

The Synthesis of Desmethylenececalin

Mitsuru NAKAYAMA, Mikoto OHNO, Shūichi HAYASHI and Kenji FUKUI

Department of Chemistry, Faculty of Science, Hiroshima University, Higashisenda-machi, Hiroshima

(Received July 3, 1970)

Recently, desmethylenececalin¹⁾ (eupatoriochrome)²⁾ was isolated along with several acetophenone derivatives from the roots of *Helianthella uniflora* and some *Eupatorium* species. Its structure was identified as 6-acetyl-7-hydroxy-2,2-dimethyl-2H-chromene (I) on the basis of the spectral evidence.^{1,2)} Encecalin (methyl ether of I) (II) was also isolated from *Encelia californica*.³⁾

The present paper will describe the synthesis of I from 7-hydroxy-2,2-dimethylchroman (III) via the corresponding acetophenone (IV).

The Hoesch reaction of III⁴⁾ with acetonitrile afforded a hydroxy-acetophenone derivative, which was then easily converted into an acetate and may be expected to have one of two structures (IV or V). The NMR spectrum of the acetophenone shows two proton signals, at δ 7.50 and 6.35 ppm (each 1H, singlet) (para positions at C-5 and C-8 on the aromatic ring). Therefore, it can be formulated as 6-acetyl-7-hydroxy-2,2-dimethylchroman (IV). The dehydrogenation of IV with 2,3-dichloro-5,6-dicyano-*p*-quinone in anhydrous benzene gave the desired chromen I. Then, the I was easily converted

into acetate (VI) and methyl ether (II) by the usual methods.

The properties of the synthetic I and II were superimposable upon those recorded for natural desmethylenececalin and encecalin.¹⁻³⁾

Experimental*1

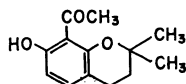
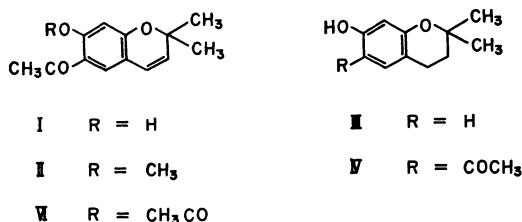
6-Acetyl-7-hydroxy-2,2-dimethylchroman (IV). A mixture of III⁴⁾ (2.0 g), acetonitrile (0.7 g), and anhydrous zinc chloride in anhydrous ether (50 ml) was saturated with dried hydrogen chloride in an ice bath and then allowed to stand for 24 hr. After the ether layer had been decanted, the ketimine hydrochloride was washed with anhydrous ether and then hydrolyzed with water (100 ml) on a steam bath for 1 hr. The precipitates were then collected and recrystallized from methanol to give IV as colorless plates; mp 119.5–120°C; yield, 0.6 g (24%). IR: 1649 (C=O) cm^{-1} . UV: λ_{max} m μ (log ϵ); 236 (3.98), 242_{sh} (3.93),*2 283 (4.18), 327 (3.85). NMR: 1.36_s (6H) ((CH₃)₂C<); 1.82_t, 2.76_t (each 2H, $J=7.0$ Hz) (–CH₂–CH₂–); 2.54_s (3H) (CH₃–COC); 6.35_s (C₈–H); 7.50_s (C₅–H); 12.38_s (OH).

Found: C, 70.80; H, 7.43%. Calcd for C₁₃H₁₆O₃: C, 70.89; H, 7.32%.

Acetate. Mp 141.5–142°C (colorless needles from ethanol). IR: 1768, 1671 (C=O) cm^{-1} . UV: λ_{max} m μ (log ϵ); 230 (4.17), 275 (4.16). NMR: 1.36_s (6H) ((CH₃)₂C<); 1.83_t, 2.80_t (each 2H, $J=7.0$ Hz) (–CH₂–CH₂–); 2.34_s (3H) (CH₃COO); 2.49_s (3H) (CH₃COC); 6.52_s (C₈–H); 7.67_s (C₅–H).

Found: C, 68.76; H, 6.83%. Calcd for C₁₅H₁₈O₄: C, 68.68; H, 6.92%.

Desmethylenececalin (6-Acetyl-7-hydroxy-2,2-dimethyl-2H-chromene) (I). A mixture of IV (0.1 g) and DDQ (0.1 g) in anhydrous benzene (30 ml) was refluxed for 1.5 hr. After the solution had then been cooled, the precipitated hydroquinone derivative was filtered off and the solvent was removed as far as possible. The chromatography of the resulting viscous oil on silica gel (8 g) with benzene gave a pale yellow solid, a solid which crystallized from ethanol as pale yellow needles,



V

1) F. Bohlmann and M. Grenz, *Chem. Ber.*, **103**, 90 (1970).

2) T. Anthonsen, *Acta Chem. Scand.*, **24**, (1970), in press.

3) L. F. Bjeldanes and T. A. Geissman, *Phytochem.*, **8**, 1293 (1970).

4) W. Bridge, A. J. Crocker, T. Cubin and A. Robertson, *J. Chem. Soc.*, **1937**, 1530.

*1 The melting points are uncorrected. The infrared spectra were measured in Nujol, while the ultraviolet spectra were measured in an ethanol solution. The NMR spectra were measured with a Hitachi R-20 spectrometer (60 MHz), using tetramethylsilane as the internal standard (δ -value in CDCl₃): s, singlet; d, doublet; t, triplet. The mass spectra were measured with a Hitachi RMS-4 mass spectrometer.

*2 sh=shoulder.

I; mp 80.5–81°C (lit, mp 77°C,¹⁾ mp 76°C²⁾; yield, 54 mg (54%). IR: 1650 (C=O) cm^{-1} . UV: λ_{max} $m\mu$ ($\log \epsilon$); 234.5 (3.95), 257.5 (4.23). NMR: 1.44_s (6H) ($(\text{CH}_3)_2\text{C}<$); 2.54_s (3H) (CH_3COC); 5.59_d, 6.32_d ($J=10$ Hz) ($-\text{CH}=\text{CH}-$); 6.37_s (C_8-H); 7.38_s (C_5-H); 12.78_s (OH). MS: M^+ m/e 218.

Found: C, 71.57; H, 6.44%. Calcd for $\text{C}_{13}\text{H}_{14}\text{O}_3$: C, 71.54; H, 6.47%.

Acetate (VI). Mp 80–81.5°C (colorless needles from ethanol). IR: 1768, 1685 (C=O) cm^{-1} . UV: λ_{max} $m\mu$ ($\log \epsilon$); 251.5 (4.55), 300 (4.12). NMR: 1.46_s (6H)

($(\text{CH}_3)_2\text{C}<$); 2.34_s (3H) (CH_3COO); 2.50_s (3H) (CH_3-COC); 5.64_d, 6.36_d ($J=10$ Hz) ($-\text{CH}=\text{CH}-$); 6.51_s (C_8-H); 7.53_s (C_5-H).

Found: C, 68.95; H, 6.23%. Calcd for $\text{C}_{15}\text{H}_{16}\text{O}_4$: C, 69.21; H, 6.20%.

Methyl Ether (II). Viscous oil. IR: 1675 (C=O) cm^{-1} . UV: λ_{max} $m\mu$ ($\log \epsilon$); 255 (4.43), 335 (3.77). NMR: 1.44_s (6H) ($(\text{CH}_3)_2\text{C}<$); 2.56_s (3H) (CH_3COC); 3.87_s (3H) (CH_3O); 5.52_d, 6.34_d ($J=10$ Hz) ($-\text{CH}=\text{CH}-$); 6.41_s (C_8-H); 7.57_s (C_5-H). MS: M^+ m/e 232. Oxime; mp 137–138°C (lit,³⁾ mp 140°C).