Tetrahedron Letters No.20, pp. 2401-2406, 1968. Pergamon Press. Printed in Great Britain.

SOME NEW FLAVONOIDS FROM PSORALEA CORYLIFOLIA

V.K. Bhalla, U. Ramdas Nayak and Sukh Dev
National Chemical Laboratory, Poona (India)

(Received in UK 25 January 1968; accepted for publication 16 February 1968)

FROM the $CHCl_3$ extract of pet. ether exhausted whole seeds of Psoralea corylifolia Linn., a series of closely related flavonoids have been isolated (Table 1) and, we summarise below the evidence leading to the structure elucidation of five of these substances.

Bavachinin, bavachin and bavachalkone

Bavachinin (m.p. 154-155°), which analyses for $C_{21}H_{22}O_4$ (Acetate, m.p. 101-102°, $[\alpha]_D$ -19.1°, $C_{23}H_{24}O_5$, M^+ at m/e 380) is clearly a flavonoid from its spectral characteristics: IR Spectrum (KBr): OH (3175, broad), C=O (1620, 1665 cm^{-1}), benzenoid absorption (1500, 1525, 1580 and 1610 cm^{-1}; UV spectrum λ_{max}^{EtOH}, mμ ($\varepsilon \times 10^{-3}$) : 232 (26.3), 272 (14.6) and 318 (6.4). The UV absorption classifies bavachinin either as an isoflavone or a flavanone*[1], though the well-defined triple absorption of the type observed for the parent compound, as well as its acetate λ_{max}^{EtOH}, mμ ($\varepsilon \times 10^{-3}$): 233 (22.1), 272 (12.8) and 317(5.7) has precedence in some flavanones[2]. Both with NaOH aq. and conc. H_2SO_4, bavachinin gives colour reactions (orange → red and dark red respectively) characteristic[3] only of a flavanone.

The PMR spectrum[4] of its acetate ($C\underline{H}_3COO$, 3H singlet at 135 c/s) clearly defines bavachinin as a flavanone[5] (I): C_2-proton (an ill-defined multiplet centred at 320 c/s, being overlapped by another 1H absorption of an olefinic H; the expected 1H double-doublet is seen centred at 337 c/s in the spectrum of bavachinin in pyridine), C_3-protons (2H multiplet centred at 168 c/s). Besides, the presence of a methoxyl group and a 3,3-dimethylallyl side chain[6] is revealed, thus accounting for all the carbon and oxygen atoms in bavachinin (I): $OC\underline{H}_3$ (3H, singlet, 232 c/s), CH_3-C=C-(6H, broad singlet, 103 c/s), -C=C$\underline{H}$- (1H absorption, buried under the C_2 resonance[CH3]), Ar-$C\underline{H}_2$-CH=C (2H, broad doublet, centred at 192 c/s, J = 7 c/s).

In accordance with its formulation as a flavanone, bavachinin is readily cleaved with NaOH aq. (10%, 10 min. at 100°) to give a deep orange chalcone[1] (m.p. 161-161.5°), $C_{21}H_{22}O_4$: λ_{max}^{EtOH} mμ ($\varepsilon \times 10^{-3}$): 235 (13.4), 300 (inflection, 8.8) and 370 (25.5). This transformation is so facile that exposure of either bavachinin or the chalcone to MeI in DMSO containing some CaO[7], produces the same trimethoxy derivative (light lemon, m.p. 85-86°) of the chalcone[8]. Refluxing the chalcone in anhydrous pyridine

*Its optical activity clearly favours a flavanone formulation.

TABLE 1. NEW FLAVONOIDS FROM PSORALEA CORYLIFOLIA

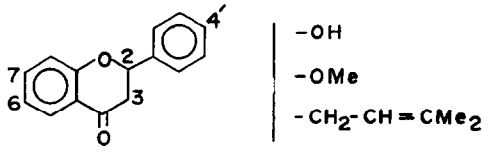
No.	Trivial name*	Mol. formula	R_{dye}+	Colour	m.p.	$[\alpha]_D^{30}$
1	Bavachalkone++	$C_{21}H_{22}O_4$	0.812	Deep orange	161-161.5°	-
2	Bavachinin	$C_{21}H_{22}O_4$	0.704	Colourless	154-55°	-10.4° ($CHCl_3$)
3**	Isobava-chalcone	$C_{20}H_{20}O_4$	0.504	Yellow	154-56°	-
4	Bavachin	$C_{20}H_{20}O_4$	0.496	Colourless	191-92°	-29.1° (EtOH)
5	Isobavachin	$C_{20}H_{20}O_4$	0.456	Colourless	187-88°	-3.94° (EtOH)
6**	-		0.234	Colourless	177-78°	-

*Based on the local name of the plant: Hindi, Bavachi; Marathi, Bavachya

+R_{dye} = $\frac{\text{Movement of substance from start in mm}}{\text{Movement of dye from start in mm}}$; Silicagel-G layer (0.3 mm); solvent, 20% EtOAc in C_6H_6; solvent front, 15 cm; temp. 25°; reference dye, Sudan-III.

++Possibly an artefact. **First isolated by G. Mehta, Ph.D Thesis, Poona University (1966).

containing some piperidine regenerates bavachinin* (80% yield after 36 hr).



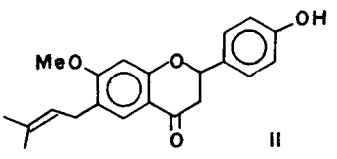
I

The overall substitution pattern of bavachinin is clear from its PMR spectrum (DMSO) in the aromatic protons region. An A_2B_2 quartet, which is seen centred at 426 c/s in its PMR spectrum, can arise only from a 4'-substituted B ring[6,9], with the doublet at 410 c/s (J = 9 c/s) being assigned to 2',6' protons and the other doublet at 442 c/s (J = 9 c/s) being assigned to 2',6' protons. That the substituent at 4' must be a hydroxyl, is clear from the batnochromic shift with enhanced intensity of absorption of the Ia band[1], when the UV spectrum of the chalcone derived from bavachinin is measured in alkaline solution: $\lambda_{max}^{EtOH-NaOH}$ 434 mμ ($\varepsilon \times 10^{-3}$ = 28.5), $\Delta\lambda$ = 64 mμ Thus, the remaining two substituents must be located in ring A. The PMR spectrum (acetone-d_6) of bavachinin further shows two one-proton singlets at 395 and

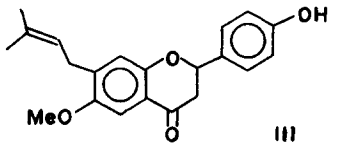
*As expected this product exhibited no optical rotation, but had the same m.p. which was not depressed on admixture with natural bavachinin.

457 c/s, assignable to the two aromatic protons of ring A. Since, these proton signals are not coupled, they must be located para to each other, the 457 c/s singlet being assigned to C_5-H, as this is expected to occur at lowest field[9], due to the anisotropic deshielding by the 4-carbonyl.

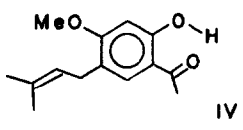
The above results enable one to formulate bavachinin as II or III, the former being preferred on biogenetic considerations[10]. A clear-cut decision in favour of II and one supporting entirely our earlier conclusions, was arrived at by the alkali cleavage of bavachinin. Treatment of bavachinin with 50% KOH aq. (2.5 hr at 180-200°) gave p-hydroxybenzoic acid (yield 80%; identified by m.p., mixed m.p. and IR) and a liquid methyl ketone, $C_{14}H_{18}O_3$ (yield ~ 80%), formulated as IV from its spectral characteristics: λ_{max}^{EtOH} mμ (ε x 10^{-3}), 232 (16.3), 272 (13.7) and 318 (6.9); IR(smear), C=O 1645, 1662 cm^{-1}; PMR, $C\underline{H}_3$-$\underset{CH_3}{C}$=C (3H singlet at 102 c/s and a 3H doublet at 104 c/s J = 1.5 c/s), Me_2C=CH-$C\underline{H}_2$- (2H doublet at 190 c/s, J = 7 c/s), Me_2C=$C\underline{H}$-CH_2- (1H triplet with further fine structure, at 314 c/s, J = 7 c/s), $C\underline{H}_3$-CO (3H singlet at 147 c/s), $C\underline{H}_3O$- (3H singlet at 230 c/s), C_3-H (1H singlet at 376 c/s), C_6-H (1H singlet at 438 c/s) and, chelated O$\underline{H}$[11] (1H singlet at 752 c/s). That the methyl ketone, indeed, has



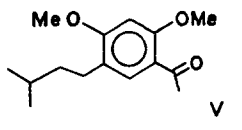
II



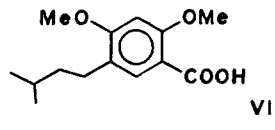
III



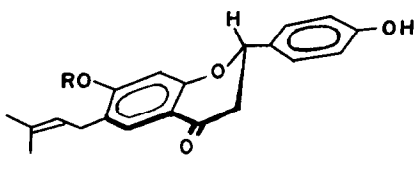
IV



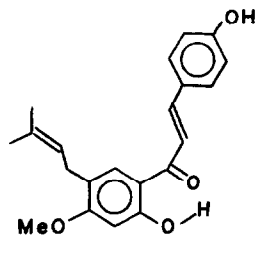
V



VI



VII



VIII

the orientation shown in IV, was proved by the catalytic hydrogenation (10% Pd-C/H_2) of its methyl ether, when the product obtained was indistinguishable (IR, PMR) from V, which was synthesised from the known[12] acid VI by its interaction with MeLi.

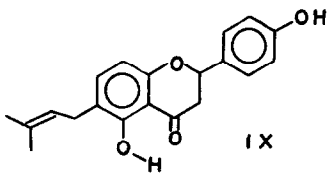
Since, the reasonable suggestion has been made[13] that probably all (-)-flavanones have S-chirality at C_2, VII (R = Me) may be considered to represent the absolute stereostructure of bavachinin.

The chalcone (bavachalcone) encountered during isolation was found to be identical with the chalcone obtained from VII and hence, must be VIII.

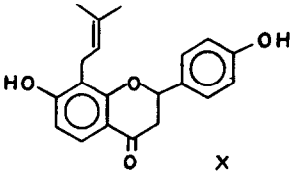
Bavachin, from its spectral characteristics appeared to be the 7-hydroxy flavanone corresponding to II. This was confirmed by its selective methylation[14] with diazomethane to bavachinin and per-methylation with MeI-CaO-DMSO to the trimethyl ether of VIII. Thus, bavachin is VII (R=H).

Isobavachin and isobavachalkone

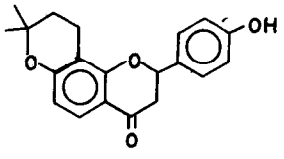
Isobavachin, m.p. 187-188°, $\nu_{KBr}^{c=o}$ 1650 cm^{-1}, was considered from its optical activity, the molecular formula ($C_{20}H_{20}O_4$) and the UV absorption (λ_{max}^{EtOH} 280 mμ, $\varepsilon \times 10^{-3}$ = 12.6) to be isomeric with the flavanone, bavachin, described earlier. The PMR spectrum of its diacetate (m.p. 116-117°, $\nu_{KBr}^{c=o}$ 1690, 1750 cm^{-1}) is in full support of above ($Me_2C=CH-CH_2$-, two 3H singlets at 94 and 98 c/s, 2H broad doublet with J = 7 c/s at 193.5 c/s, 1H triplet with further fine structure at 304 c/s; C_2 proton



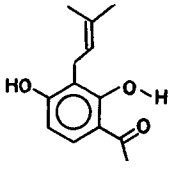
IX



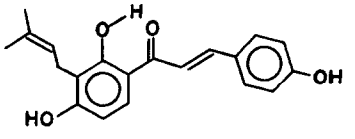
X



XI



XII



XIII

as a multiplet at 328 c/s; C_3 protons as a multiplet centred at 174 c/s) and, the splitting pattern of its aromatic protons (A_2B_2 quartet with A_2 centred at 426 c/s and B_2 at 447.5 c/s, J = 9 c/s; one AB quartet with A centred at 403 c/s and B at 466 c/s, J = 8 c/s), taken together with the accepted biogenetic origin of the A and B ring of flavonoids[10], suggested two possible structures (IX, X) for this. Since, one of the aromatic protons of ring A is considerably deshielded (at 466 c/s) and since, this can arise only when C_5 is unsubstituted (deshielding of C_5-H by 4-carbonyl), structure

IX is ruled out. This conclusion is also supported by the absence of any chelated OH proton[11] at ~750 c/s in the PMR spectrum (DMSO) of isobavachin itself.

The vicinal character of the OH and the 3,3-dimethylallyl side chain in X was confirmed by its cyclisation with AcOH-H_2SO_4 (~25°) to the chroman XI, m.p. 174-175° (Acetate, m.p. 178-180°): PMR in acetone-d_6: quaternary methyls, singlet at 80 c/s.

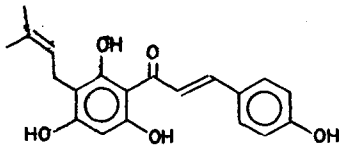
Finally, cleavage of isobavachin with alkali gave, as expected for X, p-hydroxybenzoic acid and a methyl ketone, m.p. 155-156° and having spectral characteristics, in full accord with XII: $\nu_{KBr}^{C=O}$ 1634 cm^{-1}; PMR ($CDCl_3$), $C\underline{H}_3$-C=C (3H doublet at 104 c/s with J = 1 c/s and, one 3H broad singlet at 108 c/s, $Me_2C=C\underline{H}-C\underline{H}_2$- (2H, broad doublet at 205 c/s with J = 8 c/s, 1H triplet at 316 c/s with J = 8 c/s), $C\underline{H}_3CO$ (3H singlet at 152 c/s), C_5-C_6 protons (AB quartet, with A centred at 382 c/s and B at 451 c/s, J = 8 c/s) and, chelated OH (1H singlet at 784 c/s).

The data presented above suffice to formulate isobavachin, unequivocally, as X.

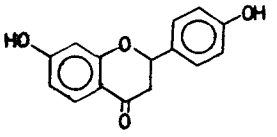
Isobavachalkone, from its spectral characteristics, which will not be discussed here, appeared to be the chalkone corresponding to X. This was proved by its cyclisation with pyridine-piperidine (reflux, 72 hr) to (±)-isobavachin; this cyclisation proceeded only to the extent of ~30% and this may be ascribed to the steric effect of the C_8-side chain in X. Thus, isobavachalkone can be formulated as XIII, a finding further supported by the conversion of isobavachin into the same chalkone by a short treatment with 10% NaOH aq.

Biogenetic considerations

The close biogenetic relationship of these flavonoids is obvious. The occurrence of bavachin (VII, R = H) and isobavachin (X) types, which differ from each other only in the position of attachment of the isoprenoid side-chain, in the same plant, is considered biogenetically significant. It is suggested that both of these types arise from the same alkylated intermediate (e.g. XIV), rather than by alkylation at different



XIV



XV

sites of an intermediate like XV. These points will be elaborated further in a detailed communication.

REFERENCES

1 L. Jurd in The Chemistry of Flavonoid Compounds (Edited by T.A.Geissman) pp.107-155 Pergamon, New York (1962).

2 M.K. Seikel and T.A. Geissman, J. Amer. Chem. Soc. 72, 5721 (1950).

3 K. Venkataraman in The Chemistry of Flavonoid Compounds (Edited by T.A.Geissman), p.72. Pergamon, New York (1962).

4 All PMR spectra were taken on ~10% solutions in CCl_4 (unless stated to the contrary) on a Varian A-60 spectrometer; the signals are recorded in c/s from tetramethylsilane as zero.

5 J. Massicot and J.P. Marthe, Bull. Soc. Chim. Fr. 1962 (1962).

6 e.g. see: L.M. Jackman in Fortschritte der Chemie Organischer Naturstoffe (Edited by L. Zechmeister) 23, pp.349-355. Springer-Verlag, Wien (1965).

7 H.C. Srivastava, S.N. Harshe and P.P.Singh, Tetrahedron Letters 1869 (1963).

8 Y. Asahina, J. Shinoda and M. Inubuse, J. pharm. Soc. Japan 48, 207 (1928).

9 T.J. Mabry, J. Kagan and H. Rosler, Nuclear Magnetic Resonance Analysis of Flavonoids, Publication No.6418, Univ. of Texas, Austin (1964).

10 For a recent summary see: J.H. Richards and J.B. Hendrickson, The Biosynthesis of Steroids, Terpenes and Acetogenins pp.27-172. W.A. Benjamin, New York (1964).

11 T.J. Batterham and R.J. Highet, Aust. J. Chem. 17, 428 (1964).

12 H.N. Khastgir, P.C.Duttagupta and P. Sengupta, Tetrahedron 14, 275 (1961).

13 W.B. Whalley in The Chemistry of Flavonoid Compounds (Edited by T.A.Geissman) pp.441-467. Pergamon, New York (1962).

14 J. Shinoda and S. Sato, J. pharm. Soc. Japan 48, 109, 117 (1928).