NMR Spectra of Some Glycoside Acetates in the Presence of Tris(dipivaloylmethanato)europium

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NMR spectra in the presence of tris(dipivaloylmethanato)europium of three acetylated glucosides, methyl 2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranoside, methyl 2,3-di-*O*-acetyl-4,6-*O*-benzylidene-*α*-D-glucopyranoside and methyl 4,6-di-*O*-acetyl-2,3-di-*O*-benzyl-*β*-D-glucopyranoside have been recorded. Complex formation with the acetoxy carbonyl groups occurs. Although the glucosides are polyfunctional with respect to complex formation with europium, preferential complex formation is observed which gives rise to significant simplifications of the NMR spectra.

Numerous reports on the use of lanthanide shift reagents in NMR spectroscopy have appeared in the last two years. The changes in chemical shifts occur by complexing of the lanthanide with free electron pairs and appear to be due to through-space effects (pseudocontant shifts). The magnitude of the change in chemical shifts is described by the McConnell and Robertson pseudocontact shift equation.[1]* A few reports on the use of shift reagents in carbohydrate chemistry have appeared.[2-7] These have mostly dealt with NMR spectra on substances which have been essentially monofunctional with respect to complexing with one molar equivalent of the lanthanide. Only one report deals with the use of lanthanides in NMR spectroscopy of carbohydrates containing several identical groups capable of forming complexes with lanthanides.[4] In the present communication we report three examples of lanthanide NMR on glycoside polyacetates. The results indicate that the complexing constants of the lanthanide with various acetoxy groups are sufficiently different to produce spectra with much better resolution than those obtained in the same solvent in the absence of lanthanides.

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* This is most conveniently expressed in the form $\varDelta\delta = k(3\cos^2\theta - 1)r^{-3}$.
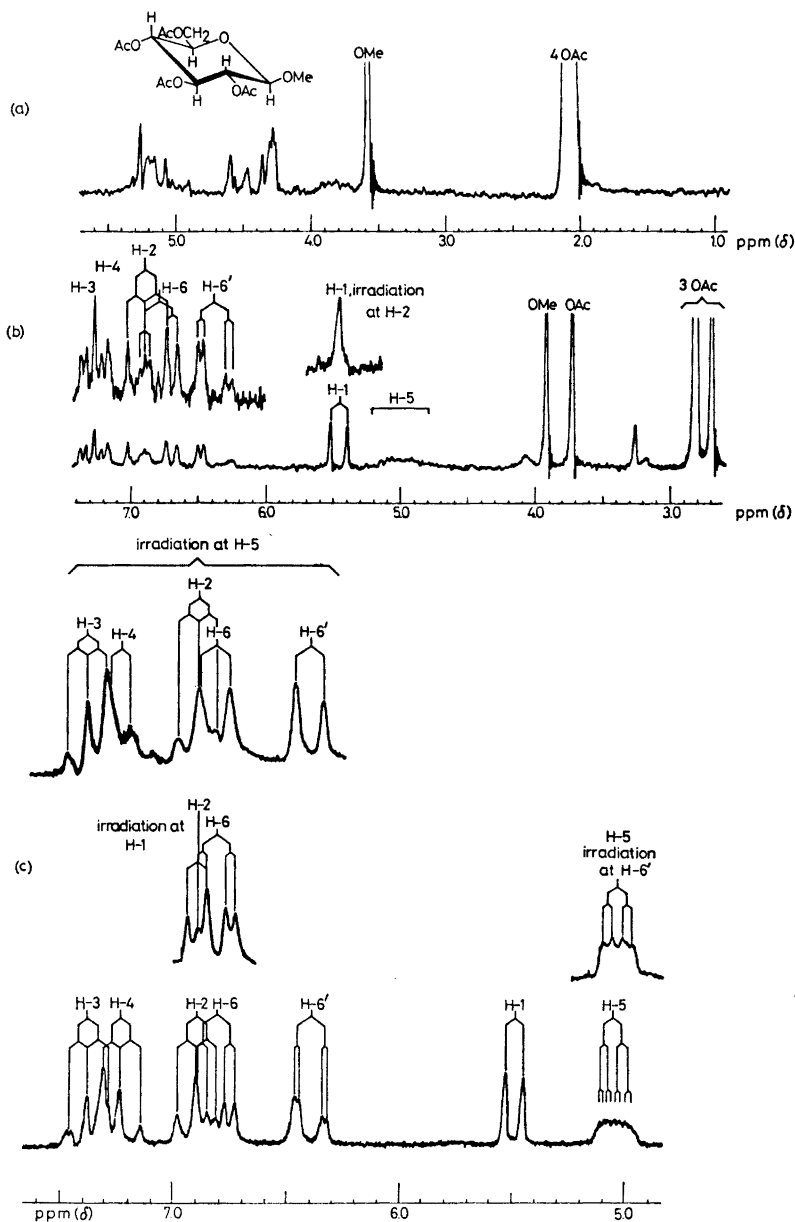
Fig. 1. NMR spectra of methyl 2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside. (a) A 60 MHz spectrum. (b) A 60 MHz spectrum in the presence of 0.80 mol (DPM)₃ Eu per mol sugar, decoupling irradiation at the H-2 signal. (c) A 100 MHz spectrum in the presence of 0.80 mol (DPM)₃Eu per mol sugar, decoupling experiments.

RESULTS

A 60 MHz spectrum of methyl 2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside in deuteriochloroform is shown in Fig. 1a. A complex second order spectrum is observed for the ring protons. A 60 MHz spectrum of this substance in the same solvent but with 0.80 molar equiv. of tris(dipivaloylmethanato)europium added is shown in Fig. 1b. This spectrum, as well as the lanthanide spectra discussed below, is optimized in the sense that the shift reagent was added in small portions; the proportion sugar:lanthanide yielding the best resolution is reported in each of the three examples. In 1b as compared to 1a, one acetoxy signal has moved to much lower field than the other three, indicating that in the equilibrium mixture the lanthanide preferentially forms a complex with one acetoxy group. The various signals were identified as follows. A distinction between the methoxy signal at 3.92 and the acetoxy signal at 3.73 ppm could be made by comparing the gradual change in the NMR spectra produced by successive additions of the complexing agent (see Fig. 4). The signals due to the ring protons were identified by spin decoupling experiments at 60 MHz
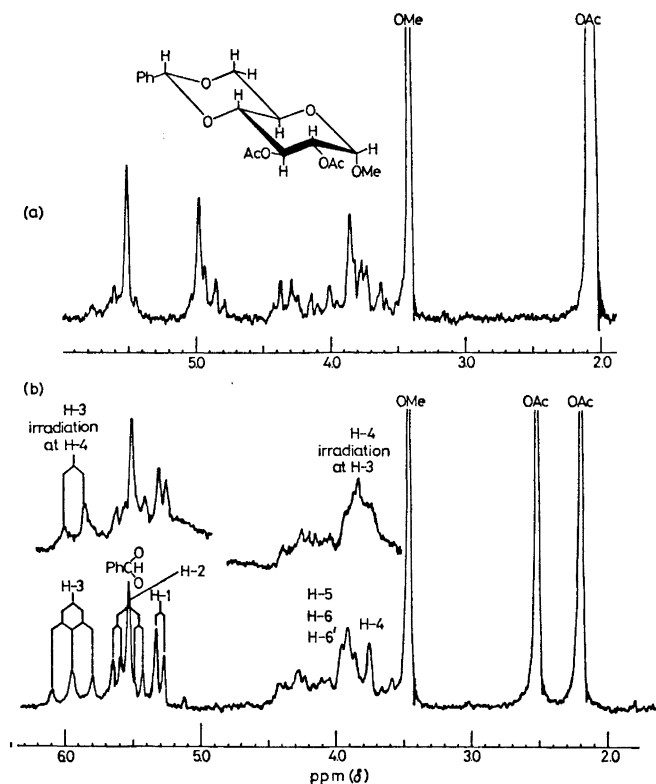

Fig. 2. NMR spectra of methyl 2,3-di-O-acetyl-4,6-O-benzylidene-α-D-glucopyranoside. (a) A 60 MHz spectrum. (b) A 60 MHz spectrum in the presence of 0.18 mol (DPM)$_3$Eu per mol sugar, decoupling experiments.

(1b) and at 100 MHz (1c) as shown in Fig. 1. Irradiation at various frequences downfield from the H-1 signal caused this to collapse into a singlet when irradiating at δ 6.90 ppm. The signal at 5.46 ppm ($J_{1,2} = 8$ Hz) therefore is due to H-1. Irradiation at H-1 conversely caused collapse of the H-2 triplet (δ 6.90 ppm $J_{1,2} = J_{2,3} = 8$ Hz) into the expected doublet. The high-field octet at 5.05 ppm is due to H-5 ($J_{4,5} = 9$ Hz, $J_{5,6} = 5$ Hz, $J_{5,6'} = 2.5$ Hz), by virtue of its coupling to three other protons as demonstrated by decoupling irradiation at its centre. This caused collapse of the H-6 signal (δ 6.82 ppm, $J_{5,6} = 5$ Hz, $J_{6,6} = 13$ Hz) and H-6' signal (δ 6.40 ppm, $J_{5,6'} = 2.5$ Hz, $J_{6,6'} = 13$ Hz) into the expected doublets and the simultaneous collapse of the H-4 signal (δ 7.24 ppm, $J_{3,4} = J_{4,5} = 8$ Hz) into the expected doublet. The remaining signal at 7.40 ppm therefore is due to H-3 ($J_{2,3} = J_{3,4} = 8$ Hz). The integrals were in accordance with the various assignments.

A partial 60 MHz spectrum of methyl 2,3-di-O-acetyl-4,6-O-benzylidene-α-D-glucopyranoside is shown in Fig. 2a. It is difficult, on the basis of the observed signals, to make any definite assignments of the resonance positions of the ring protons. Addition of the shift reagent, 0.18 mol per mol sugar, produced a mixture giving the NMR spectrum depicted in Fig. 2b. Although the 3.5 − 4.5 ppm region of the latter spectrum still is second-order, a clear resolution of the H-1, H-2 and H-3 signals is observed at lower field. The assignments are based on 60 MHz spin decoupling experiments as shown in 2b. Irradiation at the center of the presumed H-3 triplet revealed the position of H-4. Decoupling irradiation of the latter caused the H-3 triplet to collapse into a doublet. The following spectral assignments may therefore be made: H-1 δ 5.29 ppm., $J_{1,2} = 3.5$ Hz; H-2 δ 5.50 ppm, $J_{1,2} = 3.5$ Hz, $J_{2,3} = 9$ Hz; H-3 δ 5.93 ppm, $J_{2,3} = J_{3,4} = 9$ Hz.

A partial 60 MHz spectrum of methyl 4,6-di-O-acetyl-2,3-di-O-benzyl-β-D-glucopyranoside is shown in Fig. 3. Apart from signals given by acetoxy, benzylidene, and methoxy hydrogens, definite assignments of ring proton signals are most difficult. A substantial simplification in the spectrum results from the addition of 0.55 mol shift reagent per mol sugar (3b and 3c). The various assignments are based on the spin decoupling experiments outlined in the figure. Decoupling irradiation of the presumed H-2 signal (3b) caused the H-1 doublet to collapse into a singlet. Irradiation at H-1 conversely simplified the H-2 triplet, partly obscured in 3c by the methoxyl signal, into the expected doublet. Decoupling irradiation at the centre of the presumed H-5 octet caused the H-4 triplet and the H-6, H-6' quartets to collapse into the expected doublets. The following assignments can therefore be made: H-1 δ 4.59 ppm, $J_{1,2} = 7.5$ Hz; H-2 δ 3.76 ppm, $J_{1,2} = J_{2,3} = 7.5$ Hz; H-3 δ 3.91 ppm, $J_{2,3} = 7.5$ Hz, $J_{3,4} = 8.5$ Hz; H-4 δ 5.82 ppm, $J_{3,4} = J_{4,5} = 8.5$ Hz; H-5 δ 4.10 ppm, $J_{4,5} = 8.5$ Hz, $J_{5,6} = 5$ Hz, $J_{5,6'} = 2.5$ Hz; H-6 δ 5.66 ppm, $J_{5,6} = 5$ Hz, $J_{6,6'} = 12.5$ Hz; H-6' δ 5.32 ppm, $J_{5,6'} = 2.5$ Hz, $J_{6,6'} = 12.5$ Hz.

Plots of the various chemical shifts at various molar levels of complexing agent added for the three acetylated glucosides are shown in Figs. 4 − 6. The shaded areas represent uncertainty in the measurements of chemical shifts due to overlapping signals and second-order effects. The following qualitative observations may be made: In the lanthanide NMR spectra of methyl 2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside one acetoxy group forms a much stronger
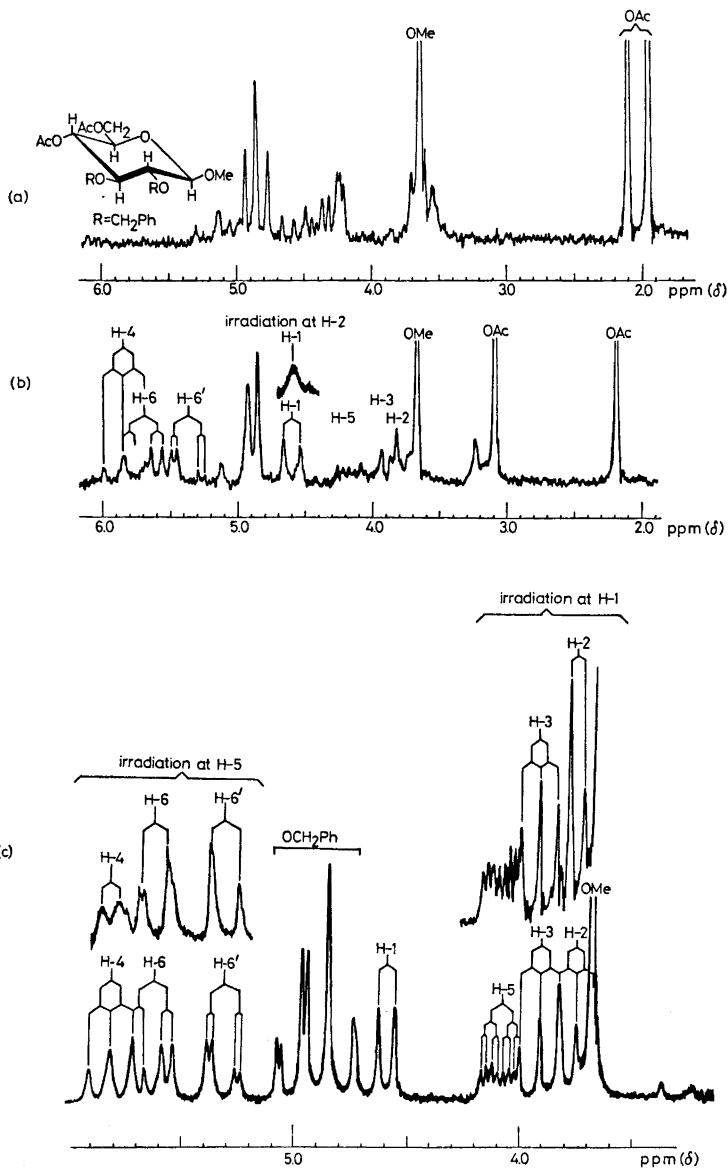
Fig. 3. NMR spectra of methyl 4,6-di-*O*-acetyl-2,3-di-*O*-benzyl-*β*-D-glucopyranoside. (a) A 60 MHz spectrum. (b) A 60 MHz spectrum in the presence of 0.55 mol (DPM)$_3$Eu per mol sugar, decoupling irradiation at the H-2 signal. (c) A 100 MHz spectrum in the presence of 0.55 mol (DPM)$_3$Eu per mol sugar, decoupling experiments.

complex than do the other three. The $\Delta\delta$ values for the ring protons are highest for the primary (H-6, H-6') protons. The overall changes in chemical
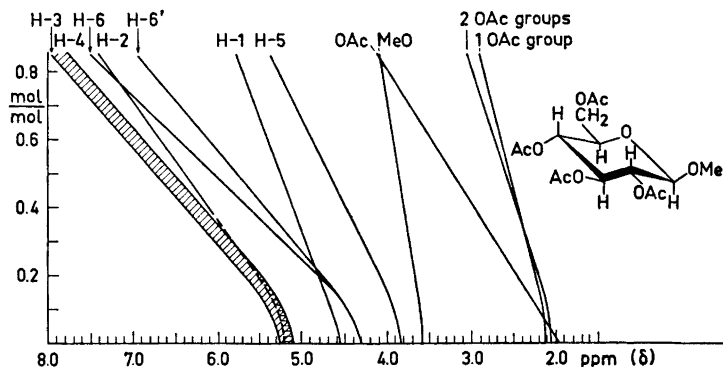
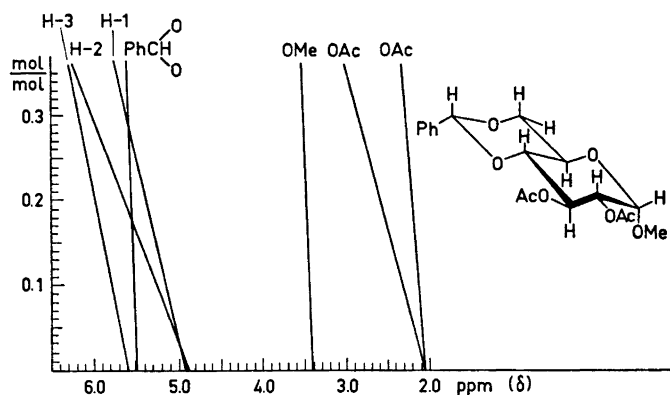*Fig. 4.* Plots of chemical shifts against mol (DPM)₃Eu per mol sugar for methyl 2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside.

Fig. 5. Plots of chemical shifts against mol (DPM)₃Eu per mol sugar for methyl 2,3-di-O-acetyl-4,6-O-benzylidene-α-D-glucopyranoside.

shifts for the various protons seem compatible with predominant complex formation with the carbonyl oxygen in the 6-position on the pyranose rings, the acetoxy group having a conformation with the carbonyl oxygen at maximum distance and pointing away from the pyranose ring and with the europium atom at least 2.5 Å distant from the oxygen.[8] A similar predominant complex would seem to account for the results depicted in Fig. 6. for methyl 4,6-di-O-acetyl-2,3-di-O-benzyl-β-D-glucopyranoside. It would seem that other conformations of the complex, *e.g.* with the europium situated above or beneath the ring, would give at least some values of θ in the McConnell-Robertson equation between 55° and 125° which would give rise to upfield changes in chemical shifts for the protons involved. A similar argument may be applied to the complex formation of the lanthanide with methyl 2,3-di-O-acetyl-4,6-O-benzylidene-α-D-glucopyranoside (Fig. 5). None of the $\varDelta\delta$ values observed are upfield. H-2 exhibits the largest change in δ with added complexing
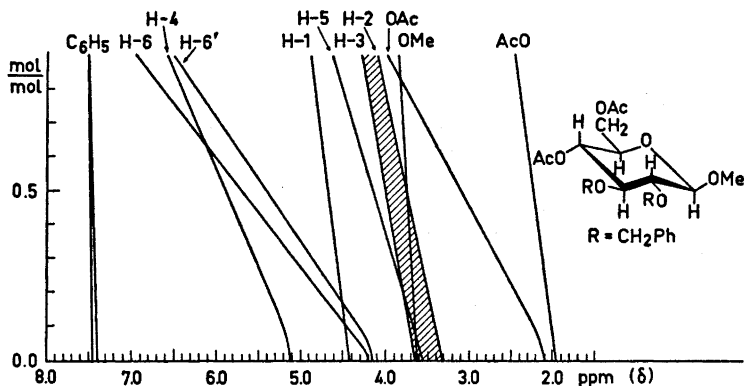
Fig. 6. Plots of chemical shifts against mol (DPM)$_3$Eu per mol sugar for methyl 4,6-di-
O-acetyl-2,3-di-O-benzyl-β-D-glucopyranoside.

agent. It may therefore be presumed that the strongest complex formation
occurs at the 2-position and that, again, the carbonyl group points away
from the pyranose ring, with the oxygen-europium distance being at least
2.5 Å. Attempts at detailed calculation of the exact average location of the
europium in the equilibrium mixtures are in progress.

DISCUSSION

The results indicate that the degree of complexing of various acetoxy
groups in polyacetylated pyranosides towards tris(dipivaloylmethanato)eu-
ropium may be sufficiently different to give preferential complex formation
and thereby significant simplifications in the NMR spectra upon the addition
of the shift reagent. The molar amount of reagent required for optimal results
depends on the substance. The fact that all shift changes are downfield in-
dicates that the europium atom is at a considerable distance from the pyranose
ring, making θ in the McConnell-Robertson equation [1] smaller than 55°. If,
for some protons, this angle were 125 – 180°, a situation which is possible provided
the europium atom is close to the pyranose ring, some of the angles to other
protons would have to come between 55 and 125°, necessitating the correspond-
ing upfield changes in some chemical shifts. Plots of chemical shifts *versus*
mol/mol lanthanide added may be useful in identifying the shifts for protons
in the absence of lanthanide. The various coupling constants are essentially
constant at various levels of lanthanide added, indicating that no significant
changes in the conformation of the pyranose ring take place upon complexing
with the lanthanide, at least not as long as the lanthanide is bound to an
equatorial substituent. The determination of the exact average location of
the europium in the various equilibrium mixtures will have to await detailed
calculations.

EXPERIMENTAL

Spectrometry. The NMR spectra were obtained on Varian A-60A and HA-100 spectrometers. Spin decoupling experiments were carried out using a V-6058A unit and a Hewlett Packard Model 202 C Audio Oscillator, respectively. The solvent used was deuteriochloroform. Tetramethylsilane was used as internal reference and chemical shifts are given in ppm downfield from this reference. The δ values were determined on a first order basis and measured from the arithmetic mid-point of the peaks.

Substances. Methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside,[9] methyl 4,6-di-*O*-acetyl-2,3-di-*O*-benzyl-β-D-glucopyranoside,[10] and methyl 2,3-di-*O*-acetyl-4,6-*O*-benzylidene-α-D-glucopyranoside [11] were made as described in the literature.

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