

Air-Induced *anti*-Markovnikov Addition
of Secondary Phosphine Oxides and
H-Phosphinates to Alkenes

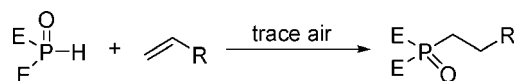
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ABSTRACT



Air (oxygen) induces the addition of secondary phosphine oxides and H-phosphinates to alkenes to selectively produce the corresponding *anti*-Markovnikov adducts in good to high yields. Mechanistic studies show that the addition probably proceeds via a radical chain mechanism.

The addition of a P(O)–H bond to an unsaturated carbon–carbon double bond is one of the most important reactions for the preparation of organophosphorus compounds.^{1,2} This addition has been achieved in the presence of radical initiators¹ such as benzoyl peroxide or AIBN, bases,¹ acids,¹ and transition metals.² Recently, the use of microwaves in this addition has attracted attention.³ Thus, Stockland reported that R₂P(O)H can efficiently add to alkenes with electron-withdrawing groups under the irradiation of microwaves.^{3a} Because the microwave-assisted reaction did not require the addition of a catalyst, it could become a cleaner synthetic process for the preparation of organophosphorus compounds.

(1) For radical and acid- or base-catalyzed addition of H–P(O), see: (a) *Organic Phosphorus Compounds*; Kosolapoff, G. M., Maier, L., Eds.; Wiley-Interscience: New York, 1972. (b) Goldwhite, H. *Introduction to Phosphorus Chemistry*; Cambridge University Press: Cambridge, 1981. Recent examples: (c) Semenzin, D.; Etemad-Moghadam, G.; Albouy, D.; Diallo, O.; Koenig, M. *J. Org. Chem.* **1997**, 62, 2414. (d) Han, L.-B.; Zhao, C.-Q. *J. Org. Chem.* **2005**, 70, 10121. (e) Casey, C. P.; Paulsen, E. L.; Beuttenmueller, E. W.; Proft, B. R.; Matter, B. A.; Powell, D. R. *J. Am. Chem. Soc.* **1999**, 121, 63. (f) Bunlaksananusorn, T.; Knochel, P. *Tetrahedron Lett.* **2002**, 5817. (g) Mimeau, D.; Gaumont, A. C. *J. Org. Chem.* **2003**, 68, 7016.

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During the course of our study on the development of new methods for the construction of phosphorus–carbon bonds by the manipulation of P(O)–H bonds,^{2a–c} we accidentally found that, to our surprise, even under mild reaction conditions a small amount of air (oxygen) can initiate the addition of secondary phosphine oxides and H-phosphinates to alkenes to give good to high yields of the corresponding *anti*-Markovnikov adducts. Compared to the microwave-assisted reactions,^{3a} this air-induced addition has a wide generality that could be applied to a variety of alkenes with or without electron-withdrawing groups.






















As shown in Table 1, under a pure nitrogen atmosphere (containing less than 1 ppm of oxygen), diphenylphosphine oxide and 1-decene did not react at 80 °C for 18 h (run 1).

Table 1. Air-Induced Addition of Ph₂P(O)H to 1-Decene

$\begin{array}{c} \text{Ph}_2\text{P(O)H} \\ + \\ \text{CH}_2=\text{CHC}_8\text{H}_{19} \end{array} \xrightarrow{80\text{ }^\circ\text{C}, 18\text{ h}} \text{Ph}_2\text{(O)P}-\text{CH}_2-\text{CH}-\text{C}_8\text{H}_{17}$		
run	atmosphere	yield % ^d
1 ^a	nitrogen	none
2 ^b	air/nitrogen	85
3 ^c	air	28

^a A vial (10 mL) was charged with Ph₂P(O)H (0.3 mmol) and 1-decene (0.6 mmol) and sealed under a nitrogen atmosphere (O₂ < 1 ppm). The vial was heated at 80 °C for 18 h. ^b Conducted under the conditions of run 1, except air (0.5 mL) was introduced to the vial before heating. ^c Heated under air without sealing the vial. ^d Determined by NMR.

Table 2. Air-Induced Addition of P(O)–H Bonds to Alkenes
$$[P(O)]-H + \text{alkene} \xrightarrow{\text{Air/N}_2} [P(O)]-CH_2-CH(R)-$$

run	[P(O)]–H	alkene	adduct	temperature, time	yield % ^a
1	<i>n</i> -Bu ₂ P(O)H	1-octene	<i>n</i> -Bu ₂ (O)P–CH ₂ –CH ₂ – <i>n</i> -C ₆ H ₁₃	80 °C, 18 h	85
2	Ph(<i>t</i> -Bu)P(O)H	1-decene	Ph(<i>t</i> -Bu)(O)P–CH ₂ –CH ₂ – <i>n</i> -C ₈ H ₁₇	130 °C, 48 h	63
3	Ph ₂ P(O)H		Ph ₂ (O)P–CH ₂ –CH ₂ – 	80 °C, 24 h	89
4		 –(CH ₂) ₄ OH	Ph ₂ (O)P–CH ₂ –CH ₂ –(CH ₂) ₄ OH	80 °C, 18 h	80
5		 –(CH ₂) ₄ CN	Ph ₂ (O)P–CH ₂ –CH ₂ –(CH ₂) ₄ CN	80 °C, 18 h	77
6		 –(CH ₂) ₄ CO ₂ Et	Ph ₂ (O)P–CH ₂ –CH ₂ –(CH ₂) ₄ CO ₂ Et	80 °C, 18 h	87
7		 –SiEt ₃	Ph ₂ (O)P–CH ₂ –CH ₂ –SiEt ₃	80 °C, 18 h	92
8		 –CN	Ph ₂ (O)P–CH ₂ –CH ₂ –CN	80 °C, 18 h	80
9		 –CO ₂ Et	Ph ₂ (O)P–CH ₂ –CH ₂ –CO ₂ Et	80 °C, 12 h	64
10		 – <i>On</i> -Bu	Ph ₂ (O)P–CH ₂ –CH ₂ – <i>On</i> -Bu	80 °C, 18 h	91
11		 –S(O)Ph	Ph ₂ (O)P–CH ₂ –CH ₂ –S(O)Ph	80 °C, 18 h	44
12		 –N	Ph ₂ (O)P–CH ₂ –CH ₂ – 	80 °C, 12 h	95
13		 –P(O)Ph ₂	Ph ₂ (O)P–CH ₂ –CH ₂ –P(O)Ph ₂	80 °C, 18 h	98
14 ^b		 –P(O)Ph(OMen)	Ph ₂ (O)P–CH ₂ –CH ₂ –P(O)Ph(OMen)	80 °C, 44 h	91
15		 –P(O)(OEt) ₂	Ph ₂ (O)P–CH ₂ –CH ₂ –P(O)(OEt) ₂	80 °C, 18 h	88
16	Ph(OEt)P(O)H	1-decene	Ph(OEt)(O)P–CH ₂ –CH ₂ – <i>n</i> -C ₈ H ₁₇	120 °C, 10 h	72
17		1-docosene	 – <i>n</i> -C ₂₀ H ₄₁	200 °C, 2 h	91
18		 –P(O)Ph ₂	 –P(O)Ph ₂	120 °C, 12 h	97
19		 –P(O)(OEt) ₂	 –P(O)(OEt) ₂	180 °C, 1 h	86
20	(<i>n</i> -BuO) ₂ P(O)H	1-decene	(<i>n</i> -BuO) ₂ P(O)–CH ₂ –CH ₂ – <i>n</i> -C ₈ H ₁₇	120 °C, 16 h	0

^a NMR yield. ^b(*R_p*)-CH₂=CHP(O)Ph(OMen), Men = (–)-menthyl.

No addition was observed when the mixture was heated at an elevated temperature (120 °C). Remarkably, however, when a trace amount of air was introduced to the vial, an 85% yield of the addition product was obtained (run 2). The addition also proceeded even under an air atmosphere (run 3), though the yield of the product was low partly due to the significant oxidation of diphenylphosphine oxide to diphenylphosphinic acid.⁴ It was further confirmed that possible impurities in diphenylphosphine oxide such as water and Ph₂P(O)OH did not initiate this addition reaction under the reaction conditions of run 1.

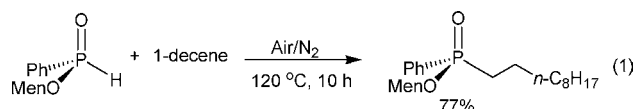
(4) Hamilton, L. A.; Landies, P. S. In *Organic Phosphorus Compounds*; Kosolapoff, G. M., Maier, L., Eds.; Wiley-Interscience: New York, 1972; Vol. 4, pp 485–487.

Table 2 shows the scope and limitations of this air-induced addition. The reaction is applicable to both secondary phosphine oxides and H-phosphinates but not applicable to H-phosphonates. Thus, similar to Ph₂P(O)H, a dialkylphosphine oxide *n*-Bu₂P(O)H also added to 1-octene to give the corresponding adduct in 85% yield (run 1). It appears that a bulky substituent on phosphorus can significantly decrease the reactivity of the phosphine oxide because a similar addition of Ph(*t*-Bu)P(O)H required a higher temperature (run 2) whereas the bulky dicyclohexylphosphine oxide did not give the corresponding adduct under similar reaction conditions. The addition of H-phosphinates to alkenes can also be initiated by a trace amount of air. For example, the addition of Ph(OEt)P(O)H to 1-decene (run 16) and the

addition of 6*H*-dibenz[*c,e*][1,2]oxaphosphorin-6-oxide to 1-docosene (run 17) afforded the corresponding adducts in 72% and 91% yields, respectively. However, a similar addition with H-phosphonates (RO)₂P(O)H could not be initiated under similar reaction conditions. For example, a mixture of (*n*-BuO)₂P(O)H and 1-decene did not give the corresponding adduct after heating at 120 °C for 16 h (run 20).

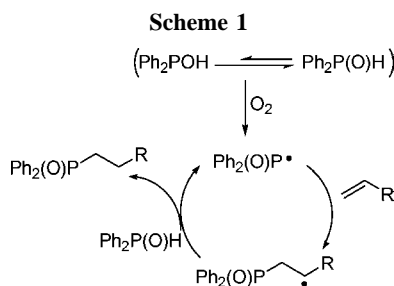
As shown in Table 2, both terminal and internal alkenes could be used as the substrates. Because a variety of functionalities were tolerant toward this air-induced addition, good to high yields of the corresponding valuable phosphorus compounds were obtained.

Finally, it was shown that this air-induced addition proceeded stereospecifically with retention of configuration at phosphorus. Thus, optically pure (*R_P*)-Ph(OMen)P(O)H (Men = (–)-menthyl) stereospecifically added to 1-decene to give the corresponding (*R_P*)-adduct in 77% yield (eq 1).



Note that the corresponding AIBN-initiated radical additions of (*R_P*)-Ph(OMen)P(O)H to alkenes also proceeds stereospecifically with retention of configuration at phosphorus.^{1c}

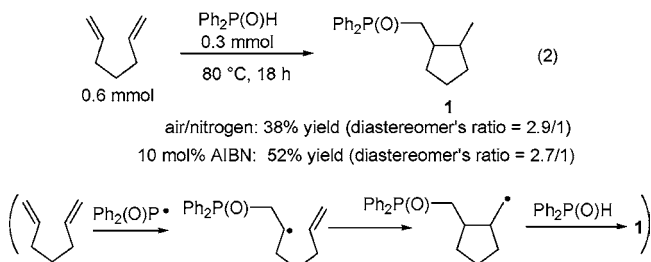
Although the detailed reaction mechanism for the air-induced addition is not clear, all these results obtained could be well explained by a radical chain mechanism as depicted in Scheme 1. As for the initiating step, the reaction



of Ph₂P(O)H (or its tautomer Ph₂P(OH))⁵ with oxygen forming a phosphinoyl radical may be the one among a few possibilities because oxidation of phosphines with oxygen

(5) [P(O)]–H compounds exist in two tautomeric forms, P(=O)H and P–OH; the former is dominant in equilibrium. Ackermann, L. *Synthesis* **2006**, 1557.

was known to proceed via a radical chain mechanism.⁶ In addition, oxygen was known to induce similar additions of a Se–H bond to carbon–carbon unsaturated bonds via a radical chain mechanism.⁷ As further evidence of this radical mechanism, it is observed that the addition of Ph₂P(O)H to 1-decene (run 2, Table 1) was completely suppressed in the presence of 4-*tert*-butylcatechol (0.3 mmol). In addition, as expected for a radical reaction, cyclization took place when 1,6-heptadiene was employed as the substrate (eq 2). Note



again that both air- and AIBN-induced reactions gave similar results.⁸

In summary, we have revealed that a trace amount of air can efficiently induce the addition of secondary phosphine oxides and H-phosphinates to alkenes via a radical chain mechanism. Compared to the hitherto known addition reactions,^{1–3} this reaction is clean, simple, and economic because only the addition of a trace amount of air is required.

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Supporting Information Available: Spectra and analytical data for new compounds; copies of NMR spectra for all products. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(6) (a) Thompson, H. W.; Kelland, N. S. *J. Chem. Soc.* **1933**, 1231. (b) Buckler, S. A. *J. Am. Chem. Soc.* **1962**, 84, 3093.

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(8) We thank a referee's suggestion for conducting this reaction to further prove the radical mechanism. In addition to **1**, 1,7-bis(diphenylphosphino)-heptane was also formed (yields based on P(O)Ph₂: air/nitrogen, 32%; AIBN, 43%). High yields of **1** could be obtained when the reaction was carried out in dilute solutions. (a) Jessop, C. M.; Parsons, A. F.; Routledge, A.; Irvine, D. *Tetrahedron Lett.* **2003**, 44, 479. (b) Cho, D.H.; Jang, D.O. *Synlett* **2005**, 59.