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Transition metal-catalyzed ring-opening, substitution, and cyclopropanation reactions via vinylcarbene complexes generated from *O*-propargyl thiocarbamates

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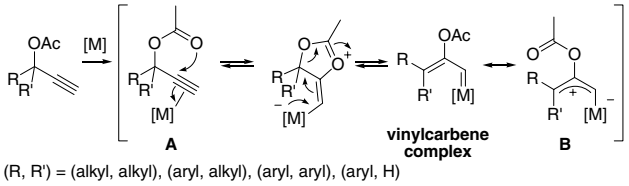
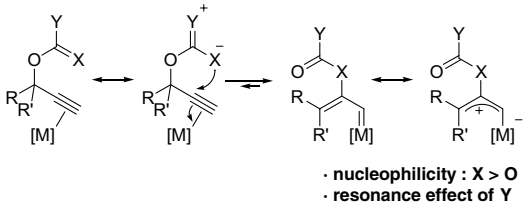
Abstract—We have developed various transition metal-catalyzed vinylcarbene transfer reactions, such as ring-opening, substitution, and cyclopropanation reactions, using *O*-propargyl thiocarbamates as carbene precursors. Platinum, ruthenium, rhodium, and gold complexes are effective for vinylcarbenoid formation. The highly nucleophilic nature and resonance effect of a thiocarbamoyl moiety readily permit the rearrangement of a thiocarbamoyl moiety from a propargylic position to an adjacent alkynyl carbon to give the intermediary vinylcarbene complexes.

Vinylcarbene transfer reactions have provided efficient access to important substructures of complex molecules in organic synthesis.[1] We have exploited the transition metal-catalyzed vinylcarbene transfer reactions, such as cyclopropanation,[2] ring-opening,[3] substitution,[3] and carbene shift reactions,[4] using propargyl carboxylates as vinylcarbene precursors.[5] 1,1-Dialkyl- or 1,1-diaryl-2-propynyl carboxylates and 1-aryl-2-propynyl carboxylates were applicable to catalytic carbene transfer reactions; however, 1-alkyl-2-propynyl and simple propargyl carboxylates did not work as vinylcarbene precursors (Scheme 1). We considered that the lack of reactivity of 1-alkyl-2-propynyl and simple propargyl carboxylates was probably due to the low stability of allyl cationic intermediates **B** (resonance form of a vinylcarbene complex), which rearranged back to alkyne complexes **A** through the equilibrium. We envisioned that a stronger nucleophilic X atom[6] than an oxygen atom and/or the resonance effect of Y surpass the limitation of carbene transfer reactions using propargyl carboxylates (Scheme 2). In this Letter, we wish to report transition metal-catalyzed vinylcarbene transfer reactions using *O*-propargyl thiocarbamates (X = S, Y = NMe_2 in Scheme 2) as vinylcarbene precursors.



Scheme 1.

When we started with the ruthenium-catalyzed ring-opening reaction of 2-methoxyfuran[3] using *O*-3-butyn-2-yl *N*,*N*-dimethylthiocarbamate (**1a**, X = S, Y = NMe_2) as a vinylcarbene precursor, we were pleased to find that the ring-opening reaction of 2-methoxyfuran[7] with **1a** took place to give triene **2a** and **2a′** in 62% total yield (**2a**/**2a′** = 82:18), which included their 6*Z*- and 6*E*-isomers (Eq. 1). On the other



Scheme 2.

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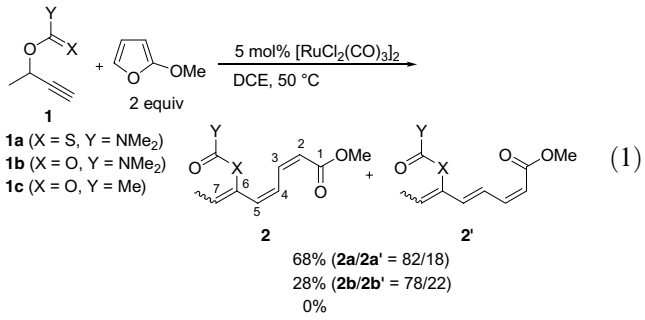
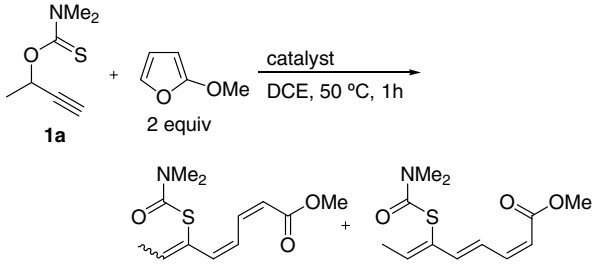


(1)

hand, 3-butyn-2-yl *N*,*N*-dimethylcarbamate **1b** (X = O, Y = NMe_2) instead of **1a** afforded a lower yield of ring-opening product (28% total yield). The reaction of acetate **1c** (X = O, Y = Me) did not take place, **1c** being recovered intact. These results indicate that the higher nucleophilicity of the sulfur atom as well as resonance of the *N*,*N*-dimethylamino moiety work effectively for the efficient generation of a vinylcarbene complex intermediate. Methoxyfuran with **1a**.

Next, we examined the ring-opening reaction with **1a** using other transition metal complexes as catalysts. The results are summarized in Table 1. Effective catalysts other than $[RuCl_2(CO)_3]_2$ include $[RuCl_2(p\text{-cymene})]_2$, $[Rh(OAc)_2]_2$, $AuCl_3$, $AuCl(PPh_3)/AgSbF_6$, and $PtCl_2$. It is noted that $[Rh(OAc)_2]_2$, which did not catalyze the reaction of propargyl acetates,[2] acts efficiently as a catalyst to give the ring-opening products **2a** and **2a′** in 50% total yield (entry 3). Among screening catalysts shown in Table 1, $PtCl_2$ was the catalyst of choice. Moreover, THF as a solvent gave better yields of products when $PtCl_2$ was used as a catalyst. Results from the platinum-catalyzed ring-opening reaction of 2-methoxyfuran with several *O*-propargyl thiocarbamates are shown in Table 2.[8] Most alkyl-substituted *sec*-*O*-propargyl thiocarbamates afforded good to excellent yields of trienes, while bulky *t*-butyl-substituted thiocarbamate **1g** gave the lowest yield of **2g** in 25% yield together with *S*-allenyl thiocarbamate **3g** (37%) (entry 5).[9] The reaction of *O*-(1-arylpropynyl) thiocarbamates **1h** and **1i** smoothly proceeded to give **2h** and **2i** in good yields with their stereoisomers (entries 6 and 7). In the reaction of the simple *O*-propargyl thiocarbamate **1j**, triene **2j** was obtained in 16% yield together with triene **4j** (7%) and 1,3-cyclohexadiene **5j** (3%) (Scheme 3). It is assumed that the products **4j** and **5j** were produced via dimerization of a vinylcarbenoid **C**, in which product **5j** was produced by the 6π-electrocyclization of initially formed *cis*-**4j**. We also examined the catalytic reaction of related heterocyclic compounds with **1a**. The reaction of 2-methylfuran with **1a** gave the corresponding trienone **6a** and **6a′** in 44% yield in a ratio of 43:57 (Eq. 2). On the other hand, when the reaction of **1a** with pyrrole was carried out, two types of substitution products **7a-H** and **8a-H** were obtained in 43% yield (**7a-H**/**8a-H** = 83:17), without ring-opening products (Eq. 3). The reaction of **1a** with *N*-methylpyrrole also gave the corresponding substitution products **7a-Me**/**8a-Me** in 36% yield.[10] When the reactions of **1a** with styrene and ethyl vinyl ether as a vinylcarbene acceptor were

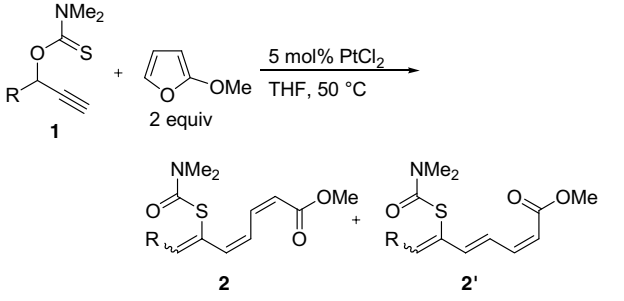
Table 1. Transition metal-catalyzed ring-opening reactions of 2-methoxyfuran with **1a**



Entry	Catalyst	Yield[a] (%) (**2a**/**2a′**)
1	$[RuCl_2(CO)_3]_2$	62 (82:18)
2	$[RuCl_2(p\text{-cymene})]_2$	65 (31:69)
3[b]	$[Rh(OAc)_2]_2$	50 (68:32)
4[c]	$AuCl_3$	68 (61:39)
5[b]	$AuCl(PPh_3)$	73 (72:28)
6	$AuCl(PPh_3)/AgSbF_6$	34 (72:28)
7	$PtCl_2$	75 (75:25)
8[d]	$PtCl_2$	82 (69:31)

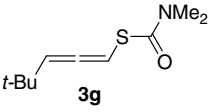
Reaction conditions: **1a** (0.50 mmol), 2-methoxyfuran (1.0 mmol), catalyst (0.025 mmol) in DCE (5.0 mL) at 50 °C for 1 h.
[a] Inseparable olefin regioisomer (2–9%) of **2a** was observed in every cases.
[b] For 2 h.
[c] For 0.5 h.
[d] In THF (5.0 mL) for 0.5 h.

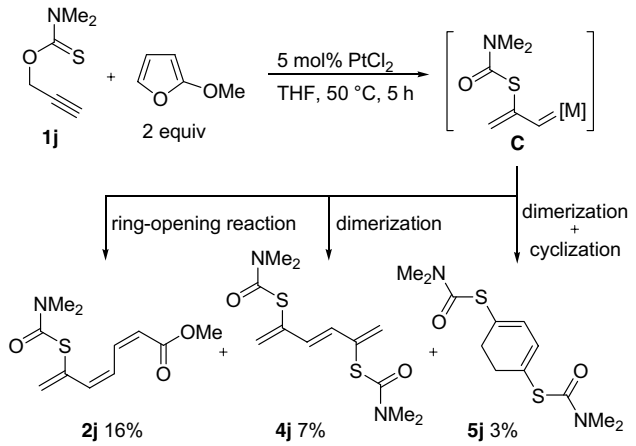
Table 2. $PtCl_2$-catalyzed ring-opening reactions of 2-methoxyfuran with *O*-propargyl thiocarbamate **1**



Entry	R	Time (h)	Yield[a] (%) (**2**/**2′**)
1	Me (**1a**)	0.5	82 (69:31)
2	*n*-Propyl (**1d**)	0.5	68 (59:41)
3	*i*-Propyl (**1e**)	0.5	90 (58:42)
4	Cyclohexyl (**1f**)	0.5	81 (63:37)
5	*t*-Butyl (**1g**)	20	25 (100:0)[b]
6	Ph (**1h**)	0.5	73 (72:28)
7	*p*-Cl–C_6H_4 (**1i**)	1.5	63 (63:37)

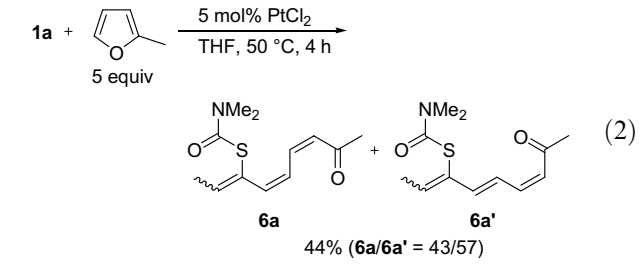
Reaction conditions: *O*-propargyl thiocarbamate **1** (0.50 mmol), 2-methoxyfuran (1.0 mmol), $PtCl_2$ (0.025 mmol) in THF (5.0 mL) at 50 °C.
[a] Inseparable olefin regioisomers (2–27%) of **2** and **2′** were included.
[b] Allene **3g** was obtained in 37% yield.



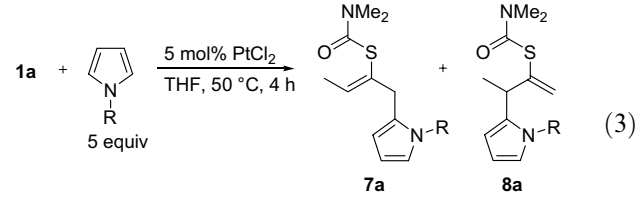


Scheme 3.

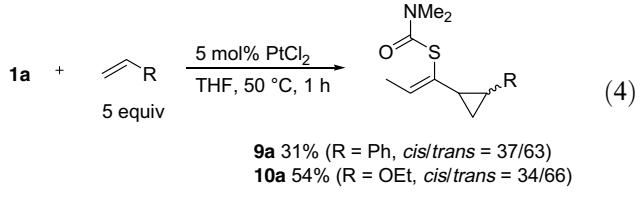
carried out, the corresponding cyclopropane **9a** and **10a**, respectively, were obtained in moderate yields (Eq. 4). These results also indicate the generation of a vinylcarbene complex from an alkyl-substituted *sec*-*O*-thiocarbamate.



(2)



(3)



(4)

In conclusion, we have developed $PtCl_2$-catalyzed vinylcarbene transfer reactions with 1-alkyl-2-propynyl and 2-propynyl thiocarbamates as vinylcarbene precursors. Ruthenium, rhodium, and gold complexes can also be employed as catalysts. By introducing a thiocarbamoyl group that involves a highly nucleophilic sulfur atom and the resonance-capable nitrogen atom, the nucleophilic migration step of a thiocarbonyl group is facilitated and therefore provides effectively a vinylcarbene species. The expanded reactivity of propargyl substrates as vinylcarbene precursors might find some application in the construction of important substructures of requisite molecules, and these approaches are under investigation in our laboratory.

Acknowledgments

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8. A representative experimental procedure of Pt-catalyzed ring-opening reactions is shown as follows: A catalytic amount of $PtCl_2$ (6.5 mg. 0.026 mmol) was placed in a flame-dried Schlenk flask under N_2. Propargyl thiocarbamate **1e** (93 mg, 0.50 mmol) and 2-methoxyfuran (92 μL, 1.0 mmol) in anhydrous THF (5.0 mL) were added to the flask at room temperature. After the mixture was stirred at 50 °C for 0.5 h, the reaction mixture was cooled to room temperature. The resulting solution was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 10:1). Compound **2e** (2*Z*,4*Z*): A pale yellow oil (52% yield, dr = 89:11); IR (neat) 1092, 1173, 1363, 1440, 1615, 1666, 1711, 2961 cm^{-1}; major isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 1.05 (d, $J = 6.8$ Hz, 6H), 2.92–3.03 (m, 7H), 3.72 (s, 3H), 5.73 (d, $J = 10.8$ Hz, 1H), 5.96 (d, $J = 10.8$ Hz, 1H), 6.28 (d, $J = 10.4$ Hz, 1H), 7.24 (dd, $J = 10.8$, 10.8 Hz, 1H), 7.32 (dd, $J = 10.8$, 10.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.2, 32.7, 36.8 (br s), 37.1 (br s), 51.1, 118.0, 125.4, 125.5, 139.6, 140.9, 147.2, 165.8, 167.0. Minor isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 0.98 (d, $J = 6.4$ Hz, 6H), 2.92–3.02 (m, 7H), 3.73 (s, 3H), 5.76 (d, $J = 11.0$ Hz, 1H), 5.97 (d, $J = 11.0$ Hz, 1H), 6.28 (d, $J = 10.4$ Hz, 1H), 7.13 (dd, $J = 11.0$, 11.0 Hz, 1H), 7.39 (dd, $J = 11.0$, 11.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.0, 29.8, 36.8 (br s), 37.1 (br s), 51.1, 118.1, 121.4, 126.3, 135.4, 140.9, 153.7, 166.6, 167.0. Anal. Calcd for $C_{14}H_{21}NO_3S$: C, 59.34; H, 7.47. Found: C, 59.34; H, 7.29. Compound **2e′** (2*Z*,4*E*): A pale yellow solid (38% yield, dr = 89/11); mp = 80.0–81.5 °C; IR (KBr) 1092, 1173, 1364, 1440, 1615, 1665, 1711, 2924 cm^{-1}; major isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 1.04 (d, $J = 6.8$ Hz, 6H), 2.94–3.15 (m, 7H), 3.72 (s, 3H), 5.64 (d, $J = 11.2$ Hz, 1H), 6.30 (d, $J = 9.2$ Hz, 1H), 6.62 (d, $J = 14.8$ Hz, 1H), 6.64 (dd, $J = 11.2$, 11.2 Hz, 1H), 7.78 (dd, $J = 11.2$, 14.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.1, 33.0, 37.0 (br s), 37.3 (br s), 51.1, 116.7, 125.7, 128.6, 143.5, 144.6, 149.6, 164.7, 166.7. Minor isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 1.08 (d, $J = 6.8$ Hz, 6H), 2.94–3.15 (m, 7H), 3.72 (s, 3H), 5.69 (d, $J = 10.8$ Hz, 1H), 6.10 (d, $J = 10.4$ Hz, 1H), 6.69 (d, $J = 10.8$, 10.8 Hz, 1H), 6.92 (d, $J = 15.1$ Hz, 1H), 7.85 (dd, $J = 10.8$, 15.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.5, 28.9, 36.9 (br s), 37.3 (br s), 51.0, 117.3, 124.7, 128.1, 136.5, 144.4, 156.4, 166.4, 166.4. Anal. Calcd for $C_{14}H_{21}NO_3S$: C, 59.34; H, 7.47. Found: C, 59.33; H, 7.32.
9. *t*-Butyl-substituted thiocarbamate **1g** in solution was gradually converted to the allenyl isomer **3g** even at room temperature. Thermal isomerization of *O*-propargyl thiocarbamates and propargyl dithiocarbonates to allenyl compounds has been reported. See: (a) Banert, K.; Fendel, W.; Schlott, J. *Angew. Chem., Int. Ed.* **1998**, *37*, 3289; (b) Banert, K.; Schlott, J. *Tetrahedron* **2000**, *56*, 5413.
10. Although the precise mechanism for the formation of **8a** is unclear at present, the electrophilic substitution of pyrrole with allyl cationic species **B** (Scheme 1) is the likely reaction mechanism.