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Synthesis and Characterization of Alkyltris(2-pyridyl)phosphonium Salts

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*Alkytris(2-pyridyl)phosphonium salts [(2-Py)$_3$PR]X **1** [**1a**, R = Et, X = Br; **1b**, R = Pr, X = Br; **1c**, R = Bu, X = Br; **1d**, R = CH_2Ph, X = Br; **1e**, R = CH_2Ph, X = Cl] were synthesised from (2-Py)$_3$P and an excess of RCl. **1c** and **1e** were found to rapidly decompose in hot acetone to 2,2′-bipyridinium(+1) bromide **2** and (2-Py)P(O)(CH_2Ph)C(OH)Me$_2$ **3**, respectively. A reaction mechanism for both products is proposed. All compounds were fully characterized, including X-ray crystallography for **1a** and **3** with **1a** being the first representative of this class of compounds characterized by this technique.*

Keywords 2-Pyridylphosphonium salts; α-hydroxyphosphine oxide; hydrolysis; X-ray

INTRODUCTION

The antitumor activity of a range of lipophilic cations including Rhodamine-123,[1] dequalinium1,[2] AA1,[3] bisquaternary ammonium heterocycles,[4] MKT-077,[5] tetrahedral bidentate phosphine Au(I) complexes,[6] and alkyltriarylphosphonium salts[7] has been well established. An antimitochondrial mode of action as a result of their lipophilic cationic character and consequent uptake into the mitochondria has been suggested. For several types of lipophilic cations (*e.g.*, Au(d*n*pype)$_2^+$, $n = 2$–4, d*n*pype = 1,2-bis(di-*n*-pyridylphosphino)ethane[6]; Ph_4PCl[8]) it was demonstrated that the

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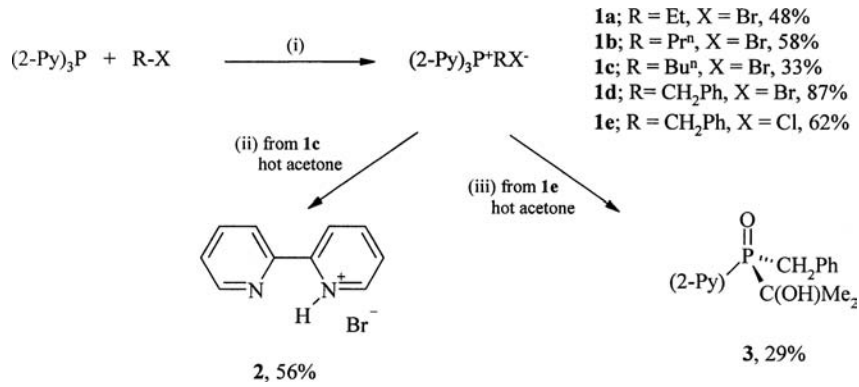
selectivity of compounds for tumor cells was increased by modifying the lipophilic/hydrophilic balance and increasing their hydrophilicity. The replacement of phenyl groups in $[Au(dppe)_2]^+$ [dppe = 1,2-bis-(diphenylphosphino)ethane][6] by hydrophilic pyridyl groups was found to be particularly promising as the systematic variation of the position of the N atom in the pyridyl ring modulated the lipophilicity and increased the selectivity for tumor cells versus normal cells. The lipophilic cation $[Au(dppe)_2]^+$ was in contrast found to be nonselective and toxic to mitochondria of all cells,[6] while the related hydrophilic cation $[Au(dpmaa)_2]^+$ [dpmaa = 1,2-bis(diphenyphosphino)maleic acid][9] showed a high water solubility and very limited activity. Following the previously mentioned study on triarylalkylphosphonium salts by Rideout et al.,[7] we had previously synthesized a series of cyclic phosphonium salts[10] that were, however, found to be unstable in water or biological fluids. It was therefore decided to investigate the potential of tris(2-pyridyl)alkylphosphonium salts that so far have found very limited interest in the chemical literature[11] as anticancer drugs. This manuscript describes the synthesis and characterization of a series of tris(2-pyridyl)alkylphosphonium bromides.

SYNTHESIS AND PROPERTIES OF $[(2\text{-Py})_3PR]X$

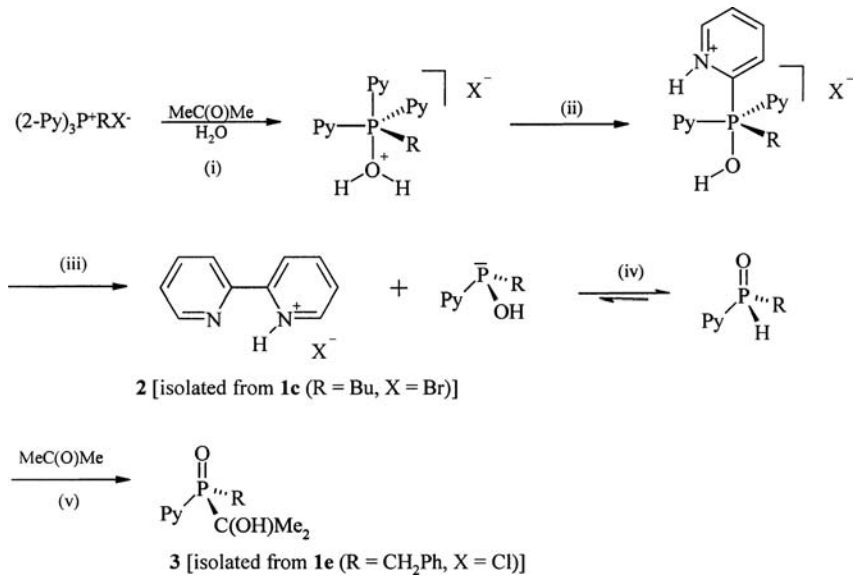
The reaction of $(2\text{-Py})_3P$[11b] with an excess of alkyl halide under reflux conditions and reaction times of several hours yielded the pyridylphosphonium salts $[(2\text{-Py})_3PR]X$ **1** ((i) in Scheme 1). In the case of the less reactive PhBr, product formation was not observed, and extended reaction times in the presence of air led instead to the formation of $(2\text{-Py})_3PO$ that was previously obtained from alkoxyphosphonium salts via an Arbuzov reaction.[12] In agreement with previous reports for tertiary



SCHEME 1 Synthesis of tris(2-pyridyl)phosphonium salts.

phosphines,[11,13a] there was no significant quaternization at the nitrogen atom (there were only minor peaks in the ^{31}P-NMR spectrum of the crude products). Preferential quaternization at the nitrogen atom has previously mainly been observed for primary phosphines RPH_2 and in cases were strong Brønsted acids (H^+) were used as electrophiles.[13] This behavior is a reflection of the higher nucleophilicity of tertiary phosphines and the higher basicity of amines. Attempts to synthesise 3-Py and 4-Py analogues of **1** under similar reaction conditions as described for $(2\text{-Py})_3$P were unsuccessful. Monitoring by ^{31}P-NMR spectroscopy showed that reactions were slower for EtBr, and prolonged heating resulted in a mixture of products that could not be separated. A similar behavior was observed for the reaction of $(3\text{-Py})_3$P with $PhCH_2X$ (X = Br, Cl), while in the case of $(4\text{-Py})_3$P and $PhCH_2Cl$, a fast reaction resulted in an unidentifiable green paste.

Phosphonium salts were colorless (**1a**, **1b**) or yellow (**1c–1e**) solids that were soluble in polar solvents such as acetone (not **1d**, **1e**) or methanol (not **1e**, due to rapid decomposition) and could be recrystallized from a mixture of polar and nonpolar solvents. When **1c** or **1e** were briefly heated in acetone to increase their solubility, they were found to decompose rapidly to the 2,2′-bipyridinium(+1) bromide **2** ((ii) in Scheme 1) and/or the phosphine oxide **3** ((iii) in Scheme 1),



SCHEME 2 Proposed reaction mechanism for the formation of **2** and **3** (*c.f.* reference 16).

respectively, which were both fully characterized including X-ray crystallography (the crystal structure of **2** was reported in ref. 14). Uchida et al.[11d,12,15,16] have previously reported in closely related systems the formation of bipyridines from (1) the reaction of 2-pyridylphosphines or 2-pyridylphosphine oxides and chlorine followed by slow hydrolysis in alcohol or water and (2) the slow reaction of pyridylphosphine oxides or **1d** with H_2O (CH_3OH) or $H_2O(CH_3OH)$/HCl, respectively. In this work, the same authors proposed a reaction mechanism (Scheme 2[11d,16]) that accounts for the formation of **2** and **3**. It involves the nucleophilic addition of water to the phosphonium salt to give a pentacoordinate phosphorous intermediate ((i) in Scheme 2), followed by proton migration to the nitrogen atom of a pyridyl ring ((ii) in Scheme 2) and reductive elimination of the bipyridine ((iii) in Scheme 2) to give the phosphinic acid (2-Py)PR(OH) and its thermodynamically favored tautomer (2-Py)P(O)(R)H ((iv) in Scheme 2). The isolation of **3** lends further support to this reaction mechanism as phosphinous acids such as (2-Py)P(O)(R)H are known to rapidly add to ketones and aldehydes to yield α-hydroxyphosphine oxides ((v) in Scheme 2) (reference 17 and references therein).

The hydrolytic instability of the phosphonium salts as evident from the rapid reaction in wet acetone was further confirmed by NMR experiments that showed that all compounds decomposed completely within 24 h in D_2O or DMSO/foetal calf serum to a number of unidentified products. Phosphine oxides similar to **3** are likely to be major components of the mixture based on signals in the ^{31}P NMR spectrum (δ 31.1–39.2) close to that of **3** (δ 39.0). This lack of stability precluded further biological testing.

Table I summarizes selected NMR spectroscopic data of pyridyl phosphorous compounds together with their phenyl analogues. The ^{13}C NMR signals of the *ipso*-C atoms of the pyridyl compounds were shielded in comparison to the phenyl derivatives as was expected from the available data for substituted pyridines and benzenes, respectively.[22] The ^{31}P NMR values of the pyridyl derivatives were in contrast deshielded by more than $\delta = 10$ if compared to the phenyl analogues. The coupling constant [^1J(CP), ^2J(HP)] of the alkyl substituents of the phosphonium salts were essentially the same in all compounds and significantly smaller than those of corresponding aryl groups. This has previously been attributed to the increased *s* character and electronegativity of the *ipso*-C atoms of the aryl substituents.[20a,23] The latter argument may also explain the much higher coupling constants of pyridyl derivatives (the presence of N should increase the electronegativity of the *ipso*-C) as compared to phenyl analogues.

TABLE I Selected NMR-Spectroscopic Data (ppm, Hz) of 2-Pyridyl Phosphorous Compounds and Their Phenyl Analogues

Compound	δ (^{31}P)	δ (^{13}C, *ipso*-Ar)	^{1}J[C(R)-P]	^{1}J[C(Ar)-P]	^{2}J(H-P)
[(2-Py)$_3$PEt]Br	15.4	142.8	50.7	115.0	14.3
[(2-Py)$_3$PPr^n]Br	13.2	142.4	48.9	114.9	m
[(2-Py)$_3$PBu^n]Br	13.5	142.9	49.4	115.0	m
[(2-Py)$_3$P(CH$_2$Ph)]Br	11.8	142.8	45.9	115.2	15.5
[(2-Py)$_3$P(CH$_2$Ph)]Cl	12.0	143.1	45.0	115.2	15.5
(2-Py)$_3$PO	14.8	154.7	—	133.1	—
(2-Py)P(O)(CH$_2$Ph) CH(OH)Me$_2$ **3**	39.0	155.6	58.4	106.5	13.6
[Ph$_3$PEt]Br[18]	26.8	117.3	51.0	85.9	12.6
[Ph$_3$PPr^n]Br[19]	24.1	118.3	50.0	—	—
[Ph$_3$PBu^n]Br[18]	25.8	117.9	49.8	85.9	—
[Ph$_3$P(CH$_2$Ph)]Br[19a]	23.6	—	—	—	—
[Ph$_3$P(CH$_2$Ph)]Cl[20]	23.2	118.5	47.2	85.6	—
Ph$_3$PO[21]	29.3	132.8	—	103.5	—

SOLID STATE STRUCTURES OF 1A AND 3

Compound **1a** is, to the best of our knowledge, the first example of a crystallographically characterized tris(2-pyridyl)phosphonium salt. It crystallizes in the triclinic space group $P\bar{1}$ with one ion pair in the asymmetric unit (Figure 1). The coordination of the phosphorous atom in the cation is essentially tetrahedral showing bond distances and angles (Table II) that are comparable to those in related triphenylphosphonium salts such as [Ph$_3$PEt]I$_3$,[24] [Ph$_3$PCH$_2$Ph]Br,[25] [Ph$_3$PMe]X (X = BF$_4$, ClO$_4$[26], X = I_3^-),[27] or [Ph$_4$P]Br·H$_2$O.[28] In contrast to the latter class of compounds, there are, however, in **1a** additional intermolecular close contacts (2 × C-H···N) between cations and between the cation and anion (4× C-H···Br), resulting in a layer structure (Table III, Figure 2). Layers are further connected via two additional, slightly longer, C-H···Br contacts (C23-H23···Br 2.97 Å, C25-H25···Br 2.99 Å) resulting in a distorted octahedral arrangement around the Br atom and thereby creating a three-dimensional network. C-H···N and C-H···Br interactions with a mean bond distance of 2.64 Å (CH···N) and 2.75 Å (CH···Br), respectively, and C-H···X angles above 140° have been discussed in recent publications.[29]

The α-hydroxyphosphine oxide **3** crystallizes in $P2_1/c$ and has one molecule in the asymmetric unit. The coordination around phosphorous is tetrahedral (Figure 3) with O-P-C angles that are slightly larger than the C-P-C angles (Table II). Bond distances and angles compare well to those of (2-Py)$_3$PO[30] or the related α-hydroxyphosphine

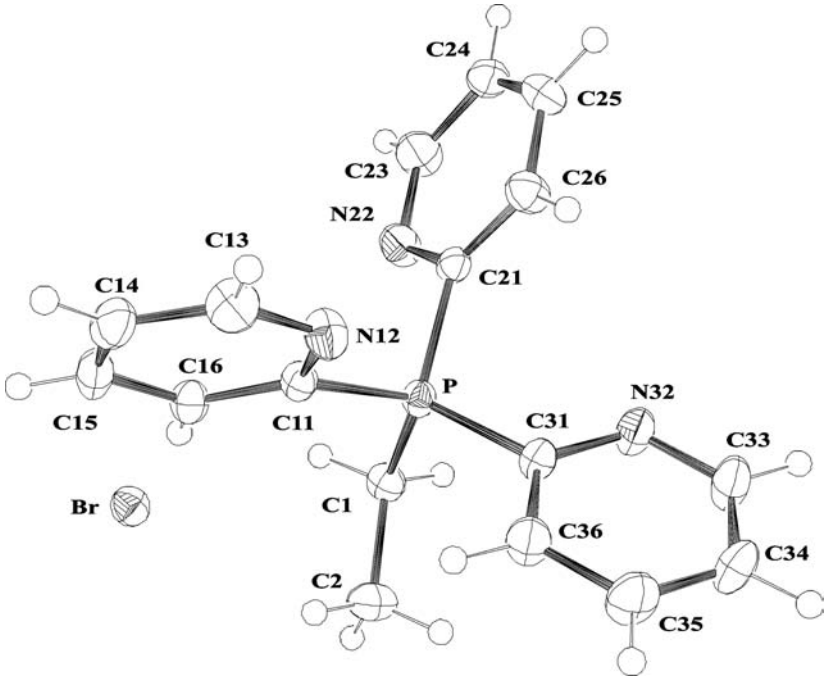


FIGURE 1 Molecular structure of [(2-Py)$_3$PEt]Br **1a**. Thermal ellipsoids are drawn on the 50% probability level. H atoms have been drawn at an arbitrary radius.

oxides PhP(O)(CH_2PH)C(Me)(Ph)OH,[31] PhP(O)(Et)C(Me)(Ph)OH,[32] Ph_2P(O)C(OH)Me_2,[33] and PhP^a(O)C(Me)$(CH_2)_2$C^{b}H$_2$(P^a-C^b).[34] The phosphorous atom of **3** is chiral (*c.f.*, the two methyl groups are inequivalent in the ^{1}H-NMR spectrum), and the two enantiomers form a

TABLE II Selected Bond Distances (Å) and Angles (°) for 1a and 3

	[(2-Py)$_3$PEt]Br **1a**	(2-Py)P(O)(CH_2Ph)CH(OH)Me_2 **3**
P-X^a	1.791 (2)	1.487 (1)
P-C11	1.805 (2)	1.817 (2)
P-C21	1.810 (2)	1.812 (2)
P-C31	1.807 (2)	1.853 (2)
X-P-C11	111.55 (9)	110.81 (7)
X-P-C21	108.68 (9)	113.34 (7)
X-P-C31	109.33 (9)	111.50 (7)
C11-P-C21	107.17 (9)	105.11 (7)
C11-P-C31	109.88 (8)	109.01 (7)
C21-P-C31	110.20 (8)	106.76 (7)

^{a}X = C1 (compound **1a**), O1 (compound **3**).

TABLE III Intermolecular Parameters (Å, °) for Compound 1a

D-H···A	D-H	H···A	D···A	D-H···A
C1-H1B···N32[a]	0.99	2.51	3.380 (2)	146
C26-H26···N12[b]	0.95	2.55	3.368 (3)	144
C1-H1A···Br	0.99	2.73	3.593 (2)	146
C14-H14···Br[c]	0.95	2.88	3.704 (2)	146
C15-H15···Br[d]	0.95	2.86	3.782 (2)	163
C16-H16···Br	0.95	2.84	3.787 (2)	174
C23-H23···Br[e]	0.95	2.99	3.756 (2)	139
C25-H25···Br[f]	0.95	2.97	3.707 (2)	135

Symmetry codes: (a) 1 − x, 1 − y, −z; (b) −x, 1 − y, −z; (c) −1 + x, y, z; (d) 1 − x, −y, 1 − z; (e) 1 − x, −y, −z; (f) −1 + x, y, −1 + z.

centrosymmetric, racemic dimer via hydrogen bonds (graph set $R_2^2(10)$) between the oxygen atom O1 of the phosphine oxide and the hydroxy functionality (Figure 4, Table IV), resulting in a molecular conformation where O1 and O2 are pointing approximately in the same direction [torsion angle O1-P-C31-O2 69.8(1)°]. This is the first example of such a structural motif in α-hydroxyphosphine oxides. Previously,

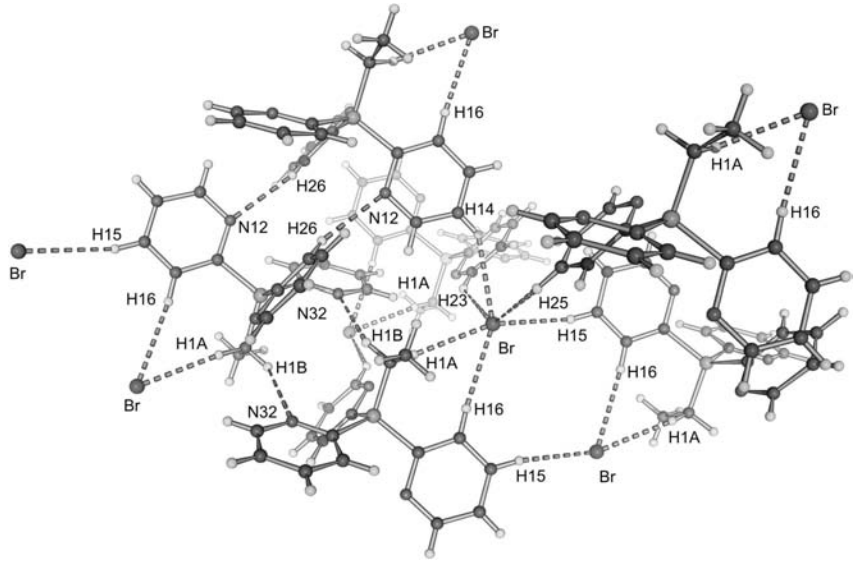


FIGURE 2 Intermolecular contacts in $[(2\text{-Py})_3\text{PEt}]\text{Br}$ **1a**.

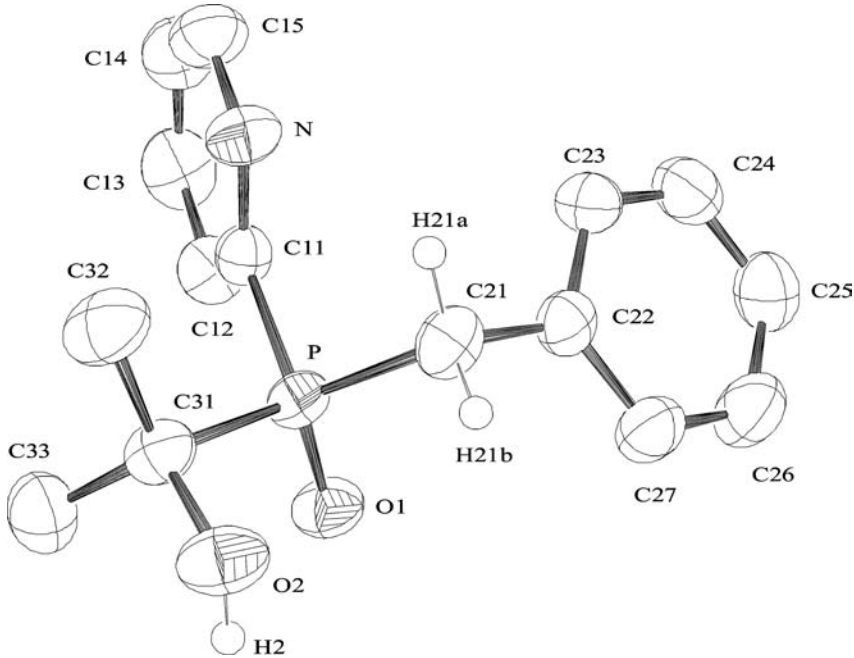


FIGURE 3 Molecular structure of (2-Py)P(O)(CH_2Ph)C(OH)Me_2 **3**. Thermal ellipsoids are drawn on the 50% probability level. H atoms (except CH_2 and OH) have been omitted for clarity.

only H-bonding resulting in infinite linear chains with O-P-C-O torsion angles in the range of 175 to 180° was observed for this class of compounds.

EXPERIMENTAL

Synthesis

Solvents were used directly as purchased from Sigma Aldrich and not dried. Deuterated solvents were degassed by freeze-drying and kept under argon and molecular sieves. NMR spectra were recorded in $CDCl_3$

TABLE IV H-bonding (Å,°) in compound 3

D-H···A	D-H	H···A	D···A	D-H···A
O2-H2···O1[a]	0.84	1.89	2.703(2)	163

Symmetry code: (a) −x, −y + 1, −z + 1.

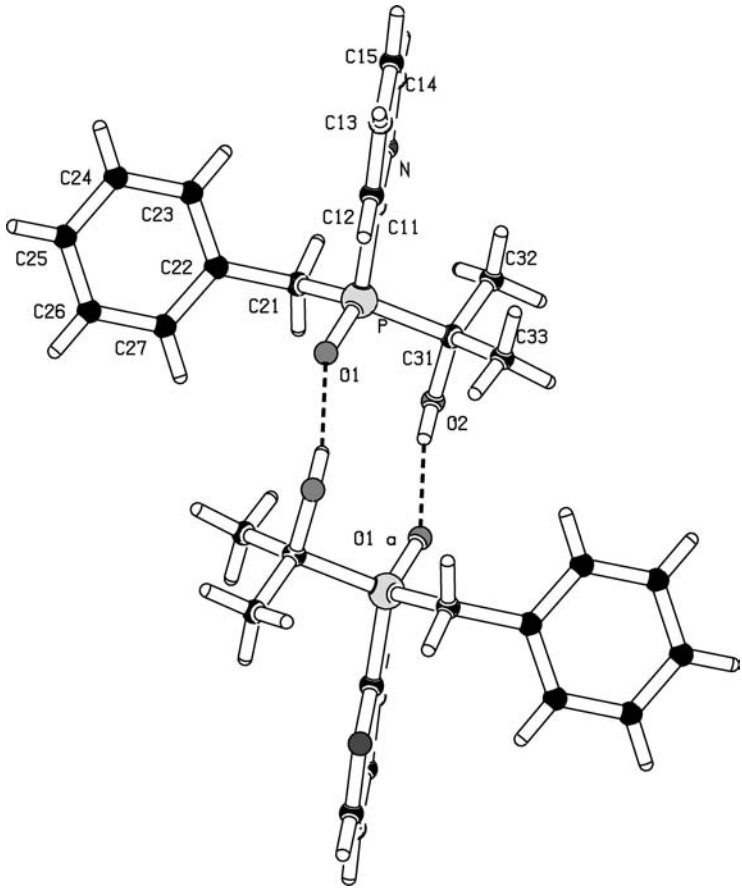


FIGURE 4 H-bonded dimer of (2-Py)P(O)(CH_2Ph)C(OH)Me_2 **3**.

at 298 K using the following Bruker instruments: *AVANCE* 300 (^{1}H, 300.13 MHz; ^{13}C, 75.5 MHz; ^{31}P 121.5 MHz), *AVANCE* DRX 400 (^{1}H, 400.13 MHz; ^{13}C, 100.6 MHz; ^{31}P, 161.9 MHz) and referenced internally to residual solvent resonances (data in δ) in the case of ^{1}H and ^{13}C spectra. The ^{31}P spectra were referenced externally to 85% H_3PO_4. All NMR spectra other than ^{1}H were proton decoupled. Hydrogen atoms in the pyridyl rings were labelled according to their respective position in the ring for an assignment of ^{1}H-NMR spectra. The first order analysis was used to assign the spectra. Melting points were recorded in unsealed capillaries and are uncorrected. Elemental analysis (empirical formulae shown) was determined by the Institute for Soil, Climate and Water, Pretoria, South Africa. The following abbreviations were used

throughout the experimental section: d = doublet, m = multiplet, q = quartet, s = singlet, and t = triplet. Coupling constants (J) are given in Hz.

Ethyltris(2-Pyridyl)phosphonium Bromide 1a

Ethyl bromide (10 mL, 133.98 mmol) was added to tris(2-pyridyl)-phosphine (0.50 g, 1.88 mmol). The mixture was refluxed at 40°C for 70 h. The excess ethyl bromide was removed in vacuo, and a white solid was obtained. The compound was recrystallized from methanol/ether at −20°C to give colorless crystals (0.32 g, 48%). m.p. (dec.): 177–178°C. Found: C, 55.7; N, 11.4; H, 4.8%; calc. for $C_{17}H_{17}BrN_3P$: C, 54.6; N, 11.2; H, 4.6%. ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ 1.35 (m, CH_3), 3.56 [overlapping qd, CH_2, ^2J(HP) 14.3 Hz, ^3J(HH) 7.5 Hz], 7.68 (m, H_5-py, 3H), 8.08 (m, H_4-py, 3H), 8.23 (m, H_3-py, 3H) and 8.83 [d, H_6-py, 3H, ^4J(HP) 4.6 Hz]. ^{31}P NMR ($CDCl_3$, 161.9 MHz): δ 15.4. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 6.2 [d, CH_3, ^2J(CP) 5.7 Hz], 14.8 [d, CH_2, ^1J(CP) 50.7 Hz], 128.2 [d, *p*-py, ^4J(CP) 3.6 Hz], 132.3 [d, *o*-py, ^2J(CP) 22.7 Hz], 138.1 [d, *m*-py, ^3J(CP) 9.8 Hz], 142.8 [d, *ipso*-C, ^1J(CP) 115.0 Hz] and 151.6 [d, CN, ^3J(CP) 19.8 Hz].

Propyltris(2-Pyridyl)phosphonium Bromide 1b

Propyl bromide (10 mL, 110.08 mmol) was added to tris(2-pyridyl)-phosphine (0.50 g, 1.88 mmol). The mixture was refluxed at 70°C for 8 h. The excess propyl bromide was removed in vacuo, and a white solid was obtained. The compound was recrystallized from acetone/hexane at −20°C to give white needle-shaped crystals (0.42 g, 58%). m.p. (dec.): 59–61°C. ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 1.15 (m, CH_3), 1.78 (m, CH_2), 3.62 (m, CH_2), 7.67 (m, H_5-py, 3H), 8.12 (m, H_4-py, 3H), 8.42 (m-H_3, py, 3H) and 8.86 [d, H_6-py, 3H, ^4J(HP) 4.7 Hz]. ^{31}P NMR ($CDCl_3$, 161.9 MHz): δ 13.2. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 14.7 [d, CH_2, ^2J(CP) 16.9 Hz], 15.3 [d, CH_3, ^3J(CP) 4.6 Hz], 21.8 [d, CH_2, ^1J(CP) 48.9 Hz], 127.9 [d, *p*-py, ^4J(CP) 3.6 Hz], 131.6 [d, *o*-py, ^2J(CP) 22.6 Hz], 137.7 [d, *m*-py, ^3J(CP) 9.9 Hz], 142.4 [d, *ipso*-C, ^1J(CP) 114.9 Hz] and 151.3 [d, CN, ^3J(CP) 19.7 Hz].

Butyltris(2-Pyridyl)phosphonium Bromide 1c

Butyl bromide (10 mL, 93.12 mmol) was added to tris(2-pyridyl)-phosphine (0.50 g, 1.88 mmol). The mixture was refluxed at 100°C for 1.5 h. The excess butyl bromide was removed in vacuo, and a sticky

brown solid was obtained. The compound was recrystallized from acetone/hexane at −20°C to yield yellow crystals (0.25 g, 33%). m.p. (dec.): 101–103°C. Found: C, 55.0; N, 10.0; H, 5.3%; calc. for $C_{19}H_{21}BrN_3P$: C, 55.5; N, 10.2; H, 5.4%. ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 0.84 [t, CH_3, ^3J(HH) 7.2 Hz], 1.50 (m, CH_2), 1.62 (m, CH_2), 3.62 (m, CH_2), 7.57 (m, H_5-py, 3H), 8.02 (m, H_4-py, 3H), 8.25 (m, H_3-py, 3H) and 8.75 [d, H_6-py, 3H, ^4J(HP) 4.6 Hz]. ^{31}P NMR ($CDCl_3$, 161.9 MHz): δ 13.5. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 13.2 (s, CH_3), 20.2 [d, CH_2, ^1J(CP) 49.4 Hz], 23.6 [d, CH_2, ^2J(CP) 12.0 Hz], 23.7 (s, CH_2), 128.2 [d, *p*-py, ^4J(CP) 3.5 Hz], 132.2 [d, *o*-py, ^2J(CP) 22.7 Hz], 138.1 [d, *m*-py, ^3J(CP) 9.8 Hz], 142.9 [d, *ipso*-C, ^1J(CP) 115.0 Hz] and 151.7 [d, CN, ^3J(CP) 19.8 Hz].

Benzyltris(2-Pyridyl)phosphonium Bromide 1d (*c.f.* [16])

Benzyl bromide (5 mL, 42.03 mmol) was added to tris(2-pyridyl)-phosphine (0.42 g, 1.58 mmol). The mixture was refluxed at 140°C for 3 h. The excess benzyl bromide was removed in vacuo to yield a yellow solid. The compound was recrystallized from methanol/ether at −20°C to give yellow crystals (0.60 g, 87%). m.p. (dec.): 163°C. Found: C, 60.1; N, 9.4; H, 4.4%; calc. for $C_{22}H_{19}BrN_3P(H_2O)_{1/2}$ (based on the ^{1}H-NMR spectrum **1d** crystallizes with $^1/_2$ equivalent of H_2O): C, 60.6; N, 9.6; H, 4.4%. ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ 5.16 [d, CH_2, ^2J(HP) 15.5 Hz], 7.07–7.13 (multiple multiplets, Ph, 5H), 7.64 (m, H_5-py, 3H), 8.03 (m, H_4-py, 3H), 8.33 (m, H_3-py, 3H) and 8.80 [d, H_6-py, 3H, ^4J(HP) 4.0 Hz]. ^{31}P NMR ($CDCl_3$, 161.9 MHz): δ 11.8. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 27.7 [d, CH_2, ^1J(CP) 45.9 Hz], 126.7 [d, *o*-Ph, ^3J(CP) 8.2 Hz], 127.4 [d, *ipso*-C, Ph, ^2J(CP) 69.7 Hz], 128.2 [d, *m*-Ph, ^4J(CP) 3.6 Hz], 128.7 [d, *p*-Ph, ^5J(CP) 3.3 Hz], 130.5 [d, *p*-py, ^4J(CP) 5.8 Hz], 133.1 [d, *o*-py, ^2J(CP) 22.6 Hz], 138.0 [d, *m*-py, ^3J(CP) 9.9 Hz], 142.8 [d, *ipso*-C, py, ^1J(CP) 115.2 Hz] and 151.4 [d, CN, ^3J(CP) 20.1 Hz].

Benzyltris(2-Pyridyl)phosphonium Chloride 1e

Benzyl chloride (10 mL, 86.89 mmol) was added to tris(2-pyridyl)-phosphine (0.42 g, 1.58 mmol). The mixture was refluxed at 120°C for 6 h. The excess benzyl chloride was removed in vacuo, and a yellow solid was obtained. The compound was triturated with acetone to give a fine pale yellow powder (0.45 g, 62%). m.p. (dec.): 107–108°C. ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ 5.28 [d, CH_2, ^2J(HP) 15.5 Hz], 6.99 (broad s, Ph, 5H), 7.60 (broad s, H_5-py, 3H), 8.01 (d, H_4-py, 3H, ^4J(HP) 5.8 Hz), 8.42 [d, H_3-py, 3H, ^3J(HP) 5.7 Hz], 8.76 [d, H_6-py, ^4J(HP) 3.5 Hz]. ^{31}P NMR ($CDCl_3$, 161.9 MHz): δ 12.0. ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 27.5

[d, CH_2, ^1J(CP) 45.0 Hz], 126.9 [d, *o*-Ph, ^3J(CP) 8.3 Hz], 128.4 [*ipso*-C, Ph, ^2J(CP) 53.4 Hz], 128.7 (s, *m*-Ph), 129.2 (s, *p*-Ph), 130.6 [d, *p*-py, ^4J(CP) 5.8 Hz], 133.1 [d, *o*-py, ^2J(CP) 22.6 Hz], 138.0 [d, *m*-py, ^3J(CP) 9.9 Hz], 143.1 [d, *ipso*-C, py, ^1J(CP) 115.2 Hz] and 151.3 [d, CN, ^3J(CP) 20.0 Hz].

2,2′-Bipyridinium(+1) Bromide 2

Butyltris(2-pyridyl)phosphonium bromide **1c** was dissolved in hot acetone/hexane to yield yellow crystals at −20°C (0.27 g, 56%). m.p. (dec.): 75°C. ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 7.79 [d, py-H, ^3J(HH) 0.8 Hz, 1H], 7.80–7.83 (m, py, 3H), 8.31–8.35 (m, py, 3H), 8.93 [d, py-H, ^3J(HH) 8.1 Hz, 1H) and 9.04 [dd, N-H, py, ^4J(HH) 0.8 Hz, ^3J(HH) 5.2 Hz, 1H]. ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 124.4 (s, *p*-py), 126.5 (s, *o*-py), 142.2 (s, *m*-py), 146.4 (*ipso*-C) and 148.0 (s, CN).

Compound 3

Benzyltris(2-pyridyl)phosphonium chloride **1e** was dissolved in hot acetone/hexane to yield yellow crystals (0.12 g, 29%) at 0°C. ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 1.41 [d, CH_3, 3H, ^3J(HP) 13.1 Hz], 1.61 [d, CH_3, 3H, ^3J(HP) 13.6 Hz], 3.51 [dd, CH_2, 1H, ^2J(HH) 14.4 Hz,^2J(HP) 16.9 Hz], 3.75 [dd, CH_2, 1H, ^2J(HP) 9.2 Hz, 1H, ^2J(HH) 14.4 Hz], OH not observed, 7.00–7.03 (multiple multiplets, Ph, 5H), 7.13–7.14 (multiple multiplets, py, 1H), 7.41–7.70 (multiple multiplets, py, 2H) and 8.70 [d, py-H, (1H), ^2J(HP) 4.8 Hz]. ^{31}P NMR ($CDCl_3$, 161.9 MHz): δ 39.0. ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 23.4 [d, CH_3, ^2J(CP) 2.8 Hz], 25.6 [d, CH_3, ^2J(CP) 8.5 Hz], 31.5 [d, CH_2, ^1J(CP) 58.4 Hz], 71.7 [d, C-OH, ^1J(CP) 76.0 Hz], 125.6 [d, Ph, J(CP) 2.9 Hz], 126.4 [d, Ph, J(CP) 2.9 Hz], 128.2 [d, Ph, J(CP) 2.3 Hz], 129.8 [d, *p*-py, ^4J(CP) 4.7 Hz], 131.4 [d, *o*-py, ^2J(CP) 8.6 Hz], 136.7 [d, *m*-py, ^3J(CP) 7.8 Hz], 148.5 [d, CN, py, ^3J(CP) 15.4 Hz] and 155.6 [d, *ipso*-C (py), ^1J(CP) 106.5 Hz]; *ipso*-C, Ph not observed.

Tris(2-Pyridyl)phosphine Oxide

Bromobenzene (10 mL, 86.89 mmol) was added to tris(2-pyridyl)-phosphine (0.42 g, 1.56 mmol). The mixture was refluxed at 120°C for 8 days. The excess bromobenzene was removed in vacuo, and a yellow solid was obtained. Colorless crystals (0.20 g, 38%) were obtained from methanol at −60°C. m.p.: 200°C. Found: C, 64.5; N, 14.9; H, 4.4%; calc. for $C_{15}H_{12}N_3PO$: C, 64.1; N, 14.9; H, 4.3%. ^{1}H NMR ($CDCl_3$,

300.13 MHz): δ 7.38 (m, H_5-py, 3H), 7.81 (m, H_4-py, 3H), 8.20 (m, H_3-py, 3H) and 8.78 [d, H_6-py, ^4J(HP) 4.5 Hz]. ^{31}P NMR ($CDCl_3$, 161.9 MHz): δ 14.8. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 125.5 [d, *p*-py, ^4J(CP) 3.3 Hz], 128.8 [d, *o*-py, ^2J(CP) 21.2 Hz], 135.9 [d, *m*-py, ^3J(CP) 9.5 Hz], 150.4 [d, CN, ^3J(CP) 19.3 Hz] and 154.7 [d, *ipso*-C, ^1J(CP) 133.1 Hz].

TABLE V Crystal Data and Refinement for Compounds 1a and 3

Compound	**1a**	**3**
Empirical formula	$C_{17}H_{17}BrN_3P$	$C_{15}H_{18}NO_2P$
M	374.22	275.27
T(K)	173 (2)	293 (2)
Wavelength (Å)	0.71073	0.71073
Crystal system	Triclinic	Monoclinic
Space group	$P\bar{1}$	$P2_1/c$
a (Å)	9.442 (1)	8.4196 (9)
b (Å)	9.549 (1)	17.2945 (19)
c (Å)	10.776 (1)	10.3595 (11)
α (°)	94.523 (2)	90
β (°)	114.379 (2)	106.796 (2)
γ (°)	97.412 (2)	90
U (Å^3)	868.1 (2)	1444.1 (3)
Z	2	4
D (calc.) Mg/m^3	1.432	1.266
μ (mm^{-1})	2.459	0.188
F (000)	380	584
Crystal size (mm^3)	0.37 × 0.36 × 0.11	0.33 × 0.28 × 0.15
Theta range for data collection (°)	2.10 to 28.27	2.36 to 28.31
Index ranges	$-12 <= h <= 9$ $-12 <= k <= 12$ $-14 <= l <= 13$	$-11 <= h <= 11$ $-23 <= k <= 17$ $-13 <= l <= 13$
Reflections collected	5926	9601
Independent reflections	4191 [R(int) = 0.017]	3568 [R(int) = 0.028]
Completeness to theta	97.0	99.3
Absorption correction	Semi-empirical from equivalents	None
Max. and min. transmission	0.7736 and 0.4631	0.9724 and 0.9406
Data/restraints/parameters	4191/0/200	3568/0/178
Goodness-of-fit on F^2	1.043	1.043
Final R indices [$I > 2$sigma(I)]	R1 = 0.028 wR2 = 0.068	R1 = 0.038 wR2 = 0.095
R indices (all data)	R1 = 0.035 wR2 = 0.072	R1 = 0.063 wR2 = 0.105
Largest diff. peak and hole (eÅ^{-3})	0.474 and −0.375	0.187 and −0.294

Crystallography

Intensity data for crystal structures were collected on a Bruker SMART 1K CCD area detector diffractometer with graphite monochromated Mo K_α radiation (50 kV, 30 mA). The collection method involved ω-scans of width 0.3°. Data reduction was carried out using the program *SAINT+*[35] and the data was processed further with the program *SADABS*.[35b] Structures were solved by direct methods using *SHELXTL*.[36] Non-hydrogen atoms were first refined isotropically followed by anisotropic refinement by full matrix least-squares calculations based on F^2 using *SHELXTL*. Hydrogen atoms (except H2 of **3**) were located from the difference map and then positioned geometrically and allowed to ride on their respective parent atoms. H2 was located from the difference map and allowed to refine freely. Further crystallographic data are summarized in Table V. Diagrams and publication material were generated using SHELXTL,[36] and PLATON,[37] ORTEP,[37] and SCHAKAL.[38]

Full crystallographic data (CCDC No. 267675 for compound **1a** and 267676 for compound **3**) have been deposited at the Cambridge Crystallographic Database Centre and are available on request from the Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Fax: +44-1223-336-033; E-mail:deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

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