UV-mediated hydrophosphinylation of unactivated alkenes with phosphinates under batch and flow conditions†

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A UV-mediated hydrophosphinylation of unactivated alkenes with H-phosphinates and hypophosphorous acid under radical free conditions is presented. The reaction affords selectively a large number of structurally diverse organophosphorous compounds in moderate to good yields under mild reaction conditions in the presence of an organic sensitizer as catalyst irradiated by UV-A LEDs. Furthermore, the high yielding hydrophosphinylation in continuous flow is disclosed.

Introduction

Organophosphorus compounds have attracted much attention due to their wide range of applications in materials, catalysis, natural bioactive products and pharmaceuticals.1 In particular, phosphinates (P(O)(OR)R1R2, R1/R2 = hydrogen and/or carbon) have been the target of numerous synthetic efforts as they are versatile precursors to organophosphorus compounds and represent a sustainable alternative to the use of phosphorous trichloride.2 Indeed, phosphinates can be considered as the synthetic equivalents of phosphorous trichloride with several advantages in terms of stability and toxicity. In this regard, the development of efficient and selective methodologies for the preparation and functionalization of phosphinates (P(O)(OR)H2) and H-phosphinates (P(O)(OR)H) has been extensively studied, mostly by the group of Montchamp.2,3 Hydrophosphinylation of unactivated alkenes is one of these routes that provide a direct access to functionalized organophosphorous compounds.4 This atom economical process has been reported to proceed via transition metal catalysis,5 or radical activation (Scheme 1a and b).6 Despite the significant progress in this chemistry, these transformations suffer from some drawbacks like the relatively harsh conditions, narrow substrates scopes and costly catalytic system thus limiting their chemical and pharmaceutical applications. Recently, Lakhdar and co-workers reported a hydrophosphinylation of unactivated alkenes with ethyl and butyl phosphinates under photocatalytic conditions (Scheme 1c),7 even though diphenyl iodonium triflate which acted as sacrificial oxidant is not a heavy metal, the use of catalytic quantity is always preferred in term of sustainability and environmental benignity. Alternatively, pioneering work from the group of Dondoni9 demonstrated that P(O)-centered radical can be generated from H-phosphonates under UV-A irradiation, in the presence of 2,2-dimethoxy-2-phenylacetophenone (DMPA) as photoinitiator, and added to alkene functionalized carbohydrates. However, the reaction requires the use of a large excess of phosphonates (100 eq.). Mathé and coworkers10 then extended this free radical hydrophosphonylation to activated and unactivated alkenes, similar reaction with hypophosphorous acid and H-phosphinates derivatives10 have not been studied previously.

In this context, we envisaged that continuous-flow systems in combination with a sensitizer irradiated by UV-A LEDs (λ = 365 nm)
nm) would result in a significant enhancement of the reaction. Over the last decade, interest has grown for flow chemistry based on microfluidic technology in particular towards large-scale application due to its significant improvement over traditional batch reactors concerning reduced consumption of chemicals, solvents and time together with enhanced yields, selectivity and control over reaction conditions. An easy scale up is also one of the characteristic of photo-reactions which are conducted in micro-reactors. In batch reactors, light penetration through the reaction media is limited which restrains the efficiency of photochemical processes. This drawback can be overcome with continuous microflow reactors since their small optical lengths improve sample irradiation and also enhance heat and mass transfer.\textsuperscript{11} Therefore, in view of the growing demand to develop efficient, mild and sustainable methods to access phosphinates and as a continuation of our interest in photocatalyzed processes,\textsuperscript{12} we herein report an original UV-mediated hydrophosphinylation of unactivated alkenes with hypophosphorous acid and less reactive H-phosphinates derivatives under batch and flow conditions.

**Results and discussion**

**Hydrophosphinylation of unactivated alkenes with H-phosphinates under batch conditions**

Initially, the hydrophosphinylation of relatively challenging H-phosphinate (1a) with octene (2a) in equimolar amounts in the presence of a photoinitiator under UV-A irradiation was selected as a model to investigate the reaction. The use of one equivalent of 4,4'-dimethoxybenzophenone (4,4'-DMBP) was found to be effective furnishing 3a after stirring in acetonitrile under an ambient inert atmosphere for 3 h (Table 1, entry 1, 42%). An investigation of solvents showed that the reaction efficiency was further enhanced when performed in DMSO (Table 1, entry 4, 69%) or acetic acid\textsuperscript{6,11} (entry 5, 70%) as previously observed for radical process with H-phosphinates, whereas moderate yields were obtained with ethyl acetate (entry 2, 46%) or DMF (entry 3, 52%). Importantly a very low catalyst loading could promote the reaction yield up to 84% (entries 6 and 7). Moreover, the loading could be further decreased but a prolonged reaction time was required (Table 1, entry 8, 86%). Interestingly, the photoinitiator DMPA (2,2-dimethoxy-2-phenylacetophenone) was not required (Table 1, entry 8, 86%). Importantly a very low catalyst loading could promote the reaction yield up to 84% (entries 6 and 7). Moreover, the loading could be further decreased but a prolonged reaction time was required (Table 1, entry 8, 86%). Interestingly, the photoinitiator DMPA (2,2-dimethoxy-2-phenylacetophenone) was not required (Table 1, entry 8, 86%).

| Entry | Photoinitiator Equivalent | Solvent | Time (h) | Yield\textsuperscript{b} (%) |
|-------|---------------------------|---------|----------|------------------|
| 1     | 4,4'-DMBP\textsuperscript{b} | 0.1     | DMSO     | 5                | 32               |
| 2     | 4,4'-DMBP\textsuperscript{b} | 0.1     | EtOAc    | 3                | 46               |
| 3     | 4,4'-DMBP\textsuperscript{b} | 0.1     | DMF      | 3                | 52               |
| 4     | 4,4'-DMBP\textsuperscript{b} | 0.1     | DMSO     | 3                | 69               |
| 5     | 4,4'-DMBP\textsuperscript{b} | 0.1     | AcOH     | 3                | 70               |
| 6     | 4,4'-DMBP\textsuperscript{b} | 0.5     | DMSO     | 3                | 72               |
| 7     | 4,4'-DMBP\textsuperscript{b} | 0.1     | DMSO     | 5                | 84               |
| 8     | 4,4'-DMBP\textsuperscript{b} | 0.05    | DMSO     | 3                | 86               |
| 9     | ——                        | ——      | DMSO     | 5                | 10               |
| 10<sup>d</sup> | 4,4'-DMBP\textsuperscript{b} | 0.1     | DMSO     | ——              | ——               |
| 11<sup>d</sup> | 4,4'-DMBP\textsuperscript{b} | 0.1     | DMSO     | 5                | 5                |
| 12    | Thioxantone\textsuperscript{b} | 0.1     | DMSO     | 5                | 76               |
| 13    | 4-MAP\textsuperscript{b}   | 0.1     | DMSO     | 5                | 19               |
| 14    | Benzophenone\textsuperscript{b} | 0.1   | DMSO     | 5                | 77               |
| 15    | DMPA\textsuperscript{b}    | 0.1     | DMSO     | 3                | 52               |
| 16    | DIBP\textsuperscript{b}    | 0.1     | DMSO     | 16               | 79 (76)%         |

\textsuperscript{a} Reaction condition: 1a (0.3 mmol, 1 equiv.), 2a (0.3 mmol, 1 equiv.), photoinitiator (x equiv.), solvent ([0.1 M]), under nitrogen and UV-A LED irradiation (\(\lambda = 365 \pm 15 \text{ nm}, 230 \text{ mW cm}^{-2}\)) at room temperature. \textsuperscript{b} Derived from \textsuperscript{1}P crude NMR spectra on integration of all formed species. \textsuperscript{c} 4,4'-DMBP = 4,4'-dimethoxybenzophenone. \textsuperscript{d} Without irradiation. \textsuperscript{e} Under ambient atmosphere. \textsuperscript{f} 4-MAP = 4-methoxyacetophenone. \textsuperscript{g} DMPA = 2,2-dimethoxy-2-phenylacetophenone. \textsuperscript{h} DIBP = 4,4'-(2-(1-methylimidazolium)ethoxy) benzophenone dibromide. \textsuperscript{i} The isolated yield is shown in parentheses.

The generality of the method was investigated, with the scope of the reaction being explored with respect to the H-phosphinate component, and the results are summarized in Table 2. Various P(O)–H compounds were employed to react with 1-octene 2a giving the corresponding 3a–g with isolated yields ranging from 30 to 76% (Table 2, entries 1–7). As expected, in all of the cases the anti Markovnikov product was observed. The reaction is not limited to H-phosphinate esters as H-phosphinate acid 1b could also deliver the desired product with a good yield (entry 2, 64%) in contrast to H-phosphinate acid 1c whose corresponding phosphinate acid product 3c was difficult to obtain in high purity (entry 3, 30%). However, H-phosphinate including unactivated alkyl and benzyl derivatives reacted successfully regardless of the ester chosen (Table 2, entries 4–6). When using (hydroxymethyl)H-phosphinate ester, which was reported to have several application,\textsuperscript{13} the branched product 3g was obtained with a significant yield of 75% (Table 2, entry 7). To further evaluate the substrate scope, a series of alkenes were tested with H-phosphinate 1a (Table 2, entries 8–12). The reaction with allyl benzene gave the corresponding product 3h with 48% of yield (Table 2, entry 8). Interestingly, 1a reacted with hindered alkenes giving 3i with a modest yield of 27% (Table 2, entry 9). Note that halogens like Br and alcohol groups were well tolerated which indicates a potential for further functionalization (Table 2, entries 10–12).
Although the detailed reaction mechanism is unclear, based on literature precedents\(^6,\)\(^16\) all these results could be well explained by a radical chain mechanism as depicted in Scheme 2. Upon irradiation, the excited state of the photoinitiator\(^17\) abstracts a proton from \(H\)-phosphinates to form the phosphoryl radical \(^18\) which adds to the terminal carbon of the alkenes. The carbon centered radical can then abstract a proton from \(H\)-phosphinate 1 to regenerate the phosphoryl radical.

**Hydrophosphinylation of unactivated alkenes with \(H\)-phosphinates under flow conditions**

With the successful results for the hydrophosphinylation under batch conditions, the reaction was then performed under continuous flow to further improve its efficiency in a shorter amount of time. The continuous flow hydrophosphinylation was performed using a continuous flow microfluidic system composed of a high pressure syringe pump delivering the homogeneous reaction mixture at specific flow rates to a commercially available microreactor (Mikroglas Dwell Device® microreactor from Invenios Europe, Langen, Germany) irradiated by HP UV-A lamp. This microreactor is made up of Foturan® glass that is transparent up to 300 nm allowing to work at a wide range of wavelengths (UV-A & visible).

We were delighted to find that \(H\)-phoshinate derivatives (3a, b, k) could be obtained with 4,4\(^0\)-DMBP as photoinitiator within a shorter reaction time than in batch (30 min vs. 5 h), indicating the importance of the short light path length provided by the microreactor, with slightly higher isolated yield, highlighting the potentials of this process (Scheme 3). This results offer the possibility to conduct the reaction on large scale without erosion of the yields.

**Hydrophosphinylation of unactivated alkenes with hypophosphorous acid under batch conditions**

To further demonstrate the utility of our protocol, we sought to test its potential for the hydrophosphinylation of various

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**Table 2** Hydrophosphinylation of alkenes with \(H\)-phosphinates\(^a\)

| Entry | \(H\)-Phosphinate 1 | Alkene 2 | Product 3 | Yield (%) |
|-------|---------------------|---------|-----------|----------|
| 1     | PHOC(O)O          | 1-Octene 2a | PhOC(O)OCy Oct | 76 |
| 2     | PH(O)OH          | 1-Octene 2a | PhOC(O)OOct | 64 |
| 3*    | PHOC(O)O          | 1-Octene 2a | PhOC(O)OCy Oct | 30^\* |
| 4     | PHOC(O)O          | 1-Octene 2a | PhOC(O)OCy Oct | 73 |
| 5     | PHOC(O)O          | 1-Octene 2a | PhOC(O)OOct | 71 |
| 6*    | PH(O)OCy         | 1-Octene 2a | PhOC(O)OOct | 51 |
| 7     | HOOC(O)OCy       | 1-Octene 2a | PhOC(O)OOct | 75 |
| 8*    | PHOC(O)O          | 2b        | PhOCyCy     | 48 |
| 9*    | PHOC(O)O          | 2c        | PhOCyCy     | 27 |
| 10    | PHOC(O)O          | Br         | 3d         | 38 |
| 11*   | PHOC(O)O          | 2e        | 3k         | 56 |
| 12*   | PHOC(O)O          | 2f        | 3l         | 69 |

\(^a\) Reaction condition: all reactions unless specified were carried out using 1 (0.3 mmol, 1 equiv.), 2 (0.3 mmol, 1 eq.), DBP (0.1 equiv.) in DMSO ([0.1 M]) under nitrogen and UV-A LED irradiation (\(\lambda = 365 \pm 15\) nm, 330 mW cm\(^{-2}\)) at room temperature for 16 h, isolated yield. 

\(^*\) Derived from \(^{31}\)P crude NMR spectra on integration of all formed species. 

\(^\circ\) (0.5 equiv.) of DBP.

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**Scheme 2** Proposed reaction mechanism for the photoinduced hydrophosphinylation of unactivated alkenes with \(H\)-phosphinates.
alkenes with hypophosphorous acid to form the previous precursor H-phosphinate acid (Scheme 4).

A slight modification of the previous batch conditions (see Table 1, ESI†) allowed us to obtain the corresponding H-phosphinates 1 with $^{31}$P NMR yield ranging from 49 to 96%. A 2 : 1 molar ratio of hypophosphorous acid–alkenes was necessary to obtain a high conversion without the formation of the disubstituted by-product. However despite the observed high conversions, isolated yields were modest due to difficult purifications. In all of the cases, the reaction was chemoselective where only mono substituted phosphinates were observed. As for H-phosphinate, the reaction proceeded well with terminal (1c–h) and cyclic alkenes (1i). Hindered alkenes delivered the desired compounds like 1j with a moderate yield of 31%, which is still higher than that obtained with H-phosphinate ester. H-Phosphinate acid 1k however was difficult to obtain in high purity. Similar to the first reaction assessed, the reaction tolerates functional groups such as amines or alcohols (1l–n) but the obtained H-phosphinate acids were not isolated. Although the scope of this reaction seems to be limited, H-phosphinate acids could be easily esterified$^{19}$ in situ and therefore the resulting procedure offers significant synthetic advantages.

**Experimental section**

**General information**

All reagents were purchased from commercial suppliers (Strem Chemicals Inc., Sigma-Aldrich or Alfa Aesar) and were used without further purification. Thin-layer chromatography (TLC) was performed on Silica gel 60 F254 plates (Merck) and visualized under UV (254 nm) or by staining with potassium permanganate or phosphomolybdic acid. Column chromatography was performed with 63–200 mesh silica gel. NMR spectra were recorded on a Bruker AVANCE 300 spectrometer at 300 MHz (75 MHz). Chemical shifts are reported in parts per million relative to solvent signal and coupling constants are reported in hertz (Hz). High-resolution mass spectra (HRMS) were performed on a Thermo LTQ Orbitrap mass spectrometer using nanoESI ionization. H-Phosphinates derivatives 1 and 4,4’-(2-(1-methylimidazolium)ethoxy)benzophenone dibromide (DIBP)$^{14}$ were prepared according to the reported procedure. The illumination was performed by UV-A LEDs (365 nm, irradiance = 230 mW cm$^{-2}$) Omnincure® AC475 model from Lumen Dynamics (Exellitas Technologies, Waltham, MA, USA). Note that the irradiance was measured at the surface of the reactor using a radiometer.

**General procedure A for the hydrophosphinylation with H-phosphinate 1 derivatives under batch conditions**

A solution of a selected H-phosphinate 1 (0.3 mmol, 1 equiv.), an alkene 2 (0.3 mmol, 1 equiv.) and DIPB (0.03–0.15 mmol, 10–50 mol%) in degassed DMSO (1.5 mL) was irradiated under 365 nm and N$_2$ for 16 h. Ethyl acetate (30 mL) was added and the reaction mixture was washed with saturated solution of NaHCO$_3$ (2 x 15 mL) and brine (2 x 15 mL). The organic layer was dried over MgSO$_4$ filtered and concentrated under reduced pressure. The residue was then purified by flash chromatography on silica gel if necessary to afford the corresponding organophosphorous compound.

**Scheme 3** Hydrophosphinylation of alkenes with H-phosphinates under batch and flow conditions. (a) Reactions conditions in batch: 1 (0.3 mmol, 1 equiv.), 2 (0.3 mmol, 1 equiv.), 4,4’-DMBP (0.1 equiv.) in DMSO ([0.1 M]) under nitrogen and UV-A LED irradiation ($\lambda = 365 \pm 15$ nm, 230 mW cm$^{-2}$) at room temperature, 5 h, isolated yield. (b) Reaction conditions in continuous flow: 1 (0.3 mmol, 1 equiv.), 2 (0.3 mmol, 1 equiv.), 4,4’-DMBP (0.1 equiv.) in DMSO ([0.1 M]) under nitrogen and UV-A LED irradiation ($\lambda = 365 \pm 15$ nm, 230 mW cm$^{-2}$) with Dowell device manufactured by Mikroglass Chemtech Mainz, Germany with a rectangular shape of dimensions 115 mm x 2 mm x 0.5 mm as photo-microreactor, at room temperature for 30 min of residence time, isolated yield.

**Scheme 4** Hydrophosphinylation of alkynes with hypophosphorous acid. All reactions (unless otherwise specified) were carried out using H$_2$PO$_2$ (0.3 mmol, 1 equiv.), 2 (0.15 mmol, 1 equiv.), DMPA (0.2 equiv.) in DMSO ([0.1 M]) under UV-A LED irradiation ($\lambda = 365 \pm 15$ nm, 230 mW cm$^{-2}$) at room temperature for 16 h. $^{31}$P crude NMR spectra on integration of all formed species.$^{19}$Isolated yield.
General procedure B for the hydrophosphinylation with hypophosphorous acid

To a 50% aqueous solution of hypophosphorous acid (79.2 mg, 0.6 mmol, 2 equiv.) in DMSO (3 mL) was added an alkene 2 (0.3 mmol, 1 equiv.), 4,4′-DMPA (15.5 mg, 0.06 mmol, 20 mol%). The reaction mixture was irradiated under 365 nm and ambient atmosphere for 16 h. Ethyl acetate (30 mL) was added and the organic layer was washed with brine (3 × 15 mL). To the organic layer a 0.03 M solution of NaHCO₃ (30 mL, 1 mmol) was added. The aqueous layer was washed with ethyl acetate (2 × 15 mL), acidified with 1 M HCl (2 mL, 2 mmol), saturated with NaCl and extracted with ethyl acetate (30 mL). The last ethyl acetate layer was dried over Na₂SO₄, filtered and concentrated under reduce pressure. The residue was then purified by flash chromatography on silica gel using 9 : 1 : 0.5 DCM-MeOH-AcOH as the eluant to afford the desired pure H-phosphinate acid 1.

Hydrophosphinylation of cyclohexyl phenyl-H-phosphinate 1a under flow condition

A solution of a cyclohexyl phenyl-H-phosphinate 20 1a (67.2 mg, 0.3 mmol, 1 equiv.), 1-octene 2a (33.6 mg, 0.3 mmol, 1 equiv.) and 10 mol% of 4,4′-dimethoxybenzophenone (7.2 mg) in degased DMSO (1.5 mL) was pumped through the Mikroglas Dwell Device reactor (V_{in} = 1.15 mL) at 38.33 µL min⁻¹, residence time of 30 min and irradiated by UV-LEDs. Ethyl acetate (30 mL) was added to the collected reaction mixture and the reaction mixture was washed with saturated solution of NaHCO₃ (2 × 15 mL) and brine (2 × 15 mL). To the organic layer was washed over MgSO₄, filtered and the solvent was removed under reduce pressure to afford 3a (85.6 mg, 0.25 mmol, 85%) as a colorless oil.

Cyclohexyl octyl(phenyl)phosphinate (3a). Following the general procedure A, using cyclohexyl phenyl-H-phosphinate 1a (67.2 mg, 0.3 mmol, 1 equiv.), 1-octene (33.6 mg, 0.3 mmol, 1 equiv.) and 10 mol% of catalyst (17.8 mg) affords 3a (76.6 mg, 0.23 mmol, 76%) as a colorless oil. 31P NMR (121 MHz, CDCl₃): δ = 43.5 (s); 1H NMR (300 MHz, CDCl₃): δ = 7.81–7.72 (m, 2H), 7.55–7.39 (m, 3H), 4.30–4.16 (m, 1H), 2.06–2.11 (m, 2H, 0.83 (t, J = 6.8 Hz, 3H); 13C NMR (75 MHz, CDCl₃): δ = 132.3 (d, J_{PC} = 122 Hz), 132.0 (d, J_{PC} = 2.7 Hz), 131.7 (d, J_{PC} = 9.7 Hz, 2C), 128.5 (d, J_{PC} = 12.2 Hz, 2C), 74.3 (d, J_{PC} = 6.8 Hz), 34.4 (d, J_{PC} = 2.9 Hz), 33.8 (d, J_{PC} = 4.3 Hz), 31.9, 31.0 (d, J_{PC} = 16.0 Hz), 30.4 (d, J_{PC} = 101 Hz), 29.1 (2C), 25.3, 23.8, 23.8, 22.7, 21.8 (d, J_{PC} = 3.7 Hz), 14.2. HRMS (ESI) m/z calcd for C₂₂H₄₆O₂P ([M + H]⁺) 373.3229, found 373.2289.

Octyl phenylphosphonic acid (3b). A solution of phenyl phosphonic acid 1b (47.4 mg, 0.3 mmol, 1 equiv.), 1-octene 2a (33.6 mg, 0.3 mmol, 1 equiv.) and DIBP (6.7 mg, 0.03 mmol, 10 mol%) in degased DMSO (3 mL) under N₂ was irradiated under 365 nm for 15 h. Ethyl acetate (30 mL) was added and the reaction mixture was washed with brine (3 × 15 mL). To the organic layer was added a 0.03 M solution of sodium bicarbonate (30 mL, 1 mmol). The aqueous layer was washed with ethyl acetate (2 × 15 mL), acidified with 1 M HCl (2 mL, 2 mmol) and extracted with ethyl acetate (30 mL). The last ethyl acetate layer was dried over Na₂SO₄, filtered and the solvent was removed under reduce pressure to afford the desired pure compound 3b (51.8 mg, 0.19 mmol, 64%). 31P NMR (121 MHz, CDCl₃): δ = 45.8 (s); 1H NMR (300 MHz, CDCl₃): δ = 11.65 (br s, 1H), 7.72–7.58 (m, 2H), 7.45–7.24 (m, 3H), 1.83–1.64 (m, 2H), 1.46–1.26 (m, 2H), 1.24–1.03 (m, 10H), 0.78 (t, J = 6.7 Hz, 3H); 13C NMR (75 MHz, CDCl₃): δ = 132.5 (d, J_{PC} = 127 Hz), 131.9, 131.2 (d, J_{PC} = 9.4 Hz, 2C), 128.4 (d, J_{PC} = 11.4 Hz, 2C), 31.9, 30.8 (d, J_{PC} = 16.3 Hz), 30.6 (d, J_{PC} = 98.7 Hz), 29.2 (2C), 22.7, 21.8 (d, J_{PC} = 2.6 Hz), 14.2; HRMS (ESI) m/z calcd for C₁₂H₁₅O₄P ([M + H]⁺) 347.3073, found 347.3073.

Butyl diocetylphosphine (3c). Following the general procedure A, using butyl octyl-H-phosphonate 1e (70.3 mg, 0.3 mmol, 1 equiv.), 1-octene 2a (33.6 mg, 0.3 mmol, 1 equiv.) and 10 mol% of catalyst (17.8 mg) affords 3d (81.2 mg, 0.22 mmol, 73%) as a colorless oil. 31P NMR (121 MHz, CDCl₃): δ = 56.5 (s); 1H NMR (300 MHz, CDCl₃): δ = 4.41–4.27 (m, 1H), 1.92–1.81 (m, 2H), 1.74–1.41 (m, 12H), 1.40–1.17 (m, 24H), 0.85 (t, J = 6.7 Hz, 6H); 13C NMR (75 MHz, CDCl₃): δ = 73.2 (d, J_{PC} = 6.8 Hz), 44.4 (d, J_{PC} = 4.3 Hz, 2C), 31.9 (2C), 31.0 (d, J_{PC} = 15.1 Hz, 2C), 29.2 (2C), 29.2 (2C), 28.9 (d, J_{PC} = 89.9 Hz, 2C), 25.4, 23.9 (2C), 22.7 (2C), 22.1 (d, J_{PC} = 3.9 Hz, 2C), 14.2 (2C); HRMS (ESI) m/z calcd for C₇₂H₁₄₀P ([M + H]⁺) 327.3225, found 327.3225.

Butyl diocetylphosphine (3c). Following the general procedure A, using butyl octyl-H-phosphonate 1f (63.6 mg, 0.3 mmol, 1 equiv.), 1-octene 2a (33.6 mg, 0.3 mmol, 1 equiv.) and 10 mol% of catalyst (89 mg) affords 3f (49.6 mg, 0.15 mmol, 51%) as a colorless oil. 31P NMR (121 MHz, CDCl₃): δ = 52.9 (s); 1H NMR (300 MHz, CDCl₃): δ = 7.28–7.16 (m, 5H), 3.96–3.76 (m, 1H), ...
Following the general procedure A, using cyclohexyl phenyl-H-phosphinate 1a (67.2 mg, 0.3 mmol, 1 equiv.), allylbenezene 2b (35.4 mg, 0.33 mmol, 1 equiv.) and 50 mol% of catalyst (89 mg) affords 3h (48.3 mg, 0.14 mmol, 48%) as a colorless oil. $^31$P NMR (121 MHz, CDCl$_3$): δ = 43.0 (s); $^1$H NMR (300 MHz, CDCl$_3$): δ = 7.74–7.64 (m, 2H), 7.49–7.33 (m, 3H), 7.21–7.00 (m, 5H), 4.24–4.09 (m, 1H), 2.66–2.49 (m, 2H), 1.98–1.04 (m, 14H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ = 141.1, 132.1 (d, $^1$J$_{PC}$ = 123 Hz), 132.0 (d, $^1$J$_{PC}$ = 2.7 Hz), 131.6 (d, $^1$J$_{PC}$ = 9.8 Hz, 2C), 128.5 (2C), 128.5 (d, $^1$J$_{PC}$ = 12.2 Hz, 2C), 128.4 (2C), 126.0, 74.4 (d, $^1$J$_{PC}$ = 6.7 Hz, 36.6 (d, $^1$J$_{PC}$ = 16.0 Hz), 34.4 (d, $^1$J$_{PC}$ = 2.9 Hz), 33.7 (d, $^1$J$_{PC}$ = 4.4 Hz), 29.8 (d, $^1$J$_{PC}$ = 101 Hz), 25.2, 23.7, 23.7, 23.5 (d, $^1$J$_{PC}$ = 3.2 Hz); HRMS (ESI) m/z calculated for C$_{21}$H$_{15}$O$_{3}$P ([M + H$^+$]) 342.1749, found 342.0564.

Cyclohexyl (3-methylbutan-2-yl)(phenyl)phosphinate (3i). Following the general procedure A, using cyclohexyl phenyl-H-phosphinate 1a (67.2 mg, 0.33 mmol, 1 equiv.), 2-methylbut-2-ene 2e (22.1 mg, 0.33 mmol, 1 equiv.) and 50 mol% of catalyst (89 mg) affords 3i (24 mg, 0.08 mmol, 27%) as a colorless oil (mixture 1: 1 of both diastereoisomers). $^31$P NMR (121 MHz, CDCl$_3$): δ = 42.7 (s); $^1$H NMR (300 MHz, CDCl$_3$): δ = 7.76–7.66 (m, 2H), 7.49–7.34 (m, 3H), 4.26–4.10 (m, 1H), 2.31–1.48 (m, 7H), 1.42–1.03 (8H), 0.96–0.79 (m, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ = 132.3 (d, $^1$J$_{PC}$ = 5.1 Hz, 2 × 0.5C), 132.2 (d, $^1$J$_{PC}$ = 5.2 Hz, 2 × 0.5C), 131.9 (d, $^1$J$_{PC}$ = 2.2 Hz, 0.5C), 131.9 (d, $^1$J$_{PC}$ = 2.2 Hz, 0.5C), 128.5 (d, $^1$J$_{PC}$ = 3.2 Hz, 2 × 0.5C), 128.3 (d, $^1$J$_{PC}$ = 3.1 Hz, 2 × 0.5C), 74.2 (d, $^1$J$_{PC}$ = 7.2 Hz, 0.5C), 74.0 (d, $^1$J$_{PC}$ = 7.1 Hz, 0.5C), 39.6 (d, $^1$J$_{PC}$ = 100 Hz 2 × 0.5C), 34.4 (d, $^1$J$_{PC}$ = 2.4 Hz, 0.5C), 34.4 (d, $^1$J$_{PC}$ = 2.3 Hz, 0.5C), 33.8 (d, $^1$J$_{PC}$ = 1.9 Hz, 0.5C), 33.8 (d, $^1$J$_{PC}$ = 1.9 Hz, 0.5C), 26.8 (d, $^1$J$_{PC}$ = 2.8 Hz, 0.5C), 26.1 (0.5C), 25.4 (2 × 0.5C), 23.8 (2 × 0.5C), 23.7 (2 × 0.5C), 22.6 (d, $^1$J$_{PC}$ = 6.1 Hz, 0.5C), 22.4 (d, $^1$J$_{PC}$ = 8.7 Hz, 0.5C), 18.3 (d, $^1$J$_{PC}$ = 3.2 Hz, 0.5C), 17.7 (d, $^1$J$_{PC}$ = 2.2 Hz, 0.5C), 7.7 (0.5C), 6.9 (d, $^1$J$_{PC}$ = 4.6 Hz, 0.5C) (1 signal missing); HRMS (ESI) m/z calculated for C$_{21}$H$_{16}$O$_{3}$P ([M + H$^+$]) 329.1821, found 329.1819.

Cyclohexyl [5-bromopentyl](phenyl)phosphinate (3j). Following the general procedure A, using cyclohexyl phenyl-H-phosphinate 1a (67.2 mg, 0.3 mmol, 1 equiv.), 5-bromo-1-pentene 2d (46.6 mg, 0.3 mmol, 1 equiv.) and 10 mol% of catalyst (17.8 mg) affords 3j (43 mg, 0.12 mmol, 38%) as a colorless oil. $^31$P NMR (121 MHz, CDCl$_3$): δ = 42.7 (s); $^1$H NMR (300 MHz, CDCl$_3$): δ = 7.82–7.72 (m, 2H), 7.56–7.39 (m, 3H), 4.31–4.18 (m, 1H), 3.34 (t, J = 6.8 Hz, 2H), 2.06–1.11 (m, 18H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ = 132.32 (d, $^1$J$_{PC}$ = 123 Hz), 132.1 (d, $^1$J$_{PC}$ = 2.7 Hz), 131.7 (d, $^1$J$_{PC}$ = 9.7 Hz, 2C), 128.6 (d, $^1$J$_{PC}$ = 12.3 Hz, 2C), 74.5 (d, $^1$J$_{PC}$ = 6.7 Hz), 34.5 (d, $^1$J$_{PC}$ = 2.9 Hz), 33.8 (d, $^1$J$_{PC}$ = 4.4 Hz), 33.5, 32.4, 32.0 (d, $^1$J$_{PC}$ = 101 Hz), 29.3 (d, $^1$J$_{PC}$ = 15.7 Hz), 25.3, 23.9, 23.8, 21.2 (d, $^1$J$_{PC}$ = 3.6 Hz); HRMS (ESI) m/z calculated for C$_{21}$H$_{14}$BrO$_{3}$P ([M + H$^+$]) 372.0854, found.
In conclusion, we developed an efficient UV-mediated hydrophosphinylolation of unactivated alkenes with 3-phosphinic acids. This reaction can be carried out using an ionic liquid soluble photosensitizer while maintaining good yield. Furthermore, the reaction with hypophosphorous acid is disclosed for the first time. Finally, a continuous flow hydrophosphinylolation was also reported which allowed faster reaction time with high yields, highlighting the potential of our methodology for rapid scale up and in-line synthesis. Taking into account the simplicity of our reaction conditions we believe this procedure will be appealing for further chemical and pharmaceutical applications.

Conflicts of interest
There are no conflicts to declare.

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