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Regio- and stereoselective addition of carboxylic acids to phenylacetylene catalyzed by cyclopentadienyl ruthenium complexes

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Abstract

The direct addition of carboxylic acids to terminal alkynes such as phenylacetylene in the presence of catalytic amount of [CpRu-$(CO)_2$Cl] (**1**) or [{$CpRu(CO)_2$}$_2$] (**2**) affords the anti-Markovnikov adducts with high selectivity. In most instances, the *E*-enol esters are the major products.
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1. Introduction

Enol esters are important reagents and useful intermediates for carbon–carbon and carbon–heteroatom bond formation reactions [1,2]. The most straightforward and atom-economic way to the synthesis of enol esters is the direct addition of carboxylic acids to 1-alkynes catalyzed by transition metal complexes which can give rise to three products (Scheme 1). Since the first report in 1983 of the [$Ru_3(CO)_{12}$]-catalyzed addition reaction under rather drastic conditions and low selectivity [3], a variety of transition metal-based catalysts have been investigated, including Ru [2,4–6], Rh [7,8], Pd [9], Ir [10], Re [11], and even bimetallic systems[12], many of which exhibited improved regio- and stereoselectivity under milder conditions. Most of these catalysts afforded selective formation of the Markovnikov adducts and only in recent years that catalysts leading to anti-Markovnikov adducts have been reported. Among the latter, with some notable exceptions [6], the *Z*-enol esters were often the predominant product obtained [4,5,8,11]. In this paper, we report a new catalytic system based on simple, air-stable and easily prepared Ru complexes that selectively affords the anti-Markovnikov and *cis*-addition products. To the best of our knowledge, this is also the first example of cyclopentadienyl ruthenium complexes catalyzing the addition of carboxylic acids to alkynes.

2. Results and discussion

The catalytic efficiency of the complexes [$CpRu(CO)_2$Cl] (**1**) and [{$CpRu(CO)_2$}$_2$] (**2**) for the addition of carboxylic acids to phenylacetylene has been studied (Table 1). The reactions were performed under relatively mild conditions and without optimization, and no special precautions against air and moisture in the handling of the complexes were needed. The products have all been characterized spectroscopically (Table 2), and the efficiencies and selectivities of the reactions have been determined by isolation, GC as well as NMR methods; many of the *Z*-isomers have been reported earlier [5,6,10,11].

Both **1** and **2** are very active catalysts for these reactions and they show similar activities. With the exception of C_6F_5COOH (**6**), the regioselectivity for the anti-Markovnikov adducts was very high. The reaction with benzoic acid (**5**) proceeded particularly well. Significant stereoselectivities

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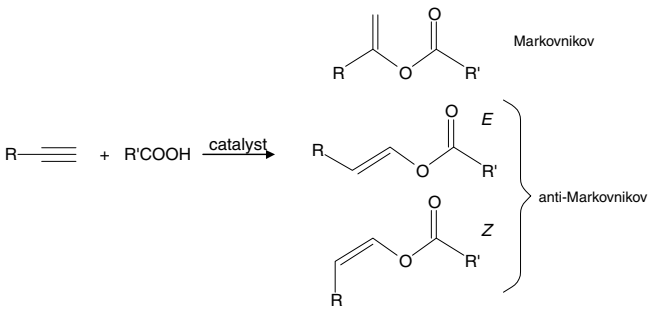


Scheme 1.

were observed for acetic acid, butyric acid and benzoic acid, and it appears that **1** afforded marginally better stereoselectivity than **2** although they showed similar regioselectivity. Although the addition reaction for **6** did proceed, regio- and stereoselectivities were low, with either **1** or **2**; separation was fairly easy, however, as the (*E*)-isomer precipitated out as a white solid from the reaction mixture upon cooling to room temperature while the (*Z*)-isomer and the Markovnikov adduct remained in solution. It has been observed that strong acids may afford products in higher regio- and stereoselectivities if the reaction temperature was kept lower [5]. However, we have found that the reaction of **6** at 70 °C did not show any improvement in selectivity. We have also found that the reaction of CF_3COOH at various temperatures ranging from 0 to 110 °C did not give any addition products; the in situ NMR spectra were always very complicated. These observations indicate that very strong carboxylic acids were not suitable substrates for this catalytic system.

In contrast to phenylacetylene, the analogous reactions using 1-hexyne proceeded with very low yields, and poorer regio- and stereoselectivities; variations in the temperature did not result in any improvement either. Thus the reaction of **5** and 1-hexyne under the same conditions gave total yields of 13% and 19% for **1** and **2**, respectively, with regioselectivity for the anti-Markovnikov product at 74.5% and 77.4%, respectively, and *E*/*Z* ratios of slightly less than unity. For the other acids, no products were formed at all. This is again in contrast to the other ruthenium systems, for which the yields of the 1-hexyne reactions are comparable or even higher than those for phenylacetylene. The reaction also failed to proceed when diphenylacetylene was employed as the alkyne substrate.

No catalytic intermediates were observable spectroscopically when stoichiometric mixtures of phenylacetylene or benzoic acid and **2** were heated over a period of 24 h; the ^{1}H NMR and IR spectra showed the presence of **2** only. In the reported $[\{Ru(RCOO)(CO)_2(L)\}_2]$ system, it was proposed that generation of the actual catalytic precursor (a mononuclear intermediate) required both an alkyne and acid [4e]; our results here therefore appear to indicate that an intermediate having both a bound alkyne and acid is involved in our system. Although we have yet to elucidate the details of the catalytic cycle for this reaction, one possible cycle that we are proposing is depicted in Scheme 2.

The similar efficiencies and selectivities shown by both **1** and **2** suggest that they are precursors to the same intermediate. However, that no observable products were formed when **5** was reacted with **2** suggests that this catalytically active species is present in only very minute amounts. The possible identity of this intermediate is $[CpRu(CO)_2(O_2CR)]$ (**A**), which may be formed from **1** via nucleophilic displacement of the Cl^- ion by the carboxylate; this would be consistent with the reaction working better with a weaker acid (and hence stronger conjugate base). This intermediate may also be formed from **2** via oxidative addition across the metal–metal bond. In either case, the equilibrium probably lies to the left-hand side, and it is the binding of the alkyne that drives the reaction forward. Indeed, we have verified that $[CpRu(CO)_2(O_2CPh)]$ does

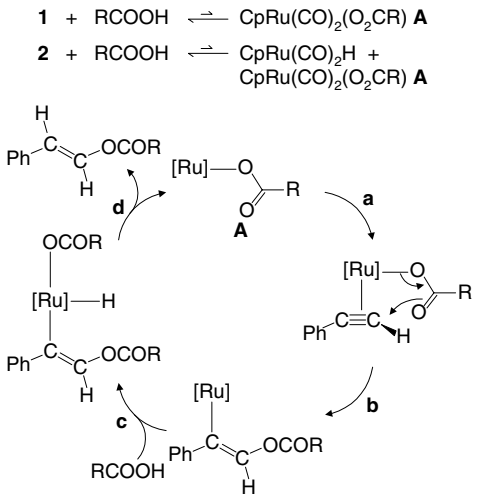
Table 1
Enol ester formation catalyzed by complexes **1** and **2**

Entry	Catalyst	Alkyne	Acid	%Conversion[a]	%Yield of adducts[b]	Selectivity[c]	*E*/*Z* ratio
1	**1**	Phenylacetylene	CH_3COOH (**3**)	84	78 (66)	97	6.0
2	**2**			92	86 (71)	97	2.9
3	**1**		$CH_3(CH_2)_2COOH$ (**4**)	80	78 (77)	97	4.1
4	**2**			79	77 (76)	97	3.0
5	**1**		C_6H_5COOH (**5**)	98.5	90 (80)	96	3.2
6	**2**			100	96 (90)	96	2.7
7	**1**		C_6F_5COOH (**6**)		(92)	47	0.8
8	**2**				(90)	61	1.0
9	**1**		$CH_3CH(Br)COOH$ (**7**)	88	48 (40)	93	1.1
10	**2**			95	75 (69)	95	1.2
11	**1**		*E*-$CH_3CH{=}CHCOOH$ (**8**)	94	91 (80)	98	5.1
12	**2**			70	68 (67)	97	5.1
13	**1**	1-Hexyne	C_6H_5COOH		(13)	74	0.8
14	**2**				(19)	77	0.9

Reaction condition: toluene, 110 °C, [alkyne] = 2 M, alkyne/acid/catalyst = 100:100:1, 24 h.
[a] Based on the consumption of alkyne, determined by GC.
[b] GC yields (isolated yields).
[c] Selectivity = anti-Markovnikov adducts/total enol esters; determined by ^{1}H NMR and GC.

Table 2
Characterization of reaction products

Acid	Product	Appearance	IR/cm^{-1}	^{1}H NMR, δ	EI-MS, *m/z*
3	β-Styryl acetate	Colorless liquid	1761 ($\nu_{C=O}$)	*E*-isomer: 7.84 (d, 1H, $^3J_{trans}$ = 12.8 Hz, =CH), 7.37–7.20 (m, 5H, Ph), 6.39 (d, 1H, =CH), 2.19 (s, 3H, Me)	162 (M^+)
			1661 ($\nu_{C=C}$)	*Z*-isomer: δ 7.58 (d, 1H, $^3J_{cis}$ = 7.4 Hz, =CH), 7.37–7.20 (m, 5H, Ph), 5.70 (d, 1H, =CH), 2.27 (s, 3H, Me)	
4	β-Styryl butyrate	Colorless liquid	1756 ($\nu_{C=O}$)	*E*-isomer: 7.87 (d, 1H, $^3J_{trans}$ = 412.8 Hz, =CH), 7.38–7.26 (m, 5H, Ph), 6.39 (d, 1H, =CH), 2.43 (t, 2H, ^3J = 7.4 Hz, CCH_2), 1.73 (m, 2H, CH_2), 1.01 (t, 3H, ^3J = 7.2 Hz, Me)	190 (M^+)
			1655 ($\nu_{C=C}$)	*Z*-isomer: 7.58 (d, 1H, $^3J_{cis}$ = 7.7 Hz, =CH), 7.38–7.26 (m, 5H, Ph), 5.70 (d, 1H, =CH), 2.52 (t, 2H, ^3J = 7.4 Hz, CCH_2), 1.78 (m, 2H, CH_2), 1.03 (t, 3H, ^3J = 7.6 Hz, Me)	
5	β-Styryl benzoate	White solid	1726 ($\nu_{C=O}$)	*E*-isomer: 8.09 (d, 1H, $^3J_{trans}$ = 12.8 Hz, =CH), 8.16–7.20 (m, 10H, Ph), 6.59 (d, 1H, =CH)	224 (M^+)
			1656 ($\nu_{C=C}$)	*Z*-isomer: 8.16–7.20 (m, 11H, Ph and =CH), 5.86 (d, 1H, $^3J_{cis}$ = 7.2 Hz, =CH)	
6	β-Styryl pentafluorobenzoate	White solid	1754 ($\nu_{C=O}$)	*E*-isomer: 7.99 (d, 1H, $^3J_{trans}$ = 13.3 Hz, =CH), 7.4–7.2 (m, 5H, Ph), 6.60 (d, 1H, =CH)	314 (M^+)
			1651 ($\nu_{C=C}$)	Z:isomer: 7.47 (d, 1H, $^3J_{cis}$ = 7.2 Hz, =CH), 7.26–7.59 (m, 5H, Ph), 5.93(d, 1H, =CH), M-adduct: 7.26–7.59 (m, 5H, Ph), 5.59 (d, 1H, $^2J_{gem}$ = 1.2 Hz, $=CH_2$), 5.23 (d, 1H, $=CH_2$)	
7	β-Styryl 2-bromopropanoate	Colorless liquid	1750 ($\nu_{C=O}$)	*E*-isomer: 7.82 (d, 1H, $^3J_{trans}$ = 12.8 Hz, =CH), 7.39–7.26 (m, 5H, Ph), 6.50 (d, 1H, =CH), 4.47 (q, 1H, ^3J = 6.8 Hz, CH), 1.92 (d, 3H, Me)	255 (M^+)
			1662 ($\nu_{C=C}$)	*Z*-isomer: 7.61 (d, 1H, $^3J_{cis}$ = 6.8Hz, =CH), 7.39–7.26 (m, 5H, Ph), 5.81 (d, 1H, =CH), 4.55 (q, 1H, ^3J = 6.8 Hz), 1.92 (d, 3H, Me)	
8	β-Styryl crotonate	Colorless liquid	1735 ($\nu_{C=O}$)	*E*-isomer: 7.98 (d, 1H, $^3J_{trans}$ = 12.8 Hz, =CH), 7.62–7.10 (m, 6H, Ph and =CH), 6.44 (d, 1H, =CH), 5.92 (dq, 1H, ^3J = 15.7 and 1.6 Hz, C*H*Me), 1.95 (dd, 3H, Me)	188 (M^+)
			1651 ($\nu_{C=C}$)	*Z*-isomer: 7.62 (d, 1H, $^3J_{cis}$ = 7.2 Hz, =CH), 7.62–7.10 (m, 6H, Ph and =CH), 6.02 (dq, 1H, ^3J = 15.7 and 1.6 Hz, C*H*Me), 5.74 (d, 1H, =CH), 1.99 (dd, 3H, Me)	
5	Hex-1-en-1-yl benzoate	Colorless liquid	1735 ($\nu_{C=O}$)	*E*-isomer: 8.2–7.2 (m, 6H, Ph and =CH), 5.60 (dt, 1H, $^3J_{trans}$ = 12.4 Hz, =CH), 2.09 (m, 2H, CH_2), 1.38 (m, 4H, 2 × CH_2), 0.90 (t, 3H, Me)	184 (M^+)
			1665 ($\nu_{C=C}$)	*Z*-isomer: 8.2–7.2 (m, 6H, Ph and =CH), 5.01 (dt, 1H, $^3J_{cis}$ = 7.2 Hz, =CH), 2.30 (m, 2H, CH_2), 1.38 (m, 4H, 2 × CH_2), 0.90 (t, 3H, Me)	



Scheme 2.

catalyze the reaction of **5** with phenylacetylene at a similar efficiency (95% yield of the adducts under the same conditions) [13]. The possibility of a vinylidene intermediate cannot be completely ruled out although it is unlikely as the predicted region- and stereoselectivities would be reversed [4g,4h,4j,5].

The possibilities for the binding of the alkyne (step **a**) include loss of a carbonyl or an $\eta^5 \rightarrow \eta^3$ ring slippage [14], although the latter has been shown to be unlikely in the closely related case of the cycloaddition of cyclooctadiene with alkyne by [CpRu(COD)Cl], which is also believed to proceed through initial loss of the Cl^- ligand [14b]. The subsequent migratory insertion (step **b**) is probably the critical step that dictates the regio- and stereoselectivity; the carboxylate ligand is probably aligned as shown with respect to the alkyne to avoid steric interaction between them, which leads to the anti-Markovnikov product. This

intramolecular nature of step **b** would also account for the stereoselectivity; indeed it is expected to lead to only the *E*-isomers. That the *Z*-isomers are also observed may be attributed to either of two possibilities: alkene isomerization, or the presence of another reaction pathway for step **b**. We have confirmed that alkene isomerization did not occur in our system; no isomerization product was found when the pure *E*-β-styryl pentafluorobenzoate and 3 mol% of **2** was refluxed in toluene for 24 h. It is therefore likely that step **b** involved two alternative pathways, the other being an intermolecular attack by carboxylate. This would seem to be consistent with the observation that stereoselectivities are poorest for the strongest acids **6** and **7**, since they would be expected to form more carboxylates in solution and hence favor the intermolecular pathway. The final two steps of the proposed cycle involve oxidative addition of the carboxylic acid (step **c**) followed by reductive elimination of the product and regeneration of the catalytically active species (step **d**).

In conclusion we have uncovered a highly efficient and selective catalytic method for the synthesis of β-styryl type enol esters by the addition of carboxylic acids to 1-alkynes using two readily available half-sandwich ruthenium complexes. In particular, they are the first examples for which high selectivity for the anti-Markovnikov, *cis*-addition products is obtained.

3. Experimental

3.1. General procedures

All manipulations were carried out under an inert atmosphere using Schlenk techniques. Catalytic reactions were performed in a thick-walled glass Carius tube equipped with a Teflon valve. ^{1}H NMR spectra were recorded as $CDCl_3$ solutions on a Bruker ACF300 NMR spectrometer; chemical shifts were referenced to the residual solvent resonance. IR spectra were recorded as CH_2Cl_2 solutions in a solution cell with NaCl windows and 0.1 mm pathlength, on a BioRad FTS-165 FTIR instrument. Mass spectra were obtained on a Finnigan Mat 95XL-T spectrometer. GC analyses were performed on a Perkin–Elmer Autosystem XL with an HP-1 column. Toluene was dried and distilled under nitrogen before use. The complexes $[CpRu(CO)_2Cl]$ (**1**) and $[\{CpRu(CO)_2\}_2]$ (**2**) were prepared according to the literature methods [15,16]. All the other chemicals were of commercial reagent grade and used as received without further purification.

3.2. A typical procedure for the catalytic runs

Acetic acid (115 μL, 2 mmol), phenylacetylene (0.22 mL, 2 mmol) and the catalyst (0.02 mmol) in toluene (1 mL) were stirred at 110 °C for 24 h. After cooling, the reaction mixture was diluted with toluene to 4 mL and *n*-nonane (70 μL) was added as internal standard. The resulting mixture was then analyzed by GC. The product was purified by silica gel column chromatography (eluant: hexane–diethyl ether, 10:1, v/v) to afford first a mixture of the *Z*- and *E*-enol esters (0.42 g) as a colorless oil, followed by the Markovnikov adduct.

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Appendix A. Supplementary data

^{1}H NMR spectra of the anti-Markovnikov products. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2005.11.023.

References

[1] C. Fischmeister, C.C. Bruneau, P.H. Dixneuf, in: S.-I. Murahashi (Ed.), Ruthenium in Organic Synthesis, Wiley–VCH, New York, 2004, p. 189 (Chapter 8).
[2] C. Bruneau, P.H. Dixneuf, Chem. Commun. (1997) 507.
[3] M. Rotem, Y. Shvo, Organometallics 2 (1983) 1689.
[4] (a) T. Mitsudo, Y. Hori, Y. Watanabe, J. Org. Chem. 50 (1985) 1566;
(b) T. Mitsudo, Y. Hori, Y. Yamakawa, Y. Watanabe, Tetrahedron Lett. 27 (1986) 2125;
(c) C. Ruppin, P.H. Dixneuf, Tetrahedron Lett. 27 (1986) 6323;
(d) Y. Hori, T. Mitsudo, Y. Watanabe, J. Organomet. Chem. 321 (1987) 397;
(e) M. Rotem, Y. Shvo, J. Organomet. Chem. 448 (1993) 189;
(f) H. Kawano, Y. Masaki, T. Matsunaga, K. Hiraki, M. Onishi, T. Tsubomura, J. Organomet. Chem. 601 (2000) 69;
(g) K. Melis, T. Opstal, F. Verpoort, Eur. J. Org. Chem. 22 (2002) 3779;
(h) K. Melis, F. Verpoort, J. Mol. Catal. A 194 (2003) 39;
(i) L. Goossen, J. Paetzold, D. Koley, Chem. Commun. (2003) 706;
(j) K. Melis, D. Vos, P. Jacobs, F. Verpoort, J. Organomet. Chem. 671 (2003) 131.
[5] H. Doucet, B. Martin-Vaca, C. Bruneau, P.H. Dixneuf, J. Org. Chem. 60 (1995) 7247.
[6] K. Melis, P. Samulkiewicz, J. Rynkowski, F. Verpoort, Tetrahedron Lett. 43 (2002) 2713.
[7] C. Bianchini, A. Meli, M. Peruzzini, F. Zanobini, C. Bruneau, P.H. Dixneuf, Organometallics 9 (1990) 1155.
[8] S. Doherty, J.G. Knight, R.K. Rath, W. Clegg, R.W. Harrington, C.R. Newman, R. Campbell, H. Amin, Organometallics 24 (2005) 2633.
[9] X. Lu, G. Zhu, S. Ma, Tetrahedron Lett. 33 (1992) 7205.
[10] H. Nakagawa, S. Okimoto, S. Sakaguchi, Y. Ishii, Tetrahedron Lett. 44 (2003) 103.
[11] R. Hua, X. Tian, J. Org. Chem. 69 (2004) 5782.
[12] P. Le Gendre, V. Comte, M. Michelot, C. Möise, Inorg. Chim. Acta 350 (2003) 289.
[13] $CpRu(CO)_2(O_2CPh)$ was prepared by an adaptation of the method from: A.S. Batsanov, O.S. Manole, Yu.T. Struchkov, G.P. Zol'nikova, D.N. Kravtsov, Izv. Akad. Nauk, Ser. Khim. (1993) 395.
[14] (a) T. Mizuta, Y. Imamura, K. Miyoshi, J. Am. Chem. Soc. 125 (2003) 2068;
(b) X. Huang, Z. Lin, Organometallics 22 (2003) 5478, and references therein.
[15] A. Eisenstadt, R. Tannebaub, A. Efraty, J. Organomet. Chem. 221 (1981) 317.
[16] N.M. Doherty, S.A.R. Knox, Inorg. Synth. 25 (1986) 180.