Synthesis of Quinolinylphosphane Oxides and -phosphonates from *N*-Arylimines Derived from Phosphane Oxides and Phosphonates

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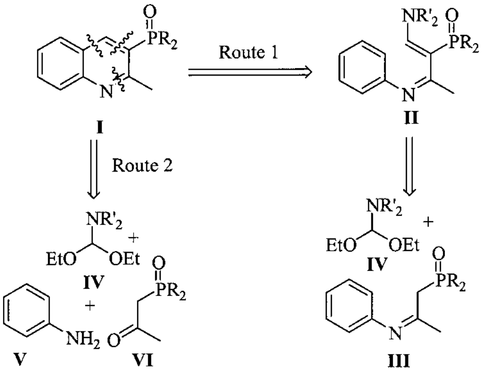
Quinolinylphosphane oxides are obtained by thermal treatment of *N*-arylimines derived from phosphane oxides with dimethylformamide diethyl acetal (DMF-DEA). An intermediate *N*-aryl-1-azadiene was isolated and cyclization thereof leads to phosphorylated quinolines. In a similar manner, quinolinylphosphonates are obtained by reaction of *N*-arylimines derived from phosphonates with DMF-DEA.

Introduction

Quinolines are widely used intermediates for functional transformations.[1,2] Simple quinolines are common units in a wide variety of natural products possessing biological activity,[3] and they are constituents of alkaloids or of antibiotics with remarkable cytotoxic and antitumor properties.[4] Furthermore, it is known that molecular modifications involving the introduction of organophosphorus functionalities could increase their biological activity.[5] For these reasons, the development of new methods for synthesis of these substrates has been an active research area in recent years.

In the case of phosphorylated quinolines, very few examples of the synthesis of these compounds have been reported. As far as we know, only the synthesis of 4-hydroxy-[6] and 4-aminoquinolinylphosphonates,[7] and very recently the preparation of biomimetic NADH models bearing a phosphonate or an oxazaphospholodine oxide, have been described.[8] We are interested in the design of new nitrogen-containing acyclic and cyclic derivatives bearing a phosphane oxide or a phosphonate moiety. In this context, we have previously described the synthesis of three-,[9] five-[10] and six-membered[11] phosphorus-substituted nitrogen heterocycles from enamines[12] and imines derived from phosphazenes, phosphane oxides or phosphonates. Continuing with our interest in the chemistry of new phosphorus-substituted compounds, we report here an easy and regioselective synthesis of quinolinylphosphane oxides (**I**, R = Ph) and -phosphonates (**I**, R = OEt) from dimethylformamide diethyl acetal (DMF-DEA, **IV**) and phosphorylated *N*-arylimines (**III**, Scheme 1, route 1), or from their precursors (Scheme 1, Route 2) such as DMF-DEA (**IV**), arylamines (**V**) and phosphorylated carbonyl derivatives (**VI**).



Scheme 1

Results and Discussion

The required *N*-arylimines derived from phosphane oxides **1**[13] were easily prepared by addition of arylamines **2** to allenes,[14] or by condensation reaction of arylamines **2** with α-carbonylphosphane oxides **3** (R^1 = H, CH_3).[7a] Thermal treatment of 2-(*N*-*p*-tolylimino)propylphosphane oxide **1a**[15] with dimethylformamide diethyl acetal (DMF-DEA) in toluene at 90 °C (24 h) gave a moderate yield (42%) of a mixture of *N*-aryl-1-azadiene **4a** (80%) (R^1 =

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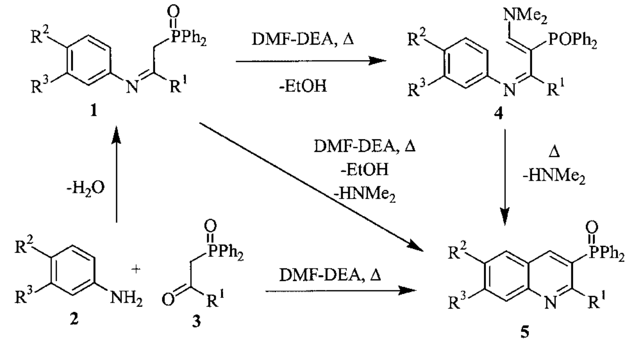
$R^2 = CH_3$, $R^3 = H$) and quinolinylphosphane oxide **5a** (20%) ($R^1 = R^2 = CH_3$, $R^3 = H$, Scheme 2). Compounds **4a** and **5a** were separated by flash chromatography and characterized on the basis of their spectroscopic data. Thus, the ^{31}P NMR spectrum of compound **4a** showed an absorption at $\delta_P = 32.3$ ppm and the ^1H and ^{13}C NMR spectra gave well-resolved doublets for the olefinic proton at $\delta_H = 7.76$ ppm ($^3J_{PH} = 15.1$ Hz) and at $\delta_C = 100.3$ ppm with a coupling constant of $^1J_{PC} = 111.8$ Hz for the carbon atom directly bonded to the phosphane oxide group of compound **4a**. Likewise, the ^{31}P NMR of compound **5a** showed an absorption at $\delta_P = 30.3$ ppm, while the ^1H NMR showed a doublet for the aromatic proton in position 4 of the quinoline ring system ($\delta_H = 7.72$ ppm, $^3J_{PH} = 15.1$ Hz) and ^{13}C NMR gave three well-resolved doublets at $\delta_C = 158.6$ ppm ($^2J_{PC} = 9.6$ Hz), $\delta_C = 125.1$ ($^1J_{PC} = 86.6$ Hz) and at $\delta_C = 142.1$ ppm ($^2J_{PC} = 11.8$ Hz) for C-2, C-3 and C-4 of the quinoline **5a**. The formation of *N*-arylazadiene **4a** can be explained by a condensation reaction of imine **1a** with DMF-DEA followed by the loss of ethanol (Scheme 2). 6π-Azaelectrocyclization of this azadiene **4a** with the loss of dimethylamine could explain the formation of quinoline **5a**, in a similar way to that reported for azapolyenes.[7c,16] In order to test whether *N*-arylazadiene **4a** is the precursor of quinoline **5a**, functionalized imine **4a** was heated at 110 °C in toluene leading to the formation of quinoline **5a** in very high yield (> 95%). As far as we know, this strategy leads to the first example of simple quinolines **5** containing a phosphane oxide group in position 3 of the ring system.



Scheme 2

With these results we tried to explore whether quinolinylphosphane oxides **5** could be obtained from *N*-arylimines **1**. Thus, thermal treatment of *N*-arylimines **1** with DMF-DEA in refluxing toluene (48 h) gave quinolinylphosphane oxides **5** in a regioselective fashion[17] and in excellent yields (Scheme 2, Table 1, Entries 1−7). The scope of the reaction was not limited to 2-alkyl-substituted ($R^1 = CH_3$, C_2H_5) quinolines **5a−5f** (Table 1 Entries 1−6), given that 2-unsubstituted quinoline **5g** ($R^1 = H$) (Table 1 Entry 7) could also be obtained. In addition, the aromatic ring (positions 6 and 7) may have electron-donating (Table 1, Entries 1, 2, 5, 6, 7), and electron-withdrawing substituents (Table 1, Entries 3, 4). From a preparative point of view, it is of interest that the synthesis of quinolinylphosphane oxide **5a** does not require the isolation and purification of the imine **1a** and the former can be obtained in "one pot" from *p*-tolylamine **2** ($R^2 = CH_3$, $R^3 = H$) and 2-oxopropyldiphenylphosphane oxide **3** ($R^1 = CH_3$) by means of "in situ" formation of the imine **1a**, followed by thermal heating with DMF-DEA (Table 1, Entry 1).

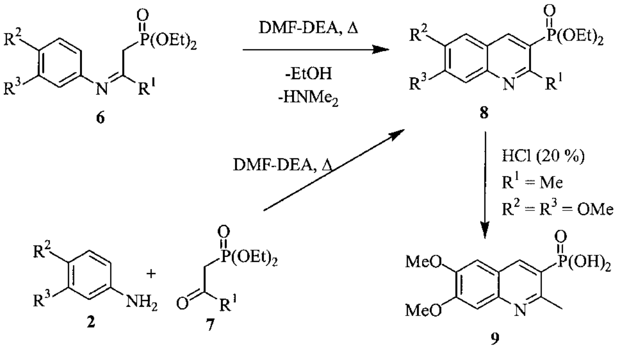
This methodology, used for the preparation of quinolinylphosphane oxides **5**, can also be extended to the synthesis of quinolines containing a phosphonate group in position 3. Reaction of *N*-arylimine derived from phosphonate **6a** ($R^1 = R^2 = R^3 = H$), easily prepared by condensation reaction of aniline **2** ($R^2 = R^3 = H$), with α-carbonylphosphonates **7** ($R^1 = H$),[7a] with DMF-DEA at 130 °C (48 h) without solvent gave quinolinylphosphonate **8a** ($R^1 = R^2 = R^3 = H$) in a good yield (Scheme 3, Table 1, Entry 8). Compound **8a** was characterized by its spectroscopic data. Thus, the ^{31}P NMR spectrum of compound **8a** showed a resonance at $\delta_P = 16.7$ ppm, while the ^1H NMR spectrum showed well-resolved doublets for the aromatic protons of

Table 1. Quinolines obtained

Entry	Compound	R^1	R^2	R^3	Yield [%][a]	M.p. [°C]	Procedure
1	**5a**	Me	Me	H	92 (90)	237−238	A[b] (C)[c]
2	**5b**	Me	OMe	H	85[d]	165−166	A[b]
3	**5c**	Me	Cl	H	72	212−213	A[b]
4	**5d**	Me	H	CF_3	86[d]	176−177	A[b]
5	**5e**	Me	Me	Me	89	175−176	A[b]
6	**5f**	Et	Me	H	91	211−212	A[b]
7	**5g**	H	OMe	H	75	181−182	B[e]
8	**8a**	H	H	H	68	oil	B[e]
9	**8b**	Me	Me	H	75	oil	C[c]
10	**8c**	Me	OMe	OMe	82	137−138	C[c]
11	**8d**	Me	H	H	72	oil	C[c]
12	**9**	Me	OMe	OMe	95	278−280[f]	

[a] Yield after purification by flash chromatography. [b] From imines **1** and DMF-DEA in toluene (110 °C). [c] "One pot" from oxo phosphonates or oxo phosphane oxides. [d] Yield from crude imines. [e] From imine **1g** or **6a** and DMF-DEA without solvent (130 °C). [f] (Decomp.).

positions 2 and 4 (δ_H = 8.95 ppm, $^3J_{PH}$ = 14.9 Hz and δ_H = 8.79 ppm, $^3J_{PH}$ = 16.0 Hz) of quinoline **8a**. It is noteworthy that quinolinylphosphonates **8** can also be directly obtained from arylamines **2** and diethyl 2-oxoalkylphosphonates **7** (R^1 = H, CH_3) by "in situ" formation of the imines derived from phosphonates **6**, followed by thermal heating with DMF-DEA (Scheme 3, Table 1, Entries 9−11). Taking into account the interest of aminophosphonic acid derivatives,[5] the ester cleavage of phosphonate was explored. Quinolinylphosphonate **8c** underwent ester cleavage with 20% aqueous hydrochloric acid to give quinolinylphosphonic acid **9** in excellent yield (Scheme 3, Table 1, Entry 12).



Scheme 3

In conclusion, the synthesis described in this paper provides an efficient and easy access to quinolines substituted with a phosphane oxide or a phosphonate group in position 3, making use of readily available starting materials. These quinolines can be prepared in a stepwise fashion or in a "one pot" reaction from arylamines, phosphorylated carbonyl compounds and dimethylformamide diethyl acetal. Functionalized quinolines are important synthons in organic synthesis and for the preparation of biologically active compounds with interest in medicinal chemistry.[1−4]

Experimental Section

General: Chemicals were purchased from Aldrich Chemical Company. Solvents for extraction and chromatography were of technical grade. All solvents used in the reactions were freshly distilled from appropriate drying agents before use. All other reagents were recrystallized or distilled as necessary. All reactions were performed under dry nitrogen. Analytical TLC was performed on Merck silica gel 60 F_{254} plates. Visualization was accomplished by UV light. Flash chromatography was carried out using Merck silica gel 60 (230−400 mesh ASTM). Melting points were determined with an Electrothermal IA9100 Digital Melting Point Apparatus and are uncorrected. ^{1}H (300 MHz), ^{13}C (75 MHz) and ^{31}P NMR (120 MHz) spectra were recorded with a Varian VXR 300 MHz spectrometer using $CDCl_3$ or CD_3OD solutions with TMS as an internal reference (δ = 0.00 ppm) for ^{1}H and ^{13}C NMR spectra and phosphoric acid (85%) (δ = 0.0 ppm) for ^{31}P NMR spectra. Chemical shifts (δ) are reported in ppm. Coupling constants (*J*) are reported in Hz. Low-resolution mass spectra (MS) were obtained at 50−70 eV by electron impact (EIMS) with a Hewlett Packard 5971 or 5973 spectrometer and by chemical ionization (CI) (N_2) with a Hewlett Packard 1100MSD. Data are reported in the form *m*/*z* (intensity relative to base = 100). Infrared spectra (IR) were taken with a Nicolet IRFT Magna 550 spectrometer, and were obtained from solids in KBr or from neat oils. Peaks are reported in cm^{-1}. Elemental analyses were performed with a LECO CHNS-932 apparatus. Imines **1a**,**b**,**f**,[14] **1g**[7a] and **6a**[7a] were synthesized according to literature procedures.

Synthesis of Imines 1c−e

{2-[(*p*-Chlorophenyl)imino]propyl}diphenylphosphane Oxide (1c): The literature procedure[14] was applied using diphenyl(1,2-propadienyl)phosphane oxide (1.20 g, 5 mmol) and 4-chloroaniline (0.64 g, 5 mmol), affording **1c** (1.41 g,77%) as a white solid. M.p. 212−213 °C. ^{1}H NMR: δ = 7.82−7.38 (m, 10 H), 7.09 and 7.01 (d, $^3J_{H,H}$ = 8.7 Hz and $^3J_{H,H}$ = 8.7 Hz, 2 H), 6.52 and 6.18 (d, $^3J_{H,H}$ = 8.7 Hz and $^3J_{H,H}$ = 8.7 Hz, 2 H), 3.53 and 3.51 (d, $^2J_{PH}$ = 14.8 Hz and $^2J_{PH}$ = 14.5 Hz, 2 H), 2.26 and 1.91 (s, 3 H) ppm. ^{13}C NMR: δ = 165.7 and 163.1, 148.7 and 141.3, 131.9−115.8 (m), 47.7 and 44.7 (d, $^1J_{PC}$ = 56.4 Hz and $^1J_{PC}$ = 61.0 Hz), 22.1 and 21.5.^{31}P NMR: δ = 29.2 and 26.5 ppm. IR (KBr): ṽ = 3170, 1696, 1617 cm^{-1}. MS: *m*/*z* (%) = 201 (100), 367 (65) [M^+]. $C_{21}H_{19}ClNOP$ (367): calcd. C 76.43, H 6.69, N 3.88; found C 76.37, H 6.72, N 3.85.

Diphenyl{2-[(*m*-trifluoromethylphenyl)imino]propyl}phosphane Oxide (1d): The literature procedure[14] was applied using diphenyl(1,2-propadienyl)phosphane oxide (1.20 g, 5 mmol) and 3-(trifluoromethyl)aniline (0.63 mL, 5 mmol), affording crude **1d** (1.70 g, 85%) as an orange solid. Purification of this compound was not possible and was used without purification in the following steps. ^{1}H NMR: δ = 7.80−7.37 (m, 14 H), 3.46 and 3.40 (d, $^2J_{PH}$ = 14.7 Hz and $^2J_{PH}$ = 14.5 Hz, 2 H), 2.25 and 1.89 (s, 3 H) ppm. ^{13}C NMR: δ = 164.7 and 162.4, 129.9−115.5 (m), 46.3 and 44.4 (d, $^1J_{PC}$ = 56.0 Hz and $^1J_{PC}$ = 61.2 Hz), 22.0 and 21.2.^{31}P NMR: δ = 29.1 and 26.3 ppm. IR (KBr): ṽ = 3182, 1690, 1610 cm^{-1}. MS: *m*/*z* (%) = 401 (100) [M^+ + 1].

{2-[(3,4-Dimethylphenyl)imino]propyl}diphenylphosphane Oxide (1e) and (*Z*)- and (*E*)-{2-[(3,4-Dimethylphenyl)amino]-1-propenyl}-diphenylphosphane Oxide (1e′): The literature procedure[14] was applied using diphenyl(1,2-propadienyl)phosphane oxide (1.20 g, 5 mmol) and 3,4-dimethylaniline (0.61 g, 5 mmol), affording a mixture of imine **1e** (1.52, 82%) and isomeric enamines **1e′** [**1e**/**1e′**(*E*)/**1e′**(*Z*) = 90:5:5] as a white solid. M.p. 127−130 °C. ^{1}H NMR: **1e:** δ = 7.83−6.45 (m, 14 H), 3.53 (d, $^2J_{PH}$ = 14.8, 2 H), 2.67 (s, 3 H), 2.11 (s, 3 H), 2.08 (s, 3 H). **1e′:** δ = 7.45−6.83 (m, 14 H), 4.78 and 4.18 (d, $^2J_{PH}$ = 17.3 Hz and $^2J_{PH}$ = 21.9 Hz, 1 H), 3.65 (s, 1 H), 2.13 (s, 3 H), 1.91 (s, 3 H), 1.90 (s, 3 H) ppm. ^{13}C NMR: **1e:** δ = 164.7, 148.0−112.6 (m), 45.1 (d, $^1J_{PC}$ = 61.4 Hz), 21.5, 19.7, 19.0. **1e′:** 160.1, 148.0−112.6 (m), 81.0 and 78.6 (d, $^1J_{PC}$ = 130.2 Hz and $^1J_{PC}$ = 114.6 Hz), 28.7, 25.9 and 22.4 (d, $^3J_{PC}$ = 5.0 Hz and $^3J_{PC}$ = 14.9 Hz), 18.7 ppm. ^{31}P NMR: **1e:** δ = 29.3 ppm. **1e′:** δ = 30.1 and 26.2 ppm. IR (KBr): ṽ = 3170, 3046, 1588.cm^{-1}. MS: *m*/*z* (%) = 201 (100), 361 (53) [M^+]. $C_{23}H_{24}NOP$ (361): calcd. C 76.43, H 6.69, N 3.88; found C 76.48, H 6.72, N 3.91.

Procedure for the Isolation of the 1-Azadiene 4a: A solution of a mixture of diphenyl[2-(*p*-tolylimino)propyl]phosphane oxide (85%) and diphenyl[2-(*p*-tolylamino)-1-propenyl]phosphane oxide (15%) (1.74 g, 5 mmol), and *N*,*N*-dimethylformamide diethyl acetal (DMF-DEA) (1.03 mL, 6 mmol) in toluene was stirred at 90 °C for 24 h. The mixture was concentrated under vacuum and the crude residue was purified by flash column chromatography eluting with MeOH/EtOAc (5:95).

[1-(Dimethylaminomethylidene)-2-(*p*-tolylimino)propyl]diphenylphosphane Oxide (4a): The procedure was applied, affording **4a** (0.68 g, 34%) as a pale yellow oil. R_f (EtOAc/Me OH, 95:5) = 0.06. ^{1}H NMR: δ = 7.89−7.82 (m, 4 H), 7.43−7.32 (m, 6 H), 6.91 (d, $^3J_{H,H}$ = 7.9 Hz, 2 H), 7.76 (d, $^3J_{PH}$ = 15.1 Hz, 1 H), 6.12 (d, $^3J_{H,H}$ = 7.9 Hz, 2 H), 2.91 (s, 6 H), 2.18 (s, 3 H), 1.70 (s, 3 H) ppm. ^{13}C NMR: δ = 167.2 (d, $^2J_{PC}$ = 9.6 Hz), 152.4 (d, $^2J_{PC}$ = 18.6 Hz), 148.4, 134.9−127.9 (m), 119.0, 100.3 (d, $^1J_{PC}$ = 111.8 Hz), 43.7, 20.7, 10.9 ppm. ^{31}P NMR: δ = 32.3 ppm. IR (film): ṽ = 2919, 1593 cm^{-1}. MS: *m/z* (%) = 402 (100) [M$^+$ + 1]. $C_{25}H_{27}N_2OP$ (401): calcd. C 74.61, H 6.76, N 6.96; found C 74.68, H 6.80, N 6.91.

General Procedure for the Synthesis of Quinolines Derived from Phosphane Oxides 5 and Phosphonates 8

Procedure A: A solution of aromatic imine **1** (5 mmol) and *N,N*-dimethylformamide diethyl acetal (DMF-DEA) (1.03 mL, 6 mmol) in toluene was stirred under reflux until TLC indicated the disappearance of imine **1** (2−3 d). The mixture was concentrated under vacuum and the crude residue was purified by flash column chromatography eluting with EtOAc/hexane.

Procedure B: A solution of aromatic imine **1g** or **6a** (5 mmol) and *N,N*-dimethylformamide diethyl acetal (DMF-DEA) (6 mL) was stirred at 130 °C until TLC indicated the disappearance of imines **1** (2−3 d). The mixture was concentrated under vacuum and the crude residue was purified by flash column chromatography eluting with EtOAc/hexane.

Procedure C: A solution of (2-oxopropyl)diphenylphosphane oxide **3** (R^1 = CH_3) (1.55 g, 5 mmol) or diethyl 2-oxopropylphosphonate **7** (R^1 = CH_3) (0.97 g, 5 mmol) and aromatic amines **2** (5 mmol) in toluene (15 mL) was stirred under reflux in a Dean−Stark apparatus. After 3 h, the reaction mixture was cooled to room temp. and *N,N*-dimethylformamide diethyl acetal (DMF-DEA) (1.03 mL, 6 mmol) was added. The mixture was stirred under reflux until the completion of the reaction (2−3 d). The mixture was then concentrated under vacuum and the crude residue was purified by flash column chromatography eluting with EtOAc/hexane.

(2,6-Dimethylquinolin-3-yl)diphenylphosphane Oxide (5a): A solution of [1-(dimethylaminomethylidene)-2-(*p*-tolylimino)propyl]diphenylphosphane Oxide (**4a**) (0.40 g, 1 mmol) in toluene (3 mL) was stirred under reflux until TLC indicated the disappearance of **4a** (36 h). The solution was then concentrated under vacuum and the crude residue was purified by flash column chromatography eluting with EtOAc, affording **5a** (0.34 g, 96%) as a pale yellow solid. This compound can also be prepared, according to Procedure A, using a mixture of diphenyl[2-(*p*-tolylimino)propyl]phosphane oxide and diphenyl[2-(*p*-tolylamino)-1-propenyl]phosphane oxide (1.74 g, 5 mmol) or applying Procedure C, using (2-oxopropyl)diphenylphosphane oxide (1.55 g, 5 mmol) and *p*-toluidine (0.54 g, 5 mmol), affording **5a** (1.64 g, 92%, Procedure A) or (1.60 g,90%, Procedure C) as a pale yellow solid. M.p. 237−238 °C. ^{1}H NMR: δ = 7.86 (d, $^3J_{H,H}$ = 8.6 Hz, 1 H), 7.72 (d, $^3J_{PH}$ = 15.1 Hz, 1 H), 7.67−7.33 (m, 12 H), 2.71 (s, 3 H), 2.40 (s, 3 H) ppm. ^{13}C NMR: δ = 158.6 (d, $^2J_{PC}$ = 9.6 Hz), 146.8, 142.1 (d, $^2J_{PC}$ = 11.8 Hz), 136.1, 133.6, 131.8, 132.1−128.3 (m), 127.7, 126.8, 125.1 (d, $^1J_{PC}$ = 86.6 Hz), 124.4, 25.3, 23.9 ppm. ^{31}P NMR: δ = 30.3 ppm. IR (KBr): ṽ = 3124, 1580, 1401 cm^{-1}. MS: *m/z* (%) = 356 (100), 357 (62) [M$^+$]. $C_{23}H_{20}NOP$ (357): calcd. C 77.30, H 5.64, N 3.92; found C 77.24, H 5.60, N 3.88.

(6-Methoxy-2-methylquinolin-3-yl)diphenylphosphane Oxide (5b): Procedure A was applied using crude [2-(*p*-methoxyphenylimino)propyl]diphenylphosphane oxide (1.82 g, 5 mmol), affording **5b** (1.58 g, 85%) as a pale yellow solid. M.p. 165−166 °C. ^{1}H NMR: δ = 7.88 (d, $^3J_{H,H}$ = 8.9 Hz, 1 H), 7.72 (d, $^3J_{PH}$ = 15.4 Hz, 1 H), 7.67−7.34 (m, 11 H), 6.81, (s, 1 H), 3.80 (s, 3 H), 2.67 (s, 3 H) ppm. ^{13}C NMR: δ = 157.4, 157.0 (d, $^2J_{PC}$ = 9.6 Hz), 144.3, 141.4 (d, $^2J_{PC}$ = 11.6 Hz), 132.1−128.4 (m), 130.7, 125.5, 125.4 (d, $^1J_{PC}$ = 99.7 Hz), 124.1, 105.4, 55.2, 25.1 ppm. ^{31}P NMR: δ = 30.5 ppm. IR (KBr): ṽ = 3224, 1619, 1599 cm^{-1}. MS: *m/z* (%) = 201 (100), 373 (64) [M$^+$]. $C_{23}H_{20}NO_2P$ (373): calcd. C 73.98, H 5.40, N 3.75; found C 74.04, H 5.37, N 3.79.

(6-Chloro-2-methylquinolin-3-yl)diphenylphosphane Oxide (5c): Procedure A was applied using [2-(*p*-chlorophenylimino)propyl]diphenylphosphane oxide (1.84 g, 5 mmol), affording **5c** (1.36 g, 72%) as a pale yellow solid. M.p. 212−213 °C. ^{1}H NMR: δ = 7.92 (d, $^3J_{H,H}$ = 9.0 Hz, 1 H), 7.70 (d, $^3J_{PH}$ = 15.0 Hz, 1 H), 7.66−7.42 (m, 12 H), 2.71 (s, 3 H) ppm. ^{13}C NMR: δ = 160.4 (d, $^2J_{PC}$ = 9.6 Hz), 146.8, 141.9 (d, $^2J_{PC}$ = 11.1 Hz), 132.3, 132.1−128.7 (m), 130.5, 126.8, 125.8 (d, $^1J_{PC}$ = 98.2 Hz), 125.5, 125.3, 25.7 ppm. ^{31}P NMR: δ = 30.1 ppm. IR (KBr): ṽ = 3118, 1626, 1573, 1394 cm^{-1}. MS: *m/z* (%) = 201 (100), 377 (63) [M$^+$]. $C_{22}H_{17}ClNOP$ (377): calcd. C 69.94, H 4.54, N 3.71; found C 70.03, H 4.58, N 3.67.

(2-Methyl-7-trifluoromethylquinolin-3-yl)diphenylphosphane Oxide (5d): Procedure A was applied using {2-[*m*-(trifluoromethyl)-phenylimino]propyl}diphenylphosphane oxide (2.01 g, 5 mmol), affording **5d** (1.77 g, 86%) as a pale yellow solid. M.p. 176−177 °C. ^{1}H NMR: δ = 8.22 (s, 1 H), 7.79 (d, $^3J_{PH}$ = 15.0 Hz, 1 H), 7.64 (d, $^3J_{H,H}$ = 8.6 Hz, 1 H), 7.69−7.38 (m, 11 H), 2.67 (s, 3 H) ppm. ^{13}C NMR: δ = 161.6 (d, $^2J_{PC}$ = 9.1 Hz), 147.4, 142.5 (d, $^2J_{PC}$ = 10.6 Hz), 132.7 (q, $^2J_{FC}$ = 32.7 Hz), 132.3, 131.7−128.7 (m), 130.2, 129.4, 126.1, 126.8 (d, $^1J_{PC}$ = 82.1 Hz), 123.4 (q, $^1J_{FC}$ = 273.0 Hz), 25.7 ppm. ^{31}P NMR: δ = 29.9 ppm. IR (KBr): ṽ = 3045, 1580 cm^{-1}. MS: *m/z* (%) = 201 (100), 411 (60) [M$^+$]. $C_{23}H_{17}F_3NOP$ (411): calcd. C 67.15, H 4.17, N 3.41; found C 67.10, H 4.20, N 3.37.

Diphenyl(2,6,7-trimethylquinolin-3-yl)phosphane Oxide (5e): Procedure A was applied, using {2-[(3,4-dimethylphenyl)imino]-propyl}diphenylphosphane oxide (1.81 g, 5 mmol), affording **5e** (1.65 g, 89%) as a pale yellow solid. M.p. 175−176 °C. ^{1}H NMR: δ = 7.64 (d, $^3J_{PH}$ = 16.0 Hz, 1 H), 7.67−7.33 (m, 11 H), 7.12, (s, 1 H), 2.60 (s, 3 H), 2.33 (s, 3 H), 2.24 (s, 3 H) ppm. ^{13}C NMR: δ = 158.7 (d, $^2J_{PC}$ = 9.6 Hz), 147.3, 142.1, 141.8 (d, $^2J_{PC}$ = 11.1 Hz), 133.6, 131.8−128.3 (m), 127.4, 127.2, 124.0 (d, $^1J_{PC}$ = 101.0 Hz), 123.2, 25.3, 20.2, 19.4 ppm. ^{31}P NMR: δ = 30.6 ppm. IR (KBr): ṽ = 3051, 2919, 1639, 1580 cm^{-1}. MS: *m/z* (%) = 201 (100), 371 (67) [M$^+$]. $C_{24}H_{22}NOP$ (371): calcd. C 77.61, H 5.97, N 3.77; found C 77.55, H 5.93, N 3.81.

(2-Ethyl-6-methylquinolin-3yl)diphenylphosphane Oxide (5f): Procedure A was applied, using a mixture of diphenyl[2-(*p*-tolylamino)-1-butenyl]phosphane oxide and diphenyl[2-(*p*-tolylimino)butyl]phosphane oxide (1.81 g, 5 mmol), affording **5f** (1.69 g, 91%) as a pale yellow solid. M.p. 211−212 °C. ^{1}H NMR: δ = 7.90 (d, $^3J_{H,H}$ = 8.6 Hz, 1 H), 7.73 (d, $^3J_{PH}$ = 15.1 Hz, 1 H), 7.66−7.39 (m, 11 H), 7.32 (s, 1 H), 3.06 (q, $^3J_{H,H}$ = 7.3 Hz, 2 H) 2.41 (s, 3 H), 1.14 (t, $^3J_{H,H}$ = 8.6 Hz, 3 H) ppm. ^{13}C NMR: δ = 163.5 (d, $^2J_{PC}$ = 9.6 Hz), 147.1, 142.4 (d, $^2J_{PC}$ = 11.6 Hz), 136.1, 133.6, 133.6−128.4 (m), 128.1, 126.9, 124.5 (d, $^1J_{PC}$ = 99.7 Hz), 124.5, 30.8, 21.1, 12.7 ppm. ^{31}P NMR: δ = 30.5 ppm. IR (KBr): ṽ = 3102, 1580, cm^{-1}. MS: *m/z* (%) = 201 (100), 371 (74) [M$^+$]. $C_{24}H_{22}NOP$ (371): calcd. C 77.61, H 5.97, N 3.77; found C 77.68, H 6.01, N 3.75.

(6-Methoxyquinolin-3-yl)diphenylphosphane Oxide (5g): Procedure B was applied, using [2-(*p*-methoxyphenylamino)vinyl]diphenylphosphane oxide (1.75 g, 5 mmol), affording **5g** (1.34 g, 75%) as a white solid. M.p. 181−182 °C. ^{1}H NMR: δ = 8.83 (dd, $^{2}J_{PH}$ = 4.4, $^{4}J_{H,H}$ = 2.0 Hz, 1 H), 8.50 (dd, $^{2}J_{PH}$ = 13.1, $^{4}J_{H,H}$ = 2.0 Hz, 1 H), 8.03 (d, $^{3}J_{H,H}$ = 9.3 Hz, 1 H) 7.76−7.45 (m, 11 H), 7.09 (d, $^{4}J_{H,H}$ = 2.7 Hz, 1 H), 3.91 (s, 3 H) ppm. ^{13}C NMR: δ = 158.4 148.3 (d, $^{2}J_{PC}$ = 12.1 Hz), 145.3, 140.3 (d, $^{3}J_{PC}$ = 7.6 Hz), 132.5, 132.3−128.6 (m), 130.7, 128.0, 3126.0 (d, $^{1}J_{PC}$ = 101.2 Hz), 124.7, 55.6 ppm. ^{31}P NMR: δ = 27.7 ppm. IR (KBr): $\tilde{\nu}$ = 3041, 1902, 1605, cm^{-1}. MS: *m/z* (%) = 201 (100), 359 (40) [M^{+}]. $C_{22}H_{18}NO_{2}P$ (359): calcd. C 73.53, H 5.05, N 3.90; found C 73.60, H 5.01, N 3.87.

Diethyl Quinolin-3-ylphosphonate (8a): Procedure B was applied, using diethyl [2-(phenylamino)vinyl]phosphonate (1.28 g, 5 mmol), affording **8a** (0.90 g, 68%) as a colorless oil. R_f (EtOAc) = 0.09. ^{1}H NMR: δ = 8.95 (d, $^{3}J_{PH}$ = 14.9 Hz, 1 H), 8.79 (d, $^{3}J_{PH}$ = 16.0 Hz 1 H), 8.00 (d, $^{3}J_{H,H}$ = 7.8 Hz 1 H), 7.89 (d, $^{3}J_{H,H}$ = 7.9 Hz, 1 H), 7.43−7.65 (m, 2 H), 4.27−4.08 (m, 4 H), 1.38−1.31 (m, 6 H) ppm. ^{13}C NMR: δ = 152.6, 147.8 (d, $^{2}J_{PC}$ = 12.1 Hz), 144.2 (d, $^{2}J_{PC}$ = 9.3 Hz), 133.0, 129.0, 126.8, 124.6, 122.1 (d, $^{1}J_{PC}$ = 186.0 Hz), 120.5, 62.3, 62.2, 16.2, 16.1 ppm. ^{31}P NMR: δ = 16.7 ppm. IR (film): $\tilde{\nu}$ = 3059, 1877, 1580, cm^{-1}. MS: *m/z* (%) = 264 (100), 265 (90) [M^{+}]. $C_{13}H_{16}NO_{3}P$ (265): calcd. C 58.87, H 6.08, N 5.28; found C 58.90, H 6.12, N 5.90.

Diethyl (2,6-Dimethylquinolin-3-yl)phosphonate (8b): Procedure C was applied, using diethyl (2-oxopropyl)phosphonate (0.97 g, 5 mmol) and *p*-toluidine (0.54 g, 5 mmol), affording **8b** (1.10 g, 75%) as a colorless oil. R_f (EtOAc) = 0.47. ^{1}H NMR: δ = 8.65 (d, $^{3}J_{PH}$ = 16.3 Hz 1 H), 7.86 (d, $^{3}J_{H,H}$ = 8.0 Hz 1 H), 7.58−7.39 (m, 4 H), 4.24−4.02 (m, 4 H), 2.86 (s, 3 H), 2.46 (s, 3 H), 1.35−1.26 (m, 6 H) ppm. ^{13}C NMR: δ = 157.8 (d, $^{2}J_{PC}$ = 12.1 Hz), 147.3, 143.5 (d, $^{2}J_{PC}$ = 9.1 Hz), 136.3, 133.9, 128.1, 127.1, 121.1 (d, $^{1}J_{PC}$ = 185.3 Hz), 62.3, 62.2, 24.9, 21.2, 16.3, 16.2 ppm. ^{31}P NMR: δ = 18.8 ppm. IR (film): $\tilde{\nu}$ = 3005, 1880, 1599, cm^{-1}. MS: *m/z* (%) = 293 (100) [M^{+}]. $C_{15}H_{20}NO_{3}P$ (293): calcd. C 61.43, H 6.87, N 4.78; found C 61.38, H 6.90, N 4.75.

Diethyl (4,6-Dimethoxy-2-methylquinolin-3-yl)phosphonate (8c): Procedure C was applied, using diethyl (2-oxopropyl)phosphonate (0.97 g, 5 mmol)and 3,4-dimethoxyaniline (1.27 g, 5 mmol), affording **8c** (1.22 g, 70%) as a white solid. M.p. 137−138 °C. ^{1}H NMR: δ = 8.62 (d, $^{3}J_{PH}$ = 15.9 Hz 1 H), 7.37 (s, 1 H), 7.08 (s, 1 H), 4.24−4.08 (m, 4 H), 4.05 (s, 3 H), 4.01 (s, 1 H), 2.87 (s, 3 H), 1.36 (t, $^{3}J_{H,H}$ = 7.0 Hz, 6 H) ppm. ^{13}C NMR: δ = 156.4 (d, $^{2}J_{PC}$ = 12.1 Hz), 153.8, 149.2, 145.7, 141.6 (d, $^{2}J_{PC}$ = 9.6 Hz), 120.0, 118.3 (d, $^{1}J_{PC}$ = 188.4 Hz), 106.7, 105.1, 61.7, 61.6, 55.6, 55.5, 24.2, 15.8, 15.7 ppm. ^{31}P NMR: δ = 18.7 ppm. IR (KBr): $\tilde{\nu}$ = 2985, 1619, 1507, cm^{-1}. MS: *m/z* (%) = 340 (100) [M^{+} + 1]. $C_{16}H_{22}NO_{5}P$ (339): calcd. C 56.63, H 6.53, N 4.13; found C 56.65, H 6.49, N 4.15.

Diethyl (2-Methylquinolin-3-yl)phosphonate (8d): Procedure C was applied, using diethyl (2-oxopropyl)phosphonate (0.97 g, 5 mmol) and aniline (0.46 mL, 5 mmol), affording **8d** (0.99 g, 72%) as a colorless oil. R_f (EtOAc) = 0.72. ^{1}H NMR: δ = 8.81 (d, $^{3}J_{PH}$ = 16.2 Hz 1 H), 8.04 (d, $^{3}J_{H,H}$ = 7.8 Hz 1 H), 7.87 (d, $^{3}J_{H,H}$ = 8.1 Hz, 1 H), 7.79 (dd, $^{3}J_{H,H}$ = 8.1, $^{3}J_{H,H}$ = 7.0 Hz 1 H), 7.56 (dd, $^{3}J_{H,H}$ = 7.8, $^{3}J_{H,H}$ = 7.0 Hz 1 H), 4.30−4.05 (m, 4 H), 2.94 (s, 3 H), 1.39−1.33 (m, 6 H) ppm. ^{13}C NMR: δ = 158.8 (d, $^{2}J_{PC}$ = 12.1 Hz), 153.1, 144.3 (d, $^{2}J_{PC}$ = 9.1 Hz), 131.6, 128.7, 126.4, 125.0, 121.1 (d, $^{1}J_{PC}$ = 185.3 Hz), 120.9, 62.2, 62.1, 25.0, 16.2, 16.1 ppm. ^{31}P NMR: δ = 17.7 ppm. IR (film): $\tilde{\nu}$ = 3041, 1854, 1590, cm^{-1}. MS: *m/z* (%) = 278 (100), 279 (95) [M^{+}]. $C_{14}H_{18}NO_{3}P$ (279): calcd. C 60.21, H 6.50, N 5.02; found C 60.16, H 6.51, N 4.99.

Procedure for the Synthesis of Quinolinylphosphonic Acid 9: 3-(Diethylphosphoryl)-4,6-dimethoxy-2-methylquinoline (**8c**) (0.34 g, 1 mmol) in HCl (20%) (5 mL) was stirred for 6 h under reflux. The solution was concentrated under reduced pressure and dissolved in methanol (1 mL). Diethyl ether was added dropwise to the solution and a solid was formed. Finally, the pale pink solid was filtered and washed with diethyl ether.

(6,7-Dimethoxy-2-methylquinolin-3yl)phosphonic Acid (9): The Procedure was applied, affording **9** (0.27 g, 95%) as a pale pink solid. Dec. temp. 278−279 °C. ^{1}H NMR: δ = 9.00 (d, $^{3}J_{PH}$ = 13.9 Hz 1 H), 7.54 (s, 1 H), 7.35 (s, 1 H), 3.96 (s, 3 H), 3.88 (s, 1 H), 2.96 (s, 3 H) ppm. ^{13}C NMR: δ = 159.9, 155.8, 153.8, 148.2 (d, $^{2}J_{PC}$ = 7.6 Hz), 138.0, 125.9 (d, $^{1}J_{PC}$ = 189.8 Hz), 124.6(d, $^{2}J_{PC}$ = 13.1 Hz), 108.0, 99.6, 57.6, 57.2, 20.5 ppm. ^{31}P NMR: δ = 8.6 ppm. IR (KBr): $\tilde{\nu}$ = 3450, 2995, 1632, cm^{-1}. MS: *m/z* (%) = 283 (100) [M^{+} + 1]. $C_{12}H_{14}NO_{5}P$ (282): calcd. C 50.89, H 4.98, N 4.95; found C 50.96, H 5.04, N 4.90.

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