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Authors

Soyoung Kim, R
Nazemi, A
Cundari, TR
et al.

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A Pd^{III} Sulfate Dimer Initiates Rapid Methane Monofunctionalization by H Atom Abstraction

R. Soyoung Kim^{a,§,‡}, Azadeh Nazemi^{b,§,‡}, Thomas R. Cundari^{b,*}, Yogesh Surendranath^{a,*}

^a Department of Chemistry, Massachusetts Institute of Technology, Cambridge, MA 02139, USA

^b Department of Chemistry, CASCaM, University of North Texas, Denton, TX 76203, USA

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ABSTRACT: An electro-generated Pd^{III}₂ species in fuming sulfuric acid is competent for rapid and concurrent methane mono-hydroxylation to methyl bisulfate (CH₃OSO₃H) and methane sulfonation to methanesulfonic acid (CH₃SO₃H). *In situ* NMR at 50 °C is used to track methane transformation exclusively to CH₃OSO₃H and CH₃SO₃H at high conversions. Integrating a set of kinetic and computational studies, the mechanism of methane monofunctionalization by Pd^{III}₂ is examined. Experimental rate laws and common kinetic isotope effects for CH₃OSO₃H and CH₃SO₃H formation suggest that both transformations proceed via a common rate-limiting C–H activation step. Introduction of O₂ or Pd^{II}₂ suppresses CH₃SO₃H generation, indicating a radical chain sequence. Although the metal–metal bonded Pd^{III}₂ complex is a net two-electron oxidant, our aggregate kinetic data point to a mechanistic model that features rate-limiting H atom abstraction by the Pd^{III}₂ complex to generate a methyl radical intermediate. The CH₃• intermediate then recombines with Pd^{II}₂ to furnish a CH₃Pd^{III}₂ intermediate that reductively eliminates CH₃OSO₃H. Alternatively, the CH₃• intermediate can enter a chain reaction with SO₃ to generate CH₃SO₃H. DFT computations support the radical-based C–H activation by Pd^{III}₂ and delineate H atom abstraction pathways with computed reaction barriers and KIEs that are consistent with experimental data. These mechanistic investigations challenge the paradigm of electrophilic C–H activation and highlight H atom abstraction as a potent pathway for selective methane C–H oxidative functionalization at high reaction rates.

KEYWORDS: Methane partial oxidation, kinetics, mechanism, electrophilic C–H activation, H atom abstraction, radical, high-valent Pd, metal–metal bond

INTRODUCTION

The selective functionalization of unactivated C–H bonds is an attractive route for the preparation of value-added chemicals from abundant hydrocarbon feedstocks.¹ Particularly, the direct partial oxidation of methane to methanol or its derivatives under mild conditions could greatly impact the efficient utilization of natural gas resources.^{2–4} Homogeneous electrophilic metal complexes in strongly acidic media are known to catalyze the selective mono-oxidation of methane to methyl esters (**Scheme 1**, top), which can then be hydrolyzed to methanol.^{5,6} Importantly, the electron-withdrawing effect of the ester functional group inhibits additional C–H activation. This “product protection” strategy has resulted in high selectivity at high conversions for methane mono-oxidation.⁷ Despite these advances, the rate of methane functionalization by this route is too low for practical deployment of these systems, **particularly considering the high cost of product separation**.⁸ This motivates renewed fundamental inquiry into new reaction pathways capable of fostering rapid methane mono-oxidation catalysis.

In the foregoing transformations, the overall driving force for methane oxidative functionalization is set by the redox potential of the chemical oxidant ([O] in **Scheme 1**, top). Since O₂ is the most practical terminal oxidant for large scale methane functionalization, any chemical oxidant must be O₂-regenerable, placing an upper bound on the redox potential of the chemical oxidant. We have used electrochemistry to overcome this limitation and drive methane functionalization at high reaction rates (**Scheme 1**, bottom).⁹ Simple Pd^{II} ions in sulfuric acid were electro-oxidized to a high-valent Pd intermediate that carried out methane mono-oxidation to methyl bisulfate (CH₃OSO₃H, MBS) with a turnover frequency of 2000 h^{–1} (at 500 psi CH₄, 140°C). Spectroscopic

studies revealed that the key high-valent intermediate is a M–M bonded dinuclear Pd complex, with the Pd centers in a formal 3+ oxidation state. In this Pd^{III}₂ species, each Pd center is pseudo-octahedrally coordinated by H_xSO₄^(x–2) oxygen donor ligands.¹⁰ In addition to MBS, the Pd^{III}₂ species also simultaneously catalyzed the sulfonation of methane to methanesulfonic acid (CH₃SO₃H, MSA) in anhydrous (fuming) sulfuric acid in which excess SO₃ is present. Whereas one equivalent of Pd^{III}₂ was consumed per one equivalent of MBS formed, no Pd^{III}₂ was consumed during the generation of MSA. The unique structure and exceptional catalytic activity of this electrogenerated Pd^{III}₂ species motivated us to probe its mechanism of C–H functionalization in detail.

Scheme 1. (Top) A general catalytic cycle for electrophilic methane functionalization by homogeneous metal ions in strong acids.^{5,11–19} The strongly electron-withdrawing ester group, X, “protects” the product from further oxidation, and the product, CH₃X, can be subsequently hydrolyzed to yield methanol. (Bottom) Structure of Pd^{III}₂ and its methane functionalization reactions.^{9,10} Generated from two-electron oxidation of Pd^{II}SO₄ in sulfuric acid, the complex acts simultaneously as a stoichiometric oxidant for MBS generation and a catalyst for MSA generation.

A common mechanistic paradigm for methane functionalization by metal ions in strong acid solvents is electrophilic C–H activation.^{5,11–19} In this mechanism, methane binds to an open coordination site on the metal and is deprotonated by an ancillary ligand or solvent to generate a M–CH₃ intermediate (**Scheme 1**, top). This mechanism is generally invoked for late- or post-transition metals that form strong metal–carbon bonds.²⁰ The M–CH₃ intermediate then proceeds to the functionalized product via a subsequent and rapid reductive elimination step. Maximizing catalyst rate for C–H functionalization via an electrophilic activation mechanism has an inherent challenge: increasing the electrophilicity of the metal center promotes C–H cleavage but also inhibits solvent/anion dissociation to expose a vacant site for methane coordination. Thus, for main group ions Hg^{II}, Tl^{III}, and Pb^{IV} with inherently labile M–L bonds, increased redox potential and the corresponding increase in metal electrophilicity was found to increase C–H functionalization rates.¹⁶ In contrast, for Pt-based systems, the high-valent Pt^{IV} species has been found to be kinetically inert for C–H activation even in strongly acidic media;^{16,21,22} instead, C–H activation takes place from the low-valent state, Pt^{II}, which then must be oxidized to Pt^{IV}–CH₃ prior to reductive elimination.²³

In light of this mechanistic understanding, the unprecedented rate of methane activation by the coordinatively saturated Pd^{III} dimer, which is ~5000-fold higher than that by Pd^{II},⁹ is intriguing. Although Pd generally features more labile ligand binding than Pt, the high redox potential (~2.3 V vs NHE) of the Pd^{III}₂ complex indicates that the Pd center is very electrophilic, which should slow down ligand dissociation. Also, despite the growing appreciation that Pd^{III} dimers are key intermediates in overall C–H functionalization catalysis, their role has typically been limited to promoting reductive elimination,^{24,25} with the C–H activation step generally occurring at Pd^{II}.^{26,27} Furthermore, the simple electrophilic C–H functionalization mechanism (**Scheme 1**, top) is unable to explain the superstoichiometric production of MSA alongside MBS (**Scheme 1**, bottom). MSA can be formed via a radical chain mechanism involving CH₃• and CH₃SO₃• radicals.²⁸ However, purely radical-based methane functionalization

sequences generally do not produce substantial quantities of MBS, although MSA can be converted to MBS under high SO₃ concentrations and at elevated temperatures.^{28,29} The ability of the electrogenerated Pd^{III}₂ complex to generate both MBS and MSA at exceptional rates suggests that it functionalizes methane by a unique mechanistic pathway.

Herein, we report a combination of NMR kinetic experiments and DFT calculations to investigate the mechanism of methane functionalization via the electrogenerated Pd^{III}₂ complex. The data points to an unconventional mechanism for methane C–H activation via H atom abstraction by a Pd^{III} dimer coordinatively saturated with H_xSO₄^(x–2) ligands. Product bifurcation proceeds from the resulting methyl radical intermediate: recombination with the mixed-valent Pd^{II,III} intermediate leads to MBS formation whereas addition with SO₃ leads to MSA formation. DFT calculations support the proposed mechanism with computed free energy barriers for H atom abstraction consistent with the experimentally measured $\Delta G^\ddagger$ values. These mechanistic insights advance the paradigm of rapid and selective methane C–H functionalization via controlled radical pathways.^{30,31}

RESULTS AND DISCUSSIONS

Experimental Observations

Rate laws from concentration-time traces

In our previous work,⁹ we measured the rate of MBS generation using electrochemical methods, but could not measure the rate of the net redox-neutral methane sulfonation reaction to generate MSA (CH₄ + SO₃ → CH₃SO₃H). In this work, we turned to NMR spectroscopy and recorded the concentrations of methane, MBS, and MSA in real time (**Figure 1a**, symbols) (see section 2 in the SI for details of the experiment). To our knowledge, such *in situ* NMR measurements in sulfuric acid for methane oxidation catalysis have not been performed previously because the reactions usually require high pressure and temperature; on the contrary, the reaction of Pd^{III}₂ could be carried out inside glass NMR tubes at mild pressures and temperatures (4–7 bar, 40–70°C). Importantly, the sum of [CH₄], [MBS], and [MSA] was constant over time (**Figure 1a**, green symbols), indicating negligible overoxidation of either MBS or MSA even at high conversion due to “product protection” by the electron-withdrawing substituents.⁷ Exchange of methane between the gas and liquid phases inside the NMR tube was unnoticeable during our experiments. It was also confirmed by UV–Vis spectroscopy that the spontaneous thermal decay of Pd^{III}₂ is negligible under the reaction conditions (see section 2.1.1 in the SI for these control studies).

The exponential concentration-time traces imply that Pd^{III}₂ reacts with methane via parallel first-order reactions to generate MBS and MSA. Initial rates estimated as the slope at $t = 0$ at varying initial [CH₄] also suggested that both MBS and MSA generation are first order in methane (**Figure S4**). Then, [MBS] and [MSA] may be expressed by the following single-exponential equations for parallel first-order reactions:³²

$$[\text{MBS}] = \frac{k_1[\text{CH}_4]_0}{k_1 + k_2} \{1 - \exp(-(k_1 + k_2)t)\} \quad \dots \quad 1$$

$$[\text{MSA}] = \frac{k_2[\text{CH}_4]_0}{k_1 + k_2} \{1 - \exp(-(k_1 + k_2)t)\} \quad \dots \quad 2$$

In equations 1 and 2, [CH₄]₀, k_1 , and k_2 stand for the initial methane concentration and the pseudo-first-order rate constants for MBS and MSA formation, i.e., $\frac{d[\text{MBS}]}{dt} = k_1[\text{CH}_4]$ and $\frac{d[\text{MSA}]}{dt} = k_2[\text{CH}_4]$. These equations were fitted over an initial time period of ~300–400 s in which [Pd^{III}₂] changes by 20% or less and [SO₃] remains virtually unchanged because it is in vast excess (>1 M) relative to both CH₄ and Pd^{III}₂ (on the order of 1–10 mM). The good

fits (**Figure 1a**, lines) indicate that MBS and MSA production are first order in $[\text{CH}_4]$. This is consistent with previous electrochemical studies that showed that MBS production is first-order in $[\text{CH}_4]$.⁹

The reaction orders in Pd^{III}_2 and SO_3 were determined by plotting the fitted pseudo-first-order rate constants k_1 and k_2 versus the initial concentrations of Pd^{III}_2 and SO_3 (**Figure 1b** and **c**; see **Table S1** for the fitted values of k_1 and k_2 and section 2.2.3 in the SI for details). MBS and MSA formation kinetics displayed divergent dependences on $[\text{Pd}^{\text{III}}_2]$ and $[\text{SO}_3]$. The rate of MBS formation displayed a clear first-order dependence on $[\text{Pd}^{\text{III}}_2]$ (**Figure 1b**, blue). In contrast, the rate of MSA formation was only marginally influenced by $[\text{Pd}^{\text{III}}_2]$ with an observed reaction order of 0.2 (**Figure 1b**, red). On the other hand, for $[\text{SO}_3]$, the rate of MSA

formation displayed an observed reaction order of 0.5 (**Figure 1c**, red) while the rate of MBS formation displayed no clear dependence on $[\text{SO}_3]$ (**Figure 1c**, blue). Given the error bars and spread of the data, MBS formation was considered to be zero-order in SO_3 . Together with the CH_4 reaction order, the following empirical rate laws were obtained.

$$\frac{d[\text{MBS}]}{dt} = k_1[\text{CH}_4] = k_{\text{MBS}}[\text{Pd}^{\text{III}}_2][\text{CH}_4] \quad \dots \quad 3$$

$$\frac{d[\text{MSA}]}{dt} = k_2[\text{CH}_4] = k_{\text{MSA}}[\text{Pd}^{\text{III}}_2]^{0.2}[\text{SO}_3]^{0.5}[\text{CH}_4] \quad \dots \quad 4$$

The foregoing kinetic data establish distinct rate expressions for MBS and MSA formation mediated by Pd^{III}_2 .

Figure 1. (a) A typical concentration-time plot from real time NMR reaction monitoring of methane oxidation by Pd^{III}_2 . Black solid lines represent fitting with equations 1 and 2. $[\text{Pd}^{\text{III}}_2] = 5.0 \text{ mM}$, $[\text{SO}_3] = 2.6 \text{ M}$. (b, c) The observed rate constants for the formation of MBS and MSA (k_1 and k_2), obtained from fitting equations 1 and 2, are plotted against varying initial concentrations of (b) Pd^{III}_2 ($[\text{SO}_3] = 2.6 \text{ M}$) and (c) SO_3 ($[\text{Pd}^{\text{III}}_2] = 5.0 \text{ mM}$). $P(\text{CH}_4) = 4\text{--}7 \text{ bar}$, $T = 50^\circ\text{C}$ for all data. See section 2.2.3 in the SI for explanation of the error bars and additional details.

Activation barriers

Variable temperature studies were performed to extract activation barriers for MBS and MSA formation. *In situ* NMR was not feasible at elevated temperatures with higher reaction rates because we cannot monitor the reaction with sufficient data density. This is not due to spectrometer sensitivity but rather due to the long ^1H nuclear spin relaxation time of the spherically symmetric methane molecule. Instead, we fitted *ex situ*-measured final concentrations of MBS, MSA, and methane to concentration-time traces simulated based on the empirical rate expressions, equations 3 and 4. The procedure yielded the rate constants k_{MBS} and k_{MSA} (see **Table S4** for the obtained rate constants and section 2.2.6 in the SI for details).

Rate constants thus measured at different temperatures gave Arrhenius activation energies (E_a) of $21.3(\pm 0.2)$ and $26.3(\pm 0.4) \text{ kcal/mol}$ for MBS and MSA, respectively (**Figure 2**). The higher E_a for MSA generation compared to MBS gave increased selectivity for MSA at increasing temperatures. Notably, the E_a for MBS measured here is lower than the value measured electrochemically at higher temperatures ($80\text{--}140^\circ\text{C}$), $25.9(\pm 2.6) \text{ kcal/mol}$.⁹ However, we consider the current E_a value to be more accurate because it isolates the kinetics of methane functionalization from the electrochemical steps required for Pd^{III}_2 generation and better accounts for changes in methane solubility across the temperature range. Indeed, the lower E_a measured in this work provides for better agreement between the rate constants measured at low temperature by NMR and at high temperature by electrochemistry (see section 2.2.7 in the SI for details). The same variable temperature data are also displayed as an Eyring plot in the SI (**Figure S6**), although interpretation of such a plot requires a mechanistic model that will be developed below. The foregoing variable temperature data evince distinct activation energies for MBS and MSA formation mediated by Pd^{III}_2 .

Figure 2. Arrhenius plots for MBS and MSA formation.

Kinetic isotope effects

KIEs were determined from separate reactions of CD_4 and CH_4 . Due to the low sensitivity of ^2H coupled with the requirement for long NMR relaxation delay times for accurate quantitation of CD_4 , *ex situ*-NMR measurements were conducted as described in the previous section. k_{MBS} and k_{MSA} independently determined for CH_4 and CD_4 at 50°C gave KIEs of $4.2(\pm 0.6)$ and $4.2(\pm 0.4)$ for MBS and MSA, respectively. Therefore, C–H bond cleavage is postulated to be rate-limiting for both reactions.³³ It was also found that there is no H/D exchange, either in the product or the starting material, which is consistent with rate-limiting C–H cleavage followed by fast subsequent reactions (**Figure S7**). The similarity of the KIE values also suggests that the rate-limiting C–H cleavage step for the two reactions may be mechanistically similar or involve a common elementary reaction.

Suppression of methanesulfonic acid generation by O_2 and $\text{Pd}^{\text{II,III}}$

As highlighted in the introduction, the generation of MSA in fuming sulfuric acid is thought to proceed via a radical chain

sequence shown below (the subscripts “rp” in the rate constants stand for radical propagation):^{28,29,34}

Even though the reaction involves free radicals, high selectivity for monosulfonation has been observed, which is attributed to the polarity effect^{5,35} and has also been noted in other radical-based methane functionalization reactions.^{18,30,31,36} To experimentally probe whether MSA generation in our system also proceeds via a radical chain sequence, O₂ was introduced as a radical scavenger that is stable in the fuming sulfuric acid medium. Co-addition of O₂ results in suppression of MSA generation and an increase in MBS production (Figure 3, hollow symbols). While the precise reason for increased MBS production is unclear, we note that O₂ can serve both as a radical scavenger and as an oxidant, potentially exposing new pathways for MBS formation. Interestingly, as seen in Figure 3, green, the sum of methane, MBS, and MSA concentrations remains unchanged over the timecourse of the reaction even in the presence of O₂, indicating that any mechanistic changes upon O₂ addition do not lead to substantial over-oxidation of the methyl group. ~~None the less,~~ Regardless, the suppression of MSA evinces the involvement of radical intermediates for MSA generation.²⁸

Figure 3. Real time concentration-time traces of CH₄ oxidation at 50°C recorded without O₂ (solid symbols) and with O₂ (hollow symbols). The volume of co-added O₂ was equal to that of CH₄ (see section 2.2.4 in the SI for details and observed rate constant values). [Pd^{III}₂] = 3.3 mM, [SO₃] = 1.9 M, T = 50°C.

In order to further investigate the radical nature of MSA generation, we studied the effect of increasing the concentration of the Pd₂^{II,III} intermediate. As described in our previous work,¹⁰ the mixed-valent dimer is in equilibrium with Pd^{II} and Pd^{III}₂, and its concentration is on the order of 10–100 μM for the Pd^{III}₂ samples used in this study. The S = ½ complex clearly inhibited MSA generation (Figure 4), indicating that it is an effective scavenger for the radical intermediates involved in MSA formation.

Figure 4. Real time concentration-time traces obtained with (solid symbols) low and (hollow symbols) high concentrations of Pd₂^{II,III}. The high [Pd₂^{II,III}] sample ([Pd₂^{II,III}] ≈ 0.2 mM; for the control sample in solid symbols, [Pd₂^{II,III}] ≤ 0.1 mM) was prepared by adding a Pd^{II} solution to a Pd^{III}₂ solution and equilibrating overnight. The slightly higher rate of MBS formation in the high [Pd₂^{II,III}] case is due to a slightly higher concentration of the Pd^{III}₂ complex in this sample (1.5 vs 1.2 mM; see section 2.2.5 in the SI for the full details of the experiment and the observed rate constants).

It was envisioned that Pd₂^{II,III} acts as a radical scavenger by recombining with the propagating radical, CH₃[•]. The recombination would generate a CH₃Pd^{III}₂ intermediate that can undergo facile reductive elimination of MBS in line with literature precedent²⁵ and our own calculations (Figure S14; see below for details of our computational modeling of the Pd^{III}₂ complex). In principle, the Pd₂^{II,III} complex may also undergo recombination with CH₃SO₃[•], the other propagating radical. However, within the overall reaction mechanism (see below), this alternative radical chain termination would be inconsistent with the observed rate law for MSA generation, which is first order in CH₄ and has a positive order in SO₃ (see section 3.1 in the SI for the derived rate law when termination proceeds via capture of CH₃SO₃[•] instead of CH₃[•]). The calculated driving force for the capture of CH₃[•] is also >20 kcal/mol more favorable than that for the capture of CH₃SO₃[•] (Figure S13). Together, this analysis leads us to conclude that radical termination proceeds via recombination of the propagating CH₃[•] with Pd₂^{II,III}.

Mechanistic models for oxidation of methane by Pd^{III}₂

Combining the foregoing experimental observations, we assemble the putative mechanistic model shown in Scheme 2 (solid lines) for methane oxidation by the Pd^{III}₂ complex. We invoke that the reaction is initiated by a rate-limiting H atom abstraction (HAA) reaction between methane and Pd^{III}₂ to generate CH₃[•] and Pd₂^{II,III}. The methyl radical can then recombine with Pd₂^{II,III} to generate a CH₃Pd^{III}₂ intermediate that reductively eliminates MBS. Alternatively, the methyl radical can add to SO₃ to form CH₃SO₃[•] and set off a radical chain sequence of MSA generation (reactions 5 and 6). The radical chain is terminated by recombination of CH₃[•] with the Pd₂^{II,III} complex.

Scheme 2. The reaction mechanism proposed on the basis of experimental results for methane oxidation by Pd^{III}₂ in fuming sulfuric acid. RLS denotes the rate-limiting step. Abbreviations for each step stand for H atom abstraction (ha), radical recombination (rrc), reductive elimination (rel), and radical propagation (rp). A parallel ionic pathway by electrophilic C–H activation (ea) is also shown with dashed line. Reactants are shown in black, intermediates in green, and byproducts in grey.

The proposed mechanism is consistent with the kinetic data. First, by virtue of the common bifurcating CH₃[•] intermediate, the mechanism explains the simultaneous formation of MBS as a stoichiometric product and MSA as a superstoichiometric co-product. The shared rate-limiting HAA step explains the high and similar KIE of 4.2 for both MBS and MSA generation (KIE_{MBS} =

4.2(±0.6) and $KIE_{MSA} = 4.2(±0.4)$; see above). The involvement of free radical intermediates explains the suppression of MSA formation by O_2 addition (**Figure 3**). Additionally, the mechanism invokes radical termination by reaction with $Pd_2^{II,III}$, and this is consistent with the suppression of MSA formation by increased $[Pd_2^{II,III}]$ (**Figure 4**). This putative termination step also directly generates a $CH_3Pd^{III}_2$ intermediate that undergoes rapid reductive elimination to generate MBS.

The putative mechanism in **Scheme 2** can be used to derive predicted rate expressions for MBS and MSA generation that match the experimental rate laws (equations 1 and 2). From the steady-state approximation,

$$\begin{aligned} \frac{d[CH_3^*]}{dt} &= k_{ha}[CH_4][Pd^{III}_2] \\ &\quad - k_{rrc}[Pd_2^{II,III}][CH_3^*] \\ &\quad + k_{rp2}[CH_4][CH_3SO_3^*] \\ &\quad - k_{rp1}[SO_3][CH_3^*] = 0 \end{aligned} \quad \dots 7$$

$$\begin{aligned} \frac{d[CH_3SO_3^*]}{dt} &= k_{rp1}[SO_3][CH_3^*] \\ &\quad - k_{rp2}[CH_4][CH_3SO_3^*] = 0 \end{aligned} \quad \dots 8$$

Therefore,

$$k_{rp1}[SO_3][CH_3^*] = k_{rp2}[CH_4][CH_3SO_3^*] \quad \dots 9$$

$$k_{ha}[CH_4][Pd^{III}_2] = k_{rrc}[Pd_2^{II,III}][CH_3^*] \quad \dots 10$$

In other words, the two radical propagation steps should have equal rates (equation 9), and the rate of initiation should equal the rate of termination (equation 10). Since reductive elimination from $CH_3Pd^{III}_2$ should be rapid (see above), the rate of MBS generation is equal to the rate of generating the $CH_3Pd^{III}_2$ intermediate, which is then equal to the rate of HAA by Pd^{III}_2 according to equation 10. Hence,

$$\frac{d[MBS]}{dt} = k_{ha}[CH_4][Pd^{III}_2] \quad \dots 11$$

As for MSA, the rate of its generation equals the rate of either of the radical propagation steps in equation 9. Rearranging equation 10 to obtain an expression for $[CH_3^*]$ and substituting it into equation 9,

$$\frac{d[MSA]}{dt} = \frac{k_{rp1}k_{ha}}{k_{rrc}}[CH_4][SO_3]\frac{[Pd^{III}_2]}{[Pd_2^{II,III}]} \quad \dots 12$$

Importantly, the derived rate laws agree with the experimental rate laws. Equation 11 is in line with the observed first-order dependence of MBS on CH_4 (**Figure 1a**) and Pd^{III}_2 and near-zero-order dependence on $[SO_3]$ (**Figure 1**, blue; equation 3). Likewise, equation 12 is in line with the observed first-order dependence on $[CH_4]$ (**Figure 1a**). Equation 12 is also in line with both the near-zero-order dependence on $[Pd^{III}_2]$ (**Figure 1**, red; equation 4) and the suppression of MSA generation by added $Pd_2^{II,III}$ (**Figure 4**). In the fully electrolyzed Pd solutions used in the Pd^{III}_2 order study (**Figure 1b**), $[Pd_2^{II,III}]$ would be effectively proportional to $[Pd^{III}_2]$ since the bulk concentration of $Pd_2^{II,III}$ is low and most of the $Pd_2^{II,III}$ species recombining with CH_3^* would be those generated *in situ* from methane H atom abstraction. When $[Pd_2^{II,III}]$ is increased deliberately by adding Pd^{II} , the inverse dependence on $Pd_2^{II,III}$ becomes observable. However, equation 12 predicts a first-order dependence on $[SO_3]$, while the experimental data shows an SO_3 order of ~0.5. In fuming sulfuric acid, SO_3 forms adducts with sulfuric acid to generate, for example, disulfuric acid ($H_2S_2O_7$).²⁰ Thus, it was postulated that the activity of SO_3 may scale nonlinearly with the nominal free SO_3 concentration. Additionally, the presence of SO_3 could perturb the local hydrogen bond network around the Pd^{III}_2 complex and hinder the approach of CH_4 or cage escape of the CH_3^* intermediate. Such influences would also

contribute to a suppression of MSA formation with increasing $[SO_3]$ that would counteract the predicted first-order SO_3 dependence in equation 12. Notwithstanding, the experimental forward order in SO_3 is consistent with equation 12. In sum, the putative mechanistic model in **Scheme 2** effectively accounts for the multitude of experimental observations.

While we cannot definitively rule out the existence of a concurrent non-radical pathway for MBS formation via electrophilic C–H activation (**Scheme 2**, dashed line; also equation 13 below), the putative HAA sequence provides the simplest explanation for all of the experimental observations. This putative HAA mechanism is, to the best of our knowledge, unprecedented for Pd–Pd bonded dimeric Pd^{III} complexes, but we note that C–H activation from Pd^{III} dimers is rare in general.^{26,37} To further probe the viability of the putative HAA sequence, DFT calculations were carried out.

Evaluation of Mechanistic Models with DFT Calculations

Computational modeling of Pd^{III}_2

The Pd^{III}_2 complex was modeled based on structural information from X-ray absorption and Raman spectroscopies,⁹ as well as literature data for analogous complexes.^{38–43} The two Pd^{III} centers are connected through a metal–metal single bond and are each ligated by five oxygen atoms from $H_xSO_4^{(x-2)}$ ligands.⁹ The sulfuric acid solvent provides for extensive hydrogen bonding, protonation/deprotonation, and ligand exchange reactions with the complex. However, due to the prohibitive computational cost associated with modeling all of these interactions, we opted to model the complex in an implicit solvation environment (see the SI for computational details). Whereas implicit solvation modeling parameters for sulfuric acid are not available, we found that the foregoing results were marginally impacted by solvent dielectric constant and proceeded to perform all calculations in an implicit water solvent in order to mimic the high dielectric constant of sulfuric acid (~100).⁴⁴ While numerous protonation states and numbers of $H_xSO_4^{(x-2)}$ ligands attached to Pd^{III}_2 are possible, computational investigations were focused on the neutral complex with six bisulfate (HSO_4^-) ligands unless it was deemed informative to explore other isomers (see below). For $Pd^{III}_2(HSO_4)_6$, 36 isomers were calculated having four different ligation geometries: the HSO_4^- ligands were attached to the Pd atoms in a monodentate (κ^1), bidentate (κ^2), or bridging (μ^2) fashion, resulting in (a) *cis*- κ^2 - μ^2 , (b) *trans*- κ^2 - μ^2 , (c) paddlewheel, and (d) unbridged geometries (**Figure 5**). All conformers of these configurational isomers had a lower computed free energy for the singlet (orange) versus triplet (green) spin state, consistent with the experimentally observed diamagnetism of Pd^{III}_2 . We found the *trans*- κ^2 - μ^2 geometry to be the most stable, and this preference was retained for the foregoing intermediates and transition states (see section 4.2 in the SI). Study of possible tautomers of this isomer shows that the symmetrically protonated hexa-bisulfate tautomer is the most stable (**Table S6**). Together, the computational survey suggests that the most stable isomer has the Pd–Pd core bridged by two HSO_4^- ligands *trans* to each other.

Figure 5. Computationally modeled Pd^{III}₂(HSO₄)₆ isomers and their computed free energies: (a) *cis*-κ²-μ², (b) *trans*-κ²-μ², (c) paddlewheel, (d) unbridged. The unbridged complex showed spontaneous Pd-Pd bond cleavage when modeled as a triplet. The free energies are values relative to the most stable isomer (conformer #3, *trans*-κ²-μ²). We provide a tentative explanation for the large singlet-triplet energy gaps between the *cis*-κ²-μ² and *trans*-κ²-μ² geometries in section 4.3.1.2 in the SI.

Electrophilic (ionic/organometallic) C–H activation

In order to first explore the feasibility of the more conventional electrophilic C–H activation mechanism, we computed the ionic/organometallic pathway according to equation 13.

The reaction proceeds in two-steps: ligand dissociation first exposes an electrophilic Pd^{III} center, which then coordinates and activates methane to form a CH₃Pd^{III}₂ species. Calculated structures of Pd^{III}₂ showed lengthening of axial Pd–O bonds (2.25±0.04 Å) by 0.15 Å on average compared to equatorial Pd–O bonds (2.10±0.03 Å) due to the *trans* influence of the Pd–Pd bond. However, calculated free energies indicated that homolysis of the axial Pd–O bond is more favorable than heterolytic dissociation by 9.3 kcal/mol (Figure S9). Even upon protonating the Pd^{III}₂ complex to dissociate a H₂SO₄ instead of a HSO₄[–], Pd–O bond homolysis was still preferred over heterolysis by 6.4 kcal/mol (Figure S9). We note that the absolute values of the reaction free energies cannot be trusted because of the large influence of solvation for these reactions. These computational studies suggest that the first step of electrophilic C–H activation, heterolytic Pd–O dissociation, is disfavored relative to Pd–O homolysis.

Although the foregoing analysis suggests that the first step of equation 13 is unfavorable, it was decided to compute the feasibility of the second step of the conventional electrophilic mechanism, i.e., methane activation from a coordinatively unsaturated Pd^{III} dimer. In particular, we searched for concerted metalation-deprotonation (CMD) pathways involving a Pd-bound

HSO₄[–], a free HSO₄[–], and a Pd-bound SO₄^{2–} proton acceptors (Figure 6). We were unable to locate a transition state involving a bound SO₄^{2–} ligand, but were able to find transition states for CMD pathways with bound and free HSO₄[–] proton acceptors (see Figure S11 for optimized structures and energies of the transition states). All of these transition state energies were found to be greater than 33 kcal/mol, irrespective of whether CMD occurred at an axial or equatorial coordination site. These barriers are substantially higher than those observed experimentally and significantly in excess of the H atom abstraction barrier computed below. Based on these results, it was concluded that Pd^{III}₂ is unlikely to activate methane via a traditional electrophilic mechanism.

Figure 6. Calculated electrophilic C–H activation pathways: concerted metalation-deprotonation (CMD) by (a) a bound bisulfate (HSO₄[–]) ion, (b) a free HSO₄[–] ion, and (c) a bound sulfate (SO₄^{2–}) ion. The located transition states for (a) and (b) are shown in Figure S11. No viable transition state could be located for (c).

Initial mechanistic model for H atom abstraction: by the products of homolytic ligand dissociation

To model methane C–H cleavage via an H atom abstraction mechanism, we initially focused on a stepwise mechanism that proceeds from the products of homolytic ligand dissociation. In sum, we identified a mechanism with favorable calculated free energies, but that is inconsistent with experimental kinetic data. Four radical abstraction pathways were modeled: abstraction of either an H atom or a methyl radical by either the Pd₂^{II,III} complex or the free bisulfate radical (Table 1). The bisulfate radical (HSO₄[•]) was found to be a much more effective radical abstracting agent than the Pd₂^{II,III} complex, and abstracting an H atom was easier than abstracting a methyl radical. The free energy barrier for H atom abstraction (HAA) by HSO₄[•] was 9.5 kcal/mol, which is highly favorable and consistent with the experimental activation barrier if combined with a modest free energy for ligand homolysis. These results suggest that C–H activation by Pd^{III}₂ could proceed through ligand homolysis to reversibly generate a reactive bisulfate radical that undergoes rate-limiting HAA with methane to generate a Pd₂^{II,III} complex and a methyl radical (equations 14 and 15). The proposed mechanism as a whole is depicted in Figure S8.

Table 1. Reaction free energies of the four possible C–H cleavage reactions following homolytic ligand dissociation from Pd^{III}₂.

Reaction	ΔG (kcal/mol)
Pd ₂ ^{II,III} + CH ₄ ⇌ HPd ^{III} ₂ + CH ₃ [•]	52.5
Pd ₂ ^{II,III} + CH ₄ ⇌ CH ₃ Pd ^{III} ₂ + H [•]	66.9
HSO ₄ [•] + CH ₄ ⇌ H ₂ SO ₄ + CH ₃ [•]	0.04

The suggested stepwise HAA reaction was, however, at odds with the experimentally observed rate laws. Applying the steady state approximation to the stepwise HAA sequence (equations 14 and 15), we arrive at the following predicted kinetic expression (see section 3.2 in the SI for details of the mathematical derivation):

$$r_{\text{MBS}} = k_{\text{ha}}[\text{CH}_4][\text{HSO}_4^\bullet] \quad \dots 16$$

$$[\text{HSO}_4^\bullet] = \frac{k_{\text{ld}}[\text{Pd}^{\text{III}}_2]}{k_{\text{ha}}[\text{CH}_4] + k_{\text{ld}}[\text{Pd}_2^{\text{II,III}}]} \quad \dots 17$$

where the subscript ha' stands for HAA from methane by $\text{HSO}_4^\bullet$ (equation 15) and the subscript ld stands for the homolytic ligand dissociation reaction (equation 14). Combining the two equations,

$$r_{\text{MBS}} = \frac{k_{\text{ha}}k_{\text{ld}}[\text{CH}_4][\text{Pd}^{\text{III}}_2]}{k_{\text{ha}}[\text{CH}_4] + k_{\text{ld}}[\text{Pd}_2^{\text{II,III}}]} \quad \dots 18$$

Equation 18 can be simplified by considering two limiting cases. First, if ligand dissociation is fast and reversible, $k_{\text{ld}}[\text{Pd}_2^{\text{II,III}}] \gg k_{\text{ha}}[\text{CH}_4]$ and $r_{\text{MBS}} \approx \frac{k_{\text{ha}}k_{\text{ld}}[\text{CH}_4][\text{Pd}^{\text{III}}_2]}{k_{\text{ld}}[\text{Pd}_2^{\text{II,III}}]}$. This is inconsistent with the observation that MBS generation is first-order in $[\text{Pd}^{\text{III}}_2]$ (Figure 1b, blue). It is also inconsistent with the observation that adding $\text{Pd}_2^{\text{II,III}}$ suppresses MSA generation but does not influence the rate of MBS generation (Figure 4). On the other hand, if $k_{\text{ld}}[\text{Pd}_2^{\text{II,III}}] \ll k_{\text{ha}}[\text{CH}_4]$, ligand homolysis becomes rate-limiting and equation 18 reduces to $r_{\text{MBS}} \approx k_{\text{ld}}[\text{Pd}^{\text{III}}_2]$. This is inconsistent with the first-order dependence of r_{MBS} on $[\text{CH}_4]$ (Figure 1a) and the observed high KIE of 4.2 for MBS formation. Similarly, the rate law for MSA generation derived from the stepwise mechanism disagrees with the experimental rate expression (see section 3.2 in the SI). The foregoing analysis indicates that methane HAA by Pd^{III}_2 does not proceed via a free bisulfate radical intermediate.

Convergence with the experimentally proposed mechanistic model: H atom abstraction by the coordinatively saturated Pd^{III}_2 complex

Based on the kinetic analysis above, it is most reasonable to invoke that H atom abstraction (HAA) proceeds directly from the Pd^{III}_2 complex. Notably, since Pd^{III}_2 is coordinatively saturated, the bound HSO_4^- ligands are expected to be the H atom acceptors rather than the Pd center itself, leading to the liberation of H_2SO_4 following the overall HAA reaction. Two pathways were calculated: the first invokes HAA by a κ^1 -bisulfate ligand on the Pd^{III}_2 complex (pathway A) whereas the other involves partial dissociation of a κ^2 -bisulfate ligand to κ^1 prior to HAA (pathway B) (Figure 7) (see section 4.4 in the SI for additional reaction pathways that were calculated). For all species in both pathways, the *trans*- κ^2 - μ^2 isomer was found to be the most stable (Table S10) and therefore DFT results suggest no substantial ligand rearrangement during the C–H activation event. All plausible spin states were also explored (Table S11).

For pathway A (Figure 7, top), transition states were found where one of the oxygen atoms in the κ^1 -bisulfate interacts with the methane H atom. Several conformations of the TS with different positions of methane relative to Pd were optimized to identify the most stable structure; all the calculated TS conformations were very similar in free energy (e.g., ΔG between the two conformations of **A-TS** in Figure 7 was 0.2 kcal/mol). The lowest free energy of **A-TS**, 27.3 kcal/mol, was significantly lower than the $\Delta G^\ddagger$'s of electrophilic C–H activation pathways computed earlier (Figure 6). The ground spin state of **A-TS** was triplet, but with the corresponding open-shell singlet being only 0.7 kcal/mol

higher in energy. The close energy match between the singlet and triplet TS electronic configurations suggests that the reaction will display a comparable free energy barrier irrespective of whether it proceeds along a singlet surface or undergoes intersystem cross along the reaction coordinate. After HAA, the methyl radical, free H_2SO_4 , and the 5,6-coordinate $\text{Pd}_2^{\text{II,III}}$ complex (**A-Int2**) display an aggregate free energy 6.8 kcal/mol above the initial state. The $\text{Pd}_2^{\text{II,III}}$ intermediate had a doublet ground state in line with prior EPR studies.¹⁰ The free methyl radical generated in this step can react with SO_3 to enter a radical propagation cycle that generates MSA. Alternatively, recombination of the $\text{Pd}_2^{\text{II,III}}$ complex with the methyl radical gave the singlet $\text{CH}_3\text{Pd}^{\text{III}}_2$ product (**A-P**) with a relative free energy of –19.5 kcal/mol, confirming the thermodynamic favorability of the reaction.

For pathway B (Figure 7, bottom), **R** first undergoes partial dissociation of a κ^2 -bisulfate ligand to yield a 5,6-coordinate Pd^{III}_2 complex (**B-Int1**). This complex is the same as the starting complex for the ionic CMD pathway shown earlier (Figure S11 and Figure 6) and was found to have a relative free energy of 4.8 kcal/mol for the closed-shell singlet ground state. A triplet spin configuration for **B-Int1** was found to be 1.5 kcal/mol above the singlet, suggesting the thermal accessibility of the bi-radical electronic configuration as depicted in Figure 7. We note that a metal-bound bisulfate radical intermediate was also invoked for an early transition metal electrocatalyst for methane functionalization.³¹ Along with the preference for ligand homolysis (see above), these results imply a significant degree of covalent character in the Pd–O bond. The transition state for HAA from **B-Int1** was 25.1 kcal/mol above **R**. Similar to **A-TS**, **B-TS** had a triplet ground state with an open-shell singlet only 0.6 kcal/mol higher in energy. Thus, as for pathway A, barrier heights are comparable for reaction progress along the singlet and triplet surfaces. Although **B-TS** is 2.2 kcal/mol more stable than **A-TS**, we consider both pathways to be equally viable, given the typical energy accuracy expectations of DFT calculations. Following HAA, the H_2SO_4 dissociated, and a nearby κ^1 -bisulfate underwent rearrangement to κ^2 to furnish **B-Int2**. Without dissociation of the H_2SO_4 , due to the weak binding strength of neutral H_2SO_4 , the $\text{Pd}_2^{\text{II,III}}$ intermediate was calculated to have a 6.5 kcal/mol higher free energy (Figure S12, bottom). On the other hand, absent the rearrangement of the nearby κ^1 -bisulfate, the 4,6-coordinate $\text{Pd}_2^{\text{II,III}}$ was found to be 4.6 kcal/mol higher in free energy than the 5,6-coordinate $\text{Pd}_2^{\text{II,III}}$ (Figure S12, top). We note that **B-Int2**, with κ^2 -bisulfate ligands in a *cis* arrangement, is a higher energy stereoisomer of **A-Int2** containing *trans* κ^2 -bisulfate ligands. Finally, recombination with $\text{CH}_3^\bullet$ yielded the $\text{CH}_3\text{Pd}^{\text{III}}_2$ complex **B-P**, which was –17.7 kcal/mol relative to **R**. Again, the principal difference between **B-P** and **A-P** is *cis* vs *trans* arrangement of the κ^2 -bisulfate ligands contributing to the small energy difference between these two final structures. Notably, the position of the methyl group (equatorial versus axial) in either **B-P** and **A-P** did not significantly affect their free energies (Figure S12, bottom right).

Taken together, the foregoing calculations provide two viable pathways for HAA-mediated methane activation by Pd^{III}_2 . Both calculated pathways are in line with the experimental activation free energies and kinetic isotope effects. Since the rate of MBS generation is equivalent to the rate of HAA under the steady-state approximation (equation 11), the values of k_{MBS} measured at variable temperatures were treated with transition state theory to give $\Delta G^\ddagger_{\text{ha}} = 20.7(\pm 0.3)$ kcal/mol (Figure S6). Given the uncertainty in the exact arrangement of ligands and interaction with the solvent, we consider this value to be in good agreement with the calculated free energy barriers of 27.3 kcal/mol and 25.1 kcal/mol for pathways A and B, respectively. From analysis of the computed vibrational frequencies at the TS using the Bigeleisen-Mayer equation,⁴⁵ pathways A and B gave calculated KIEs of 5.9

and 7.8, respectively. These substantial calculated KIE values are qualitatively consistent with the experimentally measured value, $4.2(\pm 0.6)$. As such, the computed HAA pathways in **Figure 7** are

in line with experimental activation metrics and KIE values, lending credence to a direct H atom abstraction mechanism for methane activation by the Pd^{III}_2 complex.

Figure 7. BLYP/SDD,6-311++G(d,p)/SMD-water//BLYP/SDD,6-31+G(d) computed reaction pathways for H atom abstraction from CH_4 by Pd^{III}_2 and recombination of $\text{CH}_3^\bullet$ with $\text{Pd}_2^{\text{II,III}}$. (Top) Pathway A, HAA by κ^1 -bisulfate; (bottom) pathway B, HAA by κ^2 -bisulfate after rearrangement to κ^1 . Numbers indicate free energies in kcal/mol for the most stable conformer. Calculations were done at 323 K to match experimental conditions. Pd = light green, O = red, S = yellow, H = light blue, C = magenta. Yellow highlights in the Chemdraw figures are added as a visual guide.

Mechanistic Rationalization Based on the Properties of Pd^{III}_2

The foregoing results strongly suggest that the Pd^{III}_2 complex activates methane by H atom abstraction which initiates dual mechanistic pathways for the concurrent formation of MBS and MSA at exceptional rates. This dual reactivity and the high reaction rates can be rationalized by the unique physicochemical properties of the critical Pd^{III}_2 intermediate.

First, the Pd^{III}_2 complex is potent both as a two-electron oxidant and as a one-electron oxidant. Mono-nuclear Pd^{IV} is typically confined to predominantly two-electron redox processes because of the relative instability of the odd-electron Pd^{III} state.^{46,47} In contrast, the electrogenerated Pd^{III}_2 species exhibits an overall two-electron reduction potential ($E(\text{Pd}^{\text{III}}_2/\text{Pd}^{\text{II}})$) that is within 10 mV of its one electron reduction potential ($E(\text{Pd}^{\text{III}}_2/\text{Pd}_2^{\text{II,III}})$).¹⁰ This indicates that the Pd^{III}_2 species is equally potent as a one-electron and a two-electron oxidant so that it can simultaneously initiate radical methane sulfonation and mono-oxidize methane by two electrons to MBS. Importantly, the striking similarity between the one-

electron and two-electron reduction potentials arises from the Pd–Pd bond that stabilizes the odd-electron intermediate.¹⁰

Second, the one-electron redox potential of Pd^{III}_2 is very high for methane oxidation. In particular, the driving force for an HAA reaction, which is a proton-coupled electron transfer (PCET) reaction, can be decomposed into contributions from the pK_a of the proton acceptor and the reduction potential of the electron acceptor.⁴⁸ Since the fuming sulfuric acid solvent severely restricts the basicity of any proton acceptor in the medium, the redox potential of the electron acceptor must be sufficiently high to compensate. Indeed, we find that the one-electron reduction potential of Pd^{III}_2 is ~ 2.3 V vs NHE,¹⁰ allowing it to drive facile HAA despite the poor basicity of the proton acceptor. Owing to the high redox potential of Pd^{III}_2 and the low pK_a of the acceptor, the HAA reaction is expected to be highly asynchronous, and this too could serve to lower the kinetic barrier for the reaction.⁴⁹ Importantly, because HAA can proceed with proton and electron going to different sites, the pathway no longer requires direct

methane coordination to Pd. Consequently, the HAA pathway bypasses a common impediment to rapid electrophilic C–H activation by no longer requiring the dissociation of strongly bound ligands from the high-valent metal center.

CONCLUSIONS

We examined the reaction mechanism of methane functionalization by an electrogenerated, $\text{H}_x\text{SO}_4^{(x-2)}$ -ligated Pd^{III}_2 complex in fuming sulfuric acid using an integrated set of experimental and computational studies. Experimental rate laws and common kinetic isotope effects for MBS and MSA formation suggest that both proceed via a common rate-limiting C–H activation step. The observed suppression of MSA by introduction of O_2 and $\text{Pd}_2^{\text{II,III}}$ indicate a radical chain sequence. Together, the NMR kinetic studies point to a putative mechanistic model that features rate-limiting H atom abstraction (HAA) by the Pd^{III}_2 complex to generate a methyl radical intermediate. The $\text{CH}_3^\bullet$ can then recombine with $\text{Pd}_2^{\text{II,III}}$ to furnish MBS upon reductive elimination. Alternatively, $\text{CH}_3^\bullet$ can enter a radical chain reaction with SO_3 to generate MSA. This unconventional radical-based C–H activation by a Pd^{III} dimer is supported by DFT computations that reveal the preference of the complex for homolytic Pd–O bond scission and two HAA pathways with reaction barriers in agreement with experimental data. Altogether, these mechanistic investigations highlight HAA as a potent pathway for selective methane C–H functionalization at high reaction rates.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website. Details of sample preparation, NMR measurements, concentration-time trace curve fittings and simulations, rate law derivations, and DFT computation and cartesian coordinates of calculated complexes (XYZ) are presented.

AUTHOR INFORMATION

Corresponding Authors

*Email: t@unt.edu

*Email: yogi@mit.edu

ORCID

R. Soyoung Kim: 0000-0001-7912-735

Azadeh Nazemi: 0000-0002-7326-6796

Thomas R. Cundari: 0000-0003-1822-6473

Yogesh Surendranath: 0000-0003-1016-3420

Present Addresses

§R.S.K.: Department of Chemistry, Yale University, New Haven, CT 06520, USA

§A.N.: Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, MA 02139, USA

Author Contributions

†These authors contributed equally.

Notes

The authors declare no competing financial interests.

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Abbreviations

MBS: Methyl bisulfate ($\text{CH}_3\text{OSO}_3\text{H}$)

MSA: Methanesulfonic acid ($\text{CH}_3\text{SO}_3\text{H}$)

KIE: Kinetic isotope effect

HAA: H atom abstraction

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