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Synthesis and Catalytic Study of Ruthenium Carbene Catalyst Containing a Zn-Porphyrin Ligand

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A ruthenium carbene complex containing a Zn-porphyrin ligand has been developed. The complex was characterized by ^{1}H NMR, IR, HRMS and elemental analysis. The catalytic activity of the ruthenium carbene complex for olefin metathesis reactions was also investigated. The complex exhibited excellent performance for both ring-closing and cross metathesis reactions at 35 ℃.

Keywords olefin metathesis, ruthenium carbene, catalyst, Zn-porphyrin

Introduction

Olefin metathesis is one of the most flexible, efficient and widely used methods for the construction of carbon-carbon double bonds.[1] In 1992, Grubbs and coworkers reported the first well-defined ruthenium-based olefin metathesis catalyst (**1**, Figure 1).[2] Since then, a series of modified catalysts have been synthesized including **2** in which one of the tricyclohexylphosphine ligands in **1** was replaced with a bulky *N*-heterocyclic carbene (NHC) ligand, H_2IMes (Figure 1).[3] In addition, more stable Hoveyda-type complexes **3** and **4** (Figure 1) have also been developed.[4] Complex **4**, which has an *O*-chelated NHC ruthenium isopropoxybenzylidene, is very important because it has excellent stability and remarkable catalytic activity in olefin metathesis.[5] Many other complexes based on **4** have also been designed by changing the strength of the Ru—O bond which has a pronounced effect on the catalytic activity.[6]

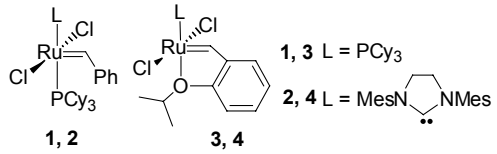

Figure 1 Catalysts for olefin metathesis.

It is well known that a change in the isopropoxystyrene ligand can result in a change in the activity of the catalyst. For example, increasing the steric bulk of the ligand can improve the leaving-group ability of the styrene ligand. Porphyrins are tetrapyrrole macrocycles that possess 22 π electrons and based on Hückel's rule, they are highly aromatic. These aromatic properties are responsible for many of the useful porphyrin applications, particularly in the field of medicine.[7,8] Bulky porphyrins also have excellent stability and can effectively stabilize Ru catalysts.[9] So, in this work the effect of using a porphyrin in the isopropoxystyrene ligand was investigated. A ruthenium carbene complex containing a Zn porphyrin ligand was synthesized, characterized and investigated as a catalyst for ring-closing and cross metathesis reactions.

Experimental

Elemental analyses were determined using an Elementar Vario EL cube analyzer. ^{1}H NMR spectra were obtained on a 400 or 500 MHz spectrometer and ^{13}C NMR spectra were obtained on a 500 MHz spectrometer with $CDCl_3$ as the solvent and TMS as the internal reference. High-resolution (HR) mass analysis was determined by Fourier transform ion cyclotron resonance mass spectrometry (MS).

The (*E*)-4-bromo-1-isopropoxy-2-(prop-1-enyl) benzene was prepared according to a literature method.[10]

Synthesis of compound 5 A flask was charged with 1.50 g (5.91 mmol) of (*E*)-4-bromo-1-isopropoxy-2-(prop-1-enyl)benzene (precursor for **5**) and 5 mL of anhydrous diethyl ether. The solution was cooled to −78 ℃, and then 4.27 mL of *n*-BuLi (1.66 mol/L in hexane, 7.08 mmol, 1.2 equiv.) was slowly added via a syringe. The reaction mixture was then allowed to slowly warm to room temperature. After stirring for 1 h at room temperature, the reaction mixture was cooled to −78 ℃. To

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this mixture, 0.43 g of DMF (5.91 mmol, 1 equiv.) was slowly added via a syringe and the resulting solution was stirred for 1 h at this temperature. The mixture was then concentrated under vacuum to obtain a thick oil residue. Next, 20 mL of dichloromethane was added to the residue. After being washed four times with water, the organic layer was dried over magnesium sulfate. Removal of the solvent by filtration gave an oil residue. The residue was purified by silica gel chromatography using pentane/CH_2Cl_2 (1∶1) as the eluent. The desired compound **5** was obtained as a yellow oil (0.67 g, 3.28 mmol, 56%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.88 (s, 1H, COH), 7.949 (s, 1H, CH), 7.70 (d, $^3J_{(H, H)}$=11.0 Hz, 1H, CH), 6.95 (d, $^3J_{(H, H)}$=8.4 Hz, 1H, CH), 6.71 (d, $^3J_{(H, H)}$=20 Hz, 1H, CH), 6.38−6.33 (m, 1H, CH), 4.71−4.67 (m, 1H, CH), 1.93 (d, $^3J_{(H, H)}$=8.0 Hz, 3H, CH_3), 1.41 (d, $^3J_{(H, H)}$=7.5 Hz, 6H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 18.9, 21.9, 70.7, 112.5, 124.8, 127.6, 128.0 128.3, 129.2, 130.2, 159.5, 190.9. Anal. calcd for $C_{13}H_{16}O_2$: C 76.44, H 7.90; found C 76.77, H 7.85.

Synthesis of compound 6 A flask was charged with compound **5** (1 g, 4.9 mmol), benzaldehyde (1.56 g, 14.7 mmol) and propionic acid (60 mL). The mixture was brought to a boil and then pyrrole (1.32 g, 19.6 mmol) was added via a syringe. The mixture was then stirred for 8 h under reflux and the propionic acid was removed under vacuum. Next, dichloromethane (50 mL) was added to the residue, and the organic layer was separated and washed four times with water. The organic layers were combined and washed with saturated salt water, dried over magnesium sulfate, filtered and concentrated. The desired product **6** was obtained as a purple solid after purification by silica gel chromatography using pentane/CH_2Cl_2 (1∶1) as the eluent. Yield: 9.1% (0.27 g, 0.33 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.95 (d, $^3J_{(H, H)}$=5.5 Hz, 2H, CH), 8.86（s, 6H, CH), 8.23 (d, $^3J_{(H, H)}$=8.0 Hz, 8H, CH), 7.77 (d, $^3J_{(H, H)}$=9.0 Hz, 10H, CH), 7.05−7.01 (m, 1H, CH), 6.40 (dd, $^3J_{(H, H)}$=8.5 Hz, 19.5 Hz, 1H, CH), 4.93−4.84 (m, 1H, CH), 1.94 (d, $^3J_{(H, H)}$=8.0 Hz, 3H, CH_3), 1.61 (d, $^3J_{(H, H)}$=7.5 Hz, 6H, CH_3), –2.72 (s, 2H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 19.0, 22.5, 71.0, 112.1, 119.9, 120.1, 120.2, 120.5, 125.9, 126.2, 126.7, 126.8, 127.7, 128.0, 133.0, 133.9, 134.0, 134.4, 134.6, 142.3, 154.5, 167.2; IR (KBr) ν: 3402, 2961, 2923, 2852, 1653, 1259, 1107, 800, 701 cm^{-1}. Anal. calcd for $C_{50}H_{40}N_4O$: C 84.24, H 7.66, N 6.86; found C 84.31, H 7.55, N 6.92.

Synthesis of compound 7 A mixture of compound **6** (165 mg, 0.23 mmol) and $Zn(OAc)_2$•$2H_2O$ (389 mg, 2.3 mmol) was dissolved in DMF (5 mL) and CH_2Cl_2 (10 mL). Then the mixture was placed in a 250 mL flask and refluxed for 20 min under N_2. After cooling to room temperature, the solvent was evaporated under vacuum. The residue was dissolved in dichloromethane and washed with water. Then the organic layer was dried with magnesium sulfate and concentrated. The desired product **7** was obtained as a purple solid after purification by silica gel chromatography using pentane/CH_2Cl_2 (1∶1) as the eluent. Yield 78.4% (140 mg, 0.18 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.99 (s, 8H, CH), 8.25 (d, $^3J_{(H, H)}$=7.5 Hz, 8H, CH), 7.81−7.77 (m, 10H, CH), 7.02 (d, $^3J_{(H, H)}$=20.0 Hz, 1H, CH), 6.43−6.37 (m, 1H, CH), 4.90−4.87 (m, 1H, CH), 1.94 (d, $^3J_{(H, H)}$=7.5 Hz, 3H, CH_3), 1.62 (d, $^3J_{(H, H)}$=7.5 Hz, 6H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 18.9, 22.5, 71.1, 112.1, 121.0, 121.1, 121.2, 121.4, 125.9, 126.1, 126.5, 126.7, 127.5, 131.9, 132.0, 132.1, 132.2, 132.8, 133.7, 134.4, 135.0, 142.8, 142.9, 143.0, 150.2, 150.3, 150.7, 154.3; IR (KBr) ν: 2922, 2850, 1596, 1484, 1439, 1339, 1242, 1122, 1068, 1003, 994, 797, 700 cm^{-1}. Anal. calcd for $C_{50}H_{38}N_4OZn$: C 77.36, H 4.83, N 7.22; found C 77.41, H 4.95, N 7.32.

Synthesis of complex 8 Grubbs catalyst **2** (17 mg, 0.020 mmol) and CuCl (2.0 mg, 0.020 mmol) were added to a Schlenk flask under N_2. A solution of **7** (14 mg, 0.018 mmol) in 5 mL dry dichloromethane was poured into the reaction mixture at room temperature. The resulting mixture was then stirred for 3 h at 40 ℃. After being cooled to room temperature, the reaction mixture was filtered and the clear filtrate was collected. The solvent from the filtrate was evaporated under vacuum to obtain a residue. The desired product **8** was obtained as a green-purple crystalline solid after purification by silica gel chromatography using pentane/CH_2Cl_2 (1∶1) as the eluent. Yield 36.2% (8 mg, 0.0065 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 16.70 (s, 1H, Ru-H), 9.03 (s, 2H, CH), 8.96−8.94 (m, 6H, CH), 8.33−8.17 (m, 7H, CH), 7.83−7.77 (m, 10H, CH), 7.18−7.16 (m, 1H, CH), 6.99−6.94 (m, 3H, CH), 5.20−5.17 (m, 1H, CH), 4.19 (s, 4H, CH_2), 2.52 (s, 12H, CH_3), 1.49 (d, $^3J_{(H, H)}$=6.4 Hz, 6H, CH_3); IR (KBr) ν: 2966, 2925, 2849, 1617, 1482, 1261, 1101, 1002, 796, 700 cm^{-1}; HRMS calcd for $C_{69}H_{59}Cl_2N_6OZnRu$ $[M-H]^+$ 1153.3085, found 1153.3088. Anal. calcd for $C_{69}H_{60}Cl_2N_6OZnRu$: C 67.56, H 4.93, N 6.85; found C 67.77, H 4.84, N 6.95.

Kinetics study of 8 and 4 A Schlenk flask was charged with catalyst (0.02 mmol, 1.0 mol%) and dry CH_2Cl_2. The sample was equilibrated at 30 ℃ and then diethyl diallylmalonate **9** was added via a syringe. Aliquots were taken from the reaction mixture at the appropriate time using a syringe and were quenched immediately with 0.1 mol/L PEI in CH_2Cl_2. The resulting solution was then subjected to short column chromatography to remove any Ru metal residue using CH_2Cl_2 as the eluent. The solvent from the collected solution was evaporated under vacuum. The conversion yield was determined by comparing the ratio of the integrals of the ^{1}H NMR methylene proton peaks in the starting material with those in the product.

Catalytic study of the ruthenium carbene complex 8 The general procedure for the metathesis reactions with the ruthenium carbene complex **8** is as follows: 0.0005 mmol of catalyst **8** suspended in 1.0 mL of dry CH_2Cl_2 was placed in a Schlenk flask, and heated to

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35 ℃ in an oil bath under nitrogen. Then, the desired amount of substrates was added with stirring. The reaction mixture was stirred for 1—12 h. At the end of the reaction, the catalysts were separated by silica gel chromatography using CH_2Cl_2 as the eluent to remove any trace amounts of the Ru residue. The yield is reported as isolated yield.

Results and Discussion

The reaction of compound **5** with benzaldehyde and pyrrole gave compound **6** which contains a porphyrin (Scheme 1). Next, **6** was treated with $Zn(OAc)_2•4H_2O$ in *N*,*N*-dimethylformamide to give ligand **7** in good yield. As described by Kingsbury *et al*,[4b] the treatment of **7** with **2** in the presence of CuCl in CH_2Cl_2 at 40 ℃ resulted in the exchange of the styrene group to give **8**, a ruthenium complex, as a green-purple crystalline solid.

The catalytic activity of **8** and the unmodified Hoveyda second generation catalyst **4** were tested for the ring-closing metathesis (RCM) reaction using diethyl diallylmalonate **9** as the substrate. The relative conversion rates are shown in Figure 2. Although **8** has a lower initiation rate than **4**, both catalysts had high RCM conversions (>95%) after 30 min.

The catalytic efficiency of complex **8** for different RCM substrates was then investigated (Table 1). The ring closure of the *N*-protected substrates **11**, **13**, **15** and **21** and the oxygen containing dienes **15**, **19** and **23** led to either five-, six-, or seven-membered rings with di-, or tri-substituted double bonds, respectively (Table 1, Entries 1—8). High yields were obtained with a low

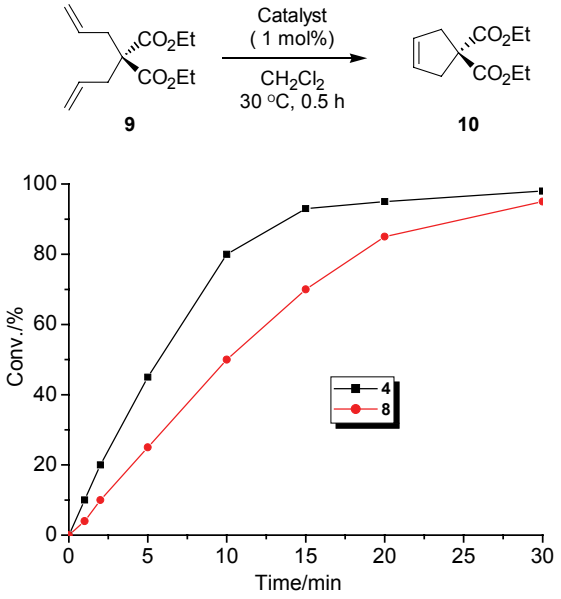


Figure 2 Catalytic activities of **8** and **4** in the RCM of diallyl diethylmalonate.

catalyst loading (0.1—0.5 mol% [Ru]).

The usefulness of catalyst **8** for the cross metathesis (CM) reaction of **25** and **26** was also examined (Table 2). Catalyst **8** exhibited a high activity in this reaction with a loading of 1.5 mol%. The dimerization of olefin **27** to *E*-stilbene was achieved which is similar to the results for **4**.[11] The reaction proceeded smoothly for methyl acrylate **26** and olefins (**25a**—**25d**) which had different substituted groups on the benzene rings including

Scheme 1 Synthesis of ruthenium carbene complex **8** (Mes=2,4,6-trimethylphenyl)

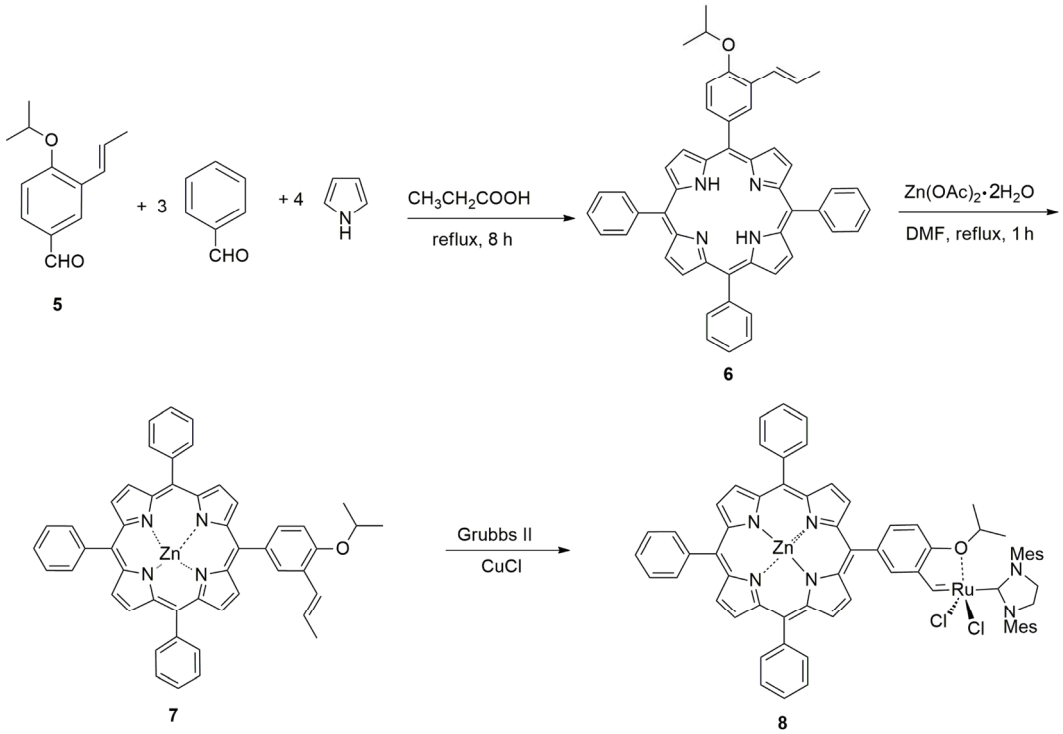
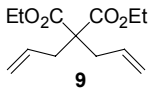
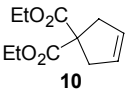
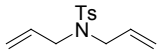
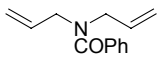
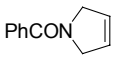
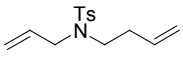
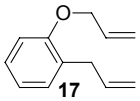
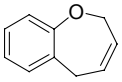
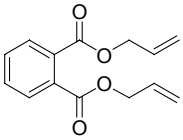
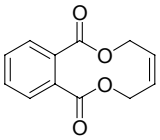
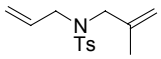
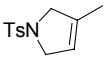
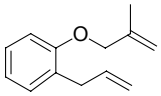
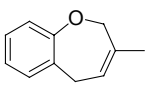
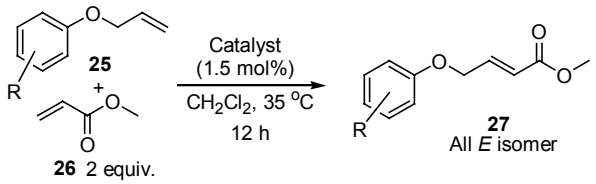


Table 1 Application of catalyst **8** to different RCM substrates[a]

Entry	Substrate	Product	Cat./mol%	*t*/h	Yield[b]/%
1	 **9**	 **10**	0.1	2.0	98
2	 **11**	 **12**	0.1	1.5	97
3	 **13**	 **14**	0.1	1.5	97
4	 **15**	 **16**	0.1	1.5	98
5	 **17**	 **18**	0.1	1.5	90
6	 **19**	 **20**	1.0	12	96
7	 **21**	 **22**	0.5	1.0	97
8	 **23**	 **24**	0.5	1.5	93

[a] Reactions were conducted in CH_2Cl_2 at 35 ℃. [b] Isolated yield.

Table 2 Application of catalyst **8** to different CM substrates



Entry	Substrate	Product	Yield[a]/%
1	**25a** (R=H)	**27a**	93
2	**25b** (R=4-OCH_3)	**27b**	98
3	**25c** (R=4-Br)	**27c**	96
4	**25d** (R=4-CH_3)	**27d**	95
5	**25e** (R=4-NO_2)	**27e**	60
6	**25f** (R=2-Br)	**27f**	40

[a] Isolated yield.

methyl, methoxyl, bromo, and nitro groups. The products (**27a**—**27e**) were obtained in good to high yields (60%—98%). Even with an *o*-substituted substrate **25f**, a moderate yield (**27f**, 40%) was obtained.

Conclusions

In summary, a new Hoveyda-Grubbs type metathesis catalyst containing a Zn-porphyrin ligand has been prepared. This complex exhibits high activity and selectivity for a series of RCM and CM reactions with different substrates.

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