Communications

Selective Oxidation of Methane to Methanol Catalyzed, with C−H Activation, by Homogeneous, Cationic Gold**

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Some of the most efficient homogeneous catalysts for the low-temperature, selective oxidation of methane to functionalized products employ a mechanism involving C−H activation[1] with an electrophilic substitution mechanism. Several such systems have been reported based on the cations Hg^{II},[2] Pd^{II},[3] and Pt^{II}.[4] These catalyst systems typically operate by two general steps that involve: A) C−H activation by coordination of the methane to the inner sphere of the catalyst (E^{n+}) followed by cleavage of the C−H bond by overall electrophilic substitution to generate E^{n+}−CH_3 intermediates, and B) oxidative functionalization involving redox reactions of E^{n+}−CH_3 to generate the desired oxidized product CH_3X.[4a] Consequently, efficient catalysts that follow this pathway would be expected to be "soft", highly electrophilic species that form relatively strong covalent bonds to carbon atoms and that are also good oxidants.

We considered that gold cations could be uniquely efficient electrophilic catalysts for methane conversion because, as shown in the conceptual catalytic cycle (Scheme 1), both Au^I and Au^{III} oxidation states could be

Scheme 1. Proposed functionalization catalytic cycles involving C−H activation by Au^I and Au^{III} species.

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active for heterolytic C−H activation as well as oxidative functionalization; this is likely because Au^I (d^{10}, two-coordinate) and Au^{III} ions (d^8, square planar) are both "soft" electrophiles that are isoelectronic and isostructural with the neighboring cations (Hg^{II} and Pt^{II}, respectively) that have been shown to be active for electrophilic C−H activation of methane.[2,4] This situation is not common, and in most catalytic systems based on "soft", redox-active electrophiles only one oxidation state of the redox couple is active for C−H activation. Thus, we sought to explore the catalytic chemistry of gold cations for the oxidation of methane. To our knowledge, while gold complexes have been reported to facilitate free-radical reactions of alkanes with peroxides in low yields,[5] no homogeneous gold catalysts that operate by heterolytic C−H activation and oxidative functionalization have been reported for the selective functionalization of alkanes. This is possibly because of the strong propensity for irreversible formation of gold metal, and any attempts to develop redox catalysis based on homogeneous Au cations must address this issue.

In strong acid solvents such as triflic or sulfuric acid, Au^{III} cations (generated by dissolution[6] of Au_2O_3) react with methane at 180°C to selectively generate methanol (as a mixture of the ester and methanol) in high yield (Table 1, entries 1 and 2). As expected, the irreversible formation of metallic gold is very evident after these reactions and, unlike reactions with Hg^{II},[2] Pt^{II},[4d] and Pd^{II}[3a] that are catalytic in 96% H_2SO_4, only stoichiometric reactions (turnover numbers (TONs) < 1) are observed with Au^{III} [Eq. (1)]. Soluble cationic gold is essential for these reactions as no methanol is observed under identical conditions without added Au^{III} ions (entry 3), or in the presence of metallic gold (entry 4) which is not dissolved in hot H_2SO_4.

$$3\,CH_4\,(27\,bar) + 2\,AuX_3 + 3\,H_2O \xrightarrow[180\,°C,\,2\,h]{HX} 3\,CH_3OH + 6\,HX + 2\,Au^0$$
$$X = HSO_4$$

$$(1)$$

Consistent with the known nobility of gold metal, no methanol formed when SO_3 or persulfate ($K_2S_2O_8$) were added as possible oxidants of metallic gold (entries 5 and 6). We considered the use of Se^{VI} ions as a more suitable oxidant. Se^{VI} ions are a more powerful oxidizing agent than S^{VI} ions ($E^o = 1.5$ V SeO_4^{2-}/H_2SeO_3, $E^o = 0.17$ V SO_4^{2-}/H_2SO_3, respectively) and, critically, the hydrated form, selenic acid (H_2SeO_4), is known to oxidize gold metal.[7] Equally important, selenic acid is also almost as acidic as sulfuric acid,[7,8] and it was anticipated that neither the acid nor the conjugate base ($HSeO_4^-$) would inhibit catalysis with electrophilic, cationic gold by blocking the required coordination of methane to the metal center.[4a]

We now report that a 3M solution of H_2SeO_4 in 96% sulfuric acid solvent containing 27 mM metallic gold (added as a 20 mesh powder) leads to catalytic oxidation of methane (27 bar) to methanol at 180°C [Eq. (2)].[9] Turnover numbers of up to 30 and turnover frequencies of about 10^{-3} s^{-1} have

$$CH_4 + H_2SeO_4 \rightarrow CH_3OH + H_2SeO_3 \qquad (2)$$

Table 1: Yield of CH_3OH under different reaction conditions.[a] [9]

Entry	Au source [mM][b]	Additives	t [h]	TON	TOF [s^{-1}]	CH_3OH (% sel)	[CH_3OH] [mM]	CH_4 (% conv)	CO_2 [mol%]
1	Au_2O_3 [50]	–	1	0.8	10^{-3}	>90	60	<2	<1
2	Au_2O_3 [50]	100% CF_3SO_3H	1	0.9	10^{-3}	>90	70	<2	<1
3	–	–	6	0	0	0	0	<1	<1
4	Au^0 [27][c]	–	1	0	0	0	0	<1	<1
5	Au^0 [27][c]	2 wt% SO_3	3	0	0	0	0	<1	<1
6	Au^0 [27][c]	0.1 M $K_2S_2O_8$	2	0	0	0	<5	<1	<2
7	Au^0 [27][c]	3 M H_2SeO_4	2	9	10^{-3}	81	240	11	3
8	Au^0 [5][c]	3 M H_2SeO_4	9	32	10^{-3}	77	178	8	2
9	Au_2O_3 [81]	3 M H_2SeO_4	10	4	10^{-3}	74	350	15	6
10	Au^0 [27][c]	3 M SeO_3 + 6 bar O_2	2	8	10^{-3}	86	215	10	2
11	Au^0 [81][c]	3 M SeO_3 + 2% SO_3	3	15	10^{-3}	94	627	28	2
12	–	3 M H_2SeO_4	6	0	–	68	69	3	<2

[a] Reaction temperature 180°C, 27 bar CH_4 with 96% D_2SO_4 as solvent. [b] Based on in situ generated Au^{III} species assuming complete dissolution of added gold. [c] Added as metallic (20 mesh) gold powder.

been observed in methanol concentrations of up to 0.6 M in sulfuric acid with >90% selectivity, (Table 1, entries 7–11). Both gold and selenic acid are required for the reaction; no methanol is observed in the absence of Se^{VI} ions with or without Au^0 (entries 3 and 4) and only small amounts of methanol are formed in the presence of selenic acid without Au^0 (entry 12). Use of 100% enriched [^{13}C]methane as well as ^{1}H, ^{13}C NMR spectroscopic, and HPLC analyses of the crude reaction mixtures confirmed that methanol is the predom-
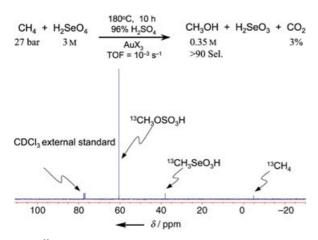

Figure 1. ^{13}C NMR spectrum of the crude reaction mixture resulting from the reaction of $^{13}CH_4$.[10]

inant liquid-phase product generated from methane. As can be seen from an NMR spectrum of the crude reaction mixture (Figure 1), only a small amount of methane selenoic acid (CH_3SeO_3H) is observed in the liquid phase. Very low levels (<5% based on added CH_4) of CO_2 is observed in the gas phase along with recovered CH_4. The observation that addition of O_2 to the reaction mixture (entry 10) has no significant effect on the reaction (compare entry 7) and the high reaction selectivity and reproducibility suggests that free radicals are not involved. Carrying out the stoichiometric reaction with Au_2O_3 at several temperatures between 100 and 200°C leads to an estimated activation barrier of about 30 kcal mol^{-1}.

Control experiments confirm that selenic acid can dissolve gold metal. Thus, addition of metallic gold powder or gold metal (separately obtained from stoichiometric reactions between Au_2O_3 and methane) to a 3 M solution of selenic acid in 96% sulfuric acid leads to rapid dissolution of the gold metal upon warming to 100°C to generate a clear yellow solution of cationic gold. While we have not obtained kinetic data on the various reaction steps proposed in Figure 1, this visual observation of rapid dissolution at low temperature suggests that the rate-determining step for methane oxidation catalyzed by cationic gold is not Au^0 reoxidation.

We have not been able to determine the exact oxidation state of the dissolved gold, but on the basis of known redox potentials we expect that Au^{III} ions are the major species. However, it is possible that Au^I ions (potentially stabilized to disproportionation by Se anions) could be present. The possibility that both Au^{III} and Au^I ions may be present in solution leads to the challenging question of whether one or both oxidation states (Au^I and Au^{III}) are active for the C–H activation of methane. This is an important point because, as discussed above, both Au^I and Au^{III} ions are potential catalysts. The observation that reactions starting from Au^{III} ions (with Au_2O_3 as the source) lead to stoichiometric conversion of methane into methanol [Eq. (1)] does not require that Au^{III} ions are the active species. The C–H activation reaction could occur with catalytic amounts of Au^I ions, formed by reduction of Au^{III} ions with adventitious reductants, and in both cases the stoichiometry shown in Equation (1) would be expected. As observed with the related Hg^{II},[2] Pt^{II},[4] and Pd^{II}[2] systems, some evidence for the formation of an Au–CH_3 intermediate is the observation that low levels of CH_3D (<2%, which is not produced in the absence of added Au^{III}) are produced when the reactions are carried out in D_2SO_4. So far, attempts at synthesizing likely Au^I–CH_3 or Au^{III}–CH_3 intermediates (without "soft" ligands such as phosphine) have been unsuccessful.

Given the synthetic challenges, we turned to DFT calculations to determine the feasibility of the steps proposed in Scheme 1. B3LYP/LACVP**++,[11] as implemented by the Jaguar 5.5 package,[12] was applied with the basis set for sulfur augmented with an extra, compact d-like polarization shell to

better describe high oxidation states.[13,14] A dielectric continuum surrounding the models at a probe radius of 2.205 Å represented the sulfuric acid solvent with $\varepsilon = 50$.[15] Enthalpies describe solutes in ideal solution at 175°C. Entropy changes, which are not accounted for, must be kept in mind as species enter and exit the models. A survey of complexes of gold ions with H_nSO_4 ($n = 0,1,2$) showed that the square planar $Au^{III}(SO_4)_2^-$ ion (1) and linear $Au^I(HSO_4)_2^-$ ion (7) are the most stable Au^{III} and Au^I species in solution. However, bidentate sulfate ions, bisulfate ions, and water made similarly strong bonds to gold, so other complexes are most likely present in equilibrium quantities.

Figure 2 illustrates the Au^{III} pathway, by which 1 reacts with methane to produce the $[Au^{III}(CH_3)(HSO_4)_3]^-$ complex 5. Calculations show that a key role of the acid solvent is the generation of various protonated states of the gold complexes, such as 2, that are sufficiently labile to allow methane to substitute into the coordination sphere of the metal. C–H activation can proceed through a number of transition states, the most accessible of which is an electrophilic substitution pathway 3^+, which features an intramolecular abstraction of a proton from methane by the neighboring bisulfate, with an activation energy of 28.1 kcal mol^{-1}. Alternative mechanisms with slightly higher enthalpies include intermolecular reactions with bisulfate ions in solution. The resulting Au^{III}–CH_3 complex 4 most likely converts into the lowest energy Au^{III}–CH_3 complex 5 before functionalization.

Oxidative functionalization of 5 proceeds with a low energy barrier ($\Delta H = 10.8$ kcal mol^{-1}) through an S_N2 type attack on the methyl group by a free bisulfate ion 6^+. This process is facilitated by the dissociation of the ligand *trans* to the CH$_3$ group. A reductive elimination mechanism was also found, but with a $\Delta H^{\ddagger}$ value of 32.9 kcal mol^{-1}.

Au^I species can follow a similar electrophilic substitution C–H activation mechanism (Figure 3) to produce $[Au^I(CH_3)(H_2SO_4)]$ (10) with an activation energy of 26.2 kcal mol^{-1} from 7. Interestingly, an oxidative addition mechanism was also found with an activation energy of 21.1 kcal mol^{-1}, somewhat lower than the electrophilic substitution. The resulting Au^{III} species 12 is a stable intermediate, but the compound is acidic enough that deprotonation would rapidly lead to the same Au^I–CH$_3$ complex 10 for the electrophilic substitution pathway.
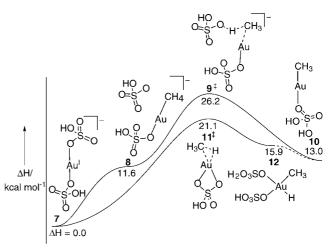

Figure 3. Calculated enthalpies (kcal mol^{-1}) at 175°C relative to 7, including solvation by sulfuric acid ($\varepsilon = 50$). For clarity, spectator H_2SO_4 groups have been omitted from some structures. The top curve illustrates electrophilic substitution, while the bottom curve illustrates oxidative addition.

While C–H activation with Au^I ions is feasible, direct functionalization from this species is not. Both reductive elimination and nucleophilic substitution yields an $Au^{-I}\cdot2H_2SO_4$ ion that is calculated to be 37.6 kcal mol^{-1} higher in energy than 10. However, 10 can most likely be oxidized to the Au^{III} species 5, either through selenic acid, sulfuric acid, or 1. Indeed, preliminary calculations show that the redox exchange $10 + 1 \rightarrow 5 + 7$ is exothermic by about 32 kcal mol^{-1}, and would thus be feasible even for the stoichiometric process.

Based on these results, it appears that oxidative addition to Au^I ions is the favored pathway, which is 7.0 kcal mol^{-1} lower in energy than the electrophilic substitution pathway for Au^{III} ions. However, these energetics do not take the relative concentrations of the Au^{III} and Au^I cations into account, and the concentration of Au^I ions should be significantly lower than Au^{III} ions in the presence of excess oxidant Se^{VI}. A difference of 7.0 kcal mol^{-1} corresponds to a ratio of approximately 2500:1 at 175°C, and thus if the ratio of Au^I to Au^{III} ions is less than 1:2500, the Au^{III} pathway would be favored. Since this is a feasible ratio, both Au^I and Au^{III}
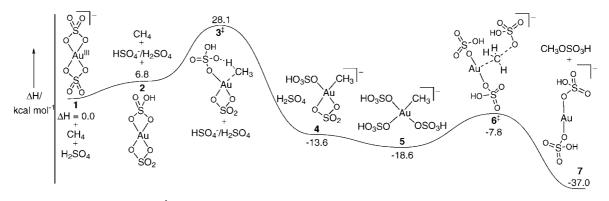

Figure 2. Calculated enthalpies (kcal mol^{-1}) relative to 1, including solvation by sulfuric acid ($\varepsilon = 50$). Spectator sulfuric acid molecules have been omitted from some structures for clarity.

remain possible active species, which is in contrast to findings for Pt^{II}[4a] and Hg^{II} ions.[2]

In summary, we report that cationic gold catalyzes the selective, low-temperature, oxidation of methane to methanol in strong acid solvent using Se^{VI} ions as the stoichiometric oxidant. The reaction does not appear to proceed through free radicals and DFT calculations indicate that Au^{I} or Au^{III} species are both viable catalysts that operate by mechanisms involving overall electrophilic C−H activation and oxidative functionalization.

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[9] In a typical reaction, a 50-mL glass-lined, stirred, high-pressure reactor containing 27 mM of 20 mesh, gold powder and 3M H_2SeO_4 (3 mL) in 96% D_2SO_4 was pressurized with methane to a final pressure of 27 bar. This reaction mixture was vigorously stirred and maintained at 180°C for 2 h. After cooling the mixture, the reaction gas phase was vented into an evacuated cylinder (to obtained both dissolved and undissolved gases) and analyzed by GC-MS. The liquid phase was analyzed by ^1H and ^{13}C NMR spectroscopy and HPLC.[4d]

[10] This NMR spectrum cannot be used to obtain quantitative information nor is it representative of the $^{13}CH_4$ dissolved under reaction conditions. See reference [9].

[11] Relativistic effects are incorporated into the Los Alamos Core-Valence Pseudopotential (LACVP) used for Au (P. J. Hay, W. R. Wadt, *J. Chem. Phys.* **1985**, *82*, 299). The 6-31G**++ basis was employed for other atoms (M. M. Francl, W. J. Pietro, W. J. Hehre, J. S. Binkley, M. S. Gordon, D. J. DeFrees, J. A. Pople, *J. Chem. Phys.* **1982**, *77*, 3654). In our experience, approximations

implied by this finite basis cause average errors of 4 kcal mol^{-1}, which the implicit solvent model will increase.

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[14] The d-like polarization shell with exponent $\alpha = 0.65$ was replaced with two shells: a single Gaussian with exponent $\alpha = 0.55$ and a two-Gaussian contraction with exponents $\alpha_1 = 7.5$ and $\alpha_2 = 1.8$ with contraction coefficients $c_1 = 0.2$ and $c_2 = 1.0$.

[15] A high-temperature (175°C) value was projected assuming the dielectric constant of sulfuric acid decays with temperature at a rate similar to that of water; $-(1/\varepsilon)\,\partial\varepsilon/\partial T = 0.0045$.