Non-Catalyzed, Atom-Economic, High-Yield Synthesis of Tertiary α-Hydroxyphosphane Selenides

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Received 12 July 2006; revised 8 August 2006

Abstract: First examples of a facile hydroxoselenophosphorylation of aldehydes are reported. Nucleophilic addition of P,Se-ambident secondary phosphane selenides to a series of aldehydes proceeds under catalyst-free conditions at room temperature to give tertiary α-hydroxyphosphane selenides in high yield.

Key words: hydroxoselenophosphorylation, α-hydroxyphosphane selenides, aldehydes, nucleophilic addition

Tertiary phosphane selenides are widely used as unique ligands for metal complex catalysts1a–h and building blocks in the synthesis of biologically active compounds, for example, anti-arthritic gold complexes.1c At the same time, being based on toxic chlorides of phosphorus and organometallic compounds, the synthesis of tertiary phosphane selenides is very often complex, multi-step, and unsafe. Almost no information on the synthesis and properties of functionalized tertiary phosphane selenides has been published until now. Therefore, the search for new facile and environmentally benign routes to the preparation of tertiary phosphane selenides, especially functionalized ones, remains an important synthetic challenge.

The employment of the addition reaction of secondary phosphane chalcogenides to the carbonyl function looks like an ideal approach to the solution of this problem. Reactions of this kind are known to proceed with 100% economy of the participating atoms (i.e. without waste) to afford chiral tertiary α-hydroxyphosphane chalcogenides. It should be noted that prior to this work, this reaction was studied only for secondary phosphane sulfides2a–h and, to a lesser degree, for secondary phosphane oxides2a–l,3a and, to the best of our knowledge, there have been no publications on the hydroxoselenophosphorylation of aldehydes with secondary phosphane selenides.

The goal of the present work was to study regularities of the reaction of secondary phosphane selenides with functional aliphatic, aromatic, and heteroaromatic aldehydes in order to develop a general, expedient, and atom-economic method for the synthesis of polyfunctional chiral tertiary phosphane selenides.

We have found that a potentially ambident nucleophile,4 bis(2-phenylethyl)phosphane selenide (1) (now readily available in two steps from styrene, elemental phosphorus and selenium5), reacts with aldehydes to give tertiary α-hydroxyphosphane selenides 3a–h in high isolated yields (80–92%). Despite the broadly varied nature of the aldehydes employed (Table 1), the potentially ambident phosphane selenide 1 behaves as a P-centered nucleophile only; in no case are the products of a selenium attack at the carbonyl group detected, which is in keeping with the X-ray crystal structure of selenide 1 as a tetracoordinated species A (Equation 1), as well as with its 31P, 1H, 13C, 73Se NMR, UV, and IR data.4

\[
\text{H}^{-} \quad \text{P}^{-} \quad \text{Se}^{-} \quad \text{H}^{-} \quad \text{P}^{-} \quad \text{Se}^{-}
\]

Equation 1

In the 1H NMR spectra of compounds 3a–h, the most typical signals are those of the OCHP=Se group. For compounds 3a,c, these signals are observed as a doublet at δ = 4.26 (3a) and 4.45 (3c) ppm, with 31P–C–1H coupling constants of 2.3 Hz and 2.6 Hz, respectively. The geminal 31P–C=H coupling constants in α-hydroxyphosphane selenides (as well as in α-hydroxyphosphane sulfides2a–c) are small, thus making the splitting of the H-atom resonance signal not always observable. As a result, the signals of tertiary phosphane selenides 3b,3d–h can show up as a singlet at δ = 4.45–5.20 ppm. In the 13C NMR spectra of compounds 3a–h, the signals of the OCHP=Se fragments appear as a typical doublet at δ = ~61.6–79.7 ppm with the 31P–13C coupling constant being equal to 41.1–49.0 Hz. The nonequivalence of two phenylethyl signals in the 1H and 13C NMR spectra of phosphane selenides 3a–h is caused by the presence of a chiral carbon atom in the HOCHP=Se fragment.

Thus, using the easily available bis(2-phenylethyl)phosphane selenide (1) it has been demonstrated that the reaction of secondary phosphane selenides with aldehydes of diverse nature is a single-step, atom-economic method for the synthesis of tertiary chiral phosphane selenides. These adducts can be utilized for the preparation of corresponding optically active phosphane selenides, which are prom-
ising ligands for transition-metal-catalyzed asymmetric reactions.

The $^1$H, $^{13}$C, and $^{31}$P NMR spectra were recorded on a Bruker DPX 400 spectrometer (at 400.13 MHz, 101.61 MHz, and 161.98 MHz, respectively) in CDCl$_3$ solutions and referenced to internal HMDS ($^1$H NMR) and external 85% H$_3$PO$_4$ ($^{31}$P NMR). IR spectra were recorded as KBr pellets or films on a Bruker IFS 25 instrument.

### Tertiary α-Hydroxyphosphane Selenides 3; General Procedure

A mixture of phosphane selenide 1 (10 mmol) and aldehyde 2 (10 mmol) in THF (4 mL) was stirred at r.t. under argon. The reaction was monitored using $^{31}$P NMR spectra that showed the disappearance of peaks of the initial secondary phosphane selenides 2 at $\delta = 2.17$ ppm and the appearance of new peaks at $\delta = 45$–53 ppm, corresponding to tertiary α-hydroxyphosphane selenides 3. The solvent was then removed under reduced pressure and the residue was recrystallized from n-hexane [compound 3c was re-precipitated from CHCl$_3$ using petroleum ether (bp 40–70 °C)].

**2,2,2-Trichloro-1-[bis(2-phenylethyl)phosphoroselenoyl]ethanol (3a)**

Colorless solid; mp 89–90 °C.

IR (KBr): 3100 (v OH), 3085, 3061, 3024 (v =CH of phenyl rings), 2940, 2906, 2857 (v CH), 1601, 1584, 1495, 1453 (v C=O of phenyl rings), 1066 (δ C=O–OH), 797, 733 (v C–Cl), 748, 698 (δ C–H of phenyl rings), 481 cm$^{-1}$ (v P=Se).

$^1$H NMR (400.13 MHz, CDCl$_3$): $\delta = 2.43$–2.63 (m, 4 H, PhCH$_2$), 2.76–2.96 (m, 4 H, CH$_2$P), 4.26 (d, 1 H, $^2$J$_{P,H} = 2.3$ Hz, PCH), 7.17–7.28 (m, 10 H, C$_6$H$_5$).

$^{13}$C NMR (100.69 MHz, CDCl$_3$): $\delta (the signal marked with an asterisk was identified in acetone-d$_6$) = 29.61 (PhCH$_2$), 30.66 (PhCH$_2$), 31.53 (d, $^3$J$_{P,C} = 35.0$ Hz, CH$_2$P), 39.33 (d, $^3$J$_{P,C} = 37.0$ Hz, CH$_2$P), 79.72* (d, $^3$J$_{P,C} = 43.6$ Hz, PCH), 98.32 (CCl$_3$), 126.91 (p-CH$_{arom}$), 128.31, 128.39, 128.92 (m-CH$_{arom}$), 139.68 (d, $^3$J$_{P,C} = 15.0$ Hz, ipso-CH$_{arom}$), 139.95 (d, $^3$J$_{P,C} = 15.0$ Hz, ipso-CH$_{arom}$).

$^{31}$P NMR (161.98 MHz, CDCl$_3$): $\delta = 53.1$.

Anal. Calcd for C$_{18}$H$_{20}$Cl$_3$OPSe: C, 46.13; H, 4.30; Cl, 22.69; P, 6.61; Se, 16.86. Found: C, 46.16; H, 4.31; Cl, 22.62; P, 6.58; Se, 16.90.

**1-[Bis(2-phenylethyl)phosphoroselenoyl] prop-2-yn-1-ol (3b)**

Light yellow solid; mp 117–118 °C.

IR (KBr): 3223 (v OH), 3085, 3067, 3026, 3003 (v =CH of phenyl rings), 2953, 2927, 2856 (v CH), 2177 (v C=O), 1602, 1585, 1495, 1454 (v C=O of phenyl rings), 1248 (δ CH$_2$), 1055 (δ COH), 847 (δ CH$_2$), 752 (δ C–H of phenyl rings), 708 (v Si–C), 699 (δ C–H of phenyl rings), 488, 471 cm$^{-1}$ (v P=Se).

### Table 1 Synthesis of Tertiary α-Hydroxyphosphane Selenides 3a–h

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$^a$ Yields were calculated based on $^{31}$P NMR spectra of the crude products.

$^b$ Isolated yield.
13C NMR (161.98 MHz, CDCl3): δ = 49.6.

Anal. Calcd for C23H34OsPSe: C, 59.50; H, 6.58; P, 6.62; Se, 17.65; Si, 6.27. Found: C, 59.29; H, 6.10; N, 6.27; P, 7.01; Se, 17.71.

**[Bis(2-phenethyl)phosphoroselenoyl](1-vinyl-1H-imidazol-2-yl)methanol (3f)**

Colorless solid; mp 178–180 °C.

IR (KBr): 3020, 2851, 1651, 1507, 1463, 1415, 1403 (C=C of phenyl and imidazole rings).

**[Bis(2-phenethyl)phosphoroselenoyl](1-ethyl-1H-benzimidazol-2-yl)methanol (3g)**

Colorless solid; mp 117–118 °C.

IR (KB): 3100 (v OH), 3130, 3108, 3082, 3060, 3027, 3006 (v =CH, =CH of vinyl group, phenyl, and imidazole rings), 2972, 2957, 2924, 2904, 2853 (v CH), 1641 (v =C of vinyl group), 1615, 1582, 1524, 1496, 1483, 1451 (v C=C, C=C of phenyl and imidazole rings), 1078 (δ =CH-OH), 751, 695 (δ CH of phenyl and imidazole rings), 499 cm−1 (v P=S).
Bis(2-phenylethyl)phosphoro- selenoyl][1-vinyl-1H-benimidazole- 2-yl]methanol (3h)
Colorless solid; mp 97–98 °C.
IR (KBr): 3100 (ν=O), 2972, 2933, 2917, 2900, 2849 (νC–H), 1642 (νC=O of phenyl group, phenyl, and benzimidazole rings), 1587, 1496, 1454 (νC=C, C=C of phenyl and benzimidazole rings), 1079 (δC=O), 481 cm⁻¹ (νP=Se).

References


Acknowledgment
Financial support from the Federal Agency on Science and Innovations (Contract No. 02.445.11.7296) and the Siberian Branch of the Russian Academy of Sciences (Integration project No. 32) is gratefully acknowledged.

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