

Letter

Efficient methoxycarbonylation of benzyl chloride without external carbon monoxide: a further application of methyl formate in synthesis using $\text{PdCl}_2(\text{PPh}_3)_2$ as catalyst

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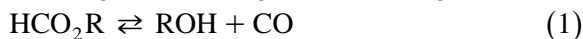
Abstract

The decarbonylation reaction of methyl formate induced by $\text{Mg}(\text{OMe})_2$, in the presence of benzyl chloride and dichlorobis(triphenylphosphine)palladium gives rise selectively to methyl phenylethanoate with turnover numbers and turnover frequencies up to ca. 2400 and 1000 h^{-1} , respectively. © 1999 Elsevier Science B.V. All rights reserved.

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1. Introduction

During the last years, alkyl formates have been extensively used as a source of carbon monoxide in many carbonylation reactions, avoiding the handling of this toxic gas [1,2].



Their decarbonylation is catalysed by either bases such as alkoxides of various metals and organic cations or organometallic catalysts [3–5]. The former are by far the best, allowing efficient decarbonylation at low or medium temperature.

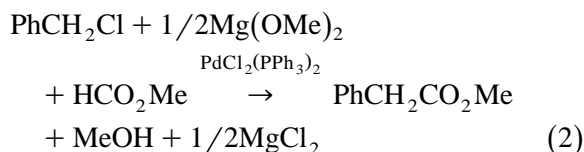
We have already reported that upon using sodium methoxide in stoichiometric amounts, the palladium catalysed methoxycarbonylation

of aryl and vinyl halides could be performed under mild conditions with methyl formate as the sole source of carbon monoxide and methanol [6]. Under the same conditions however, the use of benzyl halides as substrates led only to benzyl methyl ether production via nucleophilic attack of the methoxide anion at the electrophilic benzylic carbon atom [7,8]. Examination of literature data on the classical one-phase system of benzyl halides alkoxycarbonylation using methanol and CO [9,10] shows that the formation of benzylic ether can be limited, or suppressed in two different manners: either by a judicious choice of the base (e.g., base with low nucleophilicity such as 1,8-bis(dimethylamino)naphthalene [11], or much more covalent methoxides such as magnesium methoxide [12]), or by gradually introducing the organic halide into the solution in order to limit

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the contact with the base [13]. This last method has been recently carried out with methyl formate as the only source of CO, methanol, sodium methoxide using tetracarbonyl cobaltate anion as catalyst [14]. However, independently to the difficulty to introduce the reagent into the reactor under pressure during the course of the reaction, as usual in the case of cobalt based catalysts, turnover numbers are very low.

We wish now to report that the use of magnesium methoxide both as a base and a decarbonylation catalyst provides a useful tool for the methoxycarbonylation of benzyl chloride using methyl formate as the only source of CO under batch conditions.



2. Results and discussion

In the presence of methyl formate, methanol, magnesium methoxide (0.7 eq vs. PhCH₂Cl)

and dichlorobis(triphenylphosphine)palladium, benzyl chloride is converted into methyl phenylethanoate (58% yield) and benzyl methyl ether (see Table 1; run 1). The pressure in the autoclave rapidly reached and never exceeded about 10 bar (value mainly due to the vapor pressure of methyl formate at 120°C) showing that the decarbonylation reaction of methyl formate is globally the limiting step. Although methoxide ions are already in excess total conversion of benzyl chloride can be rapidly achieved if the quantity of magnesium methoxide increases again (1.4 eq) and 98% yield of ester is reached (run 2).

It has been recently described that the methanol solvate Mg(OMe)₂, 2MeOH under solid form decomposes in three steps depending on temperature to finally furnish MgO [15]. Other intermediate degradation products are obtained in the first step at 80°C and we believe that magnesium alkoxides in solution undergo the same kind of degradation at our working temperature. So an excess is necessary. To support this fact, a preliminary heating of Mg(OMe)₂ in methanol before adding other

Table 1

Methoxycarbonylation of benzyl chloride using methyl formate as the source of CO

run	MeOH (ml)	HCO ₂ Me (ml)	Mg(OMe) ₂ (mmol)	PdCl ₂ (PPh ₃) ₂ (μmol)	t (h)	PhCH ₂ Cl conversion (%)	ester (%) ^c	ether (%) ^c	ester selectivity (%)
1	15	35	12.3	140	5	63	58	5	92
2	15	35	24.6	140	1.5	100	98	2	98
3	15	35	24.6	14	5.5	92	86	6	93
4 ^{a,b}	15	35	24.6	14	3.5	93	85	8	91
5	15	35	18.5	14	2.25	93	92	1	99
6	25	25	18.5	14	2.25	100	96	4	96
7 ^c	25	25	18.5	14	2.25	23	11	12	48
8	40	10	18.5	14	2.25	100	88	12	88
9 ^d	25	25	37	14	2.5	100	94	6	94
10 ^{a,d}	25	25	37	7	5	93	42	51	45

The reactions were conducted in an stainless steel autoclave of 160 ml capacity at 120°C, PhCH₂Cl used as received (17.4 mmol), Mg(OMe)₂ was obtained by reaction of Mg with MeOH solvent prior to use, methanol and methyl formate were distilled.

^aFinal pressure is above 40 bar at the temperature of the reaction.

^bT = 140°C.

^cMg(OMe)₂ solution has been heated for 2 h and cooled before adding other reactants; after 20 h: 100% conversion, 43% ester, 57% ether.

^dPhCH₂Cl (34.8 mmol).

^eGLC yield based on initial PhCH₂Cl, the analyses were done on a Chrompack 9002 gas chromatograph equipped with a capillary column: CP SIL5 CB (25 m × 0.32 mm). Ethylbenzene was used as GC internal standard.

reactants was effected leading after reaction to only 11% yield of ester (compare runs 6 and 7).

The diminution of the amount of catalyst and the increase of the temperature (runs 3 and 4) have awaited effects. However it has to be noticed that at 140°C the final pressure is above 40 bar indicating that the rate of decarbonylation reaction of methyl formate is higher than the rate of methoxycarbonylation at this low catalyst content. Curiously both relatively high pressure observed during the course of the reaction, and higher temperature do not accelerate a lot the catalytic reaction. Furthermore, if the amount of base is reduced by 25% in order to limit the decarbonylation reaction, the reaction time is surprisingly divided by a factor two for the same conversion (runs 3 and 5). In fact, addition of carbon monoxide to the methyl formate/methanol medium inhibits the methoxycarbonylation reaction as proved by the experiment conducted under 10 bar of CO (Table 2, run 1), but not the decarbonylation reaction since final pressure has enhanced.

However, an identical pressure and a more important catalyst amount allow the methoxycarbonylation to run to some extent. The use of carbon monoxide in conjunction with small quantity of catalyst quenches the reaction of methoxycarbonylation. The same trend has been

noticed during alkoxy-carbonylation of aryl halides with palladium based catalysts [16,17]. CIR-FTIR studies led the authors to conclude that the irreversible formation of inactive palladium-carbonyl clusters or homopolymers occurs under CO pressure, when the phosphine-to-palladium mole ratio used is small (less than 4).

In our experiments, this ratio is 2:1 and we have checked that in the absence of methyl formate, the value of initial pressure is crucial to the progress of the reaction. The experiments were conducted at 80°C since at 120°C in pure methanol under CO pressure, ether is the predominant product (runs 5 and 6).

Thus, using 14 μmol of $\text{PdCl}_2(\text{PPh}_3)_2$ (runs 2–4), it appears that the reaction of methoxycarbonylation performed better at lower CO pressure. When methyl formate is used, the production of CO can be easily controlled via the equilibrium (1) by adjusting the ratio $\text{MeOH}/\text{HCO}_2\text{Me}$ at the beginning of the reaction (Table 1, run 6). Nevertheless optimum reaction conditions need enough methyl formate as a solvent to reduce the formation of ether (run 8).

At last, the limit of the system has been reached as the amount of catalyst was reduced again (run 10).

Table 2
Methoxycarbonylation of benzyl chloride in the presence of CO

run	MeOH (ml)	HCO ₂ Me (ml)	Mg(OMe) ₂ (mmol)	PdCl ₂ (PPh ₃) ₂ (μmol)	P _{CO} ^c (bar)	T (°C)	t (h)	PhCH ₂ Cl conversion (%)	ester (%) ^d	ether
1 ^a	15	35	18.5	14	10	120	2.25	18	trace	18
2	50	–	18.5	14	15	80	4	31	0	31
3	50	–	18.5	14	4	80	4	50	3	47
4 ^b	50	–	18.5	14	1	80	4	73	43	30
5	50	–	12.3	140	15	80	5	75	61	14
6	50	–	12.3	140	15	120	2	100	45	55

The reactions were conducted in a stainless steel autoclave of 160 ml capacity at 120°C; PhCH₂Cl used as received (17.4 mmol); Mg(OMe)₂ was obtained by reaction of Mg with MeOH solvent prior to use; methanol and methyl formate were distilled.

^aFinal pressure is above 40 bar at the temperature of the reaction.

^bThe volume of gas in the reactor is not sufficient to transform all the reactant into ester.

^cAt room temperature.

^dGLC yield based on initial PhCH₂Cl; the analyses were done on a Chrompack 9002 gas chromatograph equipped with a capillary column: CP SIL5 CB (25 m \times 0.32 mm). Ethylbenzene was used as GC internal standard.

3. Conclusions

Methyl formate has consequently a dual function, both limiting the formation of ether, the sole by-product of the reaction, by solvent effect, and producing slowly and continuously CO in situ, thus avoiding the risk of catalyst deactivation.

The system is very active since turnover numbers of 2340 has been obtained with an average turnover frequency of 930 h^{-1} (run 9). To our knowledge, this is the best result ever reported in alkoxy-carbonylation of benzyl chloride.

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