Amination of aryl bromides catalysed by supported palladium

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Abstract

Palladium particles immobilised onto a metal oxide support or Pd(0), Pd(II) and $[Pd(NH_3)_4]^{2+}$ in NaY zeolite have been prepared and characterised. They exhibit a good activity towards the amination of aryl bromides using secondary amines such as piperidine and diethyl amine with a good regio-selectivity for these reactions. Low Pd concentrations (1 mol%) are required to observe a reasonable regio-selectivity. The catalysts can easily be separated from the reaction mixture (filtration) and reused without loss of activity and selectivity. The electronic nature of the aryl halides plays an important role for both the reaction yields and the regio-control of the reaction. It depends on the relation of the direct amination via a benzyne intermediate versus the Pd-catalysed route. © 1999 Elsevier Science S.A. All rights reserved.

1. Introduction

The (regio-)selective synthesis of aromatic amines is of considerable interest for several chemical and pharmaceutical applications. As a consequence, the development of new selective, general and economical methods for their synthesis retain attention [1]. The last decade has seen the development of new homogeneous Pd-catalysed methods, mainly based on the catalytic couple Pd/bulky phosphines [2].

While the use of these homogeneous palladium catalysts constitute today an inestimable choice (high activity, high selectivity, applicability for the synthesis of fine chemicals) [1e], homogeneous catalysts are generally connected with problems of separation (purity of the products), recovery and regeneration of the catalysts. These are of economical importance, when applied for large-scale synthesis in the industry. Although recent advances in the comprehension of the mechanism of the reaction have been made, the amination of aryl halides still require a large amount of Pd catalyst

(2–5 mol% Pd/aryl halide) [3], which is generally not recovered at the end of the reaction. However, more active systems (1 mol% Pd; activation of aryl chlorides) have been reported too [2d]. In addition to the separation problems deactivation of the homogeneous catalysts has been reported at relatively high temperature [4].

The problems discussed could be principally minimised by a heterogeneously catalysed reaction. There is, to our knowledge, no report about the amination of aryl halides with supported Pd particles or Pd complexes. However, the use of metal oxides (MO_x) or zeolites as support should have several advantages: (1) the variation of the nature of the support (relative acidity/basicity) could influence the activity of the supported Pd particles [5,6], (2) the support, and more generally zeolite, are capable of stabilising small metal particles or complexes [7], and (3) zeolites as support for complexes could maintain their activity and increase their stability [8]. In addition, zeolites are known for their shape selectivity, which could enhance the selectivity of the heterogeneous catalysts [7].

Here we report for the first time that Pd/MO_x, Pd/zeolite or $[Pd(NH_3)_4]$/zeolite are active and recoverable catalysts for the regio-selective amination of aryl bromides.

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2. Results and discussion

2.1. Preparation of the catalysts

The heterogeneous palladium catalysts were prepared from metal oxide supports (MO_x) or from zeolites.

The MgO support was prepared according to modified procedures of the literature [6a], by thermal decomposition in air at high temperature of the hydroxide precursor, which was obtained by precipitation from the $MgSO_4$ with a 25% ammoniac solution. Thus, material with defined specific area was reproducibly obtained: MgO, $S = 44.2$ m^2 g^{-1}. The other oxides are commercially available, and have the following specific area: ZrO_2, $S = 48.6$ m^2 g^{-1}; TiO_2, $S = 39.1$ m^2 g^{-1}.

The supported $Pd(0)/MO_x$ catalysts (ca. 5 wt.% Pd relative to the oxide) were prepared by impregnation of the support using a solution of $Pd(acac)_2$ in benzene, followed by a reduction of the Pd(II) complex under H_2 to give the desired catalysts: Pd/MgO: 4.3 wt.%, Pd/ZrO_2: 5.5 wt.% and Pd/TiO_2: 4.4 wt.%.

The Pd-loaded NaY zeolites were prepared according to the literature [9] by an ion exchange procedure using a aqueous solution of $[Pd(NH_3)_4]Cl_2$ to give a 7 wt.% Pd zeolite. Calcination under O_2 of exchanged $[Pd(NH_3)_4]^{2+}$NaY gave the Pd(II)–NaY zeolite and subsequent reduction under H_2 lead to the formation of the Pd(0)–NaY zeolite.

2.2. Test of the catalytic activity

For the test of the catalytic activity we choose firstly aryl bromides. This choice was directed both by the real availability of these compounds and on literature basis. Aryl bromides exist with a large variety of substituents on the aromatic ring, that could be used to test the tolerance of the reaction towards other functional groups. Most of the reported work concerning this reaction were made with such derivatives, that offers us a large basis for comparison of the systems described here and to the homogeneously catalysed amination of aryl halides.

For the Pd-catalysed amination of aryl halides, particularly of aryl bromides, two independent (competing) reactions have to be regarded: (1) the direct amination of aryl bromides via a benzyne intermediate (Scheme 1, route a) leading to a mixture of two regio-isomers [10], and (2) the Pd-catalysed amination (Scheme 1, route b), which give only one isomer directed by the halogen (leaving group) and the oxidative addition of the aryl halide to the Pd(0) intermediate [2b,c,3a–c].

Since only the Pd-catalysed reaction present an interest, the studies described here were performed by comparing of each Pd-catalysed experiment with the reaction in absence of Pd catalyst and, when applying, with the reaction using homogeneous Pd catalysts under comparable conditions.

Following we will describe and discuss the results obtained in dependence on:

- the nature of the support: MO_x or NaY
- the nature of the Pd species immobilised into the zeolite: Pd(0), Pd(II) or $[Pd(NH_3)_4]^{2+}$
- the variation of the Pd concentration (catalyst amount)
- the variation of the aryl substituents
- the variation of the amine
- the variation of the base
- the recovery of the catalysts

For the studies on the influence of the support and the influence of the nature of the Pd species, we chose the reaction of *para*-bromoanisole with piperidine as model reaction (Scheme 2). This reaction was found to give reasonable yields, thereby allowing the observation of enhancement of the reaction yield and/or selectivity, both directed by these parameters.

2.3. Influence of the support

The conversion and the selectivity obtained for the $Pd(0)/MO_x$ or the Pd(0)/NaY (1 mol% Pd/aryl bro-
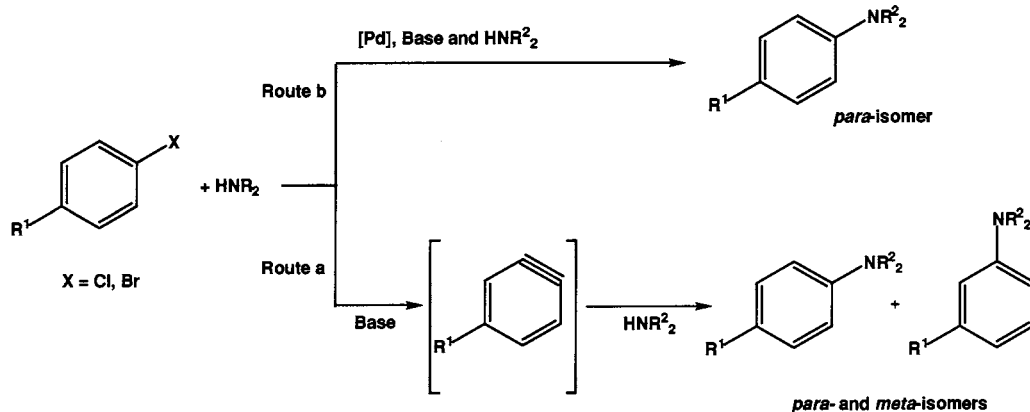
Scheme 1. Proposed reactions routes for the amination of aryl halides in presence and absence of Pd catalysts.
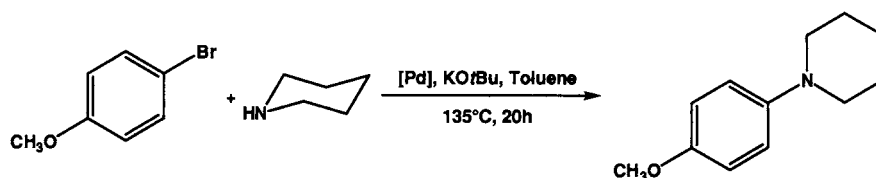
Scheme 2. Reaction conditions: 10 mmol bromoanisole, 20 mmol piperidine, 12 mmol NaO*t*Bu, 1 mol% [Pd] catalyst, 6 ml toluene, 135°C, 20 h.

mide) are reported in Table 1 and compared to the results obtained in absence of catalyst.

As expected the direct amination via a benzyne intermediate (Scheme 1, route a — Table 1, entry 6) gave a mixture of *para*- and *meta*-products in a 1:1 ratio. While the yield of this reaction is high, it does not contribute to an interesting alternative to the Pd-catalysed ones.

Table 1 shows also that the reaction yield and selectivity depend on the nature of the metal oxide support. In general the use of the heterogeneous catalysts gave better yields compared to the reaction in absence of palladium. As expected the use of zeolites gave a higher control onto the reaction selectivity probably due to the well-established 'shape selectivity'. In this case we should also note that the enhancement of the yield due to the heterogeneous catalyst is less for zeolites than for metal oxide supports, which can be attributed to diffusion limitation, decreasing the rate of the reaction. The other variations observed for the metal oxide supports could be discussed in terms of relative acidity/basicity. The following classification could be assumed from the more acidic to the more basic support [6b], although the differences are small and have to be handled with care (e.g. due to possible differences in Pd dispersion):

$$TiO_2 > ZrO_2 \gg C \gg MgO$$
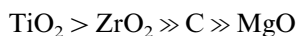
(the active carbon support C is here considered as almost neutral)

As Table 1 shows, the more acidic supports (TiO$_2$ and ZrO$_2$) gave the highest selectivity, which can be correlated to the fact that these acidic supports favour largely the reductive elimination of the products. This step constitutes, as already mentioned for the homogeneously catalysed reaction, the limiting step of the reaction [2b,c,3a–c]. This observation is correlated also by the good results obtained with the NaY zeolite as support (without any consideration of shape selectivity), these materials being generally more acidic as the other metal oxide supports.

While the Pd(0)-loaded NaY catalysts does not constitute the most active one, the enhancement in selectivity obtained by its use counter-balanced, in some way, the lower activity observed. This support was then retained for most of the other studies described below.

2.4. Influence of the nature of the Pd species entrapped into the NaY zeolite

It was previously described that the activity of the Pd-loaded zeolites used for the heterogeneously catalysed Heck reaction [11], depends on the nature of the Pd species {Pd(0), Pd(II) and [Pd(NH$_3$)$_4$]$^{2+}$} entrapped into them at the beginning of the reaction. Thus, a relation between the activity of the catalysts and the nature of the entrapped species was suggested in terms of different nature of Pd(0) species generated during the reaction and of different Pd dispersions attained during the preparation of the catalysts. Analogous to this work, we were interested in the influence that the nature of the Pd species entrapped into the zeolite cages could have onto the activity of the heterogeneous catalysts.

Table 2 shows that there is no influence due to the nature of the Pd species entrapped into the zeolite

Table 1
Results obtained for the amination of bromoanisole with piperidine (Scheme 2) with different Pd/MO$_x$, Pd(0)–NaY or without catalysts [a]

Entry	Catalyst	Total GLC yield	*Para*-:*meta*-selectivity
1	Pd/C	80.7	1.7:1
2	Pd/MgO	75.4	1.1:1
3	Pd/ZrO$_2$	83.6	1.8:1
4	Pd/TiO$_2$	79.3	2.1:1
5	Pd(0)–NaY	65.8	3:1
6	No catalyst	42.3	1:1

[a] The total GLC yields (*para*-+*meta*-isomers) are given with the selectivity *para*-/*meta*- ($\Delta_{rel} \leq \pm 10\%$).

Table 2
Results obtained for the amination of bromoanisole with piperidine (Scheme 2) with different Pd species [Pd] entrapped in NaY ([Pd]–NaY catalysts) [a]

Entry	Pd species	Total GLC yield	*Para*-:*meta*-selectivity
1	Pd(0)	65.8	3:1
2	Pd(II)	66.1	2.9:1
3	[Pd(NH$_3$)$_4$]$^{2+}$	68.3	3.1:1
4	pure zeolite NaY	37.3	1.3:1

[a] The total GLC yields (*para*-+*meta*-isomers) are given with the selectivity *para*-/*meta*- ($\Delta_{rel} \leq \pm 10\%$).

Table 3
Results obtained for the amination of bromoanisole with piperidine (Scheme 2) using different amounts of Pd(0)–NaY catalyst (Pd concentration variation) [a]

Entry	Pd concentration (mol%)	Total GLC yield	*Para-:meta-* selectivity
1	0	42.3	1:1
2	0.2	49.6	1.6:1
3	1	65.8	3:1
4	5	62.4	2.5:1

[a] The total GLC yields (*para-*+*meta-*isomers) are given with the selectivity *para-/meta-* ($\Delta_{rel} \leq \pm 10\%$).
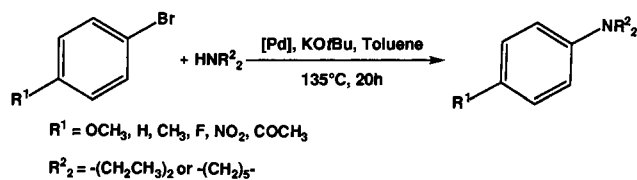
Table 4
Results obtained for the amination of bromoanisole with piperidine (Scheme 2) using 1 mol% of Pd(0)–NaY or no catalyst at different temperatures [a]

Entry	Catalyst	T (°C)	Total GLC yield	*Para-:meta-* selectivity
1	Pd(0)–NaY	60	5.3	– [b]
		100	28.7	2.6:1
		135	65.8	3:1
2	–	60	2.8	1:1
		100	22.4	1:1
		135	42.3	1:1

[a] The total GLC yields (*para-*+*meta-*isomers) are given with the selectivity *para-/meta-* ($\Delta_{rel} \leq \pm 10\%$).
[b] In this case only the *para-*isomer was detected, but this does not necessary represent the real selectivity.

R[1] = OCH$_3$, H, CH$_3$, F, NO$_2$, COCH$_3$

R$^2_2$ = -(CH$_2$CH$_3$)$_2$ or -(CH$_2$)$_5$-

Scheme 3. Reaction conditions: 10 mmol aryl bromide, 20 mmol amine, 12 mmol NaO*t*Bu, 1 mol% [Pd] catalyst, 6 ml toluene, 135°C, 20 h.

cages. Thus, only slightly better results are obtained with the entrapped [Pd(NH$_3$)$_4$]$^{2+}$ complex (Table 2, entry 3), compared to the other two types of Pd species. This is probably due to the fact that, as already mentioned above, the limiting step of the reaction is the elimination of the products, where the nature of the support plays a stronger role than the origin of the active Pd species.

In addition, we checked whether the presence of Pd species in the zeolite is responsible for the activity and the enhancement of the selectivity observed with these catalysts. Thus, the amination reaction of bromoanisole in presence of NaY zeolite (free of Pd) was done. The result is a little enhancement of selectivity and a small decrease of the reaction yield (Table 2, entry 4). This

suggests that while the zeolite shape selectivity could occur in this case, it does not explain the result obtained with the Pd-loaded zeolites in terms of selectivity and activity.

2.5. Influence of the Pd concentration and of the temperature

Since we found that the Pd species entrapped into the zeolite cages or immobilised onto a MO$_x$ support were responsible for the enhancement of the *para-* versus *meta-*selectivity, we studied the influence of the Pd concentration in order to optimise the reaction conditions.

The reaction yields and selectivities reported in Table 3 show that an optimal Pd concentration of 1 mol%/ aryl bromide is required to observe the best results. A lower concentration (0.2 mol%) causes reduction in activity and selectivity and a higher Pd concentration (5 mol%) decreased the influence of the palladium towards the selectivity. We have actually no reasonable explanation for this observation.

A complementary study was to observe the influence of the reaction temperature onto both the yield and the selectivity. The results reported in Table 4 show that at least no strong influence of the temperature for the selectivity occurs, whereas a strong decrease of the yields is observed at lower temperature for both the Pd-catalysed and the non-catalytic direct amination of aryl bromides.

2.6. Influence of the nature of the amine

While the results obtained for the amination of aryl bromides using heterogeneous Pd catalysts represent an interesting contribution when applied to the piperidine, it was interesting to study this type of reaction when applied to less reactive and more volatile amines, such as the diethyl amine (Scheme 3, R[1] = OCH$_3$).

Such a reaction represents an interesting case of generalisation of the procedure, more particularly for industrial applications, which are mainly concerned by the synthesis of basic materials (aniline derivatives).

As expected, Table 5 shows that the amination of aryl bromides using a less reactive amine such as diethyl amine lead to lower yields. The lower selectivity observed with heterogeneous catalysts suggests that a large percentage of the transformation observed for the bromoanisole is due to the direct amination route (Scheme 1, route a). This is confirmed by the lower difference observed between the yields of the reaction in presence and absence of Pd catalyst for the two amines studied.

Our attempts to improve these results were not successful. A lower reaction temperature (80 or 100°C) in order to limit the volatilisation of the diethyl amine

Table 5
Results obtained for the amination of bromoanisole with different amines (Scheme 3, $R^1 = OCH_3$) using 1 mol% of Pd catalyst or no catalyst [a]

Entry	Catalyst	Amine	Total GLC yield	Para-:meta-selectivity
1	Pd(0)–NaY	Piperidine	65.8	3:1
	Pd/TiO$_2$		79.3	2.1:1
	–		42.3	1:1
2	Pd(0)–NaY	Dietylamine	49.3	2.7:1
	Pd/TiO$_2$		52.1	1.8:1
	–		39.1	1:1

[a] The total GLC yields (para- + meta-isomers) are given with the selectivity para-/meta- ($\Delta_{rel} \leq \pm 10\%$).

lead generally to poor yields (typically between 12 and 24%). An increase in the concentration of diethyl amine (5 or 10 equivalents/aryl bromide) lead generally to slightly increased reaction yields (typically between 45 and 59%) but to a strong decrease of the reaction selectivity, which generally tends to the one reported for the amination in absence of Pd catalyst.

2.7. Influence of the aromatic substituents

As for many reactions in organic chemistry, it was interesting to study the generalisation of the heterogeneously Pd-catalysed amination of aryl bromides and its tolerance towards a variety of functional groups. Thus, we studied the amination of differently para-substituted aryl bromides (Scheme 3).

The results reported in Table 6 show that the heterogeneously Pd-catalysed amination of aryl bromide is tolerant towards a 'large' variety of functional groups. As we can observe, both the reaction yield and the product selectivity are controlled in some way by the electronic effect of the functional groups [10]. As expected, electron withdrawing groups lead to better reaction yields, since it facilitates the oxidative addition of the aryl bromide onto the Pd(0) species. An unexpected effect of the electron withdrawing groups is a lower selectivity, probably due to a larger contribution (higher reaction rate) of the direct amination of the aryl bromides via a benzyne intermediate as attested by the higher reaction yields observed in these cases.

Similar results were observed using the diethyl amine, and are reported in Table 7.

While the results obtained in these experiments are generally good, the heterogeneous Pd catalysts do not rival with the best homogeneous catalysts described in the literature which lead generally to a total regiocontrol of the reaction and often to better yields (see Table 6).

In some cases we observed that the reaction between the activated aryl bromides (p-NO$_2$C$_6$H$_4$Br or p-CH$_3$COC$_6$H$_4$Br) lead to the formation of other non-defined derivatives decreasing drastically the yield of desired products. We still have actually no explanation for these observations.

2.8. Influence of the base

As previously suggested, one important factor toward the selectivity of the heterogeneously Pd-catalysed amination of aryl bromides is the control of the contribution of the direct amination reaction via a benzyne intermediate.

Table 6
Results obtained for the amination of aryl bromides with piperidine (Scheme 3, $R^1 = OCH_3$ and $R^2 = -(CH_2)_5-$) using 1 mol% of Pd(0)–NaY or no catalyst [a]

Entry	R	Catalyst	Heterogeneous		Homogeneous [b]	
			Total GLC yield	Para-:meta-selectivity	Isolated yield (%)	Catalysts and Refs.
1	CH$_3$O	Yes	65.8	3:1	94	[P(o-Tol)$_3$]$_2$PdCl$_2$
		No	42.3	1:1		[12]
2	H	Yes	92.2	–	83	Palladacycle [c]
		No	56.2	–		[14]
3	CH$_3$	Yes	68.1	1:0	89 [d]	[P(o-Tol)$_3$]$_2$PdCl$_2$
		No	65.7	9:1		[12]
4	F	Yes	91.1	2.1:1	82	Palladacycle [c]
		No	72.3	1.2:1		[14]
5	NO$_2$	Yes	83.8	2.8:1	83	Pd$_2$(dba)/BINAP
		No	59.8	1.6:1		[13]
6	CH$_3$CO	Yes	82.3	2.4:1	89	Pd$_2$(dba)/BINAP
		No	67.8	1.7:1		[13]

[a] The total GLC yields (para- + meta-isomers) are given with the selectivity para-/meta- ($\Delta_{rel} \leq \pm 10\%$) and the results compared to reported literature for homogeneous catalysts.
[b] For the homogeneous systems generally 100% selectivity for the para product is obtained.
[c] The catalyst used in these experiments is the palladacycle: {Pd[P(o-Tol)$_2$(C$_6$H$_4$CH$_2$)](μ-OAc)}$_2$.
[d] The experiment used as reference here did not use the p-BrC$_6$H$_4$CH$_3$ but the p-BrC$_6$H$_4$$n$Bu.

Table 7

Results obtained for the amination of aryl bromides with diethyl amine (Scheme 3, $R^1 = OCH_3$ and $R^2 = -(CH_2CH_3)_2$) using 1 mol% of Pd(0)–NaY or no catalyst [a]

Entry	R	Catalyst	Total GLC yield	Para-:meta-selectivity
1	CH_3O	Yes	49.3	2.7:1
		No	39.1	1:1
2	H	Yes	62.9	–
		No	44.9	–
3	CH_3 [b]	Yes	63.4	6:1
		No	51.7	4.3:1
4	F	Yes	76.2	2:1
		No	66.1	2:1
5	NO_2	Yes	77.2	2.3:1
		No	61.8	1.5:1
6	CH_3CO	Yes	72.1	2.6:1
		No	62.3	1.3:1

[a] The total GLC yields (*para-+meta*-isomers) are given with the selectivity *para-/meta-* ($\Delta_{rel} \leq \pm 10\%$).

[b] A report using as homogeneous catalysts [P(*o*-Tol)$_3$]$_2$PdCl$_2$ attested a isolated yield of 26% for the *para*-isomer.

A way to limit this side reaction is to disfavour it or to limit its possibility by changing the base (Scheme 2). Our attempts in this direction were not very successful. The use of NaO*t*Bu instead of the KO*t*Bu results in lowered yields (typically 32–45% for the model reaction), while actually a better selectivity was observed (*para-:meta-* = 5.2:1 with the Pd(0)–NaY). In order to improve this procedure we used a mixture of NaO*t*Bu/ K$_2$CO$_3$ (1:1) in order to obtain a more reactive base, but we did not observe any enhancement of the reaction yield and no effect onto the selectivity.

2.9. Recovery of the catalysts

An important point concerning the use of heterogeneous catalysts is its lifetime, particularly for industrial applications of the amination of aryl halides.

After separation and washing, the heterogeneous catalysts were used for the same reactions (Scheme 2) under the same reaction conditions as for the initial run without any regeneration procedure.

Table 8 shows that all the catalysts still showed a good activity and comparable selectivity as for fresh catalysts.

Few selected investigations indicated some leaching (residual activity of the supernatant solution after separation of the solid) in the case of the metal oxide supports. It seems to depend on the filter and filtration procedure, respectively. However, this limited leaching can by far not explain the overall activity of the catalysts (see also recovery of the catalyst).

3. Conclusions

The heterogeneous catalysts Pd/MO$_x$ or Pd-loaded zeolites exhibit a good activity towards the amination of aryl halides using secondary amines such as piperidine and diethyl amine. While they did not rival with the best homogenous Pd catalysts, some of them gave a good regio-control for this particular reaction. This is particularly true for the Pd-loaded zeolites, which, in addition to the Pd-catalysed route for the reaction, probably lead also to shape selectivity, thus enhancing the results observed with the other heterogeneous catalysts reported here. Remarkable is the low Pd concentration (1 mol%) required to observe a reasonable activity and regio-selectivity. In addition, the results described in this paper show that these catalysts can be easily separated from the reaction mixture (filtration) and reused without loss of activity and selectivity.

We found that the electronic nature of the aryl halides plays an important role for both the reaction yields and the regio-control of the reaction. As suggested by the generally accepted reaction mechanism of the Pd-catalysed amination of aryl halides, the limiting step is the elimination of the product from the Pd(II) intermediate [2,3]. Thus, we suggest that the electronic nature of the aryl halides does not control the regio-selectivity of the heterogeneously Pd-catalysed amination of aryl halides, but it depends more on the rate ratio

Table 8

Results obtained for the amination of bromoanisole with piperidine (Scheme 3, $R^1 = OCH_3$ and $R^2 = -(CH_2)_5-$) using recovered heterogeneous Pd catalysts [a]

Entry	Catalyst	First run		Recycled	
		GLC yield	Para-:meta-selectivity	GLC yield	Para-:meta-selectivity
1	Pd(0)–NaY	65.8	3:1	60.4	2.8:1
2	Pd/TiO$_2$	79.3	2.1:1	67.2	2.0:1
3	Pd/ZrO$_2$	83.6	1.8:1	69.7	1.6:1

[a] The total GLC yields (*para-+meta*-isomers) are given with the selectivity *para-/meta-* ($\Delta_{rel} \leq \pm 10\%$) and compared to the results obtained for the first run of the catalysts.

between the direct amination via a benzyne intermediate (Scheme 1, route a) [10], which is favoured by the presence of electron withdrawing groups onto the aromatic ring, and the Pd-catalysed route, which lead to a total control of the reaction (Scheme 1, route b). The yield enhancement observed when electron withdrawing groups are bound to the aromatic ring, is due to the favoured direct amination [10] and the favoured oxidative addition of the aryl halides on the Pd(0) precursor [2,3], respectively.

Current investigation focus on the kinetic and mechanistic aspect of the heterogeneously Pd-catalysed amination of aryl halides and of the development of new heterogeneous Pd catalysts by grafting of Pd complexes onto a metal oxide support or in zeolite cages. Thus, a higher activity should be obtained, leading to more interesting heterogeneous catalysts.

4. Experimental

All preparations, manipulations and reactions were carried out under argon, including the transfer of the catalysts to the reaction vessel. All glassware was base- and acid-washed and oven dried. The other chemicals (organic reagents) were deaerated by an argon flow before they were used. The toluene used for the catalytic experiments was distilled under argon over sodium from purple benzophone ketyl and stored over activated molecular sieves (4 Å). The TiO_2 and ZrO_2 were donated by Degussa-Hüls AG and the NaY zeolite (LZ-Z-52) was purchased from Sigma-Aldrich Chemicals. These catalyst supports were dried before use at 120°C for 48 h under 5×10^{-2} mmHg. All other chemicals were used as received. NMR spectra were recorded with a Bruker AM 400 spectrometer (^{1}H-NMR were referenced to the residual protio-solvent: $CDCl_3$, $\delta = 7.25$ ppm; ^{13}C-NMR were referenced to the C signal of the deutero solvent: $CDCl_3$, $\delta = 77$ ppm). The palladium content determination of the catalysts (Pd/MO_x or Pd-loaded zeolites) was performed by AAS spectroscopy from a solution obtained by treatment of the catalysts with a 40% HF commercial solution (Pd/MO_x) or by treatment with a mixture of HBF_4, HNO_3 and HCl in a Teflon reactor at 180°C (Pd(0)-loaded zeolite). Gas–liquid chromatograms were performed on a HP 6890 series chromatograph equipped with a FID detector and a HP-1 column (cross-linked methylsiloxane, 30 m × 0.25 mm × 0.25 μm film thickness) using He as carrier gas. Alternatively, a HP 5970 series chromatograph equipped with a selective mass spectrometer detector HP 5970 and a BGB-1 column from SCP-Seitz GmbH (95% methylpolysiloxane + 5% phenylpolysiloxane, 25 m × 0.32 mm × 0.52 μm) using He as carrier gas was used.

4.1. Catalysts preparation

4.1.1. Preparation of MgO [6a]
A sample of $MgSO_4$ (1 mol, 120.3 g) was dissolved in distilled water (1 l) at 30°C. Then, 400 ml of a 25% ammoniac solution were added over 100 min under agitation. The resulting mixture was left for 20 h in order to allow the formed $Mg(OH)_2$ to precipitate. The $Mg(OH)_2$ was then filtered off and washed with distilled water until the neutrality of the filtrate is measured. The resulting material was then dried in oven at 130°C to give 33.9 g of a white powder (58.1% yield).

In a second period, 10 g of $Mg(OH)_2$ were activated by the 'addition' of a 1.4 M solution of $Mg(NO_3)_2$ in distilled water (12 ml). Then the 'wet' material was calcinated in air at 600°C for 6 h to give 7.25 g of a fine white powder (99.3% yield). The MgO thus obtained present a specific surface of $S = 44.2$ m^2 g^{-1}.

4.1.2. General procedure for the preparation of the Pd/MO_x [5]
A solution of Pd(acac)$_2$ in benzene (made from 143.1 mg of Pd(acac)$_2$ in 15 ml of benzene) was added to 1 g of MO_x. The mixture was then stirred for 1 h at room temperature (r.t.) before the benzene is evaporated to give a slightly yellow material. This was reduced under H_2 flow (150 ml min^{-1}) in a U-reactor at 70°C for 2 h to give the desired Pd/MO_x catalyst as a grey material.

AAS determinations for the different Pd/MO_x: Pd/MgO, Pd = 4.3% wt; Pd/TiO_2, Pd = 4.4% wt; Pd/ZrO_2, Pd = 5.5% wt.

4.1.3. Preparation of the [Pd(NH$_3$)$_4$]NaY catalyst [9]
A 0.1 M ammoniac solution of [Pd(NH$_3$)$_4$]Cl$_2$ (47 ml), prepared from PdCl$_2$ and a 25% ammoniac solution, was added dropwise to a suspension of the NaY (4.5 g) into bi-distilled water (100 ml/g zeolite). The mixture was stirred for 24 h at r.t. and the exchanged zeolite was filtered off and washed until no trace of chloride was detected in the filtrate (AgNO$_3$ test). Then the zeolite was allowed to dry at room temperature to give the entrapped [Pd(NH$_3$)$_4$]$^{2+}$NaY as a slightly yellow material. The [Pd(NH$_3$)$_4$]$^{2+}$NaY was then stored under an argon atmosphere to prevent a variation of the hydration. The AAS determination gave 7 ± 0.5% wt. Pd.

4.1.4. Preparation of Pd(II)–NaY [9]
The above prepared [Pd(NH$_3$)$_4$]$^{2+}$NaY was calcinated in a U-tube reactor under pure O_2 flow (180 ml min^{-1}) using a heating rate of 2 K min^{-1} from r.t. to 500°C. The temperature was maintained at 500°C for 30 min and the reactor was cooled at r.t. under a flow of argon to give the Pd(II)–NaY as a tabac-coloured powder. The Pd(II)–NaY was then stored under an argon atmosphere to prevent hydration. The AAS determination gave 7 ± 0.5% wt. Pd.

4.1.5. Preparation of the Pd(0)–NaY [9]

The above prepared Pd(II)–NaY was reduced in a U-reactor under pure H_2 flow (70 ml min^{-1}) using a heating rate of 28 K min^{-1} from r.t. to 350°C. The temperature was maintained at 500°C for 15 min and the reactor was cooled at r.t. under a flow of argon to give the Pd(0)–NaY as a black powder. The Pd(0)–NaY was then stored under an argon atmosphere to prevent hydration and re-oxidation. The AAS determination gave $7 \pm 0.5\%$ wt. Pd.

4.2. Catalytic activity

Catalytic reactions were carried out in pressure tubes under argon. The Pd catalysts were transferred under Ar. The qualitative and quantitative analysis of the reactants and the products was made by GLC. Conversion and selectivity are represented by GLC yields (= relative area of GLC signals referred to an internal standard calibrated to the corresponding pure compound, $\Delta_{rel} = \pm 10\%$).

4.2.1. General procedure for the first run and the recycling of the catalysts

A total of 10 mmol of aryl bromide, 20 mmol of amine, 12 mmol of base and 1 mol% of Pd (as heterogeneous catalyst, the amount in g of catalyst depending on the Pd loading) were introduced in a pressure tube under argon. A total of 6 ml of dry toluene previously deaerated were added and the mixture was further deaerated by an argon flow for 5 min. The reactor was then placed in a pre-heated oil bath at 135°C for 20 h with vigorous stirring and then cooled to r.t. before the reaction mixture was analysed by GLC.

For the recycling studies, a catalyst issue from a first run was used. After separation of the reaction mixture, it was washed with toluene and CH_2Cl_2 in order to remove all adsorbed organic substrates and dried at r.t.

For the studies concerning the influence of the Pd concentration, the same procedure was used, and the amount of catalyst was adapted in order to obtain 0.2, 1, or 5 mol% Pd.

4.2.2. GLC analysis

A homogeneous 3 ml sample of the reaction mixture was sampled and quenched with 5 ml water in a test tube. The layers were shortly but vigorously mixed, and the organic layer was separated. It was dried over MgSO$_4$ and filtered through a cotton pad. The resulting dry organic layer was then analysed by GLC or GLC–MS. GLC rate program: AS 100 constant pressure (130 kPa): 2 min at 100°C, heating at 15°C min^{-1} up to 170°C, 2 min at 170°C, heating at 35°C min^{-1} up to 240°C, 10 min at 240°C, heating at 50°C min^{-1} up to 270°C and 2 min at 270°C.

4.2.3. Purification of the aniline derivatives

When possible, *para*-products of the amination reactions were isolated and analysed by standard methods (^{1}H- and ^{13}C-NMR). We give here the purification methods used, followed by the characterisation data.

After separation of the heterogeneous catalyst, the reaction mixture was carefully evaporated. The residue was dissolved in CH_2Cl_2 (50 ml) and washed with water (3 × 20 ml). The organic layer was then dried over activated MgSO$_4$ and carefully evaporated. The residue was then purified by chromatography over silica gel (50 g SiO$_2$ g^{-1} organic mixture, SiO$_2$ Merck Type 7754 70–230 mesh, 60 Å) eluting with a mixture of pentane:ethyl acetate, 30:1 to give the *para*-aniline derivative. Eventually another chromatography on silica was realised in order to obtain a higher purity. The purity of the *para*-products was estimated by GLC to be $\geq 90\%$.

4.2.4. Characterisation of the aniline derivatives of piperidine: p-RC$_6$H$_4$NC$_5$H$_{10}$

4.2.4.1. Data for R = H, isolated yield 61% as yellow oil.
^{1}H-NMR, CDCl$_3$, 400.13 MHz: 7.41 (dd, $^{3}J = 8.9$ Hz and $^{3}J = 7.5$ Hz, 2H, m-C$_6$$\underline{H}_5$N); 7.10 (d, $^{3}J = 8.9$ Hz, 2H, o-C$_6$$\underline{H}_5$N); 6.99 (t, $^{3}J = 7.5$ Hz, 1H, p-C$_6$$\underline{H}_5$N); 3.31 (m, 4H, NC$\underline{H}_2$); 1.87 (m, 4H, NCH$_2C\underline{H}_2$); 1.74 (m, 2H, NCH$_2CH_2C\underline{H}_2$). ^{13}C-NMR, CDCl$_3$, 100.62 MHz: 152.06 (C–N, $\underline{C}_6$H$_5$N); 128.79 (m-$\underline{C}_6$H$_5$N); 118.98 (p-$\underline{C}_6$H$_5$N); 116.33 (o-$\underline{C}_6$H$_5$N); 50.47 ($\underline{C}$H$_2$N); 25.71 ($\underline{C}$H$_2$CH$_2$N); 24.18 ($\underline{C}$H$_2$CH$_2$CH$_2$N). C$_{11}$H$_{15}$N, M_w 161.12. MS: m/z (%): [M$^+$] 160 (25), [M$^+$ − C$_4$H$_8$] 104 (42).

4.2.4.2. Data for R = CH$_3$, isolated yield 63% as a slightly yellow oil.
^{1}H-NMR, CDCl$_3$, 400.13 MHz: 6.90 (d, $^{3}J = 9.0$ Hz, 2H, m-C$_6$$\underline{H}_4$N); 6.69 (d, $^{3}J = 9.0$ Hz, 2H, o-C$_6$$\underline{H}_4$N); 3.42 (m, 4H, NC$\underline{H}_2$); 2.71 (s, 3H, C$\underline{H}_3$); 1.92 (m, 4H, NCH$_2C\underline{H}_2$); 1.81 (m, 2H, NCH$_2CH_2C\underline{H}_2$). ^{13}C-NMR, CDCl$_3$, 100.62 MHz: 147.66 (C–N, $\underline{C}_6$H$_4$N); 128.91 (m-$\underline{C}_6$H$_5$N); 116.27 (p-$\underline{C}_6$H$_4$N); 112.43 (o-$\underline{C}_6$H$_5$N); 54.02 ($\underline{C}$H$_2$N); 28.01 ($\underline{C}$H$_2$CH$_2$N); 24.96 ($\underline{C}$H$_2$CH$_2$CH$_2$N); 21.78 ($\underline{C}$H$_3$). C$_{12}$H$_{17}$N, M_w 175.14. MS: m/z (%): [M$^+$] 174 (21), [M$^+$ − C$_4$H$_8$] 119 (36), [M$^+$ − C$_5$H$_{10}$N] 90 (19).

4.2.4.3. Data for R = F, isolated yield 34% as a light orange oil.
^{1}H-NMR, CDCl$_3$, 400.13 MHz: 7.09 (d, $^{3}J = 8.9$ Hz, 2H, m-C$_6$$\underline{H}_4$N); 6.85 (d, $^{3}J = 8.9$ Hz, 2H, o-C$_6$$\underline{H}_4$N); 3.34 (m, 4H, NC$\underline{H}_2$); 1.89 (m, 4H, NCH$_2C\underline{H}_2$); 1.78 (m, 2H, NCH$_2CH_2C\underline{H}_2$). ^{13}C-NMR, CDCl$_3$, 100.62 MHz: 157.62 (C–F, p-$\underline{C}_6$H$_4$N); 148.12 (C–N, $\underline{C}_6$H$_4$N); 116.42 (m-$\underline{C}_6$H$_5$N); 114.79 (o-$\underline{C}_6$H$_5$N); 54.72 ($\underline{C}$H$_2$N); 27.29 ($\underline{C}$H$_2$CH$_2$N); 25.97 ($\underline{C}$H$_2$CH$_2$CH$_2$N); 21.78 ($\underline{C}$H$_3$). C$_{11}$H$_{14}$NF, M_w 179.11. MS: m/z (%): [M$^+$] 178 (29), [M$^+$ − F] 159 (72); [M$^+$ − C$_4$H$_8$] 122 (49), [M$^+$ − C$_5$H$_{10}$N] 94 (16).

4.2.4.4. Data for R = OCH₃, isolated yield 39% as a yellow oil. ^{1}H-NMR, CDCl$_3$, 400.13 MHz: 6.79 (d, $^3J = 9.0$ Hz, 2H, *m*-C$_6$H$_4$N); 6.46 (d, $^3J = 9.0$ Hz, 2H, *o*-C$_6$H$_4$N); 3.92 (m, 4H, NCH$_2$); 3.34 (s, 3H, CH$_3$O); 1.87 (m, 4H, NCH$_2$CH$_2$); 1.74 (m, 2H, NCH$_2$CH$_2$CH$_2$). ^{13}C-NMR, CDCl$_3$, 100.62 MHz: 160.02 (*p*-C$_6$H$_4$N); 151.08 (C–N, C$_6$H$_4$N); 117.02 (*m*-C$_6$H$_5$N); 114.29 (*o*-C$_6$H$_5$N); 55.96 (CH$_3$); 54.27 (CH$_2$N); 26.97 (CH$_2$CH$_2$N); 25.92 (CH$_2$CH$_2$CH$_2$N). C$_{12}$H$_{17}$NO, M_w 191.13. MS: *m/z* (%): [M$^+$] 191 (33), [M$^+$ − CH$_3$] 176 (35); [M$^+$ − C$_4$H$_8$] 135 (52), [M$^+$ − C$_5$H$_{10}$N] 121 (12).

4.2.4.5. Data for R = NO₂, isolated yield 41% as an orange viscous oil. ^{1}H-NMR, CDCl$_3$, 400.13 MHz: 8.07 (d, $^3J = 9.0$ Hz, 2H, *m*-C$_6$H$_4$N); 6.87 (d, $^3J = 9.0$ Hz, 2H, *o*-C$_6$H$_4$N); 3.32 (m, 4H, NCH$_2$); 1.91 (m, 4H, NCH$_2$CH$_2$); 1.81 (m, 2H, NCH$_2$CH$_2$CH$_2$). ^{13}C-NMR, CDCl$_3$, 100.62 MHz: 150.67 (C–N, C$_6$H$_4$N); 141.47 (*p*-C$_6$H$_4$N); 125.15 (*m*-C$_6$H$_5$N); 115.14 (*o*-C$_6$H$_5$N); 54.02 (CH$_2$N); 27.28 (CH$_2$CH$_2$N); 25.92 (CH$_2$CH$_2$CH$_2$N). C$_{11}$H$_{14}$N$_2$O$_2$, M_w 206.11. MS: *m/z* (%): [M$^+$] 205 (28); [M$^+$ − NO$_2$] 159 (49); [M$^+$ − C$_4$H$_8$] 150 (62).

4.2.4.6. Data for R = CH₃CO, isolated yield 36% as an orange viscous oil. ^{1}H-NMR, CDCl$_3$, 400.13 MHz: 7.79 (d, $^3J = 8.3$ Hz, 2H, *m*-C$_6$H$_4$N); 6.92 (d, $^3J = 8.3$ Hz, 2H, *o*-C$_6$H$_4$N); 3.34 (m, 4H, NCH$_2$); 1.89 (m, 4H, NCH$_2$CH$_2$); 2.48 (s, 3H, CH$_3$); 1.77 (m, 2H, NCH$_2$CH$_2$CH$_2$). ^{13}C-NMR, CDCl$_3$, 100.62 MHz: 196.56 (CO); 149.92 (C–N, C$_6$H$_4$N); 129.63 (*m*-C$_6$H$_5$N); 124.92 (*p*-C$_6$H$_4$N); 114.33 (*o*-C$_6$H$_5$N); 51.09 (CH$_2$N); 26.04 (CH$_2$CH$_2$N); 25.12 (CH$_2$CH$_2$CH$_2$N); 26.27 (CH$_3$CO). C$_{13}$H$_{17}$NO, M_w 203.13. MS: *m/z* (%): [M$^+$] 202 (32); [M$^+$ − CH$_3$] 187 (52); [M$^+$ − CH$_3$CO] 159 (68); [M$^+$ − C$_4$H$_8$] 146 (62).

4.2.5. Characterisation of the aniline derivatives of the diethyl amine: p-RC₆H₄N(C₂H₅)₂

4.2.5.1. Data for R = H, isolated yield 52% as a slightly yellow oil. ^{1}H-NMR, CDCl$_3$, 400.13 MHz: 7.35 (m, 2H, C$_6$H$_5$N); 6.82 (m, 3H, C$_6$H$_5$N); 3.43 (m, 4H, NCH$_2$); 1.26 (m, 6H, NCH$_2$CH$_3$). ^{13}C-NMR, CDCl$_3$, 100.62 MHz: 147.53 (C–N, C$_6$H$_5$N); 128.98 (*m*-C$_6$H$_5$N); 115.20 (*p*-C$_6$H$_5$N); 111.66 (*o*-C$_6$H$_5$N); 44.03 (CH$_2$N); 12.32 (CH$_3$CH$_2$N). C$_{10}$H$_{15}$N, M_w 149.12. MS: *m/z* (%): [M$^+$] 149 (25), [M$^+$ − CH$_3$] 134 (42), [M$^+$ − C$_2$H$_5$] 120 (21), [M$^+$ − C$_2$H$_5$ − CH$_2$] 106 (47), [M$^+$ − N(C$_2$H$_5$)$_2$ + H] 77 (69).

4.2.5.2. Data for R = CH₃, isolated yield 47% as a slightly yellow oil. ^{1}H-NMR, CDCl$_3$, 400.13 MHz: 7.18 (d, $^3J = 8.5$ Hz, 2H, *m*-C$_6$H$_4$N); 6.58 (d, $^3J = 8.5$ Hz, 2H, *o*-C$_6$H$_4$N); 3.28 (m, 4H, NCH$_2$); 2.41 (s, 3H, CH$_3$); 1.22 (m, 6H, NCH$_2$CH$_3$). ^{13}C-NMR, CDCl$_3$, 100.62

MHz: 147.66 (C–N, C$_6$H$_4$N); 128.91 (*m*-C$_6$H$_5$N); 116.26 (*p*-C$_6$H$_4$N); 112.43 (*o*-C$_6$H$_5$N); 44.08 (CH$_2$N); 21.78 (CH$_3$); 12.40 (CH$_3$CH$_2$N). C$_{11}$H$_{17}$N, M_w 163.14. MS: *m/z* (%): [M$^+$] 163 (28), [M$^+$ − CH$_3$] 148 (37), [M$^+$ − C$_2$H$_5$] 134 (35), [M$^+$ − C$_2$H$_5$ − CH$_2$] 120 (68).

The other *para*-products described in this paper could not be isolated as a pure compound. We could isolate the mixture of the *para*- and *meta*-aniline derivatives with a 'purity' ≥ 88%. The NMR of this mixture was recorded in order to have an additional analytical method for the determination of the ratio *para*-/*meta*-. The mixture was then used to calibrate the GLC and the GLC–MS in order to determine GLC yields by the internal standard method. The MS obtained by GLC–MS for the *para*-isomer are given below.

4.2.5.3. Data for R = CH₃O. C$_{11}$H$_{17}$NO, M_w 179.13. MS: *m/z* (%): [M$^+$] 179 (25), [M$^+$ − CH$_3$] 163 (32), [M$^+$ − C$_2$H$_5$] 149 (42), [M$^+$ − C$_2$H$_5$ − CH$_2$] 135 (67), [M$^+$ − N(C$_2$H$_5$)$_2$ + H] 107 (71).

4.2.5.4. Data for R = F. C$_{10}$H$_{14}$NF, M_w 167.11. MS: *m/z* (%): [M$^+$] 166 (21), [M$^+$ − F] 147 (31), [M$^+$ − C$_2$H$_5$] 137 (39), [M$^+$ − C$_2$H$_5$ − CH$_2$] 123 (71).

4.2.5.5. Data for R = NO₂. C$_{10}$H$_{14}$N$_2$O$_2$, M_w 194.11. MS: *m/z* (%): [M$^+$] 194 (18), [M$^+$ − NO$_2$] 148 (35), [M$^+$ − C$_2$H$_5$] 165 (32), [M$^+$ − C$_2$H$_5$ − CH$_2$] 151 (69).

4.2.5.6. Data for R = CH₃CO. C$_{12}$H$_{17}$NO, M_w 191.13. MS: *m/z* (%): [M$^+$] 190 (17), [M$^+$ − CH$_3$] 175 (41), [M$^+$ − C$_2$H$_5$] 161 (36), [M$^+$ − CH$_3$CO] 148 (62), [M$^+$ − C$_2$H$_5$ − CH$_2$] 147 (53).

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