

## CHAPTER 1

# *Introduction*

*What is now proved was once only imagined*

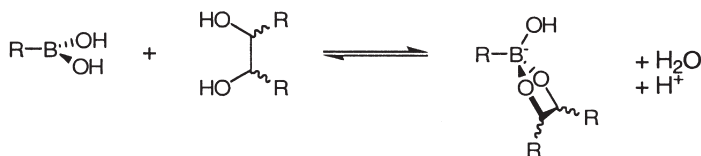
William Blake, 1757–1827

The recognition of a target molecule by a synthetically prepared receptor has captured the imagination of supramolecular chemists. Since its inception, research in this area has been instrumental in elucidating the mode of action of a great many biological events concerning recognition and catalysis.<sup>1</sup> The importance of this work was underlined with the award of the Nobel Prize in Chemistry to Cram, Lehn and Peterson in 1987 “for their development and use of molecules with structure-specific interactions of high selectivity.”<sup>2</sup> Since then the diversity of compounds studied under the umbrella of supramolecular chemistry has grown significantly. Of particular interest are chemical molecular sensors, single molecules with the ability to both recognise and signal analytes in real time.<sup>3,4</sup>

The development of coherent strategies for the selective binding of target molecules, by rationally designed synthetic receptors, remains one of chemistry’s most sought after goals. The research conducted to this end is driven by a fundamental inquisitiveness and need to monitor compounds of industrial, environmental and biological significance.

Within our research groups we have exploited the interaction between boronic acids and diols. The primary interaction of a boronic acid with a diol is covalent and involves the rapid and reversible formation of a cyclic boronate ester. The array of hydroxyl groups present on saccharides provides an ideal scaffold for these interactions and has led to the development of boronic acid-based sensors for saccharides (Scheme 1).<sup>5–18</sup>

Many synthetic receptors developed for neutral guests have relied on non-covalent interactions, such as hydrogen bonding, for recognition. It is the case, however, that in aqueous systems neutral guests may become heavily solvated. While biological systems have the capacity to expel water from their binding pockets and sequester analytes wholly, using non-covalent interactions, synthetic monomeric receptors have not yet been designed where hydrogen



**Scheme 1** *The rapid and reversible formation of a cyclic boronate ester.*

bonding has been able to compete with bulk water for low concentrations of monosaccharides.<sup>19</sup> However, it should be pointed out that progress is being made in this area and recently Davis reported a hydrogen-bonding receptor capable of binding D-glucose in water with a weak but significant stability constant.<sup>20</sup>

The capacity of boronic acid receptors to function effectively in water is reflected by the number of published sensory systems designed around them. The most popular class of the fluorescent boronic acid-based sensors utilise an amine group proximal to boron. The Lewis acid–Lewis base interaction between the boronic acid and the neighbouring tertiary amine has a dual role. First, it enables molecular recognition to occur at neutral pH. Second, it can be used to communicate binding by modulating the intensity of fluorescence emission through photoinduced electron transfer (PET), introducing an “off–on” optical response to the sensor.

The quality of the research in this area, particularly in the past few years, has led to a significant advance in the understanding of the basic science behind the generic mode of action of this class of receptor. *This book will therefore bring together and critique the contemporary scientific understanding of the fundamental processes involved in the molecular recognition of saccharides by boronic acids.* It should be noted that a comprehensive overview of this nature has not been previously reported in the scientific literature. *A literature review will then investigate the application of these sensory systems.* Although this review cannot be exhaustive, it is our intention to illustrate the current state of play in the field.