

the aldehyde product. The inactivating substrates undergo the first "electron transfer" (H-atom transfer) but do not undergo the second electron transfer due to steric and/or stereoelectronic reasons, leaving the enzyme stalled in the one-electron-reduced inactive state.

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### Reactions of Neutral Palladium Atoms in the Gas Phase: Formation of Stable Pd(alkane) Complexes at 300 K

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Some transition metals activate alkanes in low-energy conditions and others do not. For example, in the solution phase<sup>1</sup> coordinatively unsaturated Ru, Rh, Ir, and Pt centers insert into C-H bonds of alkanes, including methane. In the gas phase,<sup>2</sup> most of the 3d series bare metal cations Sc<sup>+</sup> through Ni<sup>+</sup> break C-H bonds or C-C bonds of propane and larger alkanes, leading to H<sub>2</sub> or CH<sub>4</sub> elimination products (or both). Thus far, only gas-phase cations attack C-C bonds of alkanes. Ta<sup>+</sup>, W<sup>+</sup>, Os<sup>+</sup>, Ir<sup>+</sup>, Pt<sup>+</sup>, Nb<sup>2+</sup>, Ta<sup>2+</sup>, and Zr<sup>2+</sup> dehydrogenate CH<sub>4</sub> at 300 K.<sup>3,4</sup> Neutral platinum and palladium clusters, Pt<sub>x</sub> and Pd<sub>x</sub> (x ≥ 2), activate CH<sub>4</sub>.<sup>5</sup> A key question is exactly how the electronic structure of the metal atom or metal center controls its chemical reactivity.<sup>6</sup> Gas-phase experiments in conjunction with high quality ab initio calculations<sup>7-9</sup> are beginning to show that the overall pattern of low-lying atomic states, including electron configuration and spin, strongly influences which metal atoms react and which do not.<sup>10</sup>

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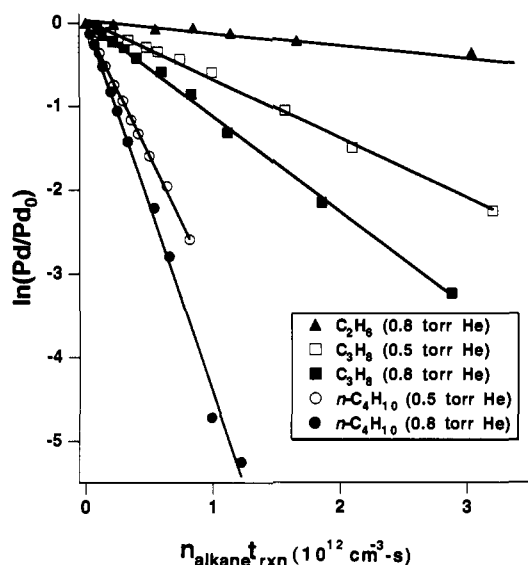


Figure 1. Semilogarithmic plots of Pd (4d<sup>10</sup>, <sup>1</sup>S<sub>0</sub>) laser-induced fluorescence intensity vs the product of hydrocarbon number density and reaction time. Reactants and He pressures as indicated.

Table I. Effective Bimolecular Rate Constants (10<sup>-12</sup> cm<sup>3</sup> s<sup>-1</sup>) for Reactions of Pd and Ni with Alkanes and Alkenes at 300 K in He Buffer Gas<sup>a</sup>

reactant	0.5 Torr of He		0.8 Torr of He	
	Pd(4d <sup>10</sup> )	Ni(3d <sup>9</sup> 4s) <sup>b</sup>	Pd(4d <sup>10</sup> )	Ni(3d <sup>9</sup> 4s) <sup>b</sup>
C <sub>2</sub> H <sub>4</sub>	10.0 ± 1.0	0.5 ± 0.1	14.5 ± 1.5	0.5 ± 0.05
C <sub>3</sub> H <sub>6</sub>	-	12 ± 2	178 ± 18	11 ± 4
1-butene	314 ± 31	175 ± 35	357 ± 36	140 ± 30
CH <sub>4</sub>	-	NR	NR	NR
C <sub>2</sub> H <sub>6</sub>	-	NR	0.15 ± 0.02	NR
C <sub>3</sub> H <sub>8</sub>	0.60 ± 0.06	NR	1.15 ± 0.12	NR
n-C <sub>4</sub> H <sub>10</sub>	3.1 ± 0.3	NR	4.4 ± 0.4	NR
cyclopropane	-	-	59 ± 6	10 ± 1

<sup>a</sup> NR means no reaction was observed ( $k \leq 3 \times 10^{-14}$  cm<sup>3</sup> s<sup>-1</sup>). Dash (-) means reaction was not studied. Ni data are from ref 12. <sup>b</sup> The reactivities of the Ni ground state 3d<sup>9</sup>4s<sup>2</sup>(<sup>3</sup>F<sub>4</sub>) and the low-lying excited state 3d<sup>9</sup>4s<sup>1</sup>(<sup>3</sup>D<sub>3</sub>) at 205 cm<sup>-1</sup> were identical.

We and others<sup>11</sup> are surveying the gas-phase reactivity of bare neutral transition metal atoms with alkanes and alkenes. In the 3d series,<sup>10,12</sup> none of the neutral atoms reacts with alkanes at 300 K, and only Sc, Ti, V, and Ni react with alkenes. Here we report our first state-specific kinetics data for the 4d series. The 4d<sup>10</sup> (<sup>1</sup>S<sub>0</sub>) ground state of the Pd atom reacts rapidly with ethylene, propylene, cyclopropane, and 1-butene and moderately rapidly with ethane, propane, and n-butane at 300 ± 5 K in 0.5–0.8 Torr of He. The latter are apparently the first clear-cut examples of gas-phase chemistry between a neutral ground-state transition metal atom and an alkane. Earlier gas-phase studies of Pd reactivity with CH<sub>4</sub> found no reaction of the Pd atom and very slow reaction of the clusters Pd<sub>x</sub>, x ≥ 2.<sup>5c</sup> CH<sub>4</sub> is inert to Rh atoms<sup>5d</sup> and to Fe atoms.<sup>5e</sup> The ground-state Pt atom *might* react with CH<sub>4</sub>, n-hexane, and cyclohexane,<sup>5a,5b</sup> but interpretation was complicated by the possible presence of excited-state atoms or of multiphoton ionization and fragmentation.

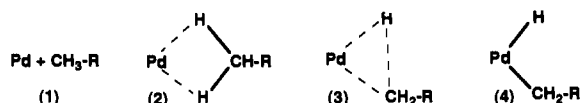
The pressure dependence of our effective bimolecular rate constants indicates that the products are collisionally stabilized Pd(hydrocarbon) adducts.<sup>13</sup> The most likely structure of the

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Pd(alkene) adducts is a donor-acceptor  $\pi$ -complex.<sup>10,12</sup> For the Pd(alkane) adducts, the structure might well be the unusual  $\eta^2$ -complex **2**, which was recently predicted by ab initio calculations.<sup>7c</sup>



The kinetics measurements are described elsewhere.<sup>12-14</sup> The disappearance of the 4d<sup>10</sup> (<sup>1</sup>S<sub>0</sub>) Pd ground state is monitored by laser-induced fluorescence (LIF).<sup>15</sup> Figure 1 gives several examples of semilogarithmic plots of Pd atom LIF signal vs hydrocarbon number density. The resulting effective bimolecular rate constants *k* at 300 K and 0.5-0.8 Torr of He are collected in Table I.

Most of the neutral 3d series metal atoms have 3d<sup>x-24s<sup>2</sup></sup> ground-state configurations.<sup>16</sup> The 4s orbital is larger than 3d,<sup>9</sup> the outer-shell 4s<sup>2</sup> configuration presents an inert-gas-like appearance to an approaching alkane or alkene, which is itself closed-shell. A substantial potential energy barrier typically prevents close approach of metal atom and hydrocarbon at 300 K. The most reactive atom in the 3d series is Ni,<sup>10,12</sup> whose low-lying 3d<sup>9</sup>4s<sup>1</sup> singlet state can form a bound Ni(alkene) complex.<sup>17</sup>

In the 4d series, the 5s and 4d orbitals are more similar in size,<sup>18</sup> which strengthens metal bonding to H and to alkyl. The 4d<sup>10</sup> ground state of Pd is unique among all neutral transition metal atoms. A simple donor-acceptor model of M-alkene bonding predicts that ground-state Pd should fall into a deep attractive well with alkenes, consistent with our observations. The Pd + 1-butene rate constant of 3.5 × 10<sup>-10</sup> cm<sup>3</sup> s<sup>-1</sup> is essentially equal to a hard-spheres collision rate, i.e., the reaction efficiency is 1. Every Pd + 1-butene collision produces an internally hot complex with a sufficiently long lifetime (~50 ns) to be stabilized by He, which implies a deep Pd-butene potential well and no barrier to complex formation.

For Pd + alkane, reaction efficiencies are small, about 5 × 10<sup>-4</sup> for C<sub>2</sub>H<sub>6</sub>, 4 × 10<sup>-3</sup> for C<sub>3</sub>H<sub>8</sub>, and 0.015 for *n*-C<sub>4</sub>H<sub>10</sub>. We observe no reaction with CH<sub>4</sub> (*k* ≤ 3 × 10<sup>-14</sup> cm<sup>3</sup> s<sup>-1</sup>). The increase in rate constant with He pressure indicates a termolecular reaction in the linear regime of pressure dependence. The lifetime of the internally hot Pd(alkane) complex<sup>13</sup> is probably ~25 ps for C<sub>2</sub>H<sub>6</sub>, ~200 ps for C<sub>3</sub>H<sub>8</sub>, and ~0.5 ns for *n*-C<sub>4</sub>H<sub>10</sub>. The reaction efficiencies suggest that the Pd(alkane) complexes are more weakly bound than the Pd(alkene) complexes. The efficiencies also indicate barriers smaller than 5 kcal mol<sup>-1</sup> between reactants and the stable Pd(alkane) complex.<sup>12</sup> Exponential decay of Pd signal vs alkane pressure over one decade at 300 K suggests<sup>19</sup> Pd-alkane binding energies of at least 8 kcal mol<sup>-1</sup> relative to ground-state reactants. These results seem consistent with matrix isolation vibrational spectroscopy<sup>20</sup> of PdCH<sub>4</sub>.

Recent high-level ab initio calculations suggest the nature of the Pd(alkane) complexes indirectly observed here. Blomberg et al.<sup>7c</sup> examined the reaction path from **1**, M + CH<sub>4</sub>, through the transition state **3** to the C-H bond insertion product **4** for all members of the 4d series. For Pd + CH<sub>4</sub>, **3** lies 16 kcal mol<sup>-1</sup> above ground-state reactants **1**; **4** is unstable by 9 kcal mol<sup>-1</sup> relative to **1**. Pd is unique in that the  $\eta^2$ -complex **2** is a stable minimum below ground-state reactants, with no barrier separating

**1** and **2**. The calculated energy of the  $\eta^2$ -complex is only 4 kcal mol<sup>-1</sup> below reactants, but the geometry was not optimized. The most plausible identity of the inferred Pd(alkane) adducts thus appears to be the  $\eta^2$ -complex.

We plan to extend these kinetics studies to the ground states of ruthenium, rhodium, and platinum to further test the utility of ab initio calculations for such electronically complex systems. We also hope to measure accurate bond energies and to study the novel  $\eta^2$ -complexes spectroscopically in the gas phase.

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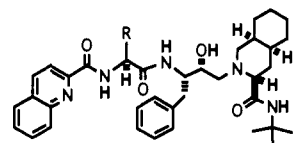
### 3'-Tetrahydrofuranlyglycine as a Novel, Unnatural Amino Acid Surrogate for Asparagine in the Design of Inhibitors of the HIV Protease

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The blockade of the HIV protease has become a major target in the search for an effective therapy for AIDS.<sup>1</sup> While many reports of potent HIV-1 inhibitors have appeared recently, the compound Ro 31-8959 remains the least selective for the HIV-1 and HIV-2 proteases.<sup>2</sup> This property may result in reduced susceptibility to resistance since these represent the genetically most divergent strains of HIV presently known to exist.



Ro 31-8959, R = CH<sub>2</sub>CONH<sub>2</sub>  
12, R = 3(R)-tetrahydrofuranlyl  
13, R = 3(S)-tetrahydrofuranlyl

Interestingly, no improvement over asparagine at the P<sub>2</sub> subsite has been reported. Computer-assisted modeling starting with the X-ray crystal structure of the L-689,502-HIV-1 protease complex<sup>3</sup> and replacing the L-689,502 inhibitor with Ro 31-8959 suggested that one feasible explanation for this preference might be hydrogen

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