Methyl(cyanomethyl)phosphines. Synthesis and Nucleophilic Reactivity

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The preparation of \( \text{Me}_2\text{PCH}_2\text{CN} \), \( \text{MeP(CH}_2\text{CN})_2 \) and \( \text{P(CH}_2\text{CN})_3 \) is described, and phosphorus lone-pair ionization potentials and second order rate constants for their reactions with benzyl bromide in acetonitrile at 35 °C are determined. The rate constant for \( \text{Me}_2\text{PCH}_2\text{CN} \) is approximately the same as that for \( \text{Ph}_3\text{P} \), whereas that for \( \text{P(CH}_2\text{CN})_3 \) is \( 2 \times 10^9 \) times smaller. This low nucleophilicity of cyanomethylphosphines is ascribed to polar effects from the cyano group(s) which contracts the phosphorus lone-pair.

(Cyanomethyl)phosphines, \( \text{R}_3\text{nP(CH}_2\text{CN})_n \), are examples of C-functionalized tertiary phosphines which have recently attracted considerable interest, mainly because of their potential as chelating ligands. Introduction of functional groups close to the phosphorus atom, however, changes the donor property of phosphorus for both steric and electronic reasons, and accordingly changes the coordinating ability (towards metal centers) and nucleophilicity (towards carbon centers). Obviously it would be valuable to have quantitative information on how different functional groups change the donor property in order to help designing new phosphines with specific properties. Functionalization at the α-carbon should give maximum effects, and many such substituted phosphines are now known, e.g., the trisubstituted phosphines \( \text{P(CH}_2\text{OH})_3 \), \( \text{P(CH}_2\text{NR}_2)_3 \), \( \text{P(CH}_2\text{PMe}_2)_3 \), \( \text{P(CH}_2\text{COOEt})_3 \), \( \text{P(CH}_2\text{COOH})_3 \) and \( \text{P(CH}_2\text{CN})_3 \). However, we are aware of only one quantitative study of the nucleophilic reactivity of α-substituted phosphines. The quaternization of some diphenylphosphinoacetic acid derivatives with ethyl iodide has been correlated with Taft \( \sigma^+ \) values and phosphorus lone-pair ionization potentials.

The present paper describes the preparation of two new α-substituted phosphines, \( \text{Me}_2\text{PCH}_2\text{CN} \) and \( \text{MeP(CH}_2\text{CN})_2 \), a new route (eqn. (4)) to the known \( \text{P(CH}_2\text{CN})_3 \), and quantitative results on their very different nucleophilic reactivities.

**Synthesis.** (Cyanomethyl)phosphines have hitherto been prepared by three methods [eqn. (1)–(3)]. The first method [eqn. (1)]

\[
\begin{align*}
\text{R}_2\text{POEt} + \text{ClCH}_2\text{CN} & \rightarrow \\
\text{R}_2\text{P(O)CH}_2\text{CN} & \xrightarrow{\text{Ph}_2\text{SiH}_2} \text{R}_2\text{PCH}_2\text{CN} \\
\text{Ph}_3\text{nP(SiMe}_3)_n + n & \text{ClCH}_2\text{CN} \rightarrow \\
\text{Ph}_3\text{nP(CH}_2\text{CN})_n + n & \text{Me}_3\text{SiCl} \\
\text{PCL}_3 + 3 \text{Bu}_3\text{SnCH}_2\text{CN} & \rightarrow \\
\text{P(CH}_2\text{CN})_3 + 3 & \text{Bu}_3\text{SnCl}
\end{align*}
\]

allows only one cyanomethyl group to be introduced but is otherwise fairly general. This method was chosen to prepare \( \text{Me}_2\text{PCH}_2\text{CN} \). The second route [eqn. (2)] involves the preparation of silylphosphines which are very reactive and sometimes difficult to obtain, and the yield is low for \( n = 3 \). The third method [eqn. (3)] seems fairly general (\( \text{Cl}_2\text{PCH}_2\text{CN} \) and \( \text{MeP(CH}_2\text{CN})_2 \) have been similarly obtained) but its drawback is the low yield synthesis of \( \text{Bu}_3\text{SnCH}_2\text{CN} \). To obtain \( \text{MeP(CH}_2\text{CN})_2 \) and \( \text{P(CH}_2\text{CN})_3 \), we therefore attempted a synthesis via the known Reformatsky reagent \( \text{BrZnCH}_2\text{CN} \) [eqn. (4)], in analogy with Podla-
hová’s successful syntheses of Ph₃-nP-(CH₂COOEt)ₙ.

The reactions when run at low temperatures (-78 °C) gave MeP(CH₂CN)₂ and P(CH₂CN)₃ in fair yields. As it is a one pot synthesis from readily obtainable starting materials, this route is considered the most attractive one to prepare (cyanomethyl)phosphines with two or three cyanomethyl groups.

\[
\text{Me}_3-n\text{P}Cl_n + n \text{BrZnCH₂CN} \rightarrow \text{Me}_3-n\text{P(CH₂CN)}_n
\]

**Nucleophilic reactivity.** P(CH₂CN)₃ reacts very slowly with alkyl halides. Several days, in refluxing acetonitrile with excess benzyl bromide, were necessary to prepare PhCH₂P⁺(CH₂CN)₂Br⁻, and refluxing with excess ethyl iodide in acetonitrile did not give appreciable amounts of a phosphonium salt after 2 days. The above benzylphosphonium salt hydrolyzes easily at room temperature to give PhCH₂P(O)(CH₂CN)₂. This reflects the good leaving group ability of the cyanomethyl group which, more surprisingly, also manifests itself in the properties of P(CH₂CN)₃. Although fairly stable to water and dilute HCl, P(CH₂CN)₃ is rapidly hydrolyzed to HPO₃²⁻ and CH₂CN by aqueous NaOH at room temperature. MeP(CH₂CN)₂ and Me₂PCH₂CN react more smoothly with alkyl halides, and only PhCH₂(Me)P⁺(CH₂CN)₂Br⁻ is somewhat prone to hydrolysis.

Quantitative results on the nucleophilic reactivity of Me₃PCH₂CN, MeP(CH₂CN)₂ and P(CH₂CN)₃ were obtained from following, by conductivity measurements, their reactions with benzyl bromide in acetonitrile at 35 °C. The second order rate constants for quantization, including that of Ph₃P for comparison, are given in Table 1, together with the Taft σ⁺ values and the phosphorus lone-pair ionization potentials (IP).

**Table 1.** Rate constants for quantization, Taft σ⁺ values and phosphorus lone-pair ionization potentials of Me₃-nP(CH₂CN)ₙ and Ph₃P.

<table>
<thead>
<tr>
<th></th>
<th>(k_2 )</th>
<th>(\Sigma \sigma^+)</th>
<th>IP (eV)</th>
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<tbody>
<tr>
<td>P(CH₂CN)₃</td>
<td>1.3×10⁻⁷</td>
<td>5.13</td>
<td>10.59</td>
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<tr>
<td>MeP(CH₂CN)₂</td>
<td>3.0×10⁻⁵</td>
<td>3.42</td>
<td>9.83</td>
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<tr>
<td>Me₂PCH₂CN</td>
<td>3.9×10⁻³</td>
<td>1.71</td>
<td>9.22</td>
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<tr>
<td>Ph₃P</td>
<td>3.0×10⁻³</td>
<td>1.80</td>
<td>7.88</td>
</tr>
</tbody>
</table>

* Second order rate constant for quantization with benzyl bromide in acetonitrile at 35 °C. *σ⁺=0.00 for Me, 0.60 for Ph and 1.71 for CH₂CN. * Vertical ionization potentials.

![Fig. 1. Plot of rate constant versus Taft σ⁺ values for the reaction R₃P+PhCH₂Br → R₃PhCH₂P⁺Br⁻ in acetonitrile at 35 °C.](image1)

![Fig. 2. Plot of rate constant versus phosphorus lone-pair ionization potential for the reaction R₃P+PhCH₂Br → R₃PhCH₂P⁺Br⁻ in acetonitrile at 35 °C.](image2)

log $k_2$ with IP for Me$_2$PCH$_2$CN, Me$_2$P(CH$_2$CN)$_2$ and P(CH$_2$CN)$_3$ indicates that the cyano groups exert a field (or inductive) effect on the lone-pair which results in a contraction of it and thereby makes it less available for reactions.

This conclusion is corroborated by CNDO/2 calculations, which show that the electron density in the lone pair region of P(CH$_2$CN)$_3$ is reduced relative to that of Me$_2$P. *Ab initio* calculations on Me$_2$PCH$_2$CN and low temperature X-ray diffraction studies on P(CH$_2$CN)$_3$ are in progress with the aim to give more evidence on the electron distribution in these cyanomethylphosphines.

**EXPERIMENTAL**

Analyses were performed by the microanalytical department of this laboratory. $^1$H and $^{31}$p NMR spectra were recorded on a JEOL FX 90 Q Fourier NMR spectrometer. Chemical shifts (ppm) are given relative to internal TMS for $^1$H spectra ($\delta_H$) and external 85 % H$_3$PO$_4$ for $^{31}$p spectra ($\delta_p$), and are given as positive for low-field shifts. The He(I) photoelectron spectra were obtained on a Perkin-Elmer PS 18 spectrometer calibrated using the 2P3/2 peaks of Ar and Xe. Ionization potentials were reproducible within $\pm 0.03$ eV. The kinetic measurements were performed at 35.0±0.2°C using the conductivity method of Henderson and Buckler. A Radiometer CDM 2 Conductivity Meter and a cell with platinumized platinum electrodes with a cell constant of 0.97 cm$^{-1}$ was used. Acetonitrile (Merck "Uvasol") was purified through a column of neutral Al$_2$O$_3$ (Woelm N-Super I) and deoxygenated by bubbling Ar through it for 10 min. The solvent thus purified had a conductivity of less than 0.2 $\mu$S/cm$^{-1}$. The solutions were prepared at 20°C and corrected for concentration changes upon heating to 35°C. The reactions were followed until a few percent of the phosphine had reacted. The rate constants were calculated from the linear approximation $kt = x/ab$. Benzyl bromide and phosphine concentrations were varied to prove that the reactions were second order. Up to ten times molar excess of benzyl bromide was used for the more slowly reacting phosphines to ensure convenient rates. The calculated rate constants (Table 1) are the results of duplicate runs, which were reproducible within $\pm 10\%$. All manipulations with phosphines were carried out under N$_2$ or Ar.

P,P-Dimethylphosphinoylacetonitrile (Me$_2$P(O)CH$_2$CN). Me$_2$POBu $^{21}$ (3.35 g, 25 mmol) was added in 0.5 ml portions to CIH$_2$CN (3.8 g, 50 mmol) at 75°C with stirring. After 1 h at 75°C BuCl and excess CIH$_2$CN were removed in vacuo and the residue recrystallized from ethyl acetate to give Me$_2$P(O)CH$_2$CN (1.90 g, 65 %), m.p. 75–78°C (hygroscopic). Anal. C$_4$H$_8$NP: C, H, N, NMR (CDCl$_3$): $\delta_p$ 38.0; $\delta_H$ 1.76 (CH$_3$, d, $^2J_{PH}$ 13.2 Hz), 3.04 (CH$_2$, d, $^2J_{PH}$ 15.1 Hz).

P,P-Dimethylphosphinooacetanitile (Me$_2$PCH$_2$CN). A mixture of Me$_2$P(O)CH$_2$CN (1.75 g, 15 mmol) and PH$_2$SiH$_2$ (2.76 g, 15 mmol) was heated with stirring to 175°C for 6 h. Vacuum distillation through a small Claisen head gave Me$_2$PCH$_2$CN (1.24 g, 82 %), b.p. 58–59°C/12 mmHg. The purity was more than 97 % according to $^1$H and $^{31}$p NMR. NMR (CDCl$_3$): $\delta_p$ -50.1; $\delta_H$ 1.19 (CH$_3$, d, $^2J_{PH}$ 3.8 Hz), 2.40 (CH$_2$, d, $^2J_{PH}$ 5.6 Hz).

Benzyl(cyanomethyl)dimethylphosphonium bromide (PhCH$_2$Me$_2$P*CH$_2$CN Br). A mixture of Me$_2$PCH$_2$CN (0.20 g, 2 mmol) and PhCH$_2$Br (0.68 g, 4 mmol) in dry ether (10 ml) was kept at 20°C for 6 days. The precipitate was washed with ether, dried and recrystallized from 2-propanol to give the product (0.33 g, 60 %), m.p. 120–121.5°C. Anal. C$_{11}$H$_8$BrNP: C, H, N, Br. NMR (CD$_2$CN): $\delta$ 31.7.

P-methylphosphonyldiacetonitile (Me$_2$P(CH$_2$CN)$_2$). A solution of BrCH$_2$CN (7.20 g, 60 mmol) in dry THF (30 ml) was added during 20 min to a stirred suspension of Zn (Riedel-de Haen "chem. rein, geraspelt", freshly etched with 0.2 M HCl followed by washing with water, acetone, ether and drying; 3.92 g, 60 mmol) in dry THF (10 ml). The temperature was kept at ca. 20°C by occasional immersion in an ice-bath. The resulting green to brown solution was cooled to -78°C and MePCl$_3$ (3.51 g, 30 mmol) in dry THF (10 ml) added with stirring during 20 min. The reaction mixture was allowed to reach room temperature slowly (over ca. 6 h), filtered through a glasswool plug and the precipitate washed with THF (2×10 ml). The solvent was removed at 10 mmHg and the residue dissolved in deoxygenated water (20 ml). The product was extracted with CH$_2$Cl$_2$ (2×20 ml) and the CH$_2$Cl$_2$ solution washed with water (20 ml) and dried (Na$_2$SO$_4$). Evaporation of the solvent and distillation in vacuo through a small Claisen head gave MeP(CH$_2$CN)$_2$ (1.13 g, 30 %), b.p. 99–102°C/0.20 mmHg. The purity was higher than 97 % according to $^1$H and $^{31}$p NMR. NMR (CDCl$_3$): $\delta_p$ -38.2; $\delta_H$ 1.37 (CH$_3$, d, $^2J_{PH}$ 5.5 Hz), 2.63 (CH$_2$, AB part of ABX spectrum, $\Delta$$_{AB}$ 0.04 ppm, $^2J_{AB}$ 17.2, $^2J_{PH}$ 5.4 and 6.0 Hz).

P-methylphosphonnoylidiacetonitile (Me$_2$P(O)(CH$_2$CN)$_2$). MeP(CH$_2$CN)$_2$ (0.13 g, 1
mmol) in CH₂Cl₂ (5 ml) was oxidized by bubbling NO₂ through the solution until a green colour remained. Evaporation of the solvent and recrystallization of the residue from abs. ethanol gave the product (0.09 g, 60 %), m.p. 93–94 °C. Anal. C₆H₁₂N₂O₂P: C, H, N. NMR ((CD₃)₂CO): δₚ 31.1; δH 1.90 (CH₃, d, 2JₚH 13.8 Hz), 3.49 (CH₂, d, 2JₚH 14.5 Hz).

Benzylid(cyanomethyl)methylphosphonium bromide (PhCH₂MeP⁺(CH₂CN)₂ Br⁻). A mixture of MeP(CH₂CN)₂ (0.50 g, 4 mmol) and PhCH₂Br (1.37 g, 8 mmol) in CH₂CN (5 ml) was refluxed for 20 h. The solvent was removed in vacuo and the residue washed with hexane to remove excess PhCH₂Br. Recrystallization from a small amount of CH₃CN gave the product (0.47 g, 40 %), m.p. 121.5–122.5 °C. Anal. C₁₂H₁₄BrN₂P: C, H, N, Br. NMR (CD₃CN): δp 33.2.

Phosphinetrityriacetonitrile (P(CH₂CN)₃). This phoshine was prepared in the same way as MeP(CH₂CN)₂, from BrCH₂CN (7.20 g, 60 mmol), Zn (3.92 g, 60 mmol) and PCl₃ (2.20 g, 16 mmol) in THF (50 ml). The reaction mixture, after reaching room temperature, was heated to reflux with active carbon and then filtered through a glasswool plug. The solvent was removed in vacuo and the brown residue was dissolved in hot, deoxygenated water (5 ml). Cooling to 0 °C gave a crystalline product which was recrystallized once from water, with addition of active carbon, to give P(CH₂CN)₃ (1.07 g, 45 %), m.p. 110–111.5 °C (lit. 110.5–112.5 °C).

Benzyltris(cyanomethyl)phosphonium bromide (PhCH₂P⁺(CH₂CN)₃ Br⁻). A mixture of P(CH₂CN)₃ (0.76 g, 5 mmol) and PhCH₂Br (3.4 g, 20 mmol) in CH₂CN (7 ml) was heated to reflux for 4 days. The precipitate, after cooling, was filtered off and recrystallized from CH₂CN to give the product (1.02 g, 64 %), m.p. 199–201 °C. Anal. C₁₅H₁₄BrN₃P: C, H, N, Br. NMR (CD₃CN): δp 31.6; δq 4.69 (CH₂CN, d, 2JₚH 15.5 Hz), 4.74 (CH₂Ph, d, 2JₚH 14.9 Hz), 7.54 (Ph).

P-benzylphosphonyloldiacetonitrile (PhCH₂P(O)(CH₂CN)₂). PhCH₂P⁺(CH₂CN)₃ Br⁻ (0.32 g, 1 mmol) and water (3 ml) were heated to give a clear solution. The product crystallized on cooling (0.19 g, 87 %), m.p. 163.5–165 °C. Anal. C₁₃H₁₁N₂O₃P: C, H, N. NMR (CD₃CN): δp 32.0; δq 3.18 (CH₂CN, d, 2JₚH 13.4 Hz), 3.52 (CH₂Ph, d, 2JₚH 14.8 Hz), 7.36 (Ph).

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REFERENCES


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