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CHENOPODIUM OIL

BY

THOMAS ANDERSON HENRY
AND
HUMPHREY PAGET

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CXCVI.—*Chenopodium* Oil.

By THOMAS ANDERSON HENRY and HUMPHREY PAGET.

THE oil distilled from *Chenopodium ambrosioides* var. *anthelminticum* is now being used on a considerable scale in the campaigns against hookworm disease that are being carried on in various parts of the Tropics under the auspices of the International Health Board of the Rockefeller Foundation.

As a result of the investigations conducted by Kremers (*Pharm. Rev.*, 1907, **25**, 155), Schimmel & Co. (Bericht von Schimmel & Co., April, 1908, p. 109), and Nelson (*J. Amer. Chem. Soc.*, 1911, **33**, 1404; 1913, **35**, 84; 1914, **36**, 2521), it is known that the oil consists chiefly of a liquid organic peroxide, ascaridole, $C_{10}H_{16}O_2$, and a mixture of liquid hydrocarbons, of which until last year only one, cymene, had been identified with certainty. To account for the optical activity and a characteristic colour reaction of the hydrocarbon fraction, Schimmel & Co. suggested the presence of sylvestrene (*loc. cit.*), but this has received no support from later

investigators (compare Wirth, *J. Amer. Pharm. Assoc.*, 1920, **9**, 139). Since the present authors began their work Nelson has re-examined the hydrocarbon fraction and produced evidence of the presence of α -terpinene and *l*-limonene (*J. Amer. Chem. Soc.*, 1920, **42**, 1204), whilst Caius and Mhaskar have stated, without adducing any experimental data, that the fraction contains cymene, terpinene, and phellandrene (*Ind. J. Med. Res.*, 1920, **7**, 570).

It has been assumed generally that the value of the oil as an anthelmintic is due to the ascaridole, but Hall and Hamilton have asserted as a result of an extensive series of pharmacological trials that the "lighter" portions (that is, the hydrocarbon fraction) are more active as anthelmintics than the "heavier" (ascaridole) fractions (*J. Pharm. Exp. Ther.*, 1918, **11**, 89). In view of this confusion, it seemed to the authors desirable that the oil should be re-examined and the nature and pharmacological action of its components definitely settled.

The pharmacological examination of the substances isolated from the oil has been undertaken by Dr. Wilson G. Smillie of the Instituto de Hygiene, San Paulo, Brazil, who has already obtained a number of interesting results, which will be recorded elsewhere.

EXPERIMENTAL.

Six lots of chenopodium oil, purchased through ordinary trade channels, were used. These had the following constants:

	(1)	(2)	(3)	(4)	(5)	(6)
d_{15}^{15}	0.9665	0.9663	0.9712	0.9723	0.9672	0.9582
Sp. rotation $[\alpha]_D^{15}$...	-5.7°	-4.5°	-5.3°	-5.3°	-6.3°	-6.8°

The oils were separated by distillation under 15 mm. pressure into three fractions: (a) b. p. below 84°, d_{15}^{15} 0.8596 to 0.8839, $[\alpha]_D^{15}$ -14° to -18°; (b) b. p. 84—104°, d_{15}^{15} 0.9200 to 1.0070, $[\alpha]_D^{15}$ -5° to -11°; and (c) b. p. 104—118°, d_{15}^{15} 1.0120 to 1.0160, $[\alpha]_D^{15}$ -0.25° to -1.18°, which usually formed about 25, 15, and 55 per cent. respectively of the whole oil. The residual 5 per cent. is chiefly ascaridole glycol. The oil is difficult to fractionate, especially in the later stages, owing to the risk of explosive decomposition of the ascaridole. Fraction (a) consisted mainly of hydrocarbons, (b) of a mixture of hydrocarbons and ascaridole, and (c) was almost pure ascaridole. Fraction (b) was further treated by carefully heating it under a reflux condenser at atmospheric pressure, when the ascaridole decomposed with considerable violence, but without loss, giving the isomeric ascaridole glycol anhydride. On steam-distilling the product, the anhydride yielded the corresponding glycol, which was not volatile in steam, so that the distillate

consisted almost wholly of hydrocarbons; this was added to fraction (a), which then formed about 30 per cent. of the whole oil.

Examination of the Hydrocarbon Fraction.

Acids.—On repeated agitation with 5 per cent. solution of sodium carbonate, the fraction yielded 0.9 per cent. of oily material having the characteristic odour of the lower fatty acids. This was converted into silver salts by neutralisation and precipitation in three portions with silver nitrate (Found : Ag = 56.27, 55.8, 57.6. Silver butyrate, $C_4H_7O_2Ag$, requires Ag = 55.4 per cent.).

Methyl Salicylate.—On further agitation of the fraction with 4 per cent. solution of sodium hydroxide, there was obtained on acidification 1.5 per cent. of a red oil, which on standing solidified in part, owing to the separation of salicylic acid (m. p. 156°), and the rest of the acid was removed by shaking the liquid portion with sodium carbonate solution. The liquid portion then boiled at $220^\circ/755$ mm., gave a benzoyl derivative, m. p. 83° , and was therefore methyl salicylate; the salicylic acid is no doubt formed by the action of the alkali on the ester during extraction.

As no evidence of the presence of other oxygenated compounds could be obtained, the mixture was then redistilled several times through a six-bulb Young dephlegmator, which separated it into three fractions boiling at $166\text{--}173^\circ$, $174\text{--}177^\circ$, and $177\text{--}180^\circ$ under 765 mm. pressure. The middle fraction formed the bulk of the mixture, and this, on redistillation, was found to consist of a product having the following constants : b. p. $176.5\text{--}177^\circ/765$ mm.; d_{15}^{20} 0.8491; $[\alpha]_D^{20}$ -18.09° ; n_D^{20} 1.48320. It had a slight lemon-like odour, and its solution in acetic anhydride gave a transient, bluish-red coloration with sulphuric acid. This product was prepared without difficulty from all six oils, and in spite of its constant boiling point was subsequently found to be a mixture of at least three hydrocarbons. The results of the analysis (Found : C = 88.14, 88.16, 88.63; H = 11.40, 11.10, 11.21) agree fairly well with those required for a mixture of terpenes, $C_{10}H_{16}$, with cymene, $C_{10}H_{14}$, in about equal proportions (namely, C = 88.9; H = 11.08 per cent.), and further evidence was obtained later of the presence of approximately this quantity of cymene.

Attempts to effect a further separation by distillation at different pressures through a twelve-bulb Young dephlegmator were unsuccessful.

Identification and Removal of α -Terpinene.—Further separation of the mixture by physical means having failed, recourse was had to the identification of the components and attempts to eliminate

these in succession. On treatment with sodium nitrite in presence of acetic acid at 0° , the mixture gave a nitrosite, which, after recrystallisation from ethyl acetate, had m. p. 155° and showed no depression of melting point on admixture with α -terpinene nitrosite made from terpinene, prepared from either turpentine oil or terpineol. The formation of α -terpinene nitrosite had already been recorded by Nelson (*loc. cit.* Compare Caius and Mhaskar, *loc. cit.*), who, however, failed to obtain any other evidence of the presence of α -terpinene. Caius and Mhaskar state that phellandrene is also present. Phellandrene gives even in small quantities an excellent yield of a nitrosite of unmistakable appearance, and the present authors were unable to find any evidence of the formation of phellandrene nitrosite along with the α -terpinene derivative in the reaction.

Baeyer has shown (*Ber.*, 1894, 27, 815) that small quantities of terpinene can be removed from its mixtures with other terpenes by repeated agitation in the cold with Beckmann's chromic acid mixture. Two hundred c.c. of the hydrocarbon fraction were treated repeatedly with small quantities of chromic acid mixture until no further absorption, and no increase in the specific rotation of the recovered oil, took place. The recovered oil, after distillation over sodium, had b. p. 176.5 — $177^{\circ}/758$ mm., d_{20}^{25} 0.8545, $[\alpha]_D^{15}$ -23.08° , n_D^{20} 1.48637 (Found : C = 89.08, 88.92, 88.80; H = 10.86, 10.59, 10.65. A mixture of terpene, $C_{10}H_{16}$, with cymene, $C_{10}H_{14}$, in the proportion of about 40 : 60 requires C = 89.04; H = 10.96 per cent.).

The recovered oil gave no crystalline nitrosite on treatment with sodium nitrite in acetic acid at 0° , but still gave the characteristic bluish-red coloration with sulphuric acid in presence of acetic anhydride, and on oxidation with potassium permanganate (see below) yielded no trace of the characteristic crystalline oxidation products of α -terpinene, whence it appears that the latter terpene had been completely eliminated by the treatment. The chromic acid mixture recovered yielded, on extraction with ether, a small quantity of a crystalline acid melting at 189° , which proved to be one of the forms of $\alpha\delta$ -dihydroxy- α -methyl- δ -isopropyladipic acid produced by the oxidation of α -terpinene (see below).

Action of Bromine. Isolation of a New Terpene Tetrabromide.—Bromine, in excess of that required to form a tetrabromide, was added to either the original mixture of hydrocarbons or the α -terpinene-free mixture (see preceding paragraph) dissolved in its own volume of chloroform and cooled to 0° . After standing for one hour, the chloroform and excess of bromine were removed by a current of dry air, leaving a viscous, dark grey oil; this, on standing for six to eight weeks, deposited a solid tetrabromide,

which after solution in ethyl acetate separated in large crystals up to about 1 gram in weight. The bulk of the brominated product remained liquid even after six months' exposure to a temperature of -15° to -20° , but on distillation under reduced pressure it yielded a considerable quantity of *p*-cymene (b. p. $175-176^{\circ}$), and the residue, on standing, then deposited a further quantity of the crystalline tetrabromide. The latter melted and decomposed at 117° , and repeated crystallisation from different solvents failed to change this melting point. Mixtures of equal parts of the tetrabromide with the tetrabromides of (a) *d*-limonene, m. p. 105° , (b) dipentene, m. p. 126° , (c) terpinolene, m. p. 112° , melted at (a) $90-95^{\circ}$, (b) $102-105^{\circ}$, (c) $100-104^{\circ}$ respectively, so that the substance is not identical with any of the well-known terpene tetrabromides. The tetrabromide is optically inactive (Found: Br = 69.88, 70.08. $C_{10}H_{16}Br_4$ requires Br = 70.17 per cent.). It is apparently the formation of this substance on bromination that led Nelson (*loc. cit.*) to assume that the hydrocarbon fraction of chenopodium oil contained *l*-limonene. The tetrabromide of the latter, however, melts at $104-105^{\circ}$, is optically active ($[\alpha]_D = -73^{\circ}$), and when crystallised with an equal quantity of *d*-limonene tetrabromide gives dipentene tetrabromide, m. p. 126° . In all these respects the new substance differs from *l*-limonene tetrabromide, and it is probably the tetrabromide of a new laevorotatory terpene.

The crystallographic examination of the new tetrabromide has been kindly undertaken for the authors by Dr. G. F. Herbert Smith of the Natural History Section of the British Museum, who reports as follows :

"The crystals are monoclinic. The prominent faces parallel to which the crystals are elongated belong to the form (110) and the faces observed at the end belong to the forms (001), (101), and $\bar{1}11$. The fundamental data are $a : b : c = 1.413 : 1 : 1.471$; $\beta = 99^{\circ} 51'$. The calculated and observed values of the biangular co-ordinates of the observed forms are given in the following table.

Form.	Calculated.		Observed.	
	ϕ .	ρ .	ϕ .	ρ .
110.....	—	—	$0^{\circ} 0'$	$35^{\circ} 42'$
$\bar{1}11$	$48^{\circ} 35'$	$42^{\circ} 12'$	$48^{\circ} 44'$	$41^{\circ} 51'$
101.....	—	—	$39^{\circ} 4'$	$90^{\circ} 0'$
001.....	—	—	$80^{\circ} 5'$	$90^{\circ} 0'$

"There is an optic axis very nearly perpendicular to the faces of the form (110) and the double refraction is high.

"The symmetry of the crystals is different from, and the measurements I have made do not harmonise at all with, those recorded by

Hintze for limonene tetrabromide (*Zeitsch. Kryst. Min.*, 1885, **10**, 252)."

No crystalline derivatives with halogen acids or nitrosyl chloride could be obtained from the mixture of hydrocarbons either before or after the removal of the α -terpinene. Sylvestrene yields a crystalline dihydrochloride.

Oxidation with Potassium Permanganate in Acetone. Isolation of p-Cymene.

The results recorded above indicate that the hydrocarbon fraction consists of α -terpinene, cymene, and a lævorotatory terpene, which forms an optically inactive, crystalline tetrabromide. It was hoped to obtain further information regarding this terpene by the oxidation of the whole hydrocarbon fraction with potassium permanganate in the cold, since the products of oxidation of α -terpinene under these conditions are well known and *p*-cymene is not attacked, so that any products of oxidation found other than those obtainable from α -terpinene might be assumed to come from the lævorotatory terpene. The oxidation was carried out in ice-cold water under the conditions prescribed by Wallach for α -terpinene (*Annalen*, 1908, **362**, 297), but it was subsequently found convenient to replace water by acetone. The hydrocarbon fraction (50 c.c.) was dissolved in acetone (150 c.c.) and a saturated solution of potassium permanganate in acetone added, 50 c.c. at a time, until the reagent was no longer decolorised immediately (*A*). After this stage, the oxidation proceeded very slowly and was completed by adding finely powdered permanganate with constant agitation until the liquid remained coloured for twenty-four hours after the last gram had been added (*B*); usually about 150 grams of permanganate were required in all. If the liquid is worked up at stage (*A*), 60 to 70 per cent. by volume of the oil originally used is recovered, and now has physical constants similar to those of the oil recovered after oxidation with cold chromic acid (p. 1717), with the exception that the highest specific rotation found was -20° in place of -23° . It roughly corresponds, therefore, with the oxidation of the α -terpinene. The oil recovered at stage (*B*) was optically inactive, and after several distillations over sodium boiled constantly at $175-176^\circ/763$ mm., and had n_D^{20} 1.49041 (Found: C = 89.2, 89.3; H = 10.4, 10.51. *p*-Cymene, $C_{10}H_{14}$, requires C = 89.57; H = 10.43 per cent.). It yielded *p*-cymenesulphonic acid (Found: for the barium salt, Ba = 24.4. Calc., Ba = 24.8 per cent.), and on oxidation with aqueous potassium permanganate solution at 100° yielded *p*-hydroxyisopropylbenzoic acid, m. p. $153-154^\circ$ (Found: C = 66.45; H = 6.8. Calc.,

C = 66.7; H = 6.7 per cent.), from which *isopropenylbenzoic acid* (m. p. 255°) was readily obtained by boiling with hydrochloric acid. The usual methods of identifying *p*-cymene are not very satisfactory. Many terpenes yield *p*-cymenesulphonic acid on treatment with sulphuric acid, and the authors have found that commercial phellandrene, on oxidation with hot permanganate, yields *p*-hydroxyisopropylbenzoic acid; special care was therefore taken in this case to prove that the recovered hydrocarbon was actually *p*-cymene. The amount recovered varied from 45 to 50 per cent. (compare p. 1716).

The products of oxidation were isolated by filtering off the manganese dioxide, distilling off the acetone, and steam-distilling the alkaline residue to recover the *p*-cymene. To the aqueous residue in the flask was added the aqueous extract obtained by suspending the manganese dioxide in water and passing through it a vigorous current of steam for two hours. The combined aqueous liquids were then reduced to low bulk in a vacuum and, when cold, extracted with ether, which removed a small amount of a viscous, neutral, yellow oil having a faint odour of mint. The liquid was then acidified and extracted repeatedly with ether, which removed a complex mixture of acids, mostly resinous, from which on standing there separated crystalline material (*A*) amounting to about 2 per cent. by weight of the oil originally used. When no more crystals would separate, the viscous acid resin was filtered off and steam-distilled. The acid distillate was neutralised with sodium hydroxide, evaporated to dryness, and mixed rapidly and completely with the quantity of sulphuric acid, cooled to -16°, required to convert the sodium into sulphate, which separated and was rapidly filtered off, leaving the volatile acids (*B*) as a dark brown liquid. The non-volatile residue in the flask was extracted with ether and yielded a large fraction of resinous acids (*C*).

Crystalline Acids (A).—A rapidly filtered solution in boiling water of the mixture of acids deposited, on standing, colourless, prismatic crystals, of which more was obtained by concentration of the mother-liquor in a vacuum. The crops were mixed and recrystallised from boiling water until of constant melting point, 203—204° (corr., decomp.). The acid was sparingly soluble in cold water or alcohol and less soluble in other solvents, and was optically inactive in aqueous solution (Found: C = 51.21, 51.12; H = 7.72, 7.82. $C_{10}H_{18}O_6$ requires C = 51.29; H = 7.69 per cent. Required for neutralisation, 8.57 c.c. of *N*-NaOH per gram. $C_8H_{16}O_2(CO_2H)_2$ requires 8.55 c.c. per gram).

The mother-liquor, on further concentration, deposited a second acid crystallising in rosettes of needles, which was recrystallised

from water until the melting point remained constant at 189° (corr., decomp.). This substance was moderately soluble in water, and optically inactive in 5 per cent. aqueous solution (Found: C = 51.0, 51.26; H = 7.86, 7.79. $C_{10}H_{18}O_6$ requires C = 51.29; H = 7.69 per cent. Required for neutralisation, 8.56 c.c. of *N*-NaOH per gram. $C_8H_{16}O_2(CO_2H)_2$ requires 8.55 c.c. per gram).

These two acids appear to be identical with the two $\alpha\delta$ -dihydroxy- α -methyl- δ -isopropyladipic acids, $C_{10}H_{18}O_6$, obtained by Wallach by the oxidation of terpinen-4-ol from marjoram oil (*Annalen*, 1907, 356, 212), which he describes as melting at 205 — 206° and 188 — 189° respectively. The acids decompose on melting and in the authors' experience the melting points can be varied from 203° to 214° and from 188° to 192° respectively by variation in the rate of heating. Wallach described the acid of higher melting point as the active and the other as the inactive acid, apparently because the latter only was produced by the oxidation of α -terpinene, which is itself optically inactive, whilst the active terpinenol from marjoram oil yielded both. The acid should, however, exist in more than one inactive modification, and both forms obtained by the present authors were inactive. It seemed likely that both these acids came from the α -terpinene, and this was confirmed by oxidising α -terpinene (prepared from terpineol) with permanganate in acetone, when the same two acids were obtained.

After the removal of the acid melting at 189° , concentration of the mother-liquor was continued, by slow evaporation at atmospheric temperature, causing the separation of a third substance, which, after several recrystallisations from water, melted at 179° (Found: C = 50.55, 50.84; H = 7.6, 7.69 per cent. Required for neutralisation, 8.38 c.c. of *N*-NaOH per gram). Mixed with either of the foregoing acids, this substance showed no depression in melting point, and it is probably merely a mixture of both.

Volatile Acids (B).—The dark brown, volatile acids isolated as already described (p. 1720) consisted mainly of acetic acid, since a series of eight fractions of silver salt prepared from them gave the following results: Ag = 62.5, 63.7, 64.4, 64.7, 65.1, 65.2, 65.3, 66.1. Silver acetate, $CH_3\cdot CO_2Ag$, requires Ag = 64.68 per cent. There is, however, present in addition a minute amount of an acid crystallising in long, slender needles, m. p. 117° , of which sufficient has not been obtained for examination; it can be isolated by steam-distilling the crude, volatile acids, stopping the distillation when the distillate begins to show only a weak acid reaction to litmus, and then extracting the residual liquor with ether.

Resinous Acids (C).—These form the bulk of the oxidation products and from them no definite substance has so far been obtained.

The only difference observed in the course of the oxidations with permanganate in (a) water and (b) acetone was that in the former case the volatile acids produced included *isobutyric* acid (Found: in the silver salt, $\text{Ag} = 55.5, 55.7$. Calc., $\text{Ag} = 55.39$ per cent.), which was separated from the acetic acid also formed by fractional crystallisation of the anilides, acetanilide, m. p. 114° , separating first from boiling water and *isobutyranilide*, m. p. 102° , last.

Oxidation with permanganate of the hydrocarbon fraction of chenopodium oil from which α -terpinene had been removed (p. 1717) yielded acetic and *isobutyric* acids and the volatile, crystalline acid melting at 117° . The latter appears, therefore, to be the only oxidation product found which may be characteristic of the *lævoro*-tatory terpene, and so far it has not been possible to obtain it in quantity sufficient for examination. From this terpinene-free fraction of the hydrocarbon mixture 58 per cent. of cymene was recovered on oxidation.

Oxidation of limonene and phellandrene, under the conditions described above, yielded none of the crystalline products obtained from the chenopodium mixture of hydrocarbons, thus confirming evidence already given of the absence of these terpenes from the mixture.

Ascaridole Fraction.

As already stated, fraction (c) consisted almost wholly of ascaridole and on redistillation had b. p. $108\text{--}110^\circ/15$ mm., d^{15}_D 1.0120, $[\alpha]^{15}_D -0.5^\circ$, constants which are in good agreement with those already on record (Found: $\text{C} = 71.63$; $\text{H} = 9.45$. Calc., $\text{C} = 71.43$; $\text{H} = 9.53$ per cent.). As stated above, ascaridole, when heated above 160° , is converted explosively into an isomeric substance, ascaridole glycol anhydride, the temperature rising to about 300° . Nelson found that the action could be readily controlled by dropping ascaridole into cymene heated at 150° . The authors found that dilution of ascaridole with any volatile, indifferent solvent boiling at about $130\text{--}150^\circ$, for example, xylene, will serve equally well. After the reaction is complete, the solvent is distilled off, leaving a residue of the anhydride which can be purified by distillation. It forms a viscous, yellow oil, b. p. $230\text{--}245^\circ/755$ mm., $122\text{--}125^\circ/20$ mm.; d^{15}_D 1.026; $[\alpha]^{15}_D -0.72^\circ$.

By treatment with steam, the anhydride is converted into ascaridole glycol, which is not volatile in steam, but can be distilled apparently unchanged under reduced pressure. Obtained in this way, it is a heavy, green, viscous oil, b. p. $135\text{--}160^\circ/15$ mm. (Found: $\text{C} = 64.55$; $\text{H} = 9.74$. Calc., $\text{C} = 64.46$; $\text{H} = 9.74$ per cent.). It was previously prepared by Nelson (*loc. cit.*) by

shaking ascaridole with ferrous sulphate solution or by hydrating the anhydride by dilute sulphuric acid. The monobenzoate melts at 136—137°, as recorded by Nelson (Found : C = 70.68; H = 7.92. Calc., C = 70.34; H = 7.55 per cent.).

Indian Chenopodium Oil.

In connexion with attempts made in recent years to cultivate chenopodium in India for the production of oil, two samples of the drug have been received from Col. A. T. Gage, Director of the Botanical Survey of India. These were labelled *C. ambrosioides* and *C. anthelminticum* and yielded 0.17 and 0.24 per cent. of oil having $d_{15}^{15^\circ}$ 0.9399, $[\alpha]_D^{15}$ + 0.07°, and $d_{15}^{15^\circ}$ 0.9080, $[\alpha]_D^{15}$ - 9.6° respectively. The quantities obtained were too small for further investigation.

Summary of Results.

1. Chenopodium oil contains minute quantities of the lower fatty acids, chiefly butyric acid, and less than 0.5 per cent. of methyl salicylate. The remainder of the oil consists of at least 60 per cent. of ascaridole with about 5 per cent. of the corresponding glycol and 30 to 40 per cent. of a mixture of hydrocarbons made up approximately of cymene 15 per cent., α -terpinene 5 per cent., and a new lævorotatory terpene, 10 per cent. No evidence has been obtained of the presence in the oil of sylvestrene, limonene, phellandrene, safrole, or camphor, all of which have been suggested or recorded as constituents.

2. The lævorotatory terpene has not been isolated from the mixture of hydrocarbons, but judging from the physical constants of its mixtures with (a) α -terpinene and cymene, and (b) cymene alone, it must have approximately the following characters: b. p. 177—178°/760 mm., $d_{15}^{15^\circ}$ 0.847, $[\alpha]_D^{15}$ - 57°, n_D^{20} 1.484. It furnishes a well-crystallised tetrabromide, m. p. 117°, which is optically inactive, and on oxidation with permanganate yields acetic and isobutyric acids and possibly a volatile, crystalline acid, m. p. 117°, not yet identified. It is interesting to note that Lewinsohn (*Arch. Pharm.*, 1906, 244, 424) isolated from myrrh oil a terpene having the following constants; b. p. 78—80°/20 mm., $d_{20}^{20^\circ}$ 0.847, $[\alpha]_D^{20}$ + 80°, yielding a tetrabromide, m. p. 115°.

3. On oxidation with permanganate in acetone, α -terpinene yields two forms of $\alpha\delta$ -dihydroxy- α -methyl- δ -isopropyladipic acid melting at 203—204° and 189° respectively; the latter has already been obtained by Wallach by oxidation of this terpene with permanganate in water at 0°, and both acids by the same author from the terpinen-4-ol of marjoram oil by the same means. The acid of higher m. p.

is described by Wallach as active, although no determination of the value is given; both acids obtained by the present authors were optically inactive in aqueous solution.

The authors desire to express their cordial thanks to Dr. Herbert Smith for the crystallographic measurements recorded above and to Mr. F. Walton for assistance in the experimental work.

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