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Straightforward Synthesis of Aromatic Imines from Alcohols and Amines or Nitroarenes Using an Impregnated Copper Catalyst

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Dedicated to Professor Miguel A. Miranda on the occasion of his 60th birthday

Keywords: Copper / Heterogeneous catalysis / Hydrogen transfer / Imines / Oxidation

The impregnated copper on magnetite catalyst is a versatile system for the synthesis of imines starting from alcohols and amines. This catalyst does not require any type of expensive and difficult to handle organic ligand or typical transition metals, and provides excellent yields achievable under mild reaction conditions. Moreover, the catalyst is very easy to remove from the reaction medium by simply using a magnet.

Introduction

Imines are crucial intermediates and their reactions are fundamental and ubiquitous in the synthesis of biologically active nitrogen compounds, such as B-lactams, dyes, fragrances, pharmaceuticals, fungicides, and agricultural chemicals.^[1] Generally, imines, including Schiff bases, are produced from the condensation of primary amines with carbonyl compounds. However, several new synthetic strategies have been developed in recent years, including the metal-catalyzed oxidation (or dehydrogenation) of primary amines to give the corresponding imines.^[2] Imines have also been prepared from symmetrical secondary amines.^[3] However, the variety of compounds obtained in this manner was very limited; the use of secondary arylamine derivatives circumvented this restriction enabling access to a much wider range of products.^[4]

The in situ oxidative imine formation process starting from alcohols and amines by manganese oxides and molecular sieves formally permitted access to several types of imines.^[5] It should be pointed out that the same intermediates have been detected in the alkylation^[6] of amines by alcohols through the hydrogen autotransfer reaction.^[7] The use of stoichiometric amounts of manganese oxidants is highly undesirable from both economical and environmental points of view. Therefore, much attention has been paid

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201200319.

The one-pot process of dehydrogenation of alcohols in the presence of aniline followed by aqueous hydrolysis gave pure alcohols in excellent yields. In addition to amines, nitroarenes could be used as the nitrogen-containing reagent. In the case of primary amines the expected imines were successfully prepared under similar reaction conditions.

to the use of catalysts to effectively carry out this transformation. In fact, some complexes and compounds derived from transition metals of the second and third row, such as ruthenium,^[8] palladium,^[9] osmium,^[10] iridium,^[11] platinum,^[12] and gold^[13] have shown promise for this imine synthesis strategy. However, the toxicities, pricing, and stability of these metals prohibits their general use for industrial purposes.

Consequently, we have recently developed a new, simple and robust method to immobilize different metal oxides^[14] onto magnetite.^[15] Along this research line, we report herein the first catalyst derived from the cheaper and safer firstrow copper transition metal impregnated on magnetite and its use in the preparation of imines by reaction of alcohols and different nitrogen-atom sources such as amines^[16] or nitroarenes.^[17]

Results and Discussion

Preparation of Imines from Alcohols and Amines

The first process evaluated was the reaction between benzyl alcohol (1a) and aniline (2a) under an Ar atmosphere to give corresponding imine (3a) as depicted in Table 1, using the impregnated copper on magnetite as catalyst. It should be pointed out that simple copper(II) acetate gave, in a similar process,^[18] the typical monoalkylated amine, rendering, in this case, N-benzylaniline. However, using the new copper catalyst, imine could be isolated after a few days of reaction in the absence of oxygen. Thus, the reaction using NaOH as base gave expected imine (3a) with



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a small amount of the corresponding N-benzylaniline, which came from the aforementioned hydrogen autotransfer process. The study of the influence of base, as well as its absence, showed that NaOH rendered the best results (Table 1, compare Entries 1-7). The effect of reaction temperature was also investigated. Temperatures below 130 °C were found to minimize formation of by-product N-benzylaniline and to enhance imine formation; ideal yields routinely resulted from reactions run at 100 °C (Table 1, Entries 1 and 8-10). Choice of solvent was also found to influence reaction yield (Table 1, Entries 10-12), with toluene providing the best results. In addition, increased reaction basicity was found to have a significantly negative effect (Table 1, Entries 13 and 14); an increase in the amount of benzyl alcohol (Table 1, Entry 15) also had a negative effect, whereas an increase in the amount of aniline had a beneficial effect on the yield, being practically quantitative (Table 1, Entry 16). The influence of catalyst concentration was also studied. Decreased catalyst concentrations led to lower reaction yields though increases in catalyst produced only marginal increases in yield (Table 1, Entries 17 and 18). The reaction was repeated in the presence of air to see if this might be the actual source of oxidant in these reactions. However, we found no difference in yield or required reaction time between the reactions performed with or without air (Table 1, Entries 16 and 19). The reaction was performed also using the commercial micro-magnetite support only. This gave expected imine 3a in moderate yield (Table 1, Entry 20), whereas the use of the most active nanopowder magnetite^[15b] afforded a comparable yield (63%).

The standard catalyst^[14b] was prepared from copper dichloride. To know the possible effect of anion on catalyst activity, similar catalysts were prepared from copper dibromide and copper dinitrate. The FXR analysis revealed that the total incorporation of copper was 1.26 and 1.35% for bromide- and nitrate-derived catalyst, respectively; both incorporations were similar to the observed for the standard chloride-derived catalyst. When these catalysts were used in reactions similar to that presented in Table 1, Entry 16, similar yields were obtained (95 and 99% using bromide- and nitrate-derived catalysts, respectively), indicating only a marginal effect of the counterion on catalytic activity.

Once the optimal reaction conditions were established, the prospect of catalyst recycling was examined. The catalyst was recovered using a magnet, from the reaction described in Table 1, Entry 16 then washed with toluene and re-used under the same reaction conditions, to render expected product **3a** but in only 72% yield. A third cycle of recovered catalyst use provided a modest yield of **3a** (44%). The phenomenon of leaching was studied by ICP-MS analysis of the resulting reaction solution mixture, and 17% of the initial amount of copper was detected (0.002% for iron), which could be due to the formation of different imine-copper complexes. To validate this hypothesis the process was repeated in the absence of amine. After 4 d of reaction with benzyl alcohol and NaOH in toluene at 100 °C the solution obtained after trapping the catalyst by Table 1. Optimization of reaction conditions.[a]

	$\begin{pmatrix} OH \\ \\ \\ \\ 1a \end{pmatrix}$ + $\begin{pmatrix} NH_2 \\ \\ \\ 2a \end{pmatrix}$	CuO-Fe ₃ O ₄ (1.3 mol-%) base, solvent	-	∼ _N -⊂⊂)
Entry	Base (mol-%)	Solvent	Т	t	Yield
			[°C]	[d]	[%][b]
1	NaOH (140)	PhMe	130	4	65 ^[c]
2	KOH (140)	PhMe	130	4	2 ^[d]
3	LiOH (140)	PhMe	130	4	39
4	Na ₂ CO ₃ (140)	PhMe	130	4	3
5	K_2CO_3 (140)	PhMe	130	4	27
6	NaOAc (140)	PhMe	130	4	1
7	-	PhMe	130	7	2
8	NaOH (140)	PhMe	25	7	27
9	NaOH (140)	PhMe	70	7	71
10	NaOH (140)	PhMe	100	4	91
11	NaOH (140)	dioxane	100	6	61
12	NaOH (140)	MeCN	100	6	18 ^[e]
13	NaOH (300)	PhMe	100	4	59 ^[f]
14	NaOH (500)	PhMe	100	4	25
15	NaOH (140)	PhMe	100	4	20 ^[g]
16	NaOH (140)	PhMe	100	4	98 ^[h]
17 ^[i]	NaOH (140)	PhMe	100	4	81 ^[h]
180	NaOH (140)	PhMe	100	4	98 ^[h]
19 ^[k]	NaOH (140)	PhMe	100	4	95 ^[h]
20[1]	NaOH (140)	PhMe	100	4	57 ^[h]

[a] Reaction carried out using compound **1a** (1.3 mmol), **2a** (1.0 mmol) in solvent (3 mL) and under an Ar atmosphere, unless otherwise stated. [b] Isolated yield after column chromatography. [c] *N*-Benzylaniline was isolated in 14% yield. [d] *N*-Benzylaniline was isolated in 89% yield. [e] *N*-Benzylaniline was isolated in 51% yield. [f] *N*-Benzylaniline was isolated in 19% yield. [g] Reaction carried out using compound **1a** (1.0 mmol), **2a** (1.0 mmol). [h] Reaction carried out using compound **1a** (1.0 mmol), **2a** (2.0 mmol). [i] Reaction carried out using 0.3 mol-% of catalyst. [j] Reaction carried out using 2.3 mol-% of catalyst. [k] Reaction carried out using entry solution carried out using 9.3 mol-% of catalyst. [k] Reaction carried out using 2.5 mol-%).

a magnetic was analyzed by ICP-MS which revealed the presence of only 9.8% of the initial amount of copper, lower that that obtained under typical reaction conditions involving the presence of amine. In another trial, quinoline (100 mol-%) was heated at 100 °C in toluene with the catalyst and subsequent ICP-MS analysis showed an incorporation of 18% of copper to the final solution which is similar to that obtained from typical reaction conditions and substantially higher than that obtained in the absence of amines. These data support our hypothesis of a leaching process. Moreover, the TEM images of the recycled catalyst showed a drastic change in copper particle size from 7.0 ± 6 nm (maximum at 3 nm) for freshly prepared catalyst to 13.0 ± 6 nm for the recycled catalyst (Figure 1). This change in particle size may affect the reactivity of the recycled catalyst. However, the BET surface area did not suffer a great change, from 6.2 m²g⁻¹ for the initial catalyst to 11.4 m²g⁻¹ for the used catalyst, which is practically the same specific area. It should be pointed out that the recycled catalyst from the aforementioned treatment without amine showed a similar particle size distribution



 $(3.7 \pm 1.5 \text{ nm})$, see Supporting Information) to that of the initial catalyst. However, the results obtained from treatment with quinoline were slightly different $(9.2 \pm 1.9 \text{ nm})$, see Supporting Information), indicating that nitrogen-containing compounds may not only favor the leaching process but may also facilitate the generation of CuO-particles.

Aromatic Imines from Alcohols and Amines or Nitroarenes



Figure 1. Size of CuO-Fe₃O₄ catalyst.

The optimized protocol was then applied to other substrates in order to study the scope of the reaction (Table 2). The protocol gave excellent results in the case of aromatic alcohols independent of the presence of electron-withdrawing or electron-donating groups; even the relative position of this substituent had no influence on reaction efficiency. However, the reaction failed when the aliphatic 3methyl-1-butanol was used as a substrate (Table 2, Entry 19). The methodology could be applied to aromatic amines, with different functional groups as well as to aliphatic amines. However, the use of aliphatic amines ren-

Table 2. Preparation of imine derivatives.[a]

	OH NH2	CuO-Fe ₃ O ₄ (1.3 mol-%)	- ~ R	
	Ar R 1 2	NaOH (140 mol-%) PhMe, 100 °C, 4 d	Ar N	
Entry	Ar	R	Product	Yield [%] ^[b]
1	Ph	Ph	3a	98
2	Ph	$3-ClC_6H_4$	3b	71
3	Ph	4-MeOC ₆ H ₄	3c	73
4	Ph	2,5-Me ₂ C ₆ H ₃	3d	41
5	Ph	<i>n</i> Bu	3e	75
6	Ph	tBuCH ₂	3f	45
7	Ph	$Me(CH_2)_{11}$	3g	77
8	$4-ClC_6H_4$	Ph	3h	80
9	$4-ClC_6H_4$	$3-ClC_6H_4$	3i	98
10	$4-MeC_6H_4$	Ph	3j	69
11	$4-MeOC_6H_4$	Ph	3k	97
12	$4-MeOC_6H_4$	$3-ClC_6H_4$	31	30
13	3-MeC ₆ H ₄	Ph	3m	99
14	$3-MeOC_6H_4$	Ph	3n	62
15	$3,5-Me_2C_6H_3$	Ph	30	74
16	3,5-Me ₂ C ₆ H ₃	$3-ClC_6H_4$	3p	86
17	3,5-(MeO) ₂ C ₆ H ₃	Ph	3q	93
18	3,5-(MeO) ₂ C ₆ H ₃	$3-ClC_6H_4$	3r	89
19	<i>i</i> PrCH ₂	Ph	3s	0

[a] Reaction carried out using compound 1 (1.0 mmol), 2a (2.0 mmol) in toluene (3 mL). [b] Isolated yield after bulb-to-bulb distillation.

dered slightly lower yields than those obtained for aromatic ones (compare, for instance, Table 2, Entries 1 and 5–7).

Preparation of Aldehydes from Alcohols and Aniline

The success obtained in preparing imines using our copper impregnated magnetite catalyst inspired us to formulate a process for synthesizing aldehydes from alcohols (Table 3).

Table 3. Preparation of arenecarbaldehydes.^[a]

	i) CuO-Fe ₃ C PhNH ₂ (2 NaOH (14 	0₄ (1.3 mol-%) a, 200 mol-%) 0 mol-%) 0 ℃, 4 d	Q
	Ar ii) HCl (3 м), 25 °C, 2 h 1	Et ₂ O	Ar H 4
Entry	Ar	Product	Yield [%] ^[b]
1	Ph	4a	99
2	$4-ClC_6H_4$	4 b	93
3	$4-MeC_6H_4$	4c	88
4	$4 - MeOC_6H_4$	4d	96
5	$3-MeC_6H_4$	4 e	85
6	$3-MeOC_6H_4$	4 f	95
7	$2,6-Cl_2C_6H_3$	4g	32
8	3,4-Cl ₂ C ₆ H ₃	4h	88
9	3,5-Me ₂ C ₆ H ₃	4i	98
10	3,5-(MeO) ₂ C ₆ H ₃	4j	94
11	3,4,5-(MeO) ₃ C ₆ H ₂	4k	81

[a] Reaction carried out using compound 1 (1.0 mmol), 2a (2.0 mmol) in toluene (3 mL) for the first step; and HCl (2 mL) and ether (2 mL) for the second step. [b] Isolated yield after extraction.

Thus, the above standard reaction of arylmethanol derivatives 1 with aniline catalyzed by impregnated copper on magnetite was followed by treatment with aqueous HCl, following catalyst removal with a magnet. The whole process provided an organic layer in which the aldehyde could be isolated in good yields and with excellent purity simply by solvent removal under low pressure. Addition of Na₂CO₃ to the aqueous solution and extraction of the resulting mixture rendered the pure aniline (2a) in good yields (79–96%), showing the possible recyclability of the integrated process. The reaction was found to proceed with excellent yields regardless of the presence of electron-donating or -withdrawing groups on the aromatic ring. Only in the case of the 2,6-dichlorophenyl derivative was the yield of the corresponding arenecarbaldehyde 4g significantly lower (Table 3, Entry 7). This is perhaps best explained by steric hindrance of the starting reagent, since the related 3,4dichlorophenyl derivative gave corresponding aldehyde 4h in good yield (Table 3, Entry 8).

Preparation of Imines from Alcohols and Nitrobenzene

A new entry to the synthesis of imines has been accomplished very recently using nitroarenes as the nitrogencontaining moiety^[8c,17] and an excess of alcohol as the source of both aldehyde and reducing agent. Date: 04-07-12 16:15:44

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The reaction of nitrobenzene (5) with four equivalents of alcohol (1) catalyzed by the impregnated copper catalyst gave expected imines 3 with reasonable yields independent of the alcohols used and substitution on the aromatic ring (Table 4). Although the process using simple amines is more effective than the one using nitroarenes, it is interesting to note that the same copper catalyst could be used for both processes and demonstrated similar activities in both scenarios.

Table 4. Preparation of N-phenyl imine derivatives.^[a]

	OH NO2	CuO-Fe ₃ O ₄ (1.3 mol-%)	. A. Ph
	Ar Ph	NaOH (300 mol-%)	Ar
	1 5	PhMe, 130 °C, 3 d	3
Entry	Ar	No.	Yield [%][b]
1	Ph	3a	70
2	$4 - MeC_6H_4$	3k	61
3	4-MeOC ₆ H	4 3 1	84
4	3-MeC ₆ H ₄	3n	58

[a] Reaction carried out using compound 1 (4.0 mmol), 5 (1.0 mmol) in toluene (3 mL). [b] Isolated yield after bulb-to-bulb distillation.

Preparation of Imines from Primary Amines

Finally, we studied the possible catalytic activity of the impregnated copper on magnetite for the preparation of imines starting from primary amines (6).^[2] Thus, the treatment of arylmethylamines with a base and substoichiometric amounts of the copper catalyst under Ar gave expected imines 7 in good yields (Table 5); the apparent discrepancy with formation of 7b was more a matter of isolation difficulties rather than of the product formation.

Table 5. Preparation of aryl imine derivatives.^[a]

	Cu NH ₂ (2.	O-Fe ₃ O ₄ 6 mol-%)	<u>^</u>
	Ar NaOH PhMe, 6	(200 mol-%) 100 °C, 3 d 7	l´ `Ar
Entry	Ar	Product	Yield [%][b]
1	Ph	7a	95
2	$4 - MeC_6H_4$	7b	49
4	$3-MeC_6H_4$	7c	71

[a] Reaction carried out using compound **6** (2.0 mmol) in toluene (3 mL). [b] Isolated yield after bulb-to-bulb distillation.

Conclusions

In conclusion, impregnated copper on magnetite has been shown to be an active, highly selective and broadly applicable catalyst for the preparation of imines starting from different feed-stocks such as alcohols and amines or nitroarenes, or primary amines. The copper-catalyzed dehydrogenation-condensation process could be integrated into a one-pot process to yield pure aldehydes, simply by aqueous acidic treatment and subsequent catalyst removal with a magnet. This catalyst does not require the use of any type of expensive and difficult to handle organic ligands, leads to excellent yields of product, and requires mild conditions.

Experimental Section

General Remarks: Melting points were obtained with a Reichert Thermovar apparatus. NMR spectra were recorded with a Bruker AC-300 (300 MHz for ¹H and 75 MHz for ¹³C) using CDCl₃ as a solvent and TMS as internal standard for ¹H and ¹³C; chemical shifts are given in δ (ppm) and coupling constants (J) in Hertz. FT-IR spectra were obtained with a JASCO 4100LE (Pike Miracle ATR) spectrophotometer. Mass spectra (EI) were obtained at 70 eV using 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 of phosphomolybdic acid, 10 g of Ce(SO₄)₂·4H₂O, 60 mL of concentrated H₂SO₄ and 940 mL of H₂O]. The chromatographic analyses were carried out with a Younglin 6100GC instrument equipped with a flame ionization detector and a 30 m capillary column (0.25 mm diameter, 0.25 mm film thickness, HP-5 stationary phase), using nitrogen (2 mL/min) as carrier gas, P = 10 psi, T_{injector} = 270 °C and T_{detector} = 270 °C; 60 °C for 3 min then at 15 °C/min to 270 °C for 15 min; t_r values are given in min under these conditions. 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 with a Thermo Elemental VGPQ-ExCell spectrometer. The X-ray Fluorescence analyses were carried out using a PHILIPS MAGIX PRO (PW2400) X-ray spectrometer equipped with a rhodium X-ray tube and a beryllium window. The reactions were performed in a 12-vessel carousel reaction station (Radleys). The CuO-Fe₃O₄ catalyst was prepared according to the literature procedure.^[14e]

General Procedure for the Synthesis of Aryl Imines Derivatives from Alcohols and Amines: To a stirred solution of the corresponding alcohol (1 1 mmol) in toluene (3 mL) under an Ar atmosphere was added CuO-Fe₃O₄ (50 mg), NaOH (56 mg, 1.4 mmol) and the corresponding amine (2, 2 mmol). The resulting mixture was stirred at 100 °C for 4 D. The catalyst was removed by a magnet and washed with EtOAc (2×5 mL). The collected organic phases were dried with MgSO₄, and the solvents were removed under reduced pressure. The product was purified either by bulb-to-bulb distillation or crystallization to give corresponding pure products 3. Imine 3a^[19] is commercially available and was characterized by comparison of its physical and spectroscopic data with those of authentic material. Yields are included in Table 2. Physical and spectroscopic data, as well as literature data for known compounds, follow:

(*E*)-*N*-Benzylidene-3-chloroaniline (3b):^[20] Pale yellow oil; $t_r = 14.8$. $R_f = 0.87$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 1622$, 1582, 1067 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 7.05-7.1$, 7.15–7.2, 7.3–7.35, 7.4– 7.5, 7.85–7.9 (5m, 1, 2, 1, 3 and 2 H, respectively, ArH), 8.4 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 119.4$, 120.9, 125.8, 128.8 (2 C), 128.9 (2 C), 130.0, 131.7, 134.7, 135.8, 153.3, 161.3 ppm. EI-MS: *m/z* (%) = 217 (31) [M + 1]⁺, 216 (45) [M]⁺, 215 (93), 214 (100), 111 (26), 89 (10), 75 (15).

(*E*)-*N*-Benzylidene-4-methoxyaniline (3c):^[4c] White solid; M.p. 66–68 °C; $t_r = 15.4$. $R_f = 0.53$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 1609$, 1581,

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1247 cm^{-1.} ¹H NMR (300 MHz, CDCl₃): δ = 3.85 (s, 3 H, CH₃), 6.95–7.0 (m, 2 H, ArH), 7.25–7.3 (m, 2 H, ArH), 7.45–7.5 (m, 3 H, ArH), 7.9–7.95 (m, 2 H, ArH), 8.51 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 55.4, 114.3 (2 C), 122.1 (2 C), 128.5 (2 C), 128.7 (2 C), 131.0, 136.4, 144.8, 158.2, 158.3 ppm. EI-MS: *m*/*z* (%) = 212 (14) [M + 1]⁺, 211 (88) [M⁺], 210 (15), 197 (15), 196 (100), 167 (22).

(*E*)-*N*-Bencylidene-2,5-dimethylaniline (3d):^[21] Orange solid; M.p. 86–90 °C (hexane); $t_r = 14.5$. $R_f = 1.5$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 3019$, 1629, 1573 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 2.31$ (s, 3 H, CH₃), 2.34 (s, 3 H, CH₃), 6.75 (s, 1 H, ArH), 6.9–6.95 (d, J = 7.6 Hz, 1 H, ArH), 7.1–7.12 (d, J = 7.6 Hz, 1 H, ArH), 7.45–7.5 (m, 3 H, ArH), 7.9–7.93 (m, 2 H, ArH) 8.36 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 17.5$, 21.2, 118.5, 126.4, 128.8 (4 C), 130.2, 131.3, 136.4, 136.7, 151.1 (2 C), 159.4 ppm. EI-MS: m/z (%) = 210 (19) [M + 1]⁺ 209 (100) [M]⁺, 208 (96), 194 (13), 193 (33), 132 (100), 131 (12), 130 (13), 117 (16), 105 (12), 103 (16), 79 (14), 77 (27).

(*E*)-*N*-Bencylidenebutan-1-amine (3e):^[9c] Brown oil; $t_r = 10.1$. $R_f = 0.56$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 3026$, 1645, 1451 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 0.95$ (t, J = 6.6 Hz, 3 H, CH₃), 1.35–1.7 (2m, 4 H, 2 CH₂), 3.6 (t, J = 6.4 Hz, 2 H, NCH₂), 7.4–7.7 (m, 5 H, ArH), 8.3 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 14.0$, 20.6, 33.1, 61.6, 128.1 (2 C), 128.7 (2 C), 130.6, 136.4, 160.9 ppm. EI-MS: m/z (%) = 161.1 (8) [M]⁺ 160.1 (21), 132 (31), 119 (29), 118 (100), 117 (10), 105 (10), 104 (30), 91 (93), 90 (9), 89 (13), 84 (19), 83 (14), 77 (15).

(*E*)-*N*-Benzylidene-2,2-dimethylpropan-1-amine (3f):^[22] Yellow oil; $t_r = 9.9$. $R_f = 0.63$ (hexane/EtOAc, 4:1). IR: $\hat{v} = 3027$, 1742, 1645 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 0.98$ (s, 9 H, 3 CH₃), 3.37 (s, 2 H, CH₂), 7.35–7.45 (m, 3 H, ArH), 7.75–7.8 (m, 2 H, ArH), 8.23 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 28.1$ (3 C), 32.8, 74.1, 128.2 (2 C), 128.7 (2 C), 130.5, 136.6, 160.9 ppm. EI-MS: m/z (%) = 175 (9) [M]⁺ 174 (21), 160 (16), 119 (37), 118 (100), 117 (10), 91 (100), 90 (9), 89 (10).

(*E*)-*N*-Benzylidenedodecan-1-amine (3g):^[10] Yellow oil; $t_r = 16.4$. $R_f = 0.6$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 3021$, 1647, 1466 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 0.88$ (t, J = 5.4 Hz, 3 H, CH₃), 1.2–1.5 (m, 18 H, 9 CH₂), 1.65–1.75 (m, 2 H, CH₂), 3.58–3.62 (t, J = 6.7 Hz, 2 H, NCH₂), 7.25–7.4, 7.7–7.75 (2m, 3 and 2 H, respectively, ArH), 8.26 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 14.0$, 22.6, 27.3, 29.3, 29.4, 29.5, 29.6 (3 C), 30.9, 31.9, 61.8, 128.0 (2 C), 128.5 (2 C), 130.3, 136.3, 160.6 ppm. EI-MS: *m/z* (%) = 273 (2) [M]⁺, 174 (16), 161 (12), 160 (100), 132 (25), 119 (16), 118 (35), 104 (11), 91 (29).

(*E*)-*N*-(4-Chlorobenzylidene)aniline (3h):^[13a] Yellow solid; M.p. 51– 54 °C; $t_r = 14.8$. $R_f = 0.7$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 1621$, 1578, 1092 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 7.15-7.2$, 7.35–7.4, 7.75–7.85 (3m, 3, 4 and 2 H, respectively, ArH), 8.37 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 120.8$ (2 C), 128.9 (2 C), 129.1 (2 C), 129.3, 129.8 (2 C), 134.6, 137.2, 151.5, 158.6 ppm. EI-MS: *m*/*z* (%) = 217 (32) [M + 1]⁺, 216 (46) [M]⁺, 215 (95), 214 (100), 104 (10), 77 (43), 51 (13).

(*E*)-3-Chloro-*N*-(4-chlorobenzylidene)aniline (3i):^[23] Brown oil; $t_r = 16.1$. $R_f = 0.67$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 3060$, 1596, 1485 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 7.2-7.35$ (m, 4 H, ArH), 7.45– 7.5 (d, J = 8.5 Hz, 2 H, ArH), 7.8–7.85 (d, J = 8.5 Hz, 2 H, ArH), 8.39 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 119.4$, 120.9, 126.1, 129.2 (2 C), 130.1 (2 C), 130.2, 134.3, 134.8, 137.8, 152.9, 159.9 ppm. EI-MS: m/z (%) = 253 (10) [M + 4]⁺, 252 (18) [M + 3]⁺, 251 (64) [M + 2]⁺, 250 (74) [M + 1]⁺, 249 (100) [M]⁺, 248 (99), 138 (19), 113 (20), 112 (13), 111 (63), 89 (26), 77 (10), 76 (12), 75 (45), 51 (10).

(*E*)-*N*-(4-Methylbenzylidene)aniline (3j):^[19] Yellow oil; $t_r = 14.3$. $R_f = 0.67$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 3027$, 1602, 1498 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 2.4$ (s, 3 H, CH₃), 7.1–7.25 (m, 7 H, ArH), 7.77–7.8 (d, J = 8.0 Hz, 2 H, ArH), 8.40 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 21.6$, 115.0 (2 C), 118.4 (2 C), 120.8, 128.7 (2 C), 129.5 (2 C), 133.5, 141.8, 145.3, 160.4 ppm. EI-MS: m/z (%) = 196 (20) [M + 1]⁺, 195 (100) [M]⁺, 194 (100), 91 (19), 77 (58), 51 (16).

(*E*)-*N*-(4-Methoxybenzylidene)aniline (3k):^[4c] Yellow solid; M.p. 45–48 °C; $t_r = 15.4$. $R_f = 0.2$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 1679$, 1600, 1245 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 3.78$ (s, 3 H, CH₃), 6.9–6.95, 7.15–7.2, 7.3–7.35, 7.75–7.85 (4m, 2,3,2 and 2 H, respectively, ArH), 8.32 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 54.8$, 113.6 (2 C), 120.4 (2 C), 125.0, 128.6 (2 C), 128.7 (2 C), 130.0, 151.8, 159.1, 161.7 ppm. EI-MS: m/z (%) = 213 (1) [M]⁺, 212 (13), 211 (88), 210 (100), 167 (12), 77 (20).

(*E*)-3-Chloro-*N*-(4-methoxybenzylidene)aniline (31):^[24] Brown oil; $t_r = 16.7$. $R_f = 0.57$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 1621$, 1597, 1243, 1027 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 3.86$ (s, 3 H, CH₃), 7.15–7.3 (m, 6 H, ArH), 7.82–7.85 (d, J = 8.5 Hz, 2 H, ArH), 8.33 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 55.2$, 113.1, 113.8 (2 C), 114.2, 118.3, 130.1 (2 C), 130.2, 134.7, 153.5, 159.5, 160.6, 162.4 ppm. EI-MS: m/z (%) = 247 (32) [M + 2]⁺, 246 (45) [M + 1]⁺, 245 (96) [M]⁺, 244 (100), 111 (23), 77 (10), 75 (17).

(*E*)-*N*-(3-Methylbenzylidene)aniline (3m):^[19] Brown oil; $t_r = 14.3$. $R_f = 0.7$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 3030$, 1627, 1584 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 2.41$ (s, 3 H, CH₃), 7.2–7.4 (m, 7 H, ArH), 7.64–7.66 (d, J = 7.4 Hz, 1 H, ArH), 7.75 (s, 1 H, ArH), 8.41 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 21.3$, 120.8 (2 C), 125.8, 126.4, 128.6, 128.9, 129.1 (2 C), 132.2, 136.1, 138.5, 152.1, 160.6 ppm. EI-MS: m/z (%) = 196 (15) [M + 1]⁺, 195 (100) [M]⁺, 194 (100), 104 (11), 91 (14), 77 (52), 51 (15).

(*E*)-*N*-(3-Methoxybenzylidene)aniline (3n):^[19] Yellow oil; $t_r = 15.2$. $R_f = 0.6$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 3005$, 1601, 1584, 1265, 1037 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 3.83$ (s, 3 H, CH₃), 7.2–7.35 (m, 8 H, ArH), 7.4 (s, 1 H, ArH), 7.8 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 55.1$, 111.6, 118.3, 120.8 (2 C), 122.3, 125.9, 129.1 (2 C), 129.5, 137.4, 151.8, 159.8, 160.3 ppm. EI-MS: m/z (%) = 212 (24) [M + 1]⁺, 211 (100) [M]⁺, 210 (100), 182 (11), 181 (26), 180 (13), 168 (10), 167 (24), 104 (18), 77 (63), 51 (16).

(*E*)-*N*-(3,5-Dimethylbenzylidene)aniline (30):^[25] Brown oil; $t_r = 14.9$. $R_f = 0.67$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 3014$, 1625, 1588 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 2.40$ (s, 6 H, 2 CH₃), 7.15–7.25 (m, 4 H, ArH), 7.35–7.4 (m, 2 H, ArH), 7.5 (m, 2 H, ArH), 8.36 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 21.3$ (2 C), 124.9 (2 C), 125.9, 126.7 (2 C), 129.2 (2 C), 133.3, 136.2, 138.1 (2 C), 152.3, 161.0 ppm. EI-MS: *m/z* (%) = 210 (44) [M + 1]⁺, 209 (100) [M]⁺, 208 (100), 194 (14), 193 (13), 165 (12), 105 (11), 104 (25), 103 (13), 91 (26), 78 (13), 77 (100), 51 (25).

(*E*)-3-Chloro-*N*-(3,5-dimethylbenzylidene)aniline (3p): Brown oil; $t_r = 16.1$. $R_f = 0.7$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 3019$, 1597, 1485 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 3.80$ (s, 6 H, 2 CH₃), 6.95–7.1 (m, 5 H, ArH), 7.82–7.85 (d, J = 8.6 Hz, 2 H, ArH), 8.33 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 21.1$ (2 C), 113.0, 114.8, 118.2, 126.0 (2 C), 129.8, 130.2, 134.7, 135.6, 138.1, 147.6, 161.9 ppm. EI-MS: m/z (%) = 245 (31) [M + 2]⁺, 244 (48) [M + 1]⁺, 243 (96) [M]⁺, 242 (100), 109 (23), 91 (12), 76 (11), 75 (13). HRMS calcd. (%) for C₁₅H₁₄ClN: 243.0815, found 243.0800.

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(*E*)-*N*-(3,5-Dimethoxybenzylidene)aniline (3q): $-^{126]}$ Brown oil. $t_r = 16.7$. $R_f = 0.5$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 3004$, 1627, 1587, 1151 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 3.84$ (s, 6 H, 2 CH₃), 6.57–6.59 (t, J = 2.3 Hz, 1 H, ArH), 7.05–7.06 (d, J = 2.3 Hz, 2 H, ArH), 7.2–7.25 (m, 3 H, ArH), 7.35–7.4 (m, 2 H, ArH), 8.4 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 55.6$ (2 C), 104.3, 106.5 (2 C), 121.0 (2 C), 126.1, 129.2 (2 C), 138.3, 152.0, 160.4, 161.1 (2 C) ppm. EI-MS: m/z (%) = 242 (37) [M + 1]⁺, 241 (100) [M]⁺, 240 (100), 226 (10), 212 (23), 211 (56), 210 (19), 196 (12), 183 (10), 182 (18), 167 (12), 154 (12), 104 (24), 78 (10), 77 (78), 51 (18).

(*E*)-3-Chloro-*N*-(3,5-dimethoxybenzylidene)aniline (3r): Red oil; $t_r = 17.9$. $R_f = 0.5$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 3004$, 1593, 1484, 1204, 1064 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 3.84$ (s, 6 H, 2 CH₃), 7.05–7.1 (m, 4 H, ArH), 7.2–7.3 (m, 3 H, ArH), 8.31 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 55.6$ (2 C), 104.4, 119.3, 120.8, 125.8, 130.1, 130.2 (2 C), 137.7, 147.6, 153.0, 160.9 (2 C), 161.2 ppm. EI-MS: m/z (%) = 277 (32) [M + 2]⁺, 276 (47) [M + 1]⁺, 275 (100) [M]⁺, 274 (99), 246 (12), 245 (21), 138 (11), 111 (20). HRMS: calcd. for C₁₅H₁₄ClNO₂ 275.0713; found 275.0730.

General Procedure for the Synthesis of Arenecarbaldehydes 4: To a stirred solution of corresponding alcohol (1 1 mmol) in toluene (3 mL) under an Ar atmosphere was added CuO-Fe₃O₄ (50 mg), NaOH (56 mg, 1.4 mmol) and corresponding aniline (2a, 0.18 mL, 2 mmol). The resulting mixture was stirred at 100 °C for 4 d. The catalyst was removed by a magnet and then HCl (2 mL) and ether (2 mL) were added. The resulting mixture was stirred for 2 h at room temperature, and then it was quenched with water (2 mL) and extracted with EtOAc ($3 \times 5 \text{ mL}$). The organic phases were dried with MgSO₄, followed by evaporation under reduced pressure to remove the solvent. The product was purified by vacuum distillation at 120 °C to give corresponding products 4. Alcohols 4a,^[27] 4b,^[28] 4c-f,^[27] 4g,^[29] 4h,^[30] 4i,^[31] 4j,^[28] and 4k^[32] are commercially available and were characterized by comparison of their physical and spectroscopic data with those of pure commercial samples. Yields are included in Table 3.

General Procedure for the Synthesis of Aryl Imines Derivatives from Primary Amines: To a stirred solution of corresponding amine (6 2 mmol) in toluene (3 mL) under air was added CuO-Fe₃O₄ (50 mg) and NaOH (120 mg, 2 mmol). The resulting mixture was stirred at 100 °C for 3 d. The catalyst was removed by a magnet and washed with EtOAc (2×5 mL). The collected organic phases were dried with MgSO₄, and the solvents were removed under reduced pressure. The product was purified either by bulb to bulb distillation or crystallization to give corresponding pure products 7. Yields are included in Table 5. Physical and spectroscopic data as well as literature data for known compounds follow:

(*E*)-*N*-Benzylidene-1-phenylmethanamine (7a):^[2g] Brown oil; $t_r = 13.9$. $R_f = 0.56$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 3061$, 3027, 1643, 1579 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 4.82$ (s, 2 H, CH₂), 7.2–7.5 (m, 8 H, ArH), 7.78–7.79 (d, J = 3.3 Hz, 2 H, ArH), 8.39 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 65.0$, 126.9, 127.9 (2 C), 128.2 (2 C), 128.5 (2 C), 128.6 (2 C), 130.7, 136.1, 139.2, 162.0 ppm. EI-MS: m/z (%) = 196 (7) [M + 1]⁺, 195 (45) [M]⁺, 194 (44), 117 (12), 92 (33), 91 (100), 89 (15), 65 (14).

(*E*)-*N*-(4-Methylbenzylidene)-1-(*p*-tolyl)methanamine (7b):^[2g] White solid; M.p.: 51–53 °C; $t_r = 15.4$. $R_f = 0.6$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 3015$, 1646, 1558 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 2.34$ (s, 6 H, 2 CH₃), 4.77 (s, 2 H, CH₂), 7.1–7.25 (m, 6 H, ArH), 7.65–7.67 (d, J = 7.8 Hz, 2 H, ArH), 8.34 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 21.1$, 21.5, 64.8, 127.9 (2 C), 128.2 (2 C), 129.1 (2 C), 129.3 (2 C), 133.6, 136.3, 136.5, 140.9, 161.7 ppm. EI-MS: m/z (%) = 223 (27) [M]⁺, 222 (12), 106 (20), 105 (100), 77 (12).

(*E*)-*N*-(3-Methylbenzylidene)-1-(*m*-tolyl)methanamine (7c):^[33] Yellow oil; $t_r = 15.2$. $R_f = 0.5$ (hexane/EtOAc, 4:1). IR: $\tilde{v} = 1652$, 1568 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 2.33$ (s, 3 H, CH₃), 2.37 (s, 3 H, CH₃), 4.77 (s, 2 H, CH₂), 7.25–7.6 (m, 6 H, ArH), 7.64 (s, 2 H, ArH), 8.35 (s, 1 H, NCH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 21.2$, 21.3, 65.1, 124.2, 125.0, 125.8, 127.7, 128.1, 128.7, 131.5, 132.6, 138.0, 138.3, 138.4, 139.1, 162.1 ppm. EI-MS: *m*/*z* (%) = 223 (35) [M]⁺, 222 (22), 208 (15), 106 (54), 105 (100), 103 (15), 91 (14), 79 (13), 77 (19).

Supporting Information (see footnote on the first page of this article): Particle size distribution and copies of the ¹H NMR and ¹³C NMR spectra.

Acknowledgments

This work was supported by the current Spanish Ministerio de Economía y Competitividad (Consolider Ingenio 2010 CSD2007-00006, CTQ2007-65218/BQU and CTQ2011-24151) and the Generalitat Valenciana (G.V.; PROMETEO 2009/03, FEDER). R. C. thanks the G.V. for a fellowship through the PROMETEO program. J. M. P. thanks the Spanish Ministerio de Educación and the Universidad de Alicante for undergraduate grants. We gratefully acknowledge the refinement of our English by Mrs. Oriana C. Townley.

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Received: March 15, 2012 Published Online:

FULL PAPER

Impregnated Copper Catalysts

Ar N^R

X = H, O

R-NX₂

The impregnated copper on magnetite catalyst is a versatile system for the synthesis of imines starting from alcohols and amines or nitroarenes. A similar synthesis of imines was accomplished using only pri-

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OF



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Straightforward Synthesis of Aromatic Imines from Alcohols and Amines or Nitroarenes Using an Impregnated Copper Catalyst

Keywords: Copper / Heterogeneous catalysis / Hydrogen transfer / Imines / Oxidation