

## Kinetics and Mechanism of Urea Hydrolysis Catalyzed by Palladium(II) Complexes

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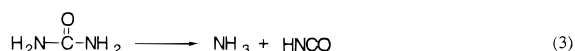
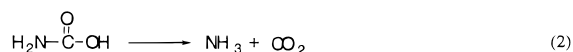
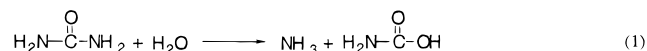
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Four palladium(II) aqua complexes catalyze hydrolytic decomposition of urea into carbon dioxide and ammonia. The initial rates of carbon dioxide formation at 313 K and pH 3.3 fall in the range  $6.7 \times 10^{-5}$  to  $1.6 \times 10^{-4}$  M min<sup>-1</sup>, depending on the catalyst. The pseudo-first-order rate constant for the formation of carbon dioxide is  $1.7 \times 10^{-3}$  min<sup>-1</sup> in the presence of 0.30 M *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> as the catalyst at 313 K and pH 3.3. This reaction is ca.  $1 \times 10^5$  times faster than the uncatalyzed decomposition of urea. The reaction catalyzed by *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> is monitored by <sup>13</sup>C and <sup>15</sup>N NMR spectroscopic methods. The following steps in the mechanism of this reaction are studied quantitatively: binding of urea to the catalyst, formation of carbamic acid (H<sub>2</sub>NCOOH) coordinated to palladium(II) via the nitrogen atom, and conversion of this intermediate into carbon dioxide and ammonia. These products are formed also by another pathway that does not involve carbamic acid. Kinetic effects of added acid and inhibition of the reaction by addition of thiourea and of bases are interpreted quantitatively. Ammonia inhibits the decomposition. When, however, this product is sequestered by metal cations, the reaction becomes relatively fast and catalytic turnover is achieved. The most effective of these sequestering agents is the silver(I) cation. Although the simple palladium(II) complexes are very different from the enzyme urease, which contains nickel(II) ions, the decomposition of urea catalyzed by both kinds of agents involves carbamic acid as the intermediate. Kinetic and mechanistic studies with metal complexes contribute to the understanding of the enzymatic mechanism.

## Introduction

The enzyme urease contains nickel and catalyzes hydrolysis of urea into ammonia and carbamic acid (eq 1). Because carbamic acid spontaneously decomposes into ammonia and carbon dioxide (eq 2), the overall hydrolysis reaction is usually written as a sum of eqs 1 and 2. The elimination reaction in eq 3, which yields isocyanic acid, occurs extremely slowly in



aqueous solution at 298 K and pH 2; the rate constant is  $3.6 \times 10^{-8}$  min<sup>-1</sup>.<sup>1</sup> To our knowledge, uncatalyzed hydrolysis of urea in aqueous solution has not been reported; because its rate constant must be smaller than that for the reaction in eq 3, an estimated upper limit of  $1 \times 10^{-8}$  min<sup>-1</sup> for the pseudo-first-order rate constant is appropriate. The catalytic power of urease can only be estimated; the enzymatic rate enhancement is at least 10<sup>14</sup>-fold at pH 7 and 311 K.<sup>2</sup> The recent X-ray crystallographic determination of the urease structure showed two nickel(II) atoms, which are 3.5 Å apart, at the active site.<sup>3,4</sup> The catalytic mechanism may involve coordination of urea via its oxygen atom to one of the nickel(II) atoms and nucleophilic attack at the carbon atom by the hydroxo ligand bound to the other nickel(II) atom.<sup>3,5</sup>

Because urease is a metalloenzyme, coordination of urea to various metal ions has been studied. Coordination via the

oxygen atom, which is more basic than the nitrogen atom, has been observed in many metal complexes, but hydrolysis of this ligand has not been reported.<sup>6–14</sup> Phenylurea coordinated to cobalt(III) decomposes in strongly acidic solution, producing carbon dioxide and the anilinium cation.<sup>8</sup> Coordination of urea through the nitrogen atom has been observed in a few complexes. In two of them, urea is activated toward decomposition into ammonia and carbon dioxide at room temperature.<sup>6–8,14–16</sup> In a rhodium(III) complex in aqueous solution, the highest conversion was 43%. More recently, in a platinum(II) complex in acetone solution, the conversion was 75% after 6 days.<sup>6</sup> In neither case was catalytic turnover reported, presumably because these metal ions form complexes that are inert to ligand substitution.

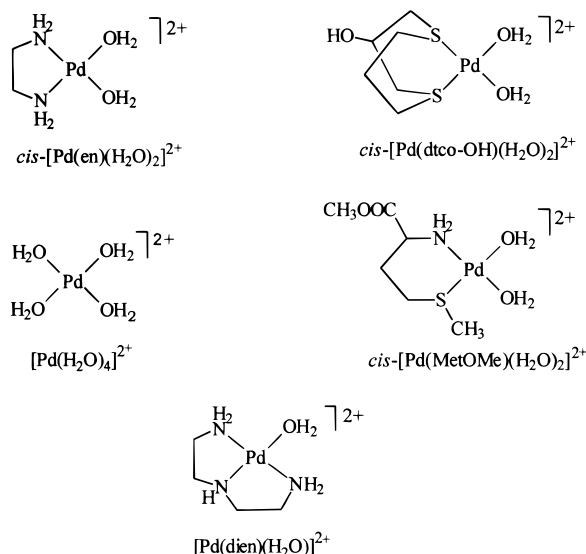
Here we report the first example of *catalytic* decomposition of urea, according to eqs 1 and 2. Because the catalysts are palladium(II) complexes, which are relatively labile in substitution reactions, turnover was achieved. Although this study is not an attempt to mimic the active site of urease or its biological function, the new catalysts may be somewhat relevant to the enzyme. Because palladium(II) is a congener of nickel(II) and

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Chart 1. The Complexes



because both the catalytic and the enzymatic reactions involve carbamic acid as an intermediate, this study may shed some light on the mechanism of action of urease.

## Experimental Procedures

**Chemicals.** The deuterium-containing compounds  $D_2O$ ,  $DClO_4$ , and  $NaOD$ , the salts silver cyanate, ammonium carbamate,  $K_2[PdCl_4]$ ,  $Ni(ClO_4)_2$ ,  $Zn(ClO_4)_2$ ,  $Cd(ClO_4)_2$ ,  $Hg(ClO_4)_2$ , and  $NaClO_4$ , and the ligand 1,5-dithiacyclooctan-3-ol (designated dtco-OH) were obtained from Sigma Chemical Co. and Aldrich Chemical Co. Anhydrous  $AgClO_4$  (strong oxidant!) and  $AgClO_4 \cdot H_2O$  were obtained from G. Frederick Smith Chemical Co. The following enriched compounds were obtained from Cambridge Isotope Laboratories: the solvent for all the reactions, acetone- $d_6$ ; the urea isotopomers containing  $^{13}C$  (99.0%), both  $^{15}N$  (98%), and  $^{13}C$  and both  $^{15}N$  together (99% and 98%, respectively); and  $NH_4NO_3$  containing both  $^{15}N$  (98%). Trifluoroacetic acid (TFA) was obtained from Fisher Scientific. These and all other chemicals were of reagent grade.

**Palladium(II) Complexes.** The following complexes were prepared by published procedures:  $cis-[Pd(en)Cl_2]$ ,  $[Pd(dien)I]I$ ,  $cis-[Pd(Me_tOMe)Cl_2]$ ,  $[Pd(H_2O)_4](ClO_4)_2$ , and  $cis-[Pd(dtco-OH)Cl_2]$ .<sup>17–20</sup> The halide ligands were removed by stirring a solution of the halo complex and an equivalent amount of  $AgClO_4 \cdot H_2O$  in acetone- $d_6$  (containing adventitious water) for 0.5 h at 25 °C, in the dark. The solid  $AgCl$  or  $AgI$  was filtered off in the dark, and a fresh solution of the aqua complex (Chart 1) was used in further experiments. The complexes  $cis-[Pd(en)(H_2O)_2]^{2+}$ ,  $[Pd(dien)(H_2O)_2]^{2+}$ ,  $cis-[Pd(MetOMe)(H_2O)_2]^{2+}$ , and  $[Pd(H_2O)_4]^{2+}$ , all with  $ClO_4^-$  as the counteranion, had the respective ultraviolet absorption maxima,  $\lambda_{max}$ , at 340–345, 365, 360, and 380–382 nm. The values for the first and the last complex, which have been published before, agree with our values.<sup>17,21–23</sup> The cyanate complexes  $cis-[Pd(en)(NCO)_x]^{(2-x)+}$  and  $[Pd(NCO)_4]^{2-}$  were synthesized in acetone- $d_6$ , according to published procedures.<sup>24–27</sup>

**Table 1.** Longitudinal Relaxation Times of  $^{13}C$  with and without the Paramagnetic Relaxation Agent, at 313 K

| sample <sup>a</sup>                   | $T_1$ , s              |                             |
|---------------------------------------|------------------------|-----------------------------|
|                                       | without $[Cr(acac)_3]$ | with 0.040 M $[Cr(acac)_3]$ |
| $(CH_3)_2CO$                          | $28.4 \pm 1.3$         | $0.65 \pm 0.01$             |
| $(NH_2)_2CO$                          | $15.9 \pm 1.2$         | $0.33 \pm 0.01$             |
| $cis-[Pd(en)(OC(NH_2)_2)(H_2O)]^{2+}$ | not detd               | $0.17 \pm 0.01$             |
| $cis-[Pd(en)(NH_2CONH_2)(H_2O)]^{2+}$ | not detd               | $0.19 \pm 0.02$             |
| $cis-[Pd(en)(NH_2COOH)(H_2O)]^{2+}$   | not detd               | $0.54 \pm 0.01$             |
| $CO_2$                                | >40                    | $1.62 \pm 0.02$             |

<sup>a</sup> For the structures of the three complexes, see Chart 2.

**Table 2.** Carbon-13 and Nitrogen-15 Chemical Shifts with Respect to the Methyl Group in Acetone- $d_6$  and the Ammonium Ion in  $NH_4NO_3$ , Respectively<sup>a</sup>

| sample  | $\delta$ , ppm        |  |
|---|-----------------------|--|
|   | $^{13}C$              | $^{15}N$   |
| $(NH_2)_2CO$  | 162.8                 | 58.0 broad   |
| $cis-[Pd(en)(OC(NH_2)_2)(H_2O)]^{2+}$                   | 165.5                 | 60.6 broad   |
| $cis-[Pd(en)(NH_2CONH_2)(H_2O)]^{2+}$                   | 158 broad             | 79.3 tr (uncoordinated)<br>–18.0 broad d (coordinated) |
| $cis-[Pd(en)(NH_2COOH)(H_2O)]^{2+}$                     | 174.3                 | –27.0 broad dd   |
| $cis-[Pd(en)(NH_3)_x(H_2O)_{2-x}]^{2+}$ ,<br>$x = 1, 2$ | none                  | –56.2 broad  |
| $CO_2$  | 125.3                 | none   |
| $NH_4^+$  | none                  | 0.0  |
| $NCO^-$   | 128.7 tr <sup>b</sup> | not detd   |
| $cis-[Pd(en)(OOCNH_2)(H_2O)]^+$                         | 187.0                 | not detd   |
| $NH_4(NH_2COO)$   | 165.4                 | not detd   |

<sup>a</sup> The temperature was 313 K, and the solvent was acetone- $d_6$ . The last three compounds were not observed in the decomposition of urea catalyzed by  $Pd(II)$  aqua complexes. <sup>b</sup> In  $D_2O$ .

**Carbon-13 Relaxation Times.** Longitudinal relaxation times ( $T_1$ ) in the presence and the absence of the paramagnetic complex  $[Cr(acac)_3]$  were determined by the inversion-recovery method,<sup>28</sup> with a Bruker DRX-400 spectrometer, at 313 K. The solvent was acetone- $d_6$ . The results are given in Table 1. The three palladium(II) complexes included there were obtained in situ, after 2 h at 313 K, in a solution that was initially 0.30 M in each  $cis-[Pd(en)(H_2O)_2]^{2+}$  and urea- $^{13}C$ . The concentrations of the last four compounds in Table 1 fell in the range 0.0030–0.15 M. In the absence of  $[Cr(acac)_3]$ , the delay between the scans was 8 min. In an independent experiment with 1.0 M free urea- $^{13}C$ , a single scan was sufficient. With other compounds, eight scans were recorded. In the presence of  $[Cr(acac)_3]$ , 30 scans were taken, with 20-s delays between them. The concentration of  $[Cr(acac)_3]$  was 0.040 M except in the experiments in which it was varied, to verify that the relaxation times do not depend on the concentration of this paramagnetic agent greater than 0.010 M.

**Carbon-13 and Nitrogen-15 NMR Spectra.** These spectra were recorded with Varian VXR-300 and Bruker DRX-400 spectrometers. The chemical shifts ( $\delta$ ) are given in ppm downfield from the internal reference, which usually was the methyl resonance of acetone- $d_6$  (the solvent in all experiments) for  $^{13}C$  NMR or the ammonium resonance of  $NH_4NO_3$  for  $^{15}N$  NMR spectroscopy (see Table 2). The internal reference in kinetic experiments was the carbonyl resonance of acetone- $d_6$  because its chemical shift is similar to the shifts of urea and carbon dioxide. The quality of the  $^{13}C$  NMR spectra was improved by their acquisition in narrow windows. In all the quantitative experiments with  $^{13}C$  and in all the experiments with  $^{15}N$ , the solution was made 0.040 M in the relaxation agent  $[Cr(acac)_3]$ . In the carbon-13 experiments the delay between the pulses was longer than  $5T_1$  for the slowest-relaxing species,  $CO_2$ ; each scan took 9.35 s. Usually 30 scans of enriched samples, and as many as 3000 scans of unenriched ones, were taken. In the nitrogen-15 experiments, the delay between pulses was

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5.0 s, each scan required 6.35 s, and as many as 1000 scans were recorded. Spectra of either nucleus were recorded with and without proton decoupling. In quantitative experiments, in which accurate relative intensities were needed, decoupling was not used. The  $^{13}\text{C}$  resonances were integrated with an estimated error of  $\pm 5\%$ . Concentrations of the compounds were determined on the basis of these integrals, the initial concentration of urea, and the known concentration of the  $^{13}\text{C}$  nuclei in the known volume of the solvent, acetone- $d_6$ . Equilibrium constants, rates, and rate constants were calculated from the known concentrations of the reactants and products, with an estimated error of 10–20%.

**Binding of Urea to Palladium(II).** These experiments were performed by  $^{13}\text{C}$  NMR spectroscopy, in acetone- $d_6$  as the solvent, at 313 K. In one series, the solutions were made 0.30 M in the catalyst,  $\text{cis}[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}$ , and 0.10, 0.15, or 0.30 M in urea- $^{13}\text{C}$ . In another series, the solutions were made 0.30 M in urea- $^{13}\text{C}$  and 0.075, 0.15, or 0.30 M in  $\text{cis}[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}$ . An average value from these six experiments was taken as the binding constant. The latter series of experiments was done in acetone- $d_6$  that was made 3.0 M in  $\text{H}_2\text{O}$ . An average value from these three experiments was taken as the binding constant of urea when it competes with water for coordination to the catalyst.

**Kinetics of Hydrolysis.** The solvent was always acetone- $d_6$ . The temperature was  $313 \pm 0.5$  K in experiments concerning the reaction mechanism and  $333 \pm 0.5$  K in those concerning catalytic turnover. The reactions in eqs 1 and 2 were followed mostly by  $^{13}\text{C}$  NMR spectroscopy. In a typical experiment, to a solution of a freshly prepared complex shown in Chart 1 were added solid  $[\text{Cr}(\text{acac})_3]$ , sometimes another chemical, and finally solid urea, to start the reaction. Acquisition of the spectra began within 1 min. The optional chemical was an acid ( $\text{DClO}_4$  or  $\text{CF}_3\text{COOH}$ ), a base ( $\text{NaOH}$  or  $\text{Et}_3\text{N}$ ),  $N,N$ -dimethylformamide, or thiourea. The final concentrations of  $[\text{Cr}(\text{acac})_3]$  and a base were 0.040 and 0.22 M, respectively. Other concentrations were variously adjusted. Addition of either base to  $\text{cis}[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}$  did not cause precipitation. When urea was added, either before or after the base, a yellow precipitate formed. It was dissolved in  $\text{H}_2\text{O}$  or  $\text{D}_2\text{O}$  and examined by  $^{13}\text{C}$  and  $^{15}\text{N}$  NMR spectroscopy.

The initial rates in Figures 1–4 and 7 were determined in the experiments in which only the first 3–5% of a reaction was followed. The rate constants  $k_1$  and  $k_2$  in Figures 5 and 6, respectively, were obtained by fitting intensities of the  $^{13}\text{C}$  NMR resonance of the intermediate for 5 half-lives of urea decomposition to the appropriate equation. The microscopic rate constants were obtained by fitting the data in Figures 5 and 6 to the appropriate equations.

All the experiments concerning the mechanism of the reactions were done with  $\text{cis}[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}$  as the catalyst. The initial solutions were usually made 0.30 M in it and in the enriched urea. The concentration of adventitious water was ca. 1.5 M.

In experiments concerning the rate law, the concentrations of the catalyst, the enriched urea, and water were varied, one at a time. Usually the initial rate of formation of  $\text{CO}_2$  was determined. At least 10 spectra were taken during 1–2 h, depending on the reaction rate.

Acidity was adjusted with  $\text{DClO}_4$  (in determinations of initial rates) or with  $\text{CF}_3\text{COOH}$  (in determinations of particular rate constants). The net acid concentration was corrected for the contribution from the stock solution of  $\text{cis}[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}$ , for which the first  $\text{pK}_a$  is 5.6.<sup>17</sup> In some experiments, ionic strength was varied with  $\text{NaClO}_4$  or the reaction was inhibited with different concentrations of  $\text{NH}_4\text{NO}_3$ .

The reactions in eqs 1 and 2 were also followed by  $^{15}\text{N}$  NMR spectroscopy, to determine the initial rate of  $\text{NH}_3$  formation. The concentrations of urea and of the products were determined from the known sum of their concentrations and the relative intensities of the corresponding resonances. Possible substitution of ammonia for an aqua ligand in  $\text{cis}[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}$  was studied with  $\text{NH}_4\text{NO}_3$  that was 98% enriched in  $^{15}\text{N}$  in both ions.

**Composition of the Reaction Mixtures.** The reactant, urea, an intermediate, carbamic acid N-bound to palladium(II), and the products, ammonia and carbon dioxide, were detected by  $^{13}\text{C}$  and  $^{15}\text{N}$  NMR spectroscopy. Assignments of resonances were confirmed by spiking the reaction mixtures with dry ice and  $\text{NH}_4\text{NO}_3$  containing 98%  $^{15}\text{N}$  in both ions. The concentration of urea continued to decrease after the

solution became saturated with carbon dioxide, at the maximum concentration of 0.10 M. The chemical shifts varied by less than  $\pm 0.10$  ppm, depending on the composition of the mixture and other conditions.

## Results and Discussion

**Use of  $^{13}\text{C}$  NMR Spectroscopy in Kinetics.** On one hand, quantitative analysis with  $^{13}\text{C}$  NMR spectroscopy is problematic, mainly because of differential relaxation and the nuclear Overhauser effect (NOE).<sup>28</sup> Because these factors affect signal intensity, concentrations are not accurately obtained from the spectrum. On the other hand,  $^{13}\text{C}$  chemical shifts conveniently span a wide range. Differential relaxation was avoided in our experiments when the delay time between the pulses was greater than  $5T_1$  of the slowest-relaxing nucleus, that in  $\text{CO}_2$ . In the presence of  $[\text{Cr}(\text{acac})_3]$ , the delay time between the pulses became sufficiently short for practical work.<sup>29</sup> The NOE problem disappeared when all the spin–spin couplings were preserved, i.e., when decoupling was not used. Initial rates were determined in the first 2 h of the reaction course, while less than 5% of the urea decomposed. In a series of quantitative experiments with urea solutions of known concentrations, the determinations based on the relative intensities of the  $^{13}\text{C}$  NMR resonances of urea and acetone- $d_6$  differed by only 2% from the actual concentrations. Evidently,  $^{13}\text{C}$  NMR spectroscopy can be a reliable tool in quantitative analysis if precautions are taken. We know only several other quantitative studies by  $^{13}\text{C}$  NMR spectroscopy and only one previous application of it in kinetics.<sup>30–33</sup>

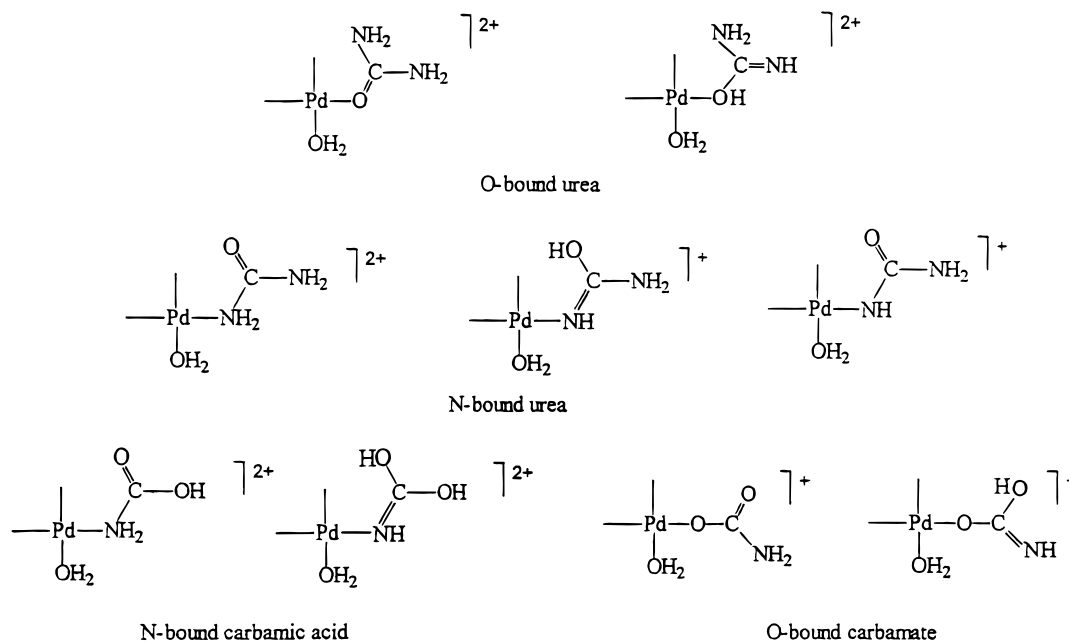
**Relaxation Times  $T_1$  of the  $^{13}\text{C}$  Nuclei.** A typical determination is shown in the Supporting Information, Figure S1. The results are given in Table 1. The undetermined  $T_1$  times were too long in the absence of the paramagnetic relaxation agent,  $[\text{Cr}(\text{acac})_3]$ , but they were conveniently determined in its presence. Raising its concentration above 0.040 M did not cause significant further shortening of the  $T_1$  times. The values in Table 1 generally increase as the number of  $^1\text{H}$  and  $^{14}\text{N}$  nuclei in the molecule decreases.

**Binding of Urea to Palladium(II).** Urea can variously coordinate to metals; unidentate terminal modes are the most common. Binding of hard metal ions, such as cobalt(III), chromium(III), and rhodium(III), via the oxygen atom is both kinetically and thermodynamically favored.<sup>7–9</sup> Platinum(II), which is a soft ion, initially loses an aqua ligand to yield the oxygen-bound isomer, which then converts into the more stable nitrogen-bound isomer.<sup>6</sup> This process occurs over hours, and the estimated equilibrium constant for it is ca. 10.

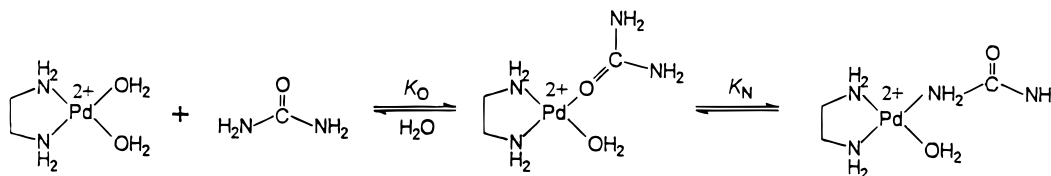
Because urea was enriched in both  $^{15}\text{N}$  and  $^{13}\text{C}$ , we applied NMR spectroscopy of both nuclei to study reactions with  $\text{cis}[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}$  and, to a lesser extent, other palladium(II) complexes in Chart 1. The  $^{13}\text{C}$  NMR spectra of mixtures containing urea and  $\text{cis}[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}$  show the resonances at 162.8, 165.5, and 158 ppm, respectively, of free urea and the O-bound and N-bound ligands shown in Chart 2. These values agree with those reported previously.<sup>6</sup> Partial coalescence of the first two resonances indicates that the exchange between

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Chart 2. Coordination Modes



Scheme 1. Coordination of Urea

**Table 3.** Equilibrium Constants for Urea Binding to [Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> Complex in Acetone-*d*<sub>6</sub>, at 313 K

| equilibrium const <sup>a</sup>                         | no H <sub>2</sub> O added | 3.0 M H <sub>2</sub> O |
|--|---------------------------|------------------------|
| <i>K</i> <sub>O</sub>                                  | 23                        | 20                     |
| <i>K</i> <sub>N</sub>                                  | 0.060                     | 0.050                  |
| <i>K</i> = <i>K</i> <sub>O</sub> <i>K</i> <sub>N</sub> | 1.3                       | 0.95                   |

<sup>a</sup> Defined in Scheme 1.

the free and O-bound urea molecules is fast on the <sup>13</sup>C NMR time scale. As expected, this coalescence was somewhat lessened at a lower temperature (283 K).

In the hydrolysis reactions catalyzed by *cis*-[Pd(dtco-OH)-(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup>, the O-bound ligand is evident in the <sup>13</sup>C NMR spectra soon after the mixing of this catalyst and urea. As Figure S2 in the Supporting Information shows, parallel disappearance of the O-bound ligand and the appearance of the N-bound ligand indicate their interconversion. This process is evident in the case of *cis*-[Pd(dtco-OH)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> but not in the case of *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup>, with which the quantitative kinetic experiments were done. Therefore this interconversion was not investigated quantitatively.

The equilibrium constants *K*<sub>O</sub> and *K*<sub>N</sub> are defined in Scheme 1. Their values, which are average results of multiple experiments by <sup>13</sup>C NMR spectroscopy, are given in Table 3. The O-bound isomer is much more abundant than the N-bound isomer. The equilibrium constants change only slightly, if at all, when the concentration of water in the acetone-*d*<sub>6</sub> solution is made 10 times higher than that of urea. Evidently, urea has a greater affinity than water for binding to the palladium(II) atom.

**Comparison of Different Complexes as Catalysts.** In the kinetic experiments reported in Table 4, the maximal concentration of carbon dioxide in solution was ca. 0.010 M, well below

**Table 4.** Initial Rate of CO<sub>2</sub> Formation in the Decomposition of Urea Catalyzed by Various Palladium(II) Complexes in Acetone-*d*<sub>6</sub>, at 313 K<sup>a</sup>

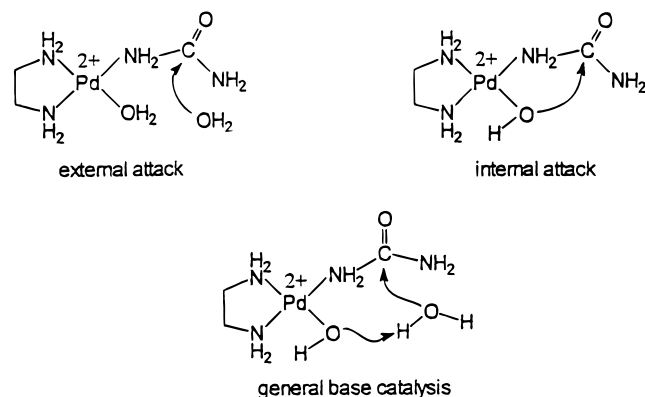
| complex   | 10 <sup>5</sup> <i>v</i> <sub>i</sub> CO <sub>2</sub> , M min <sup>-1</sup> |
|---|---|
| [Pd(H <sub>2</sub> O) <sub>4</sub> ] <sup>2+</sup>                      | 6.67 ± 0.69   |
| <i>cis</i> -[Pd(en)(H <sub>2</sub> O) <sub>2</sub> ] <sup>2+</sup>      | 13.3 ± 1.1  |
| <i>cis</i> -[Pd(OMeMet)(H <sub>2</sub> O) <sub>2</sub> ] <sup>2+</sup>  | 7.87 ± 0.55   |
| <i>cis</i> -[Pd(dtco-OH)(H <sub>2</sub> O) <sub>2</sub> ] <sup>2+</sup> | 16.5 ± 1.0  |
| [Pd(dien)(H <sub>2</sub> O)] <sup>2+</sup>                              | <1.4 × 10 <sup>-3</sup>   |

<sup>a</sup> Initial concentrations of urea and the complex were 0.30 M each, the temperature was 313 K, and the solvent was acetone-*d*<sub>6</sub>.

the solubility limit in acetone-*d*<sub>6</sub> (0.10 M under our conditions). All the unidentate and bidentate complexes in Chart 1 proved similarly effective in promoting hydrolysis of urea. No hydrolysis was detected for 5 days in the presence of the complex [Pd(dien)H<sub>2</sub>O]<sup>2+</sup>. This unreactivity can be due to two causes: (i) the very low concentration of the urea complex, undetected by <sup>13</sup>C NMR spectroscopy, and (ii) the prevention by the tridentate ligand of internal attack and general-base catalysis; see Scheme 2. External attack by a water molecule from the solvent is expected to be less efficient than the aforementioned two mechanisms.

Further kinetic experiments, described below, were done with *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> because this catalyst is easy to prepare and because an intermediate was clearly detectable in the reaction.

**Products of Urea Decomposition.** The species CO<sub>2</sub>, NH<sub>3</sub>, and NH<sub>4</sub><sup>+</sup> were readily detected by their NMR chemical shifts, listed in Table 2. Our values agree with those in the literature.<sup>6,8</sup> Ammonia occurs as a free molecule and as a ligand in *cis*-[Pd(en)(NH<sub>3</sub>)(H<sub>2</sub>O)]<sup>2+</sup> and *cis*-[Pd(en)(NH<sub>3</sub>)<sub>2</sub>]<sup>2+</sup>. The assignments were confirmed by spiking the reaction mixtures with authentic compounds, in the presence and the absence of *cis*-[Pd(en)-(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup>.

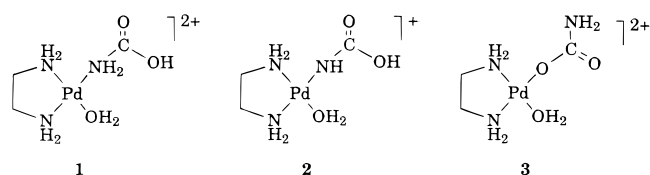
**Scheme 2.** Hydrolysis Mechanisms

**Carbamic Acid as an Intermediate in Hydrolysis.** An intermediate is consistently observed with all four palladium(II) aqua complexes shown in Chart 1 and Table 4. The fifth one is inactive, as explained above. When urea is enriched only in  $^{13}\text{C}$ , the resonance at 174.3 ppm of the intermediate is a singlet. When urea is enriched in both  $^{13}\text{C}$  and  $^{15}\text{N}$ , this  $^{13}\text{C}$  resonance of the intermediate is a doublet, owing to coupling to one  $^{15}\text{N}$  nucleus, and the  $^{15}\text{N}$  resonance at  $-27$  ppm of the intermediate is an unresolved doublet of doublets, owing to coupling to two inequivalent protons.<sup>34</sup>

Neither spectrum is consistent with the isocyanate anion,  $\text{NCO}^-$ , which was detected as an intermediate in the noncatalytic decomposition of urea.<sup>1</sup> We did not observe the characteristic resonances (Table 2) of this ion, either free or coordinated to palladium(II). Neither spectrum is consistent with an N,N- or N,O-bidentate urea ligand.

Free carbamic acid also can be ruled out; it exists as a zwitterion,  $^+\text{NH}_3\text{COO}^-$ , which decomposes into carbon dioxide and ammonia too rapidly to be detected by NMR spectroscopy.<sup>35</sup> Addition of ammonium carbamate,  $\text{NH}_4(\text{NH}_2\text{COO})$ , to solutions of  $[\text{Pd}(\text{H}_2\text{O})_4]^{2+}$  and of *cis*- $[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}$  in acetone- $d_6$  yielded complexes of O-bound carbamate, **3**, which show the  $^{13}\text{C}$  NMR resonance at 187.0 ppm, not at 174.3 ppm. The latter signal was detected only in the reaction of the coordinated urea.

The NMR spectroscopic evidence is consistent with N-coordination of carbamic acid (**1**), or of its conjugate base (**2**), to palladium(II). In most kinetic experiments, the  $\text{H}_3\text{O}^+$



concentration was 0.5 mM and the concentration of **2** would be undetectably low. With increasing acidity of the reaction mixture, the concentration of the intermediate decreased. Indeed, protonation of the amino group in compound **1** displaces carbamic acid from the complex. Compound **2** was formed when the reaction mixture was made basic; details will be given below, in the subsection on the effects of base. To conclude, the intermediate in the reaction performed under the usual conditions, in the presence of ca. 0.5 M acid, likely has the structure **1**, as shown in Scheme 3. The tautomeric iminol forms

of **1–3** are unlikely because urea and carbamic acid exist mostly in the amide form.<sup>14</sup>

**Stoichiometry of Decomposition.** Initial rates ( $v_i$ ) of the formation of carbon dioxide and ammonia, determined from  $^{13}\text{C}$  and  $^{15}\text{N}$  NMR spectra, are  $(1.33 \pm 0.10) \times 10^{-4}$  and  $(2.48 \pm 0.17) \times 10^{-4} \text{ M min}^{-1}$ , respectively. This ratio of approximately 1:2 agrees with the overall stoichiometry of urea decomposition (the sum of eqs 1 and 2). It can easily be shown that this ratio also agrees with the mechanism in Scheme 3. Only urea and the ligands formed from it are shown in the abbreviated formulas for the palladium(II) complexes in eqs 4–6. The intermediate, the complex of carbamic acid, reaches

$$v_i^{\text{CO}_2} = k_2[\text{Pd}-\text{NH}_2\text{COOH}] \quad (4)$$

$$v_i^{\text{NH}_3} = k_1[\text{Pd}-\text{NH}_2\text{C}(\text{O})\text{NH}_2] + k_2[\text{Pd}-\text{NH}_2\text{COOH}] \quad (5)$$

a steady concentration some time after mixing of urea and the catalyst. This concentration is maintained for at least 1 h, the time over which the initial rates were determined. During this hour, the intermediate is formed and consumed at the same rate, as stated in eq 6. If this rate is taken as the initial rate, eq 7 follows.

$$k_1[\text{Pd}-\text{NH}_2\text{C}(\text{O})\text{NH}_2] = k_2[\text{Pd}-\text{NH}_2\text{COOH}] \quad (6)$$

$$v_i^{\text{NH}_3} = 2v_i^{\text{CO}_2} \quad (7)$$

**The Rate Law.** As Figures 1 and 2 and Figure S3 in the Supporting Information show, the orders of the reaction with respect to urea, *cis*- $[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}$ , and water are 1, 1, and 0, respectively. The rate law in eq 8 indicates that the active

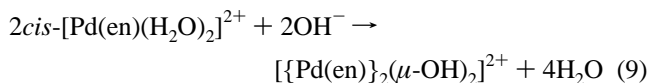
$$v_i^{\text{CO}_2} = k_{\text{obs}}[\text{NH}_2\text{C}(\text{O})\text{NH}_2][\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+} \quad (8)$$

species is a mononuclear complex of palladium(II) and that external water (as from the solvent) does not participate in the rate-limiting step.

**Inhibition of the Reaction.** As Figure 3 shows, thiourea inhibits hydrolysis of urea. At the inhibitor concentration of 0.083 M, a  $^{13}\text{C}$  NMR spectrum showed only traces of O-bound urea and gave no evidence for the N-bound isomer. Evidently, thiourea acts by preventing binding of urea to the catalyst. Fitting of Figure 3 to the mechanism in Scheme 4 gave the binding constant  $K_{\text{tu}} = 61 \pm 11$  for thiourea. As expected, this value is greater than the values for urea, given in Table 3. As Table S1 in the Supporting Information shows, dimethyl sulfoxide at the concentrations tested does not inhibit hydrolysis of urea.

**Kinetic Effects of Base.** The initial rate of carbon dioxide production does not depend on ionic strength of the solution;  $v_i^{\text{CO}_2} = (1.33 \pm 0.15) \times 10^{-4} \text{ M min}^{-1}$  when the ionic strength is 0.9–2.9 M. Evidently, moderate amounts of acids or bases may be added to the reaction mixture in acetone- $d_6$  without adjusting the ionic strength.

The inhibition of the reaction by NaOH, evident in Figure 4, can be caused by either or both of the following processes: (i) formation of the catalytically-inactive binuclear complex, shown in eq 9,<sup>23</sup> and (ii) deprotonation of the N-bound carbamic acid,

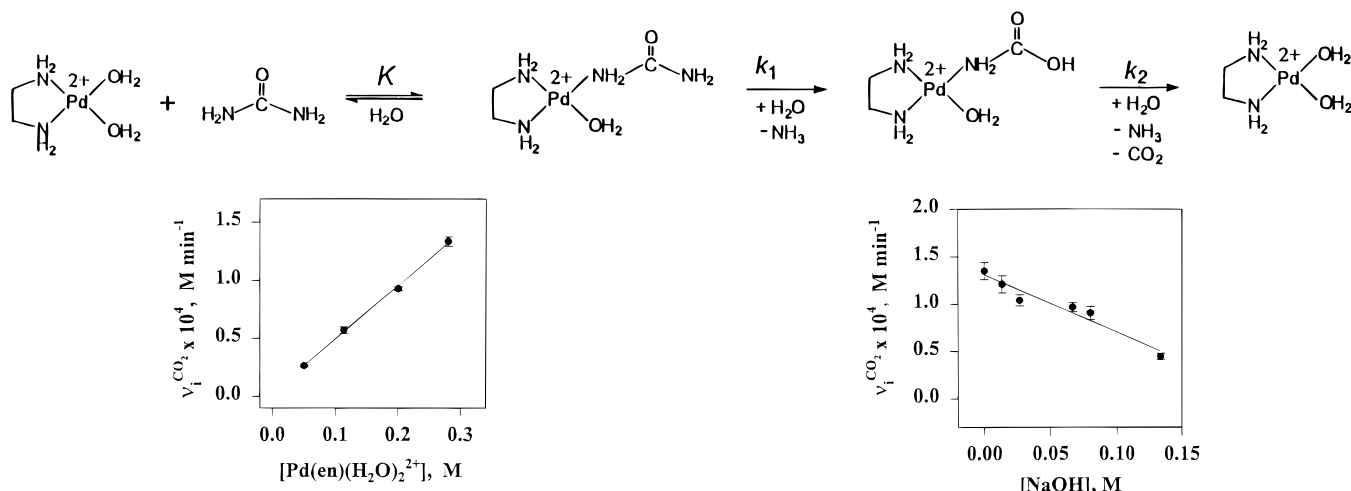


so that the more reactive intermediate **1** is converted into the less reactive intermediate **2**, which decomposes more slowly into carbon dioxide and ammonia.<sup>7</sup> Extrapolation of the plot

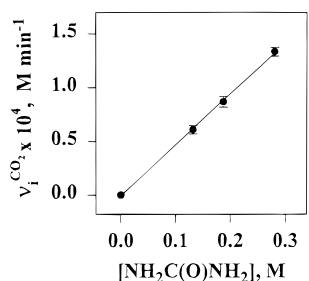
(34) Zhao, Y.; Raymond, M. K.; Tsai, H.; Roberts, J. D. *J. Phys. Chem.* **1993**, 97, 2910.

(35) Dixon, N. E.; Sargeson, A. M. In *Zinc Enzymes*; Spiro, T. G., Ed.; Wiley: New York, 1983; p 253.

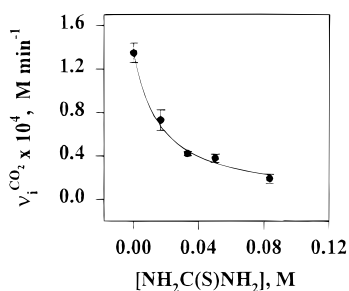
## Scheme 3. Carbamic Acid in the Intermediate



**Figure 1.** Dependence of the initial rate of CO<sub>2</sub> formation on the initial concentration of the *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> complex. The initial concentration of urea was 0.30 M, the temperature was 313 K, and the solvent was acetone-*d*<sub>6</sub>. Error bars for some of the points are smaller than the symbols.



**Figure 2.** Dependence of the initial rate of CO<sub>2</sub> formation on the initial concentration of urea. The initial concentration of the *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> complex was 0.30 M, the temperature was 313 K, and the solvent was acetone-*d*<sub>6</sub>. An error bar for one of the points is smaller than the symbols.



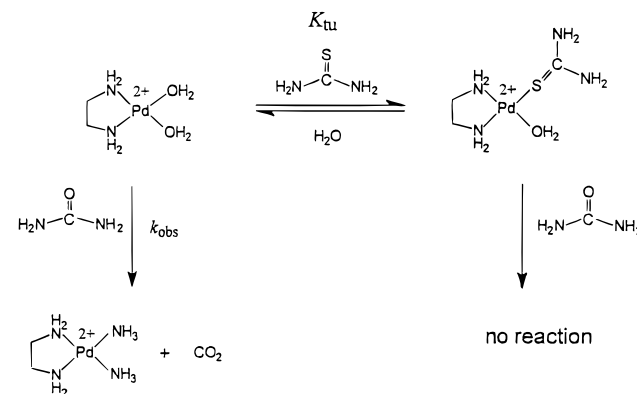
**Figure 3.** Dependence of the initial rate of CO<sub>2</sub> formation on the concentration of thiourea. The initial concentrations of urea and the *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> complex were 0.30 M each, the temperature was 313 K, and the solvent was acetone-*d*<sub>6</sub>. An error bar for one of the points is smaller than the symbols.

in Figure 4 indicates that the reaction will cease when the NaOH concentration becomes ca. 0.22 M, nearly equal to the concentration of palladium(II). This fact is consistent with either explanation above. Both dimerization and deprotonation require a Pd:OH<sup>-</sup> ratio of 1:1.

When the reaction mixture was made 0.22 M in NaOH or Et<sub>3</sub>N, a yellow precipitate appeared. It was filtered off from acetone-*d*<sub>6</sub> and dissolved in H<sub>2</sub>O. The <sup>13</sup>C NMR spectrum of the acetone-*d*<sub>6</sub> filtrate showed an abundance of free urea and traces of the compound **2**. The <sup>13</sup>C NMR spectrum of the

**Figure 4.** Dependence of the initial rate of CO<sub>2</sub> formation on the concentration of NaOH. The initial concentrations of urea and the *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> complex were 0.30 M each, the temperature was 313 K, and the solvent was acetone-*d*<sub>6</sub>.

## Scheme 4. Inhibition by Thiourea



aqueous solution, with 0.10 M acetone-*d*<sub>6</sub> for D-lock, showed, conversely, an abundance of compound **2** and traces of free urea. The <sup>15</sup>N NMR spectrum of this solution, showing the doublet at -25.4 ppm owing to coupling with one proton, confirmed this interpretation.

In conclusion, addition of base to the reaction mixture promotes formation of the observed intermediate, but it exists in the stable form **2**, rather than the reactive form **1**. Consequently, the overall decomposition of urea into CO<sub>2</sub> and NH<sub>3</sub> is inhibited.

**Kinetic Effects of Acid.** Experiments with DClO<sub>4</sub> dissolved in a mixture of D<sub>2</sub>O and acetone-*d*<sub>6</sub> and with CF<sub>3</sub>COOH dissolved in acetone-*d*<sub>6</sub> gave similar results; the rates of formation of carbon dioxide at the same [H<sup>+</sup>] differed only within the margins of error. Evidently, the anions of these acids do not affect hydrolytic decomposition of urea. Since water concentration does not affect the initial rate of CO<sub>2</sub> formation (Figure S3), the two solvent systems can be compared.

As Table 5 shows, an increase in the solution acidity inhibits coordination of urea to palladium(II) but favors the O-bound over the N-bound isomer in the diminishing fraction of urea that is coordinated. The two isomers exist in a fast equilibrium, but the N-bound one is much more acidic than the O-bound one; the respective pK<sub>a</sub> values are 3–4 and ca. 13.<sup>6,7</sup> The N-bound urea partially exists in the deprotonated form, shown in Chart 2. Its protonation by the added acid directly causes release of the N-bound isomer and, indirectly, also of the

**Table 5.** Effects of Acid on the Extent of Urea Coordination, the Mode of Its Coordination, and the Initial Rate of CO<sub>2</sub> Formation<sup>a</sup>

| added<br>[DCIO <sub>4</sub> ], M | urea<br>[bound]/[free] [O-bound]/[N-bound] |      | 10 <sup>4</sup> v <sub>i</sub> CO <sub>2</sub> ,<br>M min <sup>-1</sup> |
|----------------------------------|--|------|---|
| 0.000                            | 3.10                                       | 8.70 | 1.330 ± 0.070   |
| 0.027                            | 2.20                                       | 8.70 | 1.020 ± 0.090   |
| 0.080                            | 1.10                                       | 14.1 | 0.800 ± 0.070   |
| 0.107                            | 0.700                                      | 21.4 | 0.640 ± 0.050   |
| 0.133                            | 0.500                                      | 22.4 | 0.600 ± 0.050   |

<sup>a</sup> Initial concentrations of urea and the *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> complex were 0.30 M each, the temperature was 313 K, and the solvent was acetone-*d*<sub>6</sub>.

O-bound isomer. Therefore the concentrations of both isomers decrease with increasing acidity, but to different extents. As <sup>13</sup>C NMR spectra showed, concentration of the reactive intermediate designated **1** decreases with increasing acidity, most likely because protonation of the amino group causes release of H<sub>3</sub>N<sup>+</sup>COOH from palladium(II). Table 5 shows that, as expected, coordination to palladium(II) favors hydrolysis of urea. Figure S4 in the Supporting Information indicates that, molecule for molecule, the N-bound isomer of urea is more reactive than the O-bound isomer.

**Kinetic Profile of the Intermediate, a Complex of Carbamic Acid.** Concentration of the intermediate in Scheme 3, determined by <sup>13</sup>C NMR spectroscopy, was fitted to eq 10, and

$$[\text{Pd}-\text{NH}_2\text{COOH}] = \frac{k_1 K [\text{Pd}(\text{en})(\text{H}_2\text{O})_2]_0 [\text{NH}_2\text{C}(\text{O})\text{NH}_2]_0}{k_2 - k_1} [\exp(-k_1 t) - \exp(-k_2 t)] \quad (10)$$

rate constants  $k_1$  and  $k_2$  were obtained. Because the intermediate **1** is formed from the N-bound urea ligand, whose concentration is relatively low, the rate constant for the formation of **1** must be relatively high. As Table 6 shows, the initial rate of carbon dioxide formation is similar to the rate of disappearance of the intermediate **1** and much lower than the rate of its appearance. For all of these reasons, the larger rate constant,  $k_1$ , is assigned to the formation of the intermediate and the smaller one,  $k_2$ , to its conversion into carbon dioxide and ammonia, as in Scheme 3.

Both of these rate constants are composite quantities, for they depend on the acid concentration. Analysis of this dependence gave three microscopic rate constants, for individual steps in the reaction mechanism. These three rate constants are discussed in the next two subsections.

**The Rate Constant  $k_1$ .** This rate constant corresponds to nucleophilic attack at the carbon atom of N-bound urea, as Schemes 2 and 3 show. Although the experimental results in Figure 5 span a relatively narrow interval of acidity (or basicity), they were fitted to eq 11, derived from Scheme 5. The slope

$$k_1 = \frac{k_1' K_a}{[\text{H}^+]} + k_1'' \quad (11)$$

of the plot in Figure 5 is small, but it lies outside the experimental margin of error. Because acetone is a slightly basic solvent,<sup>37</sup> CF<sub>3</sub>COOH is a stronger acid in it than in water. This acid constituted less than 1% of the solvent volume. Therefore the small kinetic effect shown in Figure 5 is probably not due to the variations in the extent of dissociation and in the

solvent properties. Our skepticism about the kinetic effect of acid remains, even though the experiment with a much more basic solution (0.027 M NaOH in acetone-*d*<sub>6</sub>) gave the rate constants  $k_1 = 8.9 \pm 3 \text{ min}^{-1}$  and  $k_2 = (0.89 \pm 0.07) \times 10^{-3} \text{ min}^{-1}$ . The increase in  $k_1$  with decreasing acidity becomes more noticeable in a wider interval, but the aforementioned value of  $k_1$  is still much smaller than that calculated from eq 11 and the constants  $k_1'$ ,  $k_1''$ , and  $K_a$  in it. This discrepancy between the found and the expected values of  $k_1$  in the basic solution may be due to the reaction in eq 9.

The equilibrium constant  $K_a$  could not be determined experimentally because the complex *cis*-[Pd(en){NH<sub>2</sub>C(O)-NH<sub>2</sub>}(H<sub>2</sub>O)] in the lower left corner of Scheme 5 is reactive and present in a very low concentration and because the aqua ligand and urea probably have similar acidities.<sup>6,7,17</sup> Fortunately, the value of  $K_a$  could be estimated on the basis of the published value  $\text{p}K_a = 5.6$  for *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup>.<sup>17</sup> Since urea is a slightly stronger electron donor than is water (see Table 3), displacement of one aqua ligand by urea should slightly lessen the acidity of the remaining aqua ligand on palladium(II). With a reasonable estimate of  $K_a = 1 \times 10^{-6} \text{ M}$ , the slope and the intercept in Figure 5 yielded the rate constants  $k_1'' = 0.3 \text{ min}^{-1}$  and  $k_1' = 460 \text{ min}^{-1}$  in Scheme 5. There is only one relevant report in the literature, for comparison. Our values are greater than  $2.4 \times 10^{-3} \text{ min}^{-1}$ , the rate constant for conversion of N-bound urea to N-bound cyanate ligand observed in a rhodium(III) complex.<sup>7</sup> That the hydroxo complex is more reactive than the "parent" aqua complex is consistent both with internal attack and with general-base catalysis, shown in Scheme 2.

**The Rate Constant  $k_2$ .** Carbamic acid, the ligand of interest in the intermediate, can decompose when free or bound to palladium(II); the corresponding rate constants are  $k_f$  and  $k_b$ . The former reaction is extremely fast:<sup>35,36</sup>  $k_f = 6.0 \times 10^{10} \text{ min}^{-1}$ . Fitting of the slope and the intercept of the plot in Figure 6 to eq 12, derived from Scheme 6, yielded  $k_d = 9.0 \times 10^{-14} \text{ M}^{-1}$

$$k_2 = \frac{k_f K_d [\text{H}^+]}{[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}} + k_b \quad (12)$$

and  $k_b = 8.9 \times 10^{-4} \text{ min}^{-1}$ . Both values are small. Our result for  $k_b$  can be compared with the rate constants for decomposition of [Co(NH<sub>3</sub>)<sub>5</sub>(NH<sub>2</sub>COO)]<sup>2+</sup> and [Co(NH<sub>3</sub>)<sub>5</sub>(NH<sub>2</sub>COOH)], which are  $6 \times 10^2$  and ca.  $0.6 \text{ min}^{-1}$ , respectively.<sup>37</sup> The low value of the rate constant  $k_b$  may be due to the relatively high acidity of the carbamic acid ligand in our four-coordinate complex **1**, which is deprotonated to give the less reactive conjugate base, **2**.

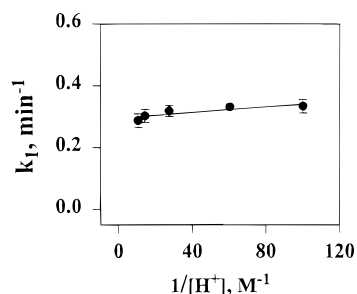
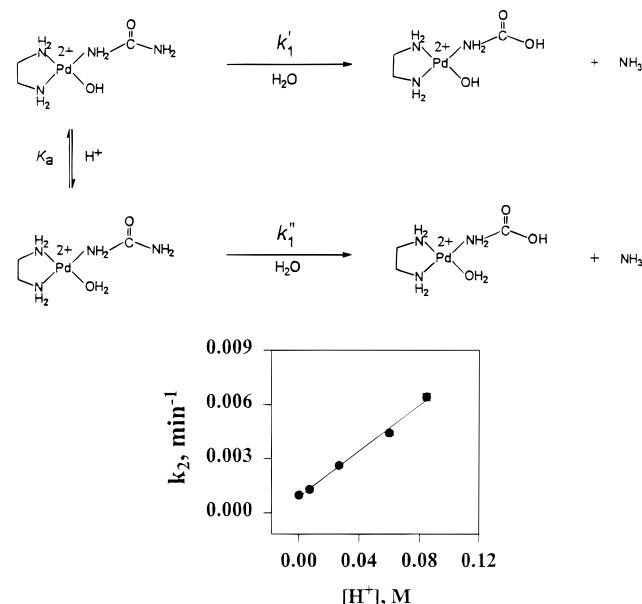
**The Overall Mechanism.** All the steps discussed so far are integrated in Scheme 7. The observed species appear in boxes. All the equilibrium constants and rate constants given in Scheme 7 have been determined. This mechanism, however, does not fully account for the kinetic results. The overall rate of the reaction (i.e., the initial rate of carbon dioxide formation in Table 6) is greater than the maximal rate of decomposition of carbamic acid, calculated from the known values of  $k_1$  and  $k_2$  and the maximal concentration of the intermediate **1**. Evidently, carbon dioxide is formed by a pathway that does not involve N-bound carbamic acid. The rate of this second pathway in Table 6 is the difference between the overall rate of carbon dioxide formation and the rate of the disappearance of the N-bound carbamic acid. Because this intermediate can plausibly be formed only from N-bound urea, the second pathway probably does not begin with N-bound urea. The reasonable alternative for the starting compound is the complex of O-bound urea, shown in Chart 2. Both pathways contribute approximately equally to the formation of carbon dioxide.

(37) Laitinen, H. A.; Harris, W. E. *Chemical Analysis*; McGraw-Hill: New York, 1975; p 120.

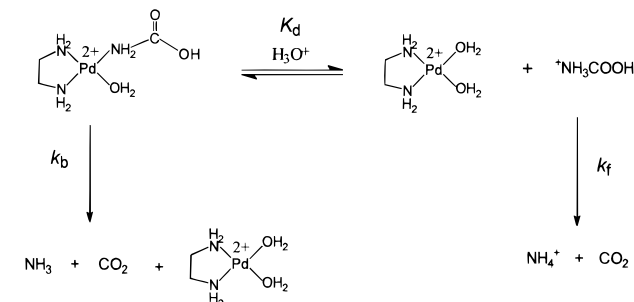
**Table 6.** Initial Rate of CO<sub>2</sub> Formation in the Decomposition of Urea by Two Paths, One of Which Involves the *cis*-[Pd(en)(NH<sub>2</sub>COOH)(H<sub>2</sub>O)]<sup>2+</sup> Complex (**1**), and Dependence of the Rate Constants for Appearance and Disappearance of This Complex on the Concentration of CF<sub>3</sub>COOH<sup>a</sup>

| added<br>[CF <sub>3</sub> COOH], M | 10 <sup>4</sup> v <sub>i</sub> CO <sub>2</sub> , M min <sup>-1</sup> |   |                |                                      |  |
|------------------------------------|--|---|----------------|--------------------------------------|--|
|                                    | total  | first pathway,<br>via Pd–NH <sub>2</sub> COOH | second pathway | 10k <sub>1</sub> , min <sup>-1</sup> | 10 <sup>3</sup> k <sub>2</sub> , min <sup>-1</sup> |
| 0.000                              | 1.33 ± 0.07  | 0.61  | 0.72           | 3.34 ± 0.2                           | 0.970 ± 0.010                                      |
| 0.007                              | 1.22 ± 0.08  | 0.58  | 0.64           | 3.31 ± 0.20                          | 1.29 ± 0.04  |
| 0.027                              | 1.02 ± 0.09  | 0.79  | 0.23           | 3.18 ± 0.10                          | 2.62 ± 0.04  |
| 0.060                              | 0.990 ± 0.020  | 0.35  | 0.64           | 3.02 ± 0.08                          | 4.42 ± 0.10  |
| 0.084                              | 0.910 ± 0.040  | 0.32  | 0.59           | 2.87 ± 0.12                          | 6.42 ± 0.21  |

<sup>a</sup> Initial concentrations of urea and the *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> complex were 0.30 M each, the temperature was 313 K, and the solvent was acetone-*d*<sub>6</sub>.

**Figure 5.** Dependence of the rate constant for the appearance of the intermediate, containing the carbamic acid complex *cis*-[Pd(en){NH<sub>2</sub>COOH}(H<sub>2</sub>O)]<sup>2+</sup>, on the concentration of trifluoroacetic acid. The initial concentrations of urea and the *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> complex were 0.30 M each, the temperature was 313 K, and the solvent was acetone-*d*<sub>6</sub>. An error bar for one of the points is smaller than the symbols.**Scheme 5.** Effect of Acid on the Formation of the Intermediate**Figure 6.** Dependence of the rate constant for the disappearance of the intermediate, the carbamic acid complex *cis*-[Pd(en){NH<sub>2</sub>COOH}(H<sub>2</sub>O)]<sup>2+</sup>, on the concentration of trifluoroacetic acid. The initial concentrations of urea and the *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> complex were 0.30 M each, the temperature was 313 K, and the solvent was acetone-*d*<sub>6</sub>. Error bars for some of the points are smaller than the symbols.

Although the palladium(II) complex containing O-bound urea is clearly evident in the NMR spectra, there are no precedents for nucleophilic attack by water at its carbon atom and formation of the O-bound carbamate anion, shown in **3**. There are precedents for the decomposition of the O-bound carbamate anion into carbon dioxide and ammonia, but this reaction is much slower than the decomposition of the N-bound carbamic

**Scheme 6.** Effect of Acid on the Decomposition of the Intermediate

acid. For example, the ratio of the respective rate constants for the decomposition of these two ligands in the coordination sphere of cobalt(III) is 1:600.<sup>38,39</sup> Since in palladium(II) complexes the O-bound urea is more abundant than the N-bound urea (see Table 3), the rate constant for the nucleophilic attack in the former (yielding the O-bound carbamate anion) must be smaller than the rate constant for the attack in the latter (yielding the N-bound carbamic acid). Under these conditions, the O-bound carbamate anion would be undetectable by the <sup>13</sup>C NMR spectroscopy. We, however, hesitate to implicate this plausible intermediate in the second pathway for urea decomposition until conversion of the O-bound urea into the O-bound carbamate anion is demonstrated.

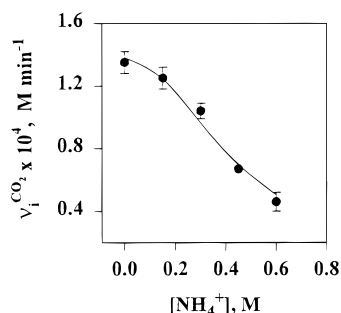
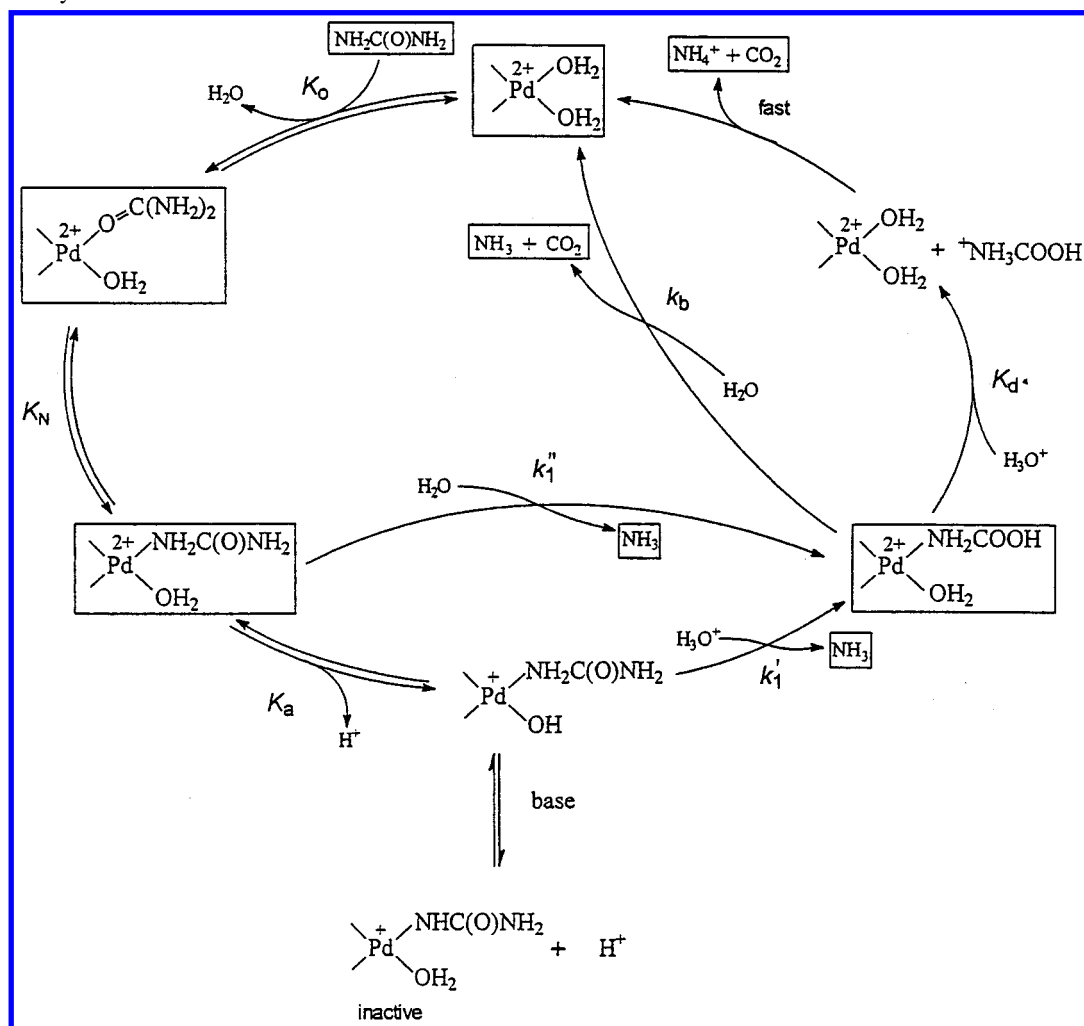
**Inhibition by Ammonia.** As Figure 7 shows, added NH<sub>4</sub>NO<sub>3</sub> inhibits decomposition of urea. The acidity of this salt is too slight to affect the rate of carbon dioxide formation. Control experiments with *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> and NH<sub>4</sub>NO<sub>3</sub> under the same conditions showed displacement of the aqua ligands by ammonia. The resulting complexes, *cis*-[Pd(en)(NH<sub>3</sub>)(H<sub>2</sub>O)]<sup>2+</sup> and *cis*-[Pd(en)(NH<sub>3</sub>)<sub>2</sub>]<sup>2+</sup>, gave broad, overlapping <sup>15</sup>N NMR resonances at -56.2 ppm. The binding constant for ammonia, estimated from the <sup>15</sup>N NMR spectra of a series of solutions with different concentrations, is 4.3 M<sup>-2</sup>.

Ammonia produced in the decomposition of urea inhibits this decomposition by converting the catalytically-active aqua complexes into the inactive ammine complexes; see Scheme 8. Fitting of the plot in Figure 7 to eq 13, derived from Scheme 8, gave the equilibrium constant K<sub>i</sub> = 4.8 ± 0.6 M<sup>-2</sup> for binding of NH<sub>3</sub> to palladium(II). This value agrees with the aforementioned estimate of 4.3 M<sup>-2</sup>. Ammonia at relatively low concentrations (≤ 0.6 M) inhibits urea hydrolysis only partially because the catalytically-active *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> is only partially converted into the catalytically-inactive ammine com-

- (38) (a) Kaminskaia, N. V.; Kostić, N. M. *J. Chem. Soc., Dalton Trans.* **1996**, 3677. (b) Buckingham, D. A.; Franics, D. J.; Sargeson, A. M. *Inorg. Chem.* **1974**, *13*, 2630.  
(39) Buckingham, D. A.; Olsen, I. I.; Sargeson, A. M.; Satrapa, H. *Inorg. Chem.* **1967**, *6*, 1027.



Scheme 7. Catalytic Mechanism



**Figure 7.** Dependence of the initial rate of CO<sub>2</sub> formation on the concentration of added NH<sub>4</sub>NO<sub>3</sub>. The initial concentrations of urea and the *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> complex were 0.30 M each, the temperature was 313 K, and the solvent was acetone-*d*<sub>6</sub>. An error bar for one of the points is smaller than the symbols.

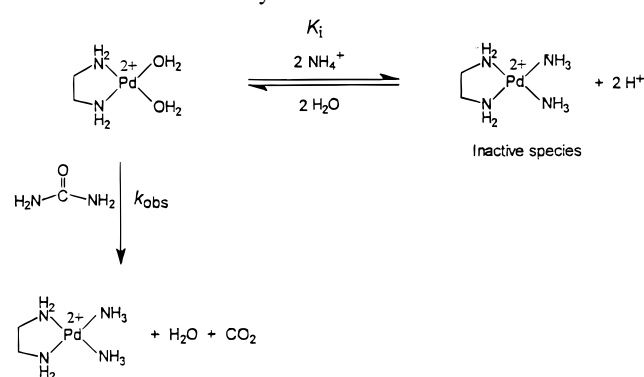
$$v_1^{\text{CO}_2} =$$

$$k_{\text{obs}}[\text{NH}_2\text{C(O)NH}_2]_0[\text{Pd(en)(H}_2\text{O)}_2^{2+}]_0 \frac{1}{1 + K_1[\text{NH}_4\text{NO}_3]^2} \quad (13)$$

plexes *cis*-[Pd(en)(NH<sub>3</sub>)<sub>2</sub>]<sup>2+</sup> and *cis*-[Pd(en)(NH<sub>3</sub>)(H<sub>2</sub>O)]<sup>2+</sup>. The remaining *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> still catalyzes urea hydrolysis. The inhibited reaction requires a longer time (4 days) and slightly higher temperature (333 K) than the reaction in the absence of the added ammonia.

**Catalytic Turnover.** Since ammonia poisons the palladium(II) catalyst and inhibits decomposition of urea, sequestration

Scheme 8. Inhibition by Product



of ammonia is expected to promote the decomposition. Indeed, Table 7 shows that this reaction is enhanced in the presence of certain metal cations. When *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> is absent, urea does not detectably decompose in the presence of Ag(I), Cd(II), Ni(II), and Zn(II) cations and decomposes very slowly in the presence of Hg(II) cations. Clearly, these cations do not directly decompose urea; they only suppress the inhibition of this reaction, catalyzed by *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup>. Stabilities of the ammonia complexes follow the order of the binding constants β<sub>1</sub> or β<sub>2</sub>: Hg(II) > Ag(I) > Ni(II) > Cd(II) > Zn(II). The order of half-lives for the reaction is remarkably similar: Hg(II) < Ag(I) < Cd(II) < Zn(II) > Ni(II). The only qualitative discrepancy between the two series is the Ni(II) ion, whose activating effect is less than is expected from its affinity

**Table 7.** Effects of Added Metal Cations, at the Concentration of 1.0 M, on the Half-life of Urea Decomposition<sup>a</sup>

| cation | $\beta_1$         | $\beta_2$            | $t_{1/2}$ , h |
|--------|-------------------|----------------------|---------------|
| Ag(I)  | $2.0 \times 10^3$ | $1.4 \times 10^7$    | 4.10          |
| Cd(II) | $3.2 \times 10^2$ | $2.9 \times 10^4$    | 18.4          |
| Ni(II) | $4.7 \times 10^2$ | $6.1 \times 10^4$    | >26.7         |
| Hg(II) | $6.0 \times 10^8$ | $3.0 \times 10^{16}$ | <2.30         |
| Zn(II) | $1.5 \times 10^2$ | $2.7 \times 10^4$    | 26.7          |

<sup>a</sup> Initial concentrations of urea and *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> were 0.30 and 0.075 M, respectively, the temperature was 333 K, and the solvent was acetone-*d*<sub>6</sub>.

**Table 8.** Effects of Ag(I) Ion Concentration on the Half-life of Urea Decomposition<sup>a</sup>

| [Ag(I)],<br>M | [Pd(en)(H <sub>2</sub> O) <sub>2</sub> ] <sup>2+</sup> ,<br>M | $t_{1/2}$ ,<br>h | [Ag(I)],<br>M | [Pd(en)(H <sub>2</sub> O) <sub>2</sub> ] <sup>2+</sup> ,<br>M | $t_{1/2}$ ,<br>h |
|---------------|---|------------------|---------------|---|------------------|
| 0.1           | 0.075   | 16.5             | 1.0           | 0.150   | 2.50             |
| 0.5           | 0.075   | 4.60             | 2.0           | 0.075   | 3.30             |
| 1.0           | 0.075   | 4.10             |               |   |                  |

<sup>a</sup> Initial concentration of urea was 0.3 M, the temperature was 333 K, and the solvent was acetone-*d*<sub>6</sub>.

for ammonia. Carbon-13 NMR spectra show Ni(II) to be the only cation out of these five that binds urea to a detectable extent under the conditions of our experiments. This intrinsic affinity for urea may be a reason for the presence of Ni(II) cations in the enzyme urease.

As Table 8 shows, when ammonia is sequestered by complexation to the Ag(I) cation, the reaction occurs with a turnover—1 equiv of *cis*-[Pd(en)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup> effects complete hydrolysis of 4 equiv of urea. When the concentration of the

Ag(I) cation or of the catalyst is raised, this reaction becomes rather fast—its half-life is less than 4 h. To our knowledge, this is the first report of catalytic decomposition of urea in the presence of a metal complex.

## Conclusions

Simple palladium(II) aqua complexes catalyze hydrolytic decomposition of urea to carbon dioxide and ammonia, via N-coordinated carbamic acid as an intermediate. In these respects, the complexes resemble the enzyme urease, the active site of which contains two nickel(II) ions. Because palladium and nickel are congeners in the periodic table, their divalent cations have similar electronic structures and behave similarly in ligand-substitution reactions. Although the simple metal complexes are very different from the enzyme, kinetic studies with them contribute to the understanding of the enzymatic mechanism.

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**Supporting Information Available:** A table showing the dependence of the rate of CO<sub>2</sub> formation on (CH<sub>3</sub>)<sub>2</sub>SO concentration and figures showing the determination of *T*<sub>1</sub> for CO<sub>2</sub>, <sup>13</sup>C NMR evidence for decomposition of urea promoted by *cis*-[Pd(dtcO-OH)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup>, independence of the rate of CO<sub>2</sub> formation on [H<sub>2</sub>O], and dependence of the rate of CO<sub>2</sub> formation on the fraction of urea coordinated via oxygen and nitrogen atoms (5 pages). Ordering information is given on any current masthead page.

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