$Ru(medtra)H_2O$ system,[15] where medtra = *N*-methylethylenediaminetriacetate. The magnitude of ΔV^* suggests the operation of an I_a rather than a limiting A mechanism.[16]

A comparison of the substitution rate constants in Table II with those reported previously[2] for the substitution of $Ru(Hedta)H_2O$, $Ru(edta)H_2O^-$ and $Ru(edta)OH^{2-}$ clearly indicates that the edta complexes are at least 1 order of magnitude more reactive and in some cases more than 2 orders of magnitude for the $Ru(edta)H_2O^-$ species. This must be due to the labilizing effect of the additional (uncoordinated) acetate ligand as compared to that of the *N*-hydroxyethyl group in the hedtra complexes, which reaches a maximum in the case of the $Ru(edta)H_2O^-$ complex, i.e. where the acetate substituent is unprotonated and H_2O is the leaving group. Nevertheless, even for the protonated form of the ligand in $Ru(Hedta)H_2O$, the acetic acid moiety still has a substantially higher labilization effect than the *N*-hydroxyethyl group. This difference is presumably due to the large difference in basicity of these ligand moieties. The intimate nature of this labilization effect remains uncertain, and various studies are presently under way to clarify this aspect.

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Registry No. $Ru^{III}(hedtra)H_2O$, 118170-06-2; K[Ru(hedta)Cl], 57132-64-6; thiourea, 62-56-6; dimethylthiourea, 534-13-4; tetramethylthiourea, 2782-91-4; thiocyanate, 302-04-5; azide, 14343-69-2.

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Contribution from the Department of Chemistry, University College, University of New South Wales, Australian Defence Force Academy, Northcott Drive, Campbell, ACT, Australia 2600, and Research School of Chemistry, The Australian National University, Canberra, ACT, Australia 2600

Cobalt-Induced Facile Degradation of Phenylurea to Ammonia, Carbon Dioxide, and Anilinium Ion and Other Reactions of Linkage Isomeric Cobalt(III) Complexes of Phenylurea

David P. Fairlie,[1a] W. Gregory Jackson,*[,1a] and George M. McLaughlin[1b]

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A search for metal ion promoted hydrolysis of urea and the factors influencing linkage isomerization on a metal has led us to prepare and examine reactivities of N- and O-bound phenylurea complexes of pentaamminecobalt(III). The N-bonded isomer reacts in aqueous acid to yield principally $[Co(NH_3)_6]^{3+}$, CO_2, and anilinium ion (ca. 70%) but also via parallel paths leading to $[(NH_3)_5CoOC(NH_2)NHC_6H_5]^{3+}$ (linkage isomerization) and $[(NH_3)_5CoOH_2]^{3+}$ (aquation). The major path involves an elimination reaction of $[(NH_3)_5CoNH_2CONHC_6H_5]^{3+}$ to give anilinium ion and $[(NH_3)_5CoNCO]^{2+}$. The latter complex, which has been isolated and characterized, is known to undergo rapid hydration (pH < 2) to $[(NH_3)_5CoNH_2CO_2H]^{3+}$, which subsequently decomposes along three parallel paths to $[Co(NH_3)_6]^{3+}$ and traces of $[(NH_3)_5CoOH_2]^{3+}$ and $[(NH_3)_5CoOCONH_2]^{3+}$. Kinetic data for the three parallel reactions of $[(NH_3)_5CoNH_2CONHC_6H_5]^{3+}$ in aqueous $HClO_4$ (1.0 M, 25.0 °C) are $k_{elim} = 1.04 \times 10^{-2}$ s^{-1} (elimination), $k_{NO} = 2.39 \times 10^{-3}$ s^{-1} (isomerization), and $k_{aq} = 1.13 \times 10^{-3}$ s^{-1} (aquation). A single-crystal structure reveals that the urea exo C–N bond is 0.11 Å longer than the endo C–N bond and, as in uncoordinated phenylurea, the electron-withdrawing phenyl ring is neither planar with nor conjugated to the urea moiety. These features are likely retained in the protonated form and account for the facility of the elimination path. By contrast, neither elimination nor hydrolysis of the O-bonded phenylurea complex was detected; instead it slowly undergoes parallel aquation and O- to N-linkage isomerization. Both processes are base-catalyzed, and each obeys a rate law of the form $k(obsd) = k_s + k_{OH}[OH^-]$. The equilibrium constant ($K'_{NO} = k_{NO}/k_{ON} = 166$) reflects the strong thermodynamic preference for the O rather than the N terminus of the neutral phenylurea molecule. However, the observed equilibrium is pH-dependent ($K'(obsd) = K'_{NO}[H^+]/(K_a + [H^+])$); for pH > 3, the N-bonded isomer is more stable due to its selective deprotonation ($K'_{NO}(obsd) \approx 10^{-5}$, pH 6.2). The single-crystal structure determination of $[(NH_3)_5CoNHCONHC_6H_5](ClO_4)_2 \cdot H_2O$ shows the cobalt in an approximately octahedral environment with phenylurea bonded as its anion through the indicated nitrogen center. As observed for the free ligand, the phenyl substituent is twisted (37°) with respect to the approximately planar urea moiety. The compound crystallizes in the monoclinic system ($\beta = 91.64°$), with $V = 1887.0$ Å^3, space group $C2/c$, $Z = 8$, $a = 15.751$ (6) Å, $b = 12.277$ (5) Å, $c = 9.762$ Å, and $R = 0.046$ and $R_w = 0.043$ for 1381 diffractometer data (244 variables) with $I \geq 3\sigma(I)$, $\mu = 105.47$ cm^{-1}, and $F(000) = 1023.96$.

Introduction

The Ni(II)-containing enzyme[2] jack bean urease catalyzes the degradation of urea to ammonia and carbon dioxide by a factor of 10^{14} (pH 7.0, 38 °C).[3] Since it is believed that specific coordination of urea to Ni(II) is intrinsic to the mechanism of catalysis,[3] there is special interest in synthesizing metal complexes of urea that might model urease by undergoing facile decomposition to NH_3 and CO_2. The enzymic degradation of urea is currently believed to be a hydrolysis[4] (eq 1) rather than the elimination reaction (eq 2) that is known[5] for nonenzymic degradation of urea in aqueous media at pH 7–14.

$$H_2NCONH_2 + H_2O \rightarrow H_2NCO_2H + NH_3 \quad (1)$$

$$H_2NCONH_2 + H_2O \rightarrow HNCO + NH_3 + H_2O \quad (2)$$

The latter process is independent of pH between 2 and 12.[6] Sumner and co-workers first demonstrated that the urease reaction yielded ammonium carbamate rather than free cyanate[7] but

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Table I. ^1H and ^{13}C NMR Chemical Shifts for Phenylurea and Its Pentaamminecobalt(III) Complexes in Me_2SO-d_6

	^1H NMR data[a]					^{13}C NMR data[a]				
compd[b]	cis NH_3	trans NH_3	NH_2	CNHC	C_6H_5[c]	C=O	C_1[d]	C_o[e]	C_m[e]	C_p[e]
$OC(NH_2)NHC_6H_5$			5.80	8.45	7.30, 7.17	156.05	140.37	128.45	117.75	121.03
$[(NH_3)_5CoOC(NH_2)NHC_6H_5]^{3+}$	4.02	2.70	6.67	8.95		161.66	137.09	129.08	121.36	123.36
$[(NH_3)_5CoNHCONHC_6H_5]^{2+}$	3.38	3.20	2.02[f]	8.25	7.28, 7.15	163.48	141.54	128.29	117.73	119.87
$[(NH_3)_5CoNH_2CONHC_6H_5]^{3+}$	3.65	3.37	*g*	9.32	7.47, 7.37					

[a] ppm downfield from TMS. [b] Perchlorate salts; [Co] = 0.2 g/1.5 mL; [free phenylurea] ≈ [complexed phenylurea]. [c] Locations of most intense spikes—resonances span 0.8 ppm. [d] Meso or bridgehead atom. [e] Ortho, meta, and para carbons (intensity ratio: 2:2:1). [f] NH singlet. [g] Not observed, average NH/free H^+ signals.

subsequently reported[8] that the former product had arisen from CO_2 and NH_3. This conclusion was later disputed in favor of $NH_4^+NH_2CO_2^-$ as the first free intermediate,[9] and some evidence for a carbamoyl-transfer reaction, based on a thymol blue/spectrophotometric assay, appears to support the latter contention.[4]

The reactivities of (urea-*N*)-[10,11] and (urea-O)pentaamminecobalt(III)[11,12] ions have been examined, but no hydrolysis of the urea ligand to bound carbamate was detected between pH 0 and 14. Instead, faster ligand substitution proceeds both intramolecularly (linkage isomerization) and intermolecularly (hydrolysis), with the O-bound form being the more kinetically and thermodynamically stable isomer[11] except under conditions where the more acidic N-bonded isomer is selectively deprotonated (pH > 3). Although $[(NH_3)_5CoNH_2CONH_2]^{3+}$ undergoes primarily linkage isomerization in acid media,[11] it was anticipated that a suitable modification to the electronic structure of the urea ligand might result in a C–N cleavage path. For example, the related cation $[(NH_3)_5CoNH_2CO_2]^{2+}$, an intermediate in the acid hydrolysis of $[(NH_3)_5CoNCO]^{2+}$, is known to decarboxylate to $[Co(NH_3)_6]^{3+}$ and CO_2.[13] The following report describes a relatively facile degradation of phenylurea, when bound through nitrogen to cobalt(III), producing anilinium ion, CO_2, and NH_3.

Results

Synthesis and Characterization. Phenylurea reacts with the labile complex $[(NH_3)_5CoOSO_2CF_3](CF_3SO_3)_2$ in poorly coordinating solvents (acetone, sulfolane) at 20 °C to yield exclusively the pink $[(NH_3)_5CoOC(NH_2)NHC_6H_5]^{3+}$ ion. This is both kinetically and thermodynamically more stable than its nitrogen-bonded linkage isomer but unstable with respect to solvolysis (Co–O cleavage) in more strongly coordinating solvents (e.g. H_2O, Me_2SO, and Me_2NCHO). The red deprotonated form of the N-bonded phenylurea complex, $[(NH_3)_5CoNHCONHC_6H_5]^{2+}$, was obtained by heating $[(NH_3)_5CoOS(CH_3)_2]^{3+}$ in Me_2SO with excess phenylurea and a sterically hindered base. This procedure has proven to be a general route to $[(NH_3)_5CoNH\text{–}R]^{2+}$ ions for carboxamides, ureas, carbamates, sulfinamides, sulfonamides, and sulfamates and is discussed in detail elsewhere.[14] The reaction involves linkage isomerization of the first-formed (phenylurea-*O*)pentaamminecobalt(III) ion to the thermodynamically favored deprotonated phenylurea-*N* complex. This ion, which is inert in neutral or basic solution but unstable in acid, can be readily identified by addition of strong acid to its cold (<0 °C) aqueous solutions, whereupon the yellow protonated form is generated.

As for urea,[11] the observed isomer equilibrium is strongly dependent on pH because of the large difference in acidity between isomers ($pK_a \approx 2$–3, N-bonded isomer; $pK_a \approx 13$, O-bonded isomer; H_2O). When phenylurea is an uncharged ligand, the O-bonded isomer is thermodynamically more stable, but above pH ≈ 3 ($[H^+] > K_a$, (3)), the N-bonded isomer assumes thermodynamic stability. Clearly, the driving force is formation of the deprotonated ion:

$$CoNH_2CONHC_6H_5^{3+} \underset{}{\overset{K'_{ND}}{\rightleftharpoons}} CoOC(NH_2)NHC_6H_5^{3+}$$

$$\Big\updownarrow K'_a$$

$$CoNHCONHC_6H_5^{2+} + H^+$$

$$K'_{ND}(obsd) = \frac{[CoOC(NH_2)NHC_6H_5^{3+}]}{[CoNH_2CONHC_6H_5^{3+}] + [CoNHCONHC_6H_5^{2+}]} = K'_{ND}[H^+]/(K'_a + [H^+]) \quad (3)$$

The colors and associated visible spectra of these three phenylurea complexes are characteristic of the bonding mode of the phenylurea ligand. Their ^1H NMR chemical shifts (Table I) in Me_2SO-d_6 also distinguish the complexes from each other as well as from free phenylurea. The positions of, and separations between, resonances for the cis- and trans-NH_3 protons (12 H:3 H) conform with observations on related pentaamminecobalt(III) complexes[11] and clearly identify the mode of coordination of the phenylurea molecule.

The ^1H NMR signals for bound or free phenylurea also serve as fingerprint identification (Table I). Coordination by oxygen of phenylurea to cobalt causes a downfield shift in all proton resonances relative to the free ligand. The absolute chemical shift for the Co–NH– proton (2.02 ppm) is consistent with values observed[11] for deprotonated urea-*N* complexes of pentaamminecobalt(III). The resonance for the C–NH–C proton of phenylurea and its Co(III) complexes also characterizes the environment of the phenylurea. For the protonated N-bonded phenylurea complex, generated in situ, the NH proton signals of the urea (except for that of C–NH–C) could not be unambiguously assigned.

The ^{13}C NMR data (Table I) also testify to the presence of phenylurea in the cobalt complexes and distinguish between isomers. The resonance due to the carbonyl carbon is distinctly different for free, O-bonded, and N-bonded phenylurea. Upon coordination, this resonance moves to lower field, the magnitude of the shift being greater for N-coordination of the anionic ligand (+7.4 ppm) than for O-coordination of the neutral ligand (+5.6 ppm). Further, the absolute chemical shift of the carbonyl carbon of free phenylurea is considerably further upfield than similar resonances[10,11] for other urea molecules. This observation is consistent with less s character for the carbonyl carbon of phenylurea, noting that a relationship has been found between the lengths of carbonyl bonds in X–CO–Y compounds (X, Y = C or N) and the degree of σ character of the carbon atom toward the oxygen atom.[15]

Of the other carbon atoms, the meso or bridgehead carbon atom (C_1) produces a resonance that is quite different for each complex, as expected from the magnetic influence of the cobalt and the differing degrees of electronic shielding of the phenylurea ligands. However, even the ring carbons, particularly those meta and para

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Table II. Product Distribution Data for Reactions of (Phenylurea-*N*)pentaamminecobalt(III)

products	R_f[b]	proportions, %[a] 1.0 M $HClO_4$	0.1 M CH_3CO_2H	Me_2SO/H^+
$[(NH_3)_5CoOC(NH_2)NHC_6H_5]^{3+}$	1.8	17.2 (15.1)	35.3 (15.7)	57.2 (38.6)
$[Co(NH_3)_6]^{3+}$	2.5	71.3	13.8 (9.3)	9.9 (9.3)
$[(NH_3)_5CoOS(CH_3)_2]^{3+}$	3.2			20.7 (34.4)
$[(NH_3)_5CoOH_2]^{3+}$	4.3	9.3 (11.4)	5.7 (12.7)	
$[(NH_3)_5CoNHCONHC_6H_5]^{2+}$	6.3		0 (32.8)	0 (6.3)
$[(NH_3)_5CoNCO]^{2+}$	9.0		45.2 (30.4)	12.2 (11.4)
$[(NH_3)_5CoOCONH_2]^{2+}$	10.4	2.2		

[a] Values in parentheses represent (uncorrected) product distribution. Other data are corrected to 100% reaction of the phenylurea-*N* complex, and allowance has also been made for the subsequent solvolysis of the O-bonded isomer and for the subsequent reactions of $[(NH_3)_5CoNCO]^{2+}$. [b] Relative distances traveled by ions on Dowex 50W-X2 (H^+ form) with an aqueous 0.23 M Na^+ (pH 6.88; 0.01 M $H_2PO_4^-$, 0.01 M HPO_4^{2-}, 0.2 M Cl^-) eluent.

to C_1, produce quite different ^{13}C resonances. These shifts for uncoordinated and N-bonded phenylurea are similar. The absolute shift differences for corresponding carbons (ca. 1 ppm) are also similar in magnitude to those observed for benzamide and its O- and N-bonded pentaamminecobalt(III) complexes.[16] However, upon O-coordination of phenylurea, the ^{13}C resonances for meta and para ring carbons move 3.6 and 2.3 ppm downfield, respectively, while the meso signal moves 3.3 ppm upfield. Clearly, the electronic shielding within the ligand has been considerably disturbed due to O-coordination.

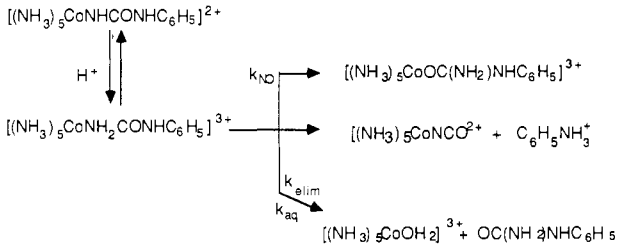
Finally, the linkage isomeric complexes are readily distinguished on the basis of their acidities and reactivities described ahead. The notable difference in the acidities of the O-bonded isomer ($pK_a > 10$) and the N-bonded isomer ($pK_a \approx 2$–3) parallels observations for similar complexes of other ureas,[10,11] carboxamides,[16] carbamates,[13,16,17] sulfinamides,[17] sulfonamides,[17] and sulfamate.[18] This property is an essential feature of the chemistry to be described.

Reactions of the N-Bonded Isomer. A solution of $[(NH_3)_5CoNHCONHC_6H_5](ClO_4)_2$ in Me_2SO-d_6 was monitored by ^1H NMR spectroscopy over a period of 1 month at 35 °C, and the complex was completely stable. However, the red solution instantly turns yellow upon acidification, and for strong aqueous acid (1.0 M $HClO_4$) it was surprising to observe that the yellow color persisted rather than being rapidly replaced by the deep pink color characteristic of the oxygen-bonded isomer, as observed for acidic solutions of other urea-*N* species, $[(NH_3)_5CoNHCOR]^{2+}$ (R = NH_2, NMe_2, NHMe).[10,11]

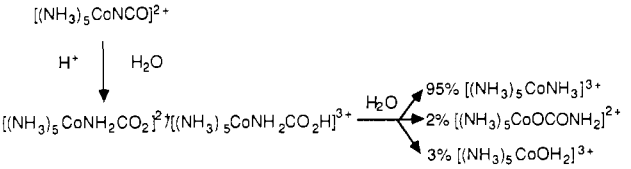
Experiments were conducted to identify and quantify the products from the reaction, and results are summarized in Table II. In 0.1–1.0 M $HClO_4$ the major products were $[Co(NH_3)_6]^{3+}$ and $[(NH_3)_5CoOC(NH_2)NHC_6H_5]^{3+}$. The latter arises from N- to O-linkage isomerization of the N-bound phenylurea ligand and is akin to those processes reported for other N-bonded ureas on Co(III).[10,11] However, formation of the more dominant product, yellow $[Co(NH_3)_6]^{3+}$, is new chemistry; this result requires, at some point, net cleavage of the CoNH–C bond.

A clue to the mechanism of the latter reaction was provided by the following experiments, noting that the reactant must first protonate before any of the subsequent processes can occur. In weakly acidic solution (0.1 M CH_3CO_2H, pH 3.7; Table II) only 14% $[Co(NH_3)_6]^{3+}$ was produced from the protonated phenylurea-*N* complex, in comparison with >70% for the strong aqueous acid media (0.1–1.0 M $HClO_4$). Moreover, a significant quantity of $[(NH_3)_5CoNCO]^{2+}$ (>40%, corrected) was observed under these low-[acid] conditions, and this ion was characterized by its rate of elution (2+ ion), electronic spectrum, and isolation in crystalline form. The isolated product had the expected elemental analysis, and the infrared and ^1H NMR spectra were identical with those for an authentic specimen.

The following scheme accommodates the results:



The detection of $[Co(NH_3)_5NCO]^{2+}$ en route to the hexaammine complex clearly establishes an elimination pathway rather than direct $CoNH_2$–C cleavage or hydrolysis of $[(NH_3)_5CoNH_2CONHC_6H_5]^{3+}$ to $[(NH_3)_5CoNH_2CO_2H]^{3+}$ (and anilinium ion), which then yields hexaammine. The pK_a of the protonated form of $[(NH_3)_5CoNHCONHC_6H_5]^{2+}$ has not been accurately determined but does not seem to be too different from that (2.9) measured[10] for $[(NH_3)_5CoNH_2CONMe_2]^{3+}$. Hence, in 0.1 M CH_3CO_2H only a small amount of $[(NH_3)_5CoNH_2CONHC_6H_5]^{3+}$ is actually formed, but more importantly the acid-catalyzed hydration of any $[(NH_3)_5CoNCO]^{2+}$, which is far more difficult to protonate,[13] is effectively halted. The isocyanate complex is known[13,19] to undergo hydration and decarboxylation in aqueous acid at a rate linear in $[H^+]$:



From the known product distribution[13] for $[(NH_3)_5CoNCO]^{2+}$ in 1.0 M $HClO_4$ and with the assumption that all of the $[Co(NH_3)_6]^{3+}$ arises via $[(NH_3)_5CoNCO]^{2+}$, it may be deduced that the observed 71.3% $[Co(NH_3)_6]^{3+}$ (Table II) implies the initial formation of 71.3 × 100/95.5 = 74.7% $[(NH_3)_5CoNCO]^{2+}$. Since the elimination path (74.7%) and N- to O-linkage isomerization (17.2%) account for only 92% of total cobalt, it is evident that there are one or more additional products. These were identified as the aqua complex, formed via a third process involving direct aquation of $[(NH_3)_5CoNH_2CONHC_6H_5]^{3+}$ to $[(NH_3)_5CoOH_2]^{3+}$ and free phenylurea, and the carbamato-*O* species.

A consideration in this evaluation is that if only 71.3% (absolutely) of the 74.7% isocyanate complex appears as $[Co(NH_3)_6]^{3+}$, the remaining 3.4% total cobalt must be from $[(NH_3)_5CoOCONH_2]^{2+}$ and $[Co(NH_3)_5OH_2]^{3+}$. Yet the reaction of $[Co(NH_3)_5NCO]^{2+}$ in acid is known to yield $[Co(NH_3)_5OH_2]^{3+}$ and $[(NH_3)_5CoOCONH_2]^{2+}$ in the ratio 3:2, whereas we observe 9.3% and 2.2%, respectively.[13] Thus, there is about 9.3 – (3/2)(2.2) = 6% $[Co(NH_3)_5OH_2]^{3+}$ unaccounted for, providing evidence for the third reaction path, direct solvolysis via Co–N cleavage. This is not too surprising since a minor Co–N cleavage pathway has been observed also for the reactions of $[(NH_3)_5CoNH_2COR]^{3+}$ (R = NH_2, NMe_2) in aqueous acid.[10,11]

Also reported in Table II is the product distribution for the reaction of $[(NH_3)_5CoNHCONHC_6H_5]^{2+}$ in acidic dimethyl sulfoxide. In this medium the initial yellow color observed disappeared with time and was replaced by a deep pink. In dry dimethyl sulfoxide the hydration of red $[(NH_3)_5CoNCO]^{2+}$ cannot occur. However N- to O-linkage isomerization and direct Co–N cleavage, leading to $[(NH_3)_5CoOSMe_2]^{3+}$, together accounted for only ca. 78% of the cobalt. The 22% balance comprised the cyanate complex and, surprisingly, some hexaammine complex; the latter arises from traces of H_2O (lattice water) in the Me_2SO. This was demonstrated in control experiments using authentic

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Table III. Specific Rates for Reactions of (Phenylurea-*N*)pentaamminecobalt(III) and Specific Rates for Solvolysis and Product Distribution Data for Reactions of (Phenylurea-*O*)pentaamminecobalt(III) at 25 °C

N-Bonded Isomer

reagent	k(obsd), s^{-1} [a]	k_{NO}, s^{-1}	k_{elim}, s^{-1}	k_{sol}, s^{-1}
1.0 M $HClO_4$ [b]	1.39×10^{-2}	2.39×10^{-3}	1.04×10^{-2}	1.11×10^{-3}
0.1 M CH_3CO_2H	4.49×10^{-4}	1.59×10^{-4}	2.65×10^{-4}	2.6×10^{-5}
Me_2SO/CF_3SO_3H	5.38×10^{-3}	3.08×10^{-3}	1.19×10^{-3}	1.11×10^{-3}

O-Bonded Isomer

reagent	% $CoNHCO\text{-}NHC_6H_5^{2+}$ [c]	% $CoOH_2^{3+}$ [c]	$10^5 k$(obsd), s^{-1} [d]
0.1 M $HClO_4$ [e]	0	100	16.1 (3.95)
0.1 M NaMES [e,f]	8.2	91.8	(4.86)
Me_2SO	0	100 [h]	48.2 (1.88)
0.1 M NaOH [e]	3.2	96.8	
0.1 M NaPhos [e,g]	8.9	91.1	

[a] Observed rates are separated into specific rates for isomerization, elimination, and solvolysis according to product distribution reported in Table II. [b] In 0.1 M $HClO_4$, k(obsd) = 9.30×10^{-3} s^{-1}; μ = 1.0 M ($NaClO_4$). [c] Data normalized to 100% reaction. [d] Means of three or more determinations at 520 nm with standard deviations ≤±3%. Numbers in parentheses are for the urea-*O* analogues under the same conditions.[11] [e] μ = 1.0 M, $NaClO_4$. [f] pH = 6.2 buffer (half-neutralized with NaOH). [g] Buffer pH = 6.88. [h] $[(NH_3)_5CoOSMe_2]^{3+}$.

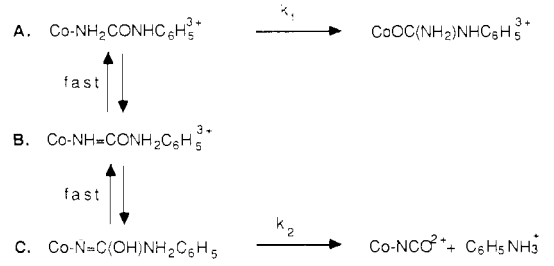
cyanate complex in acidified Me_2SO.

From the product analyses (Table II) and the observed rate constants (k(obsd)) for reactions of $[(NH_3)_5CoNHCONHC_6H_5]^{2+}$ in 1.0 M $HClO_4$, 0.1 M CH_3CO_2H, and Me_2SO/H^+ (Table III), rate constants for the individual pathways—N- to O-linkage isomerization (k_{NO}), elimination (k_{elim}), and solvolysis (k_{sol})—were determined for each medium (Table III).

The magnitude of the rate constant for N to O isomerization is similar to that for $[(NH_3)_5CoNH_2CONH_2]^{3+}$ (k_{NO} = 3.07×10^{-3} s^{-1})[11] in aqueous $HClO_4$ (μ = 1.0 M) Also, it is evident that the rate of linkage isomerization in Me_2SO is remarkably similar to that in aqueous $HClO_4$. This observation is consistent with the negligible solvent dependence of the linkage isomerization rate for $[(NH_3)_5CoNH_2CONMe_2]^{3+}$ but contrasts with the 4-fold difference in isomerization rates for $[(NH_3)_5CoNH_2CONH_2]^{3+}$ in Me_2SO and H_2O.[11] The rates of direct solvolysis of $[(NH_3)_5CoNH_2CONHC_6H_5]^{3+}$ in Me_2SO and 1.0 M $HClO_4$, while subject to substantial error due to their small contribution to the overall reaction, are also comparable.

The rates determined for 0.1 M CH_3CO_2H attract larger errors because of the extrapolation from the observed 67%–100% reaction, but it remains evident that, accompanying the elimination process, there is a greater proportion of the N- to O-linkage isomerization path compared to that for 1.0 M $HClO_4$, although not as much as witnessed for Me_2SO. In terms of reaction scheme 3, the reactive entity is $[(NH_3)_5CoNH_2CONHC_6H_5]^{3+}$, and the product distributions should be pH independent; however, the difference in ionic strengths could accommodate the differences.

The elimination reaction in 1.0 M $HClO_4$ is about 9-fold faster than that in Me_2SO/H^+. In terms of energies this is not a large difference. It could reside in the solvent dependence of the tautomer distribution for the reactive entity



or the solvent dependence of k_2/k_1; e.g., water could preferentially solvate departing $C_6H_5NH_3^+$ through H-bonding, thereby raising k_2 for H_2O vs Me_2SO. This analysis assumes that linkage isomerization and elimination arise from the specific tautomers shown. The case for A being the most abundant tautomer for the urea-*N* species in general is argued elsewhere,[10,10] and this implies $k_2 \gg k_1$, in order to accommodate the observed rates (Table III).

Reactions of the O-Bonded Isomer. The oxygen-bonded phenylurea complex $[(NH_3)_5CoOC(NH_2)NHC_6H_5]^{3+}$ aquates in 0.1 M $HClO_4$ to give exclusively $[(NH_3)_5CoOH_2]^{3+}$ and free phenylurea. The product analysis was performed by using cation-exchange chromatography and by first using an eluent (pH 6.88, 0.23 M Na^+, 0.2 M Cl^-, 0.01 M HPO_4^{2-}, 0.01 M $H_2PO_4^-$) in which other anticipated 2+ or 3+ ions could be separated. In 0.1 M NaOH (μ = 1.0 M, $NaClO_4$) some base-catalyzed O- to N-linkage isomerization competes with base-catalyzed aquation, resulting in 3% $[(NH_3)_5CoNHCONHC_6H_5]^{2+}$ and 97% $[(NH_3)_5CoOH]^{2+}$. The N-bonded isomer was shown to be absent in similar ion-exchange analyses of fresh aqueous solutions of O-bonded isomer, and thus the 3% is genuine product. In 0.1 M NaMES or NaPhos buffer (pH = 6.2 or 6.9, μ = 1.0 M ($NaClO_4$)), the O- to N-isomerization path competes much better with aquation; ca. 8.5% $[(NH_3)_5CoNHCONHC_6H_5]^{2+}$ was observed (Table III). There was no detectable (>0.5%) hydrolysis of the bound phenylurea to give the O-bonded carbamate complex in the pH range 1–14. These results directly parallel those obtained for other (urea-O)pentaamminecobalt(III) complexes.[11] Table III also presents kinetic data for the Me_2SO solvolysis of the O-bonded phenylurea complex. No O- to N-linkage isomerization was detected in Me_2SO.

The results for aqueous solution are consistent with two rate laws of the form k(obsd) = $k_s + k_{OH}[OH^-]$, one corresponding to the aquation path (k_s = 16.1×10^{-5} s^{-1}; k_{OH} not determined) and the other representing the O- to N-linkage isomerization reaction (k_s (=k_{ON}) = 1.44×10^{-5} s^{-1}; k_{OH} not determined). For comparison, some rate parameters for analogous reactions of (urea-*O*)pentaamminecobalt(III) complexes are given in Table III. The rate of aquation of the O-bonded phenylurea complex is ca. 4-fold faster than that for the corresponding O-bound urea ion, while solvolysis in Me_2SO is ca. 26-fold faster for the O-coordinated phenylurea complex. This faster aquation may result from a longer (weaker) Co–O bond for the phenylurea complex, as well as phenyl–solvent interactions that disrupt solvent–solvent structure, thereby facilitating solvent entry and ligand solvation. There may also be a contribution from steric interactions between the bulky phenyl substituent and the cis NH_3 ligands on cobalt.

The equilibrium constant for the N- and O-bonded phenylurea isomers in water (K'_{NO}, (3)) can be deduced by using the relation $K'_{NO} = k_{NO}/k_{ON}$ and the values separately determined for k_{NO} (2.39×10^{-3} s^{-1}, Table III) and k_{ON} (1.44×10^{-5} s^{-1}), as discussed elsewhere.[11] The result (K'_{NO} = 166; 25 °C, μ = 1.0 M) indicates the thermodynamic preference for the O-bound form and accommodates the inability to observe O to N rearrangement in acidic aqueous solution. For Me_2SO, a similar calculation cannot be performed, but a K'_{NO} value of at least 50 is indicated, since the protonated N-bonded isomer was observed to isomerize irreversibly. Also, as already noted, the O-bonded isomer in Me_2SO slowly yielded $[(NH_3)_5CoOSMe_2]^{3+}$ and free phenylurea, but no N-bonded isomer (<1%).

Description of the Crystal and Molecular Structure of $[(NH_3)_5CoNHCONHC_6H_5](ClO_4)\cdot H_2O$. Selected bond lengths and angles are reported in Table IV, positional parameters are given in Table V, and the molecule is represented by the ORTEP drawing in Figure 1. For the N-coordinated phenylurea ligand, the N_1–C_1 bond (1.31 Å) is considerably shorter than the N_7–C_1 bond (1.42 Å). Both the N_1–C_1 and C_1–O (1.24 Å) bond lengths are not significantly different from those of $[(NH_3)_5CoNHCOCH_3]^{2+}$ (1.34 and 1.27 Å, respectively)[20] and indicate substantial π-electron delocalization restricted to the N_1–C_1–O linkage. The N_7–C_2 bond length is identical with the N_7–C_1 distance and signifies the lack of conjugation of the phenyl group with the urea portion of the

(20) Schneider, M. L.; Ferguson, G.; Balahura, R. J. *Can. J. Chem.* **1973**, *51*, 2180.

Table IV. Selected Bond Lengths (Å) and Bond Angles (deg) for Phenylurea and $[(NH_3)_5CoY](ClO_4)_2$ (Y = $NHCONHC_6H_5$ and $NHCOCH_3$)

length	H_2NCO-NHC_6H_5[d]	Y = $NHCONHC_6H_5$[e]	Y = $NHCOCH_3$[f]
N_1–C_1	1.326 (10)	1.310 (14)	1.339 (12)
N_7–C_1	1.375 (10)	1.420 (14)	
O_1–C_1	1.245 (9)	1.240 (13)	1.267 (12)
N_7–C_2	1.419 (9)	1.420 (14)	
N_6–O_1		2.80 (1)	2.90 (1), 2.99 (1)
Co–N_1		1.907 (9)	1.910 (8)
Co–N_{trans}		2.013 (9)	1.994 (8)
Co–N_{cis}(mean)		1.982 (12)[a]	1.963 (13)
angle	H_2NCO-$NCONHC_6H_5$[d]	Y = $NHCONHC_6H_5$[e]	Y = $NHCOCH_3$[f]
$N_1C_1O_1$	122.5 (7)	124.8 (11)	122.6 (8)
$N_7C_1O_1$	122.6 (7)	119.5 (11)	119.4 (8)[b]
$N_1C_1N_7$	115.0 (7)	115.7 (10)	118.0 (9)[c]
CoN_1C_1		129.2 (8)	131.0 (7)

[a] Rms deviation from the mean. [b] Angle C_2C_1O. [c] Angle $N_1C_1C_2$. [d] Reference 15. [e] This work. [f] Reference 20.

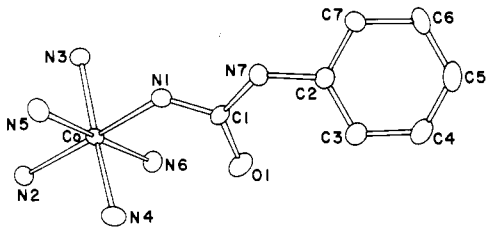


Figure 1. ORTEP diagram showing the molecular ion $[(NH_3)_5CoNHCONH(C_6H_5)]^{2+}$ and the atomic-numbering scheme.

molecule. Both the dihedral angle (37°), between the plane of the phenyl substituent and that of the urea moiety, and the N_7–C_1 bond length (1.42 Å) are somewhat greater than those of the free ligand (ca. 46°, 1.375 Å).[15a] Further, the Co–N_1 (1.91 Å) bond differs significantly from the mean Co–N_{cis} bond length (1.91 Å), a result that is interpreted as arising through bonding via π-orbitals between cobalt and the deprotonated N-bonded phenylurea ligand. Another point concerns the N_6O_1 contact, which is even shorter (2.80 Å) than that of $[(NH_3)_5CoNHCOCH_3]^{2+}$ (2.90, 2.99 Å), where hydrogen-bonding between the cis NH_3 and carbonyl oxygen has been proposed.[20]

Although we do not have solid-state structural data for the protonated phenylurea-*N* complex, it seems certain that the long C_1–N_7 bond observed for the deprotonated form is essentially preserved for the protonated form and that it is this feature which dramatically influences the chemical reactivity of $[(NH_3)_5CoNHCONHC_6H_5]^{2+}$, compared with that of $[(NH_3)_5CoNHCONH_2]^{2+}$ and $[(NH_3)_5CoNHCON(CH_3)_2]^{2+}$, in acidic media.

Discussion

In connection with the metalloenzyme urease, we have previously tried to observe activation of urea toward hydrolysis by coordination to Co(III).[10-12] However, pentaamminecobalt(III) complexes of neither N- nor O-bonded urea apparently mimicked the chemistry of urease because of preferred intramolecular (linkage isomerization) and intermolecular (aquation) ligand substitution. In contrast to the chemistry[11] of other $[(NH_3)_5CoNH_2CONRR']^{3+}$ ions, $[(NH_3)_5CoNH_2CONH$-$C_6H_5]^{3+}$ rapidly decomposes in water to CO_2, anilinium ion, and $[Co(NH_3)_6]^{3+}$. Instead of arising through CoN–C cleavage, this facile reaction proceeds via CoNC–N cleavage and thus qualifies as an elimination reaction, rather than hydrolysis, as observed for the nonenzymic decomposition of free urea in water.

The facility of this elimination path appears to be related to the ability of the pendant NRR′ of the urea in $[(NH_3)_5CoNH_2CONRR']^{3+}$ to act as a leaving group. Also, this process involves less electronic reorganization than the alternative mechanism, where nucleophilic attack of water at the carbonyl carbon requires the latter to rehybridize from sp^2 to sp^3. The anilinium ion (pK_a = 4.6) is considerably less basic that either NH_4^+ (pK_a = 9.24), $NH_3CH_3^+$ (pK_a = 10.6), or $NH_2(CH_3)_2^+$ (pK_a = 10.73), reflecting a resonance stability favoring loss of anilinium ion from the urea complex. Note however that the greater acidity of the anilinium ion is usually attributed to out-of-plane twisting rather than the inherent electron-withdrawal potential of the phenyl substituent.

Table V. Positional Parameters

atom	x/a	y/b	z/c
Co	0.0000	0.2371 (1)	0.5000
C_{11}	0.2555 (3)	0.3683 (3)	0.2820 (4)
C_{12}	0.4588 (2)	0.0988 (2)	0.4255 (4)
O_1	0.0656 (6)	−0.0140 (8)	0.4879 (12)
O_2	−0.0529 (7)	0.1214 (8)	0.1275 (10)
O_{11}	0.2524 (11)	0.2520 (9)	0.2666 (20)
O_{12}	0.3181 (8)	0.4080 (9)	0.1975 (15)
O_{13}	0.1773 (8)	0.4148 (12)	0.2517 (23)
O_{14}	0.2790 (13)	0.3933 (12)	0.4172 (15)
O_{21}	0.4618 (10)	0.0672 (12)	0.5607 (12)
O_{22}	0.5298 (7)	0.0640 (10)	0.3548 (13)
O_{23}	0.3893 (8)	0.0426 (11)	0.3633 (18)
O_{24}	0.4453 (10)	0.2109 (8)	0.4071 (13)
N_1	0.0963 (6)	0.1606 (7)	0.4353 (11)
N_2	−0.1019 (6)	0.3199 (7)	0.5635 (10)
N_3	−0.0094 (7)	0.3082 (8)	0.3199 (11)
N_4	0.0096 (7)	0.1603 (9)	0.6794 (11)
N_5	0.0774 (6)	0.3574 (8)	0.5667 (12)
N_6	−0.0754 (6)	0.1186 (7)	0.4316 (11)
N_7	0.1891 (6)	0.0234 (8)	0.3766 (12)
C_1	0.1126 (7)	0.0559 (10)	0.4384 (13)
C_2	0.2094 (7)	−0.0857 (9)	0.3417 (14)
C_3	0.1872 (7)	−0.1729 (10)	0.4226 (14)
H_3	0.1573 (7)	−0.1635 (10)	0.5050 (14)
C_4	0.2120 (9)	−0.2791 (12)	0.3745 (17)
H_4	0.1998 (9)	−0.3413 (12)	0.4284 (17)
C_5	0.2530 (10)	−0.2931 (10)	0.2524 (21)
H_5	0.2655 (10)	−0.3644 (10)	0.2209 (21)
C_6	0.2752 (9)	−0.2061 (12)	0.1784 (17)
H_6	0.3064 (9)	−0.2157 (12)	0.0974 (17)
C_7	0.2523 (8)	−0.0996 (11)	0.2207 (13)
H_7	0.2662 (8)	−0.0383 (11)	0.1664 (13)

The pK_a for the reactive $[(NH_3)_5CoNH_2CONHC_6H_5]^{3+}$ ion was not precisely determined, but it appears to be similar to those of other $[(NH_3)_5CoNH_2CONRR']^{3+}$ ions (pK_a = 2–3).[10,11] No direct ^1H NMR evidence for the site of protonation of $[(NH_3)_5CoNHCONHC_6H_5]^{2+}$ is available because the Co–NH proton appears to exchange on the NMR time scale with added H^+, even in Me_2SO-d_6 (monitored at 60 MHz). As in the case of N-bonded amides, where proton addition occurs at the carbonyl oxygen, the π-electron density seems to be restricted to the CoNC(O) atoms in $[(NH_3)_5CoNHCONHC_6H_5]^{2+}$. Indirect evidence for N- rather than O-protonation in Me_2SO-d_6 obtains from observations of the H^+/HOD resonance with time. Since this signal does not move upfield commensurate with reaction, as found for N-bound amide complexes,[16,17] O-protonation seems unlikely. No distinction as to which of the nitrogens is protonated can be made with certainty. Protonation of the outer nitrogen would favor the observed elimination reaction, but the magnitude of the pK_a and the marked change in the visible absorption spectrum on addition of H^+ are more consistent with protonation of the coordinated nitrogen, as established for two other (urea-*N*)pentaamminecobalt(III) ions.[11] (Note that the elimination process most likely does proceed via the tautomer having the proton on the exo N, but this reactive species is in much lower abundance.) Moreover, the rate of N to O isomerization for phenylurea is very similar in magnitude to those of other ureas, and this supports similar sites of protonation. Protonation at an atom more remote from the metal should decrease the rate of rearrangement due to the necessity of proton migration to the coordinated nitrogen prior to intramolecular linkage isomerization.[11]

Other workers[3] have proposed that substrates for urease might be activated toward nucleophilic attack by water through O-coordination to an active-site Ni(II) ion. The outlined mechanism

involved two nickel ions and a bridging urea ligand as an active intermediate. This proposal was based upon observations that N-coordination of carboxylic acids to Cu(II)[21a] and Co(III)[21b] does not activate amides toward alkaline hydrolysis whereas O-coordination of *N,N*-dimethylformamide to $(NH_3)_5Co^{III}$ [21c] enhances the hydrolysis of the amide by a factor of 10^4. The proposal was also based upon the structures of molecules that are substrates for urease ($RCONH_2$; R = NH_2, $NHNH_2$, NHOH, $NHCH_3$, H, CH_3) and also those that are not substrates for urease (phenyl formate, *p*-nitroformanilide, trifluoroacetamide, *p*-nitrophenyl carbamate, thiourea, and *O*-methylisouronium ion).

Concerning the former observations, while O-bonded formamides $[(NH_3)_5CoOCHNR_2]^{3+}$ certainly cleave at C–N upon alkaline hydrolysis, O-bonded ureas[10-12] and C-substituted O-bonded amides[16] do not, or at least not as readily.

The reaction of $[(NH_3)_5CoOC(NH_2)_2]^{3+}$ in water (pH 6.2) yields 24% $[(NH_3)_5CoNHCONH_2]^{2+}$ in competition with $[(NH_3)_5CoOH_2]^{3+}$, since the N-bonded isomer assumes greater thermodynamic stability under these conditions.[11] This work has shown that the phenylurea complex behaves similarly. The possibility of pH-dependent linkage isomerizations in cases of certain ambidentate ligands enables the metal ion to activate a ligand not only through initial coordination but also following rearrangement. If it is suggested that the softer Ni(II) ion has an even higher affinity for the nitrogen atom at physiological pH, the possibility that urea binds Ni(II) through nitrogen should be given credence. This possibility is strengthened by the recent X-ray structural characterization of a Ni(II) complex containing an N,O-bound hydroxamate ligand.[22] Hydroxamic acids are known inhibitors of the urease-induced hydrolysis of urea, and it is tempting to attribute this property to their ability to N-bond to Ni(II). Note than an elimination reaction of an N-bound urea has been observed on $(NH_3)_5Rh^{III}$.[23] Were a similar reaction to proceed on Ni(II) leading to an intermediate containing a bound cyanate, it is possible that its decomposition to bound ammine (for which acid-catalyzed hydration is now well-known) and CO_2 might be too fast to distinguish from a process in which carbamates were formed directly.

Regardless of the mechanism for enzymic hydrolysis of urea, this work and parallel work demonstrate that the amide substituent in $[(NH_3)_5CoNHCOR]^{2+}$ can dramatically alter the reaction course, as can the nature of the metal ion. When R = H, alkyl, or aryl, protonation gives the kinetically inert but thermodynamically unstable $[(NH_3)_5CoNH{=}C(OH)R]^{3+}$ ion, which leads very slowly to $[(NH_3)_5CoOC(NH_2)R]^{3+}$ along with, and ultimately all to, $[(NH_3)_5CoOH_2]^{3+}$.[17] For R = NH_2, NHMe, or NMe_2, protonation yields the kinetically labile ion $[(NH_3)_5CoNH_2COR]^{3+}$, which isomerizes rapidly and intramolecularly to $[(NH_3)_5CoOC(NH_2)R]^{3+}$,[10,11] whereas when R = NHC_6H_5, elimination from $[(NH_3)_5CoNH_2COR]^{3+}$ produces RH_2^+ and $[(NH_3)_5CoNCO]^{2+}$ (this work). If R = O, decarboxylation of $[(NH_3)_5CoNH_2COR]^{3+}$ results in $[Co(NH_3)_6]^{3+}$ and CO_2, except in very strong acid (R = OH) where there is substantial isomerization, producing $[(NH_3)_5CoOC(NH_2)R]^{3+}$.[13] When R = OEt, $[(NH_3)_5CoNH_2COR]^{3+}$ reacts without elimination to $[(NH_3)_5CoNCO]^{2+}$ to give approximately equal proportions of $[Co(NH_3)_6]^{3+}$, $[(NH_3)_5CoOC(NH_2)R]^{3+}$, and $[(NH_3)_5CoOH_2]^{3+}$.[16,17]

Clearly, these systems provide a variety of avenues for reaction of the coordinated ligand, and they complement our knowledge of intramolecular rearrangements as well. The effects of varying the metal ion and its oxidation state on the reaction rates and course for these and related ambidentate ligands are being actively pursued.

Experimental Section

Visible spectra were recorded on Cary 118C and 210 spectrophotometers, generally at 25 °C. ^1H NMR spectra were measured for samples in anhydrous Me_2SO-d_6, containing $SiMe_4$ as internal reference, on a Varian T60 spectrometer at 35 °C. ^{13}C NMR spectra were recorded for the same solutions on a JEOL 90FXQ spectrometer (probe temperature 30 °C) with 1,4-dioxane as internal reference. Infrared spectra were obtained for samples as Nujol mulls between KBr plates on a Jasco IRA-2 instrument. SP-Sephadex C-25 cation-exchange resin (Pharmacia) was used as supplied. Phenylurea (Aldrich) and 2,2,6,6-tetramethylpiperidine (Fluka) were obtained commercially and also synthesized,[24] purified, and characterized by established procedures. Solvents were of analytical reagent grade.

Syntheses. $[Co(NH_3)_5O_3SCF_3)](ClO_4)_2$,[25] $[Co(NH_3)_5OH_2](ClO_4)_3$, $[Co(NH_3)_6]^{3+}$, $[Co(NH_3)_5OS(CH_3)_2](ClO_4)_3{\cdot}H_2O$,[26] $[Co(NH_3)_5NC-O](ClO_4)_2$,[13] and $[Co(NH_3)_5O_2CNH_2](ClO_4)_2$[27] were prepared as reported. The documented spectroscopic parameters were closely reproduced in this work.

$[(NH_3)_5CoNHCONHC_6H_5](ClO_4){\cdot}H_2O$. $[(NH_3)_5CoOS(CH_3)_2](ClO_4)_3$ (8 g, 1.5 mmol) was dissolved in dimethyl sulfoxide (40 mL), and the solution was reacted with phenylurea (10 g, 73 mmol) and 2,2,6,6-tetramethylpiperidine (4.5 g, 32 mmol) at 80 °C for 1 h. Addition of an equal volume of 2-butanol or 2-propanol and excess diethyl ether yielded quantitatively a crimson precipitate. The total crude product was dissolved in water, sorbed onto a column of Sephadex cation-exchange resin, and eluted with 0.3 M $NaClO_4$ (pH 8, Tris buffer). Six bands were detected and successively eluted: a trace of a lilac 1+ ion (presumed to be $[(NH_3)_4Co(NHCONHC_6H_5)_2]^+$),[18] crimson red $[(NH_3)_5CoNHCONHC_6H_5]^{2+}$, a crimson brown 3+ ion, and yellow $[Co(NH_3)_6]^{3+}$ and traces of two pink, higher charged cations. The $[(NH_3)_5CoNHCONHC_6H_5](ClO_4)_2{\cdot}H_2O$ complex was isolated by rotary evaporation of solvent to a small volume and cooling (yield ca. 71%). It was recrystallized twice from warm water (pH 9, Tris) as deep crimson needles suitable for X-ray structure analysis (yield 3.95 g, 52%). Electronic spectrum: ϵ_{max} 121.0 (0.1 M Tris). Anal. Calcd for $CoC_7N_7H_{24}Cl_2O_{10}$: C, 17.39; H, 4.97; N, 20.29; Cl, 14.70. Found: C, 17.28; H, 5.03; N, 20.01; Cl, 14.68.

$[(NH_3)_5CoOC(NH_2)NHC_6H_5]_2(S_2O_6)_3{\cdot}3H_2O$. $[Co(NH_3)_5O_3SCF_3](CF_3SO_3)_2$ (6 g, 10 mmol) and phenylurea (5 g, 37 mmol) were dissolved in acetone (30 mL), and the mixture was briefly warmed (60 °C, 5 min). Anhydrous diethyl ether was then added until a pink precipitate formed in quantitative yield. This product was collected and air-dried before rapid dissolution in ice-cold water (1:1) and filtration through a finely sintered glass funnel. Addition by filtration of a one-fifth volume of a saturated aqueous solution of $Na_2S_2O_6$ or $Li_2S_2O_6$ produced pink, sparingly soluble needles of the title product from an orange filtrate, which contained the more water-soluble $[Co(NH_3)_5OH_2]_2(S_2O_6)_3$. The precipitate was collected and washed with ice-cold water (3 × 30 mL), absolute ethanol, and diethyl ether. Recrystallization was carried out by rapid dissolution of the needles in ice-cold water (21 mL), filtration through a finely sintered glass funnel, and addition of acetone (41 mL). Yield: 62%. Electronic spectrum: ϵ_{max} 86.4 (0.1 M $HClO_4$). Anal. Calcd for $CoN_7C_7H_{26}S_3O_{11.5}$: C, 15.36; H, 4.75; N, 17.92. Found: C, 15.0; H, 4.7; N, 17.6.

Product Analyses. All product analysis experiments comprised separation of reaction products on jacketed columns of SP-Sephadex C-25 cation-exchange resin, maintained at 2 °C by water circulating from a Haake thermostat bath, using a phosphate-buffered eluent to be subsequently described. Under these conditions all products elute separately. In some cases, following separation, products were removed from the column with 0.5 M $NaClO_4$ to enable isolation as solid perchlorate salts. All products were quantified by measuring absorbances and solution sample volumes and by using ϵ values reported. Typical experiments are described below.

$[(NH_3)_5CoNHCONHC_6H_5](ClO_4)_2{\cdot}H_2O$ (0.1–10 mmol) was stirred in aqueous $HClO_4$ (0.1, 1.0 M; μ = 1.0 M ($NaClO_4$)) at known temperatures for 10 half-lives (ca. 13 min; 25 °C). Reactions were quenched with ice, and products were sorbed onto 2 °C columns of cation-exchange resin and eluted with 0.23 M Na^+ (0.01 M $H_2PO_4^-$, 0.01 M HPO_4^{2-}, 0.2 M Cl^-; pH 6.88) eluent.

$[(NH_3)_5CoNHCONHC_6H_5](ClO_4)_2{\cdot}H_2O$ (0.1–10 mmol) was stirred in aqueous 0.1 M CH_3CO_2H for 2 h (18 °C). Reactions were quenched

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with ice and NaH_2PO_4 (1 g), and the products were chromatographed as above.

Solutions of $[(NH_3)_5CoNHCONHC_6H_5](ClO_4)_2 \cdot H_2O$ (0.1–10 mmol) in dimethyl sulfoxide containing CF_3SO_3H (10 mmol) were reacted for 30–40 min (16 °C). The reactions were then quenched with ice (in latter experiments the acid was first neutralized), and the products were chromatographed.

$[(NH_3)_5CoOC(NH_2)NHC_6H_5]_2(S_2O_6)_3 \cdot 3H_2O$ (10 mmol) was stirred in 0.1 M $HClO_4$, 0.1 M NaMES, or 0.1 M NaPhos (μ = 1.0 M ($NaClO_4$)) for 10 half-lives (25 °C) or in 0.1 M NaOH (μ = 1.0 M ($NaClO_4$)) for 30 s (25 °C). Product mixtures were chromatographed, eluted, and quantitated as described above. Some (incomplete) reactions were performed at lower temperatures, and product analyses are corrected to 100% reaction by using the figure determined for recovered reactant.

Kinetic studies utilized routine methods described elsewhere.[11] Rate constants for the parallel first-order reactions of the O- and N-bonded isomers were determined by the usual nonlinear least-squres analysis using absorbance–time traces (at 520 nm) recorded on a Cary 210 spectrophotometer fitted with a thermostated (25.0 ± 0.1 °C) cell block.

Crystallography. The data crystal was defined by four pairs of faces (110), (110), (100), and (111) with distances between them of 0.08, 0.073, 0.072, and 0.175 mm, respectively. Data were collected on a Philips PW1100/20 four-circle diffractometer using graphite-monochromated Cu Kα radiation. Unit cell dimensions and their estimated standard deviations were determined from the setting angles of 25 carefully centered reflections. Data within the range $3 < 2\theta(\text{Cu K}\alpha) < 100°$ spanning one unique quadrant of reciprocal space were collected, corrected for absorption effects, and reduced in the usual way.

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Registry No. $[(NH_3)_5CoNH_2CONHC_6H_5]^{3+}$, 119946-90-6; $[(NH_3)_5CoOC(NH_2)NHC_6H_5]^{3+}$, 107440-52-8; $[(NH_3)_5CoNHCONHC_6H_5](ClO_4)_2 \cdot H_2O$, 119946-93-9.

Supplementary Material Available: Table VI, giving thermal parameters (1 page). Ordering information is given on any current masthead page.

Contribution from the Department of Chemistry, University of Queensland, Brisbane, Australia 4067

NMR Study of Acid–Base Equilibria and Other Reactions of Ammineplatinum Complexes with Aqua and Hydroxo Ligands[1]

Trevor G. Appleton, John R. Hall,* Stephen F. Ralph, and Craig S. M. Thompson

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^{15}N and ^{195}Pt NMR spectra have shown that $[Pt(^{15}NH_3)_3]_2(\mu\text{-}OH)^{3+}$ slowly forms when a solution containing $Pt(^{15}NH_3)_3(H_2O)^{2+}$ and $Pt(^{15}NH_3)_3(OH)^+$ is allowed to stand. By measurement of the change in δ_N or J(Pt–N) as the pH of a solution of $Pt(^{15}NH_3)_3(H_2O)^{2+}$ was changed, the pK_a for this complex was determined (6.37 ± 0.10). Reaction of a solution of *cis*-$Pt(^{15}NH_3)_2(H_2O)_2^{2+}$ with chloride gave a solution containing *cis*-$Pt(^{15}NH_3)_2Cl(H_2O)^+$ and *cis*-$Pt(^{15}NH_3)_2Cl_2$. When the pH was increased to approximately 7, a new species, assigned as $[Pt(^{15}NH_3)_2]_2(\mu\text{-}Cl)(\mu\text{-}OH)^{2+}$, was formed. The variation of δ_N trans to water/hydroxide with pH for *cis*-$Pt(^{15}NH_3)_2Cl(H_2O)^+$ allowed the pK_a for this species to be determined (6.85 ± 0.10). Bromide behaved in an analogous way, but *cis*-$Pt(NH_3)(H_2O)_2^{2+}$ reacted with 1 mol of iodide to give $[\{Pt(NH_3)_2(\mu\text{-}I)\}_2]^{2+}$. The NMR peaks from this complex were previously wrongly assigned to *cis*-$Pt(NH_3)_2I_2$. Changes in δ_N of *cis*-$Pt(^{15}NH_3)_2(H_2O)_2^{2+}$ with pH allowed the values of pK_{a1} and pK_{a2} to be determined, at 5 °C, to reduce the rate of formation of hydroxo-bridged species (5.93 ± 0.10 and 7.87 ± 0.10, respectively).

Introduction

Despite the interest in the chemistry of the antitumor compound *cis*-$Pt(NH_3)_2Cl_2$ and its derivatives in recent years, many aspects of the solution chemistry of these complexes remain relatively unexplored. For example, there are, to our knowledge, no values in the literature from reliable experimental determinations for the acid dissociation constants of the simple species *cis*-$Pt(NH_3)_2(H_2O)_2^{2+}$ (**1**) and *cis*-$Pt(NH_3)_2Cl(H_2O)^+$ (**2**). This is despite the frequent mention of such hydrolysis products in discussions of the biochemistry of *cis*-$Pt(NH_3)_2Cl_2$.[2] Grinberg and Ryabchikov[3] reported that although *trans*-$Pt(NH_3)_2(H_2O)_2^{2+}$ with NaOH gave a simple titration curve with two distinct "breaks" corresponding to the two deprotonation steps, the cis isomer, **1**, gave a much more complex titration curve, from which they claimed that they could obtain only an average of the two acid dissociation constants. If the data given by Jensen[4] are plotted, it is clear that he, too, obtained a complex titration curve from the titration of **1** with NaOH. He nevertheless analyzed these data to give values (at 20 °C) of pK_{a1} 5.56 and pK_{a2} 7.32. Perumareddi and Adamson[5] reported values of 5.63 and 9.25, respectively, but gave no details of their procedure. We now know[6-10] that, for solutions containing moderate concentrations of *cis*-$Pt(NH_3)_2(OH)(H_2O)^+$, there is rapid formation of hydroxo-bridged oligomers, $[Pt(NH_3)_2(\mu\text{-}OH)]_n^{n+}$ (n = 2, 3). Attempts to determine the acid dissociation constants of **1** that do not take this oligomerization into account cannot be expected to produce reliable results, especially for pK_{a2} (if the constants are determined, as is usually the case, by titration of **1** with NaOH). Potentiometric determinations have been carried out on analogous complexes with other amines (e.g., *trans*-1,2-diaminocyclohexane,[11] 1,2-diaminoethane (pK_{a1} 5.8, pK_{a2} 7.6)[12]) that may be more valid because of different rates of oligomerization.

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