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SYNTHESIS OF SOME DERIVATIVES OF *N*-(2,3,4,6-TETRA-*O*-ACETYL-*β*-D-GLUCOPYRANOSYL)-*N’*-(BENZOTHIAZOLE-2’-YL) THIOUREAS

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NGUYEN DINH THANH, PHAM HONG LAN, NGUYEN THU HUYEN
Faculty of Chemistry, Hanoi University of Science, VNU

ABSTRACT

Some compounds of N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N′-(benzothiazole-2′-yl)thioureas have been synthesized from corresponding 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate and the substituted derivatives of 2-aminobenzothiazoles executing in home microwave oven. Their spectroscopic properties have been recorded and the relationships between their structures and spectral properties (IR, ^{1}H- and ^{13}C-NMR) have been discussed.

I - INTRODUCTION

Certain sugars perform important biological function [1]. They can control various gene expressions to adjust the upgrowth, development and reaction of organs. Glycosyl isothiocyanates have been widely used as valuable intermediates in the synthesis of glycosyl derivatives [2]. The isothiocyanates and glycosyl isothiocyanates have been the focus of synthetic attention during recent years because of their potential pharmacological properties [3]. They have also attracted considerable interest due to the anti-HIV activity shown by 1-deoxyno-jirimycin, castanospermine and some of their derivatives [4]. Many biologically important products have a sugar unit joined by an atom (O, S, N or C) or a group of atom [5].

In the present study, we reported on the synthesis of various peracetated glucosylthioureas containing thiazole ring executing in microwave oven. This method is becoming an increasingly popular method of heating which replaces the classical one because it proves to be a clean, cheap, and convenient method [6].

II - EXPERIMENT

Melting points of the synthesized compounds were measured on STUART SMP3 (BIBBY STERILIN-UK). The FTIS-spectra was recorded on Magna 760 FT-IR Spectrometer (Nicolet, USA) in form of KBr and using reflex-measure method. NMR was recorded on an Advance Spectrometer (Bruker, Germany) at 500 MHz, using DMSO-d_6 as solvent and TMS as an internal reference. 2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate was synthesized by known method [7, 8].

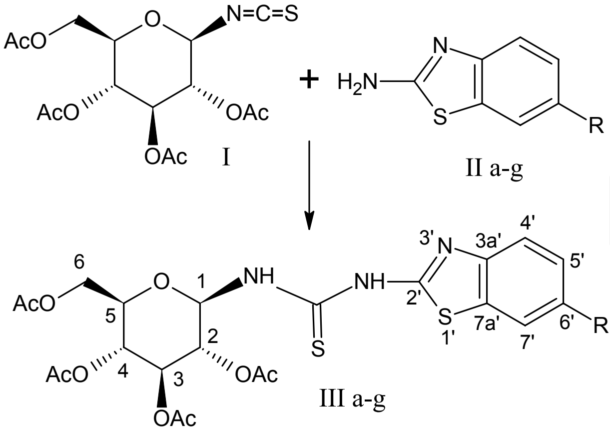
Synthesis of the derivative of N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N′-(benzothiazole-2′-yl) thioureas

Mixed (0.002 mole) of the derivatives of 2-aminobenzothiazole and 0.778 g (0.002 mole) of 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate. Then this mixture was irradiated about 5 minutes in home microwave oven. The mixture had become dark-yellow. Cooled it to room temperature, recrystallized from a mixture of ethanol and toluene (1:1 in volume) obtained ivory-white crystal. Obtained compounds were represented in table 1.

III - RESULTS AND DISCUSSION

The derivatives of N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N’-(benzothiazole-2’-yl)thioureas (III) could be easily synthesized by the addition of corresponding amino compounds (II) on isothiocyanate derivatives (I). We performed this reaction by executing in microwave oven in several minutes [9]. The synthetic processes could be represented in reaction Schema 1.

We have found that nucleophiles addition the derivatives of 2-aminobenzothiazole to 2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl isothiocyanate has taken place fairly easily. Reaction yield were rather high in this method. All these obtained thioureas could be dissolved in a mixture of ethanol and toluene (1:1 in volume) solvent, and could not be dissolved in ethanol and water. Their structures have been affirmed by spectroscopic data (such as: IR-, NMR- spectra).



II and III: a R=H; b R=Cl; c R=OEt;
d R=Me, e R=COOMe;
f R=COOEt; g R=COOPr-n

Schema 1: Synthesis of substituted N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N’-(benzothiazole-2’-yl)thioureas

In the IR spectra of above glucopyranosyl thioureas, the stretching band of C=S bond in thioureas linkage appeared in regions of 1367 - 1373 cm^{-1}, and N-H bonds in thioureas have absorption band in regions of 3490 - 3168 cm^{-1}, specified for stretching vibrations of these bonds. These bands sometimes have been superimposed each other, hence in several cases, one absorption band was appeared in their IR spectra. These bands also appeared in IR-spectra of some N-(2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl)-N’-(4’,6’-diarylpyrimidine-2-yl) thioureas [7], and N-(2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl)-N’-(4’-arylthiazole-2’-yl) thioureas [8]. The characteristics of pentaacetated glucopyranose ring was confirmed by the present of absorption band in regions of 1750-1692 cm^{-1} that specified for stretching vibration of C=O bond in ester function.

The ^{1}H-NMR spectra of these above thioureas, for example, the compound IIIc, are represented in Fig.1. There are resonance signals which specified for protons in thioureas N-H groups at δ 11.966 and 8.889 ppm. Some resonance signals are in regions δ 2.096 and 1.902 ppm belong to some protons in methyl and acetyl groups. Protons C-H in pyranose ring of monosaccharide have chemical shifts from δ 5.878 ppm to 3.986 ppm which usually are observed in ^{1}H-NMR spectra of monosaccharide compounds. Proton H-1 has chemical shift in region δ 5.878 ppm (triplet) with coupling constant J= 9.0 Hz. Resonance signal of proton H-2 appeared in triplet as region δ 5.094 ppm with coupling constant J= 5.0 Hz. The values of coupling constants correlated with *trans*-H-H coupling interactions and indicated β-anomer configuration of NH-thiourea group [9]. Other protons, such as H-3 and H-4 have triplet resonance signals in regions δ 5.452 ppm (with coupling constants $J_{3,4}$= 9.5 Hz) and δ 4.928 ppm (with coupling constants $J_{4,3} = J_{4,5} = 9.5$ Hz), respectively. Three protons in benzothiazole have two chemical shifts in regions from δ 7.617 ppm to δ 7.016 ppm.

In the COSY spectra of thiourea IIIc, it was shown that proton H-1 interacted with proton H-2 and proton in NH bond of thiourea linkage, and that these signals appeared in triplet. Protons H-2 had the interactions with proton H-3 and proton H-1. Protons in phenyl also have some interactions each other in AX type.

Table 1: Some derivatives of substituted N-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-N'-(benzothiazole-2'-yl)thioureas

Compd.	R	Melting Point, °C	Yield, %	IR spectra, cm^{-1}		
				$\nu_{N\text{-}H}$	$\nu_{C=O\ (ester)}$	$\nu_{C=S}$
IIIa	H	200-202	52	3490; 3175	1746	1373
IIIb	Cl	210-212	55	3476; 3168	1747	1367
IIIc	OEt	202-204	66	3483; 3196	1747	1371
IIId	CH_3	201-203	54	3469; 3175	1748	1370
IIIe	COOMe	202-203	57	3490; 3182	1750; 1721	1373
IIIf	COOEt	203-205	48	3469; 3175	1754; 1692	1370
IIIg	COOPr-n	205-206	60	3471; 3172	1748; 1715	1370

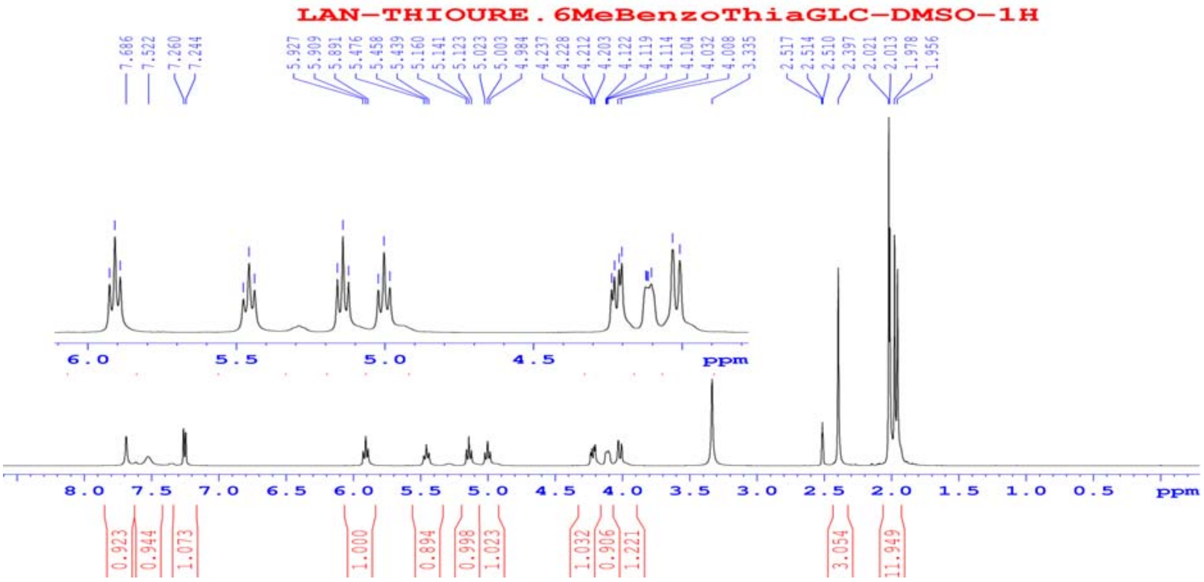


Figure 1: ^{1}H-NMR spectra of compound IIId

In the ^{13}C-NMR spectra, it could be noticed that the number of carbon atoms in spectra and this one in molecular formulas of each thioureas were identical each other. For example, the compound of thiourea IIIc is represented in Fig. 3, there were some resonance peaks in high-field region of 30.609 - 14.605 ppm that's indicated the present of ethoxy group and methyl groups on acetyl function. Six carbon atoms in pyranose ring have clearly resonance signal in region of 81.347 - 61.690 ppm. The carbon atoms in benzothiazole rings have chemical shifts in region of 115.195 - 106.004 ppm. The magnetic resonance signals of the thiocarbonyl and carbonyl groups have appeared in the low-field region of 206.473 and 169.992 - 169.336 ppm.

Table 2: ^{1}H-NMR Spectra of substituted N-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-N'-(benzothiazole-2'-yl)thioureas

Compd.	Alkyl and acetyl groups	Pyranose ring	Thiourea	Benzothiazole ring
IIIa	2.009 - 1.955	5.902 - 30.996	12.219; 9.125	8.168 - 7.566
IIIb	2.011 - 1.879	5.904 - 3.997	12.194; 9.126	8.045 - 7.443
IIIc	2.087 - 1.833; 1.345	5.894 - 3.986	11.966; 8.899	7.617 - 7.016
IIId	2.510 - 1.956	5.927 - 3.981	12.234; 8.899	7.686 - 7.244
IIIe	3.995; 2.049 - 1.878	5.919 - 3.870	12.344; 9.206	8.539 - 7.680
IIIf	2.012 - 1.955; 1.341	5.920 - 4.020	12.213; 9.231	8.567 - 7.513
IIIg	2.016 - 1.959; 1.767; 1.012	5.925 - 4.002	12.256; 9.232	8.653 - 7.889

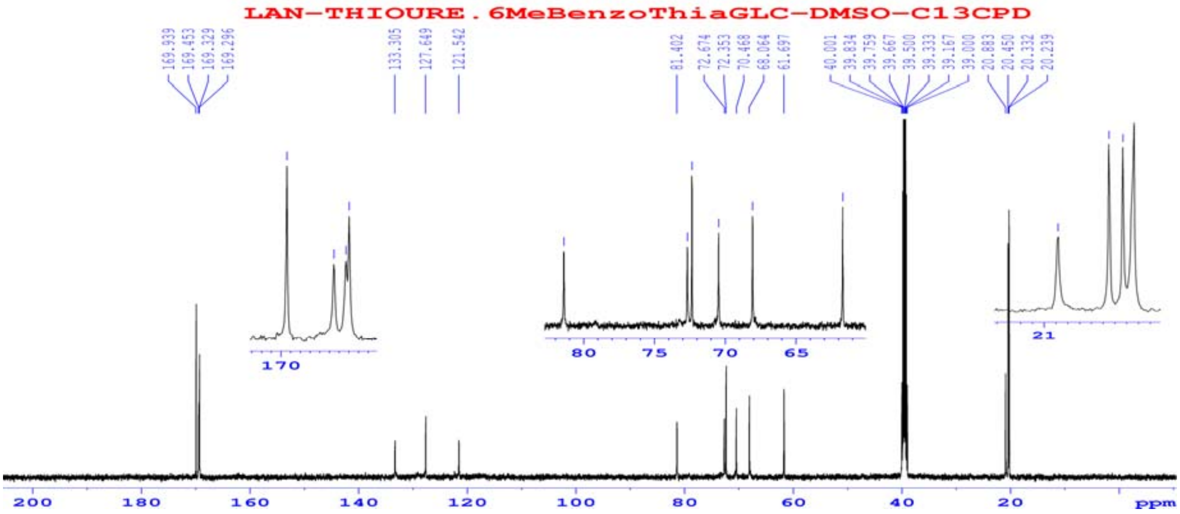


Figure 3: ^{13}C-NMR spectra of compound IIId

In NMR spectra using HMBC and HSQC experiments, the long-range and the short-range C-H interactions were shown, for example, the HSQC and HMBC spectra of IIIc in Figures 4 and 5. Carbon atom $C_{1'}$ had long-range interaction with proton $H_{2'}$ and proton H_1; carbon atom $C_{2'}$ interacted with protons $H_{2'}$ and $H_{3'}$, etc□

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Table 3: The result data analysis of ^{13}C-NMR (ppm) of substituted N-(2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl) —N'-(benzothiazole-2'-yl)thioureas

Compd.	Alkyl and Acetyl groups	Pyranose ring	Benzothiazole ring
IIIa	20.443 - 20.223 169.896 - 169.250	81.239 - 61.638	129.348 - 115. 424
IIIb	20.451 - 20.230; 169.907 - 169.263	81.245 - 61.642	127.673 - 121.579
IIIc	30.609; 20.478 - 18.485; 14.605 169.992 - 169.336	81.347 - 61.690	155.537 - 106.004
IIId	20.883 - 20.239; 169.939 - 169.296	81.402 - 61.697	133.305 - 121.542
IIIe	53.028; 21.387 - 21.169; 170.854 - 170.210; 166.702	82.184 - 62.571	128.445 - 124.828
IIIg	66.099; 21.611 - 20.230; 10.289 169.900 - 169.259; 165.304	81.315 - 61.644	127.484 - 123.871

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Corresponding author: **Nguyen Dinh Thanh**
Faculty of Chemistry, Hanoi University of Science, VNU
Email: nguyendinhthanh@hus.edu.vn