

Synthesis and antifungal evaluation of some novel benzopyridazines

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Manuscript received online 17 December 2018, Revised on 16 January 2019, accepted on 20 January 2020

Abstract : A series of some new 1-(substituted thioanilido)-8-Keto-3-substituted benzopyridazines (III) were prepared by reacting 4-aryl-3-thiosemicarbazides (I) with 2-carboxyl-(substituted benzophenones). Thiosemicarbazones(II), so formed on cyclodehydration gave the titled compounds. These benzopyridazines were screened for their antifungal activities. Based on the screening data, some structure activity relationship was established .

(Keywords: *Synthesis, Antifungal activities, Benzopyridazines*)

Introduction

Several pyridazines exhibit interesting biological activities like cardiovascular¹, hypotensive², antihypertensive³, herbicidal⁴, and fungicidal⁵. Literature is scanty with report of pesticidal properties of this ring⁶. In this communication we report the reaction of various thiosemicarbazides (I) with 2-carboxyl(substituted benzophenones) to produce thiosemicarbazones (II). These on cyclodehydration gave the titled compounds benzopyridazines(III). These were screened for antifungal activities against *Aspergillus niger* and *Aspergillus flavus*.

Experimental

Melting points of all the synthesized compounds were determined in open capillary tubes and are uncorrected. Structure elucidation were characterized by elemental and spectral data. The IR spectra were recorded in KBr on Perkin-Elmer model-157 spectrophotometer. The NMR spectra were recorded on Perkin-Elmer R-32 spectrometer in DMSO-d₆ at 90 MHz. The purity

of the compounds were checked by TLC using silicagel-G(Merck). Elemental analysis of all the compounds were satisfactory. 4-Aryl-3-thiosemicarbazides(I) required as starting material were synthesized from appropriate amines following the method of Kazakov *et al*⁷.

4-(Substituted Phenyl)-1-(2-Substituted)-Thiosemicarbazones(II)

A mixture of 4-phenyl-3-thiosemicarbazide and 2-carboxyl(substituted benzophenones) dissolved in methanol, was refluxed for 1 hour. White crystals of the thiosemicarbazones were obtained on cooling. It was filtered, washed and recrystallized with ethanol. m.p.155°C, yield 65%. Anal. Calcd C₂₁H₁₆N₃O₂SCl, C 61.72; H 3.98; N 10.46 Found C 61.53; H 3.90; N 10.25 Calculated; The other compounds prepared are given in Table 1.

1-(4-thioanilido)-8-Keto-benzopyridazines(III)

4-(chloro-phenyl)-(2-carboxy-benzaldehyde)-thiosemicarbazone was cyclodehydrated by heating under reflux in glacial acetic acid for 2h. The solid mass obtained was poured over crushed ice, m.p. >300°C, yield 77%. Anal. Calculated

C₂₂H₁₅N₃O₂SCl, C 65.37; H 3.87; N 10.54 Found C 65.10; H 3.69; N 10.35 Calculated IR(KBr) cm⁻¹; 3260 (-NH), 1690 (>C=O), 1640 (C=N), 1070 (C=S) PMR(s) : 2.2 (s, 3H, CH₃), 6.9-8.0 (m, 12H, aromatic) and 9.3-9.7 (bs, 1H, NH). Other such compounds prepared are given in Table 2.

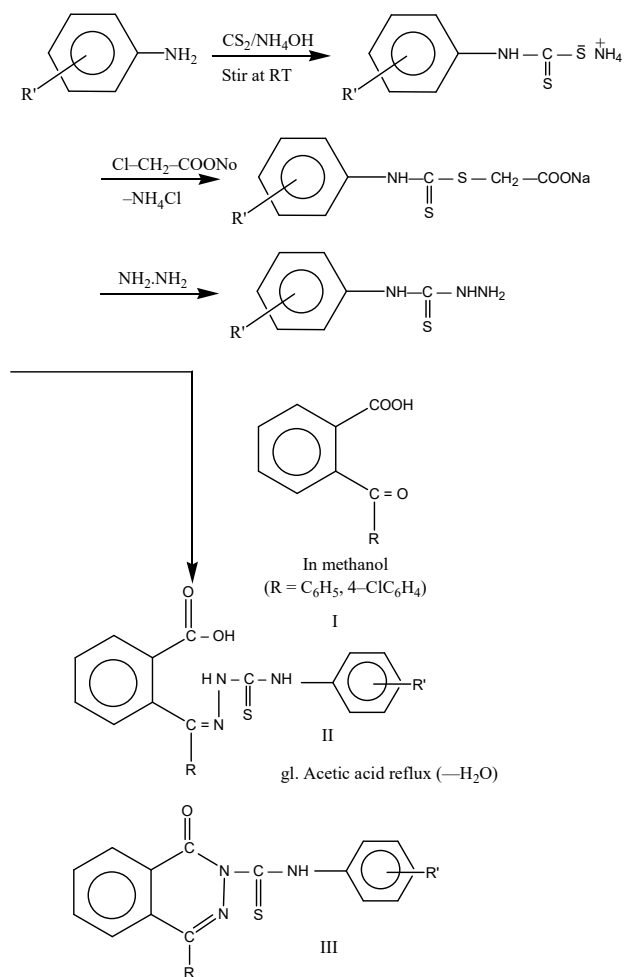


Table - 1 Physical data of thiosemicarbazones

Compound No.	R	R'	m.p.($^{\circ}\text{C}$)	Yield (%)	Molecular Formula
1	C_6H_5	H	80	73	$\text{C}_{21}\text{H}_{17}\text{N}_3\text{O}_2\text{S}$
2	C_6H_5	4-Cl	155	65	$\text{C}_{21}\text{H}_{16}\text{N}_3\text{O}_2\text{SCl}$
3	C_6H_5	3- CH_3	70	63	$\text{C}_{22}\text{H}_{18}\text{N}_3\text{O}_2\text{S}$
4	4- ClC_6H_4	H	>300	64	$\text{C}_{21}\text{H}_{16}\text{N}_3\text{O}_2\text{SCl}$
5	4- ClC_6H_4	4-Cl	>300	62	$\text{C}_{21}\text{H}_{15}\text{N}_3\text{O}_2\text{SCl}$
6	4	3- CH_3	>300	60	$\text{C}_{22}\text{H}_{18}\text{N}_3\text{O}_2\text{SCl}$
7	2,5-di ClC_6H_3	H	160	72	$\text{C}_{21}\text{H}_{15}\text{N}_3\text{O}_2\text{SCl}_2$
8	2,5-di ClC_6H_3	3- CH_3	180	66	$\text{C}_{22}\text{H}_{17}\text{N}_3\text{O}_2\text{SCl}_2$

Table - 2
Physical data of Benzopyridazines

Compound No.	R	R'	m.p.(^o C)	Yield (%)	Molecular Formula
1	C ₆ H ₅	H	94	82	C ₂₁ H ₁₅ N ₃ OS
2	C ₆ H ₅	4 - Cl	140	85	C ₂₁ H ₁₄ N ₃ OSCl
3	C ₆ H ₅	3 - CH ₃	96	80	C ₂₂ H ₁₆ N ₃ OS
4	4 - ClC ₆ H ₄	H	>300	79	C ₂₁ H ₁₄ N ₃ OSCl
5	4 - ClC ₆ H ₄	4 - Cl	>300	77	C ₂₁ H ₁₃ N ₃ OSCl ₂
6	4	3 - CH ₃	>300	75	C ₂₂ H ₁₅ N ₃ OSCl
7	2,5diClC ₆ H ₃	H	227	74	C ₂₁ H ₁₃ N ₃ OSCl ₂
8	2,5diClC ₆ H ₃	3 - CH ₃	165	70	C ₂₂ H ₁₅ N ₃ OSCl ₂

Table - 3
Antifungal activity of Benzopyridazines

S. No.	Compound as in table 2		<i>Aspergillus niger</i>			<i>Aspergillus flavus</i>		
	R	R'	1000 ppm	100 ppm	10 ppm	1000 ppm	100 ppm	10 ppm
1	C ₆ H ₅	H	54	34	20	56	40	24
2	C ₆ H ₅	4	57	36	22	60	42	32
3	C ₆ H ₅	3 - CH ₃	48	30	16	51	34	20
4	4	H	48	31	15	50	34	19
5	4	4	64	40	34	70	60	52
6	4	3 - CH ₃	52	32	20	54	36	22
7	2,5diClC ₆ H ₃	H	60	38	32	66	45	37
8	2,5diClC ₆ H ₃	3 - CH ₃	54	33	20	57	33	22
9	Carbendazim		94	90	86	96	92	88

Biological Evaluation

The newly synthesized compounds (III) were screened for their antifungal activities against *Aspergillus niger* and *Aspergillus flavus* at three different concentrations of 1000, 100 and 10 ppm

following Agar growth technique⁸, with three replications. All the tubes were incubated at 28°C in B.O.D. incubator. The results were taken after 4 days and are recorded in Table 3.

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