Chapter 5

**Answers**

**5.1.** (a) Both rotaxanes and catenanes are mechanically interlocked molecules which because of their mechanically bonded components cannot be separated without breaking or distorting chemical bonds. However, rotaxanes are considered to be topologically trivial because under continuous deformations such as stretching the macrocycle or shrinking the stoppering units, the ring and axle components may be pulled apart without breaking a chemical bond. The opposite is true for catenanes, they are a type of molecular link and so have a more complex topology then rotaxanes.

(b) The fact that the rings of a catenane cannot be separated without breaking a chemical bond means that a chemical bond must be formed in any proposed synthesis, i.e. macrocycle clipping step. However, rotaxanes, can be prepared by strategies such as shrinking, swelling and slippage, in which a pseudorotaxane intermediate becomes kinetically stabilised. The various synthetic approaches are summarised in Figure 5.4.

(c) Interactions used in template-directed MIM synthesis include; metal–ligand i.e. dative covalent bonding, π–π aromatic stacking, hydrogen bonding, hydrophobic forces, anion–hydrogen bonding and halogen bonding interactions. Non-polar solvents favour the use of weaker intermolecular forces such as hydrogen bonding and donor-acceptor π–π stacking, whilst hydrophobic and solvophobic effects are used in polar solvents, such as the inclusion complexes formed with cyclodextrin macrocycles. Whilst a strong association with the templating species is important, it is critical that these interactions template the formation of an interpenetrated assembly, i.e. a pseudorotaxane. For example, both the crown ethers in Figure 5.9 bind strongly to a secondary ammonium ion, but only the larger one is able to direct the formation of an interpenetrated assembly.

(d) Active metal templates typically deliver high yields of MIMs, require only a catalytic quantity of the metal template and form MIMs with weak inter-component interactions, beneficial for enabling dynamic properties.

e) Eglington-Glaser-Hay, Ullmann and Sonogashira reactions are all possible, using coordination of Cu(I). Likewise an oxidative Heck reaction using Pd(II) for the coupling of a boronic acid with an alkene. Ni(II) has been used to prepare a [2]rotaxane *via* bromoalkane homocoupling (see below). Importantly, all these active metal template-directed syntheses require the metal catalyst to be coordinated endotopically by the macrocycle to deliver a MIM.



**5.2.** (a) The three types of molecular motion in a MIM are translation, pirouetting and rocking, as illustrated in Figure 5.19. In a catenane the pirouetting of one ring is equivalent to the translation (or circumrotation) of the other, the terminology is dependent on the frame of reference. Typically the motion of the smaller ring is described while keeping the larger one fixed.

(b) In a non-degenerate molecular shuttle the macrocycle experiences a different interaction free energy with each station. Since station A is thermodynamically favoured, it now has the lower energy well on the potential energy profile diagram and so a higher macrocycle occupancy than station B. The population difference between these two stations will be related to their difference in free energy (Δ*G*).



(c) The free energy of guest binding (typically a gain in enthalpy due to formation of new non-covalent interactions) lowers the potential energy well for station B below that of station A, making it the favourable site for macrocycle occupancy. At constant temperature, a significant lowering in the energy of station B will increase the energy barrier the macrocycle must overcome to reach station A (Δ*G*‡) and hence slow down the kinetics of translational motion, even switching it off altogether if it does not have enough thermal energy (*kT*).



(d) Light, electrochemical (and chemical) oxidation and reduction, pH, molecular recognition (charged and neutral guests), solvent and heat (entropy shuttles) have all been used as stimuli to induce co-conformational change in molecular shuttles, by a combination of raising/lowering of wells/barriers on the potential energy landscape. The change in co-conformational bias can be characterised spectroscopically; *via* a perturbation to IR, UV-Vis-NIR absorption or fluorescence emission spectrum (e.g. change in intensity or wavelength) or NMR spectroscopy, particularly for 1H NMR where the nuclei of protons are particularly sensitive to the shielding/de-shielding effects from a proximal macrocyclic ring. A common experiment to quantify the proportion of macrocycles occupying each station uses the proton integration ratios of 1H NMR peaks for each co-conformation. To do so requires the kinetics of station exchange to be slower than the timescale of the NMR experiment, hence the sample must often be cooled down.

(e) To convert a molecular switch into a molecular motor requires the use of kinetic barriers that the macrocycle cannot pass over, essentially compartmentalising it on the axle component. This allows it to be trapped at stations that are not the lowest in energy on the potential energy landscape, a process known as ratcheting. The removal of the kinetic barrier allows the macrocycle to re-establish its equilibrium position, moving down the potential energy hill and performing work in the form of unidirectional molecular motion; the hallmark of a molecular motor.