

Kinetics of an Air- and Water-Stable Ruthenium(IV) Catalyst for the Deprotection of Allyl Alcohol in Water

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Kynurenic allyl ester reacts readily with $[CpRu(NCCH_3)_3]PF_6$ in dry acetone to yield the Ru^{IV} allyl. The complex is an effective catalyst for the hydrolysis of methyl allyl carbonate in aqueous solution in air yet decomposes rapidly in aerobic solutions of methanol. Kinetic studies are consistent with rate-limiting attack of water (or methanol) on the Ru^{IV} allyl as a key step. A polystyrene-supported version of the catalyst was active for the catalytic hydrolysis of methylallyl carbonate, but kinetic studies indicate that the Ru leaches from polystyrene upon repeated catalytic cycles.

Introduction

The rich reaction chemistry of transition metal allyl complexes has spawned a diverse array of catalytic reactions for selective bond forming and cleaving reactions.¹⁻⁴ Catalytic nucleophilic allylic substitution is a powerful synthetic method for the selective formation of carbon–carbon and carbon–heteroatom bonds.^{1–3} Allylic ethers, esters, carbonates, and carbamates are also versatile protecting groups due to their high reactivity with many transition metals.^{1,5–10} Several metals are known to cleave allyl esters/ethers in protic^{10–12} or aprotic solvents,^{6,7,13} and Ru complexes, including commercially available [CpRu(CH₃CN)₃]PF₆,^{14,15} are particularly attractive due to their tolerance to many

- (1) Trost, B. M.; Van Vranken, D. L. Chem. Rev. 1996, 96, 395-422.
- (2) Trost, B. M.; Crawley, M. L. Chem. Rev. 2003, 103, 2921–2944.
- (3) Tietze, L. F.; Ila, H.; Bell, H. P. Chem. Rev. 2004, 104, 3453–3516.
- (4) Consiglio, G.; Waymouth, R. M. Chem. Rev. 1989, 89, 257–276.
 (5) Tanaka, S.; Saburi, H.; Ishibashi, Y.; Kitamura, M. Org. Lett.
- **2004**, 6, 1873–1875.
- (6) Greene, T. W.; Wuts, P. G. M., Eds. *Protective Groups in Organic Synthesis*, 3rd ed.; John Wiley & Sons: New York, 2000.
 - (7) Tsuji, J.; Mandai, T. Synthesis 1996, 1–24.
- (8) Trost, B. M.; Fullerton, T. J. J. Am. Chem. Soc. 1973, 95, 292–294.
 (9) Tsuji, J.; Takahashi, H.; Morikawa, M. Tetrahedron Lett. 1965, 6,
- 4387–4388.
 - (10) Guibe, F. Tetrahedron 1998, 54, 2967-3042.
- (11) Genet, J. P.; Savignac, M. J. Organomet. Chem. 1999, 576, 305-317.
- (12) Genet, J. P.; Blart, E.; Savignac, M.; Lemeune, S.; Lemaireaudoire, S.; Paris, J. M.; Bernard, J. M. *Tetrahedron* **1994**, *50*, 497–503.
- (13) Tanaka, S.; Hajime, S.; Murase, T.; Ishibashi, Y.; Kitamura, M. J. Organomet. Chem. 2007, 692, 295–298.
- (14) Trost, B. M.; Older, C. M. Organometallics 2002, 21, 2544–2546.
 (15) Trost, B. M.; Fraisse, P. L.; Ball, Z. T. Angew. Chem., Int. Ed. 2002, 41, 1059–1061.
- (16) Morisaki, Y.; Kondo, T.; Mitsudo, T.-a. Organometallics 1999, 18, 4742–4746.
- (17) Hermatschweiler, R.; Ferandez, I.; Breher, F.; Pregosin, P. S.; Veiros, L. F.; Calhorda, M. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 4397–4400.
- (18) Fernandez, I.; Hermatschweiler, R.; Breher, F.; Pregosin, P. S.; Veiros, L. F.; Calhorda, M. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 6386–6391.

Scheme 1. Synthesis of Kitamura's Catalyst, 1



functional groups.^{16–21} Kitamura reported Ru complexes derived from [CpRu(CH₃CN)₃]PF₆ and quinaldic acid that are particularly effective for deallylation reactions that operate in protic solvents and feature an internal base,^{5,13,22–24} which obviates the need for additives.^{10–12} Complex **1** exhibits a wide substrate tolerance in alcoholic solvents¹³ and has been shown to reversibly allylate a variety biological molecules, including peptides and nucleic acids.^{5,23,25} As part of a program on the synthesis of water-soluble bioactive polymers,²⁶ we sought a facile method for the deprotection of allylic carbonates or carbamates in aqueous solution. Herein, we report our investigations on the kinetics and mechanism of the hydrolysis of allyl carbonates in water in the presence of both homogeneous and supported analogues of complex **1**. We also compare the rates of hydrolysis and methanolysis of allyl methyl carbonate in both aqueous and methanol solutions.

- (19) Achard, M.; Derrien, N.; Zhang, H.-J.; Demerseman, B.; Bruneau, C. Org. Lett. **2008**, *11*, 185–188.
- (20) Gruber, S.; Zaitsev, A. B.; Woirile, M.; Pregosin, P. S.; Veiros,
 L. F. Organometallics 2008, 27, 3796–3805.
 (21) Bruneau, C.; Renaud, J.-L.; Demerseman, B. Chem.—Eur. J.
- (21) Brundau, C., Kenaudi, J.-L., Demerschan, B. Chem.—Lat. J. 2006, 12, 5178–5187.
- (22) Saburi, H.; Tanaka, S.; Kitamura, M. Angew. Chem., Int. Ed. **2005**, 44, 1730–1732.
- (23) Tanaka, S.; Saburi, H.; Murase, T.; Yoshimura, M.; Kitamura, M. J. Org. Chem. **2006**, *71*, 4682–4684.
- (24) Tanake, S.; Saburi, H.; Kitamura, M. Adv. Synth. Catal. 2006, 348, 375–378.
- (25) Tanaka, S.; Hirakawa, T.; Oishi, K.; Hayakawa, Y.; Kitamura, M. *Tetrahedron Lett.* **2007**, *48*, 7320–7322.
- (26) Cooley, C. B.; Trantow, B. M.; Nederberg, F.; Kiesewetter, M. K.; Hedrick, J. L.; Waymouth, R. M.; Wender, P. A. J. Am. Chem. Soc. 2009, 131, 16401–16403.

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Scheme 2. Synthesis of the Ru Complex 4



Results and Discussion

Quinaldic acid and pyridine carboxylic acids have proven to be effective ligands for Ru-catalyzed allylation reactions and allyl alcohol/carbonate deprotection.^{5,13,22–24} We sought a readily functionalized derivative of quinaldic acid that might enable facile anchoring of Ru complexes to inorganic²⁷ or organic supports. Kynurenic acid (4-hydroxyquinoline-2-carboxylic acid), a metabolite of tryptophan,^{28,29} provided an attractive and readily available synthon. The kynurenic acid allyl ester can be readily alkylated with a variety of functional groups to generate a series of substituted kynurenic acid derivatives. The kynurenic allyl ester **2** reacts with [CPRu(NCCH₃)₃]PF₆ in dry acetone to yield the orange-yellow Ru^{IV} allyl **4**, which precipitates from concentrated solution (Scheme 2).^{22,24,30}

The Ru allyl complex **1**, derived from quinaldic acid, has been shown to be an active catalyst for the deallylation of allyl carbonates¹³ and carbamates²³ in methanolic solutions under argon (eq 1). For these reactions, it was proposed that the Ru^{IV} allyl species is the resting state and that attack of methanol on the Ru allyl is rate-limiting.^{5,13,22}

To assess the activity of the analogous Ru allyl complex **4** in aqueous solution, we investigated the kinetics of deallylation of allyl methyl carbonate in D_2O , eq 1.

$$\begin{array}{c} & \mathbf{4} \\ (0.5 \text{ mol}\%) \\ \hline \mathbf{D}_2 \mathbf{0} \end{array} \begin{array}{c} \mathsf{OH} + \mathsf{CH}_3 \mathsf{OH} + \mathsf{CO}_2 \end{array} (1)$$

In the absence of Ru, allyl methyl carbonate is stable in water for more than a week at room temperature. In the presence of the Ru complex 4 (0.6-10 mol %), allyl methyl carbonate hydrolyzes to allyl alcohol, methanol, and carbon dioxide. In the solid state, complex 4 is stable in air for months without the loss of activity. Kinetic studies carried out in air at room temperature revealed that the hydrolysis of allyl methyl carbonate was zero order in carbonate, Figure 1, and first order in Ru to give a rate law:

$$-d[\text{carbonate}]/dt = R = k_{\text{obs}}$$
 (2)

where $k_{obs} = k'[4] = (1.25 \pm 0.05) \times 10^{-3} \text{ M h}^{-1}$ (20 °C), Figure 2.

The mechanism proposed for the deprotection of allyl carbonates in alcohol solvents was proposed to involve the nucleophilic attack of the alcohol on the Ru^{IV} allyl species as a key step.^{5,13,23} An analogous mechanism for the aqueous hydrolysis of allyl methyl carbonate is shown in Scheme 3. This mechanism assumes that attack of water on the Ru^{IV} allyl generates allyl alcohol and a solvated Ru^{II} species, which subsequently reacts with allyl methyl carbonate to regenerate the Ru^{IV} allyl species **4**.

A rate law for the mechanism in Scheme 3 can be derived if a low, steady-state concentration of the Ru^{II} intermediate and the reversible formation of **4** from allyl alcohol is assumed (eqs 3 and 4).^{22,30}



With these assumptions, the rate of disappearance of allyl methyl carbonate can be derived (eq 5):

$$R = -\frac{d[C]}{dt} = \frac{k_1 k_2 [4] [H_2 O] [C]}{k_{-1} [A] + k_2 [C]}$$
(5)

where [C] = concentration of allyl methyl carbonate, [A] = concentration of allyl alcohol, and [4] = concentration of complex **4**. This rate equation would be consistent with the experimental rate law under conditions where the rate of formation of **4** from the reaction of allyl methyl carbonate with Ru^{II} is faster than the formation of **4** from the reaction of **4** from the reactin **4** from the reaction **4** from the reaction **4** from

Rate =
$$k_1[H_2O][4]$$
, where $k' = k_1[H_2O]$ (6)

These results imply that the attack of water on the Ru^{IV} allyl complex **4** is rate limiting, even in aqueous solution $([H_2O] \approx 55.5 \text{ M}; [D_2O] \approx 55.5 \text{ M}, 20 \text{ °C})$, and that the Ru^{IV} allyl complex **4** is the resting state during the catalytic

⁽²⁷⁾ Hirakawa, T.; Tanaka, S.; Usuki, N.; Kanzaki, H.; Kishimoto, M.; Kitamura, M. Eur. J. Org. Chem. 2009, 789–792.

⁽²⁸⁾ Erhardt, S.; Schwieler, L.; Nilsson, L.; Linderholm, K.; Engberg, G. *Physiol. Behav.* **2007**, *92*, 203–209.

⁽²⁹⁾ Barth, M. C.; Ahluwalia, N.; Anderson, T. J. T.; Hardy, G. J.; Sinha, S.; Alvarez-Cardona, J. A.; Pruitt, I. E.; Rhee, E. P.; Colvin,

<sup>R. A.; Gerszten, R. E. J. Biol. Chem. 2009, 284, 19189–19195.
(30) Tanaka, S. J.; Saburi, H.; Hirakawa, T.; Seki, T.; Kitamura, M.</sup>

Chem. Lett. **2009**, *38*, 188–189.



Figure 1. Plot of allyl methyl carbonate [C] vs time. Conditions: $[4]_0 = 0.0005 \text{ M in } D_2\text{O} \text{ with (a) } [C] = 0.105 \text{ M (triangles); (b) } [C] = 0.054 \text{ M (squares); (c) } [C] = 0.025 \text{ M (diamonds); (d) } [C] = 0.013 \text{ M (circles).}$



Figure 2. Plot of k_{obs} ($\mathbf{M} \cdot \mathbf{h}^{-1}$) vs Ru concentration [**4**]₀. Conditions: [allyl methyl carbonate]₀ = 0.10 M in D₂O.

reaction (i.e., $[Ru]_T \approx [\mathbf{4}]_0$) under these conditions. Analysis of the kinetics of the catalytic hydrolysis of allyl methyl carbonate reaction in a 1:1 mixture of H₂O/D₂O solvent revealed a kinetic isotope effect of $k_H/k_D = 2.5$, which is consistent with proposals by Kitamura^{5,22,30} that nucleophilic attack on the Ru^{IV} allyl is coupled to deprotonation of the nucleophile (H₂O in the present case, ROH in previous examples), presumably by the Ru carboxylate (Scheme 3).

The rate law derived in eq 5 assumes the reversible formation of 4 from allyl alcohol and the Ru^{II}, but an equally valid rate law could be derived without this assumption (i.e., $k_{-1}[A] = 0$). As CpRu complexes ligated by pyridine carboxylic acids or quinaldic acids have been shown to catalyze allylic substitutions of allyl alcohols,^{22,30-34} we sought independent kinetic evidence for the equilibrium represented in eq 3. To this end, we treated the Ru complex 4 with D₂O in acetone- d_6 and measured both the equilibrium constant and the rate of approach to equilibrium at 20 °C (see Experimental Section).³⁵ Under these conditions, the equilibrium constant (eq 3) was determined to be $K_{eq} = [Ru^{II}][A]/[4][D_2O] = 0.0075 \pm 0.0008$ with $k_1 = 0.036 \pm 0.011$ M⁻¹ h⁻¹ and $k_{-1} = 4.80 \pm 1.53$ M⁻¹ h⁻¹.

For comparison, the kinetics of the catalytic *methanolysis* of allyl methyl carbonate with **4** were examined in CD₃OD. When carried out in air at room temperature, the methanolysis of allyl methyl carbonate with **4** proceeds only to 40% conversion under these conditions. Kinetic studies revealed that the evolution of [allyl methyl carbonate] with time is linear to approximately 25% conversion; at longer times, the rate decays rapidly. Similar rates and conversions are observed in the presence and absence of 5 equiv of allyl methyl ether, suggesting that product inhibition by allyl methyl ether is not the cause of decaying rate. However, if the methanolysis of allyl methyl carbonate with **4** is carried out under argon, the reaction proceeds to full conversion in less than 90 min with a rate that is zero order in allyl carbonate, k_{obs} (methanol) = $(6.6 \pm 0.2) \times 10^{-2}$ M h⁻¹.

While we have not unambiguously determined the cause of the low conversions observed for the methanolysis in air, we propose that oxidative decomposition of the catalyst is a likely cause, due to the higher conversions observed under argon. We propose that different behaviors observed in water and methanol are due to the higher solubility of oxygen in methanol relative to water: χO_2 /water (298 K, 1 atm) = 2.3×10^{-5} ; χO_2 /CH₃OH (298 K, 1 atm) = 4.2×10^{-4} .^{36–38} As the Ru^{IV} compounds **4** and **1** are shelf stable for months in air, it is likely that oxidation of the Ru^{II} species is competitive with catalysis in methanol, whereas in water the lower solubility of O₂ leads to longer catalysts lifetimes. If borne out in further studies, this hypothesis highlights another potential advantage of water as reaction solvent.

A comparison of the rates of hydrolysis of allyl methyl carbonate in water (under air) versus the methanolysis (under argon) reveals that the deallylation of allyl methyl carbonate is considerably faster in methanol. If we assume that $k' = k_1[\text{ROH}]$ (for R = H or CH_3) and that the concentration of $[\text{D}_2\text{O}] = 55.5$ M and $[\text{CD}_3\text{OH}] = 24.6$ M, then estimates for k_1 reveal that the rate constant for nucleophilic attack by methanol is approximately 60 times that of water $(k_1(\text{methanol}) = 2.68 \pm 0.10 \text{ M}^{-1} \text{ h}^{-1}, ^{39} k_1(\text{water}) = 0.045 \pm 0.002 \text{ M}^{-1} \text{ h}^{-1})$. These estimates imply that methanol is considerably more reactive than water toward the Ru^{IV} allyl.

Further insights were obtained from measurements of the equilibration of the Ru^{IV} allyl **4** and methanol in acetone. The slow approach to equilibrium of the Ru complex **4** treated with methanol in acetone- d_6 , eq 7, was examined at 20 °C.³⁵ Under these conditions, the equilibrium constant (eq 7) was determined to be K_{eq} (methanol) = [Ru^{II}]-[AE]/[**4**][CH₃OH] = 0.0828 \pm 0.0083 with $k_1' = 0.86 \pm 0.26$ M⁻¹ h⁻¹ and $k_{-1}' = 10.4 \pm 3.3$ M⁻¹ h⁻¹ (where [AE] = concentration of allyl methyl ether). These results confirm the higher rate of attack of methanol on the Ru^{IV} allyl **4**. In either methanol or water, **4** is the predominant species at

⁽³¹⁾ Tanaka, S.; Seki, T.; Kitamura, M. Angew. Chem., Int. Ed. 2009, 48, 8948–8951.

⁽³²⁾ Sundararaju, B.; Achard, M.; Demerseman, B.; Toupet, L.; Sharma, G. V. M.; Bruneau, C. *Angew. Chem., Int. Ed.* **2010**, *49*, 2782–2785.

⁽³³⁾ Gruber, S.; Pregosin, P. S. Adv. Synth. Catal. 2009, 351, 3235-3242.

⁽³⁴⁾ Zaitsev, A. B.; Caldwell, H. F.; Pregosin, P. S.; Veiros, L. F. Chem.-Eur. J. 2009, 15, 6468-6477.

⁽³⁵⁾ Espenson, J. H. *Chemical Kinetics and Reaction Mechanisms*, 2nd ed.; McGraw-Hill: New York, 2002.

⁽³⁶⁾ Fischer, K.; Wilken, M. J. Chem. Thermodyn. 2001, 33, 1285–1308.

⁽³⁷⁾ Battino, R.; Rettich, T. R.; Tominaga, T. J. Phys. Chem. Ref. Data 1983, 12, 163–178.

⁽³⁸⁾ Steinhoff, B. A.; Stahl, S. S. J. Am. Chem. Soc. 2006, 128, 4348-4355.

⁽³⁹⁾ This corresponds to a turnover frequency of approximately 1 min^{-1} ; for comparison, water-soluble Pd catalysts catalyze the deprotection of allyl alkyl carbonates with Et₂NH with turnover frequencies of approximately 2- 10 min⁻¹ (ref 12).

Scheme 3. Proposed Mechanism for Catalytic Hydrolysis of Allyl Methyl Carbonate in Water by Ru^{IV}-Allyl Complex 4^a



^a PF₆ anion omitted for clarity.

Scheme 4. Synthesis of the Polystyrene-Supported Ru Complex 5



equilibrium, but the equilibrium constant is higher in the case of methanol than for water in acetone solution.



Studies of the catalytic hydrolysis of allyl methyl carbonate suggest **4** is air/water compatible. To facilitate removal of the catalyst from the products, we generated a solid-supported version²⁷ of the Ru catalyst. Solid-supported catalysts facilitate the removal and recycling of metal residues,⁴⁰ and several heterogeneous catalysts for (de)allylation have been reported.^{41–44} Indeed, among other solid-supported allylation catalysts,^{44–46} a heterogeneous version of **1** supported on silica was developed by Kitamura and co-workers.²⁷ The supported catalyst provided comparable yields and rates to the homogeneous analogues²⁷ and exhibited no leaching from the solid support after nine reaction cycles in methanol solvent under argon, but only one instance of water being used as a cosolvent was reported.²⁷ The amino-functionalized ligand **3** was coupled to a chloromethyl polystyrene resin (1% cross-linked, 200–400 mesh, $3.5-4.5 \text{ mmol Cl}^{-}/\text{g}$) to generate the polystyrene-supported ligand **PS-3**. Microanalysis of **PS-3** provided an estimate of 1.164 mmol/g for the amount of ligand loaded onto the polystyrene. Treatment of **PS-3** with excess [CpRu(CH₃CN)₃]-PF₆ for 1.5 h in acetone generated the polystyrene-supported complex **5**, Scheme 4.

The supported catalyst **5** is competent for the hydrolysis of allyl methyl carbonate in aqueous solution. Conducting the hydrolysis of allyl methyl carbonate under identical conditions with the supported Ru complex **5** and homogeneous analogue **4** allowed for the direct comparison of the rates, enabling an estimate of the Ru loading on the PS bead.^{47,48} When 0.9 mg of **5** was used for the hydrolysis of allyl methyl carbonate in 0.32 mL of D₂O, the rate constant, k_{obs} , from the zero-order plot of [allyl methyl carbonate] versus time of this reaction was compared to the k_{obs} versus **[4]** plot (Figure 2) to determine an effective concentration of ruthenium, [Ru]_{eff} = 1.847 ± 0.047 mM, and a catalyst loading of 0.66 ± 0.15 mmol/g of active Ru^{IV} on the **5** bead. Combustion analysis of **5** provided an independent estimate of the Ru content in **5**, [Ru] = 0.48 ± 0.04 mmol/g, which is within error of the loading determined by kinetic analysis.

After 4 h of reaction time, the supported catalyst was isolated from the reaction solution by filtering, washed with allyl alcohol and acetone, removed of volatiles under high vacuum, and subjected to identical catalytic conditions. For the second run, the rate was lower and the calculated catalyst loading on 5 was 0.53 ± 0.06 mmol/g. This process was

⁽⁴⁰⁾ Bergbreiter, D. E.; Tian, J. H.; Hongfa, C. Chem. Rev. 2009, 109, 530–582.

⁽⁴¹⁾ Miura, H.; Wada, K.; Hosokawa, S.; Sai, M.; Kondo, T.; Inoue, M. *Chem. Commun.* **2009**, 4112–4114.

⁽⁴²⁾ Li, G.; Zhao, G. Org. Lett. 2006, 8, 633-636.

⁽⁴³⁾ McNamara, C. A.; Dixon, M. J.; Bradley, M. Chem. Rev. 2002, 102, 3275–3300.

⁽⁴⁴⁾ Uozumi, Y.; Shibatomi, K. J. Am. Chem. Soc. **2001**, *123*, 2919–2920.

⁽⁴⁵⁾ Uozumi, Y.; Danjo, H.; Hayashi, T. J. Org. Chem. **1999**, 64, 3384–3388.

⁽⁴⁶⁾ Akiyama, R.; Kobayashi, S. Angew. Chem., Int. Ed. 2001, 40, 34693471.

⁽⁴⁷⁾ Demerseman, B.; Renaud, J. L.; Toupet, L.; Hubert, C.; Bruneau, C. *Eur. J. Inorg. Chem.* **2006**, 1371–1380.

⁽⁴⁸⁾ Phan, T. S.; Sluys, M. V. D.; Jones, C. M. Adv. Synth. Catal. **2006**, *348*, 609–679.





Figure 3. Plots of [allyl methyl carbonate] vs hours for the deallylation of allyl methyl carbonate in D_2O catalyzed by 5, recycled over successive runs.

repeated, and on the third run the rate was even lower, yielding an estimate of $0.31 \pm 0.03 \text{ mmol/g}$, Figure 3.

The lower rates observed on subsequent runs imply that Ru is leaching from the polystyrene support.⁴⁹ As a test for leaching, the supernatant from the washings was assessed for catalytic activity;⁴⁸ these experiments revealed that the supernatant was catalytically active albeit at a much slower rate than 5 (approximately 20 times slower). We could not detect any free kynurenic acid ligand in the supernatant by ¹H NMR or ESI-MS, implying that, in water, Ru is extracted off of the bead, presumably by solvolysis of the kynurenic ligand, leaving PS-3 intact. While similar leaching phenomena have been observed with other PS-supported Ru catalysts,^{50,51} this behavior is in contrast to that reported by Kitamura for a silica-supported version of 1, which did not exhibit loss of catalytic activity over nine recycling cycles under an argon atmosphere.²⁷ To test whether the presence of air might contribute to the higher leaching, we repeated the catalyst recycling experiments with 5 in water under argon. For these experiments, leaching was attenuated but still evident with each catalyst cycle, giving catalyst loadings of 0.84 ± 0.08 , ⁵² 0.66 ± 0.15 , and $0.31 \pm$ 0.03 mmol/g over three successive runs.

The higher degree of leaching observed for the polystyrene catalyst **5** in water, relative to the silica-supported analogue,²⁷ could be due to the nature of the solvent (water versus methanol), the nature of the modified ligands (kynurenic acid versus amide-substituted pyridine carboxylic acid), or the support itself. Arenes are known to displace coordinated ligands on Ru^{II} species.⁵³ The phenyl-rich environment of the PS bead could labilize the Ru complexes; further studies are ongoing to test these hypotheses.

Conclusions

Cyclopentadienyl ruthenium complexes of a modified natural product, kynurenic acid, were found to be an effective catalyst for the deallylation of carbonates in water. A variety of substituted kynurenic acid ligands are available using simple procedures and commercially available materials. In the presence of air, catalyst **4** exhibits increased stability in water versus methanol, although methanol is a better nucleophile toward **4**. A kynurenic acid ligand bearing a pendant amine allows for the attachment of the catalyst to a solid PS support. However, catalyst **5**, a heterogeneous version of **4**, was observed to leach from the polystyrene support upon several catalyst recycling experiments, suggesting that the stability of supported versions of these homogeneous catalysts depends sensitively on the nature of the support and reaction conditions.

Experimental Section

General Considerations. All materials were purchased from Aldrich and used as received unless stated otherwise. Tris-(acetonitrile)cyclopentadienylruthenium(II) hexafluorophosphate was purchased from Strem and used as received. All preparations of ruthenium(IV) compounds were carried out in an inert atmosphere using standard glovebox or Schlenk techniques but stored in atmosphere in closed vials. Combustion analyses were conducted on a Perkin-Elmer TGA 7 thermogravimetric analyzer.

Synthesis of Kynurenic Acid Allyl Ester. Allyl bromide (1.4 mL, 16.6 mmol) was added in a single aliquot to a vigorously stirred mixture of kynurenic acid (2.0 g, 10.6 mmol) and KHCO₃ (1.7 g, 17.4 mmol) in 60 mL of DMF. The single-neck, round-bottom flask was equipped with reflux condenser and heated to 40 °C for 15 h. The reaction was quenched with water (~60 mL) and extracted three times with ethyl acetate. Combined organics were washed with 5% aqueous NaCl, dried with MgSO₄, filtered, and removed of volatiles. Material was taken on without further purification. Yield: 1.575 g (65%). ¹H NMR (300 MHz, CDCl₃): δ 8.38 (1H, d, 8.37 Hz); 8.05 (1H, bs); 7.70 (1H, t, 7.75); 7.49 (1H, d, 8.40); 7.41 (1H, t, 7.75); 7.05 (1H, s); 6.4 (1H, m); 5.44 (2H, m); 4.93 (2H, d, 4.93). ¹³C NMR (125 MHz, CDCl₃): δ 162.9; 136.6; 130.6; 133.4; 103.8; 126.7; 126.5; 126.4; 124.8; 120.2; 118.4; 112.0; 67.8.

Synthesis of 2 (R=CH₃). Methyl iodide (0.155 mL, 2.5 mmol) was added in a single aliquot to a vigorously stirred mixture of kynurenic acid allyl ester (0.505 g, 2.2 mmol) and Cs₂CO₃ (0.803 g, 2.5 mmol) in 130 mL of acetone. The single-neck, round-bottom flask was fitted with a reflux condenser and heated to reflux for 15 h. The reaction was quenched with brine (~70 mL) and extracted three times with ethyl acetate. The combined organics were dried with MgSO₄, filtered, and removed of volatiles. Material was taken on without further purification. Yield: 0.301 g (56%). ¹H NMR (300 MHz, acetone-*d*₆): δ 8.22 (1H, d, 8.27 Hz); 8.12 (1H, d, 8.56 Hz); 7.84 (1H, t, 7.66 Hz); 7.68 (1H, t, 7.66 Hz); 7.59 (1H, s); 6.17 (1H, m); 5.44 (2H, m); 4.95 (2H, d, 5.83 Hz); 4.20 (3H, s). ¹³C NMR (125 MHz, acetone-*d*₆): δ 163.4; 149.9; 148.7; 132.9; 130.7; 130.2; 127.8; 122.2; 121.9; 118.2; 118.0; 100.3; 66.1; 56.1.

Synthesis of 4. 2 (0.21 g, 0.86 mmol) and [CpRu(NCCH₃)₃]PF₆ (0.316 g, 0.73 mmol) were added to a flame-dried Schlenk flask with a stir bar and removed from the glovebox to a Schlenk line. Under N₂, 10 mL of extra-dry acetone (Aldrich) was added via syringe. The red solution produced a yellow precipitate over 25 min. The stirring was stopped and, under N₂ flow, the supernatant was removed from the precipitate with a pipet and discarded. The precipitate was washed with approximately 1 mL of extra-dry acetone, and the precipitate was removed of volatiles under high vacuum, yielding pure 4: 0.218 g (54%). ¹H NMR (300 MHz, acetone-*d*₆): δ 8.43 (1H, d, 8.74 Hz); 8.10 (2H, m); 7.91 (1H, t, 7.12); 7.59 (1H, s); 4.87 (2H, m); 4.70 (1H, d, 10.46 Hz); 4.45 (1H, m); 4.40 (1H, m); 4.35 (1H, s). Anal. Calcd for C₁₉H₁₈F₆NO₃PRu: 41.16 C, 3.27 H, 2.53 N. Found: 41.26 C, 3.08 H, 2.53 N.

Synthesis of 3. 2-Bromoethylamine \cdot HBr (0.21 g, 1.02 mmol) was added in a single aliquot to a vigorously stirred mixture of kynurenic acid allyl ester (0.22 g, 0.87 mmol) and Cs₂CO₃ (0.8 g,

⁽⁴⁹⁾ Catalyst decomposition could also contribute to the lower rates upon recycling, but the activity of the supernatant implies that leaching of Ru occurs.

⁽⁵⁰⁾ Nguyen, S. T.; Grubbs, R. H. J. Organomet. Chem. 1995, 497, 195–200.

⁽⁵¹⁾ Nieczypor, P.; Buchowicz, W.; Meester, W. J. N.; Rutjes, F. P. J. T.; Mol, J. C. *Tetrahedron Lett.* **2001**, *42*, 7103.

⁽⁵²⁾ The initial Ru loading estimated from the rates is higher under argon atmosphere than under air.

⁽⁵³⁾ Fairchild, R. M.; Holman, K. T. Organometallics 2008, 27, 1823– 1833.

2.5 mmol) in 65 mL of acetone. The single-neck, round-bottom flask was fitted with a reflux condenser and heated to reflux for 15 h. The reaction was quenched with brine (\sim 70 mL) and extracted three times with ethyl acetate. The combined organics were dried with MgSO₄, filtered, removed of volatiles, and taken into acetone (material is self-labile when neat). Material was taken on without further purification. Yield: 0.120 g (46%). ¹H NMR (300 MHz, acetone-*d*₆): δ 8.30 (1H, d, 8.4 Hz); 7.86 (1H, d, 8.4 Hz); 7.53 (1H, t, 7.8 Hz); 7.27 (1H, t, 7.8 Hz); 7.06 (1H, s); 6.04 (1H, m); 5.41 (1H, d, 17.4 Hz); 5.22 (1H, d, 10.7); 4.79 (2H, d, 5.6); 4.36 (2H, t, 7.8); 3.59 (2H, t, 7.8 Hz); 3.48 (2H, bs). ¹³C NMR (125 MHz, acetone-*d*₆): δ 163.0; 132.3; 132.1; 126.8; 125.3; 124.2; 120.9; 118.5; 110.3; 66.8; 64.6; 54.9; 53.0; 40.6. IR (diamond anvil cell) cm⁻¹: 1708 (s, C=O); 1607 (m, 1°NH); 1564 (m, C–C aromatic); 1095 (s, C–O ester); 760 (s, 1°NH).

Synthesis of PS-3. 3 (1.23 g, 4.5 mmol) and Merrifield's peptide resin (1% cross-linked, 200–400 mesh, 0.132 g, 0.49 mmol) were added to a round-bottom flask with a stir bar. Acetone (100 mL) and Cs₂CO₃ (0.169 g, 0.52 mmol) were added, and the reaction mixture was stirred for 19 h. The crude reaction mixture was filtered, and the filtrate was washed with copious quantities of acetone. IR (diamond anvil cell) cm⁻¹: 1708 (s, C=O); 1564 (m, C-C aromatic); 1095 (s, C-O ester); 760 (s, 2°NH) (see Supporting Information).

Synthesis of 5. PS-3 (0.141 g, 0.52 mmol) and [CpRu-(NCCH₃)₃]PF₆ (0.5363 g, 1.24 mmol) were added to a flamedried Schlenk flask with a stir bar and removed from the glovebox to a Schlenk line. Under N₂, 15 mL of extra-dry acetone (Aldrich) was added via syringe, and the reaction mixture was stirred for 1.5 h. The stirring was stopped and, under N₂ flow, the supernatant was removed from the precipitate with a pipet and discarded. The precipitate was washed with copious extra-dry acetone and removed of volatiles under high vacuum. IR (diamond anvil cell) cm⁻¹: 1587 (m); 1334 (m); 833 (s) (see Supporting Information). Combustion analysis of 5: Samples were loaded onto the analytical balance of the TGA under air flow and subjected to an annealing program: 1 min hold at 50 °C, temperature ramp to 100 °C, 2 min hold at 100 °C, temperature ramp to 900 °C, 1 min hold at 900 °C, temperature ramp to 50 °C; all temperature ramps were 50 °C/min. Initial sample masses were taken after the 100 °C temperature hold and final masses at the end of the program. A sample of Merrifield's peptide resin subjected to the annealing program resulted in complete loss of mass. After subjecting 4 (1.2567 mg, 0.00227 mmol) to the annealing program, a black residue remained (0.3341 mg) that provided a molecular weight of the fully oxidized material (0.3341 $mg/0.00227 \text{ mmol} = 147.2 \text{ g/mol}; \text{RuO}_2 \text{ is } 133 \text{ g/mol}).$ In a representative annealing, 5 (1.7490 mg) was reduced to a black residue (0.1202 mg), which was taken to be 147.3 g/mol in molecular weight, yielding a Ru loading on 5 of 0.467 mmol/g. Triplicate measurements yield: 0.478 ± 0.034 mmol/g.

Kinetic Analysis to Give the Ru Loading on 5. In a typical experiment, 5 (0.9 mg) was loaded directly into an NMR tube along with D_2O (0.32 mL) and allyl methyl carbonate (3.6 μ L, 0.032 mmol), the tube was shaken to mix, and reaction progress was monitored by ¹H NMR against an internal standard (acetone). From a (zero-order) plot of [allyl methyl carbonate] versus hours (Figures 1), the slope was taken to be k_{obs} , and this value was divided by k' (the slope of the k_{obs} versus [Ru] plot generated from the solution catalysis, Figure 2) to determine a [Ru] in solution, 1.847 mM. Accounting for the solution volume and mass of 5 in the given experiment gives the loading of 5, 0.657 mmol/g of active Ru^{IV} on 5. The error of Ru loading was propagated from the rate constant errors.

Equilibration of 4 and D₂O in Acetone. Into an NMR tube under argon was added 4 (2.6 mg, 0.0047 mmol), 1.0 mL of acetone- d_6 , and D₂O (8.6 μ L, 0.4773 mmol), in order. (For methanol the amounts were 4 (2.7 mg, 0.0049 mmol), 0.5 mL of acetone- d_6 , and CD₃OD (2.0 μ L, 0.049 mmol) added in the given order.) The tube was shaken to mix, and reaction progress was monitored by ¹H NMR (see Supporting Information). Concentrations of allyl alcohol and 4 were determined by integration against an internal standard. The concentration of Ru^{II} was determined from mass balance: [Ru^{II}] = [4]_O – [4]. The reported rate and equilibrium constant errors were propagated from the error of the NMR integrations, which were taken to be ±10%.

Typical Kinetic Experiment. 4 (1.8 mg, 0.0032 mmol) was stirred with 1.1 mL of D_2O (or other solvent) to yield a 2.95 mM stock solution. In an NMR tube, 0.22 mL of stock solution was diluted with 0.43 mL of D_2O to give a final concentration of **4** (0.65 μ mol, 0.001 M), to which was added allyl methyl carbonate (7.35 μ L, 0.065 mmol, 0.100 M) via syringe. The tube was capped and shaken to mix. The reaction was monitored by ¹H NMR (see Supporting Information), and concentrations were determined versus an internal standard (acetone). The reported rate constant errors were propagated from the error of the NMR integrations, which were taken to be ±10%. When reactions were conducted under argon, the solvent was sparged with a submerged jet of gas for 2 min, and the reaction vessel was purged out before and after reagent addition.

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Supporting Information Available: ¹H NMR and IR spectra and relevant thermodynamic and kinetic data. This material is available free of charge via the Internet at http://pubs.acs.org.