Synthesis of novel fused heterocyclic system: 5-(substituted) -5-oxo-5*H*-6,12-dioxa-5λ^5–phosphabenzo (a) anthracene-7-ones

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Abstract

Synthesis of new fused phosphorus heterocyclic derivatives, phosphabenzo[a]anthracene-7-ones, is accomplished by a new methodology involving Friedel-Crafts insertion of phosphorus trichloride into 3-flavanol in the presence of $ZnCl_2$ as a catalyst and subsequent reaction of the resultant chloroxaphosphorin with various alcohols in the presence of triethylamine, followed by oxidation with H_2O_2. The structures were determined by IR, ^1H, ^{13}C, ^{31}P NMR and mass spectral (MS) studies. They were screened for antifungal and antibacterial activity.

Keywords: Chloroxaphosphorin; 5-oxo-5*H*-6,12-dioxa-5λ^5–phosphabenzo (a) anthrace-ne -7 -ones; 3-hydroxyflavone; C-phosphorylation, Friedel-Crafts reaction

Introduction

Synthesis of new multi-ring phosphorus heterocycles for applications in medicine and industry has attracted the attention of researchers in recent years.[1-5] Phosphorus analogues of α-pyrones, which act as HIV protease inhibitors,[6] have sparked additional interest. Flavonoids are a large class of natural pigments which are an integral part of the human diet acting as antioxidants.[7] They also play an important role as insecticides[8] and their photochemical properties are well known.[9-10] In view of this, syntheses of phosphorus heterocycles annulated with both α-pyrones and benzene alkoxy/ aryloxy/ alkeneoxy and alkyneoxy substituted at phosphorus have been accomplished.

Results and Discussion

The novel benzanulated phosphorus heterocyclic compounds (**4a-j**) (Scheme 1) were prepared in two steps, starting from 3-hydroxyflavone (**1**). Lewis acid catalyzed electrophilic phosphorylation of **1** with phosphorus (III) chloride,[1,2,2a] formed phosphorus dichloride

intermediate **2,** which on subsequent intramolecular Friedel-Crafts insertion in the presence of $ZnCl_2$ as catalyst formed the six membered chlorophosphorin **3**. In the second step, **3** undergoes halide displacement on reaction with various alcohols in diethyl ether at 25 °C in the presence of Et_3N as an acid acceptor. Subsequent oxidation with H_2O_2 gave the title compounds **4a-j**. The products were obtained by filtering off triethylamine hydrochloride, evaporation of the filtrate, washing the residue with water and recrystallization of the solid products using suitable solvents. Thin layer chromatography was employed to determine the purity of the products. All the title compounds **4a-j** are readily soluble in polar solvents and melt in the range of 148-182°C. Their chemical structures were established by elemental analysis, IR, ^{1}H, ^{13}C, ^{31}P NMR and MS spectra.

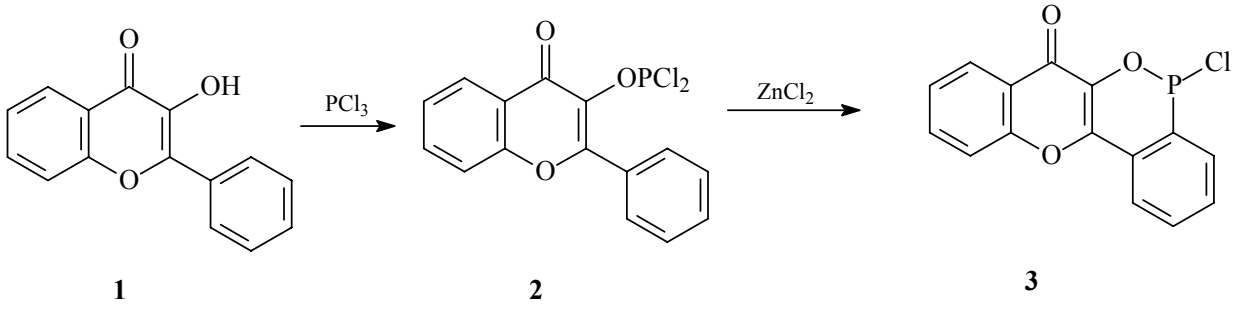
The presence of characteristic IR bands for P-O-C $_{exo}$ (901-912, 1110-1124 cm^{-1}) P-O-C $_{endo}$ (977-1043, 1191-1205 cm^{-1}), P=O (1275-1292 cm^{-1}), P-C_{arom} (1460-1480 cm^{-1}), and C=O (1611-1615 cm^{-1}) of **4a-j** [11,12] proved the formation of phosphabenzo [a]anthracene-7-ones.

^{1}H NMR data agreed well with the structures proposed for **4a-j**. The doublets at δ 7.71-7.74 (J = 7.8-8.1 Hz) and δ 8.00-8.09 (J = 7.6-7.8 Hz) are assigned to H-1 and H-4 protons. [2,4,10,11,15] The H-2 and H-3 resonated [2,4,10,11,15] as doublets of doublets at δ 7.66-7.69 (J =7.3-7.6, 1.1-1.3 Hz) and at δ 7.53-7.58 (J = 7.5-7.7, 1.3-1.8 Hz), respectively. The signals at δ 7.47-7.51(dd, J = 7.0-7.4, 1.1-1.5) are attributed [2,9,10,14] to H-9 and H-10, respectively. The H-8 and H-11 resonated [2,9,10,14] as a doublet at δ 8.25-8.27 (J = 7.1-7.4, Hz) and δ 7.17- 7.21 (J = 7.6-7.8 Hz), respectively. The chemical shifts of the protons present in the substituents appeared in the expected regions.[13]

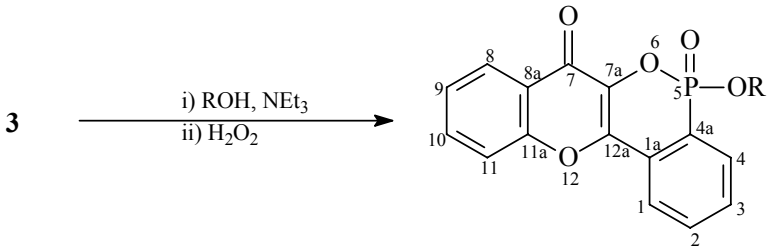
^{13}C NMR chemical shifts of **4a-j** were interpreted on the basis of additivity rules.[6,11,16] The phosphorus bonded C-4a resonated as a doublet at δ 124.8-126.1 (J = 125-142 Hz). The endocyclic oxygen bonded C-7a, gave signals as a doublet at δ 142.3-145.0 (J = 8-9 Hz). The exocyclic oxygen bonded C-1$'$ gave signals as a doublet at δ 60.3-151.2 (J = 6-7 Hz). The chemical shifts of C-1a, and C-8a appeared at δ 128.7- 130.4 and 121.0-121.9, respectively. The carbonyl carbon C-7 resonated at δ 172.9- 174.3. The remaining carbon signals are observed in the expected regions.[13]

The absence of a signal for the hydroxy proton and presence of a signal for C-4a, with a coupling constant ^1Jcp = 125-142 Hz, provided the most convincing evidence for the formation of the oxaphosphorin ring.

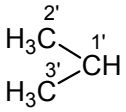
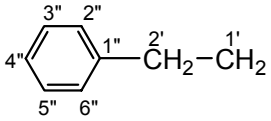
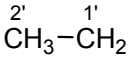
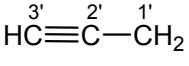
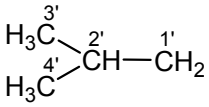
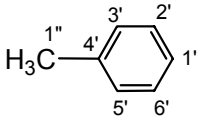
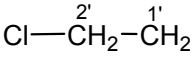
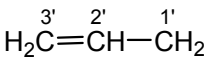
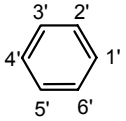
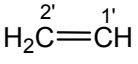
^{31}P NMR chemical shifts[17]of these compounds (**4a-j**) appeared in the region 15.3-22.3 ppm. GC Mass spectra for **4a-j** show the appearance of M^+ at the appropriate molecular weight, $[M-(OR)]^+$ at m/z 283, $[M-R, PO_3]^+$ at m/z 220, $[M-C_6H_4PO_2R]^+$ at 162 and $[M-C_8H_3O_2PR]^+$ at m/z 121, conclusively establishing the proposed molecular structures.



1 **2** **3**



4a—j

Compd.	R	Compd.	R
4a		**4f**	
4b		**4g**	
4c		**4h**	
4d		**4i**	
4e		**4j**	

Scheme 1

Antimicrobial activity

Compounds **4a-j** were screened for their antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* (10^6 cell/mL) by the disc-diffusion method[18, 19] in nutrient agar medium at various concentrations (250, 500 µg/disc) in dimethylformamide (DMF). These solutions were added to each filter disc and DMF was used as the control. The plates were incubated at 35 °C and examined for zone of inhibition around each disc after 24 h. The results were compared with

the activity of the standard antibiotic Penicillin (250 μg/disc). Their antifungal activity[20] was evaluated against *Curvularia lunata* and *Fusarium oxysporium* at concentrations of 250 and 500 μg/disc (Table 1). Griseofulvin was used as the reference compound (Table-1). Fungal cultures were grown on potato dextrose broth at 25 °C and, finally, spore suspension was adjusted to 10^5 spores/mL. Most of the compounds showed significant activity against bacteria and low activity against fungi.

Experimental Section

General Procedures

Melting points were determined on a Mel.-Temp apparatus and are uncorrected. Elemental analyses were performed at the Central Drug Research Institute, Lucknow, India. IR spectra were recorded in KBr pellets on a Perkin- Elmer 283 unit. ^{1}H, ^{13}C and ^{31}P-NMR spectra were taken on a AMX 400 MHz spectrometer operating at 400 MHz for ^{1}H, 100 MHz for ^{13}C and 161.9 MHz for ^{31}P. The compounds were dissolved in DMSO-d_6 and $CDCl_3$, and chemical shifts were referenced to TMS (^{1}H and ^{13}C) and 85% H_3PO_4 (^{31}P). Mass spectra were recorded on GC-MS instrument at 70 eV with a direct inlet system. 3-hydroxyflavone and various alcohols were procured from Lancaster, London and from Aldrich Chemical Company, USA were used without further purification.

Synthesis of 5-(isopropyl)-5-oxo-5*H*-6,12-dioxa-5λ^5–phosphabenzo (a) anthracene-7-one (4a). General procedure. A mixture of phosphorus trichloride (5.0 g, 0.036 mole) and 3-hydroxy-flavone (4.7 g, 0.02 mole) was heated gradually to 180°C over a period of 5 hours with continuous stirring. A slow sweep of nitrogen was maintained in the reaction vessel to facilitate the ready removal of evolved hydrogen chloride. The reaction flask containing the chlorophosphine precursor **2** was cooled to 25°C and 0.03 g of anhydrous zinc chloride was added to it. The temperature of the reaction mixture was increased to 210°C over a period of 2 hours and then cooled to room temperature. The reaction mixture was dissolved in 30 mL of ether, and to it was added drop wise a mixture of isopropyl alcohol (1.2 g, 0.02 mole) and triethylamine (2.0 g, 0.02 mole) in 30 mL of dry diethyl ether. The reaction mixture was stirred at 25°C for 2 hours. Triethylamine hydrochloride was removed by filtration, H_2O_2 (1.0 g 0.03 mole) was added to the filtrate and stirred for one hour. The resulting solution was extracted twice with diethyl ether and dried over anhydrous $MgSO_4$. On evaporation of solvent at room temperature a crude product was obtained. It was washed with chilled isopropanol and recrystallized from methanol to give **4a**. The progress of the reaction was monitored by TLC using ethyl acetate and hexane (3:1) mixture as mobile solvent and silica gel as adsorbent.
Compounds **4b-j** were prepared adopting the same procedure.

Table 1. Antimicrobial activity of 5-(substituted)-5-oxo-5H-6,12-dioxa-5λ^5–phospha benzo (a) anthracene-7-ones (4a-j)

Compd.	Zone of inhibition (mm)							
	Bacteria				Fungi			
	Staphylococcus aureus		*Escherichia coli*		*Curvularia lunata*		*Fusarium oxysporium*	
	250 µg/disc	500 µg/disc	250 µg/disc	500 µg/disc	250 µg/disc	500 µg/disc	250 µg/disc	500 µg/disc
4a	12.1	14.2	10.6	16.0	5.0	6.0	5.0	7.0
4b	11.7	13.5	11.4	16.8	3.0	4.0	2.0	4.3
4c	10.8	12.1	10.4	15.9	4.6	6.0	4.0	6.3
4d	16.3	19.8	14.1	16.9	4.0	5.0	6.3	7.0
4e	15.6	17.7	13.0	14.7	3.0	5.3	4.0	6.0
4f	14.2	16.8	11.4	13.7	2.0	4.0	3.0	5.3
4g	12.5	14.3	10.2	11.6	4.0	5.6	4.0	6.0
4h	16.4	18.1	10.4	12.3	5.0	6.3	5.0	7.0
4i	18.4	20.9	15.3	19.9	4.6	6.0	5.0	6.3
4j	16.7	19.2	9.4	11.1	2.0	5.0	3.0	5.3
Penicillin	22		21					
Griseofulvin					20		20	

Physical, Analytical and Spectral Data for the Compounds (4a-j)

5-(Isopropoxy)-5-oxo-5*H*-6,12-dioxa-5λ^5–phosphabenzo(a)anthracene-7-one(4a). Yield 68%. mp 167-169 °C. IR$_{(KBr)}$: ν_{max} (Cm^{-1}), C=O 1612, P=O 1287, P-C$_{Ar}$ 1476, P-O-C$_{endo}$ P-O 977, O-C 1200, P-O-C$_{exo}$, P-O 901, O-C 1123, ^{31}P NMR ($CDCl_3$, 161.9 MHz) δ: 20.9. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.73 (d, *J* = 7.9, H-1), 7.69 (dd, *J* = 7.6, 1.3, H-2), 7.56 (dd, *J* = 7.6, 1.8, H-3), 8.03 (d, *J* =7.7, H-4), 8.26 (d, *J* = 7.3, H-8), 7.42 (dd, *J* = 7.4, 1.2, H-9), 7.49 (dd, *J* = 7.3, 1.5, H-10), 7.19 (d, *J* = 7.8, H-11), 0.97 (m, 3H, CH_3), 1.12-1.13 (m, 3H, CH_3), 3.76 (m, 1H, OCH). ^{13}C NMR ($CDCl_3$ 100 MHz) δ: 127.5 (C-1), 128.5 (C-2), 131.1 (C-3), 133 (C-4), 173 (C-7), 122.9 (C-8), 124.0 (C-9), 133.9 (C-10), 117 (C-11), 129.9 (C-1a), 125.3 (d, *J* = 130.8 Hz, C-4a), 144.9 (d, $^2J_{(P\text{-}O\text{-}C\ endo)}$= 8.2 Hz, C-7a), 121.0 (C-8a), 155.4 (C-11a), 154.8 (C-12a), 66.2 (d, $^2J_{(P\text{-}O\text{-}C\ exo)}$= 6.1 Hz, C-1' O<u>C</u>H), 15.3 (<u>C</u>H_3)$_2$; GC-MS (%): 342 ($M^{+\bullet}$ 22), 326 (29), 300 (45), 283 (37), 236 (18), 220 (35), 162 (7), 147 (24), 135 (33), 121(100), 107 (25), 91 (52)., Anl Calcd for $C_{18}H_{15}O_5P$: C, 63.15; H, 4.38; Found: C, 62.89; H, 4.34%.

5-(Ethoxy)-5-oxo-5*H*-6,12-dioxa-5λ^5–phosphabenzo (a) anthracene-7one (4b). Yield 68%. mp 148-149 °C. IR$_{(KBr)}$: ν_{max} (Cm^{-1}), C=O 1614, P=O 1291, P-C$_{Ar}$ 1476, P-O-C$_{endo}$ P-O 1043, O-C 1200, P-O-C$_{exo}$, P-O 908, O-C 1121, ^{31}P NMR ($CDCl_3$, 161.9 MHz) δ: 15.3; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.73 (d, *J = 8.1*, H-1), 7.68 (dd, *J* = 7.4, 1.2, H-2), 7.54 (dd, *J* = 7.7, 1.6, H-3), 8.00 (d, *J* = 7.7, H-4), 8.25 (d, *J* = 7.1, H-8), 7.42 (dd, *J* = 7.4, 1.1, H-9), 7.48 (dd, *J* = 7.0, 1.2, H-

10), 7.19 (d, *J* = 7.7, H-11), 1.37 (t, *J* = 7.5, 3H, CH_3), 3.27 (q, 2H, OCH_2), ^{13}C NMR ($CDCl_3$ 100 MHz) δ: 127.7 (C-1), 128.3 (C-2), 130.2 (C-3), 133.6 (C-4), 173.7 (C-7), 122.2 (C-8), 124.2 (C-9), 134.2 (C-10), 118.2 (C-11), 128.8 (C-1a), 124.8 (d, *J* = 127 Hz, C-4a), 145.0 (d, $^2J_{(P\text{-}O\text{-}C\ endo)}$= 8.5 Hz, C-7a), 121.8 (C-8a), 155.9 (C-11a), 154.6 (C-12a), 64.5 (d, $^2J_{(P\text{-}O\text{-}C\ exo)}$= 6.5 Hz, C-1' O<u>C</u>$H_2$), 15.7 (<u>C</u>$H_3$); GC-MS (%):328 ($M^{+\bullet}$, 46), 312 (31), 300 (28), 283 (41), 236 (14), 220 (27), 144 (32), 135 (22), 121 (100), 119 (18), 117 (11), 91 (43).; Anl Calcd for $C_{17}H_{13}O_5P$: C, 62.19; H, 3.96; Found: C, 61.95; H, 3.93%.

5-(Isobutoxy)-5-oxo-5*H*-6,12-dioxa-5λ^5–phosphabenzo(a)anthracene-7-one(4c). Yield 70%. mp 161-163 °C. $IR_{(KBr)}$: ν_{max} (Cm^{-1}), C=O 1613 P=O 1285, P-C_{Ar} 1468, P-O-C_{endo} P-O 987, O-C 1205, P-O-C_{exo}, P-O 907, O-C 1122, ^{31}P NMR ($CDCl_3$, 161.9 MHz) δ: 22.3 ; ^1H NMR ($CDCl_3$, 300 MHz) δ: 7.71 (d, *J* = 7.9, H-1), 7.68 (dd, *J* = 7.4, 1.2, H-2), 7.54 (dd, *J* = 7.6, 1.4, H-3), 8.05 (d, *J* =7.8, H-4), 8.27 (d, *J* = 7.3, H-8), 7.42 (dd, *J* = 7.5, 1.3, H-9), 7.48 (dd, *J* = 7.1, 1.4, H-10), 7.20 (d, *J* = 7.7, H-11), 0.87-1.03 (m, 6H, $2CH_3$), 1.19-1.42 (m, 1H, CH), 3.73-4.0 (m, 2H, CH_2). ^{13}C NMR ($CDCl_3$ 100 MHz) δ: 127.1 (C-1), 128.5 (C-2), 130.4 (C-3), 132.9 (C-4), 174.2 (C-7), 122.8 (C-8), 124.4 (C-9), 133.6 (C-10), 117.8 (C-11), 129.7 (C-1a), 125.3 (d, *J* = 131 Hz, C-4a), 142.3 (d, $^2J_{(P\text{-}O\text{-}C\ endo)}$= 8.3 Hz, C-7a), 121.5 (C-8a), 155.5 (C-11a), 153.9 (C-12a), 68.1 (d, $^2J_{(P\text{-}O\text{-}C\ exo)}$= 6.3 Hz, C-1' O<u>C</u>$H_2$), 41.3 (<u>C</u>H), 21.1 $(CH_3)_2$; Anl Calcd for $C_{19}H_{17}O_5P$: C, 64.04; H, 4.77; Found: C, 63.78; H, 4.72%.

5-(2-Chloroethoxy)-5-oxo-5*H*-6,12-dioxa-5λ^5–phosphabenzo(a)anthracene-7-one (4d). Yield 68%. mp 157-159 °C. $IR_{(KBr)}$: ν_{max} (Cm^{-1}), C=O 1611, P=O 1276, P-C_{Ar} 1460, P-O-C_{endo} P-O 996, O-C 1191, P-O-C_{exo}, P-O 909, O-C 1110, ^{31}P NMR ($CDCl_3$, 161.9 MHz) δ: 18.7; ^1H NMR ($CDCl_3$, 300 MHz) δ: 7.74 (d, *J* = 8.0, H-1), 7.69 (dd, *J* = 7.3, 1.1, H-2), 7.53 (dd, *J* = 7.6, 1.3, H-3), 8.08 (d, *J* = 7.8, H-4), 8.27 (d, *J* = 7.3, H-8), 7.43 (dd, *J* = 7.3, 1.1, H-9), 7.49 (dd, *J* = 7.3, 1.4, H-10), 7.17 (d, *J* = 7.8, H-11), 4.65 (t 2H, OCH_2), 4.14 (t, 2H, CH_2Cl).; ^{13}C NMR ($CDCl_3$ 100 MHz) δ: 127.6 (C-1), 128.4 (C-2), 130.3 (C-3), 133 (C-4), 173.8 (C-7), 122.7 (C-8), 124.4 (C-9), 133.9 (C-10), 117.8 (C-11), 129.6 (C-1a), 126.1 (d, *J* = 128 Hz, C-4a), 143.4 (d, $^2J_{(P\text{-}O\text{-}C\ endo)}$= 8.9 Hz, C-7a), 121.3 (C-8a), 155.6 (C-11a), 153.5 (C-12a), 63.2 (d, $^2J_{(P\text{-}O\text{-}C\ exo)}$= 6.1 Hz, C-1', O<u>C</u>H_2), 22.4 (CH_2Cl); Anl Calcd for $C_{17}H_{12}O_5PCl$: C, 56.27; H, 3.31; Found: C, 56.10; H, 3.26%.

5-(Phenoxy)-5-oxo-5*H*-6,12-dioxa-5λ^5–phosphabenzo(a)anthracene-7-one (**4e**). Yield 75%. mp 181-183 °C. $IR_{(KBr)}$: ν_{max} (Cm^{-1}), C=O 1612, P=O 1287, P-C_{Ar} 1475, P-O-C_{endo} P-O 1035, O-C 1203, P-O-C_{exo}, P-O 912, O-C 1119, ^{31}P NMR ($CDCl_3$, 161.9 MHz) δ: 21.9; ^1H NMR ($CDCl_3$, 300 MHz) δ: 7.73 (d, *J* = 7.8, H-1), 7.66 (dd, *J* = 7.5, 1.9, H-2), 7.53 (dd, *J* = 7.6, 1.4, H-3), 8.01 (d, *J* = 7.6, H-4), 8.25 (d, *J* = 7.3, H-8), 7.40 (dd, *J* = 7.3, 1.1, H-9), 7.47 (dd, *J* = 7.2, 1.3, H-10), 7.21 (d, *J* = 7.6, H-11), 6.91-7.49 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$ 100 MHz) δ: 127.3 (C-1), 128.8 (C-2), 131.0 (C-3), 133.4 (C-4), 172.9 (C-7), 122.5 (C-8), 124.1 (C-9), 133.8 (C-10), 118.3 (C-11), 130.4 (C-1a), 125.4 (d, *J* = 129 Hz, C-4a), 144.9 (d, $^2J_{(P\text{-}O\text{-}C\ endo)}$= 8.6 Hz, C-7a), 121.9 (C-8a), 155.2 (C-11a), 154.5 (C-12a), 149.4 (d, $^2J_{(P\text{-}O\text{-}C\ exo)}$= 8.2 Hz, ipso carbon C-1'), 128.5 (C-3'&C-5'), 125.7 (C-4'), 121.4b(C-2'&C-6'); GC-MS (%):376 ($M^{+\bullet}$, 64), 300 ($M^{+\bullet}$, 46), 283 (41),

236 (53), 220 (38), 158 (13), 144 (18), 121 (100), 93 (17).; Anl Calcd for $C_{21}H_{13}O_5P$: C, 67.02; H, 3.45; Found: C, 66.84; H, 3.40%.

5-(2-Phenylethoxy)-5-oxo-5*H*-6,12-dioxa-5λ^5–phosphabenzo(a)anthra-cene-7-one (**4f**). Yield 67%. mp 163-164 °C. IR$_{(KBr)}$: ν_{max} (Cm^{-1}), C=O 1617, P=O 1279, P-C$_{Ar}$ 1468, P-O-C$_{endo}$ P-O 992, O-C 1203, P-O-C$_{exo}$, P-O 908, O-C 1120, ^{31}P NMR ($CDCl_3$, 161.9 MHz) δ: 19.8; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.71 (d, *J* = 8.0, H-1), 7.67 (dd, *J* = 7.6, 1.3, H-2), 7.56 (dd, *J* = 7.7, 1.3, H-3), 8.09 (d, *J* = 7.6, H-4), 8.26 (d, *J* = 7.4, H-8), 7.41 (dd, *J* = 7.5, 1.2, H-9), 7.50 (dd, *J* = 7.2, 1.3, H-10), 7.21 (d, *J* = 7.8, H-11), 2.81 (t, *J* = 7.3, 2H, CH_2), 4.56 (t, *J* = 7.5, 2H, OCH_2), 6.82-7.24 (m, 5H, Ar); ^{13}C NMR ($CDCl_3$ 100 MHz) δ: 127.7 (C-1), 128.2 (C-2), 131.1 (C-3), 133.7 (C-4), 173.5 (C-7), 122.6 (C-8), 124.8 (C-9), 134.5 (C-10), 118.4 (C-11), 128.7 (C-1a), 125.7 (d, *J* = 126 Hz, C-4a), 142.8 (d, $^2J_{(P\text{-}O\text{-}C\ endo)}$= 8.5 Hz, C-7a), 121.7 (C-8a), 155.4 (C-11a), 154.1 (C-12a), 136.3(ipso carbon, C-1"), 124.2 (C-2"&C-6"), 127.2 (C-3"&C-5"), 125 (C-6') 65.1 (d, $^2J_{(P\text{-}O\text{-}C\ exo)}$= 7 Hz, C-1', O<u>C</u>H$_2$), 34.8 (C-2', <u>C</u>H$_2$); Anl Calcd for $C_{23}H_{17}O_5P$: C, 68.30; H, 4.20; Found: C, 68.18; H, 4.17%.

5-(2-Yne-propoxy)-5-oxo-5*H*-6,12-dioxa-5λ^5–phosphabenzo(a)anthracene-7-one (4g). Yield 48%. mp 155-156 °C. IR$_{(KBr)}$: ν_{max} (Cm^{-1}), C=O 1614, P=O 1288, P-C$_{Ar}$ 1474, P-O-C$_{endo}$ P-O 1018, O-C 1203, P-O-C$_{exo}$, P-O 905, O-C 1122, ^{31}P NMR ($CDCl_3$, 161.9 MHz) δ: 17.6. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.72 (d, *J* = 7.8, H-1), 7.69 (dd, *J* = 7.5, 1.2, H-2), 7.58 (dd, *J* = 7.5, 1.4, H-3), 8.03 (d, *J* =7.8, H-4), 8.27 (d, *J* = 7.4, H-8), 7.44 (dd, *J* = 7.4, 1.1, H-9), 7.51 (dd, *J* = 7.1, 1.3, H-10), 7.18 (d, *J* = 7.6, H-11), 2.06 (s, 1H, CH≡C), 4.21 (s, 2H, OCH_2); ^{13}C NMR ($CDCl_3$ 100 MHz) δ: 127.4 (C-1), 128.7 (C-2), 131.3 (C-3), 132.6 (C-4), 174.1 (C-7), 122.2 (C-8), 124.6 (C-9), 133.5 (C-10), 118.2 (C-11), 129.8 (C-1a), 125.7 (d, *J* = 131 Hz, C-4a), 144.2 (d, $^2J_{(P\text{-}O\text{-}C\ endo)}$= 8.0 Hz, C-7a), 121.5 (C-8a), 155.3 (C-11a), 153.7 (C-12a), 49.8 (d, $^2J_{(P\text{-}O\text{-}C\ exo)}$= 6.8 Hz, C-1', O<u>C</u>H$_2$), 83.2 (C-2'), 67.4 (C-3'); Anl Calcd for $C_{18}H_{11}O_5P$: C, 63.90; H, 3.25; Found: C, 63.63; H, 3.22%.

5-(4-Methylphenoxy)-5-oxo-5*H*-6,12-dioxa-5λ^5–phosphabenzo(a)anthracene-7-one (4h). Yield 72%. mp 177-178 °C. IR$_{(KBr)}$: ν_{max} (Cm^{-1}), C=O 1613, P=O 1275, P-C$_{Ar}$ 1465 P-O-C$_{endo}$ P-O 989, O-C 1202, P-O-C$_{exo}$, P-O 906, O-C 1124, ^{31}P NMR ($CDCl_3$, 161.9 MHz) δ: 20.1. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.74 (d, *J* = 7.8, H-1), 7.67 (dd, *J* = 7.6, 1.3, H-2), 7.56 (dd, *J* = 7.6, 1.6, H-3), 8.06 (d, *J* = 7.6, H-4), 8.27 (d, *J* = 7.2, H-8), 7.43 (dd, *J* = 7.3, 1.4, H-9), 7.48 (dd, *J* = 7.4, 1.2, H-10), 7.18 (d, *J* = 7.8, H-11), 2.21 (s, 3H, CH_3), 6.88-7.22 (m, 4H, Ar); ^{13}C NMR ($CDCl_3$ 100 MHz) δ: 127.5 (C-1), 128.6 (C-2), 130.1 (C-3), 133.2 (C-4), 173.1 (C-7), 122.8 (C-8), 124.8 (C-9), 133.7 (C-10), 117.7 (C-11), 129.6 (C-1a), 126.0 (d, *J* = 142 Hz, C-4a), 144.8 (d, $^2J_{(P\text{-}O\text{-}C\ endo)}$= 8.2 Hz, C-7a), 121.8 (C-8a), 155.8 (C-11a), 154.0 (C-12a), 150.1 (d, $^2J_{(P\text{-}O\text{-}C\ exo)}$= 8.5 Hz, ipso carbon, C-1'), 120.3 (C-2'&C-6'), 126.4 (C-3'&C-5'), 134.3 (C-4'), 20.3 (C-1" ,<u>C</u>H$_3$); Anl Calcd for $C_{22}H_{15}O_5P$: C, 67.69; H, 3.84; Found: C, 67.43; H, 3.80%.

5-(Allyloxy)-5-oxo-5*H*-6,12-dioxa-5λ^5–phosphabenzo(a)anthracene-7-one (**4i**). Yield 60%. mp 160-162 °C. IR$_{(KBr)}$: ν_{max} (Cm^{-1}), C=O 1615, P=O 1292, P-C$_{Ar}$ 1480, P-O-C$_{endo}$ P-O 990, O-C 1204, P-O-C$_{exo}$, P-O 903, O-C 1118, ^{31}P NMR ($CDCl_3$, 161.9 MHz) δ: 18.4. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.73 (d, *J* = 7.9, H-1), 7.69 (dd, *J* = 7.5, 1.9, H-2), 7.55 (dd, *J* = 7.6, 1.8, H-3), 8.02

(d, *J* = 7.7, H-4), 8.25 (d, *J* = 7.1, H-8), 7.42 (dd, *J* = 7.3, 1.2, H-9), 7.49 (dd, *J* = 7.3, 1.3, H-10), 7.19 (d, *J* = 7.6, H-11), 4.40 (d, *J* = 1.5, OCH_2), 5.80-5.97 (m, 1H, CH), 5.34 (d, J_{trans} = 17.2, CH_2), 5.17 (d, J_{cis} = 10.0, CH_2); ^{13}C NMR ($CDCl_3$ 100 MHz) δ: 127.2 (C-1), 128.9 (C-2), 131.2 (C-3), 132.8 (C-4), 174.3 (C-7), 122.9 (C-8), 124.3 (C-9), 133.4 (C-10), 117.8 (C-11), 130.3 (C-1a), 125.1 (d, *J*= 134 Hz, C-4a), 143.3 (d, $^2J_{(P\text{-}O\text{-}C\ endo)}$= 8.7 Hz, C-7a), 121.6 (C-8a), 155.3 (C-11a), 153.7 (C-12a), 64.7 (d, $^2J_{(P\text{-}O\text{-}C\ exo)}$= 6.1 Hz,C-1', O<u>C</u>$H_2$), 136.7 (C-2'), 117.3 (C-3'); Anl Calcd for $C_{18}H_{13}O_5P$: C, 63.52; H, 3.82; Found: C, 63.38; H, 3.77%.

5-(Vinyloxy)-5-oxo-5*H*-6,12-dioxa-5λ^5–phosphabenzo(a)anthracene-7-one (4j). Yield 66%. mp 172-173 °C. $IR_{(KBr)}$: ν_{max} (Cm^{-1}), C=O 1611, P=O 1283, P-C_{Ar} 1472, P-O-C_{endo} P-O 983, O-C 1203, P-O-C_{exo}, P-O 901, O-C 1122, ^{31}P NMR ($CDCl_3$, 161.9 MHz) δ: 21.3; ^1H NMR ($CDCl_3$, 300 MHz) δ: 7.72 (d, *J* = 7.8, H-1), 7.68 (dd, *J* = 7.6, 1.3, H-2), 7.56 (dd, *J* = 7.6, 1.6, H-3), 8.03 (d, *J* = 7.6, H-4), 8.26 (d, *J* = 7.3, H-8), 7.43 (dd, *J* = 7.4, 1.2, H-9), 7.50 (dd, *J* = 7.3, 1.1, H-10), 7.21 (d, *J* = 7.8, H-11), 6.40-6.52 (m, 1H, OCH), 4.28 (d, J_{trans}=16.8, CH_2), 3.90 (d, J_{cis} = 9.8, CH_2). ^{13}C NMR ($CDCl_3$ 100 MHz) δ: 127.3 (C-1), 128.3 (C-2), 131.3 (C-3), 133.5 (C-4), 173.4 (C-7), 122.3 (C-8), 124.7 (C-9), 133.8 (C-10), 118.3 (C-11), 129.7 (C-1a), 125.3 (d, *J* = 125 Hz, C-4a), 145.4 (d, $^2J_{(P\text{-}O\text{-}C\ endo)}$= 8.1 Hz, C-7a), 121.7 (C-8a), 155.5 (C-11a), 154.7 (C-12a), 151.2 (d, $^2J_{(P\text{-}O\text{-}C\ endo)}$= 7.0 Hz, C-1'), 92 (C-2'); Anl Calcd for $C_{17}H_{11}O_5P$: C, 62.57; H, 3.37; Found: C, 62.39; H, 3.34%.

Conclusions

In conclusion, we have developed a convenient method for the synthesis of new substituted phosphabenzo [a] anthracene-7-one derivatives. These compounds exhibited moderate activity against bacteria and less activity on fungi.

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