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Synthesis, Reaction, and Recycle of Light Fluorous Grubbs−Hoveyda Catalysts for Alkene Metathesis[†]

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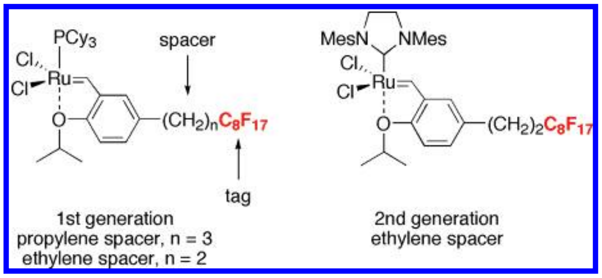

Light fluorous versions of first- and second-generation Grubbs−Hoveyda metathesis catalysts are introduced. These exhibit the expected reactivity profile, are readily recovered from reaction mixtures by fluorous solid-phase extraction, and can be routinely reused five or more times. The catalysts can be used in a stand alone fashion, or supported on fluorous silica gel.

Introduction

Organic molecules bearing small fluorous tags (C_6F_{13}, C_8F_{17}) are called light fluorous molecules.[1] Light fluorous reagents,[2] scavengers, and catalysts are especially convenient since they typically induce reactions of organic substrates under the same conditions as their nonfluorous relatives, but are reliably removed from crude reaction products by fluorous solid-phase extraction (fspe).[3] Only a handful of light fluorous catalysts, including palladium,[4a,b] platinum,[4c] and nickel[4d] complexes, have been described to date.

Alkene metathesis is among the most powerful and popular methods for carbon−carbon bond formation today, and an assortment of metathesis catalysts are now available (Figure 1).[5] Among these, first and second generation Grubbs−Hoveyda catalysts **1**[6] and **2**[7] and related molecules[8] are especially useful because of their scope and stability.[9] The high cost of these catalysts encourages recovery and reuse, even on a small scale.

An assortment of polymer- and ionic liquid-supported metathesis catalysts have been introduced to facilitate separation in metathesis reactions.[10] Recently, Yao has

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[†] Dedicated to Dr. Alfred Bader in celebration of his 80th birthday.

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(2) Representative fluorous reagents and scavengers: (a) Dobbs, A. P.; McGregor-Johnson, C. *Tetrahedron Lett.* **2002**, *43*, 2807−2810. (b) Dandapani, S.; Curran, D. P. *Tetrahedron* **2002**, *58*, 3855−3864. (c) Zhang, W.; Chen, C. H.-T.; Lu, Y.; Nagashima, T. *Org. Lett.* **2004**, *6*, 1473−1476. (d) Lindsley, C. W.; Zhao, Z.; Leister, W. H. *Tetrahedron Lett.* **2002**, *43*, 4225−4228. (e) Lindsley, C. W.; Zhao, Z. J.; Leister, W. H.; Strauss, K. A. *Tetrahedron Lett.* **2002**, *43*, 6319−6323. (f) Lindsley, C. W.; Zhao, Z.; Newton, R. C.; Leister, W. H.; Strauss, K. A. *Tetrahedron Lett.* **2002**, *43*, 4467−4470. (g) Zhang, W.; Curran, D. P.; Chen, C. H.-T. *Tetrahedron* **2002**, *58*, 3871−3875. (h) Zhang, W.; Chen, C. H.-T.; Nagashima, T. *Tetrahedron Lett.* **2003**, *44*, 2065−2068.

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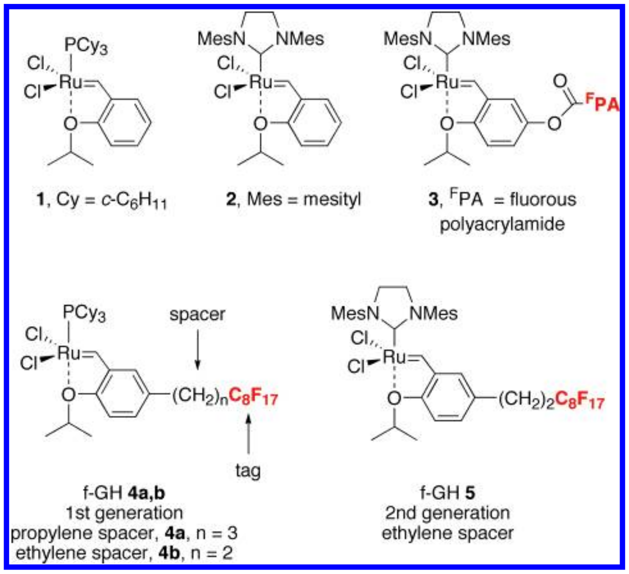


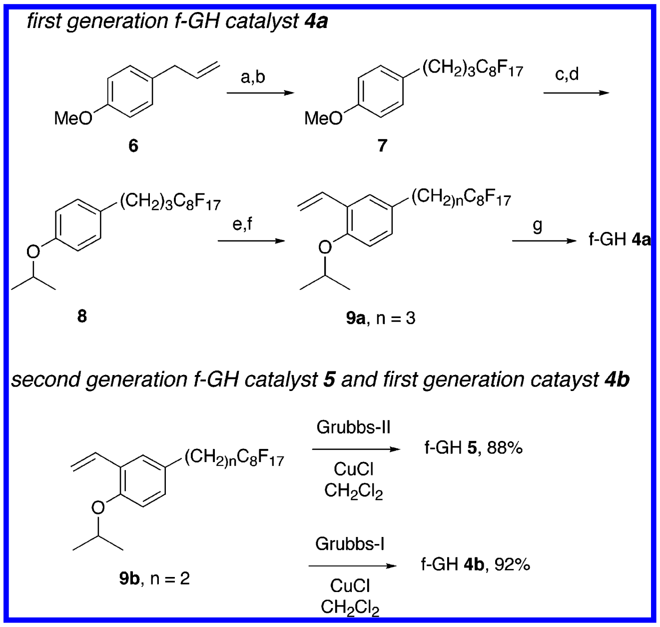
FIGURE 1. Grubbs−Hoveyda (GH) metathesis catalysts.

reported a heavy fluorous Grubbs−Hoveyda catalyst **3**.[11] The catalyst is linked to a fluorous polyacrylate and can be used in conjunction with a fluorous solvent for fluorous biphasic catalysis. We report herein complementary light fluorous Grubbs−Hoveyda (f-GH) catalysts **4a**,**b** and **5**. These induce alkene metathesis reactions under the same conditions as their nonfluorous parents but can be readily separated from crude reaction products by fluorous solid-phase extraction (fspe) when added to reaction mixtures in pure form or by filtration when added in supported form on fluorous silica gel. The catalysts are reasonably stable to both the reaction and separation conditions, and can be recovered and reused repeatedly.

Results and Discussion

Syntheses of the first- and second-generation f-GH catalysts are summarized in Scheme 1. For first-generation catalyst **4a**, addition of the fluorous tag to 1-allyl-4-methoxybenzene **6** was accomplished by standard atom transfer addition[12] and reduction[13] reactions to provide **7**. Demethylation[14] and isoproylation provided **8**. This was brominated[15] and the bromide was coupled with vinyl tributyltin[16] to provide ligand precursor **9a**. Trans-metathesis[7] with the standard first-generation Grubbs catalyst (Grubbs-I) provided the f-GH catalyst **4a** as brown crystals (mp 159.0−160.0 °C) after recrystallization from CH_2Cl_2/pentane. The crystal structure of this complex was solved, and ORTEP diagrams and full data are provided in the Supporting Information.

SCHEME 1[a]



[a] Reagents and conditions: (a) 2.2 equiv of $C_8F_{17}I$, 1 equiv of Me_3Al, 5 mol % of $Pd(PPh_3)_4$, CH_2Cl_2, rt, 64% (recrys.); (b) 1.5 equiv of Bu_3SnH, 0.2 equiv of AIBN, benzene, reflux, 81%; (c) 4 equiv of $BBr_3S(CH_3)_2$, dichloroethane, reflux, 88%; (d) 1.5 equiv of NaH, 2 equiv of ^{i}PrI, THF/DMF, rt, 94%; (e) 1.1 equiv of Br_2, 0.04 equiv of AcOH, CH_2Cl_2, rt, 94%; (f) 50 mol % of $Pd(PPh_3)_4$, 3 equiv of tributylvinylstannane, toulene, reflux, 64%; (g) 1.1 equiv of Grubbs-I, 1.25 equiv of CuCl, CH_2Cl_2, rt, 71%.

Second-generation f-GH catalyst **5** differs from **4a** by having the *N*-heterocyclic carbene (NHC) ligand[17] in place of the phosphine, and it has an ethylene spacer rather than a propylene spacer. The ethylene spacer was used because ligand precursor **9b** became commercially available during the course of this work.[18] Trans-metathesis of **9b** with standard second-generation Grubbs catalyst (Grubbs-II) gave f-GH catalyst **5** as green crystals, mp 136.5−137.5 °C, after column chromatography and recrystallization from CH_2Cl_2/pentane.

Most of the experiments with first generation f-GH catalyst **4a** were complete when styrene **9b** became available to us. However, to show that propylene- and ethylene-spacer catalysts were analogous, we also synthesized **4b** by cross metathesis from **9b** and Grubbs-I catalyst as above. Complex **4b** was isolated in 92% yield as a brown solid, mp 154.5−155.5 °C.

Complexes **4a**,**b** and **5** were air stable over several days either as solids or dissolved in solvent in an NMR tube, so no special handling or storage precautions were taken. However, **4a** and **5** slowly decomposed over several days when heated in $CDCl_3$ at 80 °C (estimated half-lives: **4a**, ~20 h; **5**, ~8 days). The better thermal stability of **5** is consistent with its better recovery in the reuse experiments described below. The catalysts were not significantly soluble in fluorous solvents such as FC-72 (per-

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(18) (a) Ligand **9b** and FluoroFlash silica gel and TLC plates were purchased from Fluorous Technologies, Inc., www.fluorous.com. FluoroFlash silica gel has a perflourooctylethyl silyl ($C_8F_{17}CH_2CH_2Si$) bonded phase. (b) DPC holds an equity interest in this company.

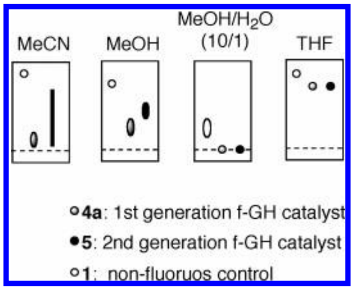


FIGURE 2. TLC behavior of **1**, **4a**, and **5** on FluoroFlash silica.

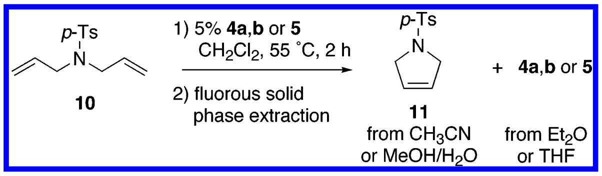
fluorohexanes), but instead dissolved in common organic solvents including diethyl ether, THF, CH_2Cl_2, and CH_3CN.

To evaluate prospects for fspe separation, we analyzed the TLC behavior of the standard and fluorous GH catalysts under typical "fluorophobic" conditions (to model the first stage of a fluorous spe) and "fluorophilic" conditions (to model the second stage) on commercial FluoroFlash fluorous silica gel.[18] The results of these informative experiments are summarized pictorially in Figure 2.

When the FluoroFlash TLC plate was eluted with 100% acetonitrile, nonfluorous catalyst **1** moved with the solvent front, as expected, while f-GH catalyst **4a** was well retained. In contrast, f-GH catalyst **5** exhibited a long streak, suggesting decomposition. In 100% methanol, both f-GH catalysts **4a** and **5** provided well-resolved spots, but the retention factors (R_f) were too high for filtration-based separation. In 10/1 MeOH/H_2O, the R_f factors of both complexes decreased significantly and they only barely moved from the baseline. In the fluorophilic solvent THF, both complexes exhibited clean spots near the solvent front. A similar behavior was observed in ether (not shown).

These results suggest that complex **4a** can be retained in a fluorophobic pass with water-free acetonitrile while aqueous methanol is preferred for **5**. Both complexes should be eluted in a fluorophilic pass with ether or THF. These experiments show how simple fluorous TLC experiments can be used to quickly identify suitable conditions for solid-phase extractions.

TABLE 1. Reuse of f-GH Catalysts 4a,b and 5 in the Metathesis of 10 to 11



entry	cat.	cyc	10 mg	cat mg	**11**,% (mg)	cat., % (mg)
1	**4a**	1	196	41	99 (180)	88 (36)
2	**4a**	2	170	36	99 (155)	72 (26)
3	**4a**	3	90	19	98 (78)	84 (16)
4	**4a**	4	76	16	99 (67)	69 (11)
5	**4a**	5	52	11	99 (46)	73 (8.0)
6	**4a**	6	28	6	99 (25)	73 (4.4)
7	**4a**	7	21	4	98 (18)	80 (3.2)
8	**4b**	1	121	25	99 (107)	84 (21)
9	**5**	1	300	64	96 (256)	91 (58)
10	**5**	2	249	53	98 (217)	91 (48)
11	**5**	3	215	46	98 (187)	85 (39)
12	**5**	4	161	35	94 (134)	89 (31)
13	**5**	5	140	30	97 (121)	90 (27)

The reaction, separation, and reuse features of f-GH catalysts **4a** and **5** were studied in detail in the conversions of *N*,*N*-diallyl-*p*-toluenesulfonamide **10** to *N*-*p*-tosyl-2,5-dihydro-1*H*-pyrrole **11**, and the results of this series of experiments are summarized in Table 1. In a typical experiment with the first-generation catalyst **4a**, 196 mg (0.8 mmol) of **10** was heated with 41 mg (5 mol %) of **4a** in dichloromethane at reflux for 2 h.[19] The cooled mixture was loaded to 1.2 g of fluorous silica gel (30× weight of the catalyst), which was eluted with 6 mL of acetonitrile to provide an organic fraction containing product **11** (180 mg, >99%) followed by 18 mL of ether to provide a fluorous fraction containing recovered catalyst **4** (36 mg, 88%).

The recovered catalyst exhibited a ^{1}H NMR spectrum similar to the starting catalyst, and it was used directly in the second cycle with appropriate adjustment of all other components to maintain the same ratio (5 mol % of catalyst). This process was continued through seven cycles with the weights and yields of product and catalyst shown in Table 1, entries 1–7. The yield of the product was uniformly high, while the yield of recovered catalyst ranged from 69% to 88%. At the end of the seventh cycle, about 10% of the original catalyst was recovered. While the recovered complex is no longer pristine (see the Supporting Information for the ^{1}H NMR spectrum), we believe that it is still active. Overall, the initial 41 mg of catalyst (0.04 mmol) was used to metathesize 633 mg (about 2.5 mmol) of **10**. No effort for further optimization of the loading or recovery was attempted.

The first-generation catalyst with the ethylene spacer **4b** was tested in a single experiment (entry 8) and gave results very comparable to those of **4a**. Based on this and the structural similarity, we suggest that **4a** and **4b** can be used interchangeably.

The second-generation catalyst **5** behaved similarly, and a series of five metathesis cycles with this catalyst are summarized in Table 1, entries 9–13.[20] Optimized fspe conditions required somewhat more fluorous silica gel (50× weight of the catalyst) compared to **4a**. The fluorophobic elution was conducted with 80% MeOH/H_2O and THF was used for the fluorophilic elution. Yields of product **11** were again high (94–98%) in each cycle, while

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[19] Tosyl amide **10** (1.00 g, 3.98 mmol) and **4a** (211 mg, 0.199 mmol, 0.050 equiv) and dichloromethane (79.6 mL, 0.05 M) were placed in a flask under an argon atmosphere and the mixture was refluxed for 2 h at 55 °C. After removal of the volatile components by evaporation, the brownish mixture was submitted to separation by fspe. A short column was packed with fluorous silica gel (6.3 g) using acetonitrile as the solvent. The crude reaction mixture was then loaded onto this column and eluted with 31.5 mL of acetonitrile to give RCM product **11** in 98% yield (865 mg). The next elution of diethyl ether (94.5 mL) afforded the catalyst **4a** in 87% yield (184 mg).

[20] Tosyl amide **10** (300 mg, 1.20 mmol) and **5** (64.2 mg, 0.060 mmol, 0.050 equiv) and dichloromethane (24 mL, 0.05 M) were placed in a flask under an argon atmosphere and the mixture was refluxed for 2 h at 55 °C. After removal of the volatile components by evaporation, the brownish mixture was submitted to separation by fspe. A short column was packed with fluorous silica gel (3.2 g) using aq 80% MeOH as the solvent. The crude reaction mixture was then loaded onto this column and eluted with 16.1 mL of aq 80% MeOH and successively 9.7 mL of THF. The evaporation of the 80% MeOH fraction and the THF fraction by vacuum centrifuge gave RCM product **11** in 96% yield (256 mg) and catalyst **5** in 91% yield (58.3 mg), respectively.

the recovery of catalyst **5** was better, ranging from 85% to 91%. At the end of five cycles, 915 mg (4.1 mmol) of product **11** was produced starting from 64 mg (0.06 mmol) of **5**, and 42% of the original catalyst mass was recovered. The catalyst recovered after cycle five is not as pure as the starting complex (see ^{1}H NMR spectra in the Supporting Information), but we expect that it is still active. And if desired, it could be repurified by chromatography or crystallization prior to reuse.

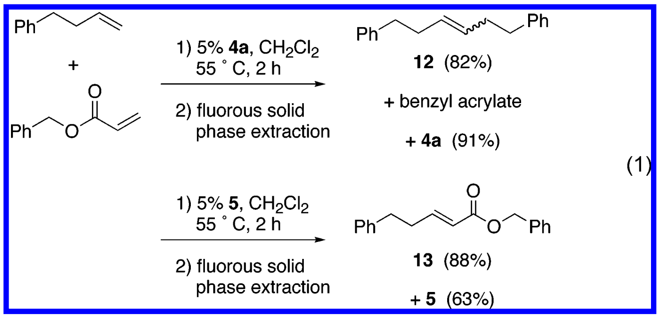
The ^{1}H NMR spectra of the products of Table 1 are clean and ligand resonances cannot be detected in either these or the ^{19}F NMR spectra (see the Supporting Information). However, the crude products are typically light tan. This, coupled with the observation that the recovered yield of the catalyst is never quantitative, suggests that the product may still contain small amounts of ruthenium. To obtain more information on residual ruthenium, we metathesized 1 g of substrate **10** with 211 mg (5 mol %) of f-GH catalyst **4a** under the standard conditions. After fspe, we recovered 965 mg (98%) of **11** along with 184 mg (87%) of the catalyst **4a**.

Crude product **11** was light tan in color, though no resonances for the ligand could be detected in either its ^{1}H or ^{19}F NMR spectrum. Spiking the product with 0.3 mol % of benzotrifluoride (an amount equivalent to 6% of the original amount of catalyst) showed that the CF_3 group of the spike was readily detected, so the fluorine content of the sample must be well below this. Elemental analysis of the crude product showed that it contained 0.15% ruthenium, which corresponds to about 6% of the original ruthenium added.[21] Because the corresponding 6% of the ligand is absent, we presume that most of this is ruthenium that has been released from the fluorous component of the ligand and is therefore not retained on the spe. Portions of the crude product were further purified by recrystallization (to give a very faint tan solid) and flash chromatography (to give a white solid). These products exhibited <0.05% ruthenium (the limit of delectability) in elemental analysis. These levels were deemed satisfactory and further trace analysis was not conducted. A similar preparative experiment with **5** gave qualitatively similar results.[22]

The scope of the new catalysts was briefly probed by conducting ring closing metathesis with five substrates under the standard conditions, and the results of these experiments are summarized in Table 2. All five substrates cyclized smoothly and in good yield with f-GH catalyst **4a**, though the cyclization of acrylate in entry 3 required 3 days. Yields of products were uniformly good (84–99%), and the catalyst was recovered in 76–92% yields. Metathesis of substrate in entry 5 was described with an ionic liquid-supported first-generation GH catalyst, but deactivation of the catalyst was observed in the third cycle.[14] We conducted three cycles of metathesis of this substrate without problem, and recovered 70% of the original catalyst mass.

Catalyst **5** was more reactive as expected, and all substrates were consumed in 2 h. However, only the products in entries 1–3 were reasonably pure as assayed by ^{1}H NMR spectroscopy. The target products from entries 4 and 5 were indeed the major components, but these samples also had significant impurities that may result from ring opening metathesis or polymerization. These products were not further purified. Recovery of the catalyst **5** was satisfactory in entries 1–4 (76–89%), but lower (62%) in entry 5.

Next, we tested the reactivity of **4a** and **5** in a representative cross-metathesis reaction between 4-phenyl-1-butene and benzyl acrylate under the standard conditions with the usual fspe separation (eq 1). First-generation catalyst **4a** provided the homodimer **12** in 82% yield alongside recovered benzyl acrylate (100%) and catalyst **4a** (91%). Second-generation catalyst **5** provided cross-coupled product **13** in 88% yield and homodimer **12** was not detected by ^{1}H NMR spectroscopy. Catalyst **5** was recovered in 63% yield. These results are in line with expectations from the nonfluorous catalysts[6,7,23] and provide additional evidence that the fluorous catalysts will exhibit reactivity profiles that can be readily anticipated from results in the standard series.



(1)

Finally, we conducted a series of experiments with a silica-supported catalyst to show that f-GH catalysts are compatible with this mode of delivery and removal. Recently, Gladysz, Bannwarth, and others have developed procedures to isolate supported fluorous compounds from reactions,[24] and Teflon and fluorous silica have been used as supports to date. In some procedures, the supported catalyst or reactant is added directly to the reaction mixture, while in others a soluble catalyst or reactant is used and the support is added after the reaction. This later approach is one of the standard ones for spe loading.[25]

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[21] A control experiment with standard catalyst **1** (14 mg) and **10** (119 mg) provided 109 mg of crude product **11** (>100%). This was a dark brown solid and was contaminated with 0.56% ruthenium, corresponding to 25% of the original amount of ruthenium added. Surprisingly, 10 mg (71%) of the original catalyst was recovered from the fluorous spe. The TLC results (Figure 2) suggest that the catalyst should not be retained, so this may be due to precipitation during spe loading or elution.

[22] The crude product **11** was light tan and contained 0.46% Ru by elemental analysis (19% of original catalyst charge; however, there may be an error in this analysis since 91% of the original catalyst mass was recovered). The chromatographed product was a white powder containing <0.09% Ru while the crystallized product was a very pale tan powder containing <0.05% Ru.

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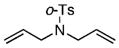
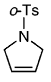
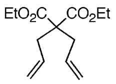
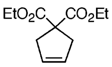
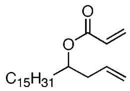
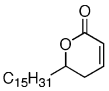
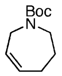
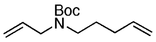
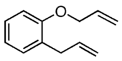
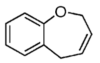
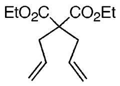
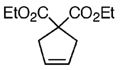
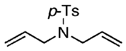
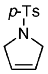
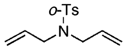
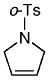
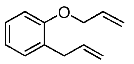
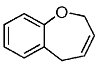
[25] See Fluoruos Technolgies, Inc. Product Application Note "Fluorous Solid-Phase Extraction": http://fluorous.com/download.html.

TABLE 2. Examples of RCM with f-GH Catalysts 4a and 5

Entry	Substrate	Product	cat	time (h)	%yld prod	%yld cat
1			**4a**	2	98	92
			5	2	92	76
2			**4a**	2	99	88
			5	2	95	80
3			**4a**	72	90	76
			5	2	82	83
			**4a**	4	87[a] (67[c])	83
4			**5**	2	92[a]	89
			**4a**[b]	2	84	89
5			**4a**[b]	2	89	83
			4a[b]	2	82	95
			5	2	51[a]	62

[a] Contains impurities. [b] Three cycles with the same original catalyst charge. [c] After flash chromatographic purification.

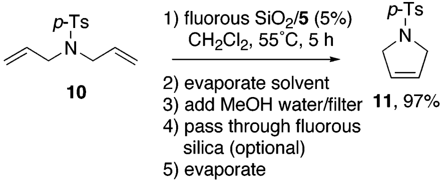
TABLE 3. Examples of RCM with Silica-Supported f-GH Catalyst 5

Entry	Substrate	Product	time (h)	%yld prod	^{19}F NMR res?[a]
					
1			1	97	Yes
2			1	98	Yes
3			1	98[b]	Yes
4			3	94	Yes[c]
5			5	97	Yes
6			6	96	No
7			2	67	Yes

[a] Yes: trace signals detected in the ^{19}F NMR, estimated less than 0.4% compared to the product. No: no clear signals in the ^{19}F NMR spectrum. [b] At 85% conversion of **10**. [c] Contains 0.4% signal relative to the product

We initially dissolved f-GH complex **5** in CH_2Cl_2, added 30× weight of fluorous silica gel, and then evaporated to dryness. The resulting green, free-flowing supported complex was then suspended in 80% MeOH/water. The powder remained green while the solution stayed clear; little or no reaction occurred when substrates were added followed by heating. As expected, the complex prefers the fluorous silica to the polar, hydrophilic solvent. However, the complex is readily extracted back from the fluorous silica by washing with the standard reaction solvent dichloromethane. Thus, simply by switching solvents, the complex can be driven onto or extracted off of the fluorous silica gel.

Equation 2 summarizes a very simple procedure that we developed to capitalize on this two-state, solvent-dependent behavior. Silica-supported **5** (180 mg of silica containing 6 mg of **5**, 5 mol %) was added to **10** (28 mg) in CH_2Cl_2 (2.2 mL). The resulting slurry was refluxed for 5 h, then the mixture was cooled and the solvent was evaporated to yield a dry green powder. Methanol/water (80%, 3 mL) was added and the slurry was filtered with a standard suction filter. The liquid phase containing the product was clear to the naked eye, yet it still contains a trace (<1%, see below) of the originally added catalyst. This material may be of sufficient purity for many uses; however, to upgrade it even further, we poured the MeOH/water solution through a small pad (60 mg) of additional fluorous silica gel. Although the solution appeared clear, a faint green line was visible at the top of the silica pad after filtration. Product **11** (24 mg, 97%) was obtained after evaporation of the solvent, and it was fluorine free according to the standard ^{19}F NMR analysis. The green silica gel from the initial filtration was washed with THF to provide the recovered catalyst **5** in 83% yield after evaporation.



(2)

Table 3 summarizes the results of several experiments conducted to probe the features of supported catalyst **5**. In these experiments, the slurry resulting from addition of MeOH/water was simply filtered and evaporated; it was not passed through an additional pad of fluorous silica. Diethyl diallyl malonate was subjected to three cycles of metathesis using the same supported catalyst charge (entries 1–3). Unlike the experiments in Table 2, we did not adjust the amount of precursor to compensate for lost catalyst (because the supported catalyst is a material and we do not know how much catalyst was lost); we simply used the same amount of precursor in each of the three cycles. Cycles 1 and 2 proceeded smoothly in the allotted time (1 h), while only 85% conversion was observed in cycle 3. Presumably this is a result of the gradual erosion of the catalyst, as in Table 2. A fourth cycle (entry 4) was conducted for 3 h, and this gave complete conversion to **11**, which was isolated in 94% yield.

All of the crude products contained tiny, but clearly visible resonances in the ^{19}F NMR spectra, which we estimate to account for less than 8% of the original amount of catalyst **5** that was added (in other words, less than 0.4 mol % compared to the product). This estimate is based on an accurate quantitation of the product of entry 4 by adding a BTF standard; this contained 0.4% of the original product. While the ^{19}F NMR assay quantities total fluorine content and does not provide structural information, we speculate that most of the trace fluorine-containing material is the catalyst because of the green band observed in filtration (see above).

Fresh fluorous silica-supported catalyst charges were used to metathesize the substrates in entries 5–7, and yields were uniformly excellent. Purities were also satisfactory, with very small ligand peaks (again possibly from the catalyst) being detected in the products from entries 5 and 7. The ^{19}F NMR from entry 6 was free from resonances. The colors of all the products were very pale tan and we judged these products to be more faintly colored than typical products from crude fspes (Table 2). The very small amounts of fluorine-containing residues in these samples are acceptable for many applications; indeed, it is only the high sensitivity of the assay that allows us to detect these otherwise spectroscopically silent contaminants. If better quality product is needed, it can be filtered through a small pad of fluorous silica gel to remove the last traces of fluorous residues.

We conducted a series of control experiments with diallyl malonate to better understand the supported procedure, and the results of these experiments are summarized in the Supporting Information. Briefly, attempts to use the standard Grubbs–Hoveyda catalyst **2** under the procedure outlined above with fluorous silica gel, reverse phase silica gel, or no silica gel at all were uniformly unsuccessful. The standard catalyst **2** simply dissolved when the 80/20 MeOH/water was added, and it ended up contaminating the product. Little or no catalyst was retained on the support or left in the flask (when support was absent).

In contrast, while the use of f-GH catalyst **5** supported on standard silica gel gave inferior results, its use supported on reverse phase silica gel or unsupported gave comparable results to the use of fluorous-supported catalyst. In the unsupported procedure, the catalyst was simply precipitated by addition of 80/20 MeOH/water, but its recovery was difficult since it clung to the flask and the stir bar. These results suggest that the prime factor behind the success of the separation in the solvent-switch procedure is the insolubility of **5** in 80/20 MeOH/water. This is not surprising, since the same insolubility drives the related fspe. Because of the mutually selective nature of fluorous interactions, we recommend fluorous silica gel as the material of first choice for this procedure, though other materials or even no material at all can potentially be used.

Conclusions

New fluorous Grubbs–Hoveyda catalysts **4a**,**b** and **5** show typical features of light fluorous catalysts; they react under similar conditions and show similar reactivity profiles to the nonfluorous analogues, but they are readily separated and recovered either by filtration (when added initially on fluorous silica gel) or by fluorous solid-phase extraction (when used in a standard solution-phase reaction). Only a small amount of fluorous silica gel is needed (30–50× weight of the catalyst), and catalysts **4a**,**b** are especially convenient because they can be retained under water-free conditions with acetonitrile. While most of the work on first-generation catalysts has been conducted with propylene-spaced complex **4a**, the commercial availability of the styrene precursor **9b** of ethylene-spaced complex **4b** and the similarities between **4a** and **4b** suggest that **4b** is presently the catalyst of choice in this series.

Standard Grubbs–Hoveyda catalysts can often be removed from crude reaction products by regular silica gel chromatography,[6,7] but this method is probably not as reliable or general as the fluorous spe; some organic molecules will have similar R_f values to standard catalysts on regular silica gel while essentially no organic molecules will be retained on fluorous spe. Furthermore, we find that both fluorous and nonfluorous Grubbs–Hoveyda catalysts tend to streak to some extent on standard silica gel. This suggests that purification of products that elute after the complexes can be a problem in standard silica gel chromatography. In contrast, on fluorous silica gel, no product ever elutes after the complex. This “one size fits all” aspect of the fluorous spe is attractive.

The recoveries of the catalyst are good (typically 75–95%) but not quantitative, at least in part because the catalysts are not fully stable to the reaction conditions. Small amounts of ruthenium are divorced from the fluorous carbene ligand during the reaction and leach into the product. The levels of contamination are tolerable for many types of multistep syntheses and can be reduced by chromatography, crystallization, or other means. On the positive side, because the fluorous spe targets a ligand and not the metal, the material recovered from the spe is largely active catalyst. In addition to reusing the catalyst, we routinely reused the fluorous silica gel after washing with THF and reconditioning with the fluorophobic solvent.

Assorted resin-bound,[9] heavy fluorous[10] and ionic liquid-supported[14] Grubbs catalysts have been reported, and these catalysts are effectively materials. Analyses of these materials are typically based on performance. This is convenient when the material is reused to repeatedly conduct the same reaction, but has detractions when the material is used to conduct different reactions. For example, degraded catalyst products or left over products or reactants from a prior reaction may remain in the active catalyst material and contaminate subsequent reactions. In contrast, the light fluorous catalysts are molecules, and can be analyzed and characterized as such. The purity of the recovered catalyst is readily assessed by NMR spectroscopy, melting point, and other means. If this is deemed unacceptable, then the catalyst can be recrystallized or otherwise purified. Standard Grubbs–Hoveyda catalysts are expensive even in small quantities, so the ability to recover and reuse the catalyst can result in significant cost savings.

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Supporting Information Available: Procedures for reactions and spe purifications, spectroscopic data for products, data for the crystal structure of **4a**, and copies of NMR spectra of typical products after spe. This material is available free of charge via the Internet at http://pubs.acs.org.

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