

isolated and some of its physical properties determined. It has been given the name "Carnosol."

7. A wax and a resin have been isolated from extractives of the plant.

8. A volatile oil has been isolated by steam distillation of the leaves of *Salvia carnososa* (Dougl.). The usual physical and chemical constants have been determined and the oil separated by fractional distillation into eight fractions.

9. It has been established that the three lots of *Salvia carnososa* (Dougl.) examined differed greatly in their content of volatile oil and carnosol.

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Salvia Carnosa (Dougl.). II—Carnosol*

By Allen I. White† and Glenn L. Jenkins‡

In a previous paper (1) the authors reported the isolation of a new crystalline compound from *Salvia carnososa* (Dougl.). This compound, called carnosol, crystallizes in white, odorless, long needles and has a melting point of 219.5° C. (uncorr.) with decomposition. It has a specific rotation of -66.00° and is soluble in ethanol, methanol, ether and chloroform, and is slightly soluble in petroleum benzin. When placed in dilute alkali, carnosol dissolves and the solution undergoes a color change from a beginning orange-red to a deep brown to blue-black. It is also soluble in concentrated sulfuric acid, producing a yellow color. Carnosol is insoluble in water, dilute hydrochloric acid and a 5% solution of sodium bicarbonate.

This paper reports the investigations made concerning the chemical nature of this new

* Abstracted from a part of the thesis presented to the Graduate Faculty of the University of Minnesota by Allen I. White in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

This is a report in a cooperative research project connected with the Indian Medicinal Plant study of the Bureau of Plant Industry, United States Department of Agriculture.

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compound which is of special interest because of the possibility that it is responsible for the bacteriological activity of extracts from which carnosol is obtained (1). Because of the insolubility in culture media of free carnosol and because of its apparent decomposition in alkali, it has been impossible to determine whether it has bacteriological activity or not.¹ It is hoped that an understanding of the chemical nature of carnosol will make it possible to prepare derivatives suitable for further bacteriological study.

EXPERIMENTAL

Reaction Tests.—A 0.1% solution of carnosol in chloroform slowly and incompletely decolorized a few drops of a 1% solution of bromine in chloroform. However, when a 2% solution of potassium permanganate in acetone was added to a 1% solution of carnosol in acetone, rapid decoloration of the permanganate with production of considerable manganese dioxide occurred. When 0.1 Gm. of carnosol was dissolved in 5 cc. of hot ethanol and 0.1 Gm. of phenylhydrazine added, no cloudiness or precipitate formed upon cooling, dilution or standing. When a drop of ferric chloride test solution was added to a 0.1% solution of carnosol in ethanol, a deep brilliant green color was produced.

¹ The bacteriological tests were conducted by Dr. R. N. Bieter, Dr. W. P. Larson, Charles H. Drake and J. Gordon Beaton of the School of Medicine, University of Minnesota.

Analysis.—Using the usual sodium decomposition procedure, it was found that carnosol did not contain sulfur, nitrogen or halogens. Using the Rast camphor method, carnosol showed a molecular weight of 306.45. Calculated for $C_{19}H_{26}O_4$: 318.21. Ultimate analysis by the combustion method gave the following results: calculated for $C_{19}H_{26}O_4$: C = 71.65%, H = 8.24%; found: C = 71.90%, H = 8.07%. An alkoxyl determination employing the technique of Viebock and Schwappach as outlined by Clark (2) showed no alkoxyl group present. In an attempt to determine the saponification equivalent of carnosol it was found impossible to carry out the necessary titration and obtain an accurate result because of the reaction of the compound to alkaline solutions with the formation of a deep dark green to black color.

Bromination.—In a large test-tube, 0.5 Gm. of the crystals was dissolved in 20 cc. of hot glacial acetic acid and 1.5 cc. of liquid bromine were added. The mixture was allowed to stand for one hour during which no appreciable diminution in the intensity of the bromine color could be observed. The mixture was poured into 100 cc. of ice water and the resulting precipitate was filtered off. It was impossible to obtain a crystalline product from dilute ethanol, but by dissolving the precipitate in a small amount of warm glacial acetic acid and diluting with warm water to the point of incipient cloudiness, crystals were obtained. They were further purified by crystallization from anhydrous ether several times. A very small yield of well-defined, rectangular, greenish brown crystals was obtained. Melting point, 189–190° C. (uncorr.).

Hydrogenation.—In a pressure bottle, 0.2 Gm. of carnosol was dissolved in 30 cc. of absolute ethanol and a small amount of platinum black was washed in with an additional 20 cc. of absolute ethanol. The mixture was shaken with hydrogen for one hour at room temperature under a pressure of 41 lbs. per sq. in. The catalyst was filtered off and the solution concentrated to 20 cc., warm water added to the point of incipient cloudiness, and the material allowed to crystallize. Melting point, 219–220° C. (uncorr.) with decomposition. Browning began at 190° C. Mixed melting point with original crystals, 219° C. (uncorr.) with decomposition. Conclusion: No hydrogenation took place.

Methylation.—In a 250-cc. Erlenmeyer flask, a dry ethereal solution of diazomethane prepared from 6.9 Gm. of *n*-nitroso methyl urea (3) was added to one-hundredth of a mole (3.18 Gm.) of the crystals dissolved in a mixture of 50 cc. of anhydrous ether and 20 cc. of anhydrous methanol cooled in an ice bath to 0° C. The flask was fitted with a calcium chloride tube, and after one hour in the ice bath it was kept at 5° C. in a refrigerator for 48 hours. At the beginning of the reaction, considerable escaping gas was observed but quickly decreased to a slow evolution. At the end of the period, the solution was poured into an evaporating dish and allowed to evaporate spontaneously to approximately 15 cc.

It was then cooled in an ice-salt bath, crystals forming. Four recrystallizations from dilute ethanol produced white platelets having a melting point of 152.5–153.5° C. (uncorr.). Yield, 1.4 Gm. (40.58%). The compound was soluble in ethanol, methanol and ether. It was insoluble in water and 10% sodium hydroxide. An alcoholic solution gave no color reaction when treated with ferric chloride test solution. Calculated for $C_{21}H_{30}O_4$: C = 72.78%, H = 8.73%; found: C = 72.98%, H = 9.08%. Methoxyl determination (2) of methylated carnosol showed the following results: calculated for $C_{21}H_{30}O_4$ (two OCH_3): 17.92%; found: 17.94%. Calculation of molecular weight from the per cent of radical found: 345.82; calculated for $C_{21}H_{30}O_4$: 346.24. By calculation, the molecular weight of carnosol would be 317.79. From these molecular weight determinations and the ultimate analyses, it is justifiable to assign the molecular formula of $C_{19}H_{26}O_4$ to carnosol and $C_{21}H_{30}O_4$ to its methylated derivative.

Saponification of Methylated Carnosol.—Since the difficulty encountered in saponification of carnosol was believed due to phenolic groups present, saponification of the methylated derivative was undertaken in the belief that this difficulty could here be avoided. The saponification equivalent as determined using an ethanolic sodium hydroxide solution was 334.41. Calculated for $C_{21}H_{30}O_4$: 346.24. The reaction mixture was then examined for an acidic saponification product as follows: The solution was made alkaline to phenolphthalein with dilute sodium hydroxide, and after the addition of 10 cc. of water, the ethanol was evaporated from the solution on a steam bath. The solution was then made acid by the addition of a few drops of dilute hydrochloric acid and a flocculent white precipitate resulted. It was removed by filtration and washed with ice water until the filtrate was acid-free to litmus. Attempts to crystallize this amorphous precipitate from dilute ethanol, benzol-petroleum benzine, dilute methanol and ether were unsuccessful. The potassium salt of the acid was readily and successfully crystallized by making an alcoholic solution of the acid alkaline with dilute potassium hydroxide and cooling the resulting solution. Fine white needles resulted. The amorphous precipitate of the free acid melted over a range of 140–160° C. The yield was 70 mg. An alcoholic solution gave no color reaction when treated with ferric chloride test solution.

An attempt to acetylate 0.1 Gm. of methylated carnosol using 2 cc. of acetic anhydride with 0.05 Gm. of fused sodium acetate was unsuccessful, indicating the methylated compound contained no free OH group.

Acetylation.—One gram of carnosol was mixed with 0.5 Gm. of powdered fused sodium acetate and 5 cc. of acetic anhydride and refluxed on a steam bath, with occasional shaking for two hours. The hot solution was then poured into ice water and allowed to stand in a refrigerator for four hours.

The solid material which had formed was collected and recrystallized four times from dilute ethanol. After drying for 24 hours in a sulfuric acid desiccator, the melting point was 165–166° C. (uncorr.). The yield was 1.03 Gm. (81.7%). An alcoholic solution gave no color reaction when treated with ferric chloride test solution. Calculated for $C_{22}H_{30}O_6$: C = 68.61%, H = 7.52%; found: C = 68.37%, H = 7.84%.

An acetyl determination was made in the following manner: Exactly 0.0992 Gm. of the compound was placed in a 250-cc. round-bottom flask and 25 cc. of approximately 0.1*N* alcoholic potassium hydroxide were added. The solution was refluxed for one hour over a small flame. The solution was then cooled and made acid with dilute sulfuric acid. Sufficient water was then added to make a volume of approximately 200 cc. The solution was carefully distilled over a low flame into exactly 50 cc. of 0.02*N* sodium hydroxide until approximately 50 cc. remained in the distillation flask. During the distillation, the adaptor dipped slightly into the sodium hydroxide solution. The sodium hydroxide solution was then titrated using a micro burette with 0.02*N* hydrochloric acid, using phenolphthalein as the indicator. Calculated for two CH_3CO groups in $C_{22}H_{30}O_6$: 21.38%; found: 20.81%.

Benzoylation.—One gram of carnosol was dissolved in 3 cc. of pyridine and 1 cc. of benzoyl chloride added. The solution was refluxed for one-half hour over a small flame after which it was poured with vigorous stirring into 10 cc. of ice water. The precipitate which formed was washed with 5 cc. of a 5% sodium carbonate solution and recrystallized four times from dilute ethanol. After drying for 24 hours in a sulfuric acid desiccator, the melting point was 172° C. (uncorr.). Yield, 1.44 Gm. or 87.27%. An alcoholic solution gave no color reaction when treated with ferric chloride test solution. Calculated for $C_{22}H_{30}O_6$: C = 75.25%, H = 6.51%; found: C = 75.20%, H = 6.87%.

Vacuum Sublimation.—Seventeen-hundredths gram of carnosol was subjected to vacuum sublimation for four hours at a temperature of 200° C. and a partial pressure of 3 mm. of mercury. In that period of time, 0.06 Gm. of an amorphous sublimate was collected. It had a light tan color mixed with white, indicating some decomposition. Recrystallization of the sublimate from dilute ethanol gave crystals having a melting point of 219° C. (uncorr.) and which caused no depression of the melting point when mixed with carnosol. An alcoholic solution gave the characteristic green color reaction when treated with ferric chloride test solution. The un-sublimed residue amounted to 0.10 Gm. and tests showed it to be unchanged carnosol. Thus, carnosol is slowly sublimable under reduced pressure with some slight decomposition.

Saponification.—One gram of carnosol was refluxed for six hours with 25 cc. of 25% aqueous potassium hydroxide. The alkaline solution was then carefully and slowly distilled until 5 cc. of distillate

had been collected. Difficulty was encountered in the distillation due to excessive frothing. The distillate was divided into two portions, one of 2 cc. and one of 3 cc.

The 2-cc. portion was used for an attempted fractionation on a semi-micro scale according to the procedure of Emich (4). Three fractions were obtained and gave the following boiling points at 730-mm. pressure using the procedure given by Emich (4).

Fraction	B. P., ° C.
1	83.0
2	91.5
3	93.0

The 3-cc. portion was used in an unsuccessful attempt to make a derivative with 3,5-dinitrobenzoyl chloride.

The alkaline reaction mixture which remained after distillation was examined by extracting with ether while alkaline and then making acid and extracting with ether. Both extractions produced uncrystallizable resinous extracts which gave green colors characteristic of carnosol when tested in ethanolic solutions with ferric chloride test solution. The presence of an alcohol with a boiling point below 100° C. as the neutral saponification product is indicated but not confirmed.

Permanganate Oxidation.—1. *In neutral acetone:* The procedure as outlined by Adams, Hunt and Clark (5) for the oxidation of tetrahydrocannabidiol was adopted. In a three-necked one-liter flask equipped with a mechanical stirrer, dropping funnel and reflux condenser, a solution of 5 Gm. of potassium permanganate in 250 cc. of acetone was added over a two-hour period to 1 Gm. of carnosol in 50 cc. of acetone. The reaction was begun at room temperature but at the end of 30 minutes a small flame was applied to speed up the reaction. At the end of this period, the solution retained the characteristic permanganate color. The solution was made acid with sulfuric acid and the excess manganese dioxide and permanganate were destroyed by the addition of sodium bisulfite. The clear, pale yellow solution was diluted with 50 cc. of water and the acetone distilled off. The remaining aqueous solution was extracted with three successive 25-cc. portions of ether and the ether solution in turn extracted with two successive 15-cc. portions of 5% sodium bicarbonate solution. The bicarbonate layer was acidified with sulfuric acid, a slight cloudiness occurring. The acidified solution was extracted with ether and the ethereal solution dried for 12 hours over anhydrous sodium sulfate. Spontaneous evaporation of the ethereal solution produced a light brown residue having a pungent, acrid odor. Yield, 0.24 Gm. The ether solution containing the sodium bicarbonate insoluble material was washed twice with water, passed through a dry filter, and allowed to evaporate spontaneously. A reddish brown residue having a slight aromatic odor but giving no color reaction with ferric chloride solution was deposited. Yield, 0.47 Gm. Attempts to crystallize both fragments

were unsuccessful. Attempts to prepare a solid derivative with *p*-nitro benzyl bromide according to the procedure of Lyons and Reid (6) and an anilide according to the procedure outlined by Kamm (7) of the sodium bicarbonate fraction were unsuccessful.

2. *Alkaline oxidation in water:* To 1 Gm. of carnosol in a three-necked one-liter flask equipped with a mechanical stirrer, reflux condenser and dropping funnel, was added gradually a 2% aqueous solution of potassium permanganate and the solution boiled over a low flame. After the addition of the first 25 cc. of the permanganate solution, 10 cc. of 10% sodium hydroxide solution were added. The addition of the permanganate solution was then continued at such a speed that the solution maintained its characteristic color. At the end of 60 minutes, approximately 6 Gm. of potassium permanganate had been consumed and the solution did not decolorize. After cooling, the manganese dioxide formed was removed and washed on a Büchner funnel and the filtrate concentrated to 10 cc. The solution was then made acid with 10% sulfuric acid, a slight cloudiness occurring. No product could be obtained from this solution even when cooled to -20° C. in an ice-salt bath. The solution had a strong, disagreeable odor.

The manganese dioxide precipitate was washed with four 20-cc. portions of ether which were combined and evaporated to dryness. A small amount of a yellowish green oil which could not be crystallized was obtained.

Zinc Dust Distillation.—Using the procedure of Clar (8), the following distillation was carried out: In a 50-cc. Pyrex distilling flask equipped with a mechanical stirrer and air condenser and resting in a Wood's metal bath, 3 Gm. of carnosol, 3 Gm. of sodium chloride, 15 Gm. of fused zinc chloride and 10 Gm. of zinc dust were brought to fusion. The temperature of the bath was slowly raised from 220° to 320° C. as a yellow, oily distillate having a light blue fluorescence was collected. The distillate was washed from the condenser by means of a small amount of anhydrous ether and the ether evaporated. Yield, 1.25 Gm. A dilute alcoholic solution of the distillate had a beautiful blue fluorescence and did not give any color reaction when treated with ferric chloride test solution. It could not be crystallized, even at low temperatures, from ethanol, dilute ethanol or ether, but was purified and dried by distillation over sodium. It was found to be soluble in ethanol, ether and chloroform, and insoluble in water, sodium hydroxide, dilute hydrochloric acid and concentrated sulfuric acid. When 0.05 Gm. of the distillate was dissolved in 2 cc. of chloroform and a drop of bromine in chloroform was added the bromine was not decolorized in five minutes. When 0.05 Gm. was dissolved in 2 cc. of acetone and 2 drops of a 2% solution of potassium permanganate were added, a slight but slow decoloration of the solution occurred at the end of three minutes. An attempt to make a picrate using the procedure suggested by Kamm (9) was unsuccessful. Boiling

point, $298-300^{\circ}$ C. $n_D^{25} = 1.5584$. Calculated for $C_{14}H_{18}$: C = 90.26%, H = 9.74%; found: C = 90.08%, H = 9.50%.

Sulfur Dehydrogenation of the Zinc Dust Distillate.—Dehydrogenation of the zinc dust distillate was carried out in the following manner: Twenty-five hundredths gram of the distillate and 0.16 Gm. of sulfur were put in a small Pyrex tube and a Pyrex air condenser fused onto it. The mixture was heated for six hours at 140° C. and then for 18 hours at 180° C. in an oil bath. Hydrogen sulfide was continuously evolved during that period. After allowing to cool, the Pyrex tube containing the black reaction mixture was crushed and the residue extracted with ether. This solution, which showed a pale blue fluorescence, produced a small amount of crystalline material upon evaporation. Recrystallization five times from small amounts of ethanol gave a product (0.06 Gm.) having a melting point of 97° C. A mixed melting point with a known sample of phenanthrene (m. p., $97.5-98.5^{\circ}$ C.) showed no depression. A picrate made in alcoholic solution produced orange-red crystals which after drying at 100° C. for 15 minutes gave a melting point of 140° C. A mixed melting point with the picrate of a known sample of phenanthrene (m. p., 141° C.) showed no depression. From these results it is concluded that the sulfur dehydrogenation product of the zinc dust distillation of carnosol is phenanthrene.

Dehydrogenation in a similar manner using selenium metal in place of sulfur produced too small an amount of crystalline material for characterization.

Pyrolysis.—To determine whether the zinc dust distillate obtained above might be a product of simple pyrolysis of carnosol, the following experiment was carried out: In a small Pyrex tube to which had been attached a distilling arm, 0.2 Gm. of carnosol was heated with a naked flame from a micro burner. The compound melted and changed into a red liquid which bubbled rapidly as the heating continued. A light red oil distilled and, upon cooling, changed into a viscous and stringy resin. A small carbonaceous residue remained in the distilling flask.

The resin-like distillate was dissolved with some difficulty in a small amount of boiling ethanol. A small portion of the solution gave no color test with ferric chloride test solution. To the remainder of the warm solution warm water was added to the point of incipient cloudiness and then placed in the refrigerator over night. A small amount of crystalline material was collected and purified by boiling with charcoal in alcohol and recrystallizing twice from dilute ethanol. The white needle crystals obtained melted at $160-162^{\circ}$ C. (uncorr.). They were insoluble in 10% sodium hydroxide but soluble in concentrated sulfuric acid, causing a deep yellow coloration. No further investigation of their nature was made.

Since it was considered possible that the gas given off when carnosol was liquefied might be carbon dioxide, the following experiment was performed: 50

mg. of carnosol were placed in a porcelain boat inside a Pyrex tube, one end of which was connected to an oxygen tank; the other end was fitted with a small glass tube which dipped into a solution of calcium hydroxide. The air was first removed from the tube by passing through oxygen until the lime water showed no precipitation. Then the tube was dipped into a fresh solution of calcium hydroxide and, while continuing the passage of oxygen through the tube, the boat was slowly heated until the crystals melted and then held at that temperature while the resulting liquid bubbled. The flow of oxygen was continued through the tube for five minutes, but no cloudiness could be observed in the solution of calcium hydroxide. Thus, the gas given off by the pyrolysis of carnosol is not carbon dioxide.

DISCUSSION

The new organic compound, carnosol, which had been isolated from *Salvia carnosia* (Dougl.) has been assigned the molecular formula, $C_{19}H_{26}O_4$. The molecular weight as determined by the Rast method and the methoxyl determination of the methylated derivative is satisfied by this formula. The results obtained by ultimate analysis of the original compound as well as of the methylated, acetylated and benzoylated derivatives also confirmed this formula.

The presence of phenolic OH groups in carnosol was suggested by the reaction of the compound to ferric chloride test solution and its solubility and oxidation in sodium hydroxide. Methylation of carnosol with diazomethane and the determination of the methoxyl added indicated that two of the four oxygens in the compound exist in phenolic OH groups. The presence of two OH groups was confirmed by the acetyl determination of the acetylated compound. That the two OH groups acetylated are the same as the two methylated was shown by the fact that the methylated compound could not be acetylated. Although alcoholic OH groups are acetylated as well as phenolic OH groups, diazomethane does not methylate alcoholic OH groups but readily methylates phenolic OH groups. Since a methoxyl determination on the unmethylated carnosol showed that it contained no methoxyl group, the value obtained from the methylated compound must be due only to groups added by diazomethane. From these facts it was concluded that the two oxygens present in OH groups are both phenolic OH groups.

Because of the oxidation of carnosol in alkaline solutions, saponification and acidity determinations could not be made on it. However, the fact that the compound was insoluble in 5% sodium bicarbonate solution indicated that no free carboxyl group was present. This was further borne out by the insolubility of the methylated compound in sodium hydroxide. The determination of the saponification equivalent of the methylated compound demonstrated the presence of an ester. This ester could be the result of methylation of a carboxyl group by diazomethane. A methyl ester and one methoxyl group would give the results obtained in the methoxyl determination. However, if this were so, the diacetate which has been shown to be formed by acetylation of carnosol must be formed on one phenolic OH group and one alcoholic OH group. The acetylation of an acid group could take place to form an anhydride, but, under the conditions of the experiment, the anhydride would be decomposed to form its component acids. The fact that there is no alcoholic OH group present has been previously shown. The evidence indicates that the ester shown to be present in the methylated compound is part of the original compound and has not been formed by methylation. The isolation of an unidentified amorphous acidic product which forms a crystalline potassium salt from the saponification of the methylated compound and the indication that a neutral product results from the saponification of carnosol, support this evidence.

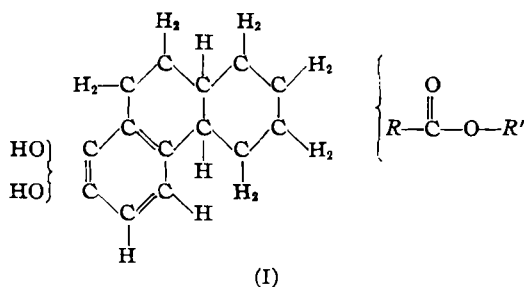
The identification of phenanthrene as the product of the sulfur dehydrogenation of the zinc dust distillate indicated that the distillate was a partially saturated phenanthrene. Ultimate analysis of the zinc dust distillate showed that it conformed to the formula $C_{14}H_{18}$. Such a hydrocarbon could be an octahydrophenanthrene. Phenanthrene has been obtained from 1,2,3,4,9,10,11,12-octahydrophenanthrene by dehydrogenation with sulfur by Fulton and Robinson (10). Further evidence that the zinc dust distillate might be an octahydrophenanthrene is contributed by its physical properties. The zinc dust distillate of carnosol boiled

at 298–300° C. Ipatieff (11) reported the boiling point of the octahydrophenanthrene which he obtained by the hydrogenation of phenanthrene to be 290–300° C. Bardhan and Sengupta (12) reported the boiling point of the 1,2,3,4,9,10,11,12-octahydrophenanthrene which they obtained synthetically to be 135° C. at 9 mm. of pressure. They also reported these other properties of their synthetic product: $n_D^{32} = 1.548575$, stable to potassium permanganate, and no decoloration of bromine in chloroform. Cook and Hewett (13) reported the 1,2,3,4,9,10,11,12-octahydrophenanthrene which they obtained synthetically was an oil which absorbed no bromine, had a boiling point of 159° C. at 15-mm. pressure, and a refractive index of $n_D^{15.2} = 1.5527$. The zinc dust distillate of carnosol gave a refractive index of $n_D^{25} = 1.5584$, absorbed no bromine, and apparently was stable to potassium permanganate. Berge, *et al.* (14), reported the 1,2,3,4,9,10,11,12-octahydrophenanthrene which they obtained synthetically to be a yellowish oil which showed a brilliant light blue fluorescence in solution. The physical properties of their product conformed to those reported above. The zinc dust distillate of carnosol showed a light blue fluorescence in solution. It also formed no picrate which conforms to the evidence of Schmidt and Mezger (15) observed on the octahydrophenanthrene they obtained by hydrogenation of phenanthrene.

Since no potassium permanganate oxidation product has been obtained to substantiate the above evidence, the presence of an octahydrophenanthrene structure in carnosol cannot be conclusively stated. Further, since the phenanthrene isolated was obtained as a result of degradation reactions which may have caused the formation of phenanthrene by dehydration and ring closure as well as dehydrogenation, the presence of an octahydrophenanthrene nucleus in carnosol can only be said to be indicated. However, based upon the experimental evidence found, (I) is tentatively proposed as the partial structural formula for carnosol.

Of the atoms in the molecular formula $C_{19}H_{26}O_4$, fifteen carbon atoms, eighteen

hydrogen atoms and the four oxygen atoms are accounted for. It is possible that the remaining four carbon atoms and eight hydrogen atoms are in the ester side chain. No evidence as to the position of the carboxyl group has been established and no values for R and R' in formula (I) are postulated.



SUMMARY AND CONCLUSIONS

The following facts relative to the chemistry of the new compound, carnosol, isolated from *Salvia carnosia* (Dougl.) have been established:

1. The usual physical and chemical properties have been determined.
2. The molecular formula, $C_{19}H_{26}O_4$, has been assigned to this compound as a result of molecular weight determinations and ultimate analyses.
3. Methyl, acetyl and benzoyl derivatives have been made and characterized.
4. It has been established that the compound contains two phenolic OH groups.
5. It has been established also that the compound contains one ester group.
6. Phenanthrene has been obtained from the compound by zinc dust distillation followed by sulfur dehydrogenation.
7. A tentative partial structural formula has been proposed for the new compound.

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The Action of Some Organo-Mercurials and Some Copper Salts on Ringworm Fungi*

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Comparative studies have been made relating chemical structure to bactericidal activity, particularly in the phenol series (1, 2). In most cases, investigators have observed a close relationship between bactericidal and fungicidal activity.

Copper and its salts possess bactericidal action (3). The successful use of copper salts as fungicides in the control of plant fungi has prompted the study of these compounds as possible effective agents in the treatment of the dermatoses. Copper deposited on the skin by iontophoresis has been used with apparent success in the treatment of "athlete's foot." Copper sulfate is reported to have given good results in the treatment of skin Aspergilliosis (4). Copper and its salts have, however, proved themselves weak fungicides on the basis of laboratory evaluation against pathogenic fungi (5).

Certain aromatic organic acids, particularly salicylic and benzoic, are employed with favorable results in the treatment of mycoses of the hands and feet. Hence, it appeared logical to investigate the fungicidal properties of a combination of the metal with the acids, that is, copper salicylate and benzoate. The effect of copper

salicylate, copper benzoate, salicylic acid and benzoic acid in inhibiting spore suspensions of two organisms commonly associated with fungous diseases of the skin is presented in Table I.

Table I.—Fungicidal-Static Activity of Two Organic Copper Salts

Compound	Highest Dilutions of Agents Effective in Inhibiting Growth in 10 Minutes	
	<i>E. interdigitale</i>	<i>A. gypsum</i>
Copper benzoate	1:40	..
Suspension 1:20		
Copper salicylate	1:300	..
Suspension 1:100		
Benzoic acid	1:400	..
Suspension 1:50		
Salicylic acid	1:700	..
Suspension 1:50		
Copper benzoate	1:300	1:450
1:50 in dioxane		
Copper salicylate	1:600	1:800
1:50 in 50% dioxane		
Benzoic acid	1:500	1:700
1:50 in dioxane		
Salicylic acid	1:1500	1:2500
1:100 in 50% dioxane		
Dioxane	No inhibition of growth with 15% dioxane	

In the field of organic mercurials there are also indications of a parallelism between bactericidal and fungicidal activity, although there are many exceptions. In the present investigation, the primary object was to compare the chlorophenylmercuric chlorides with the corresponding fluorophenyl derivatives and to observe the effect of position isomerism. In Table II are summarized the activities of six aromatic mercurials toward two strains of pathogenic fungi.

* Presented to the Scientific Section of the A. P. H. A., Detroit meeting, 1941.

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