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Synthesis of 6, 9, 11-Trihydroxy-6a, 12a-dehydrorotenoid

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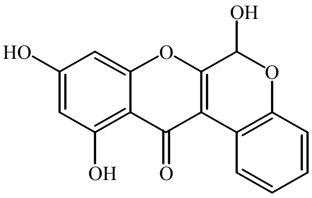
Abstract: 6, 9, 11-Trihydroxy-6a, 12a-dehydrorotenoid **1** (coccineone B) was synthesized from 2-hydroxybenzaldehyde **2** and phloroglucinol.

Keywords: Coccineone B, 6, 9, 11-trihydroxy-6a, 12a-dehydrorotenoid, synthesis.

6, 9, 11-Trihydroxy-6a, 12a-dehydrorotenoid (coccineone B) **1** is isolated from the roots of *Boerhaavia diffusa L.*, which is a plant of the family of *Nyctaginaceae* and widely used as a traditional medicine in Nepal, Srilanka, Indian, and East Africa[1]. Antitumor and antiviral effects of *Boerhaavia diffusa L.* have also been investigated[2,3]. So far the synthesis of coccineone B has not been reported.



Coccineone B **1**

The synthetic route to **1** is outlined in **Scheme 1**. 2-Hydroxybenzaldehyde **2** was reduced by KBH_4 in anhydrous methanol to afford 2-hydroxybenzyl alcohol **3**. The reaction mixture of **3** and KCN in DMF was heated to 110-130℃, which gave 2-hydroxyphenylacetonitrile **4**. Phenol hydroxyl of compound **4** was protected with benzoyl chloride, if it was not protected, the yield of 2´-benzoyloxy-5, 7-dihydroxy-2-methoxy-carbonylisoflavone **7** would be reduced, or even it would not be obtained. 2-Benzoyloxybenzyl-2, 4, 6,-trihydroxyphenyl ketone **6** was prepared by Hoesch reaction of compound **5** and phloroglucinol with a good stream of hydrogen chloride in anhydrous ether at 0℃. It is noteworthy that the presence of $ZnCl_2$•H_2O is essential for the success of this reaction. Condensation of compound **6** and ethoxalyl chloride in anhydrous pyridine and extraction with dilute hydrochloric acid gave compound **7**. Treating compound **7** with 0.1 mol/L sodium methoxide for 10 min,

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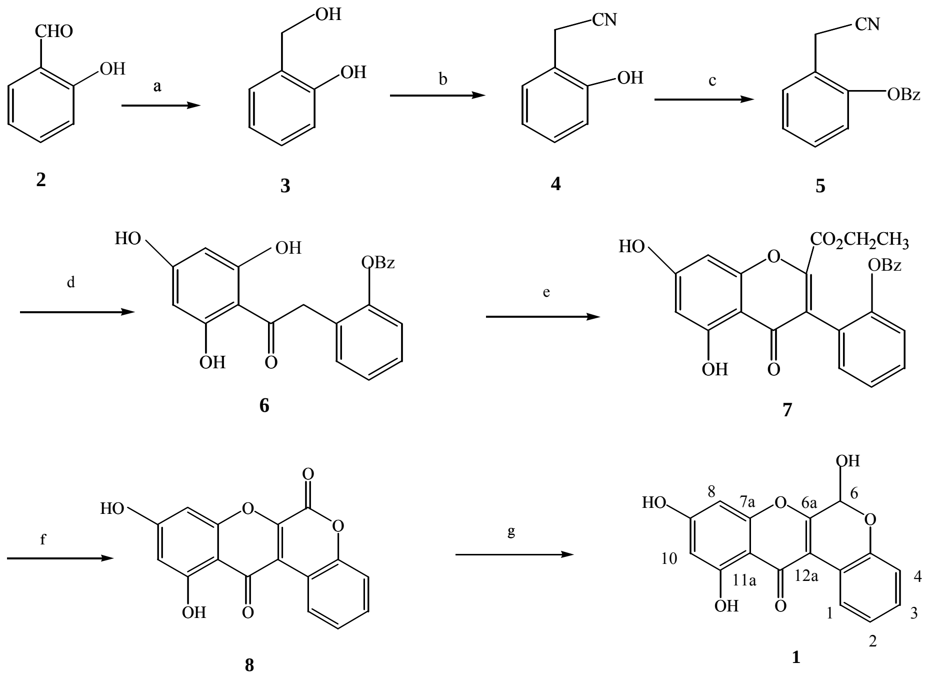
followed by acidification lactone **8** could be given. Lactone **8** was then reduced to the target molecule **1** by DIBALH.

The spectral data of synthetic product coccineone B **1** were confirmed by those of literature[4].

Scheme 1 The synthetic route of coccineone B



Reagents and Conditions: a) KBH_4, anhyd. CH_3OH, 97%; b) KCN, DMF, 110-130℃, 7h, 60%; c) BzCl, 10%NaOH solution, 2h, 87%; d) Phloroglucinol, $ZnCl_2$, anhyd. HCl, 1day, 0℃, then reflux with H_2O for 1h, 65%; e) (1) $ClCOCO_2CH_2CH_3$, anhyd. C_5H_5N, 0℃ to r.t., 24h; (2)dilute hydrochloric acid, 51%; f) 0.1mol/L $NaOCH_3$ reflux for 10min, 90%; g) DIBALH, anhyd. THF, -78℃, 24h, 80%.

Table 1 ^{1}HNMR data of compound **1** (CD_3COCD_3, δ ppm)

Synthetic **1** (300 MHz)	Natural **1** (400 MHz)
6.23 (1H, s, H-6)	6.08 (1H, s, H-6)
6.32 (1H, d, J=2.1Hz, H-8)	6.21 (1H, d, J=2.0Hz, H-8)
6.47 (1H, d, J=1.2Hz, H-10)	6.33 (1H, d, J=2.0Hz, H-10)
7.05 (1H, d, J=8.1Hz, H-4)	6.97 (1H, dd, J=8.0, 1.3Hz, H-4)
7.10 (1H, t, J=7.5Hz, H-2)	7.01 (1H, ddd, J=7.8, 7.3, 1.3Hz, H-2)
7.29 (1H, dt, J=7.7, 1.8Hz, H-3)	7.20 (1H, ddd, J=8.0, 7.3, 1.7Hz, H-3)
8.78 (1H, d, J=6.9Hz, H-1)	8.71 (1H, dd, J=7.8, 1.7Hz, H-1)

Table 2 ^{13}CNMR data of compound 1 (CD_3COCD_3, δ ppm)

Synthetic **1** (75 MHz)	Natural **1** (100 MHz)
181.1 (C-12)	181.2 (C-12)
165.5 (C-9)	165.5 (C-9)
163.5 (C-11)	163.7 (C-11)
158.0 (C-7a)	158.0 (C-7a)
157.8 (C-6a)	158.0 (C-6a)
149.8 (C-4a)	149.9 (C-4a)
129.5 (C-3)	129.5 (C-3)
128.0 (C-1)	127.6 (C-1)
122.8 (C-2)	122.9 (C-2)
118.2 (C-4)	118.1 (C-4)
117.6 (C-1a)	117.7 (C-1a)
109.8 (C-12a)	110.1 (C-12a)
105.8 (C-11a)	106.1 (C-11a)
100.2 (C-10)	100.4 (C-10)
94.7 (C-8)	94.9 (C-8)
89.2 (C-6)	89.5 (C-6)

References and Notes

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5. **1:** yellow powder. MS (FAB) *m/z* 299([M+H]$^+$, 90%), 281 ([M-OH]$^+$, 30%), 269 ([M-CHO]$^+$, 20%), HRMS *m/z* Found 299.0555 ([M+H]$^+$), Calcd for $C_{16}H_{10}O_6$ ([M+H]$^+$) 299.0550.

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