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SYNTHESIS OF PER-O-ACETYL-β-D-GLUCOPYRANOSYL THIOUREAS CONTAINING THIAZOLE RING

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Abstract. N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-(thiazol-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-aminothiazoles executing in domestic microwave oven. The 1H and 13C-NMR spectra of some derivatives of N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-(4'-arylthiazole-2'-yl)thiourea have been recorded. The magnetic signals in their NMR spectra show the relationships between the structure and positions of the substituted groups. It's also indicated that the substitution in the thiazole ring influenced on the chemical shift of proton on thiourea group. 2-Iminothiazolidin-4-ones have been synthesized from ethyl bromoacetate and substituted N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-(phenylthiazole-2'-yl)thioureas. The presence of 2-iminothiazolidin-4-one isomers were confirmed by NMR spectroscopies.

INTRODUCTION

The thiazole nucleus plays a vital role in many biological activities making it one of the extensively studied heterocycles [1-9][1] L.F. Lee, F.M. Schleppnik and R.K. Howe, J. Heterocyclic Chem. 22 (1985), pp. 1621–16Full Text via CrossRef. For example 2,4-dimethylthiazole-5-carboxamide and 2-methyl-4-trifluoromethylthiazole-5-carboxamide derivatives such as metsulfovax [10] and thifluzamide [11] are known as agricultural fungicides where the 4-trifluoromethylthiazole-5-carboxamide derivatives are usually better than the 4-methylthiazole-5-carboxamides [3]. Thiazoles occupy a prominent position among heterocycles. In nature, the thiazolium ring is the chemically active center in the coenzyme derived from vitamin B (thiamin). A large number of thiazoles obtained from microbial and marine origins exhibit important biological effects such as antitumor, antifungal, antibiotic, and antiviral activities [12]. Synthetic thiazoles have also been shown to exhibit a wide variety of biological activity [13], while others have found application as liquid crystals3 and cosmetic sunscreens [14].

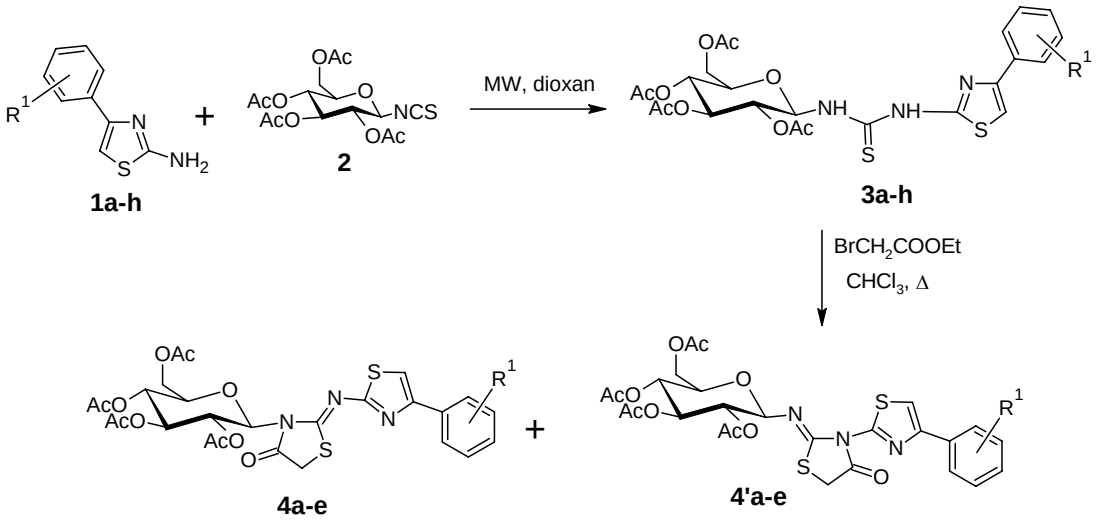
Recently, thiazole and thiadiazole analogues have been described as the possible core skeletons of A3 receptor antagonists with moderate affinity and selectivity.26,27 In this study, we report new findings of great improvement of the scaffold derivatives with subnanomolar affinity at human adenosine A3 receptors and high subtype selectivity through an SAR (structure–activity relationship) study combined with molecular modeling approaches.

In other hand, sugar isothiocyanates are among the most versatile synthetic intermediates in carbohydrate chemistry [17]. They play a pivotal role in the preparation of a

broad series of functional groups such as amide, isonitrile, carbodiimide, and N-thiocarbonyl derivatives allowing, simultaneously, the covalent coupling of a quite unrestricted variety of structures to the saccharide part [18-20]. Moreover, isothiocyanates are important reagents in heterocyclic chemistry, which may be exploited in the synthesis of nucleosides and other N-glycosyl structures [21-25].

RESULTS AND DISCUSSION

The derivatives of N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-(4'-arylthiazole-2'-yl)thioureas **3a-h** could be easily synthesized by the addition of corresponding amino compounds **1a-h** on per-*O*-acetyl-β-D-glucopyranosyl isothiocyanate **2**. We performed this reaction by executing in microwave oven in several minutes. The synthetic processes could be represented in reaction Scheme 1. We have found that nucleophiles addition of 2-amino-4-arylthiazole 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-, MS spectra).



R1=H (**a**); 3-NO_2 (**b**); 4-Cl (**c**); 4-Br (**d**); 4-Me (**e**); 4-Et (**f**); 4-OMe (**g**); 4-OMe-3-NO_2 (**h**).

Scheme 1. Synthetic pathway for N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-(4'-arylthiazole-2'-yl)thioureas and their transform.

In the IR spectra of the glucopyranosyl thioureas **3a-h**, the stretching band of C=S bond in thioureas linkage appeared in regions of 1362-1370 cm^{-1}, and N-H bonds in thioureas have absorption band in regions of 3449-3268 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. The characteristics of peracetylated glucopyranose ring was confirmed by the present of absorption band in regions of 1733-1739 cm^{-1} that specified for stretching vibration of C=O

bond in ester function.

The ^{1}H NMR and ^{13}C NMR spectral data of thioureas 3**a-h** were represented in Tables 2 and 3. From these tables, it's shown that their resonance signals in NMR spectra could be divided into some parts, as follows: region of pyranose ring, region of aromatic ring and region of acetyl function. Protons of the pyranose ring show chemical shifts from δ 4.00 to 5.90 ppm, which fit to previous results. Proton of the thiazole ring shows a single magnetic signal in region at δ 7.40-7.60 ppm. Protons of the benzene ring have chemical shifts at 7.40-7.80 ppm. The doublet signals of protons in para-substituted benzene ring sometimes appear as spin coupling A_2X_2-type ones, for example, in spectra of 1b-f. The H–H COSY spectrum of compound **3d** shows the interactions between protons H-2" and H-3", H-5" and H-6", ect… The ^{1}H-NMR spectral data of the derivatives of N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-(4'-arylthiazole-2'-yl)thiourea are represented in Table 2.

Table 1. N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-(4'-arylthiazole-2'-yl)thioureas

Entry	Compd	mp,°C	Yield, %	ν_{NH}	$\nu_{C=O}$ (ester)	ν_{C-O-C} (ester)	$\nu_{C=S}$ (thiourea)	MS, $M^{+\bullet}$
1	**3a**	200 - 202	72	3283; 3167	1733	1223; 1043	1368	565.1382
2	**3b**	215 - 216	66	3366; 3174	1748	1233; 1047	1356	
3	**3c**	238 - 240	58	3270; 3184	1738	1234; 1049	1371	643.9944/ 645.9874
4	**3d**	237 - 238	62	3368; 3175	1736	1226; 1048	1367	599.0035 /611.0135
5	**3e**	231 - 233	68	3283; 3168	1733	1229; 1051	1368	
6	**3f**	202 - 203	70	3297; 3168	1740	1234; 1045	1370	593.0920
7	**3g**	216 - 218	88	3297; 3189	1735	1253; 1033	1375	595.1475
8	**3h**	230 - 232	64	3383; 3171	1752	1225; 1048	1374	

Table 2. ^{1}H NMR spectral data of thioureas **3a-h** (in DMSO-d_6)

Proton	Compound							
	3a (δ; J; Hz)	**3b (δ; J; Hz)**	**3c (δ; J; Hz)**	**3d (δ; J; Hz)**	**3e (δ; J; Hz)**	**3f (δ; J; Hz)**	**3g (δ; J; Hz)**	**3h (δ; J; Hz)**
N-H	9,32; br	9,09; br	9,31; br	9,28; br	9,26; br	9,34; br	9,38; br	9,11; br
N'-H	11,97; s	12,07; s	11,96; s	11,96; s	11,95; s	11;95; s	11,94; s	12,01; s
H-1	5,92; t; 9,0	5,88; t; 9,1	5,89; t; 9,2	5,89; t; 9,2	5,91; t; 9,1	5,92; t; 9,1	5,92; t; 9,0	5,89; t; 9,1
H-2	5,05; t;9,0; 9,4	5,05; t; 9,1; 9,5	5,04; t; 9,2; 9,5	5,04; t; 9,2; 9,5	5,03; t; 9,1; 9,5	4,04; t; 9,1; 9,5	5,04; t; 9,0; 9,3	5,05; t; 9,1; 9,4
H-3	5,48; t; 9,4; 9,3	5,47; t; 9,5; 9,3	5,45; t; 9,5; 9,3	5,46; t; 9,5; 9,6	5,46; t; 9,5; 9,6	5,47; t; 9,5; 9.,5	5,47; t; 9,3; 9,2	5,48; t; 9,4; 9,7
H-4	5.01; t; 9.3; 9.7	5,01; t; 9,3; 9,7	5,00; t; 9,3; 9,8	5,00; t; 9,6; 9,8	4,99; t, 9,6; 9,8	5,02; t; 9,5; 9,7	5,00; t; 9,2; 9,6	5,01; t; 9,7; 9,4
H-5	4,14; m	4,13; m	4,11; m	4,11; m	4,11; m	4,13; m	4,12; m	4,13; m
H-6a	4,19; dd; 4,9; 12,4	4,20; dd; 5,3; 12,5	4,20; dd; 5,0; 12,9	4,19; dd; 3,0;12,3	4,19; dd; 4,8;12,4	4,12; dd; 5,0;12,1	4,19; dd; 4,9; 12,6	4,20; dd; 5,2; 12,6
H-6b	4,02; dd; 2,3; 12,4	4,01; dd; 2,5; 12.5	3,99; dd; 2,1; 12,9	3,99; dd; 2,1;12,3	3,99; dd; 1,8; 12,4	4,00; dd; 1,9;12,1	4,00; dd; 2,3; 12,6	4,02; dd; 2,4; 12,4
H-5'	7,58; s	7,88; s	7,63; s	7,63; s	7,49; s	7,50; s	7,41; s	7,66; s
H-2"	7,78; d; 7,5	8,71; d; 1,4	7,82; d, 8,6	7,89; d; 8,6	7,75; d; 8,0	7,79; d; 8,0	7,81; d; 8,6	8,38; d; 0,9
H-3"	7,44; t; 7,5; 7,4	-	7,62; d; 8,6	7,49; d; 8,6	7,24 d; 8;0	7,27; d; 8,0	6,91; d; 8,6	-
H-4"	7,34; t; 7,4; 7,4	8,33; d; 7,9	-	-	-	-	-	-
H-5"	7,44; t; 7,5; 7,4	7,74; t; 8,0	7,62; d; 8,6	7,49; d; 8,6	7,24 d; 8;0	7,28; d; 8,0	6,91; d; 8,6	7,44; d; 8,9
H-6"	7,78; d; 7,5	8,17; dd; 1,8; 8,8	7,82; d; 8,6	7,89; d; 8,6	7,75; d; 8,0	7,79; d; 8,0	7.81, d, 8.6	8,16; dd; 2,1; 8,3
CH_3CO	2,01; s; 2,00; s; 1,99; s; 1,98; s	2,01; s; 2,00; s; 1,99; s; 1,97; s	2,30; s; 2,02; s; 2,00; s; 1,97; s	2,01; s; 1,99, s; 1,97; s; 1,97; s	2,02; s; 1,99; s; 1,97; s; 1,97; s	2,02; s; 1,99; s; 1,97; s; 1,97; s	2,02; s; 1,99;s; 1,97; s; 1,97; s	2,01; s; 2,00; s; 1,99; s; 1,98; s
Other	-	-	-	-	2,33; s CH_3	2,50; q CH_2; 1,22; t CH_3	3,79; s OCH_3	3,98; s OCH_3

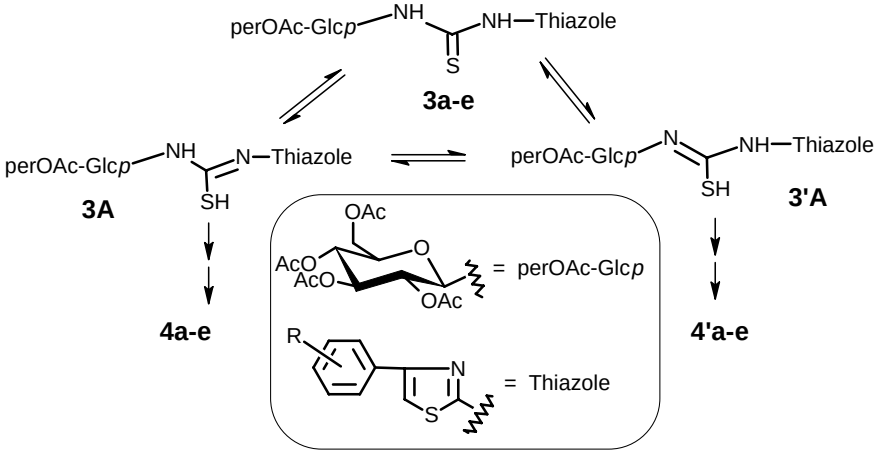
Table 3. ^{13}C NMR spectral data of thioureas **4a-h** (in DMSO-d_6)

δ (ppm)	Compound							
	3a	**3b**	**3c**	**3d**	**3e**	**3f**	**3g**	**3h**
C=S	179,2	179,2	179,2	179,2	179,2	179,2	179,2	179,2
C-1	81,0	81,0	81,0	81,1	81,1	81,0	81,1	81,0
C-2	70,5	70,5	70,4	70,4	70,5	70,5	70,4	70,4
C-3	72,3	72,3	72,3	72,3	72,4	72,3	72,3	72,3
C-4	67,9	68,0	68,0	68,0	68,0	68,0	70,0	68,0
C-5	72,5	72,4	72,5	72,5	72,5	72,4	72,5	72,4
C-6	61,7	61,6	61,7	61,7	61,7	61,7	61,9	61,6
C-2’	160,1	160,4	160,2	160,1	160,1	160,0	159,1	160,3
C-4’	148,7	148,3	147,5	*	148,9	148,8	149,0	146,2
C-5’	107,5	109,7	108,2	108,2	106,7	106,7	105,5	107,7
C-1”	133,8	131,6	132,6	132,4	137,4	131,3	*	131,1
C-2”	125,6	119,9	127,3	127,4	125,6	125,6	114,1	114,7
C-3”	128,7	130,2	128,7	128,8	129,4	128,9	127,0	126,6
C-4”	127,9	146,1	132,4	*	137,4	143,6	161,0	151,5
C-5”	128,7	135,4	128,7	128,9	129,4	128,9	127,0	139,3
C-6”	125,6	122,2	127,3	127,4	125,6	125,6	114,1	121,9
CH_3CO	20,5; 20,4; 20,3; 20,26	20,3; 20,3; 20,2; 20,2	20,4; 20,3; 20,2; 20,2	20,5; 20,4; 20,3; 20,3	20,8; 20,5; 20,4; 20,3	20,5; 20,4; 20,3; 20,3	20,5; 20,4; 20,3; 20,3	20,3; 20,2; 20,2; 20,1
CH_3CO	169,9; 169,4; 169,3; 169,3	169,8; 169,4; 169,3; 169,8	169,9; 169,4; 169,4; 169,28	170,0; 169,7; 169,5; 169,4	170,0; 170,0; 169,5; 169,4	169,9; 169,9; 169,4; 16,3	169,9; 169,9; 169,4; 169,3	169,8; 169,4; 169,3; 169,1
carbon khác	-	-	-	-	18,5 (CH_3)	27,5 (CH_2) 15,4 (CH_3)	55,1 (OCH_3)	56,8 (OCH_3)

The ^{13}C NMR spectral data of derivatives of N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N’-(4’-arylthiazole-2’-yl)thiourea **3a-h** are represented in Table 3. In their 13C-NMR spectra, six signals of pyranosyl ring appear in region from δ 82.00 to 61.00 ppm which fit with the chemical shifts of pyranose carbons. Carbon atoms in the thiazole ring have chemical shifts in region at δ 149.00-105.40 ppm, signal of carbon atom C-5’ shifts upfield and of carbon atom C-4’ shifts downfield. The reason of these phenomena is anisotropic effect of the benzene ring and electronegative influences of nitrogen and sulfur atoms in the thiazole ring. Some magnetic signals in region at δ 161.00-114.00 ppm belong to the aromatic carbon atoms. Because of the electronegative influences of sulfur atom in the thiocarbonyl group, the chemical shifts of carbon atoms in this group appear in lowest field values at δ 180.00-179.00 ppm.

The reaction of ethyl bromoacetate with corresponding *N*-(per-*O*-acetyl-β-D-glucopyranosyl)-*N'*-(phenylthiazole-2'-yl)thioureas lead to isomeric mixture of (*Z*)-3-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-2-(4"-arylthiazol-2"-ylimino)-thiazolidin-4-one (**4a-e**) and (*Z*)-2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosylimino)-3-(4"-arylthiazol-2"-yl)-thiazolidin-4-one (**4'a-e**) in parallel reaction directions A and B, respectively (Scheme 1). We used chloroform as the reaction medium and molar ratios of ethyl bromoacetate and thioureas **3a-e** were 3:1 in order to obtain the higher transformation yields. Reaction mixtures were stirred in room temperature for one hour, after that, heated with reflux for 12 h. A reaction time of over 12 h at reflux in chloroform was kept since a longer time did not improve the yield. The appearance of white precipitate in the reaction beginning was the evidence indicating the reaction was taken place. The products were insoluble in ethanol, methanol, but soluble easily in benzene, toluene, and facilitated for purification. Reaction yields are 52-62%. When the other protonic solvents (such as ethanol) were used as reaction medium, this reaction did not take place. Chloroform medium gave higher yield (up to 65%) than other mediums. 2-Aminothiazolidin-4-ones **4a-e** and **4'a-e** have structural similarity: glucopyranose and arylthiazole are at positions 3 and 2 of thiazolidine ring in isomers **4a-e**, through the direct bond with nitrogen atom or imino bond, respectively, and alternatively, in isomer **4'a-e** these moieties are at 2 and 3, respectively, of thiazolidine ring. Because of these structural similarity of **4a-e** and **4'a-e**, it's impossible to separate these isomers (by recrystallization or column chromatography).

We found that 2-iminothiazolidin-4-ones **4a-e** and **4'a-e** were formed in ratio of about 5.1-5.2/4.9-4.8. In thioureas **3a-e** the tautomers **3A** and **3'A** exist in equilibrium, the sulfur atom in thiol-tautomer play role as a nucleophile in reaction with ethyl bromoacetate (Figure 1).



Fugure 1. Reaction route in interaction of thioureas **3a-e** with ethyl bromoacetate.

IR spectra show the characteristic absorption bands at ν=1749-1743 cm^{-1} ($\nu_{C=O}$ ester), 1694-1690 cm^{-1} ($\nu_{C=O}$ lactam, shoulder), 1610-1607 cm^{-1} ($\nu_{C=N}$, shoulder), 1575-1508 cm^{-1} ($\nu_{C=C}$), 1239-1227 and 1033-1035 cm^{-1} (ν_{COC} ester). The evidences that confirm the success of reactions are the absence of NH bands in IR spectra at ν=3340-3320 cm^{-1} and chemical shifts of NH (thiourea) at δ=9-10 ppm (in ^{1}H NMR spectra). Other evidence is the disappearance of C=S signals at δ=206-208 ppm and the appearance of C=N signals at δ=163.9-160.0 ppm (in ^{13}C NMR

spectra). The ^{1}H and ^{13}C NMR spectral elucidations of these products indicated the presence of two isomers in each obtained product. The isomers **4a-e** and **4'a-e** were distinguished one isomer from another by chemical shits of protons H-1' and H-2' on pyranose ring. In isomer **4a-e** resonance signals of proton H-1' show at δ=6.42-6.35 ppm and the one of proton H-2' show at δ=5.97-5.92 ppm, while protons H-1' and H-2' in isomer **4'a-e** had chemical shifts at δ=5.97-5.92 ppm and 6.51-6.44 ppm, respectively. Proton H-1' in isomers **4'a-e** were shielded more strongly by diamagnetic anisotropy of imino group, and its resonance signal was upfield, while this effect was absent in isomer **4a-e**, so the resonance signals of proton H-1' was downfield. Isomer ratios **4a-e** and **4'a-e** have been calculated from ratio of integral curves of proton signals (Figure 2).

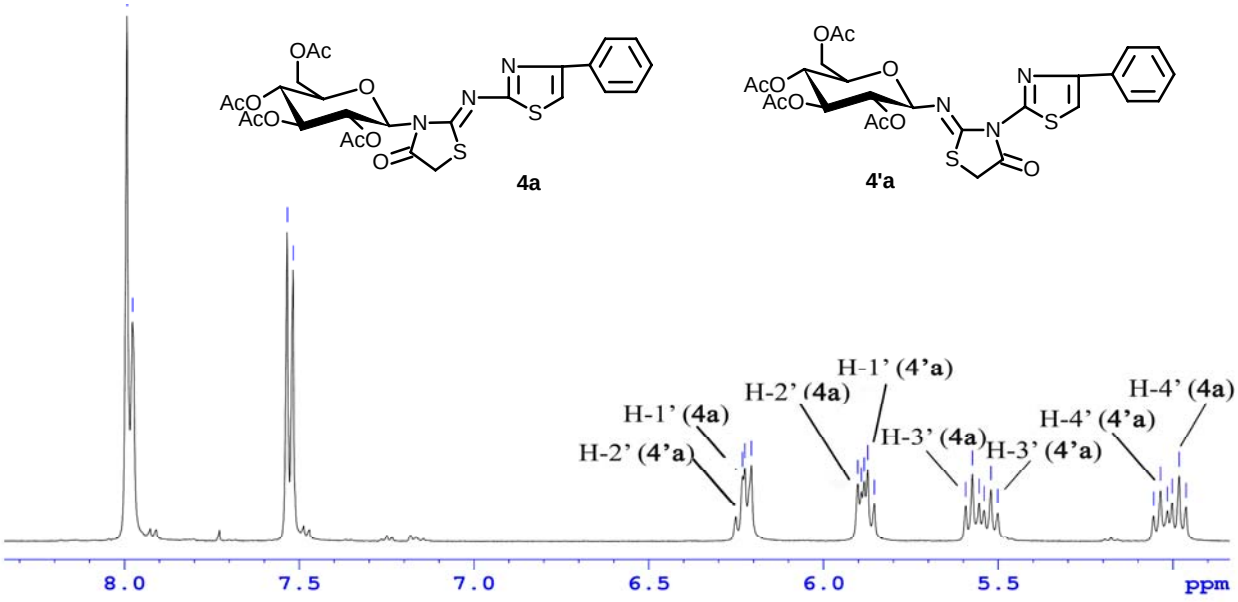


Figure 2. A part of ^{1}H-NMR spectrum of 2-aminothiazolindin-4-one **4a/4'a**.

In conclusion, the isomeric 2-iminothiazolidin-4-ones **4a-e** and **4'a-e** were obtained from reaction of corresponding thioureas **3a-e** with ethyl bromoacetate in the presence of triethylamine as catalyst in aprotonic solvents. The presences of isomers were confirmed ^{1}H NMR and ^{13}C NMR spectra.

EXPERIMENTAL

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 Avance AV500 Spectrometer (Bruker, Germany) at 500 MHz, using DMSO-d6 as solvent and TMS as an internal reference. The ^{1}H NMR and ^{13}C NMR spectra were recorded on an Advance Spectrometer (Bruker, Germany) at 500 MHz, using DMSO-d_6 as solvent and TMS as an internal reference. Chemical shifts are expressed as δ unit. Full $^{1}H/^{13}C$ assignments were carried out using HMBC,

HSQC and COSY methods. 2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate was synthesized by known method [17].

A-Synthesis of N-(2,3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-3-(4''-aryl thiazole-2-yl) thioureas (General method). Mixed 0.494 g (0.002 moles) of 2-amino-4-arylthiazole and 0.778 g (0.002 moles) of 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate. Then this mixture was irradiated about 5 minutes at 750 Watts 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 of the title thioureas.

N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-(4'-phenylthiazol-2'-yl)-thiourea (4a). From 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate (0.005 mol; 1.945 g), 2-amino-4-phenylthiazole (0.005 mol; 0.891 g), at refluxing for 25 min. Product was the white solid, yield 2.03 g (72 %), mp 200 - 202°C. MS $M^{+\bullet}$ 565.1382, calc. 565.1188 .

N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-[4'-(3"-nitrophenyl)thiazol-2'-yl]-thiourea (4b). From 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate (0.005 mol; 1.945 g), 2-amino-4-(3'-nitrophenyl)thiazole (0.005 mol; 1.116 g), at refluxing for 20 min. Product was the yellow solid, yield 2.01 g (66 %), mp 215 - 216°C.

N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'- [4'-(4"-clorophenyl)thiazol-2'-yl]-thiourea (4c). From 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate (0.005 mol; 1.945 g), 2-amino-4-(4'-clorophenyl)thiazole (0.005 mol; 1.064 g), at refluxing for 20 min. Product was the white solid, yield 1.74 g (58 %), mp 238 - 240°C.

N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-[4'-(4"-bromophenyl)thiazol-2'-yl]-thiourea (4d). From 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate (0.005 mol; 1.945 g), 2-amino-4-(4'-bromophenyl)thiazole (0.005 mol; 1.285 g), at refluxing for 20 min. Product was the pale yellow solid, yield 2.00 g (62 %), mp 237 - 238°C.

N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-[4'-(4"-metylphenyl)thiazol-2'-yl]-thiourea (4e). From 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate (0.005 mol; 1.945 g), 2-amino-4-(4'-metylphenyl)thiazole (0.005 mol; 0.962 g), at refluxing for 20 min. Product was the white solid, yield 1.97 g (68 %), mp 231 - 233°C.

N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-[4'-(4"-etylphenyl)thiazol-2'-yl]-thiourea (4f). From 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate (0.005 mol; 1.945 g), 2-amino-4-(4'-etylphenyl)thiazole (0.005 mol; 1.032 g), at refluxing for 20 min. Product was the white solid, yield 2.08 g (70 %), mp 202 - 203°C.

N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-[4'-(4"-metoxyphenyl)thiazol-2'-yl]-thiourea (4g). From 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate (0.005 mol; 1.945 g), 2-amino-4-(4'-metoxyphenyl)thiazole (0.005 mol; 1.042 g), at refluxing for 20 min. Product was the pale yellow solid, yield 2.62 g (88 %), mp 216 - 218°C.

N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-[4'-(3"-nitro-4"-metoxyphenyl)thiazol-2'-yl]-thiourea (4h). From 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate (0.005 mol; 1.945 g), 2-amino-4-(3'-nitro-4'-metoxyphenyl)thiazole (0.005 mol; 1.266 g), at refluxing for 20 min. Product was the yellow solid, yield 2.05 g (64 %), mp 230 – 232°C.

B-Synthesis of 2-iminothiazolidin-4-ones 4a-e/4'a-e. A reaction mixture of thioureas **3a-e** (5 mmol) in dried $CHCl_3$ (20 mL) was stirred vigorously. Ethyl bromoacetate (1.0 g, 0.2 mL, 6 mmol) was added dropwise with stirring for 1 h at room temperature. Then the reaction mixture was heated at reflux for 12 h and the solvent was removed under diminished pressure until the volume was in 10 mL, and ethanol (20 mL) was added and left overnight. A white separated crude product was filtered and purified by recrystallization from toluene:ethanol (1:1) to afford the title compounds **4/4'**.

3-(2',3',4',6'-Tetra-O-acetyl-β-D-glucopyranosyl)-2-[(4"-phenyl)thiazole-2"-ylimino]-thiazolidin-4-on (6a) and 2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosylimino)-3-[(4"-phenyl)thiazole-2"-yl]-thiazolidin-4-on (6'a). From N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-(4'-phenylthiazol-2'-yl)-thiourea (0.5 mmol; 0.288 g), etyl bromoacetat (1.7 mmol; 0.2 ml)/$CHCl_3$, cloroform (20 ml), at refluxing for 12 h. Product was the white solid, mp 217 - 219°C, yield 0.187 g (62 %). FTMS (ESI): calc. for $C_{26}H_{27}N_3O_{10}S_2$: 605.1138 Da, [M+H]=606.1211 Da, found: $[M+H]^{+\bullet}$=606.1297.

3-(2',3',4',6'-Tetra-O-acetyl-β-D-glucopyranosyl)-2-{[4"-(3"'-nitrophenyl)]-thiazole-2"-ylimino}-thiazolidin-4-on (6b) and 2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosylimino)-3-{[4"-(3"'-nitrophenyl)]thiazole-2"-yl}-thiazolidin-4-on (6'b). From N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-[4'-(3"-nitrophenyl) thiazol-2'-yl]-thiourea (0.5 mmol; 0.310 g), etyl bromoacetat (1.7 mmol; 0.2 ml)/$CHCl_3$, cloroform (20 ml), at refluxing for 12 h. Product was the white solid, mp 226 - 228°C, yield 0.176 g (54 %). FTMS (ESI): calc. for $C_{26}H_{26}N_4O_{12}S_2$: 650.0989 Da, [M-H]=649.0905 Da, found: $[M-H]^{+\bullet}$=649.0769.

3-(2',3',4',6'-Tetra-O-acetyl-β-D-glucopyranosyl)-2-{[4"-(4"'-clorophenyl)]-thiazole-2"-ylimino}-thiazolidin-4-on (6c) and 2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosylimino)-3-{[4"-(4"'-clorophenyl)]-thiazole-2"-yl}thiazolidin-4-on (6'c). From N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-[4'-(4"-clorophenyl) thiazol-2'-yl]-thiourea (0.5 mmol; 0.305 g), etyl bromoacetat (1.7 mmol; 0.2 ml)/$CHCl_3$, cloroform (20 ml), at refluxing for 12 h. Product was the white solid, mp 237 - 239°C, yield 0.166 g (52 %). FTMS (ESI): calc. for $C_{26}H_{26}{}^{35}ClN_3O_{10}S_2/C_{26}H_{26}{}^{37}ClN_3O_{10}S_2$: 639.0748/641.0719 Da, [M+H]=640.0821/642.0791 Da, found: $[M+H]^{+\bullet}$=640.0986/642.0965.

3-(2',3',4',6'-Tetra-O-acetyl-β-D-glucopyranosyl)-2-{[4"-(4"'-bromo-phenyl)]-thiazole-2"-ylimino}-thiazolidin-4-on (6d) and 2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosylimino)-3-{[4"-(4"'-bromophenyl)]thiazole-2"-yl}-thiazolidin-4-on (6'd). From N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-[4'-(4"-bromophenyl) thiazol-2'-yl]-thiourea (0.5 mmol; 0.328 g), etyl bromoacetat (1.7 mmol; 0.2 ml)/$CHCl_3$, cloroform (20 ml), at refluxing for 12 h. Product was the white solid, mp 242 - 244°C, yield 0.182 g (55 %). FTMS (ESI): calc. for $C_{26}H_{26}{}^{79}BrN_3O_{10}S_2/C_{26}H_{26}{}^{81}BrN_3O_{10}S_2$: 683.0243/685.0222 Da, [M+H]=684.0316/686.0295 Da, found: $[M+H]^{+\bullet}$ =684.0437/686.0431.

3-(2',3',4',6'-Tetra-O-acetyl-β-D-glucopyranosyl)-2-{[4"-(4"'-metoxy-phenyl)]thiazole-2"-ylimino}-thiazolidin-4-on (6g) and 2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosylimino)-3-{[4"-(4"'-metoxyphenyl)]thiazole-2"-yl}-thiazolidin-4-on (6'g). From N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-[4'-(4"-metoxyphenyl) thiazole2'-yl]-thiourea (0.5 mmol; 0.303 g), etyl

bromoacetat (1.7 mmol; 0.2 ml)/$CHCl_3$, cloroform (20 ml), at refluxing for 12 h. Product was the white solid, mp 224 - 226°C, yield 0.191 g (60 %). FTMS (ESI): calc. for $C_{26}H_{29}N_3O_{11}S_2$: 635.1243 Da, [M+H]=636.1316 Da, found: $[M+H]^{+\bullet}$=636.1541.

CONCLUSIONS

N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-(thiazol-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-aminothiazoles executing in domestic microwave oven. The ^{1}H and ^{13}C-NMR spectra of some derivatives of N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-N'-(4'-arylthiazole-2'-yl)thiourea have been recorded. 2-Iminothiazolidin-4-ones have been synthesized from ethyl bromoacetate and substituted *N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-*N'*-(phenylthiazole-2'-yl)thioureas. The presence of 2-iminothiazolidin-4-one isomers were confirmed by NMR spectroscopies.

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