Carbanionic displacement reactions at phosphorus. Part III.1 Cyanomethylphosphonate vs. cyanomethylenediphosphonate. Synthesis and solid-state structures

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Carbanionic Displacement Reactions at Phosphorus. Part III[1] Cyanomethylphosphonate vs. Cyanomethylenediphosphonate. Synthesis and Solid State Structures

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The result of the carbanionic reaction between acetonitrile and chlorophosphates depend strongly on the nature of the metallating agent (LiTMP, LDA, LiHMDS). According to the nature of base, the reaction can be directed towards the formation of either cyanomethylphosphonates **3** or cyanomethylenediphosphonates **5**. Electrophilic halogenation of lithiated cyanomethylphosphonate **2a** leads to the monochloro **17**, bromo **18** and iodo **19** derivatives. Only the monochloro product **17** was stable enough to be isolated in pure form. The structures of cyanobenzylphosphonate **10b**, cyanomethylenediphosphonate **5b** and its corresponding lithiated carbanion **4b** have been determined by X-ray crystallography. The polymeric structure, coupled with a wide charge delocalization, without C-Li contacts, is in agreement with the lack of reactivity towards electrophiles.

Introduction

Dialkyl cyanoalkylphosphonates are well known reagents for the two carbon chain elongation of aldehydes and ketones to α,β-unsaturated nitriles *via* the Horner-Wadsworth-Emmons (H-W-E) reaction.[2] In the past, diethyl cyanomethylphosphonate **3a** played an important role in the elucidation of the mechanism of this reaction.[3] In addition to the methodology for the olefination of carbonyl compounds, there are a number of other important and useful synthetic procedures allowing the conversion of the cyano group into amino,[4,5] amido[6] and carboxyl[7,8] groups with conservation of the phosphoryl group.

Two main routes are known for the synthesis of dialkyl cyanoalkylphosphonates. In the first one, the thermal route or Michaelis-Arbuzov reaction,[9,10] the phosphorus substrate acts as nucleophile while in the second, the carbanionic route,[11] the phosphorus substrate acts

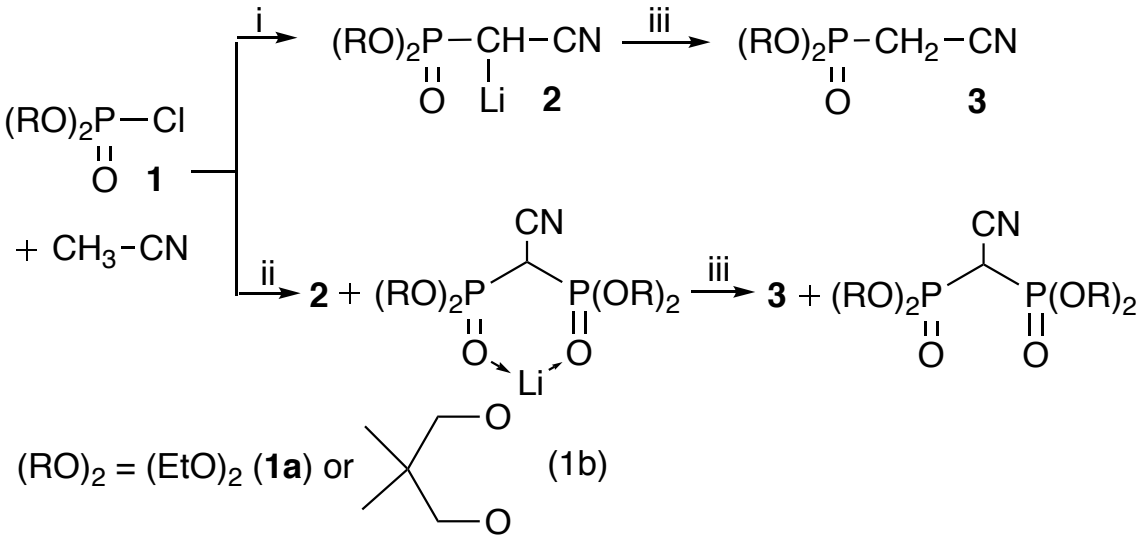
as electrophile. Generally, the thermal route is limited to the synthesis of dialkyl cyanomethylphosphonates[7,12,13] and tolerates only a methyl group on the α-carbon atom to phosphorus.[14,15] For example, the diethyl cyanomethylphosphonate **3a** was produced in 90% yield on heating triethylphosphite and chloroacetonitrile,[15] while the formation of diethyl 1-cyanoethylphosphonate **11a** from 2-bromopropionitrile resulted in only 55% yield after a 24 h reflux.[15] By contrast, the carbanionic route, described for the first time in 1975,[4] is more versatile and possesses significant synthetic advantages.[11] Cyanomethylphosphonate as well as 1-cyanoalkylphosphonates can be easily prepared in good yields by treatment at low temperature of the corresponding lithiated nitriles with chlorophosphates.[4,5] Thus, the addition of tetramethyldiaminochlorophosphate (1 eq.) at low temperature to lithiated acetonitrile (2 eq.) at -78°C provides the desired cyanomethylphosphonate in 95% yield.[4] An added advantage of the carbanionic route is that the lithiated intermediate generated *in situ* can be directly employed in a subsequent reaction.[16-22] Moreover, ester appendages at phosphorus can be easily suited. The only inconvenient of this approach is the loss of one half of the starting acetonitrile, inacceptable for the homologous nitriles and for large scale syntheses.

All subsequent anionic preparations of diethyl cyanomethylphosphonate **3a** reported in the litterature utilize LDA (2 eq.) for metallation of acetonitrile, but the yields are not so high and never exceed 53%.[23,24] Recently, our interest in the synthesis of α-monohalogenated cyanomethylphosphonates prompted us to reexamine the formation of 1-cyanoalkylphosphonates by nucleophilic substitution at phosphorus. We should like to add some useful improvements to this often quoted procedure recommended by several investigators.[16-22]

Results and discussion

By monitoring in ^{31}P-NMR the reaction of diethyl chlorophosphate **1a** with lithiated acetonitrile generated at low temperature with LDA (2 eq.), we identified in the reaction mixture two products attributed to the anions of diethyl cyanomethylphosphononate **2a** (δ_P(THF)=+43 ppm) and tetraethyl cyanomethylenediphosphonate **4a** (δ_P(THF)=+33 ppm) in a 65 / 35 ratio (Scheme 1). The same reaction mixture, in a slight different ratio, was obtained using the couple LDA (1 eq.) / *n*-BuLi (1 eq.) or LiTMP (2 eq.) as metallating agents (Table 1). These results are not dependent on the nature of the phosphoryl group since the 2-chloro-5,5-dimethyl-2-oxo-1,3,2-dioxaphosphorinane **1b** has a comparable behaviour. In marked contrast, the use of LiHMDS (2 eq.) suppresses completely the formation of the diphosphonate anions **4** and orientates the reaction towards the phosphonate anions **2**. These ones are quantitatively generated as the sole products and after acidic work-up the cyanomethylphosphonates **3** are isolated in pure form and excellent yield (Scheme 1, Table

2). In a similar way, the cyanomethylenediphosphonates **5** are cleanly obtained by using LDA, chlorophosphate and acetonitrile in a 3 / 2 / 1 ratio. Presumably, in the presence of a coordinating base as diisopropylamine, anions **2** are less aggregated and thus more reactive toward chlorophosphate **1**. In contrast, hexamethyldisilazane, a less coordinating base, do not prevent the aggregation of anions **2**, which become less reactive. The addition of salt (LiBr, 2 eq.) or the replacement of THF by DME does not change the reaction path and **2** remains the only species formed (Table 1). Consequently, by a proper choice of the metallating agent we are able to orientate the reaction between chlorophosphates **1** and acetonitrile towards the exclusive preparation of either cyanomethylphosphonate **3** or cyanomethylenediphosphonate **5** (Scheme 1).



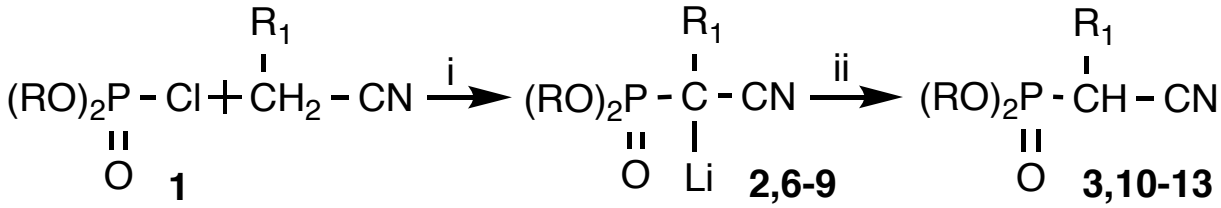
Scheme 1 Reagents and conditions: i, LiHMDS (2 eq.), THF, -78°C; ii, LDA (2 eq.), THF, -78°C; iii, HCl 3 M, 0°C.

Table 1.

Base	Solvent	**2** (%)	**4** (%)
2 LDA	THF	65	35
2 LiTMP	THF	70	30
1 *n*-BuLi + 1 LDA	THF	75	25
2 LiHMDS	THF	100	0
2 LiHMDS + 2 LiBr	THF	100	0
2 LiHMDS	DME	100	0

With these new results in hand, a general and reproducible procedure for the preparation of diethyl cyanomethylphosphonate **3a**, α-aryl- **10a** and α-alkylsubstituted **11a-13a** cyanomethylphosphonates by electrophilic phosphorylation of lithiated nitriles has been

developed (Scheme 2). As for acetonitrile, LiHMDS appears as the base of choice for the metallation of benzyl cyanide (Table 2, entries **3a** and **10a**). Owing to the difficulties frequently encountered in the slow phosphorylation of stabilized benzylic anions, the use of LiHMDS, more hindered and less basic than LDA, prevents the competing phosphorylation of the regenarated amine and consequently the protonation of the anion. For homologues alkylnitriles (R^1 = Me, Et, *n*-Pr), LiHMDS being not strong enough for their complete deprotonation, metallation proceeds in a clean manner with LDA to afford diethyl 1-lithio-cyanoalkylphosphonates **7a-9a** upon treatment with **1a**. After work-up, excellent yields of diethyl cyanoalkylphosphonates **11a-13a** are obtained (Table 2, entries **11a-13a**).



Scheme 2 Reagents and conditions: i, base (2 eq.), THF, -78°C; ii, HCl 3 M

Table 2.

Entry	R^1	δ_{PCLi} (ppm)[a]	δ_{PCH} (ppm)[b]	Base	Yields (%)
3a	H	44.7	15.2	LiHMDS	88
10a	Ph	36.3	15.0	LiHMDS	99
11a	Me	45.2	20.4	LDA	89
12a	Et	45.9	18.6	LDA	98
13a	*n*-Pr	44.8	18.7	LDA	99

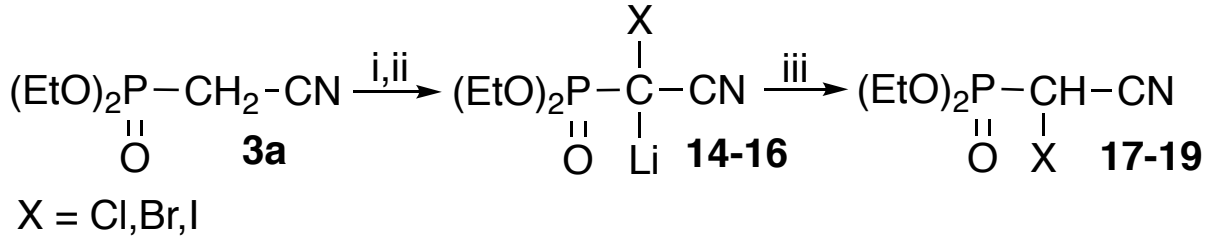
[a] In THF; [b] In $CDCl_3$

Extension of the electrophilic phosphorylation to nitriles bearing functional group (R^1 = MeO, Me_2N, F, Cl) was disappointing. As already observed by Dinizo *et al.*[25] and confirmed later,[24] even with an excess of chlorophosphate in internal quench conditions the metallation of nitriles is followed by self-condensation to afford the β-aminoacrylonitrile derivatives. Variation of base (LiHMDS, LDA, *i*-PrMgCl) or changes in reagents' addition order were totally ineffective. We found that in the best reaction conditions, by slow addition at low temperature of nitrile to the mixture of chlorophosphate and LiHMDS, the methoxy-, dimethylamino-, fluoro-, and chloroacetonitriles gave similar results and only 30% (determinated by ^{31}P NMR) of the expected cyanoalkylphosphonates were formed. However,

a general method for the preparation of fluoroalkenes by phosphorylation of lithiated fluoroacetonitrile followed by condensation on aromatic aldehydes was reported by Patrick *et al*. in 1990.[26] There are a few more examples of alkylation reactions of lithiated methoxy- and dimethylaminoacetonitrile, but these results seems not to be reproducible.[27,28]

In connection with our recent work on the selective electrophilic halogenation of α-phosphorylated carbanions protected by a trimethylsilyl group,[29-31] it became obvious that the use of silylated phosphononitriles could offer an entry into the α-monohalogenated phosphononitriles. In this purpose, the diethyl 1-lithio-cyanomethylphosphonate **2a** was reacted with TMSCl to give cleanly and quantitatively the diethyl 1-lithio-1-(trimethylsilyl)cyanomethylphosphonate (δ_P(THF)=+43.6). However, this method appears to be ineffective since this carbanion was completely inert towards electrophilic halogenation reagents. Moreover, it readily underwent desilylation on acidic work-up.

The relative inertness of diethyl 1-lithio-1-(trimethylsilyl)cyanomethylphosphonate being due to the trimethylsilyl group, we repeated the halogenation reaction without the protecting group, according to Scheme 3. The unprotected carbanion **2a** suffers facile halogenation with chlorination (C_2Cl_6), bromination ($C_2Cl_4Br_2$) and iodination (I_2) reagents to give exclusively the halogenated cyanomethylphosphonate carbanions **14-16** (δ_P(THF)=29-33 ppm). On acidic treatment, only the diethyl 1-cyanochloromethylphosphonate **17** was sufficiently stable to be isolated, while the bromo derivative **18** decomposes slowly on standing at room temperature. By contrast, the iodo derivative **19** decomposes by losing the halogen during the work-up and only the ^{31}P-NMR spectrum can be recorded.



Scheme 3 Reagents and conditions: i, LiHMDS (2 eq), THF, -78°C; ii, C_2Cl_6, $C_2Cl_4Br_2$ or I_2, -78°C; iii, HCl 3 M, 0°C

In spite of the previously reported[32] results on electrophilic fluorination of **3a**, we were unable to obtain the desired 1-cyanofluoromethylphosphonate by fluorination of **3a** using NFBS. In our conditions, a single fluorinated product was detected as a singlet in ^{19}F and ^{31}P-NMR spectra. The absence of TMS_2NF (δ_F(THF)=-176 ppm), which is usually formed during the electrophilic fluorination of stabilized carbanions, prompted us to assume an equilibrium between the nitrile and ketenimine forms of the anion, almost completely displaced in favour of the former. It seems that the more reactive ketimine form is fluorinated

on nitrogen to give the *N*-fluorophosphonoketenimine, but we cannot isolate the product. It is known that sterically hindered nitriles can be alkylated[33] or silylated[34] in the ketenimine form, but an halogenation reaction of this type has never been described.

All attempts to react the lithiated cyanomethylenediphosphonates **4** with electrophiles failed completely. These anions are also stable in aqueous solution and are protonated only by diluted hydrochloric acid. Fortunately, we succeeded to obtain X-ray quality crystals of the anion **4b** and the crystal data are compared with those of **5b**. The corresponding ORTEP projections are presented in Fig. 1 and 2.

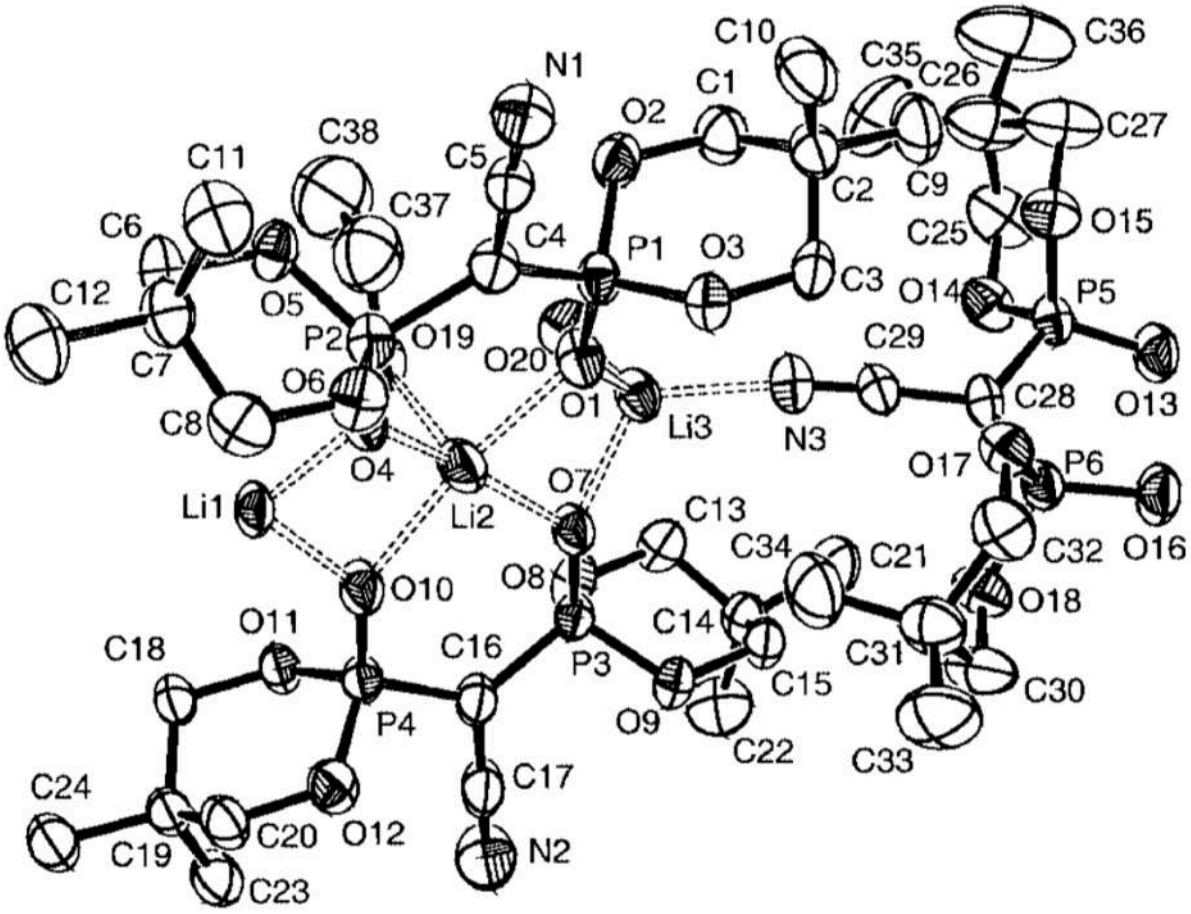


Fig. 1 Crystal structure of compound **4b**

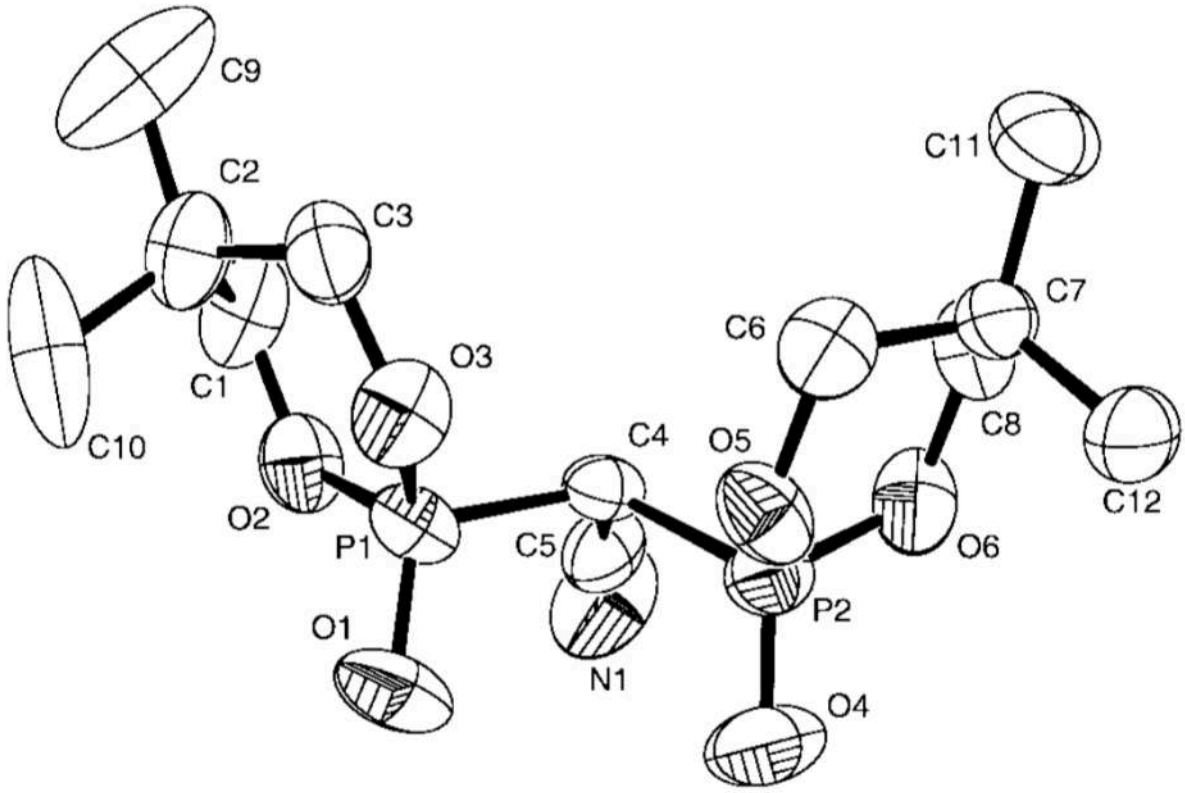


Fig. 2 Crystal structure of compound **5b**

The solid state structure of **5b** shows two monomeric units, with no contact between. The P-C and P-O distances (1.84 and 1.45 Å, respectively) are characteristic for neutral phosphonates (Fig. 1). By comparison with this, the corresponding anion **3b** crystallizes as a linear polymeric aggregate with the structural motif consisting of three lithiated diphosphonate units, with no C-Li contact. The core of the structure is constituted by three six-membered Li-O-P-C-P-O rings (which confirms the solution structure of diphosphonate anions[35] previously postulated) and two Li-O-Li-O four-membered rings, frequently found in the structures of anionic phosphonates with no C-Li contact.[36,37] There are three types of Li atoms: (a) the central one [Li(2)] is pentacoordinated to four oxygen atoms [O(1), O(4), O(7), O(10)] from two equivalent diphosphonate moieties and one oxygen atom [O(19)] from ethanol to form a tetragonal pyramide with Li(2) almost in the base plane; (b) the second [Li(1)] occupies the central position of a distorded tetrahedron composed by two oxygen atoms [O(13), O(16)] belonging to a third diphosphonate unit and two other oxygen atoms [O(4), O(10)] coming from two different diphosphonates; (c) the third one [Li(3)] is tetracoordinated by two oxygen atoms [O(1), O(7)] from two different diphosphonate moieties, one oxygen [O(20)] from a water molecule and a nitrogen atom [N(3)] from a nitrile group which form a distorted tetrahedron. The linear polymeric structure is induced by the coordination of [N(3)] to [Li(3)] (Fig. 2).

As expected, the P-C bond is significantly shortened (1.71 Å) compared to 1.84 Å in the neutral compound. Similarly, the P=O bond is a little longer (1.48 Å) than in **5b** (1.45 Å). These results, together with the planarity of the Li-O-P-C-P-O ring, suggest a wide charge delocalization involving also the nitrile group (C-C bond shortened from 1.47 Å to 1.41 Å and C≡N bond elongated from 1.13 Å to 1.15 Å). The Li-O bonds of the square-planed Li(2) are longer (2.04-2.06 Å) than those of the tetrahedral Li(1) and Li(3) (1.90-1.98 Å) or previously reported (1.86-1.90 Å).[38] In addition to these data, the ORTEP representation of compound **10b** is presented in Fig. 3.

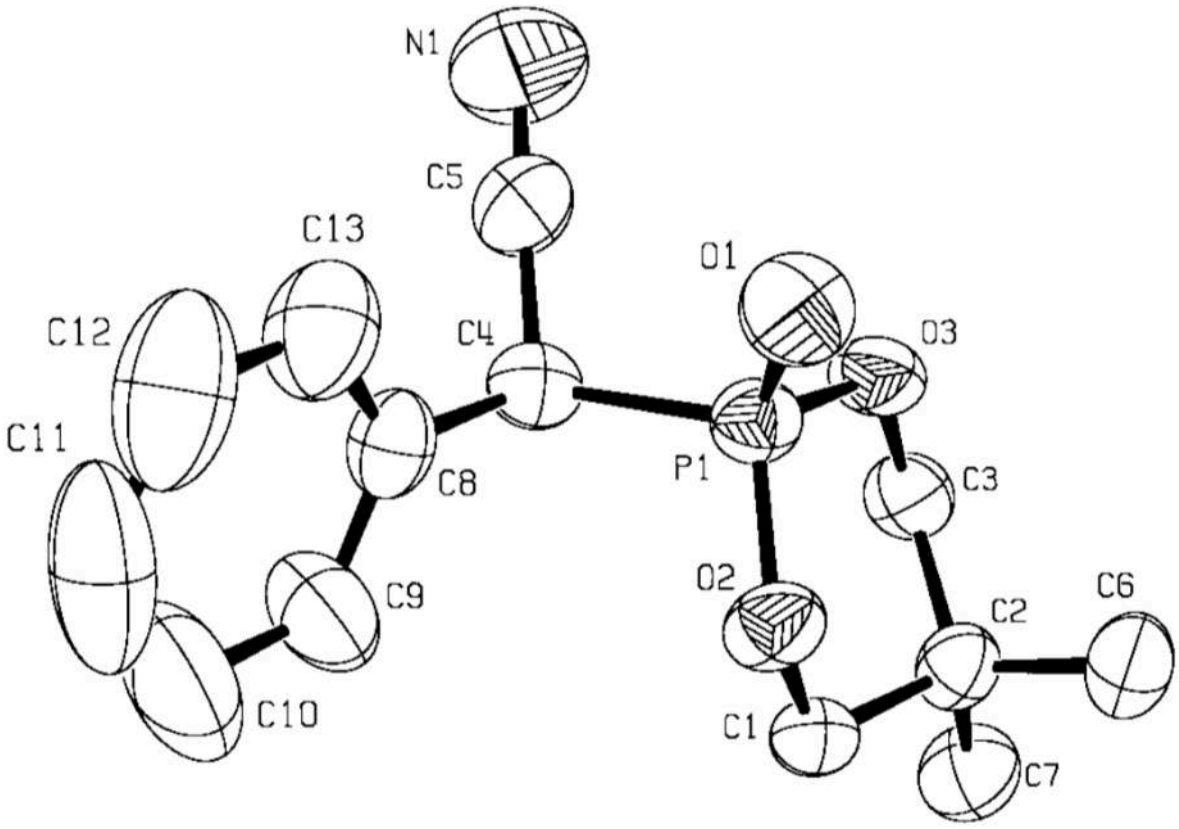


Fig. 3 Crystal structure of compound **10b**

Conclusion

We report here the reaction conditions in order to obtain in high yields and pure form either 1-cyanomethylphosphonates or 1-cyanomethylenediphosphonates. Electrophilic halogenation of 1-cyanomethylphosphonates affords cleanly the corresponding lithiated 1-cyanohalogenophosphonates, which proved to be unstable on acidic work-up for X = Br, I. The crystal structure of lithiated 1-cyanomethylenediphosphonate is described and it confirms the relative inertness of this type of structure. To our knowledge, this is the first described phosphonate anion with a polymeric structure.

Experimental

NMR spectra were recorded on a Bruker AC 200 spectrometer operating at 200 MHz for proton, 50.3 MHz for carbon, 81.01 MHz for phosphorus and 235 MHz for fluorine. ^{31}P downfield shifts (δ) are expressed with a positive sign, in ppm, relative to external 85% H_3PO_4 in H_2O. ^{1}H and ^{13}C chemical shifts (δ) are reported in ppm relative to $CDCl_3$ as internal standard. ^{19}F chemical shifts (δ) are reported in ppm relative to $CFCl_3$ as external standard. Coupling constants (*J*) are given in Hz. The following abbreviations are used: s, d, t, q, p, m for singlet, doublet, triplet, quadruplet, pentuplet and multiplet respectively. Low resolution mass spectra were recorded on a Hewlett-Packard 5989 B GC-MS spectrometer (BPX5 column, positive chemical ionisation NH_3). Organic solvents were purified by standard procedures. THF was distilled under an inert atmosphere from purple solutions of sodium-benzophenone ketyl. The synthesis of all compounds was carried out under dry nitrogen. 'Evaporation' of solvents indicates evaporation under reduced pressure using a rotary evaporator. All drying of solutions was done with anhydrous magnesium sulfate.

General method for the preparation of compounds 3a and 10-13a

n-BuLi (39.4 mL of 1.6 M solution in hexane; 63 mmol) is added to THF (40 mL) cooled to -78°C. A solution of either 1,1,1,3,3,3-hexamethyldisilazane (10.3 g; 64 mmol) (for **3a** and **10a**) or diisopropylamine (6.46 g; 64 mmol) (for **11a-13a**) in THF (30 mL) is then slowly added at this temperature *via* a dropping funnel. After 10 min. the nitrile (30 mmol) in THF (30 mL) is slowly added at the same temperature. After 30 min. a solution of diethyl chlorophosphate (5.35 g; 31 mmol) in THF (30 mL) is added at -78°C. After 15 min. at this temperature, the reaction mixture is allowed to warm-up to 0°C then poured with stirring into a mixture of 3 M HCl (50 mL), CH_2Cl_2 (50 mL) and ice (30 g). The aqueous layer is extracted with CH_2Cl_2 (2 x 50 mL). The combined organic layers are washed with H_2O (10 mL), dried and evaporated to afford the expected product which is pure enough for further reactions.

Diethyl 1-cyanomethylphosphonate 3a.[23,24] Yellowish oil (88%); δ_P(81.01 MHz; $CDCl_3$; 85% H_3PO_4) 15.2 (s); δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.32 (6 H, t, $^{3}J_{HH}$ 7.0, 2 × C*H*$_3$CH$_2$O), 2.87 (2 H, d, $^{2}J_{PH}$ 21.0, C*H*$_2$CN), 4.32 (4 H, dq, $^{3}J_{HH}$ 8.6 and *J* 7.0, 2 × CH$_3$C*H*$_2$O); δ_C(50.3 MHz; $CDCl_3$; Me_4Si) 16.7 (d, $^{3}J_{PC}$ 6.1, 2 × *C*H$_3$CH$_2$O), 16.8 (d, $^{1}J_{PC}$ 143.3, *C*H$_2$CN), 64.3 (d, $^{2}J_{PC}$ 6.6, CH$_3$*C*H$_2$O), 113.2 (d, $^{2}J_{PC}$ 7.3, CH$_2$*C*N); *m/z* (CI) 195 (M+18, 100).

Diethyl 1-cyanobenzylphosphonate 10a.[23] Yellowish oil (99%); δ_P(81.01 MHz; $CDCl_3$; 85% H_3PO_4) 15.0 (s); δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.24 (3 H, t, $^3J_{HH}$ 7.1, $(CH_3CH_2O)_A$), 1.28 (3 H, t, $^3J_{HH}$ 7.1, $(CH_3CH_2O)_B$), 3.94-4.21 (4 H, m, 2 × CH_3CH_2O), 4.31 (1 H, d, $^2J_{PH}$ 26.4, C_6H_5CHCN), 7.34-7.47 (5 H, m, C_6H_5CHCN); δ_C(50.3 MHz; $CDCl_3$; Me_4Si) 16.5 (d, $^3J_{PC}$ 5.9, 2 × CH_3CH_2O), 36.9 (d, $^1J_{PC}$ 138.6, C_6H_5CHCN), 64.6 (d, $^2J_{PC}$ 7.3, $(CH_3CH_2O)_A$), 64.9 (d, $^2J_{PC}$ 7.5, $(CH_3CH_2O)_B$), 115.7 (d, $^2J_{PC}$ 9.4, C_6H_5CHCN), 127.9 (d, $^2J_{PC}$ 7.6, C_{ipso} of C_6H_5), 128.9 (s, C_{para} of C_6H_5), 129.0 (s, 2 × C_{meta} of C_6H_5), 129.3 (d, $^3J_{PC}$ 2.6, 2 × C_{ortho} of C_6H_5); *m/z* (CI) 254 (M+1, 60), 271 (M+18, 100).

Diethyl 1-cyanoethylphosphonate 11a.[23,24,39,40] Yellowish oil (89%); δ_P(81.01 MHz; $CDCl_3$; 85% H_3PO_4) 20.4 (s); δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.26 (3 H, t, $^3J_{HH}$ 7.0, $(CH_3CH_2O)_A$), 1.28 (3 H, t, $^3J_{HH}$ 7.0, $(CH_3CH_2O)_B$), 1.44 (3 H, dd, $^3J_{PH}$ 16.9 and $^3J_{HH}$ 7.3, CH_3CH), 2.93 (1 H, dq, $^2J_{PH}$ 23.3 and $^3J_{HH}$ 7.3, CH_3CH), 4.12 (2 H, dq, $^3J_{PH}$ 8.5 and $^3J_{HH}$ 7.0, $(CH_3CH_2O)_A$), 4.14 (2 H, dq, $^3J_{PH}$ 8.5 and $^3J_{HH}$ 7.0, $(CH_3CH_2O)_B$); δ_C(50.3 MHz; $CDCl_3$; Me_4Si) 12.9 (d, $^2J_{PC}$ 6.0, CH_3CH), 16.7 (d, $^3J_{PC}$ 5.9, 2 × CH_3CH_2O), 23.9 (d, $^1J_{PC}$ 145.2, CH_3CH), 64.0 (d, $^2J_{PC}$ 7.3, $(CH_3CH_2O)_A$), 64.2 (d, $^2J_{PC}$ 6.7, $(CH_3CH_2O)_B$), 117.5 (d, $^2J_{PC}$ 9.2, $CHCN$); *m/z* (CI) 192 (M+1, 73), 209 (M+18, 100).

Diethyl 1-cyanopropylphosphonate 12a.[40-42] Yellowish oil (98%); δ_P(81.01 MHz; $CDCl_3$; 85% H_3PO_4) 18.6 (s); δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.17 (3 H, t, $^3J_{HH}$ 7.4, CH_3CH_2CH), 1.36 (6 H, t, $^3J_{HH}$ 7.0, 2 × CH_3CH_2O), 1.76-2.05 (2 H, m, CH_3CH_2CH), 2.84 (1 H, ddd, $^2J_{PH}$ 23.4, $^3J_{HH}$ 9.9 and $^3J_{HH}$ 4.8, CH_3CH_2CH), 4.18 (2 H, dq, $^3J_{PH}$ 8.4 and $^3J_{HH}$ 7.0, $(CH_3CH_2O)_A$), 4.21 (2 H, dq, $^3J_{PH}$ 8.4 and $^3J_{HH}$ 7.0, $(CH_3CH_2O)_B$); δ_C(50.3 MHz; $CDCl_3$; Me_4Si) 13.0 (d, $^3J_{PC}$ 6.0, CH_3CH_2CH), 16.9 (d, $^3J_{PC}$ 5.9, 2 × CH_3CH_2O), 21.4 (d, $^2J_{PC}$ 44, CH_3CH_2CH), 32.1 (d, $^1J_{PC}$ 144.1, CH_3CH_2CH), 64.1 (d, $^2J_{PC}$ 7.3, $(CH_3CH_2O)_A$), 64.3 (d, $^2J_{PC}$ 7.1, $(CH_3CH_2O)_B$), 116.7 (d, $^2J_{PC}$ 9.9, $CHCN$); *m/z* (CI) 206 (M+1, 59), 223 (M+18, 100).

Diethyl 1-cyanobutylphosphonate 13a.[40,41] Yellowish oil (98%); δ_P(81.01 MHz; $CDCl_3$; 85% H_3PO_4) 18.7 (s); δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.90 (3 H, t, $^3J_{HH}$ 7.3, $CH_3CH_2CH_2$), 1.30 (6 H, t, $^3J_{HH}$ 7.1, 2 × CH_3CH_2O), 1.11-1.86 (4 H, m, $CH_3CH_2CH_2$), 2.84 (1 H, dt, $^2J_{PH}$ 23.5 and $^3J_{HH}$ 7.2, CH_2CH_2CH), 3.62-4.24 (4 H, m, 2 × CH_3CH_2O); δ_C(50.3 MHz; $CDCl_3$; Me_4Si) 13.6 (s, $CH_3CH_2CH_2$), 16.7 (d, $^3J_{PC}$ 5.7, 2 × CH_3CH_2O), 21.5 (d, $^3J_{PC}$ 12.3, CH_2CH_2CH), 29.2 (d, $^2J_{PC}$ 4.4, CH_2CH_2CH), 30.0 (d, $^1J_{PC}$ 143.6, CH_2CH_2CH), 64.0 (d, $^2J_{PC}$ 6.6, $(CH_3CH_2O)_A$), 64.3 (d, $^2J_{PC}$ 6.9, $(CH_3CH_2O)_B$), 116.6 (d, $^2J_{PC}$ 9.5, $CHCN$); *m/z* (CI) 220 (M+1, 69), 237 (M+18, 100).

5,5-Dimethyl-2-oxo-2-(1-cyanobenzyl)-1,3,2-dioxaphosphorinane 10b. Following the general procedure for **10a**, the intermediate anion **6b** was precipitated with concentrated HCl (6 M) and filtrated. Colorless needles; δ_P(81.01 MHz; $CDCl_3$; 85% H_3PO_4) 4.0 (s); δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.05 (3 H, s, $(CH_3)_A$), 1.20 (3 H, s, $(CH_3)_B$), 4.13-4.29 (4 H, m, 2 × CH_2O), 4.46 (1 H, d, $^2J_{PH}$ 27.3, CHCN), 7.41-7.56 (5 H, m, C_6H_5); δ_C(50.3 MHz; $CDCl_3$; Me_4Si) 21.7 (s, CH_3), 22.3 (s, CH_3), 33.5 (d, $^3J_{PC}$ 9.2, $C(CH_3)_2$), 36.9 (d, $^1J_{PC}$ 135.8, CHCN), 79.9 (d, $^2J_{PC}$ 7.6, $(CH_2O)_A$), 80.3 (d, $^2J_{PC}$ 7.6, $(CH_2O)_B$), 116.2 (d, $^2J_{PC}$ 10.7, CHCN), 127.8 (d, $^2J_{PC}$ 7.6, C_{ipso} of C_6H_5), 129.3 (d, $^3J_{PC}$ 6.1, 2 × C_{ortho} of C_6H_5), 129.7 (d, $^5J_{PC}$ 3.0, C_{para} of C_6H_5), 129.9 (d, $^4J_{PC}$ 3.0, 2 × C_{meta} of C_6H_5); *m/z* (CI) 254 (M+1, 100), 271 (M+18, 32).

General method for the preparation of compounds 17-19

n-BuLi (6.9 mL of 1.6 M solution in hexane; 11 mmol) is added to THF (20 mL) cooled to -78°C. A solution of 1,1,1,3,3,3-hexamethyldisilazane (1.93 g; 12 mmol) in THF (10 mL) is then slowly added at this temperature *via* a dropping funnel. After 10 min. **3a** (5 mmol) in THF (10 mL) is slowly added at the same temperature. After 15 min. a solution of halogenating agent (C_2Cl_6, $C_2Cl_4Br_2$, I_2) (5.5 mmol) in THF (10 mL) is added at -78°C and the reaction mixture is allowed to warm-up to 0°C then poured with stirring into a mixture of 3 M HCl (25 mL), CH_2Cl_2 (25 mL) and ice (10 g). The aqueous layer is extracted with CH_2Cl_2 (2 x 30 mL). The combined organic layers are washed with H_2O (10 mL), dried and evaporated to afford the expected product. **17** is stable at room temperature, **18** decomposes slowly on standing and **19** decomposes during the work-up.

Diethyl 1-cyanochloromethylphosphonate 17. Yellowish oil (86%); δ_P(81.01 MHz; $CDCl_3$; 85% H_3PO_4) 8.8 (s); δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.45 (3 H, td, $^3J_{HH}$ 7.2 and $^4J_{PH}$ 0.8, $(CH_3CH_2O)_A$), 1.46 (3 H, td, $^3J_{HH}$ 7.1 and $^4J_{PH}$ 0.8, $(CH_3CH_2O)_B$), 4.31-4.48 (4 H, m, 2 × CH_3CH_2O), 4.98 (1 H, d, $^2J_{PH}$ 17.5, ClCHCN); δ_C(50.3 MHz; $CDCl_3$; Me_4Si) 17.0 (d, $^3J_{PC}$ 4.5, 2 × CH_3CH_2O), 35.5 (d, $^1J_{PC}$ 157.6, ClCHCN), 66.5 (d, $^2J_{PC}$ 5.0, $(CH_3CH_2O)_A$), 66.8 (d, $^2J_{PC}$ 6.5, $(CH_3CH_2O)_B$), 113.5 (d, $^2J_{PC}$ 4.6, ClCHCN); *m/z* (CI) 212 (M+1 ^{35}Cl, 10), 214 (M+1 ^{37}Cl, 4), 229 (M+18 ^{35}Cl, 100), 231 (M+18 ^{37}Cl, 29).

Diethyl 1-cyano-1-bromomethylphosphonate 18. Yellow oil; δ_P(81.01 MHz; $CDCl_3$; 85% H_3PO_4) 8.8 (s); δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.36 (td, $^3J_{HH}$=7.1, $^4J_{PH}$=0.6, 3H, $(CH_3CH_2O)_A$), 1.37 (td, $^3J_{HH}$=7.1, $^4J_{PH}$=0.6, 3H, $(CH_3CH_2O)_B$), 4.11-4.38 (m, 4H, CH_3CH_2O), 4.50 (d, $^2J_{PH}$=16.2, 1H, BrCHCN); δ_C(50.3 MHz; $CDCl_3$; Me_4Si) 16.7 (d,

$^3J_{PC}$=5.7, $\underline{C}H_3CH_2O$), 17.6 (d, $^1J_{PC}$=155.9, Br$\underline{C}$HCN), 66.2 (d, $^2J_{PC}$=6.6, $(CH_3\underline{C}H_2O)_A$), 66.5 (d, $^2J_{PC}$=7.3, $(CH_3\underline{C}H_2O)_B$), 113.6 (d, $^2J_{PC}$=6.0, BrCH$\underline{C}$N); *m/z* (CI) Decomposition.

Tetraethyl cyanomethylenediphosphonate 5a.[43] *n*-BuLi (20.6 mL of 1.6 M solution in hexane; 33 mmol) is added to THF (20 mL) cooled to -78°C. A solution of diisopropylamine (13.43 g; 34 mmol) in THF (10 mL) is then slowly added at this temperature *via* a dropping funnel. After 10 min. the acetonitrile (0.41 g; 10 mmol) in THF (10 mL) is slowly added at the same temperature. After 30 min. a solution of diethyl chlorophosphate (3.62 g; 21 mmol) in THF (10 mL) is added at -78°C. After 15 min. at this temperature, the reaction mixture is allowed to warm-up to 0°C then poured with stirring into a mixture of 3 M HCl (25 mL), CH_2Cl_2 (25 mL) and ice (10 g). The aqueous layer is extracted with CH_2Cl_2 (2 x 30 mL). The combined organic layers are washed with H_2O (10 mL), dried and evaporated to afford the expected product. Yellowish oil (93%); δ_P(81.01 MHz; $CDCl_3$; 85% H_3PO_4) 9.6 (s); δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.40 (12 H, t, $^3J_{HH}$ 7.0, 4 × CH_3CH$_2$O), 2.89 (1 H, d, $^2J_{PH}$ 21.0, C*H*CN), 4.21-4.36 (8 H, m, 4 × CH$_3$CH_2O); δ_C(50.3 MHz; $CDCl_3$; Me_4Si) 16.2 (s, 2 × $(CH_3CH_2O)_A$), 16.3 (s, 2 × $(CH_3CH_2O)_B$), 30.5 (t, $^1J_{PC}$ 130.7, *C*HCN), 64.9 (s, 4 × CH$_3$*C*H$_2$O), 111.7 (t, $^2J_{PC}$ 10.4, CH*C*N); *m/z* (CI) 314 (M+1, 100), 331 (M+18, 25).

1-Cyanomethylene-*bis*-(5,5-dimethyl-2-oxo-2-yl-1,3,2-dioxaphosphorinane) 5b. Following the procedure for **5a**, the intermediate anion **4b** was precipitated with concentrated HCl (6 M) and filtrated. Colorless plates (40-50%); δ_P(81.01 MHz; $CDCl_3$; 85% H_3PO_4) -0.2 (s); δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.01 (6 H, s, 2 × (CH_3)$_A$), 1.35 (6 H, s, 2 × (CH_3)$_B$), 4.15 (4 H, dd, $^3J_{PHax}$ 17.7 and $^2J_{HaxHeq}$ 10.6, 2 × CH_2O_{ax}), 4.58 (4 H, dd, $^3J_{PHeq}$ 3.2 and $^2J_{HaxHeq}$ 11.0, CH_2O_{eq}), C*H* exchanged with $CDCl_3$; δ_C(50.3 MHz; $CDCl_3$; Me_4Si) 21.1 (s, 2 × (*C*H$_3$)$_A$), 22.6 (s, 2 × (*C*H$_3$)$_B$), 29.8 (t, $^1J_{PC}$ 124.8, *C*HCN), 33.4 (d, $^3J_{PC}$ 4.4, (*C*(CH$_3$)$_2$)$_A$), 33.5 (d, $^3J_{PC}$ 4.4, (*C*(CH$_3$)$_2$)$_B$), 80.3 (s, 4 × *C*H$_2$O), 112.1 (t, $^2J_{PC}$ 10.7, CH*C*N); *m/z* (CI) 338 (M+1, 100), 355 (M+18, 88).

1-Lithio-1-cyanomethylene-*bis*(5,5-dimethyl-2-oxo-2-yl-1,3,2-dioxaphosphorinane) 3b. Compound **5b** in THF solution was deprotonated with a stoechiometric quantity of previously titrated *n*-BuLi (1.6 M in hexane). Evaporation of the THF solution gave the compound **3b** as colorless needles; δ_P(81.01 MHz; D_2O; 85% H_3PO_4) 28.8 (s); δ_H(200 MHz; D_2O; Me_4Si) 0.93 (6 H, s, 2 × (CH_3)$_A$), 1.07 (6 H, s, 2 × (CH_3)$_B$), 3.93-4.15 (8 H, m, 4 × CH_2O); δ_C(50.3 MHz; D_2O; Me_4Si) 19.3 (t, $^1J_{PC}$ 226.2, *C*LiCN), 21.8 (s, 2 × (*C*H$_3$)$_A$), 22.0 (s, 2 × (*C*H$_3$)$_B$), 33.4 (s, 2 × *C*(CH$_3$)$_2$), 78.1 (s, 4 × *C*H$_2$O), 127.4 (s, CLi*C*N).

The crystal structures of (i) 1-Lithio-1-cyanomethylene-*bis*(5,5-dimethyl-2-oxo-2-yl-1,3,2-dioxaphosphorinane) 3b, (ii) 1-Cyanomethylene-*bis*-(5,5-dimethyl-2-oxo-2-yl-1,3,2-dioxaphosphorinane) 5b and (iii) 5,5-Dimethyl-2-oxo-2-(1-cyanobenzyl)-1,3,2-dioxaphosphorinane 10b

Crystals suitable for X-ray diffraction were obtained from EtOH by slow evaporation (**3b**) or CH_2Cl_2-hexane by diffusion (**5b**, **10b**) solutions of the compounds. Data were collected at room temperature with a Nonius Kappa CCD diffractometer using MoKα radiation (λ = 0.7107 Å). The crystal structures were solved with maXus. While initial refinement was performed with the latter, final least-squares was conducted with Shelxl97.[44] Illustrations were made using Platon.[45] Crystal data are assembled in Table 4. Atomic coordinates, bond lengths and angles, and thermal parameters for compounds **3b**, **5b** and **10b** have been deposited at the Cambridge Crystallographic Data Centre. CCDC reference number 207/465. See http://www.rsc.org/suppdata/p1/b0/b003371p for crystallographic files in .cif format.

Table 4 Crystal data for the compounds **3b**, **5b** and **10b**

Compound	**3b**	**5b**	**10b**
Molecular formula	$C_{38}H_{71}Li_3N_3O_{20}P_6$	$C_{12}H_{21}NO_6P_2$	$C_{13}H_{16}NO_3P$
Molecular weight	1096.62	337.24	265.24
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1$	P21/n	P21/c
a(Å)	10.5710(2)	10.5080(5)	14.4740(9)
b(Å)	19.5690(8)	16.3980(7)	9.4720(6)
c(Å)	13.0840(5)	19.3330(8)	10.5520(5)
α(°)	90.00	90.000(3)	90.00
β(°)	101.141(2)	100.048(2)	103.753(4)
γ(°)	90.00	90.000(2)	90.00
V(Å^3)	2655.60(16)	3280.2(2)	1405.18(14)
Z	2	8	4
μ(cm^{-1})	0.275	0.289	0.195
Reflections measured	5535	12028	2870
Independant reflections	5535	6688	2870
Rint		0.041	
Reflections used	4826	3638	1963
wR2	0.1158	0.1398	0.2486
R1	0.0409	0.0537	0.0599

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