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Kinetics of the Oxidation of Quercetin by 2,2-Diphenyl-1-picrylhydrazyl (dpph$^\bullet$)

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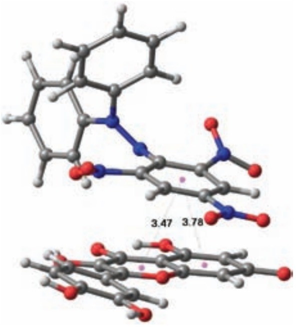
ABSTRACT



In methanol/water, dpph$^\bullet$ bleaching (519 nm) by quercetin, QH_2, exhibits biphasic kinetics. The dpph$^\bullet$ reacts completely with the quercetin anion within 100 ms. Subsequent slower bleaching involves solvent and QH_2 addition to quinoid products. The fast reaction is first-order in dpph$^\bullet$ but only ca. 0.38 order in [QH_2]. This extraordinary nonintegral order is attributed to reversible formation of π-stacked $\{QH^-/dpph^\bullet\}$ complexes in which electron transfer to products, $\{QH^\bullet/dpph^-\}$, is slow ($k_{ET} \approx 10^5$ s^{-1}).

Flavonoids are ubiquitous secondary plant metabolites.[1] A normal daily diet contains 23−34 mg of flavonoids of which the majority is quercetin[2] (3,3′,4′,5,7-pentahydroxyflavone, QH_2). Flavonoids are generally believed to provide certain health benefits, some of which appear likely to be real (e.g., their potential use as chemotheurapeutic adjuvants for lymphocytic leukemia[3]) but others (e.g., reduction in heart disease[2]) may well be imaginary. Such "benefits" are usually ascribed to the ability of flavonoids to trap free radicals, an ability common to all phenols that is generally equated to "antioxidant activity". There have, therefore, been many reports on the kinetics, products, and mechanisms of the reactions of flavonoids with free radicals. In the kinetic studies, the most popular radical has been 1,1-diphenyl-2-picrylhydrazyl (**dpph**$^\bullet$) because this radical is stable, is commercially available, and possesses a strong absorption band in the visible ($\lambda_{max} \approx 520$ nm, slightly dependent on solvent). The time-dependent 'bleaching' of this absorbance following the addition of a reducing agent (i.e., **dpph**$^\bullet \rightarrow$ **dpph**H or **dpph**$^-$) can readily be monitored. Because of its dietary abundance, quercetin has been particularly popular in these kinetic studies with at least eight reports on the QH_2/**dpph**$^\bullet$ reaction appearing over the past decade.[4] One notable feature of these eight publications is that they all (incorrectly, see below) explicitly state, or imply, that the QH_2/**dpph**$^\bullet$ reaction follows second-order kinetics (k_1, in M^{-1} s^{-1} units). However, the

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[†] CNR, Istituto di Chimica Biomolecolare.
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(1) *The science of flavonoids*; Groteworld, E., Ed.; Springer Science+Business Media, Inc: New York, 2006.

(2) Conquer, J. A.; Maiani, G.; Azzini, E.; Raguzzini, A.; Holub, B. J. *J. Nutr.* **1998**, *128*, 593–597.

(3) Russo, M.; Spagnuolo, C.; Volpe, S.; Mupo, A.; Tedesco, I.; Russo, G.-L. *Br. J. Cancer* **2010**, *103*, 642–648.

(4) (a) Dangles, O.; Fargeix, G.; Dufour, C. *J. Chem. Soc., Perkin Trans. 2* **1999**, 1387–1395. (b) Madsen, H. L.; Andersen, C. M.; Jorgensen, L. V.; Skibsted, L. H. *Eur. Food Res. Technol.* **2000**, *211*, 240–246. (c) Alluis, B.; Dangles, O. *Helv. Chim. Acta* **2001**, *84*, 1133–1155. (d) Goupy, P.; Dufour, C.; Loonis, M.; Dangles, O. *J. Agric. Food Chem.* **2003**, *51*, 615–622. (e) Butkovic, V.; Klasinc, L.; Bors, W. *J. Agric. Food Chem.* **2004**, *52*, 2816–2820. (f) Tsimogiannis, D. I.; Oreopoulou, V. *Innovative Food Sci. Emerg. Tech.* **2006**, *7*, 140–146. (g) Villano, D.; Fernandez-Pachon, M. S.; Moya, M. L.; Troncoso, A. M.; Gaecia-Parrilla, M. C. *Talanta* **2007**, *71*, 230–235. (h) Musialik, M.; Kuzmicz, R.; Pawlowski, T. S.; Litwinienko, G. *J. Org. Chem.* **2009**, *74*, 2699–2709.

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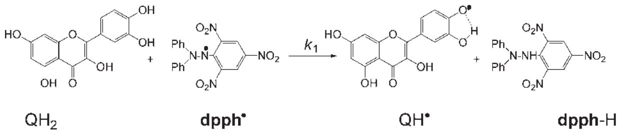
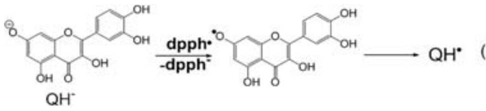
values given for k_1 in methanol at room temperature are quite diverse (ranging from a low[4g] of 264 M^{-1} s^{-1} to a high[4f] of 6433 M^{-1} s^{-1}). By far the most significant of these publications is that by Litwinienko et al.,[4h] who reported k_1 = 3000 M^{-1} s^{-1} in methanol, and who provided many useful insights into the reaction mechanism (which we are happy to accept). They also provide at least a partial explanation for the divergent values that had been reported for k_1. Specifically, these workers utilized stop-flow equipment and found *that the reaction was so fast that it was already over before any measurements of the QH_2/**dpph•** reaction kinetics could have been made in conventional spectrophotometers*! They concluded this very fast reaction involved a quercetin anion, QH^-, and followed the Sequential Proton Loss Electron Transfer (SPLET) mechanism.[5] Structure acidity relationships for ten flavonoids indicated that QH_2's 7-hydroxyl group was its most acidic (confirmed by us using NMR; see Supporting Information, SI). Thus, the initial step in the QH_2/**dpph•** process should be represented by the electron transfer of reaction 2, rather than by the H-atom abstraction shown in reaction 1.



(1)



(2)

So what was actually being measured when the apparent loss of **dpph•** was monitored in simple spectrophotometers? While answering this question, we made a most intriguing observation: *Reaction* 2 *may be bimolecular but the QH_2/**dpph•** reaction does not follow second-order kinetics!*

The 2-electron oxidation of QH_2 is known to yield quinone/quinone methide products, Q. Computations[6] indicate that Q_1 (see below) is the most stable Q (see SI). The conjugation in Q_1 produces strong absorptions in the visible, and indeed, as early as 1999 the following was reported:[4a] "In DMF, the reaction was monitored at 650 nm instead of 520 nm (DMF λ_{max} **dpph•**) in order to avoid interference with the oxidized forms of the flavonoids which absorb at the latter wavelength". Subsequently, the important fact that Q and **dpph•** both absorb at 520 nm appears to have been largely forgotten.

Our stopped-flow kinetic measurements were made in methanol/water, 80:20 (v/v), at 519 nm (λ_{max} **dpph•**) under pseudo-first-order conditions with a roughly 10-fold higher concentration of QH_2 than **dpph•**. A typical kinetic trace (Figure 1) shows that decay of the 519 nm absorption involves a "stretched" exponential, and hence more than one chemical reaction. There is a fast initial decrease within the first 100 ms after mixing the solutions of QH_2 and **dpph•**. This is due to the (quickly complete, see Figure 2) consumption of the **dpph•**, with the formation of colored products (Q) less strongly absorbing than **dpph•**. It should be emphasized that the 'grow-in' of Q will not influence the measured kinetics of the QH_2 + **dpph•** reaction; i.e., there is no actual "interference".

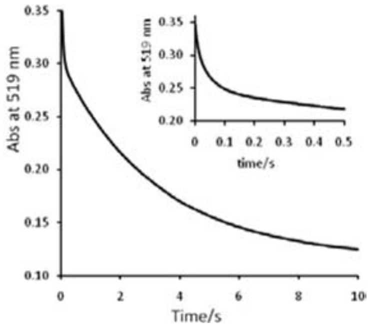


Figure 1. Time-dependent absorbance at 519 nm for reaction of quercetin (5 × 10^{-4} M) with **dpph•** (3.2 × 10^{-5} M) in methanol/water 80:20 (v/v) at 298 K. Inset: Initial portion of the same decay trace.

After the fast initial reaction, a second much slower decrease in the 519 nm absorbance occurs. "Snapshots" of the evolution of the absorption spectrum at t = 0 s, 100 ms, and 20 s are shown in Figure 2. Although the λ_{max} values for **dpph•** and for the Q products are very similar (as are the colors of the two solutions) the shoulder in the **dpph•** spectrum at ca. 660 nm is absent in the 100 ms spectrum.[7] It was this relatively slow loss of the ~520 nm absorption that so many workers[4a−g] have attributed to the **dpph•** + QH_2 reaction, *although **dpph•** was no longer present in their reaction systems!*

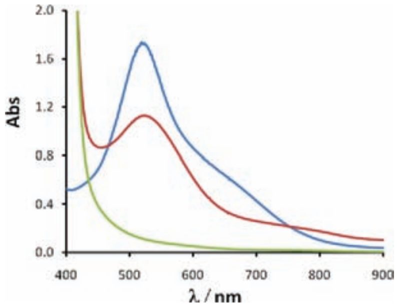


Figure 2. Absorption spectra in 80% methanol/water. *Blue*: 1.3 × 10^{-4} M **dpph•**. *Red*: ca. 100 ms after mixing a solution containing 9.7 × 10^{-4} M QH_2 with one containing 1.3 × 10^{-4} M **dpph•**. *Green*: same as for red, but after ca. 20 s.

The slow, first-order bleaching of the 519 nm absorbance at t > 0.3 s is *mainly* due to addition of two ROH solvent molecules to the 2- and 3-positions of the 2e oxidation

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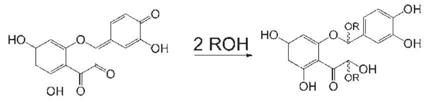
(5) Litwinienko, G.; Ingold, K. U. *Acc. Chem. Res.* **2007**, *40*, 222–230.

(6) Boersma, M. G.; Vervoort, J.; Szymuslak, H.; Lemanska, K.; Tyrakowska, B.; Cenas, N.; Segura-Aguilar, J.; Rietjens, I. M. C. M. *Chem. Res. Toxicol.* **2000**, *13*, 185–191.

(7) Q were also generated by oxidizing QH_2 with PbO_2 in CH_2Cl_2, in which Q are stable. They gave no EPR spectrum, proving that Q are not radicals. They were reduced to QH_2 by ascorbyl palmitate (see Figure S1 in the SI), a result consistent with their assigned structure.

product Q_1,[8] reaction 3.[10] Such addition products have been identified by earlier workers,[4a,c,d,g,11] and we have confirmed their observations (see SI). The quinonemethide, Q_1 (which can be regarded as a highly stabilized benzylic carbocation; see Scheme S2 in the SI), can readily undergo a proton-assisted (Michael-type) nucleophilic addition.[10] As $[QH_2]$ increases, a second Q-bleaching process becomes increasingly competitive with reaction 3. This involves the facile coupling of Q with QH_2, to give the known Q/QH_2 complex[12] (see SI).



Q_1 $\quad$ $Q(ROH)_2$ $\quad$ ROH = H_2O or MeOH $\quad$ (3)

The foregoing results in 80% $MeOH/H_2O$ extend, but are fully consistent with, Litwinienko et al.'s[4h] results in methanol and support their conclusion[4h] that in ionizing solvents the initial fast **dpph**$^\bullet$ + QH_2 reaction involves the QH^- anion.[13] In such solvents, the reaction occurs by the SPLET mechanism (as is the case for other phenols).[5]

In the only previous study[4h] of the kinetics of the *real* (i.e., initial fast) **dpph**$^\bullet$ + QH_2 reaction in ionizing solvents, it was simply *assumed* that the process was first-order in $[QH_2]$, i.e., that the reaction followed overall second-order kinetics, as it would *if the mechanism was as simple as that shown in reaction 1 or 2*. Second-order rate constants, k_1 or k_2 ($M^{-1}\ s^{-1}$), were derived from the slope of a plot of the experimental rate constants, k_{exp}/s^{-1}, at a single initial concentration of **dpph**$^\bullet$ against $[QH_2]$ and then "force fitting" a straight line through the k_{exp} points and the 0,0 origin. However, the true (least-squares) intercept in our solvent and in Litwinienko's *ionizing solvents* was never zero and the true order in $[QH_2]$ was always significantly less than 1.0.[14] In our experiments the average order in $[QH_2]$ was 0.38 (range 0.32 to 0.45; see e. g., Figure 3).

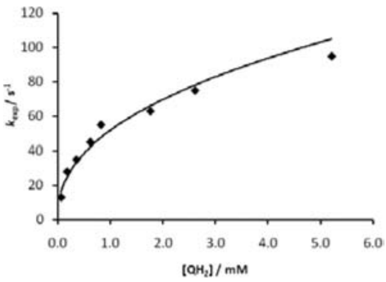


Figure 3. Plot of k_{exp} vs $[QH_2]$. The best fit-line is $k_{exp} = 52 \times [QH_2]^{0.40}$, $R^2 = 0.95$ (measurement error: *ca.* ± 10%).

Litwinienko et al.[4h] found that in dioxane and ethyl acetate, two solvents of similar hydrogen bond accepting ability to MeOH that do not support ionization, the QH_2/**dpph**$^\bullet$ reaction was very much slower than in alcohols (including alcohols + acetic acid) and the order in $[QH_2]$ was 1.0.[14] Thus, in non-ionizing solvents there is a straightforward bimolecular H-atom abstraction from QH_2 by **dpph**$^\bullet$, i.e., reaction 1. However, in ionizing solvents there is a very much faster reaction of **dpph**$^\bullet$ with the quercetin anion, but the nonintegral dependence on $[QH_2]$ of this reaction indicates that the mechanism is more complex than that shown in reaction 2. The process being monitored cannot be an elementary reaction, despite being first-order in the reagent present at the (nominally) lower concentration (**dpph**$^\bullet$). In sharp contrast, although the majority of (and probably all) **dpph**$^\bullet$ + ArOH reactions must occur by the SPLET mechanism in alcoholic solvents, these reactions are, with few exceptions,[15] first-order in [ArOH].[16,17] We are not aware of any suggested explanations for nonintegral kinetic orders in any electron transfer reaction.[18]

Such truly extraordinary kinetics required exploration. One possibility was reversible formation of noncovalent complexes between QH_2 and QH^-. In its simplest representation with dimeric complexes (Scheme 1), the order in $[QH_2]$ is about 0.5, in reasonable agreement with experiment.[19,20] Trimeric and tetrameric complexes might further reduce the observed reaction order. However, this idea had to be abandoned when Beer's Law and NMR gave no evidence for complex formation, nor did the results of extensive computations.

Scheme 1.[a]

$$QH_2 \leftrightarrows QH^- + H^+ \qquad K_a \qquad (4)$$
$$QH_2 + QH^- \leftrightarrows \{QH_2/QH^-\} \quad K_5 \qquad (5)$$

[a] *Rate law*: $-d[\mathbf{dpph}^\bullet]/dt \approx k_2(K_a\ /2K_5\ [H^+])^{0.5}[\mathbf{dpph}^\bullet][QH_2]^{0.5}$.

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[8] (a) Q are too short lived in methanol/water to isolate and identify. (b) The formation of Q from QH_2 + dpph$^\bullet$ in methanol has long been formulated as a disproportionation: $2QH^\bullet \rightarrow Q + QH_2$.[4a] The $QH^\bullet$ radical will be far more acidic than QH_2 (because the $O^\bullet$ moiety is very strongly electron-withdrawing)[9] and will rapidly ionize to give the radical anion, $Q^{\bullet-}$. Since [**dpph**$^\bullet$] > $[Q^{\bullet-}]$, we consider it far more probable that Q is formed by the reaction: $Q^{\bullet-}$ + **dpph**$^\bullet$ → Q + **dpph**$^-$.

[9] Pratt, D. A.; DiLabio, G. A.; Valgimigli, L.; Pedulli, G. F.; Ingold, K. U. *J. Am. Chem. Soc.* **2002**, *124*, 11085–11092.

[10] For example, see: Toteva, M. M.; Richard, J. P. *J. Am. Chem. Soc.* **2000**, *122*, 11073–11083. Toteva, M. M.; Moran, M.; Amyes, T. L.; Richard, J. P. *J. Am. Chem. Soc.* **2003**, *125*, 8814–8819.

[11] Hvattum, E.; Stenstrøm, Y.; Ekeberg, D. *J. Mass Spectrom.* **2004**, *39*, 1570–1581.

[12] For example, see: Krishnamachari, V.; Levine, L. H.; Pare, P. W. *J. Agric. Food Chem.* **2002**, *50*, 4357–4363. Zhou, A.; Sadik, O. A. *J. Agric. Food Chem.* **2008**, *56*, 12081–12091.

[13] Demonstrated, in part, by the large rate retarding effect of added acetic acid,[4h,14] see also SI to the present paper.

[14] We calculated, from the SI in ref 4h, kinetic orders in $[QH_2]$ for the initial fast QH_2 + **dpph**$^\bullet$ reaction as follows: Solvent, reaction order, and (in parenthesis) the reported bimolecular rate constant ($M^{-1}\ s^{-1}$). MeOH, 0.25 (3000) and 0.51 (3100); MeOH + 10 mM acetic acid, 0.53 (770) and 0.40 (720); MeOH + 100 mM acetic, 0.59 (160) and 0.51 (140); EtOH, 0.28 (4900), 0.51 (5600), and 0.57 (5800); EtOH + 5 mM acetic, 0.59 (54); + 10 mM acetic, 0.73 (41); + 50 mM acetic, 0.56 (35); + 100 mM acetic, 0.45 (25); Dioxane, 0.99 (3.0); Ethyl acetate, 1.02 (8.3) and 1.05 (10.3).

[15] The only exceptions known to us involve the reactions of **dpph**$^\bullet$ in methanol and ethanol with certain cinnamic acids for which the reaction order in [phenol] is about 0.5 and was attributed to the presence and ionization of their carboxylic acid moieties; see: Foti, M. C.; Daquino, C.; Geraci, C. *J. Org. Chem.* **2004**, *69*, 2309–2314.

[16] See: Foti, M. C.; Daquino, C.; Mackie, I. D.; DiLabio, G. A.; Ingold, K. U. *J. Org. Chem.* **2008**, *73*, 9270−9282 and references cited.

[17] This was further confirmed in the present mixed solvent by demonstrating that the reaction order is ~1.0 for 2,2,5,7,8-pentamethyl-6-hydroxychroman over a concentration range from 0.1 to 5.3 mM.

[18] This is not surprising. Such 'inconvenient' nonintegral kinetics are rare, and when they do occur, they tend to be ignored or overlooked.

[19] Kinetic rate law derivations are given in the SI.

[20] The implication of Scheme 1 is that the oxidation of QH_2 by other stable free radicals should also give nonintegral orders in $[QH_2]$, but neither TEMPO nor Galvinoxyl gave a 519 nm grow-in (indicative of Q formation) on mixing with QH_2 in $MeOH/H_2O$ (80:20, v/v).

Scheme 2. [a]

$$\mathrm{QH^- + \textbf{dpph}^\bullet \leftrightarrows \{QH^-/\textbf{dpph}^\bullet\}} \quad K_6 \qquad (6)$$

$$\mathrm{\{QH^-/\textbf{dpph}^\bullet\} \rightarrow QH^\bullet + \textbf{dpph}^-} \quad k_{\mathrm{ET}} \qquad (7)$$

[a] *Rate law*: $-\mathrm{d}[\textbf{dpph}^\bullet]/\mathrm{d}t = \{a[\mathrm{QH_2}]/(1 + b[\mathrm{QH_2}])\} \times [\textbf{dpph}^\bullet]$ where $a = k_{\mathrm{ET}}K_6K_a/[\mathrm{H}^+]$; $b = K_6K_a/[\mathrm{H}^+]$; $a/b = k_{\mathrm{ET}}$.

This forced us to reassess our initial idea of reversible formation of a noncovalent $\{\mathrm{QH}^-/$**dpph**$^\bullet\}$ complex (Scheme 2) which yields[19] an order in $[\mathrm{QH_2}]$ that varies smoothly from 1.0 at low $[\mathrm{QH_2}]$ to 0 at high $[\mathrm{QH_2}]$, with intermediate $[\mathrm{QH_2}]$ nicely accommodating our results.

Initially, Scheme 2 was abandoned, in the belief that the $\{\mathrm{QH}^-/$**dpph**$^\bullet\}$ complex would undergo intramolecular electron transfer (IET) to $\mathrm{QH}^\bullet$ + **dpph**$^-$ much more rapidly than its (kinetically required) reversible dissociation to QH^- and **dpph**$^\bullet$. Moreover, $\mathrm{QH}^\bullet$ would be expected to be such a strong acid[8b] that deprotonation would be exceedingly fast, helping to drive the reaction to completion. When Scheme 1 had to be abandoned we also abandoned our prejudices about the IET rate in the $\{\mathrm{QH}^-/$**dpph**$^\bullet\}$ complex and applied Marcus theory, Scheme 3.

Scheme 3. [a]

$$\mathrm{QH^- + \textbf{dpph}^\bullet \leftrightarrows QH^\bullet + \textbf{dpph}^-} \qquad (8)$$

$$\mathrm{\textbf{dpph}^- + \textbf{dpph}^\bullet \leftrightarrows \textbf{dpph}^\bullet + \textbf{dpph}^-} \qquad (9)$$

$$\mathrm{QH^- + QH^\bullet \leftrightarrows QH^\bullet + QH^-} \qquad (10)$$

[a] Marcus theory: $k_8 = (k_9 \times k_{10} \times K_8 \times f)^{0.5}$; since, $k_9 = 3.7 \times 10^3$ $\mathrm{M^{-1}\,s^{-1}}$, $k_{10} = 2 \times 10^9$ $\mathrm{M^{-1}\,s^{-1}}$, and $K_8 \leq 1 \times 10^{-5}$, with $f = 1$, $k_8 \leq 1 \times 10^4$ $\mathrm{M^{-1}\,s^{-1}}$ (see SI for details).

Thus, Marcus theory predicts that ET between QH^- and **dpph**$^\bullet$ cannot be particularly fast and hence dissociation of the complex $\{\mathrm{QH}^-/$**dpph**$^\bullet\}$ back to QH^- and **dpph**$^\bullet$ may well be much faster. The consequent rate law (Scheme 2) yielded for the IET process $k_{\mathrm{ET}} \approx 10^5\ \mathrm{s}^{-1}$ (see SI).

To our knowledge, bimolecular ETs have never been reported to exhibit nonintegral kinetics. However, we did find one fascinating report[21] of similar kinetics in H-atom abstraction by **dpph**$^\bullet$ from the SH group in glutathione and an analog in which the γ-glutamyl had been replaced by an α-glutamyl . The latter tripeptide was twice as reactive as the former. Some brilliant detective work demonstrated that the rate constants for the two H abstractions were equal, the measured differences in overall rates being due to differences in the equilibrium constants for complex formation between **dpph**$^\bullet$ and the two tripeptides.[21] While these tripeptides may wrap themselves around **dpph**$^\bullet$ to form the complexes, this is not possible for the quasi-planar QH^- anion for which reversible, noncovalent complex formation most probably would involve π-stacking. This led us to predict that other flavonoids would π-stack with **dpph**$^\bullet$ and give orders in [flavonoid] < 1.0 *provided the flavonoid was roughly planar*. (If planarity was seriously disrupted, there would be no π-stacking and the order in [flavonoid] would be 1.0, as with other phenols.) A brief survey of the reactions of **dpph**$^\bullet$ in $\mathrm{MeOH/H_2O}$ with three flavonoids having the same extensive π-conjugation as quercetin (fisetin, morin, kampherol), one flavonoid lacking such extensive π-conjugation ([+]-catechin), and one flavonoid (rutin) that has the same π-conjugation as $\mathrm{QH_2}$ but has a bulky sugar attached to the 3-O atom (which might partially disrupt π-stacking), gave the orders, $\boldsymbol{m}$, in [flavonoid] presented in Scheme 4.[22] These $\boldsymbol{m}$ orders support the prediction about the π-stacking with **dpph**$^\bullet$ of quasi-planar flavonoids.

Scheme 4. [a]

Quercetin ($\mathrm{QH_2}$)	$\boldsymbol{m} = 0.38$	Kampherol	$\boldsymbol{m} = 0.42$
Fisctin	$= 0.2$	[+]-Catcchin	$= 1.0$[23]
Morin	$= 0.22$	Rutin	$= 0.30$

[a] Order ($\boldsymbol{m}$) in [Flavonoid] in their fast, initial reactions with **dpph**$^\bullet$ in $\mathrm{MeOH/H_2O}$ (80:20, v/v).[22]

In conclusion, when monitored at 519 nm the **dpph**$^\bullet$ + $\mathrm{QH_2}$ reaction in $\mathrm{MeOH/H_2O}$ exhibits biphasic behavior, with both phases following first-order kinetics. The fast, initial bleaching is due to reaction of the **dpph**$^\bullet$ with the quercetin 7-anion[4h] (SPLET mechanism).[5] The quinone/quinone methide products of this reaction, Q, also absorb at 519 nm. The relatively slow bleaching of Q, which has commonly been assumed to be the **dpph**$^\bullet$ reaction,[4a−g] is really due to the addition of two solvent molecules (to give 2,3-$\mathrm{Q(ROH)_2}$) and of excess $\mathrm{QH_2}$ (to give $\mathrm{Q/QH_2}$). The fast QH^- + **dpph**$^\bullet$ reaction has a nonintegral, less than first, order dependence on $[\mathrm{QH_2}]$. Such extraordinary kinetics have not, to our knowledge, been reported for any other 1-electron transfer. We propose that these kinetics arise because of reversible formation of noncovalent π-stacked complexes between the large, planar, and extensively π-conjugated QH^- anion and **dpph**$^\bullet$.[24] Other *planar* flavonoids exhibit similar 'odd' kinetics in their reactions with **dpph**$^\bullet$ in the same ionizing solvent.

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Note Added after ASAP Publication. IUPAC name corrected in the title and reposted to the web September 9, 2011.

Supporting Information Available. Kinetic and spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(21) Viirlaid, S.; Mahlapuu, R.; Kilk, K.; Kuznetsov, A.; Soomers, U.; Jarv, J. *Bioorg. Chem.* **2009**, *37*, 125–132.

(22) Flavonoid structures are given in the SI.

(23) At low [catechin]; the order decreases at higher [catechin] as predicted by the rate law for Sheme 2; see SI.

(24) The binding energy of the $\mathrm{QH}^-/$**dpph**$^\bullet$ complex is predicted by computation (using the method in Mackie, I. D.; DiLabio, G. A. *J. Phys. Chem. A* **2008**, *112*, 10968−10976) to be 17.8 kcal/mol in the gas phase. The optimized structure of the complex is presented as the abstract figure. The interaction between the two moieties is dominated by π-stacking and by Coulomb interactions.