Synthesis and antimicrobial activity of novel 2-(heteryl-carboxamido)-2,3-dihydro-1*H*-1,2,5-oxadiazolo[3,4-*c*] [1,3,2]diazaphosphole-2-oxides

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Abstract

Some novel 2-(heterylcarboxamido)-2,3-dihydro-1*H*-1,2,5-oxadiazolo[3,4-c][1,3,2]diaza-phosphole-2-oxides (**4-13**) have been synthesized from reaction of 3,4-diamino-1,2,5-oxadiazole (**3**) with various dichlorophosphinylcarboxamides (**2**), which were prepared by C-acylation of electron-rich heterocyclic compounds with dichloro isocyanato phosphine oxide (Kirsanov isocyanate) (**1**) in dry octane, in the presence of triethylamine at 50-60 °C. Their structures were determined by IR, ^{1}H, ^{13}C, ^{31}P NMR and mass spectral (MS) studies. They were screened for antifungal and antibacterial activity against *Curvularia lunata* / *Aspergillus niger* and *Staphylococcus aureus* / *Escherichia coli*, respectively. Most of these compounds exhibited moderate activity in the assays.

Keywords: 3,4-Diamino-1,2,5-oxadiazole; 3,4-diaminofurazan; Kirsanov isocyanate; carboxamidophosphoryldichloride

Introduction

In a study of new pharmaceuticals and agrochemicals, the application of heterocycles is warranted to improve their biological activity. Diaminofurazan has been identified as an urea equivalent for histamine H_2-receptor antagonists,[1–3] and its derivatives have found increased pharmaceutical and medicinal applications.[4]

Some diazaphospholes and certain phosphinyl carbamates demonstrated insecticidal, bactericidal, antiviral, antitumor and anticarcinogenic activity.[5–15] As a part of our ongoing programme, aimed at searching for novel antibacterial and antiviral agents with high activity and low toxicity, a synthetic route has been developed to the title compounds.

Results and Discussion

The synthetic route (Chart 1) involved the C-acylation of various electron-rich heterocycles (Het–H) with Kirsanov isocyanate (**1**)[16–17] at 15-30 °C in dry octane, under inert and anhydrous conditions to furnished *N*-dichlorophosphorylheterylcarboxamides (**2**).[18] Cyclocondensation of **2** *in situ* with 3,4-diamino-1,2,5-oxadiazole (**3**)[19] in the presence of triethylamine at 50-60 °C in octane, yielded the title compounds (**4-13**). Thin layer chromatography (TLC) was employed to follow the progress of the reaction and purity of the products. The target compounds were obtained by filtering off triethylamine hydrochloride, evaporation of the filterate, washing the residue with water and recrystallization of the resulting solids, using suitable solvents. All the title compounds (**4-13**) were readily soluble in polar organic solvents and melted in the range 160-216 °C. Their chemical structures were established by IR, ^{1}H, ^{13}C, ^{31}P NMR and MS data.

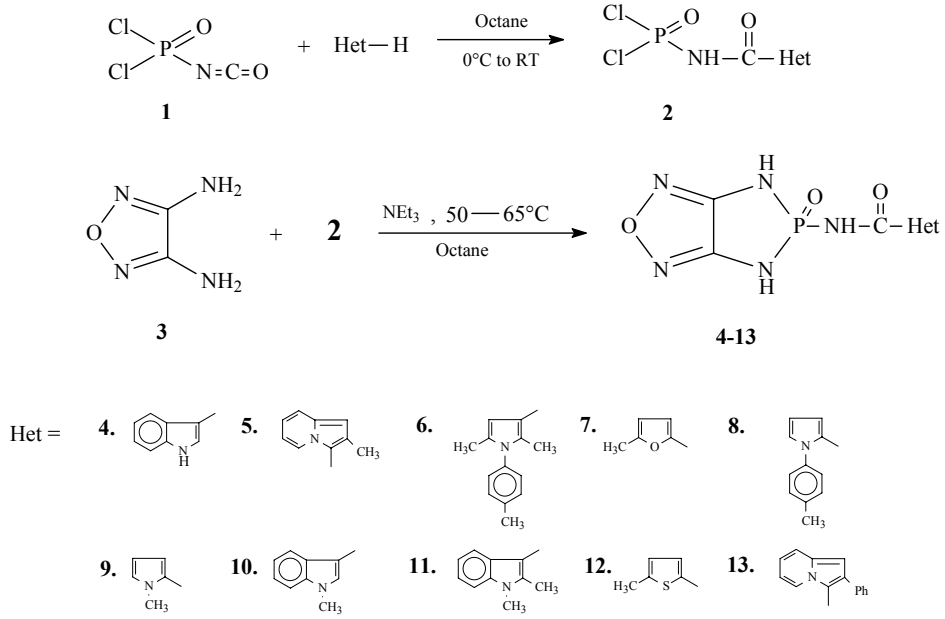

Chart 1

The presence of characteristic bands at 3222-3394 cm^{-1} (P–N-H),[20] 2948-3204 cm^{-1} (P–N-H-CO), [20] 1635-1697 cm^{-1} (C=O),[21] and 1216-1248 cm^{-1} (P=O) [22–25] in the IR spectra of **4-13** showed that cyclisation of **3** with **2** had occurred to form the furazanodiaza-phosphole. ^{1}H-NMR data agreed well with the proposed structures for **4-13**. However, it is observed that the exocyclic protons of the carboxamide group (NH–CO) of **4** and **5** resonated downfield (δ 10.69-10.89), when compared to others (δ 6.43-9.00). Endocyclic protons of N_1 and N_3 exhibited signals as doublets at δ 8.61-9.38 (J = 8.2-9.3 Hz) and 8.42-9.13 (J = 8.5-8.9 Hz) in all compounds **4-13**,[26–27] due to their coupling with phosphorus. The chemical shifts of other protons of the carboxamide moiety appeared in the expected regions.[18] It is of further interest to observe that

the protons of the carboxamide function resonated downfield, when compared to the corresponding protons in the free heterocycles. The NH proton signals were confirmed by D_2O exchange experiments.

The ^{13}C NMR chemical shifts of **4-13** were interpreted on the basis of additivity rules. The nitrogen bonded C-4 and C-5 exhibited signals at 156-165 ppm.[19] The carbonyl carbon of the carboxamide function resonated in the range δ 88-207. The other carbon chemical shifts of the carboxamide function appeared downfield (–10 ppm), when compared to the corresponding carbon chemical shifts in the respective free heterocycles. The resonances of other carbon atoms of the carboxamide moiety appeared in the expected regions. ^{31}P NMR signals of these compounds (**4-13**) appeared in the range –10.59 to 16.81 ppm. The striking appearance of two or three ^{31}P NMR signals in the spectra of **4**, **5**, **7**, **8**, **9**, **10** and **12** suggests that they may exist as two or three conformers in the solution state.[30]

The mass spectra fragmentation patterns for **4-13** are rationalized in Chart 2. Appearance of $M^{+\cdot}$ at the appropriate molecular weight, $[M–(Het)]^+$ at *m/z* 187, $[M–(NH\text{-}CO\text{-}Het)]^+$ at *m/z* 145, $[M–(H_2N\text{-}CO\text{-}Het)]^+$ at *m/z* 144, $[M–(NH–CO–Het \text{ and } H_2O)]^{+\cdot}$ at *m/z* 127 and $[M–(CO–Het)]^+$ at *m/z* 160 with the furazanodiazaphosphole-2-oxide moiety conclusively establishes their proposed molecular structure. These daughter ions being characteristic of these molecules could be used as diagnostic ions of these compounds for their monitoring in bio and eco systems.

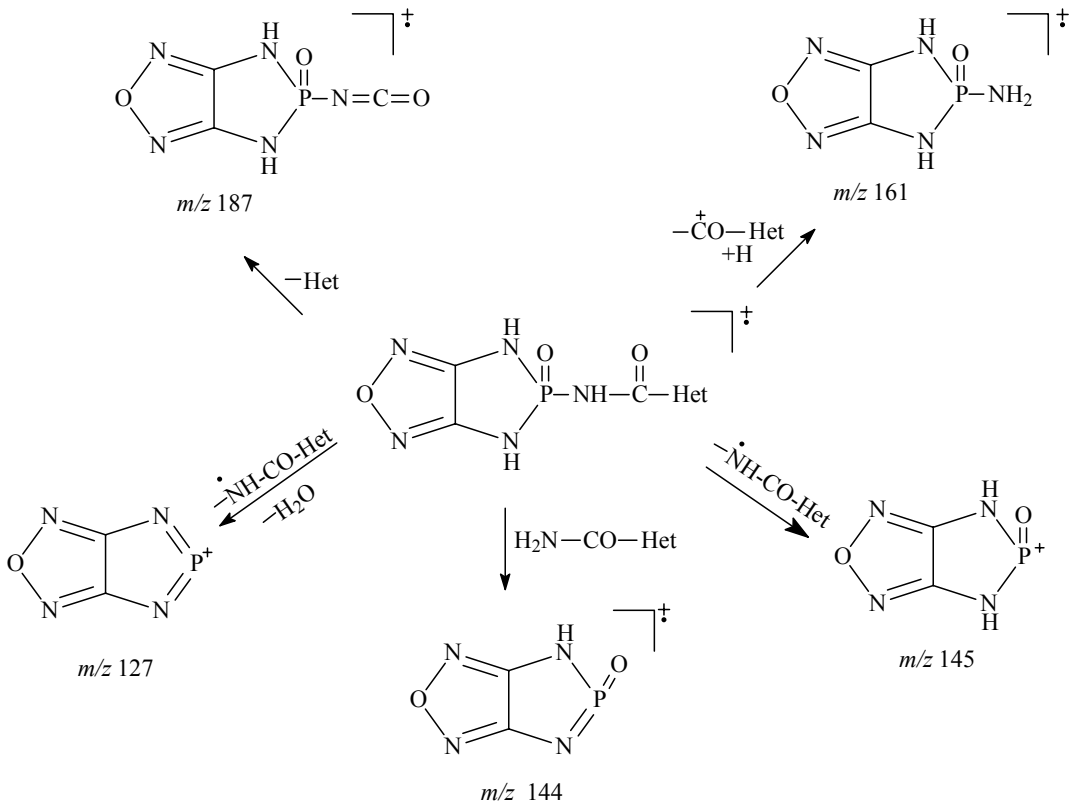

Chart 2

Antimicrobial activity

Compounds **4-13** were screened for their antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* (10^6 cell/mL) by the disc-diffusion method[28] 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 antibiotics like Penicillin and Tetracyclin (250 µg/disc). Their antifungal activity[29] was evaluated against *Curvularia lunata* and *Aspergillus niger*, at concentrations of 250 and 500 µg/disc. Griseofulvin was used as the reference compound. 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 both bacteria and fungi.

Table 1. Antimicrobial activity of 2-substituted carboxamido-2,3-dihydro-1*H*-1,2,5-oxadiazolo-[3,4-*c*][1,3,2]diazaphosphole-2-oxides (**4-13**)

Compd.	Zone of inhibition (mm)							
	Bacteria				Fungi			
	Staphylococcus aureus		*Echerichia coli*		*Curvularia lunata*		*Aspergillus niger*	
	250 µg/disc	500 µg/disc	250 µg/disc	500 µg/disc	250 µg/disc	500 µg/disc	250 µg/disc	500 µg/disc
4	14	20	10	15	6	11	8	14
5	18	22	12	19	14	20	15	23
6	3	5	4	7	–[a)]	2	–	1
7	12	15	14	18	5	8	9	12
8	15	9	6	11	–	–	–	3
9	11	19	12	19	6	11	8	13
10	13	18	12	16	5	11	7	15
11	15	22	13	21	7	15	9	18
12	19	23	21	24	8	13	10	15
13	17	21	15	18	13	18	15	21
Penicillin	24		20					
Griseofulvin					28		28	

Experimental Section

General Procedures. The melting points were determined on a Mel.-Temp apparatus and were left uncorrected. Elemental analyses were performed at the Central Drug Research Institute, Lucknow, India. IR spectra were recorded in KBr pellets and Nujol mulls 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 or $CDCl_3$, and chemical shifts were referenced to TMS (^{1}H and ^{13}C) and 85% H_3PO_4 (^{31}P). Mass spectral data was recorded on GC-MS instrument at 70 eV with a direct inlet system.

3,4-Diaminofurazan (3)[19] and isocyanatophosphoryldichloride (1)[16] were prepared according to the procedures reported. The electron-rich heterocycles (**4**, **7**, **9**, **10**, **11**, **12)**, which were procured from Aldrich Chemical Company, U.S.A and Lancaster, London, were used without further purification.

Synthesis of 2-(indole-3-carboxamido)-2,3-dihdyro-1*H*-1,2,5-oxadiazolo[3,4-c] [1,3,2]diazaphosphole-2-oxide (4). To a stirred and water-cooled solution of indole (1.17 g, 0.01 mol) in octane (10 mL), a solution of isocyanatophosphoryldichloride (1.16 g, 0.01 mol) in octane (5 mL) was added. After 30 min, the temperature of the reaction mixture was slowly raised to room temperature and stirred for another half an hour. This reaction mixture was added percolately to a cold solution (0°C) of **3** (0.01 mol) and triethylamine (0.02 mol) in 30 mL of octane. The temperature was slowly raised to 50-60°C and stirring was continued for an additional 4 h. The progress of the reaction was monitored by TLC in the 2:3 mixtures of ethyl acetate and *n*-hexane as mobile solvent. The triethylamine hydrochloride was filtered and the solvent from the filtrate was evaporated under reduced pressure. The residue was washed with water followed by chilled 2-propanol and recrystallized from ethanol to afford **4**.

Yield 2.37 g (78%), mp 160-162 °C.; IR (KBr) cm $^{-1}$: 3394 (P–N-H-Ring), 3264 (N-H–Het), 3172 (P–N-H–CO), 1640(C=O), 1230 (P=O).; ^{31}P-NMR (DMSO-d_6) δ: 1.05, 4.88.; ^{1}H-NMR (DMSO-d_6) δ : 11.83 (s, 1H, NH–Het), 10.69 (s, 1H, CO–NH), 9.38 (d, J = 9.3 Hz, 1H, N_1-H), 9.11 (d, J = 8.9 Hz, 1H, N_3-H), 8.41 (d, J = 2.8 Hz, 1H, H_2-Het), 8.17 (m, 1H, H_4-Het), 6.83-7.6 (m, 3H, $H_{5,6,7}$-Het).; ^{13}C-NMR ($CDCl_3$) δ: 207 (C=O), 165 (C-4,5), 136 (C-3′), 130 (C-9′), 129 (C-8′), 126 (C-2′), 122 (C-5′), 121 (C-4′), 118 (C-6′), 111 (C-7′).; GC-MS *m/z* (%): 304 (84, $M^{+\cdot}$), 187 (14), 160 (46), 145 (37), 142 (53), 127 (86), 117 (38), 100 (49), 99 (22), 83 (100), 78 (61): *Anal.* Calcd for $C_{11}H_9N_6O_3P$: C, 43.42; H, 2.96; N, 27.63; Found: C, 43.23; H, 2.95; N, 27.51%.

This procedure was used for the preparation of other compounds (**5-13**). The physical and spectroscopic data[31] of all the compounds are given below.

2-(2-Methylindolizine-3-carboxamido)-2,3-dihydro-1*H*-1,2,5-oxadiazolo [3,4-*c*] [1,3,2] diazaphosphole-2-oxide (5). Yield 2.26 g (71%), mp 178-182 °C; IR (KBr) cm $^{-1}$: 3312 (P–N-H), 2980 (P–N-H–CO), 1674 (C=O), 1226 (P=O); ^{31}P-NMR (DMSO-d_6) δ: – 4.28, – 9.64, – 10.59.; ^{1}H-NMR (DMSO-d_6) δ: 10.89 (s, 1H, CO–NH), 9.70 (m, 1H, H_5-Het), 8.81 (d, J = 8.2 Hz, 1H, N_1-H), 8.52 (d, J = 8.7 Hz, 1H, N_3-H), 6.83-8.00 (m, 3H, $H_{6,7,8}$-Het), 6.47 (s, 1H, H_1-Het), 2.61 (s, 3H, CH_3).; ^{13}C-NMR (DMSO-d_6) δ: 198 (C=O), 163 (C-4, 5), 149.7 (C-5′), 137.7 (C-3′), 135.9 (C-9′), 135.0 (C-7′), 124.1 (C-2′), 123.5 (C-8′), 122.5 (C-6′), 111.1 (C-1′), 13.7 (C-1″).; GC-MS *m/z* (%): 318 (63, M^{+}), 302 (56), 187 (41), 145 (32), 144 (12), 131 (34), 161 (37), 157 (51), 156 (44), 127 (82), 100 (48), 99 (23) 78 (54), 83 (100).; *Anal.* Calcd for $C_{12}H_{11}N_6O_3P$: C, 45.28; H, 3.45; N, 26.41; Found; C, 45.10; H, 3.43; N, 26.29 %.

2-[2,5-Dimethyl-1-(4-methylphenyl)pyrrole-3-carboxamido]-2,3-dihydro-1*H*-1,2,5-oxadiazolo[3,4-c][1,3,2] diazaphosphole-2-oxides (6). Yield 2.97 g (83%), mp 205-210 °C.; IR (KBr) cm^{-1}: 3223 (P–N-H), 2957 (P–N-H–CO), 1697 (C=O), 1237 (P=O);^{31}P-NMR (DMSO-d_6) δ: 14.37; ^{1}H-NMR (DMSO-d_6) δ: 9.14 (d, J = 9.1 Hz, 1H, N_1-H), 9.00 (d, J = 8.9 Hz, 1H, N_3-H), 8.31 (s, 1H, N-H–CO), 7.31 (d, J_{HH} = 7.5 Hz, 2H, o-H-Ar), 7.16 (d, J_{HH} = 7.5 Hz, 2H, m-H-Ar), 6.12 (s, 1H, H-Het), 2.44 (s, 3H, Ar-CH_3), 2.14 (s, 3H, 2-CH_3), 1.97 (s, 3H, 5-CH_3).; ^{13}C-NMR (DMSO-d_6) δ: 201 (C=O), 157 (C-4), 156 (C-5), 150 (C-6′), 143 (C-2′, 5′), 137 (C-9′), 135 (C-3′), 129 (C-8′, 10′), 128 (C-7′, 11′), 103 (C-4′), 18.4 (C-3′′), 12.2 (C-1′′, 2′′).; GC-MS *m/z* (%): 372 (42, M^+), 354 (18), 336 (31), 281 (53), 228 (64), 210 (12), 187 (38), 185 (27), 161 (28), 145 (47) 144 (15), 137 (16), 127 (85), 119 (31), 100 (21), 99 (11), 83 (100).; *Anal.* Calcd for $C_{16}H_{17}N_6O_3P$: C, 51.61; H, 4.56; N, 22.58; Found: C, 51.35; H, 4.53; N, 22.48 %.

2-(2-Methylfuran-5-carboxamido)-2,3-dihydro-1*H*-1,2,5-oxadiazolo[3,4-*c*] [1,3,2]-diazaphosphole-2-oxide (7). Yield 1.02 g (38%), mp 196°C.; IR (KBr) cm^{-1}: 3224 (P–N-H) 2963 (P–N-H–CO), 1692 (C=O), 1216 (P=O); ^{31}P-NMR (DMSO-d_6) δ: 4.67, 8.92; ^{1}H-NMR (DMSO-d_6) δ: 8.61 (d, J = 9.0 Hz, 1H, N_1-H), 8.42 (d, J= 8.7 Hz, 1H, N_3-H), 7.92 (s, 1H, N-H–CO), 7.37 (s, 1H, H_3-Het), 6.26 (s, 1H, H_4-Het), 2.30 (s, 3H, CH_3).; ^{13}C-NMR (DMSO-d_6) δ: 190 (C=O), 158 (C-4, 5), 148 (C-2′), 144 (C-5′), 117 (C-4′), 111.9 (C-3′), 13.6 (C-1′′).; *Anal.* Calcd for $C_8H_8N_5O_4P$: C, 35.68; H, 2.97; N, 26.02; Found: C, 35.53; H, 2.95; N, 25.90%.

2-(1-(4-Methylphenyl)pyrrole-2-carboxamido)-2,3-dihydro-1*H*-1,2,5-oxadiazolo[3,4-*c*][1,3,2]diazaphosphole- 2-oxides (8). Yield 2.3 g (67%), mp 216 °C ; IR (KBr) cm^{-1}: 3237 (P–N-H), 2950 (P–N-H–CO), 1696 (C=O), 1248 (P=O); ^{31}P-NMR (DMSO-d_6) δ: 8.61, 11.73; ^{1}H-NMR (DMSO-d_6) δ: 8.81 (d, J = 8.7 Hz, 1H, N_1-H), 8.63 (d, J = 8.5 Hz, 1H, N_3-H), 7.98 (m, 1H, N-H), 7.40 (d, J_{HH} = 8.5 Hz, 2H, o-H-Ar), 7.32 (d, J_{HH} = 8.5 Hz, 2H, m-H-Ar), 7.23 (s, 1H, H_5-Het), 7.19 (s, 1H, H_3-Het), 6.21 (s, 1H, H_4-Het), 2.33 (s, 3H, Ar-CH_3).; ^{13}C-NMR (DMSO-d_6) δ: 197 (C=O), 158 (C-4) 157 (C-5), 150 (C-6′), 147 (C-2′), 143 (C-5′), 137 (C-9′), 129 (C-8′, 10′), 120 (C-7′, 11′), 108 (C-3′), 107 (C-4′), 20.1 (C-1′′).; *Anal.* Calcd for $C_{14}H_{13}N_6O_3P$: C, 48.83; H, 3.77; N, 24.41; Found: C, 48.65; H, 3.75; N, 24.30%.

2-(1-Methylpyrrole-2-carboxamido)-2,3-dihydro-1*H*-1,2,5-oxadiazolo[3,4-*c*] [1,3,2]-diazaphosphole-2-oxides (9). Yield 2.06 g (77%), mp 201-203 °C; IR (KBr) cm^{-1}: 3287 (P–N-H), 2993 (P–N-H–CO), 1694 (C=O), 1244 (P=O).; ^{31}P-NMR (DMSO-d_6) δ: –4.3, 8.46, 11.36; ^{1}H-NMR (DMSO-d_6) δ: 8.91 (d, J_{HH} = 3.5 Hz, 1H, N-H–CO), 8.71 (d, J = 8.9 Hz, 1H, N_1-H), 8.53 (d, J = 8.6 Hz, 1H, N_3-H), 7.50 (m, 1H, H_5-Het), 7.22 (m,1H, H_3-Het), 6.20 (m, 1H, H_4-Het), 3.88 (s, 3H, N-CH_3).; ^{13}C-NMR (DMSO-d_6) δ: 198 (C=O), 158 (C-4, 5), 147 (C-2′), 143 (C-5′), 108 (C-3′), 107 (C-4′), 43 (C-1′′).; *Anal.* Calcd for $C_8H_9N_6O_3P$: C, 35.82; H, 3.35; N, 31.34; Found: C, 35.68; H, 3.33; N, 31.20%.

2-(1-Methylindole-3-carboxamido)-2,3-dihydro-1*H*-1,2,5-oxadiazolo [3,4-*c*] [1,3,2]-diazaphosphole- 2-oxides (10). Yield 2.67 (8.4%), mp 204-205 °C; IR (KBr) cm^{-1}: 3286 (P–N-H), 3204 (P–N-H–CO), 1637 (C=O), 1222 (P=O); ^{31}P-NMR (DMSO-d_6) δ: 12.72, 16.81; ^{1}H-NMR (DMSO-d_6) δ: 9.00 (s, 1H, CO-NH), 8.91 (d, J = 9.1 Hz, 1H, N_1-H), 8.73 (d, J = 8.6 Hz, 1H, N_3-H), 8.51 (s, 1H, H_2-Het), 8.20 (m, 1H, H_4-Het), 7.20 (m, 3H, $H_{5,6,7}$-Het), 3.90 (s, 3H,

CH_3).; ^{13}C-NMR (DMSO-d_6) δ: 197 (C=O), 165 (C-4, 5), 143 (C-2′), 137 (C-9′), 136 (C-3′), 129 (C-8′), 122 (C-5′), 121 (C-4′), 118 (C-6′), 111 (C-7′), 47.8 (C-1′′).; Anal. Calcd for $C_{12}H_{11}N_6O_3P$: C, 45.28; H, 3.45; N, 26.41; Found: C, 45.13; H, 3.43; N, 26.30%.

2-(1,2-Dimethylindole-3-carboxamido)-2,3-dihydro-1*H*-1,2,5-oxadiazolo[3,4-*c*] [1,3,2]diazaphosphole-2-oxides (11). Yield 2.62 (79%), mp 185-187 °C ;IR (KBr) cm $^{-1}$: 3273 (P–N-H), 3197 (P–N-H–CO), 1635 (C=O) 1226 (P=O) ; ^{31}P-NMR (DMSO-d_6) δ: 13.57 ; ^{1}H-NMR (DMSO-d_6) δ: 9.21 (d, J = 9.0 Hz, 1H, N_1-H), 8.96 (d, J = 8.6, 1H, N_3-H), 7.95 (m, 1H, N-H–CO), 7.60 (m, 1H, H_4-Het), 7.25 (m, 3H, $H_{5,6,7}$-Het), 3.63 (s, 3H, N-CH_3), 2.59 (s, 3H, C-CH_3).; ^{13}C-NMR (DMSO-d_6) δ: 201 (C=O), 165 (C-4), 164 (C-5), 143 (C-2′), 137 (C-9′), 135 (C-3′), 129 (C-8′), 123 (C-5′), 121 (C-4′), 120 (C-6′), 113 (C-7′), 46 (C-1′′), 12.2 (C-2′′).; *Anal.* Calcd for $C_{13}H_{13}N_6O_3P$: C, 46.98; H, 3.91; N, 25.30; Found: C, 46.76; H, 3.89; N, 25.18%.

2-(5-Methylthiophene-2-carboxamido)-2,3-dihydro-1*H*-1,2,5-oxadiazolo [3,4-*c*] [1,3,2]diazaphosphole-2-oxides (12). Yield 1.65 (58%), mp 173-176 °C; IR (KBr) cm $^{-1}$: 3256 (P–N-H), 2967 (P–N-H–CO), 1686 (C=O), 1219 (P=O); ^{31}P-NMR (DMSO-d_6) δ: – 3.7, 7.60 ; ^{1}H-NMR (DMSO-d_6) δ: 8.98 (d, J = 8.8 Hz, 1H, N_1-H), 8.82, (d, J = 8.6 Hz, 1H, N_3-H), 7.87 (m, 1H, N-H–CO), 7.46 (s, 1H, H_3-Het), 6.72 (S, 1H, H_4-Het), 2.48 (s, 3H, CH_3).; ^{13}C-NMR (DMSO-d_6) δ: 188 (C=O), 164 (C-4), 163 (C-5), 143 (C-2′), 139.6 (C-5′), 136 (C-3′), 130 (C-4′), 14.7 (C-1′′).; *Anal.* Calcd for $C_8H_8N_5O_3SP$: C, 33.68; H, 2.8; N, 24.56; Found: C, 33.51; H, 2.78; N, 24.44%.

2-(2-Phenylindolizine-3-carboxamido)-2,3-dihydro-1*H*-1,2,5-oxadiazolo [3,4-*c*] [1,3,2]diazaphosphole-2-oxides (13). Yield 1.82 g (48%), mp 163-165 °C; IR (KBr) cm $^{-1}$: 3236 (P–N-H), 2948 (P–N-H–CO), 1692 (C=O), 1233 (P=O); ^{31}P-NMR (DMSO-d_6) δ: – 8.76; ^{1}H-NMR (DMSO-d_6) δ: 9.21 (d, J_{HH} = 7.0 Hz, 1H, H_5-Het), 9.11 (d, J = 8.9 Hz, 1H, N_1-H), 8.89 (d, J = 8.8 Hz, 1H, N_3-H), 7.68 (m, 6H, H_8-Het, Ph), 7.23 (t, J_{HH} = 7.2 Hz, 1H, H_7-Het) 6.92 (t, J_{HH} = 7.2 Hz, 1H, H_6-Het), 6.76 (s, 1H, H_1-Het), 6.43 (d, J_{PH} = 9.6 Hz, 1H, N-H–CO); ^{13}C-NMR (DMSO-d_6) δ: 192 (C=O), 161 (C-4), 160 (C-5), 148 (C-5′), 140.9 (C-9′), 139 (C-3′), 137 (C-1′′), 136 (C-2′), 134 (C-7′), 130.1 (C-1′), 128.5 (C-3′′, 5′′), 127.8 (C-4′′), 126.3 (C-2′′, 6′′), 123.6 (C-6′), 123 (C-8′).; *Anal.* Calcd for $C_{17}H_{13}N_6O_3P$: C, 53.68; H, 3.42; N, 22.10; Found: C, 53.42; H, 3.40; N, 21.99%.

Conclusions

In summary, we have reported an effective and simple reaction for the synthesis of novel phosphorus heterocyclic compounds with carboxamide group. It is proved, that most of the compounds exhibited moderate activity against bacteria, less activity on fungi. It is observed that the 2-[5-Methylthiophene-2-carboxamido]-2,3-dihydro-1*H*-1,2,5-oxadiazolo[3,4-c] [1,3,2] diazaphosphole-2-oxide (**12**) has significant antibacterial activity and even higher activity than the standard penicillin against *Escherichia coli*.

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References

1. Sorba, G.; Calvino, R.; Defilippi, A.; Gasco, A.; Orsetti, M. *Eur. J. Med. Chem. Chim. Ther.* **1985,** *20*, 571.
2. Orsetti, M.; Sorba, G. *J. Pharm. Pharmacol.* **1988**, *40*, 31.
3. Sorba, G.; Gasco, A.; Orsetti, M. *Eur. J. Med. Chem.* **1989, 24**, 475.
4. For a review on the chemistry of aminofurazans sec: Andrinano, V. G.; Eremeev A. V. *Chem. Heterocycl.* Comp. (Engl. Transl.), **1984,** 937; *Khim. Geterotsikl. Soedin.* **1984,** 1155.
5. Kuranari, M.; Chugai Pharmaceutical Co., Japan Patent, **1965,** 26819; *Chem. Abstr.* **1966,** *64*, 9737 h
6. Papanastassiou, Z. B.; Bardos, T. J. *J. Med. Chem.* **1962,** *5*, 1000.
7. Zhadanov, R. I.; Buina, N. A.; Kapintanova, N. G.; Nuretdinov, I. A. *Synthesis* **1979**, 269.
8. Arnold, V. H.; Bourseaux, F.; Brock, N. *Arzneimittel Forsch* **1961,** *11*, 143.
9. Friedman, O. M.; Papanastassiou, Z.B.; Levi H. S. *J. Med. Chem.* **1963,** *6*, 82.
10. Zimmer, H.; Sill, A. *Progr. Drug. Res.* **1964,** *5*, 150.
11. Hsu, P.; Kao, I. S.; Tsai, J. S.; Chou, C. H.; Liu, M. C.; Sheu, M. L.; Meug, T. Y.; Jeu, Y. F.; Pan, R. C.; Li, S. W. *Sci. Sinica* (Peking) **1964,** *13*, 789.
12. Lemke, T. L.; Boring D. *J. Heterocyclic Chem.* **1980,** *17*, 1455.
13. Vasu Govardhana Reddy P.; Hari Babu Y.; Suresh Reddy C.; Srinivasulu D. *Heteroatom Chemistry* **2002,** *13*, 340.
14. Srinivasulu, D.; Nagaraju, C.; Devendranath Reddy, C.; Berlin, K. D. *Indian J. Chem.* **1999,** *38B*, 735.
15. Venugopal, M.; Sankar Reddy, B.; Devendranath Reddy, C.; Berlin K. D. *J. Heterocyl. Chem.* **2001,** *38*, 275.
16. Kirsanov, A. V. *Zh Obhsch Khim,* **1954,** *24*, 1033.
17. *Chem. Abstr.* **1955,** *49*, 8787a.
18. Tolmachev, A. A.; Chaikovskaya, A. A.; Smaliy, R. V.; Kudrya, T. N.; Yurchenko A. A.; Pinchuk, A. M. *Heteroatom Chemistry* **1999,** *10 (4)*, 343.
19. Zelenin, A. K.; Trudel, M. L.; *J. Heterocyclic Chem.* **1997,** *34*, 1057.
20. Chittenden, R. A.; Thomas, L. C. *Spectrochim. Acta.* **1966,** *22*, 1449.
21. Silverstein, R. M.; Webster, F. X. Spectrometric identification of organic compounds, John

Wiley & Sons, New York **1998**, 101.
22. Daash, L. W.; Smith, S. C. *Anal. Chem.* **1961,** *23*, 853.
23. Bellamy, L. J.; Beecher, L. J. *J. Chem. Soc.* **1952**, 475**.**
24. Corbridge, D. E. C. *J. Appl. Chem.* **1956**, *6*, 456.
25. Thomas, L. C.; Chittenden, R. A. *Chem. Ind.* (London) **1961**, 1913.
26. Srinivasulu, D.; Devendranath, Reddy C.; Sankar Reddy B. *Heteroatom Chemistry* **2000,** *11(5)*, 336**.**
27. Nagaprasada Rao, L.; Naga Raju, C.; Devenderanath Reddy C.; Auschwitz T. S.; Brown, W. C.; Jozef Kluck, Hickey, M. R.; Wakefield, A. C.; Berlin, K. D. *Phosphorus, Sulfur and Silicon* **2000,** *158*, 39.
28. Colle J. G.; Duguid J. P.; Fraser, A. G.; Marmion B. P.; Mackie and Mc Cartney Practical Medical Microbiology, 13th ed., vol 2, Churchil Livingstone, London **1989**.
29. Uma Maheswari Devi, P.; Srinivasa Reddy, P.; Usharani N. R.; Reddemma P. *Eur. J. Plant Pathol* **2000,** *106*, 857.
30. Haranath, P.; Anasuyamma, U.; Syam Prasad, G.; Naga Raju, C.; and Suresh Reddy,* C. Heterocyclic Communications **2004,** 10 (6), 457.
31. Silverstein, R. M.; Bassler, G. C.; Morril, T. C. *Spectrometric identification of organic compounds,* John Wiley & Sons, New York **1991**.