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# A Novel Approach to α-Silylmethylene-β-lactams via Rh-catalyzed Silylcarbonylation of Propargylamine Derivatives

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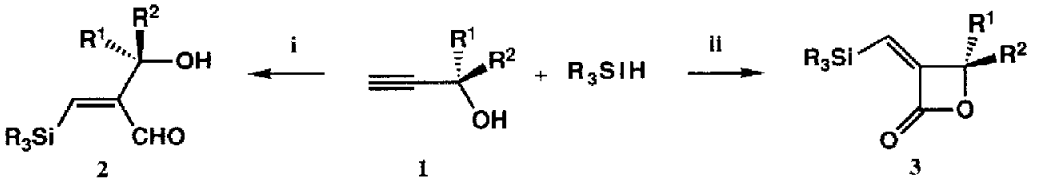
**Summary**: α-Silylmethylene-β-lactams are successfully constructed by the one-pot coupling of a substituted propargylamine derivative, a triorganosilane, and CO with the catalysis of $Rh_4(CO)_{12}$ and DBU.

We previously reported rhodium-catalyzed silylformylation of acetylenic compounds as the first synthetic method of 3-silylpropenals represented by the formal addition of triorganosilyl and formyl groups to the acetylenic bond.[1] Application of this protocol to propargyl type alcohols (**1**) also provides a general route to the corresponding 2-hydroxyalkyl-3-silylpropenals (**2**) in high yields; however, it is quite remarkable that the co-presence of base attains a one-pot cyclocarbonylation to form α-silylmethylene-β-lactones **3** in the reaction of substituted **1** under similar conditions as shown in scheme 1.[2] This unusually facile procedure to construct a four-membered ring prompts us to examine the silylformylation of propargylamine derivatives shown in eq. 1, in which the potential formation of **5** is of keen interest from the synthetic point of view. The α-alkylidene-β-lactam unit is a common structural feature included in potent β-lactamase inhibitors asparenomycins,[3] Ro 15-1903,[4] and 6-[(Z)-methoxymethylene]penicillanic acid.[5] Although a number of methods have been reported for the synthesis of this unit,[6] only a few utilized the carbonylation of certain amine derivatives.[7] We wish to describe here successful results of rhodium-catalyzed silylformylation of propargylamine derivatives, in which a series of α-silylmethylene-β-lactams is easily available by one-pot procedure.

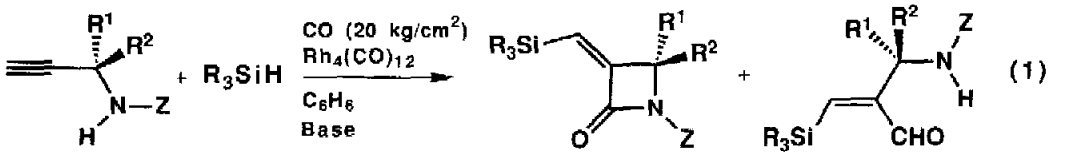
Previous reports suggest that the nonsubstituted amino group included in the starting substrates must be modified appropriately in the hydroformylation of alkenes because it participates in the consecutive




2 1 3

**Scheme 1**

**i, CO 20 kg/cm$^2$, $Rh_4(CO)_{12}$, $C_6H_6$**
**ii, CO 30 kg/cm$^2$, $Rh_4(CO)_{12}$, $C_6H_6$, Base**




4 5 6

reaction of the products under the reaction conditions[8] except for a few intramolecular version.[9] N-(1-Ethynylcyclohexyl)-p-toluenesulfonamide (**4b**) was chosen as a model compound for the β-lactam synthesis on the basis of our knowledge of the formation of **3**. Thus, carbonylation of **4b** gave two types of product, β-lactam **5b** (40 %) and 3-silylpropenal **6b** (21 %) with the aid of $Rh_4(CO)_{12}$ and $Et_3N$ at 100 °C. Isolated **6b** was not converted to **5b** under similar conditions. This suggests that two products **5b** and **6b** are formed competitively. The presence of a base such as $Et_3N$ is essential for the formation of **5b**. In fact, **6b** is the sole product in the silylformylation of **4b** under conditions excluding $Et_3N$. In contrast to the successful control of the formation of **6b**, the ratio of **5b** to **6b** was slightly improved when 10 mol % of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was added in place of $Et_3N$; it was also remarkably affected by the reaction temperature. The reaction at lower temperature (25 °C or 50 °C) apparently depressed the formation of **6b** despite an appreciable drop in the reaction rate. The exclusive formation of β-lactam **5b'** was achieved by a combined use of bulkier $^tBuMe_2SiH$ and DBU. This optimal combination of reagents realized the exclusive formation of β-lactam **5a'** in the carbonylation of **4a** under similar conditions. Other N-propargylic p-toluenesulfonamides **4d** and **4e** also gave the corresponding β-lactams **5d** and **5e**, respectively, in the one-pot procedure. On the other hand, N-propargylic carbamate **4c** and sterically less hindered sulfonamide **4f** gave a mixture of **5** and **6** even with the participation of $^tBuMe_2SiH$ and DBU. These results suggest that the path to formation of β-lactam **5** is strongly affected by the steric requirement of substrates as well as nucleophilicity of the nitrogen atom or the protonic character of N-H. Propargylamine derivatives without substituents on the propargyl carbon **4g**, **4h**, and **4i** were readily silylformylated to give **6g**, **6h**, and **6i**, respectively, in the absence of base at 25 °C; however, no attractive products were obtained in the presence of DBU. The results are summarized in Table 1.

The most notable feature of these reactions is that the $R_3Si$ group always attacks the terminal carbon of acetylenes to give **5** and/or **6**. Especially, the present one-pot procedure to form **5** provides a novel method for the synthesis of β-lactam skeletons from propargylamine derivatives, triorganosilanes, and CO. Unfortunately, a certain type of **4** does not give any cyclized product **5**; however, propenal **6** could be lead to β-lactam **5** by two additional steps, oxidation of the formyl group to give carboxylic acid and subsequent dehydrative cyclization with the aid of dicyclohexylcarbodiimide and 4-pyrrolidinopyridine.[10] Further studies are now in progress.

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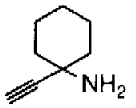
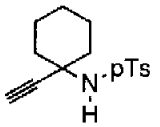
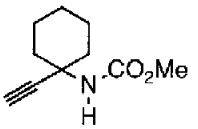
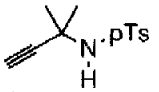
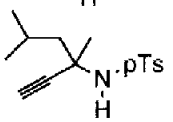
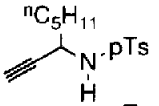
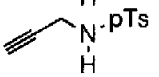
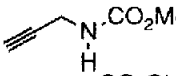
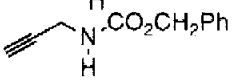
Table 1. Silylcarbonylation of **4**.[11]

| Entry | 4 | R3SiH | Conditions: Temp (°C) | Time (h) | Base [a] | Products [b]: 5 | Yield (%) | 6 | Yield (%) |
|---|---|---|---|---|---|---|---|---|---|
| 1 | **4a**  | $^t$BuMe$_2$SiH | 100 | 2 | DBU | **5a'** | 64 | -- | |
| 2 | **4b**  | Me$_2$PhSiH | 25 | 12 | -- | -- | | **6b** | 73[c] |
| 3 | | Me$_2$PhSiH | 25 | 12 | DBU | **5b** | 57 | **6b** | 2[d] |
| 4 | | Me$_2$PhSiH | 50 | 5 | DBU | **5b** | 75 | **6b** | 2[e] |
| 5 | | Me$_2$PhSiH | 100 | 2 | Et$_3$N | **5b** | 40 | **6b** | 21 |
| 6 | | Me$_2$PhSiH | 100 | 2 | DBU | **5b** | 55 | **6b** | 13 |
| 7 | | $^t$BuMe$_2$SiH | 100 | 2 | DBU | **5b'** | 81 | -- | |
| 8 | **4c**  | Me$_2$PhSiH | 100 | 2 | DBU | -- | | **6c** | 68[c] |
| 9 | | $^t$BuMe$_2$SiH | 100 | 2 | DBU | **5c'** | 28 | **6c'** | 19[c] |
| 10 | **4d**  | Me$_2$PhSiH | 100 | 2 | DBU | **5d** | 80 | -- | |
| 11 | **4e**  | Me$_2$PhSiH | 100 | 2 | DBU | **5e** | 65 | -- | |
| 12 | **4f**  | $^t$BuMe$_2$SiH | 100 | 2 | DBU | **5f'** | 14 | **6f'** | 65[f] |
| 13 | **4g**  | Me$_2$PhSiH | 25 | 12 | -- | -- | | **6g** | 81[g] |
| 14 | | Me$_2$PhSiH | 100 | 2 | DBU | -- | | -- | |
| 15 | **4h**  | Me$_2$PhSiH | 25 | 12 | -- | -- | | **6h** | 63[c] |
| 16 | **4i**  | Me$_2$PhSiH | 25 | 12 | -- | -- | | **6i** | 75[c] |

[a] The quantity of DBU was reduced to 0.1 equivalent. [b] See reference 12. [c] *Z* form only.
[d] Unchanged **4b** (29 %) was recovered. [e] Unchanged **4b** (20 %) was recovered.
[f] *Z*:*E* = 1:1.5. [g] *Z*:*E* = 1:2.

**References and notes**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11. A typical procedure is as follows: Into a glass tube containing $Rh_4(CO)_{12}$ (0.004 g, 0.005 mmol), **4b** (0.463 g, 1.67 mmol), and benzene (9 ml) saturated by CO were successively added at -70 °C under CO atmosphere by syringe $^tBuMe_2SiH$ (0.190 g, 1.64 mmol) in $C_6H_6$ (1 ml), and DBU (0.025 g, 0.16 mmol) in $C_6H_6$ (0.5 ml). The tube was put in a 100 ml of stainless steel autoclave and then the reactor was pressurized by CO to 20 kg/cm$^2$. The contents were stirred for 2 h at 100 °C and cooled to ambient temperature. After excess CO was purged in a hood, the reaction mixture was treated by the ordinary procedure to give **5b'** (81 %).
12. All these compounds were identified by $^1H$ NMR, $^{13}C$ NMR, and IR spectra. The structure of **5** was readily deduced by the presence of the diagnostic $\nu_{C=O}$ absorption around 1770 cm$^{-1}$ in the IR spectra. All new compounds gave satisfactory combustion analyses.


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