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Design, Synthesis and Multi-Spectroscopic Characterization of Aryl-Substituted Isodithiobiurets

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ABSTRACT

In the design of new bioactive compounds, the development of hybrid molecules through the combination of different pharmacophores in one frame may lead to compounds with interesting biological profiles. Serial of the **"**1-aryl-5-para-tolyl 2-s-benzyl-2-4-isodithiobiurets**"** was prepared by the interaction of 1-aryl-s-benzyl-isothiocarbamide and P-tolyl-isothiocynate in Benzene Medium. The Reaction was refluxed for 3-hours in benzene medium. After completion of the reaction, the solvent was distilled off and sticky residue obtained was triturated with petroleum ether (60-80^{o}C) to afford a pale yellow solid (IIIa). It was purified by chloroform-petroleum ether (IIIa), m.p. 170^{0}C. The elemental analysis of this new product indicated molecular formula as $C_{22}H_{21}N_3S_2$ Acylureas and biurets are noncyclic compounds which upon replacement of one or both oxygen with sulphur results into the formation of thiobiurets and dithiobiurets respectively. Isodithiobiuret derivatives shows potent biological activities such as anticonvulsant, hypnotic, analgesic, antifungal, insecticidal activity.

Keywords: P-tolyl-isothiocynate, 1-aryl-s-benzyl-isothiocarbamide etc.

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INTRODUCTION

Acyl urea and biurets are noncyclic compounds which upon replacement of one or both oxygen with sulphur results into the formation of thiobiurets and dithiobiurets respectively. Isodithiobiuret derivatives[1-2]shows potent biological activities such as anticonvulsant, hypnotic, analgesic, antifungal, insecticidal activity. Mono and dithiobiuret derivatives are effective bactericide, fungicide, herbicide, and miticides [3]Dithiobiuret derivatives are used for repelling birds, rodents, leporine animals, and ruminants[4] 1-Allyl-2-thiobiuret regulates the growth of germinating wheat and cucumber seeds[5] Oliver and coworkers[6-7] reported chemo sterilizing action of dithiobiuret derivatives in male house flies. Mono and dithiobiuret showed effective growth regulating activity[8]. Thiobiuret derivatives also showed analgesic [9], anticonvulsant, and hypnotic activity [10.] Glycosyl urea and their biuret derivatives are reported as potential glycoenzyme inhibitors

MATERIALS AND METHOD

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. ^1H 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 THERMO Finnigan LCQ Advantage max ion trap Mass spectrometer. Optical rotation $[\alpha]_D^{31}$ measured on a Equip-Tronics Digital Polarimeter EQ-800 at 31^0C 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.

Procedure

Preparation of thiourea:

In clean and dry 250ml beaker add 25ml aniline and 30ml concentrated HCl. Here hydrochloric salt is obtained. Add about 75ml of distilled water to this solution. Stir it properly. Separately prepare ammonium thiocynate solution by dissolving 20gm of ammonium thiocynate in 75ml of distilled water. Now add this solution into previously prepared solution with continuous stirring. Boil this solution till turbidity occurs. The turbidity occurs due to the separation of phenyl thiocarbamide. Add this solution into 200ml ice cold water with continuous stirring, there is a formation of precipitate into beaker. Allow the beaker to stand for 30 minutes. Filter the solution with Buchner funnel and dry the precipitate.

Preparation of 1-Aryl-*s*-benzyl isothiocarbamide:

To the ethanolic suspension of phenyl thiocarbamide was added benzyl chloride and the reaction mixture was reflux for 90 min. Afterward the reaction mixture was cooled and rendered basic with

dil. ice cold NH_4OH and a sticky residue was obtained which on standing for 1 to 2 hrs. Solidifies. It was filtered and washes with petroleum ether**.**

Preparation of P-Tolyl- Isothiocynate:[14]

Place a 500ml conical flask in freezing mixture of ice and salt. Add to it 30 ml of conc. Ammonia solution and 15ml of pure carbon disulphide. Stir the mixture and run in 19 gm of p-toluidine about 15 min. Stir for a further 30min and allow standing for another 30min. A heavy ppt of Ammonium p-toluidine dithiocarbamate separates. Filter it and dry it.

Transfer the salt to a 2lit R.B. flask. By 2-3 extractions with 100ml portion of distilled water. To this solution of 50gm of lead nitrate in distilled water with constant stirring. Lead sulphide ppt is observed. Steams distill the mixture into a receiver containing 10ml of 0.5ml H_2SO_4 as long as organic material passes over. Separate the oil; dry it over anhydrous Calcium Chloride or Magnesium Sulphate.

RESULTS AND DISCUSSION

Serial of the "1-phenyl-5-para-tolyl-2-S-benzyl-2-4-isodithiobiurets" was prepared by the interaction of the of 1-aryl-s-benzyl-isothiocarbamide and P-tolyl-isothiocynate in Benzene Medium. The Reaction was refluxed for 3-hours in benzene medium and the benzene is evaporated and then the product is recrystallized by the petroleum ether (60-800C). The identities of these new - substituted S-Benzyl isothiocarbamide have been established on the basis of usual chemical transformations and IR, 1HNMR and Mass spectral studies[11-13].

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[21-23]

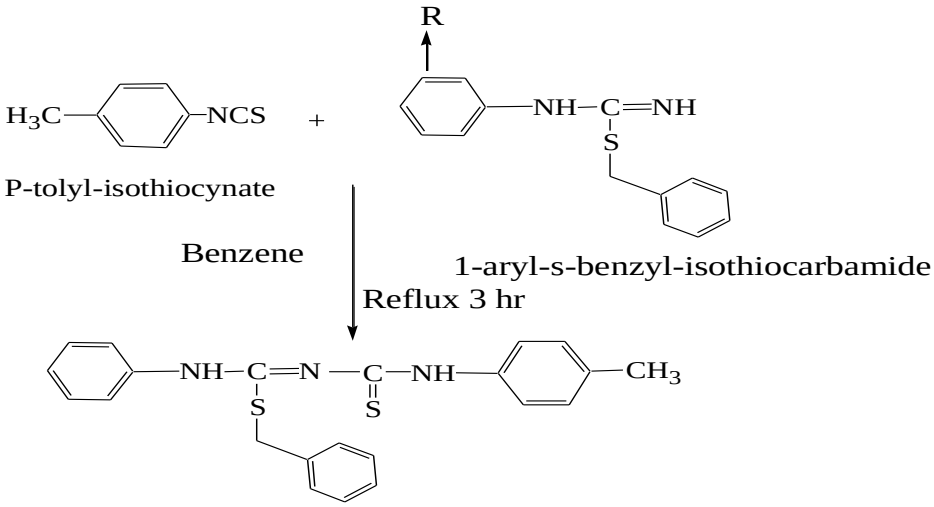
A. Spectral Studies

3.1 3a): IR (KBr):υ 3369 (N-H), 3062 (Ar-H), 2958 (Ali C-H), 1529 (C=N), 1378 (C-N), 1159 (C=S), 750 (C-S).

H NMR (δ in ppm, $CDCl_3$): δ7.156-7.321 (14H, S) δ7.508-7.438 (2H, S) Mass (m/z): 390 (M^+), 267, 225; Anal. Calcd for $C_{22}H_{21}N_3S_2$: C, 67.51; H, 5.37; N, 10.74; S, 16.36; Found: C, 67.48; H, 5.30; N, 10.70; S, 16.30.

On the basis of all above facts the product with m. p. 170˚C. was assigned the structure 1-phenyl-5 para-tolyl-2-s benzyl -2-4 isodothiobiurets (**3a)**

When the reaction of P-tolyl-isothiocynate was extended to several other 1-aryl-s-benzyl-isothiocarbamide corresponding 1-aryl-5 para-tolyl-2-s benzyl -2-4 isodothiobiurets were prepared.



1-aryl-5-para-tolyl-2-s-benzyl-2-4-isodithiobiurets

R=a) Aniline b)*o*-chloro aniline c)*m*- chloro aniline d)*p*- chloro aniline

3c: IR (KBr):υ 3363 (N-H), 3030 (Ar-H), 2980 (Ali C-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): 425 (M^+), 302, 225; Anal. Calcd for $C_{22}H_{21}N_3S_2Cl$: C, 62.11; H, 4.70; N, 9.88; S, 15.05; Found: C, 62.15; H, 4.65; N, 9.80; S, 15.10.

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

Sr. No	Compd	M.P.^{0}C	Yield %	R_f (pet ether: EtOAC) (1:1)	Analysis (%): Found (calcd)	
					N	S
1	Phenyl(3a)	170^{0}C	60%	0.65	10.70 (10.74)	16.30(16.36)
2	o-Chloro(3b)	147^{0}C	68%	0.58	9.80 (9.88)	15.10 (15.05)
3	m-Chloro(3c)	140^{0}C	62%	0.73	9.83 (9.88)	15.18 (15.05)
4	p-Chloro(3d)	142^{0}C	65%	0.48	9.93 (9.88)	15.00 (15.05)

C and H analysis was found satisfactory in all cases.

APPLICATIONS

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

CONCLUSION

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-aryl-5-para-tolyl2-s-benzyl-2-4-isodithiobiurets were synthesized and yield of product ranged from 60-70%.

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