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Efficient synthesis of mono- and diarylphosphinic acids: a microwave-assisted palladium-catalyzed cross-coupling of aryl halides with phosphinate

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ABSTRACT

A general, efficient method for the microwave-assisted synthesis of mono- and diarylphosphinic acids from anilinium phosphinate and aryl halides, using Pd(0) and Xantphos as a supporting ligand, was developed.

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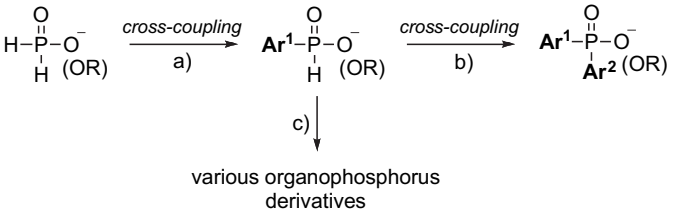
1. Introduction

Compounds containing mono- and diarylphosphinate structural motifs have attracted considerable attention in the recent years due to their various practical and scientific applications. The former include manufacturing of flame retardants,[1] advanced polymers[2] and membranes,[3] whereas the latter, construction of metal cation receptors[4,5] and peptidomimetics.[6–8] The resemblance to carboxylic group, and especially to tetrahedral intermediates formed during substitution at the sp^2-carbon, made arylphosphinates useful inhibitors in enzymatic studies[9] and efficient antagonists of biologically active carboxylic acids.[10–12] Phosphinates proved to be also superior transition state analogues for the preparation of catalytic antibodies,[13,14] and some arylphosphinates have been explored as potential therapeutics.[15]

Due to the presence of an active P–H bond, monoaryl-H-phosphinates can undergo an array of synthetically useful reactions, such as oxidation and oxidative couplings,[16] alkylation,[17] addition to carbonyl groups and imines,[18] hydrophosphinylation of multiple bonds,[19,20] or allylation[20] (Scheme 1, step c). Therefore, H-phosphinates represent versatile intermediates in the synthesis of various classes of arylated organophosphorus compounds.



Scheme 1. Synthesis of monoaryl- (a) and diarylphosphinates (b) via the cross-coupling reaction.

Apart from recent reports on copper-catalyzed reactions,[12,21] a method of choice for the synthesis of both monoaryl-H-phosphinates and diarylphosphinates remains palladium-catalyzed cross-coupling (Scheme 1).[22,23] The monoaryl derivatives are most conveniently prepared from anilinium phosphinate according to a protocol developed by Montchamp et al.,[24] but H,H-phosphinic esters can also be used as substrates (Scheme 1, step a).[4,6,23,25] In contrast to this, only on rare occasions have symmetrical diarylphosphinates been synthesized directly from H,H-phosphinates (i.e., Scheme 1, steps a and b, Ar^1=Ar^2),[5,7] and for the unsymmetrical diaryl derivatives, the reactions are much less efficient and the corresponding monoaryl-H-phosphinate have to be prepared in advance.[5,6,14,26] As far as supporting ligands for palladium are concerned, PPh_3 was used in the great majority of cases,[22–24] and other ligands were only briefly investigated.[23,24]

Recently, we have developed a very efficient procedure for cross-coupling of H-phosphonate diesters with aryl halides, under microwave irradiation.[27] Encouraged by this, and the fact that only one instance of a microwave-assisted cross-coupling of H-phosphinate with aryl triflate[12] has been described in literature, we set out to explore microwave conditions for the C–P bond formation. One should note that microwave heating seems to be perfectly suited for coupling of phosphinate salts, since as ionic species they are expected to absorb very efficiently microwave energy via a conduction mechanism.[28] With the advent of large sealed vessels[29] and automated stop-flow microwave reactors,[30] permitting direct scale-up (>1 kg) without reoptimization of the reaction conditions, microwave energy starts to become a viable alterative to conventional heating under laboratory and industrial settings.

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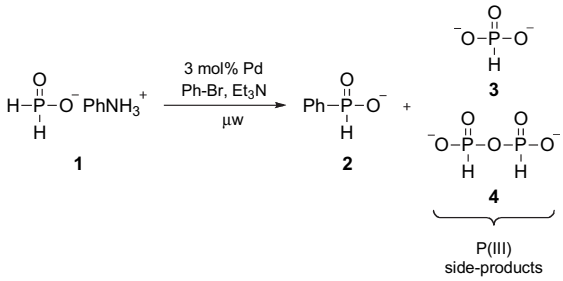
Herein, we present a systematic study on the reaction conditions for the microwave-assisted synthesis of mono-, as well as symmetrical and unsymmetrical diarylphosphinates with diverse structural features.

2. Results and discussion

We started our investigations by examining a number of common ligands for their efficiency to promote a cross-coupling between model substrates, namely bromobenzene and anilinium phosphinate **1** (Scheme 2). All experiments were performed in sealed pressure proof microwave vessels, in THF under an inert gas atmosphere, with 3 mol % palladium catalyst and triethylamine as a base. The composition of the reaction mixtures was determined by ^{31}P NMR spectroscopy after 5 min heating at 120 °C (Table 1). In addition to the starting material **1** and product **2**, in several cases signals originating from H-phosphonate (**3**) and H-pyrophosphonate (**4**) could be observed in the NMR spectra (Scheme 2). These undesired P(III) side-products were formed, most likely, due to reduction of bromobenzene to benzene via transfer hydrogenation.[24]



Scheme 2. A model reaction used for screening of the reaction conditions.

The catalyst most frequently used under thermal conditions, $Pd(PPh_3)_4$, did not produce the desired phosphinate **2**, but only oxidation products **3** and **4** (Table 1, Entry 3). Also Pd(0) with other monodentate ligands (Entries 8, 9, 12) seemed to favour transfer hydrogenation rather than cross-coupling. Among the ligands investigated, only bidentate ligands promoted synthesis of the phosphinate **2**, and the highest conversion (95%) was observed for the reaction with Xantphos (entry 11).[31]

Table 1
Ligand screening[a,b]

Entry	Catalyst[c]	Substrate **1**[d] (%)	Product **2**[d] (%)	By-products **3** &**4**[d] (%)
1	None	100	nd[e]	nd
2	$Pd_2(dba)_3{\cdot}CHCl_3$	77	nd	23
3	$Pd(PPh_3)_4$	76	nd	24
4	dppp	35	47	18
5	dppb	80	20	nd
6	dppf	14	86	nd
7	BINAP	59	24	17
8	PCy_3	83	nd	17
9	$PtBu_3$	85	nd	15
10	DPEPhos	23	50	27
11	Xantphos	3	95	2
12	IMes·HCl	77	nd	23

[a] Reaction conditions: 0.25 mmol **1**, 1.0 equiv Ph–Br, 2.5 equiv Et_3N, 3 mol % Pd catalyst and 3 mol % of the appropriate ligand (Entries 4–12) in 1 mL THF; after initial heating at 300 W, the power was adjusted to maintain the reaction temperature at 120 °C for 5 min.
[b] The full list of the tested ligands, together with ligands structures can be found in Supplementary data.
[c] In Entries 4–12 $Pd_2(dba)_3{\cdot}CHCl_3$ was used as the palladium source.
[d] Determined by ^{31}P NMR.
[e] nd=Not detected.

The fact that other wide-bite-angle ligands, e.g., dppf (Entry 6) and to smaller extent dppp and DPEPhos (Entries 4 and 10, respectively), also provided good conversions to **2**, might suggest that the reductive elimination was a turnover-limiting step of the catalytic cycle.[32] Nevertheless, one cannot exclude the importance of an attack of the phosphorus nucleophile on palladium(II) complexes (the ligand exchange process), that was found to be crucial for the overall rate of cross-couplings involving H-phosphonate diesters.[33] This step can be facilitated by ligands distorting the square planar geometry of the palladium(II) complex[34] and will be subject of separate investigations.

Next, we evaluated various solvents as reaction media for the cross-coupling reaction in Scheme 2. In order to observe clear differences between the solvents, the reaction time was shortened to 2 min, while keeping the catalyst load unchanged (3 mol %). For most solvents investigated, except acetone and dioxane (Table 2, Entries 2 and 3), the transfer hydrogenation was not the issue when standard microwave heating mode was applied (see Table 2, footnote [a]). However, significant differences in coupling rates in various solvents were observed, and only for THF (Entry 9), did a quantitative conversion to **2** occurred within 2 min, at 120 °C. For the sake of comparison, we carried out also an analogous cross-coupling reaction at 100 °C using an ordinary oil bath heating (Entry 11). Since this led to the result comparable to that of using microwave irradiation at the same temperature (Entry 10), probably, the acceleration of cross-coupling reactions by microwave heating has mostly thermal basis as predicted by the Arrhenius equation (but vide infra).

Table 2
Solvent and heating mode screening[a]

Entry	Solvent	Temperature (°C)	Substrate **1**[b] (%)	Product **2**[b] (%)	P(III) side-prod.[b] (%)
1	Toluene	120	18	82	nd[c]
2	Acetone	120	20	49	31
3	1,4-dioxane	120	46	37	16
4	MeCN	120	97	3	nd
5	DMF	120	23	77	nd
6	*i*PrOH	120	100	nd	nd
7	EtOH	120	76	24	nd
8	MeOH	120	65	35	nd
9	THF	120	nd	100	nd
10	THF	100	25	75	nd
11[d]	THF	100	36	64	nd
12[e]	THF	100	nd	64	31

[a] Reaction conditions: 0.25 mmol **1**, 1.0 equiv Ph–Br, 2.5 equiv Et_3N, 1.5 mol % $Pd_2(dba)_3{\cdot}CHCl_3$, 3 mol % Xantphos, 1 mL THF. Except for Entries 11 and 12, after initial heating at 300 W, the power was adjusted to maintain the reaction mixture at indicated temperature for 2 min.
[b] Determined by ^{31}P NMR.
[c] Not detected.
[d] Bromobenzene was added to the reaction mixture preheated to 100 °C in an oil bath, and this temperature was maintained for 2 min.
[e] After initial heating at 300 W, the reaction vessel was simultaneously cooled with a stream of air and heated with the power adjusted to maintain the reaction temperature at 100 °C for 2 min.

To find out if there was any microwave specific effect involved, we carried out an experiment in which we cooled the reaction vessel during irradiation. Under standard mode of irradiation, due to efficient absorption of microwaves by the reaction mixtures, only a minimal microwave power was required to maintain a high temperature of the sample. Heating with a simultaneous cooling increased exposure to microwave irradiation, since much higher power had to be administered to the sample to keep the temperature constant.[35] Application of such a heating mode resulted in a full conversion of the starting material even at 100 °C within 2 min (Entry 12), but unfortunately the transfer hydrogenation became a prominent reaction pathway under such conditions. This may indicate some microwave specific effect that promotes the transfer hydrogenation via thermal activation of selected chemical bonds.

Table 3
Microwave-assisted synthesis of monoarylphosphinic acids[a]

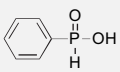
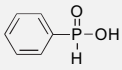
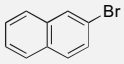
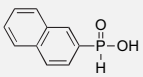
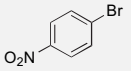
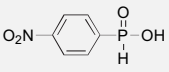
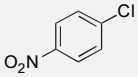
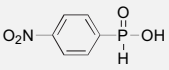
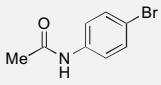
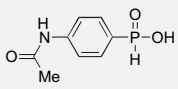
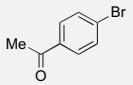
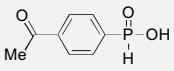
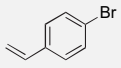
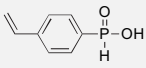
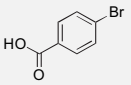
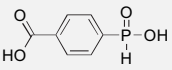
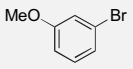
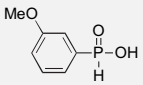
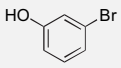
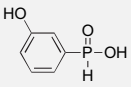
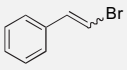
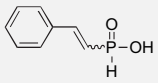
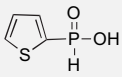
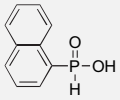
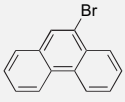
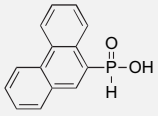
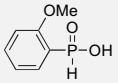
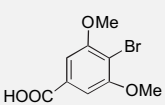
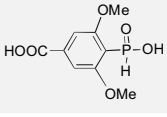
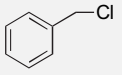
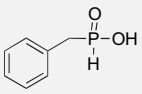
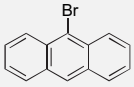
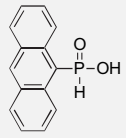
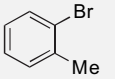
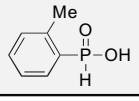
Entry	Aryl halide	Product	Prod no.	Pd (mol %)	Yield[b] (%)
1			**5**	0.1	92
2			**5**	0.1	95
3			**6**	0.1	90
4			**7**	0.1	86
5			**7**	1.0	42
6			**8**	0.1	79
7			**9**	0.1	84
8			**10**	0.1	91
9[c]			**11**	0.1	81
10			**12**	0.1	89
11			**13**	0.1	83
12[d]			**14**	0.1	89
13			**15**	0.1	73
14			**16**	1.0	73
15			**17**	1.0	78
16			**18**	1.0	84
17[c]			**19**	1.0	80

Table 3 (*continued*)

Entry	Aryl halide	Product	Prod no.	Pd (mol %)	Yield[b] (%)
18			**20**	1.0	69
17			**21**	5.0	82
18			**22**	5.0	87

[a] Reaction conditions: 1.25 mmol **1**, 1.0 equiv Ar-X, 2.5 equiv Et_3N, Pd/Xantphos ratio=1, 5 mL THF; after initial heating at 300 W, the power was adjusted to maintain the reaction temperature at 120 °C for 10 min.
[b] Isolated yield.
[c] 3.5 equiv Et_3N was used.
[d] Commercial β-bromostyrene (*Z*/*E* 1:9) was used, producing mixture of phosphinic acids (in analogous *Z*/*E* ratio).

The scope of the microwave-assisted cross-coupling of anilinium phosphinate (**1**) with aryl halides to form monoarylphosphinic acids was investigated in THF using Pd-Xantphos catalyst system and triethylamine as a base (Table 3 and Scheme 3).

Scheme 3. Microwave-assisted synthesis of monoarylphosphinic acids.

The reactivity of aryl halides strongly depended on the steric factors and for more hindered starting materials (*ortho* substituted aryls), higher catalyst loading was required (Entries 14–18). In contrast to bromides, only activated aryl chlorides (Entry 5) underwent coupling with phosphinate **1**, but a higher catalyst load was required. In this instance (Entry 5) a noticeable lower yield was due to extensive transfer hydrogenation.

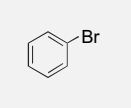
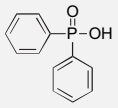
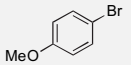
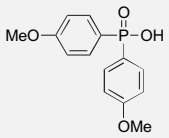
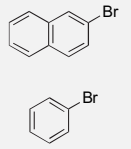
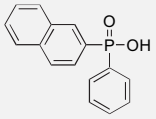
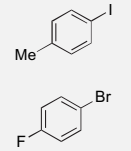
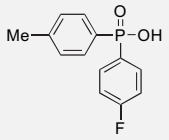
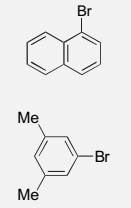
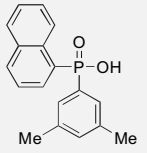
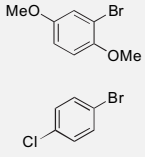
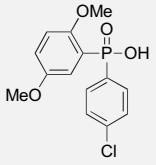
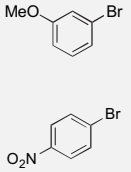
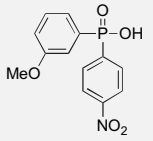
A broad spectrum of functional groups, both electron-withdrawing and electron-donating, was tolerated under this set of the reaction conditions. Notably, double bonds (Entry 7) were found to be compatible with the reaction conditions, even that a similar catalytic system [$Pd_2(dba)_3$+Xantphos] was earlier reported to promote hydrophosphinylation of alkenes.[36]

Also vinyl bromide[11] (Entry 12), 2-bromothiophene (Entry 13), and benzyl chloride (Entry 18) underwent smooth coupling with phosphinate **1** affording in good yields the corresponding phosphinates. In all instances, excellent selectivity was observed for the formation of monoaryl- over the diarylphosphinates. This feature enabled isolation of pure phosphinic acids **5**–**22** in good yields, via a simple extractive work-up.

Next, we investigated a possibility of diarylphosphinate synthesis (Scheme 4 and Table 4).

Scheme 4. Microwave-assisted synthesis of diarylphosphinic acids.

Table 4
Microwave-assisted synthesis of diarylphosphinic acids[a]

Entry	Aryl halide(s)	Product	Prod. no.	Pd (mol %)	Time (min)	Yield[b] (%)
1			**23**	2.0	15	85
2			**24**	2.0	15	89
3			**25**	0.1 2.0	10 15	83
4			**26**	0.1 2.0	10 15	79
5			**27**	1.0 3.0	10 15	81
6			**28**	1.0 3.0	10 15	86
7			**29**	0.1 2.0	10 15	76

[a] Reaction conditions: entries 1 and 2: 1.25 mmol **1**, 2.5 equiv Ar-X, 3.5 equiv Et_3N, Pd/Xantphos ratio=1, 5 mL THF; Entries 3–7: first coupling: 1.25 mmol **1**, 1.0 equiv Ar^1-X, 2.5 equiv Et_3N, Pd/Xantphos ratio=1, 5 mL THF, followed by extractive work-up, second coupling: 1.5 equiv Ar^1-X, 2.5 equiv Et_3N, Pd/Xantphos ratio=1, 5 mL THF. After initial heating at 300 W, the power was adjusted to maintain the reaction temperature at 120 °C for the time indicated for each step of the reaction.
[b] Isolated yield.

The initial experiments showed that the second coupling step (Scheme 1, step b) was much more difficult to accomplish than the attachment of the first aryl moiety (Scheme 1, step a). The most likely reason for this seemed to be reduced nucleophilicity of arylphosphinates (steric hindrance), and pointed to the importance of the ligand substitution step. To remedy this problem, higher catalyst loading and prolonged reaction times were used in the second coupling step to obtain diarylphosphinic acids in good yields (Table 4).

Under these conditions various diarylphosphinic acids without *ortho* substituents in the aromatic ring (Table 4, Entries 1–4 and 7) or bearing one *ortho* substituted aryl group (Table 4, Entries 5 and 6), were synthesized.

The symmetrical diaryl derivatives (Table 4, Entries 1 and 2) could always be obtained in high purity, just by using 2.5 equiv of the appropriate aryl halide for the reaction, followed by the extractive work-up. However, attempted one-pot synthesis of unsymmetrical phosphinic acids (e.g., Entries 4–7), by sequential addition of different aryl halides, resulted in products contaminated with symmetrical derivatives (up to 15%). Since purification of these compounds posed some problems due to their ionic nature,[37] we decided to carry out the reactions in a stepwise manner, with extractive isolation of the intermediate monoaryl phosphonic acid. Such a strategy appeared to be successful and unsymmetrical diaryl derivatives **25**–**29** could be obtained in high yields and in purity >98% (^{1}H NMR spectroscopy).

3. Conclusions

We have developed a convenient and general method for the microwave-assisted synthesis of mono- and diarylphosphinic acids catalyzed by Pd(0) and Xantphos as a supporting ligand. The procedure is highly efficient and provides a rapid access to a broad spectrum of arylphosphinate derivatives. A large range of aryl halides can be phosphinylated using 0.1 mol % of palladium, and only for sterically hindered aryl halides, the load of the catalyst has to be higher (up to 5%). Also, unsymmetrical diarylphosphinic acids could be for the first time efficiently synthesized using the developed reaction conditions.

4. Experimental section

4.1. General

All reagents were of analytical grade, obtained from commercial suppliers and used without further purification. Anilinium phosphinate **1** was obtained according to the published procedure.[24] THF, DMF, and toluene were dried using VAC solvent purifier system, and the other solvents used for the reactions were degassed by passing N_2 for 20 min. All reactions were carried out using standard Schlenk techniques.

The reactions involving microwave irradiation were conducted under N_2 atmosphere in heavy-walled glass Smith process vials sealed with aluminium crimp caps fitted with a silicon septum. The screening experiments and preparative reactions were carried out using conical 2 mL and round-bottom 5 mL vials, respectively. The microwave heating was performed in a SmithCreator single-mode microwave cavity, producing continuous irradiation of maximum 300 W at 2450 MHz (Personal Chemistry AB, Uppsala, Sweden). The reaction mixtures were stirred with a magnetic stirring bar during the irradiation.

The NMR spectra were recorded using Bruker Avance II 400 MHz instrument. The chemical shifts are reported in ppm, relative to solvent peaks (^{1}H, ^{13}C) and 2% H_3PO_4 solution in D_2O (^{31}P NMR). Assignment of the NMR signals was accomplished on the basis of 2D correlation experiments (COSY, HSQC) and DEPT spectra. High resolution mass spectra (HRMS) were recorded on Bruker MicrOTOF ESI-TOF mass spectrometer. Infrared spectra were recorded on Perkin Elmer Spectra One FTIR spectrometer.

4.2. General procedure for the synthesis of monoarylphosphinic acids 5–22

$Pd_2(dba)_3 \cdot CHCl_3$ (0.05–2.5 mol %), Xantphos (0.1–5 mol %), solid aryl halide (1.25 mmol), and anilinium phosphinate[24] (199 mg, 1.25 mmol) were placed in the microwave tube. The tube was sealed with a lid and filled with N_2, by applying three cycles of vacuum, followed by N_2. THF was introduced via the septum (5 mL), followed by liquid aryl halide (1.25 mmol) and triethylamine (432 μL, 316 mg, 3.125 mmol). The tube was then heated in the microwave oven for

10 min at 120 °C. After cooling down, the solvent was evaporated and the residue partitioned between 1 M aq NaOH (20 mL) and ether (20 mL). The organic phase was extracted two more times with 1 M aq NaOH (2×15 mL). The combined aqueous extracts were acidified with conc aq HCl (11 mL), and the resulting solution saturated with NaCl (8 g). The mixture was extracted three times with ethyl acetate (20 mL), and the combined organic extracts were dried with Na_2SO_4. Evaporation of the solvent and drying under high vacuum yielded products **5–22** of purity >95% (^{31}P NMR).

4.3. General procedure for the synthesis of symmetrical diarylphosphinic acids 23 and 24

A procedure similar to that for the preparation of monoarylphosphinic acids was applied, except that 2.5 equiv of the appropriate aryl halide (3.125 mmol), 3.5 equiv of triethylamine (605 μL, 442 mg, 4.375 mmol) and 15 min irradiation time were used.

4.4. General procedure for the synthesis of unsymmetrical diarylphosphinic acids 25–29

A procedure analogous to that for the preparation of monoarylphosphinic acids was used for the first coupling. After isolation of the monoarylphosphinic acid by extraction (see above) it was directly subjected to the second coupling reaction according to the same protocol, except that 1.5 equiv of the appropriate aryl halide (1.875 mmol) and 15 min irradiation time were used.

*4.4.1. Phenylphosphinic acid (**5**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.70 (2H, m, H2, H6), 7.62 (1H, ~tq, H4, $J_{4-3/5}$=7.2 Hz, $J_{4-6/2}$=$J_{4\text{-}P}$=1.6 Hz), 7.54 (2H, m, H3, H5), 7.48 (1H, d, *H*-P, $J_{H\text{-}P}$=548 Hz), 6.93 (b, 'PO*H*'). ^{13}C NMR (100 MHz, DMSO-d_6): δ 133.8 (d, C1, *J*=128 Hz), 132.3 (d, C4, *J*=2.6 Hz), 130.1 (d, C2, C6, *J*=11.8 Hz), 128.7 (d, C3, C5, *J*=13.3 Hz). ^{31}P NMR (162 MHz, DMSO-d_6): δ 16.5 (dt, $J_{P\text{-}H}$=548 Hz, $J_{P\text{-}2/6}$=13.6 Hz). HRMS: *m*/*z* 141.0136 ([M-H]$^-$, $C_6H_6O_2P^-$ calcd 141.0111). This compound is commercially available.

*4.4.2. Naphtalene-2-ylphosphinic acid (**6**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.35 (1H, d, H1, $J_{1\text{-}P}$=15.6 Hz), 8.10 (1H, d, H8, J_{8-7}=8.2 Hz), 8.06 (1H, dd, H4, J_{4-3}=8.4 Hz, $J_{4\text{-}P}$=3.1 Hz), 8.00 (1H, d, H5, J_{5-6}=7.9 Hz), 7.74 (1H, ddd, H3, $J_{3\text{-}P}$=11.4 Hz, J_{3-4}=8.4 Hz, J_{3-1}=1.3 Hz), 7.66 (1H, ~t, H6, J_{6-5}~8.0 Hz), 7.63 (1H, d, *H*-P, $J_{H\text{-}P}$=548 Hz), 7.62 (1H, ~t, H7, $J_{7-6/8}$~8.2 Hz). ^{13}C NMR (100 MHz, DMSO-d_6): δ 134.4 (d, C4a, *J*=2.3 Hz), 132.0 (d, C8a, *J*=14.8 Hz), 131.7 (d, C1, *J*=11.8 Hz), 131.2 (d, C2, *J*=128 Hz), 128.8 (C8), 128.3 (d, C4, *J*=13.1 Hz), 128.2 (C6), 127.8 (C5), 127.0 (C7), 125.4 (d, C3, *J*=11.8 Hz). ^{31}P NMR (162 MHz, DMSO-d_6): δ 16.4 (dt, $J_{P\text{-}H}$=548 Hz, $J_{P\text{-}1/3}$~13 Hz). HRMS: *m*/*z* 191.0274 ([M-H]$^-$, $C_{10}H_8O_2P^-$ calcd 191.0267). Known compound.[24]

*4.4.3. 4-Nitrophenylphosphinic acid (**7**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.35 (2H, dd, H3, H5, $J_{3/5-2/6}$=8.7 Hz, $J_{3/5\text{-}P}$=2.0 Hz), 7.97 (2H, dd, H2, H6, $J_{2/6\text{-}P}$=12.7 Hz, $J_{2/6-3/5}$=8.7 Hz), 7.57 (1H, d, *H*-P, $J_{H\text{-}P}$=563 Hz). ^{13}C NMR (100 MHz, DMSO-d_6): δ 149.7 (d, C4, *J*=2.8 Hz), 141.0 (d, C1, *J*=124 Hz), 131.7 (d, C2, C6, *J*=12.5 Hz), 123.5 (d, C3, C5, *J*=14.0 Hz). ^{31}P NMR (162 MHz, DMSO-d_6): δ 13.37 (dt, $J_{P\text{-}H}$=563 Hz, $J_{P\text{-}2/6}$=12.7 Hz). HRMS: *m*/*z* 185.9967 ([M-H]$^-$, $C_6H_5NO_4P^-$ calcd 185.9962). Known compound.[24]

*4.4.4. 4-Acetamidophenylphosphinic acid (**8**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.24 (1H, s, N*H*), 9.56 (b, 'PO*H*'), 7.74 (2H, dd, H3, H5, $J_{3/5-2/6}$=8.4 Hz, $J_{3/5\text{-}P}$=2.3 Hz), 7.63 (2H, dd, H2, H6, $J_{2/6\text{-}P}$=12.8 Hz, $J_{2/6-3/5}$=8.4 Hz), 7.45 (1H, d, *H*-P, $J_{H\text{-}P}$=546 Hz), 2.07 (3H, s, C*H*$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.0 (*C*═O), 142.8 (d, C4, *J*=2.9 Hz), 131.3 (d, C2, C6, *J*=12.6 Hz), 127.4 (d, C1, *J*=133 Hz), 118.5 (d, C3, C5, *J*=13.6 Hz), 24.2 (*C*H$_3$). ^{31}P NMR (162 MHz, DMSO-d_6): δ 16.2 (dt, $J_{P\text{-}H}$=546 Hz, $J_{P\text{-}2/6}$=12.8 Hz). ν_{max} (KBr): 3675–3382 (br), 3184, 2379, 1662, 1634, 1156, 985 cm^{-1}. HRMS: *m*/*z* 198.0316 ([M-H]$^-$, $C_8H_9NO_3P^-$ calcd 198.0326).

*4.4.5. 4-Acetylphenylphosphinic acid (**9**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.05 (b, 'PO*H*'), 8.07 (2H, dd, H3, H5, $J_{3/5-2/6}$=8.1 Hz, $J_{3/5\text{-}P}$=2.2 Hz), 7.84 (2H, dd, H2, H6, $J_{2/6\text{-}P}$=13.0 Hz, $J_{2/6-3/5}$=8.1 Hz), 7.53 (1H, d, *H*-P, $J_{H\text{-}P}$=554 Hz), 2.62 (3H, s, C*H*$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ 197.9 (*C*═O), 139.4 (d, C4, *J*=2.7 Hz), 138.4 (d, C1, *J*=125 Hz), 130.5 (d, C2, C6, *J*=11.9 Hz), 128.1 (d, C3, C5, *J*=13.2 Hz), 27.0 (*C*H$_3$). ^{31}P NMR (162 MHz, DMSO-d_6): δ 15.3 (dt, $J_{P\text{-}H}$=554 Hz, $J_{P\text{-}2/6}$=13.0 Hz). HRMS: *m*/*z* 183.0222 ([M-H]$^-$, $C_8H_8O_3P^-$ calcd 183.0217). Known compound.[24]

*4.4.6. 4-Vinylphenylphosphinic acid (**10**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.73–7.58 (4H, m, H2, H3, H5, H6), 7.47 (1H, d, *H*-P, $J_{H\text{-}P}$=549 Hz), 6.79 (1H, dd, Hα, $J_{α\text{-}β1}$=17.8 Hz, $J_{α\text{-}β2}$=10.9 Hz), 5.98 (1H, d, Hβ1, $J_{β1\text{-}α}$=17.8 Hz), 5.40 (1H, d, Hβ2, $J_{β2\text{-}α}$=10.9 Hz). ^{13}C NMR (100 MHz, DMSO-d_6): δ 140.7 (d, C4, *J*=3.0 Hz), 135.9 (Cα), 133.1 (d, C1, *J*=130 Hz), 130.6 (d, C2, C6, *J*=11.9 Hz), 126.2 (d, C3, C5, *J*=13.7 Hz), 116.9 (Cβ). ^{31}P NMR (162 MHz, DMSO-d_6): δ 16.0 (dt, $J_{P\text{-}H}$=549 Hz, $J_{P\text{-}2/6}$=11.6 Hz). ν_{max} (KBr): 3672–3185 (br), 2616, 2155, 1690, 1181, 1105, 972 cm^{-1}. HRMS: *m*/*z* 167.0246 ([M-H]$^-$, $C_8H_8O_2P^-$ calcd 167.0267).

*4.4.7. 4-Hydroxyphosphinoyl-benzoic acid (**11**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.08 (2H, dd, H2, H6, $J_{2/6-3/5}$=8.3 Hz, $J_{2/6\text{-}P}$=2.8 Hz), 7.82 (2H, dd, H3, H5, $J_{3/5\text{-}P}$=13.1 Hz, $J_{3/5-2/6}$=8.3 Hz), 7.53 (1H, d, *H*-P, $J_{H\text{-}P}$=554 Hz). ^{13}C NMR (100 MHz, DMSO-d_6): δ 166.7 (*C*═O), 138.3 (d, C4, *J*=124 Hz), 134.0 (d, C1, *J*=3.0 Hz), 130.4 (d, C3, C5 *J*=12.6 Hz), 129.3 (d, C2, C6, *J*=13.3 Hz). ^{31}P NMR (162 MHz, DMSO-d_6): δ 15.4 (d, $J_{P\text{-}H}$=554 Hz). HRMS: *m*/*z* 185.0013 ([M-H]$^-$, $C_7H_6O_4P^-$ calcd 185.0009). Known compound.[24]

*4.4.8. 3-Methoxyphenylphosphinic acid (**12**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.46 (1H, d, *H*-P, $J_{H\text{-}P}$=548 Hz), 7.46 (1H, td, H5, $J_{5-4/6}$=7.7 Hz, $J_{5\text{-}P}$=4.1 Hz), 7.27 (1H, ddt, H6, $J_{6\text{-}P}$=13.2 Hz, J_{6-5}=7.7 Hz, $J_{6-2/4}$~1.0 Hz), 7.21 (1H, m, H2), 7.17 (1H, m, H4), 5.46 (b, 'PO*H*'), 3.81 (3H, s, C*H*$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.1 (d, C3, *J*=16.5 Hz), 135.4 (d, C1, *J*=127 Hz), 130.1 (d, C5, *J*=15.2 Hz), 122.1 (d, C6, *J*=11.3 Hz), 118.1 (d, C4, *J*=3.0 Hz), 114.8 (d, C2, *J*=13.5 Hz), 55.3 (*C*H$_3$). ^{31}P NMR (162 MHz, DMSO-d_6): δ 16.2 (~dt, $J_{P\text{-}H}$=548 Hz, $J_{P\text{-}2/6}$~14.0 Hz). ν_{max} (KBr): 2384, 1596, 1486, 1421, 1256, 1187, 972 cm^{-1}. HRMS: *m*/*z* 171.0230 ([M-H]$^-$, $C_7H_8O_3P^-$ calcd 171.0217).

*4.4.9. 3-Hydroxyphenylphosphinic acid (**13**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.84 (1H, b, O*H*), 7.40 (1H, d, *H*-P, $J_{H\text{-}P}$=547 Hz), 7.34 (1H, td, H5, $J_{5-4/6}$=7.9 Hz, $J_{5\text{-}P}$=4.2 Hz), 7.16–7.04 (2H, m, H2, H6), 6.97 (1H, m, H4), 5.16 (b, 'PO*H*'). ^{13}C NMR (100 MHz, DMSO-d_6): δ 157.4 (d, C3, *J*=17.0 Hz), 135.0 (d, C1, *J*=128 Hz), 130.0 (d, C5, *J*=15.4 Hz), 120.5 (d, C6, *J*=11.7 Hz), 119.2 (d, C4, *J*=2.6 Hz), 116.4 (d, C2, *J*=12.4 Hz). ^{31}P NMR (162 MHz, DMSO-d_6): δ 16.26 (dtd, $J_{P\text{-}H}$=547 Hz, $J_{P\text{-}2/6}$=13.7 Hz, $J_{P\text{-}5}$=4.2 Hz). ν_{max} (KBr): 3741–2974 (br), 2375, 1595, 1437, 1162, 987 cm^{-1}. HRMS: *m*/*z* 157.0074 ([M-H]$^-$, $C_6H_8O_3P^-$ calcd 157.0060).

*4.4.10. (E)-Styrylphosphinic acid (**14**).* Contaminated with ~10% of the *Z*-isomer. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.65 (2H, m, H3, H5), 7.45–7.38 (3H, m, H2, H6, H4), 7.30 (1H, dd, Hα, $J_{α\text{-}P}$=23.3 Hz, $J_{α\text{-}β}$=17.8 Hz), 7.23 (1H, d, *H*-P, $J_{H\text{-}P}$=544 Hz), 6.67 (1H, ~t, Hβ, $J_{β\text{-}P}$=19.6 Hz, $J_{β\text{-}α}$=17.8 Hz), 5.27 (b, 'PO*H*'). ^{13}C NMR (100 MHz, DMSO-d_6): δ 145.5 (d, Cα, *J*=7.8 Hz), 134.9 (d, C1, *J*=21.5 Hz), 130.1 and 128.9 (C2, C6, C4), 127.8 (C3, C5), 121.4 (d, Cβ, *J*=127 Hz). ^{31}P NMR (162 MHz, DMSO-d_6): δ 16.4 (ddd, $J_{P\text{-}H}$=544 Hz, $J_{P\text{-}α}$=23.3 Hz, $J_{P\text{-}β}$=19.6 Hz). ν_{max} (KBr): 3711–3177 (br), 2384, 1615, 1450, 1179, 981 cm^{-1}. HRMS: *m*/*z* 167.0275 ([M-H]$^-$, $C_8H_8O_2P^-$ calcd 167.0267).

*4.4.11. Thiophen-2-ylphosphinic acid (**15**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.19 (b, 'PO*H*'), 8.01 (1H, td, H5, $J_{5\text{-}P}$=J_{5-4}=4.6 Hz,

J_{5-3}=0.9 Hz), 7.59 (1H, d, *H*-P, J_{H-P}=569 Hz), 7.58 (1H, ddd, H3, J_{3-P}=8.1 Hz, J_{3-4}=3.5 Hz, J_{3-5}=0.9 Hz), 7.26 (1H, ddd, H4, J_{4-5}=4.6 Hz, J_{4-3}=3.5 Hz, J_{4-5}=0.9 Hz). ^{13}C NMR (100 MHz, DMSO-d_6): δ 135.1 (d, C3, J=12.5 Hz), 135.0 (d, C2, J=138 Hz), 133.9 (d, C5, J=6.3 Hz), 128.5 (d, C4, J=15.7 Hz). ^{31}P NMR (162 MHz, DMSO-d_6): δ 6.2 (d, J_{P-H}=569 Hz). ν_{max} (KBr): 3681–3224 (br), 3099, 2383, 1407, 1185, 1108, 964 cm^{-1}. HRMS: *m*/*z* 146.9812 ([M-H]$^-$, $C_4H_4O_2PS^-$ calcd 146.9675).

*4.4.12. Naphtalene-1-ylphosphinate (**16**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.49 (1H, d, H8, J_{8-7}=8.6 Hz), 8.16 (1H, d, H4, J_{4-3}=8.5 Hz), 8.04 (1H, d, H5, J_{5-6}=7.8 Hz), 7.96 (1H, dd, H2, J_{2-P}=18.2 Hz, J_{2-3}=6.7 Hz), 7.83 (1H, d, *H*-P, J_{H-P}=549 Hz), 7.69–7.59 (3H, m, H3, H6, H7). ^{13}C NMR (100 MHz, DMSO-d_6): δ 133.0 (d, J=9.4 Hz) and 131.7 (d, J=10.0 Hz) (C4a, C8a), 132.6 (d, C4, J=2.8 Hz), 130.4 (d, C2, J=13.7 Hz), 130.3 (d, C1, J=126 Hz), 128.9 (C5), 127.2 and 126.6 (C6, C7), 125.3 (d, C8, J=7.3 Hz), 125.0 (d, C3, J=15.7 Hz). ^{31}P NMR (162 MHz, DMSO-d_6): δ 18.4 (dd, J_{P-H}=548 Hz, J_{P-2}=18.2 Hz). HRMS: *m*/*z* 191.0265 ([M-H]$^-$, $C_{10}H_8O_2P^-$ calcd 191.0267). Known compound.[24]

*4.4.13. Phenathrene-9-ylphosphinate (**17**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.93 (1H, d, J=7.6 Hz) and 8.89 (1H, d, J=8.7 Hz) (H4, H5), 8.55 (1H, d, H8, J_{8-7}=7.7 Hz), 8.38 (1H, d, H10, J_{10-P}=20.2 Hz), 8.15 (1H, d, H1, J_{1-2}=7.8 Hz), 7.89 (1H, d, *H*-P, J_{H-P}=553 Hz), 7.83–7.70 (4H, m, H2, H3, H6, H7). ^{13}C NMR (100 MHz, DMSO-d_6): δ 132.9 (d, C10, J=14.4 Hz), 131.2 (d, C4a, J=2.2 Hz), 129.9 (d, C8a, J=9.0 Hz), 129.8 (C1), 129.6 (d, J=16.8 Hz) and 129.3 (d, J=10.2 Hz) (C4b, C10a), 129.2 (C7), 129.2 (d, C9, $J\sim$125 Hz), 127.5, 127.4 and 127.3 (C2, C3, C6), 126.3 (d, C8, J=6.6 Hz), 123.7 and 123.0 (C4, C5). ^{31}P NMR (162 MHz, DMSO-d_6): δ 19.7 (dd, J_{P-H}=553 Hz, J_{P-10}=20.2 Hz). ν_{max} (KBr): 3668–3219 (br), 1619, 1448, 1073, 998 cm^{-1}. HRMS: *m*/*z* 241.0401 ([M-H]$^-$, $C_{14}H_{10}O_2P^-$ calcd 241.0424).

*4.4.14. 2-Methoxyphenylphosphinic acid (**18**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.1 (b, 'PO*H*'), 7.62 (1H, ddd, H6, J_{6-P}=14.3 Hz, J_{6-5}=7.3 Hz, J_{6-4}=1.7 Hz), 7.56 (1H, ~t, H4, $J_{4-3/5}$=8.0 Hz), 7.50 (1H, d, *H*-P, J_{H-P}=562 Hz), 7.14–7.03 (2H, m, H3, H5), 3.82 (3H, s, C*H*$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.8 (d, C2, J=3.8 Hz), 134.2 (d, C4, J=1.4 Hz), 131.7 (d, C6, J=7.4 Hz), 121.2 (d, C1, J=128 Hz), 120.4 (d, C5, J=12.5 Hz), 111.5 (d, C3, J=6.6 Hz), 55.8 (*C*H$_3$). ^{31}P NMR (162 MHz, DMSO-d_6): δ 11.8 (dd, J_{P-H}=562 Hz, J_{P-6}=14.3 Hz). HRMS: *m*/*z* 171.0231 ([M-H]$^-$, $C_7H_8O_3P^-$ calcd 171.0217). Known compound.[38]

*4.4.15. 4-(Hydroxyhydrophosphoryl)-3,5-dimethoxybenzoic acid (**19**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.68 (1H, d, *H*-P, J_{H-P}=586 Hz), 7.18 (2H, d, H2, H6, $J_{2/6-P}$=4.7), 3.85 (6H, s, C*H*$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ 166.5 (*C*=O), 161.4 (C3, C5), 136.0 (C1), 114.0 (d, C4, J=122 Hz), 104.8 (d, C2, C6, J=6.0 Hz), 56.1 (*C*H$_3$). ^{31}P NMR (162 MHz, DMSO-d_6): δ 8.0 (dt, J_{P-H}=586 Hz, $J_{P-2/6}$=4.7 Hz). ν_{max} (KBr): 3668–1996 (br), 1714, 1693, 1600, 1574, 1460, 1405, 1226, 1127, 991 cm^{-1}. HRMS: *m*/*z* 245.0497 ([M-H]$^-$, $C_9H_{10}O_6P^-$ calcd 245.0215).

*4.4.16. Benzylphosphinic acid (**20**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.31 (2H, t, H3, H5, $J_{3/5-2/6}$=$J_{3/5-4}$=8.3 Hz) 7.23–7.20 (3H, mm, H2, H4, H6), 6.92 (1H, d, *H*-P, J_{H-P}=531 Hz), 3.09 (2H, d, C*H*$_2$, J_{CH2-P}=18.9 Hz). ^{13}C NMR (100 MHz, DMSO-d_6): δ 131.9 (d, C1, J=7.4 Hz), 129.8 (d, C2, C6, J=6.0 Hz), 128.4 (d, C3, C5, J=3.3 Hz), 126.4 (d, C4, J=3.5 Hz), 37.7 (d, *C*H$_2$, J=85 Hz). ^{31}P NMR (162 MHz, DMSO-d_6): δ 28.3 (dt, J_{P-H}=531 Hz, J_{P-CH2}=18.9 Hz). HRMS: *m*/*z* 155.0305 ([M-H]$^-$, $C_7H_8O_2P^-$ calcd 155.0267). Known compound.[24]

*4.4.17. Anthracene-9-ylphosphinate (**21**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.02 (2H, d, H1, H8, $J_{1/8-2/7}$=9.0 Hz), 8.88 (1H, s, H10), 8.59 (1H, d, *H*-P, J_{H-P}=558 Hz), 8.17 (2H, d, H4, H5 $J_{4/5-3/6}$=8.4 Hz), 7.56 (2H, ~t, H2, H7, $J_{2/7-1/8}\sim J_{2/7-3/6}\sim$8.8 Hz), 7.58 (2H, ~t, H3, H6, $J_{3/6-4/5}\sim J_{3/6-2/7}\sim$8.8 Hz). ^{13}C NMR (100 MHz, DMSO-d_6): δ 133.1 (d, C10, J=2.8 Hz), 132.6 (d, J=9.7 Hz) and 130.5 (d, J=11.9 Hz) (C4a, C4b and C8a, C9a), 129.4 (C4, C5), 127.5 (C2, C7), 125.4 (C3, C6), 124.8 (d, C1, C8, J=11.1 Hz), 123.4 (d, C9, J=123 Hz). ^{31}P NMR (162 MHz, DMSO-d_6): δ 13.6 (d, J_{P-H}=558 Hz). HRMS: *m*/*z* 241.0400 ([M-H]$^-$, $C_{14}H_{10}O_2P^-$ calcd 241.0424). Known compound.[39]

*4.4.18. 2-Tolylphosphinic acid (**22**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.67 (1H, dd, H6, J_{6-P}=15.7 Hz, J_{6-5}=7.3 Hz), 7.55 (1H, d, *H*-P, J_{H-P}=546 Hz), 7.48 (1H, t, H4, $J_{4-3/5}$=7.5 Hz), 7.37–7.28 (2H, m, H3, H5), 2.51 (3H, s, C*H*$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ 140.1 (d, C2, J=10.4 Hz), 132.0 (d, C4, J=2.5 Hz), 131.9 (d, C1, J=126 Hz), 130.8 (d, C3, J=11.1 Hz) 130.5 (d, C6, J=13.3 Hz), 125.6 (d, C5, J=13.6 Hz), 19.5 (*C*H$_3$). ^{31}P NMR (162 MHz, DMSO-d_6): δ 17.7 (dd, J_{P-H}=546 Hz, J_{P-6}=15.7 Hz). HRMS: *m*/*z* 155.0257 ([M-H]$^-$, $C_7H_8O_2P^-$ calcd 155.0267). Known compound.[24]

*4.4.19. Diphenylphosphinic acid (**23**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.73 (4H, ddd, H2, H6, $J_{2/6-P}$=11.8 Hz, $J_{2/6-3/5}$=8.2 Hz, $J_{2/6-4}$=1.6 Hz), 7.55–7.42 (6H, m, H3, H4, H5). ^{13}C NMR (100 MHz, DMSO-d_6): δ 135.0 (d, C1, J=135 Hz), 131.5 (d, C4, J=2.4 Hz), 130.9 (d, C2, C6, J=9.9 Hz), 128.4 (d, C3, C5, J=12.6 Hz). ^{31}P NMR (162 MHz, DMSO-d_6): δ 23.4 (m). HRMS: *m*/*z* 217.0402 ([M-H]$^-$, $C_{12}H_{10}O_2P^-$ calcd 217.0424). This compound is commercially available.

*4.4.20. Bis(4-methoxyphenyl)phosphinic acid (**24**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.61 (4H, ~dd, H2, H6, $J_{2/6-P}$=11.4 Hz, $J_{2/6-3/5}$=8.7 Hz), 7.00 (4H, ~dd, H3, H5, $J_{3/5-2/6}$=8.7 Hz, $J_{3/5-P}$=2.5 Hz), 3.77 (6H, s, C*H*$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.5 (d, C4, J=2.9 Hz), 132.7 (d, C2, C6, J=11.4 Hz), 127.8 (d, C1, J=141 Hz), 113.8 (d, C3, C5, J=13.6 Hz), 55.2 (*C*H$_3$). ^{31}P NMR (162 MHz, DMSO-d_6): δ 23.9 (m). HRMS: *m*/*z* 277.0658 ([M-H]$^-$, $C_{14}H_{14}O_4P^-$ calcd 277.0635). Known compound.[40]

*4.4.21. Naphthalen-2-yl(phenyl)phosphinic acid (**25**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.41 (1H, d, H1, J_{1-P}=14.0 Hz), 8.07 (1H, d, H8, J_{8-7}=8.1 Hz), 7.98 (1H, dd, H4, J_{4-3}=8.5 Hz, J_{4-P}=3.1 Hz), 7.94 (1H, d, H5, J_{5-6}=7.7 Hz), 7.83–7.70 (3H, m, H3, H2′, H6′), 7.65–7.55 (2H, m, H6, H7), 7.54–7.43 (3H, m, H3′, H4′, H5′). ^{13}C NMR (100 MHz, DMSO-d_6): δ 135.0 (d, C1′, J=134 Hz), 134.0 (d, C4a, J=2.8 Hz), 132.3 (d, C2, J=135 Hz), 132.1 (d, C1, J=9.5 Hz), 132.0 (d, C8a, J=13.3 Hz), 131.5 (d, C4′, J=2.6 Hz), 130.9 (d, C2′, C6′, J=10.4 Hz), 128.8 (C8), 128.5 (d, C3′, C5′, J=12.6 Hz), 128.1 (d, C4, J=12.4 Hz), 128.0 (C6), 127.7 (C5), 126.9 (C7), 126.6 (d, C3, J=10.8 Hz). ^{31}P NMR (162 MHz, DMSO-d_6): δ 23.4 (m). HRMS: *m*/*z* 267.0602 ([M-H]$^-$, $C_{16}H_{12}O_2P^-$ calcd 267.0580). Known compound.[41]

*4.4.22. 4-Fluorophenyl(4-tolyl)phosphinic acid (**26**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.77 (2H, ddd, H2, H6, $J_{2/6-P}$=11.6 Hz, $J_{2/6-3/5}$=8.8 Hz, $J_{2/6-F}$=5.4 Hz), 7.62 (2H, dd, H2′, H6′, $J_{2'/6'-P}$=12.3 Hz, $J_{2'/6'-3'/5'}$=8.1 Hz), 7.33–7.25 (4H, m, H3, H5, H3′, H5′), 2.32 (3H, s, C*H*$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ 164.0 (dd, C4, J_{4-F}=253 Hz, J_{4-F}=3.3 Hz), 141.5 (d, C4′, $J_{4'-P}$=3.0 Hz), 133.6 (dd, C2, C6, J=11.7 Hz, J=8.8 Hz), ~131.7 (dd, C1, J_{1-P}=141 Hz, J_{1-F}=2.8 Hz), 131.5 (d, C1′, $J_{1'-P}$=141 Hz), 131.0 (d, C2′, C6′, $J_{2'/6'-P}$=10.3 Hz), 129.1 (d, C3′, C5′, $J_{3'/5'-P}$=13.7 Hz), 115.6 (dd, C3, C5, $J_{3/5-F}$=21.6 Hz, $J_{3/5-P}$=15.0 Hz), 21.1 (*C*H$_3$). ^{31}P NMR (162 MHz, DMSO-d_6): δ 23.0 (m). ν_{max} (KBr): 3684–3343 (br), 2962, 1364, 1226, 1201, 1123, 998 cm^{-1}. HRMS: *m*/*z* 249.0453 ([M-H]$^-$, $C_{13}H_{11}FO_2P^-$ calcd 249.0481).

*4.4.23. 3,5-Dimethylphenyl(naphthalen-1-yl)phosphinic acid (**27**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.56 (1H, d, H8, J_{8-P}=8.7 Hz), 8.19 (1H, ddd, H2, J_{2-P}=15.0 Hz, J_{2-3}=7.3 Hz, J_{2-4}=1.4 Hz), 8.01 (1H, ~d, H4, J_{4-3}=8.3 Hz), 7.85 (1H, dt, H5, J_{5-6}=7.5 Hz, J_{5-4}=J_{5-7}=2.0 Hz), 7.58–7.45 (3H, m, H3, H6, H7), 7.42 (2H, d, H2′, H6′, $J_{2'/6'-P}$=13.2 Hz), 7.11 (1H, s, H4′), 2.28 (6H, s, C*H*$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ 137.6 (d, C3′, C5′, J=14.0 Hz), 135.2 (d, C1, J=137 Hz), 133.3 (d, C2,

J=9.8 Hz), 132.9 (d, C4′, J=3.0 Hz), 132.6 (d, J=10.9 Hz) and 132.4 (d, J=11.4 Hz) (C4a and C8a), 133.5 (d, C4, J=3.0 Hz), 130.8 (d, C1′, J=132 Hz), 128.8 (C5), 128.3 (d, C2′, C6′, J=10.5 Hz), 126.8 (C7), 126.6 (d, C8, J=4.5 Hz), 126.2 (C6), 124.9 (d, C3, J=14.5 Hz), 21.1 (CH_3). ^{31}P NMR (162 MHz, DMSO-d_6): δ 34.8 (m). ν_{max} (KBr): 3807–3456 (br), 2979, 1611, 1456, 1085, 988 cm^{-1}. HRMS: m/z 295.0876 ([M-H]$^-$, $C_{18}H_{16}O_2P^-$ calcd 295.0888).

*4.4.24. 4-Chlorophenyl(2,5-dimethoxyphenyl)phosphinic acid (**28**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.72 (2H, ~dd, H2, H6, $J_{2/6\text{-}P}$=12.2 Hz, $J_{2/6\text{-}P$=8.5 Hz), 7.51 (2H, dd, H3, H5, $J_{3/5\text{–}2/6}$=8.5 Hz, $J_{3/5\text{-}P}$=3.2 Hz), 7.37 (1H, dd, H6′, $J_{6'\text{-}P}$=8.4 Hz, $J_{6'\text{–}4'}$=2.5 Hz), 7.09 (1H, dd, H4′, $J_{4'\text{–}3'}$=9.0 Hz, $J_{4'\text{–}6'}$=2.5 Hz), 7.00 (1H, dd, H3′, $J_{3'\text{–}4'}$=9.0 Hz, $J_{3'\text{-}P}$=6.5 Hz), 3.75 (3H, s, CH_3O-5′), 3.57 (3H, s, CH_3O-2′). ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.5 (d, C2′, J=4.3 Hz), 152.8 (d, C5′, J=15.5 Hz), 136.2 (d, C4, J=3.7 Hz), 134.3 (d, C1, J=140 Hz), 133.2 (d, C2, C6, J=11.8 Hz), 128.0 (d, C3, C5, J=14.6 Hz), 122.7 (d, C1′, J=132 Hz), 118.9 (d, C4′, J=2.8 Hz), 118.1 (d, C6′, J=7.2 Hz), 113.4 (d, C3′, J=9.8 Hz), 56.0 (CH_3O-2′), 55.6 (CH_3O-5′). ^{31}P NMR (162 MHz, DMSO-d_6): δ 20.2 (m). ν_{max} (KBr): 3668–3221 (br), 1602, 1475, 1434, 1226, 1175, 972 cm^{-1}. HRMS: m/z 312.0299 ([M-H]$^-$, $C_{14}H_{14}ClO_4P^-$ calcd 312.0318).

*4.4.25. 3-Methoxyphenyl(4-nitrophenyl)phosphinic acid (**29**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.28 (2H, dd, H3, H5, $J_{3/5\text{–}2/6}$=9.2 Hz, $J_{3/5\text{-}P}$=2.2 Hz), 7.98 (2H, dd, H2, H6, $J_{2/6\text{-}P}$=11.3 Hz, $J_{2/6\text{–}3/5}$=9.2 Hz), 7.42 (1H, td, H5′, $J_{5'\text{–}4'/6'}$=7.6 Hz, $J_{5'\text{-}P}$=4.3 Hz), 7.31 (1H, d, H6′, $J_{6'\text{-}P}$=12.0 Hz, $J_{6'\text{–}5'}$=7.6 Hz), 7.27 (1H, ~d, H2′, $J_{2'\text{-}P}$=13.3 Hz), 7.12 (1H, dd, H4′, $J_{4'\text{–}5'}$=7.6 Hz, $J_{4'\text{-}P}$=2.6 Hz), 3.77 (3H, s, CH_3O). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.1 (d, C3′, J=16.2 Hz), 149.2 (d, C4, J=3.0 Hz), 142.2 (d, C1, J=130 Hz), 132.2 (d, C1′, J=136 Hz), 132.4 (d, C2, C6, J=11.3 Hz), 130.2 (d, C5′, J=14.8 Hz), 123.4 (d, C3, C5, J=13.3 Hz), 123.2 (d, C6′, J=13.7 Hz), 117.6 (d, C4′, J=3.0 Hz), 116.1 (d, C2′, J=11.7 Hz), 55.3 (CH_3O). ^{31}P NMR (162 MHz, DMSO-d_6): δ 20.9 (m). ν_{max} (KBr): 3707–3456 (br), 1602, 1541, 1487, 1434, 1362, 1201, 1132, 988 cm^{-1}. HRMS: m/z 293.0441 ([M-H]$^-$, $C_{13}H_{12}NO_5P^-$ calcd 293.0453).

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Supplementary data

Supporting Information contains complete results of the ligand screening and ^{1}H-,^{13}C- and ^{31}P-NMR spectra of compounds **5–29**. Supplementary data associated with this article can be found in online version, at doi:10.1016/j.tet.2009.10.028.

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