Amination of benzylic C–H bonds by aryl azides catalysed by Co^{II}(porphyrin) complexes. A new reaction leading to secondary amines and imines†

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Co^{II}(porphyrin) complexes catalyse the reaction of aromatic azides, ArN$_3$, with hydrocarbons containing a benzylic group, R^{1}R^{2}R^{3}CH, to give the corresponding amines, R^{1}R^{2}R^{3}C-NHAr. When at least one of the R^1–R^3 substituents is hydrogen, the catalytic reaction proceeds further to give the imines R^{1}R^{2}C=NAr in good yields.

The development of metal-mediated intermolecular nitrogen atom transfer reactions, such as the amination of saturated C–H bonds, is a topic of high current interest.[1–8] Reasonably good results have only been obtained by using [*N*-(*p*-tolylsulfonyl)-imino]phenyliodinane (PhI=NTs) and related derivatives as the nitrogen source. However these compounds can only be obtained from the corresponding sulfonamides.[9] Recently, we have developed a methodology for the intermolecular allylic amination of unactivated olefins by nitroarenes in the presence of CO and ruthenium complexes as catalysts.[10] However, in these reactions only the allylic C–H bond of an olefin could be functionalised.

Aromatic azides, ArN$_3$, represent a wide class of easily synthesised compounds. We have recently reported that porphyrin complexes of cobalt(II) are able to activate aromatic azides, for the amination under mild conditions of allylic C–H bonds[11] and we report here that the same catalytic system also results in the more difficult activation of the C–H bonds of saturated organic compounds, to give secondary amines and imines. The use of organic azides as aminating agents extends considerably the number of nitrogen containing organic compounds that can be potentially obtained in catalytic reactions. Such a reaction has never been reported before. It should also be pointed out that although the condensation of ketones with primary amines is a textbook route to ketimines, the procedure is sometimes not practical for the synthesis of aromatic ketimines.[12,13]

By reaction of hydrocarbons containing a benzylic group with *p*-nitrophenyl azide catalysed by Co(II)(porphyrin) derivatives, the corresponding amines have been obtained [eqn. (1)].

$$\mathrm{R^1R^2R^3CH + ArN_3 \xrightarrow[-N_2]{Co(II)(porphyrin)} R^1R^2R^3C\text{-}NHAr} \qquad (1)$$

When at least one of the R^1–R^3 substituents is hydrogen, the catalytic reaction proceeds further to give the corresponding imines [eqn. (2)]:

$$\mathrm{R^1R^2HC\text{-}NHAr + ArN_3 \xrightarrow[-N_2]{Co(II)(porphyrin)} R^1R^2C{=}NAr + ArNH_2} \qquad (2)$$

Reaction (2) has been independently observed by preforming the amines PhCH$_2$-NHC$_6$H$_4$Y-*p* and reacting them with *p*-YC$_6$H$_4$N$_3$ (Y = NO$_2$, Cl, OMe) in the presence of the catalyst. The reaction quantitatively gives one equivalent of imine and one of *p*-YC$_6$H$_4$NH$_2$ *per* equivalent of amine while no reaction is observed in the absence of the catalyst.

Main by-products of reaction (1) are the azide-derived aniline and the diarylazo compound.

Besides Co(TPP) (TPP = dianion of *meso*-tetraphenylporphyrin) even Co(*p*-MeOTPP) [*p*-MeOTPP = dianion of *meso*-tetrakis(4-methoxyphenyl)porphyrin], Co(*p*-ClTPP) [*p*-ClTPP = dianion of *meso*-tetrakis(4-chlorophenyl)porphyrin] and Co(OEP) (OEP = dianion of β-octaethylporphyrin) were tested as catalysts. Representative results are reported in Table 1. Note that the stoichiometry in eqns. (1) and (2) implies that a maximum yield of 50% can be obtained with respect to the aryl azide when the imine is the product.

Steric hindrance lowers the selectivity, but does not prevent the reaction and with *sec*-butylbenzene, the amine was formed in 10–15% yield (Table 1).

The reaction is sensitive to the nature of the azide employed. With toluene as substrate and Co(TPP) as catalyst, electron-withdrawing substituents in the *para* position of the aromatic azide not only increase the yields of the imine, but also notably accelerate the reaction (Table 2).

To clarify the mechanism of this reaction we performed some stoichiometric reactions and a kinetic study. When Co(TPP) was reacted with excess *p*-O$_2$NC$_6$H$_4$N$_3$ at 75 °C in benzene the diazoarene *p*-O$_2$NC$_6$H$_4$N=NC$_6$H$_4$NO$_2$-*p* was catalytically obtained. When the same reaction was repeated at a lower temperature in C$_6$D$_6$, a new complex was observed whose ^{1}H NMR signals are identical to the ones of the product obtained by reaction of Co(TPP) with *p*-O$_2$NC$_6$H$_4$N=NC$_6$H$_4$NO$_2$-*p*. Observation of only one set of resonances for the aryl groups of the ArN=NAr moiety of this complex indicates that the aromatic groups of the 'ArN' moieties are equivalent. According to these preliminary results and to some similar data reported in the literature,[14] we propose that the reaction product of Co(TPP) with ArN$_3$ is the complex [Co(TPP)]$_2$(ArN=NAr), having an aryldiazene ligand bridging two porphyrin complexes.

A kinetic study was also performed employing *p*-O$_2$NC$_6$H$_4$N$_3$ and toluene as substrates and Co(TPP) as catalyst. The kinetics are first order in Co(TPP) and in azide, but show a saturation behaviour with respect to toluene concentration, the other solvent being benzene (Fig. 1, ESI†). When the selectivity was examined as a function of time for different toluene–benzene mixtures the following observations were made. (a) The amount of imine and *p*-nitroaniline grow at the same rate, in accord with the stoichiometry reported in eqns. (1) and (2). (b) The rate of formation of *p*-O$_2$NC$_6$H$_4$N=NC$_6$H$_4$NO$_2$-*p* is proportional to the one of the imine for each reaction, indicating the same dependency from the azide concentration. (c) The rate of formation (and the final selectivity) of imine increases with the toluene concentration (up to 100% toluene in the solvent mixture) while the one of the diarylazo compound decreases in the same series, indicating a common intermediate and competition for the formation of the two products.

All of the aforementioned data can be accounted for by the mechanism shown in Scheme 1.

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† Formulae of the catalysts and of the organic products and Fig. 1, the influence of the toluene concentration on the value of k_{app} are available as supplementary data. For direct electronic access see http://www.rsc.org/suppdata/cc/b0/b006136k

Table 1 Catalytic amination of benzylic compounds by p-$O_2NC_6H_4N_3$

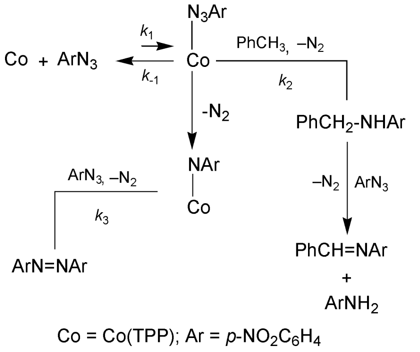
Entry	Catalyst	Substrate	t/h^a	Imine sel. (%)^b	Amine sel. (%)^b	p-Nitroaniline sel. (%)^b	p-Nitrophenylazobenzene sel. (%)^b
1^c	Co(TPP)	Isopropylbenzene	1.5	—	15.8^d(**A**)	23^d	8^d
2^c	Co(OEP)	Isopropylbenzene	6	—	27.2^d(**A**)	28^d	14^d
3^c	Co(p-MeOTPP)	Isopropylbenzene	2	—	42.3^d(**A**)	24^d	5^d
4^c	Co(p-ClTPP)	Isopropylbenzene	5.5	—	52.7^d(**A**)	20^d	15^d
5^c	Co(TPP)	*sec*-Butylbenzene	4	—	15.0^d(**B**)	8^d	21^d
6^c	Co(OEP)	*sec*-Butylbenzene	5	—	13.6^d(**B**)	24^d	10^d
7^c	Co(p-MeOTPP)	*sec*-Butylbenzene	5	—	10.3^d(**B**)	23^d	11^d
8^c	Co(p-ClTPP)	*sec*-Butylbenzene	3	—	12.2^d(**B**)	40^d	10^d
9^c	Co(TPP)	Ethylbenzene	3	25^e(**C**)	13^e(**D**)	29^e	11^e
10^c	Co(OEP)	Ethylbenzene	1	18^e(**C**)	22^e(**D**)	21^e	11^e
11^c	Co(p-MeOTPP)	Ethylbenzene	3.5	24^e(**C**)	22^e(**D**)	26^e	10^e
12^c	Co(p-ClTPP)	Ethylbenzene	4	19^e(**C**)	25^e(**D**)	33^e	2^e
13^c	Co(TPP)	Diphenylmethane	3	11.4^e(**E**)	55.2^e(**F**)	24^e	—
14^f	Co(TPP)	Fluorene	6	39.2^d(**G**)	—	41^d	12^d
15^f	Co(OEP)	Fluorene	2.5	41.4^d(**G**)	—	43^d	4^d
16^f	Co(p-MeOTPP)	Fluorene	5	36.9^d(**G**)	—	42^d	8^d
17^f	Co(p-ClTPP)	Fluorene	8	38.4^d(**G**)	—	40^d	9^d
18^f	Co(TPP)	9,10-Dihydroanthracene	12	32^g(**H**)	—	46^e	—

^{a} Time required to reach the complete conversion of the aromatic azide. ^{b} Calculated with respect to converted azide. ^{c} Reactions carried out in the substrate as solvent, T = 110 °C with cat.–azide = 1:100. ^{d} Determined by flash chromatography. ^{e} Determined by gas-chromatographic analysis. ^{f} Reactions carried out in refluxing benzene, with cat.–azide–hydrocarbon = 1:100:100. ^{g} Determined by gas-chromatographic analysis after hydrolysis of the diimine (**H**) to the diketone (**I**). The diimine (**H**) can be reduced in the same pot to the diamine (**J**) by $NaBH_4$ (28% total yield).

Table 2 Amination of toluene by p-$YC_6H_4N_3$ catalysed by Co(porphyrin)^a

Entry	Catalyst	Y	t/h^b	p-$YC_6H_4N{=}CHC_6H_5$ sel. (%)^c	p-$YC_6H_4NH_2$ sel. (%)^c	p-$YC_6H_4N{=}NC_6H_4Y$-p sel. (%)^c
1	Co(TPP)	NO_2	2	23.0(**K**)	28.0	22.0
2	Co(TPP)	Cl	5	28.0(**K**)	29.0	18.0
3	Co(TPP)	OMe	10	10.0(**K**)	14.0	25.0
4	Co(p-MeOTPP)	Cl	3	35.0(**K**)	36.0	22.0
5	Co(p-ClTPP)	Cl	2	25.0(**K**)	28.0	16.0

^{a} Reactions carried out in refluxing toluene as solvent, with cat.–azide = 1:100. ^{b} Time required to reach the complete conversion of the azide. ^{c} Determined by gas chromatographic analysis.



Scheme 1

Application of the steady state approximation to the intermediate aryl azide–porphyrin complex leads to the equation: $-d[ArN_3]/dt = k_{app}[Co(TPP)][ArN_3]$, with $k_{app} = 2k_1(k_2[\text{toluene}] + k_3)/(k_2[\text{toluene}] + k_3 + k_{-1})$, which nicely fits the data (line in Fig. 1, ESI†).‡

Finally, it is interesting to note that the reaction of p-$O_2NC_6H_4N_3$ with toluene catalysed by Co(porphyrin) is practically suppressed when carried out in the presence of the spin trap TEMPO. Since there is no reaction between Co(porphyrin) and TEMPO in the absence of the azide, this suggests that the unpaired spin density of Co(porphyrin) is partly localised on the azide nitrogen atoms in the intermediate complex.

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Notes and references

‡ The fitting affords the value k_1 = 2.6 10^{-2} $s^{-1}M^{-1}$, but, due to the form of the equation and number of data points, different groups of values for k_2, k_3, and k_{-1} give equally good fittings and only the ratios k_2/k_3 = 2.3 and k_{-1}/k_3 = 0.20 can be confidently determined.

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