

### Synthesis of Aloe-emodin.

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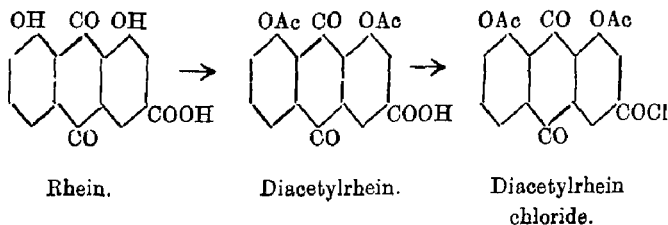
Among the hydroxyanthraquinones occurring in nature, aloemodin, the active principle of aloes, rhubarb, etc., occupies a peculiar position, because of the presence of a carbinol group. The constitution of this substance has been determined by Oesterle and others (*Arch. Pharm.*, 1911, 249, 445) by converting it into chrysophanic acid by reduction and into rhein by oxidation.

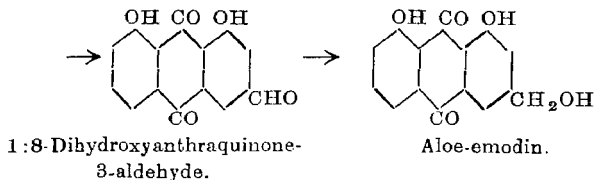
The authors have confirmed this constitution by actual synthesis, taking as the starting point rhcin which has been already synthesised (Eder and Widmer, *Helv. Chim. Acta*, 1922, 5, 3) and reducing it through the chloride and the aldehyde into the corresponding alcohol.

In order to determine the conditions of the experiment, the authors reduced anthraquinone- $\beta$ -carboxylic acid through the chloride into anthraquinone- $\beta$ -aldehyde by the method of Rosenmund and his co-workers (*Ber.*, 1918, 51, 585; 1921, 54, 425), using sulphurised quino-line as an anti-catalyst. The yield of aldehyde was, however, poor and it was subsequently found that the reaction goes on much better without any anti-catalyst.

Anthraquinone- $\beta$ -aldehyde could be successfully reduced to anthraquinone- $\beta$ -carbinol with hydrogen in presence of platinum oxide with ferrous chloride as promoter, according to the method of Roger Adams and his co-workers (*J. Amer. Chem. Soc.*, 1922, **44**, 1397 ; 1923, **45**, 1071, 2171 ; 1924, **46**, 1675).

The synthesis of aloe-emodin was accomplished<sup>2</sup> according to the following scheme.





## EXPERIMENTAL.

*Anthraquinone- $\beta$ -carboxylic acid chloride.*—Anthraquinone- $\beta$ -carboxylic acid (5 g.), prepared by oxidising  $\beta$ -methylantraquinone with chromic acid in acetic acid solution, was heated with thionyl chloride (100 g.) on a water-bath until the evolution of hydrochloric acid ceased. The excess of thionyl chloride was distilled off under diminished pressure and the acid chloride crystallised from benzene, m.p.  $146^{\circ}$ , yield theoretical.

*Anthraquinone- $\beta$ -aldehyde.*—The acid chloride (2 g.), palladiumised barium sulphate (0.7 g.) containing 5 p.c. palladium and dried *in vacuo* over phosphorus pentoxide were taken in about 40 c.c. of dry xylene in a round bottomed flask with a side-tube having a glass tube ground into it and reaching to the bottom of the flask. The flask, which was provided with a reflux condenser, was heated in an oil-bath at  $150-60^{\circ}$ . Hydrogen, carefully purified and dried by passing through strong sulphuric acid and finally through two Peligot tubes containing phosphorus pentoxide, was passed into the mixture through the side-tube until the ensuing gas was free from hydrochloric acid. The solution was then filtered from the catalyst and shaken on the machine with 10 p.c. sodium bisulphite solution. The bisulphite layer was then separated and decomposed with hydrochloric acid, m.p.  $186^{\circ}$ , yield 1g.

For studying the conversion of the aldehyde into the carbinol, anthraquinone- $\beta$ -aldehyde was prepared on a large scale directly from  $\beta$ -methylantraquinone (Ullmann and Klingenberg, *Ber.*, 1913, 46, 712).

*Anthraquinone- $\beta$ -carbinol.*—Anthraquinone- $\beta$ -aldehyde (2 g.) was dissolved in absolute alcohol, platinum oxide (0.1725 g.) prepared according to the method of Roger Adams (*loc. cit.*) was added and then 0.1 millimole of ferrous chloride. The flask containing the mixture was evacuated by means of a water-pump until the solution began to boil and then connected with a gas holder containing pure hydrogen and shaken mechanically until the theoretical amount of hydrogen

was absorbed, which in this case took only *five minutes*. The catalyst was then removed by filtration, the alcohol evaporated off and the residue treated with boiling water in which the carbinol was found to be soluble. On recrystallising from benzene it was obtained as a yellow crystalline powder, m.p. 183°. (Found: C, 75.52; H, 3.9.  $C_{15}H_{10}O_3$  requires C, 75.63; H, 4.2 per cent.).

*Diacetylchrysophanic acid*.—Chrysophanic acid was prepared from crude chrysarobin according to the method of Fischer and Gross (*J. pr. Chem.*, 1911, ii, 84, 369). It was acetylated by dissolving in acetic anhydride, cooling and adding 2 or 3 drops of strong sulphuric acid. The acetylation was almost instantaneous.

*Diacetylrhein*.—It was prepared by oxidising diacetylchrysophanic acid according to the method of Fischer and Gross (*loc. cit.*). On treating the product with dilute soda solution and acidifying, a mixture of rhein and diacetylrhein was obtained which was completely deacetylated by boiling with alcoholic potash, the rhein recrystallised from pyridine and reacetylated by heating with acetic anhydride and pyridine.

*Diacetylrhein chloride*.—It was prepared by treating diacetylrhein with thionyl chloride in the usual manner. Crystalline mass from benzene, m.p. 190°. (Found: Cl, 8.7.  $C_{19}H_{11}O_7Cl$  requires Cl, 9.2 per cent.).

*1:8-Dihydroxyanthraquinone-3-aldehyde*.—Diacetylrhein chloride was reduced to the aldehyde according to Rosenmund's method (*loc. cit.*). On decomposing the bisulphite compound by boiling with hydrochloric acid, the substance was simultaneously deacetylated. From 2 g. of the acid chloride 0.7 g. of the aldehyde was obtained. Brown glistening needles from glacial acetic acid, m.p. 218°. (Found: C, 66.85; H, 3.0.  $C_{15}H_8O_5$  requires C, 67.16; H, 3.0 per cent.).

*1:8-Dihydroxyanthraquinone-3-carbinol (Aloe-emodin)*.—The reduction of the aldehyde was effected exactly in the same way as with anthraquinone- $\beta$ -aldehyde. The carbinol was recrystallised first from dilute acetic acid and then from toluene. Orange needles from toluene, m.p. 219.20° (corr.). The m.p. was not depressed by admixture with natural aloe-emodin from Barbadoes aloes, melting at 221° (corr.). (Found: C, 67.08; H, 3.5.  $C_{15}H_{13}O_5$  requires C, 66.60; H, 3.7 per cent.).

