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New Route to the Synthesis of 2-Phenylimino-3-γ-Picolinoyl-5-Aryl/Alkylimino-1,3,4-Thiadiazolidines

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The synthesis of 2-phenylimino-3-γ-picolinoyl-5-aryl/alkylimino-1,3,4-thiadiazolidines (IV) is reported by a new route. The interaction of 1-γ-picolinoyl-4-aryl/alkyl thiosemicarbazides (I) and N-phenyl isocyanodichloride (II) on refluxing with chloroform medium for 1 h afforded (III) which on basification with dilute ammonium hydroxide solution gave the title compound (IV). The title compound on acetylation produced an acetyl derivative (V).

Key words: Synthesis, 2-Phenylimino-3-γ-picolinoyl-5-aryl/alkylimino-1,3,4-thiadiazolidines

INTRODUCTION

In the process of the synthesis of 1,3,4-thiadiazolidines, the cyclization and other routes have been employed earlier[1–5]. As a part of our research programme to explore the new route for the synthesis of heterocyclic compound[6], we now report a novel procedure for the preparation of 2-phenylimino-3-γ-picolinoyl-5-aryl/alkyl imino-1,3,4-thiadiazolidines.

RESULTS AND DISCUSSION

The reaction of 1-γ-picolinoyl-4-phenyl-thiosemicarbazide[6, 7] **(Ia)** and N-phenyl isocyanodichloride[8] **(II)** in equimolar ratio was carried out for 1 h in refluxing chloroform medium. The evolution of hydrochloric acid gas was observed. On distilling off the solvent, a semi-solid mass was left which on washing several times with petroleum ether (60–80°C) gave granular solid, crystallized from acetic acid-ethanol mixture (1 : 1), m.p. 176°C. The compound was acidic to litmus. On determination of its equivalent weight, it was found to be monohydrochloride of 2,5-diphenylimino-3-γ-picolinoyl-1,3,4-thiadiazolidine. On basification with ditute ammonium hydroxide a free base was obtained. It was crystallized from ethanol (70%), m.p. 170°C. The elemental analysis of the product indicated its m.f. to be $C_{20}H_{15}N_5OS$. (Found: C, 64.11; H, 4.00; N, 18.54; S, 8.40%; calculated for $C_{20}H_{15}N_5OS$: C, 64.34; H, 4.02; N, 18.76; S, 8.57. The IR spectrum of the compound showed absorption bands at 3423, 1677, 1596 and 688 cm^{-1} due to ν(NH), ν(C═O), ν(C═N) and ν(C—S) respectively.[9, 10]. The PMR spectrum showed peaks at δ 7.1–7.4 due to aromatic protons (10 Ar-H); pyridyl proton at δ 8.5–9.5 {4H); and at δ 10.6 for NH proton (1H).

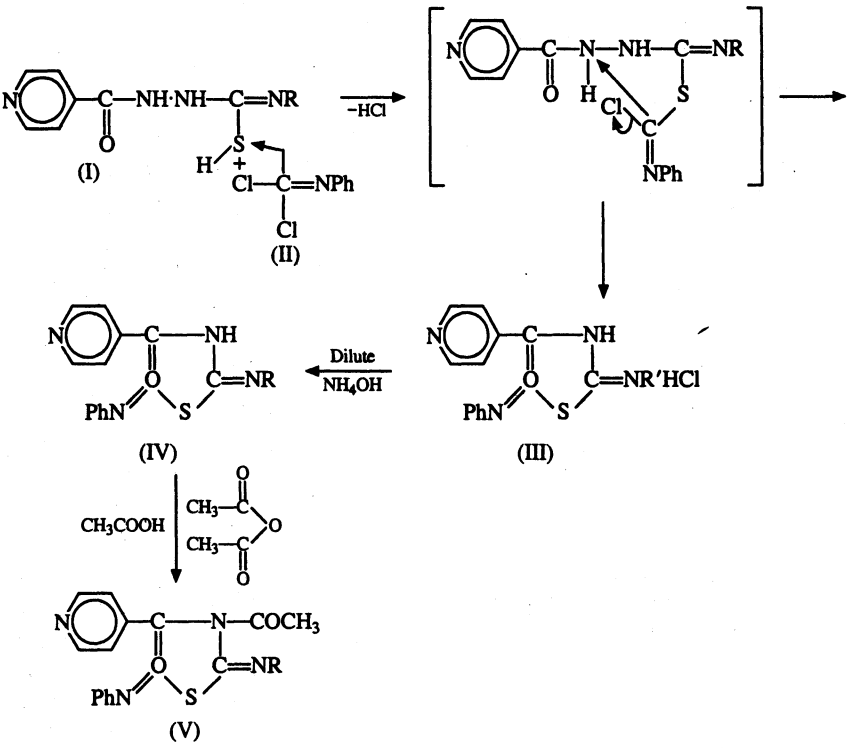
On the basis of the above fact the compound **(IVa)** has been assigned to the structure of 2,5-diphenylimino-3-γ-picolinoyl-1,3,4-thiadiazolidine.

Other compounds **(IVb–g)** were synthesized by extending the reaction of N-phenyl isocyanodichloride **(II)** to other 1-γ-picolinoyl-4-aryl/alkyl thiosemicarbazide **(Ib–g)** and related 1,3,4-thiadiazolidines **(IVb–g)** were isolated in good yield (Table-1).

2,5-Diphenylimino-3-γ-picolinoyl-1,3,4-thiadiazolidines **(IVa)** on refluxing with acetic anhydride and glacial acetic acid mixture in 1 : 1 ratio for 1 h followed by dilution with water afforded 2,5-diphenylimino-3-γ-picolinoyl-4-acetyl-1,3,4-thiadiazolidines **(Va)**. Crystallized from glacial acetic acid-ethanol, m.p. 240°C. (Found: C, 63.55; H, 4.00; N, 16.81; S, 7.64%; Calculated: C, 63.61; H, 4.09; N, 16.86; S, 7.71.)

The other related acetyl derivatives **(Vb–g)** were prepared by extending the above reaction.

The formation of 2-phenylimino-3-γ-picolinoyl-5-aryl/alkylimino-1,3,4-thiadiazolidines hydrochloride **(III)**, their free bases **(IV)** and their acetyl derivatives **(V)** is shown in Scheme-I.



where R (in **I, III, IV** and **V**):

R = a = phenyl, R = b = *o*-tolyl, R = c = *m*-tolyl, R = d = *p*-tolyl
R = e = *o*-chlorophenyl, R = f = *p*-chloro-phenyl R = g = tert-butyl

Scheme-1

TABLE-1
FORMATION OF 2-PHENYLIMINO-3-γ-PICOLINOYL-5-ARYL/ALKYL IMINO-1,3,4-THIADIAZOLIDINES AND THEIR ACETYL DERIVATIVES

1-γ-Picolinoyl-4-aryl/alkyl thiosemicarbazide (I)	2-phenylimino-3-γ-picolinoyl-5-aryl/alkylimino-1,3,4-thiadiazolidine hydrochloride (III)	Yield (%)	m.p. (°C)	Eq.wt. found (calcd.)	2-phenylimino-3-γ picolinoyl-5-aryl/alkylimino-1,3,4-thiadiazolidine (IV)	m.p. (°C)	S % found (calcd.)	2-phenylimino-3-γ-picolinoyl-4-acetyl-5-aryl/alkylimino-1,3,4-thiadiazolidine (Va)	m.p. (°C)	S % found (calcd.)
1-γ-picolinol-4-phenyl-thiosemicarbazide (Ia)	2,5-diphenylimino-3-γ-picolinoyl-1,3,4-thiadiazolidine hydrochloride (IIIa)	70	176	403 (409.5)	2,5-diphenyl-imino-3-γ picolinoyl-1,3,4-thiadiazolidine (IVa)	170	8.40 (8.57)	2,5-diphenylimino-3-γ picolinoyl-4-acetyl-1,3,4-thiadiazolidine (Va)	240	7.59 (7.71)
1-γ-picolinoyl-4-*o*-tolyl...... (Ib)	....5-*o*-tolyl (IIIb)	80	166	420.63 (423.5)	...5-*o*-tolyl (IVb)	130	7.82 (8.26)	...5-*o*-tolyl (Vb)	180	7.30 (7.45)
1-γ-picolinoyl-4-*m*-tolyll...... (Ic)	....5-*m*-tolyl (IIIc)	50	176	419.58 (423.50)	....5-*m*-tolyl (IVc)	168	8.05 (8.26)	....5-*m*-tolyl (Vc)	140	7.29 (7.45)
1-γ-picolinoyl-4-*p*-tolyll...... (Id)	....5-*p*-tolyl (IIId)	70	172	423.15 (423.50)	....5-*p*-tolyl (IVd)	164	7.88 (8.26)	....5-*p*-tolyl (Vd)	185	7.25 (7.45)
1-γ-picolinoyl-4-*o*-chlorophenyll..... (Ie)	....5-*o*-chlorophenyl (IIIe)	75	160	435.0 (444.0)	...5-*o*-chloro-phenyl (IVe)	120	7.51 (7.85)	...5-*o*-chloro-phenyl (Ve)	150	6.99 (7.11)
1-γ-picolinoyl-4-*p*-chlorophenyll..... (If)	....5-*p*-chlorophenyl (IIIf)	80	178	438.0 (444.0)	....5-*p*-chloro-phenyl (IVf)	170	7.49 (7.85)	....5-*p*-chloro-phenyl (Vf)	100	7.14 (7.11)
1-γ-picolinoyl-4-tert-butyl..... (Ig)	....5-tert-butyl (IIIg)	55	158	375.5 (389.5)	....5-tert-butyl (IVg)	140	8.62 (9.06)	...5-tert-butyl (Vg)	144	9.70 (9.90)

Note: Satisfactory C, H and N analyses found in all cases.

EXPERIMENTAL

The melting points were determined in open capillaries and are uncorrected. The infrared spectra were recorded on Perkin-elmer instrument. ^{1}H NMR spectra were recorded in DMSO/$CDCl_3$ using TMS as an internal standard. The chemical shifts are expressed in δ ppm. N-phenyl isocyanodichloride[8] (III) and 1-γ-picolinoyl-4-aryl/alkyl thiosemicarbazide (I) were prepared following earlier known procedure[6, 7].

Preparation of 2,5 - diphenylimino - 3-γ-picolinoyl - 1,3,4 - thiadiazolidine (IVa): 1-γ-Picolinoyl-4-phenyl thiosemicarbazide (**Ia**, 0.01 mole) and N-phenyl isocyanodichloride (**II**, 0.01 mole) in chloroform (20 mL) were refluxed for 1 h. On distilling off the solvent, the semi-solid mass obtained, which on washing several times with petroleum ether (60–80°C) gave a hard granular solid, yield 70%. It was crystallized from acetic acid : ethanol (1 : 1) to give light yellow solid; m.p. 176°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 (70%), m.p. 170°C. The compound was non-desulphurizable when boiled with alkaline plumbite solution.

Preparation of 2,5-diphenylimino-3-γ-picolinoyl-4-acetyl-1,3,4-thiadiazolidines (Va): 2,5-Diphenylimino-3-γ-picolinoyl-1,3,4-thiadiazolidine (**IVa**, 0.01 mole on refluxing with acetic anhydride (0.01 mole) and glacial acetic acid for 1 h followed by dilution with water afforded 2,5-diphenylimino-3-γ-picolinoyl-4-acetyl-1,3,4-thiadiazolidine (**Va**); yield 60%; m.p. 240°C. It was crystallized from acetic acid-ethanol-water.

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