HOST-GUEST CHEMISTRY

we generally consider a molecule (a ‘host’) binding another molecule (a ‘guest’) to produce a ‘host–guest’ complex or supermolecule.

Commonly the host is a large molecule or aggregate such as an enzyme or synthetic cyclic compound possessing a sizeable, central hole or cavity. The guest may be a monatomic cation, a simple inorganic anion, an ion pair or a more sophisticated molecule such as a hormone, pheromone or neurotransmitter.

More formally, the host is defined as the molecular entity possessing convergent binding sites (e.g. Lewis basic donor atoms, hydrogen bond donors etc.). The guest possesses divergent binding sites (e.g. a spherical, Lewis acidic metal cation or hydrogen bond acceptor halide anion). In turn a binding site is defined as a region of the host or guest capable of taking part in a non-covalent interaction.

The host–guest binding event may be likened to catching a ball in the hand. The hand, acting as the host, envelops the ball providing a physical (steric) barrier to dropping it (disassociation).

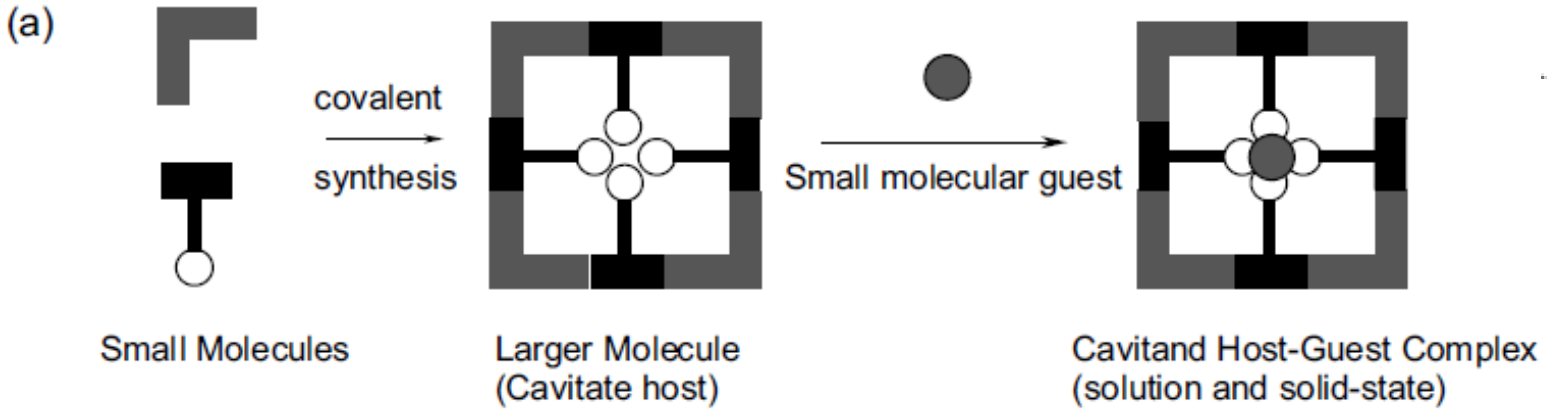
Host and guest molecules and ions usually experience an attractive force between them and hence a stabilising binding free energy.

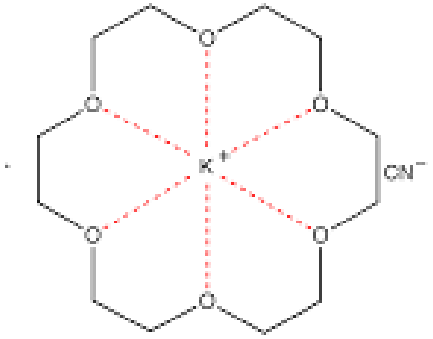
The analogy is ‘inclusion chemistry’.

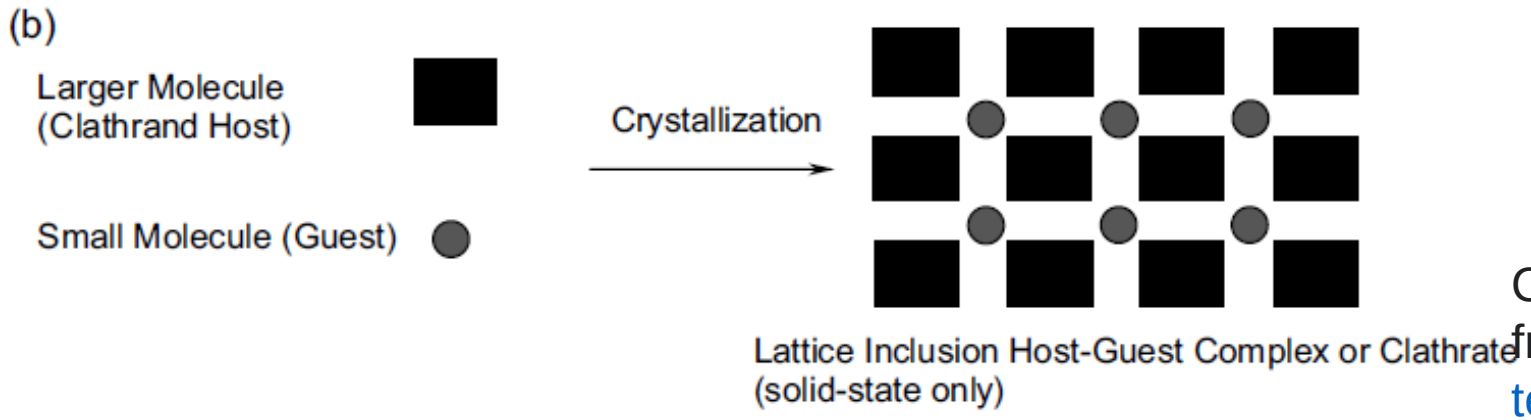
In host–guest chemistry, an inclusion compound is a chemical complex in which one chemical compound has a cavity into which a "guest" compound can be accommodated.

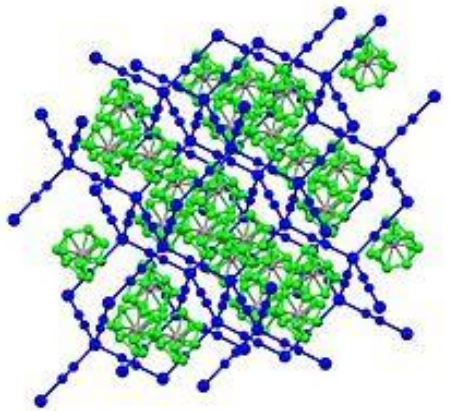
Receptors, Coordination and the Lock and Key Analogy

Host–guest (or receptor–substrate) chemistry is based upon three historical concepts:





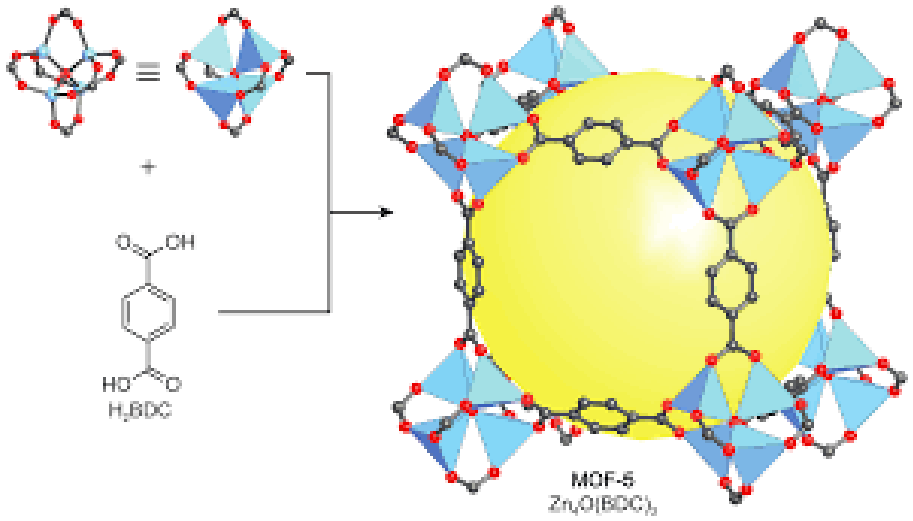


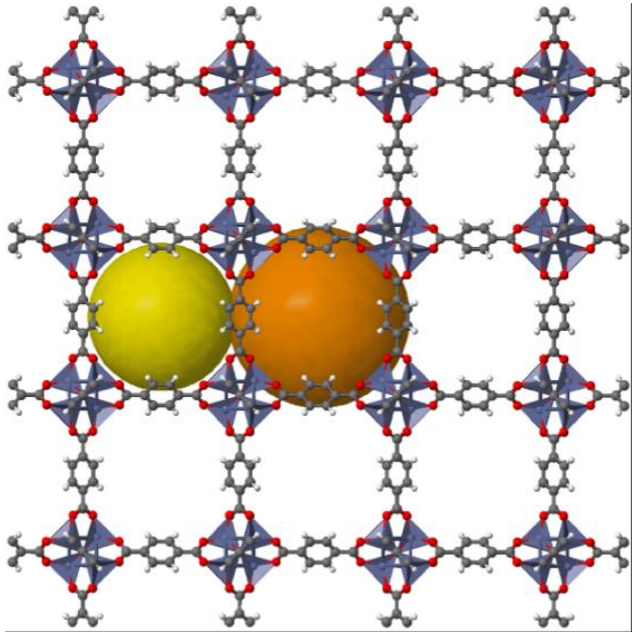


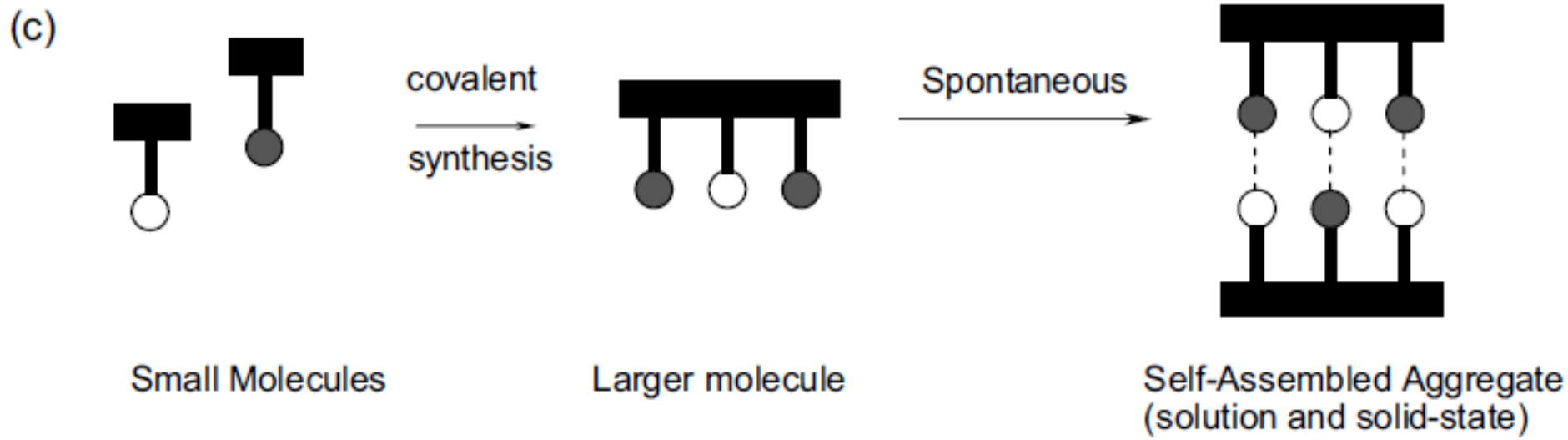
$Cd(CN)_2 \cdot CCl_4$: Cadmium cyanide clathrate framework (in blue) containing carbon tetrachloride (C atoms in gray and disordered Cl positions in green) as guest. (From Wikipedia)

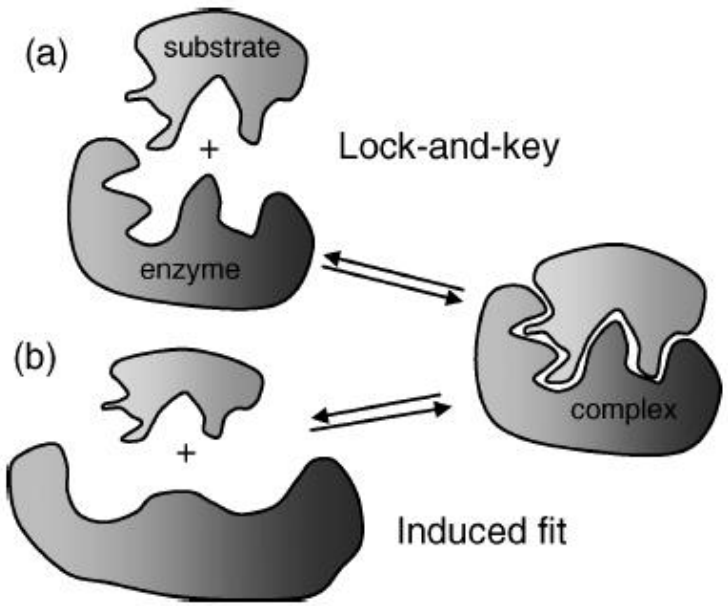
Clathrate compound

A clathrate is a chemical substance consisting of a lattice that traps or contains molecules. The word clathrate is derived from the Latin clathratus (clatratus), meaning ‘with bars, latticed’. Traditionally, clathrate compounds are polymeric and completely envelop the guest molecule, but in modern usage clathrates also include host–guest complexes and inclusioncompounds. According to IUPAC, clathrates are inclusion compounds "in which the guest molecule is in a cage formed by the host molecule or by a lattice of host molecules.









(a) Rigid lock and key and (b) induced fit models of enzyme–substrate binding.

Binding Constants

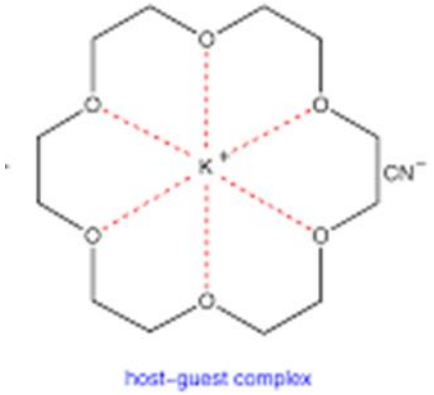
The thermodynamic stability of a host-guest (*e.g.* metal–macrocycle) complex in a given solvent (often water or methanol) at a given temperature is gauged by measurement of the binding constant, K. Strictly the binding constant is dimensionless, but it is often calculated approximately using concentrations and thus has units of $dm^3\ mol^{-1}$, or M^{-1}, for a 1:1 complex. The binding constant is also known by the terms formation constant, K_f, association constant, K_a or stability constant, K_s.

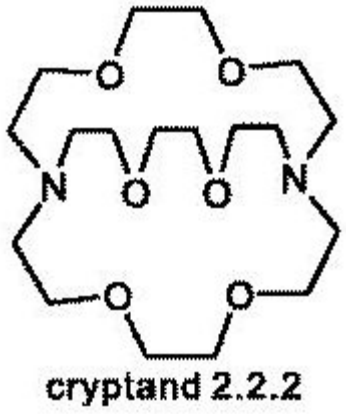
In biological systems the dissociation constant, K_d, is commonly used. This quantity is the reciprocal of the binding constant and has units of concentration. The K_d value is sometimes useful because it is a direct measure of the concentration below which a complex such as a drug-receptor complex will dissociate.

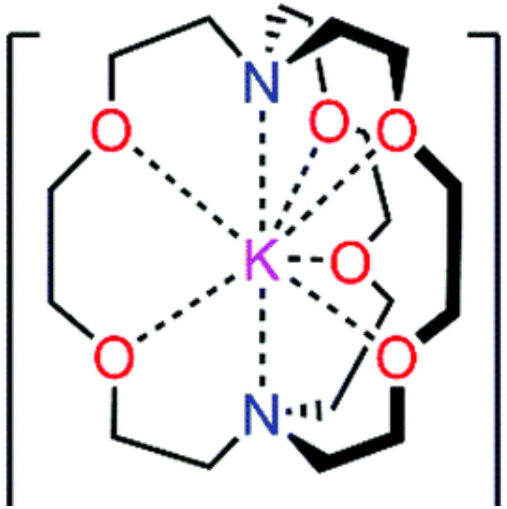
$$M(H_2O)_n^{m+} + L \rightleftharpoons ML^{m+} + nH_2O$$

$$K = \frac{[ML^{m+}]}{[M(H_2O)_n^{m+}][L]}$$

Thus a large binding constant corresponds to a high equilibrium concentration of bound metal, and hence a more stable metal–macrocycle complex. Typical binding constants for crown ethers and alkali metal cations in water are in the range 10^1–10^2. In methanol, this increases up to 10^6 for [K([18]crown-6)].The binding constant for K and [2.2.2]cryptand is about 10^{10}.







If a sequential process involving the binding of more than one metal ion is involved, then two K values may be measured for the 1:1 and 1:2 complexes, respectively: K_{11} and K_{12} (*e.g.* binding of two Na ions by dibenzo[30]crown-10).

$$M(H_2O)_n^{m+} + L \overset{K_{11}}{\rightleftharpoons} ML^{m+} + nH_2O \quad (1.3)$$

$$M(H_2O)_n^{m+} + ML^{m+} \overset{K_{12}}{\rightleftharpoons} M_2L^{(2m)+} + nH_2O \quad (1.4)$$

$$K_{12} = \frac{[M_2L^{(2m)+}]}{[M(H_2O)_n^{m+}][ML^{m+}]} \quad (1.5)$$

β_{12} may be defined for the overall process, the individual K values are then known as the stepwise binding constants:

$$\beta_{12} = K_{11} \times K_{12}$$

$$\text{Or, more generally, } \beta_{xn} = \frac{[M_x L_n]}{[M]^x [L]^n}$$

Table 1.3 Binding constants for a range of complexation processes.

Guest	Host	Solvent	K_{11}/M^{-1}	ΔG^o/kJ mol^{-1}
Na^+	ClO_4^-	H_2O	3.2	−3
Iodine	Hexamethylbenzene	CCl_4	1.35	−0.8
Tetracyanoethylene	Hexamethylbenzene	CH_2Cl_2	17	−7.1
7,7,8,8-Tetracyanoquinodimethane	Pyrene	CH_2Cl_2	0.94	~0.0
Salicylic acid	Caffeine	H_2O	44	−9.7
Hydrocortisone	Benzoate ion	H_2O	2.9	−2.5
Methyl *trans*-cinnamate	Imidazole	H_2O	1.0	0.0
p-Hydroxybenzoic acid	α-Cyclodextrin	H_2O	1130	−17.6
Caffeine	Caffeine	H_2O	19	−7.1
Phenol	Dimethylformamide	C_6H_6	442	−15.0
K^+	[18]crown-6	H_2O	100	−11.4
K^+	[18]crown-6	Methanol	10^6	−34.2
K^+	[2.2.2]cryptand	Methanol	10^{10}	−57.0
Fe^{3+}	enterobactin	H_2O	10^{52}	−296

In solution all complexation phenomena are in competition with solvation interactions and the solvent is almost invariably in a huge molar excess. Polar solvents, particularly water, compete very effectively for binding sites, particularly hydrogen bonding functionality, making hydrophobic (or solvophobic) effects of paramount importance

Indeed a common ‘trick’ to differentiate the affinity of a host for various guests is to lower the apparent binding constants by moving to a more competitive (generally more polar) solvent. Thus binding constants that are too high to measure in one solvent become lower in other solvent

Reference Book:
1. Supramolecular Chemistry: Steed and Atwood
2. Supramolecular Chemistry: A. K. Das