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Microwave Assisted One-pot Synthesis of Novel α-Aminophosphonates and Their Biological Activity

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A simple and efficient synthesis of various α-aminophosphonates (**3a-l**) by the reaction of substituted aromatic/heterocyclic aldehydes, 2-amino-6-methoxy-benzothiazole and dibutyl/diphenyl phosphites under microwave irradiation without catalyst was accomplished. The phosphonates were characterized by elemental analysis, IR, ^{1}H, ^{13}C- and ^{31}P-NMR spectra. They showed promising antimicrobial, anti-oxidant activities depending on the nature of bioactive groups at the α-carbon.

Key Words: Aminophosphonates, Microwave irradiation, Gram positive bacteria, Gram negative bacteria, Anti-oxidant activity

Introduction

Kabachnik-Fields reaction is one of the most effective synthetic methods for α-aminophosphonates. A great deal of attention is bestowed on them[1,2] as they are structural analogues of the corresponding α-amino acids. Further, heterocyclic phosphonates and ω-aminophosphonates are an important class of compounds, with several potential applications in medicine as anticancer agents,[3] potent enzyme inhibitors,[4] antiviral agents,[5] peptide mimetics,[6] haptens of catalytic antibodies, antibiotics, and pharmacological agents.[7] Their diverse applications include inhibition of synthase,[8] HIV protease,[9] renin,[10] and PTPases.[11,12] Some of these derivatives are potential antibiotics.[13] The aminophosphonic and aminophosphinic acids are of considerable interest due to their applications as agrochemicals such as plant growth regulators, pesticides and herbicides.[14] Besides the compounds containing benzothiazole moiety have been reported to have excellent fungicidal activity.[15-17] A variety of synthetic approaches have been reported for them. Of all the methods, the nucleophilic addition of phosphites to imines, catalyzed by Lewis acid or a base is the most convenient one.

Nowadays, microwave irradiation is used to accomplish certain unsuccessful or low-yielding reactions, reducing the reaction time from days to minutes, and improving yields.[18,19] Synthesis of α-aminophosphonates under microwave conditions has been scarcely investigated.

We report the synthesis of α-aminophosphonates using 2-amino-6-methoxy benzothiazole, various substituted aromatic/heterocyclic aldehydes and dibutyl/diphenyl phosphite in dry toluene under microwave irradiation in excellent yields, in a very short reaction times.

Experimental

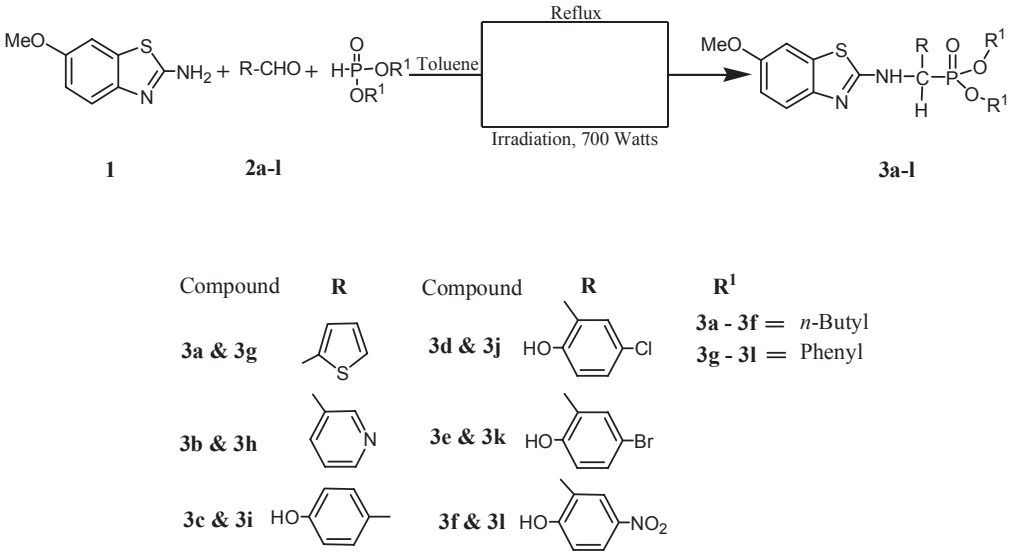
Chemistry. Sigma-Aldrich, Merck and Lancaster Chemicals were used as such. Solvents used for spectroscopic and other physical studies were reagent grade and were further purified by literature methods.[28] The reactions were carried out on Microwave Oven, CATALYST-4R, Research Model, Made in India. Melting points were determined by Guna Digital Melting Point apparatus using a calibrated centigrade thermometer. IR spectra were obtained in KBr on a Perkin-Elmer Model 281-B spectrophotometer, in wave numbers (cm^{-1}). ^{1}H and ^{13}C NMR spectra were recorded in DMSO-d_6 on a Bruker AVANCE III 500 MHz spectrometer operating at 500 MHz for ^{1}H, 125 MHz for ^{13}C and 202.4 MHz for ^{31}P NMR. The ^{1}H and ^{13}C chemical shifts were expressed in ppm with reference to tetramethylsilane and ^{31}P chemical shifts to 85% H_3PO_4. Mass spectra were recorded on a JEOL GCMATE II GC Mass spectrometer. Elemental analyses were performed by Central Drug Research Institute, Lucknow, India.

General procedure for the preparation of 3a-l.

Conventional method: To a solution of 2-amino-6-methoxy benzothiazole (**1**) (0.005 mol) and various aromatic/heterocyclic aldehydes (**2**) (0.005 mol) in anhydrous toluene (15 mL), dibutyl/diphenyl phosphite (0.005 mol) in anhydrous toluene (10 mL) was added dropwise with stirring at room temperature for half an hour. The reaction mixture was refluxed with stirring for 4 - 5 h. After completion of the reaction as indicted by TLC, ethylacetate:methanol, 4:1, the solvent was removed in a rota-evaporator, the residue was purified by column chromatography on silica gel (60 - 120 mesh) using petroleum ether-ethyl acetate (2:8) as eluent. Physical, analytical and IR spectral data of **3a-l** are given in the respective compounds. Yields of **3a-l** are in the range of 62 - 73%

Microwave irradiation: 2-Amino 6-methoxy benzothiazole (**1**) (0.005 mol) was treated with 1 equiv. of substituted various aromatic/ heterocyclic aldehydes (**2**) (0.005 mol) and 1 equiv. of dibutyl/diphenyl phosphite (0.005 mol), in anhydrous toluene were irradiated in a microwave (700 Watts), for 12 - 15 min. These are the optimized conditions for the best results. Yields of **3a-l** are in the range of 81 - 88%.

Dibutyl(6-methoxybenzo[d]thiazol-2-ylamino)(thiophen-2-yl)methylphosphonate(3a): Yield 83%. mp 177 - 182 °C. IR



Scheme 1

(KBr) ν_{max} 3381 (NH), 1210 (P=O), 758 (P-$C_{aliphatic}$); ^{1}H NMR (DMSO- d_6, 500 MHz) δ 6.77-7.26 (m, 6H, Ar-H), 5.98 (s, 1H, -NH), 5.29 (d, J = 18.5 Hz, 1H, P-C-H), 3.74-3.88 (m, 4H, -OCH_2), 3.71 (s, 3H, -OCH_3), 1.37-1.52 (m, 4H, -CH_2), 1.16-1.35 (m, 4H, -CH_2), 0.85 (t, J = 7.0 Hz, 6H, -CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 161.5, 153.9, 151.3, 139.2, 132.3, 130.8, 125.35, 120.2, 120.1, 112.9, 71.4, 69.4, 62.9, 39.9, 25.9, 20.9, ^{31}P NMR δ 20.9; Anal. Calcd for $C_{21}H_{29}N_2O_4PS_2$: C, 53.83; H, 6.24; N, 5.98; Found C, 53.71; H, 6.35, N, 5.89.

Dibutyl (6-methoxybenzo[d]thiazol-2-ylamino)(pyridin-3-yl)methylphosphonate (3b): Yield 85%. mp 175 - 177 °C. IR (KBr) ν_{max} 3392 (NH), 1220 (P=O), 759 (P-$C_{aliphatic}$); ^{1}H NMR (DMSO- d_6, 500 MHz) δ 6.72-7.5 (m, 7H, Ar-H), 6.12 (s, 1H, -NH), 5.65 (d, J =19.2 Hz, 1H, P-C-H), 3.78-3.84 (m, 4H, -OCH_2), 3.6 (s, 3H, -OCH_3), 1.50-1.54 (m, 4H, -CH_2), 1.35-1.43 (m, 4H, -CH_2), 0.85 (t, J = 6.5 Hz, 6H, -CH_3), ^{31}P NMR δ 26.0; Anal. Calcd for $C_{22}H_{30}N_3O_4PS$: C, 57.01; H, 6.52; N, 9.07; Found C, 57.11; H, 6.43, N, 9.12.

Dibutyl (4-hydroxyphenyl)(6-methoxybenzo[d]thiazol-2-ylamino)methylphosphonate (3c): Yield 86%. mp 186 - 189 °C. IR (KBr) ν_{max} 3490 (OH), 3391 (NH), 1221 (P=O), 763 (P-$C_{aliphatic}$); ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.96 (s,1H, Ar-OH), 6.69-7.32 (m, 7H, Ar-H), 5.92 (s, 1H, -NH), 5.20 (d, J = 18.5 Hz, 1H, P-C-H), 3.70-3.84 (m, 4H, -OCH_2), 3.65 (s, 3H, -OCH_3), 1.31-1.46 (m, 4H, -CH_2), 1.15-1.25 (m, 4H, -CH_2), 0.81 (t, J = 7.5 Hz, 6H, -CH_3); *Anal*. Calcd for $C_{23}H_{31}N_2O_5PS$: C, 57.73; H, 6.53; N, 5.85; Found C, 57.53; H, 6.64 N, 5.68.

Dibutyl(5-chloro-2-hydroxyphenyl)(6-methoxybenzo[d]thiazol-2-ylamino)methylphosphonate (3d): Yield 82%. mp 175 - 177 °C. IR (KBr) ν_{max} 3510 (OH), 3389 (NH), 1218 (P=O), 755 (P-$C_{aliphatic}$); ^{1}H NMR (DMSO- d_6, 500 MHz) δ 8.59 (s, 1H, Ar-OH), 6.99-7.43 (m, 6H, Ar-H), 6.05 (t, J = 20.0 Hz, 1H, -NH), 5.67 (dd, J = 23.5 Hz, J = 20.8 Hz 1H, P-C-H), 3.80-3.85 (m, 4H, -OCH_2), 3.73 (s, 3H, -OCH_3), 1.54-1.57 (m, 4H, -CH_2), 1.30-1.40 (m, 4H, -CH_2), 0.86 (t, J = 7.0 Hz, 6H, -CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 169.8, 156.7, 152.5, 143.2, 132.2, 130.5, 127.1, 124.5, 120.7, 118.3, 117.2, 115.1, 106.5, 66.9, 62.9, 35.5, 20.9, 18.5; ^{31}P NMR δ 22.8; Anal. Calcd for $C_{23}H_{30}N_2O_5PSCl$: C, 53.85; H, 5.89; N, 5.46; Found C, 53.81; H, 5.92, N, 5.56.

Dibutyl(5-bromo-2-hydroxyphenyl)(6-methoxybenzo[d]thiazol-2-ylamino)methylphosphonate (3e): Yield 81%. mp 167 - 169 °C. IR (KBr) ν_{max} 3514 (OH), 3390 (NH), 1210 (P=O), 762 (P-$C_{aliphatic}$); ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.94 (s,1H, Ar-OH), 6.75-7.37 (m, 6H, Ar-H), 6.18 (s, 1H, -NH), 5.82 (dd, J = 21.5.0 Hz, J = 19.8 Hz, 1H, P-C-H), 3.75-3.79 (m, 4H, -OCH_2), 3.71 (s, 3H, -OCH_3), 1.50-1.54 (m, 4H, -CH_2), 1.25-1.34 (m, 4H, -CH_2), 0.84 (t, J = 7.5 Hz, 6H, -CH_3); ^{31}P NMR δ 20.8; Anal. Calcd for $C_{23}H_{30}N_2O_5PSBr$: C, 49.56; H, 5.42; N, 5.03; Found C, 49.50; H, 5.36, N, 4.97.

Dibutyl(2-hydroxy-5-nitrophenyl)(6-methoxybenzo[d]thiazol-2-ylamino)methylphosphonate (3f): Yield 82%. mp 174 - 176 °C. IR (KBr) ν_{max} 3490 (OH), 3392 (NH), 1220 (P=O), 765 (P-$C_{aliphatic}$); ^{1}H NMR (DMSO-d_6, 500 MHz) δ 8.15 (s, 1H, Ar-OH), 6.55-7.75 (m, 7H, Ar-H), 6.23 (s,1H, -NH), 5.80 (d, J = 19.9 Hz, 1H, P-C-H), 3.87-3.95 (m, 4H, -OCH_2), 3.8 (s, 3H, -OCH_3), 1.45-1.52 (m, 4H, -CH_2), 1.23-1.34 (m, 4H, -CH_2), 0.82 (t, J = 6.5 Hz, 6H, -CH_3); ^{31}P NMR δ 25.5; GCMS (*m/z*; %) (523.15, 30%) $M^{+\cdot}$; Anal. Calcd for $C_{23}H_{30}N_3O_7PS$: C, 52.77; H, 5.78; N, 8.03; Found C, 52.72; H, 5.75, N, 7.98.

Diphenyl(6-methoxybenzo[d]thiazol-2-ylamino)(thiophen-2-yl)methylphosphonate (3g): Yield 80%. mp 192 - 194 °C. IR (KBr) ν_{max} 3378 (NH), 1215 (P=O), 762 (P-$C_{aliphatic}$); ^{1}H NMR (DMSO-d_6, 500 MHz) δ 6.82-7.41 (m, 6H, Ar-H), 6.1 (s, 1H, -NH), 5.81 (d, J = 21.5 Hz, 1H, P-C-H), 3.73 (s, 3H, -OCH_3); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 174.9, 155.2, 151.8, 144.5, 140.0, 131.6, 129.7, 127.2, 126.9, 125.8, 124.2, 121.0, 118.9, 118.6, 115.6, 113.6, 56.0, 52.6; ^{31}P NMR δ 24.3; GCMS (*m/z*; %) (508.38, 30%) $M^{+\cdot}$; Anal. Calcd for $C_{25}H_{21}N_2O_4PS_2$: C, 59.04; H, 4.16; N, 5.51; Found C, 59.24; H, 4.06, N, 5.61.

Diphenyl(6-methoxybenzo[d]thiazol-2-ylamino)(pyridin-3-yl)methylphosphonate (3h): Yield 81%. mp 179 - 180 °C. IR (KBr) ν_{max} 3390 (NH), 1217 (P=O), 754 (P-$C_{aliphatic}$); ^{1}H NMR (DMSO-d_6, 500 MHz) δ 6.77-8.44 (m, 17H, Ar-H), 6.07 (s, 1H,

Table 1. Antibacterial activity of α-aminophosphonates (**3a-l**) against Gram positive and Gram negative bacteria.

Compounds	*B. subtilis*		*S. aureus*		*E. coli*		*K. pneumoniae*	
	50 μg/mL	100 μg/mL	50 μg/mL	100 μg/mL	50 μg/mL	100 μg/mL	50 μg/mL	100 μg/mL
3a	7	11	9	1 0	8	11	6	10
3b	8	13	8	12	7	10	9	11
3c	6	10	7	10	6	11	8	13
3d	8	11	11	13	9	12	8	12
3e	-	-	-	-	5	9	6	8
3f	8	12	8	11	7	11	9	11
3g	7	10	6	8	10	12	7	10
3h	6	11	7	9	9	12	10	11
3i	8	13	10	15	8	10	9	11
3j	11	13	13	18	12	15	11	14
3k	10	13	13	14	11	14	13	15
3l	12	14	13	17	13	15	12	15
Penicillin	10	-	12	-	12	-	11	-

-NH), 5.40 (d, J = 18.2 Hz, 1H, P-C-H), 3.7 (s, 3H, -OCH_3); ^{31}P NMR δ 23.5; GCMS (*m/z*; %) (503.01, 45%) $M^{+\cdot}$; Anal. Calcd for $C_{26}H_{22}N_3O_4PS$: C, 62.02: H, 4.40; N, 8.35; Found C, 61.96; H, 4.37, N, 8.29.

Diphenyl(4-hydroxyphenyl)(6-methoxybenzo[d]thiazol-2-ylamino)methylphosphonate (3i): Yield 84%. mp 189 - 192 °C. IR (KBr) ν_{max} 3498 (OH), 3387 (NH), 1219 (P = O), 759 (P-$C_{aliphatic}$); ^{1}H NMR (DMSO-d_6, 500 MHz) δ 8.5 (s,1H, Ar-OH), 6.34-7.76 (m, 17H, Ar-H), 6.19 (s, 1H, -NH), 5.34 (d, J = 20.0 Hz, 1H, P-C-H), 3.69 (s, 3H, -OCH_3); *Anal*. Calcd for$C_{27}H_{23}N_2O_5PS$: C, 62.54; H, 4.47; N, 5.40; Found C, 62.42; H, 4.58, N, 5.46.

Diphenyl(5-chloro-2-hydroxyphenyl)(6-methoxybenzo[d]-thiazol-2-ylamino)methylphosphonate (3j): Yield 88%. mp 183 - 185 °C. IR (KBr) ν_{max} 3500 (OH), 3390 (NH), 1215 (P=O), 761 (P-$C_{aliphatic}$); ^{1}H NMR (DMSO-d_6, 500 MHz) δ 8.29 (s, 1H, Ar-OH), 6.74-7.38 (m, 16H, Ar-H), 6.10 (s, 1H, -NH), 5.70 (d, J = 20.5 Hz, 1H, P-C-H), 3.71 (s, 3H, -OCH_3); ^{13}C NMR (DMSO-d_6, 125 MHz) 166.6, 155.4, 154.4, 154.2, 145.2, 131.7, 128.5, 128.1, 127.5, 123.0, 119.2, 118.6, 117.8, 117.2, 115.6, 115.0, 114.0, 113.4, 106.6, 56.1, 55.9; ^{31}P NMR δ 26.1; GCMS (*m/z*; %) (552.05, 39%) $M^{+\cdot}$; Anal. Calcd for $C_{27}H_{22}N_2O_5PSCl$: C, 58.65; H, 4.01; N, 5.07; C, 58.51; H, 4.07, N, 5.12.

Diphenyl(5-bromo-2-hydroxyphenyl)(6-methoxybenzo[d]-thiazol-2-ylamino)methyl phosphonate (3k): Yield 85%. mp 181 - 184 °C. IR (KBr) ν_{max} 3505 (OH), 3397 (NH), 1190 (P=O), 760 (P-$C_{aliphatic}$); ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.94 (s, 1H, Ar-OH), 6.8-7.61 (m, 16H, Ar-H), 6.09 (s, 1H, -NH), 5.70 (dd, J = 24.5.0 Hz, J = 21.0 Hz, 1H, P-C-H), 3.73 (s, 3H, -OCH_3); ^{31}P NMR δ 21.8; Anal. Calcd for $C_{27}H_{22}N_2O_5PSBr$: C, 54.28; H, 3.71; N, 4.69; Found C, 54.22; H, 3.67, N, 4.64.

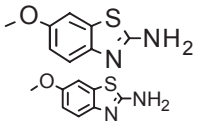
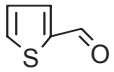
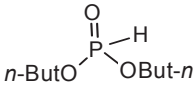
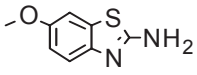
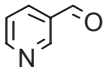
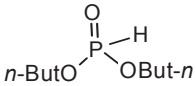
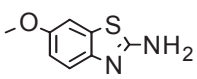
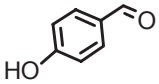
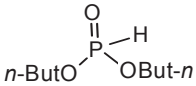
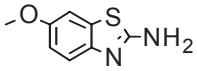
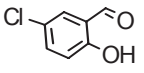
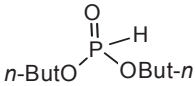
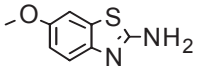
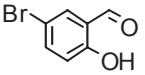
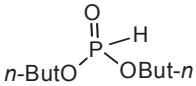
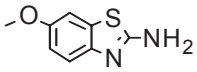
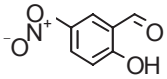
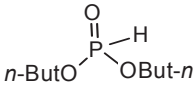
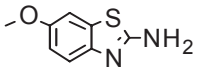
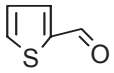
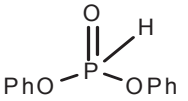
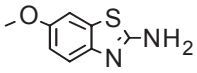
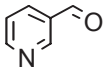
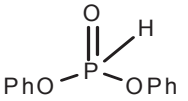
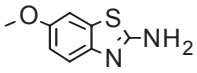
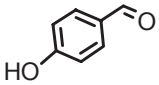
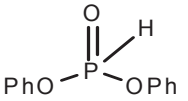
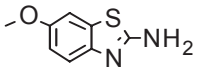
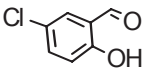
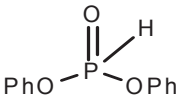
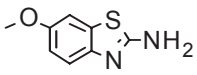
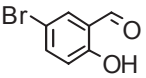
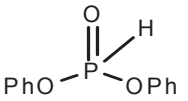
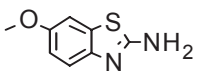
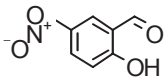
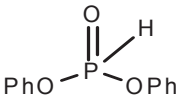
Diphenyl(2-hydroxy-5-nitrophenyl)(6-methoxybenzo[d]-thiazol-2-ylamino)methyl phosphonate (3l): Yield 84%. mp 172 - 175 °C. IR (KBr) ν_{max} 3497 (OH), 3399 (NH), 1222 (P=O), 755 (P-$C_{aliphatic}$); ^{1}H NMR (DMSO-d_6, 500 MHz) δ 8.20 (s, 1H, Ar-OH), 6.78-7.92 (m, 16H, Ar-H), 6.22 (s, 1H, -NH), 5.85 (d, J = 20.4 Hz 1H, P-C-H), 3.9 (s, 3H, -OCH_3), ^{31}P NMR δ 21.3; Anal. Calcd for $C_{27}H_{22}N_3O_7PS$: C, 57.55; H, 3.94; N, 7.46; Found C, 57.50; H, 3.87, N, 7.39.

Table 2. Antioxidant activity of α-aminophosphonates (**3a-l**) by ferric thiocyanate method

Compounds	LPO (μg/mL)
3a	92.19 ± 1.64
3b	89.71 ± 1.66
3c	86.23 ± 1.78
3d	96.88 ± 1.77
3e	89.55 ± 1.86
3f	91.27 ± 1.44
3g	89.12 ± 1.25
3h	85.32 ± 1.21
3i	71.19 ± 1.36
3j	67.72 ± 1.84
3k	69.15 ± 1.11
3l	65.26 ± 1.56
Vitamin C	82.03 ± 1.14

Antibacterial activity. Compounds **3a-l** were screened for antibacterial activity against Gram positive bacteria, *Staphylococcus aureus, Bacillus subtilis* and Gram negative bacteria, *Escherichia coli*, *Klebsiella pneumoniae* by the disc diffusion method[29,30] in nutrient agar medium at two concentrations (50, 100 μg/mL) in DMSO. The compounds were diluted in DMSO for biological assays. These solutions containing 106 cells/mL were added to each Whatmann No.1 filter paper disc (6 mm diameter) and DMSO was used as the control. For the agar disc diffusion method, the test compounds were introduced onto the disc and then allowed to dry completely to saturate the disc with the test compound. 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. Bioactivity was determined by measuring Diameter of Inhibition Zones (DIZ) in mm. The compounds **3a-l** were taken as 50 and 100 μg/mL concentrations and were evaluated by disc method. After examining

Table 3. One-pot synthesis of α-aminophosphonates (**3a-l**)

Compound	Amine	Aldehyde	Phosphite	Microwave irradiation		Conventional heating	
				Time (min)	Yield (%)	Time (h)	Yield (%)
3a				12	83	5	68
3b				12	85	5	65
3c				11	86	6	62
3d				12	82	5	69
3e				12	81	5	65
3f				12	82	5	65
3g				15	80	6	72
3h				12	81	6	67
3i				10	84	4	64
3j				15	88	7	73
3k				15	85	7	68
3l				15	84	7	69

the Petri plates for zone of inhibition around each disc, the samples were tested in triplicate and average results were recorded. Zone of inhibition is the area on an agar plate where growth of any microorganism is prevented by an antibiotic usually placed on the agar surface. If the test organism is susceptible to the antibiotic, the microorganisms will not grow. The

results were presented in **Table 1** and compared with Penicillin (50 μg/mL). The compounds **3j**, **3k** and **3l** showed very significant results against all the bacteria.

Antioxidant activity. The antioxidant activity of α-aminophosphonates was determined according to the ferric thiocyanate method in linoleic acid emulsion.[31] For stock solutions, 10 μg of test compound was dissolved in 1 mL DMSO. α-Aminophosphonates solution samples (10 - 20 μg/mL) in 2.5 mL of potassium phosphate buffer (0.04 M, pH 7.0) was added to 2.5 mL of linoleic acid emulsion in freshly prepared potassium phosphate buffer (0.04 M, pH 7.0). The mixed solution (5 mL) was incubated at 37 ^{o}C. At regular intervals during incubation, a 0.1 mL aliquot of the mixture was diluted with 3.7 mL of ethanol, followed by the addition of 0.1 mL of 30% ammonium thiocyanate and 0.1 mL of 20 mM ferrous chloride in 3.5% hydrochloric acid. The peroxide level was determined by reading the absorbance at 500 nm in a spectrophotometer. During the linoleic acid oxidation, peroxides are formed which oxidize Fe^{+2} to Fe^{+3}. The Fe^{+3} ions form a complex with thiocyanate and this complex has a maximum absorbance at 500 nm. Therefore, high absorbance indicates high linoleic acid oxidation. Solutions without added samples were used as blanks. All data on total antioxidant activity are the average of triplicate experiments. The percentage inhibition of lipid peroxidation in linoleic acid emulsion was calculated by following equation:

$$\text{Inhibition of lipid peroxidation (\%)} = [(A_{Control}-A_{Sample}) / A_{Control}] \times 100$$

The title compounds exhibited promising antioxidant activity when compared to that of Vitamin C. These findings indicate that relatively minor modifications in the chemical structure of classical α-aminophosphonates can preserve or enhance their inhibiting properties and simultaneously, amplify their antioxidant capacity to a great extent. The antioxidant activities of all the samples were concentration dependent.

Results and Discussion

Chemistry. The syntheses of **3a-l** were carried out in various conditions in order to optimize effective reaction, it was opted for microwave irradiation technique, as this reaction under conventional method was much slower and the yields were low (Table 3, entries **3a-l**).

Synthesis of novel α-aminophosphonates (**3a-l**) under microwave irradiation without catalyst afforded in 81 - 88% yields (Table 3).

The structures of the title compounds **3a-l** were established by their spectroscopic data. All the compounds **3a-l** exhibited infrared absorption bands for O-H, N-H, P=O and P-C aliphatic in the regions 3514 - 3490, 3399 - 3378, 1222 - 1190 and 754 - 769 cm^{-1} respectively.[20]

Chemical shifts for aromatic protons of the title compounds (**3a-l**) appeared as complex multiplet at δ 6.34 - 8.44.[21] P-C-H proton signals appeared as doublet and doublet of doublet[22] at δ 5.20 - 5.85 and 5.67 - 5.82 due to its coupling with the phosphorus and neighboring N-H proton. The N-H proton exhibited a singlet and triplet[22] at δ 6.05 - 6.14 indicating its coupling with neighboring proton and phosphorus.

The ^{13}C NMR spectral data of **3a-l** showed characteristic chemical shifts for aromatic carbons. The carbon chemical shifts of P-O-CH_2 and P-CH-N appeared as a doublet at 66.9 - 69.4 ppm (d, $^{2}J_{P\text{-}O\text{-}C}$ 6.5 Hz) and singlet at 56.1 - 62.9 ppm[23] respectively. The ^{31}P NMR signals appeared as singlets at 20.8 - 26.1 ppm in all the compounds.[24] The GC mass spectra of **3a-l** agreed with the proposed structures.

Antibacterial activity. MIC was determined for the compounds **3a-l**. The test compounds **3a-l** at lower concentrations have shown no bacterial growth when compared with the control tubes.[25] Compounds **3a-l** in concentrations of 0.1 - 4.1 mg/mL in steps of 100 μg/mL were evaluated. Specifically 0.1 mL of standardized inoculum (1 - 2 × 10^{7} CFU/mL) was added to each tube. The tubes were incubated aerobically at 37 ^{o}C for 18 - 24 hr. Two control tubes were maintained for each test batch. These included antibiotic control (tube containing compounds **3a-l** and the growth medium without inoculum) and organism control (the tube containing the growth medium, physiological saline and the inoculum). The highlight is that the majority of title compounds exhibited high activity against both bacteria and two compounds (**3k** and **3l**) were more effective than the standard, Penicillin.

Antioxidant activity. In the present study, antioxidant activity was determined by the thiocyanate method, in that the amount of peroxides formed in emulsion during incubation was determined spectrophotometrically by measuring absorbance at 500 nm. High absorbance is an indication of high concentrations of formed peroxides. Oxidative stress can be derived from a variety of sources and includes events such as the production of reactive oxygen species by mitochondrial oxidative phosphorylation, ionizing radiation exposure, and metabolism of exogenous compounds.[26] In addition to these sources of oxidative stress, a decrease in the activity of antioxidant enzymes, such as superoxide dismutase, glutathione peroxidase, and catalase, may contribute to oxidative stress in some disease states.[27] The title compounds showed promising antioxidant activities and were greatly influenced by the presence of different active groups.

Conclusions

A convenient synthesis of new α-aminophosphonates by using various aromatic/heterocyclic aldehydes with dibutyl and diphenyl phosphites by the Kabachnik-Fields reaction under microwave irradiation conditions is accomplished.

The compounds **3j** and **3k** showed higher activity against Gram positive bacteria and compound **3l** also showed higher activity against Gram negative bacteria when compared to that of the standard. The fragments 2-Amino-6-methoxy benzothiazole and bromo salicylaldehyde, chloro salicylaldehyde, nitro salicylaldehyde attached to phosphorus of diphenyl phosphite were found to be the most potent fragments for antibacterial and antioxidant activity (i.e., **3j**, **3k** & **3l**).

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