Microwave-assisted synthesis of benzo[*b*]phosphole oxide derivatives by oxidative addition of acetylenes and secondary phosphine oxides or alkyl phenyl-*H*-phosphinates

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Abstract:

A new and practical microwave (MW)-assisted method was developed for the fast and efficient oxidative addition of secondary phosphine oxides or alkyl phenyl-*H*-phosphinates and acetylenes. The reaction was optimized in respect of the oxidative agent, the reaction time, the temperature and the molar ratio of the starting materials. The protocol developed enabled the synthesis of novel benzo[*b*]phosphole oxide derivatives under mild conditions for a short reaction time. By the use of special reagents, such as alkyl phenyl-*H*-phosphinates or ethyl phenylpropiolate, reactive groups (phosphinic acid ester and carboxylic ester) could be integrated into the benzophosphole skeleton, which may be further functionalized towards various synthetic directions, therefore, fine-tuning the optical properties of the target molecules. The crystal structure of a benzo[*b*]phosphole oxide derivative was investigated by X-Ray diffraction, which gave structural information about the compound and its molecular interactions in the crystal.

Keywords: benzo[*b*]phosphole oxides; oxidative addition; secondary phosphine oxides; alkyl phenyl-*H*-phosphinates; X-Ray diffraction; microwave

1. Introduction

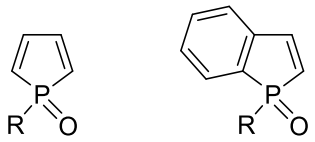
Recently, the development of conjugated organic molecules has attracted significant attention, as these types of compounds find applications as light-emitting diodes (LEDs), organic photovoltaics (OPVs) and various optical sensors [1]. These systems require an electron donor and an electron acceptor, namely an *n*- and a *p*-type semiconductor. Although a high number of organic compounds show a p-type semiconductor property, the number of n-type is relatively low. Therefore, the research for new electron acceptor molecules is a real demand.

Recently, those molecules came into the focus of development, which involve a suitable heteroatom (*e.g.*, P, B, Si, Se or Te) integrated into a delocalized electron system.

Phosphorus-containing heterocycles play an important role in several areas of life [2]. Their derivatives can be utilized in organic and material chemistry, and many can be found in the nature as well.

Benzo[*b*]phosphole derivatives may be considered as the phosphorus analogues of indole [3]. Their special electron structure provides unique physicochemical characteristics, which result in outstanding optical and electronic properties. The lone electron pair on the phosphorus atom makes these molecules suitable ligands in Pt, Pd or Rh complexes [4].

Although most compounds with a conjugated electron structure show intense luminescence in solution, due to the strong π-π contacts, this luminescence intensity is significantly decreased in conjugated or solid form [5]. This phenomenon is a huge limitation. In contrary, in case of several phosphole oxides, siloles or thiophenes, aggregation-induced luminescence was observed, the intensity was significantly higher than that of in solution. The effect is caused by the inhibited intramolecular rotation [6]. It was observed that if the phosphole oxide ring (**A**) was extended by an additional phenyl ring (resulting in benzo[*b*]phoshole oxides (**B**)), the luminescence efficiency became even higher (Figure 1).



A **B**

Figure 1. General structure of phosphole oxides (**A**) and benzo[*b*]phoshole oxides (**B**)

Benzo[*b*]phoshole oxide derivatives may be utilized in the optoelectronic industry, especially in OLEDs [7,8]. A few derivatives could be polymerized into a condensed aromatic system resulting in a luminescence active layer [9]. It is known that the optoelectronic properties can be fine-tuned by the structure, and therefore benzo[*b*]phosphole oxides bearing transformable groups mean a valuable source for further developments.

The traditional preparation of benzo[*b*]phosphole oxides involves a multistep process, starting from alkylarenes containing a phosphorus substituent in the ortho position [10]. This transformation requires a time-consuming synthesis process and the use of a strong base for the ring closure.

In recent years, the preparation of benzo[*b*]phosphole oxide derivatives is carried out by the intermolecular radical cycloaddition of a -PH(O)(Ar) compound with an internal alkyne [11]. This process means an atomic efficient and effective way for the preparation of the title derivatives. Although the oxidative addition means a huge improvement as compared to the early syntheses, the development of this reaction type is quite requiring, especially regarding the reaction time. The literature survey revealed that several oxidizing agents were tried out, however, usually a long time is needed for a complete reaction: Ag_2O – 8-10 h [6,12], AgOAc – 4-18 h [13-15], $Mn(OAc)_2/MnO_2$ – 4 h [16], $K_2S_2O_8$ – 24 h [4] and *N*-etoxy-2-methylpyridinium tetrafluoroborate – 48 h [17]. In one example, the oxidative addition could be accomplished under 30 min, however, a catalyst ($CuSO_4$) and a base (NH_3) had to be applied beside the *t*-butyl hydroperoxide oxidant [18].

The MW technique proved its significance for enabling faster and more efficient synthesis processes in organic and medicinal chemistry [19]. It is also widely used for the preparation of phosphorus-containing derivatives [20]. In order to decrease the reaction time of the oxidative addition, we studied this transformation under MW conditions.

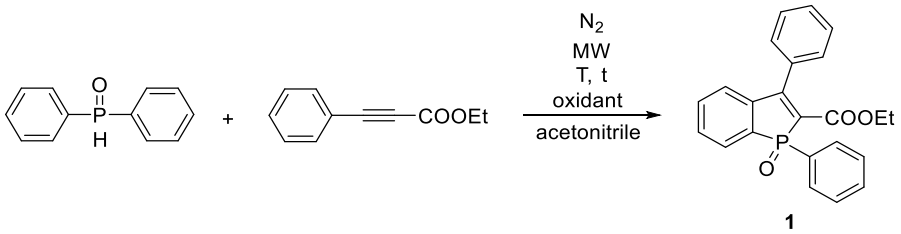
In this paper, the MW-assisted oxidative addition of secondary phosphine oxides or alkyl phenyl-*H*-phosphinates to acetylenes was investigated for the synthesis of novel benzo[*b*]phosphole oxide derivatives. The suitable selection of the starting materials enabled the introduction of reactive groups into the benzo[*b*]phosphole oxide skeleton, while the reactions could be efficiently carried out under a short reaction time applying the MW technique.

2. Results and discussion

At first, the MW-assisted cycloaddition of diphenylphosphine oxide and ethyl phenylpropiolate was optimized in respect of the oxidizing agent, the reaction temperature and the reaction time in acetonitrile as the solvent. In this reaction, the ethyl 1,3-diphenylphosphindole-2-carboxylate 1-oxide (**1**) formed regioselectively. In the first experiments, the oxidative addition was carried out in the presence of various oxidizing agents at 100 °C, applying equimolar amount of the starting materials. Using 2 equivalents of Ag_2O, a conversion of 60% was reached after 2 h (Table 1, Entry 1). Next, AgOAc was applied as oxidizing agent, and neither 2 equivalents nor 4 equivalents of the reagent were effective in the condensation since conversion of 22% and 32% was achieved, respectively (Table 1, Entries 2-3). In the presence of peroxo-type oxidants, such as oxone or 3-chloroperbenzoic acid, the cycloaddition did not occur, only diphenylphosphinic acid formed

as the result of the oxidation of the diphenylphosphine oxide (Table 1, Entries 4 and 5). Based on the above results, we continued the investigation using Ag_2O (Table 1, Entries 6-9). As the next step, the molar ratio of the dipehylphosphine oxide was increased to 1.2 equivalents, and the conversion of 79% was obtained, significantly higher than in the presence of 1 equivalent of P-component (Table 1, Entry 6). When the amount of the phosphine oxide was further increased to 1.5 equivalents, the cycloaddition became complete (Table 1, Entry 7). Based on our experiences, a higher temperature of 120 °C did not allow the decrease of the reaction time, and was not beneficial for the addition (Table 1, Entries 8 and 9). Applying the optimized parameters (1.5 equivalents of diphenylphosphine oxide, 2 equivalents of Ag_2O, 100 °C and 2 h), the target ethyl 1,3-diphenylphosphindole-2-carboxylate 1-oxide (**1**) could be isolated in a yield of 91% after column chromatography (Table 1, Entry 7).

Table 1. Oxidative addition of diphenylphosphine oxide with ethyl phenylpropiolate



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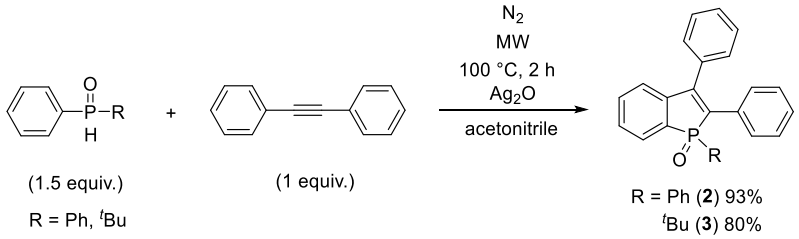
Entry	DPPO [equiv]	Oxidant	Amount of oxidant [equiv]	T [°C]	t [h]	Conversion [%][a]	Yield [%][b]
1	1	Ag_2O	2	100	2	60	–
2	1	AgOAc	2	100	2	22	–
3	1	AgOAc	4	100	2	32	–
4	1	Oxone	4	100	2	–[c]	–
5	1	3-Chloroperbenzoic acid	4	100	2	–[c]	–
6	1.2	Ag_2O	2	100	2	79	–
7	1.5	Ag_2O	2	100	2	100	**91**
8	1.5	Ag_2O	2	120	1	83	–
9	1.5	Ag_2O	2	120	2	87	–

[a]Determined by HPLC (256 nm).
[b]After column chromatography.
[c]Diphenylphosphinic acid was formed from diphenylphosphine oxide.

Using the optimal conditions, the reaction was performed with diphenyl acetylene as the coupling component. In the reaction of diphenylphosphine oxide and acetylene, the corresponding benzophosphole oxide (**2**) was obtained in a yield of 93%. The cycloaddition

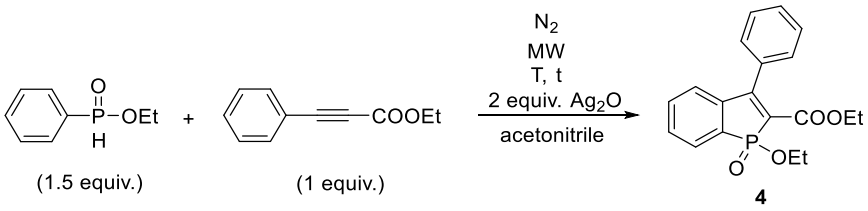
was then carried out with tert-butyl(phenyl)phosphine oxide as the P-component, and the reaction at 100 °C for 2 h resulted in a yield of 80% for compound **3**.



Scheme 1. Oxidative addition of diphenylphosphine oxide or tert-butyl(phenyl)phosphine oxide with diphenyl acetylene

In the next part, the MW-assisted oxidative addition of alkyl phenyl-*H*-phosphinates and acetylenes was optimized on the model reaction of ethyl phenyl-*H*-phosphinate and ethyl phenylpropiolate (Table 2). The first experiment was carried out using the conditions suitable for the coupling of secondary phosphine oxides, however, the reaction was not complete, and reached only a conversion of 58% (Table 2, Entry 1). When the reaction time was prolonged to 3 h, ethyl 3-phenyl-1-ethoxyphosphindole-2-carboxylate 1-oxide (**4**) formed in 100% and could be isolated in a yield of 86% (Table 2, Entry 2). The higher temperature was also unfavorable in this case (Table 2, Enties 3 and 4). Based on our experiences, the addition with ethyl phenyl-*H*-phosphinate required a slightly longer reaction time as compared to that of the diphenylphosphine oxide, which is in accordance with the reactivity of the two species and may also came from the difference in the number of the aryl rings available for the ring closure step.

Table 2. Oxidative addition of ethyl phenyl-*H*-phosphinate with ethyl phenylpropiolate.

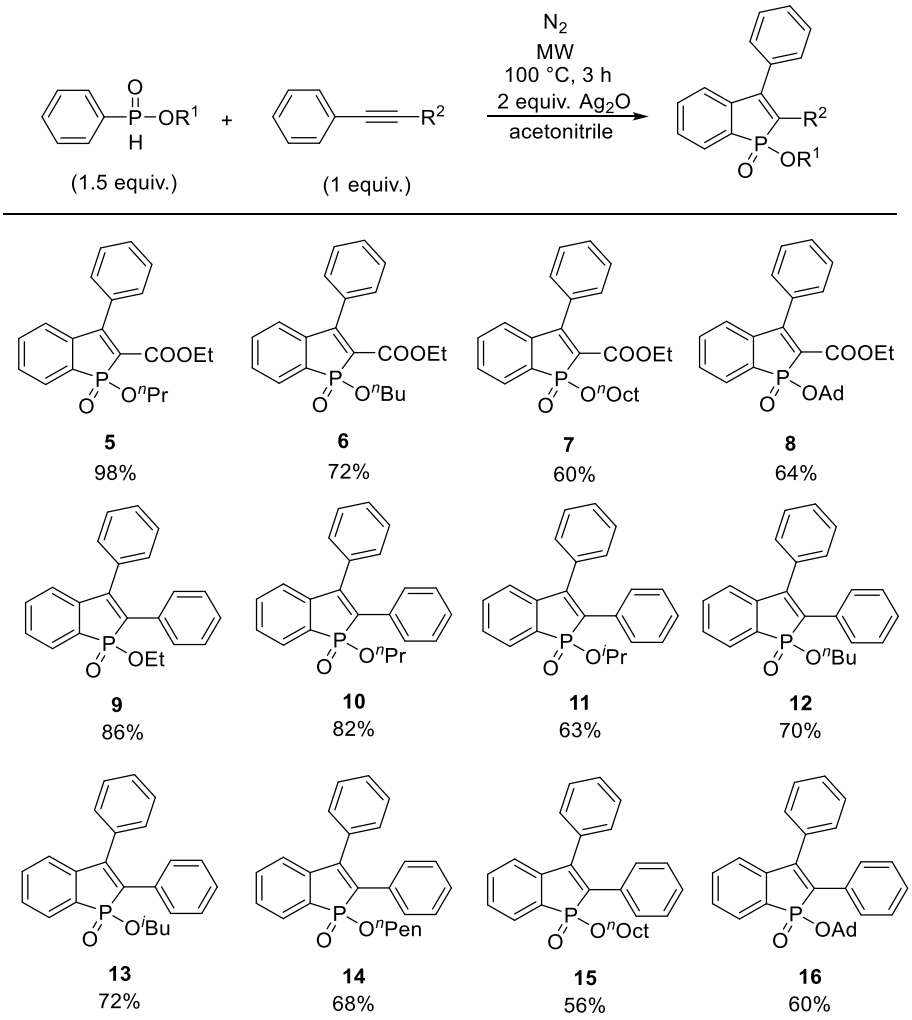


Entry	T [°C]	t [h]	Conversion[a] [%]	Yield[b] [%]
1	100	2	58	–
2	100	3	100	86
3	120	2	82	–
4	120	3	85	-

[a]Determined by HPLC (256 nm).
[b]After column chromatography.

Then, the reaction was extended for the addition of further alkyl phenyl-*H*-phosphinates (*n*-propyl-, isopropyl-, *n*-butyl-, isobutyl-, *n*-pentyl-, *n*-octyl- and adamantyl phenyl-*H*-phosphinate) and ethyl phenylpropiolate or diphenyl acetylene using the most suitable reaction conditions obtained above (Scheme 2). The addition of *n*-propyl phenyl-*H*-phosphinate or *n*-propyl phenyl-*H*-phosphinate with ethyl phenylpropiolate was similar to the above model reaction, the corresponding benzophospholes (**5** and **6**) were isolated in yields of 98% and 72%, respectively. In the reaction of *n*-octyl phenyl-*H*-phosphinate and adamantyl phenyl-*H*-phosphinate, slightly lower yields (60% and 64%) were obtained, which may be due to the steric effect of the bulky *n*-octyl and adamantyl groups.

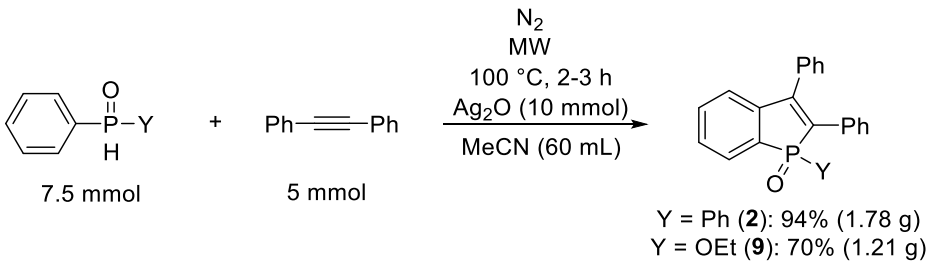
Starting from alkyl phenyl-*H*-phosphinates and diphenylacetylene, similar tendencies were observed. Performing the addition of ethyl- or *n*-propyl phenyl-*H*-phosphinate, the corresponding products (**9** or **10**) were obtained in yields of 86% or 82%, respectively. In case of the isopropyl phenyl-*H*-phosphinate, the cycloaddition resulted in a slightly lower yield, which was maybe due to the steric hindrance of the isopropyl group. The reaction of *n*-butyl- and isobutyl phenyl-*H*-phosphinate provided the benzophosphole oxides **12** and **13** in yields of 70% and 72%, respectively, which indicated that a further branching in the alkyl chain did not significantly affect the outcome. Bulky phosphinates, such as *n*-pentyl-, *n*-octyl- and adamantyl phenyl-*H*-phosphinates were less active in the cycloaddition, since compounds **14**-**16** were obtained in slightly lower yields (56-68%).



Scheme 2. Oxidative addition of alkyl phenyl-*H*-phosphinates with ethyl phenylpropiolate or diphenylacetylene.

In contrast to previous reports published in this topic [4,6,12-18], our method developed is the first MW-assisted approach for the synthesis of benzo[*b*]phosphole oxides, which allows the reactions to take place faster (2-3 h instead of 8-24 h) and applies a modestly toxic solvent (MeCN). Altogether 16 derivatives were prepared in good to high yields, among them 12 are new, which were characterized by ^{31}P, ^{1}H, and ^{13}C NMR spectroscopy, as well as by HRMS. (Copies of ^{31}P, ^{1}H, and ^{13}C NMR spectra for all compounds synthesized are presented in the Supplementary Materials.)

The scaled-up reaction of diphenyl phosphine oxide or ethyl phenyl-*H*-phosphinate and diphenyl acetylene was also carried out under MW conditions in order to demonstrate the practical utilization of the approach developed at a “gram-scale” (Scheme 3). After column chromatography the corresponding benzophosphole oxides (**2** and **9**) were isolated in yields of 94% and 70%, respectively.



Scheme 3. "Gram-scale" synthesis of benzophosphole oxides **2** and **9**.

By slow evaporation of the ethyl acetate-dichloromethane solution of 1-isopropoxy-2,3-diphenylphosphindole 1-oxide (**11**), a single crystal suitable for X-Ray diffraction study was obtained. Compound **11** crystallizes in a chiral orthorhombic *Pna*2_1 space group as an *R*-enantiomer. Single-crystal XRD analysis confirmed the molecular structure (Figure 2) and revealed the formation of two intermolecular C–H···O=P hydrogen bonding between two phenyl rings and the O=P moiety leading to hydrogen-bonded wavy layer (Figure 3, Table S2). These layers are further connected into 3D network *via* C–H···π interactions between the phenyl groups of adjacent molecules.

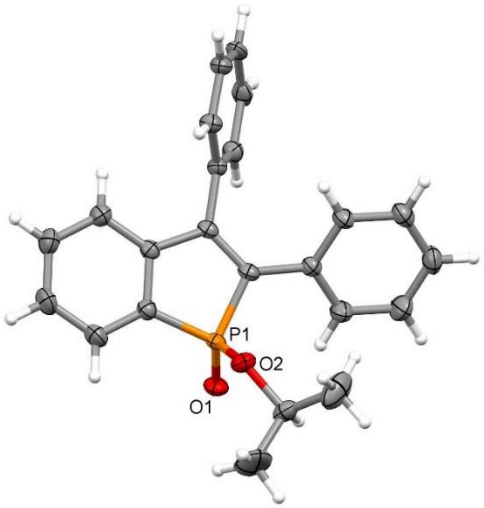
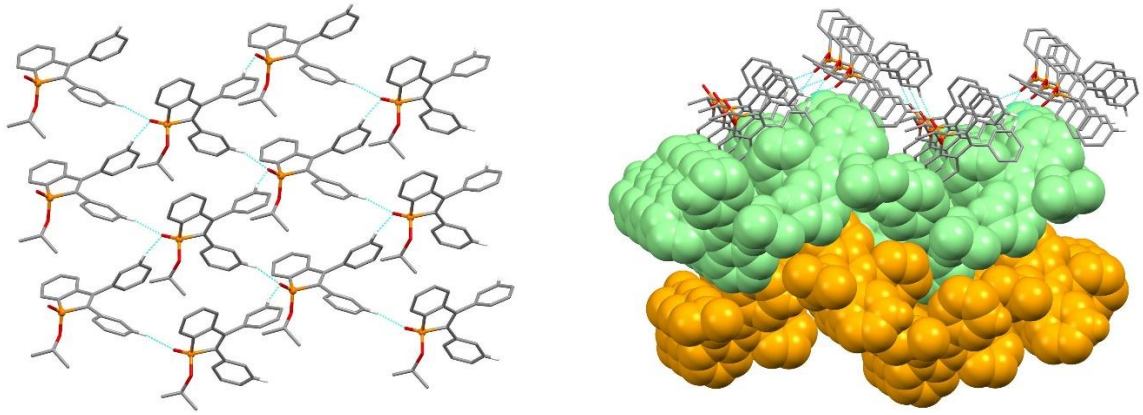


Figure 2. Molecular structure of compound **11**.



(a) **(b)**

Figure 3. Supramolecular structure of **11**. **(a)** Layer formation through C–H···O=P hydrogen bonding. **(b)** Stacking of layers into 3D network through C–H···π interactions. Blue dashed lines indicate hydrogen bonds.

3. Conclusion

In conclusion, a fast and efficient oxidative cycloaddition of secondary phosphine oxides or alkyl phenyl-*H*-phosphinates with acetylenes (diphenylacetylene or ethyl phenylpropiolate) was developed under MW conditions. The optimized synthesis enabled the preparation of the benzo[*b*]phosphole oxides in good to high yields under a short reaction time. In order to prove the practical application of the method developed, two scaled-up reactions were performed in a "gram-scale". One of the products was studied by X-Ray diffraction measurements, which provided a better understanding of their crystal structure. The target products bearing reactive phosphinic ester or carboxyl ester groups may offer a route for the further functionalization of these molecules for the realization of better optical properties.

4. Experimental section

4.1. Materials and instrumentation

Alkyl phenyl-*H*-phosphinates were prepared according to a known reference [21]. Other reagents were purchased from commercial sources and used without further purification.

The microwave-assisted experiments were performed in a 300 W CEM® Discover® focused microwave reactor (CEM Microwave Technology Ltd., Buckingham, UK) equipped with a pressure controller using 40–60 W irradiation under isothermal conditions.

High-performance liquid chromatography-mass spectrometry (HPLC-MS) measurements were performed with an Agilent 1200 liquid chromatography system coupled with a 6130 quadrupole

mass spectrometer equipped with an ESI ion source (Agilent Technologies, Palo Alto, CA, USA). Analysis was performed at 40 °C on a Gemini C18 column (150 mm × 4.6 mm, 3 μm; Phenomenex, Torrance, CA, USA) with a mobile phase flow rate of 0.6 mL/min. Composition of eluent A was 0.1% (NH_4)(HCOO) in water; eluent B was 0.1% (NH_4)(HCOO) and 8% water in acetonitrile, 0–3 min 5% B, 3–13 min gradient, 13–20 min 100% B. The injection volume was 2 μL. The chromatographic profile was registered at 254 nm. The MSD operating parameters were as follows: positive ionization mode, scan spectra from m/z 120 to 1000, drying gas temperature 300 °C, nitrogen flow rate 12 L/min, nebulizer pressure 60 psi, capillary voltage 4000 V.

The ^{31}P, ^{1}H, ^{13}C, NMR spectra were taken in $CDCl_3$ solution on a Bruker AV-300 or DRX-500 spectrometer (Bruker AXS GmBH, Karlsruhe, Germany) operating at 121.5, 75.5 and 300 or 202.4, 125.7 and 500 MHz, respectively. Chemical shifts are downfield relative to 85% H_3PO_4 and TMS.

High resolution mass spectrometry measurements were performed on a Sciex TripleTOF 5600+ high resolution tandem mass spectrometer equipped with a DuoSpray ion source. Electrospray ionization was applied in positive ion detection mode. Samples were dissolved in acetonitrile and flow injected into acetonitrile:water 50:50 flow. The flow rate was 0.2 mL/min. The resolution of the mass spectrometer was 35000.

*4.2. General Procedure for the Synthesis of 1-alkyl-1H-phoshindole-1-oxides (**1-3**) or 1-alkoxy-1H-phoshindole-1-oxides (**4-16**)*

To the mixture of 0.3 mmol of >P(O)H derivatives (diphenylphosphine oxide: 0.061 g, *t*-butylphenilphosphine oxide: 0.055 g, ethyl phenyl-*H*-phosphinate: 0.051 g, *n*-propyl phenyl-*H*-phosphinate: 0.055 g, *i*-propyl phenyl-*H*-phosphinate: 0.055 g, *n*-butyl phenyl-*H*-phosphinate: 0.059 g, *i*-butyl phenyl-*H*-phosphinate: 0.059 g, *n*-pentyl phenyl-*H*-phosphinate: 0.064 g, *n*-octyl phenyl-*H*-phosphinate: 0.076 g, or adamantyl phenyl-*H*-phosphinate: 0.083 g) and 0.2 mmol of acetylene (diphenylacetylene: 0.036 g or ethyl phenylpropiolate: 0.033 ml), 0.4 mmol (0.093 g) silver oxide was added 3 mL of acetonitrile and stirred under nitrogen atmosphere at 100-120 °C for 1-3 h in a CEM Microwave reactor (CEM Microwave Technology Ltd., Buckingham, UK) equipped with a pressure controller. The volatile components were removed in vacuum, and the residue was purified by column chromatography using silica gel as the absorbent and hexan:ethylacetate (3:1) as the eluent. The following products were thus prepared:

*Ethyl 1,3-diphenylphosphindole-2-carboxylate 1-oxide (**1**)*

Yield: 91% (0.068 g), pale yellow crystal; Mp: 127-128 °C; Mp [13]: 119-122 °C; ^{31}P (CDCl3) δ 35.7; δ[13] 35.7; $[M+H]^+_{found}$ = 375.1139, $C_{23}H_{20}NO_3P$ requires 375.1150.

*1,2,3-Triphenylphosphindole 1-oxide (**2**)*

Yield: 93% (0.070 g), pale yellow crystal; Mp: 75-76 °C; Mp [13]: 70-72 °C; ^{31}P (CDCl3) δ 39.2; δ[13] 39.0; $[M+H]^+_{found}$ = 379.1241, $C_{19}H_{23}NO_4P$ requires 379.1251.

*1-(tert-Butyl)-2,3-diphenylphosphindole 1-oxide (**3**)*

Yield: 80% (0.057 g), pale yellow crystal; Mp: 222-224°C; Mp [13]: 219-220 °C; ^{31}P ($CDCl_3$) δ 59,4; δ[13] 59,2; $[M+H]^+_{found}$ = 375.1559, $C_{24}H_{24}NOP$ requires 359.1565.

*Ethyl 1-ethoxy-3-phenylphosphindole-2-carboxylate 1-oxide (**4**)*

Yield: 86% (0.059 g), pale yellow crystal; Mp: 105-106 °C; ^{31}P ($CDCl_3$) δ 40.9; ^{13}C NMR ($CDCl_3$) δ 13.9, 16.7 (d, *J* = 6.3), 61.0, 62.7 (d, *J* = 6.5), 122.5 (d, *J* = 127.9), 126.2 (d, *J* = 13.5), 127.9 (d, *J* = 6.5), 128.0, 128.2, 128.6 (d, *J* = 140.4), 129.2, 131.6 (d, *J* = 11.5), 133.0 (d, *J* = 15.2), 133.1 (d, *J* = 2.4), 140.0 (d, *J* = 33.0), 162.4 (d, *J* = 24.4), 162.6 (d, *J* = 12.2); ^{1}H NMR ($CDCl_3$) δ 1.17 (t, 3H, *J* = 7.2), 1.42 (t, 3H, *J* = 7.1), 4.10-4.25 (m, 2H), 4.31-4.40 (m, 1H), 4.41-4.50 (m, 1H), 7.07-7.13 (m, 1H), 7.28-7.35 (m, 2H), 7.43-7.56 (m, 5H), 7.71-7.78 (m, 1H); $[M+H]^+_{found}$ = 343.1083, $C_{19}H_{20}O_4P$ requires 343.1099.

*Ethyl 3-phenyl-1-propoxyphosphindole-2-carboxylate 1-oxide (**5**)*

Yield: 98% (0.070 g), pale yellow oil; ^{31}P ($CDCl_3$) δ 41.0; ^{13}C NMR ($CDCl_3$) δ 10.1, 14.0, 24.1 (d, *J* = 6.0), 61.1, 68.1 (d, *J* = 6.9), 122.5 (d, *J* = 127.8), 126.2 (d, *J* = 13.7), 127.9 (d, *J* = 3.2), 128.0, 128.2, 128.6 (d, *J* = 140.2), 129.2, 131.6 (d, *J* = 11.5), 133.07 (d, *J* = 2.3), 133.10 (d, *J* = 15.7), 140.1 (d, *J* = 33.0), 162.4 (d, *J* = 24.7), 162.7 (d, *J* = 11.9); ^{1}H NMR ($CDCl_3$) δ 1.00 (t, 3H, *J* = 7.4), 1.17 (t, 3H, *J* = 7.2), 1.73-1.83 (m, 2H), 4.10-4.26 (m, 3H), 4.29-4.37 (m, 1H), 7.07-7.13 (m, 1H), 7.28-7.35 (m, 2H), 7.42–7.56 (m, 5H), 7.70-7.78 (m, 1H); $[M+H]^+_{found}$ = 357.1247, $C_{20}H_{22}O_4P$ requires 357.1255.

*Ethyl 1-butoxy-3-phenylphosphindole-2-carboxylate 1-oxide (**6**)*

Yield: 72% (0.053 g), pale yellow oil; ^{31}P ($CDCl_3$) δ 41.0; ^{13}C NMR ($CDCl_3$) δ 13.7, 14.0, 18.8, 32.8 (d, *J* = 6.4), 61.0, 66.4 (d, *J* = 6.9), 122.5 (d, *J* = 127.8), 126.2 (d, *J* = 13.3), 127.9, 128.2, 128.6 (d, *J* = 140.2), 129.2, 131.5 (d, *J* = 11.5), 133.0 (d, *J* = 2.3), 133.1, 140.1 (d, *J* = 33.0),

162.4 (d, *J* = 24.3), 162.6 (d, *J* = 11.9); ^{1}H NMR ($CDCl_3$) δ 0.95 (t, 3H, *J* = 7.4), 1.17 (t, 3H, *J* = 7.1), 1.41–1.51 (m, 2H), 1.69–1.78 (m, 2H), 4.10–4.23 (m, 2H), 4.23–4.30 (m, 1H), 4.33–4.42 (m, 1H), 7.07–7.13 (m, 1H), 7.29–7.35 (m, 2H), 7.41–7.56 (m, 5H), 7.70–7.77 (m, 1H); $[M+H]^{+}_{found}$ = 371.1403, $C_{21}H_{24}O_4P$ requires 371.1412.

*Ethyl 1-(octyloxy)-3-phenylphosphindole-2-carboxylate 1-oxide (**7**)*

Yield: 60% (0.051 g), pale yellow oil; ^{31}P ($CDCl_3$) δ 36.7; ^{13}C NMR ($CDCl_3$) δ 13.7, 14.1, 22.7, 25.7, 29.2 (d, *J* = 1.4), 30.6 (d, *J* = 6.8), 31.8, 61.5, 65.6 (d, *J* = 6.2), 128.0 (d, *J* = 123.4), 128.4 (d, *J* = 13.6), 128.7, 129.4, 130.4, 130.5 (d, *J* = 146.1), 131.9 (d, *J* = 10.2), 132.4 (d, *J* = 3.1), 134.0 (d, *J* = 17.1), 147.9 (d, *J* = 5.9), 166.9 (d, *J* = 13.6); ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 3H, *J* = 5.1), 1.08 (t, 3H, *J* = 7.1), 1.17–1.36 (m, 10H), 1.69–1.82 (m, 2H), 7.30–7.38 (m, 2H), 7.38–7.59 (m, 5H), 7.82–7.94 (m, 2H); $[M+H]^{+}_{found}$ = 427.2030, $C_{25}H_{32}O_4P$ requires 427.2038.

*Ethyl 1-(adamantyloxy)-3-phenylphosphindole-2-carboxylate 1-oxide (**8**)*

Yield: 64% (0.057 g), pale yellow oil; ^{31}P ($CDCl_3$) δ 37.0; ^{13}C NMR ($CDCl_3$) δ 14.1, 31.4, 35.8, 44.7 (d, *J* = 3.7), 60.8, 84.3 (d, *J* = 9.6), 123.6 (d, *J* = 135.2), 125.9 (d, *J* = 13.3), 127.7 (d, *J* = 9.2), 127.9, 128.2, 129.0, 131.0 (d, *J* = 137.0), 131.3 (d, *J* = 11.5), 132.2 (d, *J* = 2.0), 133.4 (d, *J* = 16.0), 139.6 (d, *J* = 33.0), 161.2 (d, *J* = 24.7), 162.9 (d, *J* = 11.5); ^{1}H NMR ($CDCl_3$) δ 1.21 (t, 3H, *J* = 7.1), 1.63-1.76 (m, 7H), 2.20-2.30 (m, 8H), 4.09-4.29 (m, 2H), 7.02-7.08 (m, 1H), 7.29-7,35 (m, 2H), 7.37-7.43 (m, 1H), 7.43-7.53 (m, 4H), 7.70-7.78 (m, 1H); $[M+H]^{+}_{found}$ = 449.1875, $C_{27}H_{30}O_4P$ requires 449.1882.

*1-Ethoxy-2,3-diphenylphosphindole 1-oxide (**9**)*

Yield: 86% (0.060 g), pale yellow oil; ^{31}P ($CDCl_3$) δ 44.2; δ[13] 45.8; $[M+H]^{+}_{found}$ = 347.1190, $C_{22}H_{20}O_2P$ requires 347.1201.

*2,3-Diphenyl-1-propoxyphosphindole 1-oxide (**10**)*

Yield: 82% (0.059 g), pale yellow oil; ^{31}P ($CDCl_3$) δ 46.0; ^{13}C NMR ($CDCl_3$) δ 10.0, 23.9 (d, *J* = 6.4), 67.6 (d, *J* = 6.9), 127.3 (d, *J* = 133.3), 127.7 (d, *J* = 8.7), 128.0, 128.4, 128.7, 128.97 (d, *J* = 5.5), 129.02 (d, *J* = 4.1), 130.0 (d, *J* = 125.1), 132.6 (d, *J* = 8.7), 133.0 (d, *J* = 2.3), 134.0 (d, *J* = 18.3), 142.0 (d, *J* = 34.4), 148.6 (d, *J* = 27.5); ^{1}H NMR ($CDCl_3$) δ 0.84 (t, 3H, *J* = 7.4), 1.56–1.66 (m, 2H), 3.87-4.06 (m, 2H), 7.09–7.14 (m, 1H), 7.16-7.23 (m, 2H), 7.23–7.31 (m,

2H), 7.36–7.48 (m, 7H), 7.67-7.82 (m, 1H); $[M+H]^{+}_{found}$ = 361.1347, $C_{23}H_{22}O_2P$ requires 361.1357.

*1-Isopropoxy-2,3-diphenylphosphindole 1-oxide (**11**)*

Yield: 63% (0.045 g), pale yellow oil; ^{31}P ($CDCl_3$) δ 44.7; ^{13}C NMR ($CDCl_3$) δ 24.1 (d, *J* = 4.0), 24.3 (d, *J* = 3.7), 70.9 (d, *J* = 6.8), 123.9 (d, *J* = 13.6), 127.6 (d, *J* = 9.0), 128.0 (d, *J* = 134.6), 128.3, 128.6, 129.07 (d, *J* = 2.0), 129.12 (d, *J* = 3.1), 130.6 (d, *J* = 125.1), 132.7 (d, *J* = 9.2), 132.9 (d, *J* = 2.2), 134.1 (d, *J* = 18.0), 142.0 (d, *J* = 34.4), 148.3 (d, *J* = 28.2); ^{1}H NMR ($CDCl_3$) δ 1.14 (d, 3H, *J* = 6.1), 1.28 (d, 3H, *J* = 6.2), 4.63-4.81 (m, 1H), 7.06-7.14 (m, 1H), 7.15-7.23 (m, 3H), 7.23-7.32 (m, 2H), 7.32–7.47 (m, 7H), 7.68-7.79 (m, 1H); $[M+H]^{+}_{found}$ = 361.1352, $C_{23}H_{22}O_2P$ requires 361.1357.

*1-Butoxy-2,3-diphenylphosphindole 1-oxide (**12**)*

Yield: 70% (0.052 g), pale yellow crystal; Mp: 91-92 °C; ^{31}P ($CDCl_3$) δ 46.0; δ[16] 46.0; $[M+H]^{+}_{found}$ = 375.1505, $C_{24}H_{24}O_2P$ requires 375.1513.

*1-Isobutoxy-2,3-diphenylphosphindole 1-oxide (**13**)*

Yield: 72% (0.054 g), pale yellow oil; ^{31}P ($CDCl_3$) δ 46.0; ^{13}C NMR ($CDCl_3$) δ 18.7, 29.3 (d, *J* = 6.2), 72.0 (d, *J* = 7.1), 124.0 (d, *J* = 13.5), 127.3 (d, *J* = 134.0), 127.8 (d, *J* = 8.7), 128.0, 128.4, 128.7, 129.0 (d, *J* = 2.9), 129.1 (d, *J* = 3.5), 130.1 (d, *J* = 124.8), 132.6 (d, *J* = 9.0), 133.0 (d, *J* = 2.1), 134.1 (d, *J* = 18.0), 142.1 (d, *J* = 34.3), 148.6 (d, *J* = 27.3); ^{1}H NMR ($CDCl_3$) δ 0.83 (d, 6H, *J* = 6.7), 1.78–1.96 (m, 1H), 3.67–3.89 (m, 2H), 7.08–7.16 (m, 1H), 7.16–7.22 (m, 3H), 7.23–7.32 (m, 2H), 7.33–7.51 (m, 7H), 7.67–7.82 (m, 1H); $[M+H]^{+}_{found}$ = 375.1507, $C_{24}H_{24}O_2P$ requires 375.1513.

*1-Pentoxy-2,3-diphenylphosphindole 1-oxide (**14**)*

Yield: 68% (0.053 g), pale yellow oil; ^{31}P ($CDCl_3$) δ 46.0; ^{13}C NMR ($CDCl_3$) δ 13.9, 22.1, 27.6, 30.3 (d, *J* = 6.2), 66.2 (d, *J* = 6.8), 123.9 (d, *J* = 13.3), 127.3 (d, *J* = 133.7), 127.7 (d, *J* = 8.7), 128.0, 128.7, 129.0 (d, *J* = 2.8), 129.1 (d, *J* = 3.7), 130.1 (d, *J* = 124.9), 132.6 (d, *J* = 9.0), 133.0, 134.0 (d, *J* = 18.3), 142.0 (d, *J* = 34.4), 148.6 (d, *J* = 27.6); ^{1}H NMR ($CDCl_3$) δ 0.80 (t, 3H, *J* = 6.7), 1.10–1.39 (m, 4H), 1.50–1.76 (m, 2H), 3.85–4.13 (m, 2H), 7.08–7.14 (m, 1H), 7.16–7.23 (m, 3H), 7.23–7.32 (m, 2H), 7.32–7.55 (m, 7H), 7.68–7.81 (m, 1H); $[M+H]^{+}_{found}$ = 389.1659, $C_{25}H_{26}O_2P$ requires 389.1670.

*1-Octyloxy-2,3-diphenylphosphindole 1-oxide (**15**)*

Yield: 56% (0.048 g), pale yellow oil; ^{31}P ($CDCl_3$) δ 46.0; ^{13}C NMR ($CDCl_3$) δ 14.1, 22.6, 25.4, 29.0, 29.1, 30.5 (d, *J* = 6,4), 31.7, 66.2 (d, *J* = 6,9), 123.9 (d, *J* = 13.7), 127.3 (d, *J* = 133.3), 127.7 (d, *J* = 8.7), 128.0, 128.4, 128.6, 128.97 (d, *J* = 6.9), 129.02 (d, *J* = 4.6), 130.0 (d, *J* = 124.6), 132.6 (d, *J* = 9.2), 133.0 (d, *J* = 2.2), 134.0 (d, *J* = 17.9), 142.0 (d, *J* = 34.4), 148.5 (d, *J* = 27.5); ^{1}H NMR ($CDCl_3$) δ 0.86 (t, 3H, *J* = 7.1), 1.11–1.33 (m, 10H), 1.51–1.62 (m, 2H), 3.91–4.07 (m, 2H), 7.09–7.15 (m, 1H), 7.17–7.24 (m, 3H), 7.23–7.30 (m, 2H), 7.33–7.48 (m, 7H), 7.71–7.78 (m, 1H); $[M+H]^+_{found}$ = 431.2131, $C_{28}H_{32}O_2P$ requires 431.2140.

*1-Adamantyloxy-2,3-diphenylphosphindole 1-oxide (**16**)*

Yield: 60% (0.054 g), pale yellow crystal; Mp: 145-146 °C; ^{31}P ($CDCl_3$) δ 42.3; ^{13}C NMR ($CDCl_3$) δ 31.4, 35.8, 44.7 (d, *J* = 3.7), 83.5 (d, *J* = 10.0), 123.7 (d, *J* = 13.6), 127.5, 127.6, 128.1, 128.4, 128.7, 128.8, 129.2 (d, *J* = 1.0), 129.3 (d, *J* = 5.9), 130.0 (d, *J* = 134.9), 132.0 (d, *J* = 130.1), 132.2, 133.0 (d, *J* = 9.0), 134.3 (d, *J* = 18.3), 141.7 (d, *J* = 35.0), 147.2 (d, *J* = 27.9); ^{1}H NMR ($CDCl_3$) δ 1.60 (br s, 6H), 2.00–2.25 (m, 9H), 7.02–7.11 (m, 1H), 7.13–7.22 (m, 3H), 7.22–7.30 (m, 2H), 7.31–7.44 (m, 7H), 7.67–7.82 (m, 1H); $[M+H]^+_{found}$ = 453.1972, $C_{30}H_{30}O_2P$ requires 453.1983.

*4.3. General Procedure for the gram-scale Synthesis of 1,2,3-triphenylphosphindole 1-oxide (**2**) and 1-ethoxy-2,3-diphenylphosphindole 1-oxide (**9**)*

To the mixture of 7.5 mmol of >P(O)H derivatives (diphenylphosphine oxide: 1.53 g, or ethyl phenyl-*H*-phosphinate: 1.28 g) and 5.0 mmol (0.90 g) of diphenylacetylene, 10 mmol (2.33 g) of silver oxide was added to 60 mL of acetonitrile and stirred under nitrogen atmosphere at 100 °C for 2-3 h in a CEM Microwave reactor (CEM Microwave Technology Ltd., Buckingham, UK) equipped with a pressure controller. The volatile components were removed in vacuum, and the residue was purified by column chromatography using silica gel as the absorbent and hexan:ethylacetate (3:1) as the eluent.

4.4. Single crystal X-ray diffraction measurements

Single-crystal X-ray diffraction data of compound **11** were collected on an Agilent Technologies SuperNova Dual diffractometer using Cu-Kα radiation (λ = 1.54184 Å) at 150 K. The data were processed using CrysAlis Pro [22]. Structure was solved by ShelXT [23] using intrinsic phasing and refined by a full-matrix least-squares procedure based on F^2 with ShelXL [24] using Olex2 program suite [25]. All the non-hydrogen atoms were refined anisotropically.

Hydrogen atoms were readily located in difference Fourier maps, and were subsequently treated as riding atoms in geometrically idealized positions with C–H = 0.95 Å (aromatic), 1.00 Å (methine) or 0.98 Å (methyl), and with U_{iso}(H) = kU_{eq}(C), where k = 1.5 for methyl group and 1.2 for all H atoms. The crystallographic data are listed in Table S1. Deposition Number CCDC 2111047 (for **11**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service www.ccdc.cam.ac.uk/structures.

Declaration of competing interes

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online.

Author Contributions

Á. T. and E. B. planned the experiments, B. K. and N. P.-T. carried out the experiments, F. P. performed the crystal structure analysis, E. B. contributed reagents/materials/analysis tools, Á.T. and E. B. wrote the paper. B. K. and N. P.-T. reviewed the paper. All authors have read and agreed to the published version of the manuscript.

References

[1] T. Baumgartner, Acc. Chem. Res. 47 (2014) 1613–1622.

[2] D.W. Allen, D. Loakes, J.C. Tebby, SPR - Organophosphorus Chemistry, Royal Society of Chemistry: Cambridge, United Kingdom, 2016; Volume 45.

[3] Y. Matano, H. Imahori, Org. Biomol. Chem. 7 (2009) 1258–1271.

[4] K. Fourmy, D.H. Nguyen, O. Dechy-Cabaret, M. Gouygou, M. Catal. Sci. Technol. 5 (2015) 4289–4323.

[5] A.R. Katritzky, C.W. Rees, E.F.V. Scriven (Eds.) Comprehensive Heterocyclic Chemistry II, Elsevier: Oxford, United Kingdom, 1997, Volume 4.

[6] F. Bu, E. Wang, Q. Peng, R. Hu, A. Qin, Z. Zhao, B.Z. Tang, Chem. Eur. J. 21 (2015) 4440–4449.

[7] H. Tsuji, K. Sato, L. Ilies, Y. Itoh, Y. Sato E. Nakamura, Org. Lett. 10 (2008) 2263–2265.

[8] H. Tsuji, K. Sato, Y. Sato, E. Nakamura, Chem. Asian J. 5 (2010) 1294–1297.

[9] R.F. Chen, R. Zhu, Q.L. Fan, W. Huang, Org. Lett. 10 (2008) 2913–2916.

[10] B. Wu, N. Yoshikai, Org. Biomol. Chem. 14 (2016) 5402–5416.

[11] Y.H. Budnikova, Chem. Heterocycl. Comp. 54 (2018) 269–279.

[12] Y.R. Chen, W.L. Duan, J. Am. Chem. Soc. 135 (2013) 16754–16757.

[13] Y. Unoh, K. Hirano, T. Satoh, M. Miura, Angew. Chem. Int. Ed. 52 (2013) 12975–12979.

[14] W. Ma, L. Ackermann, Synthesis 46 (2014) 2297–2304.

[15] G. Hu, Y. Zhang, J. Su, Z. Li, Y. Gao, Y. Zhao, Org. Biomol. Chem. 13 (2015) 8221–8231.

[16] O. Berger, J. Montchamp, J. Org. Chem. 84 (2019) 9239–9256.

[17] V. Quint, F. Morlet-Savary, J.F. Lohier, J. Lalevée, A.C. Gaumont, S. Lakhdar, J. Am. Chem. Soc. 138 (2016) 7436–7441.

[18] P. Zhang, Y. Gao, L. Zhang, Z. Li, Y. Liu, G. Tang, Y, Zhao, Adv. Synth. Catal. 358 (2016) 138–142.

[19] E. Bálint, G. Keglevich, The Spread of the Application of the Microwave Technique. in Milestones in Microwave Chemistry; Keglevich, G., Ed.; Springer: Cham, Switzerland, 2016, pp 1–10.

[20] E. Bálint, Á. Tajti, G. Keglevich, Materials 12 (2019) 788–803.

[21] G. Keglevich, E. Jablonkai, L.B. Balázs, RSC Adv. 4 (2014) 22808–22816.

[22] CrysAlisPro, version 1.171.39.46e; Rigaku Oxford Diffraction: Yarnton, UK, 2018.

[23] G.M. Sheldrick, Acta Cryst. A71 (2015) 3–8.

[24] G.M. Sheldrick, Acta Cryst. C71 (2015) 3–8.

[25] O.V. Dolomanov, L.J. Bourhis, R.J. Gildea, J.A.K. Howard, H. Puschmann, H. J. Appl. Cryst. 42 (2009) 339–341.