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Original Article

Synthesis characterization and antimicrobial evaluation of pyrazole amino phosphonates bearing pyrazole-5-one

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ABSTRACT

Novel derivative compounds of Pyrazole amino phosphonates containing pyrazolone were synthesized by the reaction between diethyl phosphonate and imino derivatives. The microanalysis and spectral data of the synthesized compounds are in full agreement with their molecular structure. The microbial features of the synthesized compounds were studied by a known method.

Key Words: Antibacterial; Antifungal; Phosphonates; Pyrazole; pyrazolone

INTRODUCTION

Heterocycles possessing pyrazolone and its derivatives have drawn especial wide interest by medical chemists for more than hundred years ago due to their intensting drug properties[1,] pyrazolone can be considered us intermediate compound for synthesis of various cyclic compounds of high biological activity[2-4] . These compounds have wide interesting medical and industrial applications such as anticancer[5], antiischenicefcets[6], antiflammatory[7], antifungal[8], antipyretic[9], antitubercular[10], antihypertensive[11], antiviral12 and antimicrobial[13]. In industry they are used as colorizing agents[14]. In support of our study pyrazoles and derivatives function as dyestuff, catalyst, polymerizing agents, drugs, herbicides and fungicides[15], they also possess various pharmacological activities such as anti-fungal activity[16], monoamineoxidase (MAO) inhibitory activity[17,18], antiparkinson[19], anticonvulsant[20]. Pyrazole derivatives are valuable vasodialating and vasoconstructing drugs. In view of the numerous commercial applications of organophosphorus compounds , pyrazole and its derivatives, we synthesized derivatives Pyrazole amino Phosphonates bearing pyrazolone, also they screening for possible biological and pharmacological activities.

MATERIALS AND METHODS

All the chemicals used in the present investigation were purchased from Sigma-Aldrich Chemicals company, Inc. USA. And used without further purification. TLC was performed on aluminum sheet of silica gel $60F_{254}$, E-Merk, Germany using iodine as visualizing agent. Melting point was determined in open capillary tubes on Mel-Temp apparatus and is uncorrected. Column chromatography was performed on silica gel with different solvent systems as eluents to afford the pure compound. The IR Spectra were recorded as KBr pellets on Perkin-Elmer 1000 units, instruments. All H^1 and C^{13}-NMR spectra were recorded on a Bruker DRX500MHz spectrometer operating at 400MHz for H^1-NMR and 75 MHz for C^{13}-NMR. P^{31}-NMR spectra were recorded on a Varian XL-spectrometer operating at 161.89MHz. The compounds were dissolved in DMSO-d_6 and Chemical shifts were referenced to TMS (H^1 and C^{13}-NMR) and 85% H_3PO_4 (P^{31}-NMR). Mass spectral data was recorded on FAB-MS instrument at 70ev with direct inlet system. Elemental analysis was recorded on a Carlo Erba 1108 elemental Analyzer, Central Drug Research Institute, Lucknow, India.

RESULTS AND DISCUSSION

Pyrazole amino phosphonates containing pyrazolone **(7a - f)** were synthesized by the reaction between diethyl phosphonate and imino derivatives **(6a - f),** which were derived from imino acetohydrazide derivatives **(5a - f)** and ethyl 4, 4, 4 - trifluro - 3 - oxobutanoate in presence of AOCH & ethanaol .These were prepared by reaction

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between Ethyl corresponding imino acetate derivatives **(4a - f)** and hydrazine in presence of aqueous ethanol. 4 -substituted anilines derivatives **(3a - f)** and Ethyl 2 - (3 - formyl - 4 - methyl - 1H - pyrazol - 1 - yl) acetate **(2)** and this was obtained by making reaction between 4 -methyl-1H-pyrazole-3-carbaldehyde **(1)** and ethyl 2-chloro acetate (**Fifgure-1**). The structures of the synthesized compounds **7a-f** are confirmed by IR, ^{1}H, ^{13}C & ^{31}P-NMR and MS spectra data, and are further supported by correct elemental microanalysis and given in the experimental section. Synthetic pathway for the preparation of Pyrazole amino phosphonates compounds **7a-f** is depicted in the **Figure: 1**

The IR spectrum of **7a** showed bands at 1217, 1019 and 742 cm-1, indicating presences of phosphonate functional group. ^{1}H NMR spectrum of **7a** in $CDCl_3$ showed triplet and quartet at 1.29 - 4.07 ppm for diethyl groups of phosphonate. ^{13}C NMR spectrum of **7a** showed seventeen signals in agreement with the proposed structure. ^{31}P NMR spectrum of **7a** showed signal at 19.10 ppm indicates the presence of Phosphorus in the compound. This assignment is in good agreement with literature data for Pyrazole amino phosphonates. The complete NMR data are presented in the experimental section. Further work on the structures of the synthesized compounds is underway. The mass spectra displayed the correct molecular ions (M+·) in accordance with the suggested structures.

Antimicrobial activity: Pyrazole amino phosphonates containing pyrazol-5-one moiety **(7a-f)** as synthesized as depicted in the **Figure: 1** were offered average anti-bacterial activity against the *Staphylococcus aureus* NCCS 2079, *BacillusCerus* NCCS 2106, *Escherichia coli* NCCS 2065 and *Pseudomonas aeruginosa* NCCS 2200 at the concentration of 250µg/disc. Phosphonates containing 4-methyl-1H-pyrazole moiety system consisting with nitro group **7e**, chloro **7c** and tri fluoro methyl group 7f showed more activity than other substituted derivatives of the series. The decreasing Oder of antibacterial activity of **7a-f** is as follows **"7e > 7d > 7f > 7c > 7a > 7b".**

Pyrazole Phosphonates containing pyrazol-5-one moiety **(7a-f)** were offered average antifungal activity against the *Aspergillus niger* NCCS1196 and *Candida albicans* NCCS 3471 at the concentration of 250µg/disc. Phosphonates containing 4-methyl-1H-pyrazole moiety system consisting with nitro group **7e**, chloro**7d,** trifluoro methyl **7f**, showed more activity than other substituted compounds. The decreasing Oder of antifungal activity of **7a-f** is as follows **"7e > 7d > 7f > 7c > 7a > 7b".**

The antibacterial and antifungal activity of **(7a-f)** were reported in **Table: 1.**

Experimental Section

Preparation of Ethyl 2-(3-formyl-4-methyl-1H-pyrazol-1-yl) acetate (2): A mixture of 4-methyl-1H-pyrazole-3-carbaldehyde (1), anhydrous K_2CO_3, chloroethylacetate and DMF was stirred at room temperature for 8 hours .The reaction mixture was diluted with ice cold water. The separated solid was identified as compound (2) .This was collected by filtration and recrystrecrystalized from ethanol.

Preparation Ethyl 2-(3-(((4-substituted phenyl) imino) methyl)-4-methyl-1H-pyrazol-1-yl) acetates (4a-f): Equimolar Ethyl 2-(3-formyl-4-methyl-1H-pyrazol-1-yl) acetate **(2)** and aniline (3a) were dissolve in absolute alcohol, to this three drops of acetic acid was added, then the reaction mixture was heated on a steam bath for 5-6 hours at 100^{o}C.After standing for 24hours at room temperature, the product was dried and recrystalised from warm absolute alcohol, the separated solid was identified as compound **(4a)**, The other compounds **(4b-f)** were prepared by employing the above described procedure between **(2)** and 4-sbstituted anilines **(3b-f)**.

Preparation of 2-(3-(((4-substituted phenyl) imino) methyl)-4-methyl-1H-pyrazol-1-yl) acetohydrazide (5a-f): A solution of 2-(4-methyl-3-(phenylimino) methyl)-1H-pyrazol-1-yl-) acetate (4a) and hydrazine hydrate in ethanol was refluxed for 5 hours. The reaction mixture was cooled and poured in to ice cold water with stirring. The separated solid was identified as compound **(*5a*)**.This was filtered washed with water and recrystalized from ethanol. The other compounds **(5b-f)** were prepared by employing the above described procedure between Ethyl 2-(3-(((4-substituted phenyl) imino) methyl)-4-methyl-1H-pyrazol-1-yl) acetate **(4b-f)** and hydrazine hydrate in ethanol**.**

Preparation of 1-(2-(3-(((4-substituted phenyl) imino) methyl-4-methyl-1H-pyrazol-1-yl) acetyl)-3-(trifluoromethyl)-1H-pyrazol-5(4H)-ones (6a-f): In solution of 2-(4-methyl-3-((phenylimino) methyl)-1H-pyrazol-1-yl) acetohydrazide **(5a)** in ethanol, trifluroethyl acetoacetate was added and mixture was refluxed for 12hours in presence of catalytical amount of glacial acetic acid .Excess of ethanol was removed by distillation and reside obtained was filtered, washed with ethanol, dried and recrystalized from absolute alcohol to get the compound **(6a)** in good yields. The other compounds **(6b-f)** were prepared by employing the above described procedure between 2-(3-(((4-substituted phenyl) imino) methyl)-4-methyl-1H-

pyrazol-1-yl) acetohydrazide **(5b-f)** and trifluroethyl acetoacetate**.**

Preparation of Diethyl ((((4-substituted phenyl)amino) (4-methyl-1-(2-oxo-2-(5-oxo-3-(trifluoromethyl)-4,5-dihydro - 1H-pyrazol - 1 - yl) ethyl) - 1h - pyrazol-3-yl)methyl)phosphonates(7a-f): A mixture of 1-(2-(4-methyl-3-((phenylimino) methyl)-1H-pyrazol-1-yl-) acetyl) -3-(trifluro methyl)-1H-pyrazol-5(4H)-one **(*6a*)** and diethyl phosphonate in anhydrous toluene (15 ml) was added drop wise. Sterring was continued at room temperature for another 0.5hrs, after which the mixture was heated under reflux for 4-6 hrs. The reaction was monitored by TLC on silica gel using petroleum ether, ethyl acetate (1:2V/V) as mobile phase.After completion o f the reaction ,the solvent was removed by Rota evaporator and the resulting residue was purified by Colum chromatography on silica gel (100-200 mesh) and ethyl acetate –hexane ,(3:7 ratio)as eluent to afford pure compound **(*7a*)**. The other compounds **(7b-f)** were prepared by employing the above described procedure between **6b-f** and diethyl phosphonate.

Typical spectral data for the compounds 7a-f:

Diethyl((4-methyl-1-(2-oxo-2-(5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-1-yl)ethyl-1H-pyrazol-3-yl)(phenylamino) methyl)phosphonate (7a): Yeild 65%; M.P : 161-163 ^{o}C; IR(KBr): 3052(Ar-H), 2940 & 2895 (Aliphatic -CH), 1690 (C=O), 1375-1487 (Pyrazole), 1217 (P=O), 1100 (C-F), 1019 (P-O-$C_{(aliphatic)}$), 742 P-$C_{(Aliphatic\}}$; ^{1}H-NMR (400MHZ, DMSO-d6): δ 1.29(t,6H, 2 x CH_3 of diethyl phosphonate,J=0.86), 2.04 (s,3H,-CH_3 group attached to pyrazole ring), 2.2(s,2H,-CH_2- of 3-(tri fluoromethyl)-H-pyrazol-5(4H)-One moiety),3.9(s,1H, -CH-flanked between pyrazole ring and diethyl phosphonate moiety), 4.0(s,1H,-CH-NH-phenyl ring),4.07(q,4H, 2 x CH_2 of diethyl phosphonate), 5.60(s,2H,-CH_2- flanked between pyrazole ring and carbonyl group), 6.77-7.23 (m,5H,-CH- of phenyl ring),7.40 (s,1H,-CH- of pyrazole ring); ^{13}C-NMR(75MHZ, DMSO-d6): δ 127.5, 115.6, 149.1, 8.1, 61.9, 170.7, 155.6, 22.0, 163.0, 126.2, 66.8, 147.6, 113.5, 129.5, 120.8, 62.2, 16.3. corresponding to C_1 , C_2 , C_3 , C_4 , C_5 , C_6 , C_7 , C_8 , C_9 , C_{10} , C_{11} , C_{12} , C_{13}& C_{17}, C_{14}& C_{16}, C_{15} , C_{18} & C_{20}, C_{19} & C_{21} ; ^{31}PNMR(161.89MHZ): δ 19.10; Anal.calcd(%)for $C_{21}H_{25}F_3N_5O_5P$: C 48.94% ,H 4.89% , F 11.06%, N 13.59%, P 6.01% .Found: C 48.14%, H 4.39% , F 10.26%, N 12.99% , P 5.31% .

Diethyl(((4-methoxyphenyl)amino)(4-methyl-1-(2-oxo-2-(5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-1-yl)ethyl-1H-pyrazol-3-yl) methyl) phosphonate (7b): Yeild 70%; M.P : 129-131^{o}C; IR(KBr): 3045 (Ar-H), 2940 & 2895 (Aliphatic -CH), 1685 (C=O), 1375-1487 (Pyrazole), 1225 (P=O), 1105 (C-F), 1023 (P-O-$C_{(aliphatic)}$), 747 P-$C_{(Aliphatic\}}$; ^{1}H-NMR (400MHZ, DMSO-d6): δ 1.29(t,6H,-CH_3 of diethyl phosphonate,J=0.86), 2.04 (s,3H,-CH_3 group attached to pyrazole ring), 2.2(s,2H,-CH_2- of 3-(tri fluoromethyl)-H-pyrazol-5(4H)-One moiety), 3.83(s,3H,-OCH_3 group attached to phenyl ring),3.9(s,1H, -CH-flanked between pyrazole ring and diethyl phosphonate moiety), 4.0(s,1H,-CH-NH-phenyl ring), 4.07(q,4H, 2 x CH_2-of diethyl phosphonate),5.60(s,2H,-CH_2- flanked between pyrazole ring and carbonyl group), 6.80-710 (m,4H,-CH- of phenyl ring),680 (s,1H,-CH- of pyrazole ring); ^{13}C-NMR(75MHZ, DMSO-d6): δ 127.5, 115.6, 149.1, 8.1, 61.9, 170.7, 155.6, 22.0, 163.0, 126.2, 66.8, 139.9, 115.8, 115.1, 151.7, 55.8, 62.2, 16.3. corresponding to C_1 , C_2 , C_3 , C_4 , C_5 , C_6 , C_7 , C_8 , C_9 , C_{10} , C_{11} , C_{12} , C_{13}& C_{17}, C_{14}& C_{16}, $C_{15,}$ C_{18}, C_{19} & C_{21}, C_{20} & C_{22} ; ^{31}PNMR(161.89MHZ): δ; Anal.calcd(%)for $C_{22}H_{27}F_3N_5O_6P$: C 48.44% ,H 4.99% , F 10.45%, N 12.84%, P 5.68% .Found: C 47.64%, H 4.49% , F 9.65%, N 12.24% , P 4.98% .

Diethyl((((4-flurophenyl)amino)(4-methyl-1-(2-oxo-2-(5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-1-yl)ethyl-1H-pyrazol-3-yl)methyl) phosphonate (7c): Yeild 70%; M.P : 177-179 ^{o}C; IR(KBr): 3040 (Ar-H), 2940 & 2895 (Aliphatic -CH), 1680 (C=O), 1375-1487 (Pyrazole), 1230 (P=O), 1108 (C-F), 1025 (P-O-$C_{(aliphatic)}$), 740 P-$C_{(Aliphatic\}}$; ^{1}H-NMR (400MHZ, DMSO-d6): δ 1.29(t,6H,-CH_3 of diethyl phosphite,J=0.86), 2.04 (s,3H,-CH_3 group attached to pyrazole ring), 2.2(s,2H,-CH_2- of 3-(tri fluoromethyl)-H-pyrazol-5(4H)-One moiety), 3.9(s,1H, -CH-flanked between pyrazole ring and diethyl phosphonate moiety),4.0(s,1H,-CH-NH-phenyl ring), 4.07(q,4H, 2 x CH_2-of diethyl phosphonate), 5.60(s,2H,-CH_2-flanked between pyrazole ring and carbonyl group), 7.02-7.05 (m, 4H,-CH- of phenyl ring),7.40 (s,1H,-CH- of pyrazole ring); ^{13}C-NMR(75MHZ, DMSO-d6): δ 127.5, 115.6, 149.1, 8.1, 61.9, 170.7, 155.6, 22.0, 163.0, 126.2, 66.8, 143.2, 118.9, 116.3, 155.7, 62.2, 16.3. corresponding to C_1 , C_2 , C_3 , C_4 , C_5 , C_6 , C_7 , C_8 , C_9 , C_{10} , C_{11} , C_{12} , C_{13}& C_{17}, C_{14}& C_{16}, C_{15} , C_{18} & C_{20}, C_{19} & C_{21} ; ^{31}PNMR(161.89MHZ): δ 21.80; Anal. calcd(%)for $C_{21}H_{24}F_4N_5O_5P$: C 47.29% ,H 4.54% , F 14.25, N 13.13%, P 5.81% .Found: C 46.49%, H 4.04% , F 13.45%, N 12.53% , P 5.11% .

Diethyl(((4-chlorophenyl)amino)(4-methyl-1-(2-oxo-2-(5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-1-yl)ethyl-1H-pyrazol-3-yl)methyl) phosphonate (7d): Yeild 65%; M.P : 141-143 ^{o}C; IR(KBr): 3030 (Ar-H), 2940 & 2895 (Aliphatic -

CH), 1687 (C=O), 1375-1487 (Pyrazole), 1225 (P=O), 1110 (C-F), 1017 (P-O-$C_{(aliphatic)}$), 745 P-$C_{(Aliphatic)}$, 725(-Cl) ; ^{1}H-NMR (400MHZ, DMSO-d6): δ 1.29(t,6H, 2 x CH_3 of diethyl phosphite,J=0.86), 2.04 (s,3H,-CH_3 group attached to pyrazole ring), 2.2(s,2H,-CH_2- of 3-(tri fluoromethyl)-H-pyrazol-5(4H)-One moiety), 3.9(s,1H, ,-CH-diethyl phosphite moiety), 4.0(s,1H,-CH-NH-phenyl ring), 4.07(q,4H,2 x CH_2 of diethyl phosphonate), 5.60(s,2H,-CH_2- flanked between pyrazole ring and carbonyl group), 7.10-7.27 (m, 4H,-CH- of phenyl ring),7.40 (s,1H,-CH- of pyrazole ring); ^{13}C-NMR(75MHZ, DMSO-d6): δ 127.5, 115.6, 149.1, 8.1, 61.9, 170.7, 155.6, 22.0, 163.0, 126.2, 66.8, 145.7, 114.9, 129.6, 126.1, 62.2, 16.3. corresponding to C_1 , C_2 , C_3 , C_4 , C_5 , C_6 , C_7 , C_8 , C_9 , C_{10} , C_{11} , C_{12} , C_{13}& C_{17}, C_{14}& C_{16}, C_{15} , C_{18} & C_{20}, C_{19} & C_{21} ; ^{31}PNMR(161.89MHZ): δ; Anal.calcd(%)for $C_{21}H_{24}ClF_3N_5O_5P$: C 45.87% ,H 4.40% , Cl 6.45%, F 10.37, N 12.74%, P 5.63% .Found: C 45.07%, H 3.90% , Cl 5.75%, F 9.57%, N 12.14% , P 4.93% .

Diethyl((4-methyl-1-(2-oxo-2-(5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-1-yl)ethyl-1H-pyrazol-3-yl)(4-nitrophenyl amino) methyl)phosphonate (7e): Yeild 68 %; M.P : 161-163 ^{o}C; IR(KBr): 3043 (Ar-H), 2940 & 2895 (Aliphatic -CH), 1690 (C=O), 1375-1487 (Pyrazole), 1235 (P=O), 1355 & 1330 (-NO_2), 1103 (C-F), 1022 (P-O-$C_{(aliphatic)}$), 746 P-$C_{(Aliphatic)}$; ^{1}H-NMR (400MHZ, DMSO-d6): δ 1.29(t,6H, 2 x CH_3 of diethyl phosphite,J=0.86), 2.04 (s,3H,-CH_3 group attached to pyrazole ring), 2.2(s,2H,-CH_2- of 3-(tri fluoromethyl)-H-pyrazol-5(4H)-One moiety), 3.9(s,1H, -CH-flanked between pyrazole ring and diethyl phosphonate moiety),4.0(s,1H,-CH-NH-phenylring), 4.07(q,4H, 2 x $CH_2$of diethyl phosphonate), 5.60(s,2H,-CH_2- flanked between pyrazole ring and carbonyl group), 7.30-7.70 (m, 4H,-CH- of phenyl ring),7.40 (s,1H,-CH- of pyrazole ring); ^{13}C-NMR(75MHZ, DMSO-d6): δ 127.5, 115.6, 149.1, 8.1, 61.9, 170.7, 155.6, 22.0, 163.0, 126.2, 66.8, 153.7, 114.4, 127.5, 136.3, 62.2, 16.3. corresponding to C_1 , C_2 , C_3 , C_4 , C_5 , C_6 , C_7 , C_8 , C_9 , C_{10} , C_{11} , C_{12} , C_{13}& C_{17}, C_{14}& C_{16}, C_{15} , C_{18} & C_{20}, C_{19} & C_{21} ; ^{31}PNMR(161.89MHZ): δ 23.5; Anal.calcd(%)for $C_{21}H_{24}F_3N_6O_7P$: C 45.01% , H 4.32% , F 10.17, N 15.00%, P 5.53% .Found: C 44.21%, H 3.82% , F 9.37%, N 14.40% , P 4.83% .

Diethyl((4-methyl-1-(2-oxo-2-(5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-1-yl)ethyl-1H-pyrazol-3-yl)(4-tri fluoromethyl) phenylamino) methyl)phosphonate (7f): Yeild 75 %; M.P : 183-185 ^{o}C; IR(KBr): 3035 (Ar-H), 2940 & 2895 (Aliphatic -CH), 1687 (C=O), 1375-1487 (Pyrazole), 1240 (P=O), 1106 (C-F), 1030 (P-O-$C_{(aliphatic)}$), 750P-$C_{(Aliphatic)}$; ^{1}H-NMR (400MHZ, DMSO-d6): δ 1.29(t,6H, 2 x CH_3 of diethyl phosphite,J=0.86), 2.04 (s,3H,-CH_3 group attached to pyrazole ring), 2.2(s,2H,-CH_2- of 3-(tri fluoromethyl)-H-pyrazol-5(4H)-One moiety), 3.9(s,1H, -CH-flanked between pyrazole ring and diethyl phosphonate moiety),4.0(s,1H,-CH-NH-phenylring),4.07(q,4H, 2 x CH_2 of diethylphosphonate), 5.60(s,2H,-CH_2- flanked between pyrazole ring and carbonyl group), 7.30-7.50 (m, 4H,-CH- of phenyl ring),7.40 (s,1H,-CH- of pyrazole ring); ^{13}C-NMR(75MHZ, DMSO-d6): δ 127.5, 115.6, 149.1, 8.1, 61.9, 170.7, 155.6, 22.0, 163.0, 126.2, 66.8, 150.9, 113.8, 125.9, 124.9, 124.1, 62.2, 16.3. corresponding to C_1 , C_2 , C_3 , C_4 , C_5 , C_6 , C_7 , C_8 , C_9 , C_{10} , C_{11} , C_{12} , C_{13}& C_{17}, C_{14}& C_{16}, C_{15}, C_{18}, C_{19} & C_{21}, C_{20} & C_{22} ; ^{31}PNMR(161.89MHZ): δ 20.5; Anal.calcd(%)for $C_{22}H_{24}F_6N_5O_5P$: C 45.29% , H 4.15% , F 19.25%, N 12.00%, P 5.31% .Found: C 44.49%, H 3.65% , F 18.45%, N 11.40% , P 4.61% .

Conclusion

The newly synthesized compounds of Diethyl (((4-substituted phenyl)amino) (4-methyl-1-(2-oxo-2-(5-oxo-3-(trifluoromethyl)-4,5-dihydro - 1H-pyrazol - 1 - yl) ethyl) - 1h - pyrazol-3-yl)methyl)phosphonates(7a-f):were found to be active in the study of anti-bacterial and anti-fungal activity. It can be concluded that this class of compounds certainly holds great promise towards the pursuit to discover novel classes of antimicrobial agents.

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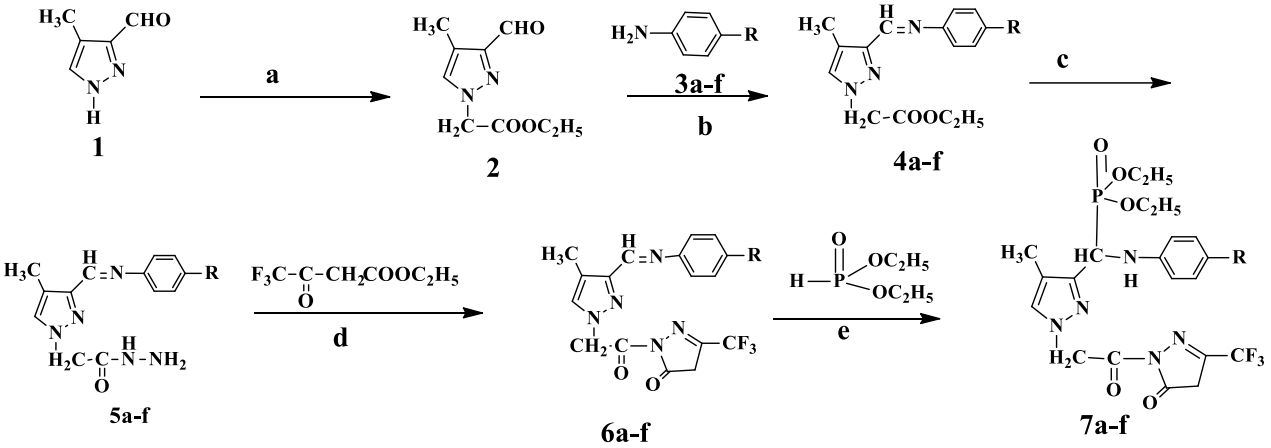
Table: 1: Antimicrobial activity of Pyrazole amino phosphonates containing pyrazolone (7a - f)

COMPOUND	Zone of inhibition(mm)					
	Staphylo cocus aureus NCCS 2079	**Bacillus Cerus NCCS 2106**	**Escherichia Coli NCCS 2065**	**Pseudomonas aeruginosa NCCS 2200**	***Aspergillus niger NCCS 1196***	***Canadida albicans NCCS 3471***
7a	10	12	09	08	08	10
7b	08	10	07	06	06	09
7c	13	15	11	10	10	12
7d	15	17	14	13	14	16
7e	17	19	18	17	16	18
7f	14	16	13	12	12	14
Amoxicillin (std. Antibacterial)	21	27	24	22	-	-
Ketoconazole (std. Anti-fungal)	-	-	-	-	22	25



Reagents and conditions: (a) Anhydrous K_2CO_3, chloro ethyl acetate, DMF, RT, rx^n mixture stirred for 8 hrs ; **(b)** Absolute alcohol, acetic acid, 100^{o}C, heated on steam bath, RT, rx^n mixture kept for 24 hrs; **(c)** H_2N-NH_2,H_2O, C_2H_5OH, refluxed for 5 hrs; **(d)** C_2H_5OH, ACOH, refluxed for 12 hrs; (e) Anhydrous toluene, RT, stirred for 0.5 hr, rx^n mixture refluxed for 6 hrs.

Compound 3/4/5/6/7	a	b	c	d	e	f
R	H	OCH_3	F	Cl	NO_2	CF_3

Figure 1. Synthetic pathway for the preparation of Pyrazole amino phosphonates compounds **7a-f**

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