Synthesis of novel fused heterocyclic system: 5-(substituted) -5-oxo-5H-6,12-dioxa-5λ5-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 ZnCl2 as a catalyst and subsequent reaction of the resultant chloroxaphosphorin with various alcohols in the presence of triethylamine, followed by oxidation with H2O2. The structures were determined by IR, 1H, 13C, 31P NMR and mass spectral (MS) studies. They were screened for antifungal and antibacterial activity.

Keywords: Chloroxaphosphorin; 5-oxo-5H-6,12-dioxa-5λ5-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 insecticides8 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,1,2a formed phosphorus dichloride
intermediate 2, which on subsequent intramolecular Friedel-Crafts insertion in the presence of ZnCl₂ 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 Et₃N as an acid acceptor. Subsequent oxidation with H₂O₂ 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, ¹H, ¹³C, ¹¹³P 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-Carom (1460-1480 cm⁻¹), and C=O (1611-1615 cm⁻¹) of 4a-j,¹¹,¹² proved the formation of phosphabenz[a]anthracene-7-ones. ¹H 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. The H-2 and H-3 resonated 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 to H-9 and H-10, respectively. The H-8 and H-11 resonated 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 ¹³C 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 ¹J cp = 125-142 Hz, provided the most convincing evidence for the formation of the oxaphosphorin ring. ¹¹³P NMR chemical shifts 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, PO₃]⁺ at m/z 220, [M-C₆H₄PO₂R]⁺ at 162 and [M-C₈H₃O₂PR]⁺ at m/z 121, conclusively establishing the proposed molecular structures.
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

### 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

<table>
<thead>
<tr>
<th>Compd.</th>
<th>R</th>
<th>Compd.</th>
<th>R</th>
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<tbody>
<tr>
<td>4a</td>
<td>(H_3C)(<em>{3'\ 1'})(</em>{2'})</td>
<td>4f</td>
<td>(4''\ 6'')(<em>{1''})(</em>{2''})(<em>{3''})(</em>{4''})</td>
</tr>
<tr>
<td>4b</td>
<td>(CH_3-CH_2)(_{1'})</td>
<td>4g</td>
<td>(3'\ 2'\ 1')</td>
</tr>
<tr>
<td>4c</td>
<td>(H_3C)(<em>{4'})(</em>{1'})(<em>{2'}) (CH-CH_2)(</em>{1'})</td>
<td>4h</td>
<td>(H_3C)(<em>{4'})(</em>{5'})(_{6'})</td>
</tr>
<tr>
<td>4d</td>
<td>(Cl-CH_2-CH_2)</td>
<td>4i</td>
<td>(3'\ 2'\ 1')</td>
</tr>
<tr>
<td>4e</td>
<td>(5'\ 6')(_{1'})</td>
<td>4j</td>
<td>(H_2C=CH)</td>
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</table>
the activity of the standard antibiotic Penicillin (250 µg/disc). Their antifungal activity was evaluated against Curvularia lunata and Fusarium oxysporum 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. 1H, 13C and 31P-NMR spectra were taken on a AMX 400 MHz spectrometer operating at 400 MHz for 1H, 100 MHz for 13C and 161.9 MHz for 31P. The compounds were dissolved in DMSO-d_6 and CDCl_3, and chemical shifts were referenced to TMS (1H and 13C) and 85% H_3PO_4 (31P). 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-5H-6,12-dioxa-5λ5–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-dioxo-5λ5-phospha benzo (a) anthracene-7-ones (4a-j)

<table>
<thead>
<tr>
<th>Compd.</th>
<th>Zone of inhibition (mm)</th>
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<tr>
<td></td>
<td>Bacteria</td>
<td>Fungi</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Staphylococcus aureus</td>
</tr>
<tr>
<td>250 µg/disc</td>
<td>500 µg/disc</td>
<td>250 µg/disc</td>
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<tr>
<td>4a</td>
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<td>16.4</td>
<td>18.1</td>
</tr>
<tr>
<td>4i</td>
<td>18.4</td>
<td>20.9</td>
</tr>
<tr>
<td>4j</td>
<td>16.7</td>
<td>19.2</td>
</tr>
</tbody>
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Penicillin 22  21

Griseofulvin 20  20

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

5-(Isopropoxy)-5-oxo-5H-6,12-dioxo-5λ5-phosphabenzo(a)anthracene-7-one (4a).
Yield 68%. mp 167-169 ºC. IR(KBr): v 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, 31P NMR (CDCl₃, 161.9 MHz) δ: 20.9. 1H NMR (CDCl₃ 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, CH₃), 1.12-1.13 (m, 3H, CH₃), 3.76 (m, 1H, OCH). 13C NMR (CDCl₃ 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 (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, J(P-O-C endo) = 8.2 Hz, C-7a), 121.0 (C-8a), 155.4 (C-11a), 154.8 (C-12a), 66.2 (d, J(P-O-C exo) = 6.1 Hz, C-1' OCH), 15.3 (CH₃₂); GC-MS (%): 342 (M⁺ 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 C₁₈H₁₅O₅P: C, 63.15; H, 4.38; Found: C, 62.89; H, 4.34%.

5-(Ethoxy)-5-oxo-5H-6,12-dioxo-5λ5-phosphabenzo (a) anthracene-7-one (4b).
Yield 68%. mp 148-149 ºC. IR(KBr): v 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, 31P NMR (CDCl₃, 161.9 MHz) δ: 15.3; 1H NMR (CDCl₃, 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, CH3), 3.27 (q, 2H, OCH2), \(^{13}\)C NMR (CDCl3 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, \(^{2}\)J(P-O-C \text{endo}) = 8.5 Hz, C-7a), 121.8 (C-8a), 155.9 (C-11a), 154.6 (C-12a), 64.5 (d, \(^{2}\)J(P-O-C \text{exo}) = 6.5 Hz, C-1'), OCH3), 15.7 (CH3); GC-MS (%): 328 (M\(^{+}\), 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 \(\text{C}_{17}\text{H}_{13}\text{O}_{5}\text{P}\): C, 62.19; H, 3.96; Found: C, 61.95; H, 3.93%.

5-(Isobutoxy)-5-oxo-5H-6,12-dioxa-5\(^{\lambda}\)-phosphabenzo(a)anthracene-7-one (4c). Yield 70%. mp 161-163 °C. IR(KBr): \(v_{\text{max}}\) (cm\(^{-1}\)), C=O 1613 P-C\(_{\text{Ar}}\) 1468, P-O-C\(_{\text{endo}}\) P-O 987, O-C 1205, P-O-C\(_{\text{exo}}\) P-O 907, O-C 1122, \(^{31}\)P NMR (CDCl3, 161.9 MHz) δ: 22.3; \(^{1}\)H NMR (CDCl3, 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, 2CH3), 1.19-1.42 (m, 1H, CH), 3.73-4.0 (m, 2H, CH2).

\(^{13}\)C NMR (CDCl3 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, \(^{2}\)J(P-O-C \text{endo}) = 8.3 Hz, C-7a), 121.5 (C-8a), 155.5 (C-11a), 153.9 (C-12a), 68.1 (d, \(^{2}\)J(P-O-C \text{exo}) = 6.3 Hz, C-1'), OCH3), 41.3 (CH1), 21.1 (CH3); Anl Calcd for \(\text{C}_{19}\text{H}_{17}\text{O}_{5}\text{P}\): C, 64.04; H, 4.77; Found: C, 63.78; H, 4.72%.

5-(2-Chloroethoxy)-5-oxo-5H-6,12-dioxa-5\(^{\lambda}\)-phosphabenzo(a)anthracene-7-one (4d). Yield 68%. mp 157-159 °C. IR(KBr): \(v_{\text{max}}\) (cm\(^{-1}\)), C=O 1611, P-C\(_{\text{Ar}}\) 1460, P-O-C\(_{\text{endo}}\) P-O 996, O-C 1191, P-O-C\(_{\text{exo}}\) P-O 909, O-C 1110, \(^{31}\)P NMR (CDCl3, 161.9 MHz) δ: 18.7; \(^{1}\)H NMR (CDCl3, 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, OCH2), 4.14 (t, 2H, CH2Cl); \(^{13}\)C NMR (CDCl3 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, \(^{2}\)J(P-O-C \text{endo}) = 8.9 Hz, C-7a), 121.3 (C-8a), 155.6 (C-11a), 153.5 (C-12a), 63.2 (d, \(^{2}\)J(P-O-C \text{exo}) = 6.1 Hz, C-1'), OCH3), 22.4 (CH2Cl); Anl Calcd for \(\text{C}_{19}\text{H}_{17}\text{O}_{5}\text{P}\): C, 56.27; H, 3.31; Found: C, 56.10; H, 3.26%.

5-(Phenoxy)-5-oxo-5H-6,12-dioxa-5\(^{\lambda}\)-phosphabenzo(a)anthracene-7-one (4e). Yield 75%. mp 181-183 °C. IR(KBr): \(v_{\text{max}}\) (cm\(^{-1}\)), C=O 1612, P-C\(_{\text{Ar}}\) 1475, P-O-C\(_{\text{endo}}\) P-O 1035, O-C 1203, P-O-C\(_{\text{exo}}\) P-O 912, O-C 1119, \(^{31}\)P NMR (CDCl3, 161.9 MHz) δ: 21.9; \(^{1}\)H NMR (CDCl3, 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 (CDCl3 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, \(^{2}\)J(P-O-C \text{endo}) = 8.6 Hz, C-7a), 121.9 (C-8a), 155.2 (C-11a), 154.5 (C-12a), 149.4 (d, \(^{2}\)J(P-O-C \text{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\(^{+}\), 64), 300 (M\(^{+}\), 46), 283 (41),
236 (53), 220 (38), 158 (13), 144 (18), 121 (100), 93 (17); Anal Calcd for C_{22}H_{13}O_{5}P: C, 67.02; H, 3.45; Found: C, 66.84; H, 3.40%.

5-(2-Phenylethoxy)-5-oxo-5H-6,12-dioxo-5λ^5–phosphabenzo(a)anthracene-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, 31P NMR (CDCl₃, 161.9 MHz) δ: 19.8. ¹H NMR (CDCl₃, 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, CH₂), 4.56 (t, J = 7.5, 2H, OCH₂), 6.82-7.24 (m, 5H, Ar); ¹³C NMR (CDCl₃ 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-O-C_{endo}) = 8.5 Hz, C-7a), 121.7 (C-8a), 155.4 (C-11a), 150.1 (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-O-C_{exo}) = 7 Hz, C-1', OCH₂), 34.8 (C-2', C₂H₂); Anal Calcd for C_{22}H_{13}O₅P: C, 68.30; H, 4.20; Found: C, 66.88; H, 4.17%.

5-(2-Yne-propoxy)-5-oxo-5H-6,12-dioxo-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, 31P NMR (CDCl₃, 161.9 MHz) δ: 17.6. ¹H NMR (CDCl₃, 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, OCH₂); ¹³C NMR (CDCl₃ 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-O-C_{endo}) = 8.0 Hz, C-7a), 121.5 (C-8a), 155.3 (C-11a), 153.7 (C-12a), 49.8 (d, 2J(P-O-C_{exo}) = 6.8 Hz, C-1', OCH₂), 83.2 (C-2'), 67.4 (C-3'); Anal Calcd for C_{18}H_{11}O₅P: C, 63.90; H, 3.25; Found: C, 63.63; H, 3.22%.

5-(4-Methylphenoxoxy)-5-oxo-5H-6,12-dioxo-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, 31P NMR (CDCl₃, 161.9 MHz) δ: 20.1. ¹H NMR (CDCl₃, 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, CH₃), 6.88-7.22 (m, 4H, Ar); ¹³C NMR (CDCl₃ 100 MHz) δ: 127.5 (C-1), 128.6 (C-2), 131.3 (C-3), 132.6 (C-4), 173.1 (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-O-C_{endo}) = 8.0 Hz, C-7a), 121.5 (C-8a), 155.3 (C-11a), 153.7 (C-12a), 49.8 (d, 2J(P-O-C_{exo}) = 6.8 Hz, C-1', OCH₂), 83.2 (C-2'), 67.4 (C-3'); Anal Calcd for C_{18}H_{11}O₅P: C, 63.90; H, 3.25; Found: C, 63.63; H, 3.22%.

5-(2-Allyloxy)-5-oxo-5H-6,12-dioxo-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, 31P NMR (CDCl₃, 161.9 MHz) δ: 18.4. ¹H NMR (CDCl₃, 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, OCH2), 5.80-5.97 (m, 1H, CH), 5.34 (d, Jtrans = 17.2, CH2), 5.17 (d, Jcis = 10.0, CH2); 13C NMR (CDCl3 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-O-C endo) = 8.7 Hz, C-7a), 121.6 (C-8a), 155.3 (C-11a), 153.7 (C-12a), 64.7 (d, 2J(P-O-C exo) = 6.1 Hz, C-1', OCH2), 136.7 (C-2'), 117.3 (C-3'); Anal Calcd for C18H13O5P: C, 63.52; H, 3.82; Found: C, 63.38; H, 3.77%.

5-(Vinyloxy)-5-oxo-5H-6,12-dioxa-5λ5-phosphabenzo(a)anthracene-7-one (4j). Yield 66%. mp 172-173 °C. IR(KBr): vmax (Cm-1), C=O 1611, P=O 1283, P-CAr 1472, P-O-Cendo P-O 983, O-C 1203, P-O-Cexo, P-O 901, O-C 1122, 31P NMR (CDCl3, 161.9 MHz) δ: 21.3; 1H NMR (CDCl3, 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, Jtrans=16.8, CH2), 3.90 (d, Jcis = 9.8, CH2). 13C NMR (CDCl3 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-O-C endo) = 8.1 Hz, C-7a), 121.7 (C-8a), 155.5 (C-11a), 154.7 (C-12a), 151.2 (d, 2J(P-O-C exo) = 7.0 Hz, C-1'); Anal Calcd for C17H11O5P: 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.

Acknowledgements

The authors express their thanks to Dr. C. Naga Raju, Department of Chemistry, Sri Venkateswara University, Tirupati, India for his academic interaction. Dr. N. Ravi Sankar, Research Scholar, Department of Botany, Sri Venkateswara University, Tirupati for his help in antimicrobial studies. Authors Dr. YHB and Dr. CSR thank CSIR and UGC, New Delhi, India for Financial Assistance.

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