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Ruthenium-catalyzed hydroesterification of alkynes and dienes based on a chelation-approach

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Abstract—Based on a chelation-assistance strategy, efficient hydroesterification of alkynes and dienes has been achieved using ruthenium catalyst without the need of high pressuric external CO atmosphere, and a diverse range of α,β-unsaturated esters and mono-olefinic esters could be obtained with high stereo- and regioselectivity. © 2003 Elsevier Science Ltd. All rights reserved.

Hydroesterification of alkenes with alkyl formates constitutes one of the most straightforward and economical ways for the formation of one-carbon elongated esters, and various catalytic protocols have been devised to achieve high efficiency and selectivity.[1] It is generally recognized that decarbonylation of activated formates occur readily to afford the corresponding alcohols and carbon monoxide during the catalytic cycles, and it offers a main reason for the decrease in overall efficiency of the reaction. To deal with this problem, external high pressure of CO has to be employed to suppress the decarbonylation pathway.[2] Catalytic alkoxycarbonylation of alkenes using alcohols and carbon monoxide, on the other hand, has been practised as a possible alternative route.[3] Despite extensive studies, there is still a strong need of efficient hydroesterification of unsaturated compounds without high pressure CO atmosphere. Recently, we reported that a chelation strategy could be successfully utilized to achieve efficient hydroesterification of alkenes in the absence of external CO.[4] High efficiency observed is believed to be derived mainly from the effective suppression of decarbonylation of activated acyl hydride intermediate by forming tight chelating transition states during the catalytic cycles. Herein, we wish to report our recent studies for expanding the scope of the chelation-assisted hydroesterification, including alkynyl- and diolefinic substrates to produce α,β-unsaturated and mono-olefinic esters, respectively.[5]

Under the previously optimized conditions for the reaction of alkenes,[4] various alkynes were allowed to react with 2-pyridylmethyl formate (**1**) in the presence of $Ru_3(CO)_{12}$ catalyst (Table 1).[6] Although conversion was completed within 12 h in all solvents examined, significant decarbonylation of formate **1** was observed when the reaction of 4-octyne was carried out in DMF and DMA (entries 1 and 2, respectively). In contrast, the reaction in DMSO proceeded smoothly without significant decarbonylation of **1**, and good yield of a conjugated *E*-ester was obtained in 85% (entry 3).[7] Judging from the results obtained, it should be noted that the reaction seems to proceed via a *syn*-addition fashion of activated acyl and hydride of formate into alkynes. It was further confirmed by the fact that we could not observe other stereoisomer, *Z*-ester, from the reaction. Diphenylacetylene also reacted with **1** to afford a *trans*-cinnamate derivative in modest yield at higher loading of the catalyst (entry 4). Although the addition was almost exclusively stereoselective (*syn*-addition) over all substrates examined, regioselectivity turned out to be rather moderate. For example, the reaction of 1-phenyl-1-butyne with **1** provided (2-pyridylmethyl) *trans*-β-ethyl cinnamate and its α-ethyl isomer with modest ratio (β/α = 85:15), which was unambiguously determined by ^{1}H NMR of the crude mixture. The fact that pyridylmethyl carboxyl group is inserted into a less bulky site of the alkynes turned out to be general over a range of internal alkynes examined (entries 5–10).[8] In contrast, with terminal alkynes, α-isomeric carboxylate was obtained as a major product (entries 11 and 12). This represents the first example of ruthenium-catalyzed hydroesterification of alkynes to the best of our knowledge.[9,10]

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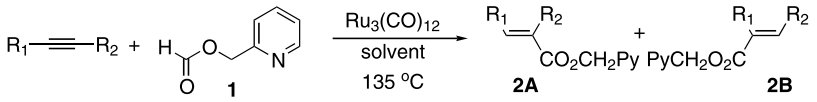
Table 1. Hydroesterification of alkynes with 2-pyridylmethyl formate **1**[a]



Entry	R_1	R_2	Solvent	Time (h)	**2A**:**2B**[b]	Yield (%)[c]
1	C_3H_7	C_3H_7	DMF	12	–	39
2	C_3H_7	C_3H_7	DMA	12	–	53
3	C_3H_7	C_3H_7	DMSO	12	–	85
4[d]	C_6H_5	C_6H_5	DMSO	18	–	60
5	C_6H_5	C_2H_5	DMSO	18	85:15	82
6	C_3H_7	CH_3	DMSO	12	65:35	76
7	$C_2H_5OTBDPS$	CH_3	DMSO	18	70:30	55
8	C_2H_5OTHP	CH_3	DMSO	8	62:38	89
9[d]	C_2H_5OBn	CH_3	DMSO	12	61:39	81
10	$C_2H_5COCH_3$	C_8H_{17}	DMSO	12	51:49	84
11	*n*-Oc	H	DMF	12	20:80	42
12	*t*-Bu	H	DMF	12	43:57	74

[a] Alkyne (3.0 equiv.), **1** (1.0 equiv.), and Ru catalyst (0.05 equiv. except entries 4 and 9) in an indicated solvent.
[b] Determined by ^1H NMR of the crude reaction mixture.
[c] Combined isolated total yield of **2A** and **2B**.
[d] Ru catalyst was used in 20 mol%.

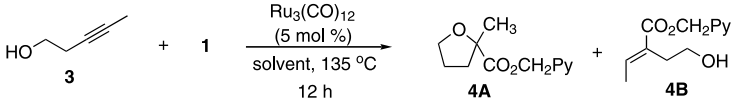
When 3-pentyn-1-ol (**3**) was allowed to react with formate **1**, a cyclized adduct **4A** was preferentially produced instead of a expected product **4B** (Scheme 1).[11] Especially, in dioxane, only the tetrahydrofuran moiety was obtained as a single product albeit with moderate yield. Although the exact route for the unexpected pathway is not clearly understood at the present stage,[12] the obtained cyclic structure is highly unique.[13]

Several types of diolefinic substrates were then reacted with formate **1** under the optimized conditions except solvents (Table 2).[14]

As demonstrated in entries 1–4, terminal olefinic site was selectively reacted in the presence of internal- or 1,1-disubstituted double bond, and only mono-esters were isolated in good to moderate yields. When a diolefinic substrate bearing a stereogenic center was allowed to react with formate **1**, almost no asymmetric induction was deduced despite the fact that regioselective addition was still observed (entry 2). The reaction of 2,5-norbornadiene with **1** afforded mono-addition product in good yield albeit with low *exo*/*endo* selectivity (entry 5). While the reaction of diallyl ether provided mono-ester in negligible yield (<5%) in organic solvents such as DMF, solvent free conditions turned out to improve the efficiency of the reaction (entry 6). With bis-styrenyl substrate, only a mono-ester was isolated in excellent yield (entry 7).

It should be noted that no isomerization of internal double bonds into terminal position was observed under the hydroesterification reaction conditions with diolefinic substrates. This is significant considering the fact that heptanoate (**5**) and hexanoate (**6**) were isolated as a mixture when 3-hexene was allowed to react with **1** under the optimal conditions (Scheme 2). Two isomeric products **5** and **6** were presumably derived from the isomerization of an internal double bond into terminal position followed by hydroesterification. This was further supported by a result that similar selectivity of linear/branched isomer was observed with comparable efficiency from the hydroesterification reaction of 1-hexene with **1** under otherwise identical conditions.[15]

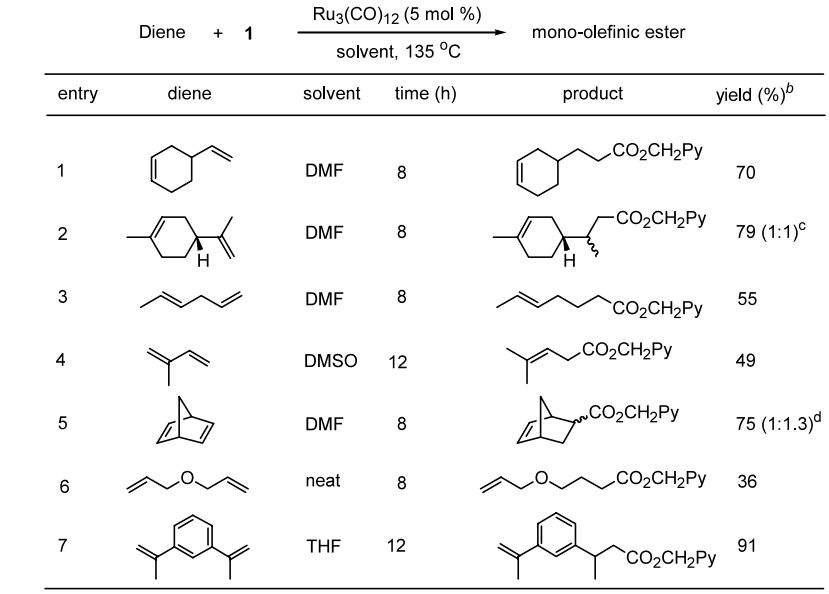
In summary, we have demonstrated that hydroesterification of alkynes and dienes proceeded efficiently with a chelating formate by the use of a ruthenium catalyst in the absence of external pressure of CO. The reaction showed a complete stereoselectivity of *syn*-addition to triple bonds with moderate regioselectivity. In addition, from the reaction of diolefinic substrates, only mono-



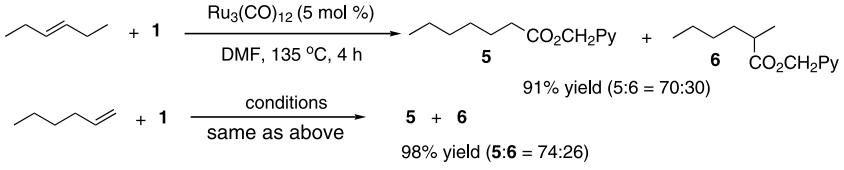
solvent	isolated yield (%, **4A**)	**4B** (%)
DMSO	23	12
Toluene	45	5
Dioxane	56	<1

Scheme 1.

Table 2. Hydroesterification of various dienes with **1** by ruthenium catalyst[a]



[a] Diene (3.0 equiv), **1** (1.0 equiv), and Ru catalyst (0.05 equiv) in an indicated solvent. [b] Refer to combined isolated yields. [c] Ratio of two diastereomers formed. [d] Ratio of *exo*/*endo* isomer.



Scheme 2.

esters were selectively produced with high efficiency without isomerization of double bonds.

Acknowledgements

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6. All new compounds were fully characterized by ^{1}H and ^{13}C NMR, IR, and HRMS.
7. Based on this result, a possibility that DMF acts as a CO source through decomposition of DMF can be ruled out. For reference of the example, see: Wan, Y.; Alterman, M.; Larhed, M.; Hallberg, A. *J. Org. Chem.* **2002**, *67*, 6232.
8. **Representative experimental procedure of hydroesterification**: To a solution of 2-pyridylmethyl formate (**1**, 40.0 mg, 0.29 mmol) in DMSO (0.2 ml) was added 4-octyne (96.5 mg, 0.88 mmol) followed by $Ru_3(CO)_{12}$ (9.3 mg, 5 mol%). The reaction mixture was stirred at 135°C for 12 h in a screw-capped vial. The crude product was extracted with ethyl acetate, washed with water, and dried ($MgSO_4$). After removal of organic solvent under

reduced pressure, the residue was purified by column chromatography on silica gel (10% ethyl acetate/hexane) to afford (2-pyridylmethyl)-2-propyl-2-pentenoate (61 mg, 85%) as a yellowish liquid: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 8.59 (d, 1H, $J=4.8$ Hz), 7.70 (td, 1H, $J=7.7$, 1.7 Hz), 7.36 (d, 1H, $J=8.0$ Hz), 7.22 (m, 1H), 6.88 (t, 1H, $J=7.5$ Hz), 5.31 (s, 2H), 2.36 (t, 2H, $J=7.9$ Hz), 2.20 (q, 2H, $J=7.4$, 7.4 Hz), 1.47 (m, 4H), 0.95 (m, 6H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 167.5, 156.4, 146.3, 143.6, 136.6, 131.9, 122.6, 121.3, 66.6, 30.6, 28.7, 22.5, 22.0, 13.9; IR (neat) 2961, 2873, 1714, 1648, 1594, 1438, 757, 602 cm^{-1}; HRMS (EI) calcd for $C_{15}H_{21}NO_2$ 247.1572 (M^+), found 247.1575.

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10. For hydroesterification of alkynes with methyl formate to methyl acrylate catalyzed by nickel catalyst, see: Yang, X.-G.; Zhang, J.-Q.; Liu, Z.-T. *Appl. Catal. A: General* **1998**, *173*, 11.
11. For a previous example of Pd-catalyzed hydroesterification of alkynols, see: El Ali, B.; Alper, H. *J. Mol. Catal. A Chem*. **1995**, *96*, 197.
12. Compound **4A** is presumed to be formed from the hydroesterification of alkynol **3** with **1** at the opposite direction compared to **4B**, and then by an intra-molecular cyclization.
13. Recently, ruthenium-catalyzed oxidative cyclization of alkynols has been reported, see: Trost, B. M.; Rhee, Y. H. *J. Am. Chem. Soc*. **2002**, *124*, 2528.
14. Alkoxycarbonylation of 1,2-polybutadiene with EtOH and CO was previously reported using Pd catalyst. See: Ajjou, A. N.; Alper, H. *Macromolecules* **1996**, *29*, 1784.
15. For ruthenium-catalyzed isomerization of internal alkenes, see: (a) Suzuki, H.; Koyama, Y.; Moro-oka, Y.; Ikawa, T. *Tetrahedron Lett*. **1979**, *20*, 1415; (b) Zoran, A.; Sasson, Y.; Blum, J. *J. Org. Chem*. **1981**, *46*, 255; (c) Wakamatsu, H.; Nishida, M.; Adachi, N.; Mori, M. *J. Org. Chem*. **2000**, *65*, 3966.