

Catalytic Intermolecular Pauson–Khand-Type Reaction: Strong Directing Effect of Pyridylsilyl and Pyrimidylsilyl Groups and Isolation of Ru Complexes Relevant to Catalytic Reaction

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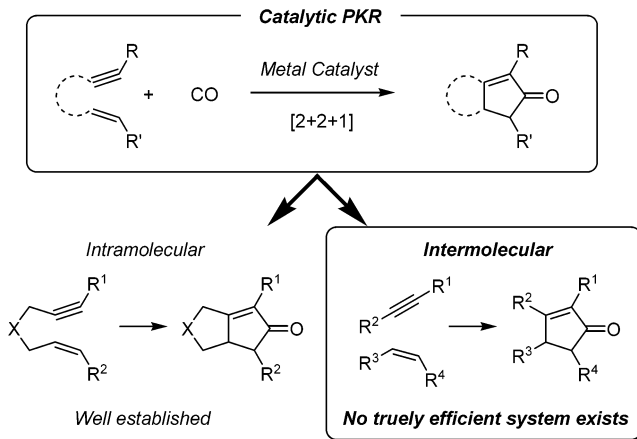
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Abstract: Some circumstantial evidence for the directing effect of the 2-pyridylsilyl group in the Ru-catalyzed intermolecular Pauson–Khand-type reaction (PKR) of alkenyl(2-pyridyl)silane, alkyne, and carbon monoxide has been provided. Most importantly, we have succeeded in isolating several monometallic Ru complexes relevant to the catalytic reaction: Ru(vinylsilane)(CO)₃ complexes and ruthenacyclopentene. While the stoichiometric reaction of the Ru(vinylsilane)(CO)₃ complex with an alkyne led to the formation of the corresponding cyclopentenone (PKR product) at 100 °C, the ruthenacyclopentene intermediate was quantitatively produced at 50 °C. This complex was also converted to a cyclopentenone upon heating at 100 °C. Moreover, it was also found that the Ru(vinylsilane)(CO)₃ complex and ruthenacyclopentene serve as catalysts in intermolecular PKR.

Introduction

The Pauson–Khand-type reaction (PKR), the metal-mediated [2 + 2 + 1] cycloaddition of alkyne, alkene, and carbon monoxide to generate 2-cyclopentenones,^{1,2} has received increasing attention in the synthetic community because it allows the construction of synthetically useful and biologically interesting five-membered carbocycles in a convergent and atom-economical manner.³ Therefore, PKR has been used as the key step in a number of natural product syntheses.⁴ Conventionally, PKR requires the stoichiometric use of Co₂(CO)₈ (heating a Co₂(CO)₆(alkyne) complex with an alkene). However, the arena of catalytic PKR (the use of a catalytic amount of metal complex

Scheme 1



to achieve this transformation) has prospered recently because of the apparent advantages (Scheme 1).⁵

Catalytic Pauson–Khand-Type Reaction. The first example of Co-catalyzed PKR was reported in 1973 by Pauson and Khand, which utilized strained (reactive) alkenes with a continuous supply of ethyne.⁶ Several other groups also attempted to render this fascinating catalytic reaction in 1980s.⁷ In 1994,

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- (2) Although the term “Pauson–Khand reaction” applies only to Co-mediated process, we refer to any closely related metal-mediated or -catalyzed [2 + 2 + 1] cycloannulation process of alkyne, alkene, and carbon monoxide (or its equivalent such as isocyanide) as “Pauson–Khand-type reaction” (PKR) in this paper.
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Jeong reported a catalytic intramolecular PKR of enynes using $P(\text{O}^i\text{Pr})_3$ as a supporting ligand for $\text{Co}_2(\text{CO})_8$.⁸ This probably is the first example of practical catalytic PKR.

Since then, extensive efforts have been made toward the modification of the original $\text{Co}_2(\text{CO})_8$ catalyst (promoter) to achieve more efficient and reliable catalytic PKR.^{9,10} However, while tremendous progress has been seen for the Co-catalyzed intramolecular PKR using enynes as substrates,⁹ the successful examples of catalytic intermolecular PKR have been limited to the utilization of strained (reactive) alkenes such as norbornene and norbornadiene or supercritical ethylene.¹⁰

The use of transition metals other than cobalt has been another area of active research. In 1993, Hoye reported a batch-catalytic protocol for intramolecular PKR using $\text{W}(\text{CO})_5 \cdot \text{THF}$ as a promoter.¹¹ Buchwald reported that titanocene complexes such as $\text{Cp}_2\text{Ti}(\text{CO})_2$ could catalyze the intramolecular PKR of enynes.¹² In 1996, the Ni-catalyzed intermolecular PKR was reported by the same group using isocyanide as a CO equivalent.^{13,14} In 1997, Murai and Mitsudo independently reported that the intramolecular PKR of enynes could be catalyzed by $\text{Ru}_3(\text{CO})_{12}$.¹⁵ In 1998, Narasaka and Jeong independently reported that rhodium complexes such as $[\text{RhCl}(\text{CO})_2]_2$ and

$[\text{RhCl}(\text{CO})(\text{dppp})]_2$ could serve as catalysts for intramolecular PKR of enynes.^{16,17} Examples of Rh-catalyzed intermolecular PKR were provided by Narasaka using reactive alkenes such as norbornene and ethylene.^{16e} However, less reactive alkenes such as styrene and 1-phenyl-3-butene were not applicable. Shibata disclosed that iridium–phosphine catalysts are effective in the intramolecular PKR of enynes and allenynes.¹⁸ An example of intermolecular reaction was also provided, but low reactivity was the apparent bane in this system as well.

Nevertheless, the synthetically most challenging catalytic intermolecular PKR has been essentially limited to the utilization of highly reactive norbornene, norbornadiene, or ethylene as an alkene component (Scheme 1). Therefore, novel catalytic conditions and/or a synthetic strategy to alleviate such limitations imposed on the alkene counterpart are strongly desired.

Directed Pauson–Khand Reaction. Where there is a lack of reactivity and/or selectivity in a certain metal-catalyzed or -mediated process, it is commonplace to tune the stereoelectronics of the catalyst or metal-containing reagent by adjusting the ligand field to enhance the reactivity or selectivity. Alternatively, a directing group (often a heteroatom that is suitably attached on the substrate) could provide a powerful strategy for enhancing the efficiency of an otherwise sluggish process and for steering the course of the reaction by taking advantage of the attractive substrate–catalyst interaction.¹⁹

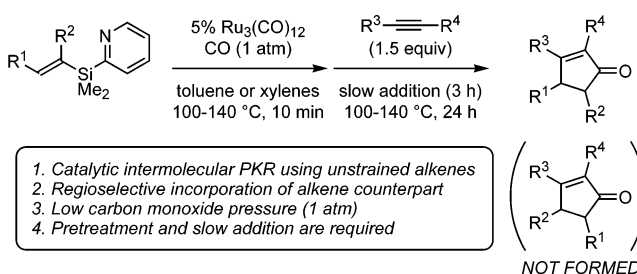
In 1988, Krafft elegantly disclosed that a coordinating heteroatom such as sulfur or nitrogen tethered to an alkene counterpart enormously enhanced the regioselectivity and productivity of the stoichiometric intermolecular PKR.^{20,21}

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Several control experiments strongly supported that the high level of regiocontrol is attributed to the attractive cobalt–heteroatom interactions during the reaction. The occurrence of such an interaction has been validated recently in the density functional study of PKR from Nakamura's laboratory.^{22,23} Moreover, these attractive cobalt–heteroatom interactions have been successfully merged into the design of efficient chiral controllers (chelating auxiliaries) for asymmetric PKR.²⁴ However, no such directing group strategy has been applied to the catalytic intermolecular PKR.²⁵ From a synthetic point of view, a directing group strategy is extremely promising for broadening the scope of applicable alkenes in catalytic PKR. In addition, the application of such a strategy to other metal-catalyzed processes (Ti, Ru, Rh, and Ir) is also intriguing since mono-metallic (noncluster) mechanisms are often proposed in other systems.

Catalytic Intermolecular Pauson–Khand-Type Reaction Directed by Pyridylsilyl Group. During the past few years, we have been particularly interested in the utilization of the dimethyl(2-pyridyl)silyl group (2-PyMe₂Si group) as a “removable directing group” in metal-catalyzed²⁶ and -mediated²⁷ processes for enhancing the total efficiency of chemical reactions.^{28,29} In such a strategy, a range of reactions can be directed through the agency of the complex-induced proximity effect

Scheme 2



(CIPE),¹⁹ yet the initial product can still be transformed into a variety of products with removal of the directing group.

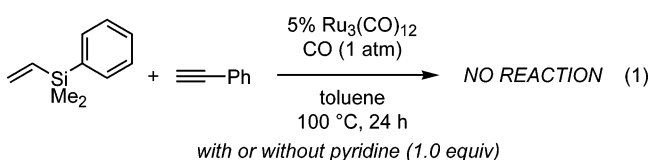
Very recently, we reported the [2 + 2 + 1] cycloaddition reaction of alkenyl(2-pyridyl)silanes, alkynes, and carbon monoxide under the influence of Ru₃(CO)₁₂ catalyst precursor,¹⁵ which would represent an important advance in the catalytic intermolecular Pauson–Khand-type reaction (Scheme 2).³⁰ The noteworthy features are that (i) it realizes a catalytic intermolecular PKR using unstrained alkenes, which was previously difficult to achieve; (ii) the pyridylsilyl group is removed from the product under the reaction conditions in most cases; (iii) it realizes a complete regioselective incorporation of the alkene counterpart (the substituent β to the silyl group always occupies the 4-position in the final 2-cyclopentenone structure); (iv) it does not require high CO pressure conditions (0.5–1.0 atm is optimal); and (v) the pretreatment of Ru₃(CO)₁₂ and alkenyl(2-pyridyl)silane and the slow addition of alkyne are often required.

Although the synthetic scope of this catalytic intermolecular PKR and its application to the synthesis of jasmone precursor were disclosed in our previous paper,^{30,31} the beneficial effects of the pyridylsilyl group have not been clarified yet. In view of the apparent significance of catalytic intermolecular PKR, we initiated our study aimed at (i) clarifying the role of the pyridylsilyl group, (ii) developing other promoting groups, and (iii) isolating Ru complexes relevant to the catalytic reaction. In this paper, we report on our investigation of this subject.

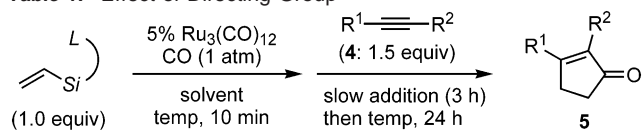
Results and Discussion

Effect of Directing Group. As can be easily concluded from our synthetic study of Ru-catalyzed PKR,^{30,31} alkenyl(2-pyridyl)silanes possess unusually high reactivity toward the catalytic intermolecular PKR. Although we have been assuming the coordination effect as an origin of their high reactivity as mentioned in the previous paper,³⁰ providing direct evidence for this is rather difficult. Thus, we conducted several control experiments to provide circumstantial evidence for the directing effect of the 2-pyridyl group on silicon.

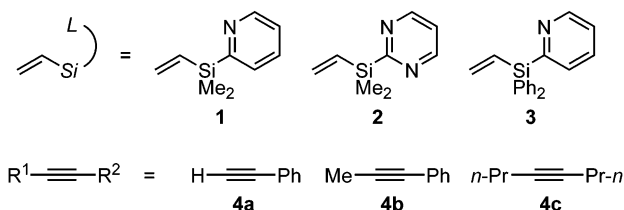
Under the catalytic influence of Ru₃(CO)₁₂ (5 mol %), no reaction occurred with dimethylphenyl(vinyl)silane (eq 1).³² The addition of pyridine (1.0 equiv) into the reaction system did not promote the reaction either. Thus, it is obvious that the (directing) pyridyl group should be attached onto silicon.



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Table 1. Effect of Directing Group^a

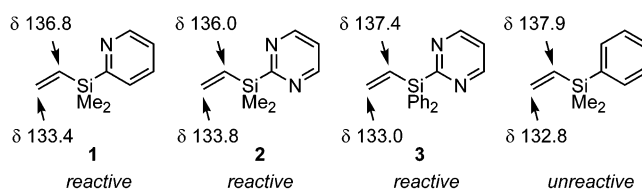
run	vinylsilane	alkyne	temp (°C)	solvent	5 (yield, %)
1	1	4a	100	toluene	5a (55)
2	1	4b	100	toluene	5b (75)
3	1	4b	120	xylenes	5b (75)
4	1	4c	120	xylenes	5c (59)
5	2	4a	100	toluene	5a (46)
6	2	4a	120	xylenes	5a (55)
7	2	4b	100	toluene	5b (75)
8	2	4b	120	xylenes	5b (91)
9	2	4c	120	xylenes	5c (50)
10	2	4c	140	xylenes	5c (65)
11	3	4b	100	toluene	5b (79)

^a

We next examined the catalytic intermolecular PKR using the congeners of dimethyl(2-pyridyl)(vinyl)silane **1** (vinylsilanes with a potentially directing heteroaromatic group on silicon) to advocate the proposed directed PKR scenario (Table 1). As for alkynes for this study, we selected phenylacetylene (**4a**), 1-phenylpropyne (**4b**), and 4-octyne (**4c**). The reactions using prototypical **1** were first examined (runs 1–4). The reaction of **1** with **4a** gave cyclopentenone **5a** in 55% yield at 100 °C (run 1). The reaction using **4b** furnished **5b** in 75% yield at 100 °C (run 2). Raising the temperature had little effect on the chemical yield (75% at 120 °C) for these substrates (run 3).

Next, we prepared the 2-pyrimidyl analogue **2** and tested it in the Ru-catalyzed PKR (runs 5–10). When **4a** was subjected to reaction with **2**, **5a** was obtained in 46% yield at 100 °C (run 5). The yield was lower than that obtained when **1** was employed as an alkene (run 2). However, at higher temperature (120 °C), **5a** could be obtained in slightly higher yield (55%, run 6). When **4b** was employed in the reaction with **2**, **5b** was obtained in 75% yield at 100 °C (run 7). At higher temperature (120 °C), **5b** could be obtained in 91% yield (run 8). The reaction using **4c** furnished **5c** in 50% yield at 120 °C (run 9). Similarly, **5c** was obtained in higher yield (65%) at higher temperature (140 °C, run 10). Throughout these reactions using **2**, we observed obvious phenomena that cannot be seen in the reactions using **1**. In many cases, a significant amount of the starting material (**2**) was recovered even after prolonged reaction time (24 h). These results clearly implicate that **2** is more stable than **1** under the reaction conditions, thereby allowing us to conduct the reaction under more forcing conditions. Indeed, the chemical yields of **5** using **2** are higher than those using **1** when

- (30) Itami, K.; Mitsudo, K.; Yoshida, J. *Angew. Chem., Int. Ed.* **2002**, *41*, 3481.
 (31) See Supporting Information for the synthetic scope (including the previous published materials) of the Ru-catalyzed intermolecular PKR.
 (32) Under identical conditions, the reaction of dimethyl(2-pyridyl)(vinyl)silane (**1**) and phenylacetylene (**4a**) furnished 2-phenyl-2-cyclopentenone (**5a**) in 55% yield.

**Figure 1.** Comparison of vinylic ¹³C NMR chemical shifts of **1**, **2**, **3**, and dimethylphenyl(vinyl)silane in CDCl₃.

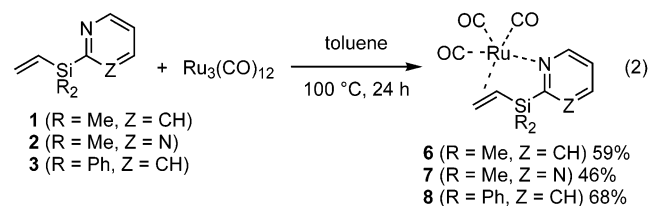
the reactions are performed at higher temperature. However, it should be mentioned that the reactivity of **2** seems to be slightly lower than that of **1** in the Ru-catalyzed intermolecular PKR.

The variation of methyl groups on the silicon atom is another interesting modification of **1**. Thus, we prepared diphenyl(2-pyridyl)vinylsilane **3** and tested it in the Ru-catalyzed PKR. When **3** was employed in the reaction with **4b**, **5b** was obtained in 79% yield at 100 °C (run 11). This implies that **3** is slightly more reactive than **1** in PKR.

These preliminary studies indicate the reactivity order to be **3** ≥ **1** > **2**, and the stability order **2** > **1** > **3**. Taking these aspects and the ease of preparation into consideration, the prototypical **1** is the choice of alkene at this stage. Nevertheless, the emergence of substantial reactivity by appending the potentially coordinating heteroaromatic groups lends credence to our proposal.

Other than the beneficial coordination effect of the pyridyl and pyrimidyl groups on catalyst ruthenium as we envisioned, it is also possible to assume that those groups on silicon might electronically activate the reacting vinyl group at a certain step of the reaction. Therefore, we compared the vinylic ¹³C NMR chemical shifts of **1**, **2**, **3**, and dimethylphenyl(vinyl)silane in CDCl₃ as indices of electron density (Figure 1).³³ Although the ¹³C NMR chemical shifts are influenced by several factors, comparison within a family is thought to allow a qualitative evaluation of electron density.³⁴ The minor chemical shift differences seem to support the notion that the through-bond electronic activation is not a viable explanation for the high reactivity of pyridyl- and pyrimidyl-substituted vinylsilanes toward catalytic PKR.

Synthesis and Structure of Mononuclear Ru(vinylsilane) Complexes. To get further insight into the role of the pyridyl and pyrimidyl groups, we conducted the stoichiometric reaction of vinylsilanes (**1**, **2**, and **3**) with Ru₃(CO)₁₂. The treatment of **1** (5.0 mmol) and Ru₃(CO)₁₂ (1.0 mmol) in toluene (30 mL) at 100 °C for 24 h furnished the Ru(vinylsilane) complex **6** (eq 2). The excess **1** was recovered from the reaction mixture. Subjection of the crude mixture to gel permeation chromatography (CHCl₃) afforded **6** in 59% yield. Similarly, the reactions using **2** and **3** gave the corresponding Ru(vinylsilane) complexes **7** and **8** in 46% and 68% yield, respectively (eq 2). No such complex was obtained by the treatment of Ru₃(CO)₁₂ with dimethylphenyl(vinyl)silane under similar conditions.



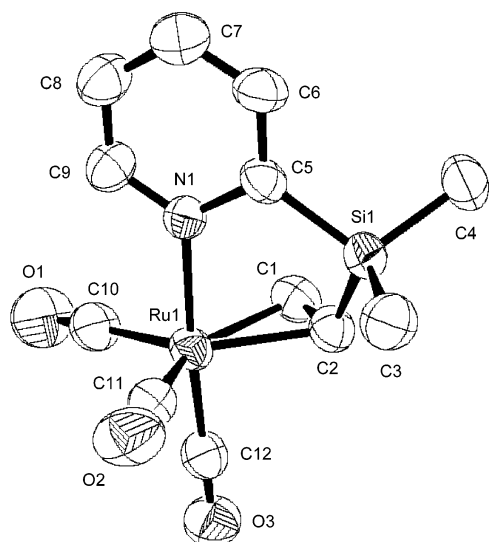


Figure 2. Structure of **6**. Thermal ellipsoids are drawn at the 40% probability level. The hydrogen atoms are omitted for clarity. Selected bond lengths (Å): Ru–N = 2.184(6), Ru–C1 = 2.182(9), Ru–C2 = 2.184(8), Ru–C10 = 1.92(1), Ru–C11 = 1.94(1), Ru–C12 = 1.86(1), C1–C2 = 1.38(1), C10–O1 = 1.12(1), C11–O2 = 1.15(1), C12–O3 = 1.19(1). Selected bond angles (deg): N–Ru–C1 = 86.5(3), N–Ru–C2 = 85.2(3), N–Ru–C10 = 93.1(3), N–Ru–C11 = 89.0(3), N–Ru–C12 = 175.9(3), C1–Ru–C2 = 36.8(3), Ru–C1–C2 = 71.7(5), Ru–C2–C1 = 71.5(5). Selected torsion angles (deg): N–Ru–C2–Si = 28.9(1), Ru–C2–Si–C5 = 32.8(1), C2–Si–C5–N = 21.4(2), Si–C5–N–Ru = –0.5(9), C1–Ru–N–C5 = –55.0(1), Ru–C1–C2–Si = –99.9(9).

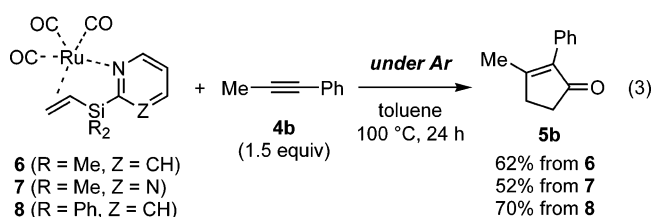
In the ^1H NMR spectra, the presence of an η^2 -complexed $\text{CH}_2=\text{CH}$ fragment was shown by three equal intensity resonances at δ 1–3 ppm (δ 1.18 dd, 1.77 dd, 2.62 dd for **6**). These resonances have chemical shifts similar to those found in other (η^2 -olefin)Ru(0) complexes,³⁵ but are quite distinct from those of a noncomplexed vinyl group of vinylsilanes, which appear at lower fields (δ 5.5–6.5). The additional coordination of the pyridyl and pyrimidyl groups to Ru was also indicated by the noticeable changes in the NMR chemical shifts. The two nonequivalent methyl groups on silicon (for **6** and **7**) in the ^1H and ^{13}C NMR spectra were consistent with the assumed vinyl–N chelation to Ru. Moreover, the three nonequivalent CO carbons (δ 201.3, 203.3, 205.1 for **6**) in the ^{13}C NMR spectra were also in line with the structure shown in eq 2. A similar structure was assumed for the $\text{Ru}(\text{CO})_2(o\text{-CH}_2=\text{CHC}_6\text{H}_4\text{PPH}_2)$ complex prepared by Bennett.³⁶

Although complex **6** is soluble in most organic solvents, it was possible to obtain a single crystal suitable for X-ray crystal structure analysis by leaving a concentrated CHCl_3 solution of **6** to stand in refrigerator. An ORTEP diagram of **6** is shown in Figure 2. Complex **6** has an approximately trigonal-bipyramidal ligand arrangement, with the vinyl group and two CO groups in equatorial positions and the pyridyl nitrogen and one CO in apical positions. This is in line with the general observation

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 (34) (a) Sardella, D. *J. Am. Chem. Soc.* **1973**, 95, 3809–3811. (b) Happ, B.; Bartik, T.; Zucchi, C.; Rossi, M. C.; Ghelfi, F.; Pályi, G.; Váradi, G.; Szalontai, G.; Horváth, I. T.; Chiesi-Villa, A.; Guastini, C. *Organometallics* **1995**, 14, 809–819. (c) Alami, M.; Liron, F.; Gervais, M.; Peyrat, J. F.; Brion, J. D. *Angew. Chem., Int. Ed.* **2002**, 41, 1578–1580.
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that the σ -donor ligands occupy the apical positions and the π -accepting ligands occupy the equatorial positions.³⁷ The vinylic C=C bond lies approximately in the equatorial plane. Overall, the structure of **6** is similar (bond lengths, bond angles, and torsion angles) to that of the $\text{PdCl}_2(\mathbf{1})$ complex prepared previously from our laboratory.^{26c} It should also be mentioned that the complexes **6–8** are stable to air and moisture (even stable to silica gel chromatography and gel permeation chromatography), which is in contrast to other Ru(0)–olefin complexes. This may be a consequence of two factors: (i) the presence of a nitrogen donor, which should favor metal–olefin π back-bonding, and (ii) the presence of vinyl–N chelation, which should reduce the tendency toward olefin dissociation.

Reactivity of Ru(vinylsilane) Complexes. The reactivity of Ru(vinylsilane) complexes toward PKR is of great interest from a mechanistic point of view. Upon heating a toluene solution of **6** (1.0 equiv) and **4b** (1.5 equiv) under argon at 100 °C for 24 h, cyclopentenone **5b** was obtained in 62% isolated yield (eq 3). The complete regioselectivity observed in the catalytic reaction was also maintained. Subjection of other Ru(vinylsilane) complexes **7** and **8** to the identical conditions afforded **5b** in 52% and 70% yield, respectively. The reactivity order (**8** > **6** > **7**) was in a good correlation to that observed in the catalytic reactions (Table 1, runs 1, 5, and 11). These stoichiometric reactions are extremely interesting because they might be relevant to our catalytic intermolecular PKR. These results clearly indicate that the reaction pathway through a mononuclear Ru complex is feasible though trinuclear $\text{Ru}_3(\text{CO})_{12}$ is employed as the catalyst precursor at the beginning.



In addition, it should be mentioned that the reactions depicted in eq 3 represent an unusual type of stoichiometric PKR. Conventionally, the stoichiometric PKR has been performed through (i) a precomplexation of an alkyne and a metal carbonyl fragment [usually $\text{Co}_2(\text{CO})_8$] and (ii) subsequent reaction with an excess amount of an alkene (Scheme 3). On the other hand, the stoichiometric reactions demonstrated in eq 3 proceed in a reverse mode to the conventional PKR with respect to the precomplexation component (alkyne \rightarrow alkene). To our knowl-

Scheme 3

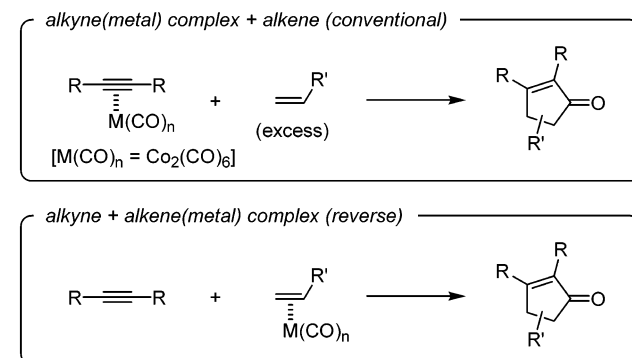


Table 2. Catalytic PKR of **1** with **4** Using Ru Complex **6**

run	Ru complex	alkyne	time (h)	5 (yield, %)
1 ^a	6	4a	24	5a (56)
2 ^b	Ru ₃ (CO) ₁₂	4a	24	5a (55)
3 ^a	6	4b	24	5b (71)
4 ^b	Ru ₃ (CO) ₁₂	4b	24	5b (75)
5 ^a	6	4b	3	5b (72)
6 ^b	Ru ₃ (CO) ₁₂	4b	3	5b (17)

^a 15 mol % of Ru complex was employed. ^b 5 mol % of Ru₃(CO)₁₂ (15 mol % Ru atom) was employed.

edge, such a stoichiometric PKR has not been reported in the literature. This may be partly because of the low coordination ability of usual alkenes compared with that of alkynes or carbon monoxide. The need of an excess amount of alkene in the conventional PKR reflects these aspects. Therefore, it may be reasonable to assume that the strong coordinating ability of vinyl(2-pyridyl)silane (through vinyl–N chelation) leads to the realization of such a stoichiometric PKR.

Moreover, we found that the Ru(vinylsilane) complex **6** serves not only as a reagent but also as a catalyst precursor for intermolecular PKR of **1** (Table 2). Thus, in the presence of a catalytic amount of **6** (15 mol %), intermolecular PKR of **1** and **4a** proceeded to afford **5a** in 56% yield (run 1). Similarly, the reactions using **4b** afforded the corresponding cyclopentenones **5b** in 71% yield (run 3). In both cases, the yields of **5** were quite similar to those obtained from Ru₃(CO)₁₂ (15 mol % Ru atom) under otherwise identical conditions (runs 2 and 4). This Ru(vinylsilane) complex **6** turned out to be the second active catalyst (precursor) in our intermolecular PKR. Interestingly, we found that the catalytic reaction using **6** proceeds much faster than that using Ru₃(CO)₁₂ at the early stage of reaction (runs 5 and 6), although the product yields after prolonged reaction time (24 h) are similar (runs 3 and 4). These results suggest the presence of an induction period in the reaction using Ru₃(CO)₁₂, most likely to generate catalytically active Ru(vinylsilane) complex. Nevertheless, these results of stoichiometric and catalytic reactions (eq 3 and Table 2) suggest that the mononuclear Ru complex **6** might be involved in the catalytic cycle of PKR using vinyl(2-pyridyl)silane **1**.

Isolation of Ruthenacyclopentene 9. While investigating the reaction of Ru(vinylsilane) complex **6** and alkyne **4b** with NMR, we found an obvious generation of a new Ru complex before the formation of cyclopentenone **5b**. After several experiments, we found that **6** is quantitatively converted to this complex by

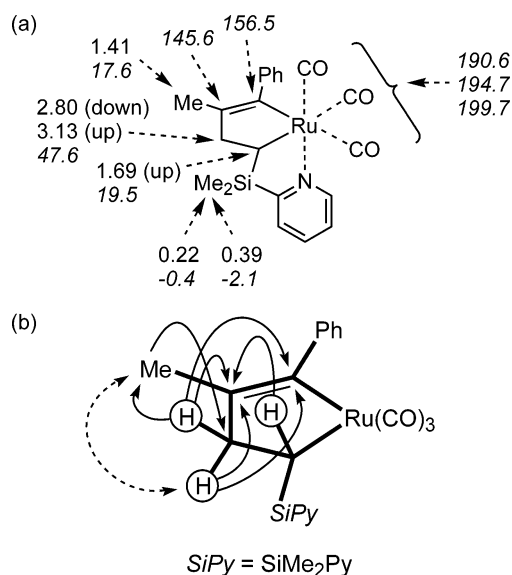
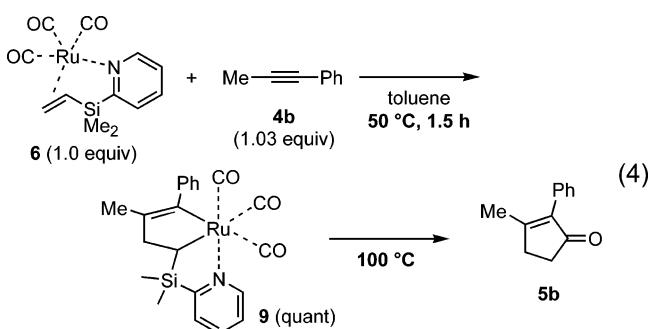


Figure 3. NMR spectra of **9**. (a) Representative proton and carbon (italics) NMR assignments. (b) Representative correlations established by HMBC (arrows) and NOESY (dotted arrow) experiments.

treatment with **4b** (1.03 equiv) in toluene at 50 °C for 1.5 h (eq 4). Because further heating of this solution at 100 °C afforded **5b**, we assume this new complex to be ruthenacyclopentene **9**, which might also be involved in the catalytic cycle.³⁸

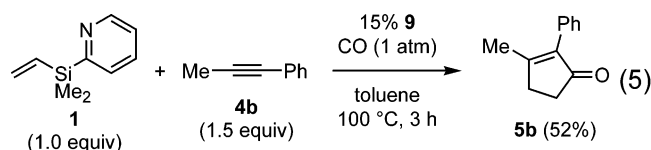
The representative NMR assignments of **9** (protons and carbons) are shown in Figure 3a, and followings are some comparisons of its NMR chemical shifts with those of Ru(vinylsilane) complex **6** and free vinylsilane **1**: (i) All ¹³C resonances of pyridine rings in **6** and **9** appear at lower field compared to those of free vinylsilane **1**, which is in line with the pyridyl-to-Ru coordination in complexes **6** and **9**. (ii) The ¹³C resonances of the carbon α to silicon (derived from the α-vinyl carbon of **1**) appear in the order of **9** (19.5 ppm) < **6** (27.6 ppm) < **1** (136.8 ppm), which is in parallel with a decrease of s-character of the α-carbon. (iii) Similarly, the ¹³C resonance of the carbon β to silicon in **9** appears at higher field (47.6 ppm) compared to that of **1** (133.4 ppm), again reflecting a decrease of s-character of this carbon. The appearance of this carbon in lower field compared with that of **6** (34.9 ppm) may be due to the allylic nature of this carbon in **9**. (iv) The ¹³C carbonyl resonances of **9** appear at slightly higher field (190.6, 194.7, 199.7 ppm) compared to those of **6** (201.3, 203.3, 205.1 ppm), which is in parallel with a decrease in Ru → π*(CO) back-donation.

Though it was not possible to obtain a single crystal of **9** suitable for X-ray crystal structure analysis, extensive NMR experiments (COSY, NOESY, HMQC, and HMBC) revealed its structure to be in line with that shown in eq 4. Important correlations established by HMBC and NOESY experiments are shown in Figure 3b. These experiments unambiguously elucidated the bond formation between the alkyne and vinylsilane moieties in the ruthenacyclopentene **9**.

(37) Rossi, A. R.; Hoffmann, R. *Inorg. Chem.* **1975**, *14*, 365–374.

(38) Selected examples for the isolation of late-metal metallacyclopentenones relevant to transition-metal-catalyzed reactions: (a) Wakatsuki, Y.; Aoki, K.; Yamazaki, H. *J. Am. Chem. Soc.* **1979**, *101*, 1123–1130. (b) Scozzafava, M.; Stolzenberg, A. M. *Organometallics* **1988**, *7*, 1073–1083. (c) O'Connor, J. M.; Closson, A.; Gantzel, P. *J. Am. Chem. Soc.* **2002**, *124*, 2434–2435.

This may be the rare example that succeeded in isolating multiple metal complexes relevant to the catalytic cycle in metal-catalyzed cycloaddition chemistry. Moreover, it should be noted that these experiments clearly revealed that the rate-determining step is not the formation of the metallacycle intermediate (oxidative cyclization step; **6** → **9**), which proceeds at 50 °C, but rather the formation of the Ru(olefin) complex (such as **6**) and/or the later steps (carbonyl insertion and reductive elimination) that require higher temperature (> 100 °C). As in the case of Ru(vinylsilane) complex **6**, this ruthenacyclopentene **9** was also found to serve as a catalyst (precursor) in the intermolecular PKR of **1** and **4b**, yielding the corresponding cyclopentenone **5b** in 52% yield (eq 5).



Mechanistic Considerations. A plausible mechanism of the Ru-catalyzed [2 + 2 + 1] cycloaddition of alkenyl(2-pyridyl)silane, alkyne, and carbon monoxide is depicted in Figure 4. The reaction is thought to begin with the formation of Ru(alkenylsilane) complex **A**. The successive coordination of an alkyne leads to the formation of Ru(alkyne)(alkenylsilane) complex **B**, which undergoes a typical oxidative cyclization process to produce ruthenacyclopentene intermediate **C**. A migratory insertion of a carbon monoxide ligand into the C(sp²)–Ru bond produces the six-membered ruthenacycle intermediate **D**. Although an alternative mechanism that involves a migratory insertion into the C(sp³)–Ru bond may also be plausible, we prefer the former simply because it retains the strong pyridyl-to-ruthenium complexation. Finally, reductive elimination furnishes the silylated cyclopentenone **F** and “Ru(CO)_n” complex **E**, which should be trapped by alkenyl(2-pyridyl)silane to regenerate Ru(alkenylsilane) complex **A**. The in situ desilylation of **F** produces **G** as the final product. It must be noted that an alternative mechanism that involves the initial coordination of an alkyne to Ru, followed by the coordination of alkenylsilane to give Ru(alkyne)(alkenylsilane) complex **B**, cannot be strictly ruled out at present.

As for the catalytically active metal species, we speculate those to be nonclustered monometallic Ru complexes rather than clustered multimetallic metal complexes (like the Co₂(CO)₈-mediated PKR). The following observations are in line with this assumption: (i) Significant improvement of reaction efficiency is observed by the pretreatment of clustered Ru₃(CO)₁₂ with alkenyl(2-pyridyl)silane (Scheme 2). (ii) Such a pretreatment most likely produces a monometallic Ru(alkenylsilane) complex **A**. (iii) The monometallic Ru(alkenylsilane) complex **A** exhibits reasonable reactivity both as reagent and as catalyst precursor (eq 3 and Table 2).

The following aspects may be the reasons for the realization of a hard-to-achieve catalytic, intermolecular, and regioselective Pauson–Khand-type reaction when alkenyl(2-pyridyl)silanes or alkenyl(2-pyrimidyl)silanes are used as alkene components.

(1) The suitably positioned pyridyl (or pyrimidyl) group should help the reacting C=C bond to coordinate to metal center through pre-coordination (complex-induced proximity effect). This should greatly enhance the coordinating aptitude of the

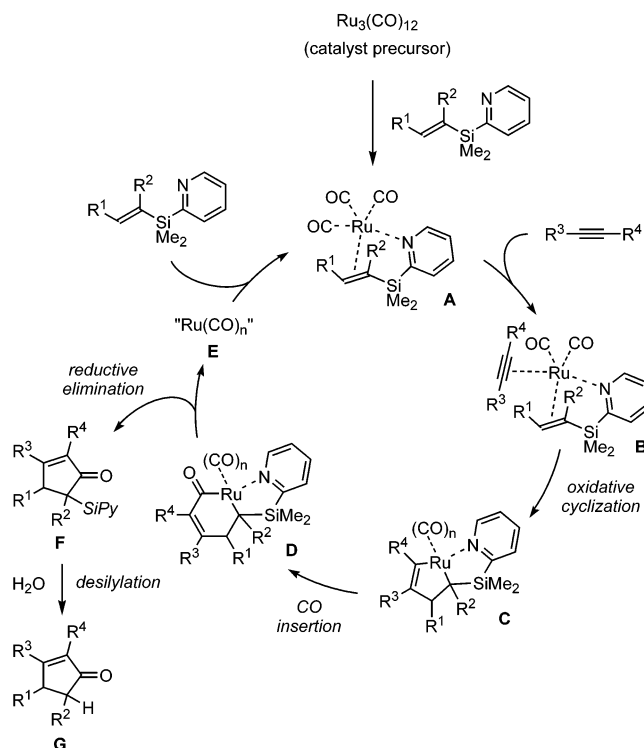


Figure 4. A plausible mechanism.

alkene counterpart, thereby making it capable of competing with alkyne and carbon monoxide for a coordination site on the metal (**A** and **B**). The well-balanced coordination abilities are extremely important for the realization of catalytic multicomponent assembly.

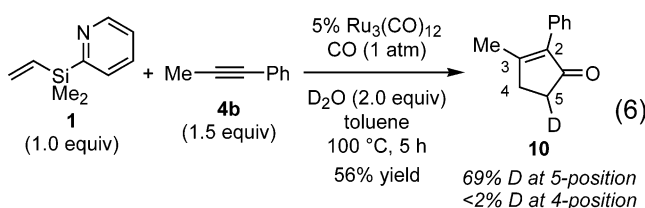
(2) In addition to the kinetic preference mentioned above, the stabilization of the metallacycle intermediate (**C**) by complexation with the suitably positioned pyridyl (or pyrimidyl) group might also contribute to accelerating the rate-determining oxidative cyclization step (**B** → **C**).²² We indeed found this to be true by the stoichiometric reaction of Ru(vinylsilane) complex **6** with alkyne **4b** (eq 4).

The complete regioselective incorporation of the alkene subunit in this catalytic intermolecular PKR is worth mentioning. The use of α - or β -substituted vinylsilane results in the regioselective production of substituted cyclopentenones with the substituent at the 5- or 4-position, respectively (**G** in Figure 4).^{30,31} This is clearly implicated in the regioselective formation of metallacyclopentene intermediate **C**. During these studies, we have been assuming that the formation of metallacyclopentene from alkyne, alkene, and low-valent metal (oxidative cyclization) may be regarded as a carbometallation reaction of an (alkyne)metal complex across an alkene (**B** → **C**). Indeed, in accord with this assumption, there are many examples indicating that the metallacycle formation occurs preferentially at the most electropositive terminus of the alkene.³⁹ Recent studies from our laboratory clearly indicated that the carbometallation (carbopalladation^{26a,e} and carbomagnesation^{27c}) across alkenyl(2-pyridyl)silane is extremely facile and regioselective

(39) (a) Pauson, P. L. *Tetrahedron* **1985**, *41*, 5855–5860. (b) La Belle, B. E.; Knudsen, M. J.; Olmstead, M. M.; Hope, H.; Yanuck, M. D.; Schore, N. E. *J. Org. Chem.* **1985**, *50*, 5215–5222. (c) Sampath, V.; Lund, E. C.; Knudsen, M. J.; Olmstead, M. M.; Schore, N. E. *J. Org. Chem.* **1987**, *52*, 3595–3603. (d) MacWhorter, S. E.; Sampath, V.; Olmstead, M. M.; Schore, N. E. *J. Org. Chem.* **1988**, *53*, 203–205. (e) Ahmar, M.; Antras, F.; Cazes, B. *Tetrahedron Lett.* **1999**, *40*, 5503–5506. (f) Reference 10b.

because of the strong complex-induced proximity effect of the pyridyl group on silicon, together with the inherent silicon α effect.

As is apparent from the regioselective incorporation of substituents on alkenylsilane, the pyridylsilyl group should be incorporated in the 5-position of the initially formed 2-cyclopentenone (**F**). However, in most cases, such silylated cyclopentenones **F** were not observed in the reaction mixture. We assume that the desilylation occurs by hydrolysis of the silyl enolate, which is produced by the [1,3]-silyl migration of 5-silylcyclopenten-2-one **F**.⁴⁰ In line with these assumptions, we detected the pyridyl-substituted disiloxane (product derived from the corresponding silanol produced by hydrolysis) in the mass spectrum of the reaction mixture. Moreover, we also found that the addition of D₂O (2.0 equiv) in the reaction of **1** and **4b** resulted in the regioselective incorporation of deuterium at the 5-position (eq 6). This result suggests that (i) the source of the hydrogen atom is residual water contained in the reaction mixture and (ii) vinylsilane **1** is incorporated in the cyclopentenone skeleton in a regioselective fashion (at the 5-position).



Experimental Section

General Method. See the Supporting Information.

Synthetic Scope of Ru-Catalyzed Intermolecular Pauson–Khand-Type Reaction of Alkenyl(2-pyridyl)silane with Alkyne. See the Supporting Information.

Synthesis of Starting Materials. See the Supporting Information.

Typical Procedure for Ru-Catalyzed Intermolecular Pauson–Khand-Type Reaction of Vinyl(2-pyridyl)silane or Vinyl(2-pyrimidyl)silane with Alkyne. A suspension of Ru₃(CO)₁₂ (16 mg, 0.025 mmol, 5 mol %) and vinylsilane (0.50 mmol) in toluene (1.5 mL) was stirred at 100 °C for 10 min under CO (1 atm). To this mixture was added alkyne (0.75 mmol) over 3 h at 100 °C, and the mixture was stirred for 24 h. After the mixture was cooled to room temperature, 1 N aqueous HCl (1 mL) was added, and the organic phase was extracted with Et₂O (3 × 2 mL). The aqueous phase was neutralized by adding NaHCO₃ and then was extracted with Et₂O (3 × 2 mL). The combined organic phase was dried over MgSO₄, and removal of solvents under reduced pressure afforded the crude product. The residue was chromatographed on silica gel to afford **5**.

Ru(vinylsilane) Complex 6. To a suspension of Ru₃(CO)₁₂ (662.7 mg, 1.04 mmol) in dry toluene (20 mL) was added a solution of **1** (791.2 mg, 5.00 mmol) in dry toluene (10 mL). After the mixture was stirred at 100 °C for 24 h, the solvent was removed under vacuum. Subjection of the crude mixture to gel permeation chromatography (CHCl₃) afforded **6** (639.5 mg, 59%) as a pale yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 0.38 (s, 3H), 0.41 (s, 3H), 1.18 (dd, J = 13.2, 1.5 Hz, 1H), 1.77 (dd, J = 13.2, 11.1 Hz, 1H), 2.62 (dd, J = 11.1, 1.5 Hz, 1H), 7.05 (ddd, J = 7.8, 5.7, 1.5 Hz, 1H), 7.35 (ddd, J = 7.8, 1.5,

0.9 Hz, 1H), 7.56 (td, J = 7.8, 1.5 Hz, 1H), 8.72 (dt, J = 5.7, 1.2 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): δ -2.0, 0.7, 27.6, 34.9, 123.8, 131.4, 135.2, 155.4, 172.4, 201.3, 203.3, 205.1. IR (neat): 1945, 1460, 1281, 1248 cm⁻¹. HRMS (FAB): m/z calcd for C₁₂H₁₃NO₃SiRu, 348.9711; found, 348.9707. X-ray data for **6**: C₁₂H₁₃NO₃SiRu, M = 348.40, triclinic, space group $P\bar{1}$ (No. 2), a = 8.9301 Å, b = 9.493(1) Å, c = 9.7181(1) Å, α = 71.094(8)°, β = 82.6320(3)°, γ = 73.3640(4)°, V = 746.20(7) Å³, Z = 2, D_c = 1.55 g/cm³, μ = 11.29 cm⁻¹. Intensity data were measured on a Rigaku RAXIS imaging plate area detector with graphite-monochromated Mo K α radiation. The data were collected at 23 ± 1 °C to a maximum 2θ value of 54.9°. A total of 3102 reflections were collected. The structure was solved by heavy-atom Patterson methods and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined isotropically. The final cycle of full-matrix least-squares refinement on F was based on 2534 observed reflections ($I > 3.00\sigma(I)$) and 177 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of R = 0.059 (R_w = 0.066). All calculations were performed using the CrystalStructure crystallographic software package.

Conclusions

In conclusion, we have succeeded in providing some circumstantial evidence for the directing effect of the 2-pyridylsilyl group in the Ru-catalyzed intermolecular Pauson–Khand-type reaction of alkenyl(2-pyridyl)silane, alkyne, and carbon monoxide. Other than the prototypical dimethyl(2-pyridyl)silyl group, dimethyl(2-pyrimidyl)silyl and diphenyl(2-pyridyl)silyl groups have been developed as new removable directing groups for catalytic intermolecular PKR. From the ¹³C NMR study of several reactive and unreactive vinylsilanes, the through-bond electronic activation seems not to be a viable explanation for the promoting effect of pyridylsilyl and pyrimidylsilyl groups. Most importantly, we have succeeded in isolating several monometallic Ru complexes relevant to catalytic intermolecular PKR: Ru(vinylsilane) complexes (**6–8**) and ruthenacyclopentene **9**. The reaction of Ru₃(CO)₁₂ with vinyl(2-pyridyl)silanes and vinyl(2-pyrimidyl)silanes produces the nonclustered monometallic Ru(vinylsilane)(CO)₃ complexes **6–8**. While the stoichiometric reactions of Ru(vinylsilane)(CO)₃ complexes **6–8** with alkynes **4** led to the formation of the corresponding cyclopentenones **5** at 100 °C, the ruthenacyclopentene intermediate **9** was quantitatively produced at 50 °C (from **6** and **4b**). This complex was also converted to a cyclopentenone **5** upon heating at 100 °C. Moreover, it was found that Ru(vinylsilane)(CO)₃ complex **6** and ruthenacyclopentene **9** also serve as catalyst precursors in intermolecular PKR. Taking all these results into account, we assume these complexes (**6–9**) to be involved in the catalytic cycle of intermolecular PKR.

In view of the apparent significance of catalytic intermolecular PKR, the present findings not only allow us to better understand the high reactivity of alkenyl(2-pyridyl)silanes and alkenyl(2-pyrimidyl)silanes in PKR, but also help us to design more efficient and/or strategic PKR in organic synthesis. In particular, the “removable directing group strategy” demonstrated herein should find many applications, and the evolution of other functional groups of this type would be easily accomplished by a relatively straightforward design.

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(40) Similar desilylation of the 2-PyMe₂Si group α to the carbonyl group was observed during the course of our investigation of Migita–Kosugi–Stille coupling reactions using 2-PyMe₂SiCH₂SnBu₃.^{26d} Namely, the Pd-catalyzed coupling reaction of 2-PyMe₂SiCH₂SnBu₃ with acid chloride produced the corresponding methyl ketone exclusively (unpublished results). Moreover, we have also discovered that the oxophilicity of the 2-PyMe₂Si group is substantially higher than that of the PhMe₂Si group,^{27b} which should render this isomerization easier.

Supporting Information Available: Synthetic scope of the Ru-catalyzed intermolecular PKR; experimental procedures and analytical and spectroscopic data of compounds (PDF). X-ray

crystallographic data (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.
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