanol, from which the product *Z*-**37** crystallized first.

It was necessary to interconvert the *Z*-species to obtain acceptable amounts of the desired *E*-stilbene. This could be achieved by irradiation of the crude stilbene mixture with sunlight in the presence of catalytic amounts of iodine in




**Scheme 7** For the catalytic, asymmetric dihydroxylation of stilbene *E*-**37** the addition of methanesulfonamide proved to be essential to yield the product **39**. Without this promotor, the dione **38** was the main product. The diol **39** was obtained with over 90% ee, but could not be enriched to enantiopurity. The enrichment was achieved at the stage of **40** and **41** by crystallization. i, NBS, *hν*; ii, $PPh_3$ (88% from **35**); iii, NaOEt; iv, 2-$BrC_6H_4CHO$; v, *hν*, heptane (68% from **36**); vi, $OsO_4$, quinine 4-chlorobenzoate; vii, $Na_2SO_3$, (~40%); viii, $OsO_4$, quinine 4-chlorobenzoate, $CH_3SO_2NH_2$; ix, $Na_2SO_3$ (~40%); x, $(MeO)_2SO_2$, KOH, DMSO (91%); xi, 2,2-dimethoxypropane, $H^+$ (76–80%); xii, Mg; xiii, $ClPPh_2$, (51% for **5**, 40% for **8**).

heptane.[15] The *E*-isomer crystallized directly within days, giving a 68% overall yield (relatively to the phosphonium salt **36**) after one additional crystallization from heptane.

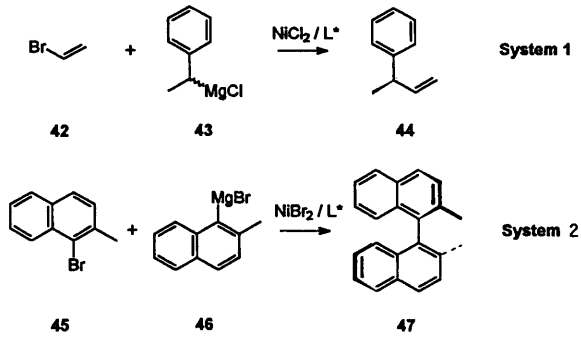
First attempts to dihydroxylate *E*-**37** using the standard catalytic ADH-procedure failed to give any product. After increasing the reaction time to weeks, a yellow crystalline material could be isolated in low yield, which turned out to be 2,2′-dibromobenzil **38**. As determined in separate experiments, benzils are formed upon elongated treatment of diphenylglycols under the usual ADH conditions (alkaline $[Fe(CN)_6]^{3-}$). Thus, to increase the rate of product formation with respect to its oxidation, the substrate:catalyst ratio had to be lowered to 100:1. In addition, methanesulfonamide had to be added as a promotor, a reagent which has proven to be beneficial for certain substrates.[17] Under these conditions both enantiomers of the desired product could be obtained in good chemical yield (60–70%) and high enantioselectivity (up to 95%) by using the esters of 4-chlorobenzoic acid with quinine and quinidine, respectively. Unfortunately, an enrichment to enantiopurity could not be achieved by crystallization. From methylene dichloride, the solvent used in the literature,[15] the racemate crystallized preferentially, but this method could not be used for an efficient enrichment of the optically active product in the mother liquor. Thus, the enrichment had to be done during the next preparation steps. For the synthesis of the bisphosphane **5**, the diol **39** was dimethylated *via* the KOH–DMSO method to yield 79% of the enantiomerically pure ether **40** after crystallization from methanol (Scheme 7). The final transformation to the bisphosphane **5** (colourless crystals) by the Grignard reagent proceeded in acceptable yield after crystallization from cyclohexane.

To obtain the rigid dioxolane phosphane **8**, the diol **39** was converted into the cyclic ether **41** by treatment with 2,2-dimethoxypropane under acidic conditions. Compound **41** could be enriched to enantiopurity by one or two crystallizations from light petroleum. The transformation into the bisphosphane **8** proceeded in only 40% yield, which could be a result of the increased steric hindrance in **8**. The $^1H$ NMR spectrum of **8** showed exceptional complexity in the aromatic region compared to that of **5**. Even after several crystallizations of **8** from methanol, a sharp melting point could not be obtained. We were not able to obtain the bisphosphanes **5** and **8** by *ortho*-lithiation of the respective (nonhalogenated) ethers.

The preparations of the ferrocenyl-containing ligand (*R*,1*S*)-PPFOMe **2**[18] and the dioxolane ligand Glyphos **1**[7] followed literature procedures.

## The catalytic systems

Most of the new optically active ligands were checked for their efficacy in two catalytic Grignard cross coupling systems (Scheme 8).




**Scheme 8** The two Grignard cross coupling systems used for testing the new ligands

The first one is the standard system of the literature. It was used to compare the new ligands with those already described. In this system, 1-phenylethylmagnesium chloride is coupled with bromoethene in the presence of nickel(0)–phosphane complexes. During this reaction one of the enantiomeric Grignard reagents formed in the fast racemization at C-1 reacts faster than the other in the sense of a kinetic resolution. This reaction usually results in medium enantioselectivities,[3b] except for some very effective systems giving selectivities up to 94%.[19]

Only *in situ* catalyses were performed, although isolated complexes usually yield higher enantioselectivities.[20] The respective ligand and nonhydrated nickel(II) chloride were mixed in dry diethyl ether at −78 °C and bromoethene and a solution of the Grignard reagent in ether were added subsequently. The mixture was allowed to warm to room temperature over 12 h before the yield and enantiomeric excess were determined by gas chromatography. Owing to the volatility of bromoethene and side reactions during the preparation of the Grignard reagent (formation of styrene by elimination and 2,3-diphenylbutane by spontaneous cross coupling) the chemical yields were in the lower range (20–60%) when using our small-scale procedure (< 1 g).

The second system allows the preparation of non-racemic, atropisomeric binaphthyls, a class of compounds successfully used as ligands in asymmetric synthesis.[21] The enantioselective formation of 2,2′-dimethyl-1,1′-binaphthyl **47** by Grignard cross coupling has been reported with varying results.[22] Since this product has $C_2$ symmetry, it seemed favourable to generate both halves from the same starting material 1-bromo-2-methylnaphthalene, which is accessible by iron-catalysed bromination of 2-methylnaphthalene.[23] As shown by GC§ and highfield NMR, the product obtained by this procedure contained about 6% of isomeric bromomethylnaphthalenes. To remove these impurities, which could not be separated by fractional distillation, a purification method was applied, which utilized the steric shielding of the bromine atom in 1-bromo-2-methylnaphthalene. In a Grignard cross-coupling reaction with

§ The following conditions proved to be useful for GC-analysis: 50 m capillary OV101 (0.3 mm i.d.), column temp. 150 °C, injector temp. 250 °C, FID temp. 250 °C, mobile phase: 2.0 bar $H_2$. A 0.4 $mm^3$ aliquot of a 0.75% sample solution in $CH_2Cl_2$ was injected. The retention time of 1-bromo-2-methylnaphthalene was 11.7 min.

sub-stoichiometric amounts of methylmagnesium bromide, 1-bromo-2-methylnaphthalene reacted significantly slower than its isomers.[24] The dimethylnaphthalenes formed were easily separated by fractional distillation, yielding 1-bromo-2-methylnaphthalene without any GC-detectable amounts of isomers.

In the Grignard cross-coupling reaction the coupling of the halogenoarene with the Grignard reagent is usually performed by preparing the Grignard reagent separately and mixing both in the presence of the catalyst. For the preparation of the $C_2$ symmetric coupling product **47** the starting material for the Grignard reagent is the halogenoarene itself. This led us to set up a simplified procedure, in which 2 equiv. of the halogenoarene were allowed to react with 1 equiv. of magnesium to give a 1:1 mixture of both reactants with known concentrations (after volume calibration). No spontaneous binaphthyl formation could be observed within months, so that this mixture proved to be storable for long periods in the absence of air, humidity and light.

The actual coupling step started with the *in situ* formation of the $Ni^{II}$-catalyst by treatment of anhydrous $NiBr_2$ with the respective ligand (atomic ratio P/Ni = 2:1) in diethyl ether or THF, resulting usually in violet mixtures. In diethyl ether suspensions formed and the presence of noncomplexed Ni-species could not be excluded. For activation (reduction to $Ni^0$), the Ni complex had to be treated with a Grignard reagent, in the literature generally methylmagnesium bromide,[5] at elevated temperatures. To simplify the procedure, we performed this activation by heating the $NiBr_2$–ligand solution with a small amount of the mixture of Grignard reagent and halogenoarene for a short period, resulting in a colour change of the mixture. After cooling, the rest of the reactant mixture was added and the reaction was allowed to proceed at room temperature for 10 to 12 days. In spite of the relatively unfavourable substrate:catalyst ratios of 100:1, the reactions proceeded generally very slowly, a fact easily explainable by steric restrictions. The product formation could be enhanced by heating but at the expense of a decrease in enantioselectivity (Table 2).

The work-up procedure started with an acid extraction to remove the magnesium compounds, followed by a column chromatography. The coupling product **47** was eluted after the less-polar starting material **45** and 2-methylnaphthalene, which was formed by hydrolysis of the excess of Grignard reagent. The enantiomeric excess of **47** was measured either by polarimetry or by HPLC. Since the HPLC method described in the literature[5] required a tedious multi-step derivatization of 2,2′-dimethyl-1,1′-binaphthyl, a new method for the direct determination of the enantiomeric excess had to be developed. A Chiralpak OT(+) column proved to be suitable for analytical enantiomer separation of 2,2′-dimethyl-1,1′-binaphthyl, if methanol at 0 °C was used as eluent. The *R*-enantiomer was eluted after the *S*-enantiomer (the latter had a much narrower elution profile than the former). The ee values determined by this HPLC technique were in accord with those determined by polarimetry.

## Results and discussion

Representative groups of ligands have been tested in the two Grignard cross coupling systems of Scheme 8. In the enantioselective formation of 3-phenylbut-1-ene **44**, the results were compared with those of Norphos, the effectivity of which has already been demonstrated.[25] Since the system **42**/**43**→**44** usually gives only modest enantioselectivity, the ligands tested in this study reach satisfactory selectivity. In particular, ligand **6** induced a high degree of enantioselectivity [68%, even better than (−)-Norphos] besides good chemical yields. Surprisingly, the structurally very similar Glyphos **1** yielded only racemic product. The phosphane **3**, the structure of which is intermediate between that of **1** and **6**, induced *ca.* 26% ee, a value lying between the selectivities of **1** and **6**. An unexpected tendency was observed within the series **4**→**7**→**10**→**13**. The simple monoether **1** yielded an enantiomeric excess of *ca.* 25%. The elongation of the side chain decreased the enantioselectivity (**7**, ~5% ee). Shifting the stereogenic centre to position 3 resulted in a substantial increase of the attainable selectivity (**10**, ~45% ee), which became a little lower, when the stereogenic centre was shifted further to position 4 (**13**, ~30% ee). Thus, the existence of a maximum and a minimum within the series of selectivities suggests the operation of (at least) two mechanisms, which make definite predictions impossible within this system.

The enantioselectivities in the system **45**/**46**→**47** (Scheme 8) showed a completely different tendency compared to the system **42**/**43**→**44**. The simplification of the standard procedure was at the cost of the attainable enantioselectivities, as clearly demonstrated for ligand PPFOMe. The highest selectivity reached with the simplified procedure was 83% ee compared to the literature value of 95% ee.[5] The difference is thought to be the result of the non-selective product formation during the activation of the Ni catalyst.

For the system **45**/**46**→**47**, in the row **1**→**3**→**6** the trend was the reverse of that for system **42**/**43**→**44**. Glyphos **1** yielded the highest, phosphane **6** the lowest enantioselectivity, provided the catalyst was prepared in THF. Whether this inversion also took place in the series **4**→**7**→**10**→**13** could not be decided, since both the chemical and optical yields were too low for reliable judgements to be made. In diethyl ether chemical and optical yields were better for the ligands **2**, **3**, **4** except for Glyphos **1**, which reached 50% ee only in the presence of THF. The negative influence of THF is thought to be due to competitive complexation of the Grignard reagent in the transition state. Only the highly donating oxygen atoms in **1** are able to displace complexed THF, giving a transition state similar to that in diethyl ether.

Compared to the system **42**/**43**→**44**, product formation in the system **45**/**46**→**47** was generally much slower. However, there were substantial differences between the individual ligands, the fastest reactions occuring with **1**, **3**, **6** and, to a limited extent, PPFOMe **2**. These ligands also gave the highest chemical yields.

Although certain trends were apparent for the reactions described in this investigation, no general rules governing the behaviour of the systems examined can be given; this is in accord with the concluding remarks of Hayashi in his recent review concerning the Grignard cross-coupling reaction.[3b]

## Experimental

Since most of the ligands were prepared in both enantiomeric forms, the configuration of the products given in this part may not be identical with those shown in the schemes. Thus, the preparation and the properties of only one enantiomer are described, with the exception of compounds **15**, **19** and **39**, where the preparation of the enantiomers was slightly different.

All procedures involving phosphanes were performed with exclusion of air using purified $N_2$. If organometallic reagents were involved, water was also excluded. Solvents used for preparative purposes were dried and deaerated according to standard procedures. Water and solvents for chromatography were deaerated by bubbling $N_2$ through the fluids for at least 12 h. Two acronyms will be used: EA for ethyl acetate and LP for light petroleum (bp 40–60 °C). Liquid starting materials were distilled under $N_2$ prior to use. Chromatographic materials [silica 60 (65–200 mm), Merck, and alumina (basic, Super I), Woelm] were heated *in vacuo* for 24 h and then saturated with $N_2$.

Melting points were determined using an SMP-20 (Büchi) and were not corrected. Polarimetric measurements (Perkin-Elmer

241) were performed, if not otherwise stated, in 1 dm cuvettes at 20.0 °C using UVASOL solvents (Merck); vibrational spectra were recorded on a Beckman-spectrometer IR 4240 or a Bruker FTIR IFS 25 either as films between NaCl-windows (film) or as KBr pellets (KBr). For mass spectroscopy, the MAT 112 S (electron impact ionization, 70 eV) and the MAT 95 (field desorption) *apparatus* (both Finnigan) were used. The intensities were relative to the basic peak ($I$ = 100%) and possible interpretations are given in brackets. Elemental analyses were performed at the Mikroanalytisches Labor of the Universität Regensburg. $^1$H NMR spectra were recorded using the following spectrometers: EM 360L (60 MHz, Varian), FT 80 A (80 MHz, Varian), AC 250 (250 MHz, Bruker), ARX 400 (400 MHz, Bruker), and VXR 500 (500 MHz, Varian). The chemical shifts are given in units of the $\delta$ scale relative to internal TMS, and $J$ values are given in Hz. The same standard was used for the $^{13}$C NMR spectra (including DEPT and APT-sequences), performed on AC 250 (63 MHz), ARX 400 (101 MHz), and VXR 500 (126 MHz) instruments. Exact peak assignments were possible after two-dimensional experiments, recorded at the ARX 400 and the VXR 500 spectrometers. For the $^{31}$P NMR spectra ($^1$H-decoupled), an AC 200 (81 MHz, Bruker, internal standard $PPh_3$) and the ARX 400 (162 MHz, external standard $H_3PO_4$) were used.

**Diphenyl(aryl)phosphanes from bromoarenes: general procedure 1**

A solution of the bromoarene [20 mmol; 10 mmol of bis(bromoarenes)] in THF (20 cm$^3$) was added slowly to activated Mg (0.50 g, 21 mmol) and the mixture heated to reflux for 1 h after completion of the addition. The Grignard solution was cooled to −5 °C by means of an ice–brine bath and a solution of distilled $ClPPh_2$ (4.0 cm$^3$, 22 mmol) in THF (20 cm$^3$) was added dropwise, a temperature < 10 °C being maintained. After 1 h at room temp. the mixture was refluxed for a further 1 h to ensure completion of the reaction. The solvent was then removed as far as possible in a stream of dry $N_2$ and deoxygenated water (25 cm$^3$) and conc. hydrochloric acid (2 cm$^3$) were added to the residue; the rest of the solvent was then removed with $N_2$. The resulting suspension was extracted with toluene (× 3) and this was followed by a product-specific work-up procedure.

**Ethers by alkylation of alkanols: general procedure 2**

The alkanol (30 mmol, 15 mmol for diols) was added to a suspension of powdered KOH (7.0 g, 110 mmol; obtained from Fluka) in DMSO (80 cm$^3$), immersed in a bath of ice–water, the alkylating agent (30–100 mmol) was added within an hour (sometimes colour changes occur during this addition) and the resulting mixture was stirred for a further 1 h. The product was usually isolated by extraction of the mixture with LP either directly or after dilution with water. The purification procedures are described together with the specific compounds.

**Sulfonic acid esters of alkanols: general procedure 3**

A solution of the appropriate alkanol (100 mmol) in a mixture of $CH_2Cl_2$ (100 cm$^3$) and pyridine (20 cm$^3$) was cooled in an ice–brine bath to −5 °C. The sulfonic acid chloride or anhydride (110 to 120 mmol per hydroxy function) was slowly added to the stirred solution at the same temperature to give an exothermic reaction and, subsequently, a precipitate. The mixture was stirred for 16 h at room temperature after which it was treated with ice (10 g) and stirring continued for a further 1 h. The organic phase was separated, washed until pyridine free with ice-cold 10% $H_2SO_4$ and then with water (50 cm$^3$). It was then filtered through a column of silica (80 cm$^3$) with $CH_2Cl_2$ as eluent, concentrated and the residue dried *in vacuo*. Further purification procedures are described together with the individual compounds.

**(2*S*)-1-(Diphenylphosphino)-2-methoxypropane 3**

A solution of compound **26** (12.2 g, 50.0 mmol) in THF (100 cm$^3$) was added to a vigorously stirred 1 mol dm$^{-3}$ solution of $LiPPh_2$ [60 cm$^3$, 60 mmol; prepared by reaction of Li (6.0 g) and $ClPPh_2$ (53 cm$^3$) in THF (280 cm$^3$)] a temperature of −10 to −5 °C being maintained. Precipitation of lithium tosylate occurred after half of the addition and rendered stirring more difficult. After the reaction mixture had been allowed to warm to room temperature overnight it was hydrolysed with deoxygenated water (50 cm$^3$) and concentrated by removal of the THF by a stream of $N_2$. The residue was extracted with LP and the extract passed through a chromatographic column ($SiO_2$) with gradient elution (LP + 2% EA→LP + 15% EA),[9] the product being eluted at a 10% EA content. The latter fractions were concentrated under reduced pressure to give the product as a colourless oil (9.1 g, 71%) (Found: C, 74.2; H, 7.3. $C_{16}H_{19}OP$ requires 74.40; H, 7.41%); $[\alpha]_\lambda$ ($\lambda$/nm) −30.6 (589), −32.4 (578), −37.2 (546), −68.4 (436) and −123 (365) ($c$ 1 in $CH_2Cl_2$); $R_F$($SiO_2$/LP–EA 20:1) 0.29; $\nu_{max}$/cm$^{-1}$ 3060, 3030 (Ar C–H), 2960, 2910, 2800 ($OCH_3$), 1575, 1465, 1420, 1360, 1110, 1070, 890, 825, 720 and 675; $\delta_H$(500 MHz; $CDCl_3$) 1.26 (3 H, dd, $J$ 6.0, $J_{PH}$ 1.0, 3-H$_3$), 2.14 (1 H, dd, $^2J$ 13.5, $J$ 7.2, 1-H), 2.47 (1 H, dd, $^2J$ 13.5, $J$ 6.1, 1-H), 3.26 (3 H, s, $OCH_3$), 3.36 (1 H, dddq, $J$ 7.2, $J_{PH}$ 7.0, $J$ 6.1, $J$ 6.0, 2-H), 7.29–7.35 and 7.42–7.47 (10 H, 2 m, $PPh_2$); $\delta_C$(126 MHz; $CDCl_3$) 20.5 (d, $J$ 8, C-3), 36.2 (d, $J$ 13, C-1), 55.9 ($OCH_3$), 74.9 (d, $J$ 32, C-2), 128.3–128.5 (m, C-3′, C-4′), 132.8–132.6 (2 d, $J$ 20, C-2′), 138.8 and 138.9 (2 d, $J$ 13, C-1′); $\delta_P$(81 MHz; $CDCl_3$) −22.2 (s); $m/z$ (EI, 70 eV) 258 (M$^+$, 48%), 227 ([M − $CH_3O$]$^+$, 5), 216 ([M − $C_3H_6$]$^+$, 10), 201 ([216 − $CH_3$]$^+$, 19), 186 ([$Ph_2PH$]$^+$, 100), 183 ([$C_{12}H_8P$]$^+$, 35), 121 ([$C_7H_6P$]$^+$, 39) and 108 ([PhP]$^+$, 66). The mass spectrum of **3** is dominated by a [2+2] fragmentation.

**(1*S*)-1-[2′-(Diphenylphosphino)phenyl]methoxyethane 4**

This compound was synthesized from compound **16** according to general procedure 1. The crude product from a 1.5-fold preparation was taken up in toluene and the solution filtered through 10 cm of silica (3.5 cm diam.) with toluene (800 cm$^3$) as eluent. Evaporation of the filtrate gave an oil which crystallized from MeOH (80 cm$^3$) upon slow cooling to 0 °C as sturdy, colourless needles. Further crystallization from MeOH (50 cm$^3$) and drying *in vacuo* yielded the title compound **4** (6.7 g, 70%), mp 90–91 °C (Found: C, 78.6; H, 6.7. $C_{21}H_{21}OP$ requires C, 78.67; H, 6.60%); $[\alpha]_\lambda$ ($\lambda$/nm) −127.7 (589), −135 (578), −157 (546), −312 (436) and −658 (365) ($c$ 1 in $CH_2Cl_2$); $R_F$($SiO_2$/toluene) 0.30; $R_F$($SiO_2$/LP–EA, 6:1) 0.49; $\nu_{max}$/cm$^{-1}$ 3060 (Ar C–H), 2970 (Aliph. C–H), 2810 ($CH_3O$), 1425, 1100 (C–O), 1070 (C–O), 755, 720 (P–C) and 675; $\delta_H$(500 MHz; $CDCl_3$) 1.27 (3 H, d, $J$ 6.3, 2-H$_3$), 3.06 (3 H, s, $OCH_3$), 5.14 (1 H, q, $J$ 6.3, 1-H), 6.89 (1 H, ddd, $J$ 7.5, $^4J_{PH}$ 4.3, $^4J$ 1.3, 3′-H), 7.17 (1 H, dt, $^4J$ 1.4, $J$ 7.5, 4′-H), 7.25–7.30 and 7.32–7.36 (10 H, 2 m, $PPh_2$), 7.40 (1 H, dt, $^4J$ 1.3, $J$ 7.5, 5′-H) and 7.55 (1 H, ddd, $J$ 7.5, $J_{PH}$ 4.2, $^4J$ 1.4, 6′-H); $\delta_C$(126 MHz; $CDCl_3$) 23.4 (C-2), 56.2 ($OCH_3$), 75.1 (d, $J$ 25, C-1), 125.5 (d, $J$ 5, C-6′), 127.4 (C-4′), 128.4–128.8 (m, C-3″ + C-4″ of $PPh_2$), 129.5 (C-5′), 133.3 (C-3′), 133.8 and 134.1 (2 d, $J$ 20, C-2″ of $PPh_2$), 134.8 (d, $J$ 15, C-2′), 136.2 and 136.8 (2 d, $J$ 10, C-1″ of $PPh_2$) and 148.3 (d, $J$ 23, C-1′); $\delta_P$(81 MHz; $CDCl_3$) −18.0 (s); $m/z$ (EI, 70 eV) 320 (M$^+$, 19%), 305 ([M − $CH_3$]$^+$, 100), 289 ([M − $OCH_3$]$^+$, 7), 227 ([305 − $C_6H_6$]$^+$, 13) and 183 ($C_{12}H_8P$, 22).

**(1*S*,2*S*)-1,2-Bis[2′-(diphenylphosphino)phenyl]-1,2-dimethoxyethane 5**

This compound was synthesized from compound **40** according to general procedure 1. The toluene extract was passed through a column of $SiO_2$ with a gradient elution (toluene→toluene + 30% $Et_2O$).[9] The product, eluted at 15% of $Et_2O$ and obtained after evaporation of the filtrate, formed light-sensitive, colourless crystals (3.1 g, 51%) from cyclohexane (50 cm$^3$) at

+4 °C; mp 163–164 °C which were relatively stable towards air (Found: C, 78.6; H, 6.5. $C_{40}H_{36}O_2P_2$ requires C, 78.67; H, 5.94%); $[\alpha]_\lambda$ ($\lambda$/nm) 150.2 (589), 158.3 (578), 186 (546), 384 (436), 828 (365) (*c* 1 in $CH_2Cl_2$); $R_F$($SiO_2$, toluene) 0.14; $R_F$($SiO_2$, LP–EA 6:1) 0.29; $\nu_{max}$/cm$^{-1}$ 3040 (Ar C–H), 2960 (Aliph. C–H), 2795 ($CH_3O$), 1460, 1415, 1070 (C–O), 725 (P–C) and 670; $\delta_H$(500 MHz; $CDCl_3$) 2.89 (6 H, s, 2 × $OCH_3$), 5.74 (2 H, 'd', *J* 6.5, 1-H, 2-H), 6.79–6.83 (4 H, m, ArH), 6.83 (2 H, md, *J* 7.5, 3′-H), 7.00 (2 H, dt, $^4J$ 1.3, *J* 7.5, 5′-H), 7.11–7.17 (2 H, m, 4′-H), 7.17–7.27 (16 H, m, $PPh_2$) and 7.73 (2 H, md, *J* 7.5, 6′-H); $\delta_C$(126 MHz; $CDCl_3$) 56.8 ($OCH_3$), 83.0–83.3 (mc, C-1, C-2), 127.8–134.3 (m, ArC), 136.6–136.7 (mc, C-2′), 137.3–137.6 (m, C-1″ of $PPh_2$) and 143.5–143.7 (mc, C-1′). Because of the complex signal multiplicities a more detailed interpretation was not possible; $\delta_P$(81 MHz; $CDCl_3$) −16.7 (s); *m*/*z* (EI, 70 eV) 610 ($M^+$, 32%), 595 ([M − $CH_3$]$^+$, 11), 579 ([M − $OCH_3$]$^+$, 30), 563 ([M − $CH_3O_2$]$^+$, 52), 425 ([M − $PPh_2$]$^+$, 9), 393 ([579 − $HPPh_2$]$^+$, 26), 377 ([563 − $HPPh_2$]$^+$, 13), 305 ([M/2]$^+$, 100), 273 ([M − $C_{24}H_{18}P$]$^+$, 12), 186 ($HPPh_2^+$, 23), 183 ($C_{12}H_8P^+$, 40), 165 ([273 − $C_6H_5P$]$^+$, 16) and 108 ($C_6H_5P^+$, 40).

**(2*R*)-2-Diphenylphosphino-4-oxapentane 6**

This compound was synthesized from the sulfonate **31**, in a manner analogous to that employed to prepare compound **3**. The crude product from a 1.4-fold preparation was chromatographed on $SiO_2$ with gradient elution (LP + 2% EA→LP + 10% EA).[9] The product contained some solid impurity ($Ph_2PPPh_2$?) after removal of the solvents and this was removed by treatment with LP (15 cm$^3$), cooling of the mixture to −30 °C and filtration at this temperature. The residue was washed with cold LP (2 × 5 cm$^3$) and the combined filtrates were concentrated under reduced pressure and dried *in vacuo* to give a colourless oil (8.4 g, 48%) (Found: C, 74.5; H, 7.4. $C_{16}H_{19}OP$ requires C, 74.40; H, 7.41%); $[\alpha]_\lambda$ ($\lambda$/nm) 22.5 (589), 23.5 (578), 27.0 (546), 49.7 (436) and 90.3 (365) (*c* 1 in $CH_2Cl_2$); $R_F$($SiO_2$, LP–EA, 20:1): 0.24; $R_F$($SiO_2$, LP–EA, 6:1) 0.51; *m*/*z* (EI, 70 eV) 258 ($M^+$, 76%), 227 ([M − $CH_3O$]$^+$, 3), 216 ([M − $C_3H_6$]$^+$, 14), 201 ([216 − $CH_3$]$^+$, 28), 186 ([$Ph_2PH$]$^+$, 100), 183 ([$C_{12}H_8P$]$^+$, 46) and 108 ([PhP]$^+$, 86); $\delta_H$(500 MHz; $CDCl_3$) 1.11 (3 H, dd, $J_{PH}$ 14.3, *J* 6.8, 3-$H_3$), 2.65 (1 H, dddq, *J* 8.6, $J_{PH}$ 4.5, *J* 3.6, *J* 6.8, 2-H), 3.24 (1 H, ddd, $^2J$ 9.3, *J* 8.6, $J_{PH}$ 5.0, 1-H), 3.28 (3 H, s, $OCH_3$), 3.44 (1 H, ddd, $^2J$ 9.3, $J_{PH}$ 7.3, *J* 3.6, 1-H), 7.30–7.37 and 7.48–7.52 (10 H, 2 m, $PPh_2$); $\delta_C$(126 MHz; $CDCl_3$) 14.7 (d, *J* 15, C-3), 31.3 (d, *J* 11, C-2), 58.7 ($OCH_3$), 75.4 (d, *J* 24, C-1), 128.3–128.7 (m, C-3′, C-4′), 133.2–133.7 (m, C-2′), 136.3 (d, *J* 12, C-1′) and 136.8 (d, *J* 14, C-1′); $\delta_P$(81 MHz; $CDCl_3$) −8.7 (s); $\nu_{max}$/cm$^{-1}$ 3070, 3050 (Ar. C–H), 2920 (Aliph. C–H), 2870, 2820 ($CH_3O$), 1470, 1430, 1100 (C–O), 730 (P–C) and 685. The mass spectrum of this substance is dominated by a [2+2] fragmentation.

**(2*R*)-2-[2′-(Diphenylphosphino)phenyl]-3,6-dioxaheptane 7**

This compound, prepared in a 2-fold scale preparation according to general procedure 1 from compound **17** (40 mmol) was obtained as a toluene solution which was charged onto a chromatographic column, prepared in the same solvent. The product was eluted in a toluene–$Et_2O$ (19:1) fraction which was concentrated under reduced pressure. The residue was recrystallized twice from MeOH (2 × 60 cm$^3$) at −30 °C and the product dried *in vacuo* to give colourless crystals (13.9 g, 77%), mp 57.5–58.5 °C (Found: C, 75.9; H, 6.8. $C_{23}H_{25}O_2P$ requires C, 75.81; H, 6.91%); $[\alpha]_\lambda$ ($\lambda$/nm) 96.2 (589), 101 (578), 118 (546), 238 (436) and 505 (365) (*c* 1 in $CH_2Cl_2$); $R_F$($SiO_2$, toluene) 0.09; $R_F$($SiO_2$, LP–EA, 6:1) 0.45; $\nu_{max}$/cm$^{-1}$ 3050 (Ar C–H), 2970 (Aliph. C–H), 2870 ($CH_3O$), 1425, 1190, 1090 (C–O), 760, 730 (P–C) and 680; $\delta_H$(500 MHz; $CDCl_3$) 1.29 (3 H, d, *J* 6.4, 1-$H_3$), 3.24–3.42 (4 H, m, 4-$H_2$, 5-$H_2$), 3.32 (3 H, s, $OCH_3$), 5.26 (1 H, q, *J* 6.4, 2-H), 6.87 (1 H, ddd, *J* 7.5, $^4J_{PH}$ 4.3, $^4J$ 1.3, 3′-H), 7.16 (1 H, dt, $^4J$ 1.4, *J* 7.5, 4′-H), 7.24–7.29 and 7.31–7.39 (10 H, 2 m, $PPh_2$), 7.39 (1 H, dt, $^4J$ 1.3, *J* 7.5, 5′-H) and 7.60 (1 H, ddd, *J* 7.5, $J_{PH}$ 4.3, $^4J$ 1.4, 6′-H); $\delta_C$(126 MHz; $CDCl_3$) 23.7 (C-1), 58.9 (C-7), 67.5 (C-5), 71.8 (C-4), 74.8 (d, *J* 26, C-2), 125.8 (d, *J* 6, C-6′), 127.4 (C-4′), 128.4–128.8 (m, C-3″ and C-4″ of $PPh_2$), 129.5 (C-5′), 133.2 (C-3′), 133.6 and 134.1 (2 d, *J* 20, C-2″ of $PPh_2$), 134.7 (d, *J* 14, C-2′), 136.2 and 136.7 (2 d, *J* 10, C-1″ of $PPh_2$) and 148.5 (d, *J* 22, C-1′); $\delta_P$(81 MHz; $CDCl_3$) −17.9 (s); *m*/*z* (EI, 70 eV) 364 ($M^+$, 7%), 305 ([M − $C_3H_7O$]$^+$, 100), 289 ([M − $C_3H_7O_2$]$^+$, 9), 227 ([305 − $C_6H_6$]$^+$, 12) and 183 ([$C_{12}H_8P$]$^+$, 12).

**(4*S*,5*S*)-4,5-Bis[2′-(diphenylphosphino)phenyl]-2,2-dimethyl-1,3-dioxolane 8**

The introduction of the diphenylphosphino functionality into **41** was performed in a manner analogous to general procedure 1. The reaction mixture was hydrolysed with a minimum of hydrochloric acid (*ca.* 1 cm$^3$) in order to avoid cleavage of the dioxolane. The toluene extract of a 2-fold scale preparation was charged onto a silica column, eluted with toluene, and concentrated to dryness. The residue was taken up in warm MeOH (500 cm$^3$) and the solution cooled slowly to −30 °C. At this temperature the solution was concentrated under reduced pressure to *ca.* 150 cm$^3$, filtered and dried *in vacuo* to afford a colourless powder (5.0 g, 40%), mp 85 °C (Found: C, 78.8; H, 6.0. $C_{41}H_{36}O_2P_2$ requires C, 79.07; H, 5.83%); $[\alpha]_\lambda$ ($\lambda$/nm) 95.0 (589), 101 (578), 120 (546), 269 (436) and 676 (365) (*c* 1 in $CH_2Cl_2$); $R_F$($SiO_2$, toluene) 0.22; $R_F$($SiO_2$, LP–EA, 6:1), 0.51; $R_F$($SiO_2$, toluene–$Et_2O$, 19:1) 0.80; $\nu_{max}$/cm$^{-1}$ 3040 (Ar C–H), 2960 (Aliph. C–H), 1460, 1415, 1350 [$C(CH_3)_2$], 1035 (C–O), 720 (P–C) and 670; $\delta_H$(500 MHz; $CDCl_3$) 1.60 (6 H, s, 2 × $CH_3$), 6.05 (2 H, 'd', *J* 7, 4-H, 5-H), 6.74 (4 H, dt, $^4J$ 1.3, *J* 7.9, ArH), 6.81 (2 H, ddd, *J* 7.8, *J* 4.0, $^4J$ 1.2, 3′-H), 6.99 (4 H, dt, $^4J$ 1.5, *J* 7.8, ArH), 7.03 (2 H, dt, $^4J$ 1.3, *J* 7.5, 4′-H), 7.08–7.16 (6 H, m, ArH), 7.23–7.27 (8 H, m, ArH) and 7.72 (2 H, dd, *J* 7.5, *J* 4.0, 6′-H); $\delta_C$(126 MHz; $CDCl_3$) 27.3 ($CH_3$), 81.9 (d, *J* 29, C-4, C-5), 109.1 (C-1), 128.0–128.5 (m, ArH), 133.1 and 133.5 (2 d, *J* 19, C-2″ of $PPh_2$), 134.4 [C-3′(?)], 136.1 (d, *J* 17, 2 × C-2′), 136.6 and 137.9 (2 d, *J* 12, C-1″ of $PPh_2$) and 140.3 (d, *J* 24, 2 × C-1′); $\delta_P$(81 MHz; $CDCl_3$) −18.8 (s); *m*/*z* (EI, 70 eV) 622 ($M^+$, 18%), 564 ([M − $C_3H_6O$]$^+$, 69), 548 ([M − $C_3H_6O_2$]$^+$, 3), 487 ([564 − $C_6H_5$]$^+$, 85), 437 ([M − $PPh_2$]$^+$, 26), 409 ([487 − $C_6H_6$]$^+$, 28), 379 ([564 − $PPh_2$]$^+$, 22), 363 ([548 − $PPh_2$]$^+$, 54), 360 ([M − $PPh_3$]$^+$, 28), 262 ([$PPh_3$]$^+$, 41), 186 ([$Ph_2PH$]$^+$, 54), 183 ([$C_{12}H_8P$]$^+$, 100) and 108 ([$C_6H_5P$]$^+$, 100). The mass spectrum is complex because of several energetically similar fragmentation mechanisms.

**(2*R*)-1-[2′-(Diphenylphosphino)phenyl]-2-methyl-1,4-dioxapentane 9**

(2*R*)-1-(2′-Bromophenyl)-2-methyl-1,4-dioxapentane **32** (9.8 g, 40 mmol) was treated with Mg (1.0 g, 42 mmol) and $ClPPh_2$ (8.0 ml, 44 mmol) as described in general procedure 1. The crude product was purified by chromatography on $SiO_2$ with toluene as eluent. After separation of a small amount of a fore-running impurity, the product-containing fractions were concentrated under reduced pressure to yield an oil (11.1 g, 79%) (Found: C, 74.25; H, 6.5. $C_{22}H_{23}PO_2$ requires C, 75.41; H, 6.62%); $[\alpha]_\lambda$ ($\lambda$/nm) 24.8 (589), 26.2 (578), 30.8 (546), 64.3 (436) and 148 (365) (*c* 1 in $CH_2Cl_2$); $R_F$($SiO_2$, $CH_2Cl_2$) 0.43; $\nu_{max}$/cm$^{-1}$ 3040 (Ar C–H), 2970, 2920, 2810 (Aliph. C–H), 1570, 1460 (Ar C–C), 1425 (Aliph. CH), 1265, 1230, 1100 (C–O), 955, 730 (P–C) and 680; $\delta_H$(400 MHz; $CDCl_3$) 1.06 (3 H, d, *J* 6.2, 6-$H_3$), 3.17 (1 H, dd, $^2J$ 10.1, *J* 5.3, 3-H), 3.21 (3 H, s, $OCH_3$), 3.30 (1 H, dd, $^2J$ 10.1, *J* 5.6, 3-H), 4.49 (1 H, ddq, *J* 5.6, *J* 5.3, *J* 6.2, 2-H), 6.68 (1 H, ddd, *J* 7.4, $J_{PH}$ 4.7, $^4J$ 1.7, 3′-H), 6.82 (1 H, tt, *J* 7.4, $^4J$ and $J_{PH}$ 0.8, 4′-H), 6.91 (1 H, ddd, *J* 8.2, $J_{PH}$ 4.4, 6′-H) and 7.28 (1 H, dddd, *J* 8.2, *J* 7.4, $^4J$ 1.7, *J* 0.8, 5′-H); $\delta_C$(100.6 MHz; $CDCl_3$) 16.7 (C-6), 59.2 (C-5), 73.1 (C-2), 75.6 (C-3), 112.0 (d, *J* 1, C-6′), 120.8 (d, *J* 1, C-4′), 126.9 (d, *J* 12, C-2′), 128.2 (d, *J* 7, C-3″), 128.5 (d, *J* 9, C-4″), 129.9 (C-5′), 133.5 (d,

*J* 2, C-3′), 134.0 + 134.1 (2 d, *J* 20, C-2″), 136.8 + 136.9 (2 d, *J* 10/11, C-1″) and 159.1 (d, *J* 14, C-1′); $\delta_P$(162 MHz; $CDCl_3$) −14.7 (s); *m/z* (EI, 70 eV) 350 ($M^+$, 3%), 319 ([M − $CH_3O$]$^+$, 4), $Ph_2PC_6H_4OH^+$, 100), 199 ($C_{12}H_8OP^+$, 70), 183 ($C_{12}H_8P^+$, 63) and 152 (28).

### (3*S*)-[2′-Diphenylphosphino)phenyl]-3-methyl-2,5-dioxahexane 10

This compound was synthesized from compound **22** by general procedure 1. The resulting toluene extract was charged onto a $SiO_2$ column and the product obtained by gradient elution (toluene→toluene + 20% $Et_2O$).[9] The combined product-containing fractions (starting with 5% $Et_2O$) were concentrated under reduced pressure and the residue was dried *in vacuo* to afford a colourless oil (6.1 g, 84%) (Found: C, 74.0; H, 6.9. $C_{23}H_{25}O_2P$ requires C, 75.81; H, 6.91%); $[\alpha]_\lambda$ (λ/nm) 4.4 (589), 4.6 (578), 5.4 (546), 10.2 (436) and 19.9 (365) (*c* 1 in $CH_2Cl_2$); $R_F$($SiO_2$, toluene) 0.12; $R_F$($SiO_2$, toluene–THF, 19:1) 0.46; $R_F$($SiO_2$, toluene–THF, 9:1) 0.65; $\nu_{max}$/cm$^{-1}$ 3050 (Ar C–H), 2970 (Aliph. C–H), 2880 ($CH_3O$), 1575, 1430, 1105 (C–O), 730 (P–C) and 680; $\delta_H$(500 MHz; $CDCl_3$) 1.04 (3 H, d, *J* 6.2, 7-$H_3$), 3.18 (1 H, dd, $^2J$ 9.9, *J* 4.7, 4-H), 3.27 (1 H, dd, $^2J$ 9.9, *J* 5.4, 4-H), 3.27 (3 H, s, $OCH_3$), 3.62 (1 H, ddq, *J* 5.4, *J* 4.7, *J* 6.2, 3-H), 4.74 (1 H, dd, $^2J$ 12.3, $J_{PH}$ 1.8, 1-H), 4.78 (1 H, dd, $^2J$ 12.5, $^4J_{PH}$ 1.8, 1-H), 6.84 (1 H, ddd, *J* 7.5, $J_{PH}$ 4.5, $^4J$ 1.2, 3′-H), 7.16 (1 H, dt, $^4J$ 1.2, *J* 7.5, 4′-H), 7.21–7.32 (10 H, m, $PPh_2$), 7.34 (1 H, dt, $^4J$ 1.2, *J* 7.5, 5′-H) and 7.57 (1 H, dd, *J* 7.5, $J_{PH}$ 4.2, 6′-H); $\delta_C$(126 MHz; $CDCl_3$) 16.9 (C–7), 59.0 (C-6), 68.8 (d, *J* 24, C-1), 73.9 (C-3), 76.3 (C-4), 127.5 (C-4′), 128.0 (d, *J* 6, C-6′), 128.4–128.6 (m, C-3″ + C-4″ of $PPh_2$), 128.9 (C-5′), 133.3 (C-3′), 133.8 (d, *J* 19, C-2″ of $PPh_2$), 135.0 (d, *J* 15, C-2′), 136.5 and 136.6 (2 d, *J* 10, C-1″ of $PPh_2$) and 143.1 (d, *J* 23, C-1′); $\delta_P$(81 MHz; $CDCl_3$) −16.2 (s); *m/z* (EI, 70 eV) 364 ($M^+$, 9%), 291 ([M − $C_4H_9O$]$^+$, 100), 275 ([M − $C_4H_9O_2$]$^+$, 15), 213 ([291 − $C_6H_6$]$^+$, 8), 197 ([275 − $C_6H_6$]$^+$, 9), 183 ([$C_{12}H_8P$]$^+$, 13) and 165 (21).

### (3*R*)-1-[2′-(Diphenylphosphino)phenyl]-3-phenyl-2,5-dioxahexane 11

This compound was synthesized in a 1.5-fold scale preparation following general procedure 1. The crude product was charged onto a silica column and subjected to gradient elution (toluene→toluene + 10% $Et_2O$).[9] The combined product-containing fractions (with 2% $Et_2O$) were evaporated to dryness to yield a yellowish syrup (5.71 g, 50%) (Found: C, 77.8; H, 6.3. $C_{28}H_{27}O_2P$ requires C, 78.85; H, 6.38%); $[\alpha]_\lambda$ (λ/nm) 51.7 (589), 54.1 (578), 61.9 (546), 110.9 (436) and 193.7 (365) (*c* 1 in $CH_2Cl_2$); $R_F$($SiO_2$, toluene–$Et_2O$, 19:1) 0.58; $\nu_{max}$/cm$^{-1}$ 3060, 3030 (Ar C–H), 2930, 2890, 2830 (Aliph. C–H), 1580 (Ar C–C), 1470, 1450, 1430 (Ar C–C), 1190, 1135, 1090 (C–O), 1020 (Ar), 735 (P–C) and 690; $\delta_H$(400 MHz; $CDCl_3$) 3.26 (3 H, s, $OCH_3$), 3.33 (1 H, dd, $^2J$ 10.4, *J* 4.7, 4-H), 3.42 (1 H, dd, $^2J$ 10.4, *J* 7.0, 4-H), 4.50 (1 H, dd, *J* 7.0, *J* 4.7, 3-H), 4.67 (2 H, s, br, 1-$H_2$); 6.87 (1 H, ddd, *J* 7.6, $J_{PH}$ 4.6, $^4J$ 1.1, 3′-H), 7.16–7.23 (6 H, m, 4′-H, CPh), 7.25–7.32 (10 H, m, $PPh_2$), 7.36 (1 H, dt, $^4J$ 1.6, *J* 7.6, 5′-H) and 7.61 (1 H, ddd, *J* 7.6, $J_{PH}$ 4.3, *J* 0.7, 6′-H); $\delta_C$(100.6 MHz; $CDCl_3$) 56.1 (C-6), 69.0 (d, *J* 25, C-1), 76.9 (C-4), 80.6 (C-3), 127.1 (C-2‴), 127.6 (C-4′), 127.8 (C-4‴), 128.1 (d, *J* 6, C-6′), 128.3–128.6 (m, C-3″, C-4″, C-3‴), 128.9 (C-5′), 133.5 (C-3′), 133.7 + 133.8 (2 d, *J* 20, C-2″), 135.1 (d, *J* 15, C-2′), 136.6 + 136.7 (2 d, *J* 10, C-1″), 139.3 (C-1‴) and 142.9 (d, *J* 24, C-1′); $\delta_P$(162 MHz; $CDCl_3$) −15.8 (s); *m/z* (EI, 70 eV) 426 ($M^+$, 0.5), 381 ([M − $C_2H_5O$]$^+$, 2), 291 ([381 + $C_7H_6$]$^+$, 100), 276 ([381 − $C_6H_5CHO$]$^+$, 27), 213 ([291 − $C_6H_6$]$^+$, 40), 183 ([$C_{12}H_8P$]$^+$, 48) and 165 (89).

### (3*S*)-1-[2′-(Diphenylphosphino)phenyl]-3-methyl-1,4-dioxapentane 12

**(a) By a Grignard reaction.** After a 1.5-fold scale preparation following general procedure 1, the crude product was charged onto a silica column and subjected to gradient elution(toluene→toluene + 5% $Et_2O$).[9] The syrup obtained after concentration of the appropriate fractions was crystallized twice from MeOH (60 cm$^3$ each, −30 °C, seeding is necessary) to yield (after drying *in vacuo*) blade–shaped, colourless crystals (6.8 g, 65%), mp 40–42 °C.

**(b) By *ortho*-lithiation.** BuLi (1.6 mol dm$^{-3}$ solution in hexane; 24.5 cm$^3$, 39.2 mmol) was added through a syringe to a solution of (3*R*)-3-methyl-1-phenyl-1,4-dioxapentane **34** (4.32 g, 26.0 mmol) and TMEDA (4.6 g, 39.7 mmol) in cyclohexane (180 ml) under $N_2$, the temperature being maintained at 0 °C by means of an ice–brine bath. After the mixture had been stirred for several hours, it was treated with a solution of $ClPPh_2$ (7.2 cm$^3$, 39.0 mmol) in dry THF (40 cm$^3$), added slowly. After being stirred for 16 h at room temperature the mixture was hydrolysed with water (25 cm$^3$) and concentrated by passage of $N_2$ through it to remove the solvent. The product, extracted with toluene and obtained by chromatography as described above, was an oil which crystallized from MeOH as a solid (4.4 g, 48%) (Found: C, 75.2; H, 6.6. $C_{22}H_{23}PO_2$ requires C, 75.41; H, 6.62%); $[\alpha]_\lambda$ (λ/nm) −5.0 (589), −5.2 (578), −5.7 (546), −7.3 (436) and −2.9 (!) (365) (*c* 1 in $CH_2Cl_2$); $R_F$($SiO_2$, toluene) 0.37; $\nu_{max}$/cm$^{-1}$ 3040 (Ar C–H), 2960, 2900, 2800 (Aliph. C–H), 1570, 1450, 1420 (Ar C–C), 1260, 1225, 1080 (C–O), 1050, 1005 (Ar), 720 (P–C) and 670; $\delta_H$(400 MHz; $CDCl_3$) 0.94 (3 H, d, *J* 6.3, 6-$H_3$), 3.22 (3 H, s, $OCH_3$), 3.37 (1 H, ddq, *J* 5.7, *J* 5.6, *J* 6.3, 3-H), 3.70 (1 H, dd, $^2J$ 9.2, *J* 5.6, 2-H), 3.97 (1 H, dd, $^2J$ 9.2, *J* 5.7, 2-H), 6.64 (1 H, ddd, *J* 7.5, $J_{PH}$ 4.7, $^4J$ 1.7, 3′-H), 6.83–6.88 (2 H, m, 4′-H, 6′-H) and 7.28–7.33 (11 H, m, 5′-H, $PPh_2$); $\delta_C$(100.6 MHz; $CDCl_3$) 16.9 (C-6), 57.1 (C-5), 71.8 (C-2), 75.1 (C-3), 110.8 (d, *J* 1, C-6′), 121.1 (C-4′), 126.1 (d, *J* 13, C-2′), 128.3 (d, *J* 7, C-3″), 128.6 (d, *J* 2, C-4″), 130.1 (C-5′), 133.3 (d, *J* 2, C-3′), 134.0 + 134.0 (2 d, *J* 20, C-2″), 136.6 + 136.7 (2 d, *J* 10, C-1″) and 160.0 (d, *J* 15, C-1′); $\delta_P$(162 MHz; $CDCl_3$) −14.9 (s); *m/z* (EI, 70 eV) 350 ($M^+$, 1%), 319 ([M − $CH_3O$]$^+$, 4), 278 $Ph_2PC_6H_4OH^+$, 100), 155 ($C_{12}H_8OP^+$, 64), 183 ($C_{12}H_8P^+$, 62) and 152 (25).

### (4*S*)-1-[2′-(Diphenylphosphino)phenyl]-4-methyl-2,5-dioxahexane 13

This compound, prepared in a 3-fold scale preparation from compound **27** according to general procedure 1, was obtained after column chromatography with toluene–$Et_2O$ (19:1) as a yellowish oil (17.9 g, 82%) (Found: C, 75.9; H, 6.9. $C_{23}H_{25}O_2P$ requires C, 75.81; H, 6.91%); $[\alpha]_\lambda$ (λ/nm) −4.9 (589), −5.6 (578), −6.4 (546), −11.2 (436) and −18.3 (365) (*c* 1 in $CH_2Cl_2$); $R_F$($SiO_2$, toluene–$Et_2O$, 19:1) 0.49; $\nu_{max}$/cm$^{-1}$ 3060 (Ar C–H), 2970 (Aliph. CH), 2880 ($CH_3O$), 1580, 1430, 1110 (C–O) and 730 (P–C), 680; $\delta_H$(500 MHz; $CDCl_3$) 1.02 (3 H, d, *J* 6.2, 7-$H_3$), 3.30 (3 H, s, $OCH_3$), 3.24–3.42 (2 H, m, 3-H, 4-H), 3.40 (1 H, dd, *J* 9.4, *J* 5.8, 3-H), 4.72 (1 H, dd, *J* 12.5, $^4J_{PH}$ 1.9, 1-H), 4.75 (1 H, dd, *J* 12.5, $^4J_{PH}$ 1.9, 1-H), 6.88 (1 H, ddd, *J* 7.5, $J_{PH}$ 4.5, $^4J$ 1.2, 3′-H), 7.19 (1 H, dt, $^4J$ 1.2, *J* 7.5, 4′-H), 7.22–7.34 (10 H, m, $PPh_2$), 7.36 (1 H, dt, $^4J$ 1.2, *J* 7.5, 5′-H) and 7.55 (1 H, dd, *J* 7.5, $J_{PH}$ 4.5, 6′-H); $\delta_C$(126 MHz; $CDCl_3$) 16.5 (C-7), 56.7 (C-6), 71.3 (d, *J* 24, C-1), 74.0 (C-3), 75.7 (C-4), 127.6 (C-4′), 127.8 (d, *J* 5, C-6′), 128.2–128.6 (m, C-3″ + C-4″ of $PPh_2$), 129.0 (C-5′), 133.4 (C-3′), 133.8 (2 d, *J* 20, C-2″ of $PPh_2$), 135.2 (d, *J* 15, C-2′), 136.5 (d, *J* 10, C-1″ of $PPh_2$) and 142.7 (d, *J* 23, C-1′); $\delta_P$(81 MHz; $CDCl_3$) −16.2 (s); *m/z* (EI, 70 eV) 364 ($M^+$, 40%), 291 ([M − $C_4H_9O$]$^+$, 100), 275 ([M − $C_4H_9O_2$]$^+$, 40), 213 ([291 − $C_6H_6$]$^+$, 11), 197 ([275 − $C_6H_6$]$^+$, 15) and 183 ([$C_{12}H_8P$]$^+$, 21).

### (1*S*)-1-(2′-Bromophenyl)ethanol 15

A mixture of 2-bromoacetophenone **14** (7.6 g, 38 mmol) and MeOH (12 ml) was hydrogenated at 80 °C/80 bar for 24 h in the presence of a ruthenium-(*S*)-BINAP catalyst (20.6 μmol) prepared according to the literature.[8] After Kugelrohr distillation at 2 mbar (130 °C oven temp.) the slowly crystallizing oil was recrystallized twice from LP at −30 °C

(first 40 $cm^3$ and then 30 $cm^3$) to yield colourless crystals (5.7 g, 75%). The corresponding *R* compound was similarly obtained from (*R*)-BINAP (Found: C, 47.8; H, 4.3. $C_8H_9BrO$ requires C, 47.79; H, 4.51%); $[\alpha]_\lambda^{30}$ ($\lambda$/nm) −54.5 (589), −57.1 (578), −65.2 (546), −114 (436) and −188 (365) (*c* 1 in $CHCl_3$) {ref. 26, $[\alpha]_D^{30}$ −54 (*c* 1 in $CHCl_3$)}; $R_F(SiO_2, CH_2Cl_2)$ 0.27; $\delta_H$(80 MHz; $CDCl_3$) 1.45 (3 H, d, *J* 6, 2-$H_3$), 2.19 (1 H, d, *J* 2, OH), 5.19 (1 H, dq, *J* 6, *J* 2, 1-H) and 6.9–7.7 (4 H, mc, ArH).

**(1*S*)-1-(2′-Bromophenyl)methoxyethane 16**

This compound was synthesized by general procedure 2 for the alkylation of alkanols. (1*S*)-1-(2′-Bromophenyl)ethanol **15** (6.75 g, 33.6 mmol) was treated with MeI (8.5 $cm^3$, 19.4 g, 136 mmol), the reaction mixture being quenched with ice–water (200 $cm^3$) after 1 h and extracted twice with LP (2 × 50 $cm^3$). The combined extracts were washed with water, dried and after work-up ($MgSO_4$) the product was distilled in a Kugelrohr apparatus at 2 mbar (60–70 °C oven temp.) to yield a colourless oil (6.60 g, 91%) (Found: C, 49.55; H, 5.1. $C_9H_{11}BrO$ requires C, 50.25; H, 5.15%). The low C% value was a result of the high vapour pressure of the substance and the analytical apparatus); $[\alpha]_\lambda$ ($\lambda$/nm) −106 (589), −111 (578), −126 (546), −219 (436) and −353 (365) {(*c* 1 in $CH_2Cl_2$) (ref. 27, $[\alpha]_D^{20}$ −100.8 (*c* 6.4 in $CH_2Cl_2$)}; $R_F(SiO_2, CH_2Cl_2)$ 0.65; $\nu_{max}/cm^{-1}$ 3050 (Ar C–H), 2910 ($CH_3$), 1455, 1430, 1200, 1100 (C–O), 1010, 735 (Ar C–H); $\delta_H$(500 MHz; $CDCl_3$) 1.40 (3 H, d, *J* 6.3, 2-$H_3$), 3.26 (3 H, s, $OCH_3$), 4.72 (1 H, q, *J* 6.3, 1-H), 7.13 (1 H, ddd, *J* 8.0, *J* 7.3, $^4J$ 1.8, 5′-H), 7.35 (1 H, ddd, *J* 7.8, *J* 7.3, $^4J$ 1.1, 4′-H), 7.47 (1 H, dd, *J* 7.8, $^4J$ 1.8, 3′-H), 7.52 (1 H, dd, $^4J$ 8.0, *J* 1.1, 6′-H); *m*/*z* (EI, 70 eV) 214 ($M^+$, 12%), 199 ($[M - CH_3]^+$, 100), 183 ($[M - OCH_3]^+$, 12), 155 ($[M - C_3H_7O]^+$, 3) and 135 ($[M - Br]^+$, 2). The same yield was obtained when $(MeO)_2SO_2$ was used for methylation.

**(2*R*)-2-(2′-Bromophenyl)-3,6-dioxaheptane 17**

This compound was synthesized by general procedure 2. A mixture of (1*R*)-1-(2′-bromophenyl)ethanol **15** and 2-methoxyethyl toluene-*p*-sulfonate **18** was stirred for 1–2 h at room temp. after which it was treated with MeOH (9 $cm^3$) and stirring continued for a further 1 h. The mixture was then poured into water and extracted with LP (3 × 100 $cm^3$). The combined extracts were washed with a little water, dried ($MgSO_4$) and evaporated under reduced pressure to yield a colourless oil (7.1–7.4 g, 91–95%), which was distilled in a Kugelrohr apparatus at 2.5 mbar/100 °C (oven temp.) (Found: C, 60.0; H, 5.85. $C_{11}H_{15}BrO_2$ requires C, 50.98; H, 5.83%); $[\alpha]_\lambda$ ($\lambda$/nm) 66.2 (589), 69.3 (578), 78.9 (546), 136 (436), 218 (365) (*c* 1 in $CH_2Cl_2$); $R_F(SiO_2, CH_2Cl_2)$ 0.40; $\nu_{max}/cm^{-1}$ 3040 (Ar C–H), 2955, 2825, 1555, 1455, 1182, 1085 (CO), 1005, 733 (Ar C–H); $\delta_H$(500 MHz; $CDCl_3$) 1.43 (3 H, d, *J* 6.4, 1-$H_3$), 3.36 (3 H, s, $OCH_3$), 3.44–3.53 (4 H, m, 4-$H_2$, 5-$H_2$), 4.83 (1 H, q, *J* 6.4, 2-H), 7.10 (1 H, ddd, *J* 7.9, *J* 7.3, $^4J$ 1.8, 5′-H), 7.32 (1 H, dt, $^4J$ 1.2, *J* 7.3, 4′-H), 7.49 (1 H, dd, $^4J$ 1.2, *J* 7.9, 6′-H) and 7.51 (1 H, dd, $^4J$ 1.8, *J* 7.3, 3′-H).

**2-Methoxyethyl toluene-*p*-sulfonate 18**

2-Methoxyethanol and toluene-*p*-sulfonyl chloride were allowed to react in a 10-fold scale preparation by general procedure 3. Distillation of the raw product gave a colourless oil (150 g, 65%), bp 130 °C/0.05 mbar; $\delta_H$(60 MHz; $CDCl_3$) 2.40 (3 H, s, Ar-$CH_3$), 3.30 (3 H, s, 4′-$H_3$), 3.6–3.7 (2 H, m, 2′-$H_2$), 4.1–4.3 (2 H, m, 1′-$H_2$), 7.30 (2 H, d, *J* 8, 2-H, 6-H) and 7.80 (2 H, d, *J* 8, 3-H, 5-H).

**(2*S*,4*RS*)-2,4-Dimethyl-3,5-dioxaheptan-1-ol 19**

This compound was synthesized according to a literature preparation [11] from (*S*)-ethyl lactate by treatment with ethyl vinyl ether and $LiAlH_4$; product yield 90%; $[\alpha]_D^{25}$ 15.0–15.3 (neat) {(ref. 11, $[\alpha]_D^{25}$ 11.3 (neat)}. The deviation results from different diastereoselectivities on C-4); $\nu_{max}/cm^{-1}$ 3460 (OH), 2990, 2945 (CH), 1460, 1385, 1345, 1135 (C–O–C), 1060 and 975; $\delta_H$(60 MHz; $CDCl_3$) 1.1–1.5 (9 H, m, 7-$H_3$, 8-$H_3$, 9-$H_3$), 3.20 (1 H, s, OH), 3.3–4.4 (5 H, m, 1-$H_2$, 2-H, 6-$H_2$), 4.70 and 5.00 [1 H, dq (q), *J* 5, *J* 2 (*J* 5), diastereotopic 4-H]. An identical procedure using (*R*)-isobutyl lactate (219 g, 1.5 mol) gave the (2*R*,4*RS*) product (188 g, 85%). Separation of the isobutyl alcohol (bp 108 °C) after the reduction step was more complex in this reaction.

**(4*S*,6*RS*)-4,6-Dimethyl-2,5,7-trioxanonane 20**

After methylation of compound **19** with $(MeO)_2SO_2$ according to general procedure 2 the product was directly extracted from the reaction mixture with LP. Initially there was a strong tendency for emulsification, but this lessened later. The organic phases were washed with a minimum amount of water (the product is water miscible!) and, after evaporation of the solvent, distilled at 56 °C/16 mbar. A preparation starting with **19** (73.5 g, 0.50 mol), KOH (51 g, about 0.77 mol) and $(MeO)_2SO_2$ (65 $cm^3$) in DMSO (500 $cm^3$) gave a colourless oil (71 g, 89%) with acetal odour (Found: C, 58.85; H, 11.1. $C_8H_{18}O_3$ requires C, 59.23; H, 11.18%); $[\alpha]_D^{20}$ −6.0 (neat); $\nu_{max}/cm^{-1}$ 2960, 2860 ($OCH_3$), 1370, 1110 (C–O–C) and 985; $\delta_H$(500 MHz; $CDCl_3$) 1.12 (1.17) [3 H, d, *J* 6.3 (6.3), 10-$H_3$], 1.18 (1.18) [3 H, t, *J* 7.0 (7.0), 9-$H_3$], 1.30 (3 H, d, *J* 5.3, 11-$H_3$), 3.28 (3.29) [1 H, dd, $^2J$ 9.7 (9.8), *J* 4.7 (4.7), 3-H], 3.34 (3.35) (3 H, s, $OCH_3$), 3.34 (3.41) [1 H, dd, $^2J$ 9.8 (9.7), *J* 6.1 (5.8), 3-H], 3.45 (3.49) [1 H, dq, $^2J$ 9.1 (9.1), *J* 7.0 (7.0), 8-H], 3.63 (3.65) [1 H, dd, $^2J$ 9.1 (9.1), *J* 7.0 (7.0), 8-H], 3.83–3.90 (1 H, m, 4-H) and 4.77 (4.79) (1 H, q, *J* 5.3 (5.3), 6-H). The product was a 1:1 diastereoisomeric mixture. Individual signals were interpreted together with data for the second isomer in brackets.

**(2*S*)-4-Oxapentan-2-ol 21**

Concentrated hydrochloric acid (10 drops) was added to a solution of (4*S*,6*RS*)-4,6-dimethyl-2,5,7-trioxanonane **20** (59.9 g, 0.37 mol) in THF (150 $cm^3$) and water (13 $cm^3$, 0.72 mol) and the mixture was stirred at room temperature for 24 h. After the water had been removed by addition of $K_2CO_3$ to the mixture it was filtered and distilled through a 20-cm Vigreux column. After separation of the low-boiling substances (THF, EtOH, $CH_3CHO$, and $H_2O$) the product distilled at 115–118 °C as a colourless liquid (28.0 g, 85%). If the water was not removed carefully, an azeotrope formed resulting in slow increase of the boiling point from 90 to 115 °C and lowering of the yield (in the absence of water the bps are sharp); $[\alpha]_\lambda$ ($\lambda$/nm) 3.0 (589) 3.2 (578), 3.6 (546), 6.1 (436) and 9.4 (365) (neat); $\nu_{max}/cm^{-1}$ 3460 (OH), 2990, 2840 ($OCH_3$), 1120 (C–O–C) and 980. $\delta_H$(500 MHz; $CDCl_3$) 1.12 (3 H, d, *J* 6.3, 1-$H_3$), 2.34 (1 H, d br, *J* 2.5, OH), 3.17 (1 H, dd, $^2J$ 9.4, *J* 8.1, 3-H), 3.35 (1 H, dd, $^2J$ 9.4, *J* 3.0, 3-H), 3.37 (3 H, s, $OCH_3$) and 3.95 (1 H, ddq, *J* 8.1, *J* 3.0, *J* 6.3, 2-H).

**(3*S*)-1-(2′-Bromophenyl)-3-methyl-2,5-dioxahexane 22**

This product resulted from etherification of (2*S*)-4-oxapentan-2-ol **21** (4.7 g, 52 mmol) with 2-bromobenzyl bromide (11 g, 44 mmol) according to general procedure 2. After removal of the LP, the residue was chromatographed on silica using $CH_2Cl_2$ as eluent with a small unidentified, fore-running impurity being discarded. The product-containing fractions were concentrated and distilled in a Kugelrohr apparatus (3 mbar/130 °C oven temp.) to yield a colourless oil (5.9 g, 52%); $[\alpha]_\lambda$ ($\lambda$/nm) 5.5 (589) 5.8 (578), 6.5 (546), 10.9 (436) and 16.7 (365) (*c* 1 in $CH_2Cl_2$); $R_F(SiO_2, CH_2Cl_2)$ 0.43; $R_F(SiO_2, CHCl_3)$ 0.57; $R_F(SiO_2$, LP–EA 6:1) 0.44; $\nu_{max}/cm^{-1}$ 2985, 2885, 1450, 1210, 1125 (C–O), 1035, 755 (Ar C–H); $\delta_H$(500 MHz; $CDCl_3$) 1.24 (3 H, d, *J* 7.2, 7-$H_3$), 3.40 (3 H, s, $OCH_3$), 3.41 (1 H, dd, $^2J$ 10.0, *J* 4.2, 4-H), 3.50 (1 H, dd, $^4J$ 10.0, *J* 5.8, 4-H), 3.78 (1 H, ddq, *J* 5.8, *J* 4.2, *J* 7.2, 3-H), 4.66 (2 H, s, 1-$H_2$), 7.13 (1 H, dt, $^4J$ 1.8, *J* 7.5, 5′-H), 7.31 (1 H, dt, $^4J$ 1.0, *J* 7.2, 4′-H), 7.52 (1 H, dd, $^4J$ 1.2, *J* 7.9, 6′-H) and 7.54 (1 H, md, *J* 7.5, 3′-H).

**(2*S*)-Ethyl 2-methoxypropanoate 24**
In a 1-dm$^3$ three-necked bulb with nitrogen inlet, thermometer, reflux condenser and dropping funnel, paraffin-free NaH (24.0 g, 1.00 mol) was suspended in anhydrous $Et_2O$ (750 cm$^3$) and the mixture was cooled to −5 to −10 °C by means of an ice–NaCl bath. A mixture of (*S*)-ethyl lactate **23** (120 g, 1.02 mol) and dimethyl sulfate (135 g, 1.07 mol) was added to the reaction mixture so that its temperature was kept < 0 °C; vigorous gas evolution and decolourization occurred. After the resulting suspension had been stirred at room temperature for 2 h it was filtered and the residue was washed thoroughly with $Et_2O$. The colourless filtrate was distilled through a 20-cm Vigreux column, the solvent at 1 bar, the product at 12 mbar (water jet vacuum) to give a colourless oil (110–120 g, 83–91%) with a sweet odour; $[\alpha]_D^{25}$ −79.8 (neat); $\nu_{max}$/cm$^{-1}$ 2980, 2820 ($OCH_3$), 1745 (C=O), 1270, 1195 and 1130 (C–O); $\delta_H$(60 MHz; $CDCl_3$) 1.50 (3 H, t, *J* 7, $CH_2CH_3$), 1.60 (3 H, t, *J* 7, 3-$H_3$), 3.60 (3 H, s, $OCH_3$), 4.10 (1 H, q, *J* 7, 2-H) and 4.50 (2 H, sextet, *J* 7, $CH_2CH_3$).

**(2*S*)-2-Methoxypropanol 25**
$LiAlH_4$ (25 g in the form of small cylinders, 0.66 mol) was placed under $Et_2O$ (300 cm$^3$) in a 1-dm$^3$ two-necked bulb with nitrogen inlet, reflux condenser and a 500-cm$^3$ dropping funnel. A solution of (2*S*)-ethyl 2-methoxypropanoate **24** (115 g, 0.87 mol) in $Et_2O$ (300 cm$^3$) was added dropwise to the stirred mixture at room temperature after which it was heated to reflux for 1 h. After cooling, the mixture was hydrolysed with a cold solution of KOH (100 g) in water (250 cm$^3$) and the ether layer was decanted; the aqueous phase was then extracted with ether (3 × 200 cm$^3$). The combined extracts were dried ($MgSO_4$) and distilled through a Vigreux column from a 100-cm$^3$ two-necked bulb. After removal of the solvent, the product distilled in the range 129–131 °C as a colourless liquid (60 g, 77%); $[\alpha]_\lambda^{25}$ ($\lambda$/nm) 16.7 (589), 17.5 (578), 19.8 (546), 32.6 (436) and 49.3 (365) (neat) {ref. 13, $[\alpha]_D^{25}$ 9.6 (neat)}; $[\alpha]_\lambda$ ($\lambda$/nm) 43.6 (589), 45.3 (578), 51.0 (546), 82.7 (436) and 122 (365) (*c* 0.5 in $CHCl_3$) {ref. 13, $[\alpha]$ 19.3 (*c* 0.5, $CHCl_3$)}; $\delta_H$(60 MHz; $CDCl_3$) 1.0–1.2 (3 H, mc, 3-$H_3$), 3.10 (1 H, s, OH), 3.35 (3 H, s, $OCH_3$) and 3.4–3.6 (2 H, mc, 1-$H_2$).

**(2′*S*)-2-Methoxypropyl toluene-*p*-sulfonate 26**
The esterification of (2*S*)-2-methoxypropanol **25** proceeded according to general procedure 3. From **25** (27 g, 0.30 mol) and toluene-*p*-sulfonyl chloride (66 g, 0.35 mol) in pyridine (60 cm$^3$) work-up gave a colourless oil (70 g, 96%) (Found: C, 53.9; H, 6.6. $C_{11}H_{16}O_4S$ requires C, 54.08; H, 6.60%); $[\alpha]_\lambda$ ($\lambda$/nm) −3.9 (589), −4.1 (578), −4.6 (546), −8.0 (436) and −12.9 (365) (neat); $[\alpha]_\lambda$ ($\lambda$/nm) −5.5 (589), −5.8 (578), −6.5 (546), −10.4 (436) and −16.3 (365) (*c* 1 in $CH_2Cl_2$); $R_F$($SiO_2$, $CH_2Cl_2$) 0.59; $\nu_{max}$/cm$^{-1}$ 2980, 2930, 2820 ($OCH_3$), 1600 (Ar C–C), 1365 (S=O), 1180 (C–O–C) and 990; $\delta_H$(500 MHz; $CDCl_3$) 1.09 (3 H, d, *J* 6.2, 3′-$H_3$), 2.43 (3 H, s, Ar-$CH_3$), 3.27 (3 H, s, $OCH_3$), 3.52 (1 H, tq, *J* 5.2, *J* 6.2, 2′-H), 3.93 (2 H, d, *J* 5.2, 1′-$H_2$), 7.33 (2 H, d, *J* 8.2, 2-H, 6-H) and 7.78 (2 H, d, *J* 8.2, 3-H, 5-H).

**(4*S*)-1-(2′-Bromophenyl)-4-methyl-2,5-dioxahexane 27**
2-Bromobenzyl alcohol (5.6 g, 30 mmol) was treated with (2′*S*)-2-methoxypropyl toluene-*p*-sulfonate **26** according to general procedure 3. After 3–4 h MeOH (8 cm$^3$) was added to the reaction mixture which was then stirred for a further 0.5 h before being poured onto ice–water (120 cm$^3$). Work-up gave a yellowish oil, which was purified by distillation in a Kugelrohr apparatus at 2 mbar and 130 °C (oven temp.) to yield a colourless oil (7.2–7.5 g, 93–96%); $[\alpha]_\lambda$ ($\lambda$/nm) −3.2 (589), −3.3 (578), −3.8 (546), −6.7 (436) and −11.0 (365) (*c* 1 in $CH_2Cl_2$); $\delta_H$(500 MHz; $CDCl_3$) 1.19 (3 H, d, *J* 6.1, 7-$H_3$), 3.42 (3 H, s, $OCH_3$), 3.51 (1 H, dd, $^2J$ 9.5, *J* 4.2, 3-H), 3.57 (1 H, dd, $^4J$ 9.5, *J* 5.5, 3-H), 3.60 (1 H, ddq, *J* 5.5, *J* 4.2, *J* 6.1, 4-H), 4.62 (2 H, s, 1-$H_2$), 7.14 (1 H, dt, $^4J$ 1.8, *J* 7.5, 5′-H), 7.32 (1 H, dt, $^4J$ 1.1, *J* 7.5, 4′-H), 7.50 (1 H, dd, *J* 7.5, $^4J$ 1.8, 6′-H) and 7.53 (1 H, dd, *J* 7.5, $^4J$ 1.1, 3′-H); *m*/*z* (EI, 70 eV) 258 (M$^+$, 9%), 199 ([M − $C_3H_7O$]$^+$, 1), 185 ([M − $C_4H_9O$]$^+$, 8), 169 ([M − $C_4H_9O_2$]$^+$, 14), 90 ([$C_4H_{10}O_2$]$^+$, 9) and 59 ([$C_3H_7O$]$^+$, 100).

**(1*R*)-1-Phenyl-3-oxabutanol 29**
Ethyl vinyl ether (20 cm$^3$, 0.21 mol) was added to the mixture of (*R*)-mandelic acid (7.6 g, 50 mmol) and toluene-*p*-sulfonic acid (15 mg) in dry THF (7.5 cm$^3$) the temperature being maintained < +5 °C. After completion of the addition, the clear mixture was stirred for 24 h at room temperature. It was then treated with $NEt_3$ (1.0 cm$^3$) to quench the reaction. After removal of the solvent, the residual oil was taken up in dry $Et_2O$ and added dropwise to a stirred suspension of $LiAlH_4$ (2.0 g, 53 mmol) in $Et_2O$. The hot mixture was refluxed for a further 1 h after which it was treated with a solution of KOH (6.0 g) in water (20 cm$^3$), added at < +10 °C. The aqueous phase was thrice extracted with $Et_2O$ and the combined extracts were dried ($K_2CO_3$) and evaporated to dryness. The product was added to a cooled (+10 °C) suspension of powdered KOH (12.7 g, 193 mmol) in dry DMSO (120 cm$^3$) followed by dimethyl sulfate (7.5 cm$^3$, 79 mmol) added in 5 portions during 1 h. After being stirred for a further 1h at room temperature the reaction mixture was diluted with water (100–150 cm$^3$) and extracted with LP. The extract was washed with a little water and evaporated and the residue was taken up in MeOH (100 cm$^3$) containing conc. HCl (10 drops). After this solution had been stirred for 2 h at room temperature, it was evaporated and fresh MeOH (100 cm$^3$) was added to the residue (pH of the solution had to be < 3, otherwise hydrochloric acid was added to it); the solution was then stirred overnight at room temperature. After MeOH had been removed, $K_2CO_3$ was added to the residue and the product was distilled *in vacuo* to yield a colourless oil (6.9 g, 91%) with a fruit-like odour; $[\alpha]_\lambda$ ($\lambda$/nm) −50.5 (589), −52.7 (578), −59.8 (546), −100.2 (436), −153 (365) (*c* 2.74 in $CH_2Cl_2$) {ref. 28, $[\alpha]_D^{20}$ −47.6 (*c* 2.75 in $CH_2Cl_2$)}; $\delta_H$(250 MHz; $CDCl_3$) 2.86 (1 H, d, *J* 2.3, OH), 3.43 (1 H, dd, $^2J$ 9.8, *J* 8.7, 2-H), 3.43 (1 H, s, $OCH_3$), 3.54 (1 H, dd, $^2J$ 9.8, *J* 3.2, 1-H), 4.89 (1 H, ddd, *J* 8.7, *J* 3.2, *J* 2.3, 1-H) and 7.25–7.40 (5 H, m, 2′-H–6′-H); $\delta_C$(62.9 MHz; $CDCl_3$) 59.0 (C-4), 72.7 (C-1), 78.2 (C-2), 126.1 (C-2′, C-6′), 127.8 (C-4′), 128.4 (C-3′, C-5′) and 140.4 (C-1′).

**(3*R*)-1-(2′-Bromophenyl)-3-phenyl-2,5-dioxahexane 30**
(1*R*)-1-Phenyl-3-oxabutanol **29** was alkylated with 2-bromobenzyl bromide following general procedure 2. The crude product obtained from the LP phase was chromatographed on silica using gradient elution (LP→LP–EA, 3:1). Concentration of the product-containing fractions, gave a colourless oil (7.9 g, 82%); $[\alpha]_\lambda$ ($\lambda$/nm) −47.8 (589), −49.9 (578), −56.7 (546), −97.1 (436) and −154.2 (365) (*c* 1 in $CH_2Cl_2$); $R_F$($SiO_2$, LP–EA, 6:1) 0.44; $R_F$($SiO_2$, $CH_2Cl_2$) 0.67; $\nu_{max}$/cm$^{-1}$ 3070, 3040 (Ar C–H), 3000, 2930, 2880 (Aliph. C–H), 1730, 1595 (Ar C–C), 1460 (Aliph. C–H), 1210, 1130, 1105 (C–O), 1035 (Ar), 755 (Ar C–H); $\delta_H$(400 MHz; $CDCl_3$) 3.41 (3 H, s, $OCH_3$), 3.53 (1 H, dd, $^2J$ 10.6, *J* 3.8, 4-H), 3.72 (1 H, dd, $^2J$ 10.6, *J* 7.8, 4-H), 4.50 (1 H, d, $^2J$ 13.3, 1-H), 4.55 (1 H, d, $^2J$ 13.3, 1-H), 4.65 (1 H, dd, *J* 7.8, *J* 3.8, 3-H), 7.12 (1 H, mt, *J* ~7.7, 5′-H), 7.32 (1 H, mt, *J* ~7.7, 4′-H), 7.30–7.35 (1 H, m, H-4″), 7.35–7.40 (4 H, m, 2″-H, 3″-H), 7.49 (1 H, dd, *J* 8.0, $^4J$ 1.2, 6′-H), 7.62 (1 H, md, *J* ~7.7, 3′-H); $\delta_C$(100.6 MHz; $CDCl_3$) 59.3 (C-6), 70.2 (C-1), 77.3 (C-4), 81.1 (C-3), 122.4 (C-2″), 127.0 (C-2′), 127.3 (C-4″), 128.1 (C-4′), 128.5 (C-3″), 128.7 (C-5′), 129.1 (C-3′), 132.3 (C-6′), 137.8 (C-1″) and 138.9 (C-1′); *m*/*z* (EI, 70 eV) 320 (M$^+$, 0.2%), 275 ([M − $C_2H_5O$]$^+$, 11), 185 ([275 − $C_7H_8$]$^+$, 23), 169 ([275 − $C_6H_5CHO$]$^+$, 44), 155 ([169 − $CH_2$]$^+$, 11), 122 ([$C_8H_{10}O$]$^+$, 13), 105 ([$C_6H_5CO$]$^+$, 63) and 77 ([$C_6H_5$]$^+$, 100).

**(2′*S*)-(4′-Oxapentan-2′-yl) toluene-*p*-sulfonate 31**
This compound was synthesized by general procedure 3 from (2*S*)-4-oxapentan-2-ol **21** (23.0 g, 256 mmol) as a colourless oil (57 g, 91%) after column filtration through $SiO_2$ (Found: C, 54.0; H, 6.5. $C_{11}H_{16}O_4S$ requires C, 54.08; H, 6.60%); $\nu_{max}/cm^{-1}$ 2980, 2930, 2880 ($OCH_3$), 1600 (Ar C–C), 1450 ($CH_3$), 1360 (S=O), 1175 (S=O), 1115 (C–O–C), 1095 (C–O–C), 915 and 765; $\delta_H$(500 MHz; $CDCl_3$) 1.25 (3 H, d, *J* 6.3, 1′-$H_3$), 2.42 (3 H, s, Ar $CH_3$), 3.22 (1 H, s, $OCH_3$), 3.34 (1 H, dd, $^2J$ 10.8, *J* 4.4, 3′-H), 3.40 (1 H, dd, $^2J$ 10.8, *J* 5.8, 3′-H), 4.69 (1 H, ddq, *J* 5.8, *J* 4.4, *J* 6.3, 2′-H), 7.31 (2 H, d, *J* 8, 2-H, 6-H) and 7.79 (2 H, d, *J* 8, 3-H, 5-H).

**(2*R*)-1-(2′-Bromophenyl)-2-methyl-1,4-dioxapentane 32**
KOBu$^t$ (7.3 g, 65.2 mmol) was added to a solution of 2-bromophenol (10.0 g, 57.8 mmol) in dry DMF (80 ml) cooled in an ice-bath. This was followed by portionwise addition of (2′*S*)-(4′-oxapentan-2′-yl) toluene-*p*-sulfonate **31** (15.9 g, 65.2 mmol). After the ice-bath had been removed the mixture was stirred at room temperature for 16 h after which it was treated with MeOH (4.0 $cm^3$) to consume uncharged sulfonate. Stirring was continued for 4 h after which the mixture was diluted with water (50 $cm^3$) and extracted with LP. The extract was washed with a small amount of water, dried ($MgSO_4$) and evaporated to leave a colourless oil (9.6 g, 68%) (Found: C, 48.7; H, 5.35. $C_{10}H_{13}BrO_2$ requires C, 49.00; H, 5.35%); $[\alpha]_\lambda$ ($\lambda$/nm) 11.7 (589), 12.3 (578), 13.8 (546), 24.4 (436) and 43.3 (365) (*c* 1 in $CH_2Cl_2$); $R_F$($SiO_2$, $CH_2Cl_2$) 0.53; $\nu_{max}/cm^{-1}$ 3060 (Ar C–H), 2980, 2920, 2880 (Aliph. C–H), 1590, 1480 (Ar C–C), 1445 (Aliph. C–H), 1280, 1250, 1115 (C–O), 1035 (Ar), 975 and 750 (Ar C–H); $\delta_H$(400 MHz; $CDCl_3$) 1.35 (3 H, d, *J* 6.3, 6-$H_3$), 3.43 (3 H, s, $OCH_3$), 3.53 (1 H, dd, $^2J$ 10.3, *J* 4.6, 3-H), 3.65 (1 H, dd, $^2J$ 10.3, *J* 5.9, 3-H), 4.54 (1 H, ddq, *J* 5.9, *J* 4.6, *J* 6.3, 2-H), 6.83 (1 H, ddd, *J* 7.9, *J* 7.4, $^4J$ 1.4, 4′-H), 6.99 (1 H, dd, *J* 8.3, $^4J$ 1.4, 6′-H), 7.23 (1 H, ddd, *J* 8.3, *J* 7.4, $^4J$ 1.6, 5′-H) and 7.53 (1 H, dd, *J* 7.9, $^4J$ 1.6, 3′-H); $\delta_C$(100.6 MHz; $CDCl_3$) 17.0 (C-6), 59.5 (C-5), 75.4 (C-2), 75.8 (C-3), 113.8 (C-2′), 116.2 (C-6′), 122.3 (C-4′), 128.3 (C-5′), 133.4 (C-3′) and 154.7 (C-1′); *m*/*z* (EI, 70 eV) 244 ($M^+$, 8%), 200 ([M − $C_2H_4O$]$^+$, 5), 172 ([200 − $C_2H_4$]$^+$, 24), 155 ([172 − OH]$^+$, 7) and 73 ($C_4H_9O^+$, 100).

**(3*S*)-1-(2′-Bromophenyl)-3-methyl-1,4-dioxapentane 33**
This compound was prepared in a similar fashion to its isomer **32** from (2′*S*)-(2′-methoxypropyl) toluene-*p*-sulfonate **26** as an alkylating reagent. After removal of the LP, the product was obtained in the form of a colourless oil (11.4 g, 81%) (Found: C, 49.0; H, 5.4. $C_{10}H_{13}BrO_2$ requires C, 49.00; H, 5.35%); $[\alpha]_\lambda$ ($\lambda$/nm) −7.1 (589), −7.4 (578), −8.4 (546), −14.9 (436) and −24.6 (365) (*c* 1 in $CH_2Cl_2$); $R_F$($SiO_2$, $CH_2Cl_2$) 0.50; $\nu_{max}/cm^{-1}$ 3070 (Ar C–H), 2990, 2940, 2830 (Aliph. C–H), 1595, 1490 (Ar C–C), 1450 (Aliph. C–H), 1290, 1255, 1160, 1110 (C–O), 1060, 1035 (Ar) and 750 (Ar C–H); $\delta_H$(400 MHz; $CDCl_3$) 1.31 (3 H, d, *J* 6.3, 6-$H_3$), 3.50 (3 H, s, $OCH_3$), 3.78 (1 H, ddq, *J* 6.0, J 4.8, *J* 6.3, 3-H), 3.91 (1 H, dd, $^2J$ 9.5, *J* 4.8, 2-H), 4.05 (1 H, dd, $^2J$ 9.5, *J* 6.0, 2-H), 6.83 (1 H, ddd, *J* 7.9, *J* 7.4, $^4J$ 1.4, 4′-H), 6.89 (1 H, dd, *J* 8.2, $^4J$ 1.4, 6′-H), 7.25 (1 H, ddd, *J* 8.2, *J* 7.4, $^4J$ 1.6, 5′-H) and 7.53 (1 H, dd, *J* 7.9, $^4J$ 1.6, 3′-H); $\delta_C$(100.6 MHz; $CDCl_3$) 17.0 (C-6), 57.5 (C-5), 72.7 (C-2), 75.3 (C-3), 112.3 (C-2′), 113.3 (C-6′), 122.0 (C-4′), 128.4 (C-5′), 133.3 (C-3′) and 155.2 (C-1′); *m*/*z* (EI, 70 eV) 244 ($M^+$, 8%), 185 ([M − $C_3H_7O$]$^+$, 2), 172 ([M − $C_4H_8O$]$^+$, 11), 155 ([172 − OH]$^+$, 12), 143 ($C_5H_5Br^+$, 13) and 73 ($C_4H_9O^+$, 100).

**(3*S*)-3-Methyl-1-phenyl-1,4-dioxapentane 34**
Phenol (4.00 g, 42.6 mmol) was added to a mixture of KOBu$^t$ (5.00 g, 44.6 mmol) and dry DMSO (80 $cm^3$) and the resulting mixture was cooled to +15 °C in a water-bath. (2*S*)-(2′-Methoxypropyl) toluene-*p*-sulfonate **26** (7.32 g, 30.0 mmol) was then added slowly to the mixture after which it was stirred overnight, diluted with an equal volume of water and extracted with LP. The extract was dried ($MgSO_4$) and evaporated to give a colourless liquid (4.32 g, 87%); $R_F$($SiO_2$, $CH_2Cl_2$) 0.54; *m*/*z* (EI, 70 eV) 166 ($M^+$, 53%), 121 ($M^+$ − $CH_2OCH_3$, 5), 94 ($C_6H_5OH^+$, 58) and 73 ($C_4H_9O^+$, 100).

**2-Bromobenzyl(triphenyl)phosphonium bromide 36**
A mixture of 2-bromotoluene (166 g, 0.97 mol) and NBS (180 g, 1.01 mol) in acetone (4 $dm^3$) was irradiated with a mercury high-pressure lamp (180 W) while $N_2$ was bubbled through it. The completion of the reaction (after 4–6 h) was checked by TLC. The mixture was then concentrated on a rotatory evaporator in a water jet vacuum to give a semi-solid residue which was taken up in $CH_2Cl_2$. The resulting dark solution was washed twice with water and then evaporated. After addition of DMF (700 $cm^3$) and $PPh_3$ (315 g) to the residue, the light yellow to brownish solution was stirred overnight while an exothermic reaction occurred accompanied by partial crystallization of the product. Precipitation of the product was completed by pouring the mixture into toluene (2–3 $dm^3$) with efficient stirring. The product was filtered off, dissolved in $CH_2Cl_2$ (2 $dm^3$) and re-precipitated by addition of $Et_2O$; it was then filtered off and dried in vacuo. This procedure was repeated to yield colourless crystals (438 g, 88%); $\delta_H$(60 MHz; $CDCl_3$) 5.6 (2 H, d, *J* 14, $CH_2P^+$) and 7.0–7.9 (19 H, m, ArH); *m*/*z* (FAB, MeOH–glycerol) 431 (cation).

**(*E*)-2,2′-Dibromostilbene *E*-37**
In a 1-$dm^3$ three-necked bulb with thermometer, dropping funnel, reflux condenser and $N_2$-inlet, compound **36** (115 g, 0.22 mol) was suspended in EtOH (500 $cm^3$) under an $N_2$ atmosphere. A separately prepared solution of Na (6.0 g, 0.26 mol) in EtOH (250 $cm^3$) was added to the reaction mixture to give an orange coloured suspension which was warmed to 30–50 °C for 30 min. After cooling in an ice-bath, the mixture was treated dropwise with a solution of freshly distilled 2-bromobenzaldehyde (40 g, 0.22 mol) in EtOH (100 $cm^3$); the colour of the mixture faded and an exothermal reaction occurred. After complete addition the mixture was heated to reflux for 1 h (maximum) although this was stopped immediately if a brown colour appeared. After cooling in an ice-bath, the reaction mixture was treated slowly with conc. hydrochloric acid (30 $cm^3$) and then evaporated to dryness. The residue was distributed between water (100 $cm^3$) and toluene (150 $cm^3$); after separation the aqueous phase was extracted with toluene (×2). The combined organic phase and extracts were then cautiously coated on $SiO_2$ (250 $cm^3$) in a rotatory evaporator. This $SiO_2$ was put on a column already filled with fresh $SiO_2$ and the product was eluted with LP (several litres were necessary for complete removal). Concentration of the eluent yielded a colourless oil which was taken up in hot heptane (250 $cm^3$) to which a few crystals of $I_2$ were added until a good violet colour remained. When the solution was exposed to the sun for a few days (in winter this time had to be extended to weeks) large, clear crystals grew on the bottom of the bulb. The solvent was decanted and the product was crystallized from heptane (150 $cm^3$) to yield highly diffracting, colourless crystals (50 g, 68%), mp 109–110 °C (Found: C, 49.5; H, 3.0. $C_{14}H_{12}Br_2$ requires C, 49.74; H, 2.98%); $R_F$($SiO_2$, $CH_2Cl_2$) 0.86; $R_F$($SiO_2$, LP) 0.33; $R_F$($SiO_2$, toluene) 0.78; $\delta_H$(500 MHz; $CDCl_3$) 7.14 (2 H, ddd, *J* 7.9, *J* 7.5, $^4J$ 1.7, 2 × 4-H), 7.33 (2 H, dt, $^4J$ 1.2, *J* 7.4, 2 × 5-H), 7.39 (2 H, s, CH=CH), 7.58 (2 H, dd, *J* 7.4, $^4J$ 1.2, 2 × 3-H), 7.71 (2 H, dd, *J* 7.5, $^4J$ 1.7, 2 × 6-H); *m*/*z* (EI, 70 eV) 336 ($M^+$, 24%), 256 ([M − HBr]$^+$, 2) and 178 ([M − $Br_2$]$^+$, 100).

**(*Z*)-2,2′-Dibromostilbene *Z*-37**
The oil obtained in the preceding preparation after column filtration was crystallized twice from MeOH with seeding to give the title compound as stout, colourless crystals (*ca.* 40%), mp 60–62 °C; $R_F$($SiO_2$, LP) 0.43; $\delta_H$(500 MHz; $CDCl_3$) 6.76 (2 H, s, CH=CH), 6.95 (2 H, dd, *J* 7.4, $^4J$ 2.0, 2 × 6-H), 6.99 (2 H,

dt, $^4J$ 1.4, $J$ 7.4, 2 × 5-H), 7.03 (2 H, dt, $^4J$ 2.0, $J$ 7.4, 2 × 4-H) and 7.55 (2 H, dd, $J$ 7.4, $^4J$ 1.4, 2 × 3-H); $m/z$ (EI, 70 eV) 336 ($M^+$, 20%), 256 ([M − HBr]$^+$, 3) and 178 ([M − $Br_2$]$^+$, 100).

**2,2′-Dibromobenzil 38**

This compound was prepared in a similar way to the diol **39** (see next experiment) provided no $MeSO_2NH_2$ was added to the mixture and the reaction was allowed to proceed at room temperature for 2 days. The residue obtained after work-up was purified by column chromatography to give initially, with LP, starting material, and then, with $CH_2Cl_2$, the title compound as a yellow zone. Evaporation of the fraction and crystallization of the residue from a minimum of $C_6H_6$ gave the product as yellow crystals (~10%), mp 115–120 °C; $R_F$($SiO_2$, toluene) 0.56; $\nu_{max}$/cm$^{-1}$ 3070 (Ar C–H), 1770, 1660 (C=O), 1580 (Ar C–C), 1430, 1260, 1200, 1025, 845 and 730 (Ar C–H); $\delta_H$(500 MHz; $CDCl_3$) 7.46 (2 H, dt, $^4J$ 2.0, $J$ 7.4, 2 × 4-H), 7.49 (2 H, dt, $^4J$ 1.5, $J$ 7.4, 2 × 5-H), 7.69 (2 H, dd, $^4J$ 1.5, $J$ 7.4, 2 × 3-H) and 7.99 (2 H, dd, $J$ 7.4, $^4J$ 2.0, 2 × 6-H); $m/z$ (EI, 70 eV) 366 ($M^+$, 1%), 287 ([M − Br]$^+$, 2), 183 ([M/2]$^+$, 100), 155 ([183 − CO]$^+$, 21) and 76 ([155 − Br]$^+$, 19).

**(1*S*,2*S*)-1,2-Bis(2′-bromophenyl)ethane-1,2-diol 39**

Bu$^t$OH (450 cm$^3$), $K_2OsO_4$·$2H_2O$ (374 mg, 1.01 mmol), the quinine ester of 4-chlorobenzoic acid (1.3 g, 2.8 mmol) and $MeSO_2NH_2$ (9.6 g, 101 mmol) were added sequentially to a solution of $K_3$[Fe(CN)$_6$] (98 g, 0.30 mol) and $K_2CO_3$ (41 g, 0.30 mol) in water (450 cm$^3$). This mixture was vigorously stirred at 0 °C for 30 min after which finely powdered (*E*)-2,2′-dibromostilbene *E*–**37** (34.3 g, 101 mmol) was added to it. The hydroxylation for 4–6 days (the reaction was screened by TLC) at 0 °C after which the excess of oxidant was destroyed by addition of $Na_2SO_3$ (50 g, 0.40 mol) to the mixture and continued stirring for 30 min. Bu$^t$OH was removed by rotatory evaporation and the residual brownish aqueous slurry was extracted with EA (3 × 150 cm$^3$). The combined extracts were dried ($Na_2SO_4$) and evaporated to give a yellowish solid which was recrystallized from cyclohexane (2 × 600 cm$^3$) to afford colourless crystals, (22.7–24.4 g, 60–65%) mp 104–105 °C; optical purity was usually >90% ee (Found: C, 45.0; H, 3.65. $C_{14}H_{12}Br_2O_2$ requires C, 45.20; H, 3.25%); $[\alpha]_\lambda^{23}$ (λ/nm) 38.7 (589), 40.1 (578), 46.0 (546), 82.0 (436) and 137 (365) ($c$ 1 in EtOH) {ref. 15, $[\alpha]_D^{23}$ 39.9 ($c$ 1 in EtOH). Thus, the optical purity of this product was *ca.* 97% ee}; $R_F$($SiO_2$, $CH_2Cl_2$) 0.13; $R_F$($SiO_2$, EA) 0.77; $\delta_H$(500 MHz; $CDCl_3$) 2.83 (2 H, 't' br, $J$ 1.7, 2 × OH), 5.32 (2 H, d, $J$ 1.7, 1-H, 2-H), 7.14 (2 H, ddd, $J$ 8.0, $J$ 7.5, $^4J$ 1.8, 2 × 5′-H), 7.35 (2 H, dt, $^4J$ 1.2, $J$ 7.5, 2 × 4′-H), 7.46 (2 H, dd, $J$ 8.0, $^4J$ 1.2, 2 × 6′-H), 7.70 (2 H, dd, $J$ 7.5, $^4J$ 1.8, 2 × 3′-H). The *R*,*R*-enantiomer was obtained similarly by using the quinidine ester of 4-chlorobenzoic acid instead of the quinine ester.

**(1*S*,2*S*)-1,2-Bis(2′-bromophenyl)-1,2-dimethoxyethane 40**

The diol **39** (7.44 g, 20 mmol) was alkylated with $(MeO)_2SO_2$ (9.0 cm$^3$, 12 g, 95 mmol) according to general procedure 2. After being stirred for 1.5 h the mixture was diluted with water (100 cm$^3$) and extracted with LP (3 × 100 cm$^3$). The combined extracts were washed with water and evaporated to dryness, and the residue was crystallized from MeOH (40 cm$^3$) to give colourless needles (6.3 g, 79%), mp 85–85.5 °C; $[\alpha]_\lambda$ (λ/nm) 107.2 (589), 112 (578), 128 (546), 227 (436) and 379 (365) ($c$ 1 in $CH_2Cl_2$); $R_F$($SiO_2$, $CH_2Cl_2$) 0.46; $\delta_H$(500 MHz; $CDCl_3$) 3.19 (6 H, s, 2 × $OCH_3$), 4.95 (2 H, s, 1-H, 2-H), 7.10 (2 H, ddd, $J$ 8.0, $J$ 7.5, $^4J$ 1.8, 2 × 5′-H), 7.32 (2 H, dt, $^4J$ 1.2, $J$ 7.5, 2 × 4′-H), 7.41 (2 H, dd, $J$ 8.0, $^4J$ 1.2, 2 × 6′-H) and 7.66 (2 H, dd, $J$ 7.5, $^4J$ 1.8, 2 × 3′-H); $m/z$ (EI, 70 eV) 199 ([M/2]$^+$, 100%).

**(4*S*,5*S*)-4,5-Bis(2′-bromophenyl)-2,2-dimethyl-1,3-dioxolane 41**

A solution of the diol **39** (7.44 g, 20 mmol) in 2,2-dimethoxypropane (25 cm$^3$, 200 mmol) was treated with conc. HCl (3 drops) and the mixture was stirred at room temperature for 16 h. After this it was evaporated and the residue treated with $NEt_3$ (3 drops). The mixture was taken up in $CH_2Cl_2$ and the solution filtered through a column of alumina and concentrated to dryness. Crystallization of the residue from LP (35 cm$^3$) and drying *in vacuo* gave the product as colourless crystals (6.1–6.4 g, 76–80%), mp 109–110 °C; $[\alpha]_\lambda$ (λ/nm) 1.8 (589), 1.9 (578), 2.2 (546), 5.4 (436) and 17.5 (365) ($c$ 1 in $CH_2Cl_2$); $R_F$($SiO_2$, $CH_2Cl_2$), 0.69; $R_F$($Al_2O_3$, $CH_2Cl_2$) 0.86; $\delta_H$(500 MHz; $CDCl_3$) 1.73 (6 H, s, 2 × $CH_3$), 5.22 (2 H, s, 4-H, 5-H), 7.15 (2 H, ddd, $J$ 8.0, $J$ 7.5, $^4J$ 1.8, 5′-H), 7.38 (2 H, dt, $J$ 7.5, $^4J$ 1.2, 4′-H), 7.42 (2 H, dd, $J$ 8.0, $^4J$ 1.2, 6′-H) and 7.72 (2 H, dd, $J$ 7.5, $^4J$ 1.8, 3′-H); $m/z$ (EI, 70 eV) 410 ($M^+$, 4%), 395 ([M − $CH_3$]$^+$, 1), 354 ([M − $C_3H_6O$]$^+$, 2), 226 ([M − $C_7H_5BrO$]$^+$, 100), 169 ([$C_7H_6Br$]$^+$, 29), 147 ([226 − Br]$^+$, 79) and 89 ([147 − $C_3H_6O$]$^+$, 68).

**Bis(phosphane)nickel-catalysed Grignard cross coupling reactions**

**(a) 3-Phenylbut-1-ene 44.** A 500-cm$^3$ two-necked bulb equipped with a reflux condenser and a dropping funnel was charged with Mg (3.20 g, 133 mmol) and a crystal of $I_2$. A portion (5 cm$^3$) of a solution of 1-phenylethyl chloride **43** (16.0 cm$^3$, 120 mmol) in dry $Et_2O$ (200 cm$^3$) was added to the mixture after which the reaction was started by cautious heating. The rest of the solution was then added in such a manner that gentle refluxing of the $Et_2O$ was maintained (faster addition gave larger amounts of 2,3-diphenylbutane and styrene). After completion of the addition, boiling was continued for 30 min by external heating. The cooled Grignard solution was filtered through glass wool and stored at −20 °C until use.

For the cross coupling, a mixture of $NiCl_2$ (5.2 mg, 40 mmol), the respective phosphane (88 mmol for monophosphanes, 44 mmol for diphosphanes) and $Et_2O$ (10 cm$^3$) was stirred in a 100-cm$^3$ bulb under $N_2$ for 20 min. After cooling of the mixture to −78 °C, the Grignard solution (20 cm$^3$, 12 mmol) was added dropwise to it, followed by the liquified bromoethene **42** (0.60–0.80 g, 5.6–7.5 mmol). The mixture was allowed to warm up to room temperature over 16 h after which it was treated with 1 mol dm$^{-3}$ hydrochloric acid (10 cm$^3$) and mesitylene (as internal standard, ~300 mg exactly weighed). The organic phase was separated, dried ($NaHCO_3$–$MgSO_4$) and injected into the GC apparatus. Enantiomeric excess and chemical yield were determined using a 40-m Lipodex C glass capillary with $H_2$ as carrier gas at 1 bar (28 °C column temp.). Retention times were 62 min (mesitylene), 82 min [(*R*)-3-phenylbut-1-ene] and 84 min [(*S*)-3-phenylbut-1-ene].

**(b) 2,2′-Dimethyl-1,1′-binaphthyl 47.** A ready-to-use mixture of 1-bromo-2-methylnaphthalene **45** and 1-(bromomagnesio)-2-methylnaphthalene **46** was prepared by treatment of a solution of 1-bromo-2-methylnaphthalene (133 g, 0.60 mol) in benzene–$Et_2O$ (1:1; 600 cm$^3$) with Mg (7.9 g, 0.33 mol) until dissolution of the metal was complete after which the reaction mixture was made up to exactly 720 cm$^3$ by addition of $Et_2O$. This mixture contained about 0.4 mol dm$^{-3}$ of each reactant.

For the Grignard cross coupling reaction, anhydrous $NiBr_2$ (55 mg, 0.23 mmol) and the respective phosphane (0.60 mmol) were deposited under $N_2$ in a 50 cm$^3$ flask with $N_2$-inlet and two-necked adaptor carrying a dropping funnel and a reflux condenser. Dry solvent (THF or $Et_2O$) was added to the mixture which was then heated to reflux for a few minutes, before the Grignard solution (1–2 cm$^3$) was added to it and heating was continued for a further few minutes. After cooling to room temperature the rest of the Grignard solution was added (30 cm$^3$ total) and the flask was closed. Stirring at room temperature was continued for 4–7 d, followed in some cases by refluxing for several hours (see Table 2). The solvent was then removed and the residue was distributed between cyclohexane and dilute hydrochloric acid. The organic phase was chromatographed on $SiO_2$ using, initially, LP, then LP–EA

**Table 1** Formation of optically active 3-phenylbut-1-ene **44** by reaction of 1-phenylethylmagnesium chloride **43** with bromoethene **42** in the presence of Ni–phosphane complexes

| Ligand | Ligand config. | Chemical yield (%) | % ee (config.) |
|---|---|---|---|
| (−)-NORPHOS | *R*,*R* | 25–60 | 55–65 (*S*) |
| **1** | *R* | 33 | 0 |
| **3** | *S* | 27–38 | 26–27 (*S*) |
| **4** | *S* | 34–56 | 24–29 (*S*) |
| **5** | *S*,*S* | 11 | 0 |
| **6** | *R* | 29–60 | 68–69 (*R*) |
| **7** | *S* | 25–43 | 3–7 (*S*) |
| **10** | *S* | 29–44 | 44–48 (*S*) |
| **13** | *S* | 29 | 31 (*S*) |

**Table 2** The asymmetric synthesis of 2,2′-dimethyl-1,1′-binaphthyl **47** by Grignard cross coupling mediated by different Ni–phosphane complexes

| Ligand | Ligand config. | Chemical yield (%) | % ee (config.) |
|---|---|---|---|
| Glyphos **1** | *R* | 40 | 50 (*S*) |
| Glyphos **1** | *R* | 57 | 34 (*S*)[a] |
| Glyphos **1** | *R* | 41 | 25 (*S*)[a,b] |
| PPFOMe **2** | *R*,1*S* | 71 | 61 (*R*) |
| PPFOMe **2** | *R*,1*S* | 63 | 83 (*R*)[a] |
| **3** | *S* | 77 | 31 (*R*) |
| **3** | *S* | 76 | 34 (*R*)[a] |
| **4** | *R* | < 10 | 14 (*R*)[c] |
| **4** | *R* | 41 | 25 (*R*)[a] |
| **5** | *S*,*S* | < 20 | 0[c] |
| **6** | *R* | 80 | 9 (*S*) |
| **7** | *R* | < 20 | 2 (*R*)[c] |
| **8** | *S*,*S* | < 20 | 4 (*S*)[c] |
| **10** | *S* | < 20 | 0[c] |
| **10** | *S* | 35 | 0[a] |
| **13** | *S* | < 20 | 4[c] |

[a] The preparation of the catalyst proceeded in $Et_2O$ instead of THF. [b] The reaction was carried out completely at the boiling point of the mixture. [c] After a 10 d reaction at room temperature, the mixture was heated to reflux for 12 h. Since the products were impure a determination of the optical purity was impossible.

(50:1). The fore-running starting material was discarded and the product-containing fractions (colourless syrups or solids, depending on the optical purity) were concentrated and weighed to determine the chemical yield. The enantiomeric excess was either determined by polarimetry or HPLC.

For HPLC, a 250-mm Chiralpak OT(+) (4.6 mm diam.) column was applied. The solvent was MeOH with a flow rate of 0.7 $cm^3$ $min^{-1}$ at a column temperature of −3.0 °C. The enantiomers (injected as 4 $cm^3$ of a 0.2% soln. in MeOH) were detected at 254 nm and had retention times of 19.5 min (*S*) and 28.5 min (*R*), respectively; $[\alpha]_\lambda$ ($\lambda$/nm) −31.3 (589), −33.0 (578), −38.6 (546), −73.3 (436) and −80.4 (365) (*c* 1 in $CHCl_3$) (the sample had an *R* configuration and an 83% ee; ref. 5, $[\alpha]_D^{23}$ −35.6, at 94% ee); $R_F(SiO_2$, LP) 0.27; $\delta_H$(60 MHz, $CDCl_3$) 2.10 (6 H, s, 2 × $CH_3$) and 7.1–8.1 (12 H, m, ArH).

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