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A new ruthenium-catalyzed cyclopropanation of alkenes using propargylic acetates as a precursor of vinylcarbenoids

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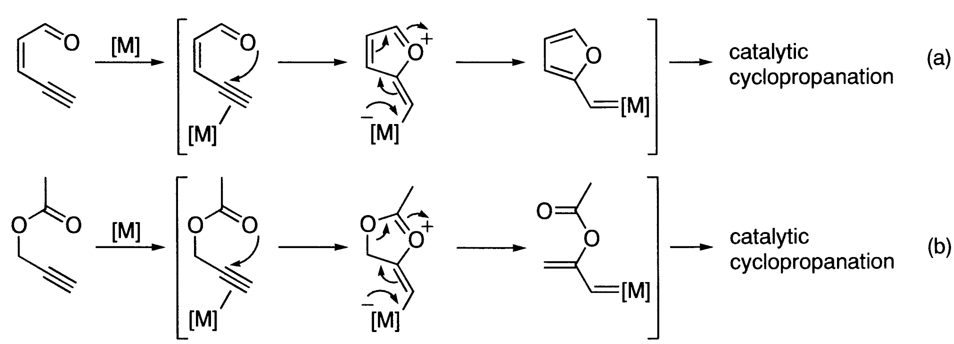
Abstract—$[RuCl_2(CO)_3]_2$ catalyzes intermolecular cyclopropanation of various alkenes with propargylic acetates to give vinylcycloropanes in good yields. The key intermediate of this reaction is a vinylcarbene complex generated by nucleophilic attack of the carbonyl oxygen of the acetate to an internal carbon of alkyne activated by the ruthenium complex. © 2003 Elsevier Science Ltd. All rights reserved.

The in situ generation of carbenoid species from diazoalkanes and transition metal complexes has been well documented and the species are most applicable to cyclopropanation and insertion reactions.[1] Recently, much attention has been paid to activation of alkynes with transition metal complexes as another method to generate carbenoid species. For example, cyclopropylcarbene–metal complexes in skeletal reorganization of α,ω-enynes,[2,3] dialkylidene ruthenium species from ω-diynes,[4] and tungsten-[5] or gold[6]-containing carbonyl ylides from *o*-ethynylphenylcarbonyl compounds are considered as new entries to carbenoid species from alkynes. Most recently, we have developed catalytic cyclopropanation of alkenes through (2-furyl)carbene complexes generated from ene–yne–carbonyl compounds (Scheme 1a).[7] A wide range of transition metal compounds, such as $Cr(CO)_5(THF)$, $[RhCl(cod)]_2$, $[RuCl_2(CO)_3]_2$, $PdCl_2$, and $PtCl_2$, was found to be effective as catalysts for the cyclopropanation. The key of the reaction is 5-*exo-dig* cyclization via nucleophilic attack of the carbonyl oxygen to an internal carbon of alkyne leading to a stable furan structure as a resonance form. This success stimulated us to develop a new method to generate a vinylcarbenoid structure from a simple propargylic carboxylate, in which nucleophilic attack of carbonyl oxygen followed by bond cleavage at propargylic position in lieu of conjugated system has been envisioned (Scheme 1b). Although this concept was invalid in most cases due to facile isomerization of propargylic acetates into allenyl acetates catalyzed by transtion metal compounds,[8] Rautenstrauch first demonstrated the validity of protocol to provide a vinylcarbenoid intermediate in palladium-catalyzed reactions of propargylic acetate with dec-1-ene.[9] Most



Scheme 1.

* Corresponding authors. Tel.: +81-75-753-5697; fax: +81-75-753-5697 (K.O.); Tel.: +81-75-753-5687; fax: +81-75-753-3573 (S.U.); e-mail: ohe@scl.kyoto-u.ac.jp; uemura@scl.kyoto-u.ac.jp

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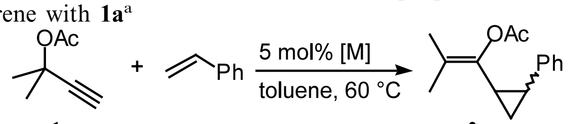
recently, Fensterbank, Malacria, and Marco-Contelles have demonstrated that intermediary vinylcarbenoids are effectively trapped by an alkenyl moiety in the molecule to give carbocycles in $PtCl_2$-catalyzed cyclization of dienynes.[10] To the best of our knowledge, however, there have been no reports on efficient intermolecular reactions of alkenes and vinylcarbenoids generated from propargylic carboxylates. In this communication, we wish to report a novel ruthenium-catalyzed intermolecular [2+1] cycloaddition (cyclopropanation) between alkenes and propargylic acetates, the latter of which can act as a vinylcarbenoid precursor.

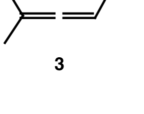
First, we examined the cyclopropanation of styrene with 2-methyl-3-butyn-2-yl acetate (**1a**) in the presence of several catalysts which have been effective for (2-furyl)carbene transfer cyclopropanation reaction.[7] Results of catalyst-screening are given in Table 1.[11] The reaction of **1a** and styrene in the presence of a catalytic amount of $[RuCl_2(CO)_3]_2$ (5 mol%) in toluene at 60°C for 18 h afforded the cyclopropanated product **2a** in 83% yield (*cis*:*trans* = 84:16), along with 5% of allenyl acetate **3** as a result of isomerization of **1a** (entry 1). The use of 10 mol% Ru catalyst completely suppressed the formation of **3** (entry 2). In contrast, $[Rh(OCOCF_3)_2]_2$ which is known as a good catalyst for carbene transfer reaction could not catalyze the present cyclopropanation, but it gave only allene **3** quantitatively (entry 3). $[IrCl(cod)]_2$ and $AuCl_3$ were also found to catalyze the cyclopropanation to give **2a** in 37% and 54% yields with 70:30 and 76:24 diastereomeric ratio, along with **3** as a byproduct (entries 4 and 5). Particularly, $AuCl_3$ was highly active to both of cyclopropanation and allene formation (entry 6). $PtCl_2$, which can act as a good catalyst for intramolecular cyclopropanation (vide supra),[10] catalyzed effectively the present reaction, along with allene formation to some extent (entry 7). $GaCl_3$ was marginally effective in the cyclopropanation to give **2a** in 26% yield with other unidentified products (entry 8). Among catalysts examined, $Cr(CO)_5(THF)$, $[(p\text{-cymene})RuCl_2]_2$, $PdCl_2$, and $PdCl_2(CH_3CN)_2$[9,12] were not effective for the present cyclopropanation.

Table 1. Transition metal-catalyzed cyclopropanation of styrene with **1a**[a]



Entry	[M]	Time	Yield (%)[b]	
			2a (*cis*:*trans*)[c]	Allene **3**
1	$[RuCl_2(CO)_3]_2$[d]	18 h	83 (84:16)	5
2	$[RuCl_2(CO)_3]_2$	15 h	90 (86:14)	0
3	$[Rh(OCOCF_3)_2]_2$[d]	30 min	Trace	99
4	$[IrCl(cod)]_2$[d]	18 h	37 (70:30)	7
5	$AuCl_3$	10 min	54 (76:24)	39
6[e]	$AuCl_3$	10 min	63 (79:21)	26
7	$PtCl_2$	1 h	91 (68:32)	9
8	$GaCl_3$[f]	28 h	26 (65:35)	0

[a] Reactions of **1a** (0.2 mmol) with styrene (1.0 mmol) in toluene (1.0 mL) were carried out in the presence of transition metal catalyst (0.01 mmol) at 60°C under N_2.
[b] GLC yield.
[c] Diastereomeric ratios were determined by ^1H NMR or GLC.
[d] 0.005 mmol.
[e] 1 mol% of $AuCl_3$ was used at room temperature.
[f] 1 M in methylcyclohexane.



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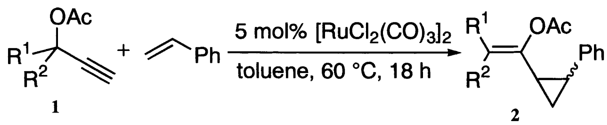
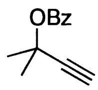
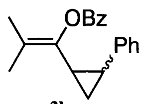
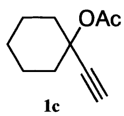
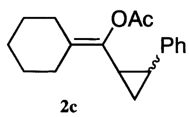
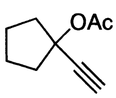
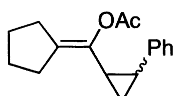
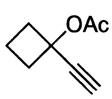
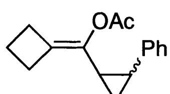
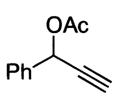
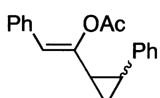
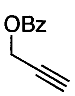
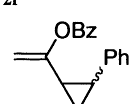
Next, we examined cyclopropanation of styrene using several propargylic acetates in the presence of $[RuCl_2(CO)_3]_2$ as a catalyst. These results are summarized in Table 2. The reaction of propargylic benzoate **1b** and styrene also gave the cyclopropanated product **2b** in 81% yield (d.r. = 88:12) (entry 1). Cyclic acetates **1c**, **1d** and **1e** reacted with styrene to give the corresponding products **2c**, **2d**, and **2e** in 91, 69, and 60% yields, respectively (entries 2–4). The reaction with secondary propargylic acetate **1f** proceeded smoothly to give **2f** in 77% yield with a 75:25 diastereomeric ratio (entry 5).[13] Primary propargylic bezoate **1g** was less reactive in the present cyclopropanation and only a trace amount of the expected products was obtained after 48 h (entry 6). Next, the reactions of **1a** with several alkenes in the presence of $[RuCl_2(CO)_3]_2$ were examined (Table 3). The reaction of 1,1-diphenylethylene with **1a** proceeded smoothly to give cyclopropane **2h** in 66% yield (entry 1). 2-Ethylbut-1-ene was slowly reacted with **1a** to give **2i** in 68% yield, although the reaction required 20 equiv. of the alkene (entry 2). On the other hand, cyclopropanation of allyltrimethylsilane, *tert*-butyl vinyl ether, or vinyl acetate with **1a** resulted in giving lower yields of products, 43% (d.r. = 67:33), 22% (*cis*:*trans* = 36:64), and 20% (*cis*:*trans* = 75:25), respectively (entries 3–5). Oct-1-ene or 3,3-dimethylbut-1-ene reacted with **1a** to give the corresponding products in lower yields (10–20%) with several unidentified products. No cyclopropanation of norbornene with **1a** under the identical conditions was observed. This result strongly supports that the present cyclopropanation proceeds via different pathway from cyclopropanation reported by Takahashi et al.[14] In the reaction of 20 equiv. of isoprene with **1a**, more substituted double bond was selectively reacted to give *trans*-**2m** in 40% yield together with 1,4-cycloheptadiene **4** in 31% yield (Scheme 2). The formation of **4** can be explained by assuming [3,3]sigmatropic rearrangement of initially produced *cis*-**2m** (Scheme 3).

In conclusion, we have developed an effective intermolecular cyclopropanation of various alkenes with propargylic carboxylates via vinylcarbene complexes. This also demonstrates versatility of alkynes as a carbene precursor in the transition metal-catalyzed reaction. The present cyclopropanation is chemically

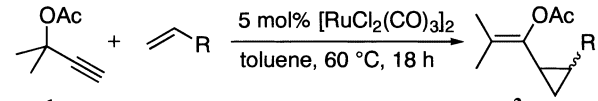
Table 2. Ru-catalyzed cyclopropanation of styrene with **1**[a]



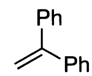
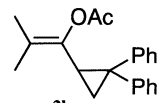
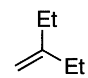
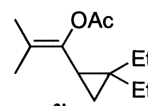
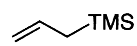
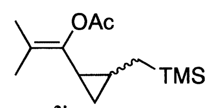
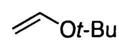
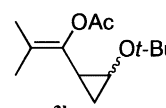
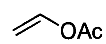
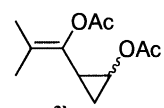
entry	1	product	yield (%)[b]	d. r.[c]
1	 **1b**	 **2b**	81	88:12
2	 **1c**	 **2c**	91	82:18
3	 **1d**	 **2d**	69	89:11
4	 **1e**	 **2e**	60	92:8
5	 **1f**	 **2f**	77	75:25
6	 **1g**	 **2g**	trace	–[d]

[a] Reactions of **1** (0.2 mmol) with styrene (1.0 mmol) in toluene (1.0 mL) were carried out in the presence of $[RuCl_2(CO)_3]_2$ (0.005 mmol) at 60°C under N_2.
[b] Isolated yield.
[c] Diastereomeric ratios were determined by ^{1}H NMR or GLC, but their configurations are not yet clear.
[d] Not determined.

Table 3. Ru-catalyzed cyclopropanation of various alkenes with **1a**[a]



1a **2**

entry	alkene	product	yield (%)[b]	*cis:trans*[c]
1		 **2h**	66	N.A.[d]
2[e]		 **2i**	68	N.A.[d]
3[e]		 **2j**	43	67:33[f]
4		 **2k**	22	36:64
5[e, g]		 **2l**	20	75:25

[a] Reactions of **1a** (0.2 mmol) with alkene (1.0 mmol) in toluene (1.0 mL) were carried out in the presence of $[RuCl_2(CO)_3]_2$ (0.005 mmol) at 60°C under N_2.
[b] Isolated yield.
[c] Diastereomeric ratios were determined by ^{1}H NMR or GLC.
[d] N.A. = not applicable.
[e] Alkene (4.0 mmol) was used.
[f] Configuration is not yet known.
[g] 42 h.

equivalent to the reaction using a combination of α-diazoketone and transition metal compounds. This system may find some applications in other catalytic vinylcarbene transfer reactions. These studies will be reported in due course.

Acknowledgements

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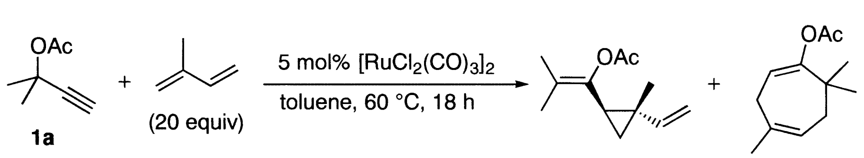
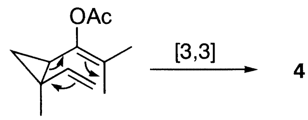


1a *trans*-**2m** (40%) **4** (31%)

Scheme 2.



cis-**2m**

Scheme 3.

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11. *General procedure for the catalytic cyclopropanation of alkenes with propargylic acetate*: To a solution of propargylic acetate **1a** (25.2 mg, 0.20 mmol) and styrene (0.11 mL, 1.0 mmol) in toluene (1.0 mL) was added $[RuCl_2(CO)_3]_2$ (2.6 mg, 0.005 mmol) at room temperature under N_2. After stirring at 60°C for 18 h, the mixture was cooled to room temperature and the amount of products was determined by GLC analysis using 2,6-dimethylnaphthalene as an internal standard. For isolation of the product, the solvent was removed under reduced pressure and the residue was subjected to column chromatography on SiO_2 (Merck silica gel 60) with hexane/AcOEt as an eluent.
    cis-**2a**: A colorless oil; IR (neat) 701, 733, 776, 1113, 1155, 1183, 1218, 1369, 1751 (C=O), 2916 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz, 25°C): δ 1.02 (ddd, J=5.4, 6.3, 6.3 Hz, 1H), 1.25 (ddd, J=5.4, 8.9, 8.9 Hz, 1H), 1.41 (s, 3H), 1.47 (s, 3H), 2.04 (s, 3H), 2.20–2.33 (m, 2H), 7.01–7.26 (m, 5H); ^{13}C NMR ($CDCl_3$, 67 MHz, 25°C): δ 11.6, 17.5, 18.6, 20.6, 21.7, 24.2, 123.2, 125.4, 127.2, 127.4, 138.1, 139.1, 169.1. Anal. calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.49; H, 7.85%.
    trans-**2a**: A colorless oil; IR (neat) 698, 760, 1102, 1159, 1196, 1214, 1369, 1749 (C=O), 2917 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz, 25°C): δ 1.02 (dd, J=7.3, 7.3 Hz, 2H), 1.57 (s, 3H), 1.79 (s, 3H), 1.94–2.09 (m, 2H), 2.16 (s, 3H), 7.06–7.30 (m, 5H); ^{13}C NMR ($CDCl_3$, 67 MHz, 25°C): δ 14.7, 18.2, 18.8, 20.6, 23.2, 23.5, 120.5, 125.7, 125.8, 128.3, 140.6, 141.9, 169.1. Anal. calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 77.96; H, 7.91%.
12. Recently, Yamamoto et al. have reported indenol ether formation from aryl alkynes via Pd–carbene intermediates. See: Nakamura, I.; Bajracharya, G. B.; Mizushima, Y.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2002**, *41*, 4328.
13. Geometry of alkenic part is temporarily assigned to *Z* due to no appreciable NOE between a vinylic proton and methyl protons of an acetyl group.
14. Takahashi et al. have already reported that cyclopropylketones were obtained from propargylic alcohols and norbornene in the presence of $[Cp'Ru(CH_3CN)_3]PF_6$ catalyst. See: (a) Kikuchi, H.; Uno, M.; Takahashi, S. *Chem. Lett.* **1997**, 1273; (b) Matsushima, Y.; Kikuchi, H.; Uno, M.; Takahashi, S. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 2475.