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Synthesis of Novel 3-Alkyl-3′,4′,5,7-Tetrahydroxyflavones

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Novel 3-alkyl-3′,4′,5,7-tetrahydroxyflavones have been prepared. The synthetic strategy involves the preparation of 1-(2-hydroxy-4,6-dimethoxyphenyl)alkan-1-ones from the Friedel–Crafts acylation of phloroglucinol followed by methylation. These key compounds were submitted to the three-step Baker–Venkataraman method, giving the 3-alkyl-3′,4′,5,7-tetramethoxyflavones, which were demethylated with boron tribromide.

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Introduction

Flavonoids are a group of low-molecular weight molecules widely distributed in the plant kingdom, and represent a significant part of the average western daily diet because they are ubiquitous in fruits, vegetables, and beverages.[1] The interest in this type of compounds has greatly grown in the past decades, owing to their antioxidant properties and to the potential health benefits in the treatment of deadly diseases involving substantial oxidative processes, such as inflammatory and heart disease, cancer, and HIV.[2–5] Among these phenolic compounds, the flavones and flavonols are the most common classes, being the first derivatives responsible for most of the important biological activities assigned to flavonoids.

Beneficial effects of flavones have been described for cancer,[3] and against bacteria,[4,5] viral infections[6] and inflammations,[5,7] but one of the most reported activities is the antioxidant one.[2,8] Several studies have reported on the qualitative structure–activity relationships for flavone-mediated antioxidant activities and have stressed the importance of the catechol moiety in the B-ring, the 4′-OH group conjugated with the 3-OH or 4-keto functions of the C-ring through the C2=C3 double bond and the additional presence of 3- and 5-hydroxyl groups in the flavone molecular structure to achieve efficient antioxidant action.[2,8] In addition, the antioxidant efficiency of hydroxyflavones has been related to the number of hydroxyl groups in the molecule, and also to their hydrogen radical-donating abilities.[8] A great number of studies have demonstrated that quercetin **1**,[2] a flavonol-type compound, and luteolin **2**,[9] a flavone-type compound, are powerful antioxidant agents (Scheme 1).

Recent studies showed that lipophilic flavones bearing methyl, isopropyl, benzyl, or isoprenyl groups enhance the binding affinity towards P-glycoprotein and the modulation of cancer cell chemoresistance.[3a] Vitamin E (α-tocopherol) **3**, a lipophilic antioxidant agent, is thought to be the major non-enzymatic antioxidant present in the lipid structures of cells and lipoproteins that reacts with peroxyl radicals, inhibiting the propagation cycle of lipid peroxidation and decreasing the modification of low-density lipoprotein, and preventing the development of atherosclerosis.[2a,10] The lipophilic character of this antioxidant agent can also be realized by its higher protection of mitochondrial membrane integrity against the effect of primary reactive oxygen species compared with other hydrophilic compounds.[11] However, a synergic effect can occur when both hydrophilic and lipophilic antioxidants are present.[8j,12] For instance, myricetin (3,3′,4′,5,5′,7-hexahydroxyflavone) reacts faster and with twice as many oxygen-centred radicals compared with vitamin E **3**, but fails to protect vitamin E-deficient microsomes from lipid peroxidation. However, compounds whose structures consist of polyhydroxylated flavones bearing lipophilic chains similar to that of vitamin E **3** on their C7 carbon circumvent this situation, being effective protectors of vitamin E-deficient microsomes.[8j] Taking into consideration these results and pursuing our studies on chromone-type compounds with potential antioxidant activity,[13] we decided to devote some attention to the synthesis of luteolin analogues bearing a lipophilic 3-alkyl chain with variable length for further biological activity. It is expected these compounds might have better pharmacokinetics in humans than other types of polyhydroxyflavones (e.g. quercetin),[14] which are not well absorbed and are extensively metabolized, and could behave as real antioxidants by scavenging free radicals. 3-Alkyl-3′,4′-dihydroxypolymethoxyflavone derivatives have already been described as inhibitors of arachidonate 5-lipoxygenase.[15]

Results and Discussion

Chemistry

The synthesis of 3-alkyl-3′,4′,5,7-tetrahydroxyflavones **9a**–**d** began with the synthesis of the key compounds 1-(2-hydroxy-4,6-dimethoxyphenyl)alkan-1-ones **4a**–**d**. Fries rearrangement of 1-acyloxy-3,5-dihydroxybenzenes was our first approach, but the treatment of 1-octanoyloxy-3,5-dihydroxybenzene with aluminium(III) chloride under different experimental conditions (using 1,2,4-trichlorobenzene as solvent or solvent-free molten conditions) did not afford the corresponding and expected ketone. In the second attempt, the direct acylation of 1,3,5-trimethoxybenzene with two molar equiv. of octanoyl chloride in the presence of $AlCl_3$[16] was attempted, but this procedure was also unproductive as the low-yield formation of a mixture

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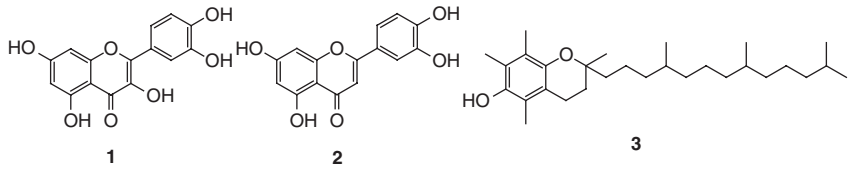
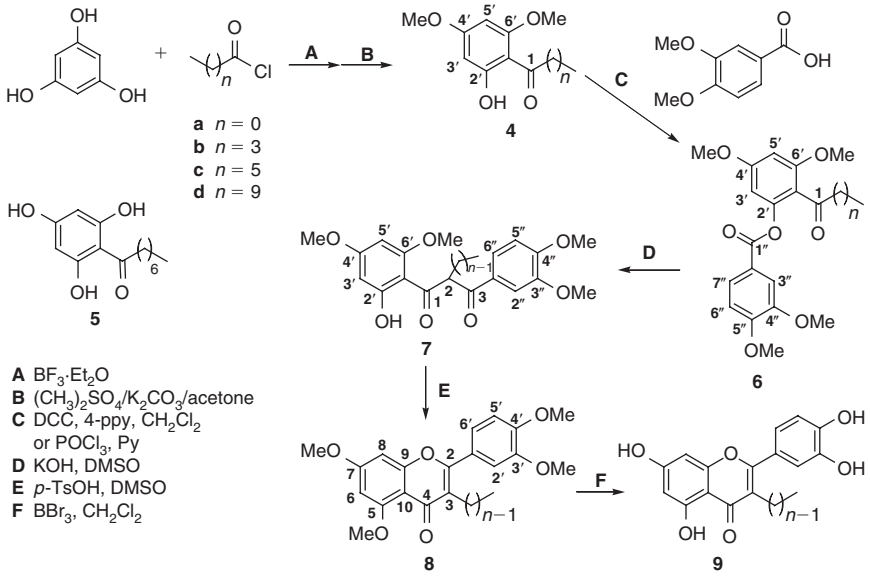


Scheme 1.



Scheme 2.

of mono- and diacylated products was obtained,[17] the monoacylated product being the minor one. Changes in reaction time (from 24 to 12 h) and amount of octanoyl chloride (from 2 to 1 equiv.) did not improve the yield of the monoacylated product. Then, we changed the Friedel–Crafts reaction catalyst to a diethyl ether solution of BF_3,[18] and the acylation of phloroglucinol with octanoyl chloride in the presence of $BF_3 \cdot Et_2O$ was attempted (Scheme 1). Attempts to isolate the corresponding 1-(2,4,6-trihydroxyphenyl)octan-1-one **5** proved to be unsuccessful, because a mixture of compounds was always obtained. To circumvent this problem, we decided to perform a quick purification of the raw material obtained by column chromatography, to eliminate most of the undesired by-products, and immediately proceeded with the protection of two hydroxyl groups by treatment of the residue obtained with methyl sulfate under basic conditions (see Experimental). The desired 1-(2-hydroxy-4,6-dimethoxyphenyl)octan-1-one **4c** was obtained in a moderate overall yield (34%). A similar procedure was applied to the reaction of phoroglucinol with propanoyl, hexanoyl, or dodecanoyl chloride, followed by methylation, affording the 1-(2-hydroxy-4,6-dimethoxyphenyl)alkan-1-ones **4a**, **b**, **d** in moderate yields (32–46%; Scheme 1).

The esterification of 1-(2-hydroxy-4,6-dimethoxyphenyl) alkan-1-ones **4a**–**d** was attempted by reaction with 3,4-dimethoxybenzoyl chloride, prepared in situ from 3,4-dimethoxybenzoic acid and phosphorous oxychloride in dry pyridine.[19] However, after an extensive study of this reaction by changing the amounts of phosphorous oxychloride (2.5 or 5 equiv.), the reaction temperatures (room temperature, 60, or 100°C) and times (12, 24, or 48 h), the expected esters **7a**–**d** were obtained in low to moderate yield (16–37%). As these results were not satisfactory, we decided to use *N*,*N*-dicyclohexylcarbodiimide (DCC) as coupling esterification agent in the presence of a catalytic amount of 4-pyrrolidinopyridine (4-ppy).[20] Treatment of 1-(2-hydroxy-4,6-dimethoxyphenyl)octan-1-one **4c** with 3,4-dimethoxybenzoic acid with an equivalent molar amount of DCC and a catalytic amount of 4-ppy in CH_2Cl_2 for 24 h led to the formation of ester **6c** in moderate yield (38%). Increasing the reaction time to 7 days improved the yield of **6c** to 72%, but it was necessary to add a new batch of DCC and 4-ppy to improve the yield up to 94% (see Experimental). Under similar conditions, esters **6a**, **b**, **d** were obtained in excellent yields (89–94%).

Baker–Venkataraman rearrangement of esters **6a**–**d** with potassium hydroxide in DMSO afforded β-diketones **7a**–**d** in good yields (60–75%); these were submitted to a cyclodehydration process with a *p*-toluenesulfonic acid/DMSO mixture, leading to the synthesis of 3-alkyl-3′,4′,5,7-tetramethoxyflavones **8a**–**d** in very good yields (77–95%).

The final step of our synthetic route consisted of the demethylation of flavones **8a**–**d**, and this was performed by treatment with boron tribromide (2.5 equiv. per methyl group) in CH_2Cl_2 for 48 h (Scheme 2). The 7-OMe was the most difficult group to be cleaved, as 3-hexyl-3′,4′,5-trihydroxy-7-methoxyflavones were obtained when the demethylation of 3-hexyl-3′,4′,5,7-tetramethoxyflavone **8c** was complete after 24 h of reaction.[21]

NMR Spectroscopy

The main features of the ^{1}H NMR spectra of each 1-(2-hydroxy-4,6-dimethoxyphenyl)alkan-1-one **4a**–**d** are the high-frequency singlet at δ_H 14.12–14.13, due to hydroxyl protons involved in intramolecular hydrogen bonds with the carbonyl groups, the two singlets at δ_H 3.82–3.86, assigned to the 4- and 6-methoxy

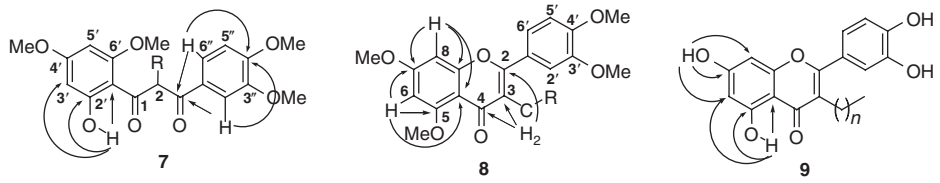


Fig. 1. Main connectivities found in the heteronuclear multiple bond coherence spectra of compounds **7**, **8**, and **9**.

groups, and the two doublets δ_H 5.92–5.93 and 6.06–6.07, attributed to the resonances of H5′ and H3′, respectively. The typical carbon resonance at δ_C 206.1–206.4 in their ^{13}C NMR spectra also confirms the presence of a ketone carbonyl group. The formation of esters **6a**–**d** can be inferred from the absence of the signals due to the hydroxyl proton singlets in their ^1H NMR spectra and the presence of an ester carbonyl group at δ_C 164.4–164.5 in their ^{13}C NMR spectra.

The appearance of only one hydroxyl resonance at high-frequency values (δ_H 13.87) in the ^1H NMR spectra of β-diketones **7a**–**d** suggests the presence of only one tautomer, as depicted in Scheme 2, and the absence of a keto–enol tautomeric equilibrium that is seen for other types of diketones.[22] These structures were also supported by the carbon resonances of two ketone carbonyl groups, appearing at δ_C 195.6–195.8 and 200.6–201.4, in their ^{13}C NMR spectra, and assigned to C3 and C1, respectively. The unequivocal assignment of these carbon resonances and those of the always difficult to differentiate C3′ and C5′[23] were confirmed by the connectivities found in the heteronuclear multiple quantum coherence (HMBC) spectra of diketones **7a**–**d** (Fig. 1).

The connectivities found in the HMBC spectra of polymethoxyflavones **8a**–**d** supported their structures and allowed the assignment of the quaternary carbons, mainly those of the A and C rings (Fig. 1). From the ^1H NMR spectra of polyhydroxyflavones **9a**–**d**, it is important to notice the high-frequency resonances, appearing as four singlets at δ_H 9.39–9.42, 9.64–9.65, 10.81–10.85, and 13.09, due to the proton resonances of 3′-OH, 4′-OH, 7-OH, and 5-OH, respectively and the important connectivities presented by two of these hydroxyl protons (Fig. 1).

Conclusions

The Friedel–Crafts acylation of phloroglucinol with appropriate long-chain alkanoyl chlorides in the presence of $BF_3{\cdot}Et_2O$, followed by methylation with methyl sulfate in alkaline medium gave 1-(2-hydroxy-4,6-dimethoxyphenyl)-1-alkan-1-ones **4a**–**d**. These compounds **4a**–**d** were esterified with 3,4-dimethoxybenzoic acid, with DCC and 4-ppy as coupling agents. Esters **6a**–**d** were submitted to a Baker–Venkataraman rearrangement, giving the β-diketones 2-alkyl-1-(2-hydroxy-4,6-dimethoxyphenyl)-3-(3,4-dimethoxyphenyl)propan-1,3-diones **7a**–**d**; these were converted to the 3-alkyl-3′,4′,5,7-tetramethoxyflavones **8a**–**d** by cyclodehydration with *p*-toluenesulfonic acid in DMSO. Finally, the demethylation of **8a**–**d** with boron tribromide afforded the novel 3-alkyl-3′,4′,5,7-tetrahydroxyflavones **9a**–**d**.

Experimental

Melting points were measured in a Griffin–Gallenkamp apparatus and are uncorrected. Positive-ion electrospray ionization (ESI) mass spectra were acquired using a Q-TOF 2 instrument (diluting 1 μL of the sample chloroform solution ($\sim 10^{-5}$ M) in 200 μL of 0.1% trifluoroacetic acid/methanol solution. Nitrogen was used as nebulizer gas and argon as collision gas. The needle voltage was set at 3000 V, with the ion source at 80°C and desolvation temperature at 150°C. Cone voltage was 35 V). The high-resolution mass spectra (electron impact (EI), 70 eV) were measured on a VG Autospec M mass spectrometer. Elemental analyses were obtained with a LECO 932 CHN analyser (University of Aveiro). ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance 300 spectrometer (at 300.13 and 75.47 MHz, respectively) unless stated otherwise; chemical shifts are reported in ppm (δ) using TMS as internal reference and coupling constants (J) are given in Hz. The ^{13}C unequivocal assignments were made with the aid of two-dimensional gradient selected heteronuclear single quantum coherence (*g*HSQC) and two-dimensional gradient selected heteronuclear multiple quantum coherence (*g*HMBC) (delays for one-bond and long-range J C–H couplings were optimized for 145 and 7 Hz, respectively) experiments. Column chromatography was performed with Merck silica gel 60.

General Procedure for the Synthesis of 1-(2-Hydroxy-4,6-dimethoxyphenyl)alkan-1-ones ***4a–d***

$BF_3{\cdot}Et_2O$ (11.1 mL, 39.8 mmol) was added dropwise to an ice-cooled mixture of 1,3,5-trihydroxybenzene (phloroglucinol) (2.00 g, 15.9 mmol) and the appropriate alkanoyl chloride (15.9 mmol). After the addition, the ice bath was removed and the reaction mixture was stirred under nitrogen at room temperature for 48 h. Then the solution was poured into ice (50 g) and water (150 mL) and the mixture obtained was extracted with ethyl acetate (3 × 150 mL); the organic layer was washed with water and the solvent was evaporated to dryness. The residue obtained was submitted to column chromatography to remove most of the impurities; the major component was collected by using a mixture of CH_2Cl_2/acetone (20:1) as eluent.

Anhydrous K_2CO_3 (8.8 g, 63.6 mmol) and $(CH_3)_2SO_4$ were added (6.02 mL, 63.6 mmol) to the crude product obtained taken up in acetone (150 mL). The reaction mixture was heated to 50–60°C under nitrogen for 1.5 h. After this period, K_2CO_3 was filtered off, washed with acetone (100 mL), and the solvent was evaporated to dryness. The residue was purified by silica gel column chromatography using a 1:1 mixture of light petroleum/CH_2Cl_2 as eluent. The solvent was evaporated to dryness and the residue was recrystallized from ethanol in each case to give 1-(2-hydroxy-4,6-dimethoxyphenyl)alkan-1-ones **4a**–**d** as white needles.

1-(2-Hydroxy-4,6-dimethoxyphenyl)propan-1-one ***4a***

Yield: (1.10 g, 33%), mp 106–107°C. δ_H ($CDCl_3$) 1.16 (3H, t, J 7.2, H3), 3.03 (2H, q, J 7.2, H2), 3.82 (3H, s, 4′-OCH_3), 3.86 (3H, s, 6′-OCH_3), 5.93 (1H, d, J 2.4, H5′), 6.07 (1H, d, J 2.4, H3′), 14.12 (1H, s, 2′-OH). δ_C ($CDCl_3$) 8.6 (C3), 37.4 (C2), 55.5 (4′,6′-OCH_3), 90.7 (C5′), 93.5 (C3′), 105.7 (C1′), 162.8 (C6′), 165.7 (C4′), 167.5 (C2′), 206.4 (C1). m/z 211 $[M+H]^+$, 233 $[M+Na]^+$. Found: m/z 210.0895. $M^{+\bullet}$ requires 210.0892.

1-(2-Hydroxy-4,6-dimethoxyphenyl)hexan-1-one ***4b***

Yield: (1.28 g, 32%), mp 74–75°C. δ_H ($CDCl_3$) 0.91 (3H, t, *J* 6.7, H6), 1.32–1.37 (4H, m, H4 and H5), 1.66 (2H, quint., *J* 7.2, H3), 2.95–3.00 (2H, m, H2), 3.82 (3H, s, 4′-OCH_3), 3.85 (3H, s, 6′-OCH_3), 5.92 (1H, d, *J* 2.4, H5′), 6.07 (1H, d, *J* 2.4, H3′), 14.13 (1H, s, 2′-OH). δ_C ($CDCl_3$) 14.0 (C6), 22.6 (C5), 24.5 (C3), 31.7 (C4), 44.2 (C2), 55.5 (4′,6′-OCH_3), 90.8 (C5′), 93.6 (C3′), 105.7 (C1′), 162.7 (C6′), 165.7 (C4′), 167.7 (C2′), 206.1 (C1). *m/z* (ESI-MS) 253 $[M+H]^+$, 275 $[M+Na]^+$. (Found: C 66.7, H 7.7. $C_{14}H_{20}O_4$ requires C 66.7, H 8.0%.)

1-(2-Hydroxy-4,6-dimethoxyphenyl)octan-1-one ***4c***

Yield: (1.52 g, 34%), mp 73–74°C. δ_H ($CDCl_3$) 0.86–0.91 (3H, m, H8), 1.29–1.34 (8H, m, H4 to H7), 1.65 (2H, quint., *J* 7.2, H3), 2.95–3.00 (2H, m, H2), 3.82 (3H, s, 4′-OCH_3), 3.85 (3H, s, 6′-OCH_3), 5.92 (1H, d, *J* 2.4, H5′), 6.06 (1H, d, *J* 2.4, H3′), 14.13 (1H, s, 2′-OH). δ_C ($CDCl_3$) 14.1 (C8), 22.6 (C7), 24.8 (C3), 29.2 and 29.5 (C4 and C5), 31.7 (C6), 44.3 (C2), 55.5 (4′,6′-OCH_3), 90.7 (C5′), 93.5 (C3′), 105.7 (C1′), 162.7 (C6′), 165.7 (C4′), 167.6 (C2′), 206.1 (C1). *m/z* 281 $[M+H]^+$, 303 $[M+Na]^+$, 583 $[2M+Na]^+$. (Found: C 68.7, H 8.4. $C_{16}H_{24}O_4$ requires C 68.5, H 8.6%.)

1-(2-Hydroxy-4,6-dimethoxyphenyl)dodecan-1-one ***4d***

Yield: (2.46 g, 46%), mp 80–83°C. δ_H ($CDCl_3$) 0.88 (3H, t, *J* 6.7, H12), 1.26–1.32 (16H, m, H4 to H11), 1.60–1.70 (2H, m, H3), 2.96–2.99 (2H, m, H2), 3.82 (3H, s, 4′-OCH_3), 3.85 (3H, s, 6′-OCH_3), 5.92 (1H, d, *J* 2.4, H5′), 6.06 (1H, d, *J* 2.4, H3′), 14.13 (1H, s, 2′-OH). δ_C ($CDCl_3$) 14.1 (C12), 22.7, 29.3, 29.53, 29.54, 29.6 and 31.9 (C4 to C11), 24.8 (C3), 44.3 (C2), 55.5 (4′,6′-OCH_3), 90.7 (C5′), 93.6 (C3′), 105.7 (C1′), 162.7 (C6′), 165.7 (C4′), 167.6 (C2′), 206.1 (C1). *m/z* (ESI-MS) 337 $[M+H]^+$, 359 $[M+Na]^+$, 695 $[2M+Na]^+$. (Found: C 71.4, H 9.6. $C_{20}H_{32}O_4$ requires C 71.4, H 9.6%.)

General Procedure for the Synthesis of 1-[2-(3,4-Dimethoxybenzoyloxy)-4,6-dimethoxyphenyl]alkan-1-ones ***6a–d***

3,4-Dimethoxybenzoic acid (0.95 g, 5.2 mmol), *N*,*N*-dicyclohexylcarbodiimide (1.07 g, 5.2 mmol) and 4-pyrrolidinopyridine (77.1 mg, 0.52 mmol) were added to a solution of the appropriate 1-(2-hydroxy-4,6-dimethoxyphenyl)alkan-1-ones **4a–d** (5.2 mmol) in CH_2Cl_2 (100 mL). The mixture was stirred under nitrogen at room temperature for 7 days, then a new portion of 3,4-dimethoxybenzoic acid (0.95 g, 5.2 mmol), *N*,*N*-dicyclohexylcarbodiimide (1.07 g, 5.2 mmol), and 4-pyrrolidinopyridine (77.1 mg, 0.52 mmol) were added and the reaction continued for another 7 days. After that period, the urea formed was filtered off and washed with CH_2Cl_2 (50 mL). The solution was concentrated under reduced pressure and purified by silica gel column chromatography using a mixture of light petroleum/ethyl acetate (5:2) as eluent. The solvent was evaporated to dryness and the residue was crystallized in each case from a mixture of light petroleum/CH_2Cl_2 to give 1-[2-(3,4-dimethoxybenzoyloxy)-4,6-dimethoxyphenyl]alkan-1-ones **6a–d** as white powders.

1-[2-(3,4-Dimethoxybenzoyloxy)-4,6-dimethoxyphenyl]propan-1-one ***6a***

Yield: (1.75 g, 90%), mp 136–138°C. δ_H ($CDCl_3$) 1.07 (3H, t, *J* 7.3, H3), 2.81 (2H, q, *J* 7.3, H2), 3.82 and 3.84 (6H, s, 4′,6′-OCH_3), 3.95 and 3.96 (6H, s, 4″,5″-OCH_3), 6.40 (2H, AB, *J* 2.3, H3′ and H5′), 6.93 (1H, d, *J* 8.5, H6″), 7.60 (1H, d, *J* 2.0, H3″), 7.78 (1H, dd, *J* 2.0 and 8.5, H7″). δ_C ($CDCl_3$) 8.2 (C3), 37.5 (C2), 55.6 and 55.9 (4′,6′-OCH_3), 56.0 and 56.1 (4″,5″-OCH_3), 96.5 and 99.9 (C3′ and C5′), 110.4 (C6″), 112.3 (C3″), 117.5 (C1′), 121.4 (C2″), 124.6 (C7″), 148.7 (C4″), 149.4 (C2′), 153.6 (C5″), 158.5 and 161.8 (C4′ and C6′), 164.6 (C1″), 203.3 (C1). *m/z* 397 $[M+Na]^+$, 413 $[M+K]^+$, 771 $[2M+Na]^+$. (Found: C 63.9, H 5.9. $C_{20}H_{22}O_7$ requires C 64.2, H 5.9%.)

1-[2-(3,4-Dimethoxybenzoyloxy)-4,6-dimethoxyphenyl]hexan-1-one ***6b***

Yield: (1.93 g, 89%), mp 93–95°C. δ_H ($CDCl_3$) 0.81 (3H, t, *J* 6.8, H6), 1.18–1.26 (4H, m, H4 and H5), 1.59 (2H, quint., *J* 7.3, H3), 2.78 (2H, t, *J* 7.3, H2), 3.81 and 3.83 (6H, s, 4′,6′-OCH_3), 3.95 (6H, s, 4″,5″-OCH_3), 6.40 (2H, AB, *J* 2.4, H3′ and H5′), 6.93 (1H, d, *J* 8.5, H6″), 7.60 (1H, d, *J* 1.9, H3″), 7.79 (1H, dd, *J* 1.9 and 8.5, H7″). δ_C ($CDCl_3$) 13.8 (C6), 22.3 and 31.2 (C4 and C5), 23.5 (C3), 44.1 (C2), 55.4 and 55.7 (4′,6′-OCH_3), 55.8 and 55.9 (4″,5″-OCH_3), 96.3 and 99.9 (C3′ and C5′), 110.2 (C6″), 112.1 (C3″), 117.4 (C1′), 121.3 (C2″), 124.4 (C7″), 148.5 (C4″), 149.3 (C2′), 153.4 (C5″), 158.4 and 161.6 (C4′ and C6′), 164.4 (C1″), 202.5 (C1). *m/z* 439 $[M+Na]^+$, 455 $[M+K]^+$, 855 $[2M+Na]^+$, 871 $[2M+K]^+$. (Found: 66.4, H 6.9. $C_{23}H_{28}O_7$ requires C 66.3, H 6.8%.)

1-[2-(3,4-Dimethoxybenzoyloxy)-4,6-dimethoxyphenyl]octan-1-one ***6c***

Yield: (2.17 g, 94%), mp 80–82°C. δ_H ($CDCl_3$) 0.84 (3H, t, *J* 6.8, H8), 1.18–1.24 (8H, m, H4 to H7), 1.57 (2H, quint., *J* 7.3, H3), 2.77 (2H, t, *J* 7.3, H2), 3.82 and 3.84 (6H, s, 4′,6′-OCH_3), 3.95 and 3.96 (6H, s, 4″,5″-OCH_3), 6.39–6.40 (2H, m, H3′ and H5′), 6.93 (1H, d, *J* 8.5, H6″), 7.60 (1H, d, *J* 2.0, H3″), 7.78 (1H, dd, *J* 2.0 and 8.5, H7″). δ_C ($CDCl_3$) 14.1 (C8), 22.6 (C7), 31.7 (C6), 24.0 (C3), 29.1 (C4 and C5), 44.3 (C2), 55.6 and 55.8 (4′,6′-OCH_3), 56.0 and 56.1 (4″,5″-OCH_3), 96.6 and 100.0 (C3′ and C5′), 110.3 (C6″), 112.3 (C3″), 117.6 (C1′), 121.4 (C2″), 124.6 (C7″), 148.7 (C4″), 149.4 (C2′), 153.6 (C5″), 158.5 and 161.7 (C4′ and C6′), 164.6 (C1″), 202.8 (C1). *m/z* 445 $[M+H]^+$, 467 $[M+Na]^+$, 483 $[M+K]^+$, 911 $[2M+Na]^+$, 927 $[2M+K]^+$. (Found: C 67.5, H 7.2. $C_{25}H_{32}O_7$ requires C 67.6, H 7.3%.)

1-[2-(3,4-Dimethoxybenzoyloxy)-4,6-dimethoxyphenyl]dodecan-1-one ***6d***

Yield: (2.45 g, 94%), mp 45–46°C. δ_H ($CDCl_3$) 0.87 (3H, t, *J* 6.7, H12), 1.21–1.29 (16H, m, H4 to H11), 1.58 (2H, quint., *J* 7.2, H3), 2.78 (2H, t, *J* 7.2, H2), 3.82 and 3.83 (6H, s, 4′,6′-OCH_3), 3.95 and 3.96 (6H, s, 4″,5″-OCH_3), 6.39 (2H, AB, *J* 2.4, H3′ and H5′), 6.92 (1H, d, *J* 8.5, H6″), 7.60 (1H, d, *J* 2.0, H3″), 7.78 (1H, dd, *J* 2.0 and 8.5, H7″). δ_C ($CDCl_3$) 14.0 (C12), 22.6 and 31.8 (C10 and C11), 23.9 (C3), 29.1, 29.2, 29.36, 29.42, 29.5 (C4 to C9), 44.2 (C2), 55.5 and 55.7 (4′,6′-OCH_3), 55.9 and 56.0 (4″,5″-OCH_3), 96.5 and 99.9 (C3′ and C5′), 110.3 (C6″), 112.2 (C3″), 117.6 (C1′), 121.4 (C2″), 124.5 (C7″), 148.6 (C4″), 149.4 (C2′), 153.5 (C5″), 158.4 and 161.7 (C4′ and C6′), 164.5 (C1″), 202.7 (C1). *m/z* 501 $[M+H]^+$, 523 $[M+Na]^+$, 539 $[M+K]^+$. (Found: C 69.7, H 7.9. $C_{29}H_{40}O_7$ requires C 69.6, H 8.1%.)

General Procedure for the Synthesis of 2-Alkyl-1-(2-hydroxy-4,6-dimethoxyphenyl)-3-(3,4-dimethoxyphenyl)propan-1,3-diones ***7a–d***

Potassium hydroxide (powder, 0.98 g, 17.5 mmol) was added to a solution of the appropriate 1-[2-(3,4-dimethoxybenzoyloxy)-4,6-dimethoxyphenyl]alkan-1-ones **6a**–**d** (3.5 mmol) in DMSO (30 mL). The solution was stirred under nitrogen at room temperature for 1 h. After that period, the solution was poured into ice (50 g) and water (150 mL), and the pH adjusted to 4 with dilute HCl. The solid obtained was removed by filtration, taken up in $CHCl_3$ (150 mL), and the organic layer was washed with water (3 × 150 mL). The mixture was purified by silica gel column chromatography using 5:2 light petroleum/ethyl acetate as eluent. The solvent was evaporated to dryness and the residue in each case was recrystallized from a mixture of light petroleum/CH_2Cl_2 to give 2-alkyl-1-(2-hydroxy-4,6-dimethoxyphenyl)-3-(3,4-dimethoxyphenyl)propan-1,3-diones **7a**–**d** as white powders.

1-(2-Hydroxy-4,6-dimethoxyphenyl)-2-methyl-3-(3,4-dimethoxyphenyl)propan-1,3-dione ***7a***

Yield: (786 mg, 60%), mp 200–202°C. δ_H (500.13 MHz, $CDCl_3$) 1.50 (3H, d, *J* 7.1, H3), 3.36 (3H, s, 6′-OCH_3) 3.80 (3H, s, 4′-OCH_3), 3.92 (3H, s, 3″-OCH_3), 3.97 (3H, s, 4″-OCH_3), 5.34 (1H, q, *J* 7.1, H2), 5.82 (1H, d, *J* 2.4, H5′), 6.09 (1H, d, *J* 2.4, H3′), 6.94 (1H, d, *J* 8.4, H5″), 7.57 (1H, d, *J* 2.0, H2″), 7.63 (1H, dd, *J* 2.0 and 8.4, H6″), 13.87 (1H, s, 2′-OH). δ_C (125.77 MHz, $CDCl_3$) 14.2 (C3), 54.3 (C2), 55.2 (6′-OCH_3), 55.6 (4′-OCH_3), 56.0 (3″-OCH_3), 56.1 (4″-OCH_3), 90.8 (C5′), 94.0 (C3′), 105.0 (C1′), 110.0 (C5″), 110.6 (C2″), 122.8 (C6″), 128.9 (C1″), 149.1 (C3″), 153.1 (C4″), 161.6 (C6′), 166.2 (C4′), 168.0 (C2′), 196.8 (C3), 201.4 (C1). *m/z* 375 $[M+H]^+$, 397 $[M+Na]^+$, 413 $[M+K]^+$, 771 $[2M+Na]^+$, 787 $[2M+K]^+$. Found: *m/z* 374.1367. $M^{+\bullet}$ requires 374.1366.

2-Butyl-1-(2-hydroxy-4,6-dimethoxyphenyl)-3-(3,4-dimethoxyphenyl)propan-1,3-dione ***7b***

Yield: (1.05 g, 72%), mp 141–143°C. δ_H ($CDCl_3$) 0.90 (3H, t, *J* 7.0, H4‴), 1.35–1.42 (4H, m, H2‴ and H3‴), 1.79–1.90 (1H, m, H1‴), 2.09–2.21 (1H, m, H1‴), 3.43 and 3.80 (6H, s, 4′,6′-OCH_3), 3.91 (3H, s, 3″-OCH_3), 3.96 (3H, s, 4″-OCH_3), 5.31 (1H, dd, *J* 4.1 and 8.6, H2), 5.84 (1H, d, *J* 2.4, H5′), 6.08 (1H, d, *J* 2.4, H3′), 6.93 (1H, d, *J* 8.3, H5″), 7.57 (1H, d, *J* 1.9, H2″), 7.60 (1H, dd, *J* 1.9 and 8.3, H6″), 13.87 (1H, s, 2′-OH). δ_C ($CDCl_3$) 13.9 (C4‴), 22.8 and 30.8 (C2‴ and C3‴), 28.7 (C1‴), 55.2 and 55.5 (4′,6′-OCH_3), 55.9 (3″-OCH_3), 56.0 (4″-OCH_3), 59.8 (C2), 90.8 (C5′), 93.9 (C3′), 105.3 (C1′), 110.0 (C5″), 110.5 (C2″), 122.6 (C6″), 129.2 (C1″), 149.0 (C3″), 153.0 (C4″), 161.7 and 166.1 (C4′ and C6′), 168.0 (C2′), 195.6 (C3), 201.0 (C1). *m/z* 417 $[M+H]^+$, 439 $[M+Na]^+$, 455 $[M+K]^+$, 855 $[2M+Na]^+$, 871 $[2M+K]^+$. (Found: C 66.2, H 6.8. $C_{23}H_{28}O_7$ requires C 66.3, H 6.8%.)

2-Hexyl-1-(2-hydroxy-4,6-dimethoxyphenyl)-3-(3,4-dimethoxyphenyl)propan-1,3-dione ***7c***

Yield: (1.17 g, 75%), mp 105–107°C. δ_H ($CDCl_3$) 0.87 (3H, t, *J* 6.8, H6‴), 1.26–1.29 (8H, m, H2‴ to H5‴), 1.79–1.90 (1H, m, H1‴), 2.08–2.21 (1H, m, H1‴), 3.43 and 3.80 (6H, s, 4′,6′-OCH_3), 3.92 (3H, s, 3″-OCH_3), 3.97 (3H, s, 4″-OCH_3), 5.31 (1H, dd, *J* 4.1 and 8.5, H2), 5.85 (1H, d, *J* 2.3, H5′), 6.09 (1H, d, *J* 2.3, H3′), 6.94 (1H, d, *J* 8.3, H5″), 7.57 (1H, d, *J* 1.9, H2″), 7.60 (1H, dd, *J* 1.9 and 8.3, H6″), 13.87 (1H, s, 2′-OH). δ_C ($CDCl_3$) 14.1 (C6‴), 22.6 and 31.6 (C4‴ and C5‴), 28.7, 29.0 and 29.5 (C1‴ to C3‴), 55.3 and 55.6 (4′,6′-OCH_3), 55.9 (3″-OCH_3), 56.1 (4″-OCH_3), 60.0 (C2), 90.9 (C5′), 94.0 (C3′), 105.4 (C1′), 110.1 (C5″), 110.6 (C2″), 122.7 (C6″), 129.3 (C1″), 149.1 (C3″), 153.0 (C4″), 161.7 and 166.1 (C4′ and C6′), 168.1 (C2′), 195.6 (C3), 200.7 (C1). *m/z* 445 $[M+H]^+$, 467 $[M+Na]^+$, 483 $[M+K]^+$, 911 $[2M+Na]^+$, 927 $[2M+K]^+$, 1356 $[3M+Na]^+$. (Found: C 67.5, H 7.1. $C_{25}H_{32}O_7$ requires C 67.6, H 7.3%.)

2-Decyl-1-(2-hydroxy-4,6-dimethoxyphenyl)-3-(3,4-dimethoxyphenyl)propan-1,3-dione ***7d***

Yield: (1.31 g, 75%), mp 114–116°C. δ_H ($CDCl_3$) 0.87 (3H, t, *J* 6.7, H10‴), 1.25–1.42 (16H, m, H2‴ to H9‴), 1.78–1.90 (1H, m, H1‴), 2.08–2.18 (1H, m, H1‴), 3.43 and 3.80 (6H, s, 4′,6′-OCH_3), 3.92 (3H, s, 3″-OCH_3), 3.97 (3H, s, 4″-OCH_3), 5.31 (1H, dd, *J* 4.2 and 8.5, H2), 5.84 (1H, d, *J* 2.3, H5′), 6.09 (1H, d, *J* 2.3, H3′), 6.94 (1H, d, *J* 8.3, H5″), 7.57 (1H, d, *J* 2.0, H2″), 7.60 (1H, dd, *J* 2.0 and 8.3, H6″), 13.87 (1H, s, 2′-OH). δ_C ($CDCl_3$) 14.1 (C10‴), 22.6 and 31.8 (C8‴ and C9‴), 28.7 (C2‴), 29.0 (C1‴), 29.3, 29.4, 29.5 and 29.8 (C3‴ to C7‴), 55.2 and 55.5 (4′,6′-OCH_3), 55.9 (3″-OCH_3), 56.0 (4″-OCH_3), 59.9 (C2), 90.8 (C5′), 93.9 (C3′), 105.3 (C1′), 110.0 (C5″), 110.5 (C2″), 122.6 (C6″), 129.2 (C1″), 149.0 (C3″), 153.0 (C4″), 161.6 and 166.1 (C4′ and C6′), 168.0 (C2′), 195.6 (C3), 200.6 (C1). *m/z* 501 $[M+H]^+$, 523 $[M+Na]^+$, 539 $[M+K]^+$, 1024 $[2M+Na]^+$. (Found: C 69.3, H 8.1. $C_{29}H_{40}O_7$ requires C 69.6, H 8.1%.)

General Procedure for the Synthesis of 3-Alkyl-3′,4′,5,7-tetramethoxyflavones ***8a–d***

p-Toluenesulfonic acid monohydrate (199.7 mg, 1.05 mmol) was added to a solution of the appropriate 2-alkyl-1-(2-hydroxy-4,6-dimethoxyphenyl)-3-(3,4-dimethoxyphenyl)propan-1,3-dione **7a**–**d** (2.1 mmol) in DMSO (30 mL). The solution obtained was heated under nitrogen at 90°C for 15 h. After that period, the solution was poured into ice (50 g) and water (150 mL), and the solid obtained was removed by filtration. The solid was taken up in $CHCl_3$ (150 mL) and the organic layer washed with water (3 × 150 mL). After solvent evaporation, the residue was purified by silica gel column chromatography using a 5:3 mixture of light petroleum/ethyl acetate as eluent. The solvent was evaporated to dryness and the residue was in each case recrystallized from a mixture of light petroleum/CH_2Cl_2 to give the 3-alkyl-3′,4′,5,7-tetramethoxyflavones **8a**–**d** as white solids.

3′,4′,5,7-Tetramethoxy-3-methylflavone ***8a***

Yield: (711 mg, 95%), mp 172–173°C. δ_H (500.13 MHz, $CDCl_3$) 2.11 (3H, s, 3-CH_3), 3.88 (3H, s, 7-OCH_3), 3.96 (9H, s, 5,3′,4′-OCH_3), 6.36 (1H, d, *J* 2.3, H6), 6.45 (1H, d, *J* 2.3, H8), 6.98 (1H, d, *J* 8.3, H5′), 7.14 (1H, d, *J* 1.9, H2′), 7.21 (1H, dd, *J* 1.9 and 8.3, H6′). δ_C (125.77 MHz, $CDCl_3$) 11.7 (3-CH_3), 55.7 (7-OCH_3), 56.0, 56.1 and 56.3 (5,3′,4′-OCH_3), 92.2 (C8), 95.8 (C6), 108.0 (C10), 110.6 (C5′), 111.7 (C2′), 117.9 (C3), 122.3 (C6′), 125.9 (C1′), 148.7 (C3′), 150.3 (C4′), 158.2 (C2), 159.6 (C9), 160.9 (C5), 163.7 (C7), 177.7 (C4). *m/z* 357 $[M+H]^+$. Found: *m/z* 356.1250. $M^{+\bullet}$ requires 356.1260.

3-Butyl-3′,4′,5,7-tetramethoxyflavone ***8b***

Yield: (786 mg, 94%), mp 164–166°C. δ_H (500.13 MHz, $CDCl_3$) 0.87 (3H, t, *J* 7.4, H4″), 1.35 (2H, sext., *J* 7.4, H3″), 1.55–1.62 (2H, m, H2″), 2.48–2.51 (2H, m, H1″), 3.86 (3H, s, 7-OCH_3),

3.949, 3.953 and 3.96 (9H, 3s, 5,3′,4′-OCH_3), 6.34 (1H, d, *J* 2.1, H6), 6.43 (1H, d, *J* 2.1, H8), 6.98 (1H, d, *J* 8.3, H5′), 7.11 (1H, d, *J* 1.8, H2′), 7.19 (1H, dd, *J* 1.8 and 8.3, H6′). δ_C (125.77 MHz, $CDCl_3$) 13.8 (C4″), 23.0 (C3″), 25.6 (C1″), 31.4 (C2″), 55.5 (7-OCH_3), 55.9 and 56.1 (5,3′,4′-OCH_3), 92.1 (C8), 95.5 (C6), 108.2 (C10), 110.5 (C5′), 111.3 (C2′), 121.5 (C6′), 122.6 (C3), 125.9 (C1′), 148.5 (C3′), 150.1 (C4′), 158.6 (C2), 159.5 (C9), 160.8 (C5), 163.5 (C7), 177.3 (C4). *m/z* 399 $[M + H]^+$, 819 $[2M + Na]^+$, 1218 $[3M + Na]^+$. (Found: C 69.4, H 6.5. $C_{23}H_{26}O_6$ requires C 69.3, H 6.6%.)

3-Hexyl-3′,4′,5,7-tetramethoxyflavone ***8c***

Yield: (761 mg, 85%), mp 107–109°C. δ_H ($CDCl_3$) 0.85 (3H, t, *J* 6.7, H6″), 1.23–1.37 (6H, m, H3″–H5″), 1.55–1.65 (2H, m, H2″), 2.46–2.51 (2H, m, H1″), 3.86 (3H, s, 7-OCH_3), 3.94, 3.95, 3.96 (9H, 3s, 5,3′,4′-OCH_3), 6.33 (1H, d, *J* 2.2, H6), 6.42 (1H, d, *J* 2.2, H8), 6.98 (1H, d, *J* 8.3, H5′), 7.11 (1H, d, *J* 1.9, H2′), 7.19 (1H, dd, *J* 1.9 and 8.3, H6′). δ_C ($CDCl_3$) 13.8 (C6″), 22.4, 29.4 and 31.3 (C3″–C5″), 25.7 (C1″), 29.0 (C2″), 55.4 (7-OCH_3), 55.7, 55.9 (5,3′,4′-OCH_3), 91.9 (C8), 95.3 (C6), 108.0 (C10), 110.4 (C5′), 111.2 (C2′), 121.4 (C6′), 122.4 (C3), 125.7 (C1′), 148.4 (C3′), 150.0 (C4′), 158.5 (C2), 159.3 (C9), 160.6 (C5), 163.4 (C7), 177.1 (C4). *m/z* 427 $[M + H]^+$. (Found: C 70.4, H 7.1. $C_{25}H_{30}O_6$ requires C 70.4, H 7.1%.)

3-Decyl-3′,4′,5,7-tetramethoxyflavone ***8d***

Yield: (780 mg, 77%), mp 65–67°C. δ_H ($CDCl_3$) 0.87 (3H, t, *J* 6.6, H10″), 1.22–1.29 (14H, m, H3″–H9″), 1.54–1.65 (2H, m, H2″), 2.45–2.50 (2H, m, H1″), 3.87 (3H, s, 7-OCH_3), 3.94, 3.957, 3.964 (9H, 3s, 5,3′,4′-OCH_3), 6.34 (1H, d, *J* 2.2, H6), 6.43 (1H, d, *J* 2.2, H8), 6.97 (1H, d, *J* 8.3, H5′), 7.10 (1H, d, *J* 1.9, H2′), 7.18 (1H, dd, *J* 1.9 and 8.3, H6′). δ_C ($CDCl_3$) 14.1 (C10″), 22.7, 31.9 (C8″, C9″), 26.0 (C1″), 29.3, 29.4, 29.60, 29.64, 30.0 (C2″–C7″), 55.6 (7-OCH_3), 56.0, 56.3 (5,3′,4′-OCH_3), 92.2 (C8), 95.7 (C6), 108.4 (C10), 110.6 (C5′), 111.4 (C2′), 121.6 (C6′), 122.8 (C3), 126.0 (C1′), 148.6 (C3′), 150.2 (C4′), 158.7 (C2), 159.6 (C9), 160.9 (C5), 163.6 (C7), 177.4 (C4). *m/z* 483 $[M + H]^+$. (Found: C 72.1, H 7.9. $C_{29}H_{38}O_6$ requires C 72.2, H 7.9%.)

General Procedure for the Synthesis of 3-Alkyl-3′,4′,5,7-tetrahydroxyflavones ***9a–d***

A solution of the appropriate 3-alkyl-3′,4′,5,7-tetramethoxyflavone **8a**–**d** (0.6 mmol) in dry CH_2Cl_2 (5 mL) was cooled in a propan-2-ol bath at −78°C and then a solution of BBr_3 in CH_2Cl_2 (1 M, 6.0 mL, 6.0 mmol) was added dropwise. After the addition, the bath was removed and the reaction mixture was stirred under nitrogen, at room temperature, for 48 h. After that period, the solution was poured into ice (10 g) and water (15 mL). The solid obtained was filtered off and washed with water (5 × 15 mL) and then with light petroleum (5 × 15 mL). The pure 3-alkyl-3′,4′,5,7-tetrahydroxyflavones **9a**–**d** were collected in each case as yellow powders.

3′,4′,5,7-Tetrahydroxy-3-methylflavone ***9a***

Yield: (176 mg, 98%), mp 281–283°C (dec.). δ_H ([D_6]DMSO) 2.02 (3H, s, 3-CH_3), 6.19 (1H, d, *J* 2.0, H6), 6.34 (1H, d, *J* 2.0, H8), 6.90 (1H, d, *J* 8.2, H5′), 7.03 (1H, dd, *J* 2.1 and 8.2, H6′), 7.10 (1H, d, *J* 2.1, H2′), 9.43 (1H, s, 3′-OH), 9.73 (1H, s, 4′-OH), 10.85 (1H, s, 7-OH), 13.09 (1H, s, 5-OH). δ_C ([D_6]DMSO) 13.6 (3-CH_3), 93.4 (C8), 98.6 (C6), 102.8 (C10), 113.5 (C3), 115.5 (C5′), 116.1 (C2′), 121.2 (C6′), 123.2 (C1′), 145.2 (C3′), 148.0 (C4′), 157.3 (C9), 161.4 and 161.5 (C2 and C5), 164.1 (C7), 181.9 (C4). *m/z* 301 $[M + H]^+$, 323 $[M + Na]^+$. Found: *m/z* 300.0630. $M^{+\bullet}$ requires 300.0634.

3-Butyl-3′,4′,5,7-tetrahydroxyflavone ***9b***

Yield: (201 mg, 98%), mp 188–191°C. δ_H ([D_6]DMSO) 0.83 (3H, t, *J* 7.3, H4″), 1.26 (2H, sext., *J* 7.3, H3″), 1.42–1.52 (1H, m, H2″), 2.40–2.45 (2H, m, H1″), 6.19 (1H, d, *J* 2.1, H6), 6.31 (1H, d, *J* 2.1, H8), 6.89 (1H, d, *J* 8.2, H5′), 6.95 (1H, dd, *J* 2.0, 8.2, H6′), 7.02 (1H, d, *J* 2.0, H2′), 9.42 (1H, s, 3′-OH), 9.65 (1H, s, 4′-OH), 10.82 (1H, s, 7-OH), 13.09 (1H, s, 5-OH). δ_C ([D_6]DMSO) 13.6 (C4″), 22.2 (C3″), 24.2 (C1″), 30.6 (C2″), 93.3 (C8), 98.5 (C6), 103.1 (C10), 115.5 (C5′), 115.8 (C2′), 118.4 (C3), 120.4 (C6′), 123.4 (C1′), 145.2 (C3′), 147.8 (C4′), 157.3 (C9), 161.5 (C5), 162.3 (C2), 164.1 (C7), 181.8 (C4). *m/z* 343 $[M + H]^+$, 365 $[M + Na]^+$. (Found: C 66.4, H 5.2. $C_{19}H_{18}O_6$ requires C 66.7, H 5.3%.)

3-Hexyl-3′,4′,5,7-tetrahydroxyflavone ***9c***

Yield: (196 mg, 88%), mp 181–183°C. δ_H ([D_6]DMSO) 0.82 (3H, t, *J* 6.6, H6″), 1.20–1.25 (6H, m, H3″–H5″), 1.41–1.49 (1H, m, H2″), 2.39–2.44 (2H, m, H1″), 6.18 (1H, d, *J* 2.1, H6), 6.31 (1H, d, *J* 2.1, H8), 6.88 (1H, d, *J* 8.2, H5″), 6.94 (1H, dd, *J* 1.9 and 8.2, H6′), 7.01 (1H, d, *J* 1.9, H2′), 9.39 (1H, s, 3′-OH), 9.64 (1H, s, 4′-OH), 10.81 (1H, s, 7-OH), 13.09 (1H, s, 5-OH). δ_C ([D_6]DMSO) 14.0 (C6″), 22.0, 30.8 (C4″, C5″), 24.4 (C1″), 28.3 (C2″), 28.7 (C3″), 93.3 (C8), 98.6 (C6), 103.1 (C10), 115.5 (C5′), 115.8 (C2′), 118.4 (C3), 120.4 (C6′), 123.4 (C1′), 145.3 (C3′), 147.8 (C4′), 157.3 (C9), 161.5 (C5), 162.3 (C2), 164.1 (C7), 181.8 (C4). *m/z* 371 $[M + H]^+$, 393 $[M + Na]^+$. (Found: C 67.7, H 6.0. $C_{21}H_{22}O_6$ requires C 68.1, H 6.0%.)

3-Decyl-3′,4′,5,7-tetrahydroxyflavone ***9d***

Yield: (220 mg, 86%), mp 173–175°C. δ_H ([D_6]DMSO) 0.85 (3H, t, *J* 6.7, H10″), 1.19–1.27 (14H, m, H3″–H9″), 1.41–1.51 (2H, m, H2″), 2.39–2.44 (2H, m, H1″), 6.18 (1H, d, *J* 2.1, H6), 6.31 (1H, d, *J* 2.1, H8), 6.88 (1H, d, *J* 8.2, H5′), 6.93 (1H, dd, *J* 2.0, 8.2, H6′), 7.01 (1H, d, *J* 2.0, H2′), 9.40 (1H, s, 3′-OH), 9.65 (1H, s, 4′-OH), 10.82 (1H, s, 7-OH), 13.09 (1H, s, 5-OH). δ_C ([D_6]DMSO) 14.0 (C10″), 22.1 and 31.3 (C8″ and C9″), 24.4 (C1″), 28.3 (C2″), 28.6, 28.7, 28.9, and 29.0 (C3″–C7″), 93.3 (C8), 98.5 (C6), 103.1 (C10), 115.5 (C5′), 115.7 (C2′), 118.4 (C3), 120.4 (C6′), 123.4 (C1′), 145.2 (C3′), 147.8 (C4′), 157.3 (C9), 161.5 (C5), 162.3 (C2), 164.1 (C7), 181.8 (C4). *m/z* 427 $[M + H]^+$, 449 $[M + Na]^+$. Found: *m/z* 426.2036. $M^{+\bullet}$ requires 426.2042.

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