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Gold Catalysis

Highly Selective Acylation of Dimethylamine Mediated by Oxygen Atoms on Metallic Gold Surfaces**

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Throughout the ages, gold has been highly valued because of its seeming chemical inertness, its luster and beauty resulting from its resistance to bulk tarnishing reactions. However, the surface of gold is not completely inert, particularly in the presence of adsorbed oxygen. Indeed, there has been a resurgence of research on heterogeneous catalysis by gold recently due to its potential for developing environmentally benign processes,[1–3] since Haruta's breakthrough observation of low-temperature CO oxidation on gold nanoparticles supported on reducible metal oxides.[4] Gold particles supported on oxide surfaces selectively promote a wide range of reactions under various conditions, including aerobic oxidation of alcohols[5–7] and amines,[8] as well as acylation of amines[9,10] as does unsupported gold powder.[11] Herein, we report for the first time the vapor-phase, surface mediated acylation of an amine to an amide on metallic gold, and we establish a molecular-level mechanism for this process based on a specific characteristic of the adsorbed amide intermediate that provides a general basis for predicting such reactions.

Amides are widely used in chemical synthesis, in pharmaceutical production, and in the synthesis of polymers, including nylon.[11] Conventional methods for synthesizing amides use either activated acid derivatives, such as acid chlorides or anhydrides, or rearrangement reactions induced by an acid or base, which often produce toxic chemical waste.[12] Amine acylation reactions catalyzed by homogeneous transition-metal complexes[13–15] in solution have been reported along with those on supported Au.[9,10] Ideally, direct synthesis of amides through heterogeneous catalytic processes with high selectivity under environmentally benign conditions would be possible.

The performance of catalytic processes can be improved through understanding the reaction mechanism at a molecular level so that the kinetics and selectivity of the overall process can be accurately predicted. A first step is to deconvolute the roles of gold and the oxide support. Our approach is to investigate O-covered Au(111), since without oxygen, Au is inert towards many reactions, including those of alcohols, aldehydes, and amines.[8,16–20]

The general concept for amine acylation on O/Au(111) originates in the chemical nature of adsorbed oxygen and other nucleophilic adsorbates formed by selective deprotonation of their conjugate acids. For example, adsorbed O on Au surfaces activates alcohols,[17] ammonia,[19,20] and amines[8] through Brønsted acid–base reactions:

$$\mathrm{RCH_2OH + O_{(a)} \rightarrow RCH_2O_{(a)} + OH_{(a)}} \tag{1}$$

$$\mathrm{RNH_2 + O_{(a)} \rightarrow RNH_{(a)} + OH_{(a)}} \tag{2}$$

These same O-covered Au surfaces are active for self-coupling of alcohols and cross-coupling between methanol and aldehydes.[16–18,21] Once the surface-bound alkoxy forms, a fraction of it undergoes β-H elimination to form the corresponding aldehyde:

$$\mathrm{RCH_2O_{(a)} + O_{(a)} \rightarrow RC(H){=}O_{(a)} + OH_{(a)}} \tag{3}$$

Esterification subsequently proceeds by nucleophilic attack on the aldehyde by the adsorbed alkoxy group at the electron-deficient aldehydic carbon, resulting in the corresponding ester through the hemiacetal intermediate (not shown):

$$\mathrm{RCH_2O_{(a)} + RC(H){=}O_{(a)} + O_{(a)} \rightarrow RC({=}O)OCH_2R_{(g)} + OH_{(a)}} \tag{4}$$

The key steps in these reactions are the initial selective activation of the RO–H bond in the alcohol by adsorbed oxygen and the nucleophilic attack of the adsorbed alkoxy on the electron-deficient carbon in the aldehyde.[16,18]

Chemical analogy and understanding of the fundamental mechanism of these reactions suggest that such reactions should occur between other adsorbed nucleophiles and electron-deficient carbon atoms. Hence, we anticipated that activation of an N–H bond in an amine [Eq. (2)] would yield an amide intermediate that should also attack the electron-deficient carbonyl carbon in aldehydes.

Here, we demonstrate the novel nucleophilic reactivity of $(CH_3)_2N$, selectively formed from activation of dimethylamine by adsorbed O on Au(111). The adsorbed $(CH_3)_2N$

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attacks the electron-deficient carbon in formaldehyde to yield *N*,*N*-dimethylformamide with nearly 100 % selectivity at low initial oxygen coverage ($\theta_O = 0.15$ ML (monolayers)). This coupling reaction occurs at temperatures as low as 175 K, indicating an extremely low activation barrier.

A single-crystal Au(111) surface was prepared in ultrahigh vacuum, on which oxygen atoms were introduced by ozone decomposition, due to the low dissociation probability of O_2 on Au(111) ($< 10^{-7}$ at 400 K).[22] The adsorption of O on Au(111) using O_3 decomposition induces formation of O-containing Au nanoparticles,[23] which serves as an excellent model for Au-based catalytic processes. The condition used for oxidation produces nanoparticles of ca. 2 nm in diameter and a low surface concentration with O bound primarily to sites with local three-fold coordination.[24,25] These Au nanoparticles are remarkably selective and active.[16,26] At higher coverage, less reactive, larger Au–O islands form a two-dimensional "oxide".[26]

Dimethylamine was initially reacted with O/Au(111) at 120 K, and then formaldehyde was adsorbed onto the surface. The selective coupling product, *N*,*N*-dimethylformamide $(CH_3)_2NC(H){=}O$ (*m*/*z* 73), evolves at ca. 175 K into the gas phase while heating the surface (Figure 1 a) along with water and unreacted dimethylamine. There is no detectable CO_2 (*m*/*z* 44) or NO_2 (*m*/*z* 46). A small amount of *N*-methyl formamide (*m*/*z* 59) was also observed at ca. 350 K.

The product was unequivocally identified by detection of the parent ion and by comparison of its fragmentation pattern to that of an authentic sample of *N*,*N*-dimethylformamide, obtained by subliming the condensed amide. Isotopic labeling was used to confirm product identification and to clarify the mechanism. Reaction of [D$_0$]formaldehyde with [D$_6$]dimethylamine exclusively yields $(CD_3)_2NC(H){=}O$, based on the mass shift of the parent ion from 73 to 79 amu (Figure 1 b). Furthermore, [D$_2$]formaldehyde reacts with [D$_0$]dimethylamine to form $(CH_3)_2NC(D){=}O$ (74 amu) (Figure 1 c). By using $H_2C^{18}O$, we established that the product contains one oxygen derived from formaldehyde (see Figure S1 in Supporting Information). These results show that the methyl groups in the amine and the carbonyl in the formaldehyde are preserved and that only the aldehydic C–H bond is broken.

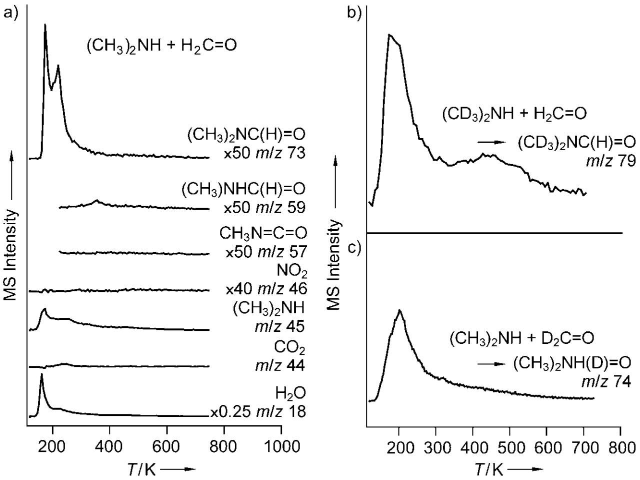


Figure 1. Reaction of dimethylamine and formaldehyde on O/Au(111) yields *N*,*N*-dimethylformamide in temperature-programmed reaction spectra obtained after introducing: a) [D$_0$]dimethylamine (9 L) and b) [D$_6$]dimethylamine ($(CD_3)_2NH$) (9 L) both followed by [D$_0$]formaldehyde (27 L) on O/Au(111) ($\theta_o = 0.15$ ML) at 120 K. In c) [D$_0$]dimethylamine (9 L) and [D$_2$]formaldehyde (27 L) were sequentially dosed onto O/Au(111) ($\theta_o = 0.15$ ML) at 120 K. The contributions from fragmentation of dimethylamine and *N*,*N*-dimethylformamide to the *m*/*z* 44 and *m*/*z* 46 signals were subtracted for clarity in (a). No reaction is detected on clean Au(111). The heating rate was 4 K s^{-1}.

By analogy to previous studies, we assert that the first step in the amine acylation reaction is deprotonation of the dimethylamine to form adsorbed $(CH_3)_2N_{(a)}$:

$$(CH_3)_2NH_{(a)} + O_{(a)} \rightarrow (CH_3)_2N_{(a)} + OH_{(a)} \tag{5}$$

The experiments with the different deuterated species show that $(CH_3)_2N_{(a)}$ must attack the aldehydic carbon in formaldehyde, presumably to form the hemiaminal:

$$(CH_3)_2N_{(a)} + H_2C{=}O_{(a)} \rightarrow (CH_3)_2NCH_2O_{(a)} \tag{6}$$

Subsequent β-hydride elimination yields *N*,*N*-dimethylformamide:

$$(CH_3)_2NCH_2O_{(a)} + O_{(a)} \rightarrow (CH_3)_2NC(H){=}O_{(g)} + OH_{(a)} \tag{7}$$

This reaction is analogous to the esterification reaction [Eq. (4)].

At high oxygen coverage, that is, $\theta_o = 1$ ML, secondary oxidation products form: NO_2, CO_2, H_2O, methyl isocyanate (*m*/*z* 57), and *N*-methylformamide were identified by quantitative mass fragmentation analysis. These products appear to form through direct oxidation of dimethylamine, as they also appear at the same temperatures in the oxidation of dimethylamine on O/Au(111) (data not shown). Apparently, at high O coverage, combustion of dimethylamine competes directly with acylation.

The selectivity for *N*,*N*-dimethylformamide from coupling between dimethylamine and formaldehyde thus decreases with initial oxygen coverage employed (Figure 2). At low initial oxygen coverage, the selectivity approaches 100 %. As the initial oxygen coverage increases, the selectivity drops to 30 % at $\theta_o = 1$ ML, where combustion reactions dominate, consistent with the general trend observed in self-coupling reactions of alcohols.[16,17]

The reaction steps involved in the selective acylation of dimethylamine, including those suggested for secondary oxidation, are summarized in Scheme 1. Evidence for specific intermediates is obtained using X-ray photoelectron spectroscopy. The evolution of the N(1s) and C(1s) X-ray photoelectron peaks with heating show that dimethylamine is first converted to $(CH_3)_2N_{(a)}$ by abstraction of the amino hydrogen (Figure 3). Secondary oxidation leads to the formation of *N*-methylformamide and methylisocyanate. (Figure 3 and Table S1, complementary reactivity data is shown in Figure S2).

Dimethylamine condensed on clean Au(111) is characterized by a single N(1s) peak with a binding energy (BE) of

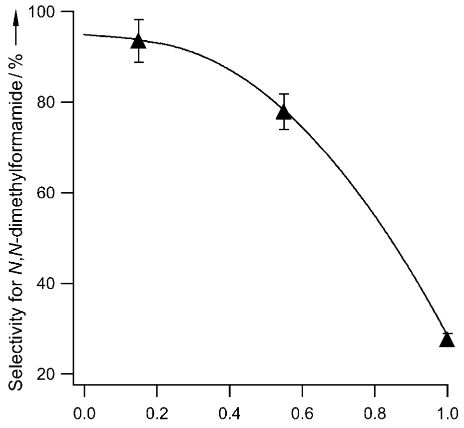


Figure 2. Selectivity for production of *N,N*-dimethylformamide (the ratio of *m/z* 73 signal to the sum of *m/z* 44 and *m/z* 73 signals, corrected for fragmentation) vs. initial oxygen coverage.

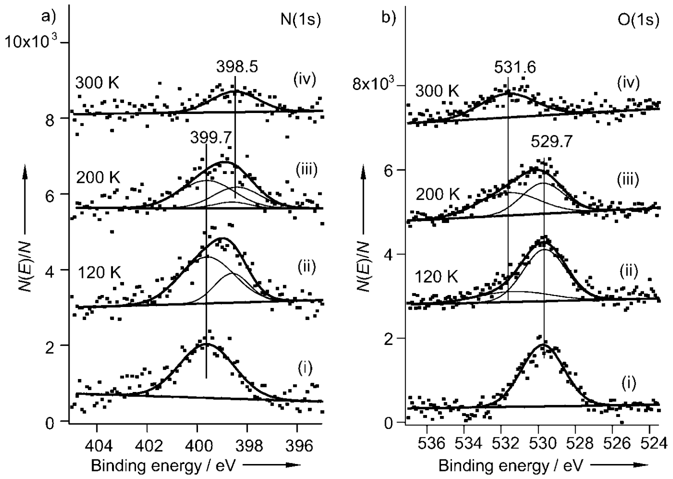
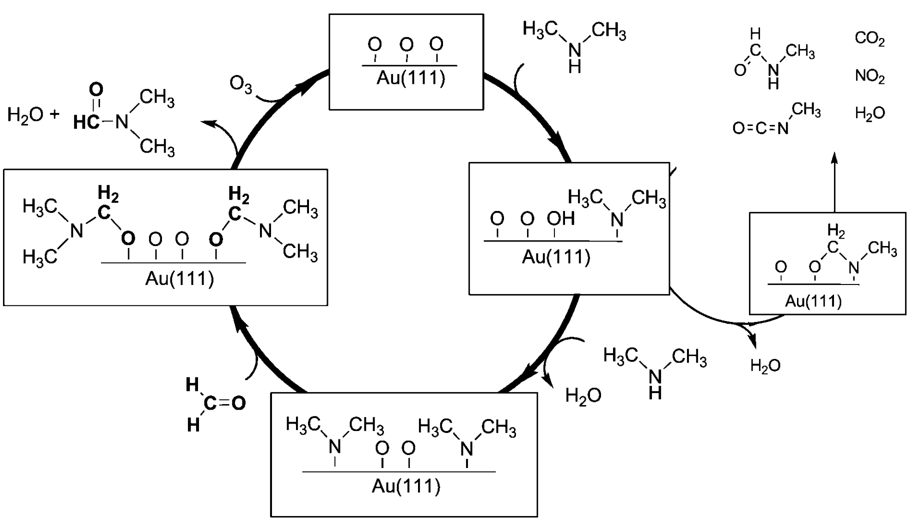


Figure 3. X-ray photoelectron spectra. a) N(1s) region following: i) condensation of dimethylamine multilayers on Au(111) at 120 K, ii) adsorption of dimethylamine on O/Au(111) ($\theta_o = 0.15$ ML) at 120 K and subsequently heated to iii) 200 K and iv) 300 K. b) O(1s) region for: i) as-prepared O/Au(111) ($\theta_o = 0.15$ ML) and ii–iv) after the same treatment as in (a), plots ii–iv. All spectra were obtained after cooling to 120 K.

399.7 eV (Figure 3a, plot i). When dimethylamine is adsorbed onto O-covered Au(111) at 120 K ($\theta_o = 0.15$ ML), the N(1s) peak broadens and shifts to lower binding energy, which is deconvoluted into a peak at 399.7 eV, assigned to molecular dimethylamine, and one at 398.7 eV, ascribed to $(CH_3)_2N_{(a)}$, (Figure 3a, plot ii). The $(CH_3)_2N_{(a)}$ formed from deprotonation of dimethylamine by the adsorbed O [Eq. (5)], is signified by a N(1s) peak at 398.7 eV, in excellent agreement with the previous identification of $(CH_3)_2N_{(a)}$ on Cu(211).[27] When the surface is heated to 200 K, the N(1s) spectrum broadens, ultimately leading to a new feature at 398.5 eV that persists when the surface is heated to 300 K (Figure 3a, plots iii and iv), and which is attributed to $CH_3NCH_2O_{(a)}$, the precursor to $CH_3N{=}C{=}O$ and $CH_3N(H)C(H){=}O$.

The concentrations of adsorbed $(CH_3)_2NH_{(a)}$ and $(CH_3)_2N_{(a)}$ decrease substantially following heating of the surface (Figure 3), based on the decrease in their characteristic N(1s) peak intensities. The $(CH_3)_2NH_{(a)}$ and $(CH_3)_2N_{(a)}$ decrease to 40% and 80%, respectively, of their amounts at 120 K after heating to 200 K. The decrease in the amount of $(CH_3)_2N_{(a)}$ is attributed to its conversion to the precursor for secondary oxidation products. This argument is supported by reactivity experiments. If after adsorbing dimethylamine on O/Au(111) ($\theta_o = 0.15$ ML) at 120 K, the surface was heated to 200 K, 250 K or 300 K and then cooled back to 120 K, very little *N,N*-dimethylformamide was formed after subsequent exposure to formaldehyde. These observations are supporting evidence that the $(CH_3)_2N_{(a)}$ is the key intermediate for the coupling to form the *N,N*-dimethylformamide. Nearly the same amount of methylisocyanate and *N*-methylformamide was formed after each of these heat treatments, consistent with the formation of the precursor to secondary oxidation below 200 K.

The O(1s) feature supports our identification of the precursor to secondary oxidation. At a coverage of 0.15 ML the O(1s) peak for adsorbed O is at 529.7 eV (Figure 3b, plot i). After dimethylamine is dosed onto the surface at 120 K, a shoulder appears at higher binding energy. When the surface is heated to 200 K, water desorbs,[28] and a peak appears at 531.6 eV (Figure 3b, plot iii), which is assigned to the precursor for the secondary oxidation products. Accordingly, this peak persists to 300 K (Figure 3b, plot iv). The atomic ratio of C:N:O in this precursor was calculated as 2:1:1 using



Scheme 1. Proposed mechanisms for the coupling of dimethylamine with formaldehyde and the secondary oxidation of dimethylamine promoted on O/Au(111).

integrated areas of C(1s), N(1s), and O(1s) peaks, corrected for their corresponding sensitivity factors. Since, aside from combustion products, the only species that evolve above 300 K are methylisocyanate and *N*-methylformamide, it is reasonable to identify the N-containing surface species at 300 K as $CH_3NCH_2O_{(a)}$, the precursor to these secondary oxidation products. We suggest this species is formed by:

$$(CH_3)_2N_{(a)} + O_{(a)} \rightarrow CH_3NCH_2O_{(a)} + OH_{(a)} \qquad (8)$$

The work reported here establishes a general mechanistic framework for anticipating an entire class of amine acylation reactions using aldehydes promoted by O-covered Au (Scheme 1). The strong parallels with the esterification of alcohols, the pattern of products formed using deuterium labeling, and the spectroscopic evidence for the key $(CH_3)_2N_{(a)}$ intermediate are strong evidence for the nucleophilic attack on the aldehydic carbon by this intermediate.

Our work also has implications for selective amine acylation over supported Au catalysts: the mechanism established here for unsupported Au in the vapor phase may also contribute to the reactive chemistry even in the liquid phase using formaldehyde as the acylation agent (e.g., in aqueous solution). The mechanism proposed is general and not limited to acylation of dimethylamine; other aldehydes may also be used. The key factor reported herein in determining selectivity is abstraction of a single H atom from the nitrogen in the amine, without associated C–H bond activation, to form an adsorbed amide. Molecular species, including water, are weakly bound to Au, so that even in solution their steady-state coverages will be low. Recent studies of benzyl amine acylation in methanol solution were explained by a combination of Au-mediated oxidative esterification of methanol and classic organic chemical solution-phase reactions. It was suggested that methylformate is catalytically formed by esterification of methanol on the Au catalyst, and that subsequent reaction steps occur in the liquid and are not mediated by Au.[10] Indeed, as noted above, oxygen-assisted esterification is facile on Au surfaces, both in the vapor and liquid phases. Importantly, we observe that methyl formate does not react with dimethylamine on Au(111) to any significant extent with or without adsorbed oxygen on Au(111) under our conditions (Figure S3), lending support to the acylation mechanism suggested by Haruta et al. in methanol solution.

In conclusion, we have established that the cross-coupling between dimethylamine and formaldehyde occurs with selectivity approaching 100% at low coverage of adsorbed O on metallic gold to form *N*,*N*-dimethylformamide through a pathway with a low activation energy. The coupling reaction occurs through the attack of nucleophilic $(CH_3)_2N_{(a)}$ on the carbonyl carbon of the aldehyde. Such reactions appear general to the coupling of alcohols and amines with aldehydes to form esters and amides, through adsorbed alkoxides and amides, respectively. Both nucleophilic reaction intermediates are formed selectively by reaction of their conjugate acids with adsorbed oxygen. We anticipate that this principle will apply to coupling of other amines and aldehydes, analogous to the the cross-coupling of alcohols and aldehydes.[18] We are currently generalizing this process to other reaction combinations to firmly extend this generality.

Experimental Section

Clean Au(111) was prepared as described previously.[26] All temperature programmed reaction data were obtained with well-established protocols.[26] The reaction products were identified by quantitative mass spectrometry (Balzers Prisma QMS 200) using fragmentation patterns obtained from authentic samples. The initial surface concentration of oxygen atoms was reproducibly varied by controlling the ozone flux. Following exposure of the oxygen-covered Au(111) to dimethylamine and formaldehyde at 120 K, temperature programmed reaction was employed to identify reaction products and to interrogate the mechanism of the reactions. The X-ray photoelectron spectra were acquired with an analyzer passing energy of 17.9 eV and a multiplier voltage of 3 kV using $Mg_{K\alpha}$ X-rays (300 W) as the excitation source. The binding energy (BE) calibration was referenced to the Au $4f_{7/2}$ peak at 83.8 eV. The N(1s) and O(1s) spectra were acquired by multiple scans (300 and 100 cycles, respectively) to enhance the signal-to-noise ratio.

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