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Highly active and selective gold catalysts for the aerobic oxidative condensation of benzylamines to imines and one-pot, two-step synthesis of secondary benzylamines

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ABSTRACT

Supported gold nanoparticles catalyze the oxidation of benzylamines to N-benzylidene benzylamines by molecular oxygen in toluene. The process is general, and *para*-substituted benzylamines as well as heterocyclic methanamines undergo oxidative condensation. 1-Phenylethanamine and diphenylmethanamine form imines with much less selectivity than benzylamines due to the unfavourable steric hindrance introduced by the substituents at the α-carbon. Secondary and tertiary dibenzyl and tribenzylamines form N-benzylidene benzylamines accompanied with aromatic ketones and oximes arising from C–N bond rupture. The efficiency of gold catalyst increases exponentially as the average particle size is reduced, and the TOF increases when the gold crystallite size is decreased. The solid support plays an important role as it has been found that gold supported on active carbon is more efficient than gold supported on anatase. Although palladium nanoparticles are also active in promoting benzylamine oxidation, only the catalyst based on platinum was found to exhibit an activity comparable to that of gold. Cross condensation of benzylamines in the presence of aromatic or aliphatic primary amines forms the mixed N-aryl or N-alkyl benzylimines with high yields. A one-pot, two-step procedure using a single gold catalyst has been devised to produce secondary symmetric and asymmetric amines derived from benzylamines with high atom efficiency.

1. Introduction

Considerable progress has been made in the recent years in developing catalytic oxidations using oxygen as the final oxidizing reagent [1,2]. In this regard, supported metal nanoparticles are selective and efficient catalysts to promote the aerobic oxidative condensation of alcohols and aldehydes [3–9].

In contrast to the interest for alcohol oxidation, catalytic oxidation of amines has attracted considerably less attention due to poor product selectivity typically achieved with these substrates [10–12]. Recently, we have reported that gold is a highly active and selective catalyst for the aerobic oxidative condensation of anilines to azobenzenes [13]. As a continuation of this work on amine oxidation, herein, we present the selective aerobic oxidative condensation of benzylamines to N-benzylidene benzylamines (Scheme 1). Benzylimines are useful synthetic intermediates that can undergo a large variety of transformations of the C=N double bond including hydrogenations, [2+2] cycloadditions and nucleophilic additions (the so-called *Strecker* reaction) [14–21]. Furthermore, following a one-pot, two-step (oxidation followed by hydrogenation) strategy in which the same gold catalyst is used, but changing the reagent from oxygen to hydrogen, it is possible to obtain symmetric and asymmetric secondary amines with very high atom efficiency. High atom efficiency is one of the major requirements in green chemistry and it is fulfilled with the process reported here [22].

A precedent to our work is the very recent reports from Angelici using bulk gold metal of micrometric size and alumina-supported gold nanoparticles (size distribution 50–100 nm) as catalysts for the aerobic oxidative condensation of benzylamine [23,24]. The main point of these reports is the unexpected activity of bulk gold as catalysts. In principle, it could be anticipated that by decreasing the gold crystallite size the activity of gold should increase. By preparing Au/TiO_2 samples with different metal crystallite sizes, we will show that the oxidation of benzylamines is a structure sensitive reaction. The Au/TiO_2 catalyst, which is also active in the hydrogenation of imines, has been found to be much less active than the Au/C catalyst in the oxidation of benzylamines, but more active in the hydrogenation of imines. Therefore, using gold as a single catalyst it has been possible to perform a one-pot, two-step process in which the initial benzylidene amine formation is coupled with subsequent hydrogenation using the same catalyst (Scheme 1). The overall result of this one-catalyst, two-step process is a novel route for symmetric and asymmetric secondary benzylamines with very high atom efficiency.

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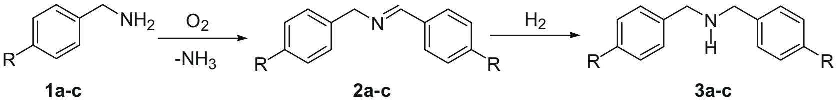


Scheme 1. Oxidative condensation of benzylamines to N-benzylidene phenylmethanamines and secondary amines.

2. Experimental

2.1. Catalyst preparation

The Au/TiO_2 catalyst consists of 1.5 wt% gold supported on TiO_2, and was supplied by the World Gold Council (reference catalysts, Type A). It can also be prepared by depositing the gold from an aqueous solution of $HAuCl_4$ (Alfa Aesar) on a sample of TiO_2 (P25 Degussa). The deposition precipitation procedure is done at 343 K and pH 9 for 2 h, using (0.2 M) NaOH to maintain the pH constant. Under these conditions, gold deposition occurs with 80% efficiency. The catalyst is then recovered, filtered, washed with deionized water and dried at 373 K overnight. Finally, the powder is calcined at 673 K in air for 4 h. Following this procedure, 3.5 nm gold nanoparticles supported on TiO_2 are obtained.

The Au/C catalyst consists of 0.8 wt% gold supported on active carbon, and was also supplied by the World Gold Council (reference catalysts, Type D).

The Au/Al_2O_3 catalyst consists of 5 wt% gold supported on γ-Al_2O_3, and was prepared by incipient wetness impregnation of 4.0 g of γ-Al_2O_3 (specific surface area of 158 m^2/g) with a solution of 0.42 g of $HAuCl_4 \cdot 3H_2O$ in 2 ml of H_2O (pH 9, milliQ). The impregnation procedure is done in air and the sample was allowed to dry overnight at room temperature. After drying in an oven at 383 K for 1 h, the solid was reduced under H_2 flow with heating at a rate of 3 K/min from room temperature to 573 K for 1 h. The catalyst was exhaustively washed with distilled water until no traces of chlorides were detected by the $AgNO_3$ test. The removal of Cl^- ions is an important process since traces of Cl^- remain strongly bonded to gold, and are highly detrimental for the overall activity. Finally, the powder is calcined at 973 K in air for 20 h. Following this procedure, 50–150 nm gold nanoparticles supported on γ-Al_2O_3 are obtained.

Pd/TiO_2 (5 wt%) and Pt/TiO_2 (5 wt%) catalysts were prepared by the impregnation of 2 g of TiO_2 (Degussa P25, 10 g, $S_{BET} = 55\ m^2\ g^{-1}$) with a solution of 0.345 g of $PdCl_2$ (Aldrich, 60% purity) or 0.28 g of $H_2PtCl_6 \cdot 6H_2O$ (Aldrich) in 7 ml of H_2O (milliQ). The slurry was stirred for 2 h at room temperature, then all the liquid was evaporated and the solid was dried at 373 K overnight and reduced with 1-phenylethanol at 433 K for 2 h. The catalyst was then washed, filtered and dried at room temperature for 12 h. The final Pd/or Pt content was found to be 5 wt% by atomic absorption analysis.

2.2. Catalytic experiments

Catalytic experiments were performed in reinforced glass semi continuous reactors equipped with temperature and pressure controllers. For each reaction, a 2 ml mixture of reactants and solvent was placed into the reactor (3 ml capacity) together with the appropriate amount of catalyst. Using toluene as a solvent, care has to be taken to avoid vapour mixtures within the explosion range. Working under the experimental conditions 373 K and 5 bar of oxygen, the composition of the vapour phase is outside the explosion mixture range. All the reactants used in this study are commercially available from Sigma–Aldrich Company with purities higher than 95%. Dodecane was always used as an internal standard for the determination of conversion level and yields. After sealing the reactor, air was purged by filling the reactor with oxygen (5 bar) and by pumping out three times before final pressurization of the reactor with O_2 at 5 bar. The reactor was deeply introduced into a silicone bath that was preheated at 373 K. During the experiment, the pressure was maintained constant and the reaction mixture was magnetically stirred at 1000 rpm. Aliquots were taken from the reactor at different reaction times. Once the catalyst particles were removed from the solution by centrifuging at 12 000 rpm, the products were analyzed by GC–MS and also by comparing the retention time with commercial (Sigma–Aldrich Company) pure samples. Only experiments with mass balances $\geqslant$95% were considered.

In the cases of experiments with a one-catalyst, two-step process in which the initial imine formed in the cross condensation is subsequently reduced to the secondary amine, the experimental conditions were the same as in the initial oxidation step. Once this reaction was complete, the hydrogenation step was carried out by flushing out the O_2 at room temperature and after sealing the reactor, hydrogen (7 bar) was charged. Then, the reactor was deeply introduced in the silicone bath that was preheated at the required temperature.

3. Results and discussion

When we were working with the supported gold nanoparticles catalysts for the oxidation of benzylamines, Angelici and co-workers [23,24] reported that the nanoparticles of gold with 50–100 nm were also able to perform the oxidation reaction. From these results, we ascertained that the direction to increasing catalyst activity was indeed to work on supported gold since, in principle, smaller gold crystallites are more active than the larger bulk gold particles as reported by Angelici and co-workers [23,24]. Then, we will present firstly the role of the gold crystallite size on the activity and selectivity for the aerobic oxidative condensation of benzylamines.

It has been reported that it is possible to prepare Au/TiO_2 catalysts with the same gold content and different crystallite sizes by depositing gold at different pHs [25–29]. Following this, three Au/TiO_2 samples were prepared, and the TEM analyses of the resulting samples (see Fig. 1) show that the Au/TiO_2 catalysts with different metal particle sizes were obtained.

When the initial reaction rate (measured from the initial slope of the plot of conversion vs. reaction time) for the oxidation of benzylamine **1a** on the three samples was determined, the results show (Fig. 2) that there is a not linear but exponential increase of activity when decreasing the crystallite size, being the activities of the Au/TiO_2 samples much larger than with gold on alumina (see Fig. 2 and Table 1).

The exponential increase of the initial reaction rate when decreasing the size of the gold crystallites and the fraction of metal surface atoms indicates that the oxidation of benzylamine to give N-benzylidene benzylamine must be a structure sensitive reaction and consequently not all the gold surface atoms are equally active. Then, from the activity results it could be expected that unsaturated gold atoms located at the corners of the crystallites, and which are proportionally numerous when decreasing the gold crystal size, should be more active.

If this is the case a higher activity for the oxidation of benzylamine to give N-benzylidene benzylamine should be obtained with

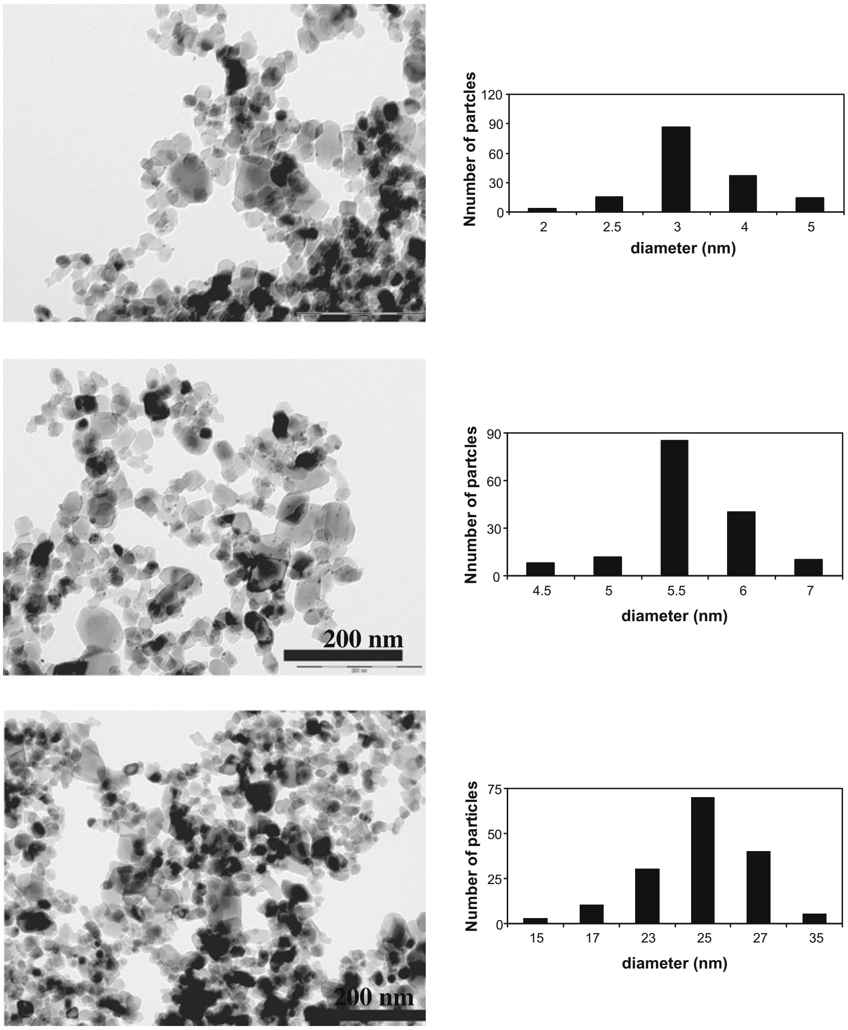


Fig. 1. TEM images and particle size distribution of three Au/TiO_2 catalysts used in this work having a very different average gold nanoparticles sizes.

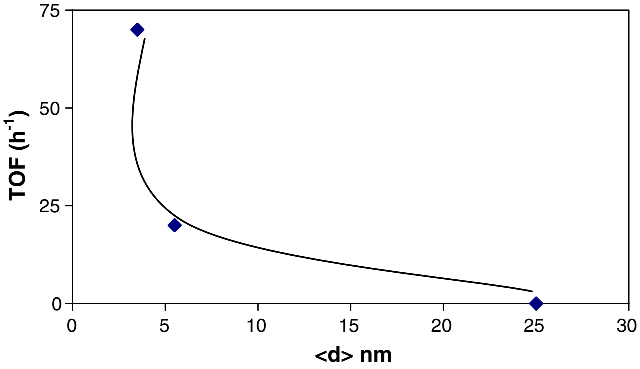


Fig. 2. Plot of the turnover frequency (TOF determined from the initial reaction rate divided by the number of gold atoms) for benzylamine oxidation vs. the average size of the gold nanoparticles for the Au/TiO_2 series. For reaction conditions, see Table 2.

Table 1
Average particle size ($\langle d \rangle$), TOF, conversion and selectivity for benzylamine oxidation catalyzed by a series of gold catalysts with different size particle sizes.

	Catalyst				
	0.8 wt% Au/C	1.5 wt% Au/TiO_2	1.2 wt% Au/TiO_2	Au/TiO_2	Au/Al_2O_3
$\langle d \rangle$ (nm)	10	3.5	5.5	25	69
TOF (h^{-1})[a]	280	70	20	0	0
Time (h)[b]	1	30	30	30	30
Conversion (%)	99	98	76	58	48
Selectivity (%)	100	94	98	97	97

[a] TOF = r_0/n_{metal}. r_0 = initial reaction rate measured from the slope of the time conversion plot at zero time. For reaction conditions, see Table 2.

[b] Results of the conversion and selectivity towards N-benzylidene phenylamine **2a** for the oxidation of benzylamine **1a** by oxygen in the presence of gold catalysts with different particle sizes.

a catalyst with a higher gold dispersion. In an attempt to achieve a higher metal dispersion we have used gold on high surface area active carbon. Thus, a 0.8 wt% Au/C was obtained from the World Gold Council [30], with a BET surface area of 1100 $m^2 g^{-1}$. However, the crystallite size of gold in Au/C was measured by TEM (see Fig. 3) and an average crystallite size larger than that of the most dispersed Au/TiO_2 (BET surface area = 50 $m^2 g^{-1}$) sample was found. Interestingly, the catalytic activity for the oxidation of benzylamine on Au/C turns out to be much higher than that with Au/TiO_2 (see Fig. 4).

In order to explain this observation, and since a strong gold/metal support interaction cannot be expected for carbon, we have to

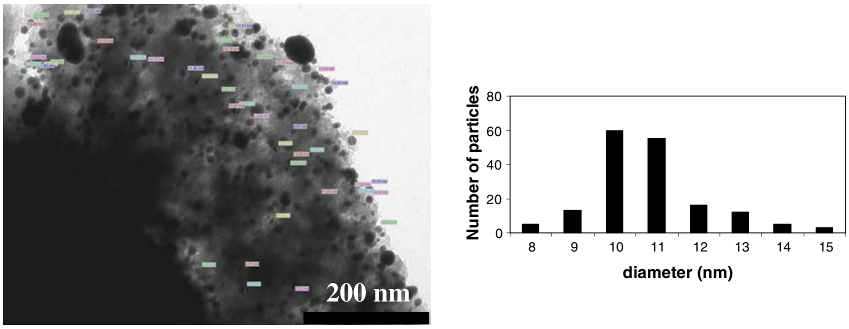


Fig. 3. TEM (left) and particle size distribution (right) of the 0.8 wt% Au/C catalyst used in this work.

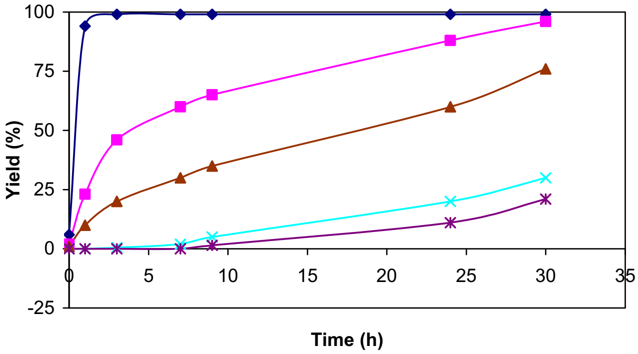


Fig. 4. Time–yield plots for the oxidation of phenylmethanamine **1a** in the presence of 0.8 wt% Au/C (10 nm) (♦), 1.5 wt% Au/TiO_2 (3.5 nm) (■), 1.2 wt% Au/TiO_2 (5.5) (△), 1.5 wt% Au/TiO_2 (25 nm) (×) and 5 wt% Au/Al_2O_3 (69 nm) (*) to the corresponding N-benzylidene phenylmethanamine **2a**. Reaction conditions: benzylamine, 1 mmol; toluene, 2 ml; oxygen pressure, 5 bar; temperature, 373 K; and Au/substrate mol ratio, 1%.

Table 2

Conversion and selectivity towards N-benzylidene phenylamine **2a–c** for the oxidation of benzylamines **1a–c** by oxygen in the presence of gold catalysts. Reaction conditions: benzylamine, 1 mmol; toluene, 2 ml; oxygen pressure, 5 bar; temperature, 373 K; and Au/substrate mol ratio, 1%.

Substrate	Catalyst	Time (h)	Product	Conversion (%)	Selectivity (%)
1a	1.5% Au/TiO_2	30	**2a**	98	94
	1.5% Au/TiO_2 (first reuse)	30		75	98
	1.5% Au/TiO_2 (second reuse)	30		66	99
	0.8% Au/C	1		99	100
	0.8% Au/C (first reuse)	1		95	100
	0.8% Au/C (second reuse)	1		72	100
	0.8% Au/C (third reuse)	1		68	100
	5% Pd/TiO_2	30		77	97
	5% Pt/TiO_2	22		99	97
1b	1.5% Au/TiO_2	22	**2b**	99	94
	0.8% Au/C	1		99	99
1c	1.5% Au/TiO_2	45	**2c**	74	92
	0.8% Au/C	1.5		100	100

assume that in the case of Au/C, the catalyst may exhibit a large number of very small particles that are difficult to be seen and to be measured by TEM, and that are very active [31,32]. Note that the initial reaction rate is more than one order of magnitude larger for Au/C than for Au/TiO_2, which makes it possible for the former to produce full conversion, with practically 100% selectivity in less than 1 h reaction time, while 30 h is necessary to achieve almost 100% conversion with 94% selectivity with Au/TiO_2 (see Table 2).

Concerning the reaction mechanism and the role of oxygen as a final oxidizing agent, we analyzed the vapour phase after the reaction to determine the presence of some nitrogen compounds. As shown in Scheme 1, the aerobic oxidative coupling expels one nitrogen atom. It was of interest to determine if ammonia, hydroxylamine or nitrogen oxides are formed as by-products in the reaction. GC–MS analyses of the head space after the reaction of phenylmethanamine **1a** to form N-benzylidene phenylmethanamine using Au/TiO_2 as a catalyst established the presence of NH_3 as the only nitrogenated compound. Although this analysis does not exclude the presence of other nitrogen compound in the liquid phase, the formation of ammonia strongly supports the fact that oxidation occurs preferentially at the C atom bond bonded to NH_2. Since water is also detected in the vapour phase, the role of oxygen is to bind hydrogen atoms that effect the oxidation and result in an unsaturated C=O or C=N bond.

Pd and Pt nanoparticles supported on TiO_2 particles are also active in promoting the oxidation benzylamines, though their activity is lower than that of gold (see Table 2).

At this point, we have a gold catalyst (Au/C) that is extraordinarily active and selective for producing N-benzylidene benzylamine by the aerobic oxidative condensation of benzylamine. It would now be interesting to study if this very active catalyst can be of general use to selectively oxidize a large number of benzylamines and can also perform what would be very relevant catalytically, i.e., the oxidative cross condensation of benzylamines and amines lacking hydrogens at the α-carbon.

3.1. Scope of the reaction

To show the generality of the catalyst a variety of substrates have been aerobically oxidized. When benzylamines with *para* substituents were reacted in the presence of Au/C (see Table 2 and Scheme 1), the corresponding N-benzylidene benzylamines **2b–c** were obtained with high conversion and almost full selectivity. Though we have only three points, a fairly good linear relationship between Hammett σ^+ constant of the *para* substituent and the initial reaction rate is observed (Fig. 5).

After this, the reactivity studies with phenylmethanamines have been extended to other heterocyclic amines (Scheme 2). It would be particularly interesting in the case of sulphur containing reactants since the sulphur compounds can act as poisons of the metal catalyst. However, taking into account that sulphur containing heterocycles are efficiently oxidized by gold nanoparticles [33], it would be interesting to explore the oxidation of pyridyl and thienylmethanamines. In the two cases, the amine was converted to the corresponding N-arylidene amine with almost complete selec-

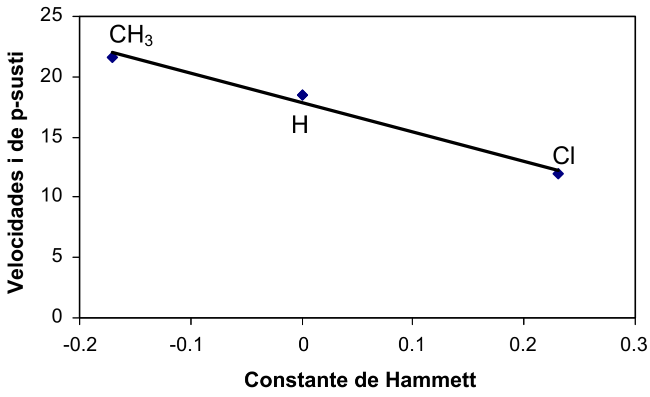
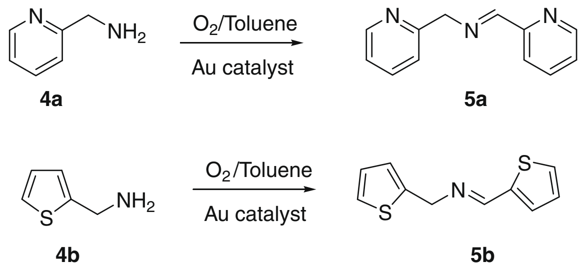


Fig. 5. Plot of the r_0 vs. σ^+ for the oxidation of *para*-substituted phenylmethanamines **1a–c** catalyzed by Au/TiO$_2$. Reaction conditions: benzylamine, 1 mmol; toluene, 2 ml; oxygen pressure, 5 bar; temperature, 373 K; and Au/substrate mol ratio, 1%.



Scheme 2. Oxidation of heteroaryl amines to the corresponding N-arylidene arylmethanamines.

tivity (Table 3). Particularly remarkable is the case of the N-pyridylmethanamine that is converted to the imine in less than 10 min under the conditions used. These heterocyclic imines are interesting synthetic intermediates and ligands.

When Au/TiO$_2$ was used as a catalyst for the oxidation of a secondary amine such as 1-phenylethanamine **6a**, besides the expected N-(α-methyl)benzylidene 1-phenylethanamine **7a**, acetophenone **8a** and acetophenone oxime **9a** were also formed in significant amounts (Scheme 3). In the oxidation of benzylamine, benzaldehyde and benzaldehyde oxime are also detected in trace quantities. Thus, although the products of the oxidation of secondary amine **6a** are similar to those observed for the oxidation of benzylamine, their relative distribution is significantly changed. We interpret the result of the lack of selectivity in the oxidation of 1-phenylethanamine **6a** as arising from the larger steric hindrance in the carbonyl group and amine due to the presence of a methyl group in the α-carbon as compared to the case of benzylamine. Due to the α-methyl group, this steric hindrance disfavours the spontaneous condensation of the aromatic ketone and benzylamine. Also the presence of the α-methyl favors oxidation at this position with the final formation of the hydroxylamine.

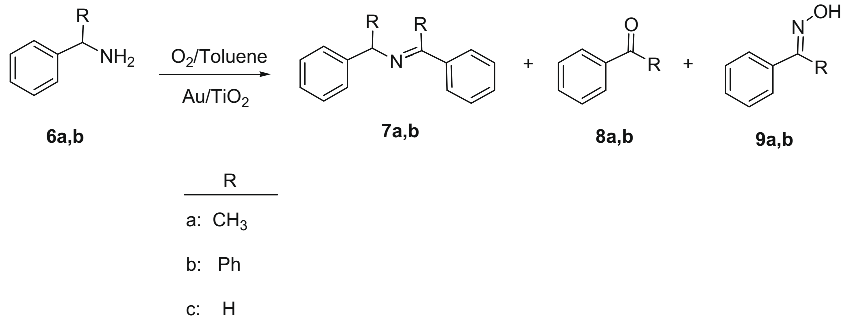
Table 3
Conversion and selectivity towards N-arylidene arylmethanamines **5a–b** for the oxidation of heteroaryl amines **4a–b** by oxygen in the presence of gold catalysts. Reaction conditions: substrate, 1 mmol; toluene, 2 ml; oxygen pressure, 5 bar; temperature, 373 K; and Au/substrate mol ratio, 1%.

Substrate	Catalyst	Time (min)	Product	Conversion (%)	Selectivity (%)
4a	0.8% Au/C	8	**5a**	96	98
4b	0.8% Au/C	120	**5b**	99	99
4b	1.5% Au/TiO$_2$	1800	**5b**	91	86

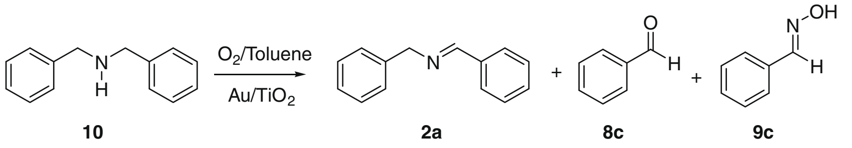
The above-mentioned hypothesis is supported by the fact that the oxidation of an even bulkier amine such as 1,1-diphenylmethanamine **6b** forms benzophenone **8b** as the prevalent product accompanied with lesser amounts of N-(diphenylmethylidene) diphenyl methinime **7b** (Scheme 3 and Table 4).

Continuing with expanding the scope to different secondary amines, Scheme 4 shows that dibenzylamine **10** undergoes dehydrogenation to compound **2a** as well as C–N bond rupture to form equivalent amounts of benzaldehyde **8c** and benzaldehyde oxime **9c** (Table 4). Recently, Baiker and co-workers have also studied this transformation using Au(AcO)$_3$ and Au(AcO)$_3$ supported on ceria as catalysts, and have reported high selectivity towards **2a** [34].

Related tertiary tribenzylamine also reacts in the presence of Au/TiO$_2$ as catalyst, and N-benzylidene benzylamine **2a** is



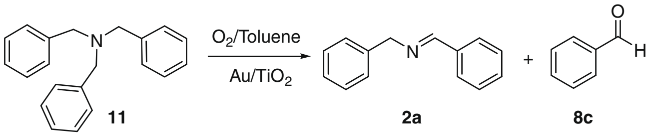
Scheme 3. Oxidation of secondary benzylamines **6a,b**.



Scheme 4. Oxidation of dibenzylamine **10** catalyzed by Au/TiO$_2$. Reaction conditions: dibenzylamine **10**, 1 mmol; toluene, 2 ml; temperature, 373 K; catalyst, 1.5 wt% Au/TiO$_2$; Au/substrate, 1 mol%.

Table 4
Conversion and selectivity towards secondary and tertiary benzylamines oxidation by oxygen in the presence of gold catalysts. Reaction conditions: amine, 1 mmol; toluene, 2 ml; oxygen pressure, 5 bar; temperature, 373 K; and Au/substrate mol ratio, 1%.

Reactive	Catalyst	Time (h)	Product	Conversion (%)	Selectivity (%)
6b	0.8% Au/C	5	**8b**	100	92
10	1.5% Au/TiO_2	20	**2a**	100	70
11	1.5% Au/TiO_2	47	**2a**	55	54



Scheme 5. Oxidation of tribenzylamine **11** catalyzed by Au/TiO_2.

Table 5
Conversion (based on benzylamine) and selectivity for the oxidative cross condensation of benzylamines and primary amines lacking α-hydrogens by oxygen in the presence of gold catalysts. Reaction conditions: benzylamine, 1 mmol; **12a,b**, 1.5 mmol; toluene, 2 ml; oxygen pressure, 5 bar; temperature, 373 K; and Au/substrate mol ratio, 1%.

Substrates	Catalyst	Time (min)	Product	Conversion (%)	Selectivity (%)
4a + **12a**	0.8% Au/C	0.5	**13a**	100	99
1c + **12a**[a]	1.5% Au/TiO_2	21	**13b**	98	41
1c + **12a**	0.8% Au/C	21	**13b**	100	99
1c + **12b**	0.8% Au/C	16	**13c**	100	99
1b + **12b**	0.8% Au/C	12	**13d**	100	99
1a + **12c**	0.8% Au/C	18	**13e**	100	99

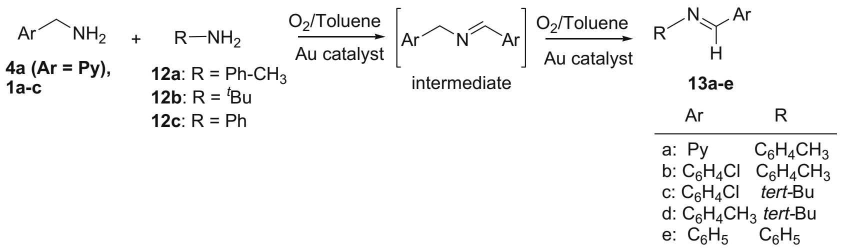
[a] Same reaction conditions using a 1:1 stoichiometry for *p*-toluidine vs. 4-chlorobenzylamine.

accompanied by the formation of almost equivalent amounts of benzaldehyde **8c**. Probably both compounds are formed simultaneously in the same oxidative C–N bond rupture (Scheme 5).

3.2. Oxidative cross condensation of benzylamines and amines lacking H in α-carbons

We have taken advantage of the remarkable influence of the support on the catalytic activity of gold to design a selective cross condensation process between benzylamines and anilines to form N-benzylidene anilines. In a previous work, we have reported that while Au/TiO_2 promotes the oxidation of anilines to azobenzenes efficiently, Au/C was inactive in catalyzing this process [13]. However, and as presented above, the reactivity for the oxidation of benzylamines was reversed and Au/C is notably more active than Au/TiO_2. Taking this into account, we could anticipate that the reaction of a mixture of benzylamines and anilines with Au/C under aerobic conditions could lead to the formation of N-arylidene anilines.

To test this cross condensation reaction, we have oxidized a mixture of 2-pyridylmethanamine **4a**, which can be rapidly transformed in **5a** and toluidine **12a** (see Scheme 6). As expected, when toluidine **12a** was in 2 equivalents with respect to amine **4a** and when Au/C was used as a catalyst, the final product was the mixed imine **13a** with very high conversion and selectivity (Table 5). The course of the reaction (Fig. 6) shows that compound **5a** is a primary and unstable product which under the reaction conditions converts to the mixed imine **13a**. Scheme 6 shows the observed product intermediacy in the formation of compound **13a**.



Scheme 6. Oxidative cross condensation of benzylamines and primary amines lacking α-hydrogens.

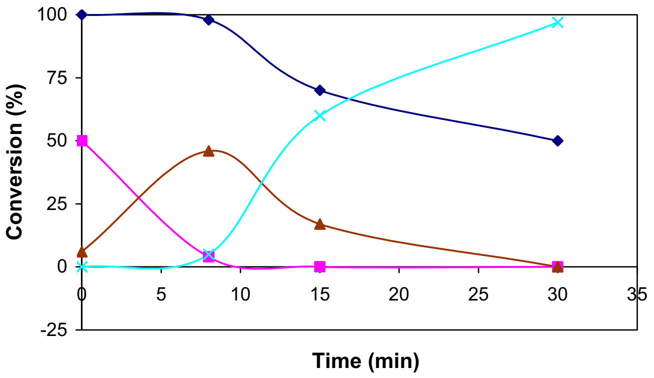


Fig. 6. Plot of time conversion for the oxidation of 2-pyridylmethanamine **4a** (■) in the presence of 1.5 equivalents of toluidine **12a** (♦) to obtain N-aryl imine **13a** (×) and intermediate imine compounds **5a** (△). Reaction conditions: compound, **4a** 1 mmol; compound **12a**, 2 mmol; toluene, 2 ml; oxygen pressure, 5 bar; temperature, 100 °C; and catalysts, 0.8 wt% Au/C (Au/**4a** mol ratio, 1%).

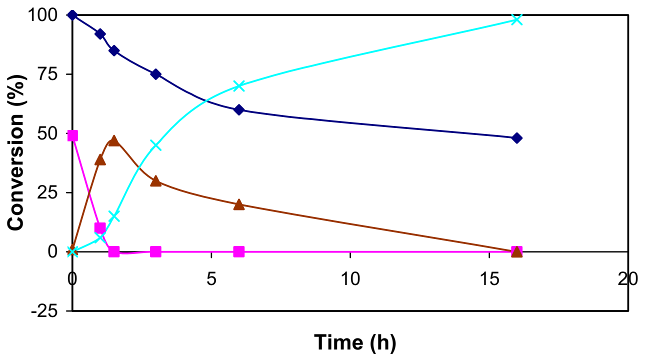
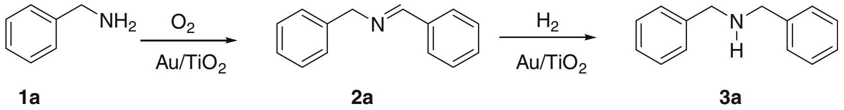


Fig. 7. Plot of time conversion for the oxidation of 4-chlorobenzylamine **1c** (■) in the presence of 1.5 excess of *tert*-butylamine **12b** (♦) catalyzed by Au/C to obtain imine compound **13c** (×) and intermediate imine compound **2c** (△). Reaction conditions: 4-chlorobenzylamine, 1 mmol; *tert*-butylamine, 2 mmol; toluene, 2 ml; temperature, 373 K; and catalyst Au/C, 1 mol%.



Total **1a** conversion 100 %
Selectivity towards **3a**: 98 %

Scheme 7. One-catalyst, two-step process in which the intermediary imine formed is subsequently reduced to the secondary amine by hydrogen by the same gold catalyst that effected the oxidation.

This concept of selective cross condensation was expanded to the formation of other aryl imines. The results are shown in Table 5. The importance of using Au/C, which is an efficient catalyst for benzylamines, is illustrated by the fact that with Au/TiO_2 a mixture of the N-aryl imine **13a** and azobenzene is obtained. The formation of azobenzene is derived from the homocoupling of aniline that occurs in the presence of Au/TiO_2 but not in the presence of Au/C [13].

Besides N-substituted anilines, tertiary aliphatic amines can also react on Au/C to produce the corresponding N-alkyl benzylimine with high selectivity and yield. Table 5 illustrates the cross condensation of *tert*-butylamine **12b** and *para*-substituted benzylamines **1b** and **1c**. Analogous to the case of 2-pyridylmethanamine **4a**, the course of the reaction shows the formation of compounds **2b** and **2c** as primary and unstable intermediates for the formation of the final mixed imines **13d** and **13c** in high yield (Fig. 7).

3.3. Catalytic synthesis of secondary benzylamines through one-catalyst, two-step process

N-alkylation of amines is classically carried out through a SN2 mechanism using alkyl halides or aliphatic compounds having good leaving groups [35]. However, this process suffers from a poor selectivity since consecutive N-alkylation of the primary product can lead to undesired by-products. An alternative process is the reductive condensation of primary amines with carbonylic compounds. Herein, considering the high product yield in benzylamine oxidation and oxidative cross condensation as well as the fact that gold catalysts can also catalyze the hydrogenation of C=N multiple bonds [7], we envision a one-catalyst, two-step process in which the initial imine formed in the cross condensation is subsequently reduced to the secondary amine. If the proposed process would take place with high efficiency and selectivity, it would be an interesting general catalytic process for the formation of secondary symmetric as well as asymmetric benzylamines. The process is shown in Scheme 7.

As anticipated based on the catalytic activity of supported gold nanoparticles we have been able to obtain different secondary amines in one-pot, two-step reactions with the same catalyst starting from benzylamine **1a**.

4. Conclusions

We have found the following:

(1) That the oxidation of amines to benzylidene amines on gold is a structure sensitive reaction that requires smaller crystallites.
(2) That gold supported on carbon selectively catalyzes full oxidative cross condensation of benzylamines and amines. Oxidative condensation also occurs efficient and selectively with heterocyclic amines containing sulphur.
(3) That gold supported on titania is able to selectively catalyze the formation of secondary benzylamines through a one-pot, two-step reaction that involves one oxidative cross condensation step followed by hydrogenation.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jcat.2009.03.015.

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