'RESEARCH JOURNEY' International E- Research Journal
Special Issue – 266(D) : Multidisciplinary Issue
Peer Reviewed Journal
E-ISSN : 2348-7143
July - 2021

Synthesis and Characterization of Nanoparticles of β-D-lactosyl Thiocarbamates

Shankesh C. Zyate , Poonam T. Agrawal*
Shri. R.L.T. College of Science, Akola
Poonamagrawal2575@rediffmail.com

Abstract:

The study includes the synthesis of nanoparticles of Lactosyl thiocarbamates and its derivatives. It appeared interesting to carry out the synthesis of nanoparticles of following Lactosyl thiocarbamates by the reaction of Lactosyl isothiocyanate with alcohols. The characterization of new thiocarbamates and biologically made nanoparticles has been carried out by usual chemical transformation, NMR, IR and Mass spectral studies and the characterization of prepared nanoparticles were done by antimicrobial activity, melting point difference, X-ray diffraction and U. V. spectroscopy.

Keywords : Thiocarbamates, nanoparticles, lactose

Introduction:

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. Highly reactive nature of *N*-linked sugar isothiocyanate and isocyanate appears to promise its great applicability in the synthesis of thiocarbamates and carbamates which find the wide spread use in the combinatorial library synthesis as well as in pharmaceutical industries. 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. 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.

Sugar isothiocyanates rank among the most versatile synthetic intermediates in carbohydrates chemistry[1-3]. They plays a vital role in the preparation of a broad series of functional groups such as thioamides[4], isonitrile, carbodiimide and *N*-thiocarbonyl derivatives[5-7] allowing, simultaneously, the covalent coupling of a quite unrestricted variety of structures to the saccharide part. More ever, isothiocyanates are important reagents in heterocyclic chemistry[8-9] which may be exploited in the synthesis of nucleosides[10] and other *N*-glycosyl[11-12] structures. Dialdehyde starch nanoparticles are useful carrier for anticancer drug because of their small size, good thermal stability, low biological toxicity and slowly anticancer drug releasing to strengthen drug effect[13].

Experimental :

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. 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. 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. Confirmation 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, UV chamber and $KMnO_4$ spray.

Method of Preparation :

Step 1 : Preparation of Lactose 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 Lactose was added in small instalments with constant stirring by maintaining the temperature below 5 ^{o}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 ^{o} C.

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

A.) Preperation of Brominating agent : 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.

B.) Addition of Brominating Agent : The fine powdered of lactose octabenzoate (10gm) was added to the brominating agent. After that flask was kept for 2 hrs at room temperature. Then 70 ml Chloroform 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-lactosyl isothiocyanate:

A) Preparation of lead thiocyanate: 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 ^{o} C.

B) Addition of lead thiocyanate: To a suspension of hepta-O-benzoyl-α-D Lactosyl 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-lactosyl isothiocyanate. M. P. 116-120 ^{o} C.

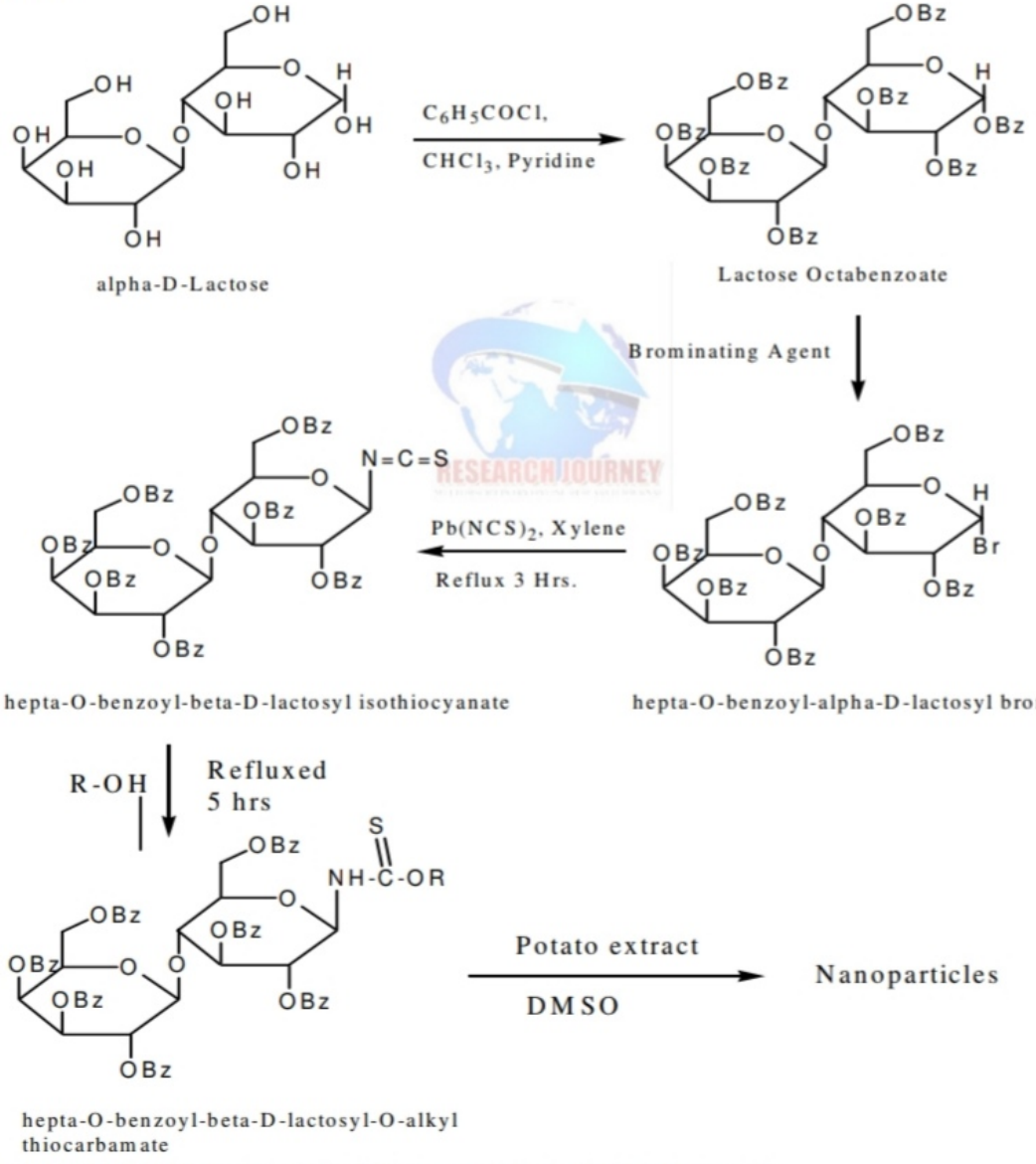
Step 4: Synthesis of N-lactosylated Thiocarbamates:

Reaction mixture of hepta-O-benzoyl-β-D-lactosyl isothiocyanate with 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 ^{o}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: **(Table 1)**

Sr. No.	Alcohols	1-hepta-O-benzoyl-β-D-lactosyl-3-aryl thiocarbamates	Yield %	Melting point of Bulk °C	Melting point of Nanoparticles °C
1.	Ethyl	O-ethyl thiocarbamate	77	125-130	152-155
2.	Methyl	O-methyl thiocarbamate	74	143	144-149
3.	n-propyl	O-n-propyl thiocarbamate	76	158-160	1142-144
4.	Isopropyl	O-isopropyl thiocarbamate	79	132-137	143-145
5.	n-butyl	O-n-butyl thiocarbamate	62	128	159-161
6.	t-butyl	O-t-butyl thiocarbamate	68	145	167-170

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 8.06 ppm and Lactosyl protons at 5.58 – 3.79 ppm. and benzoyl protons at 6.8 – 3.9 ppm. The Characterization of nanoparticles has 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.

Antimicrobial activity (Table 2)

Antimicrobials	Bulk	Nanoparticles
E. coli	11 mm	15 mm
S. aureus	10 mm	14 mm
S. typhi	12 mm	15 mm
P. vulgaris	11 mm	114 mm
Amikacin	12 mm	19 mm
Clandamycine	11 mm	16 mm
DMSO	31 mm	26 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 2) 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.

Conclusion :

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. Nanoparticles show better antimicrobial activity than bulk. Carbohydrate nanoparticles are beneficial for the medicinal purposes like anti-cancer, drug delivery system, recognition of antigens and many other pharmacological applications.

References :

1. *Ogura, H., Takahashi, H., Takeda, K., Sakaguchi, M., Nimura, N., & Sakai, M. (1975). Heterocycles., 3, 1129*
2. *Witczak, Z. J. (1986). Adv. Carbohydr. Chem. Biochem., 44, 91*

3. *De ,K. K., Shaiu, G. T. & Harmon, R. E. (1975). J. Carbohy. Nucleos Nucleot., 2, 171-176*
4. *Fernandez-bolanos, J. G., Zafra, E., Robina, I., & Fuentes, J. (1999). Carbohydr. Lett., 3, 239-246*
5. *Linkletter , B.A., & Bruice, T. C. (1998). Bioorg. Med. Chem. Lett., 8, 1285-1290*
6. *Avalos, M., Babiano, R. P.,Cintas, J. L., & Jimenez, J. C. (1993) Tetrahedron,49, 2676-2690*
7. *Arya , D.P., & T.C. Bruice. (1993). J. Am. Chem. Soc., 120, 6619-6620*
8. *Gasch, C., Pradera, M. A., Salameh, B. A. B., Molina, J. L., & J. Fuentes. (2000).Tetrahedron: Assymmetry,11, 2435*
9. *Pradera,M. A., Molina, J. L., & Fuentes, J. (1995). Tetrahedron, 51, 923*
10. *Fruentes, J., Molina, J. L., & Pradera, M. A. (1993). Tetrahedron: Assymmetry, 9, 2517-2532*
11. *Saleh, M. A. (2000). Sulfur Litt., 23(6), 265*
12. *Abdel-Megeed, M. F., Saleh, M. A., Aly ,Y. A., & Abdo, I. M. (1995). Nucleos. Nucleot. and Nucleic acids, 14, 1985*
13. *YU DanMi, XIAO SuYao, TONG ChunYi, CHEN Lin & LIU XuanMing. (2007). Chinese Science Bulletin, 52(21), 2913-2918.*