92. 1 : 3 : 8-*Trihydroxyanthraquinone.*

By W. K. Anslow, J. Breen, and H. Raistrick.

Emodic acid, obtained by the oxidation of *Frangula*-emodin, is smoothly decarboxylated by heating with copper chromite and quinoline and gives, in good yield, 1 : 3 : 8-trihydroxyanthraquinone, which has hitherto been difficult to prepare. 1 : 3 : 8-Triacetoxy- and 1 : 3 : 8-*trimethoxy-anthraquinone* are also described.

During an examination of the colouring matters present in the mycelium of a strain of *Penicillium cyclopium* Westling, which proved to be ω-hydroxyemodin (4 : 5 : 7-trihydroxy-2-hydroxymethylanthraquinone) and emodic acid (4 : 5 : 7-trihydroxyanthraquinone-2-carboxylic acid) (Anslow, Breen, and Raistrick, *Biochem. J.*, 1940, **34**, 159), and before the identity of the emodic acid was established by direct comparison with a synthetic specimen, it was considered desirable to decarboxylate this substance. This end was achieved by heating with a mixture of quinoline and copper chromite, a method originally described for the decarboxylation of acids by Kinney and Langlois (*J. Amer. Chem. Soc.*, 1931, **53**, 2189), and used by Charles, Raistrick, Robinson, and Todd (*Biochem. J.*, 1933, **27**, 499) to decarboxylate helminthosporic acid (4 : 5 : 8-trihydroxyanthraquinone-2-carboxylic acid).

The decarboxylation product from emodic acid, which must be 1 : 3 : 8-trihydroxyanthraquinone if *Frangula*-emodin is accepted as 4 : 5 : 7-trihydroxy-2-methylanthraquinone, has been described previously in a very imperfect fashion in spite of its importance in relation to *Frangula*-emodin and *Aloe*-emodin and the many naturally occurring hydroxyanthraquinones related to these substances. Oesterle (*Arch. Pharm.*, 1912, **250**, 301) converted rhein (4 : 5-dihydroxyanthraquinone-2-carboxylic acid) into the acid chloride, acid amide and amine and this substance gave, on diazotisation, a small yield of a hydroxyanthraquinone, m. p. 277—278°, acetate, m. p. 197—198°, which Oesterle believed to be 1 : 3 : 8-trihydroxyanthraquinone. Eder and Hauser (*Helv. Chim. Acta*, 1925, **8**, 126), following a synthesis of *Frangula*-emodin by Eder and Widmer (*ibid.*, 1923, **6**, 966), attempted unsuccessfully to decarboxylate its oxidation product, emodic acid, in order to determine which of the two possible trihydroxymethylanthraquinones which may theoretically arise by their method of synthesis was in fact formed. They succeeded, however, in oxidising *Frangula*-emodin 7-methyl ether (physcion) to the corresponding carboxylic acid, which was degraded through the acid chloride, acid amide and amine to give, after diazotisation and demethylation, a small yield of a hydroxyanthraquinone, m. p. 275°, which was shown by direct comparison to be identical with Oesterle's hydroxyanthraquinone. No analyses of the supposed trihydroxyanthraquinone or its acetate were given either by Oesterle or by Eder and Hauser.

Experimental.

Frangula-emodin (5 g., m. p. 255°, supplied by Schering-Kahlbaum A.G. Berlin) was acetylated at 60° for ½ hour with acetic anhydride (50 ml.) containing 2% by volume of concentrated sulphuric acid. The crude triacetylemodin (7·0 g., m. p. 193—195°) was oxidised by the method described by Fischer and Gross (*J. pr. Chem.*, 1911, **84**, 376) and yielded triacetylemodic acid (6·0 g., m. p. 218—219°), which was hydrolysed, without purification, by heating for 2 hours at 100° with 2N-sodium hydroxide (300 ml.) in an atmosphere of nitrogen. The alkaline solution was acidified with 2N-hydrochloric acid (400 ml.) and heated at 100° for 1 hour to coagulate the orange gelatinous precipitate of emodic acid, which was filtered off, washed free from chlorides, and dried. This product was crystallised from glacial acetic acid (800—900 ml.) and gave emodic acid (4·1 g.) as deep orange needles containing 1 mol. of acetic acid of crystallisation, m. p. 364—365°.

Decarboxylation of Emodic Acid.—Emodic acid (4·1 g.) was heated in an oil-bath at 225—230° for 4 hours with a mixture of pure quinoline (40 ml.) and the copper chromite catalyst (1 g.) prepared according to the method of Adkins and Folkers (*J. Amer. Chem. Soc.*, 1931, **53**, 1092), a slow stream of oxygen-free nitrogen being passed during the reaction. The decarboxylation mixture was cooled, poured into 2N-hydrochloric acid (800 ml.), and boiled. After cooling, the precipitate was separated by filtration, washed, and dried (3·8 g.). The filtrate and washings were extracted with ether and this extract was used for the extraction (Soxhlet) of the precipitate.

On removal of the solvent there remained 2·7 g. of only slightly impure 1 : 3 : 8-trihydroxyanthraquinone, m. p. 285—287°, which was purified by conversion into its acetate.

1 : 3 : 8-*Triacetoxyanthraquinone*.—The crude 1 : 3 : 8-trihydroxyanthraquinone (2·7 g.) was acetylated with acetic anhydride and concentrated sulphuric acid and the resulting acetate was crystallised first from glacial acetic acid and then from ethanol, forming fine, pale yellow needles, m. p. 194—195° (Oesterle, *loc. cit.*, gives 197—198°) (Found : C, 62·9; H, 3·8; CH_3·CO, 33·7. Calc. for $C_{20}H_{14}O_8$: C, 62·8; H, 3·7; $3CH_3$·CO, 33·8%).

1 : 3 : 8-*Trihydroxyanthraquinone*.—1 : 3 : 8-Triacetoxyanthraquinone (1·86 g.) was hydrolysed with 2N-sodium hydroxide (75 ml.) in the same way as was described for the hydrolysis of triacetylemodic acid (see p. 427). The resulting 1 : 3 : 8-trihydroxyanthraquinone (1·22 g.) crystallised from ethyl acetate in golden-brown elongated plates, m. p. 287—288° (Oesterle, *loc. cit.*, gives 277—278°; Eder and Hauser, *loc. cit.*, 275°) (Found : C, 65·5; H, 3·2. Calc. for $C_{14}H_8O_5$: C, 65·6; H, 3·15%). The quinone dissolves in cold concentrated sulphuric acid and gives a reddish-orange solution, which is somewhat less red than that given by emodin. It is readily soluble in the cold in 2% sodium carbonate solution, N-sodium hydroxide, and 2N-ammonia, the solutions all being red but with an increase in blue shade in the order given. It is insoluble in cold 2% sodium bicarbonate solution.

1 : 3 : 8-*Trimethoxyanthraquinone*.—A mixture of 1 : 3 : 8-trihydroxyanthraquinone (0·27 g.), acetone (10 ml.), and methyl sulphate (5 ml.) was boiled, and 2N-sodium hydroxide (25 ml.) added in portions to maintain an alkaline reaction. The product (0·23 g.) which separated on cooling was crystallised from ethanol (norit). 1 : 3 : 8-*Trimethoxyanthraquinone* forms large greenish-yellow plates, m. p. 195—196° (Found : C, 68·3; H, 4·7; OMe, 30·7. $C_{17}H_{14}O_5$ requires C, 68·4; H, 4·7; 3OMe, 31·2%). It is insoluble in N-sodium hydroxide, but dissolves in cold concentrated sulphuric acid to give a red solution, with a shade of blue, which is quite different from that given by 1 : 3 : 8-trihydroxyanthraquinone.

Emodic acid from *Penicillium cyclopium* Westling (0·5035 g.), freed from acetic acid of crystallisation, was decarboxylated in a similar way to that described above (see p. 427). The nitrogen issuing from the decarboxylation tube was passed through N/10-barium hydroxide. Carbon dioxide was absorbed equivalent to 92·7% of the theoretical quantity. The resulting hydroxyanthraquinone, on acetylation, gave 1 : 3 : 8-triacetoxyanthraquinone in yellow needles, m. p. 192—193°, not depressed by the synthetic specimen, m. p. 194—195° (Found : C, 62·7; H, 3·7%). On hydrolysis of the acetate, 1 : 3 : 8-trihydroxyanthraquinone, m. p. and mixed m. p. 288°, identical in its properties with the synthetic specimen, was obtained.

We desire to thank the Chemistry Research Board of the Department of Scientific and Industrial Research for a research grant.

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[*Received, January 30th*, 1940.]