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Determination of the Position of the Xanthate Groups in Glucopyranosides by Means of Nuclear Magnetic Resonance

Part 1. Position of the Xanthate Group in Mono-S-methyl Xanthates of Methyl D-Glucopyranosides

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NMR spectra have been investigated for a number of carbohydrate *O*-[(alkylthio)thiocarbonyl] derivatives. Conversion of a hydroxyl group into an *O*-[(alkylthio)thiocarbonyl] group gives rise to a shift to lower field of hydrogens on the same carbon atom as that of the *O*-[(alkylthio)thiocarbonyl] groups. This has been used in the unequivocal determination of the site of substitution in the crystalline anomeric methyl *O*-[(methylthio)thiocarbonyl]-D-glucopyranosides previously described. Contrary to the previous tentative assignment of the substituent to C-2, the results show the xanthates to be methyl 6-*O*-[(methylthio)thiocarbonyl]-D-glucopyranosides.

Despite numerous attempts, with various techniques, the pattern of substitution on the C-2, C-3, and C-6 hydroxyls in cellulose on xanthogenation, and the change in this distribution in the various stages during the viscose process is not known with certainty.[1–7] In most investigations all that has been achieved is a distinction between the degree of substitution of the hydroxyl group at C-6 on the one hand, as compared to that at the two secondary hydroxyls on the other.[1,2,4,7]

The NMR spectra of the *S*-methyl xanthates of ethanol and propan-2-ol, *O*-[(methylthio)thiocarbonyl]ethanol and 2-*O*-[(methylthio)thiocarbonyl]-propanol, were compared to those given by the parent alcohols at 60 Mcps. The solvent was carbon tetrachloride. This showed that hydrogens on the same carbon atom as that of the hydroxyl group shifted downfield on xantho-

genation. The shift from the resonance position of these hydrogens in the parent alcohols on xanthogenation was 1.0 ppm for the primary and 1.9 ppm for the secondary alcohol. A ready distinction between xanthate groups on primary and on secondary carbons could thus be made. The magnitude of the change in chemical shift, moreover, indicated a possible method for locating the xanthate groups in a partially xanthogenated glucopyranoside and for following the change in the pattern of substitution during a simulated viscose process on the glucoside. Methyl 4-*O*-methyl-β-D-glucopyranoside would appear a suitable model substance.

The findings for acyclic alcohols were confirmed by examination of the NMR spectra of 1,2:3,5-di-*O*-methylene-α-D-glucofuranoside (I), 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranoside (III), and the mono-*O*-[(methylthio)thiocarbonyl] derivatives, II and IV, respectively,[8] in deuterochloroform at 100 Mcps, (Figs. 1 and 2).

In the spectrum given by I, the doublet at 6.01 ppm (J = 3.5 cps) is due to H-1 and that at 4.49 ppm (J = 3.5 cps) to H-2. The doublet at 4.30 ppm (J = 2.5 cps) is then due to H-3 since this is the only remaining hydrogen which can couple with one proton only (H-4). The signals at 4.8 — 5.2 (4 H) are a combination of two AB systems and are given by the two methylene acetal groups. The remaining hydrogens (H-4, H-5, H-6, and H′-6) appear between 3.6 and 4.2 ppm. That H-6 and H′-6 give signals at 3.8—4.0 ppm was shown by the addition of trifluoroacetic acid which caused the OH triplet to collapse into a singlet.

The xanthate of I, (II), gives a spectrum in which the H-6 and H′-6 signals have shifted about 1 ppm downfield and appear together with the methylene protons at about 4.9 ppm. Of the four protons between 3.6 and 4.2 ppm in

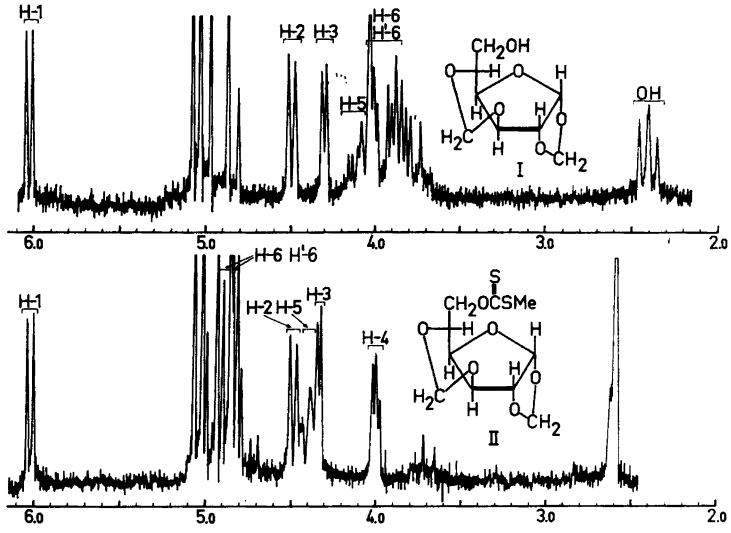

Fig. 1. NMR spctra of 1,2:3,5-di-*O*-methylene-α-D-glucofuranose (I) and its 6-*S*-methyl xanthate (II).

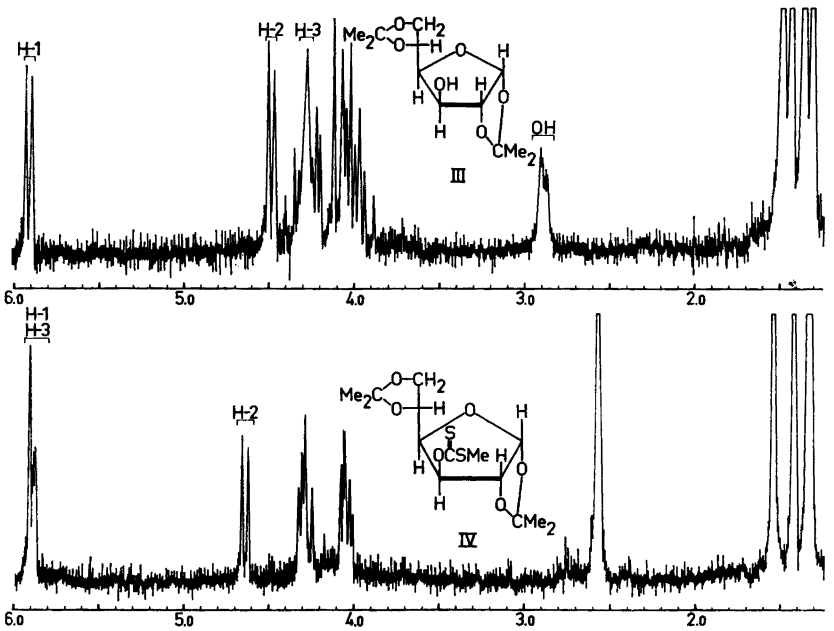

Fig. 2. NMR spectra of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (III) and its 3-*S*-methyl xanthate (IV).

the spectrum given by I only one remains, at 4.01 ppm. This is H-4 while H-5 has shifted downfield to 4.42 ppm. Spin decoupling of H-4 and H-5 confirmed that the signals given by these were at 4.01 and 4.42 ppm, respectively. The remaining hydrogens (H-1, H-2, H-3, and the four methylene protons) give the same spectrum as for I. The *S*-methyl protons appear at 2.59 ppm.

The spectra given by diisopropylideneglucose (III) and the 3-*S*-methylxanthate (IV) are shown in Fig. 2. In the spectrum given by III the doublet at 5.92 ppm (J = 3.5 cps) is due to the H-1 proton and that at 4.50 ppm (J = 3.5 cps) to H-2. The signal at 4.28 ppm is due to H-3, as shown by spin decoupling of the —OH signal at 2.89 ppm. The signals at 1.2 — 1.6 ppm are due to the acetal $-CH_3$ groups. The remaining signals at 3.8 — 4.2 ppm (4 H) are due to the remaining four protons.

The *S*-methyl xanthate (IV) of III gives a spectrum in which the signal at 5.92 (2 H) is due to H-1 and H-3. In the xanthate the H-3 signal has thus moved 1.65 ppm to lower field than in the alcohol. The doublet at 4.61 ppm (J = 3.5 cps) is due to H-2 as shown by spin decoupling at 5.92 ppm, whereby the H-2 doublet collapsed into a singlet. The signal at 2.57 ppm (3 H) is due to the *S*-methyl group.

In order to establish whether this technique could be used in the assignment of the position of xanthate groups in pyranoid rings, attention was turned to the crystalline, anomeric methyl *O*-[(methylthio)thiocarbonyl]-D

glucopyranosides previously prepared by Lieser *et al.*[9,10] The site of the xanthate groups in these derivatives was tentatively suggested to be at C-2. Willard and Pacsu [5] subsequently prepared the barium xanthate of methyl α-D-glucopyranoside as described by Lieser and Hackl [9] and converted this into the mono-*O*-[(benzylthio)thiocarbonyl] derivative.[5] This was converted into methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside by an unambigous route,[5] showing that the xanthate group was at C-6 and refuting the previous assignment of the xanthate group to C-2. In order to confirm these findings, and also to examine the position of substitution of the xanthate group in Lieser and Leckzyck's [10] derivative of methyl β-D-glucopyranoside, NMR spectra were investigated for the two anomeric methyl mono-*O*-[(methylthio)thiocarbonyl]-D-glucopyranosides, for their tri-*O*-acetyl derivatives, for methyl 6-*O*-[(benzylthio)thiocarbonyl]-α-D-glucopyranoside and its triacetate. The anomeric methyl D-glucopyranosides and the corresponding 2,3,4-tri-*O*-acetyl derivatives were used as reference materials. The solvent for the glucosides and xanthates was hexadeuterodimethylsulphoxide and for the acetylated derivatives deuterochloroform. The spectra were measured at 100 Mcps.

Comparison of the spectrum given by methyl α-D-glucopyranoside with those of the *S*-methyl xanthate and 6-*S*-benzylxanthate revealed that in the latter two, two protons had shifted from about 3.5 ppm to about 4.7 ppm, *i.e.* near the H-1 doublet which appeared at 4.54 ppm. Furthermore, the expected AB-type spectrum with $J_{AB} = 11.0$ cps with additional fine structure due to coupling with H-5 was clearly observed for both xanthates at about 4.7 ppm. This signal is therefore due to H-6 and H'-6. This fact, and the great similarity of the spectra given by the two xanthates in this respect leaves little doubt that the xanthate group in the *S*-methyl xanthate is at C-6. In these spectra the $-SCH_3$ protons give a singlet at 2.54 ppm and the $-SCH_2-$ protons in the benzyl xanthate at 4.39 ppm. Further confirmation that the xanthate group was located at C-6 was obtained by identification of the H-2 signal through spin decoupling of H-1; the H-2 signal had not shifted in the xanthates.

In the spectrum given by methyl β-D-glucopyranoside, H-1 gave a doublet at 4.05 ppm. The corresponding *S*-methyl xanthate gave a spectrum in which two hydrogens had shifted from about 3.1 ppm to 4.70 ppm. The latter signal exhibited the characteristic AB part of an ABX spectrum expected for H-6 and H'-6 coupling with H-5. The xanthate group is therefore located at C-6. The $-SCH_3$ protons appeared at 2.56 ppm. Confirmation that the xanthate group was not located at C-2 was obtained by spin decoupling of H-1; the H-2 signal for both compounds was thereby located at about 3.1 ppm.

These findings were confirmed by examination of the NMR spectra of the fully acetylated derivatives of the two anomeric *S*-methyl xanthates [10] and comparison with the spectra given by the two methyl 2,3,4-tri-*O*-acetyl-D-glucopyranosides. The spectra of these compounds, and also that of methyl 2,3,4-tri-*O*-acetyl-6-*O*-[(benzylthio)thiocarbonyl]-α-D-glucopyranoside [5] (VI) are given in Figs. 3 and 4. In the spectrum of methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside (V), the signals at 2.04 ppm (9 H) are due to the three equatorial acetyl groups. The signal due to —OH and the H-6 and H'-6 protons were located by the addition of trifluoroacetic acid. The H-5 signal then is at 3.78

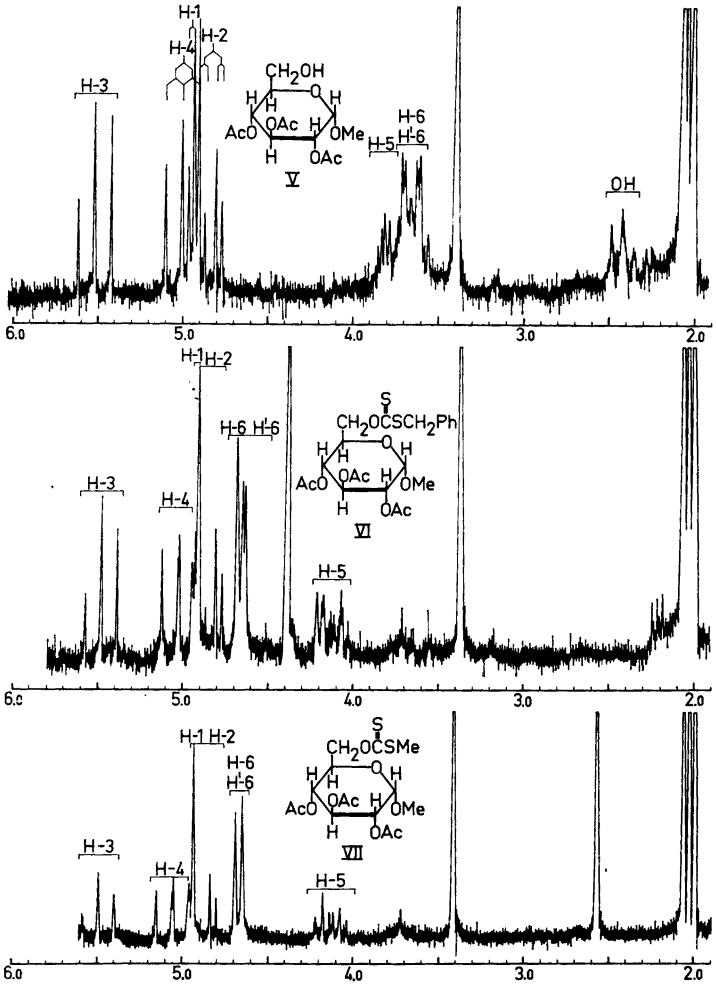

Fig. 3. NMR spectra of methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside (V), its 6-*S*-benzyl xanthate (VI) and its mono-*S*-methyl xanthate (VII).

ppm (1 H). The other signals were identified by means of "tickling" [11] experiments.

In the spectrum of the 6-*S*-benzyl xanthate of V, (VI) the new singlet at 4.39 ppm is due to the $-SCH_2-$ protons, the signal at 4.12 ppm to H-5. The H-6 and H'-6 signals have shifted to 4.6 — 4.8 ppm (2 H). The resonance position for these two protons as well as for H-4 was confirmed by spin decoupling of H-5.

Lieser and Leckzyck's methyl tri-*O*-acetyl-*O*-[(methylthio)thiocarbonyl]-α-D-glucopyranoside,[10] VII, gives a spectrum which with the exception of the

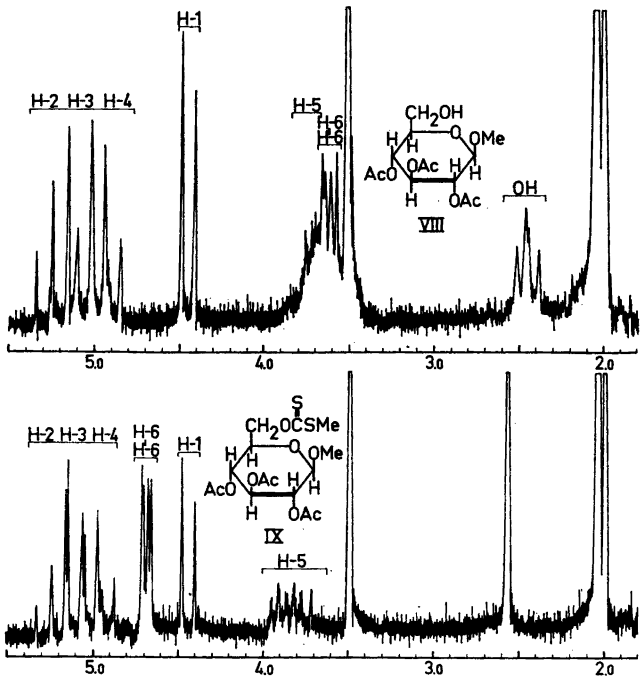

Fig. 4. NMR spectra of methyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranoside (VIII) and its mono-*S*-methyl xanthate (IX).

—SCH_3 signal at 2.56 ppm bears strong resemblance to that of VI. As in the latter, H-6 and H′-6 give signals at 4.69 ppm (2 H), this is confirmed by spin decoupling of H-5 at 4.15 ppm. Spin decoupling of H-6 and H′-6 conversely caused collapse of the H-5 signal. The xanthate group in VII is thus located at C-6.

The spectrum for methyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranoside, VIII, is shown in Fig. 4. The signals for H-6 and H′-6 were identified by spin decoupling the —OH signal and that for H-2 by decoupling at H-1. In the spectrum given by the *S*-methyl xanthate (IX) of VIII (Fig. 4) the H-6 and H′-6 signals have shifted downfield and now appear at 4.70 ppm. The assignments of the various peaks were as before confirmed by spin decoupling of H-1, H-5, H-6, and H′-6.

These findings thus show that the xanthate group in all the xanthates is located at C-6, and that Lieser *et al.*[10,11] have prepared the two anomeric methyl 6-*O*-[(methylthio)thiocarbonyl]-D-glucopyranosides and not the corresponding 2-substituted isomers.

The melting point (91—92°) for methyl 6-*O*-[(methylthio)thiocarbonyl]-α-D-glucopyranoside prepared by us is not in agreement with that previously reported (67—68°).[10,11] Repeated preparations of this compound from the silver salt as previously described and also by shaking the crude barium xan-

Table 1. Melting points and optical rotations for some xanthates. Literature values are given in brackets.

Compound	M.p. °C	$[\alpha]_D$ degrees	Rotation solvent, conc.
1,2:3,5-Di-*O*-methylene-6-*O*-[(methylthio)thiocarbonyl]-α-D-glucofuranose [8]	100—102 (97—99)	+ 25 (+ 27)	$CHCl_3$ 0.4 ($CHCl_3$)
3-*O*-[(Methylthio)thiocarbonyl]-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose [8]	59—60.5 (58—60)	—34 (—16)	$CHCl_3$ 1.0 ($CHCl_3$)
Methyl 6-*O*-[(benzylthio)thiocarbonyl]-α-D-glucopyranoside [5]	92—93 (89—92)	+ 67 (+ 80)	$CHCl_3$ 0.9 ($CHCl_3$)
2,3,4-tri-*O*-acetyl- [5]	109—109.5 (105—107)	+ 107 (+ 106)	$CHCl_3$ 1.5 ($CHCl_3$)
Methyl 6-*O*-[(methylthio)thiocarbonyl]-α-D-glucopyranoside [9,10]*	91—92 (67—68)	+ 130 + 126 (+ 123)	Me_2CO 0.8 EtOAc 1.0 (EtOAc)
2,3,4-tri-*O*-acetyl- [10]	73—75 (75—76)	+ 126 + 124 (+ 126)	$CHCl_3$ 1.2 EtOH 1.1 (EtOH)
Methyl 6-*O*-[(methylthio)thiocarbonyl]-β-D-glucopyranoside [10]	149—158 dec. (158—159)	—13 —8 (—5)	Me_2CO 1.2 EtOH 2.0 (EtOH)
2,3,4-tri-*O*-acetyl [10]	112—113.5 (112—113)	+ 2 —	$CHCl_3$ 1.3 —

* Found: C 38.2; H 5.7; S 22.7. Calc. for $C_9H_{16}O_6S_2$: C 38.0; H 5.7; S 22.6.

thate with iodomethane and isolating the product, followed by repeated crystallisation afforded crystals with m.p. 91—92° only. The optical rotation, however, is in agreement with that previously reported, as are the physical constants for the tri-*O*-acetyl derivative.

EXPERIMENTAL

All melting points are corrected. Optical rotations were measured at room temperature (20—22°).

Materials. All materials were prepared as previously described and recrystallised to analytical purity. The physical constants of the xanthates are shown in Table 1.

Spectroscopy. NMR spectra were obtained on a Varian A-60 and on a Varian HA-100 spectrometer. The spin decoupling experiments were carried out using a Hawlers Packard Model 202 C Audio Oscillator. Tetramethylsilane was used as an internal reference throughout.

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