# STUDY ON NMR SPECTRA OF SOME 4-FORMYLCOUMARIN 4-(TETRA-*O*-ACETYL-β-D-GLUCOPYRANOSYL)THIOSEMICARBAZONES

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**Nguyen Dinh Thanh**

*Faculty of Chemistry, VNU University of Science*

**Vu Ngoc Toan[2]**

*Institute of Chemical and Materials, Military Institute of Science and Technology*

TÓM TẮT

NGHIÊN CỨU PHỔ NMR CỦA MỘT SỐ 4-FORMYLCOUMARIN 4-(TETRA-*O*-ACETYL-β-D-GLUCOPYRANOSYL)THIOSEMICARBAZONES

*Các tính chất phổ $^{1}H$ và $^{13}C$ NMR của các hợp chất 6- và 7-alkoxy-4-formyl-coumarin 4-(tetra-O-acetyl-β-D-glucopyranosyl)thiosemicabazon đã được thảo luận. Các tín hiệu phổ được qui kết dựa vào phổ 2D NMR COSY, HSQC và HMBC. Hằng số ghép cặp J = 9,00–9,25 Hz giữa proton H-1' và H-2' trong hợp phần glucopyranose đã xác nhận cấu hình anomer β của các thiosemicarbazone này.*

## INTRODUCTION

The compounds containing coumarin ring are abundantly found in many natural plants [1-3]. The synthesis of organic compounds containing this ring has long been of interest because of the remarkable biological activity compounds of these [4,5]. Thiosemicarbazides exhibit various biological activities and are extensively applied in medicine, particularly in the treatment of tuberculosis [6,7]. Several compounds with a thiosemicarbazone moiety also show the biological activity [8,9]. Some peracetylated glycopyranosyl thiosemicarbazones containing coumarin ring were synthesized in good yields by the reactions of substituted 3-acetylcoumarins with 4-(tetra-*O*-acetyl-β-D-glucopyranosyl)thiosemicarbazide in our laboratory [10-12]. In progress of our works on glycopyranosyl thiosemicarbazones of coumarins, we herein report the study on the NMR spectral characteristic of some substituted 4-formylcoumarin 4-(tetra-*O*-acetyl-β-D-

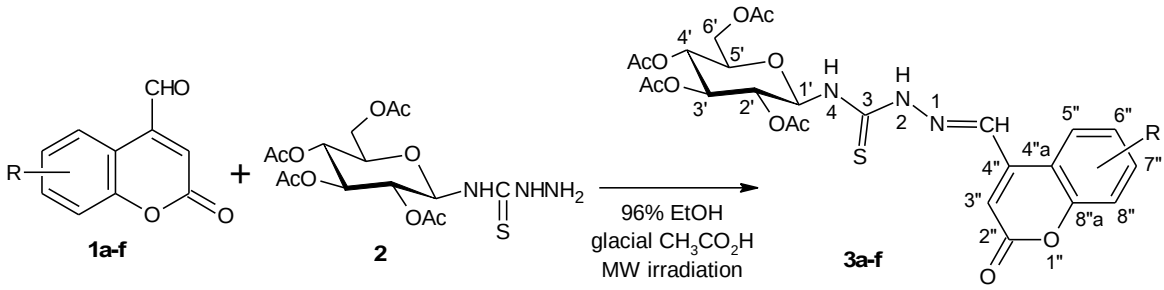
glucopyranosyl) thiosemicarbazones (*Scheme 1*).

EXPERIMENTAL PART

Substituted 4-formylcoumarin 4-(tetra-*O*-acetyl-β-D-glucopyranosyl) thiosemicarbazones 3 (*Scheme 1*) were synthesized in following procedure [5c]. Their $^{1}$H and $^{13}$C NMR spectra was recorded on FT-NMR Avance AV500 Spectrometer (Bruker, Germany) at 500.13 MHz and 125.76 MHz, respectively, using DMSO-$d_6$ as solvent and TMS as an internal standard.

RESULTS AND DISCUSSION

The assignments of $^{1}$H and $^{13}$C for 6- and 7-substituted-4-formylcoumarin 4-(tetra-*O*-acetyl-β-D-glucopyranosyl)thiosemicarbazones **3a-f** were confirmed using COSY, HMBC and HSQC methods through the case of compound **3c** (R=6-OPn). The $^{1}$H and $^{13}$C NMR spectral data of these thiosemicarbazones were listed in Tables 1 and 2. The $^{1}$H NMR spectra of these thiosemicarbazones showed resonance signals for proton NH-2 at δ=12.23–12.09 ppm (singlet), for proton NH-4 at δ=9.19–9.11 ppm (doublet) with coupling constants of $^{3}J$=9.0–9.5 Hz. The signal of NH-2 proton is in the downfield region due to the influence of anizotropic effect from adjacent azomethin bond. Protons in glucopyranose ring have resonance signals in range at δ=6.03– 3.98 ppm. Methyl groups in acetate ester have chemical shifts in range at δ= 2.00–1.92 ppm in singlet, usually as a set of four signals (*Table 1*). The coupling constants between protons H-1' (δ=6.03–5.99 ppm) and H-2' (δ=5.35–5.34 ppm) are *J*=9.00–9.25 Hz, which suggests that the link proton at position C-1' and C-2' located *trans* position to each other, meaning that the substituent in carbon C-1' is located in the β anomeric position. Especially, in the sugar region, proton H-5' (δ=4.11 ppm) has coupling interactions with proton H-6'a (δ=4.23 ppm) and H-6'b (δ=3.99 ppm). Coupling constants for these interactions are *J*=10.00–12.25, 2.5– 4.5 and ~1.75 Hz, respectively.




*Scheme 1. Substituted 4-formylcoumarin 4-(tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazones **3a-f**.*

The $^{13}C$ NMR spectral data in Table 2 show the following spectral characteristic of these thiosemicarbazones. The carbon of the aromatic ring with the signals in the δ=160.3–101.6 ppm. The carbon in the glucopyranose ring is chemical shifts in the range δ=81.7–61.7 ppm. Carbon atoms in acetyl had signals in the range δ=20.5–20.3 ppm (for methyl group) and 170.0–169.3 ppm (for carbonyl group). Resulted HMBC spectrum of compound **3b** show the long-ranged interaction that appeared in spectrum. The alkoxy groups have corresponding signals for methyl and methylene groups. The $^{1}H$-$^{1}H$ COSY spectrum of conpound **3b** shows the interactions between the two protons at the carbon atoms in the molecule together. The $^{1}H$-$^{1}H$ interactions appear in the spectrum (*Fig. 1, left*) of 4-formyl-7-ethoxycoumarin 4-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-thiosemicarbazone **3b** as follows: 9.12 (NH-4)⇔5.99 (H-1')⇔5.35 (H-2')⇔5.43 (H-3')⇔4.97 (H-4')⇔4.11 (H-5')⇔4.23 (H-6'a);3.99 (H-6'b); 4.23 (H-6'a)⇔3.99 (H-6'b) and 4.14 (-$OCH_2$-)⇔1.36 ($CH_3$).

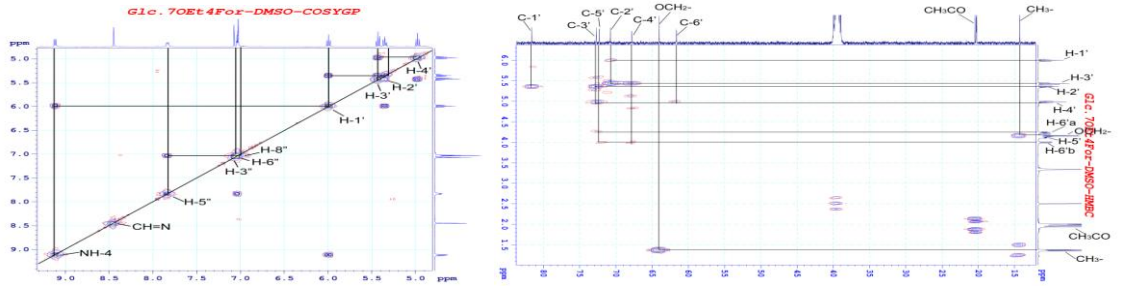



*Figure 1. $^{1}H$-$^{1}H$ COSY (left) and HMBC (right) spectra (expanded) of thiosemicarbazone **3b**.*

The obtained HMBC spectral show the indirect (long-range) interactions of the protons with the carbon atoms, for example, the carbon C=S (δ=179.0 ppm) interacts with protons NH-2 (δ=12,22 ppm) of thiosemicarbazone linkage and H-1' (δ=5.99 ppm) of the pyranose ring; carbon atom C-7" (δ=161.7 ppm) has the interaction with the proton H-5" (δ=7.83 ppm), H-6" (δ=7.03 ppm) and the – $OCH_2$– group (δ=4.14 ppm) of 7"-ethoxy. One another noteworthy interaction is the one of carbon C-5' (δ=72.3 ppm) for the protons H – 4' (δ=4.97 ppm), H-6'a (δ=4,23 ppm) and H-6'b (δ=3.99 ppm) (*Fig. 1, right*). Based on the 2D NMR spectra and the 1D NMR spectra of the thiosemicarbazone 3b, the position of the resonance signals of proton and carbon-13 has been assigned (*Tables 1 and 2*).

CONCLUSIONS

The $^{1}H$ and $^{13}C$ NMR spectra of substituted 4-formylcoumarin 4-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)thiosemicarbazone have been studied and discussed in detail. The values of the coupling constant *J*=9.00– 9.25 Hz between the protons H-1' and H-2 of component glucopyranose indicated that these thiosemicarbazones have β-anomeric configuration.

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*Table 1. $^1$H NMR spectral data of thiosemicarbazones **3a-f** [δ (ppm), multiplicity, J (Hz)]*

| Proton | 6-OBu (3a) | 6-OiBu (3b) | 6-OPn (3c) | 6-OiPn (3d) | 7-OiBu (3e) | 7-OiPn (3f) |
|---|---|---|---|---|---|---|
| CH=N | 8.54;s.1H | 8.51;s.1H | 8.55;s;1H | 8.55;s;1H | 8.45;s;1H | 8.45;s;1H |
| NH-2 | 12.09;s;1H | 12.08;s;1H | 12.09;s;1H | 12.09;s;1H | 12.22;s;1H | 12.23;s;1H |
| NH-4 | 9.17;d;1H; *J* 9.0 | 9.17;d;1H;;*J* 8.5 | 9.19;d;1H; *J* 9.0 | 9.18;d;1H; *J* 8.5 | 9.11;d;1H; *J* 9.5 | 9.12;d;1H; *J* 9.5 |
| H-1' | 6.03;t. 1H; *J* 9.25 | 6.03;t; 1H; *J* 9.25 | 6.03;t. 1H; *J* 9.25 | 6.03;t. 1H; *J* 9.25 | 5.99;t. 1H; *J* 9.0 | 5.99;t. 1H; *J* 9.25 |
| H-2' | 5.29;t. 1H; *J* 9.25 | 5.32;t; 1H; *J* 9.0 | 5.30;t. 1H; *J* 9.25 | 5.29;t. 1H; *J* 9.25 | 5.35;t. 1H; *J* 9.25 | 5.35;t. 1H; *J* 9.0 |
| H-3' | 5.43;t. 1H; *J* 9.5 | 5.43;t. 1H; *J* 9.5 | 5.43;t. 1H; *J* 9.5 | 5.43;t. 1H; *J* 9.5 | 5.43;t. 1H; *J* 9.5 | 5.43;t. 1H; *J* 9.5 |
| H-4' | 4.97;t. 1H; *J* 10.0 | 4.98;t. 1H; *J* 9.75 | 4. 97;t. 1H; *J* 9.75 | 4.97;t. 1H; *J* 9.75 | 4.97;t. 1H; *J* 9.75 | 4.97;t. 1H; *J* 9.75 |
| H-5' | 4.12;ddd;1H; *J*2.0,4.5,10.0 | 4.11;ddd;1H; *J*2.0,4.5,10.0 | 4.13;ddd;1H; *J*2.38,4.38,9.88 | 4.12;ddd;1H; *J* 2.13 | 4.10;ddd;1H; *J* 2.38,4.38,9.88 | 4.13-4.11;m;3H |
| H-6'a | 4.22;dd;1H; *J* 5.0,12.5 | 4.23;dd;1H; *J* 4.5,12.5 | 4.22;dd;1H; *J* 5.0,12.5 | 4.22;dd;1H; *J* 5.0,12.5 | 4.23;dd;1H; *J* 4.75,12.75 | 4.22;dd;1H; *J* 4.25,12.25 |
| H-6'b | 3.99;dd;1H; *J* .75,12.25 | 3.99;d;1H;*J* 11.0 | 3.99;dd;1H; *J* 2.0,12.5 | 3.99;dd;1H; *J* .75,12.25 | 4.00 – 3.98;m;1H | 3.99;d;1H; *J* 12.0 |
| H-3" | 7.32;s;1H | 7.30;s;1H | 7.34;s;1H | 7.34;s;1H | 7.07;s;1H | 7.07;s;1H |
| H-5" | 7.30;s;1H | 7.22-7.21;m;2H | 7.29;s;1H | 7.31;s;1H | 7.84;d;1H; *J* 8.0 | 7.83;d.1H; *J* 8.5 |
| H-6" | - | - | - | - | 7.06-7.05;m;2H | 7.05-7.03;m;2H |
| H-7" | 7.26;dd;1H; *J* 2.25,9.0 | 7.34;dd;1H; *J* 3.0,9.0 | 7.28;d;1H;*J* 8.25 | 7.28;dd;1H; *J* 2.5,9.0 | - | - |
| H-8" | 7.40;d;1H; *J* 9.0 | 7.22-7.21;m;2H | 7.41;d;1H; *J* 8.5 | 7.41;d;1H; *J* 9.0 | 7.06 – 7.05;m;2H | 7.05-7.03;m;2H |
| ***CH$_3$***CO | 2.00-1.93;s;12H | 2.00-1.93;s;12H | 2.00-1.92;s;12H | 2.00-1.92;s;12H | 2.00-1.93;s;12H | 2.00-1.93;s;12H |
| Other Proton | 4.05;t. 2H; *J* 6.75, O**CH$_2$**CH$_2$CH$_2$CH; 1.74;quintet. 2H; *J* 6.75,OCH$_2$**CH$_2$**CH$_2$CH$_3$; 1.46;sextet,2H; *J*6.75, OCH$_2$CH$_2$**CH$_2$**CH$_3$; 0.95;t,3H; *J*6.75, OCH$_2$CH$_2$CH$_2$**CH$_3$** | 3.77;d;2H; *J* 6.0, O**CH$_2$**CH(CH$_3$)$_2$; 2.06-2.02;m,1H, OCH$_2$**CH**(CH$_3$)$_2$; 0.99;d;6H; *J* , OCH$_2$CH**(CH$_3$)$_2$** | 4.05;t. 2H; *J*7.0, O**CH$_2$**(CH$_2$)$_3$CH$_3$;1.76;quintet. 2H; *J* 7.0, OCH$_2$**CH$_2$**(CH$_2$)$_2$CH$_3$;1.42; quintet. 2H; *J* 7.0,O(CH$_2$)$_2$**CH$_2$**CH$_2$CH$_3$;1.37;sextet .2H;*J*7.0 ,O(CH$_2$)$_3$**CH$_2$**CH$_3$ 0.90;t. 3H; *J*7.0, O(CH$_2$)$_4$**CH$_3$** | 4.08;t. 2H; *J*6.75, O**CH$_2$**CH$_2$CH(CH$_3$)$_2$ 1.65;quartet. 2H; *J*6.75, OCH$_2$**CH$_2$**CH(CH$_3$)$_2$ 1.81;septet. 1H; *J*6.75 , OCH$_2$CH$_2$**CH**(CH$_3$)$_2$ 0.95;d;6H; *J*6.75 , OCH$_2$CH$_2$CH**(CH$_3$)$_2$** | 3.87;d;2H; *J*6.5,O**CH$_2$**CH(CH$_3$)$_2$ 2.05; septet. 1H; *J*6.5, OCH$_2$**CH**(CH$_3$)$_2$ 0.99;d;6H; *J*6.5, OCH$_2$CH**(CH$_3$)$_2$** | 4.13-4.11;m;2H, O**CH$_2$**CH$_2$CH(CH$_3$)$_2$; 1.64;quartet. 2H; *J*7.0,OCH$_2$**CH$_2$**CH(CH$_3$2 1.78;septet. 1H; *J* 7.0,OCH$_2$CH$_2$**CH**(CH$_3$)$_2$ 0.93;d;6H; *J*7.0 - OCH$_2$CH$_2$CH**(CH$_3$)$_2$** |

*Table 2. $^{13}C$ NMR spectral data of thiosemicarbazones **3a-h** [δ (ppm)]*

| **Carbon** | **6-OBu (3a)** | **6-OiBu (3b)** | **6-OPn (3c)** | **6-OiPn (3d)** | **7-OiBu (3e)** | **7-OiPn (3f)** |
|---|---|---|---|---|---|---|
| C=S | 179.0 | 178.9 | 178.9 | 179.0 | 179.0 | 179.0 |
| $CH_3$***CO*** | 170.0-169.4 | 170.0-169.3 | 170.0-169.3 | 170.0-169.3 | 170.0-169.3 | 170.0-169.3 |
| C=O (lactone) | 160.1 | 160.1 | 160.1 | 160.1 | 162 | 161.9 |
| CH=N | 137.2 | 136.7 | 137.8 | 137.0 | 137.4 | 137.4 |
| C-1’ | 81.7 | 81.7 | 81.7 | 81.7 | 81.7 | 81.6 |
| C-2’ | 71.0 | 71.0 | 71.0 | 71.0 | 70.8 | 70.8 |
| C-3’ | 72.4 | 72.4 | 72.4 | 72.4 | 72.4 | 72.3 |
| C-4’ | 67.8 | 67.8 | 67.8 | 67.8 | 67.8 | 67.8 |
| C-5’ | 72.7 | 72.7 | 72.7 | 72.7 | 72.7 | 72.7 |
| C-6’ | 61.8 | 61.8 | 61.7 | 61.7 | 61.7 | 61.7 |
| C-3” | 107.6 | 107.6 | 107.6 | 107.6 | 109.2 | 109.2 |
| C-4” | 144.0 | 143.9 | 144.4 | 144.0 | 144.4 | 144.4 |
| C-4”a | 117.6 | 117.5 | 118.1 | 119.9 | 110.3 | 110.3 |
| C-5” | 120.0 | 111.8 | 113.0 | 118.1 | 125.9 | 125.8 |
| C-6” | 155.0 | 155.1 | 147.8 | 147.8 | 113.0 | 113.0 |
| C-7” | 118.1 | 118.1 | 119.9 | 117.5 | 160.3 | 160.3 |
| C-8” | 118.1 | 119.9 | 117.5 | 118.1 | 101.6 | 101.6 |
| C-8”a | 147.0 | 147.8 | 155.0 | 155.0 | 155.5 | 155.5 |
| ***CH₃***CO | 20.5-20.3 | 20.5-20.3 | 20.5- 20.3 | 20.5- 20.3 | 20.5- 20.3 | 20.5- 20.3 |
| Other carbon in alkoxy group | 67.8<br>30.7<br>18.8<br>13.7 | 74.4<br>27.8<br>19.0 | 68.1<br>28.3<br>27.7<br>21.8<br>13.8 | 67.8<br>37.4<br>24.6<br>22.4<br>14.0 | 74.0<br>74.4<br>27.6<br>18.9 | 66.9<br>37.1<br>24.6<br>22.3<br>14.0 |

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**TỔNG HỢP VÀ NGHIÊN CỨU PHỨC CHẤT**……*(tiếp theo tr.67)*


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