The total amount of crude resin corresponded to 3.5 per cent. of the weight of the plant, and from it most of the above-described crystalline substances were isolated.

The amount of essential oil obtained by the direct distillation of the air-dried plant corresponds to 0.16 per cent. of the weight of the latter. This oil had a pale yellowish brown color, an agreeably aromatic, mint-like odor, and possessed the following constants: $d = 0.9244$ at 20°; $[\alpha]_D$ —22°48′ in a 1 dcm. tube.

Among the above-mentioned substances the two crystalline alcohols, micromerol and micromeritol, are of special interest. Their empirical composition is represented by the same general formula $C_nH_{2n-14}O_4$, and, as they contain no unsaturated linkings, they are evidently cyclic compounds in which a benzene nucleus is doubtless present. As micromerol contains but one hydroxyl group, whereas micromeritol contains two such groups, they are not simple homologues, but a similarity in their general characters renders it probable that some fundamental relationship exists between them. It is of further interest to note that a crystalline, monohydric alcohol, $C_{25}H_{36}O_4$ (m. p. 300-8°; $[\alpha]_D + 64.9°$), designated as lippianol, which was recently isolated from a South African plant, *Lippia scaberrima*, Sonder (Nat. Ord. *Verbenaceae*), possesses the same general formula as those above mentioned, namely, $C_nH_{2n-14}O_4$, and has similar properties (compare Power and Tutin, *Archiv der Pharm.* **245**, 344 (1907), and *Amer. J. Pharm.*, **79**, 449 (1907)). Another compound of this class, having the formula $C_{38}H_{62}O_4$ (m. p. 278°; $[\alpha]_D + 65.9°$), and designated morindanol, has likewise been isolated in these laboratories from a West African plant, *Morinda longiflora*, G. Don (Nat. Ord. *Rubiaceae*). Cf. *J. Chem. Soc.*, **91**, 1918 (1907).

Our thanks are due to Mr. H. H. Dale, Director of the Wellcome Physiological Research Laboratories, for having conducted a test with micromerol. One gram of the substance was administered to a small dog, but no symptoms of any kind were manifested, and it therefore appears to be devoid of any pronounced physiological activity.

MARRUBIIN.[1]

By H. M. Gordin.

Received November 22, 1907.

The bitter principle, marrubiin, was discovered in horehound (*Marrubium vulgare*, Linné) by Mein and, without indicating the method by which it was obtained from the plant, sent to Harms for investigation.[2] Later

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[1] The Wm. S. Merrell Chem. Co. deserves my thanks for not only supplying the horehound but for preparing for me an extract in accord with my directions.

[2] Arch. Pharm. (2), **83**, 144; (2), **116**, 141.

the bitter principle was examined by Kromayer,[1] Hertel,[2] Morrison[3] and Matusow.[4] The different chemists employed different methods for the isolation of marrubiin, and their results differ so much from each other that it seemed advisable to undertake a thorough examination of this constituent of a popular plant. As marrubiin is only sparingly soluble in water, the yield obtained by this menstruum is extremely small. This accounts for the very small yield obtained by Harms (2 grams from 25 lbs.). On the other hand, owing to the great expense involved, ether, while a fairly good solvent for the bitter principle, is not suitable for extraction on a large scale. It seemed, therefore, that Matusow's method in which acetone is used as a menstruum was the most convenient for the purpose. Matusow's method consists in extracting the horehound with acetone, distilling off the solvent and treating the residue with hot benzene. According to Matusow, the benzene solution on cooling deposits the marrubiin in crystalline condition. I have faithfully followed Matusow's directions and obtained the crystals, but a careful examination of these showed them to be not marrubiin but potassium nitrate. The identity of the salt was established by a large number of the reactions of both the metallic and the nitrate ions, as also by a crystallographic comparison with pure potassium nitrate carried out by Prof. Kraus, of the University of Michigan. The appearance of saltpeter in considerable quantities in the acetone extract is possibly due to the presence of water in ordinary acetone. The small crystals of the salt cannot be noticed in the very dark residue left after distilling off the acetone; when the residue is heated with benzene the potassium nitrate, which is extremely easily soluble in hot water, goes into solution in the small amount of water present and crystallizes out upon cooling. Having failed to prepare marrubiin by Matusow's method, I worked out the following method. The coarsely ground horehound is extracted by percolation with cold acetone till the latter comes out nearly tasteless, the solvent distilled off and the residue digested repeatedly with considerable quantities of petroleum ether. After pouring off the petroleum ether the residue is digested several times with warm water to remove soluble inorganic salts and then dissolved in just enough hot alcohol to bring all into solution. On cooling, the whole liquid solidifies to a mass of crystals. After washing the crystals with cold alcohol, they are repeatedly recrystallized from hot alcohol, using animal charcoal freely, till their color is snow-white and their melting point is constant. The yield of pure marrubiin by this method was 0.25 per cent.; but as it had to be recrystallized nearly a dozen times and marrubiin

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[1] Arch Pharm., 108, 258.

[2] Am. J. Pharm., 1890, 273.

[3] *Ibid.*, 1890, 327.

[4] *Ibid.*, 1897, 201.

is quite soluble in cold alcohol, most of it remained in the mother liquors, from which I hope to obtain additional quantities. The melting point of marrubiin is 154.5–155.5°; under a pressure of 15 mm. it boils at 297–99°. It crystallizes from hot alcohol in two different forms. On quickly cooling the alcoholic solution the crystals are small and fine; by slow crystallization large heavy crystals can be obtained. If the hot saturated solution is free from any solid marrubiin, the solution can be kept for several hours in a supersaturated condition, and when crystallization begins, the crystals are flat and over two centimeters long. As shown by the melting point and analysis, the two modifications are chemically identical. A complete separation of the two modifications could not be effected. Following is an account of crystallographic measurements carried out by Prof. Kraus:

"Marrubiin crystallizes in two distinct modifications from a solution in alcohol. The crystals of the first modification are well developed and allowed accurate goniometric measurements to be made. The second modification does not show as well developed faces, so that for the present only approximate measurements for several angles can be given.

"*Modification One.* — These crystals are readily obtained by slow evaporation of an alcoholic solution. The crystals are usually quite small, about 2 mm., perfectly clear, and transparent. The following forms were observed: *a* (100), *m* (110), *c* (001), *d* (101), and *q* (011). Of these forms the ortho pinacoid *a* (100) and the prism *m* (110) are usually quite large, giving rise to a prismatic development. The basal pinacoid *c* (001) may, however, predominate, causing the tabular habit to result. The domes *d* (101) and *q* (001) are generally quite small but give excellent images. Fig. 1 shows the usual combination and development. In all, eight crystals were measured with the following results:

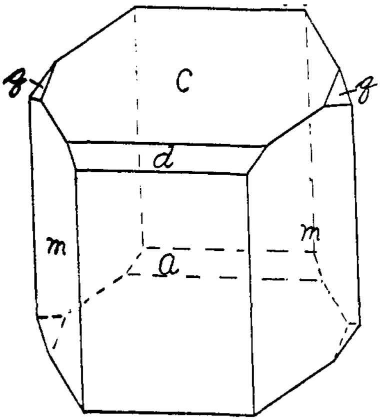

Fig. 1.

"Crystal System—Monoclinic.

"Axial Ratio—$a : b : c = 1.5551 : 1 : 0.885$, $\beta = 61° 17'$.

	Observed.	Calculated.
$a : m = (100) : (110)$ =	53° 45′	....
$a : c = (100) : (001)$ =	61° 17′	....
$c : q = (001) : (011)$ =	37° 49′	....
$a : d = (100) : (101)$ =	39° 51.3′	39° 55.7′
$c : m = (001) : (110)$ =	73° 32.5′	73° 29.5′

"*Modification Two.*—The second modification also belongs to the monoclinic system. The crystals are flat tabular in development and show a prism angle of 94° 36′. The angle between the ortho- and basal pinacoids, *a* (100) and *c* (001), is about 71° 3.5′. More accurate measurements will be made later. The above values are, however, sufficient to show a decided difference in the crystallization of the two modifications.

EDWARD H. KRAUS."

The formula of marrubiin is $C_{21}H_{28}O_4$. Analysis gave C, 73.00, 73.14, 72.90, 72.97; H, 8.28, 8.57, 8.32, 8.43; calculated for $C_{21}H_{28}O_4$: C, 73.21; H, 8.20. A molecular weight estimation by the cryoscopic method with phenol as solvent gave $M = 327$. Calculated for $C_{21}H_{28}O_4$; 344.22. Marrubiin is isomeric with the menthyl ester of acetoxy α-phenylacrylic acid and with the menthyl ester of benzoylacetic acid, which were prepared by Lapworth and Hann.[1] The first of these esters melts at 51–52°, the second is a liquid. Marrubiin is dextrorotatory. $[\alpha]_D^{24} = 45.68°$ ($c = 4.794$, solvent, acetone from bisulphite and redistilled by myself). The polariscope was a Josef and Jan Frič apparatus. Marrubiin is soluble in about 60 parts of alcohol at 20° and 20,835 parts of water at 21.5°. It is very easily soluble in acetone, chloroform, hot alcohol, warm phenol, pyridine and warm glacial acetic acid; difficultly soluble in ether or benzene. It does not reduce Fehling's solution or ammoniacal silver nitrate either before or after warming with dilute mineral acids. It does not contain CH_3O groups (by Zeisel's method) and does not decolorize bromine in glacial acetic acid solution. It has a very bitter taste and a neutral reaction. It does not react with acetic anhydride, benzoyl chloride, hydroxylamine or phenylhydrazine, showing absence of hydroxyl or carbonyl groups. In all cases unchanged marrubiin was recovered as shown by crystalline appearance, melting point and bitter taste. Cold aqueous or alcoholic potassium hydroxide has no effect upon it. Very dilute alcoholic potassium hydroxide attacks it slowly on prolonged boiling. When boiled for a short time with ten per cent. alcoholic potassium hydroxide it takes up a molecule of water and is quantitatively converted into the potassium salt of a new acid which I have named marrubic acid, $C_{20}H_{29}O_3.CO_2H$. The acid is made as follows: Ten grams marrubiin are boiled for about half an hour with 150 cc. of alcohol containing 10 to 12 per cent. of potassium hydroxide, the liquid is then diluted with twice its volume of water and concentrated till the odor of alcohol disappears, adding water from time to time. The solution is set aside in a cool place for 24 hours, and the very small amount of slimy matter which separates out removed by filtration. The filtrate is acidified with hydrochloric acid and the extremely bulky white precipitate which separates out, collected on a filter, thoroughly washed with water and recrystallized from hot alcohol to which hot water is gradually added. Yield over 98 per cent. of the theoretical. Thus obtained marrubic acid forms snow-white, long silky needles. The acid is extremely bulky and looks like quinine sulphate or caffeine, but is even fluffier than these. According to Prof. Kraus the acid crystallizes in extremely fine, long, prismatic crystals. The prism faces show, apparently, parallel extinction. The acid melts at 173–4°. Its formula

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[1] J. Chem. Soc., 81, 1497 and 1507.

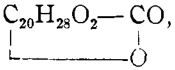
is $C_{20}H_{29}O_3.CO_2H$. Analysis gave: C, 69.02, 69.08; H, 8.76, 8.67. Calculated for $C_{20}H_{29}O_3.CO_2H$: C, 69.57; H, 8.35. Marrubic acid is very easily soluble in alcohol, warm phenol and pyridine, difficultly soluble in ether, glacial acetic acid and benzene, almost insoluble in water. It has an acid reaction in alcoholic solution. It is isomeric with antiarigenin. The latter is not an acid and becomes intensely yellow at 170° melting at 180°. Marrubic acid is very easily soluble in ammonia water, but upon concentration of the solution all the ammonia evaporates, leaving the acid unchanged. It is easily soluble in alkalies and alkali carbonates and forms salts with metals, none of which, however, could be obtained in crystalline condition. The salts all seem to be very easily soluble in water and alcohol with the exception of the copper salt, which is amorphous and difficultly soluble in water. Titration with standard alkali showed the acid to be monobasic. 0.2200 gram of the acid required 6.05 cc. N/10 KOH (phenolphthalein as indicator), and 0.3963 gram required 10.8 cc. N/10 KOH. Calculated for $C_{20}H_{29}O_3.CO_2H$, 6.1 and 10.9 cc. respectively.

Barium marrubate, $(C_{20}H_{29}O_3.CO_2)_2Ba$, was prepared by digesting marrubic acid with an excess of barium carbonate in dilute alcohol, filtering, concentrating to a small bulk, again filtering (to remove traces of barium carbonate) and evaporating to dryness. The salt is amorphous and very easily soluble in water or alcohol but insoluble in ether. It could not be obtained in crystalline form. For analysis it was converted into barium carbonate. 0.2818 gram gave 0.0645 g. $BaCO_3$, and 0.5605 g. gave 0.1293 g. $BaCO_3$. Calculated for $(C_{20}H_{29}O_3.CO_2)_2Ba$, 15.97 per cent. Ba. Found: 15.93 and 16.06 per cent. Ba. At water bath temperature marrubic acid quickly reduces ammoniacal silver nitrate or Fehling's solution. Neither the alcohol solution of the free acid nor the aqueous solution of the barium salt are colored by ferric chloride. Marrubic acid is dextrorotatory. $[\alpha]_D^{21.5} = 7.86$. ($c = 2.5456$; solvent, acetone).

When heated to 190–200° under a pressure of 15 mm. the acid boils up suddenly, loses one molecule water and changes back to marrubiin. This was shown by treating the melt with dilute sodium carbonate solution to remove traces of unchanged acid and recrystallizing the insoluble part from alcohol. The crystals were insoluble in alkali carbonates and melted at 154–5°. The same reconversion of marrubic acid into marrubiin can be effected by warming the acid with ten times its amount of acetic anhydride and a trace of zinc chloride for a few minutes to about 50°. On largely diluting the liquid, which assumes a dark yellow color, the color disappears and an oily liquid separates out, which on standing under water becomes solid. The solidified precipitate was digested with sodium carbonate and then recrystallized from alcohol. It was insoluble in alkali carbonates and melted at 154–5°. The liquid obtained by digestion with sodium carbonate gave no precipitate upon addition of excess of acid; hence the reconversion of marrubic acid into marrubiin by this method is quantitative. The acid is also reconverted into marrubiin by boiling for an hour with alcoholic hydrochloric acid (4 cc. 30 per cent. acid and 50 cc. alcohol). On throwing the solution into much water and recrystallizing the precipitate from alcohol, it was found to be marrubiin (insoluble in alkali carbonates and melted at 154–5°). Part of the acid is resinified in this reaction. On digesting a solution of marrubic acid in pyridine with benzoyl chloride (one molecule each) for 24 hours and then adding 750 cc. water an oily liquid separates out which becomes solid upon long standing. The mass was digested with dilute sodium carbonate solution and then recrystallized from alcohol. It was found again to be marrubiin. It constituted about 80 per cent. of the amount of acid taken. The part soluble in sodium carbonate does not seem to be unchanged marrubic acid. It was precipitated from the alkaline carbonate solution by addition of hydrochloric acid and recrystallized from alcohol to which hot water was gradually added. On standing fine needles separated out. They melted between 164–70° and represented most probably a benzoyl derivative of marrubic acid, but the amount was too small for an analysis.

Ethyl Marrubate.—Marrubic acid was digested with a solution of potassium hydroxide on the water bath, leaving the acid in slight excess, the liquid filtered to remove undissolved acid and evaporated to dryness. Three grams of the potassium salt thus obtained were mixed with 4 cc. ethyl iodide and 20 cc. acetone and the mixture boiled for two and a half hours under reflux condenser. The liquid was then evaporated to dryness, the residue treated with dilute sodium carbonate solution to remove possible traces of unchanged acid and recrystallized by dissolving in cold alcohol and adding water to turbidity. As the sodium carbonate solution did not give any precipitate with acids, the esterification of marrubic acid by this method must be quantitative. From a mixture of alcohol and water the ester crystallizes in very pretty glittering scales; from a mixture of ether and petroleum ether large heavy crystals can be obtained, which consist of layers of leaflets. Unlike marrubiin and marrubic acid, the ethyl ester is tasteless. It is extremely easily soluble in ether and pyridine, a little less soluble in alcohol, chloroform or benzene and still less in petroleum ether. It melts at 87°. When heated to about 100° under a pressure of 28 mm. it boils, gives up a molecule of alcohol and is reconverted into marrubiin. This was shown by recrystallizing the reaction product from alcohol and comparing it with marrubiin. For analysis an ethoxyl estimation was made by

Zeisel's method. Found: 10.78 and 11.50 per cent. of C_2H_5O. Calculated: 11.54 per cent. of C_2H_5O. The ester forms an acetyl derivative, but this and several other derivatives of marrubiin will be reported upon in my next paper. The results of the investigation so far show that marrubiin is a lactone behaving like a γ-lactone in that it easily takes up a molecule of water and changes to a hydroxy acid. The formulae of marrubiin, marrubic acid and ethyl marrubate can therefore be written as follows:



$C_{20}H_{28}O_2—CO$, $C_{20}H_{28}O_2(OH).COOH$, $C_{20}H_{28}O_2(OH)COO.C_2H_5$.

The investigation is continued.

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DECOMPOSITION CURVES OF SOME NITROCELLULOSES OF AMERICAN MANUFACTURE.[1]

BY OSWIN W. WILLCOX.

Received November 11, 1907.

In the course of a study of the test proposed by Obermuller[2] for the stability of nitrocellulose, it was observed that the rate of decomposition of an ordinary collodion cotton during a given period of time depended on whether or not the gaseous products of decomposition had been allowed to remain in contact with the sample during previous periods. As the Obermuller apparatus is perhaps the most accurate and convenient means yet devised for following quantitatively the progress of the decomposition of a nitrocellulose at temperatures below its ignition point, some of the results obtained are deemed of interest.

Obermuller's test is essentially as follows: A weighed quantity of the nitrocellulose to be tested is placed in a glass tube, which is then evacuated by means of a good air pump. When the air has been removed as much as possible, the tube is plunged into a bath previously brought to a standard temperature, which is maintained constant throughout the duration of the test. The nitrocellulose in the tube immediately begins to decompose and to give off gaseous products; the tube being in connection with a mercury manometer, the rate at which the products of decomposition are evolved is measured by the increase of pressure shown by the manometer. This rate will naturally be greater for nitrocellulose of poor stability and less for nitrocellulose of good stability. Working at a standard temperature of 140° C., and with a tube which, with its connections, had a volume of 37 cc., Obermuller

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[1] Published by permission of the Honorable the Secretary of War.

[2] Mittheilung aus dem Berliner Bezirksverein des Vereins deutscher Chemiker, October 11, 1904.