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A Novel Chelation-Assisted Hydroesterification of Alkenes via Ruthenium Catalysis

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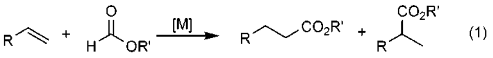
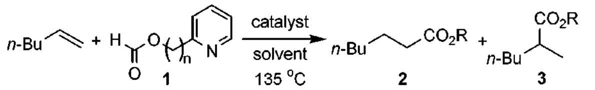
The selective C−H activation via transition metal catalysis is currently a subject of great interest, and intensive research has been carried out to ensure useful organic transformations such as C−C bond formations.[1] One of the most widely studied examples is hydroacylation in which an aldehydic hydrogen is activated by a metal catalyst followed by the addition of thus activated substrates to alkenes.[2] However, the analogous hydroesterification reaction (eq 1) still remains to be explored due to several limitations including severe reaction conditions, low yield and poor selectivity, requirement of high pressure of CO, and significant decarbonylation of alkyl formates during the course of the reaction.[3] Although some improvements have been reported with the use of Pd[4] or Ru catalysts,[5] suppression of the decarbonylation pathway is still a major challenge to overcome.[6] In the course of our studies directed toward the development of efficient catalytic reactions,[7] we have found the first example of *a highly efficient and novel chelation-assisted hydroesterification of olefins in the absence of carbon monoxide*, which will be described herein.



(1)

In recent years, directed C−H activation has been frequently employed as a key strategy in the development of selective C−C bond-forming reactions with a proper choice of directing groups.[8] Inspired by these, at the outset of our studies on the catalytic hydroesterification, we envisioned that the decarbonylation pathway could be substantially suppressed through a chelation-aided stabilization of a putative active intermediate, acyloxy metal hydride. We chose a pyridyl moiety as a possible directing group and prepared a series of 2-pyridyl-containing formates (**1a**−**1c**)[9] to verify our hypothesis (Table 1). While attempts to add benzyl formate to 1-hexene via catalysis proved totally unsuccessful, we found that same reaction with 2-pyridylmethyl formate **1b** ($n = 1$) could be effected depending on the catalyst and reaction conditions. This result clearly demonstrates that the 2-pyridyl moiety of formats serves as a coordination-directing group as already illustrated in other reactions.[8] Among numerous complexes examined, we found that $Ru_3(CO)_{12}$ effected the hydroesterification most efficiently when **1b** was used. Examination of several solvents led us to find that decarbonylation was most efficiently suppressed in DMF with this substrate,[10] providing a quantitative formation of the addition products (entry 8). It was also found that under these conditions a linear ester **2** was preferentially formed over the corresponding branched isomer **3** (**2**/**3** ≈ 3:1). Reactions at temperatures lower than 120 °C proceeded very slowly giving only decarbonylated 2-pyridinemethanol. Although 2-pyridyl formate **1a** ($n = 0$) was also efficiently activated with $Ru_3(CO)_{12}$, in this case decarbonylation was a dominant route leading to 2-hydroxypyridine instead of addition products (entry 9). Activation of **1c** ($n = 2$), bearing one more carbon chain than **1a**, was almost completely ineffective under the same conditions.

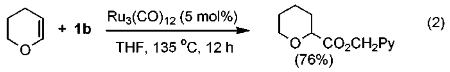
Table 1. Hydroesterification of 1-Hexene with Formates **1a**−**1c**[a]



entry	catalyst	formate	solvent	conv (%) (**2**:**3**)[b]	decarbonyl[b] (%)
1	$RuCl_2(PPh_3)_3$	**1b** ($n = 1$)	toluene	3	
2	$Ru(cod)Cl_2$	**1b**	toluene	8	5
3	$Ru(CO)H_2(PPh_3)_3$	**1b**	toluene	18	15
4	$[RuCl_2(p\text{-cymene})]_2$	**1b**	toluene	4	
5	$RhCl(PPh_3)_3$	**1b**	toluene	2	
6	$Ru_3(CO)_{12}$	**1b**	toluene	99 (57:43)	53
7[c]	$Ru_3(CO)_{12}$	**1b**	dioxane	99 (71:29)	42
8[c]	$Ru_3(CO)_{12}$	**1b**	DMF	>99 (74:26)	<1
9[c]	$Ru_3(CO)_{12}$	**1a** ($n = 0$)	DMF	99	95
10[c]	$Ru_3(CO)_{12}$	**1c** ($n = 2$)	DMF	7	5

[a] 1-Hexene (0.6 mmol), formate (0.2 mmol), and catalyst (5 mol %) were in the indicated solvent (0.1 mL) for 4 h. [b] Conversion, ratio of **2**:**3**, and extent of decarbonylated alcohols from formates **1a**−**1c** were determined by integration of ^1H NMR. [c] 2.0 mol % $Ru_3(CO)_{12}$ was used.

Our hypothesis was successfully amenable to a wide range of alkene substrates, allowing preparation of one-carbon elongated esters from olefins in high yield and good to excellent selectivity (Table 2). Preference for the formation of linear adducts dramatically soared upon increase of steric demand in substrates as exemplified by vinylcyclohexane and 3,3-dimethyl-1-butene (entries 2 and 3). Hydroesterification of styrenes with **1b** also proceeded in high yields in the presence of $Ru_3(CO)_{12}$ catalyst albeit with moderate linear-to-branched selectivity (entries 4 and 5). As in the case of aliphatic alkenes, reaction of a vinyl arene having substituents near the double bond resulted in exclusive formation of a liner ester (entry 6). Various functional groups including silyl, carbonyl, and hydroxyl groups did not affect the reaction. As expected, reaction of geminally substituted alkenes afforded exclusively linear esters presumably due to steric reasons (entries 8 and 9).[11] It is noteworthy that a conjugated olefin such as methyl vinyl ketone was also a good substrate, yielding exclusively a linear product in good yield (entry 10). Not only acyclic alkenes but also cyclic olefins turned out to be good substrates for the hydroesterification (entries 11−13). It should be addressed that reaction of 2-norbornene afforded the corresponding ester in excellent yield *with complete exo-selectivity*.[12] Notably, reaction of vinyl ethers gave a surprising result in that it provided exclusively α-adducts with no other isomeric products observed (eq 2).[13] Although the exact reason for this complete control of regioselectivity is not presently understood, it immediately affords very valuable α-alkoxyesters that are not easily available through known procedures.



(2)

Although stable hydrido acyl rhodium intermediates were previously isolated in some cases from the reaction of Rh and aldehydes,[14] no corresponding Ru species have yet been character-

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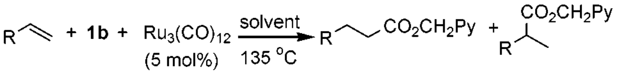
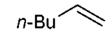
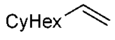
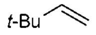
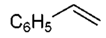
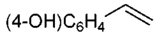
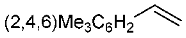
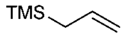
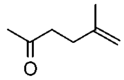
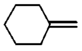
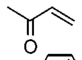
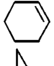
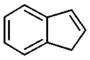
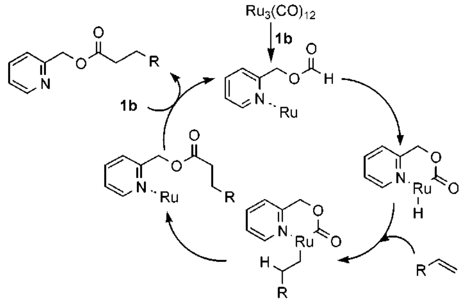
Table 2. Hydroesterification of Various Alkenes with **1b**[a]



entry	alkene	solvent	t/h	yield (%, ratio)[b]
1	 n-Bu	DMF	3	98 (74:26)
2	 CyHex	DMF	12	87 (98:2)
3	 t-Bu	DMF	3	98 (>99:1)
4	 C_6H_5	DMF	4	95 (75:25)
5	 (4-OH)C_6H_4	DMF	5	79 (65:35)
6	 (2,4,6)$Me_3C_6H_2$	$ClCH_2CH_2Cl$	7	95 (99:1)
7	 TMS	THF	5	98 (70:30)
8		DMF	5	65 (>99:1)
9		DMF	12	83 (>99:1)
10		DMF	4	68 (>99:1)
11		DMF	12	91
12		DMF	12	87 (100:0)[c]
13		CH_3CN	12	75 (82:18)[d]

[a] Alkenes (1.2 mmol) and **1b** (0.4 mmol) in a solvent (0.2 mL). [b] Refer to combined isolated yield of linear and branched isomer, whose ratio is in parentheses (determined by ^{1}H NMR of the crude reaction mixture before column). [c] Ratio of exo-/endo-isomer. [d] Ratio of 1-carboxylate/2-carboxylate determined by ^{1}H NMR of the crude reaction mixture.

Scheme 1



ized. However, on the basis of accumulating reports that low-valent Ru complexes, especially $Ru_3(CO)_{12}$, show high catalytic activity for the activation of the formyl C−H bond such as of formamides,[15a] alkyl formats,[15b] or aldehydes,[15c] we propose a plausible mechanism in Scheme 1. Although whether ruthenium acts as a mononuclear or as a cluster is not clear at the present time, coordination of the ruthenium to pyridyl nitrogen should facilitate activation of the formyl C−H bond,[16] leading to a six-membered chelation intermediate. We believe that such a chelation subsequently results in effective suppression of the decarbonylation route.[17] To demonstrate the applicability of the present process, reactions under solvent-free conditions were next tried. The neat reaction of 3,3-dimethyl-1-butene (5 equiv) with **1b** (1 equiv) proceeded with impressive efficiency, affording exclusively a linear ester in 89% isolated yield *using only 0.2 mol % $Ru_3(CO)_{12}$ catalyst* (135 °C, 5 h). The produced 2-pyridylmethyl esters could be readily hydrolyzed under mild conditions,[18] quantitatively providing the parent carboxylic acids with complete recovery of 2-pyridinemethanol.[19]

In summary, we have developed a practical useful catalytic hydroesterification reaction of alkenes guided by a chelation-assisted strategy for the first time. Using 2-pyridylmethyl formate **1b**, decarbonylation could be almost completely suppressed with a Ru catalyst during the reaction course, allowing one-carbon elongated esters starting from alkenes in high yield and excellent selectivity without requirement of high pressure CO. This result should immediately pave more opportunities for searches of efficient and selective new C−C forming catalytic reactions by means of the chelation strategies.

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Supporting Information Available: Spectral data and copies of ^{1}H and ^{13}C NMR spectra for new compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) Although a partial decomposition of DMF by Ru complexes has been reported by Lavigne et al. (*Organometallics* **1995**, *14*, 1712), decarbonylation of DMF was not observed under the present conditions.

(11) Tetrasubstituted alkenes were not reactive under these conditions.

(12) Determined by comparison with known data (ref 5d) after conversion of the 2-pyridylmethyl ester to the corresponding benzyl ester.

(13) Reaction of *n*-butyl vinyl ether with **1b** also resulted in exclusive formation of a corresponding α-adduct in 64% isolated yield in 1,2-dichloroethane (12 h, 135 °C) with $Ru_3(CO)_{12}$ (5 mol %).

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(16) A putative ruthenium hydrido peak was observed on ^{1}H NMR at −18 ppm upon heating of **1b** with $Ru_3(CO)_{12}$ (0.5 equiv) in C_6D_6 at 135 °C.

(17) Murai et al. have recently reported a chelation-assisted reductive decarboxylation reaction, in which the C−O bond of 2-pyridylmethyl esters is converted to hydrocarbons, see: Chatani, N.; Tatamidani, H.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* **2001**, *123*, 4849.

(18) See Supporting Information for details.

(19) The products were quantitatively isolated by a simple acid−base extraction according to the phase-tag procedure as described in ref 8d, thus the recovered Ru complex exhibited significantly diminished catalytic activity as compared to that of the fresh one.

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