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New cyclic phosphonium salts derived from the reaction of phosphine-aldehydes with acid

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ABSTRACT

Various cyclic phosphonium structures are formed in high yield by the deprotection of unstable phosphine-aldehydes in acidic solution. When there is a methylene spacer between the phosphine and the aldehyde, a phosphonium ion $[PHR_2CH_2CH(OEt)_2]Br_2$, R=iPrOH, Et is obtained. Reaction of these phosphonium salts with water produces the dimers $[-PR_2CH_2CH(OH)-]_2[Br]_2$ R = *i*Pr, Et. When there is an ethylene spacer as in $PPh_2CH_2CH_2CH(OCH_2CH_2O)$, a remarkable tetramer with a 16-membered ring $[-PPh_2CH_2CH_2CH\ (OH)-]_4[Cl]_4$ forms as one diastereomer in hydrochloric acid solution. Reaction of HCl with the protected phosphine-aldehyde with a propylene spacer ($PPh_2CH_2CH_2CH_2CH(OCH_2CH_2O)$) results in the formation of the monomeric phosphonium salt $[-PPh_2\ CH_2CH_2CH_2CH(OH)-]Cl$ with a 5-membered ring. Solid state structures of different ring types were determined using X-ray diffraction experiment.

1. Introduction

Phosphines are particularly versatile ligands in organometallic chemistry because of the ease in changing the substituents at phosphorus to vary their electronic and steric characteristics [1]. Additional donor groups can be attached to make mixed donor chelating ligands such as phosphorus–nitrogen [2] or phosphorus–oxygen ligands [3]. On the other hand, the synthesis and reactions of molecules with a phosphine group and an electrophilic group such as an aldehyde are less explored. Such amphoteric molecules may undergo unselective polymerization by the formation of carbon–phosphorus bonds and for this reason they require specific handling and are difficult to prepare in good yield and high purity [4]. Matt and co-workers [4a] observed that under acidic conditions a particular amphoteric phosphine-aldehyde selectively forms a stable phosphonium dimer (**1**, Scheme 1, M = Li).

A particularly useful phosphine-aldehyde, *ortho*-diphenylphosphinobenzaldehyde, is the starting material for the synthesis of chiral PNNP and PNN ligands by Schiff base condensation reactions with enantiopure amines and diamines [5]. Transition metal complexes of these ligands have found to be highly efficient and enantioselective catalysts [6]. The reason for the popularity of this phosphine-aldehyde relative to others is its stability. Recently our group showed that less stable phosphine-aldehydes derived by reactions of base with dimeric phosphonium salts **1** can also be used for the synthesis of iron(II) catalysts [7]. These precatalysts were found to be particularly active in the enantioselective transfer hydrogenation of ketones using isopropanol as the reducing agent [8].

The ease of formation of the phosphorus–carbon bonds in the synthesis of dication **1** might also be exploited in the synthesis of macrocyclic molecules (Scheme 1) to produce porous materials, anionic sensors or macrocycles. In recent years macrocyclic molecules have attracted more attention from the chemical community as a result of developments in the areas of molecular signaling, molecular motors and organometallic catalysis [9]. Macrocycles are commonly synthesized from linear molecules containing terminal reactive functional groups or from short amphoteric molecules that oligomerize into cyclic structures. Both approaches demand a high level of selectivity towards the formation of cyclic molecules over the linear ones and towards a specific size of the ring. One of the solutions to the selectivity problem is a synthesis involving a template pre-organization [10]. Here a templating molecule brings together two or more molecules with reactive functionalities by noncovalent interactions to form a highly organized structure that further undergoes chemoselective reactions.

Templating molecules are typically cationic because their coordination chemistry is well studied and understood [11]. Anions are less often employed in template syntheses because of their undesirable features, which include a high solvation energy, a low charge to radius ratio and a high pH dependence. Several examples

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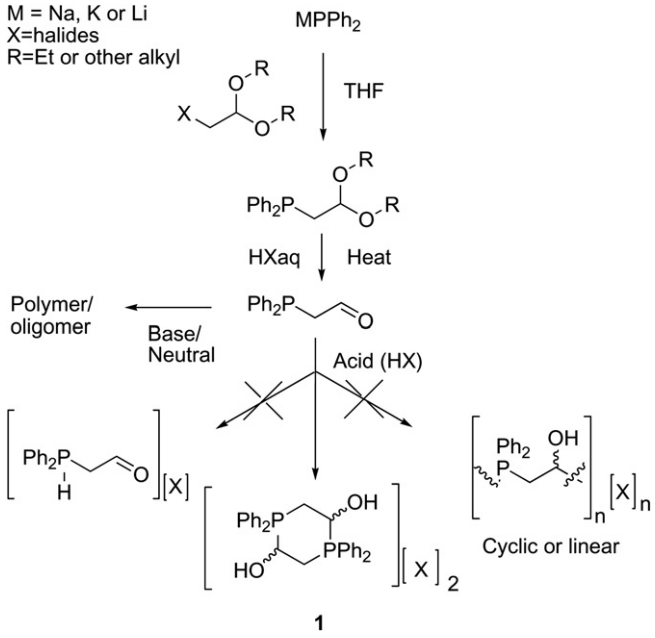


Scheme 1. Synthesis and behavior of phosphine-aldehydes under different pH conditions.

of anion-assisted formation of rotaxanes and similar macromolecules are found in the literature [12]. The only multi-component anionic template to our knowledge was reported by Rubio and co-workers [12] in the synthesis of macrocycles derived from amino acids. Unfortunately this methodology usually gives low to moderate yields of the desired product.

The ease of formation of the dimeric phosphonium compound, **1**, (Scheme 1) instead of other cyclic oligomers prompted us to explore this reaction in more detail. We wanted to investigate: (a) how is the chemoselectivity and diastereoselectivity controlled in the process of the formation of dimer **1** and (b) whether this knowledge could be used to prepare more complex and diverse molecules. This led us to discover an even simpler method of producing such phosphonium compounds when the phosphorus atoms bear electron-donating substituents and a high yielding method for the selective formation of a tetrameric macrocycle.

2. Results and discussion

2.1. One carbon spacer between the phosphorus and reactive carbon centre

Cyclic phosphonium dimers similar to that of **1** but with isopropyl or ethyl substituents at the phosphorus atoms (**2a**, **2b**) were prepared in a new, direct reaction of the secondary phosphine with the protected bromoacetoaldehyde diethyl acetal ($BrCH_2CH(OEt)_2$) to give an intermediate phosphonium salt that was then hydrolyzed (Scheme 2).

The yields of the white solids **2a** and **2b** are 81 and 40%, respectively. Compound **2a** is an air- and moisture-stable white solid that is completely soluble in methanol and/or water and insoluble in other common organic solvents. Therefore it possesses similar physical properties compared to the dimer **1**. The dimer **2b,** on the other hand, adsorbs water on prolonged exposure to the air, and is soluble only in water. However an aqueous solution of **2b** is stable toward oxidation by molecular oxygen.

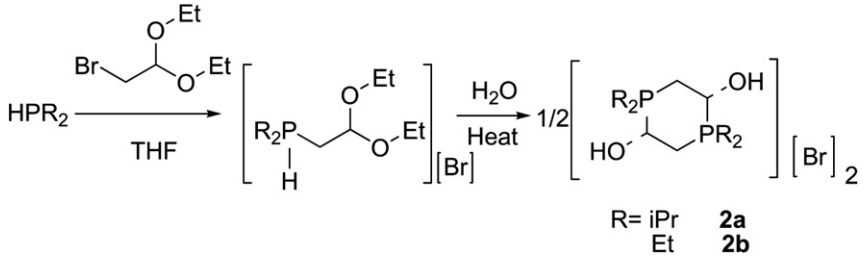
This direct reaction does not work for the less nucleophilic phosphines such as diphenylphosphine ($HPPh_2$) and di(*p*-tolyl) phosphine ($HP(p\text{-tol})_2$). These need to be converted into their corresponding more nucleophilic phosphides by reaction with potassium hydride before a successful nucleophilic attack on the protected aldehyde $BrCH_2CH(OEt)_2$ can take place (see Schemes 1 and 3). Deprotection of the phosphine-aldehyde diethyl acetals in acidic media gives the desired dimers with diphenyl (**1**, Scheme 1) or di-*p*-tolyl substituents (**2c**, Scheme 3). The new dimeric compound **2c** was obtained as a white, air-stable solid in 88% yield.

Hence the high yields and chemoselectivity in the formation of **1** and **2** are not affected by varying the electronic and steric properties of the phosphines. An explanation for the selectivity must lie in the favorable geometry of the 6-membered rings. Thus, the selectivity of the reaction appears to be primarily controlled by thermodynamic factors rather than kinetic ones.

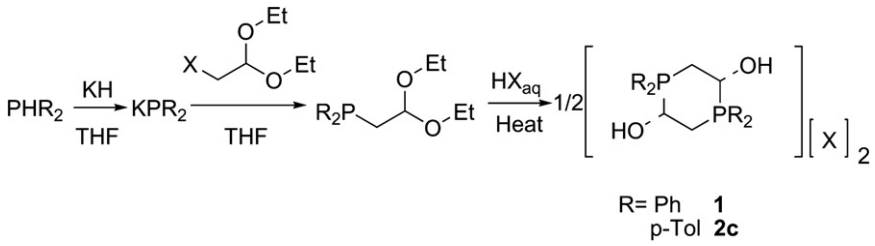
The new dimers **2a** and **2c** were fully characterized by NMR spectroscopy and X-ray diffraction experiments. These compounds show two characteristic singlets in the $^{31}P\{^1H\}$ NMR spectra in the region between 11 and 40 ppm; the two singlets observed in the $^{31}P\{^1H\}$ NMR arise from the *rac* and *meso* diastereomers. As for the ^1H NMR spectra there is a characteristic multiplet in the region between 5.3 and 6.2 ppm for the proton on the carbon with the hydroxyl group –CH(OH)–, and an absence of downfield shift of the aldehyde hydrogen resonance which is expected in the 9–10 ppm region.

Crystals of **2a** and **2c** have been analyzed by single crystal X-ray diffraction (Fig. 1). Both structures are *meso* diastereomers with the hydroxyl groups in equatorial positions for **2a** and in axial positions for **2c**. The P–C1 bond lengths are similar in both dimers and are slightly elongated compared to all other phosphorus–carbon bonds in the structures probably as a result of electron-withdrawing effect of the neighbouring oxygen atom. The bond between P1 and C6 in **2a** is longer than the bond between P1 and C3 in **2c** as expected from the larger cone angle of the *iso*propyl group compared to *p*-tolyl group. All of the angles and bond lengths of both **2a** and **2c** are comparable to those observed by Matt and co-workers [4a].

Crystals that were used for the X-ray diffraction studies were also analyzed by ^{31}P NMR spectroscopy in order to assign peaks and determine the ratio of diastereomers formed in the reaction. The $^{31}P\{^1H\}$ NMR spectra obtained for the crystals showed peaks for both diastereomers at 36.8 and 34.5 ppm for **2a** and at 16.1 and 11.2 ppm for **2c** with integration ratios of 1:2 and 3:4, respectively. On the other hand Matt and co-workers were able to selectively



Scheme 2. Direct preparation of phosphonium dimers **2a** and **2b** using secondary phosphines containing electron-donating alkyl substituents.



Scheme 3. General preparation of phosphonium dimers **1** and **2c** from potassium phosphide.

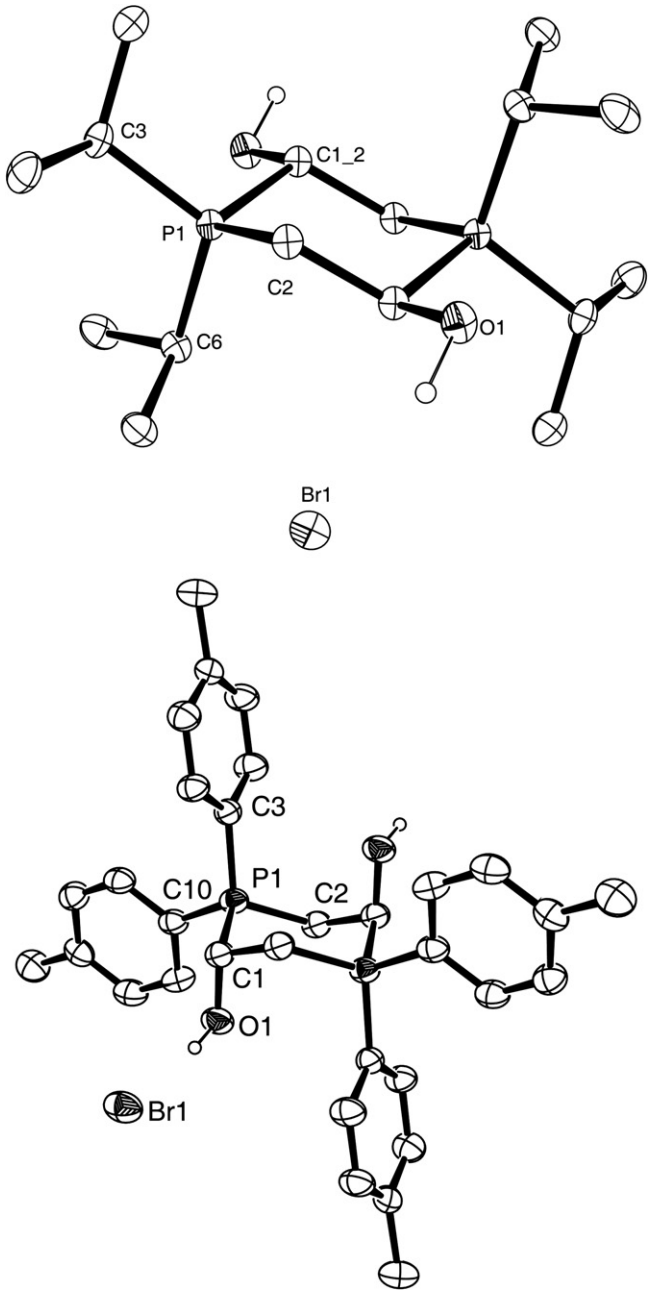


Fig. 1. ORTEP views of the molecular structures of **2a** (top) and **2c** (bottom). Thermal ellipsoids are drawn at 30% probability. Some hydrogen atoms, solvent molecules and counter ions are omitted for clarity. Selected interatomic distances [Å] and angles [o]: **2a** P1C1 1.835(3), P1C2 1.813(3), P1C6 1.825(3), P1C3 1.819(3), C1O1 1.410(3); C1P1C2 103.7(1), C1P1C3 108.4 (1); **2c** P1C1 1.847(5), P1C2 1.804(4), P1C3 1.783(3), C1O1 1.394 (4); C1P1C2 104.7(2), C10P1C3 109.1(2).

crystallize dimer **1** as the *meso* diastereomer and determine the structure by X-ray diffraction. A signal at 16.6 ppm in the $^{31}P\{^{1}H\}$ NMR spectrum was observed thus indicating that it is the minor diastereomer in the mixture of **1**. A possible explanation for the difference in distribution of diastereomers of **2a** and **2c** resulting from X-ray diffraction and $^{31}P\{^{1}H\}$ NMR analyses is that the diastereomers have similar solubility and both diastereomers co-crystallize. Thus the crystals containing the *meso* diastereomer were chosen for the X-ray diffraction accidentally. It is however possible that racemization of the pure *meso* diastereomer occurred in methanol-d_4 into a mixture of *meso* and *rac* diastereomers prior to $^{31}P\{^{1}H\}$ NMR analysis.

In order to test each of those assumptions, equimolar amounts of **1** and **2a** were mixed together in methanol-d_4 and the solution was monitored by $^{31}P\{^{1}H\}$ NMR spectroscopy. After 12 h a spectrum showed only peaks at 16.63 and 11.97 ppm (dimer **1**) and at 36.80 and 34.54 ppm (dimer **2a**). Since no mixed-substituent phosphonium dimer was produced, this indicated that the dissociation of dimers or racemization does not take place in solution (Table 1).

The various substituents at the phosphorus atom have a minor effect on the chemoselectivity of the reaction and six-membered dimers are formed over other possible species (Scheme 1). Conversely, more electron-rich substituents (*iso*propyl and ethyl) considerably increase the formation of one diastereomer over the other and thus make the reaction more diastereoselective. One can argue that the selectivity comes from the formation of the more thermodynamically favorable six-membered ring instead of the less stable cyclic or linear oligomer and polymer. In order to investigate such an assumption, we decided to increase the size of the hydrocarbon spacer between the carbonyl and phosphine groups in the phosphine-aldehyde and study the oligomerization under acidic conditions.

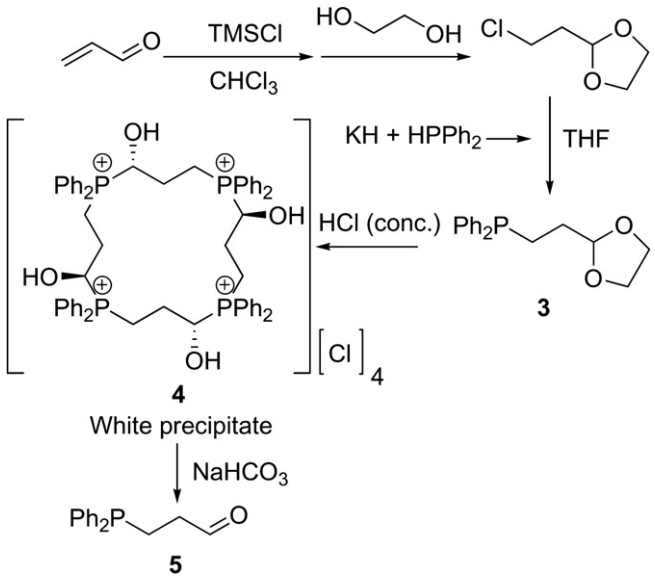
2.2. Two carbon spacer between the phosphorus and reactive carbon centre

The synthesis of 2-(2-chloroethyl)-1,3-dioxolane was previously reported by the Shrestha-Dawadi and Lugtenburg [13]. The addition of the β-chloropropionaldehyde ethylene glycol to a freshly prepared solution of the $KPPh_2$ in THF resulted in the formation of the tertiary phosphine **3** with a protected aldehyde *in situ*. Instead, the addition of a degassed, concentrated, aqueous hydrochloric acid

Table 1
Selected spectroscopic data and properties of the dimers **1, 2a, 2b, 2c**.

Dimer	$^{31}P\{^{1}H\}$ NMR minor diastereomer (ppm)	$^{31}P\{^{1}H\}$ NMR major diastereomer (ppm)	Ratio of diastereomers minor/major[a]	Yield (%) total
1[4a]	16.6	11.9	3:4	93
2a	36.8	34.5	1:2	81
2b	35.5	32.7	1:2	87
2c	16.1	11.2	3:4	88

[a] Ratios of diastereomers were determined by ^{1}H NMR.



Scheme 4. Synthesis of tetramer **4** from 2-(2-chloroethyl)-1,3-dioxolane and potassium phosphide.

solution to the reaction mixture gave **4** as a white precipitate (Scheme 4).

The molecular structure of the isolated white solid was determined by a preliminary X-ray diffraction experiment (see Experimental section) to be cyclic and tetrameric (Scheme 4). The elemental analysis and ^{1}H NMR spectra show that the crystals contain approximately 3 water molecules per tetramer. All attempts to completely remove water from the solid tetramer failed, probably due to the high affinity of the chloride ions for water. Since the $^{31}P\{^{1}H\}$ NMR spectrum of **4** in methanol-d_4 solution shows a single resonance at 27.08 ppm, we may conclude the reaction leading to its tetrameric structure is highly diastereoselective.

The formation of the specific ring size of **4** might suggest the selectivity toward its formation may be due to a template effect of monomers around the chloride ion. If this assumption is correct then the use of a more bulky counter ion in the synthesis should lead to the formation of a larger ring. To check this assumption, we synthesized the phosphine-aldehyde monomer $PPh_2CH_2CH_2CH_2C(O)H$ (**5**) by reacting the tetramer with base and extracting the product with diethyl ether. Spectral data of compound **5** were found to be similar to the one reported by Vaughn and Gladysz [4d] who synthesized and characterized this compound previously by a different method.

The reaction of **5** in THF with hydrochloric acid resulted in the complete conversion of the monomer to the tetramer **4**. Similar reactions were performed with HBr, HBF_4 and *p*-TsOH in methanol-d_4. The $^{31}P\{^{1}H\}$ NMR spectra of the reaction mixtures showed complete consumption of the starting phosphine **5** and production of the tetramer **4** along with other oligomeric species as minor products. Attempts to vary the conditions of the reaction in order to increase the yield of non-tetrameric species such as by changing the solvent, temperature and rate of addition of the reagents, failed probably as a result of the high stability of the tetramer **4** relative to the other oligomers.

2.3. Three carbon spacer between the phosphorus and reactive carbon centre

The synthesis of the protected phosphine-aldehyde precursor was carried out in a similar fashion to the previous compounds (Scheme 5).

Commercially available 2-(3-chloropropyl)-1,3-dioxolane ($ClCH_2CH_2CH_2CH(OCH_2CH_2O)$) was reacted with a freshly prepared solution of $KPPh_2$ in THF. Quenching of the reaction with concentrated hydrochloric acid gave rise to a species in solution that produced a strongly downfield-shifted resonance in the $^{31}P\{^{1}H\}$ NMR spectrum at 38.0 ppm. An X-ray diffraction study revealed that **6** is a monomeric phosphonium salt. Here the molecule has clearly "bitten its tail" to form a stable five-membered ring structure (Fig. 2). The structure of **6** revealed that bond lengths in the molecule are in comparable range to those observed in the previous cyclic oligomers. However, the C1–P1–C4 angle is smaller in compound **6** which is consistent with the observed five-membered cyclic geometry.

3. Conclusion

In conclusion, a series of oxygen-stable, cyclic phosphonium salts, derived from unstable phosphine aldehydes were synthesized and fully characterized. Chemoselective cyclization reactions strongly depended on the stability of the final product, although in the case of tetramer **4,** an anionic template effect might be operational. The variation of the carbon distance between phosphorus and carbonyl carbon from **2** to **4** resulted in the formation of different phosphonium salts: dimers with six-membered rings (compounds **1** and **2**), a tetramer with a 16-membered ring (compound **4**) and a monomer with a five-membered ring (compound **6**), respectively. All of the phosphine-aldehydes react in the presence of acid to form carbon-phosphorus bonds chemoselectively. High diastereoselectivity of oligomerization was observed in the process of formation of the dimers with electron-donating alkyl substituents at phosphorus (dimers **2a** and **2b**) and with the tetrameric oligomer **4**. The high chemoselectivity that was observed is controlled by the thermodynamic stability of the structures formed compared to other possible species (Scheme 1). This conclusion arises from observations that the dimers do not dissociate in solution into monomers and that their yields are not effected by changes in the reaction conditions as would be expected in case of kinetic control.

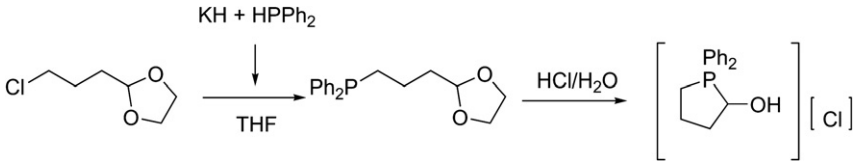
4. Experimental

4.1. General considerations

All procedures and manipulations involving air-sensitive materials were performed under an argon or nitrogen atmosphere using Schlenk techniques or a glovebox with N_2 (g). Solvents were degassed and dried using standard procedures prior to all manipulations and reactions. All other reagents used in the procedures were purchased from commercial sources and utilized without further purifications. NMR spectra were recorded at ambient temperature and pressure using Varian Gemini 400 MHz and 300 MHz spectrometers [^{1}H (400 MHz and 300 MHz), $^{13}C\{^{1}H\}$ (100 MHz and 75 MHz) and $^{31}P\{^{1}H\}$ (161 MHz and 121 MHz)]. ^{1}H and $^{13}C\{^{1}H\}$ were referenced to solvent resonances. Elemental analyses were done at the University of Toronto on a Perkin–Elmer 2400 CHN elemental analyzer.

4.2. General procedure for preparation of the dimers *2a* and *2b*

In an Ar-filled glovebox diisopropylphosphine (for **2a**) or diethylphosphine (for **2b**) (15 mmol) was dissolved in 5 mL of dry THF. Bromoacetadehyde diethyl acetal (15 mmol) was added to the resulting mixture on an Ar Schlenk line and the resulting solution was stirred for 4 h. The reaction was quenched with degassed H_2O (20 mmol) and heated for overnight at 70 °C. The solvent was



Scheme 5. Synthesis of compound **6** from 2-(3-chloropropyl)-1,3-dioxolane and potassium phosphide.

partially removed under vacuum and to give a colorless solution with a white precipitate. The solution was stored for 3 h at 5 °C. The precipitate then was filtered and washed with diethyl ether (2 × 5 mL) to give an analytically pure sample. Crystals suitable for X-ray diffraction experiments were obtained by slow diffusion of diethyl ether into a saturated solution of **2a** in methanol.

*4.2.1. Dimer **2a***

Yield: 2.93 g, 81%. The diastereomeric ratio was found to be 1:2, as determined by ^{1}H NMR. ^{1}H NMR (400 MHz, CD_3OD, resonances of two diastereomers of **2a** overlap in region δ 3.50–1.40; see below): δ 5.60 (pseudo ddd, $^3J_{HH} = 6.4$ Hz, $^2J_{HP} = 22.3$ Hz, 2H, C*H*(OH), major diastereomer; ^{31}P{^{1}H}, 5.60 (pseudo d, $^3J_{HH} = 6.5$ Hz)), 5.44 (ddd, 1H, $^3J_{HH} = 3.0$ Hz, $^3J_{HH} = 9.3$ Hz, $^2J_{HP} = 12.0$ Hz, 2H, C*H*(OH), minor diastereomer; ^{1}H{^{31}P}, 5.44 (dd, $^3J_{HH} = 3.0$ Hz, $^3J_{HH} = 9.3$ Hz)), 3.50–2.85 (m, overlap of 4H, CH(OH) CH_2P and 4H, $(CH_3)_2$C*H*P (both diastereomers); ^{1}H{^{31}P}, same), 1.60–1.40 (m, 12H, $(CH_3)_2$CHP, (both diastereomers); ^{1}H{^{31}P}, same). ^{31}P{^{1}H} NMR (161 MHz, CD_3OD): δ 36.81 (s, minor diastereomer), 34.54 (s, major diastereomer). ^{13}C{^{1}H} NMR (100 MHz, CD_3OD, signals of carbon atoms appear as multiplets with complex splitting patterns that arise from coupling to two magnetically inequivalent phosphorus atoms in the structure): δ 58.61 (m, *C*H(OH), minor diastereomer), 57.69 (m, *C*H(OH), major diastereomer), 22.93 (m, *C*H_2P, major diastereomer), 22.93 (m, *C*H_2P, minor diastereomer), 21.23 (m, *C*H_2P, major diastereomer), 21.62 (d, $^2J_{CP} = 21.8$ Hz, *C*$(CH_3)_2$P, minor diastereomer) 19.71 (d, $^2J_{CP} = 40.5$ Hz, *C*$(CH_3)_2$P, major diastereomer), 16.45–15.35 (m, overlapping peaks of *iso*propyl methyl groups, both diastereomers). Anal. Calcd for $C_{16}H_{36}P_2O_2Br_2$: C, 39.85; H, 7.52. Found: C, 39.35; H, 7.32.

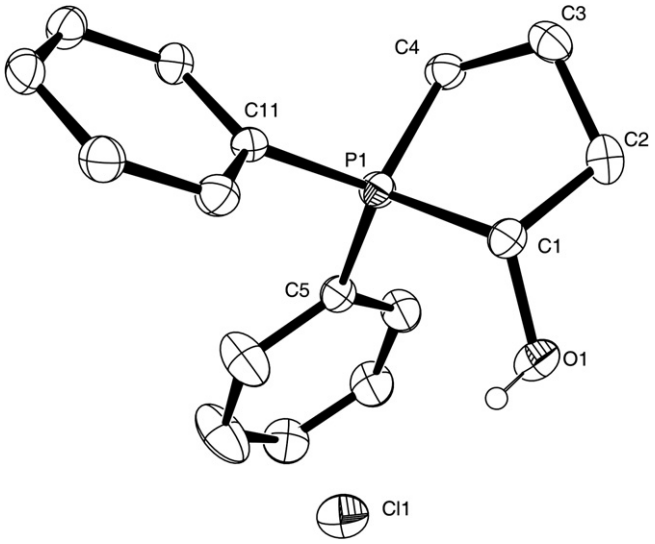


Fig. 2. ORTEP views of the molecular structure of **6**.Thermal ellipsoids are drawn at 30% probability. Some hydrogen atoms and solvent molecules are omitted for clarity. Selected interatomic distances [Å] and angles [º]: **6** P1–C1 1.870(3), P1–C4 1.799(3), P1–C5 1.782(3), C1–C2 1.519(4), C2–C3 1.523(4), C1–O1 1.410(4); C1–P1–C4 97.2(1), C1–P1–C5 111.8 (1), C1–C2–C3 108.1(2).

*4.2.2. Dimer **2b***

Yield: 2.78 g, 87%. The diastereomeric ratio was found to be 1:2, as determined by ^{1}H NMR. ^{1}H NMR (400 MHz, D_2O with a $CDCl_3$/TMS insert, resonances of two diastereomers of **2b** overlap; see below): δ 5.45–5.10 (m, 2H, C*H*(OH), diastereomers overlap; ^{1}H{^{31}P}, 5.36 (pseudo d, 2H, C*H*(OH), $^2J_{H\text{-}P} = 5.8$ Hz, major diastereomer), 5.29 (pseudo dd, 2H, C*H*(OH), $^3J_{H\text{-}H} = 3.4$ Hz, $^2J_{H\text{-}P} = 9.2$ Hz, minor diastereomer)), 3.31–2.87 (m, 4H, CH(OH)CH_2P, overlap of diastereomers; ^{1}H{^{31}P}, same), 2.58–2.08 (m, 8H, (CH_3CH_2P, overlap of diastereomers; ^{1}H{^{31}P}; same), 1.32–0.90 (m, 12H, CH_3CH_2P, overlap of diastereomers; ^{1}H{^{31}P}, same). ^{31}P{^{1}H} NMR (161 MHz, D_2O with a $CDCl_3$/TMS insert): δ 35.59 (s, minor diastereomer), 32.72 (s, major diastereomer). ^{13}C{^{1}H} NMR (100 MHz, D_2O with a $CDCl_3$/TMS insert, complex coupling of several carbon atoms results from coupling to two magnetically inequivalent phosphorus atoms in the structure): δ 58.10 (m, *C*H(OH), minor diastereomer), 57.85 (m, *C*H(OH), major diastereomer), 19.54 (m, *C*H_2P, minor diastereomer), 18.35 (m, *C*H_2P, major diastereomer), 12.50–9.12 (m, CH_3CH_2P, overlap of diastereomer), 5.42–3.72 (m, CH_3CH_2P, overlap of diastereomer). Anal. Calcd for $C_{12}H_{28}P_2O_2Br_2$: C, 33.82; H, 6.62. Found: C, 33.92; H, 6.38.

*4.3. Procedure for the preparation of the dimer **2c***

In an Ar glovebox, potassium hydride (0.521 g; 13.0 mmol) was partially dissolved in 13 mL of THF. On a Schlenk line, di(*p*-tolyl) phosphine (2.31 g; 10.8 mmol) was slowly added to the mixture. The color of the solution changed to red-orange and H_2 gas was evolved. The solution was stirred for about 30 min until no more hydrogen generation was observed. The reaction mixture was then cooled to −78 °C and bromoacetadehyde diethyl acetal (2.12 g; 10.8 mmol) was added over a 20 min period. The temperature was brought to 25 °C and 2.5 g of 48% HBr (14.8 mmol) was added. The mixture was heated at 45 °C for 2 h, and left in the freezer for 5 h. The precipitate was filtered off in the air and washed twice with 7 mL of cold water, as well as 15 mL of a 1:1 mixture of cyclohexanol:ethyl acetate. The precipitate was then recrystallized by slow diffusion of ether into in of a solution of **2c** in 1:1 methanol:toluene. The purified solid was dried under high vacuum. Yield: 2.70 g, 87.8%. Anal. Calcd for $[C_{32}H_{36}P_2O_2][Br]_2[CH_3OH][H_2O]$: C, 54.71; H, 5.84. Found: C, 54.65; H, 6.04. The diastereomeric ratio was found to be 3:4, as determined by ^{1}H NMR, and ^{31}P NMR.

*4.3.1. Diastereomer **1**. major*

^{1}H NMR (400 MHz, CD_3OD): δ 8.06 (dd, $^3J_{HH} = 8.2$ Hz, $^3J_{HP} = 12.3$ Hz, 4H, Ar*H*), 7.63–7.58 (m, 8H, Ar*H*), 7.48 (dd, $^3J_{HH} = 8.2$ Hz, $^3J_{HP} = 2.5$ Hz, 4H, Ar*H*), 6.19 (dd, $^3J_{HH} = 6.6$ Hz, $^3J_{HP} = 21.5$, 2H, PC*H*(OH)), 4.37–4.15 (m, 2H, PCH(OH)CH_2), 3.99–3.81 (m, 2H, PCH(OH)CH_2), 2.53 (s, 6H, CH_3), 2.44 (s, 6H, CH_3). ^{1}H{^{31}P} NMR (400 MHz, CD_3OD): δ 8.06 (d, $^3J_{H\text{-}H} = 8.2$ Hz, 4H, Ar*H*), 7.63–7.58 (m, 8H, Ar*H*), 7.48 (d, $^3J_{HH} = 8.2$ Hz, 4H, Ar*H*), 6.19 (d,

$^3J_{HH}$ = 6.6 Hz, 2H, PC*H*(OH)), 4.18 (dd, $^3J_{HH}$ = 6.9, 16.3 Hz, 2H, PCH(OH)C*H*$_2$), 3.93 (dd, $^3J_{HH}$ = 2.2, 16.3 Hz, 2H, PCH(OH)C*H*$_2$), 2.53 (s, 6H, C*H*$_3$), 2.44 (s, 6H, C*H*$_3$).^{31}P{^{1}H} NMR (161 MHz, CD_3OD): δ 11.12 (s). ^{13}C{^{1}H} NMR (100 MHz, CD_3OD): δ 146.9–146.8 (m, *p*-C of ArP), 146.7 (m, *p*-C of ArP), 133.7–133.6 (m, *o*-CH of ArP), 133.1–133.0 (m, *o*-C of ArP), 130.7–130.5 (m, *m*-C of ArP), 130.4–130.3 (m, *m*-C of ArP), 114.0–113.8 (m, *ipso*-C of ArP), 113.0–112.9 (m, *ipso*-C of ArP), 61.5–60.7 (m, *C*H(OH)), 22.3–21.6 (m, *C*H$_2$CH(OH)), 20.5 (s, *C*H$_3$), 20.3 (s, *C*H$_3$).

4.3.2. Diastereomer **2**. minor

^{1}H NMR (400 MHz, CD_3OD): δ 7.96 (dd, $^3J_{HH}$ = 8.3 Hz, $^3J_{HP}$ = 12.5 Hz, 4H, ArH), 7.86 (dd, $^3J_{HH}$ = 8.3 Hz, $^3J_{HH}$ = 12.0 Hz, 4H, ArH), 7.63–7.58 (m, 4H, ArH), 7.56 (dd, $^3J_{HH}$ = 8.1 Hz, $^3J_{HP}$ = 3.2 Hz, 4H, ArH), 5.81 (ddd, $^3J_{HH}$ = 2.7, 9.3 Hz, J_{HP} = 16.3 Hz, 2H, PC*H*(OH)), 4.37–4.15 (m, 2H, PCH(OH)C*H*$_2$), 3.99–3.81 (m, 2H, PCH(OH)C*H*$_2$), 2.50 (s, 6H, C*H*$_3$), 2.49 (s, 6H, C*H*$_3$). ^{1}H{^{31}P} NMR (400 MHz, CD_3OD): δ 7.96 (d, $^3J_{HH}$ = 8.3 Hz, 4H, ArH), 7.86 (d, $^3J_{HH}$ = 8.3 Hz, 4H, ArH), 7.63–7.58 (m, 4H, ArH), 7.56 (d, $^3J_{H\text{-}H}$ = 8.1 Hz, 4H, ArH), 5.81 (dd, $^3J_{HH}$ = 2.7, 9.3 Hz, 2H, PC*H*(OH)), 4.27 (dd, $^3J_{HH}$ = 9.3, 16.2 Hz, 2H, PCH(OH)C*H*$_2$), 3.83 (dd, $^3J_{HH}$ = 2.7, 16.2 Hz, 2H, PCH(OH)C*H*$_2$), 2.50 (s, 6H, C*H*$_3$), 2.49 (s, 6H, C*H*$_3$). ^{31}P{^{1}H} NMR (161 MHz, CD_3OD): δ 16.06 (s). ^{13}C{^{1}H} NMR (100 MHz, CD_3OD): δ 147.5 (m, *p*-C of ArP), 147.0–146.9 (m, *p*-C of ArP), 133.4–133.3 (m, *m*-C of ArP), 132.9–132.8 (m, *m*-C of ArP), 131.4–131.3 (m, *o*-C of ArP), 130.5–130.4 (m, *o*-C of ArP), 112.8–112.3 (m, *ipso*-C of ArP), 111.9–111.5 (m, *ipso*-C of ArP), 62.2 (pdd, *C*H(OH)), 23.6 (pdd, *C*H$_2$CH(OH)), 20.4 (s, *C*H$_3$).

4.4. Procedure for preparation of the tetramer **4**

The synthetic procedure for the preparation of 2-(2-chloroethyl)-1, 3-dioxolane was used as described [13] without major changes. Potassium hydride (3.86 g; 96.3 mmol) was partially dissolved in 25 mL of THF in an Ar glovebox. At a Schlenk line under Ar, diphenylphosphine (14.9 g; 80.0 mmol) was slowly added to the mixture. The color of the solution changed to red-orange and H_2 gas evolved. The solution was stirred until no more hydrogen generation was observed. The reaction mixture was then cooled to 0 °C and the 2-(2-chloroethyl)-1, 3-dioxolane (10.9 g; 80.2 mmol) was added over a 20 min period. The mixture was warmed to 25 °C and 20 mL of 5 M HCl was added. The mixture was heated at 45 °C over night. The volume of the solution was reduced to 2/3 of the original volume to give a milky white solution that was left in the cooler (T˜0 to −5 °C) overnight to give a white precipitate. The precipitate was filtered and washed twice with 7 mL of cold H_2O and diethyl ether (10 mL). The precipitate was then recrystallized from a saturated solution in MeOH by slow diffusion of diethyl ether. White rhombic crystals were filtered and washed with diethyl ether and pentanes to give the analytically pure product as the trihydrate. Yield: 19.6 g, 88%. ^{1}H{^{31}P} NMR (400 MHz, CD_3OD): δ 7.95–7.55 (m, 40H, ArH), 6.60 (dd, $^3J_{HH}$ = 11.2 Hz, 4H, PC*H*(OH)), 4.41–4.23 (m, 4H, C*H*$_2$CH (OH)), 3.03–2.84 (m, 4H, C*H*$_2$CH (OH)), 2.80–2.63 (m, 4H, PC*H*$_2$CH$_2$), 1.30–1.22 (m, 4H, PC*H*$_2$CH$_2$). ^{1}H NMR (400 MHz, CD_3OD): 7.95–7.55 (m, 40H, ArH), 6.60 (pd (pseudo doublet), $^3J_{HH}$ = 10.4 Hz, 4H, PC*H*(OH)), 4.41–4.23 (pq, 4H, C*H*$_2$CH (OH)), 3.03–2.84 (pq, 4H, C*H*$_2$CH (OH)), 2.80–2.63 (pt, 4H, PC*H*$_2$CH$_2$), 1.30–1.22 (bs, 4H, PC*H*$_2$CH$_2$).δ ^{31}P{^{1}H} NMR (161 MHz, CD_3OD): δ 27.08 (s). ^{13}C{^{1}H} NMR (100 MHz, CD_3OD): δ 135.0 (s, *p*-C of PhP), 134.8 (s, *p*-C of Ph'P), 134.0 (m, *m*-C of PhP), 133.4 (m, *m*-C of Ph'P), 129.9 (m, *o*-C of PhP), 129.5 (m, *o*-C of Ph'P), 115.7 (d, J_{CP} = 85 Hz, *ipso*-C of PhP), 114.7 (d, J_{CP} = 84 Hz, *ipso*-C of Ph'P), 63.1 (m, PCH(OH)), 23.7 (m, PCH$_2$CH$_2$CH(OH)), 16.5 (m, PCH$_2$CH$_2$CH(OH)). Anal. Calcd for [$C_{60}H_{64}P_4O_4Cl_4$][2MeOH][2H_2O] C, 61.29; H, 6.30. Found: C, 61.23; H, 5.84.

4.5. Procedure for preparation of the monomer **6**

Diphenylphosphine (0.500 g, 2.69 mmol) was added to a mixture of partially dissolved potassium hydride (0.129 g, 3.22 mmol) in 15 mL of THF. The color of the solution changed to red-orange and H_2 gas evolution was observed. The solution was stirred until no more hydrogen generation was observed. The reaction mixture was then cooled to 0 °C and $ClCH_2CH_2CH_2CH(OCH_2CH_2O)$ (0.404 g, 2.69 mmol) was added over a 20 min period. The mixture was warmed to 25 °C and then 10 mL of 5 M HCl was added. The mixture was heated at 45 °C overnight. The solvent was completely evaporated under vacuum to give a yellow-white solid. The solid was redissolved in a minimum amount of MeOH and diethyl ether was slowly diffused into the solution. White crystals were collected by quick filtration in air and taken into a glovebox where the recrystallization was repeated to give the analytically pure product. Yield: 0.645 g, 82%. ^{1}H NMR (400 MHz, CD_3OD): δ 8.02–7.62 (m, 10H, ArH), 5.48 (dt, $^3J_{HH}$ = 6.0 Hz, J_{HP} = 7.6 Hz 1H, C*H*(OH)), 3.22–2.99 (m, 2H, C*H*$_2$CH(OH)), 2.59–2.12 (m, 4H, PC*H*$_2$ and PCH$_2$C*H*$_2$). ^{1}H{^{31}P} NMR (400 MHz, CD_3OD):): δ 8.02–7.62 (m, 10H, ArH), 5.48 (t, $^3J_{HH}$ = 6.0 Hz, 1H, C*H*(OH)), 3.22–2.99 (m, 2H, C*H*$_2$CH(OH)), 2.59–2.12 (m, 4H, PC*H*$_2$ and PCH$_2$C*H*$_2$). ^{31}P{^{1}H} NMR (161 MHz, CD_3OD): δ 38.0 (s). ^{13}C{^{1}H} NMR (100 MHz, CD_3OD): δ 134.7 (d, J_{CP} = 3.0 Hz, *p*-C of PhP), 134.4(d, J_{CP} = 3.2 Hz, *p*-C of Ph'P), 133.7 (d, J_{CP} = 9.0 Hz, *o*-C of PhP), 132.8 (d, J_{CP} = 9.0 Hz, *o*-C of Ph'P), 130.1 (d, J_{CP} = 11.8 Hz, *m*-C of PhP), 129.4 (d, J_{CP} = 12.4 Hz, *m*-C of PhP), 118.4 (d, J_{CP} = 73.3 Hz, *ipso*-C of PhP), 115.5 (d, J_{CP} = 78.2 Hz, *ipso*-C of Ph'P), 72.5 (d, J_{CP} = 55.9 Hz, *C*(OH)), 34.5 (d, J_{CP} = 18.0 Hz, *C*H$_2$CH(OH)), 21.3 (d, J_{CP} = 38.6 Hz, PCH$_2$), 21.4 (d, J_{CP} = 17.2 Hz, PCH$_2$CH$_2$). Anal. Calcd for [$C_{16}H_{18}POCl$][MeOH]: C, 62.80; H, 6.83. Found: C, 62.33; H, 6.18. Crystals suitable for the X-ray diffraction experiment were obtained by slow diffusion of the diethyl ether into a saturated solution of **6** in methanol.

4.6. Structure determination of **2a**, **2c** and **6** by X-ray diffraction

X-ray crystallographic data were collected on a Bruker–Nonius Kappa-CCD diffractometer with use of monochromated MoKa radiation (λ = 0.71073 Å) and were measured with a combination of φ scans and ω scans with k offsets, to fill the Ewald sphere.

Table 2
Summary of crystal data and details of intensity collection and least-squares refinement parameters for **2a, 2c** and **6**.

	2a	2c	6
Empirical formula	$C_{18}H_{44}Br_2O_4P_2$	$C_{32}H_{36}Br_2O_2P_2$	$C_{17}H_{22}ClO_2P$
F_w	546.29	674.37	324.77
T [K]	150(1)	273(1)	150(1)
Space group	P_{-1}	P_{-1}	$P2_1$
A [Å]	6.9663(5)	9.1690(9)	12.5293(3)
B [Å]	9.7835(4)	10.4027(11)	15.4572(8)
C [Å]	10.4298(7)	11.3044(14)	8.8188(7)
α [°]	74.240(4)	106.400	90.00
β [°]	71.618(3)	108.023	100.445(3)
γ [°]	74.063(4)	108.758	90.00
V [Å^3]	635.17(7)	879.25(17)	1679.62(16)
Z	1	1	4
P [mgcm^{-3}]	1.428	1.274	1.284
Reflections collected	6621	3817	13 223
Unique reflections	2862 [R(int) = 0.0436]	3817 [R(int) = 0.060]	3832 [R(int) = 0.0975]
Data; parameters	2862; 128	3817; 175	3832; 208
R1; wR2	0.0356; 0.087	0.0554; 0.1532	0.0556; 0.1392

Crystals of the tetramer **4** were obtained by slow diffusion of diethyl ether into a saturated solution of **4** in methanol. The presence of large cavities in the lattice that originate from the tetrameric nature of the phosphonium ion allowed co-crystallization of a large number of solvent molecules (water and methanol as determined from ^{1}H NMR studies) that appeared to be highly disordered. Attempts to model the solvent molecules were not successful. If the SQUEEZE option in PLATON was used to minimize the overall level of the disorder in the lattice, then the density of the crystal was found to be lowered by a significant amount because of the formation of large cavities. As a result, we cannot report the crystal structure of **4** in this manuscript. On the other hand, this preliminary X-ray analysis result confirms the proposed structure with a high level of confidence. Table 2.

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Appendix A. Supplementary material

Data collection parameters and crystallographic information can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. (**2a** CCDC 749473, **2c** CCDC 749474, **6** CCDC 749475).

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