Inorg. Chem. **2007**, *46*, 4704–4712

Chemistry and Stereochemistry of the Interaction of the Water-Soluble Phosphine $[HO(CH_2)_3]_3P$ with Cinnamaldehyde in Aqueous Media

Dmitry V. Moiseev,[†] Brian R. James,*[,†] and Thomas Q. Hu[‡]

Department of Chemistry, University of British Columbia, Vancouver, British Columbia, Canada V6T 1Z1, and Pulp and Paper Research Institute of Canada, Vancouver, British Columbia, Canada V6S 2L9

Received January 29, 2007

To learn more about the bleaching action of pulps by (hydroxymethyl)phosphines, cinnamaldehyde was reacted with tris(3-hydroxypropyl)phosphine, $[HO(CH_2)_3]_3P$ (THPP), in aqueous solution at room temperature under argon. Self-condensation of the aldehyde into two isomeric products, 2-benzyl-5-phenyl-pent-2,4-dienal and 5-phenyl-2-(phenylmethylene)-4-pentenal, is observed; this implies initial nucleophilic attack of the phosphine at the β-carbon of the α,β-unsaturated aldehyde. Reaction in D_2O gives the same products in which all but the phenyl and CHO protons are replaced by deuterons. NMR studies are consistent with carbanion formation and subsequent condensation of two phosphonium-containing aldehyde moieties to generate the products with concomitant elimination of phosphine oxide. In D_2O in the presence of HCl, THPP reversibly attacks the aldehyde-C atom to form the (α-hydroxy)-phosphonium derivative $[PhCH{=}C(H)CH(OD)PR_3]Cl$ (where $R = (CH_2)_3OD$), which slowly converts into the deuterated bisphosphonium salt $[R_3PCH(Ph)CD(H)CH(OD)PR_3]Cl_2$ via the deuterated monophosphonium salt $[R_3PCH(Ph)CD(H)CHO]Cl$. The phosphonium intermediates and phosphonium products in this chemistry, although having up to three chiral carbon centers, are formed with high stereoselectivity just in enantiomeric forms. In acetone–H_2O (1:1 v/v), a cross-condensation of cinnamaldehyde with acetone to give 6-phenyl-3,5-hexadien-2-one is promoted by THPP via generation of OH^-.

Introduction

Investigations by our group have revealed recently that water-soluble phosphines, particularly tris(hydroxymethyl)-phosphine, $(HOCH_2)_3P$ (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] In efforts to investigate the bleaching mechanism, we are reacting water-soluble phosphines with various lignin model compounds and discovered recently that tris(3-hydroxypropyl)-phosphine, $[HO(CH_2)_3]_3P$ (THPP), reduces aromatic aldehydes (ArCHO) to the corresponding alcohols in aqueous solution; THPP is used because it gives cleaner reactions than does THP, which tends to lose formaldehyde.[2] This paper describes the interaction of cinnamaldehyde with THPP in aqueous media. Cinnamaldehyde possesses the phenylpropanoid backbone similar to that found in lignin chromophores where, however, the phenyl moiety contains substitutent groups.[3]

Some literature on reactions of phosphines with aldehydes and ketones in water was noted in the Introduction of our recent paper,[2] where formation of zwitterionic phosphobetaines or, in the presence of a suitable HX reagent, phosphonium salts occurs via nucelophilic attack of the phosphine at the carbonyl carbon atom.[2,4] There is also substantial

* To whom correspondence should be addressed. E-mail:brj@chem.ubc.ca.
[†] University of British Columbia.
[‡] Pulp and Paper Research Institute of Canada.

(1) (a) Hu, T. Q.; James, B. R.; Yawalata, D.; Ezhova, M. B. *J. Pulp Pap. Sci.* **2004**, *30*, 233. (b) Hu, T. Q.; James, B. R.; Yawalata, D.; Ezhova, M. B. *World Patent* (PCT WO 2004 070110 A1), Aug 2004. (c) Hu, T. Q.; James, B. R.; Yawalata, D.; Ezhova, M. B.; Chandra, R. *J. Pulp Pap. Sci.* **2005**, *31*, 69. (d) Hu, T. Q.; James, B. R.; Yawalata, D.; Ezhova, M. B. *J. Pulp Pap. Sci.* **2006**, *32*, 131. (e) Chandra, R.; Hu, T. Q.; James, B. R.; Ezhova, M. B. *J. Pulp Pap. Sci.* **2007**, *33*, in press.

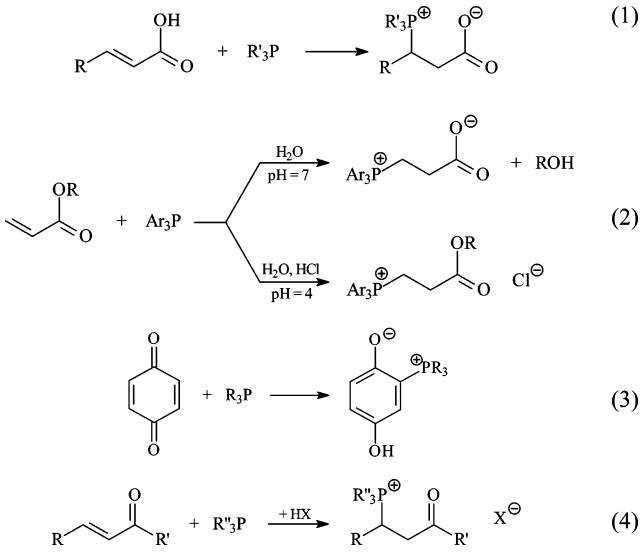
(2) Moiseev, D. V.; James, B. R.; Hu, T. Q. *Inorg. Chem.* **2006**, *45*, 10338.

(3) Morreel, K.; Ralph, J.; Lu, F.; Goeminne, G.; Busson, R.; Herdewijn, P.; Goeman, J. L.; Van der Eycken, J.; Boerjan, W.; Messens, E. *Plant Physiol.* **2004**, *136*, 4023.

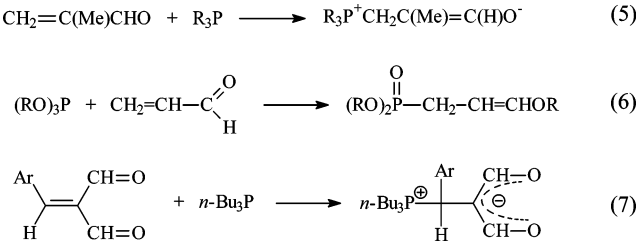
(4) (a) Lee, S. W.; Trogler, W. C. *J. Org. Chem.* **1990**, *55*, 2644. (b) Dal Canto, R. A.; Roskamp, E. J. *J. Org. Chem.* **1992**, *57*, 406. (c) Darensbourg, D. J.; Joó, F.; Katho, A.; Stafford, J. N. W.; Bényei, A.; Reibenspies, J. H. *Inorg. Chem.* **1994**, *33*, 175.

10.1021/ic0701559 CCC: $37.00
Published on Web 04/14/2007

literature describing reactivity of phosphines with α,β-unsaturated carbonyl-containing compounds, where the phosphorus nucleophile attacks the activated C═C bond.[5−9] For example, phosphobetaines are formed in water in the reactions of the sulfonated phosphines, $(m\text{-}NaSO_3C_6H_4)_3P$ and $(m\text{-}NaSO_3C_6H_4)PPh_2$, with acrylic, methacrylic, crotonic, and itaconic acids (eq 1);[5] with acrylates, hydrolysis accompanies formation of the phosphobetaine (eq 2), and, in the presence of HCl, the phosphonium salt is formed and there is no hydrolysis (eq 2).[5] In $CHCl_3$ under Ar, PPh_3 reacts with methacrylic, cinnamic, and *p*-methoxycinnamic acids to give the corresponding phosphobetaine as in eq 1,[6] while $(HOCH_2)_3P$ and methylacrylate generate the phosphine oxide $O{=}P(CH_2CH_2CO_2Me)_3$.[7] Tertiary phosphines react with *p*-quinones to give phosphobetaines of the type shown in eq 3.[8] α,β-Unsaturated ketones react with tertiary phosphines in organic solvents in the presence of an acid to form the corresponding quaternary phosphonium salt (eq 4),[9] analogous to the lower reaction shown in eq 2. Of special interest regarding potential catalytic processes for pulp bleaching, trialkylphosphines have been reported to catalyze the addition of water or methanol to α,β-unsaturated compounds such as methyl vinyl ketone, methyl acrylate, and acrylonitrile via similar attack of the phosphine at the activated C═C bond.[10]



The interaction of phosphines with α,β-unsaturated aldehydes, which provides one path for the bleaching process[1e] and is the subject of this paper, can also be a critical factor in hydroformylation processes catalyzed by Rh-phosphine species, where such aldehydes, formed via dehydration of the hydroformylation aldehyde products, have been found to react with phosphines;[11] the reaction shown in eq 5 for methacrolein has been suggested,[11b] and acrolein, methacrolein, and crotonaldehyde have been used for removing tertiary phosphines from a rhodium-containing hydroformylation reaction medium.[11a] A more complex reaction of trialkylphosphites with acrolein or crotonaldehyde in dioxane occurs via nucleophilic attack of the P atom on the C═C double bond, followed by intramolecular oxidation of P^{III} to P^{V} and migration of an alkyl radical to the aldehyde oxygen atom (eq 6).[12] Tri(*n*-butyl)phosphine is reported to react with (arylmethylene)malonaldehydes in C_6H_6 or CH_2Cl_2 at room temperature according to eq 7, but, under the same conditions, PPh_3 did not react;[13] it should be pointed out, however, that such dialdehydes are organic Lewis acids that react even with tertiary amines.[13]



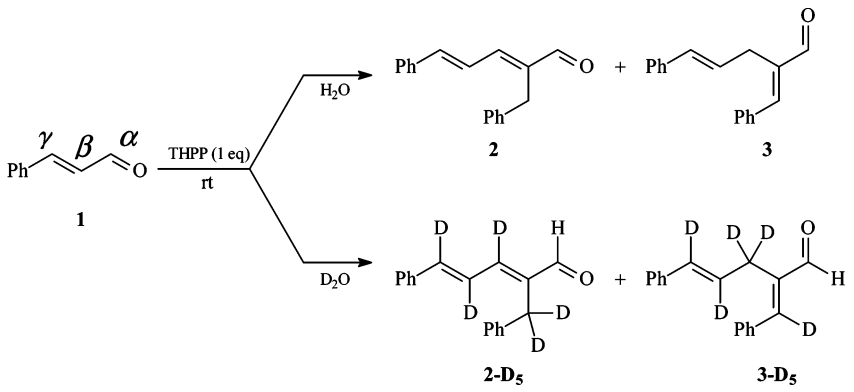
Few details are available for reactions of the type exemplified by eqs 5−7; this fact, coupled with the absence of previous reports on the interaction of phosphines with α,β-unsaturated aldehydes in aqueous media and the relevance to pulp bleaching and the catalytic production of α,β-unsaturated organics in aqueous media, prompted us to investigate the reaction of cinnamaldehyde with THPP.

Experimental Section

General. NMR spectra were recorded at room temperature (r.t., ~300 K) in situ (for reactions in H_2O/D_2O) or in $CDCl_3$ (for isolated materials) on Bruker AV400 (400 MHz for ^1H, 161 MHz for $^{31}P\{^1H\}$, 100 MHz for $^{13}C\{^1H\}$, and 61 MHz for ^2D) or Bruker AV300 (300 MHz for ^1H and 121 MHz for $^{31}P\{^1H\}$) instruments. 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, m = multiplet. *J* values are given in Hertz. When necessary, atom assignments were made by means of ^1H-^1H, ^1H-$^{13}C\{^1H\}$ (HSQC and HMBC), and ^1H-$^{31}P\{^1H\}$ NMR correlation spectroscopies. Manipulations for NMR studies were performed using standard Schlenk techniques under Ar, and, before use, distilled H_2O and D_2O were stirred for 3 h under Ar. The reactions described could also be carried out in air, but interpretations of the NMR were more complicated because varying amounts of phosphine oxide were generated. Elemental analyses were performed on a Carlo Erba 1108 analyzer. Mass spectrometry was performed on a Bruker Esquire electrospray (ESI or APCI) ion-

(5) Larpent, C.; Patin, H. *Tetrahedron* **1988**, *44*, 6107.
(6) Galkin, V. I.; Bakhtiyarova, Yu. V.; Polezhaeva, N. A.; Galkina, I. V.; Cherkasov, R. A.; Krivolapov, D. B.; Gubaidullin, A. T.; Litvinov, I. A. *Russ. J. Gen. Chem.* **2002**, *72*, 384.
(7) Valetdinov, R. K.; Zuikova, A. N. *Zh. Obsh. Khim.* **1978**, *48*, 1726.
(8) (a) Ramirez, F.; Chen, E. H.; Dershowitz, S. *J. Am. Chem. Soc.* **1959**, *81*, 4338. (b) Boekestein, G.; Buck, H. M. *Phosphorus Sulphur* **1978**, *5*, 61. (c) Müller, E.; Eggensperger, H.; Teissier, B.; Scheffler, K. *Z. Naturforshung* **1963**, *18b*, 984.
(9) Tammer, T.; Heubach, G.; Sachse, B. German patent, DE 1985, 3332716 A1.
(10) Stewart, I. C.; Bergman, R. G.; Toste, F. D. *J. Am. Chem. Soc.* **2003**, *125*, 8696.
(11) (a) Bryant, D. R.; Galley, R. A. U.S. Patent 4,283,304, Aug 1981, assigned to Union Carbide Corporation. (b) Bryant, D. R. In *Catalyst Separation, Recovery and Recycling*; Cole-Hamilton, D., Tooze, R., Eds.; Springer: Dordrecht, 2006; Chapter 2.
(12) Kamai, G.; Kuhtin, V. A. *Dokl. Akad. Nauk. USSR* **1957**, *112*, 868.
(13) Dvořák, D.; Arnold, Z. *Collect. Czech. Chem. Commun.* **1987**, *52*, 2699.

Scheme 1 [a]



[a] The *E*- or *Z*-configurations at the olefinic groups are not known with certainty, but the illustrated *E*,*E*-isomers are favored.

trap spectrometer using samples dissolved in CH_3OH or water, with positive-ion polarity.

Cinnamaldehyde (Aldrich) and hydrocinnamaldehyde (Acros Organics) were used as received. Tris(3-hydroxypropyl)phosphine (THPP, an oil, ~85% from Strem Chemicals) was used without purification; we discussed recently the difficulty in trying to purify THPP, which contains impurities that are "closely related" phosphines.[2] The hydrochloride, $[(HOCH_2CH_2CH_2)_3PH]^+Cl^-$, was prepared as we described recently.[2]

Condensation of Cinnamaldehyde (1) in the Presence of THPP in H_2O. Cinnamaldehyde (300 mg, 2.27 mmol) was added to a solution of THPP (473 mg, 2.27 mmol, assuming 100% purity) in air-free water (15 mL), and the reaction mixture was stirred under Ar at r.t. for 48 h. The resulting yellow suspension was extracted with Et_2O (6 × 10 mL), and the ether layers were dried over Na_2SO_4. The products were separated on a 3-foot silica gel column (60 mesh) using *n*-pentane/Et_2O (4/1 v/v) as eluant. The first three fractions yielded product mixtures. The fifth fraction, after in vacuo removal of solvent, gave 2-benzyl-5-phenyl-pent-2,4-dienal (**2**) as a yellow solid in 29% yield (82 mg) on recrystallization from *n*-pentane. Anal. Calcd for $C_{18}H_{16}O$: C, 87.06; H, 6.49. Found: C, 87.36; H, 6.59. ^{1}H NMR: δ 9.57 (s, 1H, C*H*O), 7.52−7.00 (m, 13H, Ph and C*H*═C*H*−C*H*═C) 3.83 (s, 2H, CH_2). APCI (MeOH): *m*/*z* 249.2 (100%) $[M + H]^+$, calcd 249.3. Compound **2** is known, but only MS(IE) data have been presented.[14] The fourth fraction, 5-phenyl-2-(phenylmethylene)-4-pentenal (**3**), an isomer of **2**, was similarly isolated and recrystallized as a yellow solid in 21% yield (58 mg). Found: C, 86.83; H, 6.56. ^{1}H NMR: δ 9.67 (s, 1H, C*H*O), 7.60−7.16 (m, 11H, Ph and C*H*═C), 6.46−6.26 (m, 2H, C*H*═C*H*), 3.46 (d, $^3J_{HH}$ = 5.1, 2H, CH_2). APCI (MeOH): *m*/*z* = 249.2 (100%) $[M + H]^+$ This compound has been isolated previously as a pale-yellow viscous oil, characterized only as the 2,4-dinitrophenylhydrazone derivative.[15]

The same reaction in D_2O gives some corresponding deuterated products (see Scheme 1):

2-D_5. ^{1}H NMR: δ 9.57 (s, 1H, C*H*O), 7.52−7.16 (m, 10H, Ph). ^{2}D NMR: δ 7.31, 7.20, 7.11 (overlapping singlets, C*D*═C*D*-C*D*═C), 3.83 (s, CD_2). ESI (MeOH): *m*/*z* = 276.1 (100%) $[M + Na]^+$, calcd 276.1. (The extraneous Na^+ is derived from silicates in glass.)

3-D_5. ^{1}H NMR: δ 9.67 (s, 1H, C*H*O), 7.61−7.18 (m, 10H, Ph). ^{2}D NMR: δ 7.47 (s, C*D*═C), 6.46 (s, PhC*D*═CD), 6.36 (s, PhCD═C*D*), 3.44 (s, CD_2). ESI (MeOH): *m*/*z* = 276.1 (100%) $[M + Na]^+$.

^{31}P{^{1}H} NMR Investigation of the Reaction of THPP and 1. Cinnamaldehyde (28 mg, 0.21 mmol) was added to a solution of THPP (44 mg, 0.21 mmol) in air-free H_2O (~2 mL) under Ar, and the mixture was stirred for 5 min at r.t.; the immediately formed yellowish suspension was transferred into a J-Young NMR tube, and the ^{31}P{^{1}H} NMR spectra were recorded periodically for days (see Results and Discussion).

NMR Investigation of the Reaction of 1 with THPP Hydrochloride (1:1). The aldehyde (6.7 mg, 0.05 mmol) was added to a solution of THPP hydrochloride (12.2 mg, 0.05 mmol) in air-free D_2O (~1 mL), and the mixture was stirred at r.t. for 10 min, before being placed into an NMR tube and monitored for 40 days; successive formation of three products was observed (see Scheme 3 and text):

7, {PhCH═CHCH(OD)P[$(CH_2)_3$OD]$_3$}Cl. ^{31}P{^{1}H} NMR: δ 37.5 s. ^{1}H NMR: δ 7.59−7.38 (m, Ph, overlapping with Ph groups of **1**, **9-D_1**, and **10-D_1**), 7.01 (dd, 1H, $^3J_{HH}$ = 15.8, $^4J_{PH}$ = 4.3, C*H*═CH−CH), 6.38 (ddd, 1H, $^3J_{HH}$ = 15.8, $^3J_{HH}$ = 7.5, $^3J_{PH}$ = 4.2, CH═C*H*-CH), 5.49 (ddd, 1H, $^3J_{HH}$ = 7.4, $^4J_{HH}$ = 0.8, $^2J_{PH}$ = 4.4, C*H*), 3.68 (t, $^3J_{HH}$ = 6.0, CH_2OH), 2.44−2.33 (m, 6H, PCH_2), 1.97−1.83 (m, 6H, PCH_2CH_2); for the CH_2 protons, the resonances overlap with corresponding proton signals of THPP hydrochloride, **9-D_1** and **10-D_1**. ^{13}C{^{1}H} NMR: 137.8 (d, $^3J_{PC}$ = 12, PhC*H*═CH), 136.4 (d, $^4J_{PC}$ = 3, C_{ipso}), 130.7 (s, *p*-*C*), 130.5 (s, *m*-*C*), 128.4 (d, $^5J_{PC}$ = 1, *o*-*C*), 121.7 (d, $^2J_{PC}$ = 2, PhCH═*C*H), 68.3 (d, $^1J_{PC}$ = 63, P*C*H), 62.5 (d, $^3J_{PC}$ = 16, *C*H_2OH), 25.1 (d, $^2J_{PC}$ = 5, PCH_2*C*H_2), 14.7 (d, $^1J_{PC}$ = 46, P*C*H_2).

9-D_1, {[DO$(CH_2)_3$]$_3$PCH(Ph)C(H)DCH(OD)$_2$}Cl. ^{31}P{^{1}H} NMR: δ 38.3 s. ^{1}H NMR: δ 4.84 (d, 1H, $^3J_{HH}$ = 8.6, C*H*(OD)$_2$), 3.94 (dd, 1H, $^2J_{PH}$ = 15.5, $^3J_{HH}$ = 2.5, C*H*(Ph)), 2.12 (ddd, 1H, $^3J_{PH}$ = 8.0, $^3J_{HH}$ = 8.5, and $^3J_{HH}$ = 2.5, C*H*D). ^{1}H{^{31}P}: δ 4.84 (d), 3.94 (d), 2.12 (dd).

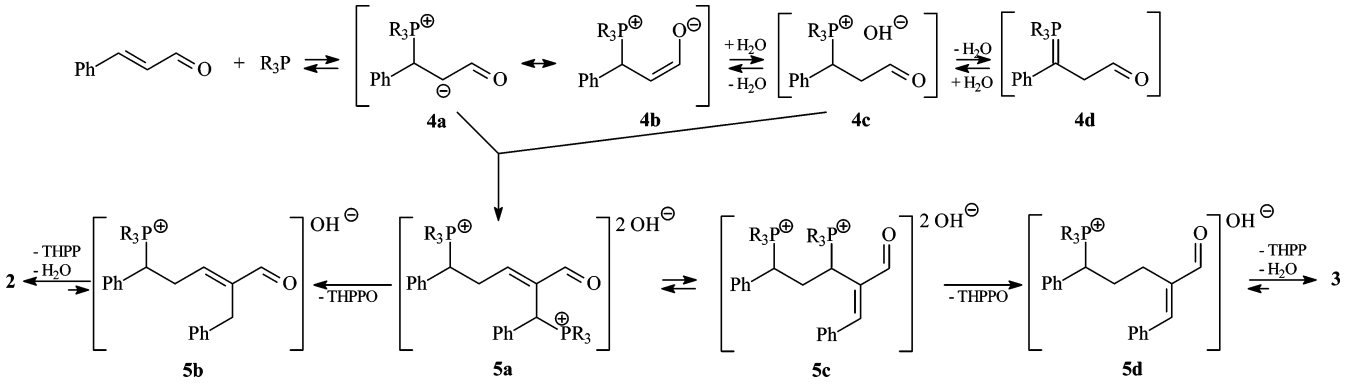
10-D_1, the bisphosphonium salt {[DO$(CH_2)_3$]$_3$PCH(Ph)C(H)-DCH(OD)P[$(CH_2)_3$OD]$_3$}Cl_2. ^{31}P{^{1}H} NMR: δ 39.1 (d, $^4J_{PP}$ = 4, *P*C(H)Ph)) and 38.6 (d, $^4J_{PP}$ = 4, *P*CH(OD)). ^{1}H NMR: δ 4.35 (d, $^3J_{HH}$ = 11.9, C*H*(OD)), 4.26 (pseudo d, $^2J_{PH}$ = 15.4, C*H*(Ph); in the ^{1}H{^{31}P} spectrum: d, $^3J_{HH}$ = 1.9), 2.46 (m, C*H*D, superimposed with the PCH_2 multiplet). ^{13}C{^{1}H} NMR: δ 131.8 (d, $^4J_{PC}$ = 2, *m*-*C*), 131.6 (d, $^5J_{PC}$ = 3, *p*-*C*), 131.0 (br s, *o*-*C*), 130.6 (d, $^2J_{PC}$ = 6, C_{ipso}), 62.9 (dd, $^1J_{PC}$ = 61, $^3J_{PC}$ = 13, P*C*H(OD)), 62.2 (d, $^3J_{PC}$ = 16, *C*H_2OD), 36.3 (dd, $^1J_{PC}$ = 46, $^3J_{PC}$ = 13, P*C*H(Ph)), 31.0 (br s, *C*HD), 25.0 (d, $^2J_{PC}$ = 4, PCH_2*C*H_2), 24.9 (d, $^2J_{PC}$ = 4, PCH_2*C*H_2), 15.8 (d, $^1J_{PC}$ = 48, P*C*H_2), 14.5 (d, $^1J_{PC}$ = 46, P*C*H_2).

Reaction of 1 with THPP Hydrochloride (1:2). The aldehyde (11.6 mg, 0.085 mmol) was added to a solution of THPP hydrochloride (42 mg, 0.170 mmol) in D_2O (~ 1.5 mL), and the procedure used was as above for the 1:1 reaction, the system being

(14) (a) Barrault, J.; Derouault, A.; Courtois, G.; Maissant, J. M.; Dupin, J. C.; Guimon, C.; Martinez, H.; Dumitriu, E. *Appl. Catal., A* **2004**, *262*, 43. (b) Sato, T.; Arai, M.; Kuwajima, I. *J. Am. Chem. Soc.* **1977**, *99*, 5827.

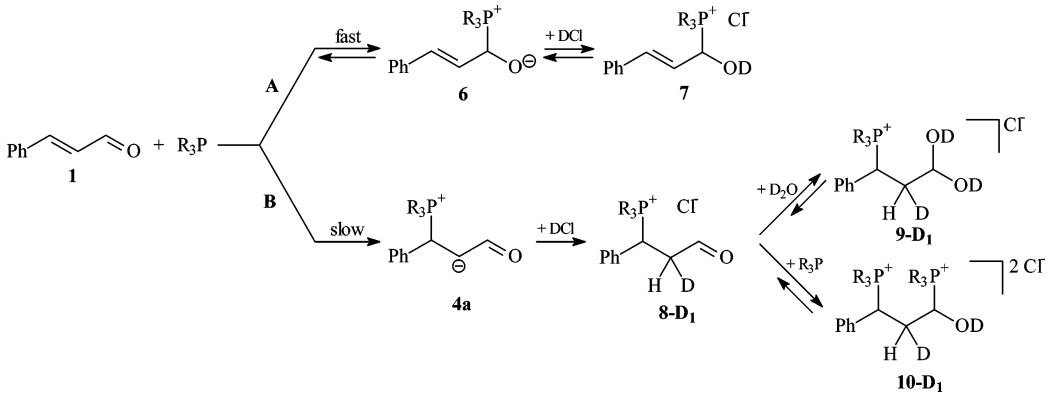
(15) Doyama, K.; Joh, T.; Shiohara, T.; Takahashi, S. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 4353.

Scheme 2 [a]



[a] R = (CH$_2$)$_3$OH.

Scheme 3 [a]



[a] R = (CH$_2$)$_3$OH.

monitored for 40 days. After in vacuo removal of water, a colorless, gluelike residue was submitted for low-resolution ESI-MS (H_2O): detected were cations of **10-D$_1$** [*m/z* 586.2 (100% [M − Cl]$^+$), calcd 586.3], **9-D$_1$** [*m/z* 360.3 (100% [M − Cl]$^+$), calcd 360.2], **8-D$_1$** [*m/z* 342.2 (63% [M − Cl]$^+$), calcd 342.2], and the protonated form of THPP [*m/z* 209.0 (58% [M + H]$^+$), calcd 209.2]. ^{2}D and ^{2}D-{^{1}H} NMR (H_2O): δ 2.61 (br s, C*D*H).

The same reaction was performed in H_2O but at 90 °C for 2 h. After removal of water, a residue was submitted for low-resolution ESI-MS (H_2O): detected were proton-containing forms of **9** [*m/z* 359.3 (100% [M − Cl]$^+$), calcd 359.2], **8** [*m/z* 341.3 (56% [M − Cl]$^+$), calcd 341.2], and the protonated form of THPP [*m/z* 209.1 (34% [M + H]$^+$)]. The ^{1}H NMR spectrum of **10** is similar to that of **10-D$_1$** (see above), except for the resonance of the second methylene proton, which appears as a broad triplet at δ 2.66, and the resonance of the C*H*(Ph) proton, which now appears as a doublet of pseudodoublets at δ 4.25 ($^2J_{PH}$ = 13.5, $^3J_{HH}$ = 11.8, coupling on the second methylene proton being unresolved).

Reaction of Hydrocinnamaldehyde with THPP Hydrochloride. The aldehyde (11.5 mg, 0.09 mmol) was added to a solution of THPP hydrochloride (21.4 mg, 0.09 mmol) in air-free D_2O (∼1.5 mL), and the NMR spectra were recorded after 10 min. ^{31}P{^{1}H} NMR: δ 36.5. ^{1}H NMR: δ 7.49−7.33 (m, 5H, Ph), 4.57 (d, 1H, $^3J_{HH}$ = 11.4, C*H*), 3.69 (t, 6H, $^3J_{HH}$ = 6.0, CH_2OH), 3.10 (m, 1H, PhCH_AH$_B$), 2.84 (m, 1H, PhCH$_A$$H_B$), 2.42−2.28 (m, 6H, PC$H_2$), 2.26−2.04 (m, 2H, PhCH$_2$CH_2), 1.94−1.72 (m, 6H, PCH$_2$CH_2). ^{13}C{^{1}H} NMR: δ 141.6 (s, C_{ipso}), 130.3 (s), 130.2 (s), 128.1 (s, *p-C*), 65.2 (d, $^1J_{PC}$ = 59, *C*H), 62.4 (d, $^3J_{PC}$ = 16, *C*H$_2$OH), 33.5 (d, $^2J_{PC}$ = 4, PhCH$_2$*C*H$_2$), 32.1 (d, $^3J_{PC}$ = 13, Ph*C*H$_2$), 25.0 (d, $^2J_{PC}$ = 4, PCH$_2$*C*H$_2$), 14.5 (d, $^1J_{PC}$ = 46, P*C*H$_2$). After removal of water, the resulting colorless, viscous residue was submitted for low-resolution ESI-MS (H_2O): detected were the cations of the phosphonium salt **11** [*m/z* 343.2 (100% [M − Cl]$^+$), calcd 343.2], the protonated form of THPP [*m/z* 209.0 (18% [M + H]$^+$)], and the reactant aldehyde [*m/z* 116.9 (10% [M − OH]$^+$), calcd 117.2].

Aldol Condensation of Cinnamaldehyde and Acetone in the Presence of THPP. A solution of THPP (21 mg, 0.1 mmol) in air-free water (2 mL) was added to a solution of cinnamaldehyde (132 mg, 1 mmol) in air-free acetone (2 mL), and the mixture was stirred under Ar for 17 h at r.t. Removal of the solvents left a brown solid that was extracted by Et_2O (2 × 5 mL); the ether layers were dried with Na_2SO_4 overnight, and the product was separated by column chromatography on silica gel (230−400 mesh) using Et_2O/*n*-pentane (2:1 v/v) as eluant. After removal of the solvents under vacuo, 6-phenyl-3,5-hexadien-2-one (**12**), a known compound,[16] was isolated as an pale yellow solid (128 mg, 74%). ^{1}H NMR: δ 7.51−7.44 (m, 2H, *o-H*), 7.41−7.23 (m, 4H, overlapping β-, *m*- and *p-H*), 7.00−6.82 (m, 2H, γ- and δ-*H*), 6.26 (d, $^3J_{HH}$ = 15, 1H, α-*H*), 2.32 (s, 3H, CH_3); these data agree well with those in one literature report[16b] but show differences to data from another report.[16c]

Results and Discussion

A 1:1 reaction of cinnamaldehyde (**1**) with THPP in water, at room temperature under O_2-free conditions over 2 days,

(16) (a) Unterhalt, B.; Weyrich, K. *Arch. Pharm.* **1980**, *313*, 913. (b) Masuyama, Y.; Sakai, T.; Kato, T.; Kurusu, Y. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 2265. (c) Nongkhlaw, R. L.; Nongrum, R.; Myrboh, B. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1300.

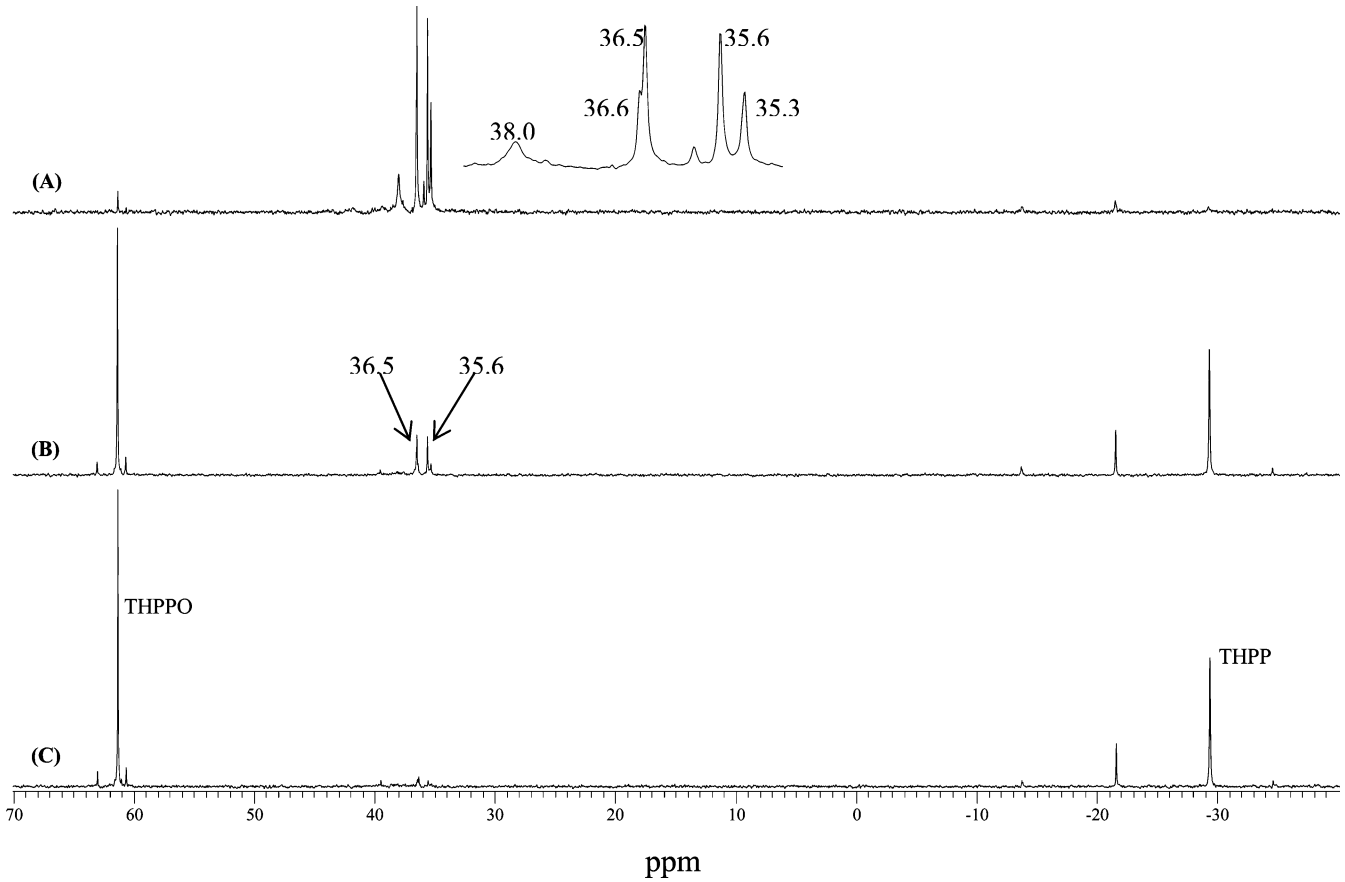


Figure 1. The $^{31}P\{^1H\}$ spectrum of the 1:1 reaction of THPP with **1** in H_2O, after (A) 10 min, (B) 48 h, and (C) 6 days; unremovable phosphine impurities are seen as singlets at δ_P −21.4 and −34.5; the singlets at δ_P 60.6 and 63.0 are the phosphine oxides formed in the redox reaction of the phosphine impurities with **1** (see ref 2).

generates mainly the two isomeric products: 2-benzyl-5-phenyl-pent-2,4-dienal (**2**) and 5-phenyl-2-(phenylmethylene)-4-pentenal (**3**) in 29% and 21% yield, respectively (Scheme 1); the net formation of **2** or **3** involves the "dimerization" of 2 mol of **1** accompanied by loss of one oxygen atom. TLC analysis shows at least five other minor organic products, which could not be isolated pure but are likely higher "oligomerization" compounds (see below). The oxygen atom is incorporated within the tris(3-hydroxypropyl)phosphine oxide product (THPPO, δ_P 61.3), and unreacted THPP (δ_P −29.3) was also seen. Monitoring the reaction by $^{31}P\{^1H\}$ NMR spectroscopy revealed that, after 10 min, no free THPP was present, while new resonances were detected in the phosphonium region (Figure 1A):[17] a broad singlet at δ_P 38.0 and two sets of singlets at δ_P 36.6, 35.3 (of equal intensity) and 36.5, 35.6 (also of equal intensity). These resonances then slowly disappeared, while resonances of THPP and THPPO simultaneously increased (Figure 1B,C), and Figure 2 illustrates the relative changes of the resonance intensities (assumed to correlate with the phosphorus-containing species) versus time.

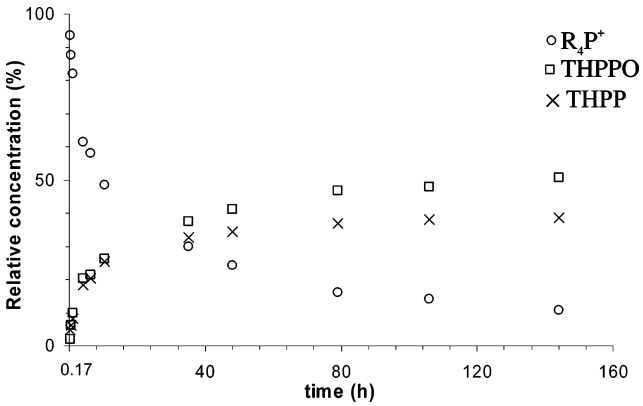
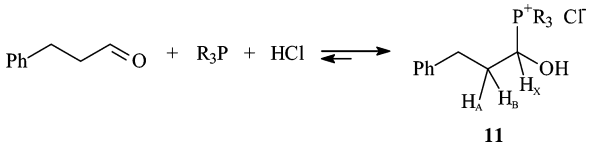


Figure 2. Relative concentration of phosphorus-containing species (according to integration of the $^{31}P\{^1H\}$ resonances of Figure 1) versus time; R_4P^+ is a mixture of **4a**−**d** and **5a**−**d** intermediates (see text). The initial THPP is consumed within the first 10 min (see Figure 1).

When the 1:1 cinnamaldehyde/THPP reaction was carried out in D_2O, the deuterated products **2-D$_5$** and **3-D$_5$** were isolated (Scheme 1). Their ^1H spectra, which show only the aldehyde proton and phenyl proton resonances, and their ^2D NMR data, which show resonances for all five deuterons in the carbon chain moiety, unambiguously prove their structures. There is a small ^1H resonance at δ_H 3.81 for **2-D$_5$**, attributable to **2-D$_4$** where deuteration is not quite complete at the benzyl position (**2-D$_5$**/**2-D$_4$** = 10/1). Similarly, the ^1H spectrum of **3-D$_5$** shows a resonance at δ_H 3.44 corresponding to **3-D$_4$**, where some protons remain in the methylene group

(17) (a) Tebby, J. C. In *Phosphorus-31 NMR spectroscopy in stereochemical analysis*; Verkade, J. G., Quin, L. D., Eds.; VCH Publishers: Weinheim, 1987; Chapter 1. (b) Fluck, E.; Heckmann, G. In *Phosphorus-31 NMR spectroscopy in stereochemical analysis*; Verkade, J. G., Quin, L. D., Eds.; VCH Publishers: Weinheim, 1987; Chapter 2. (c) Quin, L. D. *A guide to organophosphorus chemistry*; Wiley-Interscience: New York, 2000; Chapter 6. (d) Moiseev, D.; James, B. R.; Patrick, B. O.; Hu, T. *Inorg. Chem.* **2006**, *45*, 2917.

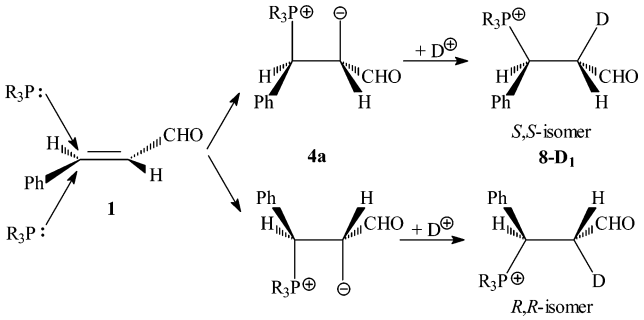
Scheme 4 [a]



11

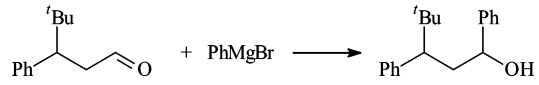
[a] R = $(CH_2)_3OH$.

Scheme 5 [a]



[a] R = $(CH_2)_3OH$; the stereochemistry is shown here for **8-D$_1$**, but the same reasoning applies to the experimentally observed diol, **9-D$_1$.**

Scheme 6



(**3-D$_5$**/**3-D$_4$** = 4/1)]. The ESI mass spectral data also show the incorporation of five deuterium atoms.

A plausible mechanism for formation of **2** and **3** is summarized in Scheme 2 (the α-, *β*-, and *γ*-positions are defined in Scheme 1 and are used throughout the text and Schemes 2−6). Initial nucleophilic attack of THPP at the *γ*-carbon (see eq 1, Introduction) would give carbanion **4a**, stabilized by the enol resonance form **4b**; in D_2O, exchange of the *β*-proton takes place. The strongly basic **4a** in H_2O would generate the phosphonium hydroxide **4c**, which could exist in equilibrium with the ylide form **4d**,[2,18] which in D_2O allows for H/D exchange of the *γ*-proton of the phenylpropanoid backbone. Evidence for the generation of OH^- is a pH increase from 9.0 to 11.2 after **1** was added to the THPP solution. The hydroxide **4c** (a mixture of *R*- and *S*-isomers) is likely the most stable intermediate because the reaction takes place in H_2O, and the broad singlet at δ_P 38.0 is tentatively assigned to this species (Figure 1A). The condensation is envisaged as reaction between **4a** and **4c** to give the diphosphonium dihydroxide **5a** (Scheme 2). Such phosphonium hydroxide salts can decompose under basic conditions to form the corresponding phosphine oxide and a 2-electron reduction product,[19] and we invoked such a step in the reduction of aromatic aldehydes to the alcohols by THPP in aqueous solution.[2] The observed generation of THPPO (Figure 2) is consistent with the same type of redox reaction, which here would lead to formation of the monophosphonium hydroxide **5b**; subsequent loss of the phosphine (which is thus regenerated) and H_2O would give **2** (Scheme 2). The coproduct **3** can be obtained from a similar sequence of the redox and elimination reactions via the diphosphonium dihydroxide **5c**, which could be formed by migration of a THPP molecule within **5a** (Scheme 2). Evidence for isomers **5a** and **5c** is the observation of two sets of two equal intensity singlets seen in the $^{31}P\{^1H\}$ spectrum (δ_P 36.6, 35.3 and 36.5, 35.6 in a 2:3 ratio; Figure 1A). These signals are attributed to two species each containing two noncoupled P centers, rather than sets of diastereomers, because their simple $^{31}P\{^1H\}$ spectra imply the presence of just two enantiomeric forms for each species (the stereochemical aspects of nucleophilic attacks by phosphine reagents are discussed below in more detail). The H/D exchange of the five protons of **2** and **3** seen in the D_2O system is readily accounted for by the mechanism shown in Scheme 2, remembering that phosphonium intermediates such as **5a**−**d** (like **4a**−**c**) can exist in equilibrium with ylide species (cf. **4d**, see above).

Of interest, we have characterized crystallographically a compound analogous to **5c**, but which was made from PEt_3 and 4-OH-3,5-$(OMe)_2$-cinnamaldehyde (sinapaldehyde); again, this compound is formed via processes showing high stereoselectivity.[20] Of note, the redox reactions involve only the phosphonium moiety at the *γ*-carbon (relative to the aldehyde group of **5a** or **5c**), which can be rationalized in terms of formation of the most stable carbanion during the redox process (see Scheme 2 in ref 2); here, stabilization would involve conjugation between a carbanion lone-pair and an adjacent α,*β*-unsaturated aldehyde moiety. At completion of the cinnamaldehyde reaction (Figure 2), the THPPO formed is ∼50% of the reactant THPP concentration (in agreement with the stoichiometry), whereas the yield of regenerated THPP is ∼40% and there is ∼10% of phosphonium species. This is consistent with the last stage of the process (**5b**→**2**, **5d**→**3**) being reversible, which is reasonable considering that **2** and **3** are α,*β*-unsaturated aldehydes that could react with THPP; such reactions would lead to further oligomerization products. Compound **2** has been made previously via condensation reactions between cinnanmaldehyde and hydrocinnamaldehyde[14a] and between an acetal and a silyl enol ether,[14b] while **3** is one product of a Rh-catalyzed hydroformylation of 1,5-diphenyl-1-penten-3-yne,[15] but neither was characterized by ^1H NMR.

Further evidence in support of Scheme 2 is seen when a 1:1 cinnamaldehyde/THPP reaction in H_2O was quenched by addition of HCl after 45 min (to prevent the redox process); the ESI mass spectrum of a MeOH solution of a residue obtained by removal of water showed a main peak at *m*/*z* 455.5, which corresponds to a monophosphonium cation generated from species such as **5a** or **5c** (with OH^- anions replaced by Cl^-) by loss of one protonated THPP moiety, $[HO(CH_2)_3PH]^+$. A minor peak at *m*/*z* 699.3 (8%) corresponds to a monocation form of **5a**/**5c**, in which one phosphonium center has presumably been neutralized by Cl^-; observed peaks at *m*/*z* 341.5 (8%) and 373.5 (7%) correspond to the cation of **4c** and its hemiacetal form, respectively.

(18) Starnes, W. H.; Lauff, J. J. *J. Org. Chem.* **1970**, *35*, 1978.
(19) (a) McEwen, W. E.; Axelrad, G.; Zanger, M.; VanderWerf, C. A. *J. Am. Chem. Soc.* **1965**, *87*, 3948, and references therein. (b) Hays, H. R.; Laughlin, R. G. *J. Org. Chem.* **1967**, *32*, 1060, and references therein. (c) Pagilagan, R. U.; McEwen, W. E. *Chem. Commun.* **1966**, 652.
(20) Moiseev, D.; James, B. R.; Patrick, B. O.; Hu, T. Q. Unpublished work.

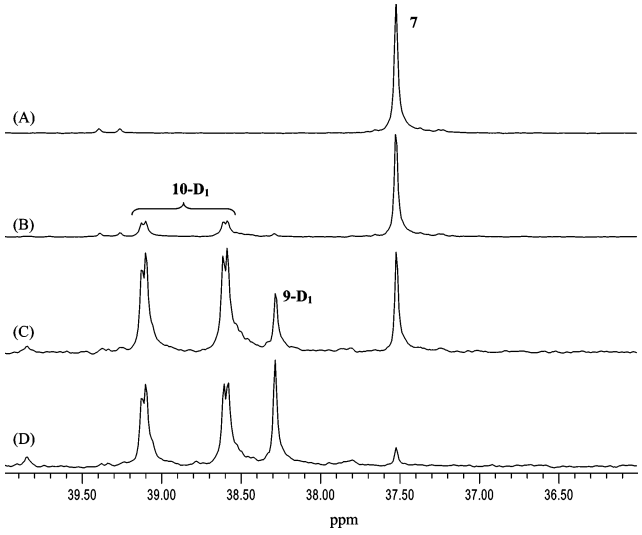


Figure 3. The phosphonium region of the $^{31}P\{^1H\}$ spectrum of the 1:1 reaction of **1** with THPP hydrochloride in D_2O at ambient conditions after (A) 10 min, (B) after 1 day, (C) after 8 days, and (D) after 40 days.

Quite different behavior is seen in the 1:1 reaction of cinnamaldehyde with THPP hydrochloride, where the P atom now attacks the carbonyl α-C atom rather than the γ-C atom (Scheme 3, path A). After 10 min of reaction in D_2O, NMR spectra are consistent with the presence of the phosphonium salt **7** (as a mixture of *R*- and *S*-enantiomers). In the $^{31}P\{^1H\}$ spectrum, there is a singlet at δ_P 37.5 (Figure 3A) and a triplet for unreacted THPP(D)$^+$ at δ_P 16.7 ($^1J_{PD} = 75$ Hz), while in the ^1H NMR spectrum the α- and β-protons appear as doublets of doublets of doublets centered at δ_H 5.49 and 6.38, respectively (see Experimental Section and the Supporting Information, Figure S1); each ddd pattern, which results from coupling to two different H atoms and the P atom, collapses in the $^1H\{^{31}P\}$ spectrum to a doublet of doublets. The α-carbon appears in the $^{13}C\{^1H\}$ spectrum as a doublet at δ_C 68.3 because of coupling to phosphorus. The ratio of **7**:**1** at the 10 min stage is ~5 (see Figure S1). Path A is an example of the kinetically favored nucleophilic attack of a phosphine at the α-carbon of **1** in acid conditions; in this experiment the pH was ~4.4. At higher pH, the reaction can be reversed to regenerate the starting materials, when the much slower chemistry outlined in Scheme 2 (involving nucleophilic attack at the γ-carbon) is evident. Indeed, even at pH 4.4, there is evidence for much slower γ-attack. After 24 h, two new doublets develop in the $^{31}P\{^1H\}$ spectrum (at the expense of the singlet of **7**) at δ_P 39.1 and 38.6 ($^4J_{PP} = 4$ Hz) (Figure 3B), which correlate in a $^{31}P\{^1H\}$-$^{31}P\{^1H\}$ COSY experiment; these are assigned to the bisphosphonium salt **10-D$_1$** (Scheme 3, path B), which also has the requisite ^1H and ^{13}C NMR data. The γ-proton appears at δ_H 4.26 as a pseudodoublet ($^2J_{PH} = 15.4$, coupling with the β-proton and deuteron being unresolved, Figure S2), which in the $^1H\{^{31}P\}$ spectrum becomes a doublet ($^3J_{HH} = 1.9$ Hz, coupling with the β-deuteron again being unresolved), and this proton correlates with the δ_P 39.1 signal in an HMQC experiment. The corresponding γ-carbon appears in the $^{13}C\{^1H\}$ spectrum as a doublet of doublets at δ_C 36.3 ($^1J_{PC} = 46$ and $^3J_{PC} = 13$ Hz). The α-proton of **10-D$_1$** appears as a doublet at δ_H 4.35 both in the ^1H and in the $^1H\{^{31}P\}$ spectra implying coupling only to the β-proton ($^3J_{HH} = 11.9$ Hz), while the α-carbon in the $^{13}C\{^1H\}$ spectrum appears as a doublet of doublets at δ_C 62.9 ($^1J_{PC} = 61$ and $^3J_{PC} = 13$ Hz). The β-proton multiplet resonance overlaps with the multiplets of the phosphorus alkyl protons, but the shift was determined by a ^1H-^1H COSY experiment in which the α- and γ-protons correlate with the resonance at δ_H 2.46 (Figure S3). The β-carbon appears as a broad singlet at δ_C 31.0 because of coupling with the deuterium and the two P atoms. As **10-D$_1$** forms, the ^1H resonances of the starting aldehyde necessarily intensify. Thus even in the acidic conditions, where the bulk of the phosphine is present as phosphonium, the γ-carbon is slowly attacked, and the suggested pathways are shown in Scheme 3: the initially formed zwitterion **4a** (cf. Scheme 2) would be stabilized by accepting a deuteron to give the monophosphonium salt **8-D$_1$** (or its diol **9-D$_1$**), which could subsequently undergo attack (preferentially to cinnamaldehyde) at the α-carbon by the phosphine to yield **10-D$_1$** (Scheme 3, path B). After 8 days of the 1:1 reaction, the $^{31}P\{^1H\}$ spectrum shows a singlet at δ_P 38.3, characteristic of a monophosphonium species that we consider to be the diol **9-D$_1$** (Figure 3C), and ^1H NMR data, which show the C*H*(OD)$_2$ proton rather than the C*H*O proton, are consistent with this formulation (Figure S2). The α-C*H*(OD)$_2$ proton appears as a doublet at δ_H 4.84 ($^3J_{HH} = 8.6$ Hz) both in the ^1H and $^1H\{^{31}P\}$ spectra; the γ-C*H*(Ph) proton in the ^1H NMR appears as the expected doublet of doublets, which becomes a clear doublet in the $^1H\{^{31}P\}$ NMR spectrum; the β-C*H*D proton is seen at δ_H 2.12 as a doublet of doublets of doublets in the ^1H NMR spectrum ($^3J_{PH} = 8.0$, $^3J_{HH} = 8.5$, $^3J_{HH} = 2.5$ Hz) and a doublet of doublets in the $^1H\{^{31}P\}$ spectrum. In the acid conditions, formation of **8-D$_1$** from **4a** will be essentially complete, and there is no opportunity for the dimerization of **4a** (cf. Scheme 2); similarly, at the 1:1 stoichiometry, **9-D$_1$** would seem to be the likely final product of the 1:1 reaction, but its formation is extremely slow at ambient conditions and is incomplete even after 40 days (Figure 3D).

When THPP hydrochloride and cinnamaldehyde were reacted in a 2:1 ratio under the same conditions as the 1:1 reaction, the stoichiometrically favored **10-D$_1$** was the final product after 40 days, and only a trace of **9-D$_1$** was detected. A resulting syrupy residue was analyzed by ^2D- and $^2D\{^1H\}$-NMR spectroscopy, which revealed only one broad singlet at δ_D 2.61 for the β-deuteron of **10-D$_1$**. The ESI-MS of an aqueous solution of the residue showed a main peak corresponding to the monochloride cation of **10-D$_1$** and smaller peaks due to the monocations of **8-D$_1$** and **9-D$_1$**. When the residue was obtained from a 2:1 reaction in H_2O (90 °C for 2 h), ESI-MS (H_2O) peaks corresponded to nondeuterated **9**; the MS data show nicely the incorporation of a single D atom in the D_2O experiment. The diastereotopic methylene protons of **10** appear in the ^1H NMR spectrum at δ_H 2.66 as a broad triplet and at δ_H 2.44 m, which overlaps with the multiplets of the phosphorus alkyl protons; however, the shifts were determined by a ^1H-^1H COSY experiment (Figures S4 and S5).

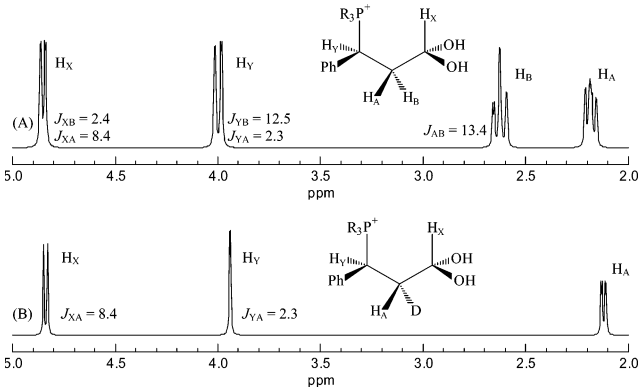
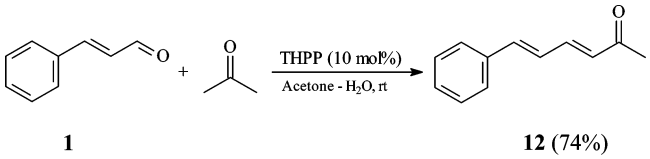


Figure 4. Simulated ^{1}H{^{31}P} NMR spectra of the labeled protons of **9** (A) and **9-D$_1$** (B); spectrum A, written arbitrarily with *S*-chirality at the γ-carbon, corresponds to $\Delta\delta_{AB}$ = 0.44 ppm.

In compound **10-D$_1$**, the proton of the C*H*(OD)(PR$_3$)$^+$ group appears in the ^{1}H- and ^{1}H{^{31}P}-NMR spectra as a doublet at δ 4.35 with coupling only to the β-proton ($^3J_{HH}$ = 11.9 Hz), and surprisingly shows no two-bond coupling to the P atom, which we have observed in **7** and in analogous phosphonium-containing species;[2] note that in **10-D$_1$,** the C*H*Ph proton does show $^2J_{PH}$ coupling to its neighboring P atom. To validate the noncoupling and clear up an a possible discrepancy in the literature,[4a,b] THPP hydrochloride was reacted with hydrocinnamaldehyde (3-phenyl-propanal) in D$_2$O at ambient conditions to give the phosphonium chloride **11** (Scheme 4). The α-proton appears at δ_H 4.57 as a pseudodoublet ($^3J_{HH}$ = 11.4 Hz) in both the ^{1}H- and ^{1}H-{^{31}P}-NMR spectra (Figures S6 and S7), again showing no $^2J_{PH}$ coupling (the β-CH$_2$ protons are diastereotopic and form an ABX spin-system in which J_{AX} is resolved and $J_{BX} \sim 0$); again the β-protons couple with phosphorus, as shown by the more complex multiplet pattern of these protons in the ^{1}H spectrum than in the ^{1}H{^{31}P} spectrum. [All three carbons of the alkyl chain appear in the ^{13}C{^{1}H} spectrum as doublets at δ_C 65.2 ($^1J_{PC}$ = 59 Hz), 33.5 ($^2J_{PC}$ = 4 Hz), and 32.1 ($^3J_{PC}$ = 13 Hz)]. The mass spectrum, obtained by low-resolution ESI of an aqueous solution of the residue from the reaction, shows the main peak at *m*/*z* 343.2, which corresponds to the phosphonium cation of **11**. The α-proton of the acetaldehyde derivatives [(CH$_3$)CH(OH)PR$_3$]Cl (R = Me and Et) has also been reported not to couple with phosphorus,[4a] while for the Ph$_3$P analogue of **11**, a doublet for the α-proton ($^2J_{PH}$ = 10.2 Hz) was attributed, likely incorrectly, to coupling with the P atom.[4b]

Compounds **9-D$_1$**, **10**, and **10-D$_1$** possess two, two, and three chiral centers, respectively, implying the corresponding existence of 4, 4, and 8 stereoisomers. However, the relative simplicity of the resonances and their multiplicities, in the ^{1}H, ^{31}P{^{1}H}, and ^{13}C{^{1}H} spectra, are consistent with the presence of just two enantiomers in each case, implying stereoselectivity in the formation of **9-D$_1$** and **10/10-D$_1$**. More explicitly, for example, for non-deuterated **9**, the ^{1}H{^{31}P} NMR spectrum of the four protons of the propyl chain form a Y-AB-X spin-system; the experimental spectrum (Figure S8) can be simulated using the *J* values shown in Figure 4A, this implying that $J_{XY} \leq 1$ Hz. If H$_B$ is specifically replaced by D, the ^{1}H system simplifies to a Y-A-X spin system (J_{YB} and J_{XB} disappear, and coupling to deuterium is unresolved) that is defined by the *J* values shown in Figure 4B, and this agrees with the experimental spectrum for **9-D$_1$** (Figure S9). If H$_A$ is replaced by D, J_{YA} and J_{XA} disappear, and the ^{1}H resonance for H$_X$ should appear as a doublet with J_{XA} = 2.4 Hz (see Figure S10). Thus, for a mixture of *R*- and *S*-isomers at the β-carbon and a fixed chirality at the γ-carbon, the final ^{1}H NMR pattern of **9-D$_1$** is expected to be a superposition of two patterns discussed above (Figure S11), and this is not observed. Thus **9-D$_1$** is considered to be a mixture of two enantiomers. Presumably, after nucleophilic attack of THPP, the chirality of the β-carbon of the carbanion **4a** is determined by an electrostatic interaction between the phosphonium and the carbanion lone pair, and subsequent addition of a deuteron must lead only to the formation of *R*,*R*- and *S*,*S*-enantiomers (Scheme 5).

Scheme 7



1 **12** (74%)

The simplicity of the ^{1}H, ^{31}P{^{1}H}, and ^{13}C{^{1}H} spectra of **10-D$_1$** shows that its formation from the *R*,*R*/*S*,*S* mixture of **8-D$_1$** (see above) involves stereospecific, nucleophilic attack of THPP at the aldehyde carbon to give just two enantiomers, implying that *R*,*R*-**8-D$_1$** generates specifically *R* (or *S*) chirality at the precursor carbonyl carbon and that the *S*,*S*-**8-D$_1$** correspondingly generates specifically *S* (or *R*). This is difficult to rationalize because the aldehyde group is remote from the γ-chiral center bearing the bulky groups. However, Arjona et al. have found that a bulky *R*-chiral center at such a γ-carbon in 3-phenyl-4,4-dimethylpentanal gives with PhMgBr predominantly *S*-chirality in the generated alcohol moiety, and, vice versa, an *S*-center generates *R*-chirality (Scheme 6). The alcohol product was obtained in 34% diastereomeric excess yield.[21] The diastereoselectivity was interpreted theoretically in terms of steric selection of transition states, and such an explanation seems relevant here, especially for attack of the more bulky nucleophile THPP at the aldehyde-C atom of, for example, **8-D$_1$**, where higher stereospecificity could lead to formation of *R*,*R*,*S*- and *S*,*S*,*R*-enantiomers of **10-D$_1$**. Some computer modeling studies are needed to help elucidate the steric effects implicated; H-bonding involving the hydroxyl groups of THPP may play a role.[17d] The possibility of accidental degeneracy within the NMR spectra of the four possible stereoisomers of **10-D$_1$** must be practically zero!

Of note, in a preliminary reaction in an acetone−H$_2$O mixture (1:1 v/v) at ambient conditions, cinnamaldehyde with THPP (10:1) was found to undergo a catalyzed condensation reaction with the acetone to afford 6-phenyl-3,5-hexadien-2-one (**12**) in 74% yield after 17 h (Scheme 7). In the absence of THPP, no condensation occurred, and presumably the phosphine is simply promoting reaction by production of

(21) Arjona, O.; Perez-Ossorio, R.; Perez-Rubalcaba, A.; Quiroga, M. L. *J. Chem. Soc., Perkin Trans. 2* **1981**, 597.

OH^- (see, for example, formation of **4c** in Scheme 2). This leads to the classic base-catalyzed aldol-type condensation involving generation of the intermediate carbanion ($^-CH_2COCH_3$) from the acetone; the maximum reported yield for **12** from such a reaction is 60%.[16] We reported recently that THPP similarly promotes a base-catalyzed aldol condensation reaction of hydrocinnamaldehyde to give 5-phenyl-2-benzyl-2-pentenal.[2]

Conclusions

The phosphine $[HO(CH_2)_3]_3P$ (THPP) interacts with cinnamaldehyde in H_2O at ambient conditions to generate slowly the known condensation, isomeric products, 2-benzyl-5-phenyl-pent-2,4-dienal and 5-phenyl-2-(phenylmethylene)-4-pentenal; the mechanism involves nucleophilic attack of the phosphine at the C═C bond to give a putative carbanion intermediate that is in equilibrium with a more stable phosphonium hydroxide. Subsequent condensation reactions generate two bisphosphonium dihydroxides, in which a [-CH-(P^+R_3)-] phosphonium center adjacent to a π-conjugation moiety is slowly converted by OH^- to the phosphine oxide and $-CH_2-$; the monophosphonium hydroxide products then eliminate THPP to give the isomer products. The same reaction carried out in D_2O gives analogous products in which all but the phenyl and aldehyde protons are replaced by deuterons. Reaction of THPP hydrochloride with cinnamaldehyde in D_2O involves an initial more rapid nucleophilic attack of the phosphine at the aldehyde-C atom within an equilibrium reaction to form the (α-hydroxy)phosphonium salt, $\{PhCH{=}C(H)CH(OD)P^+R_3\}Cl$, where $R = (CH_2)_3OD$. Over longer periods the system generates initially the more stable $\{PhCH(P^+R_3)C(D)HCHO\}Cl$ (in equilibrium with the diol) via attack of THPP at the C═C bond; however, this phosphonium aldehyde is more reactive toward the phosphine than cinnamaldehyde, and this eventually leads to the formation of the bisphosphosphonium salt $\{R_3P^+CH(Ph)-CD(H)CH(OD)P^+R_3\}Cl_2$. The phosphonium intermediates and phosphonium products in this chemistry, although having up to three chiral carbon centers, are formed with high stereoselectivity just as enantiomers. In acetone−H_2O, THPP catalyzes the cross-condensation of cinnamaldehyde with acetone via a standard aldol condensation reaction promoted by in situ generation of hydroxide.

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada for funding via a Discovery grant and an Idea to Innovation (I2I) grant and Drs. Nick Burlinson and Maria Ezhova for discussions about the NMR data.

Supporting Information Available: Various experimental ^1H-, ^1H-^1H COSY-, and $^1H\{^{31}P\}$-NMR spectra (Figures S1−S9) and predicted $^1H\{^{31}P\}$ NMR spectra for diastereomers of **9-D$_1$** (Figures S10 and S11). This material is available free of charge via the Internet at http://pubs.acs.org.

IC0701559