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### ABSOLUTE CONFIGURATION OF CARBON 2 IN THE CHROMENE RING OF GAMBOGIC ACID<sup>1</sup>

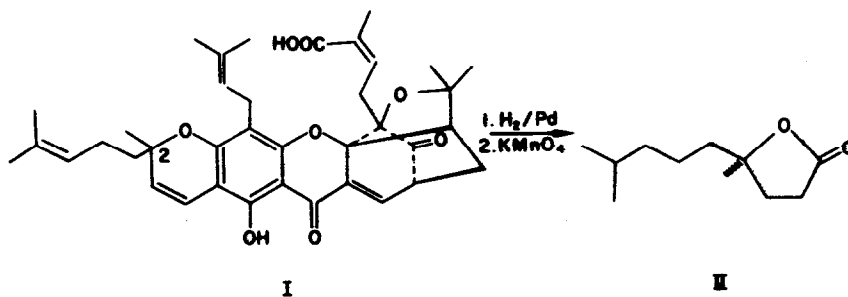
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A few 2-methyl-2(4'-methylpent-3'-enyl)-chromenes, gambogic acid (2-6), cannabichromene (7), and flemingins (8) have been recently found in Nature. Except for gambogic acid (9), they have only one asymmetric center, i.e. the carbon 2 of the chromene ring. We have now established the absolute configuration of this center in the most easily available of these chromenes, gambogic acid, by  $\text{KMnO}_4$  oxydation of the corresponding chroman (10).

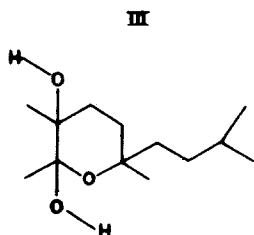
Catalytic hydrogenation of gambogic acid (I) ( $[\alpha]_D^{20} = -648^\circ$ , MeOH,  $c = 1.06$ ) in ethanol in the presence of Pd/C or Pt Adams gave a crude resinous mixture ( $[\alpha]_D^{20} = -15.2^\circ$ ,  $\text{CHCl}_3$ ,  $c = 1.07$ ) of hydrogambogic acids (11). This product was dissolved in light petroleum and treated with excess  $\text{KMnO}_4$  in 20% NaOH at room temperature. Working up as usual, followed by preparative gas chromatography (12) of the neutral fraction, afforded oily R(+)-4,8-dimethyl-4-hydroxynonanonic acid lactone (II) (Found: C, 71.98; H, 11.28.  $\text{C}_{11}\text{H}_{20}\text{O}_2$  requires: C, 71.69; H, 10.94), IR (neat) 5.65  $\mu$ , NMR ( $\text{CCl}_4$ ):  $(\text{CH}_3)_2\text{CH}-$  (6H, d, 1.07  $\delta$ ,  $J = 6$  Hz),  $\text{CH}_3-\text{C}-\text{O}-$  (3H, s, 1.35  $\delta$ ),  $-\text{CH}_2-\text{CO}-$  (m, 2.3-2.7  $\delta$ ), total protons count 20;  $[\alpha]_{589}^{20} = +8.06^\circ$ ,



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$[\alpha]_{578}^{20} = +8.63^\circ$ ,  $[\alpha]_{546}^{20} = +10.38^\circ$ ,  $[\alpha]_{436}^{20} = +18.20^\circ$ ,  $[\alpha]_{364}^{20} = +28.75^\circ$  ( $\text{CHCl}_3$ ,  $c = 0.98$ ), optical purity 92%, calculated from the data by Jeger and al. (13).

We believe that in this medium the cleavage of the chroman ring proceeds through hydro-



xylation of the aromatic double bond

(III), without affecting the asymmetric center 2. Independently from the

pathway then followed, the strongly

alkaline medium and almost absence of racemisation rule out a  $B_{AL}$  mechanism (14a). When

the oxydation was accomplished with  $\text{CrO}_3$  in

$\text{AcOH}$  and  $\text{H}_2\text{SO}_4$  (10), R(+)III with 32% optical purity was obtained (14b). Retention of configuration from the lactone ring closure has been already demonstrated (10). The overall reaction should then occur with retention of configuration, that establishes the R absolute configuration for carbon 2 in gambogic acid. The application of this method to flemingins is in progress.

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- (9) It is much likely that gambogic acid has the same configuration as morellin (see also the optical rotation values), apart from carbon 2, which is not asymmetric in the latter. The stereochemistry of morellin should have been already established by X-rays analysis: G. Kartha, G.N. Ramachandran, H.B. Bhat, P.M. Nair, V.K.V. Raghavan and K. Venkataraman, Tetrahedron Letters 459 (1963)
- (10) See the results of H. Mayer, P. Schudel, R. Rfegg and O. Isler, Helv. Chim. Acta 46, 963 (1963) on natural  $\alpha$ -tocopherol.
- (11) We have not been able to reproduce the results of Ahmad et al. (4), who give  $[\alpha]_D^{20} = +15^\circ$  ( $\text{CHCl}_3$ ,  $c=1$ ) for decahydrogambogic acid, m. 134-136°. On different preparations, at least two spots were always revealed by TLC: see ref. 3 and 6, too. However, this can not affect the stereochemistry at center 2.
- (12) Aerograph A-350-B, 20% Carbowax 20M on washed Chromosorb P 30/60 mesh in a copper column (length 2 m, diam. 0.6 cm), carrier gas He (60 ml/min.)
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