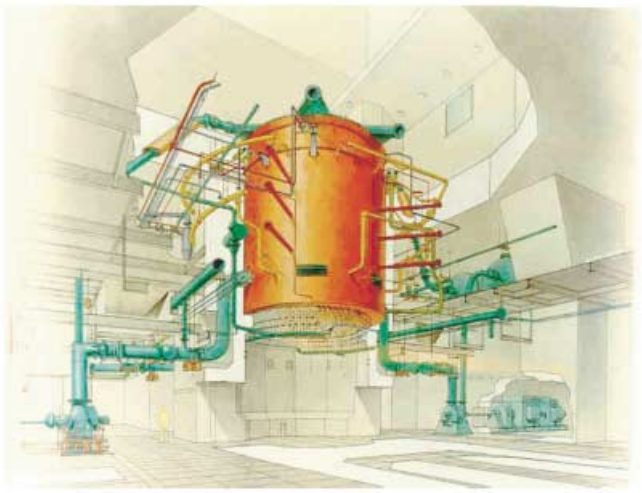
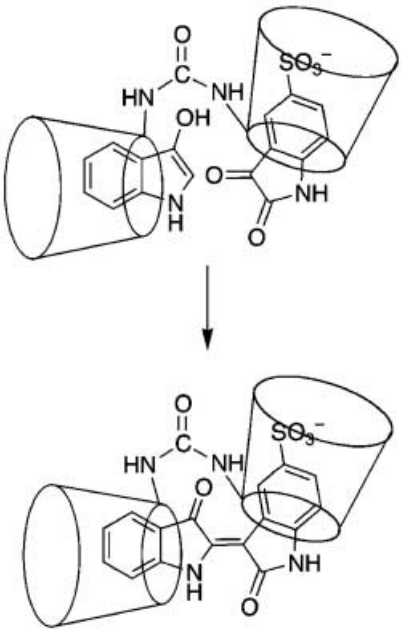
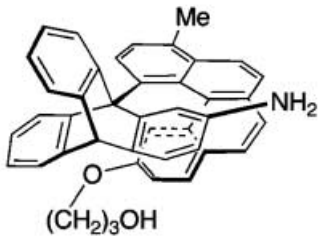
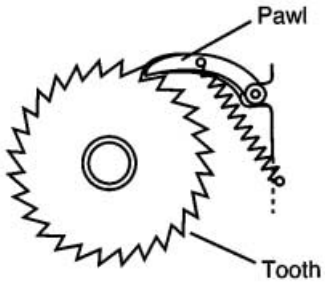
Molecular Reactors and Machines

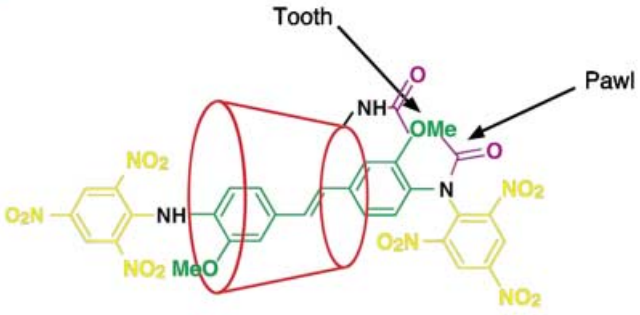




How useful are molecular mechanical devices?







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Molecular Reactors and Machines: Applications, Potential, and Limitations

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Abstract: Molecular reactors are miniature vessels for the assembly of reactants at the molecular level, in order to change the nature of chemical transformations. It seems probable that those that will find most immediate applications are those that change product ratios or give products which would not readily form in the absence of the reactors, and thereby afford easy access to materials that are otherwise difficult to obtain. Molecular machines consist of interrelated parts with separate functions and perform some kind of work, at the molecular level. Practical examples are likely to be relatively uncomplicated and not based on individual functions of single-molecule devices. Instead they will probably rely on extensive redundancy of the molecular components and their interactions and reactions, as well as of the machines themselves.

Keywords: molecular devices · molecular reactors · nanotechnology · scaffolds · template synthesis

Introduction

An examination of the recent scientific literature might lead to the conclusion that nanotechnology is only a very recent discovery. Many scientists disagree, however, arguing instead that it is simply a new label.[1] The issue is clouded further by the lack of a specific definition of the field that clearly distinguishes it from other areas of chemistry, physics and biology. Nevertheless, it would be unrealistic not to acknowledge some of the important new scientific developments that have been described under this heading and their commercial implications, as well as the way in which reports such as the construction of a molecular abacus[2] and light-harvesting devices[3] have captured the imagination. The purpose of this article is to evaluate two particular aspects of nanotechnology: those involving molecular reactors and machines. The aim is to analyse what these topics involve, to survey a selection of recent publications in the areas and to assess the potential for practical applications of the results. The emphasis is on supramolecular systems and particularly those based on cyclodextrins, since this is our principal field of interest, but many of the comments that apply to these systems are also relevant in a broader context.

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Molecular Reactors

Reactors are vats for carrying out chemical reactions. It follows that *molecular reactors are miniature vessels for the assembly of reactants at the molecular level, to change the nature of chemical transformations.* It is implicit that a molecular reactor must alter a reaction to make it different from that that would occur in a bulk medium, such as a common solvent, otherwise there is no need for a special definition.

Catalysts: The most common types of molecular reactors are molecular hosts that act as catalysts, to increase the rates of reactions of included guests or to induce those reactions to occur under less extreme conditions, such as at lower temperatures or at near neutral pH in aqueous solution. Systems of this type have been studied extensively for several decades,[4–6] and build on even earlier studies by physical organic chemists of anchimeric assistance and neighbouring-group participation. Many are based on the principles expounded more than fifty years ago in Pauling's molecular recognition and transition-state theory of enzyme catalysis,[7] and are therefore referred to as enzyme mimics or artificial enzymes.[4] Of course enzymes are themselves

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molecular reactors, but the focus of this article is on chemists' inventions.

Some quite remarkable catalysts have been reported. A most impressive example is the flavo–thiazolio–cyclophane **1** of Mattei and Diederich[8] (Figure 1), which is a model for

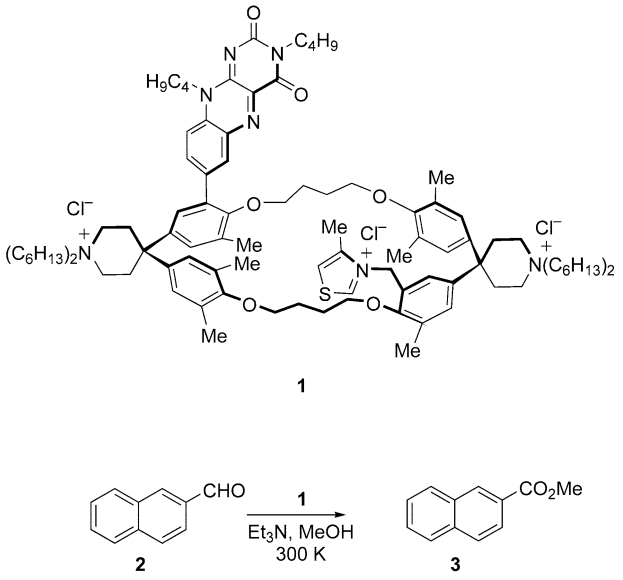
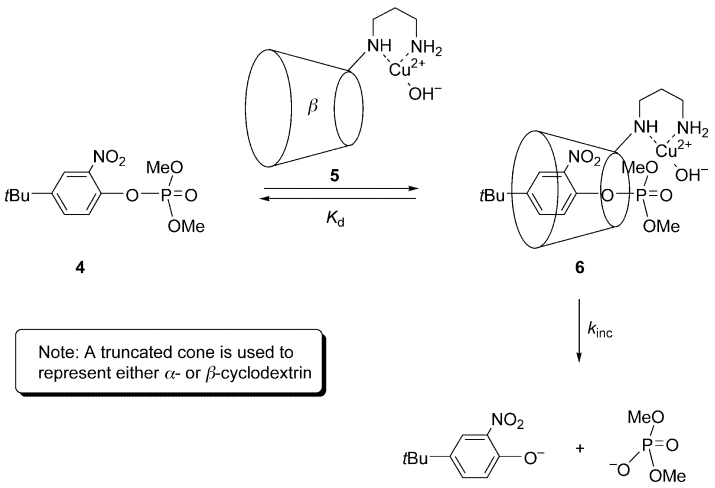


Figure 1. The pyruvate oxidase mimic of Mattei and Diederich.[8]

the enzyme pyruvate oxidase. It catalyses the oxidation of aromatic aldehydes to the corresponding methyl esters in basic methanol. The catalytic cycle has a turnover number of approximately 100 and involves the covalent attachment of a substrate to the cyclophane's thiazolium group, oxidation of the bound substrate by the flavin moiety, release of the product through methanolysis and then electrochemical re-oxidation of the reduced flavin. The conversion of the aldehyde **2** to the ester **3** is catalysed very efficiently, with $k_{cat} = 0.22\ s^{-1}$ at 300 K in 50 mM methanolic triethylamine.

In a somewhat simpler system, the metallocyclodextrin **5** is a very effective catalyst for the hydrolysis of the phosphate triester **4** (Scheme 1).[9] In aqueous solution at pH 7.0 and 298 K, the ternary complex **6** forms very readily ($K_d = 4.3 \times 10^{-3}\ mol\,dm^{-3}$) and, under these conditions, the pseudo-first-order rate constant for reaction of the included species ($k_{inc} = 3.1 \times 10^{-2}\ s^{-1}$) is 97000 times higher than that for the hydrolysis in free solution ($k_{un} = 3.2 \times 10^{-7}\ s^{-1}$).

Despite the progress that has been made through the development of these and numerous other prototype catalysts, for the most part it is unlikely that they will be exploited in practical applications to any significant extent in the near future. The science is important and innovative, but it is still only at an early stage, and as yet the majority of the catalysts offer little in the way of real advantages over other more conventional chemical systems. Furthermore, they are generally rather complicated and difficult to assemble. The conversion of aldehydes to esters is a standard transformation that is readily accomplished without the need to resort to the eighteen-step synthesis that was required to produce the cyclophane **1**. The hydrolysis of phosphate esters can be



Scheme 1. Hydrolysis of the triester **4** catalysed by the metallocyclodextrin **5**.

achieved either at elevated temperatures or under acidic or basic conditions in the absence of the metallocyclodextrin **5**. Without much more research, it is doubtful that we will be able to routinely produce useful catalytic molecular reactors that act simply by increasing the rates of reaction or by changing the conditions required for reaction.

Scaffolds and templates: Instead it seems probable that molecular reactors will find more immediate practical applications where they act as scaffolds and templates for chemical transformations,[10] to change product ratios or to give products that would not readily form in the absence of the reactors, and thereby afford easy access to materials that are otherwise difficult to obtain.

Some of the most straightforward molecular reactors of this type involve a change in the regioselectivity of reaction of a substrate as a result of access of a reagent being restricted.[11–14] In a representative example from our own work,[11] which builds on earlier studies of aromatic chlorination by Breslow et al.,[12,13] α- and β-cyclodextrin have been shown to change the ratios of products of bromination of anisole **7** and acetanilide **9** with pyridinium dichlorobromate (Scheme 2). Substitution at the *para*-position is preferred, presumably because the *ortho*-positions are shielded (Figure 2), and the effect is greatest with α-cyclodextrin.

There are evident benefits to be gained from using such a system. The cyclodextrins are now affordable and readily available. They greatly increase the solubility of the substrates **7** and **9** in water, making it practical to use this as a

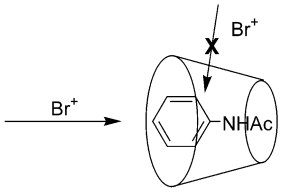


Figure 2. Effect of a cyclodextrin restricting access of a brominating agent to the *ortho* position of acetanilide **9**.

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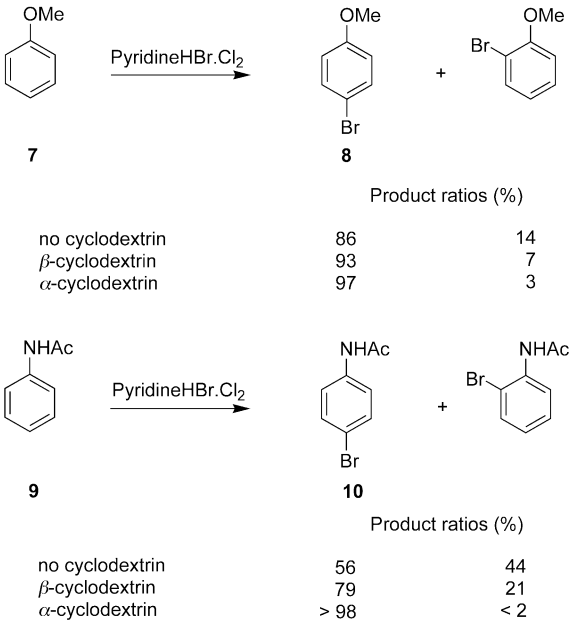

Scheme 2. Bromination of anisole **7** and acetanilide **9** with pyridinium dichlorobromate in water at 298 K.

cheap and environmentally benign alternative to the organic solvents normally employed for such transformations. The aqueous solution of the cyclodextrin can be recycled through a batch-type process, simply by adding the reagent and substrate, allowing the reaction to proceed and then removing the product by solvent extraction. The yields of the bromides **8** and **10** are increased. Lower quantities of byproducts are formed, so there is less waste, and product isolation and purification is made easier. The method is neither conceptually difficult nor technically demanding. In fact it is the simplicity that makes it so attractive, and it is difficult to imagine a more practical method for preparation of the bromides **8** and **10**, particularly on a large scale.

Of course these effects of the cyclodextrins are partly fortuitous and the demand for the bromides **8** and **10** is likely to be limited! A wider range of applications will depend on our ability to design systems to achieve particular outcomes. Although this continues to be a challenge, it has already been accomplished in a number of cases. Breslow et al.[15–17] have reported reactors for the regio- and stereoselective functionalisation of substrates at unactivated positions, including the cytochrome P450 mimic **11**, which oxidises the diester **13** to **14** and, therefore, provides ready access to the triol **15** from the diol **12** (Figure 3).[15,16] This group has also used imidazole-substituted cyclodextrins to control aldol condensations.[18] In another case involving C–C bond formation, a urea-linked cyclodextrin dimer has been used as a scaffold for the reaction of indoxyl **16** with the isatinsulfonate **17**, changing the ratio of formation of indigo **18** and the indirubinsulfonate **19** by a factor of at least several thousand (Scheme 3).[19]

Templating pericylic reactions has attracted particular attention,[20–22] probably because they are especially dependent on the orientation of the reactants. Sanders' group has used the metalloporphyrin trimers **20** and **21** to change the ratio of formation of the *exo*- and *endo*-Diels–Alder adducts **24** and **25** from the furan **22** and the alkene **23** (Figure 4).[20] We have used cyclodextrins to control the relative orientations of nitrile oxides and dipolarophiles in order to reverse the regioselectivity of their cycloadditions (Scheme 4).[21] More recently, Chen and Rebek[22] have used a resorcinarene-based tetraimide to control the regioselectivity of the

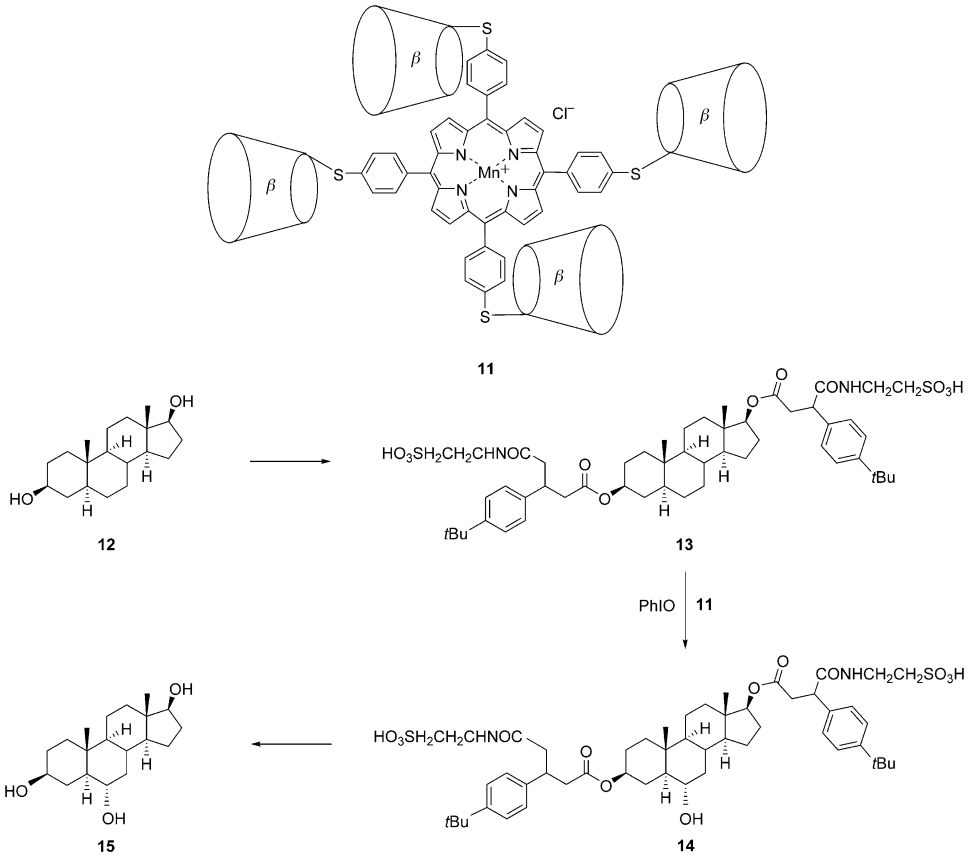

Figure 3. Regio- and stereoselective hydroxylation of the steroid **12**.

reaction of phenylazide with phenylacetylene. In addition to changing the product ratios, these molecular reactors are substrate selective and increase the rates of the reactions they template. For example, at millimolar concentrations in water at 298 K, the reaction of the nitrile oxide **27** with the

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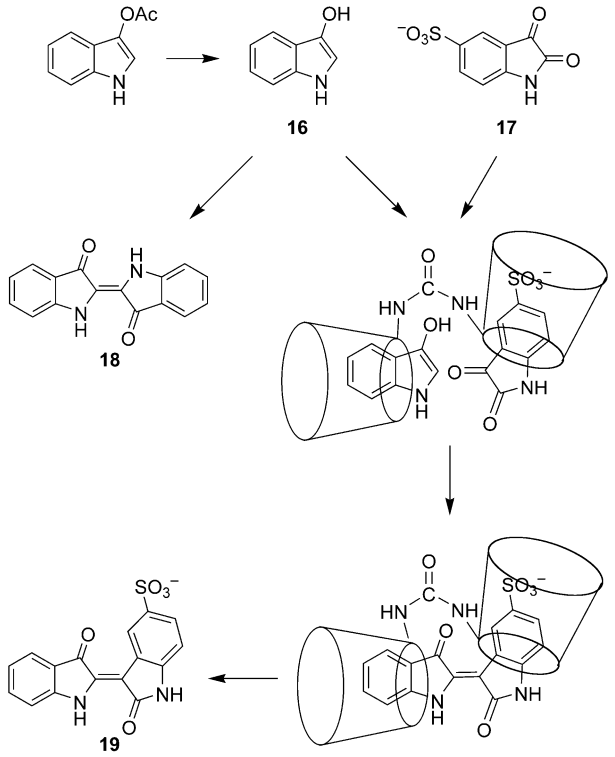

Scheme 3. Effect of a cyclodextrin dimer to template formation of the indirubinsulfonate **19**, at 298 K in 10 mM borate buffer at pH 10.0.

A limitation of many molecular reactors is that they are not catalytic, as a consequence of their design. Where they function by binding the reactants in a geometry that resembles that of the products, almost inevitably the products bind more strongly, leading to product inhibition. One way to address this is to include, within a catalytic cycle, the creation and deconstruction of interactions that are responsible for reactant and product binding. Accordingly, we are developing the use of β-cyclodextrin in a catalytic variation of the cycloaddition shown in Scheme 4.[23] Acylation of β-cyclodextrin through reaction with a nitrophenyl ester installs the dipolarophile, which then reacts with the nitrile oxide. Subsequent hydrolysis of the cyclodextrin ester releases the cycloadduct and regenerates the cyclodextrin. Consequently, binding of the reactant and the product to the cyclodextrin occurs through an ester link, which is only formed transiently.

Seeking improvements of this type continues to be an active topic of research and much more will be required in order for the full potential of the templating effects of molecular reactors to be realised. Meanwhile, the less complicated prototypes, such as that illustrated in Scheme 2, already offer distinct practical gains and it is reasonable to assume that we will soon see examples of their exploitation.

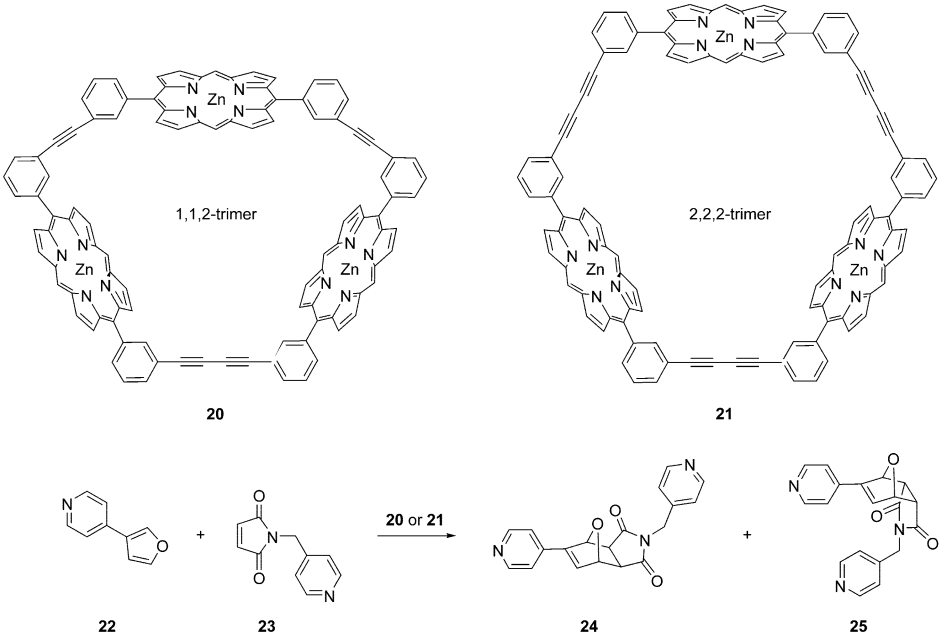

Figure 4. Effect of metalloporphyrin trimers to template a Diels–Alder reaction.

alkynylcyclodextrin **26** is at least a thousand times faster than the reactions of either *tert*-butylnitrile oxide with the alkyne **26** or the nitrile oxide **27** with propiolamide **28**.[23] Despite these effects, for the reasons outlined above, the major practical advantage with these systems is still the clean formation of products that are otherwise difficult to access.

Molecular Machines

Already molecular machines have been extensively applied. Based on the literal definition that *a machine is an apparatus, consisting of interrelated parts with separate functions, and used in the performance of some kind of work, and that a molecular machine is merely a machine that functions at the molecular level,* there are many types in everyday use. Phenolphthalein and other pH indicators, which may be protonated or deprotonated on one part to consequently change the spectroscopic properties of another, thereby providing a visible measure of proton concentration, are simple examples. Others include sensors that fluoresce on binding metal ions to give spectroscopic responses, and phase-transfer agents, which combine a binding function with an ability to move between phases, and can therefore transport chemicals across solvent interfaces. Each of these relies on distinct functions of several interacting components to operate, so they are molecular machines in the strict sense of the words. However, they are not ones that are typically identified with the topic. Instead, molecular machines are more commonly

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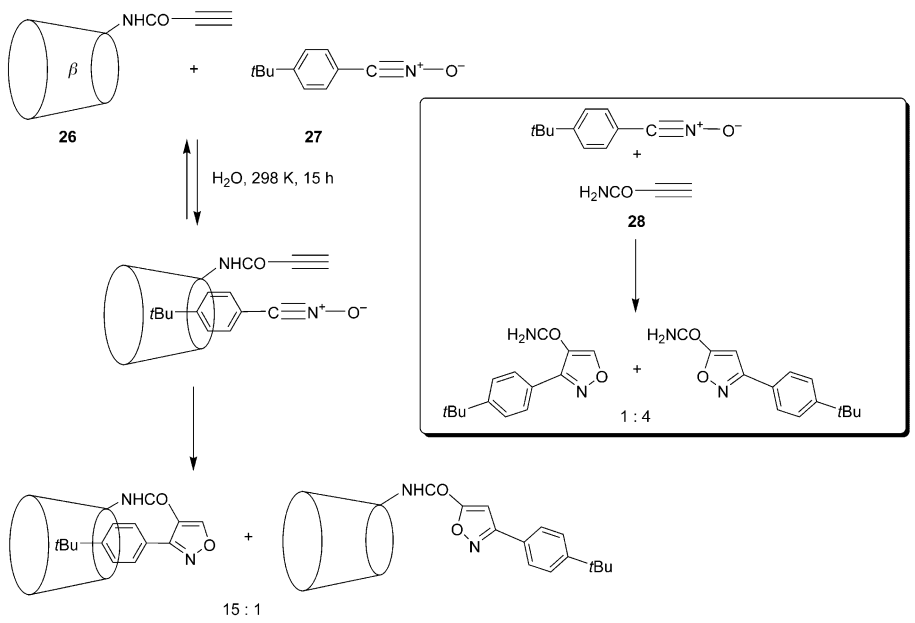
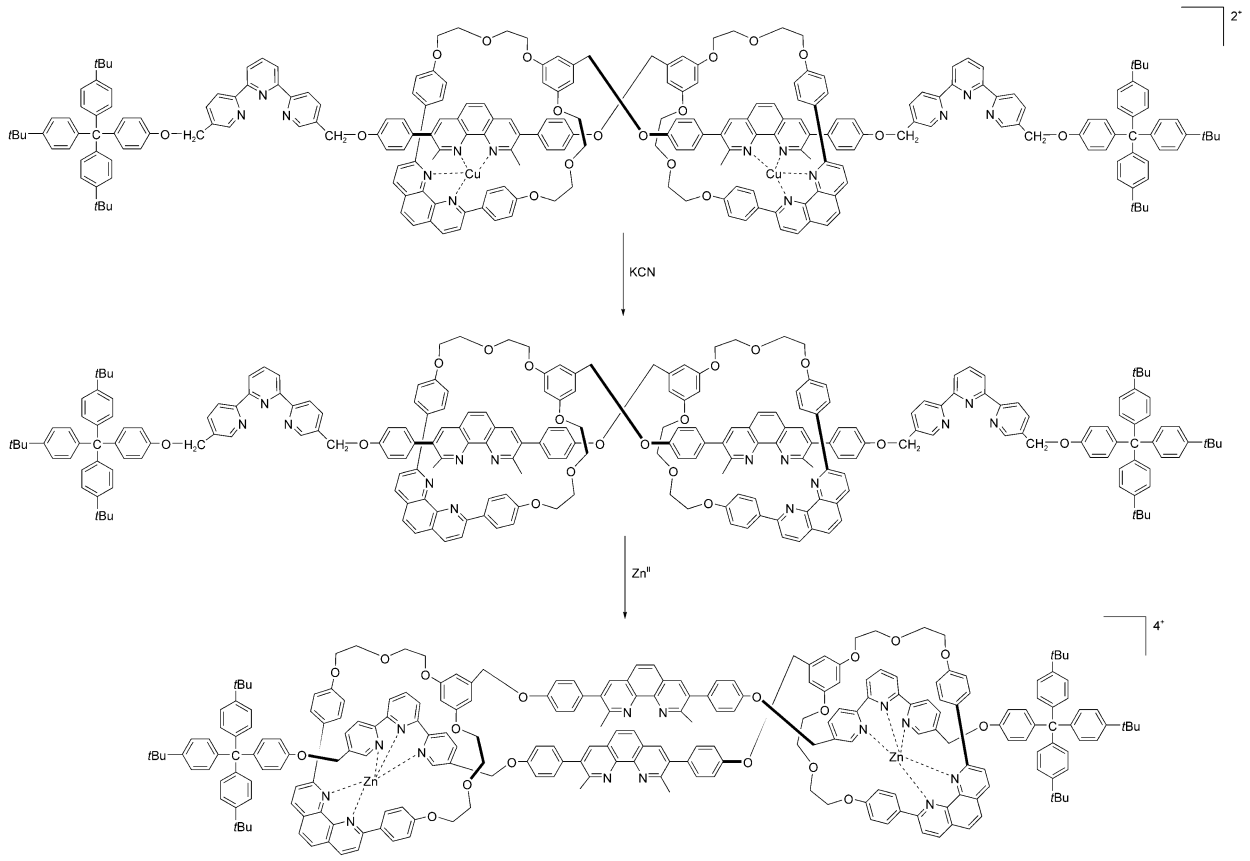


Scheme 4. Effect of a cyclodextrin to reverse the regioselectivity of a nitrile oxide cycloaddition.

associated with the Feynman concept[24,25] of constructing intricate purpose-built mechanical devices from the "bottom-up", that is, from bringing together complicated combinations of molecules, with interconnected functions, to work as complex supramolecular assemblies.[26,27] The distinction is subtle, particularly since most of the research in this very active area continues to be directed at building the component parts, which actually fit the more literal definition.

The multicomponent, multifunction machines that have been envisaged have yet to eventuate and, as is discussed in more detail below, it is not clear when or even if they will be. Despite this, during the last decade or so there have been many reports of the construction of elegant molecular gadgets such as switches,[28,29] shuttles,[30] gears,[31] ratchets,[32,33] brakes,[34] rotors,[35] lifts[36] and sensors.[37–41] Another fascinating example is the molecular muscle reported by Sauvage et al.[42,43] and is illustrated in Scheme 5; it involves the ion-induced expansion and contraction of an hermaphrodite rotaxane dimer. The molecular motors of Kelly et al.[44,45] (Scheme 6), and Feringa and coworkers[46–48] (Scheme 7) are particularly ingenious. We have developed the rotaxane **29** as the basis of a molecular ratch-



Scheme 5. Reversible ion-induced motion of a molecular muscle.

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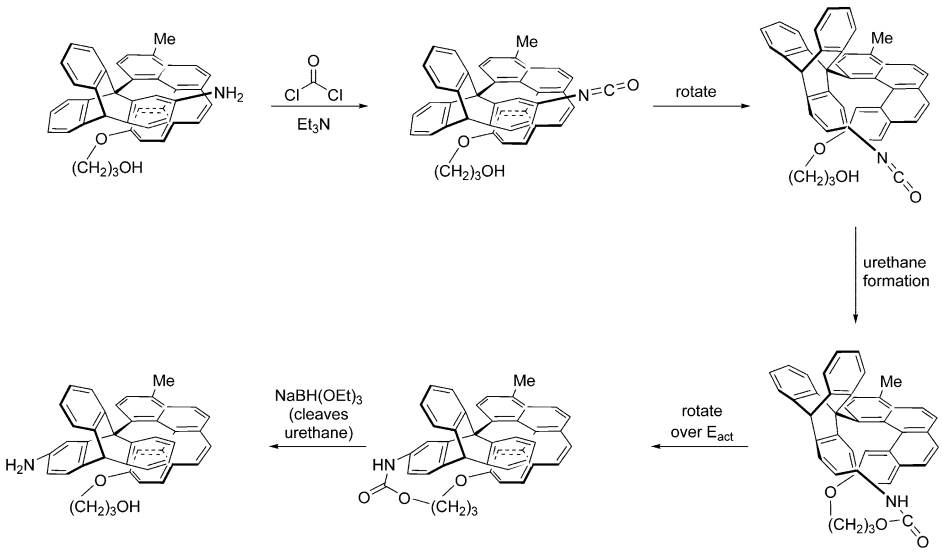
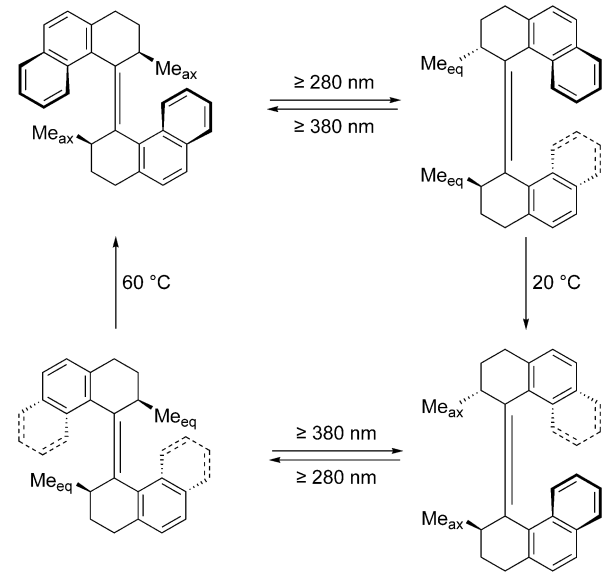


Scheme 6. A molecular motor developed by Kelly et al.[44,45]



Scheme 7. A molecular motor developed by Feringa et al.[46–48]

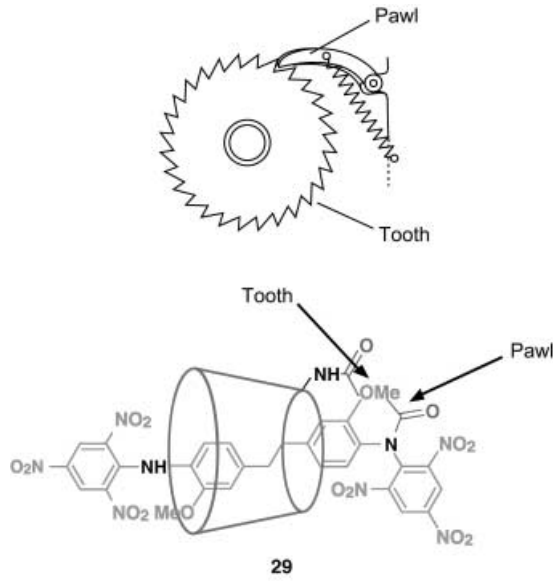


Figure 5. Towards a molecular ratchet.

et (Figure 5)[49] and explored the effect of cyclodextrins in rotaxanes to align and separate molecular fibres formed by the axle components in solid-state self-assemblies (Figure 6).[50] The result in this case is self-assembled structures that resemble co-axial cables, and it is interesting to speculate that such systems might one day find application in microelectronic devices. Already, Anderson and co-workers[51,52] have demonstrated insulating properties of the cyclodextrins of β-cyclodextrin–poly(*p*-phenylene) polyrotaxanes in solution. Other intriguing recent examples of molecular devices include a manganese(III) porphyrin threaded onto a polybutadiene strand and which moves along the strand, catalysing epoxidation of double bonds of the polymer.[53] Among the sensors that have been developed,[37–41] those of Bayley et al.[38–41] are especially innovative. These use engineered transmembrane protein pores for stochastic sensing of single-molecule binding and reaction events. The analyte is detected through its affect on the ion current through the pore.

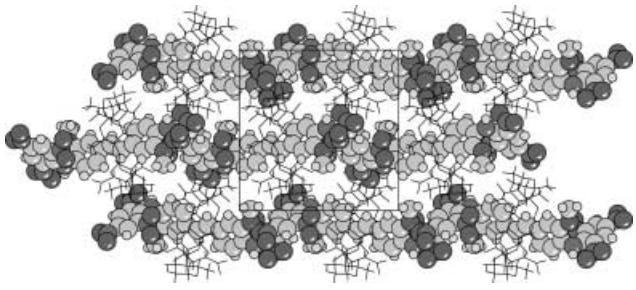


Figure 6. Insulated molecular fibres in solid-state self-assemblies of cyclodextrin rotaxanes.

Limitations of single-molecule devices: Ironically, the ability of the Bayley systems to sense single-molecule processes exposes one of the limitations of any device based on the function of an individual molecule. Chemical processes are characterised by kinetic and thermodynamic parameters that are statistical averages based on the Boltzmann distribution of the activity of many molecules. A single-molecule event may be quite different from the average and it is, therefore, not characteristic. Instead, to obtain distinctive data with the Bayley systems it is necessary to monitor repeat events in order to obtain typical patterns of behaviour, thus compromising any advantages arising from the

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ability to monitor a single-molecule process. For similar reasons, any device that depends on the activity of a single molecule is likely to behave in an unreliable and irreproducible manner, due to variations in the energetics. The problems will be exacerbated in any machines that rely on the timing of interdependent sequences of molecular events. Further, any such molecular apparatus will only function repeatedly in a predictable way if each of the events is irreversible and occurs with close to one hundred percent efficiency, and yet the system must be easily restored to its original condition for the next cycle. These are extremely daunting obstacles that must be overcome if we are to build complex single-molecule devices. We must also devise more clever ways for the molecular components of these devices to interact and for the output from these devices to be improved, in order for them to do useful work. Otherwise practical molecular analogues of machines such as the conventional petrol-driven engine, that relies on, inter alia, precision timing of the firing of cylinders, the almost inevitable response of the pistons and then their return to their original positions before the next firing, will never be realised.

Conclusion

Useful molecular machines are most likely to be relatively uncomplicated and not based on individual functions of single-molecule devices. Instead they will probably rely on extensive redundancy of the molecular components and their interactions and reactions, as well as of the machines themselves. Then the output of the machines will depend on the average behaviour of a significant number of molecules or supramolecular assemblies, and it will not be impaired as a result of either the failure of a single-molecule chemical process or statistical variations. This is the case with the majority of the prototype molecular machines that have already been reported and the concept has ample precedent in other areas. Computer data is recorded with a redundancy of approximately thirty-percent, simply to validate the basic binary code. Redundancy is also important at all levels in biological systems, which can therefore continue to survive and flourish irrespective of the malfunction of either a single molecule, cell or higher organism (even a human!). Biological systems also rely on repair mechanisms to excise errors, but it is not evident that this is a realistic objective with molecular machines.

This leads to the conclusion that most useful new molecular machines are likely to conform to the literal definition. The Feynman concept[24,25] of constructing intricate mechanical devices one molecule at a time continues to be a challenging and elusive goal. Nevertheless simple and practical molecular machines and reactors are already a reality.

Acknowledgements

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[1] See for example, A. J. Bard, *Chem. Eng. News* **1999**, *77*, 5.
[2] H. Shigekawa, K. Miyake, J. Sumaoka, A. Harada, M. Komiyama, *J. Am. Chem. Soc.* **2000**, *122*, 5411.
[3] a) L. Jullien, J. Canceill, B. Valeur, E. Bardez, J.-P. Lefevre, J.-M. Lehn, V. Marchi-Artzner, R. Pansu, *J. Am. Chem. Soc.* **1996**, *118*, 5432; b) G. Steinberg-Yfrach, P. A. Liddell, S.-C. Hung, A. L. Moore, D. Gust, T. A. Moore, *Nature* **1997**, *385*, 239; c) M. Tamura, D. Gao, A. Ueno, *Chem. Eur. J.* **2001**, *7*, 1390; d) U. Hahn, M. Gorka, F. Vögtle, V. Vicinelli, P. Ceroni, M. Maestri, V. Balzani, *Angew. Chem.* **2002**, *114*, 3747; *Angew. Chem. Int. Ed.* **2002**, *41*, 3595.
[4] W. B. Motherwell, M. J. Bingham, Y. Six, *Tetrahedron* **2001**, *57*, 4663.
[5] J. K. M. Sanders, *Chem. Eur. J.* **1998**, *4*, 1378.
[6] F. Hof, S. L. Craig, C. Nuckolls, J. Rebek Jr. , *Angew. Chem.* **2002**, *114*, 1556; *Angew. Chem. Int. Ed.* **2002**, *41*, 1488.
[7] L. Pauling, *Chem. Eng. News* **1946**, *24*, 1375.
[8] a) P. Mattei, F. Diederich, *Angew. Chem.* **1996**, *108*, 1434; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1341; b) P. Mattei, F. Diederich, *Helv. Chim. Acta* **1997**, *80*, 1555.
[9] L. Barr, C. J. Easton, K. Lee, S. F. Lincoln, J. S. Simpson, *Tetrahedron Lett.* **2002**, *43*, 7797.
[10] C. J. Easton, S. F. Lincoln, *Modified Cyclodextrins. Scaffolds and Templates for Supramolecular Chemistry*, Imperial College Press, London, **1999**.
[11] P. G. Dumanski, C. J. Easton, S. F. Lincoln, J. S. Simpson, *Aust. J. Chem.* **2003**, *56*, 1107.
[12] R. Breslow, P. Campbell, *J. Am. Chem. Soc.* **1969**, *91*, 3085.
[13] R. Breslow, H. Kohn, B. Siegel, *Tetrahedron Lett.* **1976**, *17*, 1645.
[14] M. Komiyama, H. Hirai, *J. Am. Chem. Soc.* **1984**, *106*, 174.
[15] R. Breslow, X. Zhang, Y. Huang, *J. Am. Chem. Soc.* **1997**, *119*, 4535.
[16] R. Breslow, Y. Huang, X. Zhang, J. Yang, *Proc. Natl. Acad. Sci. USA* **1997**, *94*, 11156.
[17] R. Breslow, X. Zhang, R. Xu, M. Maletic, *J. Am. Chem. Soc.* **1996**, *118*, 11678.
[18] J. M. Desper, R. Breslow, *J. Am. Chem. Soc.* **1994**, *116*, 12081.
[19] a) C. J. Easton, J. B. Harper, S. F. Lincoln, *New J. Chem.* **1998**, *22*, 1163; b) J. B. Harper, C. J. Easton, S. F. Lincoln, *Tetrahedron Lett.* **2003**, *44*, 5815.
[20] Z. Clyde-Watson, A. Vidal-Ferran, L. J. Twyman, C. J. Walter, D. W. J. McCallien, S. Fanni, N. Bampos, R. S. Wylie, J. K. M. Sanders, *New J. Chem.* **1998**, *22*, 493.
[21] a) A. G. Meyer, C. J. Easton, S. F. Lincoln, G. W. Simpson, *Chem. Commun.* **1997**, 1517; b) A. G. Meyer, C. J. Easton, S. F. Lincoln, G. W. Simpson, *J. Org. Chem.* **1998**, *63*, 9069.
[22] J. Chen, J. Rebek, Jr., *Org. Lett.* **2002**, *4*, 327.
[23] L. Barr, C. J. Easton, unpublished results.
[24] R. P. Feynman, *Eng. Sci.* **1960**, *23*, 22.
[25] R. P. Feynman, *Saturday Rev.* **1960**, *43*, 45.
[26] a) V. Balzani, A. Credi, F. M. Raymo, J. F. Stoddart, *Angew. Chem.* **2000**, *112*, 3484; *Angew. Chem. Int. Ed.* **2000**, *39*, 3349; b) V. Balzani, A. Credi, M. Venturi, *Chem. Eur. J.* **2002**, *8*, 5525; c) V. Balzani, M. Venturi, A. Credi, *Molecular Devices and Machines: A Journey into the Nanoworld*, Wiley-VCH, Weinheim, **2003**.
[27] "Molecular Machines Special Issue" (Guest Ed.: J. F. Stoddart) *Acc. Chem. Res.* **2001**, *34*, 409.
[28] a) F. M. Raymo, S. Giordanni, *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 4941; b) A. R. Pease, J. O. Jeppesen, J. F. Stoddart, Y. Luo, C. P. Collier, J. R. Heath, *Acc. Chem. Res.* **2001**, *34*, 433.
[29] J. W. Lee, K. Kim, K. Kim, *Chem. Commun.* **2001**, 1042.
[30] A. Altieri, G. Bottari, F. Dehez, D. A. Leigh, J. K. Y. Wong, F. Zerbetto, *Angew. Chem.* **2003**, *115*, 2398; *Angew. Chem. Int. Ed.* **2003**, *42*, 2296.
[31] J. Clayden, J. H. Pink, *Angew. Chem.* **1998**, *110*, 2040; *Angew. Chem. Int. Ed.* **1998**, *37*, 1937.
[32] T. R. Kelly, I. Tellitu, J. P. Sestelo, *Angew. Chem.* **1997**, *109*, 1969; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1866.
[33] T. R. Kelly, J. P. Sestelo, I. Tellitu, *J. Org. Chem.* **1998**, *63*, 3655.
[34] T. R. Kelly, M. C. Bowyer, K. V. Bhaskar, D. Bebbington, A. Garcia, F. Lang, M. H. Kim, M. P. Jette, *J. Am. Chem. Soc.* **1994**, *116*, 3657.
[35] D. A. Leigh, J. K. Y. Wong, F. Dehez, F. Zerbetto, *Nature* **2003**, *424*, 174.

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[36] V. Balzani, M. Clemente-León, A. Credi, J. N. Lowe, J. D. Badjic, J. F. Stoddart, D. J. Williams, *Chem. Eur. J.* **2003**, *9*, 5348.
[37] A. K. Hossain, H. Mihara, A. Ueno, *J. Am. Chem. Soc.* **2003**, *125*, 11178.
[38] L.-Q. Gu, O. Braha, S. Conlan, S. Cheley, H. Bayley, *Nature* **1999**, *398*, 686.
[39] H. Bayley, P. S. Cremer, *Nature* **2001**, *413*, 226.
[40] S.-H. Shin, T. Luchian, S. Cheley, O. Braha, H. Bayley, *Angew. Chem.* **2002**, *114*, 3859; *Angew. Chem. Int. Ed.* **2002**, *41*, 3707.
[41] T. Luchian, S.-H. Shin, H. Bayley, *Angew. Chem.* **2003**, *115*, 1970; *Angew. Chem. Int. Ed.* **2003**, *42*, 1926.
[42] M. C. Jiminénez, C. Dietrich-Buchecker, J.-P. Sauvage, *Angew. Chem.* **2000**, *112*, 3422; *Angew. Chem. Int. Ed.* **2000**, *39*, 3284.
[43] J.-P. Collin, C. Dietrich-Buchecker, P. Gaviña, M. C. Jiminez-Molero, J.-P. Sauvage, *Acc. Chem. Res.* **2001**, *34*, 477.
[44] T. R. Kelly, H. De Silva, R. A. Silva, *Nature* **1999**, *401*, 150.
[45] T. R. Kelly, *Acc. Chem. Res.* **2001**, *34*, 514.
[46] N. Koumura, R. W. J. Zijlstra, R. A. van Delden, N. Harada, B. L. Feringa, *Nature* **1999**, *401*, 152.
[47] B. L. Feringa, *Acc. Chem. Res.* **2001**, *34*, 504.
[48] R. A. van Delden, N. Koumura, A. Schoevaars, A. Meetsma, B. L. Feringa, *Org. Biomol. Chem.* **2003**, *1*, 33.
[49] H. Onagi, C. J. Blake, C. J. Easton, S. F. Lincoln, *Chem. Eur. J.* **2003**, *9*, 5978.
[50] H. Onagi, B. Carrozzini, G. L. Cascarano, C. J. Easton, A. J. Edwards, S. F. Lincoln, A. D. Rae, *Chem. Eur. J.* **2003**, *9*, 5972.
[51] S. Anderson, R. T. Aplin, T. D. W. Claridge, T. Goodson III, A. C. Maciel, G. Rumbles, J. F. Ryan, H. L. Anderson, *J. Chem. Soc. Perkin Trans. 1* **1998**, 2383.
[52] F. Cacialli, J. S. Wilson, J. J. Michels, C. Daniel, C. Silva, R. H. Friend, N. Severin, P. Samorì, J. P. Rabe, M. J. O'Connell, P. N. Taylor, H. L. Anderson, *Nat. Mater.* **2002**, *1*, 160.
[53] P. Thordarson, E. J. A. Bijsterveld, A. E. Rowan, R. J. M. Nolte, *Nature* **2003**, *424*, 915.

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