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# Synthesis of isopongaflavone

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The synthesis of isopongaflavone[1] **9**, a constituent of the seeds of *Tephrosia bracteolata*, is described. Phloroacetophenone **1** on treatment with chlorobutyne affords 2,6-dihydroxy-6′,6′-dimethylpyrano[2′,3′: 4,3]acetophenone **2** which on methoxymethylation yields 2,6-di(methoxymethoxy)-6′, 6′-dimethylpyrano[2′,3′: 4,3]acetophenone **5**. Alkaline condensation of **5** and benzaldehyde gives 2′, 6′-di(methoxymethoxy)-6″,6″-dimethylpyrano[2″, 3″ : 4′, 3′] chalcone **6**. DDQ treatment of 2′, 6′-dihydroxy-6″,6″-dimethylpyrano[2″, 3″ : 4′, 3′] chalcone **7**, obtained by the demethoxymethylation of **6**, furnishes 5-hydroxy-6″,6″-dimethylpyrano[2″, 3″ : 4, 3]flavone **8** which on O-methylation gives 5-methoxy-6″,6″-dimethylpyrano[2″, 3″ : 4, 3]flavone **9**.

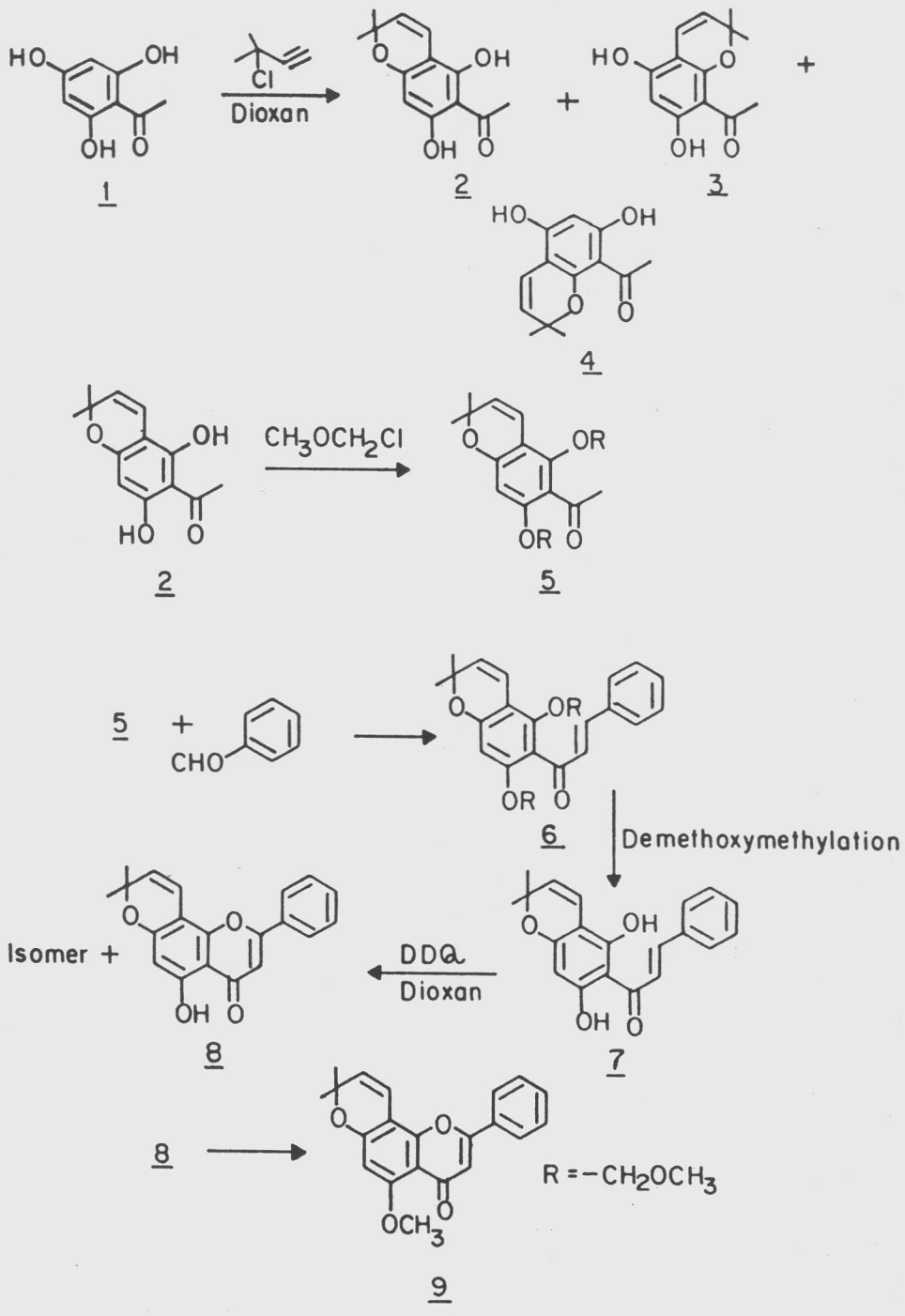
Isopongaflavone (5-methoxy-6″,6″-dimethyl pyrano [2″, 3″ : 7,8]flavone, **9**) was isolated from the seeds of *Tephrosia bracteolate*[1], and its structure assigned based on spectral data only. In this paper, we describe the synthesis of this natural product starting from phloroacetophenone **1**.

Phloroacetophenone **1** on treatment with chlorobutyne[2] (2-chloro-2-methylbut-3-yne) in dry dioxan gives three major products: 2,6-dihydroxy-6′, 6′-dimethylpyrano[2′,3′ : 4,3]acetophenone **2**, 4,6-dihydroxy-6′, 6′-dimethylpyrano [2′,3′ :3, 2]acetophenone **3** and 2,4-dihydroxy-6′, 6′-dimethylpyrano[2′,3′ :6,5]acetophenone **4**, and several other minor products. Methoxymethylation[3] of **2** using methoxymethyl chloride and potassium carbonate yielded the 2,4-di(methoxymethoxy) derivatgive **5**. Alkaline condensation of **5** with benzaldehyde gave the methoxymethylated chalcone **6** which on demethoxymethylation[3] furnished the hydroxy chalcone **7**. DDQ treatment of **7** afforded the compound **8**. Finally O-methylation of **8** gave isopongaflavone **9** (cf. Scheme I), whose m.p. and spectral characteristics agreed with those reported[1] for the natural sample. A direct comparison was not possible owing to nonavailability of the authentic sample.

## Experimental Section

**General.** Melting points were determined using an electrothermal melting point apparatus (Gallenkamp) and are uncorrected. IR spectra were recorded in KBr on a Pye-Unicam SP3-300 IR spectrophotometer ($\nu_{max}$ in $cm^{-1}$ ). $^1H$ NMR spectra were recorded on a Perkin-Elmer R-32 (90MHz) instrument in $CDCl_3$ with TMS as internal standard (chemical shifts in δ, ppm). UV spectra were recorded on LKB 4053 spectrophotometer in Ultraspeck methanol ($\nu_{max}$ in nm). TLC was performed using silica gel 60G. Mass spectra were recorded on a VG 7070E analytical mass spectrometer.

**Treatment of phloroacetophenone chlorobutyne 1.** To a solution of phloroacetophenone 1($2.97\times10^{-5}$ mmoles) in dry dioxan (80 mL) were added 2-chloro-2-methylbut-3-yne[2] (0.048 mmole), anhydrous potassium carbonate ($1.08\times10^{-4}$ mmole) and potassium iodide ($6.02\times10^{-6}$ mmole). The mixture was refluxed for 24 hr. Dioxan was removed by distillation and water added to the residue. It was extracted with ether, dried over anhydrous sodium sulphate and evaporated to dryness. The ether extract on column chromatography using petrol (40-60°C), petrol-benzene (15:1), petrol-benzene (9:1) and increasing




**Scheme I**

quantities of benzene as eluents gave the following major compounds, A-C, and several other minor compounds.

**Compound A:** It was obtained from column and purified by preparative TLC over silica gel 60G using benzene-acetone (20:1) as developing solvent. It was a semi solid mass ($6.41\times10^{-6}$ mmole) and could not be crystallized from any solvent $R_f$ 0.81 (benzene-acetone, 20:1); $M^+$ 234; UV: 228, 265; IR : 3470, 2910, 2870, 1645, 1600, 1595, 1375, 1360; $^1$H NMR: 1.43 [s, 6H, -O-C($CH_3$)$_2$], 2.45 (s, 3H, -$COCH_3$), 5.71 (d, 1H, $J$=10Hz, H-5′), 6.83 (d, 1H,

$J$=10Hz, H-4′), 7.11 (s, 1H,H-5), 8.32 and 12.75 (2s, 2H, -OH×2); [Found: C, 66.8; H, 5.6. $C_{13}H_{14}O_4$ requires: C, 66.7, H, 5.9%]. It was identified as 2,6-dihydroxy-6′, 6′-dimethylpyrano [2′,3′: 4,3]acetophenone **2.**

**Compound B:** It was purified by preparative TLC over silica gel 60G using benzene-acetone (20:1) as developing solvent affording a white semi-solid ($4.18\times10^{-6}$ mmole) which could not be crystallized from any solvent; $R_f$ 0.67 (benzene-acetone; 20:1). It was characterized as **3** ($M^+$, 234); UV: 232, 260; IR: 3450, 2910, 2890, 1640, 1605, 1600, 1375, 1365; PMR: 1.41 [s, 6H, -O-C($CH_3$)$_2$], 2.44 (s, 3H, -$COCH_3$), 5.68 (d, 1H, J=10Hz, H-5′), 6.78 (d, 1H, J=10Hz, H-4′), 7.18 (s, 1H, H-5), 12.25 (s, 2H, -OHx2) [Found: C, 66.8, H, 5.8. $C_{13}H_{14}O_4$ requires: C, 66.7; H, 5.9%]. It was identified as 4,6-dihydroxy-6′,6′-dimethyl-pyrano[2′,3′:4,3]acetophenone **3**.

**Compound C:** The fraction from column was further purified by preparative TLC over silica gel 60G using benzene-acetone (20:1) as developing solvent, and was characterized as 4 ($2.90\times10^{-6}$ mmole); $R_f$ 0.51 (benzene-acetone; 20:1); $M^+$, 234; UV: 232, 260; IR : 3470, 2910, 2890, 1645, 1605, 1600, 1375, 1365; $^1$H NMR: 1.41 [s, 6H, –O–C($CH_3$)$_2$], 2.46 (s, 3H, –$COCH_3$), 5.68 (d, 1H, $J$=10Hz, H-5′), 6.45 (s, 1H, H-3) 6.78 (d, 1H, $J$=10Hz, H-4′), 13.10 (s, 2H, -OH×2); [Found: C, 66.8, H, 5.8. $C_{13}H_{14}O_4$ requires: C, 66.7; H, 5.9%]. It was identified as 2,6-dihydroxy-6′,6′-dimethylpyrano[2′,3′:4,3]acetophenone **4.**

**Methoxymethylation of 2,6-dihydroxy-6′,6′-dimethylpyrano[2′,3′:4,3]acetophenone 2.** A mixture of 2,6-dihydroxy-6′,6′-dimethylpyrano [2′,3′ :4,3]acetophenone (**2**, $4.27\times10^{-6}$ mmole) in dry acetone (25 mL), methoxymethyl chloride ($1.16\times10^{-5}$ mmole) and anhydrous potassium carbonate ($1.80\times10^{-4}$ mmole) was refluxed for about 3 hr. The progress of the reaction mixture was moitored by TLC. After cooling, acetone was distilled off and water added to the residue. It was then extracted with ether, washed with water and dried over anhydrous $Na_2SO_4$. The organic layer was evaporated to dryness and the single methoxymethylated product **5** ($3.35\times10^{-6}$ mmole) was obtained by crystallization from petrol, m.p. 49°; $M^+$ 232; $R_f$ 0.74 (benzene-acetone; 9:1); UV: 226, 265; IR : 1645, 1600, 1595, 1375, 1365; $^1$H NMR: 1.48 [s, 6H, –O–C($CH_3$)$_2$], 2.41 (s, 3H, –$COCH_3$), 3.45 (s, 6H, -$CH_2OCH_3$ × 2), 5.51 (s, 4H, –$CH_2OCH_3$ × 2), 5.70 (d, 1H, $J$=10Hz, H-5′), 6.78 (d, 1H, $J$=10Hz, H-4′), 7.10 (s, 1H, H-5), [Found: C, 63.6; H, 6.8. $C_{17}H_{22}O_6$ requires: C, 63.4; H, 6.8%]. It was identified as 2,6-di(methoxymethoxy)-6′, 6′-dimethylpyrano [2′,3′ : 4,3]acetophenone **5.**

**2′,6′-Di(methoxymethoxy)-6″,6″-dimethyl-pyrano[2″,3″: 4′,3′]chalcone 6.** A mixture of 2,6-di(methoxymethoxy)-6′, 6′-dimethylpyrano[2′,3′: 4,3]acetophenone **5** ($5.21\times10^{-6}$ mmole) and benzaldehyde ($1.02\times10^{-5}$ mmole) in ethanolic solution of KHO (50%, 25 mL) was kept at room temperature for 3 days. The reaction mixture was diluted with ice cold water, acidified with dil. HCl and extracted with ether. The ether layer was washed with water, dried over anhydrous sodium sulphate and evaporated to dryness. The residue was purified by preparative TLC over silica gel 60G using benzene-acetone (15:1) as developing solvent. The product was crystallized from ethyl acetate to give yellow crystals ($2.73\times10^{-6}$ mmole), m.p. 71°; $M^+$ 410; $R_f$ 0.88 (benzene-acetone; 10:1); UV: 232, 260, 365; IR : 1640, 1600, 1595, 1375, 1365; $^1$H NMR : 1.41 [s, 6H, -O-C($CH_3$)$_2$], 3.48 (s, 6H, -$CH_2OCH_3$×2), 5.44 (s, 4H, -$CH_2OCH_3$×2), 5.61 (d, 1H, $J$=10Hz, H-5″), 6.58 (d, 1H, $J$=10Hz, H-4″), 6.98 (s, 1H, H-5′), 7.45 (d, 1H, $J$=9Hz, H-α), 7.58 (s, 5H, aromatic protons), 8.01 (d, 1H, $J$=9Hz, H-β); Anal. Calcd for $C_{24}H_{26}O_6$: C, 70.2; H, 6.3. Found: C, 70.5; H, 6.6%.

**2′,6′-Dihydroxy-6″,6″-dimethylpyrano[2″,3″: 4′,3′]chalcone 7.** To a solution of the above methoxymethylated chalcone **6** ($2.43\times10^{-6}$ mmole) in methanol (35 mL), HCl (3$N$, 50 mL) was added and boiled in water bath for 15 min. It was diluted with water (150 mL) and extracted with ethyl acetate. The ethyl acetate extract was washed with water, dried over anhydrous $Na_2SO_4$ and concentrated. TLC examination of the residue showed several spots and the major product was

purified by preparative TLC using ethyl acetate-benzene (1:1) as developing solvent. It crystallized from petrol as yellow needles ($2.23\times10^{-6}$ mmolw), m.p. 84°, $M^+$ 322; $R_f$ 0.61 (ethyl acetate-benzene; 1:1). It gave positive ferric chloride test. UV: 228, 372; IR : 3520, 1645, 1610, 1590, 1385, 1310; $^1$H NMR: 1.44 [s, 6H, –O–C($CH_3$)$_2$], 5.54 (d, 1H, *J*=10Hz, H-5″), 6.58 (d, 1H, *J*=10Hz, H-4″), 7.01 (s, 1H, H-5′), 7.43 (d, 1H, *J*=9Hz, H-α), 7.50 (s, 5H, aromatic protons), 8.03 (d, 1H, *J*=9Hz, H-β), 12.78 (s, 2H, –OH×2); Anal. Calcd for $C_{20}H_{18}O_4$: C, 74.5; H, 5.6. Found: C, 74.6; H, 5.6%.

**5-Hydroxy-6″,6″-dimethylproano[2″,3″: 4,3] flavone 8.** To a solution of 2′,6′-dihydroxy--6″,6″-dimethylproano[2″,3″: 4′,3′]chalcone **7** ($3.10\times10^{-6}$ mmole) in dry dioxan (150 mL) was added DDQ ($6.60\times10^{-7}$ mmole). The mixture was refluxed for 3 hr. Dioxan was removed by distillation and water was added to the residue. It was extracted with ether. The ether extract was washed with water, dried over anhydrous $Na_2SO_4$ and evaporated to dryness. The product was purified by preparative TLC over silica gel 60G using benzene as developing solvent. It crystallized from benzene-*n*-hexane as pale yellow crystals ($1.34\times10^{-6}$ mmole), m.p. 189°; $M^+$ 320); $R_f$ 0.64 (benzene); UV: 235, 275, 355; IR : 3545, 1640, 1605, 1595, 1385, 1310; $^1$H NMR: 1.44 [s, 6H, -O-C($CH_3$)$_2$], 5.54 (d, 1H, *J*=10Hz, H-5″), 6.58 (d, 1H, *J*=10Hz, H-4″), 6.62 (s, 1H, H-3), 6.95 (s, 1H, H-6), 7.50 (s, 5H, aromatic protons), 12.48 (s, 1H, –OH); Anal. Calcd for $C_{20}H_{18}O_4$: C, 75.0; H, 5.0. Found: C, 75.3; H, 5.3%.

**5-Methoxy-6″,6″-dimethylpyrano[2″,3″:4,3] flavone 9.** A mixture of 5-hydroxy-6″,6″-dimethylpyrano[2″,3″: 4,3]flavone **8** ($1.56\times10^{-6}$ mmole), dimethyl sulphate ($1.82\times10^{-6}$ mmole) and anhydrous potassium carbonate ($1.08\times10^{-4}$ mmole) in acetone (20 mL) was refluxed for 2 hr. Acetone was distilled off and water added to the residue. It was extracted with ether, washed with water and dried over anhydrous $Na_2SO_4$. The organic layer was evaporated to dryness and the product purified by preparative TLC over silica gel $GF_{254}$ using benzene-acetone(10:1) as developing solvent. It was crystallized from methanol-chloroform to give yellow crystals ($2.7\times10^{-6}$ mmole), m.p. 214-15° (lit[1]. m.p. 215-16°); $M^+$ 334; $R_f$ 0.65 (benzene-acetone; 10:1); UV: 226, 265, 355; IR: 1645, 1605, 1595, 1385, 1310; $^1$H NMR : 1.48 [s, 6H, –O–C($CH_3$)$_2$], 3.95 (s, 3H, -$OCH_3$), 5.54 (d, 1H, *J*=10Hz, H-5″), 6.58 (d, 1H, *J*=10Hz, H-4″), 6.68 (s, 1H, H-3), 6.98 (s, 1H, H-6), 7.50 (s, 5H, aromatic protons); Anal. Calcd for $C_{21}H_{18}O_4$: C, 75.4; H, 5.4. Found: C, 75.6; H, 5.4%.

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