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CHEMICAL EXAMINATION OF MICROMERIA CHAMISSONIS.

(*Yerba Buena.*)[1]

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The labiate plant *Micromeria Chamissonis* (Benth.) Greene (syn. *M. Douglassi* Benth.), commonly known as "Yerba Buena," is a perennial, trailing or creeping, sweet-scented herb, which is indigenous to the Pacific coast of the United States. The generic name is stated to be derived from the Greek *mikros*, small, and *meros*, part, on account of the small size of the flowers (compare Jepson's "Flora of Western Middle California," p. 463). A description of the anatomical characters of the plant, with illustrations, has been given by J. Moeller.[2]

The above-mentioned species of *Micromeria* is used to some extent medicinally, but, so far as known to us, it has never been the subject of chemical investigation, and we have therefore availed ourselves of the opportunity of making a complete examination of its constituents.

Experimental.

The material employed in this investigation consisted of a bale of the entire, air-dried herb, which was kindly placed at our disposal by Messrs. Burroughs, Wellcome & Co., of London. The genuineness of the material was assured by the fact that it had been specially collected for them in California under the supervision of a competent botanist, Mr. P. E. F. Perrédès, B.Sc., F.L.S.

Distillation of the Plant with Steam. Characters of the Essential Oil.

A quantity ($56^1/_4$ pounds $= 25^1/_2$ kg.) of the herb was submitted to steam distillation by Messrs. Stafford Allen & Sons, of London, and our thanks are due to them for having kindly conducted this operation for us. The amount of essential oil obtained was 42.3 grams, corresponding to 0.16 per cent. of the weight of air-dried plant. Towards the end of the distillation a small quantity (8.5 grams) of a semi-solid substance separated in the condenser and receiver. This was separately collected and examined.

The essential oil had a pale yellowish brown color and an agreeably aromatic, somewhat mint-like odor. Its density was 0.9244 at 20°, and its optical rotation $-22° 48'$ in a 1 dcm. tube. It was not completely soluble in ten times its volume of 70 per cent. alcohol, and gave no coloration with ferric chloride.

The above-mentioned, semi-solid substance was spread on a porous plate, when the oily constituent was absorbed, and a white, crystalline

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[1] Read before the New York Section of the American Chemical Society, Nov. 8, 1907.

[2] Am. J. Pharm., 1882, **54**, 461, from Pharm. Centralhalle, 1882, No. 29.

solid remained. This was crystallized from acetic acid, from which it separated in pearly leaflets, melting at 61.5°. It was analyzed with the following result:

0.0914 gave 0.2506 CO_2 and 0.1073 H_2O. $C = 74.8$; $H = 13.0$.

$C_{16}H_{32}O_2$ requires $C = 75.0$; $H = 12.5$ per cent.

This solid substance was thus identified as palmitic acid.

Examination of the Alcoholic Extract of the Plant.

For the purpose of a complete examination of the constituents of the plant, 36 pounds ($16^1/_3$ kg.) of air-dried material were extracted by continuous percolation with hot alcohol. After the removal of the greater portion of the alcohol, a dark green, thick extract was obtained, which weighed 4170 grams. Of this extract, 3.5 kg. were mixed with water, and the mixture distilled with steam until all the volatile substances present had been removed.

Volatile Constituents of the Alcoholic Extract.

The distillate obtained, as above described, had a distinctly acid reaction and contained a quantity of essential oil floating on the surface. It was extracted twice with ether, after which the ethereal liquid was washed with a little water, dried with anhydrous sodium sulphate, and the ether removed. About 20 grams of a pale yellowish brown essential oil, possessing an aromatic, mint-like odor, were thus obtained. When distilled under a pressure of 25 mm. it passed over between 80° and 160°, but the greater portion boiled between 120° and 140°. The oil had a density of 0.9450 at 20°, and an optical rotation of —26° 44′ in a 1 dcm. tube. It was readily soluble in 70 per cent. alcohol, thus differing from the essential oil distilled directly from the dried plant.

The acids contained in the aqueous distillate from which the essential oil had been removed were neutralized with baryta, and the liquid concentrated. About 3 grams of a barium salt were thus obtained in the form of a thick syrup, which afforded reactions indicating the presence in the distillate of formic, acetic, and butyric acids, the latter being relatively small in amount.

Non-volatile Constituents of the Alcoholic Extract.

After the removal of the essential oil and volatile acids by distillation with steam, as above described, there remained in the distilling vessel a reddish-brown, aqueous liquid (*A*) together with a large quantity of a dark green, soft resin (*B*). The resin was separated by filtration from the liquid, while still hot, and washed well with hot water, the washings being added to the filtrate.

Examination of the Aqueous Liquid (*A*).

The aqueous liquid, which was of a reddish brown color, and possessed a slightly bitter taste, was concentrated to a convenient bulk by heating under diminished pressure in a bath of hot water.

Isolation of a New Phenolic Substance, Xanthomicrol, $C_{15}H_{10}O_4(OH)_2$.

The concentrated aqueous liquid was extracted repeatedly with ether, and the several portions finally mixed. This ethereal liquid was washed with a little water, and then extracted with small successive portions of a saturated solution of sodium carbonate. The first few extractions with alkali afforded opaque liquids containing small amounts of a dark green, semi-solid sodium compound of a resinous nature, but neither from this nor from the products which separated on acidifying these liquids could anything crystalline be obtained. The alkaline liquids obtained by the subsequent extractions were, on the other hand, of an orange-yellow color, and, when acidified, yielded orange-yellow precipitates, which were collected, washed with water, and crystallized from alcohol. A substance was thus obtained in the form of fine, lemon-yellow, silky needles, melting at 225°, which was analyzed with the following result:

0.1114 gave 0.2535 CO_2 and 0.0453 H_2O. $C=62.1$; $H=4.5$.

After another crystallization the melting point of the substance remained unchanged, and it was again analyzed:

0.1099 gave 0.2522 CO_2 and 0.0450 H_2O. $C=62.6$; $H=4.5$.

$C_{15}H_{12}O_6$ requires $C=62.5$; $H=4.2$ per cent.

The only known compound of the empirical formula $C_{15}H_{12}O_6$, which has properties similar to those of the above substance, is the so-called "datiscetin," a hydrolytic product of datiscin (compare Beilstein's *Handbuch der org. Chemie*, Bd. III., p. 580). Datiscetin, however, is stated to melt at 237°, and its solution in sulphuric acid, which has a yellow color, shows a blue fluorescence. Although the above-described substance (m. p. 225°) also dissolves in concentrated sulphuric acid with a yellow color, its solution shows no fluorescence. It thus appears not to be identical with any substance hitherto recorded, and it is therefore proposed to designate it *xanthomicrol*, with reference to its yellow color, its phenolic properties, and the generic name of the plant from which it has been obtained.[1]

Xanthomicrol is readily soluble in alcohol, ethyl acetate, and acetone, and moderately soluble in ether, but only sparingly so in chloroform and benzene. It is practically insoluble in cold, but slightly soluble in hot water. It dissolves readily in cold aqueous alkalis, forming solu-

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[1] According to the recent investigations of Korczyński and Marchlewski (*Chem. Centralb.*, 1906, II., 1265 and 1907, II., 700) the substance designated as datiscetin, when purified, possesses the empirical formula $C_{15}H_{10}O_6$, melts at 268–269°, and contains four hydroxyl groups. It would thus be essentially different in its composition and character from xanthomicrol.

tions which are yellow when dilute and orange-red when concentrated. It is, however, not acid towards litmus, and the sodium compound, produced by shaking an ethereal solution of the substance with the theoretical quantity of sodium ethoxide, is readily decomposed on exposure to the atmospheric moisture and carbon dioxide. The property which this substance possesses of combining with alkalis is therefore to be attributed to the presence of one or more phenolic groups.

Di-acetylxanthomicrol, $C_{15}H_{10}O_6(CO.CH_3)_2$.—A small quantity of xanthomicrol was boiled for a short time with acetic anhydride, the greater part of the latter removed by distillation, and the residue poured into water. The product of the reaction, which soon solidified, was collected, washed, and dried. It was then crystallized from ethyl acetate, from which it separated in pale yellow needles, melting at 116.°

The number of acetyl groups in this compound was determined by hydrolyzing weighed portions of the substance with a solution of sodium hydroxide, subsequently acidifying with sulphuric acid, and distilling until acid ceased to pass over.

(I) 0.1763 gave an amount of acetic acid equivalent to 9.4 cc. N/10 NaOH.

(II) 0.1789 gave an amount of acetic acid equivalent to 9.7 cc. N/10 NaOH.

(I) $CH_3.CO = 22.9$; (II) $CH_3.CO = 23.3$.

$C_{15}H_{10}O_6(CO.CH_3)_2$ requires $CH_3.CO = 23.1$ per cent.

Di-acetylxanthomicrol is extremely soluble in most of the usual organic solvents, but insoluble in water. It is immediately hydrolyzed by alkalis, with the reproduction of xanthomicrol, $C_{15}H_{12}O_6$, melting at 225°.

The ethereal liquid from which the above-described new phenolic substance had been obtained, and from which nothing further was extracted on shaking with a solution of sodium carbonate, was washed with a little water, dried with calcium chloride, and the ether removed, when only a very small amount of an uncrystallizable resin remained.

The aqueous liquid (*A*) which had been extracted with ether, as above described, was found to give a deep yellow precipitate with basic lead acetate. A slight excess of the latter was therefore added, the precipitate collected, washed, suspended in water, and decomposed with hydrogen sulphide. On filtering the mixture an orange-red liquid was obtained, which gave a greenish black color with ferric chloride, thus indicating the presence of tannin, but nothing of a crystalline nature could be isolated from it.

The filtrate from the basic lead acetate precipitate was treated with hydrogen sulphide for the removal of the lead, and filtered. A portion of this liquid, when treated with phenylhydrazine acetate, readily yielded a crystalline osazone melting at 217°, and it therefore evidently contained a considerable quantity of glucose. The remainder of the filtrate was concentrated to a small bulk under diminished pressure, when a thick, dark-colored syrup was obtained, from which nothing of a crystalline nature separated, even after standing for several months.

Examination of the Resins (B).

The resin which had been separated from the aqueous liquid, in the manner previously described, was dried at 100°, and then weighed 480 grams, corresponding to 3.5 per cent. of the weight of air-dried plant. This resin was intimately mixed with purified sawdust, the mixture thoroughly dried, and then extracted in a Soxhlet apparatus with various solvents, when the following amounts of extract, dried at 100°, were obtained:

I.	Petroleum (b. p. 40–60°)	extracted	177.12	grams	=	36.9	per cent.
II.	Ether	“	178.08	“	=	37.1	“
III.	Chloroform	“	24.00	“	=	5.0	“
IV.	Ethyl acetate	“	10.56	“	=	2.2	“
V.	Alcohol	“	48.00	“	=	10.0	“
		Total	437.76	grams	=	91.2	per cent.

I. *Petroleum Extract of the Resins.*

This was a soft solid, of a dark greenish color. It was boiled for two hours in alcoholic solution with 40 grams of potassium hydroxide, when a small quantity of ammonia was evolved. After this treatment the greater portion of the alcohol was removed, water added, and the alkaline liquid repeatedly extracted with ether. The ethereal extract, which was of an orange-red color, was washed with a little water, dried with calcium chloride, and the ether removed, when an orange-colored, semisolid residue was obtained. This was distilled under diminished pressure, (25 mm.), in order to remove a small quantity of resinous matter, when it passed over between 240° and 350°. The distilled product was highly fluorescent, both in the fused state and in solution, and, on cooling, it solidified to a wax-like solid. On fractionally crystallizing the latter from ethyl acetate, it was found that the greater portion consisted of a compound which separated in small, glistening, pearly leaflets, and, after a few crystallizations, was obtained in a pure state. It then melted at 66–7°, and was analyzed:

0.1420 gave 0.4434 CO_2 and 0.1822 H_2O. $C = 85.2$; $H = 14.3$.

$C_{31}H_{64}$ requires $C = 85.3$; $H = 14.7$ per cent.

This crystalline substance was thus identified as hentriacontane.

The mother liquors from the crystallization of the hentriacontane yielded a further small quantity of a hydrocarbon, which, after repeated fractionation, melted at 71–4°, and probably consisted of pentatriacontane. The more readily soluble fraction that was finally deposited consisted of a mixture of hentriacontane with a substance which crystallized in large, thin plates. The latter substance was mechanically separated and recrystallized from a mixture of ethyl acetate and alcohol, when it was obtained in the form of pearly leaflets, melting at 135°. This compound, when dissolved in chloroform, gave, with a little acetic anhydride and a drop of sulphuric acid, the color reaction characteristic of the phytosterols.

0.1590 of the air-dried substance, heated to 105°, lost 0.0074 H_2O. $H_2O = 4.7$.

0.1480 of anhydrous substance gave 0.4536 CO_2 and 0.1622 H_2O. $C = 83.6$; $H = 12.2$.

$C_{27}H_{46}O, H_2O$ requires $H_2O = 4.5$ per cent.

$C_{27}H_{46}O$ requires $C = 83.9$; $H = 11.9$ per cent.

The ultimate mother-liquors, from which the above-mentioned hydrocarbons and phytosterol had been isolated, were collected and the solvent removed. A considerable quantity of a thick yellow oil was thus obtained, which was distilled under diminished pressure, and the product collected in two fractions. The fraction of higher boiling-point solidified on cooling, and a further quantity of phytosterol was isolated from it, whereas that of lower boiling-point consisted of a thick, gummy substance, having an unpleasant odor.

The alkaline, aqueous liquid, from which the above-mentioned neutral substances had been extracted by ether, contained an insoluble potassium salt, which was collected on a filter and separately examined. The salt was boiled with alcoholic sulphuric acid, in which it was soluble, and the liberated acid precipitated by the addition of water. The acid, after being collected and washed, was crystallized from alcohol, but, as it separated in a somewhat indefinite form, it was distilled under diminished pressure and then crystallized from ethyl acetate. It was thus obtained in the form of small, glistening plates, which, after a few recrystallizations, melted constantly at 80–2°.

0.0714 gave 0.2034 CO_2 and 0.0830 H_2O. $C = 77.7$; $H = 12.9$.

$C_{22}H_{44}O_2$ requires $C = 77.6$; $H = 12.9$ per cent.

This substance was evidently behenic acid. The mother-liquors from the crystallization of the latter gave deposits melting below 70°, but these were too small in amount to permit of further purification.

The alkaline liquid, from which the above-described potassium salt had been removed, was acidified with sulphuric acid and distilled with steam. The distillate contained a very small amount of volatile acid which, after conversion into a barium salt, afforded reactions indicating it to consist chiefly of butyric acid, with traces of formic and acetic acids. The contents of the distilling flask were subsequently extracted with ether, the ethereal solution being washed, dried, and the ether removed, when a quantity (88 grams) of a dark green, soft solid was obtained. This evidently contained a considerable amount of resinous matter, which was separated by washing with light petroleum, in which the resin was insoluble. The petroleum washings, after the removal of the solvent, yielded a quantity (46 grams) of a green, wax-like solid, which was distilled under diminished pressure. The larger portion (37 grams) passed over between 230° and 250° at 20 mm., while about 3 grams were collected above 250°. Both fractions, on cooling, solidified to a wax-like mass. The larger portion was fractionally crystallized from alcohol, when from the least soluble fractions a substance was finally isolated which melted at 71–3°, and this melting-point was not altered by further crystallization.

0.0780 gave 0.2193 CO_2 and 0.0905 H_2O. $C=76.7$; $H=12.9$.

$C_{20}H_{40}O_2$ requires $C=76.9$; $H=12.8$ per cent.

This substance was thus identified as arachidic acid.

The mother-liquors, which still contained a large proportion of the fatty acids present in the mixture, gave deposits from which, by long-continued fractionation, a substance was obtained which melted quite constantly at 55–7°, and this was analyzed.

0.1522 gave 0.4182 CO_2 and 0.1740 H_2O. $C=74.9$; $H=12.7$.

$C_{16}H_{32}O_2$ requires $C=75.0$; $H=12.5$ per cent.

It is evident that this substance was nearly pure palmitic acid.

From the portion of mixed fatty acids distilling above 250°/20 mm. a very small amount of a substance was isolated which melted at 77–8°. This apparently consisted of slightly impure behenic acid, which, as already noted, had been isolated from the insoluble potassium salt formed in the hydrolysis of the petroleum extract. The mother-liquors from the above-described compounds did not decolorize bromine, and no unsaturated acids were therefore present in the original mixture.

II. *Ether Extract of the Resins.*

This was obtained in the form of a light green powder and amounted to 178 grams. It was digested with a large volume of ether, which dissolved about one-half of the total amount of extract. The sparingly soluble portion was separated by filtration from the ethereal solution, washed with a little ether, and the two portions independently investigated.

Isolation of a New Crystalline Alcohol, Micromerol, $C_{33}H_{51}O_3\text{-}OH,2H_2O$.

The portion of the ether extract of the resins which remained undissolved by the above treatment was dissolved in alcohol, in which it was only moderately soluble, and the solution heated with animal charcoal under a reflux condenser for several hours. By this means the dark green color of the liquid was completely removed. After filtering the solution it began to deposit a quantity of a crystalline substance in the form of fine, colorless needles. The crystals were always accompanied by a relatively small amount of amorphous, fluffy matter, but it was found that this could be removed by filtration through fine muslin, which retained the crystalline substance while the amorphous matter was carried through the filter with the mother-liquor. By repeating this operation the crystalline substance was obtained in a pure condition, and further quantities of it were deposited on concentrating the mother-liquors. The compound, when rapidly heated, melts at 277°. An analysis of it gave the following results:

0.9268 of air-dried substance, when heated for 2 hours at 105°, lost 0.0667 H_2O. $H_2O = 7.2$.

(I) 0.1291 of anhydrous substance gave 0.3652 CO_2 and 0.1201 H_2O.

(II) 0.1338 of anhydrous substance gave 0.3934 CO_2 and 0.1276 H_2O.

(I) $C = 77.1$; $H = 10.3$. (II) $C = 77.3$; $H = 10.2$.

$C_{33}H_{52}O_4,2H_2O$ requires $H_2O = 6.6$ per cent.

$C_{33}H_{52}O_4$ requires $C = 77.3$; $H = 10.1$ per cent.

As no substance of the empirical formula $C_{33}H_{52}O_4$, having the properties of this compound, has hitherto been recorded, it is proposed to designate it *micromerol*, with reference to the generic name of the plant from which it has been obtained.

Micromerol is only moderately soluble in cold, but readily in hot alcohol, and is therefore easily crystallized from this solvent. It is also moderately soluble in ethyl acetate and in acetic acid, but only sparingly so in acetone, chloroform, and benzene, while in water and in light petroleum it is insoluble. It is likewise insoluble in aqueous alkalis, but if a little micromerol be dissolved in ether, and the ethereal solution shaken with a solution of sodium hydroxide, a white, insoluble sodium compound is at once precipitated. The latter compound, however, is very unstable, being decomposed through the influence of atmospheric carbon dioxide with the liberation of the original substance. On the other hand, although the micromerol is insoluble in aqueous alkalis, it immediately passes into solution if a few drops of alcohol are added, presumably as a compound soluble in alcohol, for the addition of a drop of hydrochloric acid reprecipitates the original substance, whereas the addition of water does not throw it out of solution.

Micromerol is optically active, and its specific rotatory power was determined with the following result:

0.1609 gram of the anhydrous substance, in 50 cc. of absolute alcohol, gave α_D $+0° 22'$ in a 2 dcm. tube, whence $[\alpha]_D$ $+57.0°$.

Micromerol is an extraordinarily stable substance. When fused with potassium hydroxide at a temperature of 270–80° it may be recovered for the most part unchanged. A strong solution of chromic anhydride in acetic acid does not attack it in the cold, and only slowly on heating. A strongly alkaline solution of permanganate very gradually acts upon it in the cold. It is not altered by bromine in chloroform solution, even after heating for several hours, and, therefore, evidently contains no unsaturated linkings. The presence of one hydroxyl group in micromerol was proved by the formation of both a monoacetyl and a monomethyl derivative.

Acetylmicromerol, $C_{33}H_{51}O_4(CO.CH_3)$.—This was prepared by heating the micromerol for a short time with an excess of acetic anhydride, then distilling off the greater portion of the latter, and pouring the product into water, when it solidified immediately. Some difficulty was experienced in crystallizing the product, for it was found that alcohol, which appeared to be best adapted for this purpose, hydrolyzed it quite readily, and unless the crystallization was conducted very rapidly an impure acetyl derivative was obtained. In most of the other usual organic solvents it is extremely soluble. It was ultimately ascertained that the substance could be crystallized from light petroleum containing a small proportion of ethyl acetate, whereby all danger of hydrolysis was averted. From the latter mixture of solvents it separated in fine, colorless needles, melting at 188°.

0.0823 gave 0.2272 CO_2 and 0.0726 H_2O. $C = 75.3$; $H = 9.8$.

$C_{33}H_{51}O_4(CO.CH_3)$ requires $C = 75.8$; $H = 9.7$ per cent.

$C_{33}H_{50}O_4(CO.CH_3)_2$ requires $C = 74.5$; $H = 9.4$ per cent.

For further confirmation respecting the number of acetyl groups in this compound, a weighed quantity of it was hydrolyzed by boiling with aqueous alcohol, and the acetic distillate collected in a standard solution of alkali, which was re-titrated.

0.3261 gave an amount of acetic acid requiring 6.1 cc. N/10 NaOH for neutralization. $CH_3.CO = 8.0$.

0.3261 gave, on hydrolysis, 0.3002 of $C_{33}H_{52}O_4$. $CH_3.CO = 7.7$.

$C_{33}H_{51}O_4(CO.CH_3)$ requires $CH_3.CO = 7.8$ per cent.

The optical rotatory power of this *acetyl derivative* was determined with the following result:

0.0878 gram, dissolved in 25 cc. of chloroform, gave α_D +0° 20′ in a 2 dcm. tube, whence $[\alpha]_D$ +47.1°.

Methylmicromerol, $C_{33}H_{51}O_3.OCH_3,H_2O$.—This was prepared by heating a solution of micromerol in absolute alcohol with an excess of sodium ethoxide and methyl iodide on the water-bath under a reflux condenser. After several hours the reaction was complete, when the greater portion of the alcohol was removed by distillation, and the product poured into water. The precipitated solid was then dissolved in ether, and the ethereal solution washed a few times with strong aqueous alkali, whereby any unchanged micromerol was converted into an insoluble sodium compound, which could be removed easily by filtration. The ethereal solution was then washed with a little water, dried over calcium chloride, and the ether removed, when the methyl derivative was obtained in a practically pure state.

Methylmicromerol readily crystallizes from alcohol in clusters of thin needles, which contain water of crystallization. The substance, when air-dried, melts at 116–7°, but when rendered anhydrous it melts at 167°.

0.3897 of air-dried substance, on heating at 110° for 2 hours, lost 0.0155 H_2O. $H_2O = 4.0$

(I) 0.1918, dried at 100°, gave 0.5424 CO_2 and 0.1864 H_2O.

(II) 0.1802, dried at 100°, gave 0.5102 CO_2 and 0.1656 H_2O.

(I) $C = 77.1$; $H = 10.8$. (II) $C = 77.2$; $H = 10.2$.

$C_{33}H_{51}O_3.OCH_3,H_2O$ requires $H_2O = 3.3$ per cent.

$C_{33}H_{51}O_3.OCH_3$ requires $C = 77.6$; $H = 10.3$ per cent.

$C_{33}H_{50}O_2(OCH_3)_2$ requires $C = 77.8$; $H = 10.4$ per cent.

As the combustion of this substance affords no conclusive evidence respecting the number of methoxyl groups that have entered the molecule, this was established by a separate determination of the methoxyl, for which Perkin's modification of the Zeisel method was employed.[1]

0.2175 gave 0.0993 AgI. $CH_3O = 6.0$.

$C_{33}H_{51}O_3.OCH_3$ requires $CH_3O = 5.9$ per cent.

It may be noted in this connection that the methoxyl group was attacked only with great difficulty by the hydriodic acid, it having been found necessary to heat the mixture for 3 hours at 140° before the reaction was complete. It also follows from the above result that micromerol, $C_{33}H_{52}O_4$, contains no methoxyl group.

Methylmicromerol is readily soluble in the ordinary organic solvents, but insoluble in water.

It was finally deemed desirable to determine the molecular weight of micromerol or one of its simple derivatives, and for this purpose methylmicromerol appeared to be well adapted on account of its ready solubility in cold benzene, whereas micromerol itself is only sparingly soluble in the latter.

0.3339 of anhydrous substance in 26.5 benzene gave Δt —0.121°. M.W. = 510.

$C_{33}H_{51}O_3.OCH_3$ requires M.W. = 526.

Isolation of a New Crystalline Alcohol, Micromeritol, $C_{30}H_{44}O_2(OH)_2,2H_2O$.

The more readily soluble portion of the ether extract of the resins, which, as described under Section II, had been separated by digesting the total amount of this extract with a limited quantity of ether, was examined as follows: The ethereal liquid, which was of a dark green color,

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[1] J. Chem. Soc., 83, 1367 (1903).

was first extracted with relatively small quantities of a solution of sodium hydroxide. The first extraction removed a small amount of resinous, uncrystallizable matter, whereas the next few extracts were of an orange-yellow color, and, when acidified, yielded a brown precipitate. The latter was collected, washed, and crystallized from alcohol, from which it separated in yellow, silky needles, melting at 225°. This substance, of which about 1 gram was obtained, was found to be identical with the new phenolic compound, xanthomicrol, $C_{15}H_{12}O_6$, which had been isolated from the aqueous liquid (*A*), as previously described. After all of this yellow substance had been removed by extraction with a solution of sodium hydroxide, further treatment of the ethereal liquid with the same alkali resulted in the formation of a large quantity of an insoluble, dark green sodium compound. The latter was removed by filtration, and the treatment with alkali continued until no more solid substance separated. The ethereal liquid then contained only a small amount of a thick, pitch-like resin, from which nothing crystalline could be obtained.

The above-mentioned solid sodium compound, which amounted to nearly 50 grams, was digested with dilute sulphuric acid, when a substance was liberated which was collected on a filter at the pump and well washed with water. The solution of this substance in hot alcohol was treated with animal charcoal for the purpose of removing some green coloring matter when, after filtration, a faintly yellow liquid was obtained, which was set aside to crystallize. The first deposits from this liquid were not of a distinctly crystalline character, and melted somewhat indefinitely at about 250°. They were found, however, to contain appreciable quantities of the previously described micromerol, $C_{33}H_{52}O_4$, since by treatment with an amount of ether which was insufficient to dissolve the whole, and recrystallizing the undissolved portion from alcohol, fine colorless needles were obtained which melted at 277°, and were identical with the compound previously isolated.

The alcoholic liquid from which the above-mentioned first deposits had been removed, together with the alcoholic solution of that portion of these deposits which was more readily soluble in ether, was concentrated. A gelatinous mass was first obtained, from which a further small quantity of micromerol was isolated. The mother-liquors from this gelatinous substance were further concentrated, when, after long standing, feathery needles separated which were different in character from the previously isolated micromerol. Some difficulty was experienced in isolating this compound in a pure state on account of its being accompanied by a little amorphous, fluffy matter. It was found, however, that by allowing the substance to crystallize slowly from a dilute solution it could be obtained in well-formed crystals, and by means of a fine muslin filter these were easily separated from the amorphous impurities, which passed through the filter with the mother-liquors. The substance, after washing with a little alcohol and recrystallizing from the same solvent, was finally obtained pure. It then melted at 294-6°, when rapidly heated. On analysis it gave the following results:

0.2144 of air-dried substance, when heated for 2 hours at 110°, lost 0.0158 H_2O. $H_2O = 7.4$.

(I) 0.1623 of anhydrous substance gave 0.4537 CO_2 and 0.1488 H_2O.

(II) 0.1416 of anhydrous substance gave 0.3945 CO_2 and 0.1275 H_2O.

(I) $C = 76.2$; $H = 10.2$. (II) $C = 76.0$; $H = 10.0$.

$C_{30}H_{46}O_4$, $2H_2O$ requires $H_2O = 7.1$ per cent.

$C_{30}H_{46}O_4$ requires $C = 76.6$; $H = 9.8$ per cent.

This substance evidently possesses the empirical formula $C_{30}H_{46}O_4$, and as no substance of this formula, with the same properties, has hitherto been recorded, it must be regarded as a new compound. It is therefore proposed to designate it by the distinctive name, *micromeritol*, with reference to the botanical name of the plant from which it has been obtained.

Micromeritol is moderately soluble in cold, and readily soluble in hot alcohol, from which, on cooling, it crystallizes in clusters of fine, colorless needles. It is also readily soluble in chloroform and ethyl acetate, but only moderately soluble in benzene. In water and in light petroleum it is insoluble. It is optically active, and a determination of its specific rotatory power gave the following result:

0.0543 gram of the anhydrous substance in 25 cc. of chloroform gave α_D +0°16′ in a 2 dcm. tube, whence $[\alpha]_D$ +61.4°.

Micromeritol, in its general characters, resembles micromerol. It is, for example, insoluble in aqueous alkalis, but readily yields an unstable sodium compound on shaking an ethereal solution of the substance with aqueous sodium hydroxide. Unlike micromerol, from which it differs by the elements C_3H_6, it contains two hydroxyl groups. The latter, however, are dissimilar in character, for if the diacetyl derivative be boiled with aqueous alcohol, one of the acetyl groups is eliminated while the other remains unaffected.

A property of the above-described alcohols, which is also possessed to a greater or less extent by others of a similar character and represented by the same general formula, $C_nH_{2n-14}O_4$, is that of forming colloidal solutions. If, for example, a little micromerol, $C_{33}H_{52}O_4$, be dissolved in boiling ethyl alcohol, a little ammonia added, and the liquid heated until the alcohol and ammonia have been for the most part removed, no precipitate is produced on diluting the cooled liquid with water. This clear liquid, on being allowed to stand for about an hour, forms a perfectly transparent jelly. When, however, an aqueous solution of an electrolyte, such as ammonium chloride, is added to the liquid before it has formed a jelly, the micromerol is immediately precipitated in a flocculent form. In the case of micromeritol, $C_{30}H_{46}O_4$, a slight precipitation was produced on the addition of water and the solid separated completely in a crystalline state on allowing the liquid to stand for some time, whereas complete precipitation immediately ensued on the addition of a drop of a solution of ammonium chloride. On testing the monohydric alcohol lippianol,[1] $C_{25}H_{36}O_4$, in the same manner, it was found that on diluting the ammoniacal liquid with water a crystalline precipitate was immediately produced, and the amount of this was not increased by the addition of a solution of ammonium chloride. The alcohol, morindanol,[2] $C_{38}H_{62}O_4$, when tested under the same conditions, exhibits a behavior very similar to that of micromerol, with perhaps still less tendency to deposit the solid substance except when an electrolyte is added. The tendency to the formation of these colloidal solutions, therefore, evidently increases in proportion to the molecular weight of the substance.

Di-acetylmicromeritol, $C_{30}H_{44}O_4(CO.CH_3)_2$. — When micromeritol is subjected for a short time to the action of boiling acetic anhydride, and the solution allowed to cool, the *di-acetyl derivative* separates in long, colorless needles, which melt at 204°. It can also be crystallized from ethyl acetate or from alcohol, and separates from the latter solvent in glistening plates.

0.1611 gave 0.4350 CO_2 and 0.1312 H_2O. $C = 73.6$; $H = 9.0$.

$C_{30}H_{44}O_4(CO.CH_3)_2$ requires $C = 73.6$; $H = 9.0$ per cent.

The molecular weight of the di-acetyl derivative was determined by the cryoscopic method with the following result:

0.3308 in 21.2508 benzene gave Δt —0.15°. M.W. = 509.

$C_{30}H_{44}O_4(CO.CH_3)_2$ requires M.W. = 554.

The somewhat low result of this determination is probably due to the facility with which the di-acetyl derivative loses some of its acetic acid. It, nevertheless, suffices to show that micromeritol possesses the molecular formula assigned to it.

Mono-acetylmicromeritol, $C_{30}H_{45}O_4(CO.CH_3)$.—If di-acetyl micromeritol be boiled with aqueous alcohol for a short time it loses one acetyl group, and the solution, on cooling, deposits thin, colorless needles of a *mono-acetyl compound*, which melts with decomposition at 255°. 0.3090 of the di-acetyl derivative gave 0.2846 of the mono-acetyl compound. Loss = 7.9 per cent.

$C_{30}H_{44}O_4(CO.CH_3)_2 \rightarrow C_{30}H_{45}O_4(CO.CH_3)$ requires a loss of 7.6 per cent.

Mono-acetylmicromeritol is readily soluble in chloroform, and moderately soluble in alcohol, ethyl acetate, and benzene.

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[1] Amer. J. Pharm., **79**, 455 (1907).

[2] J. Chem. Soc., **91**, 1918 (1907).

III, IV and V. *Chloroform, Ethyl Acetate and Alcohol Extracts of the Resins.*

The portion of resin extracted by chloroform (III) was relatively small in amount, and formed a hard, black, brittle mass. It consisted of a complex mixture of amorphous substances, and, with the exception of a very small quantity of micromerol, nothing of a crystalline nature could be isolated from it.

The portions of resin extracted by ethyl acetate (IV) and alcohol (V) respectively, likewise consisted of mixtures of black, amorphous substances. They were dissolved in amyl alcohol and the solutions extracted with sodium carbonate, but nothing of a crystalline character could be separated from them.

Summary.

The results of this investigation have shown that *Micromeria Chamissonis* (Benth.) Greene (syn. *M. Douglassi*, Benth.), commonly known as "Yerba Buena," contains, in addition to some essential oil, resins, and other amorphous substances, the following compounds:

1. *Xanthomicrol*, $C_{15}H_{10}O_4(OH)_2$, a new phenolic substance, which crystallizes in fine, lemon-yellow needles, melting at 225°. It yields a *di-acetyl derivative*, $C_{15}H_{10}O_6(CO.CH_3)_2$, which crystallizes in pale yellow needles, melting at 116°.

The amount of xanthomicrol obtained corresponds to about 0.02 per cent. of the weight of air-dried plant.

2. *Micromerol*, $C_{33}H_{51}O_3-OH,2H_2O$, a new monohydric alcohol, which crystallizes in fine, colorless needles, melting at 277°. It is optically active, having $[\alpha]_D +57°$. Its *acetyl derivative*, $C_{33}H_{51}O_4(CO.CH_3)$, forms colorless needles, which melt at 188° and have $[\alpha]_D +47.1°$. Its *methyl derivative*, $C_{33}H_{51}O_3.OCH_3,H_2O$, crystallizes in thin needles, which melt at 116-7° or, when anhydrous, at 167°.

The amount of micromerol obtained corresponds to about 0.25 per cent. of the weight of air-dried plant.

3. *Micromeritol*, $C_{30}H_{44}O_2(OH)_2,2H_2O$, a new dihydric alcohol, which crystallizes in fine, colorless needles, melting at 294-6°. It is optically active, having $[\alpha]_D +61.4°$. Its *di-acetyl derivative*, $C_{30}H_{44}O_4(CO.CH_3)_2$, and *mono-acetyl derivative*, $C_{30}H_{45}O_4(CO.CH_3)$, form colorless needles, which melt respectively at 204° and 255°.

The amount of micromeritol obtained corresponds to about 0.05 per cent. of the weight of air-dried plant.

4. Hentriacontane, $C_{31}H_{64}$ (m. p. 66-7°), about 0.05 per cent., with apparently a very small amount of pentatriacontane.

5. A Phytosterol, $C_{27}H_{46}O,H_2O$ (m. p. 135°), in small amount.

6. Glycerides of palmitic, arachidic, and behenic acids.

7. Formic, acetic, and butyric acids in a free state.

8. Glucose (phenylglucosazone, m. p. 217°), a considerable amount.

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.