Preliminary communication

Rhodium-catalyzed double carbonylation of diiodomethane in the presence of triethylorthoformate

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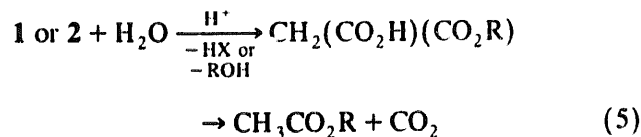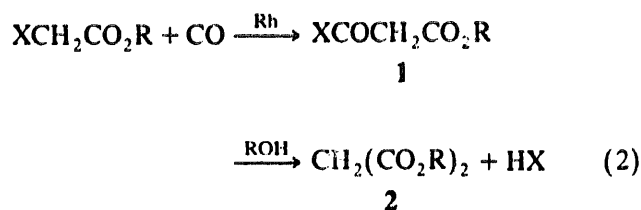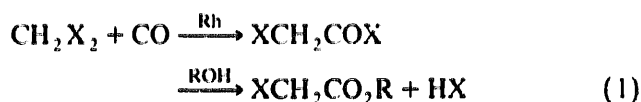
Abstract

Catalytic double carbonylation of diiodomethane in triethylorthoformate in the presence of a homogeneous rhodium complex gives diethylmalonate in a fairly good yield.

Keywords: Diiodomethane; Triethylorthoformate; Rhodium; Double Carbonylation; Catalysis

Dialkyl malonates are important intermediates in the preparation of pharmaceutical chemicals because of their expense and reactivity. The classic method of cyanation of monochloroacetic acid to cyanoacetic acid, hydrolysis to malonic acid, and esterification is the important commercial process for the synthesis of dialkyl malonates [1–5]. Currently, the most advanced technology obviating the use of toxic sodium cyanide in the manufacture of dialkyl malonates is based on the carbonylation of alkyl chloroacetates in the presence of an alcohol catalyzed by cobalt(0) carbonyl [6–12]. However, the double carbonylation of dihalomethanes to give dialkylmalonates is not an established process. There have been a few reports on the transition-metal-catalyzed double carbonylation of dihalomethanes, though the yields were quite low (less than 10%) [13,14]. In this paper, we describe our results dealing with a homogeneous rhodium catalyst system in the synthesis of diethyl malonate from diiodomethane in fairly good yields (ca. 60%), a rare example of the selective formation of a C_3 product from C_1 building blocks.

Generally, in alcohols, with a transition metal complex, considerable amounts of carbonylated dihalomethane, 1, or dialkyl malonate, 2, go to alkylacetate and CO_2 (Eq. (5)), giving low selectivity (less than 30%) [14]. Dialkyl malonates can be efficiently synthesized only if effective removal of water is accom-

plished. Since, under typical reaction conditions, water can be introduced into the system inadvertently or via side reactions such as Eqs. (3) and (4), the decarboxylation reaction is known to occur at 70°C [15], i.e. well below the reaction temperature, and without alcoholic solvent no carbonylation reaction occurs [14], then suitable reaction conditions which promote selective dialkyl malonate synthesis reactions cannot easily be found.

$$CH_2X_2 + CO \xrightarrow{Rh} XCH_2COX$$

$$\xrightarrow{ROH} XCH_2CO_2R + HX \quad (1)$$

$$XCH_2CO_2R + CO \xrightarrow{Rh} XCOCH_2CO_2R \atop \mathbf{1}$$

$$\xrightarrow{ROH} CH_2(CO_2R)_2 + HX \quad (2) \atop \mathbf{2}$$

$$HX + ROH \rightarrow RX + H_2O \quad (3)$$

$$2ROH \rightarrow ROR + H_2O \quad (4)$$

$$\mathbf{1} \text{ or } \mathbf{2} + H_2O \xrightarrow[-HX \text{ or} \atop -ROH]{H^+} CH_2(CO_2H)(CO_2R)$$

$$\rightarrow CH_3CO_2R + CO_2 \quad (5)$$

Recently, we have found that diiodomethane reacts with CO in triethylorthoformate in the presence of homogeneous rhodium complexes as catalysts to give

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Table 1
Product composition from the carbonylation of diiodomethane catalyzed by a rhodium(I) complex [a]

Base	Conversion (%)	Product composition (%) [b]		
		$CH_2(CO_2Et)_2$	$MeCO_2Et$	$EtOCH=C(CO_2Et)_2$
—	95 [c]	4.6	24	—
—	77	22	9.2	13
PPh_3	78	45	5.1	—
NEt_3	93	40	1.1	Trace

[a] $[Rh^ICl(1,5-cod)]_2$ 0.100 mmol, CH_2I_2 20.0 mmol, and base 4.00 mmol in triethylorthoformate solvent (14 ml), P_{CO} = 100 atm, 120°C, 12 h. [b] Based on CH_2I_2 consumed. Trace amounts of $CH_2(OEt)_2$, ICH_2CO_2Et and $EtOCH_2CO_2Et$ were also detected. [c] In EtOH solvent (14 ml).

Table 2
Effect of added phosphine on the carbonylation of diiodomethane catalyzed by a rhodium(I) complex [a]

PPh_3 (mmol)	Conversion (%)	Product composition (%) [b]		
		$CH_2(CO_2Et)_2$	$MeCO_2Et$	$EtOCH=C(CO_2Et)_2$
8.00	80	27	3.1	—
4.00	78	45	5.1	—
2.00	88	61	4.2	—
1.00	85	68	2.8	—
0.00	77	22	9.2	13

[a] $[Rh^ICl(1,5-cod)]_2$ 0.100 mmol and CH_2I_2 20.0 mmol in triethylorthoformate solvent (14 ml), P_{CO} = 100 atm, 120°C, 12 h. [b] Based on CH_2I_2 consumed. Trace amounts of $CH_2(OEt)_2$, ICH_2CO_2Et and $EtOCH_2CO_2Et$ were also detected.

diethylmalonate in a fairly good yield (Table 1). Even though overall conversion of diiodomethane is somewhat lower in triethylorthoformate than in ethanol, the selectivity to the malonate ester is much higher. When the reaction is carried out in the presence of a tertiary phosphine or amine, the selectivity for diethyl malonate becomes still higher. In addition to diethoxymethane,

which is produced by the reaction of EtOH and CH_2I_2, the reaction products contained ethyl iodoacetate, ethyl ethoxyacetate, ethyl acetate, and diethyl ethoxymethylene malonate as by-products. Inclusion of these by-products seen by GC, however, could not account for all the CH_2I_2 converted. There are obviously other by-products not detected by GC.

Table 3
Effect of various rhodium catalysts on the carbonylation of diiodomethane [a]

| Catalyst	Conversion (%)	Product composition (%) [b]		
		$CH_2(CO_2Et)_2$	$MeCO_2Et$	$EtOCH=C(CO_2Et)_2$
$Rh_4(CO)_{12}$ [c]	92	23	7.5	9.7
$[RhCl(1,5-cod)]_2$	85	68	2.8	—
$Rh_2(O_2CMe)_4$	69	48	5.2	Trace
$RhCl(PPh_3)_3$ [d]	58	3.2	17	—
$RhCl_3$ [d]	78	22	13	5.7

[a] Catalyst 0.100 mmol, CH_2I_2 20.0 mmol, PPh_3 1.00 mmol in triethylorthoformate solvent (14 ml), P_{CO} = 100 atm, 120°C, 12 h. [b] Based on CH_2I_2 consumed. Trace amounts of $CH_2(OEt)_2$, ICH_2CO_2Et and $EtOCH_2CO_2Et$ were also detected. [c] Catalyst 0.0500 mmol. [d] Catalyst 0.200 mmol.

Table 4
Effect of various rhodium catalysts on the carbonylation of ethyl iodoacetate [a]

Catalyst	Conversion (%)	Product composition (%) [b]			
		$EtOCH_2CO_2Et$	$CH_2(CO_2Et)_2$	$MeCO_2Et$	$EtOCH=C(CO_2Et)$
$Rh_4(CO)_{12}$ [c]	99	Trace	33	5.3	1.7
$[RhCl(1,5-cod)]_2$	99	Trace	25	5.6	3.6
$Rh_2(O_2CMe)_4$	97	Trace	28	5.2	Trace
$RhCl_3$ [d]	87	2.0	75	15	8.0

[a] Catalyst 0.100 mmol, ICH_2CO_2Et 20.0 mmol, PPh_3 1.00 mmol in triethylorthoformate solvent (14 ml), P_{CO} = 100 atm, 120°C, 12 h. [b] Based on ICH_2CO_2Et consumed. [c] Catalyst 0.0500 mmol. [d] Catalyst 0.200 mmol.

The roles of added base are to remove hydrogen iodide from the reaction field in order to promote the carbonylation and to act as a ligand. The effect of change in the concentration of PPh_3 on the reaction shows that too much PPh_3 has a detrimental effect on the selectivity toward $CH_2(CO_2Et)_2$ (Table 2) possibly by forming $(ICH_2PPh_3)^+I^-$. Various forms of rhodium catalyst precursor show catalytic activities toward double carbonylation of diiodomethane (Table 3). The fact that rhodium dimers seem to have better selectivities to diethylmalonate tells us the dinuclear pathway operates in favor of the formation of diethylmalonate (Eq. (6)). The oxidative addition to the second rhodium center must be considerably more facile than to the first, and direct synthesis of diethyl malonate without the formation of XCH_2CO_2Et prevents the formation of possible side products.

$$CH_2X_2 \xrightarrow{\text{Rh}} XH_2-Rh-X$$

$$\xrightarrow{\text{Rh}} X-Rh^{\cdots\cdot CH_2\cdots}Rh-X \qquad (6)$$
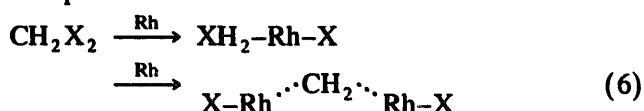
If we use ICH_2CO_2Et as a substrate instead of CH_2I_2, the rhodium monomer gives the best selectivity to diethylmalonate, as expected (Table 4), since the mononuclear carbonylation pathway is sufficient. Therefore, mononuclear and binuclear pathways must both be operating in the case of CH_2I_2, with the binuclear pathway being better for selectivity. Although the exact nature of the catalytic cycle for diethyl malonate formation is not clear, the very high selectivity obtained here is quite interesting for the use of triethylorthoformate as a solvent.

Diethyl malonate syntheses can be carried out efficiently by adding a catalytic amount of Rh complex to diiodomethane (20.0 mmol) in triethylorthoformate in a Parr 125 ml magnetically stirred autoclave equipped with a glass liner and a temperature controller. After being purged with CO several times, the reactor was pressurized to a desired pressure and heated to the desired temperature with stirring. After the required time, the liquid phase was withdrawn and analyzed by a Hewlett-Packard gas chromatograph (GC) with a flame ionization detector. For quantitative analysis, a known amount of N,N-dimethylformamide was added as an internal standard to the reaction mixture.

Acknowledgements

References

[1] J. Schwyzer, Die Fabrikation pharmazeutischer und chemischer Produkte, Springer, Berlin, 1931, p. 102.
[2] Dow Chemical Co., US Patent 2337858, 1943.
[3] A.A. Ross and F.E. Bibbins, Ind. Eng. Chem., 29 (1937) 1341.
[4] Nihon Nohyaku Co., Jpn. Kokai 76143612, 1976.
[5] N.V. Koninklijke Nederlandshe Zoutindustrie, Neth. Appl. 66013168, 1968.
[6] R.F. Heck and D.S. Breslow, J. Am. Chem. Soc., 85 (1963) 2779.
[7] T. Suzuki, T. Matsuki, K. Kudo and N. Sugita, Nippon Kagaku Kaishi, (1983) 1483.
[8] Dynamit Nobel A.-G., Ger. Offen. 2524389, 1976.
[9] Dynamit Nobel A.-G., Ger. Offen. 2603026, 1977.
[10] Asahi Denka Kogyo K.K. Jpn. Kokai 78108918, 1978.
[11] Denki Kagaku Kogyo K.K., Jpn. Kokai 80053241, 1980.
[12] Dynamit Nobel A.-G., Can. Patent 1080251, 1980.
[13] Anic S.p.A., Br. Patent 1547113, 1978.
[14] W.S. Weston, R.C. Gash and D.J. Cole-Hamilton, J. Chem. Soc. Chem. Commun., (1994) 745.
[15] D.W. Hughes, in M. Grayson and D. Eckroth (eds.), Kirk–Othmer Encyclopedia of Chemical Technology, Vol. 14, Wiley, New York, 3rd edn., 1981, p. 795.