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Nanoparticle Synthesis of 5Aryl-4-dithiobiurets Derivative of Glucose

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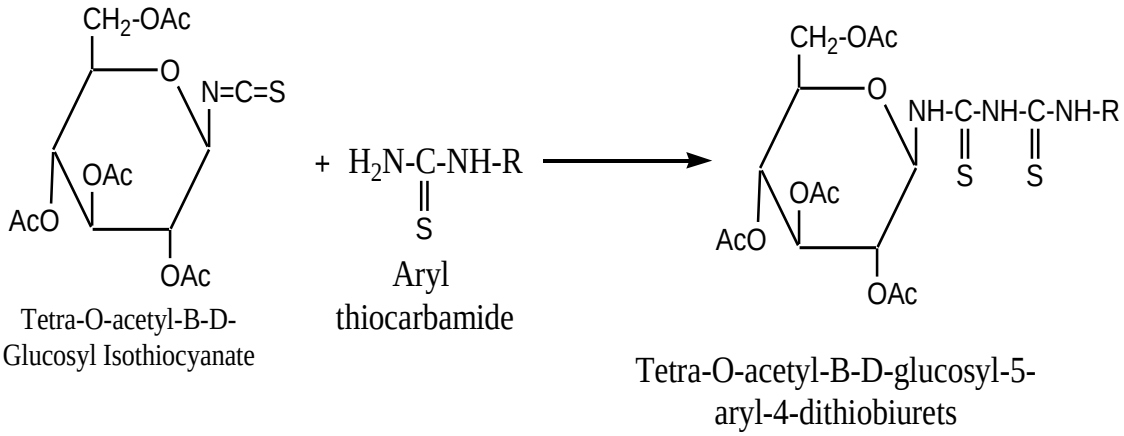
ABSTRACT

In recent years the chemistry of thiobiurets and related compounds has been attached increasing attention. Physiological and potential chemotherapeutic properties of numerous derivatives have been studied, and possible technical applications, particularly in the field of plastic and resins are embedded in an intensive patent literature.Thiobiurets and its alkylated derivatives act as antipyretics, when administered subcutaneously (to rabbits). Lethal doses cause decreases blood pressure, lung edema and general collapse.Nanotechnology also involves the synthesis of nanoparticles. These compounds arouse interest as potential biologically active substances and versatile intermediates for preparing various derivatives. To achieve the principle of green chemistry process, it leads to in search of green synthesis of nanoparticles. Here we are synthesized 1 tetra-O-acetyl-B-D. glucosyl-5aryl-4-dithiobiurets by interaction of aryl thiocarbamides and tetra-O-acetyl-B-D-glucosyl isthiocyanateThe identities of newly synthesis compounds have been established based on usual chemical transformation and U.V, IR, NMR, Mass and Partical Size analysis Analytical studies.

Keywords: *TAG Isothiocyanate ,various aryl thiocarbamide and 1-Tetra-O-acetyl- β -D-glucosyl-5-aryl 4-dithiobiuretsnanoparticles.*

Graphical Abstract



INTRODUCTION

The chemistry of thiourea of carbohydrate is extensively elaborated and well documented[**1]**. These compounds arouse interest as potential biologically active substances and versatile intermediates for preparing various derivatives. The biological properties of polyhydroxy compounds have been reported[**2,3]**.

Nanotechnology, as defined by size, is naturally very broad, including the field of science as diverse as surface science, organic chemistry, molecular biology, semiconductor physics, energy storage, microfabrication, molecular engineering, etc. The associated research and applications are equally diverse, ranging from extensions of conventional device physics to completely new approaches based upon molecular self-assembly, from developing new materials with dimensions on the nanoscale to direct control of matter on the atomic scale. Nanotechnology may create many new materials and devices with various applications, such as in Nanomedicines, Nanoelectronics, and biomaterial energy production and consumer products.

Thiobiurets and its alkylated derivatives act as antipyretics, when administered subcutaneously (to rabbits). Lethal doses cause decreases blood pressure, lung edema and general collapse[**4]**.

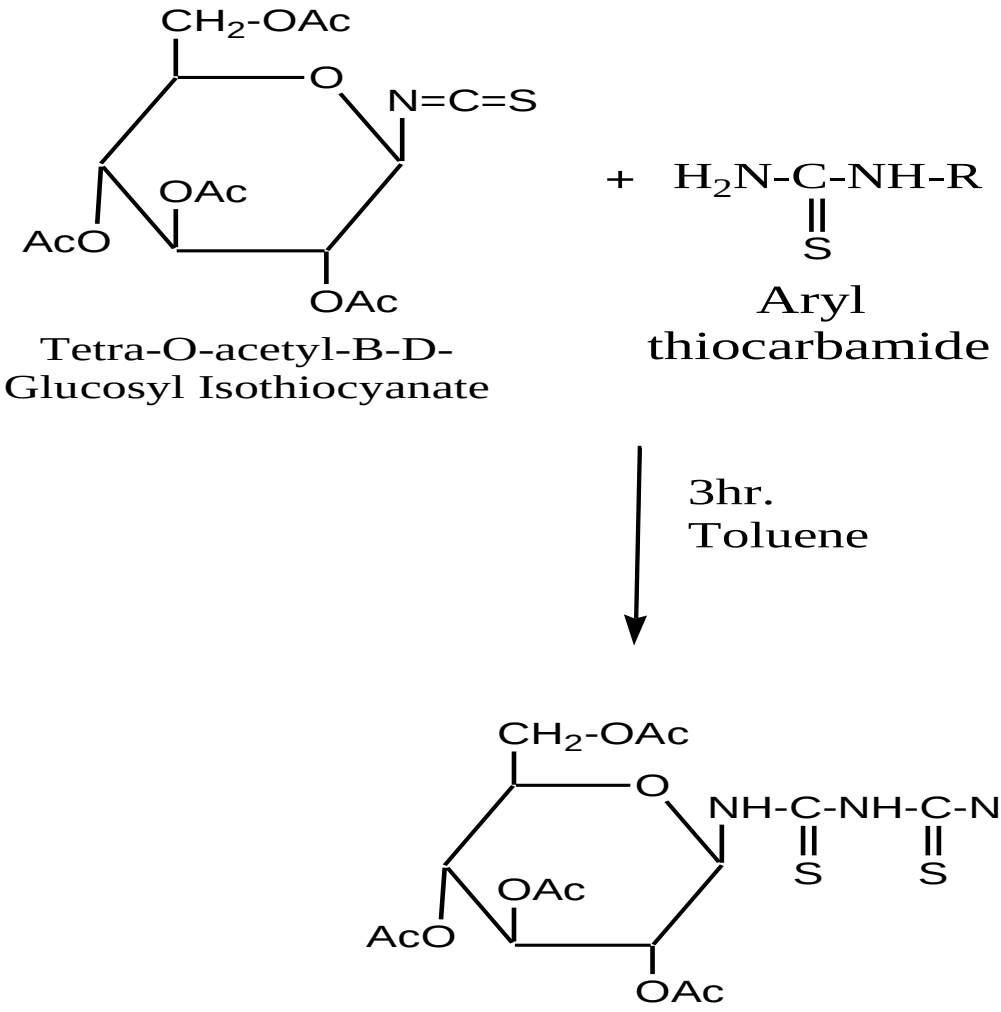
plays an important role in the field of medicinal chemistry and renders an extensive range of biological activities including anti-cancer [**5**,**6**], anti-bacterial [**7**,**8**], anti-tuberculosis [**9**,**10**], anti-diabetic [**11**], anthelmintic [**12**], anti-tumor [**13**,**14**,**15**], anti-viral [**16**,**17**], anti-oxidant [**18**], anti-inflammatory [**19**,**20**], anti-glutamate and anti-parkinsonism [**21**], anticonvulsant [**22**], muscle relaxant activities [**23**], neuroprotective [**24**], inhibitors of several enzymes and so on [**25**]. Hence, the synthesis of benzothiazoles is of considerable interest due to their potent and significant biological activities and great pharmaceutical value.

RESULTS AND DISCUSSION:

NANOPARTICLES:

A nanoparticle isa sub-classification of the ultrafine particle with lengths in two or three dimensions greater than 0.001 micrometer (1 nanometer) and smaller than about 0.1 micrometer (100 nanometers) and which may or may not exhibit a size-related intensive property. This term is a subject of controversy regarding the size range and the presence of a size-related property. Current usage emphasizes size and not properties in the definition. The length scale may be a hydrodynamic diameter or a geometric length appropriate to the intended use of the nanoparticle. The chemistry of thiourea of carbohydrates is extensively elaborated and well documented. These compounds arouse interest as potential biologically active substances and versatile intermediates for preparing various derivatives

Reaction Scheme



Interaction of tetra-O-acetyl- β -D-glycosyl isothiocyanate and phenyl thiocarbamides has been carried out in toluene medium for 3 hr. Afterwards, solvent was distilled off and viscous semisolid mass was isolated as residue. This when triturated several time with petroleum ether afforded a while solid. It was crystallized with ethanol-water,

EXPERIMENTAL

Melting points were recorded on electro thermal melting point apparatus are uncorrected. Specificrotations were measured on Equip-Tronic digital polarimeter model no. EQ 800 at 30^0C in $CHCl_3$. IRspectra were recorded on a Perkin Elmer spectrometer. ^{1}H NMR were obtained on a Bruker DRX-300(300 MHz FT NMR) NMR spectrometer in $CDCl_3$ solution with TMS as an internal reference. The massspectra were recorded on a DART mass spectrometer were recorded. Partical Size was analysis by Malvern particalsizeanalysizer.

I) Preparation of Tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate :

This has been prepared by the interaction of tetra-O-acetyl-α-D-glucopyranosyl bromide and lead thiocyanate, the former was prepared according to the procedure described earlier. Details of typical experimental are as follows :

a) Microwave assisted preparation of glucose pentaacetate :-

Peracetylation of glucose to give the acetyl derivative with small excess of acetic anhydride under the catalyst of either Potassium or Sodium acetate (anhydrous) was found practically quantitative in less than 15 min with microwave heating.

Herein, we reported first time peracetylation of glucose in molecular proportion of acetic anhydride (30 ml) using catalyst sodium acetate 0.8 gm. Under Microwave heating the reaction was complete less than 10 min. Product was isolated by pour in ice cold water with constant stirring and cooling.

The glucose penta acetate is separated out; purification of product was done under water, ethanol system. Melting point of Glucose penta acetate was found to be 110°C.

b) **Synthesis of Tetra-O-acetyl-α-D-glucopyranosyl bromide** :

The finely powdered glucose pentaacetate (21.0g) was added gradually to the brominating reagent. After the addition the flask was kept for 2 hr. at room temperature. The reaction mixture was mixed with chloroform (50 ml) then the mixture was shaken vigorously for about 15 min. The resultant mixture was pour in ice cold water.

The chloroform layer was then separated. It was washed several time with aqueous sodium bicarbonate to removed excess of acetic acid followed by the aqueous sodium meta-bisulphate to remove the excess of bromine and finely 2-3 times with water. To the chloroform layer addition of petroleum ether afforded a solid (15 g). This solid was expected tetra-O-acetyl-ά-D-glucopyranosyl brominde, it was crystallized from ethanol, m.p. 88-90°C.

d) **Preparation of lead thiocyanate :**

Lead thiocyanate was prepared by mixing aqueous solution of lead nitrate and ammonium thiocyanate. The white granular lead cyanate was filtered washed with distilled water and dried at 50°C.

Preparation of Tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate :

To a suspension of tetra-O-acetyl-α-D-glucopyranosyl bromide (21 g) in sodium dried xylene (80 ml) was added lead cyanate (15g). The reaction mixture was refluxed gently for 3 hr. with frequent shaking. This solution was then cooled and liberated lead bromide was removed by filtration. The xylene filtrate was then treated with petroleum ether (60-80°) with stirring, a pale yellow solid obtained (12 g). This solid was expected tetra-O-acetyl-β-D-glucopyranosyl isocyanate. It was purified by dissolving it in a minimum quantity of chloroform and reprecipitating with petroleum ether. m.p 115-120°C

Table No-2-: Study of synthesis of 1-tetra-*O*-acetyl-β-D-Glucosyl isothiocyanate under microwave irradiation[11]

Sr. No.	Amount of G-Bromide	Amount of Xylene	Time	Power in watt	Temp. °C	% Yield
1	10.0 gm	80 ml	35 min	P-70	120-130	90%
2	20.0 gm	120 ml	40 min	P-80	130-140	80%
3	30.0 gm	150 ml	40 min	P-80	135-145	65%

- Lead thiocyanate was taken in equimolar proportion of G-Bromide.
- G-Bromide :- 1-tetra-*O*-acetyl-□-D-Glucosyl-Bromide

Experiment No. 1:-1-Tetra-O-acetyl-β-D-glucosyl-5-phenyl-4-dithiobiuret. (IIIa)

To a toluene solution of tetra-O-acetyl- β -D-glucosyl isothiocyanate (0.005 M, 1.9g in 20 ml) was added toluene solution of phenyl thiocarbamide (0.005 M, 0.76 g in 10 ml) and reaction mixture was refluxed over boiling water bath for 3hr. Afterwards, solvent was distilled off and sticky mass obtained as residue was triturated several times with petroleum ether afford a white solid. It was crystallized with ethanol-water, m.p. 95°C. [Found: C, 50.30; H, 4.85; N, 7.93; S, 6.19, $C_{22}H_{26}O_9N_3S_2$. requires; C, 50.38, H, 4.96; N, 8.01, S, 6.10%].

The product was found soluble in ethanol, acetone, chloroform and benzene while insoluble in water and petroleum ether. It charred on heating with conc. sulphuric acid. It was found desulphurisable when boiled with alkaline plumbite solution. It was optically active and its specific rotation was found to be $[\alpha]_D^{32}$ = -136.94° (c, 0.74 in chloroform). The purity of the product was checked by TLC, Rf value 0.69 (CCl_4: EtOAc, 3:2).

ANALYTICAL AND SPECTRAL DATA OF COMPOUNDS:

Synthesis of 1-Tetra-O-acetyl-β -D-glucosyl-5-phenyl-4-dithiobiuret (IIIa).

(IIIa) IR (KBr) : ν 3234 (N-H), 1745 (C=O), 1381 (C-N), 1036, (C=S), 1235 (C-O) ,846 cm-1 (Glucose Ring), 687cm-1 (Mono substitute Ring); 1H NMR (CDCl3) : δ 7.47-7.23 (m, 5H Ar-H), 6.30 (s 1H N-H), 5.1-5.4 (m, 7H Glucopyranosyl ring), 2.1-1.6 (m, 12 H, 4COCH3); Mass : m/z 541 (M+), 331, 169, 109, Anal. Calcd. for C22H25N3O8S2; C, 48.97; H, 4.63; N, 8.24; S, 6.31; found C, 48.84; H, 4.59; N, 8.45; S 6.51%

Synthesis of 1-tetra-O-acetyl-β -D-glucosyl-5-o-tolyl-4-dithiobiuret (IIIb)

(IIIb) IR (KBr) : ν 3373 (N-H), , 1743 (C=O), 1383 (CN), 1236,(C-O)1109 (C=S) and 942 cm-1 (D-glucose ring), 822cm-1 (1,2 di substitute Ring) ; 1H NMR (CDCl3) : δ 7.3-7.2 (m, 1H, N-H), 8.0 - 7.9 (s, , N-H), 5.1-4.7 (m, 7H, glucopyranosyl ring), 2.2-1.9 (m, 12H, 4 COCH3); Mass : m/z 555 (M+ Not Located), 331, 169, 109; Anal. Calcd., C22H24N3O7S3-Cl, C, 46.07; H, 4.18; N, 7.72; S, 5.88 Found C, 46.13; H, 4.23; N, 7.21; S, 5.98%

Synthesis of 1-Tetra-O-acetyl-β -D-glucosyl-5-p-cl-phenyl-4-dithiobiuret(IIIe) :

(IIIb) IR (KBr) : ν 3415 (N-H), , 1745 (C=O), 1381 (CN), 1234,(C-O)1137 (C=S) and 941 cm-1 (D-glucose ring), 780cm-1 (1,4 di substitute Ring) ; 1H NMR (CDCl3) : δ 7.34-7.04 (m, Ar-H), 8.0 - 7.9 (s, , N-H), 6.15-4.70 (m, 7H, glucopyranosyl ring), 2.2-1.9 (m, 12H, 4 COCH3); Mass : m/z 575 (M+ Not Located), 331, 169, 109; Anal. Calcd., C22H24N3O7S3-Cl, C, 46.07; H, 4.18; N, 7.72; S, 5.88 Found C, 46.13; H, 4.23; N, 7.21; S, 5.98%

Preparation of Nanoparticles of 1-tetra-O-acetyl-β-D-glucosyl-5-phenyl-4-dithiobiurets:

Take about 1 gm of 1-tetra-O-acetyl-β-D-glucosyl-5-phenyl-4-dithiobiuret and dissolve it completely in the 20ml of solvent in a 250 ml beaker and add poly vinyl alchole as a stibilizer 1.5ml . Now put this beaker in a sonicator. The highly penetrating acoustic waves are passed through the mixture, which creates high-pressure bubbles in the beaker due to which breakdown of the bulk material took place and desired sized nanoparticles are formed. Then stirred mixture about 6hr. in magnetic stirrer at room tempeture. The size determination of nanoparticlesis done by the partical size analysizer studies

Characterization of Nanoparticles:

1. Characterization using UV-Spectrophotometer: Single Beam UV-Spectrophotometer with software BI/CI/SP/SB-S-03 of Bio Era make. The UV-Visible Spectroscopy reveals the formation of Nanoparticles Characterization of Nanoparticles was done using a visible Spectrophotometer by using a model by showing different absorption those from bulk material.

2. Size determination ofGlucose Penta Acetate, Nanoparticles by X-ray Diffraction studies(Particle Size Analysis): From the X-ray diffraction, it comes to know that size of nano Glucose Penta Acetate is 270.089 nm.

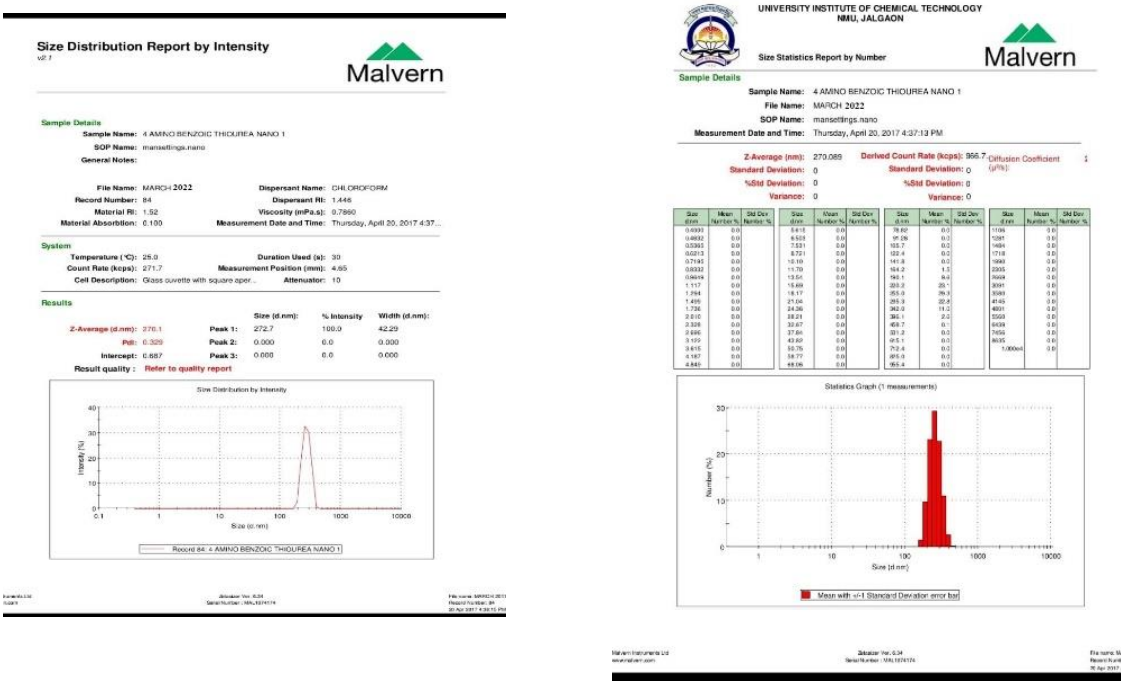


Table No. 2:-Tetra-O-acetyl-β-D-glucosyl-5-aryl-4-dithiobiurets

Sr. No.	Aryl thiocarbamides	1-tetra-O-acetyl-β-D-glucosyl-5-aryl-4-thiobiurets (III)	Yield (%)	Particle Size	M.P. (°C)
1	Phenyl….	…5-phenyl….. (IIIa)	86.10	270.089	95° C
2	o-Cl-phenyl….	…5-o-Cl-phenyl… (IIIb)	70.56		80° C
3	m-Cl-phenyl….	…5-m-Cl-phenyl... (IIIc)	85.32		101° C
4	p-Cl-phenyl….	…5-p-Cl-phenyl… (IIId)	71.69	169.75	116° C
5	o-tolyl….	…5-o-tolyl….. (IIIe)	80.00	216.65	140° C
6	m-tolyl….	…5-m-tolyl…. (IIIf)	78.12		90° C
7	p-tolyl….	….5-p-tolyl…. (IIIg)	80.36		150° C

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