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Synthesis of new α-aminophosphonates by one-pot reaction using 1,4-dimethyl piperazine as a catalyst

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ABSTRACT

The Schiff's bases were prepared by reacting 9-ethyl-3-amino carbazole with substituted aromatic aldehydes in refluxing ethanol. Dialkyl phosphite undergoes addition readily with aromatic Schiff's bases to give α-aminophosphonates(Kabachnik-Field's reaction) in presence of catalytic amount of 1,4-dimethyl piperazine. The structures of the title compounds were established by elemental analysis, IR, ^{1}H, ^{13}C, ^{31}P NMR and LCMS mass spectral data. The anti-microbial and anti-oxidant activitiy of these compounds were evaluated and they exhibited significant antimicrobial and anti-oxidant activity.

KEYWORDS

Aromatic Schiff's bases;
Dialkyl phosphite;
1,4-dimethyl piperazine;
Anti-microbial;
Anti-oxidant activity.

INTRODUCTION

α-Amino-phosphonates are important class of compounds since they are considered to be structural analogues of the corresponding α-aminoacids and find applications as enzyme inhibitors, antibiotics and pharmacological agents[1]. α-Aminophosphonates are key compounds in medicinal chemistry and pharmaceutical science[2]. In addition, they have been used as antibacterial[3], anti-HIV agents[4] and also act as peptide mimics[5].

Out of available methods, one of the main routes to α-aminophosphonates is the Kabachnik-Field's reaction, consisting of the addition of dialkyl hydrogen phosphites to compounds containing C=N bonds. A direct one -pot synthesis of α-aminophosphonates has been reported via the reaction of an aldehyde with an amine and diakyl phosphite[6-8]. In this paper, we report a mild, convenient and simple procedure using a one-pot Kabachnik- Field's reaction of an aldehyde, primary amine and dialkyl phosphite for the preparation of new α-amino phosphonates using 1,4-dimethyl piperazine as a catalyst with high yields.

EXPERIMENTAL

Chemistry

Melting points (mp) were determined in open capillary tubes using a calibrated thermometer by Guna Digital Melting Point apparatus, expressed in degrees centigrade (°C) and are uncorrected. Elemental analysis was performed on Thermo Finnigan Insturment at University of Hyderabad, Hyderabad. Infrared Spectra (υ_{max} in cm^{-1}) were recorded as KBr pellets on a Perkin – Elmer, FT-IR100 spectrophotometer.

^{1}H, ^{13}C and ^{31}P NMR spectra were recorded as

solutions in DMSO-d_6 on a Bruker AMX 500 MHz spectrometer operating at 500 MHz for ^{1}H, 125 MHz for ^{13}C and 202 MHz for ^{31}P NMR. The ^{1}H and ^{13}C chemical shifts were expressed in parts per million (ppm) with reference to tetramethylsilane (TMS) and ^{31}P chemical shifts to 85 % H_3PO_4.

Pharmacology

Antimicrobial activity

The compounds were assayed for antimicrobial activity against bacterial cultures. The bacteria includes Gram positive (*Staphyloccus aureus, Bacillus subtilis*) and Gram negative bacteria (*Escherichia coli, Klebsiella pneumoniae*) and the fungal cultures *A.niger* and *C.albicans*.

The bacterial cultures were grown in nutrient agar media and fungal cultures have been grown in the Potato Dextrose media for the better growth and sub cultured onto the petriplates for the experiments.

The α-aminophophonates were placed on the media and incubated at 37°C for 24 hrs to 72 hrs for better observation. The zone of inhibition was measured where the plaques were formed. All the experiments were carried out in duplicates and the results were expressed as Zone of Inhibition in mm.

RESULTS AND DISCUSSION

Chemistry

Syntheis of new α-aminophosphonates was accompalished in two steps. The reaction of equimolar quantities of 9-ethyl-3-amino carbazole **(1)** is treated with various aryl/hetero aryl aldehydes **(2a-l)** in anhydrous ethanol. The imines **(3a-l)** reacted with diethyl/dibutyl phosphites to give α-aminophosphonates in presence of 1,4-dimethyl piperazine in ethanol at reflux temperature for 5-6 hours with high yields (70-90%) (Scheme 1). The reaction conditions, were mild and the α-aminophosphonates formed exclusively without noticeable formation of undesired side products. The important feature of this reaction is the robustness of functional groups, such as chloro, bromo, nitro and hydroxy groups under the reaction conditions. 1,4-Dimethyl piperazine is found to be more effective than other catalysts in terms of yields, reaction time and cost of the catalyst.

The chemical structure of all the tittle compounds **(4a-l)** were characterized by IR, ^{1}H, ^{13}C, ^{31}P NMR, mass spectral data and elemental analyses and their data are presented in the experimental section. Characterstic IR stretching frequencies were observed in the region 1215-1231 cm^{-1}(P=O), 737-765 cm^{-1}(P-$C_{(aliphatic)}$), 3320-3368 cm^{-1}(N-H) respectively[9].

The proton of the methyne (P-C-H) resonated as doublet of doublet in the region δ 4.74-5.60 due to its coupling with P and the neighbouring N-H proton[10]. The carbon chemical shifts for P-O-CH_2-CH_3 and P-O-CH_2-CH_3 are observed as doublets at δ 62.2-63.4(d, J = 6.7-6.9 Hz) and at δ 15.0-16.3 (d, J =12.6-12.8 Hz) respectively. The chemical shifts for N-C-C/P are observed in the region δ 54.7-56.0. These values are in agreement with the literature data[11,12].

Synthesis of dibutyl ((2-(9-ethyl-9H-3-carbazolyl) amino)(2-thienyl)methyl)phosphonate (4l)

A mixture of 9-ethyl-3-amino carbazole **(1)** (1.04 g, 0.005 mole) and thiophene 2-carboxaldehyde **(2)** (0.5650 g, 0.005 mole) taken in round bottom flask, refluxed in anhydrous ethanol for one hour to form the corresponding aldimine (Schiff's base).The formation of Schiff's base was indicated by TLC run in hexane and ethyl acetate (1:3) as a mobile phase. Then dibutyl phosphite (0.49 mL, 0.005 mole) was added to the corresponding aldimine in presence of 1,4-dimethyl piperazine (catalyst) and the reaction mixture was stirred at reflux temperature for 4 hours. After the completion of the reaction, as indicated by TLC (silica gel) using hexane and ethyl acetate (1:3) as mobile phase, the solvent was removed in a rota-evaporator and the crude product obtained was purified by column chromatography on silica gel (60-120 mesh) using n-hexane and ethyl acetate (1:3) as an eluent to afford the pure dibutyl ((2-(9-ethyl-9H-3-carbazolyl)amino)(2-thienyl) methyl) phosphonate 4l, yield, 78%, m.p. 140-142°C.

Spectral data of synthesized compounds

Diethyl(3-bromo-2-hydroxyphenyl)-[(9-ethyl-9H-3-carbazolyl) amino] methylphosphonate (4a)

Pale brown semisolid. Yield:78. Mol.Wt 531. m.p 140-142°C. IR (KBr) ν cm^{-1}: 3365 (-NH), 1215(-P=O), 737(P-C). ^{1}H-NMR (DMSO-d_6) δ ppm: 6.87-7.01 (m, 10H, Ar-H) 5.04-5.06(dd, 1H, P-C-H), 4.95-5.2 (t, 1H, N-H), 3.86-3.88 (m, 4H P-O-CH_2-CH_3),1.12-1.15

(t, 6H, P-O-CH_2-CH_3).^{13}C-NMR (DMSO-d_6) δ ppm: 109.5(C-1), 136.7(C-3), 121.3(C-5), 121.1(C-7), 126.3(C-9), 45.3(C-1'), 131.0(C-3'), 119.9(C-5'), 37.8(-N-CH_2-CH_3), 15.3 (P-O-CH_2-CH_3),55.2(-N-C-P). ^{31}P-NMR(DMSO-d_6) δppm:22.14. Anal.cald.for $C_{25}H_{28}N_2O_4PBr$: C, 55.65; H, 5.35; N, 5.5O; Found C, 55.61; H, 5.32; N, 5.45.

Diethyl [(9-ethyl-9H-3-carbazolyl)amino]-(3-nitro phenyl)methyl]phosphonate (4b)

Pale green semisolid.Yield:71. Mol.Wt 478. m.p 156-158^{0}C. IR (KBr) v cm^{-1}: 3320 (-NH), 1230(-P=O), 741(P-C). ^{1}H-NMR (DMSO-d_6) δ ppm: 6.76-7.63 (m, 11H, Ar-H), 5.01-5.07(dd, 1H, P-C-H), 4.93-5.0 (t, 1H, N-H), 3.82-3.89 (m, 4H, P-O-CH_2-CH_3), 1.06-1.17 (t, 6H, P-O-CH_2-CH_3). ^{13}C-NMR (DMSO-d6) δ ppm: 109.1(C-1), 135.7 (C-3), 121.5(C-5), 121.3(C-7), 126.9(C-9), 53.4(C-1'), 147.7(C-3'), 129.9(C-5'), 34.8(-N-CH_2-CH_3), 17.3(-P-O-CH_2-CH_3), 52.3(-N-C-P). ^{31}P-NMR (DMSO-d_6) δ ppm: 21.12.

Diethyl [(9-ethyl-9H-3-carbazolyl)amino](1H-2-pyrrolyl)methyl]phosphonate (4c)

Pale green semisolid.Yield:83. Mol.Wt 425. m.p 156-158 ^{0}C. IR (KBr) v cm^{-1}: 3368 (-NH), 1225(-P=O), 749(P-C). ^{1}H-NMR (DMSO-d_6) δ ppm: 6.84-7.51 (m, 11H, Ar-H), 4.93-4.91(dd, 1H, P-C-H), 4.87-4.85 (t, 1H, N-H), 3.90-3.91 (m, 4H, P-O-CH_2-CH_3), 1.08-1.19 (t, 6H, P-O-CH_2-CH_3). ^{31}P-NMR (DMSO-d_6) δ ppm: 21.13. Anal.cald. for $C_{23}H_{28}N_3O_3P$: C, 64.94; H, 6.63; N, 9.88. Found: C, 63.93; H, 6.62 ;N, 9.85.

Diethyl [(9-ethyl-9H-3-carbazolyl)amino](3-pyrdiyl)methyl]phosphonate (4d)

Dark brown semisolid.Yield: 84. Mol.Wt 437. m.p 156-158^{0}C. IR (KBr) v cm^{-1}: 3350 (-NH), 1227(-P=O), 750(P-C). ^{1}H-NMR (DMSO-d_6) δ ppm: 7.81-7.91 (m, 12H, Ar-H), 4.89-4.92(dd, 1H, P-C-H), 4.61-4.54 (t, 1H, N-H), 3.98-3.99 (m, 4H, P-O-CH_2-CH_3), 1.05-1.15 (t, 6H, P-O-CH_2-CH_3). ^{31}P-NMR (DMSO-d_6) δ ppm: 22.32.

Diethyl (2,4-dichlorophenyl) (9-ethyl-9H-3-carbazolyl)amino)methyl)phosphonate (4e)

Black semisolid.Yield:88. Mol.Wt 505. m.p 156-158 ^{0}C. IR (KBr) v cm^{-1}: 3329(-NH), 1230(-P=O), 741(P-C). ^{1}H-NMR (DMSO-d_6) δ ppm: 7.89-8.01 (m, 10H, Ar-H), 5.28-5.30(dd, 1H, P-C-H), 4.93-5.02 (t, 1H, N-H), 3.77-3.81 (m, 4H, P-O-CH_2-CH_3), 1.05-1.15 (t, 6H, P-O-CH_2-CH_3). ^{31}P-NMR (DMSO-d_6) δ ppm: 23.44. Anal.cald. for $C_{25}H_{27}N_2Cl_2O_3P$: C, 59.41; H, 5.37; N, 5.54. Found: C, 59.40 H, 5.36 N, 5.50.

Diethyl ((2-(9-ethyl-9H-3-carbazolyl)amino)(2-thienyl)methyl)phosphonate(4f)

Black semisolid.Yield.Yield:80. Mol.Wt 492. m.p 143-145^{0}C. IR (KBr) v cm^{-1}: 3360 (-NH), 1235(-P=O), 765(P-C). ^{1}H-NMR (DMSO-D_6) δ ppm: 7.81-7.91 (m, 10H, Ar-H), 4.82-4.83(dd, 1H, P-C-H), 4.63-4.8 (t, 1H, N-H), 3.80-3.81 (m, 4H, P-O-CH_2-CH_3), 1.01-1.15 (t, 6H, P-O-CH_2-CH_3). ^{13}C-NMR (DMSO-d_6) δ ppm: 109.6(C-1), 136.8 (C-3), 121.0(C-5), 121.1(C-7), 126.5(C-9), 39.4(C-1'), 125.5(C-3'), 126.7(C-5'), 37.8(-N-CH_2-CH_3), 16.3(-P-O-CH_2-CH_3), 56.0(-N-C-P). ^{31}P-NMR (DMSO-d_6) δ ppm: 22.33.

Dibutyl{(3-bromo-2-hydroxyphenyl)-[(9-ethyl-9H-3-carbazolyl) amino]methyl} phosphonate(4g)

Pale green semisolid.Yield:79. Mol.Wt 586. m.p 163-165°C. IR (KBr) v cm^{-1}: 3355 (-NH), 1224(-P=O), 748(P-C). ^{1}H-NMR (DMSO-d_6) δ ppm: 6.73-7.63 (m, 10H, Ar-H), 5.01-5.07(dd, 1H, P-C-H), 4.96- 5.01 (t, 1H, N-H), 0.86-1.02 (m, 2H P-O-CH_2-CH_2- CH_2-CH_3). ^{13}C-NMR (DMSO-d_6) δ ppm: 109.7(C-1), 136.9 (C-3), 121.3(C-5), 121.2(C-7), 126.3(C-9), 44.3(C-1'), 146.7(C-3'), 127.9(C-5'), 37.8(-N-CH_2-CH_3), 16.9(-P-O-CH_2-CH_3), 55.2(-N-C-P). ^{31}P-NMR (DMSO-d_6) δ ppm: 22.35. LCMS: 538.2($M^{+\cdot}$, 100), 506.2(40), 416(20), 343(60), 210(10). Anal.cald. for $C_{29}H_{36}N_2PBrO_4$: C, 59.29; H, 6.18; N, 4.77. Found: C, 59.25; H, 6.16 N: 4.74.

Dibutyl [(9-ethyl-9H-3-carbazolyl)amino]-(3-nitro phenyl)methyl]phosphonate(4h)

Pale green semisolid.Yield:81. Mol.Wt 437. m.p 156-158 ^{0}C. IR (KBr) v cm^{-1}: 3345 (-NH), 1216(-P=O), 745(P-C). ^{1}H-NMR (DMSO-d_6) δ ppm: 7.88-7.90 (m, 11H, Ar-H), 4.91-4.93(dd, 1H, P-C-H), 4.96-5.01 (t, 1H, N-H), 0.86-1.02 (m, 2H, P-O-CH_2- CH_2-CH_2-CH_3). ^{13}C-NMR (DMSO-d_6) δ ppm: 109.8(C-1), 136.8(C-3), 121.5(C-5), 121.3(C-7), 126.4(C-

9), 54.4(C-1'), 125.3(C-3'), 127.9(C-5'), 37.8(-N-CH_2-CH_3), 16.6(-P-O-CH_2-CH_3), 52.3(-N-C-P). ^{31}P-NMR (DMSO-d_6) δ ppm: 21.12. LCMS: 566.2($M^{+\cdot}$, 100), 443.2(8.3), 392.2(12), 368.2(10), 290(17), 234(38), 211(33),182(10), 152(7), 105(8.3).

Dibutyl [(9-ethyl-9H-3-carbazolyl)amino](1H-2-pyrrolyl)methyl]phosphonate (4i)

Dark brown semisolid.Yield:74. Mol.Wt 481. m.p 157-158 ^{0}C. IR (KBr) v cm^{-1}: 3340 (-NH), 1227(-P=O), 750(P-C). ^{1}H-NMR (DMSO-d_6) δ ppm: 6.83-6.93 (m, 11H, Ar-H), 4.91-4.93 (dd, 1H, P-C-H), 4.96-5.01(t, 1H, N-H), 0.93-1.00(m, 2H, P-O-CH_2-CH_2-CH_2-CH_3) ^{31}P-NMR (DMSO-d_6) δ ppm: 22.12.

Dibutyl [(9-ethyl-9H-3-carbazolyl)amino](3-pyrdiyl)methyl] phosphonate(4j)

Pale brown semisolid..Yield:80. Mol.Wt 509. m.p 155-156 ^{0}C. IR (KBr) v cm^{-1}: 3350(-NH), 1229(-P=O), 752(P-C). ^{1}H-NMR (DMSO-d_6) δ ppm: 7.03-7.12 (m, 12H, Ar-H), 5.28-5.30 (dd, 1H, P-C-H), 4.78-4.81 (t, 1H, N-H), 0.92-1.15 (m, 2H, P-O-CH_2- CH_2-CH_2-CH_3). ^{31}P-NMR (DMSO-d_6) δ ppm: 23.12.

Dibutyl (2,4-dichlorophenyl)((9-ethyl-9H-3-carbazolyl)amino)methyl) phosphonate(4k)

Black semisolid.Yield:90. Mol.Wt 560. m.p 157-158 ^{0}C. IR (KBr) v cm^{-1}: 3340 (-NH), 1231 (-P=O), 751(P-C). ^{1}H-NMR (DMSO-d_6) δ ppm: 7.12-7.23 (m, 10H, Ar-H), 4.82-4.92 (dd, 1H, P-C-H), 4.95-5.11(t, 1H, N-H), 0.92-1.00 (m, 2H, P-O-CH_2- CH_2-CH_2-CH_3). ^{31}P-NMR (DMSO-d_6) δ ppm: 24.12. Anal.cald. for $C_{29}H_{35}N_2Cl2PO_3$: C, 65.74; H, 7.50; N, 8.20. Found: C, 65.70; H, 7.45; N, 8.17.

Dibutyl ((2-(9-ethyl-9H-3-carbazolyl)amino)(2-thienyl)methyl)phosphonate(4l)

Black semisolid.Yield:79. Mol.Wt 560. m.p 152-153 ^{0}C. IR (KBr) v cm^{-1}: 3325 (-NH), 1230 (-P=O), 741(P-C). ^{1}H-NMR (DMSO-D6) δ ppm:7.12-7.23 (m, 10H, Ar-H), 4.82-4.83(dd, 1H, P-C-H), 4.87-494 (t, 1H, N-H), 0.96-1.15 (m, 2H, P-O-CH_2- CH_2-CH_2-CH_3). ^{13}C-NMR (DMSO-d_6) δ ppm: 108.1(C-1), 137.8 (C-3), 121.9(C-5), 121.6(C-7), 125.2(C-9), 139.3(C-1'), 125.0(C-3'), 37.8(-N-CH_2-CH_3), 16.6(-P-O-CH_2-CH_3), 56.0(-N-C-P). ^{31}P-NMR (DMSO-d_6) δ ppm: 22.19. LCMS: 499.2(M^++1, 100), 471(12), 443(12), 322(50), 403(12).

PHARMACOLOGY

Antioxidant activity

Antioxidant activity was performed with two methods DPPH and Super Oxide radical scavenging activities. Scavenging capacity was measured spectrophotometrically by monitoring the decrease in absorbance at 517 nm.

DPPH radical-scavenging activity

The DPPH radical scavenging activity was measured in a reaction mixture containing 1 mM DPPH radical solution 0.1 mL, 99% ethanol 0.8 mL, and 0.1 mL of each one of the studied compounds prepared by dissolving the compound in methanol. The solution was rapidly mixed and scavenging capacity was measured spectrophotometrically by monitoring the decrease in absorbance at 517 nm.

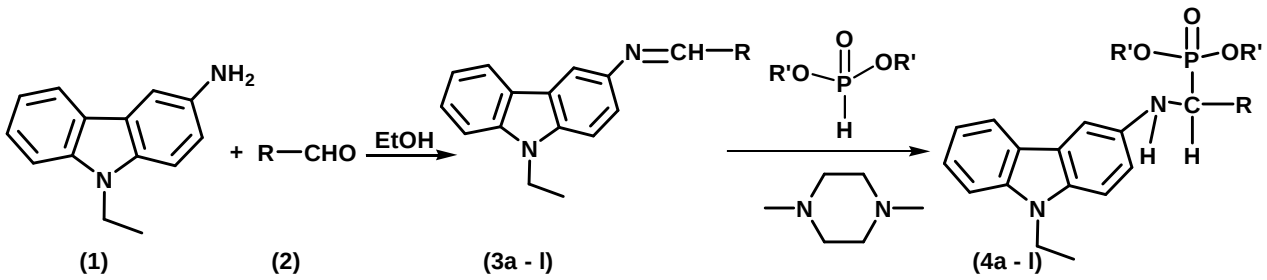
$$\text{DPPH radical scavenging activity}(\%) = \frac{\text{1 – absorbance of sample at 517nm}}{\text{Absorbance of control at 517nm}} \times 100$$

Superoxide radical scavenging activity

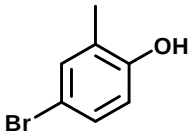
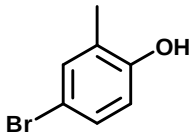
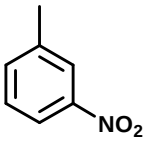
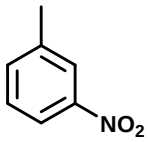
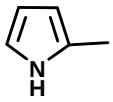
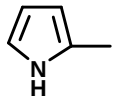
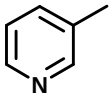
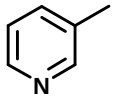
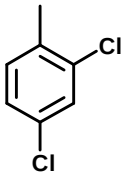
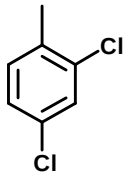
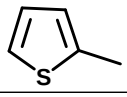
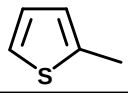
Superoxide radicals were determined using spectrophotometric measurement of the effects of various concentrations of test compounds on the reduction of nitroblue tetrazolium (NBT), according to a previously described procedure.[13] Superoxide radicals were generated in a non-enzymatic phenazine methosulfate–nicotinamide adenine dinucleotide (PMS/NADH) system. The non-enzymatic generation of superoxide radicals was measured in reaction mixtures containing various concentrations of test compounds, PMS (15 μM), NADH (73 μM), and NBT (50 μM) in phosphate buffer (20 mM, pH 7.4). After incubation for 5 min at ambient temperature, the color was read at 560 nm against blank samples.

$$\text{Superoxide radical scavenging activity}(\%) = \frac{\text{Absorbance of control} - \text{absorbance of test sample}}{\text{Absorbance of control}} \times 100$$

Reactive oxygen species (ROS), such as superoxide anion radical ($O^{2-\cdot}$), hydroxyl adicals (OH) and peroxyl radicals (ROO·) are produced as a part of nor-



Scheme 1 : Synthesis of α-aminophosphonates (4a-l)

Compound	R	R^1	Compound	R	R^1
4a		Et	4g		But
4b		Et	4h		But
4c		Et	4i		But
4d		Et	4j		But
4e		Et	4k		But
4f		Et	4l		But

mal metabolic processes.[14] The compounds **(4a-l)** showed high antioxidant activity by scavenging the free radicals and superoxide radicals.

The antioxidant activity evaluation with the 1,1-diphenyl-2-picryl-hydrazyl (DPPH), radical-scavenging assay was carried out[15] and the results are presented in TABLE 1.

Antimicrobial activity

The compounds were assayed for antimicrobial activity against bacterial cultures. The bacteria includes Gram positive (*Staphyloccus aureus, Bacillus subtilis*) and Gram negative bacteria (*Escherichia coli, Klebsiella pneumoniae*). The bacterial cultures were grown in nutrient agar media and fungal cultures have been grown in the Potato Dextrose media for the better growth and sub cultured onto the petriplates for the experiments. The cultures were diluted with sterilized saline to bring the final inoculum size of approximately 10^5-10^6 CFU/mL.

Antimicrobial activity assay

The test compounds were introduced on the disc and then allowed to dry to completely saturate the disc. Then the disc was introduced onto the upper layer of the medium with the bacteria. The Petri dishes were incubated overnight at 37°C for 24 hrs to 72 hrs for better observation and the fungal cultures were cultured on potato dextrose medium incubated at 37°C for 24 hrs to 72 hrs. These antimicrobial activities were as-

TABLE 1 : Antioxidant activities of the title compounds (4a-l)

Compound	DPPH Scavenging (%)	Superoxide Scavenging (%)
4a	71.48±1.33	65.12±1.55
4b	64.02±1.41	61.07±1.73
4c	71.13±1.21	66.45±1.64
4d	65.84±1.08	61.93±1.86
4e	71.34±1.36	68.54±1.53
4f	63.87±1.15	61.65±1.09
4g	75.68±1.12	71.19±1.37
4h	64.93±1.73	61.09±1.88
4i	72.47±1.84	69.98±1.73
4j	64.69±1.58	60.96±1.01
4k	65.23±1.06	62.87±1.12
4l	65.81±1.26	62.67±1.29
Vitamin C	83.42 ± 1.65	78.51± 1.43

TABLE 2 : Antibacterial activity[a] of title compounds (4a-l)

Entry	Zone of Inhibition(mm)			
	B. subtilis	*S.aureus*	*E.coli*	*K.Pneumoniae*
4a	8.0	7.8	8.5	7.6
4b	6.0	6.8	6.0	7.2
4c	5.7	6.4	8.5	7.4
4d	10.0	9.5	8.7	7.6
4e	11.8	14.3	9.8	11.2
4f	10.5	11.2	8.5	8.5
4g	13.5	12.5	11.1	9.9
4h	12.0	10.9	13.4	12.5
4i	11.2	13.2	12.5	11.9
4j	15.7	16.4	17.2	14.3
4k	13.4	13.5	14.4	15.5
4l	10.6	11.1	12.1	15.0
Ampicillin	16.7	17.2	17.4	16.9

[a]**concentration 100 µg/mL**

sessed based on the measurement of the diameter of the clear zone around the paper disc. The experiments were carried out in duplicates. Petri dishes were examined for the zone of inhibition around each disc and average results were recorded. The results were compared with the activity of the standard antibiotic Ampicillin(100 µg/mL). The antibacterial activity was evaluated and the results are presented in TABLE 2. The compounds **(4j)** and **(4k)** showed good activity against both the Gram positive and Gram negative bacteria when compared to that of the standard Ampicillin.

The same procedure was adopted for the antifungal activity. The compounds were screened for their antifungal activity against *A.niger* and *C.albicans* along with standard amphotericin B. The antifungal activity was evaluated and the results are presented in TABLE 3.

TABLE 3 : Antifungal activity [a] of title compounds (4a-l)

Compound	Zone of Inhibition	
	A.niger	C.albicans
4a	8.8	7.2
4b	7.2	6.5
4c	11.4	9.5
4d	7.6	11.2
4e	9.8	8.6
4f	11.1	10.3
4g	11.2	10.8
4h	6.8	6.0
4i	7.3	7.8
4j	9.3	8.4
4k	7.2	6.5
4l	9.2	9.8
AMPHOTERICIN B	13.0	12.2

[a]**concentration 100µg/mL**

The compounds **(4c)**, **(4f)** and **(4g)** exhibited good activity against fungal cultures when compared to the other compounds.

Majority of the compounds exhibited promising antioxidant, antibacterial and antifungal activity.

CONCLUSIONS

In conclusion, we have developed a convenient method for the synthesis of new α-aminophosphonates by reacting 9-ethyl-3-amino carbazole and various aryl/hetero aryl aldehydes in anhydrous ethanol. The imines were reacted with diethyl/dibutyl phosphite to get α-aminophosphonates in presence of 1,4-dimethyl piperazine in ethanol at reflux temperature for 5-6 hours with high yields. These compounds exhibited significant antioxidant, antibacterial and antifungal activity.

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