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Reactions of the Bornyl and Fenchyl Grignard Reagent with Chlorophosphanes – Diastereoselectivity and Mechanistic Implications

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The reactions of the bornyl and fenchyl Grignard reagent with the chlorophosphanes Ph_2PCl, PCl_3 and $(Et_2N)_2PCl$, respectively, were studied by multinuclear NMR spectroscopy. The diastereoselectivity was found to be independent of the diastereomeric composition of the bornyl and fenchyl Grignard reagent (e.g., the *endo*/*exo* ratio), but dependent on the chlorophosphanes used. The results are consistent with a reaction mechanism that involves SET processes and radical intermediates. No or little diastereoselectivity was observed for the reactions involving Ph_2PCl and PCl_3. The reactions of the bornyl and fenchyl Grignard reagent with $(Et_2N)_2PCl$ provided bornylP$(NEt_2)_2$ (**4a**) and β-fenchylP$(NEt_2)_2$ (**10b**) with high diastereoselectivity (of 92% and 88% *de*). The novel chiral phosphane oxides bornylPh_2PO (**2a**), isobornylPh_2PO (**2b**), α-fenchylPh_2PO (**8a**) and β-fenchylPh_2PO (**8b**), phosphinic acids bornylP(O)(H)(OH) (**5a**) and β-fenchylP(O)(H)(OH) (**11b**) and phosphonic acids bornylP$(O)(OH)_2$ (**6a**) and β-fenchylP$(O)(OH)_2$ (**12b**) were isolated as colorless crystals. The molecular structures of **2b**, **8a**, **8b**, **6a** and **12b** were determined by X-ray crystallography.

Introduction

The preparation of Grignard reagents by the direct reaction of Mg with alkyl halides proceeds via single-electron transfer (SET) and involves alkyl radical intermediates. Consequently, this method furnishes racemic Grignard reagents even if optically active alkyl halides with α-carbon atoms as sole chiral centers are used.[1] As a result, the preparation of enantiomerically enriched Grignard reagents with α-carbon atoms being the sole chiral centers requires alternative routes, which are rather tedious and somewhat limit the synthetic utility.[2] We turned our attention to diastereomeric Grignard reagents prepared by the direct method from Mg and *sec*-alkyl chlorides derived from naturally occurring inexpensive monoterpenes, such as menthol,[3] borneol and fenchol.[4] These Grignard reagents have three chiral centers and consist of configurationally stable mixtures of diastereomers, which differ only in the configuration of the α-carbon atom. Consistent with the SET mechanism, the ratio of the diastereomers is entirely independent of the initial configuration of the α-carbon atom of the alkyl chloride. The menthyl Grignard reagent contains equal amounts of menthylmagnesium chloride and neomenthylmagnesium chloride.[3] The bornyl Grignard reagent contains bornylmagnesium chloride and isobornylmagnesium chloride with an *endo*/*exo* ratio of 67:33, which can be auspiciously changed to 96:4 by thermal epimerization (refluxing toluene, 12 h). The closely related fenchyl Grignard comprises α-fenchylmagnesium chloride and β-fenchylmagnesium chloride in with an *endo*/*exo* ratio of 80:20, which can be entirely inverted to 20:80 by thermal epimerization. The diastereomeric composition of the Grignard reagents was unambiguously determined by reaction with the soft model electrophile triphenyltin chloride giving rise the formation of air-stable diastereomeric mixtures of terpenoid alkyltriphenylstannanes that were qualitatively and quantitatively assessed by ^{119}Sn, ^{13}C and ^{1}H NMR spectroscopy.[4]

We have now studied the reaction of the (epimerized) bornyl and fenchyl Grignard reagents with the selected chlorophosphanes, Ph_2PCl, PCl_3 and $(Et_2N)_2PCl$. These reactions provided diastereomeric mixtures of bornylphosphanes and isobornylphosphanes as well as α-fenchylphosphanes and β-fenchylphosphanes. Surprisingly, the diastereoselectivity of these reactions is completely independent of the initial *endo*/*exo* ratio of the Grignard reagents, but depends on the chlorophosphanes used.

Results and Discussion

The stoichiometric reactions of the (epimerized) bornyl and fenchyl Grignard reagents with the chlorophosphanes, Ph_2PCl, PCl_3 and $(Et_2N)_2PCl$, respectively, provided diastereomeric mixtures of bornylphosphanes and isobornylphosphanes (**1**–**6**) as well as α-fenchylphosphanes and β-fenchylphosphanes (**7**–**12**), which were quantitatively and qualitatively assessed by 1D and 2D ^{31}P-, ^{31}C- and ^{1}H

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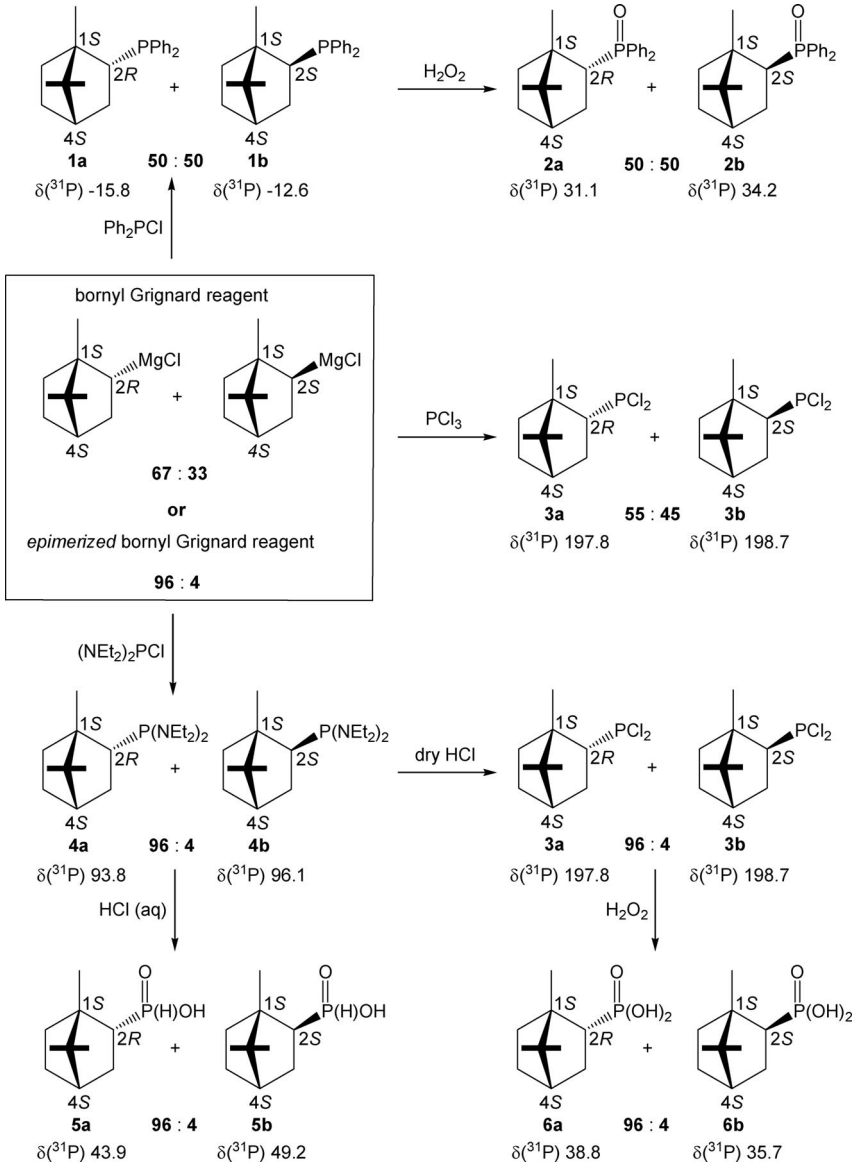
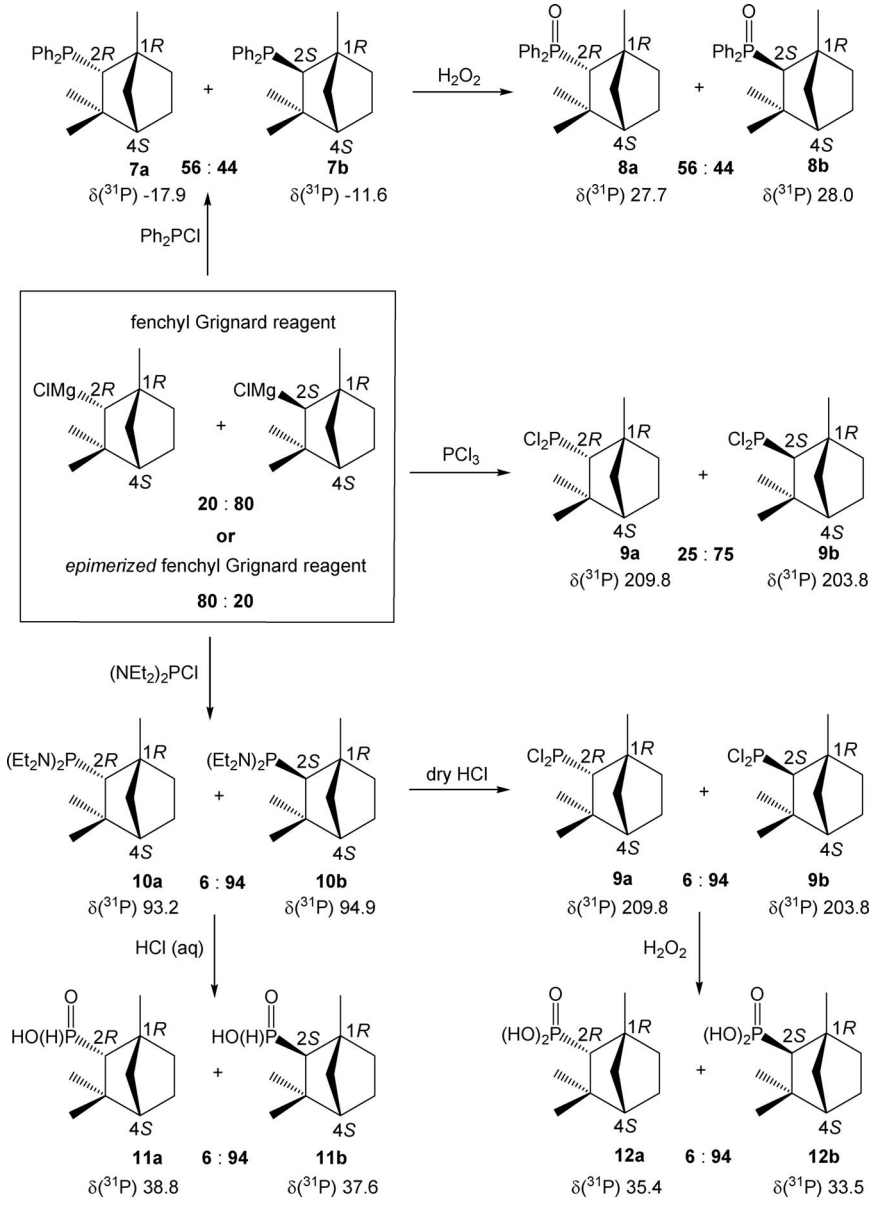
NMR spectroscopy (see Schemes 1 and 2). The assignment of the *endo* and *exo* configurations was supported by comparison of indicative $^3J(^{31}P\text{-}CC\text{-}^{13}C)$ couplings with those of *endo*- and *exo*-norbornyldimethylphosphane oxide based on the Karplus relation.[5] The diastereoselectivity varied dramatically for the chlorophosphanes used and was determined from the crude reaction mixtures by integration of the two well-separated ^{31}P-NMR chemical shifts of the *endo* and *exo* diastereomers. Surprisingly, the diastereoselectivity was found to be completely independent of the initial *endo*/*exo* ratio of the Grignard reagents.

The reaction of the bornyl and fenchyl Grignard reagent with Ph_2PCl proceeds with no and very little diastereoselectivity and produced mixtures of alkyldiphenylposphanes bornylPh_2P (**1a**) and isobornylPh_2P (**1b**) as well as α-fenchylPh_2P (**7a**) and β-fenchylPh_2P (**7b**) with *endo*/*exo* ratios of 50:50 and 56:44, respectively.

The crude yield of **1a**/**1b** and **7a**/**7b** was 58% and 48%, respectively.[6] Attempts to purify these mixtures by column chromatography lead to partial oxidation to phosphane oxides. Therefore, the crude mixtures were treated with H_2O_2 and converted into the alkyldiphenylphosphane oxides bornylPh_2PO (**2a**) and isobornylPh_2PO (**2b**) as well as α-fenchylPh_2PO (**8a**) and β-fenchylPh_2PO (**8b**), which were separated by column chromatography. Compounds **2a**, **2b**, **8a** and **8b** were isolated pure as colorless crystals in yields of 14%, 15%, 20% and 9%, respectively. The molecular structures of **2b**, **8a** and **8b** are shown in Figures 1, 2, and 3 and independently confirm the absolute (Flack parameter) and relative (*endo* or *exo*) configuration of the terpenoid residues. The $HSiCl_3$ reduction of **2b** and **8b** to **1b** and **8b**, respectively, made possible the assignment of the ^{31}P NMR chemical shifts of the crude diphenylphosphane mixtures.



Scheme 1. Synthesis of bornylphosphanes and related compounds.



Scheme 2. Synthesis of fenchylphosphanes and related compounds.

The reaction of the bornyl and fenchyl Grignard reagent with PCl_3 occurs with very little and modest diastereoselectivity and afforded mixtures of the alkyldichlorophosphanes bornylPCl_2 (**3a**) and isobornylPCl_2 (**3b**) as well as α-fenchylPCl_2 (**9a**) and β-fenchylPCl_2 (**9b**) with *endo*/*exo* ratios of 55:45 and 25:75, respectively.[7] The crude yield of **3a**/**3b** and **9a**/**9b** was 44% and 45%, respectively.[8] No attempts were made to separate these diastereomeric mixtures, due to their air sensitivity.

The greatest diastereoselectivity was observed in the reaction of the bornyl and fenchyl Grignard reagent with $(NEt_2)_2PCl$, which produced mixtures of alkylbis(diethylamino)phosphanes bornylP$(NEt_2)_2$ (**4a**) and isobornylP$(NEt_2)_2$ (**4b**) as well as α-fenchylP$(NEt_2)_2$ (**10a**) and β-fenchylP$(NEt_2)_2$ (**10b**) with *endo*/*exo* ratios of 96:4 and 6:94, respectively.[7] The crude yield of **3a**/**3b** and **9a**/**9b** was 79% and 37%, respectively.[9] Acid hydrolysis of these diastereomeric alkylbis(diethylamino)phosphane mixtures provided the phosphinic acids bornylP(O)(H)(OH) (**5a**) and isobornylP(O)(H)(OH) (**5b**) as well as α-fenchylP(O)(H)(OH) (**11a**) and β-fenchylP(O)(H)(OH) (**11b**). These acids were purified by acid base extraxction, however, all attempts to separate **5a** and **5b** as well as **11a** and **11b** by recrystallization, column chromatography and HPLC failed. Compounds **5a** and **11b** were isolated with diastereomeric purity of 92% and 88%, respectively, as colorless crystals in yields of 48% and 13%, respectively. The reaction with dry HCl converted the same diastereomeric alkylbis(diethylamino)phosphane mixtures into the chlorophosphanes bornylPCl_2 (**3a**) and isobornylPCl_2 (**3b**) as well as α-fenchylPCl_2 (**9a**) and β-fenchylPCl_2 (**9b**) without affecting the *endo*/*exo* ratios. Oxidation of the latter with H_2O_2

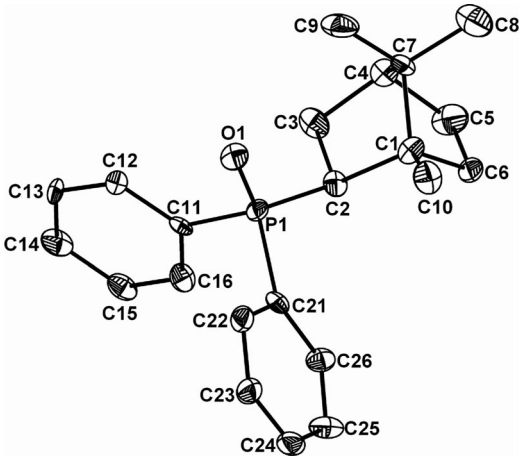


Figure 1. Structure of *exo*-isobornyldiphenylphosphane oxide (**2b**) showing 30% probability displacement ellipsoids and the numbering scheme.

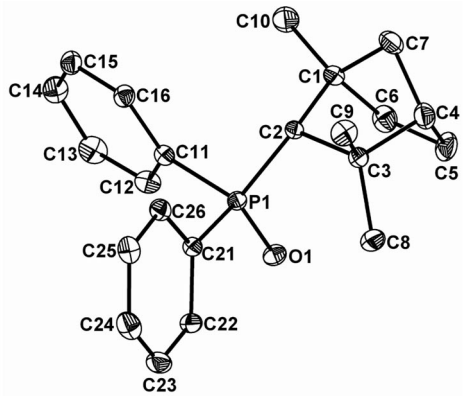


Figure 2. Structure of *endo*-α-fenchyldiphenylphosphane oxide (**8a**) showing 30% probability displacement ellipsoids and the numbering scheme.

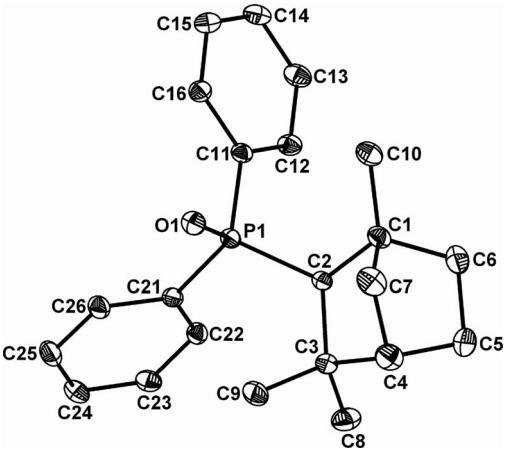


Figure 3. Structure of *exo*-β-fenchyldiphenylphosphane oxide (**8b**) showing 30% probability displacement ellipsoids and the numbering scheme.

produced the corresponding phosphonic acids bornylP(O)(OH)$_2$ (**6a**) and isobornylP(O)(OH)$_2$ (**6b**) as well as α-fenchylP(O)(OH)$_2$ (**12a**) and β-fenchylP(O)(OH)$_2$ (**12b**). The crude phosphonic acid mixtures were purified by acid base extraction and recrystallization. Compounds **6a** and **12b** were isolated pure as colorless crystals in yields of 69 and 33%, respectively. The molecular structure of **6a** is shown in Figure 4 and confirms the absolute and relative configuration of the bornyl group, **12b** is shown in Figure 5.

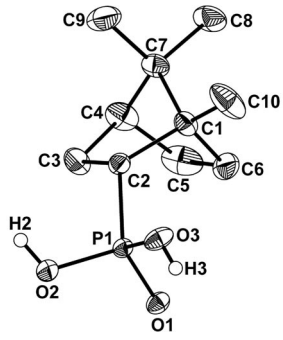


Figure 4. Structure of *endo*-bornylphosphonic acid (**6a**) showing 30% probability displacement ellipsoids and the numbering scheme.

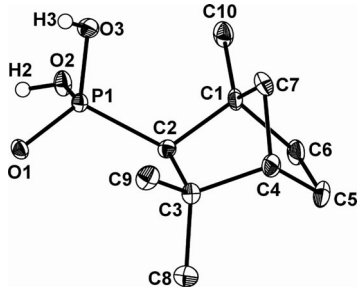


Figure 5. Structure of *exo*-β-fenchylphosphonic acid (**12b**) showing 30% probability displacement ellipsoids and the numbering scheme.

Conclusions

The reactions of the bornyl and fenchyl Grignard reagents with the chlorophosphanes, Ph_2PCl, PCl_3 and $(Et_2N)_2$-PCl, respectively, provided diastereomeric mixtures of bornylphosphanes and isobornylphosphanes as well as α-fenchylphosphanes and β-fenchylphosphanes. The diastereoselectivity of these reactions is entirely independent of the initial *endo*/*exo* ratio of the Grignard reagent, which implies that the stereochemical information of the α-carbon atoms is at least partly lost, most likely at the stage of intermediary formed bornyl and fenchyl radicals.[10] A possible substitution mechanism that accounts for radical intermediates involves an SET transfer between the Grignard reagent to the chlorophosphanes prior to combination of the radical pairs formed ("electron motion precedes nuclear motion").[2] This SET mechanism may compete with the commonly accepted SN_2 mechanism for substitution reaction at phosphorus(III). Attempts to identify possible radical or hypercoordinated phosphorus intermediates by low temperature ^{31}P NMR spectroscopy failed. The diastereoselectivity is modest for Ph_2PCl (0% and 12% *de*) and PCl_3

(10% and 50% *de*) as can be expected if radical intermediates are involved, but surprisingly high for $(NEt_2)_2PCl$. In this case, the diastereoselectivity (92% and 88% *de*) even exceeds that of the Grignard formation (34% and 60% *de*).[4] No definitive explanation can be given for this exceptionally high diastereoselectivity at this stage. However, the different diastereoselectivities may be correlated with the LUMO levels[2] of the chlorophosphanes calculated at the MP2/6-311+ g(2d,p) level of theory,[11] which increases in the order Ph_2PCl (1.5508 eV) < PCl_3 (1.5511 eV) < $(Et_2N)_2PCl$ (1.5984 eV), respectively. One other possible reason of the high diastereoselectivity of reactions involving $(NEt_2)_2PCl$ may involve the initial formation of a Lewis pair complex (N→Mg) between $(NEt_2)_2PCl$ and the Grignard reagent prior to the substitution reaction that locks the reactive centers into favorable positions. It is noteworthy that the reaction of the fenchyl Grignard reagent with $(NEt_2)_2PCl$ provides the thermodynamically less favored *exo* diastereomer β-fenchylP$(NEt_2)_2$ (**10b**) in large excess, which points to a kinetically controlled reaction pathway. The same observation was made for the formation of the fenchyl Grignard reagent.[4] Apparently, the reactions involve the same radical intermediate, namely the fenchyl radical, which has a strong bias on the formation of *exo* products.

In summary, our results suggest that the commonly accepted S_N2 mechanism for substitution reactions at chlorophosphanes[12] is not (exclusively) operative in case of sec. Grignard reagents. The investigated reactions provide evidence to suggest that an SET mechanism involving free radicals is at least partially operative.[13]

Experimental Section

General Considerations: All operations were performed under argon using standard Schlenk and vacuum line techniques. Isobornyl chloride or β-fenchyl chloride were obtained from commercially available (1S)-(–)-*endo*-borneol and (1*R*)-(+)-*endo*-α-fenchol by the Appel reaction using CCl_4/PPh_3. Bis(diethylamino)chlorophosphane $(Et_2N)_2PCl$ was prepared according to a published procedure.[14] ^{31}P-, ^{13}C- and ^1H NMR spectra were collected using a Jeol JNM-LA 400 FT spectrometer and a Jeol Eclipse+ 500 FT spectrometer. Chemical shifts are given in ppm relative to Me_4Si and H_3PO_4 (aq.). The assignment of the ^{13}C- and ^1H NMR resonances was achieved using standard 2D NMR techniques including ^1H-^1H-COSY, ^1H-^1H-NOESY, ^1H-^{13}C-HMBC and ^1H-^{13}C-HMQC. Optical rotations were measured on Perkin–Elmer 241 and Schmidt & Haensch UniPol L1000 polarimeters. Microanalyses were obtained from a Vario EL elemental analyzer. Infrared spectra were recorded using Nexus FT-IR spectrometer with a Smart DuraSamplIR.

Synthesis of the Bornyl and Fenchyl Grignard Reagent: A solution of isobornyl chloride or β-fenchyl chloride (2.00 g, 11.6 mmol) in THF (20 mL) was slowly added to a suspension of activated Mg turnings (0.4) g, 17.4 mmol) in THF (5 mL). After the addition was completed, the mixture was heated under reflux for 12 h. Prior to use, the clear solution was separated from the excess of Mg via cannula. The yield determined by titration was about 80%.[15]

Synthesis of the *epimerized* Bornyl and Fenchyl Grignard Reagent: A solution of the bornyl or fenchyl Grignard reagent was slowly distilled while toluene (50 mL) was constantly added to replace the original solvent THF. The temperature was slowly raised to 111 °C and kept there for 12 h. The yield determined by titration was between 65 and 75%.[15]

Reaction of the (*epimerized*) Bornyl and Fenchyl Grignard Reagent with Ph_2PCl, PCl_3 and $(NEt_2)_2PCl$: The appropriate Grignard reagent (11.6 mmol) was slowly added to a solution of the chlorophosphane (Ph_2PCl: 2.55 g; PCl_3: 1.59 g; $(NEt_2)_2PCl$: 2.44 g; 11.6 mmol) in THF (20 mL). The mixture was stirred for 12 h at room temperature before most of the solvent was removed in vacuo to leave an oily suspension. Hexane (20 mL) was added and the colourless precipitate filtered off. Again, the solvent was removed in vacuo to afford the crude products as oils. At this stage the crude reaction mixtures were investigated by ^{31}P NMR spectroscopy (refer to the text and references for details).

Synthesis of the Alkyldiphenylphosphane Oxides bornylPh_2PO (2a) and isobornylPh_2PO (2b) as well as α-fenchylPh_2PO (8a) and β-fenchylPh_2PO (8b): To the crude alkyldiphenylphosphanes (**1a/1b** or **7a/7b**) were dissolved in diethyl ether (100 mL), water (30 mL) and hydrogen peroxide (30 mL, 33%) were added and the two layer mixture vigorously stirred for 1 h. The layers were separated, the organic layer washed with water (2 × 40 mL) and dried with Na_2SO_4. After removal of the solvent under reduced pressure, the crude product was obtained as oil. The diastereomers were separated by column chromatography (silica; hexane/ethyl acetate = 1:1 for **2a/2b** and 2:1 for **8a/8b**). Crystallization from hexane/dichloromethane afforded colorless crystals.

2a: Yield 0.56 g, 1.65 mmol, 14%; m.p. 162 °C. $[a]_D$ = 47.2 (*c* = 3.1; $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 7.82–7.74 (m, 4 H; Ph), 7.43–7.36 (m, 6 H; Ph), 2.64–2.59 (m, 2 H; 2-H, 6_A-H), 2.93–1.85 (m, 1 H; 3-H), 1.76–1.64 (m, 3 H; 3-H, 4-H, 5-H), 1.45–1.40 (m, 1 H; 5-H), 1.31–1.26 (m, 1 H; 6_S-H), 0.89 (s, 3 H; 9-H), 0.78 (s, 3 H; 8-H), 0.41 (s, 3 H; 10-H) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ = 135.2 (d, $^1J(^{13}C$-$^{31}P)$ = 95 Hz; Ph), 134.4 (d, $^1J(^{13}C$-$^{31}P)$ = 95 Hz; Ph), 131.0 (d, $^4J(^{13}C$-$^{31}P)$ = 3 Hz; Ph), 130.7 (d, $^2J(^{13}C$-$^{31}P)$ = 70 Hz; Ph), 130.6 (d, $^2J(^{13}C$-$^{31}P)$ = 70 Hz; Ph), 128.3 (d, $^3J(^{13}C$-$^{31}P)$ = 25 Hz, Ph), 128.2 (d, $^3J(^{13}C$-$^{31}P)$ = 25 Hz; Ph), 50.6 (d, $^3J(^{13}C$-$^{31}P)$ = 11 Hz, C-7), 49.6 (d, $^2J(^{13}C$-$^{31}P)$ = 3 Hz; C-1), 44.7 (d, $^3J(^{13}C$-$^{31}P)$ = 3 Hz; C-4), 42.1 (d, $^1J(^{13}C$-$^{31}P)$ = 76 Hz; C-2), 30.8 (C-3), 30.6 (d, ($^3J(^{13}C$-$^{31}P)$ = 5 Hz; C-6), 27.7 (C-5), 18.5 (C-9), 18.2 (C-8), 15.8 (C-10) ppm. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ = 31.1 ($^1J(^{31}P$-$^{13}C)$ = 94, $^1J(^{31}P$-$^{13}C)$ = 76 Hz) ppm. IR (KBr): $\tilde{\nu}$(P=O): 1178 cm^{-1}. $C_{22}H_{27}OP$ (338.42): calcd. C 78.08, H 8.04; found C 78.06, H 7.98.

2b: Yield 0.61 g, 1.80 mmol, 15%; m.p. 166–167 °C. $[a]_D$ = 62.9 (*c* = 5.6; $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 7.91–7.87 (m, 2 H; Ph), 7.78–7.74 (m, 2 H; Ph), 7.42–7.40 (m, 3 H; Ph), 7.36–7.34 (3 H, Ph), 2.57–2.52 (m, 1 H; 2-H), 2.00–1.90 (m, 1 H; 3-H), 1.82–1.75 (m, 1 H; 5-H), 1.68–1.66 (m, 1 H; 5-H), 1.60–1.52 (m, 1 H; 6_S-H), 1.35–1.29 (m, 1 H, 6_A-H), 1.25–1.69 (m, 5 H; 3-H, 5-H, 9-H), 0.80 (s, 3 H, 8-H), 0.74 (s, 3 H, 10-H) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ = 135.5 (d, $^1J(^{13}C$-$^{31}P)$ = 96 Hz; Ph), 134.7 (d, $^1J(^{13}C$-$^{31}P)$ = 96 Hz; Ph), 130.7 (d, $^2J(^{13}C$-$^{31}P)$ = 33 Hz; Ph), 130.7 (d, $^2J(^{13}C$-$^{31}P)$ = 33 Hz; Ph), 130.6 (d, $^4J(^{13}C$-$^{31}P)$ = 3 Hz; Ph), 128.3 (d, $^3J(^{13}C$-$^{31}P)$ = 11 Hz; Ph), 128.2 (d, $^3J(^{13}C$-$^{31}P)$ = 11 Hz; Ph), 50.7 (d, $^3J(^{13}C$-$^{31}P)$ = 2 Hz; C-7), 50.0 (C-1), 45.6 (d, $^1J(^{13}C$-$^{31}P)$ = 72 Hz; C-2), 45.0 (d, $^3J(^{13}C$-$^{31}P)$ = 4.1 Hz; C-4), 41.5 (d, $^3J(^{13}C$-$^{31}P)$ = 13 Hz; C-6), 31.8 (d, ($^2J(^{13}C$-$^{31}P)$ = 4 Hz; C-3), 27.2 (C-5), 20.6 (C-9), 20.1 (C-8), 16.4 ($^3J(^{13}C$-$^{31}P)$ = 4 Hz; C-10) ppm. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ = 34.2 ($^1J(^{31}P$-$^{13}C)$ = 95, $^1J(^{31}P$-$^{13}C)$ = 71 Hz) ppm. IR (KBr): $\tilde{\nu}$(P=O): 1178 cm^{-1}. $C_{22}H_{27}OP$ (338.42): calcd. C 78.08, H 8.04; found C 78.08, H 8.02.

8a: Yield 0.76 g, 2.25 mmol, 20%; m.p. 241–243 °C. $[\alpha]_D$ = 10.5 (*c* = 5.9; $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 7.88–7.79 (m, 4 H; *o*-Ar-H), 7.35–7.29 (m, 6 H; Ar-H), 2.70–2.64 (m, 1 H; 6_A-H), 2.13–1.12 (m, 1 H; 2-H), 1.90–1.85 (m, 1 H; 5_A-H), 1.59–1.57 (m, 2 H; 4-H, 7-H), 1.39–1.32 (m, 1 H, 5_S-H), 1.06–1.02 (m, 1 H; 7-H), 0.99 (br. s, 3 H; 8-H), 0.98–0.94 (m, 1 H; 6-H), 0.93 (br. s, 3 H; 9-H), 0.54 (br. s, 3 H; 10-H) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ = 136.4 (d, $^1J(^{13}C\text{-}^{31}P)$ = 92 Hz; Ph), 130.7 (m, Ph), 128.1 (d, $^3J(^{13}C\text{-}^{31}P)$ = 10 Hz; Ph), 53.7 (d, $^1J(^{13}C\text{-}^{31}P)$ = 70 Hz; C-2), 50.8 (d, $^2J(^{13}C\text{-}^{31}P)$ = 2 Hz; C-1), 50.2 (d, $^3J(^{13}C\text{-}^{31}P)$ = 4 Hz; C-4), 47.5 (d, $^3J(^{13}C\text{-}^{31}P)$ = 15 Hz; C-7), 42.6 (C-3), 33.2 (d, ($^3J(^{13}C\text{-}^{31}P)$ = 4 Hz; C-9), 29.7 (C-6), 25.8 (C-5), 23.2 (d, ($^3J(^{13}C\text{-}^{31}P)$ = 7 Hz; C-8), 23.1 (C-10) ppm. $^{31}P\{^1H\}$ NMR: δ = 27.7 ($^1J(^{31}P\text{-}^{13}C)$ = 93, $^1J(^{31}P\text{-}^{13}C)$ = 70 Hz) ppm. IR (KBr): $\tilde{\nu}$(P=O): 1187 cm^{-1}. $C_{22}H_{27}OP$ (338.42): calcd. C 78.08, H 8.04; found C 78.09, H 8.11.

8b: Yield 0.36 g, 1.06 mmol, 9%; m.p. 241–243 °C. $[\alpha]_D$ = –74.6 (*c* = 3.8; $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 7.85–7.80 (m, 4 H; Ph), 7.37–7.34 (m, 6 H; Ph), 2.29–2.27 (m, 1 H; 7-H), 2.18 (m, 1 H; 2-H), 1.82–1.77 (m, 1 H; 5_A-H), 1.63–1.62 (m, 1 H; 6_S-H), 1.41–1.34 (m, 1 H; 5_S-H), 1.35–1.31 (m, 1 H; 6_A-H), 1.09 (br. s, 3 H; 9-H), 1.08–1.06 (m, 1 H; 7-H), 0.97 (br. s, 3 H; 8-H), 0.92 (br. s, 3 H; 10-H) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ = 138.1 (d, $^1J(^{13}C\text{-}^{31}P)$ = 92 Hz; Ph), 137.5 (d, $^1J(^{13}C\text{-}^{31}P)$ = 92 Hz; Ph), 130.5 (d, $^4J(^{13}C\text{-}^{31}P)$ = 3 Hz; Ph), 130.1 (d, $^2J(^{13}C\text{-}^{31}P)$ = 54 Hz; Ph), 130.0 (d, $^2J(^{13}C\text{-}^{31}P)$ = 56 Hz; Ph), 128.2 (d, $^3J(^{13}C\text{-}^{31}P)$ = 10 Hz; Ph), 128.1 (d, $^3J(^{13}C\text{-}^{31}P)$ = 10 Hz; Ph), 53.8 (d, $^1J(^{13}C\text{-}^{31}P)$ = 69 Hz; C-2), 50.1 (d, $^3J(^{13}C\text{-}^{31}P)$ = 3 Hz; C-4), 50.0 (C-1), 44.8 (C-7), 44.2 (d, $^2J(^{13}C\text{-}^{31}P)$ = 5 Hz; C-3), 40.8 (d, $^3J(^{13}C\text{-}^{31}P)$ = 11 Hz; C-6), 29.2 (d, ($^3J(^{13}C\text{-}^{31}P)$ = 3 Hz; C-8), 26.3 (d, ($^3J(^{13}C\text{-}^{31}P)$ = 10 Hz; C-9), 25.3 (C-5), 21.9 ($^3J(^{13}C\text{-}^{31}P)$ = 4 Hz; C-10) ppm. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ = 28.0 ($^1J(^{31}P\text{-}^{13}C)$ = 93, $^1J(^{31}P\text{-}^{13}C\text{-}2)$ = 69 Hz) ppm. IR (KBr): $\tilde{\nu}$(P=O): 1177 cm^{-1}. $C_{22}H_{27}OP$ (338.42): calcd. C 78.08, H 8.04; found C 78.02, H 8.25.

Synthesis of Alkylphosphinic Acids bornylP(O)(H)(OH) (5a) and β-fenchylP(O)(H)(OH) (11b): The crude alkylbis(diethylamino)phosphanes (**4a/4b** or **10a/10b**) were dissolved in diethyl ether (50 mL) and hydrochloric acid (50 mL, 24%) was added. The mixture stirred for 2 h before the layers were separated. The organic layer was washed with an aqueous NaOH solution (50 mL, 1 M) for 2 h before the layers were again separated. The organic layer contained only the impurities and was discarded. The crude product was recovered by acidification of the aqueous layer with hydrochloric acid (50 mL, 24%) and extraction with diethyl ether (2 × 50 mL). The combined organic layers were dried with Na_2SO_4 and the solvent was removed in vacuo. Crystallization from dichloromethane provided colorless microcrystalline products. All attempts to remove the minor epimers by fractional crystallization, column chromatography and HPLC failed.

5a: Yield 1.21 g, 5.54 mmol, 48%. Purity 92% *de*. $[\alpha]_D$ = –15.2 (*c* = 4.27; $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 12.05 (s, 1 H; OH), 6.95 (d, $^1J(^1H\text{-}^{31}P)$ = 571 Hz, 1 H; P–H), 2.07–1.95 (m, 2 H; 2-H, 3-H), 1.81–1.68 (m, 3 H; 4-H, 5-H, 6-H), 1.51–1.38 (m, 2 H; 3-H, 6-H), 1.24–1.39 (m, 1 H; 5-H), 1.03 (br. s, 3 H, 10-H), 0.85 (m, 3 H, 9-H), 0.84 (s, 3 H; 8-H) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ = 50.1 (d, $^3J(^{13}C\text{-}^{31}P)$ = 11 Hz, C-7), 48.3 (C-1), 44.7 (d, $^3J(^{13}C\text{-}^{31}P)$ = 4 Hz; C-4), 42.9 (d, $^1J(^{13}C\text{-}^{31}P)$ = 102 Hz; C-2), 30.9 (d, ($^3J(^{13}C\text{-}^{31}P)$ = 10 Hz; C-6), 29.5 (C-3), 27.9 (C-5), 18.2 (C-8 or C-9), 17.9 (C-8 or C-9), 15.0 (C-10) ppm. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ = 43.9 ($^1J(^{31}P\text{-}^{13}C)$ = 102 Hz) ppm. IR (KBr): $\tilde{\nu}$(P=O): 1176 cm^{-1}; (P–H): 2361 cm^{-1}. $C_{10}H_{19}O_2P$ (202.23): calcd. C 59.39, H 9.47; found C 59.19, H 9.54.

11b: Yield 0.61 g, 2.95 mmol, 13%. Purity 88% *de*. $[\alpha]_D$ = –29.4 (*c* = 4.7; $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 11.65 (s, 1 H; OH), 7.20 (d; $^1J(^1H\text{-}^{31}P)$ = 534 Hz, 1 H; P–H), 1.99–1.97 (m, 1 H; 7-H), 1.77–1.70 (m, 1 H; 5-H), 1.69–1.67 (m, 1 H; 4-H), 1.52–1.45 (m, 1 H; 5-H), 1.40–1.37 (m, 1 H; 6-H), 1.35 (br. s, 3 H; 10-H), 1.32 (s, 3 H; 9-H), 1.29–1.25 (m, 2 H; 6-H, 2-H), 1.13 (s, 3 H; 8-H), 1.11–1.09 (m, 1 H; 7-H) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ = 56.1 (d, $^1J(^{13}C\text{-}^{31}P)$ = 95 Hz; C-2), 49.3 (d, $^3J(^{13}C\text{-}^{31}P)$ = 3 Hz; C-4), 48.2 (C-1), 44.2 (C-7), 43.0 (d, ($^2J(^{13}C\text{-}^{31}P)$ = 5 Hz; C-3), 40.2 (d, $^3J(^{13}C\text{-}^{31}P)$ = 15 Hz; C-6), 28.6 (d, $^3J(^{13}C\text{-}^{31}P)$ = 4 Hz; C-8), 26.0 (d, $^3J(^{13}C\text{-}^{31}P)$ = 14 Hz; C-9), 25.2 (C-5), 19.6 (d, $^3J(^{13}C\text{-}^{31}P)$ = 7.3 Hz; C-10) ppm. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ = 37.6 ($^1J(^{31}P\text{-}^{13}C\text{-}2)$ = 93.3 Hz) ppm. IR (KBr): $\tilde{\nu}$(P=O): 1198 cm^{-1}; (P–H): 2357 cm^{-1}. $C_{10}H_{19}O_2P$ (202.23): calcd. C 59.39, H 9.47; found C 59.16, H 9.66.

Synthesis of Alkyldichlorophosphanes bornylPCl$_2$ (3a) and β-fenchylPCl$_2$ (9b): The crude alkylbis(diethylamino)phosphanes (**4a/4b** or **10a/10b**) were dissolved in diethyl ether (200 mL) cooled to 0 °C before gaseous hydrogen chloride was bubbled through the solution for about 5 min. The voluminous precipitate was removed by filtration. The solvent was removed in vacuo to leave the crude alkyldichlorophosphanes (**3a/3b** or **9a/9b**) as colorless oils.

Synthesis of Alkylphosphonic Acids bornylP(O)(OH)$_2$ (6a) and β-fenchylP(O)(OH)$_2$ (12b): To the crude alkyldichlorophosphanes (**3a/3b** or **9a/9b**) hydrogen peroxide (30 mL, 33%) was carefully added and the mixture heated under reflux for 2 h. Diethyl ether (50 mL) and aqueous NaOH solution (50 mL, 1 M) were added the mixture was vigorously stirred for 1 h before the layers were separated. The ether layer contained the impurities and was discarded. The crude product was recovered by acidification of the aqueous layer with hydrochloric acid (50 mL, 24%) and extraction with diethyl ether (2 × 50 mL). The combined organic layers were dried with Na_2SO_4 and the solvent was removed in vacuo. Crystallization from dichloromethane (**6a**) and ethanol (**12b**) furnished colorless crystals.

6a: Yield 1.75 g, 8.00 mmol, 69%; m.p. 201 °C. $[\alpha]_D$ = –15.7 (*c* = 0.83; EtOH). ^1H NMR (500 MHz, $CDCl_3$): δ = 10.31 (s, 2 H; OH), 6.9 (d; $^1J(^1H\text{-}^{31}P)$ = 571.0 Hz, 1 H P–H), 2.07–2.02 (m, 1 H, 2-H), 2.00–1.89 (m, 2 H; 3-H, 6-H), 1.67–1.61 (m, 2 H; 4-H, 5-H), 1.52–1.3 (m, 1 H; 3-H), 1.36–1.31 (m, 1 H, 6-H), 1.24–1.18 (m, 1 H, 5-H), 0.95 (br. s, 3 H, 10-H), 0.79 (br. s, 3 H, 8-H oder 9-H), 0.78 (3H. br. s, 8-H oder 9-H) ppm. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ = 49.6 (d, $^3J(^{13}C\text{-}^{31}P)$ = 17.6 Hz; C-7), 48.2 (d, $^2J(^{13}C\text{-}^{31}P)$ = 2.0 Hz; C-1), 44.8 (d, $^3J(^{13}C\text{-}^{31}P)$ = 5.1 Hz, C-4), 40.1 (d, $^1J(^{13}C\text{-}^{31}P)$ = 149.5 Hz, C-2), 30.6 (d, ($^3J(^{13}C\text{-}^{31}P)$ = 6.2 Hz, C-6), 30.4 (C-3), 27.6 (C-5), 18.5 (C-8 oder C-9), 18.4 (C-8 oder C-9), 15.0 (C-10) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ = 38.8 ($^1J(^{31}P\text{-}^{13}C\text{-}2)$ = 149.6 Hz) ppm. IR (KBr): $\tilde{\nu}$(P=O): 1166 cm^{-1}. $C_{10}H_{19}O_3P$ (218.22): calcd. C 55.04, H 8.78; found C 54.92, H 8.44.

12b: Yield 0.83 g, 3.82 mmol, 33%; m.p. 233 °C. $[\alpha]_D$ = –31.9 (*c* = 0.83; EtOH). ^1H NMR (500 MHz, CD_3OD): δ = 5.21 (s, 2 H; OH), 2.00–1.97 (m, 1 H, 7-H), 1.82–1.78 (m, 1 H, 5-H), 1.69–1.64 (1 H, m. 4-H), 1.55–1.48 (m, 1 H, 5-H), 1.43–1.38 (m, 1 H, 6-H), 1.35–1.32 (m, 3 H, 2-H, 6-H, 10-H), 1.30 (s, 3 H, 9-H), 1.13 (s, 3 H, 8-H), 1.10–1.07 (m, 7-H, 1 H) ppm. $^{13}C\{^1H\}$ NMR (126 MHz, CD_3OD): δ = 56.9 (d, $^1J(^{13}C\text{-}^{31}P)$ = 137.0 Hz, C-2), 50.9 (d, $^3J(^{13}C\text{-}^{31}P)$ = 5.2 Hz, C-4), 48.8 (C-1), 45.0 (C-7), 43.6 (d, ($^2J(^{13}C\text{-}^{31}P)$ = 4.1 Hz, C-3), 41.8 (d, $^3J(^{13}C\text{-}^{31}P)$ = 14.5 Hz, C-6), 28.6 (d, $^3J(^{13}C\text{-}^{31}P)$ = 4.1 Hz, C-8), 26.9 (d, $^3J(^{13}C\text{-}^{31}P)$ = 10.3 Hz; C-9), 26.0 (C-5), 21.1 (d, $^3J(^{13}C\text{-}^{31}P)$ = 4.1 Hz; C-10) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ = 33.5 ($^1J(^{31}P\text{-}^{13}C\text{-}2)$ = 136.2 Hz) ppm. IR (KBr): $\tilde{\nu}$(P=O): 1212 cm^{-1}. $C_{10}H_{19}O_3P$ (218.22): calcd. C 55.04, H 8.78; found C 54.72, H 8.39.

Supporting Information (see also the footnote on the first page of this article): General details, bond parameters as well as crystal and

refinement data of the X-ray structure analyses; indicative $^3J(^{31}P\text{-}CC\text{-}^{13}C)$ couplings related to the Karplus relation.

CCDC-749942 (**2b**), -749943 (**8a**), -749944 (**8b**), -749945 (**6a**), -749946 (**12b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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[6] Reaction of the bornyl Grignard reagent with Ph_2PCl: The ^{31}P NMR spectrum ($CDCl_3$) of the crude reaction mixture showed 3 assigned signals at δ = 80.0 (15%; Ph_2PCl), –12.6 (29%; **1b**) and –15.8 (29%; **1a**) as well as 8 minor intense signals at δ = 70.6 (4%), 42.7 (3%), 41.1 (3%), 30.1 (2%), 23.3 (8%), –17.9 (2%), –21.5 (3%) and –23.1 (3%) that were not assigned. Reaction of the fenchyl Grignard reagent with Ph_2PCl: The ^{31}P NMR spectrum ($CDCl_3$) of the crude reaction mixture showed 3 assigned signals at δ = 79.9 (35%; Ph_2PCl), –11.6 (27%, **7b**) and –17.9 (21%, **7a**) as well as 5 minor intense signals at δ = 70.6 (5%), 42.8 (5%), 40.8 (2%), –23.6 (2%) and –24.5 (3%) that were not assigned.

[7] The reaction of the bornyl Grignard reagent with PCl_3 and $(Et_2N)_2PCl$ was already reported with very similar results; however, the authors neither knew the composition of the bornyl Grignard reagent nor drew any conclusions regarding the substitution mechanism. A. Marinetti, F.-X. Buzin, L. Ricard, *J. Org. Chem.* **1997**, *62*, 297–301.

[8] Reaction of the bornyl Grignard reagent with PCl_3: The ^{31}P NMR spectrum ($CDCl_3$) of the crude reaction mixture showed 3 assigned signals at δ = 215.8 (36%; PCl_3), 198.7 (20%; **3b**) and 197.8 (24%; **3a**) as well as 5 minor intense signals at δ = 205.4 (2%), 199.3 (2%), 189 (5%), 174.6 (6%), 170.7 (5%) that were not assigned. Reaction of the fenchyl Grignard reagent with PCl_3: The ^{31}P NMR spectrum ($CDCl_3$) of the crude reaction mixture showed 3 assigned signals at δ = 215.6 (25%, PCl_3), 209.8 (15%, **9a**), 203.8 (40%, **9b**) as well as 5 minor intense signals at δ = 206.7 (3%), 206.1 (2%), 205.3 (2%), 199.8 (10%), 188.9 (3%) that were not assigned.

[9] Reaction of the bornyl Grignard reagent with $(Et_2N)_2PCl$: The ^{31}P NMR spectrum ($CDCl_3$) of the crude reaction mixture showed 3 assigned signals at δ = 154.2 (14%; $(Et_2N)_2PCl$), 96.1 (6%; **4b**) and 93.8 (73%; **4a**) as well as 1 minor intense signal at δ = 118.2 (7%) that were not assigned. Reaction of the fenchyl Grignard reagent with $(Et_2N)_2PCl$: The ^{31}P NMR spectrum ($CDCl_3$) of the crude reaction mixture showed 3 assigned signals at δ = 154.2 (18%, $(Et_2N)_2PCl$), 94.9 (35%; **10b**) and 93.2 (2%; **10a**) as well as 2 minor intense signals and 1 intense signal at δ = 128.1 (4%), 115.8 (6%), 83.8 (35%) that were not assigned.

[10] Radical intermediates are supported by MS spectrometry, which points to 2,2′-bibornanes (m/z = 274) as by-products.

[11] a) Full geometry optimizations were applied to the chlorophosphanes Ph_2Cl, PCl_3 and $NEt_2)_2PCl$ at the MP2/6-311+ g(2d,p) level of theory. Frequency analyses assured that the stationary points were true minima of the hyperpotential energy surface. b) All calculations were performed using *Gaussian*: M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, J. A. Pople, *Gaussian 03*, revision D.01, Gaussian, Inc., Wallingford, CT, **2004**.

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