

## Synthesis and Characterization of Some Novel Thiourea Having Sugar and 1,3,4-Thiadiazole Moieties

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Several novel 1,3,4-thiadiazole thioureas have been prepared by the condensation of hepta-O-acetyl- $\beta$ -D-glucosyl isothiocyanate with 2-amino-5-substituted-1,3,4-thiadiazole. The structures of these new N-glucosides have been established on the basis of  $^1\text{H}$  NMR, mass spectral and elemental analysis studies.

**Key Words:** Glucose, 1,3,4-Thiadiazole, Thiourea.

### INTRODUCTION

Carbohydrates have a wide range of biological activities. In recent years, the research of carbohydrate has been very popular<sup>1-4</sup>. N-glucosylated compounds and their derivatives are reported to be widely applied in medicinal chemistry and agricultural chemistry<sup>5-10</sup>. Thioureas derivatives have potential pharmacological properties<sup>11-16</sup> and pesticidal properties<sup>17-20</sup>, 2-amino-5-substituted thiadiazoles show some plant growth regulator and antibacterial activity<sup>21,22</sup>. Due to the importance of these compounds, a series of thiourea derivatives containing  $\beta$ -D-glucosyl substituent on the nitrogen bond were proposed. Conventional method for the synthesis of thiourea was reported based on the reaction of isothiocyanate and amines<sup>23</sup>.

### EXPERIMENTAL

A solution of **1** (12 mmol in sodium-dried toluene 20 mL) was dropped into the gently refluxing mixture of lead thiocyanate (15 mmol) and toluene (30 mL) under vigorous stirring for 3.0 h-3.5 h until TLC showed that the reaction completed. The lead salt was filtered off from the hot reaction mixture and to the filtrate petroleum ether (30-60 °C) was added to turbidity, after cooling the pure crystalline product **2** was separated and get **2** 4.21 g, yield 89 %, m.p. 110-111 °C (m.p. 112-114 °C).

A mixture of hepta-O-acetyl- $\beta$ -D-glucosyl isothiocyanate **2** (0.005 mol) and 5-substituted-1,3,4-thiadiazolyl amines (0.005 mol) in 20 mL of acetonitrile was refluxed at 90 °C for 3 h while monitoring by TLC. After completion of the reaction, the solvent was removed on a rotary evaporator

and the crude product obtained was purified by silicon-gel column eluted with ethyl acetate/petroleum ether (1:2) and a white solid (**3a-1**) was afforded. Their structures were confirmed by <sup>1</sup>H NMR spectra, elemental analyses (Tables 1 and 2).

TABLE-1  
PHYSICAL DATA OF TITLE COMPOUNDS AND  
ELEMENTAL ANALYSIS

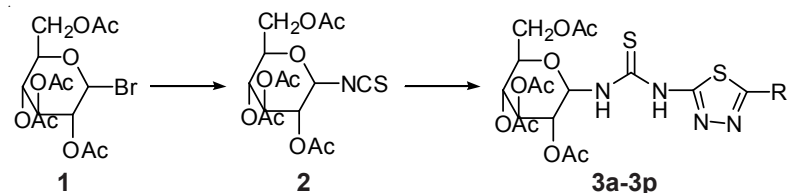
Compd.	R	Yield (%)	m.p. (°C)	Elemental analysis %		
				Found (calcd.)		
				C	H	N
<b>3a</b>	Cyclopropane	73	>200	45.64 (45.27)	5.11 (4.94)	10.55 (10.56)
<b>3b</b>	Furan	64	129-131	45.64 (45.32)	4.33 (4.35)	10.45 (10.07)
<b>3c</b>	Phenyl	74	115-118	48.88 (48.75)	4.43 (4.63)	10.05 (9.89)
<b>3d</b>	<i>p</i> -OCH <sub>3</sub> phenyl	82	193-195	48.68 (48.31)	4.43 (4.73)	9.55 (9.39)
<b>3e</b>	<i>o</i> -CH <sub>3</sub> phenyl	67	102-103	49.78 (49.65)	4.83 (4.86)	9.55 (9.65)
<b>3f</b>	<i>m</i> -CH <sub>3</sub> phenyl	64	127-129	49.48 (49.65)	4.88 (4.86)	9.65 (9.65)
<b>3g</b>	<i>p</i> -Cl phenyl	76	119-129	45.68 (45.96)	4.13 (4.19)	9.55 (9.32)
<b>3h</b>	<i>o</i> -Cl phenyl	77	119-122	45.38 (45.96)	4.14 (4.19)	9.45 (9.32)
<b>3i</b>	<i>o</i> -F phenyl	81	108-122	47.15 (47.25)	4.31 (4.31)	9.55 (9.58)
<b>3j</b>	H	73	147-149	41.55 (41.63)	4.23 (4.52)	11.45 (11.42)
<b>3k</b>	Et	69	150-152	44.01 (44.30)	4.93 (5.05)	10.55 (10.08)
<b>3l</b>	<i>iso</i> -Pr	72	111-113	44.98 (45.10)	5.13 (5.30)	10.55 (10.52)

## RESULTS AND DISCUSSION

Here, we report the synthesis of several 1,3,4-thiadiazoyl-4-(1'-N-2', 3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)thioureas **3a-1** by the condensation of hepta-O-acetyl-β-D-glucosyl isothiocyanate **2** with 2-amino-5-substituted-1,3,4-thiadiazoles. Required glucosylisothiocyanate was prepared<sup>24</sup> by the reaction of hepta-O-acetyl-β-D-glucosyl bromide **1** with lead thiocyanate (**Scheme-I**). Required 2-amino-5-substituted-1,3,4-thiadiazoles were prepared by the cyclization of substituted carboxylic acid with thiosemicarbazide<sup>25</sup>.

TABLE-2  
<sup>1</sup>H NMR (ppm) SPECTRAL DATA OF **3a-3l**

Compd.	Spectral data
<b>3a</b>	8.05 (1H, s, NH), 5.82 (dd, <i>J</i> = 8.2 Hz, 1H, C1'-H), 5.4-3.8 (m, 6H, Sugar ring C'2,3,4,6-H), 2.02-2.14 (m, 12H, 4 × CH <sub>3</sub> CO), 1.30-1.82 (m, 4H, cyclopropane rings).
<b>3b</b>	8.55 (1H, s, NH), 7.58 (d, 1H, funan ring), 7.04 (d, 1H, funan ring), 6.56 (m, 1H, funan ring), 5.73 (dd, <i>J</i> = 8.4 Hz, 1H, C1'-H), 5.26-3.8 (m, 6H, Sugar ring C'2,3,4,6-H), 2.02-2.18 (m, 12H, 4 × CH <sub>3</sub> CO).
<b>3c</b>	9.21 (1H, s, NH), 8.45-7.96 (m, 5H, phenyl ring), 5.83 (dd, <i>J</i> = 8.8 Hz, 1H, C1'-H), 5.41-3.93 (m, 6H, Sugar ring C'2,3,4,6-H), 2.00-2.15 (m, 12H, 4 × CH <sub>3</sub> CO).
<b>3d</b>	7.84 (d, 2H, phenyl ring), 6.99 (d, 2H, phenyl ring), 5.89 (dd, <i>J</i> = 9.3 Hz, 1H, C1'-H), 5.33-3.81 (m, 6H, Sugar ring C'2,3,4,6-H), 3.87 (s, 3H, OCH <sub>3</sub> ), 2.02-2.14 (m, 12H, 4 × CH <sub>3</sub> CO), 2.17 (1H, s, NH).
<b>3e</b>	7.63 (d, 2H, NH), 7.22-7.39 (m, 4H, phenyl ring), 5.89 (dd, <i>J</i> = 8.2 Hz, 1H, C1'-H), 5.31-3.80 (m, 6H, Sugar ring C'2,3,4,6-H), 2.56 (s, 3H, Ar-CH <sub>3</sub> ), 2.02-2.14 (m, 12H, 4 × CH <sub>3</sub> CO).
<b>3f</b>	7.70 (d, 2H, NH), 7.28-7.38 (m, 4H, phenyl ring), 5.69 (dd, <i>J</i> = 9.1 Hz, 1H, C1'-H), 5.33-3.80 (m, 6H, Sugar ring C'2,3,4,6-H), 2.42 (s, 3H, Ar-CH <sub>3</sub> ), 2.01-2.14 (m, 12H, 4 × CH <sub>3</sub> CO).
<b>3g</b>	8.70 (s, 1H, NH), 7.85 (d, 2H, phenyl ring), 7.42 (d, 2H, phenyl ring), 5.69 (dd, <i>J</i> = 8.9 Hz, 1H, C1'-H), 5.33-3.80 (m, 6H, Sugar ring C'2,3,4,6-H), 2.01-2.14 (m, 12H, 4 × CH <sub>3</sub> CO).
<b>3h</b>	9.53 (s, 1H, NH), 8.12 (s, 1H, phenyl ring), 7.40 (s, 1H, phenyl ring), 7.26 (s, 2H, phenyl ring), 5.58 (dd, <i>J</i> = 8.7 Hz, 1H, C1'-H), 5.23-3.77 (m, 6H, Sugar ring C'2,3,4,6-H), 2.01-2.14 (m, 12H, 4 × CH <sub>3</sub> CO).
<b>3i</b>	8.79 (s, 1H, NH), 8.23 (t, 1H, phenyl ring), 7.46 (d, 1H, phenyl ring), 7.28 (m, 2H, phenyl ring), 5.77 (dd, <i>J</i> = 8.8 Hz, 1H, C1'-H), 5.23-3.84 (m, 6H, Sugar ring C'2,3,4,6-H), 2.01-2.18 (m, 12H, 4 × CH <sub>3</sub> CO).
<b>3j</b>	11.29 (s, 1H, NH), 8.26 (s, 1H, thiazole ring), 5.67 (dd, <i>J</i> = 9.0 Hz, 1H, C1'-H), 5.21-3.74 (m, 6H, Sugar ring C'2,3,4,6-H), 2.01-2.18 (m, 12H, 4 × CH <sub>3</sub> CO);
<b>3k</b>	8.29 (s, 1H, NH), 5.88 (dd, <i>J</i> = 8.7 Hz, 1H, C1'-H), 5.20-3.78 (m, 6H, Sugar ring C'2,3,4,6-H), 2.98 (q, 2H, CH <sub>2</sub> ), 2.00-2.18 (m, 12H, 4 × CH <sub>3</sub> CO), 1.40 (t, 3H, CH <sub>3</sub> ).
<b>3l</b>	7.89 (s, 1H, NH), 5.79 (dd, <i>J</i> = 9.4 Hz, 1H, C1'-H), 5.20-3.81 (m, 6H, Sugar ring C'2,3,4,6-H), 2.00-2.18 (m, 13H, 4 × CH <sub>3</sub> CO and CH), 1.41 (d, 6H, CH <sub>3</sub> ).



a) R = cyclopropyl, b) R = furan, c) R = phenyl, d) R = *p*-OCH<sub>3</sub> phenyl, e) R = *o*-CH<sub>3</sub> phenyl, f) R = *m*-CH<sub>3</sub> phenyl, g) R = *p*-Cl phenyl, h) R = *o*-Cl phenyl, i) R = *o*-F phenyl, j) R = H, k) R = Et, l R = *iso*-Pr

**Scheme-I.** Reagents and conditions: (i) Pb(NCS)<sub>2</sub>, toluene, reflux;  
(ii) R-NH<sub>2</sub>, acetonitrile, reflux

The route shown in **Scheme-I** was used for synthesizing the title compounds. The elemental analysis and physical data are given in Table-1. The NMR spectral data are summarized in Table-2.

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