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We designed visible-light-driven molecular motors consisting of coordination complexes featuring a bis(benzoxazole)-based ligand. Complexation with various metal salts locks the non-rigid lower half of the ligand into position, resulting in well-defined unidirectional rotation upon irradiation with light. This system allows for unprecedented control over both the motor function and important motor properties, such as rotation speed, absorption wavelength, and the coupling of molecular motions during the rotation cycle.
Activating a light-driven molecular motor by metal complexation

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SUMMARY
Designing increasingly complex, responsive, and dynamic molecular systems, whose actions can be controlled by a combination of cooperative stimuli, is a key challenge toward the development of more advanced functional molecular machines. Herein, we report new photochemically driven molecular motors based on a bis(benzoxazole) ligand. Coordination of the ligand to a metal salt leads to the selective in situ activation of a well-defined motor function, which can be deactivated in the presence of a competing ligand. The rotation speed and absorption wavelength are tuned by the choice of metal, allowing unprecedented control of the molecular system. DFT calculations show that the geometry of the metal center influences the rotational barriers and the possibility to couple the rotary motion with the wagging movement at the metal center. The approach presented here will open new avenues toward more complex, dynamic, and coupled systems.

INTRODUCTION
Since the development of the first light-driven molecular motors based on overcrowded alkenes, tremendous progress has been made to further control rotary motion and elucidate key aspects of their functioning. 1–5 Concurrently with the development of other artificial molecular machines, 6–15 which include transporters, 16,17 muscles, 18–20 shuttles 21–23 and pumps, 24–27 artificial photochemically driven rotary molecular motors have found applications in distinct fields of chemistry. Their uses range from responsive surfaces and materials to enantioselective catalysis and supramolecular systems. 3–5 Intriguing examples are the use of the rotation of molecular motors to apply forces at cell-matrix and cell-cell junctions, 28 to impart unidirectional rotation in a metal-organic framework, 29,30 to achieve complex actuation in liquid crystals, 31–33 and to shift a chemical equilibrium energetically uphill. 34

The overcrowded alkene-based molecular motors have specific and fixed designs that match the properties required for the envisioned application, e.g., absorption wavelength, necessary functional groups, and rotation speed. 35 Controlling the motor properties in situ by providing an external stimulus that is orthogonal to light irradiation is a crucial step toward the goal of creating adaptive, responsive, and dynamic systems. In previous reports, different chemical stimuli have been used to modify the properties of a motor, such as its rotation speed, 36,37 absorption wavelength, 36,37 direction, 38 and the triggering or blocking of rotary motion. 39,40

Inspired by these examples and building on our earlier research on metallo-based sterically overcrowded alkenes, 41,42 we aimed to take on the challenge of regulating...
the motor characteristics even further, by designing a system in which the desired motor function is activated in situ by coordination of a ligand to a metal ion. This opens pathways toward adaptive mechanical behavior and provides unprecedented flexibility in the control and fine-tuning of the motor and its properties. In our previous approach, metal complexation was applied on structures of already functioning motors to in situ modify their properties. Our new design exploits the metal complexation to overcome the otherwise lack of rigidity in the lower half (the stator) and allows the motor to show well-defined unidirectional rotary motion (Figures 1A and 1B). Indeed, without a “locking” agent, free rotation about the single bonds that attach the lower half to the central C=C bond (the axle of rotation) leads to the rapid interconversion of various conformers, which prohibits such a defined motor function (Figure 1B). Complexation with an appropriate metal locks the lower half in a single conformation, which allows the resulting motor to go through its operational routine, as described below (Figure 1C). In addition, the rotation speed and absorption wavelength can be tuned by the choice of metal salt. Hence, we can achieve both in situ activation of the specific motor function and additional regulation of its properties with a chemical stimulus that is orthogonal to light irradiation and heat.

We designed a molecular motor based on a bis(benzoxazole) lower half to allow complexation with metal ions. Bis(oxazoline) ligands have been extensively described in terms of their synthesis and are known to coordinate to several metals, especially acting as chiral ligands featuring C2-symmetric structures, which have found widespread application in asymmetric catalysis. In the bis(benzoxazole) scaffold, the aromatic system shifts the light absorption to longer wavelengths compared with conventional aliphatic and non-conjugated bis(oxazoline) ligands. This feature has several advantages because visible light is more selectively absorbed by the chromophore than UV light, has a higher penetration depth, leads to less photodegradation in materials, and is less harmful to living cells. Furthermore, the structural similarity of the bis(benzoxazole) scaffold to the previously reported motor lower halves makes it likely that the motor will operate according to a similar mechanism as the classical 2nd generation Feringa motors.

In accordance with our previous motor designs, we envision a four-step mechanism involving the upper and lower halves rotating about the central alkene double bond (Figure 1C). The rotation cycle consists of two photochemical E-Z isomerizations, each of them followed by a thermal helix inversion (THI); in every step of the process, the helicity of the overcrowded alkene is inverted. The photoisomerization represents the “power stroke” step, where the stable folded configuration of the motor converts into a metastable twisted configuration. The methyl group changes its orientation from pseudo-axial to pseudo-equatorial in the photochemical reaction. The strain associated with the formation of the metastable isomers is released by the THI, the ratcheting step of the Feringa motors, with the irreversible formation of a second stable state.

RESULTS AND DISCUSSION
Synthesis and characterization
In L1 (Figure 2B), we installed a fluorine-bearing quaternary stereocenter both for synthetic convenience, namely, to protect the allylic position in the molecule, which could be sensitive to deprotonation, and as a handle to clearly identify the species subject to our analysis by 19F nuclear magnetic resonance (NMR) spectroscopy (see supplemental information for details about the synthesis and characterization of ligand L1). Subsequently, three metal complexes were prepared by coordinating
the ligand in CH₂Cl₂ to ZnCl₂, PtCl₂, and CuCl₂. Upon metal complexation, the UV-vis absorption band was strongly bathochromically shifted (Figures 2A and S1; Table 1). We attribute this effect mainly to the locking effect of the metal, which inhibits the free rotation of the benzoxazole rings and planarizes the structure, improving the overlap of the π-system, which is mainly involved in the first π-π* transition (see Figures 2B and 2C and discussion below).

The degree of bathochromic shift of the absorption wavelength depends on the chosen metal. The effect was the largest for the [CuCl₂L₁] complex, for which the maximum absorption wavelength shifted from 388 nm in the free ligand to 478 nm, a difference of almost 100 nm. Interestingly, the tail of absorption of [CuCl₂L₁] reaches wavelengths over 600 nm, deeper into the visible range of the spectrum than most other 2nd generation molecular motors that have been reported before.35
Crystals of the free ligand, as well as of the [ZnCl₂L₁], [PtCl₂L₁], and [CuCl₂L₁] complexes, were obtained and analyzed by single-crystal X-ray crystallography (Figure 2B; Table 1; supplemental information section X-ray structural data). The structure of L₁ in Figure 2B shows a conformation in which the benzoxazole moieties are twisted with respect to each other. Conformational disorder was found in the X-ray structure, indicating that the ligand can assume several conformations due to the
free rotation about the single bonds; consequently, the nitrogen and oxygen atoms can adopt the same position in the crystal structure randomly. In contrast, upon complexation, both nitrogen atoms in the benzoxazole moieties coordinate to the metal, leading to an overall more planar geometry. The choice of metal determines the coordination geometry in the complexes. Complexation with ZnCl₂ results in a tetrahedral geometry around the zinc atom, a d¹⁰ metal center, which is the most common four-coordinate geometry found in Zn(II) complexes.49,50 In contrast, the d⁸ Pt(II) complex gives a typical square-planar geometry around the metal center. Finally, the copper complex, featuring a d⁹ electron configuration, shows a significant distortion from the tetrahedral geometry as a result of the Jahn-Teller effect.51 To remove the degeneracy in its electron configuration, the coordination sphere is flattened, and the resulting geometry can be viewed as being between tetrahedral and square planar. This is also evident from the angle q, defined as the dihedral angle between the mean planes of the benzoxazole phenyl rings, and the coordination angle θ, which is defined as the dihedral angle of the planes by N-M-N and Cl-M-Cl. For a visual depiction, see Figure 2C.

**Irradiation experiments**

Samples of the metal complexes were irradiated at room temperature and at −40°C. However, no change in the UV-vis absorption spectra was observed. Therefore, nanosecond transient absorption spectroscopy (TAS) was used to study the effect of the metal coordination on the thermal relaxation of the complexes at room temperature. In all three complexes, excitation of a sample resulted in the formation of a red-shifted transient species that rapidly decayed on a timescale of nanoseconds or microseconds (Figures 2D and S2–S9; Table 1). In all cases, a transient signal with a positive change in optical density (ΔOD) appeared immediately after the laser pulse. The transient signal is bathochromically shifted compared with the bleaching of the absorption band of the reagent. Because this band decays back to zero over time and no degradation of the sample occurs, decomplexation can be ruled out. Instead, this induced absorption band is associated with the formation of the metastable state upon irradiation, as expected in classical Feringa motors.40,52,53 Time-dependent density functional theory (TDDFT) calculations confirm that the formation of a

<table>
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<tr>
<th>Compound</th>
<th>λmax (nm)</th>
<th>ε (M⁻¹ cm⁻¹)</th>
<th>τ (ns)</th>
<th>N–N distance (Å)</th>
<th>α (°)</th>
<th>β (°)</th>
<th>q (°)</th>
<th>θ (°)</th>
</tr>
</thead>
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<td>L₁</td>
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<td>–</td>
<td>3.84</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>[ZnCl₂L₁]</td>
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<td>1.6</td>
<td>2.83</td>
<td>116.6</td>
<td>88.5</td>
<td>169.2</td>
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<tr>
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<td>478</td>
<td>1.8 x 10⁴</td>
<td>10.3</td>
<td>2.79</td>
<td>115.7</td>
<td>88.7</td>
<td>165.1</td>
<td>51.8</td>
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<tr>
<td>[PtCl₂L₁]</td>
<td>441</td>
<td>1.2 x 10⁴</td>
<td>22.4</td>
<td>2.71</td>
<td>111.1</td>
<td>85.0</td>
<td>60.5</td>
<td>4.4</td>
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</tbody>
</table>

Summary of key properties of ligand L₁ and the metal complexes, including the maximum absorption wavelength λmax, the extinction coefficient ε, the measured lifetime (τ) of the metastable state(s), the N–N distance, the bite angle α, the N-M-N angle β, the folding angle q, which is defined as the dihedral angle between the mean planes of the benzoxazole phenyl rings, and the coordination angle θ, which is defined as the dihedral angle of the planes by N-M-N and Cl-M-Cl. For a visual depiction, see Figure 2C.
A metastable state is accompanied by a bathochromic shift in the absorption spectrum (Table S5). Notably, the transient signals in the zinc and copper complexes show only one decay lifetime each, of 1.6 and 10.3 μs, respectively, whereas the platinum complex shows a rapid decay of 22.4 ns, followed by a slower decay of 23.0 μs. Again, this result shows that the choice of metal greatly influences the behavior of the complexes.

**Mechanistic study by DFT**

We performed DFT calculations to better understand the origin of the difference in the lifetimes and the presence of a biexponential decay in the platinum complex (Figures 3 and S27–S31). All geometries were optimized at the r^2SCAN-3c level of theory using the conductor-like polarizable continuum (CPCM) (CH2Cl2) solvent model.55 Subsequently, single point energies were calculated at the PW6B95-D4/def2-TZVP,gCP(TZ)/CPCM(CH2Cl2)56–61 level of theory to correct for the electronic energy term in the computed Gibbs free energies. In the case of the Zn complex (Figure 3), we identified two possible transition states connecting the minima of the metastable and stable geometries of the motor complex. In the first transition state (TS1), the benzoxazole moieties of the lower half retain a roughly planar orientation with respect to each other, whereas in the second transition state (TS2), the benzoxazole moieties are strongly folded to allow the naphthyl upper half to move over the lower half. The second transition state was found to be considerably lower in energy, with the calculated Gibbs free energy of activation (43.1 kJ/mol) being in excellent agreement with the experimentally observed lifetime of 1.6 μs.

In the case of the Pt complex, there are two different folded geometries for both the metastable and the stable state: one in which the metal center is located on the same side as the naphthyl ring (M1 and S1 in Figure 3) and one in which the metal center is located on the opposite side of the lower half, compared with the naphthyl ring (M2 and S2). M1 and S1 were calculated to be more stable than M2 and S2, respectively, and we identified two different pathways to connect the photochemically populated metastable state M1 with S1. In the first pathway (orange), the metastable isomer M1 first adopts the less favorable folded geometry M2, through the transition state TS1, in which the metal center flips from one side of the lower half to the other side. This
transition state is 50 kJ/mol higher in energy than M1. From the less favorable conformation M2, a second transition state (TS3) completes the helix inversion of the naphthyl moiety sliding over the lower half, and this affords the stable state S1. As TS3 is lower in energy than TS1, the overall Gibbs free energy of activation of this pathway is 50.0 kJ/mol. In the second pathway (blue), the order is reversed and the helix inversion occurs directly from M1 through transition state TS2, leading to the less stable folded geometry of the stable state S2, after which the metal center moves to the other side through TS4 to adopt the more favorable conformation of the stable state S1. In this pathway, the metal flipping step also has a higher energy barrier than the THI step. Intermediate S2 is more stable than M1. Hence, the overall Gibbs free energy of activation for this second pathway is 45.2 kJ/mol, which is lower than the first pathway (50.0 kJ/mol). The second pathway is therefore predicted to be the pathway that is predominantly followed during the thermal process. Moreover, the formation of the more stable intermediate S2, associated with a barrier of 29.8 kJ/mol, followed by a higher barrier of 45 kJ/mol to form S1 is in excellent agreement with the experimental observations by TAS of a fast decay trace with a lifetime of 22.4 ns, followed by a slower decay trace of 23.0 μs. The multistep mechanism of thermal relaxation of the Pt complex is reminiscent of that of previously described molecular motors with non-rigid lower halves.62

Comparing the pathways of the zinc complex and the platinum complex, there are distinct differences. The tetrahedral geometry around the Zn complex allows for a virtually barrierless movement of the metal center, such that the different folded geometries do not constitute separate minima on the potential energy surface as calculated with r2SCAN-3c. In the case of the Pt complex, the interconversion of different strongly folded geometries was associated with high barriers as a result of the distortion of the square-planar geometry that is necessary for such movement. On the other hand, the barrier of the THI (TS2) is lower for Pt than for Zn, possibly because the tetrahedral geometry around zinc positions one chloride ligand in close proximity to the upper half in the transition state, leading to repulsion, whereas the square-planar geometry keeps the chlorine atoms further away from the upper half. Thus, the choice of metal for complexation not only influences the thermal barriers and hence the rotation speed of the motors but also leads to considerable changes in the mechanism of the thermal relaxation steps of the metal complexes.

In fact, the experimental observations in TAS and the DFT calculations suggest that in the square-planar complexes, the motion between the rotation of the upper half and the wagging motion in the lower half of the motor, consisting of the metal flipping from one side to the other, are coupled. Because this motion is barrierless in the tetrahedral complexes, these combined results show that the metal complexation can be used as an external and orthogonal stimulus to reversibly bring about coupled motions in the molecule and uncouple them by using a different metal. This feature adds another layer of tunability to the motor properties.48

**Demonstration of unidirectionality and in situ complexation/decomplexation**

To demonstrate that prolonged irradiation leads to unidirectional rotation, we also prepared a ligand (L2) with a desymmetrized lower half and its corresponding Zn, Cu, and Pt complexes (see supplemental information for details about the synthesis and characterization of ligand L2 and the corresponding metal complexes). In two sets of NMR experiments, it was shown that in situ irradiation of each isomer of the metal complexes with green light using a 530 nm LED leads to the conversion to the other isomer, reaching the same photostationary state (PSS) in each case (Figures 4A and S11–S13). Although the metastable isomers could not be directly
observed by NMR due to their very short half-life, the interconversion of both stable isomers upon irradiation with a wavelength that is not absorbed by the free ligand indicates that unidirectional rotation through the THI steps must occur. This is in agreement with the results obtained from TAS and the DFT calculations.

To exclude the possibility that the kinetic lability of the complexes could play a role on the timescale of the rotation, we performed variable-temperature exchange spectroscopy (VT-EXSY) NMR experiments on the Zn and Cu complexes (see supplemental information section exchange spectroscopy [VT-EXSY]). These experiments show that the lifetimes corresponding to the exchange reactions between the Zn complex and the free ligand are 2.6 and 2.1 ms. For the copper complex, the corresponding lifetimes are 1.3 and 1.4 ms. These values are several orders of magnitude longer than the lifetimes that were obtained from the TAS experiments for the thermal part of the rotation cycle. The exchange kinetics of the Pt complex were too slow to be studied by VT-EXSY-NMR spectroscopy, indicating that this process is much slower still. Hence, we conclude that the metal-ligand exchange kinetics do not play a significant role on the timescale of the unidirectional rotation.

Finally, we studied the possibility of activating and deactivating the motor function in situ with the addition of external chemical stimuli. Hence, the addition of one equivalent of anhydrous ZnCl₂ or CuCl₂ to a solution of the ligand in CD₂Cl₂ led to full conversion to the [ZnCl₂L₁] and [CuCl₂L₁] complexes, respectively, as determined by ¹H and ¹⁹F NMR (Figures 4, S14, and S16), as well as UV-vis spectroscopy (Figures S15 and S17). Subsequent addition of 5 μL of pyridine-d₅ as a strongly competing ligand resulted in full decomplexation and the recovery of the starting spectra. Moreover, subjecting samples of [ZnCl₂L₁] and [CuCl₂L₁] in the

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**Figure 4. NMR studies to probe the unidirectional rotation and in situ activation of a motor complex**

(A) ¹⁹F NMR spectra of solutions of (E)-[ZnCl₂L₂] and (Z)-[ZnCl₂L₂] in CD₂Cl₂ at room temperature before irradiation and after reaching PSS upon in situ irradiation with 530 nm light.

(B) ¹H NMR (left) and ¹⁹F NMR (right) spectra of (top) the ligand L₁ in CD₂Cl₂, (middle) after the addition of anhydrous ZnCl₂ (1 equiv), forming the complex [ZnCl₂L₁], and (bottom) after the addition of pyridine-d₅ (5 μL), which liberates the free ligand L₁ again.
presence of 0.2 μL pyridine to the same conditions in a TAS experiment does not lead to the formation of a transient species after excitation with a 470 nm light pulse (Figure S10). These experiments demonstrate that reversible activation of the motor function and in situ tuning of the motor properties of the Zn and Cu complexes are indeed possible. Hence, metal complexation and decomplexation serve as effective orthogonal stimuli to achieve on-demand modulation and adaptation of these light-driven molecular rotary motors. Complexation of ligand L1 with PtCl2 at room temperature in CH2Cl2 takes several days, but complete complexation can be achieved within 2 h in toluene at 100°C (Figures S18 and S19). However, due to the slow exchange kinetics of the platinum complex, the addition of a competing ligand such as pyridine or ethylenediamine leads to considerable decomposition of the complex before full decomplexation can be achieved.

Conclusions
In conclusion, we have successfully synthesized a motor ligand (L1) based on a bis(benzoxazole) scaffold and prepared and characterized the corresponding metal complexes [ZnCl2L1], [CuCl2L1], and [PtCl2L1]. We have observed that complexation is accompanied by a large redshift in the absorption spectrum, which extends to over 600 nm in the case of the [CuCl2L1] complex. Irradiation of the complexes gave rise to one or two rapidly decaying transients, which were attributed to the thermal relaxation steps in the rotation cycle. Irradiation experiments with the desymmetrized analog ligand L2 showed the directional rotary behavior of the motor complexes. Based on DFT calculations, we propose a mechanism that can account for the experimentally observed lifetimes of the Zn, Cu, and Pt complexes and that demonstrates how changing the metal center and the resulting coordination geometry strongly affects the mechanism of the thermal part of the rotation cycle. Calculations show that the square-planar geometry around the platinum metal center couples the rotary motion of the upper half to a wagging motion of the metal center in the lower half. This coupled motion is not present in the tetrahedral complexes. Finally, we have shown that the rotary motor function can be reversibly switched on or off by the metal complexation of the ligand or the addition of a competing ligand, such as pyridine, to the zinc and copper metal complexes. In summary, we can use a single light- and heat-orthogonal stimulus to simultaneously achieve in situ control over the activation of a defined motor function as well as the rotation speed, absorption wavelength, and coupling of different molecular motions. We anticipate that this unprecedented dynamic control of motor properties opens new possibilities for the design of more complex dynamic systems and advanced molecular machines.

EXPERIMENTAL PROCEDURES
Resource availability
Lead contact
Requests for further information and resources should be directed to and will be fulfilled by the lead contact, Prof. Dr. Ben L. Feringa (b.l.feringa@rug.nl).

Materials availability
All unique reagents generated in this study are available from the lead contact upon reasonable request.

Data and code availability
Crystallographic data for the structures reported in this paper have been deposited at the Cambridge Crystallographic Data Center (CCDC) under accession numbers CCDC: 2221929, 2221930, 2221931, and 2221932.
SUPPLEMENTAL INFORMATION
Supplemental information can be found online at https://doi.org/10.1016/j.chempr.2023.06.006.

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AUTHOR CONTRIBUTIONS

DECLARATION OF INTERESTS
The authors declare no competing interests.

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