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Identification of 7,4′-Dihydroxy-5-methoxyflavylium in "Dragon's Blood": To Be or Not To Be an Anthocyanin

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Abstract: The compound 7,4′-dihydroxy-5-methoxyflavylium (dracoflavylium) was identified as the major red colorant in samples of the resin "dragon's blood", extracted from the tree *Dracaena draco*. The complex network of reversible chemical reactions that dracoflavylium undergoes in aqueous solution is fully described; for the first time, all the equilibrium constants that enable a complete characterisation of the system have been obtained ($K'_a = 1.6\times10^{-4}$, $K_{a1} = 1.0\times10^{-4}$, $K_{a2} = 3.2\times10^{-8}$, $K_{Ct1} = 1.0\times10^{-7}$, $K_{Ct2} = 1.3\times10^{-10}$). It is concluded that the red colour is due to a stable quinoid base, **A**, which is the major species at pH 4–7. It is further shown that this compound does not fit the commonly accepted definitions of anthocyanidin nor 3-deoxyanthocyanidin. Similarly to synthetic flavylium salts, the natural compound 7,4′-dihydroxy-5-methoxyflavylium gives rise to several species (multistate system) reversibly interconverted by external stimuli, such as pH.

Keywords: dyes/pigments · flavylium salts · kinetics · multistate systems · natural products

Introduction

Red colorants from "dragon's blood": Synthetic flavylium salts,[1] anthocyanins[2] and natural flavylium compounds,[3] discovered in this order, all have the 2-phenyl-1-benzopyrylium chromophore in common. It is worth noting that the crucial and fundamental paper by Willstätter and Mallinson on the causes of colour in flowers and fruits[2c] tends to be forgotten, and is seldom cited as such. Moreover, the concept that the red colour of the resin named "dragon's blood" is given by natural flavylium compounds has been overlooked during the past few decades.[4]

Dragon's blood is a natural resin, presenting a rich, deep-red colour, obtained from various trees, namely, *Dracaena draco* and *Dracaena cinnabaris* belonging to the *Dracaenaceae* family. It is known that it appears in injured areas of the tree,[5] and it has been used for centuries for medical and artistic purposes.[6]

The suggestion that dracorubin (Table 1), one of the red compounds isolated from a commercial, powdered dragon's blood resin,[7] was a 2-phenyl-1-benzopyran derivative was made by Brockmann and Haase in 1936.[7a] Later, in 1943, Brockmann and Junge published the first structure of another of the red colorants, which was named dracorhodin (Table 1);[8] in their paper they concluded that dracorhodin was a natural 2-phenyl-1-benzopyrylium (a flavylium salt) that should belong to the anthocyanin family.[8] A more straightforward synthesis, and consequent confirmation of this molecule, was published by Robertson and Whalley in 1950.[9a] However, the structure of dracorubin had to wait until 1950 to be fully unveiled by Robertson and Whalley;[9b,c] and only in 1976 was it synthesised.[9d] In the meantime, two other red colorants from dragon's blood were characterised (lacking the methyl group in the 6-position)

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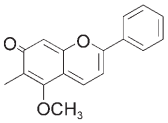
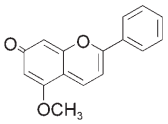
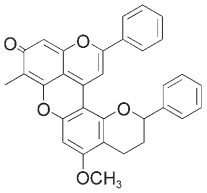
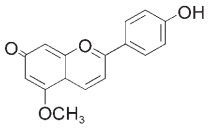
Table 1. Chemical structures responsible for the red colour in dragon's blood resins.

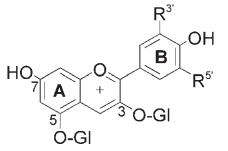
	Structure[a]	Year[b]
dracorhodin		1943, [8]1950[9a]
nordracorhodin		1971[4b]
dracorubin		1936, 1937,[7] 1950,[9b] 1976[9d]
dracoflavylium		2006

[a] The structures correspond to the quinoid bases (**A**). [b] Years in which the structures were discovered and published.

and named nordracorhodin (Table 1) and nordracorubin.[4b] Again, these compounds were obtained from a commercial batch of a resin imported from Singapore; most probably, these resins were from the palm tree *Daemonorops draco*. The most interesting aspect of Table 1 is that all of the structures are simply the quinoid base (**A**) of the respective flavylium cation ($\mathbf{A}H^+$), as can be confirmed in Scheme 1. In other words, at sufficiently acidic pH values, in all of them, the quinone is protonated and a hydroxyl group is formed, leading to the respective flavylium cation.

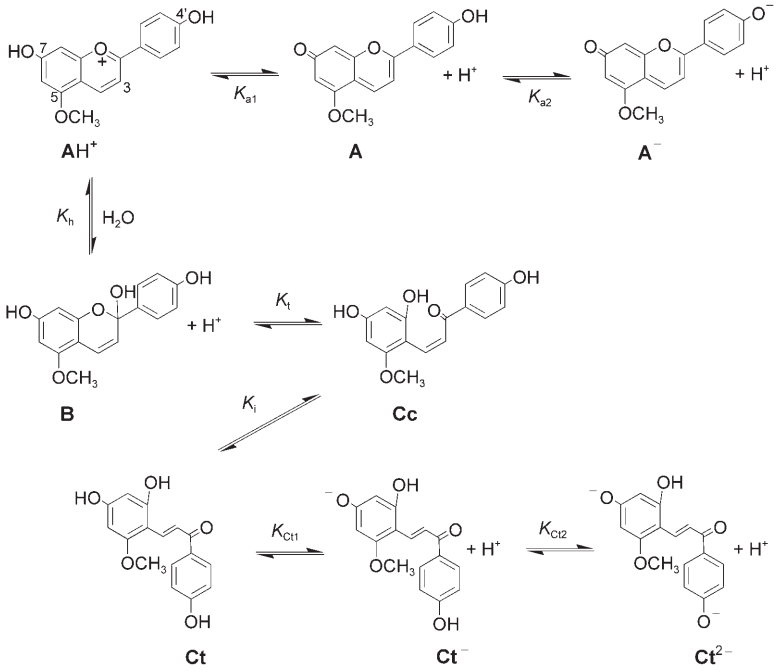
In the following years, many other compounds from dragon's blood resins—with precise geographic origins and plant species—were characterised,[10,11] but none could be responsible for the dragon's blood red colour, unlike those previously reported in Table 1,[11] owing to a lack of conjugation between the three rings, a requirement for obtaining this colour.

Equilibria in solution: As stated above, dracorhodin was regarded as a natural flavylium salt.[8] Flavylium salts are related to anthocyanins,[12] the natural colorants responsible for the exuberance of reds, blues and purples in nature. It is worth noting that the distribution of the species reported in Scheme 1 is dramatically dependent on the substitution pattern of the 2-phenyl-1-benzopyran. Anthocyanins are characterised by a hydroxyl group in positions 4′ and 7, and a sugar group in position 3 (monoglycosides) or positions 3 and 5 (diglycosides) (Scheme 2). On the other hand, in anthocyanidins the hydroxyl groups take the positions of the glycosides, leading to unstable structures in solution. On the contrary, the so-called deoxyanthocyanidins correspond to "anthocyanidins"[13] lacking the hydroxyl group in position 3 (but bearing an hydroxyl in position 5), and are quite stable in solution.



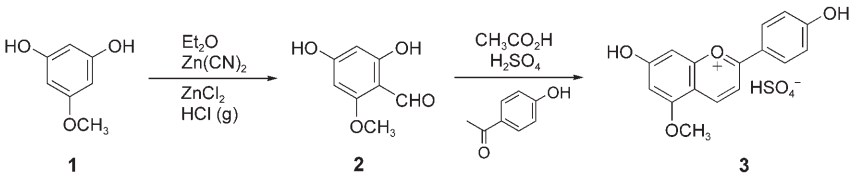
Scheme 2. In the basic chemical structure of anthocyanins, a hydroxyl group in positions 4′ and 7 is present, and a sugar (Gl) in position 3 (monoglycosides) or positions 3 and 5 (diglycosides).

In the 1970s, it was firmly established by Dubois and Brouillard (anthocyanins)[14] and McClelland (synthetic flavylium salts)[15] that both families of compounds undergo multiple structural transformations in aqueous solution, following the same basic mechanisms (Scheme 1).[16] The flavylium cation ($\mathbf{A}H^+$) is the dominant species in very acidic solutions, but with increasing pH a series of more or less reversible chemical reactions take place: 1) deprotonation leading to the quinoid base (**A**), 2) hydration of the flavylium cation giving rise to the colourless hemiacetal (**B**), 3) tautomerisation reaction, responsible for ring opening, to



Scheme 1. Network of chemical reactions for dracoflavylium.

give the pale-yellow *Z*-chalcone form (**Cc**), and finally, 4) *cis–trans* isomerisation to form the pale-yellow *E*-chalcone (**Ct**). Furthermore, at higher pH, and depending on the number of hydroxyl groups, further deprotonated species are found, such as $\mathbf{Ct}^{n-}$ and $\mathbf{A}^{n-}$. The relevant contribution for colour is given by $\mathbf{AH}^+$ and the quinoid bases.



Scheme 3. Synthetic approach for 7,4′-dihydroxy-5-methoxyflavylium/dracoflavylium.

In this work, we report on the discovery of a natural flavylium in dragon's blood resin from *Dracaena draco*, the compound 7,4′-dihydroxy-5-methoxyflavylium,[17] from here onwards called dracoflavylium (as it is the first natural flavylium discovered in a *Dracaena draco* tree). This compound does not fit the commonly accepted definition of an anthocyanidin,[13] or 3-deoxyanthocyanidin as some authors recently have proposed for analogous structures from *Arrabidaea chica*,[18] as a methoxy group was found in position 5. The dracoflavylium structure, and principally its chemical behaviour, is closer to the so-called synthetic flavylium salts,[15,17] as will be described throughout this work.

7,4′-Dihydroxy-5-methoxyflavylium (**3**) was also synthesised according to Scheme 3. Formylation of 4-methoxyresorcinol (**1**) led to salicylaldehyde **2**, which reacts with 4′-hydroxyacetophenone under acidic conditions to give flavylium salt **3**.

Results and Discussion

In order to understand the chemistry of 7,4′-dihydroxy-5-methoxyflavylium and its pH colour dependence, a complete characterisation of all equilibrium and transient species was carried out in acidic and basic media.

Acidic media: Similarly to the other flavylium compounds, 7,4′-dihydroxy-5-methoxyflavylium is involved in a complex network of chemical reactions (Scheme 1) in which the different forms can be reversibly interconverted by changing the pH: the yellow flavylium cation ($\mathbf{AH}^+$), the quinoid bases (red **A** and pink $\mathbf{A}^-$) reached by deprotonation of $\mathbf{AH}^+$, hemiketal species **B** obtained by hydration at the 2-position of $\mathbf{AH}^+$, *cis*-chalcone **Cc** formed from hemiketal **B** and *trans*-chalcone **Ct** and ionised *trans*-chalcones ($\mathbf{Ct}^-$, $\mathbf{Ct}^{2-}$), obtained from **Cc** by means of a *cis–trans* isomerisation reaction. The ionised **Cc** forms that are also formed as transient species were omitted for simplification.

The spectral variations of 7,4′-dihydroxy-5-methoxyflavylium occurring after approximately one minute upon displacing the system from equilibrium by means of a pH jump from the stock solutions at pH 1 to higher pH values are reported in Figure 1 (top). At very acidic pH the absorption band of the yellow flavylium cation, $\mathbf{AH}^+$, is dominant; by increasing the pH a new band centred at $\lambda = 493$ nm is obtained owing to the formation of the red quinoid base **A** ($pK_{a1} = 4.0$); further increase of the pH leads to an absorption band characteristic of the pink ionised base $\mathbf{A}^-$ ($pK_{a2} = 7.5$).[16a] The spectra obtained at thermal equilibrium for pH < 6 is shown in Figure 1 (bottom). The flavylium cation is again the dominant species at more acidic pH values, but for higher pH values an equilibrium is established between the base **A** (63%) and the *trans*-chalcone **Ct** (37%).

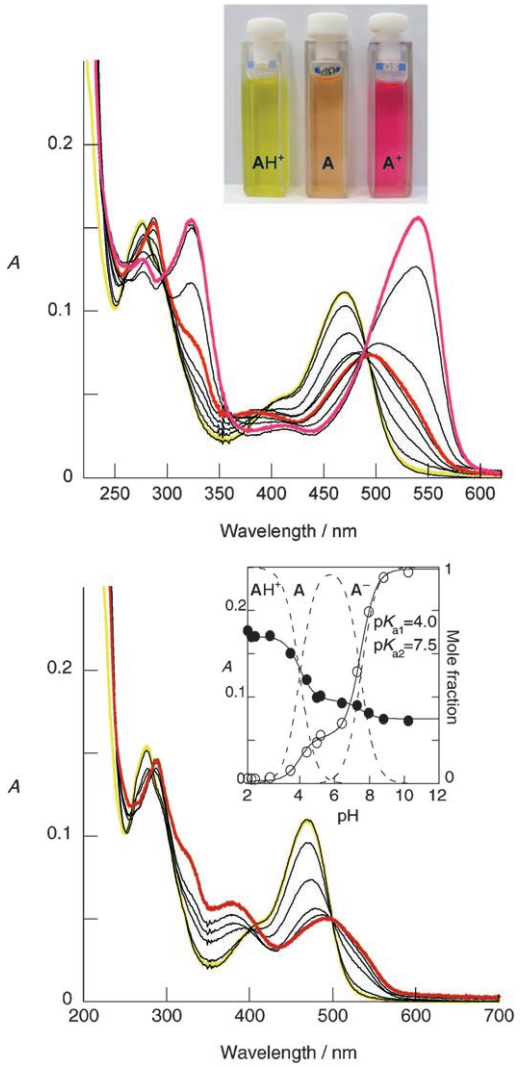


Figure 1. Top: Spectral variations occurring immediately (ca. 1 min) upon a pH jump from equilibrated solutions of the dracoflavylium (4×10^{-6} M) at pH 1.0 to higher pH values; Bottom: the same after thermal equilibration. Inset: calculated pK_{a1} and pK_{a2}.

One interesting feature of the chemistry of most 2-phenyl-1-benzopyrylium derivatives, including anthocyanins, that contributes to the different species distribution observed immediately after and at equilibrium (Figures 1 and 2) is the fact that hemiketal **B** is exclusively formed through the hydration of $\mathbf{AH}^+$, and not from the hydration of **A**.[13] In kinetic terms, the rate of formation of **B** is given by Equation (1), that is, it is proportional to the concentration of flavylium cation.

$$\frac{d[\mathbf{B}]}{dt} = k_h[\mathbf{AH}^+] - k_{-h}[\mathbf{B}][H^+] \quad (1)$$

This behaviour has implications for the kinetics of the disappearance of **A**. When a pH jump from equilibrated solutions at very acidic pH values, for example pH 1, is carried out to sufficiently high pH values, base **A** is immediately formed because proton transfer is a very fast reaction, much faster than the hydration to give **B**. Taking into account that $\mathbf{AH}^+$ and **A** are in fast equilibrium, **A** only disappears because $\mathbf{AH}^+$ leads to **B**, which in turn will evolve to **Ct**, through **Cc**. At near-neutral pH values the concentration of $\mathbf{AH}^+$ is very low, and by consequence **A** becomes a kinetic product, which evolves slowly to equilibrium ($k_{obs} = 1.7 \times 10^{-4}\ s^{-1}$ at pH 6.0).

Basic media: In moderately basic media, base $\mathbf{A}^-$ is immediately formed by deprotonation of the hydroxyl groups, and disappears through the nucleophilic attack by OH^-, leading to a final product $\mathbf{Ct}^{2-}$($\mathbf{Ct}^-$), with rate constant $55 \times [OH^-]\ s^{-1}$. At pH 8–9 the concentration of hydroxyl is very low, and by consequence $\mathbf{A}^-$ is also a kinetic product, which takes several days to reach equilibrium. The percentage of $\mathbf{A}^-$ at equilibrium, pH 8.8, is 31%, in good agreement with the value calculated by using Equation (12) in the Supporting Information. On the contrary, at pH > 12 the reaction is fast, leading to a final product that was confirmed by ^{1}H NMR spectroscopy as $\mathbf{Ct}^{2-}$.

The pK_a of the *trans*-chalcones was measured by carrying out a titration starting from $\mathbf{Ct}^{2-}$ back to acidic medium, and the spectra monitored after one minute; the values pK_{Ct2} = 9.3 ($\mathbf{Ct}^{2-}/\mathbf{Ct}^-$) and p$K_{Ct1}$ = 7.0 ($\mathbf{Ct}^-/\mathbf{Ct}$) were obtained (Figure 2). When a pH jump from equilibrated solutions at pH 12 to 1 was carried out (Figure 2) the flavylium cation formed with a rate constant of $2.1 \times 10^{-3}\ s^{-1}$, which indicates the existence of a moderate barrier for the *cis–trans* isomerisation as reported for the parent compound 7,4-dihydroxyflavylium.[16c–e] A cycle starting from pH 1 ($\mathbf{AH}^+$) to 12 ($\mathbf{Ct}^2$) and back to pH 1 allows recovery of all the initial flavylium cations, showing the excellent reversibility of the system.

As shown in the Supporting Information, the set of equilibrium constants calculated through this work, and reported in Table 2, permits the calculation of the mole fraction distribution of all species of the network at the equilibrium, as shown in the conclusive Figure 3.

Inspection of Figure 3 clearly shows that at moderately acidic pH values such as those measured for the resin, the concentration of the red base at equilibrium is very high, and for moderately basic solutions there is also a contribution from the pink colour of the ionised base, $\mathbf{A}^-$.

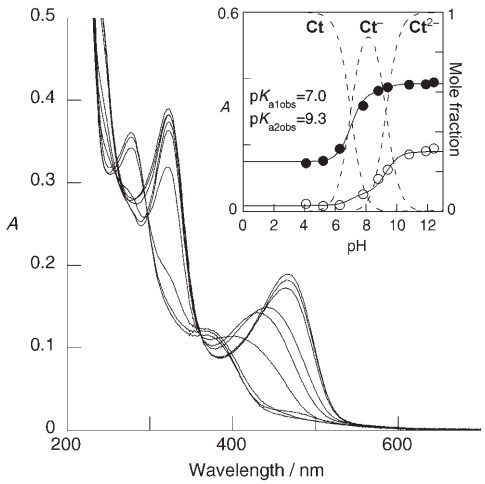


Figure 2. Spectral variations of the *trans*-chalcone species, taken immediately upon a pH jump from the equilibrated solutions at pH 12.0 to lower pH values. Inset: determination of the respective pK_a values at $\lambda = 480$ and 320 nm.

Table 2. Equilibrium constants for 7,4′-dihydroxy-5-methoxyflavylium at 25 °C (estimated error: 10%).

K'_a	K_{a1}	K_{a2}	K_{Ct1}	K_{Ct2}
1.6×10^{-4}	1.0×10^{-4}	3.2×10^{-8}	1.0×10^{-7}	1.3×10^{-10}

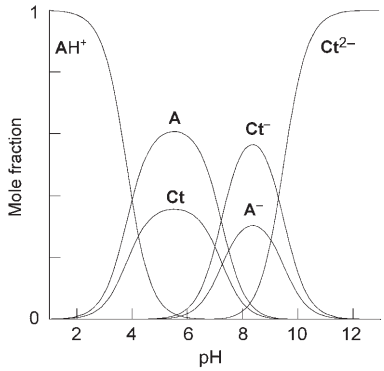


Figure 3. Variation of mole fraction distribution with pH for 7,4′-dihydroxy-5-methoxyflavylium, at 25 °C [obtained by using Eqs. (9)–(14) in the Supporting Information and the equilibrium constants reported in Table 2].

Conclusion

Dragons's blood is yellow in strongly acidic solutions, because the different species present, shown in Table 1, are flavylium cations ($\mathbf{AH}^+$) at these pH values. At moderately acidic pH values, the red quinoid base **A** is formed, which gives the resin its characteristic colour. To the best of our knowledge, this is the first known natural flavylium com-

pound for which the base is the major species at biological pH (63%). One other interesting aspect is the unusual stability of the pink ionised base: at pH≈8–9, the final equilibrium contains 30% ionised base. For the most common anthocyanins and 3-deoxyanthocyanidins[15,19] in moderately acidic to neutral pH, colourless **B** is the major species, together with **Ct.** The existence of a hydroxyl group at the 5-position and not in the 3-position leads to thermodynamically more-stable red quinoid bases; but not to the pair red ($\mathbf{AH}^+$)/blue (**A**), only to yellow ($\mathbf{AH}^+$)/red (**A**). Blue colours are formed, in anthocyanins, through beautiful and complex supramolecular structures, as brilliantly shown by GoTo, Kondo and collaborators.[20]

Finally we would like to propose the name dracoflavylium for the 7,4′-dihydroxy-5-methoxyflavylium salt, in spite of the fact that all the compounds in Table 1 should be considered bases of a flavylium compound. We would like to emphasise that the red colour in dragon's blood, extracted from *Draceana draco*, is caused by this family of molecules.

Experimental Section

General: All reagents and solvents used were of analytical grade. Solvents used for spectroscopic studies were of spectroscopic or equivalent grade, and the water used was of Millipore grade. NMR spectra were recorded on a Bruker AMX400 spectrometer operating at 400 MHz (^{1}H) or 100 MHz (^{13}C). High-resolution mass spectra (HRMS) were obtained by means of laser desorption/ionisation (LDI) with a Finnigan FT/MS 2001-DT Fourier transform ion cyclotron resonance mass spectrometer (FTICR/MS), equipped with a 3 tesla superconducting magnet and coupled to a Spectra-Physics Quanta-Ray GCR-11 Nd:YAG laser operating at the fundamental wavelength ($\lambda = 1064$ nm). Elemental analyses were obtained on a Thermofinnigan Flash EA 1112 Series instrument.

Isolation and identification of 7,4′-dihydroxy-5-methoxyflavylium: The resin was extracted from *Dracaena draco* centenary trees existing in the region of Lisbon (Autumn 2005) as well as from trees in the Funchal Natural Park (Island of Madeira, Summer 2005). The red colorants[21] were extracted by using methanol (acidified, $[H^+] \approx 10^{-2}$ M), and separated by using HPLC with a DAD detector (Thermofinnigan, Surveyor PDA 5), a RP-18 column and a water (pH 1.5)/methanol gradient.[22]

The identification of the isolated compound was made on the basis of HRMS and ^{1}H NMR spectroscopy, although complete structure confirmation required the synthesis of 7,4′-dihydroxy-5-methoxyflavylium. The isolated compound had the same retention time ($t_R = 20.50$ min), UV/Vis spectra by HPLC-DAD ($\lambda_{max} = 477$ nm) and the same molecular mass peaks (HRMS: m/z: calcd for $C_{16}H_{11}O_4^+$: 267.06628; found: 267.06646 $[M-H]^+$; calcd for $C_{15}H_9O_4^+$: 253.05063; found: 253.05025 $[M-CH_3]^+$) as the synthesised flavylium. The ^{1}H NMR spectra of the isolated and of the synthesised compounds in acidic CD_3OD are identical, except for some peak overlap owing to the presence of minor impurities in the isolated sample.

Synthesis of 7,4′-dihydroxy-5-methoxyflavylium hydrogen sulfate: The title compound was prepared from condensation of 4′-hydroxyacetophenone (0.575 g, 4.2 mmol) and 2,4-dihydroxy-6-methoxybenzaldehyde[23] (0.710 g, 4.2 mmol). The reagents were dissolved in acetic acid (20 cm^3), and concentrated sulphuric acid (5 cm^3) was added; the temperature was kept below 50 °C (≈10 min). The red solution was stirred overnight. Addition of diethyl ether led to the precipitation of a deep-red solid that was filtered, washed with cold water and with diethyl ether, and dried under vacuum to give the product (0.707 g, 46% not optimised). The product can be recrystallised from acetic acid. ^{1}H NMR (400 MHz, CD_3OD/CF_3CO_2D, 30 °C, $\mathbf{AH}^+$ form): see Table 3 (values are in agreement with published data for this compound);[24] ^{1}H NMR (D_2O/NaOD, pD > 12, 30 °C, equilibrated, $\mathbf{Ct}^{2-}$ form): $\delta = 3.59$ (s, 3H; OCH_3), 5.33 (s, 1H; H6 or H8), 6.37 (d, $J = 9.0$ Hz, 2H; H3′+H5′), 7.51 (d, $J = 15.9$ Hz, 1H; H3), 7.58–7.63 (m, 3H; H6 or H8, H2′+H6′), 8.09 ppm (d, $J = 15.9$ Hz, 1H; H4); HRMS: m/z: calcd for $C_{16}H_{11}O_4^+$: 267.06628; found: 267.06634 $[M-H]^+$; calcd for $C_{15}H_9O_4^+$: 253.05063; found: 253.04991 $[M-CH_3]^+$; elemental analysis calcd (%) for $C_{16}H_{14}O_8S \cdot 3.5H_2O$ ($M_r = 429.40$ g mol^{-1}): C 44.76, H 4.93, S 7.47; found: C 44.91, H 4.02, S 7.35.

Table 3. ^{1}H and ^{13}C NMR data[a] for 7,4′-dihydroxy-5-methoxyflavylium hydrogen sulfonate.

Position	^{1}H NMR δ [ppm] (J [Hz])	COSY	^{13}C NMR δ [ppm]	HMBC[b]
2			173.1	
3	8.09 (d, 9.2)	4	111.1	C2, C10
4	9.08 (d, 9.2)	3	149.1	C2, C9, C5
5			161.0	
6	6.78 (s)	8	100.9	C5, C10, C8
7			160.3	
8	7.03 (s)	6	96.7	C7, C10, C6
9			172.4	
10			113.8	
1′			121.0	
2′,6	8.32 (d, 9.3)	3′, 5′	133.4	C2, C4′, (C2′, C6′)
3′,5′	7.07 (d, 9.3)	2′, 6′	118.5	(C3′, C5′), C1′
4′			167.6	
5-OCH_3	4.09 (s)		57.8	C5

[a] See the Experimental Section for details. [b] Correlation from H to the indicated carbon atoms.

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[1] C. Büllow, H. Wagner, *Ber. Dtsch. Chem. Ges.* **1901**, *34*, 1782.
[2] a) R. Willsttäter, A. E. Everest, *Justus Liebigs Ann. Chem.* **1913**, *401*, 189–232; b) R. Willsttäter, H. Mallinson, *Justus Liebigs Ann. Chem.* **1915**, *408*, 15–41; c) R. Willsttäter, H. Mallinson, *Justus Liebigs Ann. Chem.* **1915**, *408*, 147–162.
[3] a) A. G. Perkin, R. Robinson, *J. Chem. Soc.* **1927**, 3015-; b) D. Pratt, R. Robinson, A. Robertson, *J. Chem. Soc.* **1927**, 1975.
[4] a) F. M. Dean, *Naturally Occurring Oxygen Ring Compounds*, Butterworths, London, **1963**, p. 388, p. 412; b) G. Cadillo, L. Merlini, G. Nasini, P. Salvadori, *J. Chem. Soc. C* **1971**, 3967–3970; c) H. G. M. Edwards, L. F. C. de Oliveira, H. D. V. Prendergast, *Analyst* **2004**, *129*, 134–138.
[5] R. Adolt, J. Pavlis, *Trees* **2004**, *18*, 43–53.
[6] Cennino Cennini in *Il libbro dell'Arte* (Eds.: F. Brunello), Neri Pozza Editore, Vicenza, **1982**, p. 44.
[7] a) H. Brockmann, R. Haase, *Ber. Dtsch. Chem. Ges. B* **1936**, *69*, 1950–1954; b) H. Brockmann, R. Haase, *Ber. Dtsch. Chem. Ges. B* **1937**, *70*, 1733–1738; c) The authors stated that the most common origin for the commercial (Merck) resin was the palm tree *Calamus draco* (*Daemonorops draco*).
[8] H. Brockmann, H. Junge, *Ber. Dtsch. Chem. Ges. B* **1943**, *76*, 751–763.
[9] a) A. Robertson, W. B. Whalley, *J. Chem. Soc.* **1950**, 1882–1884; b) A. Robertson, W. B. Whalley, J. Yates, *J. Chem. Soc.* **1950**, 3117–3123; c) A. A. Olaniyi, J. W. Powell, W. B. Whalley, *J. Chem. Soc.*

Perkin Trans. 1 **1973**, 179–184; d) E. O. P. Agbakwuru, W. B. Whalley, *J. Chem. Soc. Perkin Trans. 1* **1976**, 1392–1394.

[10] a) L. Camarda, L. Merlini, G. Nasini, *Heterocycles* **1983**, *20*, 39–43; b) A. Arnone, G. Nasini, O. V. Pava, L. Merlini, *J. Nat. Prod.* **1997**, *60*, 971–975; c) M. Masaoud, H. Ripperger, A. Porzel, G. Adam, *Phytochemistry* **1995**, *38*, 745–749; d) M. Masaoud, J. Schmidt, G. Adam, *Phytochemistry* **1995**, *38*, 795–796; e) A. G. González, F. León, L. Sánchez-Pinto, J. I. Padrón, J. Bermejo, *J. Nat. Prod.* **2000**, *63*, 1297–1299.

[11] Q. Zheng, H. Li, Y. Zhang, *Helv. Chim. Acta* **2004**, *87*, 1167–1171.

[12] E. Haslam, *Practical Polyphenolics: From Structure to Molecular Recognition and Physiological Action*, Cambridge University Press, Cambridge, **1998**, p. 263.

[13] Anthocyanidins are the aglycones of anthocyanins, and this term was proposed by R. Willstätter in 1913.[2a] The structures identified by Willstätter were the anthocyanidin chromophores; only through the work of Robinson and others was the type of the sugar groups able to be determined. It is important to remember that anthocyanidins do not exist in nature.

[14] J. R. Brouillard, J. E. Dubois, *J. Am. Chem. Soc.* **1977**, *99*, 1359.

[15] R. A. McClelland, S. Gedge, *J. Am. Chem. Soc.* **1980**, *102*, 5838.

[16] a) F. Pina, *J. Chem. Soc. Faraday Trans.* **1998**, *94*, 2109–2116; b) F. Pina, M. Maestri, V. Balzani in *Handbook of Photochemistry and Photobiology, Vol. 3: Supramolecular Photochemistry* (Eds.: H. S. Nalwa), American Scientific Publishers, **2003**, pp. 411–450; c) F. Pina, M. J. Melo, A. J. Parola, M. Maestri, V. Balzani, *Chem. Eur. J.* **1998**, *4*, 2001–2007; d) F. Pina, J. C. Lima, A. J. Parola, C. A. M. Afonso, *Angew. Chem.* **2004**, *116*, 1551–1553; *Angew. Chem. Int. Ed.* **2004**, *43*, 1525–1527; e) F. Pina, M. Maestri, V. Balzani, *Chem. Commun.* **1999**, 107–114.

[17] a) D. Amic, N. Trinajstic, *J. Chem. Soc. Perkin Trans. 2* **1991**, 891–895; b) J. M. Baranac, D. S. Amic, *J. Agric. Food Chem.* **1990**, *38*, 2111–2115.

[18] a) B. Zorn, A. J. García-Piñeres, V. Castro, R. Murillo, G. Mora, I. Merfort, *Phytochemistry* **2001**, *56*, 831–835; b) B. Devia, G. Llabres, J. Wouters, L. Dupont, M. T. Escribano-Bailon, S. Pascual-Teresa, L. Angenot, M. Tits, *Phytochem. Anal.* **2002**, *13*, 114–120.

[19] M. J. Melo, S. Moura, A. Roque, M. Maestri, F. Pina, *J. Photochem. Photobiol. A* **2000**, *135*, 33–39.

[20] a) T. Goto, T. Kondo, *Angew. Chem.* **1991**, *103*, 17–33; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 17–33; b) T. Kondo, K. Yoshida, A. Nakagawa, T. Kawai, H. Tamura, T. Goto, *Nature* **1992**, *358*, 515–518; c) T. Kondo, M. Ueda, K. Yoshida, K. Titani, M. Isobe, T. Goto, *J. Am. Chem. Soc.* **1994**, *116*, 7457–7458; d) T. Kondo, K.-I. Oyama, K. Yoshida, *Angew. Chem.* **2001**, *113*, 918–922; *Angew. Chem. Int. Ed.* **2001**, *40*, 894–897.

[21] Dracoflavylium was not identified as the major red product in all of the samples; studies are currently being carried out to understand under what conditions this compound is predominant.

[22] K. V. Casteele, H. Geiger, R. de Loose, C. F. van Sumere, *J. Chrom.* **1983**, *259*, 291–300.

[23] O. Gia, A. Anselmo, M. T. Conconi, C. Antonello, E. Uriarte, S. Caffieri, *J. Med. Chem.* **1996**, *39*, 4489–4496.

[24] L. Costantino, G. Rastelli, M. C. Rossi, A. Albasini, *J. Chem. Soc. Perkin Trans. 2* **1995**, 227–234.

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