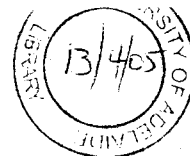


09PH
L8131



CYCLODEXTRINS: MOLECULAR WHEELS FOR SUPRAMOLECULAR CHEMISTRY

Julia Lock

Thesis submitted for the degree of
Doctor of Philosophy
in
The University of Adelaide, Department of Chemistry

July 2004



THE UNIVERSITY
OF ADELAIDE
AUSTRALIA

Contents

	Page
Declaration	iv
Acknowledgements	v
Abstract	vi
Abbreviations	viii
Chapter 1. Introduction	1
1.1 Cyclodextrins: Their Properties and Applications	1
1.2 Appropriate Guests for Cyclodextrin Inclusion Complexes and Evidence for Guest-Inclusion	3
1.3 Modified Cyclodextrins	5
1.4 Mechanically Restrained Molecular Systems	6
1.5 Molecular Devices	13
1.6 References	17
Chapter 2. Size Discrimination in Modified Cyclodextrins	23
2.1 Alicyclic-Substituted Cyclodextrins	23
2.1.1 Introduction	23
2.1.2 Results and Discussion	25
Synthesis	25
Molecular modelling	26
2D ¹ H ROESY NMR spectroscopy	28
2.1.3 Conclusion	34
2.1.4 References	35

2.2 Azacoronand-Substituted Cyclodextrins	36
2.2.1 Introduction	36
2.2.2 Results and Discussion	37
Synthesis	37
2D ¹ H ROESY NMR spectroscopy	38
Metal binding studies	49
2.2.3 Conclusion	52
2.2.4 References	52
Chapter 3. Cobalt(III)-Blocked Cyclodextrin [2]-Rotaxanes	54
3.1 Introduction	54
3.2 Results and Discussion	55
Preparation of a [2]-pseudorotaxane	55
Improvement of [2]-pseudorotaxane stability: synthesis of longer axles	59
Cobalt(III)-blocked cyclodextrin [2]-rotaxanes	68
Purification of the [2]-rotaxanes as chloro complexes	77
Rotaxane synthesis by ‘slippage’	78
A β-cyclodextrin dimer [2]-rotaxane	85
3.3 Conclusion	95
3.4 References	95
Chapter 4. Photochemically-Driven Molecular Devices	97
4.1 Introduction	97
4.2 Results and Discussion	98
Synthesis	98
Cyclodextrin dimer.stilbene inclusion complexes	103
Photochemical and thermal stimuli in molecular devices	113
Construction of three-component molecular devices	120
Movement of the <i>trans</i> stilbenes 78 and 79 inside cyclodextrin dimer hosts	132
Native cyclodextrin. <i>trans</i> stilbene inclusion complexes	133
4.3 Conclusion	146

4.4 References	147
Conclusion	149
Experimental	152
E.1 General	152
E.2 Preparation of compounds described in Chapter 2	155
E.3 Preparation of compounds described in Chapter 3	163
E.4 Preparation of compounds described in Chapter 4	175
E.5 References	179
Appendix Copies of publications	181

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 ¹H ROESY NMR spectra are consistent with the trinorbornylmethyl, cubyl and dimethylcubyl substituents of the cyclodextrins **35-37** being self-included in D₂O 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 aminoethylamine 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 ¹H 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 D₂O at pD 9, but with the substituents of the modified α -cyclodextrins **43** and **44** not being self-included in aqueous solution. In D₂O at pD 9, the substituents of **43** and **44** include in the annulus of β -cyclodextrin to form the [2]-pseudorotaxanes β CD.**43** and β CD.**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 ¹H ROESY NMR experiments to form the [2]-pseudorotaxanes β CD.**50**, α CD.**51** and β CD.**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 ¹H 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 ¹H 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 α CD.**78** inclusion complexes are $k_1(298\text{ K}) = 12.3 \pm 0.6\text{ s}^{-1}$, $k_2(298\text{ K}) = 10.7 \pm 0.5\text{ s}^{-1}$, $\Delta H^\ddagger_1 = 94.3 \pm 4.7\text{ kJ mol}^{-1}$, $\Delta H^\ddagger_2 = 93.1 \pm 4.7\text{ kJ mol}^{-1}$, $\Delta S^\ddagger_1 = 92.0 \pm 5.0\text{ J mol}^{-1}\text{K}^{-1}$ and $\Delta S^\ddagger_2 = 87.3 \pm 5.0\text{ J mol}^{-1}\text{K}^{-1}$ (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 α CD.**79** inclusion complexes are $\Delta G^0 = -910 \pm 160\text{ J mol}^{-1}$, $\Delta H^0 = 12.6 \pm 1.5\text{ kJ mol}^{-1}$ and $\Delta S^0 = 46 \pm 3\text{ J mol}^{-1}\text{K}^{-1}$ (in the direction from the less populated to more populated state).