6A-ω-Aminoalkylamino-Cyclodextrins: Their Preparation and Studies of Their Self-inclusion Complexes and Catalytic Nature.

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ABSTRACT.

This thesis describes the synthesis and characterisation of some 6^A-amino-substituted β-cyclodextrins and studies of their inclusion complexes. Particular attention is given to the role of the host/guest complexes in the de-esterification of various *p*-nitrophenyl esters by 6^A-(2-aminoethylamino)-6^A-deoxy-β-Cyclodextrin (β-CDen). The reaction kinetics for the reactions between β-CDen and the two esters *p*-nitrophenyl benzoate and *p*-nitrophenyl propanoate were investigated in both 100% water solution and a mixed solvent system of 70:30 H_2O: Acetonitrile. Reaction rates for the de-esterification of both esters show a direct concentration dependence on the host β-CDen. No instances of Michaelis-Menten kinetics where detected and the presence of an alternative reaction pathway to the reaction products was believed to be present. The addition of acetonitrile to the reaction system saw a marked reduction in overall reaction rates due to the influence of acetonitrile on the transition state solvation and diminution of the cyclodextrin "hydrophobic effect" that facilitates the formation of host-guest complexes in aqueous solution.

The synthesis and characterisation of potential "molecular knot" modified β-cyclodextrins was also investigated. The reactions of 6^A-(6-aminohexylamino)-6^A-deoxy-β-cyclodextrin with the esters *p*-Nitrophenyl noradamantane-3-carboxylate and *p*-Nitrophenyl norbornan-2-acetate lead to the formation of the corresponding 6-aminohexylamino substituted cyclodextrins. The substituents of each of these derivatives are complexed within the annulus of the modified β-cyclodextrin. Addition of adamantane-1-carboxylate to solutions of these modified cyclodextrins causes the noradamantyl and norbornyl substituents to compete for complexation within the annulus with adamantane-1-carboxylate

The reaction of1,4-bis(*p*-nitrophenoxycarbonyl)-2,3-dimethyl cubane with 6^A-(6-aminohexylamino)-6^A-deoxy-β-cyclodextrin gives a cyclodextrin dimer. The cubanyl group is complexed within the annulus f one of the cyclodextrin entities giving a product that is asymmetric on the NMR time-scale. The addition of two equivalents of adamantane-1-carboxylate to the dimer generates a symmetric 1:2 host-guest complex where the cubanyl group has been displaced from the annulus and each cyclodextrin entity has complexed a molecule of adamantane-1-carboxylate. The pK_as of these

modified 6-aminohexylamino-β-cyclodextrins were determined by potentiometric titrations.

The synthesis of modified β-cyclodextrins mono-substituted with a multi-dentate metal ion binding substituent was also attempted. Synthetic attachment of acetic acid pendant "arms" to the primary and secondary nitrogens of 6^A-(2-aminoethylamino)-6^A-deoxy-β-cyclodextrin (β-CDen) and 6^A-(3-aminopropylamino)-6^A-deoxy-β-cyclodextrin (β-CDpn) to afford the modified cyclodextrins β-CD-ED3A and β-CDPD3A. These attempts were unsuccessful due to the formation of a cyclic piperazine intermediate compound (in the former case) that barred the addition of the acetic acid pendant arm to the nitrogen attached to the $C6^A$ carbon of the β-cyclodextrin. This compound was unsuitable for metal binding and alternative methods of arm attachment resulted in similar products.

The nitrogens attached to the $C6^A$ carbon of β-CDen and β-CDpn were non-nucleophillic and no evidence was ascertained to suggest that substitution of an acetic acid arm was substituted onto the $C6^A$ attached nitrogen in either the β-CDen or β-CDpn system. Mass spectra of the isolated modified β-cyclodextrin products from each of these systems suggested that the major products of the substitution reactions between α-chloroacetic acid and β-CDen and β-CDpn were not the tri-substituted multi-dentate systems required.