

Research Article

Synthesis of 2-Arylimino-5-Tert-Butylimino-1,3,4-Thiadiazolidines

NA. Rashidi

Department of Chemistry, Mungasaji Maharaj College, Darwha, Dist:Yavatmal, Maharashtra, India.

ABSTRACT

In the present study, we have synthesized some new 2-arylimino-5-t-butylimino-1,3,4-thiadiazolidines (IVa-f). The compounds (IVa-f) were prepared by the cyclo condensation of N-aryl thiosemicarbazide (IIa-f) and tert-butyl isocyanodichloride in chloroform medium. All the newly synthesized compounds were subjected to physical characterization and spectral analysis by IR and NMR & Mass for structure elucidation.

Keywords: 1,3,4-thiadiazole derivatives, tert-butyl isocyanodichloride, cyclo condensation.

INTRODUCTION

The five member heterocyclic compounds with three hetero atoms at symmetrical position have been extensively studied. 1,3,4-thiadiazole is one such compound and literature is enriched with its various derivatives exhibiting antifungal activities^{1,9}. The different methods have been proposed for the synthesis of 1,3,4-thiadiazole and its derivatives⁷⁻⁹. Herein synthesis of various substituted 1,3,4-thiadiazolidine by cyclo condensation reaction of N-aryl thiosemicarbazide and T-butyl isocyanodichloride have been proposed. The structures of synthesized compounds were established on the basis of IR and ¹H-NMR spectra.

MATERIAL AND METHOD

Melting points were determined in open capillaries in a liquid paraffin bath and are uncorrected. The purity of compounds was checked by TLC. IR spectra were recorded using KBr disc plate technique on a Bruker FT-IR spectrophotometer. ¹HNMR spectra (DMSO-d₆ and CDCl₃) were carried out on a Bruker Advance 400 MHz spectrometer using TMS as internal reference (chemical shifts in δ , ppm).

The reagents aryl isothiocyanate¹⁰, T-butyl isocyanodichloride¹¹ were prepared by following previously reported methods.

N-aryl thiosemicarbazide(IIa-f)¹²⁻¹³ required for the synthesis of 2-arylimino-5-t-butylimino-1,3,4-thiadiazolidines (IV) were prepared as below.

Preparation of N-p-tolyl thiosemicarbazide^{12,13} (IIa)

The p-tolyl isothiocyanate (Ia) (0.01 mol) was dissolved in 20 ml chloroform and hydrazine hydrate (99%) (0.01 mol) was added drop wise

to the reaction mixture with stirring. The reaction was found to be exothermic. The resulting mixture was allowed to cool. The white solid separated within 10 minutes, was filtered, washed with water and dried. The product (IIa) was recrystallized from ethanol, yield 76%, m.p 158 °C.

(IIa) : IR spectra14: (KBr) cm⁻¹: 3296 (NH), 1619 (C=N), 1275 (C-N), 1178(C=S); **¹H-NMR** (DMSOd6) ppm: 2.2(3H, s, Ar-CH₃), 4.2 (2H, bs, N-H) 7.2-7.06 (2H, d, Ar-H), 7.03-7.37 (2H, d, Ar-H), 8.6(1H, s, N-H) .

The other N-Aryl thiosemicarbazide (IIb-f) were prepared by extending the above reaction to different aryl isothiocyanates (Ia-f).

Preparation of 2-p-tolylimino-5-t-butylimino-1,3,4-thiadiazolidine (IVa)

N-p-tolyl thiosemicarbazide (IIa) (0.01 mole) was refluxed with tert-butyl isocyanodichloride (0.01 mole) in chloroform medium over water bath for 3.0 hr. The evolution of hydrogen chloride gas was clearly noticed. On cooling the reaction mixture and distilling off chloroform afforded a sticky mass, which on washing repeatedly with petroleum ether (60-80°C) gave a granular solid, crystallised from ethanol. It was acidic to litmus and on determination of equivalent weight, it was found to be a monohydrochloride (IIIa), yield 78%, m.p. 72-74°C. It, on basification with dilute ammonium hydroxide solution afforded a free base, (IVa). It was crystallised from ethanol, m.p. 102°C. The compound was insoluble in water but soluble in organic solvents and found to be non-

desulphurizable when boiled with alkaline lead acetate solution.

molecular formula was found to be $C_{13}H_{18}N_4S$.

(IVa) : IR spectra 14: (KBr) cm^{-1} : 3392 (NH), 3228(NH), 3180-3112(Ar-H), 3026-2980 (C-H, t-Bu), 2918,2856(C-H),1487 (C=N), 1313 (C-N), 810 (C-S); **¹H-NMR** (DMSO-d₆) ppm: 1.2-1.4 (9H, m, t-Bu), 2.1(3H, s, CH₃) 6.92-7.2 (4H, m, Ar-H), 7.3 (1H, d, NH), 7.4(1H, d, NH) **(IVc)** IR: (KBr) cm^{-1} 3391(N-H) 3195-3138(Ar-H), 2969-2795 C-H),1613 (C=N), 1167 (C-N), 774(C-S); **¹H-NMR** (DMSO-d₆) ppm: 1.2-1.6 (9H, m, t-Bu), 2.1(3H, s, CH₃) 6.92-7.2 (4H, m, Ar-H), 7.4 (1H, d, NH), 8.4(1H, d, NH).

On the basis of chemical properties and spectral data, the compound (IVa) has been assigned the structure, 2-p-tolylimino-5-t-butylimino-1,3,4-thiadiazolidine (IVa). On extending the above reaction to other **N**-Aryl thiosemicarbazide (IIb-f), the related products were isolated in good yield. (Table-1)

RESULT AND DISCUSSION

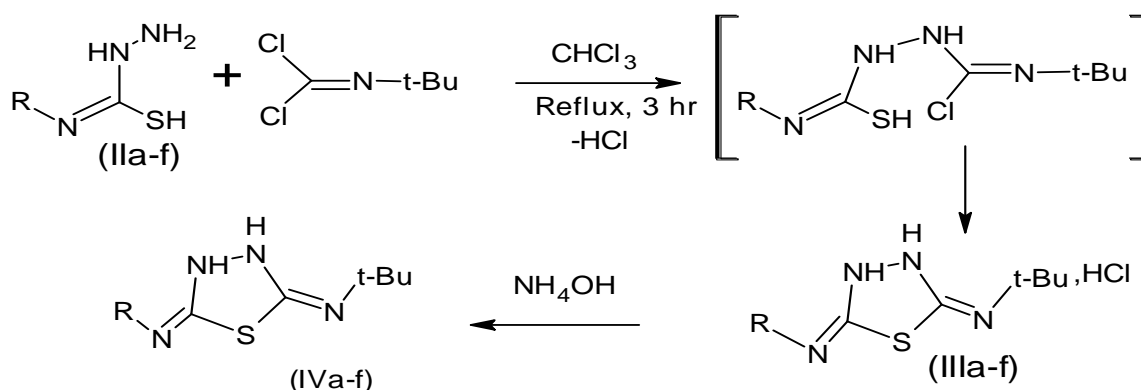
The synthetic route is outlined in Fig. 1

Six substituted aryl isothiocyanate¹⁰ (Ia-f) and T-butyl isocyanodichloride¹¹ were prepared as reported earlier. N-aryl thiosemicarbazides¹²⁻¹³ (IIa-f) was prepared as under.

The N-p-tolyl thiosemicarbazide (IIa) was prepared by the treatment of p-tolyl isothiocyanate(Ia) with hydrazine hydrate in chloroform medium. The reaction was found to be exothermic. The resulting mixture was allowed to cool. The white solid separated within 10 minutes, was filtered, washed with

water and dried. The product (IIa) was recrystallized from ethanol, yield 76% ,m.p 158 °C.

The condensation of N-p-tolyl thiosemicarbazide (IIa) (0.01 mole) with tert-butyl isocyanodichloride (0.01 mole) in chloroform medium was carried out for 3.0 hr. The evolution of hydrogen chloride gas was clearly noticed. On cooling and distilling off chloroform a sticky mass obtained, which was repeatedly washed with petroleum ether (60-80°C) gave a granular solid and crystallized from ethanol. It was acidic and found to be a monohydrochloride (IIIa) on titrimetric analysis, yield 78%, m.p. 72-74°C. It, on basification with dilute ammonium hydroxide solution afforded a free base, (IVa). It was crystallised from ethanol, m.p. 102°C. The compound was insoluble in water but soluble in organic solvents and found to be non-desulphurizable when boiled with alkaline lead acetate solution. The infrared spectra of compounds (IIa) showed a characteristic strong absorption at 1178 cm^{-1} attributable to the C=S of the thiourea residue. The cyclo condensation of (IIa) afforded substituted 1,3,4-thiadiazole(IVa). In the IR spectra of substituted 1,3,4-thiadiazole the absence of signals in the region 1400-1000 cm^{-1} established the lack of a C=S group. Also the ¹H-NMR spectra of the compound (IVa) supported the structure of the substituted 1,3,4-thiadiazole.



Where R - (I, II, III, IV, V, VI)

a= p- tolyl, b= phenyl, c = o-tolyl, d=m-tolyl,

e= o-chloro phenyl, f=p-chloro phenyl

Fig-1

Table 1: Physicochemical Properties Data

Compound	Molecular Formula	% Yield	M.P °C
Ila	C ₈ H ₁₁ N ₃ S	76	158
Ilb	C ₇ H ₉ N ₃ S	81	130
Ilc	C ₈ H ₁₁ N ₃ S	79	140
Ild	C ₈ H ₁₁ N ₃ S	75	105
Ile	C ₇ H ₈ N ₃ SCl	71	120
Ilf	C ₇ H ₈ N ₃ SCl	68	165
IVa	C ₁₃ H ₁₈ N ₄ S	78	102
IVb	C ₁₃ H ₁₈ N ₄ S	80	144
IVc	C ₁₃ H ₁₈ N ₄ S	75	115
IVd	C ₁₂ H ₁₆ N ₄ S	67	164
IVe	C ₁₂ H ₁₅ N ₄ SCl	65	110
IVf	C ₁₂ H ₁₅ N ₄ SCl	81	156

CONCLUSION

2-arylimino-5-t-butylimino-1,3,4-thiadiazolidines (IVa-f) were successfully prepared by the cyclo condensation of N-aryl thiosemicarbazide (IIa-f) and tert-butyl isocyanodichloride in chloroform medium. The structures of the synthesized compounds were established on the basis of chemical properties and IR and NMR spectral data. These compounds are expected to show antimicrobial properties.

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