rated slowly, sometimes only after agitation and concentration of the solution. A second recrystallization from water gave white needles, m. p. 190–192°.

Anal. Calcd. for $C_{13}H_{17}N_3O_4S_2$: N, 12.24. Found: N, 12.22.

3 - (*p* - Aminosulfonylphenyl) - pseudothiohydantoin (XI).—A mixture of 7.5 g. of *p*-chloroacetamidobenzenesulfonamide[9] in 150 cc. of absolute ethanol and 3.5 g. of ammonium thiocyanate was refluxed for thirty minutes. Longer heating produced no further change. The precipitate that formed was filtered, washed with 5 g. of aqueous sodium carbonate and recrystallized from water with norite. From the slow cooling of the solution, a colorless non-crystalline precipitate was obtained which darkened from 238°, melted at 258°, with decomposition.

Anal. Calcd. for $C_9H_9N_3O_3S_2$: N, 15.49. Found: N, 15.26.

(9) Jacobs and Heidelberger, THIS JOURNAL, **39**, 2429 (1917).

Summary

A number of sulfanilamide derivatives was prepared in which the amino group was substituted by various complex acyl groups and the amido group by ethanol and isopropanolamine. None showed activity comparable with sulfanilamide.

URBANA, ILLINOIS RECEIVED JUNE 16, 1939

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

Alepric, Aleprylic, Aleprestic and Aleprolic Acids, New Homologs of Chaulmoogric Acid

BY HOWARD IRVING COLE AND HUMBERTO T. CARDOSO

In analyzing *Hydnocarpus wightiana* oil by the method described by us[1] the high optical rotation and iodine numbers of the lower boiling fractions of ethyl esters indicated that there must be present at least one more optically active fatty acid besides those already known (chaulmoogric, hydnocarpic and gorlic[2] acids). By repeated fractional vacuum distillation of 200 l. of *H. wightiana* ethyl esters and fractional crystallization of the free acids we have succeeded finally in isolating two new homologs of chaulmoogric acid. The presence of two other homologs has been proved and they have been obtained 70.5 and 42% pure, respectively. Lack of sample prevented further purification. Because of their relationship to the treatment of leprosy we have named these four new homologs, alepric, aleprylic, aleprestic and aleprolic acids.

Alepric acid is the next lower homolog to hydnocarpic acid, differing from it by C_2H_4, having the formula $C_{14}H_{24}O_2$. Our final sample still contained a small amount of another unsaturated acid as indicated by the iodine number and optical rotation. The acid is colorless when liquid, white when solid, almost odorless and melts at 48°. The melted acid upon solidifying forms characteristic beautiful branching crystals rising above the surface of the acid. They are very similar to those already reported by us as characteristic of hydnocarpic and chaulmoogric acids.[3] Our purest sample of alepric acid gave a specific optical rotation of +77.12°. The theoretical value from the molecular weight–optical rotation curve is +80°.

Aleprylic acid is the next lower homolog to alepric acid containing two carbon atoms and four hydrogen atoms less than the latter. It has the formula $C_{12}H_{20}O_2$. It was obtained absolutely pure. It crystallizes in the same characteristic manner as the other homologs. Aleprylic acid melts sharply at 32° and has a specific optical rotation of +90.78°. It is colorless when liquid, white when solid and has a slight aromatic odor when warmed.

Aleprestic acid is the next lower homolog to aleprylic acid differing from it by C_2H_4 and having the formula $C_{10}H_{16}O_2$. It was obtained only 70.5% pure (Table I, 51W, 2) based upon its specific optical rotation which would be +100.5° as determined from the curve for the other homologs of this series of acids.

Although the next homolog to aleprestic acid may be present, our experimental data neither prove nor disprove its presence (Table I, 49W, 3, 4 and 5). On the other hand the second homolog below aleprestic acid is definitely proven to be present by the boiling point of the ethyl ester and the optical rotation and iodine number (Table I, 49W, 1). Computed from its rotation value we have obtained it 42% pure. We have named this lowest homolog aleprolic acid. It differs from aleprestic acid by C_4H_8 and has the

(1) Cole and Cardoso, THIS JOURNAL, **60**, 614 (1938).
(2) *Ibid.*, **60**, 612 (1938).
(3) *Ibid.*, **59**, 963 (1937).

TABLE I

FRACTIONAL DISTILLATION OF LOW BOILING ETHYL ESTERS OF *H. Wightiana* OIL

Fraction	Run	B. p., °C. (10 mm.)	Cc.	Rotation α	Specific rotation $[\alpha]^{25}D$	Iodine no.
1[a]	49W	58–66	1.5	42.4	42.68	100.2
2	49W	66–88	8.2	5.6	...	....
3	49W	88–100	2.1	8.6	...	....
4	49W	100–118	11.0	20.7	...	....
5	49W	118–120	10.0	44.0	...	....
6[b]	49W	120–122	5.0	51.0	...	....
7	49W	122–127	10.0	40.7	...	....
8	49W	127–129	5.2	24.7	...	....
9	49W	129–140	8.0	25.5	...	....
10	49W	140–146	7.0	33.1	...	....
11[c]	49W	146–148	44.0	52.6	...	....
		Fractions 49W, 2–5, redistilled				
1	50W	58–82	1.1	15.2	...	....
2[d]	50W	82–86	4.0	2.8	...	....
3	50W	86–100	5.0	6.4	...	....
4	50W	100–114	4.0	8.8	...	....
5	50W	114–120	7.0	25.3	...	....
6	50W	120–120	7.0	49.6	...	....
		Fractions 49W, 6 and 50W, 6, redistilled				
1	51W	114–122	5.0	44.8	...	....
2[e]	51W	122–122	7.0	54.6	60.94	96.64
		Ethyl aleprate (final distillation)				
1	53W	160–174	2.0	..	66.25	....
2[f]	53W	174–174	7.0	..	66.54	100.70
3	53W	174–174	2.5	..	65.41	....
		Ethyl aleprylate (final distillation)				
1[g]	31W	148	20.0	71.7	79.14	113.4
2	31W	148	20.0	71.7	79.14	113.4

[a] Ethyl aleprolate 42% pure. [b] Impure ethyl aleprestate. [c] Impure ethyl aleprylate. [d] Unidentified acids. [e] Ethyl aleprestate 70.5% pure. [f] Ethyl aleprate 94.2% pure. [g] Pure ethyl aleprylate.

formula $C_6H_8O_2$. From the curve of the other homologs its specific optical rotation would be +120.5° when pure.

In these low boiling fractions of *H. wightiana* ethyl esters there is also present an optically inactive unsaturated acid containing one double bond and probably a saturated acid. The sample at our disposal was not large enough to isolate and identify these acids (Table I, 49W, 2 and50W, 2).

Experimental

The *H. wightiana* oil used was obtained from Ernakulam, India. The ethyl esters were made in the usual manner by esterifying with ethyl alcohol and sulfuric acid and washing to remove glycerol and acid. Two hundred liters of the ethyl esters was fractionally distilled in a 2-l. still at 10 mm. The first 10% (20 l.) fractions were redistilled in the same manner. The 2 liters of low boiling esters thus obtained was refractionated carefully several times in a Podbielniak Model B high temperature fractionating apparatus at 10 mm. The apparatus and technique used were described in a previous paper.[1] Plateaus in the distillation curves were finally obtained at 122, 148 and 174° (Table I). These fractions upon being changed to acids and recrystallized several times from acetone proved to be three new homologs of chaulmoogric acid (Table I, 51W, 2; 31W, 2; 53W, 2). The fourth and lowest homolog is clearly shown to be present in fraction 49W, 1 by the very sharp drop in rotation in the next higher fraction, 49W, 2.

Alepric Acid.—Alepric acid was much more difficult to isolate than aleprylic acid as it was impossible to free it entirely from the other unsaturated acid and from palmitic acid without very great loss. We finally obtained it 96.4% pure as calculated from actual and theoretical rotations (77.1 and 80.0). The constants for alepric acid and for ethyl aleprate are given in Tables II and III.

TABLE II

CONSTANTS OF OPTICALLY ACTIVE FATTY ACIDS FOUND IN CHAULMOOGRA OILS

Acids	Mol. wt.	M. p., °C.	Sp. rot. $[\alpha]^{25}D$	Iodine no.
Chaulmoogric acid	280.2	68.5	60.3	90.5
Hydnocarpic acid	252.2	60.5	69.3	100.7
Alepric acid	224.2	48.0	77.1	113.4
Aleprylic acid	196.2	32.0	90.8	129.7
Aleprestic acid	168.1	..	100.5[a]	151.2
Homolog not found	140.1	..	110.5[a]	181.5
Aleprolic acid	112.1	..	120.5[a]	226.7
Gorlic acid	278.2	6.0	60.7	182.5

[a] Calculated.

TABLE III

CONSTANTS OF ETHYL ESTERS OF OPTICALLY ACTIVE ACIDS FOUND IN CHAULMOOGRA OILS

Compound	Mol. wt.	B. p. °C. (10 mm.)	Sp. rot. $[\alpha]^{25}D$	Iodine no.	R. index $n^{25}D$	Sp. gr. $25°/25°$
Ethyl chaulmoograte	308.3	222	55.4	82.5	1.4592	0.901
Ethyl hydnocarpate	280.2	200	61.9	90.5	1.4578	.907
Ethyl aleprate	252.2	174	66.5	100.7	1.4562	.915
Ethyl aleprylate	224.2	148	79.1	113.4	1.4550	.925
Ethyl aleprestate	196.2	122[a]	86.5[a]	129.7	1.4538[a]	...
Homolog not found	168.1	96[a]	94.1[a]	151.2	1.4526[a]	...
Ethyl aleprolate	140.1	70[a]	101.8[a]	181.5	1.4514[a]	...
Ethyl gorlate	306.3	232	55.6	167.0	1.4667	.912

[a] Calculated.

Anal. Calcd. for $C_{14}H_{24}O_2$: C, 74.93; H, 10.78; iodine no., 113.4; mol. wt., 224.2. Found: C, 74.86; H, 10.86; iodine no. (Hanus), 116.7; mol. wt., 224.5.

Aleprylic Acid.—Aleprylic acid was purified fairly easily by several fractional distillations of the ethyl ester and fractional crystallizations of the acid. The latter must be done in an electric refrigerator as the acid melts at 32°. The constants for aleprylic acid and ethyl aleprylate are given in Tables II and III. They indicate that the acid and ester were 100% pure.

Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.41; H, 10.27; iodine no., 129.7; mol. wt., 196.15. Found: C, 73.54; H, 10.24; iodine no. (Hanus), 129.6; mol. wt., 196.2.

CALCULATIONS FOR SPECIFIC OPTICAL ROTATION

Compound	Grams	$CHCl_3$, cc.	Ang. rotn. 100-mm. tube	$[\alpha]^{25}D$
Alepric acid	2.2703	25	7.00	77.12
Ethyl aleprate	2.5562	25	6.80	66.54
Aleprylic acid	2.6712	50	4.85	90.78
Ethyl aleprylate	4.0433	50	6.40	79.14

Aleprestic Acid.—Since this acid was obtained only 70.5% pure we can determine its constants only from the curves made with the other pure homologs. These probable constants are shown in Tables II and III.

Aleprolic Acid.—Fraction 49W, 1, Table I, clearly indicates the presence of this very low homolog of chaulmoogric acid. The boiling point of ethyl aleprolate should be 70° at 10 mm.; being impure it boiled slightly lower.

The homolog between ethyl aleprestate and ethyl aleprolate should boil at 96° at 10 mm. It is probably present but our final fractions were too small to attempt further fractionation to prove its presence.

An optically inactive unsaturated acid with one double bond must be present in fraction 50W, 2 to account for the iodine number found. There may also be present a saturated acid of low molecular weight.

For purposes of comparison the constants of the other known optically active acids and their ethyl esters are included in Tables II and III.

Summary

Four optically active fatty acids hitherto unknown have been discovered in *Hydnocarpus wightiana* oil. They have been named alepric, aleprylic, aleprestic and aleprolic acids.

The characteristics of these new acids and their ethyl esters are given and their relationship to their previously known homologs, hydnocarpic and chaulmoogric acids, is shown.

RIO DE JANEIRO, BRAZIL RECEIVED APRIL 20, 1939

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

Analysis of Chaulmoogra Oils. III. *Hydnocarpus Wightiana* Oil

BY HOWARD IRVING COLE AND HUMBERTO T. CARDOSO

Of the various chaulmoogra oils used in the treatment of leprosy, that expressed from the seeds of *Hydnocarpus wightiana* is by far the most generally employed. This is largely due to the fact that an oil of excellent quality is easily obtainable in large quantities at a reasonable price. *H. wightiana* occurs abundantly in southwestern India. The tree grows to a height of 7 to 10 meters. The fruit measures 6 to 12 cm. in diameter. The seed is about 2 cm. long with longitudinal grooves and a knot on the end. The species is one of the most abundant and easily accessible of the *Hydnocarpaceae*. Although *H. wightiana* oil has been so widely used for the past fifteen years in the treatment of leprosy, no accurate qualitative or quantitative analysis has ever been made due to the difficulty in separating the constituents. In 1905 Power and Barrowcliff[1] reported that the total fatty acids of this oil consisted chiefly of hydnocarpic and chaulmoogric acids and that they found evidences of a still lower homolog of the same series having the formula $C_{14}H_{24}O_2$ in the mother liquor but were unable to isolate it. Since the iodine number of the final mother liquor was so large (140.7) they concluded that it indicated the presence of an acid or acids belonging to the linolic or linolenic series. Our analysis shows that acids of neither of these series are present but that the high iodine number (and high rotation, 50.4) that they obtained are due to gorlic acid.[2] No evidence of the presence of palmitic acid was found by them and they make no mention of oleic acid. Since their analysis was made practically nothing has been added to our knowledge of the composition of this important medicinal oil. A single reference has been made to the possible presence of gorlic acid.[3] We have succeeded in analyzing *H. wightiana* oil by the method for chaulmoogra oils given in the first article of this series.[4] Our analysis is shown in Table I. It shows six fatty acids not previously reported in this oil, four of which are new homologs of chaulmoogric acid.

(1) Power and Barrowcliff, *J. Chem. Soc.*, **87**, 884 (1905).

Experimental

The sample of oil was taken from a 300-liter drum of *H. wightiana* oil, cold-pressed from fresh, selected seeds imported for the routine production of leprosy drugs for Brazil from the Ernakulam Trading Co., Ernakulam, South India. The characteristics of the oil were as follows: sp. gr. $^{25}/_{25}$, 0.9549; F. F. A. (as % oleic), 2.7; sapon. no., 201; iodine no. (Hanus), 98.4; sp. rotn.,

(2) Cole and Cardoso, THIS JOURNAL, **60**, 612 (1938).
(3) Anon., *Bull. Imp. Inst.*, **34**, 145 (1936).
(4) Cole and Cardoso, THIS JOURNAL, **60**, 614 (1938).