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Contribution to synthesis of some glucopyranosylamines containing 1,3-thiazole and 1,3-benzothiazole rings from 4,6-O-ethylidene-D-glucopyranose

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Abstract– Cyclic acetals and ketals play the important role in the synthetic chemistry of carbohydrates and widely utilized in specific protections for simultaneously two or more hydroxyl groups. In particular, alkylidene derivatives of monosaccharides are formed from interaction of these ones or their derivatives with aldehydes or ketones in the presence of acid as catalyst [1-5]. In all of alkylidene derivatives, the ethylidene ones of monosaccharides have received more attention than other particularly for the synthesis partially substituted sugars.

1. Introduction

Cyclic acetals and ketals play the important role in the synthetic chemistry of carbohydrates and widely utilized in specific protections for simultaneously two or more hydroxyl groups. In particular, alkylidene derivatives of monosaccharides are formed from interaction of these ones or their derivatives with aldehydes or ketones in the presence of acid as catalyst [1-5]. In all of alkylidene derivatives, the ethylidene ones of monosaccharides have received more attention than other particularly for the synthesis partially substituted sugars.

On the other hand, some derivatives of carbohydrate containing nitrogen include nucleic acids, coenzymes, polysaccharides, some virus components and some of the members of vitamin B group. Furthermore, these compounds made up by union of proteins with carbohydrates are of possible wide occurrence and major biological importance [5-8].

Contributing to researches in carbohydrate chemistry, in this article, some derivatives of 4,6-O-ethylideneglucopyranosylamines containing heterocyclic aromatic thiazole and benzothiazole rings have been synthesized.

2. RESULTS AND DISCUSSION

2.1. Synthesis of 4,6-O-ethylidene-D-glucose

Derivative 4,6-O-ethylidene-D-glucopiranose has been synthesized by reaction between D-glucose and paraldehyde in the presence of sulphurc acid as

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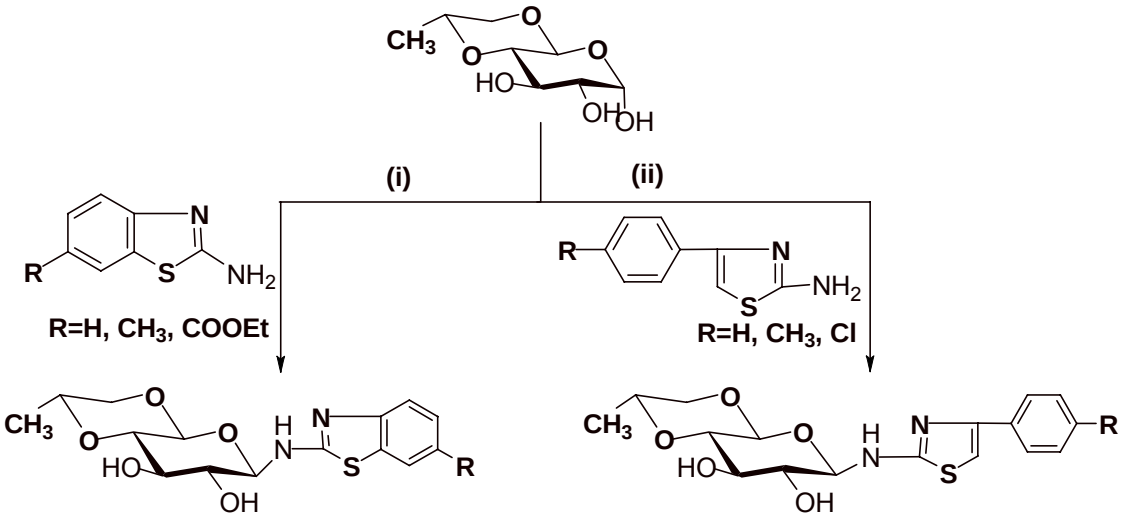
catalyst as described in reference [5], except the solid KOH has been used for neutralizing the obtained reaction solution.

2.2. Synthesis of 4,6-O-ethylidene-N-glucosylamines

The 4,6-O-ethylidene-N-glucosylamines containing thiazole and benzothiazole ring have been synthesized from 4,6-O-ethylidene-D-glucopyranose as following reactions:



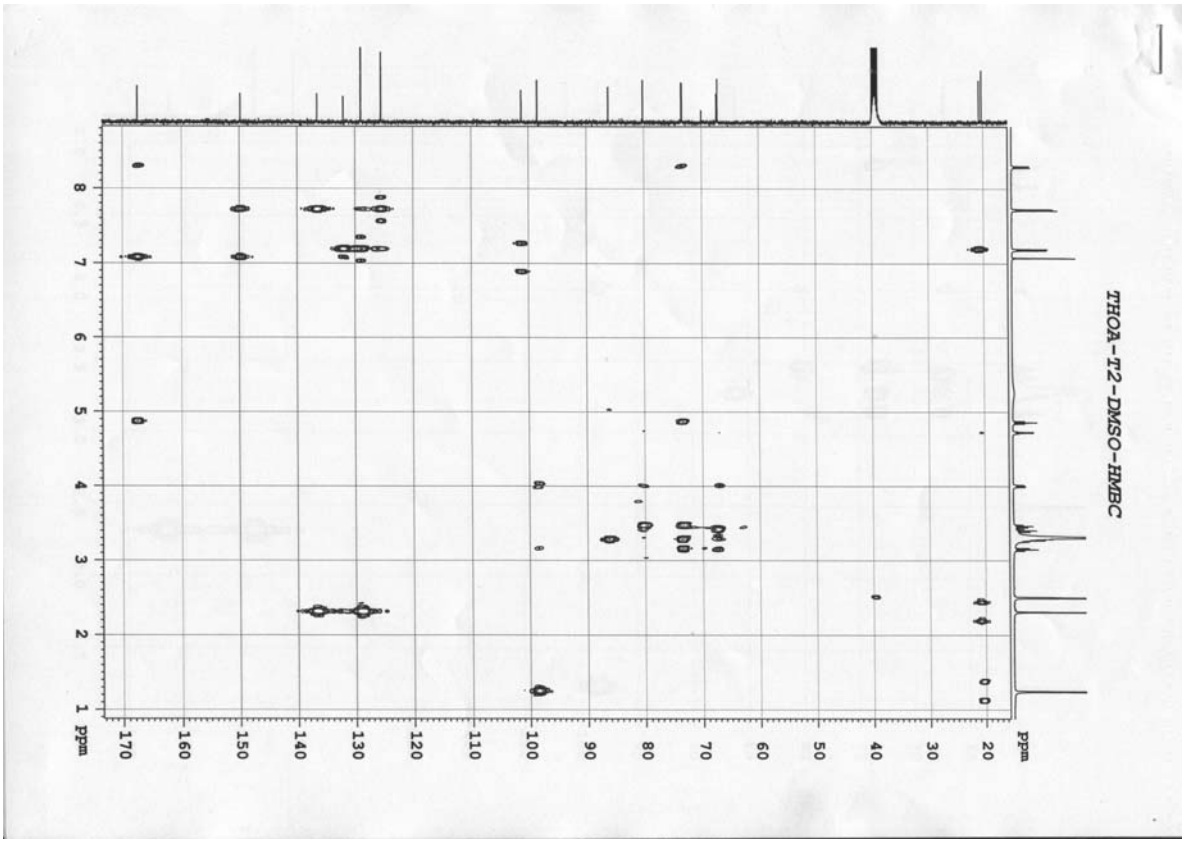
i, ii: CH_3COOH; EtOH khan; 6-8h; hs 28-40%

A simple procedure has been adopted to synthesize different N-glucosylamines of the partially protected glucose with different type of amines. Glacial acetic acid has been used as catalyst for these reactions. The amines were substituted 2-amino-4-phenylthiazoles and substituted 2-aminobenzothiazoles. Obtained N-glucosylamines were crystalline solid with high melting point, dissolving in common organic solvents (ethanol, DMF, dioxane, …). Their structures have been confirmed by using spectral methods (FTIR-, ^{1}H-NMR-, ^{13}C-NMR- and mass spectra).

The formation of the N-glucosylamines was observed by comparing the FTIR spectra of the products I-VI with the spectra of the saccharide, 4,6-O-ethylidene-D-glucopyranose and the amines. For example, when 2-amino-4-phenyl-1,3-thiazole reacted with the saccharide, the bands corresponding to the primary amine in region 3450 and 3320 cm^{-1} were absent, and that of the secondary was shifted to higher frequency due to the formation of the N-glucosylamines.

Table 1. N-(4-phenylthiazol-2-yl)-4,6-O-ethylidene-D-glucopyranosylamines and N-(benzothiazol-2-yl)-4,6-O-ethylidene-β-D-glucopyranosylamines

No.	Compound	m.p., °C	Yield,%	FTIR Spectra, cm^{-1}		
				ν_{OH}	ν_{NH}	$\nu_{C=O(este)}$
1	II, R_1=H	180-182	30	3365	3220	-
2	I, R_1=CH_3	136-138	28	3308	3114	-
3	III, R_1=Cl	170-172	35	3365	3220	-
4	IV, R_2=H	193-194	38	3466	3275	-
5	V, R_2=CH_3	239-240	40	3460	3284	-
6	VI, R_2=COOEt	228-230	38	3365	3299	1699



The vibrations corresponding to the anomeric properties of these N-glucosylamines were observed in the FTIR spectra. Strong bands were observed for (β-anomer, 750-757 and 695-698 cm^{-1}), (α-anomer, 737-745 cm^{-1}) indicating

the presence of the corresponding anomers. This is consistent with the observations made by NMR studies.

In FTIR-spectrum of 4,6-O-ethylidene-N-(benzothiazol-2-yl)-β-D-glucopyranosylamines and 4,6-O-ethylidene-N-(4-phenylthiazol-2-yl)-β-D-glucopyranosylamines, there were absorption bands in region 3460-3308 cm^{-1}, characterizing for stretching vibrations of OH-alcohol groups in carbohydrate part. The secondary amino group had an absorption band in region 3299-3114 cm^{-1}. The C=C and C=N bonds in heterocyclic aromatic have been characterized some absorption bands in regions 1549-1528 and 1465-1464 cm^{-1} (see Table 1).

^{1}H-NMR spectra of these compounds were split into two remarkable regions, corresponding with two proton types in molecules of N-(benzothiazol-2-yl)-β-D-glucopyranosylamines and N-(4-phenylthiazol-2-yl)-β-D-glucopyranosylamines: aromatic protons in benzene ring (5H) and proton at position 5 in thiazole ring (1H) had resonance signals in multiple lines in region 7.22-8.35 ppm; the protons in 4,6-O-ethylidene-D-glucopyranose had magnetic resonance signals in region 1.24-5.30 ppm. The protons of hydroxyl groups specified by the chemical shifts at 4.86-5.30 ppm, the protons in pyranose ring had signals in region 3.13-4.89 ppm, and methyl protons had chemical shifts at 1.07-2.51 ppm.

3. EXPERIMENTAL PART

Melting point of the synthesized compound was measured by using Thiele's apparatus in capillary and uncorrected. The FTIR-spectra were recorded on Magna 760 FT-IR Spectrometer (NICOLET, USA) in form of mixing with KBr and using reflex-measure method at the Petrol-Chemical Center (Hanoi University of Science, VNU). The ^{1}H-NMR was recorded on an AVANCE Spectrometer (BRUKER, German) at 500 MHz, solvent was DMSO-d_6, with the internal reference TMS (at the Room of Structural Analysis–Institute of Chemistry–Vietnam Academy of Sciences and Technology).

General Method for Synthesis of N-(4-phenyl-1,3-thiazol-2-yl)- and N-(1,3-benzo-thiazol-2-yl)- 4,6-O-ethylidene-N-glucopyranosylamines

To a solution of 0.005 mol of substituted 2-amino-4-phenyl-1,3-thiazoles or 2-amino-1,3-benzothiazoles in 20 ml of absolute ethanol was added 0.005 mol (1.03 g) of 4,6-O-ethyliden-D-glucose. Then 0.1ml of glacial acetic acid was added dropwise to obtained above solution. The mixture was heating in the bath in 6-8 hrs. After that, the solvent was evaporated in reduced pressure, filtered and crystallized from 96% ethanol.

4. CONCLUSION

Six derivatives of N-(benzothiazol-2-yl)-β-D-glucopyranosylamines and N-(4-phenylthiazol-2-yl)-β-D-glucopyranosylamines have been synthesized from corresponding substituted 2-amino-1,3-thiazoles and 2-amino-1,3-benzothiazoles

and 4,6-O-ethyliden-β-D-glucopyranose. Their structure has been confirmed using modern spectroscopic methods. The secondary amino group in these molecules had specific spectral characteristics as following, an absorption band for N-H stretching vibration in region 3385-3299 cm^{-1} in FTIR-spectra, a doublet signal for proton in NH group at 8.34-8.54 ppm.

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