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A shortcut to tris[2-(4-hydroxyphenyl)ethyl]phosphine oxide and 2-(4-hydroxyphenyl)ethylphosphinic acid *via* reaction of elemental phosphorus with 4-*tert*-butoxystyrene

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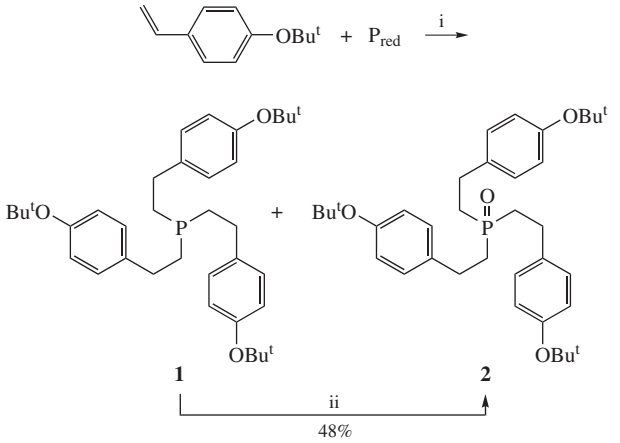
Red phosphorus reacts with 4-*tert*-butoxystyrene in KOH/DMSO system to afford (depending on the reaction conditions) tris(4-*tert*-butoxyphenylethyl)phosphine oxide (48% yield) and/or 4-*tert*-butoxyphenylethylphosphinic acid (30% yield). The treatment of these products with aqueous HCl (45 °C, 5 min) quantitatively delivers tris[2-(4-hydroxyphenyl)ethyl]phosphine oxide and 2-(4-hydroxyphenyl)ethylphosphinic acid.

Organophosphorus compounds such as phosphines, phosphine oxides, phosphinic acids are important intermediates in organic synthesis.[1] They find wide application as ligands for metal complexes, flame retardants, extractants, drug precursors, and capping ligands for the growing of nanocrystals.[1] A special attention attracts functional organophosphorus compounds bearing, for example, phenolic (hydroxylphenyl) moieties. Such compounds are used as reactive building blocks for organic synthesis[2] and additives for design of flame retardant polymer compositions.[3] However, syntheses of these compounds now are fairly laborious. For instance, tris(4-hydroxyphenyl)phosphine oxide has been prepared by the multistep method using both moisture-sensitive and aggressive compounds, *e.g.*, Grignard reagent, $POCl_3$, BBr_3.[4] Moreover, anhydrous solvents and inert atmosphere are required for this synthesis.

Here we report a novel convenient approach to the earlier unknown 4-hyroxyphenyl tethered tertiary phosphine oxide and phosphinic acid starting from commercially available 4-*tert*-butoxystyrene and elemental phosphorus.

Direct phosphorylation of 4-*tert*-butoxystyrene with red phosphorus effectively proceeded in the KOH/DMSO (H_2O) suspension at 130 °C for 3 h (the molar ratio styrene/P/KOH·0.5 H_2O/H_2O ~ 1.3:1:4.7:1.1) to afford mainly tertiary phosphine **1** and its oxide **2** in *ca.* 1:1 ratio (Scheme 1). By oxidation of this mixture with H_2O_2 (H_2O/EtOH, ambient temperature), phosphine oxide **2** was isolated in 48% yield (based on 4-*tert*-butoxystyrene).†



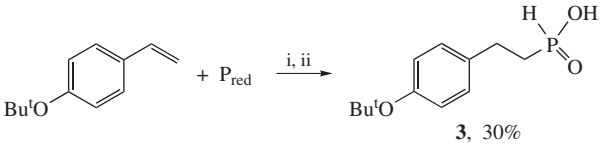
Scheme 1 *Reagents and conditions*: i, KOH/DMSO (H_2O), 130 °C, 3 h; ii, H_2O_2/H_2O/EtOH, room temperature.

Under the milder conditions (100 °C, 2 h, and the molar ratio styrene/P/KOH·0.5 H_2O/H_2O ~ 1:2.9:4.5:6.5), the major product was acid **3** (in a salt form) isolated in 30% yield (based on 4-*tert*-butoxystyrene) by acidification of the reaction mixture with aqueous HCl (Scheme 2).‡ Additionally, 2-(4-*tert*-butoxyphenyl)ethylphosphine **4** and bis[2-(4-*tert*-butoxyphenyl)ethyl]-phosphine **5** were formed as minor products (^{31}P NMR).

The structures of phosphines **1**, **4** and **5** have been confirmed by their counter synthesis *via* hydrophosphination of *tert*-butoxystyrene with PH_3/H_2 mixture in KOH/DMSO (H_2O) system at 70 °C. These results will be published elsewhere.

† ^{1}H, ^{13}C and ^{31}P NMR spectra (400.13, 100.62 and 161.98 MHz, respectively) were recorded on a Bruker DPX-400 spectrometer at ambient temperature and referenced to internal HDMS (^{1}H, ^{13}C) and external 85% H_3PO_4 (^{31}P) standards. FT-IR spectra were recorded on a Bruker Vertex 70 spectrometer. The microanalyses were performed on a Flash EA 1112 Series elemental analyzer. Melting points (uncorrected) were determined on a Kofler micro hot stage apparatus. *tert*-Butoxystyrene, KOH·0.5H_2O, DMSO (1% water content) and red phosphorus (KSAN 'SIA') were employed as purchased. The reactions with elemental phosphorus were carried out under argon atmosphere.

*Tris[2-(4-*tert*-butoxyphenyl)ethyl]phosphine oxide* **2**. A mixture of red phosphorus (0.8 g, 26 mmol), *tert*-butoxystyrene (6.0 g, 34 mmol), KOH·0.5H_2O (8.0 g, 123 mmol), DMSO (40 ml) and water (0.5 ml) was stirred at 130 °C for 3 h, cooled and analyzed. The ^{31}P NMR spectrum of the reaction mixture reveals the presence of tertiary phosphine **1** (δ_P –28 ppm) and its oxide **2** (δ_P 45 ppm) as well as minor amounts of potassium salt **3** [δ_P 19 ppm (d, $^1J_{PH}$ 465 Hz)]. The mixture was diluted with water (50 ml), passed through the glass filter and extracted with chloroform (3×20 ml). The extract was washed with water (2×40 ml) and the solvent was removed. The residue was dissolved in EtOH (10 ml) and aqueous H_2O_2 (30%, 2 ml) was added to resulting solution. The mixture was stirred at ambient temperature for 10 min, then diluted with water (30 ml) and extracted with chloroform (2×20 ml). The extract was evaporated and the residue was dried *in vacuo* (1 Torr) to give 3.15 g (48%) of phosphine oxide **2** as viscous oil. ^{1}H NMR ($CDCl_3$) δ: 1.30 (s, 27H, Me), 2.03–2.12 (m, 6H, CH_2P), 2.81–2.93 (m, 6H, $CH_2C_6H_4$), 6.84 (d, 6H, C_6H_4, $^3J_{HH}$ 8.4 Hz), 7.40 (d, 6H, C_6H_4, $^3J_{HH}$ 8.4 Hz). ^{31}P{^{1}H} NMR ($CDCl_3$) δ: 46.97. FT-IR (film, ν/cm^{-1}): 1170 (P=O). Found (%): C, 74.66; H, 8.90; P, 5.27. Calc. for $C_{36}H_{51}O_4P$ (%): C, 74.71; H, 8.88; P, 5.35.



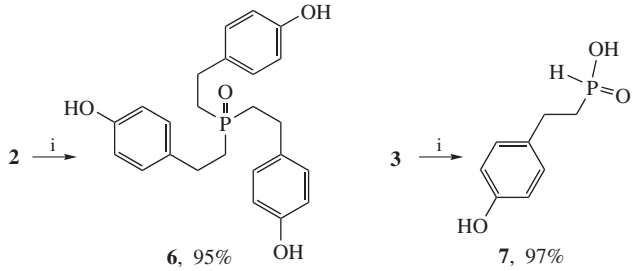
[+ 4-Bu^{t}OC$_6$H$_4$CH$_2$CH$_2$PH$_2$ + (4-Bu^{t}OC$_6$H$_4$CH$_2$CH$_2$)$_2$PH]

4 **5**

Scheme 2 *Reagents and conditions*: i, KOH/DMSO (H$_2$O), 100 °C, 2 h; ii, HCl/H$_2$O, room temperature, up to pH ~ 2–3.

Subsequently, the exhaustive removal of the *tert*-butyl group from compounds **2** and **3** was achieved by treatment with 36% aqueous HCl under mild conditions (45 °C, EtOH/H$_2$O, 5 min) to give the target phenol phosphorus derivatives **6** and **7** in nearly quantitative yields (Scheme 3).§

The synthesized compounds **3**, **6**, **7** are air-stable crystalline powders (phosphine oxide **2** is oil), soluble in polar organic



Scheme 3 *Reagents and conditions*: i, HCl/H$_2$O, EtOH, 45 °C, 5 min.

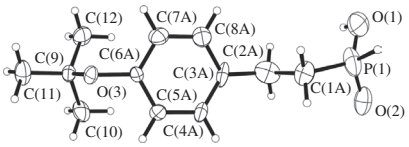


Figure 1 ORTEP diagram of acid **3** with 30% probability ellipsoids (minor disorder component B omitted for clarity).

solvents. Moreover, acid **7** is well soluble in hot water. All the compounds were characterized by ^{1}H, ^{13}C and ^{31}P NMR as well as IR spectroscopy. The molecular structure of acid **3** was established by X-ray diffractometry (Figure 1).¶ The phenylethyl fragment is disordered over two positions in 0.56(2):0.44(2) ratio. The Bu^t group and [CH$_2$P(O)OH(H)] unit are disposed on opposite sides of the average [OC$_6$H$_4$CH$_2$] plane: the value of C(9)O(3)C(2A)C(1A) torsion angle is 179.5°. The packing diagram of **3** along the *a* axis reveals the presence of strong intermolecular P=O···HO hydrogen bonding to form a 1D supramolecular array.

In summary, we have accessed hitherto unknown tris[2-(4-hydroxyphenyl)ethyl]phosphine oxide and 2-(4-hydroxyphenyl)-ethylphosphinic acid by direct reaction of red phosphorus with 4-*tert*-butoxystyrene in KOH/DMSO system, followed by treatment of the formed products with HCl to afford the target compounds. The latter are prospective ligands for design of metal complexes, building blocks for synthesis of branched molecules and 3D structures as well as promising capping agents for stabilizing of nanoparticles. Potentially, phosphine oxide **6** and acid **7** may be applied as promising antiseptics and flame-proofing additives in synthesis of phenol formaldehyde resins. Moreover, this result extends the scope of the methodology of the synthesis of important organophosphorus compounds involving cleavage of elemental phosphorus in strongly basic media.[5]

‡ *[2-(4-*tert*-Butoxyphenyl)ethyl]phosphinic acid* **3**. A mixture of red phosphorus (3.1 g, 100 mmol), *tert*-butoxystyrene (6.0 g, 34 mmol), KOH·0.5H$_2$O (10.0 g, 153 mmol), DMSO (40 ml) and water (4 ml) was stirred for 2 h at 100 °C, cooled and analyzed. The ^{31}P NMR spectrum of reaction mixture reveals the presence of potassium salt of acid **3** [δ_P 19 ppm (d, $^1J_{PH}$ 465 Hz)], primary phosphine **4** [δ_P –137 ppm (t, $^1J_{PH}$ 195 Hz)] and secondary phosphine **5** [δ_P –69 ppm (d, $^1J_{PH}$ 200 Hz)] in a 27:2:1 molar ratio. Then the mixture was diluted with water (50 ml), passed through the glass filter and extracted with chloroform (3×20 ml). The aqueous layer was acidified with aqueous HCl (up to pH ~ 2) and extracted with chloroform (3×20 ml). The extract was washed with water (2×40 ml) and dried over Na$_2$SO$_4$. The solvent was removed, then the residue was reprecipitated from water–ethanol mixture and dried *in vacuo* (1 Torr) to give 2.47 g (30%) of phosphinic acid **3**. Colourless crystals, mp 74–76 °C. ^{1}H NMR (CDCl$_3$) δ: 1.31 (s, 9H, Me), 2.02–2.11 (m, 2H, CH$_2$P), 2.83–2.91 (m, 2H, C*H*$_2$C$_6$H$_4$), 6.89 (d, 2H, C$_6$H$_4$, $^3J_{HH}$ 8.4 Hz), 7.07 (d, 1H, PH, $^1J_{PH}$ 546 Hz), 7.08 (d, 2H, C$_6$H$_4$, $^3J_{HH}$ 8.4 Hz), 11.42 (br. s, 1H, OH). ^{13}C NMR (CDCl$_3$) δ: 26.1 (*C*H$_2$C$_6$H$_4$), 28.8 (Me), 31.0 (d, CH$_2$P, $^1J_{PC}$ 93.2 Hz), 78.2 (*C*Me$_3$), 124.3 (C-3,5 in C$_6$H$_4$), 128.4 (C-2,6 in C$_6$H$_4$), 134.8 (d, C-1 in C$_6$H$_4$, $^3J_{PC}$ 15.5 Hz), 153.9 (C-4 in C$_6$H$_4$). ^{31}P{^{1}H} NMR (CDCl$_3$) δ: 36.27 (d, $^1J_{PH}$ 546 Hz). FT-IR (KBr, ν/cm^{-1}): 2349 (P–H), 1161, 1176 (d, P=O). Found (%): C, 59.45; H, 7.78; P, 12.73. Calc. for C$_{12}$H$_{19}$O$_3$P (%): C, 59.50; H, 7.91; P, 12.79.

§ *Tris[2-(4-hydroxyphenyl)ethyl]phosphine oxide* **6**. To a solution of phosphine oxide **2** (3.5 g, 6 mmol) in ethanol (10 ml), aqueous HCl (36%, 3 ml) was added and the mixture was stirred at 45 °C for 5 min. This was accompanied by evolution of gaseous products. The resulting solution was cooled to room temperature and the solvents were removed *in vacuo* (1 Torr) to give 2.36 g (95%) of phosphine oxide **6** as dough-like substance. The recrystallization of the latter from hot Pr^{i}OH gives colourless crystals, mp 213–215 °C. ^{1}H NMR (DMSO-d_6) δ: 1.90–1.97 (m, 6H, CH$_2$P), 2.66–2.72 (m, 6H, C*H*$_2$C$_6$H$_4$), 6.70 (d, 6H, C$_6$H$_4$, $^3J_{HH}$ 8.1 Hz), 7.05 (d, 6H, C$_6$H$_4$, $^3J_{HH}$ 8.0 Hz), 9.21 (br. s, 3H, OH). ^{13}C NMR (DMSO-d_6) δ: 26.2 (*C*H$_2$C$_6$H$_4$), 29.2 (d, CH$_2$P, $^1J_{PC}$ 61.7 Hz), 115.2 (C-3,5 in C$_6$H$_4$), 129.0 (C-2,6 in C$_6$H$_4$), 131.3 (d, C-1 in C$_6$H$_4$, $^3J_{PC}$ 13.0 Hz), 155.7 (C-4 in C$_6$H$_4$). ^{31}P{^{1}H} NMR (DMSO-d_6) δ: 49.81. FT-IR (KBr, ν/cm^{-1}): 3376 (OH), 1102, 1088 (d, P=O). Found (%): C, 70.14; H, 6.61; P, 7.38. Calc. for C$_{24}$H$_{27}$O$_4$P (%): C, 70.23; H, 6.63; P, 7.55.

[2-(4-Hydroxyphenyl)ethyl]phosphinic acid **7**. To a suspension of compound **3** (2.0 g, 8 mmol) in ethanol (10 ml), aqueous HCl (36%, 3 ml) was added and the mixture was stirred at 45 °C for 5 min. This was accompanied by dissolution of acid **3** precipitate and evolution of gaseous products. The resulting solution was cooled to room temperature and the solvents were removed *in vacuo* (1 Torr) to give 1.49 g (97%) of acid **7**. Colourless crystals, mp 130–132 °C (H$_2$O). ^{1}H NMR (DMSO-d_6) δ: 1.81–1.90 (m, 2H, CH$_2$P), 2.62–2.69 (m, 2H, C*H*$_2$C$_6$H$_4$), 3.96 (br. s, 1H, OH), 6.66 (d, 2H, C$_6$H$_4$, $^3J_{HH}$ 8.5 Hz), 6.94 (d, 1H, PH, $^1J_{PH}$ 520.8 Hz), 7.02 (d, 2H, C$_6$H$_4$, $^3J_{HH}$ 8.5 Hz), 9.17 (br. s, 1H, P–OH). ^{13}C NMR (DMSO-d_6) δ: 26.0 (*C*H$_2$C$_6$H$_4$), 31.7 (d, CH$_2$P, $^1J_{PC}$ 90.5 Hz), 115.3 (C-3,5 in C$_6$H$_4$), 129.0 (C-2,6 in C$_6$H$_4$), 131.0 (d, C-1 in C$_6$H$_4$, $^3J_{PC}$ 15.8 Hz), 155.7 (C-4 in C$_6$H$_4$). ^{31}P{^{1}H} NMR (DMSO-d_6) δ: 31.02 (d, $^1J_{PH}$ 520 Hz). FT-IR (KBr, ν/cm^{-1}): 3303 (OH), 2442 (P–H), 1148, 1134 (d, P=O). Found (%): C, 51.68; H, 5.91; P, 16.49. Calc. for C$_8$H$_{11}$O$_3$P (%): C, 51.62; H, 5.96; P, 16.64.

¶ *Crystal data.* X-ray quality crystals of acid **3** were obtained by slow evaporation of its ethanol solution at room temperature over several days. C$_{12}$H$_{19}$O$_3$P, M = 242.24, orthorhombic, space group $P2_12_12_1$, a = 6.068(2), b = 11.010(3) and c = 19.672(6) Å, V = 1314.3(7) Å^3, T = 200(2) K, Z = 4, d_{calc} = 1.224 g cm^{-3}, F(000) = 520.0, μ(MoKα) = 0.200 mm^{-1}, 5448 reflections collected, 1703 independent reflections (R_{int} = 0.0474), final R indexes [$I > 2\sigma(I)$]: R_1 = 0.0884, wR_2 = 0.2010; final R indexes [all data]: R_1 = 0.1304, wR_2 = 0.2463. Data were collected on a Bruker Apex II CCD diffractometer using graphite monochromated MoKα radiation (λ = = 0.71073 Å). The structure was solved by direct methods and refined by full-matrix least-squares method against all F^2 in anisotropic approximation for non-hydrogen atoms using the SHELX-97 programs set.[6] Non-hydrogen atoms were refined anisotropically using SHELX-97.[6] The phenylethyl fragment is disordered over two position in 0.56(2):0.44(2) ratio. Hydrogen atoms were included at geometrically calculated positions during the refinement using the riding model.

CCDC 950470 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2014.

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