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Gold-Catalyzed Access to Isophosphinoline 2-Oxides

Mina Hariri, Fatemeh Darvish, Karen-Pacelye Mengue Me Ndong, Nora Sechet, Geraud Chacktas, Hooriye Boosaliki, Minh Loan Tran Do, Gabin Mwande-Maguene, Jacques Lebibi, Alexander R. Burilov, Tahar Ayad, David Virieux,* and Jean-Luc Pirat*

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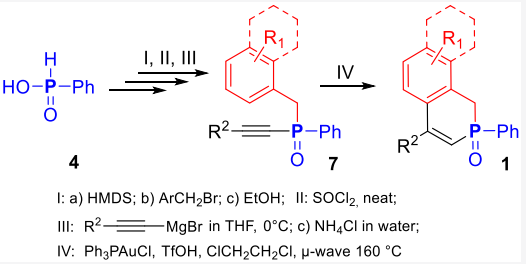
ABSTRACT: Gold(I)-catalyzed reactions of electron-poor alkynes are still a challenging process. A straightforward synthesis of phosphorus-based heterocycles, namely, 2-phenyl 1*H*-isophosphinoline 2-oxides **1**, is reported. The reaction used PPh_3AuCl precatalyst in combination with triflic acid under microwave activation and afforded isophosphinoline 2-oxides **1** in moderate to quantitative yields through a fully regioselective 6-endo-dig hydroarylation cyclization, paving the way toward an effective synthesis of phosphorus heterocycles.



Heterocyclic compounds play a determinant role in present-day living organisms, and their broad occurrence underlines this significance in several fundamental biological pathways. When practicing medicinal chemistry, the bioisosteric concept proved to be a fruitful approach in the design of new drugs with potent activity and reduced risks through modulation of the metabolic and/or pharmacokinetic properties.[1,2]

Consequently, bioisosteric replacements have known successful stories in drug discovery.[3] Phosphorus is a key ingredient of life as a vital nutrient, for instance, the transfer of energy in any leaving cells by phosphate group which is probably the most representative feature of its biological importance. In spite of the considerable amount of knowledge harvested over the last few decades, organophosphorus heterocycles are still the poor sibling in the development of new drugs.[4] Our group contributed with numerous others to the rebirth of phosphorus chemistry in life science through the development of two series of bioactive six-membered heterocycles.[5] We already demonstrated that phosphinolactone could potentially be an "ideal" bioisostere of the biologically and configurationally unstable lactol functional group.[6]

In another way, targeted covalent inhibitors are a re-emerging class of compounds in medicinal chemistry. The so-called warheads received increased attention, and an increased number of functional groups have now been exploited to target specific amino acid residues.[7] The balance between toxicity versus efficacy is the main reason for drug attrition, and covalent inhibitors benefited from several advantages, i.e., improved efficiency and lower dose response. To highlight the recent successes of this approach, more than 50 approved covalent inhibitors are on the market.[7a]

Therefore, the present paper is focused on the synthesis of phosphorus-based heterocycles, namely, the 2-phenyl *H*-isophosphinoline 2-oxides **1** (Figure 1). Such compounds can be seen as hydrolytically stable surrogates of combined coumarins **2a** and substituted flavonoids **2b**, natural compounds which express a wide range of potent activities.[8] It is also envisioned that the vinylphosphine oxide moiety may act as a new covalent inhibitor scaffold. The electrophilic character of such a functional group was thoroughly illustrated in the literature, and it was proved to react with a broad range of nucleophiles.[9] The low conjugation of the alkene moiety with the phosphoryl group makes them less electrophilic compared to the parent carbonyl derivatives.[10]

However, the lack of published synthetic approaches prompted us to develop an affordable access to variously substituted 2-phenyl *H*-isophosphinoline 2-oxides **1**. To the best of our knowledge, only Lee and colleagues and Gao and colleagues disclosed an efficient synthesis of phosphacoumarins **3** (phosphinate analogues) through catalytic approaches.[11] Our group also published a synthesis of bridgehead phosphorus heterobicycles, methanophosphocines which are eight-membered heterocycles using a gold-catalyzed cyclization of bis(arylmethyl) ethynylphosphine oxides.[12] This cascade reaction may have the potential to be extended to such target derivatives **1**, and gold-catalyzed reactions are the best effective processes.[13]

Our synthetic pathway began by the preparation of diversely substituted phenyl(arylmethyl)phosphinic acids **5**. Synthetic

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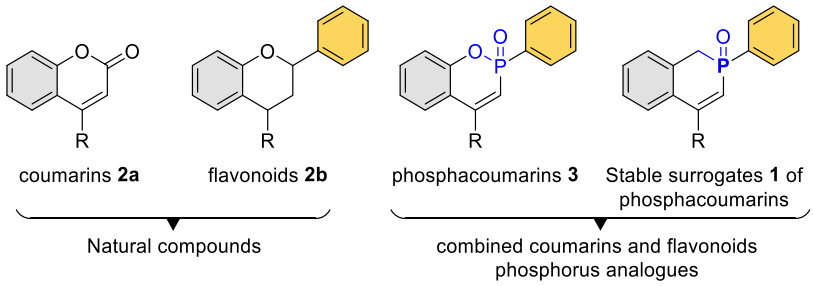
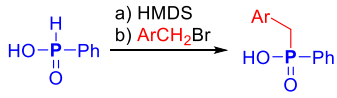


Figure 1. Isophosphinoline 2-oxide **1** as combined bioisosteres of coumarins **2a** and flavonoids **2b**, analogue of phosphacoumarins **3**.

approaches to such precursors are poorly reported in the literature. Nevertheless, Montchamp and colleagues developed an efficient Pd/xantphos-catalyzed benzylation of phenylphosphinic acid **4** using benzyl alcohol derivatives as nucleophiles,[14] and Boyd and colleagues reported a metal-free synthesis of phenyl phosphinic acid derivatives through the reaction of benzyl bromides with in situ formation of bis(trimethylsilyl)phosphonites under mild conditions.[15] Based on these precedent studies, as well as our own experiences,[12,16] we decided to use a slight modification of Boyd's procedure (instead of triethylamine or diisopropylethylamine and trimethylsilyl chloride, we used directly hexamethyldisilazane as a silylating agent (HMDS)) for the preparation of phosphinic acids **5a−h**. As highlighted in Table 1, compounds

Table 1. Synthesis of Phenyl (Arylmethyl) Phosphinic Acids 5a−h



4 **5a-i**

entry	Ar	5[a]	yield[b] (%)
1	Ph	**5a**	76
2	2-MeC_6H_4	**5b**	49
3	4-MeC_6H_4	**5c**	95
4	2-BrC_6H_4	**5d**	26
5	4-ClC_6H_4	**5e**	73
6	1-Napht	**5f**	61
7	2-Napht	**5g**	88
8	4-vinylC_6H_4	**5h**	>99

[a]Reaction run >1 mmol. [b]Isolated yields.

5 were straightforwardly obtained in moderate to quantitative yields using a two-step/one-pot sequence. The reaction involves in situ formation of bis(trimethylsilyl)-phenylphosphonite from cheap and commercially available phenylphosphinic acid **4** using hexamethyldisilazane followed by reaction with various arylmethyl halides (Table 1). It turned out that steric hindrance in the ortho position had deleterious effects leading to phosphinic acids **5b** and **5d** in 49 and 26% yields, respectively (entries 2 and 3). Similar trends were observed when the reaction was performed with hindered naphthyl derivatives. Indeed, 1-naphthylmethyl(phenyl)-phosphinic acid **2f** was obtained in 61% yield, while the less hindered 2-naphthyl derivative **2g** was isolated in 88% yield (entry 6 vs entry 7). The best yields were observed when para-substituted benzyl bromides were used whatever the nature of the para-substituents (entries 4 and 5).

With the desired phenyl(arylmethyl)phosphinic acids **5** in hand, we turned our attention to the synthesis of phenyl-(arylmethyl)(alkynyl)phosphine oxides **7** which are the key intermediates for the intramolecular hydroarylation step. Toward this end, phosphinic chlorides **6a−g** were easily obtained, generally in quantitative yields, by chlorination of the corresponding acids **5a−g** using an excess of thionyl chloride.[17] It can be noticed that phenyl(4-vinylbenzyl)-phosphinic acid **5h** failed to give the desired chloride derivative **6h** under such conditions. A polymeric content was observed in the reaction mixture. Under these conditions, phenyl-(arylmethyl)phosphinic chlorides **6a−g** were found to be sufficiently pure to be directly engaged in the next step without purification. Therefore, they were consecutively reacted with various alkynylmagnesium bromides (R^2 = H, Me, Ph), leading to the nucleophilic substitutions without any problem, thus affording a wide range of diverse phenyl(arylmethyl)(alkynyl)-phosphine oxides **7a−u** in good to excellent isolated yields (Table 2).[18] This straightforward method allowed variable aryl groups as well as different substituents to be easily introduced on the alkyne function.

The reaction conditions for the intramolecular gold-catalyzed hydroarylation were then examined, and the results are reported in Table 3. Initially, the conditions were then examined for the formation of the isophosphinoline 2-oxide **1a** starting from phenylbenzyl(ethynyl)phosphine oxide **7a** as a model reagent. The reaction was first conducted under thermic activation in 1,2-dichloroethane using Ph_3PAuCl as catalyst (2.5 mol %) in the presence of triflic acid as additive (3 equiv). Under these conditions, the reaction required 4 days to reach 89% as the relative percentage of **1a** in the crude mixture as determined by $^{31}P\{^1H\}$ NMR (entry 1). More importantly, the addition of the arene group to the alkyne appeared fully regioselective, giving as expected exclusively the 6-*endo*-dig cyclization product. The corresponding 5-*exo*-dig products were not observed, while in some cases gold-catalyzed reactions followed this mode of cyclization.[19] Microwave-assisted heating (MW) was attempted, since such technology has been shown to dramatically reduce the reaction times for processes that require prolonged heating. We were pleased to observe the formation of phosphinoline **1a** in 93% yield by running the reaction under microwave activation at 140 °C for 1.5 h (entry 2). Increasing both the temperature and the reaction time to 160 °C and 3 h, respectively, resulted in the formation of **1a** in excellent >99% yield (entry 3). By contrast, 6 h of heating at 180 °C had a detrimental effect, giving compound **1a** in lower yield 79% (entry 4). We suspected that this result could be attributed to the thermal instability of isophosphinoline 2-oxide **1a** at this temperature. This hypothesis was confirmed by a reaction time extended to 11 h, which resulted in significant yield reduction to 64% (entry

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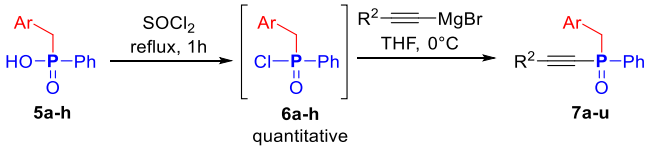
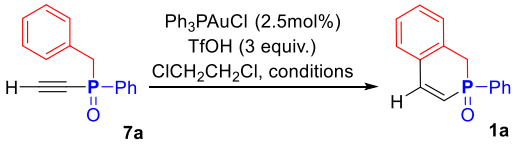
Table 2. Synthesis of Phenyl(arylmethyl)(alkynyl)phosphine Oxides 7a−u



entry	Ar	R^2	7	yield[a] (%)
1	Ph	H	**7a**	91
2	Ph	Me	**7b**	72
3	Ph	Ph	**7c**	70
4	2-MeC_6H_4	H	**7d**	53
5	2-MeC_6H_4	Me	**7e**	>99
6	2-MeC_6H_4	Ph	**7f**	75
7	4-MeC_6H_4	H	**7g**	95
8	4-MeC_6H_4	Me	**7h**	>99
9	4-MeC_6H_4	Ph	**7i**	91
10	2-BrC_6H_4	H	**7j**	60
11	2-BrC_6H_4	Me	**7k**	80
12	2-BrC_6H_4	Ph	**7l**	93
13	4-ClC_6H_4	H	**7m**	>99
14	4-ClC_6H_4	Me	**7n**	>99
15	4-ClC_6H_4	Ph	**7o**	97
16	1-Napht	H	**7p**	30
17	1-Napht	Me	**7q**	65
18	1-Napht	Ph	**7r**	77
19	2-Napht	H	**7s**	58
20	2-Napht	Me	**7t**	56
21	2-Napht	Ph	**7u**	41

[a]Isolated yields.

Table 3. Optimization of the Intramolecular Hydroarylation Reaction



entry	catalyst	additive	conditions	time	1a[a] (%)
1	Ph_3PAuCl	TfOH	80 °C	4 d	89
2	Ph_3PAuCl	TfOH	140 °C, MW	1.5 h	93
3	Ph_3PAuCl	TfOH	160 °C, MW	3 h	100
4	Ph_3PAuCl	TfOH	180 °C, MW	6 h	79
5	Ph_3PAuCl	TfOH	180 °C, MW	11 h	64
6	Ph_3PAuCl	none	160 °C, MW	3 h	0
7	none	TfOH	160 °C, MW	3 h	39

[a]Relative % of compound **1a** determined by $^{31}P\{1H\}$ NMR

5). It was already reported that alkenes can be effective substrates in intermolecular arylations and high temperature may induce over-reaction.[20] As seen in Table 3, the reaction carried out with gold catalyst alone failed to give compound **1a** (entries 6). The reaction performed with triflic acid led to the expected product **1a** in a low 38% yield. Under such conditions, 39% of the starting material **7a** remained along with the formation of 23% of side-products (entry 7). Consequently, combination of Ph_3PAuCl and triflic acid exhibited a positive synergistic enhancement of the catalytic effect.

Using the optimized conditions (160 °C, MW, 3 h), a wide range of substituted phenyl benzyl(ethynyl)phosphine oxides **7a−u** were engaged in the cyclization to evaluate the scope of the reaction (Table 4). Isophosphinoline 2-oxides **1a−n** were mostly formed in high to quantitative yields, irrespective of the nature and position of the substituents attached to both the aromatic and alkyne partners. For instance, reactions carried out with substrates bearing electron-donating substituents on the aryl group tend to give lower yields than those having electron-withdrawing substituents (entries 2−9 vs 10−13). The results depicted in Table 4 also showed that the substitution pattern on the alkyne moiety has an impact on the outcome of the reaction. Terminal alkynes tend to provide higher catalytic activity than substituted ones with isolated yields ranging from 85 to 100% (Table 4: compounds **1a**, **1d**, **1g**, **1j**, **1l**, and **1n**). It was noticed that the reaction of phenyl-substituted alkynes **7f** and **7i** also afforded the ketone resulting from the hydration of the alkyne substituent which is known to be catalyzed by gold.[21] Lee and colleagues also observed this side reaction when gold catalyst was used with silver salts. However, hydration of alkyne was drastically reduced in the presence of strong Brønsted acids (TFA, TfOH) even in the presence of silver triflate.

In summary, gold complexes were acting as mild π-Lewis acids in a facile 6-*endo*-dig arylation of electron-poor alkynes. Isophosphinoline oxides **1** were generally obtained in high yields using an unusual combination of gold(I) precatalyst with triflic acid as the sole additive. Further studies of isophosphinoline oxides **1** as the potential warhead on research applications are currently underway in our laboratory.

EXPERIMENTAL SECTION

Measurement. All experiments were carried out under a nitrogen atmosphere unless otherwise stated. Unless specified, all of the commercially available reagents and starting materials purchased from commercial sources were used as received without further purification. Thin layer chromatography (TLC) was performed on precoated plates of silica gel 60 F254 Merck. Visualization was performed with UV light and sometimes with phosphomolybdic acid solution or permanganate solution followed by heating. Flash chromatography was performed manually with silica gel (60 Å, 35−70 μm SDS). ^1H, ^{13}C, and $^{31}P\{1H\}$ NMR spectroscopic data were recorded at 400, 100, and 162 MHz, respectively. The chemical shifts are reported in ppm, and the coupling constants (J) are reported in Hz. The chemical shift values are referenced against the residual proton in the deuterated solvents. In the $^{13}C\{1H\}$ NMR spectra, signals corresponding to C, CH, CH_2, or CH_3 were assigned from the JMOD sequence. The multiplicities are given as s (singlet), d (doublet), t (triplet), q (quadruplet), and m (multiplet). Low and high resolution mass spectra were recorded with a time-of-flight mass spectrometer using electrospray ionization (ESI). Melting points were measured with an automatic melting point apparatus SMP50 from Stuart. HRMS (Q-TOF) were performed on a JEOL JMS-DX300 spectrometer (3 keV, xenon) in a *m*-nitrobenzyl alcohol matrix. Gas chromatography−mass spectra (GC-MS) were recorded on a Shimadzu QP2012-SE with a Zebron ZB-5MS (20 m × 0.18 mm), capillary nonpolar column (stationary phase: 0.18 μm film). GC-MS method: initial temperature, 50 °C; initial time, 2 min; ram, 22 °C/min; final temperature, 280 °C; final time, 15 min. Microwave reactions (MW) were performed using a CEM Discover apparatus in 10 and 35 mL sealed reactors for, respectively, small- and large-scale synthesis. Reactions were performed by maintaining the temperature to the set point. For reactions that require heating, the heat source was "heat on" systems.

Typical Procedure for the Preparation of Aryl(phenyl)-phosphinic Acids 5a−i.[12] In a dried and N_2 flushed 100 mL two-necked flask equipped with a condenser, the mixture of phenylphosphinic acid **4** (10 g, 70 mmol, 1 equiv), hexamethyldisilazane (15 mL, 70 mmol, 1 equiv), arylmethyl bromide, or arylmethyl chloride

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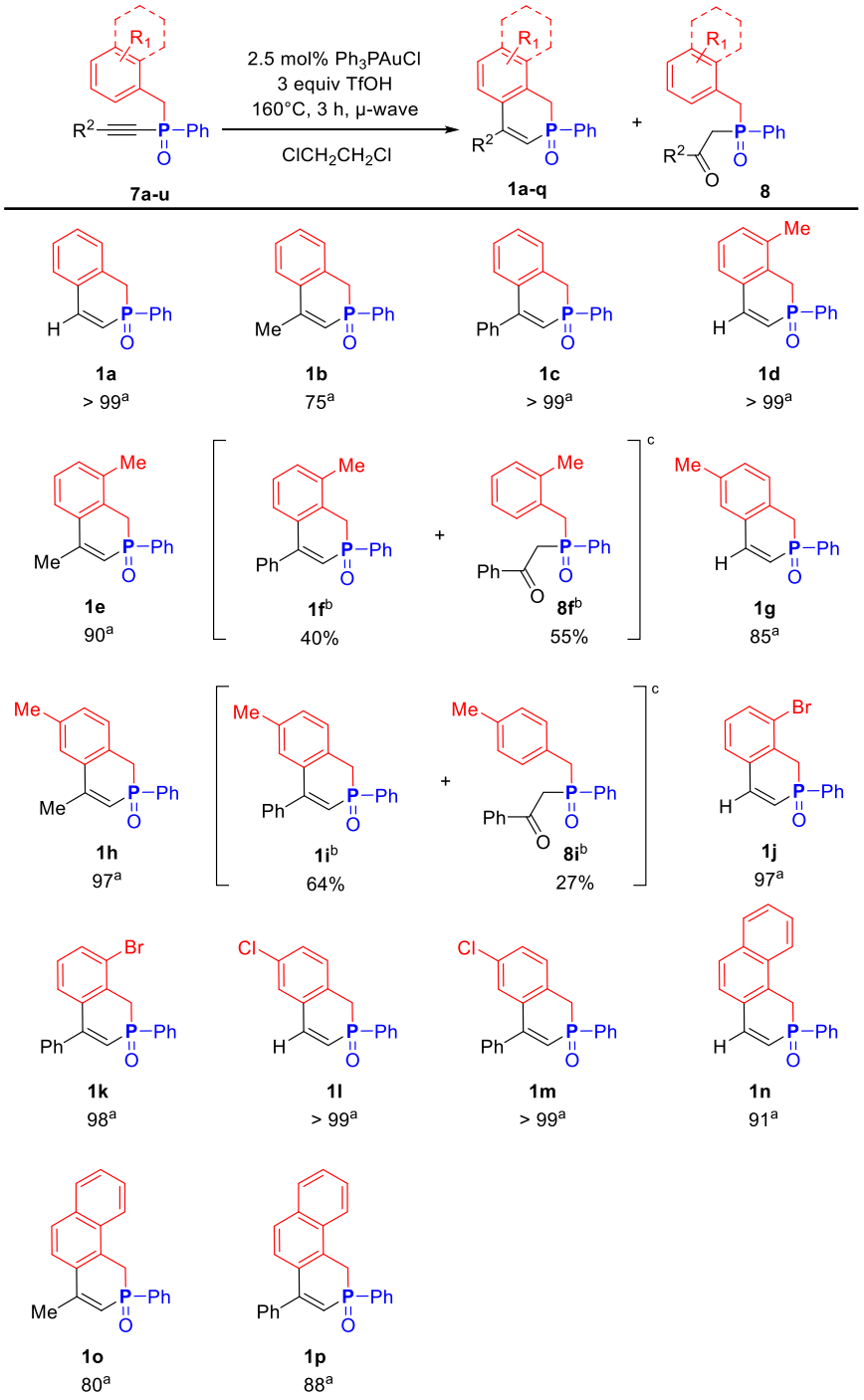
Table 4. Synthesis Isophosphinoline 2-Oxides 1a−q



[a]Isolated yields. [b]An inseparable mixture of isophosphinoline 2-oxide **1** and the ketone **8** resulting from the hydration of the alkyne function was obtained. [c]Relative % of compounds **1**/**8** determined by GC-MS analysis.

(1.5 equiv) was stirred at 105 °C for 4 h. After cooling to room temperature, ethanol (400 mL) was added and the mixture was stirred for 30 min and concentrated under a vacuum. Cyclohexane (2 × 250 mL) was added to the resulting crude, mixed, and filtered to remove the remaining excess of arylmethyl bromide or chloride. The crude was dissolved in 100 mL of 3 N HCl solution, and the solution was stirred for 10 min, then extracted with dichloromethane, dried over $MgSO_4$, and filtrated. The pure resulting solid **5** was obtained after evaporation of dichloromethane.

(Benzyl)(phenyl)phosphinic Acid (5a). Phenylphosphinic acid **4** (10 g, 70 mmol, 1 equiv), hexamethyldisilazane (15 mL, 70 mmol, 1 equiv), benzyl bromide (12.5 mL, 105 mmol, 1.5 equiv). The title product **5a** was obtained as a white solid (175.7−178.8 °C), 12.38 g (76% yield).[22]

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.66−7.56 (m, 2H), 7.55−7.48 (m, 1H), 7.43 (ddd, J = 8.6, 6.6, 3.3 Hz, 2H), 7.32 (s, 1H), 7.25−7.14 (m, 3H), 7.08 (d, J = 9.0 Hz, 2H), 3.23 (d, J = 17.6 Hz, 2H). ^{13}C{1H} NMR (101 MHz, DMSO-d_6) δ 133.6 (d, J = 126.5 Hz), 133.0 (d, J = 7.7 Hz), 131.5 (d, J = 2.7 Hz), 131.1 (d, J = 9.8 Hz), 129.8 (d, J = 5.7 Hz), 128.1 (d, J = 12.3 Hz), 127.9 (d, J = 2.7 Hz), 126.0 (d, J = 3.2 Hz), 37.9 (d, J = 92.2 Hz). ^{31}P{1H} NMRP{1H}

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NMR (162 MHz, DMSO-d_6) δ 32.87. HRMS: m/z calcd for $C_{13}H_{14}O_2P$ 233.0726 $[M + H]^+$, found 233.0729.

(2-Methylbenzyl)(phenyl)phosphinic Acid (5b). Phenylphosphinic acid **4** (4.3 g, 30.28 mmol, 1 equiv), hexamethyldisilazane (6.0 mL, 28.15 mmol, 1 equiv), 2-methylbenzyl bromide (5.7 mL, 42.22 mmol, 1.5 equiv). The title product **5b** was obtained as a white solid (160.7−171.3 °C), 3.41 g (49% yield).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.79−7.29 (m, 5H), 7.17−6.85 (m, 4H), 3.21 (d, J = 17.5 Hz, 2H), 2.14 (d, J = 1.6 Hz, 3H). ^{13}C{1H} NMR (101 MHz, DMSO-d_6) δ 136.8 (d, J = 5.7 Hz), 134.0 (d, J = 125.8 Hz), 131.6 (d, J = 2.7 Hz), 131.5 (d, J = 8.2 Hz), 131.1 (d, J = 9.8 Hz), 130.6 (d, J = 4.8 Hz), 129.9 (d, J = 3.0 Hz), 128.1 (d, J = 12.3 Hz), 126.2 (d, J = 3.4 Hz), 125.3 (d, J = 3.2 Hz), 35.6 (d, J = 92.4 Hz), 19.6 (d, J = 1.6 Hz). ^{31}P{1H} NMRP{1H} NMR (162 MHz, DMSO-d_6) δ 32.96. HRMS: m/z calcd for $C_{14}H_{16}O_2P$ 247.0882 $[M + H]^+$, found 247.0883.

(4-Methylbenzyl)(phenyl)phosphinic Acid (5c). Phenylphosphinic acid **4** (4.1 g, 28.85 mmol, 1 equiv), hexamethyldisilazane (6.1 mL, 28.85 mmol, 1 equiv), 4-methylbenzyl bromide (5.8 mL, 43.27 mmol, 1.5 equiv). The title product **5c** was obtained as a white solid (175.9−176.7 °C), 6.80 g (95% yield).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.75−7.32 (m, 5H), 7.12−6.73 (m, 4H), 3.18 (d, J = 17.6 Hz, 2H), 2.22 (d, J = 2.2 Hz, 3H). ^{13}C{1H} NMR (101 MHz, DMSO-d_6) δ 135.0 (d, J = 3.4 Hz), 133.8 (d, J = 126.2 Hz), 131.5 (d, J = 2.7 Hz), 131.1 (d, J = 9.5 Hz), 129.8 (d, J = 7.7 Hz), 129.7 (d, J = 5.7 Hz), 128.5 (d, J = 3.0 Hz), 128.1 (d, J = 12.0 Hz), 37.5 (d, J = 92.9 Hz), 20.6 (d, J = 1.1 Hz). ^{31}P{1H} NMR (162 MHz, DMSO-d_6) δ 33.09. HRMS: m/z calcd for $C_{14}H_{16}O_2P$ 247.0882 $[M + H]^+$, found 247.0887.

(2-Bromobenzyl)(phenyl)phosphinic Acid (5d).[23] Phenylphosphinic acid **4** (4.1 g, 28.85 mmol, 1 equiv), hexamethyldisilazane (6.1 mL, 28.85 mmol, 1 equiv), 2-bromobenzyl bromide (5.7 mL, 43.27 mmol, 1.5 equiv). The title product **5d** was obtained as a white solid (149−150.4 °C), 2.33 g (26% yield).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.18−7.06 (m, 3H), 7.03 (dd, J = 4.9, 4.0 Hz, 1H), 7.01−6.94 (m, 2H), 6.87 (dt, J = 7.7, 2.1 Hz, 1H), 6.81 (ddd, J = 7.8, 7.2, 0.7 Hz, 1H), 6.71−6.62 (m, 1H), 2.96 (d, J = 17.8 Hz, 2H). ^{13}C{1H} NMR (101 MHz, DMSO-d_6) δ 133.6 (d, J = 135.6 Hz), 133.0, 132.4 (d, J = 2.7 Hz), 131.8, 131.7−131.6 (m), 131.2 (d, J = 9.8 Hz), 129.0 (d, J = 3.2 Hz), 128.1 (d, J = 12.3 Hz), 127.3 (d, J = 3.2 Hz), 124.6 (d, J = 7.3 Hz), 37.9 (d, J = 91.7 Hz). ^{31}P{1H} NMR (162 MHz, DMSO-d_6) δ 31.21 (s). HRMS: m/z calcd for $C_{13}H_{13}BrO_2P$ 310.9831 $[M + H]^+$, found 310.9833.

(4-Chlorobenzyl)(phenyl)phosphinic Acid (5e).[24] Phenylphosphinic acid **4** (4.1 g, 28.85 mmol, 1 equiv), hexamethyldisilazane (6.1 mL, 28.85 mmol, 1 equiv), 4-chloromethyl-benzyl bromide (5.6 mL, 43.27 mmol, 1.5 equiv). The title product **5e** was obtained as a white solid (201.9−207.8 °C), 5.6 g (73% yield).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.72−7.56 (m, 2H), 7.54−7.33 (m, 3H), 7.32−7.18 (m, 2H), 7.10 (dd, J = 8.6, 2.4 Hz, 2H), 3.25 (d, J = 17.6 Hz, 2H). ^{13}C{1H} NMR (101 MHz, DMSO-d_6) δ 133.5 (d, J = 126.9 Hz), 132.3 (d, J = 7.7 Hz), 131.6 (d, J = 5.5 Hz), 131.1 (d, J = 9.8 Hz), 130.9 (d, J = 3.9 Hz), 128.1 (d, J = 12.0 Hz), 127.9 (d, J = 2.7 Hz), 37.2 (d, J = 92.0 Hz). ^{31}P{1H} NMR (162 MHz, DMSO-d_6) δ 32.54 (s). HRMS: m/z calcd for $C_{13}H_{13}ClO_2P$ 267.0336 $[M + H]^+$, found 267.0346.

(Naphthalen-1-ylmethyl)(phenyl)phosphinic Acid (5f).[24] Phenylphosphinic acid **4** (2.24 g, 15.8 mmol, 1 equiv), hexamethyldisilazane (3.5 mL, 15.8 mmol, 1 equiv), 1-chloromethyl-naphtalene (3.5 mL, 23.70 mmol, 1.5 equiv). The title product **5f** was obtained as a white solid (162.7−163.9 °C), 2.71 g (61% yield).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.08 (d, J = 8.1 Hz, 1H), 7.86 (d, J = 9.2 Hz, 1H), 7.75 (d, J = 7.9 Hz, 1H), 7.65 (dd, J = 11.7, 7.3 Hz, 2H), 7.57−7.38 (m, 5H), 7.34 (t, J = 7.6 Hz, 1H), 7.24 (dd, J = 7.2, 3.5 Hz, 1H), 3.72 (d, J = 17.5 Hz, 2H). ^{13}C{1H} NMR (101 MHz, DMSO-d_6) δ 134.0 (d, J = 126.3 Hz), 133.3 (d, J = 2.4 Hz), 132.0 (d, J = 4.3 Hz), 131.5 (d, J = 2.7 Hz), 131.2 (d, J = 9.8 Hz), 129.7 (d, J = 8.7 Hz), 128.3 (d, J = 6.5 Hz), 128.1, 128.1 (d, J = 12.2 Hz), 126.7 (d, J = 3.7 Hz), 125.6−125.34 (m), 125.2 (d, J = 2.1 Hz), 35.1 (d, J = 92.2 Hz). ^{31}P{1H} NMR (162 MHz, DMSO-d_6) δ 32.46. HRMS: m/z calcd for $C_{17}H_{16}O_2P$ $[M + H]^+$ 283.0882, found 283.0891.

(Naphthalen-2-ylmethyl)(phenyl)phosphinic Acid (5g). Phenylphosphinic acid **4** (0.58 g, 4.05 mmol, 1 equiv), hexamethyldisilazane (0.8 mL, 3.98 mmol, 1 equiv), 2-bromomethyl-naphtalene (1.34 g, 6.07 mmol, 1.5 equiv). The title product **5g** was obtained as a white solid (207.7−215.9 °C), 1.0 g (88% yield).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.08 (d, J = 7.9 Hz, 1H), 7.90−7.82 (m, 1H), 7.75 (d, J = 8.3 Hz, 1H), 7.70−7.58 (m, 2H), 7.55−7.38 (m, 5H), 7.35 (t, J = 7.7 Hz, 1H), 7.24 (dd, J = 6.7, 2.9 Hz, 1H), 3.72 (d, J = 17.5 Hz, 2H). ^{13}C{1H} NMR (101 MHz, DMSO-d_6) δ 134.2 (d, J = 126.5 Hz), 133.3 (d, J = 2.7 Hz), 132.0, 131.99 (d, J = 3.0 Hz), 131.6 (d, J = 9.5 Hz), 131.3 (d, J = 8.2 Hz), 128.9 (d, J = 4.3 Hz), 128.7, 128.6, 128.6, 127.9 (d, J = 1.6 Hz), 127.7, 126.5, 125.9, 38.7 (d, J = 92.0 Hz). ^{31}P{1H} NMR (162 MHz, DMSO-d_6) δ 32.44. HRMS: m/z calcd for $C_{17}H_{16}O_2P$ $[M + H]^+$ 283.0882, found 283.0886.

(4-Vinylbenzyl)(phenyl)phosphinic Acid (5h). Phenylphosphinic acid **4** (4.0 g, 28.15 mmol, 1 equiv), hexamethyldisilazane (5.6 mL, 28.15 mmol, 1 equiv), 4-vinylbenzyl chloride (3.5 mL, 42.22 mmol, 1.5 equiv). The title product **5h** was obtained as a white solid (169.2−172.2 °C), 7.3 g (yield >99%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.68−7.60 (m, 2H), 7.53 (td, J = 7.5, 1.4 Hz, 1H), 7.48−7.40 (m, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.06 (dd, J = 8.2, 2.2 Hz, 2H), 6.66 (dd, J = 17.7, 10.9 Hz, 1H), 5.76 (d, J = 17.7 Hz, 1H), 5.19 (d, J = 10.9 Hz, 1H), 3.25 (d, J = 17.8 Hz, 2H). ^{13}C{1H} NMR (101 MHz, DMSO-d_6) δ 136.9 (d, J = 2.0 Hz), 135.4 (d, J = 3.4 Hz), 134.2 (d, J = 126.5 Hz), 133.3 (d, J = 7.9 Hz), 132.0 (d, J = 2.7 Hz), 131.6 (d, J = 9.8 Hz), 130.5 (d, J = 5.9 Hz), 128.6 (d, J = 12.3 Hz), 126.2 (d, J = 3.0 Hz), 114.1 (d, J = 1.8 Hz), 38.2 (d, J = 92.0 Hz). ^{31}P{1H} NMR (162 MHz, DMSO-d_6) δ 32.68. HRMS: m/z calcd for $C_{15}H_{16}O_2P$ $[M + H]^+$ 259.0882, found 259.0892.

Typical Procedure for the Preparation of (Arylmethyl)-phenylphosphinic Chlorides 6a−g. In a 250 mL two-necked flask equipped with a condenser under N_2, the mixture of thionyl chloride (20 equiv) and (arymethyl)phenylphosphinic acid **5** (1 equiv) was refluxed at 76 °C for 30 min. The excess of thionyl chloride was removed by distillation. The resulting phosphinic chlorides **6** were consecutively engaged in the reaction with alkynylmagnesium bromides without purification.

Benzyl(phenyl)phosphinic Chloride (6a). Benzyl phenylphosphinic acid **5a** (0.8 g, 3.4 mmol, 1 equiv), thionyl chloride (5 mL, 68.9 mmol, 20 equiv). The title product **6a** was obtained as a yellow solid.

^{1}H NMR (400 MHz, chloroform-d) δ 7.80−7.67 (m, 2H), 7.59 (td, J = 7.3, 1.5 Hz, 1H), 7.47 (td, J = 7.6, 4.3 Hz, 2H), 7.25 (d, J = 6.5 Hz, 3H), 7.12 (dd, J = 4.6, 2.3 Hz, 2H), 3.89−3.58 (m, 2H). ^{31}P{1H} NMR (162 MHz, DMSO-d_6) δ 52.25 (s).

(2-Methylbenzyl)(phenyl)phosphinic Chloride (6b). (2-Methylbenzyl)(phenyl)phosphinic acid **5b** (0.8 g, 3.25 mmol, 1 equiv), thionyl chloride (4.71 mL, 64.9 mmol, 20 equiv). The title product **6b** was obtained as a yellow solid.

^{31}P{1H} NMR (162 MHz, chloroform-d) δ 51.74.

(4-Methylbenzyl)(phenyl)phosphinic Chloride (6c). (4-Methylbenzyl)(phenyl)phosphinic acid **5c** (0.8 g, 3.25 mmol, 1 equiv), thionyl chloride (4.71 mL, 64.9 mmol, 20 equiv). The title product **6c** was obtained as a yellow solid.

(2-Bromobenzyl)(phenyl)phosphinic Chloride (6d). (2-Bromobenzyl)(phenyl)phosphinic acid **5d** (0.8 g, 2.57 mmol, 1 equiv), thionyl chloride (3.73 mL, 51.42 mmol, 20 equiv). The title product **6d** was obtained as a red solid.

(4-Chlorobenzyl)(phenyl)phosphinic Chloride (6e). (4-Chlorobenzyl)(phenyl)phosphinic acid **5e** (0.8 g, 3 mmol, 1 equiv), thionyl chloride (4.35 mL, 60 mmol, 20 equiv). The title product **6e** was obtained as a yellow solid.

(Naphthalen-1-ylmethyl)(phenyl)phosphinic Chloride (6f). (Naphthalene-1-ylmethyl)(phenyl)phosphinic acid **5f** (0.7 g, 2.48 mmol, 1 equiv), thionyl chloride (3.6 mL, 49.60 mmol, 20 equiv). The title product **6f** was obtained as a yellow solid.

(Naphthalen-2-ylmethyl)(phenyl)phosphinic Chloride (6g). (Naphthalene-2-ylmethyl)(phenyl)phosphinic acid **5g** (0.59 g, 2.09

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mmol, 1 equiv), thionyl chloride (3 mL, 41.80 mmol, 20 equiv). The title product **6g** was obtained as a yellow solid.

Typical Procedure for the Preparation of (Substituted-benzyl)(phenyl)(R-yl)phosphine Oxide 7a–u. Under N_2, alkylmagnesium bromide or chloride in solution (3.5 equiv) was added dropwise to a solution of (phenyl)phosphinic chloride **6** (1 equiv) in THF at 0 °C. The mixture was stirred for 1 h at room temperature until $^{31}P\{1H\}$ NMR indicated the disappearance of the benzyl-(phenyl)phosphinic chloride. Saturated aqueous solution of NH_4Cl was added to the mixture. The aqueous layer had been separated and extracted with 2 × 5 mL of DCM, dried with $MgSO_4$, and concentrated under a vacuum. The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10.

Benzyl(ethynyl)(phenyl)phosphine oxide (7a). Benzylphenylphosphinic chloride **6a** (0.5 g, 2 mmol, 1 equiv), 0.5 M ethynylmagnesium bromide in THF (14 mL, 7 mmol, 3.5 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7a** was obtained as a brown solid (94.0–96.1 °C), 0.44 g (91% yield).

^1H NMR (400 MHz, chloroform-*d*) δ 7.68 (ddd, J = 13.3, 8.3, 1.3 Hz, 2H), 7.53 (dd, J = 7.4, 1.8 Hz, 1H), 7.48–7.32 (m, 2H), 7.25–7.09 (m, 3H), 7.14–6.96 (m, 2H), 3.45 (d, J = 16.5 Hz, 2H), 3.21 (d, J = 9.5 Hz, 1H). $^{13}C\{1H\}$ NMR (101 MHz, chloroform-*d*) δ 132.7 (d, J = 3.0 Hz), 130.8 (d, J = 10.6 Hz), 130.2 (d, J = 5.5 Hz), 130.0 (d, J = 117.6 Hz), 128.6, 128.5, 128.4, 127.3 (d, J = 3.8 Hz), 94.4 (d, J = 25.4 Hz), 77.9 (d, J = 153.6 Hz), 41.7 (d, J = 78.4 Hz). $^{31}P\{1H\}$ NMR (162 MHz, chloroform-*d*) δ 14.40 (s). HRMS: m/z calcd for $C_{15}H_{14}OP$ 241.0782 $[M + H]^+$, found 241.0781.

Benzyl(phenyl)(prop-1-yn-1-yl)phosphine Oxide (7b). Benzylphenylphosphinic chloride **6a** (0.5 g, 2 mmol, 1 equiv), 0.5 M prop-1-yn-1-ylmagnesium bromide in THF (14 mL, 7 mmol, 3.5 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7b** was obtained as a white solid, 0.36 g (72% yield).

^1H NMR (400 MHz, chloroform-*d*) δ 7.76–7.56 (m, 2H), 7.49 (dd, J = 7.5, 1.7 Hz, 1H), 7.41 (dd, J = 7.8, 3.3 Hz, 2H), 7.20 (dd, J = 4.9, 1.8 Hz, 3H), 7.05 (dd, J = 4.5, 2.8 Hz, 2H), 3.39 (d, J = 16.6 Hz, 2H), 2.03 (d, J = 3.8 Hz, 3H).

$^{13}C\{1H\}$ NMR (101 MHz, chloroform-*d*) δ 132.2 (d, J = 3.0 Hz), 131.9, 131.1 (d, J = 8.1 Hz), 130.8 (d, J = 10.4 Hz), 130.2 (d, J = 5.7 Hz), 128.4, 128.3, 128.2, 127.03 (d, J = 3.6 Hz), 105.2 (d, J = 29.3 Hz), 73.9 (d, J = 167.8 Hz), 42.2 (d, J = 78.8 Hz), 4.9 (d, J = 3.4 Hz). $^{31}P\{1H\}$ NMR (162 MHz, chloroform-*d*) δ 13.78 (s). HRMS: m/z calcd for $C_{16}H_{16}OP$ 255.0939 $[M + H]^+$, found 255.0938.

Benzyl(phenyl)(phenylethynyl)phosphine Oxide (7c). Benzylphenylphosphinic chloride **6a** (0.5 g, 2 mmol, 1 equiv), 1 M (phenylethynyl)magnesium bromide in THF (7 mL, 7 mmol, 3.5 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7c** was obtained as a white solid (150.8–152.3 °C), 0.44 g (70% yield).

^1H NMR (400 MHz) δ 7.83–7.74 (m, 2H), 7.62–7.53 (m, 3H), 7.52–7.45 (m, 3H), 7.45–7.37 (m, 2H), 7.27 (dd, J = 4.9, 1.7 Hz, 3H), 7.23–7.10 (m, 2H), 3.53 (dq, J = 16.4, 14.4 Hz, 2H). $^{13}C\{1H\}$ NMR (101 MHz, chloroform-*d*) δ 132.39 (d, J = 1.9 Hz), 132.35 (d, J = 3.0 Hz), 131.05 (d, J = 117.3 Hz), 130.82 (d, J = 10.5 Hz), 130.74 (d, J = 12.9 Hz), 130.21 (d, J = 5.7 Hz), 128.48 (d, J = 19.7 Hz), 128.43 (d, J = 16.1 Hz), 127.10 (d, J = 3.8 Hz), 119.83 (d, J = 4.0 Hz), 105.16 (d, J = 27.6 Hz), 82.15 (d, J = 162.2 Hz), 42.22 (d, J = 78.3 Hz). $^{31}P\{1H\}$ NMR (162 MHz, chloroform-*d*) δ 14.77 (s). HRMS: m/z calcd for $C_{21}H_{18}OP$ 317.1095 $[M + H]^+$, found 317.1092.

Ethynyl(2-methylbenzyl)(phenyl)phosphine Oxide (7d). (2-Methylbenzyl)(phenyl)phosphinic chloride 6b (0.5 g, 1.89 mmol, 1 equiv), ethynylmagnesium bromide 0.5 M in THF (13 mL, 6.61 mmol, 3.5 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10.The title product **7d** was obtained as a creamy solid, 0.26 g (53% yield).

^1H NMR (400 MHz, chloroform-*d*) δ 7.68–7.53 (m, 2H), 7.45 (td, J = 7.3, 1.6 Hz, 1H), 7.34 (dt, J = 7.5, 3.7 Hz, 2H), 7.12–6.88 (m, 4H), 3.66–3.21 (m, 3H), 2.05 (s, 3H). $^{13}C\{1H\}$ NMR (101 MHz, chloroform-*d*) δ 137.3 (d, J = 5.9 Hz), 132.6 (d, J = 3.0 Hz), 130.9 (d, J = 5.0 Hz), 130.7 (d, J = 10.4 Hz), 130.6 (d, J = 116.3 Hz), 130.5 (d, J = 3.4 Hz), 128.8 (d, J = 8.6 Hz), 128.5 (d, J = 13.2 Hz), 127.4 (d, J = 3.9 Hz), 125.9 (d, J = 3.6 Hz), 94.3 (d, J = 25.2 Hz), 78.1 (d, J = 199.6 Hz), 38.9 (d, J = 78.6 Hz), 19.9 (d, J = 1.8 Hz). $^{31}P\{1H\}$ NMR (162 MHz, chloroform-*d*) δ 13.84. HRMS: m/z calcd for $C_{16}H_{16}OP$ 255.0939 $[M + H]^+$, found 255.0947.

(2-Methylbenzyl)(phenyl)(prop-1-yn)phosphine Oxide (7e). (2-Methylbenzyl)(phenyl)phosphinic chloride **6b** (0.5 g, 1.89 mmol, 1 equiv), prop-1-yn-1-ylmagnesium bromide 0.5 M in THF (13 mL, 6.61 mmol, 3.5 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7e** was obtained as a red oil, 0.50 g (yield >99%).

^1H NMR (400 MHz, chloroform-*d*) δ 7.60–7.54 (m, 2H), 7.39 (d, J = 1.5 Hz, 1H), 7.35–7.19 (m, 2H), 7.08–6.73 (m, 4H), 3.54–3.19 (m, 2H), 2.02 (d, J = 1.7 Hz, 3H), 1.92 (d, J = 3.8 Hz, 3H). $^{13}C\{1H\}$ NMR (101 MHz, chloroform-*d*) δ 137.0 (d, J = 5.9 Hz), 131.9 (d, J = 3.2 Hz), 130.8, 130.6 (d, J = 5.2 Hz), 130.4 (d, J = 10.4 Hz), 130.1 (d, J = 3.2 Hz), 129.2 (d, J = 8.4 Hz), 128.1 (d, J = 12.9 Hz), 126.9 (d, J = 3.9 Hz), 125.4 (d, J = 3.6 Hz), 104.6 (d, J = 28.8 Hz), 73.8 (d, J = 166.4 Hz), 38.9 (d, J = 78.8 Hz), 19.6 (d, J = 1.4 Hz), 4.5 (d, J = 3.4 Hz). $^{31}P\{1H\}$ NMR (162 MHz) δ 12.86 (s). HRMS: m/z calcd for $C_{17}H_{18}OP$ 269.1095 $[M + H]^+$, found 269.1103.

(2-Methylbenzyl)(phenyl)(phenylethynyl)phosphine Oxide (7f). (2-Methylbenzyl)(phenyl)phosphinic chloride **6b** (0.5 g, 1.89 mmol, 1 equiv), (phenylethynyl)magnesium bromide 1 M in THF (6.5 mL, 6.61 mmol, 3.5 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7f** was obtained as a creamy solid, 0.46 g (75% yield).

^1H NMR (400 MHz) δ 7.74–7.69 (m, 2H), 7.57–7.47 (m, 3H), 7.46–7.38 (m, 3H), 7.34 (dd, J = 8.0, 6.6 Hz, 2H), 7.19–7.02 (m, 4H), 3.56 (d, J = 16.9 Hz, 2H), 2.15 (s, 3H). $^{13}C\{1H\}$ NMR (101 MHz, chloroform-*d*) δ 137.2 (d, J = 6.0 Hz), 132.2, 131.8, 130.8 (d, J = 5.1 Hz), 130.7, 130.55 (d, J = 4.1 Hz), 130.3 (d, J = 3.4 Hz), 129.2 (d, J = 8.7 Hz), 128.4, 128.3 (d, J = 13.1 Hz), 127.2 (d, J = 3.9 Hz), 125.6 (d, J = 3.7 Hz), 119.6 (d, J = 3.9 Hz), 104.6 (d, J = 27.6 Hz), 82.4 (d, J = 161.1 Hz), 39.1 (d, J = 78.6 Hz), 19.8 (s). $^{31}P\{1H\}$ NMR (162 MHz) δ 14.53 (s). HRMS: m/z calcd for $C_{22}H_{20}OP$ 331.1252 $[M + H]^+$, found 331.1259.

(Ethynyl)(4-methylbenzyl)(phenyl)phosphine Oxide (7g). (4-Methylbenzyl)(phenyl)phosphinic chloride **6c** (0.5 g, 1.89 mmol, 1 equiv), ethynylmagnesium bromide 0.5 M in THF (13 mL, 6.61 mmol, 3.5 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7g** was obtained as a red oil, 0.47 g (95% yield).

^1H NMR (400 MHz, chloroform-*d*) δ 7.63–7.57 (m, 2H), 7.40–7.39 (m, 1H), 7.33–7.30 (m, 2H), 6.93–6.86 (m, 4H), 3.34 (d, J = 9.5 Hz, 1H), 3.31 (d, J = 16.3 Hz, 2H), 2.16 (d, J = 2.6 Hz, 3H). $^{13}C\{1H\}$ NMR (101 MHz, chloroform-*d*) δ 136.5 (d, J = 3.9 Hz), 132.2 (d, J = 3.0 Hz), 130.4 (d, J = 10.6 Hz), 130.1 (d, J = 116.7 Hz), 129.7 (d, J = 5.7 Hz), 128.9 (d, J = 3.4 Hz), 128.2 (d, J = 13.3 Hz), 126.7 (d, J = 8.5 Hz), 94.2 (d, J = 25.3 Hz), 77.8 (d, J = 152.4 Hz), 41.0 (d, J = 78.8 Hz), 20.8 (d, J = 1.4 Hz). $^{31}P\{1H\}$ NMR (162 MHz) δ 14.49 (s). HRMS: m/z calcd for $C_{16}H_{16}OP$ 255.0939 $[M + H]^+$, found 255.0947.

(4-Methylbenzyl)(phenyl)(prop-1-yn-1-yl)phosphine Oxide (7h). (4-Methylbenzyl)(phenyl)phosphinic chloride **6c** (0.5 g, 1.89 mmol, 1 equiv), prop-1-yn-1-ylmagnesium bromide 0.5 M in THF (13 mL, 6.61 mmol, 3.5 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7h** was obtained as a brown oil, 0.50 g (yield >99%).

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^{1}H NMR (400 MHz, chloroform-*d*) δ 7.61−7.56 (m, 2H), 7.37 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.29−7.26 (m, 2H), 6.91−6.83 (m, 4H), 3.26 (d, *J* = 16.5 Hz, 2H), 2.16 (d, *J* = 2.4 Hz, 3H), 1.88 (d, *J* = 3.8 Hz, 3H). ^{13}C{1H} NMR (101 MHz) δ 136.4 (d, *J* = 3.9 Hz), 132.1 (d, *J* = 2.9 Hz), 130.7 (d, *J* = 10.4 Hz), 130.7 (d, *J* = 10.4 Hz), 129.9 (d, *J* = 5.7 Hz), 128.9 (d, *J* = 3.3 Hz), 128.3 (d, *J* = 13.0 Hz), 127.6 (d, *J* = 8.4 Hz), 105.0 (d, *J* = 29.0 Hz), 73.7 (d, *J* = 167.4 Hz), 41.5 (d, *J* = 79.0 Hz), 21.0 (d, *J* = 1.1 Hz), 4.7 (d, *J* = 3.3 Hz). ^{31}P{1H} NMR (162 MHz) δ 12.61 (s). HRMS: *m*/*z* calcd for $C_{17}H_{18}OP$ 269.1095 [M + H]$^+$, found 269.1104.

(4-Methylbenzyl)(phenyl)(phenylethynyl)phosphine Oxide (7i). (4-Methylbenzyl)(phenyl)phosphinic chloride **6c** (0.5 g, 1.89 mmol, 1 equiv), 1 M (phenylethynyl)magnesium bromide (6.5 mL, 6.61 mmol, 3.5 equiv) in THF. The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7i** was obtained as a yellow solid (129.6−132.1 °C), 0.56 g (91% yield).

^{1}H NMR (400 MHz) δ 7.74 (dd, *J* = 12.6, 7.6 Hz, 2H), 7.46−7.26 (m, 8H), 7.00 (s, 4H), 3.47−3.41 (m, 2H), 2.24 (s, 3H). ^{13}C{1H} NMR (101 MHz) δ 136.4 (d, *J* = 3.5 Hz), 132.0 (s, *J* = 1.6 Hz), 131.5 (s), 130.5 (d, *J* = 10.3 Hz), 130.3 (d, *J* = 4.3 Hz), 129.8 (d, *J* = 5.6 Hz), 128.8 (d, *J* = 3.2 Hz), 128.3 (s), 128.2 (d, *J* = 13.0 Hz), 127.3 (d, *J* = 8.3 Hz), 119.5 (d, *J* = 3.4 Hz), 104.7 (d, *J* = 27.3 Hz), 82.1 (d, *J* = 161.1 Hz), 41.4 (d, *J* = 78.7 Hz), 20.8 (s). ^{31}P{1H} NMR (162 MHz) δ 14.35 (s). HRMS: *m*/*z* calcd for $C_{22}H_{20}OP$ 331.1252 [M + H]$^+$, found 331.1259.

(2-Bromobenzyl)(ethynyl)(phenyl)phosphine Oxide (7j). (2-Bromobenzyl)(phenyl)phosphinic chloride **6d** (0.5 g, 1.51 mmol, 1 equiv), 0.5 M ethynylmagnesium bromide in THF (11 mL, 5.31 mmol, 3.5 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7j** was obtained as a red creamy solid, 0.29 g (60% yield).

^{1}H NMR (400 MHz) δ 7.72−7.66 (m, 2H), 7.53−7.51 (m, 1H), 7.45−7.37 (m, 4H), 7.25 (t, *J* = 7.5 Hz, 1H), 7.9−7.05 (m, 1H), 3.79−3.62 (m, *2H*), 3.27 (d, *J* = 9.6 Hz, 1H). ^{13}C{1H} NMR (101 MHz) δ 133.0 (d, *J* = 2.8 Hz), 132.8 (d, *J* = 2.9 Hz), 132.0 (d, *J* = 5.0 Hz), 130.8 (d, *J* = 10.8 Hz), 130.6 (s), 130.2 (d, *J* = 100.2 Hz), 128.9 (d, *J* = 3.5 Hz), 128.6 (d, *J* = 13.3 Hz), 127.5 (d, *J* = 3.3 Hz), 125.5 (d, *J* = 7.7 Hz), 93.9 (d, *J* = 26.0 Hz), 41.1 (d, *J* = 78.7 Hz). ^{31}P{1H} NMR (162 MHz) δ 12.71 (s). HRMS: *m*/*z* calcd for $C_{15}H_{13}BrOP$ 318.9887 [M + H]$^+$, found 318.9896.

(2-Bromobenzyl)(phenyl)(prop-1-yn-1-yl)phosphine Oxide (7k). (2-Bromobenzyl)(phenyl)phosphinic chloride **6d** (0.5 g, 1.51 mmol, 1 equiv), 0.5 M prop-1-yn-1-ylmagnesium bromide in THF (11 mL, 5.31 mmol, 3.5 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7k** was obtained as a yellow creamy solid, 0.4 g (80% yield).

^{1}H NMR (400 MHz) δ 7.69−7.64 (m, 2H), 7.48−7.29 (m, 5H), 7.19−7.15 (m, 1H), 7.05−7.00 (m, 1H), 3.63 (dd, *J* = 14.9, 13.1 Hz, 1H), 3.55 (dd, *J* = 15.6, 13.1 Hz, 1H), 1.95 (d, *J* = 3.8 Hz, 3H). ^{13}C{1H} NMR (101 MHz) δ 132.8 (d, *J* = 3.0 Hz), 132.3 (d, *J* = 3.0 Hz), 132.0 (d, *J* = 4.9 Hz), 131.3 (d, *J* = 117.9 Hz), 131.3 (d, *J* = 8.3 Hz), 130.8 (d, *J* = 10.7 Hz), 128.7 (d, *J* = 3.6 Hz), 128.4 (d, *J* = 13.2 Hz), 125.3 (d, *J* = 7.5 Hz), 105.3 (d, *J* = 30.0 Hz), 73.7 (d, *J* = 169.7 Hz), 41.3 (d, *J* = 78.7 Hz), 5.0 (d, *J* = 3.3 Hz). ^{31}P{1H} NMR (162 MHz) δ 11.97 (s). HRMS: *m*/*z* calcd for $C_{16}H_{15}BrOP$ 333.0044 [M + H]$^+$, found 333.0053.

(2-Bromobenzyl)(phenyl)(phenylethynyl)phosphine Oxide (7l). (2-Bromobenzyl)(phenyl)phosphinic chloride **6d** (0.5 g, 1.51 mmol, 1 equiv), 1 M (phenylethynyl)magnesium bromide in THF (5.5 mL, 5.31 mmol, 3.5 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7l** was obtained as a red oil, 0.55 g (93% yield).

^{1}H NMR (400 MHz) δ 7.71−7.65 (m, 2H), 7.41−7.17 (m, 10H), 7.11−7.07 (m, 1H), 6.96−6.93 (m, 1H), 3.84 (dd, *J* = 15.9, 14.6 Hz, 1H), 3.76 (dd, *J* = 18.0, 14.7 Hz, 1H). ^{13}C{1H} NMR (101 MHz) δ 133.0 (d, *J* = 2.8 Hz), 132.6 (s), 132.2 (d, *J* = 4.9 Hz), 131.3 (d, *J* = 8.4 Hz), 131.2 (dd, *J* = 63.2, 54.9 Hz), 131.1−130.8 (m, *J* = 10.7 Hz), 130.8−130.66 (m), 128.9 (d, *J* = 3.5 Hz), 128.7 (s), 128.6 (s), 128.5 (s), 127.5 (d, *J* = 3.3 Hz), 125.5 (d, *J* = 7.5 Hz), 119.9 (d, *J* = 3.9 Hz), 105.1 (d, *J* = 28.5 Hz), 82.2 (d, *J* = 164.6 Hz), 41.5 (d, *J* = 78.6 Hz). ^{31}P{1H} NMR (162 MHz) δ 12.75 (s). HRMS: *m*/*z* calcd for $C_{21}H_{17}BrOP$ 395.0200 [M + H]$^+$, found 395.0204.

(4-Chlorobenzyl)(ethynyl)(phenyl)phosphine Oxide (7m). (4-Chlorobenzyl)(phenyl)phosphinic chloride **6e** (0.5 g, 1.75 mmol, 1 equiv), 0.5 M ethynylmagnesium bromide in THF (13 mL, 6.14 mmol, 3.5 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7m** was obtained as a red solid (102.3−105.1 °C), 0.48 g (yield >99%).

^{1}H NMR (400 MHz) δ 7.66−7.61 (m, 2H), 7.51 (dt, *J* = 7.3, 3.7 Hz, 1H), 7.42 (td, *J* = 7.5, 3.4 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 6.97 (dd, *J* = 8.5, 2.5 Hz, 2H), 3.35 (d, *J* = 16.3 Hz, 2H), 3.31 (d, *J* = 9.6 Hz, 1H). ^{13}C{1H} NMR (101 MHz, chloroform-*d*) δ 133.3 (d, *J* = 4.6 Hz), 132.8 (d, *J* = 3.0 Hz), 131.4 (d, *J* = 5.7 Hz), 130.7 (d, *J* = 10.6 Hz), 129.9 (d, *J* = 117.7 Hz), 128.8 (d, *J* = 8.4 Hz), 128.7 (d, *J* = 9.2 Hz), 128.6, 94.4 (d, *J* = 25.5 Hz), 77.8 (d, *J* = 153.3 Hz), 41.2 (d, *J* = 78.1 Hz). ^{31}P{1H} NMR (162 MHz) δ 13.38 (s). HRMS: *m*/*z* calcd for $C_{15}H_{13}ClOP$ 275.0393 [M + H]$^+$, found 275.0403.

(4-Chlorobenzyl)(phenyl)(prop-1-yn-1-yl)phosphine Oxide (7n). (4-Chlorobenzyl)(phenyl)phosphinic chloride **6e** (0.5 g, 1.75 mmol, 1 equiv), 0.5 M prop-1-yn-1-ylmagnesium bromide in THF (13 mL, 6.14 mmol, 3.5 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7n** was obtained as a yellow solid (93.7 °C), 0.50 g (yield >99%).

^{1}H NMR (400 MHz) δ 7.69−7.64 (m, 2H), 7.54−7.50 (m, 1H), 7.45−7.40 (m, 2H), 7.19−7.17 (m, 2H), 7.02−6.97 (m, 2H), 3.35 (d, *J* = 16.4 Hz, 2H), 2.03 (d, *J* = 3.7 Hz, 3H). ^{13}C{1H} NMR (101 MHz) δ 133.0 (d, *J* = 4.2 Hz), 132.3 (s), 131.6 (s), 131.4 (d, *J* = 5.4 Hz), 130.7 (d, *J* = 10.5 Hz), 130.0 (d, *J* = 92.2 Hz), 129.6 (s), 128.4 (d, *J* = 12.8 Hz), 128.4 (d, *J* = 2.7 Hz), 105.4 (d, *J* = 29.4 Hz), 73.5 (d, *J* = 168.6 Hz), 41.5 (d, *J* = 78.5 Hz), 4.9 (s). ^{31}P{1H} NMR (162 MHz) δ 13.81 (s). HRMS: *m*/*z* calcd for $C_{16}H_{15}ClOP$ 289.0549 [M + H]$^+$, found 289.0557.

(4-Chlorobenzyl)(phenyl)(phenylethynyl)phosphine Oxide (7o). (4-Chlorobenzyl)(phenyl)phosphinic chloride **6e** (0.5 g, 1.75 mmol, 1 equiv), 1 M (phenylethynyl)magnesium bromide in THF (6.5 mL, 6.14 mmol, 3.5 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7o** was obtained as a yellow solid (113.2−122.8 °C), 0.59 g (97% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.77−7.72 (m, 2H), 7.57−7.42 (m, 6H), 7.38−7.34 (m, 2H), 7.21−7.19 (m, 2H), 7.05 (dd, *J* = 8.5, 2.8 Hz, 2H), 3.47 (dd, *J* = 16.5, 3.1 Hz, 2H). ^{13}C{1H} NMR (101 MHz, chloroform-*d*) δ 133.1 (d, *J* = 4.3 Hz), 132.5, 132.3, 131.4 (d, *J* = 5.2 Hz), 130.7, 130.6, 129.4 (d, *J* = 8.4 Hz), 128.6, 128.5, 119.5 (d, *J* = 3.4 Hz), 105.4 (d, *J* = 27.7 Hz), 81.9 (d, *J* = 164.2 Hz), 41.5 (d, *J* = 78.1 Hz). ^{31}P{1H} NMR (162 MHz, chloroform-*d*) δ 14.08. HRMS: *m*/*z* calcd for $C_{21}H_{17}ClOP$ 351.0706 [M + H]$^+$, found 351.0712.

(Naphthalen-1-ylmethyl)(ethynyl)(phenyl)phosphine Oxide (7p). (Naphthalene-1-ylmethyl)(phenyl)phosphinic chloride (0.75 g, 2.49 mmol, 1 equiv) **6f**, 0.5 M ethynylmagnesium bromide in THF (15 mL, 7.5 mmol, 3 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7p** was obtained as an orange solid (126.4−137.9 °C), 0.22 g (30% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.86−7.83 (m, 1H), 7.76−7.61 (m, 4H), 7.42−7.26 (m, 7H), 3.93 (dd, *J* = 16.9, 2.0 Hz, 2H), 3.16 (d, *J* = 9.5 Hz, 1H). ^{13}C{1H} NMR (101 MHz, chloroform-*d*) δ 133.8 (d, *J* = 2.7 Hz), 132.5 (d, *J* = 3.0 Hz), 132.2 (d, *J* = 4.5 Hz), 130.7 (d, *J* = 10.4 Hz), 130.4 (d, *J* = 116.9 Hz), 130.0 (d, *J* = 7.0 Hz), 128.6, 128.5, 128.4, 128.1 (d, *J* = 4.1 Hz), 126.9 (d, *J* = 9.1 Hz), 125.9 (dd, *J* = 25.9, 1.1 Hz), 125.2 (d, *J* = 4.3 Hz), 124.2 (d, *J* = 2.0 Hz), 94.4 (d, *J* = 25.4 Hz), 78.1 (d, *J* = 203.7 Hz), 38.7 (d, *J* = 78.8 Hz).

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$^{31}P\{1H\}$ NMR (162 MHz, chloroform-*d*) δ 13.85. HRMS: *m*/*z* calcd for $C_{19}H_{16}OP$ 291.0939 $[M + H]^+$, found 291.0944.

(Naphthalen-1-ylmethyl)(phenyl)(prop-1-yn-1-yl)-phosphine Oxide (7q). (Naphthalene-1-ylmethyl)(phenyl)-phosphinic chloride **6f** (0.75 g, 2.49 mmol, 1 equiv), 0.5 M prop-1-yn-1-ylmagnesium bromide in THF (15 mL, 7.5 mmol, 3 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7q** was obtained as an orange liquid, 0.49 g (65% yield).

^1H NMR (400 MHz, chloroform-*d*) δ 8.05−8.04 (m, 1H), 7.89−7.75 (m, 4H), 7.56−7.40 (m, 6H), 7.31 (dd, *J* = 7.2, 3.7 Hz, 1H), 4.06−3.94 (m, 2H), 1.91 (d, *J* = 3.8 Hz, 3H). $^{13}C\{1H\}$ NMR (101 MHz, chloroform-*d*) δ 133.8 (d, *J* = 2.7 Hz), 132.2, 132.2 (d, *J* = 3.0 Hz), 131.5 (d, *J* = 116.9 Hz), 130.7 (d, *J* = 10.4 Hz), 128.8 (d, *J* = 6.8 Hz), 128.5, 128.4, 128.2, 127.8 (d, *J* = 4.1 Hz), 127.6 (d, *J* = 8.9 Hz), 125.8−125.5 (m), 125.1 (d, *J* = 4.1 Hz), 124.4 (d, *J* = 2.0 Hz), 105.5 (d, *J* = 29.3 Hz), 74.0 (d, *J* = 167.8 Hz), 38.9 (d, *J* = 78.8 Hz). $^{31}P\{1H\}$ NMR (162 MHz, chloroform-*d*) δ 13.36. HRMS: *m*/*z* calcd for $C_{20}H_{18}OP$ 305.1095 $[M + H]^+$, found 305.1102.

(Naphthalen-1-ylmethyl)(phenyl)(phenylethynyl)-phosphine Oxide (7r). (Naphthalene-1-ylmethyl)(phenyl)-phosphinic chloride **6f** (0.66 g, 2.20 mmol, 1 equiv), 1 M (phenylethynyl)magnesium bromide in THF (6.6 mL, 6.59 mmol, 3 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7r** was obtained as a yellow solid (99.9−106.6 °C), 0.62 g (77% yield).

^1H NMR (400 MHz, chloroform-*d*) δ 7.98 (d, *J* = 8.4 Hz, 1H), 7.82−7.80 (m, 1H), 7.76−7.70 (m, 3H), 7.51−7.47 (m, 1H), 7.43−7.23 (m, 11H), 4.09−3.92 (m, 2H). $^{13}C\{1H\}$ NMR (101 MHz, chloroform-*d*) δ 133.9 (d, *J* = 3.0 Hz), 132.4 (d, *J* = 3.0 Hz), 132.3 (d, *J* = 2.0 Hz), 132.1 (d, *J* = 31.3 Hz), 130.8 (d, *J* = 10.4 Hz), 130.8, 130.6, 129.0 (d, *J* = 7.0 Hz), 128.6, 128.6, 128.5, 128.4, 128.0 (d, *J* = 4.1 Hz), 127.5 (d, *J* = 9.1 Hz), 125.8 (d, *J* = 31.6 Hz), 125.2 (d, *J* = 4.3 Hz), 124.4 (d, *J* = 2.0 Hz), 119.7 (d, *J* = 4.1 Hz), 105.3 (d, *J* = 27.5 Hz), 82.5 (d, *J* = 162.4 Hz), 39.0 (d, *J* = 78.6 Hz). $^{31}P\{1H\}$ NMR (162 MHz, chloroform-*d*) δ 14.45. HRMS: *m*/*z* calcd for $C_{25}H_{20}OP$ 367.1252 $[M + H]^+$, found 367.1261.

(Naphthalen-2-ylmethyl)(ethynyl)(phenyl)phosphine Oxide (7s). (Naphthalene-2-ylmethyl)(phenyl)phosphinic chloride **6g** (0.63 g, 2.09 mmol, 1 equiv), 0.5 M ethynylmagnesium bromide in THF (12,5 mL, 6.29 mmol, 3 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7s** was obtained as a brown creamy solid, 0.35 g (58% yield).

^1H NMR (400 MHz, chloroform-*d*) δ 7.78−7.68 (m, 5H), 7.55−7.49 (m, 2H), 7.44−7.37 (m, 4H), 7.22−7.19 (m, 1H), 3.60 (d, *J* = 16.5 Hz, 2H), 3.29 (d, *J* = 9.5 Hz, 1H). $^{13}C\{1H\}$ NMR (101 MHz, chloroform-*d*) δ 133.3 (d, *J* = 3.4 Hz), 132.7 (d, *J* = 3.0 Hz), 132.5 (d, *J* = 2.5 Hz), 130.8 (d, *J* = 10.4 Hz), 130.3 (d, *J* = 117.6 Hz), 129.2 (d, *J* = 7.5 Hz), 128.1, 128.1, 128.1, 127.8 (d, *J* = 8.6 Hz), 127.7, 126.2 (d, *J* = 1.1 Hz), 125.9 (d, *J* = 1.6 Hz), 94.3 (d, *J* = 25.2 Hz), 42.0 (d, *J* = 78.1 Hz). $^{31}P\{1H\}$ NMR (162 MHz, chloroform-*d*) δ 14.39. HRMS: *m*/*z* calcd for $C_{19}H_{16}OP$ 291.0939 $[M + H]^+$, found 291.0948.

(Naphthalen-2-ylmethyl)(phenyl)(prop-1-yn-1-yl)-phosphine Oxide (7t). (Naphthalene-2-ylmethyl)(phenyl)-phosphinic chloride **6g** (0.46 g, 1.52 mmol, 1 equiv), 0.5 M prop-1-yn-1-ylmagnesium bromide in THF (7 mL, 3.5 mmol, 2.3 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7t** was obtained as a brown solid (88.0−89.7 °C), 0.26 g (56% yield).

^1H NMR (400 MHz, chloroform-*d*) δ 7.77−7.73 (m, 1H), 7.70−7.65 (m, 4H), 7.51−7.45 (m, 2H), 7.42−7.35 (m, 4H), 7.17 (dt, *J* = 8.4, 1.9 Hz, 1H), 3.54 (d, *J* = 16.6 Hz, 2H), 1.97 (d, *J* = 3.7 Hz, 3H). $^{13}C\{1H\}$ NMR (101 MHz, chloroform-*d*) δ 133.3 (d, *J* = 3.4 Hz), 132.3 (d, *J* = 2.5 Hz), 132.2 (d, *J* = 3.0 Hz), 131.4 (d, *J* = 116.9 Hz), 130.7 (d, *J* = 10.4 Hz), 129.0 (d, *J* = 7.3 Hz), 128.6 (d, *J* = 8.9 Hz), 128.4 (d, *J* = 13.2 Hz), 128.2 (d, *J* = 4.3 Hz), 127.8 (d, *J* = 2.5 Hz), 127.60, 127.57, 127.55, 126.07 (d, *J* = 1.4 Hz), 125.76 (d, *J* = 1.8 Hz), 105.33 (d, *J* = 29.1 Hz), 73.81 (d, *J* = 167.6 Hz), 42.3 (d, *J* = 78.3 Hz), 4.8 (d, *J* = 3.2 Hz). $^{31}P\{1H\}$ NMR (162 MHz, chloroform-*d*) δ 13.95. HRMS: *m*/*z* calcd for $C_{20}H_{18}OP$ 305.1095 $[M + H]^+$, found 305.1106.

(Naphthalen-2-ylmethyl)(phenyl)(phenylethynyl)-phosphine Oxide (7u). (Naphthalene-2-ylmethyl)(phenyl)-phosphinic chloride **6g** (0.61 g, 2.02 mmol, 1 equiv), 1 M (phenylethynyl)magnesium bromide in THF (6 mL, 6.08 mmol, 3 equiv). The crude mixture was purified by flash chromatography in the respective proportions of *n*-hexane/DCM from 8:2 to 0:10. The title product **7u** was obtained as a yellow solid (170.1−173.3 °C), 0.31 g (41% yield).

^1H NMR (400 MHz, chloroform-*d*) δ 7.82−7.67 (m, 5H), 7.60−7.53 (m, 2H), 7.49−7.42 (m, 7H), 7.37−7.33 (m, 2H), 7.26−7.24 (m, 1H), 3.76−3.62 (m, 2H). $^{13}C\{1H\}$ NMR (101 MHz, chloroform-*d*) δ 133.4 (d, *J* = 3.4 Hz), 132.5, 132.5, 132.4, 131.1 (d, *J* = 117.4 Hz), 130.9 (d, *J* = 10.4 Hz), 130.7, 129.2 (d, *J* = 7.5 Hz), 128.6, 128.5, 128.5, 128.4, 128.3 (d, *J* = 4.3 Hz), 128.0 (d, *J* = 2.7 Hz), 127.7 (d, *J* = 1.8 Hz), 127.6 (d, *J* = 1.6 Hz), 126.2 (d, *J* = 1.6 Hz), 125.9 (d, *J* = 1.8 Hz), 119.8 (d, *J* = 3.9 Hz), 105.4 (d, *J* = 27.7 Hz), 82.2 (d, *J* = 162.6 Hz), 42.5 (d, *J* = 78.1 Hz). $^{31}P\{1H\}$ NMR (162 MHz, chloroform-*d*) δ 14.83. HRMS: *m*/*z* calcd for $C_{25}H_{20}OP$ 367.1252 $[M + H]^+$, found 367.1261.

Optimization of the Cyclization Conditions to Prepare 2-Phenyl-1*H*-isophosphinoline 2-oxide (1a−r). A solution of benzyl(ethynyl)(phenyl)phosphine oxide **7a** (0.2 g, 0.83 mmol, 1 equiv), Ph_3PAuCl (10 mg, 0.02 mmol, 0.025 equiv), and TfOH (0.2 mL, 2.5 mmol, 3 equiv) (see footnote [a] in Table 5) in 1,2-dichloroethane (2 mL) was stirred at room temperature, under N_2 atmosphere, before setting up the reaction conditions.

Table 5

entry	catalyst	acid	activation	time	*T* (°C)	**1a**[b] (%)
1	$(Ph)_3PAuCl$	TfOH	thermic	4 days	80	89
2	$(Ph)_3PAuCl$	TfOH	MW	1.5 h	140	93
3	$(Ph)_3PAuCl$	TfOH	MW	3 h	160	100
4	$(Ph)_3PAuCl$	TfOH	MW	6 h	180	79
5	$(Ph)_3PAuCl$	TfOH	MW	11 h	180	64
6	$(Ph)_3PAuCl$		MW	3 h	160	0
7		TfOH	MW	3 h	160	39

[a]3 equiv of TfOH was optimized in a recent paper.[12] [b]Relative % of compound **1a** determined by $^{31}P\{1H\}$ NMR.

The reaction was first conducted under thermic activation in 1,2-dichloroethane using Ph_3PAuCl as catalyst in the presence of triflic acid as additive. Under these conditions, the reaction required 4 days to reach 89% as the relative percentage of **1a** in the crude mixture as determined by $^{31}P\{^1H\}$ NMR (entry 1). More importantly, it turned out that the addition of the arene group to the alkyne is fully regioselective, giving as expected exclusively the 6-*endo*-dig cyclization product. The corresponding 5-*exo*-dig products were not observed, while in some cases gold-catalyzed reactions followed this mode of cyclization. With the aim to shorten the reaction time, microwave-assisted heating was attempted, since such technology has been shown to dramatically reduce the reaction times for processes that require prolonged heating. We were pleased to observe the formation of **1a** in 93% yield by running the reaction under microwave activation at 140 °C for 1.5 h (entry 2). Increasing both the temperature and the reaction time to 160 °C and 3 h, respectively, resulted in the formation of **1a** in excellent >99% yield (entry 3). By contrast, heating the reaction mixture at 180 °C for 6 h had a detrimental effect and gave compound **1a** in lower yield, 79% (entry 4). We suspected that this result could be attributed to the thermal instability of isophosphinoline 2-oxide **1a** at this temperature. Indeed, our hypothesis was confirmed by entry 5 when the extended reaction time of 11 h resulted in significant yield reduction, 64% (entry 5). Alkenes were already shown to be effective substrates in

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intermolecular arylations, and high temperature may induce over-reaction.[25] As can be seen in Table 3, the reaction carried out without triflic acid failed to give compound **1a**, whereas the reaction performed without gold catalyst provides the expected product **1a** in 78% yield (entries 6 and 7). It seems that Ph_3PAuCl and triflic acid have a synergistic catalytic effect.

Typical Procedure for the Preparation of Substituted 2-Phenyl-1*H*-isophosphinoline 2-Oxide 1a−q. Under N_2, to a stirred solution of Ph_3PAuCl (0.02 mmol, 2.5 mol %) in 1,2-dichloroethane (2 mL), were added TfOH (2.5 mmol, 3 equiv) and **7** (0.83 mmol, 1 equiv). The reaction mixture was heated under microwave irradiation at 160 °C for 3 h and then quenched with saturated aqueous solution of Na_2CO_3. The aqueous layer was separated and extracted with DCM. The combined organic layers were washed with water, dried over $MgSO_4$, filtered, and concentrated under a vacuum. The obtained oil was purified by flash column chromatography eluting with DCM/EtOAC (1/1 to 0/1).

2-Phenyl-1*H*-isophosphinoline 2-Oxide (1a). Benzyl(ethynyl)-(phenyl)phosphine oxide **7a** (0.2 g, 0.83 mmol, 1 equiv), Ph_3PAuCl (10 mg, 0.02 mmol, 2.5 mol %), TfOH (0.2 mL, 2.5 mmol, 3 equiv). After extraction, the combined organic layers were washed with water, dried over $MgSO_4$, filtered, and concentrated under a vacuum. The crude obtained was purified by flash column chromatography eluting with DCM/EtOAC (1/1 to 0/1). **1a** was obtained as a yellow solid (79.9 °C), 0.19 g (96% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.75−7.70 (m, 2H), 7.51−7.32 (m, 4H), 7.28−7.22 (m, 3H), 7.15−7.14 (m, 1H), 6.27 (t, J = 12.6 Hz, 1H), 3.59 (dd, J = 20.3, 17.3 Hz, 1H), 3.29 (dd, J = 17.3, 11.4 Hz, 1H). ^{13}C{1H} NMR (101 MHz, chloroform-*d*) δ 146.0 (s), 132.1 (d, J = 2.8 Hz), 131.4 (d, J = 16.4 Hz), 131.0 (d, J = 10.5 Hz), 130.5 (s), 130.5 (s), 130.4 (s), 130.2 (d, J = 7.5 Hz), 129.7 (s), 128.6 (d, J = 12.1 Hz), 127.7 (d, J = 1.0 Hz), 119.7 (d, J = 93.8 Hz), 33.9 (d, J = 71.0 Hz). ^{31}P{1H} NMR (162 MHz, chloroform-*d*) δ 18.16 (s). HRMS: m/z calcd for $C_{15}H_{14}OP$ 241.0782 $[M + H]^+$, found 241.0793.

4-Methyl-2-phenyl-1*H*-isophosphinoline 2-Oxide (1b). Benzyl(phenyl)(prop-1-yn-1-yl)phosphine oxide **7b** (0.2 g, 0.78 mmol, 1 equiv), Ph_3PAuCl (0.01 g, 0.02 mmol, 2.5 mol %), TfOH (0.2 mL, 2.34 mmol, 3 equiv). After extraction, the combined organic layers were washed with water, dried over $MgSO_4$, filtered, and concentrated under a vacuum. The crude obtained was purified by flash column chromatography eluting with DCM/EtOAC (1/1 to 0/1). The title product **1b** was obtained as a brown solid (184.3 °C), 0.15 g (75% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.76−7.71 (m, 2H), 7.55−7.39 (m, 4H), 7.29 (dt, J = 23.9, 7.5 Hz, 2H), 7.21−7.14 (m, 1H), 6.18 (d, J = 12.5 Hz, 1H), 3.60−3.51 (m, 1H), 3.32−3.25 (m, 1H), 2.40 (s, 3H). ^{13}C{1H} NMR (101 MHz, chloroform-*d*) δ 152.5, 133.3 (d, J = 13.9 Hz), 132.5 (d, J = 104.9 Hz), 131.9 (d, J = 2.7 Hz), 131.2 (d, J = 10.7 Hz), 130.6 (d, J = 9.8 Hz), 130.4 (d, J = 7.3 Hz), 129.4, 128.5 (d, J = 12.0 Hz), 127.7, 126.4 (d, J = 2.0 Hz), 117.9 (d, J = 97.4 Hz), 34.7 (d, J = 70.8 Hz), 24.1 (d, J = 15.2 Hz). ^{31}P{1H} NMR (162 MHz, chloroform-*d*) δ 17.18. HRMS: m/z calcd for $C_{16}H_{16}OP$ 255.0939 $[M + H]^+$, found 255.0951.

2,4-Diphenyl-1*H*-isophosphinoline 2-Oxide (1c). Benzyl-(phenyl)(phenylethynyl)phosphine oxide **7c** (0.2 g, 0.63 mmol, 1 equiv), Ph_3PAuCl (0.008 g, 0.016 mmol, 2.5 mol %), TfOH (0.17 mL, 1.9 mmol, 3 equiv). After extraction, the combined organic layers were washed with water, dried over $MgSO_4$, filtered, and concentrated under a vacuum. The crude obtained was purified by flash column chromatography eluting with DCM/EtOAC (1/1 to 0/1). The title product **1c** was obtained as a brown solid (187.3−193.1 °C), 0.2 g (yield >99%).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.84−7.78 (m, 2H), 7.44−7.14 (m, 12H), 6.35 (dd, J = 13.4, 1.0 Hz, 1H), 3.70−3.61 (m, 1H), 3.41 (dd, J = 16.4, 10.9 Hz, 1H). ^{13}C{1H} NMR (101 MHz, chloroform-*d*) δ 157.2 (d, J = 2.0 Hz), 140.7 (d, J = 14.5 Hz), 133.7 (d, J = 19.1 Hz), 133.2 (d, J = 13.4 Hz), 132.1 (d, J = 105.1 Hz), 132.1 (d, J = 3.0 Hz), 131.4 (d, J = 10.0 Hz), 131.0 (d, J = 7.9 Hz), 130.9 (d, J = 9.8 Hz), 130.1 (d, J = 2.3 Hz), 129.7, 128.9, 128.7, 128.6, 128.5, 127.5 (d, J = 1.8 Hz), 118.8 (d, J = 96.0 Hz), 34.8 (d, J = 71.1 Hz). ^{31}P{1H} NMR (162 MHz, chloroform-*d*) δ 17.06. HRMS: m/z calcd for $C_{21}H_{18}OP$ 317.1095 $[M + H]^+$, found 317.1107.

8-Methyl-2-phenyl-1*H*-isophosphinoline 2-Oxide (1d). Ethynyl(2-methylbenzyl)(phenyl)phosphine oxide **7d** (0.1 g, 0.39 mmol, 1 equiv), Ph_3PAuCl (0.005 g, 0.0098 mmol, 2.5 mol %), TfOH (0.1 mL, 1.17 mmol, 3 equiv). After extraction, the combined organic layers were washed with water, dried over $MgSO_4$, filtered, and concentrated under a vacuum. The crude obtained was purified by flash column chromatography eluting with DCM/EtOAC (1/1 to 0/1). The title product **1d** was obtained as a brown solid (155.4 °C), 0.1 g (yield >99%).

^{1}H NMR (400 MHz, chloroform-*d*) δ ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.77−7.71 (m, 2H), 7.51−7.15 (m, 7H), 6.28 (td, J = 12.7, 0.8 Hz, 1H), 3.56−3.47 (m, 1H), 3.22−3.15 (m, 1H), 2.26 (s, 3H). ^{13}C{1H} NMR (101 MHz, chloroform-*d*) δ 146.6, 137.7 (d, J = 9.4 Hz), 133.3 (d, J = 105.6 Hz), 132.0 (d, J = 2.8 Hz), 131.9, 131.1 (d, J = 17.1 Hz), 130.5 (d, J = 10.0 Hz), 129.1 (d, J = 2.1 Hz), 128.8, 128.7 (d, J = 12.1 Hz), 127.2, 118.8 (d, J = 93.8 Hz), 30.5 (d, J = 71.6 Hz), 19.8. ^{31}P{1H} NMR (162 MHz, chloroform-*d*) δ 18.67. HRMS: m/z calcd for $C_{16}H_{16}OP$ 255.0939 $[M + H]^+$, found 255.0952.

4,8-Dimethyl-2-phenyl-1*H*-isophosphinoline 2-Oxide (1e). (2-Methylbenzyl)(phenyl)(prop-1-yn-1-yl)phosphine oxide **7e** (0.1 g, 0.37 mmol, 1 equiv), Ph_3PAuCl (0.005 g, 0.009 mmol, 2.5 mol %), TfOH (0.1 mL, 1.11 mmol, 3 equiv). After extraction, the combined organic layers were washed with water, dried over $MgSO_4$, filtered, and concentrated under a vacuum. The crude obtained was purified by flash column chromatography eluting with DCM/EtOAC (1/1 to 0/1). The title product **1e** was obtained as a brown creamy solid, 0.09 g (90% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.74−7.69 (m, 2H), 7.50−7.34 (m, 4H), 7.06 (s, 2H), 6.15 (dd, J = 12.0 Hz, 1H), 3.52 (dd, J = 20.2, 16.7 Hz, 1H), 3.23 (dd, J = 16.7, 11.4 Hz, 1H), 2.39 (d, J = 1.3 Hz, 3H), 2.36 (s, 3H). ^{13}C{1H} NMR (101 MHz, chloroform-*d*) 153.6, 137.7 (d, J = 8.9 Hz), 133.2 (d, J = 14.6 Hz), 132.4, 132.1, 131.9, 130.8 (d, J = 8.9 Hz), 129.1 (d, J = 5.0 Hz), 128.7 (d, J = 11.4 Hz), 127.0, 124.8, 117.3 (d, J = 104.2 Hz), 30.6 (d, J = 72.0 Hz), 25.1 (d, J = 15.4 Hz), 20.7. ^{31}P{1H} NMR (162 MHz, chloroform-*d*) δ 17.66. HRMS: m/z calcd for $C_{17}H_{18}OP$ 269.1095 $[M + H]$+, found 269.1107.

6-methyl-2-phenyl-1*H*-isophosphinoline 2-Oxide (1g). Ethynyl(4-methylbenzyl)(phenyl)phosphine oxide **7g** (0.1 g, 0.4 mmol, 1 equiv), Ph_3PAuCl (0.005 g, 0.01 mmol, 2.5 mol %), TfOH (0.1 mL, 1.18 mmol, 3 equiv). After extraction, the combined organic layers were washed with water, dried over $MgSO_4$, filtered, and concentrated under a vacuum. The crude obtained was purified by flash column chromatography eluting with DCM/EtOAC (1/1 to 0/1). The title product **1g** was obtained as a brown creamy solid, 0.085 g (85% yield).

^{1}H NMR (400 MHz, chloroform-*d*) 7.75−7.70 (m, 2H), 7.51−7.29 (m, 4H), 7.09−7.04 (m, 3H), 6.25 (t, J = 12.5 Hz, 1H), 3.58 (dd, J = 20.7, 17.2 Hz, 1H), 3.27 (dd, J = 17.3, 11.5 Hz, 1H), 2.34 (s, 3H).

^{13}C{1H} NMR (101 MHz, chloroform-*d*) δ 146.4, 137.6, 132.7 (d, J = 104.0 Hz), 132.1 (d, J = 2.7 Hz), 131.3 (d, J = 2.3 Hz), 131.2, 131.0 (d, J = 10.6 Hz), 130.6, 130.5, 128.6 (d, J = 12.2 Hz), 127.2 (d, J = 7.5 Hz), 119.6 (d, J = 93.9 Hz), 33.5 (d, J = 71.2 Hz), 29.8, 21.0. ^{31}P{1H} NMR (162 MHz, chloroform-*d*) δ 19.11. HRMS: m/z calcd for $C_{16}H_{16}OP$ 255.0939 $[M + H]^+$, found 255.0948.

4,6-Dimethyl-2-phenyl-1*H*-isophosphinoline 2-Oxide (1h). (4-Methylbenzyl)(phenyl)(prop-1-yn-1-yl)phosphine oxide **7h** (0.1 g, 0.37 mmol, 1 equiv), Ph_3PAuCl (0.005 g, 0.009 mmol, 2.5 mol %), TfOH (0.1 mL, 1.11 mmol, 3 equiv). After extraction, the combined organic layers were washed with water, dried over $MgSO_4$, filtered, and concentrated under a vacuum. The crude obtained was purified by flash column chromatography eluting with DCM/EtOAC (1/1 to 0/1). The title product **1h** was obtained as a brown solid (124.3 °C), 0.097 g (97% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.74−7.69 (m, 2H), 7.48−7.46 (m, 1H), 7.43−7.38 (m, 2H), 7.34 (s, 1H), 7.06 (s, 2H), 6.15

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(dd, J = 12.3, 1.5 Hz, 1H), 3.52 (dd, J = 20.2, 16.7 Hz, 1H), 3.23 (dd, J = 16.7, 11.4 Hz, 1H), 2.39 (d, J = 1.4 Hz, 3H), 2.36 (s, 3H). ^{13}C{1H} NMR (101 MHz, chloroform-d) δ 152. 7, 137.4, 133.3 (d, J = 13.0 Hz), 132.3, 131.9 (d, J = 2.8 Hz), 131.2 (d, J = 10.7 Hz), 130.7 (d, J = 9.7 Hz), 130.2, 128.6 (d, J = 12.0 Hz), 127.4 (d, J = 7.0 Hz), 127.3 (d, J = 2.1 Hz), 118.0 (d, J = 97.6 Hz), 34.3 (d, J = 70.9 Hz), 29.8, 24.3 (d, J = 15.2 Hz), 21.4. ^{31}P{1H} NMR (162 MHz, chloroform-d) δ 17.80. HRMS: m/z calcd for $C_{17}H_{18}OP$ 269.1095 [M + H]$^+$, found 269.1106.

8-Bromo-2-phenyl-1*H*-isophosphinoline 2-Oxide (1j). (2-Bromobenzyl)(ethynyl)(phenyl)phosphine oxide **7j** (0.1 g, 0.31 mmol, 1 equiv), Ph_3PAuCl (0.004 g, 0.008 mmol, 2.5 mol %), TfOH (0.08 mL, 0.94 mmol, 3 equiv). After extraction, the combined organic layers were washed with water, dried over $MgSO_4$, filtered, and concentrated under a vacuum. The crude obtained was purified by flash column chromatography eluting with DCM/EtOAC (1/1 to 0/1). The title product **1j** was obtained as a brown creamy solid, 0.096 g (97% yield).

^{1}H NMR (400 MHz, chloroform-d) δ 7.75−7.19 (m, 9H), 6.37 (t, J = 12.5 Hz, 1H), 3.79 (dd, J = 20.6, 18.0 Hz, 1H), 3.39 (dd, J = 18.1, 10.9 Hz, 1H). ^{13}C{1H} NMR (101 MHz, chloroform-d) δ 145.3, 134.2, 133.3 (d, J = 17.3 Hz), 132.5 (d, J = 107.2 Hz), 132.4 (d, J = 3.0 Hz), 130.7 (d, J = 10.2 Hz), 130.3, 130.2, 128.9, 128.8 (d, J = 3.9 Hz), 127.2 (d, J = 10.4 Hz), 120.5 (d, J = 92.9 Hz), 33.8 (d, J = 71.5 Hz). ^{31}P{1H} NMR (162 MHz, chloroform-d) δ 18.60. HRMS: m/z calcd for $C_{15}H_{13}BrOP$ 318.9887 [M + H]$^+$, found 318.9898.

8-Bromo-2,4-diphenyl-1*H*-isophosphinoline 2-Oxide (1k). (2-Bromobenzyl)(phenyl)(phenylethynyl)phosphine oxide **7l** (0.1 g, 0.25 mmol, 1 equiv), Ph_3PAuCl (0.003 g, 0.006 mmol, 2.5 mol %), TfOH (0.07 mL, 0.76 mmol, 3 equiv). After extraction, the combined organic layers were washed with water, dried over $MgSO_4$, filtered, and concentrated under a vacuum. The crude obtained was purified by flash column chromatography eluting with DCM/EtOAC (1/1 to 0/1). The title product **1k** was obtained as a brown solid (224.0−226.0 °C), 0.098 g (98% yield).

^{1}H NMR (400 MHz, chloroform-d) δ 7.89−7.75 (m, 2H), 7.66−7.33 (m, 9H), 7.21−7.04 (m, 2H), 6.41 (dd, J = 13.5, 1.2 Hz, 1H), 3.99 (ddd, J = 19.0, 17.2, 1.2 Hz, 1H), 3.46 (dd, J = 17.2, 10.5 Hz, 1H). ^{13}C{1H} NMR (101 MHz, chloroform-d) δ 157.1 (d, J = 2.2 Hz), 140.7 (d, J = 14.6 Hz), 135.4 (d, J = 14.2 Hz), 134.2, 132.5, 132.4 (d, J = 2.8 Hz), 131.3 (d, J = 27.8 Hz), 129.6 (d, J = 1.7 Hz), 129.0 (d, J = 23.1 Hz), 128.7, 128.6 (d, J = 12.3 Hz), 128.3 (d, J = 1.7 Hz), 127.2 (d, J = 10.2 Hz), 119.9 (d, J = 95.1 Hz), 34.2 (d, J = 71.6 Hz). ^{31}P{1H} NMR (162 MHz, chloroform-d) δ 15.96. HRMS: m/z calcd for $C_{21}H_{17}BrOP$ 395.0200 [M + H]$^+$, found 395.0205.

(4-Chlorobenzyl)(ethynyl)(phenyl)phosphine Oxide (1l). (4-Chlorobenzyl)(ethynyl)(phenyl)phosphine oxide **7m** (0.1 g, 0.36 mmol, 1 equiv), Ph_3PAuCl (0.005 g, 0.009 mmol, 2.5 mol %), TfOH (0.1 mL, 1.1 mmol, 3 equiv). After extraction, the combined organic layers were washed with water, dried over $MgSO_4$, filtered, and concentrated under a vacuum. The crude obtained was purified by flash column chromatography eluting with DCM/EtOAC (1/1 to 0/1). The title product **1l** was obtained as a liquid, 0.098 g (yield >99%).

^{1}H NMR (400 MHz, chloroform-d) δ 7.75−7.69 (m, 2H), 7.53−7.44 (m, 4H), 7.29−7.24 (m, 2H), 7.13 (d, J = 8.2 Hz, 1H), 6.38 (t, J = 12.5 Hz, 1H), 3.59 (dd, J = 20.5, 17.2 Hz, 1H), 3.27 (dd, J = 17.4, 11.4 Hz, 1H). ^{13}C{1H} NMR (101 MHz, chloroform-d) δ 144.9, 133.6, 132.9 (d, J = 16.5 Hz), 132.5, 132.4, 132.3, 130.6 (d, J = 9.9 Hz), 130.3 (d, J = 2.5 Hz), 129.6, 128.9 (d, J = 12.2 Hz), 128.7 (d, J = 7.6 Hz), 128.6 (d, J = 12.4 Hz), 121.4 (d, J = 93.1 Hz), 33.4 (d, J = 71.0 Hz). ^{31}P{1H} NMR (162 MHz, chloroform-d) δ 17.62 (s). HRMS: m/z calcd for $C_{15}H_{13}ClOP$ 275.0393 [M + H]$^+$, found 275.0403.

6-Chloro-2,4-diphenyl-1*H*-isophosphinoline 2-Oxide (1m). (4-Chlorobenzyl)(phenyl)(phenylethynyl)phosphine oxide **7o** (0.1 g, 0.28 mmol, 1 equiv), Ph_3PAuCl (0.004 g, 0.007 mmol, 2.5 mol %), TfOH (0.08 mL, 0.85 mmol, 3 equiv). After extraction, the combined organic layers were washed with water, dried over $MgSO_4$, filtered, and concentrated under a vacuum. The crude obtained was purified by flash column chromatography eluting with DCM/EtOAC (1/1 to 0/1). The title product **1m** was obtained as a brown solid (174.4−178.6 °C), 0.097 g (quantitative yield)

^{1}H NMR (400 MHz, chloroform-d) δ 7.72−7.67 (m, 2H), 7.44−7.06 (m, 11H), 6.30 (d, J = 13.2 Hz, 1H), 3.58−3.49 (m, 1H), 3.32−3.25 (m, 1H).^{13}C{1H} NMR (101 MHz, chloroform-d) δ 156.4, 140.0 (d, J = 13.6 Hz), 134.9 (d, J = 12.9 Hz), 133.5, 132.7 (d, J = 9.8 Hz), 132.4, 131.0 (d, J = 9.3 Hz), 129.9, 129.6, 129.5 (d, J = 6.8 Hz), 129.4, 128.9, 128.8, 128.5, 120.2 (d, J = 96.0 Hz), 34.3 (d, J = 71.8 Hz). ^{31}P{1H} NMR (162 MHz, chloroform-d) δ 16.89 (s). HRMS: m/z calcd for $C_{21}H_{17}ClOP$ 351.0706 [M + H]$^+$, found 351.0711.

2-Phenyl-1*H*-benzo[h]isophosphinoline 2-Oxide (1n). (Naphthalen-1-ylmethyl)(ethynyl)(phenyl)phosphine oxide **7p** (0.2 g, 0.68 mmol, 1 equiv), Ph_3PAuCl (0.008 g, 0.017 mmol, 2.5 mol %), TfOH (0.2 mL, 2.06 mmol, 3 equiv). After extraction, the combined organic layers were washed with water, dried over $MgSO_4$, filtered, and concentrated under a vacuum. The crude obtained was purified by flash column chromatography eluting with DCM/EtOAC (1/1 to 0/1). The title product **1n** was obtained as a brown solid (160.9 °C), 0.18 g (91% yield).

^{1}H NMR (400 MHz, chloroform-d) δ 7.96 (d, J = 8.2 Hz, 1H), 7.82−7.76 (m, 4H), 7.59−7.36 (m, 7H), 6.41 (t, J = 12.7 Hz, 1H), 4.04 (dd, J = 21.8, 18.0 Hz, 1H), 3.64 (dd, J = 18.2, 12.0 Hz, 1H). ^{13}C{1H} NMR (101 MHz, chloroform-d) δ 147.0, 134.0, 133.8, 132.8, 132.2 (d, J = 2.8 Hz), 130.5 (d, J = 10.1 Hz), 128.8, 128.7 (d, J = 12.2 Hz), 128.3 (d, J = 18.2 Hz), 128.0, 120.0 (d, J = 2.1 Hz), 127.1 (d, J = 27.3 Hz), 126.8 (d, J = 7.1 Hz), 123.6, 119.4 (d, J = 94.0 Hz), 29.7, 29.7 (d, J = 72.2 Hz). ^{31}P{1H} NMR (162 MHz, chloroform-d) δ 18.60. HRMS: m/z calcd for $C_{19}H_{16}OP$ 291.0939 [M + H]$^+$, found 291.0948.

4-Methyl-2-phenyl-1*H*-benzo[h]isophosphinoline 2-Oxide (1o). (Naphthalen-1-ylmethyl)(phenyl)(prop-1-yn-1-yl)phosphine oxide **7r** (0.15 g, 0.49 mmol, 1 equiv), Ph_3PAuCl (0.006 g, 0.012 mmol, 2.5 mol %), TfOH (0.12 mL, 1.37 mmol, 3 equiv). After extraction, the combined organic layers were washed with water, dried over $MgSO_4$, filtered, and concentrated under a vacuum. The crude was purified by flash column chromatography eluting with DCM/EtOAC (1/1 to 0/1). The title product **1o** was obtained as a brown solid (201.9−203.1 °C), 0.12 g (80% yield).

^{1}H NMR (400 MHz, chloroform-d) δ 8.06−8.04 (m, 1H), 7.85−7.70 (m, 5H), 7.54−7.42 (m, 5H), 6.34 (d, J = 12.6 Hz, 1H), 4.08 (dd, J = 21.4, 17.6 Hz, 1H), 3.64 (dd, J = 17.5, 12.0 Hz, 1H), 2.53 (d, J = 1.3 Hz, 3H). ^{13}C{1H} NMR (101 MHz, chloroform-d) δ 153.6, 133.9, 132.1, 131.5, 131.4, 130.9 (d, J = 9.9 Hz), 128.8, 128.7 (d, J = 7.8 Hz), 127.9, 127.3, 127.1 (d, J = 33.8 Hz), 124.2, 123.7, 117.8 (d, J = 97.9 Hz), 29.8 (d, J = 71.9 Hz), 25.7 (d, J = 15.6 Hz). ^{31}P{1H} NMR (162 MHz, chloroform-d) δ 17.47. HRMS: m/z calcd for $C_{20}H_{18}OP$ 305.1095 [M + H]$^+$, found 305.1104.

2,4-Diphenyl-1*H*-benzo[h]isophosphinoline 2-Oxide (1p). (Naphthalen-1-ylmethyl)(phenyl)(phenylethynyl)phosphine oxide **7s** (0.2 g, 0.54 mmol, 1 equiv), Ph_3PAuCl (0.007 g, 0.014 mmol, 2.5 mol %), TfOH (0.14 mL, 1.64 mmol, 3 equiv). After extraction, the combined organic layers were washed with water, dried over $MgSO_4$, filtered, and concentrated under a vacuum. The crude obtained was purified by flash column chromatography eluting with DCM/EtOAC (1/1 to 0/1). The title product **1p** was obtained as a brown solid (155.1−160.2 °C), 0.175 g (88% yield).

^{1}H NMR (400 MHz, chloroform-d) δ 8.2 (d, J = 7.5 Hz, 1H), 7.79−7.71 (m, 3H), 7.57 (d, J = 8.6 Hz, 1H), 7.44−7.34 (m, 10H), 7.18 (d, J = 8.8 Hz, 1H), 6.43−6.40 (m, 1H), 4.16−4.07 (m, 1H), 3.65−3.58 (m, 1H). ^{13}C{1H} NMR (101 MHz, chloroform-d) δ 158.5 (d, J = 2.3 Hz), 141.5 (d, J = 14.5 Hz), 134.1, 133.1, 132.4 (d, J = 8.2 Hz), 132.2 (d, J = 2.7 Hz), 132.0, 131.0 (d, J = 9.8 Hz), 130.5 (d, J = 15.4 Hz), 128.9, 128.8, 128.7, 128.7, 128.6, 128.0 (d, J = 7.5 Hz), 127.3, 127.1 (d, J = 15.0 Hz), 127.0 (d, J = 2.0 Hz), 124.2, 119.0 (d, J = 97.0 Hz), 29.8 (d, J = 72.7 Hz). ^{31}P{1H} NMR (162 MHz, chloroform-d) δ 16.90. HRMS: m/z calcd for $C_{25}H_{20}OP$ 367.1252 [M + H]$^+$, found 367.1259.

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■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00648.

HR-ESI-MS, ^{1}H, ^{13}C, and $^{31}P\{1H\}$ spectra for the described compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

David Virieux − *ICGM, Univ. Montpellier, ENSCM, CNRS, Montpellier, France;* orcid.org/0000-0002-6495-9478; Email: david.virieux@enscm.fr

Jean-Luc Pirat − *ICGM, Univ. Montpellier, ENSCM, CNRS, Montpellier, France;* orcid.org/0000-0002-3688-2047; Email: jean-luc.pirat@enscm.fr

Authors

Mina Hariri − *ICGM, Univ. Montpellier, ENSCM, CNRS, Montpellier, France; Department of Chemistry, K. N. Toosi University of Technology, Tehran, Iran*

Fatemeh Darvish − *Department of Chemistry, K. N. Toosi University of Technology, Tehran, Iran*

Karen-Pacelye Mengue Me Ndong − *ICGM, Univ. Montpellier, ENSCM, CNRS, Montpellier, France; Université des Sciences et Techniques de Masuku, Franceville, Gabon*

Nora Sechet − *ICGM, Univ. Montpellier, ENSCM, CNRS, Montpellier, France*

Geraud Chacktas − *ICGM, Univ. Montpellier, ENSCM, CNRS, Montpellier, France*

Hooriye Boosaliki − *ICGM, Univ. Montpellier, ENSCM, CNRS, Montpellier, France; Department of Chemistry, K. N. Toosi University of Technology, Tehran, Iran*

Minh Loan Tran Do − *ICGM, Univ. Montpellier, ENSCM, CNRS, Montpellier, France*

Gabin Mwande-Maguene − *Université des Sciences et Techniques de Masuku, Franceville, Gabon*

Jacques Lebibi − *Université des Sciences et Techniques de Masuku, Franceville, Gabon*

Alexander R. Burilov − *Arbuzov Institute of Organic and Physical Chemistry, FRC Kazan Scientific Center of RAS, Kazan 420088, Russian Federation*

Tahar Ayad − *ICGM, Univ. Montpellier, ENSCM, CNRS, Montpellier, France;* orcid.org/0000-0003-4210-5997

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.1c00648

Notes

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