

## Synthesis of natural triisopentenylated flavanone, euchrenone a<sub>2</sub>

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**Abstract.** Euchrenone a<sub>2</sub> (7) isolated from the roots of *Euchresta japonica* has been synthesised from 3-prenylphloroacetophenone (1) by other workers. We carried out its cyclodehydrogenation with dichloro dicyano quinone (DDQ) to obtain 6-acetyl-5,7-dihydroxy-2,2-dimethylchromene (2) which was ethoxymethylated in the 7-position to give 6-acetyl-7-ethoxymethoxy-5-hydroxychromene (3). Chalcone condensation of 3 and 4-ethoxymethoxy-3-*C*-prenylbenzaldehyde (4) gave 4,6'-bisethoxymethoxy-2'-hydroxy-6'',6''-dimethyl-3-*C*-prenylpyrano (2'',3''-4,3) chalcone (5) which cyclised with methanolic sodium acetate to give protected 5,4'-bisethoxymethoxy-6'',6''-dimethyl-3'-*C*-prenylpyrano (2'',3''-7,8) flavanone (6). Deprotection of 6 with 4% methanolic HCl yielded (7) with melting point and spectral data identical to that of the natural compound.

**Keywords.** Tri-isopentenylated chalcone; tri-isopentenylated flavanone; euchrenone a<sub>2</sub>.

### 1. Introduction

Recently euchrenone a<sub>2</sub> (7) has been isolated from the roots of *Euchresta japonica* Hook. f. ex. Regel by Mizuno *et al* (1988) and has been identified as 4',5-dihydroxy-6'',6''-dimethyl-3'-*C*-prenylpyrano (2'',3''-7,8) flavanone on the basis of its UV, <sup>1</sup>H-NMR and mass spectral data.

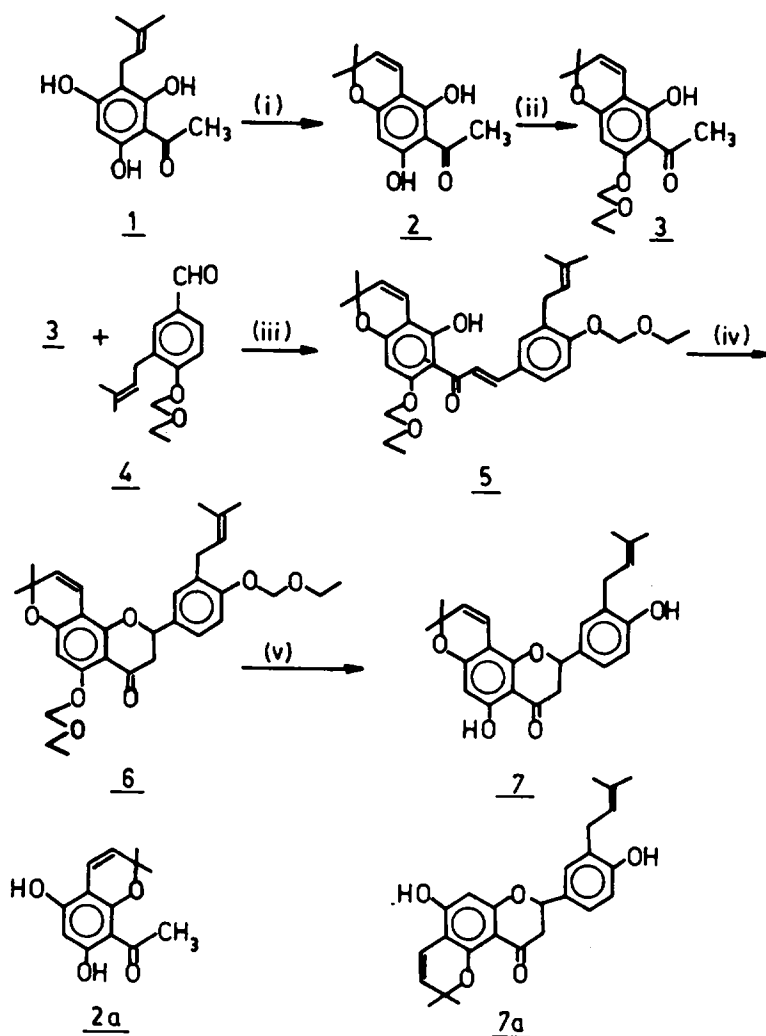
### 2. Results and discussion

All spectral data are presented in tables 1 and 2.

#### 2.1 Synthesis of euchrenone a<sub>2</sub>

3-*C*-prenylphloroacetophenone (1) prepared from phloroacetophenone according to the procedure of Collins and Shannon (1973) was cyclodehydrogenated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). It could give 2 or 2a as shown by its <sup>1</sup>H-NMR spectrum. Thus, it gives the signals of 2,2-dimethylpyran unit as two methyls at  $\delta$  1.52 (s) and two methine protons at  $\delta$  5.61 (d, *J* = 10 Hz) and 6.76 (d, *J* = 10 Hz) along with other signals of 1. The structure of the ketone is 2 because

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the final product (**7**) shows the chelated —OH group. Had it been **2a**, it would have given the isomeric flavanone (**7a**) having no chelated hydroxy group.

The ketone (**2**) was ethoxymethylated with ethoxymethyl chloride in the presence of potassium carbonate and acetone to give 6-acetyl-7-ethoxymethoxy-5-hydroxychromene (**3**). It was identified by its  $^1\text{H-NMR}$  spectrum which showed the presence of one ethoxymethoxy group as a triplet at  $\delta$  1.21 (3H,  $J = 8$  Hz), quartet at 3.69 (2H,  $J = 8$  Hz) and a singlet at  $\delta$  5.23 (2H) and one 2,2-dimethylpyran unit ( $\delta$  1.46, s,  $2 \times -\text{Me}$ ; 5.39, d,  $J = 10$  Hz and 6.60, d,  $J = 10$  Hz) along with the other protons of the parent compound. The ketone (**3**) was condensed with 4-ethoxymethoxy-3-(2,2-dimethyl-3-prenyl)benzaldehyde (**4**) (Jain and Prasad 1989) in the presence of methanolic KOH to give chalcone (**5**). It showed the characteristic  $\alpha,\beta$ -proton signals at  $\delta$  8.05 (d,  $J = 18$  Hz) and 8.36 (d,  $J = 18$  Hz) respectively in its  $^1\text{H-NMR}$  spectrum along with

Table 1. Physical and spectral data of the compounds.

Compound	m.p. (°C)	$R_f$ (solvent) <sup>a</sup>	IR absorption peaks of characteristics groups (cm <sup>-1</sup> )	UV absorption maxima (nm) (log $\epsilon$ )	Analysis (%)				Molecular formula
					Found		Calculated		
					C	H	C	H	
2	124–25°	0.46 (A)	3440, 1600, 1565 and 1475	204 (3.48), 222 sh (3.31) and 288 (3.44)	65.7	5.9	65.8	6.0	C <sub>13</sub> H <sub>14</sub> O <sub>4</sub>
3	Yellow oil	0.45 (A)	3200, 1640, 1610 and 1580	219, 272 and 350	—	—	—	—	C <sub>16</sub> H <sub>20</sub> O <sub>5</sub>
5	Orange viscous oil	0.45 (B)	3000, 1630, 1620, 1600 and 1540	214, 283 and 360	—	—	—	—	C <sub>31</sub> H <sub>38</sub> O <sub>7</sub>
6	Pale yellow viscous oil	0.40 (B)	1680, 1640 and 1580	220, 270 and 348	—	—	—	—	C <sub>31</sub> H <sub>38</sub> O <sub>7</sub>
7	145–46°	0.52 (C)	3100, 1680 and 1620	230 sh (4.30), 275 (4.65), 295 (4.00), 302 sh (3.85) and 360 (3.61)	74.0	6.5	73.9	6.4	C <sub>25</sub> H <sub>26</sub> O <sub>5</sub>

<sup>a</sup> A – benzene–chloroform (17:3); B – benzene–chloroform (19:5); C – hexane–ethyl acetate (9:4).

Table 2. <sup>1</sup>H NMR data of the compounds.

Compound	2-H	3-H	4-H	5-H	6-H	8-H	2'-H	5'-H	6'-H	4"-H	5"-H	>C(CH <sub>3</sub> ) <sub>2</sub>
2		5.61 <i>d</i> <i>J</i> = 10	6.76 <i>d</i> <i>J</i> = 10	—	—	6.10 <i>s</i>	—	—	—	—	—	1.52 <i>s</i>
3		5.39 <i>d</i> <i>J</i> = 10	6.60 <i>d</i> <i>J</i> = 10			6.22 <i>s</i>		—	—	—	—	1.46 <i>s</i>
5	7.74 <i>bs</i>			7.74 <i>bs</i>	7.74 <i>bs</i>	—	—	6.48 <i>s</i>	—	6.87 <i>d</i> <i>J</i> = 10	5.67 <i>d</i> <i>J</i> = 10	1.59 <i>s</i>
6	5.30 <i>dd</i> <i>J</i> = 12.9 & 3.1	2.64 & 2.90 2 <i>dd</i> <i>J</i> = 17.1, 3.1 & 17.1, 12.9			6.47 <i>s</i>	—	7.10 <i>m</i>	7.40 <i>m</i>	7.40 <i>m</i>	6.73 <i>d</i> <i>J</i> = 10	5.60 <i>d</i> <i>J</i> = 10	1.48 <i>s</i>
7	5.31 <i>dd</i> <i>J</i> = 12.9 & 3.1	2.80 & 3.00 2 <i>dd</i> <i>J</i> = 17.1, 3.1 & 17.1, 12.9			6.00 <i>s</i>		7.25 <i>m</i>	7.25 <i>m</i>	6.83 <i>d</i> <i>J</i> = 8.4	6.52 <i>d</i> <i>J</i> = 10	5.49 <i>d</i> <i>J</i> = 10	1.42 <i>s</i>

Compound	-CH <sub>2</sub> -CH=	-CH=C<	=C(CH <sub>3</sub> ) <sub>2</sub>	-OCH <sub>2</sub> O-	-CH <sub>2</sub> CH <sub>3</sub>	-CH <sub>3</sub> CH <sub>2</sub> -	H <sub>z</sub>	H <sub>β</sub>	-COCH <sub>3</sub>	Chelated OH	
2	—								2.72 <i>s</i>	13.95 <i>s</i>	
3					5.23 <i>s</i>	3.69 <i>q</i> <i>J</i> = 8		1.21 <i>t</i> <i>J</i> = 8	2.63 <i>s</i>	13.40 <i>s</i>	
5	3.47 <i>d</i> <i>J</i> = 6.2	5.31 <i>t</i> <i>J</i> = 6.2	1.79 <i>s</i>		5.45 & 5.47 2 <i>s</i> 2H each	3.88 (4H) <i>q</i> , <i>J</i> = 8		1.27 (6H) <i>t</i> , <i>J</i> = 8	8.05 <i>d</i> <i>J</i> = 18	8.36 <i>d</i> <i>J</i> = 18	13.80 <i>s</i>
6	3.40 <i>d</i> <i>J</i> = 6.2	5.51 <i>t</i> <i>J</i> = 6.2	1.53 & 1.74 2 <i>s</i>		5.34 & 5.36 2 <i>s</i> 2H each	3.80 (4H) <i>q</i> , <i>J</i> = 8		1.24 & 1.25 2 <i>t</i> <i>J</i> = 8 3H each			
7	3.38 <i>d</i> <i>J</i> = 6.2	5.34 <i>t</i> <i>J</i> = 6.2	1.44 <i>s</i>								12.0 <i>s</i>

the signals of one prenyl, two ethoxymethoxy and one pyran unit and the aromatic signals.

The chalcone (5) was cyclised with methanolic sodium acetate over a period of 36 h to give 5,4'-bisethoxymethoxy-6'',6''-dimethyl-3'-C-prenylpyrano (2'',3''-7,8) flavanone (6). Its <sup>1</sup>H-NMR spectrum showed the signals of two ethoxymethoxy groups at δ 1.23 and 1.25 (2*t*, *J* = 8 Hz, 2 × CH<sub>3</sub>CH<sub>2</sub>-), 3.80 (*q*, *J* = 8 Hz, 2 × -CH<sub>2</sub>-CH<sub>3</sub>) and 5.34 and 5.36 (2*s*, 2 × -OCH<sub>2</sub>O-), one prenyl group at δ 1.53 and 1.74 (2*s*, =C(CH<sub>3</sub>)<sub>2</sub>), 3.40 (*d*, *J* = 6.2 Hz, -CH<sub>2</sub>-CH=) and 5.51 (*t*, *J* = 6.2 Hz, -CH<sub>2</sub>-CH=), and one dimethyl-

pyran unit at  $\delta$  1.48 (s, 6H,  $\text{>C}(\text{CH}_3)_2$ ), 5.60 (d,  $J = 10$  Hz,  $\text{C}_{5''}\text{-H}$ ) and 6.73 (d,  $J = 10$  Hz,  $\text{C}_{4''}\text{-H}$ ). The two methyl and one methylene protons of flavanone appeared at  $\delta$  2.64, 2.90 ( $J = 17.1$  and  $3.1$  and  $17.1$ ,  $12.9$  Hz) and 5.30 ( $J = 12.0$  and  $3.1$  Hz) respectively along with the other aromatic protons.

Subsequent deprotection of flavanone (6) with methanolic HCl gave 4',5-dihydroxy-6'',6''-dimethyl-3'- $\text{C}$ -prenylpyrano (2'',3''-7,8) flavanone (7) identical in all respects (m.p.,  $R_f$ , UV,  $^1\text{H-NMR}$ ) with the natural compound euchrenone  $a_2$ .

### 3. Experimental

All melting points are uncorrected. The following spectrophotometers were used for spectral measurements: UV Shimadzu 260; IR Shimadzu 435;  $^1\text{H-NMR}$  90 MHz Perkin-Elmer R-32. UV data were taken in MeOH; IR values were recorded using nujol film or KBr disc, NMR data were recorded in  $\text{CDCl}_3$  using TMS as internal standard. Silica gel G was used for TLC and silica gel for column chromatography. The light petroleum used had a boiling range 60–80°C.  $R_f$  values are those recorded on TLC plates which were sprayed with 1% ethanolic ferric chloride or 10% aqueous  $\text{H}_2\text{SO}_4$ . The solvent systems used for TLC are indicated in table 1.

#### 3.1 6-Acetyl-5,7-dihydroxy-2,2-dimethylchromene (2)

To a solution of 3- $\text{C}$ -prenylphloroacetophenone (Collins and Shannon 1973) (1, 1.2 g) in dry benzene (80 ml) was added DDQ (1.25 g) and the whole mixture refluxed on a boiling water bath for 30 min when the colourless hydroquinone separated out. It was filtered while hot and the residue washed with dry benzene. The filtrate was evaporated to dryness and the residue column-chromatographed. Elution with ethyl acetate–petroleum ether (1:24) afforded chromene (2) as yellow flakes (250 mg) which gave a violet ferric reaction.

#### 3.2 6-Acetyl-7-ethoxymethoxy-5-hydroxy-2,2-dimethylchromene (3)

To a solution of the ketone (2, 235 mg, 1 mmol) in dry acetone (50 ml) was added anhydrous  $\text{K}_2\text{CO}_3$  (1.5 g, 10 mmol) and a solution of ethoxymethyl chloride (0.132 ml, 1 mmol) in dry acetone (10 ml). The reaction mixture was stirred at room temperature until TLC showed full conversion (1 h). It was evaporated to dryness, treated with crushed ice, extracted with ether and the oily residue purified by column chromatography. It afforded 3 as a yellow viscous oil (250 mg) which gave a violet ferric reaction.

#### 3.3 4,6'-Bisethoxymethoxy-2'-hydroxy-6'',6''-dimethyl-3'- $\text{C}$ -prenylpyrano (2'',3''-4,3) chalcone (5)

A mixture of the above chromene (3, 240 mg, 0.75 mmol) and 4-ethoxymethoxy-3- $\text{C}$ -prenylbenzaldehyde prepared according to Jain and Prasad (1989) (4, 200 mg, 0.75 mmol) was kept in contact with methanolic-KOH (500 mg/20 ml) at room temperature for 3 days. It was diluted with water (100 ml) and neutralised carefully with cold dilute HCl. The whole mixture was extracted with ether ( $2 \times 100$  ml), the

ethereal layer dried ( $\text{Na}_2\text{SO}_4$ ), evaporated *in vacuo* and the residue subjected to column chromatography. It was first eluted with petroleum ether to remove impurities and then with ethyl acetate–petroleum ether (1:49) to give **5** as a viscous orange oil (300 mg) which gave a violet green ferric reaction.

3.4 *Euchrenone a<sub>2</sub>-4',5-bisethoxymethyl ether (4',5-bisethoxymethoxy-6'',6''-dimethyl-3'-C-prenylpyrano (2'',3''-7,8) flavanone) (6)*

A methanolic solution of the above chalcone (**5**, 250 mg, 50 ml) was warmed with anhydrous sodium acetate (1.0 g) at 40–50° for 36 h, poured into cold water and extracted with ether. The ether layer was dried ( $\text{Na}_2\text{SO}_4$ ) and then evaporated under reduced pressure and the residue subjected to column chromatography. It was eluted first with petroleum ether to remove impurities and then with ethyl acetate–petroleum ether (1:49) to give **6**, as a pale yellow viscous oil (150 mg).

3.5 *Euchrenone a<sub>2</sub>(4',5-dihydroxy-6'',6''-dimethyl-3'-C-prenylpyrano (2'',3''-7,8) flavanone (7)*

A solution of the above flavanone (**6**, 125 mg) in methanol (10 ml) was warmed with 4% methanolic HCl (10 ml) for 5 min. The product was diluted with cold water, extracted with ether, the ethereal layer dried ( $\text{Na}_2\text{SO}_4$ ) and then evaporated under reduced pressure and the oily residue subjected to column chromatography. It was eluted first with petroleum ether to remove impurities and then with ethyl acetate–petroleum ether (1:19) to afford **7**. It crystallised from hexane as pale yellow plates (75 mg).

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