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SYNTHESIS OF RIPARIOCHROMENE B AND RIPARIOCHROMENE C

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The condensation of 7-hydroxy-2,2-dimethylchroman (III) and benzoyloxyacetonitrile gave 7-hydroxy-6-benzoyloxyacetyl-2,2-dimethylchroman (IV). 7-Hydroxy-6-acetoxyacetyl-2,2-dimethylchroman (VIII) was obtained from IV via four steps. The dehydrogenation of VIII with DDQ in dry toluene afforded ripariochromene B (I). Ripariochromene C (II) also was synthesized in a similar manner.

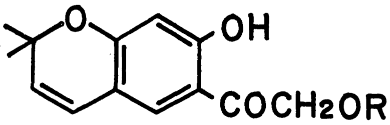
Ripariochromene B and ripariochromene C have recently been isolated from Australian Eupatorium riparium Regel along with several other chromenes.1) Those structures have been, respectively, shown to be 7-hydroxy-6-acetoxyacetyl-2,2-dimethylchromene (I) and 7-hydroxy-6-isobutyryloxyacetyl-2,2-dimethylchromene (II), which are characterized with regard to acyloxyacetyl group at the 6-position, on the basis of the spectral evidences.1) In the present paper, we wish to report the synthesis of I and II, which confirms the proposed structures of the natural ripariochromene B and ripariochromene C.

The condensation of 7-hydroxy-2,2-dimethylchroman (III) and benzoyloxyacetonitrile in the presence of freshly fused zinc chloride in dry ether gave 7-hydroxy-6-benzoyloxyacetyl-2,2-dimethylchroman (IV) [mp 141-142 °C; IR ν_{max}^{KBr} 1720, 1665 cm^{-1}; NMR $\delta_{ppm}^{CDCl_3}$ 5.48$_s$(2H)(COCH$_2$), 11.66$_s$(OH)]. IV was easily converted into 7-benzyloxy-6-benzoyloxyacetyl-2,2-dimethylchroman (V) (mp 146-147 °C; IR 1725 cm^{-1}) in the presence of anhydrous potassium carbonate with benzyl chloride in dry acetone. V was hydrolyzed in dilute hydrochloric acid to give 7-benzyloxy-6-hydroxyacetyl-2,2-dimethylchroman (VI) [mp 142-143 °C; IR 3480 cm^{-1}; NMR 5.06$_s$(2H)(COCH$_2$), 4.62$_s$(2H)($C\underline{H}_2C_6H_5$)]. The acetylation of VI with acetyl chloride in a large quantity of pyridine in an ice bath afforded 7-benzyloxy-6-acetoxyacetyl-2,2-dimethylchroman (VII) [mp 111-112 °C; IR 1740 cm^{-1}; NMR 2.14$_s$(3H)(CH$_3$CO), 5.10$_s$(2H)(COCH$_2$)]. The hydrogenolysis of VII with Pd/C in methanol yielded 7-hydroxy-6-acetoxyacetyl-2,2-dimethylchroman (dihydroripariochromene B) (VIII) [mp 131-132 °C; IR 1745 cm^{-1}; NMR 2.21$_s$(3H)(CH$_3$CO), 5.24$_s$(2H)(COCH$_2$), 11.92$_s$(OH)]. The dehydrogenation2-4) of VIII with DDQ (2,3-dichloro-5,6-dicyano-p-quinone) in boiling dry toluene gave the desired chromene (I) [mp 146-147 °C; IR 1750, 1652 cm^{-1}; UV λ_{max}^{EtOH} nm (log ε) 257 (4.51), 286(3.95), 347(3.85); NMR 1.41$_s$(6H)(CH$_3$x2), 2.20$_s$(3H)(CH$_3$CO), 5.20$_s$(2H)

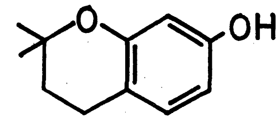
$(\mathrm{COCH_2})$, 5.54_d, 6.23_d(each J=9 Hz and 1H)(CH=CH), $6.30_s(\mathrm{C_8}$-H), $7.15_s(\mathrm{C_5}$-H), 12.20_s (OH); Found: C, 65.09; H, 5.79 %, Calcd for $\mathrm{C_{15}H_{16}O_5}$: C, 65.21; H, 5.84 %] (lit.$^{1)}$ mp 145-146 °C).

By a method similar to that described above, the isobutyrylation of VI afforded the chroman (IX) [mp 93-94 °C; IR 1740 cm^{-1}; NMR 1.23_d(6H)(J=7, $\mathrm{CH_3}$x2)($(\mathrm{C\underline{H}_3})_2\mathrm{CH}$), 2.65_m(1H)($(\mathrm{CH_3})_2\mathrm{C\underline{H}}$), 5.09_s(2H)($\mathrm{COCH_2}$)]. IX was converted into 7-hydroxy-6-isobutyryloxyacetyl-2,2-dimethylchroman (dihydroripariochromene C) (X) [mp 113-114 °C; IR 1738 cm^{-1}; NMR 1.24_d(6H)(J=7, $\mathrm{CH_3}$x2)($(\mathrm{C\underline{H}_3})_2\mathrm{CH}$), 2.65_m(1H)($(\mathrm{CH_3})_2\mathrm{C\underline{H}}$), 5.25_s(2H) ($\mathrm{COCH_2}$), 11.71_s(OH)] by hydrogenolysis. The dehydrogenation of X with DDQ gave the desired chromene (II) [mp 109.5-110.5 °C; IR 1740, 1645 cm^{-1}; UV 257(4.39), 287 (3.77), 348(3.72); NMR 1.26_d(6H)(J=7, $\mathrm{CH_3}$x2)($(\mathrm{C\underline{H}_3})_2\mathrm{CH}$), 1.45_s(6H)($\mathrm{CH_3}$x2), $2.73_{sept.}$ (1H)($(\mathrm{CH_3})_2\mathrm{C\underline{H}}$), 5.24_s(2H)($\mathrm{COCH_2}$), 5.57_d, 6.25_d(each J=9 and 1H)(CH=CH), $6.33_s(\mathrm{C_8}$-H), $7.18_s(\mathrm{C_5}$-H), 12.05_s(OH); Found: C, 67.37; H, 6.58 %, Calcd for $\mathrm{C_{17}H_{20}O_5}$; C, 67.09; H, 6.62 %] (lit.$^{1)}$ mp 109-110 °C).

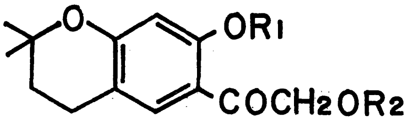
The synthetic chromene (I) and (II) were, respectively, shown to be identical with the natural ripariochromene B and ripariochromene C on the basis of a mixed-melting-point determination, NMR, IR and UV spectral comparisons.$^{5)}$



I R = $\mathrm{CH_3CO}$
II R = $\mathrm{(CH_3)_2CHCO}$



III



IV	R_1 = H	R_2 = $\mathrm{C_6H_5CO}$
V	R_1 = $\mathrm{C_6H_5CH_2}$	R_2 = $\mathrm{C_6H_5CO}$
VI	R_1 = $\mathrm{C_6H_5CH_2}$	R_2 = H
VII	R_1 = $\mathrm{C_6H_5CH_2}$	R_2 = $\mathrm{CH_3CO}$
VIII	R_1 = H	R_2 = $\mathrm{CH_3CO}$
IX	R_1 = $\mathrm{C_6H_5CH_2}$	R_2 = $\mathrm{(CH_3)_2CHCO}$
X	R_1 = H	R_2 = $\mathrm{(CH_3)_2CHCO}$

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5) The natural chromenes were kindly supplied by Dr. T. Anthonsen, Norway Institute of Technology, Norway.

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