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Regarding the Mechanism of Olefin Metathesis with Sol−Gel-Supported Ru-Based Complexes Bearing a Bidentate Carbene Ligand. Spectroscopic Evidence for Return of the Propagating Ru Carbene

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Abstract: Two isotopically and structurally labeled Ru-based carbenes (**2-*d*$_4$** and **13**) have been prepared and attached to the surface of monolithic sol−gel glass. The resulting glass-supported complexes (**18-*d*$_n$** and **19**) exhibit significant catalytic activity in promoting olefin metathesis reactions and provide products of high purity. Through analysis of the derivatized glass pellets used in a sequence of catalytic ring-closing metathesis reactions mediated by various supported Ru carbenes, it is demonstrated that free Ru carbene intermediates in solution can be scavenged by support-bound styrene ether ligands prior to the onset of competing transition metal decomposition. The observations detailed herein provide rigorous evidence that the initially proposed release/return mechanism is, at least partially, operative. The present investigations shed light on a critical aspect of the mechanism of an important class of Ru-based metathesis complexes (those bearing a bidentate styrene ether ligand).

Introduction

Research in these laboratories during the past several years has involved the synthesis and development of a variety of Ru-based catalysts (Chart 1) that promote various olefin metathesis reactions[1] efficiently and selectively.[2] Since the preparation of the first member of this family of complexes in 1996, various achiral[3] and chiral[4] Ru carbenes have been designed and developed that promote highly stereo- and enantioselective C−C bond forming reactions. The Ru complexes depicted in Chart 1 offer unique reactivity and selectivity levels that are at times not available with other catalysts.[2] Complexes **1**−**5**, shown in Chart 1, are air-stable and can be readily purified by silica gel chromatography; the majority of reactions promoted in the presence of Ru catalysts **1**−**6** can be effected in air and with undistilled commercial solvents.

The special attributes of the Ru-based complexes illustrated in Chart 1 are largely due to the presence of a bidentate carbene.[2b] As illustrated in Scheme 1, in contrast to precatalysts represented by **7** [5] and **8**,[6] which are likely activated by the loss of PCy_3 (→**c**),[7] bidentate carbenes such as **1** and **2** are converted to the catalytically active 14-electron Ru complex (**b** in Scheme 1) through dissociation of the Ru−O chelation followed by olefin metathesis involving a substrate molecule (via **a**), leading to the formation of isopropoxystyrene **9** (or a related derivative). Recent studies[8] indicate that the absence of released phosphine, which can intercept and deactivate certain Ru carbenes (e.g., **b**

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[1] For reviews on catalytic olefin metathesis, see: (a) Grubbs, R. H.; Miller, S. J.; Fu, G. C. *Acc. Chem. Res.* **1995**, *28*, 446−452. (b) Schmalz, H.-G. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1833−1836. (c) Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2036−2056. (d) Ivin, K. J.; Mol, J. C. *Olefin Metathesis and Metathesis Polymerization*; Academic Press: San Diego, CA, 1997. (e) Furstner, A. *Top. Catal.* **1997**, *4*, 285−299. (f) *Alkene Metathesis in Organic Synthesis*; Furstner, A. Ed.; Springer: Berlin, 1998. (g) Armstrong, S. K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 371−388. (h) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413−4450. (i) Randall, M. L.; Snapper, M. L. *Strem Chem.* **1998**, *17*, 1−9. (j) Phillips, A. J.; Abell, A. D. *Aldrichimica Acta* **1999**, *32*, 75−89. (k) Wright, D. L. *Curr. Org. Chem.* **1999**, *3*, 211−240. (l) Furstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012−3043. (m) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18−29. (n) *Handbook of Olefin Metathesis*; Grubbs, R. H., Ed.; VCH−Wiley: Wienheim, Germany, 2003. (o) Schrock, R. R.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 4592−4633.

[2] For brief overviews regarding supported olefin metathesis catalysts, see: (a) Kingsbury, J. S.; Hoveyda, A. H. In *Polymeric Materials in Organic Synthesis and Catalysis*; Buchmeiser, M. R., Ed.; Wiley-VCH: Weinheim, Germany, 2003; pp 467−502. (b) Hoveyda, A. H.; Gillingham, D. G.; Van Veldhuizen, J. J.; Kataoka, O.; Garber, S. B.; Kingsbury, J. S.; Harrity, J. P. A. *Org. Biol. Chem.* **2004**, *2*, 8−23.

[3] (a) Harrity, J. P. A.; Visser, M. S.; Gleason, J. D.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1997**, *119*, 1488−1489. (b) Harrity, J. P. A.; La, D. S.; Cefalo, D. R.; Visser, M. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1998**, *120*, 2343−2351. (c) Kingsbury, J. S.; Harrity, J. P. A.; Bonitatebus, P. J.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 791−799. (d) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168−8179. For a most recent supported variant of **2**, see: (e) Clavier, H.; Audic, N.; Mauduit, M.; Guillemin, J.-C. *Chem. Commun.* **2004**, 2282−2283.

[4] (a) Van Veldhuizen, J. J.; Garber, S. B.; Kingsbury, J. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2002**, *124*, 4954−4955. (b) Van Veldhuizen, J. J.; Gillingham, D. G.; Garber, S. B.; Kataoka, O.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2003**, *125*, 12502−12508. (c) Gillingham, D. G.; Kataoka, O.; Garber, S. B.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 12288−12290. See also: (d) Van Veldhuizen, J. J.; Campbell, J. E.; Giudici, R. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2005**, *127*, in press. (e) Seiders, T. J.; Ward, D. W.; Grubbs, R. H. *Org. Lett.* **2001**, *3*, 3225−3228.

[5] (a) Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2039−2041. (b) Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 100−110.

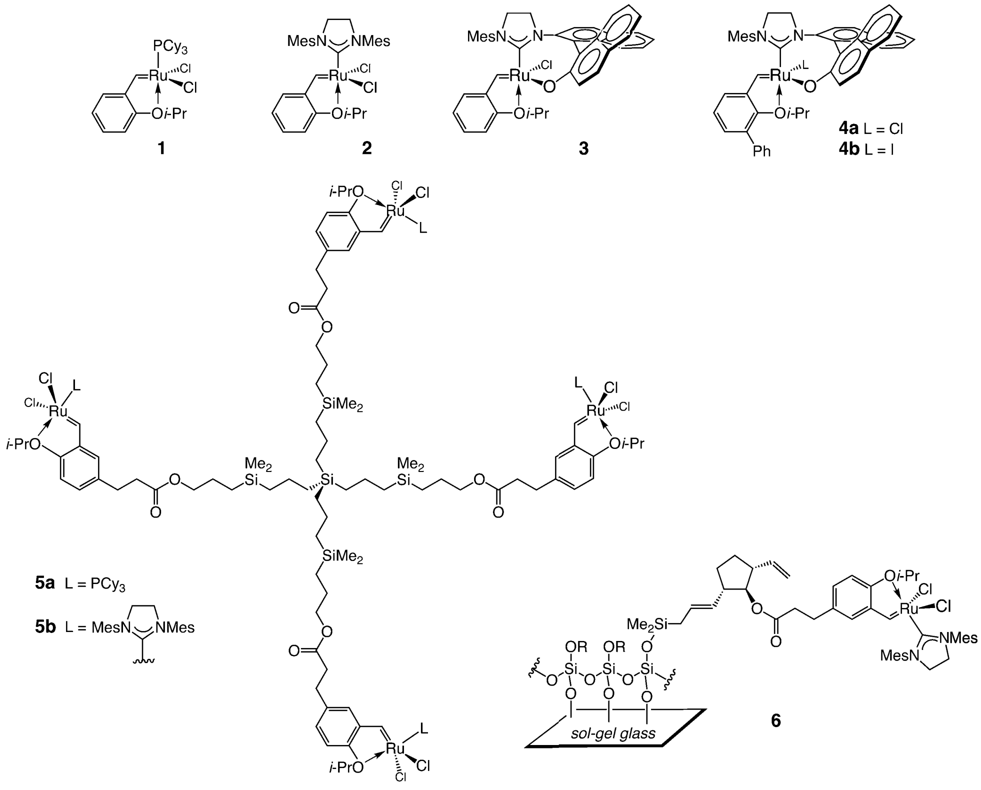
[6] Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953−956.

[7] Sanford, M. S.; Love, J. A. In *Handbook of Olefin Metathesis*; Grubbs, R. H., Ed.; VCH−Wiley: Weinheim, Germany, 2003; Vol. 1, pp 112−131, and references therein.

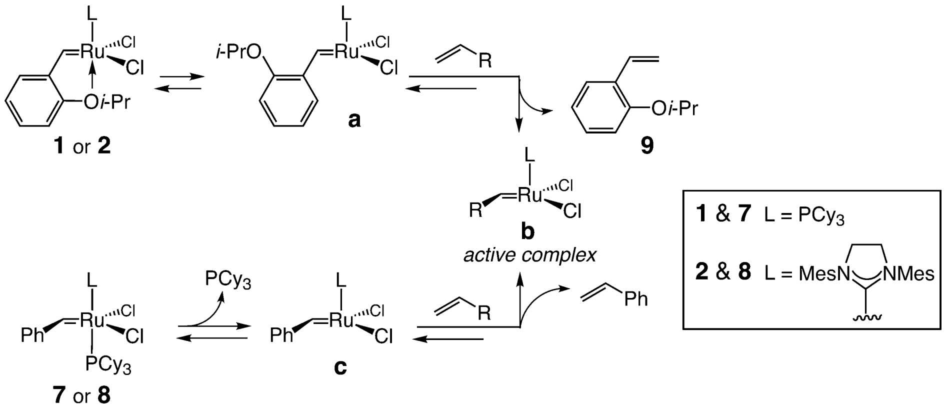
[8] (a) Love, J. A.; Morgan, J. P.; Trnka, T. M.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2002**, *21*, 4035−4037. (b) Love, J. A.; Sanford, M. S.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 10103−10109.

10.1021/ja042668+ CCC: $30.25

Chart 1



Scheme 1. Mechanisms of Formation of a Metathesis-Active Ru–Based Complex



in Scheme 1), is one of the key reasons for the unique reactivity profiles observed for complexes represented by **1** and **2**.

Another noteworthy feature that originates from the bidentate nature of the carbene ligands in **1**–**6** relates to the possibility that the achiral Ru complexes in Chart 1 operate by a release/return mechanism.[3c,d] As shown in Scheme 2, it is plausible that the initial Ru complex (e.g., **1** or **2**) can exist in equilibrium with a metal carbene (release) such as **e** (to form **9**). The original metal complex, after initiating several catalytic olefin metathesis cycles, may be regenerated through reaction of **e** with **9** (return).[9]

The release/return mechanism points to the possibility of efficient homogeneous catalysis (released carbene) through the use and recovery of a supported catalyst. Such considerations, together with the unique reactivity of **1** and **2**, have led to the development of a number of related *supported* variants.[2] One example is the sol–gel complex **6**,[10] illustrated in Chart 1, synthesized and examined in these laboratories. This supported catalyst, which can be recycled up to 20 times,[2b] benefits from at least one advantage that is imparted by the bidentate styrene ligand: because Ru carbene release from the support backbone into solution requires an initial metathesis reaction with a substrate molecule, the amount of active catalyst released is dependent on substrate concentration. The need for weighing of each catalyst sample is therefore unnecessary, an attribute that is noteworthy when the sol–gel-supported catalyst is utilized in library synthesis.

A critical question regarding the catalytic activity of Ru-based catalysts bearing bidentate styrene ligands is whether the release/return mechanism is truly operative. One plausible alternative

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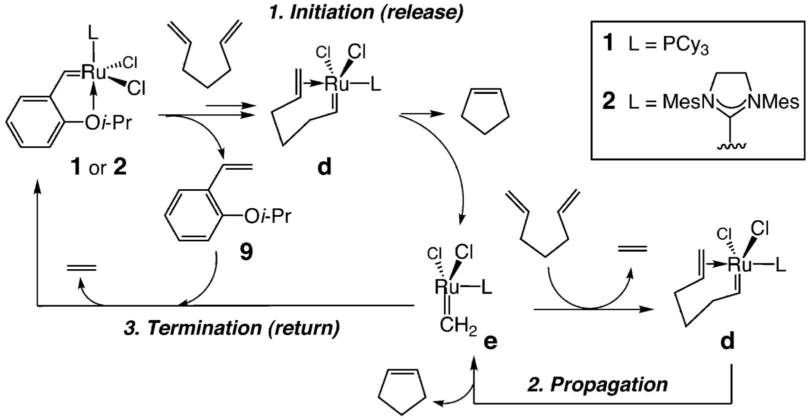
(9) For related reports on supported Ru-based complexes bearing *mono*dentate carbenes used for olefin metathesis, where a similar release/return scenario is suggested, see: (a) Barrett, A. G. M.; Cramp, S. M.; Roberts, R. S. *Org. Lett.* **1999**, *1*, 1083–1086. (b) Ahmed, M.; Barrett, A. G. M.; Braddock, D. C.; Cramp, S. M.; Procopiou, P. A. *Tetrahedron Lett.* **1999**, *40*, 8657–8662. (c) Ahmed, M.; Arnauld, T.; Barrett, A. G. M.; Braddock, D. C.; Procopiou, P. A. *Synlett* **2000**, 1007–1009.

(10) Kingsbury, J. S.; Garber, S. B.; Giftos, J. M.; Gray, B. L.; Okamoto, M. M.; Farrer, R. A.; Fourkas, J. T.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2001**, *40*, 4251–4256.

Scheme 2. Proposed Route for the Release, Catalytic Activity, and Return of Ru Complexes **1** and **2**



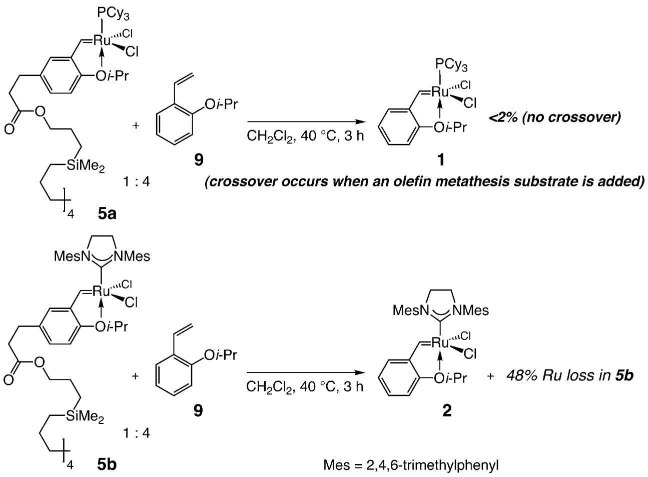
scenario is that Ru complexes such as **1** and **2**, or the supported complex **6**, serve solely as sources of highly active Ru carbenes, which, once released into solution in relatively small amounts, promote reaction at a high rate before undergoing decomposition (no return).[11] That is, the recovered catalyst sample might correspond to the portion of the initial catalyst loading that has not been liberated from the styrene ligand. Regarding the latter hypothesis, we recently illustrated that, with the more sterically hindered *chiral* Ru complexes **3** and **4** (cf. Chart 1), it is indeed likely that a return mechanism is *not* operative.[4b]

Herein, we detail the results of studies that unambiguously illustrate that measurable amounts of achiral Ru carbene released by a sol−gel-supported complex *can* return to the styrene ether attached to the support surface. These studies provide clear illustration of the validity of the release/return mechanism for Ru-based complexes such as **1**, **2**, and **6**. Mechanistic principles implied by the studies described below are relevant to the mode of action of Ru carbene derivatives prepared in other laboratories,[12] based on complexes **1** and **2**.

Results and Discussion

1. Preliminary Studies To Probe the Release/Return Mechanism. The first opportunity to test the possibility of release/return mechanism presented itself during our studies regarding the catalytic activity of **5a**, a dendritic structure based on monophosphine complex **1**. As summarized in Scheme 3, the release/return hypothesis received support since we detected efficient metal carbene transfer from dendritic to monomeric styrene ether sites within minutes *in the presence of an olefin metathesis substrate*.[3d] As depicted in Scheme 3, heating of a homogeneous solution of **5a** and **9** (1:4) in the absence of diene substrate at 40 °C (3 h, CH_2Cl_2) does not give rise to Ru crossover (**1** is not detected by 400 MHz ^1H NMR analysis). This is in stark contrast to the related experiment involving dendritic complex **5b**, one that bears an N-heterocyclic carbene (NHC). As depicted in Scheme 3, initial control experiments indicated that, under identical conditions as mentioned above (CH_2Cl_2, 40 °C, 3 h), a 1:4 mixture of the more reactive dendrimer **5b** (vs **5a**) and **9** leads to a rapid distribution of the Ru metal (52:48 ratio of dendritic:monomeric carbene proton signals).

Scheme 3



2. Initial Considerations Regarding Study of the Ru Release/Return Mechanism. The complications regarding the facile transfer of transition metal between styrene ether **9** and dendrimer **5b** caution that a similar strategy should not be used for assessment of Ru return in the case of sol−gel-supported complexes. Any metathesis reaction performed in the presence of a homogeneous styrene, such as **9** or unmetalated **5b**, cannot confirm restoration of the precatalyst resting state, since **2** or **5b** can be generated through cross-metathesis (CM) events on the sol−gel surface. Nonetheless, we realized that we could utilize advantageously the abovementioned CM reactions and design experiments that allow us to investigate rigorously the possibility of Ru-carbene return to sol−gel.

Such studies would commence with the synthesis of isotopically or structurally labeled versions of glass-supported Ru carbene **6** (Chart 1). Subsequently, a representative olefin metathesis reaction would be allowed to proceed *in the same reaction vessel* in the presence of glass samples that contain Ru complexes bearing a labeled NHC ligand as well as samples that contain unlabeled metal carbenes. After tracking of the identity of individual glass pellets, labeled and unlabeled

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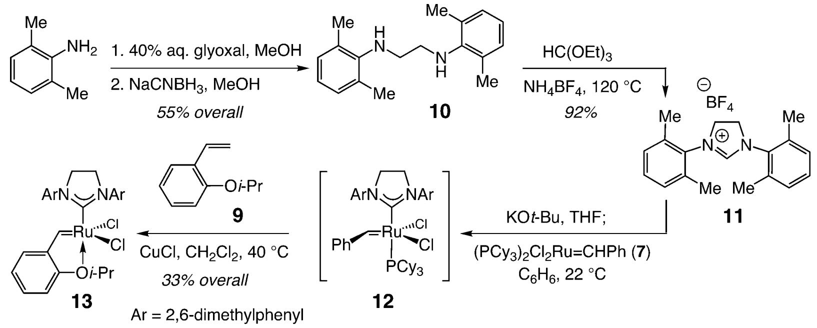
[11] Nguyen, S. T.; Trnka, T. M. In *Handbook of Olefin Metathesis*; Grubbs, R. H., Ed.; VCH−Wiley: Wienheim, Germany, 2003; Vol. 1, p 77.

[12] For example, see: (a) Grela, K.; Harutyunyan, S.; Michrowska, A. *Angew. Chem., Int. Ed.* **2002**, *41*, 4038−4040. (b) Grela, K.; Kim, M. *Eur. J. Org. Chem.* **2003**, 963−966. (c) Bujok, R.; Bleniek, M.; Masnyk, M.; Michrowska, A.; Sarosiek, A.; Stepowska, H.; Arlt, D.; Grela, K. *J. Org. Chem.* **2004**, *69*, 6894−6896. (d) Michrowska, A.; Bujok, R.; Harutyunyan, S.; Sashuk, V.; Dolgonos, G.; Grela, K. *J. Am. Chem. Soc.* **2004**, *126*, 9318−9325. (e) Wakamatsu, H.; Blechert, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 2403−2405. (f) Zaja, M.; Connon, S. J.; Dunne, A. M.; Rivard, M.; Buschmann, N.; Jiricek, J.; Blechert, S. *Tetrahedron* **2003**, *59*, 6545−6558. (g) Krause, J. O.; Zarka, M. T.; Anders, U.; Weberskirch, R.; Nuyken, O.; Buchmeiser, M. R. *Angew. Chem., Int. Ed.* **2003**, *42*, 5965−5969. (h) Krause, J. O.; Nuyken, O.; Wurst, K.; Buchmeiser, M. R. *Chem. Eur. J.* **2004**, *10*, 777−784.

Scheme 4. Synthesis of Ru-Carbene Complex **13**



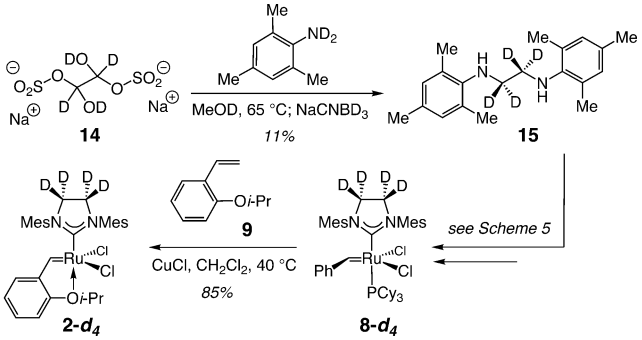
samples would be segregated. Facile exchange between styrene ether **9** and NHC-based Ru carbenes would allow us to strip the glass samples of their Ru content by treatment of the recovered sol−gel pellets with solutions of isopropoxystyrene. After recovery and chromatographic purification of *the monomeric complex (2) we would be able to establish rigorously its isotopic purity* (by ^{1}H NMR spectroscopy and/or mass spectrometry) and determine whether any crossover had occurred.

3. Synthesis of Labeled Ru Complexes. The first modified Ru complex targeted for synthesis was Ru carbene **13** (Scheme 4), a structurally altered form of **2** (a complex lacking para substitution at the two aryl groups on nitrogens). With established procedures[3d,6] in place for the synthesis of dihydroimidazolylidene ligands, we judged that it would be most efficient to use commercially available 2,6-dimethylaniline. We expected the highly deshielded carbene proton of **13** to exhibit a unique chemical shift in its ^{1}H NMR spectrum (vs complex **2**). Thus, Ru crossover from the sol−gel support to another glass support and then to **9**, based on the strategy described above, could be recognized (and quantified) through the presence of two downfield ^{1}H NMR signals (Ru═C*H*) in a region of the spectrum where trace impurities do not typically hinder analysis.

Ru complex **13** was synthesized in the manner illustrated in Scheme 4. Diamine **10** was accessed by reductive amination of the crystalline bis(imine) in the presence of NaCNBH$_3$ (55% overall yield after chromatography). Conversion to heterocycle **11** was effected upon exposure of **10** to triethyl orthoformate and ammonium tetrafluoroborate at 120 °C. Although, on the basis of previous reports, successive treatment of **11** with potassium *tert*-butoxide and (PCy$_3$)$_2$Cl$_2$Ru═CHPh (**7**) led to efficient ligand exchange, the surprising instability of **12** rendered isolation difficult. Dark red-colored bands of **12** would often elute cleanly from a silica gel column, only to decompose in solution upon standing and/or during solvent removal.[13] The solution-phase degradation can be detected visually as it is accompanied by a color change from red to dark purple. Nevertheless, when carbene **12** was isolated in pure form despite the above complications, it proved to be indefinitely stable when stored as a crystalline solid under N$_2$.

We could access sufficiently pure (>90%) samples of **12** to be used for sol−gel functionalization (see below), and the corresponding isopropoxy ether complex **13** was prepared as a two-step, one-pot process (Scheme 4).[14] However, the pronounced and unpredictable instability of **12** led us to consider using another labeled variant of Ru complex **2**. Toward this end, we judged that the diamine backbone would be the most suitable site for incorporation of isotope labels, since the imidazolinium ligand remains attached to the Ru complex[3c,d,7] (vs the isopropoxystyrene ligand, which dissociates from the metal and remains on the glass support during catalysis).

Scheme 5. Synthesis of Deuterated Ru Complexes **8-*d*$_4$** and **2-*d*$_4$**



In designing an efficient synthesis of the isotopically labeled heterocyclic ligand, we took note of a scalable synthesis of glyoxal-d_2−bis(sodium bisulfite)-*O*-d_2 reported by Bertz.[15] Thus, with NaCNBD$_3$ serving as an additional source of deuterium, syntheses of Ru complexes **8-*d*$_4$** and **2-*d*$_4$** were achieved in the manner illustrated in Scheme 5. Despite the initial low-yielding step (11%), the sequence is straightforward and allows facile access to gram quantities of labeled Ru complexes with >99 at. % D incorporation (400 MHz ^{1}H NMR analysis). Each metal carbene was easily purified by chromatography and fully characterized.

As disclosed previously,[10] we utilize ring-opening metathesis/cross-metathesis (ROM/CM) as the means for preparing, in a single operation, the tether that connects the metal complex to the glass surface in addition to the catalytically active Ru carbene bearing a bidentate styrene ether ligand (Scheme 6). This approach avoids stepwise introduction of the linker, the bidentate styrene ether, and the metal carbene. As shown in Scheme 6, ROM/CM of triene **16**[16] with Grubbs' Ru complex **8-*d*$_4$** and allylchlorodimethylsilane leads to the installment of an electrophilic silyl chloride to be used later for attachment to sol−gel glass, followed by metalation of the styrene ether moieties (→**17**). Subsequent reaction of the silyl chloride with a free

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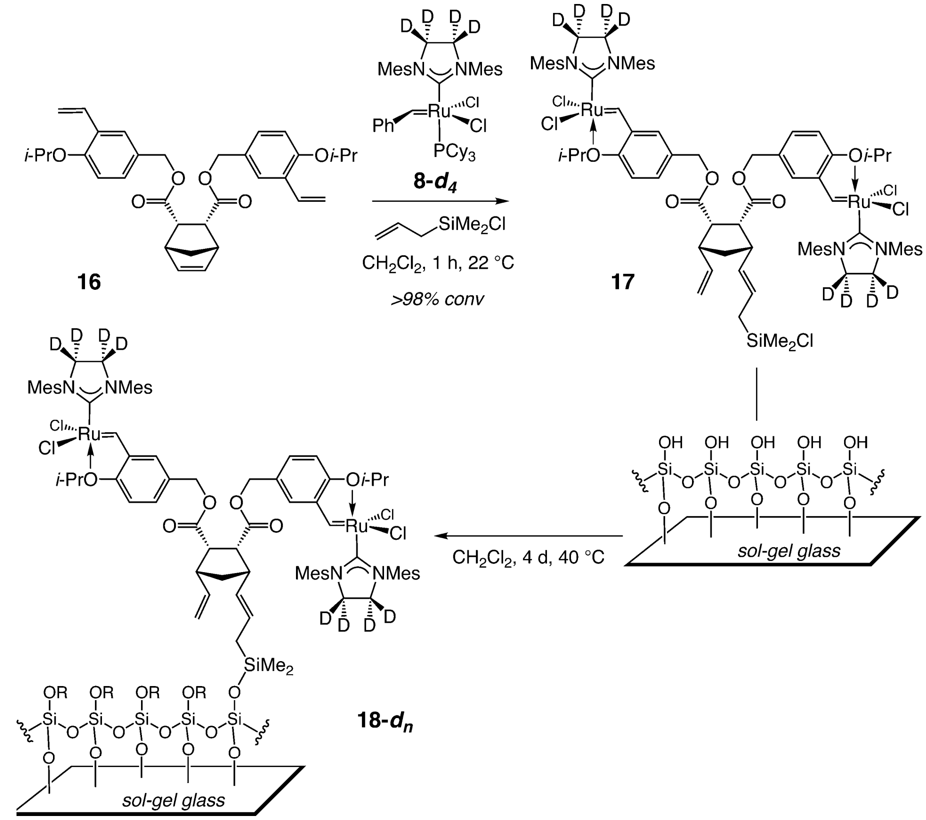
(13) Another (not necessarily mechanistically related) observation indicating that alteration of the aryl substituents of an NHC ligand can have unexpected effects on the stability and reactivity of the derived Ru carbenes can be found in a recent synthesis of a related Ru carbene bearing 2,6-diisopropylphenyl substituents on the saturated NHC; a Ru hydride was isolated as a major byproduct. See: Furstner, A.; Ackermann, L.; Gabor, B.; Goddard, R.; Lehmann, C. W.; Mynott, R.; Stelzer, F.; Thiel, O. R. *Chem. Eur. J.* **2001**, *7*, 3236−3253.

(14) See the Supporting Information for details.

(15) Bertz, S. H. *J. Org. Chem.* **1981**, *46*, 4088−4090.

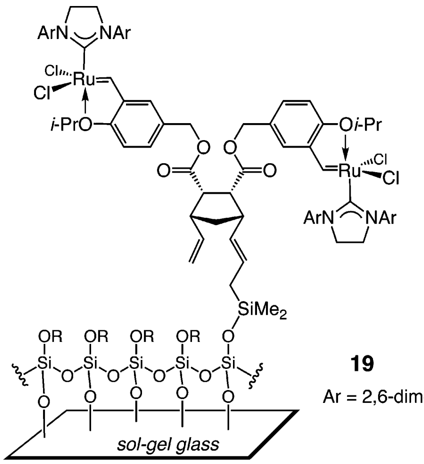
(16) This compound is easily formed by ring-opening of commercially available *cis*-5-norbornene-*endo*-2,3-dicarboxylic anhydride with 2 equiv of the functionalized benzylic alcohol; for details, see ref 10.

Scheme 6. Immobilization of Isotopically Labeled Ru Complexes



hydroxyl group on the glass surface anchors the catalyst to the support. Ru complex **18-*d*$_n$** was thus prepared as dark green glass pellets after washing with CH_2Cl_2 and drying under vacuum (Ru loading = 0.130 mmol/gram).[17]

Notwithstanding our concern regarding the stability and activity of the unimolecular bis(desmethyl) complex **13** (cf. Scheme 4), we prepared the derived polymeric variant (**19**) from a sufficiently pure (>90%) sample of carbene **12**. Supported Ru complex **19** was recovered from the procedure shown in Scheme 6 with a loading of 0.138 mmol/gram.



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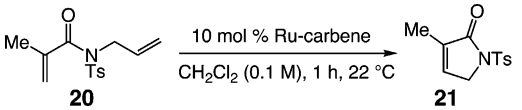
Ar = 2,6-dimethylphenyl

Table 1. Preliminary Examination of Catalytic Activity of Glass-Supported Ru Complexes



entry	catalyst	Ru loading[a] (mmol/g)	conv[b] (%)
1	**6**	0.122	83
2	**18-*d*$_n$**	0.130	92
3	**19**	0.138	63

[a] Based on mass increase upon installation of Ru carbenes. [b] Determined by 400 MHz ^{1}H NMR analysis of the unpurified reaction mixture.

4. Initial Examination of Catalytic Activity of Glass-Supported Ru Complexes. The catalytic activity of Ru-loaded glass samples **18-*d*$_n$** and **19** was examined through a study where RCM of tosyl acrylamide **20** served as the representative transformation and the activity levels of the new complexes were compared to that of the original glass-supported system **6**. As the data in entries 1 and 2 of Table 1 indicate, under identical conditions (10 mol % Ru loading, 0.1 M CH_2Cl_2), complexes **6** and **18-*d*$_n$** delivered 83 and 92% conversion, respectively, within 1 h at 22 °C.[18] The difference in activity is minor; moreover, the initial metal loading (millimoles per gram of glass), which is likely unique for a given batch of catalyst, might account for the small variation. Though measurably less efficient, samples of supported complex **19** exhibited significant olefin metathesis activity (63% conversion to **21** in 1 h; entry 3, Table 1). This finding proved critical as it allowed us to incorporate **19** in the crossover experiments (together with **6** and **18-*d*$_n$**) as a second set of supporting data. We sought to obtain additional findings due to the possibility that a minor

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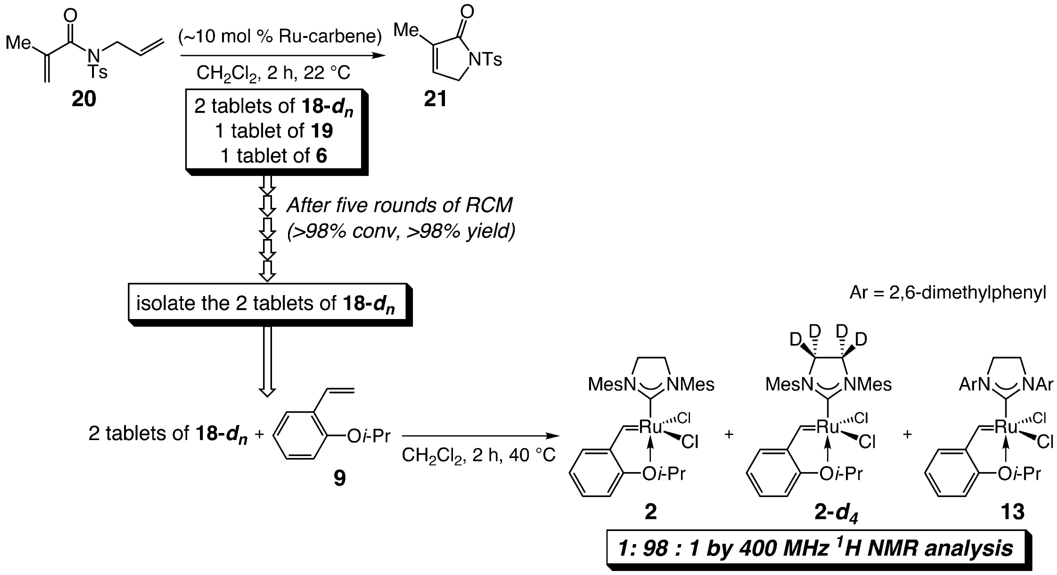
(17) The value was calculated from the mass increase following functionalization of the glass surface.

(18) If stirring is allowed to proceed for a longer period, RCM proceeds to >99% conversion for each catalyst. Reactions in Table 1 were stopped abruptly at 1 h simply by drawing the reaction mixture away from the catalyst pellet with a Pasteur pipet.

Scheme 7. Crossover Experiment with Labeled Glass-Supported Ru Complexes



impurity might give a false positive. Since we suspected that only small amounts of Ru carbene released from the glass support are likely sufficient to promote efficient conversion of **20** to **21** (see below for further discussion), we were concerned that small impurities could lead to the appearance of signals in ^{1}H NMR spectra (at ~4.18 ppm, which corresponds to the chemical shift of protons of the diamine backbone), leading to the false conclusion that there is effective crossover (see below for more detail). Inclusion of supported complex **19** would serve as an internal check by providing a second means of measuring Ru carbene transfer between different glass samples (appearance of a new carbene proton signal at 16.45 ppm corresponding to recovered **13**).

5. Crossover Experiments with Labeled Glass-Supported Ru Complexes. The key crossover experiments involving various labeled glass-supported Ru-based complexes were carried out as detailed below (Scheme 7). A total of four Ru-containing sol−gels (two pellets, 0.0149 mmol of **18-*d_n***; one pellet, 0.0079 mmol of **19**; one pellet, 0.0069 mmol of **6**; 10 mol % Ru total) were used (in the same vessel), as illustrated in Scheme 7, to catalyze five consecutive rounds of RCM on a 0.3 mmol scale (~84 mg of **20**). In each case, the reaction proceeded to >99% conversion in 2 h (0.2 M CH_2Cl_2, 22 °C), and the desired product was isolated without purification as an off-white crystalline solid in >99% yield. It is important to note that, after each run, each pellet was carefully rinsed with two portions of CH_2Cl_2 (2.0 mL for 15 min) to ensure that there were no unbound Ru complexes “trapped” within the sol−gel glass cavities.

Two important points about the Ru-catalyzed RCM reactions merit mention: (1) Each catalyst pellet contains a fingerprint of markings in the form of small chips and scratches; as is clearly shown in Figure 1, no two pellets are identical. As the first RCM reaction was set up, each gel was carefully weighed and scrutinized for its pattern of surface etchings. This allowed us to identify each individual pellet to be properly tracked throughout the course of the experiment. (2) As discussed previously,[10] continued recycling of the glass-supported Ru catalysts results in slow but steady depletion of active sites. Even though the metathesis activity of the combined three catalysts was not expended after five rounds, the second phase of the experiment was initiated at this point to ensure efficient retrieval of monomeric Ru carbenes (**2**, **2-d_4**, and **13**) for spectroscopic analysis.

After five rounds of RCM with pellets **18-d_n**, **19**, and **6**, the two pellets of **18-d_n** were separated from pellets **6** and **19** (Scheme 7). The two pellets of **18-d_n** were then placed in a vial which was charged with 0.5 mL of a 0.1 M solution of **9** in CH_2Cl_2, capped (to discourage solvent loss) and heated to 40 °C. The initially colorless solution became bright green over several hours as CM occurred. The solution was removed with a Pasteur pipet; a fresh solution of **9** was added, and the procedure was repeated until green discoloration could no longer be observed in the supernatant (total of five times). The combined styrene ether washes were concentrated to an oily green residue consisting primarily of unreacted **9**. Purification of the monomeric Ru complex was carried out by silica gel chromatography (CH_2Cl_2).

As may be expected, the major constituent of the material isolated was the perdeuterio monomer **2-d_4**. However, we established that, as depicted in Figure 2, *both Ru complex* ***2***

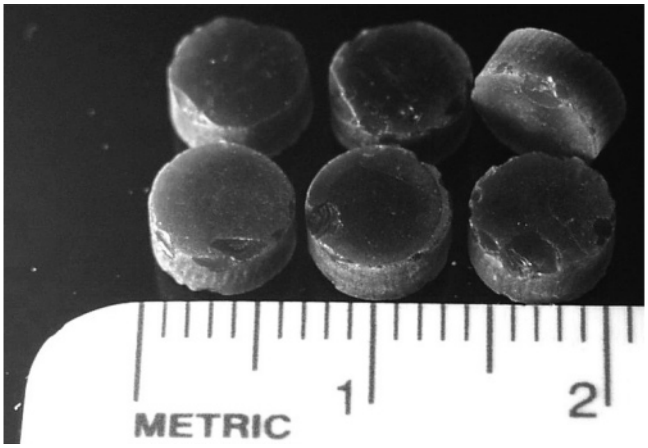


Figure 1. Dark green glass pellets of supported Ru catalyst. Though each supported Ru catalyst is recovered as dark green glass pellets, an individual piece can be readily identified by its characteristic number and pattern of surface markings.

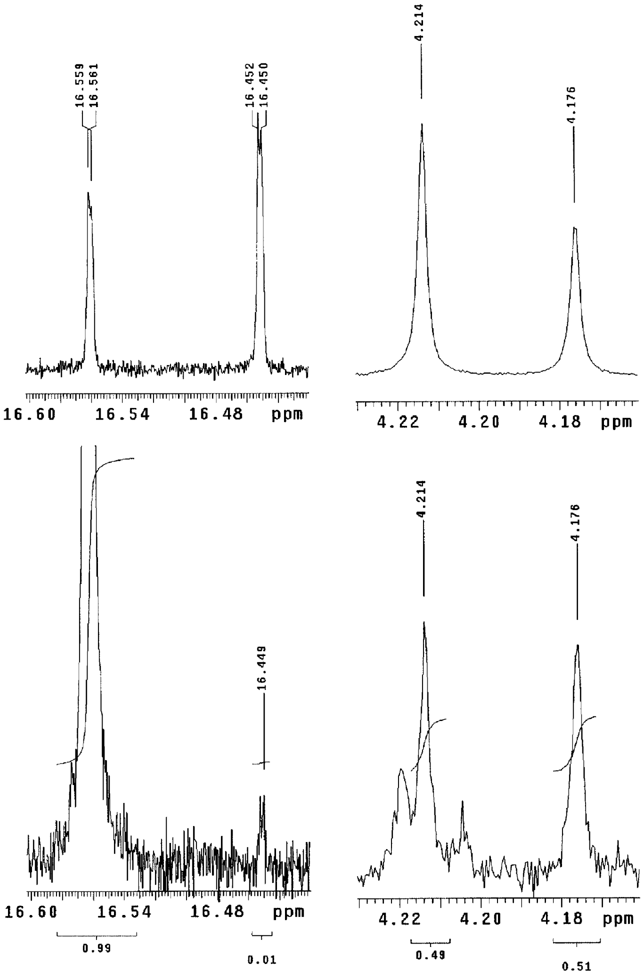


Figure 2. ^1H NMR (400 MHz) spectra for an authentic 2:3 mixture of **2** and **13** (top) and the monomeric Ru carbene recovered from complex **18-*d*$_n$** (bottom).

*(crossover from **6**) and **13** (crossover from **19**) could be cleanly detected as components of the mixture*. Also illustrated in Figure 2 (top) for comparison are the analogous regions taken from an authentic spectrum of a 2:3 mixture of **2** and **13**. The integral values provided in Figure 2 allow us to quantify the amount of Ru carbene that has been transferred from one pellet to another. Recovered Ru complex **13** thus represents 1% of the mixture, according to relative integration of the major carbene proton signal at 16.56 ppm (**2** and **2-*d*$_4$**) and the minor signal at 16.45 ppm (**13**). Moreover, an equal amount of **2** is present on the basis of the fact that the 4H singlets at 4.18 (**2**) and 4.21 ppm (**13**) are of equal intensity. *These data confirm that a measurable (2% total) amount of termination (return) occurs with glass-supported Ru catalysts.*

6. Control Experiments and Alternative Scenario. The appropriate control experiments have been carried out to validate further the conclusions mentioned above. Experiments outlined in Scheme 7 were repeated with fresh samples of catalyst *in the absence of the metathesis substrate*. The four glass samples were allowed to stir in CH_2Cl_2, and the solvent was routinely replenished in precisely the same manner as the iterative sequence of five metathesis reactions (above). The two labeled sol−gel pellets **18-*d*$_n$** were "stripped" of Ru through subjection with **9**, and the resulting monomer **2-*d*$_4$** was rigorously purified by column chromatography. Careful analysis of the resulting samples (400 MHz ^1H NMR) did not reveal any signs of pellet-to-pellet crossover. Thus, the results disclosed herein cannot be ascribed to any ill-defined effects such as insufficient rinsing of catalyst samples or the leaching of active carbenes from one gel to another; any observed crossover discussed above must therefore involve an olefin metathesis event.

Alternatively, it may be suggested that in pellets **6**, **18-*d*$_n$**, and **19** crossover may occur by dissociation of the NHC ligands instead of the styrene ether. This would be entirely inconsistent with what has been established regarding the mechanism of olefin metathesis catalyzed by Ru-based complexes that bear an NHC ligand.[7,19]

Conclusions

We have prepared two isotopically and structurally labeled Ru-based carbenes (**2-*d*$_4$** and **13**), which have been used to derivatize the surface of monolithic samples of sol−gel glass. Similar to previously reported **6**, the resulting glass-supported catalysts **18-*d*$_n$** and **19** exhibit significant catalytic activity in promoting olefin metathesis reactions and provide products of high purity without workup or purification. Analysis of glass pellets used in a sequence of RCM reactions mediated by the three supported Ru carbenes (effected in the same reaction vessel) has allowed us to establish that free Ru-carbene intermediates in solution *can* be scavenged by support-bound styrene ether ligands prior to the onset of competing Ru decomposition.

We must emphasize that the claim is not being made that the class of achiral Ru carbenes in Chart 1 operate exclusively by the release/return mechanism; we show here only that such a scenario is feasible. The observed crossover is small (2%); nonetheless, as suggested by previous observations,[20] it is possible that small amounts of released Ru carbene may be responsible for olefin metathesis activity. The above studies shed light on a critical aspect of the mechanism of achiral Ru-based complexes bearing a bidentate styrene ether ligand (e.g., **1** and **2** in Chart 1), a class of robust and air-stable carbenes that are becoming increasingly popular olefin metathesis catalysts.

The findings outlined herein imply a number of intriguing possibilities in designing catalytic olefin metathesis reactions on support.[21] One possibility would involve reaction of a polymer-bound substrate catalyzed by a glass-supported Ru carbene. In this scenario, a sterically unhindered (and preferably volatile) alkene could be used as "chaperone" to shuttle the active metal carbene through solution to the surface of the

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(19) (a) Dias, E. L.; Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1997**, *119*, 3887−3897. (b) Sanford, M. S.; Ulman, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 749−750. (c) Sanford, M. S.; Love, J. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 6543−6554. (d) Reference 8.

(20) Mechanistic studies involving chiral Ru complex **3** (Chart 1) and its deuterated derivatives indicate that catalyst recovered in high yield (90%) after olefin metathesis represents unreleased Ru carbene. Thus, even with the less active chiral complex, bearing a bidentate and sterically bulky ligand, high activity can be achieved with ≤10% released carbene. See ref 4b.

(21) For early examples of RCM with solid-supported substrates, see: (a) Miller, S. J.; Blackwell, H. E.; Grubbs, R. H. *J. Am. Chem. Soc.* **1996**, *118*, 9606−9614. (b) Schuster, M.; Pernerstorfer, J.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1979−1980. (c) van Maarsveen, J. H.; den Hartog, J. A. J.; Engelen, V.; Finner, E.; Visser, G.; Kruse, C. G. *Tetrahedron Lett.* **1996**, *37*, 8249−8252. (d) Peters, J.-U.; Blechert, S. *Synlett* **1997**, 348−350. (e) Nicolaou, K. C.; Winssinger, N.; Pastor, J.; Ninkovic, S.; Sarabia, F.; He, Y.; Vourlomis, D.; Yang, Z.; Li, T.; Giannakakou, P.; Hamel, E. *Nature* **1997**, *387*, 268−272.

polymer carrying the substrate. Such a process could be useful as a ring closure/cleavage strategy, allowing the recovery of a collection of small molecules from a solid support in parallel without purification.

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Supporting Information Available: Experimental procedures and spectral data for catalysts and products (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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