NEW FLAVONOIDS FROM BONANNIA GRAECA (L.) HALACSY

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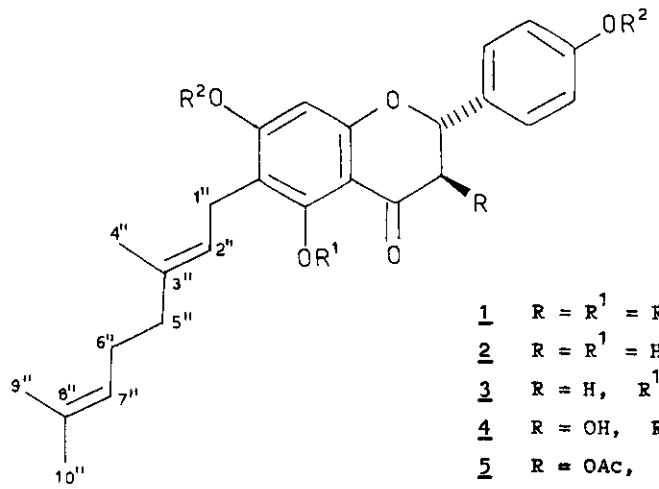
Abstract - A new C-geranylated flavanone, bonannione A, and two new C-geranylated dihydroflavonols, bonanniol A and B, were isolated from Bonannia Graeca (Umbelliferae). The structures were deduced from spectral data and chemical evidence.

Recently, we reported[1] the isolation and structural elucidation of a new irregular monocyclic diterpene, bonandiol, from Bonannia Graeca (L.) Halacsy (Umbelliferae). In our further studies of this plant, we now describe the isolation of three new flavonoids, whose structures are established as (2S)-6-C-geranyl-5,7,4'-trihydroxyflavanone (1, bonannione A), (2R,3R)-6-C-geranyl-5,7,4'-trihydroxydihydroflavonol (4, bonanniol A), and (2R,3R)-6-C-geranyl-7,4'-dihydroxy-5-methoxydihydroflavonol (6, bonanniol B).

The first of the new flavonoids (bonannione A, 1), $C_{25}H_{28}O_5$, had an IR spectrum which showed the presence of hydroxyl groups (3100-3450 cm^{-1}), a chelated carbonyl group (1640 cm^{-1}), and aromatic rings (1583 cm^{-1}). The UV spectrum (λ_{max}^{EtOH} nm 335sh, 295, $\lambda_{max}^{EtOH + NaOAc}$ 340) was characteristic of 7-hydroxyflavanone series.[2] The structure 1 followed from ^1H and ^{13}C NMR spectral data (Table 1 and 2) and those of the diacetate 2 and triacetate 3 obtained by acetylation of 1. The ppm values of ring C carbons were characteristic of a 5,7-dihydroxyflavanone structure,[3] with C-2, C-3, and C-4 at 78.8, 43.3, and 196.2 ppm, respectively, and the deshielding of the latter signal is owing to chelation effect of the 5-OH group. In fact, it remained



1 R = R^1 = R^2 = H
2 R = R^1 = H, R^2 = Ac
3 R = H, R^1 = R^2 = Ac
4 R = OH, R^1 = R^2 = H
5 R = OAc, R^1 = R^2 = Ac
6 R = OH, R^1 = Me, R^2 = H
7 R = OAc, R^1 = Me, R^2 = Ac

at 197.0 ppm in the diacetate derivative 2 whereas it was shielded in the triacetate derivative 3 by ca. 7 ppm due to the loss of hydrogen bonding. The determination of the site of alkylation at C-6 was unambiguously made on the basis of the multiplicity of the signal at 95.7 ppm in the proton coupled ^{13}C spectrum; in fact, this signal is a doublet with $^{1}J_{C,H}$ = 163.8 Hz and must be attributed to C-8, as an unsubstituted C-6 should show also a long-range interaction with the hydrogen-bonded hydroxyl proton on C-5.[4]

Mass spectral fragmentation[5] of bonannione A (1) (see Experimental) was in agreement with the assigned structure 1. The absolute stereochemistry of 1 is that depicted in the formula because of its CD curve (see Experimental) compared with those of other 2S-flavanones.[6]

It can be remarked that a product named sophoraflavanone A was reported recently[7] as a constituent of the roots of Sophora tomentosa L. and claimed to have structure 1. However, the physical and spectroscopic data in the above paper[7] are similar but not identical with those found on our product. The same authors reinvestigated the position of the geranyl chain by using the long-range selective proton decoupling method and concluded[8] that the geranyl residue was in sophoraflavanone A at C-8 instead of C-6.

The other of the new flavonoids, bonanniol A (4), was the 3 β-hydroxy derivative

Table 1. ^{1}H NMR data of compounds 1 - 7 (80MHz, $CDCl_3$, TMS as internal standard)

	1	2	3	4	5	6*	7
H-2β	5.32dd	5.40dd	5.47dd	5.02d	5.72d	4.97d	5.66d
H-3α	3.08dd	3.04dd	3.04dd				
H-3β	2.78dd	2.80dd	2.76dd	4.56d	5.38d	4.32d	5.38d
H-8	6.00s	6.31s	6.75s	6.00s	6.76s	6.17s	6.62s
H-2',6'	7.35d	7.42d	7.43d	7.42d	7.45d	7.32d	7.48d
H-3',5'	6.84d	7.11d	7.11d	6.84d	7.15d	6.77d	7.13d
H-1"	3.38brd	3.21brd	3.16brd	3.38brd	3.16brd	3.17brd	3.20brd
H-2",7"	5.09m	5.09m	5.01m	5.10m	5.02m	5.07m	5.04m
Me-4"	1.82brs	1.74brs	1.71brs	1.82brs	1.76brs	1.72brs	1.82brs
Me-9"	1.72brs	1.68brs	1.64brs	1.62brs	1.66brs	1.61brs	1.68brs
Me-10"	1.60brs	1.58brs	1.58brs	1.56brs	1.58brs	1.55brs	1.62brs
OHchel.	12.40s	12.12s		11.60s			
OMe						3.70s	3.80s
OAc		2.30s	2.38s		2.38s		2.30s
		2.29s	2.26s		2.30s		2.10s
			2.26s		2.30s		2.00s
					2.00s		

J(Hz) 1-3: 2β,3α=12; 2β,3β=4; 3α,3β=17. 4-7: 2β,3α=12. 1-7: 2',3'=8

* In DMSO solution.

Table 2. ^{13}C NMR chemical shifts (in ppm downfield from TMS) of compounds 1 - 7

	1 ($CDCl_3$)	2 ($CDCl_3$)	3 ($CDCl_3$)	4 (DMSO)	5 ($CDCl_3$)	6 (DMSO)	7 ($CDCl_3$)
C-2	78.8d[+]	78.5d	78.9d	82.9d	80.9d	82.4d	80.6d
C-3	43.3t	43.6t	45.4t	71.6d	73.5d	72.6d	74.1d
C-4	196.2s	197.0s	189.2s	198.3s	185.7s	190.6s	185.9s
C-5	161.4s•	159.6s•	149.3s	160.6s	149.8s	159.6s•	160.6s
C-6	107.1s	115.2s	121.8s	107.9s	122.7s	116.4s	123.6s
C-7	164.2s	156.6s	154.9s	164.7s	155.6s	162.8s	156.0s
C-8	95.7d	102.1d	110.0d	94.5d	110.1d	98.7d	108.2d
C-9	161.2s•	161.3s•	160.8s	160.6s	160.4s	161.6s•	160.6s
C-10	103.0s	106.1s	112.1s	100.3s	111.0s	106.1s	112.3s
C-1'	130.7s^	135.6s^	136.1s	127.8s	132.9s	128.0s	133.2s
C-2',6'	127.9d	127.2d	127.3d	129.5d	128.9d	129.4d	128.8d
C-3',5'	115.7d	122.0d	122.1d	115.0d	122.1d	114.9d	122.1d
C-4'	156.2s	151.0s	151.1s	157.9s	151.8s	157.6s	151.7s
C-1"	21.1t	21.9t	23.1t	20.6t	23.1t	21.6t	22.8t
C-2"	121.4d	121.3d	120.9d	122.6d	120.8d	123.1d^	122.0d
C-3"	139.3s	135.8s^	135.9s	134.0s	136.5s	133.9s	136.2s
C-4"	16.2q	16.1q	16.2q	15.8q	16.3q	15.9q	16.3q
C-5"	39.8t	39.6t	39.6t	39.5t	39.6t	39.3t	39.7t
C-6"	26.4t	26.6t	26.6t	26.1t	26.6t	26.2t	26.6t
C-7"	123.8d	124.3d	124.1d	124.2d	124.3d	124.2d^	124.4d
C-8"	132.0s^	131.2s	131.5s	130.7s	131.8s	130.7s	131.8s
C-9"	17.7q	17.6q	17.7q	17.4q	17.7q	17.6q	17.7q
C-10"	25.6q	25.6q	25.6q	25.4q	25.6q	25.5q	25.7q
OCH_3						61.3q	62.6q

[+] SFORD multiplicity

^ These assignments may be reversed.

of bonannione A (1). It was obtained as a colorless amorphous solid and had a molecular formula $C_{25}H_{28}O_6$. The nature and site of the substituents on the aromatic rings of compound 4 and corresponding tetraacetyl derivative 5 were obvious by comparing their ^1H and ^{13}C NMR spectral data (Table 1 and 2) with those of flavanone 1. The presence of a 3β-hydroxyl group was deduced from the chemical shift and the coupling constant ($J_{2,3}$ = 12 Hz) of the doublet at δ_H 4.56. The latter was shifted downfield in the spectrum of the acetate 5. The chemical shifts of the carbon atoms of the ring C (at 82.9, 71.6, and 198.3 ppm, respectively) were diagnostic for a 5,7-dihydroxydihydroflavonol structure and the multiplicity of the signal at 95.5 ppm (doublet with $J_{C-8,H}$ = 162.5 Hz) indicated the site of alkylation at C-6. The 2R,3R configuration of 4 is based on the magnitude of $J_{H-2,H-3}$ and the CD curve (see Experimental).[6]

The last flavonoid was named bonanniol B, with formula $C_{26}H_{36}O_6$. It possesses the structure depicted in 6, which is in complete agreement with ^1H and ^{13}C NMR spectral data (see Table 1 and 2), similar to those of compound 4. As above, the ppm values of the C-2 and C-3 carbons (at 82.4 and 72.6 ppm, respectively) agreed with a dihydroflavonol structure, whereas the carbonyl C-4 resonance was shifted by ca. 8 ppm upfield owing to removal of hydrogen bonding by 5-OH methylation. In this case, the site of alkylation at C-6 was inequivocally indicated by the considerable deshielding of the OCH_3 signal due to steric constraints of the di-ortho substitution. Furthermore, the conformation change, in which the methoxyl bond deviates from coplanarity with aryl ring, produced downfield shifts of carbon atoms C-6, C-8,and C-10, as a consequence of reduced ortho and para effects of the methoxy group.
At last, it can be noted that in all the acetate derivatives the variation of ^{13}C chemical shifts was in line with the well known acetylation effect (i.e. deshielding of ortho- and para-carbons, shielding of ipso-carbon).
The 2R,3R configuration of 6 again is based on the magnitude of $J_{H-2,H-3}$ and CD curve (see Esperimental).

EXPERIMENTAL

Mps are uncorrected. Assignments of ^{13}C NMR chemical shifts were made with the aid of off-resonance and proton coupled ^{13}C NMR experiments. Plant materials were collected in July 1983, near Palermo in Sicily, Italy, and voucher specimens were deposited in the Herbarium of the 'Istituto di Botanica' of the University of Palermo, Italy.

Extraction and isolation of the flavonoids. Dried and finely powdered Bonannia Graeca (L.) Halacsy aerial parts (200 g) were extracted with Me_2CO (7 l) at room temperature for 1 week. After filtration the solvent was evaporated yielding a gum which was subjected to dry-CC over silica gel (600 g Merck No. 7734, deactivated with 15% H_2O). Elution with petrol, petrol-EtOAc mixtures (8:2, 7:3, 6:4) yielded, in order of elution, bonandiol (5.3 g), bonannione A (1, 0.7 g), bonanniol A (4, 2.5 g), and bonanniol B (6, 0.5 g). 1 was further purified by prep.-TLC (silica gel G) using $CHCl_3$-Et_2O (7:3) (three times); compounds 4 and 6 were also purified by prep.-TLC (silica gel G) using benzene-EtOAc (75:25) (three times).

Bonannione A (1): (2S)-6-C-Geranyl-5,7,4'-trihydroxyflavanone. Mp 118°C (from benzene-petroleum ether); $[\alpha]_D^{18}$ -2.6° ($CHCl_3$, c = 0.5); ^{1}H NMR (80 MHz, $CDCl_3$): see Table 1; ^{13}C NMR (20.15 MHz, $CDCl_3$): see Table 2; EIMS (direct inlet) 75eV m/z (rel. int.): 408$[M^+]$ (38), 285$[M-C_9H_{15}]^+$(56), 219$[C_{12}H_{11}O_4]^+$(92), 165$[C_8H_5O_4]^+$(66), 121$[C_8H_9O]^+$(85), 107$[C_7H_7O]^+$(18), 69$[C_5H_9]^+$(80), 41(100); CD curve (EtOH) $\Delta\varepsilon_{332}$ +1.39 (max), $\Delta\varepsilon_{292nm}$ -6.80 (neg. max).
Found: C, 73.12; H, 6.72. $C_{25}H_{28}O_5$ requires: C, 73.52; H, 6.86.

Diacetate 2 from 1. Ac_2O-pyridine treatment of 1 for 2 h at room temperature yielded the derivative 2: mp 83°C (from acetone-petroleum ether). ^{1}H NMR (80 MHz, $CDCl_3$): see Table 1; ^{13}C NMR (20.15 MHz, $CDCl_3$): see Table 2; EIMS (direct inlet) 75eV m/z (rel. int.): 492$[M^+]$ (45), 450(15), 449(12), 381(40), 369(32), 327(68), 219(100), 203(18), 177(15), 165(40), 120(25).
Found: C, 70.91; H, 6.37. $C_{29}H_{32}O_7$ requires: C, 70.73; H, 6.50.

Triacetate 3 from 1 and 2. Ac_2O-pyridine treatment of 1 and 2 for 24 h at room temperature yielded the same derivetive 3 as a gum. ^{1}H NMR (80 MHz, $CDCl_3$): see Table 1; ^{13}C NMR (20.15 MHz, $CDCl_3$): see Table 2; EIMS (direct inlet) 75eV m/z (rel. int.): 534$[M^+]$ (1), 493(3), 492(3), 449(2), 423(1), 381(2), 369(2), 327(4), 288(3), 219(4), 189(11), 161(11), 134(16), 109(17), 43(100).

Bonanniol A (4): (2R,3R)-6-C-Geranyl-5,7,4'-trihydroxydihydroflavonol. Amorphous solid; $[\alpha]_D^{18}$ +11.1° ($CHCl_3$, c = 0.7); IR ν_{max}^{nujol} cm^{-1}: 3425(OH), 1625(C=O); UV λ_{max}^{EtOH} nm 325sh, 295; ^{1}H NMR (80 MHz, $CDCl_3$): see Table 1; ^{13}C NMR (20.15 MHz, DMSO-d_6): see Table 2; EIMS (direct inlet) 75eV m/z (rel. int.): 424$[M^+]$ (35), 406 $[M-H_2O]^+$(16), 301$[M-C_9H_{15}]^+$(73), 269$[C_{17}H_{20}O_4]^+$(43), 219$[C_{12}H_{11}O_4]^+$(17), 165$[C_8H_5O_4]^+$ (100), 136$[C_8H_8O_2]^+$(18), 107$[C_7H_7O]^+$(60), 69$[C_5H_9]^+$(85); CD curve (EtOH) $\Delta\varepsilon_{331}$ +1.70 (max), $\Delta\varepsilon_{290}$ -4.85 (neg. max).
Found: C, 70.93; H, 6.12. $C_{25}H_{28}O_6$ requires; C, 70.75; H, 6.60.

Tetracetate 5 from 4. Ac_2O-pyridine treatment of 4 for 24 h at room temperature yielded the derivative 5 as a gum. ^1H NMR (80 MHz, $CDCl_3$): see Table 1; ^{13}C NMR (20.15 MHz, $CDCl_3$): see Table 2.

Bonanniol B (6): (2R,3R)-6-C-Geranyl-7,4'-dihydroxy-5-methoxydihydroflavonol. Amorphous solid; $[\alpha]_D^{18}$ +33 ($CHCl_3$, c = 0.1); UV λ_{max}^{EtOH} nm 325sh, 283; ^1H NMR (80 MHz, DMSO-d_6): see Table 1; ^{13}C NMR (20.15 MHz, DMSO-d_6): see Table 2; EIMS (direct inlet) 75eV m/z(rel. int.): 438$[M^+]$(9), 420$[M-H_2O]^+$(12), 316$[M-122]^+$(15), 302$[C_{18}H_{22}O_4]^+$(18), 179$[C_9H_9O]^+$(78), 107$[C_7H_7O]^+$(100), 69$[C_5H_9]^+$(90); CD curve (EtOH) $\Delta\varepsilon_{337}$ +2.28 (max), $\Delta\varepsilon_{305}$ -3.04 (neg. max).
Found: C, 71.47; H, 6.32. $C_{26}H_{30}O_6$ requires: C, 71.23; H, 6.85.

Triacetate 7 from 6. Ac_2O-pyridine treatment of 6 for 24 h at room temperature yielded the derivative 7 as a gum. ^1H NMR (80 MHz, $CDCl_3$): see Table 1; ^{13}C NMR (20.15 MHz, $CDCl_3$): see Table 2.

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