

SUMMARY

Nature has developed a large number of ion channels and carriers which are complex systems that alter membrane permeability and allow the transport of alkali metal ions. This supramolecular process is of interest in the development of new transport systems to alter natural channel function for disease investigation.

Artificial ion channels with attached crown ethers as ionophores for cation transportation across lipid membranes have been extensively studied. Both semi- and fully synthetic channels have been investigated leading to a greater understanding of genetic diseases. The development and utilisation of new synthetic rigid rod channel systems have not been fully investigated.

The work presented in this thesis details the synthesis of rigid polycyclic frameworks with appended crown ethers for potential trans-membrane transport of alkali metal cations. The focus of this research is the development of new rigid-rod like compounds from the modular synthesis of polycyclic structures appended with crown ethers, with a high level of structural control. This research extends the established work on polycyclic norbornyl systems into creating new polycyclic compounds with appended crown ethers through a building block approach. The research carried out is most easily categorised by the number of carbon atoms linking the crown ether and the imide functionality (Figure I). Three systems were investigated using an ethylene (A), methylene (B) and a direct carbon link (C) described in Chapters 2, 3, and 4 respectively (Figure I).

The first stage of the research investigated a rigid polycyclic block with an ethylene attachment to a benzo-15-crown-5 ether as discussed in Chapter 2 (Figure I, A). Due to difficulties associated with this synthesis the ethylene attachment progressed towards a methylene connection (Figure I, B) of the polycyclic block and crown ether, discussed in Chapter 3.

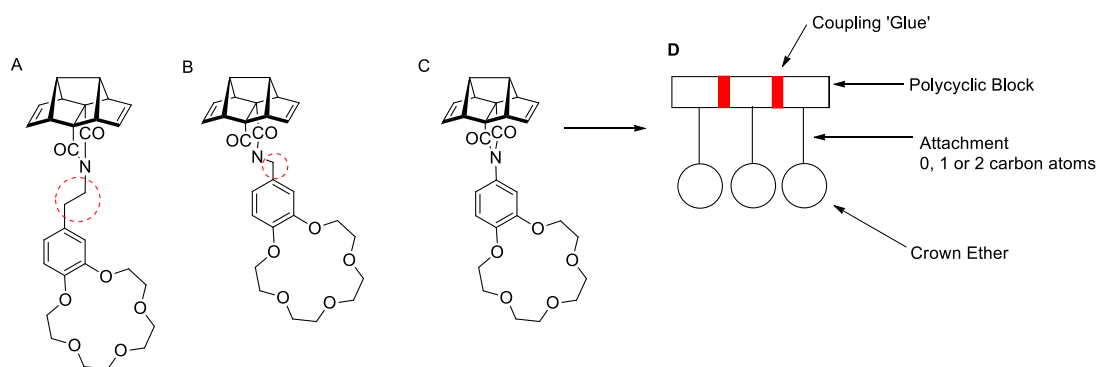


Figure I New polycyclic blocks with varying attachments between the imide and benzocrown ether, and their extension towards longer systems.

Although there was initial success in the synthesis of the compounds A and B outlined in Figure I, further synthetic procedures and methods were unable to yield coupled blocks which would see these systems extended as depicted in Figure I, D.

A new synthetic approach was required which saw all carbon units between the polycyclic norbornyl block and the crown ether removed (Figure I, C). This enabled the coupling of synthesised blocks into extended systems that were similar in length to a bilayer, and are discussed in Chapter 4.

Two tricrown systems, A and B (Figure II) were successfully synthesised and characterised by 1 and 2D NMR spectroscopy and HR-MS. Both of these tricrown systems, and similar monomer units, were analysed for complexation and transport with alkali metal ions through EIS, NMR and BLM as discussed throughout Chapter 5. Calcein release experiments were also undertaken.

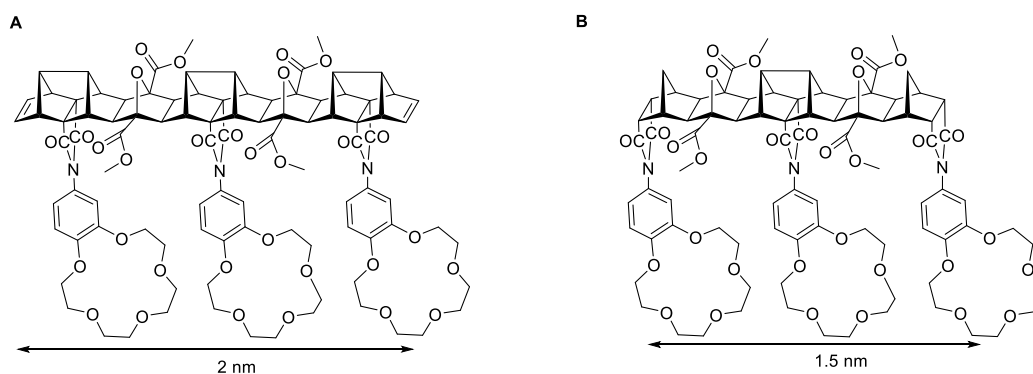


Figure II Two new polycyclic blocks with crown ethers appended for alkali metal ion transport.

The main results from these studies showed a significant trend, for both tricrown and monomer systems tested, to be the selectivity of potassium ions over sodium ions. Transport of potassium ions was monitored by the decrease in electrical resistance in EIS when the concentration of monomer was greater than 12×10^{-5} M. However the threshold concentration for transport of potassium ions with tricrown systems varied between 7×10^{-5} M and 14×10^{-5} M depending on the overall tricrown structure. These results are unusual given the preference for 15-crown-5 to complex with sodium ions rather than the larger potassium ions. However NMR complexation studies reinforced the selectivity of potassium ions (forming higher order complexes) as well as the complexation of sodium ions (1:1 and 1:2 complexes). These results are rather intriguing which require further investigation to gain a greater understanding of the potassium ion complexation as well as the mechanism of ion transport.