Chapter 2

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Oxidation of Mixtures of Thioureas: Part XII[1] – Oxidation of Mixtures of 1,3-diaryl Thioureas and Thiourea Forming 1,2,4,-thiadiazolines

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ABSTRACT

Oxidation of binary mixtures of 1,3-diaryl thioureas and thiourea in acidic alcoholic solution yields 3-amino-4-aryl-5-arylimino-Δ^2-1,2,4,-thiadiazolines. The rearrangement of the bis(formamidine)sulphide to amidinothiourea derivative has been found to be governed by the steric effect. Oxidation of binary mixtures of 1-aryl-3-(2',6'-xylyl)thiourea and thiourea in acidic alcoholic solution yields 3-amino-4-aryl-5-(2',6'-xylyl)imino-Δ^2-1,2,4,-thiadiazoline. 1-aryl--(2',5'-xylyl)thiourea, and 1-aryl-3-(2',5'-(diisopropyl phenyl)thioureas are also included in the study.

Keywords: Thioureas; thiadiazolines; amidinothiourea.

1. INTRODUCTION

Rapid developments in the field of hetrocyclic chemistry during the last few decades is viewed, world over, with owe. A survey of the chemical literature reveals that nearly one-third of the publications inorganic chemistry is in the field of heterocyclic chemistry. A wide variety of these heterocyclic derivatives have been used as fungicides, bactericides ,insecticides, herbicides, dyes ,lubricant additives, and vulcanization accelerators [1]. In this contest it is not surprising to find that there is still a lot of interest in synthesizing new derivatives of known hetrocycles and also devising newer and easier routes to their synthesis. 1,2,4,-thiadiazolines is a heterocyclic system containing two nitrogen and one sulphur atoms and is known to be a π-excessive hetroaromatic system [2]. 1,2,4-Thiadiazoles have recently attained a therapeutic and economic importance that they did not possess a few years ago. The review provides a report on developments in the synthesis of 1,2,4-thiadiazole-based compounds during the last decade. Thiadiazoles are among the privileged pharmacological building blocks due to their unique chemical properties for diverse biological and clinical applications [3,4].

Among the many methods reported for the synthesis of 1,2,4-thiadiazoline derivatives, oxidation of binary mixtures of thioureas have been used as a general method [5-18]. In these oxidations one molecule each of the thioureas is inovolved in the building up of the thiadiazoline. The structure of the final product formed is found to depend on the substitution pattern of the amidinothiourea intermediate which is formed by the isomerisation of the bis(amidino)sulphide salt. During the isomerisation of the bis(amidino)sulphide salt, of the two amidino groups, an unsubsituted [6-12] or alkyl substituted [9] amidino group is found to migrate to the aryl substituted nitrogen of the other amidino group. It has also been observed that if the aryl substituents on an amidino group are different, the amidino group which migrates preferentially goes to the nitrogen which bears the more electron releasing aryl group [10,12]. The mode of isomerisation is not altered even though one of ortho positions of aryl group is substituted by a methyl group [8]. Two products (**6** and **7**) were isolated, when both the ortho positions

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were substituted by methyl groups [15]. The yield of the product **6** was found to decrease in the order of decreasing steric hindrance. The above observations prompted us to study the electronic and steric influence during the oxidation of 1-aryl-3-aryl'thioureas and thiourea using *(**Aryl**-p-tolyl, p-anisyl, p-phenetyl & o-phenetyl).and **Aryl'**-2,6-xylyl,2,5-xylyl, 2,6-diisopropyl phenyl).*

2. EXPERIMENTAL

The IR (KBr) spectra were run on a perkin-Elmer 397 infrared spectro photometer, UV spectra in methanol on a Hitachi UV-220A spectrophotometer and ^{1}H NMR in $CDCl_3$ on R-24-B Hitachi 300 MHz high resolution NMR spectrometer with TMS as an internal standard. The mass spectra were taken on a HEW-LETT PACKARD HP-5995 mass spectrometer. Melting points were determined by capillary method and are uncorrected and the purity of the products were confirmed by TLC.

Table 1. Oxidation products of 1,3-diaryl Thioureas and Thiourea

Compound	**Ar**	**Ar'**	**Molecular formula**	**Analysis found / (reqd.)**				**m.p (^{0}C)**	**Yield (%)**
				C	**H**	**N**	**S**		
6a	Phenyl	2',6'-xylyl	$C_{16}H_{16}N_4S$	64.8 (64.9)	5.4 (5.4)	18.8 (18.9)	10.6 (10.8)	168	89
6b	p-tolyl	"	$C_{17}H_{18}N_4S$	65.7 (65.8)	5.7 (5.8)	17.9 (18.0)	10.3 (10.3)	161	77
6c	p-anisyl	"	$C_{17}H_{18}N_4OS$	62.3 (62.5)	5.3 (5.5)	17.1 (17.1)	9.9 (9.8)	141	75
6d	p-phenetyl	"	$C_{18}H_{20}N_4OS$	63.8 (63.6)	5.9 (5.9)	16.5 (16.6)	9.4 (9.3)	83	72
6e	O-phenetyl	"	$C_{18}H_{20}N_4OS$	63.7 (63.9)	5.7 (5.9)	16.5 (16.6)	9.4 (9.3)	146	70
6f	Phenyl	2',5'-xylyl	$C_{16}H_{16}N_4S$	64.7 (64.9)	5.4 (5.4)	18.8 (18.9)	10.6 (10.6	100	83
6g	p-tolyl	2',5' xylyl	$C_{17}H_{18}N_4S$	65.7 (65.8)	5.7 (5.8)	17.9 (18.0)	10.3 (10.3)	123	78
6h	Pheny	2,6-(diisopropyl) Phenyl	$C_{20}H_{24}N_4S$	68.1 (68.2)	6.8 (6.9)	15.8 15.9	9.2 9.0	181	72
6i	p-toyl	2,6-(diisopropyl)	$C_{20}H_{24}N_4S$	68.5 (68.6)	7.1 (7.1)	15.1 (15.3)	8.9 (8.7)	138	70

2.1 Oxidation of Binary Mixtures of 1-aryl-3-(2',6'-xylyl) Thioureas and Thiourea

In a typical experiment, a mixtures of 1-phenyl-3-(2',6'-xylyl)thiourea (6.05g, .025 mole) and thiourea (1.9g, .025 mole) in 1:1 ethanol-water mixture (200ml) containing con.HCl (6ml, 32%, .025mole) and oxidized with hydrogen peroxide (6 ml, 30%, .05 mole). Colloidal sulphur started separating as evidenced by a pale yellow turbidity. During the addition of H_2O_2, the reaction mixture was warmed on a waterbath. When the oxidation was complete the reaction mixture was cooled and filtered. The filtrate on basification yielded a white precipitate derived from the mixed oxidation. It was then collected, dried and crystallized from benzene-petroleum ether mixture when shining plates of the base were obtained (M.p.168^{0}C, 6.6g, 89%). T.L.C examination of this product showed the presence of only one compound and it was identified as 3-amino-4-phenyl-5-(2',6'-xylyl)imino-Δ^2-1,2,4-thiadiazoline **6**. Analysis found : C=64.8%, H = 5.4%, N = 18.8%, S = 10.6% required for $C_{16}H_{16}N_4S$, C = 64.9%, H = 5.4%, N = 18.9%, S = 10.8%; UV (MeOH) λ_{max} 220, 250, 260 nm; I.R (KBr) υ_{max} (cm^{-1}), 3450 & 3220 (s,N=H), 2970 (s), 2870 (m, C-H) 1640 (w, C=N), 1620 (s,NH_2),1025 (m) & 810 (ring skeletal vibrations of 1,2,4-thiadiazoline); N.M.R ($CDCl_3$) δ: –2.1 (s,6H, 2xCH_3 of xylyl), 4.9 (s, 2H, NH_2), 7-7.7 (non-resolved multiplet; 8H, Ar-H); Mass m/z (%) 296, (M^+, 93.3), 254 (25.2), 222 (44.3), 204 (10.1), 16.3 (1.5), 91 (30.4), 91 (30.4), 79 (17.9).

Biography of author(s)

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