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Synthesis and Structure Elucidation of Some Newer Schiff Bases Derived from Pyrimidine-5-carbonitrile Moiety

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ABSTRACT:
The condensation of 1-ethyl-2-(ethylthio)-1,6-dihydro-6-oxo-4-phenylpyrimidine-5-carbonitrile with hydrazine hydrate to yield 1-ethyl-2-hydrazinyl-1,6-dihydro-6-oxo-4-phenylpyrimidine-5-carbonitrile, which on further reaction with different aromatic aldehydes give 2-benzylidenehydrazinyl)-1-ethyl-1,6-dihydro-6-oxo-4-phenylpyrimidine-5-carbonitrile. All the final products were elucidated by ^{1}H NMR, Mass spectroscopy and IR spectra.

KEYWORDS: Pyrimidines, Benzylidinehydrazinyl; Benzaldehyde.

I. INTRODUCTION

Schiff bases are important class of compounds of medicinal chemistry. A German Scientist Hugo Schiff (1864-1915) discovered Schiff bases.[1] Schiff bases can be synthesized by treating aromatic or aliphatic primary amine with carbonyl carbon (ketones or aldehydes) under specific conditions.[2]

Schiff base, mainly those associated with heterocyclic moiety possess various pharmacological and biological activities, like cytotoxic effects, anti-fungal, anti-bacterial, anti-convulsant, anti-malarial, anti-inflammatory and antioxidant.[3-10] The large number of Schiff bases are represented by the general formula (R_1R_2) C=N-R_3 while few of these having general formula $R_1CH=NR_2$ in which carbon is attached with a hydrogen atom instead of an alkyl or aryl group.[11]

The biological activities of the Schiff bases mainly depend upon the type of the substituent linked to the aromatic ring. Schiff bases gained a great attention during recent years due to their remarkable biological and catalytic applications.[12]

Moreover, there are some reported drugs having heterocyclic Schiff base.[13-15]

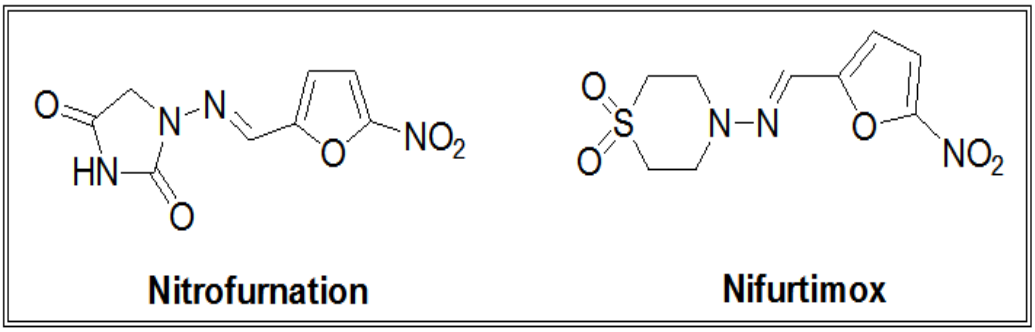

Figure-1 Some Heterocyclic Schiff base drugs

II. EXPERIMENTAL

All the chemicals, solvents and reagents were purchased from Merck and Sigma- Aldrich. All melting points are uncorrected and were taken in open capillary tubes, using a digital melting point apparatus. Follow up of the reactions and checking the purity of the compounds were made by TLC on silica gel percolated aluminium sheets and the spots were detected using UV lamp at λ254 nm. ^{1}H NMR spectra were determined by Bruker-Avance-II (400 MHz) using DMSO-d6 as a solvent and TMS as an internal standard and the chemical shift are reported as parts per million (ppm). Mass spectra were determined on Schimadzu QP 2010 Spectrometer. Infrared spectra were recorded on

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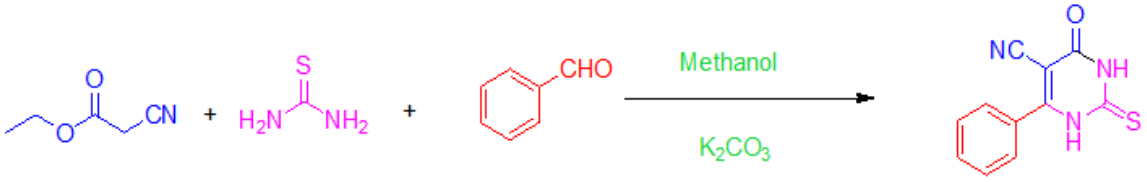
Schimadzu-FTIR-8400 Fourier transform, infrared spectrometer using KBr disc technique.

2.1 Synthesis of 1, 2, 3, 4-tetrahydro-4-oxo-6-phenyl-2-thioxopyrimidine-5-carbonitrile[16](Compound-I)

A mixture of thiourea (0.95 g, 0.01 mol), ethyl cyanoacetate (1.35 ml, 0.01 mol) benzaldehyde (1.3 ml, 0.01 mol), and potassium carbonate (1.75 g, 0.01 mol) in methanol (100 ml) was refluxed for 5 hours. The reaction mixture was cooled, poured into ice cold water. The formed precipitate was filtered, washed several times with water, dried and recrystallized with absolute alcohol.

Yield 66 % m.p. 190°C MS (EI) m/z (M+) 229; FTIR (KBr) (cm-1):1627(- CO), 2206(-CN), 3324(-CH3 Asym.), 2993 (-CH3 Sym.); 1H NMR (δ ppm) (400 MHz, DMSO) δ 1H NMR: δ 11.59 (s, 2H, NH), δ 7.48-7.74 (m,5H, Ar-H). Anal. Found C, 57.63 H, 3.08 N, 18.33 S,13.99 $C_{11}H_7N_3OS$ requires C, 56.44; H, 3.10; N, 17.65; O, 6.47; S, 12.95

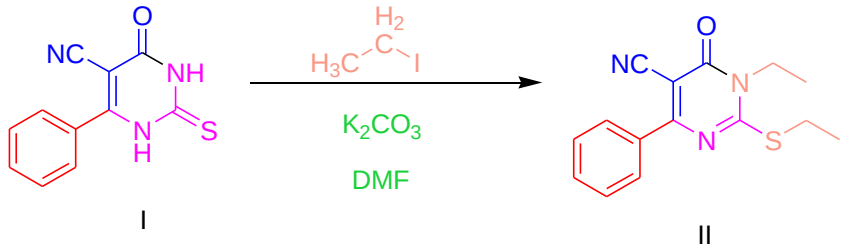


I

2.2. Synthesis of 1-ethyl-2-(ethylthio)-1,6-dihydro-6-oxo-4-phenylpyrimidine-5-carbonitrile[17](Compound-II)

A mixture of compound I (3.22 g, 0.014 mol), potassium carbonate (3.86 g, 0.028 mol) and (2.2 ml, 0.028 mol) ethyl iodide in dimethyl formamide (20 mL) was stirred 5-6 hours at room temperature. The contents were poured into water, filtered, washed with water and crystallized with absolute alcohols.

Yield 58 % m.p. 72°C MS (EI) m/z (M+) 285; FTIR (KBr) (cm-1): 1651 (C=O), 2214 (CN), 2939(C–H aliphatic); 1H-NMR δ(ppm) (400 MHz, DMSO): δ 1.29 (t,3H, SCH2-CH3), 1.36 (t,3H, N-CH2- CH3), 3.34 (q,2H, S-CH2-CH3), 4.04 (q,2H, N-CH2- CH3), 7.64-7.97 (m,5H, Ar-H). Anal. Found C, 60.25 H, 5.7 N,14.6 O, 5.1 S,11.8 $C_{15}H_{15}N_3OS$ requires C, 62.92; H, 5.96; N, 14.62; O, 5.57; S, 11.16.



I II

2.3. Synthesis of 1-ethyl-2-hydrazinyl-1,6-dihydro-6-oxo-4-phenylpyrimidine-5-carbonitrile (Compound – III)[18]

A mixture of 1-ethyl-2-(ethylthio)-1,6-dihydro-6-oxo-4-phenylpyrimidine-5-carbonitrile (0.01 mol) and hydrazine hydrate (3ml) was refluxed for 6 hours in absolute alcohol (30ml).The contents were poured into water, filtered, washed with water and crystallized with absolute alcohols.

Yield 45 % m.p. 225°C MS (EI) m/z (M+) 242; FTIR (KBr) (cm-1): 1651 (C=O), 2206 (CN), 2939(C–H aliphatic); 1H-NMR δ(ppm) (400 MHz, DMSO): δ 1.14 (t,3H, N-CH2-CH3), 3.93 (q,2H, N-CH2-CH3), 7.93 (d, 2H –NH-NH_2) δ 9.19 (s, 1H –NH) δ 7.49-7.51 (m,5H, Ar-H). Anal. Found C, 60.69; H, 5.88; N, 27.22; O, 6.22$C_{12}H_{12}N_5O$ requires C, 61.59; H, 5.72; N, 26.26; O, 5.10

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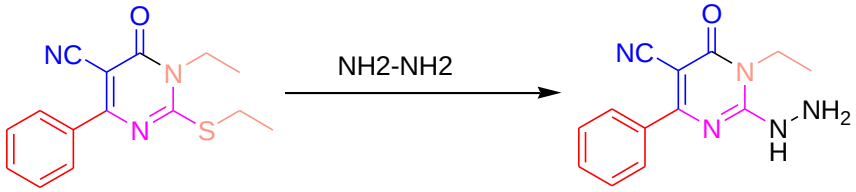
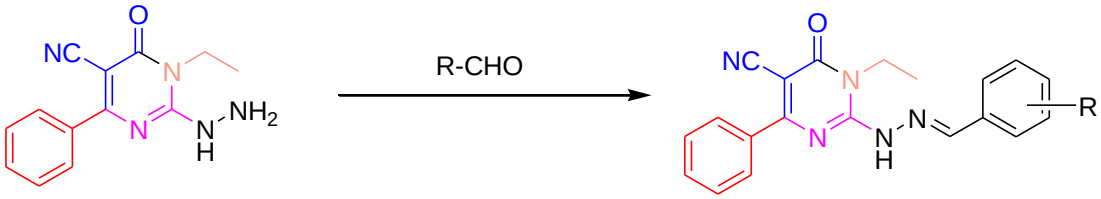


II III

2.4. Synthesis of 2-(Substituted benzylidenehydrazinyl)-1-ethyl-1,6-dihydro-6-oxo-4-phenylpyrimidine-5-carbonitrile (Compound-IV)

A mixture of 1-ethyl-2-hydrazinyl-1,6-dihydro-6-oxo-4-phenylpyrimidine-5-carbonitrile (0.01 mol) and different aromatic aldehydes (0.01 mol) was refluxed for 3 hours in absolute alcohol. The contents were poured into water, filtered, washed with water and crystallized with absolute alcohols.



III IV

Table -1 Physical Parameter of series compounds

Comp.	R	M.F.	M.W.	MP^{0}C	Yield%	N%
BS-1	-4F	$C_{20}H_{16}FN_5O$	361	>280	55	17.60
BS-2	-4-OH	$C_{20}H_{17}N_5O_2$	359	250	58	19.38
BS-3	-2-Cl	$C_{20}H_{16}ClN_5O$	377	240	52	18.44
BS-4	-4-Br	$C_{20}H_{16}BrN_5O$	422	>300	48	16.51
BS-5	-4-OCH_3	$C_{21}H_{19}N_5O_2$	373	170	56	18.65
BS-6	-3,4-$(OCH_3)_2$	$C_{22}H_{21}N_5O_3$	403	175	56	17.27
BS-7	-3-OCH_3-4-OH	$C_{21}H_{19}N_5O_3$	389	165	50	17.89
BS-8	-4-Cl	$C_{20}H_{16}ClN_5O$	377	>300	46	18.44
BS-9	-4-CH_3	$C_{21}H_{19}N_5O$	357	168	62	19.48
BS-10	-C_6H_5	$C_{20}H_{17}N_5O$	343	190	50	20.28

III. SPECTRAL ANALYSIS

^{1}H NMR

^{1}H NMR spectrum of synthesized compounds showing proton peaks of different groups at their reported region with appropriate splitting.

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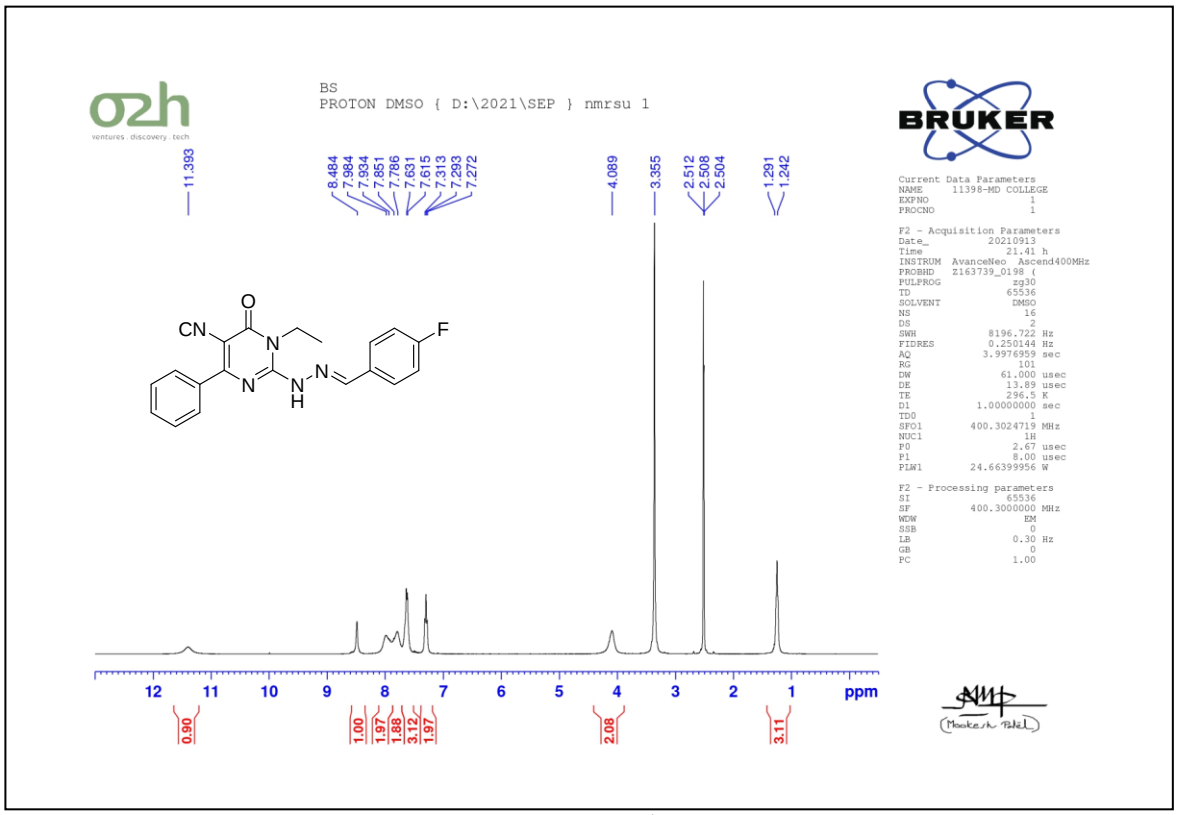

Table – 2 Spectral analysis of ^{1}H NMR

Signal Number	δ ppm	Relative no. of Protons	Multiplicity	Inference
1	1.24	3H	Triplet	-$CH_2C\underline{H}_3$
2	4.08	2H	Quartet	-$C\underline{H}_2CH_3$
3	7.2-7.9	9H	Multiplet	Ar - <u>H</u>
4	8.48	1H	Singlet	-C<u>H</u>
5	11.39	1H	Singlet	- N<u>H</u>

Mass spectra

The mass spectrum of synthesized compound gives M+1 and M-1 ion peaks in agreement with molecular weight of the respective compound.

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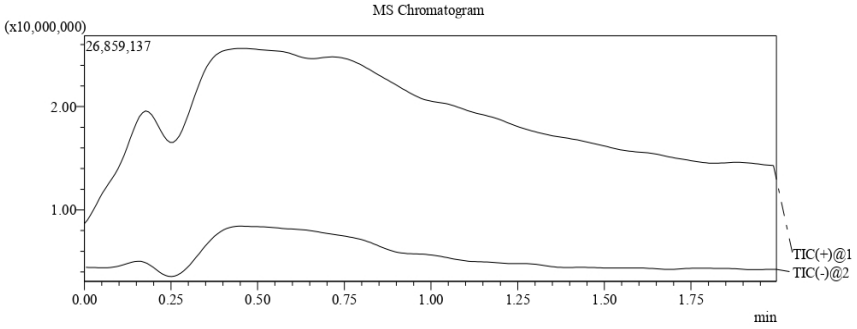
Sample Information

Acquired by	: System Administrator
Date Acquired	: 01-Dec-21 8:17:19 PM
Sample Type	: Unknown
Sample Name	: BS
Tray#	: 1
Vial#	: 9
Injection Volume	: 2
Data File	: 011221-003.lcd
Method File	: 011221SCAN.lcm
Tuning File	: ESI_07102020.lct
Processed by	: System Administrator
Date Processed	: 01-Dec-21 8:20:59 PM

MS Chromatogram



MS Spectrum

Line#:1 R.Time:----(Scan#:----)
MassPeaks:11
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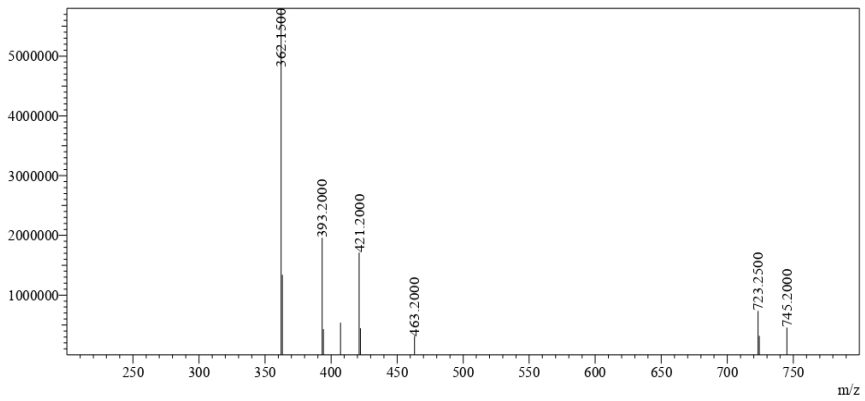
BG Mode:Averaged 0.000-0.150(1-35) Segment 1 - Event 1



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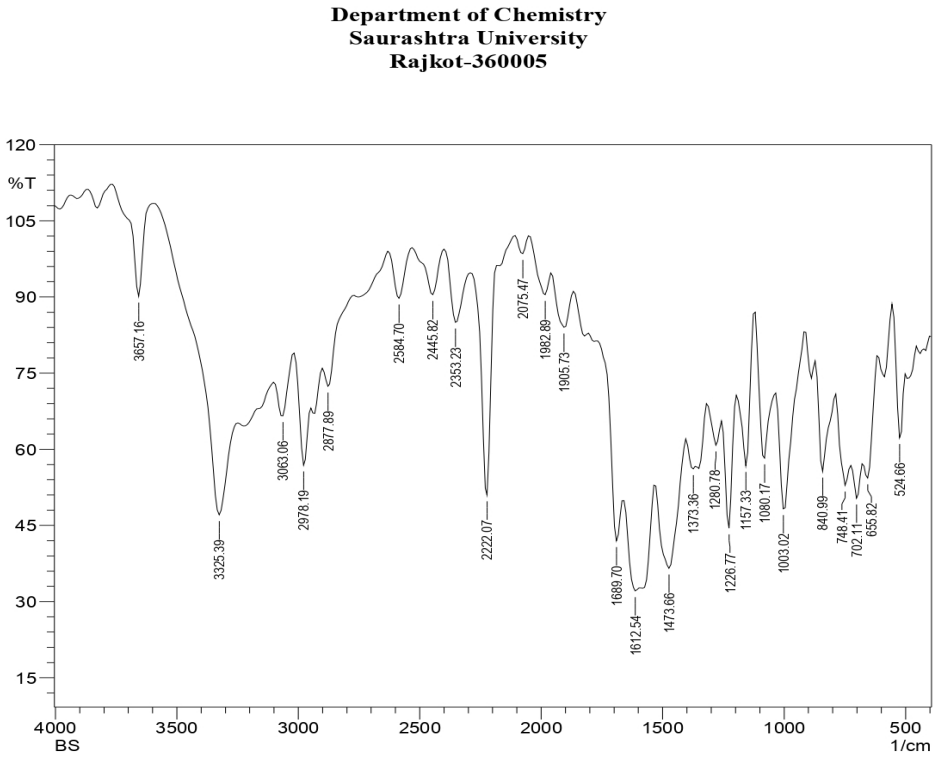
IRspectra

The infra-red spectrum of desired compound is given show the aromatic (-C-H-) stretching frequencies lie between 2993-3063cm^{-1}and C=N + C=C stretching was observed in the range of 1443 cm^{-1}. C=N stretching 2222 cm^{-1}, C=O Str. 1689 cm^{-1}, C-Br Str.



IV. CONCLUSION

The characterization of Schiff base was mainly carried out by the presence of (-C=N-) imine group. Infrequently reported 2-Substituted benzylidenehydrazinyl derivative of 4-phenylpyrimidine-5- carbonitrile was prepared by the reaction of 1-ethyl-2-hydrazinyl-1,6-dihydro-6-oxo-4-phenylpyrimidine-5-carbonitrile with different aromatic aldehydes. All the synthesized compounds are obtained in good yield, and characterization of newly synthesized compounds was carried out by Mass spectroscopy, IR and ^{1}H NMR. The spectral data reveal good agreement with the synthesized compounds.

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