

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF SUBSTITUTED ARYLTHIOUREA

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ABSTRACT

Substituted Arylthiourea have been synthesized by the action of ammonium thiocyanate with Aromatic amine in the presence of acid like conc. HCl. The synthesized compound characterized by spectral analysis and elemental analysis. It shows antimicrobial activity.

Keywords: Ammonium thiocyanates, Arylthiourea's, acid catalyst, antimicrobial activities.

INTRODUCTION

Thioureas are a group of compounds possessing a wide spectrum of biological activities. Such as antimicrobial, antifungal etc. Thompson et.al.¹ synthesized N-substituted isoquinolinl-N'-substituted phenyl thioureas, found useful for the treatment and / or prophylaxis of anxiety, mania, depression, panic disorders, migraine and defects associated with AIDS.

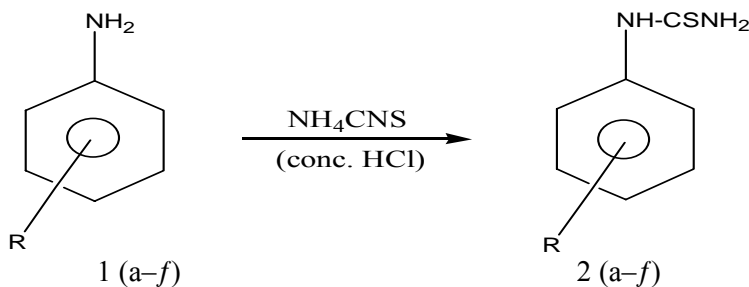
Recently Pandey et.al.² have received the bioactivity of thioureas. They exhibited antithyroidal, antibacterial and hypoglycemic activities. Biological activity of arylthiourea derivatives has been evaluated for anti convulsant⁴, antibacterial⁵⁻⁶, antiarrhythmic⁷, and anti-hyperlipidemic⁸ activities. Our considerable interest is to optimize the auxiliary group present in the aryl ring of thioureas to produce potent antimicrobial activity. It has also an important application for the protection of human skin from harmful UV irradiation¹³⁻¹⁴ and corrosion inhibitor¹⁵.

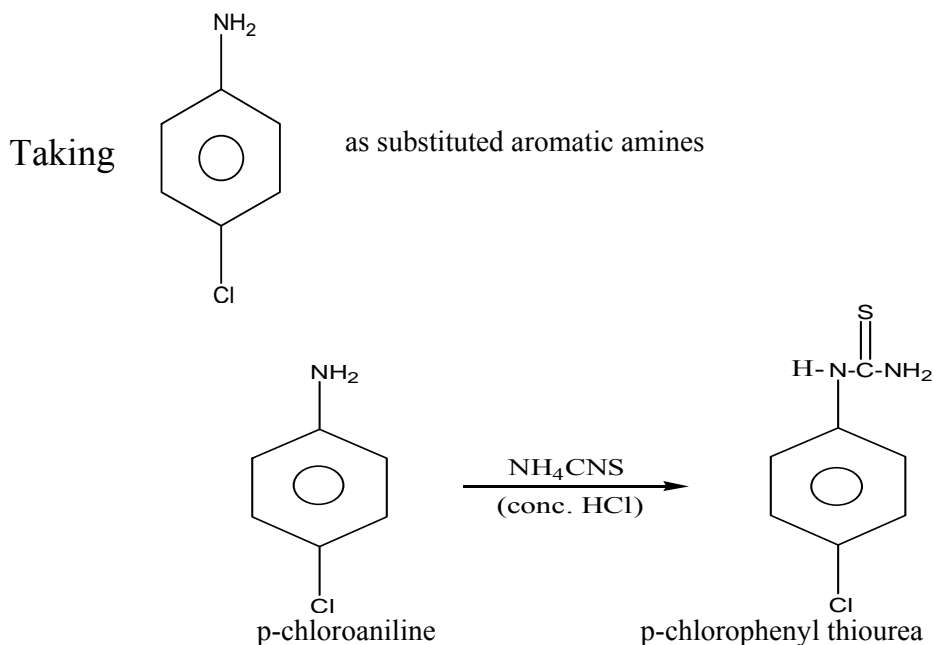
Due to these valuable findings and its need, present work has been carried out on the precipitation of substituted Arylthiourea and its derivatives.

EXPERIMENTAL

Synthesis of substituted Aryl thioureas

(0.1 mol) of substituted Aromatic amine was dissolved in 10 ml of conc. HCl and diluted to 100 ml with water in 250 ml round bottom flasks. To this added dropwise 0.1 mol of ammonium thiocyanates solution (in 50 ml warm water) in 10-15 minutes with constant stirring. The mixture was refluxed using air condenser for 30 minutes and then cooled it in an ice bath. The crystals thus obtained filtered in a pump wash with water (20-25°C) and recrystallized from absolute alcohol (Scheme-1).





Scheme-2

Melting points were determined in open capillary tubes and were found uncorrected. IR spectra were recorded on fourier transform IR spectrophotometer (shimadzu) using KBr disc methods. UV spectra were taken on Jasco model – 7800, UV spectrophotometer using methanol as solvent.

PMR spectra in CDCl_3 were recorded on Burker Advance DPx 200 MHz spectrophotomerer. The purity of the test compounds was determined by TLC. A single spot obtained confirmed the purity of substituted arylthiourea.

Physical data and spectral analysis are recorded in the following Table-1.

Table-1

Comp. No.	R	Mol. formula	M.P.	λ_{max} UV : – (Methanol)	IR (KBr; m^{-1})	[NMR/PMR] (CDCl_3 / DMSO-d_6 , δ)
2 (a)	P - Cl	$\text{C}_7\text{H}_7\text{N}_2\text{SCl}$	159°C	$\lambda_{\text{max}} = 305$ nm; 330 nm	3420 cm^{-1} (asymmetric NH stretching) 3310 cm^{-1} (symmetric NH stretching) 3030 cm^{-1} (aromatic C-H stretching) 1550 cm^{-1} (N-H bending) 1280 cm^{-1} (N-CS-N stretching) 1190 cm^{-1} (C=S stretching) 730 cm^{-1} (C - Cl stretching)	9.8 (bS, 1H, NH) 6.7 (S, 2H, CSNH ₂) 7.4 (m, 4H, aromatic)
2 (b)	P - Br	$\text{C}_7\text{H}_7\text{N}_2\text{SBr}$	171°C	$\lambda_{\text{max}} = 204$ nm; 330 nm	3420 cm^{-1} (asymmetric N-H stretching) 3300 (symmetric N-H stretching) 3020 (aromatic C-H stretching) 1550 cm^{-1} (N-H bending) 1280 cm^{-1} (N-CS-N stretching) 1200 cm^{-1} (C = S)	9.7 (bS, 1H, NH) 6.7 (S, 2H, CSNH ₂) 7.5 (m, 4H, aromatic)

					stretching) 860 cm ⁻¹ (C – Br stretching)	
2 (c)	o – OCH ₃	C ₈ H ₁₀ ON ₂ S	142 ⁰ C	λ max = 245 nm	3440 (asymmetric N–H stretching) 3220 cm ⁻¹ (symmetric N–H stretching) 3020 cm ⁻¹ (aromatic C–H stretching) 2930 cm ⁻¹ (methyl C–H stretching) 1240 cm ⁻¹ [(C–O stretch) 760 cm ⁻¹ (=(-H bending)]	9.8 (bS, 1H, NH) 6.7 (S, 2H, CSNH ₂) 7.5 (m, 4H, aromatic) 3.8 (S, 3H,OCH ₃)
2 (d)	P – CH ₃	C ₈ H ₁₀ N ₂ S	170 ⁰ C	λ max = 240 nm	3430 (asymmetric N–H stretching) 3320 cm ⁻¹ (symmetric N–H stretching) 3000 cm ⁻¹ (aromatic CH stretching) 2900 cm ⁻¹ (methyl C–H stretching) 1590 cm ⁻¹ (N–H bending) 1460 cm ⁻¹ (C – C ring stretching) 1190 cm ⁻¹ (C = S stretching)	9.9 (bS, 1H, NH) 6.8 (S, 2H, CSNH ₂) 7.5 (m, 4H, aromatic) 2.3 (S, 3H, CH ₃)

Comp. No.	R	Mol. formula	M.P.	λ max / UV (Methanol) : –	IR (KBr; m ⁻¹)	[NMR/PMR] (CDCI ₃ / DMSO-d ₆ , δ)
2 (e)	o – CH ₃	C ₈ H ₁₀ N ₂ S	129 ⁰ C	λ max = 240 nm	3420(asymmetric N–H stretching) 3320 cm ⁻¹ (symmetric N–H stretching) 3000 cm ⁻¹ (aromatic CH stretching) 2900 cm ⁻¹ (methyl C–H stretching) 1590 cm ⁻¹ (N–H bending) 1460 cm ⁻¹ (C – C ring stretching) 1190 cm ⁻¹ (C = S stretching)	9.8 (bS, 1H, NH) 6.8 (S, 2H, CSNH ₂) 7.4 (m, 4H, aromatic) 2.3 (S, 3H, CH ₃)
2 (f)	m – CH ₃	C ₈ H ₁₀ N ₂ S	95 ⁰ C	λ max = 240 nm	3425 (asymmetric N–H stretching) 3320 cm ⁻¹ (symmetric N–H stretching) 3000 cm ⁻¹ (aromatic CH stretching) 2900 cm ⁻¹ (methyl C–H stretching) 1590 cm ⁻¹ (N–H bending) 1460 cm ⁻¹ (C – C ring stretching) 1190 cm ⁻¹ (C = S stretching)	9.8 (bS, 1H, NH) 6.7 (S, 2H, CSNH ₂) 7.6 (m, 4H, aromatic) 2.35 (S, 3H, CH ₃)

Elemental Analysis

Satisfactory elemental analysis were obtained on Carlo-Erba-1108 analyzer, and the values were found to be ± 0.4 % of calculated values.

Percentage of element are recorded by elemental analysis of Wockhardt Ltd. and described in Table-2.

Table-2

Comp. No.	Mol. formula	Mol. wt.	% 'C'	% 'H'	% N	% S	% Br	% Cl	% O
2 (a)	C ₇ H ₇ N ₂ SCl	221	45.04	3.78	15.01	17.18	--	18.99	--
2 (b)	C ₇ H ₇ N ₂ SBr	185	36.38	3.05	12.12	13.87	34.57	--	--
2 (c)	C ₈ H ₁₀ ON ₂ S	182	52.72	5.53	15.37	17.59	--	--	8.78
2 (d)	C ₈ H ₁₀ N ₂ S	166	57.80	6.06	16.85	19.29	--	--	--
2 (e)	C ₈ H ₁₀ N ₂ S	166	57.40	6.46	16.75	19.39	--	--	--
2 (f)	C ₈ H ₁₀ N ₂ S	166	57.55	6.26	16.95	19.54	--	--	--

Anti-Microbial Activity

Antimicrobial study is measured invitro in order to determine the sensitivity of given micro-organism to know concentration of the synthesized drug by agar double dilution method. All the synthesized compound were screened for antibacterial activity against E. coli, S. aureus, P. aeruginosa and the data describe in Table-3.

Table-3

Comp. No.	Antibacterial activity (MIC in $\mu\text{g} / \text{mL}$)		
	E. Coli	S. aureus	P. aeruginosa
2 (a)	9.76	19.53	156.25
2 (b)	19.53	9.76	39.06
2 (c)	1250	78.12	1250
2 (d)	156.25	19.53	2500
2 (e)	2500	1250	2500
2 (f)	1250	625	78.12

RESULTS AND DISCUSSION

In the present work ammonium thiocyanate were used as the key raw material for the synthesis of substituted arylthiourea.

Compound 2 (a) – 2 (f) have been characterized on the basis of satisfactory analytical & spectral data. The UV spectra of the compounds showed absorption maxima at 204 – 333.3 nm. The IR spectra exhibits bands at 1210 ± 10 (C=S stretching), 1570 ± 20 (N–H bending), 3310 ± 10 (symmetric N–H stretching), $3430 \pm 10 \text{ cm}^{-1}$ (asymmetric N–H stretching) respectively.

The N – H proton appeared as a broad singlet in offset (δ , 9.7 – 9.9) region while another broad singlet is found in offset (δ , 2.3 – 3.8) region for –CH₃ proton respectively.

Out of the six compounds synthesized in the series 2 (a) and 2 (b) were considered better while other compounds showed good to moderate activity.

CONCLUSION

Substituted Arylthiourea and their derivatives are shown diverse antimicrobial, antifungal, effects.

ACKNOWLEDGEMENT

Thanks are due to department of Chemistry, Dr. Rafiq Zakaria College for Women, Aurangabad for providing necessary facilities during the work.

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(Received: 5 December 2009

Accepted: 25 January 2010

RJC-502)

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