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

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Received (in Cambridge, UK) 26th April 2000, Accepted 10th August 2000
First published as an Advance Article on the web 12th September 2000

The results 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 the 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 mono-chloro **17**, -bromo **18** and -iodo **19** derivatives. Only the monochloro product **17** is stable enough to be isolated in pure form. The structures of cyanobenzylphosphonate **10b**, cyanomethylenediphosphonate **5b** and its corresponding lithiated carbanion **4b** are 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

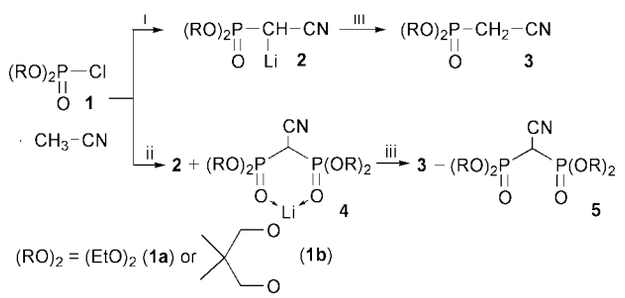
Dialkyl cyanoalkylphosphonates are well known reagents for the two-carbon-chain elongation of aldehydes and ketones to α,β-unsaturated nitriles *via* the Horner–Wadsworth–Emmons (H–W–E) reaction.[2] In the past, diethyl cyanomethylphosphonate **3a** played an important role in the elucidation of the 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 carboxy[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, diethyl cyanomethylphosphonate **3a** was produced in 90% yield on heating triethyl phosphite 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] Cyanomethylphosphonates as well as other 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 bis(dimethylamino)phosphorochloridate (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 are easily suited to the reaction conditions. The only inconvenience of this approach is the loss of one half of the starting acetonitrile, unacceptable for homologous nitriles and for large-scale syntheses.

All subsequent anionic preparations of diethyl cyanomethylphosphonate **3a** reported in the literature 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 (^{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 slightly different ratio, was obtained using the couple LDA (1 eq.)–*n*-BuLi (1 eq.) or LiTMP† (2 eq.) as metallating agent (Table 1). These results are not dependent on the nature of the



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

† *Abbreviations*. LDA, lithium diisopropylamide. LiTMP, lithium 2,2,6,6-tetramethylpiperidide. LiHMDS, lithium hexamethyldisilazide. DME, 1,2-dimethoxyethane. TMSCl, trimethylsilyl chloride. NFBS, *N*-fluorobenzenesulfonimide.

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

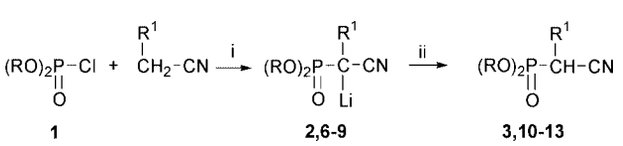
Table 2

Entry	R′	δ_P(CLi) (ppm)[a]	δ_P(CH) (ppm)[b]	Base	Yield (%)
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	Pr	44.8	18.7	LDA	99

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

phosphoryl group, since 2-chloro-5,5-dimethyl-2-oxo-1,3,2-dioxaphosphorinane **1b** shows 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 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 the proportions 3 : 2 : 1. Presumably, in the presence of a coordinating base such as diisopropylamine, anions **2** are less aggregated and thus more reactive toward chlorophosphate **1**. In contrast, hexamethyldisilazane, a less coordinating base, does 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 proper choice of the metallating agent we are able to orientate the reaction between chlorophosphates **1** and acetonitrile towards the preparation of either exclusively the cyanomethylphosphonate **3** or mixtures containing substantial amounts of the cyanomethylenediphosphonate **5** (Scheme 1).

With these new results in hand, a general and reproducible procedure for the preparation of diethyl cyanomethylphosphonate **3a**, α-aryl- **10a** and α-alkyl-substituted **11a**–**13a** cyanomethylphosphonates by electrophilic phosphorylation of lithiated nitriles has been developed (Scheme 2). As for



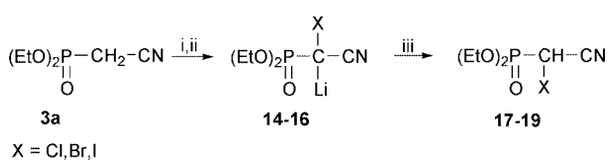
Scheme 2 *Reagents and conditions*: i, base (2 eq.), THF, −78 °C; ii, 3 M HCl.

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 regenerated amine and consequently the protonation of the anion. For homologous alkyl nitriles (R^1 = Me, Et, Pr), LiHMDS being not strong enough for their complete deprotonation, metallation proceeds in a clean manner with LDA to afford diethyl 1-lithiocyanoalkylphosphonates **7a**–**9a** upon treatment with **1a**. After work-up, excellent yields of diethyl cyanoalkylphosphonates **11a**–**13a** are obtained (Table 2, entries **11a**–**13a**).

Extension of the electrophilic phosphorylation to nitriles bearing functional groups (R′ = 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 under internal quench conditions the metallation of nitriles is followed by self-condensation to afford the β-aminoacrylonitrile derivatives. Variation of base (LiHMDS, LDA, Pr^iMgCl) 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 was 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 and Nadji in 1990.[26] There are a few more examples of alkylation reactions of lithiated methoxy- and dimethylaminoacetonitrile, but these results seem 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. For this purpose, diethyl 1-lithio(cyano)methylphosphonate **2a** was treated with TMSCl† to give cleanly and quantitatively diethyl 1-lithio-1-(trimethylsilyl)(cyano)methylphosphonate [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 lithio(trimethylsilyl)(cyano)-methylphosphonate being due to the trimethylsilyl group, we repeated the halogenation reaction without the protecting group, according to Scheme 3. The unprotected carbanion **2a**



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, 3 M HCl, 0 °C.

readily undergoes 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 diethyl 1-cyano(chloro)methylphosphonate **17** was sufficiently stable to be isolated, while the bromo derivative **18** decomposed slowly at room temperature. By contrast, the iodo derivative **19** decomposed by losing the halogen during the work-up and only the ^{31}P NMR spectrum could be recorded.

In spite of the previously reported[32] results on electrophilic fluorination of **3a**, we were unable to obtain the desired 1-cyano(fluoro)methylphosphonate by fluorination of **3a** using NFBS.† Under 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 ketenimine form is fluorinated on nitrogen to give the *N*-fluorophosphonoketenimine, but we cannot isolate the product. It is known that

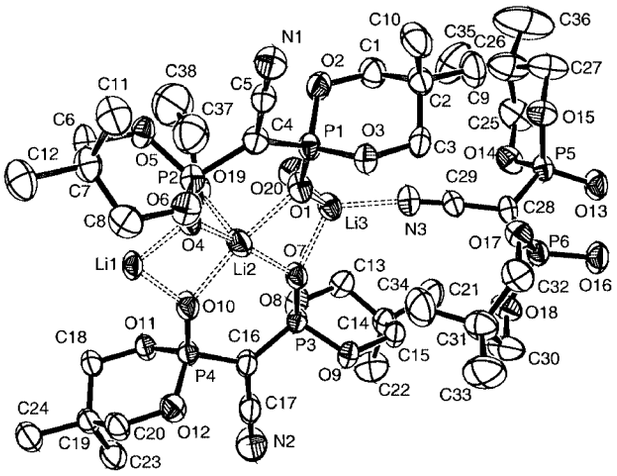


Fig. 1 Crystal structure of compound **4b**.

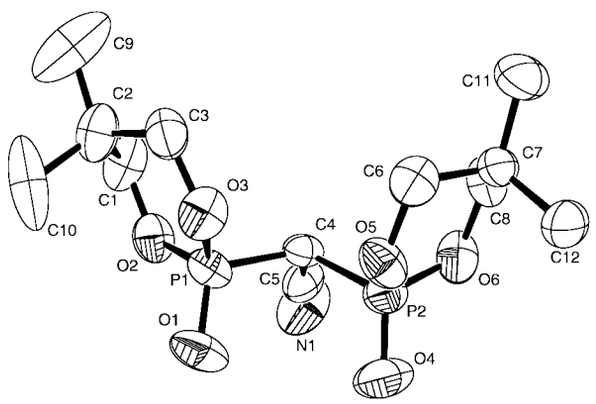


Fig. 2 Crystal structure of compound **5b**.

sterically hindered nitriles can be alkylated[33] or silylated[34] in the ketenimine form, but a halogenation reaction of this type has never been described.

All attempts to force the lithiated cyanomethylenediphosphonates **4** to react with electrophiles failed completely. These anions are also stable in aqueous solution and are protonated only by dil. hydrochloric acid. Fortunately, we succeeded in obtaining 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 Figs. 1 and 2.

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 **4b** 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 [with C(37) and C(38)] to form a tetragonal pyramid with Li(2) almost in the base plane; (b) the second [Li(1)] occupies the central position of a distorted tetrahedron composed of 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. 1).

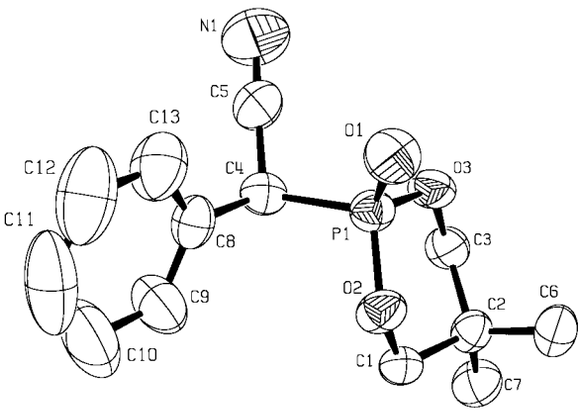


Fig. 3 Crystal structure of compound **10b**.

As expected, the P–C bond is significantly shortened (1.71 Å) compared with 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-planar 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 those previously reported (1.86–1.90 Å).[38] In addition to these data, the ORTEP representation of compound **10b** is presented in Fig. 3.

Conclusions

We report here the reaction conditions necessary 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-cyanohalogenomethylphosphonates, 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% aq. H_3PO_4. ^{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, quartet, quintet (pentuplet) and multiplet, respectively. Low-resolution mass spectra were recorded on a Hewlett-Packard 5989 B GC-MS spectrometer (BPX5 column, positive chemical ionization 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) was 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) was then slowly added at this temperature *via* a dropping funnel. After 10 min a solution of the nitrile R′CH_2CN (30 mmol) in THF (30 mL) was slowly added at the same temperature. After 30 min a solution of diethyl chlorophosphate (5.35 g, 31 mmol) in THF (30 mL) was added at −78 °C. After 15 min at this temperature, the reaction mixture was allowed to warm 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 was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with water (10 mL), dried and evaporated to afford the expected product, which was 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, $^3J_{HH}$ 7.0, 2 × CH_3CH$_2$O), 2.87 (2 H, d, $^2J_{PH}$ 21.0, CH_2CN), 4.32 (4 H, dq, $^3J_{HH}$ 8.6 and *J* 7.0, 2 × CH$_3$CH_2O); δ_C(50.3 MHz; $CDCl_3$; Me_4Si) 16.7 (d, $^3J_{PC}$ 6.1, 2 × *C*H$_3$CH$_2$O), 16.8 (d, $^1J_{PC}$ 143.3, *C*H$_2$CN), 64.3 (d, $^2J_{PC}$ 6.6, CH$_3$*C*H$_2$O), 113.2 (d, $^2J_{PC}$ 7.3, CH$_2$*C*N); *m*/*z* (CI) 195 (M + 18, 100).

Diethyl α-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$_2$O)$_A$], 1.28 [3 H, t, $^3J_{HH}$ 7.1, (CH_3CH$_2$O)$_B$], 3.94–4.21 (4 H, m, 2 × CH$_3$CH_2O), 4.31 (1 H, d, $^2J_{PH}$ 26.4, C$_6$H$_5$C*H*CN), 7.34–7.47 (5 H, m, C$_6$*H*$_5$CHCN); δ_C(50.3 MHz; $CDCl_3$; Me_4Si) 16.5 (d, $^3J_{PC}$ 5.9, 2 × *C*H$_3$CH$_2$O), 36.9 (d, $^1J_{PC}$ 138.6, C$_6$H$_5$*C*HCN), 64.6 [d, $^2J_{PC}$ 7.3, (CH$_3$*C*H$_2$O)$_A$], 64.9 [d, $^2J_{PC}$ 7.5, (CH$_3$*C*H$_2$O)$_B$], 115.7 (d, $^2J_{PC}$ 9.4, C$_6$H$_5$CH*C*N), 127.9 (d, $^2J_{PC}$ 7.6, C_{ipso} of C$_6$H$_5$), 128.9 (s, C_{para} of C$_6$H$_5$), 129.0 (s, 2 × C_{meta} of C$_6$H$_5$), 129.3 (d, $^3J_{PC}$ 2.6, 2 × C_{ortho} of C$_6$H$_5$); *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$_2$O)$_A$], 1.28 [3 H, t, $^3J_{HH}$ 7.0, (CH_3CH$_2$O)$_B$], 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$_3$C*H*), 4.12 [2 H, dq, $^3J_{PH}$ 8.5 and $^3J_{HH}$ 7.0, (CH$_3$CH_2O)$_A$], 4.14 [2 H, dq, $^3J_{PH}$ 8.5 and $^3J_{HH}$ 7.0, (CH$_3$CH_2O)$_B$]; δ_C(50.3 MHz; $CDCl_3$; Me_4Si) 12.9 (d, $^2J_{PC}$ 6.0, *C*H$_3$CH), 16.7 (d, $^3J_{PC}$ 5.9, 2 × *C*H$_3$CH$_2$O), 23.9 (d, $^1J_{PC}$ 145.2, CH$_3$*C*H), 64.0 [d, $^2J_{PC}$ 7.3, (CH$_3$*C*H$_2$O)$_A$], 64.2 [d, $^2J_{PC}$ 6.7, (CH$_3$*C*H$_2$O)$_B$], 117.5 (d, $^2J_{PC}$ 9.2, CH*C*N); *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$_2$CH), 1.36 (6 H, t, $^3J_{HH}$ 7.0, 2 × CH_3CH$_2$O), 1.76–2.05 (2 H, m, CH$_3$-CH_2CH), 2.84 (1 H, ddd, $^2J_{PH}$ 23.4, $^3J_{HH}$ 9.9, $^3J_{HH}$ 4.8, CH$_3$-CH$_2$C*H*), 4.18 [2 H, dq, $^3J_{PH}$ 8.4 and $^3J_{HH}$ 7.0, (CH$_3$CH_2O)$_A$], 4.21 [2 H, dq, $^3J_{PH}$ 8.4 and $^3J_{HH}$ 7.0, (CH$_3$CH_2O)$_B$]; δ_C(50.3 MHz; $CDCl_3$; Me_4Si) 13.0 (d, $^3J_{PC}$ 6.0, *C*H$_3$CH$_2$CH), 16.9 (d, $^3J_{PC}$ 5.9, 2 × *C*H$_3$CH$_2$O), 21.4 (d, $^2J_{PC}$ 44, CH$_3$*C*H$_2$CH), 32.1 (d, $^1J_{PC}$ 144.1, CH$_3$CH$_2$*C*H), 64.1 [d, $^2J_{PC}$ 7.3, (CH$_3$*C*H$_2$O)$_A$], 64.3 [d, $^2J_{PC}$ 7.1, (CH$_3$*C*H$_2$O)$_B$], 116.7 (d, $^2J_{PC}$ 9.9, CH*C*N); *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$_2$CH$_2$), 1.30 (6 H, t, $^3J_{HH}$ 7.1, 2 × CH_3CH$_2$O), 1.11–1.86 (4 H, m, CH$_3$CH_2-CH_2), 2.84 (1 H, dt, $^2J_{PH}$ 23.5 and $^3J_{HH}$ 7.2, CH$_2$CH$_2$C*H*), 3.62–4.24 (4 H, m, 2 × CH$_3$CH_2O); δ_C(50.3 MHz; $CDCl_3$; Me_4Si) 13.6 (s, *C*H$_3$CH$_2$CH$_2$), 16.7 (d, $^3J_{PC}$ 5.7, 2 × *C*H$_3$CH$_2$O), 21.5 (d, $^3J_{PC}$ 12.3, *C*H$_2$CH$_2$CH), 29.2 (d, $^2J_{PC}$ 4.4, CH$_2$*C*H$_2$CH), 30.0 (d, $^1J_{PC}$ 143.6, CH$_2$CH$_2$*C*H), 64.0 [d, $^2J_{PC}$ 6.6, (CH$_3$*C*H$_2$O)$_A$], 64.3 [d, $^2J_{PC}$ 6.9, (CH$_3$*C*H$_2$O)$_B$], 116.6 (d, $^2J_{PC}$ 9.5, CH*C*N); *m*/*z* (CI) 220 (M + 1, 69), 237 (M + 18, 100).

2-(α-Cyanobenzyl)-5,5-dimethyl-2-oxo-1,3,2λ^5-dioxaphosphorinane 10b. Following the general procedure for **10a**, the intermediate anion **6b** was precipitated with conc. HCl (6 M) and filtered. 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$_2$O), 4.46 (1 H, d, $^2J_{PH}$ 27.3, CHCN), 7.41–7.56 (5 H, m, C$_6$H$_5$); 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, *C*HCN), 79.9 [d, $^2J_{PC}$ 7.6, (*C*H$_2$O)$_A$], 80.3 [d, $^2J_{PC}$ 7.6, (*C*H$_2$O)$_B$], 116.2 (d, $^2J_{PC}$ 10.7, CH*C*N), 127.8 (d, $^2J_{PC}$ 7.6, C_{ipso} of C$_6$H$_5$), 129.3 (d, $^3J_{PC}$ 6.1, 2 × C_{ortho} of C$_6$H$_5$), 129.7 (d, $^5J_{PC}$ 3.0, C_{para} of C$_6$H$_5$), 129.9 (d, $^4J_{PC}$ 3.0, 2 × C_{meta} of C$_6$H$_5$); *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) was 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) was then slowly added at this temperature *via* a dropping funnel. After 10 min a solution of **3a** (5 mmol) in THF (10 mL) was 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) was added at −78 °C and the reaction mixture was allowed to warm to 0 °C, then was poured, with stirring, into a mixture of 3 M HCl (25 mL), CH_2Cl_2 (25 mL) and ice (10 g). The aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL). The combined organic layers were washed with water (10 mL), dried and evaporated to afford the expected product. **17** is stable at room temperature, **18** decomposed slowly on storage and **19** decomposed during work-up.

Diethyl chloro(cyano)methylphosphonate 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_3-CH$_2$O)$_A$], 1.46 [3 H, td, $^3J_{HH}$ 7.1 and $^4J_{PH}$ 0.8, (CH_3CH$_2$O)$_B$], 4.31–4.48 (4 H, m, 2 × CH$_3$CH_2O), 4.98 (1 H, d, $^2J_{PH}$ 17.5, ClC*H*CN); δ_C(50.3 MHz; $CDCl_3$; Me_4Si) 17.0 (d, $^3J_{PC}$ 4.5, 2 × *C*H$_3$CH$_2$O), 35.5 (d, $^1J_{PC}$ 157.6, Cl*C*HCN), 66.5 [d, $^2J_{PC}$ 5.0, (CH$_3$*C*H$_2$O)$_A$], 66.8 [d, $^2J_{PC}$ 6.5, (CH$_3$*C*H$_2$O)$_B$], 113.5 (d, $^2J_{PC}$ 4.6, ClCH*C*N); *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 bromo(cyano)methylphosphonate 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 [3 H, $^3J_{HH}$ 7.1, $^4J_{PH}$ 0.6, td, (CH_3CH$_2$O)$_A$], 1.37 [3 H, $^3J_{HH}$ 7.1, $^4J_{PH}$ 0.6, td, (CH_3CH$_2$O)$_B$], 4.11–4.38 (4 H, m, CH$_3$CH_2O), 4.50 (1 H, $^2J_{PH}$ 16.2, d, BrCHCN); δ_C(50.3 MHz; $CDCl_3$; Me_4Si) 16.7 (d, $^3J_{PC}$ 5.7, *C*H$_3$CH$_2$O), 17.6 (d, $^1J_{PC}$ 155.9, Br*C*HCN), 66.2 [d, $^2J_{PC}$ 6.6, (CH$_3$*C*H$_2$O)$_A$], 66.5 [d, $^2J_{PC}$ 7.3, (CH$_3$*C*H$_2$O)$_B$], 113.6 (d, $^2J_{PC}$ 6.0, BrCH*C*N); *m*/*z* (CI) Decomposition.

Tetraethyl cyanomethylenediphosphonate 5a[43]

n-BuLi (20.6 mL of 1.6 M solution in hexane; 33 mmol) was added to THF (20 mL) cooled to −78 °C. A solution of diisopropylamine (13.43 g, 34 mmol) in THF (10 mL) was then slowly added at this temperature *via* a dropping funnel. After 10 min a solution of acetonitrile (0.41 g, 10 mmol) in THF (10 mL) was slowly added at the same temperature. After 30 min a solution of diethyl chlorophosphate (3.62 g, 21 mmol) in THF (10 mL) was added at −78 °C. After 15 min at this temperature,

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

Compound	**4b**	**5b**	**10b**
Molecular formula	$C_{38}H_{68}Li_3N_3O_{20}P_6$ [a]	$C_{12}H_{21}NO_6P_2$	$C_{13}H_{16}NO_3P$
Relative molecular mass	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
Independent reflections	5535	6688	2870
R_{int}		0.041	
Reflections used	4826	3638	1963
$wR2$	0.1158	0.1398	0.2486
$R1$	0.0409	0.0537	0.0599

[a] $3C_{12}H_{20}LiNO_6P_2 \cdot C_2H_6O \cdot H_2O$.

the reaction mixture was allowed to warm to 0 °C, then was poured, with stirring, into a mixture of 3 M HCl (25 mL), CH_2Cl_2 (25 mL) and ice (10 g). The aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL). The combined organic layers were washed with water (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_2O), 2.89 (1 H, d, $^2J_{PH}$ 21.0, CHCN), 4.21–4.36 (8 H, m, 4 × CH_3CH_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_3CH_2O), 111.7 (t, $^2J_{PC}$ 10.4, CH*C*N); *m*/*z* (CI) 314 (M + 1, 100), 331 (M + 18, 25).

1-Cyanomethylenebis(5,5-dimethyl-2-oxo-1,3,2λ^5-dioxaphosphorinane) 5b. Following the procedure for **5a**, the intermediate anion **4b** was precipitated with conc. HCl (6 M) and filtered. 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}), CH exchanged with $CDCl_3$; δ_C(50.3 MHz; $CDCl_3$; Me_4Si) 21.1 [s, 2 × $(CH_3)_A$], 22.6 [s, 2 × $(CH_3)_B$], 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 × CH_2O), 112.1 (t, $^2J_{PC}$ 10.7, CH*C*N); *m*/*z* (CI) 338 (M + 1, 100), 355 (M + 18, 88).

Cyano(lithio)methylenebis(5,5-dimethyl-2-oxo-1,3,2λ^5-dioxaphosphorinane) 4b. Compound **5b** in THF solution was deprotonated with a stoichiometric quantity of previously titrated *n*-BuLi (1.6 M in hexane). Evaporation of the THF solution gave compound **4b** 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 × $(CH_3)_A$], 22.0 [s, 2 × $(CH_3)_B$], 33.4 [s, 2 × *C*$(CH_3)_2$], 78.1 (s, 4 × CH_2O), 127.4 (s, CLi*C*N).

The crystal structures of (i) cyano(lithio)methylenebis(5,5-dimethyl-2-oxo-1,3,2λ^5-dioxaphosphorinane) 4b, (ii) cyanomethylenebis(5,5-dimethyl-2-oxo-1,3,2λ^5-dioxaphosphorinane) 5b and (iii) 2-(α-cyanobenzyl)-5,5-dimethyl-2-oxo-1,3,2λ^5-dioxaphosphorinane 10b

Crystals suitable for X-ray diffraction were obtained from EtOH by slow evaporation (**4b**) or from CH_2Cl_2–hexane by diffusion (**5b**, **10b**) of 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 SHELXl-97.[44] Illustrations were made using PLATON.[45] Crystal data are assembled in Table 3. Atomic coordinates, bond lengths and angles, and thermal parameters for compounds **4b**, **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.

Acknowledgements

We thank Elf Atochem S.A. for financial support to B. I., and Dr M. Levard (UMR 7652) of the Ecole Polytechnique for the mass spectra.

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