

REGIOSPECIFIC DEMETHYLATION-SULFONATION OF 2',3'-DIMETHOXYFLAVONES

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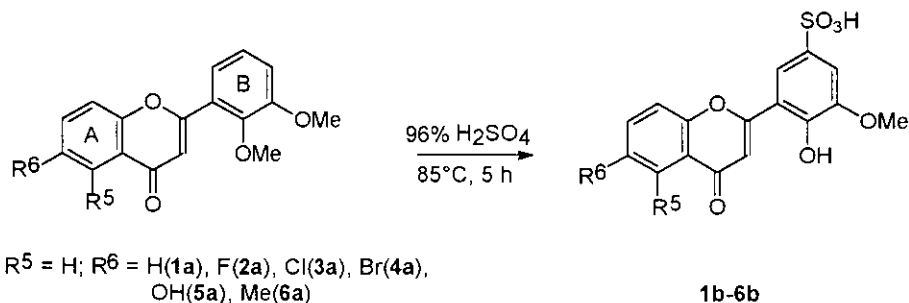
Abstract - By a careful control of the temperature at 85°C, the selective demethylation of 2',3'-dimethoxyflavones with sulfuric acid occurs at the 2'-hindered methoxy group followed by para sulfonation. At higher temperature, demethylation is complete.

INTRODUCTION

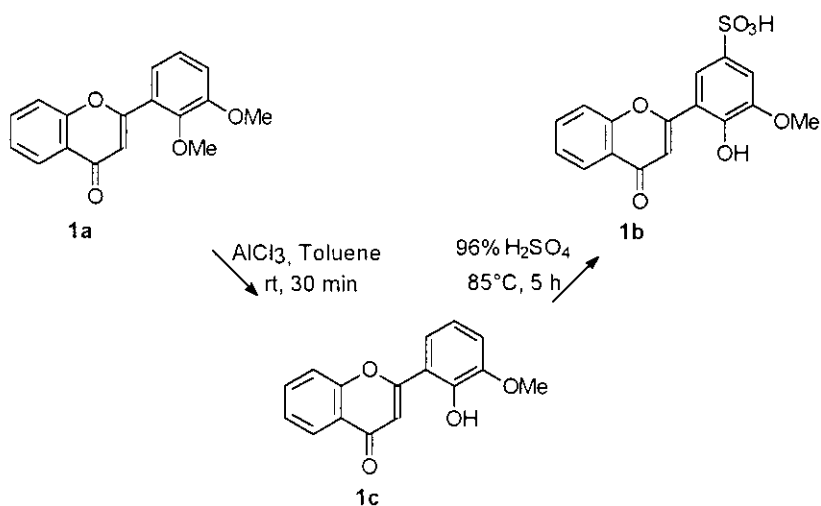
Sulfonated derivatives are valuable compounds for development of new drugs. For example, suramin, a polysulfonated naphthylurea has been used for therapy of parasitic disorders. In vitro, it is a potent inhibitor of viral transcriptase and has anti-human immunodeficiency virus activity.¹ Flavones belong to the flavonoid family which is a large group of naturally occurring compounds. They have shown to possess antiinflammatory,² antioxidant,³⁻⁵ antiviral,⁶ antimutagenic⁷ and anticarcinogenic^{8,9} properties. They may affect the activities of many enzyme systems.¹⁰ Moreover, the 1,2-dimethoxybenzene skeleton is often found in biologically active alkaloids,¹¹ albeit unusual in naturally occurring flavones.¹² In the purpose to compare biological activities of lipophylic methoxy compounds (**1a-7a**) and more water-soluble analogues two series of flavones have been synthesized, the latter was obtained by sulfonation. To our knowledge only two reports are related to the sulfonation of flavones; sulfonation with chlorosulfonic acid related to A ring¹³ and sulfonation of 3'-nitroflavones in four steps.¹⁴

RESULTS AND DISCUSSION

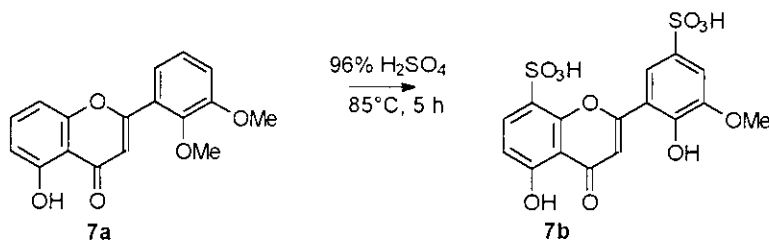
The demethylation-sulfonation was realised in one step with excellent yields, starting from 2',3'-dimethoxyflavones which except **1a**¹⁵ and **5a**¹⁶ are new compounds (Scheme 1). The sulfonation presumably occurred in two steps, demethylation of the 2' position followed by a *para* sulfonation. This is supported by obtaining first the 2'-hydroxy-3'-methoxyflavone (**1c**) using a Lewis acid,¹⁷ followed by sulfonation in the same experimental conditions (Scheme 2). With the 5-hydroxy-2',3'-dimethoxyflavone, a disulfonic flavone was obtained (Scheme 3). At higher temperature, demethylation was complete and the corresponding 2',3'-dihydroxyflavone sulfonic acid was obtained (Scheme 4).



Scheme 1

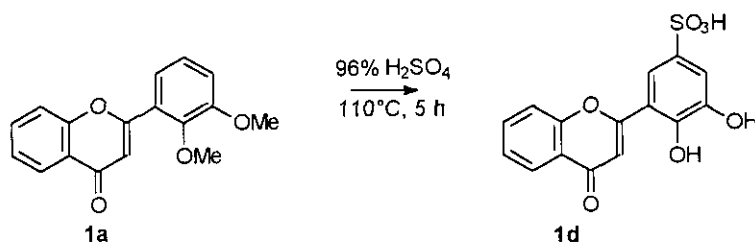


Scheme 2



Scheme 3

The 2',3'-dimethoxyflavone (1a) has been previously synthesized and the ¹³C NMR spectrum reported. But assignment of skeletal carbons was incomplete.¹⁵ The ¹³C NMR spectrum was reexamined (Table 1) based on consideration that A and B rings constitute individual spin systems.¹⁸ Carbon assignments of A-ring without any substituent are from an earlier work.¹⁹ Carbon assignments of B-ring were correlated to those obtained for 2,3-dimethoxystyrene.²⁰ For the 2'-hydroxy-3'-methoxyflavone (1c), demethylation of the 2'-methoxy group was confirmed by ¹³C NMR (resonance of the remaining methoxyl group at 56.5 ppm)



Scheme 4

For the 2'-hydroxy-3'-methoxyflavone-5'-sulfonic acid (**1b**), carbons of B ring were assigned on variations of chemical shift values reported when a methoxyl group is replaced by an hydroxyl group,^{21,22} on chemical shift values reported by Ewing²³ for the substitution of a sulfonic group and DEPT spectrum. Sulfonation of the 5' position was confirmed by a few observations. The ¹H NMR spectrum revealed two doublets ($J = 1.9$ Hz) indicative of a *meta* coupling ($H4'$, $H6'$). The chemical shift of $H3$ at 7.11 ppm is indicative of a 5'-substituent.²⁴ The ¹³C NMR revealed that the substitution did not occur in 4' position, because δ $O\text{CH}_3$ resonated at 56.6 ppm (*vide supra*).

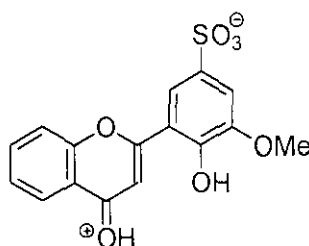


Figure 1

To confirm NMR results, the structure of 2'-hydroxy-3'-methoxyflavone-5'-sulfonic acid has been solved by X-Ray crystallography. The compound was recrystallized from water. The complete structure determination with hydrogen bonding in the crystal has been published.²⁵ The noteworthy feature is the *zwitterionic character of the structure*, the flavone being protonated at the carbonyl group (Figure 1). Such compounds should be good inhibitors of HIV protease. Structural studies with HIV protease revealed that good inhibitors have a carbonyl oxygen bonded to amide hydrogens of HIV protease residues Ile 50 and Ile 50'. The bonding is mediated by a water molecule.²⁶

The regiospecific cleavage of the 2'-methoxy group is the result of a forced rotation of the methoxy group out of the plane of the benzene ring. The methoxy group out of plane with its increased atomic charge on the oxygen atom^{27,28} is subject to a preferred nucleophilic attack of the proton.

To achieved the study, complete demethylation of B-ring was realised at higher temperature (Scheme 4).

Table 1. ^{13}C NMR chemical shifts for compounds (**1a-1d**) δ_{C} (ppm, DMSO- d_6)

	1a	1b	1c	1d
C2	161.5	160.7	160.7	161.0
C3	111.2	111.5	111.2	111.5
C4	177.0	177.7	177.2	177.5
C5	124.7	125.1	124.6	125.0
C6	125.5	125.7	125.2	125.6
C7	134.2	134.7	134.0	134.5
C8	118.4	118.6	118.3	118.5
C9	155.7	156.2	155.8	156.0
C10	123.3	123.4	123.1	123.3
C1'	125.9	117.4	117.9	117.1
C2'	147.2	147.0	146.1	145.4
C3'	153.0	147.8	148.1	146.2
C4'	115.7	111.8	114.1	115.2
C5'	124.4	138.8	119.7	138.7
C6'	120.5	117.2	119.1	116.0
OCH ₃ -2'	60.5			
OCH ₃ -3'	55.9	56.6	56.6	

EXPERIMENTAL

Materials.

2-Hydroxyacetophenones and benzoic acids were purchased from Aldrich or Merck. The ^{13}C NMR spectra were obtained at 25°C on a Bruker AC-200 spectrometer operating at 50.32 MHz using 0.5 M solution in DMSO- d_6 and taking the solvent signal as reference. All melting points (uncorrected) were taken in open capillary tubes using an Electrothermal apparatus. Sulfonic derivatives were hygroscopic. They were characterized as their *para*-toluidinium salts.²⁹

General procedure.

2',3'-Dimethoxyflavones were synthesized according to a procedure used in our laboratory.³⁰ The 2',3'-dimethoxyflavone (**1a**, 600mg, 2.12 mmol) was dissolved in concentrated sulfuric acid (96%, 20 mL, 358 mmol). The mixture is maintained at 85°C during 5 h then cooled in an ice bath. Water is poured by small quantities until complete precipitation (60 mL). The yellow solid is filtered, dried and recrystallised from absolute ethanol to afford 2'-hydroxy-3'-methoxyflavone-5'-sulfuric acid (**1b**, 666 mg, 90%). The precipitation by adding water is due to the zwitterionic structure of the flavone sulfonic acid (*vide supra*). Usually, sulfonic compounds are very soluble in water.

2',3'-Dimethoxyflavone (**1a**)

mp 83°C (47%) $^1\text{H-NMR}$ (DMSO- d_6) δ 3.81, 3.86(2s, 6H, 2xOCH₃), 6.75(s, 1H, H-3), 7.19-7.31(m, 2H, H-4',5'), 7.35(dd, J=6.7 and 2.7 Hz, 1H, H-6'), 7.49(ddd, J=7.0, 7.0 and 1.2 Hz, 1H, H-6), 7.69(dd, J=8.5 and 1.2 Hz, 1H, H-8), 7.81(ddd, J=6.9, 6.9 and 1.7 Hz, 1H, H-7), 8.05(dd, J=7.8 and 1.5 Hz, 1H,

H-5); $^{13}\text{C-NMR}$ (DMSO- d_6) see Table 1. *Anal.* Calcd for $\text{C}_{17}\text{H}_{14}\text{O}_4$: C, 72.34; H, 4.96. Found: C, 72.38; H, 4.92.

6-Fluoro-2',3'-dimethoxyflavone (2a)

mp 126°C (55%) $^1\text{H-NMR}$ (DMSO- d_6) δ 3.81, 3.86(2s, 6H, 2xOCH $_3$), 6.76(s, 1H, H-3), 7.17-7.37(m, 3H, H-4',5',6'), 7.64-7.82(m, 3H, H-5,7,8); $^{13}\text{C-NMR}$ (DMSO- d_6) δ 60.5(OCH $_3$ -2'), 55.9(OCH $_3$ -3'), 109.0-109.5(d, J=25 Hz, C-5), 110.4(C-3), 115.9(C-4'), 120.5(C-6'), 121.1-121.3(d, J=10 Hz, C-8), 122.0-122.5(d, J=25 Hz, C-7), 124.1(C-10), 124.2(C-1'), 124.4(C-5'), 147.1(C-2'), 152.2(C-9), 152.9(C-3'), 156.4-161.7(d, J=-242.5 Hz, C-6), 161.7(C-2), 176.2(C-4). *Anal.* Calcd for $\text{C}_{17}\text{H}_{13}\text{O}_4\text{F}$: C, 68.00; H, 4.33. Found: C, 68.13; H, 4.26.

6-Chloro-2',3'-dimethoxyflavone (3a)

mp 125°C (45%) $^1\text{H-NMR}$ (DMSO- d_6) δ 3.81, 3.86(2s, 6H, 2xOCH $_3$), 6.80(s, 1H, H-3), 7.19-7.32(m, 2H, H-4',5'), 7.37(dd, J=7.0 and 2.4 Hz, 1H, H-6'), 7.76(d, J=8.9 Hz, 1H, H-8), 7.85(dd, J=8.8 and 2.5 Hz, 1H, H-7), 7.97(d, J=2.4 Hz, 1H, H-5); $^{13}\text{C-NMR}$ (DMSO- d_6) δ 60.5(OCH $_3$ -2'), 55.9(OCH $_3$ -3'), 111.0(C-3), 115.9(C-4'), 120.5(C-6'), 120.8(C-8), 123.7(C-5), 124.1(C-10), 124.4(C-5'), 125.4(C-1'), 129.8(C-6), 134.0(C-7), 147.2(C-2'), 152.9(C-3'), 154.3(C-9), 161.7(C-2), 175.8(C-4). *Anal.* Calcd for $\text{C}_{17}\text{H}_{13}\text{O}_4\text{Cl}$: C, 64.45; H, 4.10. Found: C, 64.50; H, 4.08.

6-Bromo-2',3'-dimethoxyflavone (4a)

mp 130°C (46%) $^1\text{H-NMR}$ (DMSO- d_6) δ 3.80, 3.85(2s, 6H, 2xOCH $_3$), 6.79(s, 1H, H-3), 7.20-7.28(m, 2H, H-4',5'), 7.34(dd, J=7 and 2.4 Hz, 1H, H-6'), 7.66(d, J=8.9 Hz, 1H, H-8), 7.92(dd, J=8.9 and 2.5 Hz, 1H, H-7), 8.05(d, J=2.4 Hz, 1H, H-5); $^{13}\text{C-NMR}$ (DMSO- d_6) δ 60.5(OCH $_3$ -2'), 55.9(OCH $_3$ -3'), 111.1(C-3), 116.0(C-4'), 117.8(C-6), 120.5(C-6'), 121.1(C-8), 124.4(C-5'), 124.5(C-10), 125.4(C-1'), 126.8(C-5), 136.8(C-7), 147.2(C-2'), 152.9(C-3'), 154.7(C-9), 161.7(C-2), 175.7(C-4). *Anal.* Calcd for $\text{C}_{17}\text{H}_{13}\text{O}_4\text{Br}$: C, 56.50; H, 3.60. Found: C, 56.47; H, 3.68.

6-Hydroxy-2',3'-dimethoxyflavone (5a)

mp 248°C (47%) $^1\text{H-NMR}$ (DMSO- d_6) δ 3.79, 3.86(2s, 6H, 2xOCH $_3$), 6.66(s, 1H, H-3), 7.20-7.35(m, 5H, H-5,7,4',5',6'), 7.57(d, J=8.9 Hz, 1H, H-8), 10.01(s, 1H, OH); $^{13}\text{C-NMR}$ (DMSO- d_6) δ 60.5(OCH $_3$ -2'), 55.9(OCH $_3$ -3'), 107.4(C-5), 110.2(C-3), 115.6(C-4'), 119.7(C-8), 120.5(C-6'), 123.1(C-7), 124.0(C-10), 124.5(C-5'), 126.2(C-1'), 147.1(C-2'), 149.7(C-9), 153.0(C-3'), 154.9(C-6), 161.2(C-2), 176.9(C-4). *Anal.* Calcd for $\text{C}_{17}\text{H}_{14}\text{O}_5$: C, 68.45; H, 4.69. Found: C, 68.41; H, 4.74.

6-Methyl-2',3'-dimethoxyflavone (6a)

mp 105-106°C (43%) $^1\text{H-NMR}$ (DMSO- d_6) δ 2.39(s, 3H, CH $_3$), 3.80, 3.85(2s, 6H, 2xOCH $_3$), 6.71(s, 1H, H-3), 7.20-7.30(m, 3H, H-4',7,5'), 7.56-7.58(m, 2H, H-6',8), 7.81(d, J=0.8 Hz, 1H, H-5); $^{13}\text{C-NMR}$ (DMSO- d_6) δ 20.4(CH $_3$), 60.5(OCH $_3$ -2'), 55.9(OCH $_3$ -3'), 111.0(C-3), 115.7(C-4'), 118.1(C-8), 120.5(C-6'), 122.8(C-10), 124.0(C-5'), 124.4(C-5), 125.9(C-1'), 134.9(C-6), 135.2(C-7), 147.1(C-2'), 152.9(C-

3'), 154.1(C-9), 161.3(C-2), 176.9(C-4). *Anal.* Calcd for $C_{18}H_{16}O_4$: C, 72.97; H, 5.40. Found: C, 72.94; H, 5.44.

5-Hydroxy-2',3'-dimethoxyflavone (7a)

mp 102°C (27%) $^1\text{H-NMR}$ (DMSO- d_6) δ 3.82, 3.87(2s, 6H, 2xOCH $_3$), 6.82(s, 1H, H-3), 6.81(dd, J=8.1 and 0.7 Hz, H-6), 7.12(dd, J=8.4 and 0.7 Hz, 1H, H-8), 7.09-7.39(m, 3H, H-4',5',6'), 7.67(dd, J=8.4 and 8.3, 1H, H-7), 12.59(s, 1H, OH); $^{13}\text{C-NMR}$ (DMSO- d_6) δ 60.5(OCH $_3$ -2'), 55.9(OCH $_3$ -3'), 107.3(C-8), 109.8(C-3), 109.9(C-10), 110.8(C-6), 116.2(C-4'), 120.5(C-6'), 124.5(C-5'), 125.2(C-1'), 135.9(C-7), 147.3(C-2'), 153.0(C-3'), 156.0(C-5), 159.8(C-9), 162.9(C-2), 183.0(C-4). *Anal.* Calcd for $C_{17}H_{14}O_5$: C, 68.45; H, 4.69. Found: C, 68.34; H, 4.73.

2'-Hydroxy-3'-methoxyflavone-5'-sulfonic acid (1b)

Yellow solid (90 %) $^1\text{H-NMR}$ (DMSO- d_6) δ 3.89(s, 3H, OCH $_3$ -3'), 7.11(s, 1H, H-3), 7.33(d, J = 1.9 Hz, 1H, H-4'), 7.49(ddd, J = 8.6, 8.5 and 1.7 Hz, 1H, H-6), 7.75(d, J=1.9 Hz, 1H, H-6'), 7.70-7.87(m, 1H, H-7), 8.04(dd, J=7.8 and 1.3 Hz, 1H, H-5); $^{13}\text{C-NMR}$ (DMSO- d_6) see Table 1.

p-toluidinium salt³¹: mp 268°C, $C_{16}H_{11}O_7S^- \cdot C_7H_{10}N^+ \cdot 3H_2O$: *Anal.* Calcd for $C_{23}H_{27}NO_{10}S$: C, 54.22; H, 5.30; N, 2.75. Found: C, 54.28; H, 5.27; N, 2.78.

6-Fluoro-2'-hydroxy-3'-methoxyflavone-5'-sulfonic acid (2b)

Yellow solid (91 %) $^1\text{H-NMR}$ (DMSO- d_6) δ 3.88 (s, 3H, OCH $_3$), 7.11(s, 1H, H-3), 7.34(d, J=1.8 Hz, 1H, H-4'), 7.68-7.85(m, 4H, H-5,6',7,8), 10.11(s, 1H, OH); $^{13}\text{C-NMR}$ (DMSO- d_6) δ 56.5(OCH $_3$ -3'), 109.3-109.8(d, J=25 Hz, C-5), 111.0(C-3), 111.6(C-4'), 117.2(C-6'), 121.3-121.5(d, J=10 Hz, C-8), 122.3-122.8(d, J=25 Hz, C-7), 124.4(C-10), 124.6(C-1'), 139.0(C-5'), 146.9(C-2'), 147.6(C-3'), 152.5(C-9), 156.7-161.6(d, J=-245 Hz, C-6), 160.9(C-2), 176.7(C-4).

p-toluidinium salt: mp 270°C, $C_{16}H_{10}O_7FS^- \cdot C_7H_{10}N^+ \cdot 2H_2O$: *Anal.* Calcd for $C_{23}H_{24}NO_9FS$: C, 54.22; H, 4.71; N, 2.75. Found: C, 54.47; H, 4.21; N, 2.58.

6-Chloro-2'-hydroxy-3'-methoxyflavone-5'-sulfonic acid (3b)

Yellow solid (89%) $^1\text{H-NMR}$ (DMSO- d_6) δ 3.88 (s, 3H, OCH $_3$ -3'), 7.18(s, 1H, H-3), 7.34(d, J=1.8 Hz, 1H, H-5'), 7.75(d, J=1.8 Hz, 1H, H-6'), 7.80-7.83(m, 2H, H-8,7), 7.95(d, J=2.2 Hz, 1H, H-5); $^{13}\text{C-NMR}$ (DMSO- d_6) δ 56.5(OCH $_3$ -3'), 111.4(C-4'), 111.6(C-3), 116.8(C-1'), 117.2(C-6'), 121.1(C-8), 123.9(C-5), 124.5(C-10), 130.0(C-6), 134.4(C-7), 139.0(C-5'), 146.4(C-2'), 147.7(C-3'), 154.6(C-9), 161.3(C-2), 176.3(C-4).

p-toluidinium salt: mp 280°C, $C_{16}H_{10}O_7ClS^- \cdot C_7H_{10}N^+ \cdot H_2O$: *Anal.* Calcd for $C_{23}H_{22}NO_8ClS$: C, 54.38; H, 4.33; N, 2.75. Found: C, 53.93; H, 4.02; N, 2.90.

6-Bromo-2'-hydroxy-3'-methoxyflavone-5'-sulfonic acid (4b)

Yellow solid (91%) $^1\text{H-NMR}$ (DMSO- d_6) δ 3.88 (s, 3H, OCH $_3$ -3'), 7.10(s, 1H, H-3), 7.32(d, J=1.6 Hz, 1H, H-4'), 7.48-7.70(m, 2H, H-6',8), 7.95(dd, J=8.9 and 2.4 Hz, 1H, H-7), 8.1(d, J=2.4 Hz, 1H, H-5). $^{13}\text{C-NMR}$ (DMSO- d_6) δ 56.4 (OCH $_3$ -3'), 111.6(C-3), 111.6(C-4'), 116.6(C-1'), 117.1(C-6'), 117.8(C-6),

121.2(C-8), 124.8(C-10), 127.0(C-5), 137.0(C-7), 139.1(C-5'), 146.8(C-2'), 147.5(C-3'), 154.4(C-9), 160.8(C-2), 176.0(C-4).

p-toluidinium salt : mp 286°C, C₁₆H₁₀O₇BrS⁻ · C₇H₁₀N⁺ : *Anal.* Calcd for C₂₃H₂₀NO₇BrS: C, 51.68; H, 3.74; N, 2.62. Found: C, 51.46; H, 3.68, N, 2.63.

2',6-Dihydroxy-3'-methoxyflavone-5'-sulfonic acid (5b)

Yellow solid (85%) ¹H-NMR (DMSO-d₆) δ 3.87 (s, 3H, OCH₃-3'), 7.03(s, 1H, H-3), 7.23(dd, J=8.9 and 2.9 Hz, 1H, H-7), 7.30-7.33(m, 2H, H-4', 6'), 7.56(d, J=8.9 Hz, 1H, H-8), 7.73(d, J=1.7 Hz, 1H, H-5). ¹³C-NMR (DMSO-d₆) δ 56.6 (OCH₃-3'), 107.8(C-5), 110.9(C-3), 111.4(C-4'), 117.5(C-1'), 117.5(C-6'), 120.0(C-8), 123.6(C-7), 124.3(C-10), 138.7(C-5'), 146.9(C-2'), 147.8(C-3'), 149.9(C-9), 155.1(C-6), 160.4(C-2), 177.5(C-4).

p-toluidinium salt : mp 286°C, C₁₆H₁₁O₈S⁻ · C₇H₁₀N⁺ · H₂O : *Anal.* Calcd for C₂₃H₂₃NO₉S: C, 56.44; H, 4.70; N, 2.86. Found: C, 56.79; H, 4.68; N, 2.88.

2'-Hydroxy-3'-methoxy-6-methylflavone-5'-sulfonic acid (6b)

Yellow solid (89%) ¹H-NMR (DMSO-d₆) δ 2.39(s, 3H, CH₃), 3.88 (s, 3H, OCH₃-3'), 7.07(s, 1H, H-3), 7.32(d, J=1.7 Hz, 1H, H-4'), 7.60(s, 2H, H-7,8), 7.73(d, J=1.6 Hz, 1H, H-6'), 7.8(s, 1H, H-5). ¹³C-NMR (DMSO-d₆) δ 20.6(CH₃) 56.4 (OCH₃-3'), 111.5(C-3), 111.5(C-4'), 116.9(C-1'), 117.1(C-6'), 118.2(C-8), 122.9(C-10), 124.2(C-5), 135.0(C-6), 135.4(C-7), 139.1(C-5'), 146.5(C-2'), 147.5(C-3'), 154.2(C-9), 160.3(C-2), 177.3(C-4).

p-toluidinium salt : mp 294°C, C₁₇H₁₃O₇S⁻ · C₇H₁₀N⁺ : *Anal.* Calcd for C₂₄H₂₃NO₇S: C, 61.40; H, 4.90; N, 2.98. Found: C, 61.49; H, 4.96; N, 2.77.

2',5-Dihydroxy-3'-methoxyflavone-5',8-disulfonic acid (7b)

Yellow solid (58%) ¹H-NMR (DMSO-d₆) δ 3.87(s, 3H, OCH₃), 6.77 (d, J = 8.5 Hz, 1H, H-7), 7.13 (s, 1H, H-3), 7.36(d, 1H, J = 1.9 Hz, H-4'), 7.97(d, J=8.5 Hz, 1H, H-6), 8.01(d, J=1.9 Hz, 1H, H-6'). ¹³C-NMR (DMSO-d₆) δ 56.6(OCH₃-3'), 109.9(C-10), 110.1(C-3, C-6), 112.3(C-4'), 116.7(C-1'), 118.5(C-6'), 125.7(C-8), 135.0(C-7), 138.5(C-5'), 147.6(C-2'), 148.0(C-3'), 152.4(C-9), 161.2(C-5), 163.9(C-2), 183.3(C-4).

p-toluidinium salt : mp 310°C (decomp), C₁₆H₁₁O₁₁S₂⁻ · C₇H₁₀N⁺ · 4.5H₂O : *Anal.* Calcd for C₂₃H₃₀NO_{15.5}S₂: C, 43.67; H, 4.74; N, 2.21. Found: C, 43.53; H, 4.54; N, 1.91.

2'-Hydroxy-3'-methoxyflavone (1c)

White solid (60%) mp 208°C ¹H-NMR (DMSO-d₆) δ 3.86 (s, 3H, OCH₃-3'), 6.92(dd, J=8.0 and 8.0 Hz, 1H, H-5'), 7.11-7.15(m, 2H, H-3, H-4'), 7.41-7.48(m, 2H, H-6, H-6'), 7.65-7.77(m, 2H, H-8, H-7), 8.06(dd, J=7.8 and 1.5 Hz, 1H, H-5), 9.86 (s, OH). ¹³C-NMR (DMSO-d₆) see Table 1. *Anal.* Calcd for C₁₆H₁₂O₄: C, 71.64; H, 4.47. Found: C, 71.60; H, 4.51.

2',3'-Dihydroxyflavone-5'-sulfonic acid (1d)

Pale yellow solid (85%) $^1\text{H-NMR}$ (DMSO- d_6) δ 7.11 (s, 1H, H-3), 7.31(d, $J=2.0$ Hz, 1H, H-4'), 7.43-7.51(m, 1H, H-6), 7.62(d, $J=2.0$ Hz, 1H, H-6'), 7.67-7.71(m, 1H, H-8), 7.75-7.84(m, 1H, H-7), 8.02(dd, $J=7.8$ and 1.5 Hz, 1H, H-5). $^{13}\text{C-NMR}$ (DMSO- d_6) see Table 1.

p-toluidinium salt : mp 250°C, $\text{C}_{15}\text{H}_9\text{O}_7\text{S}^- \cdot \text{C}_7\text{H}_{10}\text{N}^+ \cdot \text{H}_2\text{O}$: *Anal.* Calcd for $\text{C}_{22}\text{H}_{21}\text{NO}_8\text{S}$: C, 57.51; H, 4.57; N, 3.05. Found: C, 57.54; H, 4.78; N, 2.83.

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