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# Rhodium-Catalyzed Novel Carbonylative Carbotricyclization of Enediynes

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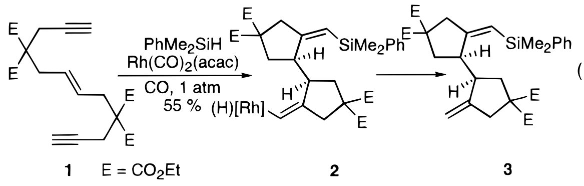
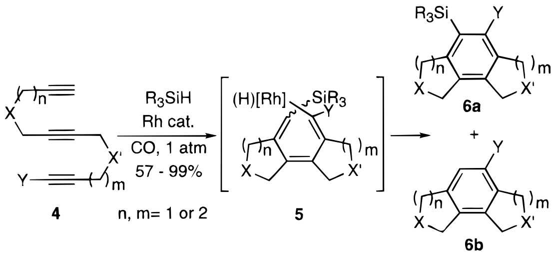
Transition metal-catalyzed carbocyclization of compounds containing organic $\pi$-systems has played an important role in organic syntheses.[1] Both the intermolecular and intramolecular carbocyclization is a powerful method for construction of cyclized compounds that are useful for further synthetic transformation. Among various metals, nickel, ruthenium, cobalt, rhodium, and palladium catalysts have been commonly used for carbocyclizations.[2−4]

In the course of our studies on silicon-initiated carbometalation reactions, silyformylation,[5a] silylcyclocarbonylation (SiCCa),[6,7] and silycarbocyclization (SiCaC)[7] have been discovered. We reported a stereospecific cascade SiCaC reaction[8] of dodec-6-ene-1,11-diynes (eq 1). In this reaction, although cyclization of the vinyl-[Rh] moiety of intermediate **2** to the vinylsilane moiety to form the third ring was conceptually possible, it did not take place. Simple reductive elimination preferentially occurred to give the corresponding biscyclopentyl **3**.



(1)

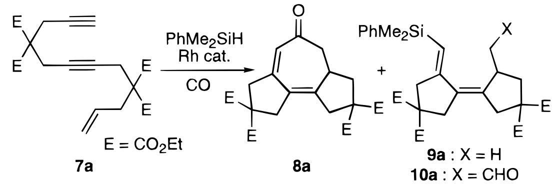
In the case of trialkynes, silylcarbotricyclization (SiCaT) takes place to give fused tricyclic compounds **6a** and **6b** in good to excellent yields (eq 2).[9] Reactions catalyzed by rhodium clusters showed high selectivity to **6a**.



(2)

As a part of our continuing studies on the metal-catalyzed, silicon-initiated carbometalations, we looked at the reaction of dedec-11-ene-1,6-diynes. To our surprise, the reaction of the enediynes with PhMe$_2$SiH in the presence of a rhodium catalyst under ambient CO afforded fused 5−7−5 ring structures incorporating CO. We describe here a novel silicon-initiated carbonylative carbotricyclization of enediynes promoted by rhodium catalysts, which provides a rapid and useful method for the construction of fused 5−7−5 ring systems.

The reaction of enediyne **7a** (0.5 mmol) with PhMe$_2$SiH (1.0 mmol) catalyzed by Rh(acac)(CO)$_2$ (1 mol %) in toluene (2.5 mL) under CO at 70 °C for 1h gave cyclopenta[e]azulene **8a** and bis(cyclopentylidene) compound **9a** as major products and aldehyde **10a** as minor product in 70% overall yield (**8a**:**9a**:**10a** = 36:43:21; isolated by column chromatography on silica gel) (Table 1, entry 1) (eq 3).



(3)

Since the one-step formation of **8a** was synthetically very attractive, we investigated the reaction variables to optimize the product selectivity for **8a**. Results are summarized in Table 1. The reactions under higher CO pressure (10 atm) suppress the formation of **9a** (entry 2). Lower reaction temperatures, smaller amounts of PhMe$_2$SiH, and higher dilution also disfavor the formation of **9a**. Addition of P(OPh)$_3$ completely suppresses the formation of **10a** (entry 3), while the use of PPh$_3$ as the additive substantially favors the formation of **10a** and reduces the yield of **8a** (entry 4). The use of THF as solvent gives better product selectivity for **8a**. Under dilute reaction conditions, the product selectivity for **8a** is dramatically increased (entries 6−8, 10, and 11). Reaction with 0.5 equiv of PhMe$_2$SiH is sufficient for high overall yield (entries 7, 10, and 11). This clearly indicates that the hydrosilane is recycled in the catalytic system. However, the reaction with 0.1 equiv of the hydrosilane does not give complete conversion in 72 h, and **8a** was isolated in 33% yield (entry 8). In the absence of PhMe$_2$SiH, no reaction takes place after 72 h, recovering enediyne **7a** (entry 9). Thus, PhMe$_2$SiH is proven necessary for this reaction to occur. The best result is achieved by using 0.5 equiv of PhMe$_2$SiH at 0.015 M concentration, giving **8a** as the single product in 92% isolated yield (entry 7). As for the catalyst, Rh(acac)(CO)$_2$, Rh$_4$(CO)$_{12}$, and [Rh(CO)$_2$Cl]$_2$ show similar efficacy. For hydrosilanes in this process, the reactions with Ph$_2$MeSiH and (EtO)$_3$SiH give **8a** exclusively although the reactions are slower than that with PhMe$_2$SiH. Trialkylsilanes behave differently, that is, the reaction with Et$_3$SiH gives a 9:1 mixture of **8a** and **9a-TES** in low conversion, while that with

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[1] For recent reviews on metal-catalyzed carbocyclization, see: Grotjahn, D. B. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Ed.; Pergamon/Elsevier Science: Kidlington, 1995; Vol. 12; pp 703, 741; Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.*, **1996**, 96, 49; Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635.

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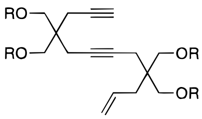
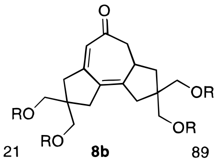
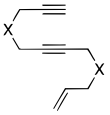
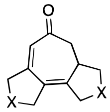
**Table 1.** Silicon-Initiated Carbonylative Carbotricyclization of **7a** [a]

| entry | cat. | R$_3$SiH (equiv.) | temp (°C) | CO (atm) | solvent (M) | time (h) | yield (%)[b] | product ratio | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | **8a** | **9a** | **10a** |
| 1 | **A** | PhMe$_2$SiH (2.0) | 70 | 1 | toluene (0.2) | 1 | 70 | 36 | 43 | 21 |
| 2 | **A** | PhMe$_2$SiH (2.0) | 60 | 10 | toluene (0.2) | 10 | 55 | 55 | 9 | 36 |
| 3[c] | **A** | PhMe$_2$SiH (1.0) | 50 | 1 | toluene (0.2) | 10 | 62 | 65 | 35 | 0 |
| 4[d] | **A** | PhMe$_2$SiH (1.0) | 50 | 1 | toluene (0.2) | 10 | 52 | 10 | 32 | 58 |
| 5 | **A** | PhMe$_2$SiH (1.0) | 22 | 1 | THF (0.2) | 12 | 65 | 70 | 15 | 15 |
| 6 | **A** | PhMe$_2$SiH (1.0) | 22 | 1 | THF (0.15) | 24 | 82 | 100 | 0 | 0 |
| **7** | **A** | **PhMe$_2$SiH (0.5)** | **22** | **1** | **THF (0.015)** | **30** | **92** | **100** | **0** | **0** |
| 8 | **A** | PhMe$_2$SiH (0.1) | 22 | 1 | THF (0.015) | 96 | 33 | 100 | 0 | 0 |
| 9 | **A** | PhMe$_2$SiH (0.0) | 22 | 1 | THF (0.015) | 96 | 0 | 0 | 0 | 0 |
| 10 | **B** | PhMe$_2$SiH (0.5) | 22 | 1 | THF (0.015) | 17 | 78 | 92 | 8 | 0 |
| 11 | **C** | PhMe$_2$SiH (0.5) | 22 | 1 | THF (0.015) | 23 | 80 | 100 | 0 | 0 |
| 12 | **A** | PhMe$_2$SiH (0.5) | 22 | 1 | THF (0.015) | 96 | 42 | 100 | 0 | 0 |
| 13 | **A** | (EtO)$_3$SiH (0.5) | 22 | 1 | THF (0.015) | 96 | 34 | 100 | 0 | 0 |
| 14 | **A** | Et$_3$SiH (0.5) | 22 | 1 | THF (0.015) | 96 | 12 | 90 | 10 | 0 |
| 15 | **A** | tBuMe$_2$SiH (0.5) | 22 | 1 | THF (0.015) | 96 | 0 | 0 | 0 | 0 |

[a] Reaction was run with endyne (0.25−0.5 mmol scale), hydrosilane and Rh-catalyst (1 mol %) in a solvent under CO. Catalyst A = Rh(acac)(CO)$_2$, B = Rh$_4$(CO)$_{12}$, C = [Rh(CO)$_2$Cl]$_2$. [b] Isolated yields. [c] P(OPh)$_3$ (3 equiv to catalyst) was added as ligand. [d] PPh$_3$ (3 equiv to catalyst) was added as ligand.

**Table 2.** Silicon-Initiated Carbonylative Carbotricyclization of **7**[a]

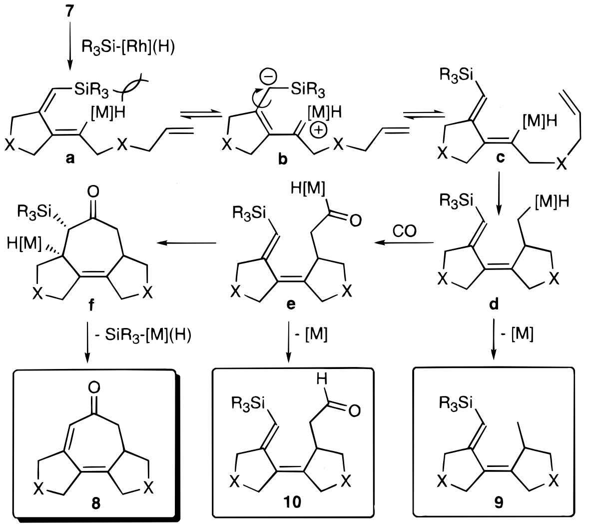
| Entry | Endiyne | Time (h) | Product | Yield (%)[b] |
|---|---|---|---|---|
| |  | |  | |
| 1 | **7b**: R = CH$_3$ | 21 | **8b** | 89 |
| 2 | **7c**: R = CH$_2$Ph | 38 | **8c** | 87 |
| 3 | **7d**: R = Ac | 39 | **8d** | 81 |
| 4 | **7e**: R = H | 20 | **8e** | 62 |
| 5 | **7f**: $\overset{\frown}{R\quad R}$ = C(CH$_3$)$_2$ | 38 | **8f** | 65 |
| |  | |  | |
| 6 | **7g**: X = NTs | 27 | **8g** | 85 |
| 7 | **7h**: X = O | 48 | **8h** | 50 |

[a] Reaction was run with an endyne (0.25 mmol), PhMe$_2$SiH (0.13 mmol) and Rh(acac)(CO)$_2$ (1 mol %) in THF (17 mL) under CO (1 atm). [b] Isolated yield.

*t*-BuMe$_2$SiH does not give any conversion after 96 h. Accordingly, PhMe$_2$SiH is the best hydrosilane for this process so far examined.

Next, other than ester groups that were included in **8a**, we looked at the heteroatom and functional group tolerance of this novel carbotricyclizaton process. Thus, various substrates containing ether, ester, hydroxyl, and sulfonamide groups were employed for the reaction. Results are summarized in Table 2. As Table 2 shows, these functional groups and heteroatoms are well tolerated in this reaction to give the corresponding expected fused 5−7−5 tricyclic compounds **8** in good to excellent isolated yields. The reaction of **7g** gives **8g** that contains two fused bispyrrolidine rings in 85% isolated yield (entry 6), while the reaction of **7h** that contains dipropargyl ether as well as propargyl allyl ether moieties is sluggish to give **8h** in 50% yield after 48 h (entry 7).

**Scheme 1**



A possible mechanism for this novel carbonylative carbotricyclization is proposed in Scheme 1. The reaction begins with the insertion of the terminal alkyne moiety into the Si−[Rh] bond of the hydrosilane−Rh oxidative adduct. Carbocyclization then occurs to give (*Z*)-dienyl[Rh](H) intermediate **a**. Because of the steric hindrance between the vinylsilane and the vinyl−[Rh] moieties, **a** isomerizes to **c** via **b** through the "Ojima−Crabtree mechansim".[5] Subsequent carbocyclization to **d**, followed by reductive elimination, should give **9**. The CO insertion to **d** gives acyl−[Rh](H) intermediate **e**. Reductive elimination of **e** should yield aldehyde **10**. Carbocyclization of **e** gives tricyclic intermediate **f** that has the silicon and the [Rh] moieties in syn positions. Subsequent $\beta$-silyl elimination[7e,9] should afford the fused 5−7−5 tricyclic product **8** and regenerate the active catalyst species, R$_3$-Si−[Rh](H). The proposed mechanism can nicely accommodate the observed three products under non-optimized conditions, dilution effects,[10] and the fact that only substoichiometric hydrosilane is needed for this novel process.

Further studies on the scope and limitation of this novel carbonylative carbotricyclization process as well as its applications to the syntheses of biologically active compounds are actively underway in these laboratories.

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**Supporting Information Available:** Experimental procedures, spectral data for all new compounds **7a**−**g**, **8a**−**h**, **9a**, and **10a** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) The observed remarkable dilution effects on the product selectivity appears to be ascribed to the relative concentration of CO in solution to those of catalyst and hydrosilane, i.e., the relative concentration of CO is higher in dilute solution if the amounts of the catalyst and hydrosilane are kept constant. As Scheme 1 illustrates, the reductive elimination of intermediate **d** can be suppressed by higher CO concentration, directing the reaction to the formation of intermediate **e**. Also, the reductive elimination of **d** and **e** is believed to be significantly accelerated by another molecule of hydrosilane.[5a,7] Thus, the low concentration of hydrosilane should slow the reductive elimination in these two steps, leading to the selective formation of intermediate **f** and then the product **8**.