"Synthesis and characterization of azopyrazole and azoisoxazole derivatives from substituted aniline"

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Abstract: In present article substituted aniline is treated with acetoacetic acid to obtained 3-(2-4-substituted-phenylhydrazono)pentane-2,4-dione which further reacted with two different nuceophile. In first stage it is reacted with 2,4-dinitrophenyl hydrazine to give 1-(2,4-dinitrophenyl)-3,5-dimethyl-4-(phenyldiazenyl)-1H-pyrazole and in second stage reacted with hydroxylamine hydrochloride to produce 3,5-dimethyl-4-(phenyldiazenyl)isoxazole. All the compounds were characterized by using IR, ^{1}H-NMR, mass spectral data and elemental analysis. The data obtained by different spectroscopic techniques matches with the structure of synthesized compounds.

Keywords: Aniline, acetylacetone, azopyrazole, azoisoxazole, ^{1}H-NMR.

I. INTRODUCTION

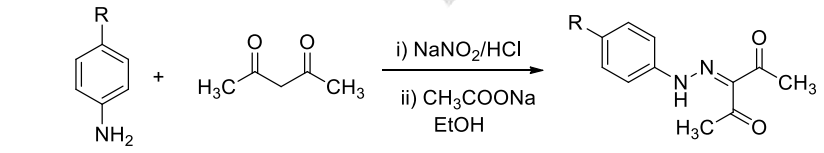
Heterocyclic compounds are cyclic compounds that have atoms of atleast two different elements as a member of its ring. Synthesis of heterocyclic compounds received a great attention in the recent years because they play an important role in drug discovery process and analysis of drugs. Heterocyclic compounds show wide variety of biological activities like antibacterial, antifungal, antitubercular, anticancer, analgesic [1-5]. Pyrazole is five membered ring organic compound with three carbon and two nitrogen, while isoxazole contain three carbon one nitrogen and one oxygen atom and shows excellent biological activities[6-10]. Isoxazole ring is found in some natural product, such as ibotenic acid. Isoxazole also form the basis for a number of drugs including the COX-2 inhibitor valdecoxib (bextra) and a neurotransmitter against AMPA.

II. EXPERIMENTAL

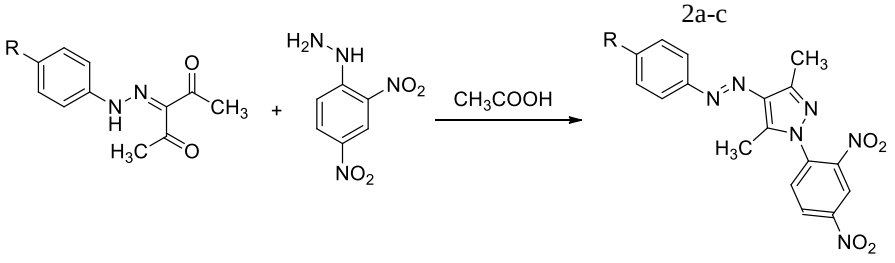
All the chemicals used were of laboratory grade and purchased from SD Fine Chemicals. Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded in KBr using Perkin Elmer model 2000 spectrophotometer and reported wave numbers are given in cm^{-1}. ^{1}H-NMR spectra were recorded in $CDCl_3$ on a Brucker Advance II 400 MHz spectrophotometer using TMS as an internal standard. Chemical shift values are shown in δ ppm. Mass spectra were recorded on Agilent 6320 Ion Trap mass spectrometer. Elemental analysis of compounds carried out by using Euro E 3000 instrument. The purity of all the synthesized compounds was checked by TLC on silica gel plates by using appropriate methanol/DCM solvents where it clearly indicates polar spots.

2.1 Synthesis of 3-(2-4-substituted-phenylhydrazono)pentane-2,4-dione (2a-c)

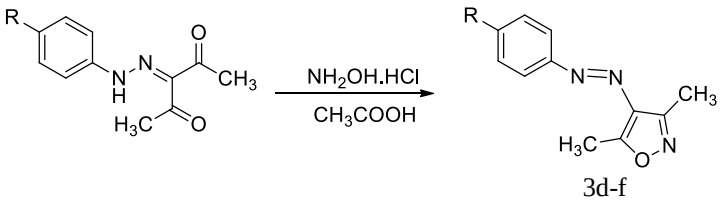
4-substituted aniline (0.01mol) was dissolved in a mixture of concentrated HCl (8ml) and water (6 ml) and cooled to 0^0 C on ice bath. A cold aqueous solution of sodium nitrite (0.02 mol) was added to it. The cold diazonium salt solution was filtered and to this sodium acetate (0.05 mol), acetyl acetone (0.01 mol) and ethanol added. Whole reaction mixture was stirred for about 2 hours and resulting solid obtained filtered, dried and purified by recrystalisation from ethanol.



2a-c



3a-c



3d-f

Fig 1 Scheme of Reaction

Table 1 Analytical data and elemental analysis of compounds

Comp.	R	Yield	Molecular Formula	M. P. (^{0}C)	Elemental Analysis		
					%C	%H	%N
					Calcd. / **Found**	Calcd. / **Found**	Calcd. / **Found**
2a	Br	72%	$C_{11}H_{11}BrN_2O_2$	110	46.66/ **46.22**	3.92/**3.27**	9.89/**9.90**
2b	OCH_3	69%	$C_{12}H_{14}N_2O_3$	116	61.53/**60.98**	6.02/**6.13**	11.96/**11.83**
2c	Cl	61%	$C_{11}H_{11}ClN_2O_2$	119	55.36/**55.31**	4.65/**4.60**	11.74/**11.63**
3a	Br	65%	$C_{17}H_{13}BrN_6O_4$	131	45.86/**44.90**	2.94/**2.27**	18.88/**18.27**
3b	OCH_3	72%	$C_{18}H_{16}N_6O_5$	125	54.54/**54.60**	4.07/**4.91**	21.20/**21.10**
3c	Cl	70%	$C_{17}H_{13}ClN_6O_4$	130	50.95/**50.27**	3.27/**3.67**	20.97/**21.30**
3d	Br	69%	$C_{11}H_{10}BrN_3O$	85	47.16/**47.00**	3.60/**3.52**	15.00/**15.95**
3e	OCH_3	64%	$C_{12}H_{13}N_3O_2$	76	62.33/**62.03**	5.67/**5.61**	18.17/**18.10**
3f	Cl	69%	$C_{11}H_{10}ClN_3O$	91	56.06/**56.13**	4.28/**4.30**	17.83/**17.80**

2.2 Synthesis of 1-(2,4-dinitrophenyl)-3,5-dimethyl-4-(phenyldiazenyl)-1H-pyrazole (3a-c)

A mixture of 3-(2-4-substituted-phenylhydrazono)pentane-2,4-dione (0.01 mol) and 2,4 dinitrophenyl hydrazine (0.01 mol) and glacial acetic acid added in R B flask and refluxed for about 4-5 hours. The resulting mixture obtained was concentrated and allowed to cool, filtered, washed, dried and recrtystallised from ethanol.

2.3 Synthesis of 3,5-dimethyl-4-(phenyldiazenyl)isoxazole (3d-f)

A mixture of 3-(2-4-substituted-phenylhydrazono)pentane-2,4-dione (0.01 mol), hydroxylamine hydrochloride (0.01 mol) and glacial acetic acid (15 ml) in RB flask refluxed for about 4-5 hours. The reaction mixture was concentrated and allowed to cool. The solid obtained was filtered, washed, dried and recrystalised from ethanol [11].

III. RESULTS & DISCUSSION

All the synthesized compounds found to be pure and their melting point can be confirmed after repeated melting point taken in laboratory. The molecular formula of all compounds can be finalized with the help of elemental analysis and the molecular ion peak as well as fragment peaks obtained in mass spectroscopic technique. The results obtained by various spectroscopic techniques consistent with the structure of synthesized compounds. All the results obtained from IR, ^{1}H-NMR and mass spectra indicates below.

3-(2-4-bromophenylhydrazono)pentane-2,4-dione (2a)

IR (KBr) ν_{max}: cm^{-1} : 3397(-NH), 3064(-Ar-CH), 2989(-Al-CH), 1689(-C=O), 1418(-C=N), 1512(-C=C): ^{1}H-NMR (DMSO-d_6) δ: 14.4(1H,s,NH), 7.4(2H,d,Ar-H), 6.9(2H,d,Ar-H), 2.5(3H,s,CH_3); MS: m/z- 281[M^+]

3-(2-4-methoxyphenylhydrazono)pentane-2,4-dione (2b)

IR (KBr) ν_{max}: cm^{-1} : 3395(-NH), 3067(-Ar-CH), 2985(-Al-CH), 1690(-C=O), 1417(-C=N),1513(-C=C): ^{1}H-NMR (DMSO-d_6) δ: 14.5(1H,s,NH), 7.2(2H,d,Ar-H), 6.7(2H,d,Ar-H), 2.6(3H,s,CH_3); MS: m/z- 234[M^+]

3-(2-4-chlorophenylhydrazono)pentane-2,4-dione (2c)

IR (KBr) ν_{max}: cm^{-1} : 3390(-NH), 3070(-Ar-CH), 2990(-Ar-CH), 1692(-C=O), 1416(-C=N),1515(-C=C): ^{1}H-NMR (DMSO-d_6) δ: 14.3(1H,s,NH), 7.2(2H,d,Ar-H), 6.6(2H,d,Ar-H), 2.8(3H,s,CH_3); MS: m/z- 236[M^+]

1-(2,4-dinitrophenyl)-3,5-dimethyl-4-(bromophenyldiazenyl)-1H-pyrazole (3a)

IR (KBr) ν_{max}: cm^{-1} : 3047(-Ar-CH), 2927(-Ar-CH), 1692(-C=O), 1408(-C=N),1577(-C=C), 1142(-C-O): ^{1}H-NMR (DMSO-d_6) δ: 7.1(2H,m,Ar-H), 7.8(2H,m,Ar-H), 2.4(3H,s, CH_3), 2.7(3H,s,CH_3); MS: m/z- 445[M^+]

1-(2,4-dinitrophenyl)-3,5-dimethyl-4-(methoxyphenyldiazenyl)-1H-pyrazole (3b)

IR (KBr) ν_{max}: cm^{-1} : 3045(-Ar-CH), 2929(-Ar-CH), 1690(-C=O), 1412(-C=N),1580(-C=C), 1141(-C-O): ^{1}H-NMR (DMSO-d_6) δ: 7.2(2H,m,Ar-H), 7.8(2H,m,Ar-H), 2.7(3H,s, CH_3), 2.8(3H,s,CH_3); MS: m/z- 397[M^+]

1-(2,4-dinitrophenyl)-3,5-dimethyl-4-(chlorophenyldiazenyl)-1H-pyrazole (3c)

IR (KBr) ν_{max}: cm^{-1} : 3044(-Ar-CH), 2925(-Ar-CH), 1695(-C=O), 1410(-C=N),1580(-C=C), 1137(-C-O): ^{1}H-NMR (DMSO-d_6) δ: 7.5(2H,m,Ar-H), 7.6(2H,m,Ar-H), 2.3(3H,s, CH_3), 2.5(3H,s,CH_3); MS: m/z- 402[M^+]

3,5-dimethyl-4-(bromophenyldiazenyl)isoxazole (3d)
IR (KBr) ν_{max}: cm^{-1} : 3051(-Ar-CH), 2925(-Ar-CH), 1680(-C=O), 1420(-C=N),1577(-C=C), 1142(-C-O): ^{1}H-NMR (DMSO-d_6) δ: 7.2(2H,m,Ar-H), 7.8(2H,m,Ar-H), 2.4(3H,s, CH_3), 2.8(3H,s,CH_3); MS: m/z- 279[M^+]

3,5-dimethyl-4-(methoxyphenyldiazenyl)isoxazole (3e)
IR (KBr) ν_{max}: cm^{-1} : 3053(-Ar-CH), 2931(-Ar-CH), 1685(-C=O), 1417(-C=N),1570(-C=C), 1142(-C-O): ^{1}H-NMR (DMSO-d_6) δ: 7.1(2H,m,Ar-H), 7.8(2H,m,Ar-H), 2.3(3H,s, CH_3), 2.7(3H,s,CH_3); MS: m/z- 233[M^+]

3,5-dimethyl-4-(chlorophenyldiazenyl)isoxazole (3f)
IR (KBr) ν_{max}: cm^{-1} : 3045(-Ar-CH), 2927(-Ar-CH), 1689(-C=O), 1418(-C=N),1575(-C=C), 1142(-C-O): ^{1}H-NMR (DMSO-d_6) δ: 7.1(2H,m,Ar-H), 7.8(2H,m,Ar-H), 2.4(3H,s, CH_3), 2.9(3H,s,CH_3); MS: m/z- 230[M^+]

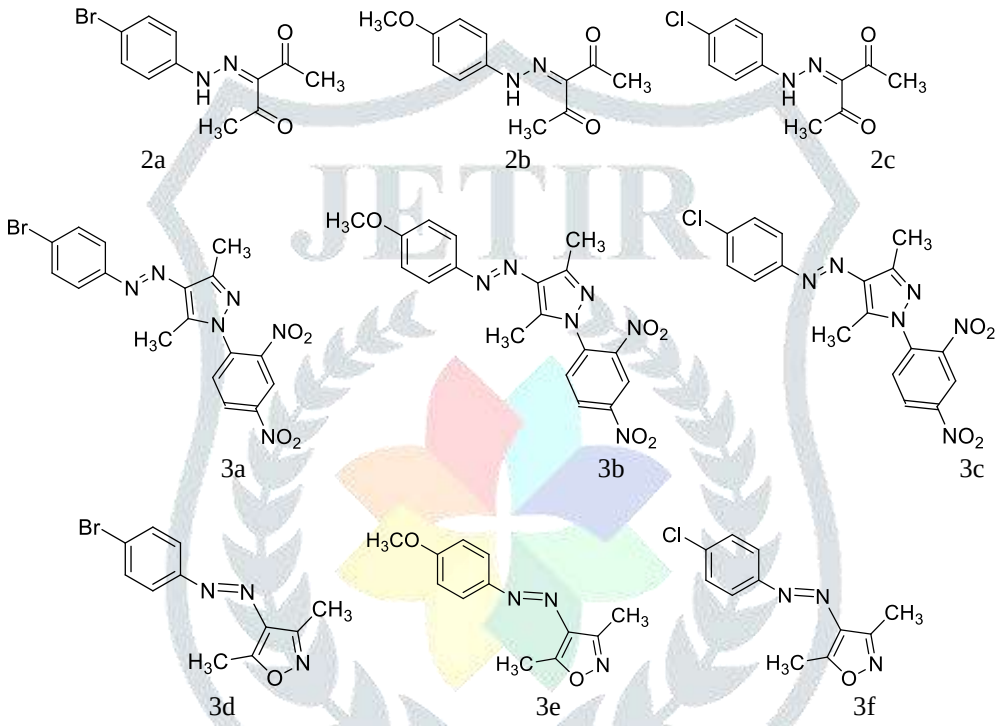


Fig 2 Structure of Synthesized Compounds

IV. CONCLUSION

In present study some azopyrazoles and isoxazoles derivatives were synthesized and found to be pure. These compounds were characterized on the basis of melting point, elemental analysis, IR, mass and ^{1}H-NMR spectroscopic techniques. The data obtained by spectroscopic techniques is matches with the structure of all compounds. Elemental analysis and molecular ion peak obtained from mass spectrum of compounds helpful for the determination of molecular formula for all compounds.

V. ACKNOWLEDGEMENT

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VI. REFERENCES

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