

of rat. Both synthetic and natural camphor act chiefly on the central nervous system, death being due to respiratory paralysis.

2. Both synthetic and natural camphor cause a depressant action on the normal frog heart.

3. Neither synthetic camphor nor natural camphor is of value in overcoming the effect of chloral hydrate on the frog heart.

4. Both synthetic camphor and natural camphor primarily depress the perfused isolated mammalian heart.

5. The effect of intravenous and subcutaneous injections of both synthetic and natural camphor on the circulation is chiefly depressant.

6. Both synthetic and natural camphor markedly stimulate the mammalian respiration.

7. The differences in action between synthetic camphor and natural camphor are chiefly quantitative and not qualitative, synthetic camphor having a more pronounced and powerful action.

8. It appears logical and justifiable from the experimental evidence obtained to substitute synthetic camphor for natural camphor for medicinal purposes.

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THE ANTHRONE DERIVED FROM BARBALOIN AND ISOBARBALOIN.*

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More than twenty years ago, Léger (1) presented evidence that the common varieties of aloin are mixtures of two isomers, barbaloin and isobarbaloin. The aloin sold in this country is prepared from Curaçao aloe and is made up largely of barbaloin with a smaller but still considerable proportion of isobarbaloin.

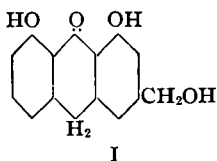
These isomers resemble each other closely in most of their properties. They have the same percentage composition, melting point and crystal form. The most notable differences are, *first*, isobarbaloin is much more soluble in methyl alcohol than is barbaloin, and *second*, isobarbaloin gives a Klunge reaction (a red color with aqueous sodium chloride and copper sulfate) in a few minutes whereas with barbaloin the color appears only after a half hour or longer. Léger also describes a number of cases in which the corresponding derivatives of the two substances dif-

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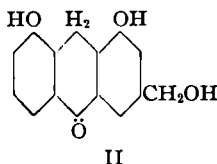
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fer, but for the most part these derivatives do not have satisfactory properties for the establishment with certainty of their purity or uniformity.

Several years ago, Hauser (2) showed that barbaloin yields an aloe-emodin anthrone on hydrolysis with an aqueous solution of borax. Later, this compound was shown by Rosenthaler (3) and by McDonnell and Gardner (4) to be aloe-emodin-9-anthrone,¹ (Formula I). Hauser in his original article suggested that



barbaloin and isobarbaloin might be derived from the two isomeric aloe-emodin anthrones. If this view were correct, isobarbaloin should yield aloe-emodin-10-anthrone (Formula II) on hydrolysis.



In order to check this hypothesis, commercial aloin was fractionally crystallized from methyl alcohol, giving four fractions. The two least soluble were combined and freed of isobarbaloin by Léger's method (1) involving subjection to the Klunge reaction. Samples of all fractions were then hydrolyzed with aqueous borax solution. The products so obtained were purified and then reduced with stannous chloride, tin and hydrochloric acid to the corresponding chrysophanic acid anthrone, and finally acetylated. The final product in all cases proved to be chrysophanic acid-9-anthranol triacetate, identical with the compound synthesized by Naylor and Gardner. This demonstrates conclusively that both barbaloin and isobarbaloin yield aloe-emodin-9-anthrone (Formula I) on hydrolysis with aqueous borax, showing that the structural difference between the two must be accounted for on some other basis than a difference in the anthracene nucleus.

EXPERIMENTAL.

Separation of Barbaloin and Isobarbaloin.—Fifty grams of commercial aloin were dissolved in 400 cc. of hot methyl alcohol. Upon cooling, yellow crystals separated (Fraction I). After filtering out Fraction I, the mother liquor was concentrated to 200 cc. Fraction II crystallized out

¹ In a paper published about a year ago, Léger (5) criticized one of us for calling this compound aloe-emodin-9-anthrone rather than aloe-emodin-9-anthranol. It should be pointed out that Meyer and Sander (6) have shown that in the tautomeric mixture of 1-hydroxy-9-anthrone and 1-hydroxy-9-anthranol, there is a scarcely detectable amount of the anthranol, despite the fact that all of the reactions expected of 1-hydroxy-9-anthranol are given. By analogy, it seems probable that the product derived from barbaloin exists chiefly in the anthrone form. Consequently, we will continue to call it aloe-emodin-9-anthrone, recognizing, however, that it is probably a mixture of that substance with a small quantity of the corresponding anthranol in dynamic equilibrium.

on cooling and was separated by filtration. The mother liquor was again concentrated to 100 cc. and Fraction III which separated on cooling was separated. Further concentration to about 25 cc. gave a mass which solidified on cooling (Fraction IV). All concentrations were carried out in a partial vacuum without access of air.

Fractions I and II were combined and dissolved in 500 cc. of hot water to which had been added 75 Gm. of sodium chloride and 25 cc. of a saturated solution of copper sulfate. The solution was heated on a boiling water-bath for ten minutes. A red color developed very quickly. Upon cooling, long yellow needles separated and were filtered from the red solution. This process was repeated until the mother liquors were no longer colored red. The dried needles were recrystallized from a mixture of two volumes of chloroform and one volume of methyl alcohol. The product corresponded in all details with Léger's description of barbaloin.

Fractions III and IV were recrystallized from methyl alcohol. Fraction IV was fairly pure isobarbaloin and Fraction III almost certainly a mixture of the two compounds.

Hydrolysis.—Each of the three fractions (Barbaloin, Fraction III and Fraction IV) was hydrolyzed with aqueous borax following Hauser's procedure (2). After thirty minutes of boiling, the solutions were acidified with hydrochloric acid and the precipitates dried and extracted with boiling toluene. The yellow crystals which separated on cooling the toluene extracts were recrystallized from 75 per cent acetic acid. All products melted within the range 198° to 201.5°. Aloe-emodin-9-anthrone melts at 201–202.5° (McDonnell and Gardner (4)).

Reduction of the Hydrolysis Products.—The specimens of aloe-emodin-9-anthrone so obtained were reduced to the corresponding chrysophanic acid anthrone with stannous chloride, tin and hydrochloric acid in glacial acetic acid solution following the procedure of McDonnell and Gardner (4). The products were recrystallized from glacial acetic acid.

Acetylation.—Each of the three specimens of chrysophanic acid-9-anthrone derived ultimately from the three aloin fractions was acetylated in the usual way with acetic anhydride and sodium acetate and the acetates were recrystallized from glacial acetic acid. Melting points alone and mixed with equal amounts of chrysophanic acid-9-anthranol triacetate (m. p. 239.8–241°) were determined. All melting points agreed within reasonable experimental and there was no depression in any case, indicating that all products were identical with chrysophanic acid-9-anthranol triacetate and with each other. All melting points were corrected. The values are given in Table I.

TABLE I.

MELTING POINTS OF THE PRODUCTS FROM THE ALOIN FRACTIONS ALONE AND WITH CHRYSOPHANIC ACID-9-ANTHRANOL TRIACETATE.

Fraction.	M. P. Alone.	M. P. Mixed.
Barbaloin	240.8–241.2	239.8–240.2
III	240.8–241.5	239.6–240.4
IV	239.4–239.8	239.6–241.0

SUMMARY.

It has been shown that all fractions obtained by the fractional crystallization of commercial aloin yield aloe-emodin-9-anthrone on hydrolysis with aqueous borax solution demonstrating that barbaloin and isobarbaloin are not derivatives of isomeric anthrones.

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