



Design, Synthesis and Characterization of Novel 1-(5-Substituted-2,4-dithiobiurete)-4-methoxyphenyl

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Abstract:

In this study, we have developed a straightforward and efficient method for synthesizing a series of 2,4-dithiobiuret derivatives. Specifically, we focused on the preparation of a novel set of compounds: 1-(5-Substituted-2,4-dithiobiurete)-4-methoxyphenyl. To achieve this, we reacted 1-(4-methoxyphenyl) thiourea with various substituted isothiocyanates in a 60% acetone-ethanol solvent mixture.

The structural characterization of the synthesized compounds was carried out using elemental analysis, assessment of chemical properties, and spectral studies. These investigations allowed us to confirm the identity and purity of the newly prepared derivatives.

Keyword: 1-(4-methoxyphenyl) thiourea, aryl / alkyl isothiocyanates, 2,4- dithiobiuretes.

Introduction:

Heterocyclic compounds derived from mono and dithiobiuretes have demonstrated significant bactericidal, fungicidal, and herbicidal activities¹⁻³. Among these, acyclic 2,4-dithiobiuretes stand out as potent biological moieties³⁻⁵. The synthesis and biological evaluation of novel 2,4-dithiobiuretes represent an intriguing area of study within organic chemistry. These compounds serve as valuable organic intermediates⁶⁻¹¹ for the construction of active heterocycles, particularly those containing nitrogen and sulfur atoms. The synthesized heterocycles play a crucial role as intermediates in the preparation of thiadiazoles, dithiazoles, thiadiazines, triazines, and Hector's bases.

Given these considerations, our research focused on the synthesis of 1-(5-substituted-2,4-dithiobiurete)-4-methoxyphenyl (III a-d). This was achieved through the reaction of equimolar amounts of 1-(4-methoxyphenyl) thiourea with various substituted isothiocyanates in a 60% acetone-ethanol solvent mixture (Scheme I).

Material and Method:

AR grade Merck and Sigma chemicals were used for synthesis. Melting points of all synthesized compounds were recorded in open glass capillaries with a SGW X-4 digital apparatus and were uncorrected. Carbon and hydrogen estimation were carried out on Carlo-Ebra-1106 analyzer while of

Nitrogen Colman-Nalyzer-29 and sulphur estimations were carried out by Carius method. IR spectra were recorded on Perkin Elmer spectrometer in the range 4000-400 cm⁻¹ in KBr pellets. PMR and C13spectra were recorded on Bruker Avance II- 400 NMR spectrometer with TMS as an internal standard using CDCl₃ and DMSO-d₆ as a solvent. Purity of the compounds was checked on silica gel - G plates by TLC with layer thickness of 3mm by using pet ether and ethyl acetate as solvent. Mass spectra were recorded on WATERS, Q-TOF micromass (ESI-MS).

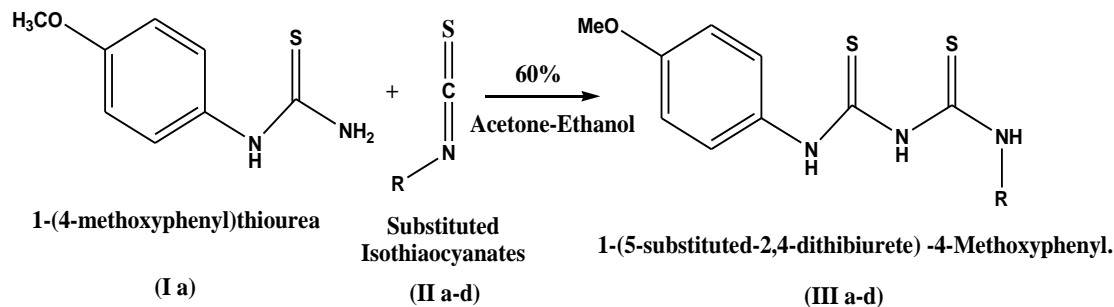
Experimental

Synthesis of 1-(5-Substituted-2,4-dithiobiurete)-4-methoxyphenyl (III a-d)

1-(5-Substituted-2,4-dithiobiurete)-4-methoxyphenyl (III a) was prepared. In 100 ml RBF reaction mixture of 1-(4-methoxyphenyl) thiourea (Ia) (0.01M) and 4-Nitroisothiocyanate (IIa) (0.01M) and in 60% acetone-ethanol medium in 1:1 molar proportion refluxed for 4 hours on water bath. The remaining solvent was distilled off. Separated Yellow crystals were washed with petroleum ether. These yellow crystals on basification with dilute ammonium hydroxide solution giving pale yellow crystals and recrystallized with aqueous ethanol. Yield 82%, M.P. – 184^oC.

Similar method has been adopted for the synthesis of remaining members of the series (IIIb to IIIId).

Reaction Scheme



R = 4-Nitrophenyl, 4-fluorophenyl, -Ethyl -Allyl

Data Analysis:

1-(5-(4-nitrophenyl)-2,4-dithibiurete)-4-methoxyphenyl (III a)

Yellowish crystalline solid, M.F. $C_{15}H_{14}N_4O_3S_2$, yield 80%, MP $184^{\circ}C$; **Elemental Analysis: Found (Calculated)** C 49.71(50.12); H 3.89(4.10); N 15.46(15.90); O 13.24(14.10); S 17.69(18.10).) 1H NMR (400 MHz, DMSO- d_6): NH protons at δ 9.8026-9.4717 ppm, Ar-H protons at δ 7.7572-7.0562 ppm, -NH protons at δ 3.5385 ppm, OCH₃ protons at δ 3.73, ^{13}C : C=S carbon at δ 183.76 ppm, Ar-C carbon at δ 140.87-120.72 ppm, CH₃ carbon at δ 40.09-38.63 ppm. **IR (KBr, cm^{-1}):** 3414 N-H stretching., 2972 C-H stretching., 1734 N=C-N stretching., 1541 N-C=S stretching., 1149 C-N stretching; **MS (ESI) (m/z)** :362(M)⁺, 363.

1-(5-(4-fluorophenyl)-2,4-dithibiurete)-4-methoxyphenyl (III b)

Brownish crystalline solid, M.F. $C_{15}H_{14}FN_3OS_2$, yield 78%, MP $196^{\circ}C$; **Elemental Analysis: Found (Calculated)** C 53.71(54.10); H 4.21(4.70); F 5.66(6.10); N 12.53(13.90); O 4.77(5.12); S 19.12(20.10).) 1H NMR (400 MHz, DMSO- d_6): NH protons at δ 9.8026-9.4717 ppm, Ar-H protons at δ 7.7572-7.0562 ppm, -NH protons at δ 3.5385 ppm, OCH₃ protons at δ 3.73, ^{13}C : C=S carbon at δ 183.76 ppm, Ar-C carbon at δ 140.87-120.72 ppm, CH₃ carbon at δ 40.09-38.63 ppm. **IR (KBr, cm^{-1}):** 3414 N-H stretching., 2972 C-H stretching., 1734 N=C-N stretching., 1541 N-C=S stretching., 1149 C-N stretching; **MS (ESI) (m/z)** :335 (M)⁺, 360.

1-(5-ethyl-2,4-dithibiurete)-4-methoxyphenyl (III c)

White crystalline solid, M.F. $C_{11}H_{15}N_3OS_2$, yield 70%, MP $222^{\circ}C$; **Elemental Analysis: Found (Calculated)** C 49.04(50.12); H 5.61(6.22); N 15.60(16.10); O 5.94(6.10); S 23.81(23.00).) 1H NMR (400 MHz, DMSO- d_6): CH₂ proton at δ 3.72 ppm, NH protons at δ 4.1026-4.3717 ppm, Ar-H protons at δ 7.7572-7.0562 ppm, -NH protons at δ 3.538 ppm, OCH₃ protons at δ 3.73, CH₃ proton at 1.00 ppm ^{13}C : C=S carbon at δ 183.76 ppm, Ar-C carbon at δ 140.87-120.72 ppm, CH₃ carbon at δ 40.09-38.63 ppm.

δ 40.09-38.63 ppm. **IR (KBr, cm^{-1}):** 3414 N-H stretching., 2972 C-H stretching., 1734 N=C-N stretching., 1541 N-C=S stretching., 1149 C-N stretching; **MS (ESI) (m/z)** :270(M)⁺, 182.

1-(5-allyl-2,4-dithibiurete)-4-methoxyphenyl (III d)

Pale yellowish crystalline solid, M.F. $C_{12}H_{15}N_3OS_2$, yield 71%, MP $210^{\circ}C$; **Elemental Analysis: Found (Calculated)** C 51.22(52.12); H 5.37(6.10); N 14.93(15.60); O 5.69(6.10); S 22.79(23.10).) 1H NMR (400 MHz, DMSO- d_6): CH₂ proton at δ 4.72 ppm, NH protons at δ 4.1026-4.3717 ppm, Ar-H protons at δ 7.7572-7.0562 ppm, -NH protons at δ 3.538 ppm, OCH₃ protons at δ 3.73, ^{13}C : C=S carbon at δ 183.76 ppm, Ar-C carbon at δ 140.87-120.72 ppm, CH₃ carbon at δ 40.09-38.63 ppm. **IR (KBr, cm^{-1}):** 3414 N-H stretching., 2972 C-H stretching., 1734 N=C-N stretching., 1541 N-C=S stretching., 1149 C-N stretching; **MS (ESI) (m/z)** :281(M)⁺, 176.

Result and Discussion

In the present research of synthesis of compounds (IIIa-III d), percentage of yield of compound (IIIa) is highest i.e. 80%. Variation in the yield of each compound is due to substitution at Nitrogen in the alky/aryl isothiocyanate (IIa-d). It is also observed that, change in the substituent at nitrogen leads not only the yield of product but also it affects the melting point.

Conclusion:

The present work is a cheaper and less time consuming method for synthesis of organic compound (III a-d). The entire synthesized compound were analyzed, found and confirmed by their elemental study, IR spectra and PMR spectra.

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Disclosure of conflict of interest

The author declare no conflict of interest

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