

# Preference of Ruthenium-Based Metathesis Catalysts toward Z- and E-Alkenes as a Guide for Selective Reactions to Alkene Stereoisomers

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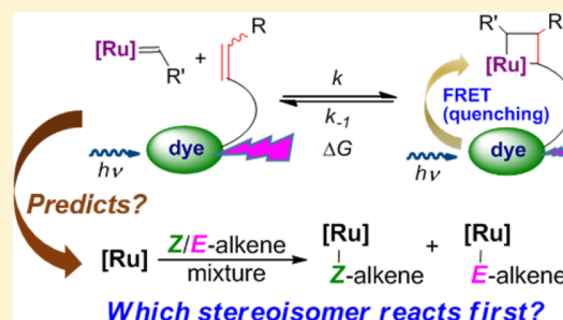
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## Supporting Information

**ABSTRACT:** As a guide for selective reactions toward either Z- or E-alkene in a metathesis reaction, the relative preference of metathesis Ru catalysts for each stereoisomer was determined by a method using time-dependent fluorescence quenching. We found that **Ru-1** prefers the Z-isomer over the E-isomer, whereas **Ru-2** prefers the E-isomer over the Z-isomer. The Z/E-alkene preference of the catalysts precisely predicted the Z/E isomeric selectivity in the metathesis reactions of diene substrates possessing combinations of Z/E-alkenes. For the diene substrates, the rate order of the reactions using **Ru-1** was Z,Z-1,6-diene > Z,E-1,6-diene > E,E-1,6-diene, while the completely opposite order of E,E-1,6-diene > Z,E-1,6-diene > Z,Z-1,6-diene was exhibited in the case of **Ru-2**.



## INTRODUCTION

Selective catalytic transformation of coexisting E- and Z-alkene stereoisomers is highly desirable in synthetic organic chemistry and has become an important goal in many areas in the chemical industry. For instance, the selective removal of trans fats from food, which possess E-alkenes and are known to be harmful to human health, has been an important issue in the food industry.<sup>1</sup> However, efficient methods enabling the selective reaction for each stereoisomer have been scarcely developed due to the lack of a guide regarding the selectivity of catalysts toward each stereoisomer. Herein, we present the preference of Ru-based metathesis catalysts for each stereoisomer, determined by a method using the principle of fluorescence resonance energy transfer (FRET)<sup>2–4</sup> as a guide for the selective reaction to each stereoisomer (Figure 1). We demonstrate that this guide is indeed consistent with the selectivity of catalysts toward alkene stereoisomers in the olefin metathesis reaction<sup>5</sup> of diene substrates possessing combinations of Z/E-alkenes.

In recent years, Schrock, Hoveyda, and Grubbs have developed Mo- and Ru-based metathesis catalysts that show highly selective reactions toward Z-alkene over E-alkene in the metathesis reactions of ethenolysis and olefins between internal and terminal alkenes.<sup>6</sup> While we chose the **Ru-1** catalyst for Z-isomer selectivity, there have been no reports on a metathesis catalyst suitable for E-isomer selectivity. We found through FRET studies that the **Ru-2** catalyst, which is the parent complex of **Ru-1**, prefers E-alkene over Z-alkene. Regarding

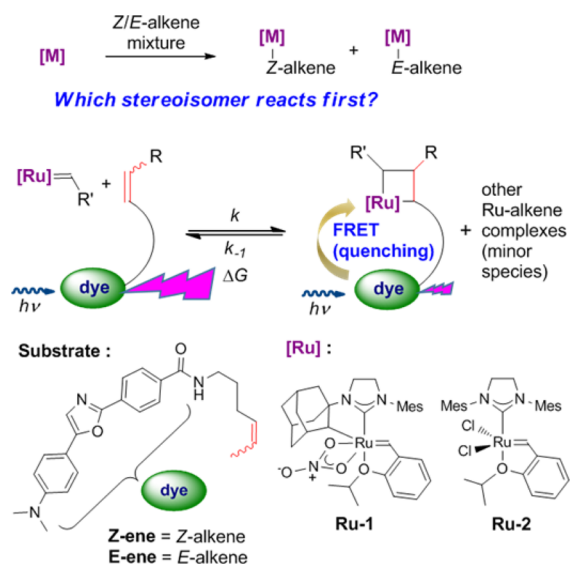
these two catalysts, it has been reported that **Ru-1** selectively generates Z-alkene,<sup>7–10</sup> while **Ru-2** does not show clear preference in the production of alkene stereoisomers in olefin metathesis.<sup>9f,11</sup> The catalysts **Ru-1** and **Ru-2** have absorbance bands in the visible light range with no fluorescence emission and thus are expected to be suitable for FRET studies as fluorescence quenchers of dye-conjugated alkene substrates when Ru-substrate complexes are formed. Measuring fluorescence quenching as a function of time could determine the relative kinetic and thermodynamic preferences, *k* and  $\Delta G$ , respectively, in the formation of an alkene-bound ruthenium alkylidene intermediate from the corresponding catalyst precursor and substrate pair.<sup>3a,c,d</sup> The higher sensitivity of the FRET-based method over other spectroscopic methods such as NMR measurements allows monitoring of small quantities of catalyst–substrate complex formation and collect data over a relatively short period of time.

## RESULTS AND DISCUSSION

For the FRET studies, we prepared dapoxy-conjugated Z- and E-alkene substrates **Z-ene** and **E-ene**<sup>3d</sup> (Figure 1). The fluorescence emission band of **Z-ene** and **E-ene** overlaps well with the absorbance band of **Ru-1** and **Ru-2** in the solvents for Ru-catalyzed metathesis reactions (see the Supporting Information). The FRET studies were carried out with the

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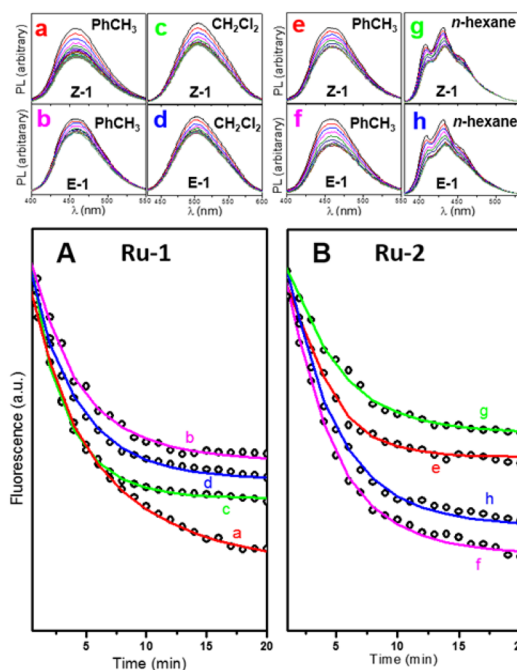
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**Figure 1.** Determination of the preference of Ru-based metathesis catalysts toward *Z*- and *E*-alkenes using the FRET-based method as a guide to predict selective catalytic transformation of coexisting *Z*- and *E*-alkenes. **Ru-1** and **Ru-2** have absorbance bands in the visible light range with no fluorescence emission and thus can act as fluorescence quenchers of dye-conjugated alkene substrates when Ru-substrate complexes are formed. Measurement of fluorescence quenching as a function of time can determine the kinetic and thermodynamic preferences,  $k$  and  $\Delta G$ , respectively, in the complex formation of a catalyst–substrate pair.

prepared dye-conjugated substrates and the catalysts. We measured the time-dependent fluorescence quenching of pairs of each of the two substrates (20  $\mu\text{M}$ ) and catalysts (30  $\mu\text{M}$ ) over a period of 20 min. Because the solvent is an important factor in both FRET studies and chemical reactions, pairs of solvents  $\text{CH}_2\text{Cl}_2$  and PhMe and PhMe and *n*-hexane for **Ru-1** and **Ru-2**, respectively, were investigated. Note that we did not consider that the altered Ru species, Ru ethylidene, plays any particular role during measurement because the difference between Ru benzylidene and ethylidene is not sufficiently pronounced regarding the functionality preference of the catalysts.<sup>3d</sup> Figure 2 shows the time-dependent fluorescence spectra of each substrate for the two catalysts and the pairs of solvents. The time-dependent fluorescence traces, representing the integrated values of the corresponding fluorescence spectra, calibrated for quenching via nonspecific complexation using the control dapoxy-conjugated alkane,<sup>3a</sup> are plotted in Figures 2A and B. Both Figures 2A and B for **Ru-1** and **Ru-2**, respectively, clearly show the dependence of the fluorescence quenching rate and amount on the substrate and solvent. While the fluorescence quenching of **Z-ene** was more rapid and to a higher degree than that of **E-ene** in the case of **Ru-1**, the reverse was observed for **Ru-2**.

For a given substrate/catalyst pair, relative kinetic and thermodynamic parameters  $k$ ,  $k_{-1}$ , and  $\Delta G$  for the complex formation between the catalyst and substrate were determined by quantitatively analyzing the fluorescence quenching traces with a set of parameters (Supporting Information). The results are summarized in Table 1. The catalyst **Ru-1** preferred **Z-ene** over **E-ene** by 3.3-fold kinetically and 13-fold thermodynamically in PhMe and 1.5-fold and 1.3-fold, respectively, in  $\text{CH}_2\text{Cl}_2$ . On the other hand, the kinetic and thermodynamic preferences of **Ru-2** for **E-ene** were 2-fold and 4-fold higher in PhMe and 4-



**Figure 2.** Time-dependent fluorescence quenching of the dye-alkenes **Z-ene** and **E-ene** due to the complex formation with (A) **Ru-1** and (B) **Ru-2**. Time-dependent fluorescence spectra (a–d for **Ru-1** and e–h for **Ru-2**) for each substrate–catalyst pair are shown above each panel. Experimental data points are shown as black circles (substrate:catalyst = 20:30  $\mu\text{M}$ ), and the theoretical curves from the global fitting analysis are represented by red and green curves for **Z-ene** and pink and blue curves for **E-ene**. The data points correspond to the calibrated integrated values of the fluorescence spectra.

fold and 4-fold higher in *n*-hexane, respectively, than those for **Z-ene**. These results indicate that the complex formation of **Ru-1** with **Z-ene** or **Ru-2** with **E-ene** is more favorable both kinetically and thermodynamically than that with the other stereoisomer along with the solvent effect in complex formation. Owing to the reversible nature of the alkene-coordinated ruthenium alkylidene intermediate, the thermodynamic preference of Ru for *Z/E*-alkenes is more important than the kinetic preference. Unlike in the case of **Ru-1**, the complex formation of **Ru-2** with both substrates in PhMe was more rapid and more favorable than that in *n*-hexane. With regard to  $\Delta G$ , the *Z*-alkene selectivity of **Ru-1** is much higher in PhMe than in  $\text{CH}_2\text{Cl}_2$  ( $\Delta\Delta G$  6.3 vs 1.7), while that of **Ru-2** is similar in both PhMe and *n*-hexane ( $\Delta\Delta G$  4.4 vs 4.5) in complex formation.

To examine whether the preference of the catalyst is valid as a selectivity guide toward each stereoisomer, we investigated the correlation between the preference and reactivity of the catalyst toward each stereoisomer. We prepared tosylamide substrates possessing *Z,Z*- (**ZZ-ene**), *Z,E*- (**ZE-ene**), and *E,E*-1,6-diene (**EE-ene**) with identical tether lengths for intramolecular olefin metathesis (Supporting Information) and evaluated the reaction rates for the three substrates with the two Ru catalysts.

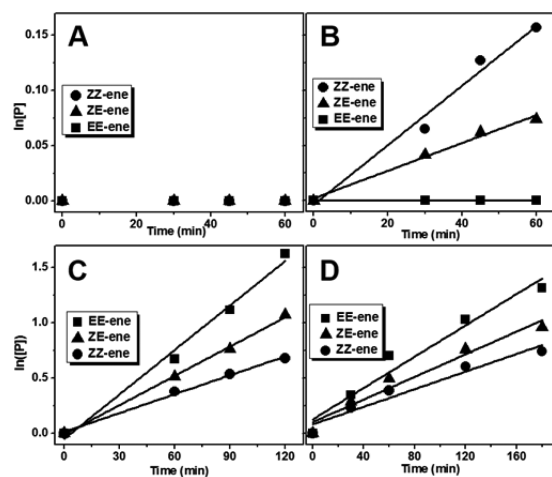
We carried out intramolecular olefin metathesis reactions of the three substrates using **Ru-1** in  $\text{CH}_2\text{Cl}_2$  and PhMe and **Ru-2** in PhMe and *n*-hexane. The reactivity of **Ru-1** with the internal alkene was much lower than that of **Ru-2**, and the reaction using **Ru-1** in  $\text{CH}_2\text{Cl}_2$  at reflux did not produce **P**,<sup>12</sup> instead leading to the recovery of intact diene substrates. At 100 °C in

**Table 1.** Relative Kinetic and Thermodynamic Parameters for the Complex Formation by the Reaction of Ru with *E/Z*-Alkene Substrates<sup>a</sup>

catalyst	solvent	substrate	$k$ ( $M^{-1} s^{-1}$ )	$k_{-1}$ ( $s^{-1}$ )	$\Delta G$ (kJ/mol)
Ru-1	PhMe	Z-ene	$5.51 \pm 0.15 \times 10^3$	$2.68 \pm 0.33 \times 10^{-2}$	$-29.8 \pm 0.30$
		E-ene	$1.68 \pm 0.07 \times 10^3$	$1.07 \pm 0.41 \times 10^{-1}$	$-23.5 \pm 0.93$
	CH <sub>2</sub> Cl <sub>2</sub>	Z-ene	$5.62 \pm 0.19 \times 10^3$	$1.35 \pm 0.07 \times 10^{-1}$	$-26.9 \pm 0.15$
		E-ene	$3.63 \pm 0.24 \times 10^3$	$1.17 \pm 0.17 \times 10^{-1}$	$-25.2 \pm 0.39$
Ru-2	PhMe	Z-ene	$2.88 \pm 0.13 \times 10^3$	$1.63 \pm 0.26 \times 10^{-1}$	$-23.8 \pm 0.40$
		E-ene	$5.88 \pm 0.17 \times 10^3$	$8.29 \pm 0.04 \times 10^{-2}$	$-27.2 \pm 0.07$
	<i>n</i> -hexane	Z-ene	$9.77 \pm 0.46 \times 10^2$	$1.11 \pm 0.15 \times 10^{-1}$	$-22.1 \pm 0.34$
		E-ene	$3.97 \pm 0.67 \times 10^3$	$1.09 \pm 0.12 \times 10^{-1}$	$-25.6 \pm 0.45$

<sup>a</sup> $k$  and  $k_{-1}$  are directly determined as fitting parameters and  $\Delta G$  is calculated as  $-RT\ln(k/k_{-1})$ .  $k$  and  $\Delta G$  represent the kinetic and thermodynamic preferences, respectively.

PhMe, the reaction of **ZZ-ene** using **Ru-1** (20 mol %) for 1 h under Ar produced **P** in 20% yield, which was unchanged for a longer period of reaction time, most likely because of catalyst decomposition.<sup>8d</sup> Thus, for **Ru-1**, the reactions occurred for 1 h at 100 °C in PhMe; both consumption of the substrate and formation of the product were monitored over time to avoid misinterpretation of the data. Despite low yields, it was clear that the reaction rate was dependent on the substrate. The rate order was **ZZ-ene** > **ZE-ene** > **EE-ene** for both substrate consumption and product formation, which is in accordance with the preference of **Ru-1** for *Z/E* isomers. In the case of **EE-ene**, the reaction did not proceed at all under the reaction conditions. The difference between the substrate consumption and the product formation was marginal; thus, only the product formation was measured over the given time period (Figure 3). Because the reaction of the diene substrates using **Ru-2** was much more rapid than that using **Ru-1**, the reaction was carried out using 2 mol % **Ru-2** at 0 °C in PhMe and *n*-hexane and monitored for 2–3 h to obtain the rate of product formation.



**Figure 3.** Log plots of product concentration versus time for metathesis reactions of **ZZ-ene**, **ZE-ene**, and **EE-ene** with **Ru-1** and **Ru-2**. Reactions with **Ru-1** in CH<sub>2</sub>Cl<sub>2</sub> (A) and PhMe (B). Reactions with **Ru-2** in PhMe (C) and in *n*-hexane (D). Symbols represent **ZZ-ene** (●), **ZE-ene** (▲), and **EE-ene** (■). Reaction conditions: substrate (150 mg, 0.535 mmol) and **Ru-1** (20 mol %) in CH<sub>2</sub>Cl<sub>2</sub> (5.35 mL) at reflux (A) and PhMe at 100 °C (B). Substrate (150 mg, 0.535 mmol) and **Ru-2** (2 mol %) in PhMe (5.35 mL) at 0 °C (C) and *n*-hexane (5.35 mL) at 0 °C (D). All reactions were carried out under Ar, and the product concentrations were obtained based on the isolated product.

The results indicated that the reaction with **Ru-2** in PhMe was more rapid than that in *n*-hexane; all of the three diene substrates underwent **P** production with the rate order of **EE-ene** > **ZE-ene** > **ZZ-ene** in both solvents. The higher reaction rate in PhMe compared with that in *n*-hexane and the rate order were also in agreement with the preference of **Ru-2** for *E*-alkene over *Z*-alkene, as shown in Table 1. For the catalyst/substrate pairs, we obtained log plots of product versus time, all of which were found to be linear (Figure 3).

From the slopes of these plots, the rate constants for the catalyst/substrate pairs were determined, the results of which are summarized in Table 2. The rate constants in Table 2

**Table 2.** Rate Constants for the Metathesis Reactions of the Three Diene Substrates with Ru Catalysts<sup>a</sup>

catalyst	solvent, T	substrate	$k$
Ru-1	PhMe, 100 °C	<b>ZZ-1</b>	$4.51 \pm 0.42 \times 10^{-5}$
		<b>ZE-1</b>	$1.99 \pm 0.16 \times 10^{-5}$
		<b>EE-1</b>	no reaction
Ru-2	PhMe, 0 °C	<b>ZZ-1</b>	$9.49 \pm 0.45 \times 10^{-5}$
		<b>ZE-1</b>	$1.47 \pm 0.05 \times 10^{-4}$
		<b>EE-1</b>	$2.24 \pm 0.16 \times 10^{-4}$
	<i>n</i> -hexane, 0 °C	<b>ZZ-1</b>	$6.14 \pm 0.57 \times 10^{-5}$
		<b>ZE-1</b>	$8.54 \pm 1.06 \times 10^{-5}$
		<b>EE-1</b>	$1.28 \pm 0.15 \times 10^{-4}$

<sup>a</sup>Rate constants were obtained from the slopes of log plots of product concentration versus time.

indicate that **Ru-1** is 2.3-fold more reactive toward **ZZ-ene** over **ZE-ene**, and this  $k$  ratio is higher than that for **Ru-2**, which is 1.5-fold more reactive toward **ZE-ene** than **ZZ-ene**. The greater  $k$  ratio for **Ru-1** over **Ru-2** (Table 2) is in accordance with the higher preference of **Ru-1** for *Z*-alkene over *E*-alkene than that of **Ru-2** for *E*-alkene over *Z*-alkene (Table 1). In the case of **Ru-2**, the higher reaction rate in PhMe than that in *n*-hexane correlates well with the more favorable complex formation of **Ru-2** in PhMe than in *n*-hexane. In these two solvents, all  $k$  ratios between the three diene substrates are similar ( $k$  ratios =  $\sim 1.5$ ), which would be attributable to almost the same  $\Delta\Delta G$  between the *Z/E*-alkenes in both solvents ( $\Delta\Delta G = \sim 4$ ). These results are in agreement with previously reported computa-



tional studies describing that the energy of the rate-determining transition state for trisubstituted ruthenacyclobutane formation is higher for the **Ru-1**/*E*-alkene pair than that for the **Ru-1**/*Z*-alkene pair due to the steric repulsion between the *N*-mesityl group and at least one substituent in the transition state for the **Ru-1**/*E*-alkene pair.<sup>6b</sup> This steric interaction in the side-bound mechanism<sup>9e,13</sup> could confer more differentiation in the preference of **Ru-1** between *Z*/*E*-isomers than that of **Ru-2**, catalyzing via the bottom-bound mechanism.<sup>14</sup> Overall, our results indicate that the preference of a metathesis Ru catalyst for an alkene stereoisomer over the other stereoisomer, determined by the FRET-based method, dictates the *Z*/*E* isomeric selectivity in the olefin metathesis reactions of diene substrates possessing combinations of *Z*/*E*-alkenes.

## CONCLUSION

In summary, we determined the relative *Z*/*E*-alkene preference of metathesis Ru catalysts using time-dependent fluorescence quenching as a guide for a selective reaction toward either *Z*- or *E*-alkene in Ru alkylidene-catalyzed metathesis. We found that **Ru-1** prefers the *Z*-isomer over the *E*-isomer, whereas **Ru-2** prefers the *E*-isomer over the *Z*-isomer. The *Z*/*E*-alkene preference of the catalysts correlated well with the *Z*/*E* isomeric selectivity in the olefin metathesis reactions of the diene substrates possessing combinations of *Z*/*E*-alkenes. The correlation indicates that the preference of a Ru catalyst for an internal alkene over the other stereoisomer would direct the *Z*/*E* isomeric selectivity in the olefin metathesis reactions of diene substrates. The results demonstrate that a guide for the selectivity of Ru alkylidene-catalyzed metathesis toward either *Z*- or *E*-alkene can be obtained using time-dependent fluorescence quenching.

## EXPERIMENTAL SECTION

**General.** Common solvents were purified before use. Tetrahydrofuran and dichloromethane were purified by distillation from sodium-benzophenone and calcium hydride, respectively. Anhydrous acetone, *N,N*-dimethylformamide, acetonitrile, ethyl acetate, and triethylamine were used as received. All reagents were reagent grade and purified where necessary. "Water" refers to distilled water. Reactions were monitored by thin layer chromatography (TLC) using silica gel plates. Flash column chromatography was performed over ultrapure silica gel (230–400 mesh). <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on a 300 or 600 MHz spectrometer using residual solvent peaks as an internal standard (CHCl<sub>3</sub>: δ 7.24 ppm for proton and δ 77.0 ppm for carbon). Multiplicities for <sup>1</sup>H NMR are designated as s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, m = multiplet, and bs = broad singlet. Infrared spectra (IR) were recorded on an FT-IR spectrometer and are reported in reciprocal centimeters (cm<sup>-1</sup>). UV–visible spectra were recorded on a UV–visible spectrophotometer. High-resolution mass spectra (HRMS) were obtained on a TOF-Q instrument.

**Synthesis of ZZ-ene.** To a mixture of *p*-toluenesulfonamide (100 mg, 0.582 mmol) and K<sub>2</sub>CO<sub>3</sub> (241 mg, 1.75 mmol) in acetone (6 mL) was added propargyl bromide (0.125 mL, 1.46 mmol), and the reaction mixture was refluxed overnight. The mixture was concentrated under reduced pressure, diluted with Et<sub>2</sub>O (30 mL), washed with brine (5 mL), dried over MgSO<sub>4</sub>, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (*n*-hexane:EtOAc = 3:1 v/v) to give 4-methyl-*N,N*-di(prop-2-yn-1-yl)benzenesulfonamide<sup>15</sup> (142.9 mg, 99%): <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.71 (d, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 7.8 Hz, 2H), 4.16 (d, *J* = 2.7 Hz, 4H), 2.42 (s, 3H), 2.14 (t, *J* = 2.7 Hz, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz): δ 21.6, 36.2, 74.4, 76.2, 128.2, 129.2, 136.9, 144.2. To a solution of 4-methyl-*N,N*-di(prop-2-yn-1-yl)benzenesulfonamide (142.9 mg, 0.578 mmol) in THF (6 mL) was

slowly added LiHMDS (1.0 M in THF, 1.20 mL, 1.20 mmol) at –78 °C, and the mixture was stirred for 30 min. After addition of MeI (0.080 mL, 1.28 mmol) at 0 °C, the resulting mixture was allowed to warm to room temperature and stirred for 3 h. Saturated aqueous NH<sub>4</sub>Cl (10 mL) was added, and the mixture was extracted with Et<sub>2</sub>O (10 mL × 3). The combined organic layer was washed with brine (5 mL), dried over MgSO<sub>4</sub>, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (*n*-hexane:EtOAc = 3:1 v/v) to give *N,N*-di(prop-2-yn-1-yl)-4-methylbenzenesulfonamide<sup>16</sup> (134 mg, 84%): <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 4.06 (m, 4H), 2.40 (s, 3H), 1.63 (s, 6H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>): δ 150.4, 144.0, 129.1, 128.1, 81.7, 74.2, 36.2, 21.5, 3.41. To a solution of *N,N*-di(prop-2-yn-1-yl)-4-methylbenzenesulfonamide (100 mg, 0.363 mmol) in EtOAc (10 mL) was added 5% Pd on CaCO<sub>3</sub> (50 mg), and the resulting suspension was stirred overnight under H<sub>2</sub> at room temperature. The mixture was filtered through Celite and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (*n*-hexane:EtOAc = 20:1 v/v) to give **ZZ-ene** (75 mg, 76%): <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.72 (d, *J* = 7.8 Hz, 2H), 7.31 (d, *J* = 7.8 Hz, 2H), 5.59 (m, 2H), 5.28 (m, 2H), 3.86 (d, *J* = 6.7 Hz, 4H), 2.45 (s, 3H), 1.61 (d, *J* = 6.8 Hz, 6H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>): δ 143.4, 137.7, 129.9, 128.6, 127.4, 125.2, 43.4, 21.7, 13.0; IR (film): cm<sup>-1</sup> 3027, 2966, 2931, 2873, 1597, 1458, 1030, 891, 771, 690, 451; HRMS (ESI) (*m/z*): calcd for C<sub>15</sub>H<sub>21</sub>NNaO<sub>2</sub>S [M + Na]<sup>+</sup> 302.1191, found 302.1189.

**Synthesis of EE-ene.** To a solution of TsNH<sub>2</sub> (250 mg, 1.45 mmol) in DMF (5 mL) was added NaH (60% in mineral oil, 132 mg, 3.19 mmol) at 0 °C, and the mixture was stirred for 10 min. To the mixture was added trans-crotyl bromide (85%, 0.33 mL, 3.19 mmol), and the resulting mixture was allowed to warm to room temperature and stirred for 4 h. Saturated aqueous NH<sub>4</sub>Cl (15 mL) was added, and the mixture was extracted with Et<sub>2</sub>O (20 mL × 3). The combined organic layer was washed with brine (10 mL), dried over MgSO<sub>4</sub>, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (*n*-hexane:EtOAc = 20:1 v/v) to afford **EE-ene** (240 mg, 60%): <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.69 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 5.56 (m, 2H), 5.24 (m, 2H), 3.73 (d, *J* = 6.6 Hz, 4H), 2.43 (s, 3H), 1.63 (d, *J* = 6.5 Hz, 6H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>): δ 142.9, 137.8, 130.2, 129.5, 127.2, 125.5, 48.4, 21.5, 17.6; IR (film): cm<sup>-1</sup> 3024, 2924, 2862, 1666, 1442, 1338, 1249, 1157, 1092, 1045, 879, 702; HRMS (ESI) (*m/z*): calcd for C<sub>15</sub>H<sub>21</sub>NNaO<sub>2</sub>S [M + Na]<sup>+</sup> 302.1191, found 302.1181.

**Synthesis of ZE-ene.** To a solution of *p*-toluenesulfonamide (500 mg, 2.92 mmol), DMAP (70 mg, 0.58 mmol), and (Boc)<sub>2</sub>O (703 mg, 3.21 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (6 mL) was added Et<sub>3</sub>N (0.485 mL, 3.50 mmol), and the mixture was stirred overnight at room temperature. At 0 °C, 1.0 M aqueous HCl (5 mL) was added, and the mixture was extracted with EtOAc (10 mL × 3). The combined organic layer was washed with saturated aqueous NaHCO<sub>3</sub> (5 mL), brine (5 mL), dried over MgSO<sub>4</sub>, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (*n*-hexane:EtOAc = 1:1 v/v) to afford *tert*-butyl prop-2-yn-1-ylcarbamate<sup>17</sup> (825 mg, 98%): <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.95 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 2.45 (s, 3H), 1.40 (s, 9H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 149.2, 144.8, 136.0, 129.6, 128.3, 84.2, 28.0, 21.8. To a mixture of *tert*-butyl prop-2-yn-1-ylcarbamate (500 mg, 1.84 mmol), PPh<sub>3</sub> (483 mg, 1.84 mmol), and propargyl alcohol (0.112 mL, 1.84 mmol) in THF (18 mL) was slowly added DEAD (40 w% in PhMe, 0.84 mL, 1.84 mmol) at 0 °C, and the reaction mixture was stirred for 3 h at room temperature. Water (10 mL) was added, and the mixture was extracted with EtOAc (15 mL × 3). The combined organic layer was washed with brine (5 mL), dried over MgSO<sub>4</sub>, filtered, and concentrated. The crude product was purified by silica gel column chromatography (*n*-hexane:EtOAc = 10:1 v/v) to afford *tert*-butyl prop-2-yn-1-yl(tosyl)carbamate<sup>18</sup> (430 mg, 76%): <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 1.34 (s, 9H), 2.31 (t, *J* = 2.3 Hz, 1H), 2.44 (s, 3H), 4.62 (d, *J* = 2.3 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H) and 7.91 (d, *J* = 8.0 Hz, 2H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 150.3, 144.3,

136.7, 129.0, 128.2, 84.7, 79.0, 74.0, 36.0, 27.8, 21.6. To a solution of *tert*-butyl prop-2-yn-1-yl(tosyl)carbamate (400 mg, 1.30 mmol) in THF (2.5 mL) was added LiHMDS (1.0 M in THF, 1.3 mL, 1.3 mmol), and the mixture was stirred for 30 min at  $-78\text{ }^{\circ}\text{C}$ . After addition of MeI (0.81 mL, 1.3 mmol), the reaction mixture was allowed to warm to room temperature and stirred for 3 h. Saturated aqueous  $\text{NH}_4\text{Cl}$  (10 mL) was added, and the mixture was extracted with  $\text{Et}_2\text{O}$  (15 mL  $\times$  3). The combined organic layer was washed with brine (10 mL), dried over  $\text{MgSO}_4$ , filtered, and concentrated under the reduced pressure. The crude product was purified by silica gel column chromatography (*n*-hexane:EtOAc = 3:1 v/v) to give *tert*-butyl but-2-yn-1-yl(tosyl)carbamate<sup>19</sup> (394 mg, 94%):  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.92 (d,  $J$  = 8.3 Hz, 2H), 7.32 (d,  $J$  = 8.2 Hz, 2H), 4.58 (q,  $J$  = 2.2 Hz, 2H), 2.45 (s, 3H), 1.84 (t,  $J$  = 2.3 Hz, 3H), 1.35 (s, 9H).  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ ): 150.4, 144.2, 136.9, 129.1, 128.2, 84.6, 79.9, 74.3, 36.3, 27.8, 21.6. To a solution of *tert*-butyl but-2-yn-1-yl(tosyl)carbamate (394 mg, 1.22 mmol) in EtOAc (15 mL) was added 5% Pd on  $\text{CaCO}_3$  (118 mg), and the resulting suspension was stirred overnight under  $\text{H}_2$  at room temperature. The mixture was filtered through Celite and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (*n*-hexane:EtOAc = 20:1 v/v) to give (*Z*)-*tert*-butyl but-2-en-1-yl(tosyl)carbamate<sup>19</sup> (237 mg 60%):  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.80 (d,  $J$  = 8.0 Hz, 2H), 7.29 (d,  $J$  = 8.0 Hz, 2H), 5.68 (m, 1H), 5.53 (m, 1H), 4.51 (d,  $J$  = 6.7 Hz, 2H), 2.43 (s, 3H), 1.77 (d,  $J$  = 6.8 Hz, 3H), 1.34 (s, 9H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ ):  $\delta$  150.7, 144.0, 137.2, 129.2, 128.1, 127.0, 125.6, 84.2, 43.5, 27.7, 21.5, 13.3. To a solution of (*Z*)-*tert*-butyl but-2-en-1-yl(tosyl)carbamate (237 mg, 0.732 mmol) in  $\text{CH}_2\text{Cl}_2$  (3 mL) was added  $\text{CF}_3\text{CO}_2\text{H}$  (1 mL) at  $0\text{ }^{\circ}\text{C}$ , and the reaction mixture was allowed to warm to room temperature and stirred for 2 h. The mixture was concentrated under reduced pressure and dissolved in  $\text{CH}_2\text{Cl}_2$  (20 mL). The solution was washed with saturated aqueous  $\text{NaHCO}_3$  (5 mL) and brine (5 mL), dried over  $\text{MgSO}_4$ , filtered, and concentrated. The residue was purified by silica gel column chromatography (*n*-hexane:EtOAc = 1:1 v/v) to afford (*Z*)-*N*-(but-2-en-1-yl)-4-methylbenzenesulfonamide<sup>19</sup> (159 mg, 97%):  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.75 (d,  $J$  = 8.0 Hz, 2H), 7.29 (d,  $J$  = 8.0 Hz, 2H), 5.52 (m, 1H), 5.29 (m, 1H), 5.13 (bs, 1H), 3.60 (m, 2H), 2.43 (s, 3H), 1.54 (d,  $J$  = 6.8 Hz, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ ):  $\delta$  143.2, 136.4, 128.7, 127.8, 126.7, 124.6, 39.5, 20.5, 12.6. To a suspension of NaH (60% in mineral oil, 32 mg, 0.78 mmol) in DMF (0.5 mL) was added a solution of the Boc-protected compound (159 mg, 0.71 mmol) in DMF (1.5 mL) at  $0\text{ }^{\circ}\text{C}$ , and the mixture was stirred for 10 min. To the mixture was added trans-crotyl bromide (85%, 0.105 mL, 0.78 mmol), and the resulting mixture was allowed to warm to room temperature and stirred for 4 h. After addition of saturated aqueous  $\text{NH}_4\text{Cl}$  (5 mL) at  $0\text{ }^{\circ}\text{C}$ , the mixture was extracted with  $\text{Et}_2\text{O}$  (10 mL  $\times$  3). The combined organic layer was washed with brine (5 mL), dried over  $\text{MgSO}_4$ , filtered, and concentrated. The residue was purified by silica gel column chromatography (*n*-hexane:EtOAc = 10:1 v/v) to give **ZE-ene** (188 mg, 95%):  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.72 (d,  $J$  = 8.1 Hz, 2H), 7.31 (d,  $J$  = 8.0 Hz, 2H), 5.56 (m, 2H), 5.28 (m, 2H), 3.85 (d,  $J$  = 6.4 Hz, 2H), 3.74 (d,  $J$  = 6.5 Hz, 2H), 2.43 (s, 3H), 1.65 (d,  $J$  = 6.4 Hz, 3H), 1.60 (d,  $J$  = 6.6 Hz, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ ):  $\delta$  143.3, 137.9, 130.6, 129.9, 128.6, 128.4, 127.5, 125.8, 125.3, 125.2, 49.1, 43.1, 21.8, 18.0, 13.1; IR (film):  $\text{cm}^{-1}$  3023, 2923, 2861, 1728, 1662, 1596, 1492, 1342, 933, 821, 724; HRMS (ESI) ( $m/z$ ): calcd for  $\text{C}_{15}\text{H}_{21}\text{NNaO}_2\text{S}$  [ $\text{M} + \text{Na}$ ]<sup>+</sup> 302.1191, found 302.1185.

**Measurement of Time-Dependent Fluorescence Quenching Signal.** The time-dependent fluorescence quenching signal was measured by a Shimadzu RF-5301PC fluorometer with excitation at 350 nm and an excitation and emission slit width of 2 nm. Samples were prepared with anhydrous solvent ( $\text{CH}_2\text{Cl}_2$ , PhMe or *n*-hexane) and measured under Ar. A solution of a substrate in solvent (3.0 mL) in a  $10 \times 10$  mm quartz cuvette was placed in the temperature-controlled holder of the fluorometer, and the fluorescence spectrum at time zero was acquired. A Ru catalyst solution (3.0 mM) was added to the substrate solution using a syringe, and the fluorescence spectra

were obtained as a function of time. The area of the fluorescence curve, designated the fluorescence intensity, was calculated.

## ■ ASSOCIATED CONTENT

### § Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01276.

UV-vis spectra of Ru catalysts, and fluorescence spectra of substrates, global fitting analysis of FRET data, and  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of new compounds and their intermediates (PDF)

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### Notes

The authors declare no competing financial interest.

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