Facile and General Synthesis of Polyphosphane Polyoxides with (O)PCP(O) Linkages

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Polyphosphane polyoxides with (O)PCP(O) linkages are powerful chelating agents for extraction of actinides from nuclear wastes. They are obtained either by the Michaelis–Arbuzov reaction of chloromethylphosphane oxides and phosphorus(III) esters, or by the reaction of phosphane oxide carbanions with chlorophosphanes. With the latter method, the addition of a phosphane oxide carbanion in excess allowed us to overcome a transmetallation reaction and thereby obtain polyphosphane polyoxides in good yields. The ^{1}H-NMR spectra of the PCH_2P groups show the influence of the different R groups attached to the phosphorus atoms. We determined the coupling constants and the chemical shifts of these spin systems.

Introduction

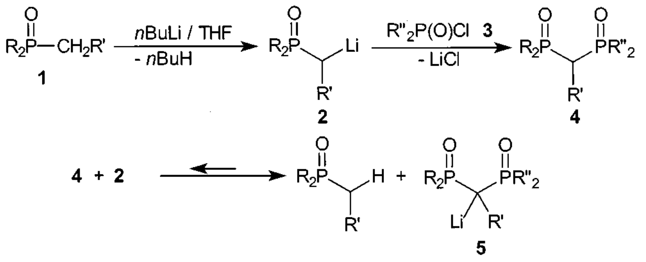
We have recently synthesized macrocyclic complexing agents[1] to achieve the extraction of actinides from nuclear wastes. These compounds were particularly efficient for plutonium and neptunium extraction, but they demonstrated low efficiency for the extraction of trivalent actinides such as americium. Therefore, we developed the synthesis of new organophosphorus compounds containing (O)PCP(O) units, in order to extract the actinides in all their valencies. The excellent extracting properties of these compounds using classical liquid-liquid extraction, or transport through supported liquid membranes, have been evaluated and are presented in a separate paper.[2] Furthermore, these kind of compounds are interesting for the treatment of bones pathologies.[3]

We chose two different pathways in order to build the (O)PCP(O) linkage. The first is a modification of the method developed by Richards et al.,[4] using a phosphane oxide carbanion and an electrophilic phosphorus compound. The second consists of a Michaelis−Arbuzov reaction between a chloromethylphosphane oxide and trivalent phosphorus esters.[5]

Results and Discussion

Reaction of Phosphane Oxide Carbanions

The reaction of *n*BuLi with an alkylphosphane oxide **1** leads to the corresponding phosphane oxide carbanion (**2**), which reacts in a second step with a diarylphosphinic chloride **3** to give the (O)PCP(O) compound **4** (Scheme 1). Generally, the yields are moderate for methylene-[4] as well as for pyridyl-substituted methylene-diphosphane dioxide,[6] or sulfide[7] The major drawback of this procedure is a successive concurrent transmetallation reaction between the initial carbanion **2** and the resulting diphosphane dioxide **4**.[8] Fortunately, the new stabilized carbanion **5** is unreactive towards **3**: indeed, the alkylation of the diphosphane dioxide carbanions **5** generally gives poor yields.[9] Furthermore, diarylphosphinic chlorides **3** probably induce more steric hindrance, in comparison to linear haloalkanes, for the electrophilic trapping of carbanion **5**.



Scheme 1. Reaction of phosphane oxide carbanions with diarylphosphinic chlorides

In order to avoid the consecutive transmetallation between **2** and **4**, it is well advised to use an excess of one equivalent of base which cannot act as a nucleophile in the reaction conditions. In such a way, using two equivalents of LDA, Savignac and Collignon groups developed an improved procedure for the reaction of phosphorylated carbanions with $ClP(O)Z_2$ as electrophiles.[10] This procedure is now widely used to prepare *gem*-diphosphorylated compounds.[11] In our case, in order to use (di)chlorophosphanes as (di)electrophiles, which are known to react easily with lithium amides, even overcrowded such as *i*Pr(Me_3-Si)NLi[12], we choosed to use simply an excess of the initial phosphane oxide carbanion **2** both as reagent and deprotonation agent: The reaction of two equivalents of phosphane oxide carbanions **2** with chlorodiphenylphosphane gives first phosphanylmethylphosphane oxides **6**, (Scheme 2), which are then oxidized, by hydrogen peroxide in dichloromethane, to the diphosphane dioxides **4a−b** in good

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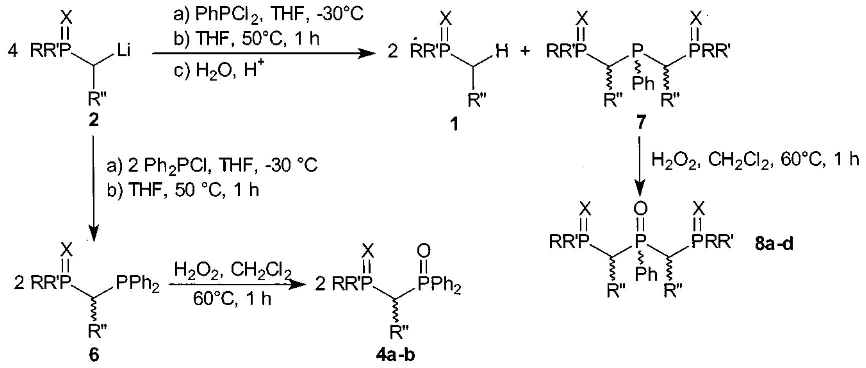


Scheme 2. Generalization of the phosphane oxide carbanions way (Table 1)

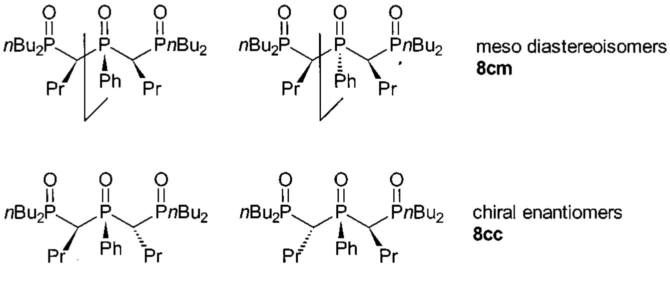
yields (Table 1). Excess of the initial phosphane oxide **1** is removed either by solubilization in hexane or by chromatography.

In the same way, the reaction of four equivalents of various phosphane oxide carbanions with dichlorophenylphosphane gives, after oxidation, triphosphane trioxides **8a−c** in good yields. This methodology was successfully applied to the synthesis of the 1,1,3,5,5-pentaphenyl-1,3,5-triphosphapentane-1,5-disulfide-3-oxide **8d** (in 27% yield) using diphenylmethylphosphane sulfide carbanion (Table 1).

Table 1. Compounds obtained by the phosphane oxide carbanions reaction

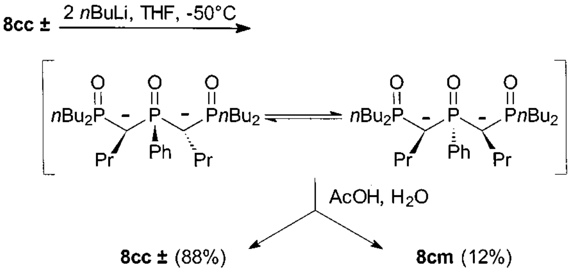
Compound	R	R′	R″	X	Yield (%)
4a	Ph	Ph	H	O	79
4b	Ph	Me	H	O	53
8a	Ph	Ph	H	O	91
8b	Ph	Me	H	O	74
8c	*n*Bu	*n*Bu	*n*Pr	O	83
8d	Ph	Ph	H	S	27

Compounds **8b** and **8c** exhibit phosphorus or carbon chiral centers: for compound **8b**, the diastereoisomers cannot be separated, but for compound **8c**, the racemic mixture of the chiral enantiomers **8cc** and one meso diastereoisomer **8cm** were separated by column chromatography, obtained in 56% and 22% yields respectively, and characterized by ^{13}C-, ^{1}H-, and ^{31}P-NMR spectra (Scheme 3). The ^{31}P-NMR spectrum shows the presence of only one meso compound.



Scheme 3. Stereoisomers of compound **8c**

In order to verify this observation, the addition of two equivalents of *n*BuLi to the **8cc** enantiomers gave the corresponding dicarbanion (Scheme 4). After equilibration at −50 °C in THF as well as in refluxing THF, the protonation by acetic acid in water leads in both cases to the formation of **8cc** and **8cm** in 88/12 ratio. The isomerization of the carbanion is probably thermodynamically controlled and the proportions of **8cc** to **8cm** depend on the relative stabilities of the different carbanions.



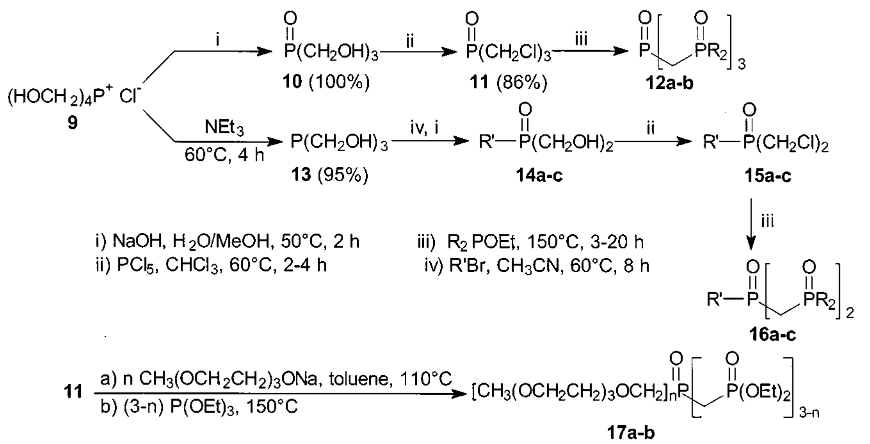
Scheme 4. Diastereoselection from (O)PCP(O) carbanions

Michaelis−Arbuzov Reactions of Chloromethylphosphane Oxides

The Michaelis−Arbuzov reactions of a phosphite or phosphinite with chloromethylphosphane oxides lead to the (O)PCP(O) compounds (Scheme 5). The chloromethylphosphane oxides are obtained using tetrakis(hydroxymethyl)phosphonium chloride **9** as a precursor. Tris(chloromethyl)phosphane oxide **11** is synthesized in two steps (in 86% yield): by reaction of **9** with sodium hydroxide to give **10**,[13] followed by the action of phosphorus pentachloride[14] on **10** to give **11**.

Triphosphane trioxides **15a−b** with lipophilic chains are obtained in four steps using tris(hydroxymethyl)phosphane **13**. In the first step, the reaction of phosphonium salt **9** with triethylamine gives **13** quantitatively.[15] **13** then reacts with bromoalkanes to afford the corresponding tris(hydroxymethyl)alkylphosphonium salts which undergo basic hydrolysis to give bis(hydroxymethyl)alkylphosphane oxides **14a−c**. Finally, chlorination of the hydroxy groups by phosphorus pentachloride affords bis(chloromethyl)phosphane oxides **15a−c** in high yields.

A third way to synthesize chloromethylphosphane oxides is by the Williamson reaction of the tris(chloromethyl)phosphane oxide **11** with an alkoxide.[16]



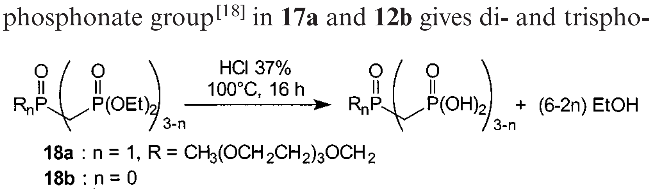
Scheme 5. Arbuzov reaction of chloromethyl phosphane oxides (Table 2)

The synthesis of PCP linkage by the Michaelis−Arbuzov reaction is carried out without solvent at 150 °C for 3 to 20 hours with a slight excess of triethyl phosphite or ethyl diphenylphosphinite and affords high yields of di-, tri-, and tetraphosphorylated compounds (Table 2). Triphosphane trioxide **16c** with *o*-nitrophenoxyoctyl chain was not obtained because the nitro group reacts with ethyl diphenylphosphinite to probably form a nitrene via a concurrent reduction reaction.[17]

Table 2. Compounds obtained by the Michaelis−Arbuzov reaction

Compound	R	R′ or *n*	Yield (%)
12a	Ph	–	31
12b	OEt	–	83
16a	Ph	$n\mathrm{C}_{12}\mathrm{H}_{25}$	84
16b	Ph	$\mathrm{PhO(CH_2)_8}$	85
16c	Ph	$o\mathrm{NO_2PhO(CH_2)_8}$	0
17a	OEt	$n = 2$	89
17b	OEt	$n = 1$	86

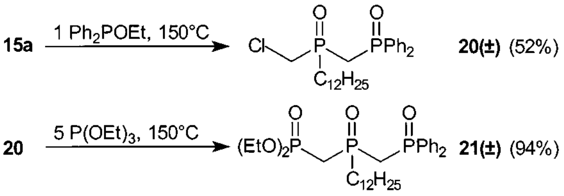
Subsequent hydrolysis, in acidic media (HCl 35%), of the phosphonate group[18] in **17a** and **12b** gives di- and trisphosphonic acid **18a** and **18b** in quantitative yield (Scheme 6).



Scheme 6. Acidic hydrolysis of the PCP phosphonates

The Michaelis−Arbuzov reaction is a very clean way to form (O)PCP(O) compounds, and the main side products are generally the less substituted ones. In the reaction of **11** with triethyl phosphite, a kinetic study of the successive Michaelis−Arbuzov reactions showed that the mono- and disubstitution steps have the same rate. However, the substitution rate of the last chloromethyl group is 1.6-fold lower. Then, by stopping the reaction before completion, the bis(*O*,*O*′-diethylphosphonomethyl)chloromethylphosphane oxide **19** can be isolated in 19% yield as a side product of the trisubstituted compound **12b** (obtained in 45% yield).

Thus, we obtained chloromethyl(diphenylphosphanylmethyl)dodecylphosphane dioxide **20** in 52% yield by the reaction of bis(chloromethyl)dodecylphosphane oxide **15a** with 1 equivalent of ethyl diphenylphosphinite. Subsequent reaction with triethyl phosphite of the free chloromethyl function lead to the mixed phosphonate−phosphane oxide compound **21** in 94% yield (Scheme 7).

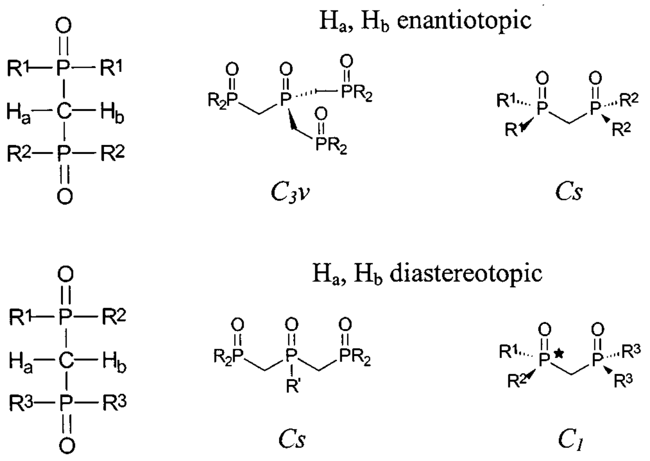


Scheme 7. Synthesis of the mixed phosphane oxide−phosphonate **21**

^{1}H- and ^{13}C-NMR Study of the (O)PCP(O) Units

The signals of the methylenic hydrogens H_a and H_b in PCH_2P groups are very sensitive to the stereoisomeric relationships[19] between the different R groups connected to the phosphorus atoms. Besides compound **4a** in which the hydrogens are equivalent and give, with the two equivalent phosphorus atoms, an A_2X_2 spin system, two different kinds of compounds are described in this work: those in which H_a and H_b are enantiotopic, i.e. related by a σ plane, and those where these hydrogens are diastereotopic, i.e. not related by any symmetry element (Scheme 8).

On the one hand, the PCH_2P group of the C_s diphosphorylated compound **17a** gives an A_2MX spin system. On the other hand, the C_{3v} tetraphosphorylated compounds **12a**, **12b**, and **18b** possess three equivalent methylene groups related by the C_3 axis in which the two hydrogens of each methylene are related by a σ plane and are enantiotopic. Thus, the spin system of these molecules is of the $[A_2M]_3X$ type. In contrast, the C_s triphosphorylated compounds **8a**, **8d**, **16a**, **16b**, **17b**, **18a**, and **19** possess two enantiotopic methylene groups, the hydrogens of which are diastereotopic, giving a $[ABM]_2X$ spin system. The last set



Scheme 8. Stereoisomeric relationships in (O)PCP(O) compounds

of compounds, **4b**, **20**, and **21**, deprived of any symmetry element, show a simple ABMX system.

The important point in the analysis of these $[ABM]_nX$ systems is the absence of any resolved coupling constants between each of the ABM parts. Then the ^{1}H-NMR spectra are made of four AB sub-spectra (Figure 1). For each spectrum, the coupling constants with the M and X phosphorus atoms can be exchanged with no effect on theoretical spectra and some double irradiation experiments involving ^{31}P were necessary to resolve this ambiguity.

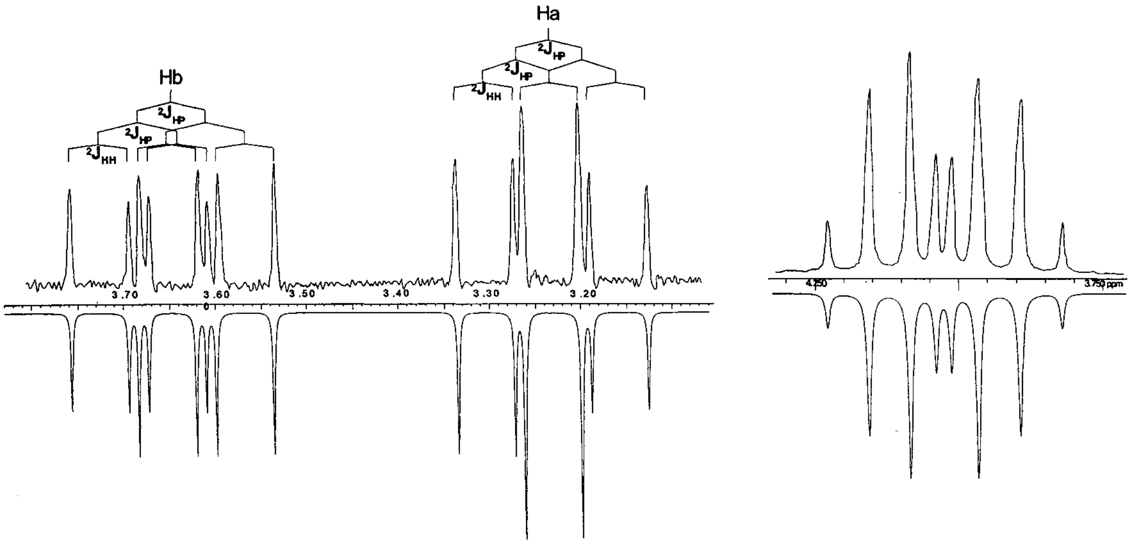
All spectra have been simulated,[20] and the resulting chemical shifts and coupling constants are listed in Table 3. The signs of the $^2J_{HH}$ coupling constants have not been determined, and are given according to the geminal coupling in *sp*^{3} hybridized system.[21] Sometimes, all the expected transitions are not observed, particularly in **8d** where the $^2J_{PH}$ couplings are equal. In the extreme cases, hydrogens in methylene groups of **19** and **18a** were accidentally isochronous and give only a doublet of doublet.

^{13}C-NMR spectra are also sensitive to the stereoisomerism of compounds, especially the carbons of diphenylphosphanyloxy and diethylphosphono groups, which appear as double signals when one phosphorus bears two identical but diastereotopic groups.

Concerning the (O)PCP(O) units, the carbon signal multiplicity due to ^{31}P-^{13}C coupling constants are dependent on the nature of the phosphorus function. The $^1J_{PC}$ couplings range from 42.8 Hz to 135.3 Hz (Table 4), but these values strongly depend on the nature of the phosphorylated group. For the phosphonic function, couplings range from 126.3 Hz to 135.5 Hz so the $^1J_{PC}$ coupling with phosphonate group can be assigned unambiguously. On the contrary, the $^1J_{PC}$ values in the phosphane oxide groups possess the same order of magnitude, between 42.8 Hz and 63.4 Hz. Thus we made some triple irradiation $\{^{31}P\}\{^1H\}$-^{13}C experiments to ascertain the attribution of each coupling constant to each phosphorus atom. The $^3J_{PC}$ couplings are rarely observed except in some esters or phosphonic acids where these values are generally weak and about 2.5 to 3.6 Hz.

Conclusion

Polyphosphane polyoxides with (O)PCP(O) bridges can be obtained in good yields using the reaction of an excess of phosphane oxide carbanions with chlorophosphanes. Additional interests of this way lie in the possible access to mixed sulfide and oxide compounds as well as in the diastereoselection occurring during the phosphination of the dicarbanionic species. Another general way to obtain the P-substituted compounds (alkyl, polyethers side chains)



16b

8d

Figure 1. Experimental and simulated ^{1}H-NMR of **16b** and **8d** at 200.13 MHz in $CDCl_3$

Table 3. ^{1}H NMR parameters and J_{PH} values of (O)PCH$_2$P(O) groups

Compound		δ (ppm)	Coupling constant (Hz)								
	[a]	H_a	H_b	P	P′[b]	$^2J_{HaHb}$	$^2J_{PHa}$	$^2J_{PHb}$	$^2J_{P'Ha}$	$^2J_{P'Hb}$	$^2J_{PP}$
4a	eq	3.54		25.37		–	14.7				–
12a[c]	en	3.65		33.90	30.10	–	13.7		13.7		15.2
12b	en	2.90		29.73	20.34	–	15.8		20.4		8.9
18b[c]	en	2.76		32.66	15.23	–	16.5		19.1		10.6
17a	en	2.42		38.51	21.62	–	13.8		20.5		12.5
4b	di	3.10	3.17	32.60	27.01	−13.5	12.9	17.2	14.9	12.4	12.0
8a	di	3.77	3.77	28.57	27.09	–	12.9		15.9		12.0
8d	di	3.94	4.12	26.85	34.41	−14.5	14.6	14.3	14.6	14.3	12.0
16a	di	3.23	3.61	39.60	25.86	−14.7	12.6	12.6	14.5	16.7	12.5
16b	di	3.23	3.64	40.42	26.60	−14.7	12.5	12.6	14.6	16.9	12.5
17b	di	2.62	2.70	34.65	20.96	−15.1	14.7	15.0	20.7	20.4	12.6
18a[c]	di	2.76	2.76	43.00	16.94	–	15.2		20.1		14.0
19	di	2.78	2.78	32.59	18.59	–	15.2		20.3		14.0
20	di	3.01	3.10	43.84	25.11	−15.1	14.9	12.7	12.0	15.6	12.6
21	di	2.73	2.80	34.99	20.67	−15.2	14.8	15.6	19.3	21.4	10.1
		3.11	3.58	34.99	22.32	−15.1	11.4	13.4	15.1	17.1	11.8

[a] eq: equivalent hydrogens, en: enantiotopic hydrogens, di: diastereototopic hydrogens. – [b] R$_2$P(O) groups (R = OH, OEt, Ph, *n*Bu). – [c] Spectra in [D$_6$]DMSO.

Table 4. ^{13}C chemical shifts and $^nJ_{PC}$ values of (O)PCP(O) groups

Compound	δ	multiplicity	$^1J_{PC}$ (Hz)	$^1J_{PC}$ (Hz)[a]	$^3J_{PC}$ (Hz)
4a	34.43	t	58.3		–
4b	34.71	dd	54.7	59.4	–
8a	32.57	dd	59.1[b]	59.9[b]	–
8cm	38.26	dd	47.7	55.6	–
8cc	37.71	dd	43.0	59.5	–
	39.99	dd	42.8[b]	43.2[b]	–
8d	35.37	dd	60.6	45.4	–
12a	32.84	dd	56.7	56.7	–
12b	26.70	ddt	63.4	131.2	2.5
16a	31.39	dd	53.6	60.5	–
16b	31.34	dd	53.6	60.6	–
17a	23.02	dd	53.1	135.3	–
17b	25.60	ddd	53.3	133.1	3.6
18a	29.11	ddd	59.8	128.3	3.2
18b	29.88	dd	63.0	126.3	–
19	25.92	ddd	63.1	132.6	3.0
20	28.42	dd	53.5	59.9	–
21	28.40	dd	57.4	133.1	–
	30.23	dd	58.8	58.8	–

[a] $^1J_{PC}$ coupling involving R$_2$P(O) groups (R = OH, OEt, Ph, *n*Bu). – [b] The $^1J_{PC}$ couplings are permutable.

is the Arbuzov reaction using chloromethylphosphane oxide reagents.

This study has shown that the ^{1}H-NMR spectra of methylene groups are strongly dependant on the stereoisomeric relationships of the R groups

Experimental Section

General Remarks: All solvents were distilled prior to use and commercially available reagents used without further purification. – All reactions were monitored by TLC (Merk, SIL G/UV$_{254}$) or ^{31}P NMR. – Merck silica gel 60 (0.063–0.20 mm) was used for column chromatography. – Melting points were determined using a Wild Leitz 350 and are given uncorrected. – ^{1}H-, ^{13}C-, and ^{31}P-NMR spectra were recorded on a Bruker AC-200 spectrometer as CDCl$_3$ solutions (unless otherwise specified). Chemical shifts are expressed in ppm and coupling constants in Hz. Reference compounds were internal TMS for ^{1}H and ^{13}C and external 85% H$_3$PO$_4$ for ^{31}P NMR. In the ^{13}C-NMR spectra of **4b** and **8a**, a few of the *J* values have not been determined due to some peak superpositions, particularly in the aromatic zone. The missing values are replaced by "–" in the descriptions of these compounds. – IR spectra were obtained with a Perkin–Elmer 377. – Mass spectra were measured with a Jeol JMS DX-300 spectrometer.

General Procedure I: To a stirred mixture of alkylphosphane oxide in anhydrous THF at −30°C, 1 equiv. of a solution of *n*BuLi (1.6 M) was added. Reaction mixture was stirred for 30 min at 0°C. After cooling to −30°C, 0.5 equiv. of diphenylchlorophosphane or 0.25 equiv. of dichlorophenylphosphane were added and refluxed for 2 hours. 20 equiv. of water were added, and THF was removed under vacuum. The same volume of CH$_2$Cl$_2$ was added and 1.2 equiv. of H$_2$O$_2$ (1 M) were slowly added at 0°C.

1,1,3,3-Tetraphenyl-1,3-diphosphapropane Dioxide (4a): Reaction according to *Procedure I* with diphenylmethylphosphane oxide and chlorodiphenylphosphane gave 79% yield of **4a** as colorless crystals, with the same spectroscopic data as described by Richards.[22]

1,1,3-Triphenyl-1,3-diphosphabutane Dioxide (4b): Reaction according to *Procedure I* with dimethylphenylphosphane oxide and chlorodiphenylphosphane gave 53% of **4b** as a yellow crystalline solid, m.p. 174°C. − IR (KBr): ṽ = 3050 cm^{-1}, 2920, 2880, 1435, 1290, 1190, 1170, 1115, 1082, 1070, 895, 880, 805, 732, 690, 545. − ^{1}H NMR: δ = 1.96 (d, $^{2}J_{HP}$ = 13.8 Hz, 3 H, PCH_3), 3.10, 3.17 (m,[23] 2 H, PCH_2P), 7.25−7.75 (m, 15 H, 3 Ph). − ^{13}C NMR: δ = 17.75 (d, $^{1}J_{PC}$ = 73.0 Hz, PCH_3), 34.71 (dd,[24] PCH_2P), 128.49, 128.57, 128.81 (3 d, $^{3}J_{PC}$ = 12.3 Hz, $^{3}J_{PC}$ = 12.1 Hz, $^{3}J_{PC}$ = 12.2 Hz, 2 *m*CH, *m'*CH), 130.22, 130.35, 130.73 (3 d, $^{2}J_{PC}$ = 10.2 Hz, $^{2}J_{PC}$ = 9.8 Hz, $^{2}J_{PC}$ = 10.1 Hz, 2 *o*CH, *o'*CH), 131.75, 131.90, 132.30 (3 d, $^{4}J_{PC}$ = 2.9 Hz, $^{4}J_{PC}$ = 2.9 Hz, $^{4}J_{PC}$ = 2.9 Hz, 2 *p*CH, *p'*CH), 132.81, 133.19, 133.44 (3 dd, $^{1}J_{PC}$ = − Hz, $^{3}J_{PC}$ = 2.7 Hz, $^{1}J_{PC}$ = − Hz, $^{3}J_{PC}$ = 2.0 Hz, $^{1}J_{PC}$ = 101.4 Hz, $^{3}J_{PC}$ = 2.3 Hz, 2 *i*C, *i'*C). − ^{31}P NMR: δ = 27.01 (d, $^{2}J_{pp}$ = 12.0 Hz, PPh_2), 32.60 (d, $^{2}J_{pp}$ = 12.0 Hz, P=O). − MS EI; *m/z* (%): 354 (15), 339 (20), 277 (31), 229 (41), 91 (93), 77 (100).

1,1,3,5,5-Pentaphenyl-1,3,5-triphosphapentane Trioxide (8a): Reaction according to *Procedure I* with diphenylmethylphosphane oxide and dichlorophenylphosphane gave 91% of **8a** as colorless crystals, m.p. 88−90°C. − IR (KBr): ṽ = 3055 cm^{-1}, 2960, 2920, 2860, 1435, 1190, 1100, 1028, 800. − ^{1}H NMR: δ = 3.77 (dd,[23] 4 H, PCH_2P), 7.05−7.90 (m, 25 H, 5 Ph). − ^{13}C NMR: δ = 32.57 (dd,[24] PCH_2P), 128.04 (d, $^{3}J_{PC}$ = 12.4 Hz, *m'*CH), 128.37, 128.55 (2 d, $^{3}J_{PC}$ = 12.3 Hz, $^{3}J_{PC}$ = 12.5 Hz, *m*CH), 130.40 (d, $^{2}J_{PC}$ = − Hz, *o'*CH), 130.73, 131.03 (2 d, $^{2}J_{PC}$ = 10.0 Hz, $^{2}J_{PC}$ = 10.3 Hz, *o*CH), 131.61, 131.89 (2 d, $^{4}J_{PC}$ = 2.9 Hz, $^{4}J_{PC}$ = 3.0 Hz, *p'*CH), 131.79 (d, $^{4}J_{PC}$ = − Hz, *p'*CH), 132.47, 133.05 (2 dd, $^{3}J_{PC}$ = 2.8 Hz, $^{3}J_{PC}$ = 3.0 Hz, $^{1}J_{PC}$ = 103.9 Hz, $^{1}J_{PC}$ = 105.2 Hz, *i*C). − ^{31}P NMR: δ = 27.09 (d, $^{2}J_{pp}$ = 12.0 Hz, 2 PPh_2), 28.57 (t, $^{2}J_{pp}$ = 12.0 Hz, P=O). − MS EI; *m/z* (%): 554 (14), 477 (75), 121 (100).

2,4,6-Triphenyl-2,4,6-triphosphaheptane Trioxide (8b) (as a mixture of *meso*- and chiral compounds): Reaction according to *Procedure I* with dimethylphenylphosphane oxide and dichlorophenylphosphane gave 74% of **8b** as colorless crystals. − IR (KBr): ṽ = 3060 cm^{-1}, 2920, 2880, 1438, 1185, 1115, 1070, 892, 810, 742, 692, 485. − ^{1}H NMR: δ = 1.61, 1.72, 2.00 (3 d, $^{2}J_{HP}$ = 13.5 Hz, $^{2}J_{HP}$ = 13.5 Hz, $^{2}J_{HP}$ = 13.7 Hz, 6 H, CH_3), 2.70−3.63 (m, 4 H, PCH_2P), 7.10−7.95 (m, 15 H, 3 Ph). − ^{31}P NMR (CD_3OD, C_6H_6): δ = 32.77 (t, $^{2}J_{pp}$ = 14.0 Hz, P=O *meso* 1), 33.67 (t, $^{2}J_{pp}$ = 12.9 Hz, P=O *meso* 2), 34.10 (t, $^{2}J_{pp}$ = 14.2 Hz, P=O chiral), 37.25 (d, $^{2}J_{pp}$ = 14.0 Hz, *P*PhMe *meso* 1), 37.40 (d, $^{2}J_{pp}$ = 14.2 Hz, *P*PhMe chiral), 38.34 (d, $^{2}J_{pp}$ = 12.9 Hz, *P*PhMe *meso* 2), 39.20 (d, $^{2}J_{pp}$ = 14.4 Hz, *P*PhMe chiral). − MS EI; *m/z* (%): 430 (4), 415 (40), 277 (80), 137 (100). − $C_{22}H_{25}O_3P_3$ (430.4): Calcd. C 60.0, H 6.1, O 12.9; found C 59.7, H 5.9, O 12.4.

5,9-Dibutyl-6,8-dipropyl-5,7,9-triphosphatridecane Trioxide (8c): Reaction according to *Procedure I* with tributylphosphane oxide and dichlorophenylphosphane gave 83% yield of **8c** as a viscous oil. Chromatographic separation using AcOEt/MeOH (97:3) as eluent gave **8cc** and **8cm** in 56% and 22% yield respectively.

***meso*-Compound 8cm:** viscous oil. − IR (KBr): ṽ = 2960 cm^{-1}, 2925, 2880, 1260, 1180, 1100, 1040, 1020, 905, 865, 820, 715. − ^{1}H NMR: δ = 0.78, 0.82, 0.93 (3 t, $^{3}J_{HH}$ = 7.0 Hz, $^{3}J_{HH}$ = 7.2 Hz, $^{3}J_{HH}$ = 6.9 Hz, 18 H, 6 CH_3), 1.07−2.40 (m, 32 H, CH_2), 3.20−3.80 (m, 2 H, PC*H*P), 7.45−7.60, 7.78−7.93 (2 m, 5 H, Ph). − ^{13}C NMR: δ = 13.51, 13.69, 14.29 (s, CH_3), 23.41, 23.47, 23.78, 23.88, 23.98, 24.12, 24.27, 24.43, 26.88 (CH_2), 28.37, 28.62 (2 d, $^{1}J_{PC}$ = 66.8 Hz, $^{1}J_{PC}$ = 64.1 Hz, PCH_2), 38.26 (dd,[24] PCH_2P), 128.49 (d, $^{3}J_{PC}$ = 11.2 Hz, *m*CH), 131.04 (d, $^{1}J_{PC}$ = 83.8 Hz, *i*CH), 131.79 (d, $^{2}J_{PC}$ = 8.3 Hz, *o*CH), 131.04 (s, *p*CH). − ^{31}P NMR: δ = 42.69 (t, $^{2}J_{PP}$ = 4.5 Hz, P=O), 52.45 (d, $^{2}J_{pp}$ = 4.5 Hz, Bu_2P=O). − MS EI; *m/z* (%): 558 (10), 528 (15), 500 (27), 341 (63), 217 (100), 201 (84).

Chiral Compound 8cc: Colorless crystals, m.p. 87−88°C. − IR (KBr): ṽ = 2960 cm^{-1}, 2930, 2870, 1465, 1190, 1165, 812, 800; 720. − ^{1}H NMR: δ = 0.65, 0.74 (2 t, $^{3}J_{HH}$ = 7.0 Hz, $^{3}J_{HH}$ = 7.0 Hz, 6 H, 2 *n*Pr CH_3), 0.78−0.96 (m, 12 H, 4 *n*Bu CH_3), 1.08−2.33 (m, 32 H, 16 CH_2), 4.09 (m, 1 H, PC*H*P), 4.58 (ddt, $^{2}J_{HP}$ = 18.5 Hz, $^{2}J_{HP}$ = 24.6 Hz, $^{3}J_{HH}$ = 6.0 Hz, 1 H, PC*H*P), 7.38−7.55, 8.00−8.17 (2 m, 5 H, Ph). − ^{13}C NMR: δ = 13.57, 13.63, 13.76 (3 s, 4 *n*Bu CH_3), 14.07, 14.20 (2 s, 2 *n*Pr CH_3), 23.25, 23.33, 23.48, 23.54, 23.63, 23.70, 23.77, 23.84, 24.05, 24.26, 24.33, 24.55, 24.76 (CH_2), 29.00, 29.11, 30.54, 30.64 (4 d, $^{1}J_{PC}$ = 64.8 Hz, $^{1}J_{PC}$ = 64.8 Hz, $^{1}J_{PC}$ = 66.6 Hz, $^{1}J_{PC}$ = 66.6 Hz, 4 PCH_2), 37.71 (dd,[24] PCH_2P), 39.99 (dd,[24] PCH_2P), 128.13 (d, $^{3}J_{PC}$ = 13.0 Hz, *m*CH), 131.54 (d, $^{1}J_{PC}$ = 85.5 Hz, *i*CH), 131.91 (d, $^{4}J_{PC}$ = 2.6 Hz, *p*CH), 132.83 (d, $^{2}J_{PC}$ = 9.4 Hz, *o*CH). − ^{31}P NMR: δ = 46.87 (dd, $^{2}J_{pp}$ = 1.3 Hz, $^{2}J_{pp}$ = 10.2 Hz, P=O), 49.35 (d, $^{2}J_{pp}$ = 1.3 Hz, Bu_2P=O), 54.96 (d, $^{2}J_{pp}$ = 10.2 Hz, Bu_2P=O). − MS EI; *m/z* (%): 558 (2), 529 (14), 501 (22), 341 (62), 217 (100), 201 (75). − $C_{30}H_{57}O_3P_3$ (646,7): Calcd. C 64.5, H 10.3, O 8.6; found C 64.5, H 10.5, O 9.0.

1,1,3,5,5-Pentaphenyl-1,3,5-triphosphapentane 1,5-Disulfide 3-Oxide (8d): Reaction according to *Procedure I* with diphenylmethylphosphane sulfide and dichlorophenylphosphane gave 24% of **8d** as colorless crystals, m.p. 251−252°C. − IR (KBr): ṽ = 3053 cm^{-1}, 2933, 2900, 2856, 1436, 1213. − ^{1}H NMR: δ = 3.94, 4.12 (m,[23] 4 H, PCH_2P), 7.08−7.92 (m, 25 H, 5 Ph). − ^{13}C NMR: δ = 35.37 (dd,[24] PCH_2P), 128.1 (d, $^{3}J_{PC}$ = 12.6 Hz, *m'*CH), 128.4, 128.6 (2 d, $^{3}J_{PC}$ = 10.5 Hz, $^{3}J_{PC}$ = 10.6 Hz, *m'*CH), 130.7 (d, $^{2}J_{PC}$ = 10.0 Hz, *o'*CH), 131.2, 131.3 (d, $^{2}J_{PC}$ = 10.9 Hz, $^{2}J_{PC}$ = 11.2 Hz, *o*CH), 131.4, 131.6 (d, $^{4}J_{PC}$ = 2.8 Hz, $^{4}J_{PC}$ = 3.1 Hz, *p*CH), 131.8 (d, $^{4}J_{PC}$ = 2.9 Hz, *p'*CH), 132.4, 133.3 (2 dd, $^{3}J_{PC}$ = 2.8 Hz, $^{1}J_{PC}$ = 85.3 Hz, $^{3}J_{PC}$ = 3.2 Hz, $^{1}J_{PC}$ = 85.7 Hz, *i*C), 132.62 (td, $^{3}J_{PC}$ = 2.2 Hz, $^{1}J_{PC}$ = 86.3 Hz, *i'*C). − ^{31}P NMR: δ = 26.8 (t, $^{2}J_{pp}$ = 12.0 Hz, 2 P=O), 34.4 (d, $^{2}J_{pp}$ = 12.0 Hz, P=S).

General Procedure II: A stirred mixture, under nitrogen, of tris(hydroxymethyl)phosphane (1.3 equiv.) and alkyl bromides (1 equiv., 0.3 mol·L^{-1}) in acetonitrile was heated for 4 h. The reaction mixture was extracted with hexane (to remove alkylbromine). The acetonitrile layer was concentrated. After addition of 30 mL of water, the reaction mixture was extracted with CH_2Cl_2, dried, and concentrated. The phosphonium salt was used without further purification.

To a stirred mixture of phosphonium salt (1 equiv., 0.3 mol·L^{-1}) in ethanol, a solution of sodium hydroxide (1.5 equiv., 0.4 mol·L^{-1}) was added and refluxed for 2 h. Ethanol was removed and the residue was extracted with $CHCl_3$. Organic layers were neutralized with 1 N HCl, dried (Na_2SO_4), and concentrated in vacuum.

Bis(hydroxymethyl)dodecylphosphane Oxide (14a): Reaction according to *Procedure II* with 1-bromododecane, purification by recrystallisation in AcOEt, gave 91% yield of **14a** as colorless crystals, m.p. 77.5°C. − IR (KBr): ṽ = 3250 cm^{-1}, 2915, 2850, 1469, 1115, 1059, 875, 482, 452. − ^{1}H NMR: δ = 0.88 (t, $^{3}J_{HH}$ = 6.2 Hz, 3 H, $^{12}CH_3$), 1.20−1.38, 1.52−1.77 (2 m, 22 H, $^{1-11}CH_2$), 3.91−4.07 (m, 4 H, PCH_2OH). − ^{13}C NMR: δ = 14.09 (s, $^{12}CH_3$), 20.69 (d, $^{2}J_{PC}$ = 4.4 Hz, $^{2}CH_2$), 22.67 (s, $^{11}CH_2$), 22.81 (d, $^{1}J_{PC}$ = 60.8 Hz, $^{1}CH_2$), 29.13, 29.34, 29.44, 29.63 (4 s, $^{4-9}CH_2$), 31.13 (d, $^{3}J_{PC}$ = 12.9 Hz, $^{3}CH_2$), 31.90 (s, $^{10}CH_2$), 56.40 (d, $^{1}J_{PC}$ = 76.4 Hz, PCH_2OH). − ^{31}P NMR: δ = 52.7 (s). − MS FAB^{+}(GT); *m/z* (%): 279 (100) $[M + H]^{+}$, 263 (7), 249 (5), 55 (18), 41 (23).

Bis(hydroxymethyl)-8-phenoxyoctylphosphane Oxide (14b): Reaction according to *Procedure II* with 8-bromo-phenoxyoctane, purification by recrystallisation in CH$_2$Cl$_2$/hexane, gave 62% yield of **14b** as colorless crystals, m.p. 100.5−101°C. − IR (KBr): $\tilde{\nu}$ = 3260 cm^{-1}, 3050, 2990, 2920, 2840, 2775, 1595, 1580, 1495, 1485, 1460, 1245, 1220, 1215, 1180, 1130, 1075, 1035, 1025, 905, 790, 690. − ^{1}H NMR ([D$_6$]DMSO): δ = 1.26−1.39, 1.57−1.82 (2 m, 14 H, $^{1-7}$CH$_2$), 3.74 (m, 4 H, PC*H*$_2$O), 3.91 (t, $^3J_{HH}$ = 6.4 Hz, ^{8}CH$_2$), 5.26 (broad s, 2 H, O*H*), 6.84−6.90 (m, 3 H, *o,p*CH), 7.19−7.27 (m, 2 H, *m*CH). − ^{13}C NMR ([D$_6$]DMSO): δ = 20.38 (d, $^2J_{PC}$ = 4.0 Hz, ^{2}CH$_2$), 22.21 (d, $^1J_{PC}$ = 65.8 Hz, ^{1}CH$_2$), 25.47 (s, ^{7}CH$_2$), 28.56, 28.65 (2 s, ^{4,5,6}CH$_2$), 30.47 (d, $^3J_{PC}$ = 12.3 Hz, ^{3}CH$_2$), 56.17 (d, $^1J_{PC}$ = 77.4 Hz, P*C*H$_2$O), 67.12 (s, ^{8}CH$_2$), 114.15 (s, *o*CH), 120.09 (s, *p*CH), 129.17 (s, *m*CH), 158.6 (s, *i*C). − ^{31}P NMR: δ = 51.4 (s).

Bis(hydroxymethyl)-8-*o*-nitrophenoxyoctylphosphane Oxide (14c): Reaction according to *Procedure II* with 8-bromo-*o*-nitrophenoxyoctane, purification by column chromatography, eluent AcOEt/EtOH (80:20), gave 77% yield of **14c** as a yellow oil. − IR (Film): $\tilde{\nu}$ = 3250 cm^{-1}, 2930, 2858, 1606, 1521, 1350, 1280, 1255, 1165, 1140, 1045, 748. − ^{1}H NMR: δ = 1.21−1.84 (m, 14 H, $^{1-7}$CH$_2$), 3.84−4.08 (m, 6 H, OCH$_2$, 2 PC*H*$_2$O), 6.98 (m, $^3J_{HH}$ = 7.9 Hz, $^3J_{HH}$ = 8.3 Hz, 1 H, ^{4}CH), 7.05 (m, $^3J_{HH}$ = 8.7 Hz, 1 H, ^{6}CH), 7.49 (m, $^3J_{HH}$ = 7.9 Hz, $^3J_{HH}$ = 8.7 Hz, $^4J_{HH}$ = 1.6 Hz, 1 H, ^{5}CH), 7.80 (dd, $^3J_{HH}$ = 8.3 Hz, $^4J_{HH}$ = 1.6 Hz, 1 H, ^{3}CH). − ^{13}C NMR: δ = 20.6 (d, $^2J_{PC}$ = 4.4 Hz, ^{2}CH$_2$), 22.8 (d, $^1J_{PC}$ = 60.8 Hz, ^{1}CH$_2$), 25.7 (s, ^{6}CH$_2$), 28.8, 28.9 (2 s, ^{4,5,6}CH$_2$), 30.9 (d, $^3J_{PC}$ = 13.0 Hz, ^{3}CH$_2$), 56.7 (d, $^1J_{PC}$ = 76.1 Hz, P*C*H$_2$OH), 69.6 (s, ^{8}CH$_2$), 114.5 (s, ^{6}CH), 120.0 (s, ^{4}CH), 125.4 (s, ^{3}CH), 134.0 (s, ^{5}CH), 139.9 (s, ^{2}C), 152.4 (s, ^{1}C). − ^{31}P NMR: δ = 50.5 (s).

General Procedure III: Phosphorus pentachloride (2.2 eq) was added slowly to a stirred mixture of bis(hydroxymethyl)phosphane oxides (1 equiv., 0.1 mol·L^{-1}) in CHCl$_3$. HCl gas was trapped by a sodium hydroxide solution. The reaction mixture was heated for 2 h and cautiously hydrolyzed by 10 equiv. of water after cooling. After extraction with CH$_2$Cl$_2$, organic layers were neutralized by Na$_2$CO$_3$ solution, dried (Na$_2$SO$_4$), and concentrated in vacuum. The crude product was purified by column chromatography or recrystallisation.

Bis(chloromethyl)dodecylphosphane Oxide (15a): Reaction according to *Procedure III* with **14a**, recrystallisation in hexane, gave 88% yield of **15a** as colorless crystals, m.p. 64°C. − IR (film): $\tilde{\nu}$ = 2990 cm^{-1}, 2970, 2920, 2850, 1470, 1455, 1410, 1395, 1245, 1229, 1212, 1180, 1135, 1120, 869, 831, 732, 720, 688. − ^{1}H NMR: δ = 0.87 (t, $^3J_{HH}$ = 6.27 Hz, 3 H, ^{12}CH$_3$), 1.22−1.41, 1.62−1.72, 1.94−2.02 (3 m, 22 H, $^{1-11}$CH$_2$), 3.71, 3.78 (m, $^2J_{HH}$ = −13.8 Hz, $^2J_{PH}$ = 5.6 Hz, $^2J_{PH}$ = 7.8 Hz, 4 H, PC*H*$_2$Cl). − ^{13}C NMR: δ = 14.07 (s, ^{12}CH$_3$), 20.78 (d, $^2J_{PC}$ = 4.5 Hz, ^{2}CH$_2$), 22.65 (s, ^{11}CH$_2$), 24.01 (d, $^1J_{PC}$ = 70.4 Hz, ^{1}CH$_2$), 28.97 (s, ^{9}CH$_2$), 29.28 (d, $^4J_{PC}$ = 1.5 Hz, ^{4}CH$_2$), 29.50, 29.57 (s, $^{5-8}$CH$_2$), 30.84 (d, $^3J_{PC}$ = 14.1 Hz, ^{3}CH$_2$), 31.87 (s, ^{10}CH$_2$), 33.78 (d, $^1J_{PC}$ = 68.3 Hz, P*C*H$_2$Cl). − ^{31}P NMR: δ = 45.6 (s).

Bis(chloromethyl)-8-phenoxyoctylphosphane Oxide (15b): Reaction according to *Procedure III* with **14b**, purification by column chromatography, eluent CH$_2$Cl$_2$/MeOH (95:5, R_f = 0.4), gave 93% yield of **15b** as colorless crystals, m.p. 62°C. − IR (KBr): $\tilde{\nu}$ = 2920 cm^{-1}, 2848, 1598, 1579, 1493, 1470, 1391, 1286, 1246, 1232, 1168, 1148, 1029, 838, 817, 751, 688. − ^{1}H NMR: δ = 1.35−1.54, 1.64−1.80, 1.92−2.06 (3 m, 14 H, $^{1-7}$CH$_2$), 3.70, 3.77 (m, $^2J_{HH}$ = −13.9 Hz, $^2J_{PH}$ = 5.6 Hz, $^2J_{PH}$ = 7.8 Hz, 4 H, PC*H*$_2$Cl), 3.94 (t, $^3J_{HH}$ = 6.4 Hz, 2 H, ^{8}CH$_2$), 6.86−6.96 (m, 3 H, *o,p*CH), 7.23−7.31 (m, 2 H, *m*CH). − ^{13}C NMR: δ = 20.75 (d, $^2J_{PC}$ = 4.5 Hz, ^{2}CH$_2$), 23.91 (d, $^1J_{PC}$ = 70.4 Hz, ^{1}CH$_2$), 25.94 (s, ^{7}CH$_2$), 28.88, 28.99, 29.19 (s, $^{4-6}$CH$_2$), 30.70 (d, $^3J_{PC}$ = 14.2 Hz, ^{3}CH$_2$), 33.82 (d, $^1J_{PC}$ = 68.2 Hz, P*C*H$_2$Cl), 67.67 (s, ^{8}CH$_2$), 114.45 (s, *o*CH), 120.45 (s, *p*CH), 129.38 (s, *m*CH), 159.05 (s, *i*C). − ^{31}P NMR: δ = 45.3 (s).

Bis(chloromethyl)-8-*o*-nitrophenoxyoctylphosphane Oxide (15c): Reaction according to *Procedure III* with **14c**, purification by column chromatography, eluent CH$_2$Cl$_2$/MeOH (90:10, R_f = 0.7) gave **15c** in 88% yield, as colorless crystals. − IR (film): $\tilde{\nu}$ = 3600−3000 cm^{-1}, 2930, 2858, 1606, 1521, 1280, 1255, 1165, 1140, 1045, 858, 748. − ^{1}H NMR: δ = 1.35−1.52, 1.63−1.84, 1.95−2.08 (3 m, 14 H, $^{1-7}$CH$_2$), 3.73, 3.79 (m, $^2J_{HH}$ = −13.8 Hz, $^2J_{PH}$ = 5.6 Hz, $^2J_{PH}$ = 7.8 Hz, 4 H, PC*H*$_2$Cl), 4.08 (t, $^3J_{HH}$ = 6.2 Hz, 2 H, ^{8}CH$_2$), 6.99 (m, $^3J_{HH}$ = 7.6 Hz, $^3J_{HH}$ = 8.0 Hz, 1 H, ^{4}CH), 7.05 (m, $^3J_{HH}$ = 8.3 Hz, 1 H, ^{6}CH), 7.49 (m, $^3J_{HH}$ = 7.6 Hz, $^3J_{HH}$ = 8.3 Hz, $^4J_{HH}$ = 1.5 Hz, 1 H, ^{5}CH), 7.79 (dd, $^3J_{HH}$ = 8.0 Hz, $^4J_{HH}$ = 1.5 Hz, 1 H, ^{3}CH). − ^{13}C NMR: δ = 20.6 (d, $^2J_{PC}$ = 4.4 Hz, ^{2}CH$_2$), 22.8 (d, $^1J_{PC}$ = 60.8 Hz, ^{1}CH$_2$), 25.7 (s, ^{7}CH$_2$), 28.8, 28.9 (2 s, $^{4-6}$CH$_2$), 30.9 (d, $^3J_{PC}$ = 13.0 Hz, ^{3}CH$_2$), 56.7 (d, $^1J_{PC}$ = 76.1 Hz, P*C*H$_2$Cl), 69.6 (s, ^{8}CH$_2$), 114.5 (s, ^{6}CH), 120.0 (s, ^{4}CH), 125.4 (s, ^{3}CH), 134.0 (s, ^{5}CH), 139.9 (s, ^{2}C), 152.4 (s, ^{1}C). − ^{31}P NMR: δ = 45.7 (s). − MS FAB$^+$ (NBA): *m/z* = 397 (70%) [M + H]$^+$, 363 (16), 258 (33), 55 (100).

General Procedure IV: A stirred mixture of chloromethylphosphane oxides (1 equiv.) and tricoordinated phosphorus ester (1.2 equiv. per chloromethyl function), under nitrogen is heated at 150°C for 5 to 20 h. Excess phosphorus ester is removed by vacuum distillation. The residue is purified by chromatography.

Compounds **12a** and **12b** were prepared according to *Procedure IV* with **11** and ethyldiphenyl phosphinite and triethylphosphite in 31% and 83% yields, respectively. Spectrometric data are given in reference[5a].

3-(1′-Dodecyl)-1,1,5,5-tetraphenyl-1,3,5-triphosphapentane 1,3,5-Trioxide (16a): Reaction according to *Procedure IV* with ethyldiphenylphosphinite and **15a**, heating for 3 h. Chromatographic separation with AcOEt/MeOH (95:5) eluent gave **16a** in 84% yield. − IR (Film): $\tilde{\nu}$ = 3140 cm^{-1}, 3055, 3010, 2922, 2850, 1188. − ^{1}H NMR: δ = 0.88 (t, $^2J_{HH}$ = 6.4 Hz, 3 H, $^{12'}$CH$_3$), 0.91−1.05, 1.12−1.41, 1.70−1.86 (3 m, 22 H, $^{1'-11'}$CH$_2$), 3.23, 3.63 (2 m,[23] 4 H, PC*H*$_2$P), 7.40−7.57, 7.72−7.89 (2 m, 20 H, CH P*Ph*$_2$). − ^{13}C NMR: δ = 14.11 (s, $^{12'}$CH$_3$), 20.99 (d, $^2J_{PC}$ = 4.6 Hz, $^{2'}$CH$_2$), 22.67 (s, $^{11'}$CH$_2$), 28.99, 29.32, 29.53, 29.58, 29.60 (5 s, $^{4'-9'}$CH$_2$), 30.67 (d, $^3J_{PC}$ = 16.4 Hz, $^{3'}$CH$_2$), 31.39 (dd,[24] P*C*H$_2$P), 31.90 (s, $^{10'}$CH$_2$), 32.61 (d, $^1J_{PC}$ = 71.3 Hz, $^{1'}$CH$_2$), 128.69, 128.75 (2 d, $^3J_{PC}$ = 12.4 Hz, $^3J_{PC}$ = 12.2 Hz, *m*CH), 130.93, 131.09 (2 d, $^2J_{PC}$ = 10.4 Hz, $^2J_{PC}$ = 10.2 Hz, *o*CH), 131.92, 131.97 (2 d, $^4J_{PC}$ = 2.6 Hz, $^4J_{PC}$ = 2.7 Hz, *p*CH), 132.99, 133.00 (2 dd, $^1J_{PC}$ = 104.1 Hz $^3J_{PC}$ = 2,5 Hz, $^1J_{PC}$ = 104.8 Hz $^3J_{PC}$ = 2.6 Hz, *i*C). − ^{31}P NMR: δ = 25.86 (d, $^2J_{pp}$ = 12.5 Hz, 2 *P*Ph$_2$), 39.60 (t, $^2J_{pp}$ = 12.5 Hz, 1 *P*(O)). − MS FAB$^+$(NBA); *m/z* (%): 646 (100) [M + H]$^+$, 431 (9), 401 (6), 263 (18), 215 (25), 199 (47). − C$_{38}$H$_{49}$O$_3$P$_3$ (646,7): Calcd. C 70.6%, H 7.6%, O 7.4%; found C 70.1, H 7.8, O 7.9.

(8′-Phenoxyoctyl)-1,1,5,5-tetraphenyl-1,3,5-triphosphapentane-1,3,5-Trioxide (16b): Reaction according to *Procedure IV* with ethyldiphenylphosphinite and **15b**, heating for 3 h. Chromatographic separation with AcOEt/MeOH (95:5) eluent gave **15b** in 85% yield. − ^{1}H NMR: δ = 1.01−1.43, 1.65−1.85 (2 m, 14 H, $^{1'-7'}$CH$_2$), 3.23, 3.63 (m,[23], 4 H, PC*H*$_2$P), 3.92 (t, $^2J_{HH}$ = 6.5 Hz, 2 H, $^{8'}$CH$_2$), 6.87−6.92, 7.18−7.28 (2 m, 5 H, *Ph*O), 7.26−7.51, 7.72−7.84 (2 m, 20 H, P*Ph*$_2$). − ^{13}C NMR: δ = 20.95 (d, $^2J_{PC}$ = 4.6 Hz, $^{2'}$CH$_2$), 25.94 (s, $^{7'}$CH$_2$), 28.87, 29.03, 29.20 (3 s, $^{4'-6'}$CH$_2$), 30.55 (d, $^3J_{PC}$ = 16.5 Hz, $^{3'}$CH$_2$), 31.34 (dd,[24] P*C*H$_2$P), 32.53 (d, $^1J_{PC}$ = 70.2 Hz, $^{1'}$CH$_2$), 67.76 (s, $^{8'}$CH$_2$), 114.48 (s, *o′*CH), 120.49 (s, *p′*CH), 128.72, 128.79 (2 d, $^3J_{PC}$ = 12.5 Hz, $^3J_{PC}$ = 12.3 Hz, *m*CH), 130.92, 131.06 (2 d, $^2J_{PC}$ = 9.8 Hz, $^2J_{PC}$ = 10.3 Hz, *o*CH), 131.87, 131.92 (2 d, $^4J_{PC}$ = 2.7 Hz, $^4J_{PC}$ = 2.8 Hz, *p*CH), 132.97, 132.99 (2 dd, $^1J_{PC}$ = 103.6 Hz, $^3J_{PC}$ = 2.4 Hz, $^1J_{PC}$ = 104.8 Hz, $^3J_{PC}$ = 2.6 Hz, *i*C), 159.08 (s, *i′*C). – ^{31}P NMR: δ = 26.6 (d, $^2J_{pp}$ = 12.5 Hz, 2 *P*Ph$_2$), 40.4 (t, $^2J_{pp}$ = 12.5 Hz, *P*(O)). – MS FAB$^+$ (NBA): *m*/*z* (%) = 683 (85) [M + H]$^+$, 215 (37), 199 (100).

Bis(2,5,8,11-tetraoxadodecyl)-*O*,*O′*-diethylphosphonomethylphosphane Oxide (17a): Reaction according to *Procedure IV* with triethylphosphite and bis(2,5,8,11-tetraoxadodecyl)chloromethylphosphane oxide, heating for 16 h. Chromatographic separation with AcOEt/MeOH (95:5) eluent gave **17a** in 89% yield. – IR (Film): $\tilde{\nu}$ = 2880–2870 cm^{-1}, 1247, 1105, 1054, 1022, 967, 821. – ^{1}H NMR: δ = 1.26 (t, $^3J_{HH}$ = 7.1 Hz, 6 H, 2 CH$_3$), 2.42 (dd,[23] 2 H, PC*H*$_2$P), 3.29 (s, 6 H, ^{12}CH$_3$), 3.43–3.48 (m, 4 H, ^{10}CH$_2$), 3.53–3.58 (m, 16 H, ^{4,6,7,9}CH$_2$), 3.67–3.72 (m, 4 H, ^{3}CH$_2$), 3.97 (d, $^2J_{HP}$ = 5.2 Hz, 4 H, ^{1}CH$_2$), 4.01–4.14 (m, 4 H, 2 POC*H*$_2$). – ^{13}C NMR: δ = 16.29 (d, $^3J_{PC}$ = 6.4 Hz, CH$_3$), 23.02 (dd,[24] P*C*H$_2$P), 58.92 (s, ^{12}CH$_3$), 62.48 (d, $^2J_{PC}$ = 6.3 Hz, PO*C*H$_2$), 66.28 (dd, $^1J_{PC}$ = 84.0 Hz, $^3J_{PC}$ = 4.2 Hz, ^{1}CH$_2$), 70.20, 70.46, 70.49, 70.54 (4 s, ^{4,6,7,9}CH$_2$), 71.86 (s, ^{10}CH$_2$), 72.99 (d, $^3J_{PC}$ = 9.5 Hz, ^{3}CH$_2$). – ^{31}P NMR: δ = 21,62 (d, $^2J_{PP}$ = 12,6 Hz, phosphonate), 38,51 (d, $^2J_{PP}$ = 12,6 Hz, phosphane oxide).

Bis(*O*,*O′*-diethylphosphonomethyl)-2,5,8,11-tetraoxadodecylphosphane Oxide (17b): Reaction according to *Procedure IV* with triethylphosphite and bis(chloromethyl)-2,5,8,11-tetraoxadodecylphosphane oxide, heating for 21 h. Chromatographic separation with AcOEt/MeOH (95:5) as eluent gave 86% yield. – IR (Film): $\tilde{\nu}$ = 2980 cm^{-1}, 2935, 2905, 1243, 1198, 1100, 1049, 1024, 970, 820. – ^{1}H NMR: δ = 1.24 (t, $^3J_{HH}$ = 7.1 Hz, 12 H, 4 CH$_3$), 2.62, 2.70 (2 m,[23] 4 H, PC*H*$_2$P), 3.26 (s, 3 H, ^{12}CH$_3$), 3.41–3.46 (m, 2 H, ^{10}CH$_2$), 3.51–3.58 (m, 8 H, ^{4,6,7,9}CH$_2$), 3.65–3.71 (m, 4 H, ^{3}CH$_2$), 4.00–4.16 (m, 10 H, ^{1}CH$_2$, POC*H*$_2$). – ^{13}C NMR: δ = 15.98 (d, $^3J_{PC}$ = 6.5 Hz, CH$_3$), 25.60 (ddd,[24] P*C*H$_2$P), 58.55 (s, ^{12}CH$_3$), 62.16 (d, $^2J_{PC}$ = 6.3 Hz, PO*C*H$_2$), 67.81 (td, $^1J_{PC}$ = 89.5 Hz, $^3J_{PC}$ = 2.8 Hz, ^{1}CH$_2$), 69.84, 70.15, 70.19, 70.26 (4 s, ^{4,6,7,9}CH$_2$), 71.60 (s, ^{10}CH$_2$), 72.58 (d, $^3J_{PC}$ = 10.9 Hz, ^{3}CH$_2$). – ^{31}P NMR: δ = 20.96 (d, $^2J_{PP}$ = 10.1 Hz, phosphonate), 34.65 (t, $^2J_{PP}$ = 10.1 Hz, phosphane oxide). – MS FAB$^+$ (NBA); *m*/*z* (%): 527 (100) [M + H]$^+$, 499 (5), 425 (4), 199 (28), 59 (98).

General Procedure V: A stirred mixture of phosphonate (0.3 mol·L^{-1}) in HCl 37% is refluxed at 100°C for 6 h. The excess HCl and water were removed by vacuum distillation. After addition of the same quantity of ethanol, the mixture is concentrated by vacuum in order to removed the traces of HCl. This last step was repeated three times.

Bis(phosphonomethyl)-2,5,8,11-tetraoxadodecylphosphane Oxide (18a): Reaction according to *Procedure V.* **18a** was obtain as a viscous oil in 98% yield. – ^{1}H NMR (D$_2$O): δ = 2.76 (dd,[23] 4 H, PC*H*$_2$P), 3.36–3.84 (m, 15 H, ^{3,4,6,7,9,10}CH$_2$, ^{12}CH$_3$), 4.15 (d, $^2J_{HP}$ = 4.9 Hz, 2 H, PC*H*$_2$O). – ^{13}C NMR (D$_2$O): δ = 29.11 (ddd,[24] P*C*H$_2$P), 60.75 (s, ^{12}CH$_3$), 63.08 (s, CH$_2$), 69.95 (d, $^1J_{PC}$ = 88.7 Hz, ^{1}CH$_2$), 72.12, 72.38 (2 s, ^{6,7,9}CH$_2$), 72.21 (d, $^4J_{PC}$ = 5.6 Hz, ^{4}CH$_2$), 74.38 (s, ^{8}CH$_2$), 75.19 (d, $^3J_{PC}$ = 11.5 Hz, ^{3}CH$_2$). – ^{31}P NMR ([D$_6$]DMSO): δ = 16.94 [d, $^2J_{pp}$ = 14.0 Hz, *P*(OH)$_2$], 43.00 (t, $^2J_{pp}$ = 14.0 Hz, *P*R$_3$). – MS FAB$^+$ (NBA); *m*/*z* (%): 415 (18) [M + H]$^+$, 401 (25), 307 (23).

Tris(phosphonomethyl)phosphane Oxide (18b): Reaction according to *Procedure V.* **18b** was obtain as a viscous oil in 98% yield. – ^{1}H NMR ([D$_6$]DMSO): δ = 2.75 (dd,[23] PC*H*$_2$P), 9.22 (broad s, OH). – ^{13}C NMR ([D$_6$]DMSO): δ = 29.88 (dd,[24] P*C*H$_2$P). – ^{31}P NMR ([D$_6$]DMSO): δ = 15.23 [d, $^2J_{pp}$ = 10.6 Hz, 3 *P*(OH)$_2$], 32.66 (q, $^2J_{pp}$ = 10.6 Hz, *P*R$_3$). – MS FAB$^-$ (NBA); *m*/*z* (%): 331 (100) [M – H$^+$], 313 (28), 295 (69), 277 (5), 235 (5), 217 (14).

Bis(*O*,*O′*-diethylphosphonomethyl)chloromethylphosphane Oxide (19): Reaction according to *Procedure IV* with triethylphosphite and **11**, and heating for 3 h. Chromatographic separation with AcOEt/MeOH (95:5) eluent gave **19** in 19% yield as a colorless solid, m.p. 104°C. – ^{1}H NMR: δ = 1.30 (t, $^3J_{HH}$ = 7.1 Hz, 12 H, CH$_3$), 2.77 (dd,[23] 4 H, PC*H*$_2$P), 3.93 (d, $^2J_{PH}$ = 7.0 Hz, 2 H, PC*H*$_2$Cl), 4.13 (m, 8 H, POC*H*$_2$). – ^{13}C NMR: δ = 16.24 (d, $^3J_{PC}$ = 6.6 Hz, CH$_3$), 25.92 (ddd,[24] P*C*H$_2$P), 37.86 (td, $^1J_{PC}$ = 73.9 Hz, $^3J_{PC}$ = 3.4 Hz, PCH$_2$Cl), 62.8, 62.9 (2 d, $^2J_{PC}$ = 6.6 Hz, $^2J_{PC}$ = 7.1 Hz, PO*C*H$_2$). – ^{31}P NMR: δ = 18.59 (d, $^2J_{pp}$ = 14.0 Hz, phosphonate), 32.59 (t, $^2J_{pp}$ = 14.0 Hz, phosphane oxide). – MS FAB$^+$ (NBA); *m*/*z* (%): 399 (100) [M + H]$^+$, 371 (4), 269 (8).

Chloromethyl(diphenylphosphanylmethyl)dodecylphosphane Dioxide (20): Reaction according to *Procedure IV* with 1 equiv. of ethyldiphenylphosphinite and 1 equiv. of **15a**, heated for 5 h. Chromatographic separation with AcOEt/MeOH (95:5) eluent gave 52% yield of **20** as colorless crystals, m.p. 105–107°C. – IR (KBr): $\tilde{\nu}$ = 3077 cm^{-1}, 3022, 3004, 2954, 1238, 1220, 839, 747, 592, 560. – ^{1}H NMR: δ = 0.86 (t, $^2J_{HH}$ = 6.4 Hz, 3 H, ^{12}CH$_3$), 1.19–1.22, 1.41–1.54 (2 m, 20 H, ^{2}CH$_2$ to ^{11}CH$_2$), 1.90–1.98 (m, 2 H, ^{1}CH$_2$), 3.01, 3.10 (m,[23] 2 H, PC*H*$_2$P), 3.67, 3.85 (m, $^1J_{HH}$ = –13.5 Hz, $^2J_{PH}$ = 6.1 Hz, $^2J_{PH}$ = 7.4 Hz, 2 H, PC*H*$_2$Cl), 7.46–7.53 (m, 6 H, *o*,*p*CH), 7.75–7.83 (m, 4 H, *m*CH). – ^{13}C NMR: δ = 14.1 (s, ^{12}CH$_3$), 20.9 (d, $^2J_{PC}$ = 4.6 Hz, ^{2}CH$_2$), 22.6 (s, ^{11}CH$_2$), 27.7 (dd, $^1J_{PC}$ = 70.5 Hz, $^3J_{PC}$ = 1.2 Hz, ^{1}CH$_2$), 28.4 (dd,[24] P*C*H$_2$P), 28.7, 29.3, 29.4 (s, $^{4-9}$CH$_2$), 30.5 (d, $^3J_{PC}$ = 15.4 Hz, ^{3}CH$_2$), 31.7 (s, ^{10}CH$_2$), 37.2 (d, $^1J_{PC}$ = 67.2 Hz, P*C*H$_2$Cl), 128.6, 128.7 (2 d, $^3J_{PC}$ = 12.5 Hz, $^3J_{PC}$ = 12.4 Hz, *m*CH), 130.4, 130.6 (2 d, $^2J_{PC}$ = 10.4 Hz, $^2J_{PC}$ = 10.2 Hz, *o*CH), 132.0, 132.1 (2 d, $^4J_{PC}$ = 2.6 Hz, $^4J_{PC}$ = 2.7 Hz, *p*CH), 132.5, 132.8 (2 dd, $^1J_{PC}$ = 104.1 Hz, $^3J_{PC}$ = 2,0 Hz, $^1J_{PC}$ = 104.8 Hz, $^3J_{PC}$ = 2.7 Hz, *i*C). – ^{31}P NMR: δ = 25.1 (d, $^2J_{pp}$ = 11.1 Hz, *P*Ph$_2$), 43.8 (d, $^2J_{pp}$ = 11.1 Hz, *P*). – MS FAB$^+$ (NBA); *m*/*z* (%): 481 (100) [M + H]$^+$, 263 (17), 215 (12), 199 (28). – $C_{26}H_{39}ClO_2P_2$ (481,0): Calcd. C 64.9, H 8.8; found C 64.9, H 8.8.

(*O*,*O′*-Diethylphosphonomethyl)(diphenylphosphanylmethyl)dodecylphosphane Dioxide (21): Reaction according to *Procedure IV* with **20** and triethyl phosphite, heated for 8 h. Chromatographic separation with AcOEt/MeOH (95:5) eluent gave 94% yield of **21** as a viscous oil. – ^{1}H NMR: δ = 0.78 (t, $^2J_{HH}$ = 6.45 Hz, 3 H, ^{12}CH$_3$), 1.07–1.28, 1.30–1.42 (m, 24 H, $^{2-11}$CH$_2$, OCH$_2$C*H*$_3$), 1.72–1.86 (m, 2 H, ^{1}CH$_2$), 2.73, 2.80 [2 m,[23] 2 H, PC*H*$_2$P(OEt)$_2$], 3.13, 3.59 (2 m,[20] 2 H, PC*H*$_2$PPh$_2$), 3.97–4.17 (m, 4 H, POC*H*$_2$),7.34–7.44 (m, 6 H, *o*,*p*CH), 7.67–7.78 (m, 4 H, *m*CH). – ^{13}C NMR: δ = 14.02 (s, ^{12}CH$_3$), 16.19, 16.24 (2 d, $^3J_{CP}$ = 6.6 Hz, $^3J_{CP}$ = 6.4 Hz, OCH$_2$*C*H$_3$), 20.96 (d, $^2J_{PC}$ = 4.6 Hz, ^{2}CH$_2$), 22.58 (s, ^{11}CH$_2$), 28.40 [dd,[24] P*C*H$_2$P(OEt)$_2$], 28.96 (d, $^4J_{PC}$ = 0.8 Hz, ^{4}CH$_2$), 29.23, 29.44, 29.50 (3 s, $^{5-9}$CH$_2$), 30.23 (dd,[24] P*C*H$_2$PPh$_2$), 30.65 (d, $^3J_{PC}$ = 16.15 Hz, ^{3}CH$_2$), 31.74 (dd, $^1J_{PC}$ = 71.4 Hz, $^3J_{PC}$ = 4.9 Hz, ^{1}CH$_2$), 31.81 (s, ^{10}CH$_2$), 62.01, 62.75 (2 d, $^2J_{PC}$ = 6.2 Hz, $^2J_{PC}$ = 6.0 Hz, PO*C*H$_2$), 128.69, 128.73 (2 d, $^3J_{PC}$ = 12.5 Hz, $^3J_{PC}$ = 12.1 Hz, *m*CH), 130.77, 130.87 (2 d, $^2J_{PC}$ = 10.3 Hz, $^2J_{PC}$ = 9.8 Hz, *o*CH), 132.03, 132.10 (2 d, $^4J_{PC}$ = 3.0 Hz, $^4J_{PC}$ = 2.9 Hz, *p*CH), 132.86, 133.37 (2 dd, $^1J_{PC}$ = 103.3 Hz, $^3J_{PC}$ = 1.8 Hz, $^1J_{PC}$ = 104.8 Hz, $^3J_{PC}$ = 3.3 Hz, *i*C). – ^{31}P NMR ([D$_6$]acetone): δ = 20.67 (d, $^2J_{pp}$ = 10.1 Hz, *P*(OEt)$_2$), 22.32 (d, $^2J_{pp}$ = 11.8 Hz, *P*Ph$_2$), 34.99 (dd, $^2J_{pp}$ = 11.8 Hz, $^2J_{pp}$ = 10.1 Hz, *P*=O).

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[23] Refers to table 3 corresponding to ^{1}H-NMR study of the methylene bridge.

[24] Refers to Table 4 corresponding to ^{13}C-NMR study of the methylene bridge.

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