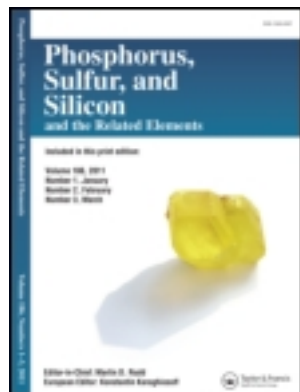


This article was downloaded by: [Ryerson University]

On: 14 May 2013, At: 06:41

Publisher: Taylor & Francis

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/gpss20>

Organophosphorus Synthesis Without Phosphorus Trichloride: The Case for the Hypophosphorous Pathway

Jean-Luc Montchamp^a

^a Department of Chemistry , Texas Christian University , Fort Worth , Texas , USA

Accepted author version posted online: 17 Sep 2012. Published online: 08 May 2013.

To cite this article: Jean-Luc Montchamp (2013): Organophosphorus Synthesis Without Phosphorus Trichloride: The Case for the Hypophosphorous Pathway, *Phosphorus, Sulfur, and Silicon and the Related Elements*, 188:1-3, 66-75

To link to this article: <http://dx.doi.org/10.1080/10426507.2012.727925>

PLEASE SCROLL DOWN FOR ARTICLE

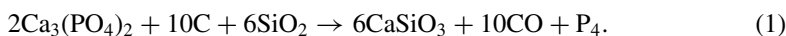
Full terms and conditions of use: <http://www.tandfonline.com/page/terms-and-conditions>

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden.

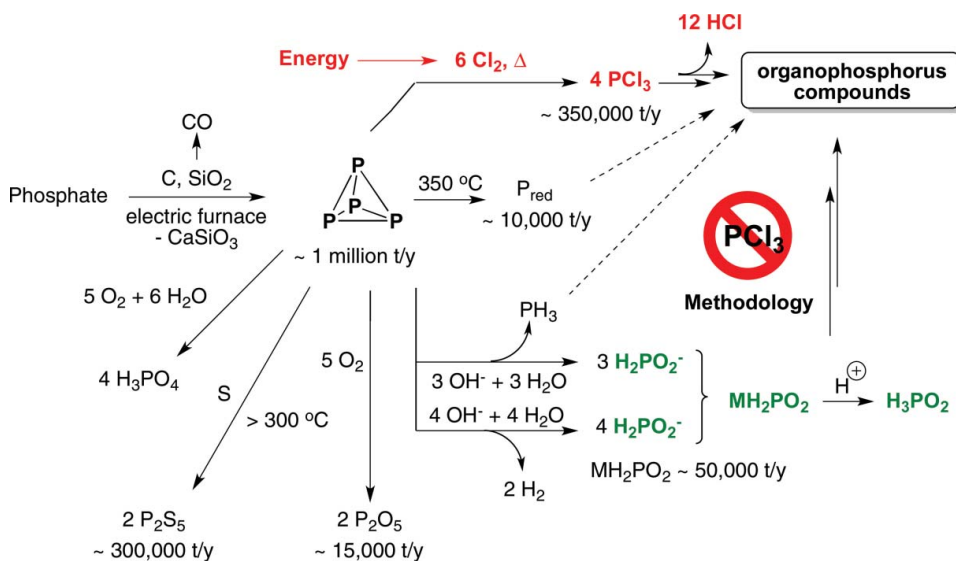
The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae, and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand, or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

INTRODUCTION

Organophosphorus compounds are of great economic importance due to their many applications, such as materials, pesticides, medicines, extractants, and flame retardants, as well as synthetic intermediates or phosphine ligands.¹ Currently, virtually any compound containing a phosphorus–carbon, phosphorus–oxygen, or a phosphorus–hydrogen bond is synthesized from elemental “white” phosphorus (P₄).² P₄ is made on an industrial scale through electrothermal manufacturing. In this process, phosphate (calcium phosphate, apatite) is reduced with coke and silica, through a combination of heat and electricity in a highly energy-consuming process (1). Calcium silicate and carbon monoxide are also produced



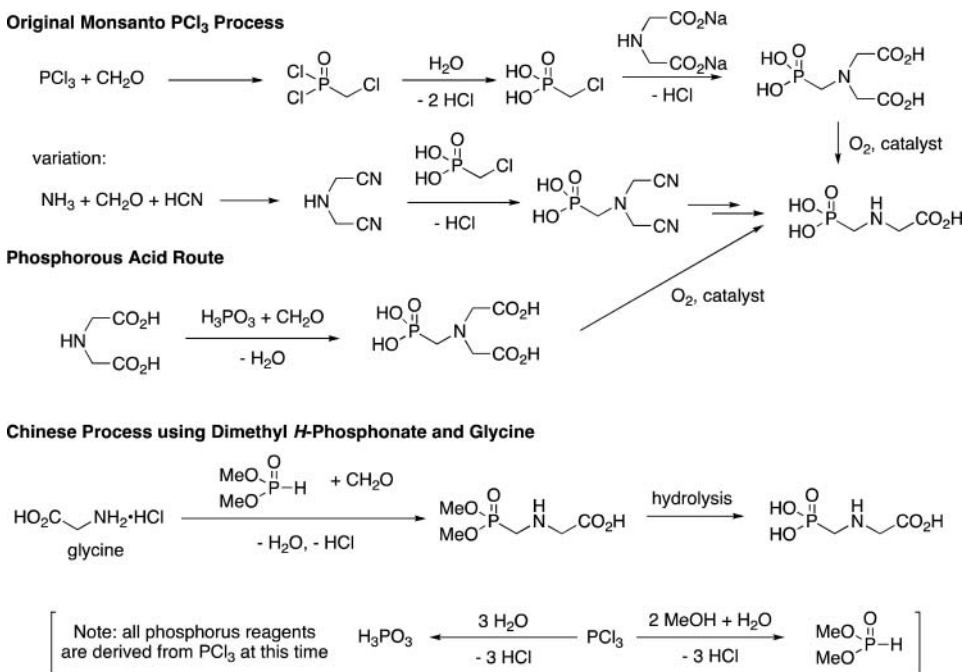
Elemental phosphorus is then converted into a variety of different inorganic phosphorus compounds, such as red phosphorus (P_{red}), phosphorus trichloride (PCl₃), phosphorus pentoxide (P₂O₅), sodium or calcium hypophosphite (M(H₂PO₂)_n), and phosphine (PH₃), which are the basis of all current organophosphorus manufacturing (Scheme 1).² A large portion of P₄ is also oxidized back to prepare high-purity phosphoric acid. For the preparation of phosphorus–carbon-containing compounds, phosphorus trichloride is by far the major intermediate, even though the final products do not contain the highly reactive phosphorus–chlorine bond. PCl₃ is produced through the direct exothermic chlorination of P₄ with chlorine, and is purified by fractional distillation. However, PCl₃ is a highly reactive and hazardous compound, and it has already been implicated in major accidents.³ Furthermore, chlorine is even more dangerous,⁴ and its preparation is energy-demanding since it is made through electrolysis. Some outdated chlorine plants are also responsible for a significant portion of preventable mercury pollution.



Scheme 1 Elemental phosphorus as a key intermediate, and other compounds of industrial relevance. t/y = metric ton/year (estimated) annual worldwide production. (Color figure available online).

Hypophosphorous derivatives (alkali hypophosphites and hypophosphorous acid) are prepared through the alkali (NaOH or Ca(OH)₂) hydrolysis of P₄.² This process is actually a complex reaction and is the source of PH₃ as well, a compound used in small amounts in the electronics industry, and as a starting material for trialkylphosphines (R₃P) and related compounds. Even though the amount of hypophosphite annually produced is only about 10% of that of PCl₃ (by weight), currently almost all of the hypophosphorous manifold goes into a single application: metal (mostly nickel) electroless plating, known as the Kanigen process. Therefore, it might not be unreasonable to increase production if hypophosphorous compounds can be used for the preparation of other important phosphorus intermediates. The main drawback is the cryptic chemistry involved during the hydrolysis of P₄, so improvements in this process would be desirable.⁵

The elaboration of PCl₃ into organophosphorus compounds always results in the formation of wasteful hydrogen chloride (HCl) and therefore is never atom-economical. For example, the manufacture of glyphosate (the world's most widely used herbicide and a major user of PCl₃) is a prime example, outlined in Scheme 2.⁶



Scheme 2 Industrial preparation of the herbicide glyphosate.

RESULTS AND DISCUSSION

Because of phosphorus trichloride's obvious drawbacks (hazardous, energy and chemically wasteful, etc.), significant research efforts have been devoted to bypass its use. A popular proposal relies on the so-called "P₄-activation" pathway.⁷ Since P₄ is already the precursor to all other organophosphorus compounds, as well as most inorganic phosphorus reagents, this appears to be a logical strategy. However, a fundamental problem

with P₄-activation is the fact that not all phosphorus atoms can be used (the only exception being its conversion to PCl₃). This is because as the phosphorus tetrahedron is broken, the reactivity of the P–P bonds decreases. Furthermore, P₄ is toxic and pyrophoric, and thereby better employed in situ, and it is also insoluble in standard organic solvents (carbon disulfide is not a convenient solvent because of its extremely low flash point and autoignition temperatures).

Two other pathways which have received significant attention to bypass PCl₃ in the preparation of organophosphorus compounds are: (a) the use of PH₃,⁸ and (b) the use of P_{red}.⁹ Both have found some support in the literature and in practice. However, PH₃ is a highly toxic and pyrophoric gas requiring very careful handling, and P_{red} uses “superbasic” conditions (aqueous KOH/DMSO, the Trofimov–Gusarova reaction)⁹ for functionalization. Additionally, the latter P_{red}-based approach requires heating white phosphorus to prepare P_{red}, and it does not solve the issue of phosphorus atom economy.

Here, we argue that hypophosphites are superior, perhaps ideal, alternatives to any other intermediates, including their P₄ precursor. This is because hypophosphorous compounds (acid and salts) are stable to air and water (H₃PO₂ is sold as a 50% w/w solution in water), nontoxic, and yet still chemically reactive so that numerous transformations can be conducted, and they are already produced on an industrial scale. Furthermore, hypophosphites can have significant solubility in various organic solvents and ionic liquids. Additionally, of all the possible alternatives to PCl₃ (Scheme 1), only two have the potential to incorporate all of the phosphorus content into an organic product: PH₃ and MH₂PO₂ (M = H, metal, or alkyl).

Another possibility to consider would be a pathway based on phosphorous acid (H₃PO₃), however, it and its derivatives are all currently mostly produced from the hydrolysis/alcoholysis of PCl₃, and H₃PO₃ is much less reactive than H₃PO₂. Perhaps with the recycling of HCl into Cl₂, either via the direct oxidation of HCl (Kel and Shell processes), or through NaCl and electrolysis, such a process might be sustainable, although significant energy is still required for the recycling. However, even if a chlorine-free preparation of *H*-phosphonates ((RO)₂P(O)H, R = H, Alk) was developed, the reactivity manifolds would intrinsically be more limited than those of hypophosphorous compounds.

Figure 1 shows some commercial prices of various phosphorus intermediates.¹⁰ Although prices from a fine chemical supplier are probably not proportional to those from an industrial supplier, it is interesting to note that hypophosphite derivatives are quite inexpensive, and always cheaper than any other P–Cl-containing compound.

H₃PO₂ \$ 7.6 / mol Ca(H₂PO₂)₂ \$ 7.4 / mol P NaH₂PO₂ \$ 7.6 / mol NH₄OPOH₂ \$ 8.8 / mol
 P_{red} \$ 3.3 / mol
 PCl₅ \$ 14.8 / mol PCl₃ \$ 13.4 / mol H₃PO₃ \$ 5.5 / mol
 (EtO)₂P(O)H \$ 10.5 / mol (MeO)₂P(O)H \$ 10.6 / mol
 (EtO)₃P \$ 5 / mol (MeO)₃P \$ 8.5 / mol

Figure 1 Commercial prices from the Sigma-Aldrich catalog, as of June 2012. The price per mol of phosphorus is calculated from the cheapest quantity of compound. (Color figure available online).

In the past, *H*-phosphinates have been derived mainly from the hydrolysis or esterification/hydrolysis of R^1PCl_2 . However, the situation has changed significantly based on the plethora of reactions now available from hypophosphorous compounds. In fact, the conversion of *H*-phosphinic acids into R^1PCl_2 may now very well be a better method than the reverse reaction.

CONCLUSIONS

Hypophosphites $\text{ROP}(\text{O})\text{H}_2$ are viable and versatile intermediates for the synthesis of a broad variety of organophosphorus compounds, including the all-important *H*-phosphinates $\text{R}^1\text{P}(\text{O})(\text{OR})\text{H}$, phosphinates $\text{R}^1\text{R}^2\text{P}(\text{O})(\text{OR})$, phosphonates $\text{R}^1\text{P}(\text{O})(\text{OR})_2$, phosphines $\text{R}^1\text{R}^2\text{R}^3\text{P}$, and sulfur-containing compounds. In spite of the rapidly growing methodologies based on hypophosphites and *H*-phosphinates, potential industrial applications to replace the environmentally problematic phosphorus trichloride are still lagging. It is hoped that this paper will promote a critical (re)evaluation of alternative strategies, especially those based on the previously neglected hypophosphorous pathway. Whereas P–C bond-forming reactions through “P₄-activation,” P_{red}-elaboration through superbasic conditions, and PH_3 -addition to olefins have all been touted in the literature as panaceae; it appears that hypophosphites are the neglected orphans, even though they might very well be the ideal solution to redesigning an environmentally friendlier, safer, more energy-efficient, and sustainable phosphorus economy. Improvements in optimizing the conversion of P_4 into hypophosphites would also be an important and desirable step. At the very least, there is a growing consensus that using chlorine, and therefore phosphorus trichloride, could and should be avoided or minimized if at all possible. In the end, current industrial processes delivering many thousands of metric tons of materials yearly are not likely to be changed in the near future. The modification of large-scale industrial processes is neither trivial nor cheap. Nonetheless, increased awareness and concerns about environmental impact and economic sustainability in industrial chemical processes might very well change this situation in the long term. If or when this takes place, it is predicted that hypophosphorous compounds could and should play a major role in revolutionizing the phosphorus industry for the better.

REFERENCES

1. For general references, see: (a) Hartley, F. R. (Ed.), *The Chemistry of Organophosphorus Compounds*, Vol. 4; Wiley: New York, **1996**. (b) Quin, L. D. *A Guide to Organophosphorus Chemistry*, Wiley: New York, **2000**. (c) Flett, D. S. *J. Organomet. Chem.* **2005**, 690, 2426–2438. (d) Savignac, P.; Iorga, B. *Modern Phosphonate Chemistry*, CRC Press: Boca Raton, **2003**. (e) Kirk-Othmer Encyclopedia of Chemical Technology, <http://onlinelibrary.wiley.com/book/10.1002/0471238961>, Online ISBN: 9780471238966, doi: 10.1002/0471238961 (accessed August 3, 2012). (f) Ullmann's Encyclopedia of Industrial Chemistry, <http://onlinelibrary.wiley.com/book/10.1002/14356007>, Online ISBN: 9783527306732, doi: 10.1002/14356007 (accessed August 3, 2012). (g) Corbridge, D. E. C. *Phosphorus: An Outline of Its Chemistry, Biochemistry and Uses*, 5th ed.; Elsevier: Amsterdam, **1995**.
2. (a), Büchel K. H.; Moretto, H.-H.; Woditsch, P. *Industrial Inorganic Chemistry*, 2nd Ed.; Wiley VCH: New York, **2000**, pp. 65–101 (ISBN 3527298495). (b) *Kirk-Othmer Encyclopedia of Chemical Technology*, Vol. 18; 4th ed.; Wiley: New York, **1999**.

3. (a) Chemical Accidents with Phosphorus Trichloride, http://www.factsonline.nl/accidents/%205405/91809_PHOSPHORUS%20TRICHLORIDE/chemical-accidents-with-phosphorus-trichloride/ (accessed August 3, 2012). (b) **1980** chemical spill: It could have been disastrous, http://www.wickedlocal.com/somerville/town_info/history/x473075243#axzz22KNpTRSA (accessed August 3, 2012). (c) Chemical leak poisons 40 in Hebei, http://www.china.org.cn/china/local/2008-05/08/content_15122906.htm (accessed August 3, 2012).
4. (a) Oceana website, "Chlorine Plants: Major, Overlooked Source of Mercury Pollution," <http://oceana.org/en/search/node/chlorine> (accessed August 3, 2012). (b) "Chlorine Gas from South Carolina Train Crash Kills Nine," *Environment News Service*, January 10, 2005. (c) "One dead, 41 injured in chemical factory blast," *LANZHOU China Daily*, January 11, 2008. (d) Tremblay, J.-F. "China Has Deadly Chlorine Accident Spill following truck collision results in 29 deaths," *C&E News* April 7, 2005. (e) "Chlorine accident kills 27 in China. *CBS News*, March 30, 2005, <http://www.cbc.ca/world/story/2005/03/30/chlorine050330.html>. (f) Chlorine was used as a chemical warfare agent during World War I.
5. Metivier, P.; Woodward, G.; Li, J., *Keynote lecture # 9, ICPC 2012, July 8–12, 2012*, Rotterdam, The Netherlands.
6. For example, see: (a) Woodburn, A. T. *Pest Manag. Sci.* **2000**, 56, 309–312. (b) Morgenstern, D. A.; Fobian, Y. M. "Process for making glyphosate by oxidizing N-substituted glyphosates," U. S. Patent 6,005,140, December 21, 1999. (c) Dutra, G. A. "Preparation of N-phosphonomethyl glycine," U. S. Patent 4,053,505, October 11, 1977. (d) Rhodia slide presentation, Glyphosate Panel, May 2008, San Antonio, Texas, https://docs.google.com/viewer?a=v&q=cache:mJiuHE1p7rEJ:www.cpda.com/CPDA/files/ccLibraryFiles/Filename/000000000164/Sellier%2520-%2520Glyphosate%2520Pannel,%2520May%25202008%2520AIC%2520Conference.pdf+process+for+glyphosate+manufacture&hl=en&gl=us&pid=bl&srcid=ADGEEsGpHNER1Q1eYICy3pvSWprGQ5nbc9ChEMymL_2hc5KmlE-af24W-Fmq0q4ABUU59gON-wgdYquFdfhCKA6zLhUIBdw4FKn0xT3Q0uZoBAA-PLtTZnxgqo07YpPxd9EpcFQ2b7Gu&sig=AHIEtbQ6EIA2UsPpp2qEAq0wjT_iPxViJw.
7. For some references on P₄-functionalization, see: (a) Cossairt, B. M.; Piro, N. A.; Cummins, C. C. *Chem. Rev.* **2010**, 110, 4164–4177; (b) Caporali, M.; Gonsalvi, L.; Rossin, A.; Peruzzini, M. *Chem. Rev.* **2010**, 110, 4178–4235; (c) Scheer, M.; Balazs, G.; Seitz, A. *Chem. Rev.* **2010**, 110, 4236–4256; (d) Lynam, J. M. *Angew. Chem. Int. Ed.* **2008**, 47, 831–833; (e) Peruzzini, M. *Speciality Chemicals Magazine* **2003**, 23, 32–35; (f) Budnikova, Y. H.; Yakhvarov, D. G.; Sinyashin, O. G. *J. Organomet. Chem.* **2005**, 690, 2416–2425; (g) Peruzzini, M.; Gonsalvi, L.; Romerosa, A. *Chem. Soc. Rev.* **2005**, 34, 1038–1047; (h) Milyukov, V. A.; Budnikova, Y. H.; Sinyashin, O. G. *Russ. Chem. Rev.* **2005**, 74, 781–805; (i) Barton, D. H. R.; Zhu, J. J. *Am. Chem. Soc.* **1993**, 115, 2071–2072; (j) Barton, D. H. R.; Vonder Embse, R. A. *Tetrahedron* **1998**, 54, 12475–12496.
8. (a) Tanaka, M. *Top. Curr. Chem.* **2004**, 232, 25–54; (b) Baillie, C.; Xiao, J. *Curr. Org. Chem.* **2003**, 7, 477–514; (c) Trofimov, B. A.; Arbuzova, S. N.; Gusarova, N. K. *Russ. Chem. Rev.* **1999**, 68, 215–227; (d) Lam, W. W.; Toia, R. F.; Casida, J. E. *J. Agric. Food Chem.* **1991**, 39, 2274–2278; (e)
9. (a) Gusarova, N. K.; Arbuzova, S. N.; Trofimov, B. A. *Pure Appl. Chem.* **2012**, 84, 439–459, and references cited therein; (b) Albouy, D.; Etemad-Moghadam, G.; Koenig, M. *Eur. J. Org. Chem.* **1999**, 861–868; (c) Trofimov, B. A.; Rakhmatulina, T. N.; Gusarova, N. K.; Malysheva, S. F. *Russ. Chem. Rev.* **1991**, 60, 1360–1367.
10. Based on Sigma-Aldrich catalog prices (June **2012**). Although these prices are obviously not the same as the industrial cost, they perhaps remain valid in a comparative sense. Note that yellow phosphorus P₄ is not available through retail chemical manufacturers.
11. Reviews: (a) Coudray, L.; Montchamp, J.-L. *Eur. J. Org. Chem.* **2008**, 3601–3613; (b) Montchamp, J.-L. *Specialty Chemicals Magazine* **2006**, 26, 44–46; (c) Montchamp, J.-L. *J. Organomet. Chem.* **2005**, 690, 2388–2406; selected examples (see also Scheme 3):

- (d) Gavara, L.; Petit, C.; Montchamp, J.-L. *Tetrahedron Lett.* **2012**, 53, 5000–5003. (accessed XX); (e) Petit, C.; Fécourt, F.; Montchamp, J.-L. *Adv. Synth. Catal.* **2011**, 353, 1883–1888; (f) Deal, E. L.; Petit, C.; Montchamp, J.-L. *Org. Lett.* **2011**, 13, 3270–3273. (g) Belabassi, Y.; Bravo-Altamirano, K.; Montchamp, J.-L. *J. Organomet. Chem.* **2011**, 696, 106–111; (h) Bravo-Altamirano, K.; Coudray, L.; Deal, E. L.; Montchamp, J.-L. *Org. Biomol. Chem.* **2010**, 8, 5541–5551; (i) Coudray, L.; Pennebaker, A. F.; Montchamp, J.-L. *Bioorg. Med. Chem.* **2009**, 17, 7680–7689; (j) Coudray, L.; Montchamp, J.-L. *Eur. J. Org. Chem.* **2009**, 4646–4654; (k) Queffélec, C.; Ribière, P.; Montchamp, J.-L. *J. Org. Chem.* **2008**, 73, 8987–8991; (l) Belabassi, Y.; Antczak, M. I.; Tellez, J.; Montchamp, J.-L. *Tetrahedron* **2008**, 64, 9181–9190; (m) Coudray, L.; Montchamp, J.-L. *Eur. J. Org. Chem.* **2008**, 4101–4103; (n) Coudray, L.; Bravo-Altamirano, K.; Montchamp, J.-L. *Org. Lett.* **2008**, 10, 1123–1126; (o) Bravo-Altamirano, K.; Abrunhosa-Thomas, I.; Montchamp, J.-L. *J. Org. Chem.* **2008**, 73, 2292–2301; (p) Belabassi, Y.; Gushwa, A. F.; Richards, A. F.; Montchamp, J.-L. *Phosphorus, Sulfur Silicon Relat. Elem.* **2008**, 183, 2214–2228; (q) Coudray, L.; Abrunhosa-Thomas, I.; Montchamp, J.-L. *Tetrahedron Lett.* **2007**, 48, 6505–6508; (r) Bravo-Altamirano, K.; Montchamp, J.-L. *Tetrahedron Lett.* **2007**, 48, 5755–5759; (s) Abrunhosa-Thomas, I.; Sellers, C. E.; Montchamp, J.-L. *J. Org. Chem.* **2007**, 72, 2851–2856; (t) Bravo-Altamirano, K.; Montchamp, J.-L. *Org. Lett.* **2006**, 8, 4169–4171; (u) Antczak, M. I.; Montchamp, J.-L. *Synthesis* **2006**, 3080–3084; (v) Gouault-Bironneau, S.; Deprèle, S.; Sutor, A.; Montchamp, J.-L. *Org. Lett.* **2005**, 7, 5909–5912; (w) Ribière, P.; Bravo-Altamirano, K.; Antczak, M. I.; Hawkins, J. D.; Montchamp, J.-L. *J. Org. Chem.* **2005**, 70, 4064–4072; (x) Bravo-Altamirano, K.; Huang, Z.; Montchamp, J.-L. *Tetrahedron* **2005**, 61, 6315–6329; (y) Deprèle, S.; Montchamp, J.-L. *Org. Lett.* **2004**, 6, 3805–3808; (z) Deprèle, S.; Montchamp, J.-L. *J. Am. Chem. Soc.* **2002**, 124, 9386–9387; (aa) Dumond, Y. R.; Montchamp, J.-L. *J. Organomet. Chem.* **2002**, 653, 252–260; (ab) Deprèle, S.; Montchamp, J.-L. *J. Organomet. Chem.* **2002**, 643–644, 154–165; (ac) Deprèle, S.; Montchamp, J.-L. *J. Org. Chem.* **2001**, 66, 6745–6755; (ad) Montchamp, J.-L.; Dumond, Y. R. *J. Am. Chem. Soc.* **2001**, 123, 510–511.
12. Selected examples: *Radical addition of hypophosphorous compounds*: (a) Nifant'ev, E. E.; Magdeeva, R. K.; Shchepet'eva, N. P. *J. Gen. Chem. USSR* **1980**, 50, 1416–1423; (b) Nifant'ev, E. E.; Solovetskaya, L. A.; Maslennikova, V. I.; Magdeeva, R. K.; Sergeev, N. M. *J. Gen. Chem. USSR* **1986**, 56, 680–688; (c) Nifant'ev, E. E.; Koroteev, M. P. *J. Gen. Chem. USSR* **1967**, 37, 1293–1294; (d) Karanewsky, D. S.; Badia, M. C.; Cushman, D. W.; DeForrest, J. M.; Dejneka, T.; Loots, M. J.; Perri, M. G.; Petrillo, E. W.; Powell, J. R. *J. Med. Chem.* **1988**, 31, 204–212. *Alkylation of *i*-PrOP(O)H₂*: (i) Gallagher, M. J.; Ranasinghe, M. G.; Jenkins, I. D. *Phosphorus Sulfur Silicon* **1996**, 115, 255–259. *Cross-Coupling*: (j) Kalek, M.; Stawinski, J. *Tetrahedron* **2009**, 65, 10406–10412; (k) Huang, C.; Tang, X.; Fu, H.; Jiang, Y.; Zhao, Y. *J. Org. Chem.* **2006**, 71, 5020–5022; (l) Rao, H.; Jin, Y.; Fu, H.; Jiang, Y.; Zhao, Y. *Chem. Eur. J.* **2006**, 12, 3636–3646; (m) Lei, H.; Stoakes, M. S.; Schwabacher, A. W. *Synthesis* **1992**, 1255–1260; (n) Schwabacher, A. W.; Zhang, S.; Davy, W. *J. Am. Chem. Soc.* **1993**, 115, 6995–6996; (o) Lei, H.; Stoakes, M. S.; Herath, K. P. B.; Lee, J.; Schwabacher, A. W. *J. Org. Chem.* **1994**, 59, 4206–4210; (p) Schwabacher, A. W.; Stefanescu, A. D. *Tetrahedron Lett.* **1996**, 37, 425–428; (q) Holt, D. A.; Erb, J. M. *Tetrahedron Lett.* **1989**, 30, 5393–5396. *Addition of ROP(O)H₂*: (r) Maier, L. *Helv. Chim. Acta* **1973**, 56, 489–491; (s) Gallagher, M. J.; Sussman, J. *Phosphorus* **1975**, 5, 91; (t) Wroblewski, A. E.; Verkade, J. G. *J. Am. Chem. Soc.* **1996**, 118, 10168–10174; (u) Fookes, C. J. R.; Gallagher, M. J.; Honegger, H. *J. Chem. Soc. Chem. Commun.* **1978**, 324–325; (v) Yamagishi, T.; Yokomatsu, T.; Suemune, K.; Shibuya, S. *Tetrahedron* **1999**, 55, 12125–12136. *Miscellaneous*: (w) Montel, S.; Midrier, C.; Volle, J.-N.; Braun, R.; Haaf, K.; Willms, L.; Pirat, J.-L.; Virieux, D. *Eur. J. Org. Chem.* **2012**, 3237–3248; (x) Yang, Y.; Coward, J. K. *J. Org. Chem.* **2007**, 72, 5748–5758; (y) Cristau, H.-J.; Coulombeau, A.; Genevois-Borella, A.; Pirat, J.-L. *Tetrahedron Lett.* **2001**, 42, 4491–4494; (z) Froestl, W.; Mickel, S. J.; Hall, R. G.; von Sprecher, G.; Diel, P. J.; Strub, D.; Baumann, P. A.; Brugger, F.; Gentsch, C.; Jaekel, J.; Olpe, H.-R.; Rihs, G.; Vassout, A.; Waldmeier, P. C.; Bittiger, H. *J. Med. Chem.* **1995**, 38, 3297–3312;

- (aa) Froestl, W.; Mickel, S. J.; von Sprecher, G.; Diel, P. J.; Hall, R. G.; Maier, L.; Strub, D.; Melillo, V.; Baumann, P. A.; Bernasconi, R.; Gentsch, C.; Hauser, K.; Jaekel, J.; Karlsson, G.; Klebs, K.; Maitre, L.; Marescaux, C.; Pozza, M. F.; Schmutz, M.; Steinmann, M. W.; van Riezen, H.; Vassout, A.; Mondadori, C.; Olpe, H.-R.; Waldmeier, P. C.; Bittiger, H. *J. Med. Chem.* **1995**, 38, 3313–3331; (ab) Baylis, E. K. *Tetrahedron Lett.* **1995**, 36, 9385–9388; (ac) Stawinski, J.; Thelin, M.; Westman, E.; Zain, R. *J. Org. Chem.* **1990**, 55, 3503–3506; (ad) Dingwall, J. G.; Ehrenfreund, J.; Hall, R. G. *Tetrahedron* **1989**, 45, 3787–3808.
13. (a) Anderson, N. G.; Coradetti, M. L.; Cronin, J. A.; Davies, M. L.; Gardineer, M. B.; Kotnis, A. S.; Lust, D. A.; Palaniswamy, V. A. *Org. Process Res. Dev.* **1997**, 1, 315; (b) Anderson, N. G.; Ciaramella, B. M.; Feldman, A. F.; Lust, D. A.; Moniot, J. L.; Moran, L.; Polomski, R. E.; Wang, S. S. Y. *Org. Process Res. Dev.* **1997**, 1, 211–216; (c)
14. *Reviews on the phosphinylidene group*: (a) Nifant'ev, E. E. *Russ. Chem. Rev.* **1978**, 47, 835–858; (b) Yudelevich, V. I.; Sokolov, L. B.; Ionin, B. I. *Russ. Chem. Rev.* **1980**, 49, 46–58; (c) Stawinski, J.; Kraszewski, A. *Acc. Chem. Res.* **2002**, 35, 952–960. *For examples of functional group interconversion related to H-phosphinates*, see: (d) Frank, A. W. *Chem. Rev.* **1961**, 60, 389–424; (e) K. Sasse (Ed.), *Methoden der Organischen Chemie (Houben-Weyl)*, Thieme: Stuttgart, **1964**, Band XII/1, pp. 294–337. (f) M. Regitz (Ed.), *Methoden der Organischen Chemie (Houben-Weyl)*, Vol. E2; Thieme: Stuttgart, **1982**. (g) Frank, A. W. In *Organic Phosphorus Compounds*, Vol. 4; G. M. Kosolapoff; L. Maier, (Eds.), Wiley: New York, **1972**, Chapter 10; (h) Karanewsky, D. S.; Badia, M. C. *Tetrahedron Lett.* **1986**, 27, 1751–1754; (i) Frank, A. W. *J. Org. Chem.* **1961**, 26, 850–852; (j) Soulier, E.; Clement, J.-C.; Yaouanc, J.-J.; des Abbayes, H. *Tetrahedron Lett.* **1998**, 39, 4291–4294.
15. *Reviews on Arbuzov*: (a) Bhattacharya, A. K.; Thyagarajan, G. *Chem. Rev.* **1981**, 81, 415–430; (b) Engel, R.; Cohen, J. I. *Synthesis of Carbon-Phosphorus Bonds*, 2nd ed.; CRC Press: Boca Raton, **2003**. *Selected examples via hydrophosphonylation*: (c) Han, L.-B.; Mirzaei, F.; Zhao, C.-Q.; Tanaka, M. *J. Am. Chem. Soc.* **2000**, 122, 5407–5408; (d) Reichwein, J. F.; Pagenkopf, B. L. *J. Org. Chem.* **2003**, 68, 1459–1463; (e) Tayama, O.; Nakano, A.; Iwahama, T.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **2004**, 69, 5494–5496.