PREPARATIVE METHODS AND NMR ANALYSIS
FOR SILYLATED DERIVATIVES OF CYCLODEXTRIN

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SUMMARY

Methods for the complete or partial (selective) silylation of β-cyclodextrin are described that provide intermediates for further derivatisation. The method is applied to the sequential attachment and attempted capping of β-cyclodextrin by a porphyrin template. Representative proton NMR spectra for a series of silyl derivatives and intermediates are analysed to demonstrate further the advantage of the method.

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INTRODUCTION

Our strategy for constructing a porphyrin-capped cyclodextrin has been described[1]. Crucial to this preparative method was a directed mono-attachment reaction that secured the component materials by an amide bond, with the provision for a subsequent cyclisation across the face of the cage molecule. The use of silylated intermediates, as protecting groups to direct reaction in the (previously functionalised) β-cyclodextrin amine, served also to solubilize the cage molecule in organic solvents and so facilitated $^1$H-nmr analysis and product purification by chromatography.

Unambiguous nmr assignments are essential to determine reaction selectivities on the cyclodextrin ring, and are of further assistance in assessing compound homogeneity. We now describe proton nmr spectra recorded at 360 MHz on samples used in the preparation of the porphyrin-cyclodextrin conjugate, as well as on model compounds, together with experimental details for these procedures.

RESULTS AND DISCUSSION

Parent and fully derivatised cyclodextrins

The simplest and most easily assigned spectra are those of cyclodextrins where each derivatisable centre (C-2, C-3 and C-6) bears the same functionality (OH, OCOCH$_3$, OSiMe$_3$, OSi$^-$BuMe$_2$). The magnitude of discrete proton coupling constants is more or less independent of the functionality, and so each proton signal can be identified from a characteristic shape (Table I). Proton chemical shifts, however, are strongly influenced by the adjacent or even distant functionality.

The proton spectra for both α- and β-cyclodextrin have the anomeric hydrogen (H-1) at lowest field, with distinct high-field signals for H-2 and H-4 (the order is inverted for these two by switching from D$_2$O to d$_6$-DMSO as solvents) (Figure 1). Inbetween a four-proton envelope for H-3, H-5, H-6 and H-6' is located. Assignments made for β-cyclodextrin were further verified by decoupling, beginning with H-1, and further by sequential inclusion of d$_6$-benzene which resolved the spectrum partially, and decoupling of the modified spectrum, which identified H-5, H-6 and H-6'.

Mono-substitution imposes some asymmetry that complicates the spectra for these compounds. Complete assignments are no longer possible, but from the characteristic signal, key shifts can be identified that are consistent