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Synthesis and Antifungal Activity of 2-Phenylimino-5-Aryl/Alkylimino-1,3,4-Thiadiazolidines

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Synthesis of several 2-phenylimino-5-aryl/alkylimino-1,3,4-thiadiazolidines (**IV**) have been reported by a new route. The interaction of aryl/alkyl thiosemicarbazides (**I**) and N-phenyl isocyano dichloride (**II**) in refluxing chloroform medium for 3 h afforded 2-phenylimino-5-aryl/alkylimino-1, 3, 4-thiadiazolidines hydrochlorides (**III**) which on basification with dilute ammonium hydroxide solution gave title compounds (**IV**). Title compunds on acetylation in 1 : 1 ratio gave monoacetyl derivatives (**V**). The structures of all these compounds were established on the basis of elemental analysis, equivalent weight determination and IR and PMR spectal studies. The synthesized compounds were assayed for their antifungal activity against tuber fungus *Rhizoctonia bataticola* with encouraging results.

Key Words: Synthesis, Antifungal activity, 2-Phenylimino-5-aryl/alkylimino-1,3,4-thiadiazolidines.

INTRODUCTION

Syntheses of various 1,3,4-thiadiazolidines by the cyclization and other routes have been reported[1–6]. As a part of our research work to explore the innovative route for the synthesis of heterocyclic compounds[7], we now report the synthesis of 2-phenylimino-5-aryl/alkylimino-1,3,4-thiadiazolidines in this communication.

RESULTS AND DISCUSSION

The reaction of 4-phenyl thiosemicarbazide (**I**) and N-phenyl isocyanodichloride (**II**)[8] in 1 : 1 ratio was carried out for 3 h in refluxing chloroform medium. The evolution of hydrochloric acid gas was noticed. On distilling off the chloroform, a sticky mass was left which on washing several times with petroleum ether (60–80°C) afforded granular solid (**IIIa**), crystallized from ethanol, m.p. 160°C. The compound was found to be acidic to litmus. On determination of equivalent weight, it was identified as monohydrochloride of 2,5-diphenylimino-1,3,4-thiadiazolidine (**IIIa**). On basification with dilute ammonium hydroxide free base (**IVa**) was obtained, crystallized from ethanol, m.p. 190°C. The elemental analysis of the product indicated its m.f. to be $C_{14}H_{12}N_4S$ (Found: C 62.35, H 4.32, N 20.48, S 11.58%; calculated for

TABLE-1
SYNTHESIS OF 2-PHENYLIMINO-5-ARYL/ALKYLIMINO-1,3,4-THIADIAZOLIDINES (IV) AND THEIR ACETYL DERIVATIVES (V)

Reactants: 4-Aryl/Alkyl-Thiosemicarbazides (I) and Phenyl Isocyanodichloride (II)

Sr. No.	4-Aryl/alkyl thiosemi-carbazide (I)	2-phenylimino-5-aryl/alkylimino-1,3,4-thiadiazolidines, HCl (III)	m.p. (°C)	Equivalent wt., found (calcd.)	m.p. free base (°C)	S* (%) found (calcd.) (free-base)	2-Phenylimino-3-acetyl 5-aryl/alkyl-1,3,4-thiadiozolide (V)	m.p. (°C)	S* (%) found (calcd.)
1.	4-phenyl—**Ia**	...-5-phenylimino—IIIa	181	304 (304.5)	183	11.58 (11.94)	-3-acetyl-5-phenylimino—**Va**	180	10.04 (10.32)
2.	4-*o*-tolyl—**Ib**	...-5-*o*-tolylimino—**IIIb**	145	311 (318.5)	163	11.02 (11.38)	-3-acetyl-5-*o*-tolylimino—**Vb**	155	9.52 (9.87)
3.	4-*m*-tolyl—**Ic**	...-5*m*-tolylimino—**IIIc**	150	313 (318.5)	170	11.08 (11.38)	-3-acetyl-5-*m*-tolylimino—**Vc**	140	9.45 (9.87)
4.	4-*p*-tolyl—**Id**	...-5-*p*-tolylimino—**IIId**	180	314 (318.5)	210	11.21 (11.38)	-3-acetyl-5-*p*-tolyllimino—**Vd**	150	9.66 (9.87)
5.	4-*p*-chlorophenyl—**Ie**	...-5-*o*-chlorophenylimino—**IIIe**	182	334 (339)	150	10.22 (10.57)	-3-acetyl-5-*o*-chlorophe- nylimino—**Ve**	168	8.98 (9.28)
6.	4-*p*-chlorophenyl—**If**	...-5-*p*-chlorophenylimino—**IIIf**	250	336 (339)	178	10.34 (10.57)	-3-acetyl-5-*p*-chloro- phenylimino—**Vf**	150	9.01 (9.28)
7.	4-*t*-butyl—**Ig**	...-5-*t*-butylimino—**IIIg**	162	278 (284.5)	156	13.54 (13.70)	-3-acetyl-5-*t*-butylimino—**Vg**	167	10.75 (11.03)

*C, H, N analyses found satisfactory in all cases.

$C_{14}H_{12}N_4S$: C 62.68, H 4.47, N 20.89 and S 11.94%). The IR spectrum of the compound showed absorption bands due to ν(NH) (3250 cm^{-1}), ν(C=N) (1570 cm^{-1}), ν(C—S) (700 cm^{-1}) and ν(N—N) (1205 cm^{-1}). The PMR spectrum of the product showed peaks at δ 9.5 ppm (2H, N—H protons) and δ 7.1–7.6 ppm (10H, Ar—H protons).

On the basis of above facts, the compound **(1Va)** has been assigned the structure as 2,5-diphenylimino-1,3,4-thiadiazolidine. Other compounds **(IVb–IVg)** were synthesized by extending the reaction of N-phenyl isocyanodichloride **(II)** to other 4-aryl/alkyl thiosemicarbazides **(Ib–Ig)** and related 1,3,4-thiadiazolidines **(IIIb–IIIg)** were isolated in good yield (Table-1). These on basification with dilute ammonium hydroxide afforded free bases **(IVb–IVg).**

2,5-Diphenylimino-1,3,4-thiadiazolidine **(IVa)** on refluxing with glacial acetic acid and acetic anhydride mixture in 1 : 1 ratio for 1 h followed by dilution with water afforded a solid **(Va),** crystallized from ethanol, m.p. 180°C. The **(Va)** gave positive test for N, S element and for $—COCH_3$ group. The elemental analysis of the product indicated its m.f. as $C_{16}H_{14}N_4OS$. (Found: C 61.52, H 4.38, N 17.86, S 10.04%. Calculated for $C_{16}H_{14}N_4OS$, C 61.93, H 4.51, N 18.06, S 10.32%).

On the basis of above facts the compound **(Va)** has been assigned the structure as 2,5-diphenylimino-3-acetyl 1,3,4-thiadiazolidine. The other related acetyl derivatives **(Vb–Vg)** were prepared by extending the above reaction.

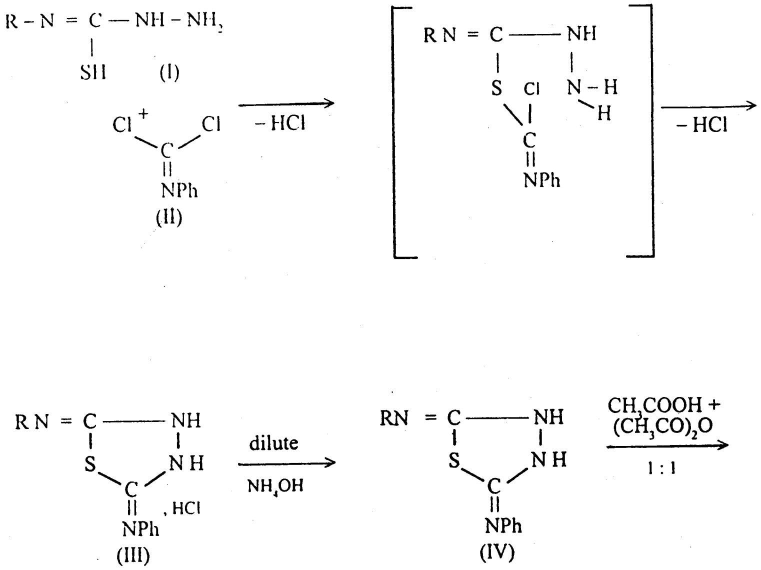
TABLE-2
ANTIFUNGAL ACTIVITY OF 2-PHENYLIMINO-5-ARYL/ALKYLIMINO-1, 3, 4-THIADIAZOLIDINES (IV)

Name of Fungus: *Rhizoctonia bataticola*

Sr. No.	Compounds	Colony diameter (mm)		% Inhibition	
		Concentration (%)			
		1	2	1	2
1.	**IV a**	13	5	84.33	93.97
2..	**IV b**	10	7	90.62	92.98
3.	**IV c**	—	—	100	100
4.	**IV d**	Nil	Nil	Nil	Nil
5.	**IV e**	NIl	Nil	Nil	Nil
6.	**IV f**	—	—	100	100
7.	**IV g**	6	5	92.77	93.97
8.	Standard (copper oxychloride)	20	—	75.90	100

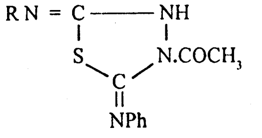
— Indicates no growth in the petri plate.

The formation of 2-phenylimino-5-aryl/alkylimino-1,3,4-thiadiazolidines hydrochloride **(III),** their free bases **(IV)** and their acetyl derivatives **(V)** are shown in the following reaction scheme.



where

R = Ph in **Ia, IIIa, IVa, Va.**
R = o-tolyl in **Ib, IIIb, IVb, Vb**
R = *m*-tolyl in **Ic, IIIc, IVc, Vc.**
R = *p*-tolyl in **Id, IIId, IVd, Vd.**
R = *o*-chlorophenyl in **Ie, IIIe, IVe, Ve.**
R = *p*-chlorophenyl in **If, IIIf, IVf, Vf.**
R = *t*-butyl in **Ig, IIIg, IVg, Vg.**


(V)

The title compounds were screened for their antifungal activity against fungus in the field of agriculture. The fungus selected was *Rhizoctoria batalicola*. The 1 and 2 per cent solutions of title compounds were screened by paper disc method. The incubation period was 72 h. The zones of incubation were measured and the percentage inhibition was calculated. Compounds **IVc** and **IVf** have shown hundred per cent inhibition, while the values of inhibition for **IVa, IVg** are considerable. The copper oxychloride was used as standard in this experiment.

EXPERIMENTAL

The melting points were determined in open capillaries and are uncorrected. The infrared spectra were recorded on Perkin-Elmer instrument. The ^1H NMR spectra wre recorded in DMSO/$CDCl_3$ using TMS as an internal standard. The chemical shifts are expressed in δ ppm. N-phenyl isocyanodichloride **(II)** was prepared by earlier known procedure[8].

Preparation of 2,5-Diphenylimino-1,3,4-Thiadiazolidine (IVa)

4-Phenyl-thiosemicarbazide (**Ia,** 0.01 mole) and N-phenyl isocyanodichloride (**II,** 0.01 mole) in chloroform (20 mL) were refluxed for 3 h. On distilling off the solvent a semisolid mass was obtained which on washing several times with petroleum ether (60–80°C) gave a hard grannular solid **(IIIa)**, yield 60%. It was crystallized from ethanol to give colourless solid, m.p. 160°C. The compound was acidic to litmus. On determination of equivalent weight by titrimetry it was found to be monohydrochloride. On basification with dilute ammonium hydroxide it gave free base, crystallized from ethanol, m.p. 190°C. The compound was non-desulplurizable with alkaline plumbite solution. Elemental analysis indicated its m.f. to be $C_{14}H_{12}N_4S$.

Preparatin of 2,5-Diphenylimino-3-Acetyl-1,3,4-Thiadiazolidine (Va)

2,5-Diphenylimino-1,3,4-thiadiazolidine (**IVa**, 0.01 mole) on refluxing with glacial acetic acid and acetic anhydride (0.01 mole) for 1 h followed by dilution with water afforded 2,5-diphenylimino-3-acetyl-1,3,4-thiadiazolidine (**Va**), yield 65%. It was crystallized from ethanol, m.p. 180°C. The product gave positive iodoform test.

The fungus *Rizotoria bataticola* causing damage to tubers like potato was chosen. Petri dishes were prepared by adding potato dextrose agar medium. The fungus was cultivated in the medium; at the same time the discs dipped in compound solution were planted in the same petri plates. The plates were incubated for about 72 h at 37°C. The zones of inhibition around the paper disc were measured in millimetres and the percentage inhibition was calculated. The solution of the test compound was prepared in DMF and copper oxychloride was used as standard (Table-2).

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