Carbohydrate Research, 39 (1975) 136–140

Note

The application of lanthanide shift reagents in the p.m.r. spectroscopy of permethyl ethers of D-galactose

ELNER B. RATHBONE* AND ALISTAIR M. STEPHEN

C.S.I.R. Carbohydrate Research Unit, Department of Organic Chemistry,
University of Cape Town (South Africa)

(Received April 29th, 1974; accepted for publication, June 4th, 1974)

The pattern of MeO signals in the p.m.r. spectra of methyl 2,3,4,6-tetra-*O*-methyl-β- (**1**) and -α-D-galactopyranoside (**2**) can be used to identify methyl ethers of D-galactose[1]. For solutions in benzene (or deuteriobenzene), five distinct methoxyl signals for both **1** and **2** were found[1,2]. In an attempt to improve the separation of these signals, the effect of europium(III) and praseodymium(III) tris-(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione) [$Eu(fod)_3$ and $Pr(fod)_3$, respectively] was investigated since these reagents can produce large lanthanide-induced shifts with relatively little line-broadening[3]. Very little work has been done on the use of lanthanide shift reagents with polyfunctional substrates[3–7] due to the complexity of such systems. No attempt will be made to furnish a quantitative explanation of the observed effects.

The effects on the MeO signals of **1** and **2** (in $CDCl_3$) of the addition of increasing proportions of either $Eu(fod)_3$ or $Pr(fod)_3$ up to a molar ratio (x) of five are shown in Fig. 1 (for **1**) and Fig. 2 (for **2**). Line-broadening is most apparent where the MeO chemical-shift changes are greatest, but the quality of the spectra was not unduly affected.

Small proportions of shift reagent produce a spread of the five MeO signals of **1** (Fig. 1A) and a crossing of the line for MeO-2 over those for MeO-4 and MeO-3 (Pr reagent), and the line for MeO-4 over those for MeO-3 and MeO-1 (Eu reagent). The chemical shifts of the MeO groups of **1** continue to increase [$Pr(fod)_3$, Fig. 1B] or decrease [$Eu(fod)_3$, Fig. 1B], gradually, with an increase in x. The shapes of the curves indicate[8] relatively low values of the equilibrium constants for the interactions between the shift reagents and the MeO oxygen atoms. The shift reagents saturate the six available donor sites slowly and simultaneously at a high value of x. For **1**, both shift reagents have the least effect on *ax* MeO-4. These results suggest rapid mono- or bi-dentate interchanges[3] (faster than the n.m.r. time-scale) of the shift reagents with

---

*Present address: National Chemical Research Laboratory, Council for Scientific and Industrial Research, Pretoria, South Africa.

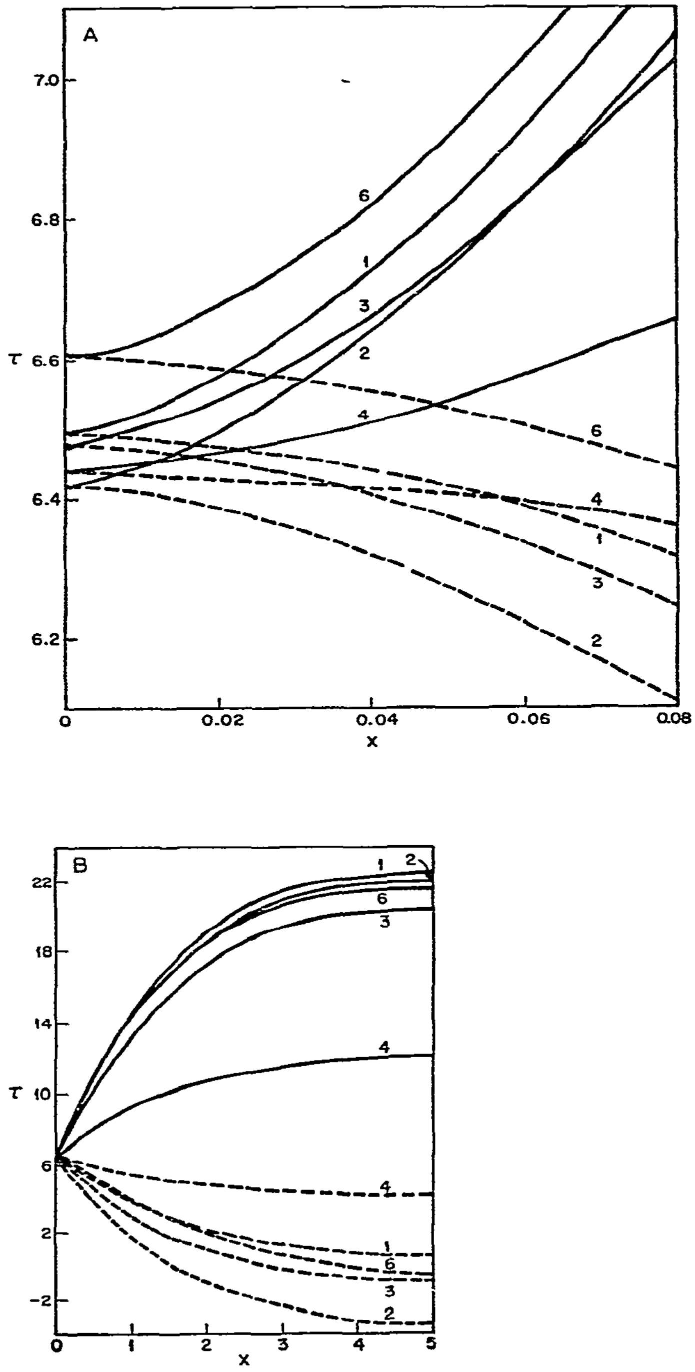

Fig. 1. The effect on the chemical shifts (τ) of MeO-1,2,3,4,6 of **1** (in deuteriochloroform) on adding small amounts (A) and larger amounts (B) of Pr(fod)$_3$ (solid lines) or Eu(fod)$_3$ (broken lines): $x = [\mathrm{LSR}]/[\mathbf{1}]$.

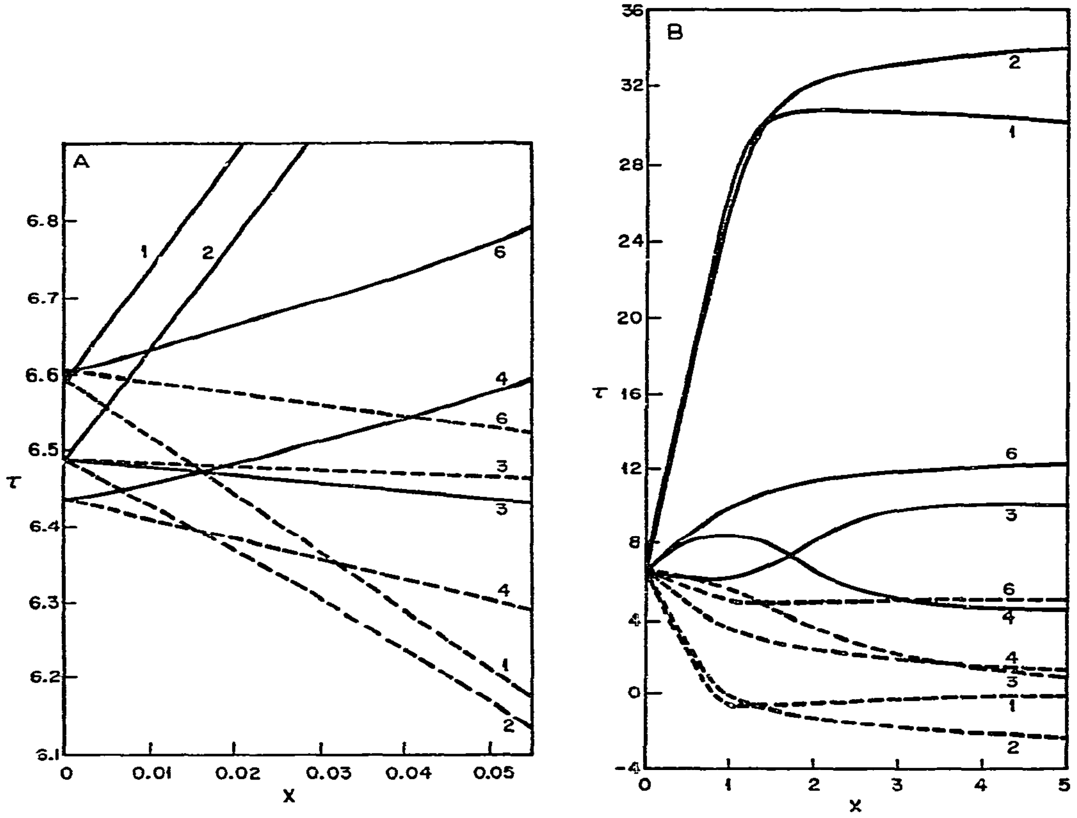

Fig. 2. The effect on the chemical shifts of MeO-1,2,3,4,6 of **2** (in deuteriochloroform) on adding small amounts (A) and larger amounts (B) of Pr(fod)$_3$ (solid lines) or Eu(fod)$_3$ (broken lines).

the equatorial oxygen atoms (and including O-5) but negligibly with the axial O-4 [in the *C1*(D) conformation]. There are no definite and consistent trends for MeO-1,2,3,6, comparing the two lanthanides: at $x = 1$, Eu(fod)$_3$ affects MeO-2 and MeO-3 more than MeO-1 and MeO-6, whereas, with Pr(fod)$_3$, this order is reversed.

The lanthanide-induced shifts for **2** (Fig. 2) are considerably different from those of **1**. The initial shapes of the curves (Fig. 2A) for **2** indicate a relatively large value of the equilibrium constant[8] for the binding at O-1 and O-2, and suggest that the first mole of shift reagent binds bidentately thereto. The lines for MeO-4 and MeO-6 are also shifted but to a much smaller extent. There is only a very slight decrease in the chemical shift of MeO-3 on addition of Eu(fod)$_3$, and whereas the effect of Pr(fod)$_3$ is small, it too produces a downfield shift (Fig. 2A). These effects on MeO-3,4,6 could be produced by long-range interaction of a shift-reagent molecule situated around O-1 and O-2. MeO-4 and MeO-6 are directly opposite a shift-reagent molecule in such a position ($\theta \sim 0°$ in the McConnell–Robertson equation[9]), whereas MeO-3 would be at an angle $\theta \sim 54°$. These trends continue up to $x = 1$.

Beyond $x = 1$ (*i.e.*, after saturation of the bidentate site at O-1 and O-2), there is a sudden increase in the induced shift of MeO-3 and a decrease for MeO-4 and MeO-1 [$Pr(fod)_3$, Fig. 2B], or MeO-6 and MeO-1 [$Eu(fod)_3$, Fig. 2B]. These trends possibly indicate[8] a change in the geometry of the complex around O-1 and O-2. The effects on **2** are slightly different with $Pr(fod)_3$ compared with $Eu(fod)_3$, which may be due to a difference in their shift mechanisms[4,10,11].

For **1**, the induced shifts are all either upfield [$Pr(fod)_3$] or downfield [$Eu(fod)_3$] indicating that the lanthanide atom is at a considerable distance from the pyranose ring[7], the angle θ towards the methoxyl protons in the McConnell–Robertson equation being $<55°$. A closer approach of the shift reagent to the pyranose ring (as would be required in the formation of a bidentate complex with **2**) could increase the angle θ to 125–180° for some protons and to 55–125° for others, so producing the abnormal shifts observed for **2**.

Thus, lanthanide shift reagents can be used to increase the dispersion of the spectra of polyfunctional molecules, even when the molecules are substituted by groups which individually have a low intrinsic affinity for the shift reagent. Furthermore, similar functional groups may be differentiated when in different structural environments. Graphs such as those in Figs. 1 and 2 may then be used to determine the optimum concentration of shift reagent required to give the best separation and spread of methoxyl signals. However, considerable line-broadening[3] is observed for high values of x.

A more exact explanation of the interactions of polyfunctional sugar molecules with lanthanide shift reagents would involve determinations of the equilibrium binding constants[12] or spin relaxation times at each donor site.

EXPERIMENTAL

P.m.r. spectra were determined on a Varian XL-100 spectrometer at 35° for solutions in $CDCl_3$ (dried over Linde Molecular Sieve type 3A) with Me_4Si as internal reference. The shift reagents, dried *in vacuo* over phosphorus pentaoxide, were added to the samples (25 mg) in the n.m.r. tubes, either dropwise as a solution in $CDCl_3$ (for the initial addition of small quantities of shift reagent) or as a solid powder. The MeO signals were identified by using partially deuteriomethylated derivatives[1] of **1** and **2**, or by extrapolation to $x = 0$ where the assignments are known[2].

ACKNOWLEDGMENTS

The authors thank Mrs. P. Davidson for determining the spectra, and Dr. D. F. Evans (Imperial College, University of London) and Professor L. D. Hall (The University of British Columbia) for advice. Financial assistance was received from the C.S.I.R. and the University of Cape Town (Staff Research Fund).

REFERENCES

1 E. B. Rathbone and A. M. Stephen, *Tetrahedron Lett.*, (1970) 1339.

2 E. B. Rathbone, A. M. Stephen, and K. G. R. Pachler, *Carbohyd. Res.*, 20 (1971) 141.

3 B. C. Mayo, *Chem. Soc. Rev.*, 2 (1973) 49.

4 A. M. Grotens, J. Smid, and E. de Boer, *J. Magn. Resonance*, 6 (1972) 612.

5 A. M. Grotens, J. Smid, and E. de Boer, *Tetrahedron Lett.*, (1971) 4863; A. M. Grotens, E. de Boer, and J. Smid, *ibid.*, (1973) 1471.

6 S. D. Gero, D. Horton, A. M. Sepulchre, and J. D. Wander, *Tetrahedron*, 29 (1973) 2963; G. E. Wright and T. Y. Tang Wei, *ibid.*, 29 (1973) 3775; N. S. Bhacca, J. Selbin, and J. D. Wander, *J. Amer. Chem. Soc.*, 94 (1972) 8719; I. Armitage and L. D. Hall, *Can. J. Chem.*, 49 (1971) 2770; I. Fleming, S. W. Hanson, and J. K. M. Sanders, *Tetrahedron Lett.*, (1971) 3733; R. F. Butterworth, A. G. Pernet, and S. Hanessian, *Can. J. Chem.*, 49 (1971) 981.

7 H. B. Borén, P. J. Garegg, Å. Pilotti, and C.-G. Swahn, *Acta Chem. Scand.*, 26 (1972) 3261.

8 J. K. M. Sanders, S. W. Hanson, and D. H. Williams, *J. Amer. Chem. Soc.*, 94 (1972) 5325.

9 H. M. McConnell and R. E. Robertson, *J. Chem. Phys.*, 29 (1958) 1361.

10 S. I. Weissman, *J. Amer. Chem. Soc.*, 93 (1971) 4920.

11 A. A. Chalmers and K. G. R. Pachler, *J. Chem. Soc. Perkin II*, (1974) 748; M. Hirayama and Y. Hanyu, *Bull. Chem. Soc. Jap.*, 46 (1973) 2687.

12 I. Armitage and L. D. Hall, *Carbohyd. Res.*, 24 (1972) 221; I. Armitage, G. Dunsmore, L. D. Hall, and A. G. Marshall, *Can. J. Chem.*, 50 (1972) 2119; A. Arduini, I. M. Armitage, L. D. Hall, and A. G. Marshall, *Carbohyd. Res.*, 31 (1973) 255.