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The First Example of Rhodium(I)-Catalyzed Regio- and Stereoselective Chloroesterification of Alkynes with Chloroformate Esters

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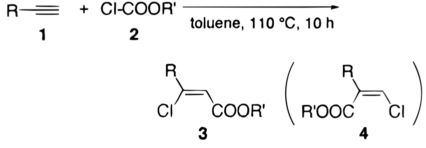
Hydroesterification of alkynes with carbon monoxide and alcohols[1] or with formate esters[2] is a process of great practical importance. However, the corresponding chloroesterification reaction, which provides a one-step synthesis of β-chloro-α,β-unsaturated esters with much synthetic potential,[3] has never been reported. In recent years we have been interested in transition metal complex-catalyzed addition reactions of E−E′ bonds (E, E′ = heteroatom or functional group) to alkynes in order to synthesize doubly functionalized alkenes in a single step.[4] Research in this area has led to the discovery of the efficient chloroesterification of alkynes with chloroformates (E = Cl, E′ = COOR).

In a representative experiment, a mixture of 1-hexyne **1** (0.2 mmol), methyl chloroformate **2a** (0.6 mmol), and a catalytic amount of $RhCl(CO)(PPh_3)_2$ (0.002 mmol) dissolved in toluene (0.5 mL) was heated at 110 °C for 10 h. GC and GC−MS analyses suggested the formation of methyl (*Z*)-3-chloro-2-heptenoate **3a** and its regioisomer **4a** in a ratio of 97:3 (eq 1; R $= n\text{-}C_4H_9$, R′ = Me). Evaporation followed by column chromatography (silica gel, 2:1 hexanes−ether) afforded a mixture of these in 79% isolated yield (**3a**/**4a** = 99/1). Spectroscopic data for these products are consistent with the proposed structures,[5] and NOE experiments (e.g., 12 and 6% enhancement between the allylic and the olefinic hydrogens in **3a** and **4a**, respectively) confirm that *cis*-addition has taken place.



(1)

Screening of various catalysts (GC yield and **3a**/**4a** ratio are shown for each case) in the reaction of **1** with **2a** under the same conditions revealed that $RhCl(CO)(PPh_3)_2$ (87%, 97/3), $RhCl(cod)(PPh_3)$ (cod = 1,5-cyclooctadiene; 91%, 97/3), and $RhBr(cod)(PPh_3)$ (91%, 98/2) are the catalysts of choice. The use of Vaska-type rhodium complexes having diphosphine ligands, such as dppf (1,1′-bis(diphenylphosphino)ferrocene; 55%, 94/6), dppe (1,2-bis(diphenylphosphino)ethane; 31%, 94/6), and dppb (1,4-bis(diphenylphosphino)butane; 26%, 91/9) gave high regioselectivities, but the yields were modest. Other rhodium complexes ligated by more basic phosphines such as $RhCl(CO)(PPh_2Me)_2$ (67%, 84/16), $RhCl(CO)(PPhMe_2)_2$ (6%, 85/15), $RhCl(CO)(PMe_3)_2$ (3%, 58/42), $RhCl(cod)(PPhMe_2)$ (19%, 64/36), and $RhCl(cod)(PMe_3)$ (5%, 65/35) resulted in lower yields and/or lower regioselectivities than $RhCl(CO)(PPh_3)_2$ and $RhCl(cod)(PPh_3)$. The activity of $IrCl(CO)(PPh_3)_2$ was very low, resulting in less than 1% yield. Rhodium complexes, either phosphine-free or having three phosphine ligands, such as $[RhCl(cod)]_2$, $RhCl(PPh_3)_3$, and $RhH(CO)(PPh_3)_3$, did not form the product at all.[6]

Ethyl **2b** and benzyl **2c** chloroformates also reacted with high regio- and stereoselectivities to afford (*Z*)-adducts in 95 and 87% isolated yields with ratios (in the isolated product) of **3b**/**4b** = 100/0 and **3c**/**4c** > 99/1, respectively. Phenyl chloroformate **2d** reacted fairly slowly and with less regioselectivity to afford a 60% total yield with **3d**/**4d** = 72/18.

The procedure can be readily scaled up and applied to other alkynes (Table 1).[7] The $RhCl(CO)(PPh_3)_2$-catalyzed addition of **2a** to 1-octyne gave an 86% yield of a **3e** and **4e** mixture in a regioisomeric ratio of 96:4. Other aliphatic alkynes substituted by a phenyl group, a bulky *tert*-butyl group, and functional groups such as chloro, cyano, and siloxy also reacted giving high regioselectivities. However, the reaction of methyl propargyl ether was rather complicated and gave the (*Z*)-adduct in only 25% yield. On the other hand, the reactions of aromatic alkynes were very clean. Thus, the reaction of phenylacetylene or 1-chloro-4-ethynylbenzene with **2a** gave methyl (*Z*)-β-chlorocinnamate **3l** or methyl (*Z*)-β-chloro-*p*-chlorocinnamate **3m** as essentially the sole product.[8] Similarly, the reaction of 4-ethynyltoluene with **2a** afforded methyl (*Z*)-β-chloro-*p*-methylcinnamate **3n**, the configuration of which was confirmed by X-ray crystrallogrophy.[9] Two ester groups could be readily introduced to 1,4-diethynylbenzene under the same reaction conditions to give **3p** as the sole product. However, all attempts to chloroesterify internal alkynes and alkenes under similar conditions have been unsuccessful to date, and the starting materials were recovered.

As far as $RhCl(CO)(PR_3)_2$ complex catalysts are concerned, the reaction can be rationalized by the mechanism illustrated in Scheme 1, which is partially substantiated by the following observations. Thus treatment of $RhCl(CO)(PR_3)_2$ complexes with

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(1) Review: (a) Pino, P.; Braca, G. In *Organic Syntheses via Metal Carbonyls*; Pino, P., Wender, I. Eds.; John Wiley and Sons: New York, 1977; Vol. 2, pp 419−516. Recent publications: (b) Hiyama, T.; Wakasa, N.; Ueda, T.; Kusumoto, T. *Bull. Chem. Soc. Jpn*. **1990**, *63*, 640. (c) Scrivanti, A.; Chinellato, R.; Matteoli, U. *J. Mol. Catal*. **1993**, *84*, L141. (d) Kushino, Y.; Itoh, K.; Miura, M.; Nomura, M. *J. Mol. Catal*. **1994**, *89*, 151. (e) Gabriele, B.; Salerno, G.; Costa, M.; Chiusoli, G. P. *J. Organomet. Chem*. **1995**, *503*, 21. (f) Xu, W.; Alper, H. *Macromolecues* **1996**, *29*, 6695−6699. (g) Piotti, M. E.; Alper, H. *J. Org. Chem*. **1997**, *62*, 8484−8489. (h) Scrivanti, A.; Beghetto, V.; Campagna, E.; Zanato, M.; Matteoli, U. *Organometallics* **1998**, *17*, 630.

(2) (a) Alper, H.; Saldana-Maldonado, M.; Lin, I. J. B. *J. Mol. Catal*. **1988**, *49*, L27. (b) El Ali, B.; Alper, H. *J. Mol. Catal*. **1991**, *67*, 29. (c) Zargarian, D.; Alper, H. *Organometallics* **1993**, *12*, 712. (d) El Ali, B.; Alper, H. *J. Mol. Catal*. **1995**, *96*, 197.

(3) For examples, see: (a) Youssef, A.-H. A.; Abdel-Maksond, H. M. *J. Org. Chem*. **1975**, *40*, 3227. (b) Youssef, A.-H. A.; Sharaf, S. M.; El-Sadany, S. K.; Hamed, E. A. *J. Org. Chem.* **1981**, *46*, 38136. (c) Seitz, D. E.; Lee, S.-H. *Tetrahedron lett.* **1981**, *22*, 4909. (d) Chalchat, J.-C.; Garry, R.-P., Lacroix; B., Michet, A.; Vessiree, R. *C. R. Hebd. Seances Acad. Sci., Ser. 2* **1983**, *296*, 253. (e) Jalander, L.; Broms, M. *Acta Chem. Scand.* **1983**, *37*, 173. (f) Barluenga, J.; Fernandez, J. R.; Yus, M. *J. Chem. Res., Synop*. **1986**, 273. (g) Grandjean, D.; Pale, P.; Chuche, J. *Tetrahedron* **1993**, *49*, 5225. (h) Mori, Y.; Asai, M.; Kawade, J.; Furukawa, H. *Tetrahedron* **1995**, *51*, 5315.

(4) (a) Han, L.-B.; Tanaka, M. *J. Am. Chem. Soc.* **1996**, *118*, 1571. (b) Han, L.-B.; Choi, N.; Tanaka, M. *J. Am. Chem. Soc.* **1996**, *118*, 7000. (c) Han, L.-B.; Choi, N.; Tanaka, M. *Organometallics* **1996**, *15*, 3259. (d) Onozawa, S.-Y.; Hatanaka, Y.; Sakakura, T.; Shimada, S.; Tanaka, M. *Organometalics* **1996**, *15*, 5450. (e) Onozawa, S.-Y.; Hatanaka, Y.; Tanaka, M. *Chem. Commun*. **1997**, 1229. (f) Han, L.-B.; Hua, R.; Tanaka, M. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 94.

(5) Reduction of **3a** to (*Z*)-3-chloro-2-hepten-1-ol **5** further confirmed the structure.

(6) In the reaction using $[RhCl(cod)]_2$, both ClCOOMe and 1-hexyne remained unreacted; however, the use of $RhCl(PPh_3)_3$ or $RhH(CO)(PPh_3)_3$ completely decomposed ClCOOMe, but 1-hexyne remained essentially intact. In the latter case, a large quantity of chloromethane was observed by ^1H and ^{13}C NMR spectroscopy.

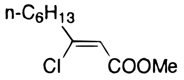
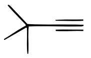
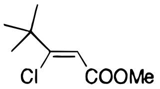
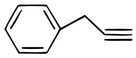
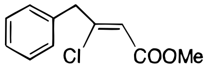
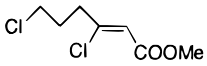
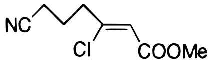
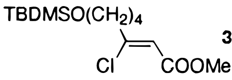
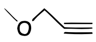
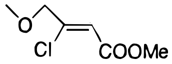
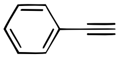
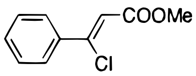
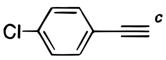
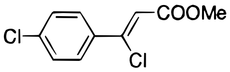
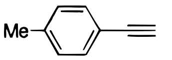
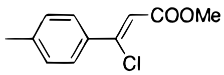
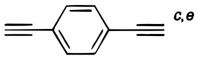
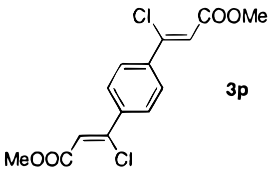
(7) A typical procedure: A mixture of **1** (410.0 mg, 5.0 mmol), **2a** (1410.0 mg, 15.0 mmol), and $RhCl(cod)(PPh_3)$ (25.4 mg, 0.05 mmol) in toluene (3.0 mL) was heated under nitrogen in a 25-mL autoclave at 110 °C for 10 h. After cooling, the solution was concentrated under reduced pressure. The residue was chromatographed on a silica gel column (hexane:ether = 2:1) to give the colorless oil adducts in 80% yield (705.0 mg, 4.0 mmol).

(8) Although the structures were not elucidated, traces of a dimer and a trimer were found by GC and GC−MS to be formed in the reaction of phenylacetylene. However, the 1-chloro-4-ethynylbenzene reaction did not form the corresponding byproducts at all.

(9) See Supporting Information for details of the crystal data.

10.1021/ja9822299 CCC: $15.00

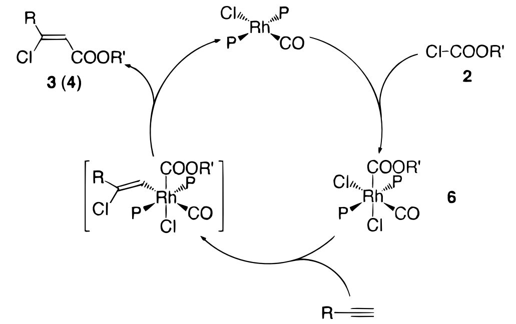
Table 1. Chloroesterification of Terminal Alkynes[a]

alkyne	adduct		% yield (**3**/**4**)[b]
n-C_6H_{13}—≡ [c]		**3e**	86 (96/4)
		**3f**	61 (100/0)
		**3g**	73 (97/3)
		**3h**	91 (94/6)
		**3i**	82 (94/6)
TBDMSO(CH_2)$_4$—≡ [c,d]		**3j**	72 (98/2)
		**3k**	25 (95/5)
		**3l**	79 (100/0)
 [c]		**3m**	84 (100/0)
		**3n**	63 (> 99/1)
 [c,e]		**3p**	64 (100/0)

[a] The reactions were carried out at 110 °C for 10 h by using 5.0 mmol alkynes, 15.0 mmol methyl chloroformate **2a** and 0.05 mmol RhCl(cod)(PPh_3) in 3 mL of toluene. [b] Isolated yield based on the alkynes used, and the ratio of **3/4** was determined by GC. [c] RhCl(CO)(PPh_3)$_2$ (0.05 mmol) was used as catalyst. [d] TBDMS stands for a *tert*-butyldimethylsilyl group. [e] 0.5 mmol alkyne, 3.0 mmol **2a**, and 0.01 mmol catalyst were used.

2a at 80 °C afforded $RhCl_2(CO)(COOMe)(PR_3)_2$ **6** ($PR_3 = PPh_3$ (**6a**), PPh_2Me (**6b**), $PPhMe_2$ (**6c**), PMe_3 (**6d**)),[10] which were confirmed by their NMR and IR spectra and/or elemental analysis.[11] The $^{31}P\{H\}$ NMR spectra of **6a**−**d** showed only one doublet (12.9 to −2.83 ppm; J_{Rh-P} = 88.2−82.4 Hz).[12] The ^1H NMR spectroscopy of **6c** displayed phosphine methyl signals as two apparent 1/2/1 triplets due to the virtual coupling. Likewise, **6b** and **6d** displayed one apparent 1/2/1 triplet. These ^{31}P and ^1H NMR spectroscopic data, in conjunction with previous observations,[13] suggest that complex **6** has the configuration shown in Scheme 1. Complex **6b**, when heated with 1-hexyne (3 equiv) at 110 °C for 3 h, gave a 93:7 mixture of **3a** and **4a** in 28% total yield. Regarding the alkyne insertion process, chlororhodation (insertion into Rh−Cl) may be more likely in view of the regioselectivity of the catalysis than alkoxycarbonylrhodation (insertion into Rh−COOR), which must proceed through congested internal attachment of rhodium.[14,15]

Scheme 1



Further investigations to clarify the mechanism and synthetic application of the products are in progress.

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Supporting Information Available: Text describing experimental details, spectroscopic and analytical details of adducts **3a**−**p** and rhodium complexes **6a**−**d**, tables of positional parameters and B_{eq} values, anisotropic thermal parameters, and bond lengths and angles for **3n** (two molecules) (18 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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[10] Oxidative addition of chloroformate with (η^5-C_5H_5)Rh(PMe_3)$_2$ is known to afford [(η^5-C_5H_5)Rh(COOMe)(PMe_3)$_2$]Cl. See: Keim, W.; Becker, J. *J. Organomet. Chem.* **1989**, *372*, 447.

[11] Complexes **6a**−**d** are unstable in solution; there exists an equibrilium between **6** and the starting materials (RhCl(CO)(PR_3)$_2$ and ClCOOMe). See Supporting Information for spectroscopic data.

[12] $^{31}P\{H\}$ NMR (C_6D_6): **6a**, 12.9 ppm (d, J_{Rh-P} = 88.2 Hz); **6b**, 9.77 ppm (d, J_{Rh-P} = 85.4 Hz); **6c**, 2.47 ppm (d, J_{Rh-P} = 82.7 Hz); **6d**, −2.83 ppm (d, J_{Rh-P} = 82.4 Hz).

[13] Deeming, A.; Shaw, B. L. *J. Chem. Soc. A* **1969**, 597.

[14] Rhodium-catalyzed chloroarylation of alkynes is reported to proceed via chlororhodation. See: Kokubo, K.; Matsumasa, K.; Miura, M.; Nomura, M. *J. Org. Chem.* **1996**, *61*, 6941.

[15] Incremental additions of PPh_3 to the RhCl(cod)(PPh_3)-catalyzed reaction system depressed the catalytic activity, suggesting that generation of monophosphine rhodium species would be involved, presumably prior to the alkyne coordination and insertion.