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A novel and convenient preparation of hypophosphite esters

Sylvine Deprèle, Jean-Luc Montchamp *

Department of Chemistry, Texas Christian University, Box 298860, Fort Worth, TX 76129, USA

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Abstract

Only a few methods have been described for the preparation of hypophosphite esters (alkyl phosphinates, $ROP(O)H_2$). As a result, comparatively few applications have been reported, and these intermediates have not been widely exploited in organophosphorus chemistry despite their synthetic potential. Herein, we describe a very general, practical, and high-yielding synthesis of hypophosphite esters, based on the reaction of hypophosphorous acid and some of its salts with alkoxysilanes. This methodology solves a number of the problems associated with previously reported reactions. Our esterification takes place at moderate temperature in a variety of solvents, and under these conditions the esters are remarkably thermally stable. Furthermore, the reagents employed are inexpensive and do not have to be strictly anhydrous. The scope and limitations of the method are discussed, and representative synthetic applications for the preparation of monosubstituted phosphinate esters are described.
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Keywords: Hypophosphite ester; Alkyl hypophosphite; Alkoxysilane; Phosphinic acid; Organic synthesis

1. Introduction

Hypophosphite esters (alkyl phosphinates, $ROP(O)H_2$) are highly sensitive to moisture, air, or heat, and have a propensity for disproportionation and decomposition. The limited number of methods available for their preparation typically do not combine generality, high yield, and experimental simplicity. Therefore, novel methods to form hypophosphite esters in high yield, from inexpensive and easily handled reagents, and under conditions compatible with a wide array of subsequent reactions, would be desirable. We now report one such reaction, in which hypophosphite esters are formed from hypophosphorous acid (or one of its salts) and an alkoxysilane ($R'_xSi(OR)_{4-x}$).

Not only are hypophosphite esters readily hydrolyzed or oxidized compounds, but they also disproportionate thermally, thereby preventing their isolation in the pure state via distillation. Even in solution, the esters (particularly the lower alkyls) rapidly decompose at room temperature with formation of a yellow solid of high phosphorus content. Therefore, the preparation and handling of hypophosphite esters require great care.

Methyl and ethyl hypophosphites ($MeOP(O)H_2$, $EtOP(O)H_2$) were first prepared by Kabachnik in 1960 [1], by the esterification of hypophosphorous acid (H_3PO_2) with diazoalkanes. A few years later, Fitch reported the esterification of crystalline H_3PO_2 with orthoformates and related compounds [2], and Nifant'ev described the direct esterification of H_3PO_2 with alcohols under azeotropic water removal (Dean–Stark trap) [3]. To date, the latter two methods are still the most commonly employed, due in part to their relative experimental simplicity, and suitability for large scale reactions. Typically, hazardous crystalline H_3PO_2 is employed, but Fitch's method allows the use of partially dried material if an excess of orthoformate is employed to scavenge the residual moisture. Nifantev's method has the advantage of not requiring any particular drying step.

Other preparations entail the alkylation of anhydrous sodium hypophosphite with triethyloxonium tetrafluoroborate [4], and the reaction of H_3PO_2 with alcohols in the presence of an activating agent (pivaloyl chloride) [5]. The transesterification of $MeOP(O)H_2$ with alcohols has also been studied [6].

However, yields are rarely quantitative in any of the above described methods. In the orthoformate-based esterification, side products formation has been exten-

* Corresponding author.

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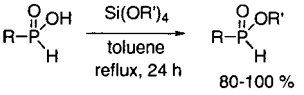
sively demonstrated [2,7]. In the Dean–Stark protocol, yields depend on reaction temperature and time [8]. In our own experience, some hypophosphorous acid always remains, disproportionation side products appear, and yields are typically in the 80–90% range. The presence of acidic components in the reaction mixture can be problematic in subsequent reactions. The other methods require the use of hazardous and/or expensive reagents which are not readily applicable to medium or large scales.

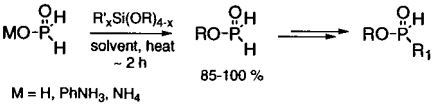
In terms of synthetic applications, Gallagher [9], Maier [10], Schwabacher [6b,11], Stawinski [5,12] and a few others [13] have been major contributors. Some of the reactions are collected in Scheme 1. Still, the synthetic scope of hypophosphite esters is limited by their lack of chemical stability, as well as the method employed in their preparation. For example, reactions under basic conditions (alkoxide, trialkylamines) have been reported to yield a number of side products [9b,14]. Also, reactions requiring heating for only a few hours at 80 °C can lead to extensive decomposition [6b,11].

As part of our ongoing efforts aiming at the preparation of biologically active phosphinic acids, we have undertaken the study of hypophosphites in organic synthesis [15]. We recently developed the room temperature radical reaction of hypophosphorous derivatives, which proceeds under conditions even compatible with hypophosphite esters prepared by the Fitch and Nifant'ev protocols [16]. However, we realized that improvements in the preparation of these esters would be valuable to both our radical reaction, and other synthetic applications.

We already reported a novel method for the esterification of monosubstituted phosphinic acids using orthosilicates and related compounds (Eq. (1)) [17]. Our reaction is highly selective for phosphinylidene (P(O)–H)-containing compounds, and monosubstituted phosphinic acids are thus esterified while disubstituted phosphinic acids remain unreacted. It occurred to us that hypophosphorous acid should also undergo the reaction. This assumption turned out to be correct, and even some hypophosphite salts can be esterified. The results of these investigations are presented herein (Eq. (2)).



(1)



(2)

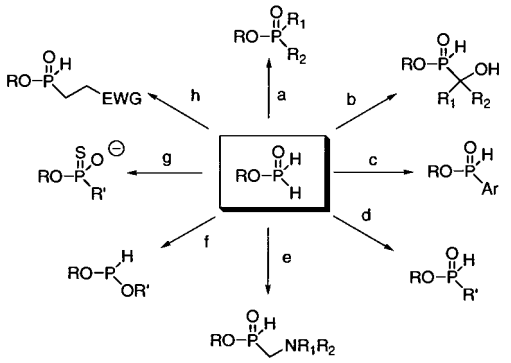
2. Results and discussion

2.1. Esterification

2.1.1. Reaction of hypophosphite salts and hypophosphorous acid with orthosilicates

In our previous work with phosphinic acids [17], we noticed that certain salts could be esterified, provided that the corresponding phosphinate remained acidic: the base must have a low pK_a, like pyridine or aniline, whereas stronger bases, like NaOH or Et_3N, produce unreactive phosphinate salts. We have introduced anilinium hypophosphite (AHP) as an inexpensive and convenient alternative to other amine salts such as the commercially available *N*-ethylpiperidinium hypophosphite (EPHP) [15,16]. Anilinium hypophosphite is a relatively non-hygroscopic crystalline solid which is easily handled and stored [18], and therefore an excellent H_3PO_2 equivalent. In our first experiment, AHP was reacted with orthosilicates, because we wanted to avoid the handling of anhydrous H_3PO_2.

The influence of various reaction parameters was studied, and the results are shown in Table 1. Reactions were monitored by ^{31}P-NMR, and the yields determined by integrating all the resonances in the spectrum. As expected, the esterification occurred smoothly and much more readily than with the corresponding anilinium phosphinates ($RPO_2H_2{\cdot}H_2NPh$) or phosphinic acids (RPO_2H_2) [17]: lower temperatures were sufficient to deliver hypophosphite esters in excellent yields (typi-



Scheme 1. Synthesis with hypophosphite esters. **1a**–**c**: CF_3CO_2H (2.5 equivalents), $H_2N(CH_2)_3Si(OMe)_3$ (2.5 equivalents), CH_3CN, reflux, 2 h. **1d**: $(BuO)_4Si$ (2.5 equivalents), cyclohexane, reflux, 2 h. (a) (i) Cl_3CCHO, 60%, [13a]. (ii) $Et_2NCH_2NEt_2$, 150 °C, 40–60%, [13b]. (iii) CH_2=$CHCH_2OAc$, *t*-Bu*O*O*t*-Bu, 130–140 °C, 25%, [13c]. (iv) Diketone, Et_3N or heat, 10–40%, [13d]. (v) $HC(OMe)_3$, cat., 20–50%, [7b,13e]. (vi) RX, *i*-PrONa, 40–95%, [9b]. (vii) See also (c) and (h). (b) (i) Acetone, r.t., [2,13l]. (ii) RCHO, Al–Li–Binol, 37–81%, [13k]. (c) ArI, Pd(0), propylene oxide or *N*-methylmorpholine, CH_3CN, 23–80%, [11,6b]. (d) (i) RX, *i*-PrONa, 50–90%, [9b]. (ii) Alkene, Et_3B, r.t., 25–80%, [16]. (e) (i) $RNH_2{\cdot}HCl$, CH_2O, Na_2CO_3, r.t., 55%, [13g]. (ii) $(AcNCH_2)_3$, 100 °C, 77%, [13h]. (f) *N*-(trimethylsilyl)succinimide, r.t., 57–60%, [13f]. PPh_3, DIAD, R′OH, [13m]. (g) S_8, 95%, [5,12]. (h) CH_2=CH(EWG), base, r.t., 60–88%, [9a,10,13i,13j].

Table 1
Esterification of hypophosphorous derivatives with orthosilicates [a]

Entry	Hypophosphite [b]	$(RO)_4Si$ equivalent	R	Solvent [c]	^{31}P-NMR % yield [d]
1	$PhNH_3{\cdot}H_2PO_2$	1.0	Bu	C_6H_6	95–100
2	$PhNH_3{\cdot}H_2PO_2$	0.5	Bu	C_6H_6	94
3	$PhNH_3{\cdot}H_2PO_2$	0.25	Bu	C_6H_6	41
4	$PhNH_3{\cdot}H_2PO_2$	1.0	Et	C_6H_6	86
5	$PhNH_3{\cdot}H_2PO_2$	1.0	Bu	CH_3CN	95–100
6	$PhNH_3{\cdot}H_2PO_2$	1.0	Et	CH_3CN	98
7	$PhNH_3{\cdot}H_2PO_2$	1.0	Me	CH_3CN	99
8	$PhNH_3{\cdot}H_2PO_2$	1.0	Bu	DMF [e]	75–83
9	$PhNH_3{\cdot}H_2PO_2$	1.0	Bu	C_6H_{12}	95
10	$PhNH_3{\cdot}H_2PO_2$	1.0	Bu	$PhCH_3$	93
11	$PhNH_3{\cdot}H_2PO_2$	1.0	Bu	Dioxane	84–87
12	$PhNH_3{\cdot}H_2PO_2$	1.0	Bu	Pyridine (dry)	61
13	$PhNH_3{\cdot}H_2PO_2$	1.0	Bu	THF	86–89
14	$PhNH_3{\cdot}H_2PO_2$	1.0	Et	THF	89
15	$PhNH_3{\cdot}H_2PO_2$	1.0	Me	THF	83
16	$NH_4{\cdot}H_2PO_2$	1.0	Bu	CH_3CN	100 [f]
17	$Et_3NH{\cdot}H_2PO_2$	1.0	Bu	CH_3CN	30
18	H_3PO_2	1.0	Bu	CH_3CN	100
19	H_3PO_2	1.0	Et	$PhCH_3$	92
20	H_3PO_2	1.0	Et	$PhCH_3$	84 [g]
21	H_3PO_2	1.0	Ph	CH_3CN	88
22	H_3PO_2	1.0	Allyl	CH_3CN	86

[a] All reactions were conducted for 2 h, under N_2.
[b] EPHP, 1-ethylpiperidine hypophosphite. H_3PO_2 was obtained by concentrating a 50 wt.% solution in vacuo.
[c] Unless otherwise noted, reagent grade solvents were employed at refluxing temperature.
[d] Determined by integration of all the signals. A range is indicated when multiple runs were conducted. The balance is unreacted starting material.
[e] 80–85 °C.
[f] NH_3 evolves.
[g] Conducted at r.t. for 5 h.

cally 85–100%, Table 1) in no more than 2–3 h. A variety of solvents could be employed (C_6H_6, cyclohexane, toluene, THF, dioxane, CH_3CN, DMF). Acetonitrile and benzene are excellent solvents for this reaction (entries 1, 4–7, 16, 18, 21, 22). DMF at 80–85 °C was less satisfactory (entry 8), presumably because its slow decomposition generates dimethylamine which forms unreactive $Me_2NH{\cdot}H_3PO_2$. Nonetheless, even under such conditions, the yields typically remained around 80%. Only pyridine did not turn out to be a very useful esterification solvent (entry 12). The fact that our esterification proceeds well in different solvents is necessary to use the resulting hypophosphite esters in subsequent reactions. Reagent grade solvents were used throughout this study, since they gave results comparable to that of strictly anhydrous solvents.

Ammonium hypophosphite also underwent esterification under our conditions, with concomitant evolution of ammonia thereby driving the reaction to completion (Table 2, entry 16). Not surprisingly, triethylammonium hypophosphite was a poor substrate for this reaction (entry 17). Hypophosphorous acid itself was esterified in high yield under the same conditions (Table 1, entries 18–22). Noteworthy is the fact that the H_3PO_2 employed was not anhydrous, but simply obtained by concentrating a commercial aqueous solution in vacuo for 20–30 min, at room temperature. Esterification could also take place at room temperature (entry 20). In fact, most of the reactions already occurred at room temperature, although heating gave better and more consistent results.

As shown in Table 1, various tetraalkylorthosilicates ($Si(OR)_4$, R = Me, Et, Bu, Allyl, Ph) could be employed. Even 0.5 equivalents of reagent delivered a high yield of butyl hypophosphite (entry 1 vs. 2), which is consistent with our previous observations with RPO_2H_2. More importantly, the hypophosphite esters formed appear to be exceptionally thermally stable under our conditions, as shown in Fig. 1. Even methyl hypophosphite is stable over at least 8 h in refluxing acetonitrile using our method, while it is reported to completely decompose within 1 h at 80 °C with the orthoformate method [6b,11]. Similarly, $EtOP(O)H_2$ suffers less than 10% decomposition over 1 day in refluxing acetonitrile. Dialkyl phosphite ($(RO)_2P(O)H$) does form slowly, and its rate of formation depends on reaction temperature and mirrors the disappearance of the alkyl hypophosphite. While ester stability is greatest in CH_3CN, it remains significant in other solvents (generally less than 20% decomposition in 1 day). Such

unprecedented thermal stability opens up a number of possibilities for synthetic applications, provided that the organosilicon by-products do not interfere.

Reactions can be conducted without difficulty up to a 100 mmol scale. Higher scales should also be appropriate, but this was not checked in this work. Concentration appears relatively unimportant. Excellent results were obtained in the 0.2–1.0 M concentration range, so we conducted the esterification at 0.5 M hypophosphite concentration as a standard procedure. The reaction also takes place in neat alkoxysilane reagent at 80 °C, although the yield is lowered, and heterogeneity can be problematic. Some of the reactions in Table 1 give heterogeneous mixtures, especially when AHP was esterified in non-polar solvents such as cyclohexane. Although it can be argued that the NMR yield might be relatively inaccurate in some of these cases, the observed precipitate appears to be related to silicon by-products and not to phosphorus, as established using trimethylphosphate as an NMR internal standard. Furthermore, these heterogeneous runs were employed in subsequent reactions with no significant lowering in the overall yield.

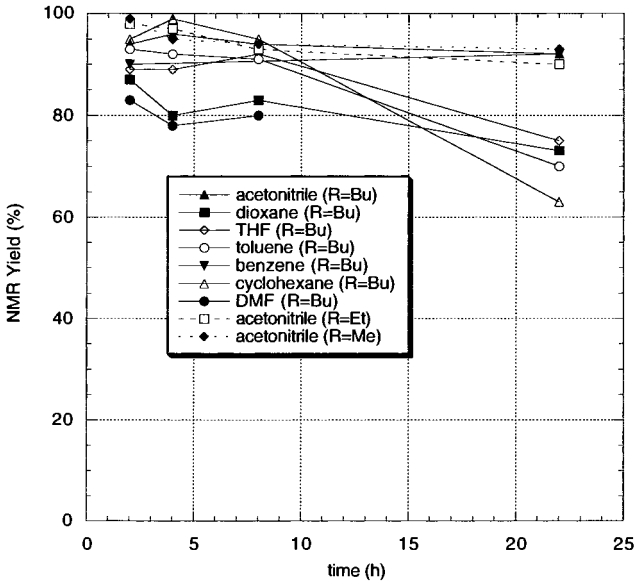


Fig. 1. Thermal stability of hypophosphite esters.

Table 2
Esterification of hypophosphorous derivatives with alkoxysilanes [a]

Entry	Hypophosphite [b]	Alkoxysilane	Solvent	^{31}P-NMR % yield [c]
1	$PhNH_3 \cdot H_2PO_2$	$PrSi(OMe)_3$	CH_3CN	90–100
2	$PhNH_3 \cdot H_2PO_2$	$PrSi(OMe)_3$ [d]	CH_3CN	40
3	$PhNH_3 \cdot H_2PO_2$	$OctSi(OEt)_3$	CH_3CN	95–100
4	$PhNH_3 \cdot H_2PO_2$	$Me_2Si(OEt)_2$ [e]	CH_3CN	85–95
5	H_3PO_2	$PrSi(OMe)_3$	CH_3CN	95–100
6	H_3PO_2	$PrSi(OMe)_3$	C_6H_{12}	67
7	H_3PO_2	$PrSi(OMe)_3$	DMF	70–80
8	H_3PO_2	$OctSi(OEt)_3$	CH_3CN	95–100
9	H_3PO_2	$OctSi(OEt)_3$	EtOH	43
10	H_3PO_2	$OctSi(OEt)_3$	*i*-PrOH	60 [f]
11	H_3PO_2	$Me_2Si(OEt)_2$ [e]	CH_3CN	94–100
12	H_3PO_2	$Me_2Si(O\textit{i}\text{-}Pr)_2$	CH_3CN	85
13	H_3PO_2	$H_2N(CH_2)_3Si(OMe)_3$	CH_3CN	11
14	H_3PO_2	$HCl \cdot H_2N(CH_2)_3Si(OMe)_3$	CH_3CN	61
15	H_3PO_2	$HCl \cdot H_2N(CH_2)_3Si(OMe)_3$	$PhCH_3$	68
16	H_3PO_2	$TFA \cdot H_2N(CH_2)_3Si(OMe)_3$	CH_3CN	90–95
17	$NaH_2PO_2 \cdot H_2O$	$(EtO)_3SiCl$	CH_3CN	100 [g]

[a] All reactions were conducted for 2–3 h, under N_2, in refluxing reagent grade solvent. Unless otherwise noted, one equivalent of alkoxysilane was employed. DMF was used at 80–85 °C.

[b] H_3PO_2 was obtained by concentrating a 50 wt.% solution in vacuo for 20–30 min.

[c] Determined by integration of all the signals. A range is indicated when multiple runs were conducted. The balance is typically unreacted starting material.

[d] 0.5 equivalent.

[e] Two equivalents were employed.

[f] *i*-$PrOP(O)H_2$ is the major product. (Other components: $MeOP(O)H_2$: 5%; H_3PO_2: 30%.)

[g] Run in duplicate.

Our reaction parallels Fitch's method [2], except that no particular excess of orthosilicate needs to be employed with concentrated H_3PO_2, and thermally stable hypophosphite esters are formed with significantly less (or no) phosphorus-derived by-products. It is also an improvement upon Nifant'ev's method [3], which normally requires an excess of alcohol, and becomes a competition between esterification and decomposition over time. As a result, our novel synthesis of hypophosphite esters is a convenient alternative to those previously reported, and should prove useful in the synthesis of organophosphorus compounds.

2.1.2. Reaction of hypophosphorous acid and anilinium hypophosphite with alkyltrialkoxysilanes and dialkyldialkoxysilanes

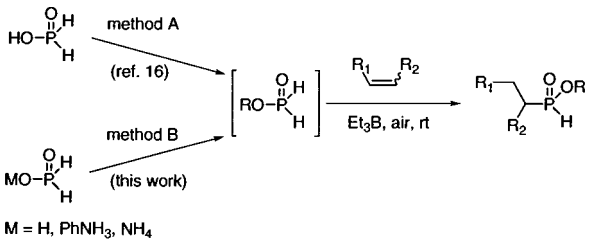
Monosubstituted phosphinic acids can also be esterified with trialkoxysilanes, although the reaction is not as general as with orthosilicates [17]. Since hypophosphorous derivatives are significantly more reactive, we focused on alkoxysilanes as esterification reagents. A wide variety of such organosilicon compounds is available inexpensively or can be prepared easily. Several alkyltrialkoxysilanes, diethoxydimethylsilane, and diisopropoxydimethylsilane were chosen as representative reagents. The results are collected in Table 2.

Again, hypophosphite esters were obtained in high yields from either AHP or concentrated H_3PO_2, and acetonitrile proved to be an optimal solvent for these reactions. The products stability profiles using alkoxysilanes were similar to those obtained using orthosilicate

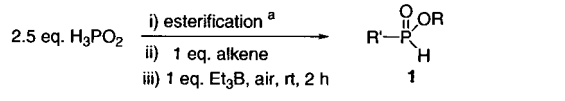
reagents (data not shown). Tri- and di-alkoxysilanes can be useful to replace orthosilicates, particularly in the case of hazardous tetramethylorthosilicate. As little as one equivalent $R'Si(OR)_3$ was necessary to bring about a nearly quantitative reaction. Diethoxydimethylsilane and diisopropoxydimethylsilane also worked well, although in this case, two equivalents were necessary to obtain the corresponding ester in high yield (entries 4, 11, 12). Again, these findings are consistent with our previous work on the esterification of monosubstituted phosphinic acids.

As expected, the alkyl hypophosphite ester is transesterified in the presence of another alcohol (Table 2, entry 10), but the reaction is incomplete, as previously reported in the literature [9]. Based on our previous experience [17], we searched for an organosilicon reagent which could be removed by extraction after a subsequent reaction. While alkoxysilane by-products are usually easy to remove by chromatography on silica gel, purification via a simple extractive work-up might be more practical. We expected and verified that 3-aminopropyltrimethoxysilane is unreactive (entry 13) as it forms a hypophosphite salt of insufficient acidity, while preformed 3-aminopropyltrimethoxysilane hydrochloride did react in moderate yield (entries 14 and 15). We also found in situ-prepared aminopropyltrimethoxysilane trifluoroacetate to be an excellent esterification reagent (entry 16). Some applications of this convenient system are described in the following section.

Finally, even commercial $NaH_2PO_2 \cdot H_2O$ was directly esterified without prior drying, using $(EtO)_3SiCl$ (entry 17), thus suggesting that other reagent systems (for example, $Me_2SiCl_2 + ROH$) could also be employed. Future improvements along these lines are underway and would provide an inexpensive and more general alternative to the alkylation of anhydrous NaH_2PO_2 with triethyloxonium tetrafluoroborate [4].



Scheme 2. Room temperature radical reaction of hypophosphite esters.



Scheme 3. Examples of room temperature radical reactions. **1a**–**c**: CF_3CO_2H (2.5 equivalents), $H_2N(CH_2)_3Si(OMe)_3$ (2.5 equivalents), CH_3CN, reflux, 2 h. **1d**: $(BuO)_4Si$ (2.5 equivalents), cyclohexane, reflux, 2 h.

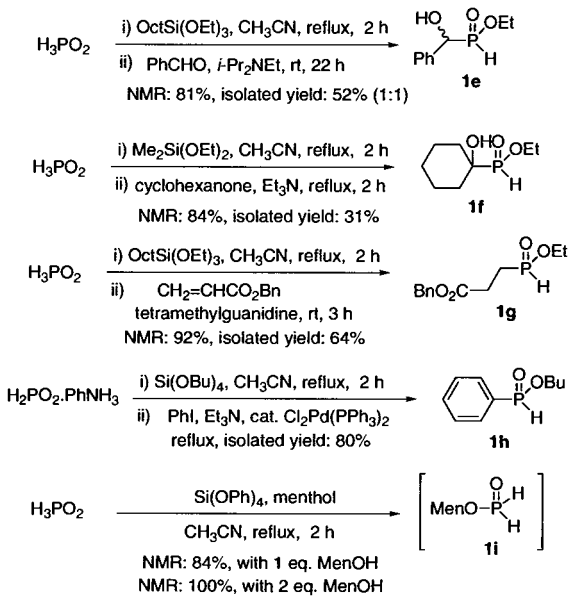
3. Synthetic applications

With a general preparation of hypophosphite esters at hand, we turned our attention to synthetic applications. If the organosilicon by-products present in the reaction mixture are not compatible with a subsequent synthetic step, our esterification would not be very useful. Fortunately, this turns out not to be the case, and some preliminary results are presented below to illustrate the practical utility of the reaction. In the following section, all isolated yields are unoptimized. More systematic studies and novel applications will be reported in due course. The remarkable thermal stability of the hypophosphite esters prepared under our conditions should allow the development of novel methodology for the synthesis of organophosphorus compounds previously not accessible using other esterifications.

3.1. Room temperature radical reaction of hypophosphite esters

Our initial motivation to develop a new synthesis of hypophosphite esters stemmed from our study of hypophosphorous derivatives in radical reactions (Scheme 2) [16]. As discussed earlier, we first used the orthoformate and Dean–Stark methods to study the Et_3B-initiated radical reaction of hypophosphite esters, and these results are described elsewhere (Scheme 2, Method A). Here, we focus our attention on the alkoxysilane-promoted esterification of AHP and H_3PO_2 and demonstrate it is an excellent method for the synthesis of monosubstituted phosphinate esters (Scheme 2, Method B).

In a typical procedure (Scheme 3), a solution of hypophosphite ester (2–2.5 equivalents) is cooled to room temperature, treated with an alkene (one equivalent), and Et_3B (1 M in hexane, 0.1–1 equivalent) is then added to the open reaction vessel. After 2–3 h, the reaction mixture is worked up and purified, affording the phosphinate ester (see Section 5). The corresponding phosphinic acid is formed in much smaller amounts than in Method A, because little or no residual H_3PO_2 contaminates the starting material. Interestingly, acetonitrile was found to be a very good solvent for this methodology, although it has not been widely used in radical reactions. Clearly, the organosilicon by-products present in the reaction mixture do not interfere with the radical process, and the reaction should be



Scheme 4. Representative reactions of hypophosphite esters.

useful for the synthesis of monosubstituted phosphinate esters.

3.2. Other reactions

Various types of reactions previously described in the literature (Scheme 1) can also be conducted. A few representative examples are shown in Scheme 4. Again, the organosilicon compounds present along with the ester do not seem to create any difficulty in the subsequent step.

Hypophosphite esters prepared with our method undergo (Scheme 4) addition to carbonyls (products **1e**, **1f**), Michael addition (product **1g**), and even palladium-catalyzed cross-coupling (product **1h**). The thermal stability of the hypophosphite esters suggests that the latter reaction could be extended to previously unreactive substrates such as aryl bromides. Work along these lines is currently in progress.

Finally, phenyl hypophosphite (Table 1, entry 21) was prepared for the first time, and its transesterification was demonstrated with the synthesis of menthyl hypophosphite (Scheme 4, **1i**). Transesterification or in situ preparation of alkoxysilanes from the corresponding chlorides should prove useful to further expand the scope of hypophosphite esters in organic synthesis.

4. Conclusions and future directions

A novel preparation of hypophosphite esters has been developed. The reaction of hypophosphorous derivatives with various alkoxysilanes is inexpensive, does not require strictly anhydrous reagents, and proceeds satisfactorily in several solvents. The broad scope of this esterification and its demonstrated applicability to further synthetic manipulations should prove a useful alternative to previously available methodology. Future directions include further optimization of the reaction conditions, the preparation of polymer supported reagents, improvements upon existing reactions of hypophosphorous esters, and more importantly the development of novel reactions for the synthesis of organophosphorus compounds. The unique thermal stability profile of the hypophosphite esters shows great promise to achieve the latter objective, and opens up several new research avenues.

Finally, with the ability to prepare various hypophosphite esters in excellent yields, we can focus our attention on harnessing the previously unrealized potential of these compounds to conduct diastereo- and enantioselective reactions [19]. Desymmetrization of the P–H bonds in $ROP(O)H_2$ should prove feasible and would provide a simple entry into P-chiral compounds. Work along these lines is actively being pursued in our laboratory, and results will be disclosed in due course.

5. Experimental

5.1. General chemistry

^{1}H-NMR spectra were recorded on a Varian XL-300 spectrometer. Chemical shifts for ^{1}H-NMR spectra are reported (in parts per million) relative to internal tetramethylsilane (Me_4Si, $\delta = 0.00$ ppm) with $CDCl_3$ as solvent. ^{13}C-NMR spectra were recorded at 75 MHz. Chemical shifts for ^{13}C-NMR spectra are reported (in parts per million) relative to $CDCl_3$ ($\delta = 77.0$ ppm) or C_6D_6 ($\delta = 128.5$ ppm). ^{31}P-NMR spectra were recorded at 121 MHz, and chemical shifts reported (in parts per million) relative to external 85% phosphoric acid ($\delta =$ 0.0 ppm). Radial chromatography was carried out with a Harrison Associates Chromatotron using 1, 2, or 4 mm layers of Silica Gel 60 PF_{254} containing gypsum (E. Merck). Ethyl acetate–hexanes mixtures were used as the eluent for chromatographic purifications. TLC plates were visualized by immersion in anisaldehyde stain (by volume: 93% C_2H_5OH, 3.5% H_2SO_4, 1% CH_3COOH, and 2.5% anisaldehyde) followed by heating. Organic solutions of products were dried over $MgSO_4$, and filtered.

5.2. Reagents and solvents

Organosilicon reagents were purchased from United Chemical Technologies, Aldrich, or Lancaster, and were used as received. *Caution*! Tetramethyl orthosilicate $(MeO)_4Si$ may cause blindness. Wear appropriate

protection. Sodium hypophosphite hydrate, and aq. hypophosphorous acid (50 wt.%), were obtained from Aldrich and used as received. Hypophosphorous acid was concentrated in vacuo on a rotary evaporator, at room temperature (r.t.) for 20–30 min before reaction. Triethylammonium hypophosphite was prepared according to Stawinski et al. [5]. Ammonium hypophosphite was prepared as described in Ref. [21]. Unless otherwise noted, HPLC grade or reagent grade solvents were used throughout. When anhydrous solvents were used, they were prepared as follows: dioxane was dried over activated 4 Å molecular sieves, and stored under N_2; pyridine and triethylamine were distilled from CaH_2 and stored under N_2 over activated 4 Å molecular sieves; tetrahydrofuran (THF) was distilled under N_2 from sodium benzophenone ketyl, and used immediately; benzene was distilled immediately before use, from CaH_2 under N_2; diisopropylethylamine was distilled from CaH_2 and stored under N_2. Anhydrous acetonitrile and DMF were obtained after drying over activated 3 Å molecular sieves, and were stored under N_2.

5.3. ^{31}P-NMR yield measurements

NMR yields were determined by integration of all the ^{31}P signals. Thermal stability studies (Fig. 1) were conducted by monitoring the reactions at timed interval. Some representative NMR data is collected in Table 3.

5.4. Anilinium hypophosphite

Anilinium hypophosphite was prepared as previously described by us [15]. Aniline (196 g, 2.1 mol) was added over 30 min via an addition funnel, to an ice-cold aq. solution of H_3PO_2 (50 wt.%, 278 g, 2.1 mol). The light brown solution rapidly turned into a thick slurry. This was filtered and the off-white crystalline precipitate was washed with cold CH_3COCH_3. The filtrate was concentrated under reduced pressure, and a second crop of crystalline hypophosphite was obtained by adding acetone. (Note: if desired, a third crop can be collected similarly, or alternatively, the mother liquor is concentrated to dryness and dried in vacuo. This crop is very slightly impure but can still be used.) The first two crops were combined and washed with ether, then dried in vacuo over P_2O_5 for 24 h. Anilinium hypophosphite (304 g, 91%) was obtained as light yellow needles (m.p. 113–114 °C). It can be stored at r.t. for several months without affecting its reactivity profile. ^{1}H-NMR (D_2O) δ 8.10–8.45 (br s, 3H), 7.12 (d, $J = 520$ Hz, 2H), 7.0–7.4 (m, 5H); ^{31}P-NMR (D_2O) δ 3.7 (t, $J_{P-H} = 520$ Hz). Anilinium hypophosphite was also reported previously [22].

5.5. Esterification: representative procedure (Tables 1 and 2)

In a typical procedure, a solution (or suspension) of the hypophosphorous compound (5 mmol), alkoxysilane (5 mmol), in solvent (10 ml) is refluxed for 2 h under N_2. At that time, the yield is determined by ^{31}P-NMR.

5.6. Synthetic applications

Isolated yields are unoptimized.

5.6.1. Room temperature radical reactions (Scheme 3)

*5.6.1.1. Methyl (2-pivaloyloxy-ethyl)phosphinate (**1a**).* Concentrated H_3PO_2 (initially 50 wt.% aq. solution, 0.678 g, 5.1 mmol) was dissolved in CH_3CN (HPLC grade, 20 ml) and the reaction flask was equipped with a reflux condenser and placed under N_2. Trifluoroacetic

Table 3
Representative ^{31}P-NMR data of hypophosphite esters in different solvents [a]

Hypophosphite	Chemical shifts (δ) (coupling constants J_{P-H} (Hz))				
	CH_3CN	C_6H_6–toluene	THF–dioxane	DMF	Other
$MeOP(O)H_2$	19.5 (566, 13)	15.5 (558, 13)	17.0 (563, 13)	19.2 (566, 13)	19.9 (575, 13) [b]
$EtOP(O)H_2$	16.2 (565, 10)	12.5 (564, 9)	13.3 (561, 10)	16.0 (564, 10)	14.1 (570) [b]
$BuOP(O)H_2$	16.5 (563, 10)	13.2 (558, 9)	14.5 (562, 9)	16.3 (564, 9)	15.6 (570) [b]
$PhOP(O)H_2$	17.6 (592)	–	–	–	–
$AllylOP(O)H_2$	17.2 (568, 11)	–	–	–	–
i-$PrOP(O)H_2$	13.0 (572, 10)				9.5 (561) [c]
$MenOP(O)H_2$	15.0 (572, 11)	–	–	–	11.3 (563, 11) [d]

[a] Esters obtained under a variety of conditions (hypophosphite starting material, concentration, alkoxysilane), generally had chemical shifts within 0.5 ppm of the given value. $ROP(O)H_2$ coupling patterns: R=Me: tq; R = Et, Bu, Allyl: tt; R=Ph, t; R=*i*-Pr, Men, td.
[b] According to Ref. [2]. The esters were obtained by the orthoformate method.
[c] According to Ref. [9b].
[d] Prepared with the Dean–Stark method, but using cyclohexane as the solvent, see Ref. [16].

acid (0.39 ml, 5.1 mmol), and 3-aminopropyltrimethoxysilane (0.90 ml, 5.1 mmol) were then added successively at r.t. An exothermic reaction immediately took place, and the mixture was heated to reflux. After 2 h, the reaction mixture was allowed to cool to r.t. The flask was open to air, vinyl pivalate (0.30 ml, 2 mmol) was added neat via syringe, followed by triethylborane (1 M in hexanes, 2.0 ml, 2 mmol), and the heterogeneous mixture was stirred in air at r.t. for 2 h. ^{31}P-NMR analysis indicated the product at δ 39 (86%). The crude reaction mixture was treated with EtOAc and aq. $KHSO_4$. The organic layer was washed successively with saturated aq. $NaHCO_3$ (1 ×), and brine (1 ×). Drying, concentration, and purification by radial chromatography (4 mm thickness, EtOAc–hexane 1:1, v/v, EtOAc) afforded **1a** (0.215 g, 55%) as a colorless oil: ^{1}H-NMR ($CDCl_3$) δ 7.20 (d, $J = 548$ Hz, 1H), 4.25–4.45 (m, 2H), 3.83 (d, $J = 12$ Hz, 3H), 2.15–2.35 (m, 2H), 1.21 (s, 9H); ^{13}C-NMR ($CDCl_3$) δ 177.6, 57.2, 52.7 (d, $J_{POC} = 7$ Hz), 38.4, 28.5 (d, $J_{PC} = 94$ Hz), 26.8; ^{31}P-NMR ($CDCl_3$) δ 36.4 (dm, $J_{P-H} = 548$ Hz).

Compounds **1b** and **1c** were prepared similarly.

*5.6.1.2. Methyl cyclohexylphosphinate (**1b**).* ^{1}H-NMR ($CDCl_3$) δ 6.80 (dd, $J = 521$, 2 Hz, 1H), 3.78 (d, $J = 11$ Hz, 3H), 1.6–2.0 (m, 6H), 1.15–1.5 (m, 5H); ^{13}C-NMR ($CDCl_3$) δ 52.8 (d, $J_{POC} = 8$ Hz), 37.4, 36.1, 35.7 (d, $J_{PC} = 89$ Hz), 25.0–26.2 (multiple peaks, could not be deconvoluted), 23.9 (d, $J_{PCC} = 6$ Hz); ^{31}P-NMR ($CDCl_3$) δ 46.7 (d, $J_{P-H} = 521$ Hz).

*5.6.1.3. Methyl (3-(tert-butoxycarbonylamino)propyl)-phosphinate (**1c**).* ^{1}H-NMR ($CDCl_3$) δ 7.09 (d, $J = 533$ Hz, 1H), 4.93 (bs, 1H), 3.79 (d, $J = 12$ Hz, 2H), 3.15–3.25 (m, 2H), 1.7–1.9 (m, 4H), 1.44 (s, 9H); ^{13}C-NMR ($CDCl_3$) δ 155.9, 52.8 (d, $J_{POC} = 7$ Hz), 40.5 (d, $J_{PCCC} = 6$ Hz), 40.4, 28.3, 25.8 (d, $J_{PC} = 94$ Hz), 21.4 (d, $J_{PCC} = 3$ Hz); ^{31}P-NMR ($CDCl_3$) δ 40.5 (dm, $J_{P-H} =$ 521 Hz).

*5.6.1.4. Butyl (4-phenylbutyl)phosphinate (**1d**) [17].* Concentrated H_3PO_2 (initially 50 wt.% aq. solution, 1.385 g, 10.5 mmol) and tetrabutoxysilane (3.233 g, 10.1 mmol) were taken up in cyclohexane (reagent grade, 20 ml). The resulting white suspension was refluxed for 2.5 h, under N_2. The reaction mixture was allowed to cool to r.t. 4-Phenyl-1-butene (0.63 ml, 4.2 mmol) was added neat via syringe, followed by triethylborane (1 M in hexanes, 4.2 ml, 4.2 mmol). The rubber septum was removed and the reaction mixture was stirred in air at r.t. for 2 h. ^{31}P-NMR analysis indicated the product at δ 39.3 (76%). The crude reaction mixture was treated with EtOAc (100 ml) and aq. HCl (1 N, 20 ml). The organic layer was washed successively with saturated aq. $NaHCO_3$ (1 ×), and brine (1 ×). Drying, concentration, and purification by radial chromatography (4 mm thickness, EtOAc–hexane 1:5, 1:1, v/v, EtOAc) afforded **1d** (0.689 g, 65%) as a colorless oil: ^{1}H-NMR ($CDCl_3$) δ 7.06 (d, $J = 530$ Hz, 1H), 7.1–7.3 (m, 5H), 3.9–4.15 (m, 2H), 2.63 (t, $J = 15$ Hz, 2H), 1.55–1.85 (m, 8H), 1.3–1.45 (2H), 0.94 (t, $J = 7$ Hz, 3H); ^{13}C-NMR ($CDCl_3$) δ 141.5, 128.2, 125.7, 65.9 (d, $J_{POC} = 7$ Hz), 35.2, 32.2 (d, $J_{POCC} = 6$ Hz), 32.0 (d, $J_{PCC} = 16$ Hz), 28.5 (d, $J_{PC} = 94$ Hz), 20.2 (d, $J_{PCCC} = 3$ Hz), 18.6, 13.4; ^{31}P-NMR ($CDCl_3$) δ 39.5 (d, $J_{P-H} = 530$ Hz).

5.6.2. Addition to carbonyls (Scheme 4)

*5.6.2.1. Ethyl(phenylhydroxymethyl)phosphinate (**1e**).* A mixture of concentrated H_3PO_2 (initially 50 wt.% aq. solution, 1.370 g, 10.4 mmol), and octyltriethoxysilane (2.855 g, 10.3 mmol), in CH_3CN (HPLC grade, 20 ml), was refluxed for 2 h under N_2 and cooled to r.t. Benzaldehyde (0.96 ml, 9.4 mmol) and anhydrous *i*-Pr_2NEt (1.80 ml, 10.3 mmol) were added via syringe to the cloudy reaction mixture. Stirring was continued at r.t. for 22 h. ^{31}P-NMR analysis indicated the product as a 1:1 mixture of diastereoisomers (δ 38.0 and 35.5) in 81% combined yield. The cloudy, biphasic mixture obtained after concentration was partitioned between EtOAc and aq. $KHSO_4$. The organic layer was washed with saturated aq. $NaHCO_3$ (1 ×), and brine (1 ×). Drying, concentration, and purification by radial chromatography (4 mm thickness, EtOAc–hexane 1:5, 1:1, v/v, EtOAc) afforded **1e** (0.992 g, 52%, 1:1 mixture of diastereoisomers) as a colorless oil: ^{1}H-NMR ($CDCl_3$) δ 7.7–7.8 (0.5H), 7.2–7.5 (m, 5H), 5.8–6.0 (0.5H), 5.5–5.9 (br, 1H), 4.8–5.0 (m, 1H), 3.8–4.1 (m, 2H), 1.1–1.3 (m, 3H); ^{13}C-NMR ($CDCl_3$) δ 135.2 (2), 128.4, 128.1 (2), 127.9, 127.5 (2), 127.4, 126.8, 126.7 (2), 71.7 (d, $J_{PC} = 98$ Hz), 71.3 (d, $J_{PC} = 110$ Hz), 63.4 (d, $J_{POC} = 7$ Hz), 63.1 (d, $J_{POC} = 8$ Hz), 30.1 (d, $J_{PCC} = 7$ Hz), 29.6 (d, $J_{PCC} = 6$ Hz), 16.1 (d, $J_{POCC} = 6$ Hz), 16.0 (d, $J_{POCC} = 7$ Hz); ^{31}P-NMR ($CDCl_3$) δ 36.6 (d, $J_{P-H} =$ 554 Hz), 32.6 (d, $J_{P-H} = 549$ Hz).

*5.6.2.2. Ethyl (1-hydroxy-cyclohexyl)phosphinate (**1f**).* Concentrated H_3PO_2 (initially 50 wt.% aq. solution, 0.678 g, 5.1 mmol) and diethoxydimethylsilane (1.372 g, 9.3 mmol) were dissolved in CH_3CN (HPLC grade, 10 ml). The resulting colorless solution was refluxed for 2 h, under N_2, then cooled to r.t. Cyclohexanone (0.54 ml, 5.2 mmol), and anhydrous Et_3N (0.72 ml, 5.2 mmol) were added, and the reaction mixture was refluxed for 2 h. EtOAc and aq. $NaHSO_4$ were added. The organic layer was washed successively with saturated aq. $NaHCO_3$ (1 ×), and brine (1 ×). Drying, concentration, and purification by radial chromatography (4 mm thickness, hexane, EtOAc–hexane 1:1, v/v, EtOAc) afforded **1f** (0.310 g, 31%) as a colorless liquid: ^{1}H-NMR ($CDCl_3$) δ 6.70 (d, $J = 530$ Hz, 1H), 4.1–4.3 (m, 2H), 1.2–1.9 (m, 10H), 1.36 (t, $J = 7$ Hz, 3H);

^{13}C-NMR ($CDCl_3$) δ 70.5 (d, $J_{PC} = 115$ Hz), 62.8 (d, $J_{POC} = 8$ Hz), 30.1 (d, $J_{PCC} = 7$ Hz), 29.6 (d, $J_{PCC} = 6$ Hz), 25.33, 19.8 (d, $J_{PCCC} = 3$ Hz), 19.7, 16.2 (d, $J_{POCC} = 5$ Hz); ^{31}P-NMR ($CDCl_3$) δ 41.3 (d, $J_{P-H} = 530$ Hz).

5.6.3. Conjugate addition (Scheme 4)

*5.6.3.1. Ethyl (2-benzyloxycarbonyl-ethyl)phosphinate (**1g**).* A mixture of concentrated H_3PO_2 (initially 50 wt.% aq. solution, 0.657 g, 5.0 mmol), and octyltriethoxysilane (1.6 ml, 5.0 mmol), in CH_3CN (HPLC grade, 10 ml), was refluxed for 2 h under N_2, then cooled to r.t. Benzyl acrylate (0.75 ml, 4.9 mmol) and 1,1,3,3-tetramethylguanidine (0.63 ml, 5.0 mmol) were added, and the cloudy reaction mixture was stirred for 3 h. ^{31}P-NMR analysis showed the product at δ 38.1. The solution was partitioned between EtOAc and aq. $KHSO_4$. The organic layer was washed successively with saturated aq. $NaHCO_3$ (1 ×), and brine (1 ×). Drying, concentration, and purification by radial chromatography (4 mm thickness, EtOAc–hexane 1:5, 1.1, v/v, EtOAc) afforded **1g** (0.819 g, 64%) as a colorless oil: ^{1}H-NMR ($CDCl_3$) δ 5.3–5.4 (bs, 5H), 7.19 (d, $J = 545$ Hz, 1H), 5.13 (s, 2H), 3.95–4.2 (m, 2H), 2.6–2.8 (m, 2H), 2.0–2.2 (m, 2H), 1.33 (t, 7 Hz, 3H); ^{13}C-NMR ($CDCl_3$) δ 171.4 (d, $J_{PCCC} = 13$ Hz), 135.2, 128.3, 128.1, 128.0, 66.6, 62.3 (d, $J_{POC} = 7$ Hz), 25.8 ($J_{PCC} = 3$ Hz), 23.2 ($J_{PC} = 95$ Hz), 15.9 ($J_{POCC} = 6$ Hz); ^{31}P-NMR ($CDCl_3$) δ 36.4 (dm, $J_{P-H} = 545$ Hz).

5.6.4. Pd-catalyzed cross-coupling (Scheme 4)

*5.6.4.1. Butyl phenylphosphinate (**1h**) [17,20].* A solution of anilinium hypophosphite (0.952 g, 6 mmol) and tetrabutoxysilane (1.933 g, 6 mmol) in CH_3CN (12 ml) was refluxed for 2 h, under N_2. After cooling to r.t., iodobenzene (0.25 ml, 2 mmol), anhydrous Et_3N (0.30 ml, 2 mmol), and $Cl_2Pd(PPh_3)_2$ (0.025 g, 0.04 mmol), were added successively. The reaction mixture was then refluxed for 5 h. At that point, the black mixture was concentrated under reduced pressure, and the residue partitioned between EtOAc and aq. $KHSO_4$. The organic layer was washed successively with saturated aq. $NaHCO_3$ (1 ×), and brine (1 ×). Drying, concentration, and purification by radial chromatography (4 mm thickness, hexane, EtOAc–hexane 1:1, v/v, EtOAc) afforded **1h** (0.300 g, 80%) ^{1}H-NMR ($CDCl_3$) δ 7.81 (d, $J = 7$ Hz, 1H), 7.76 ($J = 7$ Hz, 1H), 7.58 (d, $J = 562$ Hz, 1H), 7.55–7.6 (m, 1H), 7.45–7.55 (m, 2H), 3.95–4.15 (m, 2H), 1.6–1.8 (m, 2H), 1.35–1.5 (m, 2H), 0.92 (t, $J = 7$ Hz, 3H); ^{13}C-NMR ($CDCl_3$) δ 132.4 (d, $J_{PCCCC} = 3$ Hz), 130.3 (d, $J_{PCCC} = 12$ Hz), 129.4 (d, $J_{PC} = 132$ Hz), 128.1 (d, $J_{PCC} = 14$ Hz), 65.1 (d, $J_{POC} = 7$ Hz), 31.8 ($J_{POCC} = 6$ Hz), 18.2, 12.9; ^{31}P-NMR ($CDCl_3$) δ 25.3 (dm, $J_{P-H} = 563$ Hz).

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References

[1] M.I. Kabachnik, A.E. Shipov, T.A. Mastryukova, Bull. Acad. Sci. USSR 1 (1960) 138.
[2] S.J. Fitch, J. Am. Chem. Soc. 86 (1964) 61.
[3] E.E. Nifant'ev, L.P. Levitan, J. Gen. Chem. USSR 35 (1965) 762.
[4] H.W. Pinnick, M.A. Reynolds, Synth. Commun. 9 (1979) 535.
[5] J. Stawinski, M. Thelin, E. Westman, R. Zain, J. Org. Chem. 55 (1990) 3503.
[6] (a) M.J. Gallagher, H. Honegger, J. Chem. Soc. Chem. Commun. (1978) 54;
(b) A.W. Schwabacher, A.D. Stefanescu, Tetrahedron Lett. 37 (1996) 425.
[7] (a) M.J. Gallagher, H. Honegger, Tetrahedron Lett. 34 (1977) 2987;
(b) M.J. Gallagher, H. Honegger, Aust. J. Chem. 33 (1980) 287;
(c) M.J. Gallagher, R. Garbutt, L.Y. Hua, G.H. Lee, Phosphorus Sulfur Silicon 75 (1993) 201.
[8] I. Devedjiev, V. Ganev, R. Stefanova, G. Borisov, Phosphorus Sulfur 31 (1987) 7.
[9] (a) M.J. Gallagher, J. Sussman, Phosphorus 5 (1975) 91;
(b) M.J. Gallagher, M.G. Ranasinghe, I.D. Jenkins, Phosphorus Sulfur Silicon 115 (1996) 255;
(c) M.J. Gallagher, M.G. Ranasinghe, I.D. Jenkins, J. Org. Chem. 61 (1996) 436.
[10] L. Maier, Helv. Chim. Acta 56 (1973) 489.
[11] H. Lei, M.S. Stoakes, A.W. Schwabacher, Synthesis (1992) 1255.
[12] J. Jankowska, J. Cieslak, A. Kraszewski, J. Stawinski, Tetrahedron Lett. 38 (1997) 2007.
[13] (a) B.E. Ivanov, L.A. Kudryavtseva, Bull. Acad. Sci. USSR 7 (1968) 1544 for examples on the use of hypophosphite esters;
(b) B.E. Ivanov, L.A. Kudryavtseva, Bull. Acad. Sci. USSR 7 (1967) 1447;
(c) I.A. Aleksandrova, L.I. Ufimtseva, Bull. Acad. Sci. USSR 6 (1971) 1218;
(d) V.I. Vysotskii, A.S. Skobun, M.N. Tilichenko, J. Gen. Chem. USSR 49 (1979) 1721;
(e) M.V. Livantsov, A.A. Prishchenko, I.F. Lutsenko, J. Gen. Chem. USSR 56 (1986) 2195;
(f) M.V. Livantsov, A.A. Prishchenko, I.F. Lutsenko, J. Gen. Chem. USSR 56 (1986) 1976;
(g) I.A. Natchev, Phosphorus Sulfur 37 (1988) 133;
(h) I.A. Natchev, Liebigs Ann. Chem. (1988) 861;
(i) C.G. Caldwell, S.P. Sahoo, S.A. Polo, R.R. Eversole, T.J. Lanza, S.G. Mills, L.M. Niedzwiecki, M. Izquierdo-Martin, B.C. Chang, R.K. Harrison, D.W. Kuo, T.-Y. Lin, R.L. Stein, P.L. Durette, W.K. Hagmann, Bioorg. Med. Chem. Lett. 6 (1996) 323;
(j) A.E. Wroblewski, J.G. Verkade, J. Am. Chem. Soc. 118 (1996) 10168;
(k) T. Yamagishi, T. Yokomatsu, K. Suemune, S. Shibuya, Tetrahedron 55 (1999) 12125;
(l) E.K. Baylis, Tetrahedron Lett. 36 (1995) 9389;
(m) I.D. Grice, P.J. Harvey, I.D. Jenkins, M.J. Gallagher, M.G. Ranasinghe, Tetrahedron Lett. 37 (1996) 1087.

[14] (a) C.J.R. Fookes, M.J. Gallagher, J. Chem. Soc. Perkin Trans. 1 (1975) 1876;
(b) C.J.R. Fookes, M.J. Gallagher, H. Honegger, J. Chem. Soc. Chem. Commun. (1978) 324.
[15] J.-L. Montchamp, Y.R. Dumond, J. Am. Chem. Soc. 123 (2001) 510.
[16] S. Deprèle, J.-L. Montchamp, J. Org. Chem. 66 (2001) 6745.
[17] Y.R. Dumond, R.L. Baker, J.-L. Montchamp, Org. Lett. 2 (2000) 3341.
[18] Anilinium hypophosphite is handled in air, and can be stored for several months at room temperature in a dark glass container.
[19] To our knowledge, this has not been investigated. Shibuya and coworkers ([13k]) have conducted the enantioselective hydrophosphinylation of aldehydes, and obtained good enantiomeric excesses at the α-carbinol center, but did not observe any induction at the chiral phosphorus center.
[20] H. Dahn, V.V. Toan, M.N. Ung-Truong, Magn. Reson. Chem. 30 (1992) 1089.
[21] J.-L. Montchamp, F. Tian, J.W. Frost, J. Org. Chem. 60 (1995) 6076.
[22] H. Schmidt, Chem. Ber. 81 (1948) 477.