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Preparation of the library of fluorescent aromatic aminophosphonate phenyl and benzyl esters

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ABSTRACT

Classical hydrophosphonylation of Schiff bases have been used for the preparation of library of diphenyl and dibenzyl aromatic aminomethylphosphonates *N*-substituted with aromatic moieties. The reaction, although being capricious provided the desired products in satisfactory yields. When using harsh reaction conditions conversion of diphenyl esters into monophenyl ones was observed. On the other hand, the use of more delicate conditions resulted in lack of hydrophosphonylation. The fluorescence studies revealed that the obtained library could be used for the construction of diagnostic microarrays.

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GRAPHICAL ABSTRACT



Introduction

Diphenyl aminophosphonates and their short peptides are well recognized from their ability to inhibit serine proteinases by phosphonylating their active-site serine hydroxyl moiety.¹⁻³ It is also well acknowledged that tumor tissues are characterized by overproduction of many proteases with some of them being marker enzymes for cancerogenesis.⁴⁻⁶ Thus, the enzymatic cocktails of healthy and cancer tissues differ significantly from each other.

We speculate that the use of aminophosphonate libraries of potential inhibitors of the proteinases (and most likely phosphatases) might be useful in construction of diagnostic microarrays facilitating diagnosis based on biopsy. Indeed, libraries of short peptides have been already considered as potential diagnostic tools.⁷⁻¹⁰ In order to construct such a library the simple and efficient chemical procedures resulting in a wide variety of structurally related compounds are indispensable. In this paper, we have exploited addition of diphenyl and dibenzyl phosphites to Schiff bases obtained from aromatic aldehydes and aromatic amines as a mean to construct such a library of fluorescent inhibitors.

Results and discussion

Synthesis

The addition of phosphites to Schiff bases is one of the oldest and most commonly used procedure for aminophosphonate synthesis.^{11–13} It also seems to be a trivial and simple reaction. However, the synthesis of structurally overcrowded aminophosphonates starting from aromatic aldehydes, aromatic amines,

In memoriam of Professor Reinhard Schmutzler.

KEYWORDS Aminophosphonate library; fluorescence; hydrophosphonylation

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Scheme 1. Outline of the synthesis.

and diphenyl or dibenzyl phosphites (Scheme 1) appeared to be not an easy task. Dibenzyl and diphenyl phosphites substantially differ in nucleophilicity and thus are good models for studies on applicability of this reaction.¹⁴

The first step of the synthesis was a choice and production of appropriate Schiff bases 1. They were obtained in moderate to good yields by standard procedure. Unfortunately, none of the efforts to hydrophosphonylate bases 1za-1zg gave satisfactory results. In these cases, products were obtained in low yields as components of complex reaction mixtures.

Quite surprisingly, addition of diphenyl phosphites to the Schiff bases derived from naphth-1-yl-methylamine carried out in elevated temperature in acetonitrile provided mostly monoesters **3** instead of the expected diphenyl esters **2** (Scheme 1; Table 1). The only exception was the addition of this phosphite to Schiff base obtained from *p*-nitrobenzaldehyde, which resulted in diphenyl ester **2Axc**. The reaction of the Schiff base obtained from 1-naphthylcarboxyaldehyde afforded the mixture of both mono (compound **2Axd**) and diphenyl (compound **3Axd**) esters.

Table 1. Diphenyl and dibenzyl N-substituted aminobenzylphosphonates.

Compound $R = Ph$	Yield [%]	Compound $R = CH_2Ph$	Yield [%]
3Axa	20		
3Axb	83		
2Axc	52	2Bxc	81
2Axd + 3Axd	73	2Bxd	76
ЗАхе	85	2Bxe	79
3Axf	35	2Bxf	68
3Axg	60	2Bxg	73
2Aya	82		
		2Byb	64
2Ayc	48	2Byc	50
2Ayd	76	2Byd	69
		2Bye	67
		2Byg	43

We speculate that this effect results from high packing of the resulting diphenyl aminophosphonate molecules, which might force removal of phenol from the phosphonate moiety. On the other hand, a similar reaction using dibenzyl phosphite gave dibenzyl aminophosphonates in good to excellent yields (Table 1).

As shown in Table 1 diphenyl and dibenzyl phosphonates (compounds 2) were successfully obtained by a slight modification of the reaction conditions (reaction in THF in atmosphere of inert gas). The desired compounds were obtained with satisfactory yields (Table 1); however, their purification caused quite substantial problems. Sterically overcrowded Schiff bases obtained from o-nitrobenzaldehyde and anthracene-9-carboxyladehyde did not react with both phosphites in these conditions even after prolonged heating.

Finally, addition of tris(trimethylsilyl) phosphites, which were synthesized in situ, followed by delicate hydrolysis of trimethylsilyl esters afforded corresponding aminophosphonic acids **4** in moderate, albeit satisfactory, yields (Scheme 2; Table 2). These compounds, however, appeared to be very weakly soluble in any solvent (DMSO, alkaline and acidic water, methanol).

Fluorescence

A typical fluorescence (emission) measurement for selected aminophosphonate esters dissolved in dimethyl sulfoxide (DMSO) was determined using excitation wavelengths fixed at 254, 316, 346, and 366 nm. The best results have been obtained at 366 nm (Figure 1a). Generally, strong quenching of DMSO fluorescence by these compounds was observed.

Also fluorescence excitation measurements have been performed by fixing the detection wavelengths at 360, 400, 440, and 480 nm. The most striking results were obtained for 400 nm (Figure 1b). These studies indicated that the obtained libraries could be useful for construction of fluorescent diagnostic chips.



Scheme 2. Synthesis of N-substituted aminomethanephosphonic acids.

Experimental

All solvents and reagents were purchased from commercial suppliers, were of analytical grade, and were used without further purification. Unless otherwise specified solvents were removed with a rotary evaporator. Infrared spectra were measured on a 1600 FT-IR Perkin-Elmer spectrometer. ¹H and ³¹P NMR experiments were performed on a Bruker Avance TM DRX operating at 300.13 MHz (1H), 121.51 MHz (31P) and on Bruker Avance II Ultrashield Plus 600.58 MHz (1H), 243.12 MHz (³¹P) while ¹³C NMR studies on Bruker Avance II Ultrashield Plus 600.58 MHz (¹H) spectrometer operating 151.016 MHz (¹³C) and Bruker Ultrashield 400.13 MHz (¹H) spectrometer operating 100.61 MHz (¹³C). Measurements were made in CDCl₃ (99.8 at.%D), DMSO_{d6} (99.8 at.%D), and MeOD (99.8% at.%D) solutions at temperature 300 K, all solvents were supplied by ARMAR AG (Dottingen, Switzerland). Chemical shifts are reported in parts per million relative to tetramethylsilane (TMS) or 85% H₃PO₄ used as external standards, while coupling constants are reported in Hertz. Melting points were determined on an Electrothermal 9200 apparatus and are reported uncorrected. Electrospray mass spectra were recorded at Faculty of

Table 2. N-substituted aminobenzylphosphonates.

Compound	Yield [%]	Compound	Yield [%]
4xa	48	4xg	38
4xb	87	4ya	34
4xc	81	4yc	41
4xd	41	4yc	45
4xe	58	4yf	41
4xf	46		

Chemistry, Wroclaw University of Technology using Waters LCT Premier XE mass spectrometer (methods of ionization ESI (electrospray ionization)).

Purities of the products were determined by both thin layer chromatography (Silica Gel 60 with fluorescent indicator) and by high-performance liquid chromatography (HPLC; Waters 600 apparatus equipped with Waters 2489 UV-Vis detector, columns: SUPELCO Discovery Bio Wide pore C8 and Waters Spherisorb ODS2 analyticaL; column).

UV and fluorescence determinations have been performed using 5 mM DMSO solutions of aminophosphonates at 25°C using Gemini XSP apparatus and SofMax Pro programme. The Supplemental Materials contains sample chromatographic and spectroscopic data for representative compounds (Figures S1– S12).

Synthesis of Schiff bases (1)—general procedure

Amine (0.03 mole) was dissolved in chloroform (30 mL). The solution was heated to 40° C and the solution of appropriate aldehyde (0.03 mole) in the same solvent (15 mL) was added dropwise for 1 h with stirring. The reaction was continued at this temperature for additional 8 h and left overnight at room temperature. Then the solution was dried over anhydrous MgSO₄ and the solvent was evaporated in vacuum. Evaporation of the chloroform resulted in crude product, which was crystallized either from methanol or methanol–chloroform mixture.

Physicochemical data for Schiff bases are given in supplementary material.



Figure 1. Fluorescence spectra of chosen aminophosphonates: (a) emission spectra; (b) excitation spectra.

Addition of diphenyl phosphite to Schiff bases obtained from naphth-1-ylmethylamine

Schiff base $1 \times (0.005 \text{ mole})$ was dissolved in hot (40°C) acetonitrile (20 mL). When the solution became clear, diphenyl phosphite (0.005 mole) was added dropwise and the mixture was heated to 80°C and the reaction carried out for additional 4–20 h until precipitation of a white solid was observed. The product precipitated completely after cooling to room temperature. Filtering and washing with small portions of acetonitrile provided the desired aminophosphonates of satisfactory purity.

Phenyl N-(naphth-1-ylmethyl)amino-o-nitrobenzylphosphonate (**3Axa**)

Phenyl N-(naphth-1-ylmethyl)amino-o-nitrobenzylphosphonate (**3Axa**) was obtained as a cream color solid with a melting point of 133–134°C. ³¹P NMR (162 MHz, DMSO) δ 5.03; ¹H NMR (400 MHz, DMSO) δ 8.05 (d, *J* = 8.2 Hz, 2H), 7.88 (d, *J* = 8.2 Hz, 2H), 7.83 (d, *J* = 7.3 Hz, 1H), 7.61 (t, *J* = 8.2 Hz, 2H), 7.49–7.34 (m, 4H), 7.08 (t, *J* = 7.9 Hz, 2H), 6.92–6.81 (m, 3H), 5.20 (d, *J* = 16.4 Hz, 1H, CHP), 4.65 and 4.95 (AB system, *J* = 13.4, 2H, CH₂Ar); ¹³C NMR (101 MHz, DMSO) δ 153.02, 152.94, 148.92, 148.87, 133.69, 133.33, 132.05, 130.67, 130.00, 129.32, 129.12, 128.94, 126.97, 126.41, 125.61, 125.17, 124.13, 122.91, 120.46, 120.42, 54,48 (d, *J* = 13.3, CP), 47.63 (CH₂); HRMS (ESI-TOF) *m/z*: [MH]⁺ Calcd. for C₂₄H₂₂N₂O₅P: 449.1266, Found: 449.1280.

Phenyl N-(naphth-1-ylmethyl)amino-m-nitrobenzylphosphonate (**3Axb**)

Phenyl N-(naphth-1-ylmethyl)amino-m-nitrobenzylphosphonate (**3Axb**) was obtained as a white solid with a melting point of 223–225°C. ³¹P NMR (162 MHz, DMSO) δ 4.97; ¹H NMR (400 MHz, DMSO) δ 8.33 (s, 1H), 8.14 (d, *J* = 7.9 Hz, 1H), 8.01 (d, *J* = 8.2 Hz, 1H), 7.86 (d, *J* = 9.2 Hz, 2H), 7.78 (d, *J* = 7.5 Hz, 1H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.50–7.30 (m, 4H), 7.07 (t, *J* = 7.9 Hz, 2H), 6.95–6.77 (m, 3H), 5.05 (d, CHP, *J* = 13.4 Hz, 1H), 4.54 and 4.59 (AB system, *J* = 14.5 Hz, 2H). ¹³C NMR (101 MHz, DMSO) δ 153.36, 153.29, 147.64, 137.25, 136.68, 133.58, 132.04, 130.22, 129.96, 129.56, 129.30, 128.89, 128.62, 126.99, 126.44, 125.59, 124.45, 124.37, 122.77, 120.48, 60.12 (d, *J* = 131.3, CP), 47.86 (CH₂); HRMS (ESI-TOF) *m/z*: [MH]⁺. Calcd. for C₂₄H₂₂N₂O₅P: 449.1266, Found: 449.1273.

Diphenyl N-(naphth-1-ylmethyl)amino-p-nitrobenzylphosphonate (**2Axc**)

Diphenyl N-(naphth-1-ylmethyl)amino-p-nitrobenzylphosphonate (**2Axc**) was obtained as a white solid with a melting point of 220°C. ³¹P NMR (162 MHz, DMSO) δ 16.78; ¹H NMR (400 MHz, DMSO) δ 8.20 (d, J = 8.4 Hz, 1H), 8.16–8.08 (m, 1H), 8.04 (d, J = 8.7 Hz, 1H), 7.88–7.81 (m, 3H), 7.63 (d, J = 7.5 Hz, 1H), 7.57–7.50 (m, 1H), 7.48–7.27 (m, 4H), 7.24–7.14 (m, 3H), 7.14–7.03 (m, 3H), 6.99–6.79 (m, 3H), 4.75 (d, CHP, J = 23.6 Hz, 1H), 3.94 and 4.21 (AB system, J = 13.6 Hz, 2H, CH₂Ar); ¹³C NMR (101 MHz, DMSO) δ 150.54, 150.26, 147.64, 135.21, 133.85, 133.65, 132.02, 131.93, 130.64, 130.23, 130.14, 129.55, 129.12, 128.88, 128.79, 128.13, 127.01, 126.90, 126.12, 125.74, 125.63, 124.63, 124.41, 123.86, 123.11, 122.61, 120.91, 120.64, 58.52 (-CH₂-), 49.04 (J = 123.5 Hz, CP); HRMS (ESITOF) m/z: [MH]⁺ Calcd. for C₃₀H₂₆N₂O₅P: 525.1580, Found: 525.1573.

Diphenyl and phenyl N-(naphth-1-ylmethyl)naphth-1ylaminomethylphosphonates (**2Axd+3Axd**)

Diphenyl and phenyl N-(naphth-1-ylmethyl)naphth-1ylaminomethylphosphonates (**2Axd+3Axd**) were obtained in a molar ratio of 64:36 (diester to monoester) as determined tentatively by integration of ³¹P NMR signals. ³¹P NMR (162 MHz, DMSO) δ 18.17 (s, diester), 6.98 (s, monoester); HRMS (ESI-TOF) *m*/*z*: [MH]⁺ Calcd. for C₃₄H₂₈NO₃P: 530.1885, Found: 530.1863, while for monoester: C₃₄H₂₈NO₃P: 454.1572, Found: 454.1589.

Phenyl N-(naphth-1-ylmethyl)naphth-2-ylaminomethylphosphonate (**3Axe**)

Phenyl N-(naphth-1-ylmethyl)naphth-2-ylaminomethylphosphonate (**3Axe**) was obtained as a white solid, m.p. 224–226°C. ³¹P NMR (122 MHz, DMSO): δ 5.00; ¹H NMR (601 MHz, DMSO) δ 8.12 (d, J = 8.4 Hz, 1H), 8.05–7.72 (m, 5H), 7.72–7.55 (m, 2H), 8.55–7.29 (m, 4H), 7.27–7.02 (m, 2H), 6.93 (m, 3H), 5.00 (d, J = 13.6 Hz, 1H, CHP), 4.46 and 4.62 (AB system, J = 14.3 Hz, 2H, CH₂); ¹³C NMR (101 MHz, DMSO) δ 153.53, 133.63, 132.96, 132.82, 132.62, 132.07, 130.02, 129.87, 129.51, 129.25, 128.91, 128.74, 128.16, 127.91, 127.65, 126.93, 126.60, 126.44, 125.61, 124.37, 122.59, 120.73, 60.88 (d, J = 133.2 Hz, CP), 47.43 (CH₂); HRMS (ESI-TOF) m/z: [MH]⁺ Calcd. for C₂₈H₂₄NO₃P: 454.1572, Found: 454.1583.

Phenyl N-(naphth-1-ylmethyl)anthracen-9-ylaminomethylphosphonate (**3Axf**)

Phenyl N-(naphth-1-ylmethyl)anthracen-9-ylaminomethylphosphonate (**3Axf**) was obtained as a yellow solid, m.p. 270– 272°C. ³¹P NMR (122 MHz, DMSO): δ 1.34; ¹H NMR (601 MHz, DMSO) δ 8.26–8.17 (m, H) 8.14 (d, *J* = 8.3 Hz, 1H), 8.04 (dd, *J* = 15.1 Hz, *J* = 8.1 Hz, 2H), 7.74 (d, *J* = 7.0 Hz, 1H), 7.66 8.04 (ddd, *J* = 11.5 Hz, *J* = 8.7 Hz, *J* = 5.3 Hz, 5H), 7.55–7.44 (m, 4H), 7.33–7.23 (m, 4H), 7.20 (dd, *J* = 19.6 Hz, *J* = 11.6 Hz), 6.99 (d, *J* = 8.1 Hz, 2H), 6.99 (d, *J* = 18.4 Hz, 1H, CHP), 5.13–4.97 (m, 2H, CH₂Ar); ¹³C NMR (101 MHz, DMSO) δ 157.77, 153.01, 150.68, 133.68, 132.14, 131.62, 131.39, 130.78, 130.26, 129.92, 129.31, 128.92, 127.03, 126.63, 126.26, 125.58, 125.50, 125.11, 124.97, 124.07, 123.38, 122.95, 121.01, 120.97, 120.58, 119.20, 115.65, 55.13 (d, *J* = 133.3 Hz, CP), 48.65 (CH₂); HRMS (ESI-TOF) *m/z*: [MH]⁺ Calcd. for C₃₂H₂₆NO₃P: 504.1729, Found: 504.1732.

Phenyl N-(naphth-1-ylmethyl)phenathren-9-ylaminomethylphosphonate (**3Axg**)

Phenyl N-(naphth-1-ylmethyl)phenathren-9-ylaminomethylphosphonate (**3Axg**) was obtained as a white solid, m.p. 183– 185°C. ³¹P NMR (162 MHz, DMSO) δ 6.05; ¹H NMR (400 MHz, DMSO) δ 8.75 (dd, J = 21.1, J = 8.3 Hz, 2H), 8.42 (s, 1H), 8.10 (d, J = 8.3 Hz, 1H), 7.84 (d, J = 8.1 Hz, 2H), 7.75 (d, J = 7.5 Hz, 2H), 7.64 (d, J = 7.0 Hz, 1H), 7.58 (t, J = 7.5 Hz, 2H), 7.47 (t, J = 7.5 Hz, 1H), 7.40 (t, J = 7.5 Hz, 2H), 7.34–7.21 (m, 2H), 7.01 (t, J = 7.5 Hz, 2H), 6.90–6.78 (m, 3H), 5.24 (d, J = 14.6 Hz, 1H, CHP), 4.77 and 5.12 (AB system, J = 12.7 Hz, 2H, CH₂); ¹³C NMR (101 MHz, DMSO) δ 153.37, 153.30, 133.60, 132.09, 131.17, 130.56, 130.30, 130.19, 129.82, 129.20, 128.92, 128.81, 127.40, 127.25, 126.81, 126.34, 125.52, 124.84, 123.56, 123.09, 122.68, 120.69, 55,66 (d, J = 127.3 Hz, CP), 47.75 (CH₂); HRMS (ESI-TOF) m/z: [MH]⁺ Calcd. for C₃₂H₂₆NO₃P: 504.1729, Found: 504.1716.

Addition of diphenyl and dibenzyl phosphites to Schiff bases—general procedure

Schiff base (0.005 mole) was dissolved in THF (20 mL) and warmed to 40°C. The mixture was stirred in an atmosphere of argon until all the substrate dissolved. Then the appropriate phosphite (0.005 mole) was added dropwise during 1 h. The stirring was continued for additional 15 h and then the solvents were removed in vacuo yielding dense oils. The products were purified by Silica Gel 60 (230–400 mesh, ASTM) column chromatography using ethyl acetate-hexane (3:1 v/v) or ethyl acetate-hexane-chloroform (3:1:6 v/v) mixtures as eluents.

Dibenzyl N-(naphth-1-ylmethyl)amino-p-nitrobenzylphosphonate (**2Bxc**)

Dibenzyl N-(naphth-1-ylmethyl)amino-p-nitrobenzylphosphonate (2Bxc) was obtained as a yellow solid, m.p. 136-138 °C. ³¹P NMR (122 MHz, DMSO): δ 23.4; ¹H NMR (400 MHz, DMSO) δ 8.11 (d, J = 8.4 Hz, 2H), 8.04 (d, J = 7.9 Hz, 1H), 7.87–7.80 (m, 1H), 7.74 (d, *J* = 7.7 Hz, 1H), 7.67 (dd, *J* = 8.8, 2.0 Hz, 2H), 7.46-7.09 (m, 12H), 7.06-7.00 (m, 2H), 4.91 (d, J = 7.8 Hz, 2H, POCH₂), 4.74 and 4.81 (ABX system, J = 12.1, J = 8.1 Hz, 2H, POCH₂), 4.47 (d, J = 22.7 Hz, 1H, CHP), 3.86 and 4.09 (AB system, J = 13.6 Hz, 2H, CH₂Ar); ¹³C NMR (101 MHz, DMSO) δ 147.41, 147.37, 145.16, 136.85, 136.79, 136.70, 136.64, 135.38, 133.83, 131.87, 130.36, 130.30, 128.81, 128.78, 128.69, 128.57, 128.49, 128.05, 127.91, 126.85, 126.35, 126.08, 125.75, 124.47, 123.67, 68.31 (d, J = 6.8 Hz, POCH₂), 67.59 (d, *J* = 6.9 Hz, POCH₂), 59.34 (d, *J* = 151.7 Hz, CHP), 49.28 (CH₂Ar), 49.11 (CH₂Ar); HRMS (ESI-TOF) *m/z*: [MH]⁺ Calcd. for C₃₂H₃₀N₂O₅P: 553.1892, Found: 553.1888.

Dibenzyl N-(naphth-1-ylmethyl)naphth-1-ylaminomethylphosphonate (**2Bxd**)

Dibenzyl N-(naphth-1-ylmethyl)naphth-1-ylaminomethylphosphonate (**2Bxd**) was obtained as a cream color solid, m.p. 108–109°C. ³¹P NMR (122 MHz, DMSO): δ 24.85; ¹H NMR (601 MHz, DMSO) δ 8.22–7.78 (m, 7H), 7.71–7.06 (m, 15H), 6.92–6.74 (m, 2H), 5.30 (d, J = 21.7 Hz, 1H, CHP), 4.98 (d, J = 7.1 Hz, 2H, POCH₂), 4.43 and 4.70 (ABX system, J = 12.1, J = 7.4 Hz, 2H, POCH₂), 3.86 and 4.12 (AB system, J = 12.3 Hz, 1H, CH₂Ar); ¹³C NMR (101 MHz, DMSO) δ 137.05, 136.99, 136.67, 136.61, 135.66, 133.85, 132.89, 132.35, 131.99, 129.05, 128.79, 128.74, 128.52, 128.46, 128.25, 128.08, 127.96, 127.51, 126.91, 126.49, 126.28, 126.08, 125.89, 125.69, 124.68, 68.10 (d, J = 6.7 Hz, POCH₂), 67.26 (d, J = 6.8 Hz, POCH₂), 51.08 (d, J = 268.0 Hz, CHP), 49.14 (d, J = 17.8 Hz, CH₂Ar); HRMS (ESI-TOF) m/z: [MH]⁺ Calcd. for C₃₆H₃₂NO₃P: 558.2198, Found: 558.2207.

Dibenzyl N-(naphth-1-ylmethyl)naphth-2-ylaminomethylphosphonate (2Bxe)

Dibenzyl N-(naphth-1-ylmethyl)naphth-2-ylaminomethylphosphonate (**2Bxe**) was obtained as a white solid, m.p. 137°C. ³¹P NMR (122 MHz, DMSO): δ 24.63; ¹H NMR (601 MHz, DMSO) δ 8.14 (d, *J* = 8.2 Hz, 1H), 8.05–7.79 (m, 6H), 7.71 (d, *J* = 8.7 Hz, 1H), 7.59–7.34 (m, 6H), 7.34–7.11 (m, 8H), 7.11–6.98 (m, 2H), 4.99 (d, *J* = 7.1 Hz, 2H, POCH₂), 4.66 and 4.77 (ABX system, J = 12.0, J = 7.6 Hz, 2H, POCH₂), 4.49 (d, J = 21.7 Hz, 1H, CHP), 3.87 and 4.14 (AB system, J = 13.2 Hz, 2H, CH₂Ar); ¹³C NMR (101 MHz, DMSO) δ 137.04, 136.98, 136.84, 136.78, 135.61, 134.36, 133.86, 133.24, 133.09, 131.95, 128.83, 128.76, 128.61, 128.49, 128.36, 128.17, 128.02, 127.98, 127.72, 126.79, 126.70, 126.51, 126.32, 126.08, 125.79, 124.51, 68.07 (d, J =6.7 Hz, POCH₂), 67.35 (d, J = 6.8 Hz, POCH₂), 59.75 (d, J =153.1 Hz, CHP), 48.99 (d, J = 17.8 Hz, CH₂Ar); HRMS (ESI-TOF) m/z: [MH]⁺ Calcd. for C₄₀H₃₄NO₃P: 558.2198, Found: 558.2207.

Dibenzyl N-(naphth-1-ylmethyl)anthracen-9-ylaminomethylphosphonate (2Bxf)

Dibenzyl N-(naphth-1-ylmethyl)anthracen-9-ylaminomethylphosphonate (2Bxf) was obtained as a yellow oil. ³¹P NMR (122 MHz, DMSO): δ 25.94; ¹H NMR (601 MHz, DMSO) δ 9.31 (d, J = 8.2 Hz, 1H), 8.14 (dd, J = 19.8 Hz, J = 8.2 Hz, 3H), 7.97 (d, J = 8.5 Hz, 1H), 7.85 (d, J = 8.1 Hz, 1H), 7.76 (d, J = 8.1 Hz, 1H), 7.60–6.96 (m, 16H), 6.69 (d, J = 8.3 Hz, 2H), 5.89 (dd, J = 24.4 Hz, J = 5.8 Hz, 1H, CHP), 5.01 (d, J = 7.8 Hz, 2H, POCH₂), 4.38 and 4.62 (ABX system, J = 12.1, J = 7.5 Hz, 2H, POCH₂), 4.11–3.86 (m, 2H, CH₂Ar); 13 C NMR (101 MHz, DMSO) & 170.78, 136.96, 136.90, 136.40, 136.34, 135.48, 133.77, 131.86, 131.46, 131.39, 131.37, 130.69, 130.64, 129.72, 129.30, 129.04, 128.80, 128.73, 128.56, 128.41, 128.23, 128.13, 128.11, 127.43, 127.06, 126.87, 126.19, 126.04, 125.63, 125.28, 124.53, 124.06, 67.95 (d, J = 6.9 Hz, POCH₂), 67.25 (d, J = 6.8 Hz, POCH₂), 55.78 (d, J = 154.8 Hz, CHP), 50.01 (d, J= 16.2 Hz, CH₂Ar); HRMS (ESI-TOF) m/z: [MH]⁺ Calcd. for C₄₀H₃₄NO₃P: 608.2355, Found: 608.2349.

Dibenzyl N-(naphth-1-ylmethyl)phenathren-9-ylaminomethylphosphonate (**2Bxg**)

Dibenzyl N-(naphth-1-ylmethyl)phenathren-9-ylaminomethylphosphonate (2Bxg) was obtained as a yellow oil. ³¹P NMR (162 MHz, DMSO) δ 25.24, 22.17; ¹H NMR (400 MHz, DMSO) δ 8.85-8.77 (m, 2H), 8.15-8.05 (m, 2H), 7.95-7,81 (m, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 8.1 Hz, 1H), 7.69–7.49 (m, 6H), 7.43–7.37 (m, 1H), 7.36–7.05 (m, 10H), 7.00 (t, J =7.4 Hz, 1H), 6.78 (d, J = 7.4 Hz, 1H), 5.19 (d, J = 21.1 Hz, 1H, CPH), 5.02–4.88 (m, 2H, POCH₂), 4.77–4.48 (m, 2H, POCH₂), 3.94 and 4.20 (AB system, J = 13.2 Hz, 2H, CH₂Ar); ¹³C NMR (101 MHz, DMSO) δ 169.24, 142.98, 137.03, 136.96, 136.57, 135.67, 133.85, 132.00, 129.03, 128.92, 128.79, 128.73, 128.68, 128.66, 128.55, 128.48, 128.34, 128.24, 128.10, 127.95, 127.88, 127.83, 127.61, 127.52, 127.00, 126.85, 126.29, 126.08, 125.70, 124.70, 68.15 (d, J = 6.7 Hz, POCH₂), 67.33 (d, J =6.8 Hz, POCH₂), 63.32 (s, CH₂Ar), 48.93 (d, J = 127.8 Hz, CHP); HRMS (ESI-TOF) m/z: [MH]⁺ Calcd. for C₄₀H₃₄NO₃P: 608.2355, Found: 608.2284.

Diphenyl N-(naphth-1-yl)amino-o-nitrobenzylphosphonate (2Aya)

Diphenyl N-(naphth-1-yl)amino-o-nitrobenzylphosphonate (2Aya) was obtained as a yellow solid, m.p. 142–145°C. ³¹P NMR (243 MHz, DMSO) δ 13.49; ¹H NMR (601 MHz, DMSO) δ 8.34 (d, J = 7.0 Hz, 1H), 8.28 (d, J = 7.8 Hz, 1H), 8.13 (d,

J = 8.0 Hz, 1H), 7.83 (d, *J* = 5.8 Hz, 1H), 7.77 (t, *J* = 7.5 Hz, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.53 (d, *J* = 6.0 Hz, 2H), 7.36–7.28 (m, 4H), 7.24 (t, *J* = 7.4 Hz, 1H), 7.22–7.13 (m, 2H), 7.07 (d, *J* = 7.5 Hz, 2H), 6.97–6.91 (m, 2H), 6.75 (d, *J* = 7.5 Hz, 1H), 6.62 (d, *J* = 7.4 Hz, 1H), 6.57 (dd, *J* = 27.4, *J* = 10.0 Hz, 1H, CHP); ¹³C NMR (151 MHz, MeOD) δ 158.60, 151.27, 150.87, 150.81, 150.28, 142.92, 142.82, 135.33, 135.27, 131.36, 131.15, 130.81, 130.65, 129.23, 127.53, 127.45, 126.90, 126.02, 125.64, 123.76, 121.65, 121.23, 121.20, 120.45, 120.08, 116.50, 108.02, 68.31, 52.08 (d, *J* = 158.5 Hz, CP); HRMS (ESI-TOF) *m/z*: [MH]⁺ Calcd. for C₂₇H₂₂N₂O₅P: 511.1423, Found: 511. 1434.

Diphenyl N-(naphth-1-yl)amino-p-nitrobenzylphosphonate (2Ayc)

Diphenyl N-(naphth-1-yl)amino-p-nitrobenzylphosphonate (**2Ayc**) was obtained as a yellow solid, m.p. 116–117°C. ³¹P NMR (243 MHz, DMSO) δ 14.38; ¹H NMR (601 MHz, DMSO) δ 8.36–8.32 (m, 1H), 8.29 (d, J = 8.3 Hz, 2H), 8.19 (d, J = 8.5 Hz, 2H), 7.84–7.79 (m, 1H), 7.53–7.48 (m, 2H), 7.38–7.31 (m, 4H), 7.28 (d, J = 8.2 Hz, 1H), 7.25–7.18 (m, 3H), 7.15 (d, J = 8.1 Hz, 2H), 7.05 (d, J = 8.0 Hz, 2H), 6.82 (m, 1H), 6.76 (d, J = 7.4 Hz, 1H), 6.09 (dd, J = 27.3, 10.0 Hz, 1H, CHP); ¹³C NMR (151 MHz, DMSO) δ 150.66, 150.60, 150.35, 150.28, 147.81, 144.27, 142.17, 142.07, 134.46, 130.45, 130.29, 129.84, 128.40, 126.60, 125.88, 125.83, 125.07, 124.68, 123.91, 122.81, 120.99, 120.97, 120.79, 119.27, 119.11, 115.70, 107.57, 55.67 (d, J = 155.4 Hz, CP); HRMS (ESI-TOF) m/z: [MH]⁺ Calcd. for C₃₀H₂₅N₂O₅P: C₂₇H₂₂N₂O₅P: 511.1423, Found: 511.1438.

Diphenyl N-(naphth-1-yl)naphth-1-ylaminomethylphosphonate (2Ayd)

Diphenyl N-(naphth-1-yl)naphth-1-ylaminomethylphosphonate (2Ayd) was obtained as a brown solid, m.p. 139-144°C. ³¹P NMR (243 MHz, DMSO) δ 15.55; ¹H NMR (601 MHz, DMSO) δ 8.35 (d, J = 8.1 Hz, 1H), 8.22 (d, J = 4.7 Hz, 1H), 8.01 (d, J = 8.2 Hz, 1H), 7.93 (d, J = 8.1 Hz, 1H), 7.80 (d, J = 7.5 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.60 (t, J =7.5 Hz, 1H), 7.56–7.48 (m, 3H), 7.33 (t, J = 7.5 Hz, 2H), 7.25–7.09 (m, 8H), 6.82–6.76 (m, 1H), 6.74 (d, J = 7.9 Hz, 2H), 6.58 (d, J = 7.6 Hz, 1H), 6.51 (dd, J = 25.8, 9.5 Hz, 1H, CHP); ¹³C NMR (151 MHz, DMSO) δ 150.55 (dd, J =67.0, 9.9 Hz), 142.36, 142.26, 134.41, 133.84, 132.00, 131.83, 130.24, 130.18, 129.85, 129.34, 129.26, 128.42, 127.17, 126.75, 126.43, 126.38, 125.93, 125.75, 125.61, 125.13, 124.65, 124.07, 122.63, 121.12, 121.10, 120.49, 120.47, 119.27, 118.87, 115.71, 107.19, 65.40, 51.82 (d, J = 159.3 Hz, CP); HRMS (ESI-TOF) m/z: [MH]⁺ Calcd. for C₃₃H₂₆NO₃P: 516.1729, Found: 516. 1740.

Dibenzyl N-(naphth-1-yl)amino-m-nitrobenzylphosphonate (2Byb)

Dibenzyl N-(naphth-1-yl)amino-m-nitrobenzylphosphonate (**2Byb**) was obtained as a brownish oil. ³¹P NMR (243 MHz, DMSO) δ 22.23; ¹H NMR (601 MHz, DMSO) δ 8.62 (s, 1H), 8.28 (d, *J* = 7.8 Hz, 1H), 8.18–8.12 (m, 2H), 7.80 (d, *J* = 7.9 Hz, 1H), 7.63 (t, *J* = 7.9 Hz, 1H), 7.53–7.49 (m, 2H), 7.43–7.15

(m, 11H), 6.66 (d, J = 7.5 Hz, 1H), 6.58–6.52 (m, 1H), 5.73 (dd, J = 25.6, J = 9.2 Hz, 1H, CHP), 5.16 (d, J = 8.0 Hz, 2H, POCH₂), 5.07–4.94 (m, 2H, POCH₂); ¹³C NMR (151 MHz, DMSO) δ 148.25, 139.71, 136.82, 136.78, 136.60, 135.35, 134.41, 130.10, 128.90, 128.82, 128.77, 128.68, 128.65, 128.51, 128.48, 128.45, 128.20, 128.06, 128.04, 126.65, 126.38, 125.11, 124.38, 123.62, 123.15, 122.41, 118.64, 107.08, 68.47 (d, J = 6.9 Hz, POCH₂), 68.04 (d, J = 6.8 Hz, POCH₂), 54.70 (d, J = 151.7 Hz, CP); HRMS (ESI-TOF) *m*/*z*: [MH]⁺ Calcd. for C₃₁H₂₇N₂O₅P: 539.1736, Found: 539.1735.

Dibenzyl N-(naphth-1-ylmethyl)amino-p-nitrobenzylphosphonate (**2Byc**)

Dibenzyl N-(naphth-1-ylmethyl)amino-p-nitrobenzylphosphonate (**2Byc**) was obtained as a brownish oil. ³¹P NMR (243 MHz, DMSO) δ 21.91; ¹H NMR (601 MHz, DMSO) δ 8.24 (d, J = 8.3 Hz, 1H), 8.17 (d, J = 8.2 Hz, 2H), 7.95 (d, J = 8.6 Hz, 2H), 7.83–7.78 (m, 1H), 7.53–7.49 (m, 2H), 7.43–7.21 (m, 11H), 7.17 (t, J = 7.8 Hz, 1H), 6.59 (d, J = 7.6 Hz, 1H), 6.41 (t, J = 7.6 Hz, 1H), 5.69 (dd, J = 26.0, J = 8.9 Hz, 1H, CHP), 5.15 (d, J = 8.2 Hz, 2H, POCH₂), 5.03–4.96 (m, 2H, POCH₂); ¹³C NMR (151 MHz, MeOD) δ 148.32, 145.99, 135.21, 130.74, 130.71, 129.81, 129.71, 129.66, 129.61, 129.52, 129.48, 129.32, 129.28, 129.17, 129.07, 128.97, 128.87, 127.70, 127.41, 127.21, 126.01, 125.13, 124.53, 122.98, 119.51, 107.92, 69.37 (d, J = 6.8 Hz, POCH₂), 68.99 (d, J = 6.8 Hz, POCH₂), 55.92 (d, J = 150.0 Hz, CHP); HRMS (ESI-TOF) m/z: [MH]⁺ Calcd. for C₃₁H₂₇N₂O₅P: 539.1736, Found: 539.1735.

Dibenzyl N-(naphth-1-yl)naphth-1-ylmethylaminophosphonate (**2Byd**)

Dibenzyl N-(naphth-1-yl)naphth-1-ylmethylaminophosphonate (2Byd) was obtained as a cream color solid, m.p. 137-139°C. ³¹P NMR (243 MHz, DMSO) δ 23.25; ¹H NMR (601 MHz, DMSO) δ 8.54 (d, J = 8.3 Hz, 1H), 8.24 (d, J =8.1 Hz, 1H), 8.00 (d, J = 7.8 Hz, 2H), 7.91 (t, J = 10.9 Hz, 1H), 7.79 (d, J = 7.8 Hz, 1H), 7.63-7.57 (m, 2H), 7.55-7.45 (m, 3H),7.36–7.27 (m, 5H), 7.24 (t, J = 7.1 Hz, 1H), 7.19 (t, J = 8.3 Hz, 3H), 7.06 (t, J = 7.9 Hz, 1H), 6.95 (d, J = 7.6 Hz, 2H), 6.42 (d, J = 6.5 Hz, 2H), 6.13 (dd, J = 24.5, j = 8.5 Hz, 1H, CHP),5.17 (d, J = 8.32, 2H, POCH₂), 4.59 and 4.91 (ABX system, J = 12.8, J = 7.4 Hz, 2H, POCH₂); ¹³C NMR (151 MHz, DMSO) δ 142.20, 142.11, 136.94, 136.90, 136.48, 136.44, 134.35, 133.87, 132.82, 131.83, 131.79, 129.24, 128.84, 128.66, 128.56, 128.50, 128.22, 128.06, 127.84, 126.95, 126.65, 126.38, 126.24, 126.01, 125.86, 125.27, 124.23, 124.15, 121.87, 118.38, 106.66, 68.38 (d, J = 6.9 Hz, POCH₂), 67.98 (d, J = 6.6 Hz, POCH₂), 51.45 (d, J = 152.6 Hz, CP); HRMS (ESI-TOF) m/z: [MH]⁺ Calcd. for C₃₅H₃₀NO₃P: 544.2042, Found: 544.2048.

Dibenzyl N-(naphth-1-yl)naphth-2-ylmethylaminophosphonate (**2Bye**)

Dibenzyl N-(naphth-1-yl)naphth-2-ylmethylaminophosphonate (**2Bye**) was obtained as a brownish solid, m.p. 133–136°C. ³¹P NMR (243 MHz, DMSO) δ 23.24; ¹H NMR (601 MHz, DMSO) δ 8.27 (d, J = 7.7 Hz, 1H), 8.21 (s, 1H), 7.90 (d, J = 7.2 Hz, 2H), 7.88–7.82 (m, 2H), 7.80 (d, J = 7.3 Hz, 1H), 7.55–7.48 (m, 4H), 7.43–7.14 (m, 11H), 6.69 (d, J = 7.3 Hz, 1H), 6.41–6.34 (m, 1H), 5.60 (dd, J = 24.9, j = 8.0 Hz, 1H, CHP), 5.17 (d, J = 7.7 Hz, 2H, POCH₂), 4.88 and 5.02 (ABX system, J = 12.6 Hz, J = 7.8 Hz; 2H, POCH₂); ¹³C NMR (151 MHz, MeOD) δ 143.21, 143.12, 137.78, 137.74, 137.55, 137.51, 135.34, 135.20, 134.02, 133.85, 129.82, 129.72, 129.65, 129.55, 129.46, 129.39, 129.35, 129.18, 129.06, 129.02, 128.95, 128.86, 128.80, 128.37, 128.32, 127.54, 127.49, 127.35, 127.15, 126.01, 125.13, 122.83, 119.20, 107.93, 69.15 (d, J = 6.7 Hz, POCH₂), 68.79 (d, J = 6.8 Hz, POCH₂), 56.44 (d, J = 151.3 Hz, CP); HRMS (ESI-TOF) m/z: [MH]⁺ Calcd. for C₃₅H₃₀NO₃P: 544.2042, Found: 544.2048.

Dibenzyl N-(naphth-1-yl)phenathren-9-ylaminomethylphosphonate (**2Byg**)

Dibenzyl N-(naphth-1-yl)phenathren-9-ylaminomethylphosphonate (2Byg) was obtained as a white solid; m.p. 121°C. ³¹P NMR (122 MHz, DMSO): δ 25.94; ¹H NMR (601 MHz, DMSO) δ 8.94 (d, J = 8.2 Hz, 1H), 8.84 (d, J = 8.4 Hz, 1H), 8.62 (d, J= 8.0 Hz, 1H), 8.38 (d, J = 2.4 Hz, 1H), 8.31 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 7.9 Hz, 1H), 7.82–7.72 (m, 3H), 7.68 (t, J =7.6 Hz, 1H), 7.61 (t, J = 7.5 Hz, 1H), 7.56 (t, J = 7.5 Hz, 1H), 7.51 (t, J = 7.4 Hz, 1H), 7.34 (d, J = 7.0 Hz, 2H), 7.30–7.25 (m, 3H), 7.23–7.16 (m, 2H), 7.13 (t, J = 7.2 Hz, 2H), 7.05 (t, J = 7.8 Hz, 1H), 6.95 (d, J = 7.5 Hz, 2H), 6.56 (t, J = 7.6 Hz, 1H), 6.44 (d, J = 7.6 Hz, 1H), 6.15 (dd, J = 24.4, 8.5 Hz, 1H, CHP), 5.25–5.13 (m, 2H, POCH₂), 5.00–4.66 (m, 2H, POCH₂); ¹³C NMR (151 MHz, DMSO) δ 142.28, 142.19, 136.94, 136.90, 136.45, 136.41, 134.39, 131.31, 130.62, 130.57, 130.14, 128.98, 128.82, 128.64, 128.60, 128.54, 128.45, 128.18, 127.79, 127.62, 127.56, 127.48, 127.20, 126.67, 126.41, 125.27, 124.91, 124.37, 124.03, 123.30, 122.11, 118.48, 106.72, 68.44 (d, J = 6.8 Hz, $POCH_2$), 67.99 (d, J = 6.7 Hz, $POCH_2$), 51.66 (d, J = 148.3 Hz, CP); HRMS (ESI-TOF) m/z: [MH]⁺ Calcd. for C₃₉H₃₂NO₃P: 594.2198, Found: 594.2207.

Synthesis of N-substituted aminobenzylphosphonic acids—general procedure

Triethyl phosphite (0.23 g, 1.85 mmole) was dissolved in dichloromethane (20 mL) and trimethylsilyl bromide (2.55 g, 16.5 mmole) was added under an argon atmosphere. The obtained solution was left for 24 h.

To the solution of Schiff base (1.7 mmole) in dichloromethane (20 mL) cooled in ice-bath, a solution of tri(trimethylsilyl) phosphite was added under argon. The solution was allowed to reach room temperature and was stirred at room temperature for 20 h. Then the volatile components of the reaction mixture were evaporated and the oily residue was dissolved in a methanolic solution of water (5%, 15 mL) and stirred at room temperature for an additional 24 h. The crude product was precipitated by the addition of diethyl ether (100 mL). After washing with three portions of dry ether (10 mL each) products of satisfactory purity crystallized from the solution.

N-(Naphth-1-ylmethyl)amino-o-nitrobenzylphosphonic acid (4xa)

N-(Naphth-1-ylmethyl)amino-o-nitrobenzylphosphonic acid (**4xa**) was obtained as a white solid, m.p. 255°C. ³¹P NMR (162 MHz, DMSO) δ 15.41; NMR (601 MHz, DMSO) δ 8.35 (s, 1H), 8.17 (d, J = 8.4 Hz, 1H), 8.07–7.97 (m, 1H), 7.69–7.55 (m, 2H), 5.02 (d, J = 20.2 Hz, 1H, CHP), 4.56 (s, 2H, CH₂); ¹³C NMR (101 MHz, DMSO) δ 133.66, 131.08, 130.28, 129.61, 129.12, 27.78, 127.22, 126.74, 125.82, 123.93, 120.20, 78.49 (CH₂), CP overshadowed by DMSO; HRMS (ESI-TOF) *m/z*: [MH]⁻ Calcd. for C₁₈H₁₇N₂O₅P: 371.0797, Found: 371.0841.

N-(Naphth-1-ylmethyl)amino-m-nitrobenzylphosphonic acid (4xb)

N-(Naphth-1-ylmethyl)amino-m-nitrobenzylphosphonic acid (**4xb**) was obtained as a white solid, m.p. 215°C. ³¹P NMR (243 MHz, DMSO) δ 10.52 ¹H NMR (601 MHz, DMSO) δ 8.49 (d, *J* = 1.2 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 2H), 8.00 (d, *J* = 7.9 Hz, 2H), 7.93 (t, *J* = 10.5 Hz, 1H), 7.72 (d, *J* = 7.0 Hz, 1H), 7.68 (t, *J* = 8.0 Hz, 1H), 7.64–7.58 (m, 2H), 7.55 (t, *J* = 7.7 Hz, 1H), 5.05 and 5.12 (AB system, *J* = 14.8 Hz, 2H, CH₂), 4.67 (d, *J* = 13.4 Hz, 1H, CHP); HRMS (ESI-TOF) *m/z*: [MH]⁻ Calcd. for C₁₈H₁₇N₂O₅P: 371.0797 Found: 371.0795.

N-(Naphth-1-ylmethyl)amino-p-nitrobenzylphosphonic acid (4xc)

N-(Naphth-1-ylmethyl)amino-p-nitrobenzylphosphonic acid (**4xc**) was obtained as a white solid, m.p. 184–185°C. ³¹P NMR (243 MHz, DMSO) δ 10.82; ¹H NMR (601 MHz, DMSO) δ 8.13 (d, *J* = 8.6 Hz, 1H), 8.07 (d, *J* = 8.3 Hz, 1H), 7.95–7.90 (m, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.61 (d, *J* = 7.0 Hz, 1H), 7.55–7.48 (m, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 4.41 and 4.54 (AB system, *J* = 14.0 Hz, 2H, CH₂), 4.38 (d, *J* = 18.8 Hz, 1H, CHP); HRMS (ESI-TOF) *m*/*z*: [MH]⁻ Calcd. for C₁₈H₁₇N₂O₅P: 371.0797; Found: 371.0790.

N-(Naphth-1-ylmethyl)naphth-1-ylaminomethylphosphonic acid (**4xd**)

N-(Naphth-1-ylmethyl)naphth-1-ylaminomethylphosphonic acid (**4xd**) was obtained as a white solid, m.p. 260–264°C. ³¹P NMR (122 MHz, D₂O) δ 16.12; ¹H NMR (300 MHz, D₂O) δ 8.15 (s, 1H), 7.96–7.83 (m, 2H), 7.79 (d, J = 8.3 Hz, 1H), 7.68 (d, J = 7.9 Hz, 1H), 7.63–7.41 (m, 5H), 7.30 (t, J = 7.4 Hz, 1H), 7.25–7.14 (m, 2H), 7.07 (d, J = 6.7 Hz, 1H), 4.68 (d, J =18.5 Hz, 1H, CHP), 3.69 and 3.77 (AB system, J = 13.5 Hz, 2H, CH₂); HRMS (ESI-TOF) m/z: [MH]⁻ Calcd. for C₃₄H₂₈NO₃P: 530.1885, Found: 530.1863, while for monoester: C₂₂H₂₀NO₃P: 376.1103, Found: 376.1112.

N-(Naphth-1-ylmethyl)naphth-2-ylaminomethylphosphonic acid (**4xe**)

N-(Naphth-1-ylmethyl)naphth-2-ylaminomethylphosphonic acid (**4xe**) was obtained as a white solid, m.p. 199–200°C. ³¹P NMR (122 MHz, DMSO): δ 12.20; ¹H NMR (601 MHz, DMSO) δ 8.03–7.86 (m, 5H), 7.81 (s, 2H), 7.75–7.59 (m, 2H), 7.58–7.45 (m, 3H), 7.44–7.30 (m, 2H), 4.43 (s, 2H, CH₂), 4.28 (d, J =

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14.4 Hz, 1H, CHP); HRMS (ESI-TOF) m/z: [MH]⁻ Calcd. for C₂₂H₂₀NO₃P: 376.1103, Found: 376.1094.

N-(Naphth-1-ylmethyl)anthracen-9-ylaminomethylphosphonic acid (4xf)

N-(Naphth-1-ylmethyl)anthracen-9-ylaminomethylphosphonic acid (**4xf**) was obtained as a yellow solid, m.p. 189°C. ³¹P NMR (243 MHz, DMSO) δ 12.20; ¹H NMR (601 MHz, DMSO) δ 8.82 (d, *J* = 8.9 Hz, 1H), 8.72 (s, 1H), 8.20–8.09 (m, 3H), 8.01–7.95 (m, 2H), 7.85 (d, *J* = 9.1 Hz, 1H), 7.71 (d, *J* = 7.1 Hz, 1H), 7.69–7.53 (m, 4H), 7.52–7.48 (m, 1H), 7.46 (t, *J* = 7.7 Hz, 1H), 7.44–7.39 (m, 1H), 5.99 (d, *J* = 22.0 Hz, 1H, CHP), 4.94 and 5.01 (AB system, *J* = 13.8 Hz, 2H, CH₂); HRMS (ESI-TOF) *m/z*: [MH]⁻ Calcd. for C₂₆H₂₂NO₃P: 426.1259, Found: 426. 1251.

N-(Naphth-1-ylmethyl)phenathren-9-ylaminomethylphosphonic acid (**4xg**)

N-(Naphth-1-ylmethyl)phenathren-9-ylaminomethylphosphonic acid (**4xg**) was obtained as a yellow solid, 229°C. ³¹P NMR (243 MHz, DMSO) δ 11.81; ¹H NMR (601 MHz, DMSO) δ 8.93 (d, *J* = 8.1 Hz, 1H), 8.88 (d, *J* = 8.3 Hz, 1H), 8.34 (s, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 8.19 (d, *J* = 8.2 Hz, 1H), 8.02–7.96 (m, 2H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.79–7.67 (m, 5H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.52 (dd, *J* = 15.1, 7.4 Hz, 2H), 5.65 (d, *J* = 16.4 Hz, 1H, CHP), 4.90 and 5.24 (AB system, *J* = 13.4 Hz, 2H, CH₂); ¹³C NMR (101 MHz, DMSO) δ 133.64, 132.09, 130.80, 130.69, 130.39, 130.25, 130.12, 128.99, 128.47, 128.16, 128.06, 127.67, 127.34, 127.26, 127.06, 126.53, 125.65, 124.86, 124.24, 123.85, 123.35, 55.00 (d, *J* = 140.4 Hz, CP), 48.30 (CH₂); HRMS (ESI-TOF) *m/z*: [MH]⁻ Calcd. for C₂₆H₂₂NO₃P: 426.1259, Found: 426.1263.

N-(Naphth-1-yl)amino-o-nitrobenzylphosphonic acid (4ya)

N-(Naphth-1-yl)amino-o-nitrobenzylphosphonic acid (**4ya**) was obtained as a green-yellow solid, m.p. 130°C, decomposition 131°C. ³¹P NMR (243 MHz, MeOD) δ 16.56; ¹H NMR (601 MHz, MeOD) δ 6.67 (d, J = 8.4 Hz, 1H), 6.49 (d, J = 8.2 Hz, 1H), 6.29–6.21 (m, 2H), 6.05–5.90 (m, 4H), 5.68 (d, J = 8.2 Hz, 1H), 5.66–5.60 (m, 1H), 5.02 (d, J = 7.5 Hz, 1H), 4.68 (d, J = 22.0 Hz, 1H, CHP); ¹³C NMR (151 MHz, MeOD) δ 148.55, 139.59, 132.97, 131.35, 130.99, 126.63, 126.59, 126.50, 126.47, 124.32, 124.22, 124.00, 123.28, 122.19, 118.39, 116.56, 103.99, 50.02 (d, J = 147.30, CP); HRMS (ESI-TOF) m/z: [MH]⁺ Calcd for HRMS (ESI-TOF) m/z: [MH]⁺ Calcd for C₁₇H₁₅N₂O₅P: 359.0797, Found: 357.0744.

N-(Naphth-1-yl)amino-m-nitrobenzylphosphonic acid (4yb)

N-(Naphth-1-yl)amino-m-nitrobenzylphosphonic acid (**4yb**) was obtained as a green solid, m.p. 103–107°C. ³¹P NMR (243 MHz, MeOD) δ 20.17; ¹H NMR (601 MHz, MeOD) δ 6.91 (s, 1H), 6.64–6.53 (m, 2H), 6.38 (d, *J* = 7.7 Hz, 1H), 6.18 (d, *J* = 8.2 Hz, 1H), 5.99 (t, *J* = 7.9 Hz, 1H), 5.93 (t, *J* = 7.7 Hz, 1H), 5.88 (t, *J* = 7.6 Hz, 1H), 5.65 (d, *J* = 8.2 Hz, 1H), 5.57 (t, *J* = 7.8 Hz, 1H), 4.95 (d, *J* = 7.6 Hz, 1H), 3.81 (d, *J* = 25.3 Hz, 1H, CHP); ¹³C NMR (151 MHz, MeOD) δ 146.85, 139.44, 132.89,

132.28, 127.78, 126.55, 124.07, 124.02, 123.26, 122.64, 121.02, 120.94, 120.92, 118.57, 117.29, 105.13, 53.31 (d, J = 152.70, CP); HRMS (ESI-TOF) m/z: [MH]⁺ Calcd. for C₁₇H₁₅N₂O₅P: 359.0797, Found: 357.0703.

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N-(Naphth-1-yl)amino-p-nitrobenzylphosphonic acid (4yc)

N-(Naphth-1-yl)amino-p-nitrobenzylphosphonic acid (**4yc**) was obtained as a green solid, m.p. 123–126°C. ³¹P NMR (243 MHz, MeOD) δ 15.30, 14.98; ¹H NMR (601 MHz, MeOD) δ 6.66–6.55 (m, 3H), 6.26–6.17 (m, 4H), 6.00–5.88 (m, 3H), 5.55 (s, 1H), 3.52 (d, *J* = 22.1 Hz, 1H, CHP); ¹³C NMR (151 MHz, MeOD) δ 145.77, 144.31, 139.77, 132.83, 127.13, 127.10, 126.57, 123.97, 123.92, 123.14, 122.34, 121.39, 118.40, 55.37 (d, *J* = 144.50, CP); HRMS (ESI-TOF) *m/z*: [MH]⁺ Calcd. for C₃₀H₂₅N₂O₅P: C₂₇H₂₂N₂O₅P: 357.0640, Found: 357.0641.

N-(Napht-1-yl)anthracen-9-ylaminomethylphosphonic acid (4yf) (MG/II/25-pha)

N-(Napht-1-yl)anthracen-9-ylaminomethylphosphonic acid (**4yf**) (MG/II/25-pha) was obtained as a yellow solid and decomposed at 267°C. ³¹P NMR (243 MHz, MeOD+NaOD/D₂O) δ 20.61; ¹H NMR (601 MHz, DMSO+NaOD/D₂O) δ 8.48 (d, *J* = 13.2 Hz, 3H), 8.24 (d, *J* = 8.6 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 3H), 7.37 (d, *J* = 8.6 Hz, 3H), 7.27 (d, *J* = 7.8 Hz, 2H), 7.18 (t, *J* = 11.6 Hz, 1H), 7.13 (d, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 7.5 Hz, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 4.15 (d, *J* = 25.6 Hz, 1H, CHP); HRMS (ESI-TOF) *m/z*: [MH]⁻ Calcd. for C₂₅H₂₀NO₃P: 412.1103, Found: 412.1120.

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