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A Convenient and Applicable Route to Synthesize 2-(1-Alkynyl)phenylphosphonates

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ABSTRACT: *A convenient and applicable route has been developed to synthesize various 2-(1-alkynyl)-phenylphosphonates starting from easily available phenols via palladium-catalyzed alkynyl-dehydroxylation of 2-hydroxylphenylphosphonates.* © 2005 Wiley Periodicals, Inc. Heteroatom Chem 16:529–534, 2005; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20156

INTRODUCTION

Since conjugated alkynes are found in a wide range of natural and unnatural materials [1], as well as versatile synthetic intermediates [2], much effort has been paid to develop methods to construct organic molecules bearing alkynyl moieties. Over the last few decades, the palladium-catalyzed alkynylation reaction has been extensively studied and become one of the most general and reliable methods to form conjugated alkynes [3].

We became interested in palladium-catalyzed alkynylation reaction during the course of preparing phosphaisocoumarins via intramolecular cyclization of phosphonates to alkynes [4]. It was essential to prepare 2-(1-alkynyl)phenylphosphonates as the cyclization substrates. However, to our knowledge, there were no reports about the synthesis and application of 2-(1-alkynyl)phenylphosphonates prior to our studies. Thus, we decided to develop a convenient method to synthesize 2-(1-alkynyl)-phenylphosphonates. In this paper, we wish to report in detail our results to prepare them.

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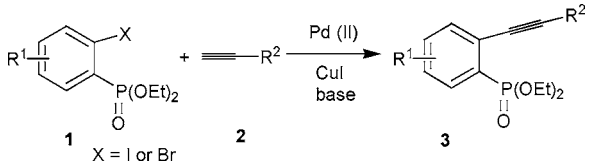
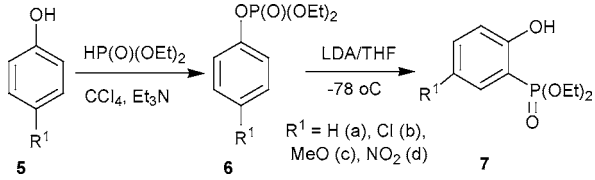
RESULTS AND DISCUSSION

Two probable methods to synthesize our aim alkynes were considered. We initially had tried to prepare the alkynes **3** through the Sonogashira cross-coupling reaction [3,5] of 2-halophenylphosphonates **1** and terminal alkynes **2** (Scheme 1). But after consulting the corresponding literature, we found that preparation of 2-halophenylphosphonate **1** ($R^1 = H$, X = I or Br) usually starts from the unstable and expensive 2-iodophenylamine and needs strong basic and irradiation conditions [6]. Furthermore, 2-iodophenylamines with other substituents in the benzene ring are not commercially available, herein it is difficult to synthesize various 2-halophenylphosphonates. Taking into account of these drawbacks, we gave up this method.

We then turned our attention to the Heck alkynylation of 2-(diethylphosphonyl)phenyl perfluoroalkanesulfonates **4** with terminal alkynes **2** (Scheme 2). It has been reported that aryl triflates [7] and aryl perfluoroalkanesulfonates [8] can undergo palladium-catalyzed cross-coupling reaction with terminal alkynes, but these procedures have not been extended to the corresponding 2-phosphonyl-substituted aryl substrates. We thought this method was feasible and applicable in the following two aspects. On the one hand, 2-hydroxyphenylphosphonates, the key starting materials to prepare compounds **4**, can be easily obtained from the



SCHEME 1



SCHEME 3

rearrangement of aryl phosphates according to the literature [9]. On the other hand, compared with the moisture-sensitive and rather expensive triflating agent (e.g. triflic anhydride) to prepare aryl triflates, perfluoroalkanesulfonyl fluoride, which is used to synthesize aryl perfluoroalkanesulfonates, is not only commercially available but also cheap and insensitive to moisture. After examination, in the end we developed a convenient route to synthesize the alkynes **3** via palladium-catalyzed alkynyldehydroxylation of 2-hydroxylphenylphosphonates.

We first prepared several 2-hydroxyphenylphosphonates **7** from the corresponding phenols **5** according to the literature [9] (Scheme 3). It is worth mentioning that the rearrangement of diethyl 4-nitrophenyl phosphate **6d** is not a literature procedure, which, we found, needs lower reaction temperature (below −85°C) and requires about 2.0 equiv. LDA.

Compounds **7** were then converted to the corresponding perfluoroalkanesulfonates **4** (Scheme 4). Compounds **7a–c** can react with perfluoroalkanesulfonyl fluoride in Et_3N at room temperature to afford **4a–c** in good yields (Table 1, entries 1–3). However, the reaction of **7d** under the above conditions gave **4d** only in 7% isolated yield, and most of the starting material **7d** was recovered (Table 1, entry 4). When this reaction was carried out in anhydrous CH_2Cl_2 by addition of 1.5 equiv. anhydrous Et_3N at room temperature, the isolated yield of **4d** has been improved to 47% (Table 1, entry 5). A probable explanation is that the nitro group's strong electron-withdrawing effect might make the formed **4d** easy to hydrolysis to **7d** under aqueous conditions.

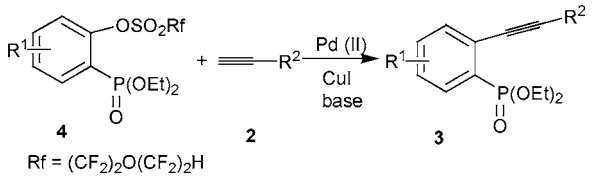
Compounds **4** reacted with a variety of terminal alkynes in the presence of $PdCl_2(PPh_3)_2$ and Et_3N at 90°C for several hours (Scheme 5), and the results are shown in Table 2. Most of the examined substrates gave the desired products **3** in moderate to high yields. Lower yields are associated with the use of electron-rich sulfonate **4c** (Table 2, entry 13) and electron-withdrawing terminal alkyne (Table 2, entry 7). It has been reported that LiCl can improve the coupling yields by acting as ligand exchanger in the initially formed organopalladium triflates [7b], and the presence of copper co-catalyst is essential for the cross-coupling reaction to proceed at room temperature [10]. Indeed, for our reaction, the yield of the reaction of **4c** with phenyl acetylene has been improved considerably from 36 to 79% by the addition of LiCl and CuI (Table 2, entries 13 and 14). Under the same conditions, the reaction of **4c** with propynl-1-ol gave the desired product **3n** in 72% yield (Table 2, entry 15).

CONCLUSIONS

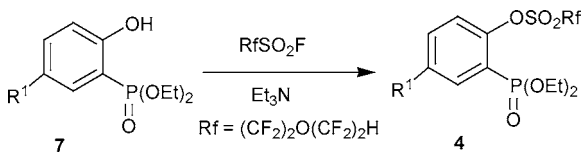
In conclusion, we have developed a convenient and applicable route to synthesize 2-(1-alkynyl)-phenylphosphonates starting from easily available phenols via the palladium-catalyzed cross-coupling reaction of 2-(diethylphosphonyl)phenyl perfluoroalkanesulfonates **4** and terminal alkynes. Since compounds **4** have the potential to react with many reagents, such as alkenes [8,11] and a variety of organometallic reagents [12], the present route may also be very useful to prepare other 2-substituted phenylphosphonates.

EXPERIMENTAL

NMR spectra were all recorded on a Varian Mercury300 spectrometer using $CDCl_3$ as a solvent



SCHEME 2



SCHEME 4

TABLE 1 The Synthesis of the Perfluoroalkansulfonates **4**[a]

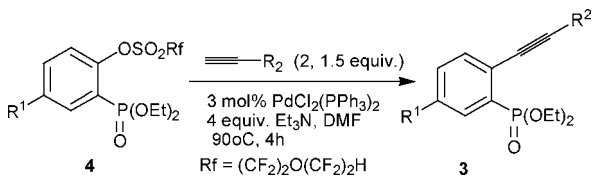
Entry	*Product*	R^1	*Solvent*	*Base*	*Yield (%)*[b]
1	**4a**	H	Et_3N	Et_3N	78
2	**4b**	Cl	Et_3N	Et_3N	75
3	**4c**	MeO	Et_3N	Et_3N	70
4	**4d**	NO_2	Et_3N	Et_3N	7
5[c]	**4d**	NO_2	CH_2Cl_2	Et_3N	47

[a]General reaction conditions otherwise specified: **7**: R_fSO_2F: Et_3N = 1 mmol: 1.2 mmol : 1 mL, at room temperature for 12 h.
[b]Isolated yield.
[c]**7d** (4.50 mmol), R_fSO_2F (6.67 mmol), Et_3N (6.83 mmol), CH_2Cl_2 (10.0 mL), at room temperature for 12 h.

unless stated. The ^1H NMR spectra and ^{13}C NMR spectra used $CDCl_3$ (with TMS) as the internal reference at 7.27 ppm and 77.0 ppm, respectively. ^{19}F NMR spectra used $CFCl_3$ as the external reference, and ^{31}P NMR spectra used the 85% H_3PO_4 as the external reference. MS spectra were determined using a HP5989A mass spectrometer. IR spectra were measured on a Y-Zoom Cursor instrument. HRMS were determined by Kratos Concept 1H series mass spectrometer. Starting materials **7a–c** were formed from the corresponding phenols as reported [9]. Fluoroalkanesulfonyl fluorides and terminal alkynes were commercially obtained. All reagents and solvents were used as received unless Et_3N and DMF used to prepare compounds **3** were distilled from calcium hydride.

Diethyl 2-hydroxy-5-nitrophenylphosphonate **7d**

7d was prepared according to a modified process of the literature [9]: the reaction of diethyl 4-nitrophenyl phosphate **6d** with 2.0 equiv. LDA under below −85°C gave **7d** as a yellow solid. Yield: 77%. ^1H NMR (300 MHz, $CDCl_3$): δ 11.15 (br s, 1H), 8.29–8.38 (m, 2H), 7.03–7.09 (m, 1H), 4.08–4.28 (m, 4H), 1.38 (t, J = 7.2 Hz, 6H). MS (EI): m/z: 275 (M^+, 36), 247 (12), 231 (13), 219 (100), 203 (31), 189 (21), 171 (42), 109 (6); IR (KBr, cm^{-1}): 3400, 2985, 1608, 1494, 1346, 1304, 1209, 1069, 1030, 987; Anal. Calcd for $C_{10}H_{14}NO_6P$: C, 43.64; H, 5.13; N, 5.09. Found: C, 43.71; H, 5.17; N, 5.12.



4 3

SCHEME 5

TABLE 2 The Synthesis of 2-(1-Alkynyl)phenylphosphonates **3**[a]

Entry	R^1	R^2	*Product*	*Yield (%)*[b]
1	H	Ph	**3a**	73
2	H	*n*-Bu	**3b**	50
3	H	H	**3c**	52[c]
4	Cl	*n*-Bu	**3d**	77
5	Cl	Ph	**3e**	81
6	Cl	*p*-EtC_6H_4	**3f**	83
7	Cl	*p*-$O_2NC_6H_4$	**3g**	47
8	Cl	CH_2OH	**3h**	78
9	Cl	CH_2OCH_3	**3i**	80
10	Cl	$SiMe_3$	**3j**	73
11	Cl	Cyclopropyl	**3k**	79
12	NO_2	*p*-EtC_6H_4	**3l**	78
13	MeO	Ph	**3m**	36
14[d]	MeO	Ph	**3m**	79
15[d]	MeO	CH_2OH	**3n**	72

[a]General reaction conditions: molar ratio of **4**: **2**: $PdCl_2(PPh_3)_2$: Et_3N is 1: 1.5: 0.03: 4, in DMF at 90°C for 4 h.
[b]Isolated yield.
[c]The total yield of **3c** by desilylation of the product of **4a** and trimethylsilyl acetelyne.
[d]By addition of 300 mol% LiCl and 10 mol% CuI.

General Procedure for the Preparation of 2-(Phosphonyl)phenyl Perfluoroalkanesulfonates **4**

To a mixture of the corresponding phenol **3** (5.5 mmol) and fluoroalkanesulfonyl fluoride (5 mmol) was added dropwise Et_3N (5 mL) at 0°C. After stirring at room temperature for 8 h, the reaction mixture was concentrated in vacuo and the residue was then dissolved in water (15 mL) and extracted with EtOAc. The organic extracts were washed with brine, dried (Na_2SO_4), and evaporated in vacuo. The residue was chromatographed on silica gel using hexane/EtOAc as an eluent to give the corresponding product **4a–c**. **4d** was prepared as in Table 1 (entry 5). The isolated yield and the physical data for **4a–d** are as follows.

2-(Diethoxyphosphonyl)phenyl 1,1,2,2-tetrafluoro-2-(1,1,2,2-tetrafluoroethoxy)ethanesulfonate **4a**. Oil. Yield: 78%. ^1H NMR (300 MHz, $CDCl_3$): δ 8.02–8.10 (m, 1H), 7.62–7.68 (m, 1H), 7.38–7.51 (m, 2H), 5.91 (tt, J_1 = 52.5 Hz, J_2 = 3.0 Hz, 1H), 4.10–4.28 (m, 4H), 1.34 (t, J = 6.9 Hz, 6H); ^{31}P NMR (121 MHz, $CDCl_3$): δ 12.14; ^{19}F NMR (300 MHz, $CDCl_3$): δ −81.77 (t, J = 12.9 Hz, 2F), −88.71 (m, 2F), −113.77 (s, 2F), −137.83 (dt, J_1 = 55.7 Hz, J_2 = 3.3 Hz, 2F); MS (EI): m/z: 510 (M^+, 2), 483 (10), 455 (14), 390 (7), 229 (5), 156 (100), 92 (9), 65 (22); IR (film, cm^{-1}): 2991, 1602, 1572, 1474, 1428, 1331, 1256, 1145, 1080, 1024, 977, 887; Anal. Calcd for $C_{14}H_{15}F_8O_7PS$: C, 32.95; H, 2.97. Found: C, 32.92; H, 3.07.

4-Chloro-2-(diethoxyphosphonyl)phenyl 1,1,2,2-tetra-fluoro-2-(1,1,2,2-tetrafluoroethoxy)ethanesulfonate **4b**. Oil. Yield: 75%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00–8.06 (m, 1H), 7.58–7.62 (m, 1H), 7.31–7.36 (m, 1H), 5.91 (tt, $J_1 = 52.5$ Hz, $J_2 = 3.0$ Hz, 1H), 4.15–4.26 (m, 4H), 1.36 (t, $J = 6.9$ Hz, 6H); ^{31}P NMR (121 MHz, $CDCl_3$): δ 10.20; ^{19}F NMR (300 MHz, $CDCl_3$): δ −81.74 (t, $J = 12.9$ Hz, 2F), −88.57 (m, 2F), −113.62 (s, 2F), −137.78 (dt, $J_1 = 55.5$ Hz, $J_2 = 3.6$ Hz, 2F); MS (EI): *m/z*: 544 (M^+, 7), 488 (2), 424 (10), 263 (2), 247 (18), 190 (100), 173 (15), 101 (25), 79 (6); IR (film, cm^{-1}): 2990, 1716, 1594, 1462, 1430, 1380, 1257, 1149, 1106, 1077, 1023, 979, 888; Anal. Calcd for $C_{14}H_{14}ClF_8O_7PS$: C, 30.87; H, 2.59. Found: C, 31.41; H, 2.51.

2-(Diethoxyphosphonyl)-4-methoxyphenyl 1,1,2,2-tetrafluoro-2-(1,1,2,2-tetrafluoroethoxy)-ethanesulfonate **4c**. Oil. Yield: 70%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50–7.56 (m, 1H), 7.26–7.31 (m, 1H), 7.08–7.12 (m, 1H), 5.90 (tt, $J_1 = 52.5$ Hz, $J_2 = 3.0$ Hz, 1H), 4.08–4.30 (m, 4H), 3.87 (s, 3H), 1.35 (dt, $J_1 = 6.9$ Hz, $J_2 = 0.6$ Hz, 6H); ^{31}P NMR (121 MHz, $CDCl_3$): δ 12.09; ^{19}F NMR (300 MHz, $CDCl_3$): δ −81.81 (t, $J = 13.8$ Hz, 2F), −88.66 (m, 2F), −113.91 (s, 2F), −137.88 (dt, $J_1 = 56.7$ Hz, $J_2 = 5.7$ Hz, 2F); MS (EI): *m/z*: 540 (M^+, 10), 259 (55), 231 (10), 215 (17), 187 (100), 171 (12), 123 (8), 65 (5); IR (film, cm^{-1}): 2988, 1738, 1582, 1477, 1371, 1254, 1150, 1074, 1029, 977, 855; Anal. Calcd for $C_{15}H_{17}F_8O_8PS$: C, 33.34; H 3.18. Found: C, 33.30; H, 3.21.

2-(Diethoxyphosphonyl)-4-nitrophenyl 1,1,2,2-tetrafluoro-2-(1,1,2,2-tetrafluoroethoxy)-ethanesulfonate **4d**. Oil. Yield: 47%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.85–8.92 (m, 1H), 8.48–8.52 (m, 1H), 7.58–7.63 (m, 1H), 5.93 (tt, $J_1 = 51.6$ Hz, $J_2 = 3.0$ Hz, 1H), 4.17–4.34 (m, 4H), 1.38 (t, $J = 6.9$ Hz, 6H); ^{31}P NMR (121 MHz, $CDCl_3$): δ 11.65; ^{19}F NMR (300 MHz, $CDCl_3$): δ −81.61 (t, $J = 11.1$ Hz, 2F), −88.41 (m, 2F), −113.21 (s, 2F), −137.90 (dd, $J_1 = 55.5$ Hz, $J_2 = 3.6$ Hz, 2F); MS (EI): *m/z*: 556 [$(M + 1)^+$, 2], 528 (27), 500 (55), 257 (100), 201 (84), 171 (62), 101 (60), 63 (32); IR (film, cm^{-1}): 2991, 1620, 1540, 1465, 1433, 1355, 1262, 1193, 1069, 1020, 862; Anal. Calcd for $C_{14}H_{14}F_8NO_9PS$: C, 30.28, H 2.54, N, 2.52. Found: C, 30.43, H, 2.57, N, 2.58.

General Procedure for the Preparation of o-Ethynylphenylphosphonic Acid Diethyl Esters **3**

To a mixture of **4** (1.0 mmol), $PdCl_2(PPh_3)_2$ (0.03 mmol), Et_3N (4.0 mmol), and DMF (3 mL) was added dropwise the terminal alkyne (1.5 mmol) at room temperature. After stirring at 80°C for 5 h under nitrogen, the reaction mixture was diluted with EtOAc and washed with aqueous NH_4Cl until neutral and brine, dried (Na_2SO_4), and evaporated in vacuo. The residue was chromatographed on silica gel using hexane/EtOAc as eluent to give the corresponding product **3**. The preparation of **3c**, **3m**, and **3n** was a little different from the above procedures (see Table 2). The isolated yield and the physical data for **3a–n** are as follows.

(2-Phenylethynyl-phenyl)-phosphonic Acid Diethyl Ester **3a**. Oil. Yield: 73%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99–8.07 (m, 1H), 7.35–7.66 (m, 8H), 4.07–4.28 (m, 4H), 1.32 (t, $J = 6.9$ Hz, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 134.18 (d, $J = 9.1$ Hz), 133.14 (d, $J = 12.3$ Hz), 131.91 (d, $J = 2.7$ Hz), 131.37, 129.71 (d, $J = 186.2$ Hz), 128.23, 128.21, 127.54 (d, $J = 14.3$ Hz), 125.64 (d, $J = 6.6$ Hz), 122.89, 94.44 (d, $J = 0.5$ Hz), 87.66 (d, $J = 6.2$ Hz), 62.10 (d, $J = 5.5$ Hz), 16.20 (d, $J = 6.8$ Hz); ^{31}P NMR (121 MHz, $CDCl_3$): δ 16.73; MS (EI): *m/z*: 314 (M^+, 100), 285 (27), 258 (30), 242 (34), 226 (23), 178 (21), 165 (37), 105 (16), 77 (7); IR (film, cm^{-1}): 2983, 2219, 1598, 1492, 1391, 1244, 1139, 1025, 970; HRMS (EI): Calcd for $C_{18}H_{19}O_3P$ (M^+): 314.10719. Found: 314.11061.

(2-Hex-1-ynyl-phenyl)-phosphonic Acid Diethyl Ester **3b**. Oil. Yield: 50%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92–7.99 (m, 1H), 7.33–7.52 (m, 3H), 4.03–4.24 (m, 4H), 2.46 (t, $J = 6.9$ Hz, 2H), 1.47–1.68 (m, 4H), 1.34 (t, $J = 6.9$ Hz, 6H), 0.95 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 134.04 (d, $J = 9.9$ Hz), 133.62 (d, $J = 12.5$ Hz), 131.86 (d, $J = 2.6$ Hz), 129.44 (d, $J = 185.8$ Hz), 126.98, 126.77 (d, $J = 1.8$ Hz), 96.21, 78.87, 62.07 (d, $J = 4.8$ Hz), 30.51, 21.94, 19.34, 16.31 (d, $J = 4.8$ Hz), 13.60; ^{31}P NMR (121 MHz, $CDCl_3$): δ 20.13; MS (EI): *m/z*: 294 (M^+, 22), 265 (19), 252 (87), 224 (35), 209 (33), 196 (100), 115 (22), 77 (9); IR (film, cm^{-1}): 2982, 2232, 1589, 1469, 1386, 1247, 1141, 1055, 1027, 966; HRMS (EI): Calcd for $C_{16}H_{23}O_3P$ (M^+): 294.13848. Found: 294.13606.

Ethynyl-phenylphosphonic Acid Diethyl Ester **3c**. Oil. Yield: 52%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.96–8.04 (m, 1H), 7.41–7.65 (m, 3H), 4.06–4.27 (m, 4H), 3.39 (d. $J = 2.7$ Hz, 1H), 1.34 (dt, $J_1 = 7.2$ Hz, $J_2 = 2.7$ Hz, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 134.35 (d, $J = 12.3$ Hz), 134.04 (d, $J = 9.5$ Hz), 131.86 (d, $J = 2.5$ Hz), 130.39 (d, $J = 186.1$ Hz), 128.18 (d, $J = 15.0$ Hz), 124.49 (d, $J = 6.6$ Hz), 82.51, 81.47 (d, $J = 6.7$ Hz), 62.29 (d, $J = 5.4$ Hz), 16.14 (d, $J = 6.3$ Hz); ^{31}P NMR (121 MHz, $CDCl_3$): δ 19.05; MS (EI): *m/z*: 238 (M^+, 100), 209 (76), 182 (67), 166 (47), 137 (29), 129

(51), 118 (51), 75 (33); IR (film, cm^{-1}): 3283, 2983, 2101, 1589, 1468, 1392, 1243, 1142, 1026, 966; HRMS (EI): Calcd for $C_{12}H_{15}O_3P$ (M^+): 238.07588. Found: 238.07819.

(5-Chloro-2-hex-1-ynyl-phenyl)-phosphonic Acid Diethyl Ester **3d**. Oil. Yield: 77%. ^1H NMR (300 MHz, $CDCl_3$): δ 7.79–7.84 (m, 1H), 7.47–7.49 (m, 2H), 4.17–4.25 (m, 4H), 2.45 (t, $J = 6.9$ Hz, 2H), 1.44–1.63 (m, 4H), 1.38 (t, $J = 6.9$ Hz, 6H), 0.95 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 134.76 (d, $J = 14.0$ Hz), 133.74 (d, $J = 10.3$ Hz), 133.00 (d, $J = 19.8$ Hz), 131.47 (d, $J = 185.3$ Hz), 131.81 (d, $J = 2.8$ Hz), 125.00 (d, $J = 6.0$ Hz), 97.16 (d, $J = 0.5$ Hz), 77.86 (d, $J = 6.0$ Hz), 62.24 (d, $J = 5.8$ Hz), 30.29, 21.81, 19.23, 16.15 (d, $J = 6.6$ Hz), 13.45; ^{31}P NMR (121 MHz, $CDCl_3$): δ 15.01; MS (EI): *m/z*: 328 (M^+, 19), 299 (15), 286 (81), 258 (32), 230 (100), 165 (10), 149 (13), 115 (12), 75 (5); IR (film, cm^{-1}): 2959, 2231, 1463, 1381, 1250, 1150, 1104, 1025, 971; HRMS (EI): Calcd for $C_{16}H_{22}ClO_3P$ (M^+): 328.09951. Found: 328.10115.

(5-Chloro-2-phenylethynyl-phenyl)-phosphonic Acid Diethyl Ester **3e**. Oil. Yield: 81%. ^1H NMR (300 MHz, $CDCl_3$): δ 7.99–8.04 (m, 1H), 7.36–7.60 (m, 7H), 4.09–4.30 (m, 4H), 1.33 (dt, $J_1 = 6.9$ Hz, $J_2 = 0.6$ Hz, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 134.27 (d, $J = 13.4$ Hz), 133.98 (d, $J = 10.0$ Hz), 133.79 (d, $J = 19.6$ Hz), 131.92 (d, $J = 3.1$ Hz), 131.79 (d, $J = 185.4$ Hz), 131.28, 128.62, 128.21, 123.94 (d, $J = 6.0$ Hz), 122.50, 95.32 (d, $J = 0.7$ Hz), 86.66 (d, $J = 6.3$ Hz), 62.32 (d, $J = 5.5$ Hz), 16.17 (d, $J = 6.7$ Hz); ^{31}P NMR (121 MHz, $CDCl_3$): δ 14.96; MS (EI): *m/z*: 348 (M^+, 100), 319 (19), 292 (30), 276 (48), 212 (17), 199 (23), 176 (46), 77 (11); IR (film, cm^{-1}): 2983, 2219, 1597, 1493, 1460, 1391, 1253, 1152, 1106, 1024, 972; HRMS (EI): Calcd for $C_{18}H_{18}ClO_3P$ (M^+): 348.06821. Found: 348.07295.

[5-Chloro-2-(4-ethyl-phenylethynyl)-phenyl]-phosphonic Acid Diethyl Ester **3f**. Oil. Yield: 83%. ^1H NMR (300 MHz, $CDCl_3$): δ 7.98–8.04 (m, 1H), 7.48–7.57 (m, 4H), 7.19–7.21 (m, 2H), 4.07–4.29 (m, 4H), 2.67 (q, $J = 7.5$ Hz, 2H), 1.33 (t, $J = 7.2$ Hz, 6H), 1.24 (dt, $J_1 = 7.5$ Hz, $J_2 = 1.2$ Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 145.34, 134.40 (d, $J = 6.6$ Hz), 134.03 (d, $J = 20.3$ Hz), 132.09 (d, $J = 2.8$ Hz), 131.81 (d, $J = 185.2$ Hz), 131.59 (d, $J = 5.5$ Hz), 131.51, 127.98, 124.41 (d, $J = 6.2$ Hz), 119.90, 95.84, 86.32, 62.52 (d, $J = 5.7$ Hz), 28.84, 16.31 (d, $J = 6.8$ Hz), 15.25; ^{31}P NMR (121 MHz, $CDCl_3$): δ 15.13; IR (film, cm^{-1}): 2968, 2218, 1512, 1461, 1390, 1253, 1152, 1025, 970; MS (EI): *m/z*: 376(M^+, 100), 347 (16), 319 (12), 287 (38), 239 (7), 189 (23), 105 (4), 77 (3); HRMS (EI): Calcd for $C_{20}H_{22}ClO_3P$ (M^+): 376.09951. Found: 376.09696.

[5-Chloro-2-(4-nitro-phenylethynyl)-phenyl]-phosphonic Acid Diethyl Ester **3g**. A red solid, mp: 123–124°C. Yield: 47%. ^1H NMR (300 MHz, $CDCl_3$): δ 8.24–8.28 (m, 2H), 7.99–8.05 (m, 1H), 7.55–7.75 (m, 4H), 4.09–4.30 (m, 4H), 1.34 (dt, $J_1 = 6.9$ Hz, $J_2 = 2.1$ Hz, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 146.36, 145.89 (d, $J = 17.4$ Hz), 133.96 (d, $J = 12.8$ Hz), 133.34, 132.57 (d, $J = 6.7$ Hz), 131.83 d, $J = 1.6$ Hz), 129.47 (d, $J = 204.2$ Hz), 129.08 (d, $J = 11.6$ Hz), 126.48 (d, $J = 1.9$ Hz), 119.05, 100.85, 86.24 (d, $J = 6.1$ Hz), 62.85 (d, $J = 6.1$ Hz), 28.79, 16.30 (d, $J = 6.3$ Hz), 15.16; ^{31}P NMR (121 MHz, $CDCl_3$): δ 17.03; MS (EI): *m/z*: 393 (M^+, 100), 365 (17), 337 (45), 321 (28), 273 (12), 244 (8), 210 (16), 199 (23), 163 (29), 105 (6), 77 (7); IR (KBr, cm^{-1}): 2981, 2323, 1593, 1456, 1340, 1249, 1106, 1043, 972; Anal. Calcd for $C_{18}H_{17}ClNO_5P$: C, 54.90; H, 4.35; N, 3.56. Found: C, 55.31; H, 4.25; N, 3.63.

[5-Chloro-2-(3-hydroxy-prop-1-ynyl)-phenyl]-phosphonic Acid Diethyl Ester **3h**. Oil. Yield: 78%. ^1H NMR (300 MHz, DMSO): δ 7.57–7.79 (m, 3H), 5.39 (t, $J = 6.0$ Hz, 1H), 4.33 (d, $J = 6.0$ Hz, 2H), 4.05–4.13 (m, 4H), 1.26 (t, $J = 6.9$ Hz, 6H); ^{31}P NMR (300 MHz, DMSO): δ 16.16; MS (EI): *m/z*: 302 (M^+, 7), 273 (7), 245 (24), 217 (49), 199 (25), 165 (10), 136 (21), 75 (11), 43 (100); IR (film, cm^{-1}): 3377, 2983, 2239, 1463, 1392, 1240, 1152, 1045, 1025, 953; Anal. Calcd for $C_{13}H_{16}ClO_4P$: C, 51.58; H, 5.34. Found: C, 51.76; H, 5.50.

[5-Chloro-2-(3-methoxy-prop-1-ynyl)-phenyl]-phosphonic Acid Diethyl Ester **3i**. Oil. Yield: 80%. ^1H NMR (300 MHz, $CDCl_3$): δ 7.92–7.98 (m, 1H), 7.42–7.52 (m, 2H), 4.36 (s, 2H), 4.08–4.24 (m, 4H), 3.48 (d. $J = 1.2$ Hz, 3H), 1.32 (t, $J = 7.2$ Hz, 6H); ^{31}P NMR (121 MHz, $CDCl_3$): δ 17.28; MS (EI): *m/z*: 316 (M^+, 2), 286 (62), 273 (5), 245 (39), 230 (100), 165 (9), 136 (16), 101 (10), 75 (7); IR (film, cm^{-1}): 2984, 2229, 1463, 1382, 1250, 1153, 1101, 1022, 963; Anal. Calcd for $C_{14}H_{18}ClO_4P$: C, 53.08; H, 5.74. Found: C, 53.02; H, 5.86.

(5-Chloro-2-trimethylsilanylethynyl-phenyl)-phosphonic Acid Diethyl Ester **3j**. Oil. Yield: 73%. ^1H NMR (300 MHz, $CDCl_3$): δ 7.94–8.00 (m, 1H), 7.41–7.53 (m, 2H), 4.04–4.26 (m, 4H), 1.35 (dt, $J_1 = 7.2$ Hz, $J_2 = 1.5$ Hz, 6H), 0.26 (d, $J = 2.4$ Hz, 9H); ^{31}P NMR (121 MHz, $CDCl_3$): δ 14.72; MS (EI): *m/z*: 344 (M^+, 10), 329 (40), 301 (6), 273 (100), 257 (13), 205 (5), 195 (16), 105 (1), 75 (25); IR (film, cm^{-1}): 2981, 2162, 1459, 1391, 1251, 1150, 1105, 1026, 973; Anal.

Calcd for $C_{15}H_{22}ClO_3P$: C, 52.24; H, 6.43. Found: C, 52.56; H, 6.69.

(5-Chloro-2-cyclopropylethynyl-phenyl)-phosphonic Acid Diethyl Ester **3k**. Oil. Yield: 79%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.88–7.95 (m, 1H), 7.39–7.41 (m, 2H), 4.04–4.25 (m, 4H), 1.43–1.52 (m, 1H), 1.36 (dt, $J_1 = 7.2$ Hz, $J_2 = 2.1$ Hz, 6H), 0.86–0.92 (m, 4H); ^{31}P NMR (121 MHz, $CDCl_3$): δ 17.95; MS (EI): *m/z*: 312 (M^+, 38), 283 (36), 255 (100), 237 (10), 220 (34), 175 (21), 139 (46), 99 (12), 75 (11); IR (film, cm^{-1}): 2983, 2234, 1464, 1383, 1249, 1152, 1025, 953; Anal. Calcd for $C_{15}H_{18}ClO_3P$: C, 57.60; H, 5.81. Found: C, 57.77; H, 6.05.

[2-(4-Ethyl-phenylethynyl)-5-nitro-phenyl]-phosphonic Acid Diethyl Ester **3l**. A yellow solid, mp: 72–74°C. Yield: 78%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.81–8.87 (m, 1H), 8.33–8.37 (m, 1H), 7.75–7.80 (m, 1H), 7.53–7.57 (m, 2H), 7.23–7.27 (m, 2H), 4.16–4.32 (m, 4H), 2.71 (q, $J = 7.5$ Hz, 2H), 1.36 (t, $J = 7.2$ Hz, 6H), 1.27 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 146.36, 145.89 (d, $J = 17.4$ Hz), 133.96 (d, $J = 12.8$ Hz), 133.34, 132.57 (d, $J = 6.7$ Hz), 131.83 (d, $J = 1.6$ Hz), 129.47 (d, $J = 204.2$ Hz), 129.08 (d, $J = 11.6$ Hz), 126.48 (d, $J = 1.9$ Hz), 119.05, 100.85, 86.24, 62.85 (d, $J = 6.1$ Hz), 28.79, 16.30 (d, $J = 6.3$ Hz), 15.16; ^{31}P NMR (121 MHz, $CDCl_3$): δ 16.11; MS (EI): *m/z*: 387 (M^+, 100), 358 (25), 330 (20), 300 (34), 221 (10), 189 (50), 143 (35), 105 (8); IR (KBr, cm^{-1}): 2968, 2211, 1597, 1515, 1385, 1343, 1255, 1145, 1020, 975; HRMS (EI): Calcd for $C_{20}H_{22}NO_5P$ ($M^+ + 1$): 388.13280. Found: 388.13084.

(5-Methoxy-2-phenylethynyl-phenyl)-phosphonic Acid Diethyl Ester **3m**. Oil. Yield: 79%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.53–7.60 (m, 4H), 7.33–7.35 (m, 3H), 7.01–7.05 (m, 1H), 4.09–4.26 (m, 4H), 3.86 (d. $J = 1.5$ Hz, 3H), 1.32 (t, $J = 6.9$ Hz, 6H); ^{31}P NMR (121 MHz, $CDCl_3$): δ 20.846; MS (EI): *m/z*: 344 (M^+, 100), 316 (11), 270 (15), 209 (5), 193 (4), 163 (14), 105 (6), 77 (3); IR (film, cm^{-1}): 2982, 1593, 1497, 1392, 1292, 1236, 1163, 1027, 971; Anal. Calcd for $C_{19}H_{21}O_4P$: C, 66.26; H, 6.16. Found: C, 66.20; H, 6.22.

[5-Methoxy-2-(3-hydroxy-prop-1-ynyl)-phenyl]-phosphonic Acid Diethyl Ester **3n**. Oil. Yield: 72%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38–7.47 (m, 2H), 6.96–7.00 (m, 1H), 4.48 (s, 2H), 4.13–4.21 (m, 4H), 3.84 (s, 3H), 3.50 (br s, 1H), 1.34 (t, $J = 7.2$ Hz, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 158.62 (d, $J = 17.9$ Hz), 134.97 (d, $J = 15.1$ Hz), 131.12 (d, $J = 187.3$ Hz), 118.57 (d, $J = 10.0$ Hz), 117.60 (d, $J = 2.8$ Hz), 117.30 (d, $J = 6.7$ Hz), 91.76, 82.81 (d, $J = 6.1$ Hz), 62.54 (d, $J = 5.6$ Hz), 55.34, 29.49, 16.21 (d, $J = 6.1$ Hz); ^{31}P NMR (121 MHz, $CDCl_3$): δ 16.47; MS (EI): *m/z*: 298 (M^+, 37), 269 (47), 241 (79), 213 (100), 195 (39), 161 (30), 77 (5); IR (film, cm^{-1}): 3404, 2985, 2239, 1598, 1479, 1394, 1296, 1146, 1026, 971; HRMS (EI): Calcd for $C_{14}H_{19}O_5P$ (M^+): 298.09786. Found: 298.09743.

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