

the use of his laboratory facilities and for his helpful suggestions, and to Dr. Alpheus W. Smith for his support of this work.

Summary

Transmission curves for several different concentrations of methyl alcohol in nitrobenzene are given for the region 2.5 to 3.7 μ , and the effects of nitrobenzene on the OH band are compared with those of other solvents. The effects of hydrogen bonding on the OH band are discussed.

A study has been made of mixtures of water with methyl cyanide, and previous work on di-

oxane-water mixtures has been extended to longer wave lengths.

Evidence for the formation of deuterium bonds between deuterium oxide and acetone and between deuterium oxide and dioxane has been obtained from observations of the spectra of mixtures of these liquids.

Chloroform has been found to produce shifts to lower frequencies of certain bands of acetone, ethyl acetate, ethyl ether and dioxane. The possibility of the formation of hydrogen bonds between chloroform and these liquids is discussed.

COLUMBUS, OHIO

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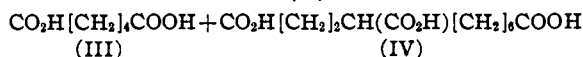
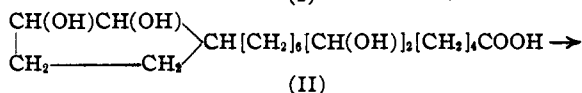
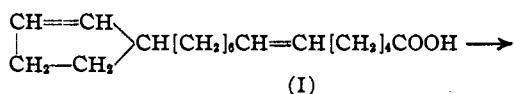
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Isolation and Properties of Gorlic Acid, an Optically Active Liquid Fatty Acid

BY HOWARD IRVING COLE AND HUMBERTO T. CARDOSO

In the course of analyzing chaulmoogra oils, several investigators have mentioned a liquid fatty acid fraction apparently containing an optically active fatty acid with a high iodine number, indicating the presence of two double bonds. Thus Dean and Wrenshall¹ obtained from a "chaulmoogra oil" a liquid acid having the constants shown in Table I. It gave no solid bromide and yielded dihydrochaulmoogric acid upon hydrogenation. They concluded that an acid $C_{18}H_{30}O_2$, corresponding to chaulmoogric acid but with a second double bond located in the side chain, was present. In 1928 André and Jouatte² reported the presence of an acid with similar characteristics in *Oncoba echinata* oil (Table I) and although they were unable to purify it completely they named it gorlic acid after the native name for *O. echinata* oil, "Gorli" oil. Recently Paget³ found in *Carpotroche brasiliensis* (sapucainha) oil a liquid fatty acid which he named dehydrochaulmoogric acid and which he showed was similar to that obtained by Dean and Wrenshall. He makes no reference to the gorlic acid of André and Jouatte. Although he also did not obtain it pure (Table I) he was able to characterize it definitely by means of its hydrogenation and oxidation products as an acid corresponding to chaulmoogric acid with one extra double bond located in the side chain be-

tween the fifth and sixth carbon atoms (formula I). Its relation to chaulmoogric acid was proved by the fact that dihydrochaulmoogric acid was obtained upon hydrogenation. The position of the second double bond in the side chain was shown by the fact that oxidation with permanganate yielded a tetrahydroxydihydrochaulmoogric acid (II)



and that this was oxidized rapidly by cold Beckmann's chromic acid mixture to adipic acid (III) and a tribasic acid, *n*-nonane- α, α', γ -tricarboxylic acid (IV).

TABLE I

COMPARISON OF CONSTANTS OF OPTICALLY ACTIVE LIQUID FATTY ACIDS FOUND IN CHAULMOOGRA OILS

Source of oil	Dean and Wrenshall	André and Jouatte	Paget	Cole and Cardoso
	Commercial chaulmoogra	<i>Oncoba echinata</i>	<i>C. brasiliensis</i>	<i>C. brasil. and O. echinata</i>
Sp. gr. 25/25	0.9322	0.9364 ¹³	...	0.9436
Ref. index, n_D^{25}	1.4745	1.4783	...	1.4782
Sp. rotation, $[\alpha]_D^{25}$	+53.1	+50.3	+45	+60.7
B. p. (10 mm.), °C.	232.5
M. p., °C.	Below 5	6
Acid value	201.2	198	201.8
Mol. wt.	278.9	277.8
Iodine no. (Hanus)	180.4 (Hubl)	169.6	138	179.7

(1) Dean and Wrenshall, *THIS JOURNAL*, **42**, 2626 (1920); *U. S. Pub. Health Reports, Bull.*, **141**, 15 (1924).

(2) André and Jouatte, *Bull. soc. chim.*, **43**, 347 (1928).

(3) Paget, *J. Chem. Soc.*, 955 (1937).

The purification of gorlic acid was made more difficult by the presence of another liquid acid, oleic. Furthermore, both André and Paget state that the acid and esters tend to decompose when distilled even at low pressures. Both the acid and the methyl and ethyl esters boil within a few degrees of oleic and chaulmoogric acids and esters as shown in Table II. All attempts to purify it

TABLE II

COMPARISON OF BOILING POINTS OF OLEIC, GORLIC AND CHAULMOOGRIC ACIDS AND ETHYL ESTERS

Compound	M. p., °C.	B. p. (10 mm.), °C.	Ethyl ester B. p., °C.
Oleic acid	14	223	209
Gorlic acid	6	232.5	214
Chaulmoogric acid	68.5	247 (20 mm.)	222

by the lead salt-ether and fractional crystallization methods or by fractional distillation of the acid met with failure. The latter might be possible except for the fact that about 20% decomposes each time it is distilled at 10 mm. pressure. However, we have been able to isolate this acid in the pure state from both *C. brasiliensis* and *O. echinata* oils by the method to be described below and have determined its constants as well as those of its methyl and ethyl esters. As we find that this acid is identical with that mentioned by André and Jouatte, who named it gorlic acid in 1928, we have adhered to this name.

Gorlic acid is a colorless, practically odorless and tasteless liquid fatty acid exhibiting a high optical activity. Its structure is the same as that of chaulmoogric acid except for the addition of one extra double bond (and hence contains two less hydrogen atoms) as shown in formula I. It is not as stable as chaulmoogric or even hydnocarpic acid. Its methyl and ethyl esters are more stable than the free acid. In the pure state the acid has not the sharp taste mentioned by André. The methyl and ethyl esters are colorless liquids with only a slight ethereal odor.

TABLE III

CONSTANTS OF PURE GORLIC ACID, METHYL AND ETHYL GORLATES

	Gorlic acid	Methyl gorlate	Ethyl gorlate
Specific gravity 25/25	0.9436	0.9228	0.9119
Refractive index, n_D^{25}	1.4782	1.4688	1.4667
Specific rotation $[\alpha]_D^{25}$	+60.7	+57.7	+55.4
B. p. (10 mm.), °C.	232.5	209	214
M. p., °C.	6	Below -10	Below -10
Molecular weight, calcd	278.2		
Molecular weight, found	277.8		
Iodine no., calcd.	182.6	178.8	165.7
Iodine no. (Hanus), found	179.7	172.8	166.2

The other characteristics of the acid and esters are given in Table III.

Method of Separation

The fatty acids of *C. brasiliensis* or *O. echinata* oil were liberated in the usual manner. After washing free of mineral acid, they were dissolved in four volumes of 80% ethyl alcohol and allowed to stand at 0° in a refrigerator overnight, then separated by filtration in a Büchner funnel. The solid acids were redissolved, recrystallized and again filtered in the same manner. The two mother liquors were combined and most of the alcohol boiled off. To change any ethyl esters formed in the above operations into acids, the mixture was resaponified and the fatty acids liberated and washed. To remove as much as possible of the solid acids remaining in solution in this liquid acid fraction, the latter was dissolved in two volumes of 80% alcohol and kept at -10° in an electric refrigerator ice compartment for two or three days and then filtered. The liquid acids were freed from the mother liquor by dilution, washed and dried. Yields of liquid acids were: *C. brasiliensis*, 25.2%; *O. echinata*, 20.8%. The liquid acids were esterified by boiling for three hours with two volumes of absolute ethyl alcohol and 3% of concentrated sulfuric acid. The esters were separated by dilution and washed. Two volumes of ether was added and free fatty acid removed by a 10% solution of sodium carbonate. The ethereal solution was washed several times, separated from the water and the ether evaporated. The ethyl esters so prepared were distilled fractionally at 10 mm. pressure in a Podbielniak Model B high temperature fractionating apparatus.⁴ Table IV shows that the small amount of palmitic and hydnocarpic acids which had remained in solution in the liquid acids (from *C. brasiliensis*) was separated easily from the ethyl oleate and gorlate on the first fractionation, while the very small amount of chaulmoograte appeared in the final fractions. A study of this table indicates the possibility of separating ethyl gorlate from ethyl oleate even though they boil only 5° apart. The fact that there was a loss of only 2.4% in distilling the ethyl esters as compared with a 20% loss when the free

TABLE IV

PURIFICATION OF ETHYL GORLATE BY FRACTIONAL DISTILLATION

Run	Fraction No.	Fraction Cc.	B. p. (10 mm.), °C.	Sp. rotn. $[\alpha]_D^{25}$	Iodine no. (Hanus)
21b	1	1	160
21b	2	8	170-191	32.33	83.6
21b	3	17.3	191-199	38.04	112.8
21b	4	11	199-211	38.47	141.0
21b	5	23.5	211-212	44.03	142.7
21b	6	25	212-214	50.05	152.0
21b	7	11.8	214	52.58	155.0
(Fractions 21b, 3-7 redistilled)					
23b	4	16	213-214	49.09	153.8
23b	5	20	214	54.76	159.8
(Final distillation)					
29b	5	10.1	214	55.4	166.2

(4) Podbielniak, *Ind. Eng. Chem., Anal. Ed.*, **2**, 181 (1931); **5**, 119 (1933).

acids were distilled helped to make the separation possible. Repeated fractionation of the fractions with high iodine number and high rotation finally gave an ethyl ester which had a constant boiling point (214° at 10 mm.) and the theoretical iodine number. The specific optical rotation of this fraction was +55.4°. This same rotation was obtained from several fractions made by the above method. Boiling points were recorded by a calibrated millivoltmeter attached to a thermocouple at the top of the column. Reflux ratios of over six to one were maintained. The pressure was kept within less than 0.3 mm. by an automatic pressure regulator.

Gorlic Acid.—After the constants of ethyl gorlate were obtained, the ester was saponified and the free acid liberated. After washing and drying, the acid was distilled at 10 mm. in the Podbielniak apparatus. It gave a horizontal distillation curve upon the first fractionation. About 20% decomposed, remaining in the distilling flask as a thick, dark brown liquid. The constants of pure gorlic acid were determined and are shown in Table III. Mol. weight, sample 0.1609 g.; 0.1 *N* potassium hydroxide 5.79 cc.; mol. wt., 277.8; calcd., 278.2.

Methyl Gorlate.—Gorlic acid was esterified with absolute methyl alcohol in the same manner as described above for the preparation of ethyl gorlate. A single distillation

in the Podbielniak apparatus gave several fractions with identical constants and a horizontal distillation curve. The constants of methyl gorlate are given in Table III.

Anal. Calcd. for C₁₅H₃₂O₂: C, 78.01; H, 11.03. Found: C, 78.00; H, 11.07.

CALCULATIONS FOR SPECIFIC OPTICAL ROTATION

Compound	Grams	CHCl ₃ , cc.	Ang. rotn. 100-mm. tube	[α] ²⁵ _D
Gorlic acid	1.7382	25	+4.22°	+60.7°
Ethyl gorlate	2.1302	25	+4.72°	+55.4°
Methyl gorlate	1.6555	25	+3.82°	+57.7°

In making the iodine number determination we observed the fact, mentioned by others, that more than the usual amount of Hanus solution must be added or the results will be low. We used three times the usual amount.

Summary

A liquid fatty acid possessing a high optical activity has been isolated from two chaulmoogra oils, *Carpotroche brasiliensis* and *Oncoba echinata*.

The constants of the pure acid and those of its methyl and ethyl esters have been determined.

RIO DE JANEIRO, BRAZIL RECEIVED JANUARY 4, 1938

[CONTRIBUTION FROM THE INTERNATIONAL LEPROSY CENTER, RIO DE JANEIRO]

Analysis of Chaulmoogra Oils. I. *Carpotroche brasiliensis* (Sapucainha) Oil

BY HOWARD IRVING COLE AND HUMBERTO T. CARDOSO

Although chaulmoogra oils have been used intensively in the treatment of leprosy for the past fifteen years, no accurate quantitative analyses of these oils have been made. They are today bought and used on the simple criteria of free fatty acid content and a certain minimal optical activity. The former indicates roughly the quality and age of the oil and the latter, supposedly, the approximate percentage of the therapeutically active hydnocarpic and chaulmoogric glycerides. Actually hydnocarpic and chaulmoogric acids differ in optical rotation by 15% and, furthermore, as we shall show, there may be present in considerable amounts a third optically active acid, gorlic acid. All attempts at quantitative analysis have failed because of the difficulty of completely separating hydnocarpic from chaulmoogric acid and of separating these two from the other acids present. None of the ordinary methods of oil analysis yield satisfactory results. We believe that the analysis of oils so extensively used medicinally is fundamental to improvement in the character of the leprosy

drugs to be made from them. If a satisfactory general method of analysis could be found the analysis of all the important chaulmoogra oils should be a comparatively easy matter. We have worked out such a method and have analyzed one of the more difficult of these oils, *Carpotroche brasiliensis*, by this method. The analyses of *Oncoba echinata*, *Hydnocarpus wighiana*, *Hydnocarpus anihelminthica* and *Taraktogenos kurzii* will follow shortly.

Carpotroche brasiliensis, Endl. (Sapucainha) is indigenous to the mountainous forests of the states of Rio de Janeiro, Minas Geraes, Espirito Santo, Bahia, São Paulo and Piahy. Peckolt, in 1869, was the first to suggest that the oil from the seeds of this tree might be used in place of chaulmoogra oil in the treatment of leprosy.¹ Machado² claimed to have found two new acids in this oil which he named carpotrochic and carpotrochic acids. Da Silva³ showed that these acids were evidently only mixtures and that the

(1) Souza Araujo, *Intern. J. Leprosy*, **3**, 50 (1935).

(2) Machado, *Ann. soc. med. cir. Rio de Janeiro*, **40**, 189 (1926).

(3) Da Silva, *Rev. brasil. med. pharm.*, **2**, 627 (1926).