

Palladium-catalyzed carbonylation of aryl halides — a detailed investigation of the alkoxy carbonylation of 4-bromoacetophenone[☆]

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Abstract

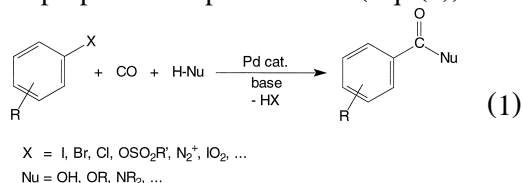
The palladium-catalyzed alkoxy carbonylation of 4-bromoacetophenone with *n*-butanol to give the corresponding benzoic acid ester has been studied systematically by evaluating the influence of critical reaction parameters such as temperature, CO pressure, solvent, base, catalyst precursor and ligand/palladium ratio. The highest catalyst efficiency was displayed at 130°C and low CO pressures using the neat alcohol as the solvent, a trialkylamine as the base and Pd(PPh₃)₄ or a PdCl₂(PhCN)₂/*n*-PPh₃-combination as the catalyst precursor. A strong dependence of the catalyst activity and stability on the phosphine concentration in the reaction mixture was found as demonstrated by the time/conversion behavior of the reaction. Thus, under the optimized conditions, catalyst productivities (turnover number = TON) of up to 7000 (70% yield of **2**) were achieved. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Carbonylation; Palladium; Homogeneous catalysis; Aromatic carboxylic acid esters

1. Introduction

Palladium-catalyzed carbonylation reactions of aryl-X derivatives constitute a powerful method of C–C-coupling reactions for the synthesis of various aromatic compounds, most importantly carboxylic acid derivatives [2–4]. The synthetic value of the reaction stems from the exceedingly low cost of carbon monoxide and from the variety of accessible carbonylation

products which can be derived by simply choosing the proper nucleophile H–Nu (Eq. (1)).



In general, the reaction of the aromatic substrate with carbon monoxide and a nucleophile is performed in the presence of a catalytic amount of a palladium compound. Apart from palladium other metals such as Co [5,6] and Ni [7,8] have been employed as catalysts. In order to neutralize the acid HX formed during the

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reaction, a stoichiometric or excess amount of a base is necessary. As substrates aryl halides, especially aryl bromides and aryl iodides, are used most frequently [9]. The much less reactive aryl chlorides are attractive starting materials due to their availability and low price. Their activation requires special catalyst systems (e.g., highly basic, pyrophoric phosphine ligands) or harsh reaction conditions [10–19]. Among the variety of possible products, carboxylic acid esters are one of the most important.

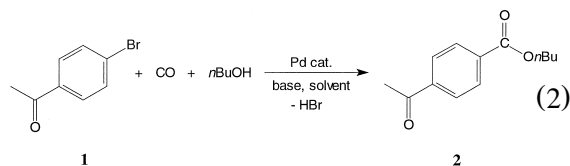
Although the palladium-catalyzed alkoxy-carbonylation reaction has been investigated by several groups throughout the last 25 years [4,9], no detailed study of the influence of the critical reaction parameters on the catalyst productivities (turnover number = TON) has appeared so far. Despite improvements, the catalyst productivities and activities for aryl-X carbonylations, which have been achieved so far, are not sufficient for industrial applications. Hence, the method is restricted to the production of higher-value fine chemicals and the synthesis of complex intermediates on a laboratory scale [20].

In the context of our efforts to develop palladium-catalyzed C–C-coupling reactions [21–24], which are useful on an industrial scale, we became interested in the carbonylation of aryl halides. Here, we present a comprehensive examination of the palladium-catalyzed alkoxy-carbonylation of an arylbromide (4-bromoacetophenone) used as a test system in order to measure the influence of reaction parameters such as temperature, pressure, ligand/metal ratio and different bases and solvents. In the course of our studies, we systematically improved the reaction conditions to achieve high catalyst TONs of up to 7000.

2. Results and discussion

In order to gain a first insight into the influence of characteristic reaction parameters and to explore new catalyst systems for aryl-X car-

bonylation reactions, we chose as a model system the reaction of 4-bromoacetophenone with *n*-butanol and CO in the presence of various bases, solvents and palladium complexes (Eq. (2)).



First, we examined the influence of the reaction temperature and the CO pressure on the yield of *n*-butyl 4-acetylbenzoate. The neat alcohol served as the solvent, triethylamine was chosen as the base and the bivalent palladium complex PdCl₂(PPh₃)₂ was employed as the catalyst precursor. Initial experiments revealed that a catalyst concentration of 0.3 mol% was ideal for the investigations. The reactions were stopped after 14 h, since separate kinetic experiments showed that after this time essentially no further conversion took place due to catalyst deactivation.

The pressure profile of the reaction at 100°C and 130°C is depicted in Fig. 1. Below 100°C and above 130°C the ester yields are lower. The selectivity for the ester is almost 100%, as in virtually all other experiments described in this paper. Almost throughout the whole pressure

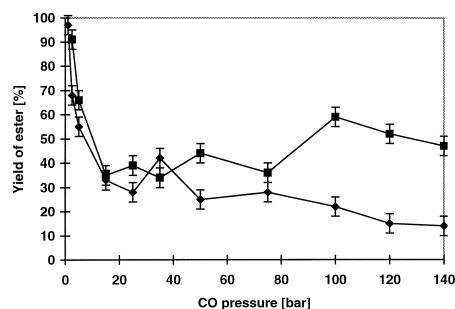


Fig. 1. Influence of the CO pressure on the ester yield at 100°C (◆-curve) and 130°C (■-curve). Reactions were run for 14 h using 7 mmol of 4-bromoacetophenone, 14 ml of *n*-butanol, three equivalents (3 eq.) of NEt₃ and 0.3 mol% PdCl₂(PPh₃)₂ as catalyst. The experiments were repeated two or three times. The fluctuation in the yield is depicted by the error bars.

range examined, a reaction temperature of 130°C turned out to be the optimum for the process. The most striking feature of the CO pressure dependence is the dramatic increase in yield when the pressure is lowered towards one atmosphere. At 130°C, it was observed that the product yield increased again at high pressures (≥ 100 bar) compared to medium pressures (15–75 bar).

These findings can be rationalized by the fact that at low partial pressures of CO the blocking of coordination sites at the metal center by CO ligands is diminished. Due to the π -acidity of CO as ligand the activity of palladium carbonyl complexes towards oxidative addition of the bromo aromatic is lower compared to palladium phosphine complexes (PdL_2 ; PdL_3 ; $\text{L} = \text{PPh}_3$). The slight increase of the yield at high pressures at 130°C may indicate a different catalytically active species under these conditions [25].

Next, we investigated how different reaction media influenced the productivity of the carbonylation process. The reaction conditions (5 bar CO pressure, 100°C temperature) were chosen for experimental convenience. When the neat alcohol was used as the solvent (2 ml per 1 mmol of the bromoarene, i.e., a 22-fold excess of the alcohol), the best ester yield (72%, entry 1, Table 1) was obtained. Furthermore, other non-polar and dipolar-aprotic solvents were tested using 5 eq. of *n*-butanol in 10.8 ml of the solvent (related to the bromoarene, entries 2–8, Table 1). However, in all cases, the yields were significantly lower in comparison to when the neat alcohol was the solvent. Interestingly, a decrease of the butanol concentration in the solvent (e.g., 10 eq. butanol, 40 ml NMP) led to a dramatic decrease of the ester yield (only 2% of butyl 4-acetylbenzoate). Therefore, we assume that the nucleophilic, base-assisted attack of the alcohol (or alcoholate ion) on the acyl palladium complex becomes the rate determining step of the reaction at low butanol concentrations.

As shown in Table 1, there is no trend regarding the polarity of the solvent. For example,

Table 1
Solvent screening for the Pd-catalyzed butoxycarbonylation of 4-bromoacetophenone^a

Entry	Solvent	Yield of ester [%] ^b
1	<i>n</i> -Butanol	72
2	<i>N</i> -Methyl-2-pyrrolidinone	53
3	Toluene	45
4	<i>N,N</i> -Dimethylacetamide	40
5	Tetramethylurea	39
6	Dimethylsulfoxide	6
7	Acetonitrile	12
8	Dichloromethane	2

^aReactions were run for 14 h at 100°C and 5 bar CO partial pressure using 7 mmol of 4-bromoacetophenone, 3.2 ml *n*-butanol (5 eq.), 10.8 ml solvent, 3 eq. NEt_3^+ and 0.3 mol% $\text{PdCl}_2(\text{PPh}_3)_2$ as catalyst.

^bDetermined by GC using diethyleneglycol dibutylether as an internal standard.

performing the reaction in the non-polar solvent toluene (entry 3, Table 1) gave a similar ester yield compared to reactions in dipolar-aprotic solvents like NMP and DMAc (entries 2, 4, Table 1). However, if the boiling point of the solvent is taken into account, it is remarkable that high-boiling solvents, apart from DMSO (entries 2–5, Table 1), give better results than more volatile solvents (entries 7, 8, Table 1).

As already mentioned in Section 1, the carbonylation reaction proceeds only in the presence of a base. The base is necessary to trap the HBr formed. We examined how different bases influence the productivity of the catalytic system. Therefore, common organic amines and inorganic salts were tested in the model reaction at 100°C and 5 bar CO partial pressure (Table 2). It turned out that trialkylamines give the best results (50–72%; entries 1–4, Table 2). Increased steric hindrance in the amine slightly decreases the yield of product (entries 3, 4, Table 2). Pyridine, an example of an aromatic amine, gave only poor results (entry 5, Table 2).

Sodium acetate and sodium carbonate led to significantly lower ester yields compared to the amine bases (entries 6, 7, Table 2). This observation is in sharp contrast to other palladium-catalyzed coupling reactions of aryl halides, e.g., Heck reactions [26,27], in which alkali carbox-

Table 2
Influence of different bases in the Pd-catalyzed butoxycarbonylation of 4-bromoacetophenone^a

Entry	Base	Eq. of base	Yield of ester [%] ^b
1	NEt ₃	3	72
2	Quinuclidine	3	68
3	NBu ₃	3	63
4	DIPEA	3	50
5	Pyridine	3	7
6	NaOAc	3	40
7	Na ₂ CO ₃	3	35
8	K ₂ CO ₃	3	2
9	NaO ^t Bu	3	3
10	NEt ₃	1.2	78
11	NEt ₃	5	52

^aReactions were run for 14 h at 100°C and 5 bar CO partial pressure using 7 mmol of 4-bromoacetophenone, 14 ml of *n*-butanol and 0.3 mol% PdCl₂(PPh₃)₂ as catalyst.

^bDetermined by GC using diethyleneglycol dibutylether as an internal standard.

ylates are, in general, superior to amines. This might be explained by the fact that the role of the base in carbonylations is not only to regenerate the Pd(0) complex from H–Pd–X complexes, but also to deprotonate the alcohol to produce butoxide ions which react more readily with the intermediate acyl palladium complex [28].

On switching over to potassium as a cation, the catalyst productivity dropped even more (entry 8, Table 2). NaO^tBu, an example of a stronger base, also failed to give any acceptable ester yields (entry 9, Table 2).

Interestingly, the variation of the concentration of triethylamine showed that a slight excess (1.2 eq., entry 10, Table 2) improves the yield in contrast to higher amounts (5 eq., entry 11, Table 2) of base.

Another important issue is the type of catalyst precursor used in the palladium-catalyzed carbonylation reaction. In this respect, we compared common Pd(II) and Pd(0) compounds, which were combined with PPh₃ as ligand in most cases (Table 3).

Comparable to PdCl₂(PPh₃)₂ (entry 1, Table 3) the oxidative insertion product of the arylbromide and Pd(PPh₃)_x [29], which is a reaction intermediate in the catalytic cycle, had roughly the same productivity (entry 2, Table 3). In contrast, a mixture of Pd(OAc)₂ and 2 eq. of PPh₃ (entry 3, Table 3) gave only poor yields of **2**. However, using Pd(OAc)₂/3 eq. PPh₃ the yield was comparable to the PdCl₂(PPh₃)₂ catalyst (entries 1, 4, Table 3). The palladacycle

Table 3
Influence of different catalyst precursors in the Pd-catalyzed butoxycarbonylation of 4-bromoacetophenone^a

Entry	Catalyst	Pd [mol%]	NEt ₃ [eq.]	Temperature [°C]	CO pressure [bar]	Yield of ester [%] ^b
<i>Pd(II) precursors</i>						
1	PdCl ₂ (PPh ₃) ₂	0.3	3	100	5	72
2	[Pd(Ar)Br(PPh ₃) ₂] ^c	0.3	3	100	5	70
3	Pd(OAc) ₂ /2 PPh ₃	0.3	3	100	5	17
4	Pd(OAc) ₂ /3 PPh ₃	0.3	3	100	5	66
5	Palladacycle ^d	0.3	3	100	5	4
6	PdCl ₂ (PPh ₃) ₂	0.1	1.2	130	2.5	86
7	PdCl ₂ (PPh ₃) ₂	0.01	1.2	130	2.5	49
<i>Pd(0) precursors</i>						
8	Pd[P(<i>o</i> -Tol) ₃] ₂	0.3	3	100	5	3
9	Pd(PCy ₃) ₂	0.3	3	100	5	55
10	Pd(PPh ₃) ₄	0.3	3	100	5	99
11	Pd(PPh ₃) ₄	0.1	1.2	130	2.5	84
12	Pd(PPh ₃) ₄	0.01	1.2	130	2.5	65

^aReactions were run for 14 h using 7 mmol of 4-bromoacetophenone and 14 ml of *n*-butanol.

^bDetermined by GC using diethyleneglycol dibutylether as an internal standard.

^cAr = 4-Acetylphenyl.

^dPalladacycle = *trans*-Di(μ-acetato)-bis[*o*-(di-*o*-tolylphosphino)benzyl]dipalladium(II) [21].

complex (derived from $\text{Pd}(\text{OAc})_2$ and $\text{P}(o\text{-Tol})_3$), which proved to be very active in Heck and Suzuki reactions [21,22], is not suitable for carbonylation reactions (entry 5, Table 3).

Using $\text{PdCl}_2(\text{PPh}_3)_2$, catalyst concentrations were lowered. With the optimized conditions established beforehand, a productivity (TON) of almost 5000 (yield 50%) was achieved (entry 7, Table 3). In addition to Pd(II) precursor complexes, we employed Pd(0)/phosphine complexes of the type $\text{Pd}(\text{PR}_3)_x$ as catalyst precursors (x depends on the steric bulk of the phosphine). With the $\text{P}(o\text{-Tol})_3$ ligand, no significant ester formation was observed (entry 8, Table 3). These results are in accordance with those obtained when the palladacycle was used as the catalyst. Obviously, the steric demand of $\text{P}(o\text{-Tol})_3$ (cone angle: 194° [30]) is too high to enable efficient carbonylation catalysis. The Pd(0) complex of the more basic, but smaller PCy_3 ligand (cone angle: 170° [30]) gave a much better catalytic productivity (entry 9, Table 3). The use of $\text{Pd}(\text{PPh}_3)_4$, however, led to an almost quantitative yield under these conditions (cone angle of PPh_3 : 145° [30]). This complex turned out to be even more efficient than $\text{PdCl}_2(\text{PPh}_3)_2$ (compare entries 1 and 10, Table 3). Even with a catalyst concentration as low as 0.01 mol% an ester yield of 65% was achieved, corresponding to a TON of 6500 (entry 12, Table 3). To the best of our knowledge this catalyst TON exceeds all others previously reported for a palladium-catalyzed aryl-X alkoxy-carbonylation in the open literature.

The improved performance of the $\text{Pd}(\text{PPh}_3)_4$ catalyst compared to $[\text{Pd}(\text{Ar})\text{Br}(\text{PPh}_3)_2]$ must be ascribed to the increased amount of ligand present in the reaction mixture. This prompted us to investigate the influence of the P/Pd ratio on the catalyst productivity. Thus, we carried out the model reaction in the presence of $\text{PdCl}_2(\text{PhCN})_2$ and various amounts of the PPh_3 ligand (see Fig. 2).

It was observed that with up to 8 eq. of PPh_3 per Pd (0.1 mol%) the catalyst productivity steadily increases to yield the ester quantita-

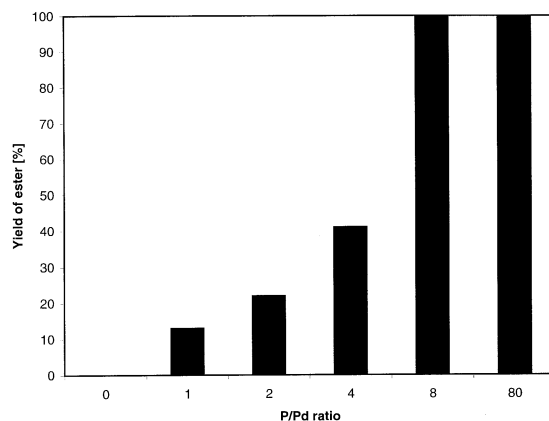


Fig. 2. Influence of the P/Pd ratio on the yield of **2** at 0.1 mol% of $\text{PdCl}_2(\text{PhCN})_2$. Reactions were run for 14 h using 7 mmol of 4-bromoacetophenone, 14 ml of *n*-butanol and 1.2 eq. of NEt_3 at 130°C and 5 bar CO partial pressure.

tively. Even at higher P/Pd ratios, 100% of the product is obtained after 14 h. In order to clarify if the drastic yield increase of **2** at higher phosphine concentrations (8, 80 eq.) is due to an increased stability or an increased activity of the catalyst, we examined the time dependent CO uptake of the reaction.

At low P/Pd ratios (up to 4 eq.), it turned out that the carbonylation stopped within the first 30 min (during the thermal equilibration of the apparatus) and the catalyst was completely deactivated after this time (no CO consumption, rapid formation of palladium metal). Using 8 eq. of the ligand compared to Pd, we observed a high activity of the catalyst system and the reaction ran to complete conversion within 1 h (Fig. 3).

On the other hand, in the presence of an 80-fold excess of the ligand, complete conversion of **1** required at least 11 h (Fig. 3). However, owing to the high stabilization of the catalyst in this case, the carbonylation proceeded also quantitatively.

In order to observe further effects, the catalyst concentration was reduced by one order of magnitude and the dependence of the ester yield on the P/Pd ratio was determined (Fig. 4).

Interestingly, the best yields (70%, TON = 7000) were observed at very high P/Pd ratios

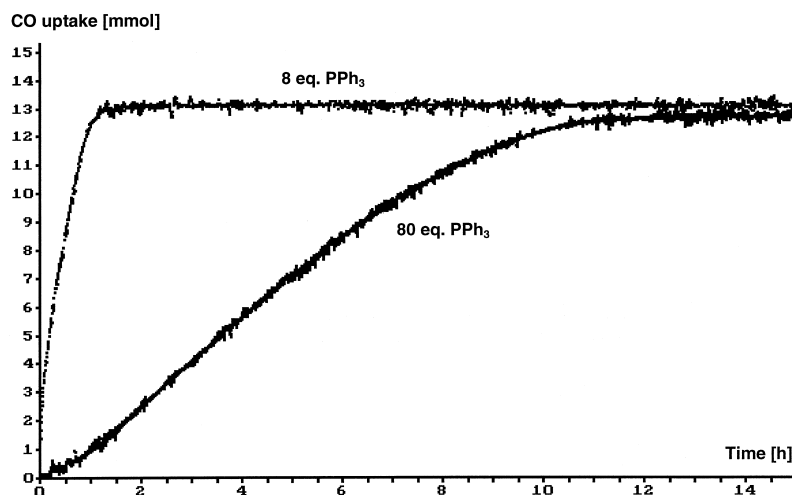


Fig. 3. Time/conversion plots at P/Pd ratios of 8 eq. and 80 eq. using 0.1 mol% of $\text{PdCl}_2(\text{PhCN})_2$. Conditions: 14 mmol of 4-bromoacetophenone, 28 ml of *n*-butanol, 1.2 eq. of NEt_3 , 130°C, 5 bar CO partial pressure.

of about 80 eq. Thus, in order to obtain high productivities when decreasing the catalyst concentration by one order of magnitude, the P/Pd ratio has to be increased by one order of magnitude. Obviously, the phosphine concentration, instead of the P/Pd ratio, has to be maintained in order to stabilize the catalyst. However, this is at the expense of the catalyst activity (compare Figs. 3 and 5), since free coordination sites of the metal center are blocked.

The fact that an optimum catalyst efficiency is achieved at relatively high P/Pd ratios is an

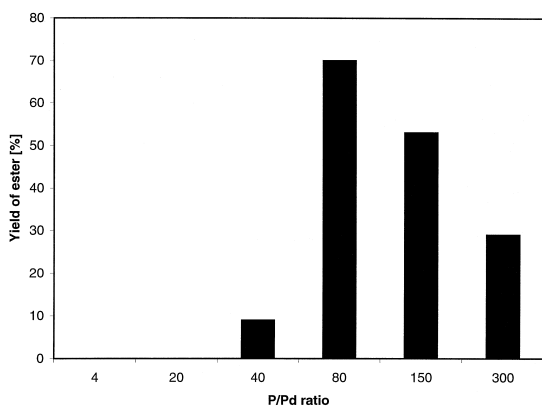


Fig. 4. Influence of the P/Pd ratio on the yield of **2** at 0.01 mol% $\text{PdCl}_2(\text{PhCN})_2$. Reactions were run for 14 h using 7 mmol of 4-bromoacetophenone, 14 ml of *n*-butanol and 1.2 eq. of NEt_3 at 130°C and 5 bar CO partial pressure.

unusual feature of this palladium-catalyzed carbonylation (compare for example: the Heck or Suzuki reaction [31]). The main problem of this reaction is the deactivation of the catalyst by reaction of the active species with CO. The CO ligands with their π -acceptor properties impede the oxidative addition of the aryl bromide because they decrease the π -electron density at the palladium center. The CO coordination can be retarded or made reversible by either lowering the CO concentration (CO pressure) or increasing the phosphine concentration. As this leads to an acceleration of the entire catalytic process, we assume that the oxidative addition step is critical above 1 bar CO pressure despite of the fact that 4-bromoacetophenone is an “activated” aryl bromide.

3. Experimental

All chemicals were purchased from the Sigma-Aldrich group and used without further purification. The CO gas (purity 99.97%) used in the carbonylation experiments was purchased from Aga Gas GmbH. The complexes $\text{Pd}[\text{P}(o\text{-Tol})_3]_2$ [32], $\text{Pd}(\text{PCy}_3)_2$ [33], palladacycle [21],

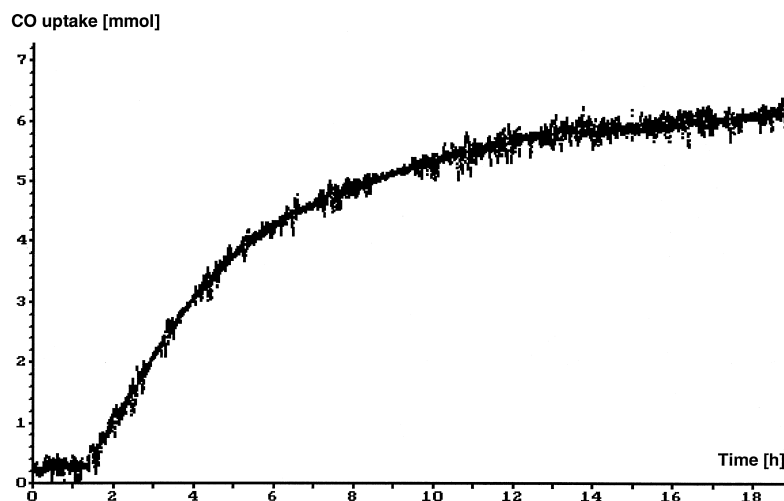


Fig. 5. Time/conversion plot at a P/Pd ratio of 80 eq. using 0.01 mol% of $\text{PdCl}_2(\text{PhCN})_2$. Conditions: 14 mmol of 4-bromoacetophenone, 28 ml of *n*-butanol, 1.2 eq. of NEt_3 , 130°C, 5 bar CO partial pressure.

$[\text{Pd}(4\text{-AcC}_6\text{H}_4)\text{Br}(\text{PPh}_3)_2]$ [29] and $\text{Pd}(\text{PPh}_3)_4$ [34] were prepared according to literature methods.

^1H , ^{13}C NMR spectra: Bruker ARX 400 with chloroform (CHCl_3) as internal standard. Infrared spectrum: Nicolet Magna 550. Mass spectrum: AMD 402/3. Column chromatography: Silica gel 60, 63–200 μm , E. Merck, Darmstadt. Carbonylation reactions were carried out in a 100 ml stainless steel Parr autoclave with a magnet-driven stirrer.

General procedure: 1.393 g (7 mmol) of 4-bromoacetophenone, 14 ml of *n*-butanol, 2.93 ml (21 mmol) of triethylamine, 14.7 mg (0.3 mol%) of $\text{PdCl}_2(\text{PPh}_3)_2$ and 200 μl of diethyleneglycol dibutylether (internal standard) were placed in the reactor. After purging three times with CO, the autoclave was pressurized with CO and heated to 130°C. Only in case of the kinetic experiments the pressure was kept constant using a pressure regulator. Here, the pressure change was determined by measuring the decrease of CO in a reservoir. After a reaction time of 14 h and cooling to room temperature, the yellow reaction mixture was diluted with 70 ml of dichloromethane and 70 ml of water. After separation of the layers, the aqueous phase

was extracted twice with 25 ml of the organic solvent. The combined organic phases were examined by GC. The product (*n*-butyl 4-acetylbenzoate) can be isolated by column chromatography using ethylacetate/hexane (1:15) as an eluent ($R_F = 0.15$).

^1H NMR (400.1 MHz, CDCl_3 , 297 K): δ [ppm] = 0.96 (t, $J = 7.3$ Hz, 3H, CH_2CH_3), 1.46 (sext, $J = 7.3$ Hz, 2H, $\text{CH}_2\text{-CH}_3$), 1.74 (quint, $J = 7.3$ Hz, 2H, $\text{O-CH}_2\text{-CH}_2$), 2.61 (s, 3H, COCH_3), 4.32 (t, $J = 7.3$ Hz, 2H, O-CH_2), 7.97 and 8.09 (m, 4H, AA'XX', C_6H_4).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100.6 MHz, CDCl_3 , 297 K): δ [ppm] = 13.70 ($\text{CH}_2\text{-CH}_3$), 19.21 ($\text{CH}_2\text{-CH}_3$), 26.84 (COCH_3), 30.64 ($\text{O-CH}_2\text{-CH}_2$), 65.27 (O-CH_2), 128.14 ($\text{C}_{\text{Aryl-3/5}}$), 129.73 ($\text{C}_{\text{Aryl-2/6}}$), 134.24 ($\text{C}_{\text{Aryl-1}}$), 140.09 ($\text{C}_{\text{Aryl-4}}$), 165.75 (CO_2R), 197.52 (COCH_3).

IR (neat, KBr): ν [cm^{-1}] = 3422 s, 3077 w, 3066 w, 3051 w, 2963 s, 2939 m, 2895 m, 2872 m, 1720 s, 1683 s, 1609 w, 1503 w, 1473 m, 1405 s, 1377 m, 1354 m, 1317 m, 1280 s, 1178 m, 1135 m, 1110 s, 1033 w, 1017 m, 965 m, 862 m, 848 w, 770 s, 740 w, 694 m, 613 m.

MS (EI, 70 eV): $m/z = 220$ (2.5, M^+), 205 (100.0, $\text{M}^+\text{-CH}_3$), 165 (77.3), 149 (78.4, $\text{M}^+\text{-CH}_3\text{-C}_4\text{H}_8$), 147 (76.1, $\text{M}^+\text{-OBU}$).

4. Conclusion

We have investigated the influence of important reaction parameters on catalyst productivities of the homogeneous palladium-catalyzed alkoxy carbonylation of an aryl bromide in detail. Using the system 4-bromoacetophenone/*n*-butanol, it was observed that temperatures between 100–130°C enable the best catalyst performance. We demonstrated that the CO pressure has a strong influence on the catalyst productivity. If the pressure was reduced towards one atmosphere of CO, the yields increased significantly indicating that the catalyst was less active at high CO concentrations. The best solvent for the reaction is the neat alcohol. Concerning the catalyst precursors, Pd(PPh₃)₄ or a combination of PdCl₂(PhCN)₂/80 eq. PPh₃ turned out to give the best productivities. With as little as 0.01 mol% Pd, we were able to achieve a TON up to 7000.

The variation of the P/Pd ratio in case of PPh₃ showed an optimum value of about 8 eq. of the ligand to Pd under our reaction conditions (0.1 mol% PdCl₂(PhCN)₂, 1.2 eq. NEt₃, 14 ml *n*-butanol, 5 bar CO, 130°C) for both high catalyst stability and activity. It is an important result that this excess of phosphine is necessary to displace CO ligands from the metal center to render the catalyst active for oxidative addition of the aryl bromide. If the catalyst concentration is lowered by one order of magnitude from 0.1 mol% Pd to 0.01 mol% Pd, the P/Pd ratio has to be increased by the same factor (80 eq.), i.e., the correct combination of phosphine and CO concentration has to be found in order to get optimum results. It is interesting to note that the P/Pd ratio is only important for a given set of reaction conditions.

Our investigations have also addressed aspects on the principal question of the rate determining step in the catalytic cycle. Despite the fact that 4-bromoacetophenone is an activated bromoarene, the oxidative addition of Ar–X to Pd seems critical. This is in contrast to the related Heck olefination or the Suzuki arylation

of 4-bromoacetophenone, for example. Compared to those C–C-coupling reactions, the carbonylation proceeds in general much slower due to the problem of catalyst deactivation. Further studies towards this problem are in progress.

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