Synthesis and Characterisation of Certain Medicinally Important Novel Pyrazolin-5-ones

Eczacılıkta Önemli Yeni Bazı Pirazolin-5-on Bileşiklerinin Sentezi ve Karakterizasyonu

Research Article

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ABSTRACT

N-(Benzene sulfonyl)-3-methyl-4-(substistuted-arylhydrazono)-pyrazolin-5-ones have been synthesized by the reaction between diazonium acetoacetic ester and benzene sulfonyl hydrazide. Pyrazolin-5-ones so obtained were characterized by elemental analysis, IR, ^{1}H NMR and mass spectra.

Key Words
Pyrazolin-5-ones, characterization, elemental analysis, IR, ^{1}H NMR and Mass spectral analysis.

ÖZET

N-(benzen sülfonil)-3-metil-4-(substite-arilhidrazon)-pirazolin-5-one bileşikleri, diazonyum asetoasetik ester ve benzen sülfonil hidrazidi reaksiyona sokmak suretiyle sentezlenmiştir. Bu şekilde elde edilen pirazolin-5-on bileşikleri elementel analiz, IR, ^{1}H NMR ve kütle spektrumları ile karakterize edilmiştir.

Anahtar Kelimeler
Pirazolin-5-on bileşikleri, karakterizasyon, elementel analiz, IR, ^{1}H NMR ve Kütle Spektrum Analizi.

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INTRODUCTION

Pyrazolin-5-ones represent important class of heterocyclic compounds possessing wide range of biological activities. Incorporation of hydrazono [1]/azo [2,3] group enhances the biological activity of heterocycles. Their diverse biological activities include antioxidant [4], vasorelaxant [5], antitumor [6], antiviral [7], analgesic [8,9], antiinflammetaory [10], antibacterial [11,12] activities. However, in the recent years, the excessive use of antibacterial agents has resulted in the development of resistance to these drugs by microorganisms [13]. Thus, antibacterial drug discovery continues to be a vital arena [14]. A number of such compounds have been synthesized by these laboratories [15, 16] The main objective of the present study is to synthesize different pyrazolin derivatives.

APPARATUS and CHEMICALS

All reagents used were of analytical reagent grade procured from Merck, India. The working solutions were prepared by using double distilled water.

The elemental analysis data for compounds under study was obtained from Central Drug Research Institute, Lucknow, India. IR spectral studies were carried out using Perkin-Elmer 983 G spectrometer with KBr pellets. Mass spectral studies were carried out using VG 70-70H Mass spectrometer.

RESULTS and DISCUSSION

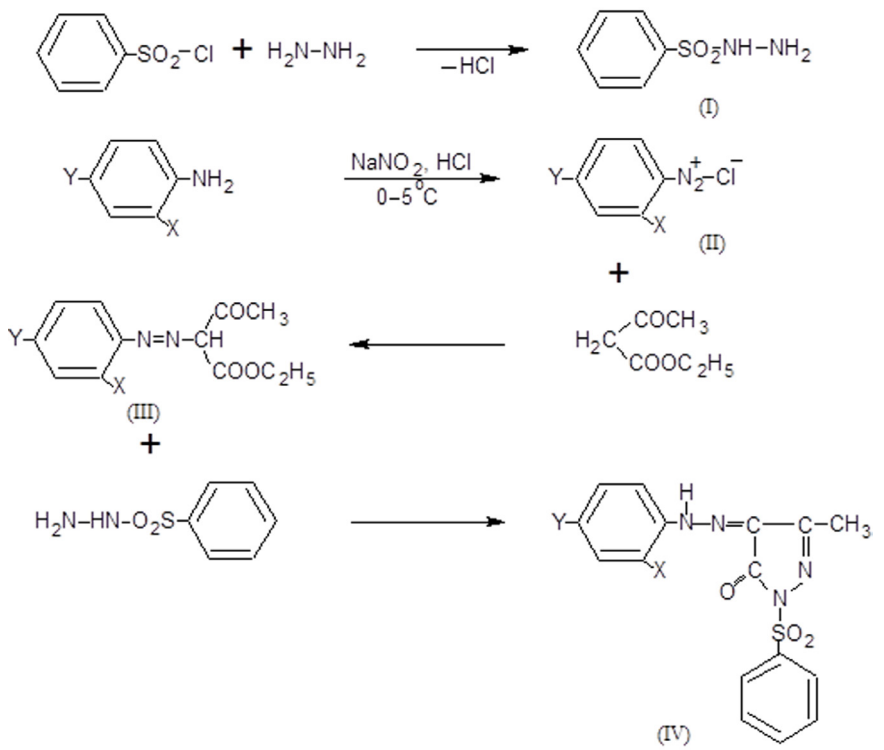
Synthesis of pyrazolin-5-ones

Preparation of toluene sulfonyl hydrazide (Scheme 1, I) [17]

A solution of benzene sulfonyl chloride in acetone and appropriate amount of hydrazine hydrate in acetone were treated with 5% NaOH solution. The mixture was shaken vigorously for ten minutes, cooled and poured into 1:1 HCl. The precipitate formed was filtered, washed with water and recrystalised from ethyl alcohol.

Preparation of substituted phenyl diazonium chloride (Scheme 1, II) [18]

The required amount of substituted aryl amine was dissolved in a suitable volume of dilute hydrochloric acid (1 Water: 3 HCl). The solution



Scheme 1. Synthesis pyrazolin-5-ones.

Table 1. Physical characteristics of pyrazolin-5-ones synthesized.

#	Substituent	Color	Melting point (°C)	#	Substituent	Color	Melting point (°C)
1	X=H, Y=H	Orange	118-119	7	X=H, Y=CH_3	Yellow	301-302
2	X=CH_3, Y=H	Yellow	243-244	8	X=H, Y=OCH_3	Yellow	304-305
3	X=OCH_3, Y=H	Yellow	215-216	9	X=H, Y=OH	Black	210-211
4	X=OH, Y=H	Black	261-262	10	X=H, Y=Cl	Yellow	268-269
5	X=Cl, Y=H	Yellow	210-211	11	X=H,Y=NO_2	Orange	181-182
6	X=NO_2, Y=H	Orange	224-225				

Table 2. Elemental analysis data of substituted arylhydrazono pyrazolin-5-ones.

S.No.	Compound	Mol. Wt.	Elemental analysis Found (Cal) %				
			C	H	N	S	Cl
1	X=H, Y=H	348	50.14 50.19	5.09 5.27	14.87 14.63	8.65 8.38	
2	X=CH_3, Y=H	362	53.30 53.33	5.49 5.79	14.73 14.63	8.60 8.38	
3	X=OCH_3, Y=H	378	53.83 53.33	5.84 5.79	14.95 14.63	8.50 8.38	
4	X=OH, Y=H	364	50.63 50.19	5.47 5.27	14.84 14.63	8.94 8.38	
5	X=Cl, Y=H	383	50.99 50.19	4.98 5.00	14.87 14.63	8.50 8.38	9.46 9.26
6	X=NO_2, Y=H	393	59.61 50.19	5.26 5.00	18.09 18.29	8.67 8.38	
7	X=H, Y=CH_3	362	53.40 53.33	5.59 5.79	14.83 14.63	8.50 8.38	
8	X=H, Y=OCH_3	378	53.73 53.33	5.94 5.79	14.85 14.63	8.61 8.38	
9	X=H, Y=OH	364	50.54 50.19	5.54 5.27	14.71 14.63	8.65 8.38	
10	X=H, Y=Cl	383	50.84 50.19	5.11 5.00	14.89 14.63	8.54 8.38	9.35 9.26
11	X=H,Y=NO_2	393	59.42 50.19	5.32 5.00	18.31 18.29	8.56 8.38	

obtained was cooled to 0°C and a little excess of an aqueous solution of sodium nitrite was added. The addition of little excess of sodium nitrite solution stabilizes the diazonium salt.

Preparation of aryl diazonium acetoacetic esters (Scheme 1, III) [19]

The respective diazonium chloride solution was added to an ice cold solution of mixture of sodium acetate and acetoacetic ester solution in methanol and the mixture was cooled. The addition of corresponding diazonium chloride was continued till crystals were separated out. The crystals were filtered, washed with water, dried and recrystallized from 1:1 dimethylformamide.

Synthesis of N-(Benzene sulfonyl)-3-methyl-4-(substituted-arylhydrazono)-pyrazolin-5-ones (Scheme 1, IV)

A mixture of appropriate amounts of diazonium acetoacetic ester and benzene sulfonyl hydrazide in ethanol was refluxed for four hours and cooled. The crystalline solid separated was filtered, washed with water, dried and recrystallized from dimethylformamide (1:1). The physical characteristics of the different compounds synthesized are presented in the Table 1.

Infrared spectral studies

The IR spectral details of the compounds are given in the Table 3.

Table 3. IR spectral data of substituted arylhydrazono pyrazolin-5-ones

Compound	1	2	3	4	5	6	7	8	9	10	11
Group	ν (cm^{-1})										
-NH-	3452	3448	3448	3440	3448	3447	3440	3448	3420	3432	3423
C-H (aromatic)	3050	3030	3028	3020	3084	3042	3020	3018	3050	3054	3022
C=O (cyclic)	1689	1686	1685	1680	1687	1701	1676	1681	1686	1684	1698
C = C (In aromatic nuclei)	1656, 1549, 1480	1654, 1544, 1475	1650, 1543, 1486	1640, 1560, 1488	1640, 1545, 1453	1614, 1575, 1501	1664, 1564, 1453	1661, 1523, 1468	1643, 1549, 1469	1640, 1546, 1467	1656, 1568, 1534
> C=N	1569	1565	1560	1559	1559	1593	1568	1558	1557	1561	1578
C-H (def)	1439	1436	1433	1431	1420	1448	1443	1446	1447	1432	1439
N = O (stretching)	----	----	----	----	----	1384	----	----	----	----	1378
S = O (Sym and Asym)	1269, 1167	1270, 1169	1269, 1165	1260, 1170	1269, 1189	1301, 1164	1268, 1178	1265, 1171	1263, 1158	1269, 1191	1289, 1172
S - aryl	1088, 1045	1086, 1040	1087, 1040	1080, 1030	1109, 1085	1048	1067, 1046	1078, 1056	1067, 1040	1134, 1067	1056
C = C (def) (out of plane)	685	683	680	668	680	678	686	686	684	685	686
C - Cl (stretching) (aromatic ring)	----	----	----	----	590	----	----	----	----	601	----

Table 4. ^{1}H NMR Spectral data of substituted arylhydrazono pyrazolin-5-ones.

	δ (ppm)				
Compound	$-CH_3$ (singlet)	$-CH_3/-OCH_3/-OH$ Attached to the aromatic ring	$-C_6H_4(R)$ (multiplet)	$-SO_2C_6H_5(R)$ (multiplet)	-NH-N=C < (singlet)
1	1.4	----------	6.9-7.1	7.4-8.1	13.4
2	1.4	2.4 ($-CH_3$)	7.1-7.3	7.6-8.2	13.4
3	1.4	4 ($-OCH_3$)	6.8-7.2	7.5-8.2	13.4
4	1.4	5.2 (-OH)	7.1-7.4	7.6-8.3	13.4
5	1.4	----------	7.0-7.4	7.6-8.2	13.4
6	1.4	----------	7.3-7.7	8.0-8.3	13.4
7	1.4	2.4 ($-CH_3$)	7.1-7.4	7.5-8.1	13.4
8	1.4	4 ($-OCH_3$)	6.8-7.3	7.5-8.1	13.4
9	1.4	5.2 (-OH)		7.5-8.3	13.4
10	1.4	----------	7.0-7.4	7.6-8.2	13.4
11	1.4	----------	7.3-7.7	7.9-8.1	13.4

The spectra showed a weak >C=N stretching frequency band at around 1565 cm^{-1}. The characteristic absorption band for –NH– group in –NH–N=C< was appeared in the region 3448 cm^{-1}. The band at around 1270 and 1400 cm^{-1} was due to the sulphone group. The band at around 1685-1701 cm^{-1} was attributed to the cyclic >C=O group.

^{1}H NMR spectral studies

The results pertaining to ^{1}H NMR spectral studies are given in the Table 4. The ^{1}H NMR spectra clearly distinguished the 2 and 4 substituted pyrazolin-5-ones (Figure 1).

Mass spectral studies

Major fragmentation pattern observed for N-(Benzene sulfonyl)-3-methyl-4-(substistuted-arylhydrazono)-pyrazolin-5-ones was due to the loss of SO_2, $-SO_2C_6H_5$, N_2, CO and $-C_6H_5$. The fragmentation pattern is presented in the Scheme 2.

CONCLUSION

N-(Benzene sulfonyl)-3-methyl-4-(substistuted-arylhydrazono)-pyrazolin-5-ones have been synthesized by the reaction between diazonium acetoacetic ester and benzene sulfonyl hydrazide.

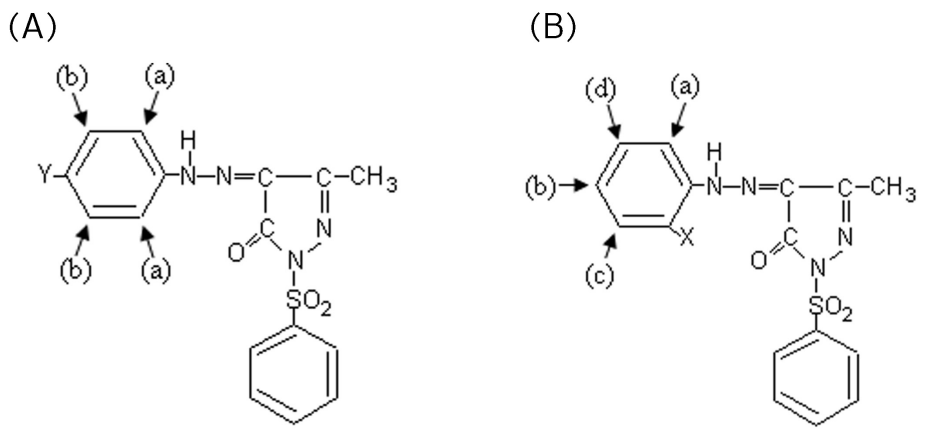
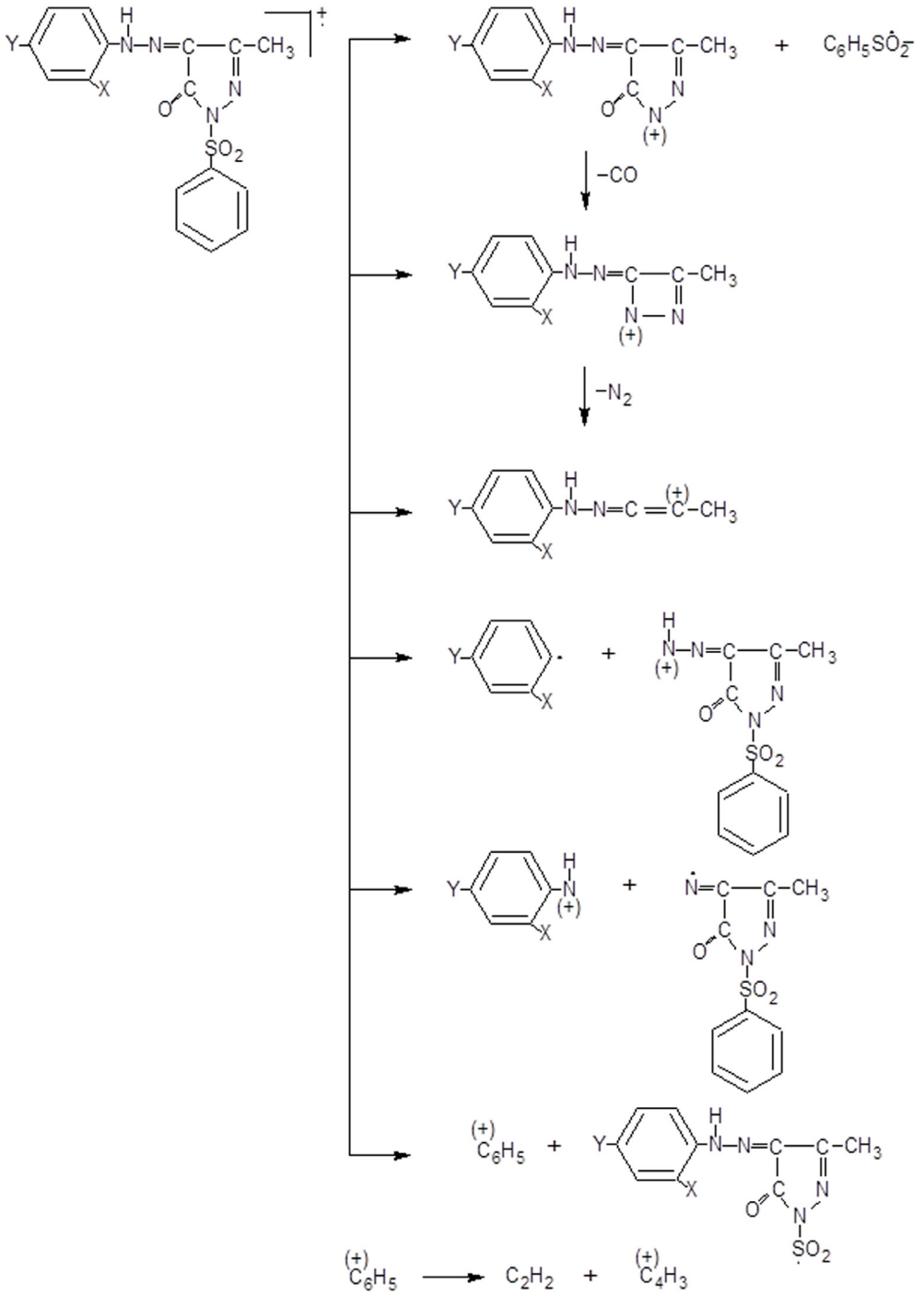


Figure 1. (A) (a) and (b) are doublets each one of them corresponds to 2 protons. (B) (a) and (c) are doublets and each one of them corresponds to 1 proton, (b) and (d) are multiplets each one of them corresponds to 1 proton.



Scheme 2. Fragmentation pattern of pyrazolin-5-ones

2-substituted (2-6) and 4-substituted pyrazolin-5-ones (7-11) are clearly distinguished by melting points and ^{1}H NMR spectra. The compounds were characterized by elemental analysis, IR, NMR and mass spectra.

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