Synthesis of Functionalized Carbamates through a Palladium-Catalyzed Reductive Carbonylation of Substituted Nitrobenzenes

Petra Wehman, Leo Borst, Paul C. J. Kamer, and Piet W. N. M. van Leeuwen*

Van't Hoff Research Institute, Department of Inorganic Chemistry, University of Amsterdam,
Nieuwe Achtergracht 166, NL-1018 WV Amsterdam, The Netherlands

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The palladium-catalyzed reductive carbonylation of *ortho* and *para*-substituted nitrobenzenes has proven to be an attractive route for the synthesis of functionalized carbamates. For the Pd(1,10-phenanthroline)$_2$(triflate)$_2$ catalyst system, the scope of the reaction has been studied. Substrates with electron-donating substituents at the *para* position were found to decrease the catalytic activity, most probably as a result of their relatively low oxidizing capacity. The selectivity towards the desired carbamate, however, was increased for these substrates. Under the influence of electron-withdrawing substituents the azoxybenzene and azobenzene derivatives became important side products. Introduction of large steric hindrance at the *ortho* position of the nitro substrates gave rise to an interesting side reaction, viz. methoxylation of the aromatic ring. The methoxylation reaction appeared to occur on an intermediate species in the catalytic cycle. Several functionalities have shown to be resistant to the reaction conditions required for the conversion of the nitro group. Especially with 4-nitrobenzoic acid, an extremely high activity and selectivity was found, thus yielding a very convenient synthesis for *N*-protected amines containing carboxylic acid functions.

Introduction

Industrially important materials like polyurethane foams and adhesives are often obtained from isocyanates. Carbamates are mostly applied in the pharmaceutical industry and as agrochemicals. The carbamate function is also widely applied as protective group for an amino function, e.g. in peptide and protein syntheses. Traditionally these products are prepared from amines obtained from nitro compounds through catalytic hydrogenation. Subsequent reaction with phosgene yields the isocyanates, which can react with an alcohol to afford the corresponding carbamates. In small scale organic syntheses the carbamate is often prepared through a reaction of the amine with methyl chloroformate[1-4].

The use of the extremely toxic phosgene and the production of HCl as side product, however, form two major disadvantages to this traditional process. Therefore research is conducted on alternative routes such as the reductive carbonylation of aromatic nitro compounds for the production of aromatic isocyanates and carbamates. In this process the nitro function is reacted directly with CO under the influence of a catalyst. When the reaction is performed in an alcohol a carbamate is obtained as major product. Thermal degradation of the carbamate yields the isocyanate (Scheme 1). A milder procedure for the dealcoholysis of the carbamate is provided by the use of chlorocatecholborane in the presence of triethylamine as a base[5].

Ever since 1962 research has been carried out on catalysts required for the reaction between the nitro function and CO. Although a lot of work has been done on the use of sulfur, selenium, or tellurium[6], attention recently has shifted to the use of group 8−10 metals. Catalyst systems based on ruthenium are often applied, especially in mechanistic studies[7]. The use of palladium as the active metal center, however, has proven to yield more active and selective catalyst systems[8,9]. This metal was first applied in a heterogeneous system with ferric chloride as cocatalyst[10]. It was soon discovered that the addition of a bidentate nitrogen-donor ligand strongly improved the catalytic activity and selectivity. In 1983 a homogeneous catalyst system consisting of palladium and a bidentate nitrogen, phosphorus, arsenic, or antimony ligand for the reductive carbonylation of aromatic nitro compounds was patented[6]. Best results until now have been obtained with palladium complexes containing rigid phenanthroline ligands, which bear mildly electron-donating substituents in the ligands and noncoordinating anions. Previous work has shown the existence of a subtle balance between various phenanthroline ligands and noncoordinating anions in the catalyst performance in the reductive carbonylation of nitrobenzene[11]. From this work we have chosen Pd(phen)$_2$(OTf)$_2$ with 4 equivalents of 1,10-phenanthroline as a stable, active, and fairly selective catalyst system to study the scope of the reaction. Although Hardy and Bennett already subjected several substituted nitroarenes to their Pd/C catalyst system[10] no systematic study of the scope of the reaction has ever been reported. Alper et al. have tried their Pd(dppp)Cl$_2$/K$_2$CO$_3$ catalyst system on a small series of six substituted nitro compounds. No attempts were made to tune the reaction conditions in such a way that the influence of the substrates on the catalytic activity could be compared; they did find that the presence of an *ortho*-methyl substituent strongly hampers the formation of the desired carbamate[12].

We set out to explore the scope of the catalytic conversion of nitro compounds into carbamates in organic synthesis. A study on the influence of various substituents on

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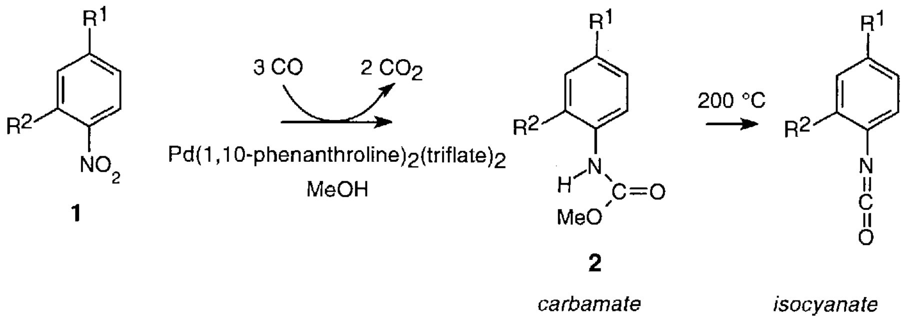
Scheme 1. Reductive carbonylation of substituted nitrobenzenes



	R^1	R^2
a	H	H
b	CF_3	H
c	CH_3	H
d	OCH_3	H
e	$N(CH_3)_2$	H
f	Cl	H
g	Br	H
h	H	Cl
i	H	CF_3
j	H	C_6H_5

	R^1	R^2
k	H	CH_3
l	H	CH_3O
m	H	i-C_3H_7
n	H	t-C_4H_9
o	CN	H
p	$C(O)CH_3$	H
q	$COOC_2H_5$	H
r	OH	H
s	COOH	H

an aromatic nitro substrate on the catalytic activity and selectivity of the $Pd(phen)_2(OTf)_2$/phen catalyst system will be reported here. Attention has been paid to the influence of electronic properties as well as of steric properties of the substrate. The resistance of several additional functional groups on the nitro substrate towards the reaction conditions also has been considered. The formation of an interesting class of (side) products in which methoxy substituents are introduced at the aryl rings during the carbonylation reaction has been studied in more detail. The accelerating effect of aniline in the reaction mixture is also considered in this study.

Results and Discussion

The various nitro substrates (**1**) have all been tested in the reductive carbonylation reaction under the influence of the $Pd(phen)_2(OTf)_2$/phen catalyst system (Scheme 1).

As all tests were performed in methanol, the corresponding methyl *N*-arylcarbamates (**2**) were always the desired products. Besides these carbamates, the corresponding urea derivatives (**3**), anilines (**4**), and azoxybenzenes (**5**) could be expected as side products under the influence of this catalyst system[11]. GC-MS measurements enabled us to qualitatively analyse the reaction products. Although the urea derivatives are thermally unstable and decompose on the GC they could be detected by their decomposition products: the anilines and isocyanates. These decomposition products always appeared together, either at exactly the same retention time or very close to one another, while the highest response was observed mostly for the isocyanate fragment. Only in a few cases could the urea derivative (**2**) be observed intact.

Apart from the common products, unexpected side products were also detected. Some of the *para*-substituted substrates yielded the corresponding azobenzene (**6**) derivative to some extent. Azobenzene had been observed before as a product in the palladium catalyzed reductive carbonylation of nitrobenzene, especially for supported Pd/C systems[8,13], but it had not been found for the $Pd(phen)_2(OTf)_2$ catalyst[11]. Other substrates, especially the *ortho*-substituted ones, gave rise to a class of side products that is even more surprising under the mild conditions used in these experiments (135°C, 60 bar CO). These side products consist of methoxy-substituted aryl carbamates (**7**) and urea derivatives (**8**, **9**). These kind of side products were detected previously in the reductive carbonylation of nitrobenzene under the influence of various Pd/4,4'-disubstituted-2,2'-bipyridine catalyst systems. However, they could only be found under more severe reaction conditions, namely at a relatively high ratio of acidic cocatalyst (*p*-toluene-sulfonic acid) to Pd or at prolonged reaction time[14]. Furthermore, a new type of side products that contains an imine function was detected for substrates **1a**, **1d**, and **1e**. These imine products, $ArN{=}CH_2$, are probably the result of a reaction between the corresponding anilines and formaldehyde, that is formed by dehydrogenation of methanol as described earlier[9,14].

The products and important side-products of the catalytic reaction were identified by comparison of analytical data with those of authentic materials[14]. On the basis of the qualitative GC-MS measurements, the reaction mixtures could be analyzed quantitatively by means of ^1H NMR since the signals of the various products were well resolved. Due to the high stability of the $Pd(phen)_2(OTf)_2$ catalyst system, the experiments were highly reproducible. Average values are presented in Table 1, 3, and 5 (see the Experimental Section for details).

Influence of Electronic Properties of the Substrate

The influence of the electronic properties of the substrate on the catalytic activity and selectivity was studied by introduction of electron-withdrawing or electron-donating substituents at the *para*-position of nitrobenzene. The donating capacity of the substituents increases in the order $F_3C < H < Me < MeO < Me_2N$. The results for the catalytic conversion of these substrates are summarized in Table 1.

Table 1. Results of the reductive carbonylation of various *para*-substituted aromatic nitro substrates with $Pd(phen)_2(OTf)_2/phen$[a]

substrate	t.o.f. (mol/mol/h)	product distribution (%)^b CA	UR	AN	AZ	AZOX
1a	234	84	7	3	0	7
1b	241	59	trace	2	6	33
1c	226	86	14	trace	0	0
1d	58	100	0	0	0	0
1e	37	100	0	0	0	0
nitrocyclohexane	0	-	-	-	-	-
α-nitrotoluene	0	-	-	-	-	-
nitrosobenzene	≥365	5	2	-	22	72

[a] See Experimental Section for the reaction conditions and analysis. – [b] CA = methyl *N*-arylcarbamate; UR = *N,N'*-diarylurea; AN = aniline derivative; AZ = azobenzene derivative; AZOX = azoxybenzene derivative.

In addition to the substrates listed, 4-chloronitrobenzene (**1f**) and 4-bromonitrobenzene (**1g**) were also tried because the chloride and bromide substituents are less powerful electron-withdrawing substituents than the trifluoromethyl group. The conversion of these substrates was strongly hampered, however, by the low solubility of the substrates as well as their products, resulting in a heterogeneous reaction mixture. Therefore the turnover frequencies (t.o.f.) of 153 and 168 mol/mol/h found for **1f** and **1g**, respectively, cannot be compared to those of the soluble substrates of Table 1. For both substrates a selectivity towards the corresponding carbamates of approximately 55% was found, while the side products consisted mainly of the azoxybenzene derivatives, together with small amounts of azobenzene, urea, and aniline derivatives.

All other *para*-substituted aromatic nitro substrates used are readily soluble in methanol, so reliable activities and selectivities could be measured. From the turnover frequencies listed in Table 1 it can be seen that the catalytic activity is reduced going from electron-withdrawing to electron-donating substituents on the substrate. Especially the strongly donating methoxy and dimethylamino functions cause a sharp decrease in catalytic activity, while the activity is only slightly enhanced by the highly electron-withdrawing trifluoromethyl substituent. A similar trend can be observed in the N–O bond strength of the nitro group under the influence of the *para*-substituents. The wavenumbers for the symmetric and asymmetric N–O vibrations are a good measure for the N–O bond strength. These data are given in Table 2.

Table 2. N–O vibrations[a] and half-wave potentials[b] of various *para*-substituted aromatic nitro compounds

compound	ν_{sym} (cm^{-1})	ν_{asym} (cm^{-1})	$E_{1/2}$ (V)
1a	1349^c	1259^c	-0.81
1b	1357	1536	-0.66
1c	1346	1517	-0.82
1d	1333	1499	-0.85
1e	1311	1486	-0.91

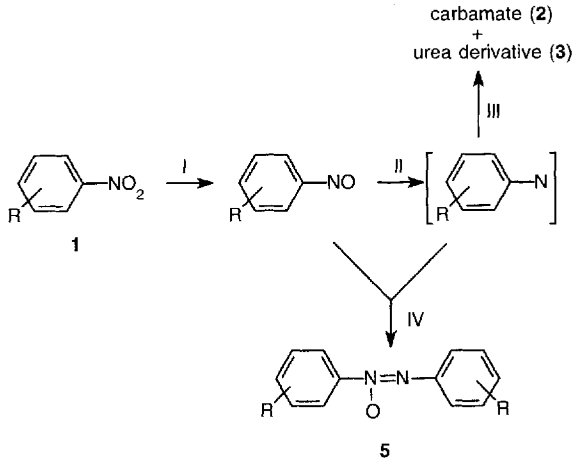
[a] IR spectra were in principal recorded in KBr. – [b] $E_{1/2}$ (V) vs. Ag/AgCl. – [c] Data recorded in a fluorolube mull.

The N–O bond strength decreases if the electron-donating capacity of the *para*-substituents increases; the lowest activity is reached for the substrate with the weakest N–O bond. This indicates that the rate determining step under the influence of the $Pd(phen)_2(OTf)_2$ catalyst system probably is not a transfer reaction of an oxygen atom from the nitro function to a coordinated CO molecule[15], because this would imply an increase in the overall activity with an increasing nucleophilicity of the oxygen atom. These is no correlation between the *nucleophilicity* of the oxygen atom and the catalytic activity.

We propose that the *oxidizing capacity* of the substrate is responsible for the differences in catalytic activity. To determine the relative oxidizing capacities of the substrates they were electrochemically reduced, and the measured half-wave potentials are listed in Table 2. In good agreement with the electron-withdrawing and electron-donating effects of the substituents, the reactivity of the nitro group in redox reactions increases in the order $F_3C > H > Me > MeO > Me_2N$. As the catalytic activity decreases in the order $F_3C > H > Me > MeO > Me_2N$, this might imply that the substrate is needed for the reoxidation of Pd^0 to Pd^{II} at some stage in the catalytic cycle. Such a substrate-assisted reoxidation might also explain the increasing amount of Pd black formed under the influence of an increasing donating capacity of the substituent on the substrate. Especially in the conversion of **1e**, a large amount of Pd black is found at the end of the catalytic runs, whereas **1a** and **1b** yield no Pd black at all. Apparently $E_{1/2}$ must be above a certain value, as can be seen from the large difference in catalytic activity for **1d** (t.o.f. = 58 mol/mol/h) and **1e** (t.o.f. = 37) compared to unsubstituted **1a** (t.o.f. = 234). Above this minimum level further increase of the oxidizing capacity only leads to a negligible enhancement of the activity (t.o.f. = 241 mol/mol/h) for **1b**. This apparent importance of the oxidizing properties of the substrate might also be the reason why the reductive carbonylation of nitrocyclohexane using the $Pd(phen)_2(OTf)_2$ catalyst completely failed under the conditions used for the aromatic nitro substrates. Aliphatic nitro compounds are known to be far less powerful oxidizing agents than their aromatic counterparts; e.g., nitromethane has a $E_{1/2}$ of -0.87 V (vs. S.C.E., at pH = 6) compared to an $E_{1/2}$ of -0.54 V (vs. S.C.E., pH = 6) for nitrobenzene[16]. Even a benzylic substrate as α-nitrotoluene showed no conversion at all.

While the activity decreases, the reaction becomes more and more selective towards the carbamate under the influence of electron-donating substituents on the substrate. Especially unreactive substrates like **1e** give 100% selectivity. Under the influence of the highly electron-withdrawing trifluoromethyl substituent, on the other hand, the selectivity towards the carbamate is lowered. For this substrate the corresponding azoxybenzene becomes an important side product. If nitrosobenzene is used as the substrate instead of nitrobenzene, azoxybenzene even becomes the major product. This substrate is completely converted within 2 h of standard reaction time, resulting in a turnover frequency larger than 365 mol/mol/h. The selectivity towards the carbamate, however, is only 5%; 70% of the product mixture consists of azoxybenzene besides 22% of azobenzene and 2% of *N*,*N'*-diphenylurea. The formation of azoxybenzene is probably favoured by the high concentration of free nitrosobenzene, which could very well react with a Pd-imido like intermediate[17,18]. In view of these results, **1b** might also react more like a nitroso substrate, probably because it is so easily reduced, which results in a relatively high concentration of the nitrosobenzene derivative. Comparable behaviour was also observed for the **1f** and **1g**, which are also better oxidizing agents than **1a** ($E_{1/2}$ for **1f** = −0.73 V, $E_{1/2}$ for **1g** = −0.72 V). These results could be explained with the simplified reaction sequence of Scheme 2, which depicts a two-step reduction of the nitro substrate to a "nitrene" intermediate through a nitroso species (Steps I and II).

Scheme 2. Simplified reaction sequence for the reductive carbonylation of aromatic nitro compounds



The nitroso intermediate could in principle exist as a free compound in solution, though it could also be coordinated to the palladium metal center as several palladium-nitrosobenzene complexes are known[19,20]. The subsequently formed "nitrene" intermediate is far too reactive to exist as a free nitrene[21] and therefore has to be coordinated to palladium to be stabilized as an imido type species. From this imido intermediate, the desired carbamate is then formed in step III through a reaction with CO and methanol.

Under the influence of a nitro substrate with a high oxidizing capacity, a fast reaction is assumed for step I, while the reaction in step II is slower but still relatively fast compared to the slow reaction of step III. The thus accumulating imido intermediate could then react with the nitroso intermediate, which would also be present in high concentration, yielding the azoxybenzene derivative in step IV. For the substrates with the electron-donating substituents, step I already will proceed much more slowly; furthermore the reaction rate of step II should be more in the range of the rate of step III. As a result of the comparable rates for the steps I–III no accumulation of the nitroso and imido intermediates takes place. This promotes the reaction between the imido intermediate and the abundant CO and methanol to form the desired carbamate instead of the reaction of step IV yielding the azoxybenzene derivative.

Influence of Steric Properties of the Substrate

The influence of the steric properties of the substrate on the activity and selectivity of the $Pd(phen)_2(OTf)_2$ catalyst was studied by introduction of substituents with increasing bulkiness at the *ortho* position of nitrobenzene. Both electron-withdrawing and electron-donating substituents were used to be able to distinguish between steric demands and electronic properties. For the electron-withdrawing substituents the effects of steric hindrance were only studied for the conversion of the nitrobenzenes with the 2-chloro (**1h**) and 2-trifluoromethyl substituent (**1i**); whereas the range of electron-donating bulky substituents was somewhat larger, comprising methyl (**1k**), methoxy (**1l**), isopropyl (**1m**), and *tert*-butyl (**1n**) substituents. A phenyl substituent (**1j**) was applied as an electronically more or less neutral, bulky substituent. All substrates were readily soluble in methanol and the results are collected in Table 3.

Table 3. Results of the reductive carbonylation of various *ortho*-substituted aromatic nitro substrates with $Pd(phen)_2(OTf)_2$/phen[a]

substrate	t.o.f. (mol/mol/h)	product distribution (%)[b]				
		CA	UR	AN	MeO-CA	MeO-UR
1h	186	84	trace	16	0	0
1i	47	46	trace	54	0	0
1j	223	76	7	10	7	trace
1k	199	42	7	7	15	trace
1l	69	55	13	10	22	trace
1m	197	31	2	16	9	2
1n	197	13	0	28	41	7

[a] See Experimental Section for the reaction conditions and analysis. – [b] CA = methyl *N*-arylcarbamate; UR = *N*,*N'*-diarylurea; AN = aniline derivative; MeO-CA = methyl *N*-(methoxyaryl)carbamate; MeO-UR = *N*,*N'*-di(methoxyaryl)urea.

Additionally, the reductive carbonylation of nitromesitylene was tried inorder to use a substrate that affords steric hindrance at both *ortho* positions with respect to the nitro function. Such a large steric bulk proved to completely deactivate the catalyst system as was concluded from the formation of a large amount of Pd black.

The *ortho*-substituted nitro substrates are less powerful oxidizing agents than their *para*-substituted analogues. For example the half-wave potential of **1b** is −0.66 V compared to −0.76 V for **1i**. The more negative values for the half-wave potentials under the influence of the ortho substituents point to steric inhibition of the conjugation of the nitro

Table 4. Half-wave potentials of various ortho-substituted aromatic nitro substrates[a]

compound	$E_{1/2}$ (V)
1h	-0.78
1i	-0.76
1k	-0.88
1l	-0.86

[a] $E_{1/2}$ (V) vs. Ag/AgCl.

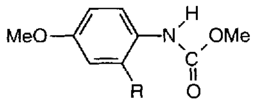
function with the aromatic ring. As a result the nitro group behaves more like an isolated or aliphatic nitro group, yielding a lower oxidizing capacity[16]. This explains that the oxidizing capacities of the substrates studied are in a narrow range. The half-wave potentials in Table 4 only vary from −0.76 to −0.8 V. A relatively small steric demand causes, therefore, a significant decrease in catalytic activity.

Comparison of the turnover frequency and selectivity obtained for **1j** (223 mol/mol/h) with the one for **1a** (234 mol/mol/h) shows that the phenyl substituent causes only little steric hindrance. This is probably due to the relative orientation of the two aryl rings in wich the phenyl substituent is almost perpendicular to the nitrophenyl plane. For the other mono *ortho*-substituted substrates, the effects on the catalytic activity and selectivity are much larger. It is evident that the influences of the ortho substituent are a combination of steric and electronic effects. Since the largest ortho substituents, namely isopropyl (**1m**) and *tert*-butyl (**1n**) still show relatively high turnover frequencies, the steric effects on the activity seem rather small. The exceptionally low t.o.f. found for the CF_3 group (**1i**) must be mainly a steric effect; the expected accelerating effect of the strongly electron withdrawing CF_3 group is not observed. The selectivity is much more influenced by the steric bulk and seems to decrease with increasing steric hindrance. Again the relation is not straightforward, which is probably a consequence of additional electronic effects.

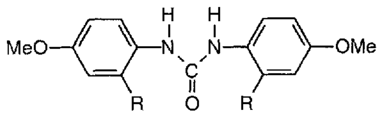
The very bulky electron donating substituents [isopropyl (**1m**) and *tert*-butyl (**1n**)] as well as the methoxy substituent (**1l**) give rise to the rapid formation of carbamates and urea derivatives with supplementary methoxy substituents on the aryl rings in addition to some other unidentified side products. The methoxy-substituted carbamate even forms the main product in the conversion of **1n**. Due to the relatively high amounts of these substituted carbamates and urea derivatives formed with these substrates we were able to separate them by means of crystallization or column chromatography. This way the exact substitution patterns could be established by ^1H NMR (Scheme 3).

The methoxy substituents were always found to be placed at the C(4) atoms of the aryl rings, which is in good agreement with the substitution patterns of these side products we found before in the reductive carbonylation of nitrobenzene under more severe reaction conditions[14]. Separation of the reaction mixture of **1n** showed the presence of methyl *N*-(2-*tert*-butyl-4-methoxy-phenyl)carbamate (**7n**) and *N,N'*-di(2-*tert*-butyl-4-methoxyphenyl)urea (**9n**) besides the carbamate (**2n**) and aniline (**4n**) products without the additional methoxy substituent. Furthermore, the formation of the methoxy substituted aniline (**10n**) in addition to the plain 2-*tert*-butylaniline (**4n**) was revealed upon separation of the mixture by means of column chromatography. No *N,N'*-di(2-*tert*-butylphenyl)urea (**3n**) could be detected, either by ^1H NMR or by GC-MS. Apparently the very bulky *tert*-butyl substituent strongly hinders the reaction that should yield the urea derivative between the aniline and isocyanate fragments. The formation of *N,N'*-di(2-*tert*-butyl-4-methoxyphenyl)urea (**9n**) is probably the result of the enhanced nucleophilicity of the amino group under the influence of the additional methoxy substituent. Separation and analysis of the reaction mixture of **1m** indicated the additional presence of the unsubstituted urea derivative (**3m**) and a nonsymmetric side product, which was probably *N*-(2-isopropylphenyl)-*N'*-(2-isopropyl-4-methoxyphenyl)-urea (**8m**).

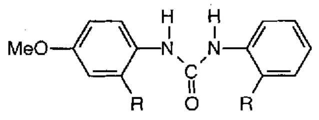
Scheme 3. Methoxy substituted side products in the reductive carbonylation of 2-(*iso*-propyl)nitrobenzene and 2-(*tert*-butyl)nitrobenzene



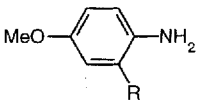
Carbamate (**7**): R = *i*-Pr, *t*-Bu.



Symmetric urea (**9**): R = *i*-Pr, *t*-Bu.



Nonsymmetric urea (**8**): R = *i*-Pr.



Aniline (**10**): R = *t*-Bu.

In the case of the substrate with the less bulky methyl substituent (**1k**) at the *ortho* position, much smaller amounts of the methoxy substituted carbamate and urea derivatives were formed.

As for the azobenzene and azoxybenzene derivatives it can be said that only traces could be detected in the conversion of 2-(trifluoromethyl)nitrobenzene, whereas these side products were found to become increasingly important under the influence of electron-withdrawing substituents at the *para* position (Table 1).

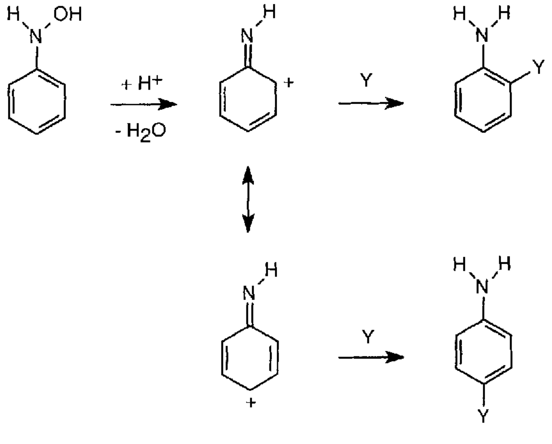
Methoxy-Substituted Side Products

Introduction of methoxy substituents without the use of halides or other good leaving groups is very attractive. Therefore this side reaction was studied in more detail. Regardless of the catalyst system and conditions used, no methoxy substituents were ever found on the aromatic nitro substrate despite the fact that a *para*-methoxy substituent has shown to hamper the catalytic conversion. Therefore, a normal nucleophilic aromatic substitution can be ruled out since under the influence of the strongly electron-withdrawing nitro function, the nitro substrate would be expected to be most prone to this kind of substitution reaction.

Experiments in which methyl *N*-phenylcarbamate (**2a**) was applied as substrate with a $Pd(OAc)_2$/bpy/*p*-toluenesulfonic acid (*p*-tsa) catalyst system at high *p*-tsa:Pd ratio showed that no reaction at all occurs starting from the carbamate. This means that the methoxy substituents are introduced neither at the nitro substrate nor at the carbamate product but at some intermediate stage in the catalytic cycle. Use of *N,N'*-diphenylurea (**3a**) as a substrate did result, however, in traces of some methoxy-substituted products. The use of aniline as substrate and $Pd(phen)_2(OTf)_2$/phen as catalyst did result in a conversion of 17% into the methoxy-substituted products. Besides these methoxy-substituted products, the regular products **2a** and **3a** were also produced. A large amount of Pd black was formed as well. Nitrobenzene yielded no methoxy-substituted products under these conditions, thus indicating that an aniline type of intermediate plays an important role in the formation of the methoxy-substituted products.

We explored whether the aniline type of intermediate reacts in a rearrangement reaction similar to the one described by Ingold for *N*-phenylhydroxylamine[22]. An acid-catalyzed nucleophilic rearrangement of *N*-phenylhydroxylamine results in aniline bearing a hydroxyl or other nucleophilic substituent at its *ortho* or *para* positions (Scheme 4)[22].

Scheme 4. Acid-catalyzed nucleophilic rearrangement of *N*-phenylhydroxylamine according to Ingold[22]



(Y = OH, OMe etc.)

Experiments under catalytic conditions (60 bar of CO, 135 °C) with *N*-phenylhydroxylamine as the substrate under the influence of the $Pd(OAc)_2$/bpy/*p*-tsa catalyst system, however, did show formation of the methoxy substituted carbamate and aniline next to the normal catalysis products, but the amount of substituted products was not increased with respect to the amount formed from nitrobenzene. Apparently, the crucial steps in the formation of the methoxy substituted carbamates, anilines, and urea derivatives do not proceed through hydroxylamines.

The Effect of Aniline

To improve the stability of the $Pd(phen)_2(OTf)_2$ catalyst system using aniline as a substrate, nitrobenzene was added to the reaction mixture. The absence of Pd black at the end of the catalytic run proved that the catalyst was indeed stabilized by nitrobenzene. The amount of methoxy substituted products was enlarged as the conversion into these products increased from 17 to 26%. Surprisingly, the overall activity of the catalyst system had also improved. Aniline had been converted into carbamate and urea derivative with a turnover frequency of 38 mol/mol/h. If the methoxy substituted (side) products are taken into account this value increases to 98 mol/mol/h. Under exactly the same conditions, nitrobenzene gave a turnover frequency of 267 mol/mol/h. The mixture of aniline and nitrobenzene in a 1-to-1 molar ratio, however, resulted in an overall t.o.f. of 422 mol/mol/h based on the conversion into carbamate, urea derivative, and azoxybenzene. If the methoxy substituted (side) products are again taken into account, the t.o.f. of the mixture amounts to 622 mol/mol/h. Obviously a large increase in catalytic activity for the conversion of nitrobenzene is caused by the presence of aniline.

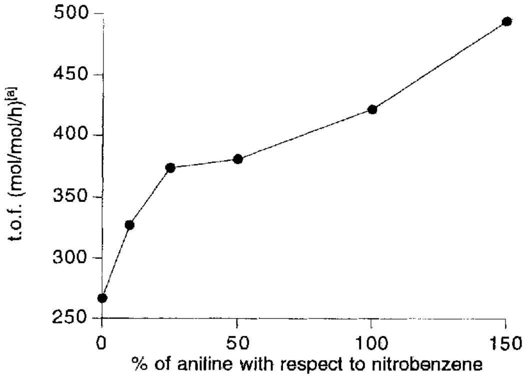
To study this effect, a series of experiments was conducted in which the amount of aniline with respect to the amount of nitrobenzene was gradually increased. The amount of nitrobenzene was kept constant at 14.6 mmol so that the total amount of substrate increased from 14.6 to 36.5 mmol. The results are depicted in Figure 1.

The turnover frequencies used in Figure 1 are based on the total conversion of nitrobenzene and aniline. The methoxy substituted side products have not been taken into account. Above 25% of aniline with respect to nitrobenzene, however, significant amounts of these products could be observed by HPLC. As a result, the steep increase in the catalytic activity shown in Figure 1 appears to flatten above the level of 25% of aniline due to the enhanced importance of the methoxy-substituted side products.

Nitro Substrates Containing a Second Functional Group

Since carbamates are useful protective groups for amines in organic syntheses[3], we tried a series of nitro substrates containing a more reactive functional group as the last part

Figure 1. The influence of the addition of aniline on the catalytic activity (t.o.f.)



[a] The t.o.f. value (mol/mol/h) is based on the conversion of aniline and nitrobenzene into methyl *N*-phenylcarbamate, *N,N'*-diphenylurea, and azoxybenzene.

of our study on the scope of the palladium catalyzed reductive carbonylation of aromatic nitro substrates. Both the stability of these additional specific groups under the reaction conditions as well as their influence on the catalytic activity and selectivity was studied. All specific groups were introduced at the *para* position of nitrobenzene in order to avoid any steric effects. Substrates containing either a cyano (**1o**), ketone (**1p**), ester (**1q**), alcohol (**1r**), or carboxylic acid (**1s**) function yield at least partly the desired carbamate and usually some of the known side products. The results of these substrates are listed in Table 5.

Table 5. Results of the reductive carbonylation of various aromatic nitro substrates containing a second functional group with Pd(phen)$_2$(OTf)$_2$/phen[a]

substrate	t.o.f. (mol/mol/h)	product distribution (%)[b] CA	UR	AN	AZ
1o	117	31	0	13	57[c]
1p	≥365	55	d	14	16
1q	157	65	0	7	0
1r	157	100	0	0	0
1s	≥365	94	0	2	0

[a] See Experimental section for the reaction conditions and analysis. – [b] CA = methyl *N*-arylcarbamate; UR = *N,N'*-diarylurea; AN = aniline derivative; AZ = azobenzene derivative. – [c] Sum of the azobenzene and the azoxybenzene derivative. – [d] Not measurable by ^{1}H NMR.

GC-MS measurements have shown that the cyano group is resistant towards the reaction conditions required for the reductive carbonylation. The ketone function also appeared to be resistant to the reaction conditions used, although 15% of the products formed could not be identified. The urea derivative probably forms part of this remaining 15% as the GC-MS measurements show both the isocyanate and the aniline fragments. The overall activity reached under the influence of the ketone substituent was very high (t.o.f. >365 mol/mol/h). This high activity can be partly ascribed to the strong oxidizing capacity of the **1p** substrate, which shows its first reduction wave at −0.63 V.

This positive effect on the catalytic activity does not occur for an ethyl ester substituent (**1q**). Though the selectivity towards the corresponding carbamate was slightly enhanced compared to the conversion of **1p**, still a considerable amount of the products remained unidentified. The activity reached in the conversion of **1r** equalled the activity found for **1q**. The selectivity under the influence of the phenolic function, however, was far better. The corresponding carbamate was formed exclusively; no other products could be detected by GC-MS or ^{1}H NMR, resulting in a simple one-pot procedure for *N*-protected hydroxyanilines.

This simple synthesis was extended to a substrate containing a carboxylic acid function. Other routes to convert such a substrate to its corresponding carbamate are far more laborious and not suitable for large scale preparations. The reductive carbonylation of 4-nitrobenzoic acid (**1s**), however, proceeded with a remarkably high activity. Complete conversion of the substrate was reached within 2 h, which is in contrast with the relatively low oxidizing capacity of this substrate ($E_{1/2} = -0.75$). In addition to this high activity, an excellent selectivity is found (94% towards the corresponding carbamate **2s**). In this manner, protected anilines containing free acid functions became easily accessible by a one-pot procedure under mild conditions. These surprising results are apparently caused by the acidic function. This supposition is confirmed by the results of addition of (benzoic) acids as cocatalyst in the reductive carbonylation of nitrobenzene (t.o.f. ≥365 mol/mol/h with selectivities towards methyl *N*-phenylcarbamate of 93–94%)[23]. Though the addition of 2,4,6-trimethylbenzoic acid has been used before in order to enhance the activity and selectivity in the palladium catalyzed reductive carbonylation of nitrobenzene[8,9,24] its effects were never found to be as profound as with the Pd(phen)$_2$(OTf)$_2$ catalyst system.

Besides the substrates mentioned in Table 5, 4-nitrobenzaldehyde and 4-nitrobenzyl chloride were also tried but none of the usual (side) products were formed. Mixtures of unidentifable or insoluble products were obtained.

Conclusion

From the study on the effects of the electronic properties of the substrate on the catalytic activity and selectivity it became clear that the activity is reduced under the influence of electron-donating substituents at the substrate, due to a decrease in the oxidizing capacity of the substrate. The selectivity toward the carbamate, on the other hand, is increased with electron-donating substituents. Under the influence of electron-withdrawing substituents the azoxybenzene and azobenzene derivatives become important side products as a result a rapid formation of the nitroso intermediate.

Under the influence of *iso*-propyl and *tert*-butyl substituents at the *ortho* position large amounts of an interesting class of side products are formed in which methoxylation at the aryl rings of the carbamates, urea derivatives, and anilines takes place.

The cyano, ketone, ester, alcohol, and acid function have shown to be resistant to the reaction conditions needed for the reductive carbonylation of the nitro group. Especially for 4-nitrobenzoic acid a remarkably high activity and selectivity was found. Reductive carbonylation thus affords a convenient synthesis of *N*-protected amine compounds containing a carboxylic acid function.

The palladium-catalyzed reductive carbonylation of aromatic nitro compounds has thus proven to be an attractive procedure for the preparation of various functionalized carbamates.

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Experimental Section

Materials and Methods: $PdCl_2$ was purchased from Degussa and used as received. All other chemicals were purchased from Aldrich or Janssen. CO 3.0 was purchased from Praxair and used as purchased. – Most of the nitro substrates were used in the catalysis experiments without further purification, except for 4-(trifluoromethyl)nitrobenzene and nitrosobenzene, which were distilled in vacuo and sublimated, respectively. The solvents were purified prior to use. Acetone was distilled from anhydrous K_2CO_3, methanol and acetonitrile from CaH_2 (5 g/l). – The Pd(1,10-phenanthroline)$_2$-$(OTf)_2$ catalyst complex was prepared from freshly synthesized $Pd(CH_3CN)_4(OTf)_2$, as was described previously[11]. – Nitromesitylene was prepared according to a literature procedure[25]. The product was purified, however, by means of a vacuum distillation (b.p. 93 °C, 4 mm Hg) instead of the prescribed steam distillation. A modified literature procedure[26] was used for the synthesis of 2-*tert*-butylnitrobenzene and 2-isopropylnitrobenzene. The synthesis of 4-(*N,N*-dimethylamino)nitrobenzene was based on a procedure by Ullmann for the synthesis of similar compounds[27]. – *N*-phenylhydroxylamine was prepared according to a literature procedure[28]. – Column chromatography was performed using silica gel (Kieselgel 60, 70–230 – mesh ASTM, purchased from Merck) as the stationary phase. – Infrared (IR) spectra were recorded on a Nicolet 510 m FT-IR spectrophotometer. ^1H-NMR spectra were obtained on a Bruker AMX 300 instrument. Chemical shifts are given in ppm. TMS was used as reference with $CDCl_3$ as internal standard. GC-MS was measured on a Hewlett-Packard GC, equipped with a 25 m capillary Ultra-2 column and a 5971 mass selective detector. Electron Impact (EI) mass spectrometry was carried out using a JEOL JMS SX/SX102A four-sector mass spectrometer, coupled to a JEOL MS-MP7000 data system. High resolution EIMS measurements of the catalytic reaction products were performed on the crude reaction mixtures. The samples were introduced via the direct insertion probe into the ion source. During the high resolution EIMS measurements a resolving power of 10000 (10% valley definition) was used. – Polarographic experiments were performed with a 626 Polarecord Metrohm, using a three-electrode system (Hg, Ag/AgCl, C). The half-wave potentials of the various nitro compounds were measured in methanol solutions, containing $10^{\ 4}$ M of the nitro compound and 0.05 M of $LiClO_4$ as the supporting electrolyte. – The reductive carbonylation of the nitro substrates to study the scope of the reaction was performed in a stainless steel (SS 316) 50 ml autoclave, equipped with a glass liner, a gas inlet, a thermocouple, and a magnetic stirrer. The results were analyzed by GC-MS (acetone) and ^1H NMR ([D$_6$]DMSO). The products were characterised by comparison of ^1H-NMR and mass spectral results with data for authentic materials[14]. Prior to the quantitative analysis by ^1H NMR, the methanol had to be evaporated at room temperature to avoid thermal decomposition of the urea derivatives. – Separate experiments validated the quantitative analysis of the reaction mixtures. The deviation of the ratios between the various products and the substrate measured by – ^1H NMR from the ratios as these were weighted in did not exceed 6%. The error introduced by the NMR apparatus if 2 samples of the same reaction mixture were measured amounted to only 0.4%. – The scatter between the experiments in duplicate for the conversion into the various products was always found within 3%, yielding a standard deviation of 0.5–1.5. – The average turnover frequencies (mol/mol/h) could be used to compare the activity of the Pd(phen)$_2$ $(OTf)_2$ catalyst with respect to the conversion of the various nitro substrates, because it was found that the reductive carbonylation of nitrobenzene is approximately zero order in substrate concentration[11]. The selectivity of the catalyst system could be expressed in a product distribution, in which the presence of small amounts of side products that only appeared in the GC-MS measurements was marked as trace. – The experiments concerning the methoxy substituted side products as well as those on the accelerating effect of aniline were conducted in a stainless steel (SS 316) 100 ml autoclave, equipped with a glass liner, a gas inlet, a thermocouple, a cooling coil, and a magnetic stirrer. The results were analysed by HPLC on a Gilson HPLC apparatus, using a Dynamax C18 column (eluent gradient: 45% water in methanol to 100% methanol in 20 minutes).

Synthesis

2-tert-Butylnitrobenzene (**1n**): A mixture of 415 ml of concentrated HNO_3 (6.46 mol) and 700 ml of concentrated H_2SO_4 was added slowly to 1000 ml of *tert*-butylbenzene (6.46 mol). During the addition the reaction mixture was cooled on an ice bath, in order to keep the temperature in the range of 20–30 °C. After complete addition of the nitrating mixture the reaction mixture was stirred at 45 °C for 1 h, after which the organic layer was separated from the water layer. The organic fraction was washed with 3 × 75 ml of 2 M NaOH and dried over $MgSO_4$. A conversion of 90% of *tert*-butylbenzene was obtained, consisting of 17% of 2-*tert*-butylnitrobenzene, 11% of 3-*tert*-butyl-nitrobenzene, and 72% of 4-*tert*-butylnitrobenzene. The remaining *tert*-butylbenzene was distilled off in a rough vacuum distillation (b.p. 84 °C, 45 mm Hg). The 2-*tert*-butylnitrobenzene was separated from the other isomers by careful distillation over a Fischer-Spaltrohr column (b.p. 145–147 °C, 34 m Hg). Yield: 40 ml of yellow liquid (0.24 mol, 4%); ^1H NMR ([D$_6$]DMSO): δ = 7.64 (d, 1 H; H_6), 7.53 (m, 2 H; H_3 + H_4), 7.39 (t, 1 H; H_5), 1.33 (s, 9 H; *t*-Bu).

2-Isopropylnitrobenzene (**1m**): The synthesis of 2-isopropylnitrobenzene was performed analogously to the synthesis of 2-*tert*-butylnitrobenzene. Concentrated HNO_3 (460 ml, 7.17 mol) and 775 ml of concentrated H_2SO_4 were reacted with 1000 ml of isopropylbenzene (7.17 mol). A total conversion of 93% was reached, consisting of 31% of 2-isopropylnitrobenzene, 7% of 3-iso-propylnitrobenzene, and 65% of 4-isopropylnitrobenzene. The remaining isopropylbenzene was first distilled off (b.p. 61 °C, 30 mm Hg) after which the 2-isopropylnitrobenzene was separated from the other isomers by distillation over the Fischer-Spaltrohr column (b.p. 137 °C, 38 mm Hg). Yield: 188 ml of yellow liquid (1.23 mol, 17%); ^1H NMR ([D$_6$]DMSO): δ = 7.79 (d, 1 H, H_6), 7.65 (m, 2 H; H_3 + H_4), 7.43 (t, 1 H; H_5), 3.21 (septet, 1 H; *i*Pr), 1.24 (d, 6 H; *i*-Pr).

4-(Dimethylamino)nitrobenzene (**1e**): 4-Nitroaniline (5 g, 36 mmol) was reacted with 10 g of dimethylsulfate (79 mmol) at 155 °C for 3 h, resulting in a brown sticky compound. The product was then treated with 5 M KOH at room temperature until an alkaline suspension was obtained. The suspension was extracted with 50 ml of dichloromethane. The organic layer was dried over $MgSO_4$ after which the solvent was evaporated. The product was purified by column chromatography using 5% of dichloromethane in hexanes as eluent. Yield: 1.19 g of yellow powder (11 mmol, 31%); ^1H NMR ([D_6]DMSO): $\delta = 8.07$ (d, 2H; $H_2 + H_6$), 6.78 (d, 2H; $H_3 + H_5$), 3.11 [s, 6H; $N(CH_3)_2$]; M.p. 161–163°C.

Catalysis

Substrate Variation: In a typical experiment using the $Pd(phen)_2(OTf)_2$/phen catalyst system the autoclave was charged with 10 ml of methanol and 14.6 mmol of a nitro substrate. 15.3 mg of $Pd(phen)_2(OTf)_2$ (0.02 mmol) and 14.4 mg of 1,10-phenanthroline (0.08 mmol) were dissolved in this mixture. The 50 ml autoclave was pressurised with 60 bar of CO and heated to 135°C within 35 minutes. The initial working pressure at 135°C was approximately 80 bar. After 2 h the autoclave was rapidly cooled down and the pressure was released. If a solid product was present the reaction mixture was diluted until all the material was dissolved to guarantee a representative sample for the analysis. In some cases the solid material turned out to be insoluble in the typical volatile organic solvents. The solvent was then completely evaporated and the resulting solid was dried and ground up before taking a sample for the analysis.

Methoxy-Substituted Side Products: Part of the experiments concerning the formation of the methoxy substitute carbamates, urea derivatives, and anilines were conducted with a $Pd(OAc)_2$/bpy/*p*-tsa catalyst system. The working procedure was in principle the same as for the substrate variation, though 9 mg of $Pd(OAc)_2$ (0.04 mmol), 99 mg of 2,2'-bipyridine (0.64 mmol), and 122 mg of *p*-toluenesulfonic acid (0.64 mmol) were used. The 100 ml autoclave was heated to 135°C within 15 minutes.

The Effect of Aniline: The working procedure for the experiments concerning the accelerating effect of aniline was in principle the same as for the substrate variation. However, in addition to 14.6 mmol of nitrobenzene an additional amount of aniline in the range of 1.46 to 21.9 mmol (10 to 150% with respect to nitrobenzene) was added. The 100 ml autoclave was heated to 135°C within 15 minutes.

Separation of Product Mixture of 2-tert-Butylnitrobenzene (**1n**): The reaction mixture was concentrated in vacuum and separated on a silicagel column [eluent CH_2Cl_2/hexanes, 95:5 (v/v)]. The following side products were identified: *Methyl N-(2-tert-Butyl-4-methoxypenyl)carbamate* (**7n**): ^1H NMR ([D_6]DMSO): $\delta = 8.50$ (br. s, 1H, NH), 6.99 (d, 1H, H_{Ar}, $^2J = 8.5$ Hz), 6.86 (d, 1H, H_{Ar}, $^3J = 2.8$ Hz), 6.78 (dd, 1H, H_{Ar}, $^2J = 8.5$ Hz, $^3J = 2.8$ Hz), 3.76 (s, 3H, OCH_3), 3.61 (br. s, 3H, $C(O)OCH_3$), 1.30 (s, 9H, *tert*-C_4H_9); GC-MS: 237 (M^+), 222 $(M - CH_3)^+$, 205 $(M - OCH_3)^+$; HRMS: exp. 237.1365, calc. for $C_{13}H_{19}NO_3$ 237.1365. – *2-tert-Butyl-4-methoxyaniline* (**10n**): ^1H NMR ([D_6]DMSO): $\delta = 6.78$ (d, 1H, H_{Ar}, $^2J = 8.8$ Hz), 6.75 (d, 1H, H_{Ar}, $^2J = 8.8$ Hz), 6.56 (s, 1H, H_{Ar}), 4.38 (br. s, 2H, NH_2), 3.78 (s, 3H, OCH_3), 1.36 (s, 9H, *tert*-C_4H_9). GC-MS: 179 (M^+), 164 $(M - CH_3)^+$, 149 $(M - 2\,CH_3)^+$; HRMS: exp. 179.1291, calc. for $C_{11}H_{17}NO$ 179.1310. – *2-tert-Butylaniline* (**4n**): ^1H NMR ([D_6]DMSO): $\delta = 7.07$ (dd, 1H, H_{Ar}), 6.90 (dt, 1H, H_{Ar}), 6.65 (dd, 1H, H_{Ar}), 6.52 (dt, 1H, H_{Ar}), 4.73 (s, 2H, NH_2), 1.35 (s, 9H, *tert*-C_4H_9). GC-MS: 149 (M^+), 134 $(M - CH_3)^+$; HRMS: exp. 149.1222, calc. for $C_{10}H_{15}N$ 149.1205. – *N,N'-Bis-(2-tert-butyl-4-methoxyphenyl)urea* (**9n**): ^1H NMR ([D_6]DMSO): $\delta = 7.69$ (br. s, NH), 7.10 (d, 2H, H_{Ar}), 6.86 (d, 2H, H_{Ar}), 6.79 (dd, 2H, H_{Ar}), 3.75 (s, 6H, OCH_3), 1.38 (s, 9H, *tert*-C_4H_9); HRMS: exp. 384.2454, calc. for $C_{23}H_{32}N_2O_3$ 384.2413.

Separation of Product Mixture of 2-Isopropylnitrobenzene (**1m**): The reaction mixture was dissolved in 30 ml of methanol and upon standing a white precipitate was formed. The white solid was filtered, washed with diethyl ether, dried in vacuum and identified as *N,N'-Bis-(2-tert-Butyl-4-methoxyphenyl)urea* (**9m**): ^1H NMR ([D_6]DMSO): $\delta = 7.89$ (br. s, NH), 7.35 (d, 2H, H_{Ar}), 6.80 (d, 2H, H_{Ar}), 6.74 (dd, 2H, H_{Ar}), 3.75 (s, 6H, OCH_3), 3.19 (m, 2H, CH), 1.19 (d, 12H, CH_3); HRMS: exp. 356.2083, calc. for $C_{21}H_{28}N_2O_3$ 384.2413. – The following other side products were identified by GC-MS and HRMS: *Methyl N-(2-Isopropyl-4-methoxyphenyl)carbamate* (**7m**): GC-MS: 223 (M^+), 208 $(M - CH_3)^+$, 191 $(M - OCH_3)^+$; HRMS: exp. 223.1206, calc. for $C_{12}H_{17}NO_3$ 223.1208. – *N-(2-Iso-Propylphenyl)-N'-(2-isopropyl-4-methoxyphenyl)urea* (**2m**): HRMS: exp. 326.1987, calc. for $C_{20}H_{26}N_2O_3$ 326.1994. – *2-Isopropyl-4-methoxyaniline* (**10m**): HRMS: exp. 165.1134, calc. for $C_{10}H_{15}NO$ 165.1154.

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[1] P. Braunstein, *Chem. Rev.* **1989**, *89*, 1927.
[2] Y. Watanabe, Y. Tsjui, R. Takeuchi, N. Suzuki, *Bull. Chem. Soc. Jpn.* **1983**, *56*, 3343.
[3] Th. W. Greene, P. G. M. Wuts, *Protective Groups in Organic Synthesis*, 2nd ed., John Wiley and sons Inc., New York, **1991**, p. 315.
[4] H. Irie, H. Nakanishi, N. Fujii, Y. Mizuno, T. Fushimi, S. Funakoshi, H. Yajima, *Chem. Lett.* **1980**, 705.
[5] V. L. K. Valli, H. Alper, *J. Org. Chem.* **1995**, *60*, 257.
[6] E. Drent, P. W. N. M. Van Leeuwen, **1983**, EP 86281.
[7] S. J. Skoog, J. P. Campbell, W. L. Gladfelter, *Organometallics* **1994**, *13*, 4137 and references cited therein.
[8] E. Alessio, G. Mestroni, *J. Mol. Catal.* **1984**, *26*, 337.
[9] S. Cenini, F. Ragaini, M. Pizzotti, F. Porta, G. Mestroni, E. Alessio, *J. Mol. Catal.* **1991**, *64*, 179.
[10] W. B. Hardy, R. P. Bennett, *Tetrahedron Lett.* **1967**, *11*, 961; American Cynamid Co., **1966**, Netherlands Patent 6513844.
[11] P. Wehman, V. E. Kaasjager, F. Hartl, P. C. J. Kamer, P. W. N. M. van Leeuwen, J. Fraanje, K. Goubitz, *Organometallics* **1995**, *14*, 3751.
[12] N. P. Reddy, A. M. Masdeu, B. El Ali, H. Alper, *J. Chem. Soc., Chem. Commun.* **1994**, 863.
[13] E. Alessio, G. Mestroni, *J. Organomet. Chem.* **1985**, *291*, 117.
[14] P. Wehman, G. C. Dol, E. R. Moorman, P. C. J. Kamer, P. W. N. M. van Leeuwen, J. Fraanje, K. Goubitz, *Organometallics* **1994**, *13*, 4856.
[15] S. P. Gupte, R. V. Chaudhari, *J. Mol. Catal.* **1986**, *34*, 241.
[16] I. M. Kolthoff, J. J. Ligane, *Polarography*, Interscience Publishers, New York, **1952**, Vol. II, p. 746; The $E_{1/2}$ values listed in this reference are measured versus S.C.E., using various acidic or buffered electrolyte solutions. As our data are measured versus Ag/AgCl in unbuffered $LiClO_4$ solutions, the absolute values of $E_{1/2}$ differ from the data reported by Kolthoff.
[17] A. F. M. Iqbal, *Chemtech* **1974**, 567.
[18] F. J. Weigert, *J. Org. Chem.* **1973**, *38*, 1316.
[19] R. G. Little, R. J. Doedens, *Inorg. Chem.* **1973**, *12*, 537.
[20] M. Calligaris, T. Yoshida, S. Otsuka, *Inorg. Chim. Acta* **1974**, *11*, L15.
[21] J. March, *Advanced Organic Chemistry*, John Wiley and sons, New York, **1992**, p. 202.
[22] H. E. Heller, E. D. Hughes, C. K. Ingold, *Nature* **1951**, *24*, 909.
[23] P. Wehman, L. Borst, P. C. J. Kamer, P. W. N. M. van Leeuwen, *J. Mol. Catal. A: Chem.*, **1996**, *112*, 23.
[24] P. Leconte, F. Metz, A. Mortreux, J. A. Osborn, F. Paul, F. Petit, A. Pillot, *J. Chem. Soc., Chem. Commun.* **1990**, 1616.
[25] G. Powell, F. R. Johnson, *Org. Synth.* **1934**, *14*, 68.
[26] D. Craig, *J. Am. Chem. Soc.* **1935**, *57*, 195.
[27] F. Ullmann, *Ann. Chem.* **1903**, *327*, 104.
[28] B. S. Furniss, A. J. Hannaford, P. W. G. Smith, A. R. Tatchell, *Vogel's Textbook of Practical Organic Chemistry*, John Wiley and sons Inc., New York, **1989**, p. 955.

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