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Nanoparticles of hepta-O-benzoyl-β-D-maltosyl thiocarbamates: Synthesis and Characterization

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Abstract:

Applications of the N-linked sugar isothiocyanate and isocyanate have gained considerable attention in recent years due to its unique characters. On the basis of experiences gained recently from work being carried out in the laboratory , it appeared quite interesting to carry out the synthesis of nanoparticles of new N-linked Maltose Thiocarbamates and their derivatives by the reaction between Maltosyl isothiocyanate and various alcohols. The characterization of new compounds and biologically made nanoparticles has been carried out by Melting point, antimicrobial activity, usual chemical transformation, NMR, IR and Mass spectral studies.

Keywords : Maltose, Thiocarbamates, Nanoparticles,

Introduction :

Day by day the field of carbohydrates becomes widely spreading because of its enormous interactions and cell-cell recognition, cell growth, fertilizations and immune responses. Nanoparticles play very important role in the development of novel diagnosis methods and in the advanced design of drug delivery system[1,2]. Silver nanoparticles and Gold nanoparticles particularly, shows an excellent anti-microbial properties and hence are rapidly being used in to medicines etc. to increase the lifestyle of human being and beneficial for mankind and environment[3,4]. Glyco-nanoparticles shows several advantages such as their synthesis can be performed under biomimetic conditions result in nanoparticles without traces of chemicals responsible for adverse cellular responses and carbohydrates which are on the surface can act as targeting molecules and trigger cellular uptake via specific receptors or mediate specific cellular responses[5]. Derivatives of Carbohydrate have been reported as inflammatory, analgesic, fungicidal, herbicidal & pesticide agents[6-8]. Because of the tremendous biological importance, carbohydrates are very essential to our daily lives. They have more importance in synthesis and medicinal chemistry[9,10]. Maltose is the second member of an important biochemical series of glucose chains. Maltose, or malt sugar, is a disaccharide formed from two units of glucose joined with an α (1→4) linkage. Maltose is not common in food, but can be formed from the digestion of starch and is heavy in the sugar in malt, the juice of barley and other grains. Nanotechnology as defined by size is naturally very broad, including field of science as diverse as surface science, organic chemistry, molecular biology, semiconductor physics, energy storage, micro fabrication, molecular engineering etc.

Isothiocyanates and isocyanates are a group of very reactive chemical compounds. Once they have reacted, the resulting product is usually less harmful than the chemical itself. This chemical is used in the manufacture of carbamates and thiocarbamates. Due to high reactivity towards compounds containing active hydrogen atom isocyanates and isothiocyanates are one of the most versatile classes of functional groups. They are important intermediates; the chemistry of these molecules is dominated by the nucleophilic addition reaction. The high yields and lack of byproducts with this type of reaction have led to their commercial exploitation in the polymer

field, agrochemicals and pharmaceuticals. Reactions with carbon nucleophiles provide a useful synthetic access to substituted amides and other derivatives.

Experimental :

The prepared Compounds and their nanoparticles have been screened for antimicrobial activity using Cup plate agar diffusion method. By measuring zone of inhibition in mm antimicrobial activity has been studied. By using DMSO as a solvent the concentration of compound were 1 mg/ ml. Amikacin (100 µg/ml) was used as a standard. Compounds were screened for antimicrobial activity against microbes (listed in table 2) in nutrient agar medium. Determining the difference between melting point of compounds and their nanoparticles is one way to test if the nanoparticle is prepared or not. So the M.P. of compounds and their nanoparticles has been taken using melting point apparatus. H^1 NMR data of the compounds were measured using $CDCl_3$ solvent on 300 MHz frequency. And their chemical shift values are in (ppm) units using TMS as a reference. IR spectral data of the compounds were recorded on FTIR-RXI spectrophotometer. Conformation of products and reaction progress carried out by TLC using Hexane : Ethyl acetate solvent system and identification of spots carried out by using iodine chamber and $KMnO_4$ spray.

Method of Preparation :

Step 1 : preparation of Maltose Octabenzoate: 55 ml dry Pyridine and 55 ml dry Chloroform were taken in a 1 lit. tight cork glass bottle and cooled in an ice-salt bath. To this solution previously prepared cooled solution of 55 ml Benzoyl Chloride in 55 ml dry Chloroform was added with constant stirring. To this mixture 20 gm. of dry powder of Maltose was added in small instalments with constant stirring by maintaining the temperature below 5 °C. After 24 hrs. mixture was washed several times with dil. Aq. Sulphuric acid, followed by aq. Sodium Bicarbonate and lastly with water. By using separating funnel Chloroform layer was separated which contains desired product. Product was triturated several times with petroleum ether until white powder obtained with M.P. 112 ° C.

Step 2 : Synthesis of hepta-O-benzoyl-α-D Maltosyl Bromide:

4 gm Red Phosphorus was added to 40 ml Glacial Acetic acid taken in a conical flask. To this mixture 15 ml molecular Bromine was added gradually with constant shaking and cooling. Mixture was allowed to stand at ice cold temperature for about 30 min. Mixture was filtered through double filter paper. The fine powdered of maltose octabenzoate (10gm) was added to the brominating agent. After that flask was kept for 2 hrs at room temperature. Then 70 ml Choroform was added to the reaction mixture followed by vigorous shaking. The resultant mixture was poured in an ice cold water to separate Chloroform layer. It was washed several times with aq. Sodium bicarbonate to remove excess of acetic acid followed by aq. Sodium metabisulphite to remove excess of bromine and finally 2-3 times with water. By using separating funnel the solution was removed and addition of petroleum ether results a solid mass (20 gm).

Step 3: Synthesis of hepta-O-benzoyl-β-D-maltosyl isothiocyanate:

Lead thiocyanate was prepared by mixing aq. Solution of lead nitrate and ammonium thiocyanate. The white precipitate was filtered washed with distilled water and dried over 50 ° C. To a suspension of hepta-O-benzoyl-α-D-maltosyl bromide (15gm) in sodium, dried xylene (60 ml) was added lead thiocyanate (5 gm). The reaction mixture was refluxed for 3 hrs, gentle

shaking. Solution was then cooled and liberated lead bromide was removed by filtration. The xylene filtrate was treated with petroleum ether with stirring, a white solid mass obtained. This solid was expected hepta-O-benzoyl-β-D-maltosyl isothiocyanate. M. P. 116-120 °C.

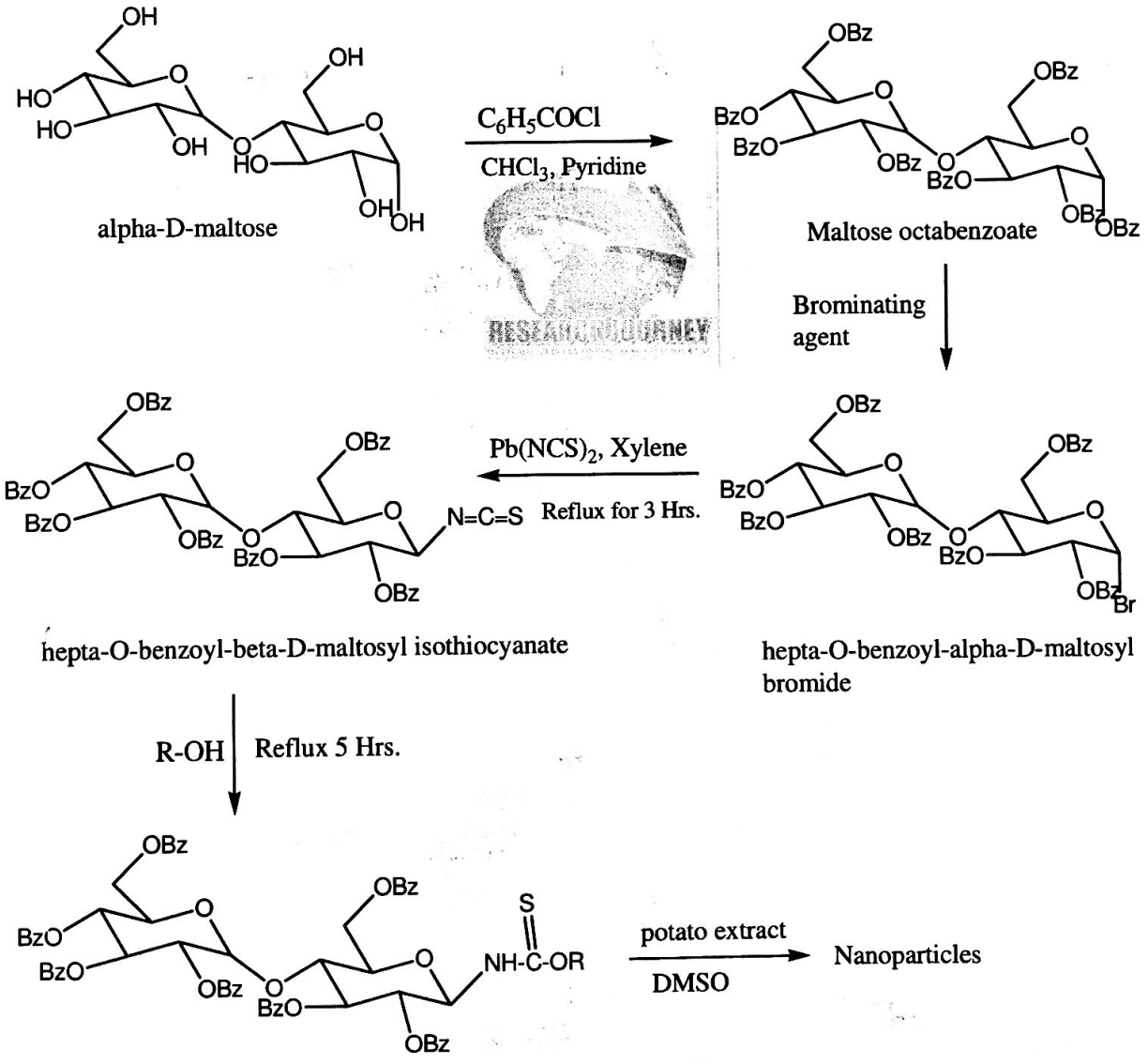
Step 4: Synthesis of N-maltosylated Thiocarbamates:

Reaction of hepta-O-benzoyl-β-D-maltosyl isothiocyanate and various alcohols has been refluxed for 5 hrs. On cooling and mixing with water most of the alcohols gave a white granular solid was purified by Chloroform-Petroleum ether. Melting point ranges from 140-170 °C for all alcohol derivatives.

Step 5 : Preparation of Nanoparticles (Biologically) :

Small pieces of potato was boiled in little amount of water in a beaker for about 10 min. Filtered the semi hot solution through filter paper, remaining filtrate obtained called potato extract. 1 gm. of compound was dissolved in 2 ml of DMSO, clear solution was obtained. Then 2,3 drops of potato extract was added to the clear solution, suddenly white precipitate of nanoparticles was obtained.

Scheme :



R= a) ethyl b) methyl c) n-propyl d) isopropyl e) n-butyl f) t-butyl

Result and Discussion: **Antimicrobial activity (Table 1)**

Antimicrobials	Bulk	Nanoparticles
E. coli	10 mm	13 mm
S. aureus	11 mm	13 mm
S. typhi	11mm	14 mm
P. vulgaris	09 mm	12 mm
Amikacin	10 mm	17 mm
Clandamycine	12 mm	14 mm
DMSO	26 mm	20 mm

**Including the well diameter of 8 mm. **Zone of inhibition in mm (15 or less) resistance, (16-20 mm) moderate and (> 20 mm) sensitive.*

The prepared Compounds and their nanoparticles have been screened for antimicrobial activity using Cup plate agar diffusion method. By measuring zone of inhibition in mm antimicrobial activity has been studied. By using DMSO as a solvent the concentration of compound were 1 mg/ ml. Amikacin (100 µg/ml) was used as a standard. Compounds were screened for antimicrobial activity against microbes (listed in table 1) in nutrient agar medium. Zone of inhibition of nanoparticles were more than bulk, which confirms better antimicrobial activity of nanoparticles in comparison to bulk one.

(Table 2)

Sr. No.	Aryl amines	1-hepta-O-benzoyl-β-D-maltosyl-3-aryl thiocarbamates	Yield %	Melting point of Bulk °C	Melting point of Nanoparticles °C
1.	Ethyl	O-ethyl thiocarbamate	71	121-123	90
2.	Methyl	O-methyl thiocarbamate	82	124	109
3.	n-propyl	O-n-propyl thiocarbamate	85	146	124-126
4.	Isopropyl	O-isopropyl thiocarbamate	81	146-149	123-129
5.	n-butyl	O-n-butyl thiocarbamate	69	141	121
6.	t-butyl	O-t-butyl thiocarbamate	76	149-155	119-123

The characterization of compounds have been confirmed by IR spectroscopy which shows C=S, N-H, C-N, C=O, C-O stretching frequencies at different absorption bands. H1 NMR shows signal due to N-H proton at 8.07 ppm and maltosyl protons at 5.58 – 3.79 ppm. and benzoyl protons at 6.78 – 3.90 ppm. The Characterization of nanoparticles have been carried out by UV visible spectroscopy. The band gap difference increases as the size of nanoparticles decreases. The decrease in melting point confirms the nanoparticles were prepared.

Conclusion :

N-linked nanoparticles have found interesting applications in a wide spectrum of biomedical utilities like imaging, sensing, drug delivery and gene targeting. The synthesised nanoparticles were characterized by antimicrobial activity, UV spectroscopy, X-Ray diffraction and melting point determination. On the basis of which nanoparticles obtained was confirmed. A nanoparticle shows better antimicrobial activity than bulk. Because of such properties of n-linked sugar derivatives provided a very facile and easy way to increase its potency and enhanced the route for biomedical analysis.

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