# Photoinduced Concerted Dual Single-bond Rotation of a Nitrogen-containing System Realized by Chalcogen Substitution

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#### Abstract

Conformational change caused by photochemical concerted multiple bond rotation is a very rare event. Thus, it is a critical challenge to expand this chemistry because it has higher potential to more precisely modulate the molecular function of molecules. Here, we describe a novel nitrogen-containing molecular system exhibiting photoinduced concerted rotation, which is the first example of successfully incorporating heteroatoms into a system exhibiting photoinduced concerted rotation. Sufficient kinetic stability and photosensitivity to realize photoinduced concerted rotation can be brought to a sterically hindered benzamide system by chalcogen substitution. The photoinduced C-N/C-C concerted rotation of the thioamide derivative can be directly observed, and it was found that the thioamide system exhibits the ability to generate different conformers depending on external stimuli. A theoretical study also supported the selective occurrence of photoinduced C-N/C-C concerted rotation. It is expected that the system can be utilized to modulate the functions of organic compounds.

#### Introduction

Conformation, the spatial orientation of atoms arising from interconversion around a single bond, mainly determines the molecular function because it is attributed to the whole three-dimensional structures of organic molecules. Thus, conformational restriction or stabilizing hidden conformations has been studied to control molecular function.<sup>1-4</sup> Conformational change, which relies on bond rotation, generally occurs in thermal processes. Photoisomerization is another possible method; however, photochemical conformational changes are less understood than thermal changes. Photoisomerization of multiple bonds, such as C=C and C=N double bonds, has been used in various fields.<sup>5-19</sup> A photoinduced concerted bond rotation, where two or more adjacent bonds rotate simultaneously, is a rare phenomenon and is known to be essentially different from the well-studied photoinduced single chemical bond rotation because the reaction product, in which two or more bonds are isomerized from the starting material, can be directly afforded without the presence of intermediate isomers.<sup>20,21</sup> A simultaneous three-bond isomerization of a conjugated triene system<sup>22</sup> and Hula Twist (HT) of a hemithioindigo (HTI) motor<sup>23,24</sup> are only experimentally demonstrated photoinduced concerted rotations involving a C=C double bond. In 2022, Dube's group serendipitously found that dual single-bond rotation (DSBR) could be induced by light irradiation,<sup>25</sup> and to our knowledge, this is the only example of the experimental verification of conformational change caused by light-induced concerted rotation. The discovery of a novel mode of photoinduced concerted rotation to alter molecular conformation is a critical challenge because concerted rotation has a higher potential to reach a structure different from that obtained by sequential bond rotation and realize different molecular movements. Despite the importance of the photoinduced concerted rotation, the complicated reaction pathway of photoisomerization proceeding on the potential energy surface (PES) in the excited state<sup>26-31</sup> has inhibited the expansion of this chemistry. Moreover, the free-rotating nature with a short time scale of single bonds makes it challenging to induce and/or detect conformational changes with precise control by light irradiation. The reported conformational change using photoinduced concerted rotation consisting only of carbon atoms allowed us to realize that a system containing a heteroatom, especially a nitrogen, generates more structural diversity. Three substituents can be attached to a nitrogen atom, and photochemical concerted rotation with a nitrogen atom can be a useful option for placing substituents in various locations with controlled conformational changes.

We planned to establish a novel nitrogen-containing system exhibiting conformational change by photoinduced concerted rotation, which is generally considered a difficult task due to the complicated reaction pathway of photoisomerization proceeding on the potential energy surface (PES) in the excited state.<sup>26-31</sup> Among nitrogen-containing chemical bonds, we focused on the amide bonds, because it is hypothesized that sp<sup>2</sup> hybridized nitrogen will act in a similar way to sp<sup>2</sup> carbon in the reported photoinduced isomerization. The E/Z stereoisomerism of amide compounds arising from their resonance structure is a general property (Fig. 1b),<sup>32</sup> and because of the ease of bond rotation, the amide C-N bond is generally regarded as a single bond. We chose an *ortho*-disubstituted tertiary benzamide system based on the following consideration to develop a novel photochemical concerted



**Fig. 1 Photoinduced concerted bond rotation. a**, Experimentally observed photoinduced concerted rotation **b**, Double bond property of the C-N bond in an amide compound arising from its resonance structure. The C-N bond generate transient E and Zisomers. c, Rotational mechanism of an *ortho*disubstituted tertiary benzamide. Each isomer could be converted to another isomer via C-N rotation or C-N/C-C concerted rotation. **d**, The effect of chalcogen substitution in the C-N rotation and C-N/C-C concerted rotation in the *ortho*-disubstituted tertiary benzamide system. A novel photoinduced C-N/C-C concerted rotation realized by the chalcogen substitution.

bond rotation. The ortho-disubstituted tertiary benzamide, which has a rotationally restricted C-C bond

and C-N, will generate four stereoisomers: stable atropisomers and transient E/Z isomers for each of

them (Fig. 1c).<sup>33-39</sup> This class of compounds has been shown to thermally isomerize through three different rotational mechanisms, i.e., rotation of the C-C or C-N axes alone and C-C/C-N concerted rotation. Generally, rotation of the C-N axis has a lower energy barrier than C-C/C-N concerted rotation, and the rotational barrier of the C-C axis alone is too energetically high and can be ignored.<sup>38</sup> A photochemical concerted rotation in a nitrogen-containing system will be realized by inducing the C-C/C-N concerted rotation by light irradiation instead of applying heat. Here, we report the development of a novel nitrogen containing systems exhibiting photoinduced C-N/C-C concerted rotation utilizing chalcogen substitution of ortho-disubstituted tertiary benzamide, and the conformational change resulting from photoinduced C-N/C-C concerted rotation can be directly observed (Fig. 1d). The conformational change arising from novel photochemical concerted bond rotation was realized by chalcogen substitution, which brings sufficient kinetic stability for the generally labile amide C-N bond under thermal conditions and photosensitivity to activate bond rotation. This system has a compact structural feature and can be easily prepared; moreover, it was found that the system exhibits the ability to generate different conformers depending on heat and light.

# **Results and Discussions**

The following issues should be solved to obtain the system showing photochemical C-N/C-C concerted rotation developed from sterically hindered benzamide. First, all isomers of benzamide should be kinetically stable under thermal conditions to decouple possible thermal isomerization; in particular, it is necessary to achieve rotational restriction of more labile C-N bonds. This kinetic stability will also

be critical to demonstrate that the observed isomerization is not the result of sequential C-N bond alone and C-C bond alone rotations. Second, the benzamide needs to be modified to become photosensitive because amide compounds generally do not isomerize when irradiated with lower energy light such as UV-A or visible light. Finally, the order of activation energy of C-N bond rotation and C-N/C-C concerted rotation under thermal conditions must be inverted to selectively induce C-N/C-C concerted rotation. We assumed that the abovementioned issues could be solved by the chalcogen substitution of the oxygen atom of the benzamide. A thioamide has been shown to exhibit a higher C-N rotational barrier than a corresponding oxoamide,<sup>41-43</sup> and the C-N bond of thioamide can be isomerized by light irradiation.44-46 Although experimental evidence has not been provided about the C-N bond rotation of selenoamide, a theoretical study also suggested that selenoamide will generate a more kinetically stable E/Z isomer.<sup>43,47</sup> On the other hand, there was no knowledge of the effect of chalcogen atoms on the C-C bond. The rotational property of chalcogenamide under photochemical conditions will be affected by steric effects as well as molecular absorption, which will be thoroughly investigated by side-byside comparison of an oxoamide, thioamide and selenoamide.<sup>48</sup>



Fig. 2 Rotational barriers of C-N axis of *ortho*-disubstituted tertiary benzamides. **a**, Activation energy of four transition states of the C-N or C-N/C-C concerted rotations in the tertiary benzamide and its chalcogen isologues calculated by density functional theory (DFT) method. **b**, The time courses of the *E* to *Z* isomerizations of the chalcogenamides observed by <sup>1</sup>H NMR spectra. The circles indicate experimental ratio of the *E* isomers at each time, and the dotted lines illustrated the theoretical curve created by curve fitting. Activation free energies ( $\Delta G^{\ddagger}$ ) were calculated by substituting the rate constants obtained from the fitting curve into the Eyring equation. **c**, The effects of the structures of benzamides on the *E/Z* isomerization. **d**, The time courses of the racemizations of the chalcogen amides by a normal phase chiral HPLC analysis. The circles indicate experimental

*ee* values at each time, and the dotted lines illustrated the theoretical curve created by curve fitting. Activation free energies ( $\Delta G^{\ddagger}$ ) were calculated by substituting the rate constants obtained from the fitting curve into the Eyring equation. **e**, The effects of the structures of benzamides on the racemization.

# Kinetic stability of stereoisomers of chalcogenoamides under thermal conditions. The potential of

chalcogen substitution for the kinetic stability of ortho-disubstituted tertiary benzamide can be shown by our initial theoretical study. Namely, the activation free energy ( $\Delta G^{\ddagger}$ ) of C-N axis rotation and C-N/C-C concerted rotation of simple ortho-disubstituted tertiary benzamide and corresponding thioamide and selenoamide were calculated by the density functional theory (DFT) method (Fig. 2a). The C-N bond rotation of oxoamide was found to impose barriers of 100.0 and 104.8 kJ/mol, depending on the rotational direction. Substitution of oxygen with sulfur or selenium atoms increases the activation energy by 11.9-21.9 and 28.9-31.3 kJ/mol, respectively. The activation energy of the C-N/C-C concerted rotation was calculated to be over 110 kJ/mol for oxoamide, and the corresponding thioamide and selenoamide showed high rotational barriers comparable to the C-C axis of BINOL  $(\Delta G^{\ddagger} = 158 \text{ kJ/mol})$ ,<sup>49</sup> a typical example of an organic compound that exists as a stable atropisomer. The obtained results suggested that the E and Z isomers of ortho-disubstituted tertiary benzothioamide and benzoselenoamide would be sufficiently stable to be separate from each other, and atropisomers arising from C-N/C-C concerted rotation would not isomerize at ambient temperature regardless of the chalcogen substitution. Next, the C-N bond rotation of ortho-disubstituted tertiary benzamides and their chalcogen isologues was experimentally investigated. Oxoamide 1-O, thioamide 1-S and selenoamide 1-Se bearing N-methyl and N-benzyl groups were prepared, and their E and Z isomers could be successfully separated by standard preparative thin-layer chromatography (P-TLC) and/or normal-phase HPLC. The isomerization reactions of isolated E isomers were conducted in CDCl<sub>3</sub> and monitored by <sup>1</sup>H NMR (Fig. 2b). For thioamides and selenoamides, the reactions were performed under dark conditions to suppress photoinduced isomerization. Oxoamide E-1-O was slowly isomerized to **Z-1-O** at 30 °C with a  $\Delta G^{\ddagger}$  value of 98.6 kJ/mol, and the  $\Delta G^{\ddagger}$  value of the corresponding reverse reaction was 100.7 kJ/mol. The half-lives of Z-1-O and E-1-O at 303 K were calculated to be 3.0 and 7.1 h, respectively, from the observed  $\Delta G^{\ddagger}$  values. The isomerization of thioamide *E*-1-S and selenoamide *E*-1-Se was too slow to determine  $\Delta G^{\ddagger}$  at 30 °C, and they were isomerized at 60 °C with  $\Delta G^{\ddagger}$  values of 111.7 and 116.1 kJ/mol, respectively. The calculated  $t_{1/2}^{303 \text{ K}}$  of Z-1-S and Z-1-Se were over 23 and 131 days, respectively, indicating that the substitution of chalcogen atoms can sufficiently improve the kinetic stabilities of the E/Z isomers. Of note, in all three cases, Z isomers were dominant after reaching equilibrium. To demonstrate the generality of the kinetic stability, the effect of ortho substituents on the rotational barrier was then investigated (Fig. 2c). The results of the substitution of bromine in 1-O and 1-S to chloride or iodine suggested that steric hindrance at the ortho substituent could increase the C-N rotational barrier, and ortho-dihalobenzoyl compounds 4-O and 4-S also showed slow C-N bond rotation. The ortho-disubstituted phenyl system could be expanded to 5-O and 5-S bearing 2-methylnaphthalenyl groups with the same trend. Next, the steric effect of the substituents on the nitrogen was examined. Oxoamide 6-O and thioamide 6-S bearing a sterically more hindered phenethyl group showed increased  $\Delta G^{\ddagger}$  by 2.5–3.3 kJ/mol. Sterically less hindered tertiary thioamide

7-S, which has methyl and ethyl groups on the nitrogen, also exhibits slow interconversion ( $\Delta G^{\ddagger}$  = 115.6 and 116.8 kJ/mol), demonstrating that the stability of *E/Z* stereoisomers is a general property of ortho-disubstituted tertiary thioamide. In all cases, the chalcogen substitution had little influence on the equilibrium positions, which are determined by the difference in activation energies between forward and reverse reactions. The possibility of the coexistence of C-N/C-C concerted rotation on the isomerization as described above was eliminated because atropisomers of 8, which pose the same substituents on the nitrogen and thus do not generate E/Z isomers, were barely racemized at 30 °C (Figs. 2d, e). Consistent with the reported atropisomerism and C-N/C-C concerted rotation of benzamide derivatives, 8-O and 9-O existed as stable atropisomers and slowly racemized in 1,2dicholoroethane at 60 °C with  $\Delta G^{\ddagger}$  values of 110.1 and 112.1 kJ/mol. The corresponding thioamides and a selenoamide were barely racemized under harsher conditions (1,2-dicholoroethane, 75 °C). The obtained results on the axial chirality clearly show the extreme stability of the thioamides and selenoamides compared to the oxoamide. The experimentally determined  $\Delta G^{\ddagger}$  value of the E/Zisomerization or racemization was consistent with our DFT calculation.

The effect of chalcogen substitution on the photoinduced isomerization. Because sufficient thermal kinetic stability with respect to E/Z isomers and atropisomers was guaranteed, we next focused on the effect of chalcogen substitution on photosensitivity. When oxoamide *Z*-1-O was irradiated in CDCl<sub>3</sub> at 4 °C by standard black light (365 nm, 27 W), the *Z* to *E* isomerization was not observed. On the other hand, thioamide *Z*-1-S r was quickly isomerized to the corresponding *E* isomer with a half-life



Fig. 4 Photo-induced isomerization of the chalcogen amides **a**, Kinetics of the Z to E isomerization mediated by a black light as a light source. **b**, Effect of the chalcogen atom and the light source on the Z to E isomerization. **c**, Kinetics of the racemization mediated by a black light. **d**, Effect of the chalcogen atom and the light source on the racemization. **e**, UV spectra of chalcogenamides measured in MeCN. The spectra of E and Z isomers were individually recorded except for oxoamide 1-O.

of 0.19 h under the same contisions (Figs. 4a, b). Selenoamide **Z-1-Se** was also isomerized under the same conditions with a slower isomerization ( $t_{1/2}^{277K} = 0.43$  h) than **Z-1-S**. Interestingly, the order of isomerization rates of **Z-1-S** and **Z-1-Se** was reversed when using a household fluorescent lamp as a light source (Fig. 4b). The UV/Vis spectra of **1-O**, *E***-1-S**, *Z***-1-S**, *E***-1-Se and <b>***Z***-1-Se** suggested that the isomerization rate reflects the maximum absorption wavelength; specifically, selenoamides **1-Se**, which show a longer absorption wavelength, could be efficiently excited by a fluorescent lamp, and thioamides would be more sensitive to the short-wavelength light, reflecting its shorter absorption wavelength (Fig. 4e). Although it is impossible to determine whether the observed isomerization

resulted from C-N bond rotation or C-N/C-C concerted rotation by this experiment, photosensitivity arising from the chalcogen substitution could be clearly demonstrated. To infer whether the photochemical E to Z isomerization proceeds via the desired C-N/C-C concerted rotation, the stability of the C-C axis under photochemical conditions was then examined. The optically enriched thioamide 8-S and selenoamide 8-Se were easily racemized under UV irradiation conditions in 1,2dichloroethane (1,2-DCE) at 4 °C (Fig. 4c), and oxoamide 8-O was stable under the same conditions. A household fluorescent lamp was also effective in inducing racemization, and a selenoamide isomerized faster than a thioamide in the same trend as Z to E isomerization (Fig. 4d). Both E/Zisomerization and racemization show the same trend and proceed on approximately the same timescale, suggesting that these two observations were the result of the same mechanism of rotation, i.e., the C-N/C-C concerted rotation; it was found that the isomerization rate was determined by the combination of the molecular absorbance, which was altered by the incorporation of sulfur or selenium, and the light source. Although it is conceivable that the photochemical C-N/C-C concerted rotation could be achieved using both a thioamide and a selenoamide, from a synthetic viewpoint, the thioamide system was selected for thorough examination of the photochemical isomerization.

**Direct observation of C-N/C-C concerted rotation.** Because the chalcogen substitution gave sufficient kinetic stability and photosensitivity to the tertiary benzamide system, our research has set the phase of direct observation of C-N/C-C concerted rotation. Thioamide **1-S** was selected as a representative to investigate the rotational mechanism, and chiral HPLC analysis of a mixture of



Fig. 5 Separation and stereochemical determination of each isomer. a, Chiral HPLC chromatograms of isolated Z-(S)-1-S, Z-(R)-1-S, E-(S)-1-S and E-(R)-1-S. b, VCD spectra of each stereoisomer of 1-S measured in CDCl<sub>3</sub>. c, Theoretical VCD spectra of Z-(R)-1-S and E-(R)-1-S calculated by DFT method at the B3PW91/6-311+G(3df,2pd) level of theory.

stereoisomers of **1-S** gave four peaks corresponding to *Z*-(*S*), *Z*-(*R*), *E*-(*S*) and *E*-(*R*) isomers. Each isomer could be separated by standard normal phase silica-gel column chromatography followed by preparative chiral column chromatography (Fig. 5a). Unfortunately, none of the isomers were crystallized to determine the stereochemistries by X-ray diffraction. Vibrational circular dichroism

(VCD) spectroscopy is a powerful tool to determine the stereochemistry of noncrystalline compounds.<sup>50,51</sup> The VCD spectra of the enantiomeric pair of *Z* isomers had the opposite signs with respect to each other, and a pair of *E* isomers also exhibited opposite VCD (Fig. 5b). The comparison of experimental and theoretical VCD spectra undoubtedly determined the stereochemistries of each isomer (Fig. 5c),<sup>52</sup> and their stereochemical information enabled us to separately observe C-N bond rotation and C-N/C-C concerted bond rotation.

The isomerization of E-(R)-1-S was conducted under thermal or photochemical conditions, and the ratio of each isomer was monitored by chiral HPLC analysis (Figs. 6a, b). When (R)-1-S was heated at 60 °C in CHCl<sub>3</sub>, E-(R)-1-S was slowly converted to Z-(R)-1-S, and finally, the reaction reached equilibrium after 48 h (Fig. 6c, E-(R):Z-(R)  $\cong$  3: 7). In this thermal isomerization, the R configuration of the stereogenic axis was completely retained, indicating that no concerted C-N/C-C rotation was involved under thermal conditions (Fig. 6d). The photoisomerization of E-(R)-1-S by black light was also investigated at 4 °C (Figs. 6c, e). As expected, E-(R)-1-S was quickly converted to Z-(S)-1-S, which was not observed under thermal conditions; Z-(R)-1-S, which would be generated by photochemical C-N bond-only rotation, was not generated at the initial stage of the reaction, suggesting that the order of C-N rotation and C-N/C-C concerted rotation under thermal conditions could be inverted by photochemical conditions. After 20 min, the ratio of E-(R)-1-S to Z-(S)-1-S became almost constant, and minor isomers Z-(R)-1-S and E-(S)-1-S were gradually generated (Figs. 6c, e). The observation of these minor isomers after reaching equilibrium between E-(R)-1-S



Fig. 6 Different rotational mode of the thioamide system. a, Experimental design for the direct observation of each isomerization. b, Possible isomers generated by the isomerization of E-(R)-1-S. c, Comparison of chiral HPLC chromatograms before and after isomerization reaction induced by heat or light. Only Z-(R)-1-S was generated from E-(R)-1-S under a thermal condition, on the other hand, the main product of the photochemical isomerization was Z-(R)-1-S. d, The time courses of the isomerization of the E-(R)-1-S under a thermal condition. e, The time courses of the photo-induced isomerization of the E-(R)-1-S. f, Reaction mechanism of the photo-induced isomerization of the thioamide. The intermediate and transition states were optimized in the lowest triplet state at the ROM06-2X/aug-cc-PVTZ [SMD(CHCl<sub>3</sub>)]//RO $\omega$ B97X-D/6-31+G(d) level of theory. TS<sup>T</sup><sub>CN/CC</sub><sup>1</sup> and TS<sup>T</sup><sub>CN/CC</sub><sup>2</sup> are the transition state of C-N/C-C concerted rotation, and TS<sup>T</sup><sub>CN</sub><sup>1</sup> is the transition state of C-N rotation. The structure of the ground state was optimized at the M06-2X/aug-cc-PVTZ

 $[SMD(CHCl_3)]//\omega B97X-D/6-31+G(d)$  level of theory.

and Z-(S)-1-S can be rationalized by the occurrence of relatively slow C-N bond rotation, demonstrating that the isomerization of E-(R)-1-S to Z-(S)-1-S was not the result of sequential C-C rotation and C-N rotation. As described above, we clearly demonstrated the photochemical C-N/C-C concerted rotation of the thioamide system. Additionally, the thioamide system exhibited the ability to generate different conformers depending on the external stimuli.

Finally, we conducted a theoretical study to elucidate the mechanism of the photochemical C-N/C-C concerted rotation. Because both singlet and triplet excited states would be involved in photoisomerization on the C-N bond of thioamide,<sup>46</sup> we performed a DFT study on the lowest triplet state of our thioamide system. In the ground state, the C=S bond and the aromatic ring are almost twisted at right angles, while the angle decreases in the triplet state, which can reduce the structural and energetic changes along the reaction coordinate to reach the transition state of the C-N/C-C concerted isomerization (Fig. 6f). The orbital shapes of the SOMO indicated that the conjugation of the radical character on the exited C=S bond to the aromatic ring would stabilize the more planar structure (Fig. S3). The C-N/C-C concerted rotation exhibited activation energies of 6.3 or 11.3 kJ/mol, and the rotational barrier of C-N rotation was found to be 27.2 kJ/mol. The calculated activation energy was consistent with the fact that both C-N rotation and C-N/C-C concerted rotation were observed at low temperature. In the triplet state, the calculated rotational barrier of C-N/C-C concerted rotation was lower than that of the C-N rotation (27.2 kJ/mol), which could be attributed to the planar structure in the triplet intermediate, and the results could also support the fact that the C-N/C-C concerted rotation proceeded selectively. Of note, this calculation does not indicate that the reaction mechanism in the lowest triplet state is the only reaction pathway for photoinduced C-N/C-C concerted rotation; thus, other reaction pathways, such as the reaction on a singlet excited state, are also possible. From now on, the detailed reaction mechanism of the C-N/C-C concerted rotation will be demonstrated by more extensive mechanistic studies.

# Conclusion

In conclusion, we developed a novel nitrogen-containing molecular system exhibiting photoinduced concerted dual single-bond rotation with the help of chalcogen substitution, and it is the first example of the direct observation of conformational change arising from photoinduced concerted rotation in a system containing a heteroatom. The incorporation of sulfur or selenium into the ortho-disubstituted tertiary benzamide can increase the rotational barrier of its C-N and C-C bonds to stabilize each conformer and its photosensitivity to induce photoisomerization. Moreover, the isolation of the kinetically stable E/Z isomers of thioamide and selenoamide demonstrated by this research was also unprecedented. The thioamide system developed here also functioned as a controlled branching unit depending on heat or light with the advantage of its compact structure and synthetic accessibility. The excellent kinetic stability of each isomer in this system and two types of molecular motions caused by different conditions emphasize the higher potential of the thioamide system. Its photoinduced concerted rotation modulates the conformation and functions of organic molecules, contributing to the expansion of the chemical space in this field.

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#### Methods

Separation of isomers and monitoring of isomerization. An *E/Z* mixture of synthesized amides, thioamides and selenoamide was purified by P-TLC or normal-phase HPLC. Each enantiomer was further purified by flash-chiral column chromatography or normal-phase chiral HPLC. For *E/Z* isomerism, a solution of compounds in CDCl<sub>3</sub> was maintained at a constant temperature, and the progress of the isomerization was monitored by <sup>1</sup>H NMR spectra. For atropisomerism or isomerization between four isomers of **1-S**, a solution of compounds in solvent was maintained at a constant temperature, and the progress of the isomerization was monitored by source, and a standard household fluorescent lamp was used as a visible-light source. The details of the preparation of compounds and monitoring of isomerization are described in the Supplemental Information.

**Structure determination utilizing VCD spectra.** Each sample was dissolved in CDCl<sub>3</sub> and placed in a 50 μm BaF<sub>2</sub> cell. VCD and IR spectra were recorded using a JASCO FVS-6000 spectrometer equipped with an MCT detector with 4 cm<sup>-1</sup> resolution for 2000 and 16 scans, respectively. Under these spectrometer settings, each sample showed a virtually mirror-image VCD spectrum to that of its enantiomer in the 1750–950 cm<sup>-1</sup> region. To obtain more accurate spectra, the VCD spectra of each sample were corrected for its enantiomer. The IR spectra were corrected by solvent spectra obtained under identical measurement conditions.

Initial gas phase conformations of each isomer of Z-(R)-1-S and E-(R)-1-S were obtained by the

Macromodel suite of the program using the MCMM method,<sup>53</sup> followed by PRCG minimization<sup>54</sup> with the OPLS3e force field.<sup>55</sup> The initial structures within 21 kJ/mol from the global minimum were further optimized by DFT calculation using Gaussian 16<sup>56</sup> at the B3PW91/6-311+G(3df,2pd) level of theory<sup>52</sup> with the IEFPCM solvation model of CHCl<sub>3</sub> to give two stable conformers for each isomer. For these geometries, VCD spectra were calculated using the same level of theory. The calculated frequencies, dipole strength, and rotational strength were converted to VCD spectra using GaussView 6<sup>57</sup> software using a peak half-width at half height of 6 cm<sup>-1</sup>. Calculated frequencies were scaled with a factor of 0.98 (harmonic). The calculated spectra were averaged based on their Boltzmann distribution at 298.2 K to generate the VCD spectra.

**DFT calculations of the rotational barrier.** All DFT calculations were performed using the Gaussian 16 program. The structures of the equilibrium or transition state in a singlet state were optimized at the  $\omega$ B97X-D/6-31+G(d) level of theory. The structures of the lowest triplet states were also optimized using the restricted-open shell (RO) method at the  $\omega$ B97X-D/6-31+G(d) level of theory. Gibbs free energies were calculated as the sum of the electronic energy (M06-2X/aug-cc-pVTZ (SMD-CHCl<sub>3</sub>) for the singlet states and ROM06-2X/aug-cc-pVTZ (SMD-CHCl<sub>3</sub>) for the triplet states) and the thermal correction term from the vibrational calculation at the same level as the optimization. The structures shown in Figs. 6f, S3, and S5 and the orbital shape (Fig. S4) were generated with CYLview20 software<sup>58</sup> and GaussView 6 software, respectively.

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# **Author Contributions**

A.K. and. S.I. designed the research and A.K., R.K., and S.I designed the experiments. A.K. performed calculation. S.N. prepared compounds, acquired experimental data for the isomerization, and measured the UV spectra. S.N. and A.K. analyzed experimental data for the isomerization. T.T. and K.M. measured the VCD spectra. S.N., A.K., R.K., T.T., K.M. and S.I. wrote the paper. All authors discussed the results and commented on the paper and have given approval to the final version of the manuscript.

# **Competing interests**

The authors declare no competing interests.

# Additional information

Supplementary information is available for this paper.