

NOVEL METHYLATED FLAVONOLS WITH UNSUBSTITUTED B RING FROM *PLATANUS ACERIFOLIA* BUDS

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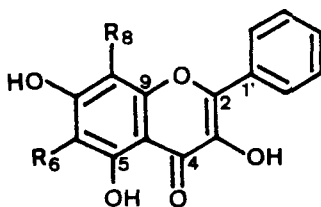
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Previous studies on *Platanus acerifolia* Willd. (Platanaceae) have yielded *O*- and *C*-prenylated- as *C*-methylated-flavonoids (1-4). The Me₂CO extract of the buds collected in spring has been examined, and during fractionation four flavonols crystallized. The isolation and structure elucidation of compounds 3-6 are reported here in the order of elution from polyamide cc.

The four compounds 3-6 are characterized by two main uv bands in MeOH, 3 (λ 272, 367 nm) and 4-6 (λ 280, 380 nm), and correspond to 5,7-dihydroxyflavonols, as indicated by the bathochromic uv shifts induced by AlCl₃/AlCl₃+HCl and NaOAc. They all exhibit an unsubstituted B ring and differ from each other by the nature and the number of substituents located at C-8 and/or C-6.

Compound 3, C₁₆H₁₂O₆ [M]⁺ *m/z* 300, is the least polar flavonol of this group. ¹H-nmr data indicated the unsubstituted B ring [δ 8.27 (2H), 7.53 (1H), and 7.50 (2H), H-2', 6', H-4',



- 1 R₆ = R₈ = H (galangin)
- 2 R₆ = H, R₈ = OH
- 3 R₆ = H, R₈ = OMe
- 4 R₆ = dimethylallyl, R₈ = OH (platanetin)
- 5 R₆ = OH, R₈ = Me (isoplatanin)
- 6 R₆ = Me, R₈ = OH (platanin)

and H-3', 5'], an isolated H (δ 6.26), and a methoxyl group (δ 3.92). The 5,7,8-trioxygenation pattern is unambiguously assigned to this molecule according to both the high-field ¹H-nmr signal of the isolated H identified with H-6 (5) and the low-field ¹³C-nmr resonance (δ 99.32) relative to C-6 (6). Compound 3 is, therefore, 8-methoxy-5,7-dihydroxyflavonol, a new natural product. The proposed structure is readily confirmed by the comparative analysis of the ¹³C-nmr spectra of both galangin [1] and 3 (Table 1), showing the shielding effect induced by the 8-*O*-substitution, more consequent on the ortho-carbons (C-7, Δδ -6.79; C-9, Δδ -7.20) than on the para-carbon (C-5, Δδ -4.76) (6,7). In addition, the fragment ion at *m/z* [M - Me]⁺ 285 (100%) and the absence of any [M - H₂O]⁺ ion in the mass spectrum of 3 are in agreement with the above-mentioned nmr discrimination between substitution at C-6 and C-8. That is, ms data relative to 6-methoxy- and 8-methoxyquercetin (8) and to 5,7-dihydroxyflavones with methoxyl at C-6 or C-8 (9) show that in the 6-OMe compounds, [M]⁺ is usually more important than [M - Me]⁺, often appearing as the base peak, whereas in those with methoxyl at C-8, the base peak is due to [M - Me]⁺. Furthermore, 6-OMe compounds exhibit [M - H₂O]⁺ greater than 10%, while in 8-OMe isomers, this ion is lower than 10%.

Compound 4, C₂₀H₁₈O₆ [M]⁺ *m/z* 354, is the only flavonol possessing a dimethylallyl chain in this group. This was shown by the ¹H-nmr peaks [δ 5.31

TABLE 1. ^{13}C -nmr Chemical Shifts of Compounds 1-6 at 50 MHz (DMSO- d_6 ; δ ppm/TMS).

Carbon	Compound					
	1	2	3	4	5	6
C-2	146.05	145.68	146.71	145.34	146.65	145.36
C-3	137.00	136.87	137.66	136.81	137.37	136.82
C-4	176.04	176.57	177.06	176.49	177.15	176.43
C-5	160.92	152.37	156.16	150.08	150.95	150.23
C-6	98.53	98.19	99.32	110.41	124.50	106.35
C-7	164.31	153.14	157.52	152.28	153.15	152.45
C-8	93.72	124.76	128.29	123.63	107.52	123.66
C-9	156.63	143.95	149.43	143.75	144.40	143.51
C-10	103.40	102.93	103.86	102.35	103.15	102.27
C-1'	131.02	131.23	131.58	131.21	131.76	131.23
C-2',6'	127.54	127.70	128.19	127.84	128.62	127.82
C-3',5'	128.32	128.48	129.50	128.37	129.37	128.39
C-4'	129.73	129.92	131.05	129.82	131.00	129.83
C-1''				21.40		
C-2''				122.33		
C-3''				130.59		
Me-6						7.79
Me-8					8.55	
Me-3''				25.47		
				17.70		
MeO-8			61.84			

(1H), 3.41 (2H), 1.80 (3H), and 1.66 (3H), H-2'', H-1'', and 2Me-3'']. As the B ring is also unsubstituted (Table 1), this chain has to be located at C-6 or C-8. According to the ^{13}C -nmr data relative to both 6-C- and 8-C-prenylated flavonoids (7), the downfield shift value δ 110.41 corresponds to the prenylated carbon (C-6). Hydroxylation at C-8 is shown by the ^{13}C -nmr signal at δ 123.63; consequently, C-9 affected by shielding is recorded at δ 143.75. These δ values are in agreement with those of the same carbons in 5,7,8-trihydroxyflavonol [2] (δ 124.76 and 143.95, C-8 and C-9) (Table 1). They support the assignment of 4 as 6-C-*gem*-dimethylallyl-5,7,8-trihydroxyflavonol. Named platanetin, this natural product has never been described in any other species.

The next two compounds, 5 and 6, are isomers of 3 ($\text{C}_{16}\text{H}_{12}\text{O}_6$ [$\text{M}]^{\dagger}$ m/z 300); their ^1H -nmr spectra are identical to those of 3, except for the aromatic H (δ 6.26) and the methoxyl group (δ 3.92). In 5 and 6, these are replaced by a C-Me (δ 2.11 in 6 and 2.16 in 5) and

-OH groups. Compounds 5 and 6 are, therefore, deduced to be 6-C-methyl-5,7,8-trihydroxy- and 8-C-methyl-5,6,7-trihydroxyflavonol. The uv spectra ($\text{AlCl}_3/\text{AlCl}_3 + \text{HCl}$) and the ^{13}C -nmr spectra are used to distinguish between these isomers. The uv spectrum of compound 6, taken in AlCl_3 and then in $\text{AlCl}_3 + \text{HCl}$, is identical to that of platanetin [4] identified with a 6-C-prenyl-8-hydroxyflavonol. This result suggests a structure based on 6-C-methylation for 6. Analysis of the ^{13}C -nmr spectrum of 6 is in agreement with the uv data because the recorded δ value at 123.66 ppm corresponds to 8-C-OH, in comparison with that at 123.63 ppm in platanetin (Table 1). This is confirmed by shielding induced by the ortho-hydroxylation on C-9 in the two compounds: δ 143.51 in 6 and δ 143.75 in 4. Consequently, these data support the assignment of 6 as the new natural product 6-C-methyl-5,7,8-trihydroxyflavonol named platanin, and compound 5 is deduced to be 8-C-methyl-5,6,7-trihydroxyflavonol or isoplatanin, another new natural prod-

uct. According to the para-hydroxylation, C-9 is, in this compound, as expected, less shielded (δ 144.40) than in **6** (δ 143.51). Finally, one can notice that all the C atoms in **5** are shifted downfield in comparison with those of **6**. Furthermore, the comparative analysis of the shift values relative to the methylated carbons (C-8 in **5** and C-6 in **6**) appears uncommon: the C-8 signal in **5** (δ 107.52) is downfield with respect to that of C-6 in **6** (δ 106.35). This reversed behavior seems to be restricted to the alkylated carbons, because the corresponding oxygenated carbons (C-6 in **5** and C-8 in **6**) are recorded in the expected order (C-6 δ 124.50, C-8 δ 123.66). The mass spectra of **5** and **6** also show differences (Table 2). The base peak of platanin [**6**] is the molecular ion, while that of isoplatanin [**5**] is $[M-H-Me-Ar]^+$; furthermore, each compound is characterized by a fragment ion: $[M-Ar]^+$ for **5**, and $[M-H-CO-CO]^+$ for **6**.

TABLE 2. Ms Data Differentiating Isomers **5** and **6**.

	<i>m/z</i>	% 5	% 6
$[M]^+$	300	24	100
$[M-H-CO-CO]^+$	243		4
$[M-Ar]^+$ ^a	223	13	
$[M-H-Me-Ar]^+$	207	100	8

^aAr = C₆H₅.

As previously reported (2-4), *P. acerifolia* buds produce a diversified flavonoid mixture involving prenylation and/or methylation. Except for 4-hydroxy-grenoblone, a minor constituent, all the flavonoids isolated from this source exhibit an unsubstituted B ring.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The source of plant material was previously reported (3). Analytical tlc was carried out on Si gel plates (E. Merck). Polyamide CC6 (Macherey Nagel) was used for cc. Uv spectra were measured in MeOH on a Beckman 25 spectrometer. ¹H- and ¹³C-nmr spectra were run on AM300 and AC200 Bruker spectrometers, respectively. Ei

mass spectra were recorded on Nermag apparatus (70 eV).

ISOLATION OF THE FLAVONOLS.—Fresh buds of *P. acerifolia* (1450 g) were rinsed with petroleum ether (40-60°) (3 liters) to defat the exudate material and then extracted with Me₂CO (3 liters) at room temperature. The hydroacetic extract was partitioned against petroleum ether; the upper phase was concentrated and then subjected to cc on polyamide. Elution was accomplished with C₆H₆ and increasing quantities of Me₂CO. Fifteen 120-ml fractions were collected and monitored by tlc on Si gel in petroleum ether-CHCl₃-Me₂CO (3:3:1). The four major flavonols **3** (30 mg), **4** (110 mg), **5** (19 mg), and **6** (19 mg) crystallized in the corresponding fractions 5, 8, 12, and 13, respectively.

8-METHOXY-5,7-DIHYDROXYFLAVONOL [3].—Yellow crystalline compound; uv λ MeOH 367, 307 sh, 295 sh, 272, 237 sh, 220 sh; /AlCl₃=AlCl₃+HCl 425, 342, 310 sh, 279, 251, 240 sh, 220; /NaOAc 400, 335 sh, 307 sh, 282, 250 sh, 220; /NaOMe 425, 332 sh, 285, 252 sh, 215 nm; ms (70 eV) *m/z* (%) $[M]^+$ 300 (48), 285 (100), 257 (26), 223 (4), 205 (3), 185 (13), 167 (12), 139 (48), 129 (26), 119 (22), 111 (35), 89 (50), 77 (35); ¹H nmr (CD₃OD, 300 MHz) δ 11.83 (1H, s, HO-5), 8.27 (2H, dd, *J*=8.5, 2 Hz, H-2',6'), 7.53 (1H, ddd, *J*=8, 8, 2 Hz, H-4'), 7.50 (2H, dd, *J*=8.5, 8 Hz, H-3',5'), 6.26 (1H, s, H-6), 3.92 (3H, s, MeO-8); ¹³C nmr see Table 1.

6-C-gem-DIMETHYL-ALLYL-5,7,8-TRIHYDROXY-FLAVONOL (PLATANIN) [4].—Ocher amorphous powder; uv λ MeOH 380, 330 sh, 315 sh, 280, 232 sh, 210; /AlCl₃ 490, 385 sh, 362, 340, 300, 280 sh, 255 sh, 230; /AlCl₃+HCl 437, 357, 315 sh, 285, 255 sh, 237, 225 sh; /NaOAc 560, 350, 295 sh, 252 sh, 222; /NaOMe 550, 350, 290, 250 sh nm; ms (70 eV) *m/z* (%) $[M]^+$ 354 (51), 339 (2), 337 (5), 325 (1), 311 (19), 298 (100), 285 (1), 270 (2), 269 (2), 181 (0.5), 167 (0.5), 142 (1), 139 (0.5), 129 (5), 119 (2), 118 (2), 111 (1), 101 (2), 89 (28), 77 (16); ¹H nmr (CD₃COCD₃, 300 MHz) δ 11.87 (1H, s, HO-5), 8.33 (2H, dd, *J*=8.5, 2 Hz, H-2',6'), 7.56 (1H, ddd, *J*=8, 8, 2 Hz, H-4'), 7.53 (2H, dd, *J*=8.5, 8 Hz, H-3',5'), 5.31 (1H, m, *J*=7, 1, 1 Hz, H-2''), 3.41 (2H, br d, *J*=7 Hz, H-1''), 1.80 (3H, br s, Me-3''), 1.66 (3H, br s, Me-3''); ¹³C nmr see Table 1.

8-C-METHYL-5,6,7-TRIHYDROXYFLAVONOL (ISOPLATANIN) [5].—Dark red-orange amorphous powder; uv λ MeOH 380, 327 sh, 317 sh, 280, 245 sh, 215; /AlCl₃ 495, 420 sh, 360, 342, 300, 277 sh, 255 sh, 230; /AlCl₃+HCl 440, 355, 322 sh, 285, 255 sh, 242, 225 sh; /NaOAc 555, 352, 292, 250, 220; /NaOMe 550, 350, 292, 250, 225 sh nm; ms (70 eV) *m/z* (%) $[M]^+$

300 (24), 299 (8), 284 (7), 271 (7), 256 (3), 236 (3), 223 (13), 207 (100), 185 (41), 167 (27), 139 (48), 133 (80), 129 (47), 122 (90), 119 (95), 111 (72), 109 (75), 101 (30), 89 (37), 77 (19); ^1H nmr (CD_3COCD_3 , 300 MHz) δ 11.85 (1H, s, HO-5), 8.33 (2H, dd, $J=8.5$, 2 Hz, H-2',6'), 7.57 (1H, ddd, $J=8$, 8, 2 Hz, H-4'), 7.54 (2H, dd, $J=8.5$, 8 Hz, H-3',5'), 2.16 (3H, s, Me-8); ^{13}C nmr see Table 1.

6-C-METHYL-5,7,8-TRIHIDROXYFLAVONOL (PLATANIN) [6].—Ocher amorphous powder; uv λ MeOH 380, 327 sh, 315 sh, 280, 237 sh, 216; / AlCl_3 492, 382 sh, 362, 337, 300, 277 sh, 252 sh, 229; / $\text{AlCl}_3 + \text{HCl}$ 437, 355, 312 sh, 283, 253, 242 sh, 220; / NaOAc 555, 350, 285, 250, 242 sh, 218; / NaOMe 550, 350, 293, 251, 240 sh, 210 nm; ms (70 eV) m/z (%) [$\text{M}]^+$ 300 (100), 299 (30), 284 (4), 283 (1), 271 (12), 256 (6), 243 (4), 226 (2), 207 (8), 206 (1), 185 (4), 167 (12), 139 (11), 129 (62), 122 (34), 119 (22), 113 (40), 111 (46), 101 (28), 89 (34), 77 (42); ^1H nmr (CD_3OD , 300 MHz) δ 11.86 (1H, s, HO-5), 8.33 (2H, dd, $J=8.5$, 2 Hz, H-2',6'), 7.51 (1H, dd, $J=8$, 8 Hz, H-4'), 7.48 (2H, dd, $J=8.5$, 8 Hz, H-3',5'), 2.11 (3H, s, Me-6); ^{13}C nmr see Table 1.

ACKNOWLEDGMENTS

The authors are grateful to Drs. P.R.

Henika and J.T. McGregor (U.S. Department of Agriculture, Berkeley) for the generous gift of an authentic sample of 5,7,8-trihydroxyflavonol used for ^{13}C -nmr analysis.

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Received 17 September 1987