Active Cross-Linkers that Lead to Active Gels**
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This communication describes the design, synthesis, and structure of the first ruthenium-complex-based hyper-cross-linker for creating a novel type of active gels as a chemomechanical soft material. Gels, which are soft materials composed of a three-dimensional (3D) network and a large amount of liquid, have found a wide range of applications, from biomedicine (for example, as a medium for tissue engineering[8]) to consumer products (for example, hair gels). Cross-linking, physically or covalently, is the fundamental and necessary attribute to produce a 3D network in a gel. Unlike supramolecular gels,[7] which are constructed through reversible, non-specific, and physical cross-linking, polymeric gels[3] usually rely on bifunctional cross-linkers (for example, bisacrylamide[9]) that become inactive after the formation of the covalent cross-links during the polymerization.

Whereas most cross-linkers in synthetic networks are less active, cross-linkers in biopolymer networks are active. For example, the cytoskeleton of muscle cells has myosin motors as the active cross-linkers to cross-link actin filaments.[5] Inspired by this process of converting chemical energy into mechanical motion, researchers have spent considerable efforts on using actin and myosins to create active gels in vitro to explore the structures and dynamics of these minimal active networks.[4] Encouraged by these developments, we developed an active cross-linker based on the tris(bipyridine) ruthenium complex ([Ru(bipy)3]n+), n = 2 or 3 for the construction of novel polymer networks (Scheme 1). We made such a choice for several reasons: First, although active or functional molecules are increasingly used for making supramolecular gels,[7] such as self-healing soft materials,[7a,8] it is rather rare to generate polymeric gels by active cross-linkers.[8b,9] Second, [Ru(bipy)3]3+, a well-known coordination compound,[10] has a long-lived excited state that has both oxidizing and reducing properties, which has attracted enduring research interests. Although its derivatives have served as photosensitizers,[11,12] electrochemiluminescent components,[13] the core of bacteria-sensing elements[14] components for conducting polymers,[15] and as cores of star polymers,[16] the capacity of [Ru(bipy)3]3+ as an active or hyper cross-linker has yet to be explored. Third, [Ru(bipy)3]3+, in particular, also serves as a redox catalyst for a well-established chemical oscillator, namely the Belousov–Zhabotinsky (BZ) reaction.[17] The redox switch of the [Ru(bipy)3]3+ complex has led to the development of a self-oscillating gel that swells in its oxidized state (RuIII) and shrinks in its reduced state (RuII) during the BZ reactions.[18] However, in that type of gel, N,N'-methylenebis(acrylamide) (BIS)[19] is the cross-linker and the ruthenium(I/III) complex is the pendant of the cross-linked chains of poly(N-isopropylacrylamide).[14,20] Because of the stereochemical configuration of the [Ru(bipy)3]3+ complex, its application as a cross-linker would result in an unprecedented molecular architecture for developing active gels as chemomechanical materials.

Based on the above-described rationale, to evaluate the correlation between the molecular architecture and the chemomechanical behavior of a soft material, we used the [Ru(bipy)3]3+ based active cross-linker 1 (Figure 1a) and two distinct monomers, N-isopropylacrylamide (NIPAAm) and allylamine, for the polymerization that results in two active polymers,[16] the capacity of [Ru(bipy)3]3+ as an active or hyper cross-linker has yet to be explored. Third, [Ru(bipy)3]3+, in particular, also serves as a redox catalyst for a well-established chemical oscillator, namely the Belousov–Zhabotinsky (BZ) reaction.[17] The redox switch of the [Ru(bipy)3]3+ complex has led to the development of a self-oscillating gel that swells in its oxidized state (RuIII) and shrinks in its reduced state (RuII) during the BZ reactions.[18] However, in that type of gel, N,N'-methylenebis(acrylamide) (BIS)[19] is the cross-linker and the ruthenium(I/III) complex is the pendant of the cross-linked chains of poly(N-isopropylacrylamide).[14,20] Because of the stereochemical configuration of the [Ru(bipy)3]3+ complex, its application as a cross-linker would result in an unprecedented molecular architecture for developing active gels as chemomechanical materials.

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Scheme 1. Conceptual illustration of the active hyper-cross-linker that gives rise to active gels, and the volumetric oscillation of the gels induced by the redox switch of the active hyper-cross-linker 1 during the BZ reaction (side chains of the polymers are omitted for clarity).
reduced state. In contrast to Gel1 and Gel2, the gels Gel3 and Gel4 use [Ru(bipy) \textsubscript{2}L' \textsuperscript{n+} (L' = 4-methyl-4'-vinyl-2,2'-bipyridine, n = 2 or 3; Supporting Information, Scheme S1) as the pendants attached to the networks of poly(N-isopropylacrylamide) and poly(allylamine), respectively. Under the same conditions of the BZ reaction used for Gel1 and Gel2, Gel3 swells, and Gel4 exhibits little change in volume when the pendants are present in their oxidized state ([Ru(bipy)\textsubscript{2}L' \textsuperscript{3+}). Such drastic contrasts in volume changes confirm that the molecular architecture determines the chemomechanical behavior of the active gels. Moreover, the transformation of a thermally insensitive polymer (such as poly(allylamine)) into a self-oscillatory material by using active cross-linkers, suggests that polymerization with active cross-linkers is an effective approach to generate active gels.

Figure 1a shows a concise, two-step synthesis of the active hyper cross-linker 1. First, 4,4'-dicarboxyl-2,2'-bipyridine \textsuperscript{[20]} was reacted with two equivalents of allylamine in the presence of coupling reagents to form N,N'-diallyl-(2,2'-bipyridine)-4,4'-dicarboxamide. Second, six equivalents of N,N'-diallyl-(2,2'-bipyridine)-4,4'-dicarboxamide reacted with one equivalent of dichloro(p-cymene)ruthenium(II) dimer\textsuperscript{[22]} in DMF at 120°C under N\textsubscript{2} for 12 h. After the reaction had reached completion, purification by column chromatography\textsuperscript{[23]} and removal of the solvent afforded active cross-linker 1 as a red powder in a total yield of 52%. The UV/Vis spectrum of the active cross-linker 1 exhibits four absorption bands at 200, 250, 305, and 465 nm (Supporting Information, Figure S1). The 200 nm and 305 nm bands arise from ligand-centered (LC) π–π* transitions,\textsuperscript{[24]} the remaining intense bands at 250 and 465 nm belong to metal-to-ligand charge-transfer (MLCT) d–π* transitions, and the shoulder at 350 nm reflects metal-centered (MC) transitions.\textsuperscript{[25]} These peaks indicate that the active cross-linker 1 electronically resembles the [Ru(bipy)\textsubscript{3}]\textsuperscript{2+} complex, thus it should be able to function as the desired redox catalyst of the BZ reaction\textsuperscript{[17f,g]} for the evaluation of the active cross-linker and the corresponding gels. Furthermore, we obtained a crystal structure of the cross-linker (Figure 1b). The three bipyridine ligands around the Ru atom form a propeller-like trigonal arrangement. The coordination of the nitrogen atoms is close to octahedral. The results indicate that the active hyper cross-linker 1 retains a similar geometry to the known crystal structure of [Ru(bipy)\textsubscript{3}]\textsuperscript{2+}. Among the six N-allylacetamide groups, two of them, which are located on different bipyridine ligands, are rigid; the other four show small flexibilities. The stereochemical configuration of the active hyper cross-linker 1 makes it an inherent 3D cross-linker.

Figure 1. a) A simple route for synthesizing the active hyper cross-linker 1. b) Crystal structure of the active hyper cross-linker 1. Thermal ellipsoids set at 50% probability. For clarity, the Cl\textsuperscript{-} counterions and all hydrogen atoms have been omitted. DIEA = disopropylethylamine, DMF = N,N-dimethylformamide, HBTU = O-(benzotriazol-1-yl)-N,N',N'-tetramethyluronium hexafluorophosphate.
with proper elasticity were obtained (Figures S2 and S3). For example, Gel1, formed by the polymerization of the active cross-linker 1 and the monomer in a ratio of 0.004, achieves an optimal cross-linking density and undergoes a change in volume during the BZ reaction (see below). Whereas Gel2, formed by the polymerization of the active cross-linker 1 and the monomer as Gel1, the molar ratios of the monomer, ruthenium catalyst [Ru(bipy)2L2]Cl2, and the cross-linker (BIS) are 1:0.015:0.012 for the syntheses of Gel3 or Gel4.

To understand the microstructure in the gels made using the active cross-linker 1, we used confocal microscopy to image Gel1 and Gel2 at the reduced state as the active cross-linker, in its reduced state, fluoresces strongly and stably upon excitation at 488 nm. Fluorescence images (Figure 2) indicate that Gel1 and Gel2 have different microstructures. For example, whereas Gel1 shows largely homogeneous fluorescence (Figure 2a) and some elliptical fluorescent dots (3.3×2.5 μm), Gel2 exhibits a fluorescent porous network composed of interconnected micrometer-size clots (Figure 2b). Furthermore, the 3D images (Figure 2c and d) obtained from a Z-scan series of fluorescence confocal images of Gel1 and Gel2 further confirm that the cross-linkers are distributed more homogeneously in Gel1 than in Gel2, despite the inhomogeneity of the cross-linkers in both Gel1 and Gel2. In comparison, the fluorescence images and the 3D images of Gel3 and Gel4 (Supporting Information, Figure S4) all show quite homogeneous fluorescence, which suggests that the [Ru(bipy)2L2]Cl2 complexes, here used as pendants, distribute evenly in Gel3 and Gel4. Furthermore, Gel1 (or Gel3) and Gel2 (or Gel4) also exhibit different appearances. For example, Gel1 (or Gel3) is more transparent than Gel2 (or Gel4), a difference that likely originates from the different polymer backbones. These results indicate that although differences in monomer structure hardly influence the distribution of the pendants in Gel3 and Gel4, the monomers most likely contribute to the heterogeneous distribution of the cross-linkers in Gel1 and Gel2.

Indeed, the differences in the microstructures of the active gels result in different chemomechanical behavior during redox reactions (Figure 3). Upon oxidation by a cerium sulfate solution, both Gel1 and Gel2 shrink, but Gel2 exhibits a bigger change in volume than Gel1. The shrinkage

![Figure 2. Confocal fluorescence images of a) Gel 1 and b) Gel 2, and the 3D images c) Gel 1 and d) Gel 2.](image)

![Figure 3. Optical images (top view) of Gel 1, Gel 2, Gel 3, and Gel 4 (the polymer chains are shown in the first row) in their reduced state (by treating with Ce(NO3)3) and oxidized state (by treating with a Ce(SO4)2 solution) at 24°C. The dotted circles indicate the edges of the gels.](image)
exhibits a temperature-dependent phase transition in its reduced and oxidized states, similar to results reported in the literature.\[18\] Unlike Gel1, Gel2, and Gel3, the volume of Gel4 is essentially independent of the redox state or temperature (Figure 4d). Furthermore, although Gel1 contains significantly fewer (1/5) Ru centers than Gel3 does, the maximum difference in relative diameters for the reduced and oxidized states of Gel1 reaches half of the difference for Gel3, which implies a higher efficiency in chemomechanical conversion per redox center (Ru II/III) when it serves as the joint center of several polymer chains. As the [RuL$_3$]$_{3}^{3+}$ are highly restricted in movement within the hyper-cross-linked network, upon oxidation, the [RuL$_3$]$_{3}^{3+}$ cross-linkers attract extra counterions into the network. In fact, the influx of counterions increases the electrostatic interactions between the ions, which likely expels water molecules out of the network and eventually induces the collapse of the polymer network. Although other factors may contribute to the volume shrinkage, the results obtained by confocal imaging and SEM confirm that the active cross-linker plays a critical role in the chemomechanical volume change of the active gels.

In conclusion, by designing and synthesizing the first octahedral ruthenium bipyridine complex that bears six polymerizable vinyl groups as the active cross-linkers, we have illustrated a new way to control molecular architecture for active materials, in which the active hyper-cross-linkers of the polymer network determine the material properties. This result suggests that the application of an active catalyst as the hyper-cross-linker of a polymer network may lead to a new way of making active soft materials.\[30\] Moreover, this work also increases the diversity of active materials, thus laying the foundation for combining counteracting components to construct sophisticated chemomechanical systems or materials.\[31\] Furthermore, this work offers a key building block for the construction of other new redox active polymers using the new octahedral ruthenium complex.

Keywords: cross-linkers · gels · polymers · ruthenium · soft materials

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Active Cross-Linkers that Lead to Active Gels

Chemomechanical reaction: The first octahedral ruthenium bipyridine complex that bears six polymerizable vinyl groups is used as an active cross-linker (see Scheme, left). It is a key building block for cross-linked polymeric networks (right) thus allowing the construction of molecular architectures in chemomechanical soft materials.