On the Ligand-to-Metal Charge-Transfer Photochemistry of the Copper(II) Complexes of Quercetin and Rutin

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In contrast to the UV-photoinduced ligand photoionization of the flavonoid complexes of Fe^{III}, redox reactions initiated in ligand-to-metal charge-transfer excited states were observed on irradiation of the quercetin (**1**) and rutin (**2**) complexes of Cu^{II}. Solutions of complexes with stoichiometries [Cu^{II}L$_2$] (L = quercetin, rutin) and [Cu$^{II}_2$L$_n$] ($n = 1$, L = quercetin; $n = 3$, L = rutin) were flash-irradiated at 351 nm. Transient spectra observed in these experiments showed the formation of radical ligands corresponding to the one-electron oxidation of L and the reduction of Cu^{II} to Cu^I. The radical ligands remained coordinated to the Cu^I centers, and the substitution reactions replacing them by solvent occurred with lifetimes $\tau < 350$ ns. These are lifetimes shorter than the known lifetimes ($\tau > 1$ ms) of the quercetin and rutin radical's decay.

Introduction. – Flavonoids, *e.g.*, quercetin (= 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4*H*-1-benzopyran-4-one; **1**) and rutin (= 3-{[6-*O*-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy}-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4*H*-1-benzopyran-4-one; **2**), constitute a large and important class of naturally occurring 4*H*-1-benzopyran-4-one derivatives with a broad spectrum of biological activities. Among the reported biofunctions are the antioxidant [1–4], anticarcinogenic [5][6], antiviral [7], and anti-allergic [8] activities. Some of the flavonoids' antioxidant activity has been related to the chelation of metal ions [9][10]. In this role, they trap the metal ions, in particular iron and copper ions, that catalyze the decomposition of lipid hydroperoxides
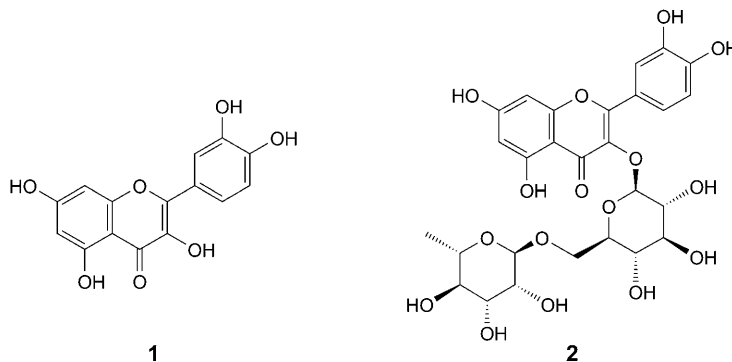
forming in this process the deleterious OH$^\cdot$ radical [11–13]. Some of the aforementioned activities have also been found in transition-metal complexes of the flavonoids [14], and these complexes are sometimes more effective than the uncomplexed flavonoids [15][16]. Redox properties of some flavonoids and flavonoid complexes have been investigated by electrochemical [17–19], pulse radiolysis [20–22], and photochemical [22][23] methods. For example, interesting aspects of the photochemistry of flavonoid- and related phenolatoiron(III) complexes have been communicated early in the literature [22][23]. Irradiation of the tris(phenolato)iron(III) complexes at 274 or 254 nm produces short-lived excited states, *i.e.*, lifetime < 1 ps, which are scavenged by a halocarbon solvent but form no products in polar solvents such as MeCN [23]. In contrast to the 274 or 254 nm photolysis, the photoionization process is induced when the [Fe^{III}(phenolato)] complexes are irradiated at 193 nm. It has also been reported that the photoionization process occurs when Fe^{III} complexes of gallocatechins are irradiated at 248 nm [22]. These are striking experimental observations since the reduction of Fe^{III} to Fe^{II} and the oxidation of the phenolato ligands is the expected reaction initiated in the ligand-to-Fe^{III} charge-transfer excited states of the Fe^{III} complexes. Questions arise, therefore, about the presence of low-energy photoreactive excited states other than the ligand-to-metal charge-transfer (LMCT) excited states where these photoreactions are initiated. The complexes of Cu^{II} with quercetin and rutin (*Fig. 1*) whose structural characteristics are known [20][21][23][24] were used in this work. Their photoinduced redox reactions were investigated *via* 351 nm flash photolysis to test the general validity of the photoprocesses observed with similar Fe^{III} complexes.

Results. – The 351 nm flash irradiations of the Cu^{II} complexes of quercetin and rutin were carried out in deaerated solutions buffered at pH 10. Concentrations of L = quercetin or rutin and Cu^{II} ion of a 10^{-4} M order of magnitude led to the formation of either [Cu^{II}L$_2$] or [Cu$^{II}_2$L$_n$] ($n = 1$, L = quercetin; $n = 3$, L = rutin) according to [20][21][23][24]. Transient spectra in *Figs. 2* and *3* were recorded with a minimum delay of 10 ns and a maximum delay of 800 ns from the 351 nm laser irradiation. Changes in the photogenerated spectra were observed within this period. Spectra recorded with a delay equal or shorter than 50 ns after the flash irradiation of the [Cu^{II}L$_2$] (*Fig. 2*) have a resemblance with the corresponding spectrum of the quer(OH)$_4$O$^\cdot$ and rut(OH)$_3$O$^\cdot$ radicals[1]) [25–28]. However, the absorbance in the 600–650 nm region is larger, relative to the absorbance at ≤ 475 nm, than in the spectra of the radicals produced by the oxidation of quercetin and rutin. This discrepancy with the spectra of the radicals is attributed to the formation of complexes containing the quer(OH)$_4$O$^\cdot$ and rut(OH)$_3$O$^\cdot$ as radical ligands (*Eqn. 1*).

$$[\text{Cu}^{II}\text{L}_2] \xrightarrow{h\nu,\phi} [\text{Cu}^I\text{L}\,(\text{L}^{\cdot+})] \qquad\qquad (1)$$

Also the flash-generated spectra recorded with solutions of the [Cu$^{II}_2$L$_n$] species in *Fig. 3* could be related to the formation of species containing the quer(OH)$_4$O$^\cdot$ and rut(OH)$_3$O$^\cdot$ radical ligands (*Eqn. 2*).

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[1])   The notation used for the radicals follows those used in [28].

a)

b)

c)
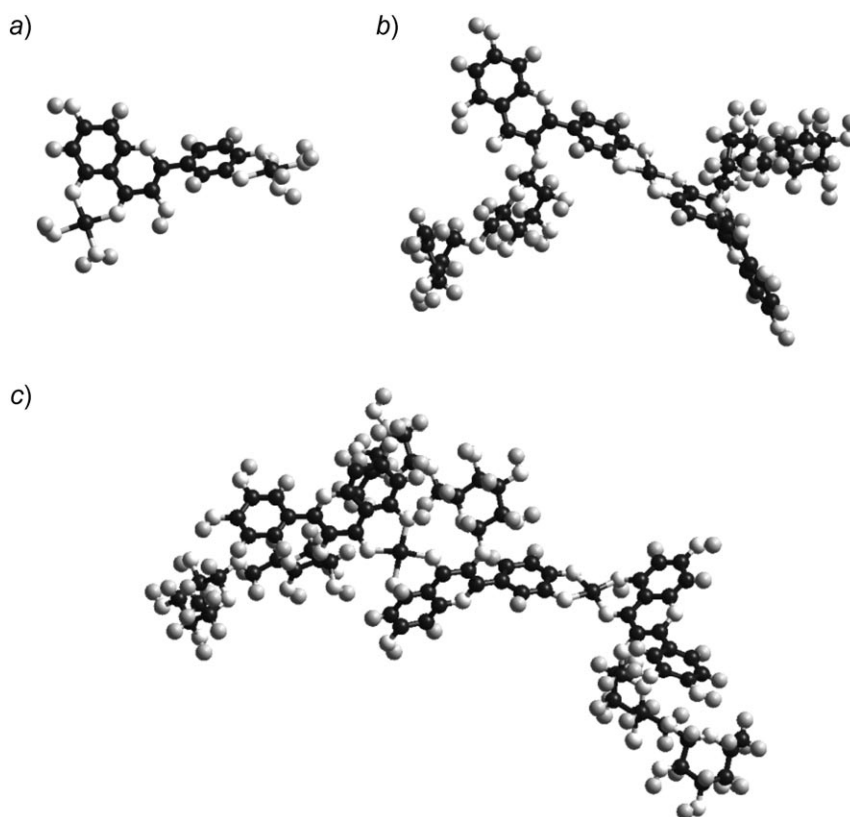
Fig. 1. *Model structures for* a) *the [Cu₂L]* (L = quercetin), b) *the [CuL₂]* (L = rutin), *and* c) *the [Cu₂L₃]* (L = rutin) *complexes.* The models are based on the published structural features of each species [20][21][23][24] and optimized with the HiperChem program.

$$[Cu^{II}_2L_n] \xrightarrow{h\nu,\phi} [Cu^{II}L_{n-1}Cu^I(L^{\cdot+})] \tag{2}$$
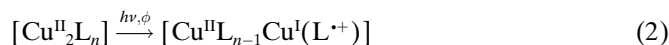
The bleach of the solutions of the $[Cu^{II}L_2]$ or $[Cu^{II}_2L_n]$ complexes at $\lambda < 450$ nm (quercetin complexes) and $\lambda < 400$ nm (rutin complexes) is consistent with the photoreduction of Cu^{II} to Cu^I. This spectroscopic assignment was confirmed when 10^{-4} M $[Cu^{II}L_2]$ or $[Cu^{II}_2 L_n]$ was reduced by the solvated electron in pulse-radiolysis experiments. Reduction of the Cu^{II} center in the complexes by e^-_{aq} bleached the solutions of the complexes at the same wavelengths as those observed in *Figs. 2* and *3*. Typical results of the pulse-radiolysis experiments are shown in *Fig. 4*. In agreement with the known properties of the radicals, the $quer(OH)_4O^\cdot$ and $rut(OH)_3O^\cdot$ radicals generated in our pulse-radiolysis experiments decayed on a time scale $t \gg 1$ ms [25][26].

The spectra in *Figs. 2* and *3* underwent transformations in the 10 ns to 1 µs time domain. The transformations of the photogenerated spectra in *Fig. 2* revealed the spectra of the $quer(OH)_4O^\cdot$ and $rut(OH)_3O^\cdot$ radicals at the end of the processes. To
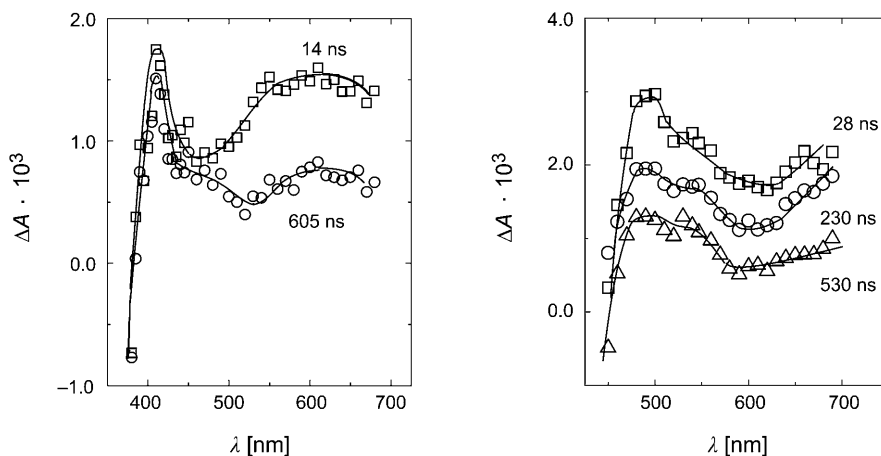
Fig. 2. *Transient spectra recorded when deareated solutions of the [CuL₂] complexes were irradiated at 351 nm.* The delays from the laser flash are indicated in the figure. Spectra in the left-hand figure were recorded with a pH 10 solution containing $1.0 \cdot 10^{-4}$ M Cu^{2+} and $2.0 \cdot 10^{-4}$ M quercetin. The spectra in the right-hand figure were recorded with a pH 10 solution containing $1.0 \cdot 10^{-4}$ M Cu^{2+} and $2.0 \cdot 10^{-4}$ M rutin.
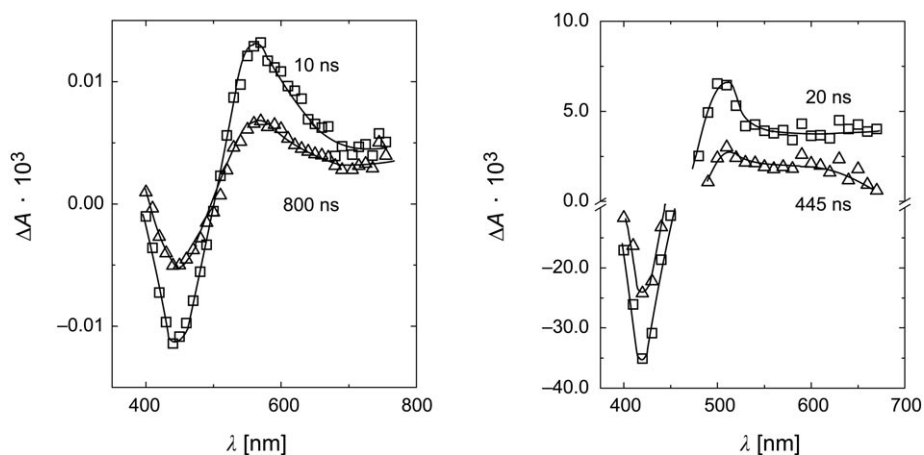

Fig. 3. *Transient spectra recorded when deareated solutions of the [Cu₂Lₙ] complexes were irradiated at 351 nm.* The delays from the laser flash are indicated in the figure. Spectra in the left-hand figure were recorded with a pH 10 solution containing $2.0 \cdot 10^{-4}$ M Cu^{2+} and $1.0 \cdot 10^{-4}$ M quercetin. The spectra in the right-hand figure were recorded with a pH 10 solution containing $2.0 \cdot 10^{-4}$ M Cu^{2+} and $1.0 \cdot 10^{-4}$ M rutin.

investigate the kinetics of the processes occurring in the 10 ns to 1 µs time domain, oscillographic traces were recorded at various wavelengths where the change of the absorbance is sufficiently large. The traces were fitted to exponentials with the rate constants, k_{ob}, listed in the *Table*. It must be emphasized that the lifetimes, $\tau = 1/k_{ob}$, of the photogenerated $[Cu^{I}L(L^{\bullet +})]$ and $[Cu^{II}(L)_{n-1}Cu^{I}(L^{\bullet +})]$ complexes were considerably shorter than those for the decay of the radicals measured in our experiments and
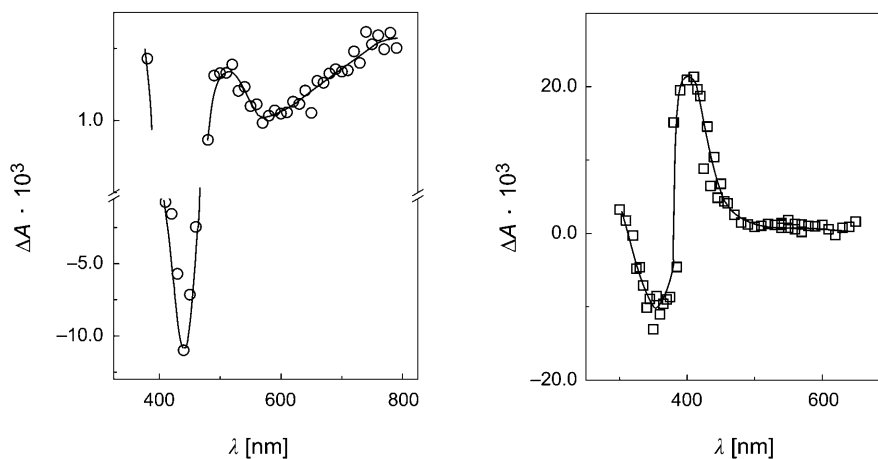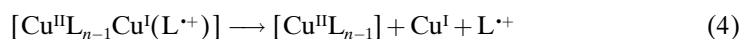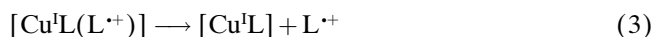
Fig. 4. *Comparison of the spectra obtained after the solvated-electron reduction of [Cu(rutin)₂]* (left) *and rutin* (right) *in a N₂ saturated solution containing 0.1M MeOH as a scavenger of OH· and H· radicals*

those published in [25] [26]. Therefore, neither the spectroscopic transformations in the 30 ns to 1 µs time domain nor the lifetime of these processes can be explained in terms of the decay of the $quer(OH)_4O·$ and $rut(OH)_3O·$ radicals *via* association or disproportionation.

Table. *Rate Constants for the Detachment of the L·⁺ Radicals in* Eqns. 3 *and* 4

	k_{ob}[a]) [s^{-1}]	
	L = rutin (n = 3)	L = quercetin (n = 1)
[CuL₂]	$3.7 \cdot 10^6$	$1.8 \cdot 10^7$
[Cu₂L$_n$]	$3.1 \cdot 10^6$	$4.0 \cdot 10^6$

[a]) Errors $\leq 15\%$.

$$[Cu^I L(L·^+)] \longrightarrow [Cu^I L] + L·^+ \tag{3}$$

$$[Cu^{II}L_{n-1}Cu^I(L·^+)] \longrightarrow [Cu^{II}L_{n-1}] + Cu^I + L·^+ \tag{4}$$

Discussion. – The 351 nm photochemistry of the quercetin and rutin complexes of Cu^{II}, namely of the $[Cu^{II}L_2]$ and $[Cu^{II}_2L_n]$ complexes, contrasts markedly with the photochemistry of the corresponding complexes of Fe^{III}. The Cu^{II} complexes undergo a photoinduced reduction of one copper ion and the simultaneous oxidation of L (*Eqns. 1* and *2*). This is the type of photoprocess expected when L-to-Cu^{II} charge-transfer excited states are the reactive excited states. Moreover, the complexation of rutin and quercetin by Cu^{II} ions induce pronounced changes in the UV spectrum of the ligands. New absorption bands and shoulders with extinction coefficients in the order of 10^3 M^{-1} cm^{-1} appear in the wavelength region 400 – 550 nm. These new absorption bands can be

assigned to phenolato-to-Cu^{II} charge-transfer transitions by comparison to the position of similar optical transitions in the spectrum of [Fe^{III}(catecholato)] complexes [29]. To a large extent, absorption bands positioned at wavelengths shorter than 400 nm must be associated with intraligand (IL) electronic transitions. In the case of the Cu^{II} complexes, the IL excited states populated when the complexes are irradiated at 351 nm must be converted with a finite yield to the reactive LMCT excited states. On the other hand, it is possible that the photoreactive excited state(s) of the [Fe^{III}(phenolato)] complexes are the IL excited state or that the LMCT excited state(s) have acquired a large character of IL excited state.

It has been proposed that the products of the LMCT excited states are Cu^{I} complexes with coordinated $L^{\bullet +} = quer(OH)_4O^{\bullet}$ and $rut(OH)_3O^{\bullet}$ radical ligands (*Eqns. 1* and *2*). The lifetime of these [Cu^{I}(radical ligand)] species is not surprising since these radicals are still monodentate ligands. Examples of transient long-lived complexes with a radical ligand have been provided by the photoredox dissociation of [Co^{III}(carbonate)] complexes [30]. In this regard, the spectroscopic transformations in *Figs. 2* and *3* can be explained in terms of the substitution of the radical ligand by solvent (see above, *Eqns. 3* and *4*).

Inspection of the rate constants in the *Table* reveals that those of the species [$Cu^{II}L_2$] and [$Cu^{II}_2L_3$] when L = rutin have very close values. It is suggestive of the $rut(OH)_3O^{\bullet}$-ligand detachment from positions in the Cu^{I} coordination sphere of these species offering similar structural characteristics. It is also possible to see in the *Table* a significant difference between the rate constants of the [$Cu^{II}L_2$] complexes with L = quercetin and rutin. These difference can be attributed to the absence of the pendent disaccharide moiety in the quercetin ligand. If this is the case, the smaller value of the rate constant of the rutin complex suggests a stabilizing effect from the disaccharide moiety. Finally, the $L^{\bullet +}$ radicals produced in *Eqns. 3* and *4* probably have the same fate as the $L^{\bullet +}$ radicals generated by other chemical methods [25][26]. It is not possible, however, to rule out reactions of these radicals with the [$Cu^{II}L_2$] and [$Cu^{II}_2L_n$] complexes. If these reactions occur under our experimental conditions, they must be as slow as the decay of the radicals in the absence of the complexes.

Experimental Part

General. Quercetin and rutin were purchased from *Fluka* and used as received. Other chemicals were reagent grade and used without further purification.

Photochemical Procedures. Absorbance changes, ΔA, occurring on a time scale longer than 15 ns were investigated at r.t. with a flash-photolysis apparatus described elsewhere [31]. In these experiments, 15 ns flashes of 351 nm light were generated with a *Lambda-Physik-SLL-200* excimer laser. The intensity of the laser flash was attenuated to values equal to or less than 35 mJ by absorbing some of the laser light in a filter soln. of $Ni(ClO_4)_2$ having the desired optical transmittance, $T = I_t/I_0$ where I_0 and I_t are the intensities of the light arriving to and transmitted from the filter soln., resp. The transmittance, $T = 10^{-A}$, was routinely calculated by using the spectrophotometrically measured absorbance, A, of the filter soln. A right-angle configuration was used for the pump and the probe beams.

Solution Preparation. In flash-photolysis experiments, concentrations of the chromophores in the soln. were adjusted to provide homogeneous concentrations of photogenerated intermediates over the optical path ($l = 1$ cm) of the probe beam. To satisfy this optical condition, solns. were made with an absorbance equal to or less than 0.1 over the 0.2 cm optical path of the pump. Solns. containing appropriate amounts of a given ligand and a Cu^{II} salt were prepared at least 2 h before the pulse-radiolysis or flash-photolysis experiments. The perchlorate and sulfate salts of Cu^{II} were indistinctively used for the preparation of the solns. which were buffered at pH 10 with the potassium tetraborate buffer. Streams of O_2-free N_2 were passed through the solns. before and during the experiments to deaerate and to keep them free of O_2.

Pulse-Radiolysis Procedures. The instrument for the pulse-radiolysis experiments and the computerized data collection for time-resolved UV/VIS spectroscopy and reaction kinetics have been described elsewhere [32]. Reductions of the complexes by e^-_{aq} were effected in solns. containing *ca.* 10^{-4} M complex and 0.01M MeOH and deaerated with streams of N_2.

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