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Carbonylation of chloroacetone to methyl acetoacetate

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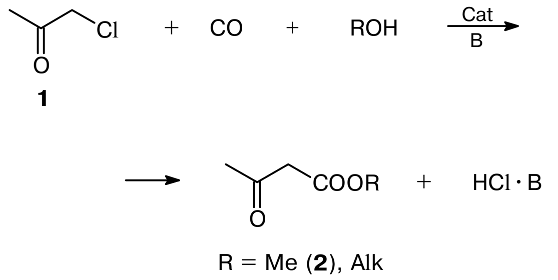
Methyl acetoacetate was prepared by the selective carbonylation of chloroacetone in the presence of a homogeneous palladium catalyst at 100 °C and under a CO pressure of 1.5 MPa.

Key words: chloroacetone, palladium catalysts, carbonylation; methyl acetoacetate, acetoacetic ester.

The catalytic carbonylation of halogen-containing compounds[1,2] makes it possible to introduce the ester group instead of the halogen atom into the substrate molecule in one step using palladium,[2a] cobalt,[2b—d] or iron[2e] catalysts. Esters of aromatic[2a,d] and aliphatic[2b,d,e] acids and phenylacetic[2a—c] and malonic acids[2b,c] are thus synthesized.

Acetoacetic ester is a large-scale commercial product, which usually obtained by the Claisen condensation of ethyl acetate.[3] Another possible way for the synthesis of acetoacetic esters, the carbonylation of chloroacetone (**1**) in the presence of the corresponding alcohols (Scheme 1), is yet poorly studied.

Scheme 1



Cat is catalyst
B is base

The synthesis of acetoacetic esters by the carbonylation of chloroacetone in the presence of the cobalt catalyst is licensed.[4] The catalyst activity is low: at its concentration of 10 mol.% the turnover number is at most 1.4 per h. The kinetics of the carbonylation of RCH_2Cl compounds, including chloroacetone, in the presence of cobalt carbonyl, has been studied.[5] The gas phase carbonylation of halogen compounds, including chloroacetone, over the supported rhodium catalyst, has been investigated.[6] However, the yield of acetoacetic ester is only 2% under these conditions. As far as we know, palladium catalysts were not applied earlier for chloroacetone carbonylation. The only known example for the carbonylation of α-haloketones on the Pd catalysts is bromoacetophenone carbonylation in the presence of $PdCl_2(PPh_3)_2$ at 80 °C and a CO pressure of 1.3 MPa. Methyl benzoylacetate was obtained[7] in 64% yield within 48 h.

The purpose of this work is to study the carbonylation of chloroacetone (**1**) in the presence of the Pd catalysts, to develop a method for the synthesis of methyl acetoacetate (**2**), and to reveal the influence of the nature of the catalyst and base precursors, temperature, and pressure.

Results and Discussion

Preliminarily we tested the catalytic activities of various palladium compounds. Tributylamine was used as a base. The catalyst concentration was 1 mol.%. The $PdCl_2$ and $Pd(OAc)_2$ salts are inactive in this reaction (Table 1, entries *1* and *2*). When using the Pd complexes with the weakly coordinating ligands, $PdCl_2(PhCN)_2$ and $PdCl_2(ImH)_4$, the yield of compound **2** was only

Table 1. Carbonylation of chloroacetone (**1**) in the presence of various palladium compounds

Entry[a]	Catalyst	Conversion of **1**[b]	Yield of **2**[b]
		(%)	
1	$PdCl_2$	60	Traces
2	$Pd(OAc)_2$	70	Traces
3	$PdCl_2(PhCN)_2$	65	5
4	$PdCl_2(ImH)_4$	62	5
5	$PdCl_2(PPh_3)_2$	100	94
6[c]	$Pd(dba)_2$ + 2 PPh_3	100	95

[a] Experimental conditions: molar ratio Pd : **1** : NBu_3 = 1 : 100 : 150, T = 110 °C, P = 1.5 MPa, 1 h.
[b] According to GLC data.
[c] Dibenzylideneacetone is abbreviated as dba.

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5% (see Table 1, entries *3* and *4*). In these cases, a great amount of Pd black forms. The $PdCl_2(PPh_3)_2$ complex exhibited a high activity. The yield of compound **2** reached 94% at a complete conversion of the substrate (see Table 1, entry *5*). Similar results were obtained when $Pd(dba)_2$ with the addition of 2 mol.% PPh_3 was used (see Table 1, entry *6*).

A stoichiometric amount of a base is needed for binding the HCl evolved during the reaction. In the absence of a base, the reaction did not occur (Table 2, entry *1*). The application of $CaCO_3$, K_2CO_3, or pyridine did not give positive results: only traces of compound **2** were formed (see Table 2, entries *2—5*). In the presence of NaOAc, product **2** was obtained in 15% yield, and in the presence of Na_2CO_3 the yield was 46% (see Table 2, entries *6* and *7*). Tributylamine is the most appropriate base of those applied by us. In its presence, the yield of ester **2** was 94% at 110 °C (see Table 2, entry *8*). The concentration of tributylamine in the reaction mixture affects the reaction rate. So, when the amount of NBu_3 was decreased from 1.5 to 1.1 equiv. per substrate, the yield of ester **2** lowered from 94 to 53% (see Table 2, entries *8* and *9*).

A study of the temperature dependence of the yield of compound **2** (Fig. 1) showed that an increase in the temperature from 60 to 130 °C (at a pressure of 1.5 MPa) increases the yield of ester **2** from 15 to 97%, and at 110 °C the yield is 94%. Thus, the 110—130 °C temperature interval can be regarded as optimum.

The synthesis at atmospheric CO pressure is inefficient. At 60 °C for 5 h compound **2** was obtained in 3% yield only (see Table 2, entry *12*). *n*-Butyl alcohol (b.p. 118 °C) was used as an alcohol component to increase the reaction temperature to 110 °C if necessary. Under these conditions, the yield of butyl acetoacetate was 25% within 5 h (see Table 2, entry *13*), and the reaction could be continued, which is indicated by the dynamics of CO absorption (Fig. 2).

Table 2. Carbonylation of chloroacetone (**1**) in the presence of $PdCl_2(PPh_3)_2$

Entry[a]	Base (number of equiv.)	T/°C	P/MPa	Yield of **2** [b] (%)
1 [c]	–	110	6.0	0
2 [c]	$CaCO_3$ (1.1)	110	6.0	Traces
3 [c]	K_2CO_3 (1.5)	110	6.0	Traces
4	Py (1.5)	110	1.5	Traces
5	Py (1.5)	150	1.5	1.5
6	NaOAc (1.5)	110	1.5	15
7	Na_2CO_3 (1.5)	110	1.5	46
8	NBu_3 (1.5)	110	1.5	94
9	NBu_3 (1.1)	110	1.5	53
12 [d]	NBu_3 (1.1)	55	0.1	3
13 [d,e]	NBu_3 (1.1)	110	0.1	25 [f]

[a] Molar ratio Pd : **1** = 1 : 100.

[b] According to GLC data.

[c] Duration of experiment is 3 h.

[d] Catalyst $Pd(dba)_2$ + 2 PPh_3, duration of experiment is 5 h.

[e] BuOH was used instead of MeOH.

[f] The yield of butyl acetoacetate is indicated.

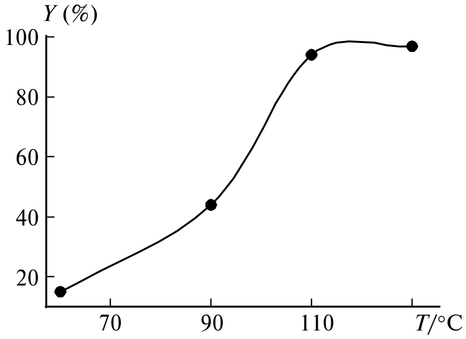


Fig. 1. Influence of the reaction temperature on the yield of compound **2** (Y); molar ratio Pd : **1** : NBu_3 = 1 : 100 : 150, P = 1.5 MPa, 1 h.

The proposed mechanism for chloroacetone carbonylation is shown in Scheme 2. This mechanism is similar to that proposed[1a,b,2a] for the carbonylation of benzyl and aryl halides. The Pd^0 complexes stabilized by the PPh_3 ligands are the true catalysts. Our data show that the reaction does not virtually occur in the absence of PPh_3. An alkylpalladium intermediate is formed by the oxidative addition of compound **1** to the catalytic complex. The next step is the migrative insertion of CO resulting in the acylpalladium complex. Its alcoholysis gives the reaction products and completes the catalytic cycle. The base binds the hydrohalic acid that evolved and also catalyzes, most likely, the alcoholysis of the acylpalladium complex to afford the product.[1a,b] The dependence of the reaction rate on the NBu_3 concentration indicates that the alcoholysis step is the limiting stage in the case. However, the synthesis at an atmospheric pressure results in a sharp decrease in the reaction rate. Probably, under a low CO pressure the formation of the acyl complex becomes the limiting stage.

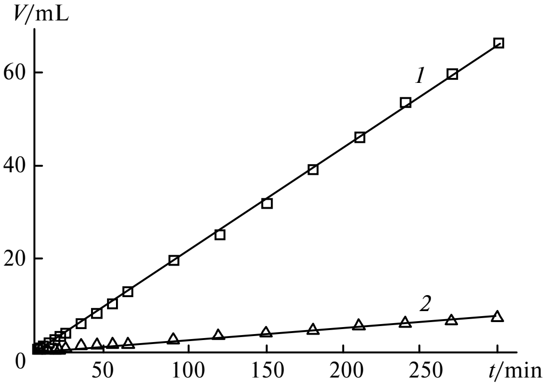
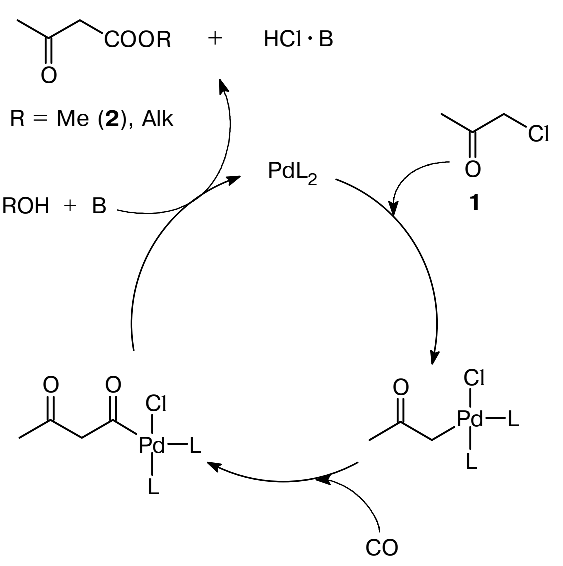


Fig. 2. Dynamics of CO absorption during carbonylation of compound **1** according to the reaction $CH_3COCH_2Cl + CO + ROH \rightarrow CH_3COCH_2COOR$ at an atmospheric pressure, T = 60 °C, R = Me (*1*); T = 110 °C, R = Bu (*2*); V is the volume of absorbed CO.

Scheme 2



L is PPh$_3$, CO
B is base

Thus, we performed the selective carbonylation of chloroacetone to methyl acetoacetate on the $PdCl_2(PPh_3)_2$ catalyst. The reaction in the presence of NBu_3 at 110—130 °C and 1.5 MPa affords ester **2** selectively in 94—97% yield.

Experimental

^{1}H NMR spectra were recorded on a Bruker WM-250 mass spectrometer (250 MHz) using Me_4Si as internal standard and $CDCl_3$ as solvent. GLC was carried out on an Autokhrom UE5 PID instrument with a 30 m×0.25 mm quartz capillary column, the SE-30 stationary phase, helium as carrier gas, and *n*-octanol as internal standard.

The starting chloroacetone was prepared by the chlorination of acetone.[8]

Chloroacetone carbonylation under elevated pressure was carried out in a steel rotating 150-mL autoclave heated with an electric furnace. Compound **1** (1 mL, 12.6 mmol), the catalyst (0.126 mmol), the corresponding amount of the base, and MeOH (25 mL) were loaded into a glass liner. The liner was placed in the autoclave, which was purged with CO, closed, and thermostated at a required temperature. Then CO was introduced to achieve a necessary pressure, and the rotation of the autoclave was switched on. After the end of the reaction, the reaction mixture was analyzed by GLC. Ester **2** was isolated by distillation, b.p. 168—170 °C. ^{1}H NMR, δ: 2.25 (s, 3 H, CH_3CO); 3.45 (s, 2 H, CH_2); 3.72 (s, 3 H, OCH_3).

Carbonylation under atmospheric pressure was carried out in a glass reactor equipped with a magnetic stirrer, reflux condenser, jacket for heating, and burette for measuring absorbed CO.

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