Phytochemistry, 1977, Vol. 16, pp. 1995–1997. Pergamon Press. Printed in England.

THE STRUCTURE AND SYNTHESIS OF NEOBAVACHALCONE, A NEW COMPONENT OF *PSORALEA CORYLIFOLIA*.

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(*Received* 27 *May* 1977)

Key Word Index—*Psoralea corylifolia*; Papilionaceae; flavonoids; formylated chalcone; 5′-formyl-2′,4-dihydroxy-4′-methoxychalcone;

Abstract—Reinvestigation of the seeds of *P. corylifolia* has given, besides known compounds, a new formylated chalcone named neobavachalcone whose structure has been deduced as 5′-formyl-2′,4-dihydroxy-4′-methoxychalcone from spectral data and confirmed by synthesis. Its dimethyl ether has also been synthesised by an alternative procedure.

In our preliminary communication [1] the isolation of a new formylated chalcone from the seeds of *P. corylifolia* was reported. The present paper describes the details of the experiments along with the synthesis of neobavachalcone and its diMe ether. The EtOH extract of the defatted seeds was fractionated into alkali soluble and insoluble fractions. The former on column chromatography gave the known compounds [2] bavachin, psoralidin and neobavaisoflavone along with a new compound named neobavachalcone. The alkali insoluble portion of the EtOH extract yielded 4′-O-Mebavachalcone, bavachromene, 7-O-Mebavachin and isobavachalcone as has been reported earlier [2]. The identity of the known compounds was established by direct comparison with authentic samples.

Neobavachalcone crystallized from EtOH as yellow prisms. Elemental analysis and a M^+ peak at m/e 298 gave its molecular formula as $C_{17}H_{14}O_5$. It gave brown colour with alcoholic $FeCl_3$, yellow with aq. NaOH and orange with conc H_2SO_4. Its UV absorption at 230, 265 and 375 nm indicated a chalcone structure. A bathochromic shift of the longer wavelength band with $AlCl_3$ and the absence of any shift with NaOAc showed the presence of a chelated OH group and the absence of a 4′-OH. A negative Gibb's test indicated that the position *para* to the OH is blocked. The IR (KBr) showed two carbonyl absorptions; absorption at 1625 cm^{-1} was due to the chalcone carbonyl (chelated) and the other at 1700 cm^{-1} was characteristic of an aromatic aldehyde group. The presence of the latter was also indicated by the positive Tollen's reduction test. The compound contained one OMe group (micro Zeisel) and formed a diMe ether (M^+ m/e 326). The difference of 28 mass units in the M^+ of the diMe ether and that of the parent compound indicated the presence of two OH groups in the latter.

PMR ($CDCl_3$) of the diMe ether showed the presence of 3 OMe groups and a singlet at δ 10.1 due to an aldehydic proton. Further there were two *ortho* coupled doublets centered at δ 6.87 and δ 7.50 integrating for 4 protons of an A_2B_2 system of a *para* substituted phenyl ring. The substitution pattern of the benzoyl group was indicated by the presence of a singlet at δ 6.46 for the 3′-proton and another downfield singlet at δ 8.15 for the 6′-proton deshielded by the carbonyl. The α and β protons of the chalcone molecule appeared as singlet at δ 7.23 (2H). The nature of the substitution of the phenyl ring was also supported by the appearance of a peak at 835 cm^{-1} characteristic of a *para* substituted benzene ring in the IR spectrum of neobavachalcone. The substituent at the 4-position was found to be OH by identifying *p*-hydroxybenzoic acid as a product of alkali hydrolysis of neobavachalcone. Considering the occurrence of other chalcones derived from isoliquiritigenin in *P soralea* seeds and based on the above spectral data, neobavachalcone has been given the structure as 5′-formyl-2′,4-dihydroxy-4′-methoxychalcone (**1**).

Synthesis of neobavachalcone (1)

Formylation of 4-O-methylresacetophenone by Gattermann–Adam's reaction gave two new products viz., 3-acetyl-2-hydroxy-6-methoxybenzaldehyde (**4**) and 5-acetyl-4-hydroxy-2-methoxybenzaldehyde (**5**). These two isomers could easily be distinguished from each other by PMR and the Gibb's test. The former gave a positive Gibb's test, the latter a negative one indicating that the position *para* to the OH is blocked. In the PMR spectrum of **4**, there were two doublets (J = 9Hz), each integrating to one proton, characteristic of *ortho* coupled protons whereas the spectrum of **5** showed two singlets due to uncoupled *para* protons. Condensation of **5** with *p*-hydroxybenzaldehyde in a strongly alkaline medium gave 5′-formyl-2′,4-dihydroxy-4′-methoxy chalcone which was identical with natural neobavachalcone in all respects. The MS of neobavachalcone and its diMe ether are also in agreement with the assigned structures.

Alternative synthesis of neobavachalcone diMe ether (2)

Resacetophenone on formylation gave besides the known 3-acetyl-2,6-dihydroxybenzaldehyde (**6**) [3] as a major product, a small amount of a new isomeric 5-acetyl-2,4-dihydroxybenzaldehyde (**7**). **7** on condensation with anisaldehyde in a strongly alkaline medium gave 5′-formyl-2′,4′-dihydroxy-4-methoxy chalcone (**3**).

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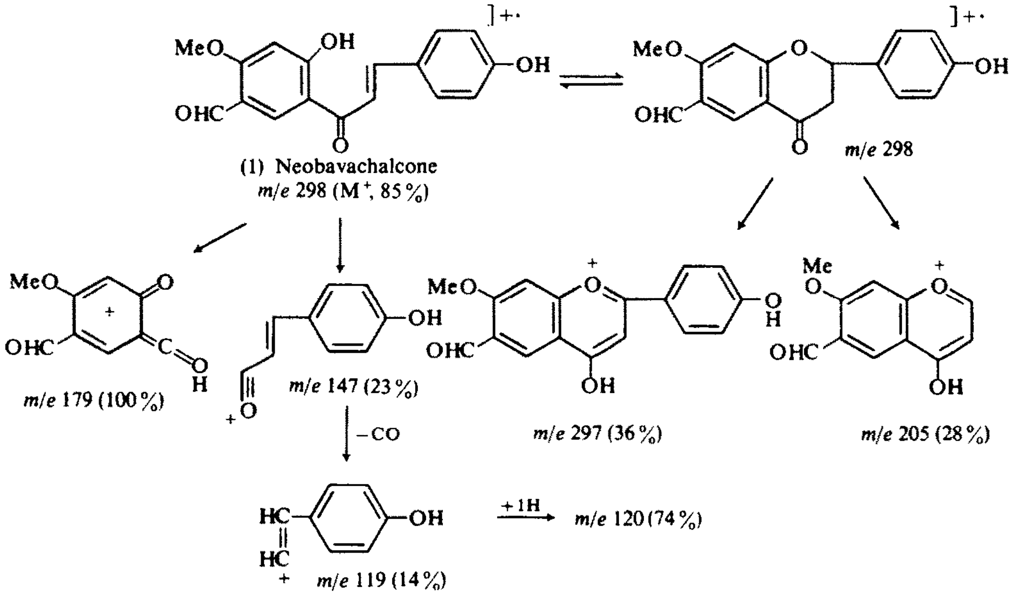
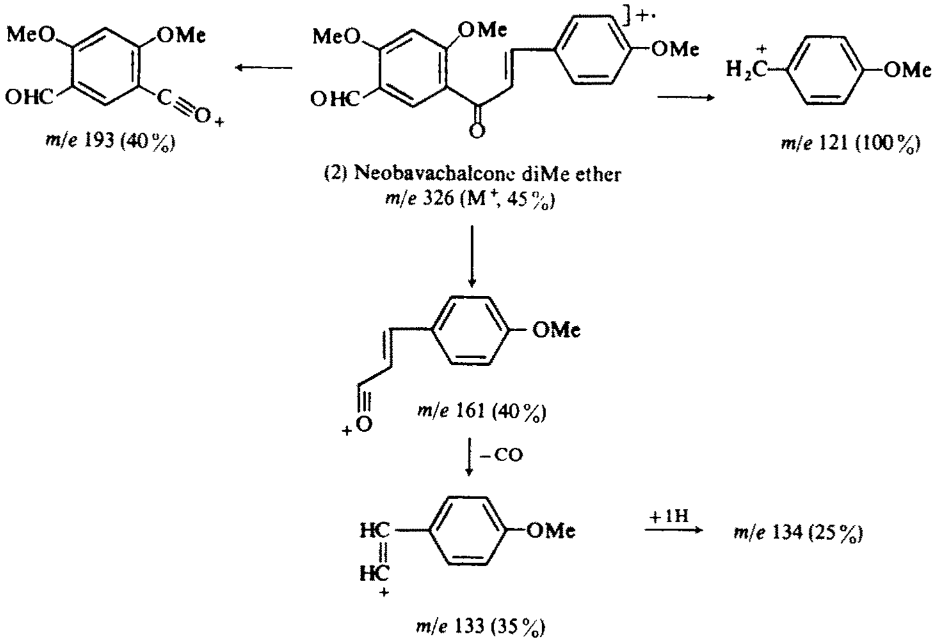
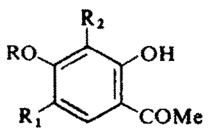
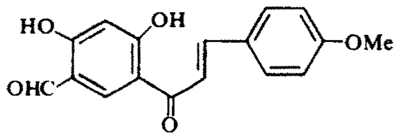




This differs from neobavachalcone in the position of the OMe group. However, methylation of **3** gave 5′-formyl-2′,4,4′-trimethoxychalcone which was identical with the diMe ether of neobavachalcone in all respects (TLC and superimposable IR).



(4) $R_1 = H; R = Me; R_2 = CHO$
(5) $R_2 = H; R = Me; R_1 = CHO$
(6) $R = R_1 = H; R_2 = CHO$
(7) $R = R_2 = H; R_1 = CHO$



(3)

EXPERIMENTAL

Unbroken seeds (2 kg) were extracted successively with petrol (3 × 3l.) and EtOH (3 × 3l.) at room temp. for 48 hr. The EtOH extract concentrate was dissolved in EtOAc (300 ml) and extracted with 5 % aq. Na_2CO_3. The alkali soluble portion on acidification at 0° gave an oily product which was extracted with EtOAc. Removal of the solvent under red. pres. afforded a viscous mass (12 g) which was chromatographed on a Si gel column (400 g). Elution with C_6H_6–EtOAc (49 : 1) gave bavachin whereas C_6H_6–EtOAc (19 : 1) gave psoralidin followed by neobavachalcone (**1**) and neobavaisoflavone. Neobavachalcone crystallized from EtOH as yellow prisms (60 mg), mp 232–35° (decomp.); brown Fe^{3+} reaction, orange with conc H_2SO_4; reduced Tollen's reagent. Negative Gibb's test. $\nu_{\max}^{\mathrm{KBr}}$: 3300 cm^{-1} (chelated —OH), 1700 cm^{-1} (HC=O), 1625 cm^{-1} (chalcone $>$C=O) and 835 cm^{-1} (*p*-substituted benzene ring). $\lambda_{\max}^{\mathrm{MeOH}}$ (log ε): 230 (2.91), 265 (3.91), 375 (4.03) nm; + $AlCl_3$: 247, 313, 429 nm; + NaOAc: 268, 378 nm; + NaOMe: 250, 325, 421 nm. MS *m/e* (%): 298 (M^+, 85), 297 (36), 269 (9), 205 (28), 179 (100), 147 (23), 120 (74), 119 (14), 107 (18), 91 (18). (Found: C, 68.2; H, 4.4; —OMe, 10.1; $C_{16}H_{11}O_4$ (OMe) requires C, 68.4; H, 4.7; —OMe, 10.4 %).

Neobavachalcone diMe ether (**2**). Neobavachalcone (25 mg) in dry Me_2CO (15 ml) was refluxed with Me_2SO_4 and K_2CO_3 (2 g) until it no longer gave a colour with $FeCl_3$. The Me_2CO soln was filtered and the product obtained from the filtrate crystallized from C_6H_6–petrol as colourless plates (19 mg), mp 140–41°; $\nu_{\max}^{\mathrm{KBr}}$: 1695 (HC=O), 1650 ($>$C=O) and 840 cm^{-1} (*p*-substituted benzene ring); PMR (δ, $CDCl_3$): 3.95 (*s*, 6H, 2—OC$\underline{H}_3$), 3.81 (*s*, 3H, 1—OC$\underline{H}_3$); 10.1 (*s*, 1H, —C$\underline{H}$O); 6.87 and 7.50 (2*d*, each *J* = 9Hz, 4H, aromatic protons of ring B in 3,5 and 2,6 positions); 6.46 (*s*, 1H, H–3'); 8.15 (*s*, 1H, H–6') and 7.23 (*s*, 2H, α- and β-H). MS *m/e* (%): 326 (M^+, 45), 311 (17.5), 297 (17.5), 193 (40), 161 (40), 134 (25), 133 (35), 121 (100). (Found: C, 69.8; H, 5.1; $C_{19}H_{18}O_5$ requires C, 69.9; H, 5.5 %).

Alkali hydrolysis of neobavachalcone. 1.1 mg was refluxed with aq. KOH (50 %, 2.5 ml) for 3 hr, the soln cooled, acidified and extracted with Et_2O. The Et_2O soln was extracted with aq. $NaHCO_3$, the alkaline soln neutralized and then re-extracted with Et_2O. The concd Et_2O extract contained *p*-hydroxybenzoic acid as shown by PC in *n*-BuOH satd with H_2O (R_f: 0.75) by comparison with an authentic sample.

Na_2CO_3 insoluble fraction. The EtOAc soln left after extraction of the EtOH extract with 5 % Na_2CO_3 was concd to a syrupy mass (500 g). A portion (2 g) was chromatographed on a column of Si gel (60 g). The column was eluted successively with C_6H_6 and C_6H_6–EtOAc mixture when the known compounds 4'-*O*-Me bavachalcone, bavachromene, 7-*O*-Me bavachin and isobavachalcone were isolated as reported earlier [2].

Synthesis of neobavachalcone (**1**). *Formylation of 4-O-Me resacetophenone.* To a soln of 4-*O*-Me resacetophenone (15 g; 1 mol) in dry Et_2O (250 ml) cooled in a freezing mixture, $Zn(CN)_2$ (21 g; 2 mol) was added followed by anhydrous $AlCl_3$ (24 g; 2 mol) dissolved in dry Et_2O (100 ml). Dry HCl gas was rapidly passed for 4 hr into the continuously stirred mixture. After 24 hr at 0° the Et_2O was decanted, the aldimine-HCl washed × 3 with 30 ml dry Et_2O and dissolved in H_2O (100 ml) and the soln then heated at 100° for 30 min. It was kept in refrigerator for 24 hr when a dark brownish-red solid separated which was filtered, dried and subjected to column chromatography on Si gel. First elutions with petrol and petrol–C_6H_6 (3 : 1) gave unreacted 4-*O*-Me resacetophenone. Subsequent eluates with petrol–C_6H_6 (1 : 1) contained 5-acetyl-4-hydroxy-2-methoxybenzaldehyde (**5**) which crystallized from EtOH as colourless plates (350 mg), mp 132°, reddish-brown Fe^{3+} colour; negative Gibb's test. $\nu_{\max}^{\mathrm{KBr}}$: 1685 (—HC=O), 1630 ($>$C=O) cm^{-1}. PMR (δ, $CDCl_3$): 2.5 (*s*, 3H, —COC$\underline{H}_3$), 3.96 (*s*, 3H, —OC$\underline{H}_3$), 6.36 (*s*, 1H, H-3), 8.25 (*s*, 1H, H-6), 10.3 (*s*, 1H, —C$\underline{H}$O) and 13.3 (*s*, 1H, —O$\underline{H}$). (Found: C, 61.6; H, 5.0; $C_{10}H_{10}O_4$ requires C, 61.8; H, 5.2 %). Further elution of the column with petrol–C_6H_6 (1 : 3) gave a yellowish white crystalline solid (600 mg) which was a mixture of two compounds as shown by TLC ($CHCl_3$). Further column chromatography on Si gel and elution with C_6H_6 gave 3-acetyl-2-hydroxy-6-methoxy benzaldehyde (**4**) which crystallized from EtOH as yellowish-white needles (400 mg), mp 124°; reddish-brown Fe^{3+} reaction; positive Gibb's test. $\nu_{\max}^{\mathrm{KBr}}$: 1667 (—HC=O), 1626 ($>$C=O) cm^{-1}. PMR (δ, $CDCl_3$): 2.5 (*s*, 3H, —COC$\underline{H}_3$), 4 (*s*, 3H, —OC$\underline{H}_3$), 6.41 (*d*, *J* = 10Hz, 1H, H-5), 8.06 (*d*, *J* = 10Hz, 1H, H-4), 10.4 (*s*, 1H, —C$\underline{H}$O) and 13.4 (*s*, 1H, —O$\underline{H}$). (Found: C, 61.8; H, 5.1 : $C_{10}H_{10}O_4$ requires C, 61.8; H, 5.2 %).

5'-Formyl-2',4-dihydroxy-4'-methoxychalcone (**1**). To a soln of 5-acetyl-4-hydroxy-2-methoxybenzaldehyde (5.1 mg) and *p*-hydroxybenzaldehyde (80 mg) in EtOH (5 ml), aq. KOH (50 %, 0.5 ml) was added slowly and the reaction mixture kept out of contact with air at room temp. for 3 days. It was then diluted with H_2O (5 ml) and acidified at 0° with HCl. The resulting solid was filtered, dried and crystallized from EtOH when chalcone (**1**) was obtained as yellow prisms (9 mg), mp 232–34° (decomp.). The mmp with the natural sample of neobavachalcone was undepressed and the IR were superimosable.

Synthesis of neobavachalcone diMe ether (**2**). *Formylation of resacetophenone.* Resacetophenone (15 g; 1 mol) was formylated in a similar way as described for 4-*O*-Me resacetophenone. The aldimine-HCl was decomposed by heating at 100° for 20 min. The product was filtered and crystallized from EtOH using charcoal when 3-acetyl-2,6-dihydroxybenzaldehyde (**6**) was obtained as colourless needles (8 g), mp 111–13° (lit. [3], mp 112–14°); brownish-red Fe^{3+} colour; $\nu_{\max}^{\mathrm{KBr}}$: *ca* 1653 cm^{-1} (broad, two carbonyls); PMR (δ, $CDCl_3$); 2.56 (*s*, 3H, —COC$\underline{H}_3$); 6.4 (*d*, *J* = 9Hz, 1H, H-5); 7.8 (*d*, *J* = 9Hz, 1H, H-4), 10.4 (*s*, 1H, C$\underline{H}$O), 12.6 (*br*, 1H, —OH) and 14 (*s*, 1H, —OH). (Found: C. 60.2; H, 4.0; $C_9H_8O_4$ requires C, 60.0; H, 4.4 %). The mother liqour was concd to a small vol. and kept in refrigerator overnight when some more 3-acetyl-2,6-dihydroxy benzaldehyde crystallized as light brown needles (500 mg). The mother liquor after the second crystallization was chromatographed on a Si gel column (50 g), and eluted with C_6H_6. First few eluates of C_6H_6 on crystallization from EtOH gave **6** and later ones on crystallization from EtOH gave 5-acetyl-2,4-dihydroxy benzaldehyde (**7**) as small colourless needles (100 mg), mp 144–45°, reddish-brown Fe^{3+} reaction; $\nu_{\max}^{\mathrm{KBr}}$: *ca* 1667 cm^{-1} (broad, two carbonyls), PMR (δ, $CDCl_3$): 2.6 (*s*, 3H, —COC$\underline{H}_3$); 6.4 (*s*, 1H, H-3); 8 (*s*, 1H, H-6); 9.83 (*s*, 1H, —C$\underline{H}$O); 11.6 (*br*, 1H, —O$\underline{H}$) and 13.1 (*s*, 1H, —O$\underline{H}$). (Found: C, 59.9; H, 4.2; $C_9H_8O_4$ requires C, 60.0; H, 4.4 %).

5'-Formyl-2',4'-dihydroxy-4-methoxychalcone (**3**). To a soln of 5-acetyl-2,4-dihydroxy benzaldehyde (7.9 mg) and freshly dist. anisaldehyde (0.1 ml) in EtOH (5 ml) was added aq. KOH (50 %, 0.5 ml) and the soln kept out of contact with air at room temp. for 3 days. The deep reddish-brown soln was diluted with H_2O (5 ml) and extracted with Et_2O to remove unreacted anisaldehyde. The aq. soln was carefully acidified at 0° with HCl and kept for 3 hr. The resulting solid was filtered and purified by column chromatography on Si gel. Elution with C_6H_6 gave first unreacted **7** followed by the required chalcone (**3**) which crystallised from MeOH as yellow prisms (13 mg); mp 190–92°, brown Fe^{3+} reaction; $\nu_{\max}^{\mathrm{KBr}}$: 1667 cm^{-1} (—HC=O), 1639 cm^{-1} ($>$C=O), 830 cm^{-1} (*p*-substituted phenyl ring); $\lambda_{\max}^{\mathrm{MeOH}}$: 251, 349, 380 nm; + $AlCl_3$: 305; 360; 425 nm; + NaOAc: 250, 277, 345, 390 nm; + NaOMe: 250, 335, 395 nm. (Found: C, 68.1; H, 4.4; $C_{17}H_{14}O_5$ requires C, 68.4; H, 4.7 %).

5'-Formyl-2',4,4'-trimethoxychalcone (**2**). The chalcone (3.1 mg) in dry Me_2CO (10 ml) was refluxed with Me_2SO_4 (0.05 ml) and ignited K_2CO_3 (1 g) until the reaction mixture gave no colour with EtOH–$FeCl_3$. The Me_2CO soln was filtered and the product obtained from the filtrate crystallized from C_6H_6–petrol as colourless plates (6 mg), mp 140–41°, mmp with the neobavachalcone diMe ether was undepressed and it had superimposable IR.

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