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Short Communication

Synthesis of 1-Phenyl-3-Substituted Phenyl Benzothiazolyl Thiocarbamide

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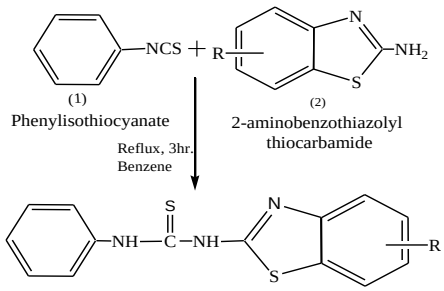
ABSTRACT

Several 1-phenyl, 3-substituted phenyl benzothiazolyl thiocarbamide (3a-j) have been synthesized by the interaction of various substituted benzothiazoles (2a-j) with phenyl isothiocynate. The newly synthesized compounds have been characterized by analytical and IR, ^{1}HNMR and Mass spectral studies.

Graphical Abstract



1-Phenyl,3-substituted-phenyl benzothiazolyl thiocarbamide

Where R= (a) Phenyl, (b) o-Cl-phenyl, (c) m-Cl-phenyl, (d) p-Cl-phenyl, (e) o-nitro-phenyl, (f) m-nitro-phenyl, (g) p-nitro-phenyl, (h) o-tolyl, (i) p-tolyl. (j) o-tolyl

Keywords: Phenyl isothiocynate, substituted benzothiazoles, benzothiazolyl thiocarbamides.

INTRODUCTION

Benzothiazole is a heterocyclic compound weak base, having varied biological properties and still of great scientific interest now a day. They are widely found in bioorganic and medicinal chemistry with application in drug discovery. They have also found application in industry as an antioxidant, vulcanization accelerators various benzothiazole such as 2-aryl benzothiazole received much attention due to unique structure and its uses as radioactive amyloidal imagining agent [1] and anticancer agent[2]. Benzothiazole are bicyclic ring system with multiple applications. A number of 2-aminobenzothiazole were intensively studied in medicinal chemistry [3, 4] and reported cytotoxic on cancer cells [5]. 2-aminobenzothiazole, substituted benzothiazole have found application in several areas of chemistry. 2-

aminobenzothiazole are broadly found in bioorganic and medicinal chemistry with application in drug discovery and development of treatment of diabetes[6], epilepsy[7-8], thrombin inhibitors[9] inflammation[10] amyotrophic lateral scelorosis[11] analgesic[12], tuberculosis[13-14] and viral infection [15]. Raksha S. Bokade and Gajanan V. Korpe have been reported the Synthesis, Characterization and Microbial Studies of N-Lactosylated Isothiobiurets[16].

MATERIALS AND METHODS

All chemicals were research grade. Melting points determined are uncorrected. IR spectra were recorded in KBr on a FT-IR Perkin-Elmer RXI (4000-450cm^{-1}) spectrophotometer. ^{1}H NMR measurements were performed on a Bruker DRX-300 (300 MHz FT NMR) NMR spectrometer in $CDCl_3$ solution with TMS as internal reference. The Mass spectra were recorded on a WATERS, Q-TOF MICROMASS (LC-MS) Mass spectrometer. Optical rotation $[\alpha]_D^{31}$ measured on a Equip-Tronics Digital Polarimeter EQ-800 at 31^{0}C in $CHCl_3$. Thin layer chromatography (TLC) was performed on silica Gel G and spots were visualized by iodine vapour. The compounds describe in this paper were first time synthesized by the multistep reaction protocol.

Preparation of Phenyl Isothiocynate[20] **(1):** The required phenyl isothiocyanate is prepared by already known procedure.

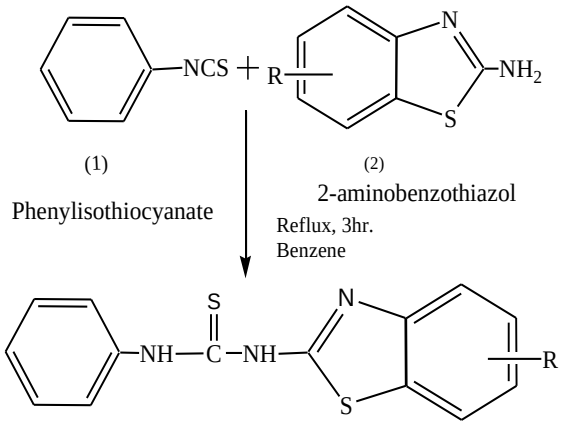
Preparation of Substituted Benzothiazoles (2a-f): The required substituted benzothiazole has been prepared by the oxidative cyclization of aryl thiocarbamide with the help of molecular bromine [21,22]. Prepare Chloroformic paste of previously prepared phenyl thiocarbamide (5gm) by adding chloroform (10ml) in a clean china dish. In this chloroformic paste add molecular bromine (20%) in chloroform with constant stirring, until a slight excess of bromine was added as evident from an orange red colour. It was then allow standing for 5-6 hours. After that adds a small amount of ethanol and basifies with cold ammonium hydroxide solution, benzothiazole is obtained. Filter the solution and dry the precipitate.

3a:- **Synthesis of 1-phenyl, 3-phenyl benzothiazolyl thiocarbamide:** A benzene solution of phenyl isothiocynate (1) (0.1 M, 1.35 g in 10 mL) was mixed with suspension of 2-amino benzothiazole (2a) (0.1 M, 1.50g in 20 mL) and the mixture after shaking for some time was refluxed over a boiling water bath 3 h. After heating, benzene was distilled off and the sticky mass obtained as residue was triturated several times with petroleum ether (60-80^{o}C). Finally it was treated with ethanol then a white solid (1.5 g) was obtained. It was crystallized from aqueous ethanol, m.p. 151^{o}C.

3a: IR (KBr):υ 3363 (N-H), 3030 (Ar-H), 1629 (C=N), 1438 (C-C), 1309 (C-N), 1159 (C=S), 750 (C-S). H NMR (δ in ppm, $CDCl_3$): δ7.156-7.321 (9H, S) δ7.508-7.438 (2H, S) Mass (m/z): 285 (M^+), 225, 151; Anal. Calcd for $C_{14}H_{11}N_3S_2$: C, 65.26; H, 3.85; N, 14.75; S, 22.45; Found: C, 65.20; H, 3.81; N, 14.71; S, 22.42.

On the basis of all above facts the product m. p. was 151^{o}C. assigned and the structure 1-phenyl, 3-phenyl benzothiazolyl thiocarbamide (**3a).**

When the reaction of phenyl isothiocynate was extended to several other 2-amino benzothiazole corresponding 1-Phenyl-3-Substituted Phenyl Benzothiazolyl Thiocarbamide were prepared.



1-Phenyl,3-substituted-phenyl benzothiazolyl thiocarbamide

Where R= (a) Phenyl, (b) *o*-Cl-phenyl, (c) *m*-Cl-phenyl, (d) *p*-Cl-phenyl, (e) *o*-nitro-phenyl, (f) *m*-nitro-phenyl, (g) *p*-nitro-phenyl, (h) *o*-tolyl, (i) *p*-tolyl. (j) *o*-tolyl,

3c: IR (KBr):υ 3363 (N-H), 3030 (Ar-H), 1629 (C=N), 1438 (C-C), 1309 (C-N), 1159 (C=S), 750 (C-S). H NMR (δ in ppm, $CDCl_3$): δ7.156-7.321 (9H, S) δ7.508-7.438 (2H, S) Mass (m/z): 319 (M^+), 320, 280, 246; Anal. Calcd for $C_{14}H_{10}N_3S_2Cl$: C, 52.66; H, 3.13; N, 13.16; S, 20.06; Found: C, 52.70; H, 3.15; N, 13.20; S, 20.10.

3f: IR (KBr):υ 3363 (N-H), 3030 (Ar-H), 1629 (C=N), 1438 (C-C), 1309 (C-N), 1159 (C=S), 750 (C-S). H NMR (δ in ppm, $CDCl_3$): δ7.156-7.321 (9H, S) δ7.508-7.438 (2H, S) Mass (m/z): 330 (M^+), 329, 151, 148; Anal. Calcd for $C_{14}H_{10}N_4S_2O_2$,: C, 50.90; H, 3.03; N, 16.96; S, 19.39; Found: C, 50.94; H, 3.08; N, 16.92; S, 19.40.

4h: IR (KBr):υ 3363 (N-H), 3030 (Ar-H), 1629 (C=N), 1438 (C-C), 1309 (C-N), 1159 (C=S), 750 (C-S). H NMR (δ in ppm, $CDCl_3$): δ7.156-7.321 (9H, S) δ7.508-7.438 (2H, S) Mass (m/z): 299 (M^+), 251, 225; Anal. Calcd for $C_{15}H_{13}N_3S_2$,: C, 60.20; H, 4.34; N, 14.04; S, 21.40; Found: C, 60.24; H, 4.38; N, 14.10; S, 21.44.

Table -1: Physical data for characterization of compounds (3a-j) C

Sr. No	Compd	Yield %	M.P. ^{0}C	R_f (pet ether: EtOAC) (1:1)	Analysis (%): Found (calcd)	
					N	S
1	Phenyl(3a)	80.00	151	0.65	14.71 (14.75)	22.44(22.45)
2	o-Chloro(3b)	79.00	121	0.58	13.12(13.16)	20.08(20.06)
3	m-Chloro(3c)	82.00	110	0.73	13.20(13.16)	20.10 (20.06)
4	p-Chloro(3d)	81.00	132	0.48	13.18(13.16)	20.02(20.06)
5	o-nitro-(3e)	78.00	129	0.63	16.94(16.96)	19.33(19.39)
6	m-nitro-(3f)	84.25	137	0.70	16.92(16.96)	19.40(19.39)
7	p-nitro-(3g)	80.00	146	0.68	16.98(16.96)	19.43(19.39)
8	o-tolyl(3h)	74.02	133	0.55	14.10(14.04)	21.44(21.40)

9	m-tolyl(3i)	65.50	126	0.60	14.02(14.04)	21.38(21.40)
10	p-tolyl(3j)	75.00	144	0.80	14.00(14.04)	21.45(21.40)

C and H analysis was found satisfactory in all cases.

RESULTS AND DISCUSSION

Several 1- Phenyl, 3-substituted phenyl benzothiazolyl thiocarbamides (3a-j) have been synthesized by the interaction of various substituted benzothiazoles (2a-j) with phenyl isothiocyanate (1). A benzene solution of phenyl isothiocynate (1) (0.1 M, 1.35 g in 10 mL) was mixed with suspension of 2-amino benzothiazole (2a) (0.1 M, 1.50g in 20 mL) and the mixture after shaking for some time was refluxed over a boiling water bath 3 h. After heating, benzene was distilled off and the sticky mass obtained as residue was triturated several times with petroleum ether (60-80^{o}C). Finally it was treated with ethanol then a white solid (1.5 g) was obtained. It was crystallized from aqueous ethanol. The IR spectra of products shows bands due to Ar-H, N-H, C=S, C=N, C-N, C-S stretching and ^{1}HNMR spectra of products distinctly displayed signals due to aromatic protons and N-H Protons. The Mass spectrum of product was also observed. The identities of these new *N*-lactosides have been established on the basis of usual chemical transformations and also IR, ^{1}H NMR and Mass spectral studies [17-19].

APPLICATIONS

The synthesized benzothiazolyl thiocarbamides lead for the development of new drugs due to the nature presence of sulphur and nitrogen present in it. The applicability of synthesized compounds is also supported by the various references quoted in the script.

CONCLUSIONS

In this research work, the characterizations of newly synthesized products were established on the basis of UV, IR, ^{1}H NMR, & Mass spectral studies. Various 1- Phenyl, 3-substituted phenyl benzothiazolyl thiocarbamides were synthesized and yield of product ranged from 65-82%.

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