A MICROWAVE ASSISTED SYNTHESIS OF 1-TETRA-*O*-ACETYL-*B*-*D*-GLUCOSYL-3-ARYL-CARBAMIDE AND THEIR COMPARATIVE STUDIES

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ABSTRACT

The use of microwave irradiation in organic synthesis has become increasingly popular within the pharmaceutical and academic arenas, because it is a new enabling technology for drug discovery and development. A huge number of research papers have appeared over the last decades on the application of microwave technology in organic synthesis. The chemistry of thiourea of carbohydrate is extensively elaborated and well documented. By taking advantage of this efficient source of energy, These compounds arouse interest as potential biologically active substances and versatile intermediates for preparing various derivatives. They have been found useful in the treatment of hypertension, as appetite suppersant and as a potential anti oxidant cardio protective agent.. Several glucosyl carbamide derivatives has been prepare by condensation of tetra-O-acetyl-B-D-glucosyl isocyanate with various aryl thiocarbamides by microwave method. The identites of newly synthesis co,mpounds have been established on the basis of usual chemical transformation and IR, NMR, Mass spectral.

Keywords: *Tetra-O-acetyl-B-D-glucosyl isocyanate, Aryl thiocarbamides , glucosyl carbamides*

Introduction

Microwave technology has been applied beneficially into a number of organic reactions. The microwave assisted hydrolysis of esters is well-known but the regioselective hydrolysis of esters at the anomeric position in sugars under this condition has not been described.

Microwave assisted organic synthesis has become an important tool to medicinal chemists for rapid organic synthesis. A huge number of research papers have appeared over the last decades on the application of microwave technology in organic synthesis.[1] Some of the major advantages include spectacular decrease in reaction time, improved conversions, clean product formation and wide scope for the development of new reaction conditions.

The use of polymer-supported reagents and scavengers is a powerful technique for expedited synthesis and purification.[2] Rapid transformations using microwave technology has shifted the bottleneck from synthesis to the work-up and purification step. Therefore, chemists are increasingly looking for an expedited synthesis and purification strategy that would combine the use of microwave heating with polymer-assisted solution-phase organic synthesis. This overview [3] covers the recent literature on the significant new applications of polymer-supported reagents and scavengers using microwave heating.

Carbohydrates derivatives have been extensively investigated including synthesis, characterization and biological activity. Partly due to the facts that many natural occurring saccharides and synthesized analogues exhibit various and potent biological activities and they have been widely employed as agrochemicals and pharmaceuticals[4-7].

Carbohydrates exist in a large elemental as well as stereochemical variety, as they are built up from monosaccharides of various kinds, forming diverse branched or linear oligomers as well as different class of poly-saccharides. Carbohydrates possess large numbers of functionalities, at least one carbonyl and several hydroxyl functions per monosaccharides and often carry further kinds of functional groups. They are compounds with several steriocenter and thus the carbohydrate group consists of a large numbers of sterioisomers. Synthetic carbohydrate chemistry, as a result of the structural complexity of carbohydrates is a challenging field for organic chemist. The initial carbohydrate chemistry deals with the structure of carbohydrate and solved basic question of the stereochemistry problem connected with it. This was mainly due to Emil Fischer, who solved all these basic questions, by the end of nineteenth century. Later in the 1960's all main

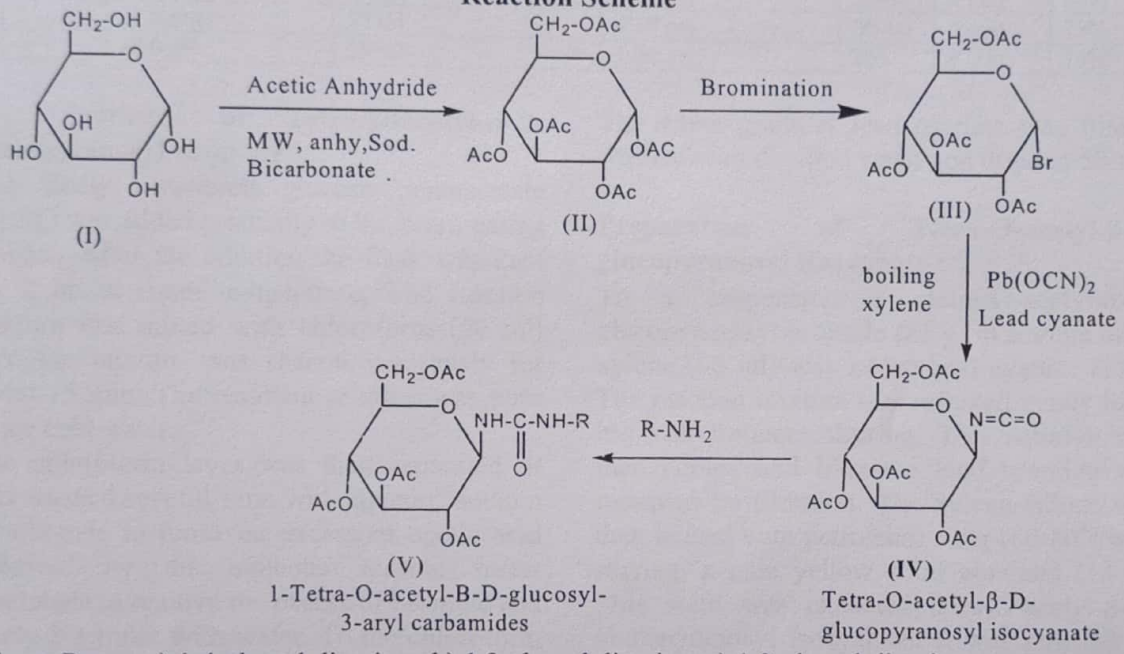
aspects of the roles play by carbohydrates in the storage and supply of energy in biochemical system were understand and the mechanism of biosynthesis and biodegradation of carbohydrates were clarified. The art of chemical transformations of monosccharides synthesis was further developed, motivated by the isolation of biological active compounds from micro-organism, such as antibiotics.

Because of tremendous biological importance, carbohydrates have aroused much interest to synthetic and medicinal chemistry[8-9].

The N-glucosylated compounds have been known for their great biological importance. They have been found several applications in paper[10], textile[11,12] and food industries[13]. Besides these applications they have been found use as divertic agents, analgesics, antidiabetic compounds, bacteriosatic agents and in many other ways[14]. Some of them have been found to be valuable oxidation dyes[15] for printing and padding the animals and vegetable fibers by standard oxidation dyeing methods. Quite few of them have antitumor and tuberculostatic activity[16].

Interaction of Tetra-O-acetyl-β-D-glucosyl isocyanate (I) and Aryl amines(IIa) has been carried out in boiling benzene medium for 5min. under microwave irradiation to afford product the solvent benzene was distilled off and sticky mass was isolated as residue. This when triturated several times with petroleum ether was convert to granular solid. crystallized from ethanol-water, m.p 112-114°C .

Reaction Scheme



Where, R = a) 1,4 phenyl diamine b) 1,3 phenyl diamine c) 1,2 phenyl diamine

I = Glucose **II** Glucose Penta acetat **III** Tetra-O-acetyl –B-D-Glucosyl Bromide

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 spectrometerwere recorded. Purity of the compounds was checkedby thin layer chromatography using Merck silica gel coated aluminum plates and petroleum ether: ethylacetate as eluent.

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

This has been prepared by the interaction of tetra-O-acetyl-α-D-glucopyranosyl bromide

and lead cyanate, the former was prepared according to the procedure described earlier. Details of typical experimental are as follows :

a) Microwave assisted preparation of glucose penta acetate :-

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.

Table No.1:- Preparation of glucose penta-acetate using acetic anhydride and appropriate amount of catalyst

Sr. No.	Amount of Glucose	Vol. of acetic anhydride	Amount of catalyst	Power	Time	Yield
1	10.0 gm	20 ml	0.89 gm	20-60	5 min	80%
2	10.0 gm	30 ml	0.89 gm	20-60	3 min	90%
3	10.0 gm	25 ml	0.89 gm	20-60	4 min	78%
4	10.0 gm	15 ml	0.89 gm	20-60	4 min	65%
5	10.0 gm	35 ml	0.49 gm	20-60	4 min	75%
6	10.0 gm	25 ml	1.29 gm	20	8 min	70%

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 cyanate :**

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

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

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 [Found C, 48.17; H, 5.99; N, 3.65; for $C_{15}H_{19}O_{10}N$ requires; C, 48.25; H, 5.09; N, 3.75%].

Table No-2-: Study of synthesis of 1-tetra-*O*-acetyl-□-D-Glucosyl isocyanate under microwave irradiation

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

Experiment No. 1:- synthesis of 1- tetra-*O*-acetyl-β-D-glucosyl-3-p-amino phenyl carbamides under microwave irradiationBenzene solution of 1-tetra-O-acetyl-β-D-glucopyranosyl isocyanate (0.005 M, 1.0 g in 20 ml) was added to benzene solution of 1,4 phenyl diamine (0.005 M, 0.35 g in 10 ml) and reaction mixture was kept under microwave irradiation . Afterwards, solvent benzene was removed by distillation and resultant syrupy mass was triturated several times with petroleum ether, a granular solid was obtained, crystallized from ethanol-water, m.p. 90-95°C. [Found: C, 50.70; H, 5.40; N, 5.05; S, 6.35, $C_{22}H_{25}O_{11}N_2S$ requires; C, 50.28, H, 4.63; N, 5.33, S, 6.09%].

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 non-desulphurisable when boiled with alkaline plumbite solution. The product was optically active and its specific rotation was found to be $[\alpha]_D^{28}$ = 150.20° (c, 0.96 in chloroform). The purity of the product was checked by TLC, Rf value 0.93 (CCl_4 : EtOAc, 3:2).

Analytical And Spectral Data of Compounds

1) Synthesis of 1-tetra-O-acetyl-β-D-glucosyl-3-*p*-amino phenyl carbamide
Yield 78 (%); . Mp.90-95^{0}C;$[\alpha]_D^{32}$150.42°(0.1,in $CHCl_3$);R*f* (Hexane:EtOAC)(1:1)0.93; **IR (KBr)cm- 1**:ν 3367 (N-H)str 3055 (Ar-H)str ,1753 (C=O)str, 1624(C=N) str, , 1242 (C-N)str, 939(char. of glucopyranosyl ring), 900 (mono Substituted Benzene) str.. **^{1}HNMR (CDCl3)ppm:** 7.49-7.19 (m,8H, Ar-H), 5.17-5.99 (m, 7H, glucosyl-H), 2.31-2.01 (m, 12H,OAc),. **MS**(m/z) : 481 (M+),387, 331, 169, 108.(Anal.Calcd. For Found (C, 54.00; H, 5.50;N, 5.91; $C_{27}H_{33}O_{10}N_3$, requires; C, 54.07; H, 5.57; N, 6.00%).

2) Synthesis of 1-tetra-O-acetyl-β-D-glucosyl-3-*m*-amino phenyl carbamide
Yield72(%); Mp.115-120^{0}C;$[\alpha]_D^{32}$220 (0.1, in $CHCl_3$);R*f* (Hexane:EtOAC)(1:1)0.83;**IR(KBr)cm- 1**:ν 3000-3292 (Ar-H)str ,1742(C=O)str, 1430 (C-N)str, 927(char. of glucopyranosyl ring), 750 (1,3 disubstituted benzene) str. **^{1}HNMR (CDCl3)ppm:** 7.46-6.32(m,8H, Ar-H), 5.57-3.87 (m, 7H, glucosyl-H), 2.31-2.01 (m, 12H,OAc),. **MS**(m/z) :M+ 496, 331, 263, 261, 169, 108.(Anal.Calcd. For Found (C, 55.18; H, 5.75; N, 5.70; for $C_{27}H_{33}O_{10}N_3$ requires; C, 55.22; H, 5.83; N, 5.83%]).

3) Synthesis of 1-tetra-O-acetyl-β-D-glucosyl-3-*O*-amino phenyl carbamide
Yield 85 (%); Mp.130-135^{0}C;[α]185 (0.1, in $CHCl_3$);R*f* (Hexane:EtOAC)(1:1)0.78 **IR (KBr)cm- 1**:ν 3000-3292 (Ar-H)str ,1755 (C=O)str, 1425 (C-N)str, 927(char. of glucopyranosyl ring), 745 (1,2disubstituted benzene) str.. **^{1}HNMR (CDCl3)ppm:** 7.46-6.32 (m,8H, Ar-H), 5.57-5.59 (m, 14H, lactosyl-H), 2.31-2.01 (m, 12H,OAc),.. **MS**(m/z) : :M+ 496, 331, 263, 261, 169, 108.(Anal.Calcd. For Found Anal.Calcd. For Found (C, 55.18; H, 5.75; N, 5.70; for $C_{27}H_{33}O_{10}N_3$ requires; C, 55.22; H, 5.83; N, 5.83%]).

Table No.3:- Characterization data of synthesis of 1-tetra-*O*-acetyl-β-D-glucosyl-3-aryl carbamides:-

Sr. No.	Aryl Amines	1-tetra-O-acetyl-β-D-glucosyl-3-aryl carbamides	m.p. (OC)	Yield (%)	Optical Rotation [α]D32	Rf value
1	1,4 phenyl diamine	1-tetra-o-acetyl B-D-glucosyl-3-p-amino phenyl carbamides	90-95	78	[α]D28 = 150.20° (c, 0.96 in chloroform)	0.93
2	1,3 phenyl diamine	1-tetra-o-acetyl B-D-glucosyl-3-m-amino phenyl carbamides	115-120	72	[α]D28 = 220.83° (c, 0.96 in chloroform).	0.83
3	1,2 phenyl diamine	1-tetra-o-acetyl B-D-glucosyl-3-o-amino phenyl carbamides	130-135	85	[α]D28 = 185.20° (c, 0.96 in chloroform).	0.78

As above product is reported by conventional heating. Here we reported this product by microwave heating just 26 min. using benzene at P-70.

Table No.4:- Comparative study of conventional and microwave assisted synthesis of 1-tetra-*O*-acetyl-β-D-glucosyl-3-aryl carbamides:-

Sr.No.	Amines	M.P. °C	Conventional method		Microwave Method	
			Time (hrs)	% Yield	Time (min.)	% Yield
1	1,4 phenyl diamine	90-95	3	65.12	12	78
2	1,3 phenyl diamine	115-120	3	70,07	12	85
3	1,2 phenyl diamine	130-135	3	60.31	12	72

From above comparative study it is conclude that microwave assisted synthesis is faster and gives cleaner product with higher yield than conventional.

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