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Organophosphorus Chemistry without PCl_3: A Bridge from Hypophosphorous Acid to H-Phosphonate Diesters

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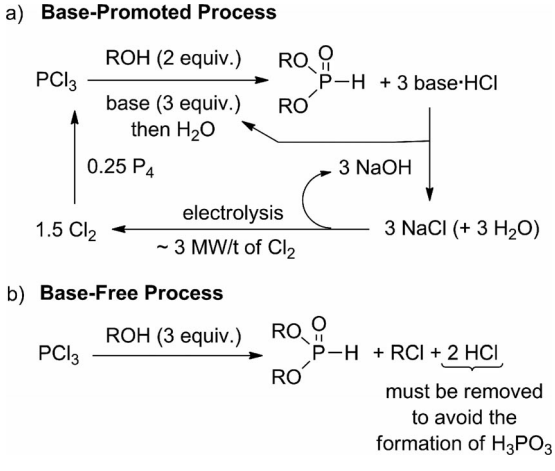
A process for the conversion of hypophosphorous acid (H_3PO_2, HPA) and alcohols into various H-phosphonate diesters [$(RO)_2P(O)H$] is described. The new reaction provides a missing bridge between HPA and important H-phosphonates, completely avoiding the use of PCl_3. Nickel chloride or nickel on silica catalyze the oxidative phosphorylation of alkyl phosphinates with various alcohols or water. The reaction is atom economic and avoids the formation of waste products. The previous need for both chlorine and base is completely avoided.

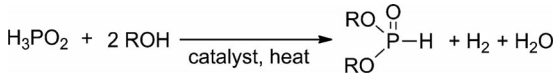
Introduction

Organophosphorus compounds are currently made from PCl_3 even though chlorine is not incorporated into the major industrial products.[1] As a result, much interest has been devoted to finding alternatives to PCl_3. Possibilities include the direct functionalization of elemental phosphorus (white P_4 and red P_{red}) and phosphine PH_3.[2] Based on their superior solubility and considerably lower toxicity, we have proposed the use of phosphinates [hypophosphorous acid (HPA) and its derivatives] as the best practical alternative to PCl_3.[3] Additional support for phosphinates resides in their synthetic flexibility in terms of the wide range of accessible functionalities, and the fact that each phosphorus atom can be incorporated into products.[3]

H-Phosphonate diesters [$(RO)_2P(O)H$] and phosphorus acid (R = H) are a major class of intermediates used in fine and industrial organophosphorus chemistry.[4] They are currently prepared from the alcoholysis of PCl_3 (Scheme 1). Both the base (such as Et_3N) and chlorine can be recycled, but the process requires extensive manipulations and electrical power. The exception is with phenol, which does not require any base because PhCl cannot form. Herein, we describe the catalytic oxidative phosphorylation of various alcohols with HPA to form H-phosphonate diesters in a simple, yet chlorine- and base-free process (Scheme 2).



Scheme 1. Preparation of H-phosphonate diesters.



Scheme 2. Synthesis of H-phosphonate diesters from HPA.

Results and Discussion

We have previously reported two catalytic phosphorus–oxygen bond-forming reactions.[5,6] For example, with H_3PO_2 (1.5 equiv.) and an alcohol (1 equiv.) using either Pd/C or $Ni/Al_2O_3/SiO_2$ as catalysts, we were able to prepare H-phosphonate monoesters.[6] These compounds are normally prepared from PCl_3 or a reagent derived from it.[7] The work exploited the well-known transfer hydrogenation pathway[8] for the preparation of organophosphorus compounds through catalytic P–O bond formation. Until this work, the fate of the hypophosphite in transfer hydrogenation was largely overlooked because it was the organic product that was desired.[8] However, Dorfman and Aleshkova reported in 1998 the results of a seminal study on the oxidation of sodium hypophosphite by alcohols using palladium or nickel catalysts.[9] The reaction produces

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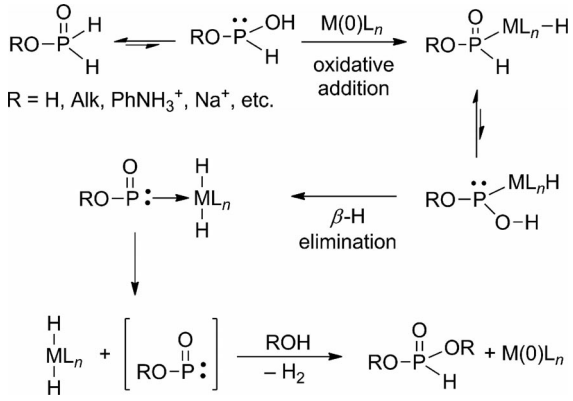
ROP(O)(ONa)H and an equivalent amount of hydrogen.[9] The authors proposed a radical pathway.

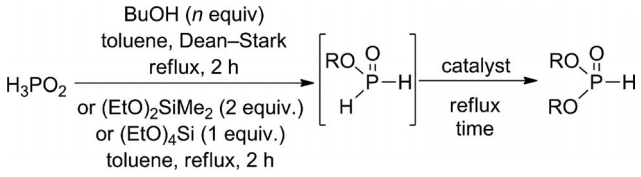
However, dialkyl H-phosphonates are much more important industrially than the monoesters because dialkyl phosphonates are ubiquitous. Perhaps the best illustration is the synthesis of *N*-phosphonomethylglycine, the active component of the herbicide glyphosate. Industrial preparations of glyphosate rely either on PCl_3 or its derivatives: Phosphorus acid or dialkyl H-phosphonates.[1a,10]

Alkyl phosphinates [$ROP(O)H_2$] can be prepared in several ways from HPA.[11] The most general and inexpensive methods use alkoxysilanes[11a,11b] or the Dean–Stark method for higher boiling alcohols.[11c–11e] It occurred to us that alkyl phosphinates might be converted into symmetrical H-phosphonate diesters as long as excess alcohol ROH is available. Therefore conditions that maximize the transfer hydrogenation when both $ROP(O)H_2$ and excess ROH are combined were optimized. The proposed mechanism is shown in Scheme 3.



Scheme 3. Proposed mechanism for the metal-catalyzed formation of H-phosphonate diesters.

Ligandless metals are expected to catalyze the transfer hydrogenation process through facile β-hydrogen elimination. Also, because of their strong reducing properties, alkyl phosphinates are able to reduce metal salts easily.[12] Scheme 4 summarizes the conditions that were investigated.



Scheme 4. Reaction conditions employed for the synthesis of H-phosphonate diesters.

Table 1 shows the results of various experiments. First, a solution of $EtOP(O)H_2$ was treated with nickel chloride. Entries 1 and 2 show the influence of the amount of catalyst on the transformation. To avoid any additional silicate reagent, we next focused on $BuOP(O)H_2$ prepared by the Dean–Stark reaction,[11,12] because in this case excess alcohol could be used as the source of the second ester group. The decomposition of $ROP(O)H_2$ is well known,[13] but entry 3 shows that this uncatalyzed process is inefficient as a synthetic procedure. The addition of $NiCl_2$ results in a clean reaction with the quantitative formation of $(BuO)_2$-P(O)H. Entries 4 and 5 show that the reaction is fast and that even inexpensive nickel chloride hexahydrate is an excellent catalyst.

Table 1. Optimization of the reaction conditions for the synthesis of H-phosphonate diesters.

Entry	R	ROH [equiv.]	Catalyst	Catalyst [mol-%]	Time [h]	^{31}P NMR yield [%] (isolated yield [%])[a]
1[b]	Et	0	$NiCl_2$	1.5	3	36
2[b]	Et	0	$NiCl_2$	3	3	95
3	Bu	2.5	none	0	18	17
4	Bu	3	$NiCl_2$	3	3	95
5	Bu	2.5	$NiCl_2{\cdot}6H_2O$	3	3	95
6	Bu	2.5	$NiBr_2$	3	3	99
7	Bu	2.5	NiI_2	3	3	95
8	Bu	2.5	$Ni(OAc)_2$	3	3	51
9	Bu	2.5	$Ni(acac)_2$	3	3	67
10	Bu	2.5	Ni powder	3	3	27
11[b,c]	Et	0	Ni/SiO_2	3	16	53
12	Bu	2.5	Ni/SiO_2	3	3	55
13[d]	Bu	2.5	Ni/SiO_2	5	30	77
14	Bu	(solvent)	Ni/SiO_2	5	18	100 (84)
15	Bu	3	Ni/SiO_2	5	18	100 (90)
16[e]	Bu	3	Ni/SiO_2	5	18	100 (75)
17	Bu	2.5	Pd/C	2	3	65
18	Bu	3	Pd/C	5	16	72 (71)
19	Bu	2.5	$PdCl_2$	3	3	78
20	Bu	2.5	CuCl	3	3	16
21	Bu	2.5	$CuCl_2$	3	3	26
22	Bu	2.5	Cu powder	3	3	17

[a] NMR yields were determined by the integration of all resonances in the ^{31}P NMR spectra. For isolation, see the Exp. Sect. [b] Prepared by the alkoxysilane method. [c] An extra equivalent of $(EtO)_2SiMe_2$ was added in the second step. [d] Catalyst was added at the start (before esterification). [e] The catalyst from entry 14 was recycled and used for this experiment on a 25 mmol scale.

Not surprisingly, other nickel(II) halides also reacted satisfactorily (entries 6 and 7). On the other hand, nickel(II) acetate, nickel acetylacetonate, and nickel powder gave poorer results. Nickel on silica was investigated next because it had given good results in the synthesis of H-phosphonate monoesters.[6] This catalyst is clearly less efficient than $NiCl_2$ (entries 4 and 5), but increasing the reaction time gave clean reactions and high conversions (entry 15). Note that addition of catalyst from the start of the reaction was unsatisfactory (entry 13). The use of *n*-butanol as solvent instead of toluene also gave excellent results (entry 14 vs. 15). This might be useful for the easy recycling of BuOH in industrial processes. In spite of lower activity, one advantage of Ni/SiO_2 over $NiCl_2$ is that it can be recycled (entry 16). Finally, palladium (entries 17–19) and copper catalysts (entries 20–22) were investigated but did not offer better results.

After the above investigation, it was concluded that $NiCl_2$ is the best catalyst for converting $ROP(O)H_2$ into $(RO)_2P(O)H$, but, because Ni/SiO_2 can be recycled, it pro-

vides a greener process. Next we turned our attention to the scope of the reaction under conditions similar to those in Scheme 4. The results are shown in Table 2. For low boiling alcohols like ethanol, which cannot be conveniently esterified by the azeotropic removal of water, the alkoxysilane method was used. Diethyl H-phosphonate was prepared by this method in good yield (entry 1). For diisopropyl H-phosphonate, the intermediate phosphinate was prepared by using a Soxhlet extractor with molecular sieves (3 Å) to remove water and by substituting cyclohexane for toluene to give the product in excellent yield (entry 2).

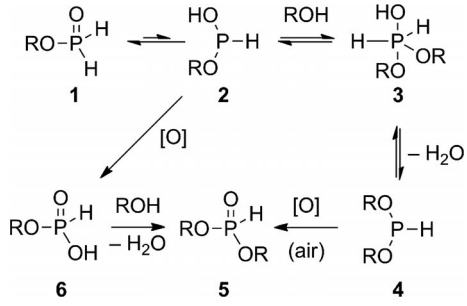
Table 2. Scope of the synthesis of H-phosphonate diesters.[a]

Entry	R	Catalyst	^{31}P NMR yield [%] (isolated yield [%])[b]
1[c–e]	Et	Ni/SiO_2	92 (75)
2[f]	*i*Pr	Ni/SiO_2	100 (87)
3	*i*Bu	Ni/SiO_2	100 (84)
4[g]	*n*Pent	Ni/SiO_2	100 (55)
5	Cy	Ni/SiO_2	100 (75)
6	Bn	Ni/SiO_2	68 (64)
7	$PhCH_2CH_2$	Ni/SiO_2	100 (81)
8	(–)-menthyl	Ni/SiO_2	100 (49)
9	fenchyl	Ni/SiO_2	100 (82)
10	Cl_3CCH_2	Ni/SiO_2	81 (26)
11	1-adamantyl	$NiCl_2$	68 (60)
12[h]	H	Ni/SiO_2	100 (84)
13[h]	Na	Ni/SiO_2	14[i]
14[h,j]	Na	Ni/SiO_2	53[i]
15[k]	3-butynyl	none	83 (51)
16[k]	$ClCH_2CH_2$	none	100 (68)
17[k]	Ph	none	74[l] (63)

[a] Unless otherwise noted, the reactions were conducted with ROH (3 equiv.) and 5 mol-% of catalyst for 18 h. [b] NMR yields are determined by integration of all the resonances in the ^{31}P NMR spectra. For isolation, see the Exp. Sect. [c] Prepared by the alkoxysilane method. [d] Reaction time of 40 h. [e] Anhydrous ethanol (3 equiv.) was added in the second step. [f] Cyclohexane was used as the solvent. [g] Reaction time of 87 h. [h] Water was used as the solvent. [i] Reaction time of 2 h. [j] The balance is NaH_2PO_4. [k] The H-phosphonate diester was obtained in the absence of catalyst during the esterification step. [l] The remainder was PhOP(O)(OH)H.

Overall, a wide range of primary and secondary alcohols were transformed into the corresponding H-phosphonate diester (entries 3–10), and in the vast majority of examples chromatographic purification was completely avoided. In some cases isolation was difficult, for example, the H-phosphonate prepared from (–)-menthol, which azeotropes off with the starting alcohol during distillation (entry 8). The product prepared from trichloroethanol was difficult to separate from the dechlorinated products formed during the reaction (entry 10). 1-Adamantanol reacted in moderate yield (entry 11), which supports the intermediacy of a highly reactive phosphinidene oxide (Scheme 3).[13] Other tertiary alcohols were problematic because of competing elimination in the esterification step. In the preparation of phosphorus acid (H_3PO_3), because HPA is a 50 wt.-% solution in water, which is the desired nucleophile, heating the solution in the presence of catalyst gave an excellent yield of product. Similar results were obtained with Ni/Al_2O_3 (71% isolated yield). In a control experiment without any catalyst, HPA remained unchanged. This type of metal-catalyzed process was described more than 100 years ago with both Cu and Pd.[14] The industrial potential of the transformation of HPA to H_3PO_3 has not yet been realized. The case of sodium hypophosphite is interesting because, unlike with HPA, over-oxidation to sodium dihydrogen phosphate is the dominant pathway in our hands (entry 13). Shortening the reaction time improved the yield significantly (entry 14), but a large amount of phosphate was still formed.

Surprisingly, 3-butyn-1-ol, 2-chloroethanol, and phenol (entries 15–17, respectively) were mostly or completely converted into the H-phosphonate diester during the Dean–Stark esterification step. Although a rationale for the reaction can only be speculative at this time, it must rely on minute variations in the tautomeric equilibria of ROP(O)H_2 that depend on the nature of the R group and the reactivity of the P^{III} tautomer. Our laboratory is actively trying to understand these effects both experimentally and computationally.[15] A plausible mechanism for the uncatalyzed process is proposed in Scheme 5.



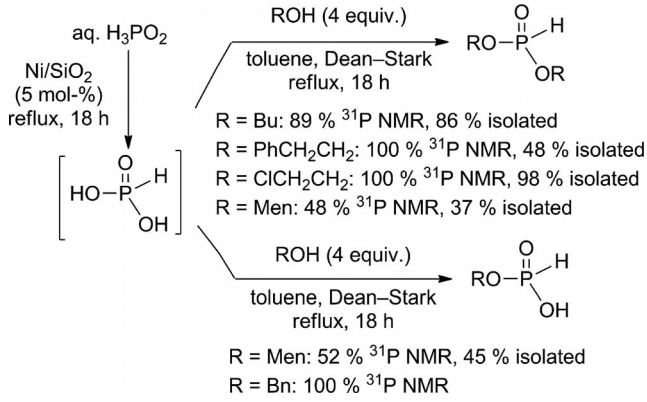
Scheme 5. Plausible mechanism for the uncatalyzed formation of H-phosphonate diesters.

As before (Scheme 3), tautomerization of alkyl phosphinate **1** into P^{III}-**2** occurs but now oxidative addition can take place with the alcohol to form pentacoordinate **3**. Intermediate **3** can isomerize by Berry pseudorotation to ultimately form dialkoxyphosphine **4**, which can be oxidized by air to the H-phosphonate diester **5**. There is significant support for this mechanism. Gallagher and Honegger proposed a virtually identical mechanism for the transesterification of alkylphosphinates[16] and Stec et al. characterized a species with a structure related to **3** by using ^{1}H NMR spectroscopy.[17] Several dialkoxyphosphines **4** have been synthesized and some are so easily oxidized in the pure state that the reaction is pyrophoric.[18] Finally, in some Dean–Stark esterifications, the presence of NMR signals corresponding to small amounts of **4** can sometimes be detected. An equally possible alternative mechanism is the oxidation of **2** followed by esterification of the H-phosphonate monoester (see below).

Because HPA can be oxidized easily to H_3PO_3, an alternative approach to bypassing PCl_3 is to use H_3PO_3. As mentioned earlier, glyphosate can be manufactured by using H_3PO_3. In terms of H-phosphonate diesters, we briefly investigated the Dean–Stark esterification of H_3PO_3. This kind of reaction has been described previously.[19] In our

process, the intermediate H_3PO_3 does not need to be isolated because it is formed in quantitative yield (see Table 2, entry 12).

Although the conversion of HPA into H_3PO_3 is known,[14] our method is mild even if the subsequent conversion of H_3PO_3 into $(RO)_2P(O)H$ is limited, often only giving the monoester or a mixture of mono- and diester (Scheme 6).[19]



Scheme 6. One-pot conversion of HPA into $(RO)_2P(O)H$ via H_3PO_3.

2-Chloroethanol is an excellent substrate, which suggests that the transformation of **2** into **6** in Scheme 5 might be an explanation for the uncatalyzed process observed in Table 2 (entry 16). The ease of oxidation of $ClCH_2CH_2OP(O)H_2$ would be due to the higher availability of its P^{III} tautomer. The Dean–Stark esterification of H_3PO_3 with phenol is slow (3 days) and gives a mixture of products (Table 2, entry 17), which also suggests that ROP(O)(OH)H might be an intermediate.

Conclusions

There are numerous literature methods for preparing H-phosphonate diesters, including transesterification.[20] However, to the best of our knowledge, the methodology presented herein is the only one that does not rely on PCl_3 at any point and is atom economic. Our reaction is greener than the alternatives because it only uses HPA, an alcohol, and nickel on silica gel as a catalyst, which might perhaps be reused, and no byproducts were formed. Although nickel chloride is a superior catalyst for this transformation, it cannot be reused. The present reaction thus provides an important link between hypophosphorous chemistry and key intermediates that are normally prepared by using PCl_3. Thus, it is another tool in the growing methodological toolbox for a phosphorus economy based on hypophosphites. Also, the reaction via $ROP(O)H_2$ appears to be much more general than the direct esterification of phosphorus acid. Our process not only provides access to an important class of industrial intermediates, it could also provide valuable hydrogen instead of hydrogen chloride, which is produced with PCl_3. The elucidation and prediction of subtle effects in phosphinylidene P(O)H chemistry are currently being investigated.

Experimental Section

General Procedure for the Nickel-Catalyzed Transformation of HPA into $(RO)_2P(O)H$: As an example, see Table 1, entry 14. Aqueous H_3PO_2 (50 wt.-%, 25 mmol) was concentrated in vacuo for 15 min at room temp. [Note: this step can be omitted as long as the esterification time is monitored]. Butanol (3 equiv., 75 mmol) followed by toluene (reagent grade, 50 mL) was added to the flask to which a Dean–Stark trap filled with excess toluene was fitted. The reaction mixture was heated at reflux for 2 h under nitrogen. The solution was cooled and the yield of $BuOP(O)H_2$ was quantitative, as determined by ^{31}P NMR spectroscopy. The Dean–Stark trap was removed and Ni/SiO_2 (64 wt.-%, 5 mol-%) was added to the $BuOP(O)H_2$ solution. The solution was heated at reflux under nitrogen for 18 h. After cooling, the reaction was filtered through Celite® and rinsed with ethyl acetate (20 mL). The organic layer was washed with brine (50 mL) and the aqueous layer was further extracted with ethyl acetate (3 × 15 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to afford dibutyl H-phosphonate as a pale-yellow liquid in 4.37 g (90% isolated yield). ^1H NMR (300 MHz, $CDCl_3$): δ = 6.83 (d, $^1J_{HP}$ = 691.9 Hz, 1 H, P-H), 4.09 (q, ^3J = 7.46 Hz, 4 H, CH_2), 1.70 (quint, ^3J = 6.68 Hz, 2 H, CH_2), 1.43 (quint, ^3J = 7.25 Hz, 2 H, CH_2), 0.96 (t, ^3J = 5.33 Hz, 6 H, CH_3) ppm. ^{31}P NMR (121.46 MHz, $CDCl_3$): δ = 7.82 (dquint, $^1J_{PH}$ = 693.23, $^3J_{POC}$ = 9.72 Hz) ppm.[21,22]

Diethyl H-Phosphonate:[21] Aqueous H_3PO_2 (50 wt.-%, 25 mmol) was concentrated in vacuo for 30 min at room temp. Octyltriethoxysilane (1 equiv., 25 mmol) and toluene (reagent grade, 50 mL) were added, and the reaction was heated at reflux for 3 h. After completion, the solution was cooled to room temp. and Ni/SiO_2 (64 wt.-%, 5 mol-%) and anhydrous ethanol (3 equiv., 75 mmol) were added. The reaction was heated at reflux and allowed to react under nitrogen for 40 h. After cooling, the reaction mixture was filtered through Celite® and the residue rinsed with ethyl acetate (20 mL). The organic layer was concentrated and subsequently dissolved in CH_3CN (HPLC grade, 50 mL). The CH_3CN layer was partitioned with hexanes (4 × 15 mL) and concentrated in vacuo to obtain a discolored liquid in 2.59 g (75% isolated yield). ^1H NMR (400 MHz, $CDCl_3$): δ = 6.82 (d, $^1J_{HP}$ = 692.8 Hz, 1 H, P-H), 4.16 (quint, ^3J = 7.20 Hz, 4 H, CH_2), 1.37 (t, J = 6.80 Hz, 6 H, CH_3) ppm. ^{31}P NMR (161.97 MHz, $CDCl_3$): δ = 7.77 (dm, $^1J_{PH}$ = 691.61 Hz) ppm.

Diisopropyl H-Phosphonate:[21–23] Aqueous H_3PO_2 (50 wt.-%, 62.5 mmol) was concentrated in vacuo for 30 min at room temp. Isopropanol (7 equiv., 438 mmol) and cyclohexane (92 mL) were added and a Soxhlet extractor was placed on the reaction flask with molecular sieves (3 Å) placed inside the extraction thimble. The solution was heated at reflux for a total of 18 h with the molecular sieves replaced after 4 and 8 h. Ni/SiO_2 (64 wt.-%, 5 mol-%) was added to the *i*PrOP(O)H_2 solution (25 mmol, 50 mL) and heated at reflux for 18 h under nitrogen. The cooled solution was filtered through Celite® and concentrated in vacuo to obtain a clear liquid in 4.15 g (87% isolated yield). ^1H NMR (400 MHz, $CDCl_3$): δ = 6.85 (d, $^1J_{HP}$ = 687.60 Hz, 1 H, P-H), 4.74 (m, 2 H, CH), 1.36 (d, ^3J = 8.40 Hz, 12 H, CH_3) ppm. ^{31}P NMR (161.97 MHz, $CDCl_3$): δ = 4.45 (dt, $^1J_{PH}$ = 686.75, $^3J_{POC}$ = 8.10 Hz) ppm.

Diisobutyl H-Phosphonate:[22,23] After concentration, 4.08 g (84%) of a light-yellow liquid was obtained. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.83 (d, $^1J_{HP}$ = 692.7 Hz, 1 H), 3.88–3.82 (m, 4 H), 1.97 (m, 1 H), 0.97 (d, ^3J = 6.9 Hz, 6 H) ppm. ^{31}P NMR (121.46 MHz, $CDCl_3$): δ = 7.99 (d, $^1J_{PH}$ = 693, $^3J_{POC}$ = 7.76 Hz) ppm.

Dineopentyl H-Phosphonate:[23] After kugelrohr distillation of excess alcohol, 3.06 g (55%) of a light-yellow liquid was obtained. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.85 (d, $^1J_{HP}$ = 693.6 Hz, 1 H), 3.77–3.73 (quint, ^3J = 6.8 Hz, 4 H), 0.98 (s, 18 H) ppm. ^{31}P NMR ($CDCl_3$, 161.97 Hz): δ = 8.38 (d, $^1J_{PH}$ = 695, $^3J_{POC}$ = 8.10 Hz) ppm.

Dicyclohexyl H-Phosphonate:[23] After kugelrohr distillation of excess alcohol, 6.16 g (75%) of a clear liquid was obtained. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.89 (d, $^1J_{HP}$ = 688.4 Hz, 1 H), 4.46–4.44 (m, 2 H), 1.96–1.93 (m, 4 H), 1.78–1.74 (m, 4 H), 1.58–1.53 (m, 6 H), 1.37–1.1.30 (m, 6 H) ppm. ^{31}P NMR (161.97 MHz, $CDCl_3$): δ = 4.46 (d, $^1J_{PH}$ = 688 Hz) ppm.

Dibenzyl H-Phosphonate:[24] After kugelrohr distillation of excess alcohol, 4.20 g (64%) of a light-yellow liquid was obtained. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.37 (m, 10 H, ArCH), 6.97 (d, $^1J_{HP}$ = 706.8 Hz, 1 H, P-H), 5.08 (m, 4 H, CH_2) ppm. ^{31}P NMR (161.97 MHz, $CDCl_3$): δ = 7.74 (dquint, $^1J_{PH}$ = 706, $^3J_{POC}$ = 9.3 Hz) ppm.

Bis(2-phenethyl) H-Phosphonate:[25] After kugelrohr distillation of excess alcohol, 7.26 g (81%) of a light-yellow liquid was obtained. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.33–7.23 (m, 10 H), 6.66 (d, $^1J_{HP}$ = 700.8 Hz, 1 H), 4.24–4.20 (m, 4 H) ppm. ^{31}P NMR (161.97 MHz, $CDCl_3$): δ = 7.65 (dquint, $^1J_{PH}$ = 700, $^3J_{POC}$ = 8.10 Hz) ppm.

Dimenthyl H-Phosphonate:[26] After kugelrohr distillation, 4.39 g (49%) of a clear liquid was obtained. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.91 (d, $^1J_{HP}$ = 686.8 Hz, 1 H), 4.28–4.18 (m, 2 H), 2.20–2.16 (m, 2 H), 2.15–2.04 (2 m, 2 H), 1.69, 1.65 (2 br. s), 1.47–1.44 (m, 2 H), 1.26–1.16 (m, 2 H), 1.07–0.96 (m, 4 H), 0.92 (2 d, ^3J = 1.32, ^3J = 1.68 Hz, 12 H), 0.89–0.84 (m, 2 H), 0.82 (d, ^3J = 1.68 Hz, 3 H), 0.79 (d, ^3J = 1.68 Hz, 3 H) ppm. ^{31}P NMR (161.97 MHz, $CDCl_3$): δ = 5.45 (dt, $^1J_{PH}$ = 686.8, $^3J_{POC}$ = 8.73 Hz) ppm.

Difenchyl H-Phosphonate: After kugelrohr distillation of excess alcohol, 7.27 g (82%) of a light-brown liquid was obtained. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.89 (d, $^1J_{HP}$ = 686.4 Hz, 1 H), 4.06–3.98 (m, 2 H), 1.74–1.70 (m, 6 H), 1.56–1.53 (m, 2 H), 1.49–1.44 (m, 2 H), 1.23–1.20 (m, 2 H), 1.14 (d, ^3J = 8.6 Hz, 6 H), 1.09 (m, 8 H), 0.96 (s, 3 H), 0.94 (s, 3 H) ppm. ^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 89.3 (d, $^2J_{COP}$ = 7.3 Hz), 49.1, 40.9, 39.5, 29.8, 25.8, 21.4, 19.3 ppm. ^{31}P NMR (161.97 MHz, $CDCl_3$): δ = 8.12 (dt, $^1J_{PH}$ = 688.4, $^3J_{POC}$ = 10.6 Hz) ppm. HRMS (ESI): calcd. for $C_{20}H_{35}O_3P$ $[M + H]^+$ 355.2402; found 355.2489.

Bis(2,2,2-trichloroethyl) H-Phosphonate:[27] After kugelrohr distillation of excess alcohol and column chromatography, 2.24 g (26%) of a light-yellow liquid was obtained. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.22 (d, $^1J_{HP}$ = 746 Hz, 1 H), 4.75–4.66 (m, 4 H) ppm. ^{31}P NMR (161.97 MHz, $CDCl_3$): δ = 7.23 (dquint, $^1J_{PH}$ = 753, $^3J_{POC}$ = 8.75 Hz) ppm.

Diadamantyl H-Phosphonate: After kugelrohr distillation of excess alcohol, 5.61 g (60%) of a white solid was obtained. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.04 (d, $^1J_{HP}$ = 680 Hz, 1 H), 2.18 (m, 6 H), 2.10 (m, 12 H), 1.63 (m, 12 H) ppm. ^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 82.3 (d, $^2J_{COP}$ = 7.62 Hz), 44.0 (d, $^3J_{CCOP}$ = 4.51 Hz), 35.7, 31.0 ppm. ^{31}P NMR (161.97 MHz, $CDCl_3$): δ = –4.06 (d, $^1J_{PH}$ = 680 Hz) ppm. HRMS (ESI): calcd. for $C_{20}H_{31}O_3P$ $[M + H]^+$ 351.2089; found 351.2104.

Phosphorous Acid:[28] After concentration of water, 1.72 g (84%) of a clear liquid was obtained. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.72 (d, $^1J_{HP}$ = 663.2 Hz, 1 H) ppm. ^{31}P NMR (161.97 MHz, $CDCl_3$): δ = 4.37 (d, J_{PH} = 664 Hz) ppm.

Dibutynyl H-Phosphonate: After kugelrohr distillation of excess alcohol, 2.37 g (51%) of a clear liquid was obtained. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.95 (d, $^1J_{HP}$ = 711 Hz, 1 H), 4.28–4.17 (m, 4 H), 2.65–2.61 (td, ^3J = 6.68, ^4J = 2.64 Hz), 2.07 (t, ^4J = 2.64 Hz) ppm. ^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 79.3, 70.7, 63.5 (d, $^2J_{COP}$ = 6.01 Hz), 20.9 (d, $^3J_{CCOP}$ = 6.26 Hz) ppm. ^{31}P NMR (161.97 MHz, $CDCl_3$): δ = 7.74 (dquint, $^1J_{PH}$ = 712, $^3J_{POC}$ = 9.72 Hz) ppm. HRMS (ESI): calcd. for $C_8H_{11}O_3P$ $[M + H]^+$, 187.0524; found 187.0570.

Bis(2-chloroethyl) H-Phosphonate:[23] After kugelrohr distillation of excess alcohol, 5.17 g (68%) of a clear liquid was obtained. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.02 (d, $^1J_{HP}$ = 720.8 Hz, 1 H), 4.40–4.33 (m, 4 H), 3.76–3.71 (t, ^3J = 8.4 Hz, 4 H) ppm. ^{31}P NMR (161.97 MHz, $CDCl_3$): δ = 8.18 (dquint, $^1J_{PH}$ = 720, $^3J_{POC}$ = 8.9 Hz) ppm.

Diphenyl H-Phosphonate:[29] After kugelrohr distillation of excess alcohol, 3.69 g (63%) of a light-yellow liquid was obtained. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.22 (m, 10 H), 7.34 (d, $^1J_{HP}$ = 728.4 Hz, 1 H) ppm. ^{31}P NMR (161.97 MHz, $CDCl_3$): δ = 0.34 (d, $^1J_{PH}$ = 733 Hz) ppm.

Preparation of Dibutyl H-Phosphonate from Phosphorus Acid: Ni/SiO_2 (64 wt.-%, 5 mol-%) was added to a round-bottomed flask containing aqueous H_3PO_2 (50 wt.-%, 25 mmol), and the mixture was heated at reflux for 18 h under nitrogen. [*Note:* if the reaction was conducted open to air, the reaction time was lowered to 6 h.] Once cooled, ^{31}P NMR analysis showed that the formation of phosphorus acid was complete. The solution was filtered through Celite® and rinsed with several aliquots of deionized water (ca. 20 mL total). The acid was concentrated and butanol (4 equiv., 100 mmol) and toluene (reagent grade, 50 mL) were added. A Dean–Stark trap prefilled with toluene was attached to the reaction vessel and the solution was heated at reflux for 18 h under nitrogen. After cooling, the solution was extracted with brine (50 mL), dried with $MgSO_4$, and concentrated in vacuo to afford a light-yellow liquid in 4.18 g (86%) isolated yield.

Supporting Information (see footnote on the first page of this article): General chemistry, method for determining yields by ^{31}P NMR, purification of H-phosphonate diesters, ^1H, ^{13}C, and ^{31}P NMR spectra.

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