THE UNIVERSITY of ADELAIDE

SUPRAMOLECULAR CHEMISTRY OF BETA– AND GAMMA– CYCLODEXTRIN DIMERS

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CONTENTS

ABSTRACT

Native and modified cyclodextrins (CDs) act as robust hosts for a variety of guest species in water, and therefore are at the centre of supramolecular chemistry. Covalently linked CD dimers provide many advantages over native CDs in complexation of guest species in terms of their stability, selectivity or flexibility. The studies underpinning this thesis are based on the β-cyclodextrin dimers, *N*,*N*′-bis((2^{A}S,3^{A}S)-3^{A}-deoxy-β-cyclodextrin-3^{A}-yl) succinamide, 33βCD$_2$suc, and *N*,*N*′-bis(6^{A}-deoxy-β-cyclodextrin-6^{A}-yl) succinamide, 66βCD$_2$suc, and the γ-cyclodextrin dimers, *N*,*N*′-bis((2^{A}S,3^{A}S)-3^{A}-deoxy-γ-cyclodextrin-3^{A}-yl) succinamide, 33γCD$_2$suc, and *N*,*N*′-bis(6^{A}-deoxy-γ-cyclodextrin-6^{A}-yl) succinamide, 66γCD$_2$suc, in which the two βCD or γCD cavities are joined together through either the C_3^A or C_6^A carbons of altropyranose or glucopyranose units, respectively.

Often in supramolecular systems, several competing equilibria exist, as exemplified by host–guest complexation and guest aggregation. The complexation of dimerising cationic pyronines B and Y, PB^+ and PY^+, by βCD and the βCD dimers, 33βCD$_2$suc and 66βCD$_2$suc, has been studied by UV–vis, fluorescence and ^{1}H NMR spectroscopy. The complexation constants for the 1:1 host–guest complexes are reported as are the dimerisation constants for PB^+ and PY^+. The modes of complexation, dimerisation and fluorescence quenching are discussed in light of the structural differences and the 1D and 2D ^{1}H NMR spectroscopic data.

The competitive equilibria between the dimerisation and host–guest complexation of hematoporphyrin, HP^{2-}, by γCD and two newly synthesised γCD dimers, 33γCD$_2$suc and 66γCD$_2$suc, have been simultaneously quantified by UV–vis and fluorescence spectroscopy. The competing equilibrium constants, thermodynamic parameters and molecular modelling are reported and the nature of interaction between HP^{2-} and γCD and the γCD dimer hosts is discussed.

The new 3% randomly substituted 1-naphthyl-sulfonamide poly(acrylate)s, PAA1NSen and PAA1NShn, have been prepared by 3% random substitution of either *N*-(2-aminoethyl)-1-naphthyl-sulfonamide or *N*-(6-aminohexyl)-1-naphthyl-sulfonamide onto the poly(acrylate) backbone. The complexation of the 1-naphthyl substituents by βCD and γCD and their succinamide–linked dimers, 33βCD$_2$suc, 66βCD$_2$suc, 33γCD$_2$suc and 66γCD$_2$suc, have been quantified by fluorescence spectroscopy. The competition between 1-naphthyl substituent aggregation and host–guest complexation by the linked CD dimers and the 1-naphthyl substituents in forming inter–polymer strand cross–links is examined in aqueous solution at the macroscopic level by rheology and at the molecular level by 2D ^{1}H NOESY NMR and fluorescence spectroscopy.

DECLARATION

This is to declare that the work presented herein is original and has been carried out at the University of Adelaide during the period 2007–2010. This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution to Huy Tien Ngo and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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PUBLICATIONS

Based on the research carried out during the period of PhD candidature

1. Ngo, H. T., Clements, P., Easton, C. J., Pham, D.-T., Lincoln, S. F., Supramolecular Chemistry of Pyronines B and Y, β-Cyclodextrin and Linked β-Cyclodextrin Dimers, *Aust. J. Chem.*, **2010**; *63*, 687-692.

2. Pham, D.-T., Ngo, H. T., Lincoln, S. F., May, B. L., Easton, C. J., Synthesis of $C6^{A}$-to-$C6^{A}$ and $C3^{A}$-to-$C3^{A}$ Diamide Linked γ-Cyclodextrin Dimers, *Tetrahedron*, **2010**, *66*, 2895-2898.

ABBREVIATIONS

1. General

Å	Ångström (10^{-10} m)
Ar	aryl
a.u.	arbitrary unit
calcd.	calculated
d	density (g cm^{-3})
δ	chemical shift (ppm)
ΔG^o	Gibbs free energy
ΔH^o	enthalpy change
ΔS^o	entropy change
ε	molar absorptivity (mol^{-1} dm^3 cm^{-1})
Eqn.	equation
et al.	*et alia*
GC-MS	Gas chromatography - mass spectrometry
Hz	Hertz
I	ionic strength (mol dm^{-3})
I_F	fluorescence intensity
J	coupling constant (Hz)
K	stability constant (dm^3 mol^{-1})
K_d	dimerisation constant (dm^3 mol^{-1})
K_1	stability constant for 1:1 host–guest complexes (dm^3 mol^{-1})
K_2	stepwise stability constant for 1:2 host–guest complexes (dm^3 mol^{-1})
lit.	literature
m/z	mass/charge ratio
M^+	molecular ion
MS	mass spectrometry

NMR	nuclear magnetic resonance
NOE	nuclear Overhauser enhancement
NOESY	nuclear Overhauser enhancement spectroscopy
pH	$-\log[H^+]$
ppm	parts per million
R_f	retention factor (in TLC)
R_c	relative retention factor to native cyclodextrins (in TLC)
ROESY	rotating frame Overhauser effect spectroscopy
T	temperature (K)
TLC	thin–layer chromatography
UV–vis	ultraviolet–visible

2. Chemicals

α-, β-, γCD	α-, β-, γ-cyclodextrin
2βCDTs	2^A-*O*-(4-methylbenzenesulfonyl)-β-cyclodextrin
2γCDTs	2^A-*O*-(4-methylbenzenesulfonyl)-γ-cyclodextrin
6βCDTs	6^A-*O*-(4-methylbenzenesulfonyl)-β-cyclodextrin
6γCDTs	6^A-*O*-(4-methylbenzenesulfonyl)-γ-cyclodextrin
6γCDTPBS	6^A-*O*-(2,4,6-triisopropylbenzenesulfonyl)-γ-cyclodextrin
23βCDO	2^A,3^A-manno-epoxide-β-cyclodextrin
23γCDO	2^A,3^A-manno-epoxide-γ-cyclodextrin
3βCDNH$_2$	3^A-amino-3^A-deoxy-(2^AS,3^AS)-β-cyclodextrin
3γCDNH$_2$	3^A-amino-3^A-deoxy-(2^AS,3^AS)-γ-cyclodextrin
6βCDNH$_2$	6^A-amino-6^A-deoxy-β-cyclodextrin
6γCDNH$_2$	6^A-amino-6^A-deoxy-γ-cyclodextrin
33βCD$_2$suc	*N*,*N*′-bis((2^AS,3^AS)-3^A-deoxy-β-cyclodextrin-3^A-yl) succinamide

33γCD_2suc	*N*,*N*′-bis((2^{A}S,3^{A}S)-3^A-deoxy-γ-cyclodextrin-3^A-yl) succinamide
66βCD_2suc	*N*,*N*′-bis(6^A-deoxy-β-cyclodextrin-6^A-yl) succinamide
66γCD_2suc	*N*,*N*′-bis(6^A-deoxy-γ-cyclodextrin-6^A-yl) succinamide
TsCl	*p*-toluenesulfonyl chloride
PB^+	pyronine B, 3,6-bis(diethylamino)xanthylium chloride
PY^+	pyronine Y, 3,6-bis(dimethylamino)xanthylium chloride
HP^{2-}	hematoporphyrin (doubly negatively charged species)
en	1,2-diamino ethane
hn	1,6-diamino hexane
1NSNP	4-nitrophenyl naphthalene-1-sulfonate
1NSen	*N*-(2-aminoethyl)-1-naphthyl-sulfonamide
1NShn	*N*-(6-aminohexyl)-1-naphthyl-sulfonamide
PAA	poly(acrylic acid)s or poly(acrylate)s
PAA1NSen	3% randomly 1NSen substituted PAA
PAA1NShn	3% randomly 1NShn substituted PAA