cyanide in 45 ml. of 50% alcohol yielded 8.0 g. of crude 2-ethylbutyl nitrile, b. p. 164–166°. This was refluxed for three hours with 20 g. of ethylmagnesium bromide in an atmosphere of nitrogen. The reaction mixture, decomposed with ice water, strongly acidified with sulfuric acid and steam distilled, gave 4.5 g. of an oil, b. p. 98–100° at 50 mm. and 171–173° at 74.5 mm., characterized by its semicarbazone.

Anal. Calcd. for $C_{10}H_{21}ON_3$: C, 60.3; H, 10.5. Found: C, 60.5; H, 10.2.

The ketone from hydrolysis of the semicarbazone was distilled: $n^{20}D$ 1.4237.

Anal. Calcd. for $C_9H_{18}O$: C, 76.1; H, 12.7. Found: C, 75.8; H, 13.0.

5-Methylhexanone-3.—This ketone was prepared by adding 25 g. of isovaleraldehyde to 39 g. of ethylmagnesium bromide and oxidizing the resulting secondary alcohol (10 g.) with chromic acid solution. Semicarbazone: plates from methyl alcohol.

Anal. Calcd. for $C_8H_{17}ON_3$: C, 56.1; H, 9.9. Found: C, 55.9; H, 10.0.

3-Methylhexanone-2.—For preparation of this ketone see Clarke[2] and Jones.[3] Semicarbazone: plates from petroleum ether.

Anal. Calcd. for $C_8H_{17}ON_3$: C, 56.1; H, 9.9. Found: C, 55.9; H, 10.2.

4-Methylhexanone-2.—For preparation of this ketone see Kohler[4] and Clarke.[5] Semicarbazone: white needles from water.

Anal. Calcd. for $C_8H_{17}ON_3$: C, 56.1; H, 9.9. Found: C, 56.2; H, 10.0.

Semicarbazone of 5-Methylhexanone-2.—This semicarbazone crystallizes from ether in leaflets, m. p. 146–147° rather than 141°.[6]

(2) Clarke, THIS JOURNAL, **33**, 529 (1911).
(3) Jones, *Ann.*, **226**, 293 (1884).
(4) Kohler, *J. Chem. Soc.*, **38**, 526 (1911).
(5) Clarke, THIS JOURNAL, **30**, 1150 (1908).
(6) Darzens, *Compt. rend.*, **140**, 153 (1905); Freylon, *Ann. chim.*, [8] **19**, 559 (1910); Fournier, *Bull. soc. chim.*, [4] **7**, 838 (1910).

Anal. Calcd. for $C_8H_{17}ON_3$: C, 56.1; H, 9.9. Found: C, 56.2; H, 9.8.

6-Methyloctanone-4.—*dl-s*-Butylcarbinol (30 g.), prepared by the action of formaldehyde on *s*-butylmagnesium iodide, reacted with phosphorus and iodine to yield 44.0 g. of the corresponding iodide, b. p. 137–140°. This in turn reacted with 4.8 g. of magnesium to form a Grignard reagent. Addition of 15 g. of *n*-butyraldehyde and subsequent purification of the reaction product gave 8.0 g. of propyl-*dl-s*-butylcarbinol, b. p. 157–163°. Chromic acid oxidation of this carbinol yielded 2.0 g. of the corresponding ketone which was characterized through its semicarbazone.

Anal. Calcd. for $C_{10}H_{21}ON_3$: C, 60.3; H, 10.6. Found: C, 60.6; H, 10.3.

Preparation of Semicarbazones.—The following procedure was followed in all preparations: 0.2 g. of the ketone was suspended in 5 ml. of water and enough ethyl alcohol added to produce homogeneity. A solution of 1.0 g. of semicarbazide hydrochloride and 2.0 g. of potassium acetate in 10 ml. of water was then added and, after standing several hours at room temperature, the mixture was refrigerated until crystallization occurred.

TABLE I

	Ketone	B. p. °C.	B. p. Mm.	Semicarbazone m. p., °C.
1	5,5-Dicarbethoxyheptanone-2	136–138	2	116.5–117.5
2	5-Carboxy, 5-carbethoxyheptanone-2	71–73	2	114–115
3	5-Carboxyheptanone-2	135–137	2	127–129
4	5-Carbmethoxyheptanone-2	75	2	108
5	5-Ethylheptanone-3	171–173	760	133–134
6	5-Methylhexanone-3	135–137	760	149–150
7	3-Methylhexanone-2	136–139	760	69–70
8	4-Methylhexanone-2	137–139	760	127–128
9	5-Methylhexanone-2	143–144	760	146–147
10	6-Methyloctanone-4	.....	..	75

Conclusion

Several new ketones have been prepared and characterized through their semicarbazones.

MIDDLETOWN, CONN. RECEIVED JANUARY 13, 1936

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF WASHINGTON UNIVERSITY]

The Preparation and Hydrolysis of Some Polyhydroxyanthraquinone Glucosides[1,2]

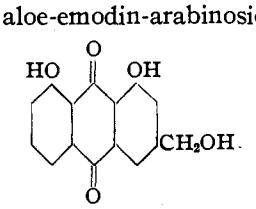
BY HARLAN FOSTER WITH JOHN H. GARDNER

Since it has been known for a long time that barbaloin on hydrolysis in acid solution gives a complex mixture from which aloe-emodin (1,8-dihydroxyanthraquinone-3-carbinol, Formula I) and *d*-arabinose are the only constituents which have as yet been identified, that substance has been regarded as either an arabinoside or an arabinose ether of aloe-emodin.[3] More recently, it has been found that barbaloin, on hydrolysis with an aqueous solution of borax, gives an aloe-emodin-anthrone (1,8-dihydroxy-9,10-dihydro-9-ketoanthracene-3-carbinol, Formula II).[4] Because of this, barbaloin has been formulated as an

(1) No. X in this series of Anthracene Studies: IX, THIS JOURNAL, **57**, 1074 (1935).
(2) Based upon a dissertation submitted by Harlan Foster in partial fulfilment of the requirements for the degree of Doctor of Philosophy, June, 1935.
(3) Leger, *Ann. chim.*, [9] **6**, 318 (1916).
(4) (a) Hauser, *Pharm. Acta Helv.*, **6**, 79 (1931); (b) Rosenthaler, *ibid.*, **9**, 9 (1934); (c) McDonnell and Gardner, THIS JOURNAL, **56**, 1246 (1934).

aloe-emodin-anthrone-*d*-arabinoside,[4b] or as the isomeric *d*-arabinose ether.[4a] It is difficult to see how either of the last formulas can be reconciled with the formation of aloe-emodin. Further, both of the ether formulas would give barbaloin an aldehyde group or an aldehyde–lactone group such as is found in the sugars. This seems inconsistent with the fact that, while barbaloin will readily reduce Fehling's solution and Tollens' reagent, it will not form a phenylhydrazine derivative.[5] These apparently contradictory results might appear consistent with Leger's arabinoside formula if it could be shown that, under the conditions of the borax hydrolysis of barbaloin, the arabinose would reduce aloe-emodin to the anthrone.

In the preceding paper of this series, the hydrolysis of the β-*d*-glucoside and β-*d*-arabinoside of α-hydroxyanthraquinone in the presence of hydrochloric acid, potassium hydroxide and borax was studied. It was found that the reactions did not proceed in a way similar to the hydrolysis of barbaloin, being in every case much more rapid, and that the non-sugar hydrolysis product was always α-hydroxyanthraquinone, with very little if any evidence of reduction. Since α-hydroxyanthraquinone differs in many of its properties from aloe-emodin, this investigation has been extended to include the β-*d*-glucosides of 1,5- and 1,8-dihydroxyanthraquinone and of chrysophanic acid (1,8-dihydroxy-3-methylanthraquinone). The results obtained differed in general only in the fact that the hydrolyses in the presence of potassium hydroxide were relatively more rapid, as might have been expected since these glucosides are soluble in alkali. In no case was any evidence of reduction detected. These results seem to us to indicate definitely that barbaloin cannot be an aloe-emodin-arabinoside.



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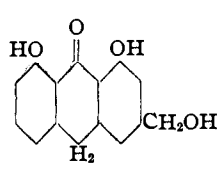

II

Experimental

Tetraacetylglucosides.—The tetraacetylglucosides were prepared from acetobromo-*d*-glucose and the anthraquinone derivatives by the method of Takahashi.[6] The yields and melting points are given in Table I and the analyses in Table II.

TABLE I

No.	Tetraacetylglucoside of -anthraquinone	Yield, %	M. p., °C. Found	M. p. given by Takahashi
I	1,5-Dihydroxy-	71	214.4 (Corr.)	
II	1,8-Dihydroxy-	62	216 (Corr.)	214.5 (Uncorr.)
III	1,8-Dihydroxy-3-methyl (chrysophanic acid)	45.7	217.3 (Corr.)	213 (Uncorr.)

TABLE II

ANALYSES

No.	Calcd. for.....	C, %	H, %	Found C, %	Found H, %
I	$C_{28}H_{26}O_{13}$	58.95	4.56	59.35, 58.25	4.64, 4.28
II	Not analyzed				
III	$C_{29}H_{28}O_{13}$	59.59	4.79	59.68, 59.73	4.80, 4.69

Glucosides.—These were prepared by the hydrolysis of the tetraacetylglucosides, by the method of Takahashi.[6] The yields and melting points are given in Table III and the analyses in Table IV.

TABLE III

No.	Glucoside of -anthraquinone	Yield, %	M. p., °C. Found (Corr.)	M. p. given by Takahashi
I	1,5-Dihydroxy-	53.5	255.2	...
II	1,8-Dihydroxy-	79	240.0	237 (slow heating)
III	1,8-Dihydroxy-3-methyl (chrysophanic acid)	61	255.2	248 (rapid heating) 256

TABLE IV

No.	Calcd. for.....	C, %	H, %	Found C, %	Found H, %
I	$C_{20}H_{18}O_9$	59.70	4.48	59.30 59.24	4.33 4.02
II	$C_{20}H_{18}O_9$	59.70	4.48	59.85 59.33	4.61 4.27
III	$C_{21}H_{20}O_9$	60.57	4.81	60.48 60.66	4.89 4.83

Hydrolysis.—Hydrolyses were carried out in 0.05 *N* hydrochloric acid, 0.05 *N* potassium hydroxide and in solutions of borax containing 100 mg. per cc. of water. The samples were prepared and the hydrolyses carried out as described by Gardner, McDonnell and Wiegand[1] except that approximately one-fifth the quantities were used. All weighings were made on a micro balance sensitive to 0.001 mg. In each case the degree of hydrolysis was calculated from the weight of material obtained from the solution at the end of the reaction, the potassium hydroxide and borax solutions being acidified with hydrochloric acid before filtering. The degree of hydrolysis was calculated from the formula

$$R = S(1 - \alpha) + S(A/G)$$

where α = degree of hydrolysis, A, the molecular weight of the algycone, G, the molecular weight of the glucoside, R, the weight of the residue and S, the weight of the sample.

Identification of the Algycone.—With each glucoside and with each solvent, the melting point of the residue after complete hydrolysis was determined. In each case it was found to agree with that of the anthraquinone derivative from which the glucoside was prepared, and in no case was there any depression in a mixed melting point. It must be concluded that in no case was there any reduction accompanying the hydrolysis.

Results and Discussion

The results are shown graphically in Figs. 1, 2 and 3. Since the three glucosides do not show

(5) Rosenthaler, *Pharm. Acta Helv.*, **4**, No. 9 (1929).

(6) Takahashi, *J. Pharm. Soc. Japan*, **585**, 969 (1925). The authors wish to express their thanks to Dr. Shiro Tashiro of the University of Cincinnati for the translation of this article.

any marked difference, they can be discussed together. In each case, it will be noted that the hydrolysis with potassium hydroxide was most rapid, borax second and hydrochloric acid slowest. This is as would be expected since the glucosides are completely soluble in the hot potassium hydroxide solution, almost completely soluble in the hot borax solution and nearly insoluble in hydrochloric acid. The fact that hydrolysis was complete even in acid solution in not more than one hundred and eighty minutes, without any complicating side reactions, shows a marked contrast with the behavior of barbaloin. The latter requires months for hydrolysis in acid solution and yields a complex mixture of products regardless of the reagent used for hydrolysis. This confirms the view expressed in connection with the previous work on glucosides of α-hydroxyanthraquinone[1] that, if reasoning by analogy is permissible, barbaloin is not an arabinoside of aloe-emodin. Furthermore, since it is well established that barbaloin gives aloe-emodin among other products on treatment with hydrochloric acid, it does not seem reasonable to regard it as an arabinoside of aloe-emodin-9-anthrone. Analyses of barbaloin which will be published elsewhere tend to further substantiate this view.

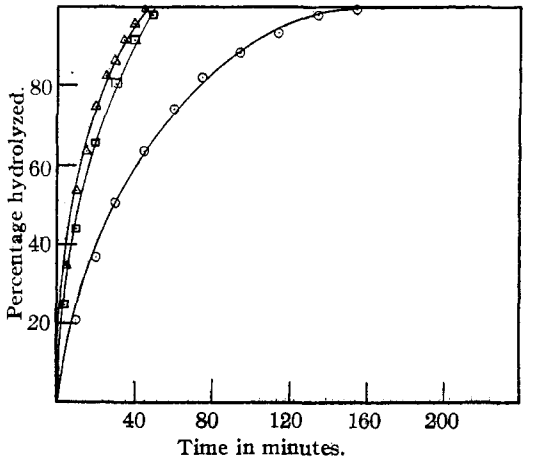

Fig. 1.—Hydrolysis of 1,5-dihydroxyanthraquinone-β-*d*-glucoside: △, KOH; ⊙, HCl; ⊡, Borax.

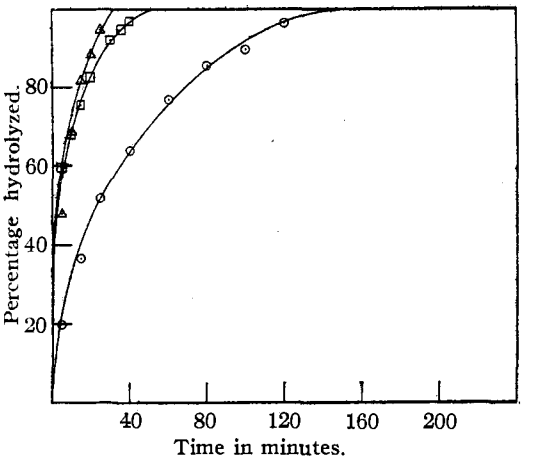

Fig. 2.—Hydrolysis of 1,8-dihydroxyanthraquinone-β-*d*-glucoside: △, KOH; ⊙, HCl; ⊡, Borax.

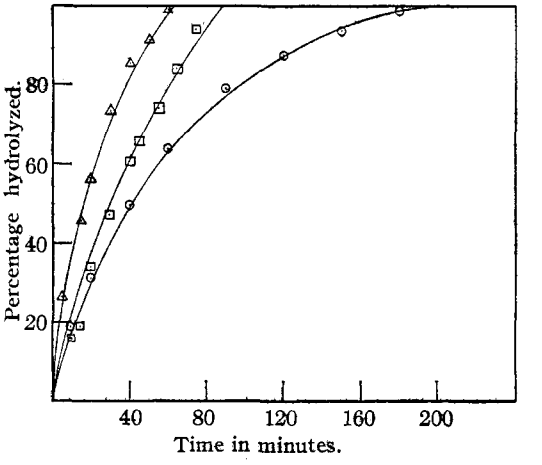

Fig. 3.—Hydrolysis of chrysophanic acid-β-*d*-glucoside: △, KOH; ⊙, HCl; ⊡, Borax.

Summary

1. Several polyhydroxyanthraquinone glucosides have been prepared and their rates of hydrolysis in dilute hydrochloric acid, potassium hydroxide and borax solutions determined.

2. It has been shown that in each case the reaction is simple hydrolysis, not accompanied by any reduction of the anthraquinone nucleus.

3. Further evidence by analogy is presented to show that barbaloin is not an arabinoside of aloe-emodin.

4. It is concluded that barbaloin does not belong to the glucoside type.

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