



Synthesis of enol and vinyl esters catalyzed by an iridium complex

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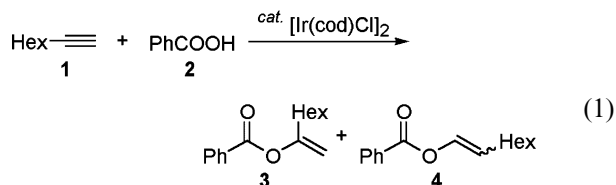
Abstract—Enol and vinyl esters were successfully synthesized by the use of an iridium complex as a catalyst. The reaction of carboxylic acid with terminal alkynes in the presence of catalytic amounts of $[\text{Ir}(\text{cod})\text{Cl}]_2$ and Na_2CO_3 gave the corresponding 1-alkenyl esters. The addition of carboxylic acids to alkynes principally took place in the Markovnikov fashion. In addition, by the use of an Ir complex combined with NaOAc various vinyl esters were prepared through the transvinylolation between carboxylic acids and vinyl acetate. © 2002 Elsevier Science Ltd. All rights reserved.

Enol and vinyl esters are frequently used as intermediates in organic synthesis and pharmaceutical chemistry.¹ Hence, a wide variety of methods have been developed for their preparation; e.g. transvinylolation of carboxylic acids with vinyl or isopropenyl acetate catalyzed by transition metal complexes,² oxidative acetoxylation of olefins by $\text{Pd}(\text{OAc})_2$ which is an important industrial process,³ treatment of enols or enolates with an appropriate acid anhydride or acid chloride.⁴ For enol ester synthesis, the direct addition of carboxylic acids to terminal alkynes catalyzed by mercury salts is a straightforward atom-economical process, but a major disadvantage of this method is the use of toxic mercury salts.⁵ In 1983, Rotem and Shvo first reported that a ruthenium complex facilitates the addition of carboxylic acids to terminal alkynes.⁶ After this finding, much attention has been paid to the ability of ruthenium complexes, and now the reaction is achieved with high selectivity.⁷ However, only a few reports have appeared for the reaction using transition metal complexes other than Ru complexes.⁸

Recently, we have shown that an iridium complex serves as an efficient catalyst for several synthetic organic transformations.⁹ As a part of our studies, we wish to disclose here an enol ester synthesis from the reaction of terminal alkyne with carboxylic acid catalyzed by an $[\text{Ir}(\text{cod})\text{Cl}]_2/\text{P}(\text{OMe})_3/\text{Na}_2\text{CO}_3$ system.

Additionally, vinyl esters were successfully synthesized by means of transvinylolation between carboxylic acids and vinyl acetates in the presence of catalytic amounts of $[\text{Ir}(\text{cod})\text{Cl}]_2$ and NaOAc. To the best of our knowledge, there is no report dealing with the preparation of enol and vinyl esters using an iridium complex as a catalyst.

The reaction of 1-octyne (**1**) with benzoic acid (**2**) was chosen as a model reaction and examined using an iridium complex as a catalyst under various reaction conditions. The representative results are summarized in Table 1. When **1** was allowed to react with **2** in the presence of a catalytic amount of $[\text{Ir}(\text{cod})\text{Cl}]_2$, benzoic acid 1-hexylvinyl ester (**3**) and benzoic acid 1-octenyl ester (**4**) corresponding to Markovnikov and *anti*-Markovnikov adducts were formed in 45 and 20% yields, respectively, along with 2-octanone (7%) (entry 1). A similar result was obtained by the use of an iridium cation complex such as $[\text{Ir}(\text{cod})_2]\text{BF}_4$, while the Vaska complex and IrCl_3 were found to be inactive (entries 2–4) (Eq. (1)).



Interestingly, the yield of **3** remarkably increased by allowing **1** to react with **2** catalyzed by $[\text{Ir}(\text{cod})\text{Cl}]_2$ combined with $\text{P}(\text{OMe})_3$ in the presence of a small

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Table 1. Reaction of **1** with **2** under various reaction conditions^a

Entry	Ligand (mol%)	Base (mol%)	Conv. (%)	Yield (%)	
				3	4 (E/Z)
1			98	45	20 (43/57)
2 ^b			97	53	14 (43/57)
3 ^c			18	12	3 (40/60)
4 ^d			<1	<1	<1
5	P(OMe) ₃ (4)	Na ₂ CO ₃ (2)	99	79	17 (41/59)
6 ^e	P(OMe) ₃ (4)	Na ₂ CO ₃ (2)	98	80	17 (41/59)
7	P(OMe) ₃ (4)	Na ₂ CO ₃ (1)	99	79	16 (43/57)
8	P(OMe) ₃ (4)		63	41	14 (40/60)
9	P(OMe) ₃ (4)	Li ₂ CO ₃ (2)	99	82	15 (40/60)
10	P(OMe) ₃ (4)	NaHCO ₃ (2)	99	79	16 (37/63)
11	P(OMe) ₃ (4)	K ₂ CO ₃ (2)	71	55	14 (36/64)
12	P(OMe) ₃ (4)	Cs ₂ CO ₃ (2)	72	50	14 (36/64)
13		Na ₂ CO ₃ (2)	97	51	23 (50/50)
14	P(O ⁱ Pr) ₃ (4)	Na ₂ CO ₃ (2)	98	74	8 (34/66)
15	P(OPh) ₃ (4)	Na ₂ CO ₃ (2)	98	45	41 (43/59)
16	dppp (2)	Na ₂ CO ₃ (2)	95	5	4 (30/70)
17	PPh ₃ (4)	Na ₂ CO ₃ (2)	29	14	8 (25/75)
18 ^{e,f}	P(OMe) ₃ (4)	Na ₂ CO ₃ (2)	82	32	21 (36/64)

^a **1** (1 mmol) was allowed to react with **2** (2 mmol) in the presence of [Ir(cod)Cl]₂ (1 mol%) in toluene (1 mL) at 100°C for 15 h under Ar.

^b [Ir(cod)₂]BF₄ was used as a catalyst.

^c [IrCl(CO)(PPh₃)₂] was used as a catalyst.

^d IrCl₃ was used as a catalyst.

^e For 3 h.

^f [Rh(cod)Cl]₂ was used as a catalyst.

amount of Na₂CO₃, and the reaction was completed within 3 h (entries 5 and 6).¹⁰ The reaction took place smoothly even in the presence of 1 mol% of Na₂CO₃, while in the absence of Na₂CO₃ the reaction was retarded (entries 7 and 8). Among the bases examined, sodium and lithium salts were found to be more effective than potassium and cesium salts (entries 9–12).

The regioselectivity of the addition of carboxylic acid **2** to **1** was affected by the phosphite ligands employed. Although the reaction lacking the phosphite ligand gave unsatisfactory results, the addition of P(OMe)₃ or P(OⁱPr)₃ to the catalytic system led to the preferential formation of Markovnikov adduct **3** (entries 6, 13 and 14). However, P(OPh)₃ brought about increase of *anti*-Markovnikov adduct **4** (entry 15). Previously, we have reported that the reduction of α,β -unsaturated carbonyl compounds with 2-propanol was successfully achieved by the use of the [Ir(cod)Cl]₂/Cs₂CO₃/dppp (dppp: diphenylphosphino-propane) system.^{9c} In the present reaction, however, a bidentate phosphine ligand like dppp resulted in a complex mixture of products (entry 16). The PPh₃ ligand considerably retarded the reaction (entry 17). On the other hand, [Rh(cod)Cl]₂ catalyst in place of [Ir(cod)Cl]₂ produced several unidentified oligomers of **1** in addition to **3** and **4** (entry 18).

Table 2 shows the reaction of 1-octyne (**1**) and phenylacetylene (**5**) with several carboxylic acids using the [Ir(cod)Cl]₂/P(OMe)₃/Na₂CO₃ system. The reactions of **1** led to the Markovnikov adducts as major products in preference to the *anti*-Markovnikov adducts (entries 1–5).

Phenylacetylene (**5**) also produced the corresponding adducts, but the yields and selectivities of the products were somewhat lower than those of **1** owing to the formation of dimers of **5** as side-products (entries 6 and 7). Miyaoura et al. reported that terminal alkynes are easily dimerized by iridium complexes.¹¹

Werner and co-workers have reported that the [Ir(μ -O₂CCH₃)(C₂H₄)₂]₂ complex prepared from [Ir(C₂H₄)₂-Cl]₂ and CH₃CO₂Na·3H₂O reacts with HC≡Ph to form [IrH(C≡CPh)(η^2 -O₂CCH₃)(PⁱPr₃)₂] complex in the presence of PⁱPr₃.¹²

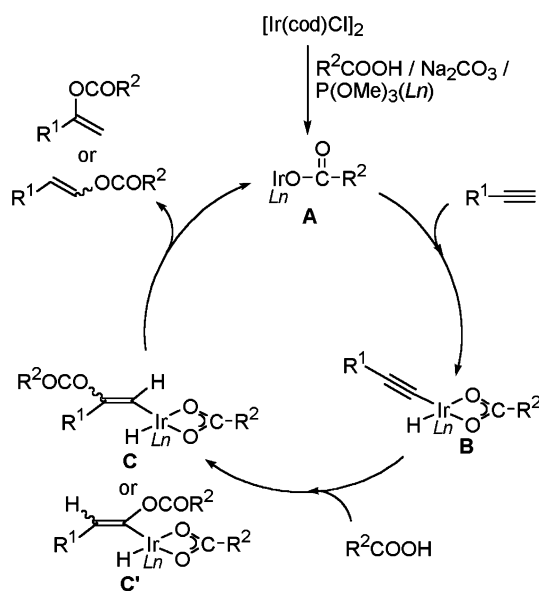
Although the reaction mechanism of the present Ir-catalyzed addition of carboxylic acids to alkynes leading to enol esters is unclear at this stage, it seems likely that [Ir(cod)Cl]₂ reacts initially with carboxylic acid under the influence of Na₂CO₃ to give an intermediate (**A**), followed by oxidative addition of alkyne forming [IrH(C≡CR¹)(η^2 -O₂CR²)Ln] (Ln=P(OMe)₃) (**B**) in a similar way as reported by Werner (Scheme 1). The addition of carboxylic acid to the triple bond on the resulting **B** furnishes **C** or **C'**, which subsequently undergoes reductive elimination to form the corresponding adducts and iridium complex **A**.

Vinyl esters are highly desirable compounds which can be converted into a variety of end-use polymer products. The synthesis of vinyl esters through transition metal-catalyzed transvinylolation undoubtedly qualifies as one of the most useful processes.² For example, palladium-catalyzed transfer vinylations between carboxylic acids and vinyl acetate are common and well-

Table 2. Reaction of **1** or **5** with several carboxylic acids^a

Entry	Carboxylic Acid	Product	(Yield/%, E/Z)
1 ^b			7 (79)
			8 (16, 35/65)
2 ^{b,c}			10 (67)
			11 (16, 38/62)
3 ^b	CH ₃ COOH		13 (77)
			14 (18, 47/53)
4 ^b			16 (62)
			17 (17, 43/57)
5 ^{b,d}			19 (52)
			20 (11, 33/67)
6 ^e	2		21 (51)
			22 (33, 19/81)
7 ^e	12		23 (22)
			24 (32, 22/78)

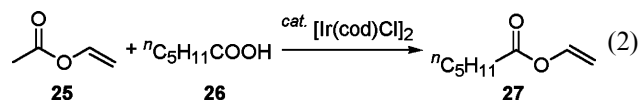
^a 1-Octyne (**1**) or phenylacetylene (**5**) (1 mmol) was allowed to react with carboxylic acid (2 mmol) in the presence of [Ir(cod)Cl]₂ (1 mol%), P(OMe)₃ (4 mol%) and Na₂CO₃ (2 mol%) in toluene (1 mL) at 100 °C for 15 h under Ar. ^b **1** was used. ^c For 4 h. ^d For 5 h. ^e **5** was used.

**Scheme 1.** A possible reaction pathway.

established as industrial methodology.^{2f} It has also been reported that some ruthenium compounds enhance the transvinylolation, but these reactions sometimes require relatively higher reaction temperature (130–150°C).^{2c}

In a previous paper, we reported a novel versatile method for the synthesis of vinyl ethers by treatment of alcohols with vinyl acetate under the influence of [Ir(cod)Cl]₂ combined with Na₂CO₃.^{9a} Our interest thus turned to develop another class of iridium-catalyzed synthesis of vinyl esters from the reaction of carboxylic acids and vinyl acetate.

Caproic acid (**26**) was allowed to react with 10 equiv. of vinyl acetate (**25**) in the presence of catalytic amounts of [Ir(cod)Cl]₂ (1 mol%) and NaOAc (3 mol%) without any ligands in toluene at 100°C for 15 h to afford vinyl caproate (**27**) in 94% selectivity at 94% conversion (Eq. (2), Table 3, entry 1).¹⁴ The reaction without NaOAc afforded **27** in slightly lower conversion (entry 2). The vinylation was found to take place even at 90°C

**Table 3.** Reaction of vinyl acetate (**25**) with several carboxylic acids^a

Entry	Carboxylic Acid	Conv./% ^b	Product	Select./% ^c
1	26	94	27	94
2 ^d	26	65	27	91
3 ^e	26	85	27	91
4 ^f	26	79	27	91
5		89		94
6		88		89
7	15	94		88
8	18	80		98
9	2	77		91

^a Carboxylic acid (1 mmol) was allowed to react with vinyl acetate (**25**) (10 mmol) in the presence of [Ir(cod)Cl]₂ (1 mol%) and NaOAc (3 mol%) in toluene (3 mL) at 100 °C for 15 h under Ar. ^b Based on carboxylic acid used. ^c Based on carboxylic acid consumed. ^d In the absence of NaOAc. ^e At 90 °C. ^f **25** (5 mmol) was used.

(entry 3), though the ruthenium-catalyzed transvinylation was usually carried out at 130–150°C.^{2c} The yield of **27** decreased when the amount of **25** was halved, since the reaction lies in equilibrium (entry 4). Under these reaction conditions, various vinyl esters were successfully synthesized from carboxylic acids and **25** in good to excellent selectivities by the iridium-catalyzed transvinylation (entries 5–9).

In summary, we have shown the development of a synthetic method of enol and vinyl esters by the use of an iridium complex as a catalyst. The addition of carboxylic acids to alkynes was facilitated by [Ir(cod)Cl]₂ combined with small amounts of P(OMe)₃ and Na₂CO₃ giving Markovnikov adducts as major products. In addition, the transvinylation between carboxylic acids and vinyl acetate was realized in good yields using the [Ir(cod)Cl]₂/NaOAc system. Further studies for the optimization of the reaction conditions as well as for the reaction pathway are now in progress.

Acknowledgements

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References

- (a) March, J. *Advanced Organic Chemistry*; Wiley: New York, 1985; (b) Monthéard, J. P.; Camps, M.; Seytre, G.; Guillet, J.; Dubois, J. C. *Makromol. Chem.* **1978**, *72*, 45.
- (a) Lobell, M.; Schneider, M. P. *Synthesis* **1994**, 375; (b) Seidel, A.; Jägers, E.; Bylsma, F. Eur. Pat. 0574725 A1, 1993; (c) Murray, E. R.; Lincoln, D. M. *Catal. Today* **1992**, *13*, 93; (d) Murray, R. E. Eur. Pat. 0351603 A2, 1989; (e) Mondal, M. A. S.; van der Meer, R.; German, A. L.; Heikens, D. *Tetrahedron* **1974**, 4205; (f) Henry, P. M. *Acc. Chem. Res.* **1973**, *6*, 16; (g) Rothman, E. S.; Serota, S.; Swern, D. *J. Org. Chem.* **1966**, *31*, 629.
- (a) Nicoleau, I.; Colling, P.; Johnson, L. Int. Pat. WO 94/08714, 1994; (b) Colquhoun, H. M.; Holton, J.; Thompson, D. J.; Twigg, M. V. *New Pathways for Organic Synthesis*; Plenum Press: New York, 1985; p. 350.
- (a) Schultz, R. G.; Gross, D. E. *Adv. Chem. Ser.* **1968**, *70*, 97; (b) Kitching, W.; Rapport, Z.; Winstein, S.; Young, W. G. *J. Am. Chem. Soc.* **1966**, *88*, 2054.
- Hudrlik, P. F.; Hudrlik, A. M. *J. Org. Chem.* **1973**, *38*, 4254.
- Rotem, M.; Shvo, Y. *Organometallics* **1983**, *2*, 1689.
- (a) Kawano, H.; Masaki, Y.; Matsunaga, T.; Hiraki, K.; Onishi, M.; Tsubomura, T. *J. Organometallic Chem.* **2000**, *604*, 69; (b) Bruneau, C.; Dixneuf, P. H. *Chem. Commun.* **1997**, 507; (c) Doucet, H.; Martin-Vaca, B.; Bruneau, C.; Dixneuf, P. H. *J. Org. Chem.* **1995**, *60*, 7247; (d) Kita, Y.; Maeda, H.; Onari, K.; Okuno, T.; Tamura, Y. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2999; (e) Bruneau, C.; Neveux, M.; Kabouche, Z.; Rupp, C.; Dixneuf, P. H. *Synlett* **1991**, 755; (f) Söderberg, B. C.; Turbeville, M. J. *Organometallics* **1991**, *10*, 3951; (g) Rupp, C.; Dixneuf, P. H.; Lecolier, S. *Tetrahedron Lett.* **1988**, *29*, 5365; (h) Mitsudo, T.; Hori, Y.; Yamakawa, Y.; Watanabe, Y. *J. Org. Chem.* **1987**, *52*, 2230; (i) Rupp, C.; Dixneuf, P. H. *Tetrahedron Lett.* **1986**, *27*, 6323; (j) Mitsudo, T.; Hori, Y.; Watanabe, Y. *J. Org. Chem.* **1985**, *50*, 1566.
- (a) Lu, X.; Zhu, G.; Ma, S. *Tetrahedron Lett.* **1992**, *33*, 7205; (b) Bianchini, C.; Meli, A.; Peruzzini, M.; Zanobini, F.; Bruneau, C.; Dixneuf, P. H. *Organometallics* **1990**, *9*, 1155.
- (a) Okimoto, Y.; Sakaguchi, S.; Ishii, Y. *J. Am. Chem. Soc.* **2002**, *124*, 1590; (b) Sakaguchi, S.; Kubo, T.; Ishii, Y. *Angew. Chem., Int. Ed. Engl.* **2001**, *40*, 2534; (c) Sakaguchi, S.; Yamaga, T.; Ishii, Y. *J. Org. Chem.* **2001**, *66*, 4710; (d) Higashino, T.; Sakaguchi, S.; Ishii, Y. *Org. Lett.* **2000**, *2*, 4193; (e) Kubo, T.; Sakaguchi, S.; Ishii, Y. *Chem. Commun.* **2000**, 625.
- A typical reaction procedure is as follows: To a toluene solution (1 mL) of [IrCl(cod)]₂ (0.01 mmol) P(OMe)₃ (0.04 mmol) and Na₂CO₃ (0.02 mmol) were added **1** (1 mmol) and **2** (2 mmol) under Ar. The reaction mixture was stirred at 100°C for 15 h. After quenching with wet ether, the product was isolated by column chromatography (230–400 mesh silica gel).
- Ohmura, T.; Yorozya, S.; Yamamoto, Y.; Miyaura, N. *Organometallics* **2000**, *19*, 365.
- Werner, H.; Poelsma, S.; Schneider, M. E.; Windmuller, B.; Barth, D. *Chem. Ber.* **1996**, *129*, 647. Quite recently, Tani and co-workers have reported that the iridium carboxylate complex like [IrCl(H)(μ-O₂CCH₃){(s)-binap}] was formed by treating [IrCl{(s)-binap}]₂ with acetic acid.¹³
- Tani, K.; Hoshida, K.; Yamagata, T. In Symposium on Organometallic Chemistry, Japan, Abstract, 2001, 168.
- A typical reaction procedure is as follows: To a toluene solution (3 mL) of [IrCl(cod)]₂ (0.01 mmol) and NaOAc (0.03 mmol) were added **26** (1 mmol) and **25** (10 mmol) under Ar. The reaction mixture was stirred at 100°C for 15 h.