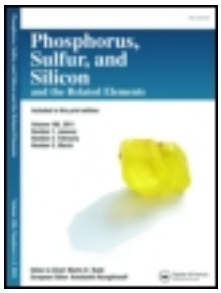

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REACTION OF $[HO(CH_2)_3]_3P$ WITH α,β-UNSATURATED KETONES CONTAINING A PHENYLPROPANOID BACKBONE

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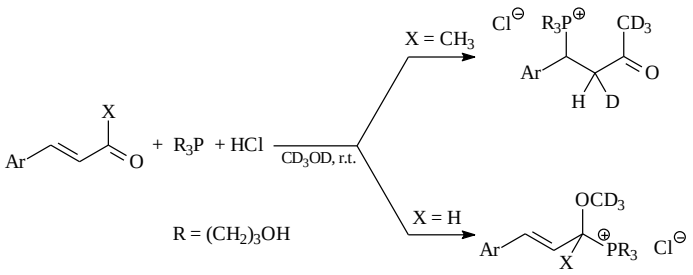
Abstract *Interaction of 3,4-(MeO)$_2$-benzylideneacetone with [HO(CH$_2$)$_3$]$_3$P (THPP) was studied in CD$_3$OD by NMR to compare reactivity of a phenylpropanoid α,β-unsaturated ketone with a corresponding α,β-unsaturated aldehyde. In the presence of HCl, both the ketone and a related cinnamaldehyde first establish an equilibrium with the product formed by nucleophilic attack of the THPP at the C=O bond, [ArCH=CHCX(OD)PR$_3$]$^+$Cl$^-$ (X = H or CH$_3$, Ar = Ph or 3,4-(MeO)$_2$C$_6$H$_3$). The ketone salt then slowly transforms into [R$_3$PCH(Ar)CH(D)C(O)CD$_3$]$^+$Cl$^-$, the phosphonium product of nucleophilic attack of THPP at the C=C bond, whereas the final product from the aldehyde is the (α-ether)phosphonium chloride [ArCH=CHCH(OCD$_3$)PR$_3$]$^+$Cl$^-$. In aqueous media, in the absence of HCl, 4-HO-benzylideneacetone, which is similar to a lignin-type, α,β-unsaturated aldehyde model compound, interacts with THPP to afford a stable phosphonium zwitterion, in contrast to the previously studied aldehyde model, which forms dimeric, bisphosphonium products.*



Keywords (Hydroxyalkyl)phosphines; α,β-unsaturated ketones and aldehydes; phosphonium salts; phosphonium zwitterions; lignin models

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INTRODUCTION

Interaction of tertiary phosphines with activated olefins is of importance in organic synthesis. Scheme 1 exemplifies some syntheses catalyzed by such phosphines, which act as nucleophiles and attack the C=C bond to generate a carbanionic site; subsequent attack at the reactant olefin gives, after elimination of the phosphine, a dimerization product (the Rauhut-Currier reaction, path A);[1] in the presence of aldehydes, the carbanion attacks the C=O bond to afford 1,2-addition products (the Morita-Baylis-Hillman reaction, path B);[2] the carbanion can also be used to generate nucleophiles which then react with the olefin substrate to afford products with a new C–O[3] or C–C bond[4] (path C). The activated olefinic substrates are generally *α*,*β*-unsaturated ketones and esters, and nitriles such as acrylonitrile.

We have reported previously on the interaction of tertiary (and secondary) phosphines with lignin model compounds, including *α*,*β*-unsaturated carbonyl compounds,[5] in relation to the discovery of the bleaching activity of water-soluble phosphines on mechanical pulps,[6] in which, for example, cinnamaldehyde derivatives containing OH and/or MeO groups in the aromatic ring are considered to be a major chromophore responsible for the lignin color.[7] Our investigations revealed that, in aqueous media, the water-soluble phosphine $[HO(CH_2)_3]_3P$ (abbreviated as THPP) promotes homocondensation of aliphatic aldehydes[8] and cross-condensation of cinnamaldehyde with acetone;[5a] these reactions are thought to involve generation of OH^- via nucleophilic attack of THPP at the C=O or C=C bond (see also Scheme 2 below), the OH^- anion then initiating the condensation process. Related to the cinnamaldehyde reaction, in the presence

of a stoichiometric amount of THPP, this aldehyde undergoes "reductive condensation" to give two isomeric products (Scheme 2).[5a] Similar to the Scheme 1 reactions, the first stage of the process is nucleophilic attack of THPP at the C=C bond and generation of the zwitterion which, in aqueous media, is in equilibrium with the phosphonium hydroxide. Dimerization of these two phosphonium species, followed by oxidation of one molecule of THPP (analogous to decomposition of quaternary phosphonium hydroxides)[8,9] and elimination of the second THPP, leads to the products. Phosphine oxides are also formed in Wittig[10], Mitsunobu[11] and Staudinger[12] reactions.

The topic of the current paper is interaction of THPP with *α,β*-unsaturated ketones containing a phenylpropanoid backbone, as in the aldehyde reactant in Scheme 2, and the findings reveal some interesting differences. Unsaturated ketones are known to react with tertiary phosphines (Scheme 1), but generally show low and often different reactivity: for example, benzylideneacetone (4-phenyl-3-buten-2-one), the closest analogue of cinnamaldehyde, in MeOH does not afford the corresponding hydro(methoxy) product (Scheme 1, path C),[3] and the divinyl ketone, 5-phenyl-1,4-dien-3-one, the C=C bond of the Ph–C=C moiety does not participate in a dimerization reaction (Scheme 1, path A).[13]

RESULTS AND DISCUSSION

The $^{31}P\{^{1}H\}$ spectrum of a 1:1 reaction of THPP with 3,4-$(MeO)_2$-benzylideneacetone (**I**) in CD_3OD (r.t., Ar) after 20 min showed a new, low intensity singlet (~3% of the THPP resonance at δ_P –29.5) at δ_P 39.1, and this is attributed to the phosphonium cation **III** (Scheme 3).[5b] The ^{1}H NMR data revealed relatively fast H/D-exchange of the H^1 and CH_3 protons in the reactant ketone (Scheme 4); e.g. after the 20 min, the intensity of the H^1 doublet (δ_H 6.68, $^{3}J_{HH}$

16.2 Hz) is ~3% of that of the H^2 resonance, which is seen as a broad singlet at δ_H 7.58 that disappears slowly over 4 days. During this time, the $^{31}P\{^1H\}$ spectrum is essentially unchanged except for the appearance of a weak singlet at δ_P –29.8, possibly due to $[DO(CH_2)_3]_2P[CH(D)(CH_2)_2OD]$, the phosphine monodeuterated in the α-position. H/D-exchange of a proton α to the P-atom typically shifts the $^{31}P\{^1H\}$ resonance upfield by up to ~ 0.3 ppm,[5e,8,14] whereas such exchange of a PH proton, for example, as in $(DOCH_2)_2PH$ and $DOCH_2P(D)H$, gives upfield shifts of 1.6 and 1.1 ppm, respectively.[15] The low-resolution MS-EI of a residue from the reaction (dissolved in MeOH) revealed main peaks at *m/z* 211 (75%, [*M*]) and 193 (100%, [$M - CD_3$]), which correspond to the fully deuterated ketone **I-D$_5$**.

In the presence of less THPP (8 mol%), the H/D-exchange slows down. Figure 1 shows the loss of intensity of the H^1, H^2 and CH_3 proton signals with time, relatively to the "stable" signals of the aromatic protons. After 15 min, a triplet (δ_H 2.33, $^2J_{HD}$ 2.2 Hz) due to CH_2D was detected near the singlet of the CH_3 protons (δ_H 2.35); after 3 h, the CH_3 resonance has almost disappeared, and a quintet (δ_H 2.32, $^2J_{HD}$ 2.2 Hz) due to the CHD_2 group is apparent. Figure 1 shows that the rate of the H/D-exchange of the H^1 and CH_3 protons is essentially identical and, after ~20 h, the intensity of both these proton signals levels out at ~3–4%. The H/D-exchange of the H^2 proton is again slow and, after 3 days, the signal intensity is reduced by only ~20%. The $^{31}P\{^1H\}$ spectrum of the reaction mixture again revealed the resonances of THPP and small amounts of the phosphonium cation (δ_P 39.1) throughout the 72 h experiment. The low-resolution MS-EI of a residue obtained from the reaction after this time showed main peaks at

m/z 210 (80%, [*M*]) and 192 (100%, [*M* – CD_3]), which correspond to the deuterated ketone **I-D_4**.

The H/D-exchange of the ketone-CH_3 protons is likely due to the keto-enol tautomerism catalyzed by a base and facilitated by C=C–C(OD)=C conjugation.[16] The fast exchange of H^1 is due to reversibility of the nucleophilic attack of THPP at the C=C bond (Scheme 5). The strong base CD_3O^- generated is thought to lead to reversible formation of the ylide and thus to the slow exchange of H^2 (Scheme 6). Exchange of the α-proton of the THPP hydroxypropyl group can also occur via a similar ylide intermediate.[8,14]

In the corresponding reaction of THPP with 3,4-$(MeO)_2$-cinnamaldehyde (1:1, CD_3OD, r.t., Ar), the fast H/D-exchange of the α-H and the slow exchange of the β-H of the C=C bond were similarly observed. In the $^{31}P\{^1H\}$ spectrum, a low intensity, broad singlet at δ_P 38.1 (~9% of the THPP resonance) was detected. This system, however, is unstable, and the δ_P 57.3 singlet of THPP=O appears, this coinciding with a more complex ^1H spectrum. The findings are closely related to those found for generation of this oxide (δ_P 61.3 in D_2O)[5a,8] in aqueous redox systems, where cinnamaldehyde undergoes 'reductive condensation' (Scheme 2)[5a] and 3,4-$(MeO)_2$-benzaldehyde is converted to the benzyl alcohol.[8]

The 1:1 reaction of **I** with THPP hydrochloride ($THPPH^+Cl^-$) in CD_3OD (r.t., Ar) differs from that with THPP in that, although the CH_3 protons of the ketone again undergo D-exchange within 30 min, the product is the ketone **I-D_3** (see Scheme 7) which then reacts further. The $^{31}P\{^1H\}$ spectrum after the 30 min (Figure 2A) shows the reactant phosphonium cation $[DO(CH_2)_3]_3P^+D$ (t, δ_P 19.5, $^1J_{PD}$ 78 Hz – very similar to the data in D_2O)[5a,8] and three new

species in the phosphonium region (δ_P 46.3, 38.4 and 37.6). Analysis of the accompanying ^{1}H spectrum reveals that the δ_P 46.3 signal pertains to species **IV** formed via nucleophilic attack of THPP at the carbonyl carbon of **I-D$_3$** (Scheme 7). The H^1 and H^2 vinyl protons are seen as two doublets of doublets centered at δ_H 6.22 ($^3J_{PH}$ 3.8 Hz) and 6.85 ($^4J_{PH}$ 5.0 Hz), respectively, with the $^3J_{HH}$ value of 16.2 Hz implying a *trans* conformation;[17] that $^4J_{PH}$ is > $^3J_{PH}$ is not unusual within such phosphonium species.[5a] The maximum relative concentration of **IV** (~20%) is seen within 1 h of the reaction (Figs. 2 and 3). Nucleophilic attack at the C=O bond was found also for the reaction of THPP with cinnamaldehyde in aqueous media in the presence of HCl[5a] and in MeOH (see below); secondary phosphines and tertiary mono(α-hydroxyalkyl)phosphines also preferably attack the C=O bond of α,β-unsaturated aldehydes.[5d]

As **IV** disappears in the solution, the δ_P 38.4 signal becomes more intense and reaches a maximum concentration of ~35% after 8 h (Fig. 3), which is assigned to the enol species **V** (Scheme 8). The ^{1}H spectrum of this species shows two doublets of doublets at δ_H 4.70 ($^2J_{PH}$ = 16.2, $^3J_{HH}$ = 11.0 Hz) and δ_H 4.98 ($^3J_{PH}$ = 7.9, $^3J_{HH}$ = 11.0 Hz); the former is due to H^2, the $^2J_{PH}$ value being typical for protons adjacent to a phenyl ring and a phosphonium cation,[5a,5b,5e,14] and the latter is assigned to the H^1 proton – the closest analogy that we could find for the latter is the δ_H 5.02 value (with $^3J_{PH}$ = 7.1 Hz, and $^3J_{HH}$ = 12.3 Hz coupling to a benzyl proton) for the corresponding proton of the enol $Ph_2PCH(Ph)CH=CH(OH)$, detected in the 1:1 reaction of cinnamaldehyde with $Ph_2PCH(OH)Ph$ in CD_3OD.[5d] Of note, there is a further analogy with this hydroxyphosphine system,[5d] in that the $^{31}P\{^1H\}$ NMR profile of the reaction is similar to that

seen here for the ketone/THPP/HCl reaction (Figs. 2 and 3); in the hydroxyphosphine reaction, the $Ph_2PCH(Ph)CH=CH(OH)$ and a co-product, $PhCH(OH)CH=CH(PPh_2)$, were considered to be formed by migration of PPh_2 and OH, respectively, within a detected intermediate $PhCH=CHCH(OH)PPh_2$, and so similarly **V** could be formed via migration of the THPP moiety within **IV** (Scheme 9). In this case, the minor, unassigned resonance at δ_P 37.6 (Fig. 2, A and B) might be associated with an intermediate such as **VI** (Scheme 9).

Other reasonable pathways for formation of **V** are shown in Scheme 8. In path A, a carbocation generated at the benzyl C-atom of the ketone would contain the enol moiety, and subsequent nucleophilic attack of THPP would give **V**; in path B, attack of THPP at the C=C bond would generate an intermediate phosphonium carbanion, with subsequent deuteron capture generating the final product, a mixture of **VII-D$_4$** and associated hemiketal **VIII-D$_8$** (see below, Scheme 10), but in this case **V** would not be detected, and so B is not considered a major pathway.

During the course of the ketone/$THPPH^+Cl^-$ reaction in CD_3OD (Figs. 2 and 3), the enol **V** slowly transforms into the ketone **VII-D$_4$**, which is monodeuterated in the α-position (Scheme 10) and, under these conditions, this is in equilibrium with the hemiketal **VIII-D$_8$** (see below); the $^{31}P\{^1H\}$ spectrum shows respective signals at δ_P 39.1 and 39.9 (see below), and the **VII-D$_4$** : **VIII-D$_8$** ratio of 3:2 is, as expected, constant within Figures 2B–D. [Note that the δ_P 39.1 value is the same as that seen for **III** (Scheme 3), in which the Me is non-deuterated.]

The same ketone/THPPH$^+$Cl$^-$ reaction was carried out in MeOH. After 48 h, the solvent was removed and an isolated residue showed a single MS-ESI+ peak at *m/z* 415.0, corresponding to the nondeuterated phosphonium cation **VII** (Scheme 11). The $^{31}P\{^1H\}$ spectrum of a D_2O solution of the residue was unchanged over time, and revealed one singlet at δ_P 39.0, and the ^1H spectrum confirmed formation of **VII**: δ_H 2.22 (s, CH_3), 4.35 (H_M), 3.73 (H_A, which overlaps with the C*H*$_2$OD resonance), and 3.28 (H_B). The H_M, H_A and H_B resonances form a MABX pattern due to additional coupling to the P-atom: J_{MA} = 11.2, J_{MB} = 3.2, J_{AB} = 18.1, Δ_{MA} = 185.8, Δ_{AB} = 132.9, J_{XM} = 15.4, J_{XA} = 5.9, J_{XB} = 9.0 Hz. Formation of phosphonium salts analogous to **VII** has been reported by

others.[3,18] The $^{31}P\{^1H\}$ spectrum of the residue in CD_3OD solution initially revealed singlets at δ_P 39.9 and 39.1 in a 1:8 ratio and, over 24 h, their intensities changed and became roughly equal. The initial ^1H spectrum, associated with the δ_P 39.1 species, is similar to that in D_2O and corresponds to that of **VII**: δ_H 2.18 (s, CH_3), 4.36 (H_M), 3.60 (H_A, which again overlaps with the C*H*$_2$OD resonance), and 3.25 (H_B); the MABX pattern is simulated using J_{MA} = 10.4, J_{MB} = 3.4, J_{AB} = 18.0, Δ_{MA} = 225.4, Δ_{AB} = 105.0, J_{XM} = 15.2, J_{XA} = 6.8, J_{XB} = 10.5 Hz. The protons of **VII-D$_4$** (Scheme 10) are seen in the ^1H spectrum as two three-spin systems, MAX and MBX, in an integration ratio of ~4:3 for the two distereoisomers present; the spectra are well simulated by the parameters: $\delta(H_M)$ 4.35, $\delta(H_A)$ 3.58, J_{MA} = 10.4, Δ_{MA} = 230.0, J_{XM} = 15.2, J_{XA} = 6.2 Hz, and $\delta(H_M)$ 4.35, $\delta(H_B)$ 3.23, J_{MB} = 3.4, Δ_{MB} = 336.3, J_{XM} = 15.2, J_{XB} = 10.3 Hz. The chirality at the methylene C-atom does not affect the $^{31}P\{^1H\}$ spectrum, which shows just the one singlet at δ_P

39.1. Nucleophilic attack of CD_3OD at the C=O of **VII-D$_4$** to afford the third chiral center in **VIII-D$_8$** is apparently stereospecific because only one ^{31}P resonance is seen at δ_P 39.9. That this is due to the hemiketal **VIII** (Scheme 11) is supported further in that the linked, analyzable ^1H resonances are shifted upfield from those assigned for **VII**, consistent with conversion of C=O to C–OD; e.g., the CH_3 singlet is seen at δ_H 1.04, and the CH_M multiplet is shifted to δ_H 3.92 (J_{MA} = 7.6, J_{MB} = 4.0, J_{XM} = 16.6 Hz), which now overlaps with the resonance of the MeO substituent in the aromatic moiety of **VII**. The H_A and H_B signals are hidden by the more intense resonances of the CH_2CH_2 protons of the THPP. Of interest, hemiacetals formed from addition of CD_3OD to the corresponding α,β-unsaturated aldehyde derivatives are a mixture of diastereomers with different ^1H and $^{31}P\{^1H\}$ chemical shifts.[5d,5e,19]

The 1:1 reaction of $THPPH^+Cl^-$ with cinnamaldehyde in CD_3OD under Ar at r.t., like the benzylideneacetone system, involves nucleophilic attack at the C=O bond, with the two equilibria outlined in Scheme 12 being established by NMR data: that between aldehyde and hemiacetal (**IX),** and that between aldehyde and the (α-deuteroxy)phosphonium salt (**X)**, which then *very* slowly converts to the (α-ether)phosphonium chloride $[PhCH=CHCH(OCD_3)PR_3]^+Cl^-$ (**XI**) (Scheme 12). After 2 h, only trace aldehyde is seen in the ^1H spectrum, in which the H^1, H^2 and H^3 protons of both **IX** and **X** are readily indentified. Figure 4, taken after 16 days when some **XI** has also been formed, shows the well resolved proton signals that, as illustrated, are readily assigned. The $^{31}P\{^1H\}$ spectrum after 2 h shows the triplet of $[DO(CH_2)_3]_3PD^+$ (δ_P 19.5, $^1J_{DP}$ = 78 Hz) and the singlet of **X** (δ_P 38.0) in about a 1:1 ratio. These resonances slowly disappear and are replaced by a singlet at δ_P 38.5, attributed to the final product **XI** (Scheme 12); after 37 days the **XI/X** ratio is ~ 8. After removal of the solvent at this stage, the MS-ESI+ of a residue

(dissolved in MeOH) showed the main peak at *m/z* 358.3 (100%) corresponding to the phosphonium cation of **XI**. Of note, and in contrast, in aqueous media the 1:1 reaction between $THPPH^+Cl^-$ and cinnamaldehyde (1:1) leads to the final product $R_3P^+CH(Ph)CH_2CH(OH)_2$, formed by nucleophilic attack at the C=C bond, although intermediate **X** was observed as the analogous (α-hydroxy)phosphonium salt.[5a]

A 1:1 reaction of 4-HO-benzylideneacetone with THPP in D_2O (r.t., Ar) rapidly gives the phosphonium zwitterion **XII-D$_5$**, which is likely in fast equilibrium with the phosphonium deuteroxide **XIII-D$_5$** (Scheme 13). Just one singlet (δ_P 37.8) is seen in the $^{31}P\{^1H\}$ spectrum, and the ^1H spectrum shows just a doublet at δ_H 4.17 due to the H^2 proton ($^2J_{PH}$ = 14.6 Hz), the H^1 and CH_3 protons having been replaced by deuterons (*cf*. the 1st step of Schemes 2[5a,b] and 4). The MS-ES+ spectrum in MeCN of a reaction residue showed peaks at *m/z* 373.3 (90%), 374.3 (100%), 375.3 (95%) and 376.3 (55%) of which the highest corresponds to **XII-D$_5$** protonated at the phenoxide oxygen; the lower mass peaks are thought to result from H/D-exchange caused by trace water in the MeCN. In contrast to the zwitterions derived from α,β-unsaturated aldehydes (Scheme 2),[5a,b] **XII-D$_5$/XIII-D$_5$** are stable under the reaction conditions and do not undergo dimerization.

A 1:1 reaction of 4-HO-benzylideneacetone with THPP in acetone (r.t., Ar) again generates **XII**, but now slowly, and it precipitates as a yellow solid (Scheme 14), similar to reactivity shown by lignin-type, α,β-unsaturated aldehydes such as coniferaldehyde and sinapaldehyde.[5e]

The $^{31}P\{^{1}H\}$ spectrum of **XII** in D_2O shows a singlet at δ_P 37.8, the same as that observed for the corresponding reaction in D_2O (see above). The initial ^{1}H spectrum reveals a singlet at δ_H 2.23 for the CH_3 protons, and broadened doublets at δ_H 4.22 (the H^2 proton) and δ_H 3.20 (one of the CH_2 protons). Over 24 h, H/D exchange occurs and the CH_2 signals disappear, while the CH_3 singlet is replaced by a quintet assigned to CD_2H. The MS-ESI+ spectrum (MeCN solution) revealed the main peak at *m/z* 371.3, corresponding to the protonated phosphonium cation of **XII**. The elemental analysis for **XII** is in reasonable agreement with the calculated values, but this is likely fortuitous because the ^{1}H data also show a significant amount of the reactant ketone, and this is not due to dissociation of **XII** in solution since no ^{1}H signals of THPP are seen; co-precipitation of ketone as an anion (formed via deprotonation of the phenolic-OH) with the protonated **XII** as a phosphonium cation seems plausible.

CONCLUSIONS

Thus, 3,4-$(MeO)_2$-benzylideneacetone, an example of *α,β*-unsaturated ketones containing a phenylpropanoid backbone and closely related to lignin-type, *α,β*-unsaturated aldehydes, reacts with $[HO(CH_2)_3]_3P$ in methanol to give within an equilibrium the phosphonium cation $R_3P^+CH(Ar)CH_2C(O)CH_3$; at room temperature, the equilibrium strongly favours the reactants but is detected by H/D-exchange in CD_3OD. The presence of HCl shifts the equilibrium to the product $[R_3P^+CH(Ar)CH_2C(O)CH_3]Cl^-$, formation of which occurs via the (*α*-hydroxy)phosphonium intermediate $[ArCH=CHC(CH_3)(OH)PR_3]^+Cl^-$ and the enol $[R_3P^+CH(Ar)CH=C(OH)CH_3]Cl^-$. Similar reaction with cinnamaldehyde affords only the (*α*-ether)phosphonium salt $[PhCH=CHCH(OMe)PR_3]^+Cl^-$. Similar to lignin-type, *α,β*-unsaturated aldehydes containing a *p*-OH substituent, 4-HO-benzylideneacetone quantitatively reacts with

$[HO(CH_2)_3]_3P$ in aqueous media to afford the zwitterion $R_3P^+CH(C_6H_4\text{-}O^-)CH_2C(O)CH_3$ which, unlike phosphonium zwitterions derived from lignin-type aldehydes, is stable in water.

EXPERIMENTAL

General. Cinnamaldehyde and 4-OH-benzylideneacetone were purchased from Aldrich and used as received. 3,4-$(MeO)_2$-benzylideneacetone and 3,4-$(MeO)_2$-cinnamaldehyde were prepared by condensing 3,4-$(MeO)_2$-benzaldehyde (Aldrich) with acetone and with acetaldehyde (Aldrich), respectively. Tris(3-hydroxypropyl)phosphine (THPP, an oil, ~85% from Strem Chemicals) was used without purification. We have discussed the difficulty in attempts to purify THPP because of impurities that are "closely related" phosphines;[8] the phosphonium hydrochloride, $\{[HO(CH_2)_3]_3PH\}^+Cl^-$ (abbreviated $THPPH^+Cl^-$) was prepared as described.[8] Distilled water and D_2O were saturated with Ar for 3 h under stirring; organic solvents were dried over the appropriate agents, distilled under N_2, degassed and then saturated with Ar. CD_3OD (Cambridge Isotope Laboratories) was used as received. NMR spectra were recorded at ~300 K on Bruker AV400 (400 MHz for ^1H, 161 MHz for ^{31}P) or AV300 (300 MHz for ^1H; 121 MHz for $^{31}P\{^1H\}$) instruments, with a residual deuterated solvent proton and 85% aq. H_3PO_4 being used as references; s = singlet, d = doublet, t = triplet, m = multiplet. ^1H and $^1H\{^{31}P\}$ spectra were simulated using the gNMR Version 4 program, with *J* values to ± 0.3 Hz. Mass spectrometry was performed on a Kratos MS-50 (EI) or on a Bruker Esquire electrospray (ESI) ion trap instrument with samples dissolved in MeOH or MeCN, with positive ion polarity, scanning from 100–1000 *m/z*. The elemental analysis of **XII** was carried out in this department by M. Lakha using a Carlo Erba 1108 analyzer.

NMR investigations of 1:1 reactions of THPP with organics. In a glove-box, THPP (25 mg, 0.12 mmol, assuming 100% purity) was added to a solution of 3,4-$(MeO)_2$-benzylideneacetone

(25 mg, 0.12 mmol) in CD_3OD (1.1 mL), and a sample (~0.7 mL) of the solution was placed under Ar in a J-Young NMR tube; NMR spectral changes were then monitored as a function of time. The same reaction with less THPP (2 mg, 0.01 mmol) was performed similarly. The 1:1 reactions of THPP with 3,4-$(MeO)_2$-cinnamaldehyde (23 mg, 0.12 mmol) in CD_3OD, and with 4-HO-benzylideneacetone (19 mg, 0.12 mmol) in D_2O (1 mL) were also studied in the same way, as were the 1:1 reactions in CD_3OD (1.1 mL) of THPP hydrochloride (12 mg, 0.05 mmol) with 3,4-$(MeO)_2$-benzylideneacetone (10 mg, 0.05 mmol), and of THPP hydrochloride (22 mg, 0.09 mmol) with cinnamaldehyde (11 μL, 0.09 mmol).

Synthesis of the phosphonium salt, XII (Scheme 14). A r.t. reaction of a stirred mixture of THPP (100 mg, 0.48 mmol) with 4-HO-benzylideneacetone (77 mg, 0.48 mmol) was carried out in acetone (1.5 mL), when a yellow precipitate was formed after 24 h. This was collected, washed with acetone (2 × 2 mL), and dried under vacuum overnight; yield ~100 mg, ~70% based on ~85% purity of THPP. Anal. Calcd. for $C_{19}H_{31}O_5P$ (370.42): C 61.61; H 8.43. Found: C 61.2; H 8.4. ^1H and $^{31}P\{^1H\}$ NMR data in D_2O are discussed in the Results and Discussion section.

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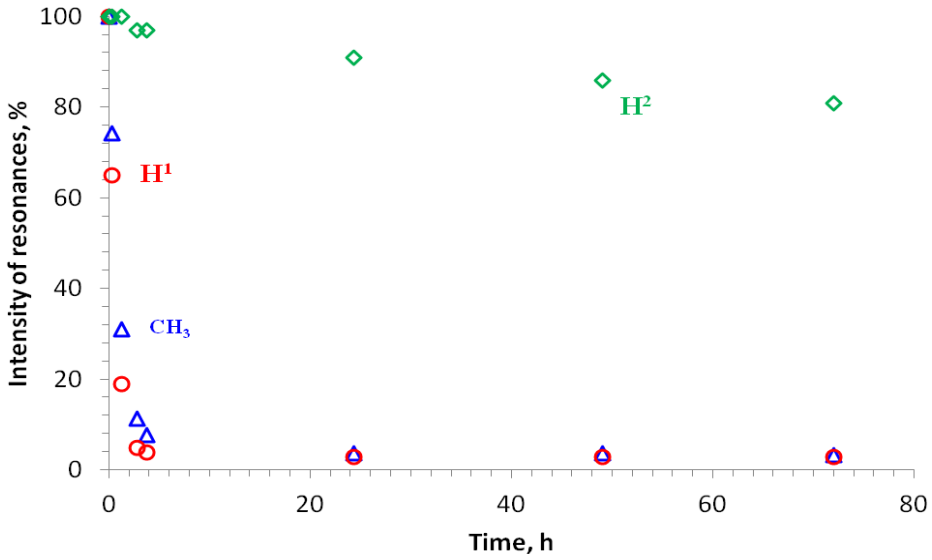


Figure 1. Decreasing intensity (%) of the protons H1, H2 and CH_3 of the ketone **I** in CD_3OD in the presence of 8 mol% THPP.

IV **V** R_3P^+D

A δ_P 37.6

B

C

VII-D$_4$

VIII-D$_8$

D

ppm

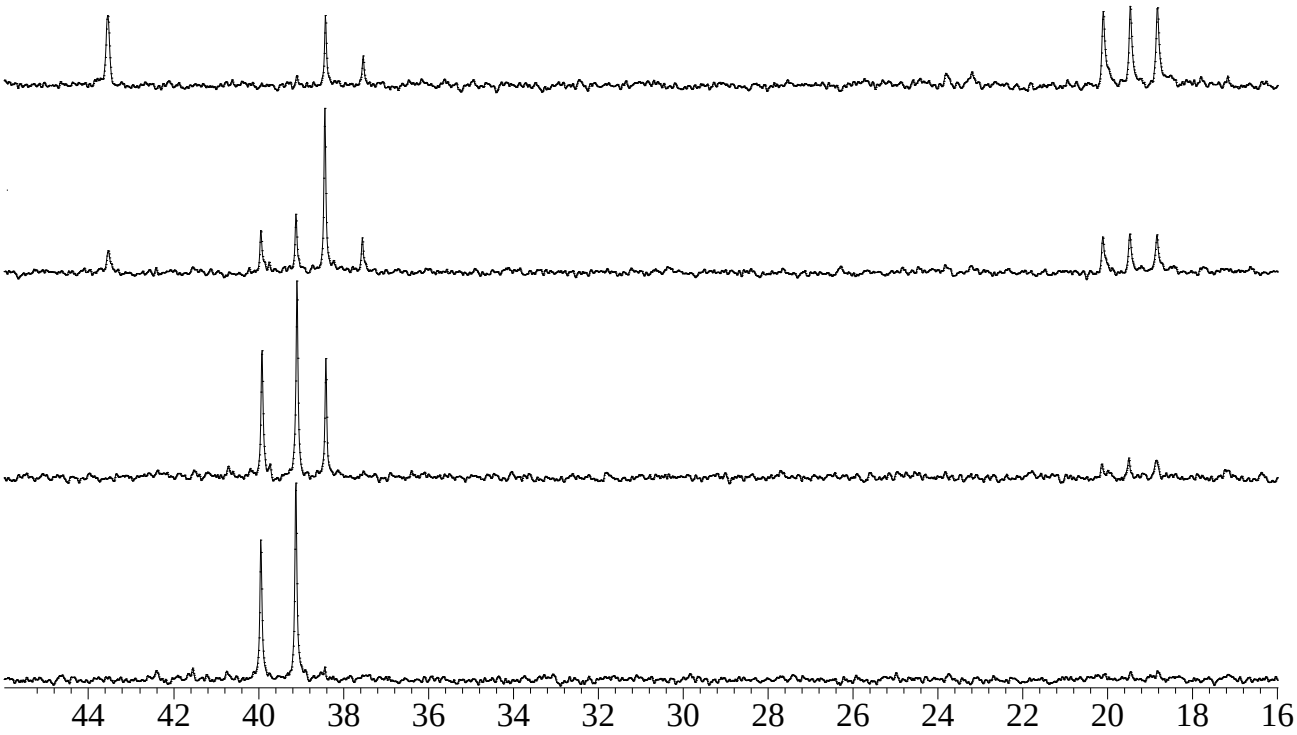


Figure 2. The $^{31}P\{^{1}H\}$ spectrum of the 1:1 reaction of the ketone **I** and THPP hydrochloride (CD_3OD, r.t., Ar) after: (A) 30 min, (B) 5 h, (C) 24 h, (D) 72 h; R = $(CH_2)_3OD$.

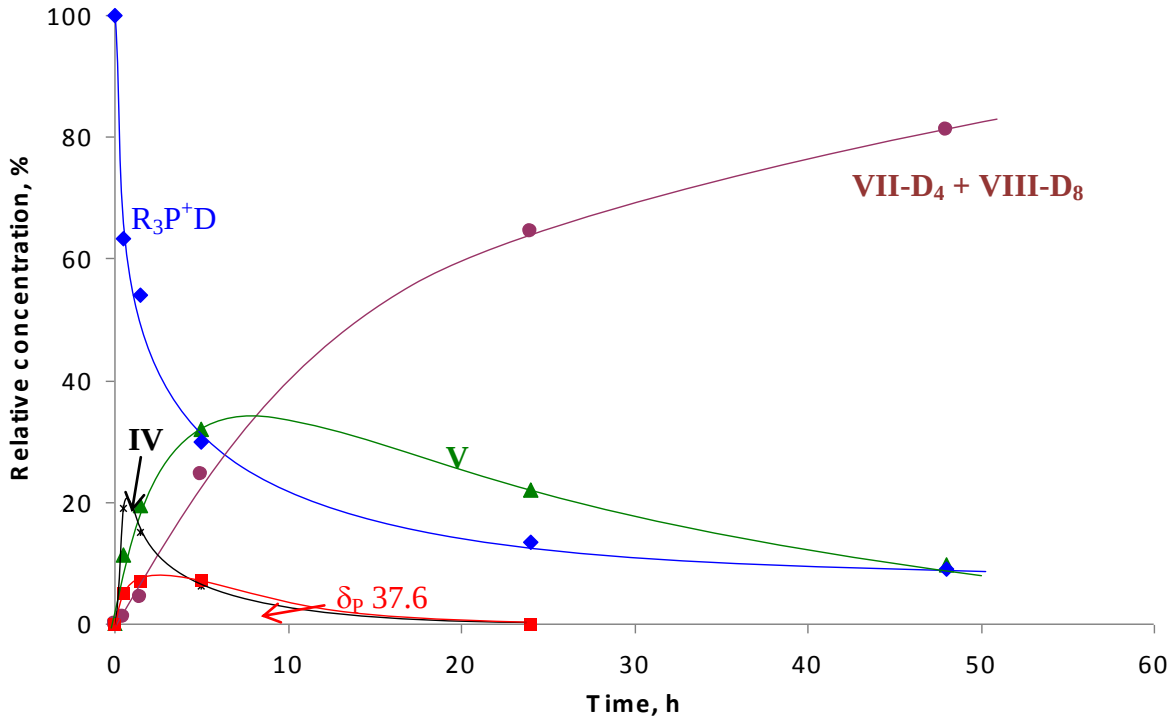


Figure 3. Relative concentration of phosphorus-containing species in the course of the reaction of THPP hydrochloride with the ketone **I** (1:1, CD_3OD, r.t., Ar; R = $(CH_2)_3OD$).

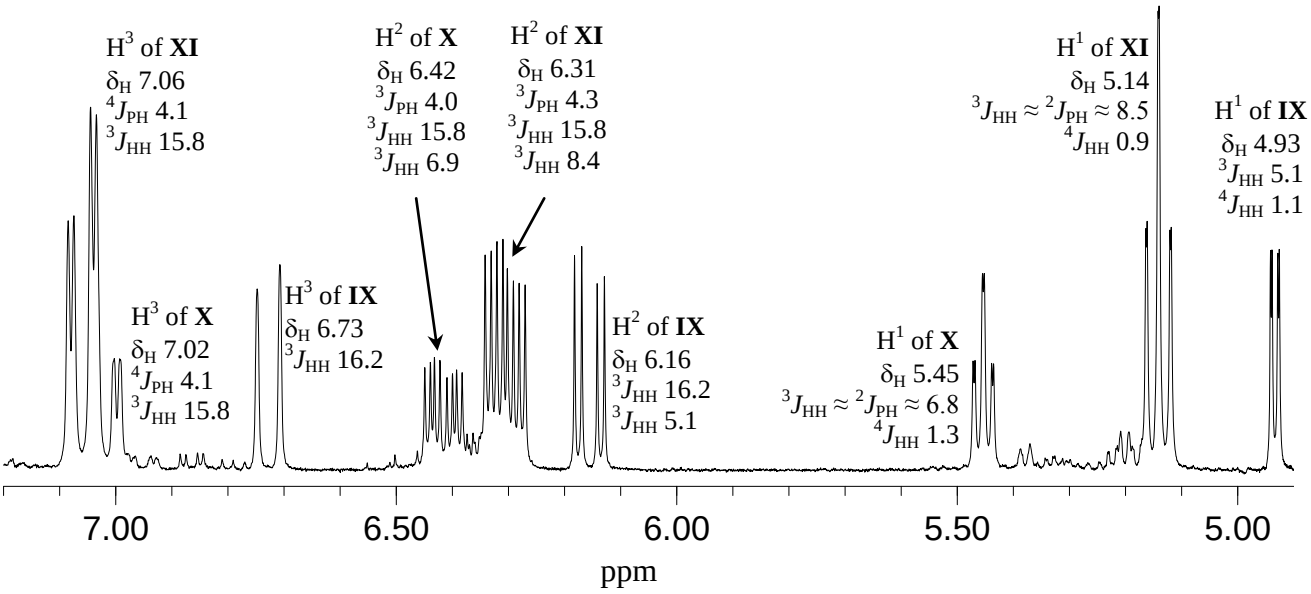
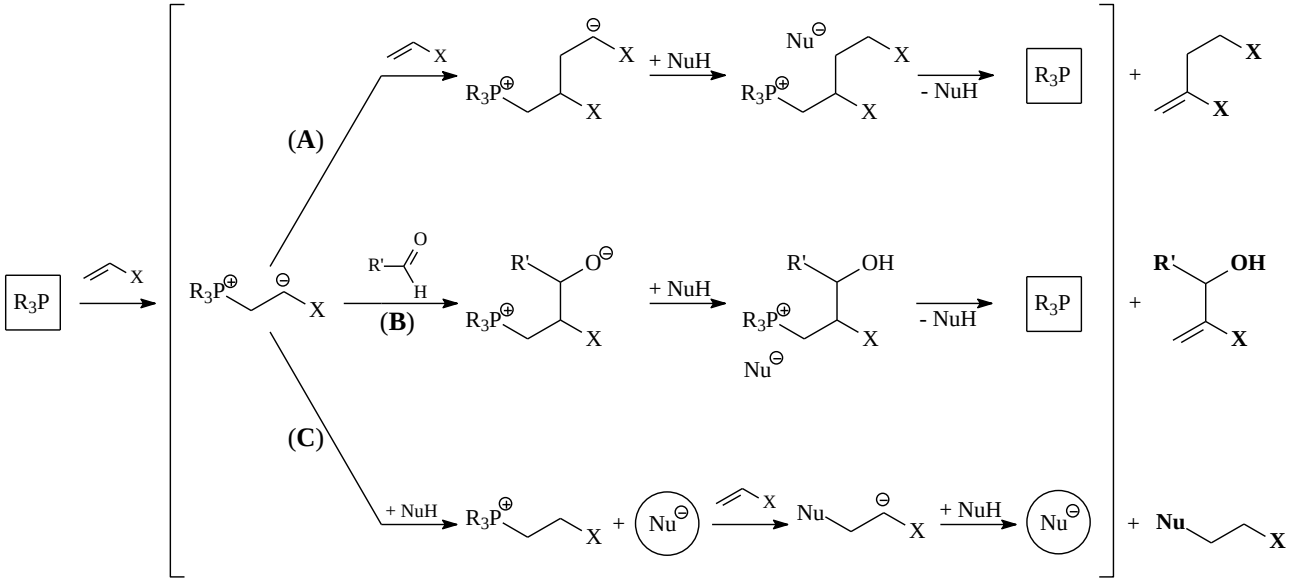
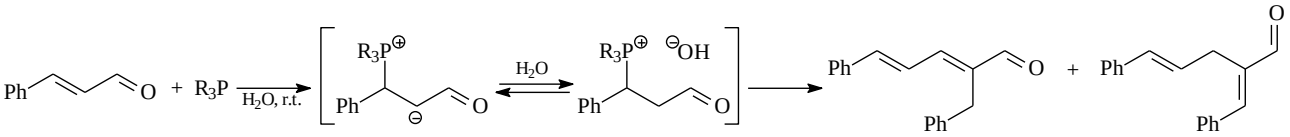


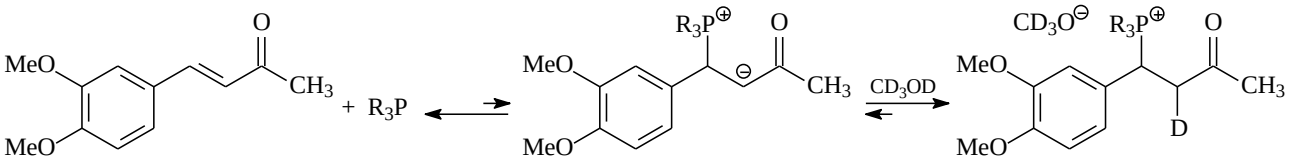
Figure 4. A part of the ^{1}H spectrum of the reaction between THPP hydrochloride and cinnamaldehyde (1:1, CD_3OD, r.t., Ar) recorded after 16 days.



Scheme 1 Reactions catalyzed by R_3P; X = electron-withdrawing group; NuH = proton donor

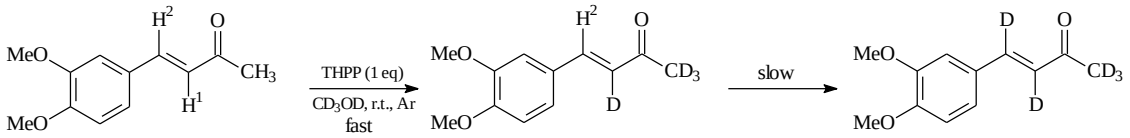


Scheme 2 Reaction of $[HO(CH_2)_3]_3P$ with cinnamaldehyde;[5a] r.t. = room temperature (~20 °C)



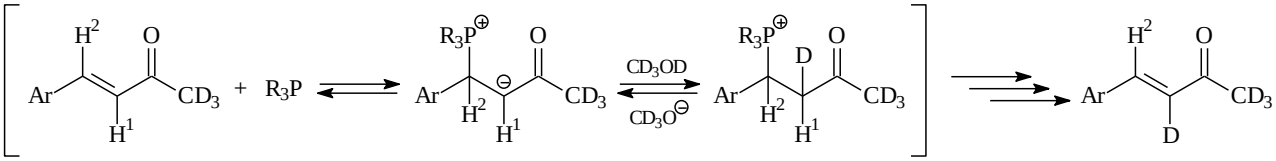
I **II** **III**

Scheme 3 Reaction of THPP with 3,4-$(MeO)_2$-benzylideneacetone

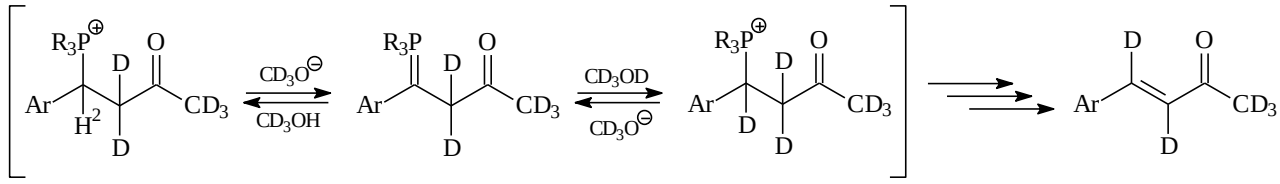


I **I-D$_4$** (M = 210.12) **I-D$_5$** (M = 211.12)

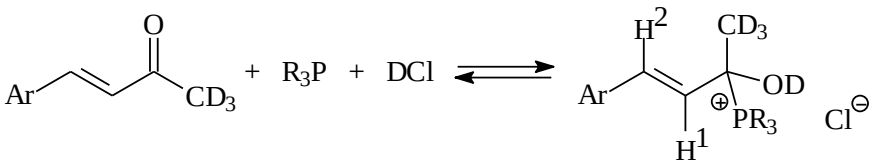
Scheme 4 H/D exchange in 3,4-$(MeO)_2$-benzylideneacetone



Scheme 5. Fast H/D exchange; R = $(CH_2)_3OD$, Ar = 3,4-$(MeO)_2C_6H_3$

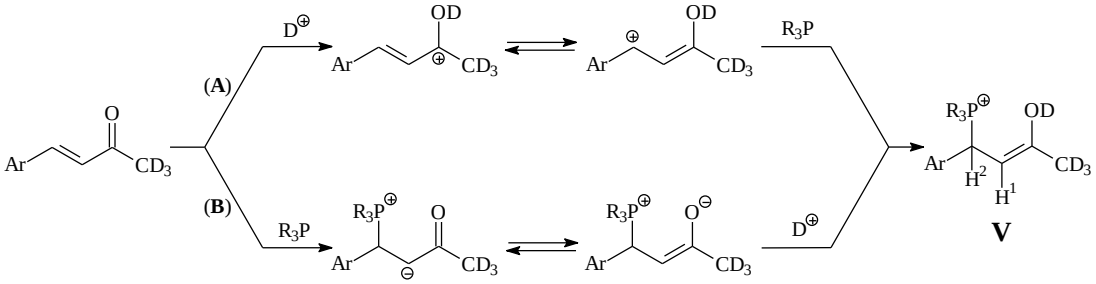


Scheme 6 Slow H/D exchange; R = $(CH_2)_3OD$, Ar = 3,4-$(MeO)_2C_6H_3$



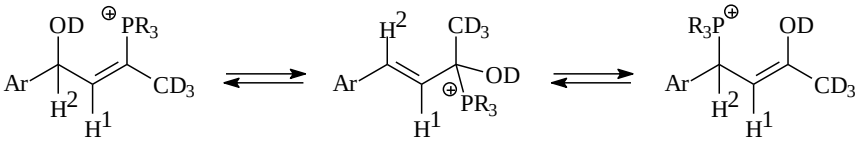
I-D$_3$ **IV**

Scheme 7 Reaction of **I** with THPP and HCl in CD_3OD; R = $(CH_2)_3OD$, Ar = 3,4-$(MeO)_2C_6H_3$



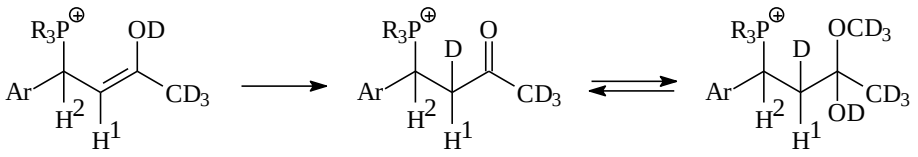
V

Scheme 8 Plausible pathways for formation of **V**; R = $(CH_2)_3OD$, Ar = 3,4-$(MeO)_2C_6H_3$



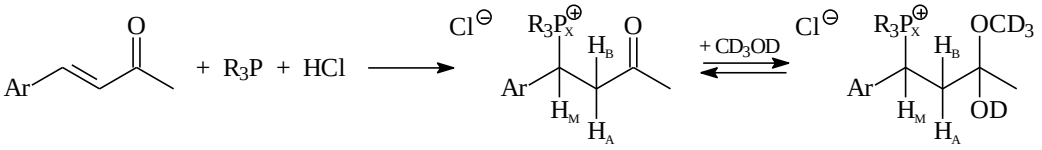
VI **IV** **V**

Scheme 9 Formation of **V** via **VI**; R = $(CH_2)_3OD$, Ar = 3,4-$(MeO)_2C_6H_3$



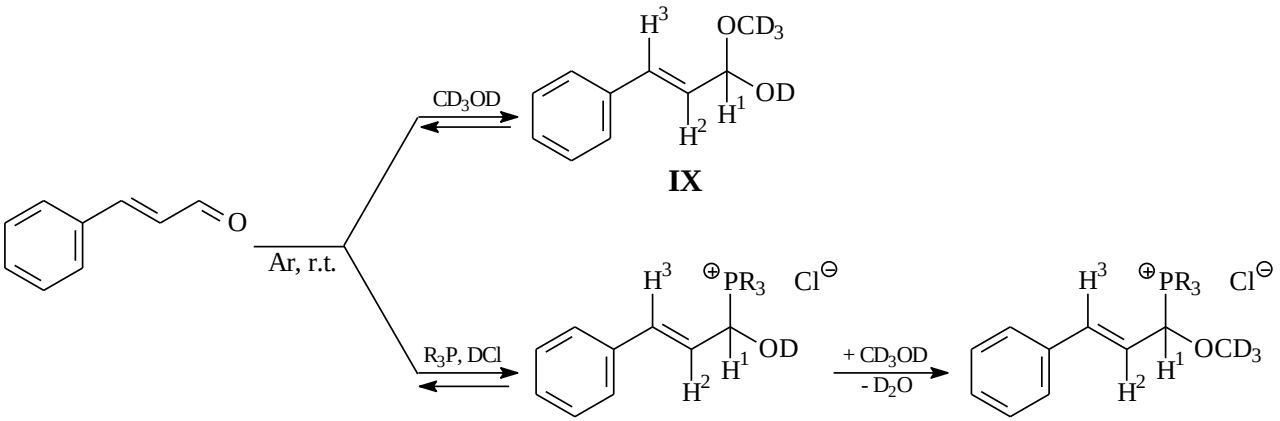
V **VII-D$_4$** **VIII-D$_8$**

Scheme 10 Transformation of **V**; R = $(CH_2)_3OD$, Ar = 3,4-$(MeO)_2C_6H_3$; the D-count in **V** does not include the D-atoms in the R_3P moiety.



I **VII** **VIII**

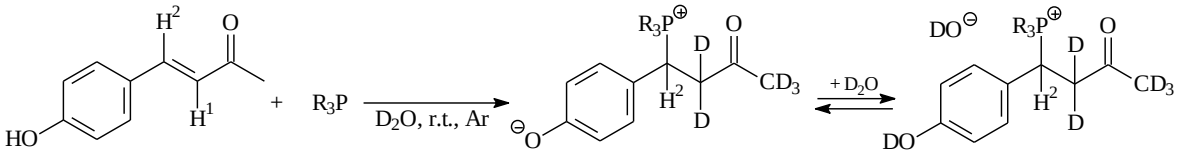
Scheme 11 Reaction of **I** with THPP and HCl in MeOH; R = $(CH_2)_3OH$, Ar = 3,4-$(MeO)_2C_6H_3$



IX

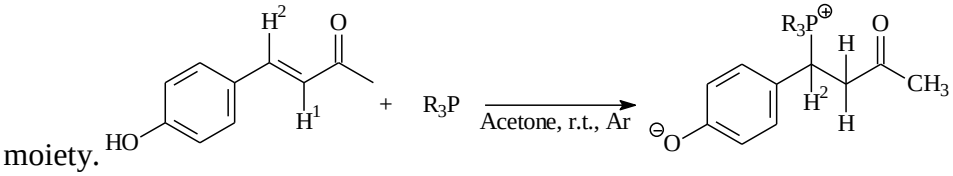
X **XI**

Scheme 12 Reaction of cinnamaldehyde with THPP and HCl in CD_3OD; R = $(CH_2)_3OD$



XII-D$_5$ **XIII-D$_5$**

Scheme 13 Reaction of 4-OH-benzylideneacetone with THPP in D_2O; R = $(CH_2)_3OD$; the D-count in **XII-D$_5$** and **XIII-D$_5$** does not include the D-atoms in the R_3P moiety.



XII

Scheme 14 Reaction of 4-OH-benzylideneacetone with THPP in acetone; R = $(CH_2)_3OH$