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Synthesis, Characterization and Biological Activities of (3-Nitrophenyl)(5-Substituted Phenyl- 1,3,4-Thiadiazol-2-Yl) Methanediamine

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ABSTRACT

Synthesis of phenyl (5-substituted phenyl-1,3,4-thiadiazol-2-yl) methanediamine (TDZ-A to TDZ-C), reaction between aryl aldehydes and Thiosemicarbazide yielded thiosemicarbazone. Thiosemicarbazone in the presence of citric acid and sodium acetate gives 2-amino-5-aryl -1,3,4-thiadiazole, which is treated with aniline in the presence of formaldehyde to obtained targeted compounds phenyl(5-substituted phenyl-1,3,4-thiadiazol-2-yl)methanediamine. The synthesized Thiadiazoles have been characterized on the basis of analytical spectral data. The resulted compounds were screened for their antibacterial, antifungal and antioxidant activities.

Keywords: Aromatic aldehydes, Thiosemicarbazide, Formaldehyde, Antioxidant activity, Antibacterial activity, Antifungal activity.

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INTRODUCTION

Molecular structure influences the biological activity of a compound[1-3]. The interest biological activities of a novel heterocyclic like Thiadiazole have stimulated considerable research work. Substituted 1, 3, 4-Thiadiazoles have become very useful compounds in medicine[4], agriculture[5]and in many fields of technology[6,7]. Some of the technological applications involve dyes, lubricating compositions, optically active liquid crystals, photographic materials and many others[8]. A large number of 1, 3, 4-Thiadiazoles have been patented in the agricultural field as herbicides[9], fungicides[10] and bactericides[11]. From these findings our work is designed for the synthesis of 5-phenyl substituted, 2-amino 1, 3, 4 Thiadiazole derivatives and determination of its molecular properties by suitable computational programmes[12-14].

MATERIALS AND METHOD

The melting point of organic compounds were determined by Thiel's melting point tube (Capillary tube method). The IR spectra of the compounds were carried out in FT-IR-Spercle Elmer DHF1FT-IRBruker. The ^{1}HNMR and ^{13}C NMR spectra of the compounds were carried out in Bruker AMX 400 MHz, the solvent used was Dueterated chloroform and ethanol.

Methods

Procedure for synthesis of phenyl (5-substitutedphenyl-1,3,4-thiadiazol-2-yl) methanediamine: Aldehydes (0.2 mol) in warm alcohol (300 ml) and Thiosemicarbazide (0.2 mol) in 300 ml hot water were mixed slowly with continuous stirring to obtained product Thiosemicarbazone. The precipitate obtained was filtered and washed with distilled water, recrystallized from suitable solvents. Thiosemicarbazone (0.05 mol) and Ferric chloride (0.15 mol) in 300 ml distilled water were heated to 80-90^{0}C for 45 min, the solution was filtered. A mixture of citric acid (0.11 mol) and sodium citrate (0.05 mol) was added to the solution and stirred. After cooling the solution was neutralization with aqueous ammonia (10%)to get the compound 2-amino-5-aryl - 1,3,4-thiadoazole. A mixture of 2-amino- 5-aryl-1, 3, 4-thiadoazole (2.22g, 0.01 mol) and 3-nitro aniline (1.38g, 0.01 mol) and formaldehyde (2ml) were taken in a beaker. The mixture was refluxed in water for 4hrs. After the completion of reaction, ice-cold water was added to the reaction mixture and dried to get the targeted compounds 2-nitrophenyl-5-aryl-1,3,4-Thiadoazol-2-yl-methanediamine (TDZ-A to TDZ-C).

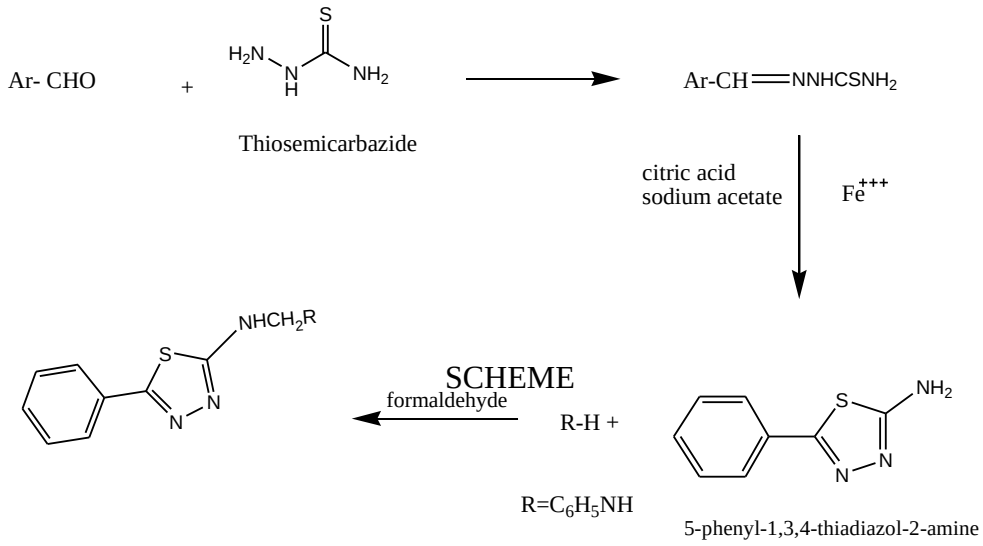
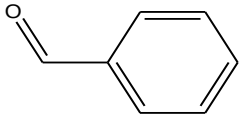
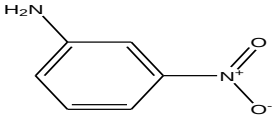
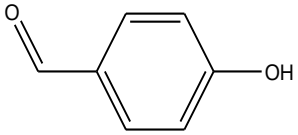
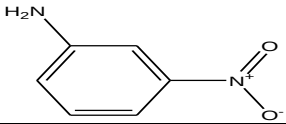
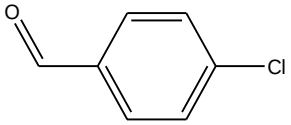
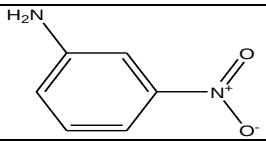


Table 1: List of Various Aldehydes and Aniline used for Scheme

S.No	Code	R	Ar
1.	TDZ – A		
2.	TDZ - B		
3.	TDZ - C		

Spectral Data

TDZ-A: 3-nitrophenyl-5-phenyl- 1, 3, 4 -thiadoazol-2-yl-methanediamine

IR (KBr Pellet, υ in cm^{-1}):C=C (1542.35 Str),C=N (1694.84 Str),C-N (1009.47 Str),C-S (759.92 Str),C-H (2835.90 Str), N-H (3420.69 Str). NO_2(Sym & Asym 1310.59&1608.88); **^{1}HNMR** (DMSO-d6, δ in ppm): 2.008-2.083 (4H, s, NH_2), 7.024-8.037 (8H, s, Ar-CH).

TDZ-B: 4-(5-(diamino(3-nitrophenyl) methyl)-1,3,4-thiadiazol-2-yl)phenol

IR (KBr Pellet, υ in cm^{-1}): C=C(1597.31Str), C=N(1683.91 Str),C-S (706.63 Str),C-H(3025.31 Str), N-H(3416.29 Str), NO_2(1343.04&1523.83 Str), OH(3741.97 Str);**^{1}HNMR** (DMSO-d6, δ in ppm): 2.003-2.008(4H, s, NH_2), 5.121(1H, s, OH), 6.932-8.037(8H, s,Ar-CH); **^{13}CNMR** (DMSO-d6, δ in ppm): 79.03(^{3}C), 116.32(^{2}C), 119.1(^{5}C), 123.21(^{7}C), 126.1 (^{4}C), 128(^{10}C), 122 (^{11}C),

122(^{12}C), 132(^{15}C), 134(^{6}C), 149(^{8}C), 163(^{13}C), 176(^{1}C), 132(^{9}C), 133.1(^{14}C); **MS:** m/z - 344.2 1 (M^+).

TDZ-C:(5-(4-chlorophenyl)-1,3,4-thiadiazol-2-yl) (3nitrophenyl) methanediamine

IR (KBr Pellet, υ in cm^{-1}):C=C(16015Str),C=N(1643.28Str),C-S(640.22Str),C-H(3025.41Str), N-H_2 (3344.76Str), NO_2 (1358.68&1529.53 Str), OH(3667.17 Str), C-Cl (718.13 Str); **^{1}HNMR** (DMSO-d6, δ in ppm): (DMSO-d6, δ in ppm): 2.008-2.083 (4H, s, NH_2), 6.932-8.037(8H, s, Ar-CH); **^{13}CNMR** (DMSO-d6, δ in ppm): 78.03(^{3}C) ,116.5 (^{2}C), 116.3(^{15}C) ,119.64(^{7}C), 123.21(^{4}C), 132.50(^{5}C), 134.31(^{6}C),126.44(^{12}C), 128.41(^{11}C), 132(^{15}C), 150.6(^{8}C), 173.13(^{13}C), 176.35(^{1}C), 132.59(^{9}C).

Tab.2.Characterization data of Synthesized compounds

Compound Code (TDZ)	Molecular Formula	Molecular Weight. (g/mole)	Time(hrs)	Melting Point (^{0}C)	Yield (%)	R_f*
TDZ -A	$C_{15}H_{13}N_5O_2S$	327.36	4	270-274	60.37	0.78
TDZ -B	$C_{15}H_{13}N_5O_3S$	343.36	4	225-227	52.87	0.85
TDZ - C	$C_{15}H_{12}ClN_5O_2S$	361.81	4	230-234	62.12	0.88

BIOLOGICAL ACTIVITY

Newly synthesized compounds were evaluated for their antimicrobial and antioxidant activities.

Antimicrobial Activity

Synthesized Thiadiazole compounds were subjected for antibacterial and antifungal activities.

Antibacterial activity

Synthesized 1,3,4-Thiadiazole derivatives were evaluated for Antibacterial activity against Gram $^{+ve}$ and Gram^{-ve} bacteria's with cup plate method[12] at concentrations of 250µg/ml and 500µg/ml. Standard was taken as streptomycin Control was taken as ethanol. The results were tabulated in Tab.3.

Table 3: Antibacterial Activity of Synthesized Compound

S.NO	Compound Code (TDZ)	Zone of Inhibition (mm)			
		Gm $^{+Ve}$ S.aureus		Gm $^{-Ve}$ E.Coli	
		250µg/ml	500µg/ml	250µg/ml	500µg/ml
1	TDZ -A	10	12	8	8
2	TDZ - B	10	11	12	15
3	TDZ -C	8	12	8	8
Control	DMSO	8		8	
Standard	Streptomycin (250 µg/ml)	18		20	

Antifungal activity of the Synthesized Compounds

Synthesized 1,3,4-Thiadiazole derivatives were evaluated for Antifungal activity with cup plate method[13] at concentrations of 250µg/ml and 500µg/ml .Standard was taken as Fluconazole. Control was taken as DMSO. The results were tabulated in Tab.4.

Tab.4: Antifungal Activity of Synthesized Compounds

S.NO	Compound Code (TDZ)	Zone of Inhibition (mm)			
		Aspergillus niger		Penicilliumnotatum	
		250µg/ml	500µg/ml	250µg/ml	500µg/ml
1	TDZ - A	11	12	16	24
2	TDZ - B	13	12	17	19
3	TDZ - C	9	13	17	18
Control	DMSO	8	8	8	8
Standard	Fluconazole (250 µg/ml)	25		28	

Antioxidant Activity

All 3derivates of synthesized compounds were evaluated for their antioxidant activity by Nitric oxide radical scavenging activity method[14]at the concentration of 25µg/ml, 50µg/ml, 75 µg/ml, and 100 µg/ml using Ascorbic acid as standard shown in the Table 5.

Table 5: Antioxidant Activity of the synthesized compounds

Compound Code (TDZ)	Percentage of inhibition (%)			
	25µg/ml	50µg/ml	75µg/ml	100µg/ml
TDZ - A	35	44	63	78
TDZ - B	24	36	54	70
TDZ - C	31	43	63	79
Control	0.92			
Standard (Ascorbic acid)	61	76	84	96*

RESULTS AND DISCUSSION

Novel 1,3,4-Thiadiazoles synthesized by aromatic aldehydes mixed with Thiosemicarbazide in the presence hot water to obtained Thiosemicarbazones. Thiosemicarbazones (0.05 mol) and Ferric chloride (0.15 mol) in 300 ml distilled water were heated to 80-90^{0}C for 45 min, the solution was filtered. A mixture of citric acid (0.11 mol) and sodium citrate (0.05 mol) was added to the solution to get the compound 2-amino-5-aryl - 1,3,4-thiadoazole. A mixture of 2-amino- 5-aryl-1, 3, 4-thiadoazole (2.22g, 0.01 mol) and 3-nitro aniline (1.38g, 0.01 mol) and formaldehyde (2ml) were refluxed in water for 4hrs to get the targeted compounds 2-nitrophenyl-5-aryl-1,3,4-Thiadoazol-2-yl-methanediamine (TDZ-A to TDZ-C).Synthesized compounds were recrystallized with appropriate solvents. All compounds were identified and characterized by IR, ^{1}H NMR, ^{13}C

NMR and Mass spectral data. Synthesized TDZ-A to TDZ-C derivatives were evaluated for Antibacterial and Antifungal activities with cup plate method at concentrations of 250µg/ml and 500µg/ml. TDZ - B is found have moderate antibacterial activity against both Gram $^{+ve}$ and Gram $^{-ve}$. Other compounds TDZ–A and TDZ-C showed insignificant activity when compared to standard Streptomycin. TDZ-A, TDZ-B and TDZ-C were found have moderate antifungal activity when compared to standard Fluconazole. Synthesized compounds were evaluated for antioxidant activity by nitric oxide radical scavenging activity method. Compounds TDZ–A and TDZ–C showed moderative activity when compared with Ascorbic acid as standard.

CONCLUSION

Novel 1,3,4-Thiadiazoles synthesized by aromatic aldehydes mixed with Thiosemicarbazide in the presence hot water to obtained Thiosemicarbazones. All compounds were identified and characterized by IR, ^{1}H NMR, ^{13}C NMR and Mass spectral data. Synthesized compounds were evaluated for Anti-bacterial activity, anti-fungal activity and antioxidant activity by using suitable standard.

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