CYCLODEXTRINS: MOLECULAR WHEELS FOR SUPRAMOLECULAR CHEMISTRY

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Contents

Abstract

This work describes the construction and characterisation of a variety of supramolecular architectures based on cyclodextrins.

The trinorbornylmethyl-, cubyl-, dimethylcubyl- and adamantyl-substituted cyclodextrins **35**, **36**, **37** and **38** were prepared by the acylation of 6^A-(6-aminohexyl)amino-6^A-deoxy-α-cyclodextrin **34** by the 4-nitrophenyl esters **25**, **26**, **27** and **28**, respectively. 2D ^{1}H ROESY NMR spectra are consistent with the trinorbornylmethyl, cubyl and dimethylcubyl substituents of the cyclodextrins **35-37** being self-included in D_2O to give **35'-37'**, but with the adamantyl substituent of **38** being too large to be self-included. The mechanism for the acylations involves reaction of the 4-nitrophenyl esters with the aminohexylamine substituent of **34** outside of the cyclodextrin; subsequent inclusion of the substituents of **35-37** in aqueous solution produces **35'-37'**.

The azacoronand-substituted cyclodextrins **43-46** were prepared by the acylation of 6^A-(6-aminohexyl)amino-6^A-deoxy-α-cyclodextrin **34** or 6^A-(6-aminohexyl)amino-6^A-deoxy-β-cyclodextrin **24** by either of the 4-nitrophenyl esters **41** or **42**. 2D ^{1}H ROESY NMR spectra are consistent with the substituents of the modified β-cyclodextrins **45** and **46** being self-included to give **45'** and **46'** in D_2O at pD 9, but with the substituents of the modified α-cyclodextrins **43** and **44** not being self-included in aqueous solution. In D_2O at pD 9, the substituents of **43** and **44** include in the annulus of β-cyclodextrin to form the [2]-pseudorotaxanes βCD.**43** and βCD.**44**. β-Cyclodextrin includes the central section of the hexyl chain of **43** or **44**. Metal-locking of the azacoronand moiety of **45/45'** was investigated, and pK_a values of 5.84 and 8.49 and metal complex stability constants (log(K) values) of <2 ([**45/45'**.Ca]$^{2+}$), 6.34 ([**45/45'**.Zn]$^{2+}$) and 5.38 ([**45/45'**.La]$^{3+}$) were determined for this system.

The water-soluble axles **50** and **51** were prepared and shown by 2D ^{1}H ROESY NMR experiments to form the [2]-pseudorotaxanes βCD.**50**, αCD.**51** and βCD.**51** in aqueous solution. The cobalt(III)-blocked α-cyclodextrin and β-cyclodextrin [2]-rotaxanes **57**, **58** and **59** were prepared in good yields, by the reaction of the terminal tetramine groups of the axle in each of the corresponding [2]-pseudorotaxanes with sodium triscarbonatocobalt(III). 2D ^{1}H ROESY NMR experiments provided evidence for the structures of the [2]-rotaxanes. The

β-cyclodextrin [2]-rotaxanes **57** and **59** were obtained as almost pure products directly from the reaction mixtures. Each of the [2]-rotaxanes was further purified as the chloro complex analogue. The [2]-rotaxane **57** can also be formed by a slippage mechanism, while the [2]-rotaxane **59** forms very slowly by slippage and the α-cyclodextrin [2]-rotaxane **58** does not form by such a mechanism. Work towards the synthesis of a [2]-rotaxane containing the urea-linked β-cyclodextrin dimer *N,N'*-bis(6^{A}-deoxy-6^{A}-β-cyclodextrin-6^{A}-yl)urea **73** was carried out, but was hindered by the low water-solubility of the corresponding [2]-pseudorotaxane.

Photo-controlled molecular devices were constructed utilising the urea-linked cyclodextrin dimers *N,N'*-bis(6^{A}-deoxy-6^{A}-β-cyclodextrin-6^{A}-yl)urea **73** and *N*-(6^{A}-deoxy-α-cyclodextrin-6^{A}-yl)-*N'*-(6^{A}-deoxy-β-cyclodextrin-6^{A}-yl)urea **77** and the stilbenes *trans*/*cis*-4-*t*-butyl-4'-oxystilbene **78**$^{-}$/**80**$^{-}$ and *trans*/*cis*-4-*t*-butyl-4'-carboxystilbene **79**$^{-}$/**81**$^{-}$. In these molecular devices, one annulus of the cyclodextrin dimer is occupied by the *t*-butylphenyl end of the stilbene, while the other annulus is alternately occupied and vacated by the phenoxy or benzenecarboxy end of the stilbene, as the stilbene is isomerised between the *trans* and *cis* configurations. 4-Methylbenzoate **94**, 4-methylphenolate **95** and 4-methylbenzenesulfonate **96** were utilised as second guests which are alternately included and excluded from one annulus of the cyclodextrin dimer during the stilbene isomerisation reactions to give rise to three-component molecular devices. The switching of the devices was followed by 2D ^{1}H ROESY NMR and UV/Vis experiments. Examination of the inclusion of the *trans* stilbenes **78**$^{-}$ and **80**$^{-}$ inside native α-cyclodextrin and β-cyclodextrin revealed a significant influence of the annulus size on the nature of the inclusion complex. Each β-cyclodextrin.stilbene complex exists either with β-cyclodextrin in a single orientation, or as two inclusion isomers in fast equilibrium, while each α-cyclodextrin.stilbene complex exists as two inclusion isomers in slow equilibrium at room temperature. Rate constants and activation parameters for exchange between the two isomeric αCD.**78**$^{-}$ inclusion complexes are k_1(298 K) = 12.3 ± 0.6 s^{-1}, k_2(298 K) = 10.7 ± 0.5 s^{-1}, $\Delta H^{\ddagger}_1$ = 94.3 ± 4.7 kJ mol^{-1}, $\Delta H^{\ddagger}_2$ = 93.1 ± 4.7 kJ mol^{-1}, $\Delta S^{\ddagger}_1$ = 92.0 ± 5.0 J mol^{-1} K^{-1} and $\Delta S^{\ddagger}_2$ = 87.3 ± 5.0 J mol^{-1} K^{-1} (where the subscripts 1 and 2 refer to the less and more populated states, respectively). The ground state parameters for exchange between the two isomeric αCD.**79**$^{-}$ inclusion complexes are ΔG^0 = -910 ± 160 J mol^{-1}, ΔH^0 = 12.6 ± 1.5 kJ mol^{-1} and ΔS^0 = 46 ± 3 J mol^{-1} K^{-1} (in the direction from the less populated to more populated state).