

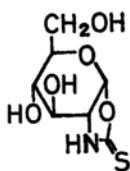
The Structure of the Oxazolidine-2-thione Derivative of D-Glucose*¹

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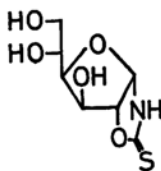
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Some reducing sugars¹⁻³⁾ have been reported to give crystalline condensation products having an oxazolidine-2-thione ring by reaction with thiocyanic acid. The structural studies on the mode of condensation between oxazolidine-2-thione ring and sugar ring in these compounds have been mainly performed for the corresponding glucose derivative (I).



A



B

Zemplen *et al.*¹⁾ gave the formula A for I, however, the formula B has generally been accepted from the following facts. Edward and Martlew⁴⁾

showed by paper chromatography the presence of l-aminoglucose and diglucosylamine in the hydrolysate of I, but no glucosamine was demonstrated which was expected from the formula A. Wickström and Wold⁵⁾ also supported the formula B by comparison of the pK_a value of I with those of simple oxazolidine-2-thiones. As for the ring size of the sugar moiety in I, Schwarz⁶⁾ concluded the presence of a furanose ring from the facts that one mole of formaldehyde was liberated by periodate oxidation and orthoformate was formed by treatment with ethyl orthoformate.

Recently Jochims *et al.*⁷⁾ reported on the synthesis and the structure of I and its homologues in which I was proved to be D-glucofurano[1', 2': 4, 5]-oxazolidine-2-thione (formula B) from the NMR data in dimethylsulfoxide- d_6 . H_1 (the proton attached to the C-1 of the sugar moiety) was found to be weakly coupled to NH and H_4 not to any hydroxyl protons. The authors have also obtained the same results by NMR studies of some derivatives of I.

It will be rationally expected that the N-acetylation of I should affect most strongly the chemical

*¹ This paper was presented at the 20th Annual Meeting of The Chemical Society of Japan, April, 1967.

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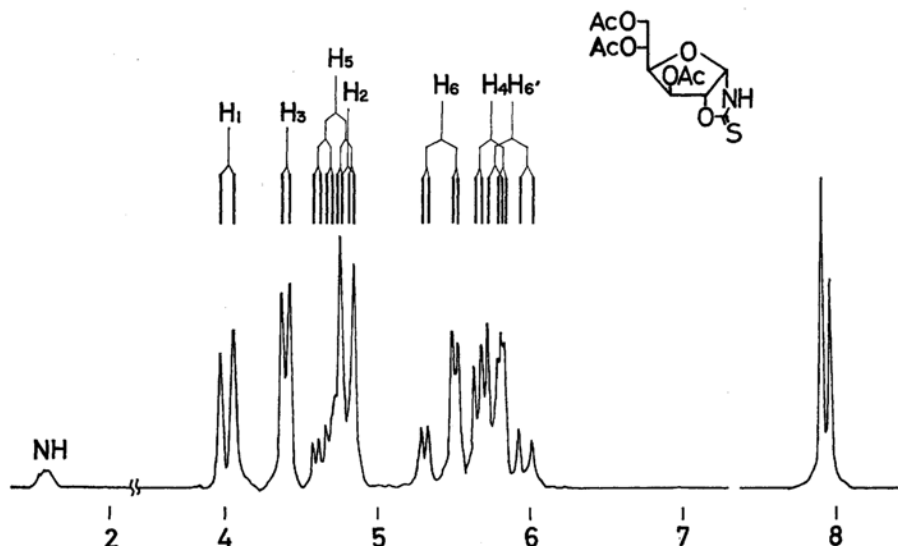
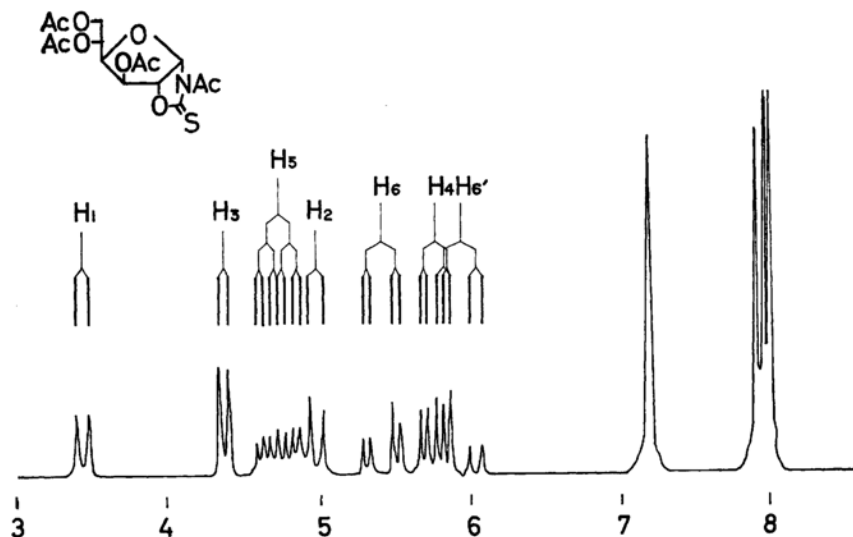
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4) J. T. Edward and E. F. Martlew, *Chem. Ind. (London)*, **1952**, 1034.

5) A. Wickström and J. K. Wold, *Acta. Chem. Scand.*, **13**, 1129 (1959).

6) J. P. C. Schwarz, *J. Chem. Soc.*, **1954**, 2644.

7) J. C. Jochims, A. Seeliger and G. Taigel, *Chem. Ber.*, **100**, 845 (1967).

Fig. 1. NMR spectrum of II in CDCl_3 at 60 Mc.Fig. 2. NMR spectrum of III in CDCl_3 at 60 Mc.

shift of the proton on the carbon attached to the nitrogen atom. In comparison of the NMR spectra of the tri-*O*-acetate (II) and tetra-*N*, *O*-acetate (III) of I¹⁰ (Figs. 1 and 2), it was observed that the chemical shift of H_1 was shifted far to the lower field, but that of H_2 was slightly to the higher field although those of other ring protons were almost identical (Table I). This fact indicates that the nitrogen is attached to C-1 of the sugar ring. The unexpected shift of H_2 will be explained by the prevention of the contribution from the en-thiol structure in the *N*-acetyl derivative.

The dihedral angles in compounds II and III calculated from observed coupling constants by

the modified Karplus equation of Abraham and coworkers⁸⁾ were 40° and 42° between H_1 and H_2 , 80° and 80° between H_2 and H_3 , and 53° and 53° between H_3 and H_4 respectively. These values imply that the furanose ring in these compounds has a "twist" conformation in which C-2 and C-3 are out of the plane containing the other ring members as shown in the case of 1,2-*O*-isopropylidene- β -glucofuranose and its derivatives.⁸⁾

The presence of the furanose ring in I was also ascertained by chemical methods. It is known

8) R. J. Abraham, L. D. Hall, L. Hough and K. A. McLauchlan, *J. Chem. Soc.*, **1962**, 3699.

TABLE 1. THE NMR SPECTRAL DATA OF D-GLUCOFURANO[1',2':4,5]OXAZOLIDINE-2-THIONE DERIVATIVES

Chemical shifts (τ values)

Compound	H ₁	H ₂	H ₃	H ₄	H ₅	H ₆	H _{6'}	OH
II	4.03 d	4.82 d	4.41 d	5.75 q	4.73m	5.42 q	5.89 q	—
III	3.50 d	5.02 d	4.43 d	5.81 q	4.78m	5.46 q	5.98 q	—
IV	4.12 d	4.92 d	5.80 d	6.37 q	5.68m	6.10 q	6.18 q	4.28 d
V	4.00 d	4.75 d	5.18 d	4.84 t
VI	4.05 d	4.90 d	5.65 b	6.12 q	5.60m	5.90 q	6.05 q	4.20 d

Compound	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	$J_{H,OH}$
II	5.1	<0.5	3.0	9.0	2.6	5.4	12.3	—
III	4.8	<0.5	3.0	9.0	2.7	5.7	12.3	—
IV	5.4	<0.5	2.5	6.0	6.0	6.0	6.5	5.0
V	6.0	<0.5	2.0	ca. 5.0
VI	5.4	<0.5	2.5	5.0	6.0	6.0	6.0	ca. 5.0

d: doublet, t: triplet, q: quartet, m: multiplet, b: broad.

— These peaks were not resolved.

that the glucopyranose ring can not be isopropylidened,⁹⁾ however, I gave a mono-isopropylidene derivative (IV), whose NMR spectrum measured in dimethyl sulfoxide- d_6 showed the hydroxyl signal at 4.28 (τ value) in doublet, indicating the presence of the secondary hydroxyl group. Therefore, IV should be 5', 6'-O-isopropylidene-D-glucufurano[1', 2':4, 5]oxazolidine-2-thione, but not the corresponding 3', 5'-O-isopropylidene derivative.

When I was benzylidenated with benzaldehyde and zinc chloride, two isomers which showed mp 232—233°C (V) and 186—188°C (VI) respectively were obtained. In the NMR spectra of these compounds also measured in dimethyl sulfoxide- d_6 , each hydroxyl proton appears at 4.83 in triplet and at 4.20 in doublet, indicating the presence of a primary and a secondary hydroxyl group respectively. So V and VI were proved to be 3', 5'-O-benzylidene- and 5', 6'-O-benzylidene-D-glucufurano[1', 2':4, 5]oxazolidine-2-thione respectively.

Experimental

NMR spectra were measured on JNM-3H-60 spectrometer at 60 Mc in deuteriochloroform for II and III, and in dimethyl sulfoxide- d_6 for IV, V and VI respectively. Tetramethylsilane was used as an internal reference in each case.

5', 6'-O-Isopropylidene-D-glucufurano[1', 2':4, 5]-oxazolidine-2-thione (IV). To a suspension of I (2.4 g) in dry acetone (60 ml) concentrated sulfuric

acid (0.8 ml) was added dropwise with stirring in an ice-water bath, and the stirring was continued for a few hours. The reaction mixture was poured into ice-water containing sodium bicarbonate (5 g), and extracted with methylene chloride (100 ml). Methylene chloride layer was washed with water and dried over anhydrous sodium sulfate. Evaporation of methylene chloride gave white residue, which was recrystallized from ethanol, mp 220—221°C, $[\alpha]_D^{25} +33.0^\circ$ (c 1.8, pyridine), yield 1.7 g.

Found: C, 46.05; H, 5.74; N, 5.48%. Calcd for $C_{10}H_{15}O_5NS$: C, 45.97; H, 5.79; N, 5.36%.

3', 5'-O-Benzylidene- and 5', 6'-O-Benzylidene-D-glucufurano[1', 2':4, 5]oxazolidine-2-thione (V and VI). A suspension of I (2.5 g) and anhydrous zinc chloride (3.0 g) in benzaldehyde (20 ml) was shaken for 1 hr to give a clear solution. The reaction mixture was poured into ice-water, stirred with petroleum ether, and the petroleum ether layer was decanted. It was repeated twice more to give a mixture of crystals and hard sirup. When this mixture was dissolved in hot ethanol (ca. 30 ml), a small amount of crystals was remained undissolved, which was filtered and recrystallized from a little larger amount of ethanol to give V as white crystals, mp 232—233°C, $[\alpha]_D^{25} +66.5^\circ$ (c 1.0, pyridine), yield 0.2 g.

Found: C, 54.27; H, 4.84; N, 4.57%. Calcd for $C_{14}H_{15}O_5NS$: C, 54.36; H, 4.89; N, 4.53%.

From the filtrate, another crystals were separated and recrystallized from ethanol to give VI, mp 186—188°C, $[\alpha]_D^{25} +68.1^\circ$ (c 1.0, pyridine), yield 0.6 g.

Found: C, 54.43; H, 4.92; N, 4.68%. Calcd for $C_{14}H_{15}O_5NS$: C, 54.36; H, 4.89; N, 4.53%.

The authors thank Mr. T. Tanaka of Science University of Tokyo for the oxazolidine-2-thione derivative of D-glucose.

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