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SYNTHESIS OF ARYLAZOPYRAZOLES AND THEIR ANTIMICROBIAL EVALUATION

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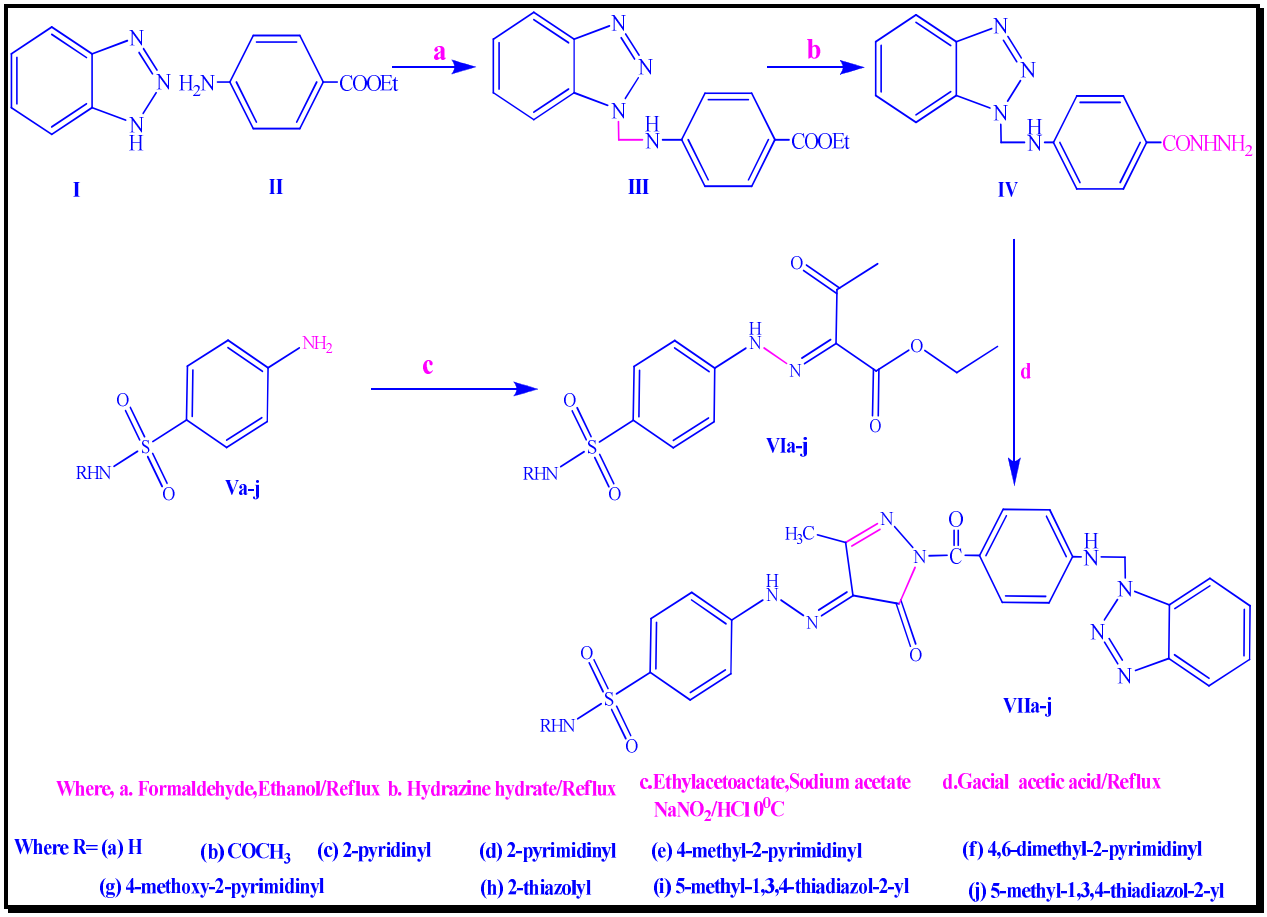
Abstract: Mannich reaction of benzotriazole **(I)**, ethyl-p-amino benzoate **(II)** and formaldehyde afforded 4-(1H)-benzotriazoyl methyl amino benzoate **(III)**, which react with hydrazine hydrate results in the 4-(1H)-benzotriazoyl methyl amino benzoyl hydrazide **(IV)**. This compound on condensation with pre-prepared different ethyl-3-oxo-2-(2-(3-(N-alkyl sulfamoyl)phenyl) hydrazono) butanoates**(VIa-j)**,furnished3-(2-(1-(4-((1H-benzo[d][1,2,3]triazol-1-yl) methyl amino) benzoyl) -3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene) hydrazinyl)-N-alkylbenzene sulfonamides**(VIIa-j)**. All the compounds **(VIIa-j)** were characterized by spectral studies. The compounds showed significant antimicrobial activity against various bacteria and fungi.

Keywords: Synthesis, heterocyclic substituted benzoyl hydrazide derivatives, oxobutanoates derivatives, pyrazolone derivatives, antimicrobial activity.

INTRODUCTION

Many pyrazolines and substituted pyrazolines derivatives are well known for their biological and pharmacological activities[i-v], which exhibit an anti-inflammatory[vi],fungicidal[vii,viii], bactericidal, antipyretic[ix,x],antidepressant[xi-xiv], anticonvulsant[xiii,xiv] and protein kinase inhibitors[xv,xvi]. These pyrazolone derivatives were investigated as thermal stabilizers for rigid PVC[xvii, xviii]. On the other hand, many azopyrazolone dyes have been utilized as chromogenic reagents for colourimetric determinations[xix,xx] and as indicator for complexometric titrations[xxi]. Also, there are some arylazopyrazolone dyes having potent antimicrobial activities[xxii]. Arylazopyrazoles are generally prepared by combination of aryl-azo-ethyl actoacetate derivatives and hydrazine derivatives[xxiii-xxvii]. The benzotriazole is found as an important heterocyclic compound. They reveal valuable pharmacological properties and clinical applications[xxviii-xxxi]. Their prime application is as corrosion inhibitors for copper or copper alloys[xxxii,xxxiii]. The area in which the merged molecule like aryl azo pyrazole-benzotriazole has not been developed in spite of good biological properties of both these compounds. Hence the present paper comprises the synthesis and characterization of aryl azo pyrazole-benzotriazole derivatives shown in Scheme 1.

REACTION SCHEME



MATERIALS AND METHODS

Measurements

All chemicals used were of laboratory grade. Benzocain, Benzotriazole and various sulfonamide derivatives **Va-j** were prepared by reported method [xxxiv]. Melting points were determined in open capillary tubes and were uncorrected. IR spectra were recorded in KBr pellets on a Nicolet 760D spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded in DMSO with TMS as internal standard on a Bruker spectrometer at 400 MHz and 100 MHz, respectively. LC-MS of selected samples taken on LC-MSD-Trap-SL_01046 instrument.

PREPARATION OF 4 - (1H) - BENZOTRIAZOLYL METHYL AMINO BENZOATE III

A mixture of 1H-Benzotriazole **I** (0.02mole), formaldehyde (0.02mole) and ethyl-4-amino benzoate **II** (0.02mole) in ethanol (50ml) was heated under reflux for 4hrs. Subsequequently, ethanol was distilled off and the pasty mass obtained, which was triturated with petroleum ether (40-60˚C). The solid 4-(1H)-benzotriazolyl methyl amino benzoate **III**, which was isolated and dried. Yield 68% , m.p.146-147˚C. IR [ν,cm^{-1},KBr]: 3086-3034(C-H aromatic), 2965(CH_2), 2910-2890,1456 (C-H),1725(C=O of ester),1255-1197(C-N). ^{1}HNMR [400 MHz, δ, ppm, DMSO- d_6] :8.21-6.56 (m, 8H,Ar-H),5.7 (s, 2H, CH_2),4.32(q,2H,-O-CH_2),3.2(s,1H,NH), 1.32 (t,3H,-CH_3).^{13}C NMR [100 MHz, δ, *ppm*, DMSO]: 170.4(CO),149.1-114.3(Ar-C), 75.7 (CH_2), 62.1(CH_2),13.9(CH_3). LC-MS: *m/z*

305(M^+).Anal. Calcd for $C_{16}H_{16}N_4O_2$ (296)C, 64.85; H, 5.44; N, 18.91.Found; C, 64.8; H, 5.4; N, 18.9.

PREPARATION OF 4-(1H) - BENZOTRIAZOLYL METHYL AMINO BENZOYL HYDRAZIDE IV

4-(1H)-benzotriazolyl methyl amino benzoate **III** (0.05mole) was refluxed with hydrazine hydrate (0.05mole) in absolute ethanol for 8 to10 hours. It was cooled and kept overnight. The solid so obtained was filtered and recrystallized from ethanol. Yield 63%, m.p.77-78˚C. IR [ν,cm^{-1},KBr]:3450(NH_2),3086-3034(C-H aromatic),2965(CH_2), 1725 (C=O of ester), 1630 (NH_2), l255-1197 (C-N). ^{1}H NMR [400MHz, δ ,ppm, DMSO- d_6] : 9.66(s,1H,CONH),8.21-6.56 (m, 8H,Ar-H), 5.7(s,2H,CH_2), 3.95(s,2H,NH_2), 3.2(s,1H, NH). ^{13}C NMR [100 MHz, δ, *ppm*, DMSO]: 170.4 (CO), 149.1-114.3 (Ar-C),75.7 (CH_2). LC-MS: *m/z* 291 (M^+). Anal. Calcd for $C_{14}H_{14}N_6O$ (282): C, 59.56; H, 5.00; N, 29.77.Found : C, 59.5; H, 4.9; N, 29.7.

PREPARATION OF ETHYL-3-OXO-2-(2-(3-(N-ALKYLSULFAMOYL) PHENYL) HYDRAZONO)BUTANOATES (VIa-j)

To a various sulphonamide derivatives **Va-j** (0.01 mole) was dissolved in a mixture of HCl (8 ml) and water (6 ml) and cooled to 0°C in ice bath. To it a cold aqueous solution of sodium nitrite (0.03 mole) was added. The diazonium salt solution was filtered into a cooled solution of ethyl aceto acetate (0.01 mole) and sodium acetate (0.12 mole) in ethanol (50 ml). The resulting solid was washed with water and recrystallized from ethanol/methanol to give pure desired product **VIa-j**.

VIa: ethyl 3-oxo-2-(2-(4-sulfamoylphenyl)hydrazono)butanoate.

Yield 84%; m.p. 166-168°C. IR[ν,cm^{-1},KBr]:3369(N-H),3086-3034(C-H aromatic), 920 (CH_3,CH_2), 1765-1725(C=O),1695-1540(C=N),1465(CH_3,CH_2),1325(SO_2),1290(C-N), 1148 (C-O), 905(S-N), 706-585(C-S). ^{1}HNMR [400MHz, δ, ppm ,DMSO-d_6]: 11.62 (s,1H,NH),7.42(s,2H,NH),7.67-6.90 (m,4H,ArH),4.29(q,2H,$COCH_2$), 2.35(s,3H, $COCH_3$), 1.34(t,3H,CH_3). ^{13}C NMR [100MHz, δ, *ppm*, DMSO]:195.4,165.4(CO),143.6-114.8 (Ar-C), 26.9, 14.2 (CH_3), 61.4 (CH_2). LC-MS:*m/z* 321 (M^+). Anal. Calcd for $C_{12}H_{15}N_3O_5S$ (313): C, 46.00; H, 4.83; N, 13.41; S, 10.23.Found; C, 45.9; H, 4.8; N, 13.4; S, 10.2.

VIb: ethyl 2-(2-(4-(N-acetylsulfamoyl)phenyl)hydrazono)-3-oxobutanoate.

Yield 81%;m.p.156-158°C.IR[ν,cm^{-1},KBr]: 3369(N-H),3086-3034(C-H aromatic), 2920 (CH_3,CH_2), 1765-1725(C=O),1695-1540(C=N),1465(CH_3,CH_2),1325(SO_2),1290(C-N), 1148(C-O), 905(S-N), 706-585(C-S).^{1}H NMR[400MHz, δ,ppm, DMSO-d_6]:11.62 (s, 1H, NH),7.67-6.90 (m,4H, ArH), 7.45 (s,1H,NH),4.29(q,2H,$COCH_2$),2.37(s,6H, $COCH_3$), 1.34 (t,3H,CH_3).^{13}C NMR [100 MHz, δ,*ppm*, DMSO]: 195.4, 192.4,165.4(CO), 143.6-114.8 (Ar-C),61.4(CH_2), 26.9, 22.3, 14.2(CH_3). LC-MS: *m/z* 367(M^+). Anal. Calcd for $C_{14}H_{17}N_3O_6S$ (355): C,47.32; H,4.82; N,11.82; S,9.02.Found C,47.3; H, 4.8; N,11.8; S, 8.9.

VIc: ethyl 3-oxo-2-(2-(4-(N-pyridin-2-ylsulfamoyl)phenyl)hydrazono)butanoate.

Yield 76%; m.p.173-175°C. IR [ν,cm^{-1},KBr]:3369(N-H),3086-3034(C-Haromatic), 2920 (CH_3,CH_2), 1765-1725(C=O),1695-1540(C=N),1465(CH_3,CH_2),1290(C-N),1148(C-O), 1325 (SO_2), 905(S-N), 706-585(C-S).^{1}H NMR [400MHz, δ ,ppm,DMSO- d_6]:11.62 (s,1H, NH),7.72-6.90(m,8H, ArH), 7.54(s,1H, NH),4.29(q,2H,$COCH_2$),2.35(s,3H,$COCH_3$), 1.34(t, 3H,CH_3).^{13}C NMR [100MHz,δ, *ppm*, DMSO]:195.4,165.4(CO),154.6-114.8(Ar-C),64.8(CH_2),26.9,14.2(CH_3).LC-MS:*m/z* 402 (M^+). Anal. Calcd for $C_{17}H_{18}N_4O_5S$(390): C, 52.30; H, 4.65; N, 14.35 ;S, 8.21. Found; C, 52.2; H, 4.6; N, 14.3; S, 8.1.

VId: ethyl 3-oxo-2-(2-(4-(N-pyrimidin-2-ylsulfamoyl)phenyl)hydrazono)butanoate.
Yield 78%;m.p.148-149°C. IR [ν,cm^{-1},KBr]: 3369(N-H),3086-3034(C-Haromatic),2920 (CH_3,CH_2), 1765-1725(C=O),1695-1540(C=N),1465(CH_3,CH_2),1325(SO_2),1290(C-N), 1148(C-O), 905(S-N), 706- 585 (C-S). ^{1}H NMR [400MHz,δ,ppm, DMSO- d_6]:11.62(s, 1H, NH),7.73-6.90 (m,7H,ArH), 7.42 (s,1H,NH),4.29(q,2H,$COCH_2$),2.35(s,3H,$COCH_3$),1.34 (t, 3H, CH_3). ^{13}C NMR [100 MHz, δ, *ppm*, DMSO] : 195.4, 165.4 (CO),170.6-114.8(Ar-C), 61.4 (CH_2), 26.9,14.2 (CH_3).LC-MS:*m/z* 406 (M^+). Anal. Calcd for $C_{16}H_{17}N_5O_5S$ (391): C, 49.10; H, 4.38; N, 17.89; S, 8.19. Found; C, 49.0; H, 4.3; N, 17.8; S, 8.1.

VIe:ethyl2-(2-(4-(N-(4-methylpyrimidin-2-yl)sulfamoyl)phenyl)hydrazono)-3-oxo butanoate.
Yield 77%; m.p.143-145°C. IR [ν,cm^{-1},KBr]:3369(N-H),3086-3034(C-Haromatic),2920 (CH_3, CH_2), 1765-1725(C=O),1695-1540 (C=N), 1465(CH_3,CH_2),1325(SO_2),1290(C-N), 1148(C-O),905(S-N), 706-585(C-S).^{1}H NMR [400MHz, δ ,ppm, DMSO- d_6] : 11.62(s,1H, NH),8.30-6.90(m, 6H, ArH), 7.44(s,1H,NH),4.29(q,2H,$COCH_2$),2.35(s,3H,$COCH_3$),2.34(s,3H,CH_3),1.34(t,3H,CH_3).^{13}CNMR [100 MHz, δ, *ppm*,DMSO]:195.4,165.4(CO),170.6-114.8 (Ar-C),61.4 (CH_2),26.9,24.5,14.2 (CH_3). LC-MS:*m/z* 413(M^+).Anal.Calcd for $C_{17}H_{19}N_5O_5S$ (405): C, 50.36; H, 4.72; N, 17.27; S, 7.91. Found; C, 50.3; H, 4.7; N, 17.2; S, 7.9.

VIf: ethyl 2-(2-(4-(N-(4,6-dimethyl pyrimidin-2-yl)sulfamoyl) phenyl) hydrazono)-3-oxo butanoate.
Yield 76%;m.p.145-147°C.IR[ν,cm^{-1},KBr]: 3369(N-H),3086-3034(C-Haromatic),2920 (CH_3,CH_2), 1765-1725(C=O),1695-1540(C=N),1465(CH_3,CH_2),1325(SO_2),1290(C-N), 1148 (C-O), 905 (S-N), 706-585(C-S).^{1}H NMR [400MHz,δ,ppm,DMSO-d_6]: 11.62(s,1H, NH),8.30-6.90(m,5H, ArH), 7.44 (s,1H,NH),4.29(q,2H,$COCH_2$),2.35(s,3H,$COCH_3$),2.34(s, 6H,CH_3),1.34(t,3H,CH_3).^{13}C NMR [100 MHz, δ, *ppm*, DMSO] : 195.4,165.4 (CO),170.6-114.8 (Ar-C), 61.4 (CH_2), 26.9, 24.7, 24.5, 14.2 (CH_3). LC-MS:*m/z* 427(M^+). Anal. Calcd for $C_{18}H_{21}N_5O_5S$ (419): C, 51.54; H, 5.05; N, 16.70;S, 7.64. Found; C, 51.5; H,4.9; N, 16.6;S, 7.6.

VIg: ethyl 2-(2-(4-(N-(4-methoxy pyrimidin-2-yl) sulfamoyl) phenyl) hydrazono-3-oxo butanoate.
Yield 76%; m.p.147-149°C. IR [ν,cm^{-1},KBr]: 3369(N-H), 3086-3034(C-H aromatic),2920 (CH_3, CH_2),1765-1725 (C=O), 1695-1540 (C=N),1465(CH_3,CH_2),1380(C-O),1325(SO_2), 1290 (C-N), 1148 (C-O),905 (S-N), 706-585(C-S).^{1}H NMR [400MHz, δ ,ppm, DMSO- d_6] : 11.62 (s,1H,NH),7.67-6.90 (m,6H,ArH),7.42(s,1H,CH_3),4.29(q,2H,$COCH_2$),3.92(s,3H,CH_3),2.35(s,3H,$COCH_3$),1.34(t, 3H,CH_3). ^{13}C NMR[100MHz,δ,*ppm*,DMSO] :195.4,165.4 (CO), 167.6-114.8 (Ar-C), 61.4(CH_2),50.8,26.9, 14.2 (CH_3). LC-MS:*m/z* 436 (M^+). Anal. Calcd for $C_{17}H_{19}N_5O_6S$ (422): C, 48.45; H, 4.54; N, 16.62; S, 7.61. Found; C, 48.4; H, 4.5; N, 16.6; S, 7.6.

VIh: ethyl 3-oxo-2-(2-(4-(N-thiazol-2-ylsulfamoyl)phenyl)hydrazono)butanoate.
Yield 78%; m.p.141-143°C. IR [ν,cm^{-1},KBr]: 3369(N-H),3086-3034(C-Haromatic),2920 (CH_3, CH_2), 1765-1725 (C=O), 1695-1540 (C=N), 1465(CH_3,CH_2),1325(SO_2),1290(C-N), 905 (S-N),706-585(C-S).^{1}H NMR [400MHz,δ,ppm, DMSO- d_6]:11.62(s,1H,NH), 7.50-6.90(m,6H,ArH),7.42 (s, 1H, NH),4.29(q,2H,$COCH_2$),2.35(s,3H,$COCH_3$),1.34(t,3H, CH_3). ^{13}C NMR [100 MHz, δ, *ppm*, DMSO] : 195.4,165.4(CO), 171.8-114.8(Ar-C), 61.1 (CH_2), 26.9, 14.2(CH_3).LC-MS: *m/z* 408 (M^+). Anal. Calcd for $C_{15}H_{16}N_4O_5S_2$ (396): C, 45.44; H, 4.07; N, 14.13; S, 16.18. Found; C, 45.4; H, 3.9; N, 14.1; S, 16.1.

VIi:ethyl-2-(2-(4-(N-(5-methyl-1,3,4-thiadiazol-2-yl)sulfamoyl)phenyl)hydrazono)-3-oxo butanoate.

Yield 81%; m.p.142-144°C. IR [ν,cm^{-1},KBr]: 3369(N-H),3086-3034(C-Haromatic),2920 (CH_3, CH_2),1765-1725(C=O),1325(SO_2),1695-1540 (C=N),1465 (CH_3,CH_2), 1290 (C-N), 706-585(C-S). ^{1}H NMR[400 MHz, δ, ppm, DMSO-d_6]:11.62(s,1H,NH),7.50-6.90(m,4H, ArH),7.42(s,1H,NH),4.29(q, 2H,$COCH_2$), 2.66(s,3H,CH_3), 2.35 (s,3H,$COCH_3$),1.34(t,3H, CH_3). ^{13}C NMR [100 MHz, δ, ppm, DMSO]: 195.4, 165.4 (CO),174.8-114.8(Ar-C), 61.1 (CH_2),26.9,19.3,14.2(CH_3).LC- MS: *m/z* 423 (M^+). Anal. Calcd for $C_{15}H_{17}N_5O_5S_2$ (411): C, 43.79; H, 4.16; N, 17.02; S, 15.59.Found; C, 43.7; H, 4.1; N, 16.9; S, 15.5.

VIj: ethyl 2-(2-(4-(N-(3,4-dimethylisoxazol-5-yl)sulfamoyl)phenyl)hydrazono)-3-oxobutanoate.

Yield 83%; m.p.139-141°C. IR [ν,cm^{-1},KBr]: 3369(N-H),3086-3034(C-Haromatic),2920 (CH_3,CH_2), 1765-1725(C=O),1325(SO_2), 1695-1540(C=N), 1465(CH_3,CH_2), 1290(C-N), 1040(O-N),706-585(C-S).^{1}HNMR [400M Hz, δ ,ppm, DMSO-d_6]:11.62 (s,1H,NH),7.50-6.90 (m,4H,ArH),7.42(s,1H, NH), 4.29(q,2H,$COCH_2$),2.35(s,3H,$COCH_3$), 2.25(s,6H,CH_3),1.34(t,3H,CH_3).^{13}C NMR [100 MHz, δ, *ppm*, DMSO]: 195.4,165.4(CO), 162.8-114.8(Ar-C),61.1(CH_2),26.9 14.2,11.8, 9.5 (CH_3).LC-MS:*m/z* 416 (M^+). Anal. Calcd for $C_{17}H_{20}N_4O_6S$ (408) : C, 49.99; H, 4.94; N, 13.72; S,7.85.Found; C, 49.9; H, 4.9; N, 13.7; S, 7.8.

PREPARATION OF 4-(2-(1-(4-((1H-BENZO[D][1,2,3]TRIAZOL-1-YL)METHYL AMINO) BENZOYL)-3-METHYL-5-OXO-1H-PYRAZOL-4(5H)-YLIDENE)HYDRAZINYL)-N-SUBSTITUTED BENZENE SULFONAMIDE VIIa-j.

The compound ethyl 3-oxo-2-(2-(4- substituted sulfamoyl phenyl) hydrazono) butanoate **VIa-j** (0.002mole) dissolved in glacial acetic acid (20ml), a solution of 4-((1H-benzo[d][1,2,3]triazol-1-yl) methylamino)benzo hydrazide **IV** (0.002 mole) in 25ml of glacial acetic acid was added and the mixture was refluxed 10-12 hrs. It was then cooled and allowed to stand overnight. The resulting solid was filtered off dried and crystallized from methanol.

VII*a: 4-(2-(1-(4-((1H-benzo[d][1,2,3]triazol-1-yl)methylamino)benzoyl)-3-methyl-5-oxo-1H-pyrazol -4(5H)-ylidene)hydrazinyl)benzenesulfonamide.*

Yield 66%; m.p.220-221°C. IR [ν,cm^{-1}, KBr]:3369(NH_2),3086-3034(C-H aromatic), 2920 (CH_3, CH_2), 1765-1725(C=O),1695-1540(C=N),1465(CH_3,CH_2), 1325 (SO_2),1290 (C-N), 706-585(C-S). ^{1}HNMR [400MHz,δ,ppm,DMSO-d_6] : 11.62 (s,2H,NH), 8.05-6.80 (m,12H, ArH),7.42(s,2H,NH_2), 6.97 (s,2H,NH),5.64(s,2H,CH_2),2.35(s,3H,CH_3).^{13}CNMR[100 MHz, δ, *ppm*, DMSO] : 170.1, 164.3 (CO),151.6-110.8(Ar-C), 129.4(C=N), 59.8(CH_2), 14.2 (C=N), 11.6 (CH_3). LC-MS:*m/z* 543 (M^+). Anal. Calcd for $C_{24}H_{21}N_9O_4S$ (531): C, 54.23; H, 3.95; N, 23.72; S, 6.02. Found; C, 54.2; H, 3.9; N, 23.7; S, 5.9.

VII*b: N-(4-(2-(1-(4-((1H-benzo[d][1,2,3]triazol-1-yl)methylamino)benzoyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)phenylsulfonyl) acetamide.*

Yield 64%; m.p.216-218°C.IR [ν,cm^{-1},KBr]: 3369(N-H), 3086-3034(C-H aromatic),2920 (CH_3,CH_2), 1765-1725 (C=O), 1695-1540(C=N), 1465 (CH_3,CH_2),1325(SO_2), 1290(C-N), 706-585 (C-S). ^{1}HNMR [400 MHz, δ,ppm,DMSO- d_6] : 11.62(s, 2H,NH), 8.05-6.80 (m, 12H, ArH), 7.42(s,1H,NH), 6.97 (s,2H,NH),5.64(s, 2H,CH_2), 2.42-2.35(s, 6H,CH_3). ^{13}C NMR [100 MHz, δ, *ppm*, DMSO] : 151.6 -110.8(Ar-C), 170.1,164.3(CO), 129.4(C=N), 59.8(CH_2), 21.8, 11.6 (CH_3),14.2 (C=N). LC-MS:*m/z* 582 (M^+). Anal. Calcd for $C_{26}H_{23}N_9O_5S$ (573): C, 54.44; H, 4.04; N, 21.98; S, 5.59. Found; C, 54.4; H, 3.9; N, 21.9; S, 5.5.

VII*c: 4-(2-(1-(4-((1H-benzo[d][1,2,3]triazol-1-yl)methyl amino) benzoyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(pyridin-2-yl)benzene sulfonamide.*

Yield 67%; m.p.223-225°C. IR [ν,cm^{-1},KBr]: 3369(N-H), 3086-3034(C-Haromatic), 2920 (CH_3, CH_2), 1765-1725 (C=O), 1695-1540(C=N), 1465 (CH_3,CH_2), 1325 (SO_2), 1290(C-N), 706 -585 (C-S). ^{1}HNMR [400 MHz,δ, ppm, DMSO-d_6] :11.62(s,2H, NH), 8.05-6.80(m, 16H, ArH), 7.42 (s,1H, NH), 6.97 (s,2H, NH), 5.64(s, 2H,CH_2),2.35(s,3H,CH_3). ^{13}C NMR [100 MHz, δ, *ppm*, DMSO] : 170.1,164.3(CO),152.9-110.8(Ar-C), 129.4(C=N), 59.8 (CH_2),14.2 (C=N),11.6 (CH_3).LC-MS: m/*z* 619(M^+). Anal. Calcd for $C_{29}H_{24}N_{10}O_4S$ (608): C, 57.23; H, 3.97; N, 23.01; S, 5.27. Found; C, 57.2; H, 3.9; N, 22.9; S, 5.2.

VII*d: 4-(2-(1-(4-((1H-benzo[d][1,2,3]triazol-1-yl)methylamino)benzoyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(pyrimidin-2-yl)benzene sulfonamide.*

Yield 68%;m.p.216-219°C.IR[ν,cm^{-1},KBr]: 3369(NH_2),3086-3034(C-Haromatic),2920 (CH_3, CH_2), 1765-1725 (C=O), 1695-1540 (C=N), 1465 (CH_3,CH_2), 1325 (SO_2), 1290(C-N),706-585 (C-S).^{1}HNMR [400MHz, δ ,ppm, DMSO-d_6] : 11.62 (s,2H,NH), 8.05-6.80(m,15H, ArH), 7.42 (s, 1H, NH_2), 6.97(s,2H,NH), 5.64 (s,2H,CH_2),2.35(s,3H,CH_3). ^{13}C NMR [100 MHz, δ, *ppm*, DMSO] :170.1,164.3(CO),152.9-110.8(Ar-C),129.4(C=N), 59.8(CH_2),14.2(C=N),11.6 (CH_3). LC-MS: m/*z* 622 (M^+). Anal. Calcd for $C_{28}H_{23}N_{11}O_4S$ (609): C, 55.17; H, 3.80; N, 825.27; S, 5.26. Found; C, 55.1; H, 3.7; N, 25.2; S, 5.2.

VII*e: 4-(2-(1-(4-((1H-benzo[d][1,2,3]triazol-1-yl)methylamino)benzoyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(4-methylpyrimidin-2-yl)benzene sulfonamide.*

Yield 65%; m.p.215-216°C. IR [ν,cm^{-1},KBr]: 3369(NH_2),3086-3034(C-Haromatic), 2920(CH_3, CH_2),1765-1725(C=O), 1695-1540 (C=N), 1465 (CH_3,CH_2), 1325 (SO_2), 1290(C-N),706-585 (C-S).^{1}HNMR [400MHz, δ ,ppm, DMSO-d_6] :11.62 (s,1H,NH), 8.05 -6.80(m,14H, ArH),7.42 (s,1H,NH),6.97(s,1H,NH),5.64(s,2H,CH_2),2.35-2.32(s, 6H,CH_3). ^{13}C NMR [100 MHz, δ, *ppm*, DMSO]:170.1,164.3(CO),152.9-110.8(Ar-C),129.4 (C=N), 59.8(CH_2),24.6(CH_3),14.2(C=N), 11.6 (CH_3). LC-MS: m/*z* 636 (M^+). Anal. Calcd for $C_{29}H_{25}N_{11}O_4S$ (623): C, 55.85; H, 4.04; N, 24.71; S, 5.14. Found; C, 55.8; H, 3.9; N, 24.6; S, 5.1.

VII*f:4-(2-(1-(4-((1H-benzo[d][1,2,3]triazol-1-yl)methylamino)benzoyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(4,6-dimethylpyrimidin-2-yl)benzene sulfonamide.*

Yield 66%; m.p.220-221°C. IR [ν,cm^{-1},KBr]: 3369(NH_2),3086-3034(C-Haromatic),2920 (CH_3,CH_2), 1765-1725(C=O),1695-1540(C=N),1465 (CH_3,CH_2), 1325 (SO_2), 1290(C-N), 706 -585(C-S). ^{1}HNMR [400MHz, δ ,ppm, DMSO-d_6] : 11.62 (s,1H,NH), 8.05-6.80(m, 13H, ArH),7.42 (s,1H, NH), 6.97(s,1H,NH),5.64(s,2H,CH_2),2.35-2.32(s,9H,CH_3).^{13}CNMR [100 MHz, δ,*ppm*, DMSO]:170.1, 164.3 (CO),152.9-110.8(Ar-C),129.4 (C=N), 59.8 (CH_2), 24.6(CH_3),14.2(C=N),11.6(CH_3).LC-MS:m/*z*650(M^+).Anal.Calcd for $C_{30}H_{27}N_{11}O_4S$ (637): C, 56.51; H, 4.27; N, 24.16; S, 5.03. Found; C, 56.5; H, 4.2; N, 24.1; S, 4.9.

VII*g: 4-(2-(1-(4-((1H-benzo[d][1,2,3]triazol-1-yl)methylamino)benzoyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(4-methoxypyrimidin-2-yl)benzene sulfonamide.*

Yield 62%; m.p.211-213°C.IR[ν,cm^{-1},KBr]:3369(NH_2),3086-3034(C-Haromatic), 2920 (CH_3, CH_2), 1765-1725 (C=O), 1695-1540 (C=N), 1465 (CH_3,CH_2), 1325 (SO_2), 1290(C-N),1148 (C-O),706-585 (C-S).^{1}HNMR [400MHz, δ ,ppm, DMSO-d_6] :11.62(s,1H, NH), 8.05-6.80(m,14H, ArH), 7.42 (s,1H, NH), 6.97(s,1H,NH), 5.64(s,2H,CH_2), 3.92(s,3H, CH_3), 2.35(s,3H,CH_3). ^{13}C NMR[100 MHz, δ, *ppm*, DMSO] :170.1,164.3 (CO),172.8-110.8(Ar-C),129.4(C=N),59.8(CH_2),54.8(CH_3), 14.2(C=N), 11.6

(CH_3). LC-MS:m/*z* 648(M^+). Anal. Calcd for $C_{29}H_{25}N_{11}O_5S$ (639): C, 54.45; H, 3.94; N, 24.09; S, 5.01. Found; C, 54.4; H, 3.9; N, 23.9; S, 4.9.

VII*h*: *4-(2-(1-(4-((1H-benzo[d][1,2,3]triazol-1-yl)methylamino)benzoyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(thiazol-2-yl)benzene sulfonamide.*

Yield 62%; m.p.211-213°C.IR [ν,cm^{-1},KBr]: 3369(NH_2),3086-3034(C-Haromatic),2920 (CH_3, CH_2),1765-1725 (C=O),1695-1540 (C=N),1465 (CH_3,CH_2),1325 (SO_2),1290 (C-N), 1148(C-O),706-585(C-S).^{1}HNMR[400MHz,δ,ppm,DMSO-d_6]:11.62(s,2H,NH),8.05-6.80 (m,14H,ArH), 7.42(s,1H, NH), 6.97(s,2H,NH), 5.64 (s,2H,CH_2),2.35(s,3H,CH_3). ^{13}C NMR [100MHz, δ,*ppm*, DMSO]:170.1, 164.3(CO),172.2-110.8(Ar-C),129.4(C=N), 59.8 (CH_2), 14.2(C=N),11.6(CH_3). LC-MS: m/*z* 627 (M^+). Anal. Calcd for $C_{27}H_{22}N_{10}O_4S_2$(614): C, 52.76; H, 3.61; N, 22.79; S, 10.43. Found; C, 52.7; H, 3.5; N, 22.7; S, 10.4.

VII*i*: *4-(2-(1-(4-((1H-benzo[d][1,2,3]triazol-1-yl)methylamino)benzoyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(5-methyl-1,3,4-thiadiazol-2-yl)benzene sulfonamide.*

Yield 60%; m.p.208-210°C.IR [ν,cm^{-1},KBr]: 3369(NH_2),3086-3034(C-Haromatic),2920 (CH_3,CH_2), 1765-1725(C=O),1695-1540 (C=N),1465 (CH_3,CH_2),1325 (SO_2),1290 (C-N), 1148(C-O),706-585(C-S).^{1}HNMR[400MHz,δ,ppm,DMSO-d_6]:11.62(s,1H,NH),8.05-6.80(m,12H,ArH),7.42(s,1H,NH), 6.97 (s, 1H, NH),5.64(s,2H,CH_2),2.68-2.35(s,6H,CH_3).^{13}C NMR [100 MHz, δ, *ppm*, DMSO]:170.1, 164.3 (CO),172.2-110.8(Ar-C),129.4(C=N),59.8 (CH_2),20.2 (CH_3),14.2(C=N),11.6(CH_3).LC-MS:m/*z* 637 (M^+). Anal. Calcd for $C_{27}H_{23}N_{11}O_4S_2$ (629): C, 51.50; H, 3.68; N, 24.47; S, 10.18. Found; C, 51.4; H, 3.6; N, 24.4; S, 10.1.

VII*j*:*4-(2-(1-(4-((1H-benzo[d][1,2,3]triazol-1-yl)methylamino)benzoyl)-3-methyl-5-oxo-1H-yrazol-4(5H)-ylidene)hydrazinyl)-N-(3,4-dimethylisoxazol-5-yl)benzene sulfonamide.*

Yield 61%; m.p.209-211°C.IR[ν,cm^{-1},KBr]:3369(NH_2),3086-3034(C-Haromatic), 2920 (CH_3,CH_2), 1765-1725 (C=O),1695-1540 (C=N),1465 (CH_3,CH_2),1325 (SO_2),1290 (C-N), 1148 (C-O),1040(O-N),706-585(C-S).^{1}HNMR[400MHz, δ ,ppm, DMSO-d_6] : 11.62 (s, 1H, NH),8.05-6.80(m,12H, ArH), 7.42(s,1H,NH),6.97(s,1H,NH),5.64(s,2H,CH_2),2.38-2.35 (s,9H,CH_3).^{13}CNMR [100MHz,δ, *ppm*, DMSO] : 170.1,164.3(CO),172.2-110.8(Ar-C), 129.4(C=N), 59.8 (CH_2),14.2 (C=N), 11.6,10.8, 9.5 (CH_3). LC-MS:m/*z* 634(M^+). Anal. Calcd for $C_{29}H_{26}N_{10}O_5S$ (626): C, 55.58; H, 4.18; N, 22.35; S, 5.12. Found; C, 55.5; H, 4.1; N, 22.3; S, 5.1.

RESULTS AND DISCUSSION

The compound **IV** (hydrazide) has been synthesized successfully as the Mannich reaction reported previously(22-26). The synthesis of **(Va-j)** has been performed based on the method reported (33). From these compounds the novel compounds **(VIa-j)** have been synthesized. The compounds **(VIa-j)** reacted with **IV** to give the corresponding compounds **(VIIa-j)**. All the compounds were confirmed on the basis of the elemental analysis and spectroscopic investigation. IR spectrum of **IV** revealed characteristic bands at 3450, 1630(NH_2) and confirmatory by ^{1}H NMR δ 3.95(s, 2H, NH_2). Further, IR spectroscopic investingation of (**VIa-j)** reveals bands at 1640-1596(C=N) and ^{1}H NMR δ 11.62 (s,1H,NH). IR spectra of compounds 7a-j shows 3369(N-H),1640-1596(C=N), 1255 -l197(C-N), and ^{1}H NMR 11.62(s,1H,NH).The examination of these data reveals that the IR band and ^{1}H NMR signals are appropriate to the correspond structure of compound.The final structure of all compounds was confirmed by ^{13}C NMR and LC- MS data, i.e. The compounds **VIIa** shows the molecular ion peak *m/z* 628 give the molecular weight of **VIIa** i.e. 614. All these facts confirm the structures (**VIIa-j)**.

ANTIMICROBIAL ACTIVITY

Antibacterial activities of all the compounds were studied against Gram–positive Bacteria (*Bacilus subtilis* and *Staphyllococcus aureus*) and Gram-negative Bacteria (*E.coil, Salmonella typhi* and *Klebsiella promioe*) at a concentration of 50µg/ml by Agar cup plate method[xxxv-xxxvii]. Methanol system was used as control in this method. Under similar condition using sulphonamide as a standard for comparison carried out control experiment. The area of inhibition of zone measured in mm. Compound **VIIe** and **VIIf** found more active against the above microbes. Other compounds were found more active against the above microbes. The antibacterial activity of all the compounds are shown in Table-1.

Table 1: Antibacterial activity of the compounds **(VIIa-j)**

Compounds	Zone of Inhibition(mm) (Activity Index)[std]				
	Gram +ve		Gram –ve		
	Bacillus Subtilis	***Staphylococcus Aureus***	***Kllebsiella promioe***	***Salmonella typhl***	***E.coil***
VIIa	57 (0.64)	50 (0.84)	70 (0.81)	65 (0.89)	71 (0.93)
VIIb	50 (0.56)	54 (0.91)	79 (0.91)	67 (0.91)	69 (0.90)
VIIc	84 (0.94)	51 (0.86)	80 (0.93)	68 (0.93)	66 (0.86)
VIId	85 (0.95)	53 (0.89)	78 (0.90)	65 (0.89)	71 (0.93)
VIIe	88 (0.98)	58 (0.98)	84 (0.97)	71 (0.97)	74 (0.97)
VIIf	86 (0.96)	56 (0.94)	82 (0.95)	69 (0.94)	73 (0.96)
VIIg	82 (0.92)	54 (0.91)	78 (0.90)	64 (0.87)	70 (0.92)
VIIh	84 (0.94)	52 (0.88)	80 (0.93)	67 (0.91)	68 (0.89)
VIIi	81 (0.91)	52 (0.88)	75 (0.87)	64 (0.87)	71 (0.93)
VIIj	79 (0.88)	51 (0.86)	79 (0.91)	66 (0.90)	71 (0.93)
Sulphonamide	89	59	86	73	76

(Activity Index) [std] ***= Zone of Inhibition of the sample/ Zone of Inhibition of the standard***

Conclusion:

The present study reports the synthesis of novel heterocyclic pyrazolinone from the corresponding precursors ethyl-3-oxo-2-(2-(3-(N-alkyl sulfamoyl)phenyl) hydrazono) butanoates **(VIa-j)** and 4-(1H)- benzotriazolyl methyl amino benzoyl hydrazide **(IV)**. The antimicrobial activity of 3-(2-(1-(4-((1H-benzo [d][1,2,3] triazol-1-yl)methyl amino) benzoyl) -3-methyl-5-oxo-1H-pyrazol- 4(5H)-ylidene) hydrazinyl) N-alkyl benzene sulfonamides **(VIIa-j)** was carried out against some strain bacteria. The results show that the synthesized compounds were toxic against the bacteria. The investigation of antibacterial screening reveals that the compounds **VIIe** and **VIIf** have exhibited good antibacterial activity comparable to the standard drugs.

References

i. Elguero, J.; Goya, P.; Jagerovic, N.; Silva, A. M. S. *In Targets in Heterocyclic Systems, Attanasi, O. A.; Spinelli, D. Eds, Italian Society of Chemistry*, Roma, Italy 2002,**6,**52.
ii. Bekhit, A. A.; Ashour, H. M.; Guemei, A. A., *Arch. Pharm*. (Weinheim), 2005,**338,**167.
iii. Pattan, S.R.; Rabara, P.A.; Pattan, J.S.; Bukitagar, A.A.; Wakale, V.S.; Musmade, D.S., *Indian J Chem*, 2009,**48,** 1453.
iv. Scheibye, S.; El-Barbary, A. A.; Lawesson, S. O.;Fritz, H. and Rihs, G., *Tetrahedron*, 1982,**38,**3753.
v. El-Hawash, S.A.; Habib, N.S. and Kassem, M., *Arch. Pharm. Chem. Life Sci*, 2006, **339,**564**.**
vi. Hiremith, S. P.; Rudresh, K. and Saundan, A. R., *Indian J. Chem.,*2002,**41B(2)**,394.
vii. Nadia Adil SALIH, *Turk J. Chem*.,2008,**32**,229-235.
viii. Dhol. P.N.; Achary, T. E. and Nayak, A., *J. Indian Chem. Soc.,* 1975,**52,**1196.
ix. Souza, F. R.; Souza, V. T.; Ratzlaff, V.;Borges, L. P.;Olivera, M. R. and Bonacorso, H. G.,*Eur.J. Pharma*,2002, **45 (2),**141.
x. McTavish, J. R., *Aspirin and Related Drugs*,2004,25.
xi. Palaska, E.; Aytemir, M.; Uzbay, I.T.; Erol, D.,*Eur. J. Med. Chem*.,2001,**36,**539.
xii. Rajendra, P. Y.; Lakshmana, R. A.; Prasoona, L.;Murali, K.; Ravi, K. P., *Bioorg. Med. Chem. Lett.*, 2005,**15,**5030.
xiii. Ozdemir, Z.; Kandilici, H.B.; Gumusel, B.; Calis, U.; Bilgin, A.A., *Eur. J.Med. Chem*., 2007, **42,**373.
xiv. Ruhogluo, O.; Ozdemir, Z.; Calis, U.; Gumusel, B.; Bilgin, AA.,*Arzneimittelforschung*, 2005,**55**,431.
xv. Singh, J. and Tripathy, R., *PCT Int. Appl*.,2001,138.
xvi. Abdallah, M., *Materials Chemistry and Physics*, 2003,**82,**786.
xvii. Sabaa, M. W.;Oraby, E. H.; Abdul Naby, A. S.; Mohamed, R. R., *Polym. Degrad. Stab*., 2006,**91,** 911.
xviii. Sabaa, M. W.;Oraby, E. H.; Abdul Naby, A. S.; Mohamed, R. R., *J.Appl. Polym. Sci*., 2006,**101,**1544.
xix. Miyara, H.,*Bull. Chem. Soc. Jpn,*1963,**36,**382.
xx. Toeik, *Bull. Chem. Soc. Jpn*, 1965,**38** 1050.
xxi. Khalifa, H. and Issa, R. M., *Egypt J. Chem.,*1974, **17,**581.
xxii. Azarifar, D. and Shaebanzadeh, M.,*Molecules*,2002, **7,** 885.
xxiii. Amir, M.; Siddiqui, A. A. and Rizwan, S.,*Oriental J Chem*.,2003, **19(3),** 629.
xxiv. Bhatt, A. K.; Shah, P. R.; Karadiyya, H. G. and Patel, H. D.,*Oriental J.Chem*., 2003,**19(3),** 643.
xxv. Patel, K. V. and Singh, A., *E-Journal of Chem*., 2009, **6(1),** 281.
xxvi. Kartritzky, A. R.; Rachwal, S. B., *J.Chem. Soc. Perkin Trans.,*1987,**1,**805.
xxvii. Kartritzky, A. R.; Manju, K.; Singh, S. K. and Meher, N. K.,*Tetrahedron*,2005,**61,**2555.
xxviii. Long, J.W.; Vecek, L. V.,Sherwin-Williams Co *U S,1982*,4663914.

xxix. Hageolorn, F. and Evertz, W.,*Bayer U S,1984*,4424360.
xxx. Sanna, P.; Carta, A.; Nikookar, M. E., *Eur. J. Med. Chem*, **2000**, 35, 535-543.
xxxi. Kopanska, K.; Najda, A.; Zebrowska, J.; Chomicz, L.; Piekarczyk, J.; Myjak, P. and Bretner, M.,*Bioorg. Med. Chem*., **2004**, 12, 2617-2624.
xxxii. Boido, A.; Vazzana, I.; Mattioli, F.; Sparatore, F. ,*Il Farmaco*, **2003**, 58, 33-44.
xxxiii. Biagi, B.; Calderone, V.; Giorgi, I.; Livi, O.; Scartoni, V.; Baragatti, B.; Martinotti, E., *Il Farmaco*, **2001**, 56, 841-849.
xxxiv. Vogel, A. I.,*A Texts Book of Practical Organic Chemistry5thedn*.,1989,701,1162,883.
xxxv. Baily, W. R. and Scott, E. G.,*Diagnostic Microbiology,The C.V. Moshy Co. St. Lovis*, 1966,257.
xxxvi. Banty,A. L.,*The Antimicrobial Susceptibility test; The Principal and practice edited by Illus lea and Febiger (Philadelphia. Pa USA),*1976,180.
xxxvii.Simoncini,F.; Rangone, R. and Calani, C., *Farmaco.Ed.Prat*,1968,**23(10),**559.

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