Reversible decomposition of mono(α-hydroxy)-phosphines and their reaction with α,β-unsaturated aldehydes

Dmitry V. Moiseev, Paolo Marcazzan, and Brian R. James

Abstract: The mono(α-hydroxy)phosphines $R_2PCH(OH)R'$ (R = Ph, R′ = H, Et, CH_2Ph, Ph, *p*-X-C_6H_4; R = cyclohexyl, R′ = Ph) are prepared under solvent-free conditions by a 1:1 reaction of Ph_2PH with the appropriate aldehyde, and their stabilities (with respect to reversible dissociation into reactants), studied in DMSO, Et_2O, and MeOH, increase with decreased basicity of the hydroxyphosphine; for example, for the $Ph_2PCH(OH)C_6H_4$-*p*-X phosphines, stability decreases in the order: X = CN > Cl > F > H > Me > OMe. A 1:1 room-temperature reaction of the (α-hydroxy)phosphines (except for R′ = H) with cinnamaldehyde in DMSO slowly yields the known mono- and di-phosphines $Ph_2PCH(Ph)CH_2CHO$ (**4a**) and $Ph_2PCH(Ph)CH_2CH(PPh_2)OH$ (**10a**), and the corresponding R′CHO aldehyde. In MeOH, the sequentially formed intermediates, $PhCH{=}CHCH(OH)PPh_2$, $PhCH(OH)CH{=}CHPPh_2$, and $Ph_2PCH(Ph)CH{=}CHOH$, were detected en route to **4a** and **10a**. Reaction of cinnamaldehyde with Ph_2PCH_2OH gives **4a** and the hemiacetal $Ph_2PCH_2OCH_2OH$ formed from the reactant hydroxyphosphine with the co-product formaldehyde. Reactions carried out in MeOH are faster because of the formation of hemiacetals from the phosphine-containing aldehyde products; thus, **4a** is seen as $Ph_2PCH(Ph)CH_2CH(OMe)(OH)$, which on dissolution in Et_2O, reverts to the aldehyde. The reaction rates and equilibrium concentrations of the various species depend on the R′ group of the reactant phosphine; the rates of consumption of the hydroxyphosphines in the reactions with cinnamaldehyde decrease in the order: $Ph_2PCH(OH)Ph > Ph_2PCH(OH)Et > Ph_2PCH(OH)CH_2Ph >> Ph_2PCH_2OH$. The reactivity pattern of $Ph_2PCH(OH)Ph$ with sinapaldehyde [3,5-$(OMe)_2$-4-OH-cinnamaldehyde] in DMSO follows that seen for cinnamaldehyde. Reaction of Ph_2PH with cinnamaldehyde in DMSO affords **4a** and **10a** via the same intermediates seen with the $Ph_2PCH(OH)R'$ reagents, but these latter reactions are thought to occur via direct attack on cinnamaldehyde by the hydroxyphosphine rather than via Ph_2PH.

Key words: (α-hydroxy)phosphines, α,β-unsaturated aldehydes, diphenylphosphine, hydrophosphination.

Résumé : On a préparé des mono(α-hydroxy)phosphines $R_2CH(OH)R'$ [R = Ph, R′ H, Et, CH_2Ph, Ph, *p*-X-C_6H_4; R = cyclohexyle; R′ = Ph] dans des conditions sans solvant, en faisant réagir des quantités équimoléculaires (1:1) de Ph_2PH et de l'aldéhyde approprié. On a de plus étudié leurs stabilités par rapport à leur dissociation en réactifs dans le DMSO, Et_2O et MeOH qui augmente avec une diminution de la basicité de l'hydroxyphosphine; par exemple, pour les phosphines $Ph_2PCH(OH)C_6H_4$-*p*-X, la stabilité diminue dans l'ordre X = CN > Cl > F > H > Me > OMe. Une réaction de quantités équimoléculaires des (α-hydroxy)phosphines (à l'exception de celle dans laquelle R′ = H) et de cinnamaldéhyde, dans le DMSO, conduit lentement à la formation des mono- et diphosphines connues, $Ph_2PCH(Ph)CH_2CHO$ (**4a**) et $Ph_2PCH(Ph)CH_2CH(PPh_2)OH$ (**10a**), ainsi qu'à l'aldéhyde correspondant, R′CHO. Dans le méthanol, les produits $PhCH{=}CH(OH)PPh_2$, $PhCH(OH){=}CHPPh_2$ et $Ph_2PCH(Ph)CH{=}CHOH$, qui se forment successivement comme intermédiaires entre **4a** et **10a**. La réaction du cinnamaldéhyde avec le Ph_2PCH_2OH conduit à la formation du produit **4a** et de l'hémiacétal, $Ph_2PCH_2OCH_2OH$, qui résulte de la réaction du réactif hydroxyphosphine avec le formaldéhyde obtenu comme coproduit. Les réactions effectuées dans le MeOH sont plus rapides en raison de la formation d'hémiacétals à partir des produits aldéhydiques contenant une phosphine; ainsi, le produit **4a** observé sous la forme de $Ph_2PCH(Ph)CH_2CH(OMe)(OH)$ qui, par dissolution dans Et_2O se retransforme en aldéhyde. Les vitesses de réaction et les concentrations à l'équilibre des diverses espèces dépendent de la nature du groupe R′ présent sur la phosphine; les vitesses de consommation des hydroxyphosphines dans les réactions avec le cinnamaldéhyde diminuent dans l'ordre $Ph_2PCH(OH)Ph > Ph_2PCH(OH)Et > Ph_2PCH(OH)Ph > Ph_2PCH(OH)CH_2Ph > Ph_2PCH_2OH$. Le patron de réactivité du $Ph_2PCH(OH)Ph$ avec le sinapaldéhde [3,5-(Ome)2-4-OH-cinnamaldéhyde], dans le DMSO, est similaire à celui du cinnamaldéhyde. La réaction du Ph_2PH avec le cinnamaldéhyde, dans le DMSO, conduit à la formation des produits **4a** et **10a** par le biais des mêmes intermédiaires que ceux observés avec les réactifs $Ph_2PCH(OH)R'$; on croit toutefois que ces dernières réactions se produisent par le biais d'une attaque directe de l'hydroxyphosphine sur le cinnamaldéhyde pluṭt que par le biais d'une attaque via Ph_2PH.

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Mots-clés : (α-hydroxy)phosphines, aldéhydes α,β-insaturés, diphénylphosphine, hydrophosphination.

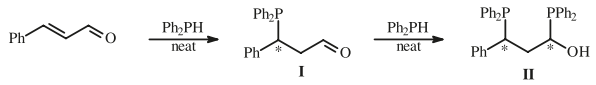
[Traduit par la Rédaction]

Introduction

Collaborative research involving our group has revealed that (hydroxymethyl)phosphines, particularly $P(CH_2OH)_3$ (abbreviated THP), are excellent bleaching and brightness stabilization agents for pulps, and interaction of such phosphines with conjugated carbonyl components of lignin is important in the bleaching process.[1] A current, widely used pulp-bleaching agent is sodium dithionite ($Na_2S_2O_4$), industrially called "hydrosulfite", and the collaborative studies revealed a remarkable synergistic effect in the use of a combination of THP and $Na_2S_2O_4$ for the bleaching;[2] this led us to study the complicated interaction between these two chemicals in aqueous solution, where some bis(hydroxymethyl)phosphine $PH(CH_2OH)_2$ was observed.[3] This encouraged us to study the reaction of secondary phosphines with lignin-model compounds, exemplified by cinnamaldehyde, where use of neat reagents gave isolable products from hydrophosphination of first the C=C and subsequently the C=O bonds (Scheme 1).[4] The isolated (α-hydroxy)phosphine **II** was found in solution to decompose reversibly to **I** and Ph_2PH with rates that were highly solvent-dependent.[4] The analogous reversible decomposition of $Ph_2PCH(OH)Et$ to propionaldehyde and Ph_2PH was also demonstrated,[4] and this confirmed the generality of such a process, which was first noted for the benzaldehyde/Ph_2PH system;[5] a more recent study with phenolic aldehydes has also demonstrated such equilibria.[6] This chemistry was clearly relevant for our studies involving THP, a tris(α-hydroxy)phosphine, and we decided to investigate reactivity between cinnamaldehyde and mono(α-hydroxy)phosphines, which could well be present in the bleaching systems formed via addition of PH of the observed $PH(CH_2OH)_2$ across carbonyl and (or) olefinic functionalities. This paper presents our findings on these systems, studied in organic solvents. The studies complement those of our recent papers, which describe the interactions in aqueous solution between cinnamaldehyde and $P[(CH_2)_2OH]_3$,[7] and between substituted cinnamaldehydes and non-functionalized tertiary phosphines.[8]

There is literature describing reactivity of (α-hydroxy)phosphines (mostly THP) with α,β-unsaturated carbonyl-containing compounds in organic solvents, where the phosphorus atom attacks the activated C=C bond followed by loss of an aldehyde; e.g., THP with acrylonitrile gives $P(CH_2CH_2CN)_3$ with loss of formaldehyde, the net reaction being addition of P–H across the C=C bond (eq. [1]).[9,10] Similarly, reaction of the bis(α-hydroxy)phosphines $RP(CH_2OH)_2$ (R = Me, Et) with acrylonitrile can lead to formation of $RP(CH_2CH_2CN)_2$.[11] Reaction of THP with methyl acrylate in organic solvents generates the phosphine oxide $O=P(CH_2CH_2CO_2Me)_3$ formed because of the presence of trace water,[12] while THP (formed from the tetrakis(hydroxy)phosphonium salt $[P(CH_2OH)_4]Cl$ and base) reacts with acrylamide to give a mixture of $[(HOCH_2)P(CH_2CH_2NHCH_2OH)_3]OH$ and $O=P(CH_2CH_2NHCH_2OH)_3$, and with acrylic acid to yield a phosphobetaine (eq. [2]).[10] In this relatively early literature work, studied during the early days of ^{31}P NMR, the products, although likely correct, were not always well-characterized.

Scheme 1. 1:1 and 2:1 reactions of Ph_2PH with cinnamaldehyde; * indicates a chiral centre (ref. 4).



$$[1]\quad P(CH_2OH)_3 + 3CH_2{=}CHCN \rightarrow P(CH_2CH_2CN)_3 + 3CH_2O$$

$$[2]\quad [P(CH_2OH)_4]Cl + NaOH + CH_2{=}CHCO_2H \rightarrow (HOCH_2)_3P^+CH_2CH_2CO_2^- + CH_2O + H_2O + NaCl$$

Our studies reported here describe mainly reactions of cinnamaldehyde with the hydroxyphosphines $R_2PCH(OH)R'$ (R = Ph, R′ = H, Et, CH_2Ph, Ph, or *p*-substituted-Ph) in DMSO and in MeOH, as well as reversible decomposition of the hydroxyphosphines.

Experimental section

Cinnamaldehyde, sinapaldehyde [3,5-$(OMe)_2$-4-OH-cinnamaldehyde], PhCHO, and 4-X-C_6H_4CHO (X = CN, Cl, F, Me, and MeO), all Aldrich products, were distilled under reduced pressure or recrystallized, and stored under Ar before use. Ph_2PH and Cy_2PH (Cy = cyclohexyl) from Strem Chemicals were used as received. Ph_2PCH_2OH was prepared as reported from Ph_2PH and paraformaldehyde,[13] but purified by trituration using hexane/$CHCl_3$ (6:1), while $Ph_2PCH(OH)Et$, $Ph_2PCH(OH)CH_2Ph$, $Ph_2PCH(OH)Ph$, and $Cy_2PCH(OH)Ph$ were prepared from the appropriate secondary phosphine and aldehyde by our recently described procedure under Ar using Schlenk glassware or a glovebox.[4] ^1H, $^1H\{^{31}P\}$, and $^{13}C\{^1H\}$ NMR data for a DMSO-d_6 solution, and elemental analyses, of the new (α-hydroxy)phosphines are given in Table S1 (see Supplementary data). The $^{31}P\{^1H\}$ singlets for these phosphines in different solvents are listed in Table S2 (see Supplementary data). Organic solvents were dried over the appropriate reagents, and then distilled under Ar, while CD_3OD and DMSO-d_6 (Cambridge Isotope Laboratory) were used as received. $^{31}P\{^1H\}$ NMR spectra were recorded on a Bruker AV300 spectrometer (121 MHz) at 300 K unless otherwise stated; ^1H and ^{13}C NMR spectra were similarly recorded on an AV400 instrument (400 MHz for ^1H, 100 MHz for $^{13}C\{^1H\}$). A residual deuterated solvent proton (relative to external $SiMe_4$) and external 85% aq. H_3PO_4 were used as references: br = broad, s = singlet, d = doublet, t = triplet, p = pentet, and m = multiplet. *J* values are given in Hertz. When necessary, atom assignments were made by means of ^1H–^1H, ^1H–$^{13}C\{^1H\}$ (HMQC and HMBC) and ^1H–$^{31}P\{^1H\}$ NMR correlation spectroscopies.

Stability (with respect to reversible dissociation) of mono(α-hydroxy)phosphines in organic solvents

In a glovebox, the phosphine (0.05 mmol) was dissolved in 1 mL of a selected solvent, and a sample (~0.7 mL) of the solution was placed under Ar in a J-Young NMR tube; $^{31}P\{^{1}H\}$ NMR spectral changes were then monitored as a function of time at 300 K.

Reactions of Ph_2PH with aromatic aldehydes in MeOH

In a glovebox, Ph_2PH (18.6 mg, 0.1 mmol) was added to a MeOH solution of the aldehyde (0.1 mmol in 1 mL), and $^{31}P\{^{1}H\}$ NMR spectral changes of a sample were then monitored as described above.

Reactions of Ph_2PH or a mono(α-hydroxy)phosphine with an α,β-unsaturated aldehyde

As above, the phosphine (0.1 mmol) was added under Ar to a solution of the aldehyde (0.1 mmol) in air-free DMSO/DMSO-d_6 or MeOH/CD_3OD (1 mL), and a sample was monitored by NMR spectroscopy at 300 K.

Results and discussion

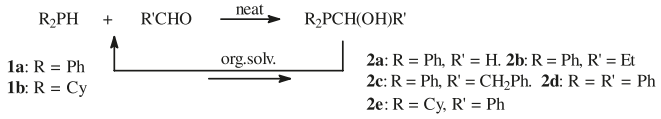
Synthesis and decomposition of (α-hydroxy)phosphines

The (α-hydroxy)phosphines **2a**–**2e** were prepared quantitatively as white solids by reaction of Ph_2PH (**1a**) or Cy_2PH (**1b**) with the corresponding aldehydes under solvent-free conditions at room temperature (Scheme 2), following the procedure reported earlier for **2b**;[4] the ^{1}H, $^{1}H\{^{31}P\}$, and $^{13}C\{^{1}H\}$ NMR data in DMSO-d_6 (Table S1 of the Supplementary data) are assigned as done previously for **2b**.[4] We have shown[4] that **2b** in solution at ambient conditions reversibly decomposes into Ph_2PH and propionaldehyde, greater stability being seen generally in higher donor number (DN) solvents such as DMSO, DMF, and pyridine,[14] and for this reason, the NMR data obtained in DMSO-d_6 are listed. The $^{31}P\{^{1}H\}$ data in four solvents (Table S2 of the Supplementary data) reveal a qualitative decomposition trend, and semiquantitative studies on **2a**–**2e** were undertaken in DMSO, Et_2O, and MeOH by monitoring the $^{31}P\{^{1}H\}$ singlet; decomposition in $CHCl_3$ and CH_2Cl_2 was significantly faster.

In DMSO (DN = 29.8), **2a**–**2d** are stable, with only trace amounts of **1a** being detected even after several hours, while **2e** essentially decomposes completely over 12 h (Fig. S1). In Et_2O (DN = 19.2), **2e** fully decomposes within 5 min, while Fig. S2 shows decomposition curves for **2b**–**2d** in this solvent, where the rates and degree of decomposition of **2d** are the highest, an equilibrium with ~90% conversion being set up with $t_{1/2} \approx 5$ h; for **2c**, an equilibrium is established with ~45% conversion ($t_{1/2} \approx 12$ h), while for **2b**, there is only ~60% conversion after 10 days, and no decomposition is evident for **2a**.

In MeOH, although a good donor (DN = 30.0), all the (hydroxy)phosphines show some instability, because they now decompose to the secondary phosphine and some hemiacetal formed from the aldehyde and MeOH; data in Fig. S3 show that the rates and the degree of decomposition decrease in the order: **2e >> 2b > 2d > 2c > 2a** (with **2e,** the $^{31}P\{^{1}H\}$ spectrum after 5 min showed only the resonance of **1b**). Rapid removal of the aldehyde as hemiacetal impedes regeneration of the (hydroxy)phosphines. Methanol is the only solvent studied where decomposition of **2a** was observed (~15% equilibrium, with $t_{1/2} \approx 3$ h). Establishing overall equilibria requires that measureable equilibria exist also between the aldehyde and its methanol hemiacetal, which is consistent with literature data, for example, in the case of **2d**, for benzaldehyde[15] (see below). The decompositions of **2a**–**2d** occur faster and to a greater extent in MeOH than in Et_2O, and hemiacetal formation must be one factor, although the presence of trace water in the MeOH possibly plays a role by favouring formation of a phosphonium intermediate. We have suggested previously[4] that decomposition of (α-hydroxy)phosphines could occur via an acid–base interaction between the OH proton and phosphine lone pair to give a phosphonium intermediate that re-arranges to the aldehyde and secondary phosphine (Scheme 5 in ref. 4); this implies also that a more electron-rich P atom gives a less stable (α-hydroxy)phosphine, and the above data for $Ph_2PCH(OH)Ph$ (**2d**) versus those for $Cy_2PCH(OH)Ph$ (**2e**) support such a premise. Of note, the tertiary phosphines $P[(CH_2)_nOH]_3$ (n = 1, 3) react quite differently with benzaldehyde in aqueous solution at ~90 °C via a redox reaction to give benzyl alcohol and the corresponding phosphine oxide.[16]

Scheme 2. Preparation and reversible decomposition of (α-hydroxy)phosphines.



We then investigated, by NMR-scale reactions in MeOH (see Experimental section), the effect of a *p*-substituent (X) in a series of benzaldehydes on the stability of the (α-hydroxy)phosphines derived from Ph_2PH (eq. [3]). The data are summarized in Fig. S4, which shows that the rates and degrees of formation of the (α-hydroxy)phosphines decrease in the order: CN > Cl > F > H > Me > OMe; an excellently linear Hammett relationship results from plotting the relative equilibrium concentration vs. σ (Fig. S5). Thus, similar to the effect of the nature of the secondary phosphine, electron-withdrawing groups of the aldehyde favour the formation of the (α-hydroxy)phosphines and, consistent with this, the pentafluorophenyl derivative $Ph_2PCH(OH)C_6F_5$ is known to be stable.[5] It should be pointed out that the linearity of the Hammett plot may be fortuitous in that the presence of the aldehyde ⇌ hemiacetal equilibria is ignored, while the degree of formation of the hemiacetal is reported to be favoured with increasing electron-withdrawing nature of X.[15] Indeed, experimental NMR and enthalpy data[15] imply relatively little hemiacetal formation for the benzaldehydes that we studied, although there are significant discrepancies between some of the measured and calculated values;[15] one set of data is X = OMe (1.5% formation of hemiacetal), Me (2.1%), H (3.7%), and Cl (13%). The data of Figs. S4 and S5 must reflect the effect of X on (α-hydroxy)phosphine stability because the effect of X on the hemiacetal equilibria would itself give an apparent decrease in formation of the hydroxyphosphines by removal of the aldehyde.

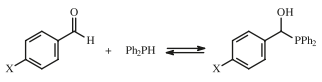
[3] 

Fig. 1. The in situ $^{31}P\{^{1}H\}$ spectrum during reaction of cinnamaldehyde (**3a**) with Ph_2PCH_2OH (**2a**) (1:1, Ar, 300 K, DMSO-d_6): (A) after 2 days and (B) 22 days.

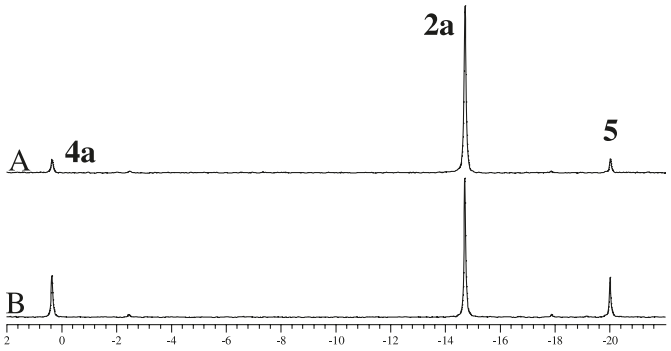
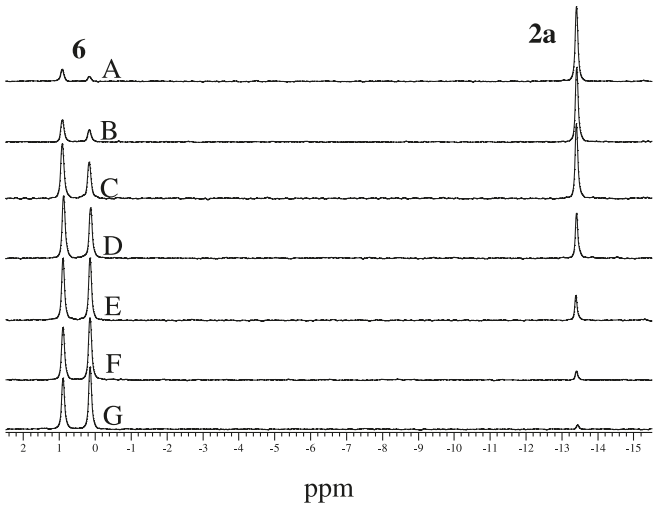
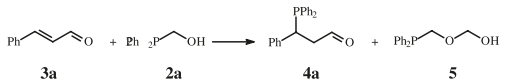


Fig. 2. The in situ $^{31}P\{^{1}H\}$ spectrum of the reaction of cinnamaldehyde (**3a**) with Ph_2PCH_2OH (**2a**) (1:1, Ar, 300 K, MeOH): (A) after 25 min, (B) 50 min, (C) 2 h, (D) 4 h, (E) 8 h, (F) 22 h, and (G) 48 h.

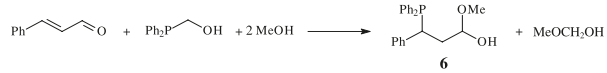


Reactions of (α-hydroxy)phosphines with α,β-unsaturated compounds

On a 1:1 reaction of Ph_2PCH_2OH (**2a**) with cinnamaldehyde (**3a**) in DMSO-d_6, the $^{31}P\{^{1}H\}$ resonance of **2a** (δ_P –14.7) was very slowly displaced by two almost equal intensity singlets at δ_P 0.4 and –20.0 (Fig. 1A); ^{1}H–^{1}H COSY and ^{1}H–$^{31}P\{^{1}H\}$ HMQC data (Figs. S6 and S7) show that the singlets are associated, respectively, with the known phosphine **4a** (**I** in Scheme 1)[4] and the phosphinated hemiacetal co-product **5** (eq. [4]). The net reaction would seem to be the formation of **4a** by nucleophilic attack of **2a** at the C=C bond of **3a** (but see below), with concomitant liberation of formaldehyde, which is not detected because it interacts via the OH group of **2a** to afford **5**. The P–CH_2 protons of **5** appear in the ^{1}H spectrum as a doublet at δ_H 4.27 ($^{2}J_{PH}$ = 5.0 Hz), which collapses to a singlet in the $^{1}H\{^{31}P\}$ spectrum. The corresponding protons of **2a** appear at δ_H 4.25 as a doublet of doublets due to extra coupling to the OH proton ($^{2}J_{PH}$ = 6.8, $^{3}J_{HH}$ = 5.5 Hz), and this reduces to a doublet in the $^{1}H\{^{31}P\}$ spectrum. The CH_2OH protons of **5** appear as a doublet at δ_H 4.67 both in the ^{1}H and $^{1}H\{^{31}P\}$ spectra ($^{3}J_{HH}$ = 7.9 Hz), and the OH proton is seen as a triplet at δ_H 6.45. After 22 days, integration of the $^{31}P\{^{1}H\}$ signals (Fig. 1B) shows that **4a** and **5** are each formed in ~20% yield (based on **2a**). Attempts to isolate pure **5** from reaction of CH_2O with **2a**, which itself is prepared from the reversible reaction of CH_2O with Ph_2PH,[13] have thus far been unsuccessful. Phosphines of this type have been synthesized previously from CH_2O and the (α-hydroxy)phosphine $P(CH_2OH)_3$.[17] There is no evidence for hemiacetal formation from **4a** and **2a**, consistent with higher reactivity (electrophilicity) of CH_2O versus that of **4a**.

[4] 

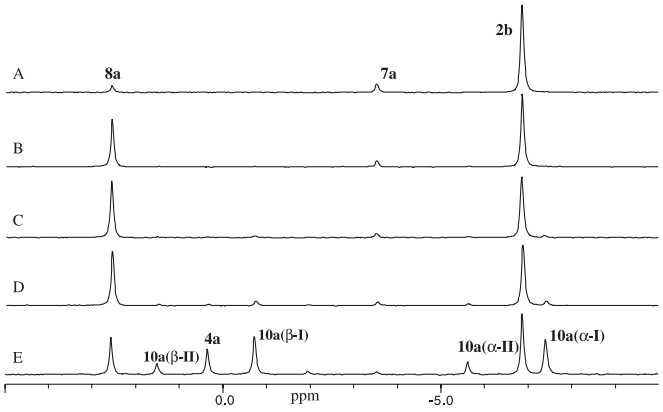
The reaction of **2a** with **3a** in MeOH is much faster than that in DMSO, the products now being the hemiacetal **6** (formed from **4a** and MeOH) and formaldehyde–hemiacetal (seen in CD_3OD as CD_3OCH_2OD, δ_H 4.65). Compound **6** is formed as a mixture of diastereomers (eq. [5]), observed in the $^{31}P\{^{1}H\}$ spectrum as two singlets δ_P 0.9 and 0.1 (Fig. 2), the diastereomeric ratio (d.r.) of a presumed mixture of *S*,*S*/*R*,*R*- and *S*,*R*/*R*,*S*-enantiomers changing from 0.37 (after 25 min) to 1.25 (after 2 days). The phosphine **4a** is almost insoluble in MeOH, but slowly dissolves as the hemiacetal **6**, when the δ_P 0.9 diastereomer is again initially preferred, the d.r. changing from 0.65 (90 min) to 1.25 (5 days) (Fig. S8). The same d.r. values result from integration of the ^{1}H signals, where the C*H*(OD)-protons appear as ddd

[5] 

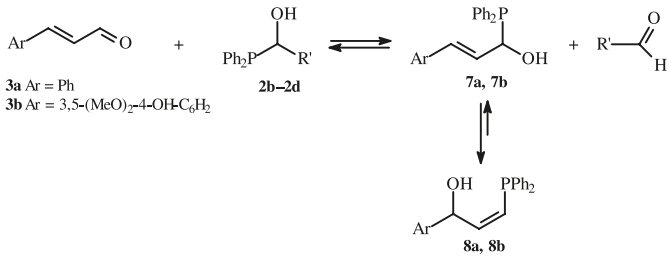
patterns at δ_H 4.17 and 4.09 with similar coupling constants ($^{3}J_{HH}$ = 8.9, $^{3}J_{HH}$ = 2.7, and $^{4}J_{PH}$ = 0.8 Hz), and the PhC*H*-protons are seen as overlapping ddd patterns at δ_H 3.76 and 3.73 ($^{3}J_{HH}$ = 12.0, $^{3}J_{HH}$ = 3.4, and $^{2}J_{PH}$ = 6.7 Hz). $^{13}C\{^{1}H\}$ NMR data for **6** are as follows: δ 142–127 (s and d, Ph groups), δ 97.9 (s, *C*HOMe), 42.2 (d, $^{1}J_{PC}$ = 11.0, Ph*C*H), and 41.7 (d, $^{2}J_{PC}$ = 20.6, *C*H_2) for one diastereomer; δ 97.8 (s, C*H*OMe), 42.1 (d, $^{1}J_{PC}$ = 11.3, Ph*C*H), and 41.0 (d, $^{2}J_{PC}$ = 20.6, *C*H_2) for the second diastereomer; the assignments for the Ph*C*H and *C*H_2 carbons, although unusual in that $^{2}J_{PC} > {}^{1}J_{PC}$, are based on definitive correlation NMR data for the corresponding C atoms of **4a**, which have such δ and *J* values.[4]

Of note, we have previously synthesized **4a** by the reaction of **3a** with Ph_2PH using neat reagents[4] (Scheme 1 in the Introduction), and it is plausible that the formation of **4a** illustrated in eq. [4] might involve the same chemistry, Ph_2PH being formed by decomposition of **2a** with formaldehyde as co-product (Scheme 2). This will be discussed later when data from reactions of cinnamaldehydes with the other (hydroxy)phosphines **2b**–**2d** have been considered (here, a different set of products and intermediates were observed). For example, a 1:1 reaction of $Ph_2PCH(OH)Et$ (**2b**) with cinnamaldehyde (**3a**) in DMSO-d_6 generates after 30 min two new singlets at δ_P –3.5 and 2.6 in the $^{31}P\{^{1}H\}$ spectrum

Fig. 3. The in situ $^{31}P\{^{1}H\}$ spectrum of the reaction of cinnamaldehyde (**3a**) with $Ph_2PCH(OH)Et$ (**2b**) (1:1, Ar, 300 K, DMSO): (A) after 30 min, (B) 6 h, (C) 22 h, (D) 46 h, and (E) 12 days; **10a** is a mixture of diastereomers (**α-I** and **β-I**) and (**α-II** and **β-II**) (Ref. 4).



Scheme 3. Formation of intermediates in reactions of (α-hydroxy)-phosphines with α,β-unsaturated compounds.



(Fig. 3A), which are assigned to the racemates of the phosphines species **7a** and **8a**, respectively (Scheme 3). A kinetic intermediate, (α-hydroxy)phosphine **7a**, is formed by nucleophilic attack of the P atom at the aldehyde C atom. In the ^{1}H spectrum (Fig. S9), the γ- and β-vinyl protons (δ_H 6.43 and 6.19, respectively) give dd and ddd patterns, which collapse to a doublet and a doublet of doublets in the $^{1}H\{^{31}P\}$ spectrum, respectively (Fig. S10) [$^{3}J_{HH}$ (trans H atoms) = 16.0, $^{4}J_{PH}$ = 3.3, $^{3}J_{PH}$ = 4.6 Hz]; the α-H appears as a broad doublet centered at δ_H 5.21 both in the ^{1}H and in the $^{1}H\{^{31}P\}$ spectrum, and the broad singlet of the OH proton is seen at δ_H 5.73. Intramolecular re-arrangement within **7a**, involving OH migration from the α- to the γ-C, affords **8a**. The downfield shift of the ^{31}P resonance (compared to that for **7a**) is consistent with the relative positions of the C=C moiety. The β- and α-vinyl ^{1}H proton signals are upfield-shifted (dd and ddd at δ_H 4.78 and 4.48, respectively) versus those for **7a**, the $^{3}J_{HH}$ value of 10.8 Hz implying a cis conformation ($^{2}J_{PH}$ = 6.5, $^{3}J_{PH}$ = 6.6 Hz), while the γ-H signal appears at δ_H 6.23 and overlaps with the β-H resonance of **7a**; the $^{1}H\{^{31}P\}$ spectra support the assignments (Figs. S9 and S10). The cis conformation might entail hydrogen-bonding between the OH proton and the P atom. The $^{1}H–^{31}P\{^{1}H\}$ correlation spectra of **7a** and **8a** are shown in Fig. S11. The eventual higher concentration of **8a** (vs. that of **7a**) implies a higher thermodynamic stability of the former (Figs. 3A–3D).

The hydroxyphosphines (**2c**–**2d**) also react with cinnamaldehyde (**3a**) according to Scheme 3. Figure 4 shows the rate of consumption of **2b**–**2d** in the reaction with **3a** under iden-

Fig. 4. The consumption of the starting phosphine in the reactions: (A) **2c** + **3a**, (B) **2b** + **3a**, (C) **2d** + **3b**, (D) **2d** + **3a**, and (E) **1a** + **3a**. Reactions were carried out under standard conditions (1:1, Ar, 300 K, DMSO).

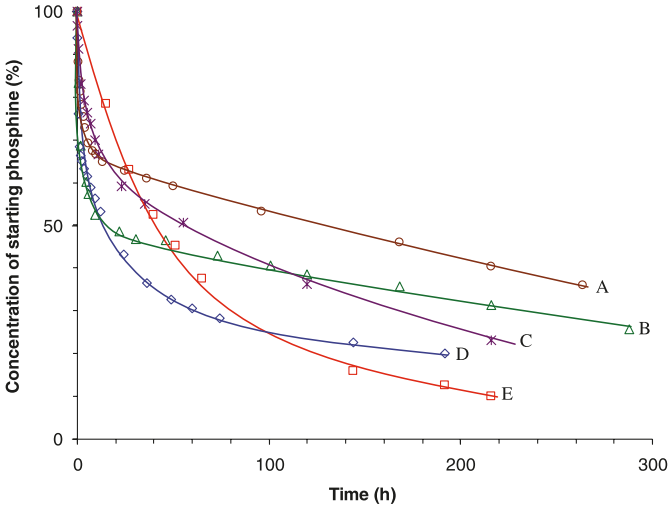


Fig. 5. The relative concentration of the intermediate **7** in the reactions: (A) **2c** + **3a**, (B) **2b** + **3a,** (C) **2d** + **3b,** (D) **2d** + **3a, and** (E) **1a** + **3a**. Reactions were carried out under standard conditions (1:1, Ar, 300 K, DMSO).

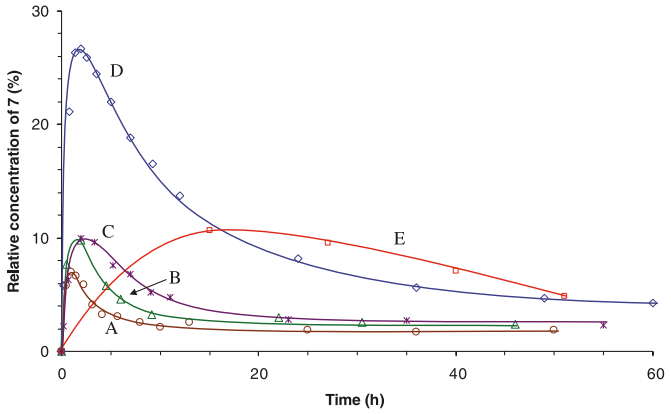


Fig. 6. The relative concentration of the intermediate **8** in the reactions: (A) **2c** + **3a**, (B) **2b** + **3a,** (C) **2d** + **3b,** (D) **2d** + **3a,** and (E) **1a** + **3a**. Reactions were carried out under standard conditions (1:1, Ar, 300 K, DMSO).

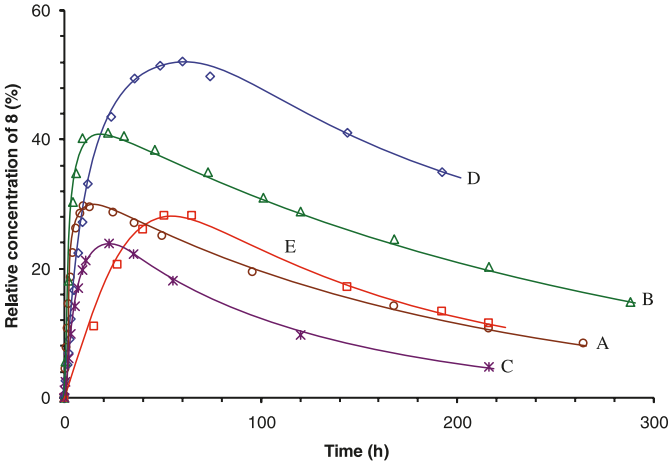


Fig. 7. The relative concentration of the diphosphine **10** in the reactions: (A) **2c** + **3a**, (B) **2b** + **3a,** (C) **2d** + **3b,** (D) **2d** + **3a,** and (E) **1a** + **3a**. All reactions were carried out under standard conditions (1:1, Ar, 300 K, DMSO).

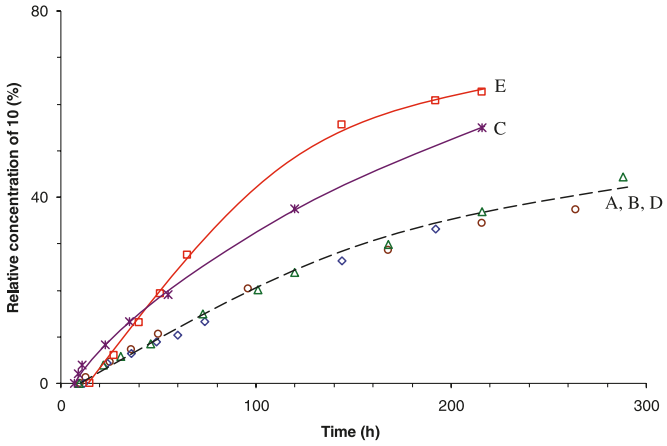
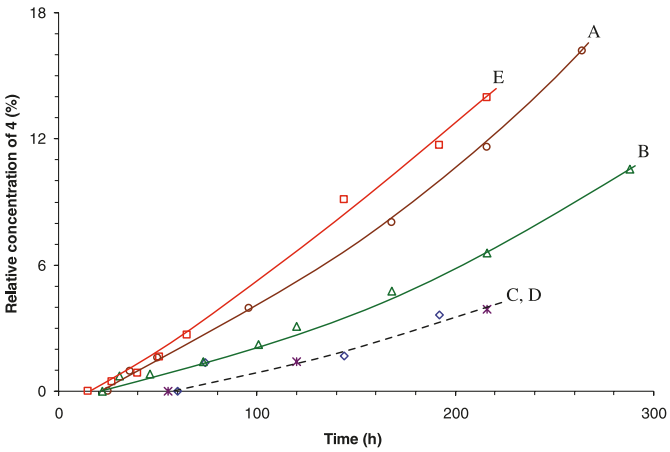


Fig. 8. The relative concentration of the phosphine **4a** or **4b** in the reactions: (A) **2c** + **3a,** (B) **2b** + **3a,** (C) **2d** + **3b,** (D) **2d** + **3a,** and (E) **1a** + **3a**. All reactions were carried out under standard conditions (1:1, Ar, 300 K, DMSO).



tical conditions (1:1, DMSO, 300 K, Ar), while Figs. 5 and 6 show the relative concentrations of the corresponding intermediates **7** and **8**, respectively. The degree of the consumption of **2b**–**2d** in their reaction with **3a** to form **7a/8a** (Scheme 3) decreases in the order: **2d** > **2b** > **2c** (Fig. 4), and also the extents of generation of **7a** (Fig. 5) and of **8a** (Fig. 6) decrease in the same order. This means that within the upper reaction of Scheme 3, benzaldehyde is a better "leaving group" than propionaldehyde, which is better than phenylacetaldehyde; with a more electrophilic aldehyde component of the reactant hydroxyphosphine, this equilibrium will be shifted to the left, and recall that in the reaction of **2a** (involving CH_2O, the most electrophilic of aldehydes) with **3a**, intermediates of the type **7** or **8** were not detected, and **4a** and **5** were the products (see above).

With the **2b**–**2d** systems, the concentrations of **7a** and **8a** do decrease slowly with formation of **4a** (Figs. 3, 5, and 6). However, **4a** can also then react with the starting phosphine **2b**–**2d** to generate the known diphosphine **10a** as a mixture of diastereomers, which is seen in the $^{31}P\{^1H\}$ spectrum as two sets of two equal intensity singlets (δ_P 1.5, –5.6 and –0.7, –7.4) (Figs. 3C-3E); eqs. [6] and [7] summarize the later stages of the chemistry (**9a** was detected in MeOH, see below). In recent work, we have characterized **10a**, where it was isolated from reaction of cinnamaldehyde with Ph_2PH via intermediate formation of **4a**[4] (see Scheme 1 in the Introduction) where **4a** and **10a** are labelled **I** and **II**, respectively.

Of note, the concentration of **10a** generated is independent of the reactant phosphine (**2b**–**2d**) used (Fig. 7), while the rate of formation of **4a** depends on the starting phosphine and decreases in the order: **2c** > **2b** > **2d** (Fig. 8). These findings can be rationalized qualitatively by considering the reverse reactions of the aldehydes with the diphosphine **10a** (eq. [7], Figs. 4 and 8), where again a more reactive aldehyde will shift the equilibrium to the left. The concentrations of **2b** and **8a** decrease simultaneously after the relatively fast stage (10 h), while the concentration of **7a** remains constant (Figs. 4–6), and this requires the upper reaction of Scheme 3 to be an equilibrium. This was confirmed by addition of EtCHO (the precursor to **2b**) to a solution containing **7a** and **8a** such as the one used to measure spectrum A in Fig. 3: the **7a**:**2b** ratio decreased rapidly from 0.15 to 0.02 on addition of two equiv. of EtCHO to the solution, while the **8a**:**2b** ratio increased from 0.15 to 0.30. The final product in these systems is **4a** (evident after 2 months!), and this requires also the reaction of eq. [7] to be reversible, and this was confirmed by addition of EtCHO to a DMSO solution of **10a**, when production of **2b** and **4a** was seen by using $^{31}P\{^1H\}$ NMR spectroscopy.

Evidence that **4a** likely derives from **7a** via the enol intermediate **9a** (formed from **7a** by migration of the Ph_2P group from the α- to γ- position) (eq. [6] was obtained by carrying out 1:1 reactions of **2b**–**2d** with cinnamaldehyde in MeOH/CD_3OD, which are much faster than the reaction in DMSO. Figure 9 shows a $^{31}P\{^1H\}$ NMR profile of the reaction for **2d** in MeOH, which is complete in 1 h. The final products of the reaction are the diastereomeric mixture of the hemiacetal **6** formed from **4a** (eq. [5], Fig. 9) and traces of the diastereomers of diphosphine **10a**. The 1:1 stoichiometry determines that **6** is essentially the sole product, while the observed intermediacy of **10a** again reveals the reversibility of the eq. [7] reaction. The **10a** diastereomers are detected at δ_P 2.6, –4.5, and 0.3, –6.6 (Fig. 9C). Figure 10 shows the ^1H–$^{31}P\{^1H\}$ HMQC correlation spectrum of this system in CD_3OD recorded after ~10 min, when the intermediates **7a,** **8a**, and **9a** are readily identified. The ^{31}P signals of **7a** (δ_P –2.3) and **8a** (δ_P 3.9) are downfield-shifted from those seen in DMSO, while the associated α-, β-, and γ-proton signals are at chemical shifts similar to those observed in DMSO-d_6 (see above) but are better resolved; e.g., the α-H of **7a** appears at δ_H 5.17 as a pseudo-doublet of triplets ($^2J_{PH}$ = $^4J_{HH}$ = 1.5, $^3J_{HH}$ = 6.5 Hz). Three ^1H resonances correlating with the $^{31}P\{^1H\}$ resonance at δ_P –0.7 in the ^1H–$^{31}P\{^1H\}$ HMQC spectrum (Fig. 10) are assigned to the enol species **9a**: the vinyl α- and β-protons appear at δ_H 4.10 and 5.02, respectively, as dd and ddd patterns ($^4J_{PH}$ = 6.8, $^3J_{PH}$ = 7.1, $^3J_{HH}$ = 9.1 Hz), the $^3J_{HH}$ value again implying a cis conformation at the olefinic bond, while the γ-H appears as a dd pattern centered at δ_H 6.15 and overlaps with the γ-H of **7a**; the $^3J_{HH}$ coupling constant to the β-H is 12.3 Hz ($^2J_{PH}$ is diffi-

Fig. 9. The in situ $^{31}P\{^{1}H\}$ spectrum of the reaction of cinnamaldehyde (**3a**) with $Ph_2PCH(OH)Ph$ (**2d**) (1:1, Ar, 300 K, MeOH): (A) after 8 min, (B) 11 min, (C) 20 min, (D) 30 min, (E), and (F) 50 min; **10a** is a mixture of diastereomers (**α-I** and **β-I**) and (**α-II** and **β-II**) (Ref. 4).

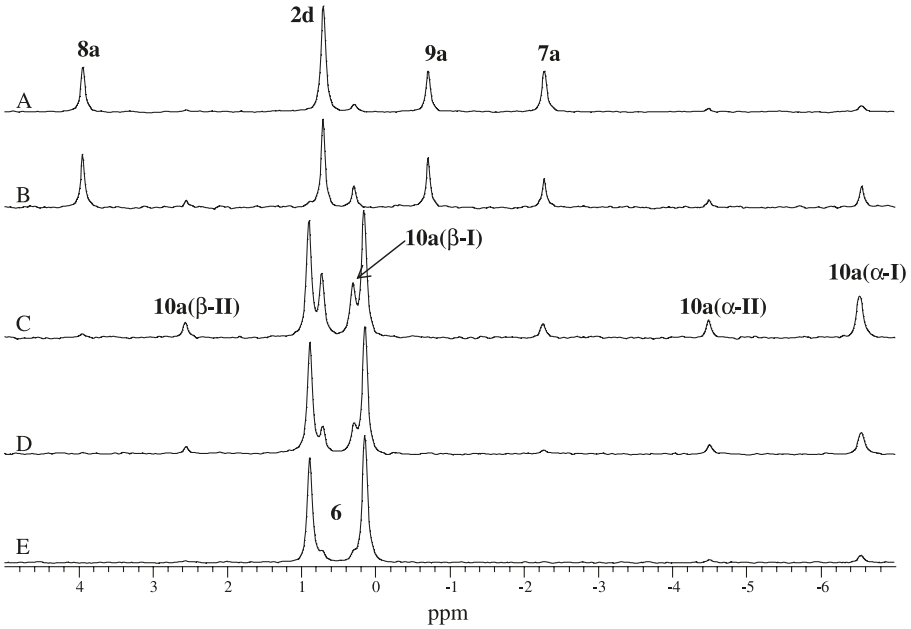


Fig. 10. The in situ $^{1}H–^{31}P\{^{1}H\}$ HMQC spectrum of the reaction of cinnamaldehyde (**3a**) with **2d** (1:1, Ar, 300 K, CD_3OD) after ~10 min.

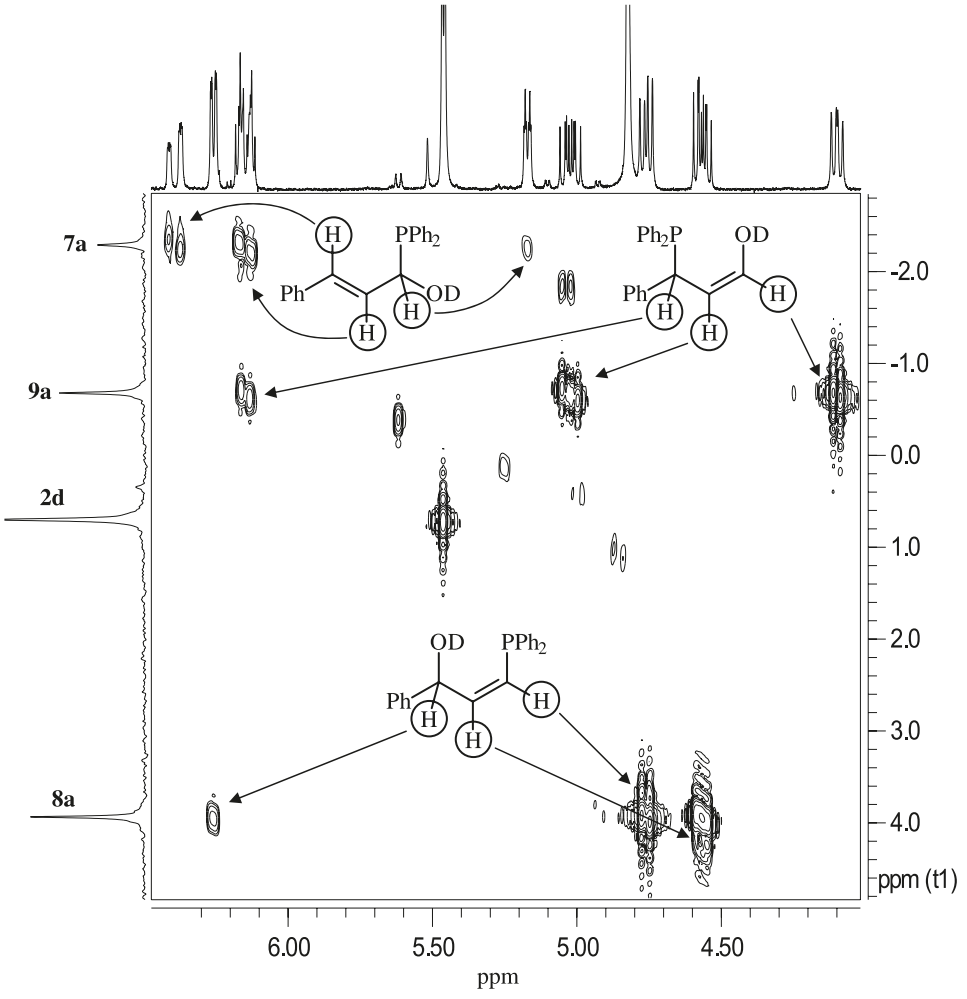
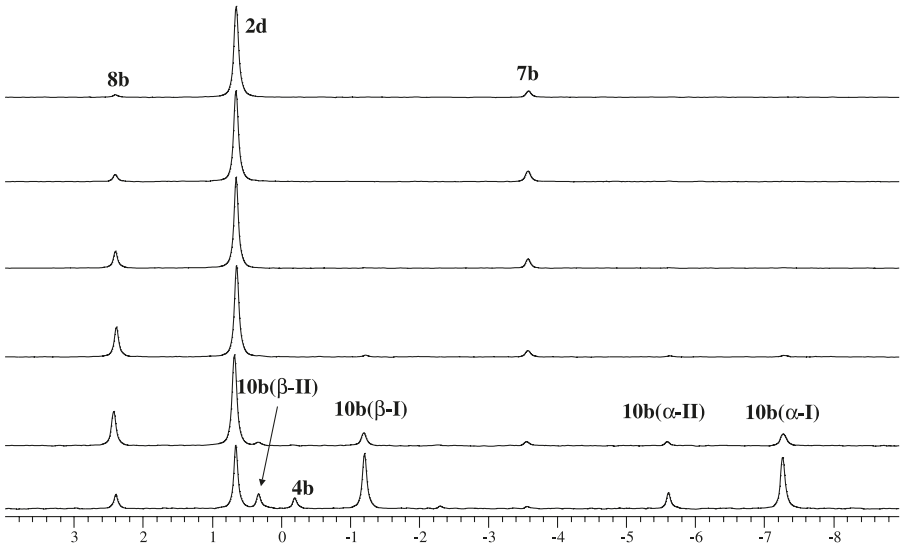
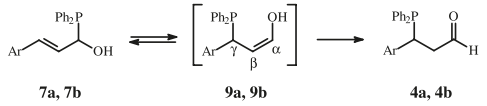


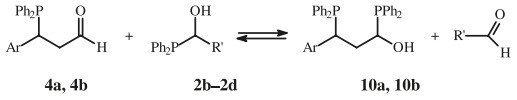
Fig. 11. The in situ $^{31}P\{^{1}H\}$ spectrum of the reaction of sinapaldehyde (**3b**) with $Ph_2PCH(OH)Ph$ (**2d**) (1:1, Ar, 300 K, DMSO): (A) after 40 min, (B) 3 h, (C) 7 h, (D) 24 h, (E) 5 days, and (F) 12 days; **10a** is a mixture of diastereomers (**α-I** and **β-I**) and (**α-II** and **β-II**) (Ref. 4).



cult to determine). In CD_3OD, the product **6** is monodeuterated in the β-position, consistent with an enol-OD intermediate being involved in the formation of **4a**.

[6] 

7a, 7b **9a, 9b** **4a, 4b**

[7] 

4a, 4b **2b–2d** **10a, 10b**

Sinapaldehyde (**3b**), a lignin-type aldehyde,[18] was also reacted with $Ph_2PCH(OH)Ph$ (**2d**) in DMSO to compare its reactivity with that of cinnamaldehyde (**3a**). The reason for this study was that the presence of an OH group para to the unsaturated aliphatic chain of **3a** has been shown to change significantly in aqueous solution the interaction of such aldehydes with PR_3 phosphines, where R does not contain an α-OH group.[8] However, in DMSO, the reactivity of **2d** with **3b** is found to be similar to that with **3a**, with corresponding intermediates and products (**4b**, **7b, 8b**, and **10b**) being detected by NMR (Fig. 11). Data in Figs. 4–6 (C curves) show that the consumption of **2d** is slower in the reaction with **3b**, leading to lower concentrations of **7b** and **8b** at a selected reaction time; the resulting higher concentration of **2d** leads to a higher concentration of **10b** (Fig. 7, eqs. [6] and [7]), although the rate of the generation of phosphine product **4b** is the same as for **4a** (Fig. 8).

It cannot be completely ruled out that **4a** and **4b** derive via **9a** and **9b**, respectively, formed at least partially by initial direct nucleophilic attack of a hydroxyphosphine at the C=C bond of the α,β-unsaturated aldehyde (eq. [6]). Further, **10a/10b**, which are hydroxyphosphines, could react with the cinnamaldehydes to form **4a/4b** giving intermediates **7a/7b** as co-products (cf. Scheme 3, upper equilibrium). However, the NMR studies support strongly the overall chemistry as presented in Scheme 3 and eqs. [6] and [7], and, although complicated because of the various equilibria involved, the reaction pathways are considered substantiated.

Because Ph_2PH (**1a**) is a decomposition product of the (α-hydroxy)phosphines (**2a**–**2d**) in organic media (Scheme 2), **1a** was always detected by $^{31}P\{^{1}H\}$ and ^{1}H NMR in small amounts (<6%) in all the reactions discussed above (δ_P –39.7 in DMSO, δ_P –39.8 in MeOH; δ_H 5.22, d, $^{1}J_{PH}$ = 222 Hz; see Figs. S9 and S12), and further, since **1a** is known to react with **3a** to give **4a**,[4] we thus studied the reaction of **3a** with **1a** in DMSO to see the plausibility of whether **4a** was being formed by this "decomposition" route. The expected intermediates and product discussed above (**7a**, **8a**, and **4a**) were detected; the consumption rate of Ph_2PH was slower than in the case of the hydroxyphosphines **2c** and **2d** (Fig. 4), presumably due to the lower nucleophilicity of the secondary phosphine compared with that of the tertiary phosphines and, as a result, the generation of **7a** and **8a** is also slower (Figs. 5 and 6). The formations of monophosphine **4a** (Fig. 8) and diphosphine (**10a**) (Fig. 7) are faster because no aldehyde is present in the reaction mixture (see the reversible reactions involving R′CHO shown in Scheme 3 and eq. [7]). The slower reactions seen with Ph_2PH (vs. **2c** and **2d**) are consistent with reaction pathways for the hydroxyphosphines via their direct attack on the unsaturated aldehydes rather than via Ph_2PH, although this latter route might contribute also; direct attack is expected to form (via nucleophilic attack of the phosphine at the C=O moiety) an (α-hydroxy)phosphonium intermediate such as $PhCH{=}CHCH(OH){-}R_2P^{+}CH(O^{-})R'$,[8,17b,19] which subsequently forms **7a** with release of R′CHO (Scheme 3). When Ph_2PH was reacted with **3a** (1:1) in MeOH, intermediates **7a**–**10a** were seen, while the only final product was hemiacetal **6** (see eq. [5]) formed from **4a** (see Scheme 1, where **I** ≡ **4a**); removal of the MeOH yielded **6** as a pink, viscous liquid, which could be dissolved in Et_2O and then removal of the Et_2O regenerated **4a** (see also the discussion on eq. [5]). From an experimental point of view, the solid mono(α-hydroxy)phosphines are useful storage agents for Ph_2PH, a foul smelling, easily oxidizable liquid.

Conclusions

Several synthesized mono(α-hydroxy)phosphines, $R_2PCH(OH)R'$, are confirmed to be generally reversibly unstable in organic solvents to give R_2PH and R′CHO, the degree of decomposition depending on the following: (a) the solvent, where stability typically increases with solvent donor number, except in the case of MeOH for which hemiacetal formation promotes decomposition, and (b) the nature of substituents R and R′, where more basic phosphines promote decomposition. Reactions of the phosphines with cinnamaldehyde in DMSO and in MeOH yield the known phosphine $Ph_2PCH(Ph)CH_2CHO$ (**4a**) and, depending on R′, the known diphosphine $Ph_2PCH(Ph)CH_2CH(PPh_2)OH$ (**10a**), as well as the liberated R′CHO aldehyde and hemiacetal co-products that result from interactions between aldehyde and alcohol functionalities. A series of sequential intermediates, more readily detected in MeOH, includes $PhCH=CHCH(OH)PPh_2$, $PhCH(OH)CH=CHPPh_2$, and $Ph_2PCH(Ph)CH=CHOH$; relative rates of formation of **4a**, **10a**, and the intermediates as a function of R′ in various equilibria are described. The reactions are thought not to proceed via Ph_2PH, which is formed by decomposition of the $Ph_2PCH(OH)R'$ compounds, although the secondary phosphine reacts with cinnamaldehyde to give the same products and intermediates.

Supplementary data

Supplementary data for this article are available on the journal Web site (canjchem.nrc.ca) or may be purchased from the Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, ON K1A 0R6, Canada. DUD 3905. For more information on obtaining material, refer to cisti-icist.nrc-cnrc.gc.ca/cms/unpub_e.shtml.

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