

MINIMAL SYNTHETIC SELF-REPLICATING SYSTEMS - A HOST-GUEST APPROACH

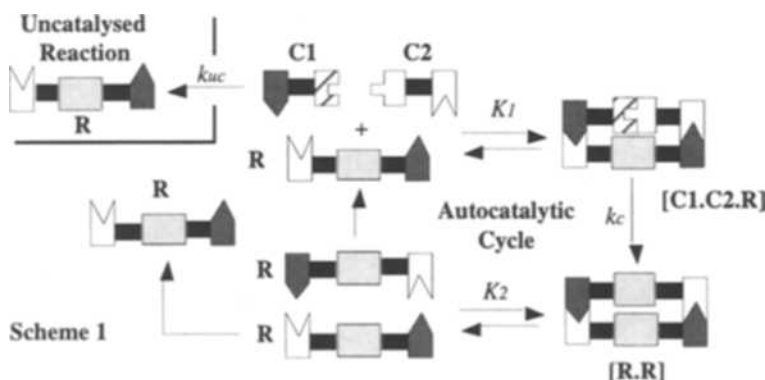
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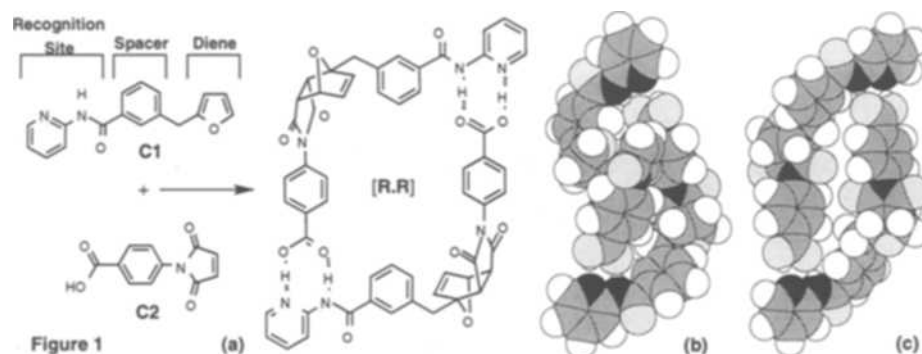
The engineering of nanometre-scale (nanoscale) structures has fascinated and inspired¹ the scientific community for a quarter of a century. Although there are no fundamental thermodynamic² or quantum mechanical³ impediments to the development of nanoscale architectures, there is a growing realisation⁴ that "engineering down" approaches, *i.e.* a reduction in the size of structures generated by lithographic techniques below the present 1 μm lower limit, are impractical. It has therefore become increasingly clear that only by extension of our knowledge of the self-assembly⁵ of large-scale biological structures which exist and function at and beyond the nanoscale *downwards* and the extension of our knowledge regarding the chemical synthesis of small scale structures *upwards*, can the gap between the promise and the reality of nanosystems be closed. This approach to nanoscale structures and systems may be termed the "bottom-up" or "engineering-up" approach.⁶

A pivotal role in the development in the field of nanotechnology will be played by systems which are capable of templating and catalysing their own synthesis – *self-replicating systems*. In the present context, we are developing a series of systems which can reproduce themselves efficiently without external co-factors, *i.e.* non-enzymatic replicators. Most of the non-enzymatic self-replicators which have appeared in the literature to date are based on the minimal model⁷ shown in **Scheme 1**.



Two reaction channels exist. The first is the uncatalysed bimolecular reaction of **C1** and **C2** to give **R**. The second is the *autocatalytic cycle*. **C1** and **C2** bind to **R** to form the catalytic ternary complex [**C1.C2.R**]. Bond formation occurs between **C1** and **C2** to give the product duplex [**R.R**] which then dissociates to return *two* molecules of **R** to the autocatalytic cycle. The importance of the autocatalytic cycle to the overall reaction rate depends on the magnitude of K_1 , K_2 and k_c compared with k_{uc} .

By utilising a variety of recognition sites and bond forming reactions, we have created a series of four replicators systems. **Figure 1** shows calculated structures of the catalytic ternary complex (**Figure 1b**) and product duplex (**Figure 1c**) of one of our self-replicating systems which is based on the molecular recognition between a carboxylic acid and an amidopyridine and utilizing the Diels-Alder reaction in the bond forming step. The synthesis and kinetic behavior of this and our other replicating systems will be reported.



¹ R.P. Feynman *Eng. & Sci.* **1960**, 23(2), 22; K.E. Drexler *Engines of Creation*, Fourth Estate, London, **1990**.

² C.H. Bennett *Int. J. Theor. Phys.* **1982**, 21, 905.

³ J.R.P. Feynman *Found. Phys.* **1986**, 16, 507.

⁴ F.L. Carter *Physica* **1984**, 10D, 175; D. Haarer *Angew. Chem. Int. Ed. Engl.* **1989**, 28, 1544.

⁵ J.S. Lindsey *New. J. Chem.* **1991**, 15, 153; D. Philp, J.F. Stoddart *Synlett* **1991**, 445; G.M. Whitesides, J.P. Mathias, C.T. Seto *Science (Washington DC)* **1991**, 254, 1312; D.S. Lawrence, T. Jiang, M. Levett *Chem. Rev.* **1995**, 95, 2229; D. Philp, J.F. Stoddart *Angew. Chem. Int. Ed. Engl.* **1996**, 35, May Issue.

⁶ R.C. Haddon, A.A. Lamola *Proc. Natl. Acad. Sci.* **1985**, 85, 1874; J.S. Miller *Adv. Mater.* **1990**, 2, 378, 495, 601.

⁷ See, for example, G. von Kiedrowski *Angew. Chem. Int. Ed. Engl.* **1986**, 25, 932; T.K. Park, Q. Feng, J. Rebek Jr *J. Am. Chem. Soc.* **1992**, 114, 4529 A. Terfort, G. von Kiedrowski *Angew. Chem. Int. Ed. Engl.* **1992**, 31, 654. M. Famulok, J.S. Nowick, J. Rebek Jr *Acta Chem. Scand.* **1992**, 46, 315.