Synthesis, Biological Activities and Spectral Characterization of some new 2-amino-4, 6-diethyl-5-(4'-Sulphonamoyl) Azopyrimidine derivatives of Sulphonamides

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Abstract

2-amino-4,6-diethyl-5-(4'-sulphonamoyl)azopyrimidines were synthesized by condensation of 2-(4'-sulphonamoyl)hydrazono-3,5-heptanedione with Guanidine Nitrate in the molar ratio 0.01M yield the corresponding synthesized compounds respectively. The following sulpha drugs viz. (Sulphanilamide, Sulphaguanidine, Sulphadiazine Sulphadimidine, Sulphathiazole and Sulphapyridine etc.) were used in this synthesis. The structure of synthesized compounds was elucidated by elemental analyses, UV-vis, FT-IR, ^{1}H, NMR and mass spectrometry and purity of newly synthesized compounds were checked by TLC.The New products have been assessed for antifungal and antibacterial activities against certain microorganism.

Keywords: Sulpha Drugs, 3, 5-Heptanedione, Guanidine Nitrate, UV-vis; FT-IR; and ^{1}H, NMR; spectrometry, antifungal and antibacterial activities.

Introduction

The pyrimidines is widely distributed in every living cell in the form of cytidine, thymine and uracil in nucleic acid so they are involved in various biological processes [1-2]. Some pyrimidine derivatives have biological and diverse type of pharmacological activities [3-8]. Sulphonamides are frequently used in medicine on account of their antibacterial activity and incorporation of azo group further enhances the biological activity of these drug.Condensed pyrimidine derivatives have been reported as anti-microbial [9], analgesic, anti-viral, anti-inflammatory [10], anti-HIV [11], anti-tubercular [12], anti-tumour [13], anti-neoplastic [14], anti-malarial [15], diuretic [16], cardiovascular [17] agents. Their compounds are also used as hypnotic drugs for the nervous system [18], calcium-sensing receptor antagonists [19] and also for antagonists of the human A2A adenosine receptor [20]. Looking the importance of substituted pyrimidines a series of new arylazopyrazoles has been synthesized for assessing their biological potentialities.

In the present study diazonium salt of sulphanilamide in which sodium acetate was used as catalyst were coupled with 3,5-heptanedione and resulting hydrazones(1a-f) were condenced with guanidine nitrate to obtain new arylazopyrimidines, 2-amino-4,6-diethyl-5-(4'-sulphonamoyl)azopyrimidines (2a-f). The synthesized compounds were adequately characterized by their elemental and spectral analysis.

Experimental

Materials and methods

Sulpha drugs viz.Sulphanilamide,Sulphaguanidine, Sulphadizine, Sulphadimidine Sulphathizole, guanidine nitrate, and 3,5-heptane dione were obtained from Sigma Aldrich. Some other chemicals and organic solvents (ethanol, methanol, diethyl ether, acetone, dimethylformamide (DMF) and dimethylsulfoxide (DMSO) were reagent grade and were used without futher purification.

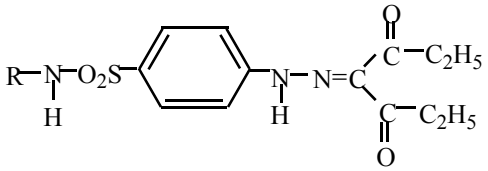
Physical measurements

The elemental analysis (C, H, N) was carried on a truspec CHN/ CHNS analyzer .The FT-IR spectra (250-4000cm^{-1}) of the compounds were recorded as KBr discs using Perkin Elmer-Spectrum RX-IFTIR instrument, the ^1H, NMR spectra of the compounds was obtained on BRUKER AVANCE II 400 NMR Spectrometer and Mass spectra was obtained on WATERS, Q-TOF MICROMASS (LC-MS). Compounds were routinely checked for their purity on silica gel G-plates.

2.3 2-(4'-sulphonamoyl) hydrazono-3, 5-heptanedione (1a-f)

The sulphanilamide (0.01 mol; 1.72 gm) was dissolved in a mixture of concentrated HCl (3ml) and water (4ml) and cooled to 0^0C in an ice salt bath. To this, cold aqueous solution of sodium nitrite (0.69 gm 0.01 mol) was added in small portions with constant stirring. Instantaneous formation of diazonium salt started. The diazonium salt so obtained was filtered in to already cooled solution mixture of sodium acetate (8gm) and coupled with 3, 5-heptane dione (0.01 mol; 1.01 gm) in ethyl alcohol (25 ml) and solution was stirred vigorously. The resulting compound (1a) so obtained was washed thoroughly with cold water and recrystallized from ethyl alcohol, the colour of the synthesized compound was orange, m.p 207^0C yield (60%). The other hydrazono compounds (1b-f) of this series have been synthesized in the similar manner. And their characteristics have been given in Table-I (a-f).

Calculated for $C_{13}H_{17}N_30_4S$, C=50.2 %, H=5.3%, N=25.1% found C= 50.8%, H= 5.7%, N=19.60%,υ^{KBr}_{max} 3410 (NH_2) cm^{-1}, 1675 (C=N or C=N) cm^{-1}, 1645 (C=O) cm^{-1}, 1130 (SO_2) cm^{-1}, 3100 cm^{-1} (NH) cm^{-1} 1520 (-NH-N) $cm^{-1}$and 750 cm^{-1} ;(DMSO-d_6) 7.10-8.2 δ multiplate (substituted phenyl) 14.2 δ singlet (-NH Protons hydrogen bonding) .The following structure is assigned to the compound on the basis of spectral studies.

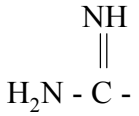
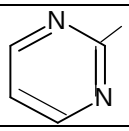
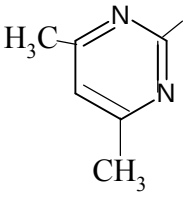
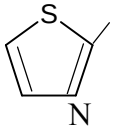
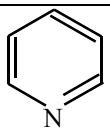


Synthesis 2-amino-4, 6-diethyl-5-(4'-sulphonamoy)azopyrimidine(2a-f)

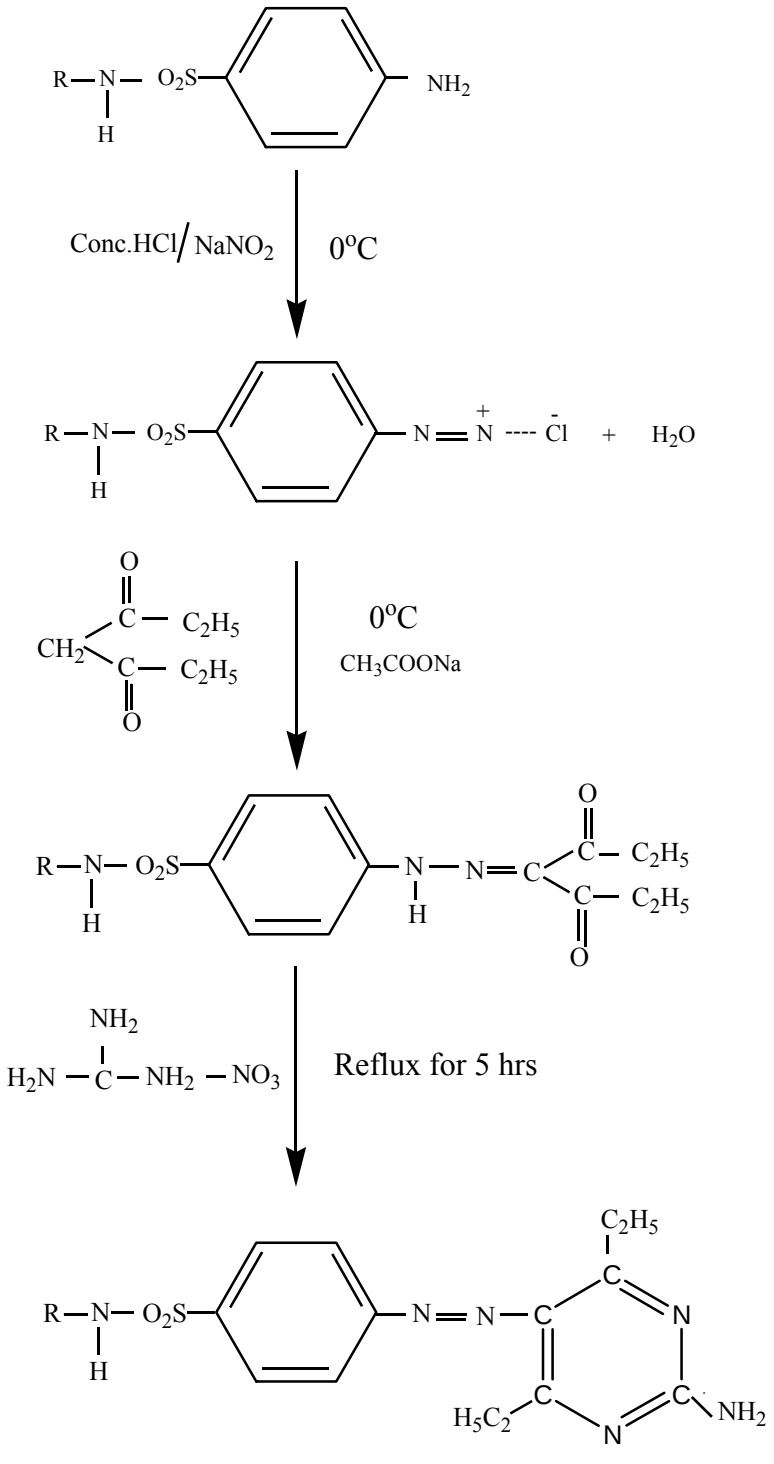
An alcoholic solution of 2-(4'-sulphonamoyl) hydrazono-3,5-heptanedione (0.004 mol) was added to a solution of guanidine nitrate (0.004 mol) in a methanolic 10 N NaOH (10 ml).

The mixture was refluxed for 5 hrs and than was left overnight. Solid product separated out was filtered and washed with methanol and hot water. It was recrystallised from DMF-ethanol mixture, orange needle crystals were obtained yield 60% M.P. 224^{0}C. Calculated for $C_{14}H_{18}N_6O_2S$ C =50.29%, H = 5.38%, N = 25.14% found C = 50.8, H = 5.9%, N = 25.7%. The following structure is assigned to the compound on the basis of spectral studies. The other compounds [2b-f] of this series have been synthesized in the similar manner.

The following drugs were used in the synthesis of 2-(4'-sulphonamoyl) hydrazono-3, 5- heptane dione and 2-amino-4, 6-diethyl-5-(4'-sulphonamoyl)azopyrimidines (1a-f to 2a-f).Where R represent various substituents, such as –

S.No.	-R	Compounds Name
1.	-H	Sulphanilamide
2.		Sulphaguanidine
3.		Sulphadiazine
4.		Sulphadimidine
5.		Sulphathiazole
6.		Sulphapyridine

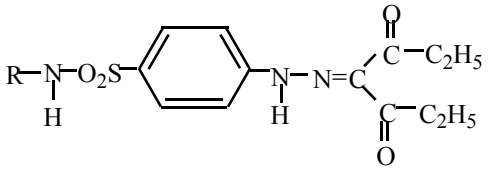
Reaction Scheme

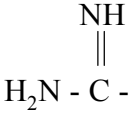
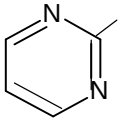
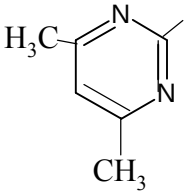
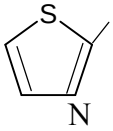
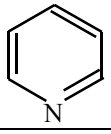


Results and discussion

Compounds were soluble in solvents like DMSO and DMF but insoluble in some common organic solvents. The compositions were established on the basis of analytical parameter (Table-I & II), spectral analysis (Table III, IV), and are discussed in detail in above section.

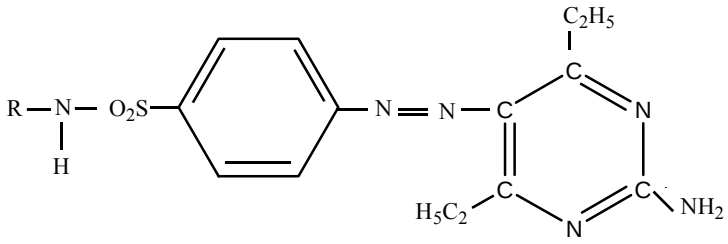
Table I (1a-f) Characteristics of 2-(4'-sulphonamoyl) hydrazono-3,5-heptane dione

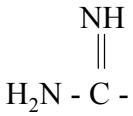
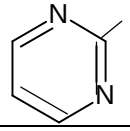
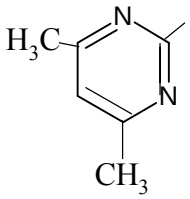
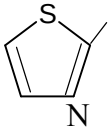
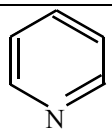


S.NO.	-R	Molecular Formula	Colour	M.P.(0^oC)	Yield (%)
1.	-H	$C_{13}H_{17}N_3O_4S$	Orange	207^0C	60%
2.		$C_{14}H_{19}O_4N_5S$	Golden yellow	215^0C	58%
3.		$C_{17}H_{19}O_4N_5S$	Dark yellow	200^0C	60%
4.		$C_{18}H_{20}N_5O_4S$	Yellow	205^0C	55%
5.		$C_{17}H_{19}O_4N_4S_2$	Orange	208^0C	60%
6.		$C_{18}H_{10}N_4O_4S$	Dark Orange	210^0C	55%

All compounds gave consistent C, H, and N analyses.

Table-II (2a-f) Characteristics of 2-amino-4,6-diethyl-5-(4'-sulphonamoyl)azopyrimidine



S.NO.	-R	Molecular Formula	Colour	M.P.0°C	Yield %
1.	-H	$C_{14}H_{18}N_6O_2S$	Orange	224^{0}C	60%
2.		$C_{15}H_{22}N_8O_2S$	Dark brown	228^{0}C	58%
3.		$C_{15}H_{24}N_8O_2S$	Radish yellow	238^{0}C	60%
4.		$C_{20}H_{27}N_8O_2S$	Dark yellow	232^{0}C	55%
5.		$C_{18}H_{25}N_7O_2S_2$	Dark Orange	240^{0}C	60%
6.		$C_{19}H_{27}N_7O_2S$	Radish-Orange	236^{0}C	55%

All compounds gave consistent C, H and N analyses.

Table-III (NMR Spectral data) Spectral data of 2-amino-4, 6-diethyl-5-(4'-sulphonamoyl)azopyrimidines

S.NO	Signal- δ Value	Assigned Structure
1.	2.48 (singlet)	(6H,S,CH_3),
2.	7.2-7.8 (Multiplate)	(4H,m,Substited Phenylring)
3.	4.8 (Multiplate)	(2H ,S,NH_2)

Table-IV (FT-IR Spectral Data)

S.NO.	Functional Group	Vibrational Frequencies
1.	$-NH_2-$	3330 cm^{-1}
2.	$-SO_2-$	1138 cm^{-1}
3.	-C=N- or C=C	1162 cm^{-1}
4.	-N=N-	1620 cm^{-1}
5.	Substituted phenyl	752 cm^{-1}

The synthesized 2-amino-4, 6-diethyl-5-(4'-sulphonamoyl) azopyrimidines deals with the biological evaluation the tests were performed to evaluate antifungal and antibacterial activity against various micro-organism by disc diffusion technique.

Anti-fungal activity

2-amino-4,6-diethyl-5-(4'-sulphonamoyl)azopyrimidines completely inhibited the growth of candida albicans. Inhibition of growth was partial in case of dermathophytes and Aspergillus species.

All the compounds gave satisfactory results of analysis.

(a) 2-amino-4,6-diethyl-5-(4'-sulphanyl sulphonamoyl)azopyrimidines,

(b) 2-amino-4,6-diethyl-5-(4'-guanidinyl sulphonamoyl)azopyrimidines, and

(c) 2-amino-4, 6-diethyl-5-(4'- thiazolyl sulphonamoyl) azopyrimidines

It have remarkable antifungal activities against Candida Aspergillus and dermatophytes other arylazopyrimidines found to be inactive against the species tested.

Anti-bacterial activity

The six arylazopyrimidines derivatives (a,b,c,d,e,and f) were tested against staph aureus staph albus, staph epidermidis, strepto cocci,Esch coli, Klebsilla and salmonella species by disc diffusion technique at 100 ml / ml concentration. The product did not show antibacterial activity.

Conclusion

The reaction of 2-(4'-sulphonamoyl) hydrazono-3,5-heptane dione with guanidine nitrate occurred in the molar ratio 0.01 : 0.01 mol, forming azopyrimidines. Elemental, analytical data and spectral data (FT-IR,^{1}HNMR), of the compounds were used for characterization.

Acknowledgment

The authors are thankful to the Head, SAIF Punjab University, Chandigarh- 160014 for elemental, and FT-IR,^{1}HNMR, analyses. The author is also thankful to Dr. Ajay Kumar from the department of biotechnology ITM University Gwalior for providing antifungal activity.

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