Structure of a New Homoisoflavanone from *Caesalpinia pulcherrima*

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The structure of 8-methoxybonducellin isolated from the stem part of *Caesalpinia pulcherrima* has been shown to be **2**, by unambigous synthesis of both 7,8-dimethoxy-3-(4′-hydroxybenzylidene)-chroman-4-one (**1**) and 7-hydroxy-8-methoxy-3-(4′-methoxybenzylidene)-chroman-4-one (**2**).

McPherson *et al.*[1] have reported the isolation of a new homoisoflavanone, namely 8-methoxybonducellin, from the stem part of *Caesalpinia pulcherrima*. They show in a diagram the structure of the natural product as 7,8-dimethoxy-3-(4′-hydroxybenzylidene)-chroman-4-one (**1**), while in the text they mention its structure as 7-hydroxy-8-methoxy-3-(4′-methoxybenzylidene)-chroman-4-one (**2**).[1] Since both compounds are new, and since the above authors isolated their compound in trace amounts as a gum, it was felt necessary to synthesize both compounds and confirm the constitution of the natural product.

7,8-Dimethoxychromone (**3**)[2] on hydrogenation with Pd–C gave the hitherto unknown 7,8-dimethoxychromanone (**4**), which on condensation with 4-hydroxybenzaldehyde in boiling acetic anhydride gave 7,8-dimethoxy-3-(4′-acetoxybenzylidene)-chroman-4-one (**5**). Compound **5** on saponification yielded compound **1** (Scheme 1). Similarly, 7-benzyloxy-8-methoxychromone (**7**), obtained by the ring closure of 2-hydroxy-3-methoxy-4-benzyloxyacetophenone (**6**)[3] with sodium and ethyl formate, gave on hydrogenation 7-hydroxy-8-methoxychromanone (**8**). Chromanone **8** on condensation with 4-methoxybenzaldehyde in boiling acetic anhydride gave 7-acetoxy-8-methoxy-3-(4′-methoxybenzylidene)-chroman-4-one (**9**), which on saponification gave compound **2** (Scheme 2). Both the compounds **1** and **2** on exhaustive methylation gave 7,8-dimethoxy-3-(4′-methoxybenzylidene)-chroman-4-one (**10**).

McPherson *et al.*[1] obtained 8-methoxybonducillin as a yellow gum, but we isolated both the compounds **1** and **2** as yellow solids having melting points of 208–210 °C and 167–168 °C, respectively. McPherson *et al.*[1] have reported bathochromic shifts in the UV spectrum of the natural product, induced by sodium acetate and sodium methoxide of 20 nm and 42 nm, respectively. We have observed shifts of the same order in the UV spectrum of compound **2**, while compound **1** showed a bathochromic shift in the presence of sodium methoxide but not in the presence of sodium acetate. In the mass spectrum of compounds **1** and **2**, we observed peaks for two main fragments as shown in Scheme 3. The natural sample showed main peaks at *m/z* 146 and 167,[1] and no peaks at *m/z* 181 and 132. However, a direct comparison of the natural product[1] with synthetic **1** and **2** could not be made because of the non-availability of the former.

Thus, on the basis of the above observations, the correct structure of the natural product occurring in *Caesalpinia pulcherrima* should be 7-hydroxy-8-methoxy-3-(4′-methoxybenzylidene)-chroman-4-one (8-methoxybonducellin, **2**).

Experimental

Melting points were determined on a Nalge micro-melting point apparatus and are uncorrected.

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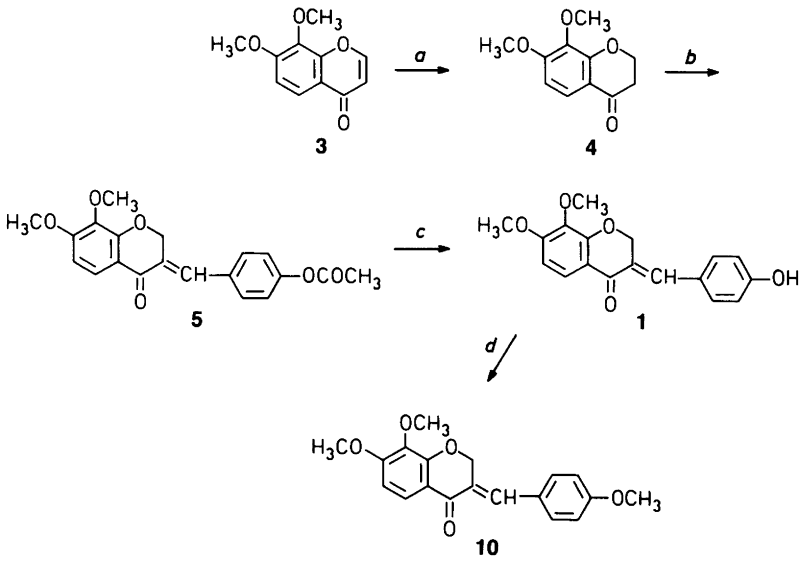


Reagents used:

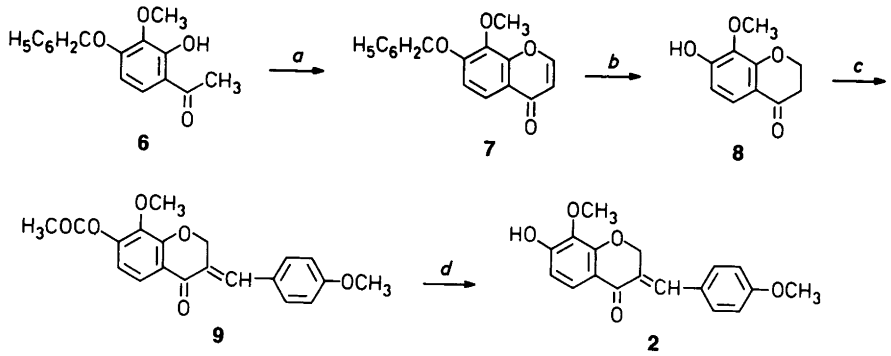
a: H_2/Pd-C, CH_3OH: $CH_3CH_2OCOCH_3$ (1:1)

b: p-HO · C_6H_4CHO, $(CH_3CO)_2O$

c: 10% Na_2CO_3

d: $(CH_3)_2SO_4$, K_2CO_3, CH_3COCH_3

Scheme 1.



Reagents used:

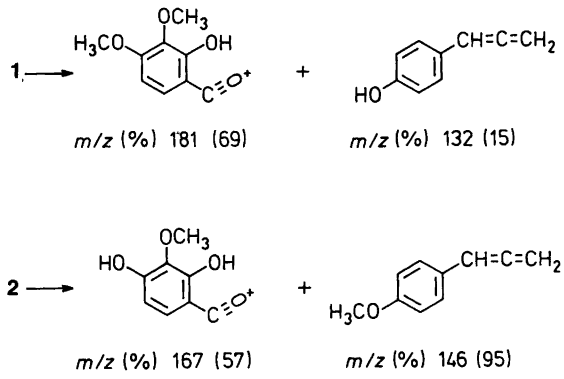
a: Na/$HCOOC_2H_5$

b: H_2/Pd-C, CH_3OH: $CH_3CH_2OCOCH_3$ (1:1)

c: p-CH_3O · C_6H_4 · CHO, $(CH_3CO)_2O$

d: 10% Na_2CO_3

Scheme 2.



Scheme 3.

Silica gel was used for column chromatography and TLC. UV Spectra were recorded on a Perkin Elmer 554 spectrophotometer, IR spectra (KBr discs) were recorded on a Shimadzu model 535 spectrophotometer (ν_{max} in cm^{-1}), mass spectra on a Varian 311 A instrument [reported as *m/z* (% rel. int.)] and ^1H NMR spectra on a 90 MHz Perkin Elmer R-32 or 200 MHz Jeol JNM FX-200 FT-NMR spectrometer. Chemical shifts are given as δ (ppm) values.

7,8-Dimethoxychromanone (**4**). 7,8-Dimethoxychromone[2] (**3**, 2 g) was hydrogenated in a mixture of methanol and ethyl acetate (1:1, 120 ml) with Pd–C catalyst (10 %, 900 mg) for 40 h. The product crystallized from methanol as colourless crystals (**4**, 1.5 g), m.p. 92–93 °C. Anal. $C_{11}H_{12}O_4$: C,H. UV[λ_{max}(MeOH, nm]: 204, 212, 231, 279 and 320(sh). IR(ν_{max}): 2880, 1665, 1590, 1495, 1440, 1376, 1362, 1275, 1190, 1115, 1080, 1015, 984 and 810. ^1H NMR ($CDCl_3$): 7.60 (1H, d, *J* 9 Hz, C–5H), 6.59 (1H, d, *J* 9 Hz, C–6H), 4.55 (2H, t, *J* 7 Hz, C–2H), 3.90 (3H, s, OCH_3), 3.83 (3H, s, OCH_3) and 2.74 (2H, t, *J* 7 Hz, C–3H).

7,8-Dimethoxy-3-(4'-acetoxybenzylidene)chroman-4-one (**5**). To a boiling solution of 7,8-dimethoxychromanone (**4**, 500 mg) in acetic anhydride (15 ml), was added *p*-hydroxybenzaldehyde (500 mg) in portions over a period of 6 h and reflux was continued for 24 h. The solid obtained after decomposition of the mixture with ice-water crystallized from chloroform/petroleum ether as colourless plates (**5**, 350 mg), m.p. 157–158 °C. Anal. $C_{20}H_{18}O_6$: C,H. UV[λ_{max}(MeOH), nm]: 208, 320 and 354. IR(ν_{max}): 2850, 1760, 1660, 1580, 1495, 1460, 1365, 1282, 1160, 1090, 970, 920 and 810. ^1H NMR ($CDCl_3$): 7.87 (1H, t, *J* 1.8 Hz, C–9H), 7.82 (1H, d, *J* 9 Hz, C–5H), 7.42 (2H, d, *J* 9 Hz, C-2' and 6'-H), 7.36 (2H, d, *J* 9 Hz, C-3' and 5'-H), 6.77 (1H, d, *J* 9 Hz, C–6H), 5.42 (2H, d, *J* 1.8 Hz, C–2H), 3.95 (3H, s, OCH_3), 3.86 (3H, s, OCH_3) and 2.31 (3H, s, $OCOCH_3$).

7,8-Dimethoxy-3-(4'-hydroxybenzylidene)chroman-4-one (**1**). Saponification of 7,8-dimethoxy-3-(4'-acetoxybenzylidene)chroman-4-one (**5**, 200 mg) with aq. sodium carbonate (8 ml, 10 %) gave a yellow solid which crystallized from methanol as yellow needles (150 mg), m.p. 208–210 °C. Anal. $C_{18}H_{16}O_5$: C,H. UV[λ_{max}(MeOH), nm]: 204, 276, 320 and 357; +NaOMe: 206, 224, 288 and 436. IR(ν_{max}): 3200, 2880, 1640, 1582, 1500, 1430, 1389, 1275, 1160, 1100, 920, 810 and 780. ^1H NMR (acetone-d_6): 7.70(1H, t, *J* 1.8 Hz, C–9H), 7.66 (1H, d, *J* 9 Hz, C–5H), 7.32 (2H, d, *J* 9 Hz, C-2' and 6'-H), 6.96 (2H, d, *J* 9 Hz, C-3' and 5'-H), 6.60 (1H, d, *J* 9 Hz, C–6H), 5.44 (2H, d, *J* 1.8 Hz, C–2H), 3.88 (3H, s, OCH_3) and 3.76 (3H, s, OCH_3). MS: 312 (M^+, 100), 311 (16), 281 (8), 182 (7), 181 (69), 180 (20), 179 (13), 165 (8), 152 (53), 151 (19), 149 (7), 137 (27), 132 (15), 131 (26), 123 (5), 122 (7), 121 (12), 120 (16), 115 (5), 109 (15), 103 (7), 94 (10), 78 (6), 77 (13), 66 (8), 63 (5) and 51 (7).

7-Benzyloxy-8-methoxychromone (**7**) . A solution of 2 hydroxy-3-methoxy-4-benzyloxyacetophenone[3] (**6**, 3.5 g) in ethyl formate (120 ml) was added in small portions to powdered sodium (3.5 g). The mixture was left overnight. The mixture was then decomposed with ice cold 10 % HCl, ethyl formate was removed by evaporation on a steam bath and the separated oil was heated for 20 min. The crude product which solidified on cooling was purified by crystallization from ethyl acetate/petroleum ether to give light yellow crystals (**7**, 2 g), m.p. 105–106 °C. UV[λ_{max}(MeOH), nm]: 213, 243, 249 and 296. IR(ν_{max}): 2980, 1645, 1612, 1575, 1500, 1421, 1405, 1276, 1210, 1178, 1063, 1005, 835 and 800. ^1H NMR ($CDCl_3$): 7.84 (1H, d, *J* 6 Hz, C–2H), 7.80 (1H, d, *J* 9 Hz, C–5H), 7.33 (5H, s, $OCH_2C_6H_5$), 7.00 (1H, d, *J* 9 Hz, C–6H), 6.20 (1H, d, *J* 6 Hz, C–3H), 5.15 (2H, s, $OCH_2C_6H_5$) and 3.93 (3H, s, OCH_3).

7-Hydroxy-8-methoxychromanone (**8**). 7-Benzyloxy-8-methoxychromone (**7**, 1.5 g) was hydrogenated in a mixture of methanol and ethyl acetate (1:1, 100 ml) with Pd–C catalyst (10%, 800 mg) for 32 h. The solid obtained after evaporating the solvent crystallized from methanol as colourless crystals (**8**, 800 mg), m.p. 161–162 °C. Anal. $C_{10}H_{10}O_4$: C,H. UV[λ_{max}(MeOH), nm]: 215, 233 and 280; +NaOAc: 212, 232, 258, 280 and 332; +NaOMe: 208, 253 and 334. IR(ν_{max}): 3200, 2984, 1650, 1570, 1494, 1440, 1378, 1320, 1285, 1218, 1180, 1135, 1100, 1010, 894, 818, 800 and 680. ^{1}H NMR ($CDCl_3$): 7.63 (1H, d, *J* 9 Hz, C–5H), 6.70 (1H, d, *J* 9 Hz, C–6H), 4.66 (2H, t, *J* 7 Hz, C–2H), 3.95 (3H, s, OCH_3) and 2.92 (2H, t, *J* 7 Hz, C–3H).

7-Acetoxy-8-methoxy-3-(4′-methoxybenzylidene)-chroman-4-one (**9**). To a boiling solution of 7-hydroxy-8-methoxychromanone (**8**, 500 mg) in acetic anhydride (15 ml) was added anisaldehyde (500 mg) in portions over a period of 24 h. The solid obtained after working up the reaction mixture crystallized from $CHCl_3$/petroleum ether as colourless plates (**9**, 350 mg), m.p. 124–125 °C. Anal. $C_{20}H_{18}O_6$: C,H. UV[λ_{max}(MeOH), nm]: 206, 236, 328 and 360. IR(ν_{max}): 1758, 1680, 1586, 1502, 1458, 1440, 1418, 1360, 1295, 1250, 1195, 1164, 1070, 1010, 945, 895, 810, 760 and 700. ^{1}H NMR ($CDCl_3$): 7.90 (1H, t, *J* 1.8 Hz, C–9H), 7.84 (1H, d, *J* 9 Hz, C–5H), 7.35 (2H, d, *J* 9 Hz, C-2′ and 6′-H), 7.03 (2H, d, *J* 9 Hz, C-3′ and 5′-H), 6.83 (1H, d, *J* 9 Hz, C–6H), 5.50 (2H, d, *J* 1.8 Hz, C–2H), 3.89 (6H, s, $2 \times OCH_3$), 2.36 (3H, s, $OCOCH_3$).

7-Hydroxy-8-methoxy-3-(4′-methoxybenzylidene)-chroman-4-one (**2**). Saponification of 7-acetoxy-8-methoxy-3-(4′-methoxybenzylidene)chroman-4-one (**9**, 200 mg) with aq. sodium carbonate (10 ml, 10%) gave a yellow solid which crystallized from methanol as yellow needles (**2**, 125 mg), m.p. 167–168 °C. Anal. $C_{18}H_{16}O_5$: C,H. UV[λ_{max}(MeOH), nm]: 205, 228, 328 and 355; +NaOAc: 207, 268, 332 and 370; +NaOMe: 207, 270, 314 and 394. IR(ν_{max}): 3050, 2880, 1640, 1564, 1505, 1480, 1445, 1430, 1370, 1340, 1245, 1256, 1220, 1190, 1168, 1082, 1035, 1015, 978, 808 and 710. ^{1}H NMR (Acetone-d_6): 7.72 (1H, t, *J* 1.8 Hz, C–9H), 7.61 (1H, d, *J* 9 Hz, C–5H), 7.44 (2H, d, *J* 9 Hz, C-2′ and 6′-H), 7.08 (2H, d, *J* 9 Hz, C-3′ and 5′-H), 6.67 (1H, d, *J* 9 Hz, C–6H), 5.47 (2H, d, *J* 1.8 Hz, C–2H), 3.86 (3H, s, OCH_3) and 3.82 (3H, s, OCH_3). MS: 312 (M+, 100), 311 (40), 297 (10), 281 (7), 167 (57), 166 (15), 165 (7), 147 (11), 146 (95), 145 (9), 138 (20), 137 (15), 131 (11), 123 (5), 115 (5), 103 (14), 77 (9) and 51 (5).

7,8-Dimethoxy-3-(4′-methoxybenzylidene)chroman-4-one (**10**). 7,8-Dimethoxy-3-(4′-hydroxybenzylidine)chroman-4-one (**1**, 75 mg) was dissolved in dry acetone (5 ml) and to the solution were added K_2CO_3 (1.5 g) and dimethyl sulphate (0.04 ml). The mixture was heated under reflux for 5 h. After working up the reaction mixture, the solid obtained crystallized from methanol as yellow crystals (**10**, 75 mg), m.p. 111–112 °C. Anal. $C_{19}H_{18}O_5$: C,H. UV[λ_{max}(MeOH, nm]: 325 and 356. IR(ν_{max}): 2900, 1660, 1580–1500, 1430, 1360, 1270, 1240, 1160, 1086 and 810. ^{1}H NMR ($CDCl_3$): 7.87 (1H, t, *J* 1.8 Hz, C–9H), 7.82 (1H, d, *J* 9 Hz, C–5H), 7.35 (2H, d, *J* 9 Hz, C-2′ and 6′-H), 7.02 (2H, d, *J* 9 Hz, C-3′ and 5′-H), 6.75 (1H, d, *J* 9 Hz, C–6H), 5.46 (2H, d, *J* 1.8 Hz, C–2H), 3.97 (3H, s, OCH_3) and 3.87 (6H, s, $2 \times OCH_3$). The same compound (**10**) was obtained by methylation of compound **2** under similar conditions.

References

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