Phosphorus Acids as Highly Efficient Promoters for the Palladium-Phenanthroline Catalyzed Carbonylation of Nitrobenzene to Methyl Phenylcarbamate[†]

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Abstract: A new family of promoters, based on phosphorus acids, is reported for the catalytic carbonylation of nitrobenzene to methyl phenylcarbamate by palladium-phenanthroline complexes. With the new promoters, unprecedented reaction rates (TOF up to 6000/h) and catalyst stability (TON up to 10^5)

Introduction

The carbonylation of organic nitro compounds is a process with a high potential synthetic and industrial interest, since many products can be obtained from nitro compounds and CO, including isocyanates, carbamates and ureas.^[1-3] Ureas and carbamates are important final products and intermediates in the synthesis of pesticides and fertilizers and mono- and diisocyanates are important intermediates in the manufacture of pesticides, polyurethane foams plastics, synthetic leather, adhesives, and coatings.

The classical method for the production of isocyanates requires the intermediate reduction of the nitro compound to amine, followed by reaction with phosgene. However, phosgene is a very toxic and corrosive material and an enormous effort has been applied to the development of phosgene-free routes to isocyanates. Among these, the catalytic carbonylation of nitro compounds, particularly of aromatic ones, represents one of the most interesting alternatives, but the direct carbonylation of nitro compounds to the corresponding isocyanates has proved to be a difficult reaction. However, in the presence of an alcohol, carbamates can be obtained more easily and with a high selectivity [Eq. (1)]:

ArNO₂ + ROH + 3 CO
$$\longrightarrow$$
 ArNHCOOR + 2 CO₂ (1)

If the isocyanate is the desired product, this can be obtained by thermal cracking of the carbamate [Eq. (2)]:

ArNHCOOR $\xrightarrow{\Delta}$ ArNCO + ROH (2)

could be reached. The best promoter is phosphoric

acid, which is also very cheap, nontoxic and easily

Keywords: carbamates; carbonylation; homogeneous

separable from the reaction products.

catalysis; nitroarenes; palladium

Despite an intense effort both in industrial and academic laboratories, no process has been developed up to now which may compete from an economical point of view with the established technology employing phosgene. This is mostly due to the insufficient turnover numbers (generally in the hundreds or even less) that even the most efficient catalysts can achieve, making catalyst recycle too expensive. In recent years the catalytic system based on palladium-phenanthroline complexes has emerged as the most active and promising for a possible industrial application.^[4-31] Several groups have reported that the addition of acidic co-catalysts (carboxylic acids^[11,12,15,18,31] or phenanthrolinium salts^[20–22,24]) markedly improves both rate and selectivity of the carbonylation of nitroarenes to give isocyanates or carbamates. We were intrigued by van Leeuwen's observation^[15] that no correlation was present between the acidity of the carboxylic acid employed as promoter and the rate increase. This suggested to us that a bifunctional activation process may be operative and we decided as a working hypothesis to investigate the promoting activity of a series of substances that may have a better bifunctional activation ability than carboxylic acids. Although we must stress that at the moment we only have some preliminary mechanistic data indicating that a bifunctional activation is indeed occurring, this working hypothesis proved fruitful and allowed us to markedly improve the efficiency of the catalytic system in terms of both reaction rate and catalyst life. A preliminary communication of part of this work has been published.^[32]

Table 1.	Comparison	of different	promoters.	[a]
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Catalyst	Promoter	Promoter/ Pd mol ratio	<i>T</i> [°C]	PhNO ₂ conv. [%] ^[b]	PhNHCO ₂ Me sel. [%] ^[c]	PhNH ₂ sel. [%] ^[c]	PhN(O)=NPh sel. [%] ^[c]
$[Pd(Phen)_2][BF_4]_2$	_	_	135	20.7	90.5	_	_
$[Pd(Phen)_2][OTf]_2$	_	_	135	13.0	79.2	1.1	1.4
$[Pd(Phen)_2][BF_4]_2$	PhCOOH	25	135	19.9	98.4	_	_
$[Pd(Phen)_2][OTf]_2$	PhCOOH	25	135	16.5	86.0	0.5	1.1
$\left[Pd(Phen)_2 \right] \left[BF_4 \right]_2$	$Ph_2P(O)OH$	25	135	39.3	96.9	_	_
$[Pd(Phen)_2][OTf]_2$	$Ph_2P(O)OH$	25	135	22.4	88.2	0.4	1.0
$[Pd(Phen)_2][BF_4]_2$	2-HO,5-ClPy	25	135	23.8	81.1	0.5	2.4
$[Pd(Phen)_2][OTf]_2$	2-HO,5-ClPy	25	135	14.5	85.4	0.8	1.1
$[Pd(Phen)_2][BF_4]_2$	2-HOPy	25	135	21.8	81.7	0.6	0.3
$[Pd(Phen)_2][BF_4]_2$	$[PhenH][PF_6]^{[d]}$	7	135	18.0	92.0	3.2	_
$[Pd(Phen)_2][BF_4]_2$	[PhenH][PF ₆]	25	135	25.8	74.0	5.6	2.8
$[Pd(Phen)_2][BF_4]_2$	[PhenH][PF ₆]	16	135	31.7	80.8	2.9	2.0
$[Pd(Phen)_2][BF_4]_2$	-	_	150	45.1	89.7	_	2.9
$[Pd(Phen)_2][BF_4]_2$	PhCOOH	25	150	45.3	95.4	_	1.7
$[Pd(Phen)_2][BF_4]_2$	$Ph_2P(O)OH$	25	150	83.7	91.2	_	0.5
$[Pd(Phen)_2][BF_4]_2$	_	_	170	87.0	90.4	_	5.7
$[Pd(Phen)_2][BF_4]_2$	PhCOOH	25	170	96.7	90.0	_	2.6
$[Pd(Phen)_2][BF_4]_2$	$Ph_2P(O)OH$	25	170	98.0	92.4	2.2	0.8

^[a] Experimental conditions: Catalyst = 2.0×10^{-2} mmol, mol ratios Pd/Phen/PhNO₂ = 1:4:730, P_{CO} = 60 bar, in methanol (10 mL) for 1.5 h.

^[b] Calculated with respect to the starting PhNO₂.

^[c] Calculated with respect to the converted PhNO₂. Most of the remaining mass balance is due to diphenylurea, which was observed, but not quantified by GC. Trace amounts (selectivity <1%) of azobenzene were also detected.

^[d] Phen/cat. = 3.

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Results and Discussion

As candidates for bifunctional activation we initially investigated 2-hydroxypyridine,^[33] previously shown by us to be also a promoter for the reaction of Eq. (1) when [Rh(CO)₄]⁻ is employed as catalyst,^[34] its 5-chloro analogue and a phosphorus acid: diphenylphosphinic acid.^[33,35] Van Leeuwen and co-workers have reported on the promoting efficiency of carboxylic acids only in conjunction with $[Pd(Phen)_2][TfO]_2$ (TfO⁻ = CF₃SO₃⁻, Phen = 1,10-phenanthroline) as catalyst and at 135 °C.^[15,18] However, in another paper,^[14] the same authors reported that the related $[Pd(Phen)_2][BF_4]_2$ complex affords better results. We have compared both these complexes in the presence of the aforementioned promoters, also including benzoic acid and [PhenH][PF₆] for comparison and in a broader range of temperatures. The results are reported in Table 1. The main conclusions that can be drawn from the data reported are the following:

We confirm that benzoic acid increases both conversion and selectivity when employed at 135 °C with [Pd(Phen)₂][TfO]₂ as catalyst. However, with the more active tetrafluoroborate catalyst, no effect on conversion is observed at either 135 or 150 °C, although an increase in selectivity is still observed. Only at 170 °C we could observe a positive effect of

benzoic acid even on the reaction rate with $[Pd(Phen)_2][BF_4]_2$.

- 2) 2-Hydroxypyridine and its chlorinated analogue show some promoting effect, but, at least for the triflate catalyst, the effect is smaller than the one of benzoic acid and they were not investigated further.
- 3) Mestroni's promoter [PhenH][PF₆] is also effective with the tetrafluoroborate catalyst, in accord with what is reported in the literature.^[20–22,24] The reaction was performed both at the molar ratio promoter/Pd employed by Mestroni, 7:1, and at the one employed by us, 25:1. Since by increasing the promoter/Pd ratio even the total amount of phenanthroline is increased, we also performed a reaction at an intermediate ratio, 16:1, which indeed gave the best results. Under these conditions [PhenH][PF₆] affords better conversions, but lower selectivities with respect to benzoic acid.
- 4) Diphenylphosphinic acid is clearly the best promoter, and increases rate and selectivity with both catalysts and at all temperatures.
- 5) When the temperature is increased, the azoxybenzene amount also increases, especially in the absence of promoters.

By working at 60 bar CO, the reaction temperature and the amounts of phenanthroline and diphenylphosphinic acid were optimized. The catalytic ratio was in-

Phen /Pd mol ratio	PhNO ₂ conv. [%] ^[b]	PhNHCO ₂ Me sel. [%] ^[c]	$\frac{\text{PhNH}_2}{\text{sel. }[\%]^{[c]}}$	PhN(O)=NPh sel. [%] ^[c]
15	33.5	93.3	1.3	2.8
18	49.7	92.3	1.7	3.2
22	82.2	94.6	1.7	2.8
30	77.9	84.8	1.2	2.8
40	72.1	88.0	2.2	3.0

Table 2. Influence of the Phen/Pd ratio.^[a]

^[a] Experimental conditions: $[Pd(Phen)_2][BF_4]_2 = 2.0 \times 10^{-2}$ mmol, mol ratios $Pd/Ph_2P(O)OH/PhNO_2 = 1:150:2190$, $P_{CO} = 60$ bar, T = 170 °C, in methanol (30 mL), for 1 h.

^[b] Calculated with respect to the starting PhNO₂.

^[c] Calculated with respect to the converted PhNO₂. Most of the remaining mass balance is due to diphenylurea, which was observed, but not quantified by GC. Trace amounts (<1%) of azobenzene were also detected in some cases.

Table 3. Influence of the reaction temperature and the Ph₂P(O)OH/Pd ratio.^[a]

Entry	<i>T</i> [°C]	Ph ₂ P(O)OH/Pd mol ratio	PhNO ₂ conv. [%] ^[b]	PhNHCO ₂ Me sel. [%] ^[c]	PhNH ₂ sel. [%] ^[c]	PhN=NPh sel. [%] ^[c]	PhN(O)=NPh sel. [%] ^[c]
1	170	25	55.7	85.8	2.0	_	6.2
2	180	25	83.6	76.9	1.4	1.6	13.6
3	190	25	85.6	65.1	1.2	3.1	23.1
4	200	25	80.1	57.8	1.2	3.2	26.6
5	170	75	68.2	91.0	1.4	_	3.0
6	180	75	84.9	88.5	1.8	0.8	4.3
7	190	75	80.8	81.7	1.6	1.9	12.0
8	170	100	78.7	93.6	1.4	_	3.3
9	170	150	82.2	94.6	1.7	0.6	2.8
10	170	225	79.8	94.8	1.7	_	2.5
11	170	300	78.5	90.6	1.7	0.6	3.6

^[a] Experimental conditions: $[Pd(Phen)_2][BF_4]_2 = 2.0 \times 10^{-2} \text{ mmol}$, mol ratios Pd/Phen/PhNO₂ = 1:22:2190, P_{CO} = 60 bar, T = 170 °C, in methanol (30 mL), for 1 h.

^[b] Calculated with respect to the starting PhNO₂.

^[c] Calculated with respect to the converted PhNO₂. Most of the remaining mass balance is due to diphenylurea, which was observed, but not quantified by GC.

creased three-fold to avoid reaching complete conversion.

The results of the experiments performed with different Phen/Pd ratios are reported in Table 2. The effect is very marked. By increasing the Phen/Pd ratio from 15 to 22, the nitrobenzene conversion increases from 33 to 82%. Higher ratios cause a decrease in the conversion, but the effect is smaller. Such an effect has already been observed by us for a related catalytic system for the synthesis of isocyanates^[11] and is probably due to a series of complexation equilibria [Eq. (3)], where only the complex with one phenanthroline is catalytically active.

$$[Pd]^{2*} \xrightarrow{\text{Phen}} [Pd(Phen)]^{2*} \xrightarrow{\text{Phen}} [Pd(Phen)_2]^{2*}$$

$$- \text{Phen} - \text{Phen} \qquad (3)$$

The selectivity is also highest at the 22:1 ratio and the corresponding phenanthroline concentration has been

chosen as a standard for the following optimization reactions.

The effect of temperatures higher than $170 \,^{\circ}\text{C}$ was then examined (Table 3, entries 1–7). The reactions were investigated both at mol ratios Ph₂P(O)OH/Pd = 25 and 75. The first is the same as the one used for the experiments in Table 1, but corresponds to a lower acid concentration in solution, since the volume was increased from 10 to 30 mL. The second ratio keeps the acid concentration equal to the one of the first series of experiments, although the acid/Pd ratio is changed.

The results show that the selectivity is always highest at 170 °C, although the conversion is higher at 180 and 190 °C. At temperatures higher than 170 °C, formation of some metallic palladium was observed at the end of the reaction. The increase in reaction temperature also causes a steady increase in the amount of azoxybenzene formed, confirming the trend previously observed, which is only partly moderated by an increase in the

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Figure 1. Influence of the $Ph_2P(O)OH/Pd$ mol ratio on the $PhNO_2$ conversion. Data in Table 3, entries 1, 5, 8–11. The curve was manually drawn and does not correspond to any mathematical fitting.

acid amount. A higher acid amount accelerates the reaction at 170 °C, but not at the higher temperatures, likely because the catalytic system decomposes.

Keeping the temperature and the phenanthroline amount constant, the $Ph_2P(O)OH$ amount was then optimized (Table 3, entries 1, 5, 8–11, Figure 1). The reaction rate increases up to a mol ratio $Ph_2P(O)OH/Pd = 150$, then it decreases a little. The selectivity is almost indistinguishable between the ratios 100 and 225, but it is lower outside this range.

By halving the amount of palladium and doubling the reaction time (Table 4), the conversion decreased from 82 to 62%, but by further reducing the amount of palladium to ca. 1/5 of the initial one and increasing the reaction time five times (five hours, molar ratio nitrobenzene/Pd = 10000, or catalyst = 10^{-2} mol %) the conversion even increased to 97.8%. The selectivity lowered from 94.6 to 73.5 along the series, but it raised back to 87.4 when 1 mL of 2,2-dimethoxypropane was added to the reaction mixture, the conversion remaining virtually unchanged (Table 4, entries 3, 4). Dimethoxypropane acts as an internal drying agent and its addition has already been shown to be beneficial for this reaction.^[20-24] This shows that the reaction is complex but the system does not deactivate on prolonged working. On the contrary, decreasing five-fold the palladium concentration increases the turnover frequency. Under these conditions (Table 4, entries 4-7), the reaction shows an induction time of about one hour, after which it proceeds with a zero order in PhNO₂ without showing any rate decrease due to possible decomposition of the catalytic system (Figure 2). The reaction is 5.4 times slower during the first hour than in any of the following ones. It should be noted that the autoclave takes about 15 min to reach the final temperature when immersed in the preheated oil bath (see Experimental Section), but the reaction does surely start well before full equilibration has been achieved. Even a full 15 min delay time in the first hour, however, would by itself cause the



Figure 2. Dependence of PhNO₂ conversion on reaction time. Data in Table 5, entries 4-7. The linear regression affords a line with equation: Conv. $\% = 23.49 \text{ t} - 18.56 \text{ (R}^2 = 0.999).$

reaction to be only 1.3 times slower in the first hour than in the following ones.

Since aniline is known to be intermediately formed in several catalytic carbonylation reactions of nitroarenes,^[1–3,19] we investigated the effect of its addition since the beginning. As shown in Table 5, the addition of aniline in a 4% molar amount with respect to the starting nitrobenzene accelerates the reaction in the first hour by a factor of about 4. Thus it is clear that the induction time is for the most part due to the required generation of aniline, which is slow in the dry solvent employed. The addition of an equimolar amount of aniline with respect to nitrobenzene has been previously reported to accelerate the rate of the reaction with a palladium-phenanthroline catalyst,^[16] but in the presence of such an high amount of aniline the selectivity of the reaction much decreased and large amounts of azoxybenzene were formed.

At this stage other phosphorus acids were tested. A comparison of the data in Table 6 shows that the introduction of an electron-donating group on the phenyl rings of diphenylphosphinic acid has a small positive effect, but the electron-withdrawing chloride is not tolerated. Phenylphosphonic acid and its substituted analogues are a better class of promoters, but phenylphosphinic acid, which has a hydrogen atom directly linked to the phosphorus atom and can act as a reductant towards palladium, completely deactivated the catalytic system, apparently because of fast formation of inactive palladium metal. Even the more acidic dithiodiphenylphosphinic acid was not a suitable promoter. Worthy of note, this acid is known not to be a good bifunctional catalyst.^[33] Very interestingly, the best conversion was obtained with commercial 85% phosphoric acid ! This is an ideal promoter in terms of cost, absence of toxicity and ease of separation from the reaction products. The 1:1 mixture of mono- and dimethyl phosphate, obtained by reaction of P_4O_{10} with the stoichiometric amount of methanol, was less efficient, but still retained a high

Entry	cat. [mmol]	<i>t</i> [h]	PhNO ₂ /Pd mol ratio	PhNO ₂ conv. [%] ^[b]	PhNHCO ₂ Me sel. [%] ^[c]	PhNH ₂ sel. [%] ^[c]	PhN=NPh sel. [%] ^[c]	PhN(O)=NPh sel. [%] ^[c]	TOF $[h^{-1}]$
1	$2.0 imes 10^{-2}$	1	2190	82.2	94.6	1.7	0.6	2.8	1800
2	$1.0 imes10^{-2}$	2	4380	62.0	90.2	1.8	traces	4.9	1359
3	4.4×10^{-3}	5	10000	97.8	73.5	3.1	3.8	7.5	1959
4 ^[d]	$4.4 imes10^{-3}$	5	10000	97.7	87.4	2.0	0.5	1.1	1956
5 ^[d]	$4.4 imes 10^{-3}$	1	10000	4.4	82.2	17.8	_	_	442
6 ^[d]	$4.4 imes10^{-3}$	2	10000	28.1	90.6	7.9	_	1.4	1404
7 ^[d]	$4.4 imes10^{-3}$	3.5	10000	65.7	94.7	2.7	_	1.4	1878

Table 4. Influence of high catalytic ratios and reaction time.^[a]

^[a] Experimental conditions: Catalyst = $[Pd(Phen)_2][BF_4]_2$, Phen = 0.44 mmol, Ph₂P(O)OH = 3.00 mmol, P_{CO} = 60 bar, T = 170 °C, in methanol (30 mL).

^[b] Calculated with respect to the starting PhNO₂.

^[c] Calculated with respect to the converted PhNO₂. Most of the remaining mass balance is due to diphenylurea, which was observed, but not quantified by GC.

^[d] 2,2-Dimethoxypropane (1 mL) was also added.

Table 5. Influence of the addition of aniline.^[a]

<i>t</i> [h]	PhNH ₂ /Pd mol ratio	PhNO ₂ conv. [%] ^[b]	PhNHCO ₂ Me sel. [%] ^[c]	PhNH ₂ sel. [%] ^[c, d]	PhN(O)=NPh sel. [%] ^[c]
1	_	14.9	93.8	6.2	_
1	100	43.2	95.1	1.8	0.8
1.5	100	86.0	93.8	2.0	0.6
1	200	59.6	96.9	0.8	0.8

^[a] Experimental conditions: $[Pd(Phen)_2][BF_4]_2 = 2.8 \text{ mg}$, $4.4 \times 10^{-3} \text{ mmol}$, mol ratios Pd/Phen/Ph₂P(O)OH/PhNO₂ = 1:100:682:5000, P_{CO} = 60 bar, T = 170 °C, in methanol (30 mL) + 2,2-dimethoxypropane (1 mL).

^[b] Calculated with respect to the starting PhNO₂.

^[c] Calculated with respect to the converted PhNO₂. Most of the remaining mass balance is due to diphenylurea, which was observed, but not quantified by GC. Azobenzene was below the detection limit (0.1%).

^[d] Calculated considering only the aniline amount in excess with respect to the initially charged one.

promoting efficiency, showing that a partial esterification of the acid does not block catalytic activity. Such esterification does indeed occur during the reaction, but to a small extent. Under the conditions of Table 3 but for a longer time (6 h), 32% of the added phenylphosphonic acid was transformed into the monomethyl ester and no diester was detectable by ³¹P NMR. The esterification is a purely organic transformation and essentially the same amount of monoester (30%) is obtained under the same conditions, but in the absence of the metal and nitrobenzene.

The fact that 85% H_3PO_4 gave a better conversion than the pure acid is at first sight surprising, since in the first case some water is also added. The results show that the addition of this water is beneficial, despite the fact that the addition of a drying agent is also positive. The apparent inconsistency can be at least qualitatively explained by considering the complex role of aniline in the catalytic system. Depending on the reaction mechanism, aniline can be, and often is, an intermediate in the carbonylation reaction of nitrobenzene, but it is also a by-product. It can be produced by reaction of nitrobenzene, CO, and water and is also involved in several reactions under the reaction conditions, some of which regenerate water. We have previously discussed some of these problems in the palladium-catalyzed carbonylation reactions of nitroarenes^[1,19] and detailed the complex situation present when the same reaction is catalyzed by Ru₃(CO)₁₂/[Et₄N][Cl].^[36] Preliminary mechanistic studies on the present catalytic system indicate that at least three different mechanisms are operating at the same time. Discussing them now is premature, but the results reported here indicate anyway that further room exists for optimization of the experimental conditions. Concerning the action of dimethoxypropane, it is worth noting that in this work we could not detect the formation of acetone, the product of its reaction with water, because this last compound is too volatile to be separated from the much larger amount of methanol, employed as solvent. However, in a related work^[31] we could indirectly evidence its formation by observing small amounts of isopropylidene-phenylimine, the Schiff base derived from the condensation of acetone with aniline, among the products.

Table 6.	Comparison	of different	phosphorus	promoters. ^[a]
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Promoter	Promoter/Pd mol ratio	PhNO ₂ conv. [%] ^[b]	PhNHCO ₂ Me sel. [%] ^[c]	PhNH ₂ sel. [%] ^[c]	PhN(O)=NPh sel. [%] ^[c]
_	_	4.6	13.7 (11.0) ^[d]	_[d]	51.0
$Ph_{2}P(O)OH$	682	37.0	89.5 (87.9) ^[d]	_[d]	1.8
$(4-MeC_6H_4)_2P(O)OH$	682	37.8	93.3 (91.7) ^[d]	_[d]	1.9
$(4-ClC_6H_4)_2P(O)OH$	682	7.7	$64.0 (60.3)^{[d]}$	_[d]	_
$PhP(O)(OH)_2$	682	42.5	86.8	< 0.1	1.6
$4 - MeC_6H_4P(O)(OH)_2$	682	49.2	90.3	0.4	1.6
$4-\text{ClC}_6\text{H}_4\text{P(O)(OH)}_2$	682	34.6	86.4	0.7	2.1
Ph ₂ P(S)SH	682	_	_	_	_
PhPH(O)OH	682	_	_	_	_
H ₃ PO ₄ 100%	682	42.6	93.5	2.8	_
H ₃ PO ₄ 100%	753	47.9	89.0	0.9	_
H ₃ PO ₄ 85%	682	55.1	87.1	3.0	1.7
$OP(OMe)(OH)_2/OP(OMe)_2(OH)$ 1:1	682	33.4	85.4 (84.0) ^[d]	_[d]	<1
PhCOOH	682	17.1	83.6 (77.3) ^[d]	_[d]	18.6
[PhenH][PF ₆]	227	10.6	83.8 (81.3) ^[d]	_[d]	_
H ₃ PO ₄ 85% ^[e]	682	64.0	84.4	5.5	3.0
H ₃ PO ₄ 85% ^[f]	682	63.0	84.9	4.4	2.4

^[a] Experimental conditions: $[Pd(Phen)_2][BF_4]_2 = 1.4 \text{ mg}$, $2.2 \times 10^{-3} \text{ mmol}$, mol ratios Pd/Phen/PhNH₂/PhNO₂ = 1:100:200:7500, P_{CO} = 60 bar, in methanol (15 mL) + 2,2-dimethoxypropane (0.5 mL) for 1 h.

^[b] Calculated with respect to the starting PhNO₂.

^[c] Calculated with respect to the converted PhNO₂. Aniline selectivity is calculated considering only the aniline amount in excess with respect to the initially charged one. Most of the remaining mass balance is due to diphenylurea, which was observed, but not quantified by GC. Azobenzene was below or very close to the detection limit (0.1%).

^[d] Less aniline was found at the end of the reaction with respect to the initially charged one. The value in parentheses refers to the selectivity with respect to the sum of PhNO₂ and PhNH₂ reacted.

^[e] 3,4,7,8-Tetramethyl-1,10-phenanthroline (TMPhen) was employed in place of Phen: mol ratio TMPhen/Pd = 100.

^[f] 3,4,7,8-Tetramethyl-1,10-phenanthroline (TMPhen) was employed in place of Phen: mol ratio TMPhen/Pd = 67.

Benzoic acid and [PhenH][PF₆] were also tested under the optimized conditions (Table 6) and gave results markedly inferior to all phosphorus acids, with the obvious exceptions of phenylphosphinic and dithiodiphenylphosphinic acids, although the TONs observed are anyway higher than those previously reported for these same promoters.

Mestroni and we have previously noted that 3,4,7,8tetramethyl-1,10-phenanthroline (TMPhen) generally affords better conversions and sometimes even better selectivities than unsubstituted Phen in carbonylation reactions of nitrobenzene catalyzed by palladium complexes.^[7-9,11] Under our conditions (Table 6) and with 85% H₃PO₄ as the acid, TMPhen increased the conversion from 55.1 to 64.0%, but the selectivity in carbamate decreased slightly (from 87.1 to 84.4%). Since TMPhen is a stronger ligand than Phen and the ideal TMPhen/Pd ratio is usually lower than the ideal Phen/Pd ratio,^[11] we also repeated the reaction at a lower TMPhen/Pd ratio (67 instead of 100), but the results are indistinguishable within the limits of the experimental error. Since TMPhen is much more expensive than Phen, it is questionable if the small rate increase observed may justify its use on a large scale.

The influence of the CO pressure was finally investigated employing 85% phosphoric acid as promoter. The reaction is clearly first order in CO pressure (Table 7, Figure 3). Because of technical limits, we could not investigate initial pressures higher than 100 bar, but they should clearly afford even better results. It should be noted that the best result corresponds to a turnover frequency (TOF) of almost 6000/h. The highest value previously reported in the open literature for the carbonylation reaction of nitrobenzene to afford methyl phenylcarbamate is 960/h.^[23] The catalytic system is very stable and by decreasing the palladium amount we could obtain an unprecedented TON of 10⁵ in 24 h, albeit with a somewhat lower selectivity (77.5%),^[37] reaching the limit for which a commercial application can be considered.

An analysis of the data in Tables 1, 3, and 6 indicates that the beneficial effect of all promoters on the selectivity is due to the decrease in the amount of azoand azoxybenzene formed. These last by-products are formed more easily at higher temperatures and are only very slowly converted to carbonylated products. The effect of the promoter may be that of (a) avoiding their formation or (b) accelerating their conversion to carbamate.^[38] When azoxybenzene was used as a substrate in place of nitrobenzene (under the conditions of Table 1, but at a molar ratio azoxybenzene/Pd = 365) in the absence of promoters, only a 4.9% conversion was

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P_{CO} [bar]	PhNO ₂	PhNHCO ₂ Me	PhNH ₂	PhN=NPh	PhN(O)=NPh
		sei. [70]	sei. [70] ^e	SCI . [70] ¹³	sei. [70] ^e
40	37.0	82.4	2.8	-	3.0
60	55.1	87.1	3.0	traces	1.7
80	65.1	87.9	4.0	-	1.0
100	81.2	87.5	3.0	-	0.8

Table 7. Influence of CO pressure.^[a]

^[a] Experimental conditions: $[Pd(Phen)_2][BF_4]_2 = 1.4 \text{ mg}, 2.2 \times 10^{-3} \text{ mmol}, \text{ mol ratios } Pd/Phen/PhNH_2/85\% \text{ H}_3PO_4/PhNO_2 = 1:100:200:682:7500, in methanol (15 mL) + 2,2-dimethoxypropane (0.5 mL) for 1 h.$

^[b] Calculated with respect to the starting PhNO₂.

^{c]} Calculated with respect to the converted PhNO₂. Aniline selectivity is calculated considering only the aniline amount in excess with respect to the initially charged one. Most of the remaining mass balance is due to diphenylurea, which was observed, but not quantified by GC.



Figure 3. Influence of CO pressure on PhNO₂ conversion. Data in Table 7. The linear regression affords a line with equation: Conv. $\% = 0.713 P_{CO} + 9.69 (R^2 = 0.989)$.

observed. The only observable product was azobenzene, 58.5%. When $Ph_2P(O)OH$ was added $[Ph_2P(O)OH/Pd=25]$, the conversion increased to 9.5% and azobenzene remained the dominant product (67.4%). This increase in reactivity is much too low to account for the increase in selectivity observed in the catalytic reaction, especially on considering that azobenzene is clearly converted at an even slower rate than azoxybenzene, but is always present in a much lower amount. Thus it is clear that the promoter depresses the formation of azoxybenzene and not simply accelerates its conversion.

Conclusion

In conclusion we have found an improved catalytic system for the carbonylation of nitrobenzene that, for the first time, yields activities and catalyst life in the range necessary for industrial applications. Preliminary results indicate that the improved features also apply to the economically very important dinitrotoluenes. Optimization of the experimental conditions with these substrates is in progress.

Experimental Section

General Procedure

All solvents were dried by standard procedures, distilled and stored under dinitrogen before use. [Pd(Phen)₂][BF₄]₂,^[7] $[Pd(Phen)_2][OTf]_2,^{[14]}$ [PhenH][PF₆],^[39] and Ph₂P(S)SH^[40] were prepared as reported in the literature. $(4-MeC_6H_4)_{2-1}$ ^[41] and $(4-ClC_6H_4)_2P(O)OH^{[42]}$ were synthesized by the method of Kosalapoff and Struck,^[43] but employing H₂O₂ as the oxidant in place of Br₂, as also reported in ref.^[42], and characterized by comparison of their analytical data with the published ones.^[41,42] 4-MeC₆H₄P(O)(OH)₂ and 4-ClC₆H₄P(O)(OH)₂ were synthesized by reaction of triethyl phosphite with 4-MeC₆H₄Br and 4-ClC₆H₄Br, respectively, in the presence of NiBr₂, following the method of Tavs,^[44] followed by hydrolysis of the ester with 37% HCl as in ref.^[45] They were characterized by comparison of their analytical data with those reported in the literature.^[46] Nitrobenzene was purified by shaking with 10% H₂SO₄, washing with water, and drying with Na₂SO₄, followed by distillation under dinitrogen and storage under an inert atmosphere. Aniline was distilled and stored under dinitrogen before use. All other reagents were commercial products and were employed as received.

Catalytic Reactions

In a typical catalytic reaction, the catalyst, Phen, PhNO₂, and, when required, PhNH₂ and the acidic promoter were weighed in a glass liner. In the cases in which less than 2 mg catalyst had to be weighed, a solution of the catalyst in nitrobenzene was prepared instead, and a known volume of the solution was added, in order to avoid large errors in weighing very small amounts of catalyst. The liner was placed inside a Schlenk tube with a wide mouth under dinitrogen and was frozen at -78 °C with dry ice, evacuated and filled with dinitrogen, after which the solvent was added. After the solvent was also frozen, the liner was closed with a screw cap having a glass wool-filled open mouth which allows gaseous reagents to exchange and rapidly transferred to a 200-mL stainless steel autoclave with magnetic stirring. The autoclave was then evacuated and filled with dinitrogen three times. CO was then charged at room temperature at the required pressure and the autoclave was immersed in an oil bath preheated at the required temperature;

the autoclave took about 15 min to fully equilibrate at the final temperature. Other experimental conditions are reported in the captions to the tables and figures. At the end of the reaction the autoclave was cooled with an ice bath, vented and the products were analyzed by gas chromatography (Dani 8620 gas chromatograph, equipped with a PS 255 column; naphthalene as an internal standard).

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References and Notes

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