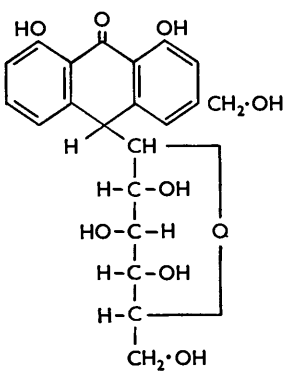
605. *The Aloins. Part I. The Structure of Barbaloin.*

By J. Evelyn Hay and L. J. Haynes.

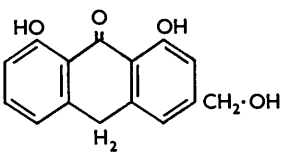
Evidence is presented supporting the formulation of barbaloin as (I).

Barbaloin, $C_{21}H_{22}O_9$, is a lemon-yellow crystalline constituent of the inspissated juices (aloes) of certain species of the aloe plant, particularly Cape aloes obtained from *A. ferox* Mill and *A. perryi* Baker growing in South and East Africa, and Curaçao aloes obtained from *A. vera* Linn. (*A. vulgaris* Lam.) growing in the West Indies. The proportion of barbaloin in the different species varies from 9% in Cape aloes to 25% in Curaçao aloes. The aloes, a dark-brown resin, is extracted with hot water, and insoluble calcium salts are precipitated with lime-water and ammonia. These are collected and treated with strong hydrochloric acid to give a yellow powder known commercially as aloin, a constituent of many purgative medicines. Barbaloin, the major component, is obtained by careful recrystallisation of this aloin. Barbaloin was first isolated [1] over a hundred years ago and has been closely studied in attempts to determine its constitution.

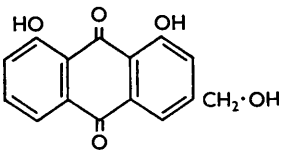
Recent papers by Mühlemann [2] and Birch and Donovan [3] concerning the constitution of barbaloin prompt us to report some work which supports Mühlemann's formulation of this compound as (I).



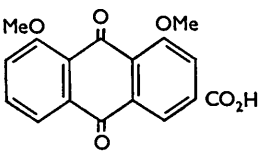
(I)



(II)



(III)



(IV)

In a study of the formation of hydroxyanthraquinone and hydroxyanthrone glycosides, Mühlemann has shown that the reaction of aloe-emodin anthrone (II) (obtained by the action of aqueous sodium borate at 100° on barbaloin [4]) with tetra-acetyl-α-D-glucopyranosyl bromide in aqueous acetone in the presence of sodium hydroxide gives a tetra-acetyl-barbaloin which on deacetylation gives barbaloin. (The paper gives the quantity of

[1] T. and H. Smith, *Chem. Gaz.*, 1851, 107.
[2] Mühlemann, *Pharm. Acta Helv.*, 1952, **27**, 17.
[3] Birch and Donovan, *Austral. J. Chem.*, 1955, **8**, 523.
[4] Hauser, *Pharm. Acta Helv.*, 1931, **6**, 79.

sodium hydroxide as 0·1 mol., but this is probably a misprint for 1 mol.) This synthesis has been repeated by Böhme and Bertram,[5] who have advanced further evidence as to the identity of the natural and the synthetic product. It would be expected that the product from such a reaction would be a glycoside derived either from a phenolic hydroxyl, the aliphatic hydroxyl, or the anthranol hydroxyl group, the (amended) conditions involved being exactly those used by Gardner and McDonnell [6] for the preparation of anthranol D-glucoside. However, Mühlemann considered that his deacetylated product had the structure (I).

The chief evidence for this was the behaviour of the product on acetylation and the fact that it could not be hydrolysed with acid under the usual laboratory conditions. Acetylation of barbaloin with acetic anhydride in the presence of zinc chloride according to the method of Zinn and Gerecs [7] gave a hepta-acetate, m. p. 129°, which was colourless and did not fluoresce in solution and was therefore considered by Mühlemann to be an anthrone derivative. Acetylation of the synthetic tetra-acetate by Zinn and Gerecs's method also gave the hepta-acetate, m. p. 129°, but acetylation with acetic anhydride and pyridine gave an amorphous yellow powder which could not be crystallised. In one experiment, Mühlemann obtained a second crystalline hepta-acetate, m. p. 202—204°, by this method of acetylation, but the preparation could not be repeated. Since the product was yellow and showed a blue fluorescence in solution, it was considered to be an anthranol derivative. When the hepta-acetate, m. p. 129°, was further acetylated with acetic anhydride and pyridine, a yellow amorphous solid was obtained. Chromatography of this gave an amorphous product which was considered, from the analytical results, to be an octa-acetate contaminated with some hepta-acetate.

Birch and Donovan [3] recently studied the acetylation of barbaloin and were unable to detect the formation of an octa-acetate. From a consideration of the ultraviolet spectrum of barbaloin, its hepta-acetate (m. p. 129°), and its heptamethyl ether and various 2 : 2′-disubstituted benzophenones, they concluded that barbaloin contained an aloe-emodin anthrone nucleus. Since aloe-emodin anthrone readily formed a tetra-acetate in which the anthrone nucleus had been converted into an anthranol, and barbaloin formed only a hepta-acetate whose absorption spectrum suggested that the anthrone nucleus remained, it was concluded that the anthrone residue in barbaloin could not enolise, that is, that it was disubstituted at $C_{(10)}$. Since barbaloin is a C_{21} compound, and is known to be degraded to D-arabinose,[8] it was suggested that these substituents could be represented as C_1 and C_5 groups, the C_5 group giving rise to the D-arabinose.

A more direct demonstration of the anthrone nucleus in barbaloin is obtained from a study of its infrared spectrum (see Table). Flett [9] has shown that anthrone has a single

Compound	C=O frequency ($cm.^{-1}$)	Compound	C=O frequency ($cm.^{-1}$)
Anthrone [9]	1654	Anthraquinone [9]	1676
1 : 8-Dihydroxyanthrone	1636	Aloe-emodin (III)	1674, 1626
Aloe-emodin anthrone (II)	1631	1 : 8-Dihydroxyanthraquinone [9]	1675, 1622
Barbaloin (I)	1630	Rhein dimethyl ether (IV)	1726, 1672, 1649
Barbaloin methyl ether	1680		

band in the carbonyl stretching-frequency region at 1654 $cm.^{-1}$; this band is displaced to 1633 $cm.^{-1}$ in 1-hydroxyanthrone because of the strong hydrogen bonding between the carbonyl group and the neighbouring hydroxyl group. A similar effect is observed with 1 : 8-dihydroxyanthrone (dithranol) and aloe-emodin anthrone whose spectra show bands at 1636 and 1631 $cm.^{-1}$ respectively. (This observation confirms Gardner and McDonnell's formulation [10] of aloe-emodin anthrone as the 9-anthrone rather than the 10-anthrone.)

[5] Böhme and Bertram, *Arch. Pharm.*, 1955, **288**, 510.
[6] Gardner and McDonnell, *J. Amer. Chem. Soc.*, 1937, **59**, 857.
[7] Zinn and Gerecs, "Beitrage zur Kenntnis von Kapaloe und Kapaloin," Diss., Eidgenoss. Techn. Hochschule, Zürich, 1945, quoted in ref. 2.
[8] Léger, *Ann. Chim.* (*France*), 1916, **6**, 318; 1917, **8**, 265; cf. Oesterle, *Arch. Pharm.*, 1899, **237**, 811.
[9] Flett, *J.*, 1948, 1441.
[10] Gardner and McDonnell, *J. Amer. Chem. Soc.*, 1934, **56**, 1346; see also Gardner and Naylor, *ibid.*, 1931, **53**, 4114, and ref. 11.

Barbaloin shows a single band in this region of the spectrum at 1630 cm.$^{-1}$. The fact that only a single band is shown in this region of the spectrum also disposes of earlier suggestions that barbaloin is an anthraquinone derivative; as would be expected from Flett's observations, the spectrum of aloe-emodin (III) shows two bands in the carbonyl stretching-frequency region, one at 1674 cm.$^{-1}$ due to the unassociated carbonyl group, the other at 1626 cm.$^{-1}$ due to the hydrogen-bonded carbonyl group; if barbaloin were an anthraquinone derivative, it would similarly be expected to show two bands in this region of its spectrum.

The infrared spectrum of rhein dimethyl ether (IV), which is produced by permanganate oxidation of barbaloin methyl ether,[11] shows bands in the carbonyl stretching-frequency region at 1726, 1672, and 1649 cm.$^{-1}$. Of these, the first may presumably be assigned to the carboxyl-carbonyl group and the second to the unassociated carbonyl group of the anthraquinone nucleus. The third band must then be assigned to the carbonyl group with the neighbouring methoxyl groups: this is somewhat surprising since Flett's results with other methoxyanthraquinones would lead one to predict that this band should be between 1680 and 1670 cm.$^{-1}$. It is possible that the position of this band is affected by the carboxyl group in the *para*-position to the carbonyl group. There can be little doubt of the correctness of the formulation of the compound in view of its rigid identification by Cahn and Simonsen [11] and the fact that analysis shows the presence of two methoxyl groups.

Barbaloin heptamethyl ether [11] shows an infrared band at 1680 cm.$^{-1}$ attributable to a carbonyl group, and Cahn and Simonsen have shown that it forms a dinitrophenylhydrazone. Hence of the nine oxygen atoms present in barbaloin, seven are present in hydroxyl groups and one in a carbonyl group. If this is so, then barbaloin cannot be a glycoside, since this would involve the presence of two ether-oxygen atoms.

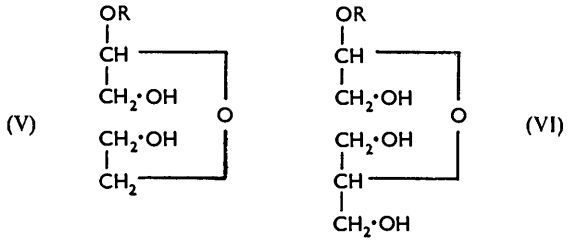
Periodate oxidation of barbaloin at 0°, under conditions in which aloe-emodin anthrone is unaffected by the reagents involved, results in a rapid uptake of two mols. of oxidant with the formation of formic acid, no further oxidant being consumed during 24 hours. This shows the presence of a –CH(OH)·CH(OH)·CH(OH)– system and confirms that the glucose residue is present in the pyranose ring form. This being so, then all the oxygen is accounted for and the glucose residue cannot be associated with any of the hydroxyl groups in the anthrone nucleus. The only likely remaining position for attachment of the glucose residue is $C_{(10)}$ of the anthrone nucleus.

Barbaloin, although an anthrone derivative, does not give the colour reactions [12] given by an anthrone with a free $>CH_2$ group; moreover, no intermediate oxidation product corresponding to the oxidation of the anthrone to the anthraquinone residue has ever been described. We have found that oxidation of barbaloin with limited amounts of ferric chloride gives merely aloe-emodin and unchanged barbaloin. These observations also argue for the attachment of the glucose residue to $C_{(10)}$ in the anthrone nucleus.

Early in our work, it became clear that the degradation of barbaloin to aloe-emodin and D-arabinose by treatment with acid for several months, as described by Léger,[8] was not a hydrolysis but an atmospheric oxidation. Oxidation of barbaloin with aqueous ferric chloride was shown by Cahn and Simonsen [11] to give aloe-emodin in good yield. By removal of inorganic material from the mother-liquors of this reaction by an ion-exchange technique, we have been able to isolate a second product, D-arabinose, which we have identified by melting point, mixed melting point, rotation, paper chromatography, and the preparation of the diphenylhydrazone (mixed m. p.). This reinforces Léger's identification of the products obtained by prolonged acid treatment of barbaloin. In view of Mühlemann's demonstration of the formation of barbaloin from a glucose derivative, and hence the virtual certainty that barbaloin contains a glucopyranosyl residue (see below), this degradation is of considerable interest, and we are at present engaged in an examination of it. Mühlemann's synthetic product examined under these conditions also gives arabinose (identified by paper chromatography) as the sole sugar-like material. Anthranol D-glucoside [6] gives only D-glucose under these conditions.

[11] Cahn and Simonsen, *J.*, 1932, 2573.
[12] Kariyone, *J. Pharm. Soc. Japan*, 1954, **74**, 234; Rosenthaler, *Pharm. Acta Helv.*, 1931, **6**, 115.

An unusual feature in this structure for barbaloin lies in the way in which the glucose residue is attached to the anthrone residue by a direct carbon–carbon linkage instead of a glycosidic carbon–oxygen–carbon linkage. Smith and van Cleve [13] recently described a method for the determination of the ring size of glycosides in which the glycoside is oxidised with periodate and the resulting dialdehyde is reduced with sodium borohydride to compounds of the types (V) and (VI). These compounds are acetals and are readily hydrolysed



by dilute acid to give, among other products, ethylene glycol and glycerol respectively. These products can be related to the ring system present in the original glycoside. This method has been modified to a convenient micromethod for the determination of the ring size of glycosylamines (" nitrogen glycosides ") by Viscontini, Hoch, and Karrer.[14] We have found that the method of Viscontini *et al.* gives very good results with methyl α-D-glucopyranoside (glycerol), adenosine (glycerol), sucrose (glycerol), and methyl β-D-xylopyranoside (ethylene glycol). (Sucrose gave two spots on the paper chromatogram when examined by this method, one due to glycerol, the other presumably to dihydroxyacetone.) Now, since barbaloin is not a glycoside, the dialcohol produced by reduction of the dialdehyde would be an ether and not an acetal, and so should not be degraded by acid to either ethylene or glycerol: in fact, neither ethylene glycol nor glycerol could be detected after treatment of barbaloin by this method. However, glycerol was detected after treatment of borohydride-reduced periodate-oxidised barbaloin with ferric chloride. This, taken with the results from the direct periodate oxidation, provides an independent confirmation of the presence of a hexopyranose residue.

In our early work on barbaloin, we found that the ultraviolet absorption spectra of barbaloin methyl ether in ethanol and ethanolic sodium ethoxide are virtually identical: since we considered that an anthrone or mono-10-substituted anthrone would be converted under these conditions into the salt of the corresponding anthranol with a considerable change in the absorption spectrum, it seemed that the anthrone nucleus in barbaloin must be disubstituted at $C_{(10)}$. Re-examination of this shows that the spectrum of barbaloin methyl ether in ethanolic sodium ethoxide in fact undergoes a slow change. The enolisation of the anthrone residue must involve the shift of the glucosyl residue into the plane of the anthranol residue and it is probable that this slows the rate of enolisation. This would explain the difficulty of converting barbaloin into its octa-acetate.

In the earlier work on barbaloin, difficulty in the interpretation of the experimental results lay in conflicting results of analytical and molecular-weight determinations. In 1942, Owen and Simonsen [15] reported that barbaloin methyl ether had a molecular weight of 521 as determined by *X*-ray crystallography, and showed that the analyses required a heptamethyl ether $C_{21}H_{17}O_2(OMe)_7$ (*M*, 518·6), implying a molecular formula for barbaloin itself of $C_{21}H_{24}O_9$. Dr. C. A. Beevers (to whom we express our thanks) has confirmed Simonsen and Owen's value for the molecular weight of barbaloin methyl ether, but in view of doubts that the formation of the methylated product may have involved some structural change in the barbaloin molecule, it was desirable to have some data on barbaloin itself.

A complete analysis by Mr. F. H. Oliver, of the Imperial College of Science and Technology, London, of a sample of carefully purified barbaloin dried to constant weight

[13] Smith and van Cleve, *J. Amer. Chem. Soc.*, 1955, **77**, 3091.
[14] Viscontini, Hoch, and Karrer, *Helv. Chim. Acta*, 1955, **38**, 642.
[15] Owen and Simonsen, *J. Amer. Chem. Soc.*, 1942, **64**, 2516.

in vacuo gave the figures: C, 60·2, 60·3; H, 5·5, 5·5; O, 34·7, 34·4%; the dried material readily absorbed moisture (1—2 mols.) in air. Barbaloin crystallises as long yellow crystal bundles, and an *X*-ray photograph of a crystal from one of these bundles showed a typical fibre-diagram. However, a few specimens were found, each less than 0·1 mm. wide, which appeared to be single crystals. *X*-Ray crystallography of one such crystal gave a probable value for the molecular weight of air-dried barbaloin of 449 ± 12. Although these single crystals represent only a very small proportion of any sample of crystalline barbaloin, they are always present even in the most carefully purified samples and we consider that it is unlikely that they are not barbaloin. These analytical figures indicate a molecular formula for barbaloin of $C_{21}H_{22}O_9$ (Required: C, 60·3; H, 5·3: O, 34·4%. $C_{21}H_{22}O_9,H_2O$: *M*, 436).

[*Added, May 2nd*, 1956.] Since this paper was submitted for publication, Owen [16] has made a preliminary communication describing the hydrogenolysis of barbaloin to a deoxybarbaloin in which the hydroxymethyl group of barbaloin has been converted into a methyl group, thus demonstrating that the sugar residue in barbaloin is not attached to the hydroxymethyl group of aloe-emodin anthrone. Periodate oxidation of this material, its dimethyl ether obtained by the action of diazomethane, and of barbaloin, results in the consumption of two mols. of oxidant with the formation of one mol. of formic acid but no formaldehyde.

Experimental

Barbaloin.—Commercial aloin (from Curaçao aloes) (450 g.) was recrystallised twice from water (1·5 l.) and then several times from methanol. Barbaloin (200 g.) was thus obtained as lemon-yellow needles, m. p. 148—148·5° [Found (arithmetic mean of five analyses): C, 57·5; H, 5·7; OMe, 0; loss over P_2O_5 *in vacuo* at 100°, 5·1. Calc. for $C_{21}H_{22}O_9,H_2O$: C, 57·5; H, 5·6; H_2O, 4·1%]. The weight lost was recovered by anhydrous barbaloin in air during 2 days (Found, in material dried to constant weight *in vacuo* immediately before analysis: C, 60·2, 60·3; H, 5·5, 5·5; O, 34·7, 34·4. Calc. for $C_{21}H_{22}O_9$: C, 60·3; H, 5·3; O, 34·4%).

Molecular-weight determination (by Dr. C. A. Beevers). The material showed as long yellow crystal bundles with striations parallel to the length, often breaking up into narrower fibres at the ends. An *X*-ray photograph (Cu-*K*α radiation, 50 kv, 25 ma, 2 hours' exposure) of one of these crystals showed a typical fibre diagram. A few specimens (less than 0·1 mm. wide) appeared to be single crystals under the polarising microscope and showed parallel extinction. One such single crystal (0·07 × 0·01 × 0·5 mm.; estimated wt. 0·5 μg.) was picked up by a fine glass fibre which had been slightly greased. It was orientated by microscope on a Weissenberg *X*-ray goniometer, and a series of 10° oscillation photographs (1 hr. each) was taken. These showed distinct spots on the first- and the second-layer lines, with a few spots on the zero- and the third-layer lines. Upper and lower layers were identical. The layer-line spacing corresponds to an axial dimension of 9·54 ± 0·1 Å, and this may be taken as the *b* axis. All the spots observed (approx. 22 in first- and second-layer lines) could be indexed on the basis of orthogonal axes of dimensions $a = 21·1 \pm 0·3$, $c = 20·3 \pm 0·3$ Å. The *b* axis is perpendicular to the others, thus the cell is orthorhombic and has a volume of 4080 Å^3. Referred to the axes, the largest face on the crystal is (001).

When some of the material was stirred in chloroform a few crystals sank although the majority floated. Thus a density of 1·48 g./c.c. was suggested, giving a value of 3590 for the molecular weight of the cell contents. On the assumption of 8 molecules per unit cell, this gives a value of the molecular weight of 449 ± 12.

Insufficient spots were observed to enable the space-group to be determined. However, the general planes (*h*,*k*,*l*) seem all to be present, indicating the primitive lattice P. There seems to be a definite series of absences in the (*h*,0,*l*) planes when *l* is odd. For the (0,*k*,*l*) planes only the (008) was observed. For the (*h*,*k*,0) planes all reflexions were present. In the cases of the pinacoidal reflexions there are insufficient results to establish any definite absences. These findings leave a number of possible space-groups.

Reaction of Barbaloin with Aqueous Sodium Borate (cf. Hauser [4] and Rosenthaler [17]).—An aqueous solution (100 ml.) of barbaloin (5 g.), sodium borate (10 g.), and phenylhydrazine hydrochloride (2 g.) was refluxed during 2 hr. in an atmosphere of nitrogen. The dark red

[16] Owen, *Chem. and Ind.*, 1956, R 37.
[17] Rosenthaler, *Pharm. Acta Helv.*, 1932, **7**, 19.

solution was acidified with dilute hydrochloric acid, and the precipitated yellow solid was extracted into ether (*ca.* 500 ml.). Evaporation of the washed and dried (Na_2SO_4) ether extract gave a reddish solid which on crystallisation from acetic acid (charcoal) gave aloe-emodin anthrone (1·5 g., 51%) as yellow needles, m. p. 199° (Cahn and Simonsen [11] give m. p. 199°). Repetition of the experiment without the phenylhydrazine hydrochloride gave only an 11% yield of the anthrone (m. p. 199°). When the phenylhydrazine hydrochloride was replaced by hydrazine, the yield of anthrone was 34%, but the product had m. p. 190—192° and could not readily be purified.

Attempted Acid Hydrolysis.—Barbaloin was heated at 100° with N-hydrochloric acid for 2 hr. or with hydrobromic acid (38%) for 4 hr. Paper chromatography did not disclose sugar-like materials.

Periodate Oxidation.—An aqueous solution of barbaloin (436 mg.) and 0·2M-sodium metaperiodate (20 ml.) were mixed, the volume was made up to 100 ml. with distilled water, and the solution set aside at 0°. The yellow barbaloin solution immediately became red. Titration of aliquot parts showed that reaction was complete in 3 hr. (consumption, 2·1 mols. of periodate). In a second reaction, when the oxidation was complete the solution was steam-distilled : formic acid was detected in the distillate by its colour reactions with chromotropic acid.[18]

Reduction and Attempted Hydrolysis of the Periodate Oxidation Product (cf. Viscontini, Hoch, and Karrer [14]).—Sodium metaperiodate (10 mmoles, 2 mg.) was added to a solution of barbaloin (5 mmoles, 2 mg.) in water (0·2 ml.), and the whole was kept at 0° for 4 hr. Potassium borohydride (2 mg.) in water (0·1 ml.) was added and the yellow solution kept overnight at 0°. Samples were hydrolysed at 100° (*a*) with N-hydrochloric acid (0·2 ml.) for 15 min., and (*b*) with 38% hydrobromic acid (0·2 ml.) for 15 min. and 1 hr. Adenosine, sucrose, methyl α-D-glucopyranoside, and methyl β-D-xylopyranoside were also treated as above except that the solutions were kept at room temperature. Hydrolysis was effected with N-hydrochloric acid (0·2 ml.) at 100° for 15 min.

The hydrolysates were placed on a paper chromatogram, with spots of ethylene glycol and glycerol as markers, and allowed to run in ethyl acetate–pyridine–water (10 : 4 : 3). The air-dried papers were sprayed with aqueous sodium metaperiodate (0·5%), set aside for 5 min., then sprayed with benzidine solution (0·5 g. in 20 ml. of acetic acid and 80 ml. of ethanol) (N.B. : avoid breathing the benzidine spray). Glycerol (R_F 0·42) and ethylene glycol (R_F 0·51) yield white spots on a blue ground. Adenosine, sucrose, and methyl α-D-glucopyranoside gave the same white spot with R_F 0·42, and methyl β-D-xylopyranoside one with R_F 0·51. Sucrose gave a second white spot of R_F 0·23, possibly due to dihydroxyacetone. Barbaloin gave no white spot. However, a white spot with R_F 0·42, identifiable as glycerol, was given by barbaloin which had been treated as follows.

Barbaloin was oxidised and reduced as described above. The aqueous solution was saturated with salt and extracted with pentyl alcohol. The residue, after removal of the alcohol, was refluxed with aqueous ferric chloride solution (20%) at 115° for 15 min. and 125° for 6 hr. The reaction mixture was filtered and the filtrate passed through a column of Amberlite resin IR-120 (H) to remove ferrous ions. This solution was examined chromatographically as described above.

Ferric Chloride Oxidation (cf. Cahn and Simonsen [11]).—A solution of barbaloin (10 g.) and ferric chloride (50 g.) in water (150 ml.) was heated under reflux at 115° for 15 min. and then at 125° for 6 hr. A dark-brown solid separated from the hot solution. The solution was cooled and the solid collected, dried, and extracted (Soxhlet) into boiling toluene. Removal of the toluene yielded aloe-emodin (4 g., 64%) which on recrystallisation from ethanol gave reddish-orange needles, m. p. 216—219° (Cahn and Simonsen give m. p. 218°; Oesterle [8] gives m. p. 223°). Sublimation of this material at 160—170°/0·2 mm. gave orange needles, m. p. 224—226°.

The dark red filtrate obtained after collection of the solid aloe-emodin was extracted with pentyl alcohol (10 × 30 ml.). The pale yellow aqueous solution was passed through columns of Amberlite resin IR-120 (H) until the eluate was free from ferrous ions. The colourless solution thus obtained was passed through columns of Amberlite resin IR-4B (OH) until all chloride ions had been removed. The neutral solution was concentrated to a small volume. A little ferric hydroxide separated and was removed and the solution was again passed through cation- and anion-exchange resins. The colourless solution was concentrated *in vacuo* to a pale yellow syrup which crystallised on treatment with ethanol. Recrystallisation from aqueous

[18] Feigl, " Spot Tests," English translation by R. E. Oesper, Vol. II, Elsevier, Amsterdam, 1954, p. 245.

methanol gave D-arabinose (0·7 g.), m. p. and mixed m. p. 155·5—156·5°, $[\alpha]_D^{18}$ −104° (*c* 0·42 in H_2O) (lit., $[\alpha]_D$ −105°). The material was identical with authentic D-arabinose when examined by paper chromatography with two solvent systems and formed a diphenylhydrazone, m. p. 197°, undepressed on admixture with an authentic specimen of m. p. 199°.

Ferric Chloride Oxidation of Synthetic Barbaloin.—Tetra-acetylbarbaloin was synthesised by Mühlemann's method. The product (500 mg.) was refluxed in dilute hydrochloric acid for 0·5 hr. A solution of ferric chloride (2·5 g.) in water (5 ml.) was added and the oxidation carried out as above. The sugar isolated from the mother-liquors was identified as arabinose by paper chromatography.

Barbaloin Heptamethyl Ether (cf. Cahn and Simonsen).—Methyl iodide (147 g.) and silver oxide (64·8 g.) were gradually added during 8 hr. to a gently refluxing solution of dry barbaloin (14 g.) in dry acetone (315 ml.) under nitrogen. The mixture was cooled, the solid was collected, and the solvents were removed from the filtrate, leaving a dark red syrup (14·1 g.). This residue was methylated twice with dry acetone (45 ml.), methyl iodide (73 g.), and silver oxide (32 g.). The resulting syrup (13·2 g.) was dissolved in benzene; no crystals separated. The syrup, dissolved in benzene, was run on to an alumina column and eluted with benzene. Evaporation of the solvent from the first fraction left a syrup which crystallised. Recrystallisation from ethanol gave barbaloin heptamethyl ether (1·5 g.), m. p. 180—182°, $[\alpha]_D^{19}$ −12·3° (*c* 1·46 in $CHCl_3$) {Cahn and Simonsen record m. p. 177—179°, $[\alpha]_{5461}$ −12·05° (*c* 1·40 in $CHCl_3$)} [Found : C, 64·8; H, 6·95; OMe, 42·3. Calc. for $C_{21}H_{15}O_2(OMe)_7$: C, 65·1; H, 7·0; OMe, 42·1%].

Molecular weight (by Dr. C. A. BEEVERS) (cf. Owen and Simonsen [15]). A few crystals were available in the form of clear, almost square prisms of length 1 mm. and width about 0·2 mm., showing under the polarising microscope an extinction parallel to their length. The crystals gave excellent *X*-ray spots and an oscillation photograph and Weissenberg photographs of the zero- and the first-layer lines were obtained, the crystal being rotated about the prism axis. From these it appears that the crystal system is orthorhombic with axes $a = 8{\cdot}47 \pm 0{\cdot}10$ Å; $b = 17{\cdot}35 \pm 0{\cdot}05$ Å; $c = 18{\cdot}28 \pm 0{\cdot}05$ Å. There are screw axes in the structure parallel to *b* and *c*, the lattice being a primitive one. The cell volume is thus 2686 Å^3. The observed density is 1·28 g./c.c., giving a molecular weight for the cell contents of 2065. For four molecules per unit cell, this gives a molecular weight for barbaloin methyl ether of 516 ± 10. The crystal used exhibits 011 planes to make up its prismatic shape parallel to the *a* axis.

Permanganate oxidation (cf. Cahn and Simonsen). Barbaloin methyl ether (1 g.) was mixed to a paste with a little hot water, and 2·5% aqueous potassium permanganate (107 ml.) was added during 45 min. The mixture was stirred and heated on the water-bath during 3 hr. Acidification, with dilute hydrochloric acid, of the orange solution obtained after removal of manganese dioxide gave rhein dimethyl ether (250 mg., 41%), m. p. 287—289° [Found : OMe, 22·3. Calc. for $C_{15}H_6O_4(OMe)_2$: OMe, 19·9%].

We thank Professor E. L. Hirst, F.R.S., for advice and encouragement, Dr. E. S. Stern and J. F. Macfarlan and Company for gifts of chemicals, Dr. L. J. Bellamy and Dr. M. St. C. Flett for infrared spectra, the Department of Scientific and Industrial Research for a Maintenance Allowance (to J. E. H.), and Messrs. J. I. Henderson, J. Muir, and J. C. Paxton for assistance in some of the experimental work.

DEPARTMENT OF CHEMISTRY,
THE UNIVERSITY, EDINBURGH, 9.

[*Received, January 30th*, 1956;
revised, April 9th, 1956.]