

Predicting Gold-Mediated Catalytic Oxidative-Coupling Reactions from Single Crystal Studies

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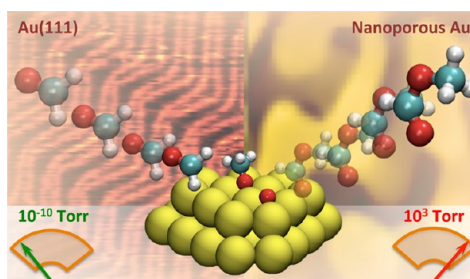
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CONSPECTUS

Though metallic gold is chemically inert under ambient conditions, its surface is extremely reactive and selective for many key oxidative chemical transformations when activated by atomic oxygen. A molecular-level understanding of the mechanism of these processes could allow researchers to design “green” catalytic processes mediated by gold-based materials. This Account focuses on the mechanistic framework for oxidative-coupling reactions established by fundamental studies on oxygen-activated Au(111) and the application of these principles to steady-state catalytic conditions. We also discuss the importance of the paradigms discovered both for predicting new oxidative-coupling reactions and for understanding existing literature.

The mechanistic framework for the oxidative coupling of alcohols on gold surfaces predicts that new oxidative-coupling reactions should occur between amines and aldehydes and amines and alcohols as well as through alcohol carbonylation. Adsorbed atomic oxygen on the gold surface facilitates the activation of the substrates, and nucleophilic attack and β -H elimination are the two fundamental reactions that propagate the versatile chemistry that ensues. In the self-coupling of primary alcohols, adsorbed atomic oxygen first activates the O–H bond in the hydroxyl group at ~ 150 K, which forms the corresponding adsorbed alkoxy groups. The rate-limiting step of the self-coupling reaction is the β -H elimination reaction of alkoxy groups to form the corresponding aldehydes and occurs with an activation barrier of approximately 12 kcal/mol. The remaining alkoxy groups nucleophilically attack the electron-deficient aldehyde carbonyl carbon to yield the adsorbed “hemiacetal”. This intermediate undergoes facile β -H elimination to produce the final coupling products, esters with twice the number of carbon atoms as the starting alcohols. This mechanistic insight suggests that cross-coupling occurs between alcohols and aldehydes, based on the logic that the nucleophilic reaction should be independent of the origin of the aldehydes, whether formed in situ or introduced externally. As a further example, adsorbed amides, formed from deprotonation of amines by atomic oxygen, can also attack aldehydes nucleophilically to yield the corresponding amides.

Our mechanistic framework can also explain more elaborate gold-mediated chemistry, such as a unique carbonylation reaction via two subsequent nucleophilic attacks. These model studies on well-defined Au(111) at low pressure predict steady-state catalytic behavior on nanoporous gold under practical conditions. The fundamental principles of this research can also explain many other oxygen-assisted gold-mediated reactions observed under ambient conditions.



Introduction

The development of highly selective, energy-efficient, and environmentally benign processing is a “holy grail” for the chemical industry. Heterogeneous catalysts offer a promising approach toward this goal. Fundamental studies of surfaces with well-defined structures and composition can

be used to identify rate-limiting reaction intermediates, the rate constants for their reactions, and the overall catalytic cycle(s) in order to advance the discovery and development of catalysts. In addition, first-principles theory-based calculations offer molecular-level understanding of the energetics and activation barriers of elementary steps. This

Account provides an overview of our recent advances in model mechanistic studies of oxygen-assisted gold-mediated oxidative-coupling reactions on Au(111) and their practical relevance to gold-based catalysts under working catalytic conditions.

Partial oxidation of methanol to formaldehyde on gold was reported in 1920, challenging the assumption of the chemical inertness of gold surfaces. In the 1980s, modest catalytic activity of gold supported on refractory metal oxides was reported.¹ The current interest in heterogeneous Au catalysis was set off by the discovery that gold nanoparticles supported on reducible metal oxides catalyze CO oxidation to CO₂ using O₂ at temperatures as low as -70 °C.² Subsequently, catalysis of a range of key transformations by gold-based materials has been demonstrated,³ including selective oxidation of alcohols.^{2,4–6}

Explanations for the catalytic activity of Au include quantum size effects, charge transfer to or from Au, dissolution of Au into the lattice of the metal oxide and electronic effects at the gold–oxide perimeter. Recent reports on the high catalytic activity for oxidative coupling reactions^{7,8} clearly show that bulk gold promotes reaction without an oxide support. Moreover, single crystal gold surfaces also promote a wide range of selective oxidation⁹ reactions if properly activated.^{10–13}

Ironically, the catalytic activity of metallic gold is a direct result of its *difficulty* to activate molecular oxygen because adsorbed O is required for bond activation, leading to high selectivity. Explanations for the activity of supported Au include direct dissociation of O₂ on or adjacent to gold nanoparticles, spillover of O_(a) from the support, formation of O_{2(a)}, and formation of OH_(a) in basic solution.¹⁴ We have chosen to focus on the reactions of atomic oxygen adsorbed on Au(111), a representative facet of Au particles, as a model. The mechanistic framework established by these studies explains reactivity of gold powder, nanoporous gold, and supported gold particles under working catalytic conditions, while also predicting new reactions, which have been verified.

Due to the extremely low dissociation probability of O₂ on Au(111), adsorbed atomic oxygen is formed by other methods: electron bombardment of NO₂, O₂⁺ sputtering, or exposure to ozone¹⁵ or atomic oxygen. Binding of atomic O to the Au(111) surface induces release of Au atoms from the surface to form nanoparticles containing Au and O,¹⁶ as illustrated by the scanning tunneling microscopy (STM) images (Figure 1).

The bonding environment of the adsorbed oxygen depends sensitively on the deposition rate and preparation temperature (Figure 1), because these are kinetically controlled structures. When oxygen is deposited at 200 K, nanoparticles containing both oxygen and Au (O/Au)

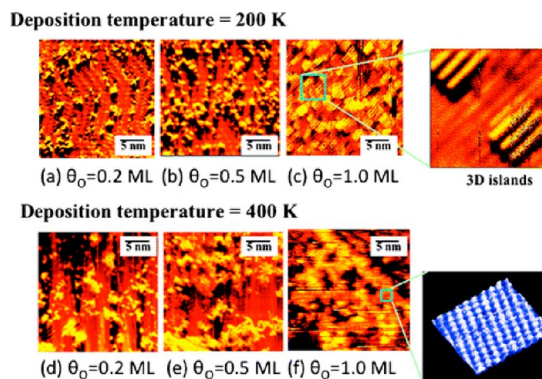


FIGURE 1. Scanning tunneling microscopic images showing the formation of nanoparticles on Au(111) after deposition of O_(a) via O₃ decomposition at two different surface temperatures. Insets, zoomed-in images with atomic-level detail. The size of the nanostructures increases with increasing O concentration and with surface temperature. Reprinted with permission from ref 16. Copyright 2006 American Chemical Society.

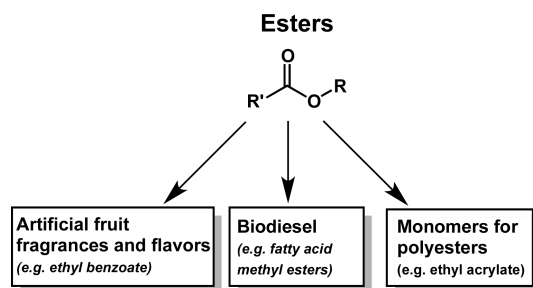
appear when the surface coverage of atomic oxygen is below 0.5 monolayer (ML), and the characteristic herringbone reconstruction of Au(111) is partially lifted (Figure 1). Further increase in the surface coverage of atomic oxygen results in 2D or 3D oxide-like structures.¹⁶ A combination of vibrational spectroscopy and *ab initio* molecular dynamics calculations reveals that at low coverages (<0.2 ML), atomic oxygen prefers to bind to the 3-fold FCC hollow sites, with a gradual transition to an oxide-like phase as the coverage of the O_(a) increases.¹⁶ The size and order of the O/Au particles increase when atomic oxygen is deposited at 400 K due to enhanced diffusion of gold (Figure 1d,e).¹⁶

The development of Au-mediated oxidative-coupling processes is a step in the direction of sustainable chemistry, and thus, we focus on this class of reactions. On O/Au, they are facile and highly selective; on nanoporous gold, they occur readily under mild ambient conditions. Esters are the main products of the coupling reactions of alcohols and aldehydes and have wide applications (Scheme 1). Esters also serve as solvents, surfactants, and critical intermediates to various derivatives. Amides, widely used as precursors to nylons, are the coupling product of amines and oxygenates.

Selective Oxidation of Alcohols: A Key Step en Route to Coupling Reactions

Selective oxidation of alcohols to the corresponding aldehydes on gold is a key initial step in the self-coupling of alcohols. The observation of formaldehyde production via partial oxidation of methanol on Au at high temperatures (>790 K) dates back to the early 20th century; a significant decrease in temperature (570 K) was reported more than

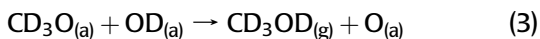
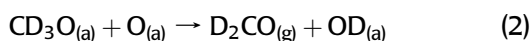
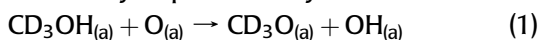
SCHEME 1. Major Industrial Applications of Esters



half a century later *in excess oxygen*. It was not until the late 1990s that selective oxidation of alcohols under milder conditions on supported Au catalysts¹⁷ or Au-containing alloys was reported.³ More recently, facile, selective oxidation of C₁–C₄ primary alkyl alcohols has been reported on O/Au(111); the corresponding aldehydes are formed at 200–250 K, indicating rapid kinetics of formation.¹²

Temperature-programmed reaction spectroscopy (TPRS) has been employed here as the primary method to investigate reactivity and mechanism of the selective oxidation and oxidative-coupling reactions. In conjunction with isotopic labeling, the identity of reaction intermediates, the rate-determining step, and the selectivity of the reaction are determined. For example, formaldehyde-*d*₂, methyl formate-*d*₄, and CO₂ (not shown) are identified by reacting CD₃OH with O/Au (Figure 2); the temperature at which each product evolves reflects directly the rate constant of the reaction(s) from which it emanates.

The key elementary steps for aldehyde formation are



These steps were deduced based on detailed analysis of the temperature-programmed reaction and spectroscopic data. This mechanism can be generalized to other alcohols (Scheme 2); it involves (1) oxygen-assisted deprotonation of the alcohol forming the corresponding alkoxy (reaction 1) and (2) β-H elimination of alkoxy to the corresponding aldehydes (reaction 2). First-principles calculations also support these conclusions.^{10,12,18–20} Importantly, *adsorbed atomic oxygen is required for the activation step*, because methanol adsorbs reversibly without reaction on clean Au(111).

The identity of the key reaction intermediate is supported by vibrational spectroscopy (Figure 3). Adsorbed O exhibits a vibrational feature at 370 cm⁻¹ (Figure 3a). Exposing

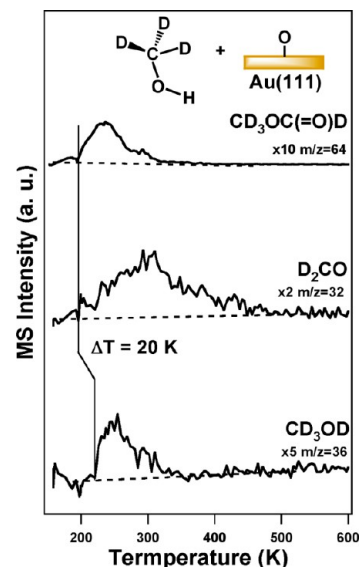
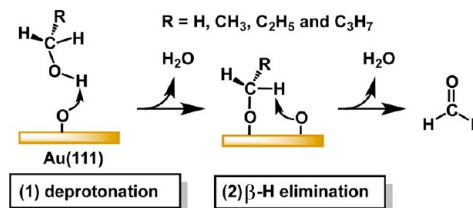


FIGURE 2. Oxidation of CD₃OH on O/Au(111) ($\theta_{\text{O}} = 0.05$ ML) yields selective and total oxidation products. Methanol was introduced to the O/Au(111) at 150 K, and the surface then heated at 5 K/s. Reprinted with permission from ref 19. Copyright 2011 Royal Society of Chemistry. No residual oxygen was detected in any of TPRS experiments reported in this Account.

SCHEME 2. Reaction Mechanism for Selective Oxidation of Alcohols to the Corresponding Aldehydes



O/Au(111) to methanol at 160 K gives rise to vibrational peaks characteristic of methoxy at 1060, 1170, 1500, and 3010 cm⁻¹ (Figure 3b).¹² When the surface is heated to 225 K, the intensities of the vibrational features for methoxy diminish significantly as methoxy reacts away, and features of adsorbed formate appear at 1500 and 1380 cm⁻¹ due to secondary oxidation of formaldehyde (Figure 3d). Alkoxy corresponding to activation of other primary alkyl alcohols by O/Au(111) have also been confirmed by vibrational spectroscopy.^{10,18,19}

The β-H elimination from CH₃O_(a) leading to formaldehyde was identified experimentally as the rate-limiting step from the measured kinetic isotope effect for CH₃O_(a) vs CD₃O_(a).¹² Consequently the energetics and activation barriers for β-H elimination of methoxy were investigated by DFT calculations for transfer to (1) the gold surface, (2) O_(a), (3) OH_(a), and (4) CH₃O_(a) (Figure 4). The oxygen-assisted

pathway has the lowest activation barrier (0.49 eV), suggesting that it is the favored reaction channel if there is sufficient adsorbed oxygen. The other three pathways were calculated to have similar barriers, approximately 0.15 eV higher than that of the oxygen-assisted pathway.²⁰ A limited amount of combustion occurs and is attributed to the further oxidation of aldehydes.^{12,18} For example, the carbonyl carbon in formaldehyde is nucleophilically attacked by adsorbed atomic oxygen to form adsorbed dioxymethylene

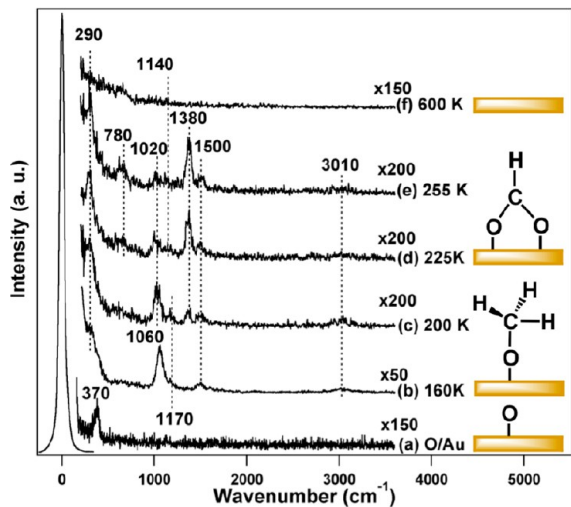


FIGURE 3. Vibrational spectra of intermediates formed during the reaction of methanol with O/Au(111). (a) O/Au(111) with 0.1 ML atomic oxygen; (b) O/Au(111) with 0.1 ML atomic oxygen exposed to methanol at 160 K; (c–e) gradual formation of adsorbed HCOO after heating to 200, 225, and 255 K, which disappears after heating to 600 K. All spectra were collected at 160 K. Reprinted with permission from ref 12. Copyright 2009 Wiley.

(Scheme 3), which subsequently dehydrogenates to formate (Figures 3c,d). Decomposition of formate leads to CO₂ and water.^{12,20}

Self-Coupling of Primary Alcohols: Mechanistic Framework

Self-coupling of primary alcohols is the reaction of two molecules of the same alcohol to form a molecule of the corresponding ester. Methyl formate-*d*₄ is the dominant product from reaction of CD₃OH on O/Au(111) (Figure 2). Mechanistically, the coupling derives from the partial oxidation of alcohols to aldehydes described in the previous section. Though self-coupling of methanol on O/Au(111) is exemplified here (Scheme 4), the mechanistic framework established applies to self-coupling reactions of all primary alcohols.

As the β -H elimination of a fraction of the adsorbed methoxy commences, the coexistence of the *adsorbed* formaldehyde, with an electron-deficient carbonyl carbon atom, and the remaining methoxy, with an electron-rich oxygen, sets the stage for a nucleophilic reaction.¹² Methoxy attacks the electron-deficient carbonyl carbon in the formaldehyde spontaneously forming the “hemiacetal” surface intermediate. According to separate DFT calculations, they react with no activation barrier (Figure 5a–c).²⁰ β -H elimination from the hemiacetal to form methyl formate then occurs; with the assistance of adsorbed oxygen, there is no energy barrier (Figures 5d–f).²⁰ Even without the aid of adsorbed O, the energy barrier for formation of the ester is only 0.22 eV.

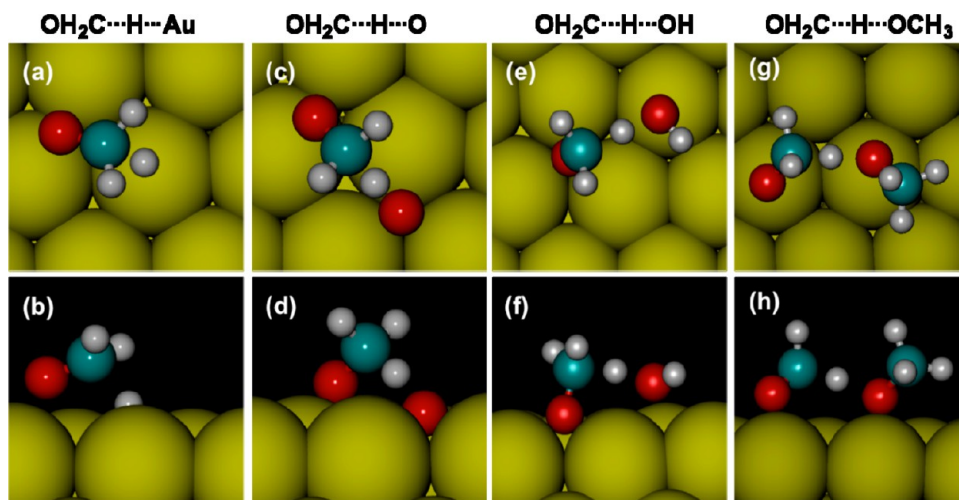
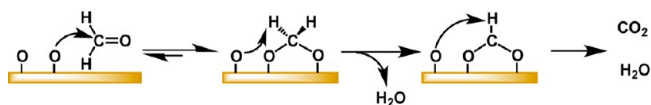
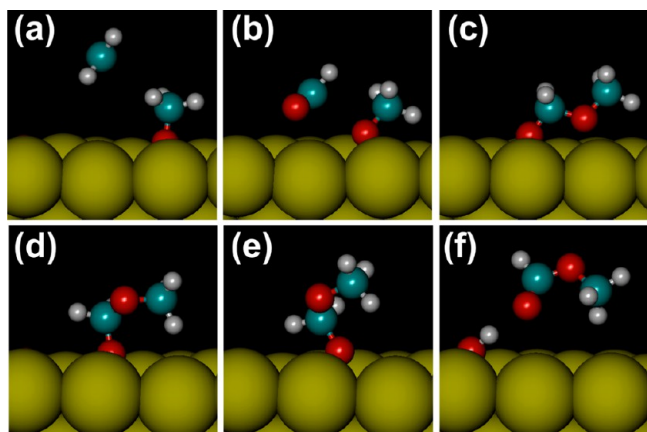
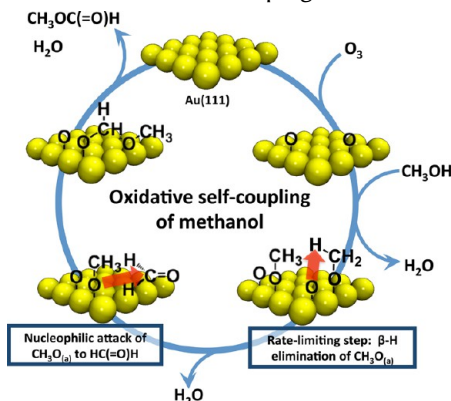


FIGURE 4. Transition state structures [top and side views] for formaldehyde formation via β -H transfer from methoxy on Au(111) to (left to right) (a, b) neighboring Au ($E_a = 0.64$ eV), (c, d) an adsorbed O atom ($E_a = 0.49$ eV), (e, f) adsorbed OH ($E_a = 0.63$ eV), and (g, h) an adjacent methoxy ($E_a = 0.66$ eV). Large yellow spheres, red spheres, blue spheres, and small white spheres represent Au, O, C, and H atoms, respectively.

SCHEME 3. Mechanism for Acid Formation and Combustion Reactions by Further Oxidation of Formaldehyde on O/Au(111)**SCHEME 4.** Mechanism for the Self-Coupling of Methanol on O/Au(111)**FIGURE 5.** Calculated reaction process of nucleophilic attack of methoxy on formaldehyde forming hemiacetal (a–c) and atomic-oxygen-assisted β -H elimination of hemiacetal forming methyl formate (d–f). The atomic oxygen in β -H elimination is blocked in view by the front Au atoms in (a–e); however, it was in all calculations.

The negligible barriers for nucleophilic attack and β -H elimination from the hemiacetal identify β -H elimination of methoxy as the rate-limiting step in the self-coupling of methanol in agreement with the kinetic isotope shift for the evolution of methyl formate- d_4 compared with that of methyl formate- d_0 .¹² Detailed analysis of the temperature-programmed reaction spectra of CD_3OH on O/Au(111) reveals that the onset of formaldehyde and methyl formate evolution coincide (Figure 1), consistent with the theoretical prediction of the β -H elimination of methoxy being rate

limiting.¹⁹ Moreover, separate investigations of reactions of formaldehyde and adsorbed methoxy show that they couple readily (see below).

One of the reasons that oxidative coupling occurs on Au whereas other coinage metals, for example, Ag, favor partial oxidation to formaldehyde is that bonding of methoxy and formaldehyde is relatively weak. There are two important consequences of this weak bonding. First, the attack of the aldehyde by the methoxy requires that the CH_3O move off its preferred binding site, requiring partial loss of O–Au bonding in the transition state. The weak bonding leads to a lower barrier than is expected for other metals that have stronger metal–O bonding.²¹ The second consequence is that the reactant species are very mobile on the surface due to the low barrier for diffusion.

Coupling of other primary alcohols (ethanol, 1-propanol, and 1-butanol) follows the same mechanism (Scheme 4) but with important differences.¹⁹ The selectivity for aldehyde production rises with increasing length of the alkyl chains at the expense of the ester formation. This is attributed to the greater ease of the β -H elimination for longer chain alkoxy.¹⁹ The yield of the ester depends on the surface coverage of the alkoxy, aldehyde, and adsorbed oxygen; the higher rate of β -H elimination depletes the surface alkoxy, thus reducing the rate of formation of the adsorbed hemiacetal.¹⁹ Accordingly, 1-butanol almost exclusively forms the aldehyde, $\text{CH}_3(\text{CH}_2)_2\text{CH}(\text{=O})$. This example demonstrates how the mechanism provides a general understanding of these oxidative processes.

Coupling of Alcohols and Aldehydes: Predictions from the Mechanism

The power of mechanistic studies lies not only in rationalizing the existing results in the literature, but more importantly in predicting new reactions. The mechanistic framework for self-coupling of alcohols on O/Au(111) establishes a guiding principle for oxidative coupling more generally, that attack of formaldehyde by methoxy is nucleophilic in nature (Scheme 4 and Figure 5). This being so, the nucleophile can be introduced externally, reacting directly with the adsorbed alkoxy. Indeed, this is readily observed (Figure 6a, bottom trace). Moreover, the evolution temperature for methyl formate from adding formaldehyde to $\text{CH}_3\text{O}_{(\text{a})}$ is ~ 40 K lower. These results are a clear indication that supplying formaldehyde circumvents the rate-limiting β -H elimination from methoxy, lowering the overall activation barrier.¹³

A second and more far-reaching implication of the identification of the nucleophilic attack as the key mechanistic

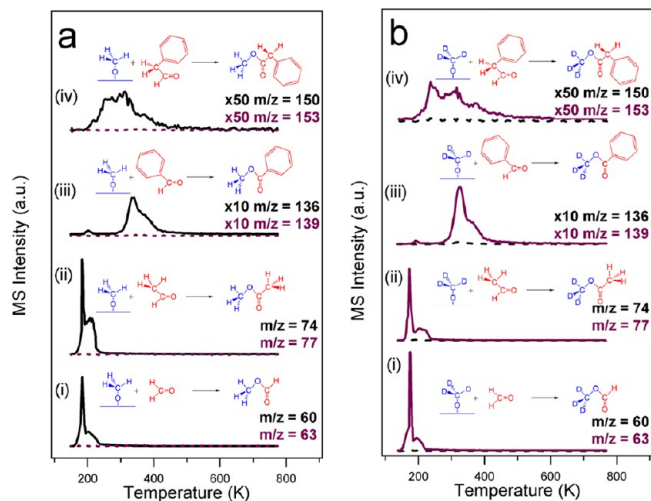


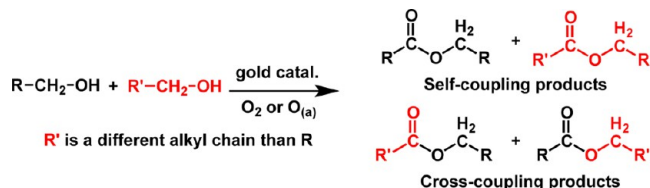
FIGURE 6. Coupling reactions of (a) methoxy- d_0 and (b) methoxy- d_3 on O/Au(111) ($\theta_{\text{O}} \approx 0.05$ ML) with (i) formaldehyde, (ii) acetaldehyde, (iii) benzaldehyde, and (iv) benzeneacetaldehyde. The dashed lines are the traces obtained for the masses shown in the corresponding color to establish the isotopic purity of the products in the two cases. Reprinted with permission of ref 13. Copyright 2009 Nature Publishing Group.

step is that similar reactions are likely to occur with other surface nucleophiles and electrophiles, opening a path for the discovery of numerous new families of reactions. Essentially, we can represent these reactions as attack of an electron-deficient center by an electron-rich species. Aldehydes, having the common terminal carbonyl group and the β -hydrogen, are the natural analogues of formaldehyde as the electrophile. Indeed, cross-coupling of methanol and various aldehydes readily occurs on O/Au(111) (Figure 6) to selectively form the corresponding esters. The introduction of acetaldehyde, benzaldehyde, and benzeneacetaldehyde to the methoxy covered O/Au(111) produces methyl acetate, methyl benzoate, and benzeneacetic acid methyl ester, respectively (Figure 6).¹³ All coupling processes occur at very low temperatures, especially for the smaller reactants, with evolution of the esters as low as 200 K. Isotopic labeling confirms that the methoxy group is preserved in the coupling reactions. The observed cross-coupling reactions of methanol with aldehydes firmly supports the mechanistic framework for oxidative-coupling reactions on gold (Scheme 4). Cross-coupling of alcohols and aldehydes has been reported on nanoporous gold⁸ and polymer stabilized gold particles²² in gas and liquid phases, demonstrating the generality of the mechanism.

Cross-Coupling of Dissimilar Alcohols: Selectivity Control

Alcohols are more desirable raw materials than aldehydes for producing esters due to their wider availability and lower

SCHEME 5. Possible Ester Products (Not All Are Actually Formed) from the Cross-Coupling of Two Dissimilar Alcohols

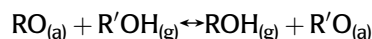


cost. Cross-coupling of dissimilar alcohols can, in principle, form the same variety of esters as cross-coupling of alcohols and aldehydes. However, reaction of dissimilar alcohols on O/Au(111) normally yields a mixture of esters from both self-coupling and cross-coupling reactions via competitive reactions of the coadsorbed alkoxy (Scheme 5). Therefore, a key challenge for selectively cross-coupling dissimilar alcohols is to effect the production of one or a few desired esters while suppressing the rest. To that end, understanding the mechanism is quite important.

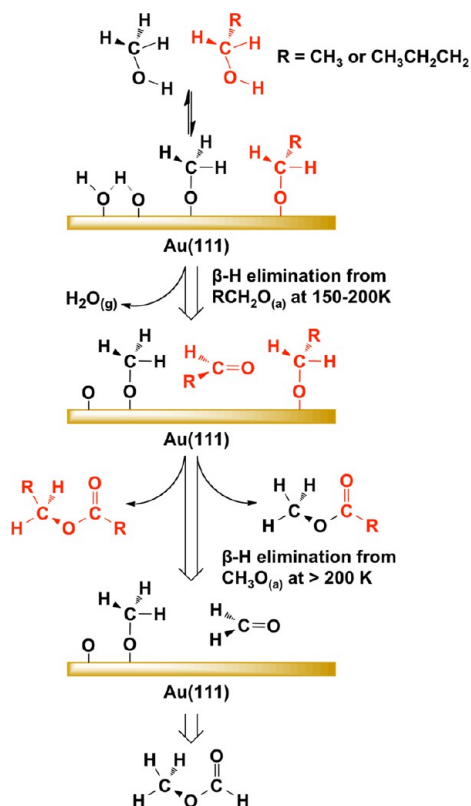
Cross-coupling of dissimilar alcohols on O/Au(111) follows the same elementary steps as the self-coupling of alcohols, though with more potential branching pathways (Scheme 6). Reacting a mixture of primary alkyl alcohols with O/Au(111) at 150 K yields a mixture of adsorbed alkoxy intermediates.¹⁰ Differences in the rates of β -H elimination of dissimilar alkoxy, due to the differing strengths of the β -C-H bonds of alkoxy, play a critical role in determining the product distribution.¹⁰ Since the strengths of the β -C-H bonds decreases with increasing molecular weight, formation of the higher molecular weight aldehyde will commence first. Reaction of this aldehyde with the two alkoxy species will compete. The dominant coupling products are thus the self-coupling product of the higher molecular weight alcohol and the cross-coupling product of the lower molecular weight alkoxy and higher molecular weight aldehyde.

Since the formation of the aldehydes and the subsequent reactions with the adsorbed alkoxy species form a competitive network of reactions, the product distribution depends sensitively on the relative concentrations of the adsorbed alkoxy as well as on their relative β -C-H bond strengths. The relative stability of the surface-bound alkoxy is in increasing order, $\text{CH}_3\text{O}_{(\text{a})} < \text{C}_2\text{H}_5\text{O}_{(\text{a})} < \text{C}_3\text{H}_9\text{O}_{(\text{a})}$.¹⁰

Consequently for a mixture of reactants, the surface concentration of alkoxy species will be determined by the equilibrium



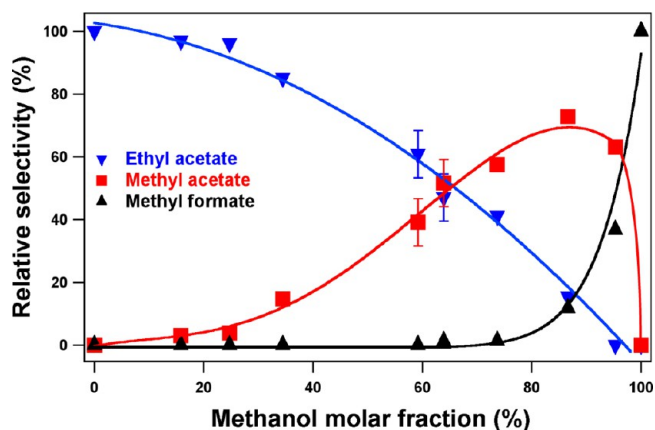
The product distribution of cross-coupling of methanol and ethanol on O/Au(111) as a function of the relative

SCHEME 6. Schematic of the Competing Coupling Reactions between Dissimilar Alcohols on O/Au(111) with Heating of the Surface^a

^aβ-H elimination of higher molecular weight alkoxy (ethoxy or n-butoxy) occurs more readily than that of methoxy; therefore no higher molecular weight alkoxy is left on the surface when formaldehyde is formed. Reprinted with permission from ref 10. Copyright 2010 American Chemical Society.

concentrations of methanol and ethanol illustrates the importance of the two factors (Figure 7).¹⁰ No ethyl formate is formed at any composition of the alcohol mixture; due to the lower β-C–H bond strength in ethoxy, acetaldehyde forms preferentially, and the acetate esters dominate the products except at the highest methanol concentrations; formaldehyde is not formed in the presence of ethoxy. Ethyl acetate, from the self-coupling of ethanol, and methyl acetate, from the cross-coupling of methanol and ethanol, always form together since they share a common electrophile, acetaldehyde. For the same reason, no methyl formate, the self-coupling product of methanol, is detected at methanol molar fractions below 70%, consistent with depletion of the adsorbed ethoxy prior to the onset of formaldehyde formation. At high methanol molar concentrations (>70%), adsorbed methoxy is in excess, leading to the formation of methyl formate.

These mechanistic principles also govern the product distribution pattern for coupling of dissimilar alcohols in

**FIGURE 7.** Selectivity variation as a function of methanol molar fraction for reaction of mixtures of CH₃OH and CH₃CH₂OH on O/Au(111) (θ_{O} = 0.1 ML). No ethyl formate was detected. All alcohol mixtures were introduced (6 L) at 150 K. Reprinted with permission from ref 10.

liquid phase. For example, when 1-hexanol and benzyl alcohol are oxidized in methanol solution on Au supported on TiO₂, methyl hexanoate and methyl benzoate are the exclusive coupling products, with yields close to 100%.²³ The relatively weak β-C–H bond of 1-hexanoyl and benzyl alkoxy ensures the selective formation of their corresponding aldehydes. Furthermore, the high concentration of methanol as solvent ensures that there will be a significant amount of methoxy on the catalyst despite its presumed lower binding energy. Dominant formation of both methoxy and the higher molecular weight aldehydes leads to the exclusive production of methyl hexanoate and methyl benzoate, respectively. High yields of methyl esters from cross-coupling of methanol and higher molecular weight alcohols have also been observed on polymer stabilized Au,²⁴ Au nanoparticles supported on silica,²⁵ and potassium titanate nanowires,²⁶ showing the general applicability of the mechanistic insight.

Coupling of a Secondary Amine and Aldehydes: Expanding the Arsenal of Nucleophiles

The coupling of methanol with a family of aldehydes indicates the generality of nucleophilic attack by the adsorbed alkoxide. The self-coupling of other primary alcohols also confirms that other alkoxy groups also can serve as nucleophiles in these oxidative-coupling reactions on Au. A step further in this direction is to find other surface intermediates that serve as nucleophiles and exhibit similar patterns of reactivity. Surface-bound amides (RR'N_(a)), which form from the oxygen-assisted deprotonation of the corresponding amines are promising candidates due to their structural and electronic similarity to alkoxy groups.

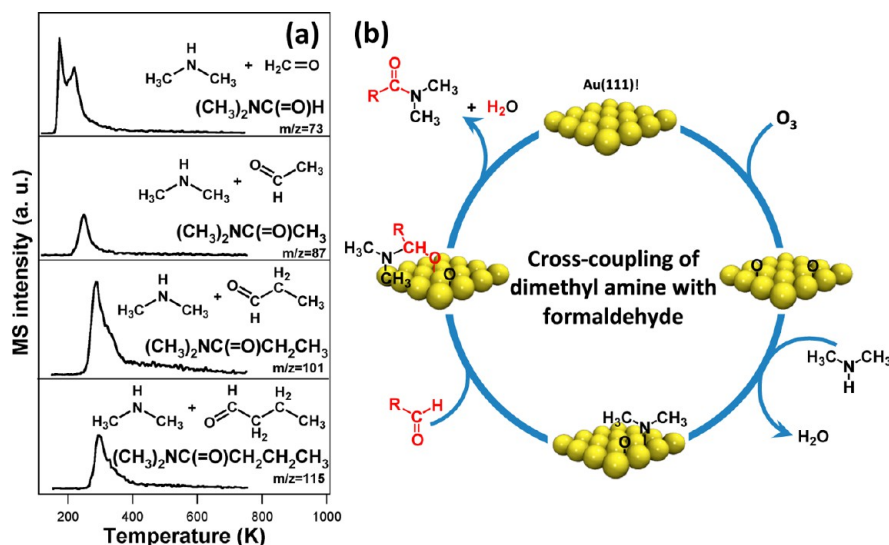


FIGURE 8. (a) Cross-coupling of dimethyl amine with formaldehyde (top), acetaldehyde (second to top), propanal (second to bottom), and butanal (bottom) on O/Au(111) ($\theta_{\text{O}} = 0.1$ ML) produces the corresponding amides. (b) Mechanism for oxidative coupling of dimethyl amine and aldehydes.

Indeed, cross-coupling of dimethyl amine and aldehydes (formaldehyde, acetaldehyde, propanal, and butanal) occurs readily on O/Au(111), forming the corresponding amides (Figure 8).¹¹ The oxygen activation of N–H in dimethyl amine on O/Au(111) leads to the formation of surface-bound dimethyl amide.¹¹ When exposed to an aldehyde, the nitrogen attacks the carbonyl carbon in the aldehyde, leading to the formation of the surface-bound “hemiaminal” intermediate (Figure 7b), before β -H elimination to form the amide. Dimethyl amine, the simplest secondary amine, was chosen as the model amine to avoid multiple N–H activations on O/Au(111); however, a similar mechanism applies to other amines.

This paradigm for oxidative-coupling reactions offers mechanistic insight into reactions reported in the literature that might appear rather mysterious in origin. For example, the coupling reaction observed among three components (benzaldehyde, piperidine, and phenylacetylene) on semiconductor–Au nanocomposites shown in Scheme 7a²⁷ is likely to proceed in two steps: (1) cross-coupling between piperidine and benzaldehyde via the oxidative-coupling mechanism described above forming the amide and (2) a dehydration reaction between the amide formed in step 1 and phenylacetylene via an adsorbed phenylacetylide, which can be formed by reaction of adsorbed O with the acidic acetylenic hydrogen. (Scheme 7b). Imines, with the C=N double bond analogous to the C=O double bond in aldehydes, have been reported to aerobically couple with pyrrolidine, a secondary amine (Scheme 7c),⁷ likely via the nucleophilic attack by the electron-rich amide, formed via deprotonation of pyrrolidine, on the electron deficient

carbon in the imine (Scheme 7d). The final product could be formed by a β -H elimination step of the surface-bound intermediate resulting from the previous step (Scheme 7d).

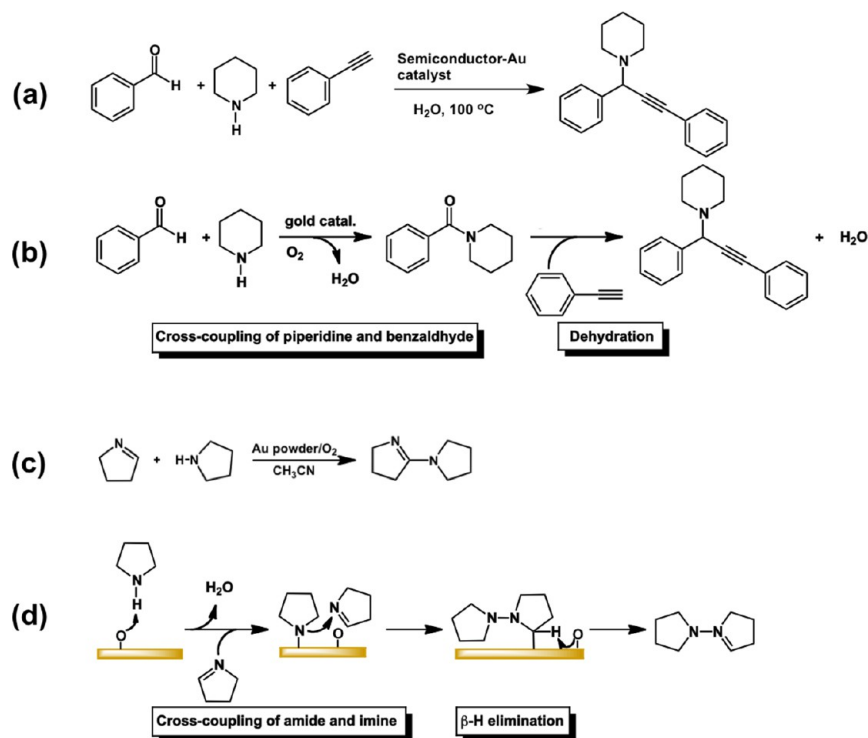
Taken together, the principles developed for simple oxidative coupling reactions on O/Au(111) can be generalized to provide a rationale for complex reactions reported in the literature on metallic gold, even in solution.

Generalization to Carbonylation Reactions

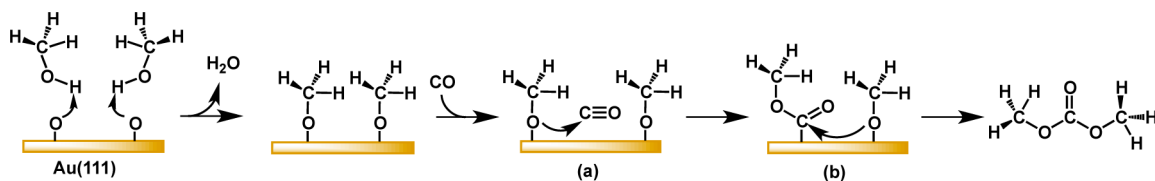
The nucleophilic reactions can be further generalized, as illustrated by the recent discovery of the direct methoxycarbonylation reaction.²⁸ In this reaction, surface-bound methoxy attacks adsorbed CO at temperatures as low as 150 K to form a stable surface-bound methoxycarbonyl, with CO inserting into the O–Au bond (Scheme 8).²⁸ Calculations suggest that it bonds to Au(111) via the carbonyl carbon on the atop site (Figure 9).²⁸ The carbonyl carbon in methoxycarbonyl, bonded to two oxygen atoms, is susceptible to further nucleophilic attack of adjacent methoxy (Figure 9b), leading to the final coupling product, dimethyl carbonate.

Methoxycarbonyl can be employed as a synthetic intermediate in cross-coupling reactions, exploiting nucleophilic attack by other nucleophiles, for example, ethoxy, phenoxy, and dimethyl amide (Figure 10a). The subsequent attack of the methoxycarbonyl by these nucleophiles leads to the formation of the corresponding coupling products (Figure 10b). The two-step nucleophilic attack mechanism offers potential synthetic routes for a wide range of chemical transformations, such as carboxymethylation and transesterification on atomic oxygen activated metallic gold.

SCHEME 7. Schematics of (a) Overall Coupling Reactions Involving Three Components (Benzaldehyde, Piperidine, And Phenylacetylene) on Semiconductor–Au Nanocomposites (ref 27), (b) a Mechanism Proposed Based on the Mechanistic Framework for Oxidative-Coupling of Alcohols on Au, and (c) the Cross-Coupling Reaction of an Imine with a Secondary Amine (ref 7), along with (d) the Proposed Mechanism Following Our General Framework



SCHEME 8. Two-Step Mechanism for Carbonylation of Methanol Forming Dimethyl Carbonate



Application of the Mechanistic Concepts to Steady State Heterogeneous Catalysis on Metallic Gold under Catalytic Conditions

The mechanistic studies on model surfaces described above have direct applicability to processes with gold catalysts under practical working conditions, provided the reaction conditions are chosen appropriately. The catalyst must provide adsorbed atomic oxygen at low coverages from O₂ dissociation, and the reaction intermediates formed must react sufficiently fast to provide reasonable turnover rates. Oxygen can be supplied to the gold surface in a minimum of two ways: (1) migration of atomic oxygen from a reducible oxide or (2) dissociation of O₂ on specific sites on the gold catalyst. Here we focus on the latter case, using a free-standing metallic catalyst, nanoporous Au.

Nanoporous materials offer the possibility of both relatively high surface area (and thus effective utilization of metal) and selective reactivity. Of relevance here are dilute metal alloys with gold that effect the activation of dioxygen, while retaining the characteristic reactivity of gold. Nanoporous gold (npAu) is actually a dilute Ag/Au alloy. At silver concentrations of 1–3%, strong parallels are observed for the self-coupling of alcohols on the model system (O/Au(111)) at low pressure and on nanoporous gold catalysts, that is, unsupported metallic gold in nanoporous form, with molecular oxygen as the oxidant at atmospheric pressure.²²

The parallel between npAu and model Au(111) surfaces has been established by experiments both in UHV and in steady-state catalytic reactors.^{8,29,30} Nanoporous gold readily dissociates dioxygen upon exposure to O₂ both in

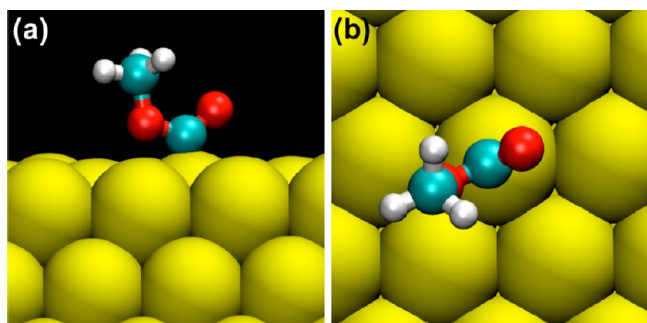


FIGURE 9. Calculated structure of methoxycarbonyl on Au(111): (a) side view and (b) top view. Large yellow spheres, red spheres, blue spheres, and small white spheres represent Au, O, C, and H atoms, respectively. Reprinted with permission from ref 28. Copyright 2011 American Chemical Society.

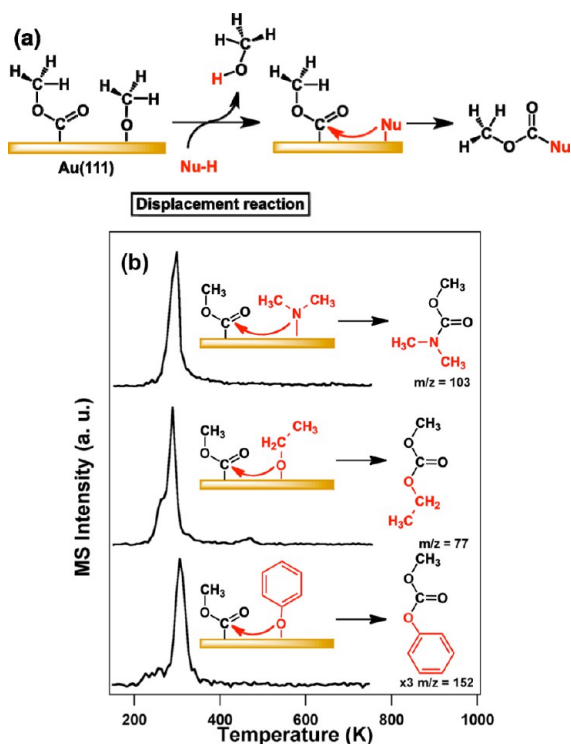


FIGURE 10. (a) Schematics for coupling of methoxycarbonyl with other surface nucleophiles than methoxy, introduced by displacement reactions. (b) Methoxycarbonyl nucleophilically attacked by dimethyl amide, ethoxy, and phenoxy forming the corresponding coupling products. Reprinted with permission from ref 28. Copyright 2011 American Chemical Society.

vacuum and at higher pressures,²⁹ likely with the involvement of the trace amounts of silver in the material. With atomic oxygen adsorbed, npAu then readily self-couples methanol, yielding methyl formate at 300 K in temperature-programmed reaction, similar to the result observed in with O/Au(111) (Figure 11a).

The distribution of products and their temperatures suggest identical mechanisms on the two surfaces. Further, in

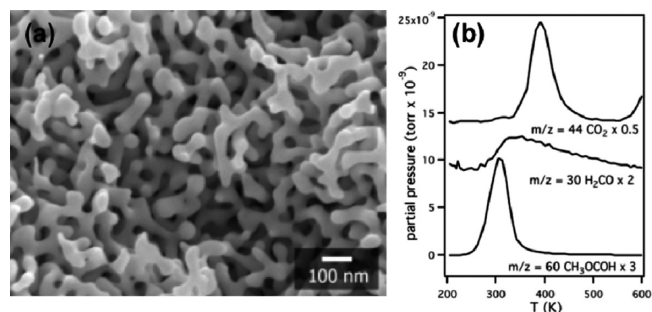


FIGURE 11. (a) Scanning-electron micrograph of a cross-section of a nanoporous gold disk. Reprinted with permission from ref 30. Copyright 2012 Wiley. (b) Temperature-programmed reaction of selective oxidative coupling of methanol by O adsorbed on npAu. The adsorbed O was created by exposure to O₂ at 300 K; CH₃OH was subsequently dosed at 210 K. Reprinted with permission from ref 29. Copyright 2013 Elsevier.

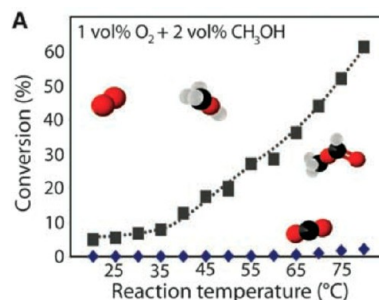


FIGURE 12. Oxidation of methanol over nanoporous gold. Total oxidation (blue rhombuses) and oxidation to form the coupled product (gray squares) increase with temperature (no other products than methyl formate and CO₂ were detected). Reprinted with permission from ref 8. Copyright 2010 American Association for the Advancement of Science.

the catalytic steady state, gaseous mixtures of O₂ and methanol yield methyl formate with selectivities approaching 100% at temperatures between 30 and 80 °C (Figure 12).²⁹ These catalytic reactions were *predicted* on the basis of the model studies on O/Au(111), and the extension of these predictions from O/Au(111) to other reactions is apparent.

Further, self-coupling of alcohols in *liquid phase* also shows similar product distributions, indicating that similar mechanistic steps are involved.^{6,31} Most of the elementary steps in the catalytic self-coupling of alcohols in the liquid phase can be mediated by the Au surface alone, although the possibility of the involvement of liquid-phase reactions cannot be excluded. We attribute the excellent transferability from the model studies to the following key characteristics of the gold surface: (1) alcohols and other hydrocarbons are activated only when adsorbed atomic oxygen is present, preventing the buildup of surface spectators; (2)

water binds only weakly and leaves the surface rapidly around 200 K ($\text{OH}_{(a)}$ is unstable with respect to formation and desorption of water, so the surface coverage of OH is minimal at all times³²); (3) OH is not thermodynamically stable with respect to disproportionation; (4) the dissociation probability for O_2 is extremely low on Au, leading to the low surface concentrations of atomic oxygen under steady-state conditions.

Conclusions

A general mechanistic framework has been established for oxidative coupling reactions on Au-based catalysts. The mechanistic insight is that the key elementary step is the gold-mediated nucleophilic attack of an alkoxy on an aldehyde. This understanding leads to the general prediction of oxidative-coupling reactions between surface adsorbed nucleophiles and electrophiles. This guiding principle has been verified by demonstration of the cross-coupling of alcohols and aldehydes, as well as amines and aldehydes. The generality of the oxidative mechanistic framework is further established by the discovery of the carboxymethylation of alcohols. Strong parallels between the mechanistic studies on the model single crystal and reactions in gas/liquid-phase firmly establish the practical relevance of the fundamental surface science studies.

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FOOTNOTES

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