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New chiral phosphetanes: synthesis and use in the palladium-catalyzed allylic alkylation

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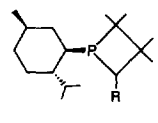
Abstract

The new chiral phosphetane–acetals **4a–d** and **10a–d** were synthesized and evaluated as coligands for the palladium-catalyzed allylic alkylation of 1,3-diphenyl-2-propenyl acetate with sodium malonate. For each set of epimeric phosphetanes, the enantiomeric excesses are highly dependent on the relative configurations of the various chiral centers. The highest asymmetric induction was observed with phosphetane **4a**. An X-ray crystal structure of the complex (allyl)PdCl(**4a**) is also reported.

Keywords: Phosphetane; Palladium; Catalysis; Acetals

1. Introduction

Chiral phosphetanes having the general structure **1** are ligands which are well adapted to palladium-catalyzed asymmetric reactions. Thus, high activity and significant enantiomeric excesses have been obtained in the hydrosilylation of olefins with phosphetane **1a** as chiral ligand [1].



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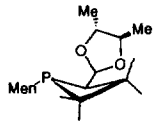


1a P(R), C(R)(R,R)

Men = *l*- menthyl

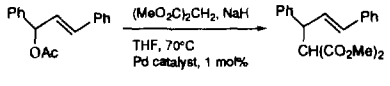
The four-membered ring of **1a** bears a chiral 4,5-dimethyl-1,3-dioxolan-2-yl group, α to the phosphorus atom. By comparison with other substituents, e.g. R = H, CH_2Ph, $SiMe_3$, the dioxolane moiety increases the enantioselectivity of the hydrosilylation reaction when the relative configurations of the various chiral centers of the ligand are appropriately selected.

On the basis of these encouraging results we envisaged an extension of our investigations, to include new phosphetanes bearing acetal functions and to develop new catalytic applications of these ligands.

We report here on the synthesis and characterization of some new phosphetane–acetals and their use in the palladium-catalyzed allylic alkylation reaction.

2. Results and discussion

The potential of ligands other than diphosphines in the asymmetric catalytic allylic substitutions has been recognized recently (for a recent review see Ref. [2]). Amongst others, heterotopic chelate ligands such as phosphino-oxazolines [3,4], phosphino-carboxylic acids [5] and phosphino-ether derivatives [6,7] permit highly enantioselective synthesis. In this context, P–O bidentate phosphetanes could be expected to afford valuable catalysts, and phosphine **1a** was selected to check the potential of phosphetanes in palladium-catalyzed allylic alkylations. The usual model substrate, 1,3-diphenyl-2-propenyl acetate in reaction with the sodium salt of dimethyl malonate (Eq. (1)) was considered.



(1)

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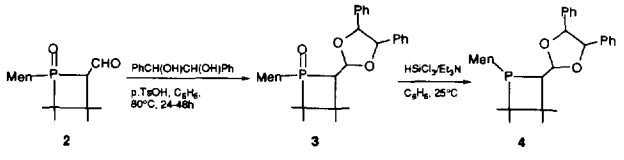
We assumed that the phosphetane–acetal would act as a P–O bidentate ligand; therefore, a phosphine:palladium ratio of 1:1 was used to prepare the catalyst solution from $[(allyl)PdCl]_2$ and **1a** in tetrahydrofuran (THF). A satisfactory catalytic activity was observed: the substitution reaction was complete after about 24 h in refluxing THF. Under these conditions an enantiomeric excess of 43% was obtained, with the *R*(+) enantiomer predominating. The level of enantioselectivity afforded by ligand **1a**, albeit moderate, is significant and justifies further systematic testing of phosphetane–acetals in allylic substitution reactions.

Recent work by Frost and Williams [7] concerning the use of P–O, N–O and S–O bidentate acetal ligands in the reaction in Eq. (1) shows that the 4,5-diphenyl-1,3-dioxolan-2-yl-substituted moieties are more efficient chiral auxiliaries than their dimethyl analogs. Therefore, diphenyl-1,3-dioxolan-2-yl-substituted phosphetanes were expected to afford more enantioselective catalysts than ligand **1a**. To test this hypothesis, the ligand optimization process was oriented toward diphenyl-substituted phosphetane–acetals and refined via variations of two main structural parameters: the relative configurations of the chiral centers and the distance between the phosphorus and oxygen atoms.

Four epimers of the diphenyl analog of phosphetane **1a** have been prepared in separate, two-step syntheses from the 2-formylphosphetane oxides **2a,b** [1] and the enantiomeric 1,2-diphenylethanediols, as shown in Eq. (2).



(2)

Substrate	Diol	Product **3**	Yield (%)	Product **4**
2a P(*S*)C(*R*)	*R*,*R*	**3a** P(*S*)C(*R*)(*R*,*R*)	79	**4a** P(*R*)C(*R*)(*R*,*R*)
	S,*S*	**3b** P(*S*)C(*R*)(*S*,*S*)	90	**4b** P(*R*)C(*R*)(*S*,*S*)
2b P(*R*)C(*S*)	*R*,*R*	**3c** P(*R*)C(*S*)(*R*,*R*)	20	**4c** P(*S*)C(*S*)(*R*,*R*)
	S,*S*	**3d** P(*R*)C(*S*)(*S*,*S*)	27	**4d** P(*S*)C(*S*)(*S*,*S*)

Acetalization of **2** with 1,2-diphenylethanediol takes place in refluxing benzene in the presence of catalytic amounts of *p*-toluenesulfonic acid. Yields of **3** varied significantly as a function of the relative stereochemistries of the phosphetane oxide and diol, nevertheless, it must be noted that reaction conditions were not optimized.

Reduction of the phosphetane oxides **3a–d** with $HSiCl_3$–Et_3N proceeds stereospecifically with assumed retention of the phosphorus configuration [8,9]. The new

Table 1
Selected NMR data for compounds **3a–d** and **4a–d**

	^{31}P	^{1}H			^{13}C				
		PC^4H	$CH(O-)_2$	CH(Ph)O	PC^4H	C^3	PC^2	$CH(O-)_2$	CH(Ph)O
3a *	64.1	2.65	6.10	4.67, 4.77	48.5	40.7	53.3	102.6	86.8
		(8.5)[5.4]	(8.5)[2.5]	(8.1)	[55.2]	[13.7]	[47.9]		85.5
3b	66.7	2.57	5.76	4.60, 4.66	48.7	40.7	53.5	101.7	86.3
		(8.3)[5.7]	(8.3)[3.4]	(7.8)	[55.1]	[13.6]	[49.8]		84.2
3c	63.3	2.80	5.90	4.62, 4.68	55.5	42.0	48.1	102.2	86.4
		(8.3)[5.1]	(8.3)[4.3]	(8.1)	[46.2]	[13.7]	[58.0]		84.9
3d	64.9	2.84	5.82	4.73	53.8	41.7	48.9	102.3	86.9
		(8.4)[5.2]	(8.4)[3.0]		[45.7]	[13.9]	[57.8]		84.9
4a *	19.5	2.60	5.76	4.59, 4.74	42.9	37.0	41.9	107.0	86.9
		(8.4)[5.7]	(8.4)[1.5]	(10.0)		[4.2]	[3.0]	[24.3]	85.8
4b	21.6	2.51	5.60	4.66, 4.72	43.1	36.9	41.8	106.2	86.7
		(6.6)[6.6]	(7.0)[3.0]	(7.8)		[5.6]	[4.6]	[19.5]	84.3
4c	18.8	2.75	5.74	4.69, 4.74	43.1	37.0	44.8	106.9	86.5
		(7.6)[6.4]	(7.6)[2.5]	(7.9)	[2.8]	[7.8]	[4.3]	[21.8]	84.7
4d	18.5	2.72	5.58	4.69	43.7	37.2	43.1	106.5	87.4
		(6.1)[6.1]	(6.1)[3.0]		[5.2]	[6.7]	[3.3]	[18.2]	84.6

Spectra measured in $CDCl_3$ or C_6D_6(*): chemical shifts in ppm; J_{HP} (Hz) coupling constant in brackets, J_{HH} (Hz) coupling constants in parentheses. Atoms are numbered as follows: P–$C^2(Me_2)$–$C^3(Me_2)$–$C^4H(R)$–. The C(2) and C(3) assignments for phosphetanes **4a–d** may be reversed.

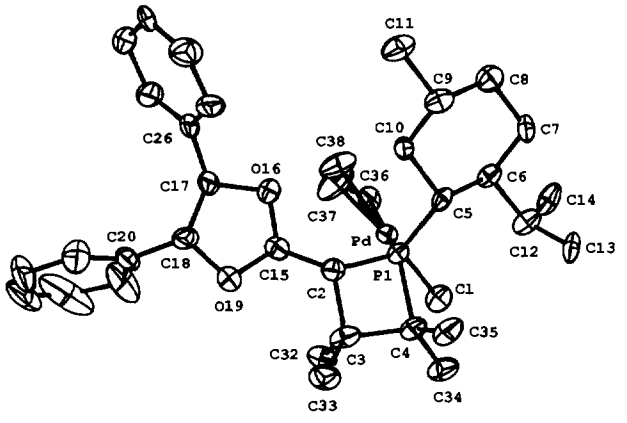
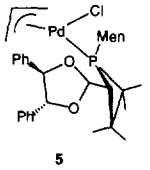


Fig. 1. ORTEP drawing of the palladium complex **5**.

compounds **3a–d** and **4a–d** were fully characterized by NMR and mass spectroscopy. The main NMR data are reported in Table 1.

Concerning the stereochemistry of phosphetanes **4**, the phosphorus configuration and the equatorial position of the dioxolane ring were initially extrapolated on the basis of previous results (see Refs. [1,9] and references cited therein). They were confirmed by an X-ray crystal structure of the palladium complex **5**, obtained from **4a**, which afforded the required stereochemical data.



5

The ORTEP drawing of complex **5** is given in Fig. 1. The main bond angles and distances are reported in Table 2.

Table 2
Selected bond angles and distances for complex **5**

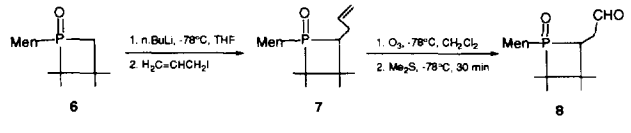
Distances (Å)		Angles (deg)	
Pd–P	2.3190(9)	P–Pd–C38	94.9(1)
Pd–C38	2.155(5)	P–Pd–Cl	102.86(4)
Pd–C37	2.144(6)	Cl–Pd–C36	92.0(1)
Pd–C36	2.217(4)	C2–P–C4	76.7(2)
Pd–Cl	2.358(1)	C2–P–Pd	117.7(1)
P–C(2)	1.840(4)	C4–P–Pd	123.1(1)
P–C(4)	1.886(4)	C5–P–Pd	112.4(1)
P–C(5)	1.838(4)	P–C2–C15	120.5(3)
C(2)–C(15)	1.480(6)	P–C2–C3	90.1(3)

The X-ray structure shows *R*-configurations for both the phosphorus and the intracyclic α-carbon atoms of ligand **4a**.

Complex **5** and its analogs were used as the catalyst precursors for most of the catalytic tests given in Table 3 (see below). The synthesis of **5** may be found in Section 3.

In phosphetanes **4**, the dioxolane substituent is directly bound to the intracyclic α carbon atom. This involves a three bond separation between the phosphorus and oxygen atoms and implies the formation of a five-membered ring when **4** behaves as a chelating ligand toward transition metals. As the chelate ring size is an important structural parameter in most organometallic catalysts (see for example Ref. [10]), it seemed worthwhile to compare phosphetanes which give various ring sizes upon complexation. Thus, the synthesis of phosphetane–acetals with an additional one-carbon spacer between the dioxolane moiety and the four-membered ring was undertaken as follows.

The two epimers of the phosphetane oxide **6** [9] were metalated separately with *n*-BuLi in THF at −78 °C and reacted then with one equivalent of allyl iodide to afford the corresponding allyl-substituted phosphetanes **7a** and **7b** (Eq. (3)).



6 **7** **8** (3)

Substrate	Product **7**	Yield (%)	Product **8**	Yield (%)
6a P(*R*)	**7a** P(*S*)C(*S*)	73	**8a** P(*S*)C(*S*)	57
6b P(*S*)	**7b** P(*R*)C(*R*)	85	**8b** P(*R*)C(*R*)	41

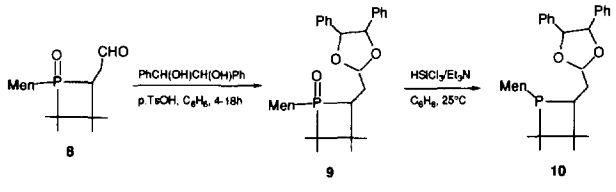
When starting from the phosphetane oxide **6a**, ^{31}P NMR of the crude reaction mixture showed two signals at δ 72.7 and 71.6 ppm respectively in 80:20 ratio. Only the major product was isolated in pure form after chromatography and fully characterized. A single isomer, **7b**, was observed in the alkylation of **6b**.

Based on previous results [1,9] concerning the stereochemistry of various metalation–alkylation reactions of **6**, the allyl substituent of **7a** is assumed to occupy the equatorial position, anti to the menthyl group. ^{13}C NMR data support this hypothesis: the $^2J_{CP}$ coupling constants of the allylic CH_2 carbons, of 5.9 Hz and 4.4 Hz for **7a**

Table 3
Asymmetric allylic alkylations catalyzed by phosphetane–Pd complexes

Entry	Ligand	*e.e.* (%)
1	**1a** P(*R*)C(*R*)(*R*,*R*)	43 (*R*)
2	**4a** P(*R*)C(*R*)(*R*,*R*)	82 (*R*) [a]
3	**4b** P(*R*)C(*R*)(*S*,*S*)	65 (*R*)
4	**4c** P(*S*)C(*S*)(*R*,*R*)	0
5	**4d** P(*S*)C(*S*)(*S*,*S*)	24 (*R*)
6	**10a** P(*R*)C(*S*)(*R*,*R*)	4 (*R*)
7	**10b** P(*R*)C(*S*)(*S*,*S*)	31 (*R*)
8	**10c** P(*S*)C(*R*)(*R*,*R*)	24 (*R*)
9	**10d** P(*S*)C(*R*)(*S*,*S*)	51 (*R*)
10	**4a**– preformed Pd complex **5**	81 (*R*)
11	**4a** Pd:L = 1:2	91 (*R*) [a]

Reaction conditions are not optimized; a maximum reaction time of 24 h was selected arbitrarily. Yields vary between 50 and 95%; *e.e.* were determined by HPLC with chiral column (Chiralcel OD, hexane:^{i}PrOH = 200:1. The *R* enantiomer elutes first, with a retention time of 22 min). The absolute configuration was determined by comparison of the optical rotation with literature values [4] (*R*(+), $[\alpha]_D = +22.4$ ($c = 1.8$, $CHCl_3$)).
[a] 90% yield.



(4)

Substrate	Diol	Product **9**	Yield (%)	Product **10**
8a P(*S*)C(*S*)	*R*,*R*	**9a** P(*S*)C(*S*)(*R*,*R*)	60	**10a** P(*R*)C(*S*)(*R*,*R*)
	S,*S*	**9b** P(*S*)C(*S*)(*S*,*S*)	78	**10b** P(*R*)C(*S*)(*S*,*S*)
8b P(*R*)C(*R*)	*R*,*R*	**9c** P(*R*)C(*R*)(*R*,*R*)	47	**10c** P(*S*)C(*R*)(*R*,*R*)
	S,*S*	**9d** P(*R*)C(*R*)(*S*,*S*)	46	**10d** P(*S*)C(*R*)(*S*,*S*)

Stereospecific, quantitative reductions of **9a–d** to **10a–d** take place at room temperature under the standard conditions described in Eq. (4). Phosphetanes **10a–d** are air-sensitive compounds which must be handled and stored under an inert atmosphere.

The synthetic work described so far has provided four epimers of each phosphetane–acetal **4** and **10**. The *l*-menthyl group bound to phosphorus is a fixed chiral auxiliary, while the stereochemistries of the remaining chiral centers, the phosphorus atom, the α-carbon and the dioxolane moiety, vary in a controlled, known fashion. All these new ligands have been tested in the palladium-catalyzed allylic alkylation reaction of Eq. (1), in order to compare their respective enantioselectivities and to select the best candidate for further studies. Table 3 summarizes the results of the catalytic tests.

As shown in Table 3, the *R*(+) configuration is favored in the final product, regardless of the absolute configuration of the acetal moiety, which exerts generally only a moderate influence on the steric course of the reaction (as examples compare entries 2 vs. 3 and 4 vs. 5). However, the nature of the substituents of the dioxolane ring plays a significant role: the diphenyl-substituted acetal is markedly more enantioselective than the corresponding dimethyl acetal (entries 1 vs. 2).

In two cases, an increased distance between the phosphorus atom and the dioxolane group lowers the enantiomeric excesses (entries 2 vs. 6 and 3 vs. 7). The reverse effect is observed in the two other cases (entries 4 vs. 8 and 5 vs. 9). Rationalization of these data is not obvious at present.

Most notably, results reported in Table 3 indicate phosphetane **4a** as the most suitable ligand for Pd-catalyzed asymmetric allylic alkylations: the *R*(+) enantiomer was obtained in *e.e.* higher than 80%.

The same *R* enantiomer was obtained in significant *e.e.* (65%) by using the epimeric ligand **4b**, despite the presence of dioxolane moieties with opposite configurations. This is a quite surprising result when considering that the dioxolane oxygen atom should chelate to Pd in the catalytic species, which raises questions concerning the actual nature of the catalyst.

and **7b** respectively, compare well with those of the corresponding carbon atoms in analogous benzyl-substituted phosphetanes of known anti stereochemistry ($^2J_{CP} = 4.7$ and 4.4 Hz) [9].

Both isomers of the phosphetane **7** were treated successively with ozone and dimethylsulfide at low temperature in order to convert the olefin function into a formyl substituent. Compounds **8a** and **8b** were obtained in acceptable yields after chromatography on alumina. The main NMR data for the new phosphetane oxides **7** and **8** are reported in Section 3.

Aldehydes **8** were converted to the corresponding acetals, **9**, by reaction with the enantiomeric 1,2-diphenylethanediols (Eq. (4)), according to the procedure already discussed for the synthesis of **3**. The lower sterical hindrance around the formyl group makes the acetalization of **8** easier than that of **3**: complete transformation was achieved after 5–18 h in refluxing benzene.

If phosphetane–acetals give labile palladium–oxygen bonds, then complexes bearing two phosphorus ligands could be formed 'in situ' and may take part in the reaction shown in Eq. (2). In an attempt to elucidate this point, we increased to 2:1 the phosphine:palladium ratio in the catalyst solution. As shown in the last entry of Table 3, a phosphetane to palladium ratio of 2:1 did not alter the catalytic activity significantly and increased the *e.e.* to about 90%. Results obtained with one and two equivalents of phosphine were, however, too similar to confirm unambiguously that different species were involved.

More accurate studies will be needed to clarify and optimize the catalytic behavior of the phosphetane–acetal ligands; nevertheless, the results above show that ligands **4a** are an efficient chiral auxiliary in the palladium-promoted allylic alkylation. Further investigations and extension of this work to other catalytic reactions are in progress.

3. Experimental section

All reactions were carried out under nitrogen in dry solvents. Homochiral 1,2-diphenylethanediols are commercially available. NMR spectra were recorded on a Bruker AC 200 SY spectrometer operating at 200.13 MHz for ^{1}H, 50.32 MHz for ^{13}C and 81.01 MHz for ^{31}P.

3.1. Typical procedure for the allylic alkylation reaction (Eq. (1)) [11]

A solution of the chiral ligand (0.01 mmol) in THF (0.5 ml) was added to a solution of $[(allyl)PdCl]_2$ (0.005 mmol) in 0.5 ml THF and stirred at room temperature for about 10 min. A suspension of sodium malonate (2.0 mmol) was prepared from NaH (80 mg, 60% dispersion in mineral oil) and dimethyl malonate (0.23 ml) in 4 ml THF at 0–25 °C. A solution of 1,3-diphenyl-2-propenyl acetate [11] (0.25 g, 1 mmol) in THF (1 ml) and the catalyst solution were added successively to the sodium malonate. The mixture was refluxed for 24 h. After acidic work-up (acetic acid, 4 ml), column chromatography on silica gel with a hexane–ethyl acetate gradient as eluent afforded the final product as a colorless solid. The purity of each sample of methyl 2-carbomethoxy-3,5-diphenylpent-4-enoate was checked by ^{1}H NMR spectroscopy [12].

3.2. Synthesis of the phosphetane oxides 3a–d

The synthesis of **3a** is given as a representative procedure. A solution of **2a** (0.3 g, 0.96 mmol), (*R*)-(−)-1,2-diphenyl-1,2-ethanediol (0.2 g, 0.96 mmol) and *p*-toluenesulfonic acid (catalytic amount) in benzene was heated at 75 °C for about 24 h (reaction times of 48 h are required for the synthesis of **3c** and **3d**. If necessary, $MgSO_4$ was added to the reaction mixture to remove water). The final product was purified by column chromatography on alumina with hexane–ether 1:1 as eluent ($R_f = 0.7$ in ether).

3a was obtained in 79% yield as a colorless solid: m.p. 204 °C (crystallized from an hexane–ether mixture). Selected NMR data for **3a** are given in Table 1. Additional ^{13}C NMR data: δ 16.9 (d, $^{2}J_{C-P} = 4.2$ Hz, Me), 17.3 (Me), 21.7 (Me), 22.1 (Me), 22.6 (Me), 22.7 (Me), 24.6 (d, $^{3}J_{C-P} = 11.3$ Hz, CH_2), 25.3 (d, $^{3}J_{C-P} = 20.3$ Hz, Me), 30.8 (d, $^{3}J_{C-P} = 3.4$ Hz, $CHMe_2$), 33.7 (d, $^{3}J_{C-P} = 12.9$ Hz, CHMe), 34.3 (CH_2), 34.8 (CH_2), 39.8 (d, $^{1}J_{C-P} = 43.1$ Hz, PCH), 41.1 (CH), 137.3, 139.4 (C); mass spectrum *m/e* 508 (M, 9%), 425 ($M - C_6H_{11}$, 20%), 275 (48%), 180 ($Ph_2C_2H_2$, 100%). Anal. Found: C, 75.52; H, 8.99. $C_{32}H_{45}O_3P$. Calc.: C, 75.56; H, 8.92%. $[\alpha]_D = -126$ ($c = 1$, $CHCl_3$).

3.3. Reduction of phosphetane oxides 3 to 4 (Eq. (2))

Reduction of **3a** is given as a representative example: the phosphetane oxide **3a** (0.21 g, 0.4 mmol) was dissolved in dry benzene (5 ml), then triethylamine (0.11 ml, 0.8 mmol) and trichlorosilane (0.08 ml, 0.8 mmol) were added at 5 °C. The solution was stirred at room temperature and the progress of the reaction was monitored by ^{31}P NMR. After 2 h, the solution was cooled to 5 °C, and 20% aqueous NaOH solution (1.5 ml) was added dropwise. The organic layer was directly chromatographed, under argon, on a short alumina column with hexane–ether (90:10) as eluent. **4a** was obtained in 95% yield as a colorless solid; mass spectrum *m/e* 493 (M + 1, 32%), 297 (100%); $[\alpha]_D = -235$ ($c = 1$, benzene).

4b–d were obtained through the same procedure. All reductions are quantitative according to ^{31}P NMR analysis of the crude reaction mixtures. Yields ranging from 60% to 95% were obtained after chromatography; reaction times vary between 2 h (for **3a**) and 4.5 h (for **3d**). Selected NMR data for phosphetanes **4** are given in Table 1.

3.4. Synthesis of the (allyl)PdCl(4a) complex, 5

$[(Allyl)PdCl]_2$ (37 mg, 0.1 mmol) was dissolved in CH_2Cl_2 (1 ml). A solution of **4a** (0.10 g, 0.2 mmol) in CH_2Cl_2 was then added at room temperature. After about 1 h, the solvent was evaporated and the final product was crystallized from hexane at −20 °C. **4a** is formed as a mixture of two interconverting isomers in a 2:1 ratio (^{31}P NMR (CH_2Cl_2) δ 60.8 and 61.6 ppm respectively). The various interconversion processes between diastereomeric allyl–palladium complexes and their implications regarding Pd-catalyzed allylic substi-

tutions are discussed in Ref. [2]; see also Ref. [13]. Anal. Found: C, 62.23; H, 7.58. $C_{35}H_{50}O_2ClPPd$. Calc.: C, 62.22; H, 7.46%.

3.5. Synthesis of the α-allylphosphetanes 7 (Eq. (3))

n-BuLi (4.8 ml, 1.6 M solution in hexane, 7.7 mmol) was added to a THF solution (100 ml) of phosphetane oxide **6a** (or **6b**) (2.0 g, 7 mmol) at −78 °C. After a few minutes a solution of allyl iodide (0.77 ml, 8.4 mmol) in THF (1 ml) was added. After 15 min at −78 °C the reaction mixture was warmed to room temperature and checked by ^{31}P NMR. When starting from the phosphetane oxide **6a** we observed two signals at δ 72.7 and 71.6 ppm respectively in 80:20 ratio. The minor product is presumed to be the isomeric phosphetane oxide having a P(*S*)C(*R*) configuration. (By using allyl bromide as alkylating agent, a smaller amount of the second isomer was formed; however, a significant amount of unreacted starting material was recovered.) After hydrolysis and extraction with ether, the final product was purified by chromatography on alumina with hexane–ethyl acetate 1:1 as eluent.

After chromatography, a single isomer of phosphetane **7a** was obtained in 73% yield (1.7 g) as a colorless solid: m.p. 149 °C (hexane). Selected NMR data: ^{31}P NMR (C_6D_6) δ 66.9; ^{1H} NMR (C_6D_6) δ 0.76 (d, $^3J_{H-H}$ = 6.9 Hz, $CHMe_2$), 0.79 (s, Me), 0.85 (d, $^3J_{H-H}$ = 5.7 Hz, CHMe), 0.88 (d, $^3J_{H-P}$ = 18.0 Hz, Me), 1.06 (d, $^3J_{H-H}$ = 6.6 Hz, $CHMe_2$), 1.08 (d, $^3J_{H-P}$ = 16.3 Hz, Me), 1.32 (s, Me),... 2.5 (m, 2H), 4.88 (m, $^3J_{H-H}$ = 10.1 Hz, 1H, $=CH_2$), 4.99 (m, $^3J_{H-H}$ = 17.0 Hz, 1H, $=CH_2$), 5.6 (m, 1H, CH=); ^{13}C NMR (C_6D_6) δ 16.8 (d, $^2J_{C-P}$ = 4.5 Hz, Me), 17.2 (Me), 21.5 (Me), 21.7 (Me), 22.1 (Me), 22.6 (Me) 24.4 (d, $^3J_{C-P}$ = 10.0 Hz, CH_2), 25.0 (d, $^3J_{C-P}$ = 22.8 Hz, Me), 28.7 (d, $^2J_{C-P}$ = 5.9 Hz, $CH_2CH=$), 30.7 (d, *C*HMe_2), 33.4 (d, $^3J_{C-P}$ = 12.2 Hz, *C*HMe), 34.3 (CH_2), 35.1 (CH_2), 40.6 (d, $^1J_{C-P}$ = 42.5 Hz, P*C*H), 41.0 (CH), 41.7 (d, $^2J_{C-P}$ = 12.2 Hz, *C*), 48.7 (d, $^1J_{C-P}$ = 53.2 Hz, P*C*), 49.3 (d, $^1J_{C-P}$ = 51.8 Hz, P*C*H), 115.6 ($=CH_2$), 138.3 (d, $^3J_{C-P}$ = 11.8 Hz, CH=) ppm; mass spectrum *m/e* 324 (M, 61%), 171 (100%). Anal. Found: C, 74.19; H, 11.53. $C_{20}H_{37}OP$. Calc.: C, 74.03; H, 11.49%. $[\alpha]_D = -63$ (*c* = 1, $CHCl_3$).

7b. A single isomer of **7b** was observed in the crude reaction mixture. **7b** was obtained in 85% yield as a colorless solid. ^{31}P NMR (C_6D_6) δ 63.6; ^1H NMR (C_6D_6) δ 0.75 (d, $^3J_{H-H}$ = 6.8 Hz, $CHMe_2$), 0.81 (Me), 0.83 (d, $^3J_{H-H}$ = 6.9 Hz, Me), 0.90 (d, $^3J_{H-H}$ = 6.8 Hz, $CHMe_2$), 0.98 (d, $^3J_{H-P}$ = 16.3 Hz, Me), 1.14 (d, $^3J_{H-P}$ = 15.6 Hz, Me), 1.36 (Me),... 4.95 (m, $^3J_{H-H}$ = 10.0 Hz, 1H, $=CH_2$), 5.06 (m, $^3J_{H-H}$ = 17.0 Hz, 1H, $=CH_2$), 5.7 (m, 1H, =CH); ^{13}C NMR (C_6D_6) δ 15.8 (Me), 17.8 (d, $^2J_{C-P}$ = 4.4 Hz, Me), 21.1 (Me), 21.5 (Me), 21.7 (Me), 22.7 (Me), 24.6 (d, $^3J_{C-P}$ = 10.6 Hz, CH_2), 25.2 (d, $^3J_{C-P}$ = 22.8 Hz, Me), 28.8 (d, $^2J_{C-P}$ = 4.4 Hz, $CH_2CH=$), 30.0 (d, $^3J_{C-P}$ = 3.8 Hz, *C*HMe_2), 33.1 (d, $^3J_{C-P}$ = 12.1 Hz, *C*HMe), 34.7 (CH_2), 35.6 (CH_2), 42.3 (d, $^2J_{C-P}$ = 3.9 Hz, CH), 42.7 (d, $^2J_{C-P}$ = 12.3 Hz, *C*), 44.0 (d, $^1J_{C-P}$ = 40.8 Hz, P*C*H), 47.7 (d, $^1J_{C-P}$ = 56.6 Hz, P*C*), 51.8 (d, $^1J_{C-P}$ = 47.8 Hz, P*C*H), 115.8 ($=CH_2$), 138.2 (d, $^3J_{C-P}$ = 13.7 Hz, CH=) ppm; $[\alpha]_D = -38$ (*c* = 1, $CHCl_3$).

3.6. Synthesis of the formyl–phosphetane oxides 8 (Eq. (3))

Ozonolysis of the C=C double bond of **7** was performed on a 1 g scale (3 mmol) in CH_2Cl_2 (100 ml) at −78 °C. The reaction was complete in about 0.5 h. Reduction of the intermediate ozonide with an excess of dimethylsulfide (10 ml) takes place between −78 °C and 25 °C. After evaporation of the solvent and excess sulfide under reduced pressure, the residue was chromatographed on a short alumina column with hexane–ethyl acetate 2:1 as eluent to afford **8**.

8a was obtained in 57% yield (0.57 g): colorless solid, m.p. 144 °C (hexane–ether); ^{31}P NMR (C_6D_6) δ 67.5; ^1H NMR (C_6D_6) δ 0.72 (d, $^3J_{H-H}$ = 6.8 Hz, $CHMe_2$), 0.80 (s, Me), 0.84 (d, $^3J_{H-P}$ = 17.9 Hz, Me), 0.87 (d, $^3J_{H-H}$ = 6.4 Hz, CHMe), 1.02 (d, $^3J_{H-P}$ = 16.6 Hz, Me), 1.03 (d, $^3J_{H-H}$ = 6.8 Hz, $CHMe_2$), 1.11 (s, Me),... 2.4–2.6 (m, 2H), 9.30 (t, $^3J_{H-H}$ = 1.0 Hz, CHO); ^{13}C NMR (C_6D_6) δ 17.0 (d, $^2J_{C-P}$ = 4.4 Hz, Me), 17.2 (Me), 21.3 (Me), 22.0 (Me), 22.3 (Me), 22.6 (Me), 24.3 (d, $^3J_{C-P}$ = 10.8 Hz, CH_2), 24.7 (d, $^3J_{C-P}$ = 22.2 Hz, Me), 30.8 (d, $^3J_{C-P}$ = 3.8 Hz, *C*HMe_2), 33.3 (d, $^3J_{C-P}$ = 12.4 Hz, *C*HMe), 34.1 (CH_2), 34.3 (CH_2), 38.6 (d, $^2J_{C-P}$ = 4.5 Hz, *C*H_2CHO), 40.8 (d, $^1J_{C-P}$ = 41.3 Hz, P*C*H), 41.0 (d, $^2J_{C-P}$ = 2.4 Hz, CH), 41.3 (d, $^2J_{C-P}$ = 12.0 Hz, *C*), 42.3 (d, $^1J_{C-P}$ = 52.0 Hz, P*C*H), 48.8 (d, $^1J_{C-P}$ = 54.1 Hz, P*C*), 199.5 (d, $^3J_{C-P}$ = 10.6 Hz, CHO) ppm; mass spectrum (C.I.) *m/e* 327 (M + 1, 100%). Anal. Found: C, 69.15; H, 10.33. $C_{19}H_{35}O_2P$. Calc.: C, 69.90; H, 10.81%. $[\alpha]_D = -50$ (*c* = 1, $CHCl_3$).

8b was obtained in 41% yield (0.41 g) as a colorless solid. ^{31}P NMR (C_6D_6) δ 64.5; ^1H NMR (C_6D_6) δ 0.84 (d, $^3J_{H-H}$ = 6.8 Hz, $CHMe_2$), 0.90 (s, Me), 0.93 (d, $^3J_{H-H}$ = 6.5 Hz, CHMe), 1.02 (d, $^3J_{H-H}$ = 6.7 Hz, $CHMe_2$), 1.07 (d, $^3J_{H-P}$ = 16.7 Hz, Me), 1.08 (d, $^3J_{H-P}$ = 19.4 Hz, Me), 1.21 (s, Me),... 2.6 (m, 1H), 2.9 (m, 1H), 9.46 (s, CHO); ^{13}C NMR (C_6D_6) δ 15.8 (Me), 18.1 (d, $^2J_{C-P}$ = 4.2 Hz, Me), 20.9 (Me), 21.6 (Me), 22.4 (Me), 22.7 (Me), 24.6 (d, $^3J_{C-P}$ = 10.8 Hz, CH_2), 24.8 (d, $^3J_{C-P}$ = 21.6 Hz, Me), 30.3 (d, $^3J_{C-P}$ = 4.3 Hz, *C*HMe_2), 33.1 (d, $^3J_{C-P}$ = 12.1 Hz, *C*HMe), 34.7 (CH_2), 35.4 (d, $^2J_{C-P}$ = 2.0 Hz, CH_2), 38.6 (d, $^2J_{C-P}$ = 4.2 Hz, *C*H_2CHO), 42.3 (d, $^2J_{C-P}$ = 16.9 Hz, *C*), 42.4 (CH), 44.0 (d, $^1J_{C-P}$ = 41.1 Hz, P*C*H), 44.8 (d, $^1J_{C-P}$ =

48.9 Hz, PCH), 48.0 (d, $^{1}J_{C-P}$ = 56.6 Hz, PC), 199.5 (d, $^{3}J_{C-P}$ = 11.6 Hz, CHO) ppm.

3.7. Synthesis of the phosphetane oxides 9 (Eq. (4)): general procedure

A solution of **8a** (or **8b**) (0.3 g, 0.92 mmol), (*R*)-(−)-1,2-diphenyl-1,2-ethanediol (or the corresponding *S* enantiomer; 0.20 g, 0.95 mmol) and *p*-toluenesulfonic acid (catalytic amount) in benzene was heated at 75 °C for 5 h (reaction times of 18 h are required for the synthesis of **9c** and **9d**). $MgSO_4$ was added to the reaction mixture to remove water. The final product was purified by column chromatography on alumina with hexane–ethyl acetate 80:20 (ethyl acetate for **9d**) as eluent (R_f = 0.6 in ethyl acetate).

9a was obtained in 50% yield as a colorless solid. ^{31}P NMR ($CDCl_3$) δ 70.5; ^{1}H NMR ($CDCl_3$) (selected data) δ 2.2–2.3 (m, 2H), 2.59 (q, $^{3}J_{H-H} \sim {}^{2}J_{H-P}$ = 6.7 Hz, PCH), 4.72 (s, CHPh), 5.53 (t, $^{3}J_{H-H}$ = 5.3 Hz, $CH(O-)_2$); ^{13}C NMR ($CDCl_3$) δ 17.0 (d, $^{2}J_{C-P}$ = 4.3 Hz, Me), 17.2 (Me), 21.9 (Me), 22.2 (Me), 22.4 (Me), 22.6 (Me), 24.2 (d, $^{3}J_{C-P}$ = 10.7 Hz, CH_2), 25.1 (d, $^{3}J_{C-P}$ = 23.0 Hz, Me), 28.8 (d, $^{2}J_{C-P}$ = 5.5 Hz, $CH_2CH(O-)_2$), 30.8 (d, $^{3}J_{C-P}$ = 3.1 Hz, $CHMe_2$), 33.2 (d, $^{3}J_{C-P}$ = 12.4 Hz, CHMe), 34.0 (2 CH_2), 40.3 (d, $^{1}J_{C-P}$ = 40.6 Hz, PCH), 41.1 (d, $^{2}J_{C-P}$ = 1.8 Hz, CH), 41.5 (d, $^{2}J_{C-P}$ = 12.6 Hz, C), 44.6 (d, $^{1}J_{C-P}$ = 52.5 Hz, PCH), 48.8 (d, $^{1}J_{C-P}$ = 54.6 Hz, PC), 84.9 (CHPh), 87.0 (CHPh), 104.6 (d, $^{3}J_{C-P}$ = 11.5 Hz, $CH(O-)_2$), 126.4, 126.8, 128.2, 128.6, 128.7, 136.7, 138.4 (Ph) ppm; mass spectrum (C.I.) *m/e* 522 (M, 10%), 180 ($Ph_2C_2H_2$, 100%). $[\alpha]_D$ = −26 (*c* = 1, $CHCl_3$).

9b was obtained from the (*S,S*) diol in 78% yield (0.48 g) as a colorless solid. ^{31}P NMR ($CDCl_3$) δ 70.5; ^{1}H NMR ($CDCl_3$) (selected data) δ 2.1–2.3 (m, 2H), 2.5–2.6 (m, 1H), 4.67 (s, CHPh), 5.45 (t, $^{3}J_{H-H}$ = 5.4 Hz, $CH(O-)_2$); selected ^{13}C NMR data: ($CDCl_3$) δ 29.5 (d, $^{2}J_{C-P}$ = 4.8 Hz, $CH_2CH(O-)_2$), 40.4 (d, $^{1}J_{C-P}$ = 41.3 Hz, PCH), 41.4 (d, $^{2}J_{C-P}$ = 12.3 Hz, C), 44.5 (d, $^{1}J_{C-P}$ = 53.0 Hz, PCH), 48.7 (d, $^{1}J_{C-P}$ = 54.0 Hz, PC), 84.8 (CHPh), 86.6 (CHPh), 104.7 (d, $^{3}J_{C-P}$ = 12.9 Hz, $CH(O-)_2$) ppm.

9c was obtained from the (*R,R*) diol in 47% yield (0.23 g) as a colorless solid. ^{31}P NMR ($CDCl_3$) δ 67.1; ^{1}H NMR ($CDCl_3$) (selected data) δ 2.6–2.8 (m, 1H), 4.74 (s, CHPh), 5.50 (t, $^{3}J_{H-H}$ = 5.3 Hz, $CH(O-)_2$); selected ^{13}C NMR data: ($CDCl_3$) δ 29.4 (d, $^{2}J_{C-P}$ = 3.3 Hz, $CH_2CH(O-)_2$), 42.2 (d, $^{2}J_{C-P}$ = 12.5 Hz, C), 44.4 (d, $^{1}J_{C-P}$ = 39.4 Hz, PCH), 46.3 (d, $^{1}J_{C-P}$ = 49.8 Hz, PCH), 48.1 (d, $^{1}J_{C-P}$ = 56.6 Hz, PC), 84.9 (CHPh), 86.7 (CHPh), 104.7 (d, $^{3}J_{C-P}$ = 11.1 Hz, $CH(O-)_2$) ppm.

9d was obtained from the (*S,S*) diol in 46% yield (0.22 g) as a colorless oil. ^{31}P NMR ($CDCl_3$) δ 66.7; ^{1}H NMR ($CDCl_3$) (selected data) δ 2.7–2.8 (m, 1H), 4.69 (*AB*, $^{3}J_{AB}$ = 8.1 Hz, CHPh), 4.75 (A*B*), 5.52 (dd, ^{3}J = 6.3 Hz, ^{3}J = 3.7 Hz, $CH(O-)_2$); selected ^{13}C NMR data: ($CDCl_3$) δ 29.0 (d, $^{2}J_{C-P}$ = 4.5 Hz, $CH_2CH(O-)_2$), 42.2 (d, $^{2}J_{C-P}$ = 9.2 Hz, C), 43.8 (d, $^{1}J_{C-P}$ = 39.7 Hz, PCH), 46.4 (d, $^{1}J_{C-P}$ = 50.2 Hz, PCH), 47.8 (d, $^{1}J_{C-P}$ = 56.5 Hz, PC), 84.5 (CHPh), 86.7 (CHPh), 104.4 (d, $^{3}J_{C-P}$ = 13.5 Hz, $CH(O-)_2$) ppm.

3.8. Reduction of phosphetane oxides 9 to 10 (Eq. (4))

The same reduction procedure as for **3** was used. All reductions were quantitative, according to ^{31}P NMR analysis of the reaction mixture. Yields ranging from 50 to 95% were obtained after chromatography. Phosphetanes **10** are air-sensitive compounds.

10a: ^{31}P NMR ($CDCl_3$) δ 31.0; ^{1}H NMR ($CDCl_3$) (selected data) δ 0.66 (d, $^{3}J_{H-H}$ = 6.7 Hz, $CHMe_2$), 0.76 (d, $^{3}J_{H-H}$ = 6.4 Hz, CHMe), 0.86 (d, $^{3}J_{H-H}$ = 6.7 Hz, $CHMe_2$), 0.90 (s, Me), 0.97 (d, $^{3}J_{H-P}$ = 15.6 Hz, Me), 1.15 (s, Me), 1.15 (d, $^{3}J_{H-P}$ = 9.0 Hz, Me),... 4.64 (CHPh), 5.38 (t, $^{3}J_{H-H}$ = 5.3 Hz, $CH(O-)_2$); ^{13}C NMR ($CDCl_3$) δ 16.7 (Me), 22.3 (d, J_{C-P} = 9.6 Hz, Me), 22.4 (Me), 22.7 (Me), 22.8 (d, J_{C-P} = 4.9 Hz, Me), 23.7 (d, $^{2}J_{C-P}$ = 22.0 Hz, Me), 24.9 (d, $^{3}J_{C-P}$ = 10.4 Hz, CH_2), 25.5 (d, J_{C-P} = 8.5 Hz, Me), 29.9 (d, $^{3}J_{C-P}$ = 12.6 Hz, $CHMe_2$), 33.5 (d, $^{3}J_{C-P}$ = 6.2 Hz, CHMe), 34.7 (d, $^{1}J_{C-P}$ = 3.6 Hz, PCH), 34.8 (CH_2), 35.6 (d, $^{2}J_{C-P}$ = 16.2 Hz, $CH_2CH(O-)_2$), 36.2 (d, $^{1}J_{C-P}$ = 28.8 Hz, PCH), 36.9 (d, $^{2}J_{C-P}$ = 5.1 Hz, CH_2), 37.0 (d, J_{C-P} = 5.8 Hz, C), 42.4 (d, J_{C-P} = 3.9 Hz, C), 48.5 (d, $^{2}J_{C-P}$ = 21.2 Hz, CH), 84.6 (CHPh), 86.9 (CHPh), 105.0 (d, $^{3}J_{C-P}$ = 10.7 Hz, $CH(O-)_2$), 126.3, 126.8, 128.1, 128.4, 128.5, 136.9, 138.6 (Ph) ppm.

10b: ^{31}P NMR ($CDCl_3$) δ 29.1; ^{1}H NMR ($CDCl_3$) (selected data) δ 4.72 (CHPh), 5.48 (dd, $^{3}J_{H-H}$ = 5.7 Hz, $^{3}J_{H-H}$ = 4.1 Hz, $CH(O-)_2$); ^{13}C NMR ($CDCl_3$) (selected data) δ 34.7 (d, $^{1}J_{C-P}$ = 3.5 Hz, PCH), 36.3 (d, $^{1}J_{C-P}$ = 28.5 Hz, PCH), 36.6 (d, $^{2}J_{C-P}$ = 17.2 Hz, $CH_2CH(O-)_2$), 36.7 (d, J_{C-P} = 4.4 Hz, C), 42.3 (d, J_{C-P} = 4.5 Hz, C), 48.6 (d, $^{2}J_{C-P}$ = 21.4 Hz, CH), 84.9 (CHPh), 86.6 (CHPh), 105.2 (d, $^{3}J_{C-P}$ = 12.2 Hz, $CH(O-)_2$) 137.0, 138.2 (Ph) ppm.

10c: ^{31}P NMR ($CDCl_3$) δ 25.3; ^{1}H NMR ($CDCl_3$) (selected data) δ 4.72 (CHPh), 5.44 (dd, $^{3}J_{H-H}$ = 6.9 Hz, $^{3}J_{H-H}$ = 3.8 Hz, $CH(O-)_2$); ^{13}C NMR ($CDCl_3$) (selected data) δ 35.3 (d, $^{2}J_{C-P}$ = 17.4 Hz, $CH_2CH(O-)_2$), 39.7 (d, $^{1}J_{C-P}$ = 31.8 Hz, PCH), 36.6 (d, J_{C-P} = 6 Hz, C), 43.3 (d, J_{C-P} = 4.3 Hz, C), 47.2 (d, $^{2}J_{C-P}$ = 11.0 Hz, CH), 84.9 (CHPh), 86.7 (CHPh), 105.2 (d, $^{3}J_{C-P}$ = 14.1 Hz, $CH(O-)_2$) 136.9, 138.6 (Ph) ppm.

10d: ^{31}P NMR ($CDCl_3$) δ 26.6; ^{1}H NMR ($CDCl_3$) (selected data) δ 4.68 (*AB*, $^{3}J_{H-H}$ = 7.7 Hz, CHPh), 4.71 (A*B*, CHPh), 5.46 (dd, $^{3}J_{H-H}$ = 6.8 Hz, $^{3}J_{H-H}$ = 3.5 Hz, $CH(O-)_2$); ^{13}C NMR ($CDCl_3$) (selected data) δ 35.0 (d, $^{2}J_{C-P}$ = 16.1 Hz, $CH_2CH(O-)_2$), 39.6 (d, $^{1}J_{C-P}$ = 30.1 Hz, PCH), 36.4 (d, J_{C-P} = 7.6 Hz, C), 43.2

(d, $J_{C-P} = 4.6$ Hz, C), 47.2 (d, $^2J_{C-P} = 11.5$ Hz, CH), 84.6 (CHPh), 86.8 (CHPh), 105.2 (d, $^3J_{C-P} = 13.6$ Hz, $CH(O-)_2$) 137.1, 138.7 (Ph) ppm.

3.9. X-ray structure determination for 5

Crystals of **5**, $C_{35}H_{45}ClO_2PPd$, were grown from an hexane–ether solution of the compound. Data were collected at -150 ± 0.5 °C on an Enraf Nonius CAD4 diffractometer using Cu Kα radiation ($\lambda = 1.54184$ Å) and a graphite monochromator. The crystal structure was solved and refined using the Enraf Nonius MOLEN package. The compound crystallises in space group $I222$ (23), $a = 26.367(3)$ Å, $b = 18.691(2)$ Å, $c = 16.229(2)$ Å; $V = 7997.8(2.8)$ Å^3; $Z = 8$; $d_{calc} = 1.114\,g\,cm^{-3}$; $\mu = 50.2\,cm^{-1}$; $F(000) = 2792$. A total of 4107 unique reflections were recorded in the range $2 \leq 2\theta \leq 150.0°$ of which 273 were considered as unobserved ($F^2 < 3.0\sigma(F^2)$), leaving 3834 for solution and refinement. Direct methods yielded a solution for all atoms. The hydrogen atoms were included as fixed contributions in the final stages of least squares refinement while using anisotropic temperature factors for all other atoms. A non-Poisson weighting scheme was applied with a p factor equal to 0.08. The final agreement factors were $R = 0.062$, $R_\omega = 0.099$, G.O.F. = 2.21.

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