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Synthesis and antimicrobial activity of 2,4,8,10,13-pentamethyl-6-substituted-13,14-dihydro-12H-6λ^5-dibenzo[d,i] [1,3,7,2]dioxazaphosphecin-6-oxides, sulphides and selenides

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Synthesis of novel 2,4,8,10,13-pentamethyl-6-substituted-13,14-dihydro-12H-6λ^5-dibenzo[d,i][1,3,7,2]dioxazaphosphecin-6-oxides was accomplished by condensation of bis(2,4-dimethyl-2-hydroxybenzyl)methylamine with phosphorus-containing dichlorides in the presence of triethylamine at 40–50°C. Corresponding oxides, sulphides and selenides were prepared in a two-step process. Bis(2,4-dimethyl-2-hydroxybenzyl) methylamine was condensed with phenyldichlorophosphine and ethyldichlorophosphite to obtain the trivalent phosphorus intermediate compounds. In the second step, the latter compounds were treated with hydrogen peroxide, sulphur and selenium to obtain the corresponding oxides, sulphides and selenides, respectively. Their structures were established by elemental analysis, IRS, NMR (^{1}H, ^{13}C and ^{31}P) and mass spectral data. Their antimicrobial activity was also evaluated.

Key words: dioxazaphosphecin-6-oxides, sulphides and selenides, dichlorides, antimicrobial activity.

INTRODUCTION

Organophosphorus compounds containing important pharmacophoric moieties are used in agriculture as pesticides and in medicine as drugs [1]. Phosphorus macrocycles containing P(III) in view of their unique structures (i.e. host molecules) possess complexation abilities [2, 3]. Phosphorus macrocycles have already found numerous industrial [4] and biological [5] applications.

Phosphorus-containing macrocycles are interesting molecules with potential applications in supramolecular and synthetic organic chemistry. They have been synthesized as phosphine oxides, phosphines, phosphonium salts, phosphates, phosphonates and phosphoranes [6]. The importance of these molecules, as phosphorus analogues of crown ethers, is derived from their potential catalytic activity and ion carrying properties. The design of host molecule capable of binding neutral organic molecules as guests is an area of rapidly expanding interest [7]. Cram [8] and Vogtle [9] have made significant advances in the field of host-guest complexation [10]. Phosphorus-containing macrocycles are expected to function as good 'hosts' in the 'host-guest chemistry'. In view of these and several other possible applications, phosphorus macroheterocycles with oxygen and nitrogen as donor atoms, have been synthesized, characterized and their antimicrobial activity has been evaluated.

RESULTS AND DISCUSSION

6-Substituted-dioxazaphosphecin-6-oxides (**3a-c**) containing oxygen, nitrogen and phosphorus atoms in the ten-membered heterocycles were synthesized by reacting equimolar quantities of bis(2,4-dimethyl-2-hydroxybenzyl) methylamine (**1**) with 4-nitrophenyl phosphorodichloridate (**2a**), bis(2-chloroethyl)phosphoramidic dichloride (**2b**) and 4-chlorophenyl-phosphorodichloridate (**2c**) in toluene in the presence of triethylamine at 40–50°C. The intermediate trivalent phosphorus compounds (**5a,b**) were prepared by cyclocondensation of **1** with phenyldichlorophosphine and ethyl dichlorophosphite in toluene in the presence of triethylamine at 10–30°C. Compounds **5a** and **5b** were converted into the corresponding oxides, sulphides and selenides (**6a–f**) by reacting with hydrogen peroxide, sulphur and selenium, respectively, in refluxing toluene. Physical data of **3a–c** and **6a–f** are given in Table 1.

The title compounds **3a–c** and **6a–f**, exhibited characteristic bands [11, 12] in their IR spectra, in the regions 1241–1304 cm^{-1}, 954–964 and 1196–1128 cm^{-1} for P=O, P–O–C (Ar), respectively. Characteristic bands were also observed for P=S and P=Se groups in the expected regions 737–774 and 678–687 cm^{-1}, respectively.

Proton NMR spectral data of the title compounds **3a–c** and **6a–f** showed a singlet in the region δ 3.00–3.24 for N–CH_3. The methylene protons (C-12 & C-14) (4H) resonated [13] as a multiplet at δ

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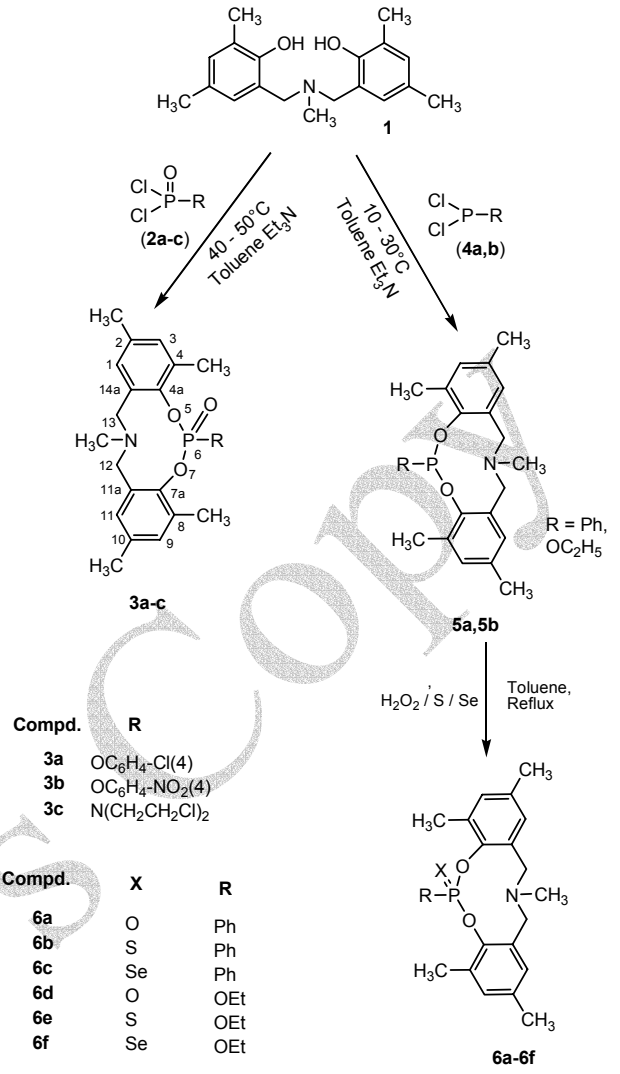
3.59–4.48. The aromatic protons showed complex multiplet in the region δ 6.50–8.28. Nitrogen mustard group (**3c**) resonated as two multiplets, one at δ 3.94–4.06 (m, 4H, –N–CH_2–) and the other at δ 3.01–3.04 (m, 4H, –CH_2Cl). The 6-ethoxy group in **6d–f** gave a quartet at δ 4.20–4.25 for –OCH_2– and a triplet at δ 1.31–1.40 for –CH_3.

The ^{13}C NMR chemical shifts of **3a–c** and **6a–f** were interpreted based on additivity rules, computed chemical shifts of starting compound **1,** intensity of signals and carbon coupling with phosphorus. The oxygen bearing carbons in **4a** and **7a** resonated in the region 147.8–151.6 ppm [14]. The methylene carbons (C-12 & C-14) resonated in the region 52.2–57.9 ppm. The N–CH_3 (C-13) resonated in the region 35.20–38.90 ppm as a signlet. The methyl carbons (C-2 & C-10) and (C-4 & C-8) gave signals at δ 20.2–20.6 and at 17.2–17.9, respectively. The two methylene carbons [2C–N(CH_2)$_2$] directly bonded to nitrogen atom of the mustard group in **3c** resonated as a doublet at δ 50.8 [$^2J_{PN–C}$ = 6.3 Hz] due to their coupling with phosphorus atom. A singlet was observed for the chloro-substituted methylene carbons [2C–(CH_2Cl)$_2$] at δ 42.6. Other carbon chemical shifts appeared in the expected region.

^{31}P Resonance signals appeared within the region –3.65 to –10.85 ppm for compounds **3a–c**. ^{31}P NMR resonances of **6b** & **6c** and **6e** & **6f** appeared in the region 79.65, 88.82 and 68.00 & 78.06 ppm due to its attachment to the sulphur and selenium atoms respectively. The compound **6a** and **6d** showed their ^{31}P NMR signals at δ 12.80 and 18.00 respectively [15, 16]. The compounds **3c, 6a** and **6c g**ave $m^{+\bullet}$ ions in their FAB at m/z 420 (19.6), 421 (16.6 M +1) and 484 (98), respectively.

EXPERIMENTAL

Melting points were determined using a Mel-Temp apparatus and were uncorrected. Elemental analyses were performed at the Central Drug Research Institute, Lucknow, India. The IR spectra were recorded as KBr pellets on a Perkin-Elmer 1000 unit. The ^{1}H, ^{13}C and ^{31}P {^{1}H} NMR spectra were recorded on AMX 400 MHz spectrometer operating at 400 MHz for ^{1}H, 100 MHz for ^{13}C and 161.9 MHz for ^{31}P. The compound was dissolved in DMSO-d_6 and the chemical shifts were referenced to TMS (^{1}H & ^{13}C) and 85% H_3PO_4 (^{31}P). Fast atom bombardment (FAB) mass spectra were recorded on JEOL SX 102/DA-6000 system using Argon/Xenon (6 keV, 10 mA) as the FAB gas, at RSIC, Central Drug Research Institute (CDRI), Lucknow, India.



Scheme 1.

GENERAL PROCEDURES

Bis(2,4-dimethyl-2-hydroxybenzyl)-methylamine **(1)** was prepared according to the reported procedure [17].

Synthesis of 2,4,8,10,13-pentamethyl-6-(4-nitro-phenoxy)-13,14-dihydro-12H-6λ^5-dibenzo[d,i][1,3, 7,2]dioxazaphosphecin-6-oxide (**3b**). A solution of 4-nitrophenylphosphorodichloridate (520 mg, 2 mmol) in 25 mL of dry toluene was added dropwise over a period of 20 minutes to a stirred solution of bis(2,4-dimethyl-2-hydroxybenzyl)methylamine (600 mg, 2 mmol) and triethylamine (404 mg, 4 mmol) in 20 mL of dry toluene in the course of 20 minutes at 10°C. After the addition, the temperature of the reaction mixture was raised to room temperature and stirred for 3 h, later the reaction mixture was stirred at 40–50°C for another 3 h. The progress of the reaction was monitored by TLC analysis (ethyl acetate-hexane, 1:2) on silicagel as adsorbent. The precipitated triethylamine hydrochloride was sepa-

rated by filtration and the filtrate was evaporated in a rotary-evaporator. The residue was washed with water and recrystallised from chloroform-hexane (1:3), yield 560 mg (69%); m.p. 132–133°C. Compounds **3a**,**c** were prepared by applying the above procedure.

Preparation of the compounds **6a-c.** A solution of phenyl dichlorophosphine (**4a**, 300 mg, 2 mmol) in 25 mL of dry toluene was added dropwise over a period of 20 minutes to a stirred solution of bis(2,4-dimethyl-2-hydroxybenzyl) methylamine (**1**, 600 mg, 2 mmol) and triethylamine (404 mg, 4 mmol) in 25 mL of dry toluene at 0°C under N_2 atmosphere. After the addition, the temperature of the reaction mixture was raised to room temperature and stirred for 3 h, later the reaction mixture was stirred at 30°C for another 3 h. The triethylamine hydrochloride was removed by filtration. To the filtrate (**5a**) hydrogen peroxide (30%) (200 mg, 2 mmol) was added at 5–10°C and stirred for 3 h at 50–60°C. The progress of the reaction was monitored by TLC analysis (ethyl acetate-hexane, 1:2) on silica gel. The solvent was removed in a rotary-evaporator. The residue was washed with water and recrystallised from 2-propa-nol, yield 860 mg (58%), m.p. 205–207°C. Com-pounds **6b** and **6c** were prepared by reacting with sulphur and selenium respectively by applying the above procedure.

Preparation of the compounds **6d-f.** A solution of ethyl dichlorophosphite (**4b**, 300 mg, 2 mmol) in 20 mL of dry toluene was added dropwise over a period of 20 minutes to a stirred solution of bis(2,4-dimethyl-2-hydroxybenzyl)methylamine (**1**, 600 mg, 2 mmol) and triethylamine (404 mg, 4 mmol) in 25 mL of dry toluene at 0°C under N_2 atmosphere. After the addition, the temperature of the reaction mixture was stirred at 20–30°C for another 2 h. The triethylamine hydrochloride was removed by filtration. To the filtrate (**5b**) selenium (200 mg 2 mmol) was added at 10–20°C and stirred for 3 h at 60–70°C. The progress of the reaction was monitored by TLC analysis (ethyl acetate-hexane, 1:2) on silicagel. The solvent from the reaction mixture was removed in a rotary-evaporator. The residue was washed with water and recrystallised from 2-propanol to obtain **6f**, yield 620 mg (62%); m.p. 156–158°C. Com-pounds **6d** and **6e** were prepared by using hydrogen peroxide and sulphur respectively by adopting the above procedure.

SUMMARY

A new class of substituted 13,14-dihydro-12H-6λ^5-dibenzo[d,i][1,3,7,2]dioxazaphosphecin-6-oxides, sulphides and selenides were conveniently synthesized and shown to have high antimicrobial activity.

ANTIMICROBIAL ACTIVITY

The antibacterial activity of all the title compounds (**3a–c**) and (**6a–f**) was assayed [18] against the growth of *Staphylococcus aureus* (gram +ve) and *Escherichia coli* (gram –ve) at two different concentrations (100, 50 ppm) (Table 1). The majority of the compounds exhibited high activity against both kinds of bacteria. The achievement is that three compounds, **3c**, **6c** and **6f** were more effective than that of the standard penicillin.

The compounds **3a–c** and **6a–f** were screened for their antifungal activity against *Aspergillus niger* and *Helminthosporium oryzae* species along with the standard fungicide *Griseofulvin* (Table 2) by the disc diffusion method [19] at two different concentrations (100, 50 ppm). It is rewarding to observe that the majority of the compounds **3a–c** and **6a–f** exhibited higher antifungal activity when compared with that of the standard *Griseofulvin* .

The great success is the fact that **3b, 6c** and **6f** exhibited higher activity than that of the standard *Griseofulvin* against both kinds of fungi. Thus, new compounds with much higher antimicrobial activity than that of the presently used commercial bactericides/fungicides have been discovered.

Table 1. Antibacterial activity of the compounds (**3a–c**) and (**6a–f**).

Compound	Zone of inhibition, mm			
	Escherichia coli		*Staphylococcus aureus*	
	100	50	100	50
3a	13	7	12	9
3b	12	9	13	6
3c	16	10	18	10
6a	10	8	10	8
6b	12	6	11	6
6c	18	11	16	11
6d	15	5	12	5
6e	13	6	14	7
6f	18	10	16	10
Penicillin	15	8	15	8

Table 2. Antifungal activity of the compounds (**3a–c**) and (**6a–f**).

Compound	Zone of inhibition, mm			
	Aspergillus niger		*Helminthosporium oryzae*	
	100	50	100	50
3a	10	7	12	9
3b	14	10	15	12
3c	11	8	10	8
6a	9	5	11	6
6b	12	6	12	10
6c	15	12	13	6
6d	10	7	10	9
6e	9	8	12	7
6f	14	10	15	10
Griseofulvin	12	8	12	8

2,4,8,10,13-Pentamethyl-6-(4-chlorophenoxy)-13,14-dihydro-12H-6λ⁵-dibenzo-[d,i][1,3,7,2]-dioxazaphosphecin-6-oxide (**3a**). Yield 64%; m.p. 164–166°C. IR (KBr) cm^{-1}: 1262 (P=O), 959 (P–O), 1228 (O–C); ^{1}H-NMR (DMSO-d_6) δ: 6.76–7.92 (m, 8H, Ar–H), 3.72–4.35 (m, 4H, CH_2), 3.09 (s, 3H, N–CH_3), 2.21 (s, 12H Ar–CH_3); ^{13}C-NMR(DMSO-d_6) δ: 128.6 (C-1 & C-11), 130.6 (C-2 & C-10), 124.5 (C-3 & C-9), 131.6 (C-4 & C-8), 133.5 (C-11a & C-14a), 52.5 (C-12 & C-14), 148.5 (d, J = 8.4 Hz, C-4a & C-7a), 35.5 (N–CH_3), 20.4 (C-2 & C-10, Ar–CH_3), 17.5 (C-4 & C-8, Ar–CH_3), 149.0 (d, J = 7.3 Hz, C-1′), 121.2 (C-2′ & C-6′), 125.5 (C-3′ & C-5′), 133.3 (C-4′); ^{31}P-NMR (DMSO-d_6), δ-10.85. Anal.Calcd. for $C_{25}H_{27}ClNO_4P$: C, 63.63; H, 5.77; N, 2.97. Found: C, 63.55; H, 5.72; N, 2.90%.

2,4,8,10,13-Pentamethyl-6-(4-nitro-phenoxy)-13, 14-dihydro-12H-6λ⁵-dibenzo-[d,i] [1,3,7,2]-dioxazaphosphecin-6-oxide (**3b**). Yield 62%; m.p. 178–180°C. IR (KBr) cm^{-1}: 1290 (P=O), 954 (P–O), 1218 (O–C); ^{1}H-NMR (DMSO-d_6) δ: 6.70–8.30 (m, 8H, Ar–H), 3.68–4.40 (m, 4H, CH_2), 3.00 (s, 3H, N–CH_3), 2.27 (s, 12H, Ar–CH_3) ^{13}C-NMR (DMSO-d_6) δ: 128.4 (C-1 & C-11), 130.4 (C-2 & C-10), 124.7 (C-3 & C-9), 131.5 (C-4 & C-8), 133.7 (C-11a & C-14a), 52.2 (C-12 & C-14), 148.3 (d, J = 8.2 Hz, C-4a & C-7a), 35.2 (N–CH_3), 20.5 (C-2 & C-10, Ar–CH_3), 17.2 (C-4 & C-8, Ar–CH_3), 149.5 (d, J = 7.2Hz, C-1′), 120.8 (C-2′ & C-6′), 125.3 (C-3′ & C-5′), 133.4 (C-4′). ^{31}P-NMR (DMSO-d_6) δ: –3.65. Anal. Calcd. for $C_{25}H_{27}N_2O_6P$: C, 62.24; H, 5.64; N, 5.81. Found: C, 62.18; H, 5.60; N, 5.76%.

2,4,8,10,13-Pentamethyl-6-[bis-2-chloroethyl)-amino]-13,14-dihydro-12H-6λ⁵-dibenzo-[d,i][1,3,7,2]dioxazaphosphecin-6-oxide (**3c**). Yield 60%; m.p. 180–182°C. IR (KBr) cm^{-1}: 1292 (P=O), 954 (P–O), 1220 (O–C); (DMSO-d_6) δ: 6.70–7.33 (m, 4H, Ar–H), 3.78–3.87 (m, 4H, CH_2), 3.15 (s, 3H, N–CH_3), 2.21 (s, 12H, Ar–CH_3), 3.94–4.06 (t, 4H, N–CH_2), 3.27–3.24 (t, 4H, CH_2Cl); ^{13}C-NMR (DMSO-d_6) δ: 128.5 (C-1 & C-11), 130.5 (C-2 & C-10), 124.6 (C-3 & C-9),131.4 (C-4 & C-8), 133.6 (C-11a & C-14a), 52.3 (C-12 & C-14), 148.6 (d, J = 8.6 Hz, C-4a & C-7a), 35.4 (N–CH_3), 20.6 (C-2 & C-10, Ar–CH_3), 17.4 (C-4 & C-8, Ar–CH_3), 50.8 (d, J = 6.3 Hz, N–CH_2), 42.6 (–CH_2Cl). ^{31}P-NMR (DMSO-d_6) δ: –8.20; FAB m/z (%): [420 (19.6) M^+], 380 (15), 362 (16), 300 (100), 246 (20), 215 (17), 164 (26), 135 (60), 91(20). Anald. Calcd. for $C_{23}H_{31}Cl_2N_2O_3P$: C, 56.91; H, 6.44; N, 5.77. Found: C, 56.84; H, 6.39; N, 5.71%.

2,4,8,10,13-Pentamethyl-6-phenyl-13,14-dihydro-12H-6λ⁵-dibenzo-[d,i][1,3,7,2]-dioxazaphosphecin-6-oxide (**6a**). Yield 58%; m.p. 157–159°C; IR (KBr) cm^{-1}: 1241 (P=O), 748 (P–C aryl); ^{1}H-NMR (DMSO-d_6) δ: 6.82–7.94 (m, 9H, Ar–H), 3.71–4.35 (m 4H, CH_2), 3.20 (s, 3H, N–CH_3), 2.20 (s, 12H, Ar–CH_3); ^{13}C-NMR (DMSO-d_6) δ: 128.7 (C-1 & C-11), 130.7 (C-2 & C-10), 125.3 (C-3 & C-9), 131.7 (C-4 & C-8), 134.1 (C-11a & C-14a), 56.5 (C-12 & C-14), 147.8 (d, J = 8.5 Hz, C-4a & C-7a), 38.5 (N–CH_3), 20.6 (C-2 & C-10, Ar–CH_3), 17.4 (C-4 & C-8, Ar–CH_3), 131.1 (C-1^1), 126.6 (C-2^1 & C-6^1), 128.0 (C-3^1 & C-5^1), 124.3 (C-4^1); ^{31}P-NMR (DMSO-d_6) δ: 12.80; FAB m/z (%): [421 (16.6), M+1], 406 (11), 328 (20), 300 (100), 273 (75, 257 (11), 194(10), 164 (17), 154(23), 135 (50), 119(12); Anal. Caled. for $C_{25}H_{28}NO_3P$: C, 71.24; H, 6.70; N, 3.32 Found: C, 71.17; H, 6.65; N, 3.28%.

2,4,8,10,13-Pentamethyl-6-phenyl-13,14-dihydro-12H-6λ⁵-dibenzo-[d,i][1,3,7,2]-dioxazaphosphecin-6-sulfide (**6b**). Yield 52%; m.p. 162–164°C; IR (KBr) cm^{-1}: 774 (P=S), 751 (P–C aryl); ^{1}H-NMR (DMSO-d_6) δ: 6.85–8.25 (m, 9H, Ar–H), 3.70–4.26 (m, 4H, CH_2), 3.25 (s, 3H, N–CH_3), 2.20 (s, 12H, Ar–CH_3); ^{13}C-NMR (DMSO-d_6) δ: 131.8 (C-1 & C-11), 130.8 (C-2 & C-10), 126.6 (C-3 & C-9); 133.2 (C-4 & C-8), 134.2 (C-11a & C-14a), 57.0 (C-12 & C-14), 149.0 (d, J = 8.2 Hz, C-4a & C-7a), 38.4 (N–CH_3), 20.4 (C-2 & C-10, Ar–CH_3), 17.5 (C-4 & C-8, Ar–CH_3), 131.2 (C-1^1), 127.8 (C-2^1 & C-6^1), 128.0 (C-3^1 & C-5^1), 122.3 (C-4^1); ^{31}P-NMR (DMSO-d_6) δ: 79.65; Anal. Calcd for $C_{25}H_{28}NO_2PS$: C, 68.63; H, 6.45; N, 3.20. Found: C, 68.70; H, 6.40; N, 3.17%.

2,4,8,10,13-Pentamethyl-6-phenyl-13,14-dihydro-12H-6λ⁵-dibenzo-[d,i][1,3,7,2]-dioxazaphosphecin-6-selenide (**6c**). Yield 56%; m.p. 216–218°C; IR (KBr) cm^{-1}: 695 (P=Se), 955 (P–O), 1260 (O–C), 753 (P–C aryl); ^{1}H-NMR (DMSO-d_6) δ: 6.96–8.28 (m, 9H, Ar–H), 3.87–4.24 (m, 4H, CH_2) 3.24 (s, 3H, N–CH_3), 2.24 (s, 12H, Ar–CH_3); ^{13}C-NMR (DMSO-d_6) δ: 131.7 (C-1 & C-11), 130.7 (C-2 & C-10), 126.5 (C-3 & C-9), 132.7 (C-4 & C-8), 133.8 (C-11a & C-14a) 56.4 (C-12 & C-14), 149.3 (d, J = 8.3 Hz, C-4a & C-7a), 38.3 (N–CH_3), 20.4 (C-2 & C-10, Ar–CH_3), 17.9 (C-4 & C-8, Ar–CH_3), 131.4 (C-1^1), 126.0 (C-2^1 & C-6^1), 128.3 (C-3^1 & C-5^1), 122.3 (C-4^1); ^{31} P-NMR (DMSO-d_6) δ: 88.82; FAB m/z (%): [484 (98), $M^{+\bullet}$], 483 (22), 482 (21), 422 (35), 441 (20) 440 (100), 407 (19), 406 (13), 241 (15), 164 (30),. 135 (48); Anal. Calcd for $C_{25}H_{28}NO_2PSe$: C, 61.98; H, 5.83; N, 2.89. Found: C, 61.93; H, 5.80; N, 2.85%.

2,4,8,10,13-Pentamethyl-6-ethoxy-13,14-dihydro-12H-6λ⁵-dibenzo-[d,i][1,3,7,2]-dioxazaphosphecin-6-oxide (**6d**). Yield 62%; m.p. 156–158°C; IR (KBr) cm^{-1}: 1256 (P=O), 689 (P–O), 1265 (O–C); ^{1}H-NMR (DMSO-d_6) δ: 6.73–7.26 (m, 4H, Ar–H), 3.81–4.20

(m, 4H, CH_2), 3.20 (s, 3H, N–CH_3), 2.22 (s, 12H, Ar–CH_3) 4.20–4.10 (q, 2H OCH_2), 1.31 (t, 3H –CH_3); ^{13}C-NMR (DMSO-d_6) δ: 131.4 (C-1 & C-11), 129.7 (C-2 & C-10), 126.9 (C-3 & C-9), 132.6 (C-4 & C-8), 133.8 (C-11a & C-14a), 56.2 (C-12 & C-14), 151.6 (d, *J* = 8.5 Hz, C-4a & C-7a), 38.4 (N–CH_3), 20.2 (C-2 & C-10, Ar–CH_3), 17.5 (C-4 & C-8, Ar–CH_3), 65.6 (d, *J* = 8.6 Hz, OCH_2), 17.0 (CH_3); ^{31}P-NMR (DMSO-d_6) δ: 18.00; Anal. Calcd. for $C_{21}H_{28}NO_4P$: C, 64.77; H, 7.25; N, 3.60. Found: C, 64.80 H, 7.20; N, 3.56%.

2,4,8,10,13-Pentamethyl-6-ethoxy-13,14-dihydro-12H-6λ^5-dibenzo-[d,i][1,3,7,2]-dioxa zaphosphecin-6-sulfide (**6e**). Yield 60%; m.p. 161–163°C; IR (KBr) cm^{-1}: 737 (P=S), 678 (P–O), 1265 (O–C aryl); ^{1}H-NMR (DMSO-d_6) δ: 6.65–8.10 (m, 4H, Ar–H), 3.59–3.72 (m, 4H, CH_2), 3.17 (s, 3H N–CH_3), 2.21 (s, 12H, Ar–CH_3), 4.23 (q, 2H, OCH_2), 1.36 (t, 3H, CH_3); ^{13}C-NMR (DMSO-d_6) δ: 131.7 (C-1 & C-11), 130.7 (C-2 & C-10), 126.6 (C-3 & C-9), 132.3 (C-4 & C-8), 133.6 (C-11a & C-14a), 57.9 (C-12 & C-14), 149.2 (d, *J* = 8.4 Hz, C-4a & C-7a), 38.9 (N–CH_3), 20.3 (C-2 & C-10, Ar–CH_3), 17.5 (C-4 & C-8, Ar–CH_3), 65.9 (d, *J* = 8.4 Hz, OCH_2), 17.2 (CH_3); ^{31}P-NMR (DMSO-d_6) δ: 68.0; Anal. Calcd. for $C_{21}H_{28}NO_3PS$: C, 62.20; H, 6.96; N, 3.45. Found: C, 62.14; H, 6.90, N, 3.40%.

2,4,8,10,13-Pentamethyl-6-ethoxy-13,14-dihydro-12H-6λ^5-dibenzo-[d,i][1,3,7,2]-dioxazaphosphecin-6-selenide (**6f**). Yield 61%; m.p. 154–156°C; IR (KBr) cm^{-1}: 687 (P=Se), 715 (P–O), 1260 (O–C aryl); ^{1}H-NMR (DMSO-d_6) δ: 6.50–7.23 (m, 4H, Ar–H), 3.75–4.28 (m, 4H, CH_2), 3.18 (s, 3H, N–CH_3), 2.24 (s, 12H, Ar–CH_3), 4.25 (q, 2H, OCH_2), 1.40 (t, 3H, CH_3); ^{31}P-NMR (DMSO-d_6) δ: 78.07; Anal. Calcd. for $C_{21}H_{28}$ NO_3PSe: C, 55.75; H, 6.24; N, 3.10. Found: C, 55.65; H, 6.20; N, 3.04%.

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СИНТЕЗ И АНТИМИКРОБНА АКТИВНОСТ НА 2,4,8,10,13-ПЕНТАМЕТИЛ-6-ЗАМЕСТЕНИ-13,14-ДИХИДРО-12Н-6λ^5-ДИБЕНЗО[d,i][1,3,7,2]ДИОКСАЗАФОСФЕЦИН-6-ОКСИДИ, СУЛФИДИ И СЕЛЕНИДИ

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(Резюме)

Проведен е синтез на нови 2,4,8,10,13-пентаметил-6-заместени-13,14-дихидро-12Н-6λ^5-дибензо[d,i][1,3,7,2] диоксазафосфецин-6-оксиди чрез кондензация на бис(2,4-диметил-2-хидроксибензил)метиламин със съдържащи фосфор дихлориди в присъствие на триетиламин при 40–50°С. В двустадиен процес са синтезирани съответните оксиди, сулфиди и селениди. Бис(2,4-диметил-2-хидроксибензил)метиламин кондензира с фенилдихлорфосфин и етилдихлорфосфит до междинни съединения съдържащи тривалентен фосфор. Във втория стадий, тези съединения взаимодействат с хидропероксид, сяра и селен до получаване на съответните оксиди, сулфиди и селениди. Структурата им е установена чрез елементен анализ, ИЧС, ЯМР (^{1}Н, ^{13}С и ^{31}Р) и масспектрометрия. Оценена е също и тяхната антимикробна активност.