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A General Protocol for the Synthesis of *H*-α-Hydroxyphosphinates

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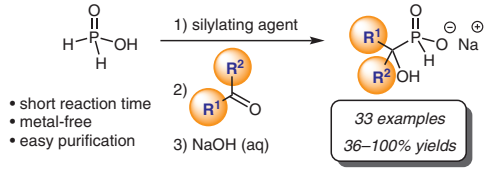

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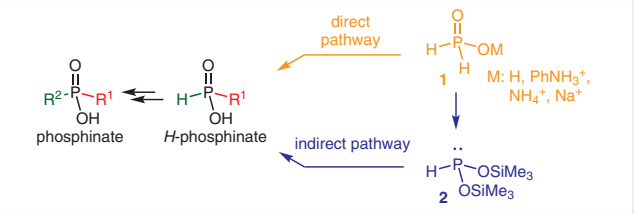
Abstract A general synthetic procedure was developed for *H*-α-hydroxyphosphinates via Abramov reaction. The present work is a complementary study to those reported till now. This methodology has the advantage that it can be applied to various aliphatic and (hetero)aromatic substrates. The *H*-α-hydroxyphosphinates were easily purified and obtained in good to excellent yields in shorter times. A ^{31}P NMR spectroscopy study has shown that only 2 equivalents of a silylating agent were required.

Keywords α-hydroxyphosphinate, synthetic methods, phosphorus, phosphonylation, *H*-phosphinate

Phosphinates are an important class of organophosphorus compounds with a phosphorus atom attached to two oxygens $R^1R^2P(O)(OR)$ ($R^1/R^2/R$ = hydrogen/carbon chain). The P–C bond in phosphonates and even more in phosphinates, provides a high stability and the ability to mimic phosphate esters and carboxylates. Phosphinates represent consequently interesting scaffolds for the development of novel therapeutic molecules.[1] More particularly, *H*-phosphinates (R^1 = H, R^2 = carbon chain) can be precursors of phosphinates (R^1/R^2 = carbon chain) as phosphinic acid pseudopeptides. These peptide isosteres contain a non-hydrolyzable phosphinic acid function instead of a peptide bond that can mimic the substrate transition state for hydrolytic enzymes[2] as matrix metalloproteinases (MMPs)[3] and aspartic acid proteinases.[4] Moreover, peptidomimetic phosphinates are potent inhibitors in different pathologies as cancer, neurodegenerative diseases, parasitic, and viral diseases.[5]

In this context, a straightforward and convenient access to *H*-phosphinates still represents a major issue for the synthesis of bioactive molecules. Several commonly general synthetic pathways are reported in the literature to obtain *H*-phosphinates from hypophosphite derivatives (direct pathway) or from bis(trimethylsilyl)phosphonite $(TMSO)_2PH$ (indirect pathway) (Scheme 1). The direct pathway involves either a radical addition of hypophosphorous acid to alkenes in the presence of a radical initiator (Et_3B/O_2; AIBN)[6] or a palladium-catalyzed cross-coupling reaction of various hypophosphites $MOP(O)H_2$ (M = H, $PhNH_3^+$, NH_4^+, Na^+) and halide substrates RX [R = (hetero)aryl, alkenyl, allylic, benzylic; X = I, Br, OTf, Cl, CH_2Cl].[7] The indirect pathway usually involves the addition of excess in situ preformed phosphonite $(TMSO)_2PH$ on various electrophiles[8] such as alkyl halides,[9] aldehydes/ketones,[10] imines,[11] and α,β-unsaturated esters.[12] For this indirect pathway, the preparation of $(TMSO)_2PH$ is crucial and often inconvenient as its preparation involves a large amount of silylating agent ($TMSCl/Et_3N$ or BSA) or refluxing in the presence of HMDS for several hours. Besides, the subsequent reactions between $(TMSO)_2PH$ and the various electrophiles often required extended reaction times. A large quantity of $(TMSO)_2PH$ is often used in order to avoid the formation of symmetrical disubstituted phosphinates.[8,10g] Although the two-step strategy is well documented in the literature, no general procedure can be efficiently used on various functionalized substrates.

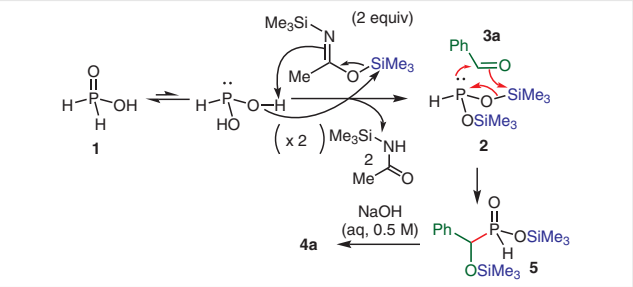


Scheme 1 Synthetic pathways to phosphinates and *H*-phosphinates

For the past years our team has already studied and reported the synthesis of substituted phosphinic acids.[13] Herein, we disclose a complementary study in order to propose an easily handled general protocol for Abramov reaction to synthesize α-hydroxyphosphinates. Our approach does not necessitate the previous inconvenient preparation of a hypophosphite salt and the use of excess amount of $(TMSO)_2PH$. Furthermore, our methodology furnishes easily purified compounds in very satisfying yields and shorter times than previously reported in the literature.[8]

At the outset of this study, the equimolar Abramov reaction was conducted with hypophosphorous acid (**1**) and benzaldehyde (**3a**) in the presence of *N*,*O*-bis(trimethylsilyl)acetamide (BSA) in dichloromethane at 0 °C (Table 1). Initially, BSA (3 equiv) was dropwise mixed with hypophosphorous acid (**1**) over 40 minutes to generate in situ the bis(trimethylsilyl)phosphonite (**2**), which was subsequently added over 20 minutes to a solution of benzaldehyde (1 equiv) in dichloromethane at 0 °C (Table 1, entries 1–3: method A). A ^{31}P NMR spectrum after 1 hour indicated a total conversion and the expected α-hydroxyphosphinate **4a** was easily isolated as a solid sodium salt in a good yield of 70% (entry 1). We were also surprised that the reaction was already complete at the end of the bis(trimethylsilyl)phosphonite (**2**) addition (entries 3 vs. 1 and 2). Moreover, symmetrically disubstituted phosphinate was not formed as was generally observed in many other works.[8,10h] Indeed, the excess of BSA could silylate the *H*-α-hydroxyphosphinate to form a P(III) silylphosphonite. This P(III) specie may compete with **2** for the addition onto **3a** and thus form a symmetrically disubstituted phosphinate as a side-product. Thereafter, the previous procedure was modified in order to easily handle the reaction, by directly adding the solution of benzaldehyde (**3a**) onto the in situ bis(trimethylsilyl)phosphonite (**2**) (entry 4: method B). We were pleased to observe the formation of the expected α-hydroxyphosphinate **4a** in a higher yield (85%). As previously mentioned, symmetrically disubstituted phosphinate was not detected. Then, the reaction was carried out by decreasing the amount of BSA (2 equiv) in the first step followed by the method B procedure (entry 5). The reaction was successful and the product **4a** was obtained in an excellent yield (96%). Although a large quantity of silylating agent is often used in the literature to form the bis(trimethylsilyl)phosphonite (**2**) starting from hypophosphorous acid (**1**), only 2 equivalents are actually required to perform the silylation based on the postulated reaction mechanism shown in Scheme 2.

This reaction indeed could proceed because of the P(V)/P(III) species equilibrium existing between hypophosphorous acid (**1**) and its phosphonite form. The silylation actually allows the equilibrium displacement by trapping the phosphonite. Then, the attack of **2** onto **3a** may proceed by a concerted five-membered-ring transition state in which the TMS moiety may activate the aldehyde as a Lewis

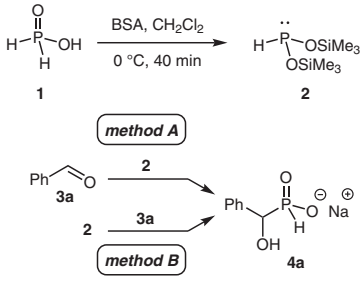


Scheme 2 Postulated mechanism of the Abramov reaction between hypophosphorous acid (**1**) and benzaldehyde (**3a**) in the presence of BSA as silylating agent

acid. The hydrolysis of the silylated α-hydroxyphosphinate **5** finally leads to the resulting sodium α-hydroxyphosphinate **4a**.

Under the method B conditions, the reaction progress was followed by $^{31}P\{^1H\}$ and ^{31}P NMR in order to identify the different P(III) and P(V) species proposed above (Figure 1). First of all, when the silylating agent BSA is added to hypophosphorous acid (**1**), we observed the fast disappearance of its signal (**1**, 12.8 ppm) and an emerging sole signal in the P(III) region corresponding to the bis(trimethylsilyl)phosphonite (**2**, 141.4 ppm). The coupling ^{31}P NMR spectra (in blue) show the fitting multiplicities a triplet for

Table 1 One-Pot Abramov Reaction of Benzaldehyde **3a** and Hypophosphorous Acid (**1**) in the Presence of *N*,*O*-Bis(trimethylsilyl)acetamide (BSA)[a]



Entry	BSA (equiv)	Method[b]	Time (min)[c]	Yield (%)[c,d]
1	3	A	80	70
2	3	A	35	70
3	3	A	20	71
4	3	B	20	85
5	2	B	20	96

[a] Reaction conditions: To a solution of **1** (10 mmol) in anhyd CH_2Cl_2 (2 mL) was added dropwise BSA (20 mmol) under an argon atmosphere at 0 °C. After 40 min, the adequate solution (method A or B) was added dropwise to the reaction mixture under argon atmosphere at 0 °C, then the mixture was quenched with aq 0.5 M NaOH.
[b] For details, see experimental section.
[c] The reaction was monitored by ^{31}P NMR spectroscopy. The indicated time includes the time of addition.
[d] Isolated yield of α-hydroxyphosphinate **4a**.

1 ($^1J_{PH}$ = 568.1 Hz) and a doublet for **2** ($^1J_{PH}$ = 174.6 Hz), respectively. After the addition of benzaldehyde (**3a**), the bis(trimethylsilyl)phosphonite (**2**) signal disappeared in favor of a new signal at 22.1 ppm [P(V) area] correlated to the silylated α-hydroxyphosphinate **5** formation. After hydrolysis, ^{31}P NMR signal shifted to 26.7 ppm corresponding to **4a**. This signal multiplicity is an expected doublet of doublets ($^1J_{PH}$ = 517.2 Hz; $^2J_{PH}$ = 8.7 Hz). It was noted that a small quantity of silylated phosphorous acid **6** was detected at –14.1 ppm probably due to the bis(trimethylsilyl)phosphonite (**2**) oxidation leading to the disodium salt **7**. As previously mentioned, we never detected any signal corresponding to the symmetrically disubstituted phosphinate formation even in excess of BSA.[8,10h]

Under these optimized conditions, the scope of the Abramov reaction was studied on various aromatic and alkyl substituted aldehydes (Scheme 3). Most of the reactions were almost complete after only 30 minutes to afford sodium α-hydroxyphosphinates **4a–v** after simple washes in good to excellent yields (60 to 99%). The introduction of halogen on *ortho*- or *para*- positions of benzaldehyde successfully led to the expected α-hydroxyphosphinates **4b–d**, albeit a lower yield was obtained starting from the 2-chlorobenzaldehyde (**3b**) probably due to the steric hindrance. As a general trend, the substitution of an electron-donating group at the *para*-position of benzaldehyde by an electron-withdrawing group provided the α-hydroxyphosphinates **4f–h** in similar excellent yields (85–98%).

However, when the reaction was carried out with hypophosphorous acid (**1**) and *m*-nitrobenzaldehyde (**3i**), the corresponding α-hydroxyphosphinate **4i** was obtained in a lower yield of 49%. Moreover, the reaction was also successful even in the presence of bulkier aromatic and heteroaromatic aldehydes **3j–o** and gave the α-hydroxyphosphinates **4j–o** in good to excellent yields (60 to 100%).

We then performed the reaction between various alkyl aldehydes **3p–v** and hypophosphorous acid (**1**) in the presence of BSA under the optimized conditions. Remarkably, the reaction was successful in the presence of challenging aldehydes like formaldehyde (**3p**) and acetaldehyde (**3q**). In the first case, the gaseous formaldehyde, in situ generated by depolymerization of paraformaldehyde,[14] was bubbled

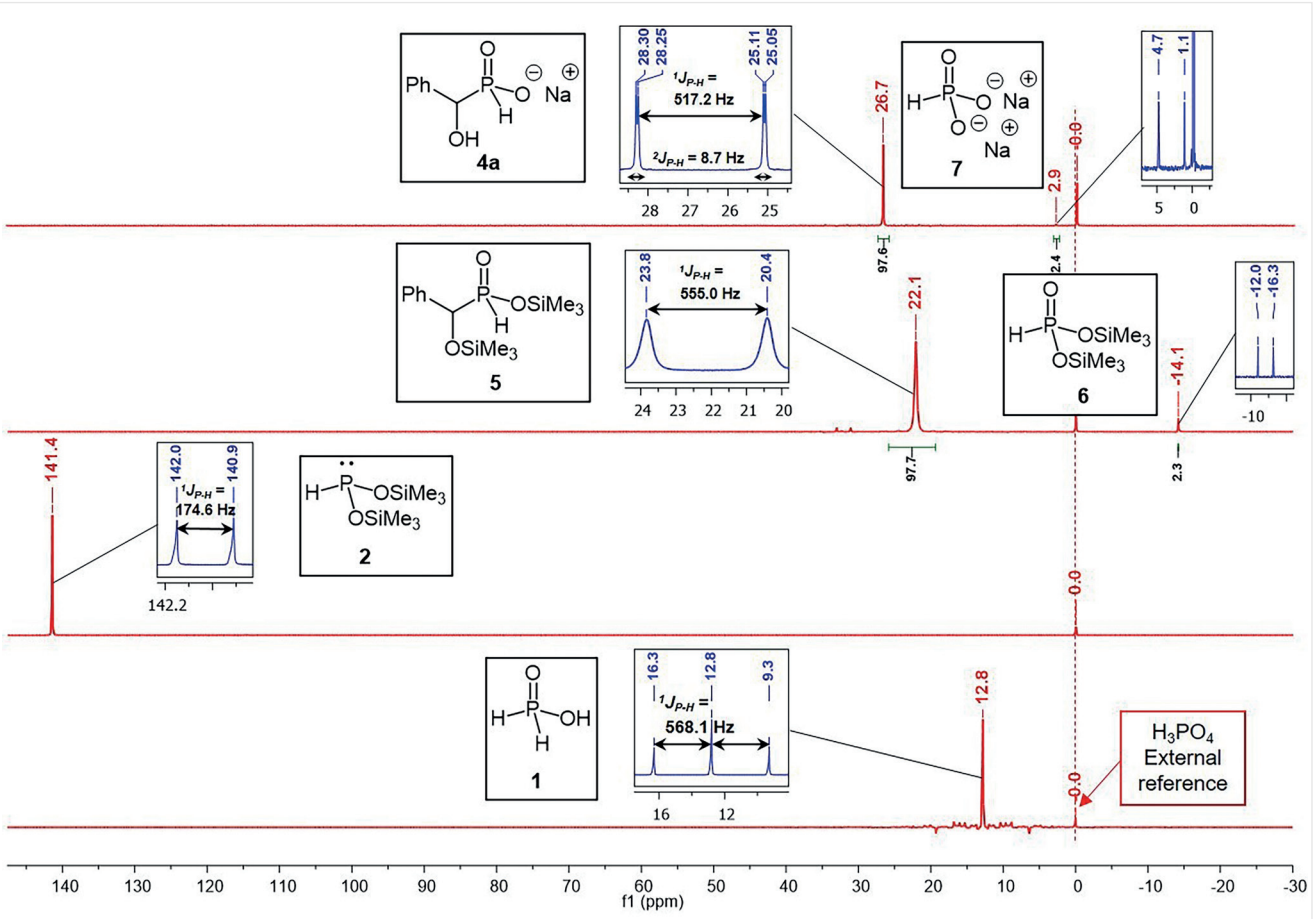
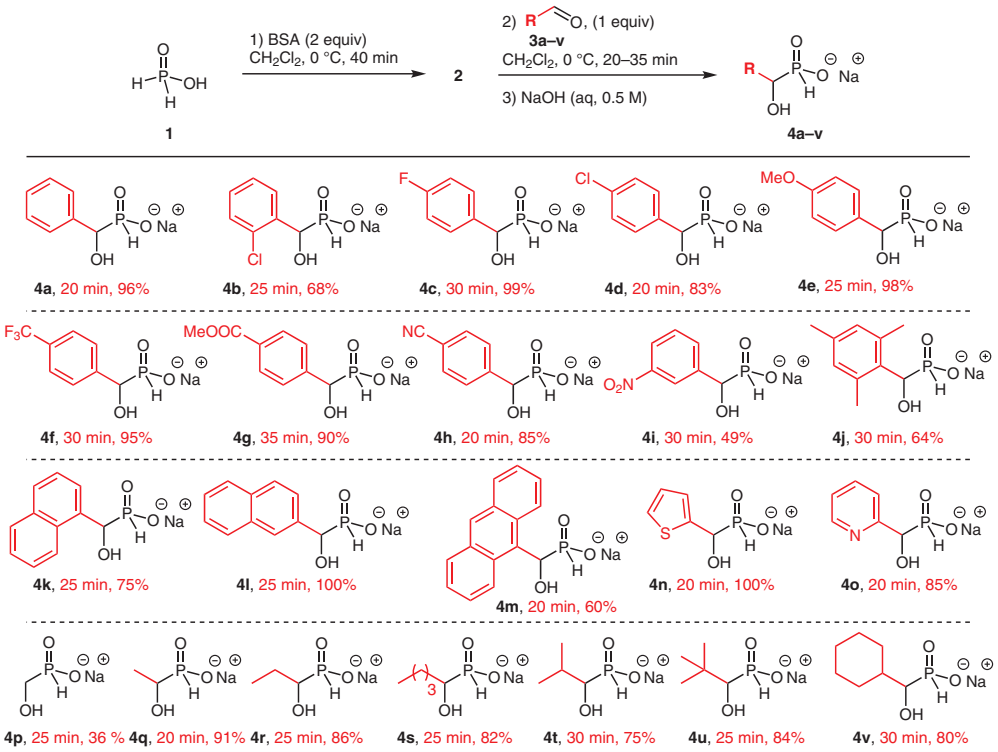


Figure 1 ^{31}P{^{1}H} (in red) and ^{31}P (in blue) NMR monitoring of the Abramov reaction between hypophosphorous acid (**1**; 1 equiv) and benzaldehyde (**3a**; 1 equiv) in the presence of BSA (2 equiv)

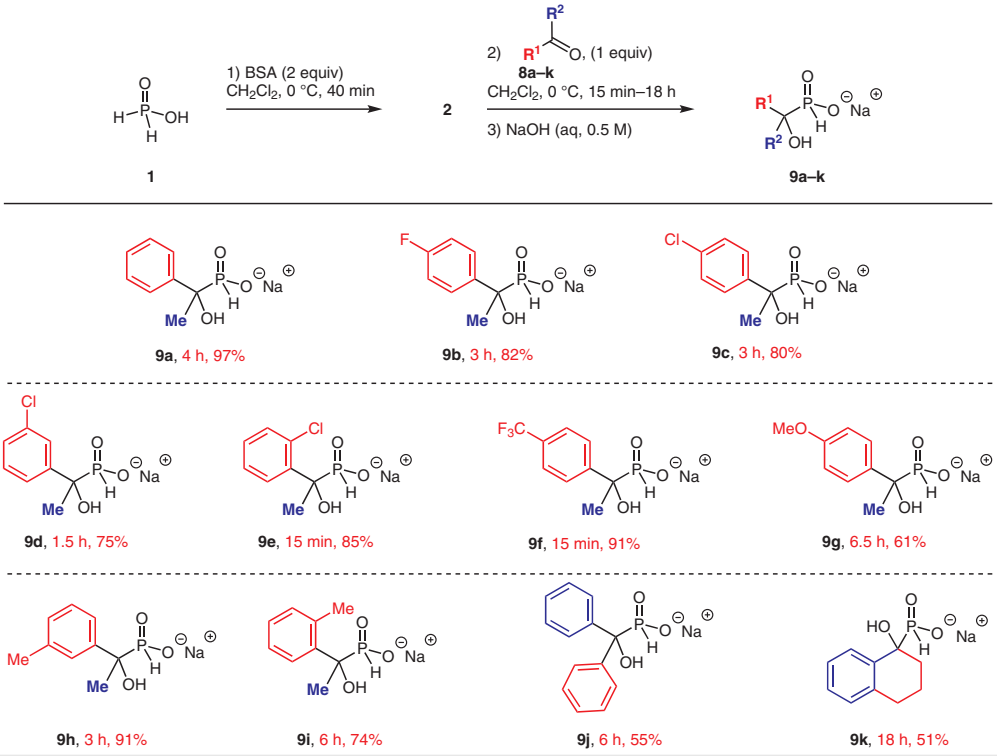


Scheme 3 Scope of aldehydes

through the phosphonite solution at 0 °C under an argon flux. The reaction conversion did not exceed 45% even after extended time. However, the corresponding α-hydroxyphosphinate **4p** was still isolated in a yield of 36%. This significant and unoptimized result is the first example for the synthesis of (1-hydroxymethyl)phosphinate (**4p**) under mild conditions. Indeed, only few work reported the synthesis of **4p** under harsh conditions and long reaction time.[15] It was also noted that the reaction conversion was quite low in the presence of paraformaldehyde (<5%) even after extended time and refluxing. When the reaction was conducted in the presence of volatile acetaldehyde, the corresponding silylated α-hydroxyphosphinate was formed after only 20 minutes. The expected α-hydroxyphosphinate **4q** was then isolated in an excellent yield of 91%. The other aliphatic aldehydes **3r–v** also allowed to achieve the reaction in very good yields (75–86%). It is important to notice that we never detected any side-product resulting from the α-hydrogen elimination on aliphatic aldehydes compared to previous reported work.[10a]

Thereafter, the same mild reaction conditions were tested on various ketones as electrophile in order to enlarge the scope of the reaction (Scheme 4). As a general trend, the reaction rates are slower in the presence of ketones than aldehydes. For the range of studied ketones, the reactions were complete after 1.5–18 hours. After purification, the corresponding sodium salts were obtained in rather good yields (51–97%). The Abramov reaction between acetophenone (**8a**) and hypophosphorous acid (**1**) in the presence of BSA as a silylating agent gave the desired α-hydroxyphosphinate **9a** in an excellent yield (97%). *para*-Substituted halogenoacetophenones **8b**,**c** also furnished the products **9b**,**c** in 3 hours. In addition, it was noted that the introduction of a chlorine on *meta*- and *ortho*-positions of acetophenone allowed to dramatically reduce the reaction time to 1.5 hours and 15 minutes, respectively, in similar yields (75 and 85%). The α-hydroxyphosphinate **9f** substituted by a trifluoromethyl group was successfully obtained only after 15 minutes in 91% yield while we observed a slower reaction rate in the presence of 4-methoxyacetophenone (**8g**). Furthermore, we unsurprisingly found that the replacement of a 3-methyl group (**8h**, **9h**) by a 2-methyl moiety (**8i**, **9i**) on acetophenone doubled the reaction time. Finally, the reaction was also successfully conducted in the presence of bulkier ketones such as benzophenone (**8j**) and tetralone (**8k**) and led to the desired α-hydroxyphosphinates **9j**,**k** in moderate yields (51 and 55%) involving longer reaction times.

In conclusion, we have proposed a general protocol for the equimolar Abramov reaction between carbonyl compounds and hypophosphorous acid (**1**) in the presence of only 2 equivalents of BSA as a silylating agent. This general method has been successfully applied to various substituted aliphatic and aromatic aldehydes and ketones leading to easily purified *H*-α-hydroxyphosphinates in good to excel-



Scheme 4 Scope of ketones

lent yields and shorter reaction times than those reported methods.[10] Moreover, the reaction is also effective in the presence of challenging aldehydes such as formaldehyde and acetaldehyde. Furthermore, symmetrically disubstituted phosphinates were not formed nor even detected unlike the previous reported work.[8,10g] Current efforts are now focused on testing this methodology to other electrophiles and this will be reported in due course.

Reagents were purchased from common commercial suppliers (Sigma-Aldrich, Alfa Aesar, Acros Organics) and used as delivered. All solvents were extra-dried grade prior used. BSA was purchased from Alfa Aesar (LOT: J24T014). Anhyd H_3PO_2 was prepared from commercial aq H_3PO_2 solution (50% w/w) according to the procedure reported by Montchamp et al.[16] Reactions requiring inert conditions were carried out in flame-dried glassware under an argon atmosphere.

NMR spectra were recorded at 20 °C on a Bruker Avance III 400 spectrometer (^{1}H: 400 MHz, ^{13}C: 101 MHz, ^{31}P: 162 MHz, ^{19}F: 377 MHz). Chemical shifts (δ) are given in ppm, the number of protons (n) for a given resonance was indicated by nH, and coupling constants *J* in Hz. ^{1}H NMR spectra were calibrated on non-deuterated solvent residual peak (H_2O: 4.79 ppm) while H_3PO_4 (85% in H_2O) was used as an external standard for ^{31}P NMR notably for the monitoring of the Abramov reaction. Standard abbreviations were used for ^{1}H, ^{13}C, ^{31}P and ^{19}F NMR spectra to indicate the signal multiplicity. All ^{13}C NMR spectra were measured with ^{1}H-decoupling while ^{31}P and ^{19}F NMR spectra were measured with ^{1}H coupling (zoom on the spectrum) and ^{1}H decoupling. ^{1}H experiments with H_2O presaturation were performed with D_1 = 2 s and 128 scans. The reactions were followed by ^{31}P and ^{31}P{^{1}H} NMR experiments (the spectra were recorded without lock and shims). High-resolution mass spectra (HRMS) were performed on a Bruker maXis mass spectrometer in negative (ESI-) mode by the 'Fédération de Recherche' ICOA/CBM (FR2708) platform. MS analyses were performed using a Q-TOF Impact HD mass spectrometer equipped with the electrospray (ESI) ion source (Bruker Daltonics). The instrument was operated in the negative mode with an ESI source on a Q-TOF mass spectrometer with an accuracy tolerance of 2 ppm. Samples were diluted with MeCN and H_2O (15:85) and were analyzed by mass spectrometry in continuous infusion using a syringe pump at 200 µL/min. The mass profiles obtained by ESI-MS were analyzed using DataAnalysis software (Bruker Daltonics). IR spectra were recorded on a ThermoFisher scientific Nicolet 380 FT-IR spectrophotometer. Smart OMNI-Sampler Germanium ATR Sampling accessory was used. The Smart OMNI-Sampler utilized an extremely rugged germanium ATR crystal. The wave numbers were expressed in cm^{-1} and comprised between 4000 and 675 cm^{-1}. The samples were analyzed neat. The following abbreviations were used for IR spectra to indicate the signal intensities: w (weak), m (medium), s (strong), br (broad).

One-Pot Abramov Reaction, Method A (Table 1); General Procedure

To a dry and argon flushed 100 mL three-necked flask equipped with a thermometer, an argon inlet, and an addition funnel, were successively introduced anhyd H_3PO_2 (**1**; 0.660 g, 10.0 mmol) and anhyd CH_2Cl_2 (2 mL) under an argon atmosphere. BSA (6.11 g, 30.0 mmol) was added dropwise at 0 °C under argon and the mixture was stirred for 40 min. The reaction conversion was monitored by ^{31}P NMR spec-

troscopy. To another dry and argon flushed 100 mL three-necked flask equipped with a thermometer, an argon inlet, and an addition funnel, were successively introduced the respective aldehyde **3** (10.0 mmol) and anhyd CH_2Cl_2 (2 mL). The bis(trimethylsilyl)phosphonite solution prepared as above was added dropwise at 0 °C to the aldehyde solution. The reaction was monitored by ^{31}P NMR spectroscopy. The reaction mixture was quenched by adding aq 0.5 M NaOH (10 mL) to adjust the pH value to 7.0. Then, CH_2Cl_2 was evaporated under reduced pressure and the solution was lyophilized. The crude residue was washed with MeOH (H_3PO_3 removal) and EtOH (acetamide removal) to give the product as a pure solid.

Optimized Method B for the Synthesis of α-Hydroxyphosphinate Sodium Salts 4a–v and 9a–k

To a dry and argon flushed 100 mL three-necked flask equipped with a thermometer, an argon inlet, and an addition funnel, were successively introduced anhyd H_3PO_2 (**1**; 0.660 g, 10.0 mmol) and anhyd CH_2Cl_2 (2 mL) under an argon atmosphere. BSA (4.07 g, 20.0 mmol) was added dropwise at 0 °C under argon and the mixture was stirred for 40 min. The reaction conversion was monitored by ^{31}P NMR spectroscopy. A solution of the respective aldehyde **3** or ketone **8** (10.0 mmol) in anhyd CH_2Cl_2 (2 mL) was added dropwise at 0 °C and the reaction was monitored by ^{31}P NMR spectroscopy. The mixture was quenched by adding aq 0.5 M NaOH (10 mL) to adjust the pH value to 7.0. Then, CH_2Cl_2 was evaporated under reduced pressure and the solution was lyophilized.

Purification procedure for α-hydroxyphosphinate sodium salts **4a–o** and **4r–v**: After lyophilization, the crude residue was washed with MeOH (Na_2HPO_3 removal) and EtOH (acetamide removal) to give the product as a pure solid.

Purification procedure for α-hydroxyphosphinate sodium salts **9a–k**: After lyophilization, the crude solid was dissolved in a minimum volume of EtOH. When Et_2O was slowly added to the resulting solution cooled at 0 °C, a solid was formed. The pure solid was collected by filtration.

[Hydroxy(phenyl)methyl]phosphinate Sodium Salt (4a)

White powder; yield: 1.86 g (96%).

IR (neat): 3181br (O–H), 2935w (C–H_{Ar}), 2901w (C–H), 2325w (P–H), 1498w (C=C_{Ar}), 1188s (P=O), 1061m (C–OH), 1019m (P–O), 731w cm^{-1} (C–P).

^1H NMR (400 MHz, D_2O): δ = 6.85 (d, $^1J_{PH}$ = 516.0 Hz, PH), 7.47–7.33 (m, 5 H_{arom}), 4.69 (d, $^2J_{PH}$ = 8.0 Hz, 1 H, PCH).

^{13}C NMR (101 MHz, D_2O): δ = 137.3 (C_2), 128.5 (d, $^4J_{PC}$ = 2.0 Hz, C_4, C_6), 127.9 (d, $^5J_{PC}$ = 3.0 Hz, C_5), 127.0 (d, $^3J_{PC}$ = 5.1 Hz, C_3, C_7), 73.8 (d, $^1J_{PC}$ = 105.0 Hz, C_1).

$^{31}P\{^1H\}$ NMR (162 MHz, D_2O): δ = 26.5 (s).

^{31}P NMR (162 MHz, D_2O): δ = 26.5 (dd, $^1J_{PH}$ = 516.0 Hz, $^2J_{PH}$ = 8.0 Hz).

These data are in agreement with those previously reported by Kaboudin et al.[17]

[(2-Chlorophenyl)(hydroxy)methyl]phosphinate Sodium Salt (4b)

White powder; yield: 1.41 g (68%).

IR (neat): 3163w (O–H), 2933w (C–H_{Ar}), 2816w (C–H), 2367w (P–H), 1152s (P=O), 1022m (C–OH), 1013m (P–O), 743m (C–Cl), 705w cm^{-1} (C–P).

^1H NMR (400 MHz, D_2O): δ = 7.48 (d, $^3J_{HH}$ = 7.7 Hz, 1 H, H_7), 7.42 (d, $^3J_{HH}$ = 7.9 Hz, 1 H, H_4), 7.35 (t, $^3J_{HH}$ = 7.4 Hz, 1 H, H_6), 7.32–7.24 (m, 1 H, H_5), 6.85 (d, $^1J_{PH}$ = 521.7 Hz, PH), 5.20 (d, $^2J_{PH}$ = 9.7 Hz 1 H, PCH).

^{13}C NMR (101 MHz, D_2O): δ = 135.6 (C_2), 132.4 (d, $^3J_{PC}$ = 6.2 Hz, C_3), 129.5 (C_5), 129.2 (d, $^4J_{PC}$ = 2.4 Hz, C_4), 128.6 (d, $^3J_{PC}$ = 4.9 Hz, C_7), 127.4 (d, $^5J_{PC}$ = 2.0 Hz, C_6), 70.2 (d, $^1J_{PC}$ = 104.2 Hz, C_1).

$^{31}P\{^1H\}$ NMR (162 MHz, D_2O): δ = 25.8 (s).

^{31}P NMR (162 MHz, D_2O): δ = 25.8 (dd, $^1J_{PH}$ = 521.7 Hz, $^2J_{PH}$ = 9.7 Hz).

These data are in agreement with those previously reported by Kaboudin et al.[17]

[(4-Fluorophenyl)(hydroxy)methyl]phosphinate Sodium Salt (4c)

White powder; yield: 2.10 g (99%).

IR (neat): 3167w (O–H), 2988w (C–H_{Ar}), 2901w (C–H), 2322w (P–H), 1608w (C=C_{Ar}), 1511m (C-F), 1187s (P=O), 1067m (C–OH), 1022m (P–O), 742w cm^{-1} (C–P).

^1H NMR (400 MHz, D_2O): δ = 7.47 (d, $^1J_{PH}$ = 517.6 Hz, PH), 7.42–7.34 (m, 2 H, H_3, H_7), 7.15 (t, $^3J_{HH}$ = 8.9 Hz, 2 H, H_4, H_6), 4.68 (d, $^2J_{PH}$ = 8.4 Hz, 1 H, PCH).

^{13}C NMR (101 MHz, D_2O): δ = 162.2 (dd, $^1J_{FC}$ = 243.2 Hz, $^5J_{PC}$ = 3.0 Hz, C_5), 133.1 (C_2), 128.8 (dd, $^3J_{FC}$ = 8.4 Hz, $^3J_{PC}$ = 5.3 Hz, C_3, C_7), 115.2 (dd, $^2J_{FC}$ = 21.6 Hz, $^4J_{PC}$ = 2.0 Hz, C_4, C_6), 73.0 (d, $^1J_{PC}$ = 105.4 Hz, C_1).

$^{19}F\{^1H\}$ NMR (377 MHz, D_2O): δ = –115.4 (d, $^6J_{FP}$ = 4.2 Hz).

^{19}F NMR (377 MHz, D_2O): δ = –115.3 to –115.5 (m).

$^{31}P\{^1H\}$ NMR (162 MHz, D_2O): δ = 26.2 (d).

^{31}P NMR (162 MHz, D_2O): δ = 26.2 (dm, $^1J_{PH}$ = 517.6 Hz).

MS (ESI–): *m*/*z* = 189.01 $[M - H]^-$, 401.01 $[2 M - 2 H + Na]^-$.

HRMS (ESI–): *m*/*z* $[M - H]^-$ calcd for $C_7H_7FO_3P$: 189.0122; found: 189.0122.

[(4-Chlorophenyl)(hydroxy)methyl]phosphinate Sodium Salt (4d)

White powder; yield: 1.89 g (83%).

IR (neat): 3159w (O–H), 2988w (C–H_{Ar}), 2901w (C–H), 2327w (P–H), 1492w (C=C_{Ar}), 1185s (P=O), 1068m (C–OH), 1021m (P–O), 829w (C–Cl), 739w cm^{-1} (C–P).

^1H NMR (400 MHz, D_2O): δ = 7.40 (d, $^3J_{HH}$ = 8.5 Hz, 2 H, H_3, H_7), 7.33 (d, $^3J_{HH}$ = 8.5 Hz, 2 H, H_4, H_6), 6.80 (d, $^1J_{PH}$ = 518.6 Hz, PH), 4.66 (d, $^2J_{PH}$ = 8.8 Hz, 1 H, PCH).

^{13}C NMR (101 MHz, D_2O): δ = 135.9 (d, $^2J_{PC}$ = 3.2 Hz, C_2), 132.9 (C_5), 128.5–128.4 (m, C_3, C_4, C_6, C_7), 73.1 (d, $^1J_{PC}$ = 104.5 Hz, C_1).

$^{31}P\{^1H\}$ NMR (162 MHz, D_2O): δ = 25.9 (s).

^{31}P NMR (162 MHz, D_2O): δ = 25.9 (dd, $^1J_{PH}$ = 518.6 Hz, $^2J_{PH}$ = 8.8 Hz).

These data are in agreement with those previously reported by Kaboudin et al.[17]

[Hydroxy(4-methoxyphenyl)methyl]phosphinate Sodium Salt (4e)

White powder; yield: 2.19 g (98%).

IR (neat): 3167br (O–H), 2944w (C–H_{Ar}), 2834w (C–H), 2312w (P–H), 1670w (C=C_{Ar}), 1612w (C=C_{Ar}), 1245m (C–OMe), 1189s (P=O), 1069m (C–OH), 1020m (P–O), 743w cm^{-1} (C–P).

^1H NMR (400 MHz, D_2O): δ = 7.30 (d, $^3J_{HH}$ = 8.6 Hz, 2 H, H_3, H_7), 6.98 (d, $^3J_{HH}$ = 8.6 Hz, 2 H, H_4, H_6), 6.79 (d, $^1J_{PH}$ = 514.9 Hz, PH), 4.59 (d, $^2J_{PH}$ = 8.1 Hz, 1 H, PCH), 3.79 (s, 3 H, OCH_3).

^{13}C NMR (101 MHz, D_2O): δ = 158.5 (d, $^5J_{PC}$ = 2.5 Hz, C_5), 129.6 (d, $^2J_{PC}$ = 31.5 Hz, C_2), 128.5 (d, $^3J_{PC}$ = 5.5 Hz, C_3, C_7), 114.0 (d, $^4J_{PC}$ = 1.7 Hz, C_4, C_6), 73.2 (d, $^1J_{PC}$ = 106.5 Hz, C_1), 55.3 (OCH_3).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 26.5 (s).

^{31}P NMR (162 MHz, D_2O): δ = 26.5 (dd, $^1J_{PH}$ = 514.9 Hz, $^2J_{PH}$ = 8.1 Hz).

MS (ESI–): *m*/*z* = 201.03 [M – H]$^-$, 425.05 [2 M – 2 H + Na]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_8H_{10}O_4P$: 201.0322; found: 201.0322.

{Hydroxy[4-(trifluoromethyl)phenyl]methyl}phosphinate Sodium Salt (4f)

White powder; yield: 2.48 g (95%).

IR (neat): 3165w (O–H), 2987w (C–H_{Ar}), 2325w (P–H), 1621w (C=C_{Ar}), 1324m (C–F), 1188m (P=O), 1067s (C–OH), 1018m (P–O), 759w cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 7.60 (d, $^3J_{HH}$ = 7.9 Hz, 2 H, H_4, H_6), 7.41 (d, $^3J_{HH}$ = 7.9 Hz, 2 H, H_3, H_7), 6.71 (d, $^1J_{PH}$ = 521.4 Hz, PH), 4.66 (d, $^2J_{PH}$ = 8.8 Hz, 1 H, PCH).

^{13}C NMR (101 MHz, D_2O): δ = 141.6 (C_2), 129.0 (dd, $^2J_{FC}$ = 32.1 Hz, $^5J_{PC}$ = 2.9 Hz, C_5), 127.2 (d, $^3J_{PC}$ = 4.9 Hz, C_3, C_7), 125.4–125.1 (m, C_4, C_6), 124.3 (q, $^1J_{FC}$ = 271.2 Hz, C_8), 73.4 (d, $^1J_{PC}$ = 102.6 Hz, C_1).

^{19}F{^{1}H} NMR (377 MHz, D_2O): δ = –62.29 (s).

^{19}F NMR (377 MHz, D_2O) δ = –62.29 (s).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 25.6 (s).

^{31}P NMR (162 MHz, D_2O): δ = 25.6 (dd, $^1J_{PH}$ = 521.4 Hz, $^2J_{PH}$ = 8.8 Hz).

MS (ESI–): *m*/*z* = 239.01 [M – H]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_8H_7F_3O_3P$: 239.0090; found: 239.0090.

{Hydroxy[4-(methoxycarbonyl)phenyl]methyl}phosphinate Sodium Salt (4g)

White powder; yield: 2.14 g (90%).

IR (neat): 3165w (O–H), 2957w (C–H_{Ar}), 2911w (C–H), 2320w (P–H), 1725m (C=O), 1611w (C=C_{Ar}), 1281m (C–O), 1187s (P=O), 1110m (C–O), 1071m (C–OH), 1024m (P–O), 748w cm^{-1} (C–P).

Water presaturation ^{1}H NMR (400 MHz, D_2O): δ = 7.99 (d, $^3J_{HH}$ = 8.2 Hz, 2 H, H_4, H_6), 7.57–7.40 (m, 2 H, H_3, H_7), 6.82 (d, $^1J_{PH}$ = 521.8 Hz, PH), 4.78 (d, $^2J_{PH}$ = 9.1 Hz, 1 H, PCH), 3.88 (s, 3 H, CO_2CH_3).

^{13}C NMR (101 MHz, D_2O): δ = 169.2 (C_8), 143.2 (C_2), 129.4 (C_4, C_6), 128.6 (C_5), 126.8 (C_3, C_7), 73.5 (d, $^1J_{PC}$ = 102.3 Hz, C_1), 52.5 (CO_2CH_3).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 25.6 (s).

^{31}P NMR (162 MHz, D_2O): δ = 25.6 (dd, $^1J_{PH}$ = 521.8 Hz, $^2J_{PH}$ = 9.1 Hz).

MS (ESI–): *m*/*z* = 229.03 [M – H]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_9H_{10}O_5P$: 229.0271; found: 229.0272.

[(4-Cyanophenyl)(hydroxy)methyl]phosphinate Sodium Salt (4h)

White powder; yield: 2.14 g (85%).

IR (neat): 3188w (O–H), 2978w (C–H_{Ar}), 2903w (C–H) 2324w (P–H), 2239w (C≡N), 1671w (C=C_{Ar}), 1611w (C=C_{Ar}), 1187s (P=O), 1068m (C–OH), 1022m (P–O), 750w cm^{-1} (C–P).

Water presaturation ^{1}H NMR (400 MHz, D_2O): δ = 7.75 (d, $^3J_{HH}$ = 8.0 Hz, 2 H, H_4, H_6), 7.51 (d, $^3J_{HH}$ = 7.0 Hz, 2 H, H_3, H_7), 6.82 (d, $^1J_{PH}$ = 523.8 Hz, PH), 4.79 (d, $^2J_{PH}$ = 9.7 Hz, 1 H, PCH).

^{13}C NMR (101 MHz, D_2O): δ = 143.4 (C_2), 132.4 (C_4, C_6), 127.2 (d, $^3J_{PC}$ = 4.4 Hz, C_3, C_7), 119.8 (C_8), 109.9 (d, $^5J_{PC}$ = 2.3 Hz, C_5), 73.4 (d, $^1J_{PC}$ = 101.5 Hz, C_1).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 25.1 (s).

^{31}P NMR (162 MHz, D_2O): δ = 25.1 (dd, $^1J_{PH}$ = 523.8 Hz, $^2J_{PH}$ = 9.5 Hz).

MS (ESI–): *m*/*z* = 196.02 [M – H]$^-$, 415.02 [2 M – 2 H + Na]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_8H_7NO_3P$: 196.0169; found: 196.0168.

[Hydroxy(3-nitrophenyl)methyl]phosphinate Sodium Salt (4i)

Brown powder; yield: 2.29 g (49%).

IR (neat): 3145w (O–H), 2988w (C–H_{Ar}), 2901w (C–H), 2332w (P–H), 1667w (C=C_{Ar}), 1526m (C–NO_2), 1356m (C–NO_2), 1190m (P=O), 1060s (C–OH), 1019m (P–O), 751w cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 8.21 (s, 1 H, H_7), 8.15 (d, $^3J_{HH}$ = 8.1 Hz, 1 H, H_5), 7.74 (d, $^3J_{HH}$ = 7.5 Hz, 1 H, H_3), 7.59 (t, $^3J_{HH}$ = 8.1 Hz, 1 H, H_4), 6.86 (d, $^1J_{PH}$ = 523.1 Hz, PH), 4.83 (d, $^2J_{PH}$ = 8.7 Hz, 1 H, PCH).

^{13}C NMR (101 MHz, D_2O): δ = 147.9 (C_6), 139.4 (C_2), 133.4 (d, $^3J_{PC}$ = 4.7 Hz, C_3), 129.5 (d, $^4J_{PC}$ = 2.1 Hz, C_4), 122.7 (d, $^5J_{PC}$ = 2.6 Hz, C_5), 121.5 (d, $^3J_{PC}$ = 4.9 Hz, C_7), 72.9 (d, $^1J_{PC}$ = 102.7 Hz, C_1).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 25.0 (s).

^{31}P NMR (162 MHz, D_2O): δ = 25.0 (dd, $^1J_{PH}$ = 523.1 Hz, $^2J_{PH}$ = 8.7 Hz).

MS (ESI–): *m*/*z* = 216.01 [M – H]$^-$, 152.04 [M – H – HPO_2]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_7H_7NO_5P$: 216.0067; found: 216.0068.

[Hydroxy(mesityl)methyl]phosphinate Sodium Salt (4j)

White powder; yield: 1.51 g (64%).

IR (neat): 3172w (O–H), 2948w (C–H_{Ar}), 2910w (C–H), 2317w (P–H), 1670w (C=C_{Ar}), 1611w (C=C_{Ar}), 1394w (CH_3), 1170m (P=O), 1100w (C–O), 1060s (C–OH), 1041m (P–O), 743w cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 7.31 (dd, $^1J_{PH}$ = 517.3, $^3J_{HH}$ = 2.8 Hz, PH), 6.92 (s, 2 H, H_4, H_6), 5.06 (dd, $^2J_{PH}$ = 16.4 Hz, $^3J_{HH}$ = 2.8 Hz, 1 H, PCH), 2.33 (s, 6 H, 8-CH_3, 9-CH_3), 2.20 (s, 3 H, 10-CH_3).

^{13}C NMR (101 MHz, D_2O): δ = 137.8 (C_5), 137.7 (d, $^2J_{PC}$ = 4.7 Hz, C_2), 131.1 (C_3, C_7), 129.6 (C_4, C_6), 71.5 (d, $^1J_{PC}$ = 105.2 Hz, C_1), 20.5 (8-CH_3, 9-CH_3), 19.9 (10-CH_3).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 25.9 (s).

^{31}P NMR (162 MHz, D_2O): δ = 25.9 (dd, $^1J_{PH}$ = 517.3 Hz, $^2J_{PH}$ = 16.3 Hz).

MS (ESI–): *m*/*z* = 213.07 [M – H]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_{10}H_{14}O_3P$: 213.0686; found: 213.0685.

[Hydroxy(naphthalen-1-yl)methyl]phosphinate Sodium Salt (4k)

White powder; yield: 1.83 g (75%).

IR (neat): 3687w (O–H), 3172w (O–H), 2988w (C–H_{Ar}), 2900w (C–H), 2372w (P–H), 1596w (C=C_{Ar}), 1147s (P=O), 1083m (C–OH), 1041m (P–O), 744m cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 8.15 (d, $^3J_{HH}$ = 8.0 Hz, 1 H, H_5) 7.99–7.92 (m, 1 H, H_7 or H_{10}), 7.89 (d, $^3J_{HH}$ = 8.2 Hz, 1 H, H_7 or H_{10}), 7.70–7.63 (m, 1 H, H_3), 7.63–7.51 (m, 3 H, H_4, H_8, H_9) 6.93 (dd, $^1J_{PH}$ = 519.4 Hz, $^4J_{PH}$ = 1.9 Hz, PH), 5.53 (d, $^2J_{PH}$ = 10.1 Hz, 1 H, PCH).

^{13}C NMR (101 MHz, D_2O): δ = 133.7 (C_2), 133.4 (C_6), 130.6 (d, $^3J_{PC}$ = 4.3 Hz, C_{11}), 128.6 (C_7), 128.1 (d, $^4J_{PC}$ = 2.9 Hz, C_{10}), 126.3, 126.0 (C_8, C_9), 125.7 (d, $^4J_{PC}$ = 2.8 Hz, C_4), 124.9 (d, $^3J_{PC}$ = 6.4 Hz, C_3), 123.8 (C_5), 70.4 (d, $^1J_{PC}$ = 104.4 Hz, C_1).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 26.8 (s).

^{31}P NMR (162 MHz, D_2O): δ = 26.8 (dd, $^1J_{PH}$ = 519.4 Hz, $^2J_{PH}$ = 10.1 Hz).

These data are in agreement with those previously reported by Kaboudin et al.[17]

[Hydroxy(naphthalen-2-yl)methyl]phosphinate Sodium Salt (4l)

White powder; yield: 2.44 g (100%).

IR (neat): 3172w (O–H), 2988w (C–H_{Ar}), 2900w (C–H), 2372w (P–H), 1596w (C=C_{Ar}), 1147s (P=O), 1083m (C–OH), 1041m (P–O), 744m cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 7.99–7.84 (m, 4 H, H_4, H_{11}, H_9, H_6), 7.60–7.46 (m, 3 H, H_3, H_7, H_8), 6.88 (d, $^1J_{PH}$ = 518.1 Hz, PH), 4.85 (d, $^2J_{PH}$ = 8.4 Hz, 1 H, PCH).

^{13}C NMR (101 MHz, D_2O): δ = 135.1 (C_2), 132.9 (d, $^4J_{PC}$ = 2.0 Hz, C_{10}), 132.6 (d, $^5J_{PC}$ = 1.6 Hz, C_5), 128.0 (d, $^4J_{PC}$ = 1.3 Hz C_4), 127.9, 127.6 (C_6, C_9), 126.5, 126.2 (C_7, C_8), 125.6 (d, $^3J_{PC}$ = 6.6 Hz, C_{11}), 125.1 (d, $^3J_{PC}$ = 4.1 Hz, C_3), 73.9 (d, $^1J_{PC}$ = 104.4 Hz, C_1).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 26.4 (s).

^{31}P NMR (162 MHz, D_2O): δ = 26.4 (dd, $^1J_{PH}$ = 518.1 Hz, $^2J_{PH}$ = 8.4 Hz).

MS (ESI–): *m*/*z* = 221.04 [M – H]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_{11}H_{10}O_3P$: 221.0373; found: 221.0374.

[Anthracen-9-yl(hydroxy)methyl]phosphinate Sodium Salt (4m)

Yellow powder; yield: 1.77 g (60%).

IR (neat): 3161w (O–H), 2930w (C–H_{Ar}), 2923w (C–H), 2347w (P–H), 1675m (C=C), 1622w (C=C_{Ar}), 1590w (C=C_{Ar}), 1580w (C=C_{Ar}), 1187w (P=O), 1069w (C–OH), 1050w (P–O), 730m cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 8.63–8.36 (m, 3 H, H_9, H_4, H_{14}), 8.02 (d, $^3J_{HH}$ = 8.1 Hz, 2 H, H_7, H_{11}), 7.53–7.41 (m, 4 H, H_5, H_6, H_{12}, H_{13}), 7.25 (d, $^1J_{PH}$ = 522.5 Hz, PH), 6.10 (d, $^2J_{PH}$ = 16.3 Hz, 1 H, PCH).

^{13}C NMR (101 MHz, D_2O): δ = 137.7 (C_2), 131.4 (C_8, C_{10}), 130.0 (d, $^3J_{PC}$ = 5.1 Hz, C_3, C_{15}), 129.2, 129.1 (C_7, C_{11}), 128.5 (C_4, C_{14}), 126.2 (C_9), 125.3 (C_5, C_6, C_{12}, C_{13}), 70.8 (d, $^1J_{PC}$ = 104.4 Hz, C_1).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 25.3 (s).

^{31}P NMR (162 MHz, D_2O): δ = 25.3 (dd, $^1J_{PH}$ = 522.5 Hz, $^2J_{PH}$ = 16.3 Hz).

MS (ESI–): *m*/*z* = 271.05 [M – H]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_{15}H_{12}O_3P$: 271.0530; found: 271.0530.

[Hydroxy(thiophen-2-yl)methyl]phosphinate Sodium Salt (4n)

White powder; yield: 2.00 g (100%).

IR (neat): 3157w (O–H), 2984w (C–H_{Ar}), 2905w (C–H), 2326w (P–H), 1196s (P=O), 1070m (C–OH), 1023m (P–O), 727w cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 7.41 (d, $^3J_{HH}$ = 5.0 Hz, 1 H, H_5), 7.12–7.07 (m, 1 H, H_3), 7.07–7.03 (m, 1 H, H_4), 6.86 (d, $^1J_{PH}$ = 520.8 Hz, PH), 4.90 (d, $^2J_{PH}$ = 9.0 Hz, 1 H, PCH).

^{13}C NMR (101 MHz, D_2O): δ = 139.8 (C_2), 127.2 (d, $^4J_{PC}$ = 1.8 Hz, C_4), 126.1 (d, $^4J_{PC}$ = 2.5 Hz, C_5), 126.0 (d, $^3J_{CP}$ = 6.9 Hz, C_3), 69.5 (d, $^1J_{PC}$ = 108.7 Hz, C_1).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 24.6 (s).

^{31}P NMR (162 MHz, D_2O): δ = 24.6 (dd, $^1J_{PH}$ = 520.8, $^2J_{PH}$ = 9.0 Hz).

MS (ESI–): *m*/*z* = 176.98 [M – H]$^-$, 376.94 [2 M – 2 H + Na]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_5H_6O_3PS$: 176.9781; found: 176.9781.

[Hydroxy(pyridin-2-yl)methyl]phosphinate Sodium Salt (4o)

White powder; yield: 1.66 g (85%).

IR (neat): 3151w (O–H), 2989w (C–H_{Ar}), 2911w (C–H), 2345w (P–H), 1591w (C=C_{Ar}), 1193s (P=O), 1068m (C–OH), 1026s (P–O), 744w cm^{-1} (C–P) .

^{1}H NMR (400 MHz, D_2O): δ = 8.46 (d, $^3J_{HH}$ = 4.6 Hz, 1 H, H_6), 7.86 (t, $^3J_{HH}$ = 7.7 Hz 1 H, H_4), 7.47 (d, $^3J_{HH}$ = 7.9 Hz, 1 H, H_3), 7.39–7.31 (m, 1 H, H_5), 6.88 (d, $^1J_{PH}$ = 525.7 Hz, PH), 4.76 (d, $^2J_{PH}$ = 9.8 Hz, 1 H, PCH).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 25.3 (s).

^{31}P NMR (162 MHz, D_2O): δ = 25.3 (dd, $^1J_{PH}$ = 525.7 Hz, $^2J_{PH}$ = 9.8 Hz).

MS (ESI–): *m*/*z* = 172.02 [M – H]$^-$, 367.02 [2 M – 2 H + Na]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_6H_7NO_3P$: 172.0169; found: 172.0170.

(1-Hydroxymethyl)phosphinate Sodium Salt (4p)

To a dry and argon flushed 100 mL three-necked flask equipped with a thermometer, an argon inlet, and an addition funnel, were successively introduced anhyd H_3PO_2 (**1**; 0.660 g, 10.0 mmol) and anhyd CH_2Cl_2 (2 mL) under an argon atmosphere. BSA (4.07 g, 20.0 mmol) was added dropwise at 0 °C under argon and the mixture was stirred for 40 min. The reaction conversion was monitored by ^{31}P NMR spectroscopy. Gaseous formaldehyde generated by heating paraformaldehyde was bubbled via a cannula into the cooled silylated phosphonite solution for 25 min under an argon flux. The reaction was monitored by ^{31}P NMR spectroscopy. The reaction mixture was quenched by adding aq 0.5 M NaOH (10 mL) to adjust the pH value to 7.0. Then, CH_2Cl_2 was evaporated under reduced pressure and the solution was lyophilized. After lyophilization, the crude residue was washed with EtOH (acetamide removal). After trituration of the solid with MeOH, the mixture was filtered (NaH_2PO_2 partial removal) and the filtrate was evaporated in vacuo. The resulting colorless oil was triturated with ethanol until the formation of a precipitate (Na_2HPO_3 removal). The supernatant was collected and finally evaporated in vacuo to afford a colorless oil; yield: 0.483 g (36%, purity = 88%).

IR (neat): 3169w (O–H), 2960w (C–H), 2917w (C–H), 2308w (P–H), 1168s (P=O), 1048m (C–OH), 1039m (P–O), 756w cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 6.93 (dt, $^1J_{PH}$ = 511.2 Hz, $^3J_{HH}$ = 2.3 Hz, PH), 3.59 (dd, $^2J_{PH}$ = 6.1 Hz, $^3J_{HH}$ = 2.3 Hz, 2 H, PCH_2).

^{13}C NMR (101 MHz, D_2O): δ = 60.9 (d, $^1J_{PC}$ = 106.8 Hz, C_1).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 24.5 (s).

^{31}P NMR (162 MHz, D_2O): δ = 24.5 (dt, $^1J_{PH}$ = 511.2 Hz, $^2J_{PH}$ = 6.1 Hz).

These data are in agreement with those previously reported by Cristau et al.[15b]

(1-Hydroxyethyl)phosphinate Sodium Salt (4q)

After lyophilization, the crude residue was dissolved in a minimum amount of H_2O and washed several times with EtOAc (acetamide removal). The aqueous layer was evaporated to give a colorless oil; yield: 1.20 g (91%).

IR (neat): 3170w (O–H), 2963w (C–H), 2915w (C–H), 2310w (P–H), 1170s (P=O), 1050m (C–OH), 1040m (P–O), 757w cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 6.73 (dd, $^1J_{PH}$ = 505.7 Hz, $^3J_{HH}$ = 1.5 Hz, PH), 3.70 (qdd, $^3J_{HH}$ = 7.1 Hz, $^2J_{PH}$ = 2.7 Hz, $^3J_{HH}$ = 1.5 Hz, 1 H, PCH), 1.29 (dd, $^3J_{PH}$ = 16.6 Hz, $^3J_{HH}$ = 7.1 Hz, 3 H, CH_3).

^{13}C NMR (101 MHz, D_2O): δ = 66.2 (d, $^1J_{PC}$ = 109.7 Hz, C_1), 14.7.

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 30.2 (s).

^{31}P NMR (162 MHz, D_2O): δ = 30.2 (dqd, $^1J_{PH}$ = 505.7 Hz, $^3J_{PH}$ = 16.6 Hz, $^2J_{PH}$ = 2.7 Hz).

These data are in agreement with those previously reported by David et al.[18]

(1-Hydroxypropyl)phosphinate Sodium Salt (4r)

White powder; yield: 1.17 g (86%).

IR (neat): 3171w (O–H), 2962w (C–H), 2915w (C–H), 2309w (P–H), 1169s (P=O), 1049m (C–OH), 1040m (P–O), 758w cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 6.74 (d, $^1J_{PH}$ = 520.7 Hz, PH), 3.49–3.39 (m, 1 H, PCH), 1.75–1.65 (m, 1 H, H_{2a}), 1.61–1.45 (m, 1 H, H_{2b}), 1.00 (t, $^3J_{HH}$ = 7.4 Hz, 3 H, CH_3).

^{13}C NMR (101 MHz, D_2O): δ = 72.1 (d, $^1J_{PC}$ = 110.0 Hz, C_1), 22.5 (d, $^2J_{PC}$ = 3.7 Hz, C_2), 9.8 (d, $^3J_{PC}$ = 12.1 Hz, C_3).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 29.2 (s).

^{31}P NMR (162 MHz, D_2O): δ = 29.2 (dm, $^1J_{PH}$ = 505.4 Hz).

MS (ESI–): *m*/*z* = 123.02 [M – H]$^-$, 269.03 [2 M – 2 H + Na]$^-$, 415.04 [3 M – 3 H + 2 Na]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_3H_8O_3P$: 123.0216; found: 123.0216.

(1-Hydroxypentyl)phosphinate Sodium Salt (4s)

White powder; yield: 1.43 g (82%).

IR (neat): 3163w (O–H), 2953w (C–H), 2926w (C–H), 2854w (C–H), 2310w (P–H), 1168s (P=O), 1073m (C–OH), 1045m (P–O), 764w cm^{-1} (C-P) .

^{1}H NMR (400 MHz, D_2O): δ = 6.75 (br d, $^1J_{PH}$ = 503.8 Hz, PH), 3.59–3.48 (m, 1 H, PCH), 1.77–1.62 (m, 1 H, H_{2a}), 1.62–1.44 (m, 2 H, H_{2b}, H_{3a}), 1.44–1.23 (m, 3 H, H_{3b}, H_4), 0.89 (t, $^3J_{HH}$ = 6.0 Hz, 3 H, CH_3).

^{13}C NMR (101 MHz, D_2O): δ = 70.4 (d, $^1J_{PC}$ = 110.0 Hz, C_1), 28.6 (d, $^3J_{PC}$ = 3.0 Hz, C_3), 27.2 (d, $^2J_{PC}$ = 12.1 Hz, C_2), 21.7 (C_4), 13.2 (C_5).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 29.6 (s).

^{31}P NMR (162 MHz, D_2O): δ = 29.6 (br d, $^1J_{PH}$ = 503.8 Hz).

MS (ESI–): *m*/*z* = 151.05 [M – H]$^-$, 325.09 [2 M – 2 H + Na]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_5H_{12}O_3P$: 151.0529; found: 151.0530.

(1-Hydroxy-2-methylpropyl)phosphinate Sodium Salt (4t)

White powder; yield: 1.20 g (75%).

IR (neat): 3170br (O–H), 2956w (C–H), 2326w (P–H), 1180s (P=O), 1063m (C–OH), 1017m (P–O), 753w cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 6.82 (d, $^1J_{PH}$ = 507.1 Hz, PH), 3.31–3.20 (m, 1 H, PCH), 2.07–1.92 (m, 1 H, H_2), 0.96 (d, $^3J_{HH}$ = 7.6 Hz, 3 H, 3-CH_3 or 4-CH_3), 0.94 (d, $^3J_{HH}$ = 7.3 Hz, 3 H, 3-CH_3 or 4-CH_3).

^{13}C NMR (101 MHz, D_2O): δ = 75.6 (d, $^1J_{PC}$ = 108.7 Hz, C_1), 29.0 (d, $^2J_{PC}$ = 3.2 Hz, C_2), 19.0 (d, $^3J_{PC}$ = 7.7 Hz, 3-CH_3 or 4-CH_3), 17.3 (d, $^3J_{PC}$ = 7.6 Hz, 3-CH_3 or 4-CH_3).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 28.5 (s).

^{31}P NMR (162 MHz, D_2O): δ = 28.5 (dm, $^1J_{PH}$ = 507.1 Hz).

MS (ESI–): *m*/*z* = 137.04 [M – H]$^-$, 297.06 [2 M – 2 H + Na]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_4H_{10}O_3P$: 137.0373; found: 137.0371.

(1-Hydroxy-2,2-dimethylpropyl)phosphinate Sodium Salt (4u)

White powder; yield: 1.46 g (84%).

IR (neat): 3278br (O–H), 2953w (C–H), 2867w (C–H), 2326w (P–H), 1186s (P=O), 1058s (C–OH), 1026m (P–O), 738w cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 6.87 (d, $^1J_{PH}$ = 508.3 Hz, PH), 3.17 (d, $^2J_{PH}$ = 6.8 Hz, 1 H, PCH), 0.98 (s, 9 H, *t*-C_4H_9).

^{13}C NMR (101 MHz, D_2O): δ = 78.4 (d, $^1J_{PC}$ = 105.7 Hz, C_1), 33.8 (d, $^2J_{PC}$ = 3.3 Hz, C_2), 25.9 [d, $^3J_{PC}$ = 5.6 Hz, $C(CH_3)_3$].

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 27.3 (s).

^{31}P NMR (162 MHz, D_2O): δ = 27.3 (dd, $^1J_{PH}$ = 508.3 Hz, $^2J_{PH}$ = 6.8 Hz).

MS (ESI–): *m*/*z* = 151.05 [M – H]$^-$, 325.09 [2 M – 2 H + Na]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_5H_{12}O_3P$: 151.0529; found: 151.0528.

[Cyclohexyl(hydroxy)methyl]phosphinate Sodium Salt (4v)

White powder; yield: 1.6 g (80%).

IR (neat): 3235br (O–H), 2921w (C–H), 2852w (C–H), 2303w (P–H), 1173s (P=O), 1076m (C–OH), 1037m (P–O), 745w cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 6.86 (dd, $^1J_{PH}$ = 507.1 Hz, $^3J_{HH}$ = 1.1 Hz, PH), 3.29 (br t, $^2J_{PH}$ = 5.9 Hz, 1 H, PCH), 1.89–1.79 (m, 1 H, H_{3a} or H_{7a}), 1.79–1.65 (m, 4 H, H_2, H_{4a}, H_{6a} H_{3a} or H_{7a}), 1.65–1.55 (m, 1 H, H_{5a}), 1.33–1.03 (m, 5 H, H_{5b}, H_{4b} H_{6b}, $H_{3b,}$ H_{7b}).

^{13}C NMR (101 MHz, D_2O): δ = 75.1 (d, $^1J_{PC}$ = 108.5 Hz, C_1), 38.9 (d, $^2J_{PC}$ = 2.7 Hz, C_2), 29.5, 28.0 (2 d, $^3J_{PC}$ = 7.4 Hz, C_3, C_7), 25.8, 25.7, 25.5 (C_4, C_5, C_6).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 28.4 (s).

^{31}P NMR (162 MHz, D_2O): δ = 28.4 (dt, $^1J_{PH}$ = 507.1 Hz, $^2J_{PH}$ = 6.1 Hz).

MS (ESI–): *m*/*z* = 177.07 [M – H]$^-$, 377.13 [2 M – 2 H + Na]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_7H_{14}O_4P$: 177.0686; found: 177.0685.

(1-Hydroxy-1-phenylethyl)phosphinate Sodium Salt (9a)

White powder; yield: 2.02 g (97%).

IR (neat): 3157w (O–H), 2973w (C–H_{Ar}), 2901w (C–H), 2320w (P–H), 1579w (C=C_{Ar}), 1171m (P=O), 1066w (C–OH), 1044 (P–O), 750w cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 7.52–7.45 (m, 2 H, H_3, H_7), 7.45– 7.38 (m, 2 H, H_4, H_6), 7.38–7.32 (m, 1 H, H_5), 6.66 (d, $^1J_{PH}$ = 515.3 Hz, PH), 1.65 (d, $^3J_{PH}$ = 13.9 Hz, 3 H, CH_3).

^{13}C NMR (101 MHz, D_2O): δ = 141.4 (C_2), 128.3 (d, $^4J_{PC}$ = 2.0 Hz, C_4, C_6), 127.3 (d, $^5J_{PC}$ = 2.5 Hz, C_5), 125.8 (d, $^3J_{PC}$ = 3.9 Hz, C_3, C_7), 74.6 (d, $^1J_{PC}$ = 106.4 Hz, C_1), 21.6 (d, $^2J_{PC}$ = 6.2 Hz, CH_3).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 31.0 (s).

^{31}P NMR (162 MHz, D_2O): δ = 31.0 (dq, $^1J_{PH}$ = 515.3 Hz, $^3J_{PH}$ = 13.9 Hz).

MS (ESI–): *m*/*z* = 185.04 [M – H]$^-$, 393.06 [2 M – 2 H + Na]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_8H_{10}O_3P$: 185.0373; found: 185.0373.

[1-(4-Fluorophenyl)-1-hydroxyethyl]phosphinate Sodium Salt (9b)

White powder; yield: 1.85 g (82%).

IR (neat): 3240w (O–H), 2967w (C–H_{Ar}), 2913w (C–H), 2320w (P–H), 1682w (C=C_{Ar}), 1601w (C=C_{Ar}), 1163s (P=O), 1131w (C–F), 1043s (C–OH), 1013w (P–O), 747w cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 7.48–7.37 (m, 2 H, H_3, H_7), 7.10 (t, ^3J = 8.9 Hz, 2 H, H_4, H_6), 6.63 (d, $^1J_{PH}$ = 516.1 Hz, PH), 1.61 (d, $^3J_{PH}$ = 14.3 Hz, 3 H, CH_3).

^{13}C NMR (101 MHz, D_2O): δ = 161.8 (dd, $^1J_{FC}$ = 243.1 Hz, $^5J_{PC}$ = 2.8 Hz, C_5), 137.1 (C_2), 127.7 (dd, $^3J_{FC}$ = 8.3 Hz, $^3J_{PC}$ = 3.8 Hz, C_3, C_7), 114.8 (dd, $^2J_{FC}$ = 21.4 Hz, $^4J_{PC}$ = 2.0 Hz, C_4, C_6), 73.7 (d, $^1J_{PC}$ = 107.1 Hz, C_1), 21.6 (d, $^2J_{PC}$ = 6.7 Hz, CH_3).

^{19}F{^{1}H} NMR (377 MHz, D_2O): δ = –116.6 (d, $^6J_{FP}$ = 3.9 Hz).

^{19}F NMR (377 MHz, D_2O): δ = –116.5 to –116.7 (m).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 31.4 (d, $^6J_{FP}$ = 3.9 Hz).

^{31}P NMR (162 MHz, D_2O): δ = 31.4 (dq, $^1J_{PH}$ = 516.1 Hz, $^3J_{PH}$ = 14.2 Hz).

MS (ESI–): *m*/*z* = 203.03 [M – H]$^-$, 429.04 [2 M – 2 H + Na]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_8H_9FO_3P$: 203.0279; found: 203.0277.

[1-(4-Chlorophenyl)-1-hydroxyethyl]phosphinate Sodium Salt (9c)

White powder; yield: 1.95 g (80%).

IR (neat): 3223br (O–H), 2988w (C–H_{Ar}), 2902w (C–H), 2339w (P–H), 1666w (C=C_{Ar}), 1580w (C=C_{Ar}), 1168m (P=O), 1093w (C–OH), 1024s (P–O), 841w (C–Cl), 729w cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 7.43–7.33 (m, 4 H, H_3, H_4, H_6, H_7), 6.62 (d, $^1J_{PH}$ = 516.4 Hz, PH), 1.60 (d, $^3J_{PH}$ = 14.3 Hz, 3 H, CH_3).

^{13}C NMR (101 MHz, D_2O): δ = 140.1 (C_2), 132.5 (C_5), 128.1 (d, $^4J_{PC}$ = 2.1 Hz, C_4, C_6), 127.5 (d, $^3J_{PC}$ = 3.8 Hz, C_3, C_7), 73.8 (d, $^1J_{PC}$ = 106.3 Hz, C_1), 21.6 (d, $^2J_{PC}$ = 6.3 Hz, C_8).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 31.1 (s).

^{31}P NMR (162 MHz, D_2O): δ = 31.1 (dq, $^1J_{PH}$ = 516.4 Hz, $^3J_{PH}$ = 14.3 Hz).

MS (ESI–): *m*/*z* = 219.00 [M – H]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_8H_9ClO_3P$: 218.9983; found: 218.9982.

[1-(3-Chlorophenyl)-1-hydroxyethyl]phosphinate Sodium Salt (9d)

White powder; yield: 1.82 g (75%).

IR (neat): 3163w (O–H), 2987w (C–H_{Ar}), 2926w (C–H), 2332w (P–H), 1620w (C=C_{Ar}), 1595w (C=C_{Ar}), 1568w (C=C_{Ar}), 1176s (P=O), 1045s (C–OH), 1016w (P–O), 797 (C–Cl), 735 cm^{-1} (C–P) .

^{1}H NMR (400 MHz, D_2O): δ = 7.48 (s, 1 H, H_3), 7.40–7.25 (m, 3 H, H_5, H_6, H_7), 6.64 (d, $^1J_{PH}$ = 517.9 Hz, PH), 1.62 (d, $^3J_{PH}$ = 14.4 Hz, 3 H, CH_3).

^{13}C NMR (101 MHz, D_2O): δ = 143.9 (C_2), 133.6 (d, $^4J_{PC}$ = 2.5 Hz, C_4), 129.7 (d, J_{PC} = 1.9 Hz, C_5 or C_6), 127.2 (d, J_{PC} = 2.4 Hz, C_5 or C_6), 125.9 (d, $^3J_{PC}$ = 3.8 Hz, C_3), 124.3 (d, $^3J_{PC}$ = 3.7 Hz,C_7), 73.9 (d, $^1J_{PC}$ = 105.9 Hz, C_1), 21.7 (d, $^2J_{PC}$ = 5.8 Hz, CH_3).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 30.9 (s).

^{31}P NMR (162 MHz, D_2O): δ = 30.9 (dq, $^1J_{PH}$ = 517.9 Hz, $^3J_{PH}$ = 14.4 Hz).

MS (ESI–): *m*/*z* = 219.00 [M – H]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_8H_9ClO_3P$: 218.9983; found: 218.9983.

[1-(2-Chlorophenyl)-1-hydroxyethyl]phosphinate Sodium Salt (9e)

White powder; yield: 2.1 g (85%).

IR (neat): 3160w (O–H), 2973w (C–H_{Ar}), 2901w (C–H), 2341w (P–H), 1581w (C=C_{Ar}), 1174s (P=O), 1096w (C–OH), 1036s (P–O), 753m (C–Cl), 738w cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 7.54–7.48 (m, 1 H, H_7), 7.31 (d, $^3J_{HH}$ = 7.7 Hz, 1 H, H_4), 7.22 (t, $^3J_{HH}$ = 7.4 Hz, 1 H, H_6), 7.01 (d, $^1J_{PH}$ = 533.4 Hz, PH), 2.54 (t, $^3J_{HH}$ = 7.4 Hz, 1 H, H_5), 1.66 (d, $^3J_{PH}$ = 13.9 Hz, 3 H, CH_3).

^{13}C NMR (101 MHz, D_2O): δ = 139.3 (d, $^2J_{PC}$ = 3.3 Hz, C_2), 131.5 (d, $^3J_{PC}$ = 4.5 Hz, C_3), 131.4 (d, $^4J_{PC}$ = 1.3 Hz, C_4), 129.0 (d, $^4J_{PC}$ = 1.9 Hz, C_6), 128.4 (d, $^3J_{PC}$ = 4.4 Hz, C_7), 127.1 (C_5), 75.2 (d, $^1J_{PC}$ = 103.6 Hz, C_1), 22.0 (d, $^2J_{PC}$ = 4.4 Hz, CH_3).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 27.9 (s).

^{31}P NMR (162 MHz, D_2O): δ = 27.9 (dq, $^1J_{PH}$ = 533.4 Hz, $^3J_{PH}$ = 13.9 Hz).

MS (ESI–): *m*/*z* = 219.00 [M – H]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_8H_9ClO_3P$: 218.9983; found: 218.9981.

{1-Hydroxy-1-[4-(trifluoromethyl)phenyl]ethyl}phosphinate Sodium Salt (9f)

White powder; yield: 2.51 g (91%).

IR (neat): 3167w (O–H), 2987w (C–H_{Ar}), 2900w (C–H), 2316w (P–H), 1618w (C=C_{Ar}), 1412w (C–F), 1167s (P=O), 1073w (C–OH), 1025m (P–O), 745w cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 7.70 (d, $^3J_{HH}$ = 8.0 Hz, 2 H, H_4, H_6), 7.61 (d, $^3J_{HH}$ = 8.0 Hz, 2 H, H_3, H_7), 6.67 (d, $^1J_{PH}$ = 519.3, PH), 1.66 (d, $^3J_{PH}$ = 14.3 Hz, 1 H, CH_3).

^{13}C NMR (101 MHz, D_2O): δ = 145.8 (C_2), 128.5 (dd, $^2J_{FC}$ = 32.2 Hz, $^5J_{PC}$ = 2.5 Hz, C_5), 126.3 (d, $^3J_{PC}$ = 3.6 Hz, C_3, C_7), 125.3–124.9 (m, C_4, C_6), 124.3 (q, $^1J_{FC}$ = 271.2 Hz, C_9), 74.1 (d, $^1J_{PC}$ = 105.1 Hz, C_1), 21.7 (d, $^2J_{PC}$ = 5.7 Hz, C_8).

^{19}F{^{1}H} NMR (377 MHz, D_2O): δ = –62.3 (s)

^{19}F NMR (377 MHz, D_2O): δ = –62.3 (s).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 30.8 (s).

^{31}P NMR (162 MHz, D_2O): δ = 30.8 (dq, $^1J_{PH}$ = 519.3 Hz, $^3J_{PH}$ = 14.3 Hz).

MS (ESI–): *m*/*z* = 253.02 [M – H]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_9H_9F_3O_3P$: 253.0247; found: 253.0248.

[1-Hydroxy-1-(4-methoxyphenyl)ethyl]phosphinate Sodium Salt (9g)

White powder; yield: 1.45 g (61%).

IR (neat): 3199w (O–H), 2930w (C–H_{Ar}), 2835w (C–H), 2320w (P–H), 1610w (C=C_{Ar}), 1251m (C–O), 1175s (P=O), 1095w (C–OH), 1033s (P–O), 750 cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 7.39 (dd, $^3J_{HH}$ = 8.8 Hz, $^4J_{PH}$ = 1.9 Hz, 2 H, H_3, H_7), 6.98 (d, $^3J_{HH}$ = 8.8 Hz, 2 H, H_4, H_6), 6.62 (d, $^1J_{PH}$ = 513.6 Hz, PH), 3.80 (s, 3 H, OCH_3), 1.60 (d, $^3J_{PH}$ = 14.2 Hz, 3 H, CH_3).

^{13}C NMR (101 MHz, D_2O): δ = 157.9 (C_5), 133.9 (C_2), 127.3 (d, $^3J_{PC}$ = 3.9 Hz, C_3, C_7), 113.7 (d, $^4J_{PC}$ = 1.9 Hz, C_4, C_6), 73.6 (d, $^1J_{PC}$ = 107.8 Hz, C_1), 55.3 (OCH_3), 21.4 (d, $^2J_{PC}$ = 6.9 Hz, CH_3).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 31.7 (s).

^{31}P NMR (162 MHz, D_2O): δ = 31.7 (dq, $^1J_{PH}$ = 513.6 Hz, $^3J_{PH}$ = 14.3 Hz).

MS (ESI–): *m*/*z* = 215.05 [M – H]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_9H_{12}O_4P$: 215.0479; found: 215.0477.

[1-Hydroxy-1-(*m*-tolyl)ethyl]phosphinate Sodium Salt (9h)

White powder; yield: 2.01 g (91%).

IR (neat): 3207w (O–H), 2981w (C–H_{Ar}), 2905w (C–H), 2379w (P–H), 1668w (C=C_{Ar}), 1607w (C=C_{Ar}), 1150s (P=O), 1089w (C–OH), 1036m (P–O), 747w cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 7.39–7.18 (m, 3 H, H_3, H_6, H_7), 7.12 (d, $^3J_{HH}$ = 6.7 Hz 1 H, H_5), 6.61 (d, $^1J_{PH}$ = 516.8 Hz, PH), 2.29 (s, 3 H, ArCH_3), 1.59 (d, $^3J_{PH}$ = 14.3 Hz, 3 H, CH_3).

^{13}C NMR (101 MHz, D_2O): δ =141.5 (C_2), 138.3 (C_4), 128.3 (d, $^5J_{PC}$ = 2.0 Hz, C_5), 127.8 (d, $^4J_{PC}$ = 2.5 Hz, C_6), 126.4 (d, $^3J_{PC}$ = 3.9 Hz, C_3), 127.1 (d, $^3J_{PC}$ = 3.9 Hz, C_7), 74.0 (d, $^1J_{PC}$ = 106.8 Hz, C_1), 22.0 (d, $^2J_{PC}$ = 6.1 Hz, CH_3), 20.6 (ArCH_3).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 31.5 (s).

^{31}P NMR (162 MHz, D_2O): δ = 31.5 (dq, $^1J_{PH}$ = 516.8 Hz, $^3J_{PH}$ = 14.3 Hz).

MS (ESI–): *m*/*z* = 199.05 [M – H]$^-$, 421.09 [2 M – 2 H + Na]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_9H_{12}O_3P$: 199.0530; found: 199.0529.

[1-Hydroxy-1-(*o*-tolyl)ethyl]phosphinate Sodium Salt (9i)

White powder; yield: 1.71 g (74%, purity >96%).

IR (neat): 3157w (O–H), 2988m (C–H_{Ar}), 2900m (C–H), 2313w (P-H), 1580w (C=C_{Ar}), 1174m (P=O), 1076m (C–OH), 1046s (P–O), 745w cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 7.45–7.40 (1 H, H_7), 7.25–7.17 (m, 3 H, H_4, H_5, H_6), 6.82 (d, $^1J_{PH}$ = 518.1 Hz, PH), 2.54 (s, 3 H, ArCH_3), 1.69 (d, $^3J_{PH}$ = 14.1 Hz, 3 H, CH_3).

^{13}C NMR (101 MHz, D_2O): δ = 139.4 (C_2), 137.2 (d, $^3J_{PC}$ = 4.5 Hz, C_3), 132.5 (C_4), 127.5 (d, $^4J_{PC}$ = 2.1 Hz, C_7), 127.3 (d, $^3J_{PC}$ = 4.7 Hz, C_5 or C_6), 125.7 (d, $^5J_{PC}$ = 1.4 Hz, C_5 or C_6), 75.9 (d, $^1J_{PC}$ = 105.8 Hz, C_1), 22.6 (d, $^2J_{PC}$ = 5.3 Hz, CH_3), 22.1 (ArCH_3).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 30.7 (s).

^{31}P NMR (162 MHz, D_2O): δ = 30.7 (dq, $^1J_{PH}$ = 518.1 Hz, $^3J_{PH}$ = 14.1 Hz).

MS (ESI–): *m*/*z* = 199.05 [M – H]$^-$, 421.10 [2 M – 2 H + Na]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_9H_{12}O_3P$: 199.0530; found: 199.0530.

(Hydroxydiphenylmethyl)phosphinate Sodium Salt (9j)

White powder; yield: 1.49 g (55%).

IR (neat): 3400w (O–H), 2988w (C–H_{Ar}), 2901w (C–H), 2338w (P–H), 1597w (C=C_{Ar}), 1170m (P=O), 1059s (C–OH), 1036w (P–O), 750w cm^{-1} (C–P).

^{1}H NMR (400 MHz, D_2O): δ = 7.43–7.36 (m, 4 H, H_3, H_7, H_9, H_{13}), 7.32–7.19 (m, 6 H, H_4, H_5, H_6, H_{10}, H_{11}, H_{12}), 6.84 (d, $^1J_{PH}$ = 528.7 Hz, PH).

^{13}C NMR (101 MHz, D_2O): δ = 141.3 (d, $^2J_{PC}$ = 2.0 Hz, C_2, C_8), 128.3 (C_4, C_6, C_{10}, C_{12}), 127.7 (d, ^5J = 1.3 Hz, C_5, C_{11}), 127.3 (d, $^3J_{HH}$ = 4.9 Hz, C_3, C_7, C_9, C_{13}), 78.8 (d, $^1J_{PC}$ = 105.4 Hz, C_1).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 30.5 (s).

^{31}P NMR (162 MHz, D_2O): δ = 30.5 (d, $^1J_{PH}$ = 528.7 Hz).

MS (ESI–): *m*/*z* = 247.05 [M – H]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_{13}H_{12}O_3P$: 247.0530; found: 247.0527.

(1-Hydroxy-1,2,3,4-tetrahydronaphthalen-1-yl)phosphinate Sodium Salt (9k)

White powder; yield: 1.20 g (51%).

IR (neat): 3155w (O–H), 2995w (C–H_{Ar}), 2900w (C–H), 2312w (P–H), 1650w (C=C_{Ar}), 1172s (P=O), 1089w (C–OH), 1053s (P–O), 749m cm^{-1} (C–P) .

^{1}H NMR (400 MHz, D_2O): δ = 7.52–7.47 (m, 1 H, H_3), 7.29–7.20 (m, 2 H, H_4, H_5), 7.20–7.14 (m, 1 H, H_6), 6.76 (d, $^1J_{PH}$ = 514.1, PH), 2.83–2.63 (m, 2 H, H_{10}), 2.28–2.16 (m, 1 H, H_{8a}), 2.03–1.68 (m, 3 H, H_{8b}, H_{9a}, H_{9b}).

^{13}C NMR (101 MHz, D_2O): δ = 138.6 (d, $^2J_{PC}$ = 5.1 Hz, C_7), 135.9 (C_2), 129.2 (C_6), 127.6 (C_5), 127.5 (d, $^3J_{PC}$ = 5.9 Hz, C_3), 126.1 (C_4), 71.7 (d, $^1J_{PC}$ = 110.6 Hz, C_1), 30.9 (d, $^3J_{PC}$ = 4.8 Hz, C_8), 29.0 (C_{10}), 18.5 (d, $^2J_{PC}$ = 4.7 Hz, C_9).

^{31}P{^{1}H} NMR (162 MHz, D_2O): δ = 32.9 (s).

^{31}P NMR (162 MHz, D_2O): δ = 32.9 (dt, $^1J_{PH}$ = 514.1 Hz, $^3J_{PH}$ = 12.8 Hz).

MS (ESI–): *m*/*z* = 211.05 [M – H]$^-$.

HRMS (ESI–): *m*/*z* [M – H]$^-$ calcd for $C_{10}H_{12}O_3P$: 211.0530; found: 211.0528.

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