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Homogeneous Catalysis

Recycling a Homogeneous Catalyst through a Light-Controlled Phase Tag**

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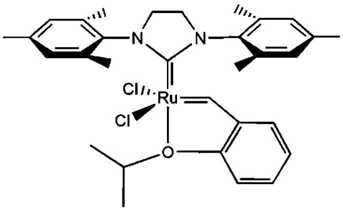
Homogeneous catalysts, which exist in the same phase as the reactants, are known to have superior behavior and selectivity compared to heterogeneous catalysts. However, recovery of a catalyst from a reaction has remained a fundamental problem as separating it from the end products is usually costly and inefficient.[1] To overcome tedious separation processes, several catalysts such as interphase,[2] clathrate-enabled,[3] ionic-tagged,[4] fluorous-tagged,[5] redox-switchable phase tagged,[6] and solid- or polymer-supported catalysts[7] have been developed. Some of these methods,[8–12] such as aqueous biphasic catalysts for propene hydroformylation, phase-switchable catalysts using CO_2 for the switch, as well as other catalysts have been so successful that some of them have been commercialized.[8,9] Strategies involving ionic-tagged catalysts that can be used for olefin metathesis are also attractive because these catalysts can be easily repeatedly recycled from the reaction mixture.[13] However, these systems require expensive ionic liquids as the support materials, result in heterogeneity, and thus slows down the reaction rate in the subsequent reactions. In addition, these methods often result in impurities in the recycled catalysts, such as decomposed catalyst, which may accelerate the catalyst decomposition in future reactions.

The catalytic activity of Ru catalysts influenced by light has been reported recently.[14] Herein, however, the use of a light-controlled phase tag to separate homogeneous catalysts from their reaction products is demonstrated. These types of light-controlled phase tags can be switched between a neutral (lipophilic) phase and a charged (lipophobic) phase through the use of a tag-centered photoreaction. The photoreaction results in drastic changes in the polarity and solubility of the catalyst. Thus, it is possible to optimize the solubility of the catalyst in different solvents and thereby improve extraction and separation of the catalyst from the products.

To demonstrate this new concept, the Hoveyda–Grubbs boomerang-shaped ruthenium–carbene complex **1**[15a] was selected as the catalyst precursor because it is a known effective catalyst.[15] Furthermore, numerous recycling methods have already been tested using this high-value catalyst.[4a,b,5b,6a,b,d] A nitrobenzospiropyran ((*R*/*S*)-SP) unit was chosen as the light-active group because it undergoes rapid and reversible photo transitions (with high quantum yield) between a colorless spiro (SP) state and a colored merocyanine (ME) state without generating photoproducts.[16,17]



1: Hoveyda–Grubbs catalyst

Scheme 1 illustrates the synthetic route for the (*R*/*S*)-SP-tagged Ru complex **6**. The (*R*/*S*)-SP tagged ligand **5** was synthesized in a reaction that produced moderate to good yields using 4-bromo-1-isopropoxy-2-propenyl-benzene (**2**) as the starting material. Treatment of **2** with the second-generation Grubbs catalyst in the presence of CuCl with CH_2Cl_2 as the solvent at 40 °C, as described by Hoveyda and co-workers,[15a] resulted in the exchange of the styrene group and produced a good yield (64.7 %) of the (*R*/*S*)-SP-tagged Ru complex **6** as a green crystalline solid.

As expected, irradiation of complex **6** with light caused the (*R*/*S*)-SP tag to convert from the neutral (lipophilic) phase to the charged (lipophobic) phase, thus forming complex **7**. In the absence of light complex **7** converted back into complex **6**. A typical experiment to demonstrate this conversion was conducted in CH_3CN. When irradiated with light ($\lambda >$ 380 nm), an absorption band at 563 nm appeared in the UV spectra, thus indicating the formation of *trans*-ME (Figure 1 a). Then after two minutes the absorption peak reached a maximum, thus indicating the complete conversion of (*R*/*S*)-SP into *trans*-ME. In the absence of light complex **7** completely converted back into complex **6** as indicated by the disappearance of the absorption band at 563 nm (Figure 1 b).

Further study indicated that the aforementioned tag-centered reaction was significantly affected by the solvent (Figure 1 c and d). The reaction was very rapid, reaching its peak within 2 minutes in light when cyclohexane and CH_3CN were used as the solvents. Whereas the reaction rate of complex **7** completely converting back into complex **6** was fastest when CH_2Cl_2 was the solvent. The transformation was completely reversible in cyclohexane, CH_3CN, and CH_2Cl_2 and was repeated eight times.

Significantly, complexes **6** and **7** have remarkable dissimilar characteristics of solubility as a result of the different polarities of the (*R*/*S*)-SP and *trans*-ME tags. Hence, the

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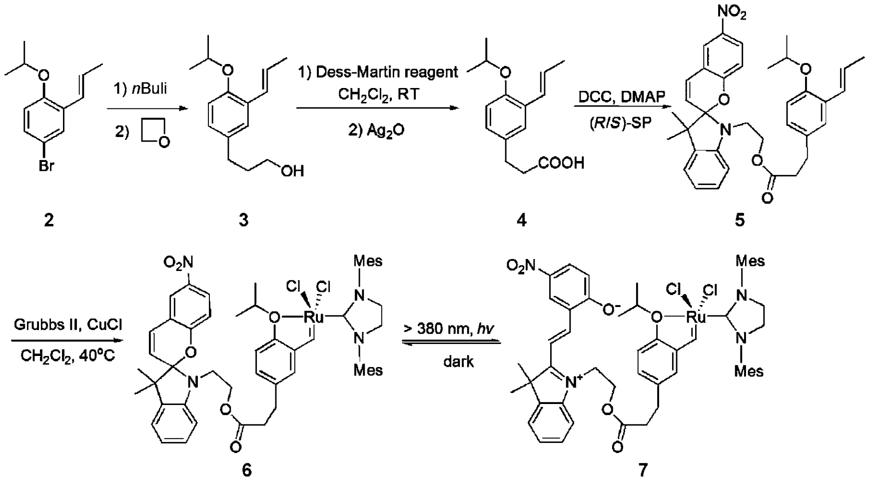


Scheme 1. Synthesis of (*R*/*S*)-SP-tagged ruthenium–carbene complex **6**. DCC = 1,3-dicyclohexylcarbodiimide, DMAP = 4-dimethylaminopyridine, Mes = mesityl.

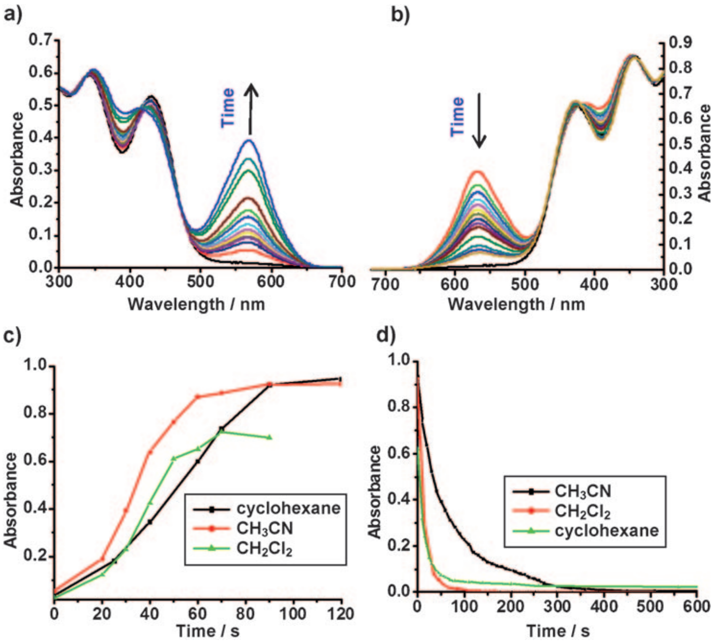


Figure 1. Evolution of the absorption spectrum for the catalyst (1.0×10^{-4} M, 25 °C: a) Irradiation with light ($\lambda > 380$ nm) in CH_3CN. b) In the absence of light in CH_3CN. c) Irradiation of the sample in CH_3CN, CH_2Cl_2, and cyclohexane. d) Sample in different solvents in the absence of light.

solubility of the two complexes can be adjusted by switching the (*R*/*S*)-SP tag by irradiation. A conventional experiment that exhibits the aforementioned concept was conducted in a biphasic system containing cyclohexane as the nonpolar solvent and a mixture of glycol and methanol (3:2:1, by volume) as the polar solvent (Figure 2). Complex **6** with a neutral (*R*/*S*)-SP tag showed very good solubility in cyclohexane (Figure 2a: upper layer). Only traces of the former compound, complex **6**“, were recovered from the polar solvent mixture (lower layer). When the sample was irradiated with light, the (*R*/*S*)-SP tag immediately transformed into the ionic *trans*-ME tag to produce complex **7**, which, subsequently completely dissolved in the polar phase (Figure 2b: lower layer). In the absence of light and at room temperature, the ionic *trans*-ME tag converted back into the neutral (*R*/*S*)-SP tag and produced complex **6**. Afterwards, **6** shifted back to the cyclohexane layer. The cycle was repeated seven times, thus proving that the usage of light to transform complex **6** into **7** between the two solvents is significantly reversible (Figure 2c).

The (*R*/*S*)-SP-tagged ruthenium–carbene **6** is a highly active catalyst for ring-closing metathesis (RCM) reactions. Kinetic studies using diethyl diallymalonate **8** as a test diene indicated that under similar reaction conditions, the catalytic activity of **6** is comparable to that of complex **1**. A high conversion (> 98 %) was achieved after 1 hour for the RCM of **8** at 30 °C (see Figure S1 in the Supporting Information). Further study showed that the ring closure of N-protected substrates **10**, **12**, **14**, **16**, and **18**, sulfur-containing substrate **20**, or oxygen-containing dienes **22**, **24**, and **26** led to either five-, six-, or seven-membered rings with a di-, tri-, or tetra-substituted double bond, respectively (Table 1, entries 1–9). The products were obtained in high yield by using a small loading of complex **6** (0.5–2.5 mol %). Cross metathesis of olefins **28** and **29** also produced high yields when 2.5 mol % of complex **6** was used (Table 1, entry 11). Good yields were also obtained in ring-closing reactions of olefins **31** and **33** through enyne metathesis (Table 1, entries 12 and 13). Thus, complex **6** is a highly active catalyst for a wide range of RCM reactions. Moreover, it is active with many functional groups which is similar to its parent compound **1**.

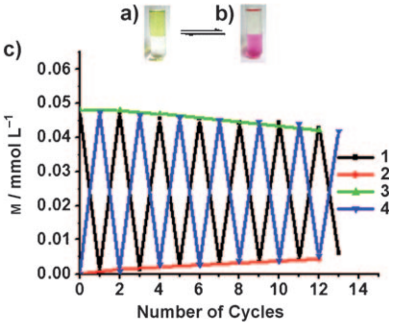
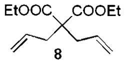
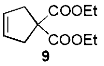
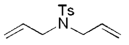
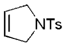
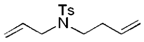
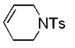
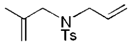
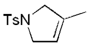
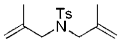
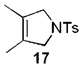
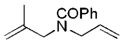
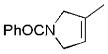
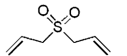
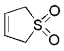
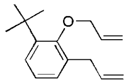
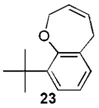
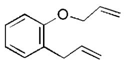
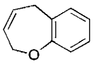
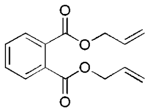
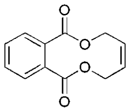
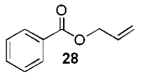
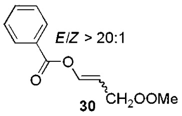
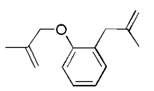
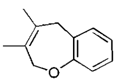
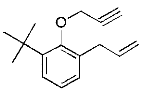
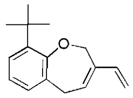


Figure 2. Shuttling of complex **6** between a two-phase system containing cyclohexane, glycol, and methanol (3:2:1, by volume) through a light-controlled tag-centered reaction: a) In the absence of irradiation. b) After irradiation with light. c) Concentration of complex **6** in the upper layer; 1) upper solution (by UV analysis); 2) lower solution (by ICP-MS analysis); 3) upper solution (by ICP-MS analysis); 4) lower solution (by UV analysis).

In contrast to other tagged or supported catalysts, the (*R*/*S*)-SP-tagged complex **6** can be easily recycled by manip-

Table 1: Metathesis and recycle study of catalyst **6** for different dienes.[a]

Entry	Diene	Product	**6** [$\times 10^{-4}$ mmol] (Ru [mol %])	Convn. [%][b] (yield [%])[c]	Remaining **6**[d] [$\times 10^{-4}$ mmol]	Recovered **6**[e] [$\times 10^{-4}$ mmol] (rate [%])[f]
1	 **8**	 **9**	0.5 (4.8)	> 98 (95)	4.0	3.9 (96)
2	 **10**	 **11**	0.5 (4.8)	> 98 (97)	4.2	4.1 (97)
3	 **12**	 **13**	0.5 (4.8)	> 98 (97)	4.2	4.1 (97)
4	 **14**	 **15**	0.5 (4.8)	> 98 (97)	4.5	4.2 (94)
5	 **16**	 **17**	2.5 (24.2)	> 95 (93)[g]	16.9	16.3 (96)
6	 **18**	 **19**	1.0 (9.7)	> 98 (97)	8.4	7.8 (94)
7	 **20**	 **21**	0.5 (4.8)	> 98 (96)	4.3	4.1 (96)
8	 **22**	 **23**	0.5 (4.8)	> 98 (94)	4.4	4.2 (95)
9	 **24**	 **25**	0.5 (4.8)	> 95 (90)	4.3	4.1 (96)
10	 **26**	 **27**	1.0 (9.7)	> 90 (87)	7.2	6.9 (95)
11	 **28**  **29**	 *E*/*Z* > 20:1 **30**	2.5 (24.2)	> 90 (85)	17.9	16.8 (94)
12	 **31**	 **32**	2.5 (24.2)	> 90 (85)[h]	18.1	17.2 (95)
13	 **33**	 **34**	1.0 (9.7)	> 85 (80)	6.1	5.9 (97)

[a] Reactions were conducted at 35 °C in CH_2Cl_2. [b] Conversion of substrate was determined by ^1H NMR spectroscopy. [c] Yield of isolated product. [d] The available complex **6** was detected by UV analysis. [e] Based on the residual complex **6**. [f] Relative rate of conversion. See the Supporting Information [g] In toluene at 80 °C. [h] In CH_2Cl_2 at 45 °C. Ts = 4-toluenesulfonyl.

ulating the (*R*/*S*)-SP tag using the absence or presence of light. The recovery of complex **6** from its products is demonstrated in Figure 3. After the RCM reaction, the solvent was removed under vacuum. Cyclohexane and a mixture of glycol and methanol (2:1, by volume) were later added to the residue. At this time, the catalyst, products, and unchanged dienes were dissolved in the upper (cyclohexane) layer. The system was then irradiated with light to transform the (*R*/*S*)-SP tag into the *trans*-ME tag, thus producing catalyst **7**, which completely shifted into the lower layer (glycol/methanol). The products, which remained in the upper (cyclohexane) layer, were subsequently separated. As some polar products, such as compounds **11**, **13**, **15**, **17**, **19**, and **21** (see Table S1 in the Supporting Information), were partly dissolved in the polar phase, four to five extractions were necessary to remove them completely. For less polar products, such as compounds **23**, **25**, **27**, **32**, and **34** (see Table S1 in the Supporting Information), two to three extractions were sufficient to remove them completely. After elimination of the products, CH_2Cl_2 (or cyclohexane) was added again to start a new biphasic system. The catalyst was not directly recovered from the polar phase owing to the strong hydrogen

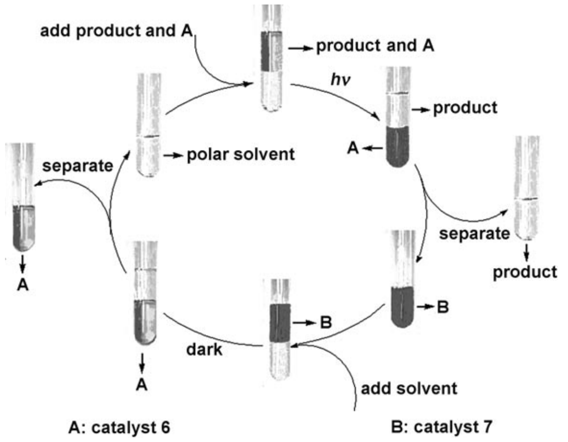
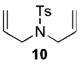
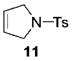


Figure 3. Schematic for the separation of homogeneous catalyst **6** from the products.

Table 2: Recycling of **6** for RCM of dienes **10**.[a]

Substrate	Product	Ru cat. [mol %]	Cycle	TOF h^{-1}[b] (convn. [%])[c]				
				3 min	5 min	8 min	10 min	Final
 **10**	 **11**	1.0	1	620 (34)	575 (48)	569 (76)	551 (92)	490 (98)[d]
			2	602 (33)	575 (48)	561 (75)	545 (91)	447 (97)[e]
			3	602 (33)	575 (48)	554 (74)	545 (91)	415 (97)[f]
			4	565 (31)	563 (47)	531 (71)	533 (89)	415 (97)[g]
			5	547 (30)	539 (45)	524 (45)	527 (88)	387 (97)[h]
			6	437 (24)	527 (44)	516 (69)	515 (86)	366 (98)[i]

[a] Reaction conditions are the same as those in Table 1. [b] TOF is the average turnover frequency measured within 3–16 minutes of the reaction starting (TOF = TON/time). [c] Conversion was determined by ^{1}H NMR spectroscopy. [d] At 12 min. [e] At 13 min. [f] At 14 min. [g] At 14 min. [h] At 15 min. [i] At 16 min.

bonding. The mixture was stored in the dark for 3–5 minutes (7–8 h for cyclohexane) to allow the *trans*-ME tag in complex **7** to convert into the neutral (*R*/*S*)-SP-tagged complex **6**, which then shifted back to the bottom (CH_2Cl_2) layer. Removal of solvent from the separated bottom layer produced the recycled catalyst, complex **6**. In this manner, the RCM products were obtained in excellent yields (80–95 %), and good recovery of the catalyst was achieved (94–97 %; Table 1). As some of the catalyst decomposed during the reactions, recovery were based on the observed residual catalyst after the reactions. The catalyst decomposition products were retained in the polar layer and were readily separated from the catalyst.

Compared with previously reported solid-[18] or polymer-supported ruthenium–carbene catalysts,[19] no supporting media were necessary during the catalytic reaction with complex **6**. Thus, the numerous problems caused by the supporting media that were encountered in other methods, such as heterogeneity or slower reaction rates, were avoided. The light-sensitive phase tag is an organic group, and it has no effect on the catalytic activity of the ruthenium–carbene catalyst. The catalytic reaction and the separation were performed in a common organic solvent system. Hence, it is more desirable than the ionic-tagged[13,20–22] or fluorous-tagged ruthenium–carbene,[5] which have to be recycled using ionic liquids or fluorous solvents, respectively. The use of light, a clean and environmentally friendly resource, as the driving force to alter the polarity of the catalyst makes this method more viable than ferrocene redox-switchable tagged ruthenium–carbene catalysts—these require oxidizing and reducing reagents to switch the polarity of the catalysts. Comparing the various methods of recovery, the current method enabled the separation of pure homogeneous catalyst from the products by simple extraction using a light-controlled process. The ^{1}H NMR spectra showed that the recycled catalyst complex **6** was pure (see the Supporting Information). Therefore, **6** can be directly used for numerous applications. The recovered catalyst exhibited good catalytic activity, which was comparable with the parent catalyst. The recovered catalyst retained almost the same activity for six cycles performed under similar reaction conditions (Table 2). Inductively coupled plasma mass spectrometry (ICP-MS) analysis of product **11** after the first recycle using catalyst **6** (1 mol % of Ru) indicates only 9.245 ppm of Ru contamination in the crude product (see the Supporting Information), which is similar to results obtained by previously reported methods.[13b,22]

In conclusion, an (*R*/*S*)-SP ruthenium–carbene catalyst **6**, which can be recovered using a light-controlled process, has been developed. This method of recycling and recovery of homogeneous catalysts offers significant advantages because it uses light—a cheap and clean resource—as the driving force. It also requires no temperature changes. Moreover, it does not require expensive supporting media. Thus, this method can be an attractive and viable alternative for industrial applications. With the increasing interest in the development of recyclable catalysts for different tasks in organic synthesis, this strategy can be applied to the design of other transition-metal-based catalysts, template-synthesis, and other related research areas.

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