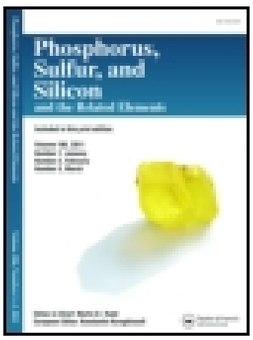

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2-Phenoxyethyldiphenylphosphine oxide as an equivalent of diphenylvinylphosphine oxide in nucleophilic additions

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ABSTRACT

A facile method for the synthesis of β-functionalized ethyldiphenylphosphine oxides is developed based on readily available 2-phenoxyethyldiphenylphosphine oxide used as an equivalent of diphenylvinylphosphine oxide in the reactions of addition of different PH- and NH-nucleophiles in DMSO in the presence of KOH. The transformations of labile phosphine oxides of a general formula $Ph_2P(O)CH_2CH_2OR$, where R = Ph, H, or $Ph_2P(O)CH=CH_2$, in aq.KOH/DMSO and solid KOH/DMSO systems are explored in the absence of nucleophilic reagents.

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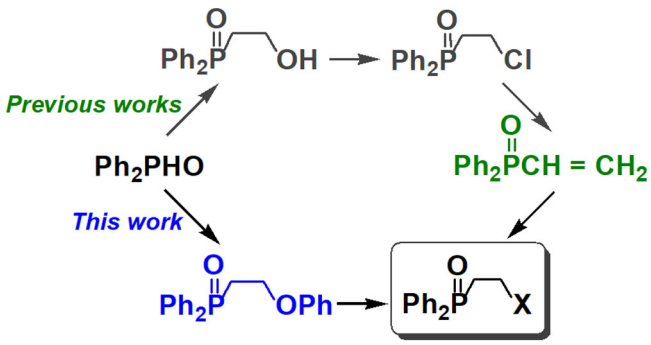
GRAPHICAL ABSTRACT



Introduction

In the chemistry of organophosphorus compounds, as well as in organoelement chemistry in general, the most valuable reagents are those that enable easy introduction of a phosphorus-containing group, resulting in the formation of a carbon–element or carbon–carbon bond. One of these reagents is diphenylvinylphosphine oxide **1**, which was described for the first time as early as 1961.[1,2] Due to its ability to add readily various nucleophilic agents, it is widely used in synthetic practice as a 'donor' of the 2-diphenylethylphosphoryl group in the synthesis of β-O-,[3–5] C-,[3] N-,[3,5–9] and P-[3,5,10,11] substituted ethyldiphenylphosphine oxides. This led to the development of numerous synthetic routes to the starting oxide **1** from various P(III) and P(V) acid derivatives, which are shown in Supporting Information Scheme S1.

Optically active β-phosphorylated aminophosphine oxides[8,12] and (β-diphenylphosphino)ethyldiphenylphosphine oxide[13] derived from vinylphosphine oxide **1** are of interest as ligands for metal complex catalysts; nonsymmetrical ethylenediphosphine dioxides[14] and P-containing podands[4,14] demonstrate high efficiency and selectivity toward the alkali metal cations. Aza-podands[15] and carbamoylphosphine oxides obtained from the secondary *N*-alkyl-*N*-(β-phosphorylethyl)-amines[16] are effective extractants for rare earth metals(III) from the acidic media.

We have previously found,[17] that to obtain the products of nucleophilic addition of NH- and PH-acids to vinyldiphenylphosphine oxide **1**, β-hydroxyethyldiphenylphosphine oxide **2**,[18] which is an intermediate compound in the synthesis of the oxide **1**,[19] can be used, thereby allowing to exclude the steps of its preparation, as well as β-ethoxyethyldiphenylphosphine oxide.[17] These advances were preceded by several reports on successful replacement of β-alkoxy groups in phosphine oxides for $R_2P(O)$-substituents.[20,21] However, the modified method was limited only to the active NH- and PH-nucleophiles.

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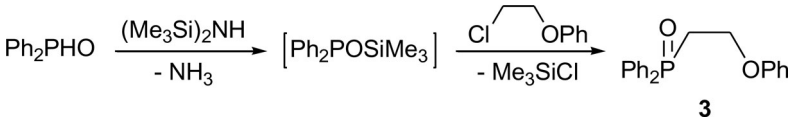


Scheme 1. Synthesis of 2-phenoxyethyldiphenylphosphine oxide **3**.

Results and discussion

In the present work, we used 2-phenoxyethyldiphenylphosphine oxide **3** as an equivalent of vinylphosphine oxide **1** in the reactions with different nucleophilic reagents for the synthesis of β-functionalized ethyldiphenylphosphine oxides. Note that a convenient and efficient synthetic route to compound **3** was devised by our research group starting from diphenylphosphinous acid and hexamethyldisilazane based on the Arbuzov rearrangement of O-trimethylsilyldiphenylphosphinite[19] with β-chloroethylphenyl ether (Scheme 1). Earlier the analogous reactions were successfully accomplished with ethyl chloroacetate[22] and oligo(ethylene glycol) ditosylates and dihalogen derivatives.[23]

The reactions of phosphine oxide **3** with a range of PH- and NH-nucleophiles were carried out in DMSO in the presence of aqueous or solid KOH at 60–70 °C. Under these conditions, PhO^- leaving group is readily substituted for different nucleophilic moieties (Scheme 2). The reactions were monitored using 31P NMR spectroscopy.

Table 1 lists the conditions for the synthesis and main characteristics of resulting β-substituted ethyldiphenylphosphine oxides **4**–**12**.

The structures of all the compounds obtained were unambiguously confirmed based on the $^{31}P\{^1H\}$, ^1H, and $^{13}C\{^1H\}$ NMR spectroscopic data. The ^1H signals were assigned based on the fully proton-decoupled ^{13}C NMR spectra. The signals of the carbon nuclei were assigned based on the results of 2D NMR experiments using HMBC and HSQC pulse sequences. It should be noted that $^2J_{HP}$ and $^3J_{HP}$ coupling constants of the doublet of triplets corresponding to α- and β-methylene protons of the $P(O)CH_2CH_2$ moiety in the NMR spectra of secondary amines **6**–**8** are in the range of 11.2–11.4 Hz. In the case of tertiary amine **12**, the value of $^3J_{HP}$ coupling constant appeared to be twice as much as that of $^2J_{HP}$ (20.7 Hz vs. 10.3 Hz).

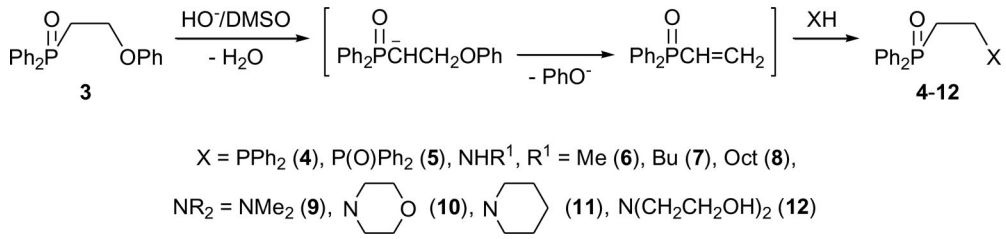
The reactions with active diphenylphosphine and diphenylphosphinous acid in the presence of the aqueous alkali proceeded smoothly and completed in 30–60 min at 60–80 °C. According to the results of the $31P\{^1H\}$ NMR monitoring of the reaction course, the yields of the target products were quantitative (Table 1). Dimethylamine and morpholine were readily alkylated with phosphine oxide **3** under the same conditions and afforded β-aminoethylphosphine oxides **9** and **10** in high yields within 2.5 h, respectively. These reactions start with the rapid generation of vinylphosphine oxide **1** upon interaction of phenoxyethyl precursor **3** with the alkali (Scheme 1). According to the 31P NMR spectrum, the reaction mixture obtained immediately after mixing oxide **3**, morpholine, and aq.KOH/DMSO at 25 °C contains 21% of vinylphosphine oxide **1** (23.7 ppm) and 79% of the starting oxide (29.9 ppm).

The alkylation of piperidine and diethanolamine was performed in the solid KOH/DMSO superbasic medium at 70 °C for 1 and 2.5 h, respectively. In these cases, the resulting reaction mixtures contained side products along with target phosphine oxides **11** and **12**. In the first case, the 31P NMR spectrum of the reaction mixture displayed two signals which refer to target oxide **11** (31.3 ppm, 94%) and tetraphenylethylene diphosphine dioxide **5** (32.4 ppm, 6%). The most complex pattern was observed in the spectrum of the reaction mixture with diethanolamine. After heating for 0.5 h, the spectrum showed the phosphorus resonances of starting oxide **3** (29.1 ppm, 24%) and vinylphosphine oxide **1** (23.7 ppm, 7%), and the signals of four side products: hydroxyethylphosphine oxide **2** (32.9 ppm, 6%), dioxide **5** (32.3 ppm, 6%), bis(2-diphenylphosphinyl)ethyl ether **13** (29.4 ppm, 4%), potassium diphenylphosphinate **14** (17.8 ppm, 6%), and an oxide derivative (30.4 ppm, 35%), which is likely to result from the HO-addition of diethanolamine to oxide **1**. After 2 h of heating, the reaction mixture contained only three products: target phosphine oxide **12** (81%, 35.3 ppm), dioxide **5** (6%, 32.4 ppm), and potassium diphenylphosphinate $Ph_2P(O)O^-K^+$ **14** (13%, 17.6 ppm).

The phosphorus signals of the side products in the reaction mixtures were assigned based on the comparative analysis of δ values for proposed compounds **5**, **13**, and **14**, as well as the data of the NMR spectra of $CDCl_3$ solutions of the mixed samples obtained by addition of individual compounds **1**, **2**, **5**, and **14** to the reaction mixture.

The same side products were observed during alkylation of primary amines RNH_2 (R = Me, Bu, Oct). In these cases, the yields of secondary amines strongly depended on the ratio of the reagents and the medium basicity. The reaction of oxide **3** with $BuNH_2$ (1:4) in aq.KOH/DMSO at 25 °C for 6 h led to a mixture of secondary amine **7** (56%, 31.5 ppm), tertiary amine $[Ph_2P(O)CH_2CH_2]_2NBu$ (3%, 31.3 ppm), and hydroxyethylphosphine oxide **2** (41%, 33.5 ppm). The use of a tenfold excess of butylamine provided 96% yield of secondary amine **7** upon heating at 70 °C for 1.5 h. The side product appeared to be dioxide **5** (4%) (Table 1). The reaction of hydroxyethylphosphine oxide **2** under the same conditions during heating for 6 h afforded amine **7** in 85% yield together with the corresponding tertiary amine and the potassium salt **14** (Scheme 3).

It is noteworthy, that replacing bipolar DMSO, which solvates potassium cations well, with nonpolar dioxane leads to a significant decrease in the rate of conversion of phenoxy derivative **3** to diphenylvinylphosphine oxide **1** (Scheme 2). Thus, the reaction with piperidine at 60 °C in DMSO occurs within 45–60 min, whereas in dioxane under the same conditions, after 1 h the reaction mixture contains 80% of the starting oxide **3** (^{31}P NMR) and as low as 13% after 8 h.

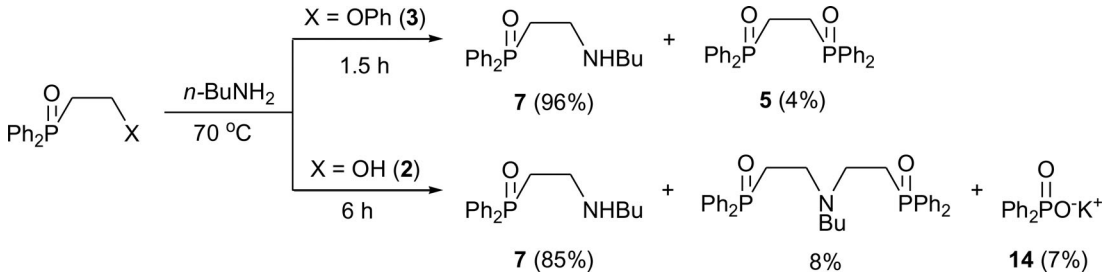


Scheme 2. Syntheses of 2-substituted ethyldiphenylphosphine oxides **4**–**12**.

Table 1. Conditions for the synthesis, yields and main characteristics of β-functionalized ethyldiphenylphosphine oxides $Ph_2P(O)CH_2CH_2X$ **4**–**12**.

№	X	Molar ratio of the reagents **3** : aq.KOH : XH	Heating temperature, °C	Heating time, h	Yield,[a] %	M. p., °C (solvent)
4	PPh_2	1 : 1.5 : 1	80	1	100 (95)	193–194 [b](ethanol)
5	$P(O)Ph_2$	1 : 1.5 : 1.1	60	0.5	100 (89)	266–268[c] (methanol)
6	NHMe	1 : 1.5 : 10	70	1	97 (79)	61–63[d, e]
7	NHBu	1 : 1.5 : 10	70	1	96 (80)	66.5–68[d, f] (*c*-hexane)
8	NHOctyl	1 : 1.5 : 6	70	3	97 (74)	75–77[d, g] (ethyl acetate)
9	NMe_2	1 : 1.5 : 3	70	2.5	100 (80)	112.5–113.5[h] (*c*-hexane)
10		1 : 1.5 : 1	60–70	2.5	94 (67)	126–128[i] (hexane–ethyl acetate)
11		1 :1.5[j]: 1.5	60	1	94 (89)	111–112[k] (hexane–ethyl acetate)
12	$N(CH_2CH_2OH)_2$	1 :1.5[j]: 1.5	70	2	81 (52)	oil[d]

[a]According to the ^{31}P NMR data (yields of isolated products).
[b]Literature m.p. 193–194 °C.[17]
[c]Literature m.p. 269–270 °C[3,17]; 271–272 °C.[18]
[d]purified by column chromatography.
[e]Literature m.p. 28–30 °C.[24]
[f]Literature m.p. 64–65° C.[25]
[g]Literature m.p. 35 °C.[9]
[h]Literature m.p. 114 °C.[6]
[i]Literature m.p. 133 °C.[6]
[j]solid KOH.
[k]Literature m.p. 115 °C[17]; 112–113 °C.[6]

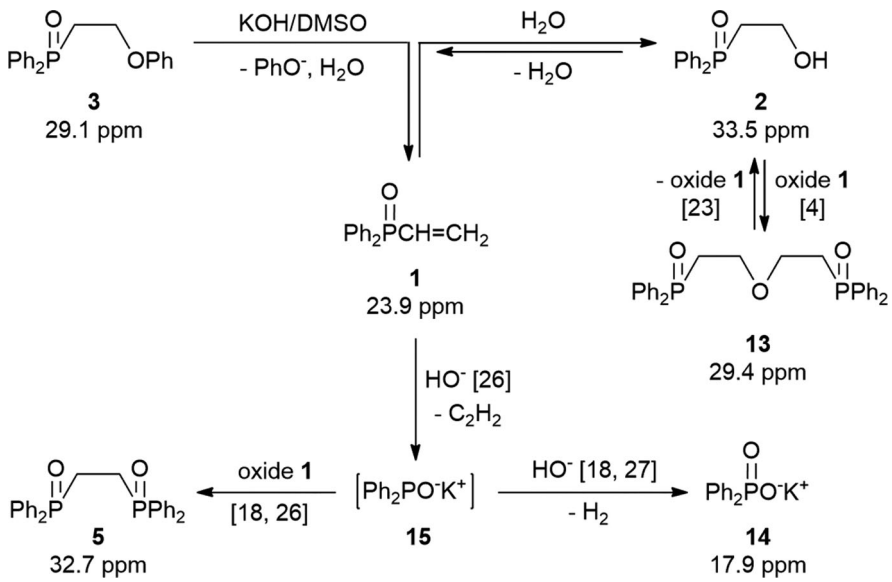


Scheme 3. Reactions of butylamine with phosphine oxides **2** and **3** (1:10) in aq.KOH/DMSO.

In the superbasic medium (solid KOH/DMSO), the reaction of oxide **3** with $BuNH_2$ (1:2) led to a mixture of secondary amine **7** and tertiary amines (48% and 25%, respectively), as well as four side products, including phosphine oxides **1** (3%) and **2** (8%), dioxide **5** (7%), and potassium diphenylphosphinate **14** (9%).

Hence, the application of sixfold–tenfold excess of the initial primary amine allows for suppression of the competing reactions of addition of water to vinylphosphine oxide **1** and alkylation of the resulting secondary amine. It should be noted that the melting points of resulting secondary amines **6** and **8** are higher than those detected earlier for the amine samples obtained by other routes by 33 °C and 45 C, respectively (Table 1). Nevertheless, their structures and compositions were unequivocally confirmed by the ^{1}H, ^{13}C, and 31P NMR spectroscopic data as well as microanalyses (Table 1).

To confirm the identity of the side products, we performed the analogous experiments without the addition of nucleophilic reagents. The transformations of oxide **3** in the aqueous and solid KOH/DMSO systems at 25 °C and 70 °C were monitored by 31P NMR spectroscopy. The analogous experiments were carried out also with intermediate vinylphosphine oxide **1** and 2-hydroxyethylphosphine oxide **2**. The resulting data are summarized in Scheme 4.



Scheme 4. Transformations of phosphine oxides **1**, **2**, and **3** in aqueous and solid KOH/DMSO.

In the presence of the base, oxide **3** starts to convert to vinylphosphine oxide **1**. In the medium of aq.KOH/DMSO, initial oxide **3** afforded at room temperature after 2 h a mixture containing 40% of dioxide **5** (32.4 ppm), 7% of vinylphosphine oxide **1** (23.8 ppm), and 6% of hydroxyethyl-substituted phosphine oxide **2** (32.8 ppm). After heating of oxide **3** under these conditions at 70 °C for 1 h, the 31P NMR spectrum showed the resonances of vinylphosphine oxide **1** (23.8 ppm, 82%), phosphine oxide **2** (32.9 ppm, 14%), and bis(phosphorylated) diethyl ether **13** (29.4 ppm, 4%), which resulted from the addition of water and phosphine oxide **2** to oxide **1**. Heating for 8 h afforded a mixture of dioxide **5** (34%) and potassium diphenylphosphinate **14** (36%) as the main products along with oxides **1** (16%) and **2** (8%).

In the superbasic medium solid KOH/DMSO during heating at 70 °C for 1 h, oxide **3** almost fully converted to vinylphosphine oxide **1** (23.8 ppm, 92%), affording only a small amount of 2-hydroxyethylphosphine oxide **2** (32.8 ppm, 8%). In 10 h, the main reaction product appeared to be potassium salt **14** (58%) with a mixture of oxides **1** (13%) and **2** (8%), ether **13** (3%), and dioxide **5** (8%).

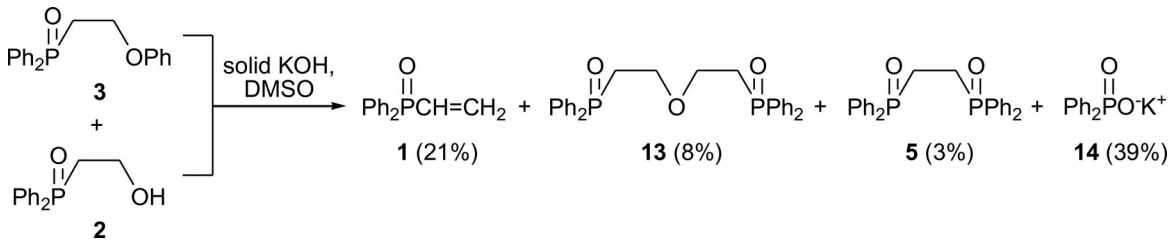
Product **5** results from the cleavage of the P–C bond in vinylphosphine oxide **1** under the action of the alkali, which affords acetylene and diphenylphosphinite anion Ph_2PO^-,[26] followed by the addition of the latter across the double bond of oxide **1**[18,26] (Scheme 4). Earlier it was shown that oxide **1** quantitatively converts to dioxide **5** during stirring in a water–methanol solution of NaOH at room temperature for 24 h.[26] The analogous result was obtained upon heating of the bis(phosphorylated) diethyl ether in a water–alcohol medium at a temperature >30 °C in the presence of diphenylphosphinous acid and an alkaline agent (NaOH, EtONa, NaH, or K_2CO_3).[23]

In the superbasic medium, diphenylphosphinite anion Ph_2PO^- **15** is readily and rapidly oxidized to diphenylphosphinate anion $Ph_2P(O)O^-$ **14**.[18,27] It is known that diphenylphosphinous acid is oxidized (80%) in aq.KOH/DMSO at 25 °C during 20 h or at 60 °C during 5 h.[18] In the experiment performed with the solid alkali, Ph_2PHO quantitatively converted to $Ph_2P(O)O^-K^+$ **14** at 25 °C for 2 h. An attempt to synthesize bis(phosphorylated) diethyl ether **13** from phenoxyethylphosphine oxide **1** and hydroxyethyl counterpart **2** in the solid KOH/DMSO system afforded a mixture with potassium salt **14** as a main product (Scheme 5).

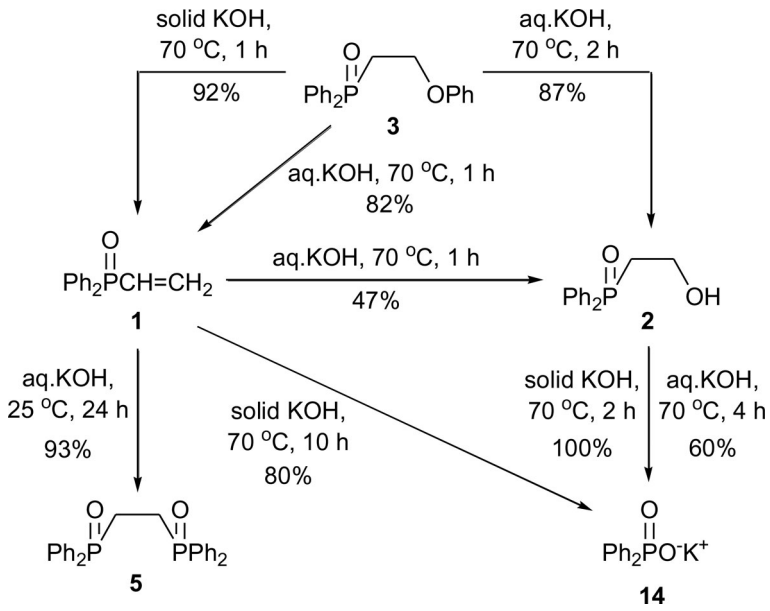
The results obtained suggest that the reaction mixture consisting of oxide **3**, KOH, and DMSO is a very labile system (Scheme 4). In the absence of compounds that can rapidly bind *in situ* generated diphenylvinylphosphine oxide **1**, oxides **2** and **13** are readily formed. The transformations between compounds **1**, **2**, and **13** represent reversible addition/elimination reactions. Upon addition of a nucleophilic reagent, the equilibrium shifts to the formation of vinylphosphine oxide **1** and further to β-substituted ethyldiphenylphosphine oxide. In the case of the less active nucleophilic reagents, the addition proceeds slowly and the competing cleavage of the P–C bond of vinylphosphine oxide **1** becomes predominant, resulting in the formation of diphenylphosphinite anion **15**[26] and its following conversion to stable dioxide **5**[18,26] and/or oxidation to potassium salt **14**[18,27] depending on the medium basicity and the reaction time (Scheme 4).

Scheme 6 shows the conditions for conversion of oxides **1**–**3** in the absence of nucleophilic reagents to stable *P,P,P',P'*-tetraphenylethylenediphosphine dioxide **5** and potassium salt **14**. In the aqueous medium, the formation of dioxide **5** prevails, whereas in the superbasic medium, the main product is potassium diphenylphosphinate **14**.

Thus, phenoxyethylphosphine oxide **3** is readily transformed into labile vinylphosphine oxide **1**, which quantitatively converts to dioxide **5** in aq.KOH/DMSO at 25 °C during 6 h and affords potassium salt **14** in 80% yield in the superbasic medium at 70 °C after 10 h. More stable



Scheme 5. Composition of the reaction mixture of oxides **3** and **2** after heating at 60 °C for 14 h.



Scheme 6. Conditions for the transformation of oxides **1**–**3** in KOH/DMSO into tetraphenyldiphosphine dioxide **5** and potassium phosphinate **14**.

hydroxyethylphosphine oxide **2** remains unchanged in aq.KOH/DMSO at room temperature for 24 h, whereas at 70 °C it converts to salt **14** in 60% yield for 4 h. Under the superbasic conditions, the P–C bond in oxide **2** is completely cleaved within 2 h (Scheme 6).

Conclusions

Hence, we developed a facile synthetic route to β-functionalized ethyldiphenylphosphine oxides using readily available 2-phenoxyethyldiphenylphosphine oxide instead of diphenylvinylphosphine oxide in nucleophilic additions. The advanced method for obtaining the target β-functionalized derivatives allows for avoiding the multistep synthesis of the vinyl-substituted phosphine oxide. The investigations on the transformations of starting phenoxyethylphosphine oxide and intermediate β-hydroxyethyl- and vinyl-containing counterparts in KOH/DMSO in the absence of nucleophilic reagents enabled complete identification of the side products. It was shown that in the KOH/DMSO medium, 2-phenoxyethyl-, 2-hydroxyethyl-, and diphenylvinylphosphine oxides are labile compounds that readily convert to each other. The application scope of the suggested method was explored for a range of PH- and NH-nucleophiles. It was found that the reactions with less reactive nucleophilic reagents afford tetraphenylethylenediphosphine dioxide as the main side product in aq.KOH/DMSO, whereas in the solid KOH/DMSO superbasic medium, the main side product is potassium diphenylphosphinate. The use of phenoxyethyldiphenylphosphine oxide allows one to perform the reactions with nucleophilic reagents at lower temperatures (10–30 °C) and with shorter reaction times (0.5–2.5 h) than the analogous processes with 2-hydroxyethyl-substituted counterpart, thus, decreasing the amount of the side products in the resulting mixture.

Experimental section

The 1H, 13C{^{1}H}, and 31P{^{1}H} NMR spectra of solutions of the resulting compounds and reaction mixtures in $CDCl_3$ were measured with a Bruker Avance III NanoBay 300 and a Bruker Avance^{TM} 600 instrument at 300.28 and 600.22 MHz (^{1}H), 75.51 and 150.925 MHz (^{13}C), and 121.495 and 242.974 MHz (^{31}P), respectively. The chemical shifts of hydrogen and carbon nuclei were referenced to the residual signal of chloroform (7.27 ppm) or the signal of $CDCl_3$ (77.0 ppm) and calculated relative to TMS. ^{31}P NMR chemical shifts are given with respect to 85% solution of H_3PO_4 in D_2O as external standard. Electrospray ionization mass spectrometry (ESI-MS) spectra of synthesized compounds in methanol solutions were recorded on with electrospray mass spectrometer AmaZon Bruker Daltonik GmbH in the UltraScan positive and negative ionization mode (*m*/*z* range: 70–2200). The Supporting

Information contains sample ^{1}H, ^{13}C, and ^{31}P NMR spectra of the products (Figures S1–S34)

All the manipulations with trivalent phosphorus derivatives were performed under an inert atmosphere of argon. The solvents in use were dried according to the standard procedures.[28] Column chromatography was carried out using Fluka silica gel 70-230 mesh, 60 Å. The melting points were determined with Anshuts thermometers in a special unit using capillaries.

Diphenylvinylphosphine oxide **1**,[19] 2-hydroxyethyldiphenylphosphine oxide **2**,[18] and diphenylphosphinous acid[29] were synthesized according to the published procedures.

Diphenylphosphine

A two-neck flask equipped with a capillary, a Wurtz adapter, and a descending condenser, was charged with 121.2 g (0.60 mol) of diphenylphosphinous acid[29] and 6.5 g (0.03 mol) of diphenylphosphinic acid.[18,30] The resulting mixture was heated under vacuum at 175–180 °C (bath) and on distillation yielded diphenylphosphine (b.p. 156–160 °C/10 torr). Yield: 50.2 g (90%), δ_P (DMSO): 39.0 ppm, J_{PH} = 215.4 Hz.

The stillage residue was heated at 80–90 °C with a solution of 20 g of KOH in 150 mL of water until complete dissolution. The resulting mixture was cooled to room temperature, filtered, and acidified with dilute H_2SO_4 to pH = 3–4. The resulting precipitate was filtered off, rinsed with water, and dried in air to give 66.0 g (100%) of diphenylphosphinic acid. M. p. 193–195 °C (Literature m.p.: 193–195 °C[18]).

2-Phenoxyethyldiphenylphosphine oxide (3)

A mixture of 30.0 g (148 mmol) of diphenylphosphinous acid[29] and 48 mL (37.1 g, 230 mmol) of hexamethyldisilazane was stirred at 120 °C for 1 h. Then, 19.7 g (126 mmol) of 2-phenoxyethylchloride[31] was added dropwise under an argon flow at the same temperature over 30 min. The reaction mixture was heated at 180–200 °C for 3 h, distilling trimethylchlorosilane (vapor temperature: 57–97 °C), then, cooled to room temperature, diluted with CCl_4 (70 mL) and $CHCl_3$ (30 mL), and stirred at 40–50 °C for 3 h. After addition of 50 mL of H_2O, the organic layer was separated, sequentially washed with saturated aqueous solution of K_2CO_3 (5 × 10 mL)[1], H_2O (2 × 10 mL), 5% aq. HCl (10 mL), and H_2O (2 × 10 mL), dried over anhydrous Na_2SO_4, and evaporated under vacuum. The resulting residue (39.2 g, yellow oil) was crystallized upon addition of 50 mL of Et_2O. The crystals obtained were collected by filtration (38 g). According to the $^{31}P\{^{1}H\}$ NMR spectrum, the crude product contained 94% of phosphine oxide **3** and 6% of dioxide **5**. A heterogeneous mixture of the crystalline product and 100 mL of EtOAc was passed through a silica gel (30 g) column (eluent: EtOAc, 500 mL). The eluate obtained was evaporated under vacuum. The resulting residue (35.5 g, 88%; m. p. 103–105 °C) was recrystallized from EtOAc to give 34.9 g (86%) of phosphine oxide **3**. M. p.: 105–106 °C (Literature m.p.: m. p. 105–106 °C[32]).

^{1}H NMR (300.28 MHz): δ = 2.86 (dt, $^{3}J_{HH}$ = 7.4 Hz, $^{2}J_{HP}$ = 11.7 Hz, 2H, PCH_2); 4.34 (dt, $^{3}J_{HP}$ = 9.3 Hz, $^{3}J_{HH}$ = 7.4 Hz, 2H, CH_2O); 6.73 (d, $^{3}J_{HH}$ = 8.6 Hz, 2H, *ortho*-CH_{OPh}); 6.91 (t, $^{3}J_{HH}$ = 7.4 Hz, 1H, *para*-CH_{OPh}); 7.21 (d, $^{3}J_{HH}$ = 7.3 Hz, 2H, *meta*-CH_{OPh}); 7.44–7.58 (m, 6H, *meta*-CH_{PPh} + *para*-CH_{PPh}), 7.78 (ddd, $^{3}J_{HP}$ = 11.7 Hz, $^{3}J_{HH}$ = 7.9 Hz, $^{4}J_{HH}$ = 1.6 Hz, 4H, *ortho*-CH_{PPh}). ^{13}C NMR (75.50 MHz): δ = 30.6 (d, $^{1}J_{CP}$ = 70.7 Hz, PCH_2); 61.6 (s, CH_2O); 114.7 (s, *ortho*-CH_{OPh}); 121.3 (s, *para*-CH_{OPh}), 129.0 (d, $^{3}J_{CP}$ = 12.0 Hz, *meta*-CH_{PPh}); 129.6 (s, *meta*-CH_{OPh}); 131.0 (d, $^{2}J_{CP}$ = 9.6 Hz, *ortho*-CH_{PPh}); 132.3 (d, $^{4}J_{CP}$ = 3.1 Hz, *para*-CH_{PPh}); 132.6 (d, $^{1}J_{CP}$ 100.6 Hz, *ipso*-C_{PPh}); 158.2 (s, *ipso*-C_{OPh}). 31P NMR (75.50 MHz): δ = 29.9. ESI-MS, *m/z* (I_{rel}, %): 323 (23) $[M+H]^+$, 345 (95) $[M+Na]^+$, 667 (34) $[2M+Na]^+$.

Continuing elution with methanol allowed for collecting the dioxide fraction. The eluate was evaporated under vacuum. The residue obtained (2.1 g, 6%; m. p. 265–268 °C) was recrystallized from ethanol to give 1.4 g (4%) of dioxide **5**, m.p.: 268–269 °C. Literature m.p.: 269–270 °C,[3] 271–272 °C.[18] A description of the spectra of dioxide **5** is given in the procedure of its synthesis at page 12, its actual spectra are provided in Supporting Information.

P,P,P′,P′-Tetraphenylethylenediphosphine monooxide (4)

A mixture of 2-phenoxyethyldiphenylphosphine oxide **3** (3.98 g, 12.4 mmol), diphenylphosphine (2.31 g, 12.4 mmol), and 50% aqueous solution of KOH (18.6 mmol) in DMSO (15 mL) was rigorously stirred under an argon flow at 80 °C for 1 h and diluted with water (30 mL). The resulting precipitate was filtered off, washed with water, and recrystallized from ethanol Yield: 4.87 g (95%); m.p.: 193–194 °C. Literature m.p. 193–194 °C.[17] (Table 1). ^{1}H NMR (600.22 MHz): δ = 2.30 (br. s, 4H, CH_2CH_2); 7.30–7.68 (m, 20H, Ph). ^{13}C NMR (150.925 MHz): 19.2 (dd, J_{CP} = 15.0 Hz, $^{2}J_{CP}$ = 4.2 Hz, CH_2P); 25.9 (dd, J_{CP} = 69.6 Hz, $^{2}J_{CP}$ = 16.5 Hz, $CH_2P{=}O$); 128.6 (d, $^{3}J_{CP}$ = 6.9 Hz, *meta*-CH_{PPh}); 128.8 (d, $^{2}J_{CP}$ = 11.6 Hz, *ortho*-CH_{PPh}); 129.0 (s, *para*-CH_{PPh}); 130.8 (d, $^{3}J_{CP}$ = 9.3 Hz, *meta*-$CH_{P(O)Ph}$); 131.9 (d, J_{CP} = 2.6 Hz, *para*-$CH_{P(O)PPh}$); 132.4 (d, J_{CP} = 98.3 Hz, *ipso*-$C_{P(O)Ph}$); 132.8 (d, $^{2}J_{CP}$ = 18.5 Hz, *ortho*-$CH_{P(O)Ph}$); 137.3 (d, J_{CP} = 13.1 Hz, *ipso*-C_{PPh}). ^{31}P NMR (121.56 MHz): δ = 15.0 (d, $^{3}J_{PP}$ = 49.5 Hz, CH_2P); 30.0 (d, $^{3}J_{PP}$ = 49.5 Hz, $CH_2P{=}O$).

P,P,P′,P′-Tetraphenylethylenediphosphine dioxide (5)

P,P,P',P'-Tetraphenylethylenediphosphine dioxide (5) was obtained in analogy to monooxide **4** from phosphine oxide **3** (3.45 g,10.7 mmol), diphenylphosphinous acid[29] (2.38 g, 11.8 mmol), and 50% aqueous solution of KOH (0.90 g, 16.0 mmol) in DMSO (14 mL) (60 °C, 30 min). Obtained product was recrystallized from ethanol. Yield: 4.10 g (89%); m.p.: 266–268 °C. Literature m.p. 269–270 °C,[3,17] 271–272 °C.[18] (Table 1). ^{1}H NMR (600.22 MHz): δ = 2.49, 2.50 (two s[2], 4H, CH_2P); 7.42 (t, $^{3}J_{HH}$ = 7.5 Hz, 8H, *meta*-CH); 7.47 (t, $^{3}J_{HH}$ =

[1]The organic layer was washed until precipitation of $Ph_2P(O)OH$ during acidification of the washings.

[2]Two conformers (1:1).

7.4 Hz, 4H, *para*-CH); 7.68 (dd, $^{3}J_{HH}$ = 7.5 Hz, $^{3}J_{HP}$ =12.0 Hz, 8H, *ortho*-CH). ^{13}C NMR (150.925 MHz): δ = 21.4, 21.9 (two dd, J_{CP} = $^{2}J_{CP}$ = 31.4 Hz, PCH_2, two conforms); 128.9 (two overlapping d, $^{3}J_{CP}$ = 5.9 Hz, *meta*-CH); 130.8 (two overlapping d, $^{2}J_{CP}$ = 4.8 Hz, *ortho*-CH); 131.9 (m, *ipso*-C); 132.1 (s, *para*-CH). ^{31}P NMR (121.56 MHz): δ = 32.8. ESI-MS: *m/z* (I_{rel}, %): 431 (20) $[M+H]^+$, 453 (100) $[M+Na]^+$.

General procedure for the synthesis of 2-substituted ethyldiphenylphosphine oxides 6–12

A mixture of 2-phenoxyethyldiphenylphosphine oxide **3** (10 mmol), the corresponding nucleophilic reagent (10–100 mmol), and KOH (15 mmol) (50% aqueous solution or solid) in DMSO (15 mL) was vigorously stirred at 60–70 °C for 1–4.5 h. The reaction course was monitored by 31P NMR spectroscopy. The resulting mixture was diluted with 20 mL of water, and the target product was extracted with $CHCl_3$ (3 × 15 mL). The extract was washed with 30% aq. KOH (3 × 10 mL), dried over anhydrous Na_2SO_4, and evaporated under vacuum. The resulting residue was kept at 50 °C (1 torr)[3] for 1 h and dissolved in 5% aq. HCl (15 mL). The solution obtained was washed with benzene (3 × 10 mL), alkalized with a saturated aqueous solution of K_2CO_3 until pH = 12, and extracted with $CHCl_3$ (3 × 10 mL). The extract was dried over anhydrous Na_2SO_4 and evaporated under vacuum. The resulting residue was recrystallized (amines **9**–**11**) or purified by column chromatography on silica gel using a $CHCl_3$–CH_3OH mixture (20:2) as an eluent (amines **6**–**8**, **12**). The reaction conditions in each particular case, yields and main characteristics of amines **6**–**12** are summarized in Table 1.

2-Methylaminoethyldiphenylphosphine oxide (6)

2-Methylaminoethyldiphenylphosphine oxide (6) was synthesized according to the general procedure using 1.37 g (5.3 mmol) of phosphine oxide **3**, 4.3 mL 40% aqueous solution of methylamine (3.86 g, 124 mmol), 50% aqueous solution of KOH (1.1 g, 18.6 mmol) and DMSO (10 mL) (70 °C, 1 h). The resulting residue was purified by column chromatography on silica gel ($CHCl_3$–MeOH, 20:2). Yield: 2.80 g (79%); m.p.: 61–63 °C. Literature m.p. 28–30 °C.[24] ^{1}H NMR (300.28 MHz): δ = 1.68 (br s, 1H, NH); 2.36 (s, 3H, CH_3); 2.48 (dt, $^{2}J_{HP}$ = 11.3 Hz, $^{3}J_{HH}$ = 7.4, 2H, PCH_2); 2.89 (dt, $^{3}J_{HP}$ = 11.4 Hz, $^{3}J_{HH}$ = 7.4 Hz, 2H, $PCH_2\underline{CH_2}$); 7.41–7.54 (m, 6H, *meta*-CH + *para*-CH); 7.72 (ddd, $^{3}J_{HP}$ = 11.5 Hz, $^{3}J_{HH}$ = 7.9 Hz, $^{4}J_{HH}$ = 1.6 Hz, 4H, *ortho*-CH). ^{13}C NMR (75.50 MHz): δ = 30.3 (d, J_{CP} = 71.1 Hz, PCH_2); 36.4 (s, CH_3); 45.1 (d, $^{2}J_{CP}$ = 2.0 Hz, $PCH_2\underline{CH_2}$); 128.9 (d, $^{3}J_{CP}$ = 11.6 Hz, *meta*-CH); 130.9 (d, $^{2}J_{CP}$ = 9.4 Hz, *ortho*-CH); 132.0 (d, $^{4}J_{CP}$ = 2.7 Hz, *para*-CH); 133.1 (d, J_{CP} = 98.6 Hz, *ipso*-C). ^{31}P NMR (121.56 MHz): δ = 31.4. ESI-MS: *m/z* (I_{rel}, %): 260 (100) $[M+H]^+$, 282 (12) $[M+Na]^+$, 519 (94) $[2M+H]^+$, 541 (80) $[2M+Na]^+$. Anal. Calcd. for $C_{15}H_{18}NOP$: C, 69.48; H, 7.00; N, 5.40; P, 11.95. Found: C, 69.29; H, 7.11; N, 5.42; P, 12.00%.

[3]To remove the DMSO residues into a trap cooled with liquid nitrogen.

2-Butylaminoethyldiphenylphosphine oxide (7)

2-Butylaminoethyldiphenylphosphine oxide (7) was synthesized according to the general procedure using phosphine oxide **3** (6.0 g, 18.6 mmol), 13.6 g (18 mL, 186.0 mmol) butylamine, 50% aqueous solution of KOH (1.6 g, 27.9 mmol) and DMSO (15 mL) (70 °C, 1 h). The resulting residue was purified by column chromatography on silica gel ($CHCl_3$–MeOH, 20:2). Yield: 5.0 g (89%); m.p.: 66.5–68 °C (*c*-hexane). Literature m.p. 64–65 °C.[25] ^{1}H NMR (300.28 MHz): δ = 0.84 (t, $^{3}J_{HH}$ = 7.2 Hz, 3H, CH_3); 1.25 (sextet, $^{3}J_{HH}$ = 7.3 Hz, 2H, CH_2Me); 1.37 (quintet, $^{3}J_{HH}$ = 7.2 Hz, 2H, CH_2Et); 1.73 (s, 1H, NH); 2.49 (dt, $^{2}J_{HP}$ = 11.2 Hz, $^{3}J_{HH}$ = 7.4 Hz, 2H, PCH_2); 2.52 (t, $^{3}J_{HH}$ = 7.0 Hz, 2H, CH_2Pr); 2.92 (dt, $^{3}J_{HP}$ = 11.3 Hz, $^{3}J_{HH}$ = 7.4 Hz, 2H, $PCH_2\underline{CH_2}$); 7.40–7.53 (m, 6H, *meta*-CH + *para*-CH); 7.72 (ddd, $^{3}J_{HP}$ = 11.5 Hz, $^{3}J_{HH}$ = 7.8 Hz, $^{4}J_{HH}$ = 1.7 Hz, 4H, *ortho*-CH). ^{13}C NMR (75.50 MHz): δ = 14.1 (s, CH_3); 20.5 (s, CH_2Me); 30.5 (d, J_{CP} = 71.0 Hz, PCH_2); 32.2 (s, CH_2Et); 43.1 (d, $^{2}J_{CP}$ = 2.1 Hz, $PCH_2\underline{CH_2}$); 49.5 (s, CH_2Pr); 128.8 (d, $^{3}J_{CP}$ = 11.7 Hz, *meta*-CH); 130.8 (d, $^{2}J_{CP}$ = 9.4 Hz, *ortho*-CH); 131.9 (d, $^{4}J_{CP}$ = 2.8 Hz, *para*-CH); 133.2 (d, J_{CP} = 98.8 Hz, *ipso*-C). ^{31}P NMR (121.56 MHz): δ = 31.6. ESI-MS: *m/z* (I_{rel}, %): 302 (100) $[M+H]^+$, 324 (33) $[M+Na]^+$, 340 (9) $[M+K]^+$, 603 (18) $[2M+H]^+$, 625 (11) $[2M+Na]^+$.

2-Octylaminoethyldiphenylphosphine oxide (8)

2-Octylaminoethyldiphenylphosphine oxide (8) was synthesized according to the general procedure using phosphine oxide **3**, 14.8 g (19 mL, 114.6 mmol) octylamine, 50% aqueous solution of KOH (1.6 g, 28.6 mmol) and DMSO (15 mL) (70 °C, 3 h). The resulting residue was purified by column chromatography on silica gel ($CHCl_3$–MeOH, 20:2) and recrystallized from ethyl acetate. Yield: 5.0 g (74%); m.p.: 79.5–80.5 °C. Literature m.p. 35 °C.[9] ^{1}H NMR (300.28 MHz): δ = 0.86 (t, $^{3}J_{HH}$ = 6.5 Hz, 3H, CH_3); 1.17–1.35 (m, 10H, $C_5H_{10}Me$); 1.41 (quintet, $^{3}J_{HH}$ = 6.7 Hz, 2H, CH_2Hex); 2.52 (dt, $^{2}J_{HP}$ = 11.2 Hz, $^{3}J_{HH}$ = 7.3 Hz, 2H, PCH_2); 2.55 (t, $^{3}J_{HH}$ = 7.1 Hz, 2H, CH_2Hept); 2.95 (dt, $^{3}J_{HP}$ = 11.0 Hz, $^{3}J_{HH}$ = 7.3 Hz, 2H, $PCH_2\underline{CH_2}$); 7.41–7.55 (m, 6H, *meta*-CH + *para*-CH); 7.73 (ddd, $^{3}J_{HP}$ = 11.5 Hz, $^{3}J_{HH}$ = 7.9 Hz, $^{4}J_{HH}$ = 1.7 Hz, 4H, *ortho*-CH). ^{13}C NMR (75.50 MHz): δ = 14.1 (s, CH_3); 22.6 (s, CH_2Me); 27.3 (s, CH_2Pent); 29.2 (s, CH_2Pr); 29.5 (s, CH_2Bu); 30.0 (s, CH_2Hex); 30.4 (d, J_{CP} = 71.0 Hz, PCH_2); 31.8 (s, CH_2Et); 42.9 (d, $^{2}J_{CP}$ = 1.4 Hz, $PCH_2\underline{CH_2}$); 49.8 (s, CH_2Hept); 128.7 (d, $^{3}J_{CP}$ = 11.7 Hz, *meta*-CH); 130.7 (d, $^{2}J_{CP}$ = 9.4 Hz, *ortho*-CH); 131.8 (d, $^{4}J_{CP}$ = 2.7 Hz, *para*-CH); 133.0 (d, J_{CP} = 98.7 Hz, *ipso*-C). ^{31}P NMR (121.56 MHz): δ = 31.2. ESI-MS: *m/z* (I_{rel}, %): 358 (99) $[M+H]^+$, 380 (40) $[M+Na]^+$, 715 (12) $[2M+H]^+$, 737 (13) $[2M+Na]^+$. Anal. Calcd. for $C_{22}H_{32}NOP$: C, 73.92; H, 9.02; N, 3.92; P, 8.66. Found: C, 73.99; H, 8.99; N, 4.01; P, 8.47%.

2-(N,N-Dimethylaminoethyl)diphenylphosphine oxide (9)

2-(N,N-Dimethylaminoethyl)diphenylphosphine oxide (9) was synthesized according to the general procedure using phosphine oxide **3** (3.5 g, 10.9 mmol), 4.6 mL 38% aqueous solution of *N,N*-dimethylamine (1.5 g, 32.6 mmol), 50% aqueous solution of KOH (0.9 g, 16.3 mmol) and DMSO (10 mL) (70 °C, 2.5 h). The resulting residue was twice recrystallized from *c*-hexane. Yield: 2.4 g (80%); m.p.: 112.5–113.5 °C. Literature m.p. 114 °C.[6] ^{1}H NMR (300.28 MHz): $\delta = 2.22$ (s, 6H, CH_3); 2.43–2.55 (m, 2H, PCH_2); 2.57–2.68 (m, 2H, PCH_2CH_2); 7.42–7.57 (m, 6H, *meta*-CH + *para*-CH); 7.74 (ddd, $^{3}J_{HP} = 11.6$ Hz, $^{3}J_{HH} = 7.9$ Hz, $^{4}J_{HH} = 1.6$ Hz, 4H, *ortho*-CH). ^{13}C NMR (75.50 MHz): $\delta = 28.5$ (d, $J_{CP} = 70.5$ Hz, PCH_2); 45.2 (s, NMe_2); 52.2 (s, PCH_2CH_2); 129.0 (d, $^{3}J_{CP} = 11.7$ Hz, *meta*-CH); 131.0 (d, $^{2}J_{CP} = 9.3$ Hz, *ortho*-CH); 132.1 (d, $^{4}J_{CP} = 2.9$ Hz, *para*-CH); 133.2 (d, $J_{CP} = 99.3$ Hz, *ipso*-C). ^{31}P NMR (121.56 MHz): $\delta = 31.1$.

2-Morpholinoethyldiphenylphosphine oxide (10)

2-*Morpholinoethyldiphenylphosphine oxide* (10) was synthesized according to the general procedure using phosphine oxide **3** (2.0 g, 6.2 mmol), morpholine (0.8 mL, 0.8 g, 9.3 mmol), 50% aqueous solution of KOH (0.5 g, 9.3 mmol) and DMSO (10 mL) (60–70 °C, 2.5 h). The resulting residue was twice recrystallized from hexane-ethyl acetate. Yield: 1.32 g (67%); m.p.: 126–128 °C. Literature m.p. 133 °C.[6] ^{1}H NMR (300.28 MHz): $\delta = 2.41$ (t, $^{3}J_{HH} = 4.7$ Hz, 4H, NCH_2); 2.44–2.57 (m, 2H, PCH_2); 2.65–2.77 (m, 2H, PCH_2CH_2); 3.60 (t, $^{3}J_{HH} = 4.7$ Hz, 4H, CH_2O); 7.42–7.56 (m, 6H, *meta*-CH + *para*-CH); 7.74 (ddd, $^{3}J_{HP} = 11.6$ Hz, $^{3}J_{HH} = 7.8$ Hz, $^{4}J_{HH} = 1.6$ Hz, 4H, *ortho*-CH). ^{13}C NMR (75.50 MHz): $\delta = 27.7$ (d, $J_{CP} = 70.7$ Hz, PCH_2); 51.4 (s, PCH_2CH_2); 53.4 (s, NCH_2); 67.0 (s, CH_2O); 128.9 (d, $^{3}J_{CP} = 11.7$ Hz, *meta*-CH); 130.9 (d, $^{2}J_{CP} = 9.5$ Hz, *ortho*-CH); 132.0 (d, $^{4}J_{CP} = 2.8$ Hz, *para*-CH); 133.2 (d, $J_{CP} = 99.4$ Hz, *ipso*-C). ^{31}P NMR (121.56 MHz): $\delta = 30.7$.

2-Piperidinoethyldiphenylphosphine oxide (11)

2-Piperidinoethyldiphenylphosphine oxide (11) was synthesized according to the general procedure using 3.3 g (10.0 mmol) of phosphine oxide **3**, piperidine (1.5 mL, 1.35 g, 15 mmol), solid KOH (0.8 g, 15 mmol) and DMSO (10 mL) (60 °C, 1 h). The resulting residue was twice recrystallized. Yield: 2.8 g (89%); m.p.: 112–113 °C. Literature m.p. 112–113 °C.[6] ^{1}H NMR (300.28 MHz): $\delta = 1.39$ (quintet, $^{3}J_{HH} = 5.8$ Hz, 2H, $NCH_2CH_2CH_2$); 1.52 (quintet, $^{3}J_{HH} = 5.5$ Hz, 4H, NCH_2CH_2); 2.36 (t, $^{3}J_{HH} = 5.4$ Hz, 4H, NCH_2); 2.45–2.59 (m, 2H, PCH_2); 2.63–2.72 (m, 2H, PCH_2CH_2); 7.41–7.55 (m, 6H, *meta*-CH + *para*-CH); 7.74 (ddd, $^{3}J_{HP} = 11.6$ Hz, $^{3}J_{HH} = 7.9$ Hz, $^{4}J_{HH} = 1.6$ Hz, 4H, *ortho*-CH). ^{13}C NMR (75.50 MHz): $\delta = 24.4$ (s, $NCH_2CH_2CH_2$); 26.1 (s, NCH_2CH_2); 27.8 (d, $J_{CP} = 70.4$ Hz, PCH_2); 51.7 (s, PCH_2CH_2); 54.4 (s, NCH_2); 128.8 (d, $^{3}J_{CP} = 11.7$ Hz, *meta*-CH); 130.9 (d, $^{2}J_{CP} = 9.3$ Hz, *ortho*-CH); 131.9 (d, $^{4}J_{CP} = 2.8$ Hz, *para*-CH); 133.2 (d, $J_{CP} = 99.0$ Hz, *ipso*-C). ^{31}P NMR (121.56 MHz): $\delta = 31.3$. ESI-MS: 314.06 $[M+H]^+$; 336.07 $[M+Na]^+$; 649.22 $[2M+Na]^+$.

Di[(2-hydroxyethyl)aminoethyl]diphenylphosphine oxide (12)

Di[(2-hydroxyethyl)aminoethyl]diphenylphosphine oxide (12) was synthesized according to the general procedure using phosphine oxide **3** (3.00 g, 9.3 mmol), di(2-hydroxyethyl)amine (1.3 mL, 1.47 g, 13.9 mmol), solid KOH (0.78 g, 13.9 mmol), and DMSO (10 mL) (70 °C, 2 h). The resulting residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH, 20:2). Yield: 1.6 g (52%) as an oil. ^{1}H NMR (300.28 MHz): $\delta = 2.48$ (dt, $^{2}J_{HP} = 10.3$ Hz, $^{3}J_{HH} = 5.9$ Hz, 2H, PCH_2); 2.55 (t, $^{3}J_{HH} = 4.8$ Hz, 4H, NCH_2); 2.87 (dt, $^{3}J_{HP} = 20.7$ Hz, $^{3}J_{HH} = 5.9$ Hz, 2H, PCH_2CH_2); 3.41 (t, $^{3}J_{HH} = 4.8$ Hz, 4H, CH_2OH); 4.67 (s, 2H, OH); 7.44–7.58 (m, 6H, *meta*-CH + *para*-CH); 7.76 (ddd, $^{3}J_{HP} = 11.5$ Hz, $^{3}J_{HH} = 8.0$ Hz, $^{4}J_{HH} = 1.7$ Hz, 4H, *ortho*-CH). ^{13}C NMR (75.50 MHz): $\delta = 28.1$ (d, $J_{CP} = 71.1$ Hz, PCH_2); 47.8 (d, $^{2}J_{CP} = 5.5$ Hz, PCH_2CH_2); 57.0 (s, NCH_2); 59.5 (s, CH_2OH); 129.1 (d, $^{3}J_{CP} = 11.8$ Hz, *meta*-H); 130.9 (d, $^{2}J_{CP} = 9.4$ Hz, *ortho*-CH); 132.2 (d, $^{4}J_{CP} = 2.7$ Hz, *para*-CH); 132.3 (d, $J_{CP} = 99.7$ Hz, *ipso*-C). ^{31}P NMR (121.56 MHz): $\delta = 35.5$. Anal. Calcd. for $C_{18}H_{24}NO_3P$: C, 64.85; H, 7.26; N, 4.20; P, 9.29. Found: C, 64.58 H, 7.01; N, 4.11; P, 9.03%.

General procedure for the experiments without nucleophilic reagents

A mixture of phosphine oxide **1**, **2**, **3**, or Ph_2PHO[29] (1 mmol) and 50% aqueous solution of KOH or the solid alkali (5 − 2.5 mmol) in DMSO (5 mL) was rigorously stirred at 25 °C or 70 °C for 1 − 24 h. The reaction course was monitored by 31P NMR spectroscopy. The ^{31}P NMR signals of the side products in the reaction mixtures were assigned based on the comparative analysis of the corresponding phosphorus resonances of the proposed side compounds as well as the data of the NMR spectra of $CDCl_3$ solutions of the mixed samples obtained by addition of individual compounds **1**, **2**, **5**, and **13** to the reaction mixture.

NMR spectra (^{1}H, ^{13}C, ^{31}P) for the products **3 − 11** are contained in the Supporting Information (Figures S6–S34).

Conflict of interests

The authors declare no conflict of interests.

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