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Article

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Wet and Dry Processes for the Selective Transformation of Phosphonates to Phosphonic Acids Catalyzed by Brønsted Acids

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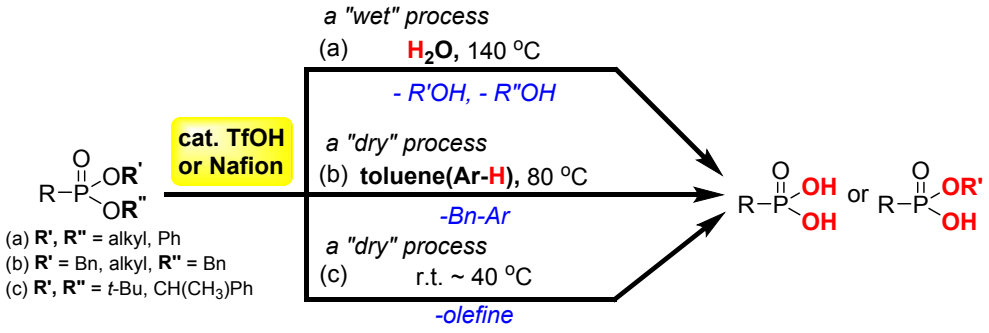
Abstract: A "wet" process and two "dry" processes for converting phosphonate esters to phosphonic acids catalyzed by a Brønsted acid have been developed. Thus, in the presence of water, a range of alkyl, alkenyl and aryl substituted phosphonates can be generally hydrolyzed to the corresponding phosphonic acids in good yields catalyzed by trifluoromethyl sulfonic acid (TfOH) at 140 ^{o}C (the wet process). On the other hand, with specific substituents of the phosphonate esters, the conversion to the corresponding phosphonic acids can be achieved under milder conditions in the absence of water (the dry process). Thus, the conversion of dibenzyl phosphonates to the corresponding phosphonic acids took place smoothly at 80 ^{o}C in toluene or benzene in high yields. Moreover, a selective conversion of benzyl phosphonates RP(O)(OR')(OBn) to the corresponding mono phosphonic acids RP(O)(OR')(OH) can also be achieved under the reaction conditions. The dealkylation via the generation of

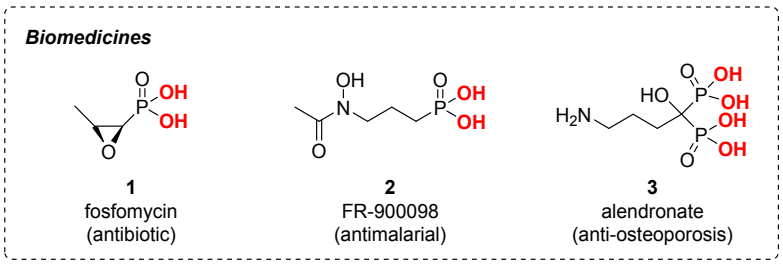
isobutene of di*tert*-butyl phosphonate and related catalyzed by TfOH took place even at room temperature to give the corresponding phosphonic acids in good to high yields. Nafion also shows high catalytic activity for these reactions. By using Nafion as the catalyst, phosphonic acids could be easily prepared in a large scale via a simple process.

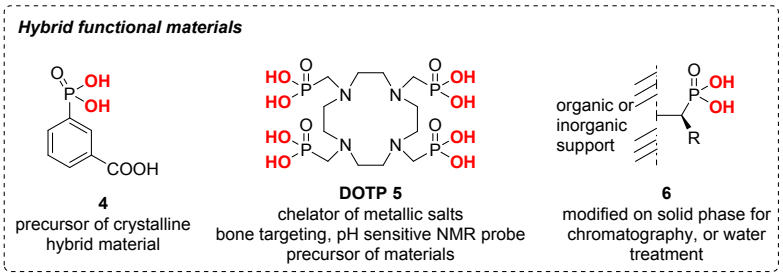


INTRODUCTION

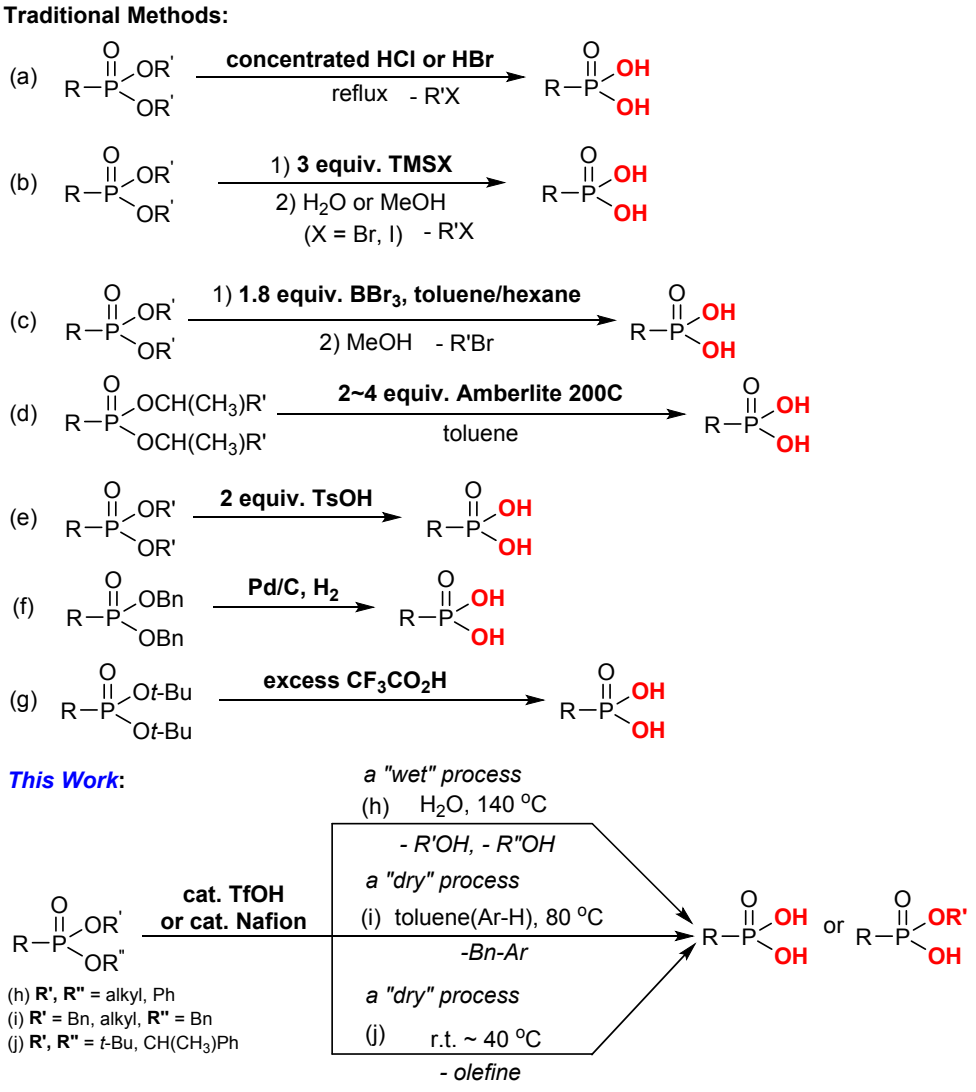
Phosphonic acids are an important class of compounds in medical and agricultural chemistry.[1] For examples, fosfomycin is a clinically used antibiotic, FR-900098 is an antimalarial, and alendronate is a widely employed anti-osteoporosis (Scheme 1).[2a-2c] These phosphonic acids are also widely used in the preparation of hybrid functional materials, as exemplified by compounds **4**, **DOTP 5** and **6** (Scheme 1).[2d-2f] Despite the importance, efficient and general methods for their synthesis are limited (Scheme 2).[1a,3-8]

Scheme 1. Selected Examples of Biomedicines and Hybrid Materials of Phosphonic Acids.





Scheme 2. Synthesis of Phosphonic Acids.



Currently, phosphonic acids are generally prepared via the hydrolysis of dialkyl phosphonates in hot concentrated hydrochloric acid (Scheme 2a)[3] or using halotrimethylsilanes (Scheme 2b).[4] However, the former requires a rather harsh reaction conditions and the later uses expensive halosilanes. Two equivalents of the toxic R'X were concomitantly generated from the reactions. In addition, the purification

of the obtained phosphonic acids from the mixture was also a hard work. Dealkylation of dialkyl phosphonates could also be achieved by using BBr_3 (Scheme 2c).[5] Nitta et al reported the reaction of phosphonates with a cation-exchange resin (Amberlite 200C) (Scheme 2d)[6a] or TsOH (Scheme 2e)[6b] to prepare phosphonic acids. However, all these reactions require an excess amount of BBr_3, cation exchange resin (Amberlite 200C) or TsOH. Hydrolysis by the palladium-catalyzed debenzylation with hydrogen was also known (Scheme 2f).[7] However, the contamination of the heavy metal in the resulted phosphonic acids could be a problem. Di*tert*-butyl phosphonate was also used to prepare the corresponding phosphonic acid by treating it with a large excess amount of trifluoroacetic acid (Scheme 2g).[8]

Herein, we report two catalytic ways for converting phosphonate esters to phosphonic acids, i.e. *the wet process*: a Brønsted acid TfOH can catalyze the hydrolysis of phosphonate esters to produce the corresponding phosphonic acids in good to high yields in the presence of water (Scheme 2h), and *the dry process*: in the absence of water, benzyl phosphonates can be converted to the corresponding phosphonic acids under mild conditions in toluene (Scheme 2i). In addition, monosubstituted phosphonic acids could be selectively obtained by using this dry process from the corresponding benzyl phosphonates (Scheme 2i). Moreover, *tert*-butyl phosphonates and related can readily give the corresponding phosphonic acids even at room temperature (Scheme 2j). The recyclable solid acid Nafion also shows high catalytic activity for these reactions. By using Nafion as the catalyst, phosphonic acids can be easily prepared from the corresponding phosphonate esters in gram-scale reaction via a simple process.

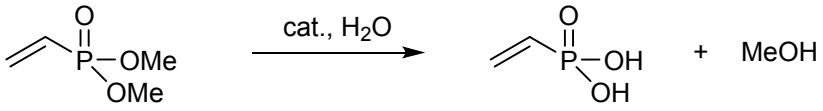
RESULTS AND DISCUSSION

The "wet" process for converting phosphonate esters to phosphonic acids.

As an extension of our study on the selective cleavage of C–O and P–O bonds of phosphites $(RO)_3P$ catalyzed by a Brønsted acid,[9] we found that TfOH was able to catalyze the C–O cleavage of dimethyl vinylphosphonate (**1a**) to generate the corresponding vinylphosphonic acid in the presence of water. As shown in Table 1,

92% yield of **2a** was obtained by heating a mixture of **1a** and water in the presence of 10 mol% H_3PO_3 (Table 1, entry 1). Only 27% yield of **2a** was formed under similar reaction conditions without the acid (Table 1, entry 2). When **1a** was treated with a perfluorinated sulfonic acid (TfOH) under similar conditions, the yield of **2a** increased to 96% (Table 1, entry 3). The yield of **2a** reduced to 52% when the reaction was conducted at 120 °C (Table 1, entry 4). This reaction also took place smoothly by using only 2 equivs water (Table 1, entry 5). Under similar reaction conditions, **1a** was heated at 140 °C for 8 h and 16 h to produce **2a** in 65% and 93% yield, respectively (Table 1, entries 6 and 7). Practically importantly, a solid acid Nafion[10] is equally active as the catalyst, affording almost a quantitative yield of **2a** under similar reaction conditions (Table 1, entry 8). As described below, the use of Nafion catalyst can dramatically simplify the preparation process of phosphonic acids since unlike the difficult removal of TfOH from the products[8a] Nafion can be easily separated from the products by a simple filtration.[10]

Table 1. A Brønsted Acid-Catalyzed Hydrolysis of 1a.[a]



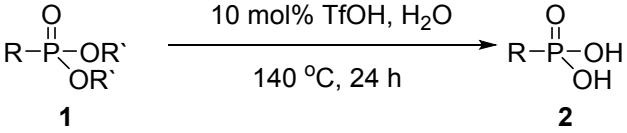
1a **2a**

entry	cat.	H_2O	temperature/℃	time	yield[b] (**2a**)
1	H_3PO_3	0.2 mL	140	24 h	92%
2	none	0.2 mL	140	24 h	27%
3	TfOH	0.2 mL	140	24 h	96%
4	TfOH	0.2 mL	120	24 h	52%
5	TfOH	2 equiv.	140	24 h	88%
6	TfOH	0.2 mL	140	8 h	65%
7	TfOH	0.2 mL	140	16 h	93%
8[c]	Nafion	0.2 mL	140	24 h	95%

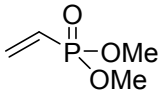
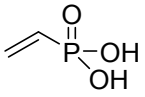
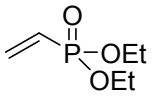
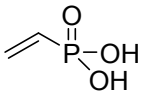
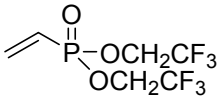
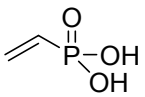
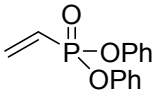
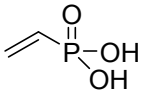
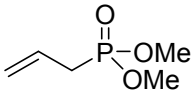
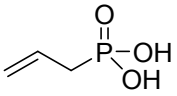
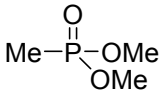
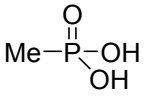
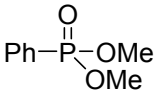
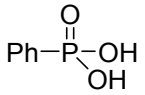
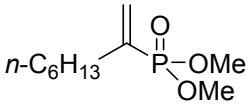
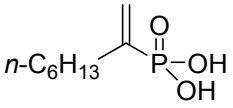
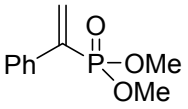
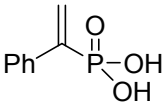
[a]Reaction conditions: a mixture of **1a** (2.53 mmol), catalyst (10 mol%) and H_2O was heated for 24 h in a 10 mL sealed glass tube. [b]Yields based on ^{31}P NMR analysis. [c]10 mg was used.

This hydrolysis reaction was rather general for the synthesis of phosphonic acids. A variety of phosphonate esters under the present reaction conditions gave the

Table 2. Hydrolysis of Phosphonate Esters Catalyzed by TfOH.[a]



1 **2**

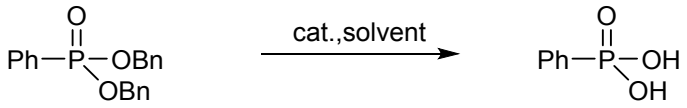
entry	substrate **1**		product **2** (isolated yield)	
1		**1a**		**2a,** 91%
2[b]		**1b**		**2a,** 76%
3		**1c**		**2a,** 96%
4		**1d**		**2a,** 95%
5		**1e**		**2e**, 89%
6		**1f**		**2f**, 93%
7[b]		**1g**		**2g**, 90%
8		**1h**		**2h**, 54%
9		**1i**		**2i**, 81%

[a]Reaction conditions: a mixture of **1** (2.53 mmol), 10 mol% TfOH and 0.2 mL H_2O was heated under air in a 10 mL sealed glass tube at 140 °C for 24 h. [b]48 h.

corresponding phosphonic acids **2** in good to excellent yields. As shown in Table 2, compared to dimethyl vinylphosphonate **1a**, the hydrolysis of diethyl vinylphosphonate **1b** (Table 2, entry 2) was slow and 76% yield of vinylphosphonic acid was obtained after 48 h heating. In contrast, bis(2,2,2-trifluoroethyl) vinylphosphonate **1c** readily produced vinylphosphonic acid **2a** in 96% yield (Table 2, entry 3). Therefore, an

electron-deficient group fastens the hydrolysis. Similarly, diphenyl vinylphosphonate **1d** (Table 2, entry 4) was also readily hydrolyzed to give a high yield of vinylphosphonic acid **2a** under the standard conditions. Under similar conditions, allylphosphonic acid **2e** was obtained in 89% yield by the hydrolysis of the corresponding dimethyl allylphosphonate **1e** (Table 2, entry 5). Methylphosphonic acid **2f** and phenylphosphonic acid **2g** were also obtained from the hydrolysis of the corresponding dimethyl phosphonates **1f** and **1g**, in high yields (Table 2, entries 6 and 7), respectively. Similarly, the hydrolysis of dimethyl 1-octen-2-yl-phosphonate **1h** and dimethyl (1-phenylvinyl)phosphonate **1i** (Table 2, entries 8 and 9) produced good yields of the corresponding phosphonic acids **2h** and **2i**, respectively.

Table 3. A Brønsted Acid-Catalyzed Debenzylation of 1j.[a]



1j **2g**

entry	cat.	solvent	temperature/°C	time	yield[b] (**2g**)
1	TfOH	toluene	80	4 h	25%
2	TfOH	toluene	80	6 h	54%
3	TfOH	toluene	80	8 h	>99%
4	TfOH	toluene	60	8 h	8%
5	TfOH	toluene	40	8 h	2%
6	TfOH	benzene	80	8 h	35%
7	TfOH	benzene	80	12 h	68%
8	TfOH	benzene	80	16 h	>99%
9	TfOH	CH_2Cl_2	80	8 h	trace
10	TfOH	H_2O	80	8 h	N.D.
11	none	toluene	80	8 h	N.D.
12	H_3PO_3	toluene	80	8 h	N.D.
13[c]	Nafion	toluene	80	8 h	>99%

[a]Reaction conditions: a mixture of **1j** (0.5 mmol) and a catalyst (10 mol%) in a solvent (1 mL) was heated in a 10 mL sealed glass tube. [b]Yields based on ^{31}P NMR analysis dissolved in methanol. [c]10 mg was used.

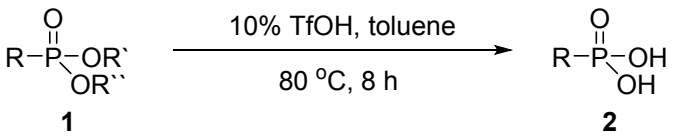
"Dry" processes for converting phosphonate esters to phosphonic acids.

As described above, the wet process by the hydrolysis of phosphonates with water

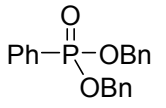
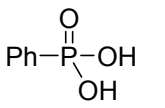
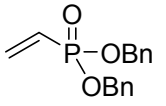
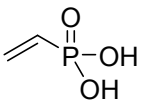
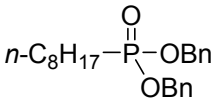
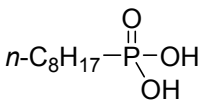
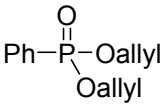
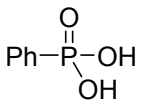
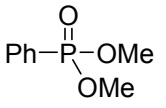
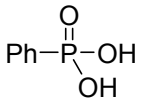
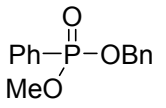
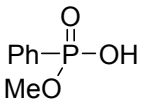
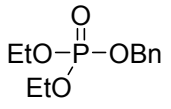
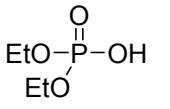
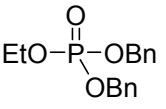
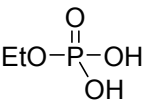
catalyzed by a Brønsted acid could give the corresponding phosphonic acids. However, a long-time heating at a high temperature (140 °C) was necessary. In addition, the removal of water from the products under vacuum also takes a long time. Therefore, a more efficient process for converting phosphonate esters to phosphonic acids under *dry and mild conditions* is desirable. Fortunately, we could solve this problem. Thus, to our delight, we found that, *in the absence of water*, by simply heating dibenzyl phenylphosphonate **1j** in benzene or toluene at 80 °C in the presence of a catalytic amount of TfOH, the debenzylation took place efficiently to produce the corresponding phosphonic acid **2g** in high yields (Table 3). For example, in the presence of 10 mol% TfOH, **1j** was heated in toluene at 80 °C for 4 h and 6 h to produce **2g** in 25% and 54% yield, respectively. (Table 3, entries 1 and 2).[11] When the reaction time was extended to 8 h, a quantitative yield of **2g** was obtained (Table 3, entry 3). However, only 8% and 2% yields of **2g** were obtained when the reactions were performed at 60 °C and 40 °C, respectively (Table 3, entries 4 and 5). The debenzylation took place slowly in benzene, and 35% and 68% yields of **2g** were obtained at 80 °C in 8 h and 12 h, respectively (Table 3, entries 6 and 7). When the reaction time was extended to 16 h, a quantitative yield of **2g** was also produced (Table 3, entry 8). In CH_2Cl_2, only a trace amount of product was detected (Table 3, entry 9). For comparison, **2g** could not be observed at all in water (Table 3, entry 10). No reaction took place in the absence of the acid catalyst (Table 3, entry 11) or with H_3PO_3 (Table 3, entry 12), showing the exceptional catalytic reactivity of the perfluorinated sulfonic acids for this reaction. Solid Nafion was also active for this reaction, and gave a quantitative yield of **2g** under similar reaction conditions (Table 3, entry 13).

This efficient debenzylation reaction could be applied to other substrates. As shown in Table 4, dibenzyl vinylphosphonate **1k** and octylphosphonate **1l** also gave the corresponding vinylphosphonic acid **2a** and octylphosphonic acid **2l** in 93% and 95% yield, respectively, under similar conditions (Table 4, entries 2 and 3). Similarly, diallyl phenylphosphonate produced phenylphosphonic acid **2g** in 75% yield (Table 4, entry 4). However, phenylphosphonic acid **2g** was not formed at all from dimethyl phenylphosphonate (Table 4, entry 5) under this water-free condition. This novel

Table 4. Selective Generation of Phosphonic Acids by Debenzylation of Benzyl Phosphonates and Related Catalyzed by TfOH.[a]



1 **2**

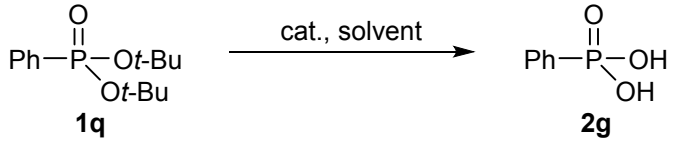
entry	substrate **1**		product **2** (isolated yield)	
1		**1j**		**2g,** 90%
2		**1k**		**2a**, 93%
3[b]		**1l**		**2l**, 95%
4[c]		**1m**		**2g,** 75%
5		**1g**		**2g,** N.D
6		**1n**		**2n**, 82%
7		**1o**		**2o**, 93%
8		**1p**		**2p**, 94%

[a]Reaction conditions: a mixture of **1** (0.5 mmol), 10 mol% TfOH and 1 mL toluene was heated in a 10 mL sealed glass tube at 80 °C for 8 h. [b]100 °C, 24 h. [c]120 °C, 24 h.

difference in reactivity between methyl and benzyl groups makes the generation of monosubstituted phosphonic acids possible via selective dealkylation of phosphonates and related. For example, the benzyl group was selectively removed from benzylmethyl phenylphosphonate **1n** to produce methyl phenylphosphonic acid **2n** in 82% yield (Table 4, entry 6). Similarly, benzyldiethyl phosphate and dibenzylethyl phosphate

were selectively debenzylated to selectively produce the disubstituted phosphoric acid diethyl phosphoric acid **2o** and monosubstituted phosphoric acid monoethyl phosphoric acid **2p** in 93% and 94% yield, respectively (Table 4, entries 7 and 8). Note that a selective synthesis of these phosphoric acid derivatives is rather difficult and required complicated manipulations.

Table 5. A Brønsted Acid-Catalyzed De*tert*-butylation of 1q.[a]



1q **2g**

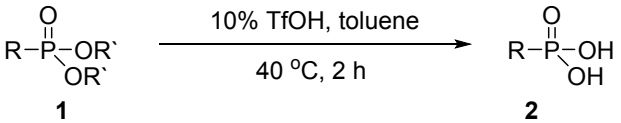
entry	cat.	solvent	temperature/°C	time	yield[b] (**2g**)
1	TfOH	toluene	80	30 min	>99%
2	TfOH	toluene	60	30 min	>99%
3	TfOH	toluene	40	2 h	>99%
4	TfOH	toluene	r.t.	5 h	>99%
5	TfOH	benzene	r.t.	5 h	92%
6	TfOH	CH_2Cl_2	r.t.	5 h	90%
7	none	toluene	r.t.	5 h	N.D.
8	H_3PO_3	toluene	r.t.	5 h	N.D.
9[c]	Nafion	toluene	r.t.	8 h	>99%

[a]Reaction conditions: a mixture of **1q** (0.5 mmol) and a catalyst (10 mol%) in a solvent (1 mL) was heated in a 10 mL sealed glass tube. [b]Yields based on ^{31}P NMR analysis dissolved in methanol. [c]10 mg was used.

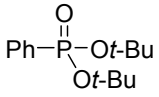
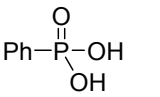
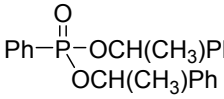
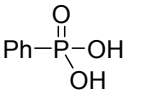
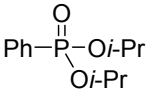
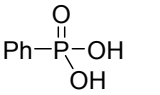
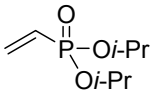
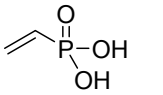
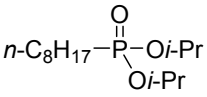
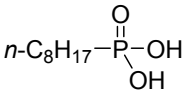
Worth noting is that, when the benzyl group was replaced by *tert*-butyl, the reaction could take place at room temperature to give almost a quantitative yield of the corresponding phosphonic acid **2g** (Table 5). For example, in the presence of 10 mol% TfOH, **1q** was heated in toluene at 80 °C or 60 °C for 30 minutes to produce **2g** in quantitative yield (Table 5, entries 1 and 2). A quantitative yield of **2g** was also obtained by carrying out the reaction at 40 °C for 2 h or at room temperature for 5 h (Table 5, entries 3 and 4). Similarly, the dealkylation also took place in benzene or CH_2Cl_2 to give **2g** in 92% and 90% yield, respectively (Table 5, entries 5 and 6). It was noted that no reaction took place in the absence of the acid (Table 5, entry 7) or with H_3PO_3 (Table 5, entry 8), showing the exceptional catalytic reactivity of the perfluorinated sulfonic

acids for this reaction. Solid Nafion was also active for this reaction, and gave a quantitative yield of **2g** under similar reaction conditions (Table 5, entry 9).

Table 6. Generation of Phosphonic Acids by Dealkylation Catalyzed by TfOH.[a]



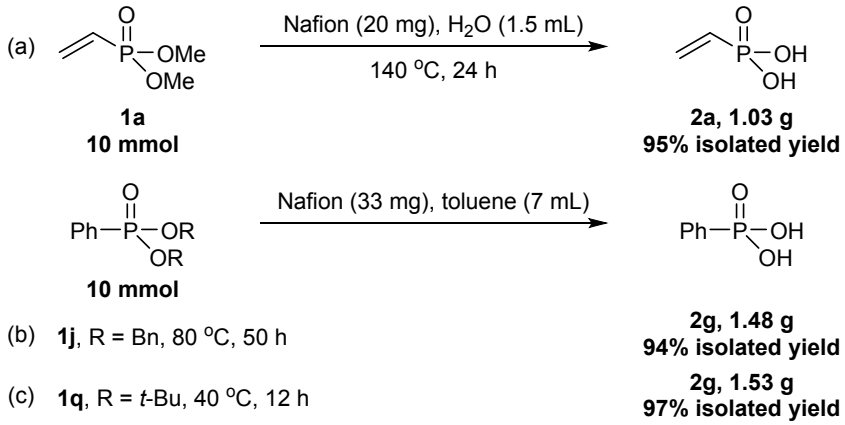
1 **2**

entry	substrate **1**		product **2** (isolated yield)	
1		**1q**		**2g,** 95%
2		**1r**		**2g,** 94%
3[b]		**1s**		**2g**, 92%
4[b]		**1t**		**2a**, 92%
5[c]		**1u**		**2l,** 61%

[a]Reaction conditions: a mixture of **1** (0.5 mmol), 10 mol% TfOH and 1 mL toluene was heated in a 10 mL sealed glass tube at 40 °C for 2 h. [b]120 °C, 24 h. [c]120 °C, 50 h.

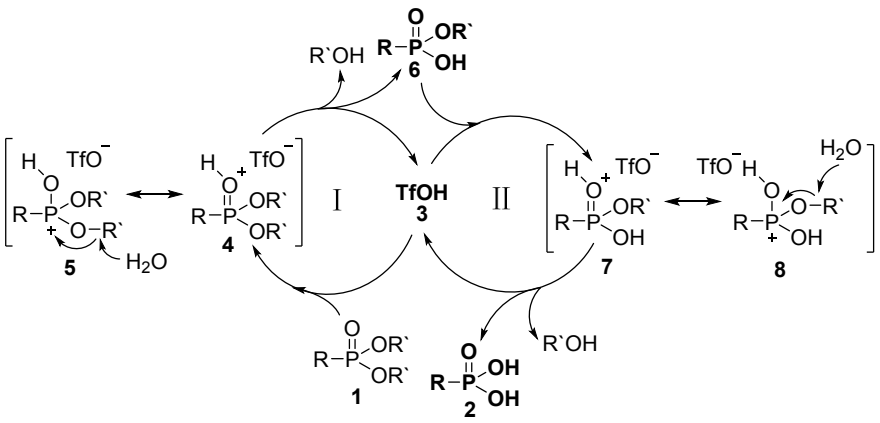
This efficient dealkylation reaction could also be applied to other *sec*-alkyl substituent phosphonates. As shown in Table 6, di(1-phenylethyl) phenylphosphonate **1r** also gave the corresponding phenylphosphonic acid **2g** in 94% yield under similar conditions (Table 6, entry 2). Moreover, diisopropyl phenylphosphonate **1s** also produced phenylphosphonic acid **2g** in 92% yield under similar conditions, though a higher temperature was required (Table 6, entry 3). Similarly, diisopropyl vinylphosphonate and octylphosphonate were deisopropylated to produce the corresponding vinylphosphonic acid **2a** and octylphosphonic acid **2l** in 92% and 61% yield, respectively (Table 6, entries 4 and 5).

Scheme 3. 10 mmol-Scale Reactions Using Solid Acid Nafion as the Catalyst.



The advantages of the present methods compared to the old ones are apparent (See ESI for details) as demonstrated in Scheme 2.[10] As shown in Scheme 3a, a trace amount of Nafion catalyst effectively catalyzed the conversion of **1a** to **2a** in a 10 mmol scale reaction of dimethyl vinylphosphonate **1a** with water. After the reaction, a simple filtration removing the solid catalyst Nafion followed by evaporation of the solution under vacuum could give highly pure vinylphosphonic acid in a high yield. Similarly, as shown in Scheme 3b and 3c, all the reactions are very efficient for the conversion of **1j** and **1q**, to give the corresponding phosphonic acid **2g** in 94% and 97% isolated yields, respectively, by simply removing the solid catalyst via filtration.

Scheme 4. A Proposed Mechanism of the Hydrolysis of Dialkyl Phosphonates Catalyzed by a Brønsted Acid in Water.



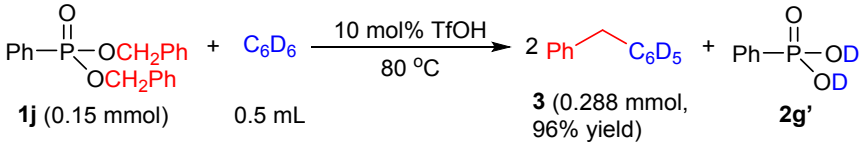
On the bases of the literatures reported,[12,13] a plausible mechanism of the hydrolysis

of dialkyl phosphonates catalyzed by Brønsted acid in water was proposed (Scheme 4). Firstly, TfOH may protonize dialkyl phosphonate **1** to give the intermediate **4** which was transformed to phosphonium salt **5**. Phosphonium salt **5** may undergo C–O cleavage via a S_N2-type attack of H_2O at the R' group of **5** to give intermediate **6**, R'OH, and regenerate TfOH, as TfO^- is a weak nucleophile.[14] On the one hand, the regenerated TfOH may then protonize **6** to give the **7** and **8**. Subsequently, phosphonium salt **8** reacts with water to produce **2**, R'OH, and regenerate TfOH.

It should be noted that the above S_N2-type C–O bond cleavage mechanism might not be applicable to diphenyl phosphonates $RP(O)(OPh)_2$. Alternatively, a P–O bond cleavage, rather than an O–Ph bond cleavage, might take place in cases of $RP(O)(OPh)_2$.[1a]

On the other hand, to probe the debenzylation reaction mechanism in toluene or benzene, control reactions were conducted (Scheme 5) (See ESI for details). When dibenzyl phenylphosphonate **1j** was allowed to debenzylate in benzene-d_6 catalyzed by TfOH under the standard reaction conditions, **3** having a C_6D_5 unit was produced in almost a quantitative yield as determined by ^1H NMR spectroscopy using 1,4-dioxane as an internal standard, indicating that the reaction took place as shown in Scheme 5.[15]

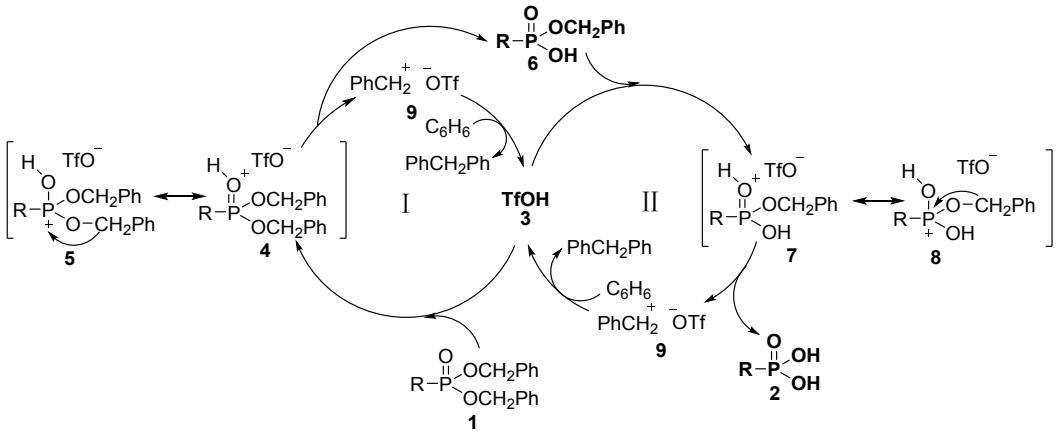
Scheme 5. The Reaction of Dibenzyl Phenylphosphonate (1j) with Benzene-d_6 Catalyzed by TfOH.



The mechanism is not fully understood at present. A plausible mechanism of the debenzylation of dibenzyl phosphonates catalyzed by a Brønsted acid in benzene was shown in Scheme 6.[6,11] TfOH may firstly protonize dibenzyl phosphonate **1** to give the intermediate **4** which could be transformed to phosphonium salt **5**. Phosphonium salt **5** may directly decompose undergo C–O cleavage via a S_N1-type mechanism to give **9** and intermediate **6**. Then **9** reacts with benzene to give diphenylmethane that could be

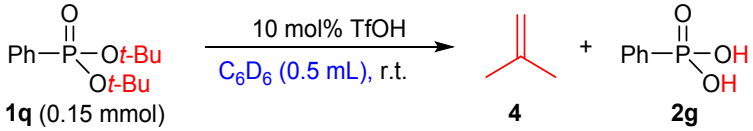
detected by GC-MS[16] and regenerates TfOH. The regenerated TfOH then should further react with **6** to produce **2**.

Scheme 6. A Proposed Mechanism of the Debenzylation of Dibenzyl Phosphonate (1j) Catalyzed by Brønsted Acid in Benzene.



The de*tert*-butylation reaction was considered as a similar reaction with the well-employed regeneration of an alcohol ROH from *t*-BuOR by the deprotection of the *tert*-butyl group.[17] Indeed, when di*tert*-butyl phenylphosphonate **1q** was allowed to react in benzene-d_6 in the presence of TfOH under the standard reaction conditions, isobutene **4** was generated as confirmed by ^{1}H NMR spectroscopy (Scheme 7).

Scheme 7. The De*tert*-butylation of Di*tert*-butyl Phenylphosphonate (1q) in Benzene-d_6 Catalyzed by TfOH.



In summary, we have developed a wet and two dry methods to prepare phosphonic acids from phosphonate esters catalyzed by Brønsted acids. A variety of phosphonates could be efficiently protonated in water or, in the absence of water, in toluene and benzene. Furthermore, selective monodealkylation of dialkyl phosphonates could be achieved by employing this Brønsted acid-catalyzed method in toluene under mild conditions. The reusable solid acid Nafion could be used as the catalyst for these

reactions, that made the preparation of phosphonic acids simple and easy.

EXPERIMENTAL SECTION

General Information

Unless otherwise noted, reactions with water were carried out in Schlenk tubes under air atmosphere, and reactions with toluene were carried out in oven-dried Schlenk tubes under Ar atmosphere. All reagents were purchased and used as received. Phosphonate esters were either purchased or prepared from the corresponding alcohols and phosphorochloridate according to literature procedures.[6a] Mass spectra were recorded at Shimadzu GCMS-QP 2010 plus spectrometer. Flash column chromatography was performed using 200-300 mesh silica gel. ^{1}H, ^{13}C, and ^{31}P NMR were recorded on a JEOL JNM-ECS400 (400 MHz for ^{1}H, 100 MHz for ^{13}C, and 162 MHz for ^{31}P spectroscopy). Chemical shifts for ^{1}H NMR are referred to internal Me_4Si (0 ppm) and reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz) and integration. Chemical shifts for ^{31}P NMR were relative to H_3PO_4 (85% solution in D_2O, 0 ppm).

(a) A typical procedure for TfOH-catalyzed hydrolysis of phosphonate esters in H_2O: To a 10 mL Schlenk tube in air was added dimethyl vinylphosphonate **1a** (0.59 mL, 5 mmol), H_2O (0.4 mL) and trifluoromethanesulfonic acid (44.2 μL, 10 mol%). The tube was heated at 140 °C using a heating aluminum block for 24 h and **1a** was consumed as confirmed by ^{31}P NMR spectroscopy. After removal of the volatiles, the residues (light brown oil) were purified by passing through a short silica gel column (200-300 mesh, dichloromethane/methanol = 4:1 as eluent) to obtain pure product **2a** (colorless oil) in 91% isolated yield (491.5 mg) after removing the volatiles under vacuum (ca 20 Pa) at 130 °C overnight.

(b) 10 mmol-Scale hydrolysis of dimethyl vinylphosphonate with H_2O using Nafion as catalyst: To a 10 mL Schlenk tube was added dimethyl vinylphosphonate **1a** (1.19 mL, 10 mmol), H_2O (1.5 mL) and Nafion (20 mg). The tube was then heated at 140 °C for 24 h. Pure **2a** was obtained after filtration removing Nafion and evaporation under vaccum removing volatiles in 95% isolated yield (1.03 g).

(c) A typical procedure for TfOH-catalyzed debenzylation of phosphonates in toluene: To a 10 mL Schlenk tube was added dibenzyl phenylphosphonate **1j** (676.8 mg, 2 mmol), trifluoromethanesulfonic acid (17.7 μL, 10 mol%) and toluene (2 mL)

under Ar. The tube was then heated at 80 °C for 24 h. The product precipitated as a light brown solid. After removal of the liquids, the residues (light brown solid) were purified by passing through a short silica gel column (200-300 mesh, dichloromethane/methanol = 3:1) to obtain **2g** (white solid) in 91% isolated yield after drying under vacuum (287.8 mg).

(d) 10 mmol-Scale debenzylation of phosphonates in toluene using Nafion as catalyst: To a 25 mL Schlenk tube was added dibenzyl phenylphosphonate **1j** (3.4 g, 10 mmol), Nafion (33 mg) and toluene (7 mL) under Ar. The tube was then heated at 80 °C for 50 h. Water was added to dissolve the product precipitated out and then Nafion was removed by filtration. The aqua solution was collected and volatiles were pumped off under vacuum to give pure **2g** as a white solid in 94% isolated yield (1.48 g).

(e) A typical procedure for TfOH-catalyzed de*tert*-butylation of phosphonates in toluene: To a 10 mL Schlenk tube was added di*tert*-butyl phenylphosphonate **1q** (540.6 mg, 2 mmol), trifluoromethanesulfonic acid (17.7 μL, 10 mol%) and toluene (2 mL) under Ar. The tube was then heated at 40 °C for 2 h and **1q** was completely consumed. The product precipitated out as a light brown solid. After removal of the liquid mixture, the residues (light brown solid) were purified by passing through a short silica gel column (200-300 mesh, dichloromethane/methanol = 3:1 as eluent) to obtain pure product **2g** in 92% isolated yield (white solid, 290.9 mg).

(f) 10 mmol-Scale de-*tert* butylation of phosphonates in toluene catalyzed by Nafion: To a 25 mL Schlenk tube was added di*tert*-butyl phenylphosphonate **1q** (2.7 g, 10 mmol), Nafion (33 mg) and toluene (7 mL) under Ar. The tube was then heated at 40 °C for 12 h. The product precipitated as a white solid. 7 mL MeOH was added to dissolve the white solid. Pure **2g** was obtained after filtration removing Nafion and pumping off the volatiles under vacuum in 97% isolated yield (white solid, 1.53 g).

(g) The reaction of dibenzyl phenylphosphonate (1j) in benzene-d_6 catalyzed by TfOH: To an NMR tube was added dibenzyl phenylphosphonate **1j** (50.8 mg, 0.15 mmol) and C_6D_6 (0.5 mL), and its ^{1}H NMR was taken. Trifluoromethanesulfonic acid (1.3 μL, 10 mol%) was then added to the NMR tube. The tube was gently shaken at room temperature for ca. 0.5 h, and was subjected to ^{1}H NMR measurement again. The tube was then heated at 80 °C, and its ^{1}H NMR were taken after 1 h and 13 h, respectively. ^{1}H NMR revealed that the reaction completed after 13 h at 80 °C. 1,4-Dioxane (25.7 μL, 0.3 mmol) was added to the NMR tube as an internal standard, and ^{1}H NMR showed that diphenylmethane-d_5 was obtained in 96% yield (0.288 mmol).

(h) The de*tert*-butylation of di*tert*-butyl phenylphosphonate (1q) in benzene-d_6 catalyzed by TfOH: To an NMR tube was added di*tert*-butyl phenylphosphonate **1q** (40.6 mg, 0.15 mmol) and C_6D_6 (0.5 mL) and subjected to ^{1}H NMR measurement. Trifluoromethanesulfonic acid (1.3 μL, 10 mol%) was then added to the NMR tube. The tube was slightly shaken at room temperature and was subjected to ^{1}H NMR measurement after 0.5 h, 1.5 h, 3.5 h and 5 h, respectively. ^{1}H NMR showed that the reaction completed after 5 h and isobutene **4** was generated.

^{1}H, ^{13}C and ^{31}P NMR Spectral Data of the Products

Vinylphosphonic acid (2a).[18a] Colorless oil (248.7 mg, 91%). ^{1}H NMR (400 MHz, D_2O): δ 5.70–5.66 (m, 2H), 5.64–5.63 (m, 1H). ^{13}C{1H} NMR (100 MHz, D_2O): δ 133.8, 126.7 (d, $J_{C\text{-}P}$ = 176.6 Hz). ^{31}P NMR (162 MHz, D_2O): δ 16.7.

Allylphosphonic acid (2e).[18b] White solid (274.8 mg, 89%). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ 8.89 (s, 2H), 5.90 (s, 1H), 5.34–5.27 (m, 2H), 2.74–2.71 (m, 2H). ^{13}C{1H} NMR (100 MHz, $(CD_3)_2CO$): δ 128.5 (d, $J_{C\text{-}P}$ = 20.0 Hz), 119.6 (d, $J_{C\text{-}P}$ = 10.9 Hz), 32.6 (d, $J_{C\text{-}P}$ = 140.1 Hz). ^{31}P NMR (162 MHz, $(CD_3)_2CO$): δ 28.4.

Methylphosphonic acid (2f).[18c] Colorless oil (225.9 mg, 93%). ^{1}H NMR (400 MHz, D_2O): δ 1.28 (dt, J = 17.2 Hz, 5.2 Hz, 3H). ^{13}C{1H} NMR (100 MHz, D_2O): δ 11.7 (d, $J_{C\text{-}P}$ = 135.7 Hz). ^{31}P NMR (162 MHz, D_2O): δ 31.1.

Phenylphosphonic acid (2g).[6a] White solid (71.1 mg, 90%). ^{1}H NMR (400 MHz, D_2O): δ 7.63–7.57 (m, 2H), 7.45–7.41 (m, 1H), 7.37–7.32 (m, 2H). ^{13}C{1H} NMR (100 MHz, D_2O): δ 132.3 (d, $J_{C\text{-}P}$ = 2.7 Hz), 130.5 (d, $J_{C\text{-}P}$ = 182.2 Hz), 130.4 (d, $J_{C\text{-}P}$ = 10.4 Hz), 128.7 (d, $J_{C\text{-}P}$ = 14.8 Hz). ^{31}P NMR (162 MHz, D_2O): δ 17.2.

Oct-1-en-2-ylphosphonic acid (2h).[18d] White solid (262.6 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.59 (s, 2H), 5.96 (d, J = 23.6 Hz, 1H), 5.63 (d, J = 49.6 Hz, 1H), 2.28–2.21 (m, 2H), 1.50–1.48 (m, 2H), 1.27–1.25 (m, 6H), 0.88–0.85 (m, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$): δ 139.9 (d, $J_{C\text{-}P}$ = 176.6 Hz), 127.4 (d, $J_{C\text{-}P}$ = 9.4 Hz), 31.8, 31.7, 28.9, 27.9 (d, $J_{C\text{-}P}$ = 5.7 Hz), 22.7, 14.1. ^{31}P NMR (162 MHz, $CDCl_3$): δ 21.9.

1-Phenylvinylphosphonic acid (2i).[18e] White solid (377.3 mg, 81%). ^{1}H NMR (400

MHz, $(CD_3)_2CO$): δ 9.94 (s, 2H), 7.65–7.64 (m, 2H), 7.47–7.43 (m, 3H), 6.32 (d, J = 22.0 Hz, 1H), 6.17 (d, J = 46.0 Hz, 1H). $^{13}C\{1H\}$ NMR (100 MHz, $(CD_3)_2CO$): δ 141.5 (d, $J_{C\text{-}P}$ = 174.5 Hz), 137.1 (d, $J_{C\text{-}P}$ = 10.4 Hz), 130.2, 128.7, 128.5, 127.7. ^{31}P NMR (162 MHz, $(CD_3)_2CO$): δ 17.6.

n-Octylphosphonic acid (2l).[18f] White solid (92.2 mg, 95%). ^1H NMR (400 MHz, $CDCl_3$): δ 9.04 (s, 2H), 1.78–1.69 (m, 2H), 1.65–1.55 (m, 2H), 1.36–1.26 (m, 10H), 0.89–0.86 (m, 3H). $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$): δ 31.9, 30.5 (d, $J_{C\text{-}P}$ = 17.1 Hz), 29.1, 26.2, 24.7, 22.7, 22.1 (d, $J_{C\text{-}P}$ = 4.6 Hz), 14.1. ^{31}P NMR (162 MHz, $CDCl_3$): δ 37.8.

Methyl phenylphosphonic acid (2n).[6a] White solid (70.6 mg, 82%). ^1H NMR (400 MHz, D_2O): δ 7.59–7.53 (m, 2H), 7.43–7.41 (m, 1H), 7.37–7.32 (m, 2H), 3.42 (dd, J = 4.0 Hz, 11.6 Hz, 3H). $^{13}C\{1H\}$ NMR (100 MHz, D_2O): δ 132.6 (d, $J_{C\text{-}P}$ = 2.4 Hz), 131.0 (d, $J_{C\text{-}P}$ = 10.0 Hz), 128.8 (d, $J_{C\text{-}P}$ = 14.8 Hz), 128.4 (d, $J_{C\text{-}P}$ = 182.7 Hz), 52.5 (d, $J_{C\text{-}P}$ = 5.0 Hz). ^{31}P NMR (162 MHz, D_2O): δ 20.4.

Diethyl phosphoric acid (2o).[6a] White solid (71.7 mg, 93%). ^1H NMR (400 MHz, D_2O): δ 3.88–3.84 (m, 4H), 1.12 (t, J = 7.0 Hz, 6H). $^{13}C\{1H\}$ NMR (100 MHz, D_2O): δ 63.5 (d, $J_{C\text{-}P}$ = 5.4 Hz), 15.5 (d, $J_{C\text{-}P}$ = 6.6 Hz). ^{31}P NMR (162 MHz, D_2O): δ 0.6.

Ethyl phosphoric acid (2p).[6a] Colorless oil (59.2 mg, 94%). ^1H NMR (400 MHz, D_2O): δ 3.78–3.70 (m, 2H), 0.98 (dt, J = 2.4 Hz, 7.2 Hz, 3H). $^{13}C\{1H\}$ NMR (100 MHz, D_2O): δ 63.5 (d, $J_{C\text{-}P}$ = 5.1 Hz), 15.3 (d, $J_{C\text{-}P}$ = 6.4 Hz). ^{31}P NMR (162 MHz, D_2O): δ 0.2.

ASSOCIATED CONTENT

Supporting Information.

The Supporting Information is available free of charge on the ACS Publications website at http://pubs.acs.org. Details of the typical produces, the control experiments of the mechanistic studies and copies of ^1H, ^{31}P and ^{13}C NMR spectra.

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Notes

The authors declare no competing financial interest.

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