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$Re(CO)_5Br$-Catalyzed Addition of Carboxylic Acids to Terminal Alkynes: A High Anti-Markovnikov and Recoverable Homogeneous Catalyst

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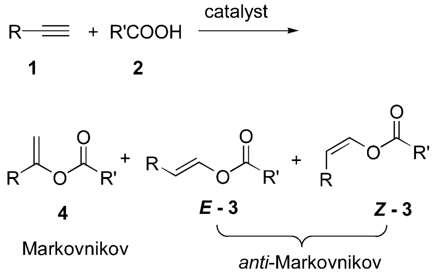
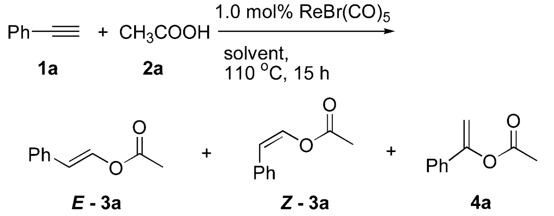
Abstract: The addition of carboxylic acids to terminal alkynes is efficiently catalyzed by the early transition-metal complex $Re(CO)_5Br$ in toluene or *n*-heptane at 110 °C in an air atmosphere, affording the anti-Markovnikov adducts in good yields with high selectivity. In most cases, the reactions afford unusual *Z*-adduct predominantly. When *n*-heptane was used as solvent, $Re(CO)_5Br$ can be partly recovered from the reaction mixture.

Transition-metal-catalyzed addition of carboxylic acids **1** to terminal alkynes **2** is an efficient, atom-economic method for the synthesis of 1-alkenyl esters. The addition reaction often affords a mixture of three possible 1-alkenyl esters (one Markovnikov-type adduct and two anti-Markovnikov-type *E* and *Z* adducts) (eq 1). Therefore, it is interesting and important to develop the catalyst system for the high regio- and stereocontrol of the addition reaction. Since Rotem and co-worker first reported the example of the addition reaction in 1983 using $Ru_3(CO)_{12}$ as catalyst,[1] a variety of other catalytic systems have been employed including Ru,[2] Rh,[3] Pd,[4] and Ir[5] complexes. In most cases, the addition reactions either gave the Markovnikov-type adduct as the major product or afforded a mixture of three adducts with low selectivity. The aims of our study are to develop a simple, efficient, and recoverable new catalyst system to catalyze the addition of carboxylic acids to terminal alkynes with high selectivity of the anti-Markovnikov adduct. In this paper, we describe our findings of an early transition-metal complex $Re(CO)_5Br$-catalyzed addition reaction of carboxylic acids to terminal alkynes with high selectivity to afford anti-Markovnikov adducts. To the best of our knowledge, this is the first example of early transition-metal-catalyzed addition of carboxylic acids to alkynes.



(1)

TABLE 1. Effect of Solvent on the Selectivity in the Addition of 2a to 1a Catalyzed by $Re(CO)_5Br$[a]



entry	solvent	yield of adducts (%)[b]	selectivity of **3a** (%) (E/Z)[c]
1	*n*-heptane	72 (60)	99 (27/73)
2	toluene	73	100 (28/72)
3	$CHCl_2CHCl_2$	69	100 (26/74)
4	di-*n*-butyl ether	73	95 (26/74)
5	DMF	30	94 (37/63)
6	$CH_3COOC_2H_5$	35	50 (44/56)
7	THF	20	40 (77/23)
8	acetone	4	29 (38/62)
9	CH_3CN	3	62 (42/58)

[a] Reactions were carried out with 2.0 mmol of **1a**, 2.5 mmol of **2a**, and 0.02 mmol of $Re(CO)_5Br$ in 1.0 mL of solvent at 110 °C for 15 h. [b] GC yields based on the amount of **1a** used. Values in parentheses are isolated yields. [c] Determined by GC.

We chose the reaction of phenyl acetylene **1a** with acetic acid **2a** in the presence of $Re(CO)_5Br$ as a model reaction to optimize the reaction conditions. The yields of adducts were determined by gas chromatographic analysis, using $C_{16}H_{34}$ as an internal standard. When a solution of 2.0 mmol of **1a**, 2.5 mmol of **2a**, and 0.02 mmol of $Re(CO)_5Br$ in 1.0 mL of *n*-heptane, in an air atmosphere of a closed glass tube, was stirred at 110 °C for 15 h, the GC and GC-MS analyses of the reaction mixture showed the formation of three adducts in a ratio of <1:73:27 (retention time order) in 72% GC yield. The ^1H NMR spectroscopic data of the reaction mixture disclosed that the addition reaction gave only a trace amount of the Markovnikov adduct **4a** (<1%). On the basis of the coupling constants of the olefinic protons of the anti-Markovnikov adducts, it was confirmed that the ratio of *Z*-**3a**:*E*-**3a** was 73:27. These results are in accordance with the GC quantitatively analytical data (Table 1, entry

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(1) Rotem, M.; Shvo, Y. *Organometallics* **1983**, *2*, 1689−1691.

(2) (a) Mitsudo, T.; Hori, Y.; Watanabe, Y. *J. Org. Chem.*, **1985**, *50*, 1566−1568. (b) Ruppin, C.; Dixneuf, P. H. *Tetrahedron Lett.* **1986**, *27*, 6323−6324. (c) Mitsudo, T.; Hori, Y.; Yamakawa, Y.; Watanabe, Y. *J. Org. Chem*. **1987**, *52*, 2230−2239. (d) Rotem, M.; Shvo, Y. *J. Organomet. Chem*. **1993**, *448*, 189−204. (e) Doucet, H.; Martin-Vaca, B.; Bruneau, C.; Dixneuf, P. H. *J. Org. Chem*. **1995**, *60*, 7247−7255. (f) Bruneau, C.; Dixneuf, P. H. *Chem. Commun*. **1997**, 507−512. (g) Opstal, T.; Verpoort, F. *Synlett* **2002**, *6*, 935−941. (h) Melis, K.; Opstal, T.; Verpoort, F. *Eur. J. Org. Chem*. **2002**, *22*, 3779−3784. (i) Melis, K.; Verpoort, F. *J. Mol. Catal.* A: Chem. **2003**, *194*, 39−47. (j) Goossen, L. J.; Paetzold, J.; Koley, D. *Chem. Commun*. **2003**, 706−707. (k) Melis, K.; Vos, D.; Jacobs, P.; Verpoort, F. *J. Organomet. Chem*. **2003**, *671*, 131−136.

(3) Bianchini, C.; Meli, A.; Peruzzini, M.; Zanobini, F. *Organometallics* **1990**, *9*, 1155−1160.

(4) Lu, X.; Zhu, G.; Ma, S. *Tetrahedron Lett.* **1992**, *33*, 7205−7209.

(5) Nakagawa, H.; Okimoto, S.; Sakaguchi, S.; Ishii, Y. *Tetrahedron Lett.* **2003**, *44*, 103−106.

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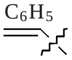
TABLE 2. Addition of Carboxylic Acids to Terminal Alkynes Catalyzed by Re(CO)$_5$Br[a]

entry	R	R′	adducts; yield (%)[b]	selectivity of **3** (%) (E/Z)[c]
1	C_6H_5	C_6H_5	**3b**; 70(67)	99 (13/87)
2	*p*-MeC_6H_4	CH_3	**3c**; 81(73)	100 (24/76)
3[d]	*n*-C_6H_{13}	CH_3	**3d**; 80 (51)	>99 (45/55)
4	*n*-C_6H_{13}	C_6H_5	**3e**; 57 (50)	98 (36/64)
5[d]	*n*-C_6H_{13}		**3f**; 77 (45)	>99 (44/56)
6	*t*-C_4H_9	CH_3	**3g**; 78	99 (67/33)
7[e]	*t*-C_4H_9	CH_3	**3g**; 76[f]	f
8	NC(CH_2)$_3$	CH_3	**3h**; 70 (65)	96 (40/60)
9	CH_3OCO	CH_3	**3i**; 51 (33)	100 (96/4)

[a] Reactions were carried out with 2.0 mmol of alkynes **1**, 2.5 mmol of **2**, and 0.02 mmol of Re(CO)$_5$Br in 1.0 mL of toluene. [b] GC yields based on the amount of **1** used. The values in parentheses are isolated yields. [c] Determined by GC. [d] Reaction in *n*-heptane. [e] Reaction in C_6D_6. [f] Yield and ratio of *E*:*Z* (67:33) were determined by ^{1}H NMR.

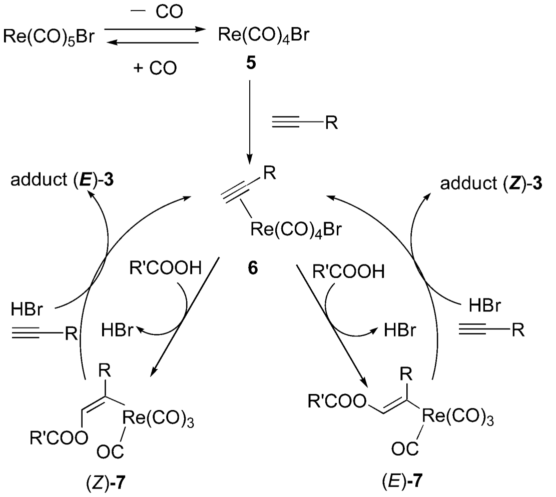
1). In addition, the ratio of *Z*-**3a** and *E*-**3a** could not be changed by a prolonged reaction time (25 h).[6]

Table 1 summarizes the results of the effect of solvents on the distribution of adducts in the reaction of **1a** with **2a**. The distribution of Markovnikov product and anti-Markovnikov products, as well as the distribution of *E*-**3a** and Z-**3a** stereoisomer, depends greatly on the nature of the employed solvents. When toluene, 1,1,2,2-tetrachloroethane, and di-*n*-butyl ether were used as solvents, the addition reactions afforded the anti-Markovnikov adduct **3a** exclusively (Table 1, entries 2 and 3) or with high selectivity (Table 1, entry 4). The obtained yields and the ratios of *E*-**3a** and *Z*-**3a** were similar to or the same as those observed in *n*-heptane solvent. In contrast to the nonpolar solvents, when the addition reactions were carried out in polar solvents such as DMF, ethyl acetate, THF, acetone, and acetonitrile, Re(CO)$_5$Br showed low catalytic activity (entries 5−9). In addition, except for DMF, the use of polar solvents resulted in the increase of the Markovnikov adduct **4a**. In the cases of THF and acetone, the addition reaction gave **4a** as the main product (Table 1, entries 7 and 8).

We also tested the catalytic activity of Re$_2$(CO)$_{10}$ in the reaction of **1a** with **2a** under identical reaction conditions (as shown in Table 1, entry 2); however, a very low yield (ca. 10%) of adducts mixture was obtained.

The Re(CO)$_5$Br-catalyzed addition reaction can be readily applied to other terminal alkynes and carboxylic acids. In *n*-heptane or toluene, all the addition reactions afforded the anti-Markovnikov adduct exclusively or with high selectivities. The results are summarized in Table 2. Addition of benzoic acid **2b** to **1a** afforded adducts **3b** in 70% GC yield with 99% of selectivity, and the ratio of *E*-**3b** and *Z*-**3b** was 13:87 (Table 2, entry 1). *p*-Methylphenylacetylene reacted with **2a** to give the adducts **3c** in high yield with high selectivity as **1a** did. Alkyl alkynes also facilitated the present catalytic addition reactions to afford the anti-Markovnikov adducts with high selectivities. For example, the addition reactions of 1-octyne with **2a**, **2b**, and acrylic acid furnished the anti-Markovnikov adducts in good yields, and in all these cases, the *Z*-adducts were predominant (Table 2, entries 3−5). However, in the case of the sterically congested 3,3-dimethyl-1-butyne used, the addition reaction with **2a** took place to produce the *E*-adduct predominantly (Table 2, entry 6). A study of ^{1}H NMR of the addition reaction in C_6D_6 also confirmed the reversal of stereoselectivity of adducts (Table 2, entry 7). In addition, the functional group-bearing alkynes such as 5-hexynenitrile and methyl propiolate also reacted with **2a** to give the adducts **3h** and **3i** in 70% and 51% yields, respectively (Table 2, entries 8 and 9). I When methyl propiolate was employed, the *E*-adduct was obtained in very high selectivity (*Z*-**3i**: *E*-**3i** = 4:96). Since methyl propiolate is an active alkyne, we examined the reaction in the absence of catalyst, and no addition reaction occurred at all.

SCHEME 1. Proposed Mechanism for the Addition of Carboxylic Acids to Terminal Alkynes



Although the mechanism of the present rhenium-catalyzed addition of carboxylic acids to alkynes remains to be elucidated, one of the possible catalytic cycles proposed is shown in Scheme 1. We suggest that the catalytic reaction is initiated by the decarbonylation of Re(CO)$_5$Br to give 16-electron intermediate Re(CO)$_4$Br (**5**).[7] The formation of the vinylrhenium intermediates (*E*)-**7** and (*Z*)-**7**, which arise from the reaction of the alkyne-coordinated intermediate **6** with carbonylic acid, leads eventually to the formation of the anti-Markovnikov adducts (*Z*)-**3** and (*E*)-**3**. The stereoselective formation of the adducts (*Z*)-**3** or (*E*)-**3** depends on the formation of intermediate (*E*)-**7** or (*Z*)-**7**, respectively. Intermediate (*E*)-**7** exists the steric repulsion between the substituent R and the R′COO groups, while (*Z*)-**7** has the steric repulsion between the CO ligand and the R′COO group. On the basis of the observation of adduct (*Z*)-**3** obtained predominantly in most cases, it seems that there is much stronger steric repulsion between the CO ligand and the R′COO group than between the R and the R′COO groups, resulting in the favored formation of (*E*)-**7**. Accordingly,

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(6) In the presence of Re(CO)$_5$Br (1.0 mol %), heating a solution of the isolated *E*-**3a** and *Z*-**3a** (*E*-**3a**/*Z*-**3a** = 28/72) in *n*-heptane at 110 °C for 10 h could not change the ratio of *E*-**3a** and *Z*-**3a**. This observed result indicated that the isomerization between *E*-**3a** and *Z*-**3a** could not occur.

(7) The formation of 16-electron Re(CO)$_4$Br (**5**) through the decarbonylation of Re(CO)$_5$Br has already been reported: (a) Jolly, P. W.; Stone, F. G. A. *J. Chem. Soc.* **1965**, 5259−5263. (b) Zingales, F.; Sartorelli, U.; Canziani, F.; Raveglia, M. *Inorg. Chem.* **1967**, *6*, 154−157.

it is reasonable to explain that when benzoic acid **2b** was used instead of acetic acid **1b**, the ratios of the adducts (*Z*)-**3**:(*E*)-**3** were increased (Table 1, entry 2 vs Table 2, entry 1; Table 2, entry 3 vs entry 4), since phenyl (R′ = Ph, **2b**) is bulkier than methyl (R′ = Me, **1b**).

On the other hand, when R is a bulky group (e.g. *t*-Bu), the steric repulsion between the R and the R′COO group becomes important. Therefore, in the case of 3,3-dimethyl-1-butyne, the addition reaction gave (*E*)-**3g** predominantly. However, the highly selective formation of (*E*)-**3i** from the reaction of methyl propiolate with **2a** is not clear.

Additionally, when the addition reaction was carried out in *n*-heptane, $Re(CO)_5Br$ could be recovered partly after the reaction. For example, if the reaction mixture (shown in Table 2, entry 3) was cooled to ambient temperature, the white crystals were formed.[8] The IR data of the isolated crystals were in accordance with those of the authentic sample of $Re(CO)_5Br$,[9] and the molecular structure of the crystals was unequivocally confirmed by the X-ray structure analysis.[10] Furthermore, the recovered $Re(CO)_5Br$ showed the same catalytic activity and selectivity in *n*-heptane as fresh $Re(CO)_5Br$ employed in the reactions of 1-octyne with acetic acid to give **3d** in 81% GC yield (*Z*-**3d**/*E*-**3d** = 55:45).

In conclusion, we have developed the first early transition-metal complex $Re(CO)_5Br$-catalyzed addition of carboxylic acids to terminal alkynes under an air atmosphere. The catalytic procedure has three characteristics: (1) the reactions take place in *n*-heptane or toluene to give anti-Markovnikov adducts with high selectivities; (2) in most cases, the addition reactions afford unusual *Z*-adducts predominantly; and (3) the catalyst $Re(CO)_5Br$ can be partly recovered after the catalytic reactions in *n*-heptane solvent.

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Supporting Information Available: Detailed experimental procedure, the ORTEP structure of the recovered $Re(CO)_5Br$, and the charts of ^1H, ^{13}C NMR of **3a**−**i**. This material is available free of charge via the Internet at http://pubs.acs.org.

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[8] $Re(CO)_5Br$ could be recovered in 46−61% as precipitate with *n*-heptane as solvent.

[9] IR(KBr): 2030, 2025, 1975, 600 cm^{-1}.

[10] For the ORTEP structure of $Re(CO)_5Br$, see the Supporting Information.