Supramolecular Chemistry: An Overview

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Abstract

The field of supramolecular chemistry is among the most interesting and promising areas in modern chemistry. Supramolecular chemistry or "chemistry beyond molecules" covers all intermolecular interactions where covalent bonds are not involved in the components of the interaction. Many of these interactions are based on host-guest interactions. Nowadays the area of supramolecular chemistry stretches from molecular recognition in natural and artificial complexes to applications in chemical technologies, in medicine, in biology and in new materials. Recent studies on the artificial host-guest systems have revealed that molecular recognition is the essential conceptual basis for supramolecular chemistry and nanotechnology.

Introduction

In view of the advantages of supermolecular chemistry and the design principles of synthetic enzymes, many supramolecular synthetic enzymes were formulated based on various supramolecular materials, including macrocycals and container molecules (such as cyclodextrin, calicarene, cyclophanes, crown anther, cryptophane, Capsules). Others) and self-assembled nanometer-sized objects (eg, ligand-anchoring supramolecular complexes, micelles, vesicles, and nanotubes) and so A fascinating member of this class of molecules is cyclodextrins (CDs).

1. Cyclodextrins (CDs)

Cyclodextrins, also known as Schredingerdextrins, cyclomyelosides, and cycloglucoamyloids, comprising a family of cyclic oligosaccharides associated with six (A-CD), seven (þ-CD), eight (Y-CD) or more glucopyropause units is 1,4) Bonds. Cyclodextrins are extremely attractive components of artificial enzymes and other biomimetic materials. Cyclodextrins possess a hydrophobic cavity and which is water soluble and pose no risk when used together with nutrients. Cyclodextrins are biodegradable, used as selective micro vessels of host in many thermal, photo chemical, organic reactions. Much of the current interest in CD arises from its ability to form a wide range of guest species, partially or completely within their annuities, to form host – guest complexes. Their ability to create host-guest campuses has used the CDs of many entrepreneurs.

1.1. Structural Features of Cyclodextrins

From X-ray structures it appears that the secondary hydroxyl groups (C2 and C3) in CD are located on the broad edge of the ring and the primary hydroxyl group (C6) on the other edge, and that apolar C3 and C5 are hydrogen and ether-like Oxygen is inside molecules like torus. This results in a molecule with a hydrophilic, which can dissolve in water, and an apolar cavity, which provides a hydrophobic matrix, described as a micro heterogeneous environment. The absence of formic acid or formaldehyde in

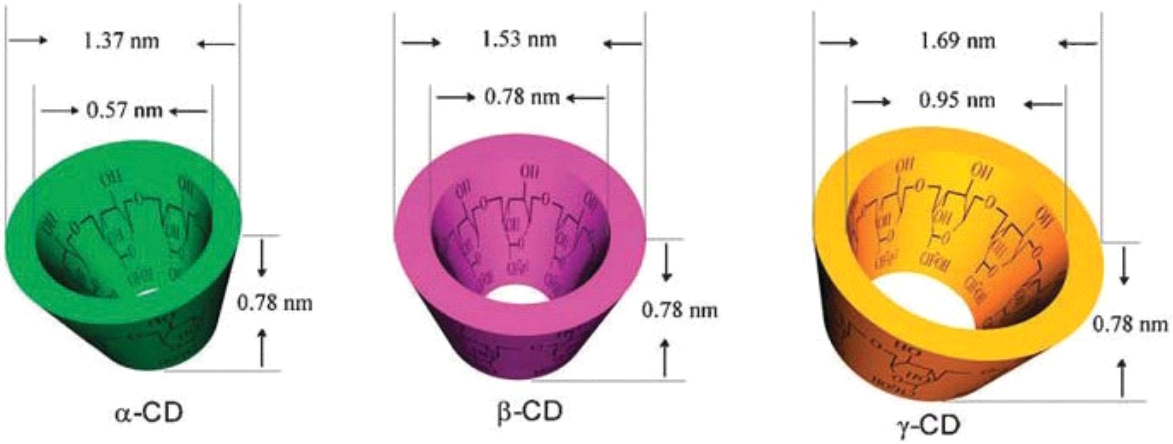
periodic oxidation of A, y- and y-Cd proves that cyclodextrin does not have free end groups. CDs have no reducing end groups and give positive characteristic test for non-reducing carbohydrates. CDs are stable in alkaline solutions, but are the only product susceptible to acid hydrolysis and glucose. On methylation followed by hydrolysis, CDs give 2,3,6- trimethylglucose only, indicating the presence of free hydroxyl groups at 2,3 and 6 positions. Under normal experimental conditions (pH greater than 3.5 and temperature below 60° C) all CDs are quite stable. The shape of the cavity is variable depending on the type, variable, or y-CD, and the melting and reactive characteristics can be changed through modification of hydroxyl groups, making CD a better alternative to other common host compounds. Huh. Table 1.1 gives some physiochemical properties of cyclodextrin.

Table: Physicochemical Properties of Cyclodextins

	a	þ	y
No. of glucose units	6	7	8
Empirical formula (anhydrous)	C36H60O30	C42H70O35	C48H80O40
Mol. Wt. (anhydrous)	972.85	1134.99	1297.14
Cavity length, Å	8	8	8
Cavity diameter, Å (approx)	~5.2	~6.6	~8.4
a_D, deg	+150.5	+162.0	+177.4
Heat capacity (anhyd. solid), J. mol^{-1} K^{-1}	1153	1342	1568
Heat capacity (infinite diln), J. mol^{-1} K^{-1}	1431	1783	2070
pK_a (25°)	12.33	12.20	12.08
OH^0 (ionization), kcal.mol^{-1}	8.36	9.98	11.22
OS^0 (ionization), cal.mol^{-1} K^{-1}	-28.3	-22.4	-17.6
Solubility (water, 25°), mol L^{-1}	0.1211	0.0163	0.168
OH^0 (solution), kcal.mol^{-1}	7.67	8.31	7.73
OS^0 (solution), cal.mol^{-1} K^{-1}	13.8[a]	11.7[a]	14.7[a]

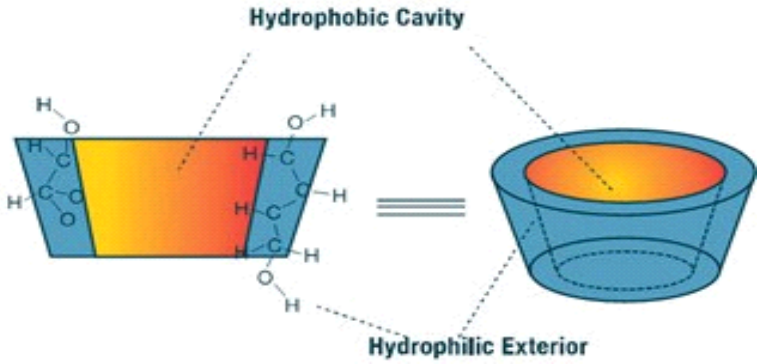
a = Mole Fraction Standard State

Figure 1.1: Structures of a-, þ- and y- cyclodextrins



n = 1 a-cyclodextrin, n = 2 þ-cyclodextrin, n = 3 y-cyclodextrin

Figure 1.2: Side View of Cyclodextrin



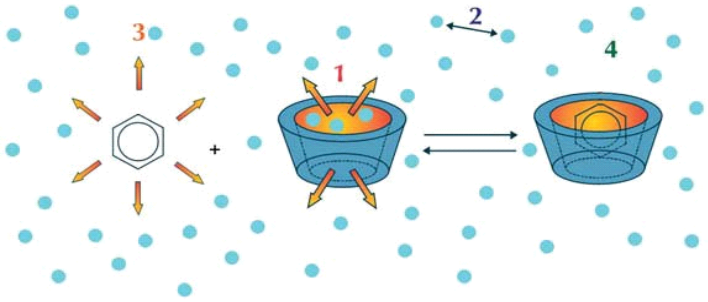
2. Inclusion Complex Formation

Complex formation is a one-dimensional fit between the host cavity and the guest molecule. The main interest in cyclodextrins lies in their ability to form inclusion complexes with many compounds. The lipophilic cavity of the CD molecule provides a microenvironment consisting of suitably nonpolar pieces that can enter the inclusion complexes. CDs have profound effects on the physicochemical properties of guest molecules, leading to beneficial modification of guest molecules that would not otherwise be obtained. No covalent bond is formed during the formation of the inclusion complex.

3. Driving Force for Inclusion Complex Formation

The ability of a cyclodextrin to form an inclusive complex with a guest molecule is a function of two major factors. The first is sticky and depends on the relative size of the guest molecule of the CD or some major functional groups within the guest. The second important factor is the thermo-dynamic interactions between the various components of the system (CD, guest and solvent).

Figure 1.3: The Driving Force for Forming Cyclodextrin Inclusion Complex with a Guest Molecule



As shown in Figure 1.3, there are four energetically favorable interactions that help shift the balance toward complex formation:

- Displacement of polar water molecules from the apolarcyclodextrin cavity
- Increased number of hydrogen bonds formed as displaced water returns to larger pool
- Lack of repulsive interactions between hydrophobic guests and the aquatic environment, and
- As a guest inserts itself into the apolarcyclodextrinkity as hydrophobic interactions increase.

The inclusion is a thermodynamic equilibrium process with an association constant K. The 1:1 (CD: Guest) stoichiometry is the most common type of CD complexes. The combination of CD and guest (G)

molecules, and the separation of the formed CD / guest complex, is controlled by a thermodynamic equilibrium,

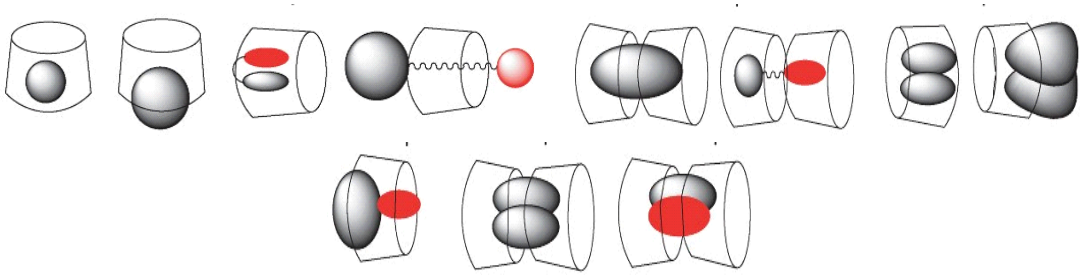
$$CD + GCD.GK^{11} = [CD.G][CD][G]$$

Apart from the release of high-energy water from the CD cavity, the other forces responsible for the complex formation are: van der Waals interactions, hydrophobic interactions, strain energy of the macrocyclic ring, hydrogen bonding dipole-dipole, charge-transfer and electrostatic interactions.

4. Higher Order Complexes

The ability of þ-CD to form inclusion complex is highly affected by the size, shape, and hydrophobicity of guest molecules. Usually, a single guest molecule is accommodated into the þ-CD cavity, with a host/guest stoichiometry of 1:1. However, inclusion complexes of 1:2, 2:1, or 2:2 stoichiometry are also known (Figure 1.4).[17a-i] In addition to these binary inclusion complexes, there are ternary inclusion complexes that contain þ- CD(s) and two different kinds of guests.[18a-i]

Figure 1.4: Schematic Representation of Various Types of Cyclodextrin Inclusion Complexes



4.1. Binding Constants

CD inclusion complexes are formed as a result of bimolecular processes. For example, let us consider the formation of the following three simplest premises by balance:

$$S + L \quad SL$$
$$SL + L \quad SL_2$$
$$S + SL \quad S_2L$$

The step wise binding constants are calculated as K_{11}, K_{12} and K_{21} from the following equations:

$$K11 = [SL]\,[S][L]$$
$$K12 = [SL_2]\,[SL][L]$$
$$K21 = [S_2L]\,[S][SL]$$

Each K value has the unit $M.^{-1}$ Equilibrium constants for molecular association (also known as binding constants, complexation constants, association constants, formation constants) have been measured using a variety of chemical approaches including micro-calorimetry, UV/Visible, fluorescence, circular dichroism, NMR spectroscopy and gas and liquid chromatography. The binding constant (K) for the inclusion of a guest molecule into the cavity of þ-CD [1:1 complex] was calculated from the absorption and emission spectral data by using Benesi–Hildebrand Equations (1) and (2).

5. UV-Visible Spectroscopy

Modification of UV spectra in the presence of cyclodextrin provides evidence for the formation of an inclusion complex. Spectrophotomeric determinations of CD complexes rely on the difference in the absorptivities of free and complexed substrate. On adding CD to the substrate solution in a suitable solvent, there is a hike in the absorbance in most cases, followed by a red/blue shift in absorbance maximum in a few cases. The addition of þ-CD shifts the absorption peak of indole at 285 nm to the red by about 1-5 nm and increases the absorbance. Despite the considerable amount of experimental and theoretical work on CD inclusion complexes, there is no general agreement as to how substrates interact with CDs and how the solvents affect the stability of the complexes. Some authors have suggested that binding is mainly due to dipolar interactions between the substrate and the cyclodextrin with the solvent having a minor role in stabilizing the complexes.

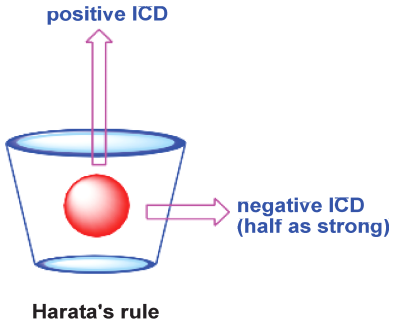
6. Fluorescence Spectroscopy

One of the most dramatic effects of molecular inclusion within cyclodextrin is fluorescence enhancement. Changes in the fluorescence spectra provide evidence for the hydrophobicity of the cavity. Cramer et al. first noticed that 8-(phenylamino)-l-naphthalenesulfonate exhibited a more intense emission in the presence of þ-cyclodextrin and presumed a 1:1 complex was formed. Since then other authors have reported enhancement of fluorescence of benzene and its derivatives in cyclodextrin. The increase in fluorescence is clearly demonstrated by the fluorescence spectra of pyrene phospholipids, Riboflavin, Naphthalene and pirixicam in the absence andin the presence of cyclodeodextrin in aqueous solution. 6-p-Toluidinylnaphthalene-2-sulphonate (TNS) is known for a fluorescent probe for the discovery of hydrophobic regions. The fluorescence of this probe is quenched in water, but in hydrophobic environments such as proteins, it is cultured with a shift of emission maxima toward shorter wavelengths and higher amounts of TNS fluorescence. TNS fluorescence increases markedly when a- or xt-cyclodextrins were added to the aqueous solution. Consequently the changes of fluorescence spectra provide evidence of the hydrophobicity of the cavity. Thus, hydrophobic bonding has been suggested as an important driving force in the formation of the inclusion complex between the dye and cyclodextrin. Recently, various fluorescent probes have been developed to study biological phenomena in living cells where fluorescence resonance energy transfer (FRET) has been used. Selective recognition and optical sensing for organic neutral molecules with artificial fluorescent cyclodextrins are also of current interest.

8. Induced Circular Dichroism (ICD)

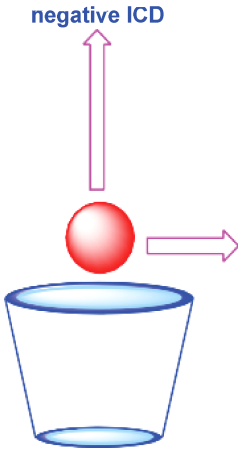
Circular dichroism is a spectroscopic technique that detects the differential absorption of spherically polarized light passing through a spiral material. a-, þ - and y-CD, which are not themselves absorbed in UV-Vis. Wavelength range and therefore, despite being a spiral compound, show no circular dipole signal (Figure 1.5). However, CDs can induce intermolecular (in particular inner molecular) circular dichroism, If they form complexes with achiral compounds affecting the incumbent chromophoric groups. A measurement of the presence of IISc due to this phenomenon is a measure of complex formation and allows determination of a constant equilibrium for association or dissociation.

Figure 1.5: Schematic Representation of CD with an Achiral Guest having Chromophore and its Induced Circular Dichroism



The analysis of the ICD spectral pattern of the chromophore of aromatic compounds are used for elucidation of the inclusion complexes, where the chromophores are situated inside the CDs cavity. According to Harata's rule, the ICD of a chromophore located inside the cyclodextrin cavity will always be positive when its electric transition dipole moment is parallel to the principal axis of the cyclodextrin. Furthermore, if the alignment inside the cavity is perpendicular to the principal axis of the host, the resulting ICD was postponed to be negative. Later, based on the Kirkwood–Tinoko theoretical calculation, Kodaka proposed that if the chromosome is located outside the guest cavity, the situation is completely reversed. Different cases are depicted in Figure 1.6.

Figure 1.6: Illustration of Harata's and Kodaka's Rule



ICD of bicyclic azo compounds in cyclodextrins has been investigated. The fascination for the study of such simple sis-azocalcanes arises from the fact that the azo group (-N = N-) is one of the smallest and simplest chromophores, but in contrast the carbonyl group (which can compete in size Is) It has a non-vanishing electric dipole transition moment ("allowed"), which facilitates interpretations of the ICD spectra.

The strong split-type ICD spectra, like an exciton coupling effect, has been observed frequently and this typical spectral change suggests the formation of a 1:2 (CD:guest) inclusion complex where a chiral dimer is trapped within the CD cavity. Studies of the complexation between y- cyclodextrin and pyrene by ICD and spectrofluorimetry have shown that two pyrene molecules can be included by a slow process

to form an *S*-helical configuration, as judged from the change in sign of the band corresponding to the ^1L_a transition. At elevated temperatures (> 66° C) a transformation into the 1:1 complex takes place.

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