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# Reactions of Tertiary Phosphines with Alcohols in Aqueous Media

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The phosphines $R_2R'P$ [R = R′ = Me, Et, $^n$Pr, $^i$Pr, $(CH_2)_3OH$; $Me_2PhP$ and $MePh_2P$] react with 2- or 4-hydroxybenzyl alcohols, including "lignin-type" vanillyl, syringyl, and α-methylvanillyl alcohols, in a 1:1 ratio in aqueous media, to give zwitterionic phosphobetaine products; these on treatment with aq HCl form the corresponding phosphonium chlorides in good to excellent yields. The syringyl derivative $[3,5\text{-}(OMe)_2\text{-}4\text{-}OH\text{-}C_6H_2CH_2PEt_3]Cl$ was structurally characterized by X-ray analysis. Kinetically, the reactivity of the benzyl alcohols, studied with the water-soluble $[HO(CH_2)_3]_3P$, decreases with substituents in the order 2-hydroxy > 4-hydroxy > vanillyl > syringyl > α-methylvanillyl, while 3-hydroxybenzyl alcohol is unreactive; the trend is consistent with reactivity requiring the presence of an *ortho*- or *para*-OH substituent in the aromatic ring of the alcohol, and that the reactions proceed via a carbocation species stabilized as a quinone methide. Triethylphosphine reacts with coniferyl alcohol at the C═C moiety to give a zwitterionic intermediate that is again converted by aq HCl to a phosphonium chloride; no reaction was observed with cinnamyl alcohol. The effect on a phenolic $pK_a$ by incorporation of a phosphonium substituent is also measured.

## Introduction

Collaborative research involving our group has revealed that water-soluble, hydroxymethyl-phosphines, particularly $(HOCH_2)_3P$ (abbreviated THP), are excellent bleaching and brightness stabilization agents for pulps, and interaction of such phosphines with conjugated carbonyl components of lignin is likely involved in the bleaching process.[1] Investigations on this topic revealed that reaction of $[HO(CH_2)_3]_3P$ (THPP, a more stable entity than THP) with several aromatic aldehydes (ArCHO, where Ar = substituted phenyl) in aqueous solution generated the corresponding alcohols, the phosphine being oxidized to the monooxide.[2] However, with syringaldehyde $(3,5\text{-}(OMe)_2\text{-}4\text{-}OH$-benzaldehyde, a lignin-type component), the initially formed alcohol product is more reactive toward THPP than is the starting aldehyde, and the final product is a zwitterionic phosphobetaine;[2] we noted briefly that the phosphobetaine could be protonated using HCl to generate the corresponding phosphonium chloride[2] (see Scheme 1). The presence of the 4-OH substituent seemed important, and to investigate further such chemistry, we extended the studies to other substituted benzyl alcohols [3-MeO-4-OH- (vanillyl), and α-methylvanillyl alcohol, IUPAC names are as follows: vanillyl alcohol = 4-(hydroxymethyl)-2-methoxyphenol; syringyl alcohol = (4-hydroxymethyl)-2,6-dimethoxyphenol; α-methylvanillyl alcohol = 4-(1′-hydroxyethyl)-2-methoxyphenol; coniferyl alcohol = 4-(3′-hydroxyprop-1′-enyl)-2-methoxyphenol], cinnamyl alcohol and coniferyl alcohol (3-OMe-4-OH-cinnamyl), as well as to other tertiary phosphines.

It should be noted that formation of quaternary phosphonium salts via reaction of tertiary phosphines with alcohols *in the presence of a strong acid* has long been known and is exemplified indirectly by the reactions shown in eqs 1 and 2 (R′ = alkyl, cycloalkyl, alkenyl, or benzyl).[3,4] The reactions of eq 2 involved a reflux procedure in benzene or THF, and a similar procedure in MeCN or $CHCl_3$ has been reported more recently using $ArCH_2OH$ alcohols, where Ar = $p\text{-}NMe_2\text{-}C_6H_4$ or a 2-thiophene moiety.[5] Reaction of $[Ph_3PH]Br$ with saturated and unsaturated alcohols in the absence of solvent at 160 °C also affords quaternary

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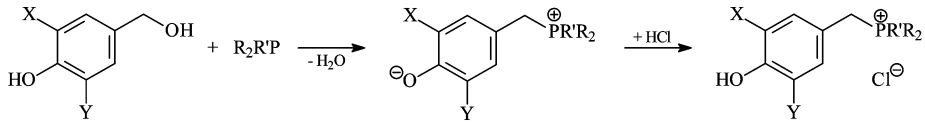
**Scheme 1**



**1a**; X = OMe,Y = H
**1b;** X = Y = H
**1c;** X = Y = OMe

**2**

| | $^{31}P\{^1H\}$, $\delta$ |
|---|---|
| **3a;** X = OMe,Y = H, R = R′ = Et | 38.0 |
| **3b;** X = Y = H, R = R′ = Et | 38.0 |
| **3c;** X = Y = OMe, R = R′ = Et | 39.0 |
| **3d;** X = OMe,Y = H, R = R′ = Me | 26.8 |
| **3e;** X = OMe,Y = H, R = R′ = $^n$Pr | 32.4 |
| **3f;** X = OMe,Y = H, R = R′ = $^i$Pr | 41.7 |
| **3g;** X = OMe,Y = H,R = R′ = $(CH_2)_3OH$ | 34.8 |
| **3h;** X = OMe,Y = H, R = Me, R′ = Ph | 23.9 |
| **3i;** X = OMe,Y = H, R = Ph, R′ = Me | 23.7 |

phosphonium salts,[6] and similarly alkyl, allyl and benzyl alcohols react with $Ph_3P$ in trifluoroacetic acid[7] or HCl[8] to give phosphonium salts. Such systems appear to involve direct nucleophilic displacement by the tertiary phosphine of the anion of an alkyl/aryl intermediate RX (X = halogen, $OCOCF_3$, etc.), and will be further discussed later.

$$[PH_4]I + 4ROH \rightarrow [R_4P]I + 4H_2O \quad (1)$$

$$[R_3PH]Br + R'OH \rightarrow [R_3PR']Br + H_2O \quad (2)$$

Our studies described here will demonstrate formation of phosphonium chlorides by addition of HCl to a zwitterionic phosphobetaine formed directly from the alcohol and phosphine *in aqueous media*. Detailed NMR data and, in one case, crystallographic data fully establish the identities of the phosphonium chlorides and, less directly, the phosphobetaines.

## Experimental Section

**General Procedures.** Vanillyl-, α-methylvanillyl-, coniferyl-, and cinnamyl-alcohols were purchased from Aldrich, while syringyl alcohol, and the 4-, 3-, and 2-hydroxybenzyl alcohols, were Lancaster products; all were used as supplied. $Et_3P$, $Me_2PhP$, $MePh_2P$, $^nPr_3P$, $^iPr_3P$, and $Et_2P(CH_2)_2PEt_2$ (Strem products), and the Aldrich products $[(HOCH_2)_4P]Cl$ and $Me_3P$ (1.0 *M* solution in toluene) were also used without purification; $[HO(CH_2)_3]_3P$ (an oil, > 80%, from Strem) was difficult to purify, as discussed previously;[2] $(NCCH_2CH_2)_3P$ was prepared according to a literature method.[9] Before use, distilled $H_2O$ and $D_2O$ were stirred for 3 h under Ar; organic solvents were dried over the appropriate agents, and then distilled under $N_2$. $CD_3OD$ (Cambridge Isotope Laboratories) was used as received. $^{31}P$ NMR spectra were recorded in $D_2O$ on a Bruker AV300 (121 MHz for $^{31}P$), while $^1H$- and $^{13}C$ NMR spectra were recorded on an AV400 spectrometer (400 MHz for $^1H$; 100 MHz for $^{13}C$). A residual, deuterated solvent proton (relative to external $SiMe_4$) or external to 85% aq $H_3PO_4$ was used as a reference; br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; *J* values are given in Hertz. All NMR data were measured at 300 K in $D_2O$ solution, except those for **3i** which was poorly soluble in water and $CD_3OD$ was used. Elemental analyses were performed on a Carlo Erba 1108 analyzer. Mass spectrometry was performed on a Bruker Esquire electrospray (ESI) ion-trap instrument using samples dissolved in MeOH, with positive ion-polarity, scanning from 60 to 800 *m*/*z*. UV−vis data were recorded on an HP 8452A Diode-Array spectrophotometer at 298 K using a 1 cm quartz cell; pH values of 6.00 to 11.40 in aqueous solution were maintained by the use of phosphate or borate buffers, NaOH and aq HCl.

**Preparation of [3-MeO-4-OH-$C_6H_3CH_2PEt_3$]Cl (3a).** Vanillyl alcohol (308 mg, 2.00 mmol) and $Et_3P$ (0.30 mL, 2.0 mmol) were mixed under Ar in deoxygenated water (8 mL), and the mixture was stirred for 18 h at 90 °C. Then HCl (0.17 mL of 37% aq solution, 2.0 mmol) was added, and the water was removed under vacuum. The residue was dried under vacuum at ∼50 °C for 1 h and washed with acetone (∼10 mL). The resulting white sold was separated and dried under vacuum overnight; yield 490 mg (84%). $^{31}P\{^1H\}$ NMR: $\delta$ 38.0 s. $^1H$ NMR: $\delta$ 6.91 (d, $^3J_{HH}$ = 8.1, 1H, *m-H*), 6.87 (pseudo t, $^4J_{HH} \approx {}^4J_{PH} \approx 2$, 1H, *o-H*), 6.78 (d of pseudo t, $^3J_{HH}$ = 8.1, $^4J_{HH} \approx {}^4J_{PH} \approx 2$, 1H, *o-H*), 3.85 (s, 3H, $OCH_3$), 3.56 [d, $^2J_{PH}$ = 14.0, 2H, $ArCH_2$ (s in $^1H\{^{31}P\}$ spectrum)], 2.15 (dq, $^2J_{PH}$ = 12.7, $^3J_{HH}$ = 7.6, 6H, $PCH_2CH_3$), 1.18 (dt, $^3J_{PH}$ = 18.3, $^3J_{HH}$ = 7.6, 9H, $PCH_2CH_3$). $^{13}C\{^1H\}$ NMR: $\delta$ 149.1 (d, $^4J_{PC}$ = 3.0, *C*-OMe), 146.2 (d, $^5J_{PC}$ = 3.6, *C*-OH), 124.0 (d, $^3J_{PC}$ = 5.3, *o-C*), 121.3 (d, $^2J_{PC}$ = 8.4, $C_{ipso}$), 117.3 (d, $^4J_{PC}$ = 3.1, *m-C*), 114.9 (d, $^3J_{PC}$ = 4.3, *o-C*), 57.2 (s, $OCH_3$), 25.6 (d, $^1J_{PC}$ = 45.9, $ArCH_2$), 12.0 (d, $^1J_{PC}$ = 49.0, $PCH_2CH_3$), 5.8 (d, $^2J_{PC}$ = 5.4, $PCH_2CH_3$). Anal. Calcd for $C_{14}H_{24}O_2ClP$: C, 57.83; H, 8.32. Found: C, 58.2; H, 8.7. Low-resolution ESI MS: *m*/*z* = 255.1 $[M - Cl]^+$. $M_{calc}$ = 290.2.

**[4-OH-$C_6H_4CH_2PEt_3$]Cl (3b).** The procedure used follows that given for **3a** except that 248 mg (2.00 mmol) of 4-hydroxybenzyl alcohol was used; 480 mg of a white solid (75%) were isolated. Elemental analysis, MS, and NMR data ($^{31}P\{^1H\}$, $^1H$, $^1H\{^{31}P\}$, $^{13}C\{^1H\}$) for **3b** (and for **3c**−**j**), all white solids, are given in the Supporting Information, Table S1.

**[3,5-$(OMe)_2$-4-OH-$C_6H_2CH_2PEt_3$]Cl (3c).** The procedure used follows that given for **3a** except that 409 mg (2.00 mmol) of syringyl alcohol was used; yield 315 mg (61%).

**[3-MeO-4-OH-$C_6H_3CH_2PMe_3$]Cl (3d).** The procedure used follows that given for **3a** but with $Me_3P$ added as 1.0 M solution in toluene (2 mL, 2.0 mmol) and a stirring time of 24 h; yield 443 mg (89%).

(6) Hamanaka, N.; Kosuge, S.; Iguchi, S. *Synlett.* **1990**, 139.
(7) Lee, K. Y.; Kim, J. N. *Bull. Korean Chem. Soc.* **2000**, *21*, 763.
(8) Ruther, W.; Ruland, A. German Patent 3331008, 1985.
(9) Vullo, W. J. *Ind. Eng. Chem. Prod. Res. Dev.* **1966**, *5*, 346.

**[3-MeO-4-OH-$C_6H_3CH_2P^nPr_3$]Cl (3e).** The procedure for **3d** was used, but with $^nPr_3P$ (0.41 mL, 2.0 mmol); yield 379 mg (57%).

**[3-MeO-4-OH-$C_6H_3CH_2P^iPr_3$]Cl (3f).** The procedure for **3c** was used but with $^iPr_3P$ (0.39 mL, 2.0 mmol); yield 452 mg (68%).

**{3-MeO-4-OH-$C_6H_3CH_2P[(CH_2)_3OH]_3$}Cl (3 g).** The procedure to isolate **3c** was used, but with THPP (416 mg, 2.00 mmol, assuming 100% purity); yield 427 mg (56%).

**[3-MeO-4-OH-$C_6H_3CH_2PMe_2Ph$]Cl (3 h).** The procedure for **3c** was used, but with $Me_2PhP$ (0.29 mL, 2.0 mmol); yield 595 mg (96%).

**[3-MeO-4-OH-$C_6H_3CH_2PMePh_2$]Cl (3i).** The procedure for **3c** was used, but with $MePh_2P$ (0.38 mL, 2.0 mmol); yield 484 mg (65%).

**[3-MeO-4-OH-$C_6H_3CH(Me)PEt_3$]Cl (3j).** The procedure for **3a** was used, but with α-methylvanillyl alcohol (336 mg, 2.00 mmol); yield 522 mg (86%).

**Reaction of $Et_2PCH_2CH_2PEt_2$ with Vanillyl Alcohol to Give {[3-OMe-4-OH-$C_6H_3CH_2PEt_3$-$CH_2$-]$_2$}$^{2+}Cl_2$ (4).** The procedure used follows that given for **3a**, but using instead 0.24 mL (1.0 mmol) of the diphosphine; 511 mg (93%) of the white solid product was obtained. $^{31}P\{^1H\}$ NMR: $\delta$ 37.9 s. $^1H$ NMR: $\delta$ 6.87 (d, $^3J_{HH}$ = 7.9, 2H, *m-H*), 6.84 (br s, 2H, *o-H*), 6.72 (br d, $^3J_{HH}$ = 7.9, 2H, *o-H*), 3.81 (s, 6H, $OCH_3$), 3.65 [d, $^2J_{PH}$ = 13.4, 4H, $ArCH_2$ (s in $^1H\{^{31}P\}$ spectrum)], 2.33−2.23 (m, 8H, $PCH_2CH_3$), 2.14 [pseudo d, $^2J_{PH}$ = 6.7, 4H, $PCH_2CH_2P$ (s in $^1H\{^{31}P\}$ spectrum)], 1.22 (dt, $^3J_{PH}$ = 18.9, $^3J_{HH}$ = 7.6, 12H, $PCH_2CH_3$). $^{13}C\{^1H\}$ NMR: $\delta$ 149.6 (s, *C*-$OCH_3$), 146.9 (s, *C*-OH), 124.0 (br s, *o-C*), 120.2 (t, $^2J_{PC}$ = 8.9, $C_{ipso}$), 117.7 (s, *m-C*), 114.7 (s, *o-C*), 57.3 (s, $OCH_3$), 25.6 (d, $^1J_{PC}$ = 45.6, $ArCH_2$), 12.0 (d, $^1J_{PC}$ = 48.6, $PCH_2CH_3$), 5.8 (d, $^2J_{PC}$ = 5.0, $PCH_2CH_3$). Anal. Calcd for $C_{26}H_{42}O_4Cl_2P_2$: C, 56.63; H, 7.68. Found: C, 56.3; H, 8.0. Low-resolution ESI MS: *m/z* = 515.3 [100%, M − Cl]$^+$, 343.3 [45%, M − 2Cl − $CH_2C_6H_3(OH)(OMe)$]$^+$, *m/2z* = 240.2 [60%, M − 2Cl]$^{2+}$; $M_{calc}$ = 550.2.

**[4-HO-3-MeO-$C_6H_3CH(PEt_3)CH_2CH_2OH$]Cl (6).** A mixture of coniferyl alcohol (360 mg, 2.00 mmol) and $Et_3P$ (236 mg, 2.00 mmol) in water (8 mL) was heated at 90 °C for 20 h to give a yellow solution. After any unreacted phosphine was pumped off, HCl (0.17 mL of 37% aq solution, 2.00 mmol) was added, and water was then removed under reduced pressure. The resulting viscous residue was dissolved in EtOH (5 mL), and $Et_2O$ (5 mL) was added to precipitate an oil, which, after drying under vacuum, gave a white foam of **6** (300 mg, 45%). Anal. Calcd for $C_{16}H_{28}O_3ClP$: C, 57.40; H, 8.43. Found: C, 57.3; H, 8.7. $^{31}P\{^1H\}$ NMR: $\delta$ 40.4 s. $^1H$ NMR: $\delta$ 6.98 (d, $^3J_{HH}$ = 8.2, *m-H*), 6.97 (br s, 1H, *o-H*, superimposed with *m*-H), 6.91 (dt, $^3J_{HH}$ = 8.2, $^4J_{PH}$ = $^4J_{HH}$ = 2.2, 1H, *o-H*), 3.88 (s, 3H, $OCH_3$), 3.83 (ddd, $^3J_{HH}$ = 2.6, $^3J_{HH}$ = 12.8, $^2J_{PH}$ = 15.5, 1H, *CH*; $^1H\{^{31}P\}$: dd), 3.64 (m, 1H, $CH_AH_BOH$; $^1H\{^{31}P\}$: ddd), 3.38 (m, 1H, $CH_AH_BOH$; $^1H\{^{31}P\}$: ddd), 2.35 (m, 1H, $CH_AH_B$), 2.22 (dq, $^3J_{HH}$ = 7.6, $^2J_{PH}$ = 12.6, 6H, $PCH_2$), 2.15 (m, 1H, $CH_AH_B$, overlapped with $PCH_2$), 1.16 (dt, $^3J_{HH}$ = 7.6, $^3J_{PH}$ = 17.7, 9H, $CH_3$). $^{13}C\{^1H\}$ NMR: $\delta$ 149.4 (d, $^4J_{PC}$ = 2.5, *C*-$OCH_3$), 146.9 (d, $^5J_{PC}$ = 3.3, *C*-OH), 124.4 (d, $^2J_{PC}$ = 6.1, $C_{ipso}$), 123.7 (br s, *o-C*), 117.5 (d, $^4J_{PC}$ = 2.5, *m-C*), 114.7 (br s, *o-C*), 59.3 (d, $^3J_{PC}$ = 14.0, $CH_2OH$), 57.4 (s, $OCH_3$), 35.4 (d, $^1J_{PC}$ = 45.3, *PC*H), 31.0 (s, $CH_2$), 11.7 (d, $^1J_{PC}$ = 47.7, $PCH_2$), 3.6 (d, $^2J_{PC}$ = 5.6, $CH_3$). Low-resolution ESI MS: *m/z* = 299.2 (100%) [M − Cl]$^+$, 281.2 (30%) [M − Cl − $H_2O$]$^+$; $M_{calc}$ = 334.1.

**X-ray Crystallographic Analysis.** An X-ray quality, colorless crystal of **3c** was obtained by crystallization from a saturated DMSO solution of the compound. Selected crystallographic data are shown in Table 1 and more details are provided in the Supporting Information. Measurements were made at 173 (±0.1) K on a Bruker X8 APEX diffractometer using graphite-monochromated Mo Kα radiation (0.71073 Å). Data were collected to a maximum $2\theta$ value of 52.8°, in a series of $\phi$ and $\omega$ scans in 0.50° oscillations with 20.0 s exposures; the crystal-to-detector distance was 38.95 mm. Of the 8292 reflections collected, 3322 were unique ($R_{int}$ = 0.034; Friedels not merged); equivalent reflections were merged. Data were collected and integrated using the Bruker SAINT software package.[10] Data were corrected for absorption effects using the multiscan technique (SADABS),[11] with minimum and maximum transmission coefficients of 0.831 and 0.987, respectively. The data were corrected for Lorentz and polarization effects, and the structure was solved by direct methods.[12] All non-H atoms were refined anisotropically. H1o was located in a difference map and refined isotropically. All other H atoms were included in calculated positions but were not refined.

**Table 1.** Crystallographic Data for **3c**

| | |
|---|---|
| empirical formula | $C_{15}H_{26}O_3PCl$ |
| fw | 320.78 |
| cryst color, habit | colorless, tablet |
| cryst size, mm | 0.04 × 0.10 × 0.25 |
| cryst. syst | orthorhombic |
| space group | $P2_12_12_1$ ( No. 19) |
| *a*, Å | 8.1209(4) |
| *b*, Å | 11.0776(5) |
| *c*, Å | 18.0926(9) |
| *V*, Å$^3$ | 1627.6(1) |
| *Z* | 4 |
| $\mu$, cm$^{-1}$ | 3.38 |
| total reflns | 8292 |
| unique reflns | 3322 |
| $R_{int}$ | 0.034 |
| no. variables | 190 |
| *R*1 ($I > 2.00\sigma(I)$) | 0.035 (2931 obsd reflns) |
| wR2[a] | 0.088 (all data) |
| gof | 1.06 (all data) |

[a] $w = 1/[\sigma^2(F_o^2) + (0.0448P)^2 + 0.0000P]$, where $P = (F_o^2 + 2F_c^2)/3$.

## Result and Discussion

As discussed in our earlier paper,[2] the 1:1 reaction of syringyl alcohol (**1c** in Scheme 1) with $[HO(CH_2)_3]_3P$ (THPP), in $H_2O/D_2O$ under Ar at 90 °C for 16 h, generated the zwitterionic phosphobetaine **2** (X = Y = OMe, Scheme 1) as a highly hygroscopic, sticky greenish solid. The formulation of **2** is consistent with the $^1H$-, $^{31}P\{^1H\}$-, $^1H\{^{31}P\}$-, and $^{13}C\{^1H\}$-NMR data, and MS data, although satisfactory elemental analysis (EA) was difficult to obtain; for example, the EA was 0.56% low in C and 0.73% low in H.[2] One likely difficulty here is that **2** is isolated partly in a protonated form as a phosphonium hydroxide.[2,13] In the present work, the analogous phosphobetaine (X = OMe, Y = H, Scheme 1) obtained from vanillyl alcohol (**1a**) had similar limitations in characterization, but more conclusive proof of the formulation was obtained by treating the phosphobetaine with 1 equiv of HCl to generate the phosphonium chloride (**3g**), see below. Several such phosphonium chlorides (**3a**−**i**), all highly water-soluble except **3i**, were

(10) *SAINT*, Version 7.03A; Bruker AXS Inc.: Madison, WI, 1997−2003.
(11) *SADABS. Bruker Nonius area detector scaling and absorption correction*, V2.10; Bruker AXS Inc.: Madison, WI, 2003.
(12) Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G. L.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A. G. G.; Polidori, G.; Spagna, R. *J. Appl. Crystallogr.* **1999**, *32*, 115.
(13) Moiseev, D.; James, B. R.; Patrick, B. O.; Hu, T. Q. *Inorg. Chem.* **2007**, *46*, 9389.

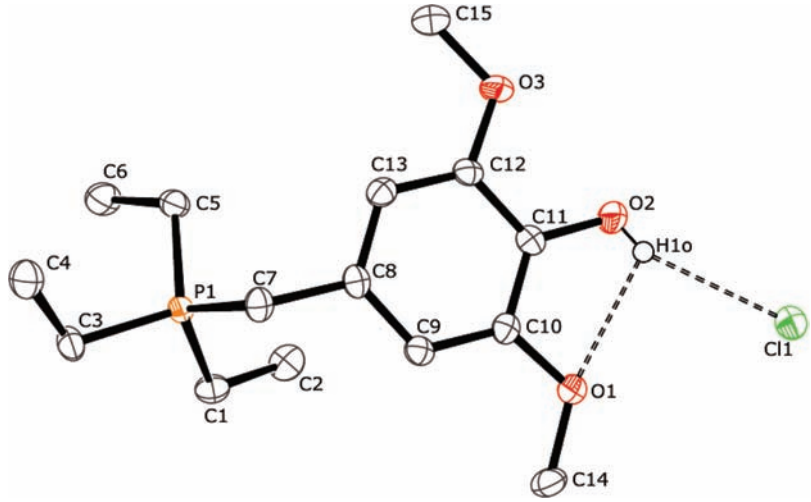



**Figure 1.** ORTEP diagram of **3c** showing 50% probability thermal ellipsoids; H-atoms omitted for clarity.

similarly made in 57−96% yields by the 1:1 reaction of vanillyl-, syringyl-, and 4-OH-benzyl alcohol with tertiary phosphines, followed by treatment with 1 equiv of HCl (Scheme 1).

Except for the purely aqueous THPP systems, all the other reactions (involving alkyl-containing phosphines) were 2-phase at the start, but the initially formed emulsions had turned into homogeneous solutions by completion of the reactions; it would be difficult to monitor the 2-phase systems by NMR. The characterization of **3a** will serve as an example for characterization of the other chlorides **3b**−**i**, whose NMR, MS, and EA data are given in the Supporting Information, Table S1; corresponding data for **3j**, made from $Et_3P$, 3-MeO-4-OH-$C_6H_3CH(Me)OH$ (a Me-substituted vanillyl alcohol) and HCl, are also given in Supporting Information, Table S1. In the case of the $Et_3P$/syringyl alcohol system, an X-ray quality crystal of the phosphonium chloride **3c** was isolated, and its structure fully confirmed the nature of these compounds.

The phosphonium chloride **3a** (Scheme 1) in $D_2O$ is characterized by a $^{31}P\{^1H\}$ singlet at $\delta$ 38.0, in the correct range for a phosphonium compound.[2,13,14] The benzyl protons appear in the $^1H$ spectrum at $\delta$ 3.56 as a doublet ($^2J_{PH}$ = 14.0 Hz), which collapses to a singlet in the $^1H\{^{31}P\}$ spectrum; the $CH_2$ and $CH_3$ resonances of the $Et_3P$ moiety appear in the $^1H$ NMR, respectively, as an expected doublet of quartets at $\delta$ 2.15 and a doublet of triplets at $\delta$ 1.18. Resonances for the other protons are also readily assigned (see Experimental Section), although that of the *p*-OH was not seen because of H/D exchange. The phenolic $^1H$ signal in aprotic solvents for the benzyl alcohols used here is solvent-dependent and appears in the range $\delta$ 9.0−6.0. The $^{13}C\{^1H\}$ resonances, including that of the benzyl carbon, a doublet at $\delta_C$ 25.6 ($^1J_{PC}$ = 45.9 Hz), are also readily assigned. The phosphonium chlorides **3b** and **3c** formed from $Et_3P$ with 4-hydroxybenzyl alcohol (**1b**) and syringyl alcohol (**1c**), respectively, reveal NMR data similar to those of **3a**.

A colorless crystal of **3c** was obtained by crystallization of the salt from DMSO. The molecular structure (Figure 1) and selected geometrical parameters (Table 2) are standard for a P atom exhibiting tetrahedral coordination, with

**Table 2.** Selected Bond Distances and Angles for **3c** with Estimated Standard Deviations in Parentheses

| bond | length (Å) | bond | angle (deg) |
|---|---|---|---|
| C (1)−P (1) | 1.794 (2) | C (1)−P (1)−C (7) | 112.07 (12) |
| C (3)−P (1) | 1.796 (2) | C (3)−P (1)−C (7) | 107.37 (12) |
| C (5)−P (1) | 1.798 (3) | C (5)−P (1)−C (7) | 109.43 (11) |
| C (7)−P (1) | 1.804 (2) | C (8)−C (7)−P (1) | 115.51 (16) |
| C (11)−O (2) | 1.361 (3) | C (11)−O (2)−H (1o) | 115 (2) |
| O (2)−H (1o) | 0.70 (3) | O (2)−H (1o)···Cl (1) | 158 (3) |
| H (1o)···Cl (1) | 2.47 (3) | O (2)−H (1o)···O (1) | 110 (3) |
| H (1o)···O (1) | 2.38 (3) | | |

C−P−C angles in the range of 106.35−112.07°.[13–15] Of note, the H atom of the phenolic hydroxide is H-bonded to the $Cl^-$ and to the O atom of an MeO group. Within the O(2)···H···Cl and O(2)···H···O(1) bonds (with respective angles of 158 and 110°), the O(2)···H, H···Cl, and the H···O(1) distances are 0.70, 2.47, and 2.38 Å, respectively, with corresponding O(2)···Cl and O(2)···O(1) distances of 3.134 and 2.700 Å.

The α-methyl-substituted vanillyl alcohol (**1d**) reacts with $Et_3P$ in the same manner as **1a** and affords the phosphonium salt **3j** in 86% yield after 20 h (Scheme 2); in the $^{31}P\{^1H\}$ spectrum, the singlet $\delta_P$ appears at 40.9, while the benzyl proton appears in the $^1H$ spectrum at $\delta_H$ 3.80 as a doublet of quartets (due to $^3J_{HH}$ and $^2J_{PH}$ coupling), which collapses in the $^1H\{^{31}P\}$ spectrum to a quartet (Supporting Information, Table S1).

The tertiary phosphines $Me_3P$, $^nPr_3P$, $^iPr_3P$, $[HO(CH_2)_3]_3P$, $Me_2PhP$, and $MePh_2P$ react with vanillyl alcohol in the same manner as $Et_3P$ and give, after treatment with HCl, the corresponding phosphonium salts **3d**−**i** (Scheme 1). $^{31}P$ chemical shifts are listed in Scheme 1. A reaction of vanillyl alcohol with $(NCCH_2CH_2)_3P$ affords many products, as judged by a multitude of $^{31}P\{^1H\}$ NMR signals seen in a $D_2O$ solution of a product residue; hydrolysis of CN groups is suspected.

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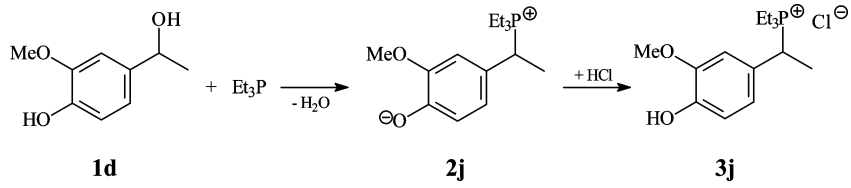
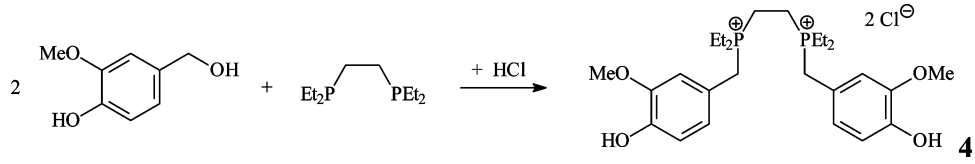
**Scheme 2**




**Scheme 3**




A 2:1 reaction of vanillyl alcohol with the diphosphine $Et_2PCH_2CH_2PEt_2$ and 2 equiv of HCl gave cleanly the water-soluble bisphosphonium salt (**4**) in 93% yield (Scheme 3); the EA, NMR, and MS data are fully consistent with the formulation shown.

Worth noting is the related chemistry in a patent that reports formation of $[(3,5(alkyl)_2\text{-}4\text{-}OH\text{-}C_6H_2CH_2)_4P]Cl$ (used as an antioxidant in polypropylene production) from reaction of $[(HOCH_2)_4P]Cl$ with the appropriate 4-OH-benzyl chloride in dioxane in the presence of $Et_3N$.[16] We did test the reaction of vanillyl alcohol with $[(HOCH_2)_4P]Cl$ in water at 90 °C under Ar in the absence of added base, and preliminary NMR and MS data[17] appear consistent with formation of $[(3\text{-}MeO\text{-}4\text{-}OH\text{-}C_6H_3CH_2)_4P]Cl$ in high yield, thus showing that benzyl alcohols can possibly be used as reactants via a "greener" method in aqueous media instead of the corresponding chlorides in dioxane solution.

Because of our interest in the kinetics of reactions of water-soluble phosphines (such as THP and THPP) with lignin-type alcohols and the **2**:**3** product ratio at a selected pH (deprotonated to protonated form, cf. Scheme 1), we measured the p$K_a$ of the phenol-OH of a phosphonium chloride product (**3**) by a standard UV−vis/pH titration method.[18] Data for the α-methylvanillyl alcohol (**1d**) system (Scheme 2) are shown in Figure 2: at pH 6.00, absorption maxima for the protonated form (**3j**) are seen at 206, 234, and 282 nm, while increasing pH leads to deprotonation to give the zwitterion (**2j**) with maxima at 214, 256, and 296 nm, and the titration reveals a clean system with 3 isosbestic points (224, 242, and 282 nm). Standard analysis of the data at 256 nm via the Henderson−Hasselbalch equation[19] yields a p$K_a$ value of 9.14 ± 0.02 (Supporting Information, Figure S1). As expected, the presence of the phosphonium moiety increases significantly the acidity of the phenolic-OH group, the p$K_a$ value for **1d**, under the same conditions, being 9.83.[20] To the best of our knowledge, this is the first report of the effect on a phenolic p$K_a$ of inclusion of a phosphonium group into a phenol. Attempts to determine the p$K_a$ of **3g** were thwarted by difficulty in handling this air-sensitive material; related to this was the difficulty in trying to prepare a THPP analogue of **3j**, this leading to a white, foam-like solid that over a few hours turned to a pink, viscous residue. The

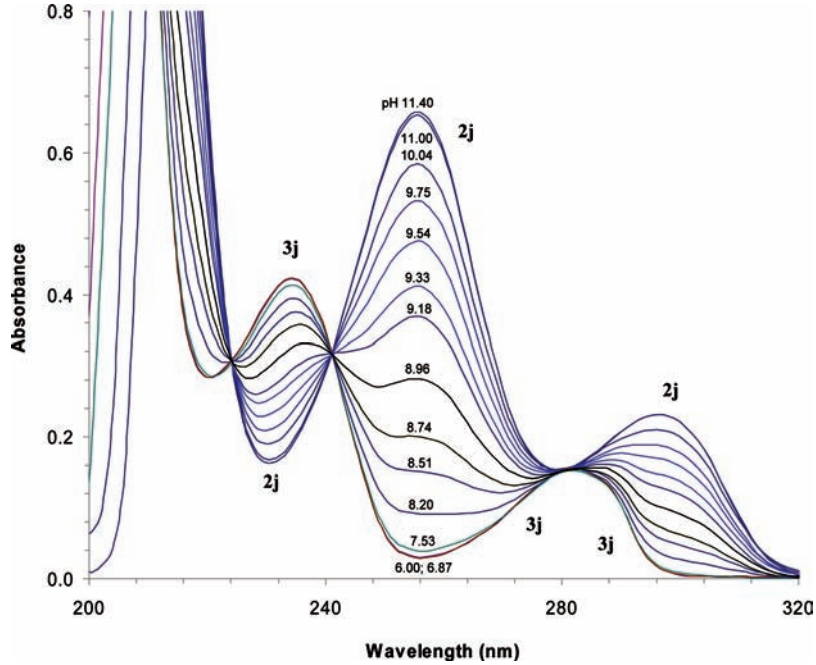
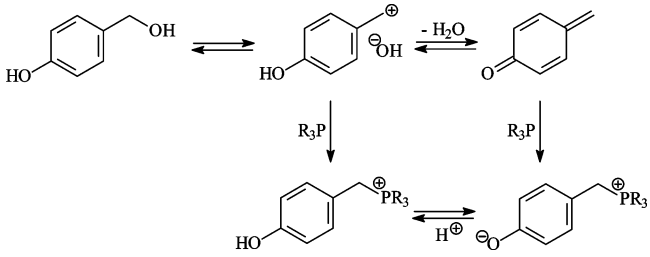
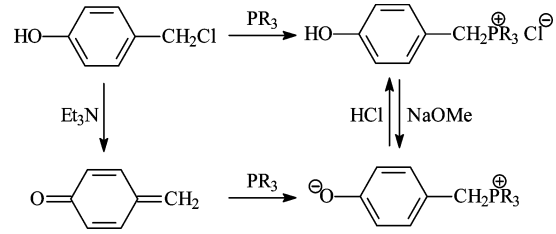



**Figure 2.** pH-Dependence of the UV−vis spectrum of buffered solutions of **3j** (see Scheme 2) at 25 °C; initial [**3j**] = $5.01 \times 10^{-5}$ M.

**Scheme 4**



**Scheme 5**



incorporation of an OH group into the phosphine renders the phosphonium salts much more difficult to handle and purify, as noted previously in the reaction of THPP with syringyl alcohol.[2]

To estimate a reactivity trend of benzyl alcohols toward a tertiary phosphine, NMR-scale reactions of the water-soluble phosphine THPP with **1a**−**d**, and with 2- and 3-OH-benzyl alcohols, were carried out under selected conditions (1:1, $H_2O$, Ar, 90 °C); the product is a type-**2** zwitterion (in its free and/or protonated form). Consumption of THPP ($\delta_P$ −29.3) was monitored by $^{31}P\{^1H\}$ NMR, and the data are presented in Supporting Information, Figure S2. The reactivity decreases in the order **1d** > **1c** ≥ **1a** > **1b** > 2-OH-benzyl alcohol, while 3-OH-benzyl alcohol was unreactive: with **1d**, 97% consumption of THPP is reached after 2 h, while the corresponding times for **1c** and **1a** were 6 and 8 h, respectively; with **1b** only 88% of THPP had reacted after 12 h. Reactivity toward 2-OH-benzyl alcohol is lower (50% conversion after 12 h) than with the 4-OH (**1b**). The type-**2** products in these reactions react rapidly with 1 equiv of HCl to generate the respective phosphonium chlorides. Direct addition of HCl to the benzyl alcohols in the absence or presence of phosphine generated emulsions that must contain the corresponding benzyl chlorides, the observation implying that benzyl alcohols react faster with HCl than with phosphines.

A plausible mechanism for the reaction of phosphines with lignin-type alcohols in aqueous solution involves initial generation of a carbonium ion, with the phenolic-OH then deprotonated to give a form stabilized by the quinone methide resonance structure; subsequent nucleophilic attack by the phosphine would give the phosphonium salt in protonated or zwitterionic form (Scheme 4). That 3-OH-benzyl alcohol is unreactive is consistent with this suggested mechanism because the *m*-substituted alcohol cannot form a quinone methide intermediate. Increasing *m*-substitution of OMe groups presumably increases reactivity (**1c** ≥ **1a** > **1b**) by stabilizing the carbocation, while replacement of a benzyl hydrogen of the 4-OH alcohol by methyl increases reactivity more significantly (**1d** has the highest reactivity), presumably again by stabilizing the carbocation. The reactivity order is also in general agreement with the fact that electron-donor substituents increase stability of quinone methides.[21] There was no reaction of benzyl alcohol itself with THPP, consistent again with the requirement of an *o*- or *p*-OH substituent to form the zwitterion/phosphobetaine intermediate; in the presence of HCl, the alcohol is converted into benzyl chloride which can react with tertiary phosphines via a standard nucleophilic substitution reaction.

Supporting the mechanism of Scheme 4, formation of a quinone methide via dehydrochlorination with $Et_3N$ in benzene of the substituted benzyl chloride, 3,5-$^t$Bu$_2$-4-OH-$C_6H_2CH_2Cl$, and subsequent reaction with $^n$Bu$_3$P has been shown to generate the phosphonium cation.[22] This report also demonstrates nicely the two approaches to formation of phosphonium salts from a 4-OH-benzyl chloride: direct nucleophilic substitution of $Cl^-$ by phosphine, or via the phosphine/quinone methide reaction (Scheme 5). In our systems, the quinone methide has to be generated from a benzyl alcohol by a net loss of $H_2O$. Related chemistry is seen in a report on formation of an *o*-phosphonium zwitterion from 4-nitro-2-(chloromethyl)phenol and $Ph_3P$ (or $Pr_3P$) following dehydrochlorination with a base.[23] In a patent describing syntheses of 2-, 3-, and 4-OH-benzylphosphonium chlorides from the corresponding benzyl alcohol and phosphine in the presence of HCl,[8] the systems must involve initial formation of the benzyl chlorides and direct nucleophilic displacement of the chloride by the phosphine since the 3-OH (*m*-substituted) undergoes reaction.

The interaction of $Et_3P$ with coniferyl alcohol (**5**) was also studied (Scheme 6). This alcohol (a substituted cinnamyl alcohol) is, like the substituted benzyl alcohols, also a precursor to polymeric units in lignin,[24] but interaction with the phosphine is different from that seen for **1a**−**d**: $Et_3P$ now attacks the C═C bond at the carbon adjacent to the aromatic ring. After treatment with HCl, the phosphonium salt **6** is isolated in 45% yield. The formulation is substantiated by EA, low-resolution MS ESI, and NMR data (see Experimental Section and Supporting Information, Figure S3, which shows a $^1H-^1H$ COSY experiment). The $\gamma$-H appears in the $^1H$ spectrum as a doublet of doublets of doublets at $\delta$ 3.83 ($^3J_{HH}$ = 2.6, $^3J_{HH}$ = 12.8, $^2J_{PH}$ = 15.5 Hz), while the diastereotopic α-protons, correlating in a $^1H-^{13}C\{^1H\}$ HSQC experiment with a doublet at $\delta_C$ 59.3 ($^3J_{PC}$ = 14.0), appear

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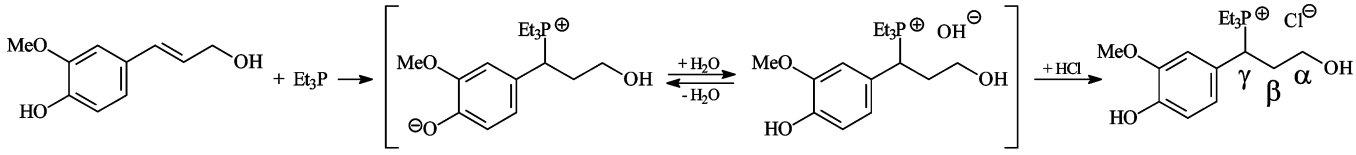
**Scheme 6**




**5** **6**

as multiplets centered at $\delta$ 3.64 and 3.38. The diastereotopic $\beta$-protons, correlating in the $^1H-^{13}C\{^1H\}$ HSQC experiment with a singlet at $\delta_C$ 31.0, appear as multiplets centered at $\delta$ 2.35 and 2.15. The $^{31}P\{^1H\}$ singlet is seen at $\delta$ 40.4. The suggested mechanism shown in Scheme 6 follows that from our studies on the interaction of phosphines with unsaturated aromatic aldehydes including coniferaldehyde.[13] Evidence for the intermediate zwitterion was seen in an NMR-scale, 1:1 reaction of **5** with THPP in $H_2O$ that was complete in 5 h; the $^{31}P\{^1H\}$ singlet of THPP was gradually replaced by a new singlet at $\delta_P$ 37.2, assigned to the corresponding phosphonium zwitterion (or an equilibrium mixture of the zwitterion and its protonated form (cf. Scheme 4)). When the same reaction was carried out in $D_2O$, slow H/D-exchange of the $CH_2$ protons adjacent to the P atom and the $\gamma$-proton was observed; such exchange, noted in an earlier paper describing reaction of THPP with syringyl alcohol,[2] almost certainly occurs via ylide intermediates (see Scheme 6 in ref 2).

Reactions of the type shown in Scheme 6, which reduce the extent of conjugation, could certainly contribute to a pulp bleaching process, while possible reactions of alcohols with phosphines should be considered when alcohols are products from reactions catalyzed by metal-phosphine complexes, particularly where in situ catalysts are generated using excess phosphine.

No reaction was observed between THPP and cinnamyl alcohol under the same conditions used for the benzyl alcohol systems. Presumably, compared to **5**, the absence of the *p*-OH substituent prevents reactivity at the C═C and $CH_2OH$ moieties (cf. Schemes 4 and 6). Halogen-substituted alcohols (e.g., chlorohydrins) have been shown to react with tertiary phosphines but with replacement of the halide to form products of the type $[R_3P(CH_2)_2OH]X$, where X is typically Cl.[15,25]

## Conclusions

Research on the use of water-soluble phosphines for the bleaching of pulps led us into aqueous solution studies on the interaction of tertiary phosphines with organic components found in lignin, in this case aromatic alcohols mainly containing -OH and/or -OMe substituents in the aromatic ring. The products are zwitterionic phosphobetaines that are difficult to isolate as pure compounds, but treatment with HCl converts these to phosphonium chlorides which are well characterized, in one case by X-ray crystallography. Reactivity requires the presence of an *o*- or *p*-OH substituent in the alcohol, and this is consistent with a mechanism via carbocation and quinone methide intermediates. The mechanism complements that invoked in non-aqueous solvents for formation, for example, of a phosphonium chloride, involving conventional nucleophilic displacement of the chlorine of an aromatic or alkyl chloride by a tertiary phosphine.

**Acknowledgment.** We thank the Natural Sciences and Engineering Research Council of Canada for funding via a Discovery Grant.

**Supporting Information Available:** Elemental analyses, MS, and NMR data ($^{31}P\{^1H\}$, $^1H$, $^1H\{^{31}P\}$, $^{13}C\{^1H\}$) for the phosphonium chlorides **3b**−**j**; CIF file for **3c**; analysis for $pK_a$ from the data of Figure 2; reactivity data for alcohols toward THPP; $^1H-^1H$ COSY data for **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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