Helical Complexes and Beyond

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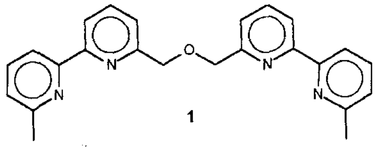
Abstract: Helical complexes have been much studied as examples of self-assembled supramolecular units. Their structural features are analysed in terms of the metal ion, the binding site on the ligand and the bridging group linking these sites. Understanding these elements allows the controlled assembly of multicomponent systems. Preliminary results show the complexes to have high stability, arising from the inertness of the self-assembled species.

Keywords: helical structures · self-assembly · supramolecular chemistry

Why have helical complexes been the object of such attention over the past ten years? The notion of helicity in coordination chemistry is almost as old as the subject itself, dating back to the recognition by Alfred Werner that the 1,2-diaminoethane (en) ligands in $[Co(en)_3]^{3+}$ could twist either clockwise (Λ) or anticlockwise (Δ) around the C_3 symmetry axis of the complex. However, it is reasonable to associate the beginning of current interest in helical complexes with a paper by Lehn[1] in 1987 in which the oligobidentate ligands **1** and **2** were shown to form double helical complexes, which were dubbed "helicates", with respectively two and three Cu^I ions. These complexes showed two features which have characterised the study of helical complexes ever since: a polynuclear structure, in which ligand strands twist around the metal–metal axis, and a remarkable facility of synthesis—simple mixing of ligands and metal ions in the stoichiometric ratio leading to rapid and complete formation of complexes. The formation of a helicate is thus a prototypical self-assembly reaction,[2] and it is this that has prompted their study. Here we summarise some of the most important results on the structures and properties of these complexes.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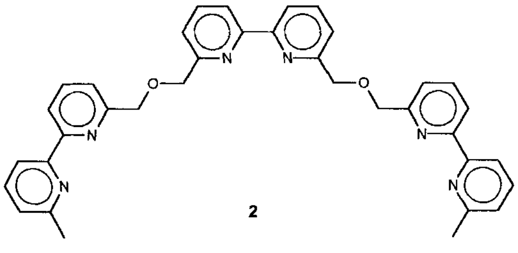
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We will consider complexes in which the helical axis is defined by two or more metal ions, and the ligands form the strands of the helix, twisting around the axis and held in place by complexation to the metal ions. Many polynuclear helical complexes, both double[3] and triple,[4] had been reported in the literature before 1987, although their helical nature was often not commented upon. The principles of the construction of helicates are shown in Figure 1. The three basic elements of the structure are the metal ion, the binding site on the ligand and the bridge that joins binding sites, coordinating different metals. The metal ion will in general have a more or less strongly preferred coordination geometry, defined by a coordination number and a geometrical disposition: tetrahedral for Cu^I, octahedral for low-spin Fe^{II}, coordination number of 8 or 9 for the larger lanthanides, and so on. The coordination preference of the metal is the first element of structural control. The binding site of the ligand is the second element and is characterised by a denticity, that is, the number of atoms that bind to the metal: 2 (didentate) for bipy or catechols, 3 (tridentate) for terpy, etc. Clearly it is necessary for the total number of atoms bound to the metal to satisfy its coordination preference: thus a tetrahedral ion as used by Lehn[1] will require two didentate sites, and therefore two strands, while an octahedral metal will require three didentate sites, giving a triple helix,[5] or two tridentate sites, giving a double helix.[6] Similarly, the coordination requirements of a lanthanide may be satisfied by three tridentate sites, giving a coordination number of nine.[7] The final structural element is the bridge: it must be flexible enough to allow the ligand as a whole to wrap around the helical axis, but sufficiently rigid to prevent the second binding site from twisting round to coordinate to the first metal, and to ensure that the helical chirality of one metal is transferred to its neighbour.

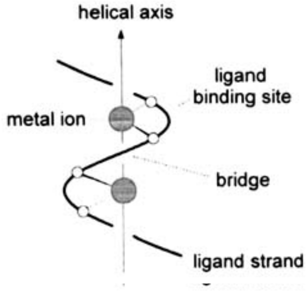

Figure 1. The different structural elements of a helical complex. Only one ligand strand is shown.

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Its size will determine the separation between the metals, and thus their interactions and the pitch of the helix. Figure 2 shows three crystal structures of helicates illustrating these principles.

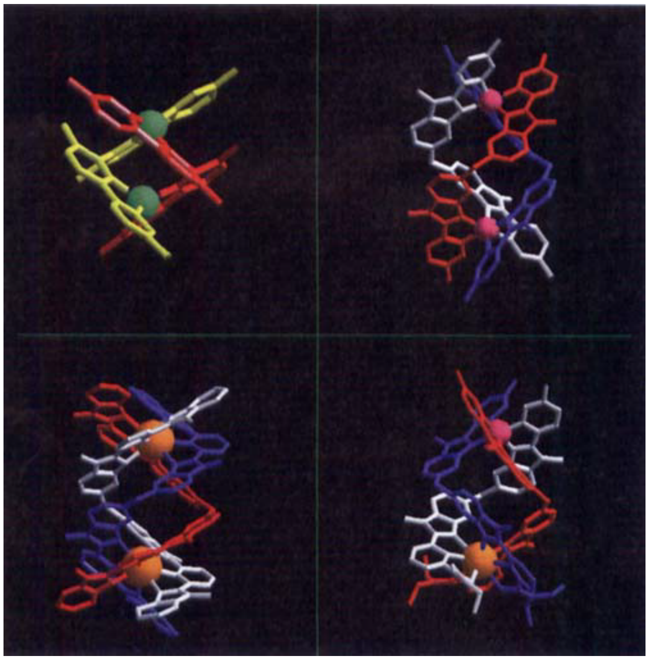
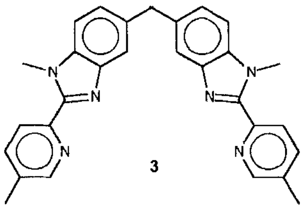


Figure 2. Selected helical complexes showing different metal coordination numbers. Upper left: a double helix with two tetrahedral Cu^{I} ions [3c]; upper right: a triple helix with octahedral Co^{II} in $[Co_2(3)_3]^{4+}$ [14]; lower left: a triple helix with 9-coordinate Eu^{III} $[Eu_2(5)_3]^{6+}$ [7]; lower right: a heteronuclear triple helix with Fe^{II} in an octahedral site and La^{III} in a 9-coordinate site (C. Piguet and G. Bernardinelli, private communication).

The metal ions used are generally labile. This property allows rapid and reversible formation of coordinate bonds, and the position of thermodynamic stability can thus be reached through a trajectory over the potential energy hypersurface, even though this may entail the formation of many chemical bonds (12 for $[Cu_3(2)_2]^{3+}$ and $[Co_2(3)_3]^{4+}$, 18 for $[Eu_2(5)_3]^{6+}$). The three structural elements given above may be varied by the chemist to control which product or structure is formed.

Control through the metal ion: The polypyridyls such as **6** have been extensively investigated by Constable[8] and Potts.[9] Ligand **6** shows very nicely the effect of metal ion coordination preference, since it may act as a hexadentate, a bis(tridentate) or a tris(didentate) ligand. With the large Eu^{III} ion the ligand wraps around to occupy six coordination sites, giving essentially a mononuclear single helix;[10] with octahedral metal ions such as Cd^{II}, Fe^{II} and Mn^{II} it gives a dinuclear double helix, and with Cu^{I} and Ag^{I} a trinuclear double helix.[6] Ligands **3** and **4**, on the other hand, may only act as as bis(didentate) ligands; with tetrahedral Cu^{I}, **4** forms a dinuclear double helix M_2L_2, but the octahedral Co^{II} ion requires three didentate ligands, and thus forms a helix M_2L_3 with three strands. A metal such as Zn^{II} with no strong stereochemical preferences forms both M_2L_2 and M_2L_3 depending on the stoichiometry.[11]



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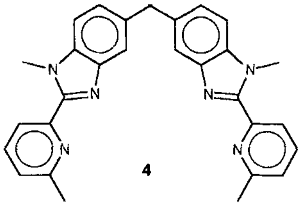

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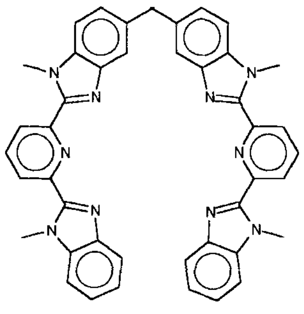

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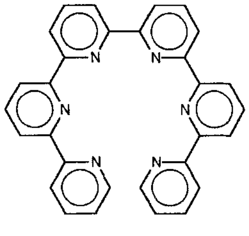

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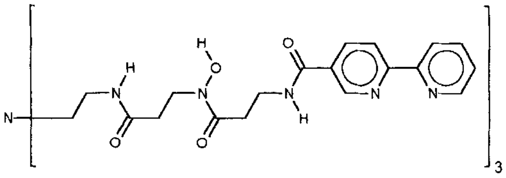
Binding site of the ligand: The vast majority of ligands used to form helical complexes possess either didentate or tridentate binding sites. Monodentate links normally allow torsion about the M–L bond axis and thus do not give a sufficiently rigid helix. Heterocyclic nitrogen ligands such as pyridyls, phenanthrolines and benzimidazoles predominate, but catechols and hydroxamic acids have also been used. An interesting example of using the ligand site to select the metal ion has been given by Shanzer[12] with the ligand **7**. With Fe^{II} the bipyridyl site is favoured, but upon oxidation the metal ion displaces itself to the hydroxamate site for which Fe^{III} has a much greater affinity. More subtle effects may be obtained by suitable substitution of the ligands. The dipyridyl ligands **1** and **2** are substituted at the 6,6′ positions; this would lead to steric interactions between ligands if three ligands bind to an octahedral metal, but not if two ligands bind to a tetrahedral metal. Substitution at the 5,5′ sites does not lead to such repulsion, and so mixing **2** and **8** with tetrahedral Cu^{I} and octahedral Ni^{II} results in exclusive complexation of Cu^{I} by **2** and of Ni^{II} by **8**.[13] More subtle effects are seen if only one side of the didentate site is substituted. Ligands **3** and **4** form triple helical complexes with octahedral Co^{II} and Fe^{II}; with **3** the complex of Co^{II} may be readily oxidised to Co^{III}, but not with **4** where the steric repulsion of the methyl groups pre-



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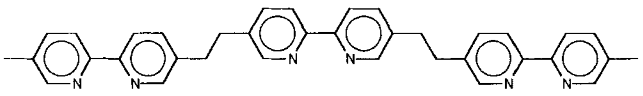

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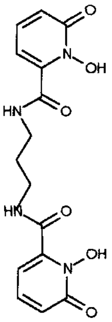
vents the contraction of the coordination sphere required on oxidation.[14] With iron(II) the complex with **3** is low spin, while that with **4** is high spin.[15]

The bridging unit: The choice of the bridging unit is certainly crucial for the construction of the helix, but little systematic investigation has been carried out so far. Most data is available for the catechol and related helicates with varying bridging units (ligands **9**–**13**); these ligands all form triple helicates with octahedral metals, and show varying pitch and metal–metal distance as the bridge is varied.[16] When the bridge is too flexible, a *meso* helicate, where the metal ions have opposing chirality, may be formed.[16c] The complex $[Fe_2(\mathbf{9})_3]^{6-}$ [4a] is much more twisted than the other complexes, but this may also be associated with the use of a $3d^5$ metal ion rather than the spherical d^0 or d^{10} species used in the other studies. The most spectacular effect of the bridging unit recorded to date concerns the double helical complex $[Cu_2(\mathbf{14})_2]^{2+}$ used as a precursor for the synthesis of a molecular knot by Dietrich-Bucheker and Sauvage. The initial work used a flexible -$(CH_2)_4$- bridge and gave a very low yield of 3% for the knot after cyclisation.[17] Replacement of this bridge by a more rigid 1,3-phenylene unit strongly favoured the formation of the double helical precursor over the alternate side-by-side structure, and increased the overall yield of the synthesis to 30%.[18]



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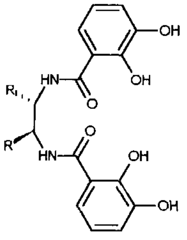

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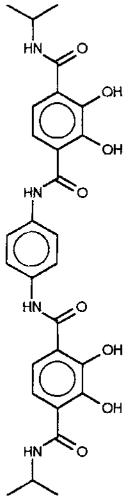

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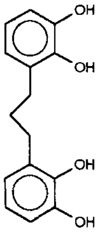

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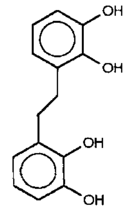

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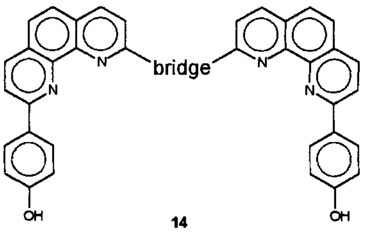

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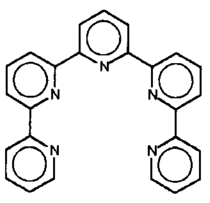
Multicomponent systems: The next step in developing self-assembly reactions is to increase the number of components, and we may divide the systems into heteronuclear, where one ligand and two different metals are used, and heteroleptic, where one metal is used with two ligands. Pentadentate ligands such as **15**–**17** are particularly adapted to heteronuclear complexes, since they generally behave as didentate and tridentate species—this is indeed structurally defined in the segmental ligands **16** and **17**, and further control may be introduced by modifying the substitution of the didentate group. Quinquepyridyl (**15**) reacts with tetrahedral Ag^I and octahedral Co^{II} to give $[CoAg(\mathbf{15})_2]^{3+}$,[19] while **16** binds Ag^I and Fe^{II} to give $[FeAg(\mathbf{16})_2]^{3+}$, [20] both double helical species. In **17** the methyl substituent of the didentate site no longer hinders octahedral coordination, and a triple helix with an octahedral ion (Fe^{II} or Zn^{II}) in a trisdidentate site and a lanthanide in a tris tridentate site is formed.[21] This system has been investigated in some detail by Piguet, and modification of the tridentate site has very recently led to the preparation of very stable luminescent lanthanide complexes.[22] The basis of the selectivity in these systems is matching the number of coordination sites of the metal ions to the number offered by the ligand strands. It is important to note, however, that, although the heteronuclear species represent minima on the energy surfaces, a homonuclear species will be formed in the absence of one or other metal; it is only when the correct stoichiometry is obeyed that the assembly of the heteronuclear species occurs in high yield.



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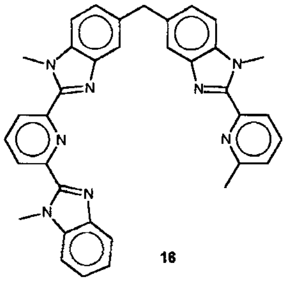

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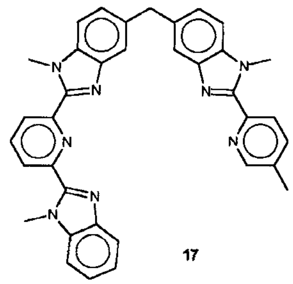

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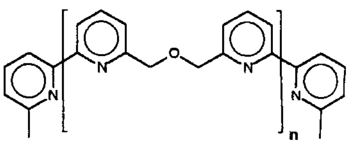
Heteroleptic systems have been less studied, although Lehn has published some interesting results. Thus, a mixture of bis-, tris-, tetrakis- and petakisdidentate ligands (**BP*n***, $n = 2$–5; **18**) in the presence of Cu^I leads to a mixture of double helical complexes $[Cu_nL_2]^{n+}$ in which both ligands are identical—no mixed ligand species are observed.[13] Although, in terms of number of coordination sites, a complex such as $[Cu_4(\mathbf{BP4})(\mathbf{BP2})_2]^{4+}$ satisfies the matching principle, it is readily seen that it is entropically less favourable than two homoleptic systems $[Cu_4(\mathbf{BP4})_2]^{4+} + 2[Cu_2(\mathbf{BP2})_2]^{2+}$ (Figure 3). For this reason attempts to prolong helices by the Vernier principle[2] have been unsuccessful. In a system such as Co^{II} + **15** there is an incommensurability between the six-coordinate metal ion and the pentadentate ligand. The Vernier principle would predict the formation of $[Co_5(\mathbf{15})_6]^{10+}$, but this is not observed (Figure 4). Stable species may be obtained by adding simple ligands or solvent



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n = 1 - BP2
n = 2 - BP3
n = 3 - BP4
n = 4 - BP5

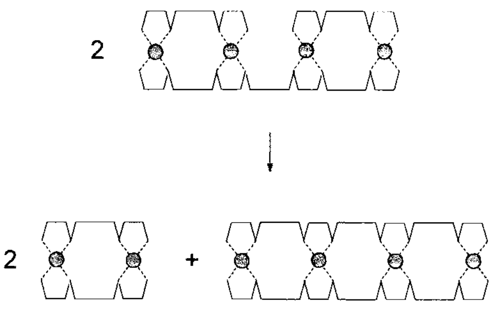

Figure 3. Entropy considerations favouring the maximum number of particles render mixed ligand species unstable.

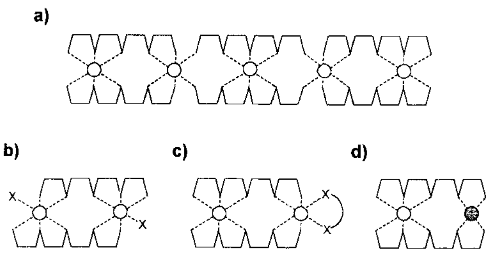

Figure 4. The incommensurability between pentadentate ligands and octahedral metals may be resolved in different ways: a) the Vernier type extension, disfavoured on entropy grounds; b) and c) completing the coordination sphere with monodentate or bidentate ligands; d) replacing one octahedral metal by a tetrahedral metal.

molecules to satisfy the metal ion coordination as in $[\mathrm{Co_2(\mathbf{15})_2(\eta^2\text{-}O_2CCH_3)}]^{3+}$,[23] by adopting a heteronuclear structure as in $[\mathrm{CoAg(\mathbf{15})_2}]^{3+}$ mentioned above or, in the case of copper, by undergoing an oxidation state change, $\mathrm{Cu^I}$ species showing lower coordination numbers than $\mathrm{Cu^{II}}$. The mixed valence species $[\mathrm{Cu_2(\mathbf{15})_2}]^{3+}$ with four-coordinate $\mathrm{Cu^I}$ and six-coordinate $\mathrm{Cu^{II}}$ obeys the matching principle.[24] Copper(II) frequently shows a coordination number of 5, and this may be satisfied by assembly of a heteroleptic helix with one tridentate strand, and the other didentate, as recently reported for a trinuclear complex by Lehn.[25]

An astonishing example of a three-component system was reported very recently:[26] reaction of **8** with $\mathrm{FeCl_2}$ yields the complex $[\mathrm{Fe_5(\mathbf{8})_5Cl}]^{9+}$ in which the iron atoms form the apices of a pentagon with the ligand strands twisting around the edges, and the chloride ion firmly bound at the centre. This cyclic, toroidal triple helix contrasts with the classical linear triple helix $[\mathrm{Ni_3(\mathbf{8})_3}]^{6+}$,[27] and suggests the role of the chloride ion to be crucial. Not surprisingly, given the topological complexity of the complex, the synthesis requires a night's reflux at 170 °C to proceed to completion.

The properties of helical complexes have received much less attention than their structure and synthesis. The most obvious property, their chirality, has been little studied, mainly because the syntheses usually start with achiral ligands and consequently the helicate is formed as a racemic mixture of plus (P) and minus (M) enantiomers. Lehn et al. observed a spontaneous partial resolution of a trinuclear triple helical complex of nickel(II), $[\mathrm{Ni_3(\mathbf{8})_3}]^{6+}$,[27] but the only complete resolution that has been reported to date was achieved by oxidation of $[\mathrm{Co_2(\mathbf{3})_3}]^{4+}$ to the cobalt(III) complex $[\mathrm{Co_2(\mathbf{3})_3}]^{6+}$ to ensure kinetic inertness, followed by resolution by crystallisation.[28] The circular dichroism and optical rotation of the complex correspond to roughly twice that of enantiomerically pure $[\mathrm{Co(bpy)_3}]^{3+}$; this shows that there is little interaction between the two metal centres. Chiral ligands have been used to induce helices of one particular chirality.[16a, 29]

The thermodynamic data available suggest that, provided the formation of the helix does not produce any particular strain in the ligands, the polynuclear species are very stable. Thus formation of $[\mathrm{Co_2(\mathbf{3})_3}]^{4+}$ is essentially quantitative in acetonitrile solution even at concentrations as low as $10^{-5}\,\mathrm{M}$.[14] It appears, on the basis of the limited data available,[11, 15, 30] that the formation pathway involves initial complexation around one metal ion, followed by complexation of the second metal in the preorganised site [Eq. (1)]. Since the formation reactions are generally

$$\mathrm{M} + n\mathrm{L} \longrightarrow [\mathrm{ML}_n] \longrightarrow [\mathrm{M_2L}_n] \qquad (1)$$

observed to be rapid (with the interesting exception of the higher nuclearity copper(I) systems[13]), high stability requires very slow dissociation. This is indeed observed in the very low rates of racemisation observed for enantiomerically pure $[\mathrm{Co_2(\mathbf{3})_3}]^{4+}$[31] and partially resolved nickel triple helix.[27] Electron transfer has been studied, and the systems may be classed according to whether the redox reaction entails no change in stereochemical preferences ($\mathrm{Co^{II}}$,[14] $\mathrm{Fe^{II}}$ and $\mathrm{Ru^{II}}$[32]) or not. The $\mathrm{Cu^I/Cu^{II}}$ couple is the most studied example of the latter category, and usually a major structural rearrangement occurs upon electron transfer.[6, 8, 9] Energy transfer between metal sites has been observed in heteronuclear lanthanide complexes, and in the quenching of europium luminescence in $[\mathrm{FeEu(\mathbf{17})_3}]^{5+}$.[22, 33]

This brief survey has concentrated on concepts, and practical aspects such as the characterization of the helicates have not been discussed, although advances such as the application of electrospray mass spectrometry have been of vital importance. Two applications of helical complexes have appeared: templating precursors to topologically complex molecules such as knots[17] and doubly interlaced catenanes,[34] and combining a weakly binding lanthanide ion with a strongly binding transition metal to give a stable heteronuclear complex. More generally, the study of polynuclear helical complexes has encouraged coordination chemists to think of metal ions not merely in terms of the metal centre or its immediately bound atoms, but as structure-generating units. In this context, the helicates are closely related to other fields such as molecular boxes formed by coordination reactions,[35] extended coordination polymers[36] and the general construction of large molecular architectures by coordination reactions.[37] Many of the lessons learnt from helicate self-assembly will be of value in other fields. Finally, we should not forget the aesthetic pleasure offered by these complex structures when viewed by modern computer graphics packages!

Received: October 11, 1996 [C493]

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