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Impregnated palladium on magnetite as catalyst for multicomponent reductive amination reactions and other related reducing processes

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ABSTRACT

The impregnated palladium on magnetite catalyst is a versatile system for different reduction processes using inexpensive polymehtylhydrosiloxane, including multicomponent reductive amination reactions, and aldehyde, imine, sulfinimide and sulfoxide reductions. This catalyst avoids the use of any type of expensive and quite expensive organic ligand, showing excellent yields, under mild reaction conditions. The catalyst is easily removed from the reaction medium, just by using a magnet. The catalytic system is very selective permitting the discrimination between ketones and aldehydes in the reductive amination process.

1. Introduction

The multicomponent[1] reductive amination of carbonyl compounds is very attractive in organic synthesis because ketones and aldehydes can be transformed directly into the corresponding primary or secondary amines,[2] with hydrogen and borohydride derivatives being the common source of reductive agent. In general, it is necessary to use an excess of amines in order to limit or prevent the competitive reduction of the carbonyl compound. In addition, the reduction agents are expensive, highly toxic, explosive, flammable and they must be handled with care and frequently generate undesirable wasteful salts.

Polymethylhydrosiloxane (PMHS) has been reported as air and moisture stable, inexpensive, non-toxic, versatile and widely used reducing agent in organic synthesis,[3] with minimal or non-reducing ability in the absence of a catalyst. This fact has made this reagent an ideal reductive agent since it could partially overcome the drawbacks of the classical reductive amination protocols. Besides the aforementioned possible advantage, its use for this process has been scarcely tested in homogeneous conditions,[4,5] with the only heterogeneous catalyst tested (palladium on charcoal) giving very disappointed results (yields lower than 60%).[4]

On the other hand, we have recently prepared, by impregnation[6] on magnetite,[7] different catalysts derived from copper,[8] ruthenium[9] and palladium.[10,11] With this study we would like to show that palladium impregnated on magnetite can be used as an excellent heterogeneous catalyst for multicomponent reductive amination reactions as well as in other reduction processes.

2. Results and discussion

2.1. Multicomponent reductive amination of aldehydes

First of all, we explored the most complicated multicomponent amination process and, in order to optimize the reaction conditions, we studied the reaction between a poor nucleophilic amine, such as aniline (**1a**), with benzaldehyde (**2a**), both in strict stoichiometric amounts, and PMHS to give the corresponding benzylated aniline **3a**, as depicted in Table 1. After a week, the reaction rendered a poor yield of the expected product **3a** at 75 °C using only nano-particles of magnetite. The catalyzed reaction with different impregnated metallic systems, including those derived from cobalt, nickel, copper and ruthenium gave miserable chemical yields after a two days reaction, with the use of bimellatic systems not showing any important difference. However, the reaction using the palladium derivative gave the expected product in only 3 h with an excellent yield (Table 1, entry 6).

Once the best catalyst was established, we focused on the optimization of other parameters of the reaction (Table 2).

As it was expected, the reaction failed in the absence of reducing silane agent. The yield was even modest in the case of using stoichiometric amount of PMHS, and meanwhile the use of 2 equiv of

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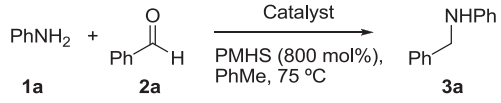
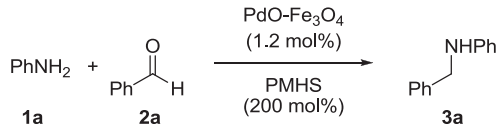
Table 1
Catalyst optimization



Entry	Cat. (mol %)	t (h)	Yield **3a** (%)[a]
1	Fe_3O_4 (65)	168	18
2	CoO–Fe_3O_4 (1.4)	48	2
3	NiO–Fe_3O_4 (1.0)	48	3
4	CuO–Fe_3O_4 (1.3)	48	2
5	Ru_2O_3–Fe_3O_4 (1.4)	48	3
6	PdO–Fe_3O_4 (1.2)	3	96
7	Ni(II)–Cu–Fe_3O_4 (0.9–1.1)	48	4
8	Pd(II/0)–Cu–Fe_3O_4 (1.5–0.8)	48	9

[a] Isolated yields after column chromatography (silica gel: hexane/ethyl acetate).

Table 2
Reaction-condition optimization



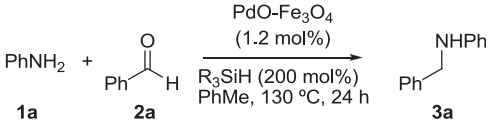
Entry	Solvent	T (°C)	t (h)	Yield **3a** (%)[a]
1	PhMe	75	5[b]	2
2	PhMe	75	2[c]	64
3	PhMe	75	0.25	97
4	PhMe	75	0.25[d]	96
5	PhMe	25	0.25	97
6	PhMe	130	0.25	93
7	PhMe[e]	25	1	13
8[f]	PhMe	25	0.25	95
9[g]	PhMe	25	1	45
10	—	25	1	15
11	MeCN	25	1	20
12	1,4-Dioxane	25	0.25	92
13[h]	PhMe	25	0.5	10
14[i]	PhMe	25	0.25	94
15[j]	PhMe	25	0.5	8
16[k]	PhMe	25	3	2

[a] Isolated yields after column chromatography (silica gel: hexane/ethyl acetate).
[b] Reaction performed in absence of PMHS.
[c] Reaction performed using 100 mol % of PMHS.
[d] Reaction performed using 300 mol % of PMHS.
[e] Reaction performed using 2.4 mol % of catalyst.
[f] Reaction carried out using ten-fold solvent volume.
[g] Reaction performed using 0.2 mol % of catalyst.
[h] Reaction performed adding KF (400 mol %).
[i] Reaction performed adding PhCl (10 mol %).
[j] Reaction performed adding KF (400 mol %) and PhCl (10 mol %).
[k] Reaction performed adding camphorsulfonic acid (10 mol %).

reductant gave a satisfactory yield in only 15 min; the further increase of this amount did not produce any significant change (compare entries 1–4). The temperature did not seem to be very important since the same results were obtained independently of the temperature employed (from 25 to 130 °C). However, the dilution of the reaction (entry 7) and the decrease of the amount of the catalyst (entry 9) had a negative impact on the yields. The nature of solvent (or its absence) is also important, with the best results being obtained in either toluene or 1,4-dioxane (compare entries 5 and 10–12). Finally, we examined the possible activation of the silane reagent by the addition of KF,[12] chlorobenzene,[13] or camphorsulfonic acid,[14] but in all cases the results were far more inferior to those obtained in absence of silane activator.

Although the PMHS has many advantages as reducing agent compared with other silanes, we also tested other simple reagents to be sure of the previous results. The comparison of entry 6 in Table 2 with all results from Table 3 demonstrated that PMHS gave the best results.

Table 3
Silane reagent optimization



Entry	R_3SiH	Yield **3a** (%)[a]
1	$(EtO)_3SiH$	0
2	Ph_3SiH	55
3	Ph_2SiH_2	3

[a] Isolated yields after column chromatography (silica gel: hexane/ethyl acetate).

Once the optimal reaction conditions were established, the problem of recycling was examined. The catalyst recovered by a magnet from the reaction described in the entry 2 of Table 2 was washed with toluene and re-used under the same reaction conditions, obtaining the expected product **3a** in 72% yield. In the third re-use the yield was 57%, indicating that there is a small decrease in the activity of the catalyst, probably due to the adsorption of different salts on the surface of the catalyst (SiO_2). The XPS studies on the used catalyst showed the partial reduction from the initial palladium(II)[10] to a 1:4 mixture of Pd(II/0) species, respectively. To understand if the formed Pd(0) species was less reactive than the initial one, the initial palladium impregnated magnetite catalyst was reduced with $NaBH_4$ to produce Pd–Fe_3O_4.[15] The standard reaction using this reduced and impregnated palladium on magnetite gave the expected product **3a** with a similar yield (94%), albeit the reaction time should be increased up to 5 h. However, this recycled catalyst was ineffective, rendering compound **3a** in 14% yield in a second cycle after one day reaction time, pointing out a faster leaching of Pd(0) compare to Pd(II) nano-particles, which is also a possible explanation for the decrease on the catalytic activity of the initial Pd(II) system. Moreover, the XPS study of the recycled PdO–Fe_3O_4 showed the adsorption of silica (41%) at the surface (1 nm depth). Finally, the ICP-MS analysis of the reaction solution showed the presence of palladium (0.13% of the initial amount) and iron (0.001% of the initial amount). It should be pointed out that the nano-size distribution of the standard palladium oxide particles at the surface of the catalyst was about 65% between 2.0 and 3.5 nm (Fig. 1), whereas the reported size of the related reduced palladium particles was higher (5 nm).[15] Therefore, there are three phenomena, at least, which could make more difficult the recycling process: the partial reduction of palladium species, the incorporation of silica at the surface, and the leaching of palladium.

Once the best conditions were found (Table 2 entry 5), we conducted the study with other primary amines **1** and aldehydes **3** under these conditions (Table 4).

The obtained yields were independent of the aniline derivative used, as well as the presence of substituents with electron-donating or -withdrawing groups. Even the reaction gave an excellent result in the case of using aliphatic amines, with the use of a α-unbranched amine requiring longer reaction times (compare entries 1–8). However, when the reaction was performed with the very poor nucleophilic 2-pyridyl-amine, the reaction had to be heated up to 130 °C in order to obtain good results (entry 9). The reaction failed when the less nucleophilic 4-methylbenzenesulfonamide was used. The reaction could be carried out with any type of aromatic and aliphatic aldehydes with similar results (entries 10–14). Even 2-pyridylamine could react with different aldehydes only increasing the reaction temperature (entries 15–18). The selectivity of the

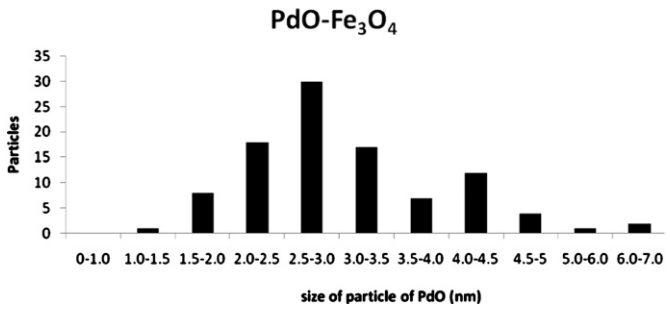
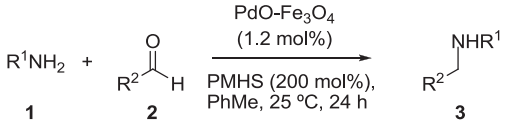


Fig. 1. Size of PdO particles in the catalyst.

Table 4
Impregnated palladium on magnetite catalyzes the multicomponent reductive amination process



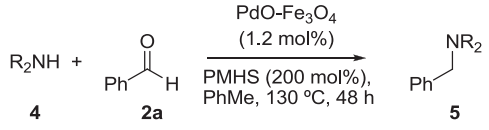
Entry	R^1	R^2	Product	Yield (%)[a]
1	Ph	Ph	**3a**	97
2	4-$MeOC_6H_4$	Ph	**3b**	95
3	2-$MeOC_6H_4$	Ph	**3c**	87
4	3-ClC_6H_4	Ph	**3d**	74
5	3,5-$(CF_3)_2C_6H_3$	Ph	**3e**	90
6	1-Naphthyl	Ph	**3f**	68
7	$(CH_2)_5CH$	Ph	**3g**	86
8	$Me(CH_2)_7$	Ph	**3h**	81[b]
9	2-Pyridyl	Ph	**3i**	15[b] (79)
10	Ph	1-Naphthyl	**3j**	91[c]
11	Ph	4-$MeOC_6H_4$	**3k**	19[b] (85)[c]
12	Ph	4-ClC_6H_4	**3l**	12[b] (95)
13	Ph	4-$MeCOC_6H_4$	**3m**	85
14	Ph	$(CH_2)_5CH$	**3n**	74[c]
15	2-Pyridyl	4-MeC_6H_4	**3o**	20[b] (77)
16	2-Pyridyl	4-$MeOC_6H_4$	**3p**	16[b] (87)
17	2-Pyridyl	2-$MeOC_6H_4$	**3q**	9[b] (86)
18	2-Pyridyl	4-ClC_6H_4	**3r**	11[b] (89)

[a] Isolated yields after column chromatography (silica gel: hexane/ethyl acetate). The yields after 7 days reaction at 130 °C appear in parenthesis.
[b] Yield after 7 days reaction time.
[c] Yield after 2 days reaction time.

catalyst was highlighted by the use of 4-acetylbenzaldehyde, since the reaction occurred exclusively through the most electrophilic aldehyde group (entry 13).

After the success obtained using primary amines, we studied the scope of the reaction using secondary amines. The protocol could be used for this type of amines only by increasing the reaction temperature, as it is depicted in Table 5. The reaction gave satisfactory yields for amines **5**, including acyclic and cyclic derivatives, albeit somehow higher for the later.

Table 5
Multicomponent reductive amination process using secondary amines



Entry	R_2	Product	Yield (%)[a]
1	$(PhCH_2)_2$	**5a**	62
2	$(^nBu)_2$	**5b**	71
3	$(CH_2)_2O(CH_2)_2$	**5c**	95
4	$(CH_2)_2CHMe(CH_2)_2$	**5d**	89

[a] Isolated yields after column chromatography (silica gel: hexane/ethyl acetate).

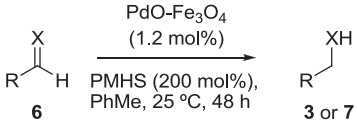
Finally, it should be pointed out that reproducibility in the preparation of the catalyst was very high, obtaining always values of palladium incorporation around 2.55–2.70%, The catalyst did not required any special type of treatment for its storage, as low temperature or inert atmosphere. For instance, the yield obtained in the preparation of compound **5d** using PdO–Fe_3O_4 was similar with the fresh-prepared catalyst (89%) and with the six-month old one (84%).

2.2. Other reduction processes

Encouraged by the previous successes, we examined other reducing process,[3] starting from the classical reduction of aldehydes.[16] This transformation has an important drawback and it is the over-reduction process that gives the corresponding alkane.[17] However, we anticipated that the impregnated palladium catalyst could be selective enough to stop the reaction after the initial hydrosilylation process. Thus, the reaction of different aromatic or aliphatic aldehydes rendered the expected alcohols **7** at room temperature with excellent yields (Table 5, entries 1–5).

Not only aldehydes but also simple imines[18] could reduce successfully using this protocol (Table 5, entry 6). Moreover, the reaction with a preformed sulfonimide derivative gave the expected sulfonamide **7f** with a modest yield, but this gives an idea of the broad scope of this catalyst to reduce different aldehyde derivatives (Table 6).

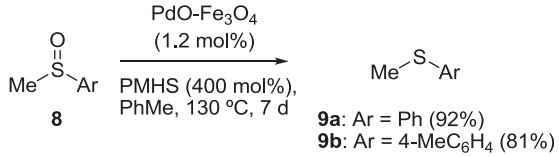
Table 6
Impregnated palladium on magnetite catalyzes the reduction of aldehyde and imine derivatives



Entry	R	X	Product	Yield (%)[a]
1	Ph	O	**7a**	92
2	4-$MeOC_6H_4$	O	**7b**	82
3	4-ClC_6H_4	O	**7c**	90
4	$(CH_2)_4CH$	O	**7d**	95
5	$Me(CH_2)_8$	O	**7e**	12
6	Ph	NPh	**3a**	99[b]
18	Ph	NSO_2Ph	**7f**	46

[a] Isolated yields after column chromatography (silica gel: hexane/ethyl acetate).
[b] Yield after 24 h reaction time.

The deoxygenative reduction[19] of sulfoxides **8** to give the corresponding sulfides **9** could also be performed by a catalyzed process using impregnated palladium on magnetite (Scheme 1). The reaction gave the expected products **9** with very good chemical yields.



Scheme 1. Reduction of sulfoxides.

3. Conclusion

In conclusion, impregnated palladium magnetite has shown to be an active and highly selective catalyst for different reducing processes using the air and moisture stable, inexpensive and non-toxic reducing agent polymehtylhydrosiloxane, including the multicomponent amination reaction, reduction of aldehydes,

simple imines, sulfonimides and sulfoxides. The catalyst is selective and permits the discrimination between two close electrophilic carbonyl groups, such as aldehydes and ketones.

4. Experimental section

4.1. General information

Melting points were obtained with a Reichert Thermovar apparatus. NMR spectra were recorded on a Bruker AC-300 (300 MHz for ^{1}H and 75 MHz for ^{13}C) using $CDCl_3$ as a solvent and TMS as internal standard for ^{1}H and ^{13}C; chemical shifts are given in δ (parts per million) and coupling constants (J) in Hertz. FT-IR spectra were obtained on a Nicolet Impact 400D spectrophotometer. Mass spectra (EI) were obtained at 70 eV on a Himazdu QP-5000 spectrometer, giving fragment ions in m/z with relative intensities (%) in parentheses. Thin layer chromatography (TLC) was carried out on Schleicher & Schuell F1400/LS 254 plates coated with a 0.2 mm layer of silica gel; detection by UV254 light, staining with phosphomolybdic acid [25 g phosphomolybdic acid, 10 g $Ce(SO_4)_2\cdot 4H_2O$, 60 mL of concentrated H_2SO_4 and 940 mL of H_2O]. Column chromatography was performed using silica gel 60 of 35–70 mesh. All reagents were commercially available (Acros, Aldrich, Fluorochem) and were used as received. The ICP-MS analyses were carried out on a Thermo Elemental VGPQ-ExCell spectrometer. The X-ray Fluorescence analyses were carried out on a PHILIPS MAGIX PRO (PW2400) X-ray spectrometer equipped with a rhodium X-ray tube and a beryllium window. The BET analyses were carried out on an automatic volumetric AUTOSORB-6 from Quantachrome and its degasser unit. N_2 at 77 K was used as gas. X-ray photoelectron spectroscopy analyses were carried out on a VG-Microtech Multilab 3000 equipped with a hemispheric electron analyzer with 9 channeltrons (pass energy between 2–200 eV) and an X-ray tube with Mg and Al anodes. TEM analyses were carried out on a JEOL JEM-2010 microscope.

4.2. Procedure for the PdO–Fe_3O_4 catalyst preparation

To a stirred solution of $PdCl_2$ (177 mg, 1 mmol), KCl (1 g, 13 mmol) in deionized water (120 mL) was added commercially available Fe_3O_4 (4 g, 17 mmol, powder <5 μm, BET area: 9.86 m^2/g). After 10 min at room temperature, the mixture was slowly basified with NaOH (1 M) until pH around 13. The mixture was stirred during one day at room temperature in air. After that, the catalyst was filtered and washed with deionized water (3×10 mL). The solid was dried at 100 °C during 24 h in a standard glassware oven, obtaining the expected catalyst: incorporation of palladium of 2.6% according to XRF; by XPS the palladium on the surface was determined as 24.8%; the BET area surface was 13.6 m^2/g.

4.3. General procedure for the reductive amination process

To a stirred solution of aldehyde (**2**, 1 mmol) in toluene (2 mL) were added PdO–Fe_3O_4 (50 mg, 1.2 mol % of Pd), PMHS (2 mmol, 0.12 mL) and the corresponding amine (**1** or **4**, 1 mmol). The resulting mixture was stirred at room temperature or at 130 °C until the end of reaction. The catalyst was removed by a magnet and the resulting mixture was quenched with water and extracted with EtOAc. The organic phases were dried over $MgSO_4$, followed by evaporation under reduced pressure to remove the solvent. The corresponding products **3** or **5** were purified by chromatography on silica gel (hexane/ethyl acetate).

*4.3.1. N-Benzylaniline (**3a**)*[9]. Pale yellow solid; mp 37–40 °C (hexane); IR (cm^{-1}): 3414, 1603; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.98 (s, br, 1H), 4.3 (s, 2H), 6.6–6.65, 6.65–6.75, 7.1–7.2, 7.25–7.4 (4m, 2, 1, 2 and 5H, respectively); ^{13}C NMR (75 MHz, $CDCl_3$): δ 48.2, 112.8 (2C), 117.5, 127.2, 127.5 (2C), 128.6 (2C), 129.2 (2C), 139.4, 148.1; EI-MS m/z: 184 (M^++1, 13%), 183 (M^+, 100), 182 (38), 180 (10), 106 (20), 91 (100), 77 (18), 65 (14).

*4.3.2. N-Benzyl-4-methoxyaniline (**3b**)*[9]. Brown oil; IR (cm^{-1}): 3405, 1525, 1281; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.5–3.8 (s, br, with a s at 3.68, 1 and 3H, respectively), 4.22 (s, 2H), 6.55–6.6 (m, 2H), 6.7–6.75 (m, 2H), 7.2–7.35 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 49.1, 55.6, 114 (2C), 114.8 (2C), 127, 127.4 (2C), 128.5 (2C), 139.6, 142.3, 152; EI-MS m/z: 214 (M^++1, 16%), 213 (M^+, 100), 212 (11), 198 (11), 122 (78), 91 (65), 65 (11).

*4.3.3. N-Benzyl-2-methoxyaniline (**3c**)*[9]. Pale yellow oil; IR (cm^{-1}): 3423, 1603, 1509, 1292; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.84 (s, 3H), 4.3 (s, 2H), 4.61 (s, br, 1H), 6.55–6.9, 7.2–7.4 (2m, 4 and 5H, respectively); ^{13}C NMR (75 MHz, $CDCl_3$): δ 48, 55.4, 109.3, 110, 116.6, 121.3, 127.1, 127.5 (2C), 128.5 (2C), 138.1, 139.5, 146.7; EI-MS m/z: 214 (M^++1, 16%), 213 (M^+, 100), 212 (21), 198 (34), 120 (12), 92 (13), 91 (70), 65 (15).

*4.3.4. N-Benzyl-3-chloroaniline (**3d**)*[9]. Brown oil; IR (cm^{-1}): 3420, 1585, 1077; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.2 (s, br, 1H), 4.39 (s, 2H), 6.6–6.65, 6.75–6.8, 6.85–6.9, 7.2–7.25 (4m, 1, 1, 1 and 1H, respectively), 7.45–7.55 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 47.7, 110.9, 112.3, 117, 127.2 (2C), 127.3 (2C), 128.5, 130.1, 134.8, 138.6, 149; EI-MS m/z: 219 (M^++1, 21%), 218 (M^+, 15), 217 (64), 216 (19), 91 (100).

*4.3.5. N-Benzyl-3,5-bis(trifluoromethyl)aniline (**3e**)*[20]. Pale yellow oil; IR (cm^{-1}): 3420, 1620, 1516, 1473, 1273, 1169, 1120; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.35 (d, J=5.1 Hz, 2H), 4.42 (t, br, J=5.1 Hz, 1H), 6.96 (s, 2H), 7.14 (s, 1H), 7.2–7.3, 7.3–7.4 (2m, 1 and 4H, respectively); ^{13}C NMR (75 MHz, $CDCl_3$): δ 48, 110.4, 112, 123.5 (q, $^1J_{C-F}$=273 Hz, 2C), 127.6 (2C), 127.9 (2C), 128.9 (2C), 132.4 (q, $^2J_{C-F}$=32.6 Hz, 2C), 137.6, 148.6; EI-MS m/z: 319 (M^+, 42%), 300 (11), 91 (100).

*4.3.6. N-Benzylnaphthalen-1-amine (**3f**)*[21]. Brown solid; mp 55–58 °C (hexane), IR (cm^{-1}): 3432, 1577, 1525, 1495, 805, 786, 770, 742, 699; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.49 (s, 2H), 4.7 (s, br, 1H), 6.6–6.65, 7.2–7.45, 7.75–7.85 (3m, 1, 9 and 2H, respectively); ^{13}C NMR (75 MHz, $CDCl_3$): δ 48.7, 104.9, 117.7, 119.9, 123.4, 124.8, 125.7, 126.6, 127.4, 127.7 (2C), 128.7 (3C), 134.2, 138.9, 143; EI-MS m/z: 233 (M^+, 17%), 232 (21), 231 (100), 230 (86), 154 (19), 128 (18), 127 (52), 126 (15), 115 (17), 91 (17), 77 (13).

*4.3.7. N-Benzylcyclohexanamine (**3g**)*[22]. Pale yellow oil; IR (cm^{-1}): 1495, 1449, 731, 696; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.05–1.3, 1.55–1.6, 1.7–1.75, 1.85–1.95 (4m, 6, 1, 2 and 2H, respectively), 2.48 (tt, br, ^1J=10.3 Hz, ^2J=3.8 Hz, 1H), 3.8 (s, 2H), 7.2–7.25, 7.3–7.35 (2m, 1 and 4H, respectively); ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.9 (2C), 26.1, 33.5 (2C), 51, 56.1, 126.7, 128 (2C), 128.3 (2C), 141; EI-MS m/z: 189 (M^+, 31%), 147 (12), 146 (97), 132 (13), 91 (100), 65 (12).

*4.3.8. N-Benzyloctan-1-amine (**3h**)*[23]. Pale yellow oil; IR (cm^{-1}): 1495, 1454, 729; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.87 (t, J=7 Hz, 3H), 1.2–1.35, 1.45–1.55 (2m, 10 and 3H, respectively), 2.61 (t, J=7.2 Hz, 2H), 3.78 (s, 2H), 7.2–7.25, 7.3–7.35 (2m, 1 and 4H, respectively); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14, 22.6, 27.3, 29.2, 29.5, 30, 31.8, 49.4, 54, 126.7, 128 (2C), 128.2 (2C), 140.4; EI-MS m/z: 219 (M^+, 3%), 121 (11), 120 (100), 106 (13), 92 (11), 91 (100).

*4.3.9. N-Benzylpyridin-2-amine (**3i**)*[9]. Yellow solid; mp 94–96 °C (hexane); IR (cm^{-1}): 3217, 1598, 1578, 1529; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.46 (d, J=5.8 Hz, 2H), 5.26 (s, br, 1H), 6.3–6.35 (m, 1H),

6.5–6.55 (m, 1H), 7.3–7.35 (m, 6H), 8.0–8.05 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 46.1, 106.6, 112.9, 127, 127.2 (2C), 128.5 (2C), 137.3, 139.1, 148, 158.6; EI-MS *m*/*z*: 185 (M^++1, 14%), 184 (M^+, 100), 183 (52), 107 (18), 106 (75), 91 (36), 79 (26), 78 (20), 65 (12).

*4.3.10. N-(Naphthalen-2-ylmethyl)aniline (**3j**)*[24]. Pale yellow solid; mp 64–66 °C (Hexane), IR (cm^{-1}): 3407, 1598, 1502, 1474, 799, 790, 779, 749, 691; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.93 (s, br, 1H), 4.68 (s, 2H), 6.6–6.65, 6.7–6.75, 7.15–7.2, 7.35–7.4, 7.45–7.5, 7.75–7.8, 7.85–7.9, 8–8.05 (8m, 2, 1, 2, 1, 3, 1, 1 and 1H, respectively); ^{13}C NMR (75 MHz, $CDCl_3$): δ 46.3, 112.7 (2C), 117.5, 123.5, 125.5, 125.8, 126, 126.3, 128.1, 128.7, 129.3 (2C), 131.5, 133.8, 134.3, 148.2; EI-MS *m*/*z*: 233 (M^+, 27%), 232 (12), 231 (61), 230 (100), 141 (76), 127 (18), 115 (16), 77 (22).

*4.3.11. N-(4-Methoxybenzyl)aniline (**3k**)*[9]. Pale yellow oil; IR (cm^{-1}): 3412, 1603, 1259; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.91 (s, 3H), 4.1 (s, br, 1H), 4.37 (s, 2H), 6.75–6.8, 6.85–6.9, 7–7.05, 7.3–7.36, 7.4–7.45 (5m, 2, 1, 2, 2 and 2H, respectively); ^{13}C NMR (75 MHz, $CDCl_3$): δ 47.5, 55, 112.7 (2C), 113.8 (2C), 117.2, 128.6 (2C), 129.1 (2C), 131.3, 148.1, 158.6; EI-MS *m*/*z*: 213 (M^+, 29%), 122 (10), 121 (100), 77 (10).

*4.3.12. N-(4-Chlorobenzyl)aniline (**3l**)*[9]. Pale yellow oil; IR (cm^{-1}): 3419, 1596, 1089; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.04 (s, br, 1H), 4.3 (s, 2H), 6.55–6.65, 6.7–6.75, 7.15–7.2, 7.25–7.3 (4m, 2, 1, 2 and 4H, respectively); ^{13}C NMR (75 MHz, $CDCl_3$): δ 47.6, 112.8 (2C), 117.8, 128.7 (2C), 128.7 (2C), 129.3 (2C), 132.8, 138, 147.8; EI-MS *m*/*z*: 219 (M^++1, 21%), 218 (M^+, 14), 217 (63), 216 (15), 182 (12), 127 (33), 125 (100), 106 (10), 89 (13), 77 (12).

*4.3.13. 1-{4-[(Phenylamino)methyl]phenyl}ethanone (**3m**)*[25]. Brown oil; IR (cm^{-1}): 3378, 1730, 1600, 1573; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.56 (s, 3H), 4.1 (s, br, 1H), 4.39 (s, 2H), 6.55–6.6, 6.65–6.75, 7.1–7.2 (3m, 2, 1 and 2H, respectively), 7.44 (d, *J*=8.3 Hz, 2H), 7.91 (d, *J*=8.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.5, 47.8, 112.8 (2C), 117.8, 127.2 (2C), 128.7 (2C), 129.2 (2C), 136.1, 145.2, 147.7, 197.7; EI-MS *m*/*z*: 225 (M^+, 2%), 224 (16), 223 (100), 222 (49), 180 (10), 179 (35), 104 (14), 77 (42), 51 (11).

*4.3.14. N-(Cyclohexylmethyl)aniline (**3n**)*[5e]. Pale yellow oil; IR (cm^{-1}): 3408, 1600, 1505, 1470, 1447, 745, 691; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.9–1.05, 1.15–1.3, 1.5–1.65, 1.65–1.85 (4m, 2, 3, 1 and 5H, respectively), 2.94 (d, *J*=6.7 Hz, 2H), 3.69 (s, 1H), 6.58 (d, *J*=7.7 Hz, 2H), 6.66 (t, *J*=7.3 Hz, 1H), 7.16 (dd, ^1J=7.7 Hz, ^2J=7.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.9 (2C), 26.6, 31.3 (2C), 37.5, 50.5, 112.6 (2C), 116.8, 129.2 (2C) 148.6; EI-MS *m*/*z*: 189 (M^+, 18%), 107 (9), 106 (100), 77 (12).

*4.3.15. N-(4-Methylbenzyl)pyridin-2-amine (**3o**)*[9]. White solid; mp 73–77 °C (hexane); IR (cm^{-1}): 3210, 1599, 1570, 1521; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.32 (s, 3H), 4.42 (d, *J*=5.7 Hz, 2H), 5.02 (s, br, 1H), 6.3–6.35 (m, 1H), 6.5–6.6 (m, 1H), 7.12 (d, *J*=7.9 Hz, 2H), 7.22 (d, *J*=7.7 Hz, 2H), 7.3–7.4 (m, 1H), 8.05–8.1 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21, 46, 106.6, 112.9, 127.3 (2C), 129.2 (2C), 136, 136.7, 137.3, 148.1, 158.6; EI-MS *m*/*z*: 199 (M^++1, 15%), 198 (M^+, 100), 197 (45), 183 (16), 120 (71), 105 (49), 79 (22), 78 (19), 77 (14).

*4.3.16. N-(4-Methoxybenzyl)pyridin-2-amine (**3p**)*[9]. White solid; mp 128–130 °C (hexane); IR (cm^{-1}): 3231, 1603, 1574, 1531, 1506, 1238; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.77 (s, 3H), 4.40 (d, *J*=5.5 Hz, 2H), 5.01 (s, br, 1H), 6.3–6.4 (m, 1H), 6.5–6.6 (m, 1H), 6.86 (d, *J*=8.5 Hz, 2H), 7.26 (d, *J*=8.6 Hz, 2H), 7.35–7.4 (m, 1H), 8.05–8.1 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 45.7, 55.2, 106.7, 112.9, 113.9 (2C), 128.6 (2C), 131.1, 137.3, 148.1, 158.6, 158.7; EI-MS *m*/*z*: 215 (M^++1, 10%), 214 (M^+, 68), 213 (14), 136 (22), 121 (100), 78 (18).

*4.3.17. N-(2-Methoxybenzyl)pyridin-2-amine (**3q**)*[9]. Yellow solid; mp 54–56 °C (hexane); IR (cm^{-1}): 3256, 1607, 1234; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.79 (s, 3H), 4.46 (d, *J*=6.1 Hz, 2H), 5.2 (s, br, 1H), 6.3–6.35 (m, 1H), 6.45–6.5 (m, 1H), 6.8–6.9, 7.15–7.3 (2m, 2 and 2H, respectively), 7.3–7.35 (m, 1H), 8–8.05 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 41.4, 55.1, 106.5, 110, 112.6, 120.3, 126.9, 128.1, 128.5, 137.2, 147.9, 157.2, 158.8; EI-MS *m*/*z*: 215 (M^++1, 12%), 214 (M^+, 77), 213 (14), 199 (27), 184 (15), 183 (100), 181 (14), 180 (13), 136 (36), 121 (27), 107 (14), 105 (12), 91 (63), 79 (19), 78 (30), 66 (13).

*4.3.18. N-(4-Chlorobenzyl)pyridin-2-amine (**3r**)*[9]. White solid; mp 103–105 °C (hexane), IR (cm^{-1}): 3225, 1607, 1570, 1533, 1081; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.4 (d, *J*=5.9 Hz, 2H), 5.44 (s, br, 1H), 6.25–6.30 (m, 1H), 6.5–6.55 (m, 1H), 7.2–7.3 (m, 4H), 7.3–7.35 (m, 1H), 7.95–8 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 45.3, 106.6, 113, 128.5 (2C), 128.5 (2C), 132.6, 137.4, 137.7, 147.9, 158.4; EI-MS *m*/*z*: 220 (M^++1, 33%), 219 (M^+, 27), 218 (100), 217 (41), 142 (32), 140 (98), 127 (16), 125 (45), 107 (11), 89 (17), 79 (31), 78 (22).

*4.3.19. Tribenzylamine (**5a**)*[26]. White solid; mp 86–88 °C (hexane), IR (cm^{-1}): 1492, 1451, 1365, 741, 696; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.55 (s, 6H), 7.15–7.25, 7.3–7.35, 7.35–7.4 (3m, 3, 6 and 6H, respectively); ^{13}C NMR (75 MHz, $CDCl_3$): δ 57.9 (3C), 126.8 (3C), 128.2 (6C), 128.7 (6C), 139.6 (3C); EI-MS *m*/*z*: 287 (M^+, 18%), 210 (29), 196 (21), 92 (14), 91 (100), 65 (10).

*4.3.20. N-Benzyl-N-butylbutan-1-amine (**5b**)*[27]. Yellow oil; IR (cm^{-1}): 1687, 1494, 1453, 731, 696; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.87 (t, *J*=7.3 Hz, 6H), 1.29 (m, 4H), 1.4–1.5 (m, 4H), 2.39 (t, *J*=7.1 Hz, 4H), 3.53 (s, 2H), 7.2–7.3 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1 (2C), 20.6 (2C), 29.2 (2C), 53.5 (2C), 58.6, 126.5, 128 (2C), 128.8 (2C), 140.3; EI-MS *m*/*z*: 219 (M^+, 3%), 177 (11), 176 (83), 91 (100).

*4.3.21. 4-Benzylmorpholine (**5c**)*[26]. Brown oil; IR (cm^{-1}): 1494, 1454, 1114; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.43 (m, 4H), 3.48 (s, 2H), 3.69 (m, 4H), 7.2–7.35 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 53.5 (2C), 63.4, 66.9 (2C), 127, 128.1 (2C), 129.1 (2C), 137.6; EI-MS *m*/*z*: 177 (M^+, 32%), 146 (30), 106 (10), 105 (13), 92 (12), 91 (100), 86 (19), 77 (11), 65 (11).

*4.3.22. 1-Benzyl-4-methylpiperidine (**5d**)*[28]. Pale yellow oil; IR (cm^{-1}): 1494, 1454, 1118, 821, 733, 696; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.9 (d, *J*=6.4 Hz, 3H), 1.25 (td, ^1J=12 Hz, ^2J=3.3 Hz, 2H), 1.3–1.35 (m, 1H), 1.57 (d, *J*=12 Hz, 2H), 1.92 (td, ^1J=12 Hz, ^2J=2.5 Hz, 2H), 2.84 (d, *J*=12 Hz, 2H), 3.47 (s, 2H), 7.2–7.3 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.9, 30.7, 34.3 (2C), 53.9 (2C), 63.5, 126.8, 128 (2C), 129.2 (2C) 138.6; EI-MS *m*/*z*: 189 (M^+, 52%), 188 (71), 112 (43), 98 (38), 92 (13), 91 (100), 65 (12).

4.4. General procedure for the reduction of aldehydes and imines

To a stirred solution of aldehyde or imine (**6**, 1 mmol) in toluene (2 mL) were added PdO–Fe_3O_4 (50 mg, 1.2 mol % of Pd) and PMHS (2 mmol, 0.12 mL). The resulting mixture was stirred at room temperature during two days. The catalyst was removed by a magnet and the resulting mixture was quenched with water and extracted with EtOAc. The organic phases were dried over $MgSO_4$, followed by evaporation under reduced pressure to remove the solvent. The corresponding products **3a** or **7** were purified by chromatography on silica gel (hexane/ethyl acetate).

*4.4.1. Phenylmethanol (**7a**)*[29]. Colourless oil; IR (cm^{-1}): 3324, 1495, 1453, 1207; ^1H NMR (300 MHz, $CDCl_3$): δ 2.62 (s, br, 1H), 4.59 (s, 2H), 7.25–7.3 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 65, 126.9 (2C), 127.5, 128.4 (2C), 140.8; EI-MS *m*/*z*: 108 (M^+, 62%), 107 (48), 79 (68), 77 (100).

*4.4.2. (4-Methoxyphenyl)methanol (**7b**)*[16j]. Colourless oil; IR (cm^{-1}): 3335, 1586, 1511, 1243, 1173; ^1H NMR (300 MHz, $CDCl_3$): δ 2.57 (s, br, 1H), 3.77 (s, 3H), 4.53 (s, 2H), 6.85 (d, *J*=8.6 Hz, 2H), 7.23 (d, *J*=8.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.1, 64.6, 113.8 (2C), 128.5 (2C), 133.1, 158.9; EI-MS *m*/*z*: 138 (M^+, 88%), 137 (61), 136 (76), 135 (100), 77 (74).

*4.4.3. (4-Chlorophenyl)methanol (**7c**)*[16h]. Colourless solid; mp 68–71 °C (hexane), IR (cm^{-1}): 3337, 1490, 1450, 798; ^1H NMR (300 MHz, $CDCl_3$): δ 2.1 (s, br, 1H), 4.63 (s, 2H), 7.27 (d, *J*=8.6 Hz, 2H), 7.32 (d, *J*=8.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 64.4, 128.2 (2C), 128.6 (2C), 133.3, 139.2; EI-MS *m*/*z*: 144 (M^++1, 16%), 143 (M^+, 13%), 142 (78), 141 (40), 140 (65), 139 (92), 125 (18), 113 (30), 112 (17), 111 (54), 107 (56), 105 (10), 89 (15), 79 (64), 77 (100).

*4.4.4. Cyclopentylmethanol (**7d**)*[30]. Colourless solid; mp 121–123 °C (hexane), IR (cm^{-1}): 3341, 1196; ^1H NMR (300 MHz, $CDCl_3$): δ 1.2–1.25, 1.5–1.6, 1.7–1.75 (3m, 2, 4 and 2H), 2–2.15 (m, 1H), 2.5 (s, br, 1H), 3.48 (d, *J*=6.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.3 (2C), 29 (2C), 42, 67.1; EI-MS *m*/*z*: 100 (M^+, 4%), 99 (54), 98 (33), 81 (38), 80 (10), 70 (12), 69 (100), 67 (20), 57 (47).

*4.4.5. Decan-1-ol (**7e**)*[31]. Colourless oil; IR (cm^{-1}): 3326, 1465, 1377, 1056, 721; ^1H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, *J*=6.5 Hz, 3H), 1.25–1.35 (m, 14H), 1.56 (p, *J*=6.9 Hz, 2H), 2.1 (s, 1H), 3.61 (q, *J*=4.9 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14, 22.6, 25.7, 29.3, 29.4, 29.5, 29.6, 31.8, 32.7, 62.8; EI-MS *m*/*z*: 112 (30%), 111 (26), 98 (18), 97 (48), 84 (52), 83 (83), 82 (31), 71 (17), 70 (96), 69 (85), 68 (32), 67 (17), 57 (42), 56 (75), 55 (100), 54 (10).

*4.4.6. N-Benzylbenzenesulphonamide (**7f**)*[9]. White solid; mp 85–87 °C (hexane); IR (cm^{-1}): 3325, 1611, 1586, 1318, 1161, 676; ^1H NMR (300 MHz, $CDCl_3$): δ 4.13 (d, *J*=6.2 Hz, 2H), 5.38 (t, *J*=6.1 Hz, 1H), 7.15–7.3, 7.45–7.5, 7.55–7.6, 7.85–7.9 (4m, 5, 2, 1 and 2H, respectively); ^{13}C NMR (75 MHz, $CDCl_3$): δ 47, 126.9 (2C), 127.6, 127.7 (2C), 128.5 (2C), 129 (2C), 132.5, 136.2, 139.7; EI-MS *m*/*z*: 247 (M^+, 0.2%), 106 (100), 104 (12), 91 (14), 79 (15), 78 (13), 77 (37), 51 (11).

4.5. General procedure for the sulfoxide reduction process

To a stirred solution of aryl methyl sulfoxide (**8**, 1 mmol) in toluene (2 mL) were added PdO–Fe_3O_4 (50 mg, 1.2 mol % of Pd) and PMHS (4 mmol, 0.24 mL). The resulting mixture was stirred at 130 °C during a week. The catalyst was removed by a magnet and the resulting mixture was quenched with water and extracted with EtOAc. The organic phases were dried over $MgSO_4$, followed by evaporation under reduced pressure to remove the solvent. The corresponding products **9** were purified by chromatography on silica gel (hexane/ethyl acetate).

*4.5.1. Methyl(phenyl)sulfane (**9a**)*[19b]. Colourless oil; IR (cm^{-1}): 1581, 1529, 736; ^1H NMR (300 MHz, $CDCl_3$): δ 2.48 (s, 3H), 7.1–7.15, 7.25–7.3 (2m, 1 and 4H, respectively); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.8, 125, 126.6 (2C), 128.8 (2C), 138.7; EI-MS *m*/*z*: 124 (M^+, 100%), 109 (41), 91 (29), 78 (30), 65 (12).

*4.5.2. Methyl(p-tolyl)sulfane (**9b**)*[32]. Pale yellow oil; IR (cm^{-1}): 1583, 1528, 763; ^1H NMR (300 MHz, $CDCl_3$): δ 2.3 (s, 3H), 2.45 (s, 3H), 7.09 (d, *J*=8.1 Hz, 2H), 7.18 (d, *J*=8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.5, 20.9, 127.3 (2C), 129.6 (2C), 134.7, 135; EI-MS *m*/*z*: 138 (M^+, 100%), 123 (30), 92 (10), 91 (57), 79 (11), 77 (10).

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2011.08.063. These data include MOL files and InChiKeys of the most important compounds described in this article.

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