

1,3:4,6-Di-*O*-benzylidene-2,5-*O*-3,6,9,12-tetraoxatetradecane-1,14-diyl-D-mannitol and the Solution State Structure of its Molecular Complex with the Benzylammonium Cation. A Variable-temperature ^1H N.M.R. Spectroscopic Investigation

Steven E. Fuller, Brian E. Mann, and J. Fraser Stoddart

Department of Chemistry, The University, Sheffield S3 7HF, U.K.

The results of variable-temperature ^1H n.m.r. spectroscopic investigations, including both multiple irradiation experiments and qualitative measurements of nuclear Overhauser effects, on D-(2)-PhCH₂NH₃ClO₄ indicate that the conformation (H_a/H_c) in which the phenyl ring in the cation is oriented over one of the 1,3-dioxan rings in D-(2) becomes increasingly preferred in CD₂Cl₂ solution as the temperature is lowered.

Previously, ^1H n.m.r. spectroscopic investigations of the 1:1 complexes formed between 1,3:4,6-di-*O*-methylene-2,5-*O*-3,6,9,12-tetraoxatetradecane-1,14-diyl-D-mannitol D-(1) (see preceding communication) and PhCHR'NH₃⁺ClO₄⁻ salts (where R' = H, Me, CO₂Me) revealed¹ the existence in CD₂Cl₂ solution of a dipole-induced dipole interaction² between one of the 1,3-dioxan rings in D-(1) and the phenyl ring in the bound PhCHR'NH₃⁺ ion. Thus, it came as a surprise to us to learn that, in the solid state structure³ of the 1:1 complex formed between 1,3:4,6-di-*O*-benzylidene-2,5-*O*-3,6,9,12-tetraoxatetradecane-1,14-diyl-D-mannitol D-(2) (see preceding communication) and PhCH₂NH₃ClO₄, the phenyl group in the cation is oriented above the (OCH₂CH₂)₅O loop and away from the carbohydrate portion of D-(2). This structure has been designated³ as the H_a/H_b conformation and is shown in Figure 1 along with the conformations for the other two possible rotamers, H_b/H_c and H_a/H_c , produced on torsion about the C-N bond in the complex.† In this communication, we describe the results of variable-temperature ^1H n.m.r. spectroscopic investigations at 400 MHz in CD₂Cl₂ solution on (i) the free crown, D-(2), and on (ii) the 1:1 complex formed between D-(2) and PhCH₂NH₃ClO₄.

A comparison of the chemical shifts of the protons associated with the dioxan rings in the carbohydrate portion of D-(2) between (a) the free crown, D-(2), at ambient temperature, and the 1:1 complex, D-(2)-PhCH₂NH₃⁺, at (b) ambient temperature and (c) at -49 °C is presented diagrammatically in Figure 2. The proton assignments at ambient temperatures (Figure 2a, b) were made on the basis of multiple-irradiation experiments involving decoupling of appropriate spin systems and the qualitative measurements

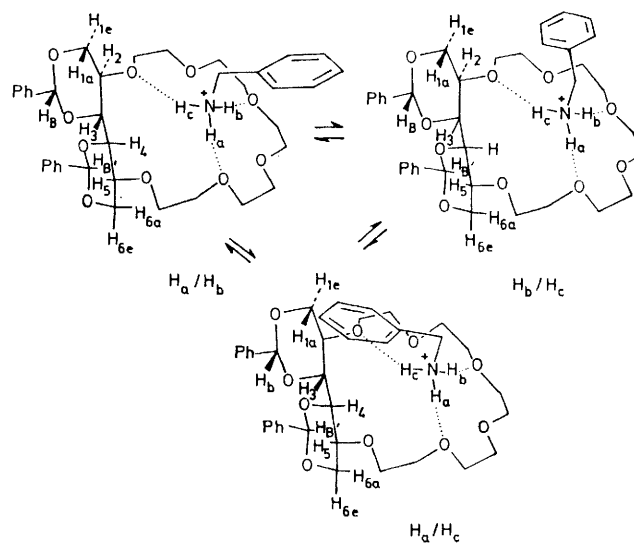


Figure 1. The proposed interconversion between conformational diastereoisomers of D-(2)-PhCH₂NH₃⁺ in solution.

of nuclear Overhauser effects from difference spectra. (Nuclear Overhauser effects were observed in experiments in which the pulse spacing was not arranged to be at least 5 times that of the maximum T_1 value.)

The partial spectrum of D-(2), reproduced in Figure 3, shows splitting patterns and associated coupling constants. On addition of 1.0 mol. equiv. of PhCH₂NH₃ClO₄ to the CD₂Cl₂ solution of D-(2), low-frequency shifts were observed (Figure 2a) for $H_{B/B'}$, $H_{3/4}$, and $H_{1a/6a}$ as well as additional signals (Figure 4a) for protons in the complexed PhCH₂NH₃⁺ ion. When the signal for the phenyl protons in this cation was irradiated, enhancements of signal intensities were observed for $H_{B/B'}$, $H_{1a/6a}$, $H_{3/4}$, and the OCH₂CH₂O protons in D-(2) as well as for the benzylic methylene protons of the cation. On cooling the CD₂Cl₂ solution down to -49 °C the signals for $H_{B/B'}$, $H_{1e/6e}$, $H_{3/4}$, and $H_{1a/6a}$

† If it is assumed that the hydrogen bonding pattern involving the NH₃H₃H₃⁺ centre of the PhCH₂NH₃⁺ ion and the (OCH₂CH₂)₅O loop of D-(2) is similar to that observed (ref. 3) in the solid state, then three rotational isomers resulting from torsion about the C-N bond in the cation can be identified according as to whether the phenyl group is staggered between H_a and H_b, H_b and H_c, or H_a and H_c. The three isomers are therefore referred to as the H_a/H_b , H_b/H_c , and H_a/H_c conformations, respectively.

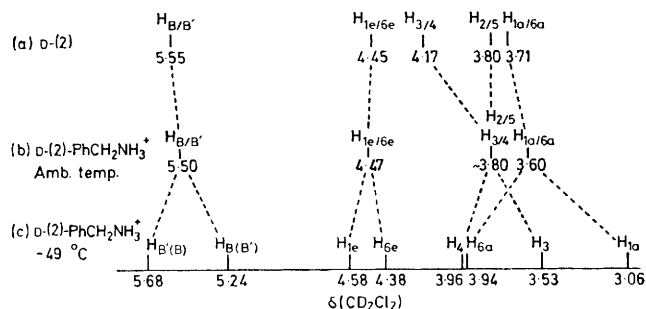


Figure 2

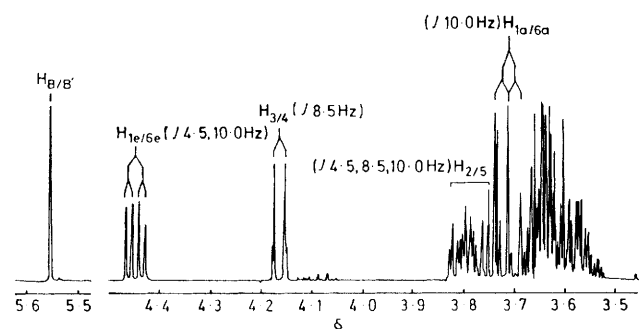


Figure 3. The partial ^1H n.m.r. spectrum of *D*-(2) recorded in CD_2Cl_2 at ambient temperature on a Bruker WH400 spectrometer. Irradiation of the following protons resulted in the following percentage enhancements in signals for neighbouring protons: irr. $\text{H}_{\text{B/B}'}$ \rightarrow $\text{H}_{3/4}$ (11%) and $\text{H}_{1\text{a}/6\text{a}}$ (6%); irr. $\text{H}_{3/4} \rightarrow$ $\text{H}_{\text{B/B}'}$ (14%).

separate out (Figure 4b) into two signals in each case. When the high-field triplet ($J_{1\text{a},1\text{e}} = J_{1\text{a},2} = 10.5$ Hz) at δ 3.06, which can be assigned to $\text{H}_{1\text{a}}$, is irradiated, the difference spectrum reveals an increase in intensity for a signal at δ 3.94, which can thus be assigned to $\text{H}_{6\text{a}}$. This signal lacks multiplicity because of saturation transfer⁴ from $\text{H}_{1\text{a}}$ to $\text{H}_{6\text{a}}$ by chemical exchange. Likewise, irradiation of the signal at δ 4.58 results in saturation transfer by chemical exchange to afford a signal centred upon δ 4.38. A conventional decoupling experiment allows these two signals to be assigned to $\text{H}_{1\text{e}}$ and $\text{H}_{6\text{e}}$, respectively. A similar combination[‡] of double irradiation experiments allows signals at δ 3.53 and δ 3.96 to be assigned to H_3 and H_4 , respectively. These spectral changes can be interpreted in terms of equilibration[§]

[‡] Irradiation of the signal centred on δ 3.53 resulted in the appearance of a signal at δ 3.96 as a consequence of saturation transfer by chemical exchange. This assignment was confirmed by carrying out a similar double-irradiation experiment at -49°C after addition of a further 1.0 mol. equiv. of *D*-(2) to the CD_2Cl_2 solution of the 1:1 complex. Irradiation of the signal at δ 4.17 for $\text{H}_{3/4}$ in the free crown, *D*-(2), led to the emergence of two broadened doublets ($J_{2,3} = \text{ca. } J_{4,5} = \text{ca. } 9$ Hz) centred upon δ 3.96 and δ 3.53 corresponding to H_4 and H_3 , respectively, in the 1:1 complex, *D*-(2)- $\text{PhCH}_2\text{NH}_3^+$. In this experiment, saturation transfer by chemical exchange is occurring as a result of equilibration between the free crown and the 1:1 complex.

[§] The free energy of activation (ΔG^\ddagger) for this cation dissociation process has been calculated to be *ca.* 11.3 kcal mol⁻¹ (1 kcal = 4.18 kJ) at the coalescence temperature (T_c *ca.* -35°C at 220 MHz) given an observed limiting peak separation of 107 Hz between the equal intensity singlets H_{B} and $\text{H}_{\text{B}'}$, at -80°C .

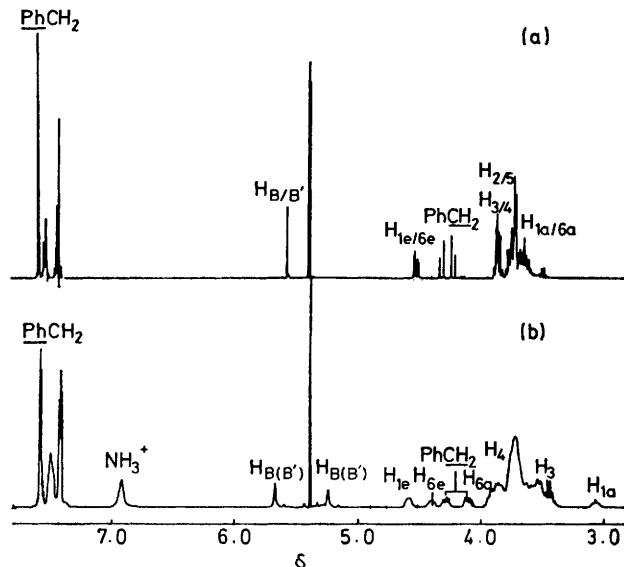


Figure 4. The ^1H n.m.r. spectra of the 1:1 complex formed between *D*-(2) and the $\text{PhCH}_2\text{NH}_3^+$ ion recorded on a Bruker WH400 (a) at ambient temperature and (b) at -49°C .

of the $\text{PhCH}_2\text{NH}_3^+$ ion between the homotopic faces of *D*-(2). The dramatic upfield shifts of $\text{H}_{1\text{a}}$ and H_3 in the low temperature spectrum of *D*-(2)- $\text{PhCH}_2\text{NH}_3^+$ indicate that conformation $\text{H}_{\text{a}}/\text{H}_{\text{b}}$, in which the phenyl ring in the cation is oriented[¶] over one of the dioxan rings in *D*-(2), is preferred in CD_2Cl_2 solution at -49°C . This stereochemical relationship is reflected in the shielding of the three axial protons, H_{B} , $\text{H}_{1\text{a}}$, and H_3 , by the phenyl group. The changes in chemical shifts of these protons and those with which they are undergoing site exchange indicate that the contribution of conformation $\text{H}_{\text{a}}/\text{H}_{\text{c}}$ to the equilibrium (Figure 1) increases^{**} as the temperature of the solution is lowered.

Received, 11th June 1982; Com. 669

References

- 1 D. A. Laidler and J. F. Stoddart, *Tetrahedron Lett.*, 1979, 453.
- 2 J. E. Anderson, *Tetrahedron Lett.*, 1965, 4713; K. D. Carlson, C. R. Smith, and I. A. Wolff, *Carbohydr. Res.*, 1970, 13, 403.
- 3 S. E. Fuller, J. F. Stoddart, and D. J. Williams, *J. Chem. Soc., Chem. Commun.*, 1982, preceding communication.
- 4 M. L. Martin, G. J. Martin, and J. J. Delpuech, 'Practical NMR Spectroscopy,' Heyden, London, 1980, p. 315.

[¶] The magnitude of the coupling constant ($J_{3,4} < 2$ Hz) between H_3 and H_4 observed in the double-irradiation experiment described in footnote[‡] indicates a *gauche* relationship between these two protons and suggests that the interannular bond adopts the same conformation in solution as it does (ref. 3) in the solid state.

^{**} The average chemical shift of H_{B} and $\text{H}_{\text{B}'}$ at -49°C is δ 5.46 compared with the observed chemical shift of δ 5.50 for $\text{H}_{\text{B/B}'}$ at ambient temperature. The average chemical shift of $\text{H}_{1\text{a}}$ and $\text{H}_{6\text{a}}$ at -49°C is δ 3.50 compared with the observed chemical shift of δ 3.60 for $\text{H}_{1\text{a}/6\text{a}}$ at ambient temperature. Moreover, as the temperature of the CD_2Cl_2 solution of the 1:1 complex is lowered to -66°C and -80°C , the triplet for $\text{H}_{1\text{a}}$ continued to drift towards higher (δ 2.97) and higher (δ 2.84) field. This behaviour supports the view that the population of conformation $\text{H}_{\text{a}}/\text{H}_{\text{c}}$ in CD_2Cl_2 solution increases as the temperature of the solution decreases.