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Ru-Catalyzed Cyclocarbonylation of α- and β-Allenic Sulfonamides: Synthesis of γ- and δ-Unsaturated Lactams

Suk-Ku Kang,*,† Kwang-Jin Kim,† Chan-Mo Yu,† Jeong-Wook Hwang,‡ and Young-Kyu Do‡

Department of Chemistry and BK-21 School of Molecular Science, Sungkyunkwan University, Suwon 440-746, Korea, and Department of Chemistry, and BK-21 School of Molecular Science, Korea Advanced Institute of Science and Technology, Taejon 305-701, Korea

skkang@chem.skku.ac.kr.

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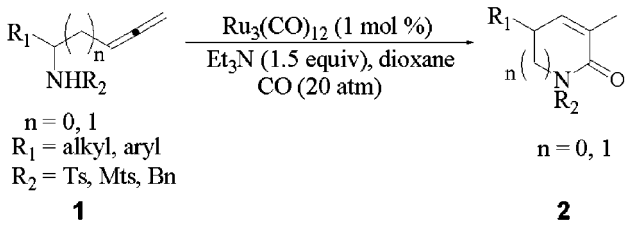
ABSTRACT



The Ru-catalyzed cyclocarbonylation of α- or β-allenic sulfonamides in the presence of $Ru_3(CO)_{12}$ (1 mol %) and Et_3N (1.5 equiv) under CO atmosphere (20 atm) in dioxane at 100 °C for 9 h gave heterocyclic γ- and δ-unsaturated lactams in good yields.

The palladium-catalyzed coupling reaction of allene-substituted alcohols and amine has received much attention in recent years.[1] The palladium-catalyzed carbonylative cyclization of various allenic alcohols and sulfonamides has been known[2,3] to be an efficient entry to heterocyclic ring systems. Recently Takahashi et al.[4] used a ruthenium catalyst in carbonylative coupling and reported that a successful cyclocarbonylation of allenic alcohols to form γ- and δ-lactones was accomplished. Alternatively Murai et al.[5] reported the Ru-catalyzed carbonylative [4 + 1] cycloaddition of α,β-unsaturated imines with carbon monoxide to form α,β-unsaturated γ-lactams. As an extension of our research efforts to utilize allenic sulfonamides in carbonylative cyclization,[6] we attempted to investigate the $Ru(CO)_3$-catalyzed cyclocarbonylation of α- and β-allenic sulfonamides to form γ- and δ-unsaturated lactams.

To find an optimum condition for the cyclization, a series of experiments were performed; the results are shown in Table 1. For the cyclization reaction of **1a**, the catalysts tested were $Ru_3(CO)_{12}$, $[RuCl_2(CO)_3]_2$, $RuCl(PPh_3)_3$, and $Ru(CO)H_2(PPh_3)_3$. Both $Ru_3(CO)_{12}$ and $[RuCl_2(CO)_3]_2$ were equally effective for the cyclization reaction of **1a**. The use of Ru_3-

† Sungkyunkwan University.
‡ Korea Advanced Institute of Science and Technology.

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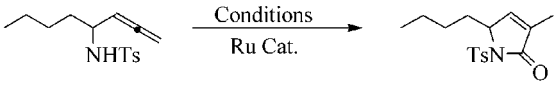
Table 1. Ru-Catalyzed Cyclocarbonylation of α-Allenic Sulfonamide **1a**



1a **2a**

entry	catalysts (mol %)	base (equiv)	solvent	CO pressure (atm)	isolated yield (%)
1	$Ru_3(CO)_{12}$ (1)	Et_3N (1.5)	dioxane	10	42
2	$Ru_3(CO)_{12}$ (3)	Et_3N (3.0)	dioxane	10	58
3	$Ru_3(CO)_{12}$ (5)	Et_3N (3.0)	dioxane	15	82
4	$Ru_3(CO)_{12}$ (5)	Et_3N (3.0)	THF	20	45
5	$Ru_3(CO)_{12}$ (5)	Et_3N (1.5)	CH_3CN	20	53
6	$Ru_3(CO)_{12}$ (5)	K_2CO_3 (3.0)	DMF	20	0
7	$Ru_3(CO)_{12}$ (5)	Et_3N (3.0)	DMF	20	43
8	$Ru_3(CO)_{12}$ (1)	Et_3N (1.5)	dioxane	20	85
9	$[RuCl_2(CO)_3]_2$ (1)	Et_3N (1.5)	dioxane	20	85
10	$RuCl_2(PPh_3)_3$ (1)	Et_3N (1.5)	dioxane	20	61
11	$Ru(CO)H_2(PPh_3)_3$ (1)	Et_3N (1.5)	dioxane	20	0

$(CO)_{12}$ or $[RuCl_2(CO)_3]_2$, Et_3N as a base, and dioxane as solvent under 20 atm pressure of carbon monoxide afforded γ-unsaturated lactam **2a** in 85% yield. (entries 8 and 9 in Table 1).[7] Nevertheless, we chose $Ru_3(CO)_{12}$ as the catalyst for further studies.

Table 2. $Ru_3(CO)_{12}$-Catalyzed Cyclocarbonylation of Allenic Sulfonamide Derivatives

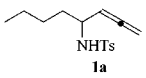
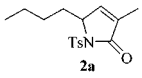
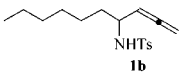
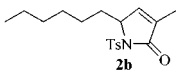
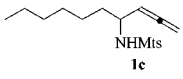
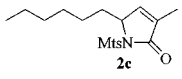
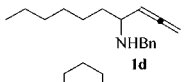
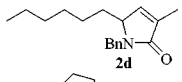
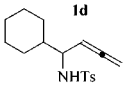
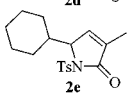
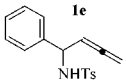
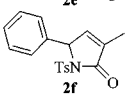
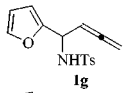
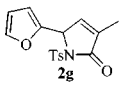
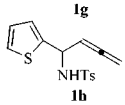
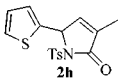
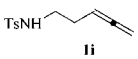
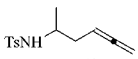
entry	substrate	time (h)	product	isolated yield (%)
1	 **1a**	9	 **2a**	85
2	 **1b**	9	 **2b**	91
3	 **1c**	9	 **2c**	68
4	 **1d**	9	 **2d**	54
5	 **1e**	16	 **2e**	70
6	 **1f**	16	 **2f**	80
7	 **1g**	12	 **2g**	95
8	 **1h**	14	 **2h**	76
9	 **1i**	9	 **2i**	81
10	 **1j**	9	 **2j**	80

Table 2. The α-allenic sulfonamide **1a** reacted in the presence of $Ru_3(CO)_{12}$ (1 mol %) in dioxane at 100 °C under CO (20 atm) for 9 h to produce the cyclized unsaturated γ-lactam **2a** in 85% yield (entry 1 in Table 2). Under the same conditions the α-allenic 2,4,6-trimethylbenzenesulfonamide **1c** was smoothly cyclized to **2c** in 68% yield (entry 3). For the α-allenic benzylamine **1d** the reaction proceeded to provide **2d** in 54% yield (entry 4). Treatment of cyclohexyl-substituted α-allenic sulfonamide **1e** under the same conditions gave the lactam **2e** in 70% yield (entry 5). With phenyl-, 2-furyl-, and 2-thienyl-substituted sulfonamides **1f**, **1g**, and **1h** as substrates, the γ-lactams **2f**, **2g**, and **2h** were obtained in 80%, 95%, and 76% yields, respectively (entries 6−8).

For the compound **2f**, the structure was unambiguously confirmed by X-ray crystallography (Figure 1). This protocol was extended to β-allenic sulfonamide **1i**. The reaction of **1i** with $Ru_3(CO)_{12}$ catalyst in the same reaction conditions

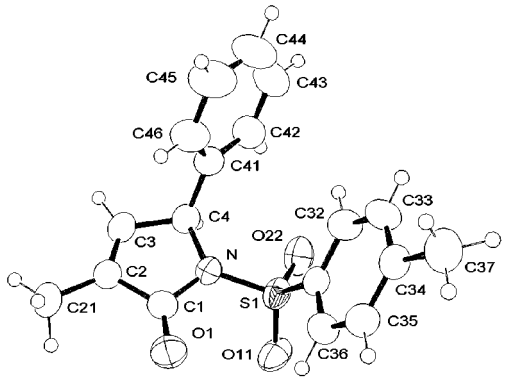
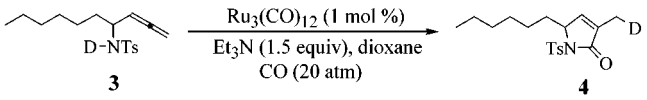


Figure 1. ORTEP drawing of **2f**.

afforded the unsaturated δ-lactam **2i** in 81% yield (entry 9). Alternatively, for α-methyl-substituted β-allenic sulfonamides **1j** the cyclocarbonylation under Ru-catalysis afforded α-methyl-substituted δ-lactam **2j** in 80% yield (entry 10).

To confirm the proposed mechanism we have conducted studies on the carbocyclization of the deuterium-substituted α-allenic sulfonamide **3** by means of 500 MHz ^{1}H NMR spectrometry and high resolution mass spectrometry. It was found that the deuterium was totally transferred to the product lactam **4**[8] (Scheme 1).

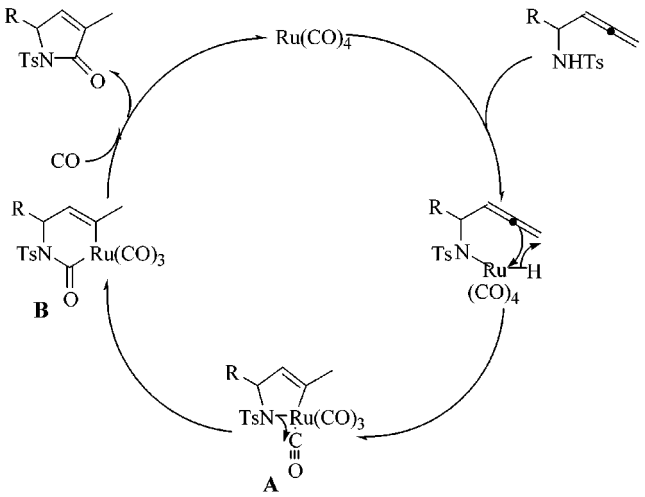
Scheme 1



3 **4**

For the formation of lactams **2** by the Ru-catalyzed cyclocarbonylation, the plausible mechanism is shown in Scheme 2. It is presumed that oxidative insertion of Ru(CO)$_4$ to the N−H bond of the NHTs group in compound **1** followed by syn-addition of the Ru−H bond to the terminal allene produces the intermediate **A**. Carbonyl insertion to the N−Ru bond gives the intermediate **B**, which reacts with CO to provide the product lactam with liberation of Ru(CO)$_4$ (Scheme 2).

Scheme 2



In conclusion, the Ru-catalyzed cyclocarbonylation of allenic sulfonamides under CO (20 atm) to form γ- or δ-lactams was accomplished successfully.

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Supporting Information Available: Typical experimental procedures and characterization for **2a**−**i** and **2j**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(7) **Typical Procedure.** A stainless autoclave was charged with allenic sulfonamide **1a** (70 mg, 0.25 mmol), 1.4-dioxane (3 mL), triethylamine (38 mg, 0.38 mmol), and $Ru_3(CO)_{12}$ (1.6 mg, 1 mol %), and the system was flushed with 20 atm of CO three times. It was then pressurized to 20 atm, and the reaction mixture was stirred at 100 °C for 9 h. The mixture was cooled and then evaporated in vacuo. The crude product was separated by SiO_2 column chromatography (hexanes/EtOAc, 1:5) to give the product **2a** (63 mg, 85%). **2a**: colorless oil; IR (neat) 3056, 2987, 1724, 1424, 1359, 1266, 1171 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.85 (t, 3H, J = 7.63 Hz), 1.09 (m, 2H), 1.28 (m. 2H), 1.81 (t, 3H, J = 1.76 Hz), 1.83 (m, 1H), 2.14 (m, 1H), 2.43 (s, 3H), 4.73 (m, 1H), 6.82 (t, 1H, J = 1.76 Hz), 7.32 (d, 2H, J = 8.21 Hz), 7.97 (d, 2H, J = 8.21 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 145.5, 145.5, 136.8, 134.3, 130.2, 128.7, 63.0, 32.7, 26.6, 23.2, 22.4, 14.6, 11.4; HRMS calcd for $C_{16}H_{21}NO_3S$ 307.1242, found 307.1236.

(8) Spectral and physical data of **3** and **4**. **3**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.85 (t, 3H, J = 7.63 Hz), 1.20 (m, 8H), 1.50 (m, 2H), 2.42 (s, 3H), 3.80 (m, 1H), 4.63 (m, 1H), 4.72 (m, 1H), 4.96 (m, 1H), 7.30 (d, 2H, J = 8.21 Hz), 7.75 (d, 2H, J = 8.21 Hz); HRMS calcd for $C_{17}H_{24}DNO_2S$ 308.1668, found 308.1646. **4**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.87 (t, 3H, J = 7.63 Hz), 1.06 (m, 1H), 1.12 (m, 1H), 1.22 (m, 6H), 1.81 (t, 2H, J = 1.76 Hz), 1.82 (m, 1H), 2.13 (m, 1H), 2.43 (s, 3H), 4.73 (m, 1H), 6.81 (t, 1H, J = 1.76 Hz), 7.32 (d, 2H, J = 8.21 Hz), 7.97 (d, 2H, J = 8.21 Hz); HRMS calcd for $C_{18}H_{24}DNO_3S$ 336.1617, found 336.1616.