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# Oxidation of Catechin and Rutin by Pentaammineruthenium(III) Complexes

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The reaction of catechin and rutin with $Ru(NH_3)_5L^{3+}$ (L = *N*-methylpyrazinium ($pzCH_3^+$), pyrazine (pz), and isonicotinamide (isn)) complexes underwent a two-electron oxidation on the catechol ring (B ring) with the formation of quinone products. The kinetics of the oxidation, carried out at $[H^+] = 0.01-1.0$ M and pH = 4.0−7.6, suggested that the reaction process involves the rate determining one-electron oxidation of the flavonoids in the form of $H_2X$ ($k_0$), $HX^-$ ($k_1$), and $X^{2-}$ ($k_2$) by $Ru(NH_3)_5L^{3+}$ complexes to form the corresponding semiquinone radicals, followed by the rapid scavenge of the radicals by the Ru(III) complexes. The specific rate constants ($k_0$, $k_1$, and $k_2$) were measured and the results together with the application of the Marcus theory were used to estimate the self-exchange parameters for the one-electron couples of the flavonoids, $H_2X/H_2X^{+\bullet}$, $HX^-/HX^\bullet$, and $X^{2-}/X^{-\bullet}$.

## Introduction

Flavonoids are a group of naturally occurring polyphenolic compounds widely distributed in plants.[1] During the past decade, flavonoids have received growing interest since many studies have demonstrated that they possess properties which have beneficial effects on human health.[2−5] These highly potent biological activities are thought to result from their antioxidation activity, particularly their ability to scavenge the free radical.[6]

In order to understand the antioxidative activity of flavonoids, it would be helpful to investigate the oxidation of this class of compounds. In the present work, we carried out the kinetic study of the oxidation of catechin and rutin (Scheme 1) by $Ru(NH_3)_5L^{3+}$ (L = $pzCH_3^+$, pz, isn) complexes over a pH range 0−7.6. Catechin belongs to the flavanol subclass of flavonoids and is primarily found in green and black teas and in red wine.[7] It is assumed to be responsible for the protective effect of tea against the development of certain cancers, coronary heart disease, and stroke.[8] Rutin (quercetin O-rutinose) is one of the most bioactive flavonoids, also known as vitamin P, and is thought to be an activating factor for vitamin C.[9] Rutin has displayed a broad range of physiological and pharmacological activities[10−13] and is found in many typical nutrimental plants, particularly in buckwheat, apple, and black tea.[14]

Since it has been proposed that the presence of the catechol moiety in the B ring of the flavonoids is the main factor controlling the antioxidative activity of flavonoids,[1,15,16] the kinetics of the oxidation of catechol also was studied under the same pH range for comparison. We will focus our interest on the investigation of intrinsic reactivities of flavonoids and catechol in different forms by the analysis of kinetic results

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(1) Harborne, J. B.; Williams, C. A. *Phytochemistry* **2000**, *55*, 481.
(2) Erlund, I. *Nutr. Res. (N.Y.)* **2004**, *24*, 851.
(3) Cabrera, C.; Artacho, R.; Gimenez, R. *J. Am. Coll. Nutr.* **2006**, *25*, 79.
(4) Sowers, M. R.; Crawford, S.; McConnell, D. S.; Randolph, J. F.; Gold, E. B.; Wilkin, M. K.; Lasley, B. *J. Nutr.* **2006**, *136*, 1588.
(5) Soleas, G. J.; Grass, L.; Josephy, P. D.; Goldberg, D. M.; Diamandis, E. P. *Clin. Biochem.* **2006**, *39*, 492.
(6) Heim, K. E.; Tagliaferro, A. R.; Bobilya, D. J. *J. Nutr. Biochem.* **2002**, *13*, 572.
(7) Manach, C.; Scalert, A.; Morand, C.; Remesy, C.; Jimenez, L. *Am. J. Clin. Nutr.* **2004**, *79*, 727.
(8) Arls, I. C. W.; van de Putle, B.; Hollman, P. C. H. *J. Agric. Food Chem.* **2000**, *48*, 1752.
(9) Zoulis, N. E.; Efstathiou, C. E. *Anal. Chim. Acta* **1996**, *320*, 255.
(10) Peters, U.; Poole, C.; Arab, L. *Am. J. Epidemiol.* **2001**, *154*, 495.
(11) Higdon, J. V.; Frei, B. *Crit. Rev. Food Sci. Nutr.* **2003**, *43*, 89.
(12) Cook, N. C.; Samman, S. *J. Nutr. Biochem.* **1996**, *7*, 66.
(13) Robak, J.; Gryglewski, R. *Biochem. Pharmacol.* **1998**, *37*, 837.
(14) Hetrog, M. L. G.; Hollman, P. C. H.; Katan, M. B. *J. Agric. Food Chem.* **1992**, *40*, 2379.
(15) Pietta, P. G. *J. Nat. Prod.* **2000**, *63*, 1035.
(16) Silva, M. M.; Santo, M. R.; Caroco, G.; Rocha, R.; Justino, G.; Mira, L. *Free Radical Res.* **2002**, *36*, 1019.

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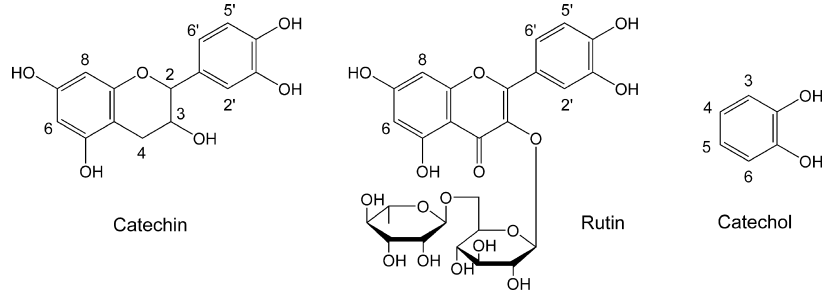
**Scheme 1.** Structures of Catechin, Rutin and Catechol




according to the Marcus theory. The information of the self-exchange rate constants of catechol compounds is quite lacking in the literature.

## Experimental Section

**Materials.** (+)-Catechin (Sigma), rutin (Beijing Company of Chemical Agents), and catechol (Fluka) were purchased and used as received. $[Ru(NH_3)_5(pzCH_3)](ClO_4)_4$[17] and $[Ru(NH_3)_5L](ClO_4)_3$ (L = pz,[17] isn[18]) complexes were prepared according to the cited literature methods. The doubly distilled water was obtained by passing house-line distilled water through a Barnstead NANO water purification system.

**Instrumentation.** UV−vis spectra were measured on a Hewlett-Packard HP 8453 diode-array spectrophotometer. An Orion 420 pH meter with a standard 91-51 line electrode was used for pH measurements. $^1$H NMR spectra were obtained in $DCl/D_2O$ solution on a Varian Inova 600 spectrometer at National Chung Hsing University. Electrochemistry were performed on a PAR model 273A potentiostat/galvanostat system as described before.[19] The kinetic studies for the oxidation of flavonoids at various pH were carried out on the Hi-Tech CH-61 stopped-flow spectrophotometer. Because of the low solubility, the dissolution of high concentrations of catechin and rutin was assisted by the addition of a small amount of methanol. For the studies at pH ≥ 4, the pH and the ionic strength were controlled in the flavonoid solutions, and the Ru(III) complexes were prepared in a slightly acidic medium ($\sim 1 \times 10^{-3}$ M) in order to avoid the disproportionation. The measurements were performed at an ionic strength of 1.0 under pseudo-first-order conditions with flavonoids in excess. The reactions were monitored by following the formation of $Ru(NH_3)_5L^{2+}$ complexes at their band maxima. The pseudo-first-order rate constants were obtained by the slopes of the linear least-squares fits of $\ln(A_\infty - A_t)$ vs time plots.

## Results

**Characterization of the Reactions.** The stoichiometry of the reactions between flavonoids and $Ru(NH_3)_5L^{3+}$ complexes under study were determined by the spectrophotometric titrations of flavonoids with Ru(III) complexes at all pH conditions. The titrations were monitored at the MLCT band maxima of the $Ru(NH_3)_5L^{2+}$ complexes. A 2:1 (Ru(III)/flavonoids) ratio was found in the titration, indicating an overall tw- electron stoichiometric oxidation of the reactions.

**Table 1.** $^1$H-NMR Chemical Shifts of Catechin, Rutin and Catechol[a]

| | catechin | | rutin | | | catechol | |
|---|---|---|---|---|---|---|---|
| proton | $H_2X$ | X | $H_2X$ | X | proton | $H_2X$ | X |
| H-2′ | 6.89 | 6.26 | 7.53 | 7.11 (5.48[b]) | H-3, 6 | 6.77 | 6.40 (6.43[c]) |
| H-5′ | 6.81 | 6.42 | 6.88 | 6.49 (6.48[b]) | H-4, 5 | 6.86 | 7.15 (7.06[c]) |
| H-6′ | 6.86 | 7.19 | 7.44 | 7.71 (7.81[b]) | | | |
| H-2 | 4.71 | 4.71 | | | | | |
| H-3 | 4.16 | 4.27 | | | | | |
| H-4 | 2.50 | 2.52 | | | | | |
| | 2.80 | 2.87 | | | | | |
| H-6 | 6.04 | 6.08 | 6.20 | 6.29 (6.24[b]) | | | |
| H-8 | 5.96 | 6.00 | 6.37 | 6.47 (6.40[b]) | | | |

[a] In $D_2O$, $\delta$ in ppm. [b] In $CD_3OD$ solvent, ref 20. [c] In $CDCl_3$ solvent, ref 21.

The $^1$H NMR spectra further suggested that the oxidation went to the catechol (B) ring of the flavonoids with the formation of quinone products. The chemical shifts of $^1$H NMR spectra of catechin, rutin, catechol and their corresponding oxidized products are listed in Table 1. As shown in the Table, there are significant upfield shifts (>0.39 ppm) in $\delta$ values at 2′, 5′ protons and downfield shifts (>0.27 ppm) at 6′ protons for both catechin and rutin, similar to that observed for the catechol. On the other hand, only a little change occurred in chemical shifts for protons on the A and the C rings. Figure 1 shows the $^1$H NMR spectra of rutin and its oxidized product. The results of stoichiometry and NMR spectra of the products suggest that the reaction follows eq 1

$$2Ru(NH_3)_5L^{3+} + H_2X \rightarrow 2Ru(NH_3)_5L^{2+} + X + 2H^+ \quad (1)$$

where $H_2X$ and X are catechin, rutin, catechol and the corresponding quinone products, respectively.

**Kinetics of Oxidation.** A nice linear relationship was found for plots of $\ln(A_\infty - A_t)$ vs time with either flavonoid or Ru(III) complex as the limiting reagent, suggesting that the reaction is first order in both reactants. From the reaction stoichiometry, the rate law therefore can be expressed as

$$-\frac{d[Ru(NH_3)_5L^{3+}]}{dt} = 2k[Ru(NH_3)_5L^{3+}][H_2X] \quad (2)$$

The second order rate constants, $k$, were obtained from the slopes of $k_{obs}$ vs $[H_2X]$ plots, and the results are listed in Table S1−S2, Supporting Information. The values of $k$ decrease with increasing acidity, but not linearly. Figure 2 shows typical plots of this kind at $[H^+] = 0.01-1.0$ M. The kinetic behaviors of catechin and rutin are similar to that of the catechol. Since previous studies have found that the oxidation of the catechols are formally analogous to the

(17) Creutz, C.; Taube, H. *J. Am. Chem. Soc.* **1973**, *95*, 1086.
(18) Gaunder, R. G.; Taube, H. *Inorg. Chem.* **1970**, *9*, 2627.
(19) Chen, M. H.; Lee, S.; Liu, S.; Yeh, A. *Inorg. Chem.* **1996**, *35*, 2627.
(20) Dangles, O.; Fargeix, G.; Dufour, C. *J. Chem. Soc. Perkin Trans. 2* **1999**, 1387.
(21) Fattahi, A.; Kass, S. R.; Liebman, J. F.; Matos, M. A. R.; Miranda, M. S.; Morais, V. M. F. *J. Am. Chem. Soc.* **2005**, *127*, 6116.

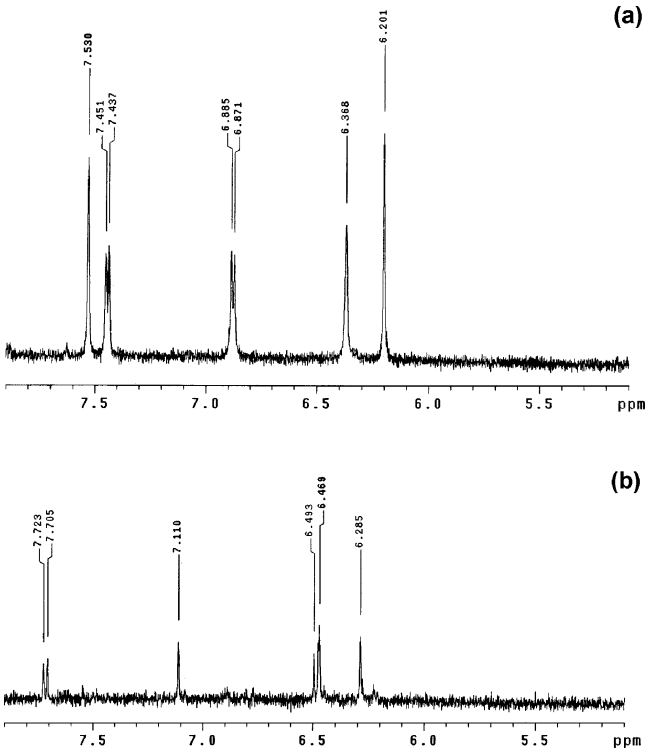



**Figure 1.** $^1$H NMR spectrum of rutin (a) and the corresponding quinone (b) in 0.1 M DCl/$D_2O$ solution.

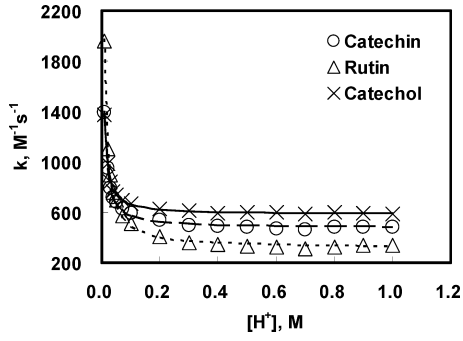



**Figure 2.** $k$ vs [$H^+$] plot for the oxidation of flavonoids by $Ru(NH_3)_5(pzCH_3)^{4+}$ complex at [$H^+$] = 0.01−1.0 M. $\mu$ = 1.0 $HClO_4$/$LiClO_4$. (○) Catechin, (Δ) rutin, (×) catechol.

ascorbic acid,[22,23] the mechanism of the reaction therefore can be expressed in eqs 3−10.[24]

$$H_2X \overset{Ka_1}{\rightleftharpoons} H^+ + HX^- \quad (3)$$

$$HX^- \overset{Ka_2}{\rightleftharpoons} H^+ + X^{2-} \quad (4)$$

$$Ru(NH_3)_5L^{3+} + H_2X \xrightarrow{k_0} Ru(NH_3)_5L^{2+} + H_2X^{\bullet+} \quad (5)$$

$$Ru(NH_3)_5L^{3+} + HX^- \xrightarrow{k_1} Ru(NH_3)_5L^{2+} + HX^{\bullet} \quad (6)$$

$$Ru(NH_3)_5L^{3+} + X^{2-} \xrightarrow{k_2} Ru(NH_3)_5L^{2+} + X^{\bullet-} \quad (7)$$

$$Ru(NH_3)_5L^{3+} + H_2X^{\bullet+} \xrightarrow{\text{fast}} Ru(NH_3)_5L^{2+} + 2H^+ + X \quad (8)$$

$$Ru(NH_3)_5L^{3+} + HX^{\bullet} \xrightarrow{\text{fast}} Ru(NH_3)_5L^{2+} + H^+ + X \quad (9)$$

$$Ru(NH_3)_5L^{3+} + X^{\bullet-} \xrightarrow{\text{fast}} Ru(NH_3)_5L^{2+} + X \quad (10)$$

According to this mechanism, $k$ can be expressed as

$$k = \frac{k_0[H^+]^2 + k_1K_{a_1}[H^+] + k_2K_{a_1}K_{a_2}}{[H^+]^2 + K_{a_1}[H^+] + K_{a_1}K_{a_2}} \quad (11)$$

The values of p$K_{a1}$ and p$K_{a2}$ are 8.79, 13.25 (catechin[25]), 8.8, 11.04 (rutin[26]), 9.23 and 13.05 (catechol[27]), respectively.

At [$H^+$] = 0.01−1.0 M, [$H^+$] ≫ $K_{a1}$, $K_{a2}$, and $k_0$[$H^+$]$^2$ + $k_1K_{a1}$[$H^+$] ≫ $k_2K_{a1}K_{a2}$, eq 11 can be reduced to

$$k = \frac{k_0[H^+] + k_1K_{a_1}}{[H^+]} \quad (12)$$

With the $Ru(NH_3)_5(pzCH_3)^{4+}$ complex as the oxidant, the only Ru(III) complex strong enough to oxidize flavonoids, a nice linear relationship of $k$ vs 1/[$H^+$] plots was obtained in the oxidation of flavonoids at [$H^+$] = 0.01−0.3 M, as shown in Figure 3. The values of $k_0$ and $k_1$, as obtained from the nonlinear least-squares fits of $k$ vs [$H^+$] according to eq 12, are listed in Table 2. At [$H^+$] = 0.4−1.0 M, $k$ was insensitive to the change in acid concentrations, suggesting that in this region $k_0$[$H^+$] ≫ $k_1K_{a1}$, and $k \approx k_0$. Taking the average over this range, we found that $k_0$ = (4.8 ± 0.2) × $10^2$, (3.3 ± 0.2) × $10^2$, and (5.9 ± 0.1) × $10^2$ $M^{-1}$ $s^{-1}$ for catechin, rutin, and catechol, respectively, agree well with those obtained from eq 12.

At pH ≥ 4.0, the $Ru(NH_3)_5(pzCH_3)^{4+}$ complex introduced a serious disproportionation, and only the oxidations by $Ru(NH_3)_5(pz)^{3+}$ and $Ru(NH_3)_5(isn)^{3+}$ complexes were investigated. At pH = 4.0−5.6, [$H^+$] ≫ $K_{a1}$, $K_{a2}$, and eq 11 reduces to

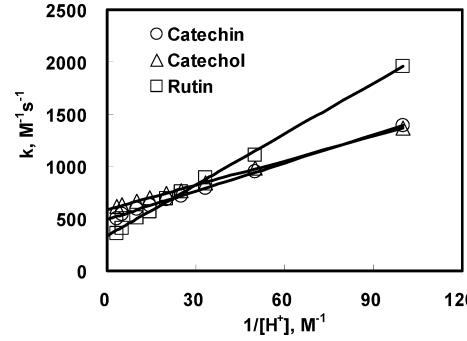



**Figure 3.** $k$ vs 1/[$H^+$] plot for the oxidation of flavonoids by $Ru(NH_3)_5(pzCH_3)^{4+}$ complex at [$H^+$] = 0.01−0.3 M. $\mu$ = 1.0 $HClO_4$/$LiClO_4$. (○) Catechin, (□) rutin, (Δ) catechol.

(22) Xu, J.; Jordan, R. B. *Inorg. Chem.* **1990**, *29*, 4180.
(23) Hoddenbagh, J. M. A.; Macartney, D. H. *J. Chem. Soc., Dalton Trans.* **1990**, 615.
(24) Lin, L. M.; Lien, M. H.; Yeh, A. *Int. J. Chem. Kin.* **2005**, *37*, 126.

$$k = \frac{k_0[H^+]^2 + k_1K_{a_1}[H^+] + k_2K_{a_1}K_{a_2}}{[H^+]^2} \quad (13)$$

However, nice linear plots of $k$ vs $1/[H^+]$ passing through the origin were observed, as shown in Figure 4, which further indicated that $k_1K_{a1}[H^+] \gg k_0[H^+]^2 + k_2K_{a1}K_{a2}$, and $k$ followed eq 14.

$$k = \frac{k_1K_{a_1}}{[H^+]} \quad (14)$$

Values of $k_1$, obtained from the slopes of the one-parameter linear least-squares fits of the plots, are listed in Table 2.

At pH $\geq$ 6.0, since the contribution of $k_0[H^+]^2$ is negligible and $[H^+]^2 \gg K_{a1}[H^+] + K_{a1}K_{a2}$, eq 11 becomes

$$k = \frac{k_1K_{a_1}[H^+] + k_2K_{a_1}K_{a_2}}{[H^+]^2} \quad (15)$$

At this pH, the kinetic measurement were interfered by the disproportionation of $Ru(NH_3)_5(pz)^{3+}$ complex, and only $Ru(NH_3)_5(isn)^{3+}$ complex was used for oxidation. For the oxidation of rutin, at pH = 6.0−6.8, linear relationships were observed for $k[H^+]$ vs $1/[H^+]$ plots, as Figure 5a showed. Because of the higher $pK_{a2}$, similar kinetic behaviors were observed in the oxidation of catechin and catechol only at pH $\geq$ 6.4. Figure 5b shows the plots of $k[H^+]$ vs $1/[H^+]$ plots for the oxidations of catechin and catechol. Nonlinear least-squares fits of $k$ vs $[H^+]$ according to eq 15 with given $k_1$, $K_{a1}$, $K_{a2}$ values yielded values of $k_2$, as shown in Table 2. We were unable to measure the rate of the reduction at pH $\geq$ 8.0 due to the interference of the disproportionation of the Ru(III) complexes. Moreover, the rate of the reaction was beyond the limit of the instrument.

## Discussion

The substitution inertia of $Ru(NH_3)_5L^{3+}$ complexes suggests that the reactions can be viewed as outer-sphere electron transfer reactions that follow the Marcus theory[28,29] as expressed in eqs 16−20.

$$k_{12} = \sqrt{k_{11}k_{22}K_{12}f_{12}}W_{12} \quad (16)$$

$$\ln f_{12} = \frac{[\ln K_{12} + (w_{12} - w_{21})/RT]^2}{4[\ln(k_{11}k_{22}/10^{22}) + (w_{11} + w_{22})/RT]} \quad (17)$$

$$W_{12} = \exp[-(w_{12} + w_{21} - w_{11} - w_{22})/2RT] \quad (18)$$

$$w_{ij} = \frac{z_iz_je^2}{D_sa_{ij}(1 + \beta a_{ij}\sqrt{\mu})} \quad (19)$$

$$\beta = \left(\frac{8N\pi e^2}{1000D_sk_BT}\right)^{1/2} \quad (20)$$

where $k_{11}$ and $k_{22}$ are self-exchange rate constants for Ru(III) complexes and flavonoids, respectively; $k_{12}$ and $K_{12}$ are rate

**Table 2.** Rate Constants for the Reduction of $Ru(NH_3)_5L^{3+}$ Complexes[a]

| | | $Ru(NH_3)_5L^{3+}$ | | |
|---|---|---|---|---|
| $H_2X$ | $k_n$ | L = $pzCH_3^+$ | L = pz | L = isn |
| catechin | $k_0$ | (4.92 ± 0.05) × $10^2$ | | |
| | $k_{22}$ | 2.8 × $10^7$ | | |
| | $k_1$ | (5.56 ± 0.08) × $10^9$ | (1.62 ± 0.03) × $10^7$ | (2.26 ± 0.02) × $10^6$ |
| | $k_{22}$ | 2.7 × $10^{11}$ | 2.2 × $10^{10}$ | 1.6 × $10^{10}$ |
| | $k_2$ | | | (1.5 ± 0.2) × $10^{11}$ |
| | $k_{22}$ | | | 2.8 × $10^{11}$ |
| rutin | $k_0$ | (3.37 ± 0.12) × $10^2$ | | |
| | $k_{22}$ | 4.1 × $10^6$ | | |
| | $k_1$ | (1.02 ± 0.02) × $10^{10}$ | (7.32 ± 0.05) × $10^6$ | (1.26 ± 0.01) × $10^6$ |
| | $k_{22}$ | 8.5 × $10^{11}$ | 2.2 × $10^9$ | 1.8 × $10^9$ |
| | $k_2$ | | | (4.7 ± 0.1) × $10^{10}$ |
| | $k_{22}$ | | | 3.7 × $10^{11}$ |
| catechol | $k_0$ | (5.86 ± 0.04) × $10^2$ | | |
| | $k_{22}$ | 4.6 × $10^6$ | | |
| | $k_1$ | (1.33 ± 0.02) × $10^{10}$ | (1.82 ± 0.02) × $10^7$ | (3.62 ± 0.06) × $10^6$ |
| | $k_{22}$ | 2.0 × $10^{11}$ | 1.3 × $10^9$ | 1.2 × $10^9$ |
| | $k_2$ | | | (1.33 ± 0.14) × $10^{11}$ |
| | $k_{22}$ | | | 3.4 × $10^{10}$ |

[a] $\mu$ = 1.0 M $HClO_4/LiClO_4$, $T$ = 25 °C, all in $M^{-1}$ $s^{-1}$.

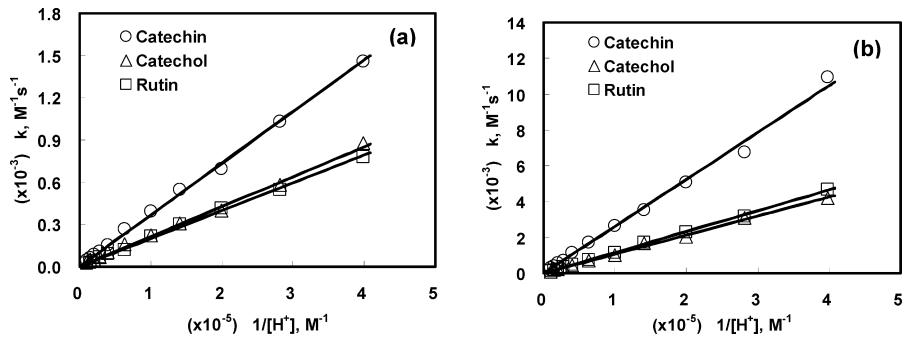



**Figure 4.** $k$ vs $1/[H^+]$ plots for the oxidation of flavonoids by $Ru(NH_3)_5L^{3+}$ at pH = 4.0−5.6. $\mu$ = 1.0 $LiClO_4$. (a) $L$ = isn (b) $L$ = pz. (○) Catechin, (□) rutin, (Δ) catechol.

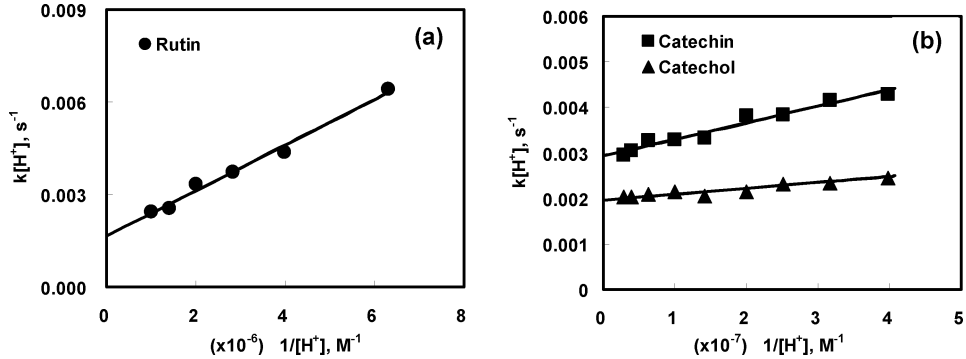



**Figure 5.** $k[H^+]$ vs $1/[H^+]$ plots for the oxidation of flavonoids by $Ru(NH_3)_5(isn)^{3+}$ complex at pH = 6.0−7.6. $\mu$ = 1.0 $LiClO_4$. (a) Rutin (b) catechin and catechol. (•) rutin, (■) catechin, (▲) catechol.

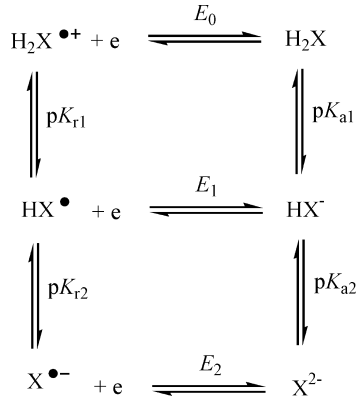
**Table 3.** Potentials and Self-Exchange Rate Constants

| reactants | | $r$ (Å) | $E$ (V) | $k_{ex}$ |
|---|---|---|---|---|
| $Ru(NH_3)_5(pzCH_3)^{4+/3+}$ | | 3.9[a] | 0.92(0.92[b]) | 39[a] |
| $Ru(NH_3)_5(pz)^{3+/2+}$ | | 3.8[a] | 0.53(0.53[b]) | $1.4 \times 10^4$[a] |
| $Ru(NH_3)_5(isn)^{3+/2+}$ | | 3.9[a] | 0.41(0.38[b]) | $1.1 \times 10^5$[a] |
| catechin | $H_2Q/H_2Q^{+\bullet}$ | 4.2[c] | 1.17 | $2.8 \times 10^7$ |
| | $HQ^-/HQ^\bullet$ | | 0.59 | $1.9 \times 10^{10}$ |
| | $Q^{2-}/Q^{-\bullet}$ | | 0.079 | $2.8 \times 10^{11}$ |
| rutin | $H_2Q/H_2Q^{+\bullet}$ | 5.5[c] | 1.15 | $4.1 \times 10^6$ |
| | $HQ^-/HQ^\bullet$ | | 0.57 | $2.0 \times 10^9$ |
| | $Q^{2-}/Q^{-\bullet}$ | | 0.17 | $3.6 \times 10^{11}$ |
| catechol | $H_2Q/H_2Q^{+\bullet}$ | 3.4[c] | 1.12 | $4.6 \times 10^6$ |
| | $HQ^-/HQ^\bullet$ | | 0.52 | $1.2 \times 10^9$ |
| | $Q^{2-}/Q^{-\bullet}$ | | 0.043 | $3.4 \times 10^{10}$ |

[a] Ref 29. [b] Measured at $\mu$ = 0.1 M, ref 29. [c] Calculated from equation $4\pi r^3/3 = M/(\rho N)$ using measured density ($\rho$), ref 35.

constant and equilibrium constant of the cross reaction; $z_i$ and $z_j$ are the charges of the reacting species; $a_{ij}$ is the internuclear distance and is taken to be equal to the sum of radius of the reductants; and $D_s$ is the static dielectric constant of water.

The reduction potentials of $Ru(NH_3)_5L^{3+/2+}$ couples, measured at 1.0 M ionic strength (Table 3) are in good agreement with values measured at $\mu$ = 0.10 M.[29] The reduction potentials of flavonoids for $H_2X^{+\bullet}/H_2X$ ($E_0$), $HX^\bullet/HX^-$ ($E_1$), and $X^{-\bullet}/X^{2-}$ ($E_2$) couples are related to each other according to the thermocycle[28]




$$E_0 = E_2 + 0.059(pK_{a1} + pK_{a2} - pK_{r1} - pK_{r2}) \quad (21)$$

$$E_1 = E_2 + 0.059(pK_{a2} - pK_{r2}) \quad (22)$$

Taking $pK_{r2}$ = 4.6,[30] 4.3,[30] and 5.0[31] for catechin, rutin and catechol, respectively, and assuming $pK_{r1} = -1$ (taken to be equal to that of catechol[32]), $E_0$ and $E_1$ can be calculated according to eqs 21 and 22 with reported values of $E_2$,[31,33,34] and the results are shown in Table 3. With the reduction potentials and the self-exchange rate constants of Ru(III) complexes, the self-exchange rate constants of the flavonoids can be calculated from eqs 16−20, and the results are shown in Table 2.

As shown in the table, $k_{22}$ value of $H_2X/H_2X^{+\bullet}$ couple for catechol ($4.6 \times 10^6$ $M^{-1}$ $s^{-1}$) agrees with the literature[31] reported value of $2 \times 10^6$ $M^{-1}$ $s^{-1}$. However, there is a big difference in the $k_{22}$ values for $HX^-/HX^\bullet$ couple obtained from the oxidation by $Ru(NH_3)_5(pzCH_3)^{4+}$ complex as compared to those obtained from the $Ru(NH_3)_5(pz)^{3+}$ and $Ru(NH_3)_5(isn)^{3+}$ complexes where they agree fairly well with each other. In order to account for this discrepancy, we have carried out the oxidation of the ascorbic acid ($H_2A$) at $\mu$ = 1.0 M in acidic medium by $Ru(NH_3)_5(pzCH_3)^{4+}$ ($[H^+]$ = 0.01−1.0 M) and $Ru(NH_3)_5(isn)^{3+}$ ($[H^+]$ = 0.01−0.1 M) complexes. The values of $k$ are listed in Table S3, Supporting Information. For L = $pzCH_3^+$, the measured $k_0$ ($(5.4 \pm 0.4) \times 10^2$ $M^{-1}$ $s^{-1}$) agreed with the Marcus predicted value of $3.8 \times 10^2$ $M^{-1}$ $s^{-1}$, but the $k_1$ value ($(2.64 \pm 0.05) \times 10^7$ $M^{-1}$ $s^{-1}$) was greater than the calculated value of $1.0 \times 10^6$ $M^{-1}$ $s^{-1}$ by an order of magnitude. However, the $k_1$ value ($(1.06 \pm 0.02) \times 10^3$ $M^{-1}$ $s^{-1}$) for L = isn agreed reasonably well with Marcus predicted value of $5.8 \times 10^2$ $M^{-1}$ $s^{-1}$. Moreover, Haim et. al,[29] in their study of the oxidation of ascorbic acid by a series of $Ru(NH_3)_5L^{3+}$ complexes at pH = 1−3 also found that the measured $k_1$ for L = $pzCH_3^+$ was ∼10-fold greater than the calculated value. However, the measured $k_1$ values for L = pz and isn are comparable with the theoretical values. On the basis of the kinetic results of the oxidation of the ascorbic acid, we therefore tend to believe that the $k_{22}$ for $HX^-/HX^\bullet$ couple obtained from the oxidation of pz and isn complexes is more reliable. Taking average values obtained from these two complexes, the self-exchange rate constants of $HX^-/HX^\bullet$ couples are listed in Table 3. The similarity of self-exchange rate constants of catechin and rutin with that of catechol in all three forms provides further evidence that the oxidation of the flavonoids goes to the B-ring.

Although the oxidation of catechol compounds by transition metal complexes has been extensively studied,[23,31,36−40] most of the works are interested in the investigation of the

(25) Slabbert, N. P. *Tetrahedron* **1977**, *33*, 821.

reactivities of the metal complexes, and little effort was devoted to that of the catechols. So far only the self-exchange rate constant for the $H_2X/H_2X^{+\bullet}$ couple has been reported;[31] no information is available for either the mononegative ($HX^-$) or dinegative ($X^{2-}$) form. We were able to obtain the self-exchange rate constants of all three forms from the measured specific rate constants over a wide pH range. The results may provide important information for the redox reactions involving this class of compounds, especially when the reaction is carried out at high pH where the contributions of $HX^-$ ($k_1$) and $X^{2-}$ ($k_2$) are significant.

It has been reported that flavonoids possess more effective antioxidation activities than vitamins C and E.[41] Our results further support this argument, at least in respect to the intrinsic reactivities. The self-exchange rate constants of the ascorbic acid are $2 \times 10^3$ ($H_2A/H_2A^{+\bullet}$),[28] $1.6 \times 10^5$ ($HA^-/HA^{\bullet}$),[42] and $2 \times 10^5$ ($A^{2-}/A^{-\bullet}$)[28] $M^{-1}$ $s^{-1}$, respectively. Compared to the flavonoids we found that $k_{ex(fla)}/k_{ex(asc)}$ are $10^3$, $10^4$, $10^5$ for $H_2X/H_2X^{+\bullet}$, $HX^-/HX^{\bullet}$, and $X^{2-}/X^{-\bullet}$ couples, respectively. The greater $k_{22}$ for the flavonoids may arise from the ability of the delocalization of the semiquinone radical on the catechol ring which will stabilize the intermediate and lower the activation energy.

Since there are other hydroxyl groups in catechin and rutin, they may undergo further oxidation after the catechol ring is oxidized. However, we found that the formation of Ru(II) complexes after the correction of possible disproportionation is less than 5% upon the addition of Ru(III) complexes to the solutions in all pH ranges in 3 h. The oxidation of the hydroxyl groups in A and C rings, if any, is therefore rather slow as compared to the oxidation of the catechol ring, at least under our experimental conditions.

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**Supporting Information Available:** Tables S1 and S2 listing specific rate constants of the oxidation of catechin, rutin and catechol at $[H^+] = 0.01-1.0$ M and pH = 4.0−7.6. Table S3 listing the specific rate constants of the oxidation of ascorbic acid in $[H^+] = 0.01-1.0$ M. This material is available free of charge via the Internet at http://pubs.acs.org.

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(26) Mielczarek, C. *Eur. J. Pharm. Sci.* **2005**, *25*, 273.
(27) Tyson, C. A.; Martell, A. E. *J. Am. Chem. Soc.* **1968**, *90*, 3379.
(28) Macartney, D. H.; Sutin, N. *Inorg. Chim. Acta* **1983**, *74*, 221.
(29) Akhtar, M. J.; Haim, A. *Inorg. Chem.* **1988**, *27*, 1608.
(30) Jovanovic, S. V.; Steenken, S.; Tosic, M.; Marjanovic, B.; Simic, M. G. *J. Am. Chem. Soc.* **1994**, *116*, 4846.
(31) Steenken, S.; Neta, P. *J. Phys. Chem.* **1979**, *83*, 1134.
(32) Pellzzetti, E.; Mentasti, E.; Balocchi, C. *J. Phys. Chem.* **1976**, *80*, 2979.
(33) Steenken, S.; Neta, P. *J. Phys. Chem.* **1982**, *86*, 3661.
(34) Jovanovic, S. V.; Steenken, S.; Hara, Y.; Simic, M. G. *J. Chem. Soc. Perkin Trans. 2* **1996**, 2497.
(35) Kimura, M.; Yamabe, S.; Minato, T. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1699.
(36) Brodovitch, J. C.; McAuley, A.; Oswald, T. *Inorg. Chem.* **1982**, *21*, 3442.
(37) Macartney, D. H.; McAuley, A. *J. Chem. Soc., Dalton Trans.* **1984**, 103.
(38) Herbert, J. W.; Macartney, D. H. *J. Chem. Soc., Dalton Trans.* **1986**, 1931.
(39) Kamau, P.; Jordan, R. B. *Inorg. Chem.* **2002**, *41*, 3076.
(40) Lam, W. W. Y.; Lee, M. F. W.; Lau, T. C. *Inorg. Chem.* **2006**, *45*, 315.
(41) Rice-Evans, C. A.; Miller, N. J.; Paganga, G. *Trends Plant Sci.* **1997**, *2*, 152.
(42) Wanat, A.; van Eldik, R.; Stochel, G. *J. Chem. Soc., Dalton Trans.* **1998**, 2497.