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A Unidirectional Open–Close Mechanism of Metal-Ion-Driven Molecular Hinges with Adjustable Amplitude

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Abstract: A basic requirement for each molecular system that is supposed to perform work is a synchronized and unidirectional movement. Unidirectionality can be achieved by a change of configuration or conformation that is controllable by external stimulation. Molecular hinges based on a bipyridine unit work unidirectionally and are able to reach an amplitude of motion that amounts to about 180°. To analyze if it is possible to adjust the height of the unidirectional amplitude of motion, three planar chiral molecular hinge systems with a 2,2′-bipyridine unit as functional element were designed and stimulated with various divalent metal ions in different solvents. The configurations of the hinges were determined by DFT calculations using B3LYP and the 6-31G* basis set and experimentally verified by 2D NMR NOESY spectra. Circular dichroism (CD) and UV spectroscopy were used to study the properties of the hinges by the addition of metal ions (primarily Zn^{2+} and Hg^{2+}) in dichloromethane and methanol. The choice of metal ions and solvents determines whether or not and how far the hinges are closed. Furthermore, a drastic change in the height of the amplitude of motion can be reached by modifying the position of the bipyridine unit in the hinge. Amplitude values from 45 up to 190° were obtained from quantum mechanical calculations. This control of the amplitude of motion can in the future be used for more complex switching processes of molecular machines.

Keywords: bipyridine · chirality · circular dichroism · molecular devices · unidirectional rotation

Introduction

In recent years, the development of molecular motors that are able to perform an externally stimulated directional movement has become more and more important because it allows for the imitation and a deeper understanding of biochemical processes.[1,2]

A multitude of molecular devices have already been designed, for example, rotors,[3] shuttles,[4] switches,[5] tweezers,[6] and so on, but only a few systems show a unidirectional course of movement caused by a change of configuration or conformation that is controllable by external stimulation.[3,7,8] A synchronized and unidirectional movement is, however, a basic requirement for work to be done. The energy obtained from such work can be used to perform a task. Work is defined as the amount of energy transferred by a force acting through a distance. It becomes greater the higher the distance and the larger the force is. For molecular systems that perform a synchronized and unidirectional movement by external stimulation, this means that the higher the amplitude of motion and the stronger the stimulus is, the more work is performed. Possible stimulants causing a unidirectional movement are light or a chemical reaction. One example for a system with a light-induced unidirectional mechanism of motion would be molecular scissors,[9] the blades of which perform a movement with a relative amplitude of 49° triggered by irradiation ($\lambda = 350$ nm). Here the molar conversion amounts to 89%.[9b] A system with a much higher relative amplitude of motion ($\approx 180°$) and almost quantitative conversion can be achieved by utilizing 2,2′-bipyridines.[10] Using such bipyridines as switching units is simple and effective: by adding divalent metal ions, a complete conversion to the respective bipyridine–metal complexes takes place.[11] Subsequently, the bipyridine can be easily turned back to the original state by removing the metal ion using a stronger metal complexing agent. Thus an unlimited repetition of switching is possible. In 1979 and 1984, Rebek et al. already reported the effective use of 2,2′-bipyridine units for metal-ion switchable rotation in allosteric receptors,[10h,i] and also many other groups introduced

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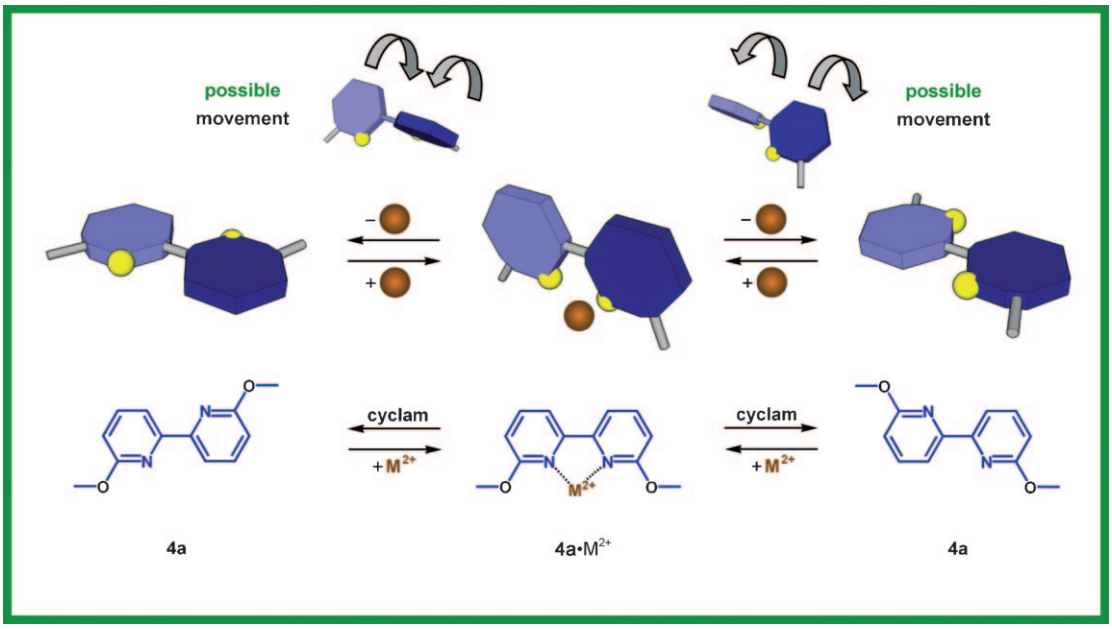
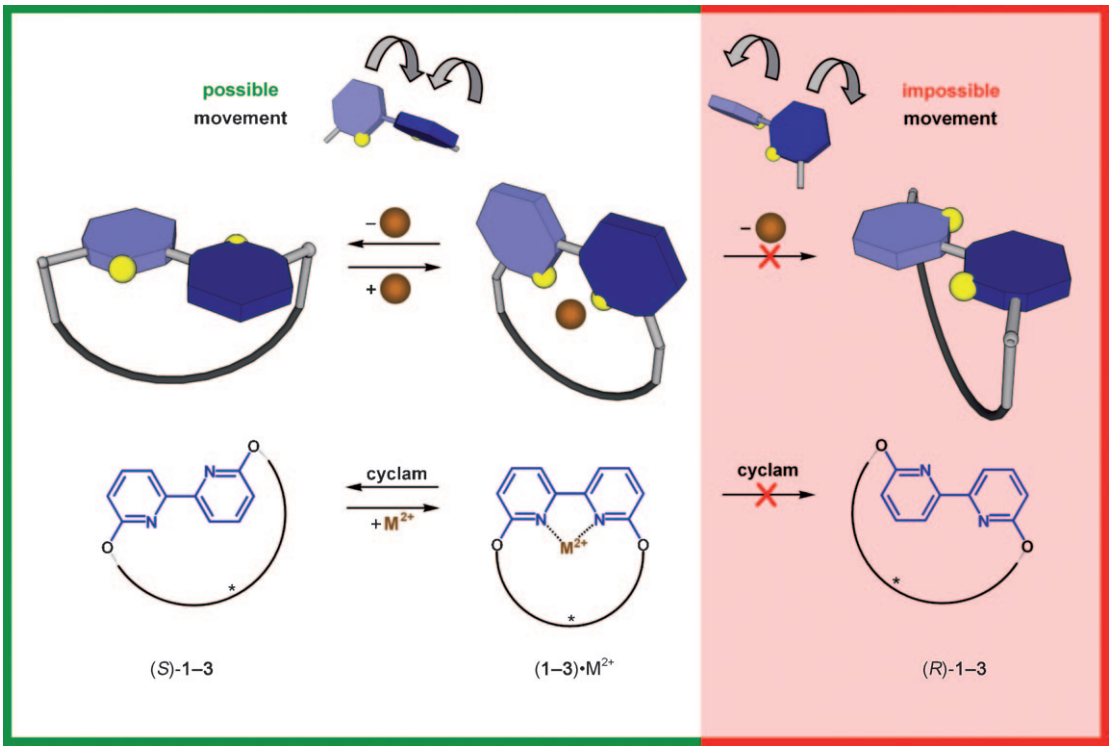


Scheme 1. Schematic representation of an achiral 2,2′-bipyridine hinge with a bidirectional open–close motion.

2,2′-bipyridines as switchable elements.[10] In these systems, however, it is not possible to control the direction of movement because a rotation around the C–C′ biypridine axis is possible in both directions (see Scheme 1): the system exhibits two states, the open form **4a** and the complex **4a**·M^{2+}. However, the transition from one state to the other can take place in two different ways, and thus a control of the orientation of the rotation is not possible. Recently we managed to create a system with a unidirectional movement of the bipyridine: we synthesized a copper-ion-controlled molecular hinge[8] with a central 2,2′-bipyridine unit (compound **1** in Scheme 2). The unidirectionality of movement is realized by fixation to a rigid chiral clamp, which induces a chiral planarity within the noncomplexed bipyridine unit. Only one



Scheme 2. Schematic representation of a chiral hinge with a unidirectional open–close motion.

configuration (given as *S* in Scheme 2) is adopted when the unit is opened (by removal of metal ions) and the closing process (by the addition of metal ions) can likewise only be performed out of this configuration. Accordingly, the green-framed area of Scheme 2 depicts the only way through which such passage is possible.

A restriction for almost all previously described unidirectional rotation movements is the fact that with a given rotation unit, only a singular amplitude of a nonvariable value can be achieved. A design of systems whose unidirectional motion amplitude can be varied by simple changes of the reaction conditions would be more interesting. Accordingly, our aim was to analyze whether it is possible to provide a unidirectional open–close process with adjustable amplitude and, to be more precise, whether the unidirectional open–close motion can be controlled by treating our bipyridine hinge with different metal ions in various solvents. Moreover, we wanted to find out if the amplitude of motion can be varied by modification of the chiral clamp and/or the bipyridine unit.

Results and Discussion

Principle and design: As a central element for the hinges with unidirectional open–close mechanism, a 2,2′-bipyridine unit was chosen. Noncomplexed 2,2′-bipyridines exhibit an N-C-C′-N′ dihedral angle of 180° (open state) that can be switched to 0° when divalent metal ions are added (closed state). The driving force behind the opening process is the repulsive interaction between the protons in the *ortho* position to the rotation axis and the lone-pair repulsion of the nitrogen atoms, whereas the driving force behind the closing process is the rapid and energetically preferred formation of the metal(II)–bipyridine complex. The complexation is a completely reversible process because the metal ion can easily be removed by a strong complexing agent like cyclam. Thus, the open–close motion is a rapid process that can be repeated as often as desired. 2,2′-Bipyridines like **4a** (Figure 1) can freely rotate around the C2–C2′ axis in both directions. The calculated energy profile in Figure 1 demonstrates that a change of the N1-C2-C2′-N1′ dihedral angle results in two energetic minima in each direction of rotation. The minima at +35.2 and −35.2° can be assigned to the axial chiral configurations *aS* and *aR*. These states are, however, not adopted because of their high energy relative to the states at 180° (a dihedral angle of +180° corresponds to a dihedral angle of −180°). In bipyridines like **4a** without a connecting unit between the oxygen atoms, both planar states with a dihedral angle of 180° are identical. Thus, in **4a** only one noncomplexed state exists in solution. The direction of the movement from the noncomplexed to the complexed state is not controllable (see Scheme 1). In bipyridines that are *meta*-bridged by means of an achiral unit, the bipyridine unit becomes planar chiral and can take a *pR* or *pS* configuration. Thus, in such systems there are two possible states with a N1-C2-C2′-N2′ dihedral angle of 180°, which are enantiomeric.

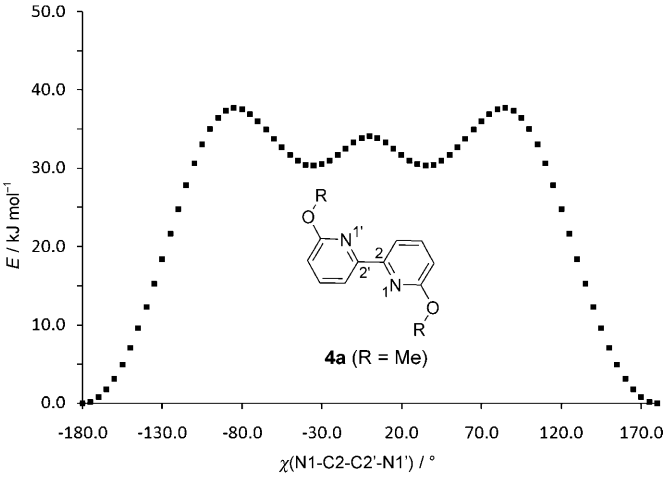


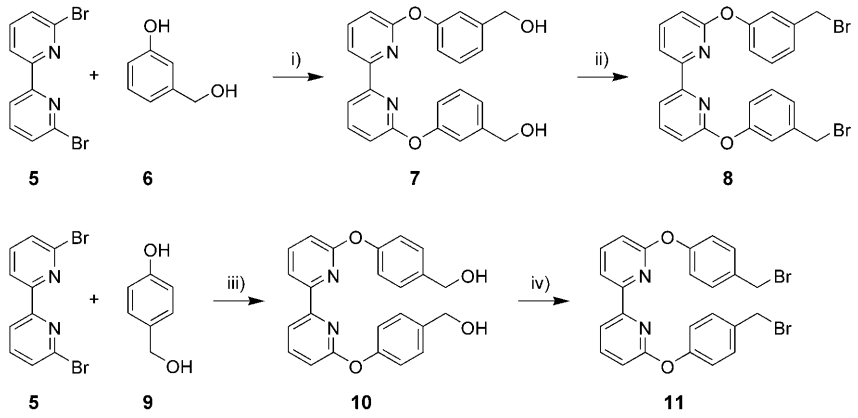
Figure 1. Calculated energy profile of bipyridine **4a** in relation to the dihedral angle χ (N1-C2-C2′-N1′) using B3LYP/6-31G*.

Bipyridines that are *meta*-bridged by means of a chiral unit result in two diastereomeric states with a dihedral angle of 180°. An adequate choice of the chiral bridging unit allows a stabilization of one of these planar chiral conformations, so that only one noncomplexed conformation is selectively adopted in solution (Scheme 2). Furthermore, if the bridge is small enough, only one complexed state can be adopted, too. Therefore the control of planar chirality makes a unidirectional open–close mechanism possible: the addition of metal salts causes a closing motion in only one direction (from 180 to 0°). An overrotation in the other direction (from 180 to 360°) would lead to a complex in which the metal ion is not positioned between the bipyridine and the chiral clamp, but rather outside. However, due to the small bridge this is not possible. The opening process induced by the removal of the metal ion is also unidirectional, as only one noncomplexed state is formed. Only the green-framed area of Scheme 2 is passed through. The amplitude of motion in this unidirectional process amounts to 180°.

Although the conformations in bipyridine **4a** with dihedral angles of +35 and −35° show high energy values compared with the minima at 180° and are therefore not adopted, it is imaginable to design a system that has a unidirectional open–close mechanism and in which one of the axial chiral conformations is somehow stabilized at room temperature so that the open–close motion can be effected from that state. The amplitude of this unidirectional process would amount to about 35°. The result would be an adjustable system that can be adapted to further requirements depending on whether a higher or a lower amplitude is required.

Synthesis: To study the control of the motion amplitude of bipyridine units, we tried to build up four hinge systems. The different hinges were designed by simple modular combination of four (2×2) basic building blocks.

The bipyridine bridges **8** and **11** (Scheme 3) were obtained by the reaction of bipyridine **5** with hydroxybenzyl alcohol **6** or **9** in basic medium (NaH) and subsequent bromination with thionyl bromide.

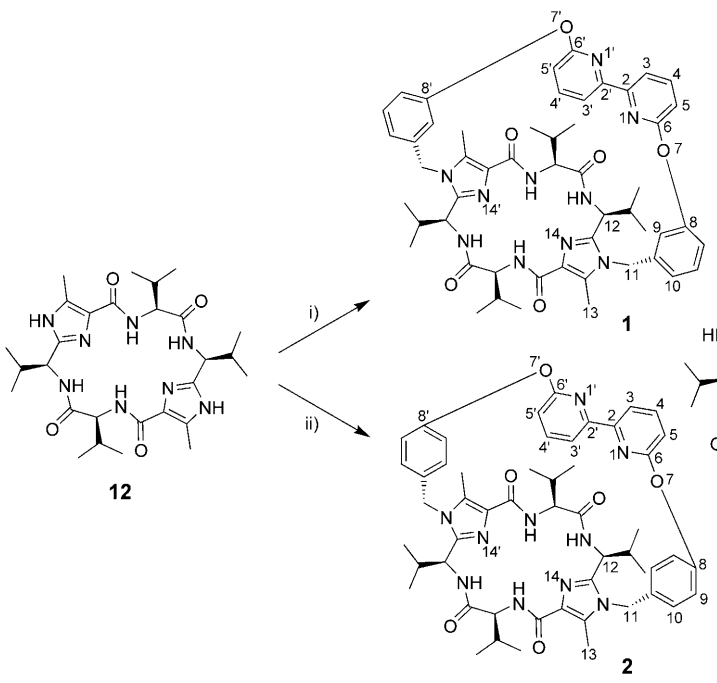


Scheme 3. Preparation of the bridges for the hinges. Reaction conditions: i) NaH, DMSO, Δ, 30%; ii) $SOBr_2$, CH_2Cl_2, 98%; iii) NaH, DMSO, Δ, 16%; iv) $SOBr_2$, CH_2Cl_2, 89%.

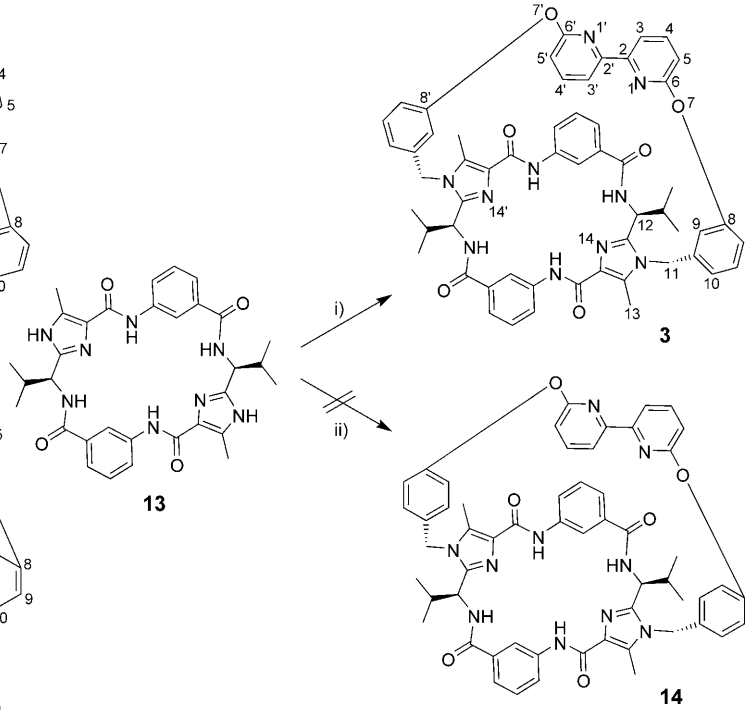
As further building blocks we used the chiral cyclopeptidic imidazole clamps **12** and **13**, which were already utilized in former studies and can be built up in a multistep synthesis from L-valine and α-amino-β-oxobutanic acid.[12] The preparation of the bridged clamps was accomplished by simple alkylation of the imidazole **12** or **13** using caesium carbonate (Schemes 4 and 5).

There are four possibilities of combining the bridges and clamps, but only the synthesis of the hinges **1**–**3** was successful. One reason for the failure of the synthesis of **14** can be seen in the mismatched proportions of bridge **11** and clamp **13**: due to the aromatic unit in the peptidic scaffold clamp **13** is larger than clamp **12**. The distance between the nitrogen atoms N14 and N14′ in a derivative of **13** amounts to 11.19 Å, whereas the same distance in a derivative of **12** is only 6.85 Å.[13] Bridge **8** shows a better tension angle because the aromatic substituents are arranged at an angle of 120°. Accordingly, the connection of **8** with both clamps was performed without any difficulties. Bridge **11** is much smaller because of the linear aromatic substitution. The coupling to the smaller clamp **12** is already difficult (yield: 16%) and fails with the larger clamp **13**.

Calculated molecular structures and energy profiles: As described above, an essential property of the hinges is an energetic discrimination of one diastereomer. To determine the energetically lowest configuration, DFT calculations were carried out and the energy differences of the four possible



Scheme 4. Preparation of the chiral molecular hinges **1** and **2**. Reaction conditions: i) **8**, Cs_2CO_3, CH_3CN, Δ, 25%; ii) **11**, Cs_2CO_3, CH_3CN, Δ, 16%.



Scheme 5. Preparation of the chiral molecular hinge **3**. Reaction conditions: i) **8**, Cs_2CO_3, CH_3CN, Δ, 34%; ii) **11**, Cs_2CO_3, CH_3CN, Δ, 0%.

isomers were computed.[14] The structures of (*S*)-**1**–**3** and (*R*)-**1**–**3** were determined by geometry optimizations using B3LYP and the 6-31G* basis set. In Table 1 the energy differences of the configurations of the hinges **1**–**3** are illustrated in comparison with the bipyridine **4a**. Figures 2, 3, and 4 show the calculated molecular structures of the two lowest energy minima of the hinges **1**–**3**.

Table 1. Calculated energy differences and dihedral angles (χ; N1-C2-C2′-N1′) of the hinges **1**–**3** and bipyridine **4a** using B3LYP/6-31G*.[14]

Compound	Conformer	χ (N1-C2-C2′-N1′) [°]	ΔE[a] [kJ mol^{-1}]
4a	(*pS*)-**4a**	+180.0	0.0
	(*aS*)-**4a**	+35.2	30.3
	(*aR*)-**4a**	−35.2	30.3
	(*pR*)-**4a**	−180.0	0.0
1	(*pS*)-**1**	+177.5	0.0
	(*aS*)-**1**[b]	+35.0	56.5
	(*aR*)-**1**	−33.3	57.6
	(*pR*)-**1**	−163.1	42.4
2	(*pS*)-**2**	+138.3	3.1
	(*aS*)-**2**	+44.2	0.0
	(*aR*)-**2**[b]	−44.0	31.7
	(*pR*)-**2**[b]	−138.0	57.6
3	(*pS*)-**3**	−171.8	0.0
	(*aS*)-**3**[b]	+35.0	81.7
	(*aR*)-**3**	−41.2	65.1
	(*pR*)-**3**	+175.2	19.8

[a] Relative energy relating to the lowest energy conformer. [b] No minima were found. The dihedral angles χ were fixed to the values given in the table, whereas all other structural parameters were optimized.

The calculations demonstrate that for hinge **1** the *pS* configuration exhibits the lowest energy value. For the *pR*-configured structure, a substantially higher energy value (difference relative to *pS*: 42.4 kJ mol^{-1}) is obtained. The energy values found for the axial chiral configuration are even higher and almost twice as large as the energy difference between the axial and planar chiral conformations in the non-fixed bipyridine **4a**. For conformer *aS* no minimum was found. Whereas **4a** shows four minima from which two are stabilized by 30 kJ mol^{-1}, the fixing of the bipyridine resulting in hinge **1** leads to a destabilization of three minima by 26–42 kJ mol^{-1}. Therefore only the *pS* isomer of **1** should be present in solution. Similar results were obtained for hinge **3**: here again the *pS* isomer is the conformer with the lowest energy, whereas the *pR* conformer shows a higher energy by 19.8 kJ mol^{-1}; for the axial configurations even higher values were calculated. The energy difference relative to the *pS* isomer amounts to 65.1 kJ mol^{-1} for the *aR* isomer and 81.7 kJ mol^{-1} for the *aS* conformer. For the latter no minimum was found. The large energy gap between the isomers of **1** and **3** can be explained by the different positions of the bipyridine units relative to the peptidic scaffolds: in the *pS* isomers, the C2–C2′ and N14–N14′ axes are almost perpendicular, whereas in the *pR* isomers they are parallel (Figures 2 and 4). As a result, the C8–C8′ distances in the *pR* conformers are larger. That causes tension in the rigid scaffold and leads to the high energy difference. In (*pS*)-**1** the C8–C8′ distance amounts to 8.99 Å, whereas in (*pR*)-**1** it is calculated to be 9.80 Å. In **3** there is even a greater difference between the isomers: for (*pS*)-**3**, the C8–C8′ distance amounts to 9.05 Å and for (*pR*)-**3** it is 10.44 Å. The high energy differences lead to the conclusion that hinges **1** and **3** adopt the configurations (*pS*)-**1** and (*pS*)-**3** also in solution at room temperature.

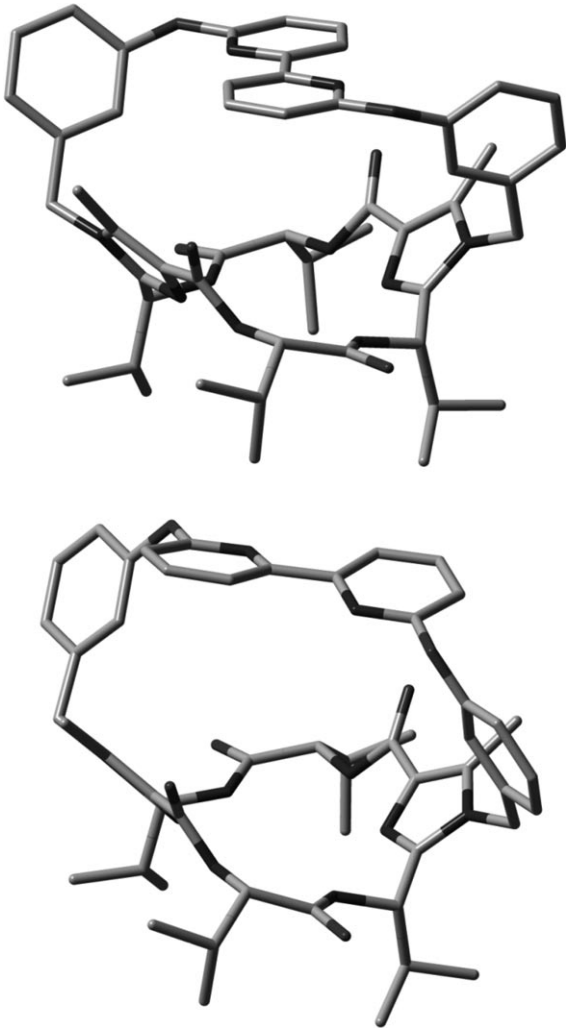


Figure 2. Molecular structures of (*pS*)-**1** (top) and (*pR*)-**1** (bottom) calculated using B3LYP/6-31G*. All hydrogen atoms have been omitted for clarity.

Energy calculations for hinge **2** provide two similarly low energy states. The energetically lowest isomer is the *aS* isomer, but the *pS* isomer is calculated to be only 3.1 kJ mol^{-1} less stable. For the isomers (*aR*)-**2** and (*pR*)-**2** no minima were found. The energy values calculated for the *R* conformers with fixed dihedral angles (31.7 and 57.6 kJ mol^{-1}, respectively) show that both conformations are significantly less stable than those of the *S* isomers. The marginal energy difference between (*aS*)-**2** and (*pS*)-**2** can be ascribed to the small *para*-substituted bridge **11**: to equalize tensions in the molecular scaffold, the bipyridine unit has to be slightly twisted. As a result, both conformers are quite similar (see Figure 3) and the difference between the

Figure 3. Molecular structures of (*pS*)-**2** (top) and (*aS*)-**2** (bottom) calculated using B3LYP/6-31G*. All hydrogen atoms have been omitted for clarity.

N1-C2-C2′-N1′ dihedral angle of the bipyridine units amounts to only 94.1°. Whereas **4a** shows four minima, of which two are stabilized by 30 kJ mol^{-1}, the fixing of the bipyridine resulting in hinge **2** leads to a destabilization of three minima by 30–86 kJ mol^{-1}. Thus, in contrast to compounds **1** and **3**, which exhibit only one configuration (*pS*), hinge **2** can exist as both *S* conformers, (*aS*)-**2** and (*pS*)-**2**.

Apart from the energies, the N1-C2-C2′-N1′ dihedral angles of the bipyridine units in the different conformers can be received from theoretical calculations. These angles are of interest because they allow statements about the height of the amplitude of motion. For (*pS*)-**1**, a dihedral angle of +177.5° was calculated. Therefore **1** can reach an amplitude of motion that amounts to approximately 180° because complexation with metal ions leads to a dihedral angle of about 0°. (*pS*)-**3** exhibits an N1-C2-C2′-N1′ angle of

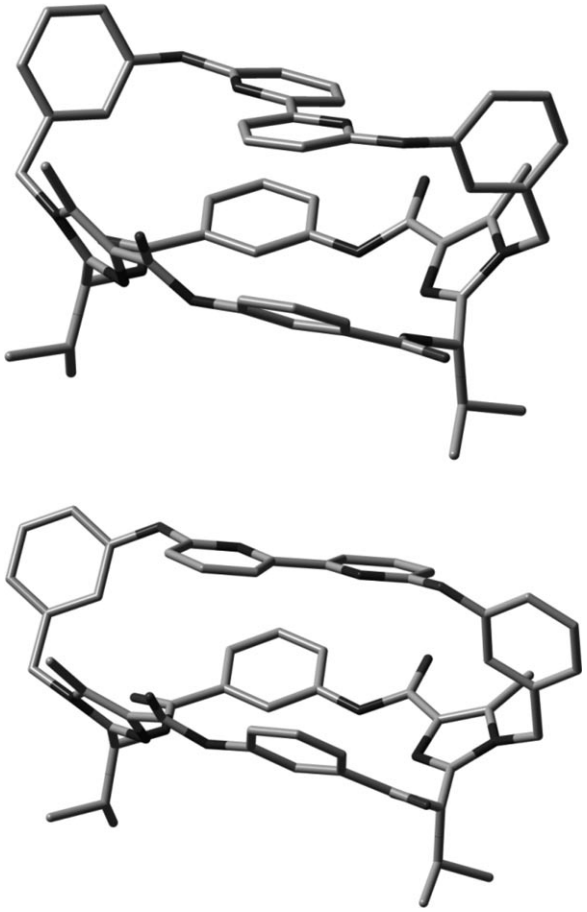


Figure 4. Molecular structures of (*pS*)-**3** (top) and (*pR*)-**3** (bottom) calculated using B3LYP/6-31G*. All hydrogen atoms have been omitted for clarity.

−171.8°, which means that the amplitude of motion during complexation can amount to almost 190°. (*pS*)-**2** as well as (*aS*)-**2** show a much lower amplitude of motion with 138.3 and 44.2°, respectively. But only the closing process from +44 to approximately 0° is unidirectional because both *S*-configured states are adopted in equilibrium. Therefore the amplitude for the unidirectional process amounts to only 44°.

These results show that the amplitude of motion of the bipyridine unit can be influenced by two different factors. On the one hand, the height of the amplitude can be controlled by using clamps of different size, as proved by the comparison of (*pS*)-**1** und (*pS*)-**3**. On the other hand, it is possible to obtain a very low amplitude of motion by embedding the bipyridine unit into a small bridge like **11**, as demonstrated by the comparison of the structures (*pS*)-**1** and (*pS*)-**2**.

NOESY experiments: To prove that the theoretical determination of the configurations is consistent with experimental observations, some 2D NOESY spectra were analyzed to determine diverse H–H distances in the structures **1** and **3**. In Table 2 the atomic distances obtained from NMR spectra are compiled in comparison to theoretical values.

Table 2. Atomic distances [Å] for **1** and **3** obtained from NMR spectroscopic experiments and calculated values of atomic distances [Å] for the conformers (*pS*)-**1**, (*pS*)-**3**, (*pR*)-**1**, and (*pR*)-**3** using B3LYP/6-31G*.

	Experimental[a]		Calculated[b]			
	1	**3**	(*pS*)-**1**	(*pR*)-**1**	(*pS*)-**3**	(*pR*)-**3**
O7–O7′	–	–	8.25	8.12	8.25	8.12
C8–C8′	–	–	8.99	9.80	9.05	10.44
H11a–H11b	1.75[c]	1.75[c]	1.75	1.75	1.76	1.75
H11a–H10	2.18	2.22	2.35	2.99	2.34	2.60
H13–H11a	2.41	2.41	2.50	2.46	2.52	2.57
H13–H10	3.02	2.74	3.53	4.99	3.01	4.04
H13–H9	3.00	3.38	3.73	2.48	4.19	3.24
H13–H5	–[d]	–[d]	5.03	2.98	5.91	2.88
H13–H4	2.49	–[d]	2.98	3.58	3.47	3.78
H13–H3	2.36	4.03	2.73	4.93	3.45	5.95

[a] Values obtained from NMR spectroscopy. [b] Values calculated by using B3LYP/6-31G*. [c] The distance between the diastereotopic protons H11a and H11b was used as the reference distance for calibration. [d] In the 2D NOESY spectrum, no cross-peaks were observed.

Both **1** and **3** show a striking difference between the *pS* and *pR* isomers in the atomic distances of the protons H13 and H5 and the distance of the protons H13 and H3, respectively. Whereas large H13–H5 distances (5.03 for **1**, 5.91 Å for **3**) and small H13–H3 distances (2.73 and 3.45 Å, respectively) are calculated for the *S* isomer, there are small H13–H5 distances (2.98 and 2.88 Å, respectively) and large H13–H3 distances (4.93 and 5.95 Å, respectively) for the *R* isomer. Considering that the maximum atomic distance that still leads to a corresponding cross-peak amounts to 4 Å, it is possible to determine the configuration of **1** and **3** in solution by a comparison with the calculated values: for the atoms H13 and H5 no corresponding cross-peak is observed in the 2D NOESY spectrum, which is a first hint that **1** and **3** indeed exist exclusively as *S* configurations. This result is confirmed by a comparison of the H13–H3 distances: for both **1** and **3** corresponding cross-peaks are obtained in the NMR spectrum, from which atomic distances of 2.36 and 4.03 Å, respectively, can be calculated. This again is consistent with the theoretical H13–H3 distance of the *S* isomers. Thus it is proved that the theory, according to which the *S* isomer is energetically more favored and is therefore formed preferentially, agrees with the experimental results.

From calculations for hinge **2**, two similar energetically stable conformers were obtained. This indicates a higher flexibility of the molecular structure **2** than of structure **1** or **3**. Furthermore the protons H9 and H10 in structure **2** are not fixed spatially because the *para*-substituted aromatic unit, in contrast to the *meta*-substituted unit in **1** and **3**, can rotate freely. A distance determination by means of NOESY data is therefore not expedient.

CD and UV spectroscopy experiments: To understand more precisely the closing process of the hinges by complexation with divalent metal ions, the reference system **4a** (R = Me), **4b** (R = Ph), and the hinge **1** were analyzed by means of CD and UV spectroscopy in different solvents.

In the case of bipyridine **4**, the addition of $Cu(OTf)_2$, $Zn(OTf)_2$, $Cd(OTf)_2$, and Hg(OTf) (OTf = trifluoromethanesulfonate) in a mixture of dichloromethane and acetonitrile leads to a complexation that is visible in the UV spectrum as a bathochromic shift of the bipyridine band from 307 nm to a maximum of 331 nm. The formation of the complex is completed when for example, 1.0 equiv of Zn^{2+} or 1.5 equiv of Hg^{2+} are added. When a mixture of methanol/acetonitrile is used, a different behavior is observed: only the addition of Hg^{2+} results in a complex formation, whereas no complexation is found with Zn^{2+} ions. For saturation, 3.0 equiv of Hg^{2+} are needed and again a bathochromic shift from 307 to 331 nm is observed.

Analogously to the reference system **4** the closing process of hinge **1** was analyzed in different solvents. Especially the addition of Zn^{2+} and Hg^{2+} ions in dichloromethane and methanol leads to very contrary effects that will be discussed in detail. A formation of the Zn^{2+} complex by adding $Zn(OTf)_2$ to a solution of (*pS*)-**1** in dichloromethane/acetonitrile can be observed in the UV and CD spectrum (see Figure 5). In the UV spectrum this can be seen by a bathochromic shift of the bipyridine band from 307 to 331 nm. Here the complexation is complete after adding 1.0 equiv of Zn^{2+}. In the CD spectrum the conformational change caused by the complexation can also be observed. The positive Cotton effects at 242 and 272 nm as well as the negative Cotton effects at 255 and 296 nm in the uncomplex-

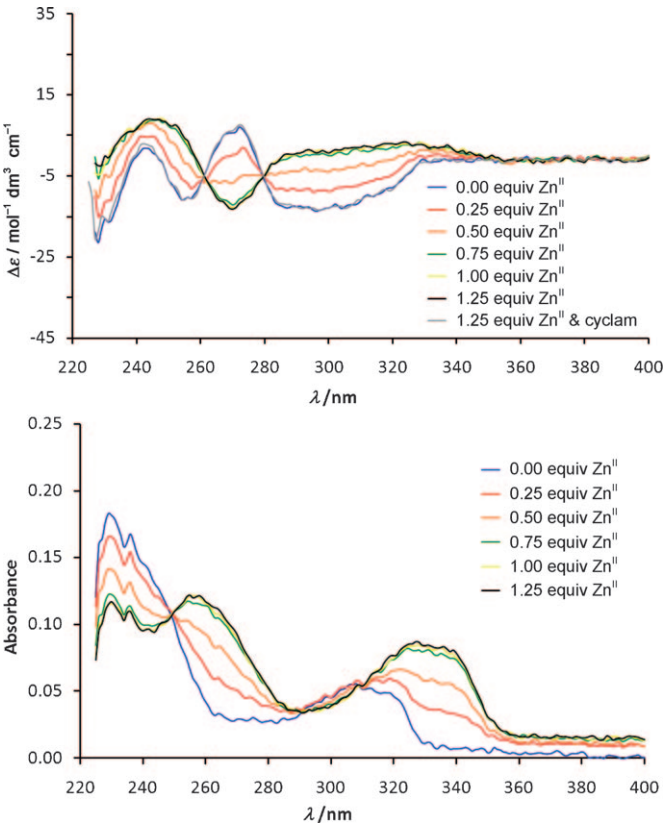


Figure 5. CD spectra (top) and UV spectra (bottom) of hinge **1** with different equivalents of $Zn(OTf)_2$ in dichloromethane/acetonitrile (96:4).

ated state change drastically: the broad negative band at 296 nm disappears completely and the positive Cotton effect at 272 nm turns into a negative band at 266 nm. These results are consistent with the behavior of the hinge, which shows a planar chirality in the uncomplexed state that is lost during complexation. The Zn^{2+} complex shows merely the chiral elements of the clamp.

When an excess of the strong metal-ion complexing agent cyclam is added, the hinge opens and shows again the positive and negative Cotton effects at 272 and 296 nm that can be ascribed to the planar chirality of (*pS*)-**1**. Analogous measurements in methanol do not lead to complex formation: in the CD spectrum as well as in the UV spectrum there is no visible change when Zn^{2+} is added. This is consistent with the reference system.

If the larger Hg^{2+} ion is used instead of the Zn^{2+} ion, contrary effects are observed during complexation in dichloromethane and methanol (see Figures 6 and 7). In the UV and CD spectra only minimal effects can be detected by addition of Hg^{2+} ions in dichloromethane/acetonitrile. Even after the addition of 5.0 equiv of Hg^{2+}, there is neither a bathochromic shift that would indicate the formation of the complex nor a disappearance of the bands that indicate the planar chirality.

In methanol/acetonitrile, however, a complexation of **1** is detectable, but it is not complete until 3.0 equiv of Hg^{2+} are added. The UV and CD curve progression is here similar to

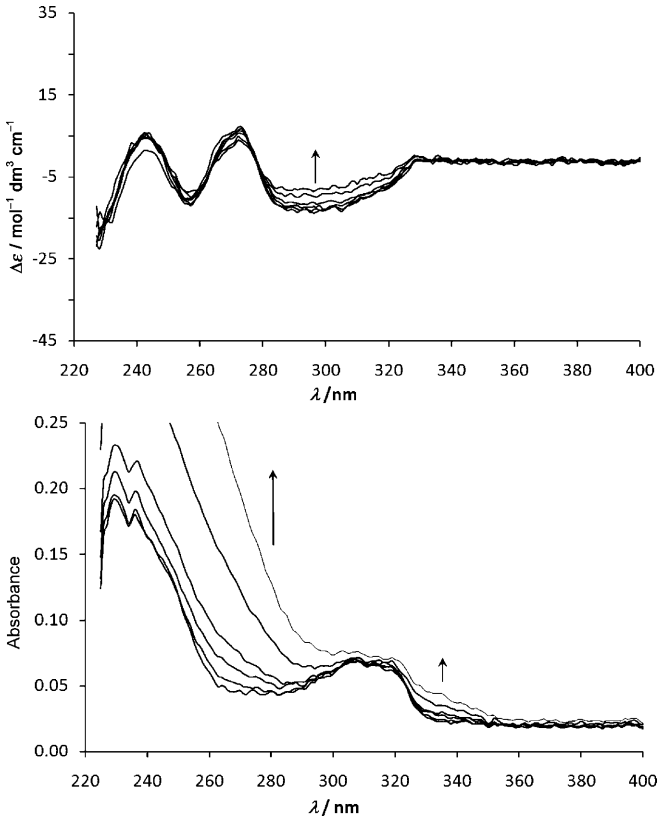


Figure 6. CD spectra (top) and UV spectra (bottom) of hinge **1** with different equivalents of $Hg(OTf)_2$ in dichloromethane/acetonitrile (96:4).

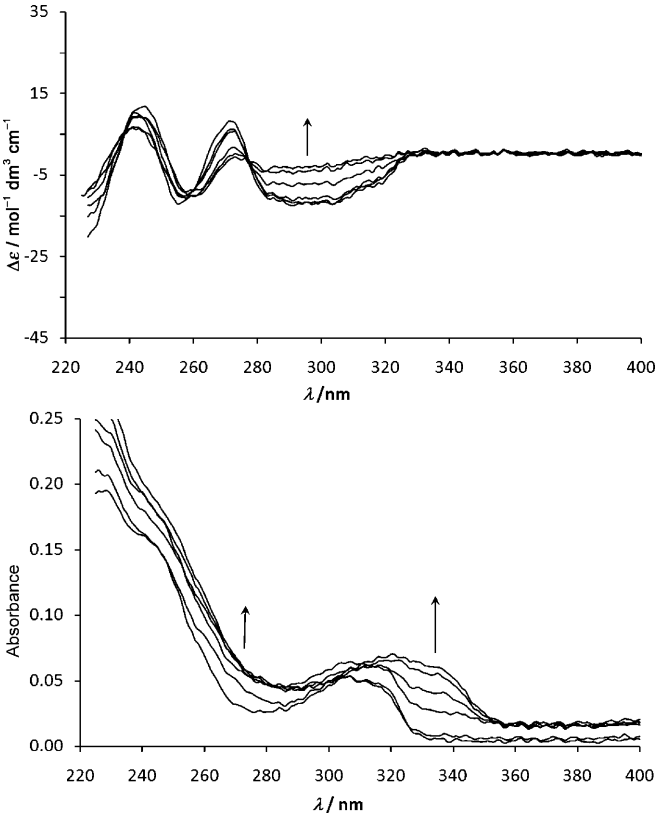


Figure 7. CD spectra (top) and UV spectra (bottom) of hinge **1** with different equivalents of $Hg(OTf)_2$ in methanol/acetonitrile (96:4).

the formation of the Zn^{2+} complex in dichloromethane/acetonitrile, but the bathochromic shift of the bypridine band from 307 to 320 nm is lower.

The reference measurements described above show that the Zn^{2+} complex of **4a** in dichloromethane and the Hg^{2+} complex of **4a** in methanol exhibit a bathochromic shift of the bipyridine band from 307 to 331 nm and from 307 to 328 nm, respectively. Therefore the slightly smaller bathochromic shift of the Hg^{2+} complex of **1** in methanol cannot be ascribed to solvent effects but rather to different bonding relations within the metal complex. It should be possible to draw a conclusion from the geometry of the complex because the location of the absorption maximum depends on the N1-C2-C2′-N1′ dihedral angle. To estimate the dihedral angle in the Hg^{2+} complex of **1**, UV spectra of the reference system **4a** with $[M(solvent)_2]^{2+}$ in relation to the dihedral angle were calculated using time-dependent density functional theory (TD-DFT) methods. We used Zn^{2+} as the metal ion M^{2+}, and as solvent molecules we used CH_3CN. The reason for this is the fact that the location of the maxima depends neither on the solvent nor on the metal ion, and the chosen complex is the one with the lowest numbers of electrons and conformers. In Figure 8 the shifts of the absorption maximum relative to $[\mathbf{4a}{\cdot}Zn(CH_3CN)_2]^{2+}$ with an ideal dihedral angle of 0° are illustrated. It becomes evident that a shift of 10 nm corresponds to a dihedral angle of about 30°. If this value is assigned to the Hg^{2+} complex

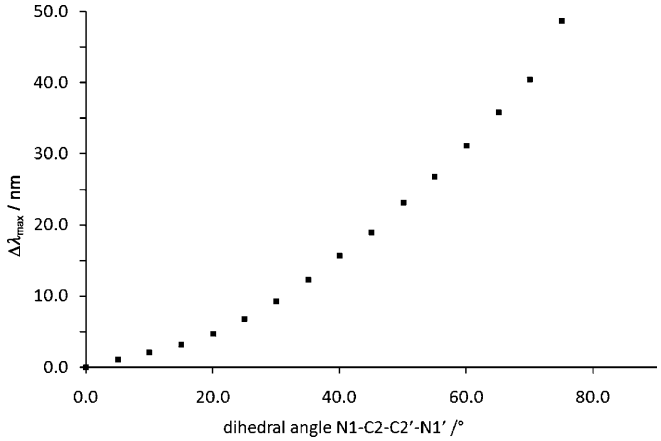


Figure 8. Relative shift of the absorptions maximum ($\Delta\lambda_{max}$) of the bipyridine band of the complex $[\mathbf{4}\cdot Zn(MeCN)_2]^{2+}$ in relation to the dihedral angle N1-C2-C2′-N1′ calculated by TD-DFT/6-31G* ($\lambda_{max}=326$ nm for N1-C2-C2′-N1′ = 0°).

of **1** in methanol, the amplitude of motion in the closing process amounts to 150° and is much lower than with Zn^{2+} in dichloromethane/acetonitrile.

The fact that the formation of the complex is successful in methanol with Hg^{2+} whereas no complex is found in dichloromethane/acetonitrile can probably be ascribed to the metal ions that are differently solvated in distinct solvents: in dichloromethane/acetonitrile the large Hg^{2+} ion is complexed by acetonitrile and therefore it is too large to get into the cavity between the bipyridine unit and the clamp. As mentioned before, a complex in which the metal ion is placed outside the cavity cannot be formed. In methanol/acetonitrile the Hg^{2+} ion is complexed by the smaller methanol molecules so that it can get into the cavity. Nevertheless, no ideal complex is formed and the resulting enlargement of the cavity by Hg^{2+} leads to a dihedral angle that differs from 0° and amounts to approximately 30°.

The hinges **2** and **3** show a similar behavior to (*pS*)-**1**. The same solvent and metal ion effects can be observed, but the changes in the CD and UV spectra are less distinctive. Hinge **3** shows, for example, a bathochromic shift of the bipyridine band from 306 to 331 nm upon addition of Zn^{2+} in dichloromethane, which is almost identical to the values found for **1**. This is consistent with the above-described calculations that predict a motion amplitude of 190°.

There is also an experimental affirmation of the calculations made for **2**. According to the calculations, the dihedral angles of (*pS*)-**2** and (*aS*)-**2** differ significantly from 180°. This has to result in a shift of the maximum of the absorption band of the bipyridine. In the UV spectrum there is indeed an absorption maximum located at 295 nm that is shifted hypsochromically (12 nm) compared to the absorption maximum of **1**. A specific value for the amplitude of motion of **2** cannot be deduced from the spectra, but in accordance with the calculation, it should be much lower than that for hinge **1**.

Conclusion

All in all, we were able to show that it is possible to control the unidirectional open–close mechanism of metal-ion-driven molecular hinges. Whether or not and to what extent that mechanism works can be determined by the choice of the solvent, the choice of the metal ion, and the choice of the combination of bridges and clamps. By variation of the metal ions and the clamp-bridge combinations, the height of the amplitude of motion can be influenced. Quantum mechanical calculations show that it is possible to reach amplitudes from 45 up to 190°. This combination of initializing or preventing a movement by choosing the adequate chemical conditions and the control of the amplitude of motion can be used for more complex switching or motion processes of molecular machines.

Experimental Section

General remarks: All chemicals were reagent grade and used as purchased. Reactions were monitored by TLC analysis using silica gel 60 F_{254} thin-layer plates. Flash chromatography was carried out on silica gel 60 (230–400 mesh). ^1H and ^{13}C NMR spectra were measured using Bruker Avance DMX 300 and Avance DRX 500 spectrometers. All chemical shifts (δ) are given in ppm relative to TMS at 25 °C. The spectra were referenced to deuterated solvents indicated in brackets in the analytical data. HRMS spectra were recorded using a Bruker BioTOF III Instrument. IR spectra were measured using a Varian 3100 FTIR Excalibur Series spectrometer. UV and CD absorption spectra were taken using a Jasco J-815 spectrophotometer.

Hinge 1: Caesium carbonate (130 mg, 0.400 mmol) was added to a solution of scaffold **12** (27 mg, 0.048 mmol) and bipyridine **8** (25 mg, 0.048 mmol) in anhydrous acetonitrile (35 mL) and the mixture was heated to reflux at 90 °C for 5 h. After cooling to room temperature, ethyl acetate (60 mL) and water (15 mL) were added. The organic layer was washed with water (3×10 mL), dried ($MgSO_4$), and concentrated in vacuo. Column chromatography of the residue on silica gel (CH_2Cl_2/EtOAc/MeOH, 75:25:3) afforded hinge **1** (11 mg, 25 %) as a white solid. M.p. >250 °C; ^1H NMR (500 MHz, $CD_3OD/CDCl_3$): $\delta=7.62$ (dd, $^3J(H,H)=7.7$ Hz, $^3J(H,H)=7.7$ Hz, 2H; H_{ar}), 7.33 (dd, $^3J(H,H)=7.9$ Hz, $^3J(H,H)=7.9$ Hz, 2H; H_{ar}), 7.06 (d, $^3J(H,H)=8.1$ Hz, 2H; H_{ar}), 7.00 (dd, $^3J(H,H)=8.0$ Hz, $^4J(H,H)=1.8$ Hz, 2H; H_{ar}), 6.84 (d, $^3J(H,H)=7.5$ Hz, 2H; H_{ar}), 6.80 (dd, $^3J(H,H)=8.1$ Hz, $^4J(H,H)=0.6$ Hz, 2H; H_{ar}), 6.30 (s, 2H; H_{ar}), 5.27 (d, $^2J(H,H)=16.7$ Hz, 2H; CH_2), 4.95 (d, $^3J(H,H)=6.5$ Hz, 2H; NHC*H*CH), 4.87 (d, $^2J(H,H)=16.7$ Hz, 2H; CH_2), 4.36 (d, $^3J(H,H)=6.5$ Hz, 2H; NHC*H*CH), 2.46 (s, 6H; imidazole CH_3), 2.14–2.04 (m, 4H; $CHCH(CH_3)_2$), 0.94 (d, $^3J(H,H)=6.9$ Hz, 6H; $CH(CH_3)_2$), 0.92 (d, $^3J(H,H)=6.8$ Hz, 6H; $CH(CH_3)_2$), 0.87 (d, $^3J(H,H)=6.8$ Hz, 6H; $CH(CH_3)_2$), 0.86 ppm (d, $^3J(H,H)=6.7$ Hz, 6H; $CH(CH_3)_2$); ^{13}C NMR (125 MHz, $CD_3OD/CDCl_3$): $\delta=170.2$, 162.0, 161.5, 155.8, 152.4, 146.1, 141.3, 135.0, 132.5, 130.0, 129.6, 121.7, 120.3, 117.7, 114.7, 112.0, 58.1, 50.4, 46.8, 34.0, 32.3, 19.1, 18.5, 18.3, 17.6, 9.6 ppm; IR (KBr): $\tilde{\nu}=3327$, 2920, 2851, 1724, 1660 cm^{-1}; UV/Vis (MeOH): λ ($\log\varepsilon$) = 307 nm (3.92) ; HRMS (ESI): m/z calcd for $C_{52}H_{61}N_{10}O_6$ $[M+H]^+$: 921.4776; found: 921.4796.

Hinge 2: Caesium carbonate (98 mg, 0.300 mmol) was added to a solution of scaffold **12** (19 mg, 0.034 mmol) and bridge **11** (18 mg, 0.034 mmol) in anhydrous acetonitrile (25 mL) and the mixture was heated to reflux at 90 °C for 5 h. After cooling to room temperature, ethyl acetate (30 mL) and water (15 mL) were added. The organic layer was washed with water (3×10 mL), dried ($MgSO_4$), and concentrated in vacuo. Column chromatography of the residue on silica gel (CH_2Cl_2/EtOAc/MeOH, 75:25:2) provided hinge **2** (5.0 mg, 16 %) as a white solid.

M.p. >250 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.74 (dd, ^3J(H,H) = 7.7 Hz, ^3J(H,H) = 7.7 Hz, 2H; H_{ar}), 7.42 (d, ^3J(H,H) = 7.7 Hz, 2H; H_{ar}), 6.99 (d, ^3J(H,H) = 7.7 Hz, 2H, H_{ar}), 6.77 (d, ^3J(H,H) = 8.6 Hz, 4H; H_{ar}), 6.61 (d, ^3J(H,H) = 8.6 Hz, 2H; H_{ar}), 5.33 (d, ^2J(H,H) = 16.2 Hz, 2H; CH_2) 4.98 (d, ^3J(H,H) = 6.6 Hz, 2H; NHC*H*CH), 4.75 (d, ^2J(H,H) = 16.2 Hz, 2H; CH_2), 4.52 (d, ^3J(H,H) = 6.6 Hz, 2H; NHC*H*CH), 2.28–2.20 (m, 4H; CHC*H*$(CH_3)_2$), 2.18 (s, 6H; imidazole CH_3), 1.05 (d, ^3J(H,H) = 6.8 Hz, 6H; CH$(CH_3)_2$), 1.04 (d, ^3J(H,H) = 6.8 Hz, 6H; CH$(CH_3)_2$), 1.00 (d, ^3J(H,H) = 6.8 Hz, 6H; CH$(CH_3)_2$), 0.90 ppm (d, ^3J(H,H) = 6.8 Hz, 6H, CH$(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.3, 171.2, 162.9, 162.4, 156.1, 156.0, 146.3, 146.2, 140.2, 133.8, 129.8, 129.3, 127.1, 120.0, 118.6, 113.8, 58.7, 50.8, 47.1, 33.9, 31.1, 19.5, 18.8, 18.2, 18.1, 10.1 ppm; UV/Vis (MeOH): λ (log ε) = 296 nm (3.90); IR (KBr): $\tilde{\nu}$ = 2960, 2917, 2849, 1737, 1655 cm^{-1}; UV/Vis (MeOH): λ (log ε) = 295 nm (3.90); HRMS (ESI): *m*/*z* calcd for $C_{56}H_{61}N_{10}O_6$ $[M+H]^+$: 921.4776; found: 921.4767.

Hinge 3: Caesium carbonate (110 mg, 0.33 mmol) was added to a solution of scaffold **13** (25 mg, 0.04 mmol) and bridge **8** (20 mg, 0.04 mmol) in anhydrous acetonitrile (60 mL) and the mixture was heated to reflux at 90 °C for 3 h. After cooling to room temperature, ethyl acetate (30 mL) and water (15 mL) were added. The organic layer was washed with water (3×10 mL), dried ($MgSO_4$), and concentrated in vacuo. Column chromatography of the residue on silica gel (CH_2Cl_2/EtOAc/MeOH, 75:25:2) led to hinge **3** (13 mg, 34%) as a yellowish solid. M.p. >250 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.57 (s, 2H; CON*H*Ph), 8.27–8.25 (m, 2H; H_{ar}) 7.88–7.86 (m, 2H; H_{ar}), 7.58–7.54 (m, 2H; H_{ar}), 7.36–7.33 (m, 4H; H_{ar}), 7.16–7.14 (m, 2H; H_{ar}), 6.88–6.86 (m, 2H; H_{ar}), 6.78–6.76 (m, 2H; H_{ar}), 6.53 (s, 2H; CON*H*CH), 6.38–6.37 (m, 2H; H_{ar}), 6.05–6.03 (m, 2H; H_{ar}), 5.50 (d, ^2J(H,H) = 16.2 Hz, 2H; CH_2) 5.36–5.32 (m, 2H; NHC*H*CH), 5.07 (d, ^2J(H,H) = 16.2 Hz, 2H; CH_2), 2.46 (s, 6H; imidazole CH_3), 2.26–2.17 (m, 2H; CHC*H*$(CH_3)_2$), 1.05 (d, ^3J(H,H) = 6.7 Hz, 6H; CH$(CH_3)_2$), 0.87 ppm (d, ^3J(H,H) = 6.7 Hz, 6H; CH$(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.7, 161.9, 154.5, 147.8, 140.7, 137.3, 135.7, 133.3, 132.7, 130.1, 129.7, 125.5, 124.9, 123.0, 121.7, 119.3, 116.5, 116.4, 113.8, 112.5, 111.1, 50.7, 47.1, 35.6, 19.1, 18.7, 9.7 ppm; IR (KBr): $\tilde{\nu}$ = 3453, 3382, 3062, 2958, 2924, 2854 cm^{-1}; UV/Vis (MeOH): λ (log ε) = 267 (4.18), 307 nm (3.82); HRMS (ESI): *m*/*z* calcd for $C_{56}H_{52}N_{10}O_6Na$ $[M+Na]^+$: 983.3964; found: 983.3984.

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